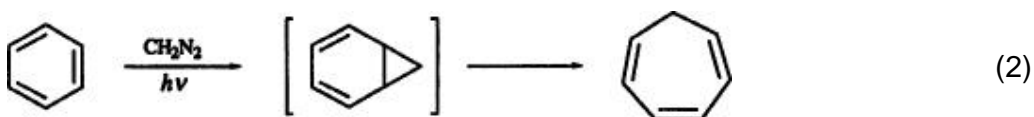


# Divinylcyclopropane-Cycloheptadiene Rearrangement

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## 1. Introduction

The first documented report of a possible Cope rearrangement was probably that of Baeyer, who prepared eucarvone by hydrobromination of carvone in 1894. (1) Although the transformation was briefly studied at that time, it was not until the 1950s that this and other Cope-type rearrangements received detailed attention. The thermal isomerization of *cis*-divinylcyclopropane to cycloheptan-1,4-diene (Eq. 1) was reported by Vogel in 1960 during his studies of the Cope rearrangement of 1,5-hexadienes annulated by a homologous series of carbocyclic rings. (2, 3) Scores of mechanistic studies followed this discovery upon the realization that the rearrangement could be related to the conceptually similar vinylcyclopropane–cyclopentene isomerization discovered a year earlier. (4-6) It was also recognized that this rearrangement might be operating in the formation of cycloheptatriene from norcaradiene during photolysis of diazomethane in benzene, studied by von Doering in 1950 (Eq. 2). (7-9) The topic received considerable attention in the 1960s, an era of mechanistic investigations of various concerted transformations. During the 1970s it enjoyed exploitation in many synthetic strategies, and the following decade the elements of this rearrangement were incorporated into tandem or multistep procedures in a preconceived manner. Many aspects of the various permutations of the Cope rearrangement have been previously reviewed. (10-16)

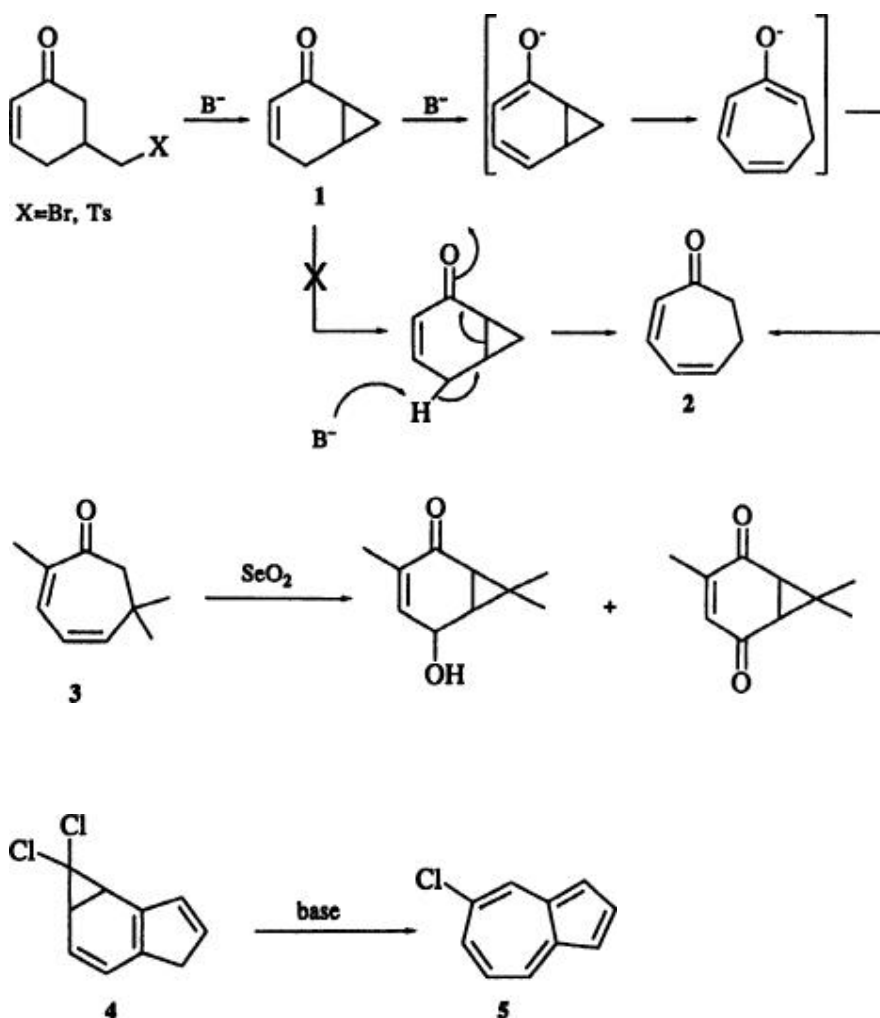


The purpose of this review is to summarize the mechanistic, stereochemical, and practical results in this area in the context of the evolution of synthetic achievements during the last 40 years. Also described in this chapter are the transformations of several of the simple heteroatom permutations of this rearrangement in order to render appropriate comparisons of various systems. The following discussion therefore addresses those rearrangements of cyclopropanes, oxiranes, thiiranes, and aziridine rings substituted with vicinal vinyl groups. Excluded from this review are rearrangements of those divinyl-substituted three-membered rings that contain more than a single heteroatom within the reacting manifold. Brief mention of these systems along with a guide to the literature is found in the last section of this chapter.

The literature is covered through December 1990. Many of the principal researchers in this field have been contacted during the compilation of this review, and many unpublished transformations have been included in the tables.

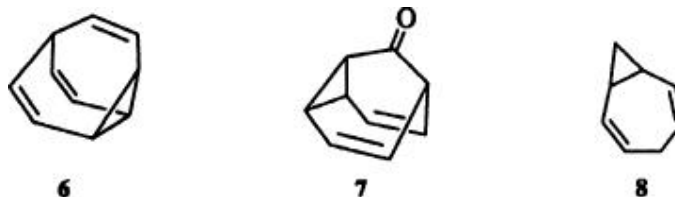
## 2. Mechanism

Close inspection of the early literature suggests that the divinylcyclopropane rearrangement went unnoticed as such for some time. Aside from the ring expansion of norcaradiene mentioned above, (7-9) the base-catalyzed rearrangement of cyclopropyl enone **1** to cycloheptadienone **2** may very well have proceeded via the Cope rearrangement shown below, rather than by the direct unravelling of the cyclopropyl system from the  $\gamma$  position as originally proposed. (17-21) Curiously, the reverse of this reaction is observed during the oxidation of cycloheptadienone **3** with  $\text{SeO}_2$ . (22-25) Chloroazulene (**5**) was isolated from the base-catalyzed reaction of the dichlorocarbene adduct **4**. (26) Finally,

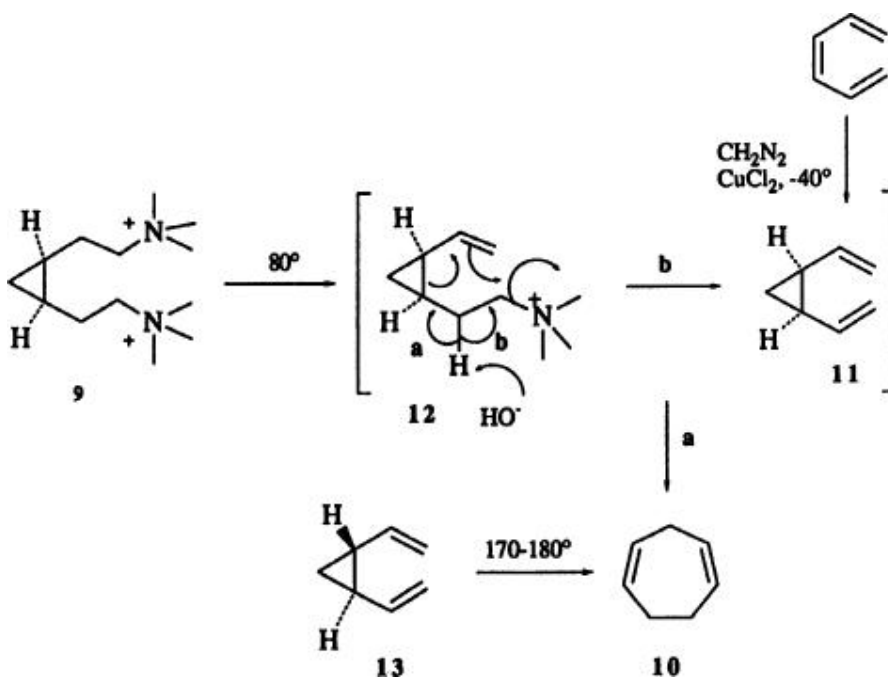


the rearrangements of various bullvalenes, semibullvalenes, or isobullvalenes such as **6** or **7** also proceed through a degenerate Cope rearrangement. (27-31) Such rearrangements were observed during the studies of fluxional

molecules, the simplest being 3,4-homotropilidene (**8**). (27) The heteroatom analogs of



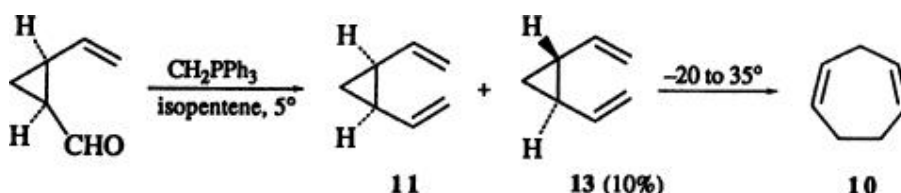
fluxional molecules have also been studied. (29-33) The earliest mechanistic observations recognized that *trans*-divinylcyclopropane cannot rearrange to cycloheptadiene in a concerted fashion because such a rearrangement would result in a *trans* olefin constrained in a seven-membered ring. The mechanism was studied in the early 1960s in the context of then-popular valence isomerism, and a number of reports appeared from the laboratories of Vogel (2, 3, 34-36) and von Doering (27, 37, 38) during this period. During an attempt to prepare *cis*-divinylcyclopropane, Vogel et al. noted that the Hofmann elimination of salt **9** gives cycloheptadiene **10** at 80°, presumably via the elusive



cyclopropane **11**. (3) The corresponding *trans* isomer **13** required a temperature of 180° to undergo similar rearrangement to **10**. An explanation was advanced by von Doering and Roth, who generated **10** even at -40° during the copper-catalyzed cyclopropanation of *cis*-hexatriene. (27) They postulated synchronous opening of *cis*-divinylcyclopropane (**11**) and a diradical opening of the *trans* isomer followed by either a diradical closure to **10** or isomerization to the *cis* compound and subsequent reorganization to

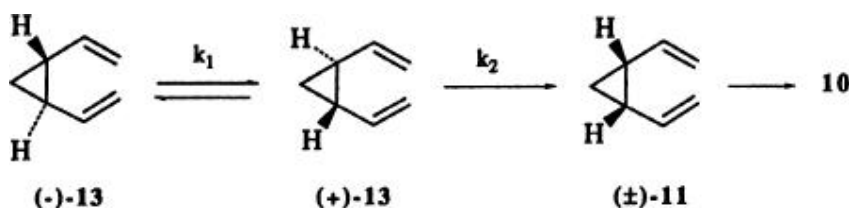
cycloheptadiene (**10**). (37, 38) An additional explanation of Vogel's experiment can be seen as postulated in path **a** in the base-catalyzed elimination of the first intermediate of the Hofmann process. (37, 38) Although possible, such a process seems more complex in terms of net electron movement than the generation of **11** by a simple E2 elimination (path **b**). von Doering has estimated the activation energy for this isomerization to be 20.6 kcal/mole. (37, 38)

*cis*-Divinylcyclopropane was prepared and characterized in 1973. (39) *cis*-1-Vinylcyclopropane-2-carboxaldehyde was converted to **11** by a low-temperature Wittig reaction; the product was distilled at low temperature

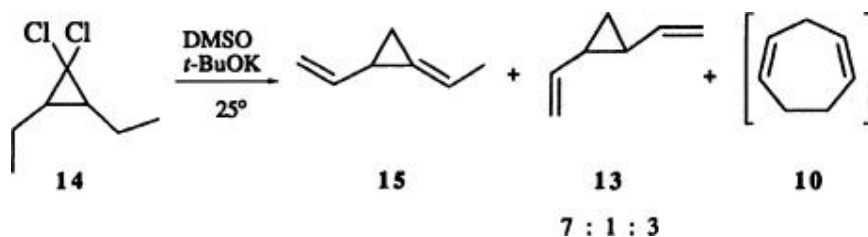


and then characterized by  $^1\text{H}$  NMR at  $-20^\circ$ . The rearrangement was complete below  $35^\circ$ , and the free energy of activation was 20 kcal/mole, in agreement with von Doering's postulate. (37) The rate of the rearrangement was  $7.7 \times 10^3 \text{ s}^{-1}$  at  $35^\circ$ .

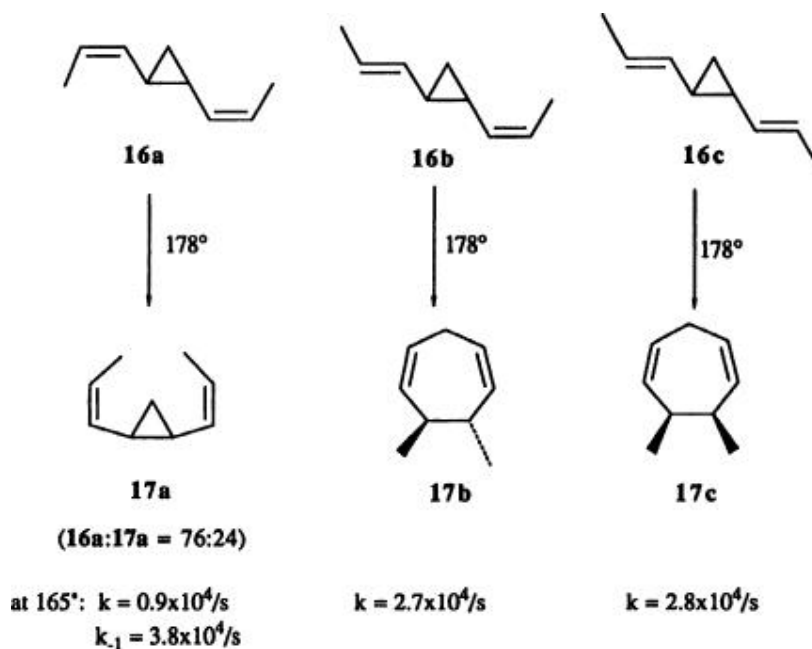
*trans*-Divinylcyclopropane was examined in detail in 1972. (40) Optically active **13** was prepared by resolution of the precursory *trans*-2-vinylcyclopropane carboxylic acid in 14% optical purity. The rate of isomerization of (+)-**13** to (±)-**11**,  $k_2$ , was  $1.5 \times 10^4 \text{ s}^{-1}$  at  $170^\circ$ , the temperature of conversion of **13**



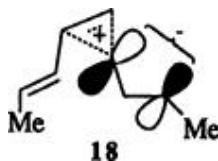
to cycloheptadiene (**10**). The corresponding rate of interconversion of enantiomers,  $k_1$ , was  $0.54 \times 10^4 \text{ s}^{-1}$  at  $170^\circ$ . These results were interpreted to mean that the observed racemization has no electrocyclic component and is therefore diradical in nature. Comparisons have been invoked between this racemization and the similar process for 1,2-diphenylcyclopropane and 1,2-divinyloxiranes. (41) *trans*-Divinylcyclopropane and its isomerization have been observed at a much lower temperature during the dehydrohalogenation of dichlorocyclopropane (**14**). (42, 43) The initially formed cycloheptadiene **10** gives, under the reaction conditions, its conjugated isomer.



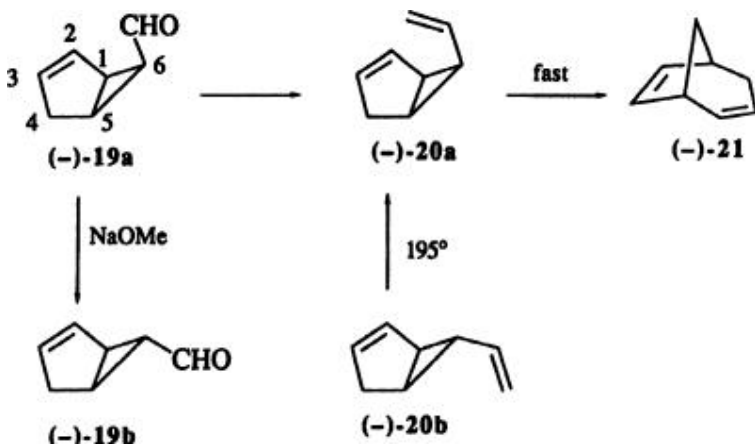
The rearrangement of the three possible isomers of *trans*-divinylcyclopropane (**16**) was studied mechanistically. (44, 45) The results were interpreted as



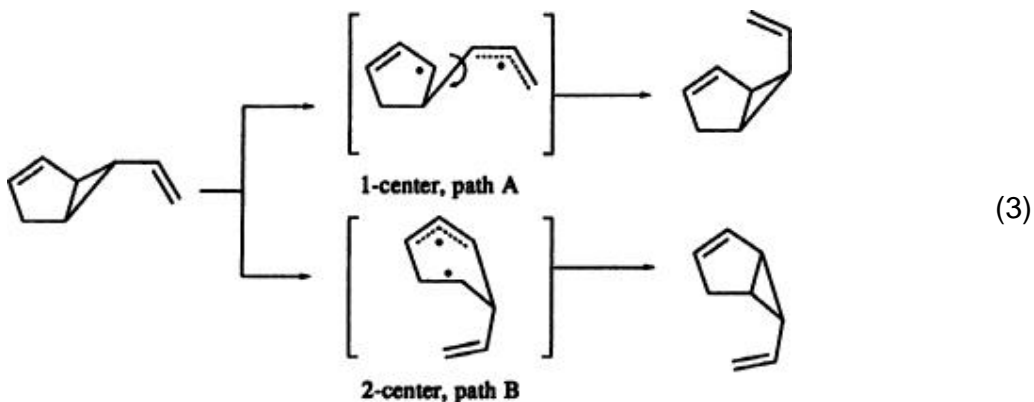
electrocyclic closures exhibiting some zwitterionic character, as shown in **18**, and compared with the thermal isomerization of 1-alkylidene-2-alkylcyclobutanes. (46) Thus two opposing mechanistic interpretations of racemizations and rearrangements of dialkenylcyclopropanes were advanced: a concerted and a diradical picture.



The one-center epimerization interpretation versus a two-center question was readdressed in 1976. (47) *endo*-Cyclopropylcarboxaldehyde (**19a**), prepared by peroxyacid oxidation of norbornene, was resolved with ephedrine and converted to *endo*-vinylcyclopropane (**20a**). Epimerization of **19a** with sodium methoxide gave the *exo* isomer **19b**, which furnished the corresponding *exo*-vinylcyclopropane



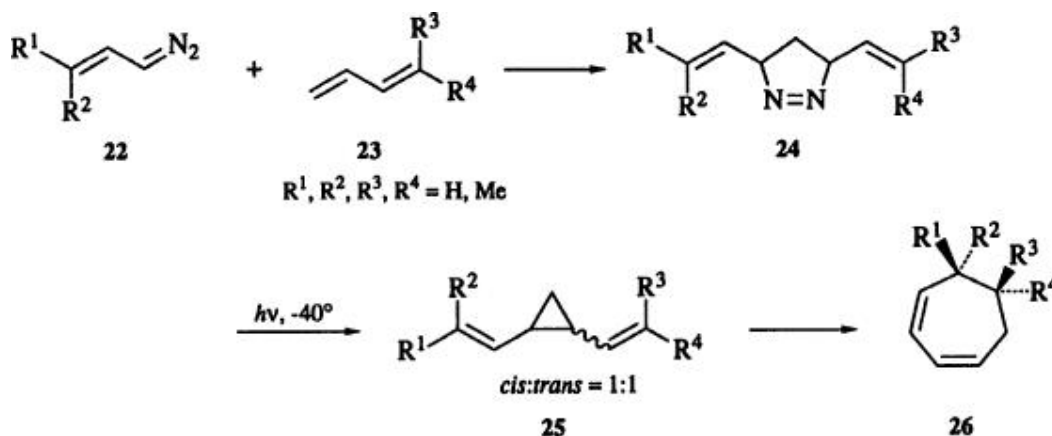
**20b**. Through comparison of optical rotations it became evident that only the C(1) — C(6) bond suffered cleavage during the *trans*–*cis* isomerization, as no enantiomer of **21** was detected. Thus in this reaction, the absence of racemization excludes a two-center process (path B, Eq. 3). The *endo* isomer of racemic **20a** was isolated in 1965. (48) Similar studies are available on the deuterated analog of **20a**. (49)



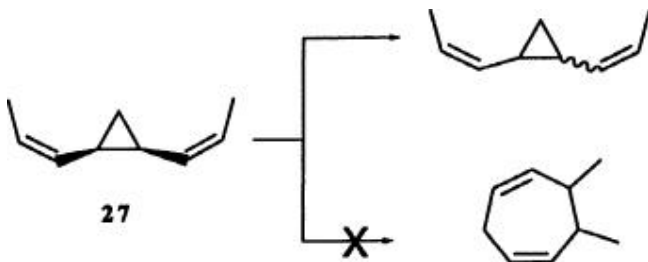
As in the vinylcyclopropane–cyclopentene rearrangements, the major dispute over the mechanism involves diradical versus concerted pathways. (10-15) This dispute is, for the moment, unresolved. Discussion of this mechanistic

duality can be found in recent reviews of the Cope (10-16) and vinylcyclopropane-cyclopentene (11, 16, 50-54) rearrangements.

Among the *cis* and *trans* phenylvinylcyclopropanes, only the hydroxy-substituted compounds undergo the Cope rearrangement in the presence of base. (55) The thermal (56) and photochemical (57) rearrangements of several divinylcyclopropanes prepared by the addition of vinyl diazomethanes **22** to dienes **23** (56, 58) have been studied. (56-59) The *cis* isomers rearrange readily between  $-20^\circ$  and  $90^\circ$ , whereas the *trans* compounds require temperatures above  $160^\circ$ .



The results of the experiments described above confirm an earlier observation that substitution on the vinyl moieties is an important factor with regard to rate. (44) *cis*-(Di-*cis*-propenyl)cyclopropane (**27**) does not rearrange at all and



undergoes only *cis-trans* isomerization. These results have been rationalized by invoking a concerted  $[\sigma^2s + \pi^2s + \pi^2s]$  process and a boat-like, cisoid conformation in the transition state, (59) and are quite analogous to the known tendency of similarly functionalized vinylcyclopropanes. (10, 11, 16, 50, 52, 53) *cis*-Divinylcyclopropane rearranges 5800 times faster than *cis*-vinylpropenyl-cyclopropane. (59) The Cope rearrangement of divinylcyclopropanes is highly stereoselective in some cases. Thus cyclopropyl system **16** rearranges with retention of stereochemistry at the olefinic termini. (45) A boat-like transition state has been proposed to account for this and



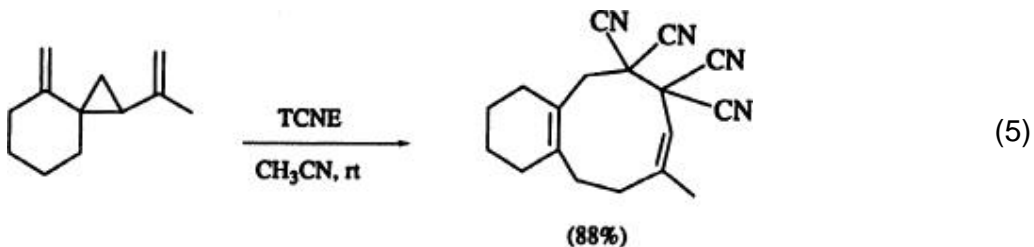
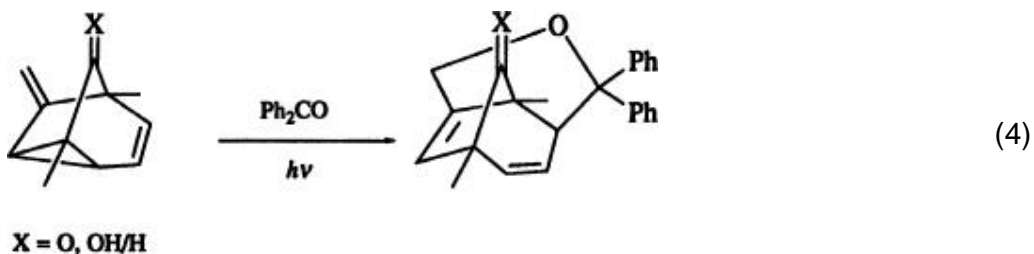
other observations. (59, 60)

A molecular orbital treatment of the *cis*-divinylcyclopropane system suggests that a minimum-energy transition state with an activation energy of 17–18 kcal/mole is available by considering structure **28**. (60) An experimental value of 22.3 kcal for the rearrangement of **29** has been reported (39) and is in good



agreement with the calculated value. (59, 60) Studies of the rearrangements of divinylcyclobutanes indicate that the Cope rearrangements indeed proceed through a concerted rearrangement in *cis* compounds and diradical isomerization of *trans* isomers to *cis* prior to rearrangement. (10, 12, 15, 59-61) This is in contrast to studies that suggest one-center epimerization pathways. (47)

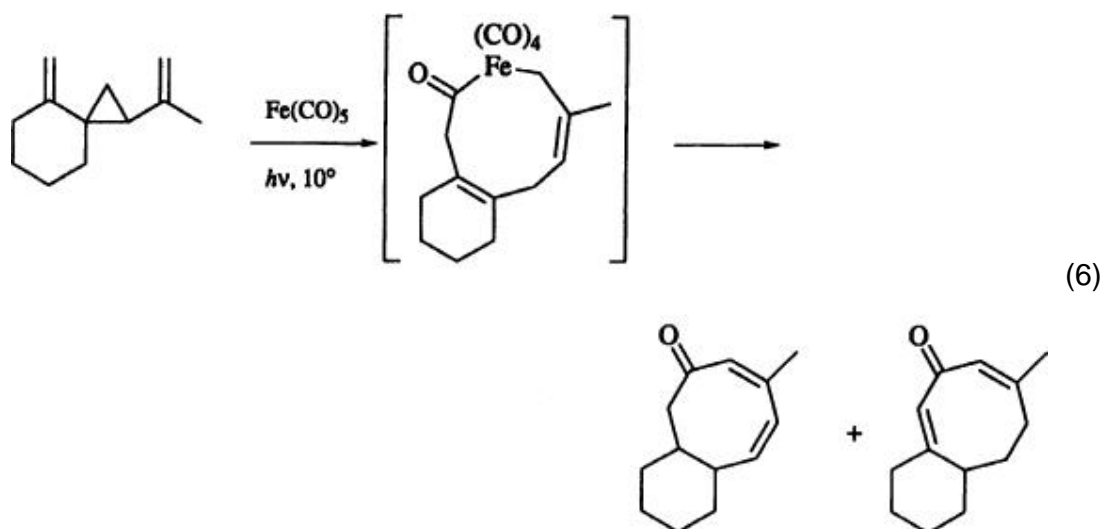
Isolated examples of photochemical rearrangements exist and appear to involve diradical intermediates. (62, 63) In some cases a diradical intermediate may cyclize with an external  $\pi$  system, as in Eq. 4, where benzophenone inserts across the photochemically generated diradical of a sterically constrained divinylcyclopropane. (64, 65) A thermally induced insertion of this type has also been reported (66) and involves a  $[(^2\pi + ^2\sigma + ^2\pi) + ^2\pi]$  cycloaddition, presumed concerted (Eq. 5).



Rearrangements of divinylcyclopropanes catalyzed by transition metals are known and proceed in analogy to the reactive tendencies of simple vinylcyclopropanes (11, 16, 50, 52) or cyclopropanes. (67) Usually the rearrangement proceeds via initial ring opening to a metallocycle, which either undergoes further cycloadditions or results in an overall ring expansion (Eq. 6). (68, 69) In analogy with similar insertions into simple vinylcyclopropanes, (50, 67) the mechanism involves initial formation of an iron complex. A transition-metal-catalyzed Cope rearrangement has been reported. (70, 71) Initial complexation followed by generation of a bis- $\pi$ -allyl system and electrocyclic closure to cycloheptadiene have been invoked (Eq. 7).

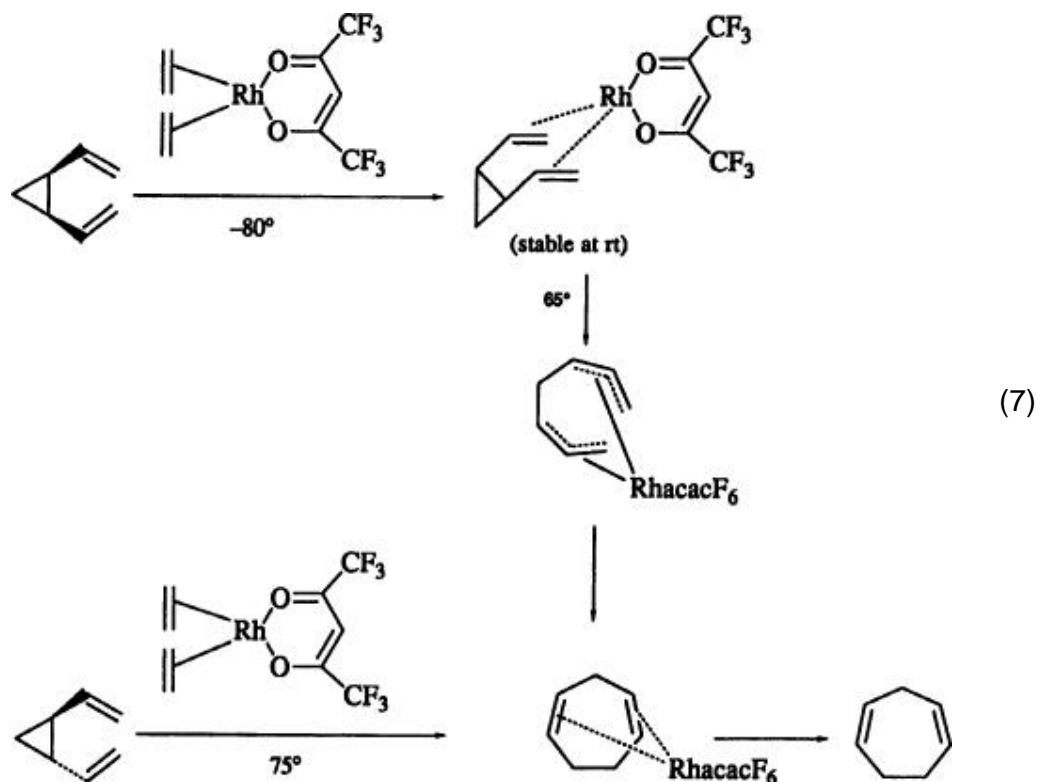
Recently, a Cope rearrangement has been reported under conditions that involve rhodium-catalyzed cyclopropanation of dienes with vinyl diazo compounds. (72) The cyclopropanations frequently generate *endo* divinylcyclopropanes, which produce cycloheptadienes under the reaction conditions. The participation of the metal in these rearrangements cannot be ruled out.

In summary, the mechanism and the stereochemical consequences of the Cope rearrangement of *cis*- or *trans*-divinylcyclopropanes may be generalized



to state that *cis* isomers rearrange by a low  $E_{\text{act}}$  pathway that is most likely a concerted one. The *trans* isomers suffer a diradical or one-center epimerization prior to the energy-releasing rearrangement to cycloheptadiene through a boat-like transition state. Stereoelectronic effects that operate in this rearrangement are governed by the usual rules of sigmatropic migrations or

diradical closures. (73, 74) Prediction of experimental results should be possible by considering the closest mechanistic analogy, the vinylcyclopropane system. (10, 11, 16, 50, 52, 53) Mechanistic investigations addressing the Cope rearrangement have been reviewed. (12-14, 75) Most recently, a detailed review summarizing

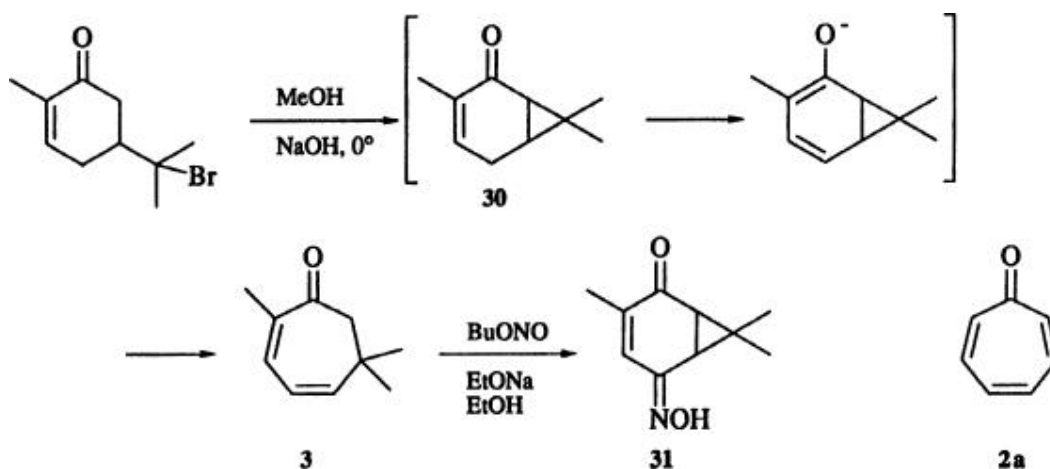


the mechanistic and synthetic aspects of the divinylcyclopropane rearrangement has been compiled. (15)

### 3. Scope and Limitations

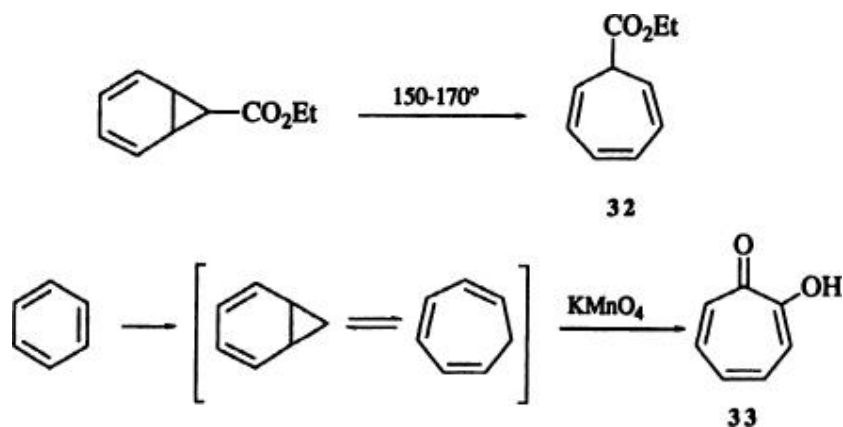
#### 3.1. Simple Cycloheptadienes

The first synthesis of a cycloheptadiene via a divinylcyclopropane rearrangement was undoubtedly the preparation of eucarvone (**3**) by Baeyer almost 100 years ago by treatment of carvone hydrobromide with base. Baeyer also proposed the possible intermediacy of the cyclopropyl ketone **30**. (1) This transformation was studied mechanistically by Wallach in 1905, (76, 77) Lapworth in 1910, (78) and van Tamelen in 1956 with the conclusion that a Cope rearrangement was indeed operating in this transformation. (19-21) The stability of simple cyclopropyl ketones to base investigated by Zelinskii in 1922 (79) also rendered unlikely the mechanism proposed by Wallach, (76, 77) who suggested

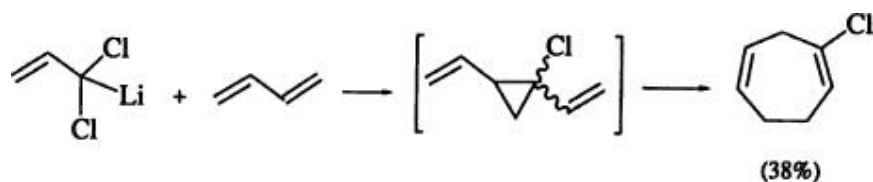


opening of the cyclopropane ring by the action of external nucleophiles (OH<sup>-</sup>). The reverse of this process occurs in the preparation of oxime **31** from eucarvone. (22, 24, 25) This procedure was applied to the synthesis of tropone (**2a**) and its derivatives. (19, 80)

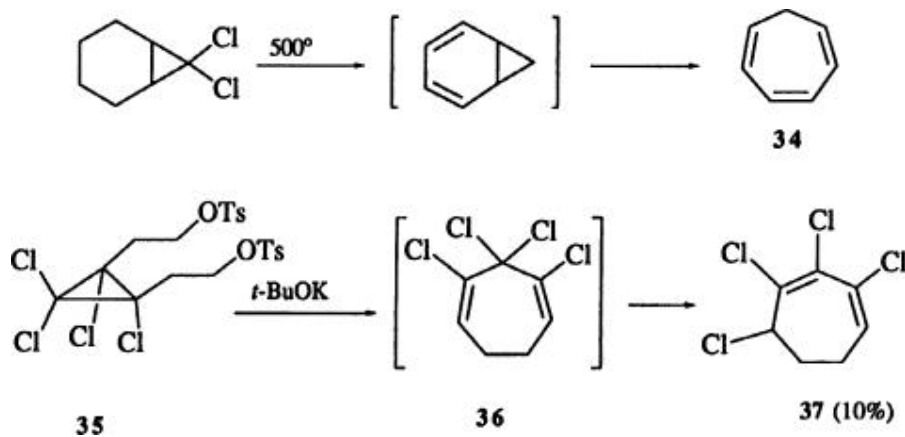
Norcaradienecarboxylates rearrange at 150–170° to cycloheptatrienes **32**. (81) Tropolone (**33**) was prepared by irradiating a solution of diazomethane



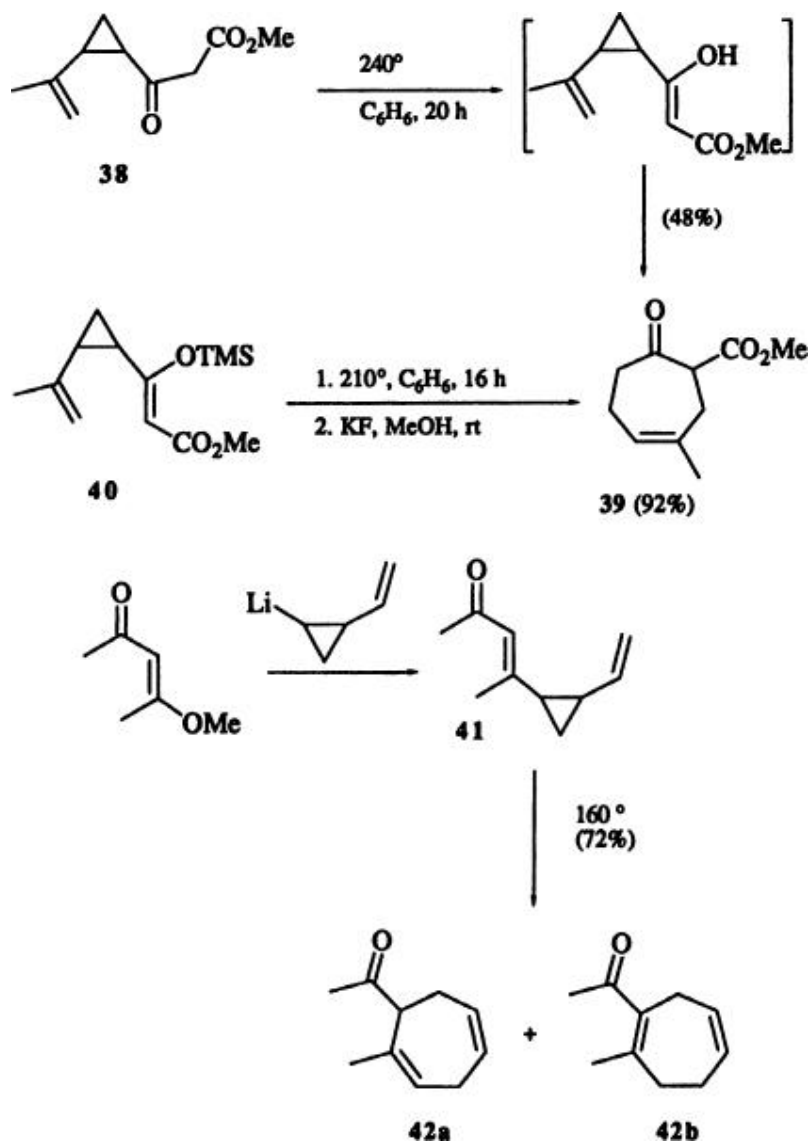
in benzene at 365 nm, (7) followed by oxidation of the norcaradiene–cycloheptatriene equilibrium mixture. Addition of dichloroallyllithium to butadiene gives intermediate chlorodivinylcyclopropanes, which rearrange to chlorocycloheptadiene



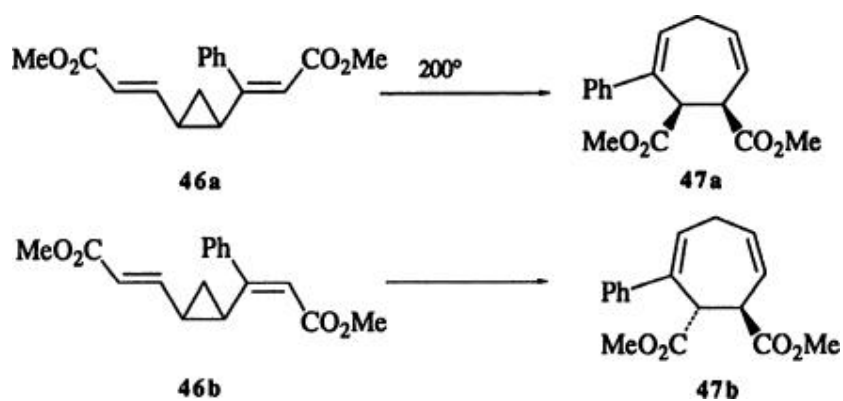
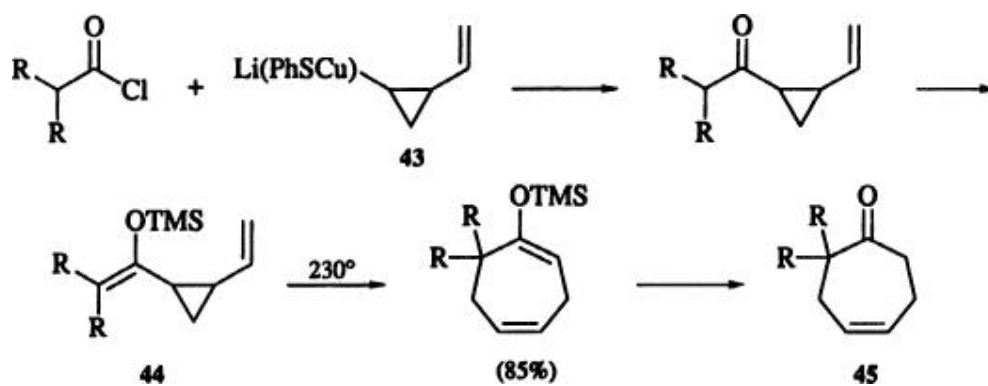
at 25° (from *cis*) and 190° (from *trans*). (82) Cycloheptatrienes such as 34 are prepared by dehydrohalogenation of dichlorobicyclo[4.1.0]heptanes. (83) A low yield of tetrachlorodiene 37 is observed during base-catalyzed elimination of ditosylate 35. (84) The initially formed 1,4-cycloheptadiene 36 isomerizes to 37 via an allylic shift.



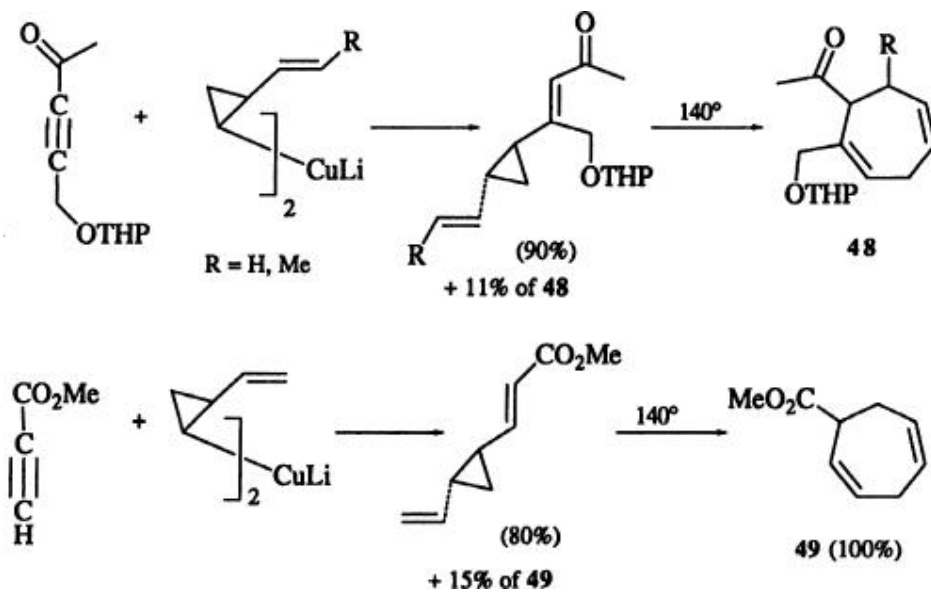
More highly functionalized cycloheptanes are prepared by using the Cope rearrangement in such a way as to incorporate one of the olefins into an enol ether. When vinylcyclopropyl keto ester **38** is heated, a 48% yield of cycloheptenone **39** is realized. (85) This transformation can be improved by performing the rearrangement with trimethylsilyl enol ether **40** at a lower temperature. The addition of lithiovinylcyclopropanes or their cuprates to enones substituted with alkoxy or halo groups at the  $\beta$  position provides a convenient synthesis of divinylcyclopropanes such as **41**. The metallation of bromovinylcyclopropanes as well as the addition is stereospecific. (86) The half-life of *cis*-**41** is 30 minutes at 80°, whereas the half-life of *trans*-**41** is 38 minutes at 160°. The isomeric cycloheptadienes **42a** and **42b** are produced in 72% yield. (86) Conversion of acid chlorides to divinylcyclopropanes **44** is accomplished with thiophenylvinylcyclopropane cuprate **43** followed by conversion of the ketones to their silyl enol ethers. Thermolysis provides high yields of cycloheptenones **45**. (87, 88) Divinylcyclopropanes substituted on the vinyl moiety rearrange to cycloheptenes in a stereospecific fashion. The *Z* isomer **46a** furnishes *cis*



diester **47a** while the *E* isomer gives only the *trans* diester **47b**. (89, 90) The stereospecificity has been rationalized by invoking a concerted rearrangement of the *cis*-divinylcyclopropane system through a boat transition state. (90)  
 Addition



of vinylcyclopropyl cuprates to propargylic esters or ketones provides a convenient route to divinylcyclopropane precursors of cycloheptadienes such as **48** and **49**. (91)

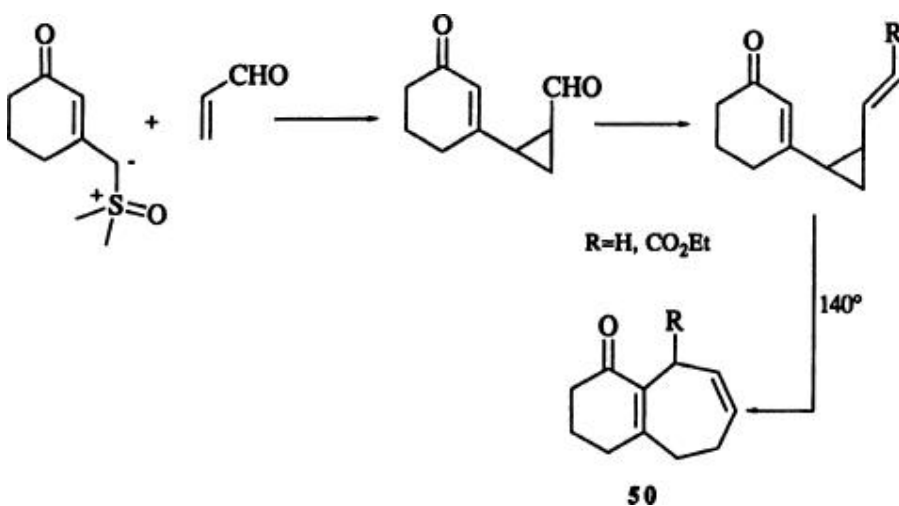




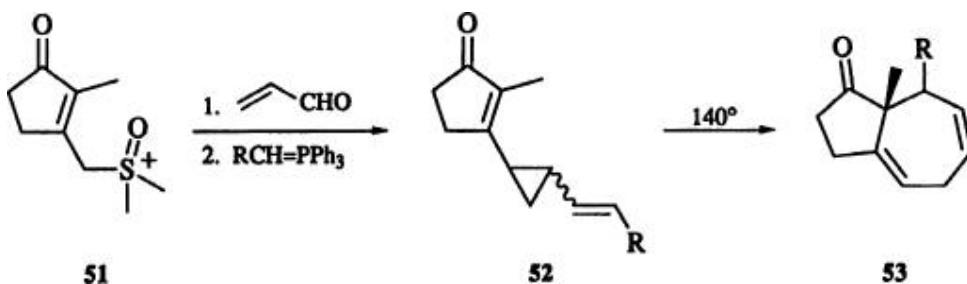
Substituted cycloheptadienes are easily prepared by the Cope rearrangement. New and mild methods for this rearrangement continue to appear; for the latest applications the reader should consult Table I.

### 3.2. Annulation Procedures

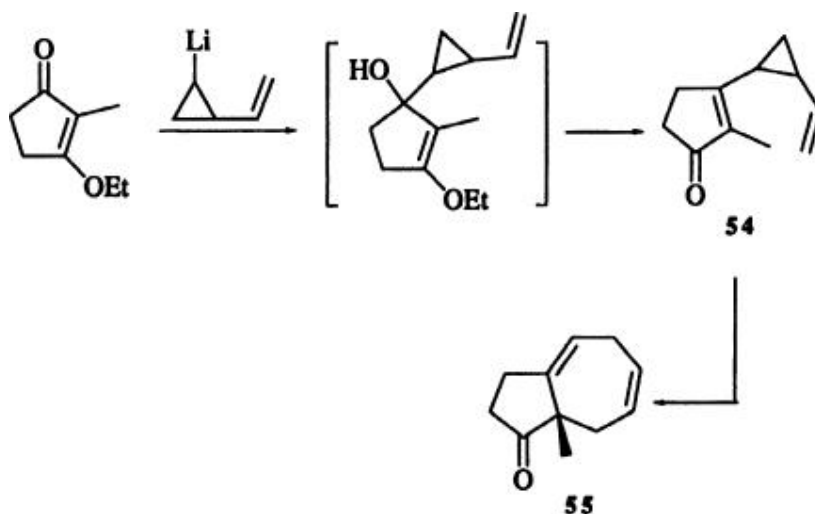
The rearrangement of functionalized divinylcyclopropanes is used in several annulation protocols. Thus divinylcyclopropanes prepared by sulfoxonium ylide addition to Michael acceptors followed by Wittig reaction are thermolyzed to annulated cycloheptadienes such as **50**. The  $\beta$ ,  $\gamma$ -olefin isomerizes to conjugation under the conditions of the rearrangement. (92, 93)  $\alpha$ -Methylcyclopentenones of type **51** are similarly converted to divinylcyclopropanes which rearrange to angularly methylated bicyclo[5.3.0]decanes **53**. In analogy with the rearrangements of vinylcyclopropanes, (11, 16, 50) the *cis* isomer



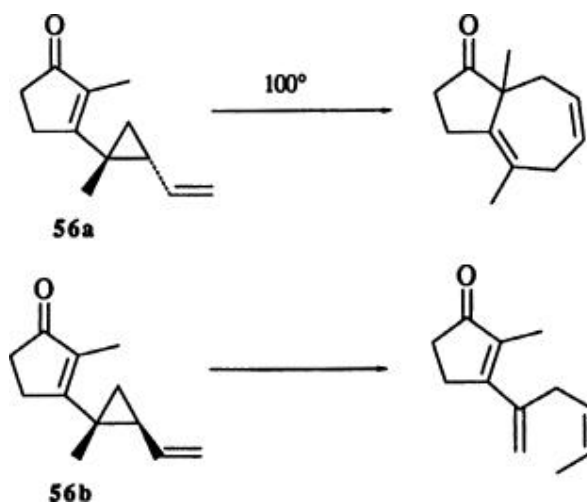
of **52** does not undergo the rearrangement, presumably because of steric inhibition in the transition state. (94)



Divinylcyclopropanes such as **54** are generated by the addition of lithium vinylcyclopropanes to enol ethers of cyclic  $\beta$ -diketones. (86) The resulting divinylcyclopropanes produce the annulated cycloheptenes **55** at 80° or 160° for *cis* and *trans* isomers, respectively. When the cyclopropane is substituted with a methyl group, only the *trans* isomer **56a** rearranges to cycloheptene, (91)

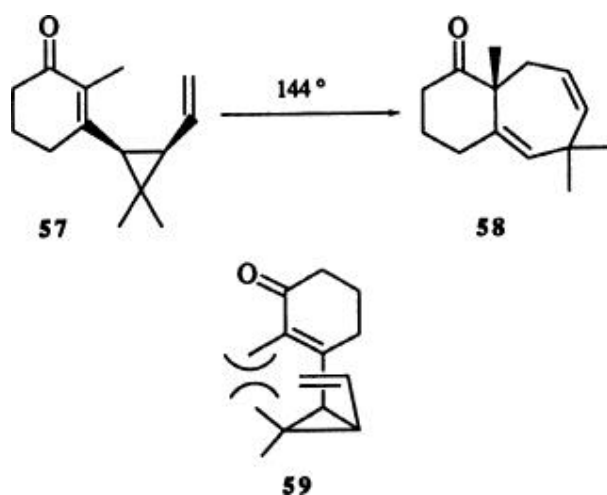


whereas the *cis* compound gives the product of [1,5]-homodienyl shift in analogy with similar processes in *cis*-alkylvinylcyclopropanes. (11, 16, 50, 52, 73) Further substitution on the cyclopropane ring leads to rate retardation as seen for the rearrangement of the *cis* isomer **57** to bicyclo[5.4.0]undecanone **58**. (95)

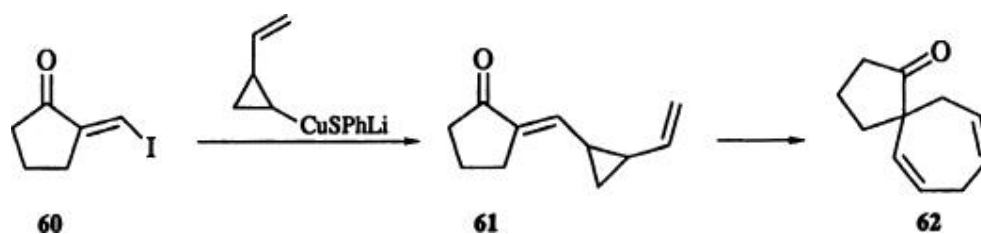


The required boat transition state **59** cannot be attained because of hindrance by the *gem* dimethyl group. (95) Numerous examples of this protocol exist for

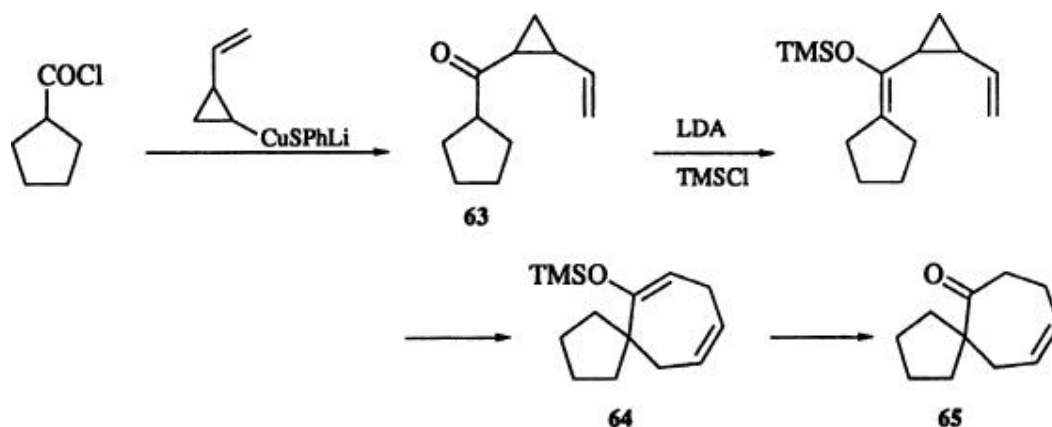
the construction of fused bicyclic systems. (86, 91-97) The spirocyclic annulation



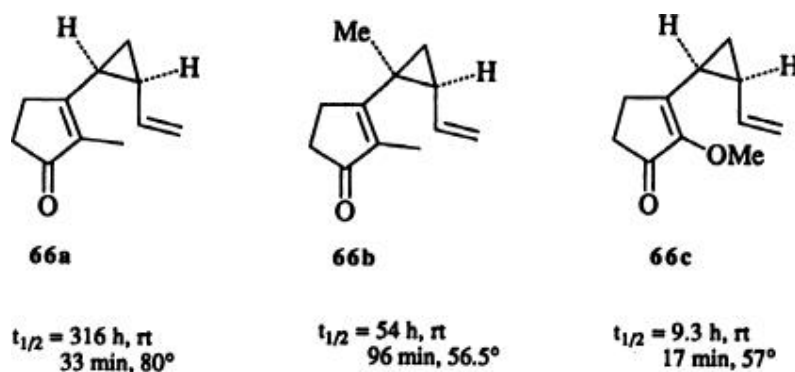
based on this rearrangement has also been reported. (98) Generation of divinylcyclopropane **61** from iodo enone **60** leads to spirocyclic system **62** in 64%



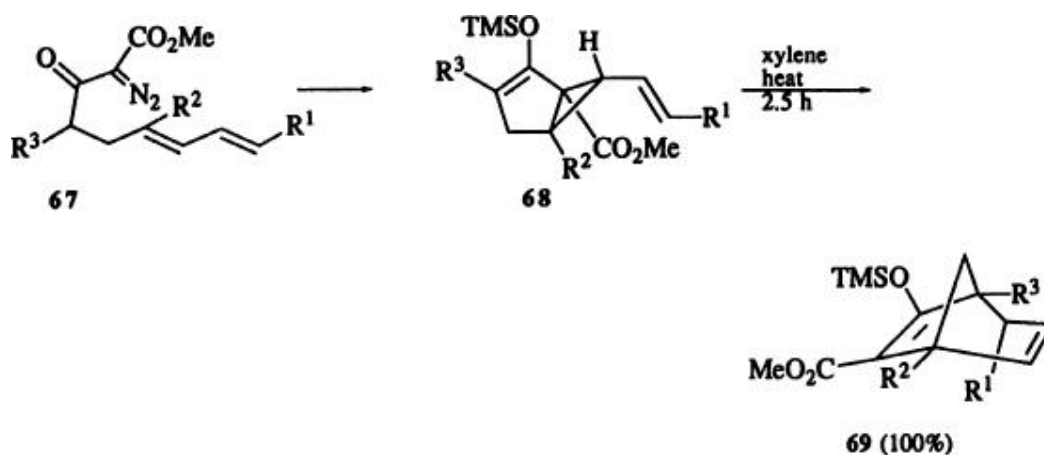
yield. (98) The aforementioned conversion of acid chlorides to cycloheptenones can be adapted for spiroannulation, as shown for cycloheptanone **65**. (87) This protocol is sometimes complicated by the generation of regioisomeric enol ethers (87, 98) from unsymmetrical ketones such as **63**.



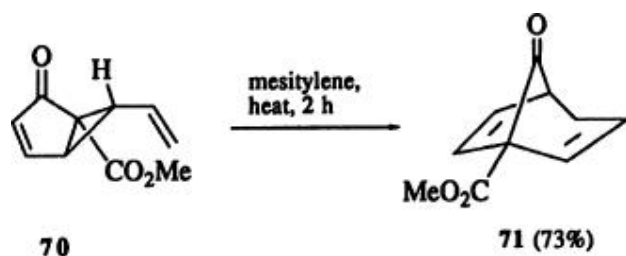
In general, the rearrangements of divinylcyclopropanes to annulated bicyclic systems proceed smoothly below 200° and are complicated only by the competing [1,5] shifts of *cis*-alkylvinylcyclopropanes or rate retardation due to increased olefin substitution in the divinylcyclopropane system, again in direct analogy to the criteria governing the vinylcyclopropane–cyclopentene rearrangement. (11, 16, 50, 52, 73, 74) A comparison of rate differences as a result of a substitution pattern has been made. (99) There may be a special ionic component in the transition state involving the rearrangement of **66c** that is accelerated compared to either of the alkyl-substituted analogs **66a** or **66b**.



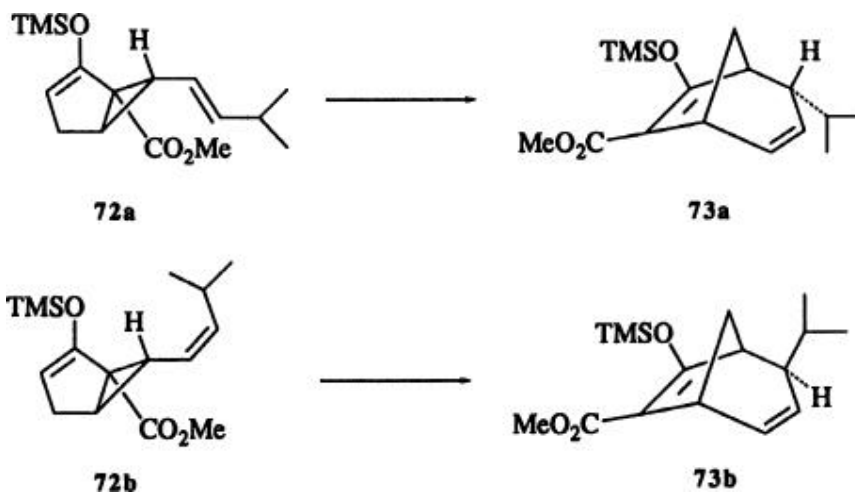
Bicyclo[5.3.0]decanes (86, 91, 94) and bicyclo[5.4.0]undecanes (86, 92, 93, 95) of varying substitution pattern are readily available. Bridged bicyclic systems are also accessible by modifying the topology of the rearrangement. Several approaches to bicyclo[3.2.1]octanes are described in the literature and differ only in the methods used to construct the precursory divinylcyclopropanes. The rearrangement of trimethylsilyl ethers such as **68**, generated via the intramolecular cyclopropanation (51) of diazo keto esters **67** followed by silylation



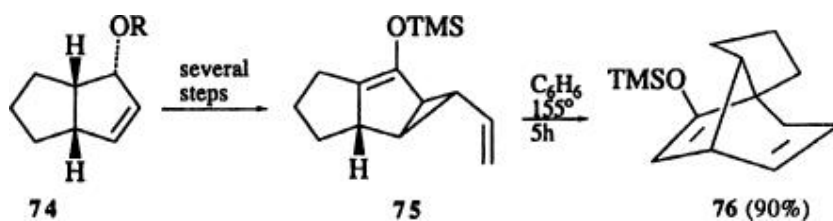
of the intermediate keto vinylcyclopropanes, provides excellent yields of bridged systems **69** upon refluxing in xylene. (100) The regiomerie rearrangement of vinylcyclopropane **70** gives keto ester **71** in 73% yield. (100) The stereospecificity



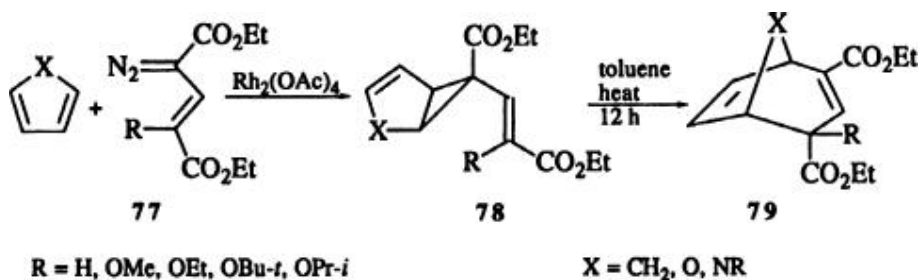
of this rearrangement has been confirmed by comparison of the *cis* and *trans* isomers of divinylcyclopropanes **72a** and **72b**. Each rearranges smoothly to the *endo*- and *exo*- isopropylbicyclo[3.2.1]octane systems, respectively. (101) More highly functionalized systems are attained by the rearrangement of divinylcyclopropane **75**, in which the vinylcyclopropyl portion



is introduced via ethyl diazoacetate cyclopropanation of allylic ether **74**. The tricyclic system **76** is obtained in high yields by sealed-tube thermolysis of **75**. (101)

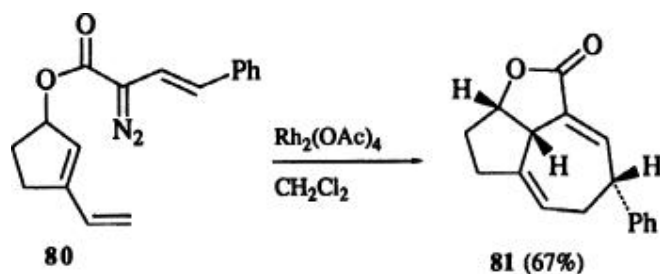


The rhodium-catalyzed cyclopropanation of some conjugated dienes with unsaturated diazo esters gives vinylcyclopropanes of type **78** exclusively in an



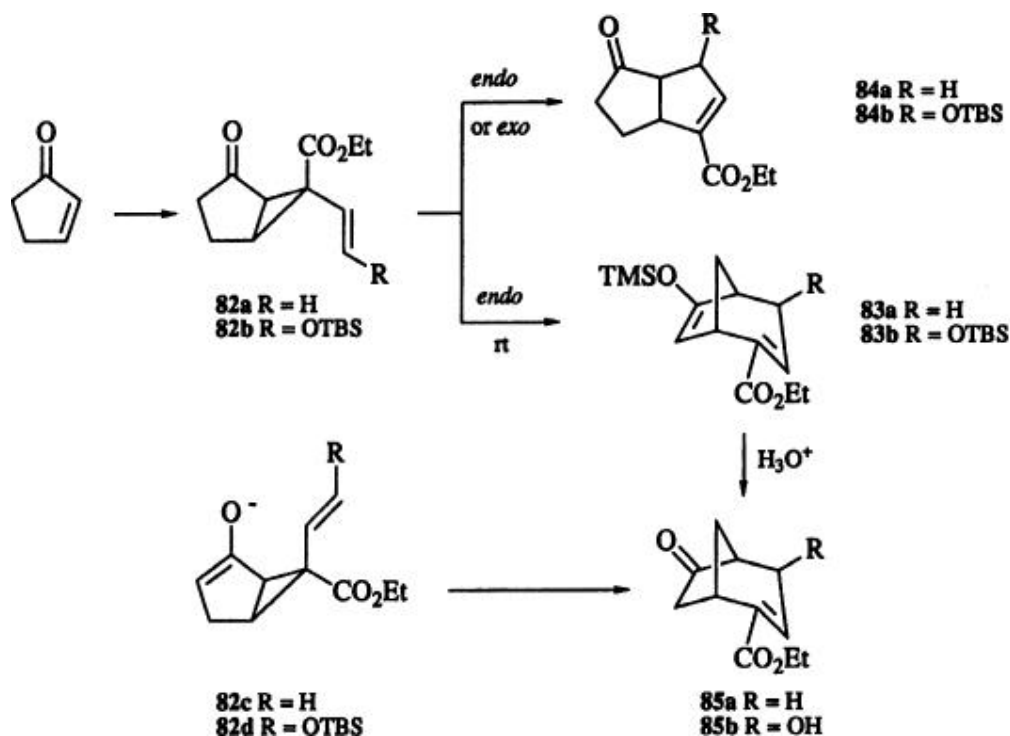
*endo* fashion, and the subsequent rearrangement to **79** is stereospecific. (72, 102-107) This process has been extended to include cyclopropanation of furans and pyrroles, leading to the corresponding bridged heterocycles. (106, 107) The intramolecular version of this reaction leads to the preparation of

fused cycloheptadienes such as **81** without isolation of the intermediate divinylcyclopropane.



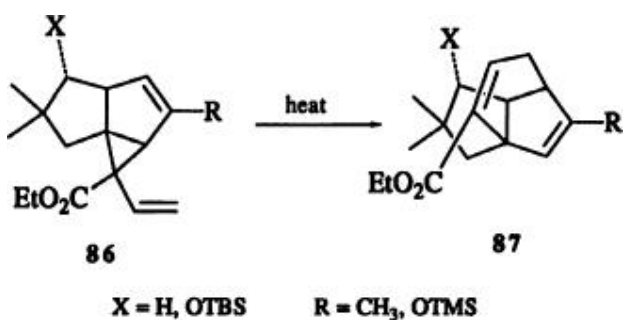
The reaction is stereospecific in most cases and it is not clear whether rhodium catalysis is only the agent responsible for cyclopropanation or whether it also serves a function in the subsequent Cope rearrangement. (104) Carboethoxy or phenyl substitution on the unsaturated diazo ester unit seems essential.

The Cope rearrangement to trimethylsilyl enol ethers derived from **82a** (in its *endo* form) occurs at low temperature. (108) This process represents an overall



[3 + 4] annulation of enones via vinylcyclopropanes **82a**, which can also be rearranged to annulated cyclopentenones such as **84a** in an overall [2 + 3] sequence. (108-112) The trimethylsilyl enol ether of *exo*-**82a** undergoes the Cope rearrangement only at temperatures above 180°, presumably via a

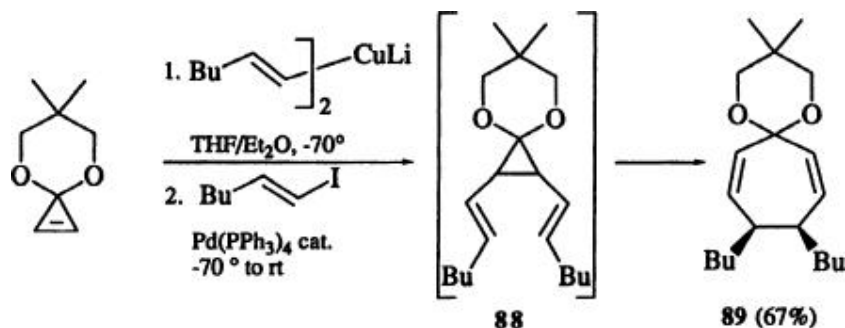
diradical cleavage and isomerization to *endo*-**82a**. The consequence of this competition is the formation of cyclopentene **84a** along with **85a**. (108-110) Interestingly, **82c**, the enolate anion of **82a**, undergoes the Cope rearrangement at lower temperatures ( $-10^{\circ}$  to room temperature). A remote charge acceleration has been invoked to explain this phenomenon. (110, 113) A study of this rearrangement and its application to the synthesis of bridged systems such as **87** has been made. (109)



A new vinylcyclopropane–cyclopentene rearrangement that proceeds under extremely mild conditions has been reported. (110, 111) Silyl enol ether terminated vinylcyclopropanes of type **82b** (both *exo* and *endo* isomers) rearrange at  $-78^{\circ}$  to the corresponding siloxycyclopentenenes of type **84b** upon treatment with trimethylsilyl iodide (TMSI) and hexamethyldisilazane (HMDS). (111) The stereochemistry of this process depends on the precise conditions of the rearrangement or the Lewis acid used. On the other hand, generation of the trimethylsilyl enol ether of **82b**, via its enolate anion **82d**, leads to almost quantitative production of **83b**. (112) This control of the mode of rearrangement can also be applied to the six-membered analogs of **82b**. Interestingly, **82d**, the lithium enolate anion of **82b**, also rearranges to **85b** at low temperatures, even though the enolate of **82a** requires higher temperatures, at which decomposition begins to compete with the rearrangement. (110-112) There are other reports of Cope rearrangements of divinylcyclopropanes in which one of the olefins is an enolate anion: the descarboethoxy derivative of **82a**, which does not rearrange, (114) whereas a divinylcyclopropane in which one of the participating olefins is an ester enolate anion does rearrange at low temperature. (115) The mechanism of either the cyclopentene rearrangement or the Cope rearrangement of the silyl enol ether terminated vinylcyclopropanes remains unknown at this point, but preliminary evidence (low-temperature NMR monitoring of the reaction progress) suggests the existence of charged species as intermediates. (116) Remote charge acceleration from the silyl enol ether center or secondary orbital participation of the carboxylate heteroatoms is suspected. (112, 116)

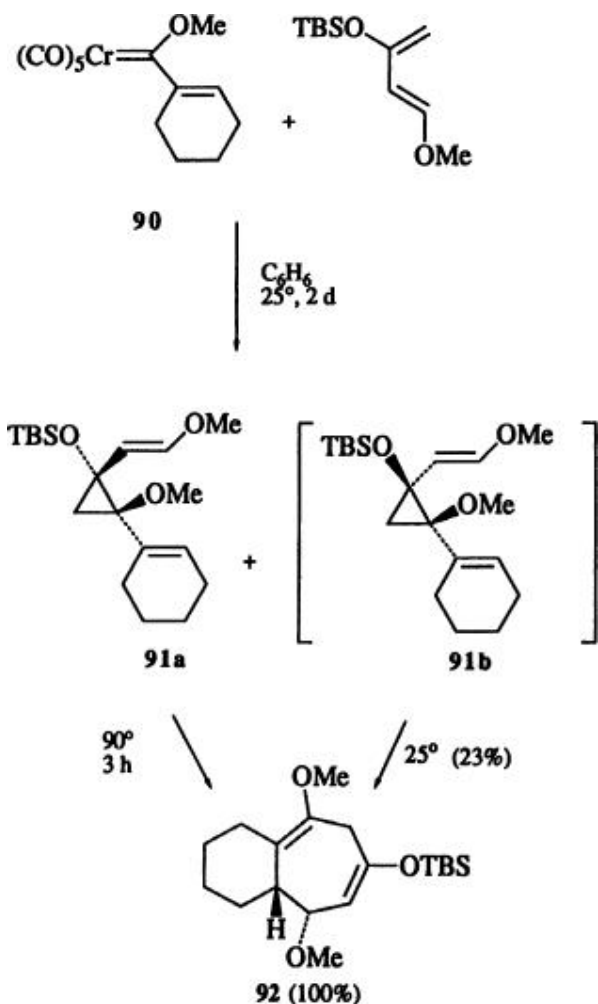


Two procedures for the formation of cycloheptadienes via organometallic intermediates have recently appeared. The addition of vinyl cuprates to the ketals of cyclopropanes, followed by palladium-catalyzed coupling with vinyl halides, leads to intermediate divinylcyclopropanes **88**, which rearrange below room temperature to *cis*-functionalized cycloheptadienes **89**. (117) In the reaction



of chromium carbenoid **90** with conjugated dienes, divinylcyclopropanes **91a** and **91b** are formed in a ratio of 1.7 to 1. The *cis* isomer rearranges to annulated cycloheptene **92** during the reaction (23% in the final mixture), whereas the *trans* isomer gives **92** quantitatively at 90°. (118)

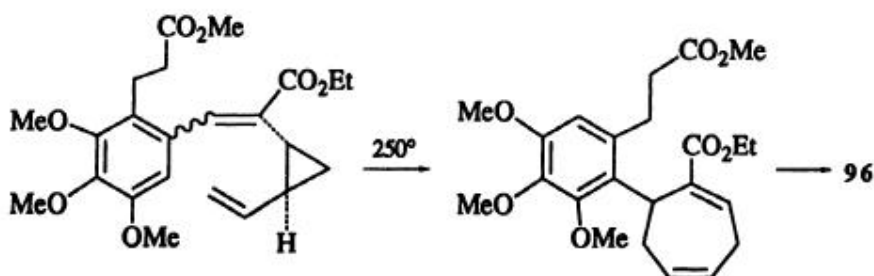
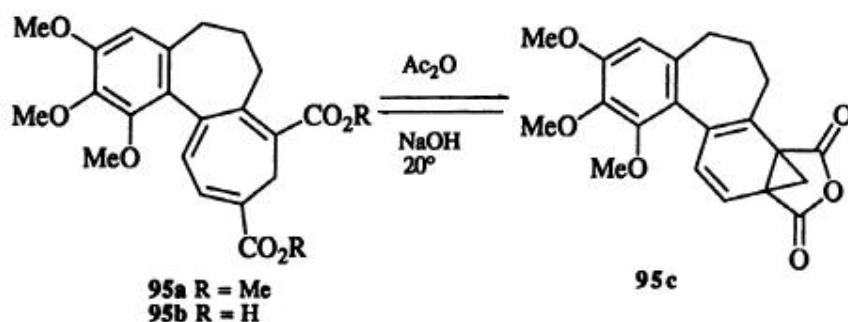
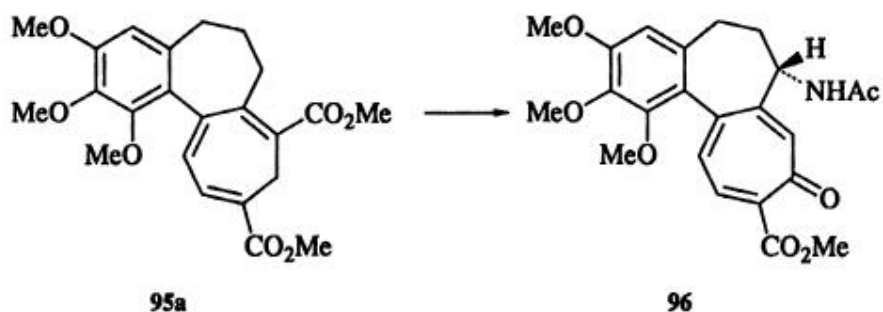
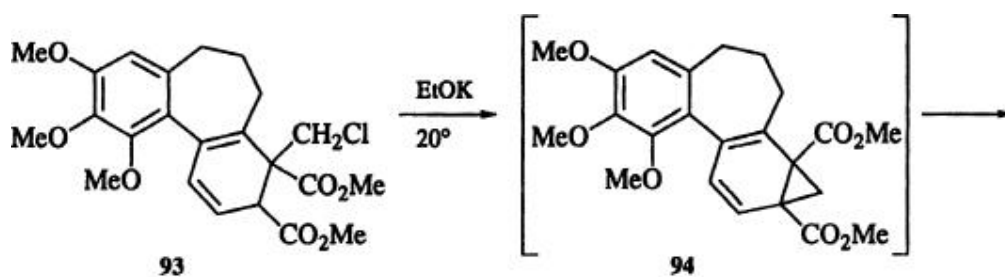
The Cope rearrangement of divinylcyclopropanes leads to a number of interesting annulation protocols that furnish fused, bridged, or spiroannulated ring systems. Further refinements of this technology that will possibly eliminate the need for pyrolysis and thereby allow survival of sensitive



functional groups can be expected. Recent reviews incorporate the annulation protocols. (10-15)

### 3.3. Applications to Natural Product Synthesis

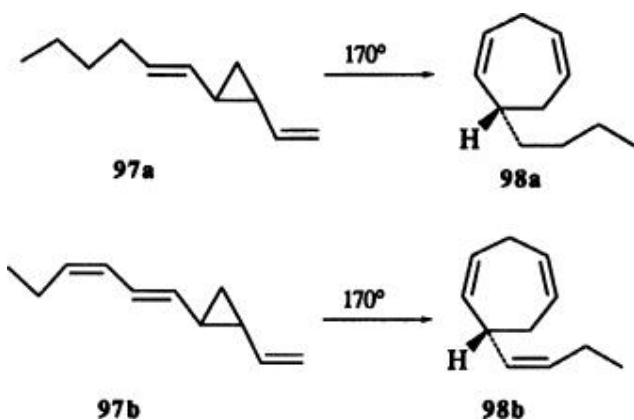
The Cope rearrangement of divinylcyclopropanes has been used in the synthesis of natural products containing functionalized seven-membered rings. Among the first applications following the eucarvone synthesis (1) was the Eschenmoser synthesis of colchicine (96), which features the norcaradiene Cope rearrangement of diester 94, generated by intramolecular displacement of chloride 93. (119) Curiously, cycloheptatriene 95b, undergoes equilibration with norcaradiene anhydride 95c. This type of equilibrium has been observed in a number of structurally similar compounds. (11-15, 22-25, 27) The Cope rearrangement has been applied to a formal total synthesis of colchicine (Eq. 8). (120) The key step in this synthesis is the generation of an appropriately functionalized *trans*-divinylcyclopropane via diazopyruvate cyclopropanation of butadiene followed by a Wittig reaction.



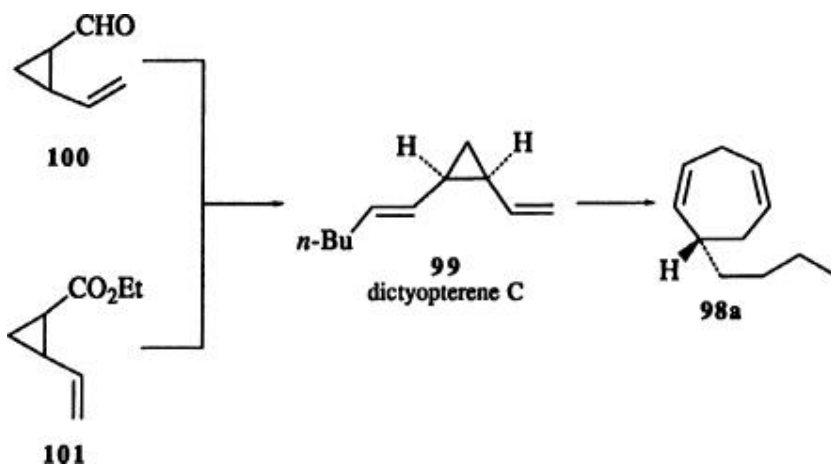
(8)

Two *trans*-substituted divinylcyclopropanes, dictyopterene A (**97a**) and dictyopterene B (**97b**), as well as their isomers, have been isolated from the essential oil of *Dictyopteris*. (121-125) A proposal for their biogenesis involving the Cope rearrangement has been advanced. (126) These hydrocarbons have been synthesized and found to rearrange with some degree of stereospecificity to cycloheptadienes **98a** and **98b**. (123) The energies of activation for the two rearrangements are 37.4 and 28.5 kcal/mole,

respectively, suggesting that the mechanism has radical character. This assumption rests on the partial racemization



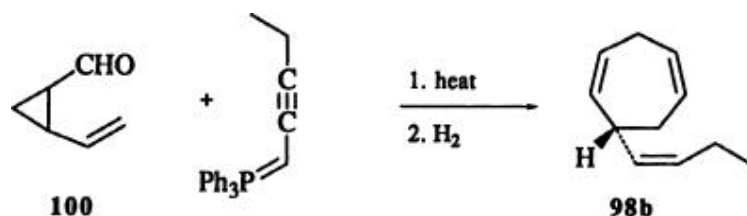
observed in the products and the differences in the energies of activation, corresponding roughly to the resonance stabilization of the allylic radical expected in the rearrangement of **2**. (123) The enantiomers of **98a** and **98b** have also been isolated from the essential oil, (122) and dictyoptere C (**99**) has been proposed as their in vivo progenitor, as it seems unlikely that either dictyoptere A or B could serve as a biogenetic precursor. (123) The racemic



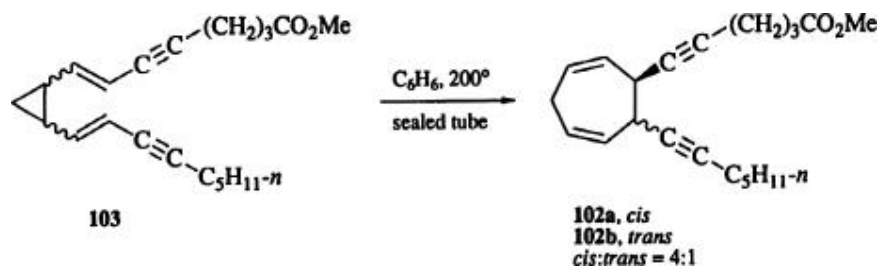
isomers of **99** have been prepared, and their rearrangement to the racemate of **98a** has been tested. (127-129) Thus, both *trans* and *cis* olefinic isomers of *trans*-substituted cyclopropane **99** give **98a** at 175°. The *cis*-olefinic isomer of *cis*-cyclopropane **99** requires 75° to rearrange, while the *trans* isomer of *cis*-**99** rearranges at 15°. (127) These results are in accord with the steric requirements of the Cope rearrangement. (10-16) Dictyoptere has been synthesized from vinylcyclopropane carboxaldehyde (**100**), (127) and by cyclopropanation of butadiene with ethyl diazoacetate and subsequent elaboration of vinylcyclopropane **101**. (130) The thermal and photochemical

behavior of all four stereoisomers of dictyopterene *A* and the related dictyopterene *B* has been studied. (126, 127) Accurate kinetic data and comparison of  $E_{\text{act}}$  and  $\Delta S^\ddagger$  values for dictyopterenes with those of various model systems leads to the conclusion that the rearrangement may be concerted ( $E_{\text{act}} \sim 32$  kcal/mole for various isomers of **97a** and **99**, 28 kcal/mol for **97b**). Isomerization (*trans*–*cis*) was rationalized in terms of diradical intermediates. Photochemical isomerization of the *cis*,*trans* isomers of **97a** to **99** proceeds at 40° in benzene and produces mixtures of **99** and **98a**. Diradical intermediates and their recombination to various stereoisomers of **97a** or to cycloheptadiene **98a** have been invoked in explanation. (126, 127)

A synthesis of cycloheptadiene **98b**, the racemate of the sperm-attractant sirenin isolated from the female gametes of the brown alga *Ectocarpus siliculosus*, starts from **100**. (131) No correlation of optical rotation was made to compare this substance to dictyopterenes *C* or *D*. (123, 125, 129) Synthesis of these naturally occurring cycloheptadienes has also been accomplished in a chiral sense. (132, 133)

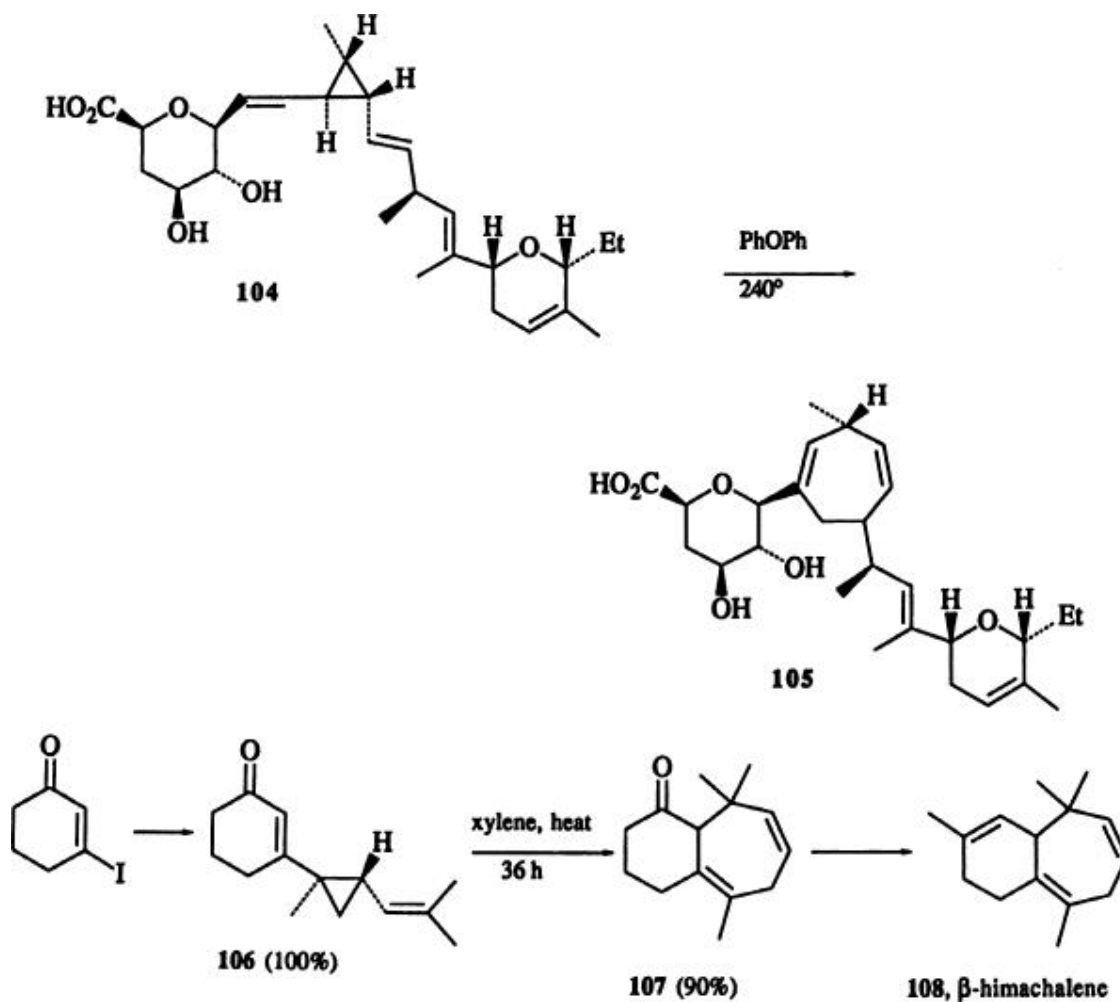


Arachidonic acid analogs **102a** and **102b** have been prepared via the Cope rearrangement of divinylcyclopropanes **103**. (134) A naturally occurring divinylcyclopropane



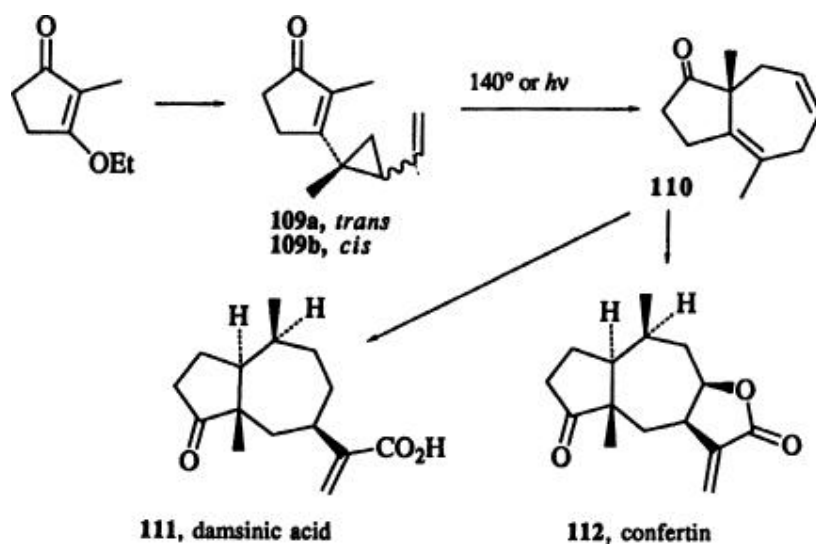
antibiotic **104** from *Polyangium cellulorum* var. Fulrum is thermolyzed to cycloheptadiene **105**, which is inactive against pathogenic fungi. (135)  $\beta$ -Himachalene (**108**) has been synthesized via a Cope rearrangement of divinylcyclopropane **106** generated by conjugate addition of an appropriate cuprate. The thermolysis of **106** gives annulated cycloheptadiene **107**, which is

converted to  $\beta$ -himachalene. (136) Damsinic acid (111) and confertin (112) have been prepared by manipulation of a common intermediate, fused cycloheptadiene 110. (63) Noteworthy in this synthesis is the solution to the problem of competing rearrangements such as the [1,5]-homodienyl shift of *cis*-alkyldivinylcyclopropanes 109b. Whereas the thermolysis of 109a leads to 110 in 100% yield, 109b furnishes this compound in only 20% yield at the expense of the retro ene process. Irradiation of 109b at 98° leads to cycloheptadiene

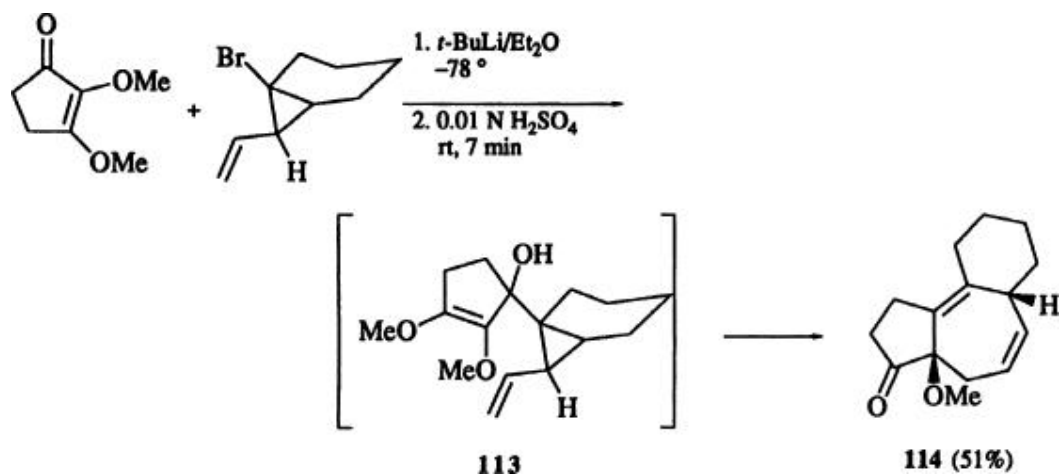


110 in 80–90% yield, presumably by generating the *cis*-divinylcyclopropane which then undergoes thermolysis. (63)

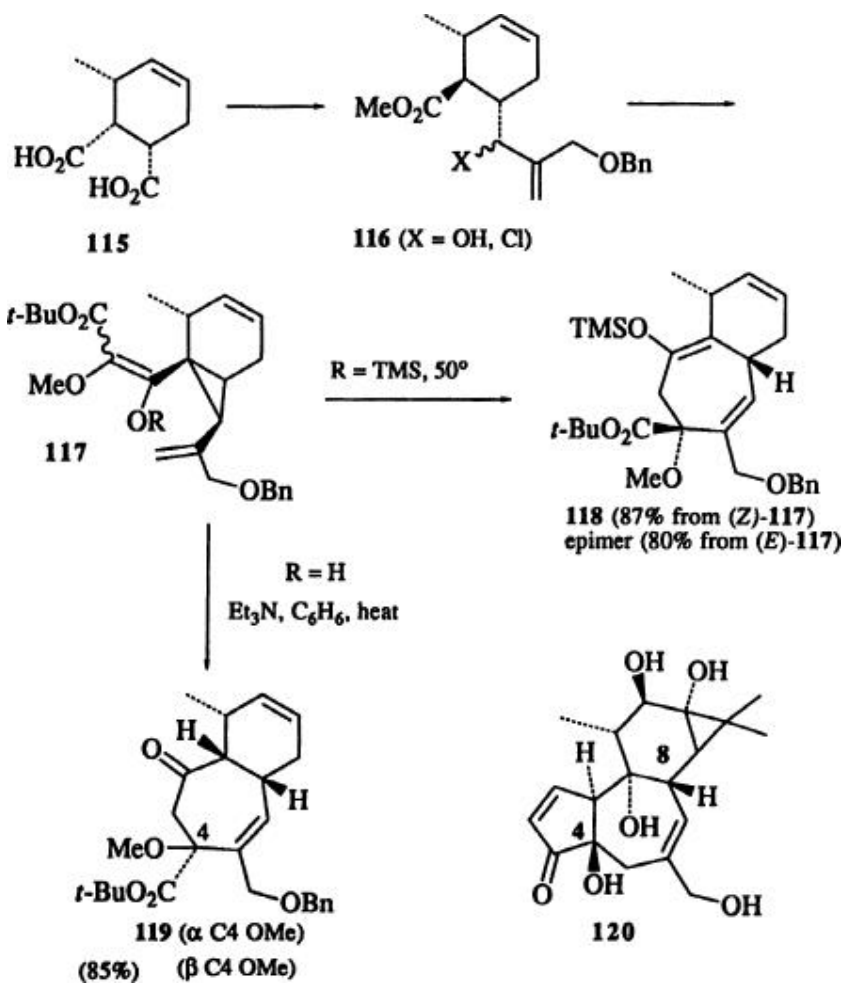
A model study aimed at the synthesis of phorbol (120) led to the preparation



of tricyclic ketone **114** via the Cope rearrangement of divinylcyclopropane **113**, which takes place under acidic (solvolytic) conditions, perhaps



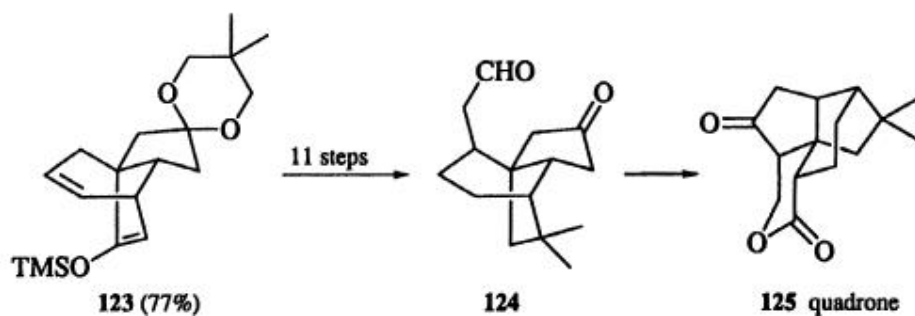
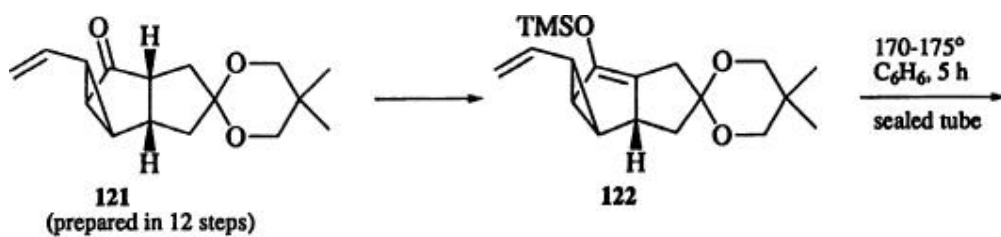
accelerated by a partial remote charge. (99) A more recent study toward phorbol-type compounds features the base-catalyzed formation of one of the vinyl units in divinylcyclopropane **117**. The *E* and *Z* stereochemistry determines



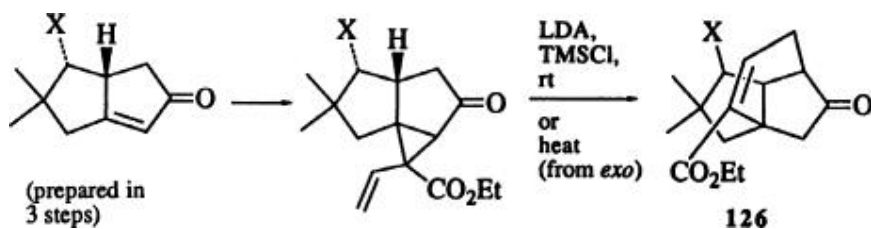
the stereochemistry of cycloheptadiene **118** or its hydrolysis product, bicyclic ketone **119**. The *E* enolate in **117** is preferentially formed from the precursory  $\beta$ -keto ester by refluxing it in benzene–triethylamine, where an internally hydrogen bonded enol form would predominate. The bicyclic ketone **119** possesses the C-4, C-8 stereochemistry found in phorbol (**120**). (137)

A formal synthesis of quadrone (**125**) has been accomplished via the rearrangement of trimethylsilyl enol ether **122**, available in 13 steps. The Cope rearrangement takes place at  $170^\circ$  to generate bridged tricyclic **123**, which is converted to keto aldehyde **124** in 11 steps. (138) The structurally similar system

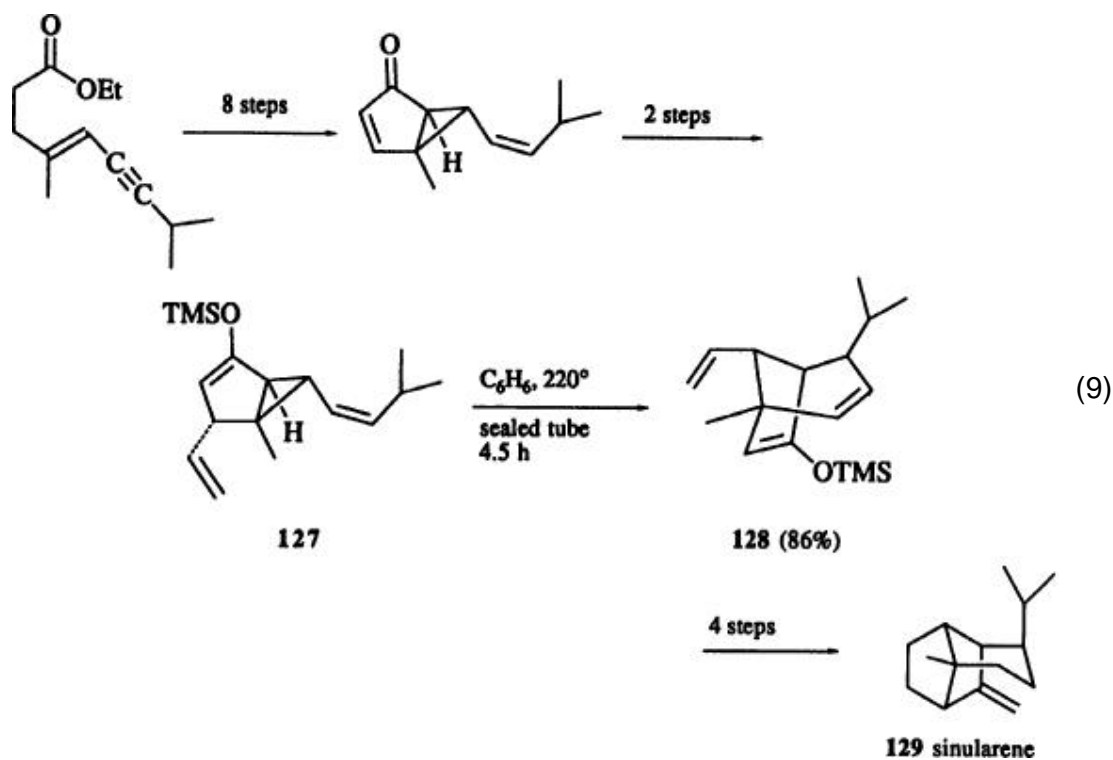




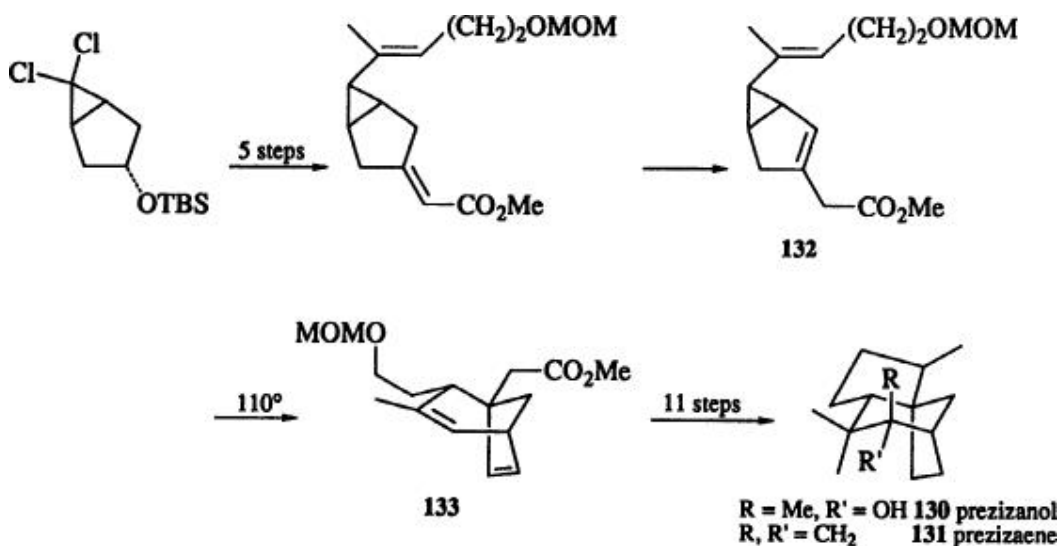
**126** has also been synthesized via a [3 + 4] annulation sequence. (108, 109)  
The



synthesis of sinularene (**129**) was accomplished by the sequence shown in Eq. 9. The Cope rearrangement of **127** proceeds in 86% yield to furnish the precursor to the natural product, bicyclic enol ether **128**. (139) Prezizanol (**130**)



and prezizaene (**131**) are obtained by a similar strategy. Only the *endo* isomer **132** rearranges to bicyclo[3.2.1]octane **133** in 98% yield. This compound was converted to the sesquiterpenes **130** and **131** in 11 steps. (**140**)



It can be expected that this rearrangement will continue to be used in the total syntheses of complex natural products because of its simplicity, low energy of rearrangement, and high degree of stereocontrol. The development of tandem

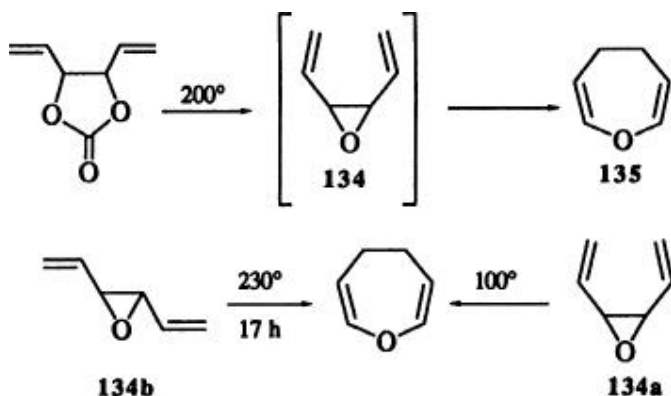
processes of increasing complexity that generate the divinylcyclopropanes under mild conditions will aid in further applications of this rearrangement.

## 4. Heterocyclic Systems

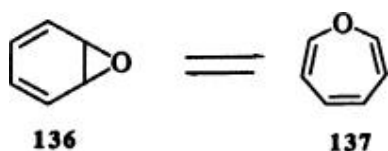
The Cope rearrangement of divinylcyclopropanes in which one or more atoms along the periphery of the reacting system has been replaced by a heteroatom is also known. (10-16, 27, 51, 52) In such systems the mechanism can operate from additional manifolds: electrocyclic zwitterionic processes, fully ionic processes involving nucleophilic ring opening followed by alkylative reclosure, and diradical cyclizations. The regiochemistry as well as the topology of heteroatom variations of the Cope rearrangement, like those of the heteroatom analogs of the vinylcyclopropane system, are therefore more complex than for the carbocyclic system. (51, 52)

### 4.1. Divinyloxiranes

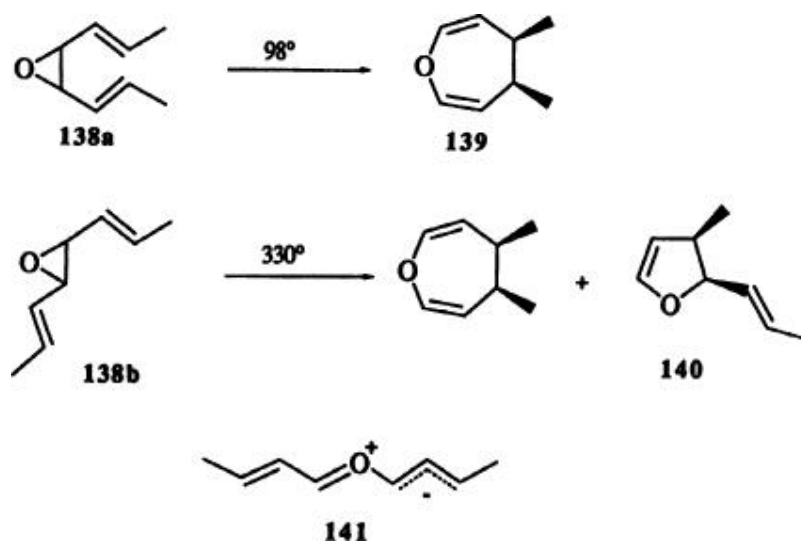
The rearrangement of divinyloxiranes to oxepines has been investigated in detail. 4,5-Dihydrooxepine (**135**) was isolated during an attempted preparation of divinylethylene oxide by pyrolysis of divinylethylene carbonate. (141) The intermediate in this reaction is oxirane **134**; thermolysis of its *cis* and



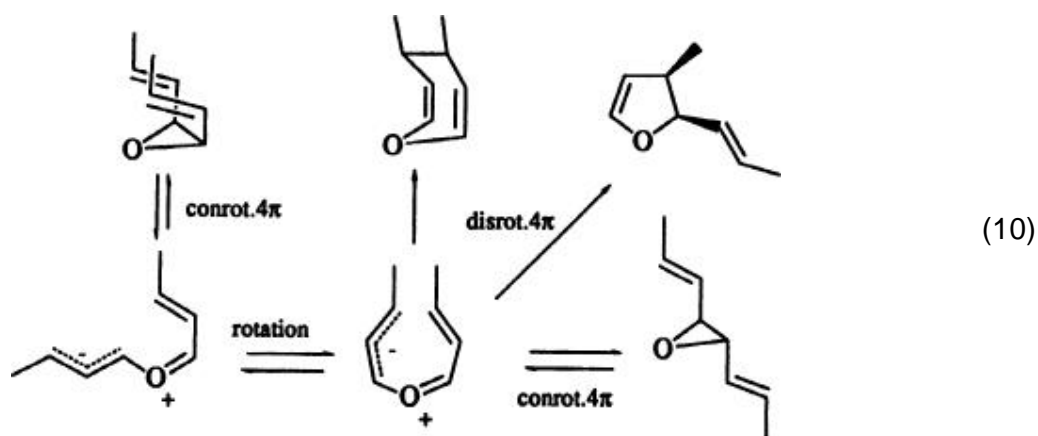
*trans* isomers resembles that of the carbocyclic analogs. (142) The *cis*- and *trans*-divinyloxiranes have  $\Delta H^\ddagger$  of 24.6 kcal/mole and 36 kcal/mole, and  $\Delta S^\ddagger$  of  $-11.3 \text{ cal deg}^{-1} \text{ mole}^{-1}$  and  $-0.4 \text{ cal deg}^{-1} \text{ mole}^{-1}$ , respectively. This suggests that a boat transition state and a diradical cleavage of the C-C bond operate in the oxepine rearrangement. (143) Benzene oxide-oxepine valence tautomerism has been compared to the norcaradiene-cycloheptatriene rearrangement. (143) The kinetics of the equilibrium of **136** and **137** as well as substituted derivatives of these systems have been reviewed. (143, 144)



*trans*-Divinyloxiranes yield vinylidihydrofurans in competing rearrangements. The kinetics of racemization of chiral *trans*-divinyloxirane ( $k_{160^\circ} = 5.5 \times 10^6 \text{ s}^{-1}$ ), suggest an electrocyclic process for the ring opening. (145) An isotope effect study suggests that oxepines or vinylidihydrofurans are produced competitively from a common zwitterionic intermediate. (146) A carbonyl ylide mechanism has been proposed to account for these observations. (147) Disrotatory closure of **141** would lead to dihydrofuran **140** (with inversion). Conrotatory

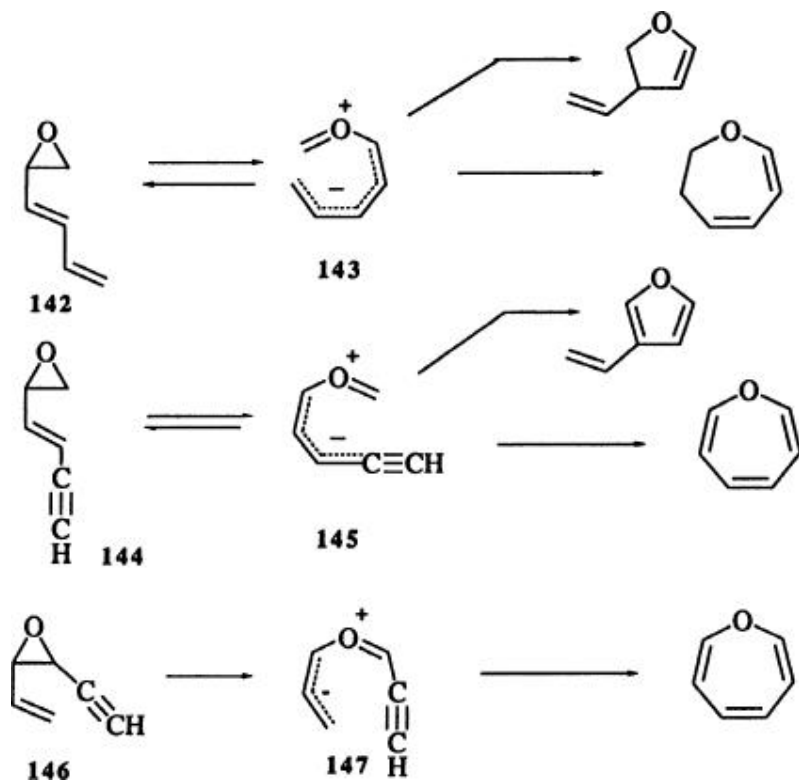


closure would yield the *cis* oxirane, which undergoes closure to oxepine **139** stereospecifically. (141, 148, 149) A summary of mechanistic options is shown in Eq. 10.



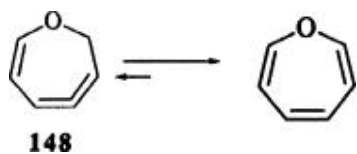
Eberbach (149-158) and Chucho (148, 159-165) studied the mechanism and

applications of this rearrangement extensively. An interesting comparison can be made between the systems studied by Eberbach, which involved mainly dienyl or enynyl epoxides, and those of Chuche, who investigated the divinyl or vinyllynyl oxiranes. In both instances oxepines of the appropriate unsaturation level are obtained, with competing rearrangements to vinylidihydrofurans or in some cases to cyclopropyl carbonyl compounds. The concerted closures of zwitterions such as **141**, **143**, **145**, and **147** were invoked as mechanistic options



in both thermal and photochemical rearrangements of oxiranes of type **138**, **142**, **144**, and **146**, respectively. (**148**) Only *Z* isomers of **142** lead to oxepins, whereas either *Z* or *E* isomers lead to vinylidihydrofurans. (**157**, **158**)

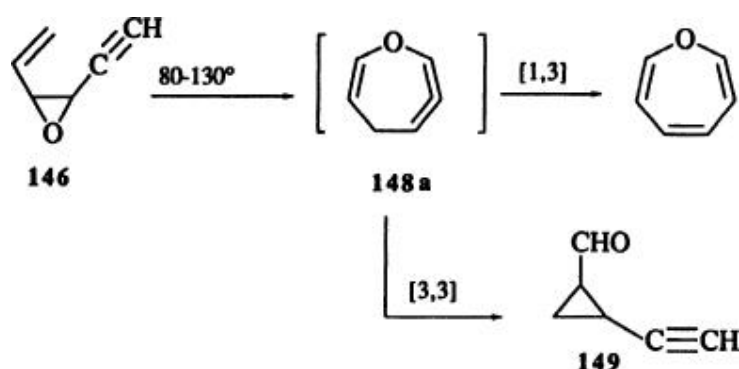
The alkynyl compounds **144** rearrange at 170° to either vinylfurans or oxepins. (**150-152**) The intermediate in these reactions is the cyclic allene **148**,



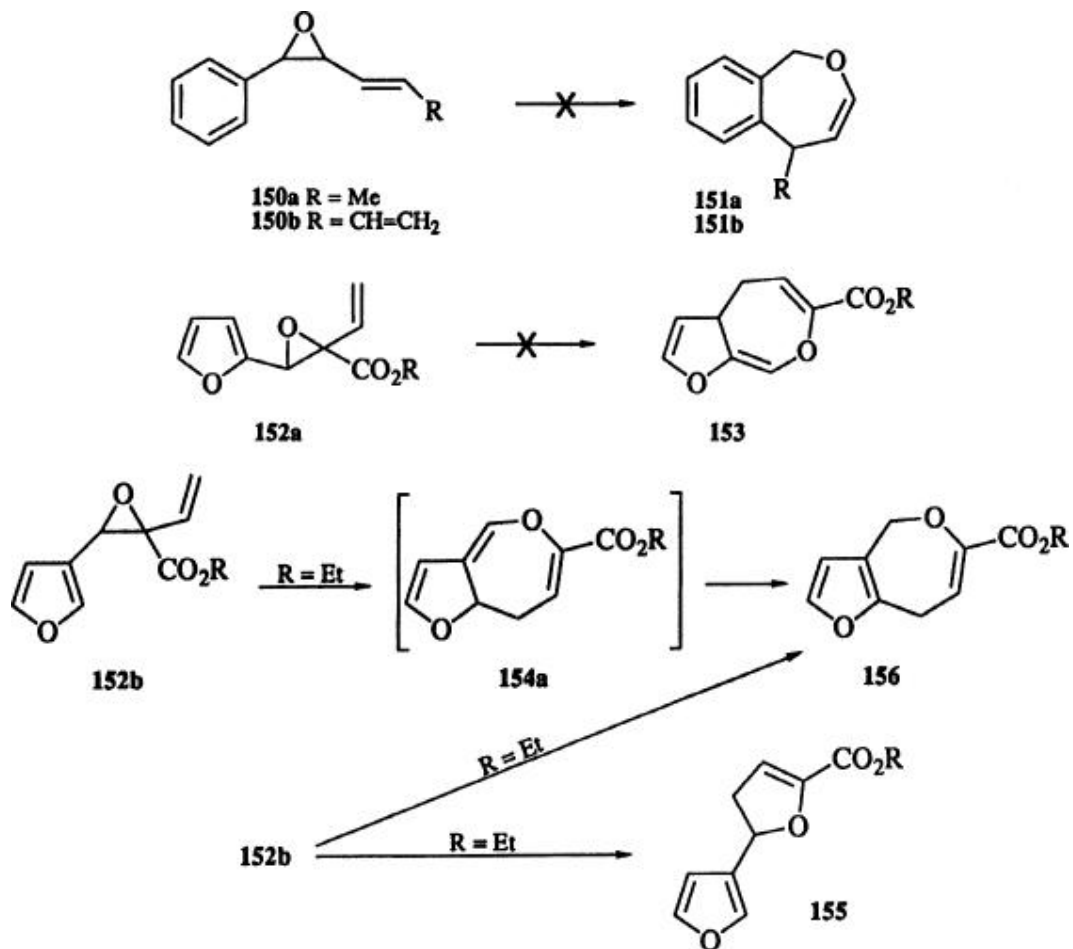
which isomerizes to an oxepine under thermolytic conditions. (**153**) A similar intermediate, **148a**, has been proposed (**159**) to account for the formation of

oxepine from **146** and the formation of ethynylcyclopropylaldehyde **149**. (**159**, **160**) This transformation has been studied in gaseous and liquid phases and found somewhat controllable. (**161**)

This rearrangement is sometimes useful in the synthesis of fused oxepines or benzoxepines. Under certain conditions aromatic olefins participate in the rearrangement. (**166-168**) However, the rearrangement of oxiranes such as

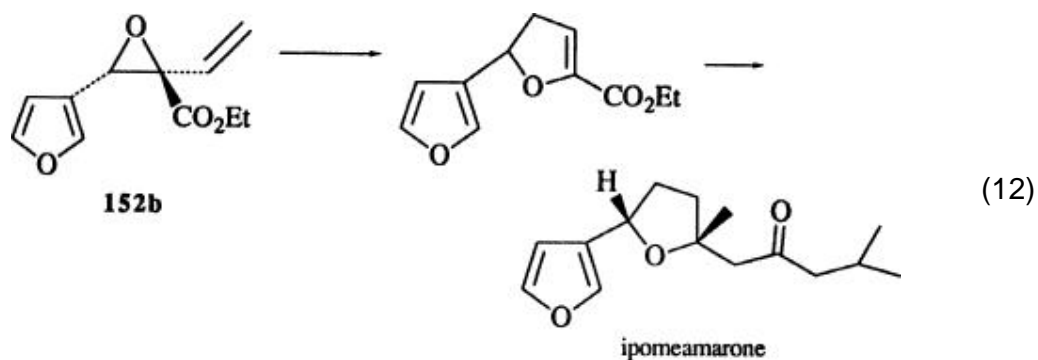
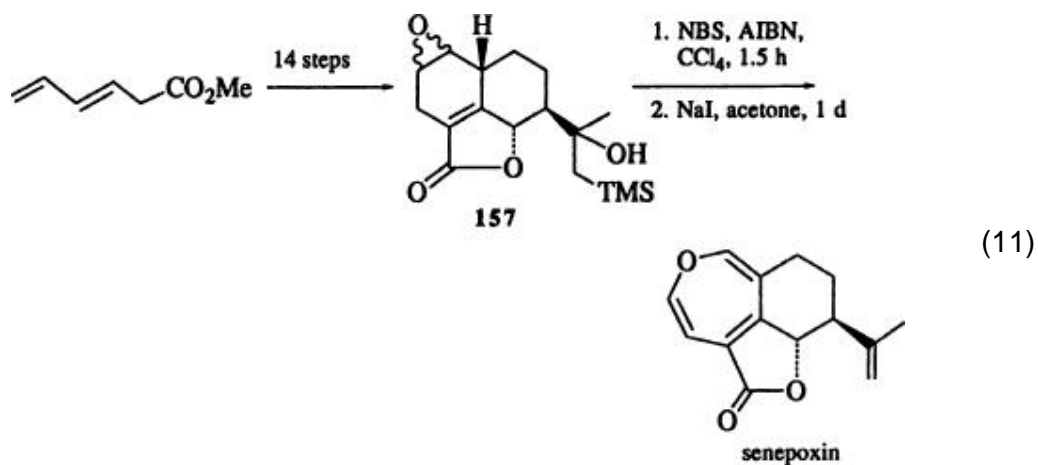


**150a,b** (**148**) is sluggish, as is the rearrangement of the 2-furyl derivative **152a**. (**166**) On the other hand, 3-furyl derivative **152b** provides smoothly the intermediate oxepine **154a**, which gives the fully aromatic compound **156** under the reaction conditions. (**166**) This difference in reactivity can be attributed to unfavorable resonance stabilization of carbonyl ylides of type **141** derived from the 2-furyl compounds, which yield dihydrofurans rather than oxepins upon thermolysis. (**148**, **166**) Control in the rearrangement of compounds such as **152b** to either oxepines **156** or dihydrofurans **155** depends on the temperature profile of the

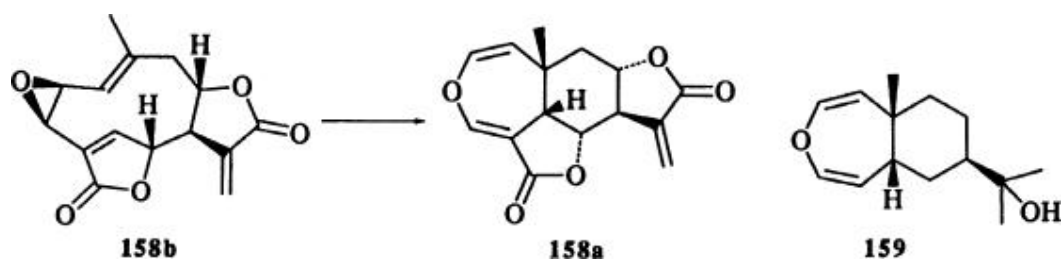


pyrolysis. (166-168) Apart from the detailed mechanistic studies, few examples of this rearrangement in the synthesis of more complex molecules have been reported. Senepoxin has been synthesized by allylic bromination of epoxide **157**, available in 14 steps from methyl 3,5-hexadienoate, followed by in situ generation of the divinylloxirane precursor, which gave senepoxin in 22% yield, Eq. 11. (169) Control of the dihydrofuran–oxepine mode of the rearrangement allows the conversion of oxirane **152b** to ipomeamarone, a furanosesquiterpene from the sweet potato *Ipomea batatas* (Eq. 12). (167)

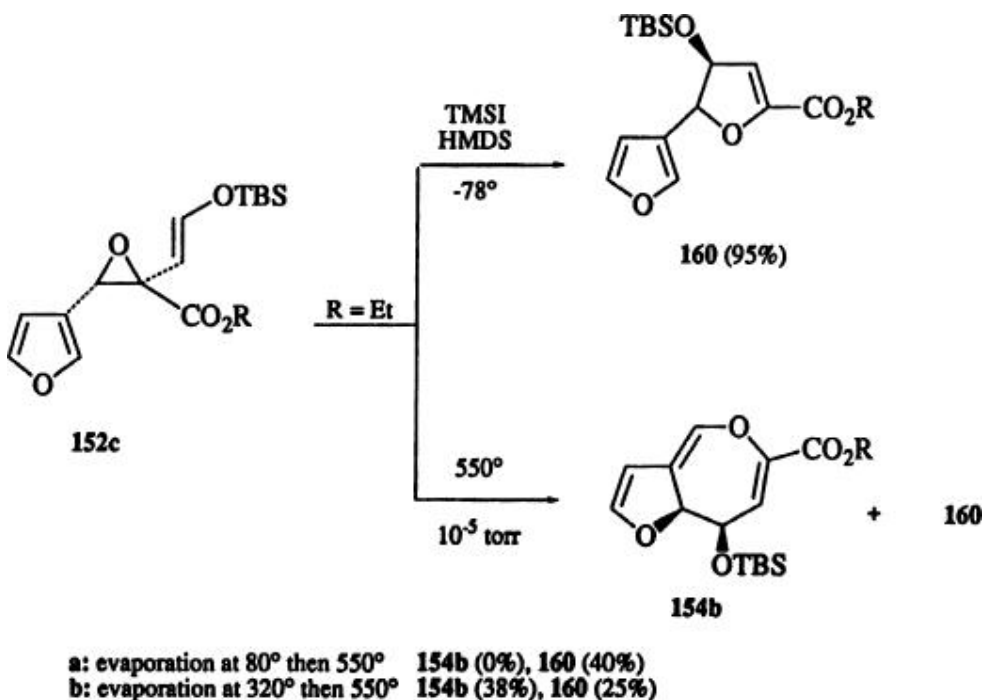




One example of a biological divinylloxirane–oxepine rearrangement has been reported in the context of stereochemical studies in sesquiterpenoids. A minor constituent of the extract of *Mikania* species, miscandenin (**158a**), has been assigned the indicated stereochemistry by X-ray crystallography, in analogy with a similar assignment to occidenol (**159**). The suggested Cope rearrangement responsible for the formation of these compounds is shown. (**170**)



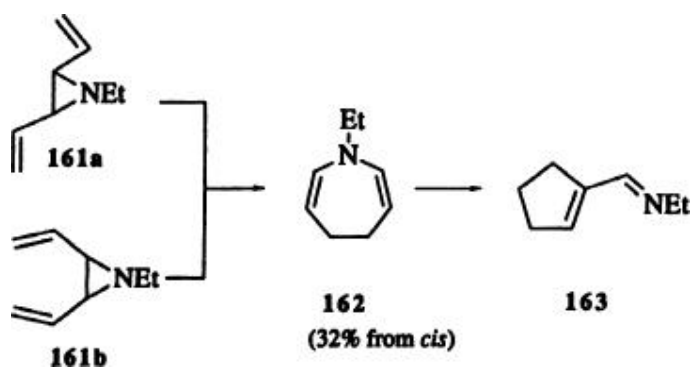
An example of this rearrangement that proceeds under extremely mild conditions involves the synthesis of oxepine **154b** from the silyl enol ether-terminated vinyloxirane **152c**. Either oxepines **154b** or dihydrofurans **160** are available by controlled thermal rearrangement of the oxirane. The dihydrofurans such as **160** become exclusive products of the low temperature



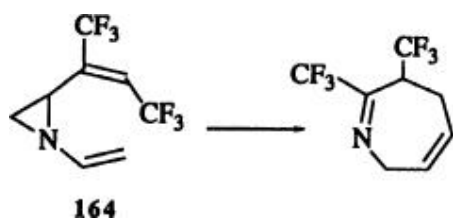
rearrangement of **152c** mediated by trimethylsilyl iodide–hexamethyldisilazane, (**168**) in direct analogy to the rearrangement of the silyl enoether-terminated vinylcyclopropanes. (**111**) The mechanism of this intriguing rearrangement is at present unknown. (**116**, **168**)

#### 4.2. Divinylaziridines

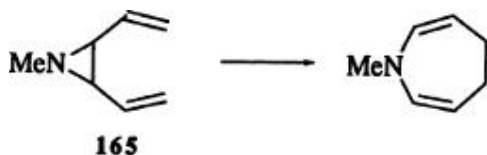
Transformations analogous to the Cope rearrangement occur with both divinylaziridines and vinylaryl- or vinylalkynylaziridines. These processes have been studied in parallel with the corresponding oxygenated analogs. (**159**, **160**, **165**) The rearrangement of *cis*- and *trans*-divinylaziridines **161a,b** to azepines **162** occurs during the ring opening of divinylloxiranes with ethylamine. (**171**)



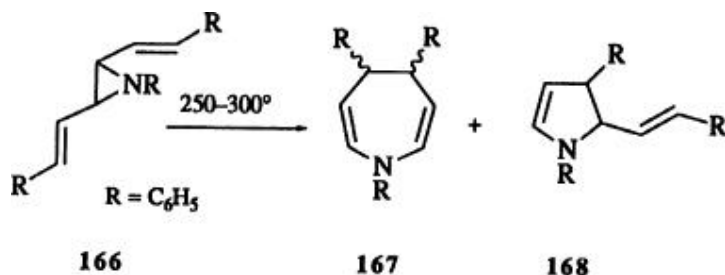
In the presence of moisture, the ring-contracted cyclopentene imine **163** is observed. The rate of the valence isomerization of *cis*-divinylaziridine **164** to its azepine is  $k_{25^\circ} = 1.28 \times 10^{-4} \text{ s}^{-1}$ . (172) It is noteworthy that several



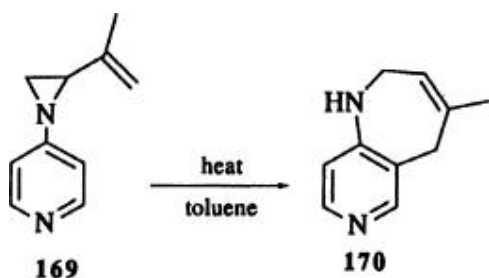
regioisomeric divinylaziridines can exist as a consequence of the trivalent nitrogen. Thus the substitution pattern in the resulting azepines can also differ.



The  $D H^\ddagger$  for the isomerization of **165** is 18.5 kcal/mole, a value substantially lower than that for carbon analogs in the Cope rearrangement. (173) *cis*-Divinylaziridines give azepines whereas *trans* compounds furnish pyrrolines, in analogy with the rearrangements of divinylloxiranes. Concerted closures of zwitterionic intermediates have been postulated as mechanistic explanations for thermal rearrangements. (174) Aziridines **166**, in which only one of the vinyl

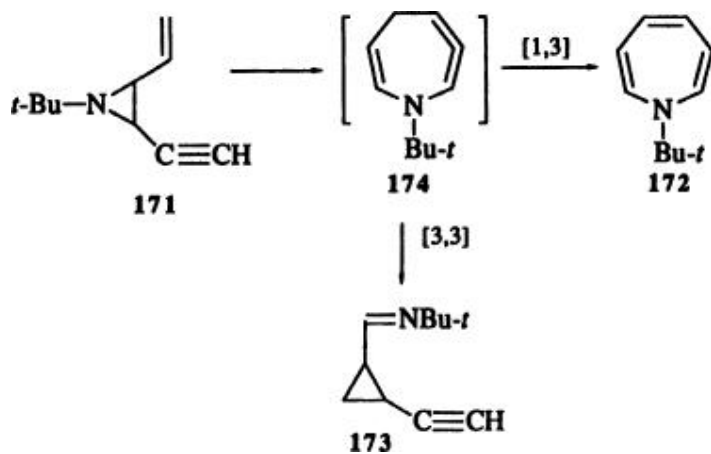


groups is confined in an aromatic nucleus, prefer the pyrroline pathway, (174) but *N*-substituted vinylaziridines **169** give pyridoazepines **170** on thermolysis. (175)



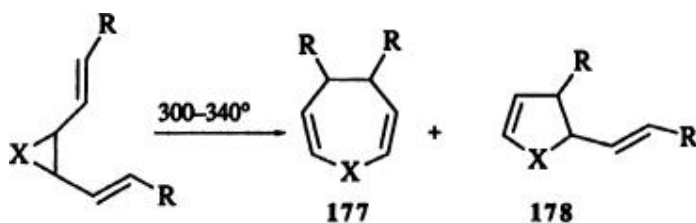
Cycloadditions of vinylaziridines to acetylenes have been reported to involve intermediates similar to the ylides obtained on thermolysis of divinylaziridines. (176-178)

The vinylalkynylaziridines **171** behave like their divinylloxirane analogs. (159-161) The chief product is azepine **172**; however, ring contraction and transformation to cyclopropylalkynylimines **173** has also been observed. Allene **174** has been postulated as an intermediate. (159)



### 4.3. Divinylthiiranes

*cis*-Divinylthiirane **175** isomerizes to 4,5-dihydrothiepine at 340° (flow system). (179) Kinetic measurements (176 in CCl<sub>4</sub> solution, 110°) show that the rearrangement is slower than that of oxiranes, cyclopropanes, or aziridines (Table A) (179) with  $k_1 = 14 \times 10^{-3} \text{ min}^{-1}$  at 118°. The rearrangement has been suggested to proceed through an ylide intermediate. The competing formation of vinylidihydrothiophene **178** (29%) is also observed. (179)



**175**, R = H  
**176**, R = Me

Table A

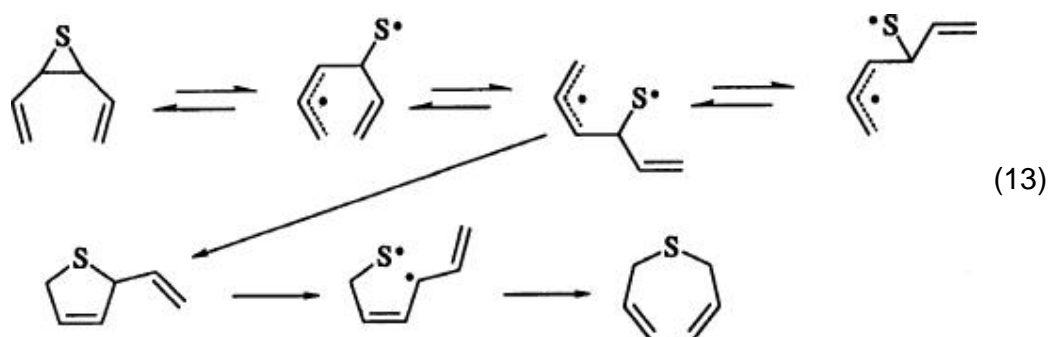
X	$\Delta H^\ddagger$ (kcal/mole)
CH <sub>2</sub>	17.8
NR	18.5
O	22.7
S	25.0

Table A.

X	$\Delta H^\ddagger$ (kcal/mole)
CH <sub>2</sub>	17.8
NR	18.5
O	22.7
S	25.0

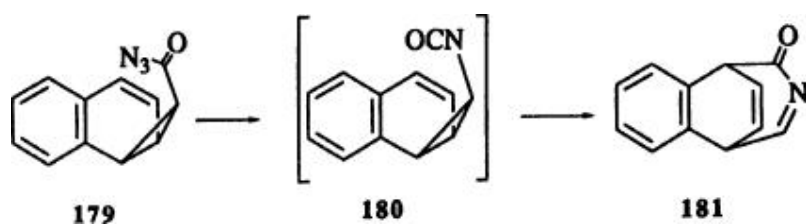
The *cis*- and *trans*-divinylthiiranes are stable at room temperature. The *cis* isomer rearranges above 90° and the *trans* isomer at 120°. (180) Loss of sulfur and formation of hexatrienes as well as isomerizations of thiepienes are the major complications. (179, 180) Diradical intermediates have been invoked to

explain the competing process. The *cis*- or *trans*-divinylthiiranes can rearrange according to the postulate shown in Eq. 13. (180) No use in synthetic methodology has been reported.



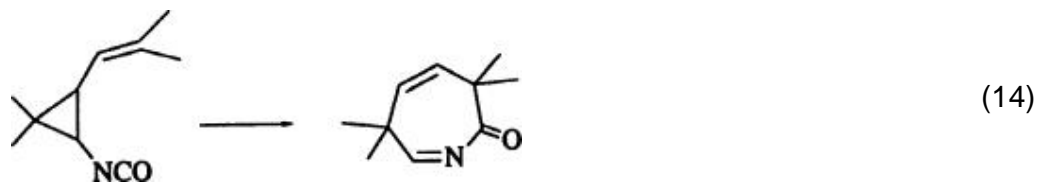
#### 4.4. Miscellaneous Compounds

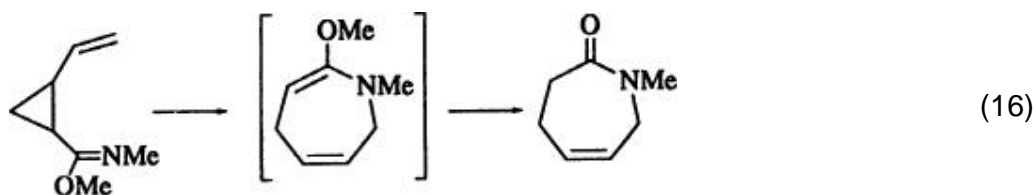
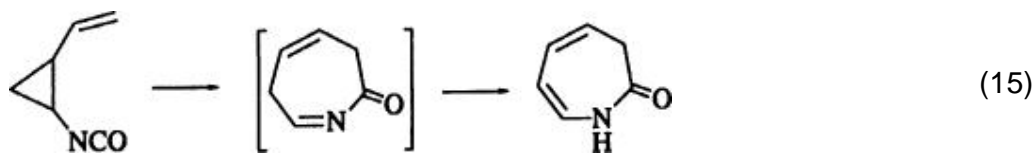
Essentially any combination of heteroatoms, both within and outside the three-membered ring, is subject to the Cope rearrangement. Acyl azide **179** gives an unusual rearrangement product on attempted Schmidt reaction. (181)



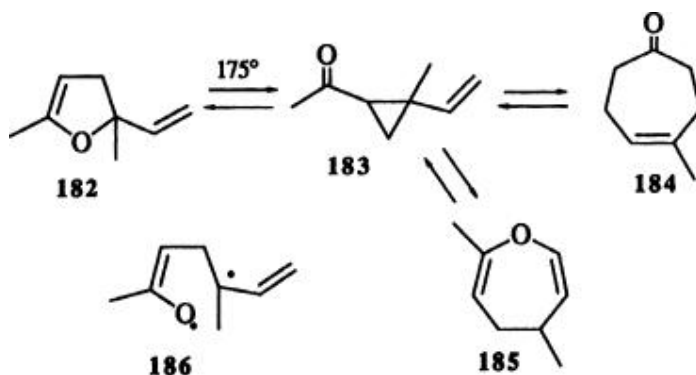
The product was identified as imino ketone **181**, arising via Cope rearrangement of isocyanate **180**.

Rearrangement of vinylcyclopropyl isocyanates have been reported to give azepinones (Eq. 14) (182) or lactams (Eq. 15). (34, 35) Azepinamides are also obtained from vinylcyclopropyl imidates, (Eq. 16). (32) Similarly, vinylcyclopropyl carbonyl





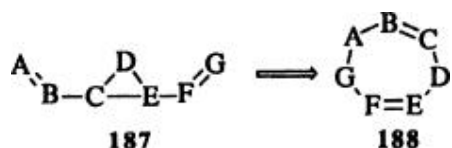
compounds **183** can yield oxepines **184** or vinylidihydrofurans **182** through thermal equilibration involving diradicals such as **186**. (**183**)



A study of substituent effects on the outcome of the rearrangement of most of the analogs of the Cope rearrangement discussed in this chapter has appeared. (**184**) Further examples of the Cope-like transformations of three-membered ring systems substituted with a variety of unsaturated side chains containing heteroatoms can be found in a recent compilation on the transformation of ring heterocycles. (**185**, **186**) This review summarizes only the most common types of the rearrangement, excluding those three-membered rings that contain more than a single heteroatom.

## 5. Summary

The potential of the seven-atom assembly represented by a Cope system appears limitless. Ample mechanistic precedent has been set, and it appears that synthetic utility should be forthcoming, especially in the heteroatomic cases. It appears that a system such as **187** (where A–G can represent any combination of atoms or functionalities that satisfy their valence requirements)



can effectively yield the product of its Cope rearrangement, **188**, where the final topography is dictated by the relative energetics of the particular bonds that participate in the rearrangement. Finally, applications of the Cope rearrangement to enantiocontrolled synthesis will no doubt appear as methods are developed that both lower the temperature of the rearrangement and provide means of chirality transfer or retention during the rearrangement.



## 6. Experimental Procedures

### 6.1.1.1. *cis*-6,7-Dimethylcyclohepta-1,4-diene (44)

A 40- $\mu$ L sample of *trans,trans,trans*-dipropenylcyclopropane (98.6%) was degassed through three or four freeze-pump-thaw cycles at  $10^{-4}$  torr, then sealed under vacuum in a base-washed and thoroughly dried ampule, and heated in an oil bath at 178° for 4.2 hours. The reaction mixture contained one product (98.8%) and no starting material according to GLPC analyses. The  $^1\text{H}$  NMR spectrum ( $\delta$  5.58, 3.07, 2.61, 2.55, 0.99) was identical with that of an authentic sample of *cis*-dimethylcyclohepta-1,4-diene.

### 6.1.1.2. 7-*n*-Butyl-1-*tert*-butyldimethylsiloxy-1,4-cycloheptadiene (87)

To a cold ( $-78^\circ$ ) stirred solution of lithium diisopropylamide (1.4–1.5 mmol/mmol of ketone) in dry THF (4 mL/mmol of base) under an atmosphere of argon was added slowly a solution of *n*-butyl-*trans*-2-vinylcyclopropyl ketone (1.19 mmol) in dry THF (1 mL/mmol of ketone), and the resulting solution was stirred at  $-78^\circ$  for 45 minutes. A solution of freshly sublimed *tert*-butyldimethylsilyl chloride (1.6 mmol/mmol of ketone) in dry THF (1 mL/mmol of chloride) was added, followed by dry HMPA (0.5 mL/mmol of ketone). The solution was stirred at  $-78^\circ$  for 15 minutes and at room temperature for 2–3 hours, and then it was partitioned between saturated aqueous sodium bicarbonate and pentane (10 mL and 20 mL/mmol of ketone, respectively). The aqueous phase was washed twice with pentane. The combined extract was washed four times with saturated aqueous sodium bicarbonate and twice with brine, and then dried ( $\text{MgSO}_4$ ). Removal of the solvent, followed by bulb-to-bulb distillation of the remaining oil, gave the corresponding silyl enol ether as a colorless oil that exhibited no IR carbonyl stretching absorption. Thermolysis of the silyl enol ether was accomplished by heating (neat, argon atmosphere) at 230° (air-bath temperature) for 30–60 minutes. Direct distillation (140–150°/12 torr) of the resultant materials provided the cycloheptadiene in 85% yield: IR (film) 1660, 1260, 840  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  0.09 (s, 6H), 0.88 (s, 9H), 0.7–2.75 (m, 14H), 4.8 (t, 1H,  $J = 5.5$  Hz), 5.5–5.9 (m, 2H).

### 6.1.1.3. 1,2,3,7-Tetrachloro-1,3-cycloheptadiene (84)

To a solution of *cis*-1,2,3,3-tetrachloro-1,2-cyclopropane diethyl bis(*p*-toluenesulfonate) (1.15 g, 2 mmol) in THF (80 mL) was added dropwise at  $-50^\circ$  under a nitrogen atmosphere *t*-BuOK (960 mg, 8.5 mmol) in THF (15 mL). After 1 hour at  $-50^\circ$ , the solution was allowed to warm to room temperature over 2 hours. It was evaporated in vacuo at 25°. The residue was extracted with chloroform and ether. The solvent was evaporated and the crude product purified by column chromatography ( $\text{SiO}_2/\text{CHCl}_3$ ) followed by preparative TLC ( $\text{SiO}_2/\text{CHCl}_3$ ) yielding 1,2,3,7-tetrachloro-1,3-cycloheptadiene (10%): UV ( $\text{CDCl}_3$ ) 257  $\text{cm}^{-1}$ ; IR (film)

3040, 2940, 2850, 1590, 1570, 1440, 1340, 1315, 1180, 1140, 1120, 840, 750, 710  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  2.3 (m, 2H), 2.6 (m, 2H), 4.92 (dd, 1H,  $J = 6, 8$  Hz), 6.56 (t, 1H,  $J = 7.1$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  24.7 (t), 43.8 (t), 59.1 (d), 127.6 (s), 128.5 (s), 134.1 (d), 136.3 (s).

6.1.1.4. *12,12-Diphenyl-5-methyl-11-oxa-7-oxo-tetracyclo[6.4.0.0<sup>5,9</sup>.0<sup>6,9</sup>]dodec-3-ene* (65)

A solution of benzophenone (91 mg, 0.5 mmol) and 5,8-dimethyl-9-methylenetricyclo[3.3.1.0<sup>2,8</sup>]non-3-en-7-one (87 mg, 0.5 mmol) in benzene (5 mL) was irradiated (RPR-100 photoreactor, 350-nm lamps) at room temperature for 8 hours. After the solvent was removed in vacuo, the resulting residue was separated by TLC on silica gel using ether–hexane (1:1) as the eluant to give the starting material (10 mg, 10%) and the cycloadduct (95 mg, 69%). The product was recrystallized from ethanol to give colorless crystals (mp 182–183°): IR (KBr) 1705, 1595, 1035  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.95 (s, 3H), 1.47 (s, 3H), 1.86 (d, 1H,  $J = 18.8$  Hz), 2.34 d, 1H,  $J = 18.8$  Hz), 2.45 (s, 1H), 3.43 (d, 1H,  $J = 6.8$  Hz), 4.06 (d, 1H,  $J = 11$  Hz), 4.62 (d, 1H,  $J = 11$  Hz), 5.5 (dd, 1H,  $J = 8, 6.8$  Hz), 5.79 (d, 1H,  $J = 8$  Hz), 7.05–7.77 (m, 10H); MS [ $m/e$  (rel.int)] 356 ( $\text{M}^+$ ), 132 (100).

6 $\alpha$  )-( $\pm$ )-3,3a,6,7-Tetrahydro-6-methyl-7-phenyl-1H-cyclohepta[c]furan-1-one (105)

A solution of (2*E*, 4*E*)-2,4-hexadienyl 2-diazo-4-phenyl-3-butanoate (5 mmol) in dichloromethane (10 mL) was added dropwise over 10 minutes to a stirred mixture of rhodium(II) acetate (0.021 g, 0.05 mmol) in dry dichloromethane (10 mL) and heated under reflux in an argon atmosphere. After heating for an additional 10 minutes, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica with ethyl acetate–hexane (1:9) as solvent to give (3 $\alpha$   $\alpha$ , 6  $\alpha$ , 7  $\alpha$  )-( $\pm$ )-3,3a,6,7-tetrahydro-6-methyl-7-phenyl-1*H*-cyclohepta[c]furan-1-one as a white solid (mp 104–106°) in 76% yield: IR (Nujol) 1755, 1670  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.0 (d, 3H,  $J = 6.7$  Hz), 3.16 (m, 1H), 3.69 (m, 1H), 4.09 (dd, 1H,  $J = 8.7, 8.7$  Hz), 4.21 (m, 1H), 4.66 (dd, 1H,  $J = 8.7, 8.7$  Hz), 5.36 (ddd, 1H,  $J = 10, 6.4, 3.0$  Hz), 5.68 (ddd, 1H,  $J = 10, 2.1, 2.1$  Hz), 6.92 (dd, 1H,  $J = 5.3, 3.2$  Hz), 7.13–7.75 (m, 5H); Anal. Calcd for  $\text{C}_{16}\text{H}_{16}\text{O}_2$ : C, 79.97; H, 6.71. Found C, 79.99; H, 6.75.

6.1.1.6. Diethyl

*endo*-1,5-Dimethyl-8-oxabicyclo[3.2.1]octa-2,6-diene-2,4-dicarboxylate (103)

A solution of diethyl 4-diazo-2-pentenedioate (1.06 g, 5 mmol) in dichloromethane (10 mL) was added dropwise over 10 minutes to a stirred mixture of rhodium(II) acetate (0.021 g, 0.05 mmol) and 2,5-dimethylfuran (25 mmol) in dichloromethane (5 mL) and heated under reflux in an argon atmosphere. After heating for an additional 10 minutes, the solvent was evaporated under reduced pressure and the residue was purified by

chromatography on silica with ether–petroleum ether (15:85 to 20:80) as gradient to give diethyl *endo*-1,5-dimethyl-8-oxabicyclo[3.2.1]octa-2,6-diene-2,4-dicarboxylate (0.98 g, 70%): IR (neat) 1720, 1705, 1622  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (  $\text{CDCl}_3$ )  $\delta$  1.27 (t, 3H,  $J = 7.1$  Hz), 1.30 (t, 3H,  $J = 7.1$  Hz), 1.60 (s, 3H), 1.67 (s, 3H), 3.48 (d, 1H,  $J = 2.7$  Hz), 4.13–4.23 (m, 4H), 5.72 (d, 1H,  $J = 5.7$  Hz), 6.47 (d, 1H,  $J = 5.7$  Hz), 6.53 (d, 1H,  $J = 2.7$  Hz);  $^{13}\text{C}$  NMR (  $\text{CDCl}_3$ )  $\delta$  13.9, 19.7, 23.9, 49.4, 60.3, 60.8, 83.8, 84.9, 131.2, 133.9, 140.7, 143.3, 165.4, 168.7; Anal. Calcd for  $\text{C}_{15}\text{H}_{20}\text{O}_5$ : C, 64.27; H, 7.19. Found: C, 64.41; H, 7.20.

#### 6.1.1.7. 2,3-Dicarbomethoxy-6-phenyl-4,7-dihydro-1H-azepine (176)

To a solution of 2-phenyl-2-vinylaziridine (0.44 g, 3 mmol) in methylene chloride (10 mL) was added dimethyl acetylenedicarboxylate (0.4 g) at  $0^\circ$ . Removal of the solvent led to

2,3-dicarbomethoxy-6-phenyl-4,7-dihydro-1H-azepine (95%, mp  $122\text{--}123^\circ$ ): IR (neat) 3300, 1730  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (  $\text{CDCl}_3$ )  $\delta$  3.46 (d, 2H,  $J = 7$  Hz), 3.72 (s, 3H), 3.85 (s, 3H), 4.4 (d, 2H), 4.75 (broad s, 1H), (  $\text{D}_2\text{O}$  exchange: signal at 4.75 disappeared and signal at 4.44 collapsed to a singlet), 6.36 (t, 1H,  $J = 7$  Hz), 7.4 (s, 5H).

#### 6.1.1.8. 3,6-Dihydro-3,3,6,6-tetramethyl-2H-azepin-2-one (182)

A solution of *cis*-2,2-dimethyl-3-isobutenylcyclopropyl isocyanate (3.5 g, 21.2 mmol) in dry *o*-xylene (30 mL) was refluxed under a dry nitrogen atmosphere for 60 hours. After evaporation of *o*-xylene, the residue was distilled under a nitrogen stream to give 3,6-dihydro-3,3,6,6-tetramethyl-2H-azepin-2-one (2.1 g, 60%) as colorless oil (bp  $79^\circ/2$  torr).

#### 6.1.1.9. Eucarvone (24)

Freshly distilled carvone (200 g, 1.33 moles) was added to a solution of hydrogen bromide (296 g, 3.66 moles) in glacial acetic acid at  $6\text{--}11^\circ$ . The rate of addition was determined by the effectiveness of the cooling and stirring; with a good paddle-type stirrer and a cooling bath at  $-30^\circ$ , 15–30 minutes was required. The cooling bath was removed and stirring continued for 15 minutes. The resulting dark solution was poured into 2 L of water, the lower layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with water, then with saturated potassium bicarbonate solution until basic to litmus, and finally with water until neutral. The ether solution was dried roughly over sodium sulfate, then dropped into a well-stirred and cooled solution of 145 g of potassium hydroxide in 550 mL of methanol. After completion of the addition, the resulting stirred suspension was refluxed for 15 minutes and poured onto ice-sulfuric acid to precipitate the eucarvone. The yellow oil was separated and the aqueous layer was extracted with ether. The ether solution was washed with saturated potassium bicarbonate solution and transferred to a steamdistillation apparatus along with

20 g of barium bicarbonate. After the ether had distilled, 9 L of distillate was collected, saturated with salt, and extracted with ether. The combined extracts were dried over sodium sulfate, concentrated in vacuo to a yellow oil, and fractionated in a spinning band column of approximately 25 plates to yield a total of 146.5 g (73%) of eucarvone (bp 82.5–84°/8 torr;  $n_D^{(21)} = 1.5080$ ).

## 7. Tabular Survey

The tables are organized according to the type of rearrangement and its product. In many cases the requisite divinylcyclopropane or its analog is generated from suitable precursors under the conditions of the rearrangement. The starting material is shown along with the intermediate in brackets, and the system is listed according to the carbon number of the reactive intermediate. Table I lists only thermal rearrangements of divinylcyclopropanes leading to simple cycloheptadienes, whereas the rearrangements resulting in the formation of products that contain more than one ring are found in Table II. Photochemical rearrangements are listed in Table III, and those occurring under transition-metal catalysis are found in Table IV. In some cases the rearrangement takes place in a reaction medium containing transition metals, but these may not be directly involved in the mechanism of product formation. For clarity such rearrangements are also listed in Table IV. Tables V–VII contain compilations of Cope-type rearrangements of divinylloxiranes, divinylaziridines, and divinylthiiranes, respectively. Finally, Table VIII lists a few examples of Cope-type rearrangements of systems containing other heteroatoms in the reacting matrix.

In those cases where multiple references exist for a given compound, only those that deal with the actual preparation are given. References to rate studies or additional references to preparation are found in the text. The following abbreviations are used in the tables:

Bn	benzyl
Bz	benzoyl
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
HMDS	hexamethyldisilazane
HMPA	hexamethylphosphoric triamide
LDA	lithium diisopropylamide
NBS	<i>N</i> -bromosuccinimide
rt	room temperature
TBS	<i>tert</i> -butyldimethylsilyl
TFA	trifluoroacetyl
THF	tetrahydrofuran
THP	tetrahydropyranyl
TMS	trimethylsilyl
Ts	<i>p</i> -toluenesulfonyl

(-) no yield given

**Table I. Thermal Rearrangements of Divinylcyclopropanes to Cycloheptadienes**

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**Table II. Thermal Rearrangements of Divinylcyclopropanes to Annulated Systems**

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**Table III. Photochemical Rearrangements of Divinylcyclopropanes**

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**Table IV. Transition-Metal-Catalyzed Rearrangements of Divinylcyclopropanes**

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**Table V. Rearrangements of Divinyloxiranes**

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**Table VI. Rearrangements of Divinylaziridines**

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**Table VII. Rearrangements of Divinylthiiranes**

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**Table VIII. Rearrangements of Miscellaneous Systems**

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TABLE I. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO CYCLOHEPTADIENES

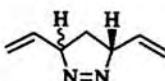
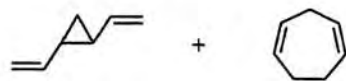



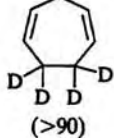




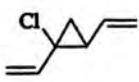
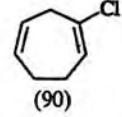
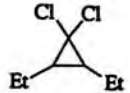
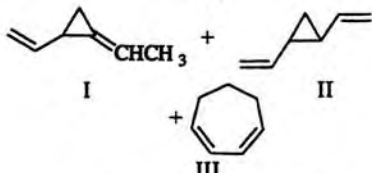
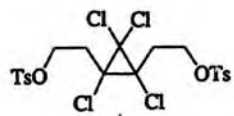
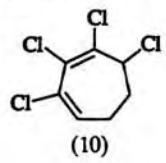
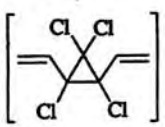

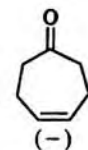
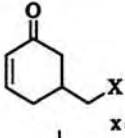
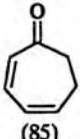
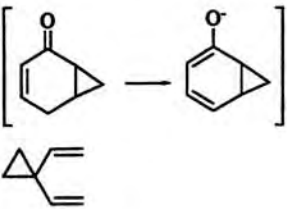
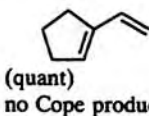
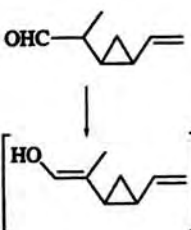
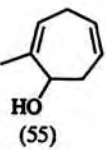
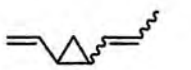
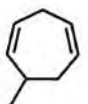
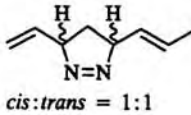
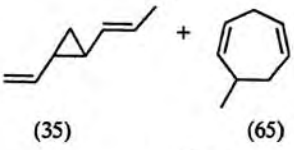
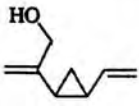
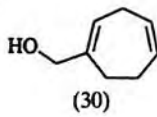


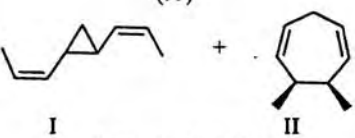
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>7</sub> 	Heat		58
<i>cis</i> + <i>trans</i>	Heat	(53) (47)	58
<i>cis</i>	Heat	(38) (62)	57
<i>trans</i>	Heat	(37) (63)	57
<i>cis</i> + <i>trans</i>	45°	(38.1) (61.5)	187
<i>cis</i> + <i>trans</i>	75°	(36.6) (63.0)	187
<i>cis</i> + <i>trans</i>	100°	(32.4) (67.0)	187
	-20 to 20° in NMR probe		39, 40, 59
44 	-40°		27, 34
	80°	(-)	3
	-10°		188
	160° in NMR probe	(>90)	39, 40, 59
	190°		27, 34
	170-180°		3
		(-)	2, 3, 7
	160-190°		82
	<i>t</i> -BuOK, DMSO, 25°, 2.3 h		42, 43
	Pentane, 100°, 44 h	(52) I:II:III = 7:1:3 (53) I:II:III = 4:1:5	
	<i>t</i> -BuOK, THF, -50°, 1 h; -50° to rt, 2 h		84
			
	Thermolysis or base		189
		(-)	



TABLE I. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO CYCLOHEPTADIENES (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs
 <p>X = Br, OTs</p>	NaOH, H <sub>2</sub> O, rt	 <p>(85)</p>	19-21
	238-288° 4-12 torr, gas phase	 <p>(quant) no Cope product</p>	190, 191
<p>C<sub>4</sub></p> 	180°, 12 h	 <p>(55)</p>	189
			59
<p><i>cis</i> (E) <i>cis</i> (Z) <i>trans</i> (E) <i>trans</i> (Z)</p>  <p><i>cis:trans</i> = 1:1</p>	-10 to 30° in NMR probe 50-98° in NMR probe 160° in NMR probe 160° in NMR probe 30-60°	<p>(-) (-) (-) (-)</p>  <p>(35) + (65)</p>	59, 126
	180°, 12 h	 <p>(30)</p>	189
<p>C<sub>5</sub></p> 			59
<p><i>cis</i> (E,E) <i>cis</i> (Z,Z)</p>	-10 to 30° in NMR probe 50-98° in NMR probe	<p>(-)</p> <p><i>cis-trans</i> isomerization, no Cope product</p>	59 59
<p><i>trans</i> (E,E)</p>	160° in NMR probe 178°, 4.2 h sealed tube	<p>(-) (99)</p>	59 44, 45
<p><i>trans</i> (Z,Z)</p>	179°, 4.2 h, sealed tube	 <p>I + II</p> <p>I:II = 1.21:1.76</p>	44

46

C<sub>4</sub>

47

C<sub>5</sub>

TABLE I. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO CYCLOHEPTADIENES (*Continued*)

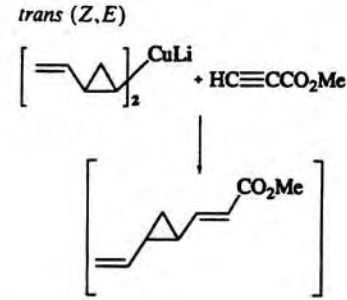
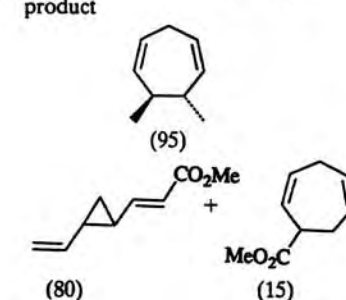
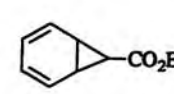
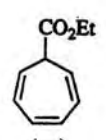
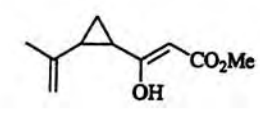
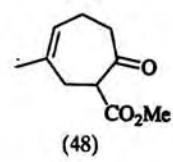
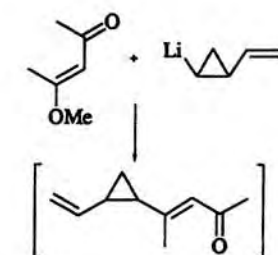
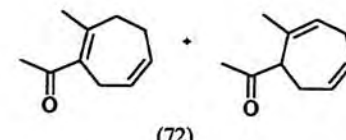
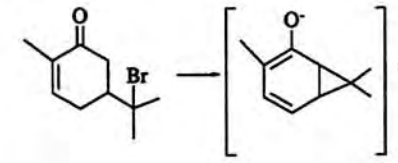
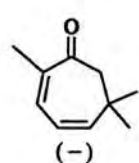
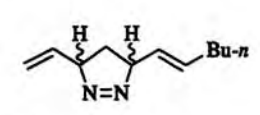
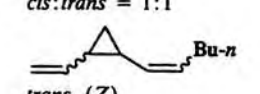
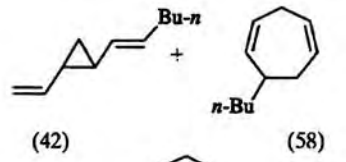

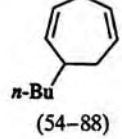
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	160° in NMR probe	<i>cis-trans</i> isomerization, no Cope product	59
<i>trans</i> ( <i>Z,E</i> ) 	178°, 4.2 h, sealed tube -78°	 (80) + (95)	44, 45
	150-170°	 (-)	81
	C <sub>6</sub> H <sub>6</sub> , 240°, 20 h 1. TMSCl, Et <sub>3</sub> N, Et <sub>2</sub> O, rt 2. C <sub>6</sub> H <sub>6</sub> , 210°, 16 h 3. KF, MeOH, rt	 (48) (88)	85 85
	1. -78°, THF, H <sub>3</sub> O <sup>+</sup> 2. heat	 (72)	86
	NaOH, MeOH, 0°	 (-)	1, 17-19, 21, 24, 76-78
C <sub>11</sub>  <i>cis:trans</i> = 1:1  <i>trans</i> , ( <i>Z</i> )	30-60°	 (42) + (58)	126
 <i>trans</i> , ( <i>E</i> ) Dictyoptere A	130-165° 2.3-22 h	 (54-88)	62
	129-165° 2-26 h (for racemate)	(56-82)	62, 124-127, 129, 130, 132, 133

TABLE I. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO CYCLOHEPTADIENES (Continued)

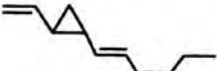
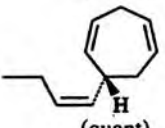

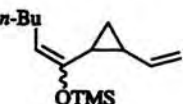
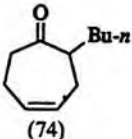
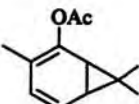
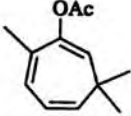

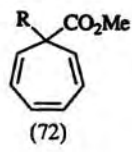
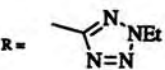

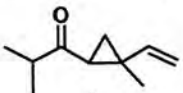
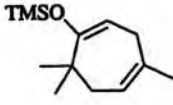
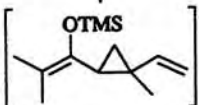
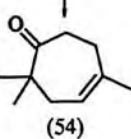
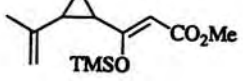
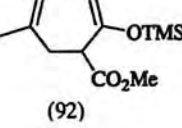
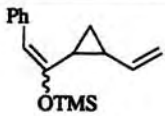
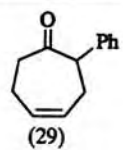
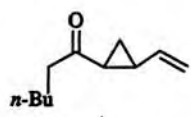

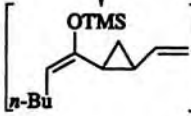
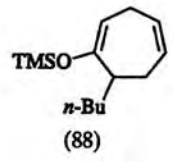
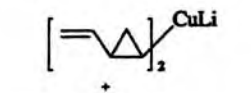
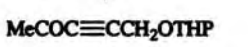
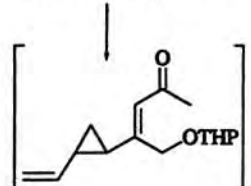
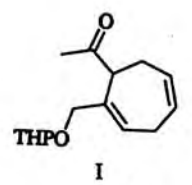
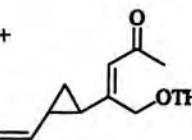
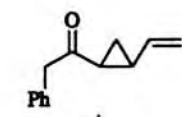

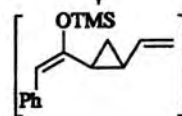
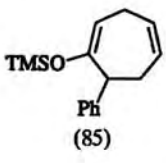
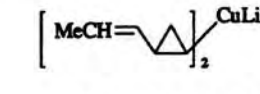
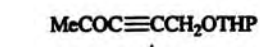
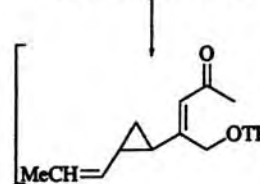
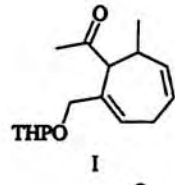
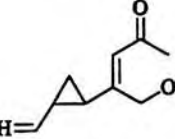
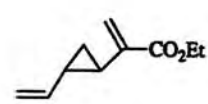

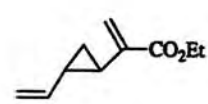
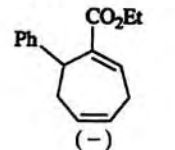
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	170° [for (-) isomer]	(S-), 16% opt. pure Dictyoptereene C'	123, 132
<i>cis</i> , (Z)	75°, 5 h, sealed tube	(R-), (quant) Dictyoptereene C	123 132, 133
	66–78°, 1.2–4.5 h 15°	(-) (66–80)	62 123, 133
Dictyoptereene B	70°	 (quant) Dictyoptereene D'	123, 128 129, 131
<i>cis</i> isomer Dictyoptereene D	20°	(30) (racemate = sirenin)	131
	180°, 3 h	(quant)	129
	100–110°, 30 min; H <sub>3</sub> O <sup>+</sup>	<i>cis-trans</i> isomerization <i>cis:trans</i> = 1:3 no Cope product	182
		 (74)	87, 88
C <sub>12</sub>			
	rt		25
	C <sub>6</sub> H <sub>6</sub> , 70°	 (72)	192
R = 			
C <sub>13</sub>			
	170°, 3 h	<i>cis-trans</i> isomerization <i>cis:trans</i> = 1:2.6 no Cope product	182
	LDA, TMSCI 165–175°		86
		 (54)	
<i>cis + trans</i>			
	210°, C <sub>6</sub> H <sub>6</sub> , 16 h	 (92)	85

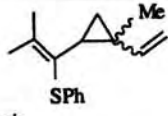
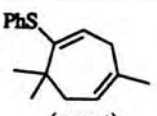
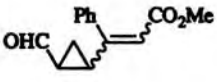
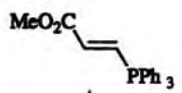
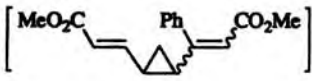
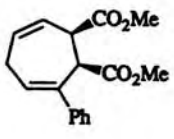
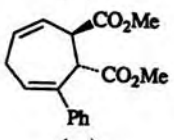
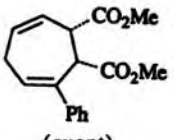
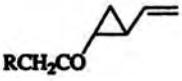
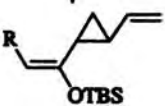
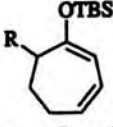
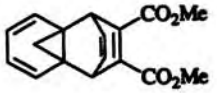
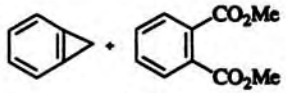
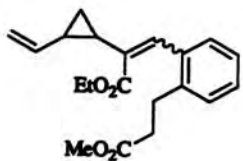
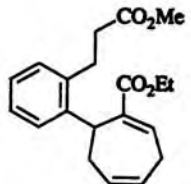
TABLE I. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO CYCLOHEPTADIENES (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	100–110°, 30 min H <sub>3</sub> O <sup>+</sup>	 (29)	88
C <sub>14</sub>   	LDA, THF, -78°; TMSCl, Et <sub>3</sub> N, -78° to rt; 100–110°, 30 min, neat	 (88)	87
C <sub>15</sub>  + MeCOC≡CCH <sub>2</sub> OTHP  	-78°	 I +  II (90) I:II = 1:8	91
C <sub>16</sub>   	LDA, THF, -78°; TMSCl, Et <sub>3</sub> N, -78° to rt, 1 h; 100–110°, 30 min, neat	 (85)	87
 + MeCOC≡CCH <sub>2</sub> OTHP  	-78°	 I +  II (90) I:II = 1:8	91
  	Xylene, reflux, 24 h	 (90) (-)	120

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TABLE I. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO CYCLOHEPTADIENES (*Continued*)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
 <i>cis</i> <i>trans</i>	25° 160°, sealed tube	 (quant) (70)	193
C <sub>17</sub>  +   <i>cis</i> , (Z)	THF, reflux	 (76)	89
<i>cis</i> , (E)	THF, reflux	 (-) (quant)	89
<i>trans</i> , (Z)	200°, 5 h	(quant)	90
<i>trans</i> , (E)	200°, 5 h	 (quant)	90
  OTBS	LDA, THF, -78°; TBSCl, HMPA, -78° to rt, 2-3 h; 230°, 30-60 min	 R = <i>n</i> -Bu (85) R = <i>t</i> -Bu (74)	87
 CO <sub>2</sub> Me CO <sub>2</sub> Me	400°, 1 torr	 (45) no Cope product	194
C <sub>31</sub>  EtO <sub>2</sub> C MeO <sub>2</sub> C	Xylene, reflux, 24 h	 (93)	120

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TABLE I. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO CYCLOHEPTADIENES (Continued)

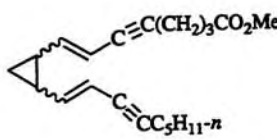
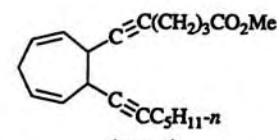
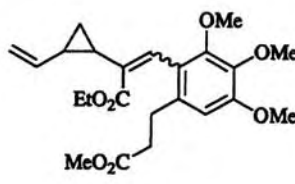
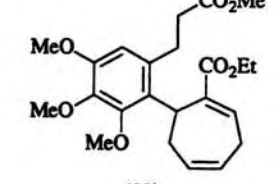
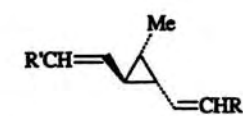
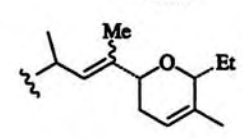
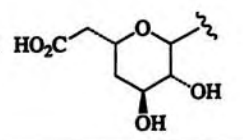
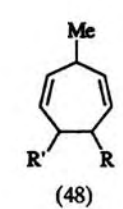
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs
<p>C<sub>21</sub></p> 	200°, C <sub>6</sub> H <sub>6</sub> , sealed tube	 (quant) <i>cis:trans</i> = 4:1	134
<p>C<sub>23</sub></p> 	Xylene, reflux, 24 h	 (92)	120
<p>C<sub>28</sub></p>  <p>R = </p> <p>R' = </p>	Diphenyl ether, 240°, 10 min	 (48)	135

TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS

	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs
C <sub>4</sub>		THF	no Cope product	114
		Thermolysis 25°: t <sub>1/2</sub> = 1 d 40°: t <sub>1/2</sub> = 25 min 53°: t <sub>1/2</sub> = 6 min  60°, THF, ether		48, 49 187, 195  195
57		NMR (degenerate rearrangement)		27
C <sub>5</sub>		rt		196
		30-60°		56
		Pyridine, piperidine, 100°, 2h		197
	R = CO <sub>2</sub> H			

TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (Continued)

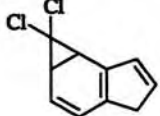
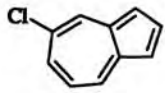
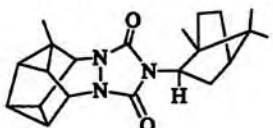
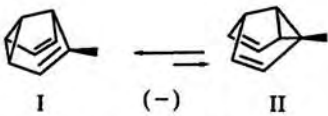
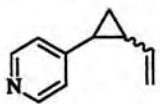
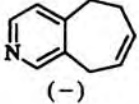


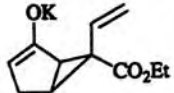
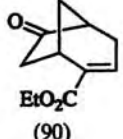
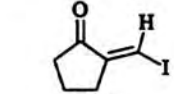
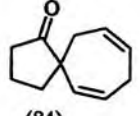
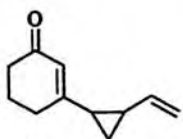
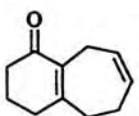
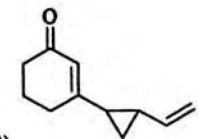
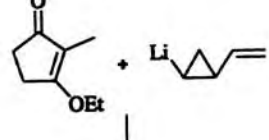
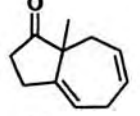
	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
58		Indene, Na, CHCl <sub>3</sub>	 (-)	2, 26
		1. NaOH 2. MnO <sub>2</sub>	 I (-) II I:II = 85:15 at rt	198
		Xylene, 142°, 18 h	 (-)	199
		rt		30, 31
59		rt	 EtO <sub>2</sub> C (90)	110
		Heat	 (84) (64)	88 96, 98
		THF, heat	 +  (90)	92, 96
		-78°, THF, H <sub>3</sub> O <sup>+</sup> , heat	 (72)	86, 96



TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (*Continued*)

	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs
		-78°, THF, H <sub>3</sub> O <sup>+</sup> , heat	(77)	86, 96
09		C <sub>6</sub> H <sub>6</sub> , <i>t</i> -C <sub>3</sub> H <sub>7</sub> ONa, reflux, 2 h	(18)	18
		NaOH, EtOH, 100°, 5 h	(21)	21
		NaOH, EtOH, 100, 5 h	(21)	21
		C <sub>6</sub> H <sub>5</sub> OK, EtOH, 121°, 20 h	(45)	55
		C <sub>6</sub> H <sub>5</sub> OK, EtOH, 121°, 20 h	(45)	55
		-78°, THF; H <sub>3</sub> O <sup>+</sup> , heat	(74)	86, 96
		Xylene, 140°, 10 h	(92)	97
		Xylene, 140°, 10 h	(82)	95
61		THF, -78°, 1 h; -20°, 1 h; 180°, 15 min	(77)	98
		142°, 18 h	(43)	199

TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (*Continued*)

	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
		THF, reflux, 3 h		197
		140°, 2 h		49
C <sub>13</sub>		80°, CHCl <sub>3</sub> , 4 h		199
		LDA, -78°		115
		-78°, THF; H <sub>3</sub> O <sup>+</sup> , heat		86
		LDA, THF, -78°; TMSCl, Et <sub>3</sub> N, -78° to rt, 1 h; 100-110°, 30 min, neat		87, 88
		100-110°, 30 min; H <sub>3</sub> O <sup>+</sup>		87, 88
		Hexane, reflux, 4 h		95, 96

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TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (Continued)

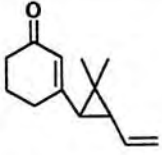
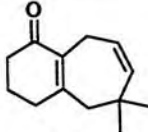
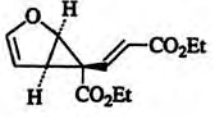
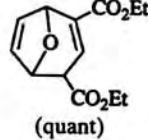
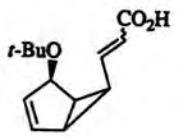
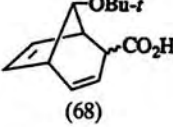
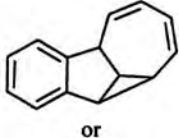
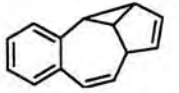
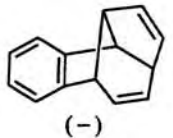
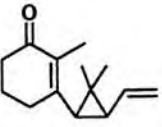
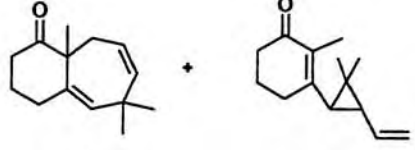
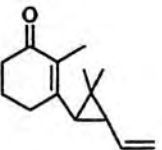
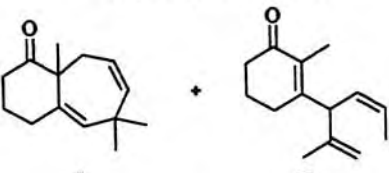
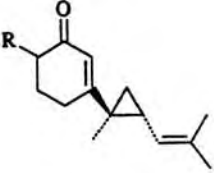
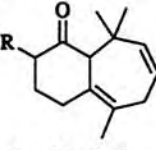
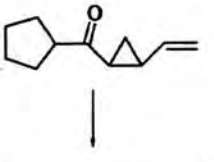
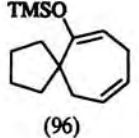
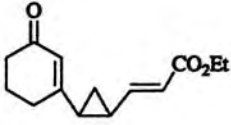
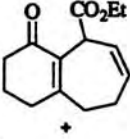
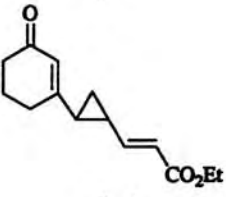
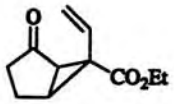
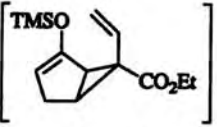
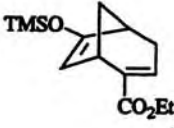
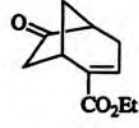
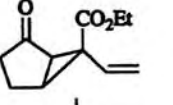
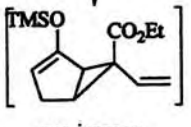
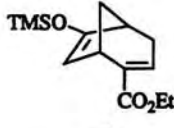
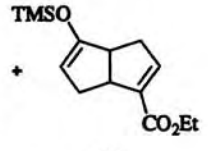
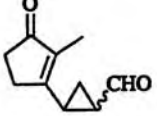
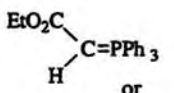
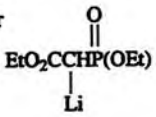
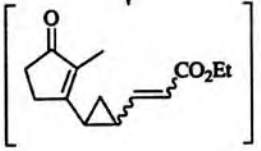
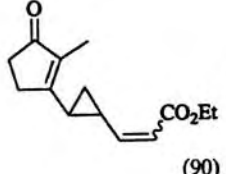
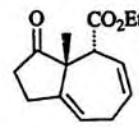
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	<i>o</i> -Dichlorobenzene, sealed tube, 220°, 8 h	 (59)	95
	40°	 (quant)	72, 106
	Pyridine, piperidine, 100°, 2 h	 (68)	197
 or 	330°	 (-)	200
	A. <i>o</i> -Dichlorobenzene, reflux, 3 h B. <i>o</i> -Xylene, reflux, 48 h	 I + II	95, 96
		A. (91) I:II = 0.8:1.0 B. (84) I:II = 2.7:1.0	
	<i>o</i> -Dichlorobenzene; sealed tube, 220°, 12 h	 I + II	95
		(87) I:II = 1:4	
	Xylene, reflux, 3 h; LDA, THF, HMPA, -78°; CH <sub>3</sub> I	 R = H (-) R = Me (90)	201
	LDA, THF, -78°; TMSCl, Et <sub>3</sub> N, -78° to rt, 1 h; 100-110°, 30 min	 (96)	87, 88

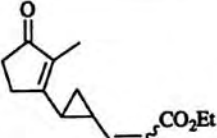
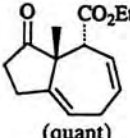
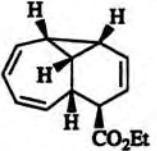
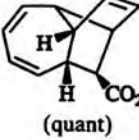
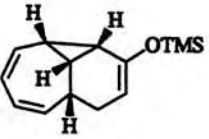
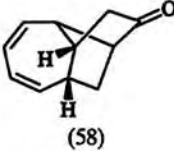
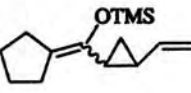
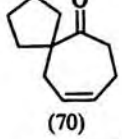
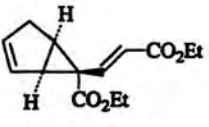
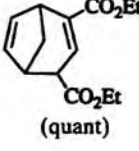
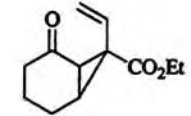
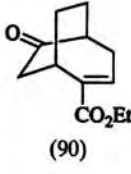
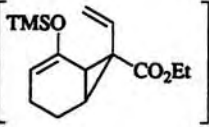
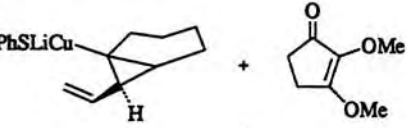
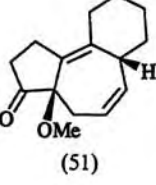
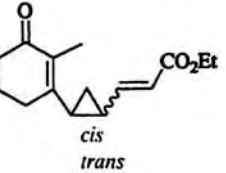
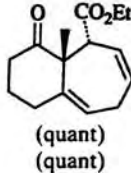
TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	THF, heat	 +  (-)	92
 ↓  <i>endo isomer</i>	TMSI, HMDS, -20° to rt	 —  (quant)	108, 109
 ↓  <i>exo isomer</i>	1. TMSI, HMDS 2. Flash vacuum pyrolysis, 550°	 +  I                      II (90) I:II = 58:42	108, 109
 +  or  ↓ 	rt	 (90) + 	94

99

67

TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	100–140°; CHCl <sub>3</sub> , sealed tube	 (quant)	94
	CCl <sub>4</sub> , 55°, 88 h (in NMR tube)	 (quant)	202
	THF, reflux, 18 h; MeOH, 45°, 2 h	 (58)	202
	100–110°, 30 min, H <sub>3</sub> O <sup>+</sup>	 (70)	87, 88
	40°	 (quant)	106
	TMSI, HMDS, –20° to rt; H <sub>3</sub> O <sup>+</sup>	 (90)	110
			
	0.01 N H <sub>2</sub> SO <sub>4</sub> , acetone (1:1), rt, 7 min	 (51)	99
	20° Xylene, reflux	 (quant) (quant)	97, 203 203

89

C<sub>15</sub>

69

TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (Continued)

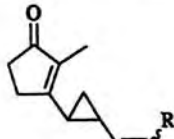
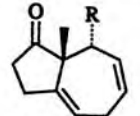
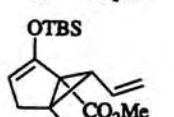

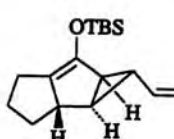
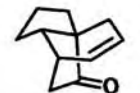
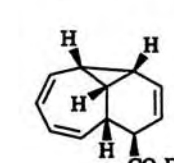
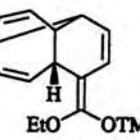
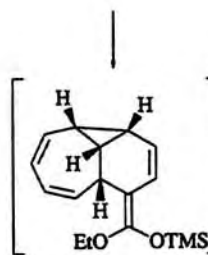
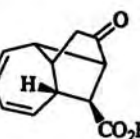
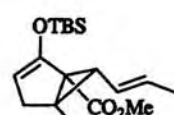
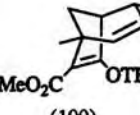
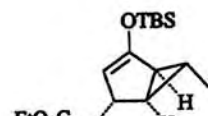
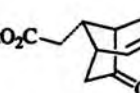
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.												
	$C_6H_6$ , $t-C_3H_7ONa$ , reflux, 3 h		18												
	100–110°, 30 min, $H_3O^+$		87, 88												
	130°	 (-)	97												
	Xylene; reflux, 2.5 h	 (quant)	100, 101												
	$C_6H_6$ , 2.5 h; 200°, sealed tube; 1 N HCl, THF, rt	 (81)	204												
	$Ph_3P=CHSPh$	 (65)	92												
 (15)	THF, rt														
	$R-CH=CH-PPh_3$ or $R-CH(OEt)P(OEt)_2$	 I	94												
 II	THF, rt														
		<table border="1"> <thead> <tr> <th>R</th> <th>I</th> <th>I + II</th> </tr> </thead> <tbody> <tr> <td>SPh</td> <td><i>cis:trans</i> = 1:1</td> <td>(67)</td> </tr> <tr> <td>SOPh</td> <td><i>cis</i></td> <td>(81)</td> </tr> <tr> <td>SO<sub>2</sub>Ph</td> <td><i>trans</i></td> <td>(80)</td> </tr> </tbody> </table>	R	I	I + II	SPh	<i>cis:trans</i> = 1:1	(67)	SOPh	<i>cis</i>	(81)	SO <sub>2</sub> Ph	<i>trans</i>	(80)	
R	I	I + II													
SPh	<i>cis:trans</i> = 1:1	(67)													
SOPh	<i>cis</i>	(81)													
SO <sub>2</sub> Ph	<i>trans</i>	(80)													

70

C<sub>16</sub>C<sub>17</sub>

71

TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
 <p>R = SPh R = SO<sub>2</sub>Ph</p>	CHCl <sub>3</sub> , 100–140°, sealed tube	 <p>R = SPh (quant) R = SO<sub>2</sub>Ph (quant)</p>	94
	Xylene, reflux, 2.5 h	 <p>(100)</p>	100, 101
	C <sub>6</sub> H <sub>6</sub> , sealed tube, 155°, 5 h; <i>n</i> -Bu <sub>4</sub> NF, THF, rt	 <p>(84)</p>	15
	LDA, THF, -78°, 45 min; TMSCl, -78°, 20 min; rt, 20 min; CCl <sub>4</sub> , 100°, 2 h; 70°, 15 h	 <p>(-)</p>	202
 <p>I</p>	CCl <sub>4</sub> , 18 h; THF:H <sub>2</sub> O = 2:1, 2 h, 25°	 <p>(40) + I (23)</p>	202
	Xylene, reflux, 2.5 h	 <p>(100)</p>	100, 101
	C <sub>6</sub> H <sub>6</sub> , 200°, 2.5 h, sealed tube; 1 N HCl, THF, rt	 <p>(81)</p>	204

72

73

C<sub>18</sub>

TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (Continued)

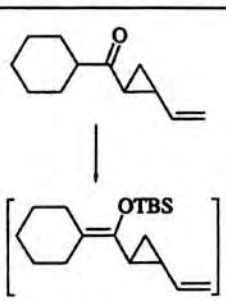
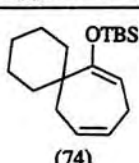
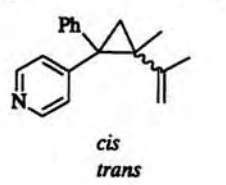
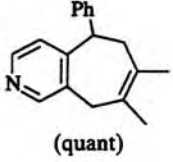
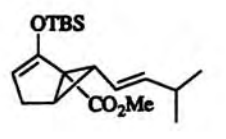
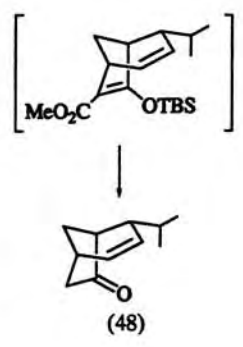
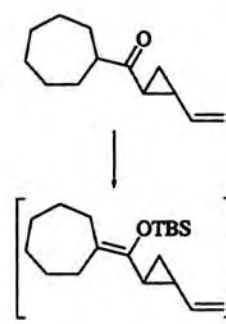
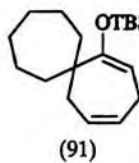
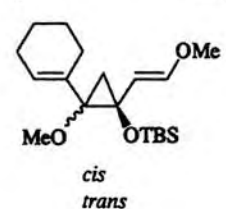
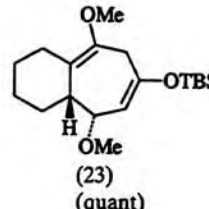
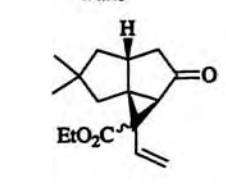
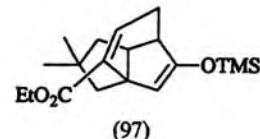
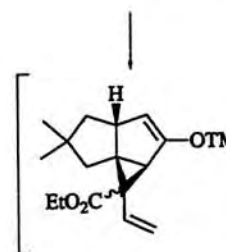
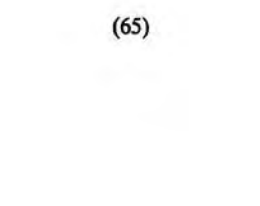
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	<p>LDA, THF, <math>-78^{\circ}</math>,                      TBSCl, HMPA; <math>-78^{\circ}</math>                      to rt, 2-3 h; <math>230^{\circ}</math>, 30-                      60 min, neat</p>	 (74)	87
<p>74</p>  <p><i>cis</i> <i>trans</i></p>	<p>rt                      CH<sub>3</sub>CN, <math>81^{\circ}</math>, 6 h</p>	 (quant)	199
<p>C<sub>19</sub></p> 	<p>C<sub>6</sub>H<sub>6</sub>, <math>200^{\circ}</math>, 2.25 h, sealed                      tube; <i>n</i>-Bu<sub>4</sub>NF, THF,                      rt; 1 N HCl, THF,                      reflux</p>	 (48)	204
	<p>LDA, THF, <math>-78^{\circ}</math>;                      TBSCl, HMPA, <math>-78^{\circ}</math>                      to rt, 2-3 h; <math>230^{\circ}</math>, 30-                      60 min, neat</p>	 (91)	87
<p>75</p>  <p><i>cis</i> <i>trans</i></p>	<p><math>25^{\circ}</math>  <math>90^{\circ}</math>, 3 h</p>	 (23) (quant)	118
	<p>(<i>endo</i>) TMSI, HMDS,  <math>-20^{\circ}</math> to rt</p>	 (97)	108, 109
	<p>(<i>exo</i>) TMSI, HMDS, <math>550^{\circ}</math></p>	 (65)	



TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (Continued)

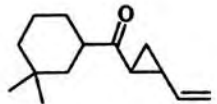
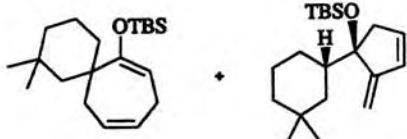
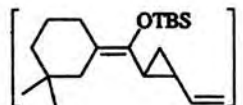
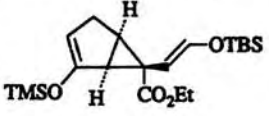
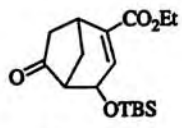
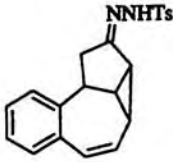
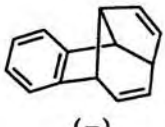
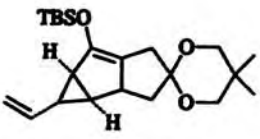

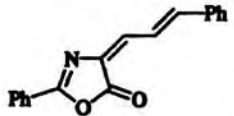
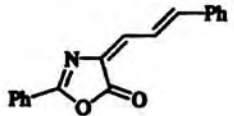
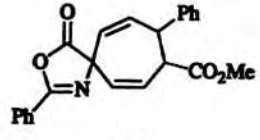
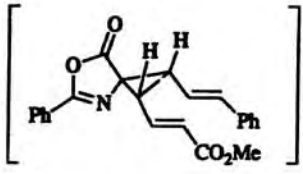
	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>20</sub>		LDA, THF, -78°; TBSCl, HMPA; -78° to rt, 2-3 h; 230°, 30- 60 min		87
76			(-)	
		-78° to rt, H <sub>3</sub> O <sup>+</sup>		110, 112
			(quant)	
C <sub>21</sub>		0°		200
			(-)	
C <sub>22</sub>		C <sub>6</sub> H <sub>6</sub> , 170-175°, 5 h, sealed tube; <i>n</i> -Bu <sub>4</sub> NF, THF		138
			(-)	
C <sub>23</sub>				
77				
	+ Me <sub>2</sub> S=CH-CH=CHCO <sub>2</sub> Me	THF, 3 h		205
			(-)	
				

TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (*Continued*)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
<p>78</p>	EtOK, 20°		119
<p>C<sub>12</sub></p>	<p>(endo) TMSI, HMDS, -20° to rt (exo) TMSI, HMDS, 550°</p>	<p>(97)</p> <p>(76)</p>	108, 109
<p>79</p> <p>C<sub>17</sub></p>	Et <sub>3</sub> N, C <sub>6</sub> H <sub>6</sub> , reflux	<p>(85)</p> <p>+</p> <p>(trace)</p>	137

TABLE II. THERMAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES TO ANNULATED SYSTEMS (*Continued*)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.								
<p>C<sub>21</sub></p> <p> <chem>Me2S=CHC(Ph)=CHCO2Me</chem> </p>	<p>A. THF, 3 h                      B. THF, 42 h                      C. C<sub>6</sub>H<sub>6</sub>, reflux</p>	<p>  I   II                 </p> <table border="0"> <tr> <td>I</td> <td>II</td> </tr> <tr> <td>A. (4)</td> <td>(9)</td> </tr> <tr> <td>B. (-)</td> <td>(32)</td> </tr> <tr> <td>C. (-)</td> <td>(50)</td> </tr> </table>	I	II	A. (4)	(9)	B. (-)	(32)	C. (-)	(50)	205
I	II										
A. (4)	(9)										
B. (-)	(32)										
C. (-)	(50)										
<p>C<sub>30</sub></p>	<p>A. TMSCl, Et<sub>3</sub>N, DMF, 50°                      B. NaH, TMSCl, THF</p>	<table border="0"> <tr> <td>I</td> <td>II</td> </tr> <tr> <td>A. (trace)</td> <td>(87)</td> </tr> <tr> <td>B. (85)</td> <td>(trace)</td> </tr> </table> <p>  I   II                 </p>	I	II	A. (trace)	(87)	B. (85)	(trace)	137		
I	II										
A. (trace)	(87)										
B. (85)	(trace)										

TABLE III. PHOTOCHEMICAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES






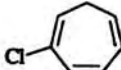
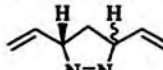


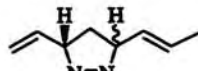
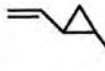
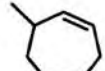

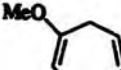

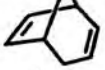
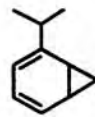
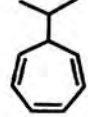
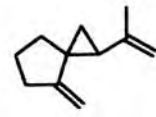
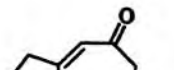
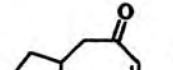
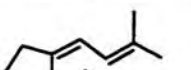
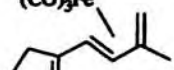
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
<p>C<sub>7</sub></p>  <p>from benzene solution of CH<sub>2</sub>N<sub>2</sub></p>	<p><i>hν</i></p>	 (-)	7, 9
	<p>313 nm 240-390 nm 300-390 nm</p>		206
		 (-)	
 <p>from chlorobenzene solution of CH<sub>2</sub>N<sub>2</sub></p>	<p><i>hν</i>, acetone, 3 d</p>	 (30)	9
 cis + trans trans	<p><i>hν</i></p>	 +  (49) (49) (42) (56) (56) (42)	187 57 57
<p>C<sub>8</sub></p>  cis:trans = 1:1	<p><i>hν</i>, <i>n</i>-pentane, 0°, Pyrex</p>	 +  (60) (40)	126
 <p>from anisole solution of CH<sub>2</sub>N<sub>2</sub></p>	<p><i>hν</i>, acetone, 3 d</p>	 (71)	9
	<p><i>hν</i>, 0°, rt</p>	 (-)	187
<p>C<sub>10</sub></p>  <p>from dioxane solution of C<sub>6</sub>H<sub>5</sub>C<sub>3</sub>H<sub>7</sub>-<i>i</i> and CH<sub>2</sub>N<sub>2</sub></p>	<p><i>hν</i></p>	 (16)	8
<p>C<sub>11</sub></p> 	<p><i>hν</i>, Fe(CO)<sub>5</sub>, petroleum ether, 4 h</p>	 +  (15) (15)  +  (36) (24)	69

TABLE III. PHOTOCHEMICAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES (Continued)

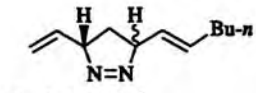
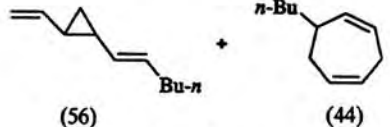
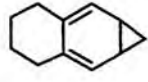
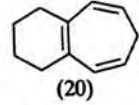
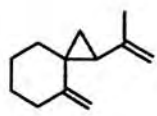
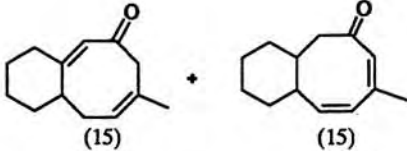
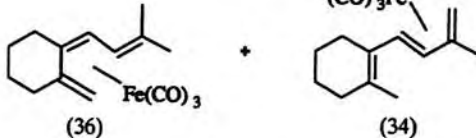
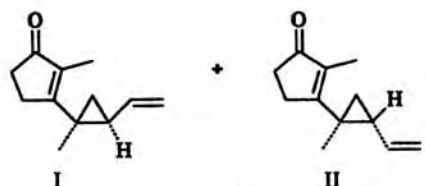
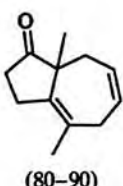

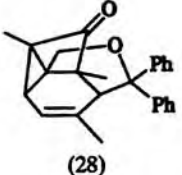

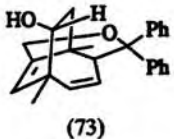
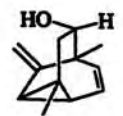
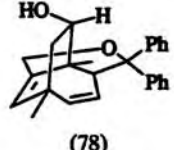

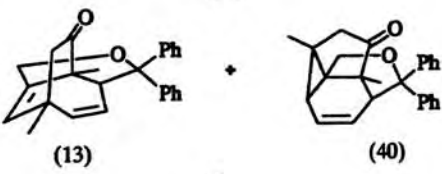

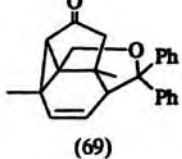
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs
 <i>cis + trans 1:1</i>	$h\nu$ , <i>n</i> -pentane, 0°, Pyrex	 (56) + (44)	126
 (20)	$h\nu$	 (20)	8
 C <sub>12</sub>	$h\nu$ , Fe(CO) <sub>5</sub> , petroleum ether, 4 h	 (15) + (15)	69
		 (36) + (34)	
 I + II I:II = 1:4	$h\nu$ , 98°	 (80-90)	63
	$h\nu$ , 12 h, Ph <sub>2</sub> CO	 (28)	65
	$h\nu$ , 3 h, Ph <sub>2</sub> CO	 (73)	65
	$h\nu$ , 8 h, Ph <sub>2</sub> CO	 (78)	65
	$h\nu$ , 3.5 h, Ph <sub>2</sub> CO	 (13) + (40)	65
	$h\nu$ , 8 h, Ph <sub>2</sub> CO	 (69)	65

TABLE III. PHOTOCHEMICAL REARRANGEMENTS OF DIVINYLCYCLOPROPANES (Continued)

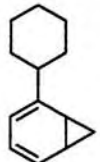
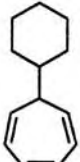
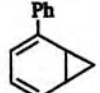

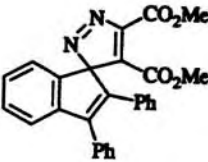
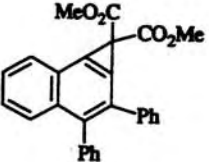
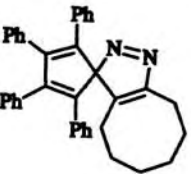
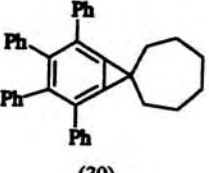
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
<p>C<sub>13</sub></p>  <p>from dioxane solution of cyclohexylbenzene and CH<sub>2</sub>N<sub>2</sub></p>	<i>hν</i>	 <p>(13)</p>	8
 <p>from dioxane solution of biphenyl and CH<sub>2</sub>N<sub>2</sub></p>	<i>hν</i>	 <p>(9)</p>	8
<p>C<sub>27</sub></p> 	<i>hν</i>	 <p>(30)</p>	207
<p>C<sub>37</sub></p> 	<i>hν</i>	 <p>(30)</p>	208

TABLE IV. TRANSITION-METAL-CATALYZED REARRANGEMENTS OF DIVINYLCYCLOPROPANES

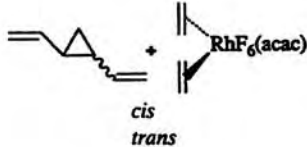

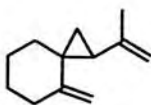
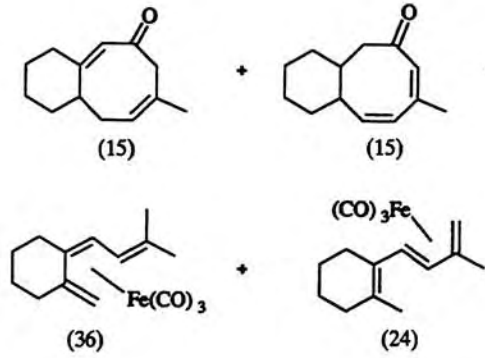
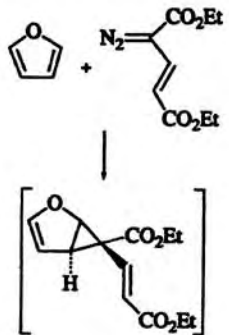
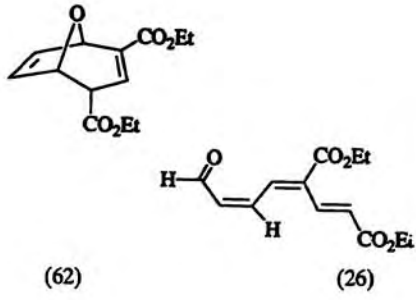
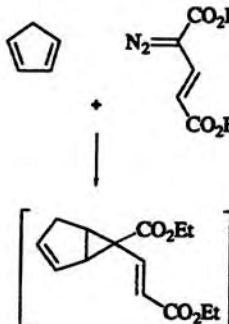
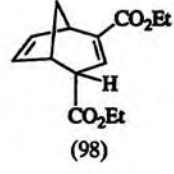
	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs
88	<p>C<sub>7</sub></p> 	<p>rt rt</p>	 (-) (-)	<p>70, 71 70</p>
	<p>C<sub>12</sub></p> 	<p><i>hν</i>, Fe(CO)<sub>5</sub>, petroleum ether, 4 h</p>		<p>69</p>
	<p>C<sub>13</sub></p> 	<p>Rh<sub>2</sub>(OAc)<sub>4</sub>; CH<sub>2</sub>Cl<sub>2</sub>, reflux, 10 min</p>		<p>72, 103</p>
68	<p>C<sub>14</sub></p> 	<p>Rh<sub>2</sub>(OAc)<sub>4</sub>; CH<sub>2</sub>Cl<sub>2</sub>, reflux, 10 min</p>		<p>102</p>

TABLE IV. TRANSITION-METAL-CATALYZED REARRANGEMENTS OF DIVINYLCYCLOPROPANES (*Continued*)

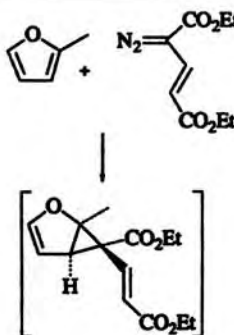
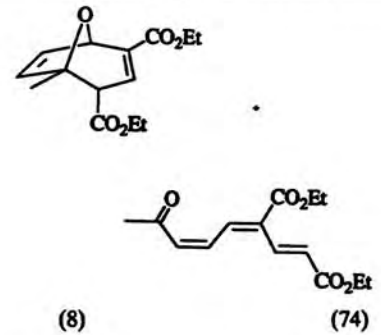
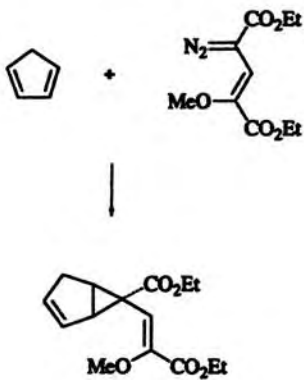
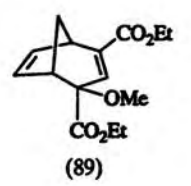
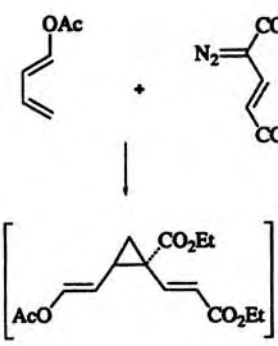
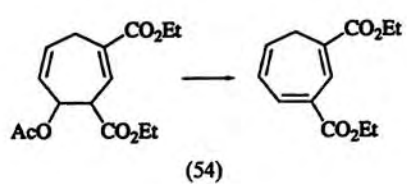
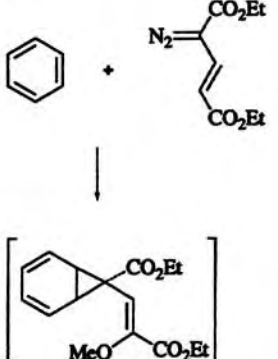
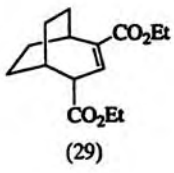
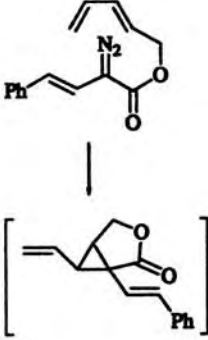
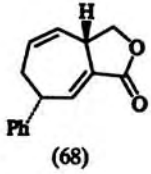
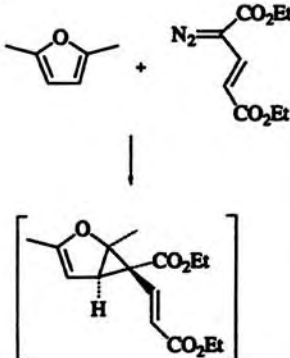
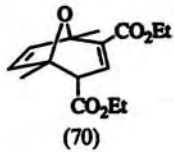
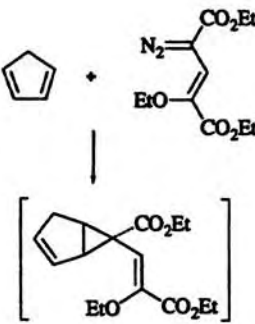
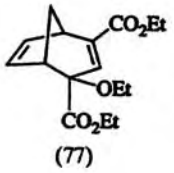
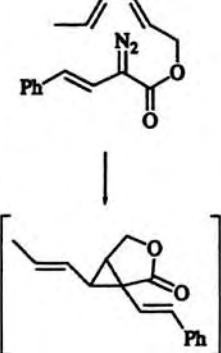
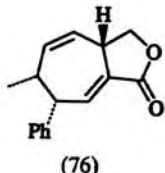
	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
06		$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min		72, 103
C <sub>15</sub>		$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min		102
		$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min		107
16		$\text{Rh}_2(\text{TFA})_4$ ; $\text{H}_2$ , Pd/C		107



TABLE IV. TRANSITION-METAL-CATALYZED REARRANGEMENTS OF DIVINYLCYCLOPROPANES (*Continued*)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min	 (68)	105
	$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min	 (70)	72, 103
<p><math>\text{C}_{10}</math></p> 	$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min	 (77)	102
	$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min	 (76)	105

92

$\text{C}_{10}$

93

TABLE IV. TRANSITION-METAL-CATALYZED REARRANGEMENTS OF DIVINYLCYCLOPROPANES (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
<p>94</p>	<p><math>\text{Rh}_2(\text{OAc})_4</math>; <math>\text{CH}_2\text{Cl}_2</math>, reflux, 10 min</p>	<p>(60)</p>	105
	<p><math>\text{Rh}_2(\text{OAc})_4</math>; <math>\text{CH}_2\text{Cl}_2</math>, reflux, 10 min</p>	<p>(68)</p>	105
<p>95</p>	<p><math>\text{Rh}_2(\text{OAc})_4</math>; <math>\text{CH}_2\text{Cl}_2</math>, reflux, 10 min</p>	<p>I</p> <p>II</p> <p>(54) I + II</p>	103
	<p><math>\text{Rh}_2(\text{OAc})_4</math>; <math>\text{CH}_2\text{Cl}_2</math>, reflux, 10 min</p>	<p>(5)</p>	105

TABLE IV. TRANSITION-METAL-CATALYZED REARRANGEMENTS OF DIVINYLCYCLOPROPANES (Continued)

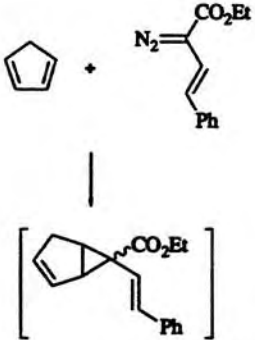
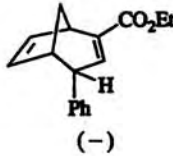
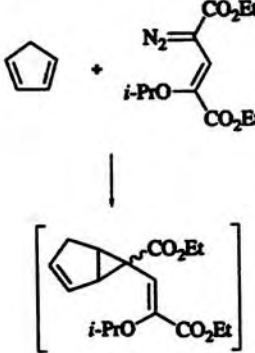
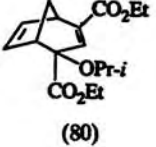
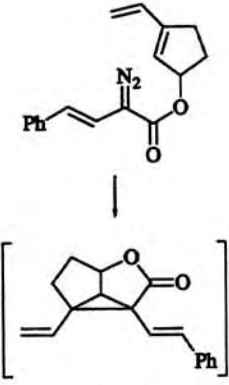
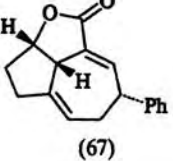
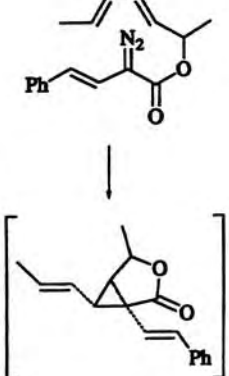
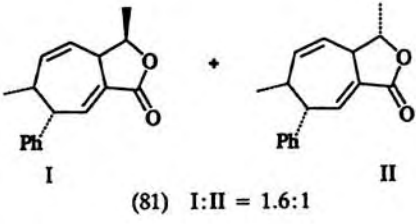
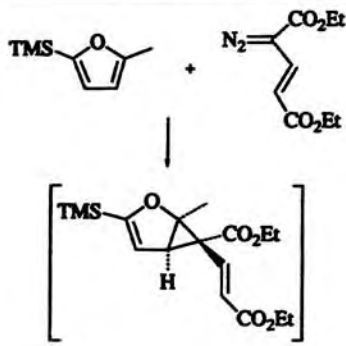
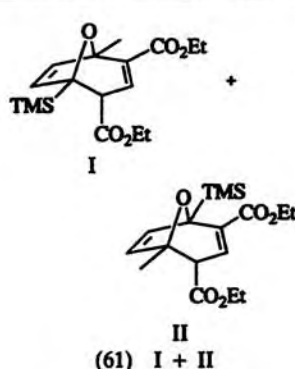
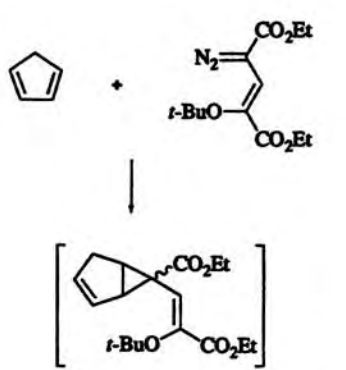
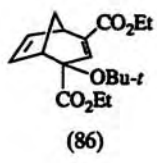
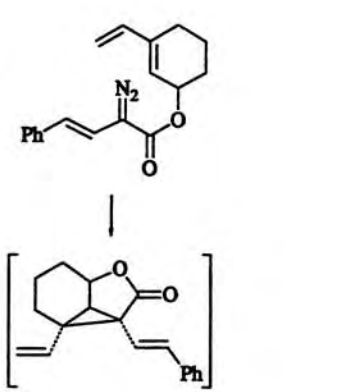
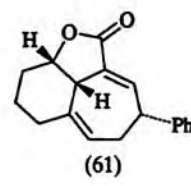
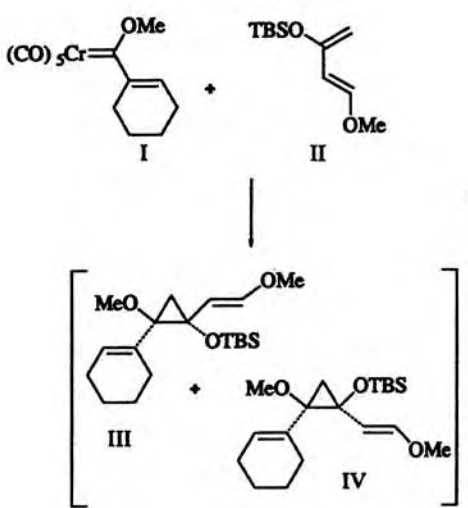
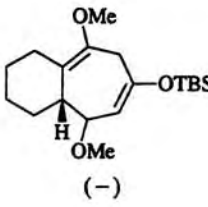
	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>17</sub>		Rh <sub>2</sub> (OAc) <sub>4</sub> ; CH <sub>2</sub> Cl <sub>2</sub> , reflux, 10 min		104
96		Rh <sub>2</sub> (OAc) <sub>4</sub> ; CH <sub>2</sub> Cl <sub>2</sub> , reflux, 10 min		102
		Rh <sub>2</sub> (OAc) <sub>4</sub> ; CH <sub>2</sub> Cl <sub>2</sub> , reflux, 10 min		104
97		Rh <sub>2</sub> (OAc) <sub>4</sub> ; CH <sub>2</sub> Cl <sub>2</sub> , reflux, 10 min		105

TABLE IV. TRANSITION-METAL-CATALYZED REARRANGEMENTS OF DIVINYLCYCLOPROPANES (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min	 (61) I + II	103
<p>C<sub>11</sub></p> 	$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min	 (86)	102
	$\text{Rh}_2(\text{OAc})_4$ ; $\text{CH}_2\text{Cl}_2$ , reflux, 10 min	 (61)	104
<p>C<sub>19</sub></p> 	I + II, 25°, 2 d, $\text{C}_6\text{H}_6$ ; (III, 40%) III, 90°, 3 h	 (-)	118

86

66

TABLE IV. TRANSITION-METAL-CATALYZED REARRANGEMENTS OF DIVINYLCYCLOPROPANES (*Continued*)

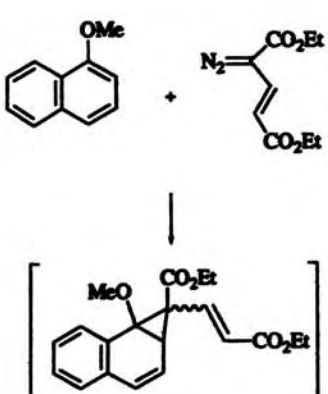
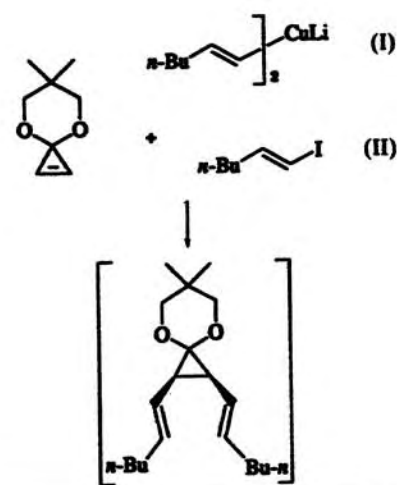
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
<p>C<sub>3</sub></p> 	<p>Rh<sub>2</sub>(OAc)<sub>4</sub>; CH<sub>2</sub>Cl<sub>2</sub>, reflux, 10 min</p>	<p>(41)</p>	107
	<p>I. THF, Et<sub>2</sub>O, -70° or II. Pd(Ph<sub>3</sub>P)<sub>4</sub> (cat.) -70° to rt</p>	<p>(67)</p>	117

TABLE V. REARRANGEMENTS OF DIVINYLOXIRANES

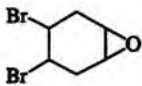
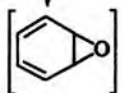
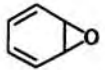

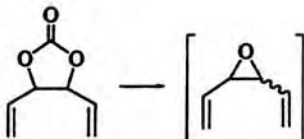







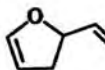

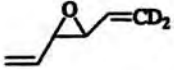
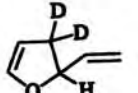
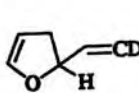
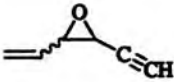

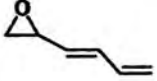

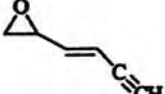
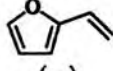
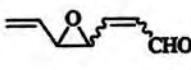
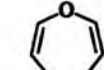
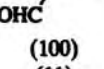
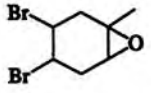
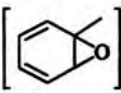
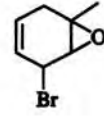


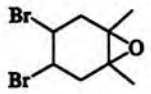

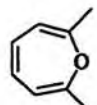
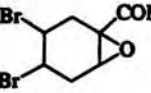
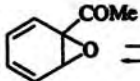
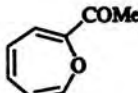
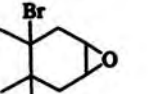
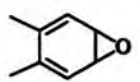
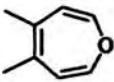

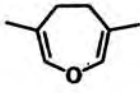
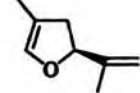

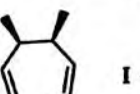
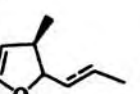
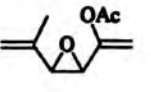
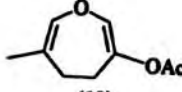
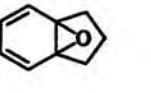
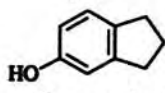
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
 	CH <sub>3</sub> ONa	 =  (80)	143, 144
	γ-Collidine	Phenol (0)	209
	LiCl, 200°	 +  (-)	141
 +  (64) (28)	Heat (steam bath), overnight	 +  (62) (38)	142
pure <i>cis</i> pure <i>trans</i>	CCl <sub>4</sub> , sealed tube, 98° Sealed tube, 230°, 17 h	(48) (0)	(43) (quant) 142 147, 173
	CCl <sub>4</sub> , sealed tube, 98°	 +  (-)	148
	192°, 600 torr, 22 h, break seal technique	 +  52: 48	146
	80–130°	 (-)	159, 160
	170°	 (-)	157, 158
	170°	 (-)	150–152
	cis, ( <i>Z</i> ) trans, ( <i>Z</i> )	 (100)	210, 211
		 (11)	

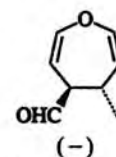
TABLE V. REARRANGEMENTS OF DIVINYLOXIRANES (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
 I  II 	I. NaOMe II. KOBu- <i>t</i>	 =  (-)	143
	CH <sub>3</sub> ONa	 =  (-)	143
	1,5-Diazabicyclo[4.3.0]non-5-ene	 =  (-)	143
	CH <sub>3</sub> ONa	 =  (-)	143
 <i>trans</i>	Vapor phase; 330° CCl <sub>4</sub> , sealed tube, 98°	 I +  II I:II = 3:2 I (quant)	147, 148
 <i>cis</i>	Vapor phase; 330° CCl <sub>4</sub> , sealed tube, 98°	 I +  II I:II = 1:1 I (quant)	147, 148
	100°, 14 h	 (80)	212
	H <sup>+</sup> , Et <sub>2</sub> O, H <sub>2</sub> O	 HO no Cope product	143

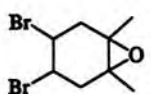
C<sub>s</sub>



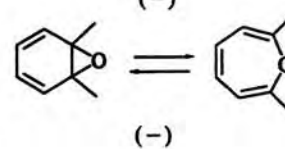
95°, 3.5 h, CCl<sub>4</sub>



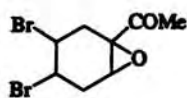
210



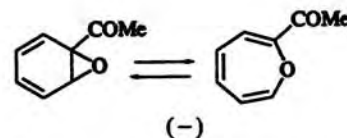
CH<sub>3</sub>ONa



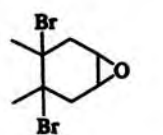
143



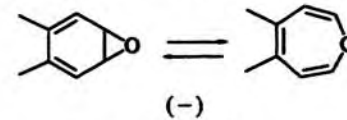
1,5-Diazabicyclo[4.3.0]non-5-ene



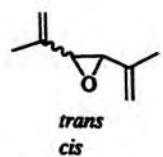
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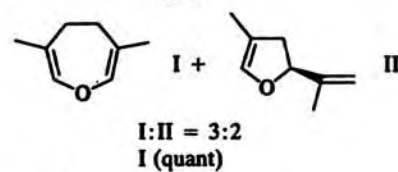
CH<sub>3</sub>ONa



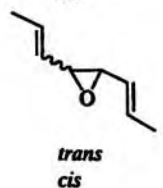
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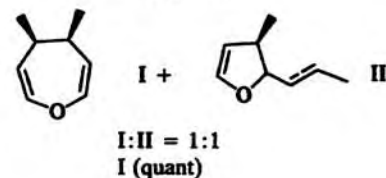
Vapor phase; 330°  
CCl<sub>4</sub>, sealed tube, 98°



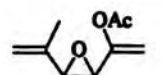
147, 148



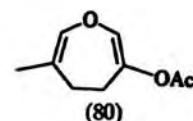
Vapor phase; 330°  
CCl<sub>4</sub>, sealed tube, 98°



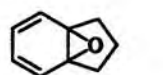
147, 148



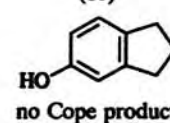
100°, 14 h



212



H<sup>+</sup>, Et<sub>2</sub>O, H<sub>2</sub>O



143

C<sub>s</sub>

TABLE V. REARRANGEMENTS OF DIVINYLOXIRANES (Continued)

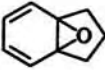
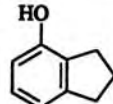

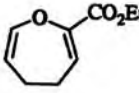
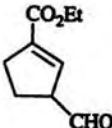
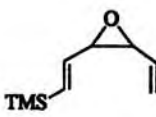
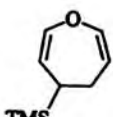
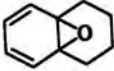
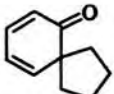
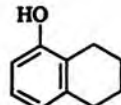
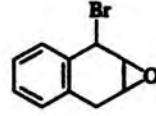
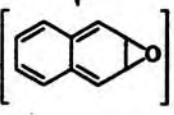
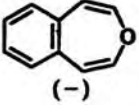

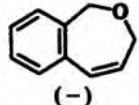
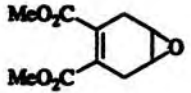
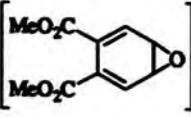
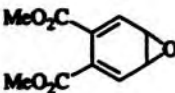
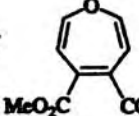
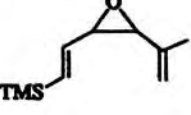
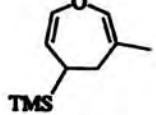
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	Lewis acid, Et <sub>2</sub> O, H <sub>2</sub> O	 no Cope product	143
	Flash vacuum thermolysis, 600° Flash vacuum thermolysis, 400°	 (33) (67) +  (33) (0)	166
	90°, CCl <sub>4</sub> , 22 h	 (67) some loss of product due to volatility	213
<b>C<sub>10</sub></b> 	H <sup>+</sup> , H <sub>2</sub> O, Et <sub>2</sub> O	 —  (quant), no Cope product	143
   	<i>t</i> -BuOK, Et <sub>2</sub> O	 (-)	143
	Thermolysis	 (-)	158
   	NBS, NaI, acetone	 =  (-)	143
	120°, CCl <sub>4</sub> , 15 h	 (85)	213



TABLE V. REARRANGEMENTS OF DIVINYLOXIRANES (Continued)

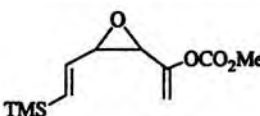
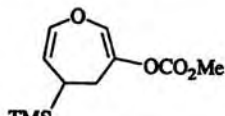
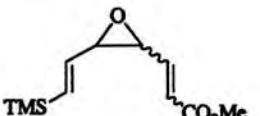
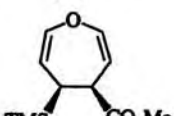
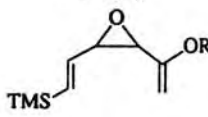
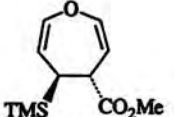
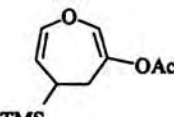
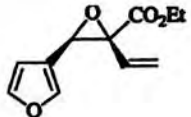
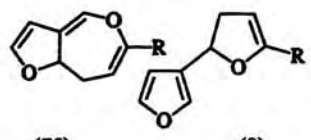
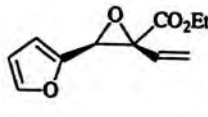
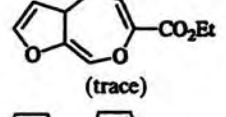
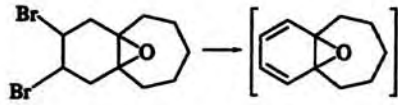
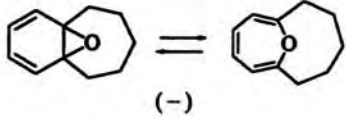
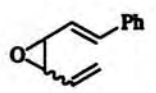
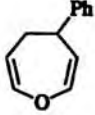
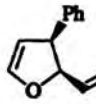
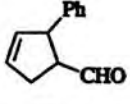
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
<p>C<sub>11</sub></p> 	125°, CCl <sub>4</sub> , 12 h	 (77)	213, 214
 <i>trans</i> , ( <i>E</i> ) <i>cis</i> , ( <i>E</i> )	165°, CCl <sub>4</sub> , 24 h 100°, CCl <sub>4</sub> , 12 h	 (20) (84)	213
 <i>trans</i> , ( <i>Z</i> ) <i>cis</i> , ( <i>Z</i> )	145°, CCl <sub>4</sub> , 42 h 130°, CCl <sub>4</sub> , 24 h	 (14) (62)	213
<p>R = Ac R = SO<sub>2</sub>CF<sub>3</sub> R = TMS</p>	135°, CCl <sub>4</sub> , 24 h 90°, CCl <sub>4</sub> , 12 h 120°, CCl <sub>4</sub> , 12 h	 (94) (77) (78)	213, 214 212 212
	Flash vacuum thermolysis, 400° Flash vacuum thermolysis, 550°	 (75) (trace) R = CO <sub>2</sub> Et (0) (75)	166
	Flash vacuum thermolysis, 500°	 (trace) (49)	166
 KOBu- <i>t</i> , ether		 (-) (-)	143
<p>C<sub>12</sub></p>  <i>cis:trans</i> = 40:60	400°, 15 torr, neat	 (38)	160
		 (13)	
		 (6)	

TABLE V. REARRANGEMENTS OF DIVINYLOXIRANES (Continued)

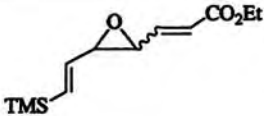
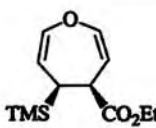
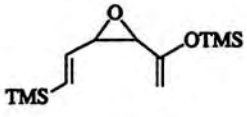
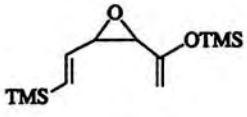
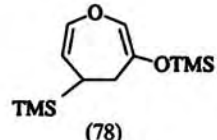
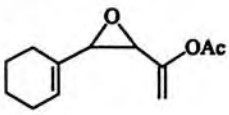
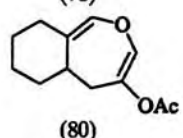
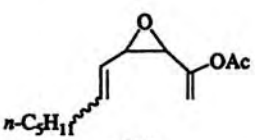
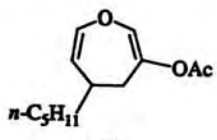
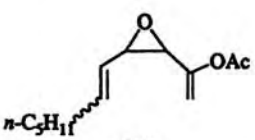
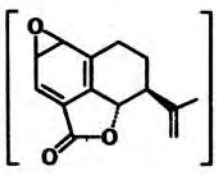
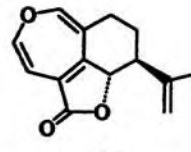
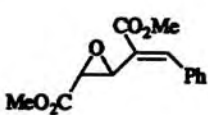
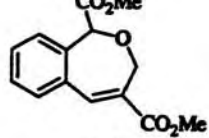
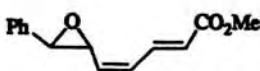
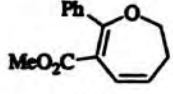
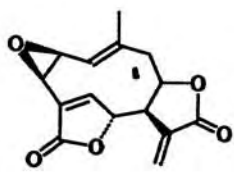
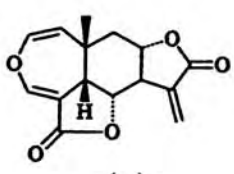
	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	 <i>trans</i>	16°, CCl <sub>4</sub> , 26 h	 (31)	213
	 <i>cis</i>	95°, CCl <sub>4</sub> , 20 h	(77)	
110		120°, CCl <sub>4</sub> , 12 h	 (78)	214
		150°, 2 h	 (80)	212
C <sub>13</sub>	 (E)	140°, 13 h	 (86)	
	 (Z)	150°, 26 h	(61)	212
C <sub>14</sub>		NaI, acetone, 1 d	 (22) Senepoxin	169
		Heat	 (–)	158
111		Heat	 (55)	157
C <sub>15</sub>		Biotransformation	 (–)	170

TABLE V. REARRANGEMENTS OF DIVINYLOXIRANES (Continued)

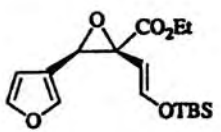
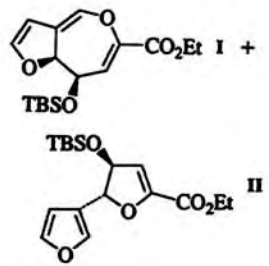
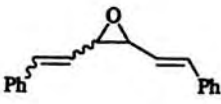
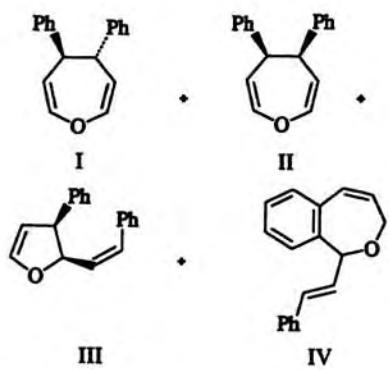
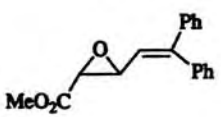
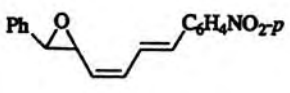
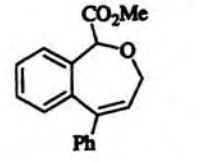
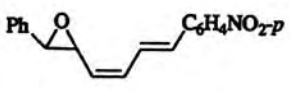
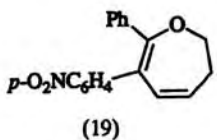
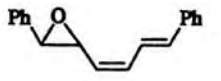
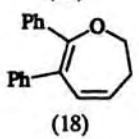
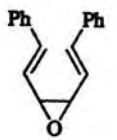
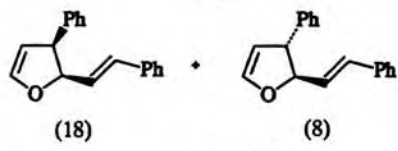
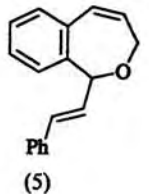
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.												
<p>C<sub>17</sub></p> 	<p>320°, then 550°, 10<sup>-5</sup> torr 80°, then 550°, 10<sup>-5</sup> torr TMSI, HMDS, -78°</p>	 <p>I (38) + II (25) II (40) II (95)</p>	168												
<p>C<sub>18</sub></p> 															
<p><i>trans Z,E</i> <i>cis E,E</i></p> 	<p>C<sub>6</sub>H<sub>5</sub>Cl, reflux, 2 h Toluene, reflux, 2 h</p>	<table border="1"> <thead> <tr> <th>I</th> <th>II</th> <th>III</th> <th>IV</th> </tr> </thead> <tbody> <tr> <td>(10)</td> <td>(3)</td> <td>(18)</td> <td>(6)</td> </tr> <tr> <td>(0)</td> <td>(50)</td> <td>(0)</td> <td>(0)</td> </tr> </tbody> </table>	I	II	III	IV	(10)	(3)	(18)	(6)	(0)	(50)	(0)	(0)	160
I	II	III	IV												
(10)	(3)	(18)	(6)												
(0)	(50)	(0)	(0)												
	Heat		158												
	Heat	 <p>(19)</p>	157												
	Heat	 <p>(18)</p>	157												
	Toluene, 15 torr, 350°	 <p>(18) + (8)</p>	160												
<p><i>cis:trans</i> = 2:3</p>		 <p>(5)</p>													

TABLE V. REARRANGEMENTS OF DIVINYLOXIRANES (*Continued*)


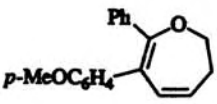
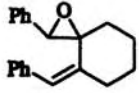
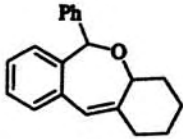
	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>19</sub>		Heat	 (18)	157
C <sub>20</sub>		370°, 10–15 s	 (-)	158

TABLE VI. REARRANGEMENTS OF DIVINYLAZIRIDINES

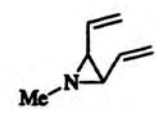
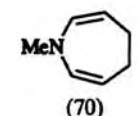
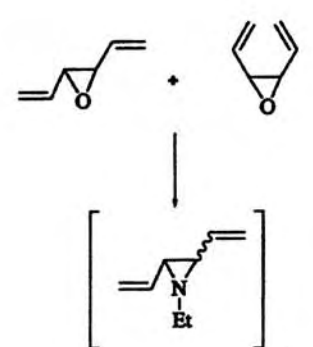
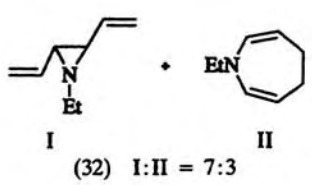
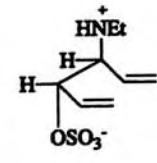
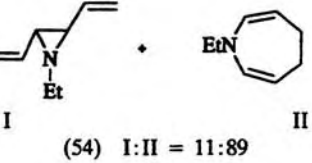
	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>7</sub>		C <sub>6</sub> H <sub>6</sub>	 (70)	173
C <sub>8</sub>		EtNH <sub>2</sub> , HCl; ClSO <sub>3</sub> H; NaOH	 I + II (32) I:II = 7:3	171, 172
		50% NaOH; steam distillation	 I + II (54) I:II = 11:89	171

TABLE VI. REARRANGEMENTS OF DIVINYLAZIRIDINES (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	rt, overnight or several hours at elevated temperatures, vacuum distillation	 (-)	172, 176
	C <sub>6</sub> H <sub>6</sub> , heat	 (-)	173, 215
	Toluene, reflux	 (60)	216
	80°, 1 h	 (quant)	174
	250°	 (-)	174
	Toluene, reflux	 (40)	216
	50°, 1-2 h; vacuum distillation	 (-)	172
 <i>trans</i> <i>cis</i>	320-340° 80-130°	 (85) (-)	165 159

TABLE VI. REARRANGEMENTS OF DIVINYLAZIRIDINES (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	$h\nu$ , THF, rt; toluene, reflux 130°	 (-) (-)	175 216
	$h\nu$ , THF, rt; toluene, reflux	 + (-)	175, 216
	140°, 1 d	 (37)	216
$C_{11}$ 	 $[CF_3-C(=O)-O-Rh-O-C(=O)-CF_3]_2$	 (-)	215
	$h\nu$ , THF, rt; toluene, reflux	 (-)	175
	Distillation or chromatography	 (-)	217
$C_{12}$ 	Distillation or chromatography	 (-)	217
	300°	 (-)	174
	Distillation or chromatography	 (-)	217

TABLE VI. REARRANGEMENTS OF DIVINYLAZIRIDINES (Continued)

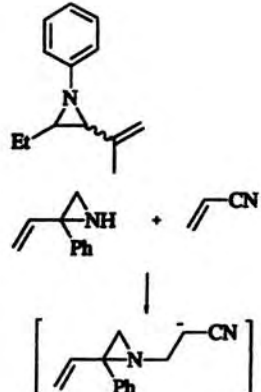
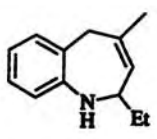
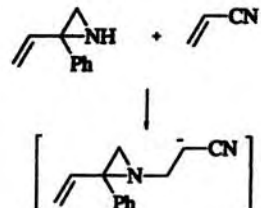
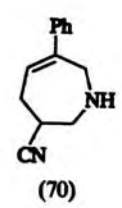
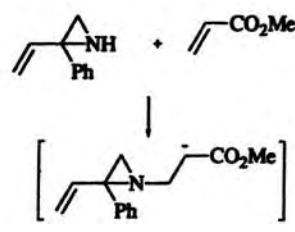
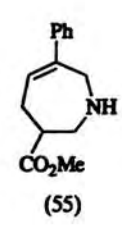
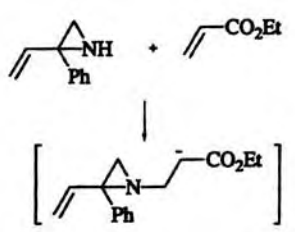
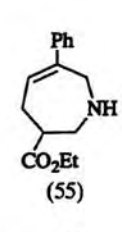
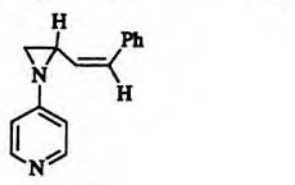
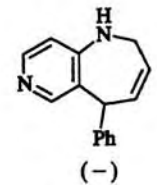
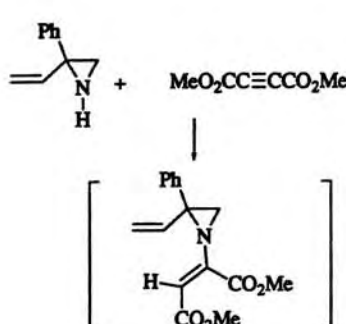
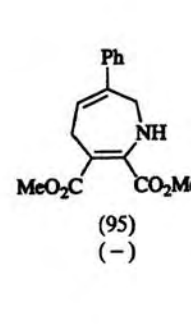
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
<p>C<sub>13</sub></p> 	<p>Distillation or chromatography</p>	 <p>217</p>	
	<p>CH<sub>3</sub>CN, reflux</p>	 <p>(70)</p>	<p>176, 178</p>
<p>C<sub>14</sub></p> 	<p>80°</p>	 <p>(55)</p>	<p>178</p>
<p>C<sub>15</sub></p> 	<p>80°</p>	 <p>(55)</p>	<p>176</p>
	<p><i>hν</i>, THF, rt; toluene, reflux</p>	 <p>(-)</p>	<p>175</p>
<p>C<sub>16</sub></p> 	<p>CH<sub>2</sub>Cl<sub>2</sub>, 0°</p> <p>-20°</p>	 <p>(95)</p> <p>(-)</p>	<p>176</p> <p>178</p>



TABLE VI. REARRANGEMENTS OF DIVINYLAZIRIDINES (Continued)

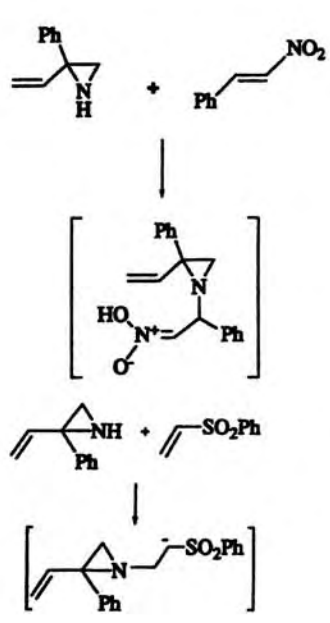
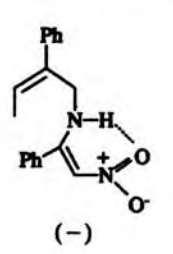
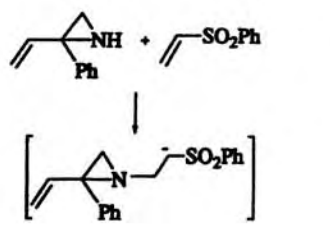
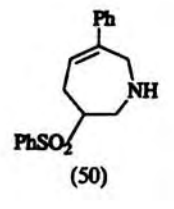
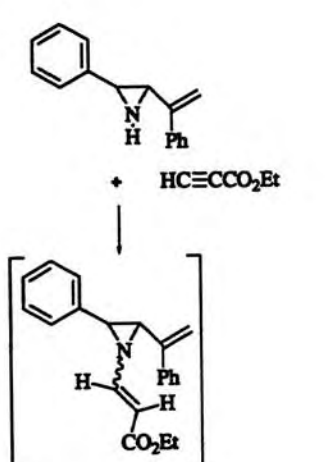
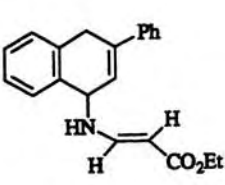
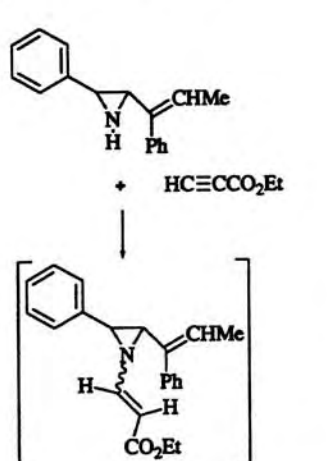
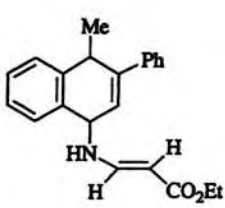
	Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>18</sub>		C <sub>6</sub> H <sub>6</sub> , 20 h, reflux	 (-)	176
		CH <sub>3</sub> CN, reflux	 (50)	176, 178
C <sub>21</sub>		DMSO, Celite, 24 h, 20–30°		177
C <sub>22</sub>		DMSO, Celite, 24 h, 20–30°		177

TABLE VI. REARRANGEMENTS OF DIVINYLAZIRIDINES (*Continued*)

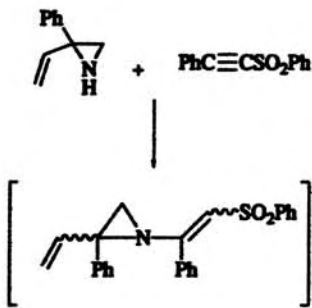
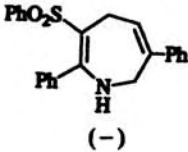
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
<p data-bbox="204 1012 239 1042">C<sub>24</sub></p> 	C <sub>6</sub> H <sub>6</sub> , 2 d, reflux	 <p data-bbox="1274 1242 1315 1265">(-)</p>	176

TABLE VII. REARRANGEMENTS OF DIVINYLTHIRANES

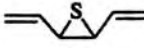










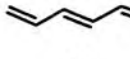


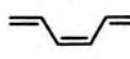
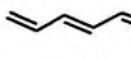

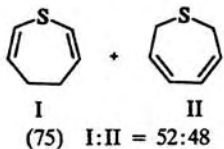
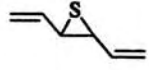
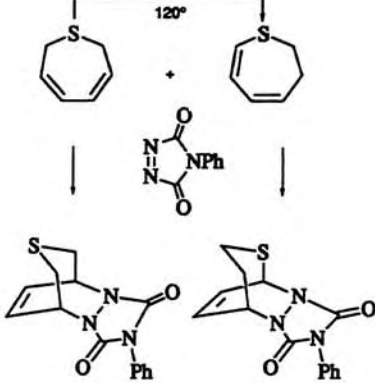
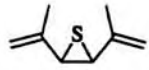
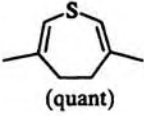
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs																														
 	340°	 (quant)	179																														
	420° 400° 390° 370°	 I +  II +  III   IV +  V	<table border="1"> <thead> <tr> <th></th> <th>I</th> <th>II</th> <th>III</th> <th>IV</th> <th>V</th> </tr> </thead> <tbody> <tr> <td>(100)</td> <td>29</td> <td>15</td> <td>0</td> <td>10</td> <td>46</td> </tr> <tr> <td>(96)</td> <td>28</td> <td>10</td> <td>12</td> <td>18</td> <td>32</td> </tr> <tr> <td>(91)</td> <td>30</td> <td>11</td> <td>16</td> <td>16</td> <td>27</td> </tr> <tr> <td>(66)</td> <td>25</td> <td>8</td> <td>30</td> <td>11</td> <td>26</td> </tr> </tbody> </table>		I	II	III	IV	V	(100)	29	15	0	10	46	(96)	28	10	12	18	32	(91)	30	11	16	16	27	(66)	25	8	30	11	26
	I	II	III	IV	V																												
(100)	29	15	0	10	46																												
(96)	28	10	12	18	32																												
(91)	30	11	16	16	27																												
(66)	25	8	30	11	26																												
 	Static system break seal technique 90-120°	 I +  II (20-25) I:II = 1:4	180																														
 	Static system break seal technique 90-120°	 I +  II (20-25) I:II = 1:4	180																														

TABLE VII. REARRANGEMENTS OF DIVINYLTHIRANES (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	90°	 <p>I (75) I:II = 52:48</p>	180
	100-125°	 <p>120°</p>	180
	110°, CCl <sub>4</sub> or 300° (vapor phase)	 <p>(quant)</p>	179

C\*

TABLE VIII. REARRANGEMENTS OF MISCELLANEOUS SYSTEMS

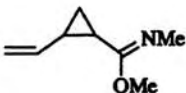
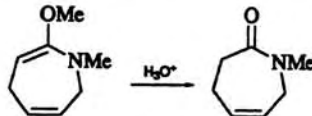

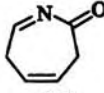
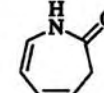
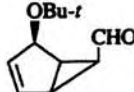
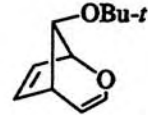
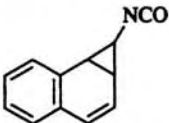
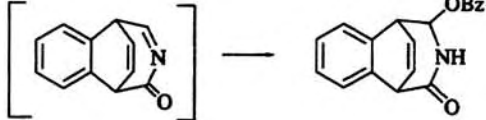

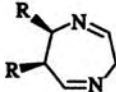
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_8$ 	110–130°		32
	<i>o</i> -Xylene, reflux, 60 h	 (-) (60)	32
<i>cis</i> <i>trans</i>	80° 350°	 (-) (-)	34, 35, 36
$C_{11}$ 	0°, NMR tube	 equilibrium: $k = 1.1$	197

TABLE VIII. REARRANGEMENTS OF MISCELLANEOUS SYSTEMS (Continued)

Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs
C <sub>12</sub> 	Thermolysis, BzOH		34, 35
C <sub>15</sub>  R = phenyl, <i>p</i> -tolyl, mesityl, <i>o</i> -hydroxyphenyl, <i>tert</i> -butyl	Thermolysis	 from <i>trans</i> : (49–66) from <i>cis</i> : (34–90)	218

## **8. Acknowledgment**

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# Organocopper Reagents: Substitution, Conjugate Addition, Carbo/Metallocupration, and Other Reactions

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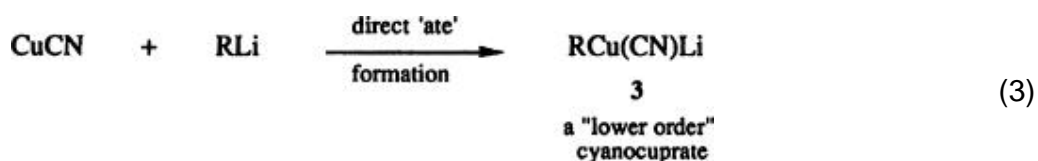
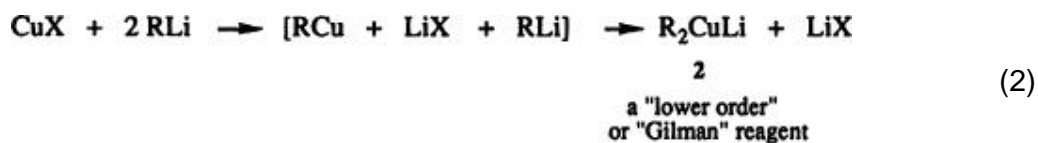
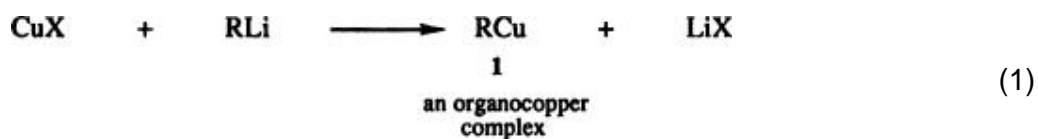
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## 1. Introduction

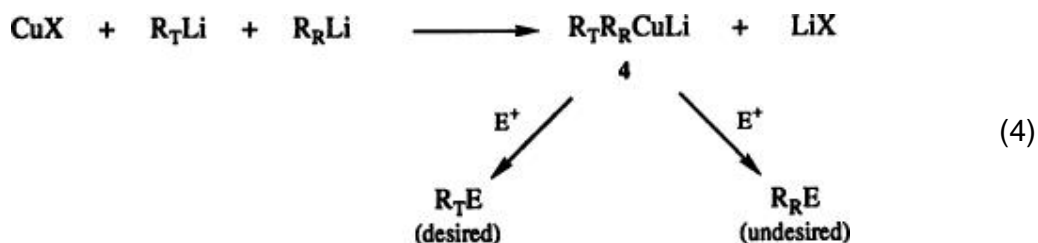
Well over a decade ago, two reviews were contributed to the *Organic Reactions* series covering substitution and conjugate addition reactions in organocopper chemistry. (1) Their appearance, which highlighted most of the early work in this field, served not only as a source of invaluable references to original literature reports, but also stimulated a vast number of subsequent studies on the properties and uses of organocopper complexes. That these reagents are of tremendous value to the domain of synthetic organic chemistry is hardly open to debate; (2) indeed it is rare *not* to find a copper-mediated carbon-carbon bond-forming transformation in journals that cater to organic chemistry. Collman and Hegedus summed up the situation some years ago in their text on organotransition metal chemistry by stating, "Of all the transition-metal organometallic reagents developed for application to organic synthesis, organocopper complexes are by far the most heavily used and enthusiastically accepted by the synthetic chemist, ...." (3) Research in this area since these remarks of 1980 has expanded considerably. Fortunately, numerous reviews addressing specific subdivisions of organocopper chemistry have filled the need to keep pace with the advances being made. (4)

The work cited in this chapter, which dates from ca. 1975, concerns in large measure uses of organocopper complexes originating from either catalytic or stoichiometric quantities of a copper(I) halide together with a Grignard (RMgX) or organolithium (RLi) reagent. These combinations form either neutral organocopper reagents RCu (1) or copper(I) monoanionic salts  $R_2CuM$  ( $M = Li$  or  $MgX$ ), commonly referred to as "lower-order" species. The latter *ate* complexes with lithium as gegenion (i.e., 2) are also known as "Gilman reagents" in recognition of their origins (Eqs. 1 and 2). (5) Copper(I) cyanide is also an excellent precursor, affording homogeneous mixtures of lower order cyanocuprates  $RCu(CN)Li$ , 3, upon treatment with an equivalent of an organolithium (Eq. 3). The strength of the  $Cu - CN$  linkage presumably accounts for direct cuprate formation with 1 equivalent of the organolithium, rather than the metathesis that occurs with copper(I) chloride, bromide, or iodide.



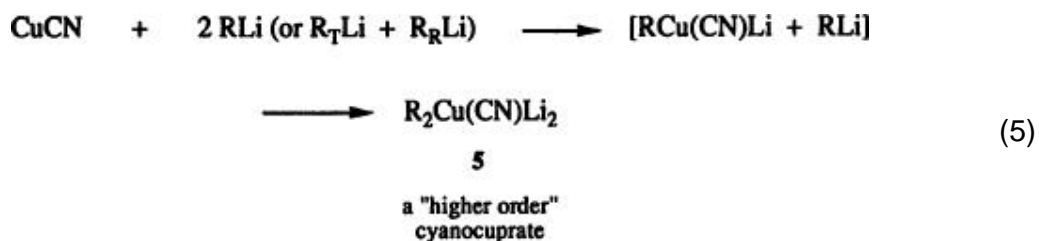


While use of reagents **1**, **2**, and **3** alone can be aptly classified as broad-based and intense, their importance has further encouraged extensive development of variations on these themes (i.e., their composition and reactivity profiles). Reagents **1–3** have been found to be unexpectedly compatible with certain electrophilic additives at low temperatures, which substantially alter their reactivity. Rather than forming **2** from 2 equivalents of the same RLi, different organolithiums can be utilized to give  $\text{R}_T\text{R}_R\text{CuLi}$ , **4**, conserving potentially valuable RLi. This scenario raises the question of controlling the selectivity of transfer of the desired ligand  $\text{R}_T$  rather than the anticipated residual (or “dummy”) group  $\text{R}_R$  from copper to electrophilic carbon (Eq. 4). Fortunately, many solutions to this problem now exist.



The most recent arrivals to the fold of organocopper chemistry are those species resulting from a composite of the principles delineated in Eqs. 2–4.

That is, admixture of 2RLi (or R<sub>1</sub>Li + R<sub>2</sub>Li) with copper(I) cyanide proceeds beyond the stage of **3** to ultimately arrive at copper(I) dianionic complexes **5**, the so-called “higher-order” cyanocuprates (Eq. 5). (6) Undoubtedly it is the cyano ligand, with its π -acidic nature, which enables copper to accept a third negatively charged ligand. Although reagents **5** do not yet share in all of the



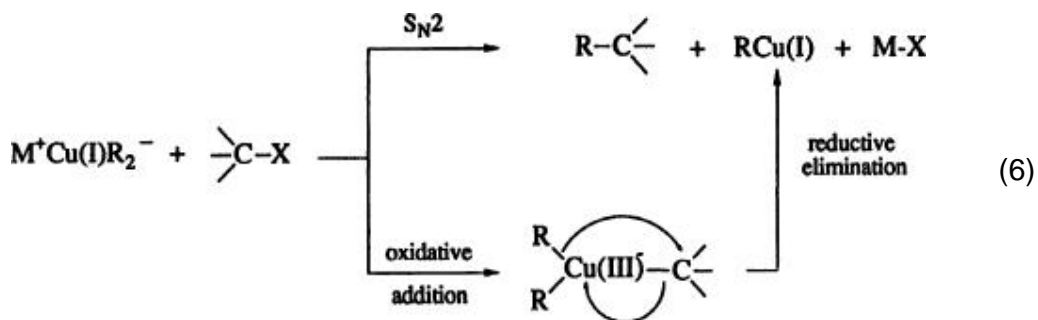
benefits offered by time in comparison with their lower-order counterparts, they nicely complement prior art. Moreover, as with species **1–4**, they continue to evolve, providing the synthetic community with alternatives for highly selective and efficient means of making key carbon–carbon bonds.

## 2. Mechanism

The popularity of organocopper complexes as reagents in organic synthesis has spawned numerous mechanistic investigations of both substitution and conjugate addition schemes. Studies of the former, most often involving homogeneous solutions of cuprates (rather than neutral organocopper species,  $\text{RCu}$ ), corroborate an earlier assessment that no single interpretation can account for all of the mechanistic and stereochemical results gathered to date. (7) Variations in the nature of the leaving group, the hybridization of the carbon undergoing the reaction in the substrate, and the effects of other functionality located within the molecule may all contribute to the course followed. In addition, since it now appears that the organocuprate itself within a given class [e.g., lower-order homocuprates,  $\text{R}_2\text{CuLi}$  (7) or higher-order cuprates  $\text{R}_2\text{Cu}(\text{CN})\text{Li}_2$  (8)] may vary as a function of solvent, mode of preparation, and presence of additives, the likelihood of finding a common denominator seems slim. However, there are many valuable generalizations concerning specific substrate types that can be made and utilized to advantage in synthetic situations.

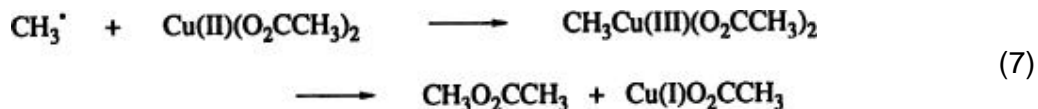
### 2.1.1.1. Substitution Reactions

Proposed mechanisms for substitutions of halides or sulfonates usually involve a direct displacement by  $\text{R}$  in  $\text{R}_2\text{CuLi}$  in an  $\text{S}_{\text{N}}2$  process, or attack by the cuprate itself to afford a transient  $\text{Cu}(\text{III})$  intermediate, followed by reductive elimination (Eq. 6). An early case opposing

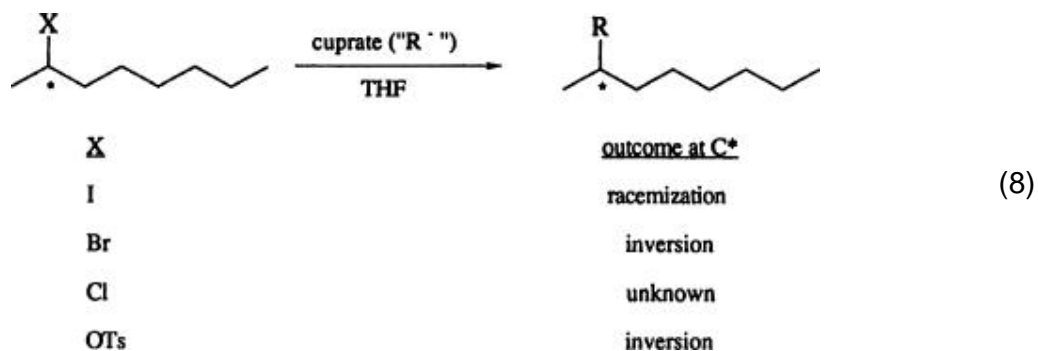


involvement of a  $\text{Cu}(\text{III})$  species has been made, (9) as has an alternative proposal invoking a dimeric cuprate wherein each copper atom donates one electron [i.e., to form two  $\text{Cu}(\text{II})$  atoms] toward a net two-electron change, thereby avoiding a highly unstable  $\text{Cu}(\text{III})$  oxidation state. (10) Examples of copper complexes of this formal oxidation level are known; however, they generally tend to require good  $\sigma$ -donor ligands for stabilization. (11-15) Arguments in favor of a  $\text{Cu}(\text{III})$  intermediate are further strengthened by analogy to reactions of dialkylgold(I) reagents, (16) which give documented  $\text{Au}(\text{III})$  intermediates. (17) Reductive elimination from the  $\text{Cu}(\text{III})$  to the  $\text{Cu}(\text{I})$

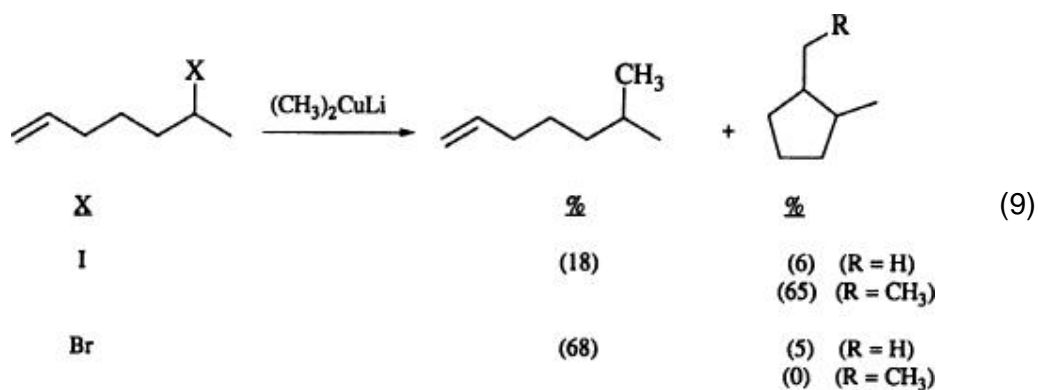
state, as with the corresponding aurates, occurs following their generation via alkyl radical addition to cupric acetate (Eq. 7). (18)



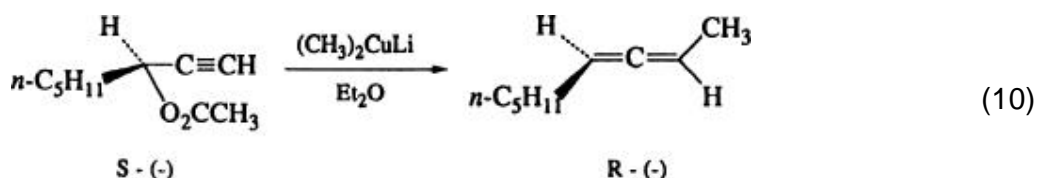
Implied in both mechanisms (Eq. 6) is the stereochemistry at the reacting carbon center, which is predicted to undergo a net inversion. Tosylates (19) and epoxides (20) do give products of inversion, but recent evidence shows that such is not the case with all reactive halides. (21, 22) That is, iodides typified by



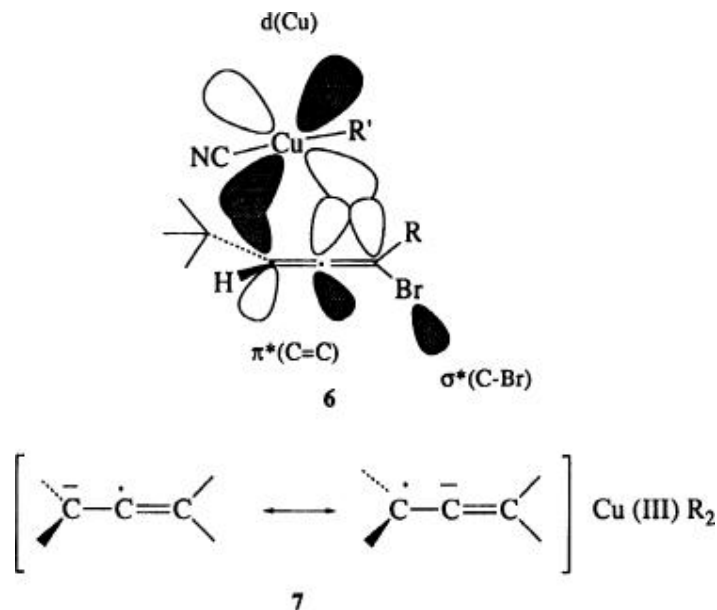
(+)-2-iodooctane lead to racemized products, while chiral nonracemic bromides give results akin to sulfonates (Eq. 8). (21, 22) The necessity for a pathway proceeding through free radicals in the case of iodides is borne out from experiments with various radical traps, for example, 6-halo-1-heptenes (Eq. 9). (23) With  $X = \text{I}$ , cyclopentane-containing products predominate by ratios of 3–4:1 over straight-chain products of substitution. Even bromides lead to finite percentages of cyclic material, implying that more than one mechanism is operative.  $\alpha$ -Deuterium and  $^{13}\text{C}$  secondary kinetic isotope effects associated with these displacements have also been measured. (24)



Several more recent reports have appeared suggesting Cu(III) intermediates in reactions of widely varying systems, including allylic (25) and propargylic (26-30) halides, sulfonates and esters, allenes, (31)  $\alpha$ -dihalo esters, (32, 33) and others. (34) Propargylic acetates, tosylates, and halides produce substituted allenes resulting from predominantly *anti* addition (Eq. 10). Trapping experiments at low temperatures implicate a Cu(III) intermediate, which gives a coupling

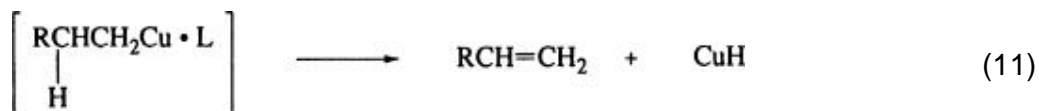


product upon warming. (26) Allenic bromides, likewise and in concert, are converted back into the corresponding acetylenes without loss of stereochemical information, perhaps via initial "bidentate binding" as illustrated in complex 6. (31) Interestingly, these same cuprates, as well as those derived from Grignard reagents with catalytic amounts of copper(I) halides, racemize (unactivated) chiral allenes, probably by way of radical anions 7 formed by electron transfer from R<sub>2</sub>CuLi. Rates of loss of optical activity are greater in tetrahydrofuran than in diethyl ether solutions. (35)



Single electron transfer (SET) chemistry of organocuprates has also been observed with several other substrate types. Many alkyl aryl ketones (36) and diaryl ketones (37) of varying substitution patterns and reduction potentials react in a 1,2 sense with  $R_2CuLi$ , presumably by way of electron transfer. It is often not possible, though, to rule out the direct 1,2 addition by electron-rich  $d^{10}$  copper(I) in  $R_2Cu^-$ , even though this should be disfavored by “ $\alpha$ -effect” (38-40) repulsion. Similar intermediate roles for anion radicals are described in reactions of  $Me_2CuLi$  with cyclopropyl ketones 41a and enones, 41b and of  $Ph_2CuMgBr$  on nitrosobenzene. (42) Supporting studies on the oxidation potentials of cuprates (e.g.,  $[PhCuOR]^-$ ) (43) and  $RCu$ , (44) as well as on reduction potentials of selective substrates in ethereal media, have also been reported. (45)

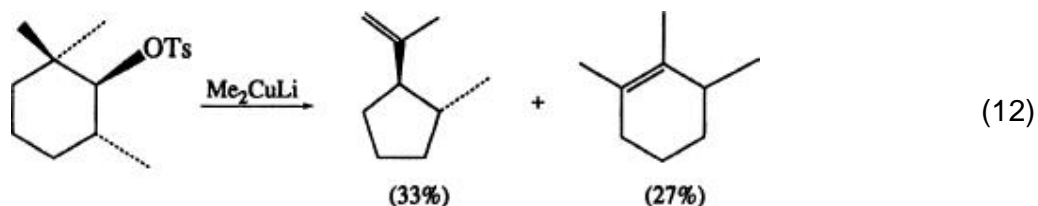
Reductions of alkyl halides, a competitive pathway in cuprate couplings, have been suggested to take place by way of copper hydrides,  $CuH \cdot L$ , formed



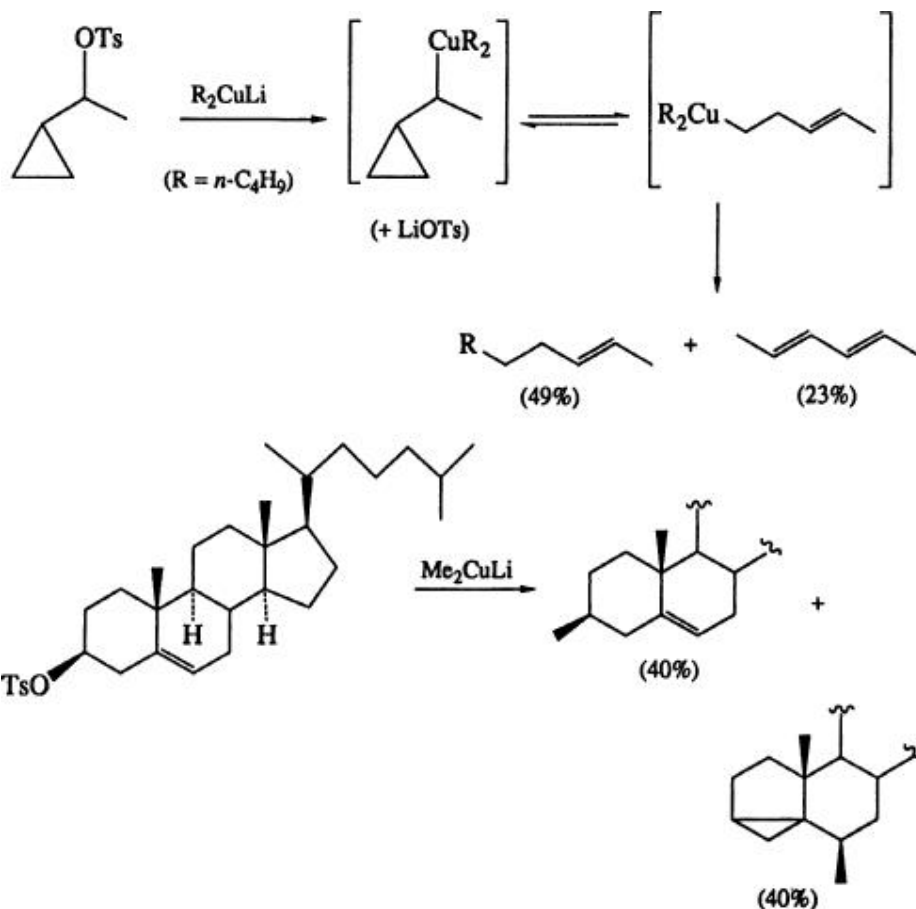
via  $\beta$  elimination from an organocopper species (Eq. 11). (46) Similar outcomes, however, are realized when  $\beta$ -hydride elimination is unlikely or cannot occur, for example, with  $Ph_2CuLi$  or  $Me_2CuLi$ . (47) The ultimate source of hydrogen in the reduced product has yet to be ascertained. Functional group replacements by hydrogen in olefinic (48) and (hetero)aromatic substrates (49) have also been reported, where single-electron transfer

processes may play a role.

Alkyl tosylates in hindered systems, rather than undergoing reduction, react through a concerted *anti*-elimination mechanism involving  $\text{Li}^+$  as a Lewis acid in a “push–pull” process. When such an action induced by  $\text{R}_2\text{CuLi}$  ( $\text{R} = \text{Me}, \text{Ph}$ ) is precluded, skeletal reorganization ensues (Eq. 12). (50)



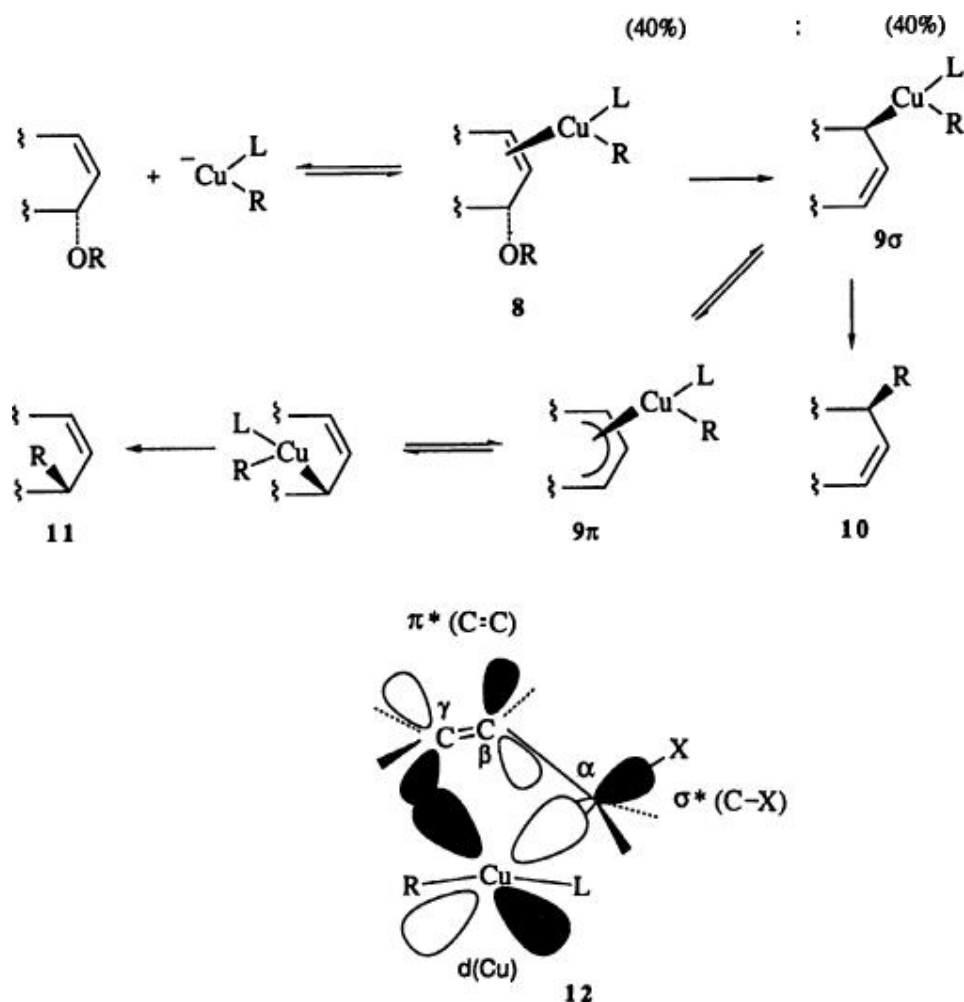
The proximity of certain functional groups to the  $sp^3$  carbon bearing a leaving group can dramatically alter both the anticipated products and the mechanistic picture. Cyclopropyl tosylates give ring-opened materials, a process that may involve a “cuprate(I)–cation complex”. (51) Homoallylic steroidal tosylates (e.g., of cholesterol) of defined stereochemistry react with  $\text{R}_2\text{CuLi}$  with retention of configuration, suggesting participation of the 5,6 double bond. (51)



Alkylations of cyclic and acyclic allylic systems in particular have been scrutinized as to their regio- and stereochemical outcomes in reactions with organocuprates. In general, products reflecting *anti* stereochemistry are favored, although this can be reversed (i.e., to give *syn* products) depending upon the leaving group, [52,53a,b](#) steric factors, [\(54-57\)](#) and type of substrate. [53a,c](#) Early views promoted the orbital distortion technique, suggesting an initial radical anion. [\(58\)](#) More recent studies point to a rate-determining formation of a  $\sigma$ -allylcopper(III) complex **9  $\sigma$** , originating from  $S_N2'$  attack by copper following prior cuprate complexation with the olefin (as in complex **8**). [\(59, 60\)](#) Reductive elimination from **9  $\sigma$**  with retention of configuration would give *anti* product **10**. Alternatively, copper species **9  $\sigma$**  may rapidly isomerize to a  $\pi$ -allyl species **9  $\pi$**  (L = alkyl), resulting in the potential loss of regiocontrol. Intermediate **9** may then partition itself between products **10** and **11** depending on stereoelectronic and steric factors. It should be noted that formation of **10** and/or **11** indicates that rates of reductive elimination vs. isomerization can be altered by changes of the ligand L on copper. [\(61\)](#) Similar mechanistic interpretations have been advanced for Cu(I)-catalyzed Grignard couplings. [\(62\)](#) An alternative view postulates overlap between a diffuse copper(I) *d*



orbital and the appropriate LUMO of the allylic system, as in **12**. Simultaneous  $d\pi^*$



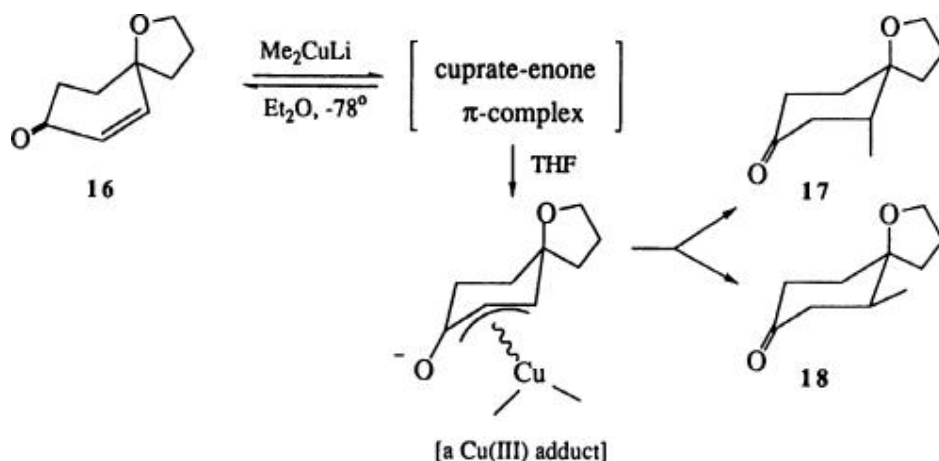
(at the  $\gamma$  carbon) and  $d\sigma^*$  (at the  $\alpha$  carbon) bonding accounts for the  $S_N2\phi$  preference with net *anti* stereochemistry. (39)

#### 2.1.1.2. Conjugate Additions

The mechanistic picture for cuprate conjugate addition reactions is no less complicated than that put forth for substitution reactions. Several different proposals have evolved over the past decade, for the most part based on studies involving Gilman lithio cuprates ( $R_2CuLi$ ). With the advent of additives (e.g., boron trifluoride etherate, chlorotrimethylsilane) now commonly employed in reactions of this type, the situation has been made all the more complex.

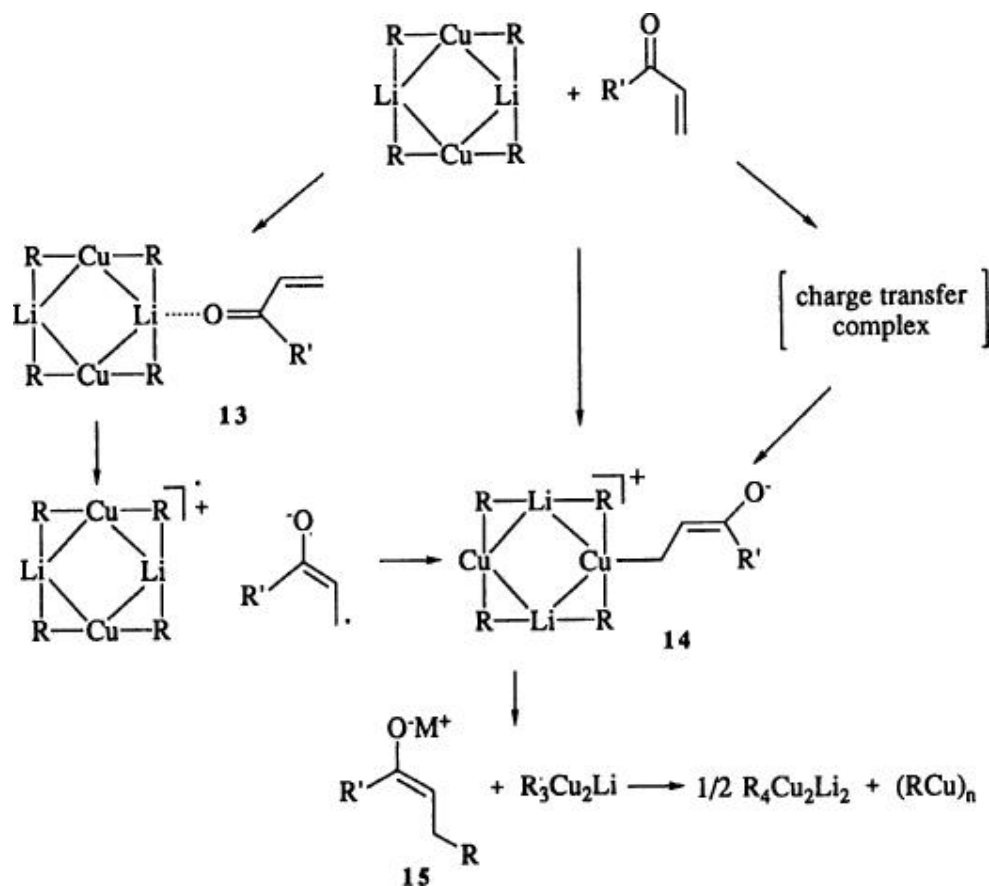
The correlation of reduction potentials of  $\alpha$ ,  $\beta$ -unsaturated carbonyl systems with cuprate reactivity, and the generally recognized need for oxygen as part of

the chromophore, have given rise to a proposal involving a single electron transfer mechanism. (63, 64) Initial Lewis acid–Lewis base interaction (13, Scheme 1) encourages transfer of an electron from a dimeric cuprate to the enone (or enoate), followed by formation of a copper–carbon bond as in species 14. Reductive elimination from the Cu(III) species 14 affords the enolate, although the exact nature of M in species 15 is still an open question. (65-67) Intermediate 14 can also arise by way of an initial charge transfer complex. (68, 69) Still more direct would be the addition of the reagent to the  $\beta$  carbon atom



of the substrate. (19, 70, 71) Kinetic data on these Michael reactions indicate the existence of an equilibrium between reactants and some intermediate that goes on to form a Cu(III) species in an intramolecular manner, placing copper at the  $\beta$  carbon of an enolate. (72-74) Lithium ion coordination with the carbonyl oxygen would assist when geometrically possible from within the cuprate cluster, or when free LiX is present. (73)

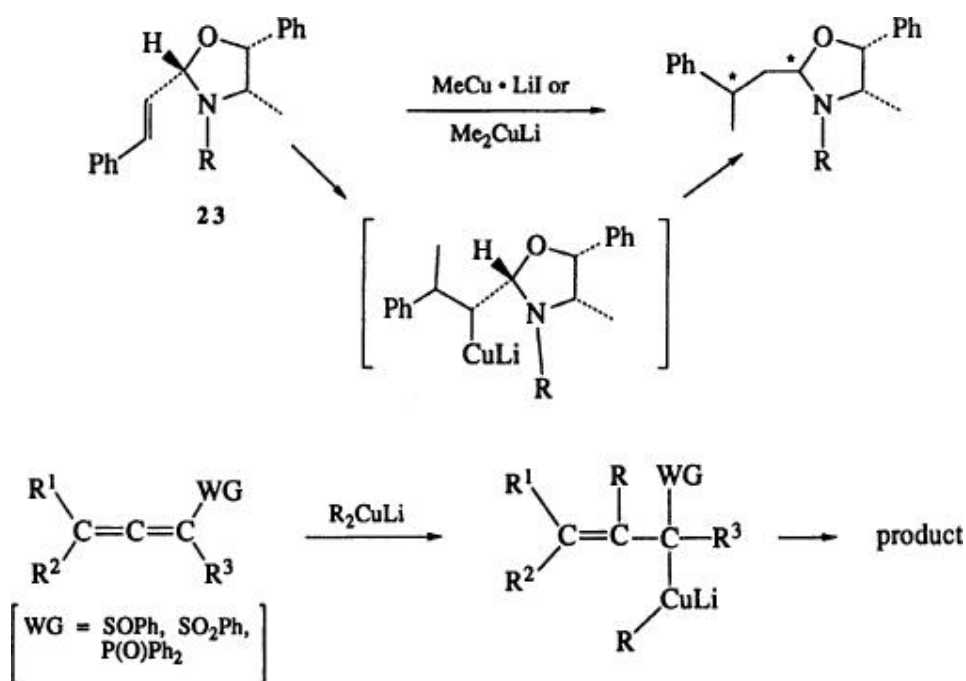
**Scheme 1.**



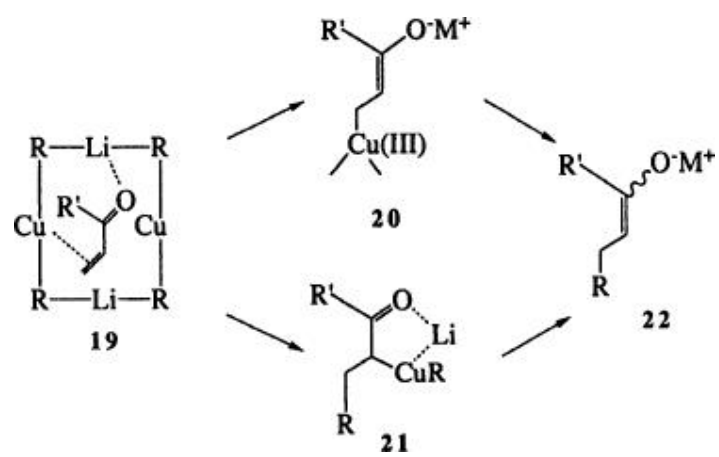
This notion of an early intermediate complex (beyond that of simple  $\text{Li}^+$  coordination) has gained considerable momentum since being originally put forth. (75) Cogent evidence for binding between copper and  $\pi^*$  of the enone comes both from infrared spectroscopic studies of reactions involving unsaturated esters, (76) as well as low-temperature  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy (77, 78) of reactions of  $\text{Me}_2\text{CuLi}$  or  $\text{Me}(2\text{-thienyl})\text{CuLi}$  with cinnamate esters. Complexation between copper(I) and olefins is supported by Hartree–Fock–Slater (HFS) calculations suggesting involvement of metal  $3d$   $\pi$  alkene  $\pi^*$  interactions. (79) Experiments designed to further substantiate the spectroscopic data using enone 16 suggest that, following reversible  $d\pi^*$  interaction, the cuprate adds to the  $\beta$  position (also in a reversible sense) to afford a Cu(III) adduct. This intermediate can then go on to product(s) 17 and/or 18 depending on solvent(s) and the presence (or lack) of chlorotrimethylsilane in the medium. In diethyl ether at  $-78^\circ$ , a yellow precipitate is observed and can be separated from the solution. Subsequent redissolution in tetrahydrofuran leads to the expected products (17, 18), implying that the unknown material is a cuprate–enone complex. (80)

Thus, on the basis of existing information, conjugate additions of lithio cuprates to  $\alpha, \beta$ -unsaturated ketones and esters involve an initially reversible copper(I)–olefin/lithium–oxygen association to form 19, which is stable at very

low temperatures (Scheme 2). Formation of **19** is favored in poor donor solvents and by the absence of donor ligands. (66, 67) Warming leads to another intermediate, likely to be a fleeting  $\beta$ -carbon-bonded Cu(III) species **20**, which then undergoes reductive elimination. A carbocupration step to afford species **21** is a reasonable alternative along the reaction coordinate, since rapid migration of copper to oxygen (**21**  $\leftrightarrow$  **22**, M = CuR) cannot as yet be unambiguously ruled out. (81) This pathway is given further credence by the surprising results obtained from reactions of dimethylcopperlithium with chiral vinyloxazolidine **23**, which contains an unactivated double bond. (82, 83) The stereoselectivities observed (as a function of solvent, time, and temperature) are best accommodated by an initial carbometalation. Moreover, it is well established that  $\alpha$ -acetylenic ketones, (84) esters and acids, (85-87) as well as  $\alpha$ -allenic carbonyl systems, (88) follow this more classical organometallic insertion route. Such is also the case with related sulfoxides, 89a sulfoxides, 89a and phosphine oxides. 89b,90 Mechanistic details for carbocuprations of isolated triple bonds are even more sketchy. (91)



Scheme 2.



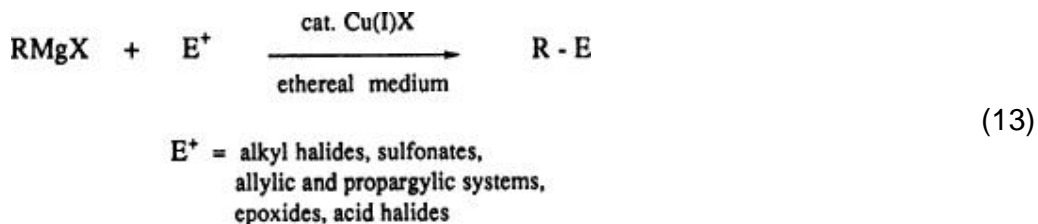
### 3. Scope and Limitations

#### 3.1. Grignard-Derived Organocopper Reagents

##### 3.1.1. Copper-Catalyzed Reactions of $RMgX$

###### 3.1.1.1. Substitution

The pros and cons of using Grignard reagents alone as organometallic components in displacement reactions have been known for some time. (92) In general, a Grignard reagent is not likely to afford coupling products in synthetically useful yields, although there are some exceptions (e.g., allylic and benzylic systems). (92) While the prognosis can be significantly improved when these reactions are run in the presence of catalytic amounts of transition metals (93-95) (e.g., Ni, (94) Pd, (95) Fe (96)), copper(I) salts have found by far the most widespread use in this capacity. One highly valued precursor,  $Li_2CuCl_4$ , (9, 96) in quantities oftentimes less than 1 mole percent, is quite effective in cross couplings of a Grignard reagent with alkyl halides and tosylates. These reactions encounter competing disproportionation processes when applied to less reactive secondary and especially tertiary halides. Several other electrophiles ( $E^+$ ) are also amenable, including acid halides, epoxides, and  $\beta$ -lactones. Allylic leaving groups allow for particularly valuable  $S_N2'$  reactions, while propargylic configurations offer excellent inroads to allenic systems (Eq. 13).

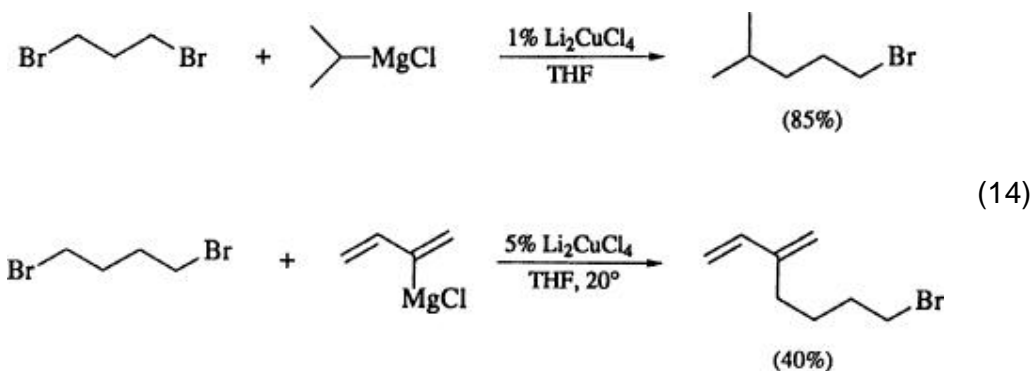


The attraction to Grignard-based substitution methodology is certainly in part due to the availability of most Grignard reagents. Moreover, the need for only catalytic amounts of copper(I) halides adds substantially to the merits of this technology from the fiscal perspective. Primary, secondary, and tertiary Grignard reagents, under the influence of a copper(I) halide, show strong tendencies to react at the carbon bearing the original halide, while propargylic and allylic Grignard reagents may couple at either terminus. Vinylic Grignard reagents are available in high isomer purities by way of carbocupration of acetylenes (Table III), and their subsequent displacement reactions occur with retention of double-bond geometry. Hence, various olefins of well-defined stereochemistry are accessible by way of this chemistry. Many examples of Grignard-based reactions are listed in Tables I, II, and III, addressing catalytic

processes, stoichiometric displacements and 1,4 additions, and carbocuprations, respectively.

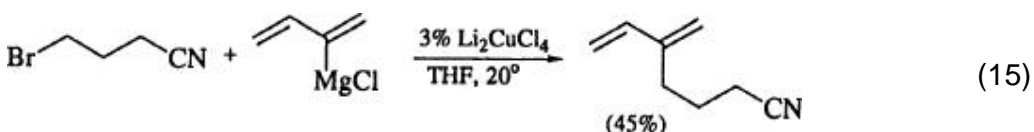
### 3.1.1.1.1. Alkyl Halides and Sulfonates

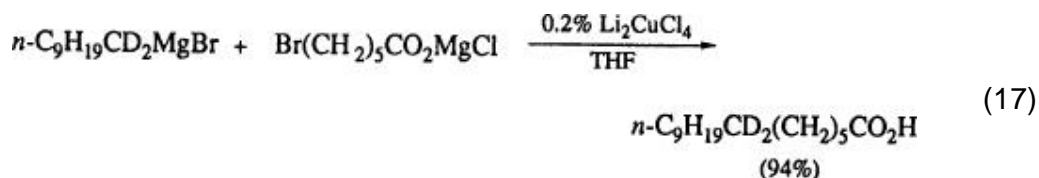
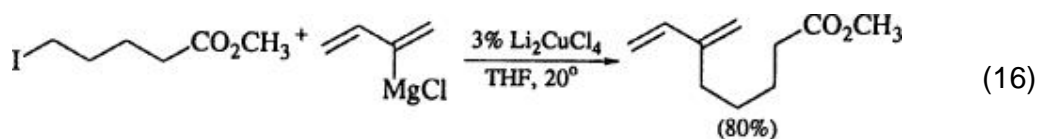
With regard to displacement at  $sp^3$ -based centers bearing halogen, essentially all uses rely on the greater reactivity of bromides and especially iodides relative to the far more sluggish chlorides (Table 1A). Generally speaking, couplings tend to be consistently more effective using stoichiometric rather than catalytic amounts of a copper(I) halide. However, the advent of the soluble catalyst  $Li_2CuCl_4$  has generated a resurgence of interest in this catalytic mode of carbon–carbon bond construction. (9, 96) Several features of this process are noteworthy. Selective couplings with substrates possessing multiple electrophilic sites have been achieved. Thus  $\alpha, \omega$ -dibromides react with 1 equivalent of a Grignard reagent to give



monosubstituted products (Eq. 14). With  $\alpha, \beta$ -dibromides, however, the reaction fails because of favorable  $\beta$  elimination. (97) Alkyl iodides in bifunctional molecules containing an aryl halide (e.g., *p*-Br group) react at the primary aliphatic center. (98) A methylene group containing both halide and an organometallic residue (e.g.,  $R_3Sn -$ ) is also quite reactive. (99) With 2 or more equivalents of Grignard reagent, double displacements take place. (100)

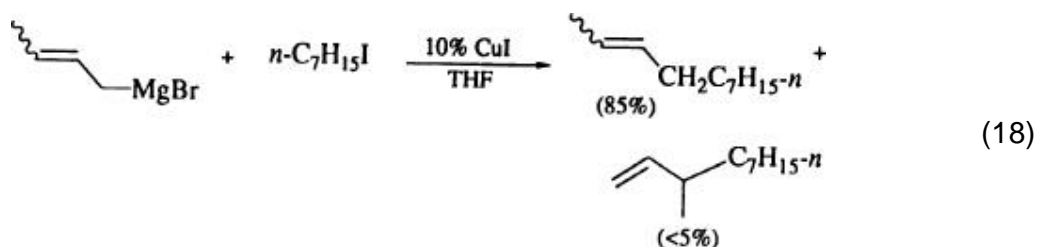
Certain functional groups can be tolerated within the substrate. Esters, (98, 101) acids, (102, 103) and nitriles (98) are relatively inert, and lead to selective couplings (Eqs. 15–17). A high-yield route to deuterium-labeled materials involves treatment of an  $\omega$ -bromo acid with a labeled Grignard reagent which gives,





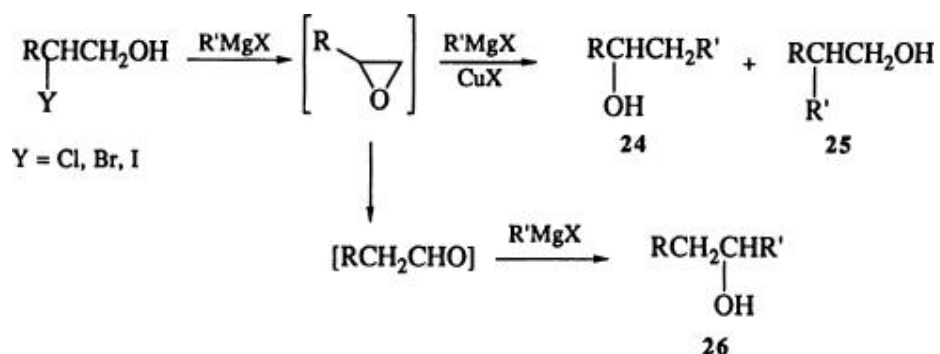
for example, 7,7-*d*<sub>2</sub>-palmitic acid in excellent yield (Eq. 17). (102) Similar couplings occur between deuterated tosylates and Grignard reagents. (104)

Grignard/catalytic CuX substitutions of 1,2-halohydrins provide interesting outcomes. In contrast to ethylene bromohydrin, (101) substituted halohydrins give mixtures of products, accounted for in Scheme 3. (105) The product distribution (24:25:26) depends upon the nature of X (Cl, Br, I), as well as on R MgX. While alkyl Grignard reagents are less regioselective, vinyl, allyl, or phenyl Grignard reagents predominantly afford isomer 25, (105) the formal product of direct substitution. Propargyl Grignard reagents produce ca. 20% of the corresponding allenyl adducts of ring opening. (105) Crotyl reagents react at the more-substituted carbon with >80% regioselectivity. (105) Extreme departures from this generalization have been noted with alkyl halides, as in Eq. 18. (106)



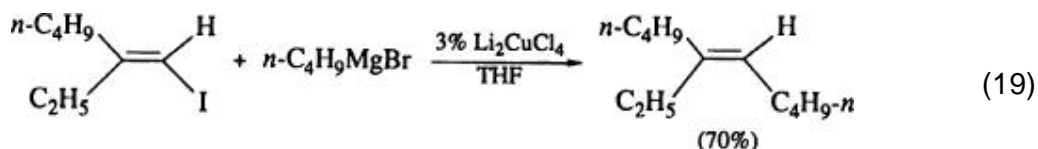
Scheme 3.





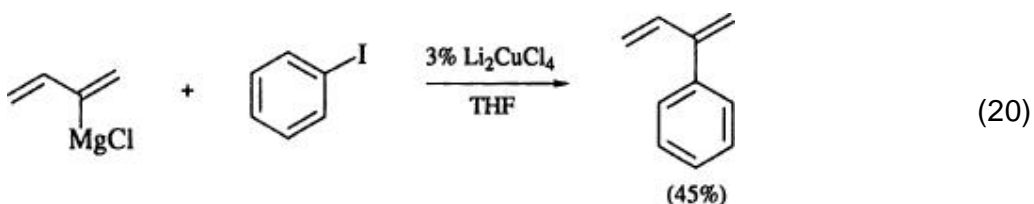
### 3.1.1.1.2. Vinyl/Aryl Halides

Copper-catalyzed Grignard additions to  $sp^2$  carbons are not facile. Substitutions of vinyl halides are better achieved through nickel-catalyzed (94) or palladium-catalyzed (95) reactions or by stoichiometric organocopper reagents (vide infra). Nevertheless,  $\text{Li}_2\text{CuCl}_4$ -catalyzed substitution of a vinyl iodide occurs with retention of olefin geometry (Eq. 19). (107)



This transformation is limited, however, to alkyl or allylic Grignard reagents, and even in these cases significant amounts of alkene (from metal-halogen exchange) are also obtained.

Copper-catalyzed substitutions of aryl halides by Grignard reagents likewise are not synthetically useful. Again, nickel (94) and palladium (95) catalysts, as with vinyl halides, are far superior in this respect. However, in one reaction, the use of  $\text{Li}_2\text{CuCl}_4$  allows substitution, albeit in moderate yield (Eq. 20). (98)

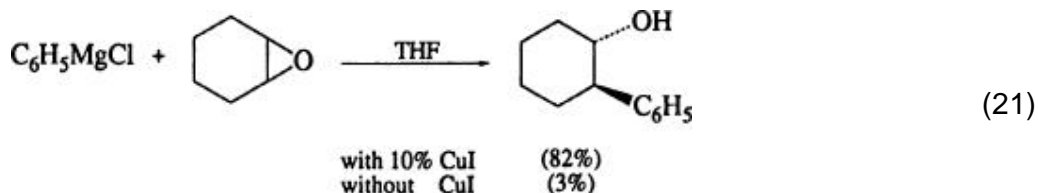


More examples of copper-catalyzed substitution reactions are listed in Table I-A.

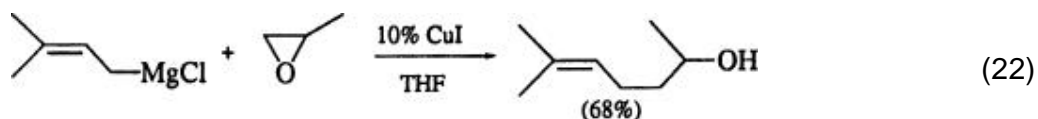
### 3.1.1.1.3. Epoxides

Ring opening of epoxides can be achieved on occasion with Grignard reagents alone; however, complications may arise due to either the Lewis acidity or basicity of the reagent. (108, 109) These problems can be remedied to a

significant degree by using catalytic amounts of copper(I) salts (Eq. 21). (110, 111)



Monosubstituted epoxides give better yields with good regioselectivity (attack at the less-hindered site) with alkyl Grignard reagents/catalytic copper(I), whereas vinyl, benzyl, or aryl Grignard reagents give comparable yields with or without copper catalysts. (110, 111) Unlike crotyl Grignard reagents (cf. Eq. 18), prenyl Grignard reagents react with epoxides (Eq. 22) exclusively at their primary positions (a attack), (111) presumably due to both stereoelectronic



and steric effects. Reactions with disubstituted epoxides are slow, but afford the *trans* alcohol stereospecifically. (110) Oxetane can also be cleaved by Grignard reagents in the presence of 10% CuX, although longer reaction times are required. (110) Care must be taken as to the quality of the Grignard reagent and the copper(I) salt, since many byproducts are formed when less pure reagents are used. (112, 113)

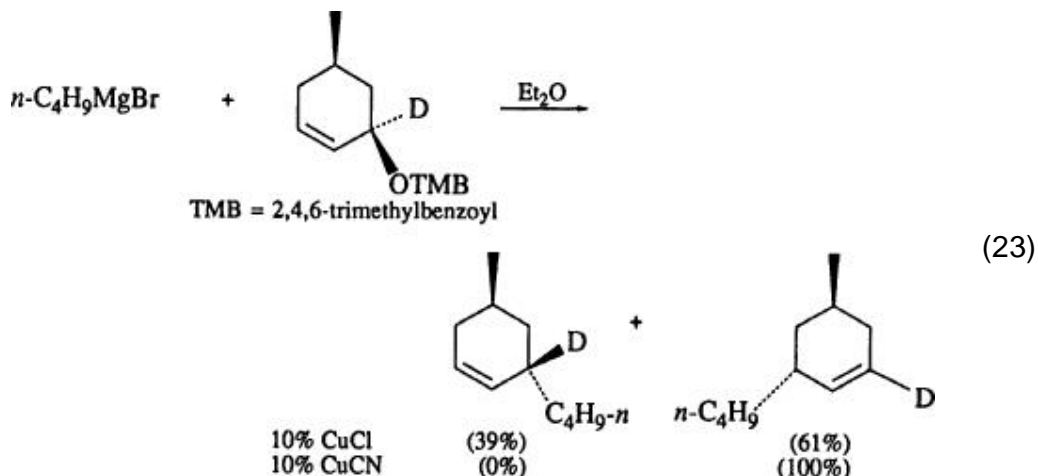
See Table I-C for additional examples.

#### 3.1.1.1.4. Allylic Substrates

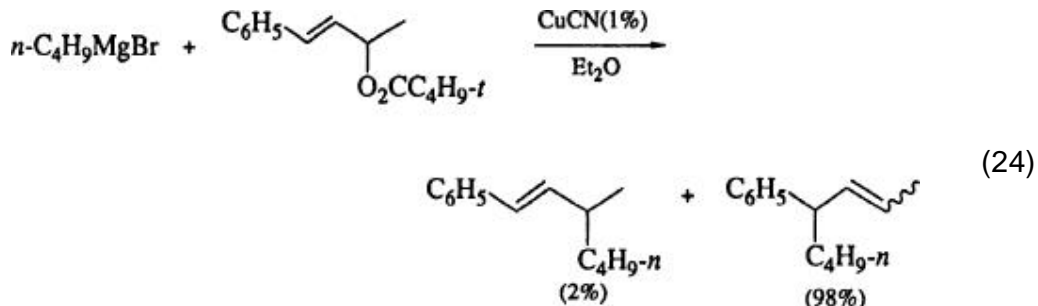
Nucleophilic displacements by Grignard reagents themselves at allylic carbons usually lead to both normal ( $S_N2$ ) and rearranged ( $S_N2'$ ) products. (92, 114) Although a catalytic amount of a copper(I) salt is likely to increase the overall yields of these reactions, the regioselectivity depends upon several parameters, including the nature of the Grignard reagent, the copper salt, and steric effects in both substrate and reagent (see Table I-B).

Through an extensive study of alkylation of allylic carboxylates, it has recently been concluded that such reactions are more efficient, both in terms of yield and regiochemistry, if the Grignard reagent/catalytic CuX system is used. With alkyl Grignard reagents, the regioselectivity of alkylation is principally governed by the nature of the copper salt: whereas copper(I) halides produce a mixture

of both  $\alpha$  and  $\gamma$  alkylated products, copper(I) cyanide affords exclusive  $\gamma$  alkylation (Eq. 23). [62a](#) This pattern holds as well for acyclic

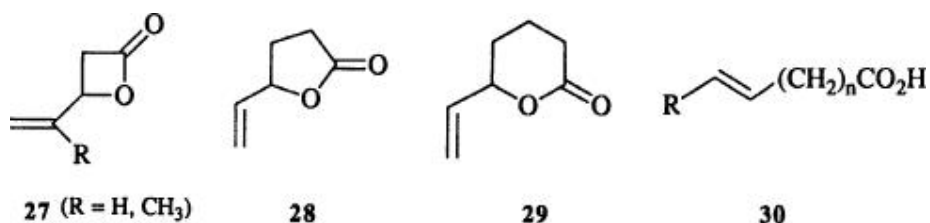


systems, as long as an alkyl Grignard reagent is involved. For example, an  $\alpha$ -methylcinnamyl pivalate derivative affords 98%  $\gamma$  alkylation using *n*-butylmagnesium bromide/1% copper(I) cyanide (Eq. 24), even though this system is thermodynamically biased to form the  $\alpha$  adduct so as to maintain styryl conjugation.



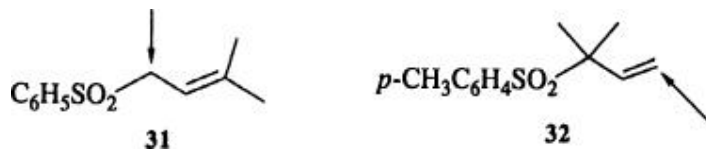
These results are in striking contrast to those obtained from stoichiometric copper reagents (both lithium and magnesium *homocuprates*). The mixed lower-order cyanocuprate  $\text{BuCu}(\text{CN})\text{MgBr}$  has been proposed as the reactive species in the catalytic processes described above, [62a](#) although the presence of a higher-order reagent  $[\text{Bu}_2\text{Cu}(\text{CN})(\text{MgBr})_2]$  was not ruled out. What remains puzzling at this time though is that aryl or vinyl Grignard reagents, even in the presence of copper(I) cyanide, show poor regioselectivity in unbiased systems. [62a](#) A further point of interest is that with butylmagnesium bromide, alkylations of both cyclic and acyclic pivalates are highly stereoselective, if not stereospecific. Thus, 1% copper(I) cyanide is sufficient to direct the alkylation to the  $\gamma$  position with 98% *anti* stereoselectivity. [62b](#) On

the other hand, 1% copper(I) chloride effects  $\alpha$  alkylation ( $S_N2$  displacement) with inversion of configuration. [62b](#)



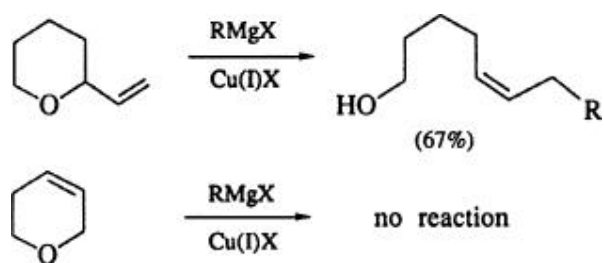
An interesting variation of an  $S_N2'$  reaction on allylic carboxylates is the use of allylic lactones [27–29](#) as substrates. Copper-catalyzed Grignard additions to these substrates occur exclusively at the vinyl terminus. Reaction of [27](#) (R = CH<sub>3</sub>) with a prenyl or geranyl Grignard reagent containing copper(I) iodide paved the way for the syntheses of homoterpenoic acids, ([115](#)) although better yields could be obtained using homocuprates. These additions appear to be general, as vinyl lactones [27](#) (R = H), ([116](#)) [28](#), ([117](#)) and [29](#) ([117](#)) are excellent precursors to alkenoic acids [30](#) of predominantly *E* configuration.

Allylic sulfones have also been extensively studied. ([118](#)) Reactions of this class of substrate with Grignard reagents in the presence of 1% copper(II) acetylacetonate are highly susceptible to steric congestion in the allylic fragment. Thus hexylmagnesium bromide attacks exclusively the less-hindered positions indicated in [31](#) and [32](#). ([118](#)) The yields of these reactions depend upon both solvent (tetrahydrofuran better than ether) and substrate;  $\alpha$ -unsubstituted allylic sulfones produce poorer yields because of competing  $\alpha$  metalation. Therefore, a higher percentage of the catalyst (10%) is required to obtain acceptable results. ([118](#)) On the other hand, yields in excess of 80% are achieved when allyl phenyl sulfones are coupled with Grignard reagents using 5% copper(II) chloride-triphenylphosphine (1:1). ([119](#))

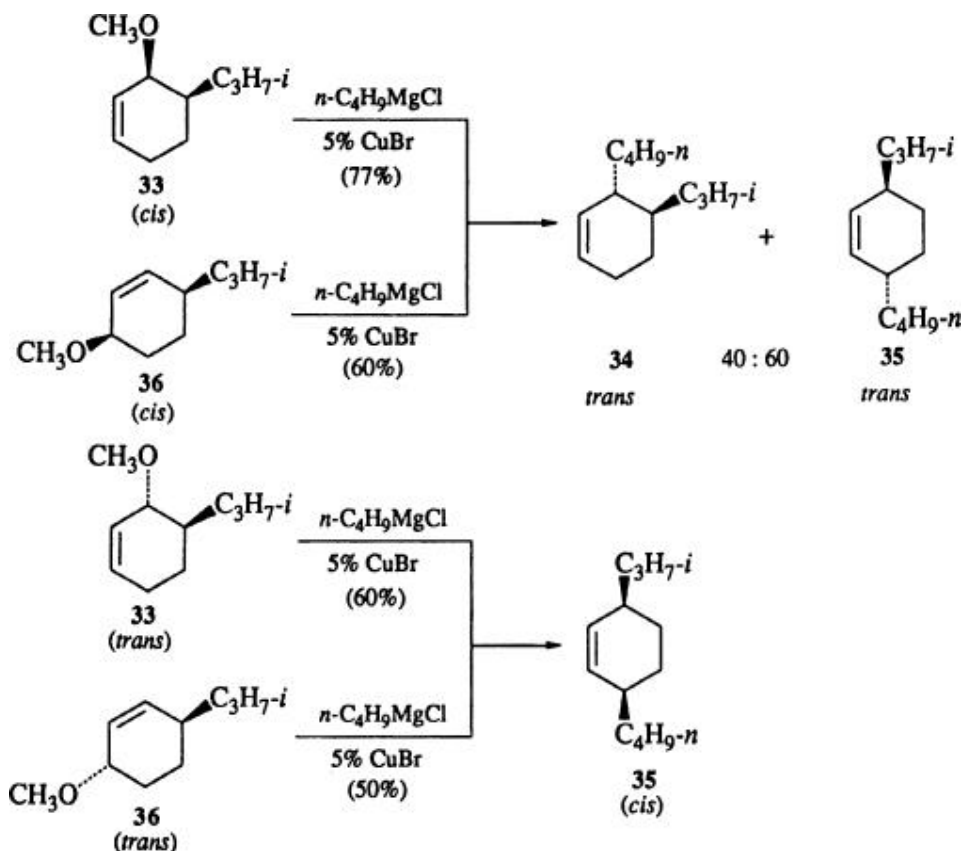


$\alpha$ -Unsubstituted allylic phosphates undergo exclusive  $S_N2$  displacement with a variety of Grignard reagents (alkyl, alkenyl, aryl) containing 5% copper(I) bromide. ([120](#)) An  $\alpha$ -methyl substituent, however, shifts the regiochemistry of alkylation toward  $\gamma$  attack ( $\gamma : \alpha = 9:1$ ), ([121](#)) an observation elegantly exploited in the synthesis of the sex pheromone of the African Monarch butterfly. ([121](#))

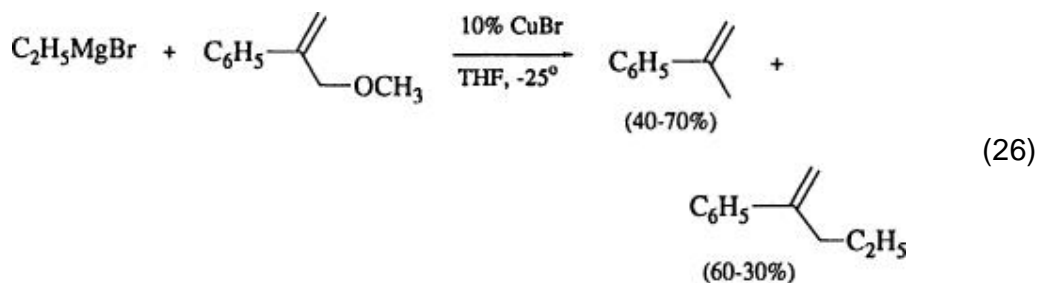
Copper-catalyzed Grignard additions to allylic acetals and allylic ethers have been studied. In the former reaction, (122) irrespective of the substitution pattern, complete allylic transposition occurs. Reactions with acyclic allylic ethers are more susceptible to steric effects, and the Grignard reagent is delivered to the less-substituted end of the allylic system. (123) Cyclic allylic ethers give interesting stereochemical information on these displacement reactions (Scheme 4). (124) The reactions of *cis*-33 and *trans*-36 are five times slower than those of *cis*-36 and *trans*-33. In the former two reactions, steric hindrance forces the methoxy group to adopt a pseudoequatorial position, whereas in the others the methoxy group can comfortably occupy a pseudoaxial configuration. Thus it appears that a pseudoorthogonal relationship between the  $\pi$  system and the nucleofuge is essential for success, further illustrated by the examples in Eq. 25. (124)



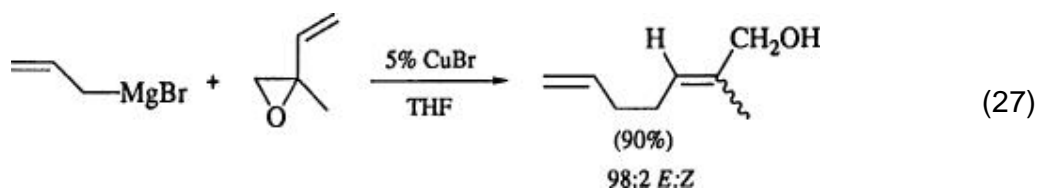
Scheme 4.



Allylic ethers with a phenyl substituent, however, undergo extensive hydrogenolysis when treated with ethylmagnesium bromide and 10% copper(I) bromide, the ratio of products varying as a function of solvent and reaction temperature (Eq. 26). (125, 126)



Alkenyl oxiranes undergo predominant  $\text{S}_{\text{N}}2'$  substitution with organocopper

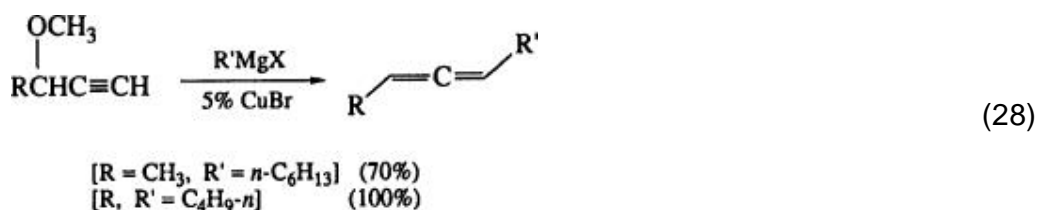


reagents. (127) A copper-catalyzed Grignard reaction of this type is synthetically quite appealing in view of the high *E/Z* ratio of products obtained, reflecting a preferential *s-trans* over *s-cis* transition state (Eq. 27). Insofar as allylic systems are concerned, therefore, leaving group aptitude falls off in the order  $\text{ArSO}_2 > \text{OAc} > \text{Cl} > \pi \text{ OR}$ , (118) with allylic epoxides representing a special class of ethers showing increased reactivity because of ring strain.

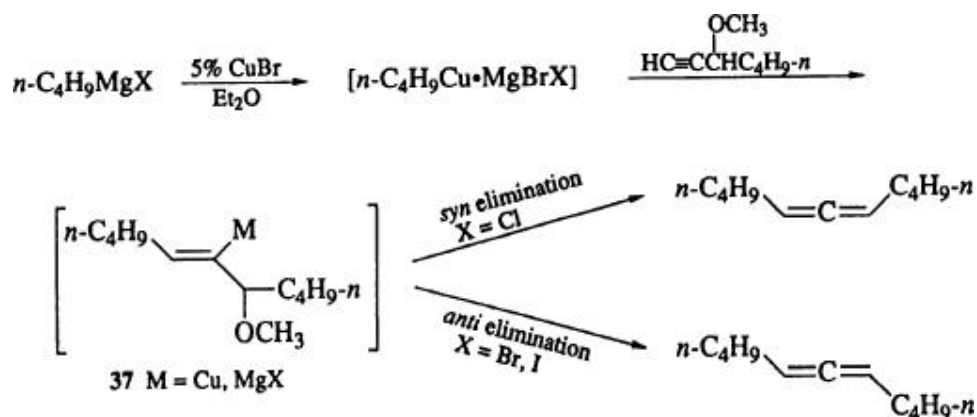
### 3.1.1.1.5. Propargylic Systems

A formal 1,3 displacement ( $\text{S}_{\text{N}}2'$  mode) of a leaving group on a propargylic carbon would give rise to an allene. Organocopper reagents are especially efficient tools for allene formation from propargylic ethers and sulfonates (Table I-D). Although use of stoichiometric copper(I) is more common in this type of transformation, a few examples exist in the literature where Grignard reagents are used together with catalytic amounts of copper(I) salts.

The overall process involving propargyl ethers as substrates to generate allenes is one which effects *anti* substitution (Eq. 28). (128, 129) Related materials of defined stereochemistry have been examined (128, 129) and the optical yields of

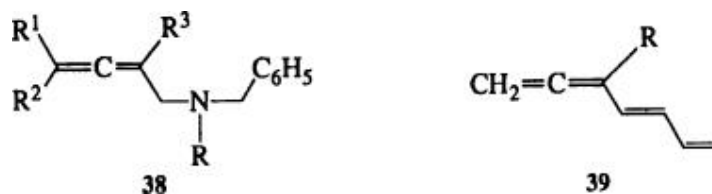


the resulting allenes used as indicators for mechanistic considerations. Initially, low optical yields (ca. 16%) were obtained, (128) although in light of the known propensity of allenes to racemize in the presence of organocopper species, (35) the results remained inconclusive. It was later shown (129) that not only can the racemization be minimized if phosphine ligands are added, but also that a *syn* carbocupration precedes the 1,2-elimination step (Scheme 5). (129) **Scheme 5.**



Quenching of intermediate **37** at  $-40^\circ$  gives the corresponding allyl ether of strictly *E* stereochemistry. More difficult to explain is the outcome when *n*-butylmagnesium chloride (as opposed to the corresponding bromide or iodide) is used, as only *syn* elimination occurs to give the overall *syn* substitution product, perhaps via the vinyl Grignard reagent (**37**,  $M = \text{MgCl}$ ) rather than a vinylcopper intermediate (**37**,  $M = \text{Cu}\cdot\text{MgBrX}$ ).

From the synthetic point of view, these allene-forming reactions can be used to prepare allenic amines, some (**38**) (**130**) of which are known inhibitors of mitochondrial monoamine oxidase. Various 1,2,4,6-tetraenes (**39**) have



also been synthesized for purposes of subsequent cyclizations to vinylcyclopentenones. (**131**, **132**) Other propargylic substrates, including tosylates, (**133**, **134**) epoxides, (**127**) acetals, (**135**, **136**)  $\beta$ -propiolactones, (**137**) and methanesulfonates, (**128**) undergo couplings via the catalytic  $\text{CuX}$ /Grignard system. The sulfonyl leaving group has been employed to produce chiral allenes. (**128**) Choice of reaction parameters can be crucial here, since in tetrahydrofuran (but not ether), propargylic substrates may be reduced by mixtures of  $\text{RMgX}$ -catalytic  $\text{CuX}$ . (**128**, **138**)

#### 3.1.1.1.6. Substitution Reactions of Other Substrates

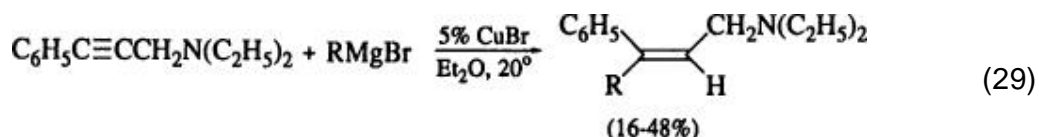
Copper(I)-catalyzed substitution reactions of allenyl ethers with Grignard reagents also produce alkynes via an apparent 1,3-substitution reaction. (**139**) *N*-Acylpyridinium salts are attacked exclusively at the 4 position when copper(I) salts are used with Grignard reagents. (**140**, **141**) Both nitrosobenzene (**142**) and carbon disulfide (**142**) also react. While acid chlorides are converted to ketones under catalytic conditions, (**143-145**) stoichiometric organocopper reagents give better yields.



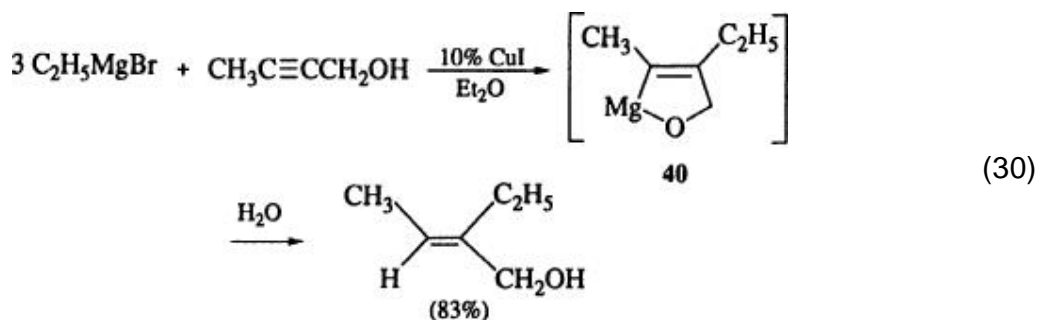
See Table I-E for related examples.

### 3.1.1.2. Carbocupration

Additions across an acetylene triple bond can be effected with a Grignard reagent alone, but require forcing conditions. Catalytic amounts of copper(I) salts allow for milder conditions and routinely afford products of *syn* addition (Eq. 29). (139) With propargyl alcohols, however, the

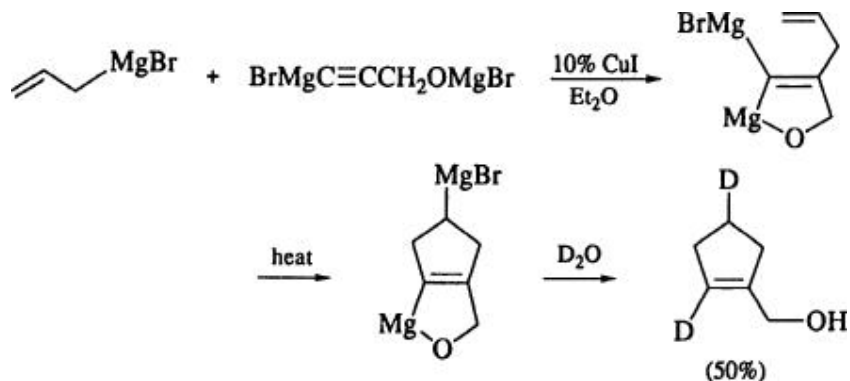


addition takes place in an *anti* fashion because of formation of a cyclic intermediate **40** (Eq. 30). (146, 147) This pattern is followed by Grignard reagents, irrespective of the presence of copper(I) salts.



An interesting variation of this carbometalation process concerns the copper-catalyzed addition of allyl magnesium bromide across the dianion of propargyl alcohol leading ultimately to (labeled) cyclic allylic alcohols (Scheme 6). (148)

Scheme 6.



Acetylene itself can be carbometalated with Grignard reagents in the presence of Cu(I); however, the reaction stops after ca. 40% completion. (149)

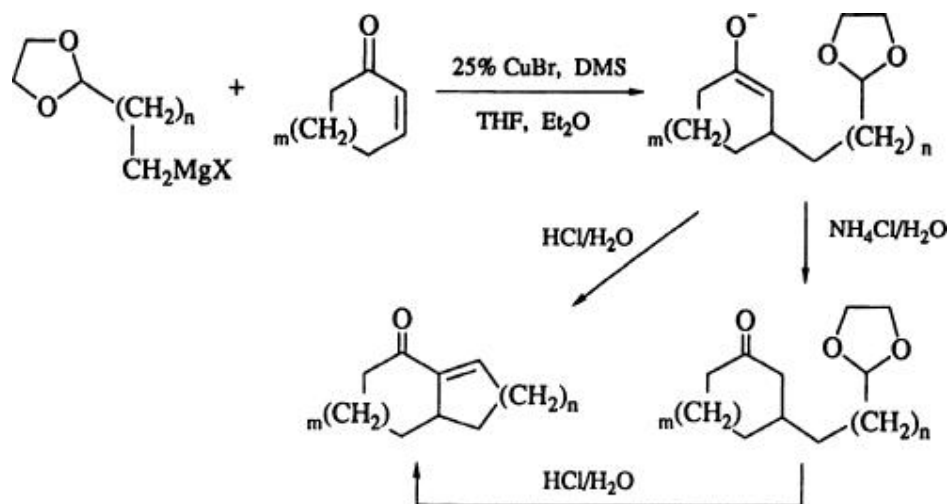
Stoichiometric copper reagents, on the other hand, effect carbocupration with ease and excellent selectivity.

### 3.1.1.3. Conjugate Additions

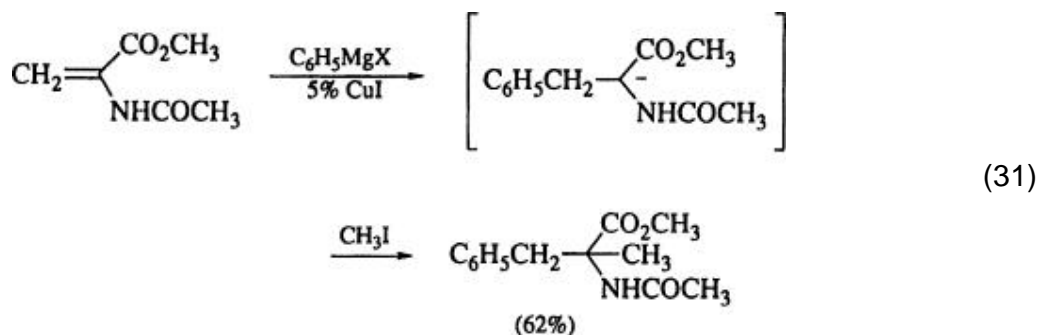
Copper-catalyzed additions of Grignard reagents to  $\alpha$ ,  $\beta$ -unsaturated ketones were first shown to occur in a 1,4 fashion in 1941. (150) The advent of stoichiometric copper reagents, because of their coupling efficiency and lower basicity, has diverted attention somewhat from the use of Grignard reagents in this context. Where permitted in terms of functionality present in the educt, however, the catalytic CuX/Grignard reagent approach is often a popular first choice (see Table I-F).

1,4 Additions of acetal-containing Grignard reagents with catalytic CuX and dimethyl sulfide (DMS) form the basis of a novel annulation process (Scheme 7). (143-145) By varying the chain length in the Grignard reagent, annulation of cyclic enones with either five- ( $n = 1$ ), six- ( $n = 2$ ), or seven-membered ( $n = 3$ ) rings can be realized. The sequence can be executed in one pot with yields ranging from 40–80%.

Scheme 7.

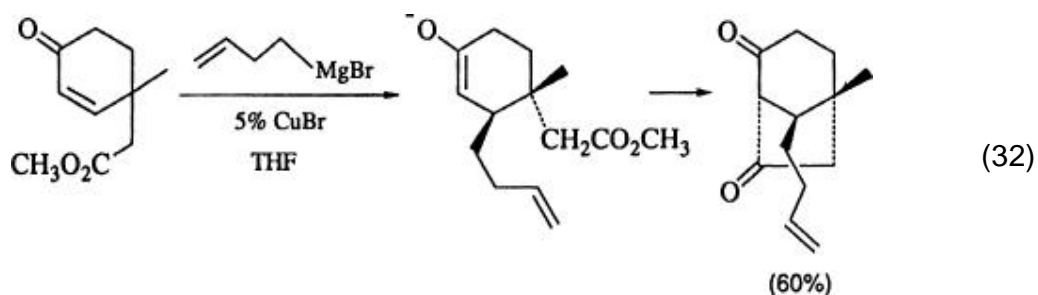


2-Acetamidoacrylic esters participate in copper-catalyzed additions of Grignard reagents (Eq. 31). (151) The conjugate addition is facile, and the intermediate carbanion can be trapped with methyl iodide to give  $\alpha$ -substituted

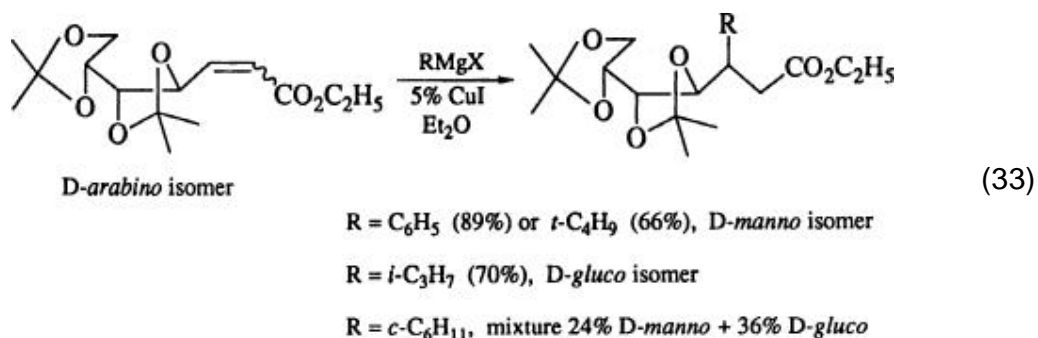


amino acid derivatives. The reaction is somewhat medium-dependent, with best results (60–80% yields) obtained in mixed solvents (tetrahydrofuran–ether–benzene). Interestingly, lower-order lithio cuprates ( $\text{R}_2\text{CuLi}$ ) give either no 1,4 addition or complex product mixtures. (151)

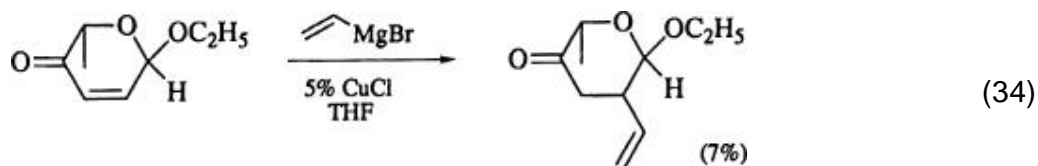
Intramolecular trapping of an incipient enolate by an internal electrophile, following a copper-catalyzed Grignard addition to an enone, can provide rapid access to elaborated carbon frameworks. This concept has been applied to a quick entry into the gibberellic acid skeleton (Eq. 32). (152)



Copper-catalyzed conjugate additions to an enoate prepared from a carbohydrate precursor lead to interesting stereoselectivity. Thus starting with a pure diisopropylidene *D-arabino* enoate, reactions of phenyl and *tert*-butyl Grignard reagents give 1,4-addition products of strictly *D-manno* configuration. (153)

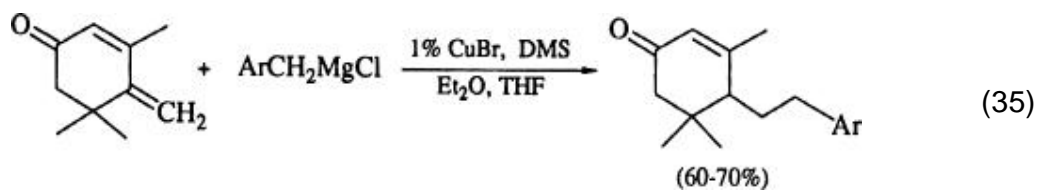


Surprisingly, isopropylmagnesium bromide produces the D-*gluco* isomer, while the reaction with cyclohexyl Grignard is nonselective (Eq. 33). (153) Similar stereoselectivity is also evident in a cyclic system, where the approach of the Grignard reagent is directed to the face away from the ethoxy group at the anomeric center (Eq. 34). (154)

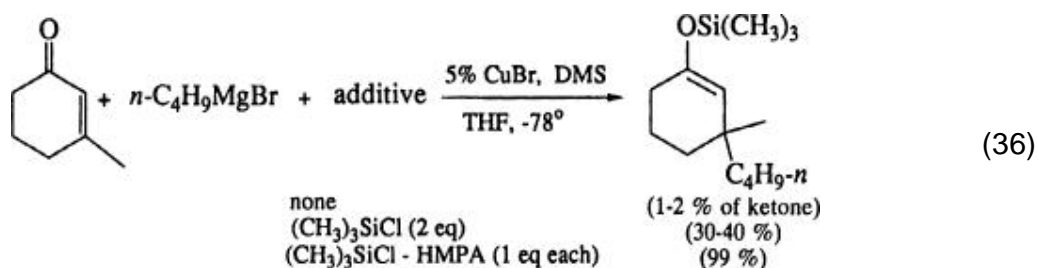


Addition-eliminations in β-chlorocinnamates can be highly stereoselective in copper-catalyzed Grignard reactions, depending upon the stereochemistry of the starting ester. (155) The *Z* isomer reacts with retention of configuration, whereas reaction of the corresponding *E* isomer shows no stereochemical preference. (155)

Benzyl Grignard reagents add to dienones in a 1,6 sense when combined with 1% copper(I) bromide dimethyl sulfide (Eq. 35). (156) Only minor amounts of 1,2 and 1,4 adducts are observed. Without copper catalysts, however, these become the major products.

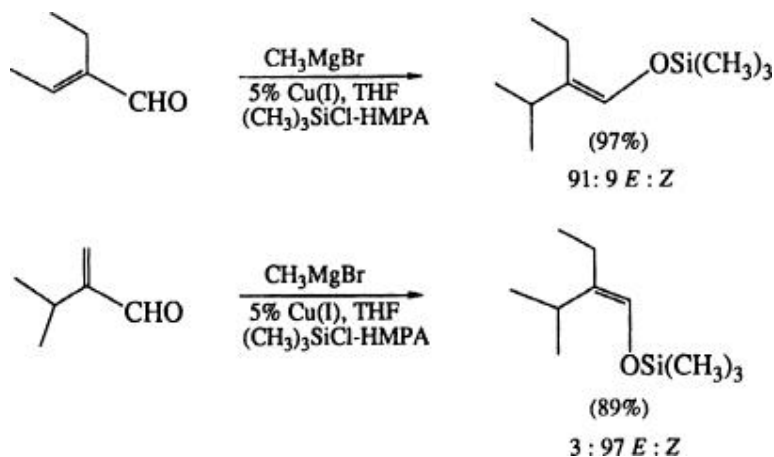


The value of the catalytic CuX/Grignard reagent mixture for inducing Michael reactions has been boosted significantly by the recent finding that chlorotrimethylsilane/hexamethylphosphoric triamide (HMPA) in THF leads to highly accelerated additions (Eq. 36). (157) Silyl enol ethers can be made from  $\alpha$ ,  $\beta$ -unsaturated aldehydes with excellent control of olefin geometry. (157) Thus,

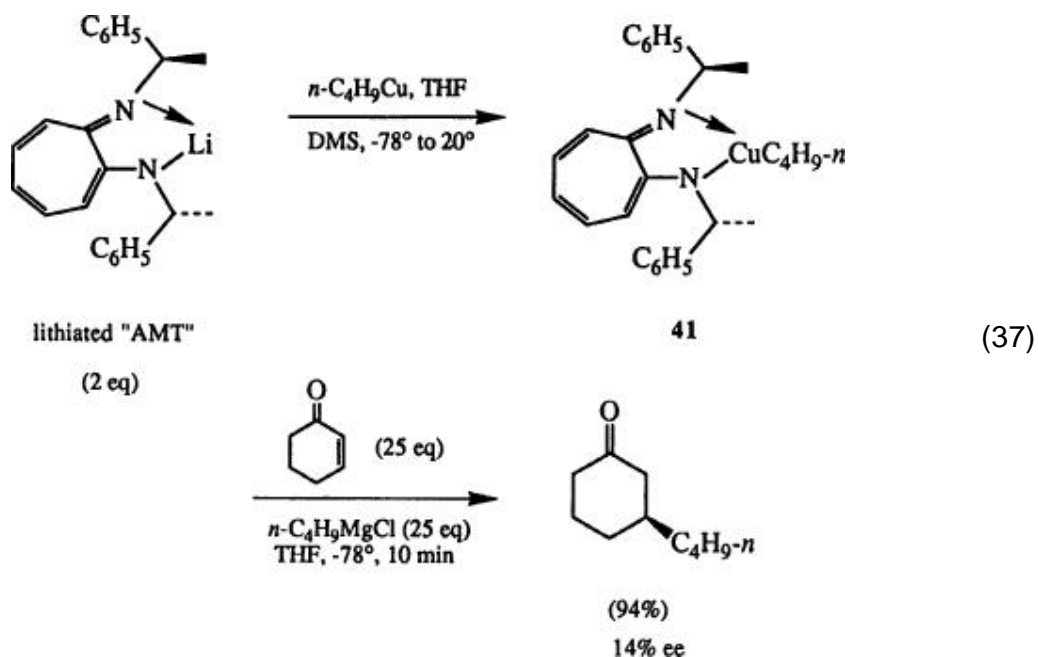


both (*E*) and (*Z*) enol silyl ethers of a particular aldehyde are available by this method (Scheme 8). (157)

Scheme 8.



A very recent and promising development for effecting chiral induction in conjugate additions involves prior complexation of RCu with a catalytic amount of a novel nonracemic, lithiated aminotroponimine (AMT) to form **41** in situ. Simultaneous addition of tetrahydrofuran solutions of *n*-butylmagnesium chloride (25 equivalents) and cyclohexenone at  $-78^\circ$  over a 5-minute period leads to the conjugate adduct (Eq. 37). 158a Although the reported ee is low, further refinements in the catalyst system increase the chiral efficiency of the coupling substantially. 158b

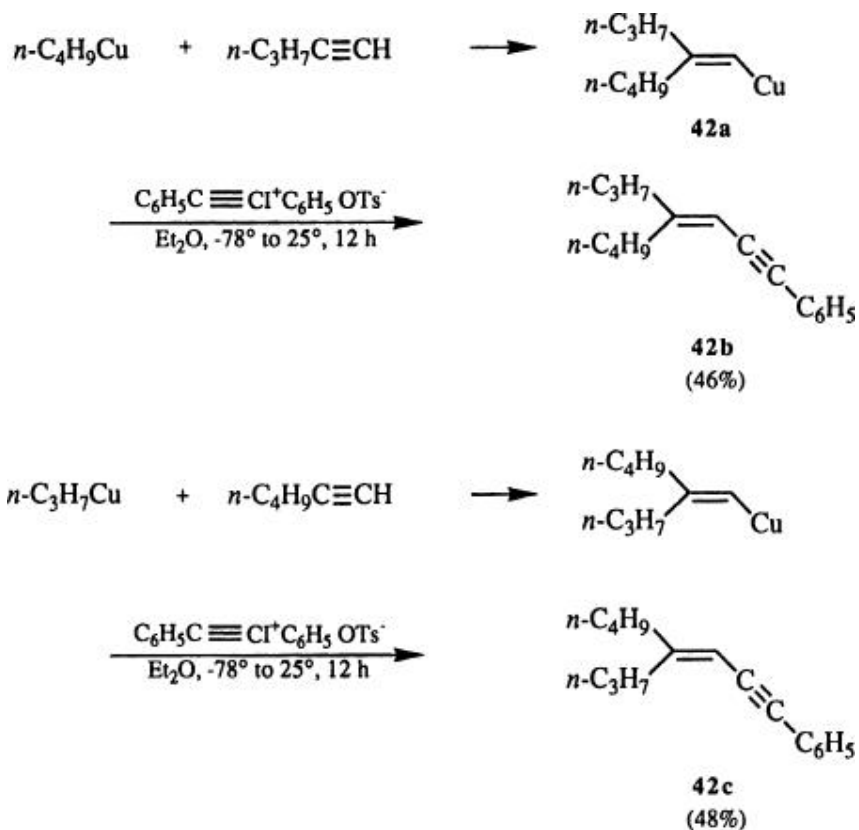


### 3.1.2. Stoichiometric Cuprate Reactions

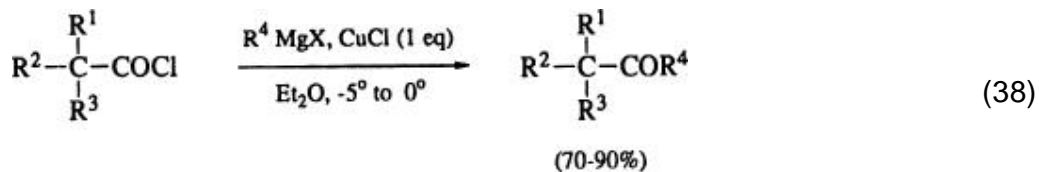
#### 3.1.2.1. Substitution

Displacement reactions by cuprates formed in situ from (usually) an excess of a Grignard reagent and a catalytic quantity of a copper(I) halide or  $\text{Li}_2\text{CuCl}_4$  can often result in quite satisfactory yields of products with newly formed carbon–carbon bonds. Hence, relatively few examples have materialized where 0.5 equivalent of copper(I) halide is called for in reactions at either  $sp^3$  or  $sp^2$  carbon centers (see Table II-D). Couplings with acetylenic halides, however, are best performed with  $\text{RCu-MgX}_2$  to obtain good yields (60–80%) of disubstituted alkynes. (159) Conjugated enynes are now available via a streamlined route involving coupling between vinyl–copper reagents and alkynyl bromides/iodides (159) or alkynyliodonium tosylates. (160) Carbocupration of a terminal acetylene with  $\text{RCu}$ , which affords the requisite neutral organometallic **42a**, reacts with phenylalkynyliodonium tosylate to give product **42b** with virtually complete control of double-bond geometry. (160) Especially noteworthy is the opportunity for choosing the resulting olefin stereochemistry (compare **42b** and **42c**) simply by reversing the order in which the alkylcopper is added to the alkyne. (160) This new method nicely complements the alternative palladium-catalyzed procedures (161) as a route to this functionality.

Stoichiometric  $\text{CuX/Grignard}$  reagent is often applied to reactions of carbonyl-containing



substrates, notably with acid halides (see Table II-A). Even highly hindered acid chlorides can be transformed to diversely substituted

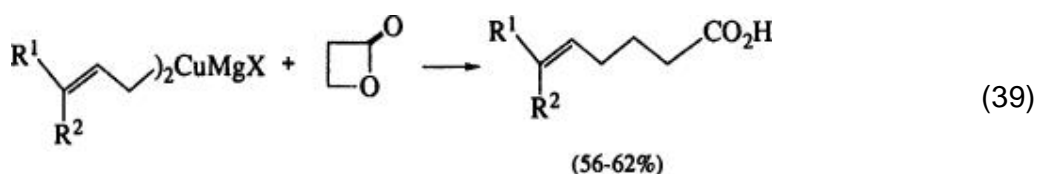


ketones using 1 equivalent each of CuCl and a Grignard reagent (Eq. 38). (162) Likewise, mixed cuprates [e.g., R(CH<sub>3</sub>)CuMgBr] prepared from methylcopper and RMgBr, efficiently transfer the Grignard-derived organic ligand to acid chlorides to form ketones in high yields. (163) The methyl group is the most effective nontransferrable ligand compared with thiophenyl, *tert*-butoxy, or 3,3-dimethylbutynyl groups. (163)

Thiocarbonyl compounds, such as carbon disulfide (142) and dithioesters, (164) are susceptible to exclusive carbophilic attack by Grignard-derived organocopper or cuprate reagents. By contrast, Grignard reagents alone normally follow a thiophilic pathway. (165)

While nucleophilic ring opening of  $\beta$ -propiolactones *en route* to  $\beta$ -substituted

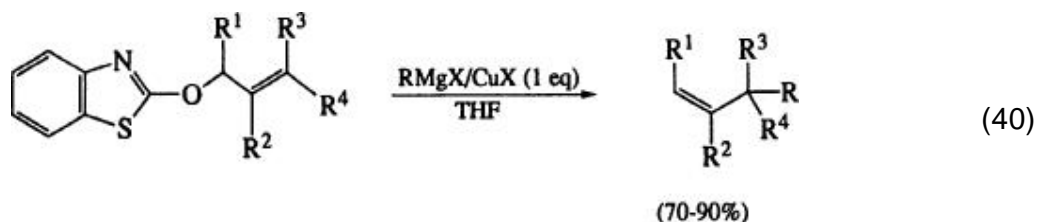
propionic acids is conveniently carried out under catalytic CuX/Grignard conditions, (166, 167) vinylic and especially allylic Grignards give unsatisfactory results. In fact, allylic Grignards attack the carbonyl group of the lactone, and virtually no  $\beta$  substitution is observed under copper-catalyzed conditions. (167) On the other hand, the use of diallylmagnesium cuprates, formed from allyl Grignards and 0.5 equivalent of copper(I) salts, provide 56–62% of the desired  $\beta$ -substituted products. (167, 168) Similarly, divinylmagnesium cuprates give better yields (85%) as compared to those realized (59%) via the catalytic mode. (167, 168) Magnesium cuprates appear to be superior to lithium cuprates in ring-opening reactions of  $\beta$ -propiolactones (Eq. 39). (168)



#### 3.1.2.1.1. Allylic Substrates

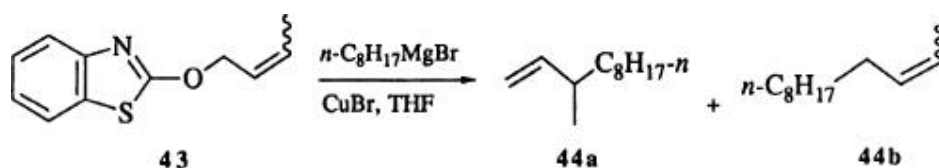
Although most allylic substitutions by Grignard reagents are copper catalyzed, a number of workers have utilized stoichiometric amounts of copper salts for these purposes (see Table II-B). Magnesium cuprates ( $R_2CuMgX$ ) displace allylic pivalates in a highly regioselective fashion with predominant formation of  $S_N2'$  products. (169) Lithium cuprates show complementary behavior in forming the product of direct displacement ( $S_N2$ ) from the same substrates. (169) Displacement reactions on allylic pivalates fail, however, when exposed to  $RCu \cdot MgX_2$ , an observation attributed to the relatively insoluble nature of many  $RCu$  species. (62) On the other hand, equimolar mixtures of a Grignard reagent and copper(I) cyanide are quite efficient owing to the lack of metathesis with this salt, (62) thereby generating a more reactive mixed cuprate of the type  $RCu(CN)MgBr$ .

Benzothiazol-2-yl allyl ethers constitute an allylic system with a leaving group possessing sites of potential coordination. Organocopper reactions with this system are highly regioselective (98:2), giving rise to  $S_N2'$  products (Eq.





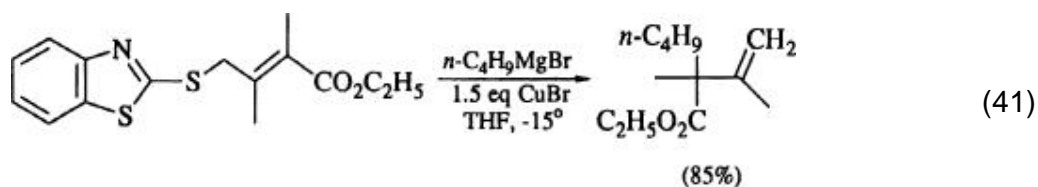
40). (170, 171) Moreover, these displacements appear to be independent of steric demands of the substituents on the allyl framework. The product olefins are obtained exclusively as the *E* isomers, underscoring this stereochemically controlled pathway. 171a However, there are exceptions, as with the crotyl ether derivative 43. Factors such as substrate–copper salt contact time play a prominent role in controlling the percentages of products 44a and 44b. Short exposure times prior to addition of the Grignard reagent lead exclusively to the  $S_N2'$  product 44a. Longer periods of aging (6 hours) prior to addition of the Grignard reagent afford the  $S_N2$  adduct 44b predominantly (95% 44b:5% 44a). This anomaly has been rationalized by invoking two different intermediates,



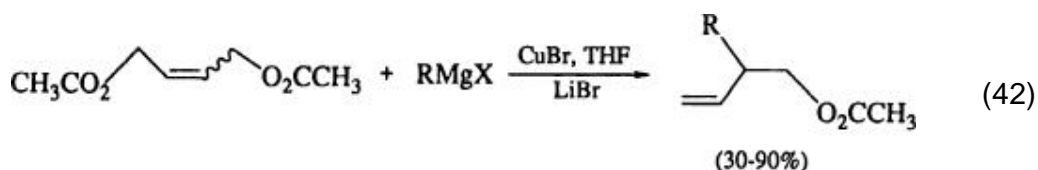
45a and 45b, for the two sets of reaction conditions, respectively. In the former, the readily derived RCu forms a  $\pi$  complex with the substrate, and proximity-induced delivery of the “R” residue gives the  $S_N2'$  product. Alternatively, if 43 and copper(I) bromide are allowed sufficient time to interact, complex 45b is formed and is attacked by the Grignard reagent at the less-hindered  $\alpha$  site. Complexes of type 45b have been independently synthesized, 171b and their reactions with Grignard reagents do indeed give  $S_N2$  products, thus adding credence to these hypotheses. 171a



Benzothiazol-2-yl allyl thioethers are also well-behaved substrates. The  $S_N2'$  products are likewise exclusively obtained from an intermediate similar to 45a. 172a However, this reaction is solvent dependent, with ether favoring the  $S_N2'$  pathway, whereas tetrahydrofuran encourages  $S_N2$  delivery. Placement of a carboalkoxy group on the double bond, as in a  $\gamma$ -(benzo-thiazol-2-thio)-substituted  $\alpha, \beta$ -enoate (Eq. 41), does not direct  $\text{RCu}\cdot\text{MgX}_2$  toward 1,4 addition, this pathway being completely overridden by the 1,3-displacement mode. 172b

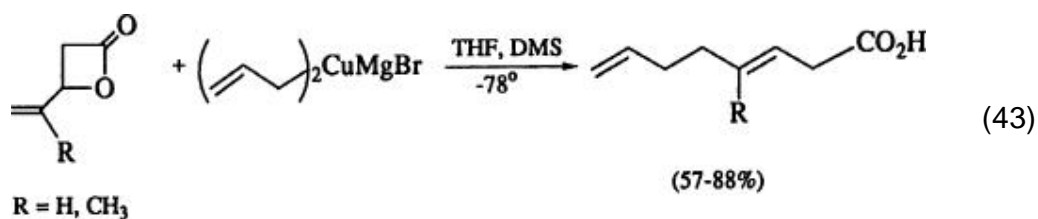


Allylic acetates are among the least useful substrates for reactions with catalytically formed organocopper reagents, the main drawback being competing attack at the carbonyl center. (62, 169) However, an equimolar mixture of Grignard reagent and  $\text{LiCuBr}_2$  [prepared from lithium bromide and copper(I) bromide]

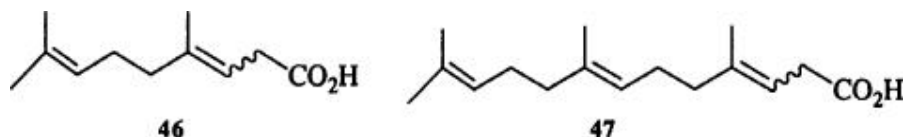


effectively reacts with allylic diacetates to give monosubstituted products of the  $S_N2'$  variety exclusively when run in tetrahydrofuran (Eq. 42). (173) Use of a medium rich in ether leads to a mixture of  $S_N2$  and  $S_N2'$  isomers.

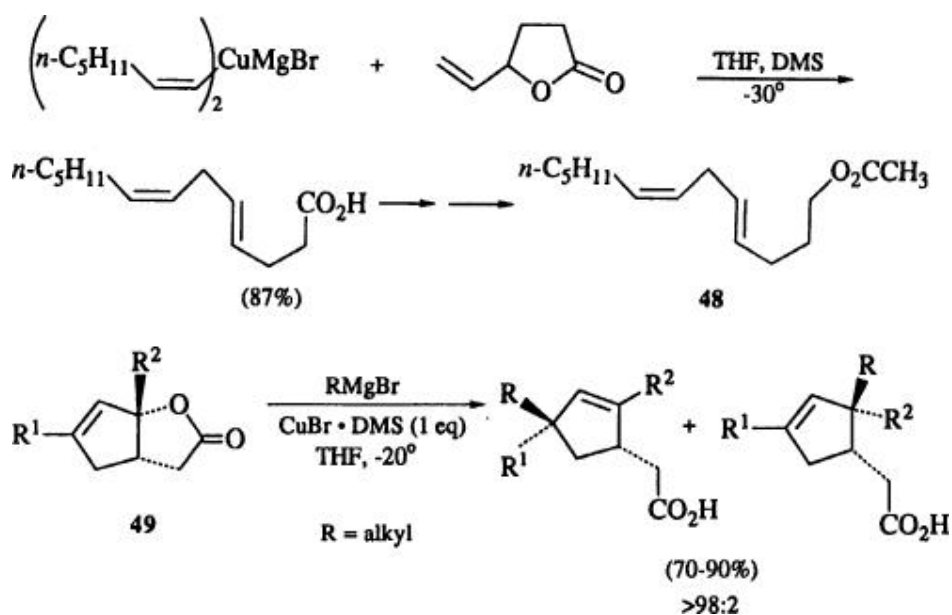
As with copper-catalyzed Grignard additions to  $\beta$ -vinyl- $\beta$ -propiolactones, diorganomagnesium cuprates react readily to give good yields of 3-alkenoic acids, predominantly with *E* stereochemistry (Eq. 43). (115, 116) With allylic Grignards as precursors, however, synthetically useful yields are obtained only



with diallylmagnesium cuprates. (115, 116) This methodology has been utilized to prepare homoterpenoic acids 46 and 47. (116)

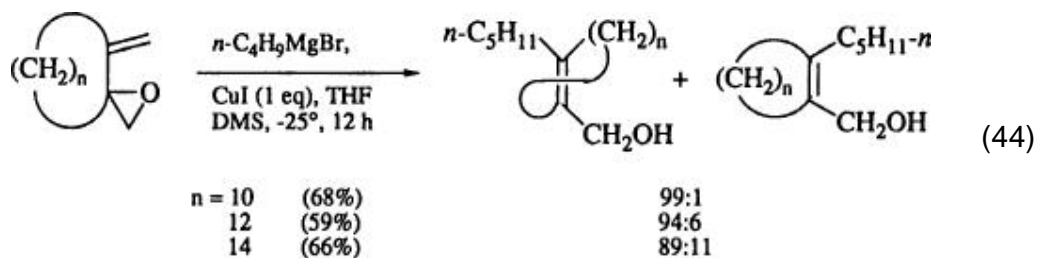


Allylic displacements can also be carried out on  $\gamma$ -vinyl- $\gamma$ -butyrolactone and  $\delta$ -vinyl- $\delta$ -valerolactone, (117) using  $R_2CuMgX$ . A simple synthesis of the tridecadienyl acetate **48**, the sex pheromone of *phthorimaea operculella*, relies on vinylcopper addition to the electrophilic  $\beta$  position of a vinylbutyrolactone. (117) The vinyl appendage may also be contained within a ring, as found for the  $RCu\cdot MgBr_2$ -mediated opening of cyclopentafuranones, **49**. These  $S_N2'$

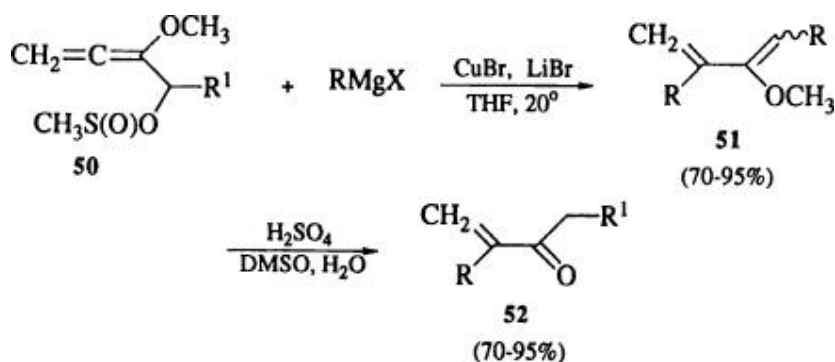


additions are both highly regio- and stereoselective, irrespective of the substitution pattern in the substrate. (174) Products reflect the normal preponderance of *anti* opening, (62) and thus are formed in a virtually pure stereoisomeric state. (174) Such is not the case in reactions of **49**, when either catalytic quantities of copper(I) salts are used, or lithium cuprates replace this stoichiometric Grignard reagent-based methodology.

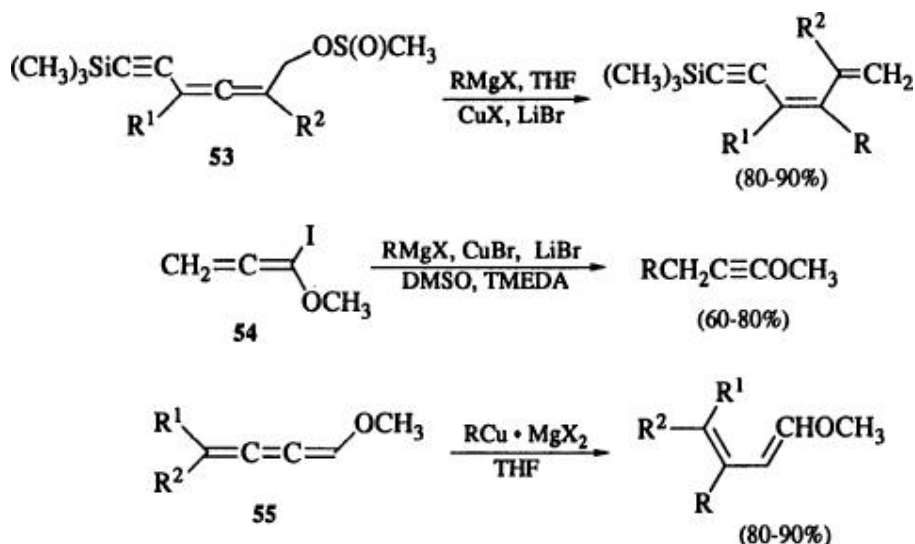
In sharp contrast to the typical *anti*  $S_N2'$  attack found in rigid cycloalkene epoxides, the more flexible 10-, 12-, and 14-membered cycloalkylidene oxiranes are susceptible to *syn*  $S_N2'$  opening with  $RCu\cdot MgX_2$ . (175) Stereoselectivities ranging from 9:1 to 99:1 are observed, with the smaller ring size (10 carbons) displaying the strongest preference for *syn* approach (Eq. 44).



Allylic substitution with Grignard reagents and 1 equivalent of a copper salt can be extended to compounds in which the double bond is part of a cumulene. The product dienes **51**, formed from consumption of  $\alpha$ -allenic methanesulfinates **50**, can be hydrolyzed with ease to give  $\alpha$ ,  $\beta$ -unsaturated ketones **52**. (176) It is essential here that  $\text{RCu}\cdot\text{MgX}_2$  be used, since cuprate reagents attack at sulfur. Addition of lithium bromide (1 equivalent) to copper(I) bromide, prior to introduction of  $\text{RMgX}$ , also has a beneficial effect on the yield and reaction rate. (176)



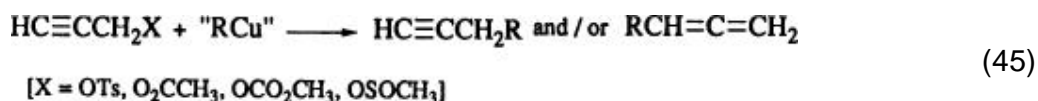
Formal 1,3 substitution is also reported for several other allenic and cumulenenic systems (Table II-B), including as examples acetylenic derivative **53**, (177) the iodomethoxypropadiene **54** [in the presence of dimethyl sulfoxide (DMSO) and tetramethylethylenediamine (TMEDA)], (178) and the methoxybutatriene **55**. (179, 180)



### 3.1.2.1.2. Propargylic Substrates

Acetylene derivatives with a leaving group at the propargylic center react with Grignard-derived organocopper reagents to produce allenes (see Table II-C). This scheme represents one of the most versatile routes to allenes of predictable geometry. Several leaving groups can be used for such purposes, namely tosylates, (134, 181) acetates, (182) and methanesulfonates. (183, 184) The organocopper component is usually  $\text{RCu}\cdot\text{MgX}_2$ , with or without added lithium bromide. (185) As with cumulenes, magnesio cuprates are not commonly used here, especially with methanesulfonates, for which predominant attack at sulfur is observed. (186)

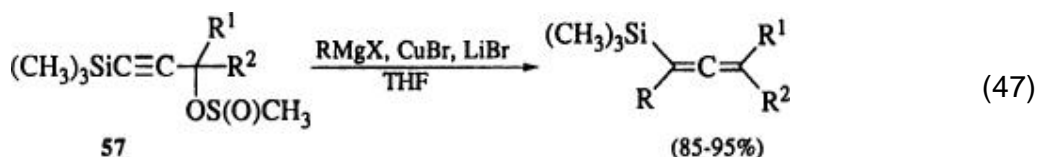
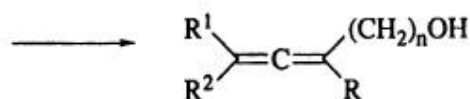
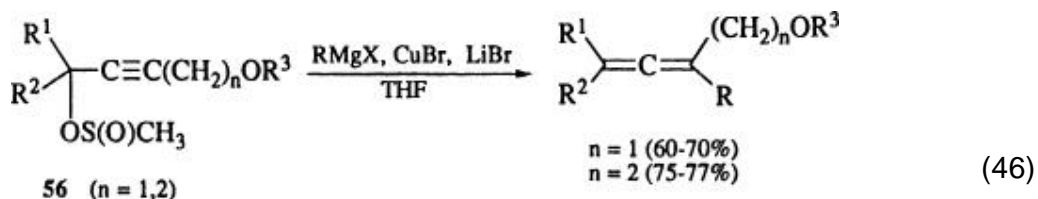
Factors affecting the reactions of propargylic substrates with organocopper species have been examined in some detail. (182) Two major displacement products can be envisioned, depending upon regiochemical biases (Eq. 45). When



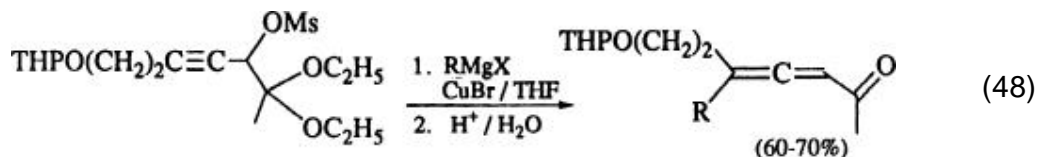
either  $\text{R}_2\text{CuMgBr}$  or  $\text{RCu}\cdot\text{MgX}_2$  is used, irrespective of solvent (ether or tetrahydrofuran) and substitution pattern of the substrate, mixtures of  $\alpha$ -substituted acetylenes and allenes are formed, with the former predominating. However, when the copper reagent is derived from an equimolar mixture of a Grignard reagent and copper(I) bromide·lithium bromide complex, and the reaction performed in tetrahydrofuran, near-exclusive formation of the allene is observed. Remarkably, there is no reaction in ether. This highly regioselective

pathway is not hampered by the presence of substituents at the acetylenic terminus and is followed irrespective of the departing moiety (e.g., acetate, carbonate, or tosylate). (182) This dramatic impact of lithium bromide on the reactivity patterns of organocopper reagents derived from Grignard reagents (185) (but not to the same extent on lithium cuprates (187)) has been applied to propargylic displacement reactions and carbocuprations.

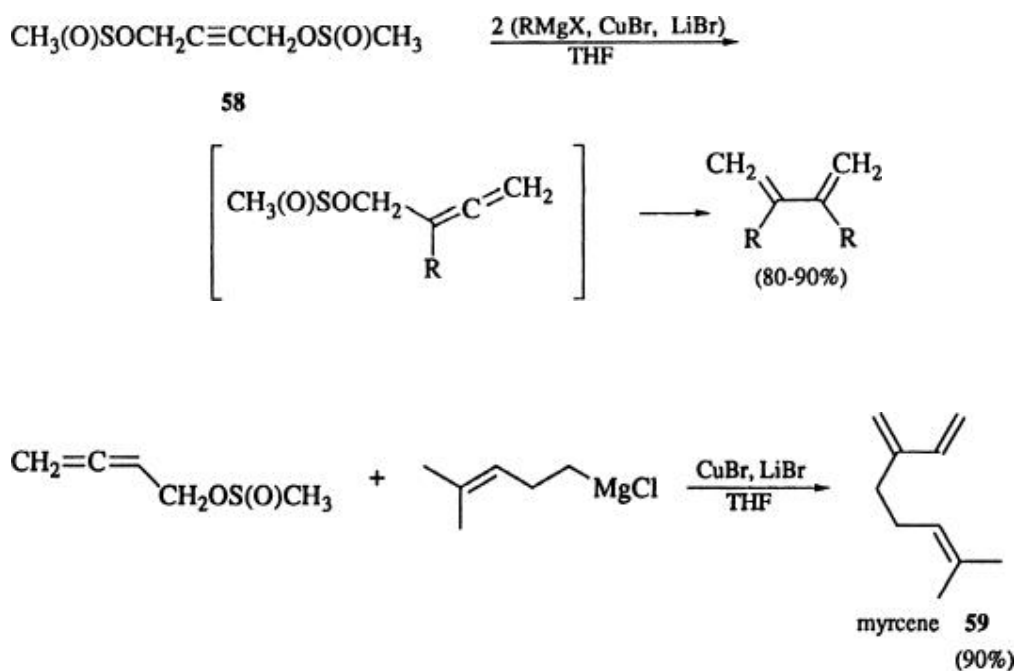
The use of methanesulfinate as a leaving group, together with the copper(I) bromide·lithium bromide complex as the source of copper(I), has eliminated most of the potential complications associated with Grignard reactions with propargylic substrates. The advantages of the methanesulfonates include higher yields, ease of preparation, and virtually complete regiochemical control (1,3 addition). For example, methanesulfonates **56** and **57** react to afford high yields of allenic alcohols (188) and trimethylsilyllallenes, (183) respectively (Eqs.



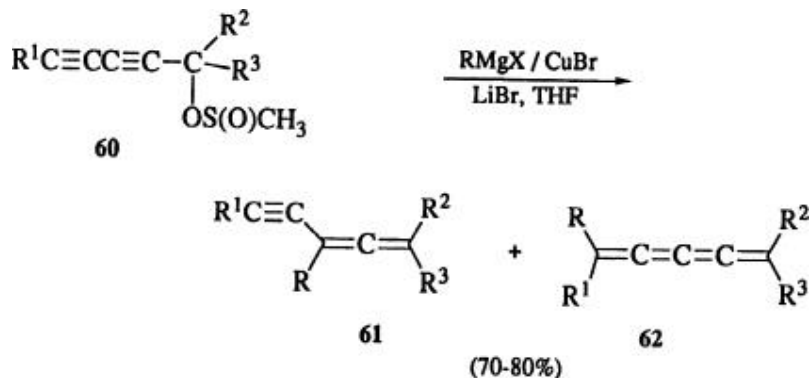
46 and 47). Since cuprates  $\text{R}_2\text{CuMgX}$  are occasionally not compatible with this functionality, the option to enlist methanesulfonates (mesylates) still exists, (183) as found in a short two-step sequence to  $\alpha$ -allenic ketones (Eq. 48). (189)



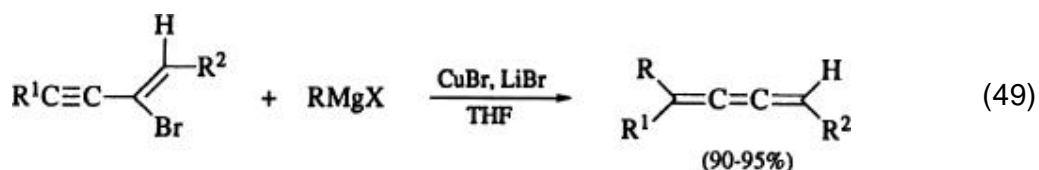
Symmetrically substituted 1,3-dienes are produced in good yields from bis(sulfinate) **58**. (29) The reaction of **58** with 2 equivalents of  $\text{RCu-MgX}_2\cdot\text{LiBr}$  cannot be stopped after the first substitution and hence loses its potential for introduction of two different R groups in a one-pot operation. The problem can be somewhat mitigated by using a preformed methanesulfinate from an  $\alpha$ -allenic alcohol, (188) and this strategy has been exploited in a short synthesis of myrcene (**59**). (29)



The regiochemistry of Grignard attack on 2,4-pentadiynyl methanesulfonates **60** in the presence of  $\text{LiCuBr}_2$  depends upon both steric effects in the substrate and the Grignard reagent-derived organocopper species. (184) Thus when  $\text{R}^1$  is hydrogen, attack is regiorandom, and both allenyne **61** and pentatetraene **62** are formed. However, when  $\text{R}^1$  is a bulkier methyl or trimethylsilyl group, steric effects direct organocopper attack in a 1,3 sense, giving rise to **61** with >95% selectivity. On the other hand, if  $\text{R}^2$  and  $\text{R}^3$  are bulky groups, then 1,5 attack to afford **62** is favored for hindered copper species. (184)

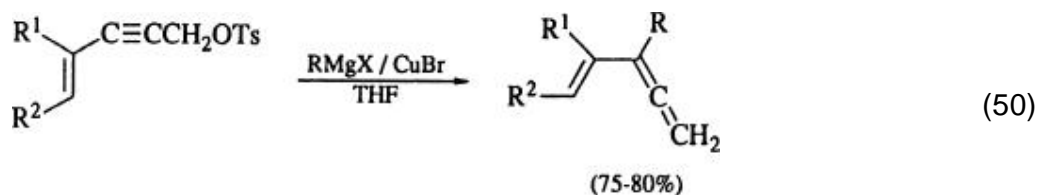


Geometrically pure butatrienes are obtained by the reactions of 3-bromo-3-alken-1-ynes with LiCuBr<sub>2</sub>-modified Grignard reagents. Although the reaction occurs with complete retention of the substrate configuration in



the product, it is limited to the use of secondary and tertiary Grignard reagents (Eq. 49). (190)

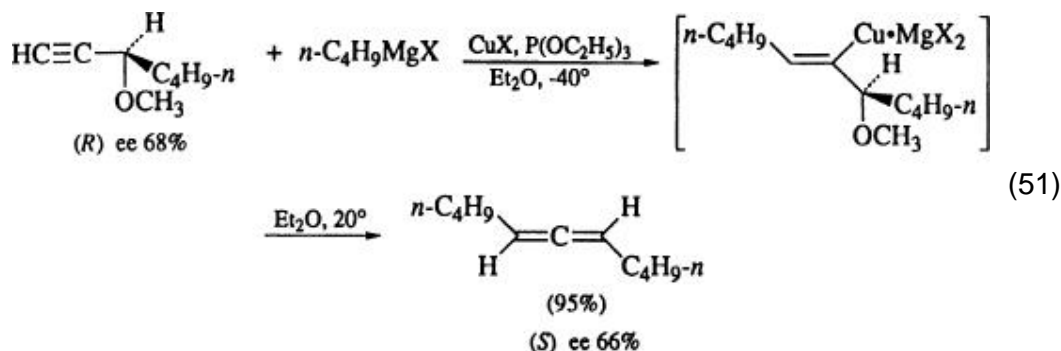
Vinylallenes, which are useful precursors to cyclopentanones, can be readily prepared by organocopper displacements from propargylic substrates (Eq. 50). (134, 181)



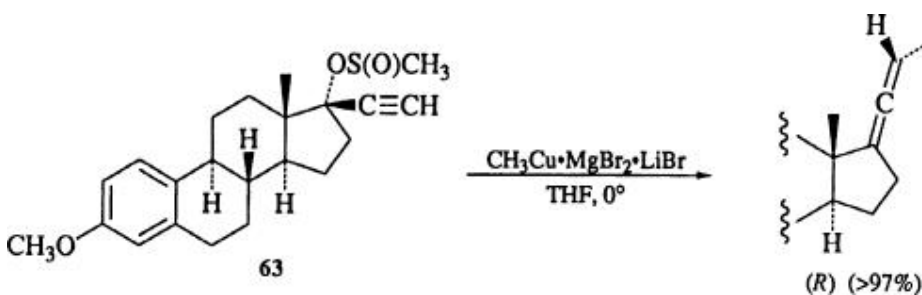
Organocopper-induced 1,3 substitution of acyclic propargylic systems takes place exclusively in an *anti* fashion. Optically active allenes have been synthesized from chiral precursor propargylic methanesulfonates, (191) taking advantage of the stereospecificity of these couplings. With poorer leaving groups such as methoxy, an initial *syn* carbocupration followed by *anti*



elimination has been proposed (Eq. 51); the overall process, however, is still tantamount to *anti* addition. (135)

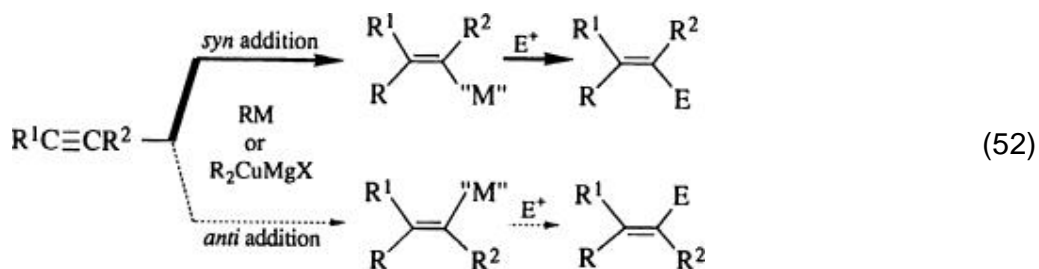


Akin to acyclic propargylic systems, the methanesulfinates derived from both epimers of 17-ethynyl-17-hydroxyestrone undergo 1,3-substitution exclusively in the *anti* mode, illustrated for the  $\alpha$  epimer **63**. (186, 192)

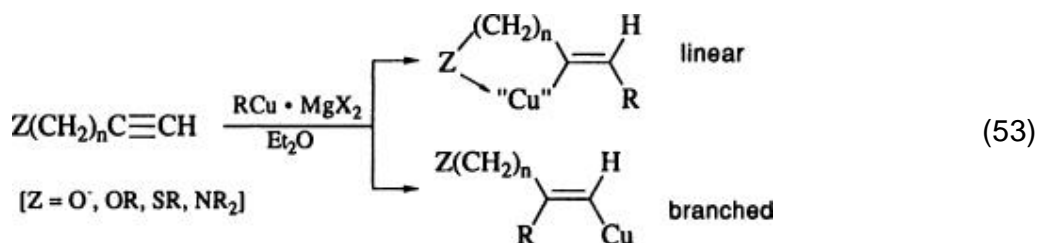


### 3.1.2.2. Carbocupration

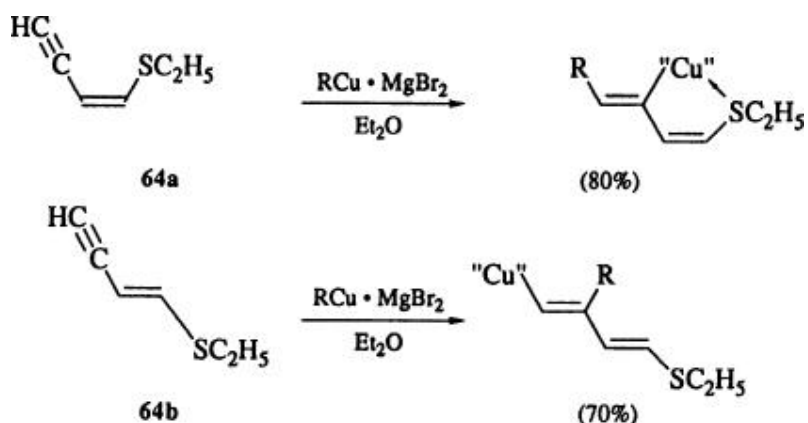
Carbometalations of alkynes using stoichiometric organocopper or cuprate reagents offer a powerful tool for preparing olefins with rigidly defined substitution patterns. (193) The addition of both carbon and copper atoms across an acetylene, which occurs in a strictly *syn* Markovnikov sense, (194) creates a new alkenylcopper species that can subsequently be replaced by reaction with an appropriate electrophile  $E^+$  (Eq. 52). This process can be particularly valuable in syntheses of insect sex pheromones, where bioactivity can be critically dependent upon alkene isomeric purity. A recent



review deals with carbocupration chemistry in some detail (see also Table III). 4f Initial research on carbocupration was limited to the basic process itself (i.e., Eq. 52,  $\text{E}^+ = \text{H}^+$ ), with variations on the part of substrate, alkyne, and Grignard reagent. With alkyl-substituted acetylenes, the usual mode of organocopper addition is observed (*syn*, Markovnikov). Opportunities for chelation in the resulting vinyl organometallic via placement of a heteroatom (e.g., OR,  $\text{O}^-$ ,  $\text{NR}_2$ , SR) in the side chain of the 1-alkyne, however, can dictate the regio- and stereochemistry of the carbocupration. (195) This effect does not extend beyond two carbon-carbon bond lengths (i.e.,



past five-membered ring formation), at which point normal reactivity to give a “branched” vinylcopper is restored. In homopropargylic substrates (Eq. 53,  $n = 2$ ), the proportion of “linear” adducts increases for the series —  $\text{OCH}_3 < \text{—SC}_2\text{H}_5 < \text{—N}(\text{C}_2\text{H}_5)_2$ , (195) an order that parallels the ligating power of these groups for copper. Geometrical orientation is also important in determining the “branched” to “linear” ratio, as illustrated in the cases of *E* and *Z* enynic thioethers 64a,b. (195) With homopropargylic ethers and acetals,



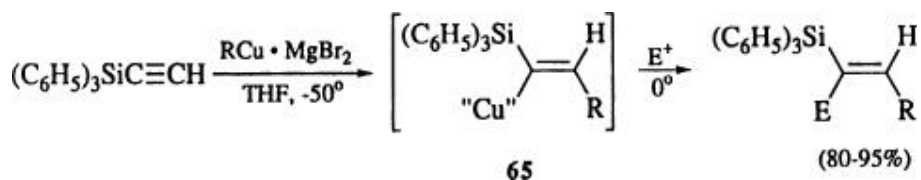
reactions run in tetrahydrofuran favor the normal mode of addition, while mixtures are usually observed when ether is the solvent. (195) Propargylic substrates (Eq. 53,  $n = 1$ ) behave akin to their homologs insofar as reactivity profiles and solvent effects are concerned. (196)

An internal acetylene requires a large excess of dialkylmagnesium cuprate in tetrahydrofuran at room temperature to effect carbocupration (vs.  $-20$  to  $0^\circ$  with monosubstituted alkynes). The same reaction in ether follows a completely different course, with *cis* reduction of the acetylene observed from *syn* addition of a copper hydride species. (197) Internal propargylic alcohols,  $R'C \equiv CCH_2OH$ , undergo either *cis* reduction in ether (when R is alkyl) or hydroxy-directed *anti*-Markovnikov addition in ether or tetrahydrofuran (when R is phenyl). (197) Similar hydroxy participation is also known for the copper-catalyzed Grignard addition to propargyl alcohol (vide supra). (139, 145, 198)

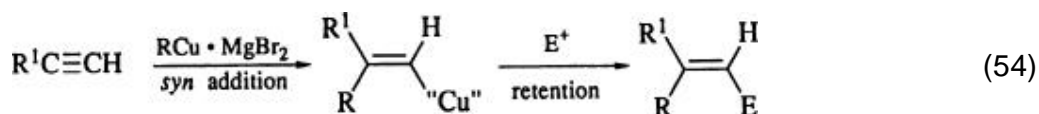
Carbocupration of the triple bond in enynes can be effected with  $R_2CuMgX$ , (199) and has led to a short synthesis of myrcene (59) (200) (compare with route on page 170). 1,3-Diynes are not regioselective in their carbocupration reactions. (201)

Heteroatom-substituted alkynes, including ynamines (202) and alkoxyacetylenes, (202) react with  $RCu \cdot MgX_2$  in tetrahydrofuran to give the respective heterovinylcoppers. Reverse regiochemistry of addition is observed with alkylthioacetylenes (202) and acetylenic sulfones. (202)

Silylacetylenes provide access to vinylsilanes via carbocupration. (203-205) The regiochemistry of cuprate additions to silylacetylenes is reversed from that to acetylenes, which places the R group from the Grignard reagent beta to silicon (cf. 65). Apparently this is inherent to silicon, and not due to alterations in reaction parameters (e.g., a solvent effect).

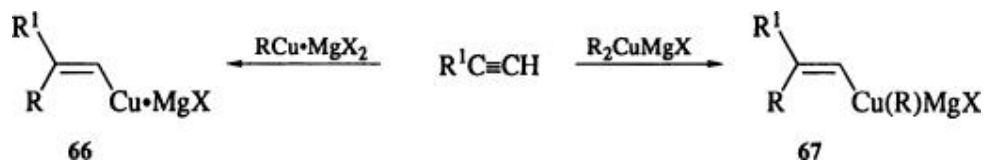


Parlaying the initial adducts of carbocupration (vinylcopper complexes) into more highly functionalized olefins now figures prominently in synthetic chemistry. Since molecular elaborations of this sort offer such virtues as single-pot processes and >99% retention of double-bond configuration, a wide range of electrophiles has been enlisted for this purpose (Eq. 54).



Heteroatom groups that have been introduced in this fashion include, as examples, halogens (Cl, Br, I), (206-208) triphenylstannyl, (209) diphenylphosphino, (209) methylthio, (209) and sulfone (210) (see Table III). Chlorotrimethylsilane does not react with vinylcopper species from carbometalations with Grignard reagents, although lithium cuprates, following carbocupration, are smoothly silylated to *cis*-vinylsilanes. (211) Vinylcopper adducts, when treated with ground-state oxygen, are transformed into symmetrical 1,3-dienes with retention of olefin geometry. (208)

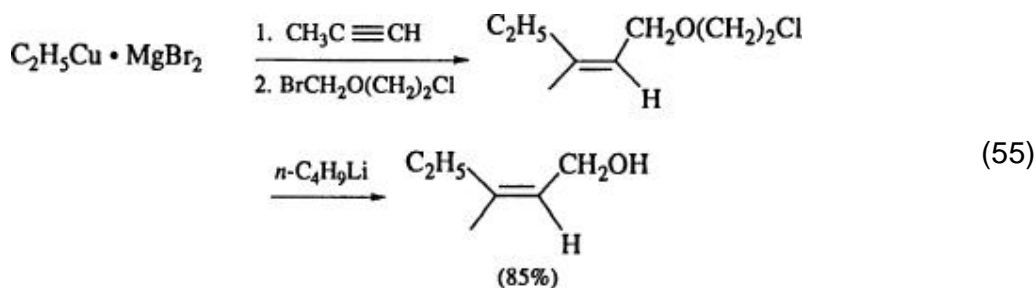
Carbon-centered electrophiles are among the most important coupling partners in synthetic transformations with vinylcopper derivatives. The preliminary choice of copper reagent for the carbocupration step has great impact on the efficiency of the secondary process. Thus, having started with  $\text{RCu} \cdot \text{MgX}_2$ , vinylcopper **66** is obtained, whereas magnesio cuprates give rise to mixed cuprates of type **67**. In the latter reaction, 2 equivalents of electrophile are needed since both groups on copper may be transferred. In fact, in some



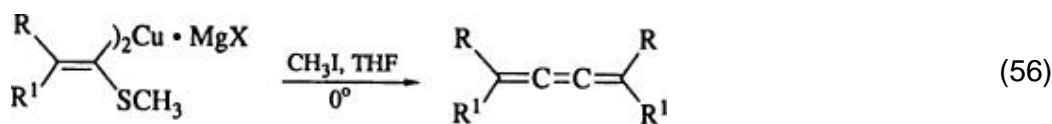
reactions (e.g., with 1 equivalent of methyl iodide), only the undesired R group on copper from **67** may react leaving the vinyl group, which presumably is protonated on workup. (209) On the other hand, species **66** are not especially

reactive toward common, unactivated alkylating agents, although they do couple with allyl bromide, (208) methyl iodide, (208) isoprene oxide, (127)  $\alpha$ -epoxy-alkynes, (127) and  $\gamma$ -vinyl- $\gamma$ -butyrolactone. (117)

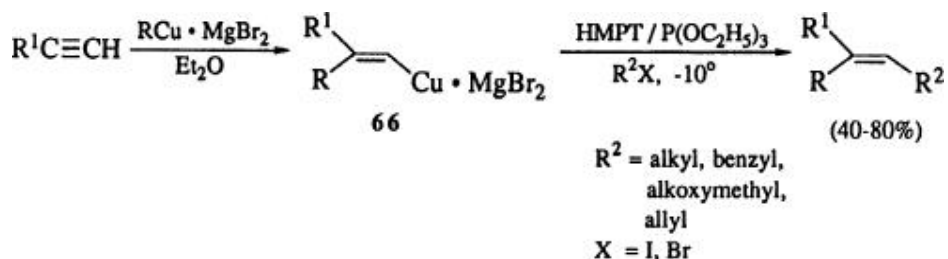
Solutions to these obstacles have been extensively investigated and recommendations have been offered. It is suggested that, if possible, synthetic schemes that bypass 67 should be considered unless the alkylating agent is relatively inexpensive. The alternative route via 66 (X = Br) may be far more effective, since 2 equivalents of hexamethylphosphorous triamide (HMPT) and 3 equivalents of a trialkyl phosphite stabilize 66 to the extent that they have sufficient lifetimes to react with a wide variety of alkyl halides (Scheme 9). (208) Simple alkyl bromides and iodides are most effective, whereas chlorides, ethers, tosylates, and esters are completely inert. Such discrimination on the part of vinylcopper 66 can be advantageous for carrying out selective transformations, as in the preparation of allylic alcohols by this methodology (Eq. 55). (212) *gem*-Alkylthiovinyl coppers, however, are anomalous in their reactions with methyl iodide, and *cis*-butatrienes result, possibly



via alkylation on sulfur, leading to a vinylcarbenoid species which dimerizes (Eq. 56). (213) On the other hand, reactions with allylic halides (rather than  $\text{CH}_3\text{I}$ ) produce the expected alkylated products. (213)

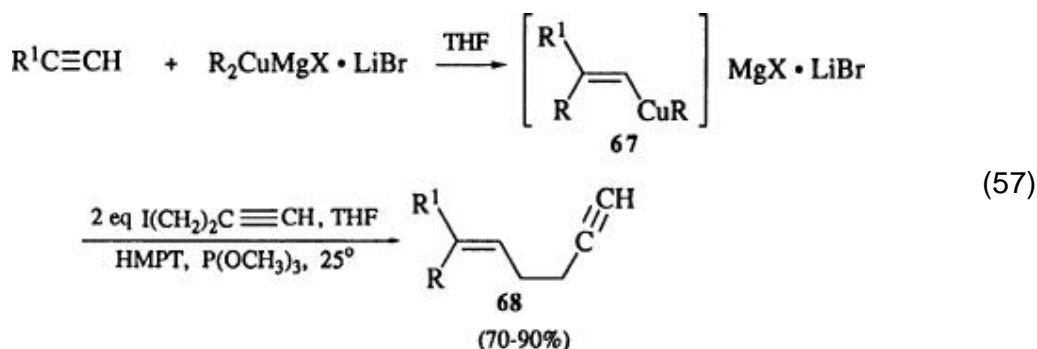


Scheme 9.

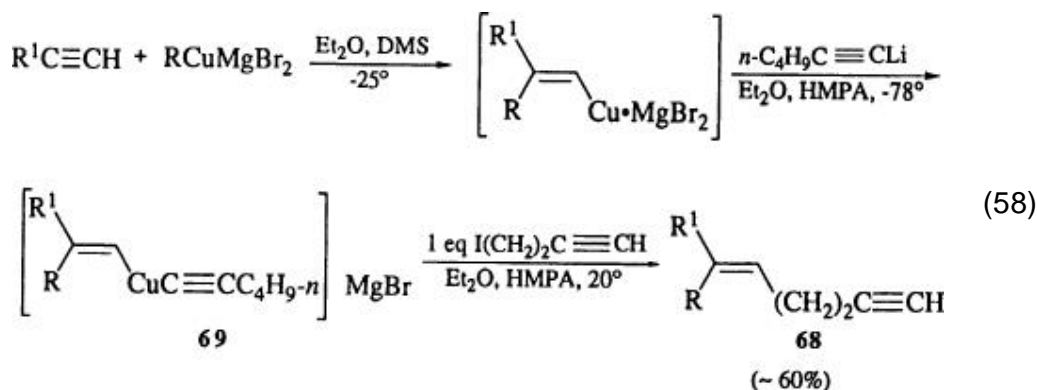


The 1,5 disposition of trisubstituted olefins in compounds of natural origin has been recognized as obtainable via alkylation of vinylcopper species with

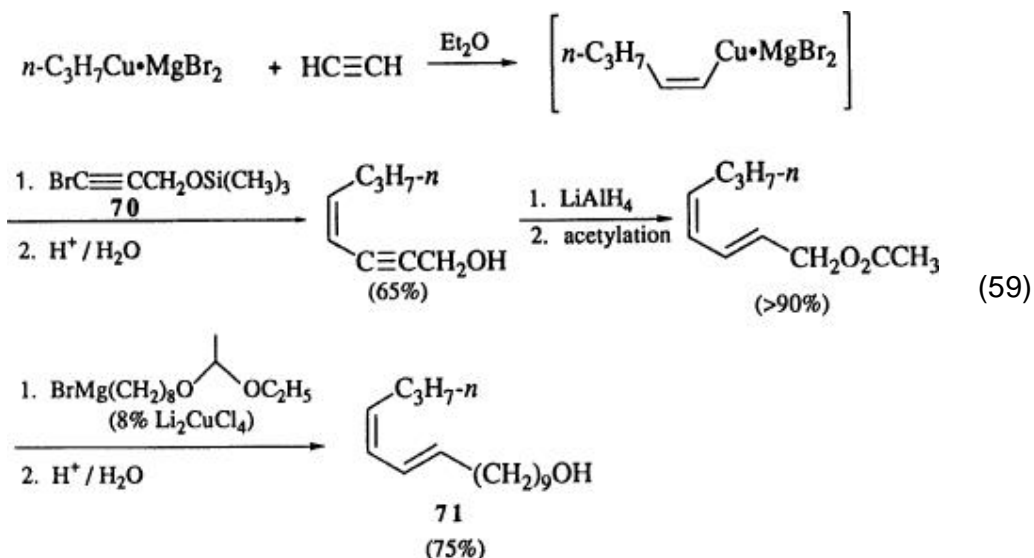
homopropargylic substrates. Unfortunately, this approach has met with little success and can only be reduced to practice through the agency of lithium bromide-complexed mixed vinylcuprates **67**, X = Br (Eq. 57). (214) Both HMPT



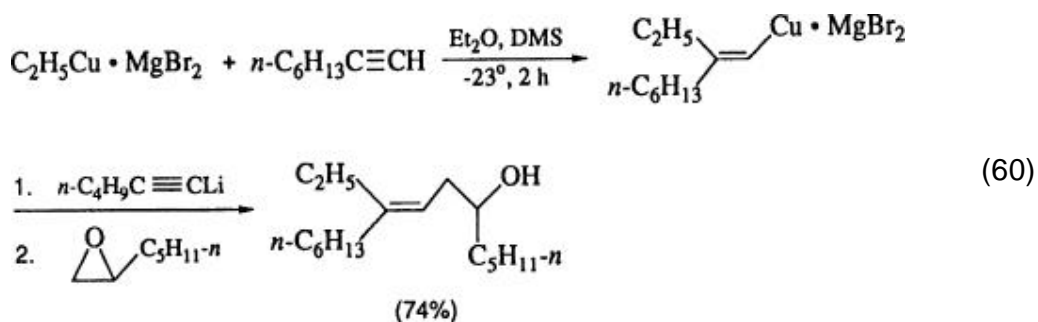
and trimethyl phosphite are again essential for the displacement, as is an excess ( $\geq 2$  equivalents) of alkylating agent, otherwise results are disappointing. (191, 214) A better alternative is to first transform the initial vinylcopper in situ to a mixed cuprate **69** by addition of a nontransferrable ligand (such as 1-pentynyl, vide infra) which then reacts with 1 equivalent of a homopropargylic iodide to give **68** in an unoptimized 60% yield (Eq. 58). (215) Enynes **68** can be further extended using the same carbometalation/alkylation strategy, as in the total synthesis of juvenile hormones. (216)



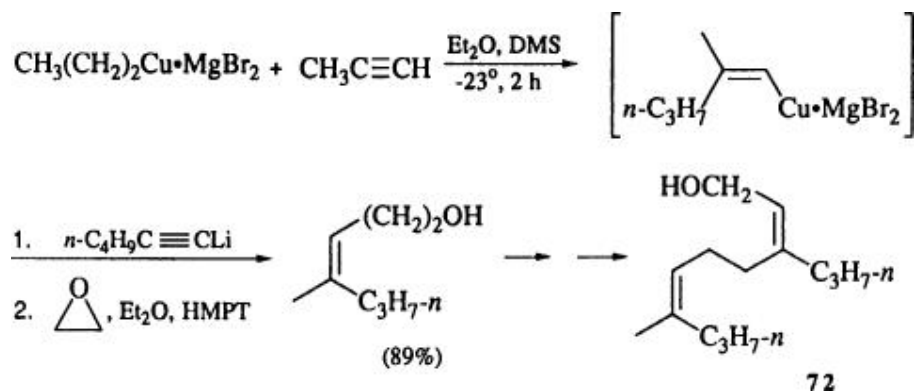
Alkylation of vinylcopper complexes with 1-haloalkynes affords conjugated enynes. (159) The reaction conditions require use of 2 equivalents of TMEDA for reasonable yields. Use of functionalized 1-haloalkynes allows for further manipulation. Use of the trimethylsilyl-protected 1-bromopropargyl alcohol **70** provides a streamlined route to bombykol (**71**) (Eq. 59). (159)



Another well-studied aspect of vinylcopper reagents is their reactions with epoxides. In general, oxiranes are only moderately reactive. (217) However, the use of mixed cuprates such as 69 enhances the reactivity of these copper reagents, and alkylations with epoxides proceed in good yields. (218) Monosubstituted epoxides are regioselectively attacked at the less-hindered carbon, giving rise to homoallylic alcohols, key intermediates in the synthesis of, for example, linear terpenoids (Eq. 60). Styrene oxide, however, gives mixtures of regioisomers, and with the less-reactive cyclohexene oxide the yield decreases to ca. 25%. 218b Another application of vinylcopper alkylation using

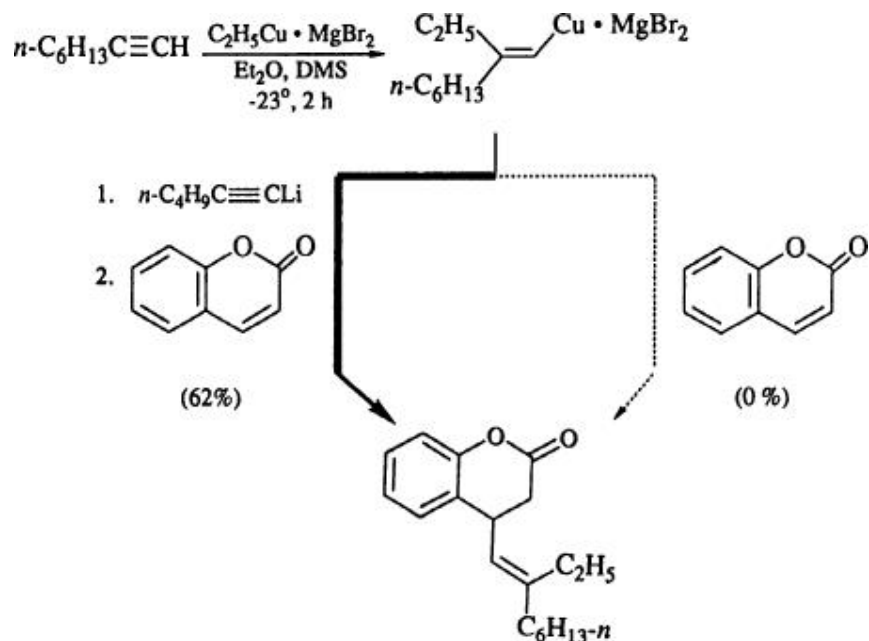


an epoxide includes a key step in the stereospecific total synthesis of the codling moth constituent 72. (215)



The enhanced reactivity of mixed cuprates has also found extension to conjugate addition schemes. That is, following carbocupration, the vinylcopper species can be converted to the *ate* complex **69** in situ with a lithiated acetylene, and then reacted with an  $\alpha$ ,  $\beta$ -unsaturated carbonyl compound. (215, 218) Double-bond geometry is retained in the adduct. (218) The alkenylcopper itself is unreactive (Scheme 10).

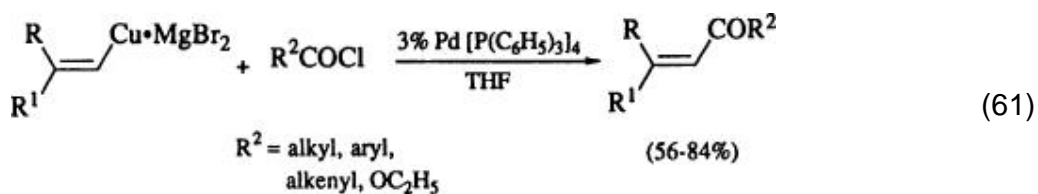
Scheme 10.



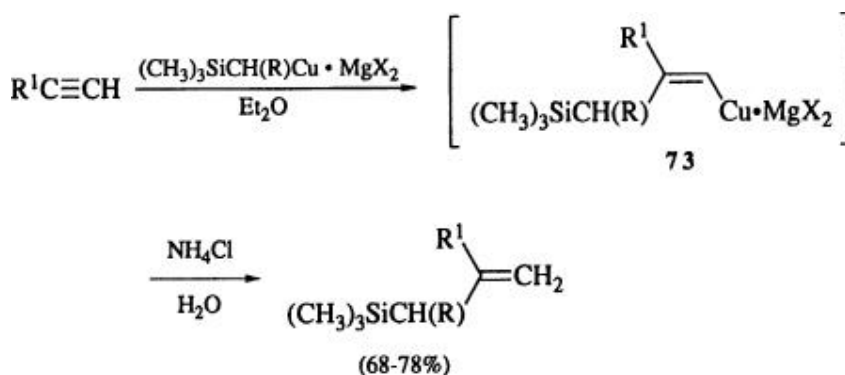
Acylation of vinylcoppers offers a straightforward route to stereodefined  $\alpha$ ,  $\beta$ -unsaturated carbonyl compounds. Attempts to directly acylate alkenylcopper species give irreproducible results with acid chlorides. (219) Lithium dialkenylcuprates are not useful because of their further 1,4 addition to the product enones. (220) Fortunately,  $\text{RCu}\cdot\text{MgX}_2$  ( $\text{R}$  = alkenyl) reacts smoothly with acyl chlorides, or with mixed-acid anhydrides if a catalytic amount of  $\text{Pd}^0$  is present. (221) The original olefin geometry is maintained throughout,



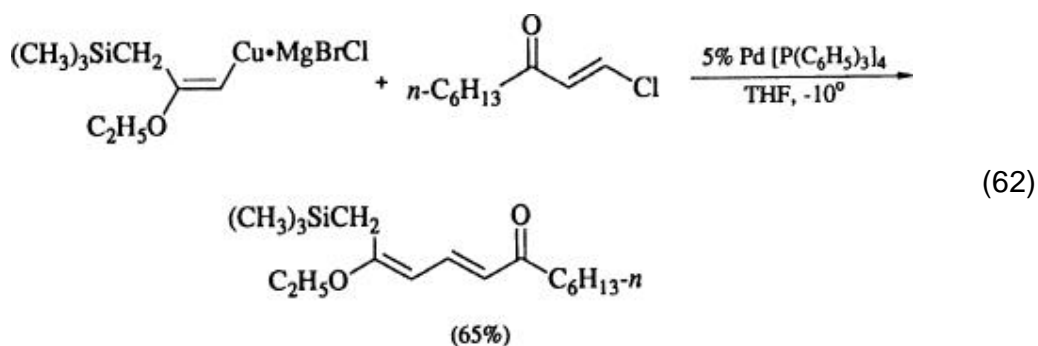
although complete isomerization (from *Z* to *E*) of the initially formed enone can be achieved via dilute acid catalysis. (221) Thus  $\alpha$ ,  $\beta$ -unsaturated ketones of either *E* or *Z* stereochemistry can be prepared with ease (Eq. 61).



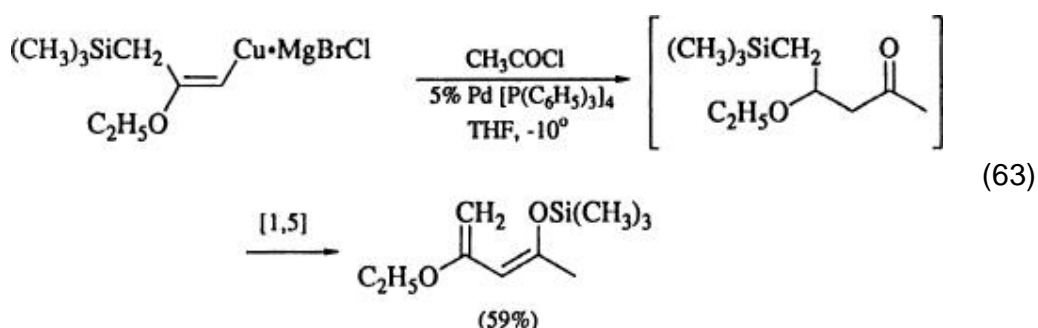
$\gamma$ -Silylated vinylcopper species **73** have recently been prepared through carbocupration of acetylenes with  $\alpha$ -silylated organocopper reagents. (222) Intermediates **73** undergo a variety of further transformations in addition to simple protonolysis to produce allylsilanes **222b** (see Table III). Oxidative dimerization



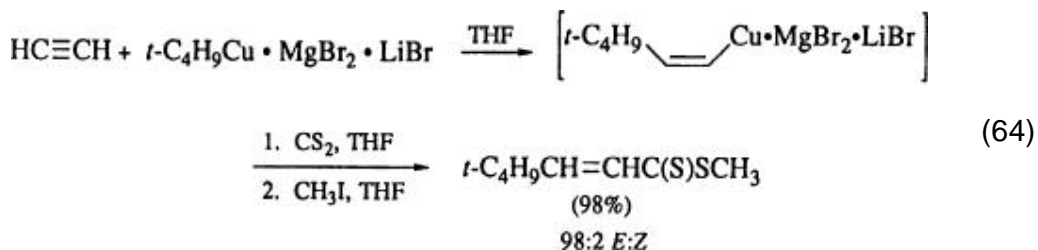
occurs in the presence of  $\text{Li}_2\text{CuCl}_4$ , and alkylations can be carried out with  $sp^3$ -centered halides. **222c** In the presence of  $\text{Pd}^0$  as catalyst, vinyl halides couple to produce highly functionalized dienes in which the stereochemistry of both components is retained (Eq. 62). **222c**



More highly functionalized organocopper reagents (e.g.,  $\omega$ -alkoxy-containing derivatives) also participate in carbocupration schemes. [222d](#) Acylation of  $\gamma$ -silylvinylcopper species in the presence of catalytic amounts of  $\text{Pd}^0$  leads to a 1,5-sigmatropic silyl shift in the initially formed  $\gamma$ -silyl- $\alpha, \beta$ -unsaturated ketone (Eq. [63](#)). [222c](#) The dienol diethers, produced in high stereoisomeric purity, are regioisomeric with those commonly referred to as “Danishefsky's dienes,” ([223](#)) and hence are promising for applications in Diels–Alder chemistry.

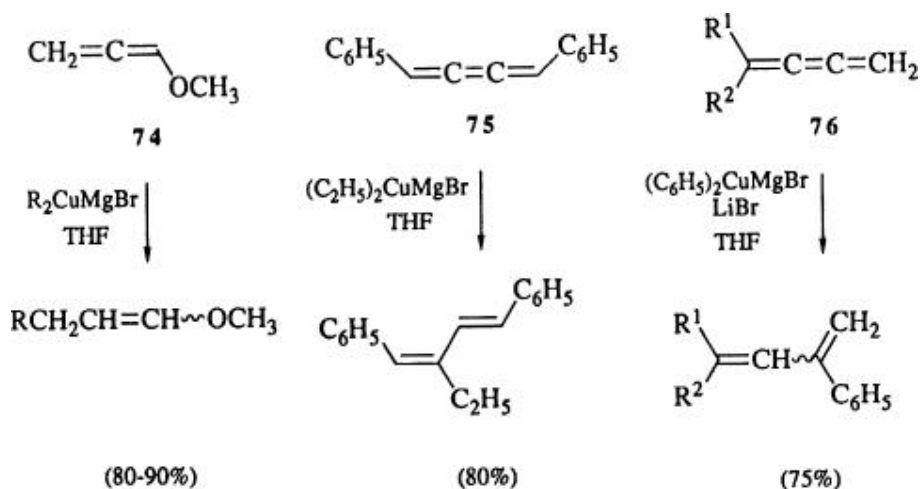


Further useful reactions of vinylcoppers or divinylmagnesium cuprates include carboxylation with carbon dioxide, ([215](#), [224](#), [226](#)) aminomethylation with aminothioacetals, ([225](#)) aminocarbonylation via phenylisocyanate, ([226](#)) cyanation with cyanogen chloride, ([227](#)) and chain extension with  $\beta$ -propiolactone. ([167](#), [228](#)) Reactions with carbon disulfide involve inversion of olefin configuration to the more stable *E* isomer (Eq. [64](#)). ([142](#))



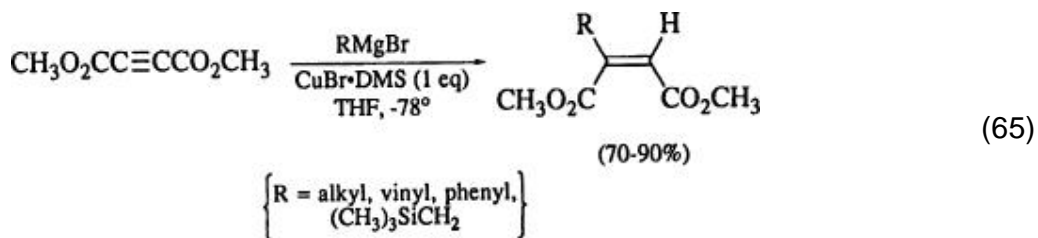
Certain cumulenes also undergo carbocupration when treated with dialkylmagnesium cuprates. The regiochemistry of attack is highly dependent on both reagent and substrate structure, as well as on reaction conditions. The

cumulenes studied so far are methoxypropadiene (**74**), ([229](#)) *cis*-1,4-diphenylbutatriene (**75**), ([230](#)) and *gem*-disubstituted butatrienes **76**. ([231](#))



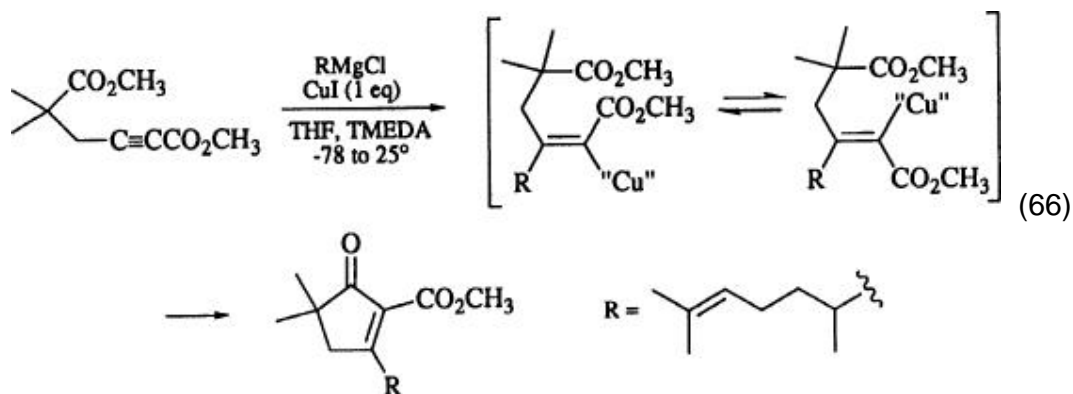
### 3.1.2.3. Conjugate Addition

Although Michael additions of organic ligands delivered with  $\text{RCu}\cdot\text{MgX}_2$  are less popular than those effected by lower-order cuprates, ([232](#), [233](#)) many examples of these couplings have appeared, most of which are illustrated in Table II-E. While reactions with cyclohexenone proceed in moderate yields (ca. 65%), acyclic enones and cyclopentenone afford inferior results. [218b](#) Acetylenic esters, however, are common acceptors toward  $\text{RCu}\cdot\text{MgX}_2$ , ([234](#)) the stereochemical outcomes of which suggest involvement of a carbocupration process. For example,  $\text{RCu}\cdot\text{MgX}_2$  reacts with dimethylacetylene dicarboxylate in tetrahydrofuran–dimethyl sulfide to give exclusively the 2-substituted maleates from *syn* addition (Eq. [65](#)). ([235](#))



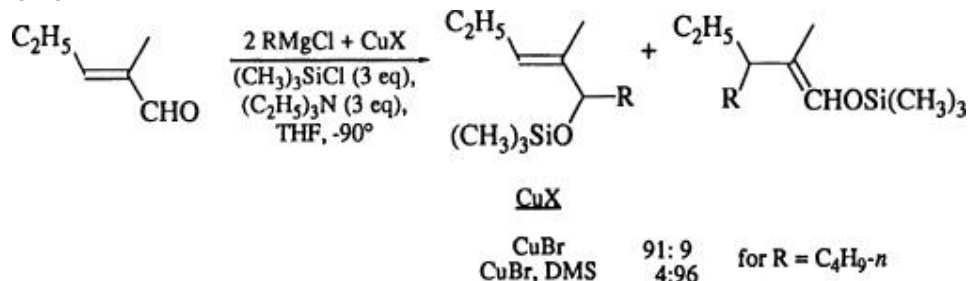
One extension of this chemistry involves  $\text{RCu}\cdot\text{MgX}_2$  addition to  $\omega$ -alkoxycarbonylacetylenic esters to form cyclopentenones (Eq. [66](#)). ([236](#)) The initial vinylcopper (via *syn* addition) probably equilibrates with its *anti* isomer,

which then undergoes intramolecular acylation. The many examples involving functionalized Grignard reagents suggest good generality to this one-pot procedure, although yields tend to be moderate (35–45%). (236)



Conjugate additions to  $\alpha, \beta$ -ethylenic carbonyl compounds appear to be more efficient when magnesio cuprates ( $R_2CuMgX$ ) are employed. (233, 237-239) An important achievement in this field is the highly selective 1,4 addition of  $R_2CuMgCl$  to  $\alpha, \beta$ -unsaturated aldehydes. (240) Reactions of lithio cuprates with  $\alpha, \beta$ -enals are usually accompanied by products of 1,2 addition. Similarly, addition of *n*-butylmagnesium chloride to  $\alpha$ -methylpent-2-enal in the presence of copper(I) bromide alone (0.5 equivalent) gives a 91:9 ratio of adducts in favor of 1,2 addition. (240) However, using the copper(I) bromide-dimethyl sulfide complex in the presence of chlorotrimethylsilane (3 equivalents), the product ratio is dramatically changed to 96:4, now in favor of the 1,4 adduct (Scheme 11). Whether chlorotrimethylsilane is present prior to or after introduction of the substrate does not affect the product distribution. Thus dimethyl sulfide appears to be the critical component responsible for this ratio reversal

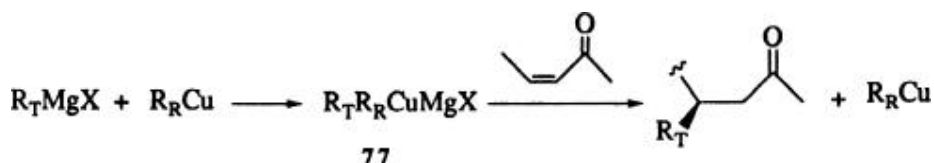
Scheme 11.



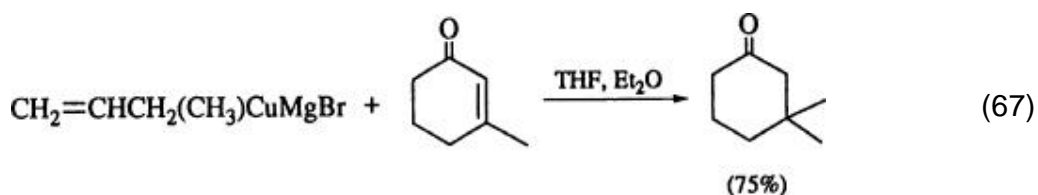
Also quite significant is that even acrolein, a notoriously poor substrate toward Michael donors, reacts with *n*-butylmagnesium chloride to give exclusively the conjugate addition product when one-half equivalent of copper(I) bromide-dimethylsulfide (and chlorotrimethylsilane) is used. Allyl Grignard, however, gives no 1,4 addition under these conditions. (240) In the sequence

of [Scheme 11](#), chlorotrimethylsilane can be omitted and bromine used to trap the incipient enolate, thereby producing  $\alpha$ -bromoaldehydes in good yields. (240) Recently it has been shown that use of chlorotrimethylsilane in copper-catalyzed Grignard reactions with enals has a rate-accelerating effect and is not merely stabilizing an initially formed enolate. (157)

The use of homocuprates  $R_2CuMgX$  has the particular disadvantage that one of the organic residues  $R$  is wasted in the coupling process, since the byproduct  $RCu$  is relatively unreactive. Many mixed cuprates such as [77](#), which selectively transfer only the desired  $R_T$  group ( $T =$  transferrable), have been developed. Such mixed cuprates can be prepared by adding 1 equivalent of  $R_TMgX$  to an  $R_RCu$  ( $R =$  residual) species, and selective transfer of  $R_T$  from the cuprate to the substrate results in full utilization of the valued Grignard reagent. Several so-called "dummy ligands" ( $R_R$  in [77](#)) have been utilized for this purpose, including thiophenyl, (241, 242) *tert*-butoxy, (243) 1-pentynyl, (244) trimethylsilylethynyl, (245) and methyl groups. (246-250) The efficiency of each dummy ligand is quite variable and depends upon the nature of  $R_T$  in

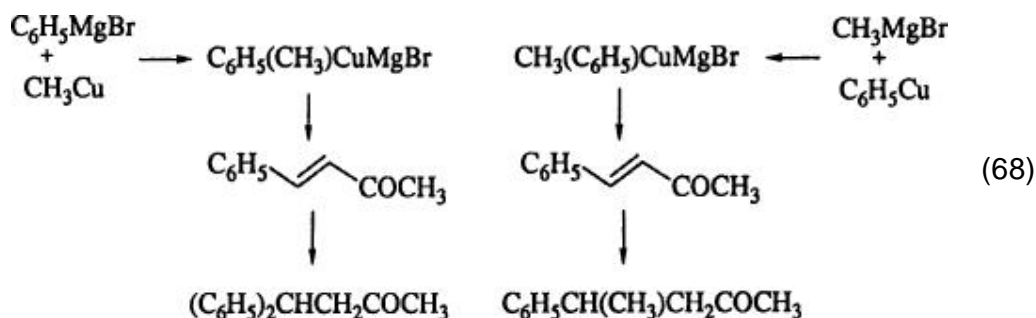


the mixed cuprate. With increasing steric requirements between cuprate and educt, the efficiency of selective transfer decreases. (251) For [77](#),  $R_R =$  methyl, in all cases studied the methyl group is transferred to some extent, but especially so when  $R_T$  is allyl or benzyl (Eq. 67). (246, 248)

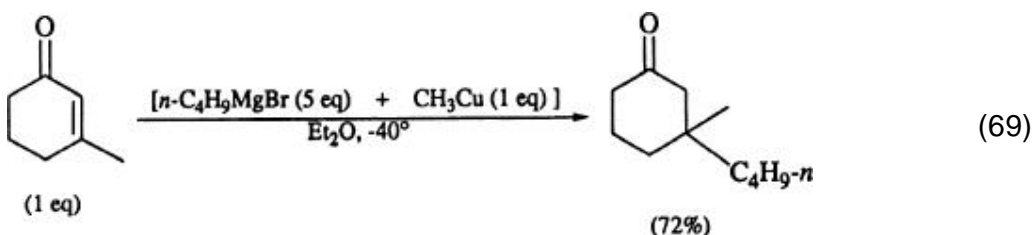


The mixed-cuprate  $R_T(CH_3)CuMgX$  (e.g.,  $R_T = C_6H_5$ ) can be prepared either by addition of a Grignard reagent to  $CH_3Cu$  or by addition of  $CH_3MgX$  to  $RCu$  (Eq. 68). The mode of formation notwithstanding, the cuprate ligand which is preferentially transferred to the enone is the one which originates with the Grignard reagent. (248) This signifies that magnesio mixed cuprates, unlike their lithio counterparts, (248) do not rapidly exchange their individual ligands. (248) These observations suggest that mixed magnesio cuprates containing divalent cations as part of the clusters' gegenion may have unique features

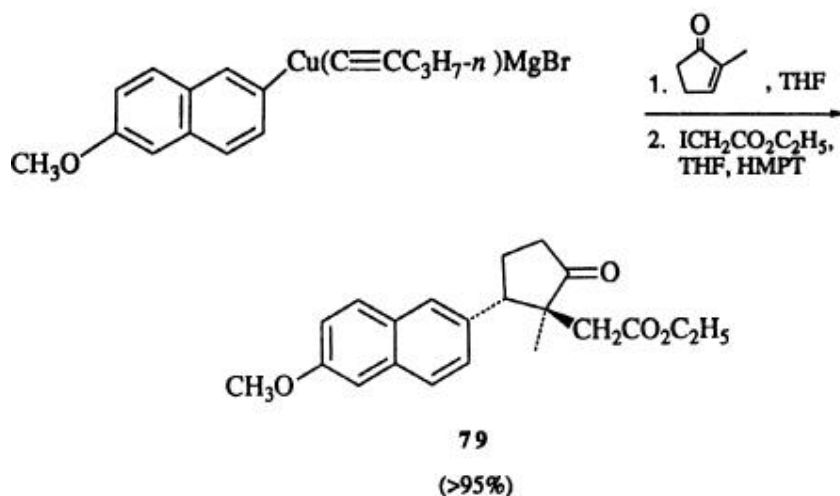
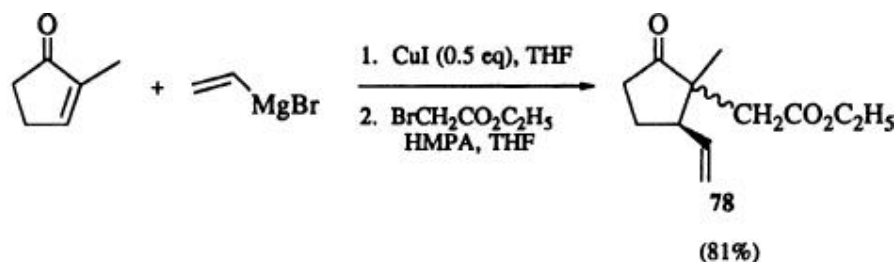
associated with their structures, and that several factors such as ligand basicity, steric bulk, and/or coordinating ability may be but part of the story behind the selective release of one group over another from copper. (252)



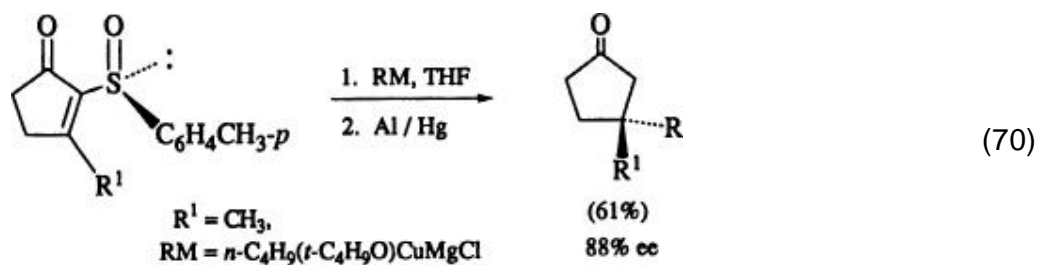
A related study using 5 equivalents of *n*-butyl Grignard and methylcopper on 3-methylcyclohexenone demonstrates that not only does the selectivity of butyl:methyl transfer remain high (98:2), but also only a minor amount (<2%) of 1,2-addition product occurs. (247) With 5 equivalents of both Grignard and substrate, similar yield and selectivity (97% butyl transfer) are observed. This last experiment, albeit indirectly, involves the use of a catalytic amount (20%) of methylcopper, a technique that appears very promising in mixed-cuprate chemistry (Eq. 69). (247)



Magnesium cuprates are widely used as reagents in the fields of organocopper conjugate addition–enolate trapping chemistry 4h and natural products synthesis. Fragments such as 78 and 79, utilized in the total synthesis of steroids, (244, 253) are representative outgrowths of this powerful approach.

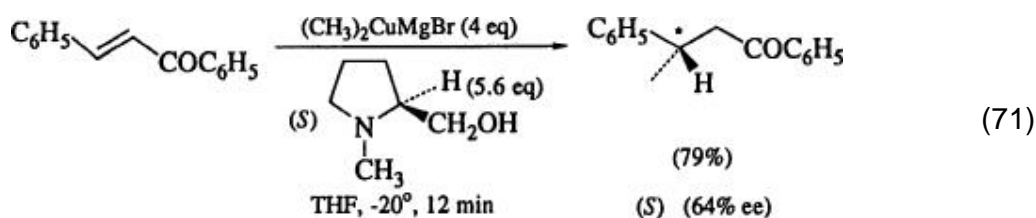


A few reports have appeared on asymmetric induction in conjugate additions of magnesio cuprates. Diastereofacial differentiations in Michael reactions of mixed cuprates  $R_T R_R CuMgCl$  to optically active 2-(*p*-toluene-sulfinyl)cyclopentenones give fairly good enantiomeric excesses (Eq. 70). (243) Conjugate additions to unsaturated imides, prepared from optically pure 2-imidazolones, also proceed with impressive diastereoselectivities. (254) Related results can be obtained with lithium cuprates (*vide infra*).



The use of chiral mixed cuprates, on the other hand, enables enantioface

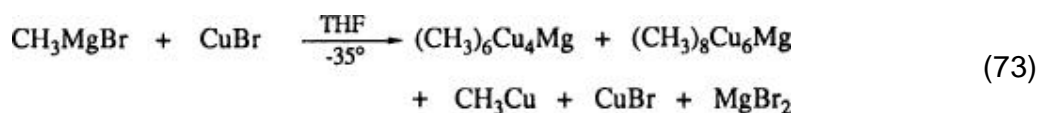
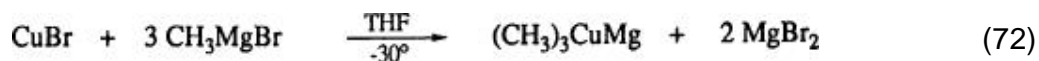
differentiation of acyclic  $\alpha$ ,  $\beta$ -enones. (255-257) Thus in the presence of (*S*)-*N*-methyl-2-hydroxymethylpyrrolidine and copper(I) bromide, methyl Grignard reacts with benzylideneacetophenone to produce the 1,4 adduct in 64% optical yield (Eq. 71). (255) The enantiomeric excess induced in this reaction depends upon the reaction times; short exposures (~0.2 hours) give best results. A later study showed that this particular chiral auxiliary was the most effective among those screened for this purpose. 257a



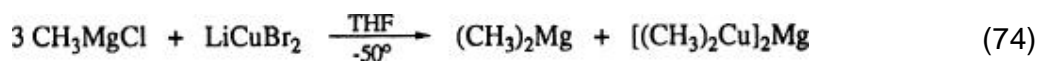
#### 3.1.2.4. Composition Studies

Although there are relatively few reports which scrutinize the solution composition of various RMgX to CuX ratios, an impressive bank of information has already been amassed. (258-262) Early work based on enolate trapping experiments with acetic anhydride, following 1,4 additions with inhomogeneous mixtures of 2EtMgBr + CuI, pointed to the presence of at least three unidentified reactive species in ether solutions. (258) Admixture of equimolar quantities of copper(I) bromide and methylmagnesium bromide in tetrahydrofuran at  $-60^\circ$  also does not afford a homogeneous solution. Nonetheless, to the extent that the copper(I) bromide does dissolve (ca. one third),  $^1\text{H}$  NMR analysis at  $-85^\circ$  reveals formation of monomeric  $(\text{CH}_3)_3\text{CuMg}$  plus magnesium bromide. (259, 260) Increasing the amount of Grignard by a factor of 3 and warming to  $-30^\circ$  gives more  $(\text{CH}_3)_3\text{CuMg}$  ( $\delta - 1.54$  ppm vs. tetramethylsilane), as all of the copper salt is solubilized (Eq. 72). Maintaining the 1:1 mixture at  $-60$  to  $-40^\circ$  over time, however, leads to several other complexes, the identity of which depends upon the extent of CuBr dissolution (Eq. 73). Confirming the existence of  $(\text{CH}_3)_8\text{CH}_6\text{Mg}$  by independent synthesis using copper(I) bromide and dimethylmagnesium was particularly enlightening, and revealed an inclination toward disproportionation to 2 MeCu and  $(\text{CH}_3)_6\text{Cu}_4\text{Mg}$ . (259) Taken together with other supporting documentation (e.g., elemental analyses of both solid and liquid phases of numerous combinations), 259a these observations have led to the deduction that "Normant" reagents (RMgBr + CuBr) in tetrahydrofuran at about  $-35^\circ$  consist of at least five components (Eq. 73). 259a Each cuprate possesses a different stability profile, but in no case does halogen constitute an integral part of these complexes. 259a

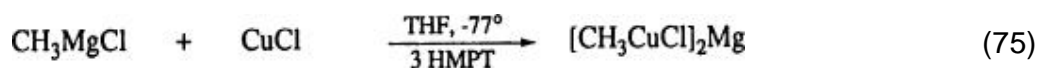




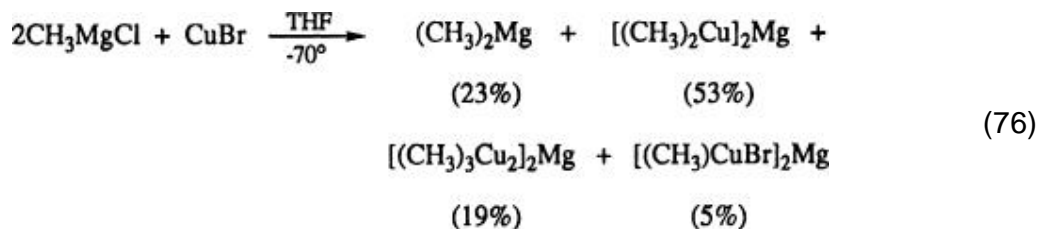
This state of affairs is made somewhat more intricate in that studies by another laboratory pursuing identical goals arrived at conclusions which are not in complete harmony with those cited above. (262) For example, treatment of CuBr·LiBr with 3 equivalents of CH<sub>3</sub>MgCl in tetrahydrofuran at -50° gives rise to two species in equal amounts (Eq. 74). Attempts to combine

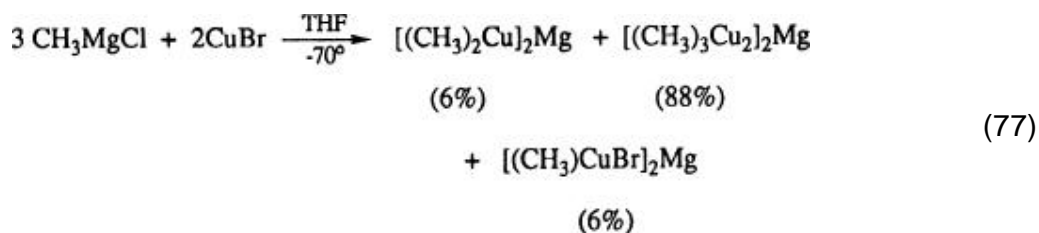


CuBr with 3 equivalents of CH<sub>3</sub>MgBr at -80° give four signals of roughly comparable intensities in the <sup>1</sup>H NMR spectrum of this mixture, with the signal at δ - 1.53 ppm assigned to [(CH<sub>3</sub>)<sub>2</sub>Cu]<sub>2</sub>Mg (262) rather than to (CH<sub>3</sub>)<sub>3</sub>CuMg. (258-260) Use of excess HMPT to completely solubilize these reagents allows for direct <sup>1</sup>H NMR examination of CH<sub>3</sub>MgCl + CuCl at reduced temperatures, which shows a single line in the spectrum (δ - 1.2 to -1.3 ppm) corresponding to [CH<sub>3</sub>CuCl]<sub>2</sub>Mg (Eq. 75). Although this additive apparently

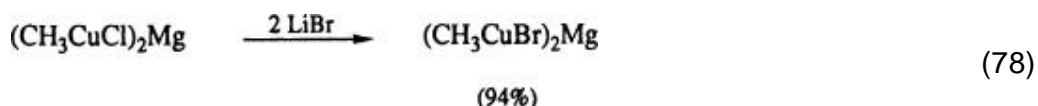


enhances the tendency toward halocuprate formation, (263) it is not obligatory, since CH<sub>3</sub>MgCl / CuBr in both 2:1 and 3:2 ratios in tetrahydrofuran without HMPT produce small percentages of bromocuprates (Eqs. 76 and 77). (262) Bromocuprates are more stable than chlorocuprates, since addition of

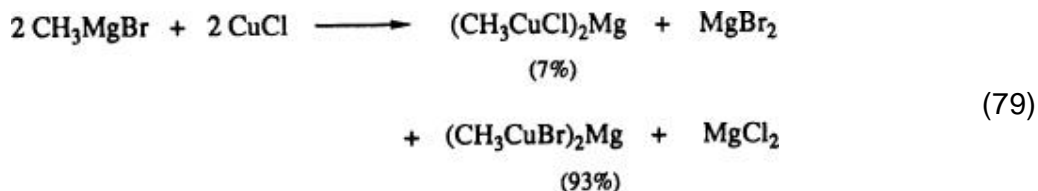




LiBr to  $(\text{CH}_3\text{CuCl})_2\text{Mg}$  [ $\delta(\text{CH}_3) - 1.31$  ppm] efficiently exchanges bromide for chloride ion to form  $(\text{CH}_3\text{CuBr})_2\text{Mg}$  [ $\delta(\text{CH}_3) - 1.25$  ppm] (Eq. 78). Hence,



using either  $\text{RMgBr} + \text{CuCl}$  or  $\text{RMgCl} + \text{CuBr}$  generates predominantly the bromomagnesium cuprate  $(\text{RCuBr})_2\text{Mg}$ , otherwise written as  $2\text{RCu}\cdot\text{MgBr}_2$  (Eq. 79).



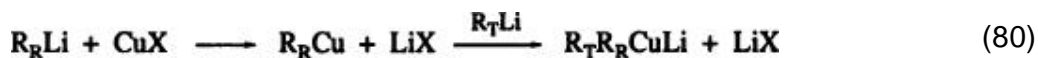
Thus, while some degree of discrepancy remains, what does emerge from this work is that cuprates stoichiometrically represented as  $\text{RCu}\cdot\text{MgX}_2$  or  $\text{R}_2\text{CuMgX}$  are often far from discrete entities. Depending on the relative ratios of reagents ( $m\text{RMgX}:n\text{CuX}$ ), temperature of formation, solvent(s), and additives, a multitude of species may be present. However, by the judicious selection of values for  $m$  and  $n$ , these spectroscopic experiments provide considerable insight as to potential substrate–reagent compatibility, and hence may assist in selection of a magnesium-based reagent for a specific application. (264)

### 3.1.3. Chemistry of Lower-Order Lithio Cuprates

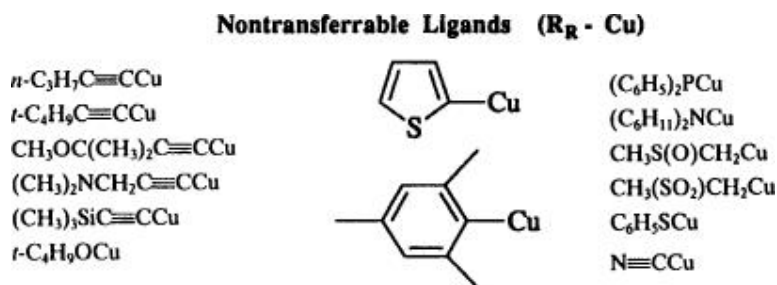
#### 3.1.3.1. Substitution

In the prior review of this topic, the scope and limitations of reactions of lower-order cuprates [Gilman reagents,  $\text{R}_2\text{CuLi}$ ] were discussed with respect to structural variations within both the substrate and the cuprate. (1) The mode of preparation of various  $\text{R}_2\text{CuLi}$  was also outlined. In the intervening years, a heightened awareness of the role of ligands during the carbon–carbon bond-forming step has developed. That is, while yields based on educt were

oftentimes high, those viewed with an eye toward conservation of nontrivial organolithium precursors ( $R_TLi$ ) cannot exceed 50%, since one of the two required  $R_TLi$  in  $(R_T)_2CuLi$  is usually lost (as the protonated species) upon workup. A need for more economical utilization of  $R_TLi$  has spawned several alternative nontransferrable, or “dummy,” ligands  $R_R$  which permit full utilization of potentially valuable  $R_TLi$ . Such mixed cuprates  $R_TR_RCuLi$  are generally prepared via prior formation of  $R_RCu(R_RLi + CuX)$  to which is added the organolithium  $R_TLi$  possessing the ligand of interest (Eq. 80).



The most popular nontransferrable ligands are the 1-alkynyl residues. These include pentynyl-, (265) *tert*-butylethynyl-, 63b (3-methyl-3-methoxybutynyl)-, (266) trimethylsilylethynyl-, (267) and 3-(dimethylamino)propynylcopper-, (268) Each has its advantages and disadvantages with regard to selectivity of transfer, solubility (in ether vs. tetrahydrofuran), and cost effectiveness.



Other mixed cuprates which provide alternatives to homocuprates include mesityl- (269) and heteroatom-containing ligands. Examples of the latter class include the *tert*-butoxy (270) and thiophenoxy groups, (270) as well as the underutilized 2-thienyl moiety derived from metalation of thiophene. (78) More recently, heterocuprates formed from lithium diphenylphosphide and lithium dicyclohexylamide, 271a,b have shown improved reactivity toward primary alkyl halides, acid chlorides, and unhindered epoxides. (271)  $\alpha$ -Heteroatom-stabilized carbanions as ligands represent another type of  $R_RLi$ , with both sulfonyl (272) and sulfoxide (273)  $\alpha$ -anions functioning in this regard. The nitrile ligand, (274) isoelectronic with acetylides, can also be an excellent choice, as it is the only member of this class of ligands which does not require any manipulation (i.e., lithiation followed by metathesis with  $CuX$ ).

The explanations behind the selectivity of ligand release (91, 275) from copper vary according to  $R_R$ , and while speculative, do provide some guidelines for use of mixed reagents. Ligands capable of strong backbonding between

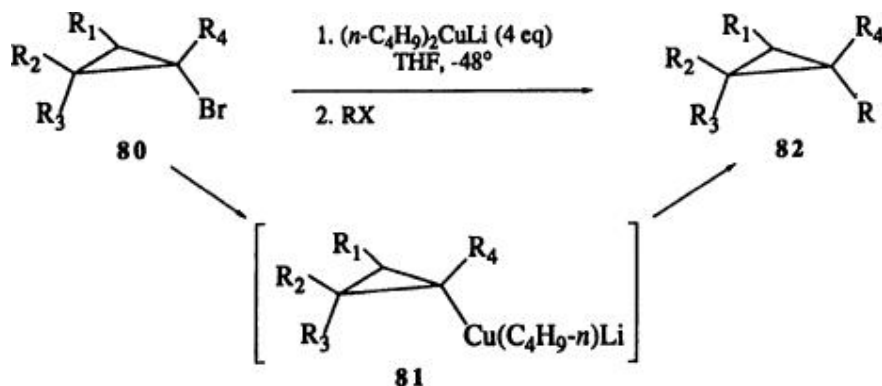
copper  $d$  electrons and  $\pi^*$  orbitals of acetylenic groups  $\sigma$  bound to the metal tend to negate their release relative to other  $sp^3$ - and  $sp^2$ -hybridized carbon atoms. Cuprates composed of ligands bearing heteroatoms attached to copper may be less prone toward release of these groups based on the  $pK_a$  of the ligand's conjugate acid. That is, the cuprate preferably delivers the more basic ligand, leaving behind the more stable RCu. Alternatively, the relative strengths of the resulting bonds as felt in the transition states (carbon–carbon vs. carbon–heteroatom) may also be a factor which contributes to the discriminating nature of mixed heterocuprates.

Ultrasonication can be employed to generate mixed lithio cuprates by combining lithium sand, pentynylcopper·HMPA complex, and an organic halide. (276) Lower-order cuprates mounted on a polymer support can be prepared and show comparable reactivity to homogeneous solutions of  $R_2CuLi$ . (277)

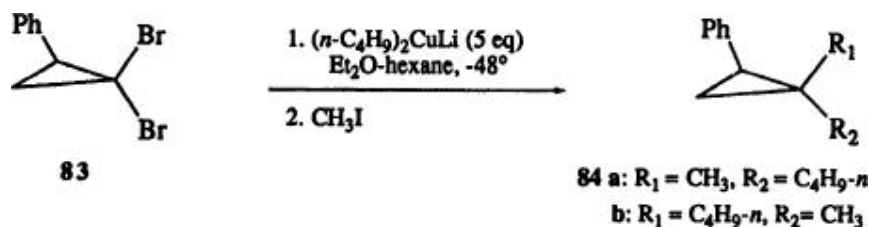
#### 3.1.3.1.1. Alkyl and Alkenyl Substrates

Examples of substitution reactions of lower-order lithio cuprates with various halides and sulfonates are listed in Table IV-A. This methodology has enabled the preparation of specifically labeled compounds with  $^{11}C$  and  $^{13}C$  tracers. (278, 279) One can also take advantage of the difference in leaving group aptitude between tosylates, halides, and alkoxides to effect selective coupling in multifunctional substrates. (280, 281) Since organocuprates are less basic than their Grignard or organolithium precursors, their substitution reactions with nonracemic substrates possessing enolizable centers are relatively free of racemization. This has been effectively exploited in chain elongations of L-serine and L-homoserine derivatives. (282) Likewise, optically active  $\alpha$ -tosyloxy acids undergo substitution with inversion of configuration at the asymmetric center in the presence of lithium dimethylcuprate. (283)

Reactions of halocyclopropanes with lithium dibutylcuprate provide an atypical route to products of substitution. When bromocyclopropane **80** is treated with dibutylcopperlithium (4 equivalents) in tetrahydrofuran and subsequently with an alkyl halide, alkylated cyclopropanes **82** are formed rather than the expected butyl-substituted compounds. (284) The coupling occurs with retention of configuration, accounted for on the basis of an intermediate mixed cuprate **81**. (284) Dibutylcopperlithium and tetrahydrofuran are both necessary for this reaction to occur. Dimethylcopperlithium in a dimethoxyethane–ether mixture induces ‘normal’ substitution of monoiodocyclopropanes in high yields. (285)

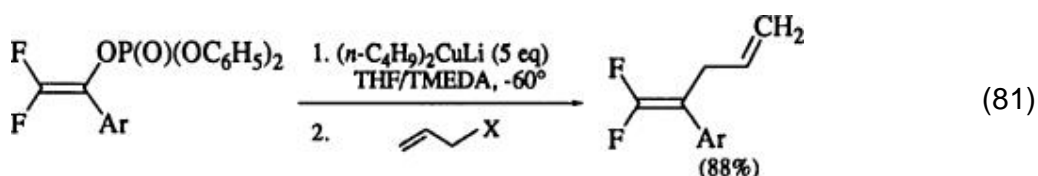


Geminal dibromocyclopropanes are susceptible to double replacement using excess dibutylcopperlithium. For example, treatment of 1,1-dibromo-2-phenylcyclopropane (**83**) with 5 equivalents of dibutylcopperlithium in ether–hexane, followed by addition of methyl iodide, results in a mixture of the dialkylated products **84a** and **84b** (4:1). <sup>284b</sup> A mechanism consistent with preferential alkylation *cis* to the phenyl group consists of (1) an initial copper–halogen exchange at the least-hindered site (*trans* to phenyl); (2) butyl migration from copper to cyclopropane carbon displacing halogen with inversion; and (3) alkylation of the resulting organocopper with methyl iodide with retention of configuration. <sup>284b</sup> Here again, dibutylcuprate is the reagent of choice since dimethyl- and divinylcuprates lead to “normal” substitution processes proposed to proceed via Cu(III) intermediates. <sup>284b,285</sup>



Substitution of enol diphenyl phosphates or triflates with lower-order cuprates provides an efficient route to olefins starting from ketones. Enol triflates react with diorganocuprates in a stereospecific manner and in high yields. (<sup>286</sup>) On the other hand, while dibutylcuprate reacts with enol diphenyl phosphates in 50–74% yields, the reaction essentially fails with dimethylcuprate. (<sup>287</sup>) Enol phosphates from  $\beta$ -keto esters or  $\beta$ -diketones couple efficiently with dialkylcuprates, resulting in a general, high-yield synthesis of stereochemically well-defined  $\alpha$ ,  $\beta$ -unsaturated carbonyl compounds. Both cyclic and acyclic

systems undergo this transformation, although cuprates derived from secondary and tertiary alkyl residues tend to give somewhat lower yields. (288) In contrast,  $\beta$ ,  $\beta$ -difluoro enol phosphates, when treated with dibutylcuprate followed by allyl halides, undergo substitution of the phosphate moiety with the allyl group (Eq. 81). (289) An intermediate vinylorganocopper is thought to be the alkylating agent. The reaction of analogous diethyl phosphates, however, gives substitution of fluorine (*cis* to the aryl group) by butyl. Replacement of the aryl group with an alkyl moiety results in cleavage of the phosphate function to the corresponding enolate. (289)

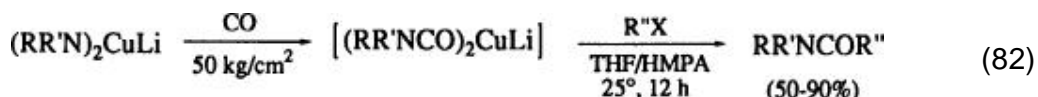


Reactions of (*E*)- $\beta$ -haloalkenyl sulfones with lower-order cuprates give substitution products with retention of olefin geometry. (290, 291) The corresponding *Z* isomers are less stereoselective, affording an isomeric mixture of products. (291) The reaction of a  $\beta$ -bromostyrene system is even more complex, resulting in several products. (291) Couplings of heteroaromatic halides with dimethylcopperlithium are synthetically unattractive because reduction products predominate. (292)

### 3.1.3.1.2. Miscellaneous Couplings

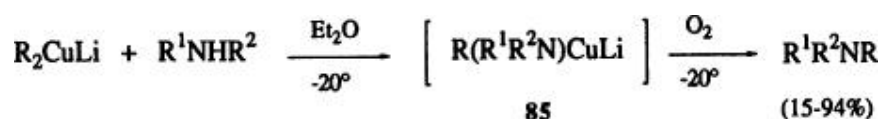
Reactions of lower-order cuprates with heteroatomic electrophiles represent a relatively new area in organocopper chemistry. Chiral sulfoxides of high optical purity are obtained from treatment of (–)-menthyl-(*S*)-arylsulfonates with diorganocuprates. (293) Similarly, phosphinate chloro esters derived from cinchonine and dichlorophenylphosphine react with aryl cyanocuprates to produce chiral phosphines and phosphine oxides. (294) Electrophilic amination of dialkynylcuprates with *N,N*-dimethylhydroxylamine-*O*-phosphinate has also been reported. (295)

Lithium bis(*N,N*-dialkylamino)cuprates react with carbon monoxide to form the corresponding bis(dialkylcarbamoyl)cuprates; the latter behave as efficient carbamoylating agents toward alkyl halides, epoxides, and acid chlorides (Eq. 82). (296, 297)

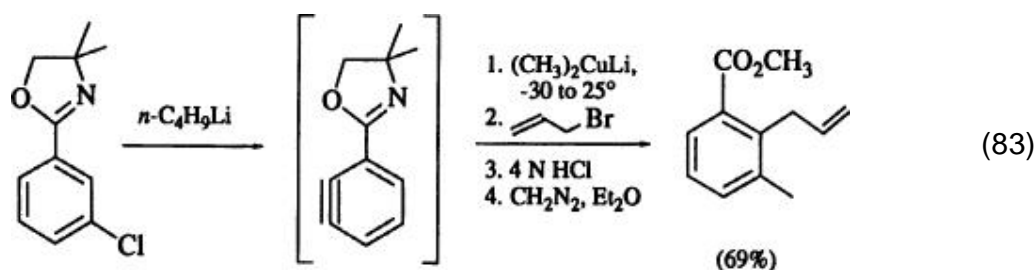


While homocuprates produce varying yields of dimers upon autooxidation, (298, 299) di(*o*-alkoxyaryl)cuprates lead to the corresponding phenols in moderate yields, accompanied by only minor amounts of dimers. (300) An alternative synthesis of phenols from diarylcuprates via reaction with diborane and then alkaline peroxide oxidation has also appeared, (301) although there seems to be no particular advantage in using cuprates instead of organolithium reagents.

Oxidative coupling of anilidocyanocuprates with *o*-lithio benzamides provides a one-step synthesis of *N*-arylanthranilamides, which can then be easily cyclized to acridone derivatives. (302) On a similar note, the heterocuprates **85**, in the presence of oxygen, offer a mild and convenient *N*-alkylation procedure for primary and secondary amines. (303)



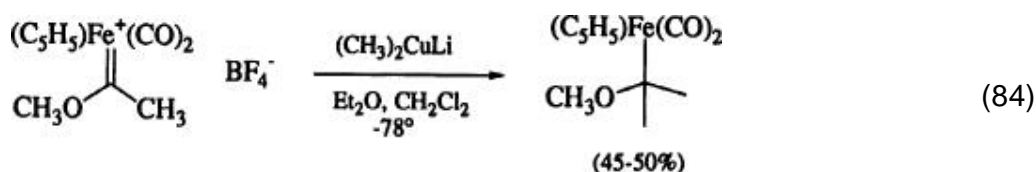
A one-pot sequence to 2,3-disubstituted benzoic acids is available by way of lower-order cuprate addition to *o*-oxazolinobenzynes (Eq. 83). (304) Another in situ derivatization involves halide displacement on an  $\alpha$ -phosphonyl carbenoid with dialkylcuprates to give good yields of  $\alpha, \alpha$ -disubstituted methylphosphonates, (305) highly valued precursors for Horner–Emmons olefination reactions.



Couplings of dialkyl and diaryl cuprates with organomercurials have been studied, but appear to be synthetically unattractive. (306)

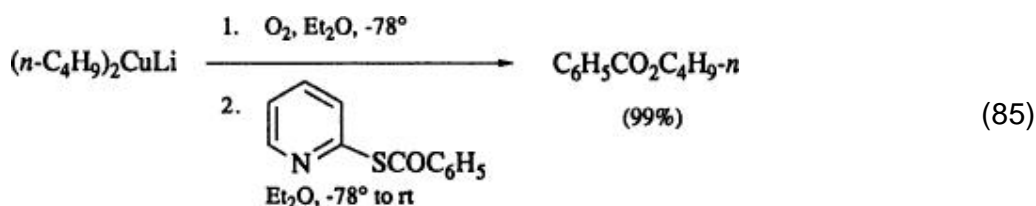
Dimethylcupperlithium can also be utilized in substitution reactions with

transition metal complexes, as reported for (arene)manganese tricarbonyl cations, (307) and Fischer-type iron–carbene complexes (Eq. 84). (308)

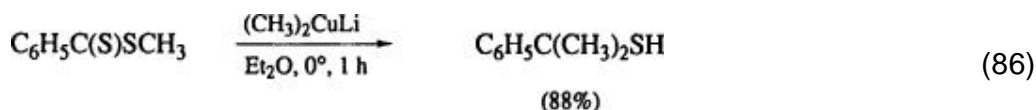


### 3.1.3.1.3. Carbonyl Compounds

Lower-order cuprate-induced substitutions of acid chlorides are efficient procedures for preparing ketones. (282, 309-311) Alternatives do exist, however, including use of selenoesters as substrates. (312) Organocuprate displacements on *S*-2-pyridylthioates also afford ketones in high yields, observations which have figured prominently in sequences leading to total syntheses of erythronolide A (313) and monensin. (314) If, however, oxygen is bubbled through solutions of  $\text{R}_2\text{CuLi}$  prior to addition of the thioester, the corresponding carboxylic esters are produced in high yields (Eq. 85). (315) An intermediate alkoxy cuprate has been suggested as the reactive reagent.



Dithioesters undergo carbophilic attack, giving rise ultimately to tertiary thiols through the intermediacy of thioketones (Eq. 86). (164) Related regiochemistry is observed in reactions of diphenyl-, dimethyl-, and di(*n*-butyl)cuprates with 1,3-thiazole-5-(4*H*)thiones, (316) although di(*tert*-butyl)copperlithium affords solely reduction products.



Additional examples can be found in Table IV-F.

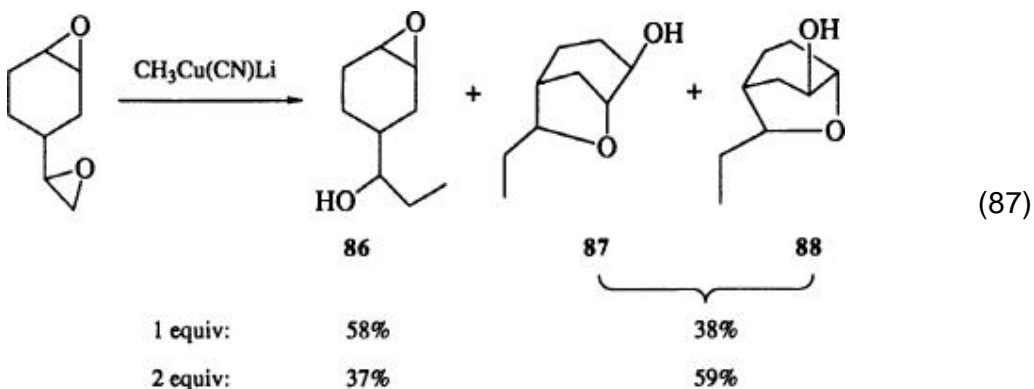


#### 3.1.3.1.4. Epoxides

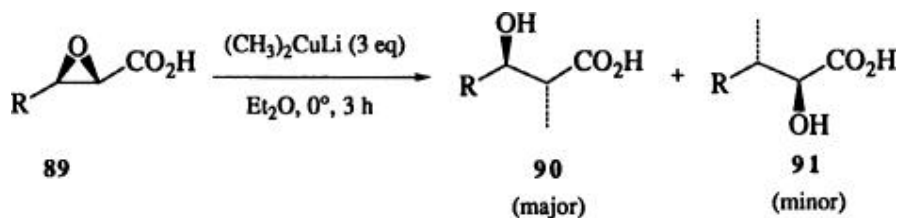
Ring opening of oxiranes with lithiodiorganocuprates represents a powerful, highly utilized synthetic methodology (see Table IV-B). Monosubstituted epoxides make excellent substrates for lower-order cuprate couplings, the regiochemistry of which favors attack at the least-hindered site.

1,1-Disubstituted oxiranes are opened regiospecifically, while 1,2-disubstituted examples often give mixtures of regioisomers or byproducts of elimination or rearrangement. Trisubstituted examples are best opened with higher-order reagents (Table IX-A). Mixed lower-order cuprates, for example,  $\text{RCu}(\text{CN})\text{Li}$ , offer an economical route to alcohols, where full utilization of the organic ligand can be anticipated, especially with acyclic epoxides (except for styrene oxide). (317) With cyclic systems (e.g., cyclohexene oxide), however, yields are only moderate. (317)

Cuprate couplings with epoxides containing neighboring functionality can often result in secondary processes. Thus 4-vinylcyclohexene dioxide, on being treated with 1 equivalent of  $\text{CH}_3\text{Cu}(\text{CN})\text{Li}$ , undergoes ring opening of the less-hindered pendant epoxide (Eq. 87). (318) The initial ring-opened product **86** then reacts further to induce an intramolecular (regiorandom) ring opening of the cyclic oxirane forming **87** and **88**. The proportion of these two bicyclic materials increases when 2 equivalents of the cuprate are used, conceivably owing to mixed heterocuprate formation between the alkoxide of **86** and residual (or additional) cyanocuprate. (318)

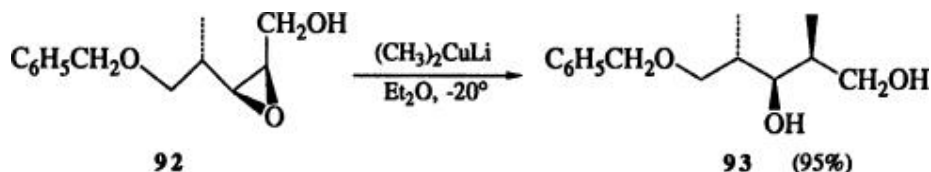


Nonracemic 2,3-epoxy acids react with diorganocuprates in a regioselective manner. The *trans*-epoxy acids **89** are preferentially attacked at the more electrophilic C-2 position, with selectivities of **90:91** between 8:1 and 30:1

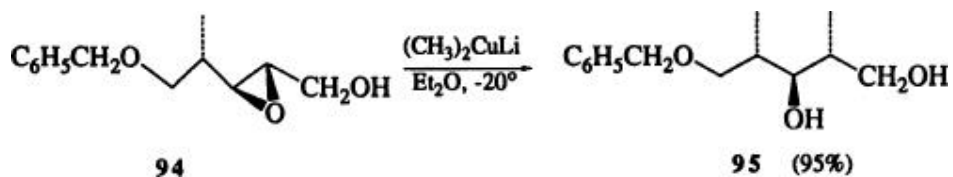


reaching a maximum for the *tert*-butyldiphenylsilyloxy derivative **89**, R = CH<sub>2</sub>OSi(*t*-Bu)(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>. (319) The *cis*-epoxy acids, on the other hand, are attacked at the C-3 center. These results complement the known regioselectivity of cuprate attack on α, β-epoxy esters. (320, 321)

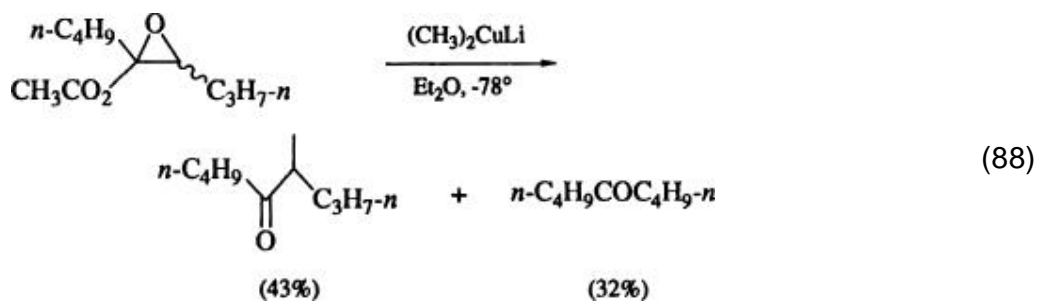
Cuprate-mediated opening of epoxy alcohols **92** is highly stereoselective and leads to structural subunits such as **93**, commonly encountered in many



polyacetate/propionate-derived natural products. Dimethylcopperlithium attacks the *cis*-epoxide **92** exclusively at the 2-position (i.e., away from the methyl group at C-4) to form **93** in 95% yield. (322) The origin of this regioselectivity is hindrance from the C-4 methyl moiety, rather than chelation effects associated with the hydroxy group. In the absence of the alkyl appendage at C-4, the regioselectivity is lost. (322) The *trans*-epoxide **94** shows complementary behavior with dimethylcopperlithium and produces exclusively the corresponding diastereomer **95**. (322)



Ring opening of α-acyloxyepoxides by diorganocuprates was envisioned as a good method for nucleophilic α-alkylation of ketones. Unfortunately the yields are modest, since undesired side reactions, principally involving competitive electron transfer to form unsubstituted (reduced) products, predominate (Eq. 88). (323)

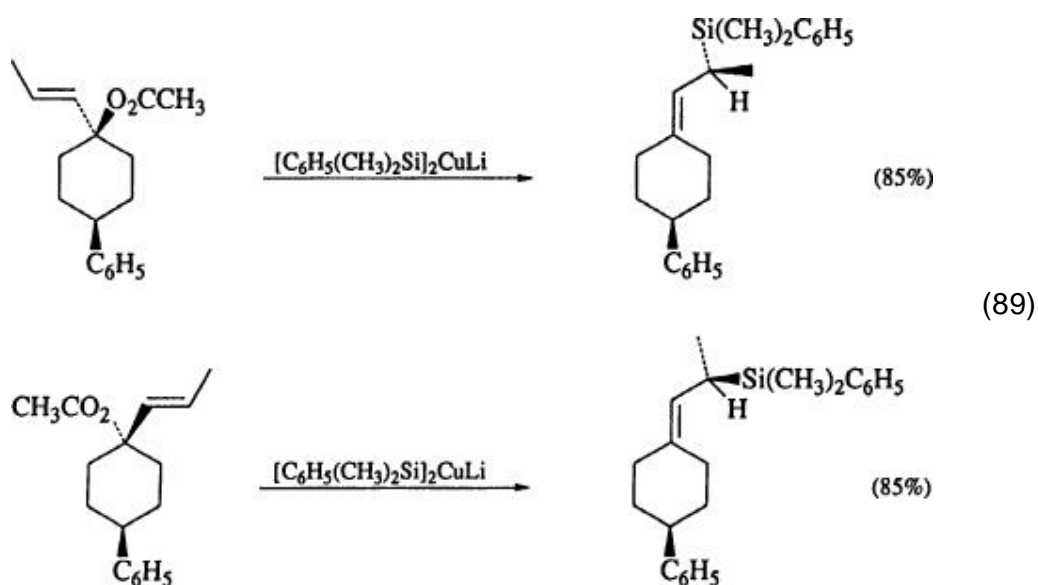


Reactions of cyclohexene oxide with organocuprates containing nonracemic ligands have been investigated. In all cases the  $\beta$ -substituted alcohols so formed reflect very low levels of optical induction. (324)

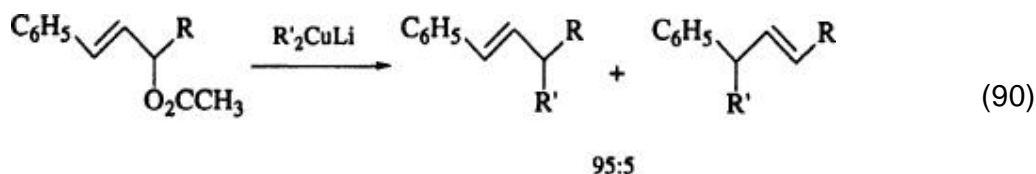
#### 3.1.3.1.5. Allylic Substrates

The predominant mode of lower-order cuprate reactions with allylic substrates is one of allylic inversion; that is, an  $S_N2'$  addition which occurs in a stereoselectively *anti* fashion.

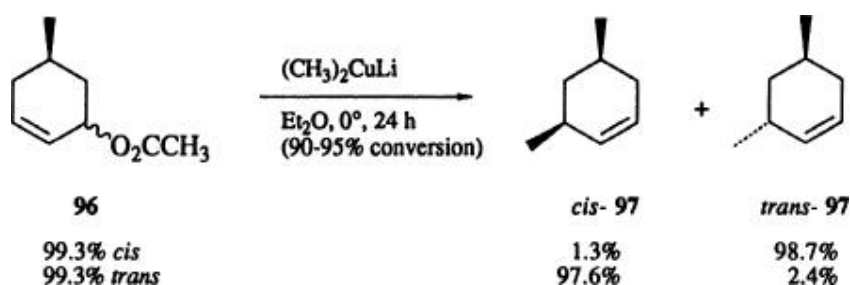
Synthetic uses of these 1,3 displacements with diorganocuprates are listed in Table IV-C. Readily available allylic acetates function nicely in this regard. Coupling (in an *anti* –  $S_N2'$  mode) with silylcuprate reagents stereospecifically produces allylsilanes (Eq. 89). (325)



The regio- and stereoselectivity of alkylation of allylic acetates and pivalates with lower-order cuprates has been studied. [53c,59,60,326](#) Examination of cinnamyl acetates reveals an overwhelming preference for regioselective  $\alpha$  attack, the conjugated olefin comprising 95% of the product mixture (Eq. [90](#)). [59c,d](#) For

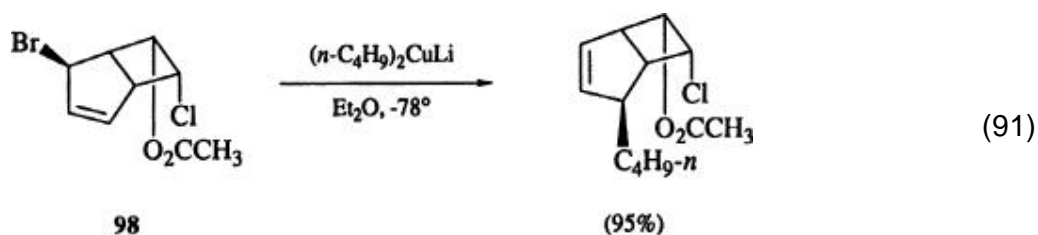


*cis*- and *trans*-5-methyl-2-cyclohexenyl acetates [96](#), which are regiochemically unbiased systems, the reaction with dimethylcopperlithium is stereospecific: *cis*-[96](#) gives *trans*-[97](#) and vice versa. [59e](#) Deuterium labeling studies show that this reaction occurs primarily (>80% selectivity) via the *anti*  $S_N2'$  mode. [53c,59e](#) The steric effects associated with these couplings have also been assessed. ([327](#)) Preparatively, however, cuprate couplings with allylic acetates are accompanied by ester cleavage thus lowering yields, and hence use of trimethyl-benzoates

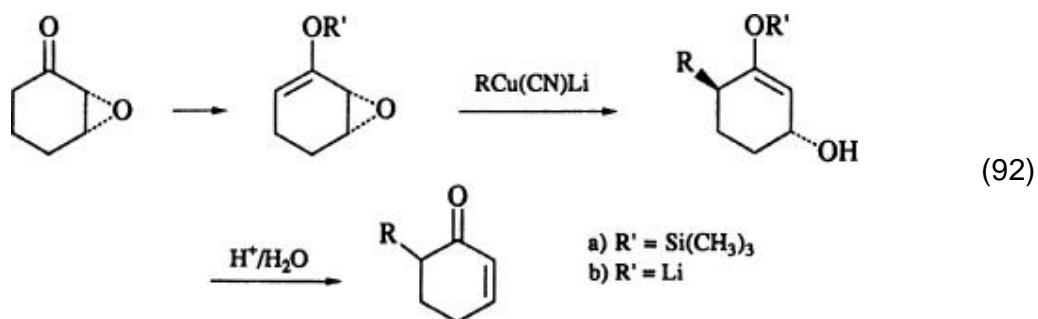


is recommended. [53c](#) Best results are obtained by copper(I) cyanide-catalyzed Grignard reactions of organocuprates with allylic acetates. ([62](#)) Recently, the involvement of a copper *d*-orbital with the appropriate  $\pi^*$  and  $\sigma^*$  orbitals of the substrate has been proposed to explain the *anti*-stereochemistry in  $S_N2'$  reactions with cuprates (cf. [12](#), page 145). ([39](#))

In sharp contrast to the *anti*- $S_N2'$  outcome from reactions of allylic esters with  $R_2CuLi$ , the corresponding carbamates show typically a *syn*-reaction mode, although maintaining an  $S_N2'$  -type addition. [52,53b](#) Mechanistic proposals for this reaction have also been put forth. [53b](#) Departure from *anti* selectivity can also occur because of steric effects. Thus in the cyclopentenyl bromide [98](#), the pendant acetate and chloride groups hinder approach of the cuprate from the side opposite the bromine and dictate *syn*- $S_N2'$  attack (Eq. [91](#)). ([328](#), [329](#))

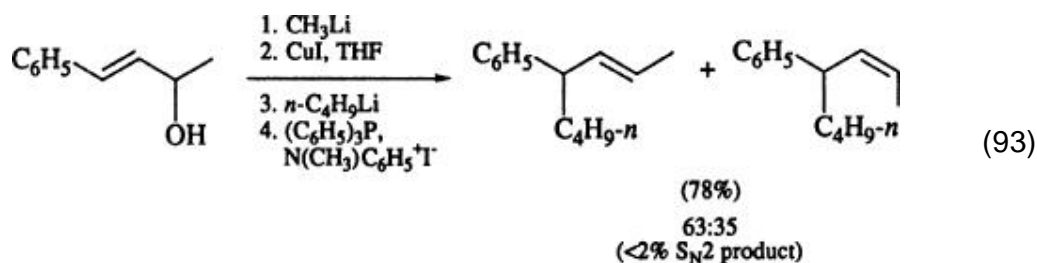


Reactions of homocuprates with acyclic vinyloxiranes are known to occur with allylic rearrangement, although such dogma does not prevail in the case of cyclic systems, where both 1,2 and 1,4 additions are observed. (330, 331) The mixed cyanocuprates, however, not only conserve potentially valuable organic residues, but also favor 1,4 attack with over 90% selectivity. (331) A variation of this methodology involves the trimethylsilyl enol ethers of  $\alpha$ ,  $\beta$ -epoxycyclohexanones. Addition (*anti*- $S_N2'$ ) to these substrates is equivalent to nucleophilic substitution at the  $\alpha'$  position of cyclohexenones [Eq. 92,



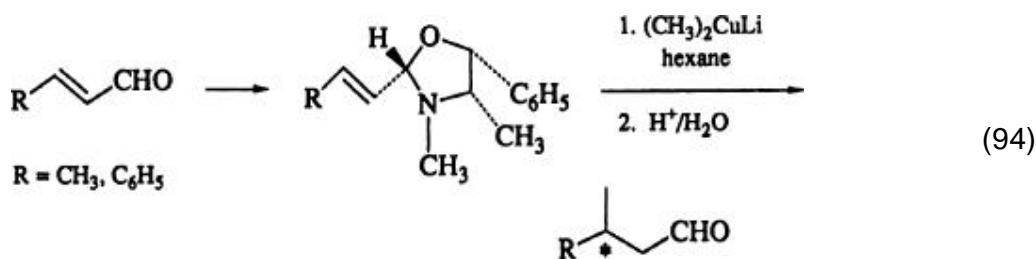
$\text{R}' = \text{Si}(\text{CH}_3)_3$ ]. (332, 333) The lithium enolates of  $\alpha$ ,  $\beta$ -epoxycycloalkanones (Eq. 92,  $\text{R}' = \text{Li}$ ) behave in the same fashion, (333) and the resulting allylic alcohols can be converted into  $\alpha'$ -substituted cyclohexenones by acid hydrolysis, elimination, and rearrangement. (332, 333)

Lithium alkoxides of allylic alcohols together with an equivalent of cuprous iodide, (methylphenylamino)triphenylphosphonium iodide, and an organolithium, combine to effect  $S_N2'$  substitutions (Eq. 93). 334a,b This four-step,



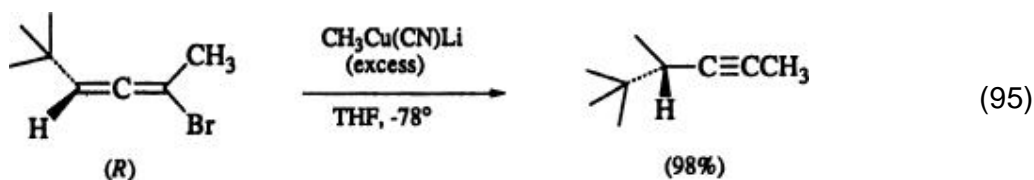
one-pot process, for which mechanistic studies have been carried out, gives >96%  $\gamma$ -alkylation. [53a](#) An allyloxyphosphonium salt and a lower-order mixed amidocuprate are believed to be the reactive partners. The sequence has since been extended to propargylic alcohols from which allenes are obtained in good yields, also in a single reaction vessel. [334c](#)

Nonracemic oxazolidines derived from  $\alpha$ ,  $\beta$ -unsaturated aldehydes and (+)- or (-)-ephedrine are receptive toward lower-order cuprate additions, producing optically active aldehydes after hydrolysis (Eq. [94](#)). ([82](#), [83](#), [335](#), [336](#)) This,



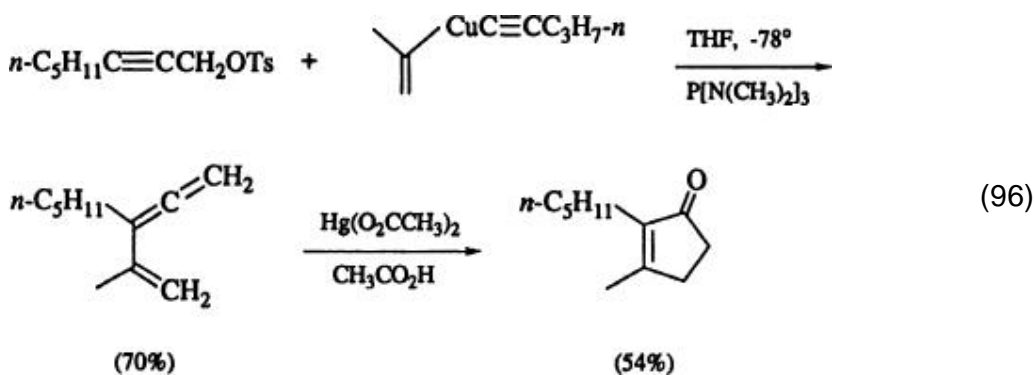
of course, is tantamount to asymmetric conjugate addition to enals. Best results are obtained in hexane with enantiomeric excesses (ee) up to 80%. [335c](#) When the  $\beta$  carbon contains an electron-withdrawing carbomethoxy group, the cuprate adds to the enoate (reversing the regiochemistry of addition) to give diastereomeric excesses (de) on the order of 95% along with good chemical yields. ([336](#)) This methodology has provided a short synthesis of (*R*)-(+)-citronellal of 85% optical purity. ([83](#))

Alkylcyanocuprates react with optically active bromoallenes preferentially (>97%) via an *anti*-S<sub>N</sub>2' mode to afford optically active acetylenes (Eq. [95](#)). The combination of sterically hindered bromoallenes together with bulky cuprates, however, redirects the coupling to favor straight substitution. ([31](#))

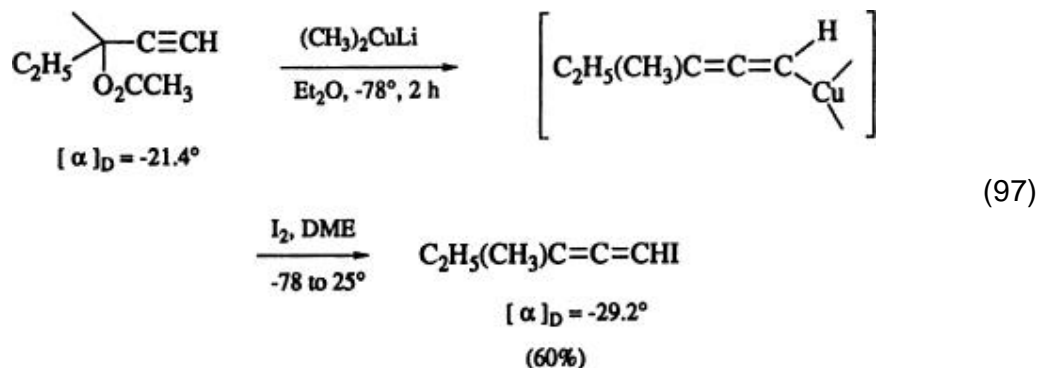


### 3.1.3.1.6. Propargylic Substrates

Displacement reactions of propargylic systems in an  $S_N2'$  sense to afford allenes are usually best effected by organocopper (RCu) or Grignard-derived (catalytic) copper reagents. (180) Nevertheless, there are scattered reports discussing reactions of lower-order cuprates with propargylic substrates for the preparation of stereodefined allenylsilanes, 325b as well as diversely substituted allenes. (28) Additional examples can be found in Table IV-D. Vinylallenes have been formed via related couplings which set the stage for their facile conversion to cyclopentenones (Eq. 96). (337)



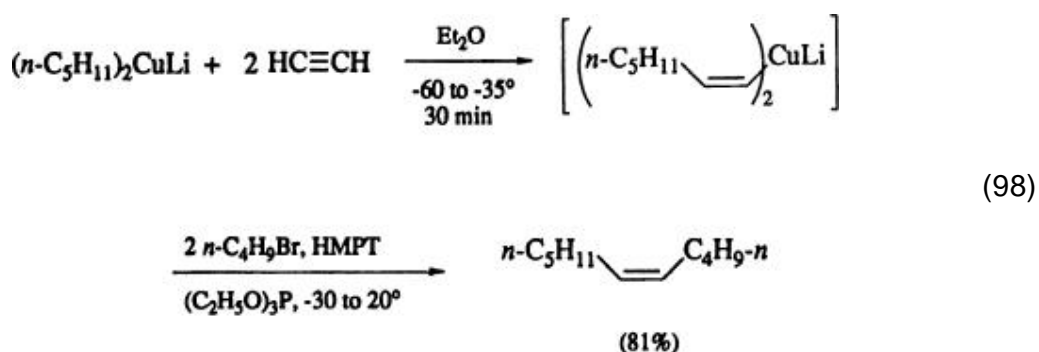
Reactions of homocuprates with propargylic acetates occur in an *anti*- $S_N2'$  sense, possibly via a two-step mechanism involving a transient Cu(III) allenyl intermediate. (338, 339) Such an intermediate can be trapped with iodine and subsequently utilized in a synthesis of chiral iodoallenes (Eq. 97). (339) Another



route to chiral allenes involves homocuprate displacement of diastereomerically pure propargylic carbamates, although net chiral induction is only moderate. (340) Problems associated with chirality control in allene formation from propargylic substrates stem from the fact that various organocuprates may induce racemization of chiral allenes. (35) Occasionally, reactions of propargylic substrates with cuprates are accompanied by considerable amounts of reduction products which may be preparatively useful. (341, 342)

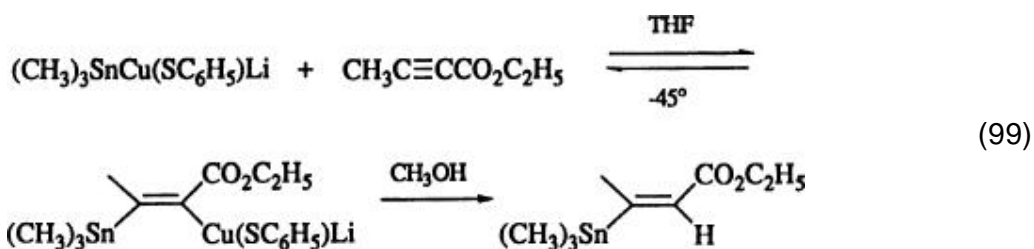
### 3.1.3.2. Carbocupration

Carbocupration of terminal acetylenes can be plagued by removal of the acetylenic hydrogen. (343) Nonetheless, acetylene itself undergoes efficient carbocupration with lower-order cuprates in ether to afford dialkenylcuprates (transfer of both ligands from  $\text{R}_2\text{CuLi}$  occurs), which go on to participate in various electrophilic substitution processes (Eq. 98; see also Table V). (344-350)

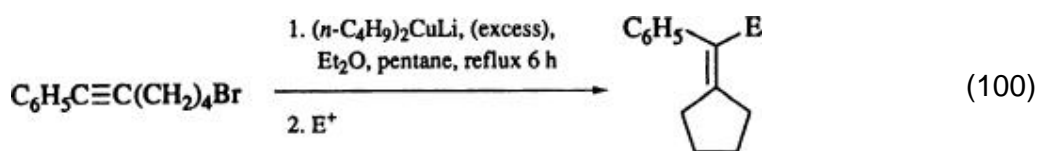


Stannylicupration of acetylenes is facile, but involves a dynamic equilibrium which can be driven forward only with protons as electrophiles. (351, 352) Hence, disubstituted but not trisubstituted vinylstannanes can be realized (Eq. 99).

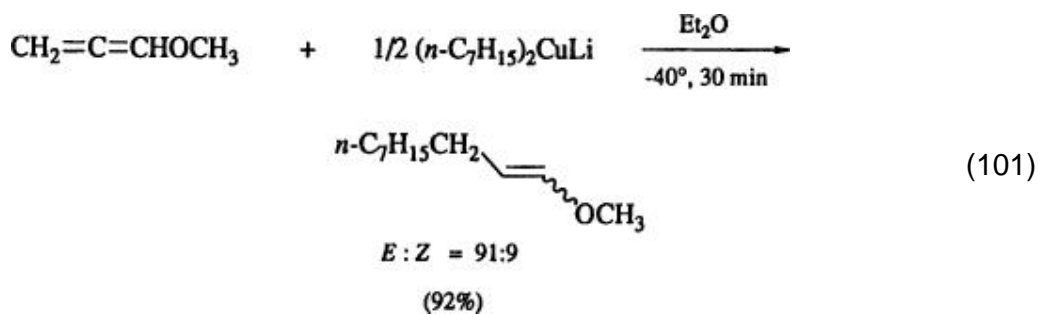




Reactions of  $\omega$ -bromophenylacetylenes with dibutylcuprate followed by quenching provides an efficient means of preparing exocyclic alkenes. (353) The reaction is highly solvent-dependent, with best results obtained in pentane–ether (7:1). Presumably the reaction proceeds via initial bromine–copper exchange and then intramolecular carbocupration (Eq. 100).

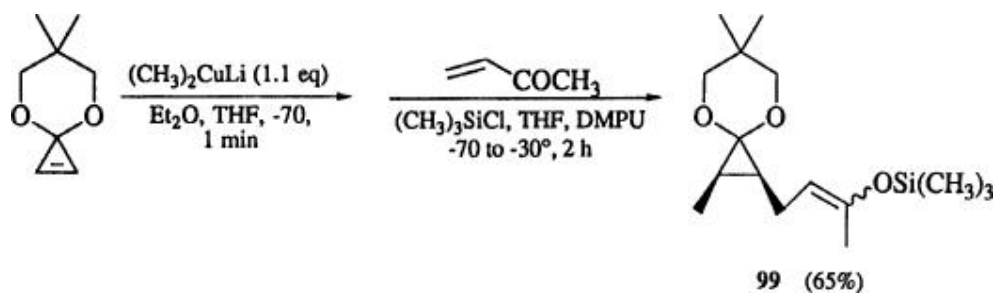


Whereas organocopper (RCu) species in tetrahydrofuran give *Z*-selective enol ethers as products, reactions of methoxyallene with dialkylcuprates in ether produce *E*-selective vinyl ethers (Eq. 101). (354)



The first and only known example of carbocupration of an olefin has recently appeared. (355) Lower-order lithio cuprates add efficiently to the double bond of a cyclopropenone ketal, the corresponding cuprate from which can be further elaborated by subsequent reactions with electrophiles such as alkyl

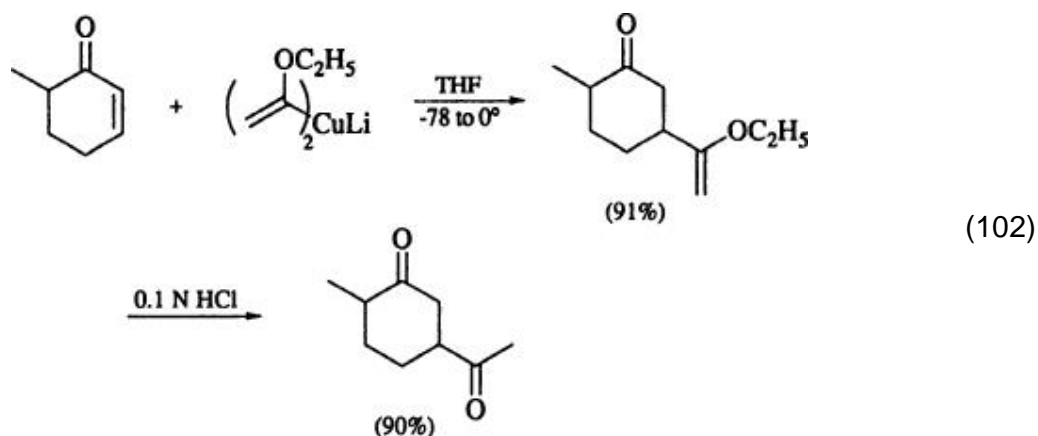
and vinyl halides. The latter class, however, requires the presence of a Pd<sup>0</sup> catalyst. Conjugate addition also readily occurs, assisted by chlorotrimethylsilane and *N,N*-dimethylpropyleneurea (DMPU), to afford from methyl vinyl ketone the *cis*-disubstituted cyclopropanone ketal **99** in good yield.



### 3.1.3.3. Conjugate Addition

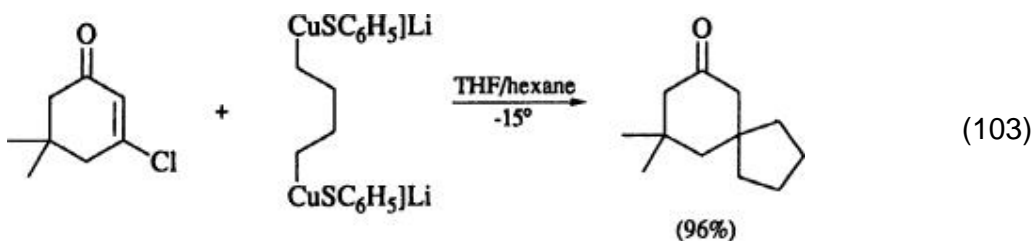
1,4 Additions of carbon- and heteroatom-based ligands (R<sub>3</sub>Si- or R<sub>3</sub>Sn-) from R<sub>2</sub>CuLi to unsaturated systems, best performed in the absence of good donor solvents, are usually quite efficient, facile, and highly tolerant of other functionality present in the educt. As a consequence, this methodology represents one of the most frequently used tools for structure elaboration in organic chemistry. Beyond the reports cited below, which allude to such topics as functionalized reagents, tandem conjugate addition/enolate trapping, variations in substrate makeup, and asymmetric synthesis, many more examples can be found in Table VI.

The utility of functionalized cuprates is of considerable synthetic value, since the 1,4 adducts offer opportunities for further manipulation. As an illustration, 1,4-diketones are readily available via the conjugate addition of  $\alpha$ -methoxyvinyl cuprates (Eq. 102). [356a](#) Other examples include those



deric  $\alpha$ -vinylacetals [356a,359](#) and  $\alpha$ -vinyl ethers. [360,356c](#)  $\alpha$ -Alkoxy cuprates have also recently been described. ([361](#)) While all of these reagents are potentially useful, they unfortunately show reduced reactivity relative to unfunctionalized diorganocuprates, and in the extreme (e.g.,  $\alpha$ -carbethoxyvinyl cuprates) may find their chemoselectivity altered such that 1,2 addition takes place. ([362](#))

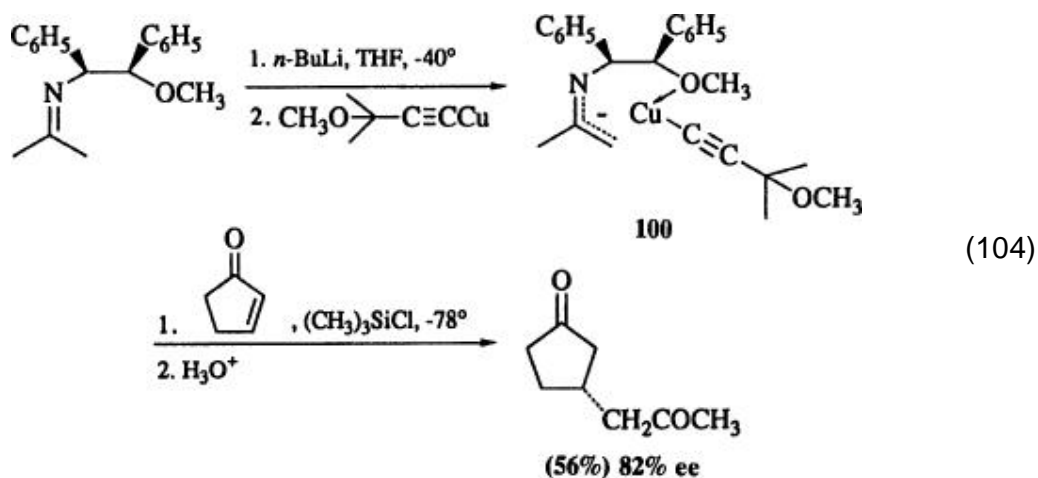
Spirocyclic systems can be generated in a single operation by use of novel bisorganocuprates (e.g., Eq. [103](#)). ([363](#)) Although  $\beta$ -halo enones are easy to come



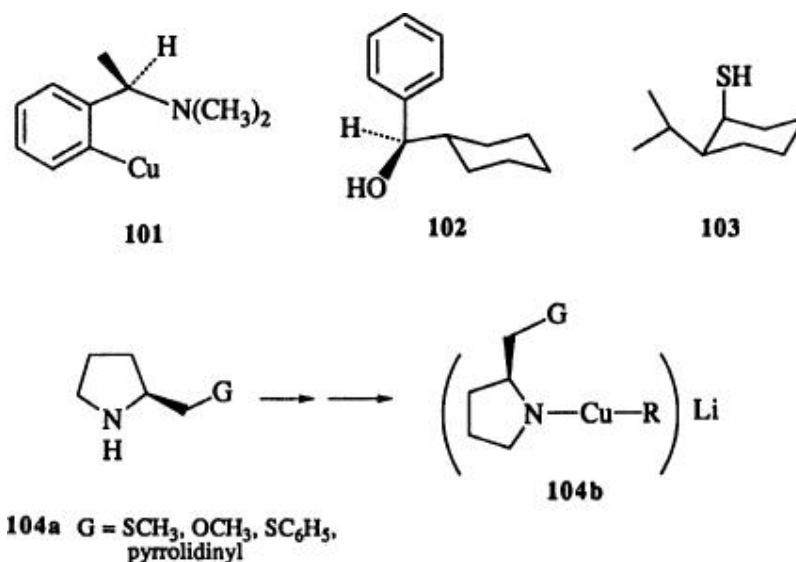
by, preparation of  $\alpha, \omega$ -dianions, especially those bearing functionality, is the limiting feature of this route. Aryl and olefinic residues can be introduced, however, as part of the newly formed ring. ([363](#))

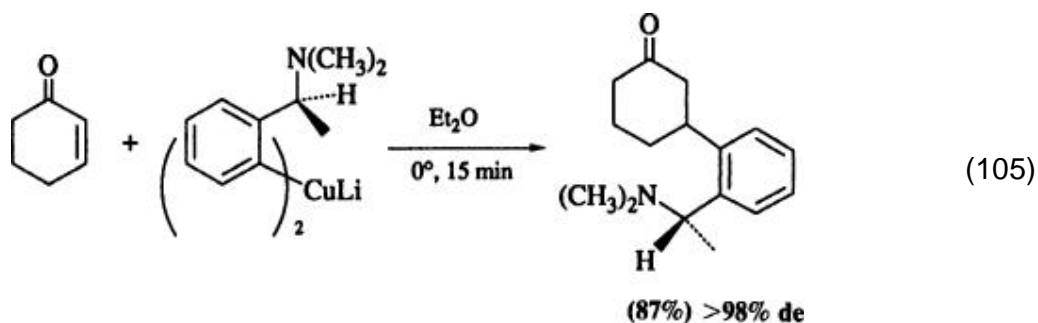
One-pot conjugate addition–enolate alkylation is the theme of two recent reviews. [4h,364](#) Many examples of this concept exist in the cuprate literature, especially concerning the syntheses of prostaglandins and steroids (vide infra and Tables [XI-C](#) and [XI-E](#)). However, the alkylation of an enolate derived from a cuprate conjugate addition is still not a well-understood process. Although it has been claimed that such enolates are lithium bound, ([365](#)) their reactivity differs from that of “normal” lithium enolates. A common practice for alkylation of such enolates is to use chlorotrimethylsilane as a trapping agent to form the isolable silyl enol ether which can be subsequently exploited as desired. Direct alkylation of enolates derived from conjugate addition does not follow any obvious pattern and is usually highly dependent on solvent and the nature of the alkylating agent. ([366](#))

Asymmetric conjugate addition employing predominantly lithio, rather than magnesio, ([254, 256, 257](#)) cuprates has been approached from various directions. Use of a chiral auxiliary *en route* to chiral mixed cuprates ( $R_T^*R_R\text{CuLi}$ ), such as that derived from azaenolate [100](#) affords ee's up to 82% (Eq. [104](#)). ([367](#)) The

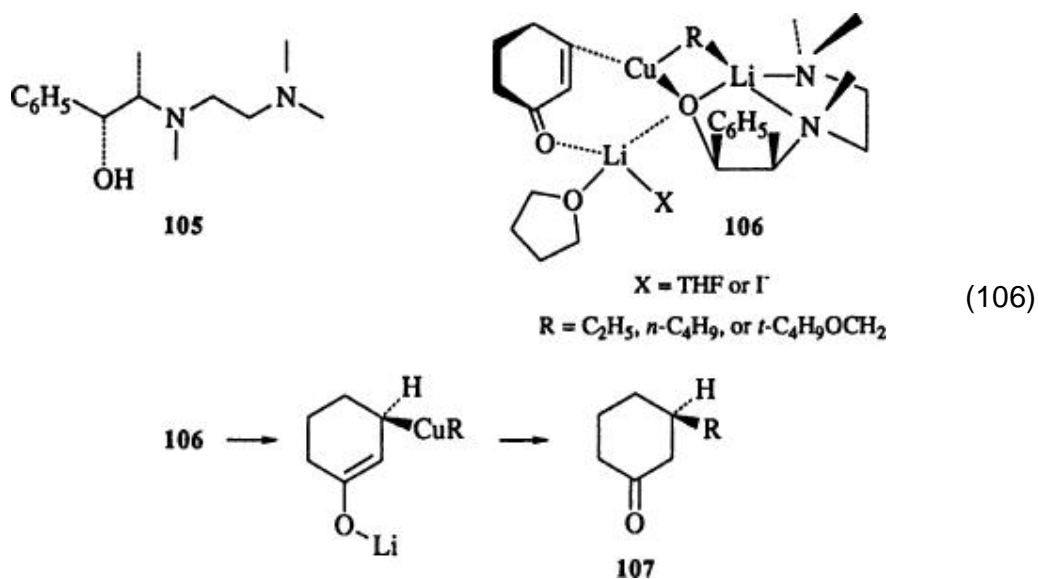


use of chiral mixed cuprates ( $R_T R_R^*$ )  $\text{CuLi}$  has been examined. (368, 369) The chiral nontransferring ligands used include metalated, optically active  $\alpha$ -alkylphenethylamine derivatives (101), alcoholates of 102, and thiolates of 103. Although ee's are low (0 to ~15%), there is an indication here that  $R_R^*$  is involved in the transition state of the 1,4 addition. 369b In contrast, when the chiral amine is part of the  $R_T$  within the homocuprate, very high de's can be obtained (Eq. 105). (370) Various prolinol derivatives (104a) pursued on the basis of earlier observations (257) have also given enantioselectivities as high as 83% when incorporated into 104b. (371) Thus far, best results (ee > 95%) emanate

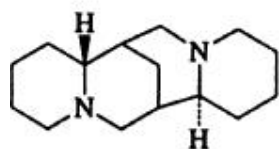




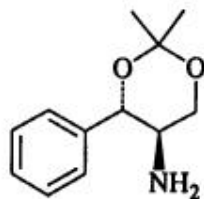
from cuprate clusters incorporating the modified ephedrine **105**. (372) Model **106** has been advanced which envisions complexation of both lithium ions in solution ( $\text{RR}'\text{CuLi}$  and  $\text{LiX}$ ) and predicts cuprate attack from the *re* face of the enone leading to product **107** (Eq. 106).



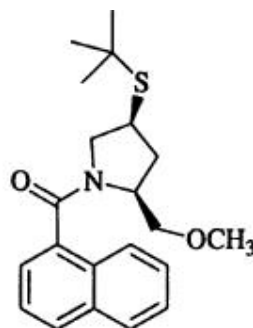
Another approach to asymmetric conjugate addition relies on the presence of optically pure additives in the reaction mixture, unsuccessfully attempted initially using sparteine (**108**) as the chiral ligand. (373) Chiral amine modified cuprates [ $\text{RCu}(\text{NR}_2)_2\text{Li-Amine}$ , e.g., Amine = **109**] have recently been used



108



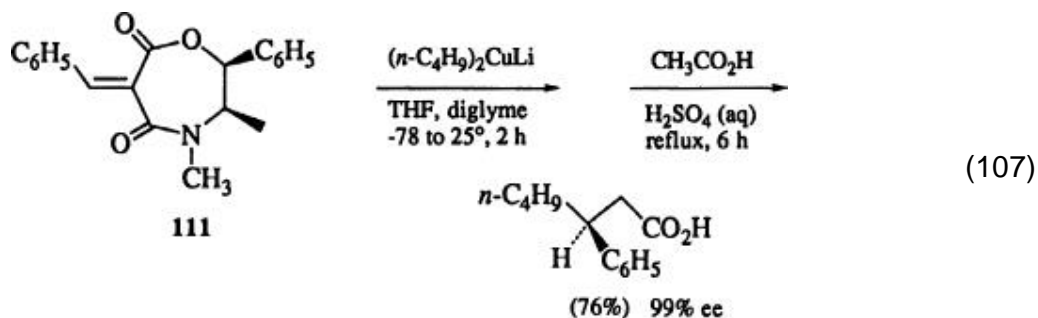
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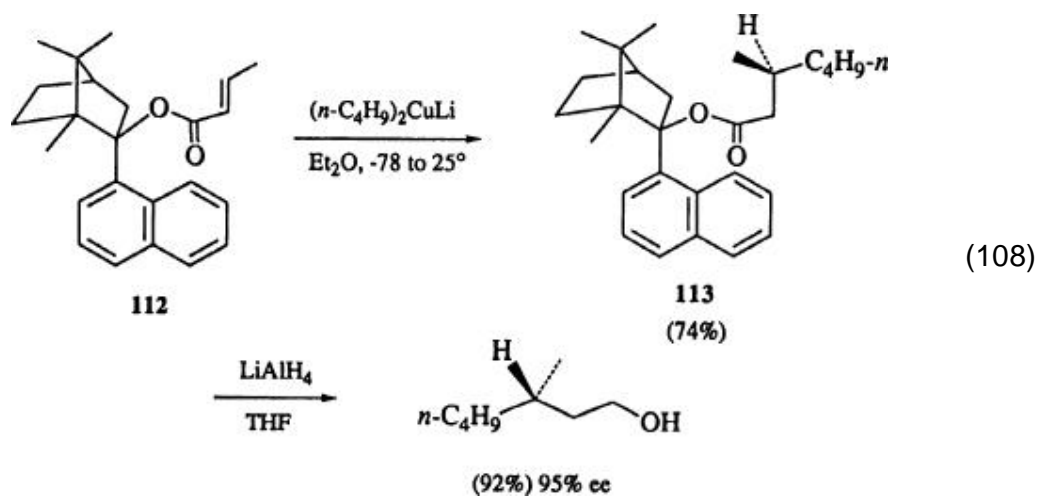
110

to afford ee's up to 50%. (374) Low optical purities (up to 15% ee) are obtained when optically active cosolvents (*R,R*)- or (*S,S*)-1,4-(dimethylamino)-2,3-dimethoxybutane are used as the only source of chirality in the medium. (375) However, with (–)-*N*- $\alpha$ -naphthoyl-2*S*-methoxymethyl-4*S*-(*tert*-butyl)thiopyrrolidine (110) as a chiral additive,  $\beta$ -methylation of chalcone in 95% ee is realized with lithium dimethylcuprate. (376)

1,4 Additions to chiral enoates are yet another means of inducing asymmetry at newly formed carbon–carbon bonds. Such reactions can be successfully carried out with chiral alkylidene perhydro-1,4-oxazepine-5,7-diones 111, the conjugate adducts from which can be easily hydrolyzed to  $\beta$ -substituted alkanolic acids in 56–99% optical yields (Eq. 107). (377) On the same theme,

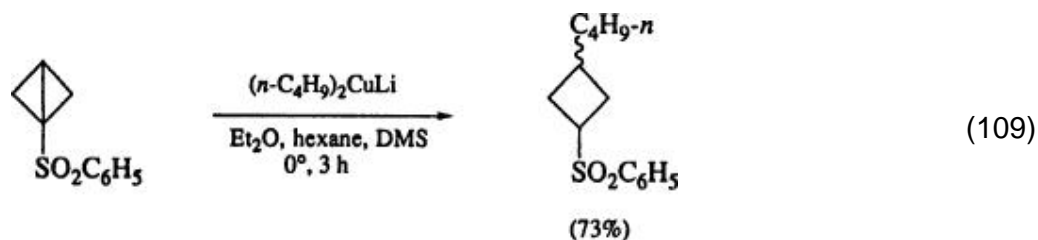


(–)-menthyl acrylates (378) and atropisomers of  $\beta$ -chloro- $\beta$ -(2-methylnaphthyl)methyl acrylates (379) have also been investigated, although with less impressive results. Recently, optically active 1,3-dioxanone derivatives have been found to direct cuprate 1,4 additions with high facial selectivities. (380) Likewise, nonracemic enoate 112, derived from (+)-camphor, induces excellent diastereoselectivity (95% de) in its reaction with lithium dibutylcuprate. The conjugate adduct 113, on treatment with lithium tetrahydroaluminate, gives the corresponding alcohol in high chemical (92%) and optical (95%) yields (Eq. 108). (381) Conjugate additions of cuprates to chiral vinyl sulfoximines also give excellent diastereomeric excesses. (382)



Apart from enones and enoates as conventional substrates, conjugate additions of cuprates to acetylenic sulfones (383) and acetylenic esters are also of interest. The latter class of compounds usually gives *cis* addition; reactions with diallyl- or dihexadienylcuprates follow the same pattern but are non-regioselective on the part of the cuprate ligand. (384) Reactions of lower-order cuprates with dienones occur primarily via 1,6 addition. (385) Cuprate additions to  $\alpha$ -allenic ketones and sulfones have been studied, (386) as have reactions with vinylphosphonates, (387) *N*-nitrosoenamines, (388) 2(1*H*)-pyrimidinones, (389) and dialkoxyphosphinylketene-*S,S*-acetals. (390) Polymerization of methyl methacrylate occurs with lithium dibutylcuprate as initiator. (391)

Cyclopropane ring opening by lower-order cuprates may be classified as homoconjugate addition, a few examples of which are in the literature. (64, 392, 393) In most cases the cyclopropane ring in the substrate is either in conjugation with an enone or is geminally deactivated. Nucleophilic ring opening takes place similarly with 1-arylsulfonylbicyclo[1.1.0]butanes and lithium diorganocuprates (Eq. 109). (394)

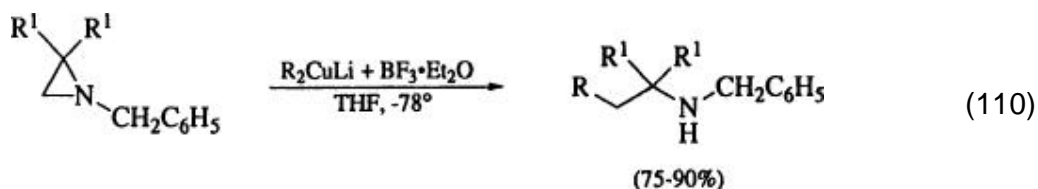


### 3.1.4. Reactions in the Presence of Additives

One of the more recently emerging aspects of organocuprate chemistry is the impact made by additives on reactions of lower-order cuprates. Although phosphorus-containing compounds (e.g., phosphines, phosphites) have been utilized for decades with the intention of solubilizing copper(I) salts and as stabilizing ligands, the apparent compatibility of electrophilic species such as boron trifluoride etherate and chlorotrimethylsilane with Gilman cuprates has significantly expanded the scope of this methodology. In general, the presence of additives of this type (i.e., electron-deficient reagents) tends to increase both rates and yields of cuprate–educt couplings. Hence, since no changes in the usual protocols for cuprate use are necessary aside from the introduction of the additive, it is not surprising that their frequency of deployment continues to grow. Most applications can be found in natural product total-synthesis endeavors, and are listed in Tables XI-A to XI-F.

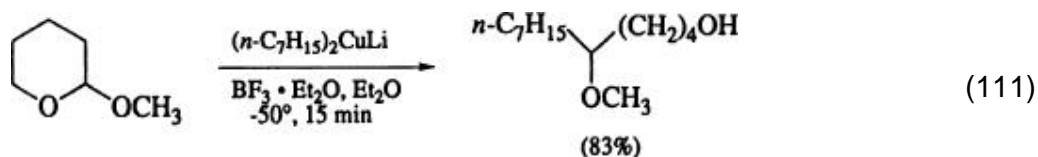
#### 3.1.4.1. Substitution

The admixture of a lower-order cuprate with (usually excess) boron trifluoride etherate at low temperatures represents a most potent combination for effecting displacements of oxygen- and nitrogen-containing functional groups. For example, cyclohexene oxide is opened by a lithium dipentylcuprate–boron trifluoride complex within 10 minutes at  $-78^\circ$  in 92% yield, (395) whereas homo- or heterocuprates alone tend to need higher temperatures and longer reaction periods with corresponding decreases in overall efficiency. Similar enhanced reactivity is reported for isoprene monoepoxide. (395) Ether is the best solvent for such reactions; the order of mixing of the cuprate, the substrate, and boron trifluoride does not have any effect on the reaction pathway. (395) Aziridines also undergo alkylation with lithium diorganocuprates in the presence of boron trifluoride etherate; (396) very poor yields (~10%) are obtained when this Lewis acid is absent (Eq. 110).



Acetals and ketals, which are usually stable toward organocupper reagents alone, can be easily cleaved when boron trifluoride etherate is added to the reaction mixture. (395) Various lower-order cuprates can be used, and ether as a solvent is indispensable (Eq. 111). With orthoesters, an interesting selectivity

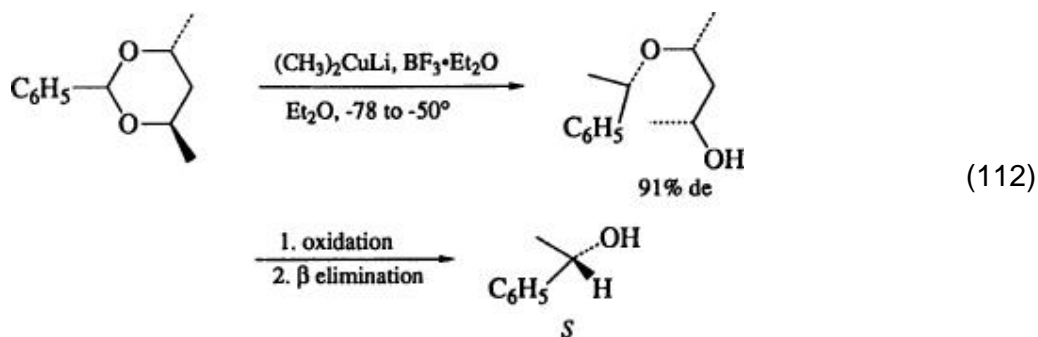




is found in this cleavage process; when the reaction is performed in tetrahydrofuran, it stops at the acetal stage. (395)

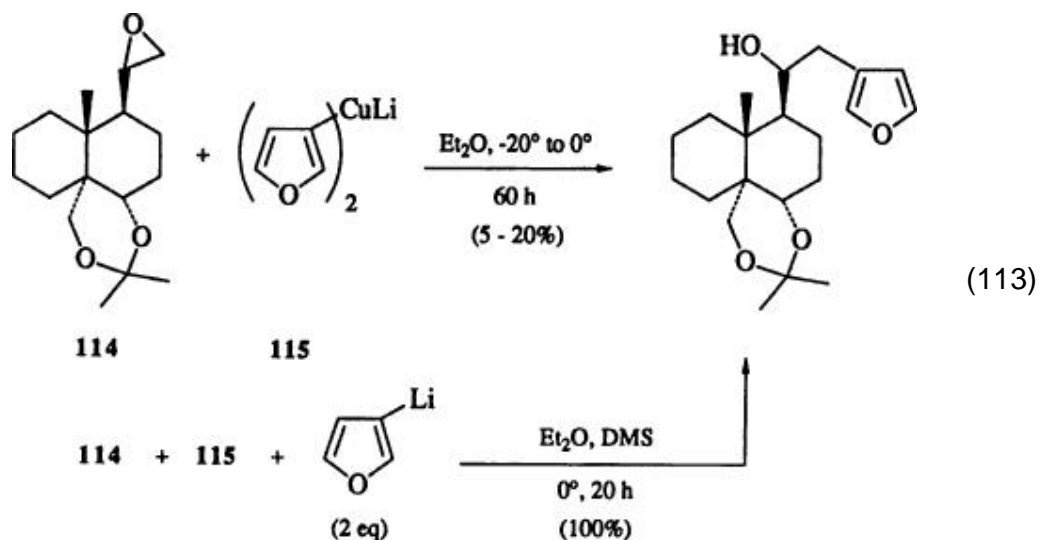
Cleavage of allylic acetals with Grignard reagents in the presence of copper(I) catalysts shows excellent  $S_N2'$  selectivity. (122) Although use of  $R_2CuLi \cdot BF_3$  enhances the reaction rate, only marginal regioselectivity is observed, (397) while complexes  $RCu \cdot BF_3$  show high regioselectivity. (398) The *anti*- $S_N2'$  coupling of a diarylcuprate can be mediated by boron trifluoride etherate. (399)

Diastereoselective cleavage of chiral acetals with  $R_2CuLi \cdot BF_3$  offers a new route to optically pure secondary alcohols (Eq. 112). (400) Selectivity is dependent



upon not only the nature of the acetal (alkyl vs. aryl), but also on the organocopper species and the Lewis acid, a diorganocuprate- $BF_3 \cdot Et_2O$  being the best choice. Titanium tetrachloride in conjunction with  $R_2CuLi$  gives low yields, probably because of the incompatibility of cuprates with this powerful Lewis acid. (399, 401)

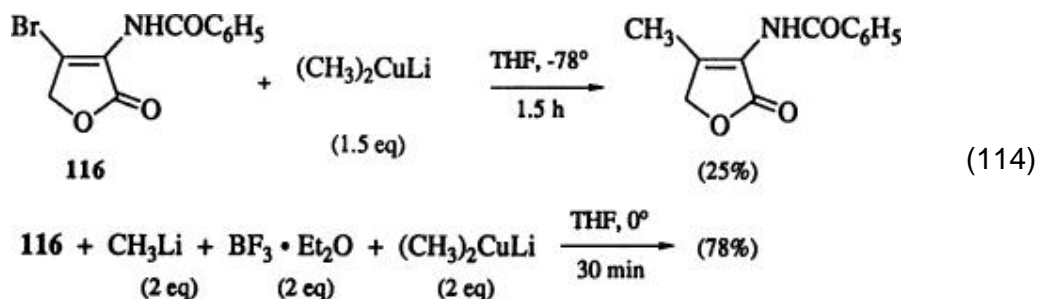
Judging from the importance of lithium ions to cuprate reactivity (see discussion on mechanism of conjugate additions and effects of crown ethers), it follows that extra alkyllithium added to solutions of  $R_2CuLi$  can also be considered an additive. For example, delivery of a 3-furyl group regioselectively to the least-hindered center of substituted epoxides occurs best when the epoxide 114/Gilman homocuprate 115 mixture contains two additional equivalents of 3-furyllithium (Eq. 113). (402) Substitution reactions of cyclic,



alicyclic, and aryl halides also give good results with  $\text{Me}_2\text{CuLi}\cdot\text{MeLi}$ . (403) As expected with enones, however, the presence of free methyllithium can lead to competitive products of 1,2 addition. (404)

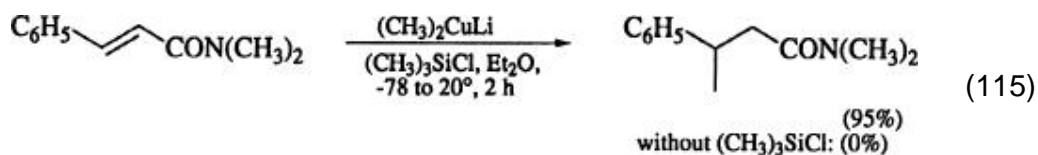
#### 3.1.4.2. Conjugate Addition

The effects of different additives on conjugate additions of lower-order cuprates can be quite varied. Tri-*n*-butylphosphine is a commonly employed solubilizing ligand which can greatly assist in maintaining homogeneity throughout the course of a cuprate reaction. This has been used to advantage in studies on additions of  $(\text{CH}_3)_2\text{CuLi}$  to allenic phosphine oxides 405a and ketones. 405b Triphenylphosphine (406) and lithium bromide (186) have been claimed to increase the rates and yields of 1,4 additions. Inhibitory effects have been noted with tetracyanoethylene (406) and 12-crown-4-ether, (407) the latter additive acting to sequester  $\text{Li}^+$  from the cuprate cluster. Anomalous results have been obtained with aluminum chloride together with lithium dibutylcuprate on maleates and fumarates. (408) The Lewis acid of choice, as with substitution reactions, seems to be boron trifluoride etherate. Both boron trifluoride etherate (2 equivalents) and excess methyllithium (2 equivalents) enhanced the rates and yields of cuprate conjugate additions to didehydrohomoserine- $\gamma$ -lactone 116 (Eq. 114). (409) Boron trifluoride etherate has

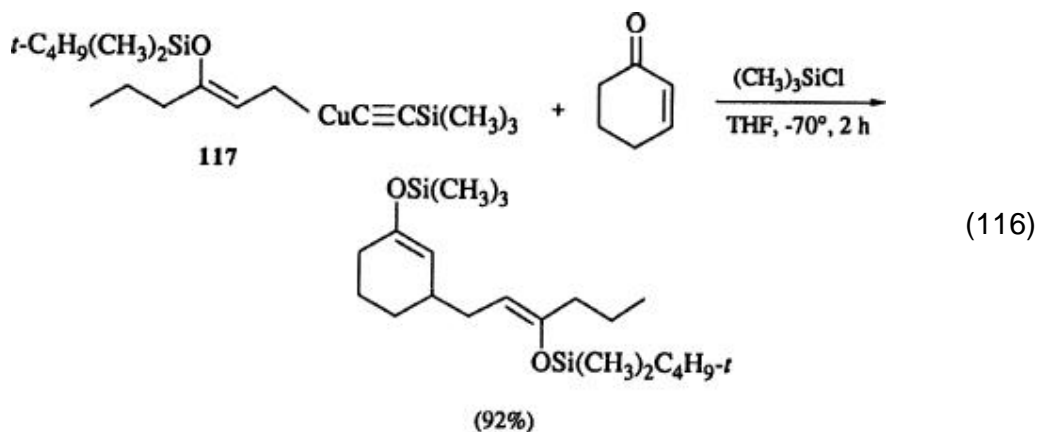


also been used to gauge the extent of topological bias associated with a 1,4 addition of dimethylcupperlithium to a chiral acetal enone. (410)

Several papers attest to the dramatic rate increases observed when chlorotrimethylsilane is present during a conjugate addition reaction of a lower-order cuprate. This seemingly incongruous pair is especially effective for reactions of enones, (80, 361, 411) enoates, (412, 413) and even with  $\alpha$ ,  $\beta$ -unsaturated amides, in which case no reaction is normally observed without chlorotrimethylsilane (Eq. 115). (412)  $\alpha$ ,  $\beta$ -Unsaturated nitriles, however, give both 1,2-and 1,4-addition products. (412)

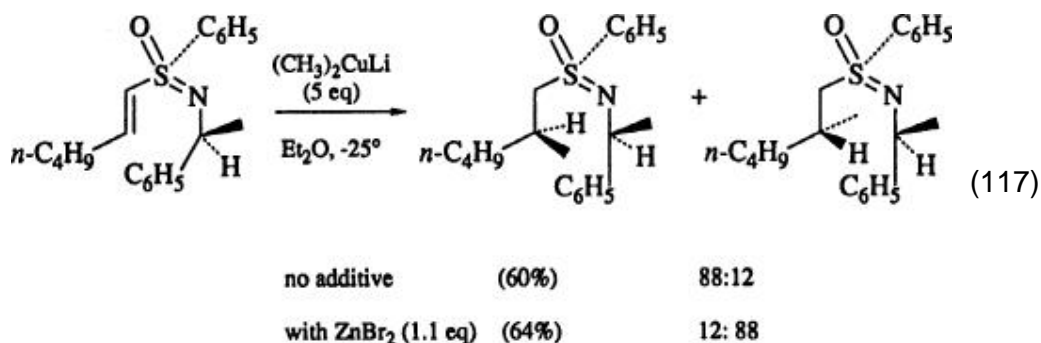


The effect of chlorotrimethylsilane together with HMPA or 4-dimethylaminopyridine is also dramatic and is particularly useful for conjugate additions to  $\alpha$ ,  $\beta$ -unsaturated aldehydes. (414) Chlorotrimethylsilane can also influence rates of conjugate additions of mixed cuprates, where an otherwise unreactive allylic ligand, as part of mixed cuprate 117, is delivered in high yield (Eq. 116). (414)



Magnesium bromide is an essential ingredient for a successful 1,4 addition of a Gilman cuprate in a route to levuglandin E<sub>2</sub>. (415)

Zinc bromide can have a major impact on Michael addition reactions of dialkylcopperlithiums to nonracemic vinylsulfoximines. (382) With (CH<sub>3</sub>)<sub>2</sub>CuLi·LiI alone, the imine directs delivery of the methyl group to afford an 88:12 ratio of diastereomers. Removal of the lithium iodide raises the selectivity to 94:6. With the zinc bromide premixed with the substrate, cuprate attack occurs mainly from the opposite direction, and the ratio is completely reversed (Eq. 117).

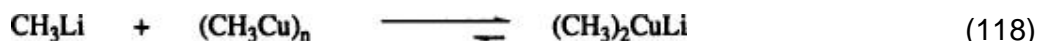


### 3.1.5. Composition Studies

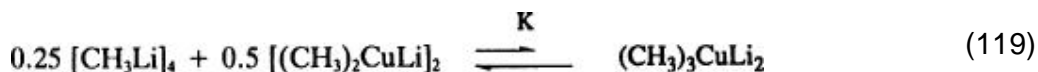
#### 3.1.5.1. Solution Experiments

An appreciation for the chemical makeup of lower order lithio cuprates has been slow to materialize. Much of the insight stems from NMR spectral studies using multinuclear and variable temperature techniques. Early <sup>1</sup>H NMR observations on dimethylcopperlithium in ether at -60° showed only the

presence of a single species, implying that any equilibrium of the type shown in Eq. 118 must lie heavily toward the cuprate. (416)

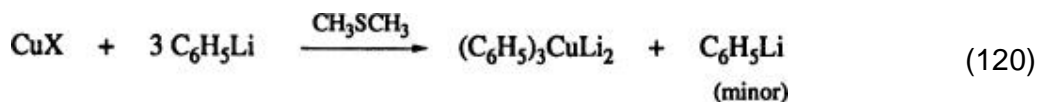


A  $^{13}\text{C}$ -NMR spectrum also gave a singlet at  $\delta -9.6$  ppm. (417) Admixture of dimethylcopperlithium with additional methyllithium in ether did not give rise to a third signal at any temperature. Later work, however, performed in *dimethyl ether* at very low temperatures, provided the first demonstration of the existence of a higher-order cuprate trimethylcopperdilithium ( $\text{Me}_3\text{CuLi}_2$ ) (418) This species exists in equilibrium with the lower-order reagent and free methyllithium, with  $K$  values always favoring the monoanionic salt ( $K < 1$ ; Eq. 119). (418, 419)  $^1\text{H}$  NMR data on various  $n\text{-BuCu}:n\text{-BuLi}$  ratios containing



coordinating phosphine ligands ( $n\text{-Bu}_3\text{P}$ ) suggest that both  $(\text{Bu}_2\text{CuLi})_2$  and  $\text{Bu}_4\text{CuLi}_3$  exist in ether solutions, while  $(\text{Bu}_2\text{CuLi})_2$  and  $\text{Bu}_3\text{CuLi}_2$  are formed in pentane. (420) Extensive use of  $^7\text{Li}$  NMR, together with  $^1\text{H}$  NMR spectroscopy and supporting chemical experiments, however, did not indicate such occurrence of higher-order cuprates  $\text{Me}_3\text{CuLi}_2$  derived from  $\text{CuX}$ ,  $\text{X} = \text{Br}, \text{I}$ , in either tetrahydrofuran or diethyl ether. (7)

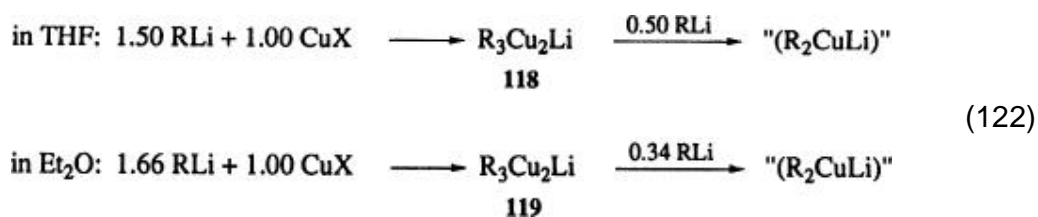
Recent spectral studies ( $^{13}\text{C}$  and  $^6\text{Li}$  NMR) of cuprates derived from mixtures of copper(I) iodide or bromide and phenyllithium in dimethyl sulfide provide evidence for the existence of higher-order species  $\text{Ph}_3\text{CuLi}_2$  in this medium (Eq. 120). (421) Such is not the case in tetrahydrofuran, however, where only  $\text{Ph}_2\text{CuLi}$  and  $\text{PhLi}$  are observed, (421) corroborating an earlier assessment. (7)



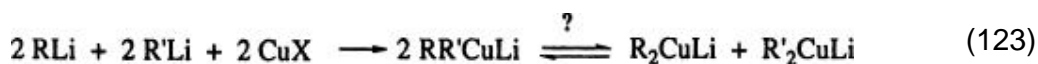
The nature of the lower-order species dimethylcopperlithium has also been found to be a function of the manner in which it is prepared. (7) Solutions of dimethylcopperlithium in tetrahydrofuran, from which the lithium salts have been removed, give an equilibrium mixture of three components with  $K_{\text{eq}} = 11$  (Eq. 121). (7, 422) With an equivalent of  $\text{LiX}$  left in solution as the byproduct



of metathesis between MeLi + CuX, Eq. 121 no longer holds because rapid exchange of both lithium ions (between cuprates and LiX) and methyl groups [between the aggregate Me<sub>3</sub>Cu<sub>2</sub>Li and (Me<sub>2</sub>CuLi)<sub>2</sub>] takes place even at very low temperatures (423, 424) on the NMR time scale. In ether, irrespective of the presence or absence of lithium salts, no such equilibrium is found. (7) Surprisingly, the species Me<sub>2</sub>CuLi prepared in ether, upon addition of tetrahydrofuran, is spectroscopically different from that formed initially in the same final ether/tetrahydrofuran ratio. Individually, these spectra point to the fundamental reagents 118 and 119 prepared first upon addition of RLi to CuX, which vary according to solvent. In tetrahydrofuran a ratio of 1.50 RLi:1.00 CuX leads first to R<sub>3</sub>Cu<sub>2</sub>Li, (418, 419) while in ether 1.66 RLi:1.00 CuX generates R<sub>5</sub>Cu<sub>3</sub>Li<sub>2</sub>. (425) Addition of the remaining RLi (0.50 and 0.34, respectively), which brings the ratio up to the “normal” 2:1 value, converts each aggregate to a form of R<sub>2</sub>CuLi (Eq. 122).

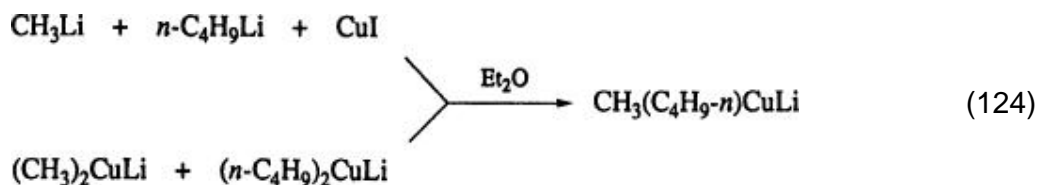


Information concerning mixed lower-order lithio cuprates RR<sup>1</sup>CuLi is even more sparse. The question arises as to whether a 1:1:1 mixture of RLi, R<sup>1</sup>Li, and CuX affords RR<sup>1</sup>CuLi as the sole species in solution, or whether it exists in equilibrium with percentages of homocuprates R<sub>2</sub>CuLi and R<sup>1</sup><sub>2</sub>CuLi (Eq. 123). (426, 427) If the latter is true, which reagent effects the chemistry? It has



been shown that treatment of CuI·*n*-Bu<sub>3</sub>P with MeLi and *t*-BuLi (in a 1:1:1 ratio) affords a species, presumably Me(*t*-Bu)CuLi, which gives a methyl singlet in the <sup>1</sup>H NMR spectrum at δ – 1.70 ppm. (428) In contrast, the spectrum recorded for an equimolar mixture of Me<sub>2</sub>CuLi and (*t*-Bu)<sub>2</sub>CuLi (together with *n*-Bu<sub>3</sub>P) shows the methyl resonance at δ – 1.25 ppm, both experiments having been run under identical conditions of solvent (2:1 ether:pentane), temperature (–20°), and concentration (0.33 M). The implication here is that

ligands in lower-order cuprates do not scramble. However, more recent spectroscopic results ( $^1\text{H}$  NMR) with the  $\text{Me}(n\text{-Bu})\text{CuLi}$  system (no phosphine present) have unequivocally shown that both formulations lead to the same species which displays two singlets for the methyl group on copper, indicative of *cis-trans* isomers of a presumed dimeric cluster (Eq. 124). (250) None of the



individual homocuprates could be detected by NMR. Moreover, exposure of preformed  $\text{Me}_2\text{CuLi}$  to 1 equivalent of  $n\text{-BuLi}$  leads to the same spectrum of  $\text{Me}(n\text{-Bu})\text{CuLi}$ , along with the appearance of 1 equivalent of free  $\text{MeLi}$  (Eq. 125). (250) Thus, while the example of *t*-BuLi-delivered lower-order cuprates



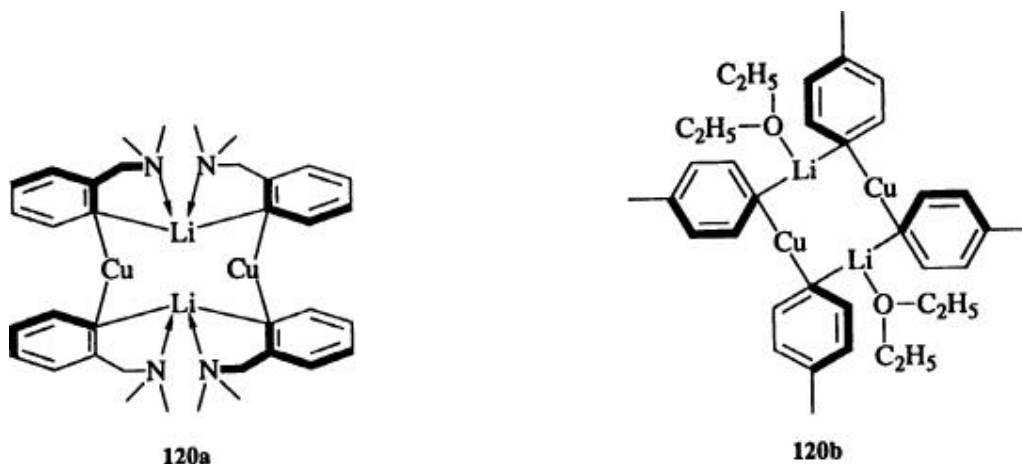
may be unique, (428) and the effects of added phosphine ligands yet to be fully determined, it seems clear that alkyl ligands may move on and off of  $\text{Cu(I)}$  monoanions with ease. The factors that govern ligand mixing between homocuprates, however, are still not fully understood.

The conclusions drawn from these studies are that (1) several distinct forms of " $\text{R}_2\text{CuLi}$ " appear to exist, (429) and (2) the fashion in which a lower-order cuprate is originally constituted [i.e., with regard to lithium salts, choice of solvent(s), etc.] may well need to be considered a reaction variable having impact not only on product yields but also on reproducibility.

### 3.1.5.2. Solid-State X-Ray Analyses

The sensitivity of most lithio organocuprates to moisture, oxidation, and temperature has seriously hampered efforts to obtain crystalline materials suitable for X-ray analysis. Although successful investigations describing mononuclear species  $\text{M}^+[\text{R}_2\text{Cu(I)}]^-$  are rare, several neutral complexes with cluster geometries have been reported, particularly in the phenyl series where bridging aryl groups are common. These include  $\text{Cu}_2\text{Li}_2(\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2)_4$ , (430)  $[\text{Li}_2\text{Cu}_3\text{Ph}_6]_2[\text{Li}_4\text{Cl}_2(\text{Et}_2\text{O})_{10}]$ , (431)  $[\text{Li}(\text{THF})_4] - [\text{Cu}_5\text{Ph}_6]$ , (432) and  $[\text{Li}(\text{Et}_2\text{O})_4][\text{LiCu}_4\text{Ph}_6]$ . (433) Perhaps the species most relevant to synthetic uses of lower-order cuprates is **120a**, the first example of a lithium cuprate containing Li and Cu in a 1:1 ratio as part of the central core. (430, 434) This X-ray structure supports the concept of a dimeric model for  $\text{Me}_2\text{CuLi}$  proposed earlier based on solution X-ray scattering, molecular weight measurements,

and kinetic data from reactions with methyl iodide in ether under carefully controlled conditions. (10) The *ortho*-*N,N*-dimethylaminomethyl residues in **120a** serve as “well-positioned intramolecular solvent molecules,” completing the preference of lithium for tetracoordination. The cuprate (*p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>)<sub>4</sub>Cu<sub>2</sub>Li<sub>2</sub>, (435) crystallized from benzene and solubilized upon addition of 2 equivalents of ether, is likely to have related structure **120b**, in which



case ether occupies two vacant coordination sites on lithium. Solution NMR studies (<sup>1</sup>H and <sup>13</sup>C) on both **120a** and **120b** also point to a dimeric array involving asymmetrically bridging ligands, 73,252,436a,b apparently a feature intrinsic to other metal 1B—lithium clusters (i.e., Ar<sub>4</sub>M<sub>2</sub>Li<sub>2</sub>, M = Ag, Au). 434–436a,437

Placement of bulky organic groups on copper has led to characterization of monomeric complexes [Cu(dppe)<sub>2</sub>][Cu(C<sub>6</sub>H<sub>2</sub>Me<sub>3</sub>)<sub>2</sub>] (438) (dppe = 1,2-diphenylphosphinyethane) and [Li(THF)<sub>4</sub>][Cu(C(SiMe<sub>3</sub>)<sub>3</sub>)<sub>2</sub>]. (439) Another technique for realizing pure lower-order cuprate monoanions relies on the lithium-ion-sequestering properties of 12-crown-4 ether, which has led to salts represented as [Li(12-crown-4)<sub>2</sub>][CuR<sub>2</sub>], R = Me, Ph. (440) Recently, crystalline [Cu(PMe<sub>3</sub>)<sub>4</sub>][CuMe<sub>2</sub>] (**121a**) (441) and RCuP(*t*-C<sub>4</sub>H<sub>9</sub>)<sub>2</sub>Li (**121b**) (442) have yielded to X-ray inspection, which for the former established its ionic composition as implied by conductivity measurements. A comparison of solution <sup>1</sup>H NMR data for **121a** and the lithio cation counterpart ([Li][CuMe<sub>2</sub>]), for which large upfield shifts for protons on carbon attached to copper are common, leads to the conclusion that interactions between R and Li<sup>+</sup> in R<sub>2</sub>CuLi are involved, as found for **120a**. (430) Extended Hückel calculations for dimeric Me<sub>2</sub>CuLi, on the other hand, predict preferential ligand bonding to copper rather than to lithium. (443) Lithio cuprate **121b**, a novel heteroligand-containing species, is also monomeric. (442) Some interesting features of **121b** have been noted, including the strong association of the lithium cation with one phosphorus atom rather than two, as in [Cu(*t*-C<sub>4</sub>H<sub>9</sub>)<sub>2</sub>P]<sub>2</sub>[Li(THF)<sub>2</sub>]. (444) As a result, four-coordinate lithium relies on



three molecules of tetrahydrofuran as ligands, and hence **121b** is more accurately described as  $[\text{RCuP}(\overline{t\text{-C}_4\text{H}_9})_2\{\text{Li}(\text{THF})_3\}]$ . (442) Thus, while much has been learned about lower-order lithio cuprates (445) since their introduction four decades ago, (5) there is still no unequivocal proof of structure for the original species,  $\text{Me}_2\text{CuLi}$ .

## 3.2. Organocopper and Organocopper–Lewis Acid–Ligand Reagents

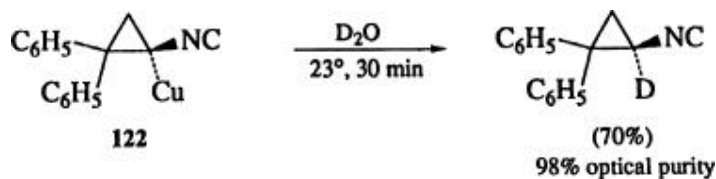
### 3.2.1. Reactions of Organocopper Reagents

Metathesis between an organolithium (RLi) and Cu(I)X salt, X = I, Br, Cl, (1:1 ratio) leads to an organocopper complex RCu. These reactions, driven in part by the large difference ( $>3$  V or  $\sim 80$  kcal/mol) in reduction potentials (446) between  $\text{Li}^0$  ( $E_{\text{red}} = -3.04$  V) and  $\text{Cu}^0$  ( $E_{\text{red}} = +0.15$  V), tend to be rapid and quantitative, although the resulting species have stability, aggregation state, and solubility characteristics dependent upon the nature of the organic ligand.

In terms of reactivity, neutral reagents RCu tend to be far less robust than their lithio or magnesio anionic counterparts (cuprates). Presumably this accounts for their relatively limited use, although excellent compatibility with Lewis acids has greatly expanded their value as agents for carbon–carbon bond formation.

#### 3.2.1.1. Substitution

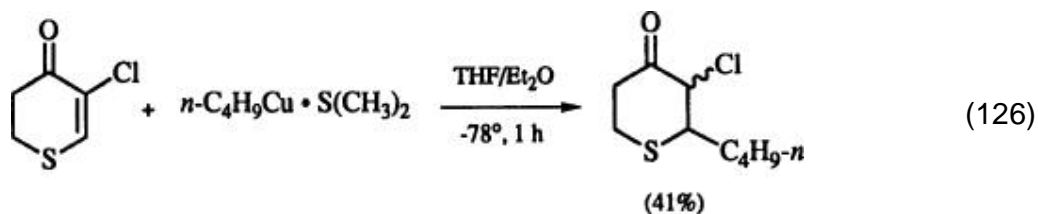
Substrates which undergo substitution with neutral complexes RCu range from allylic and propargylic systems to activated alkenyl halides. The occasional enhanced stability of an organocopper species, in comparison with the parent organolithium, has permitted preparation of optically active cyclopropylcopper reagents (e.g., 122) which maintain their configurational integrity. (447)



More examples of substitution reactions using RCu are illustrated in Table VII.

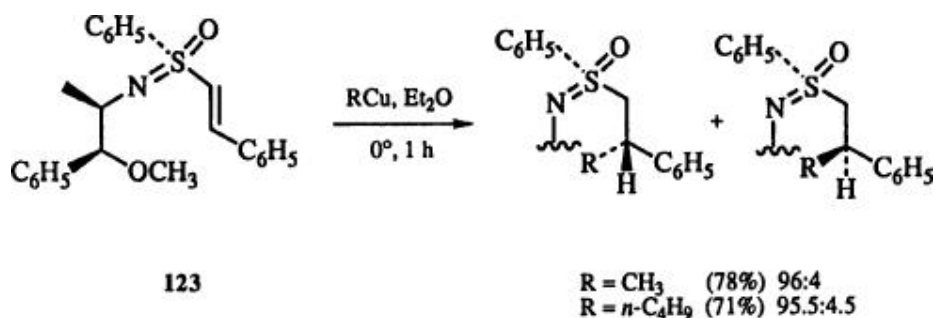
#### 3.2.1.2. Conjugate Addition

For most circumstances, 1,4 additions mediated by copper reagents fall under the domain of lower-order lithio or magnesio cuprates. However, there are instances where RCu reagents give better results than conventional cuprates. Such examples are found in the chromone and thiachromone systems (Eq. 126). (448, 449)

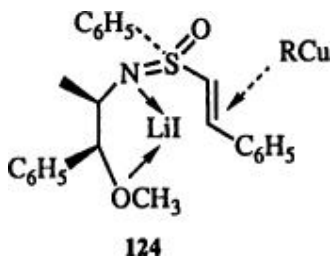


Organocopper reagents add to  $\alpha$ ,  $\beta$ -acetylenic sulfoxides in nearly quantitative yields and exclusively in a *cis* fashion. (450)

Dimethylcopperlithium shows similar reactivity, but other cuprates tend to attack at sulfur. This chemistry has been extended to optically active acetylenic sulfoxides. (451)  $\beta$ -iodovinyl sulfones undergo attack by RCu to displace the halide with strict retention of double-bond geometry. (290, 450) Nonracemic vinyl sulfoximines **123** react in

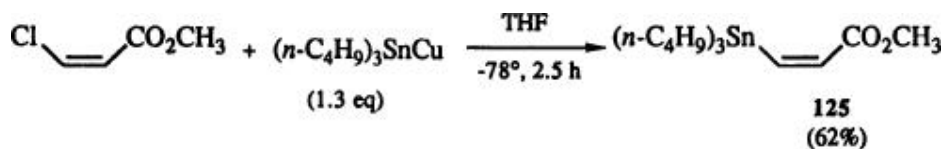


ether to generate high diastereomeric excesses of 1,4 adducts. (452) With Lil-free RCu, the selectivity is in the same direction, but only on the order of 2:1. A model (**124**) consistent with these results is proposed where Lil is



chelated followed by addition of RCu from the less sterically demanding  $\pi$  face. With both lower- and higher-order cuprates, the opposite approach is favored to the extent of ca. 15:85. (452)

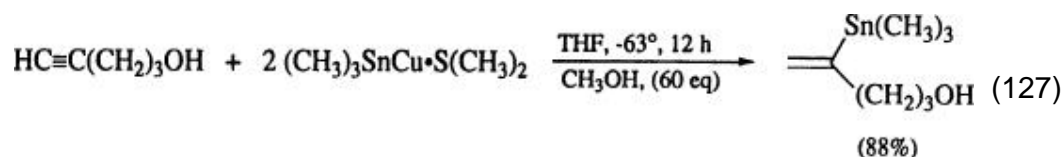
$\beta$ -Haloacrylates behave as Michael acceptors toward tributylstannylcopper to give (stereospecifically) geometrically defined  $\beta$ -stannylacrylates (**125**). (453)



Tosylate and thiophenoxide leaving groups require higher temperature (ca. 25°), and with the latter appendage, stereospecificity is lost. Reactions involving organocuprates give lower yields. (453)

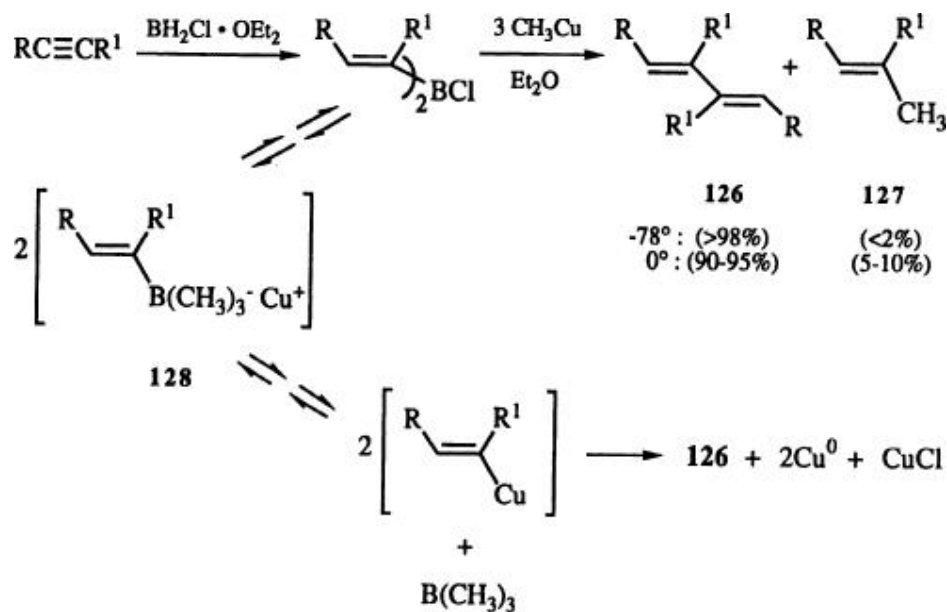
### 3.2.1.3. Reactions of Acetylenes

Stannylcupration of 1-alkynes with  $(\text{CH}_3)_3\text{SnCu}\cdot\text{S}(\text{CH}_3)_2$  is believed to be a reversible process which necessitates an in situ proton source to quench the intermediate vinylcopper species. (351, 352) The reaction is highly regioselective, with less than 8% of the 1,2-disubstituted alkene being formed (Eq. 127). (351)



Methylcopper (3 equivalents) converts acetylenes via divinylchloroboranes into symmetrical (*E,E*)-1,3-dienes **126** in high yields (Scheme 12). (454) Suppression of the formation of byproduct **127**, presumably formed by competitive reductive elimination from a copper(I) boronate complex **128** resulting from a series of redistribution equilibria, is achieved by starting the reaction at  $-78^\circ$  and warming to ambient temperature.

Scheme 12.



### 3.2.2. Reactions of Organocopper Reagents in the Presence of Additives

Although neutral organocopper complexes (RCu) alone are utilized infrequently, their modification upon addition of Lewis acids leads to

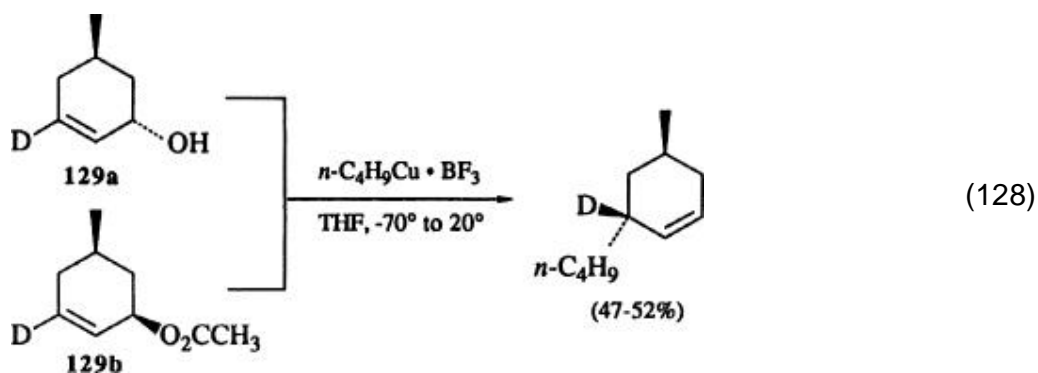
substantially improved reactivity profiles which are often unique by comparison with either RCu or anionic organocuprates. Since the initial report using boron trifluoride etherate for such purposes, (455) various other Lewis-acid candidates have also been screened. A review of this novel aspect of organocopper chemistry has recently appeared. 4i Lewis acids that can be used for activating RCu include boron trifluoride, magnesium bromide, and aluminum chloride, along with some other boranes and alanes. Other additives which significantly modify neutral organocopper species are chlorotrimethylsilane–tetramethylethylenediamine (TMEDA) mixtures and the extensively used phosphines.

### 3.2.2.1. Substitution

Although arylcopper reagents are usually quite unreactive, (456) in the presence of phosphine ligands (e.g., triphenylphosphine) they will add to formaldehyde, (457) carbon dioxide, (458) and carbon disulfide. (459-461) Similar behavior has been noted (using tri-*n*-butylphosphine) for alkynylcopper species as well. (462) See Table VIII for some related reactions of [RCu + additives].

The butylcopper–aluminum chloride mixture is effective in displacing a  $\gamma$  substituent (in an S<sub>N</sub>2 sense) from cyclic  $\gamma$ -acetoxy- $\alpha$ ,  $\beta$ -unsaturated esters. (463) By contrast, dibutylcuprate gives products of reduction. (463) Displacements on allylic acetals and ethers can be achieved with the RCu·BF<sub>3</sub> combination. Without the Lewis acid present, these reactions either fail or give complex mixtures. (397, 400)

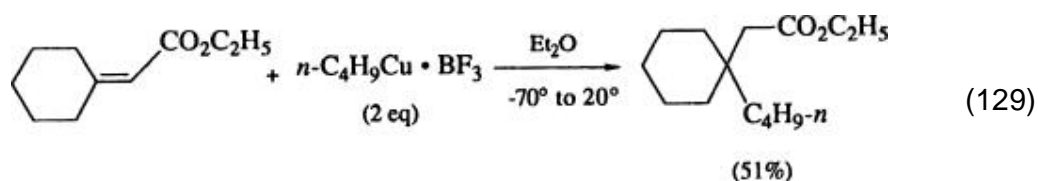
Various Lewis acids, including boron trifluoride, boron trichloride, titanium tetrachloride, and aluminum chloride, were examined as additives in reactions of RCu with cinnamyl and crotyl chlorides. (464) Best results (>95%  $\gamma$  selectivity) were realized using RCu·BF<sub>3</sub>. Similar regioselectivity from unprotected allylic alcohols is observed as long as excess (3 equivalents) reagent is utilized (Eq. 128). (464) With a free hydroxy group as part of the cyclohexenyl



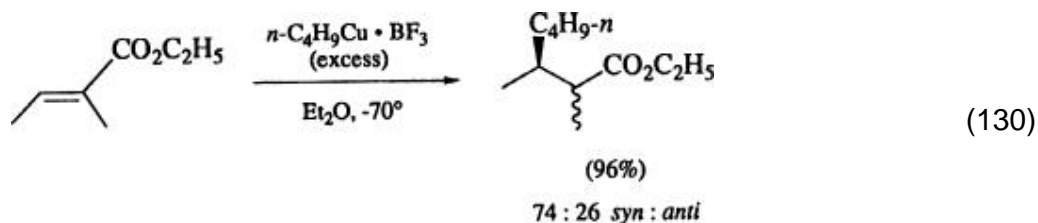
framework **129a**, the cuprate is guided toward *syn* delivery, whereas the inverted acetate **129b** gives the product of *anti* S<sub>N</sub>2' attack by the organocupper reagent. No significant stereochemical bias is seen from either the corresponding *cis* or *trans* allylic chloro congeners.

### 3.2.2.2. Conjugate Addition

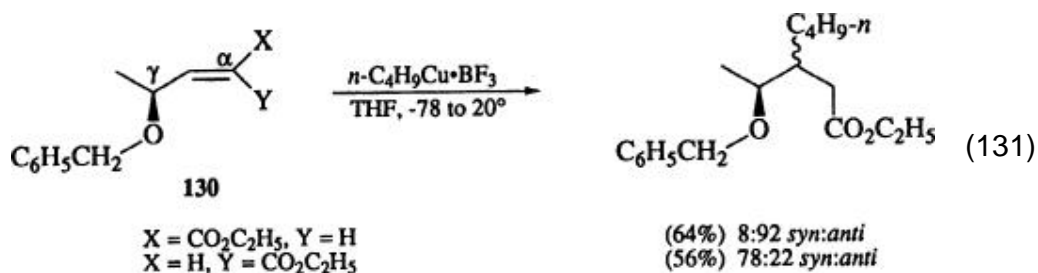
Modified, neutral organocupper reagents are used for a multitude of conjugate addition schemes, **4i** and can be especially valuable for hindered substrates where conventional cuprates are slow to react. Sterically congested enones, (**465**) and most notably enoates, react smoothly with RCu reagents in the presence of boron trifluoride etherate (Eq. **129**). (**465**) When



$\alpha$ -substituted enoates are involved, RCu·BF<sub>3</sub> delivers the organic ligand in the usual way, the *syn* isomer being preferentially obtained upon quenching and workup (Eq. **130**). (**466**)



Chemoselectivity differences between RCu·BF<sub>3</sub> and R<sub>2</sub>CuLi·BF<sub>3</sub> are vividly illustrated in their behavior toward  $\gamma$ -alkoxyenoates. (**467**) The neutral complexes (RCu) add in a Michael sense to give a mixture of *syn* and *anti* products, the ratio of which is governed by the olefin geometry in **130** (Eq. **131**). Both the

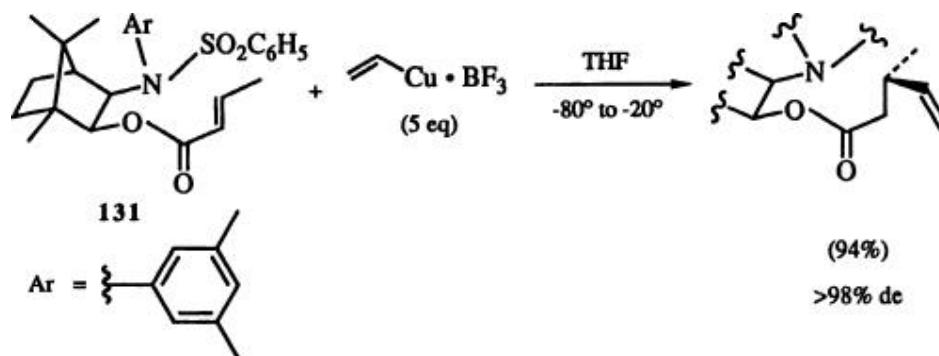


boron trifluoride-modified cuprate and R<sub>2</sub>CuLi alone, however, prefer an S<sub>N</sub>2 pathway, giving products of allylic substitution at the α position.

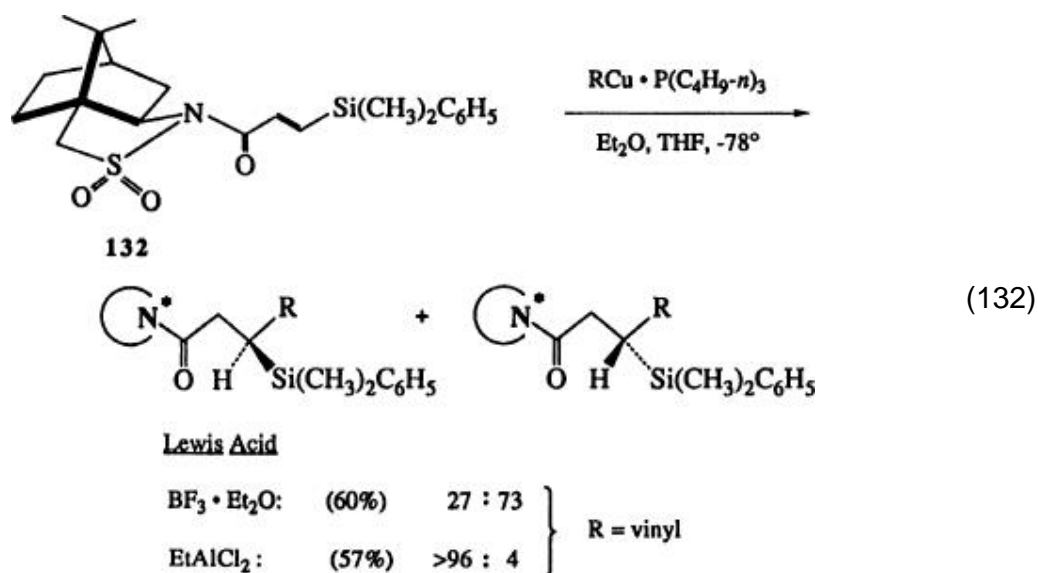
Enhanced reactivity is also reported for the tributylphosphine–RCu mixture, with nearly quantitative yields of conjugate adduct being claimed with such challenging substrates as isophorone. (468, 469)

Equimolar amounts of RCu and aluminum chloride are effective for adding to β-cyclopropyl enones in a 1,4 manner. (470, 471) This is in sharp contrast to dialkylcuprates where mixtures of 1,4 and 1,6 adducts are the norm, the latter reflecting cleavage of the three-membered ring. (64, 392, 393)

One of the more advanced applications of additive-altered RCu reagents is in the field of asymmetric conjugate addition reactions. Chiral enoates such as **131**, derived from camphor, (472) undergo highly diastereoselective (de >98%)

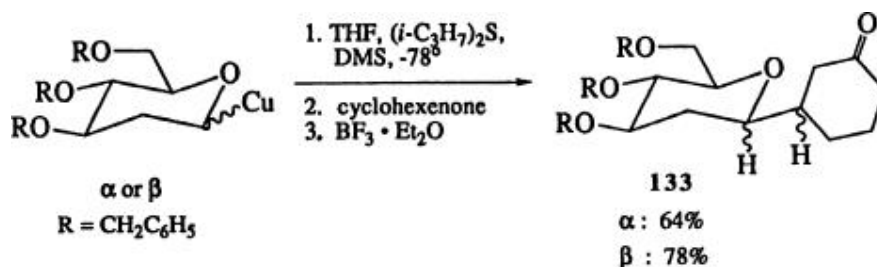


conjugate additions with RCu·BF<sub>3</sub> complexes. (473-475) The selection of a Lewis acid can affect the stereodifferentiation of an addition; thus *N*-enoilsultam **132** reacts with RCu·P(C<sub>4</sub>H<sub>9</sub>-*n*)<sub>3</sub> in the presence of boron trifluoride to give C(β)-*si* face selection, whereas with ethylaluminum dichloride, strong preference for the C(β)-*re* face by RCu is observed (Eq. 132). (474, 475)



A detailed examination of  $\alpha$ -alkoxy organocopper reagents (476, 477) reveals that conjugate additions to enones occur readily in the presence of boron trifluoride etherate. (476) The process is sensitive to the nature of the copper(I) salts used in their preparation, with best results obtained from freshly recrystallized copper(I) bromide-dimethyl sulfide complex (478, 479) which has been pretreated with 5 mol % of isopropylmagnesium bromide [to remove Cu(II) impurities] prior to addition of an  $\alpha$ -alkoxylithium species. This chemistry can be utilized as a means of introducing a hydroxymethyl anion equivalent, and also for purposes of preparing unusual C-glycosides, such as 133.

Functionalized organocopper complexes  $\text{RCu}\cdot\text{P}(\text{C}_4\text{H}_9\text{-}n)_3$  are the presumed outcome from treatment of the corresponding halides with highly

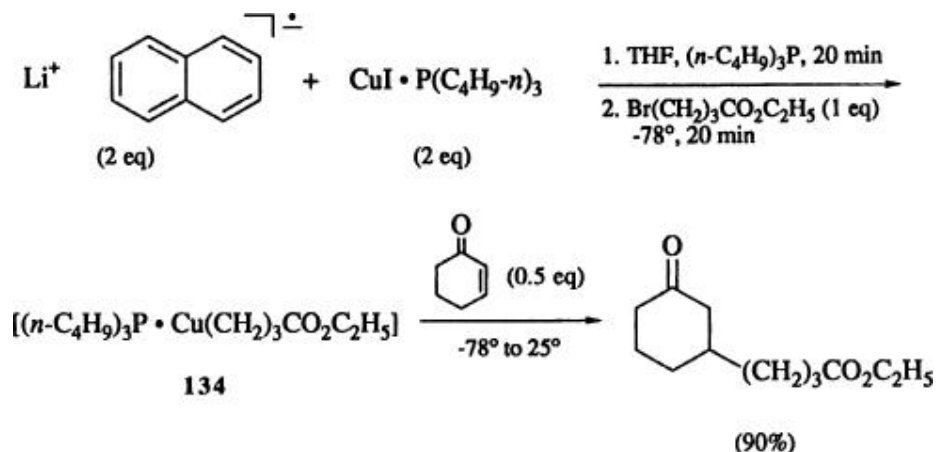


activated copper metal. (480-482) Reagent formation (e.g., 134) occurs in tetrahydrofuran following lithium naphthalenide reduction of  $\text{CuI}\cdot\text{P}(\text{C}_4\text{H}_9\text{-}n)_3$ . Aside from undergoing 1,4 additions (Scheme 13) (481) and cross couplings with acid chlorides (480) and allylic and benzylic halides, (480) ring openings of epoxides 482a can also be carried out. Organocopper complexes generated



in this fashion may also contain remote epoxides within the reagent, subsequent intramolecular cyclization of which occurs upon warming to  $-35^{\circ}$ . [482b](#) The mode of ring closure can be controlled by solvent as well as the nature of the alkyl groups located on the epoxide. Yields are good to excellent and other functionalities such as halogens and nitriles are unaffected by the oxidation sequence. Should no external electrophile be present, efficient dimerization can be effected as reaction temperatures warm above  $0^{\circ}$  in the presence of  $\text{Et}_3\text{P}$ . ([480](#))

**Scheme 13.**



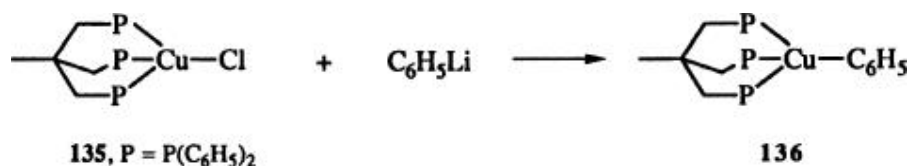
Several additional examples of the reactions of additive-modified organo-copper reagents can be found in Table [VIII-B](#).

### 3.2.2.3. Composition Studies

Essentially all of the composition data dealing with neutral organocopper complexes is based on structural information emanating from X-ray crystallographic studies. While the compounds examined may be of little obvious synthetic merit, these analyses do provide considerable insight as to potential aggregation states and other solution phenomena which may help explain reagent reactivity and the role of ligands as additives (e.g., phosphines) ([483](#), [484](#)) in reactions of  $\text{RCu}$  complexes. Perhaps equally important is the reminder that their chemistry may not involve monomeric species. Of course, when considering these compounds, the potentially vital role which solvents play in their couplings cannot be ignored.

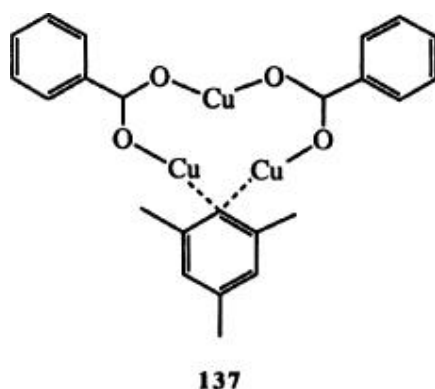
A review of the structural chemistry of organocopper(I) compounds appeared in 1977, ([485](#)) and another in 1982, ([67](#)) which contain a number of citations concerning mixed metal clusters involving  $\text{Cu(I)}$  [including as examples  $\text{Ir}$ ,  $\text{Fe}$ ,  $\text{Re}$ ,  $\text{Ru}$ ,  $\text{Hg}$ , and even  $\text{Cu(II)}$ ], in addition to X-ray analyses of more traditional  $\text{RCu}$  complexes. A spectrum of differing levels of aggregation states and bonding situations exists, ranging from monomeric to octameric lattices with the majority bearing aryl, alkenyl, and/or acetylenic groups. Structural studies of more recent vintage are described below.

Phenylcopper, containing a tetrahedral array around the metal (**136**), exists as a monomeric species in the presence of 1,1,1-tris[(diphenylphosphino)-methyl]ethane or “triphos” [CH<sub>3</sub>C(CH<sub>2</sub>PPh<sub>2</sub>)<sub>3</sub>]. **486a** It can be formed by treatment of [(triphos)CuCl, **135**] with phenyllithium in tetrahydrofuran. A similar



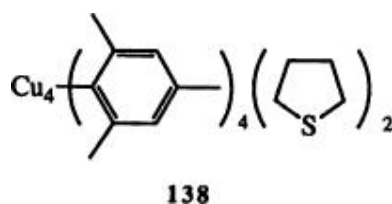
arrangement has been noted for the silylcopper species Ph<sub>3</sub>SiCu·3PMe<sub>3</sub> of approximately tetrahedral configuration which forms yellow crystals of monomeric material from toluene. The copper–silicon bond was found to be 2.340(2) Å, interestingly slightly longer than the composite of the covalent radii (2.28 Å). **486b**

A stable trinuclear complex **137** consisting of a mesityl (Mes) and two benzoyl (OBz) ligands on copper can be prepared (40% yield) via intraaggregate exchange of Cu<sub>5</sub>Mes<sub>5</sub> with Cu<sub>4</sub>(OBz)<sub>4</sub> in benzene. (**487**) The cluster contains



two bridging benzoate groups and a three-center, two-electron bonded mesityl ligand bridging two copper ions.

Several tetrameric complexes have been prepared, including the bistetrahydrothiophene-containing tetramesitylcopper(I) compound **138**. (**488**) It



is derived from cyclic pentameric  $(\text{CuMes})_5$  and tetrahydrothiophene in >80% yield, and forms a puckered eight-membered ring with four copper atoms arranged in one plane. A tetranuclear compound  $[\text{Cu}_4[4\text{-CH}_3\text{C}_6\text{H}_4)\text{CH}_3\text{C}\equiv\text{C} - (\text{C}_6\text{H}_4\text{N}(\text{CH}_3)_2)_2]_2(\text{C}_6\text{H}_4\text{N}(\text{CH}_3)_2)_2$ , containing both aryl and alkenyl bridging groups, has been crystallized and consists of a central core of copper atoms in a rhombus-like configuration. (489) The olefinic and aryl moieties each occupy adjacent edges of the  $\text{Cu}_4$  core.

### 3.3. Higher-Order Organocuprates

#### 3.3.1. Reagents from $\text{CuCN}$

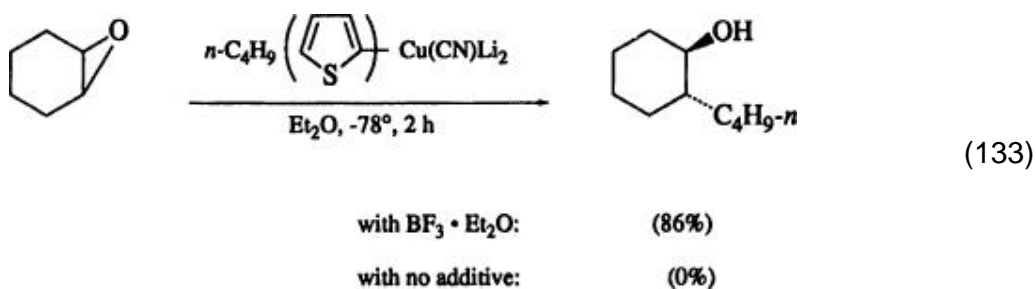
Subsequent to the two previous reviews on the chemistry of higher-order cuprates, 6a,b much additional information has been learned about these still relatively new reagents. 6c There has been no shortage of examples of their use either, as they continue to infiltrate the mainstream of synthetic methodology. That the dianionic cyanocuprates  $\text{R}_2\text{Cu}(\text{CN})\text{Li}_2$  are truly unique species, as compared to monoanionic Gilman reagents  $\text{R}_2\text{CuLi}$ , was recently established based upon a cuprate oxidation scheme using *o*-dinitrobenzene. (490) These results are fully consistent with earlier IR and NMR spectral studies which provided physical evidence to this effect. (491) A general study evaluating the effectiveness of all of the commonly used sources of  $\text{Cu}(\text{I})$ , including  $\text{CuBr}$ ,  $\text{CuBr}\cdot\text{Me}_2\text{S}$ ,  $\text{CuI}$ ,  $\text{CuCN}$ ,  $\text{CuSCN}$ , and  $\text{CuOTf}$ , (492) led to the conclusion that  $\text{CuCN}$  (along with  $\text{CuBr}\cdot\text{Me}_2\text{S}$ ) is a "superior" precursor for cuprate formation in ether or tetrahydrofuran. However, only conjugate additions to cyclohexenone were considered in this report, (492) and it is the more challenging process of substitution where higher-order reagents may often stand alone. (493, 494)

In the discussion which follows, an emphasis is placed on new developments which have not been highlighted in prior reviews. (6) A full listing of reactions involving higher-order cuprates can be found in Table IX. Their uses in natural products-related endeavors are dispersed throughout Table XI.

##### 3.3.1.1. Substitution

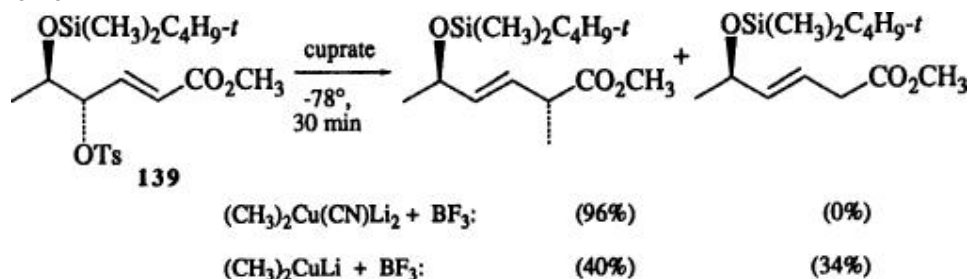
In general, higher-order cyanocuprates tend to be more reactive reagents than lower-order cuprates toward halide displacements and epoxide openings, perhaps because of their buildup of negative charge in the cluster (i.e., as dianions rather than as monoanions with  $\text{R}_2\text{CuLi}$ ). Most noteworthy in this respect are their couplings of secondary iodides and bromides, (493, 494) and displacements on trisubstituted oxiranes. (494, 495) They are fully "compatible" with boron trifluoride etherate and usually lead to enhanced rates and yields in reactions of epoxides in the presence of this additive. 496a Hence,  $\text{R}_2\text{Cu}(\text{CN})\text{Li}_2$  [or  $\text{RR}'\text{Cu}(\text{CN})\text{Li}_2$ ] provides many of the same benefits realized by lower-order reagents. 4i For example, the ligand-conserving mixed 2-thienylcuprates  $\text{R}(2\text{-Th})\text{Cu}(\text{CN})\text{Li}_2$ , 496b together with boron trifluoride

etherate, combine to open epoxides efficiently at low temperatures (Eq. 133).  
496a

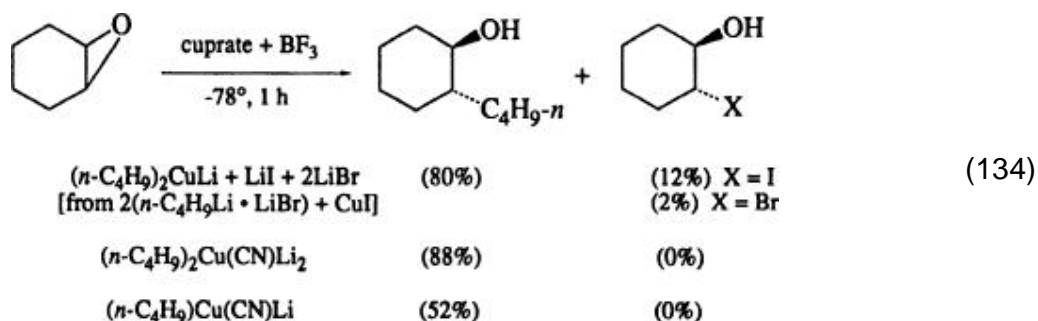


Chirality transfer in a 1,3 sense in acyclic  $\gamma, \delta$ -dioxxygenated enoates (e.g., 139) is effected with excellent stereocontrol using higher-order cyanocuprates in conjunction with boron trifluoride etherate. 497a  $\alpha$ -Alkylations usually occur with >99% diastereoselectivity, an outcome which is also obtainable with lower-order reagents in the presence of this Lewis acid. 497b The advantage offered by the higher-order cuprates lies in the net efficiency of the process; Gilman cuprates invariably lead to competing products of  $\gamma$ -alkylation and/or reduction, while use of  $\text{R}_2\text{Cu}(\text{CN})\text{Li}_2$  affords yields in excess of 94% (Scheme 14). (497)

Scheme 14.

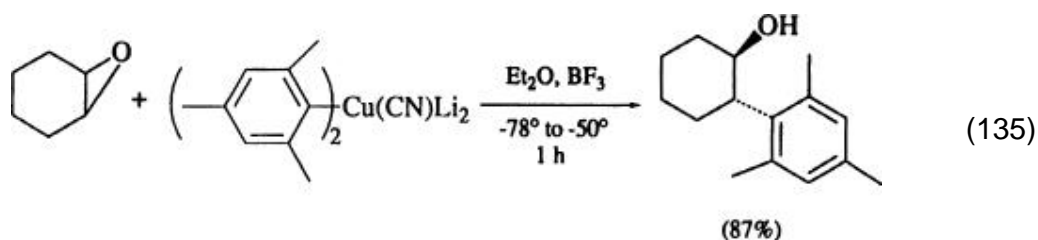


Higher-order cyanocuprates modified by boron trifluoride etherate have also been critically examined in terms of their ring-opening reactions of various epoxides. (498) This extensive study reveals that while lower-order cuprates ( $\text{R}_2\text{CuLi}$ ), which generate lithium halide salts in their preparation, always give halohydrin byproducts, in no case is this observed using either lower- or higher-order cyanocuprates alone in either tetrahydrofuran or ether. Yields for reactions of  $\text{R}_2\text{Cu}(\text{CN})\text{Li}_2$  versus  $\text{RCu}(\text{CN})\text{Li}$  are, not surprisingly, (495) considerably higher (Eq. 134). This combination is apparently so potent that even



the mesityl moiety is transferred in excellent yield, (498) an especially noteworthy example in light of its reputation as a generally nontransferrable ligand (Eq. 135). (269)

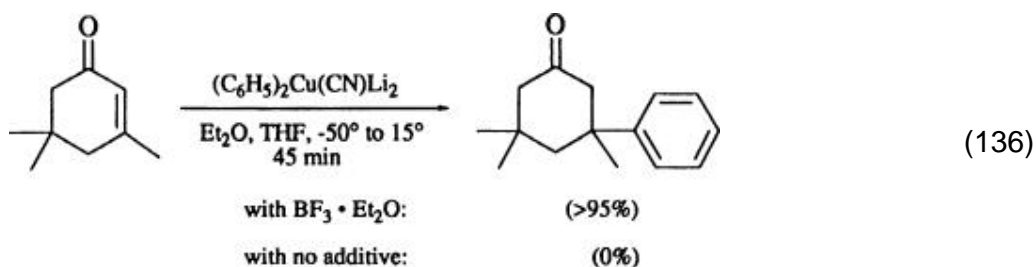
Additional citations are compiled in Table IX-A.



### 3.3.1.2. Conjugate Addition

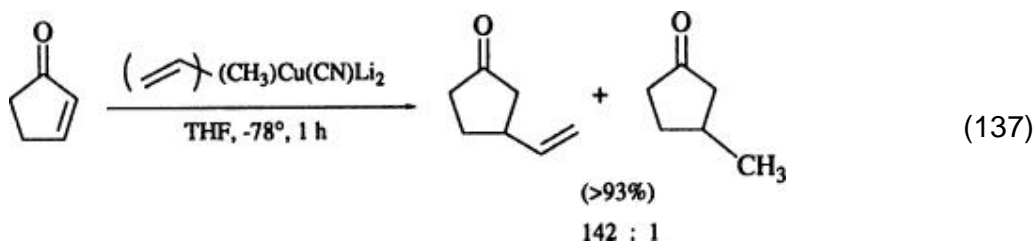
Reactions of higher-order cyanocuprates with  $\alpha$ ,  $\beta$ -unsaturated ketones and esters have been studied with regard to such variables as selectivity of ligand transfer, solvent and additive effects, and substrate variability. (499, 500)

Those prepared from 2 equivalents of the same organolithium and 1 equivalent of copper(I) cyanide are the more reactive species relative to those containing a second residual ligand  $R_R$  [i.e., mixed cuprates  $R_T R_R \text{Cu(CN)Li}_2$ ]. Even highly congested enones can usually be considered good Michael acceptors, and with especially difficult cases the use of boron trifluoride etherate can further assist. (496) Thus the hindered educt isophorone, together with the relatively unreactive aryl cuprate  $(\text{C}_6\text{H}_5)_2\text{Cu(CN)Li}_2$ , successfully form the product of 1,4-phenyl delivery in >95% yield when boron trifluoride etherate is present (Eq. 136). (496) Without this additive, essentially



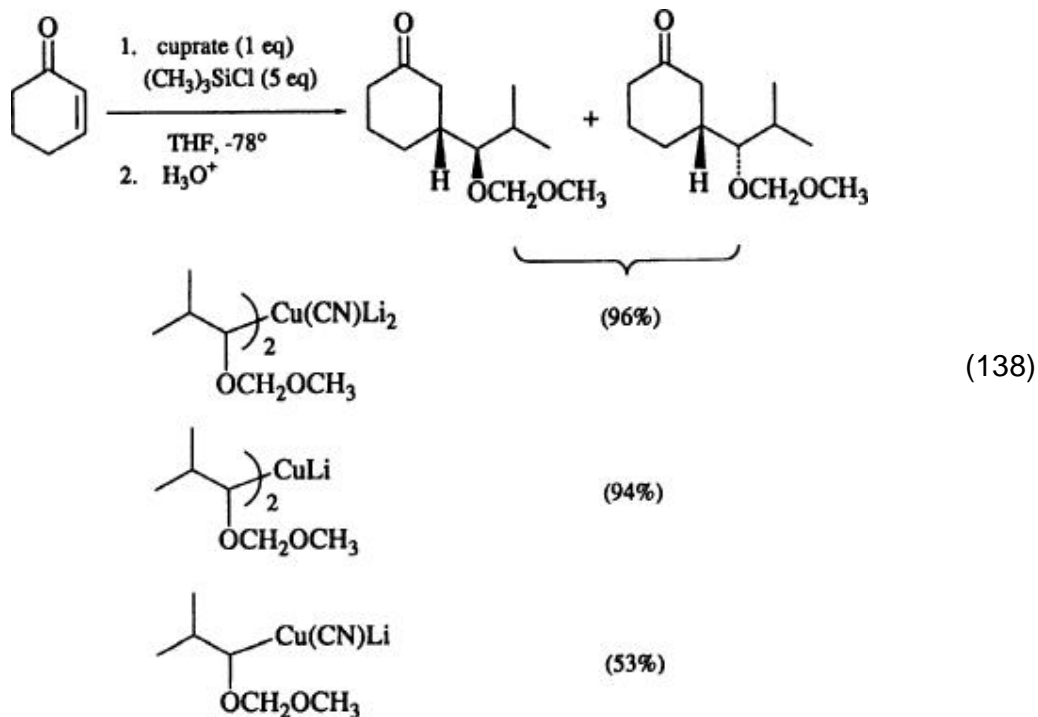
none of the desired product is obtained with this or any other cuprate reagent. Although tetrahydrofuran and dimethoxyethane work well as solvents for simpler systems, ether is by far the medium of choice with  $\beta$ ,  $\beta$ -disubstituted enones. (499, 500)

Contrary to results using mixed alkyl vinyl cuprates in displacement reactions where the  $sp^3$ -based ligands are selectively released from copper, (494) in conjugate addition schemes the vinylic group is delivered rather than the alkyl moiety (Eq. 137). (499, 500) This pattern holds as well for mixed Gilman

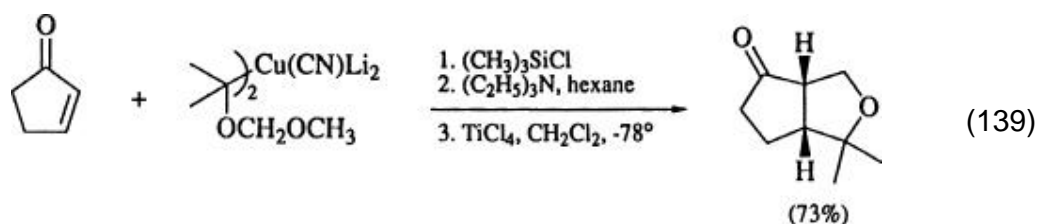


cuprates, although the ratio of vinyl to alkyl transfer is somewhat lower (ca. 25:1). (501)

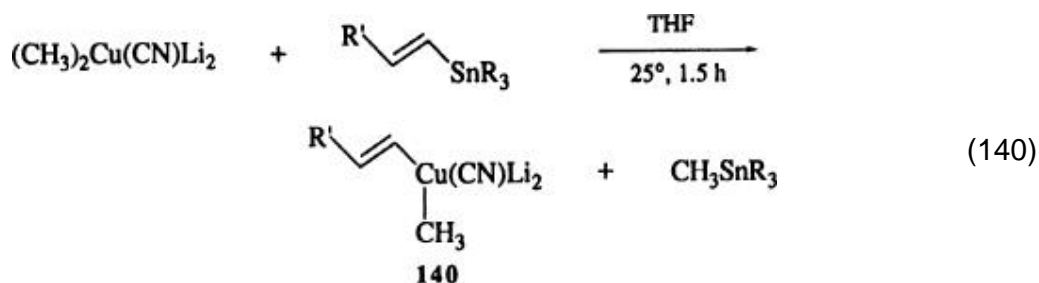
Compounds formally arising from homoenolate aldol reactions can be constructed via Michael additions of higher-order  $\alpha$ -alkoxycuprates to enones (Eq. 138). (361, 502) The reagents are easily prepared from the stannane precursors using successive transmetalations from tin to lithium to copper. Yields are greatest when both the higher-order species and chlorotrimethylsilane (5 equivalents) are used. The diastereoselectivity is in the 3:1 range, although



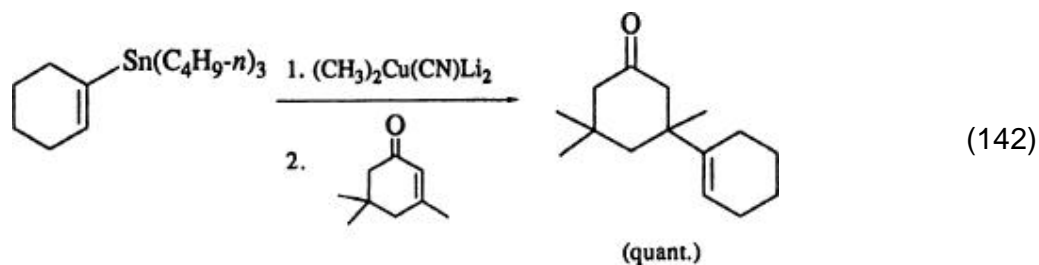
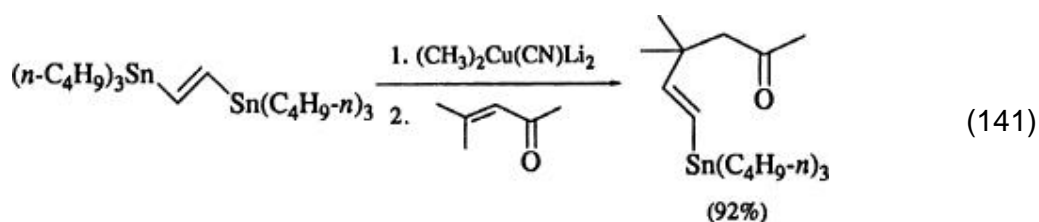
the relative relationships within either isomer have not been established.  $\alpha$ ,  $\beta$ -Disubstituted enones likewise give synthetically useful yields of conjugate adducts. More highly congested systems (e.g., isophorone), notwithstanding the presence of excess chlorotrimethylsilane, do not follow productive pathways, as dimeric materials reflecting cuprate decomposition prevail. The methodology has been applied to the preparation of a variety of substituted tetrahydrofurans (Eq. 139). (503)



A novel route for the preparation of mixed higher-order vinyl cuprates relies on a transmetalation scheme between a vinylstannane and  $\text{Me}_2\text{Cu}(\text{Cn})\text{Li}_2$  (Eq. 140). (504) Simply mixing the two organometallics in tetrahydrofuran



at room temperature produces mixed cuprate **140** quantitatively, which then selectively delivers the vinylic ligand in a 1,4 manner to various  $\alpha$ ,  $\beta$ -unsaturated ketones (Eqs. **141** and **142**). This in situ process, unlike traditional cuprate formation, does not require pregeneration of the corresponding vinyl lithium species.



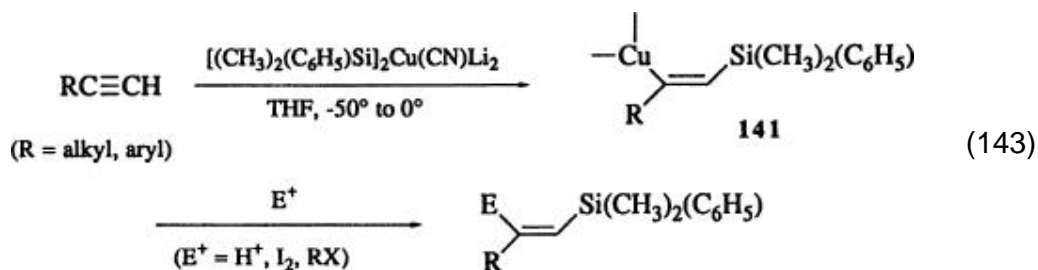
### 3.3.1.3. Carbocupration–Metallo cupration

Addition of a carbon–copper bond across a terminal acetylene using a higher-order cuprate has not been successful to date, presumably because of their greater basicity relative to Gilman reagents. Thus proton abstraction from the alkyne simply leads to a nonreactive salt and an inert copper complex returning starting material upon workup.

Less basic reagents consisting of silyl or germyl ligands, however, readily add to acetylenes, affording products which are useful synthetic intermediates. The stereo- and regiochemistry of addition are such that, for silylcupration, (**505**) products of *syn* addition are formed exclusively with the silyl substituent at the

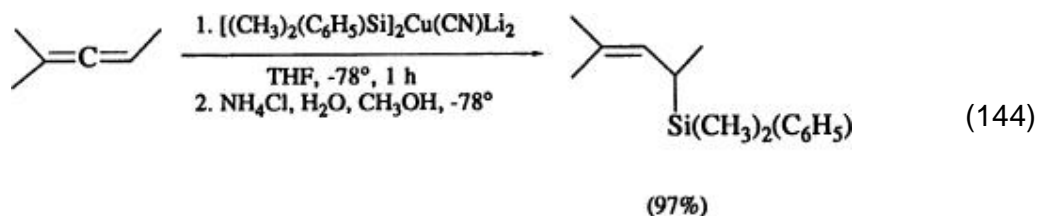


terminus. The initial vinylcopper species **141** may be transformed further upon introduction of an electrophile  $E^+$  (Eq. **143**). When mixed alkyl silyl



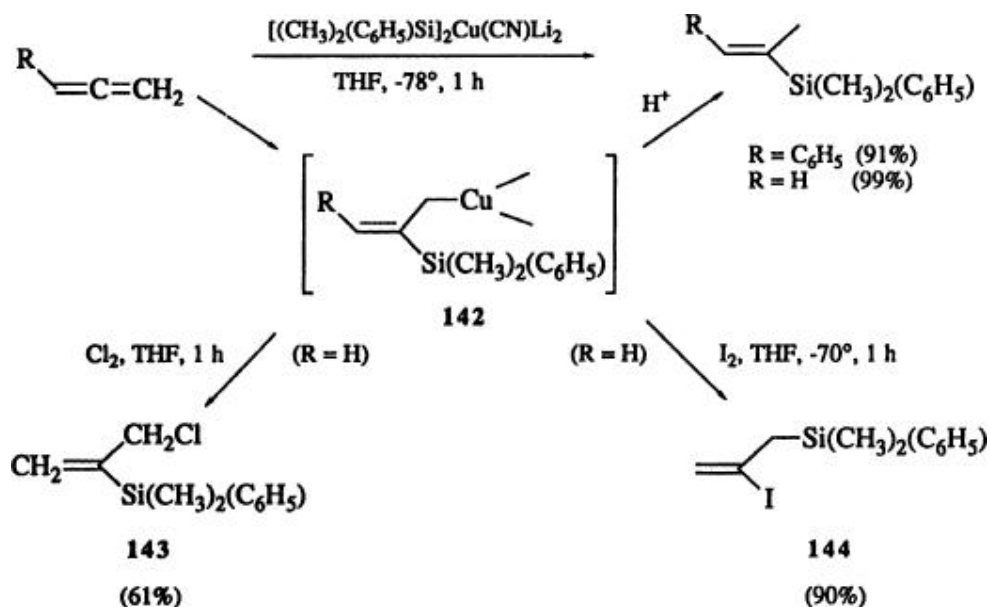
cuprates (e.g.,  $\text{CH}_3[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]\text{Cu}(\text{CN})\text{Li}_2$ ) are involved, the more electropositive ligand is transferred selectively. This observation applies not only in silylcupration reactions with acetylenes, but also in substitution and conjugate addition processes as well. **505b**

Allenes undergo *syn*-metallo-metalations with  $(\text{Me}_2\text{PhSi})_2\text{Cu}(\text{CN})\text{Li}_2$  to give either vinyl- or allylsilanes. (**506**) Simple alkylallenes react quickly at low temperatures to give products cleanly. The cuprate delivers the silyl ligand not only to give allylsilanes, but also in a manner which places this group at the less-substituted position in unsymmetrical situations (Eq. **144**).

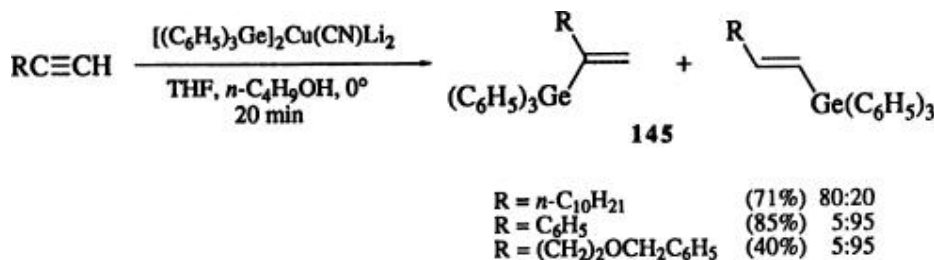


Allene itself, as with phenylallene and unlike the case above, gives a single (*E*)-vinylsilane upon workup following *syn* addition of the cuprate (**Scheme 15**). (**507**) Remarkably, when the intermediate bis-organometallic **142** is quenched with iodine at low temperature, a rearrangement ensues to afford the iodoallylsilane **144**. Such is not the case with chlorine as electrophile, which leads to vinylsilane **143**.

**Scheme 15.**



Higher-order triphenylgermyl cuprates  $(\text{Ph}_3\text{Ge})_2\text{Cu}(\text{CN})\text{Li}_2$  display less well-behaved regiochemical patterns with terminal alkynes. (508) Simple alkylsubstituted systems give ca. 4:1 ratios of terminal olefins **145**, an outcome



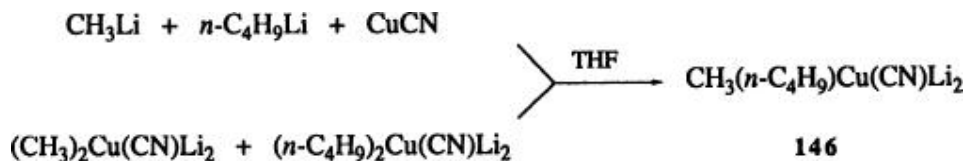
opposite to that with silyl cuprates. Moreover, the additions are sensitive to stereoelectronic factors, since phenylacetylene and internal heteroatoms reverse this ratio. Similar observations have been made with trialkylstannylcuprates. (1695)

Further illustrations of these 1,4 additions can be found in Table IX-B.

#### 3.3.1.4. Composition Studies

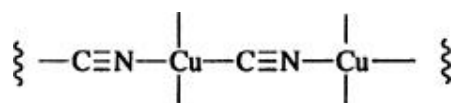
Insofar as cyanocuprates  $\text{R}_2\text{Cu}(\text{CN})\text{Li}_2$  are concerned (for the discussion on  $\text{R}_3\text{CuLi}_2$ , see the related section on lower-order lithio cuprates), their discrete nature has been established by IR and NMR spectroscopy. (491) Addition of increasing amounts of methyllithium to a tetrahydrofuran solution of  $\text{MeCu}(\text{CN})\text{Li}$  at  $-20^\circ$  results in the conversion of the lower order into the higher-order cyanocuprate  $\text{Me}_2\text{Cu}(\text{CN})\text{Li}_2$ , as shown by  $^1\text{H}$  NMR spectroscopy. The mixed cuprate  $\text{Me}(n\text{-Bu})\text{Cu}(\text{CN})\text{Li}_2$  (146) in tetrahydrofuran gives two

sharp singlets for the methyl group on copper, as well as two triplets for the methylene of the butyl ligand attached to the metal.



The doubling of signals, confirmed by  $^{13}\text{C}$  NMR, (491, 509) and also seen with lower-order reagents  $\text{RR}'\text{CuLi}$ , (250) is attributed to geometrical isomers within a dimeric cluster. The mixed cuprates appear to form irrespective of their mode of preparation; sequential addition of methyllithium and *n*-butyllithium to copper(I) cyanide gives the identical spectrum to that observed upon mixing  $\text{Me}_2\text{Cu}(\text{CN})\text{Li}_2$  with an equimolar quantity of *n*- $\text{Bu}_2\text{Cu}(\text{CN})\text{Li}_2$ .

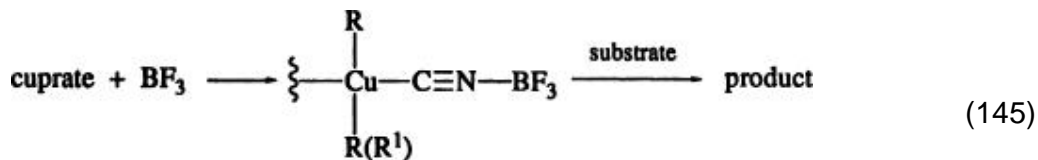
In diethyl ether, as is true with lower-order systems, (420) these species are different because of the absence of a good Lewis base to act as occupant of the fourth coordination site on copper. Such a circumstance encourages the nitrile ligand to fill this void, thereby generating oligomeric cuprates, as manifested by their spectral properties. Proton NMR spectra for **146** are now illdefined, displaying broad resonances at  $-20^\circ$  for both the methyl and methylene groups. (491) Surprisingly, upon cooling to  $-65^\circ$ , free methyllithium is observed, indicative of an equilibrium between lower-order species and free organolithium, which nonetheless does not usually interfere with their conjugate addition reactions. Infrared spectra of **146**, which also show sharp absorptions for the nitrile groups (bridging and nonbridging) in tetrahydrofuran, lose their definition as well when recorded in diethyl ether. (491) Hence, to date, the evidence seems to suggest that higher-order cyanocuprates are dimeric in tetrahydrofuran. In ether, they appear to be in a higher aggregation state, bridged via nitrile ligands, as in **147**. (491, 510)



**147**

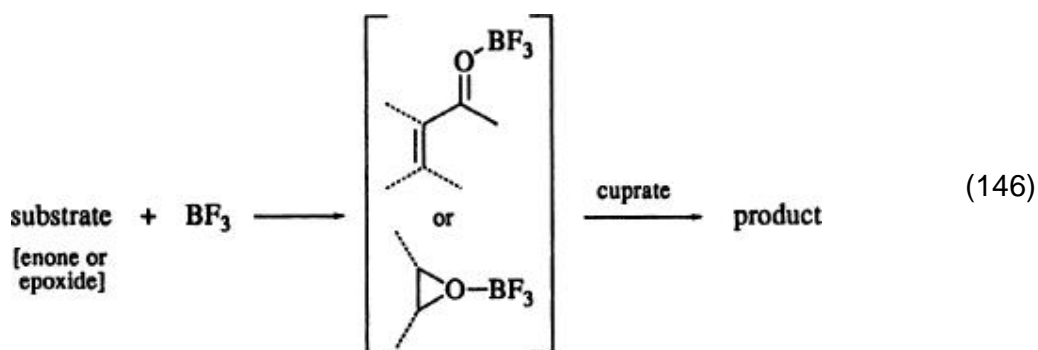
The influence of additives on reactions of cyanocuprates has been addressed to determine whether they affect the substrate, the cuprate, or both. Couplings run in the presence of boron trifluoride etherate ( 2 equivalents), which can dramatically alter reaction rates and yields in both 1, 4 additions (496) and epoxide openings, (496, 498) may now be viewed as potentially involving a modified reagent. (511) Admixture of either a homo-  $[\text{R}_2\text{Cu}(\text{CN})\text{Li}_2]$  or mixed  $[\text{RR}'\text{Cu}(\text{CN})\text{Li}_2]$  cuprate with this Lewis acid generates a nitrile bound reagent

**148.** The inclusion of boron trifluoride into the cluster introduces a more powerful Lewis acid relative to a lithium cation and is suggested to account for the enhanced rates of these reactions (Eq. 145). This notion is contrary to the more commonly held view that initial enone (or oxirane) activation by the

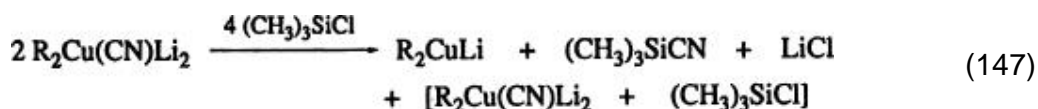


148

Lewis acid occurs followed by a second bimolecular reaction with the cuprate (Eq. 146). 4i



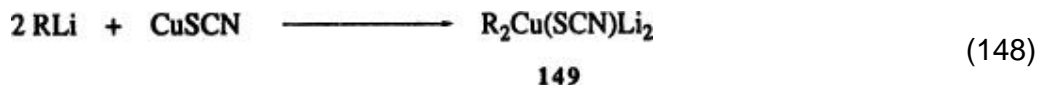
The other additive of considerable popularity in terms of accentuating cuprate couplings is chlorotrimethylsilane. The effects of this (and related) species on higher-order reagents have also been studied, and the results are quite surprising. (512) Even at very low temperatures (< -75°), introduction of R<sub>3</sub>SiX to a cuprate (prior to adding the educt) leads to immediate sequestering of the cyanide ligand from copper by the silyl halide to afford a lower-order cuprate as the predominant copper-containing species in the medium (Eq. 147).



### 3.3.2. Reagents from CuSCN

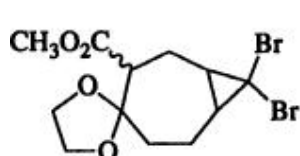
Although copper(I) thiocyanate was originally thought of as a source of lower-order cuprates, (5) it has been found to function akin to copper(I)

cyanide upon treatment with 2 equivalents of an organolithium reagent. (513) Thus, rather than metathesis occurring to generate lithium thiocyanate, a higher-order species  $R_2Cu(SCN)Li_2$  (149) results (Eq. 148). The nature of the bonding

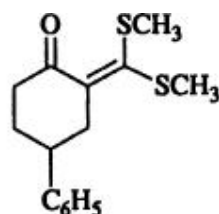


between copper and the ambident thiocyanate ligand was investigated using integrated absorption intensities (514) from IR spectra of these reagents relative to 1,4-dicyanobenzene. The data, in line with the hard/soft acids and bases model, (515) confirmed that sulfur (soft) in  $SCN^-$  is attached to copper (soft), rather than nitrogen (hard).

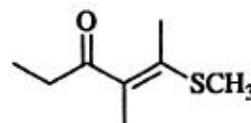
Only a few examples citing the use of these reagents have materialized since the initial report. (513) Geminally dihalogenated cyclopropanes (e.g., 150) undergo double displacements with reagents 149, (516) as do  $\alpha$ -oxoketene dithioacetals (e.g., 151) (517, 518) and vinylogous thioesters (e.g., 152). (519)



**150**



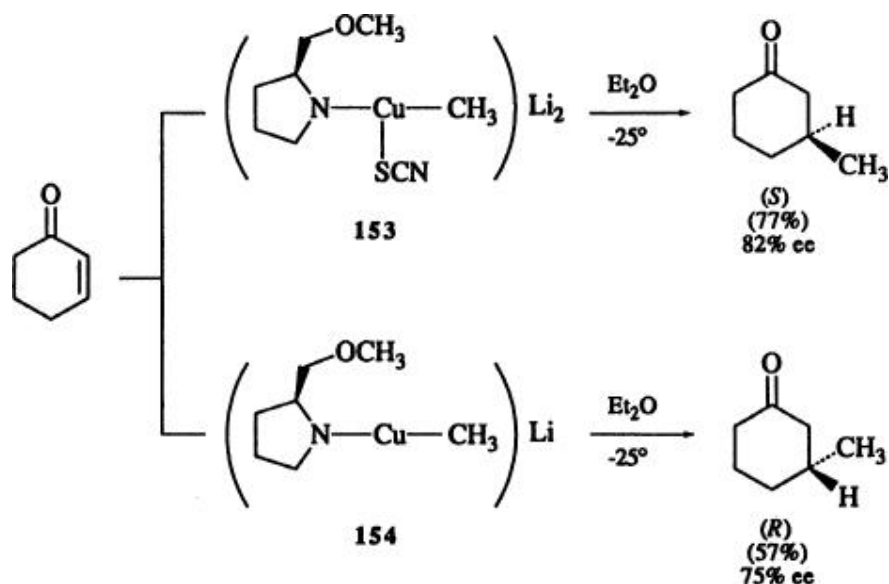
**151**



**152**

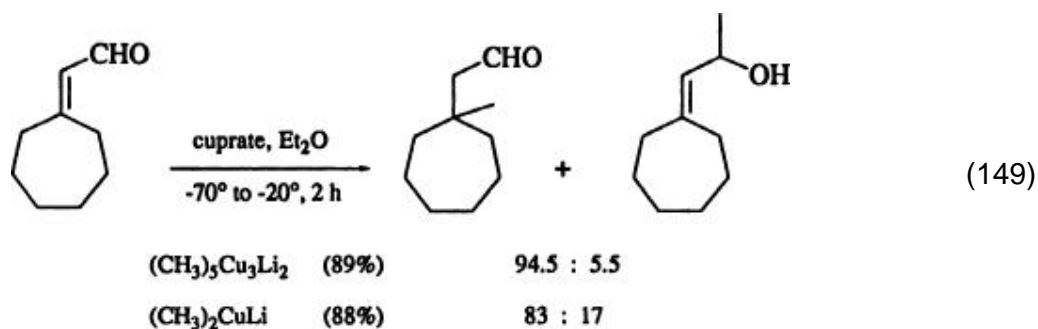
During an extensive study on Michael additions of cuprates containing nonracemic ligands, higher-order thiocyanate reagent 153 was evaluated in terms of its chirality transfer properties. (520) The extent of asymmetric induction found in the product ketones varied depending upon solvent and substrate. What is particularly striking is that the sense of chiral induction observed with this higher-order reagent is opposite to that seen with lower-order analogs 154 (Scheme 16).

**Scheme 16.**



### 3.4. Reactions of Other Organocopper Species

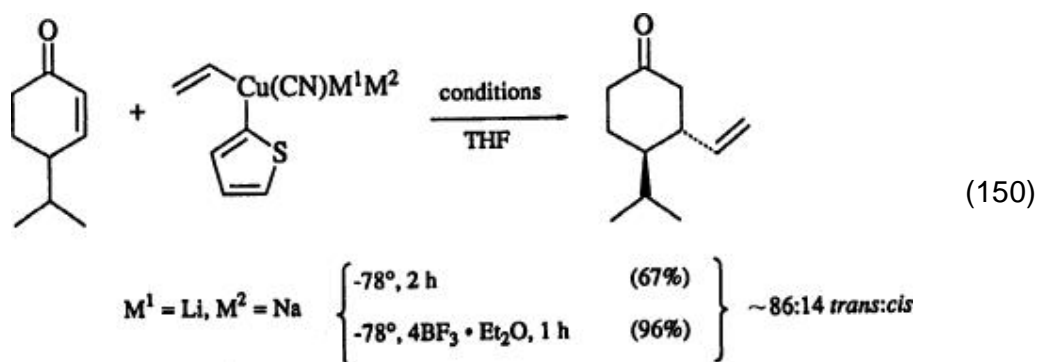
Cuprates prepared from nonintegral ratios of organolithium to copper halide, for example,  $\text{R}_3\text{Cu}_2\text{Li}$  and  $\text{R}_5\text{Cu}_3\text{Li}_2$  (see section on composition studies of lower-order lithiocuprates), have also been screened for their synthetic potential. (403, 404) Organometallics of general formula  $\text{R}_3\text{Cu}_2\text{M}$ , with  $\text{M} = \text{Li}$  or  $\text{MgBr}$ , are excellent reagents for effecting carbocupration of 1-alkynes. (521) Lithium bromide is a required additive for these reagents, which are claimed to be superior to both the  $\text{RCu}\cdot\text{MX}_n$  and  $\text{R}_2\text{CuM}$  formulations. The trinuclear copper complex  $(\text{CH}_3)_5\text{Cu}_3\text{Li}_2$  is quite effective in conjugate methylation of  $\alpha, \beta$ -unsaturated aldehydes, (425) and reagents of this type (i.e.,  $\text{R}_5\text{Cu}_3\text{Li}_2$ ) may actually not have reached their full potential in light of developments using in situ activators such as chlorotrimethylsilane. They are less prone toward competing 1,2 addition, although in highly hindered compounds they offer little advantage over Gilman reagents (Eq. 149).



Several bimetallic reagents can be added across acetylenes under the influence of copper(I) salts to form highly functionalized alkenes. Examples

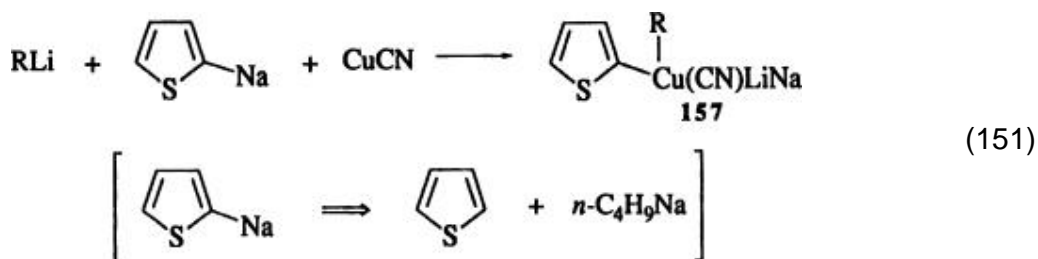


perhaps some new elements of chemoselectivity. Replacement of a lithium by a sodium cation in higher-order reagents, thereby generating the mixed metal cluster  $R_2Cu(CN)LiNa$  [or  $RR'Cu(CN)LiNa$ ] tends to decrease reactivity toward enones, as higher reaction temperatures are needed and yields are somewhat depressed compared to their dilithio counterparts. (533) Use of these mixed clusters with boron trifluoride etherate, however, can significantly improve the outcome (Eq. 150). Both monosodio lower-order ( $R_2CuNa$ ) and



disodio higher-order [ $RR'Cu(CN)Na_2$ ] cuprates are also relatively unreactive toward 2-cyclohexenone. (534) In these couplings, chlorotrimethylsilane increases yields substantially, while both 12-crown-4 and 15-crown-5 ethers retard ligand transfer.

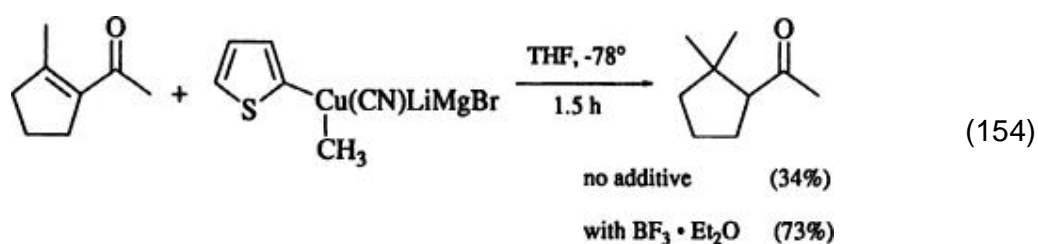
The corresponding change from  $RR'Cu(CN)Li_2$  to the magnesium halide analog  $RR'Cu(CN)LiMgX$  (158) has a similar dampening effect on cuprate reactivity. (535) As with the sodio cuprates 157, (533) they are formed by the admixture of copper(I) cyanide with an equivalent each of  $RLi$  and  $R'MgX$ ,  $RLi$  plus  $R'Na$ , or 2 equivalents of  $RNa$  (Eqs. 151–153). Epoxide openings





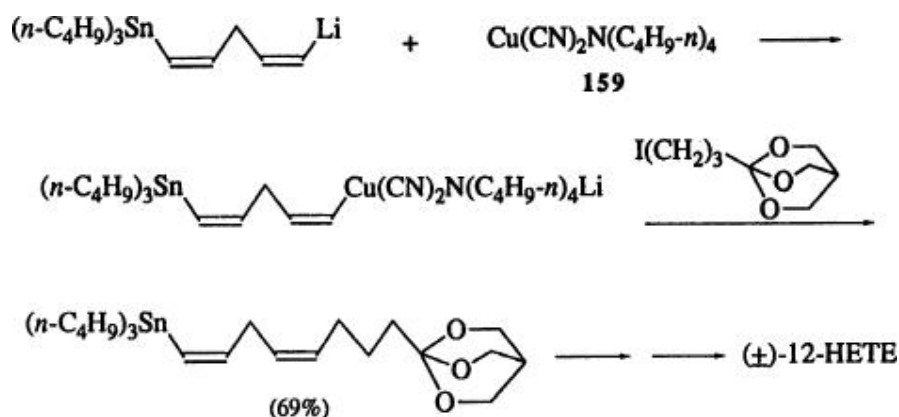


with **158** (R = 2-thienyl), especially with substrates that are challenging (e.g., cyclohexene oxides) can be plagued by competing 1,2-halohydrin formation, which suggests that **158** is not a discrete reagent. **(535)** 1,1-Disubstituted oxiranes are simply too hindered to react, and may also be consumed by cationic polymerization. Monosubstituted epoxides and primary halides, however, afford good results using **158**. Conjugate additions of **158** are acceptable for uncongested enones, and where tolerable, boron trifluoride etherate can drastically affect the level of success realized (Eq. **154**).



A higher-order dicyano cuprate,  $\text{RCu(CN)}_2[(n\text{-C}_4\text{H}_9)_4\text{N}]\text{Li}$ , derived from the addition of  $\text{RLi}$  to  $\text{Cu(CN)}_2\text{N(C}_4\text{H}_9\text{-}n)_4$  (**159**), effects both substitution and conjugate addition reactions with unhindered substrates. **(536)** The lower-order isolable species **159** is derived from copper(I) cyanide and  $(n\text{-C}_4\text{H}_9)_4\text{NCN}$ , which are mixed in methanol at room temperature. The unusual association of two attenuating cyanide ligands together with the non-Lewis acidic tetraalkylammonium counterion combine to take a severe toll in terms of reactivity. Nonetheless, for specific needs, as in the case of a synthesis of  $(\pm)$ -12-hydroxyeicosa-5,8,14(*Z*), 10(*E*)-tetraenoic acid (HETE), **(536)** it is the reagent of choice (Scheme 19).

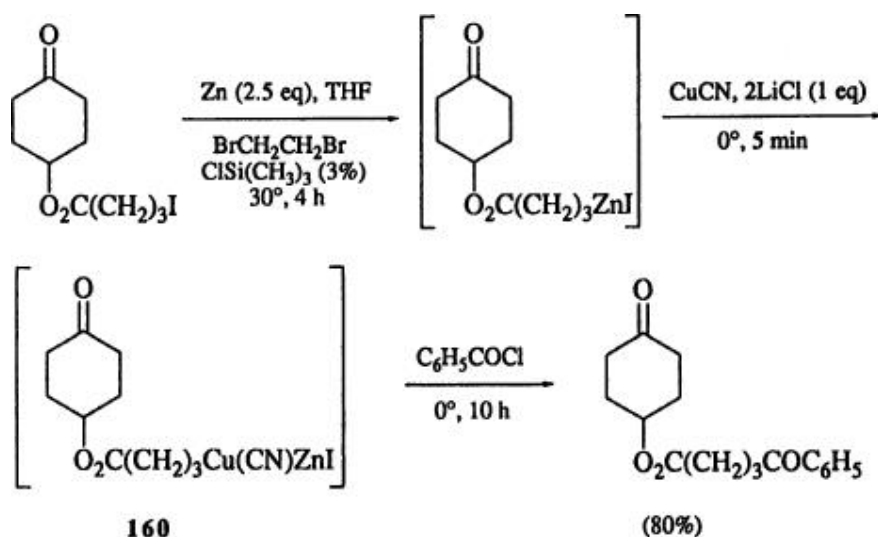
Scheme 19.



Recently, zinc halide salts of lower-order cyanocuprates have been promoted

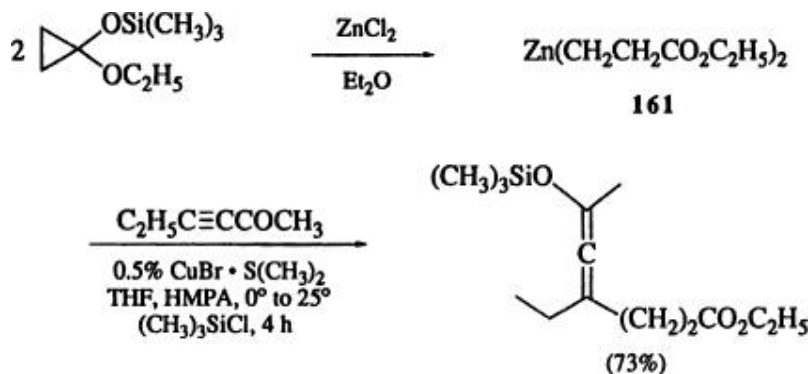
as especially mild and selective reagents which show excellent functional group tolerance within the cuprate. They can be made by oxidation of zinc metal in a mixture that contains dibromoethane and chlorotrimethylsilane as activators/initiators (Scheme 20). (537) Exposure of the organozincate to copper(I) cyanide solubilized with lithium chloride leads to the mixed reagents **160**, which can then effect several standard cuprate-mediated carbon–carbon bond-forming events. The use of both a deactivating ligand (cyano) and gegenion (zinc iodide) accounts for their internal compatibility with many electrophilic centers.

Scheme 20.



Mixed copper(I) and zinc halide dimetallic reagents lead to products of *gem*-dialkylation in good yields. (538) Organozincates, including Reformatsky reagents, undergo typical cuprate displacements on activated halides with copper(I) salts in the pot. (539, 540) Zinc homoenolates (e.g., **161**) are especially valuable synthetic tools which undergo Michael additions to enones and ynones in the presence of copper(I) bromide dimethyl sulfide, with HMPA and chlorotrimethylsilane playing essential roles (Scheme 21). (541, 542)

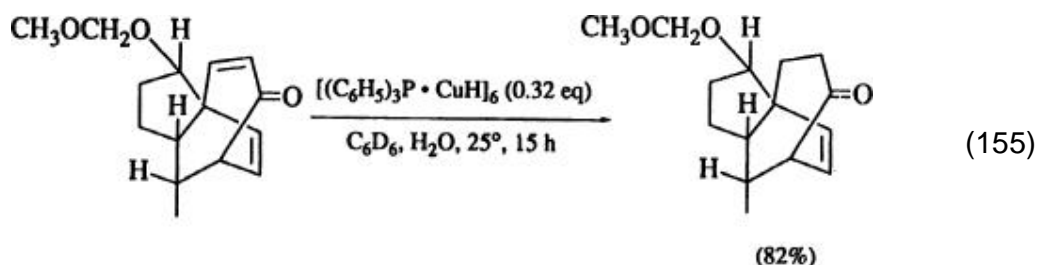
Scheme 21.



Several hydrido cuprates of general formula Li<sub>n</sub>Cu<sub>m</sub>H<sub>(m+n)</sub> are known, some of which have interesting and potentially useful synthetic properties. Li<sub>4</sub>CuH<sub>5</sub> is

reputed to be a more efficient reagent for alkyl halide reduction than is lithium aluminum hydride, whereas  $\text{Li}_2\text{CuH}_3$  behaves as a Michael donor of hydride. (543) The subsequently discovered lower-order hydride species  $\text{RCu(H)Li}$ , with  $\text{R} = \text{SC}_6\text{H}_5$  or  $t\text{-C}_4\text{H}_9\text{O}$ , can function in a similar way. (544) Related complexes of lesser-known constitution have been generated from  $\text{LiAl(OC}_4\text{H}_9\text{-}t\text{)}_3\text{H}$  and  $\text{NaAl(OCH}_2\text{CH}_2\text{OCH}_3)_2\text{H}_2$  solutions containing copper(I) bromide. (545, 546) Interestingly, methylcopper catalyzes the conjugate reduction of  $\alpha$ ,  $\beta$ -unsaturated ketones with diisobutylaluminum hydride, the aluminum enolate from which can be trapped with various activated electrophiles. (547, 548) Other hydride-containing copper(I) species derived from a mixture of  $\text{CuCl}$ ,  $\text{MgBr}_2$ ,  $\text{Et}_3\text{N}$ , and  $\text{NaBH}_4$  (or  $\text{NaH}$ ), (549) or  $(n\text{-C}_4\text{H}_9)_3\text{SnH}$  and  $(\text{CH}_3)_2\text{CuMgBr}$ , (550) add to terminal acetylenes to afford products of symmetrical coupling: (*E*, *E*)-1,3-dienes and *E*-disubstituted olefins.

Although the phosphine-stabilized hexameric copper hydride  $[\text{CuH}\cdot\text{P}(\text{C}_6\text{H}_5)_3]_6$  and related complexes have been known for some time, (551, 552) their ability to deliver hydride in a 1,4 sense has only recently been unveiled (Eq. 155). (553) Competing 1,2 addition does not occur. The reagent is fully compatible with chlorotrimethylsilane and can be used in the presence of water.



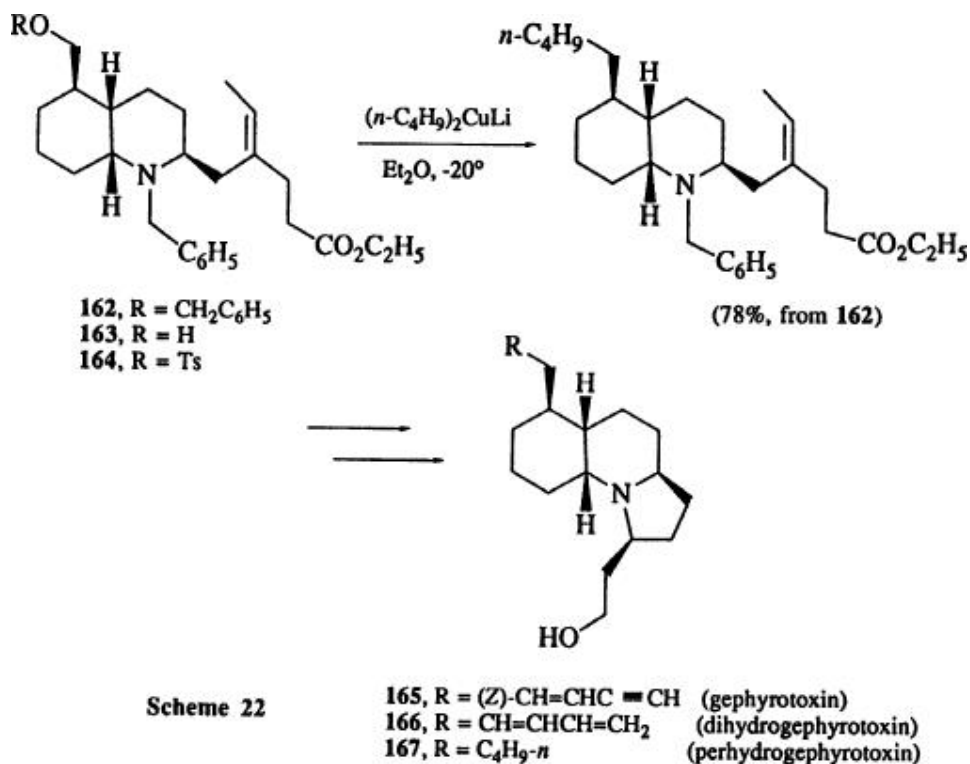
### 3.5. Applications of Organocopper–Organocuprate Reagents to Natural Products Syntheses

The true measure of the value of an organotransition metal reagent lies in the extent to which it is successfully employed, allowing a transformation to be realized which might otherwise require multiple steps to achieve. In this sense, the organocopper reagent is, perhaps, without peer. A multitude of strategies toward a vast array of complex natural products have embraced the benefits of organocopper reagent-based carbon–carbon bond constructions. In this section, a brief representative sampling of some uses of the various copper reagents within the context of total synthesis is described. Tables XI-A through F contain an extensive listing of examples found in the literature, classified according to the ultimate target structure.

In the alkaloid area, ( $\pm$ )-perhydrogephyrotoxin (167) was synthesized with the

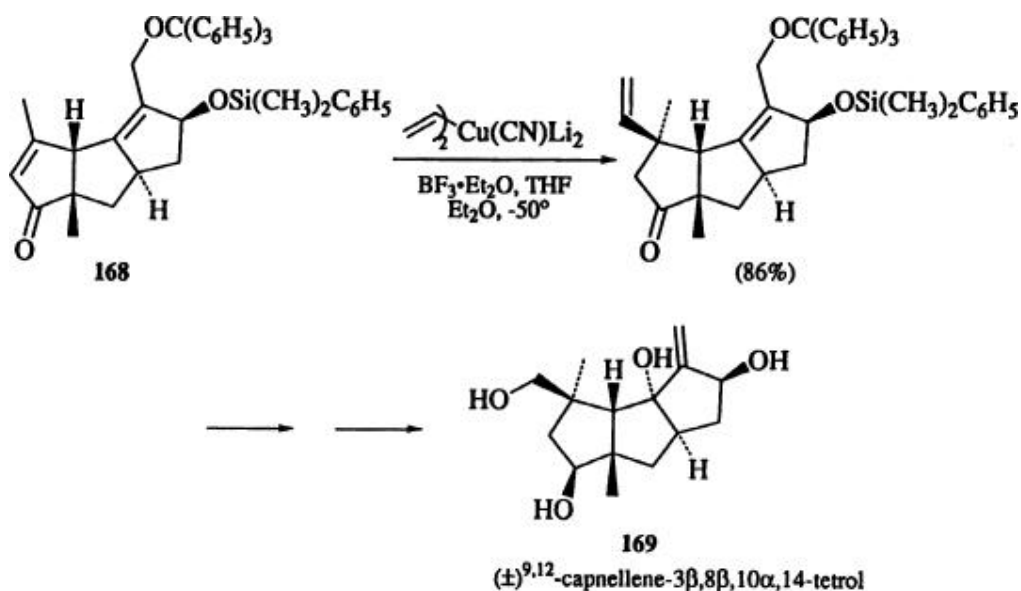
aid of the lower-order cuprate  $(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ . (554) Primary tosylate **164**, derived sequentially from precursors **162** and **163**, undergoes smooth displacement in ether at  $-20^\circ$  to arrive at the *n*-pentyl side chain characteristic of the saturated analog of naturally occurring gephyrotoxin (**165**), and dihydrogephyrotoxin (**166**) (Scheme 22). (554)

Scheme 22.



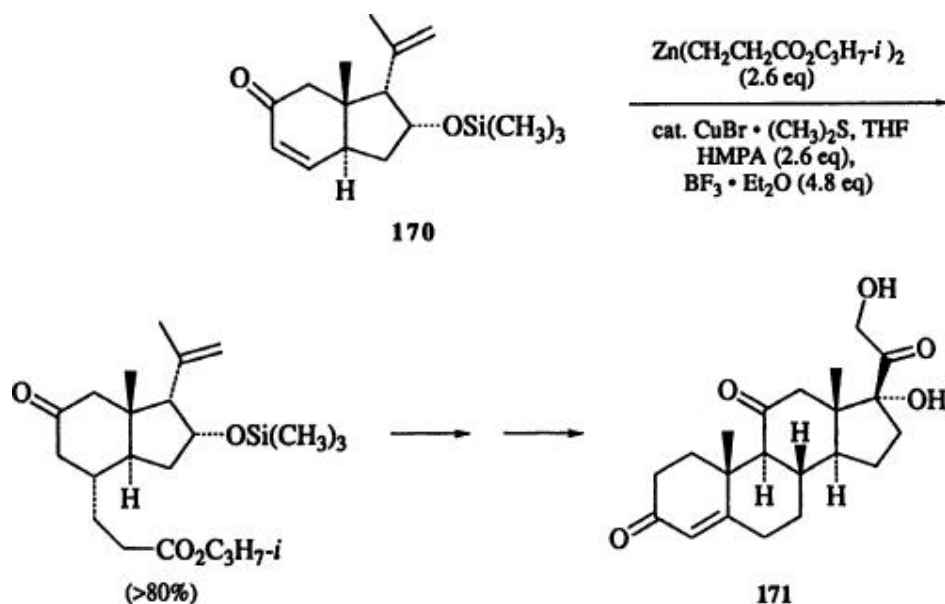
Terpenoid natural products have attracted a tremendous amount of synthetic effort over the past decade, and with these efforts has come a considerable dependence on organocopper reagents for key bond constructions. The potent combination of a higher-order cyanocuprate in the presence of boron trifluoride etherate has been used for establishing quaternary centers in the triquinane sesquiterpenoid area. (511) The vinyl lithium-derived reagent  $(\text{CH}_2 = \text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$ , useful as a hydroxymethyl group equivalent, (476, 477) adds to tricyclic enone **168** in a Michael sense exclusively from the  $\beta$  face in excellent yield. (555) Subsequent manipulations of the ethenyl residue (i.e., vicinal dihydroxylation, oxidative cleavage, and hydride reduction) give the required one-carbon appended material which was ultimately converted into the highly oxygenated capnellene tetraol **169** (Scheme 23). (555) A methyl group has also been introduced via this technology *en route* to coriolin, (556) while a synthesis of forskolin has been significantly assisted through the use of  $(\text{CH}_2 = \text{CH}_2)\text{Cu}(\text{CN})\text{Li}_2$  plus boron trifluoride etherate. (557)

Scheme 23.



A total synthesis of ( $\pm$ )-cortisone, representing applications of cuprate chemistry in the steroid area, employs a boron trifluoride etherate-activated, copper(I)bromide-dimethyl sulfide assisted 1,4 addition of a zinc homoenolate to bicyclic enone **170**. (558) The stereochemistry at the newly formed center, > 95%  $\alpha$  under the conditions shown (Scheme 24), depends upon the additive; without boron trifluoride etherate a 1:1 mixture of diastereomers is unexpectedly obtained. Further transformations of the three-carbon chain build up the A and B rings of the cortisone nucleus (171). (558)

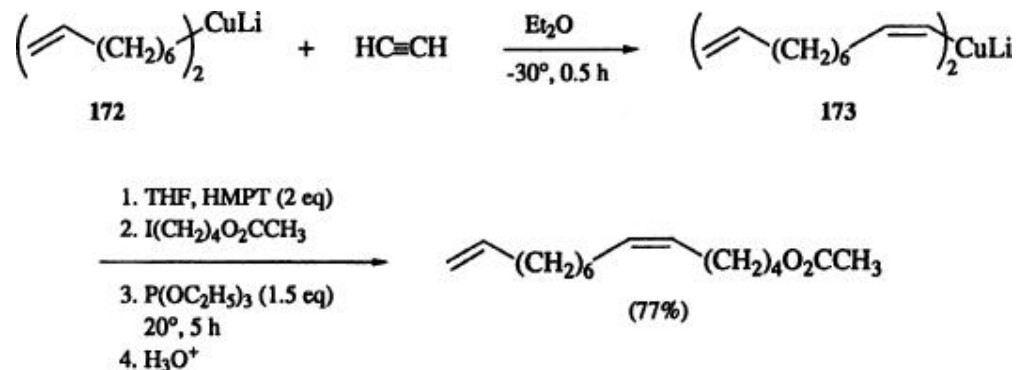
Scheme 24.



The essentially stereospecific *syn* addition of lower-order lithio cuprates across acetylenes provides a quick synthetic entry into pheromones where the purity of a *Z* olefinic component is crucial. Large-scale production of the insect pheromone *Cossus cossus* has been achieved via carbocupration of acetylene

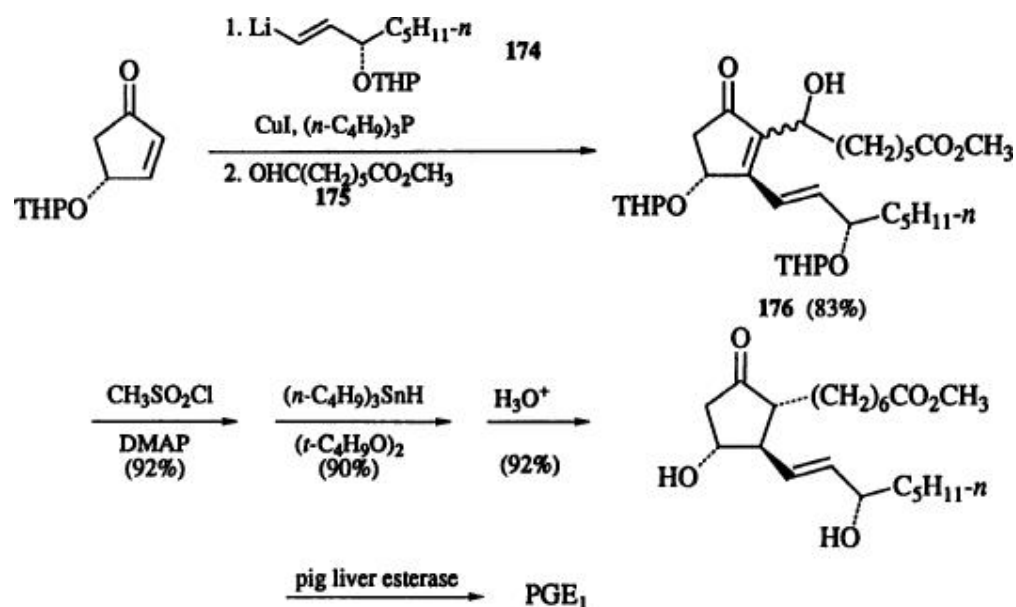
with preformed cuprate **172**, followed by alkylation of the resulting vinyl cuprate intermediate **173** with an iodoacetate in the presence of added phosphite (Scheme 25). (559) Similar sequences have been executed on a 180-mmol scale with yields in the 77–92% range and isomeric purities typically >99.9%.

Scheme 25.



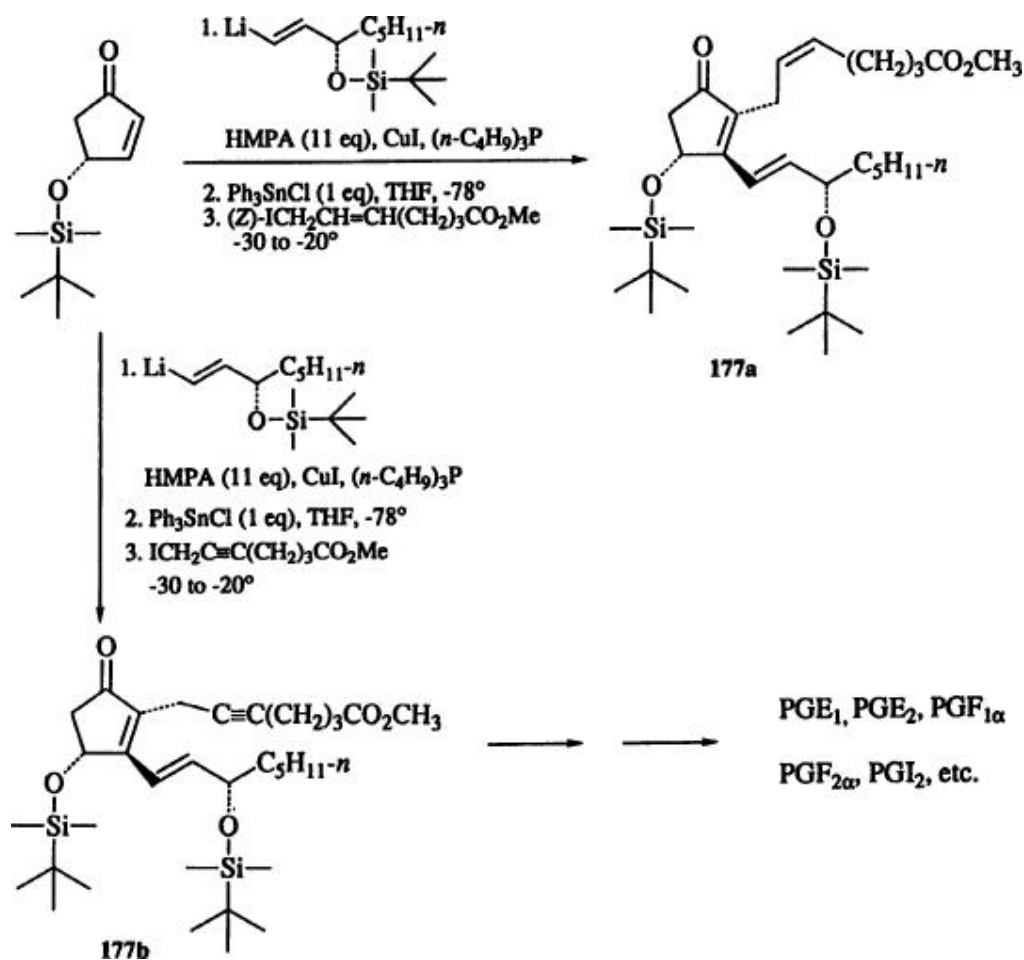
A one-pot, “three-component-coupling” sequence involving the conjugate addition of a phosphine-stabilized organocopper complex to a substituted cyclopentenone, followed by enolate trapping, configures the prostaglandin skeleton in a remarkably rapid fashion. (560) A nonracemic THP-protected enone, upon treatment with the species derived from vinyl lithium **174** and copper(I) iodide (1:1 mix) solubilized with tri-*n*-butylphosphine, affords the adduct enolate which can be quenched with aldehyde ester **175** (Scheme 26). (561-563) The overall yield of **176** from this series of reactions is 83%, with the remaining steps (mesylation, elimination, reduction, hydrolysis) to arrive at (–)-PGE<sub>1</sub> methyl ester all proceeding very efficiently as well (84–92%). (564) Natural material was then obtained by ester hydrolysis using pig liver esterase (86%).

Scheme 26.

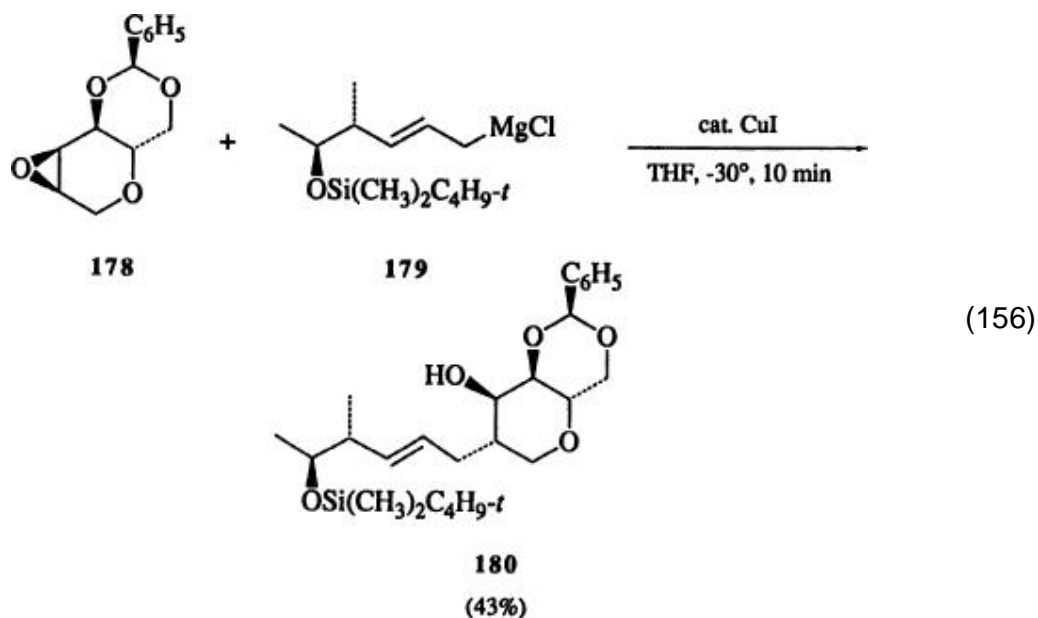


Similar tactics can be applied to the three-step preparation of PGE<sub>2</sub> from an optically active trialkylsilyl-protected 4-hydroxycyclopentenone. (561, 562) Coupling in these cases was accomplished with both allylic and propargylic iodides of the derived intermediate triphenyltin enol ethers to afford **177a** and **177b**, respectively (Scheme 27).

Scheme 27.



Many other types of compounds of natural origin have been synthesized using copper reagents to effect critical bond formations. In a total synthesis of (+)-methyl pseudomonate C from carbohydrate precursors, a copper-catalyzed ring opening of epoxide **178** with the Grignard reagent **179** formed from the corresponding allylic chloride is utilized (Eq. 156). (565) The realization

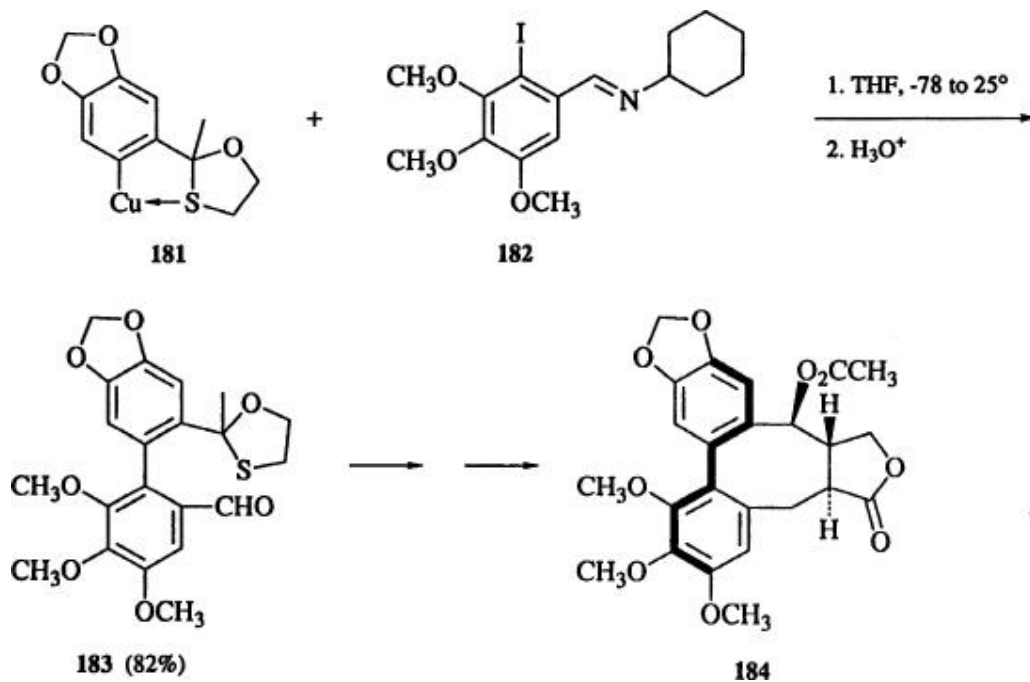


of product **180**, via **179**, represents one of the rare successful uses of an unbiased, substituted allylic magnesio (or lithio) cuprate. Many remarkable features of this coupling were noted, including (1) the regiochemistry of oxirane cleavage is cleanly derived from *trans*-diaxial attack of the reagent; (2) the site specificity of coupling in the “normal” ( $\alpha$ -), rather than “rearranged” ( $\gamma$ -) mode by the allylic cuprate; and (3) the maintenance of *E* double-bond geometry.

The construction of the biphenyl-containing lignan steganacin **184**, isolated from *Steganotaenia araliacea* and found to have antileukemic properties, relies on an intermolecular, ambient-temperature Ullmann coupling which proceeds by way of an internal ligand-stabilized arylcopper species **181**. (566) Treatment of the precursor bromide with *n*-butyllithium followed by the copper(I) iodide-triethylphosphite complex forms the organocopper reagent **181**. Introduction of the iodoimine **182** at  $-78^\circ$  gives upon warming to room temperature and hydrolysis the product biaryl **183**, presumed to arise by way of a Cu(III) intermediate (Scheme 28).

**Scheme 28.**





Several other uncategorized examples of natural product syntheses which rely on copper reagents are shown in Table [XI-F](#).

## 4. Experimental Procedures

### 4.1.1.1. 1,3-Dimethoxy-5-(*n*-pentyl)benzene (“Olivetol Dimethyl Ether”) (Dilithium-tetrachlorocuprate-Catalyzed Coupling of a Grignard with an Alkyl Halide) (567)

Under dry nitrogen, 5-chloro-1,3-dimethoxybenzene (40 g, 0.23 mol), magnesium (6 g, 0.25 mol) and a small amount of 1,2-dibromoethane in tetrahydrofuran (80 mL) were heated under reflux for 6 hours. The solution was cooled in ice and a mixture of 1-iodopentane (42.6 mL, 0.325 mol) and dilithiumtetrachlorocuprate (30 mL of a 0.2 M solution in tetrahydrofuran, 6 mmol) was added dropwise over a period of 30 minutes. The resulting black mixture was stirred at 0° for 90 minutes and at 20° for an additional 16 hours. The almost solid reaction mixture was acidified with 6 N hydrochloric acid (160 mL) and extracted with ether (2 × 200 mL). The organic extract was washed with 15% aqueous ammonia (60 mL) and water (60 mL), dried with magnesium sulfate, and evaporated in vacuo. According to the <sup>1</sup>H NMR spectrum of the residual product, olivetol dimethyl ether was formed in 74% yield. Distillation afforded the pure product (31.9 g, 66%) as a colorless liquid, bp 152–156° (12 mm).

### 4.1.1.2. *trans*-2-Phenylcyclohexanol [Copper(I) Iodide-Catalyzed Opening of an Epoxide with a Grignard] (568)

To 10.9 g (0.45 mol) of magnesium in 100 mL of tetrahydrofuran was added 73.0 g (0.465 mol) of bromobenzene in 100 mL of tetrahydrofuran over 1 hour. The resulting mixture was stirred for 30 minutes and then 8.85 g (46.5 mmol) of cuprous iodide was added and the mixture cooled to –30°. A solution of 29.45 g (0.30 mol) of cyclohexene oxide in 50 mL of tetrahydrofuran was then added dropwise. After the addition was complete, the mixture was stirred for 3 hours and then quenched by being poured into 100 mL of cold saturated aqueous ammonium chloride solution. The solution was extracted with ether and the organic layers were combined, dried, and concentrated to afford a liquid that was distilled at 80° (0.23 mm) to afford 43.1 g (81%) of a yellow solid which was recrystallized from pentane, mp 56.5 – 57.0°; IR: 3592, 3461, 2941, 2863, 1604, 1497, 1451 cm<sup>-1</sup>; <sup>1</sup>H NMR (361 MHz) δ : 7.35–7.17 (m, 5H), 3.64 (ddd, 1H, *J* = 5.4, 10.8, 10.8 Hz), 2.42 (ddd, 1H, *J* = 5.4, 10.8, 16.5 Hz), 2.11 (m, 1H), 1.84 (m, 2H), 1.76 (m, 1H), 1.62 (s, 1H), 1.53–1.25 (br m, 4H); <sup>13</sup>C NMR (90 MHz) δ : 143.4 (s), 128.7 (d), 127.9 (d), 126.7 (d), 74.3 (d), 53.3 (d), 34.6 (t), 33.4 (t), 26.1 (t), 25.1 (t); mass spectrum, *m/z*: 176(M<sup>+</sup>), 158, 143, 130, 117, 104, 91 (base).

### 4.1.1.3. *n*-Heptanoic Acid [Copper(I) Chloride-Catalyzed Opening of a Lactone with a Grignard] (166)

*n*-Butylmagnesium bromide (1 M in ether, 2.4 mL, 2.4 mmol) was slowly added to a suspension of cuprous chloride (4 mg, 0.04 mmol) in 6 mL of

tetrahydrofuran at 0° under argon.  $\beta$ -Propiolactone (0.144 g, 2 mmol) in 2 mL of tetrahydrofuran was next added dropwise. The mixture was stirred at 0° for 15 minutes and quenched by adding 3 N hydrochloric acid solution. From the organic layer, heptanoic acid was extracted with 3 N sodium hydroxide solution. The alkaline solution was acidified, extracted with ether, and concentrated to give pure heptanoic acid in 90% yield; bp 65° (1.0 mm).

#### 4.1.1.4. 3-(2-Methylpent-2-en-5-yl)furan ("Perillene")

*(Dilithiumtetrachlorocuprate-Catalyzed Coupling of an Allylic Halide with a Grignard)* (99)

To 0.104 g (4.29 mmol) of magnesium turnings covered with 3 mL of tetrahydrofuran under argon was added 0.5 g (4.29 mmol) of 3-chloromethylfuran in 2 mL of tetrahydrofuran in one portion. The mixture was allowed to stir for 30 minutes at room temperature, then warmed in a preheated 50° oil bath for 30 minutes to provide a golden-yellow solution. The solution was chilled in an ice-water bath and 0.448 g (4.29 mmol) of freshly distilled 1-chloro-3-methyl-2-butene in 2 mL of tetrahydrofuran was added in one portion followed immediately by the addition of 0.15 mL of a 0.1 M solution of dilithiumtetrachlorocuprate in tetrahydrofuran. The resulting black suspension was stirred for 5 minutes at 0°, poured into petroleum ether (50 mL), washed with 5% aqueous sodium bicarbonate solution (50 mL) and water (50 mL), and dried over sodium sulfate. Concentration in vacuo provided a pale yellow liquid which was purified by bulb-to-bulb distillation to give 0.547 g (85%) of perillene as a colorless liquid, bp 80° (20 mm).

#### 4.1.1.5. *trans*-3-*n*-Butyl-1-deuterio-5-methylcyclohexene [Copper(I)

*Cyanide-Catalyzed Substitution of an Allylic Mesitoate with a Grignard]* 62a

A flask equipped with a magnetic stirrer and septum was charged with 54 mg (0.6 mmol) of cuprous cyanide. After flushing with dry nitrogen, 2 mL of anhydrous ether was added and the suspension was chilled to -10°. An ether solution of *n*-butylmagnesium bromide (6 mmol, prepared from 987 mg of 1-bromobutane and 146 mg of magnesium in 8 mL of ether) was added through a cannula, and after stirring the mixture for 10 minutes, a solution of 778 mg (3 mmol) of  $\alpha$ -deuterio-*cis*-5-methyl-2-cyclohexenyl mesitoate in 2 mL of ether was added. The cooling bath was removed and the mixture stirred at room temperature for 6.5 hours, after which it was quenched with 2 mL of aqueous ammonium chloride solution. The resulting mixture was filtered, the precipitate washed with ether, and the ether solution dried over magnesium sulfate. Removal of solvent by fractionation followed by column chromatography (silica gel, pentane/ether) and vacuum distillation gave 289 mg (63% yield) of a clear mobile oil, bp 58–60° (7.4 mm); IR (neat): 3020, 2945, 2910, 2900, 2860, 2840, 2820, 2240, 1640, 1465, 1455, 1430, 1375, 895, 730, 710 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 5.63 (br s, 1H), 2.20–1.90 (br m, 2H), 1.90–1.68 (br m, 1H), 1.68–1.50 (m, 9H), 1.05–0.70 (m, 3H), 0.93 (d, 3H),

$J = 7.5$  Hz); high-resolution mass spectrum, calculated for  $C_{11}H_{19}D$   $m/e$  153.1622, found  $m/e$  153.1628.

4.1.1.6. 3-[3-(1,3-Dioxolan-2-yl)propyl]cyclohexanone [Copper(I) Bromide-Catalyzed Conjugate Addition of a Grignard to an  $\alpha, \beta$ -Unsaturated Ketone] (143)

Magnesium turnings (0.60 g, 25 mmol) were ground for a few minutes with a mortar and pestle and were immediately placed into a nitrogen-filled flask. A solution of 2-(3-chloropropyl)-1,3-dioxolane (1.2 mL, 8.3 mmol), 1,2-dibromoethane (0.05 mL), and tetrahydrofuran (1.6 mL) was added at 25°, and the mixture was stirred in a 70°-bath at which temperature the reaction began. The reaction flask was then placed in a 25° bath and stirred for 30 minutes, diluted with additional tetrahydrofuran (5 mL), stirred for 1.25 hours, and cooled to -78°. A solution of cuprous bromide–dimethyl sulfide complex (0.41 g, 2.0 mmol) and dimethyl sulfide (4 mL) was then added dropwise and the mixture was stirred at -78° for 1 hour. A solution of cyclohexenone (0.65 mL, 6.8 mmol) and ether (7 mL) was then introduced dropwise over a 7 minute period, and the mixture stirred at -78° for 2.5 hours and then warmed in an ice-water bath. After being stirred at 0° for 5 minutes, the mixture was quenched by the addition of a saturated aqueous solution (5 mL) of ammonium chloride (adjusted to pH 8 with aqueous ammonia) and stirred at 25° for 1.5 hours. The dark-blue aqueous layer was removed, the ether layer washed with two additional 10-mL portions of water and a saturated aqueous solution (15 mL) of sodium chloride, and dried over magnesium sulfate. Concentration by rotary evaporation gave 1.28 g of the crude product, which was purified by flash chromatography (silica gel, 1:1 hexanes/ethyl acetate) to give 1.05 g (75%) of the product as a colorless oil. The analytical sample was obtained by bulb-to-bulb distillation [oven temperature 80° (0.2 mm)]; IR (neat): 2950, 1712  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ )  $\delta$ : 4.83 (t, 1H,  $J = 4.8$  Hz), 3.90 (m, 4H), 1.15–2.55 (m, 15H); Anal. Calcd for  $C_{12}H_{20}O_3$ : C, 67.89; H, 9.50. Found: C, 67.76; H, 9.53%.

4.1.1.7. 1-Trimethylsilyloxynon-1-ene [Copper(I) Bromide-Catalyzed Conjugate Addition of a Grignard to an  $\alpha, \beta$ -Unsaturated Aldehyde in the Presence of Chlorotrimethylsilane and Hexamethylphosphoric Triamide] (157)

To a cooled (-78°) tetrahydrofuran solution (60 mL) of *n*-hexylmagnesium bromide (prepared from 35 mmol of 1-bromohexane and 37.5 mmol of magnesium in 85–90% yield), hexamethylphosphoric triamide (10.5 mL, 60 mmol) [**CAUTION: Potent Carcinogen**], and cuprous bromide–dimethyl sulfide complex (257 mg, 1.25 mmol) was added dropwise a mixture of acrolein (1.67 mL, 25 mmol) and chlorotrimethylsilane (6.4 mL, 50 mmol) in 20 mL of tetrahydrofuran over 30 minutes. After 3 hours, triethylamine (7 mL) and hexane (100 mL) were added. The organic layer was washed with water to remove hexamethylphosphoric triamide and dried over magnesium sulfate.

The product (3.86 g, 83%; 94% *E* by GLC analysis) was obtained by distillation (74°, 1 mm).

*4.1.1.8. 4-Methylbenzophenone (Substitution of an Aryl Halide with Arylmethylcoppermagnesium Bromide) (163)*

In a 1-L, flame-dried, three-necked, round-bottomed flask equipped with an overhead stirrer and low-temperature thermometer, a bright yellow suspension of methylcopper was prepared by the reaction 30 mL of a 1.73 M (51.9 mmol) ether solution of methyllithium (0.11 M in residual base) with a -78° suspension of 9.6 g (50.8 mmol) of cuprous iodide in 100 mL of tetrahydrofuran. The bright yellow color characteristic of methylcopper formed when this reaction mixture was warmed to 25°. It was then cooled to -70° and 26 mL of a 1.96 M (51.0 mmol) ether solution of 4-methylphenylmagnesium bromide was added with a syringe. The resulting suspension was allowed to warm to 25° and after cooling the deep purple solution to -78°, a solution of benzoyl chloride (13.0 mL, 112 mmol) in tetrahydrofuran (30 mL) was added dropwise by syringe. The reaction mixture was then warmed to 25° and allowed to stir for 30 minutes. It was quenched with 8 mL of absolute methanol and then added to 600 mL of saturated aqueous ammonium chloride solution. Stirring for 2 hours dissolved the copper salts, the ethereal phase was separated, and the aqueous portion was washed with two 100-mL portions of ether. The combined organic fractions were washed once with 100 mL of 0.1 N aqueous sodium thiosulfate, three times with 100 mL of 1.0 N sodium hydroxide, and once with 200 mL of saturated sodium chloride, and then dried over potassium carbonate. The product 4-methylbenzophenone was isolated by distillation (7.8 g, 79% yield), bp 120–130° (0.6 mm); IR (methylene chloride) 1670 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ : 7.1–7.9 (m, 9H), 2.4 (s, 3H).

*4.1.1.9. trans-4-Methyl-2-cyclopentene-1-acetic Acid [Stoichiometric Copper(I) Bromide-Mediated S<sub>N</sub>2ϕ Opening of a Vinylactone with a Grignard] (174)*

To a solution of cuprous bromide–dimethyl sulfide complex (71.0 g, 0.35 mol) in dimethyl sulfide (300 mL) and tetrahydrofuran (700 mL) at -20° was added methylmagnesium bromide (125 mL, 2.85 M in tetrahydrofuran, 0.35 mol). After stirring at -20° for 1 hour, a solution of 2*H*-cyclopenta[*b*]furan-2-one (21.5 g, 0.18 mol) in tetrahydrofuran (200 mL) was added dropwise via an addition funnel. The mixture was stirred at -20° for 5 hours, poured into 1 N sodium hydroxide solution, and stirred for 2 hours. The organic layer was separated and the aqueous layer was acidified to pH ~ 2 with 1 N hydrochloric acid. After extraction with ether, the organic phase was washed with water and brine, dried over magnesium sulfate, and concentrated in vacuo to provide a yellow oil (23.65 g, 97.6%). This was characterized as its methyl ester (prepared by standard diazomethane treatment); IR (CHCl<sub>3</sub>): 1730 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ : 5.65 (m, 2H), 3.65 (s, 3H), 3.14 (br m, 1H), 2.80 (br m, 1H), 2.30 (AB portion of ABX, 2H), 1.67 (m, 2H), 0.97 (d, 3H); Anal. Calcd for C<sub>9</sub>H<sub>14</sub>O<sub>2</sub>: C, 70.10; H, 9.15. Found: C, 70.01, H, 9.19%.

4.1.1.10. 3-Methoxy-17-[(1 $\beta$ -methyl)ethan-1,2-dien-2-yl]-1,3,5(10)-estratriene [Stoichiometric Copper(I) Bromide-Mediated Substitution of a Propargylic Steroidal Sulfinate with a Grignard] (185)

A solution of methylmagnesium chloride (0.03 mol) in tetrahydrofuran (30 mL) was added cautiously to a stirred suspension of cuprous bromide (0.03 mol) in tetrahydrofuran (50 mL) at  $-50^{\circ}$  and stirred at  $-30^{\circ}$  for 30 minutes. 17 $\alpha$ -Ethynyl-17 $\beta$ -methanesulfinyloxy-3-methoxy-1,3,5(10)-estratriene (5.58 g, 0.015 mol) in tetrahydrofuran (10 mL) was then added at  $-50^{\circ}$  over 10 minutes. The reaction mixture was raised to  $20^{\circ}$  within 10 minutes. After 45 minutes, it was poured into a saturated solution of ammonium chloride in water (200 mL) containing sodium cyanide (2 g). It was then extracted with hexane ( $3 \times 50$  mL) and the combined extracts were washed with water and then dried over magnesium sulfate. Evaporation of solvent in vacuo afforded the product (4.55 g, 98%) which was recrystallized from ethanol, mp  $71.0\text{--}71.5^{\circ}$ ;  $[\alpha]_{\text{D}}^{25}$  in methylene chloride:  $-16.05^{\circ}$ .

4.1.1.11. 2-(Trimethylsilylmethyl)hex-1-ene [Copper(I) Bromide-Mediated Carbocupration of an Acetylene with a Grignard in Ether] 222b

To a suspension of cuprous bromide (2.2 g, 15 mmol) and lithium iodide (1 N solution in ether, 20 mL, 20 mmol) in ether (50 mL) was added, at  $0^{\circ}$ , a solution of trimethylsilylmethylmagnesium chloride (2.90 M in ether, 17 mL, 15 mmol). The mixture first gave a yellow precipitate and then a homogeneous pale green solution which was stirred at  $-5^{\circ}$  for 1 hour. After addition of 1-hexyne (1.0 g, 12.5 mmol), the mixture was allowed to warm to  $10^{\circ}$ , stirred at this temperature for 18 hours (brown solution) and then hydrolyzed with 100 mL of buffered ammonia solution. The mixture was filtered and decanted; the organic layer was washed with brine (10 mL) and dried over magnesium sulfate. The solvent was evaporated and the residue distilled through a 10-cm Vigreux column to afford 1.8 g (78%) of pure product, bp  $70^{\circ}$  (10 mm);  $^1\text{H NMR}$  ( $\text{CCl}_4$ )  $\delta$ : 4.8 (s, 1H), 4.6 (s, 1H), 2.0 (t, 2H), 1.8 (s, 2H), 1.4 (m, 4H), 0.98 (t, 3H), 0.05 (s, 9H). Anal. Calcd for  $\text{C}_{10}\text{H}_{22}\text{Si}$ : C, 70.50; H, 13.01. Found: C, 70.40; H, 13.03.

4.1.1.12. (E)-4-Methyl-3-decen-1-ol [Copper(I) Bromide-Mediated Carbocupration of an Acetylene Followed by Opening of an Oxirane with the Derived Vinylcopper] 218b

To a mixture of cuprous bromide–dimethyl sulfide (0.82 g, 4.0 mmol), ether (5 mL), and dimethyl sulfide (4 mL) at  $-45^{\circ}$  under nitrogen was added a 2.90 M solution (1.39 mL, 4.0 mmol) of methylmagnesium bromide in ether over a 2-minute period. After 2 hours, 1-octyne (0.52 mL, 3.5 mmol) was added over 1 minute to the yellow-orange suspension. The mixture was stirred at  $-23^{\circ}$  for 120 hours, and then the resulting dark green solution was cooled to  $-78^{\circ}$ . A solution of 1-lithio-1-pentyne (prepared from 4.0 mmol of *n*-butyllithium and 4.0 mmol of 1-pentyne), ether (5 mL), and hexamethylphosphoric triamide

(1.4 mL, 8.0 mmol) [**Caution: Potent Carcinogen**] was transferred to the green solution. After 1 hour, ethylene oxide (0.21 mL, 4.0 mmol), which had been condensed at  $-45^{\circ}$ , was added with a dry-ice-cooled syringe over a 0.5-minute period. The resulting mixture was stirred at  $-78^{\circ}$  for 2 hours, allowed to stand at  $-25^{\circ}$  for 24 hours, quenched at  $0^{\circ}$  by addition of an aqueous solution (5 mL) of ammonium chloride (adjusted to pH 8 with ammonia), and then partitioned between ether and water. The crude product (90% pure by GLPC) was purified by column chromatography on silica gel (methylene chloride) to give a colorless oil (0.44 g, 75%); IR (neat): 3300, 1669, 874  $\text{cm}^{-1}$ ;  $^1\text{H NMR } \delta$ : 5.05 (t, 1H,  $J = 7$  Hz), 3.55 (t, 2H,  $J = 7$  Hz), 1.58 (s, 3H), 2.40–0.65 (br m, 16H); high-resolution mass spectrum:  $m/z$  calculated for  $\text{C}_{11}\text{H}_{22}\text{O}$ , 170.1667; found, 170.1691.

*4.1.1.13. (E)-1-Ethoxy-1-phenylpenta-1,4-diene (Lithium Dibromocuprate-Mediated Carbocupration of an Acetylene by a Grignard Followed by Alkylation of the Derived Vinylcopper with an Allylic Halide) (569)*

To a stirred solution of phenylcopper [prepared in situ by stirring phenylmagnesium bromide (0.01 mol) with 0.01 mol of the tetrahydrofuran-soluble complex lithium dibromocuprate at  $-50^{\circ}$  for 1 hour] in tetrahydrofuran (35 mL) was added 0.01 mol of ethoxyacetylene at  $-50^{\circ}$ . The mixture was then stirred for 1 hour at  $-20^{\circ}$ . Subsequently, allyl bromide (0.01 mol) was added and the mixture stirred for 3 hours. It was then poured into an aqueous ammonium chloride solution (200 mL) containing sodium cyanide (2 g) and extracted with pentane ( $3 \times 50$  mL). The combined extracts were washed with water ( $6 \times 100$  mL) to remove tetrahydrofuran and dried over magnesium sulfate. The solvent was removed in vacuo and the residue purified by column chromatography eluting with pentane. Because of the instability of the product the chromatography was performed within 2 hours; 96% yield, 95% pure by GLC; IR (neat): 3080, 3060, 1645, 1600, 1495, 1238, 1128, 910, 770, 700  $\text{cm}^{-1}$ ;  $^1\text{H NMR } (\text{CCl}_4) \delta$ : 7.5–7.1 (m, 5H), 5.82 (m, 1H,  $J = 6.0, 9.5, 17.5$  Hz), 5.07 (br d, 1H,  $J = 17.5$  Hz), 4.98 (br d, 1H,  $J = 9.5$  Hz), 4.70 (t, 1H,  $J = 8.0$  Hz), 3.73 (q, 2H,  $J = 7.0$  Hz), 2.78 (m, 2H,  $J = 6.0, 8.0$  Hz), 1.25 (t, 3H,  $J = 7.0$  Hz); mass spectrum,  $m/z$ : 188 ( $\text{M}^+$ ), 105 (100).

*4.1.1.14. 3-Vinyl-2-methyl-1-trimethylsilyloxycyclopentene (Conjugate Addition of Divinylmagnesium Cuprate to an  $\alpha, \beta$ -Unsaturated Ketone and in situ Trapping of the Enolate with Chlorotrimethylsilane) (253)*

To magnesium (6.07 g, 250 mmol) and one crystal of iodine in tetrahydrofuran (100 mL) was added vinyl bromide (70.5 mL, 1 mol) in tetrahydrofuran (60 mL) at a rate to maintain the reaction temperature at  $45^{\circ}$ . After all the magnesium had disappeared, the solution was heated at  $45^{\circ}$  under a stream of nitrogen to remove excess vinyl bromide. The mixture was then cooled to  $-5^{\circ}$ , cuprous iodide (25.7 g, 135 mmol) added, and the solution stirred until it was jet black. The mixture was quickly chilled to  $-70^{\circ}$  and 2-methylcyclopentenone (10.56 g, 110 mmol) in tetrahydrofuran (40 mL) was added dropwise and the solution

stirred at  $-40^{\circ}$  for 45 minutes. After subsequent cooling to  $-60^{\circ}$ , chlorotrimethylsilane (34 mL, 365 mmol), hexamethylphosphoric triamide (70 mL) [**Caution: Potent Carcinogen**], and triethylamine (50 mL) were added sequentially. The reaction mixture was allowed to warm to room temperature over a period of 2 hours. Aqueous petroleum ether workup, followed by distillation, gave a colorless liquid (19.19 g, 89%); bp  $64\text{--}66^{\circ}$  (3.1 mm); IR (neat): 2990, 1690, 1640, 1250, 1210, 1090, 990, 840  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CCl}_4$ )  $\delta$ : 5.70 [overlapping (5 lines) ddd, 1H,  $J = 17.5, 10, 9$  Hz], 5.00 (dd, 1H,  $J = 17.5, 2.5$  Hz), 4.93 (dd, 1H,  $J = 9, 2.5$  Hz), 3.00 (m, 1H), 2.5–1.4 (m, 4H), 1.47 (br s, 3H), 0.22 (s, 9H). Anal. Calcd for  $\text{C}_{11}\text{H}_{20}\text{OSi}$ : C, 67.28; H, 10.26. Found: C, 67.04; H, 10.18.

4.1.1.15. *4-tert-Butyldimethylsilyloxy-3-(7-tert-butyldimethylsilyloxyheptyl)cyclopent-2-en-1-one (Conjugate Addition–Elimination of a  $\beta$ -Chlorocyclopentenone with a Diorganomagnesium Cuprate)* (232)

The required Grignard reagent was prepared by adding a solution of 7-bromo-1-(*tert*-butyldimethylsilyloxy)heptane (6.19 g, 20 mmol) in tetrahydrofuran (15 mL), over 1.5 hours to magnesium (491 mg, 20.2 mmol) in refluxing tetrahydrofuran (15 mL). The consumption of magnesium was complete after heating at reflux for a further 3 hours. The concentration of reagent was measured by standard titration of an aliquot (1 mL) after hydrolysis. A suspension of cuprous iodide (78 mg, 0.4 mmol) in tetrahydrofuran (2 mL) containing 3-chloro-4-[*tert*-butyldimethylsilyloxy]cyclopent-2-en-1-one (100 mg, 0.4 mmol) was stirred vigorously at  $-10^{\circ}$  under argon. Dropwise addition of the above Grignard reagent (0.41 M in tetrahydrofuran, 1.85 mL, 0.76 mmol) produced a green solution which was stirred at  $-10^{\circ}$  for 10 minutes. The reaction was rapidly quenched with saturated aqueous ammonium chloride solution (5 mL), and after addition of ether (5 mL), the mixture was stirred at room temperature for 1 hour before dilution with water (10 mL) and extraction with ether ( $5 \times 10$  mL). The combined extracts were washed with brine ( $2 \times 5$  mL), dried over magnesium sulfate and evaporated. Preparative thin-layer chromatography [silica gel, methylene chloride/methanol (50:1, v/v)] gave the product as a colorless oil (167 mg, 95%), bp (Kugelrohr)  $135^{\circ}$  at 0.2 mm; IR: 1720  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$ : 0.04 (s, 6H), 0.12 (s, 3H), 0.14 (s, 3H), 0.88 (s, 9H), 0.91 (s, 9H), 1.16–1.80 (m, 10H), 2.25 (dd, 1H,  $J = 18.0, 3.0$  Hz), 2.44 (br t, 2H,  $J = 8$  Hz), 2.72 (dd, 1H,  $J = 18.0, 6.0$  Hz), 3.60 (t, 2H,  $J = 6.0$  Hz), 4.76 (dd, 1H,  $J = 6.0, 3.0$  Hz), 5.90 (m, 1H); Anal. Calcd for  $\text{C}_{24}\text{H}_{48}\text{O}_3\text{Si}_2$ : C, 65.40; H, 11.0. Found: C, 65.65; H, 10.8.

4.1.1.16. *1,4-Diphenyl-2,3-O-isopropylidene-L-threitol (Substitution of an Alkyl Tosylate with Lithium Diphenylcuprate)* (570)

To a solution of 3.0 g of cuprous iodide in 10 mL of dry ether, stirred at  $0^{\circ}$  under dry argon, was added dropwise 20 mL of 2.1 M phenyllithium solution in 75% benzene/25% hexane. A solution of 1.93 g of



2,3-*O*-isopropylidene-L-threitol ditosylate in 12 mL of ether and 3 mL of tetrahydrofuran was added dropwise to the resulting green solution and the mixture was stirred at 25° for 2 hours. Saturated aqueous ammonium chloride was added and the volatile solvents were removed under reduced pressure. The aqueous residue was extracted with several portions of ether, and the extracts were washed with saturated brine solution, dried, and concentrated. The yellow oily residue was chromatographed on 20 g of silica gel, eluting first with hexane to remove biphenyl, then with hexane–ethyl acetate (3:1) to elute the product. Distillation at 140° (0.1 mm) yielded 650 mg (47%) of the colorless product; IR (neat): 3080, 3060, 3010, 2940, 2880, 1620, 1500, 1460, 1380, 1370, 1240, 1215, 1160, 1075, 1050, 750, 695 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ : 1.4 (s, 6H), 2.8 (m, 4H), 4.0 (m, 2H), 7.25 (s, 10H).

*4.1.1.17. 1-Chloro-4-cyclopropylbutane (Selective Coupling of a Dihaloalkane with Lithium Dicyclopropylcuprate) (281)*

A solution of 1:1 M cyclopropyllithium in ether (660 mL) was added over 45 minutes at –35° to a slurry of 73 g (0.38 mol) of cuprous iodide in 660 mL of tetrahydrofuran. After a Gilman test was negative, 1-bromo-4-chlorobutane (54 g, 0.32 mol) was rapidly added to the mixture which was held at –35° for 1.5 hours. Aqueous saturated ammonium sulfate was then added and the mixture was filtered. The product was extracted with 2 L of ether–pentane (1:1). The organic layer was washed several times with water, then with brine. After drying over calcium sulfate, the extract was distilled through a 45-cm Vigreux column to remove solvents. The pot residue was then short-path distilled to yield 37.4 g (90%) of the product, bp 58–59° (17 mm); IR (neat): 3084, 3008, 2941, 2864, 1024 cm<sup>-1</sup>; <sup>1</sup>H NMR (CCl<sub>4</sub>) δ : 3.48 (t, 2H, *J* = 6 Hz); mass spectrum (70 ev): *m/z* 55 (base).

*4.1.1.18. 1-(2-Deuterio-1-phenylethenyl)naphthalene (Substitution of a Vinyl Bromide with Lithium Diphenylcuprate) (571)*

Lithium diphenylcuprate was prepared at 0° by slowly adding 25 mL of 1.86 M (46.5 mmol) phenyllithium solution to a suspension of 5.03 g (24.4 mmol) of cuprous bromide–dimethyl sulfide complex in 20 mL of dry ether. A yellow precipitate formed initially which changed to a homogeneous green solution after complete addition. After 40 minutes at 0°, a solution of 1.36 g (5.81 mmol) of 1-(1-bromo-2-deuterioethenyl)naphthalene (*E:Z* = 4.1) in 3 mL of dry ether was then added. After 4.5 hours at 0°, the reaction mixture was poured into aqueous saturated ammonium chloride solution (pH 9 by addition of ammonium hydroxide), and this was stirred for 1.5 hours. The ether layer was separated, washed twice with brine, and then dried. Removal of solvent afforded a light yellow oil which was purified by short-path distillation, collecting the fraction with bp 124–134° (1 mm). The yield was 0.80 g (60%) of the product which was crystallized from methanol, mp 57.5–58.5°; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ : 5.36 (s, 0.2H), 5.93 (s, 0.8H), 6.8–7.9 (m, 12H); the *Z* isomer predominated 4:1.

4.1.1.19. *4-tert-Butyl-1-methylcyclohexene (Substitution of a Vinyl Trifluoromethanesulfonate with Lithium Dimethylcuprate) (286)*

A solution of 2.0 M methyllithium in hexane (5.5 mL, 10.8 mmol) was added to a stirred slurry of cuprous iodide (1.43 g, 7.5 mmol) in 15 mL of tetrahydrofuran at 0°. A solution of 1-trifluoromethanesulfonyloxy-4-*tert*-butylcyclohexene in 5 mL of tetrahydrofuran was added, and the reaction mixture was stirred at -15° for 12 hours. It was then diluted with hexane, filtered through a pad of Florisil, and concentrated on the rotary evaporator. Chromatography of the residue on silica gel provided the product (250 mg, 75%); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ : 5.38 (m, 1H), 1.87 (m, 4H), 1.63 (s, 3H), 1.25 (m, 3H), 0.84 (s, 9H).

4.1.1.20. *Methyl*

*c-6-Benzyloxy-t-2-hydroxy-1,c-3-dimethylcyclohexane-r-1-carboxylate (Opening of an Epoxide with Lithium Dimethylcuprate) (572)*

To a solution of lithium dimethylcuprate (from 6.4 mL of 0.75 M methyllithium and 490 mg of cuprous iodide) in ether under nitrogen at 0° was added methyl *c-6-benzyloxy-t-2,3-epoxy-1-methylcyclohexane-r-1-carboxylate* in ether and the mixture was stirred at 20° for 18 hours. Addition of saturated aqueous ammonium chloride and extraction with ether gave the product as a colorless oil (125 mg, 85%); IR (film): 3560, 1720, 1270, 1060 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ : 1.05 (d, 3H, *J* = 6 Hz), 1.20 (s, 3H), 1.46–1.89 (m, 5H), 2.99 (d, 1H, *J* = 2.9 Hz), 3.64 (s, 3H), 3.87 (m, 1H), 3.98 (dd, 1H, *J* = 2.9, 10.7 Hz), 4.28 (d, 1H, *J* = 11.7 Hz), 4.52 (d, 1H, *J* = 11.7 Hz), 7.28 (m, 5H).

4.1.1.21. *1-Hydroxymethyl-2-isopropyl-3-methylcyclohexene (S<sub>N</sub>2 Substitution of a Vinyl Epoxide with Lithium Dimethylcuprate) (573)*

To a stirred suspension of 2.8 g (15.0 mmol) of cuprous iodide in 45 mL of dry ether cooled to 0° was added dropwise 16.5 mL (30.0 mmol) of methyllithium. After 5 minutes, 850 mg (5.6 mmol) of *cis-(E)-1-epoxy-2-ethylidene-3-methylcyclohexane* was added in 9 mL of ether. After being stirred at 0° for 30 minutes, the reaction mixture was poured into saturated aqueous ammonium chloride solution containing ammonium hydroxide (pH 9). After the mixture was stirred for 10 minutes, the layers were separated, the aqueous layer was extracted with ether, and the organic layers were combined, washed with water, dried, and concentrated *in vacuo*. The residue was distilled (Kugelrohr) to give 810 mg (86%) of the product as a colorless oil, bp 60° (0.02 mm); IR (CCl<sub>4</sub>): 3615, 3572–3200 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ : 4.11 (M, 2H), 2.79 (septet, 1H, *J* = 7 Hz), 2.30 (m, 1H), 2.10 (m, 2H), 1.73–1.36 (br m, 5H), 1.09–1.04 (br m, 9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ : 144.42, 129.03, 62.59, 31.03, 30.37, 29.38, 27.83, 22.99, 21.33, 20.91, 17.60; Anal. Calcd for C<sub>11</sub>H<sub>20</sub>O: C, 78.51; H, 11.98. Found: C, 78.36; H, 12.01.

4.1.1.22. *(S)-(+)-1,3-Di-n-butylallene (Substitution of a Propargylic Carbamate with Lithium Dibutylcuprate) (340)*

To a solution of lithium dibutylcuprate (3.5 mmol) in ether (15 mL), at  $-78^{\circ}$  was added an ethereal solution (25 mL) of 1.04 g (3.5 mmol) of (*R,R*)-3-[*N*-2-(1-naphthyl)ethylcarbamyloxy]hept-1-yne over 10 minutes. After being stirred for an additional 7 hours at  $-78^{\circ}$ , it was allowed to come to  $0^{\circ}$ , quenched with aqueous saturated ammonium chloride solution (20 mL), and stirred for 15 minutes. The mixture was filtered and the organic layer was separated, washed with aqueous saturated ammonium chloride solution (20 mL), dried over magnesium sulfate, and concentrated under reduced pressure. Molecular distillation of the residue afforded 0.4 g (76%) of the product;  $[\alpha]_{\text{D}}^{25} + 54.5^{\circ}$  (3.6,  $\text{CHCl}_3$ ); IR (film):  $1945\text{ cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CCl}_4$ )  $\delta$ : 0.9 (t, 6H), 1.3 (m, 8H), 1.95 (m, 4H), 4.95 (quintet, 2H).

*4.1.1.23. 2-Methyl-6-(3-oxobutyl)cyclohexanone Dimethylhydrazone (Conjugate Addition of the Cuprate Derived from an  $\alpha$ -Lithiocyclohexanone Dimethylhydrazone to an  $\alpha,\beta$ -Unsaturated Ketone) 357b*

A precooled (ca.  $-30^{\circ}$ ) clear solution of 0.96 g (5 mmol) of cuprous iodide in 2.88 mL (20 mmol) of diisopropyl sulfide and 10 mL of tetrahydrofuran was added dropwise with stirring at  $-78^{\circ}$  to a suspension of 6-lithio-2-methylcyclohexanone dimethylhydrazone [5 mmol, generated from 1.54 g (10 mmol) of 2-methylcyclohexanone dimethylhydrazone and lithium diisopropylamide (10 mmol)] in 40 mL of tetrahydrofuran. The lithium compound dissolved during warming of the orange reaction mixture from  $-78^{\circ}$  to  $-20^{\circ}$  over 30 minutes and from  $-20^{\circ}$  to  $0^{\circ}$  over 10 minutes, resulting in a clear golden yellow solution. It was cooled again to  $-78^{\circ}$ , and 0.41 mL (5 mmol) of methyl vinyl ketone was added dropwise. After 2 hours, the reaction was slowly warmed to room temperature over a period of 12 hours. The black-brown reaction mixture was poured into a mixture of saturated ammonium chloride containing ammonium hydroxide (pH 8) and repeatedly extracted with methylene chloride. The organic phase was shaken several times with ammonium chloride-ammonium hydroxide solution until the aqueous phase was no longer blue. The combined aqueous phase was again extracted with methylene chloride, and the combined organic phases were then dried over sodium sulfate. After removal of the solvent in a rotary evaporator, the crude product (1.19 g, spectroscopic yield 100%) was purified by distillation to give 0.42 g (85%) of a light-yellow oil, bp  $100^{\circ}$  (0.05 mm).

*4.1.1.24. 3-(cis-2-Ethoxyethenyl)cyclohexanone [Conjugate Addition of Lithium Di-(cis-2-ethoxyethenyl)cuprate to an  $\alpha,\beta$ -Unsaturated Ketone] (574)*

A solution of *cis*-2-ethoxyvinyl lithium was prepared from 2.18 g (6.04 mmol) of *cis*-1-ethoxy-2-tri-*n*-butylstannylethylene and *n*-butyllithium (1.1 equivalent) in 15 mL of tetrahydrofuran at  $-78^{\circ}$  over 1 hour. A solution of 0.577 g (3.03 mmol) of purified cuprous iodide and 0.89 mL (12.1 mmol) of dimethyl sulfide in 5 mL of tetrahydrofuran was then added over 5 minutes. After stirring for 1 hour at  $-78^{\circ}$ , 0.264 g (2.75 mmol) of cyclohexenone in 5 mL of tetrahydrofuran was

added over 10 minutes. After stirring for 1 hour, the mixture was warmed to  $-40^{\circ}$  during 30 minutes, quenched with aqueous 20% ammonium chloride solution, and extracted with ether. The product was purified by column chromatography (silica gel, chloroform) to afford 0.379 g (82%) of the desired product; IR (film): 1715, 1668, 1125  $\text{cm}^{-1}$ ;  $^1\text{H NMR } \delta$  : 5.93 (d, 1H,  $J = 6$  Hz), 4.28 (dd, 1H,  $J = 6, 9$  Hz), 3.78 (q, 2H,  $J = 7$  Hz), 1.42–3.30 (br m, 9H), 1.22 (t, 3H,  $J = 7$  Hz); Anal. Calcd for  $\text{C}_{10}\text{H}_{16}\text{O}_2$ ; C, 71.39; H, 9.59. Found: C, 71.78; H, 9.79.

*4.1.1.25. 3-Dimethylphenylsilyl-3,5,5-trimethylcyclohexanone [Conjugate Addition of Lithium Di-(dimethylphenylsilyl)cuprate to an  $\alpha, \beta$ -Unsaturated Ketone] (575)*

Dimethylphenylchlorosilane (3.4 g, 2 mmol), lithium shot (100 mg, 14 mmol), and dry tetrahydrofuran (35 mL) were stirred under nitrogen for 18 hours. The resulting red solution was titrated to determine its concentration and used without further purification. A tetrahydrofuran solution of the above reagent (1 mmol) was added to cuprous iodide (95 mg, 0.5 mmol) at  $-23^{\circ}$  under nitrogen and the mixture stirred at this temperature for 4 hours. Then 3,5,5-trimethylcyclohexanone (0.5 mmol) was added, and the mixture was stirred at  $-23^{\circ}$  for a further 30 minutes, poured onto a mixture of ice (25 g) and hydrochloric acid (5 mL), and extracted with chloroform ( $3 \times 25$  mL). The extracts were filtered and washed with 3 M hydrochloric acid (25 mL), water (25 mL), saturated sodium hydrogen carbonate solution (25 mL), and water (25 mL) and dried over sodium sulfate. Evaporation in vacuo followed by preparative TLC [silica gel, ether/light petroleum (3:7),  $R_f$  value 0.4] gave the product (68% yield) as prisms (from ethanol), mp  $60^{\circ}$ ; IR ( $\text{CCl}_4$ ): 1710 ( $\text{C} = \text{O}$ )  $\text{cm}^{-1}$ ;  $^1\text{H NMR } (\text{CCl}_4) \delta$  : 7.6–7.3 (m, 5H), 2.5–1.3 (m, 6H), 1.16 (s, 3H), 1.10 (s, 3H), 1.05 (s, 3H), 0.38 (s, 6H); mass spectrum:  $m/z$  274 (10,  $\text{M}^+$ ), 273 (10), 259 (100), 135 (60).

*4.1.1.26. Methyl 3-Phenylbutanoate [Conjugate Addition of Lithium Methyl(2-thienyl)cuprate to an  $\alpha, \beta$ -Unsaturated Ester in the Presence of Chlorotrimethylsilane] 78a*

*n*-Butyllithium (2.5 mmol) was added to a solution of thiophene (3 mmol) in ether (5 mL) at  $0^{\circ}$  and the solution was warmed to and stirred at room temperature for at least 40 minutes. Then another 2.5 mL of ether was added, the mixture was cooled in an ice bath, and finally powdered cuprous iodide (2.5 mmol) was added. Then the mixture was stirred until the Gilman test for free alkylolithium was negative (about 5 minutes). The color of the cuprate solution was either yellow or light green. The reaction mixture was then cooled to about  $-50^{\circ}$  and methyl cinnamate (2 mmol) in ether (2.5 mL) was added. The addition resulted in a shiny yellow color. Within 1 minute from the substrate addition, chlorotrimethylsilane (5 mmol) was added. The temperature was allowed to rise to  $0^{\circ}$  and the reaction was followed by GLC. The reaction mixture was hydrolyzed by addition of aqueous ammonium

chloride–aqueous ammonia mixture (pH 8) and extracted with ether. The crude product dissolved in pentane was chromatographed through silica gel in order to remove trimethylsilylthiophene and was then eluted with ether to obtain 0.268 g (75%) of the product; bp 133–135° (22 mm).

4.1.1.27. *(SR,1S,2R,2 $\phi$ S)-N-(1-Methoxy-1-phenyl-2-propyl)-S-phenyl-S-(2 $\phi$ -methyl-1 $\phi$ -hexyl)sulfoximine (Asymmetric Conjugate Addition of Methylcopper to a Chiral Vinyl Sulfoximine) (452)*

To a stirred suspension of cuprous iodide (486 mg, 2.56 mmol) in ether (12.8 mL) at –25° was added methylolithium (2.56 mmol). After 30 minutes, *(SR,1S,2R)-N-(1-methoxy-1-phenyl-2-propyl)-S-(1-hexenyl)-S-phenylsulfoximine* (190 mg, 0.511 mmol) in ether (2 mL) was added, and the mixture was stirred at –25° for 1 hour. It was then allowed to warm to 0° over a period of 1 hour and after an additional 1 hour at 0°, the reaction was quenched with aqueous ammonium chloride (20 mL). The layers were separated and the ether layer dried and concentrated. Analysis of the crude reaction mixture by HPLC indicated two compounds with retention volumes 2.9 and 3.4 in a ratio of 3.5 to 96.5, respectively. Purification of the crude material by preparative TLC [ethyl acetate/hexane (2.3)] gave the product as a colorless oil; <sup>1</sup>H NMR  $\delta$  : 7.70–7.01 (m, 10H), 3.90 (d, 1H,  $J$  = 7.6 Hz); 3.32–2.89 (m, 2H), 3.20 (s, 3H), 2.73 (dd, 1H,  $J$  = 7.6, 14.2 Hz), 2.02 (m, 1H), 1.54–1.0 (m, 6H), 1.32 (d, 3H,  $J$  = 5.9 Hz), 0.86 (t, 3H), 0.77 (d, 3H,  $J$  = 6.8 Hz); <sup>13</sup>C NMR  $\delta$  : 141.22, 138.86, 131.95, 129.15, 128.76, 128.13, 127.62, 127.08, 89.24, 63.45, 57.11, 56.13, 36.35, 28.47, 28.28, 22.51, 21.83, 19.89, 13.95; mass spectrum (chemical ionization, methane):  $m/e$  388 (18, M<sup>+</sup> + 1), 356 (22), 266 (79), 125 (100).

4.1.1.28. *3-[(E)-3-(Tetrahydropyran-2-yloxy)-1-octenyl]cyclopentanone (Conjugate Addition of an Organocopper to an  $\alpha$ ,  $\beta$ -Unsaturated Ketone in the Presence of Tri-*n*-butylphosphine) (468)*

Cuprous iodide (300 mg, 1.57 mmol) was placed in a 180-mL ampule equipped with a rubber septum. After the atmosphere was replaced by argon, dry tetrahydrofuran (20 mL) followed by tri-*n*-butylphosphine (1.02 mL, 4.10 mmol) were added at room temperature. The suspension was stirred until a clear solution resulted. In a 30-mL test tube equipped with a rubber septum were placed (*E*)-1-iodo-3-tetrahydropyran-2-yloxyoctene (528 mg, 1.56 mmol) and dry ether (6 mL). After cooling to –95°, *tert*-butyllithium (1.68 mL, 3.12 mmol) in pentane was added to this solution with stirring over 1 minute. The mixture was stirred at –78° for 2 hours. The resulting white suspension was added at –78°, with stirring, to the above prepared ethereal solution of the cuprous iodide–phosphine complex through a stainless-steel cannula under a slight argon pressure. After the mixture was stirred at –78° for 10 minutes, to this solution was then added slowly, along the cooled wall of the reaction vessel, a solution of cyclopentenone (103 mg, 1.25 mmol) in cold (–78°) tetrahydrofuran (10 mL) through a stainless-steel cannula under a slight argon pressure over 50 minutes. The mixture was stirred at –78° for 1 hour. A

saturated aqueous solution of ammonium chloride (15 mL) was added at  $-78^{\circ}$  and the mixture shaken vigorously. The organic layer was separated and the aqueous layer extracted with ether (30 mL). The combined extracts were dried over magnesium sulfate, evaporated, and chromatographed on triethylamine-treated silica gel (30 g) using 2000:100:1 hexane–ethyl acetate–triethylamine mixture as eluent to give the 1, 4 adduct (310 mg, 84%, mixture of diastereomers) as a colorless oil; IR (neat):  $1741$  ( $C = O$ ) $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CCl}_4$ )  $\delta$ : 0.90 (t, 3H,  $J = 6.5$  Hz), 1.1–3.1 (m, 21H), 3.3–3.7 (m, 1H), 3.7–4.2 (m, 2H), 4.65 (br s, 1H), 5.2–5.8 (m, 2H); mass spectrum,  $m/z$  calculated for  $\text{C}_{13}\text{H}_{19}\text{O}_3(\text{M}^+ - \text{C}_5\text{H}_{11})$ : 223.13464. Found 223.13404.

*4.1.1.29. (2S-(–)-Benzyl 2-Hydroxypent-4-enyl Ether [Opening of a Chiral Epoxide with Dilithium (2-Thienyl)vinylcyanocuprate] 496b*

Thiophene (88  $\mu\text{L}$ , 1.1 mmole) was added to tetrahydrofuran (1 mL), at  $-78^{\circ}$ , followed by *n*-butyllithium (0.39 mL, 1.1 mmol). The cooling bath was removed and the temperature raised to  $0^{\circ}$  over 5 minutes and stirred for an additional 30 minutes. The faint yellow anion was then transferred via cannula into a two-neck flask containing cuprous cyanide (89.6 mg, 1 mmol) and tetrahydrofuran (1 mL), which was previously purged with argon and cooled to  $-78^{\circ}$ . Warming to  $0^{\circ}$  produced a light tan solution which was cooled to  $-78^{\circ}$  and vinylolithium (0.5 mL, 1 mmol) was injected, with immediate warming to  $0^{\circ}$  (no visible change). It was then cooled to  $-78^{\circ}$  and to it was added via cannula a precooled solution of (2S)-benzyl 2-epoxypropyl ether (149 mg, 0.91 mmol) in tetrahydrofuran (1 mL). After 2.5 hours at  $0^{\circ}$ , the reaction was quenched with 5 mL of a 90% saturated ammonium chloride–concentrated ammonium hydroxide solution, extracted with ether ( $2 \times 10$  mL) and dried over sodium sulfate. Concentration, followed by chromatography on silica gel (230–400 mesh) with ether/Skelly Solve (2:3) afforded 141 mg (92%) of a clear liquid, bp  $90^{\circ}$  (0.1 mm);  $R_f$ : 0.33 (1/1 ether/Skelly Solve);  $[\alpha]_D - 2.2^{\circ}$  (c 3, chloroform); IR (neat): 3400, 3070, 3030, 1640, 1100, 740, 700  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 7.33 (s, 5H), 5.90–5.75 (m, 1H), 5.1 (M, 2H), 4.55 (s, 2H), 3.90 (m, 1H), 3.6–3.4 (m, 2H), 2.41 (d, 1H,  $J = 3.3$  Hz), 2.26 (t, 2H,  $J = 6.9$  Hz); mass spectrum,  $m/e$  192 ( $\text{M}^+$ , 1), 92 (25), 91 (100);  $m/z$  calculated for  $\text{C}_{12}\text{H}_{16}\text{O}_2$ : 192.1150. Found: 192.1161.

*4.1.1.30. 3-Vinylcyclopentanone (Conjugate Addition of Dilithium Divinylcyanocuprate to an  $\alpha$ ,  $\beta$ -Unsaturated Ketone) (499)*

Cuprous cyanide (89 mg, 1 mmol) was placed in a dry two-necked flask containing a serum cap and a T-joint with access to argon and a vacuum. It was evacuated and flushed with argon 4–5 times and left under a static argon pressure. Dry tetrahydrofuran (2 mL) was introduced and the slurry cooled to  $-78^{\circ}$ , to which was added vinylolithium (0.96 mL, 2.0 mmol) and the mixture warmed to  $0^{\circ}$ . It was recooled to  $-78^{\circ}$  and cyclopentanone (75  $\mu\text{L}$ , 0.9 mmol) was added. After 45 minutes at  $-78^{\circ}$ , the reaction was quenched with 10% ammonium hydroxide in saturated aqueous ammonium chloride solution,

stirred at room temperature for 30 minutes, and extracted with ether. Analysis by VPC indicated formation of the product in 93% yield against 3-methylcyclopentanone as internal standard; IR (neat): 1740, 990, 910  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (  $\text{CDCl}_3$ )  $\delta$  : 1.5–3.0 (m, 7H), 5.1 (m, 2H), 5.8 (m, 1H); high resolution mass spectrum,  $m/z$  calculated for  $\text{C}_7\text{H}_{10}\text{O}$ : 110.0732. Found: 110.0733.

*4.1.1.31. 3-Butyl-3,5,5-trimethylcyclohexanone [Conjugate Addition of Dilithium *n*-Butyl(methylsulfoxymethyl)cyanocuprate to an  $\alpha$ ,  $\beta$ -Unsaturated Ketone] (273)*

The lithio anion of dimethyl sulfoxide was generated as a 0.2 M solution in tetrahydrofuran by treatment of dimethyl sulfoxide with *n*-butyllithium (1 equivalent) at  $0^\circ$  for 15 minutes. This was then transferred to a slurry of cuprous cyanide (1 equivalent) in tetrahydrofuran at  $-78^\circ$  via cannula. The mixture was warmed to  $0^\circ$ , resulting in a light green slurry which was recooled to  $-78^\circ$ , and *n*-butyllithium (1 equivalent) was added and allowed to warm to  $0^\circ$  to ensure cuprate formation. It was then cooled to  $-78^\circ$  and a solution of 3,5,5-trimethylcyclohexen-1-one (0.45 equivalent) in tetrahydrofuran was added via syringe. After 3 hours at  $-78^\circ$  and an additional 1 hour at  $0^\circ$ , the reaction was quenched with a saturated ammonium chloride solution containing 10% ammonium hydroxide. After stirring for 15 minutes, it was suction filtered through Celite; the filter cake was washed with ether and the aqueous phase extracted with more ether. Analysis of the combined organic phases by VPC showed the product had formed in 95% yield;  $^1\text{H}$  NMR (  $\text{CDCl}_3$ )  $\delta$  : 2.19–2.08 (m, 4H), 1.59 (t, 2H,  $J = 15$  Hz), 1.49 (d, 2H,  $J = 14$  Hz), 1.26–1.21 (m, 4H), 1.03 (s, 3H), 1.02 (s, 3H), 0.98 (s, 3H), 0.88 (t, 3H,  $J = 7$  Hz).

## 5. Tabular Survey

Tables I–XI are organized in the sequence used in the Scope and Limitations section. Literature coverage from 1976 through 1987 is as exhaustive as possible, using both computer scanning services and hand searches. Many 1988 references are also included, although coverage for that year is not complete. In addition, some selected references for the period 1989–1991 were inserted during the proof stage. Citations for which critical data such as conditions and yields are missing are not included. Unspecified conditions are indicated by—, and unspecified yields are indicated by (—).

Tables I–X are ordered by increasing carbon number of the basic structural unit of the educt, omitting the carbon count of, for example, protecting groups or the alcohol portion of a carboxylic ester. Table XI provides examples of the use of copper reagents in the synthesis of a target structure (or analog) of a natural product. Entries in each subtable of Table XI are arranged by target molecule in alphabetical order, with the following exception. When essentially identical chemistry was used for two or more different target molecules, only one set of structures is given, and the other target molecules (not in alphabetical order) are listed with the pertinent references, but without conditions or structures.

Abbreviations used in all tables are as follows:

Ac	acetyl
acac	acetylacetonate
Bn	benzyl
BT	benzothiazol-2-yl
COD	1,5-cyclooctadienyl
Cp	cyclopentadienyl
diglyme	diethylene glycol dimethyl ether
DMA	<i>N,N</i> -dimethylacetamide
DMAP	<i>p-N,N</i> -dimethylaminopyridine
DME	1,2-dimethoxyethane
DMPU	<i>N,N</i> ¢-dimethylpropyleneurea
DMS	dimethyl sulfide
ether or Et <sub>2</sub> O	diethyl ether
EE	ethoxyethyl, C <sub>2</sub> H <sub>5</sub> OCH(CH <sub>3</sub> ) —
HMPA	hexamethylphosphoric triamide
HMPT	hexamethylphosphorous triamide



LDA	lithium diisopropylamide
MOM	methoxymethyl
MPTP	$C_6H_5N(CH_3)P^+(C_6H_5)_3I^-$
Ms	methanesulfonyl
NBS	<i>N</i> -bromosuccinimide
NCS	<i>N</i> -chlorosuccinimide
PPTS	pyridinium <i>p</i> -toluenesulfonate
Py	pyridine
TBDMS	<i>tert</i> -butyldimethylsilyl
Tf	trifluoromethylsulfonyl
THF	tetrahydrofuran
THP	tetrahydropyranyl
TMEDA	<i>N,N,N',N'</i> -tetramethylethylenediamine
TMS	trimethylsilyl
Ts	<i>p</i> -toluenesulfonyl
xs	excess

Copper reagents used with the Grignard reagent in Tables I–III are as follows:

- A  $Li_2CuCl_4$
- B  $CuCl$
- C  $CuBr$
- D  $CuI$
- E  $CuBr \cdot (CH_3)_2S$
- F  $CuCl_2 \cdot P(C_6H_5)_3$
- G  $CuCN$
- H  $Cu(acac)_2$
- I  $CuBr \cdot LiBr$

**Table I. Copper-Catalyzed Reactions of Grignard Reagents**

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**Table II. Substitution and Conjugate Addition Reactions of Stoichiometric Cu(I)-RMgX Reagents**

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**Table III. Carbocupration Reactions of Stoichiometric Cu(I)-RMgX Reagents**

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**Table IV. Substitution Reactions of Lower-Order Lithioorganocuprates**

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**Table V. Carbocupration Reactions of Lower-Order Lithioorganocuprates**

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**Table VI. Conjugate Addition Reactions of Lower-Order Lithioorganocuprates**

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**Table VII. Substitution Reactions of Organocopper Reagents, RCu**

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**Table VIII. Reactions of RCu in the Presence of Additives**

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**Table IX. Reactions of Higher-Order Cuprates**

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**Table X. Reactions of Other Organocopper Species**

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**Table XI. Organocopper Compounds in Synthesis of Natural Products**

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TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS

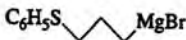

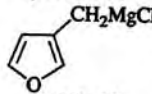
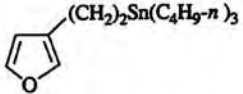
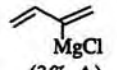
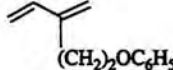
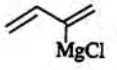
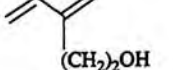
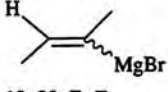
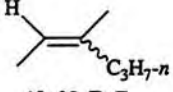
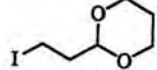
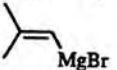
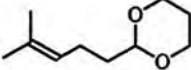
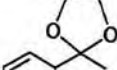
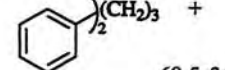
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
A. Reactions of Alkyl/Alkenyl Halides and Sulfonates				
C <sub>1</sub>				
CD <sub>3</sub> I	 (0.01% A)	THF, 20°, 30 min	 (57)	576
( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>3</sub> SnCH <sub>2</sub> I	 (0.4% A)	THF, 0°, 5 min	 (95)	99
C <sub>2</sub>				
ClMgO <sub>2</sub> CCH <sub>2</sub> Br	<i>n</i> -C <sub>5</sub> H <sub>11</sub> MgBr (4% A)	THF, -20°	<i>n</i> -C <sub>6</sub> H <sub>13</sub> CO <sub>2</sub> H + HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H (26) (40)	103
Br(CH <sub>2</sub> ) <sub>2</sub> O <sub>2</sub> CCH <sub>3</sub>	<i>n</i> -C <sub>7</sub> H <sub>15</sub> MgCl (5% C)	THF, (C <sub>2</sub> H <sub>5</sub> O) <sub>3</sub> P, -25°	<i>n</i> -C <sub>9</sub> H <sub>19</sub> O <sub>2</sub> CCH <sub>3</sub> (75)	101
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (5% C)	THF, (C <sub>2</sub> H <sub>5</sub> O) <sub>3</sub> P, -25°	<i>i</i> -C <sub>3</sub> H <sub>7</sub> CH <sub>2</sub> CH <sub>2</sub> O <sub>2</sub> CCH <sub>3</sub> (53)	101
Br(CH <sub>2</sub> ) <sub>2</sub> OC <sub>2</sub> H <sub>5</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (5% D)	THF, -10°, 4 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> OC <sub>2</sub> H <sub>5</sub> (76)	101
	C <sub>6</sub> H <sub>11</sub> MgCl (5% D)	THF, -25°, 12 h	C <sub>6</sub> H <sub>11</sub> (CH <sub>2</sub> ) <sub>2</sub> OC <sub>2</sub> H <sub>5</sub> (48)	101
Br(CH <sub>2</sub> ) <sub>2</sub> OC <sub>6</sub> H <sub>5</sub>	 (3% A)	THF, 65°, 3 h	 (78)	98
Br(CH <sub>2</sub> ) <sub>2</sub> OH	C <sub>6</sub> H <sub>11</sub> MgCl (3 eq) (5% C)	THF, (C <sub>2</sub> H <sub>5</sub> O) <sub>3</sub> P, 15°, 1 h	C <sub>6</sub> H <sub>11</sub> (CH <sub>2</sub> ) <sub>2</sub> OH (78)	101
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (3 eq) (5% C)	THF, (C <sub>2</sub> H <sub>5</sub> O) <sub>3</sub> P, -15°, 0.5 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> (CH <sub>2</sub> ) <sub>2</sub> OH (56)	101
I(CH <sub>2</sub> ) <sub>2</sub> OH	 (2 eq) (3% A)	THF, 65°, 2 h	 (75)	98
C <sub>3</sub>				
ClMgO <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> Br	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub> MgBr (4% A)	THF, -20°	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>4</sub> CO <sub>2</sub> H (77)	103
<i>n</i> -C <sub>3</sub> H <sub>7</sub> I	 10:90 <i>E</i> : <i>Z</i> (10% D)	THF, 0°, 1.5 h	 12:88 <i>E</i> : <i>Z</i> (97)	577
Br(CH <sub>2</sub> ) <sub>3</sub> Br	C <sub>6</sub> H <sub>5</sub> MgBr (1 eq) (5% C)	THF:HMPA (12:1), reflux, 4 h	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>3</sub> Br + C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>3</sub> C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>5</sub> 81:16:3 (—)	578
	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> MgBr (3.5 eq) (cat. A)	THF, 20°, 24 h	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> (CH <sub>2</sub> ) <sub>3</sub> C <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub> - <i>p</i> (—)	579
	 (5% D)	THF, 0°, 2 h	 (59)	580
	 (2 eq) (5% C)	THF:HMPA (12:1), reflux, 4 h	 + 60.5:34 (—)	578

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

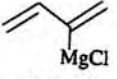
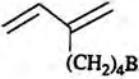
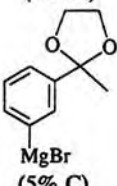
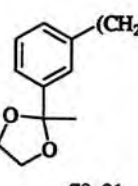
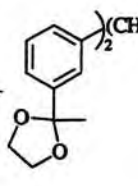
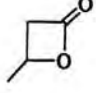
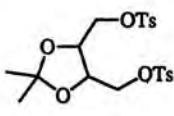
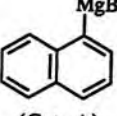
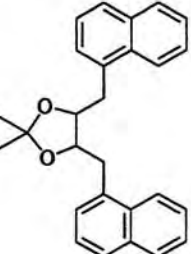
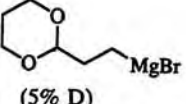
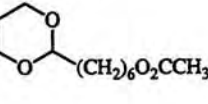
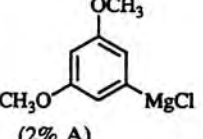
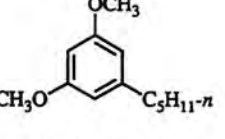
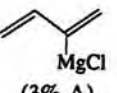
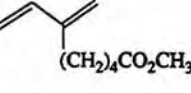
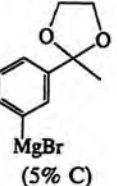
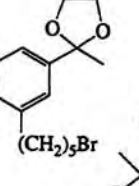
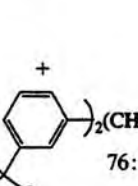
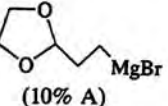
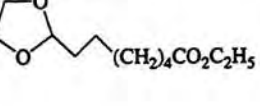
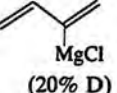
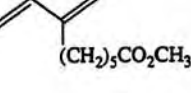
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.	
C <sub>4</sub>	Br(CH <sub>2</sub> ) <sub>4</sub> Br	 (1 eq) (5% A)	THF, 20°, 16 h	 (40)	98
	 (1 eq) MgBr (5% C)	THF:HMPA (12:1), reflux, 4 h	 (CH <sub>2</sub> ) <sub>4</sub> Br +  (CH <sub>2</sub> ) <sub>4</sub>	(—)	578
		ClMgO(CH <sub>2</sub> ) <sub>10</sub> MgCl (5% A)	THF, -10°, 1 h	HO(CH <sub>2</sub> ) <sub>10</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CO <sub>2</sub> H (73)	581
		 (Cat. A)	Ether		(—)
I(CH <sub>2</sub> ) <sub>4</sub> O <sub>2</sub> CCH <sub>3</sub>	 (5% D)	THF, -80° to reflux, 8 h	 (77)	583	
C <sub>5</sub>	n-C <sub>5</sub> H <sub>11</sub> I	 (2% A)	THF, 20°, 16 h	 (66)	567
	C <sub>2</sub> H <sub>5</sub> (CH <sub>3</sub> )C- (OMgCl) CH <sub>2</sub> Br	n-C <sub>4</sub> H <sub>9</sub> MgCl (5% C)	Ether, 10°, 2h	C <sub>2</sub> H <sub>5</sub> (CH <sub>3</sub> )C(OH)C <sub>5</sub> H <sub>11-n</sub> (68)	584
	ClMgO <sub>2</sub> C(CH <sub>2</sub> ) <sub>4</sub> Br	s-C <sub>4</sub> H <sub>9</sub> MgBr (4% A)	THF, -20°	s-C <sub>4</sub> H <sub>9</sub> (CH <sub>2</sub> ) <sub>4</sub> CO <sub>2</sub> H (88)	103
	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>4</sub> I	 (3% A)	THF, 0-20°, 16 h	 (80)	98
	Br(CH <sub>2</sub> ) <sub>5</sub> Br	 (5% C)	(1 eq) THF:HMPA (12:1), reflux, 4 h	 (CH <sub>2</sub> ) <sub>5</sub> Br +  (CH <sub>2</sub> ) <sub>5</sub> 76:18	(—)
C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>4</sub> Br	 (10% A)	THF, -10°, 1.5 h	 (77)	585	
C <sub>6</sub>	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>5</sub> I	 (20% D)	THF, -30 to 0°, 2 h	 (68)	98

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

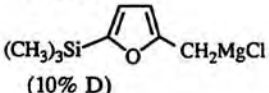
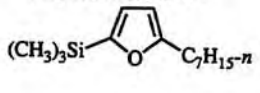
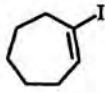
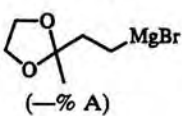
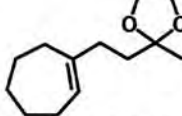
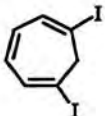
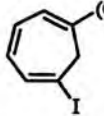
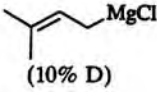
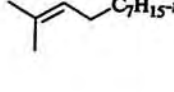
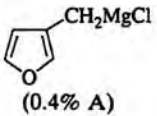
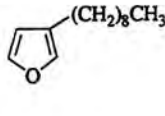
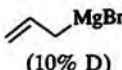
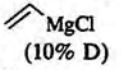
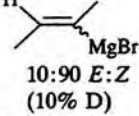
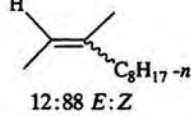
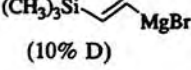
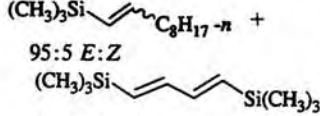
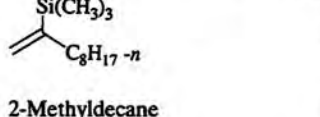
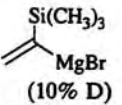
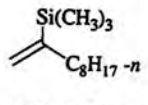
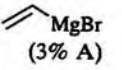
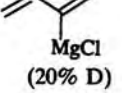
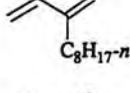
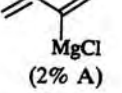
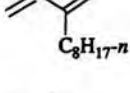
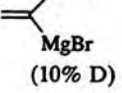
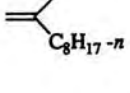
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
Br(CH <sub>2</sub> ) <sub>6</sub> Br	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgBr (1 eq) (5% C)	THF:HMPA (12:1), 25°, 4 h	<i>i</i> -C <sub>3</sub> H <sub>7</sub> (CH <sub>2</sub> ) <sub>6</sub> Br + <i>i</i> -C <sub>3</sub> H <sub>7</sub> (CH <sub>2</sub> ) <sub>6</sub> C <sub>3</sub> H <sub>7</sub> - <i>i</i>	(44) (16) 579
<i>n</i> -C <sub>6</sub> H <sub>13</sub> I	 (10% D)	THF	 C <sub>7</sub> H <sub>15</sub> - <i>n</i>	(70) 586
C <sub>7</sub> C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Cl	<i>i</i> -C <sub>4</sub> H <sub>9</sub> MgCl (0.25% A)	THF, 30°, 2 h	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C <sub>4</sub> H <sub>9</sub> - <i>t</i>	(84) 587
	 (—% A)	THF, 0°, 8 h		(60) 588
	(CH <sub>3</sub> O) <sub>2</sub> CH(CH <sub>2</sub> ) <sub>2</sub> MgBr (1.4 eq) (2% A)	Ether, THF, -20°, 1 h	 (CH <sub>2</sub> ) <sub>2</sub> CH(OCH <sub>3</sub> ) <sub>2</sub>	(60) 589
<i>n</i> -C <sub>7</sub> H <sub>15</sub> X (X = I, Br, OTs)	 (10% D)	THF, 0°, 2 h	 C <sub>7</sub> H <sub>15</sub> - <i>n</i>	(80–90) 106
C <sub>8</sub> 1-Iodooctane	 (0.4% A)	THF, 0°, 5 min	 (CH <sub>2</sub> ) <sub>8</sub> CH <sub>3</sub>	(92) 99
	 (10% D)	Ether, 0°, 1.5 h	1-Undecene	(80) 106
	 (10% D)	THF, 0°, 1.5 h	1-Decene	(82) 577
	 10:90 <i>E</i> : <i>Z</i> (10% D)	THF, 0°, 1.5 h	 C <sub>8</sub> H <sub>17</sub> - <i>n</i>	(96) 577
	(CH <sub>3</sub> ) <sub>3</sub> Si-  (10% D)	THF, 0°, 1 h	(CH <sub>3</sub> ) <sub>3</sub> Si-  C <sub>8</sub> H <sub>17</sub> - <i>n</i> + 95:5 <i>E</i> : <i>Z</i> (CH <sub>3</sub> ) <sub>3</sub> Si-  Si(CH <sub>3</sub> ) <sub>3</sub> (12)	(77) 577
	 (10% D)	THF, 0°, 1 h	 C <sub>8</sub> H <sub>17</sub> - <i>n</i>	(97) 577
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgBr (3% A)	THF, 65°, 2 h	2-Methyldecane	(78) 98
	 (3% A)	THF, 20°, 16 h	1-Decene	(36) 98
	 (20% D)	THF, 0°, 2 h	 C <sub>8</sub> H <sub>17</sub> - <i>n</i>	(60) 98
	 (2% A)	THF, 20°, 16 h	 C <sub>8</sub> H <sub>17</sub> - <i>n</i>	(95) 98
<i>n</i> -C <sub>8</sub> H <sub>17</sub> OTs	 (10% D)	THF, 0°, 3 h	 C <sub>8</sub> H <sub>17</sub> - <i>n</i>	(80) 577

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

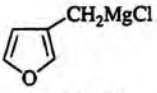
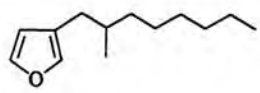
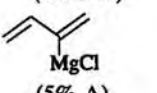
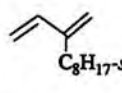
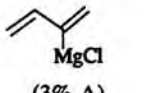
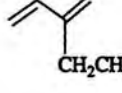
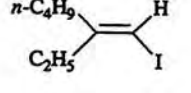
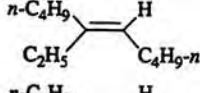
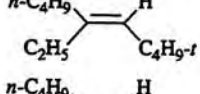
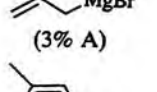
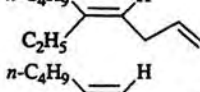
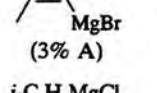
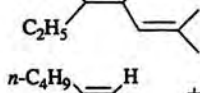
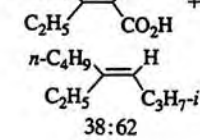
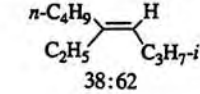
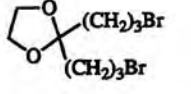
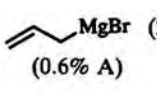
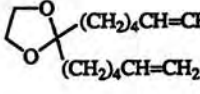
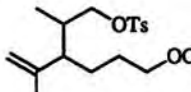
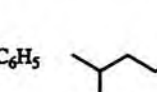
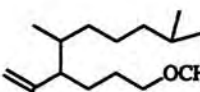
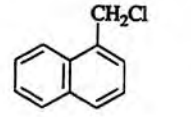
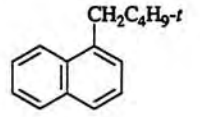
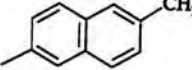
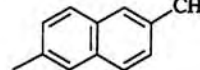
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.	
2-Iodooctane	 (0.4% A)	THF, 0°, 5 min		(89) 99	
	 MgCl (5% A)	THF, 20°, 16 h	 C <sub>8</sub> H <sub>17-s</sub>	(45) 98	
<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CH <sub>2</sub> I	 MgCl (3% A)	THF, 20°, 16 h	 CH <sub>2</sub> CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> Br- <i>p</i>	(87) 98	
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (3% A)	THF, -20°		(70) 107	
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (3% A)	THF, -20°		(70) 107	
	 MgBr (3% A)	THF, -20°		(70) 107	
	 MgBr (3% A)	THF, -20°		(50) 107	
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (5% A)	THF, -20°, 0.5 h, then CO <sub>2</sub> , H <sup>+</sup>	 +  38:62	(—) 107	
C <sub>9</sub>	 (CH <sub>2</sub> ) <sub>3</sub> Br (CH <sub>2</sub> ) <sub>3</sub> Br	 MgBr (2 eq) (0.6% A)	THF, 0°, 3 h	 (CH <sub>2</sub> ) <sub>4</sub> CH=CH <sub>2</sub> (CH <sub>2</sub> ) <sub>4</sub> CH=CH <sub>2</sub>	(—) 100
C <sub>10</sub>	 OTs OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	 MgBr (3% A)	Ether, THF, 20°, 6 h	 OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	(85) 590
C <sub>11</sub>	<i>n</i> -C <sub>10</sub> H <sub>21</sub> CD <sub>2</sub> OTs	C <sub>2</sub> H <sub>5</sub> MgBr (1% A)	THF, 25°, 16 h	<i>n</i> -C <sub>10</sub> H <sub>21</sub> CD <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	(67) 104
	<i>n</i> -C <sub>10</sub> H <sub>21</sub> CD <sub>2</sub> OTs	<i>n</i> -C <sub>10</sub> H <sub>21</sub> MgBr (1% A)	THF, 25°, 16 h	( <i>n</i> -C <sub>10</sub> H <sub>21</sub> ) <sub>2</sub> CD <sub>2</sub>	(83) 104
	ClMgO <sub>2</sub> C(CH <sub>2</sub> ) <sub>10</sub> Br	<i>n</i> -C <sub>5</sub> H <sub>11</sub> MgBr (2% A)	THF, -20°	<i>n</i> -C <sub>15</sub> H <sub>31</sub> CO <sub>2</sub> H	(94) 103
	Br(CH <sub>2</sub> ) <sub>10</sub> CO <sub>2</sub> Na	(CH <sub>3</sub> ) <sub>3</sub> SiO(CH <sub>2</sub> ) <sub>4</sub> MgBr (—% A)	THF, -20°, 2 h	HO(CH <sub>2</sub> ) <sub>14</sub> CO <sub>2</sub> H	(87) 591
		<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (0.25% A)	THF, 30°, 2 h		(86) 587
C <sub>12</sub>	Br(CH <sub>2</sub> ) <sub>12</sub> Br	THPO(CH <sub>2</sub> ) <sub>11</sub> MgBr (2% A)	THF, 20°, 12 h	THPO(CH <sub>2</sub> ) <sub>23</sub> Br	(51) 592
		<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (0.25% A)	THF, 30°, 2 h		(91) 587

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

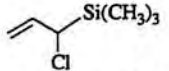
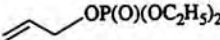
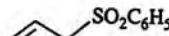
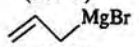
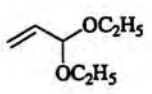



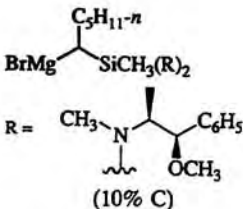
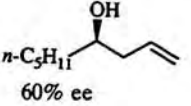



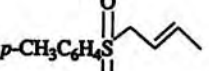
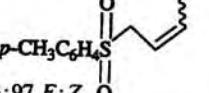
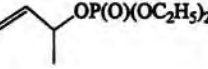
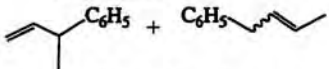
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
<i>B. Reactions of Allylic Substrates</i>				
C <sub>3</sub>				
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (10% D)	THF, 0°, 30 min	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> CH=CHSi(CH <sub>3</sub> ) <sub>3</sub>	(83) 595
	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> MgBr (5% C)	Ether, 0°, 12 h	4-Phenyl-1-butene	(88) 120
	<i>n</i> -C <sub>7</sub> H <sub>15</sub> MgCl (5% C)	Ether, 0°, 12 h	1-Decene	(92) 120
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> C≡CMgCl (5% C)	Ether, 0°, 12 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> C≡C-CH=CH <sub>2</sub>	(78) 120
	C <sub>6</sub> H <sub>5</sub> MgBr (5% H or F or A)	THF, 60°, 4 h	Allylbenzene	(94-96) 119
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (5% F)	THF, 60°, 4 h	1-Heptene	(96) 119
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (5% F)	THF, 60°, 4 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -CH=CH <sub>2</sub>	(52) 119
	 (5% F)	THF, 60°, 4 h	1,5-Hexadiene	(87) 119
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (5% C)	THF, -5°, 2 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -CH=CH-CH <sub>2</sub> CO <sub>2</sub> H <sub>5</sub> 35:65 <i>E</i> : <i>Z</i>	(76) 122
	 (5% C)	THF, -5°, 2 h	 33:65 <i>E</i> : <i>Z</i>	(91) 122
	 (10% C)	1. THF, 0° 2. 6 N HCl, 20°, 6 h 3. 90% H <sub>2</sub> O <sub>2</sub> , KHF <sub>2</sub> , DMF	 <i>n</i> -C <sub>2</sub> H <sub>11</sub> -CH(OH)-CH=CH <sub>2</sub> 60% ee	(51) 594
C <sub>4</sub>				
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (5% C)	THF, -15°, 12 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -CH=CH-CH <sub>2</sub> CO <sub>2</sub> H <sub>5</sub> 24:76 <i>E</i> : <i>Z</i>	(83) 122
	THPO-CH <sub>2</sub> -CH <sub>2</sub> -C≡CMgBr (5% C)	THF, 60°, 1 h, 25°, 36 h	 -C≡C(CH <sub>2</sub> ) <sub>3</sub> OTHP	(67) 595
	C <sub>6</sub> H <sub>5</sub> -CH <sub>2</sub> -CH <sub>2</sub> -MgBr (10% D)	THF, HMPA, -30°, 30 min	C <sub>6</sub> H <sub>5</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH=CH <sub>2</sub> 60:40 <i>E</i> : <i>Z</i>	(78) 596
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (1% H)	THF, 20°, 20 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> -CH=CH <sub>2</sub>	(69) 188
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (1% H)	THF, 20°, 20	<i>n</i> -C <sub>6</sub> H <sub>13</sub> -CH=CH <sub>2</sub> + <i>n</i> -C <sub>6</sub> H <sub>13</sub> -CH=CH <sub>2</sub> 26:74 11:89 <i>E</i> : <i>Z</i>	(40) 118
	C <sub>6</sub> H <sub>5</sub> MgBr (10% D)	Ether, 25°, 12 h	 + C <sub>6</sub> H <sub>5</sub> -CH=CH <sub>2</sub> 10:90 68:32 <i>E</i> : <i>Z</i>	(96) 121



TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$\text{CH}_2=\text{C}=\text{CHCH}_2\text{OP}(\text{O})(\text{OC}_2\text{H}_5)$ $n\text{-C}_6\text{H}_{13}\text{MgBr}$ (10% D)	Ether, 25°, 12 h	 $\text{C}_6\text{H}_{13}\text{-}n$ 6:94 48:52 <i>E:Z</i>	(91) 121
	$\text{CH}_2=\text{C}=\text{CHMgBr}$ (-% D)	Ether, -10°	 $\text{CH}_2=\text{C}=\text{CH}$	(-) 597
	 $\text{MgBr}$ (5% C)	THF, -25°, 1 h	 $\text{CH}_2\text{OH}$	(92) 127
	$\text{MgBr}$ (-% D)	Ether, -78°	 HO HO	(-) 598
			18:82	
	$n\text{-C}_6\text{H}_{13}\text{MgBr}$ (1% H)	THF, 20°, 20 h	$n\text{-C}_6\text{H}_{13}$ + $n\text{-C}_6\text{H}_{13}$ 16:84 40:60 <i>E:Z</i>	(65) 118
	$n\text{-C}_7\text{H}_{15}\text{MgCl}$ (5% C)	THF, 20°, 5 h	 $\text{C}_7\text{H}_{15}\text{-}n$	(85) 123
87:13 <i>E:Z</i>			93:7 <i>E:Z</i>	
	$n\text{-C}_7\text{H}_{15}\text{MgCl}$ (5% C)	THF, 20°, 5 h	 $\text{C}_7\text{H}_{15}\text{-}n$ + $\text{C}_7\text{H}_{15}\text{-}n$	(90) 123
			9:91	
	$n\text{-C}_4\text{H}_9\text{MgCl}$ (2.5% D)	THF, ether, -80°	 $n\text{-C}_4\text{H}_9$	(82) 599
	$\text{C}_6\text{H}_{11}\text{MgCl}$ (2.5% D)	THF, ether, -80°	 $\text{C}_6\text{H}_{11}$	(76) 599
	$t\text{-C}_4\text{H}_9\text{MgCl}$ (2.5% D)	THF, ether, -80°	 $t\text{-C}_4\text{H}_9$	(85) 599
	$n\text{-C}_4\text{H}_9\text{MgCl}$ (5% C)	THF, -15°, 12 h	 $n\text{-C}_4\text{H}_9$	(75) 122
	$n\text{-C}_4\text{H}_9\text{MgCl}$ [5% C, 2P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ]	THF, -15 to 10°, 15 h	 $n\text{-C}_4\text{H}_9$	(66) 122
			45:55 <i>E:Z</i>	
C <sub>4</sub> , C <sub>5</sub>	$\text{R}'\text{R}''\text{C}=\text{C}=\text{C}=\text{CHOCH}_3$ RMgX (10% C) R = $n\text{-C}_4\text{H}_9$ , C <sub>2</sub> H <sub>5</sub> , $i\text{-C}_3\text{H}_7$ , $c\text{-C}_6\text{H}_{11}$ , CH <sub>3</sub> , C <sub>6</sub> H <sub>5</sub>	THF or ether, 35°, 1 h	$\text{R}'\text{R}''\text{C}=\text{C}=\text{C}=\text{CH}$ R	(80-90) 179
R', R'' = H, CH <sub>3</sub>				
C <sub>5</sub>		Ether, 25°, 12 h	 $\text{OCH}_2\text{C}_6\text{H}_5$ 78:22 <i>E:Z</i>	(88) 121
	 $\text{MgCl}$ (10% D)		+ 84:16	
	 $\text{MgBr}$ (10% D)	Ether, 25°, 12 h	 $\text{OCH}_2\text{C}_6\text{H}_5$ + (91)	121
			61:39 <i>E:Z</i>	
			 $\text{OCH}_2\text{C}_6\text{H}_5$	
			95:5	

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	 (2 eq) (10% D)	THF, -50 to 25° 4 h		(60) 106
	 (5% D)	THF, -15°, 1.5 h	 96:4 E:Z	(79) 127
				(19)
	 (5% C)	THF, -25°, 1 h	 92:8 E:Z	(90) 127
	CH <sub>3</sub> MgBr (2% D)	THF, DMS (20:1), -100°, 15 min	 92:8 E:Z	(70) 116
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2% D)	THF, DMS (20:1), -100°, 15 min	 90:10 E:Z	(94) 116
	<i>s</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2% D)	THF, DMS (20:1), -100°, 15 min	 88:12 E:Z	(96) 116
	 (2% D)	THF, DMS (20:1), -78°, 15 min	 78:22 E:Z	(56) 116
				(5)
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgCl (1% H)	THF, 20°, 20 h		(2) 118
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgCl (10% H)	THF, 20°, 20 h		(65) 118
	<i>n</i> -C <sub>7</sub> H <sub>15</sub> MgCl (5% C)	THF, 20°, 5 h	 97:3	(83) 123
	THPO(CH <sub>2</sub> ) <sub>6</sub> MgCl (5% A)	THF, -70°, then (CH <sub>3</sub> CO) <sub>2</sub> O, C <sub>3</sub> H <sub>5</sub> N	 (CH <sub>2</sub> ) <sub>5</sub> O <sub>2</sub> CCH <sub>3</sub>	(82) 600
	C <sub>6</sub> H <sub>5</sub> MgBr (4% A)	THF, 0°, 1 h	 C <sub>6</sub> H <sub>5</sub>	(70) 601
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2% D)	THF, DMS (10:1), -78°, 1 h	 73:27 E:Z	(92) 115
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2% D)	THF, DMS (10:1), -78°, 1 h	 72:28 E:Z	(88) 115
	 (2% D)	THF, DMS (10:1), -30 to 0°, 3 h	 74:26 E:Z	(48) 115

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$C_6H_5MgBr$ (2% D)	THF, DMS (10:1), $-78^\circ$ , 1 h	 72:28 <i>E:Z</i>	(84) 115
	$n-C_4H_9MgBr$ (2% D)	THF, DMS (20:1), $-30^\circ$ , 1 h	 86:14 <i>E:Z</i>	(93) 117
	$s-C_4H_9MgCl$ (2% D)	THF, DMS (20:1), $-30^\circ$ , 1 h	 83:17 <i>E:Z</i>	(90) 117
	$MgBr$ (2% D)	THF, DMS (20:1), $-30^\circ$ , 1 h	 67:43 <i>E:Z</i>	(59) 117
	$n-C_8H_{17}MgBr$ (—% D)	THF, $20^\circ$ , 40 min	 $n-C_8H_{17}$ + $C_8H_{17-n}$	(80) 602
	$(CH_3)_3SiCH_2MgCl$ (3.5 eq) (5% A)	THF, $-40$ to $-20^\circ$ , 6.5 h	 (89)	603
	$C_2H_5MgBr$ (3% G)	Ether, $0^\circ$ , 5 h	 (68)	62a
	$C_6H_{11}MgBr$ (3% G)	Ether, $0^\circ$ , 5 h	 (75–87)	62a
	$MgBr$ (3% G)	Ether, $-60$ to $0^\circ$ 5 h	 (66)	62a
	$MgBr$ (6% G)	Ether, THF (1:1), $0^\circ$ , 5 h	 (56)	62a
	$C_6H_5MgBr$ (3% G)	Ether, $0^\circ$ , 5 h	 (92)	62a
	$s-C_4H_9MgCl$ (3% D)	THF, DMS (20:1), $-45^\circ$ , 1 h	 83:17 <i>E:Z</i>	(94) 117
	$C_6H_5MgBr$ (3% D)	THF, DMS (20:1), $-45^\circ$ , 1 h	 67:33 <i>E:Z</i>	(56) 117
	$n-C_4H_9MgBr$ (3% D)	THF, DMS (20:1), $-45^\circ$ , 1 h	 $n-C_4H_9$ + $n-C_4H_9$	(51) 117
	$n-C_4H_9MgBr$ (3% D)	THF, DMS (20:1), $-45^\circ$ , 1 h	 $n-C_4H_9$ + $n-C_4H_9$	(39) 117
	$n-C_4H_9MgBr$ (3% D)	THF, DMS (20:1), $-45^\circ$ , 1 h	 $n-C_4H_9$ + $n-C_4H_9$	(8) 117
	$CH_3MgBr$ (20% D)	Ether	 (94)	604
	THPO $(CH_2)_3MgCl$ (4% A)	1. THF, $-10$ to $0^\circ$ , 1h 2. TsOH, $CH_3OH$ 3. $(CH_3CO)_2O$ , $C_3H_5N$	 (65)	605



TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (*Continued*)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$C_6H_5MgBr$ (2 eq) (1% G)	Ether, 25°, 1 h	 $C_6H_5$ + D $C_6H_5$ (80)	62a
	$n-C_4H_9MgCl$ [5% C, 3P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ]	THF, 25°, 15 h	 (77)	124
	$n-C_4H_9MgCl$ [5% C, 3P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ]	THF, 25°, 3 h	 (60)	124
	$n-C_4H_9MgCl$ [5% C, 3P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ]	THF, 25°, 3 h	 (60)	124
	$n-C_4H_9MgCl$ [5% C, 3P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ]	THF, 25°, 1 h	 (83)	124
	$CH_3MgBr$ (15% D)	THF, reflux	 (82)	609
	$n-C_4H_9MgCl$ (5% C)	THF, 20°, 5 h	 (72)	123
	$C_2H_5MgBr$ (excess) (10% C)	THF, -25°	$C_6H_5CH=CHCH_3$ + $C_6H_5CH_2CH=CH_2$ + $C_6H_5CH=CHC_3H_7-n$ (—)	126
	$CH_2MgCl$ (0.4% A)	THF, 0°, 5 min	 (79)	99
	$C_6H_5CH_2O$ $MgBr$ (4% A) (2 eq)	THF, 0°, 1 h	 (79)	601
	$C_2H_5MgBr$ (10% D)	THF, HMPA, -30°, 30 min	 (85)	596
	$TMSC\equiv CMgBr$ (4% A)	THF, 22°, 3 h	 (87)	610

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	TMSCH <sub>2</sub> MgCl (20% E)	—		(80) 611
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2 eq) (1% G)	Ether, 25°, 1 h		(98) 62a
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2 eq) (1% B)	Ether, 25°, 1 h		(96) 62a
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2 eq) (1% G)	Ether, 25°, 1 h		(91) 62a
	C <sub>6</sub> H <sub>5</sub> MgBr (2 eq) (1% G)	Ether, 25°, 1 h		(76) 62a
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (10% H)	THF, 20°, 20 h		(80) 118
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl [5% C, 3P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ]	THF, 25°, 1 h		(83) 124
	( <i>i</i> -C <sub>3</sub> H <sub>7</sub> O) <sub>2</sub> (CH <sub>3</sub> )SiCH <sub>2</sub> MgCl (10% D)	THF, -50 to 0°, 5.5 h		(96) 612
	C <sub>2</sub> H <sub>5</sub> MgBr [5% H, P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ]	THF, 60°, 4 h		(54) 119
	HC≡C—MgBr (5% C)	Ether, 0°, 12 h		(92) 120
	RMgBr (5–10% B)	THF, -40 to -10°		(~100) 613
			R = C <sub>2</sub> H <sub>5</sub> , C <sub>6</sub> H <sub>5</sub> , CH <sub>2</sub> =CH, <i>t</i> -C <sub>4</sub> H <sub>9</sub> , C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> , 2-Thienyl	
C. Reactions of Epoxides and Related Substrates				
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (10% C)	THF, 0°, 2 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> OH	(88) 110

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>3</sub>				
	CH <sub>2</sub> MgBr (10% D)	THF, -30°, 1.5 h		(81) 111
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (10% D) C <sub>6</sub> H <sub>5</sub> MgBr (10% D)	Ether, 20°, 20 h THF, 20°, 20 h	<i>n</i> -C <sub>7</sub> H <sub>15</sub> OH C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>3</sub> OH	(75) 110 (52) 110
		Ether, 20°, 20 h		(50) 110
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (10% C) C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> MgCl (10% C)	THF, 0°, 2 h THF, 0°, 2 h	<i>n</i> -C <sub>3</sub> H <sub>11</sub> CH(CH <sub>3</sub> )OH C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub> CH(CH <sub>3</sub> )OH	(93) 110 (91) 110
		THF, -30°, 1.5 h		(68) 110
		THF, -30°, 17 h		(54) 143
	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub> MgBr (20% D)	THF, DMS (20:1), -30°		(90) 614
		THF, -30°, 2 h		(80) 615
	<i>n</i> -C <sub>6</sub> H <sub>17</sub> MgBr (—% D)	THF, ether		(83) 616
		Ether, THF, -73 to -30°, 5 h		(81) 617
C <sub>4</sub>				
	THPO(CH <sub>2</sub> ) <sub>6</sub> MgCl (3% C)	THF, -50°, 15 h		(81) 618
		THF, ether, -25°		(72) 619
	BrMg	THF, -30 to 0°, 17 h		(83) 620
		1. THF, DMS, 0°, 12 h 2. H <sup>+</sup> , H <sub>2</sub> O		(84) 621
		—		(90) 622

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

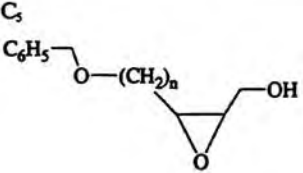
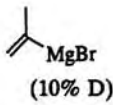
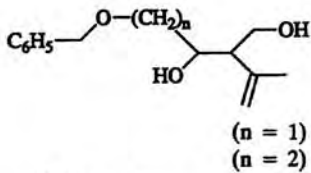
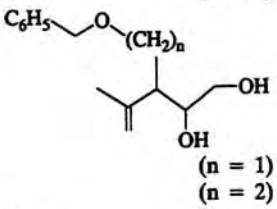
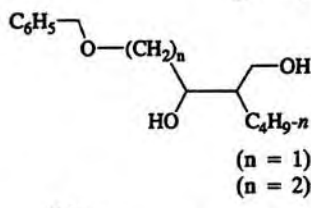
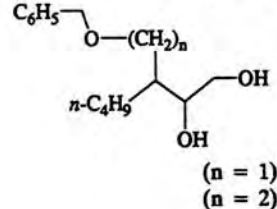
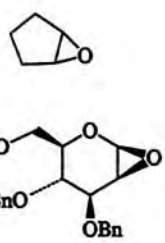
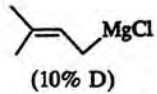
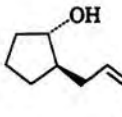
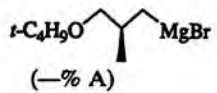
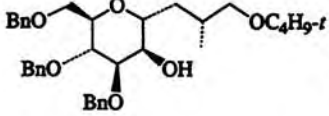
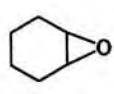
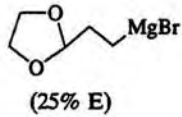
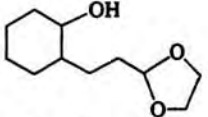
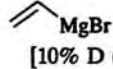
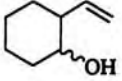
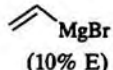
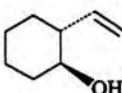
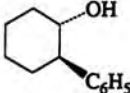
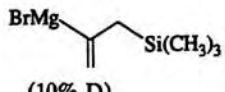
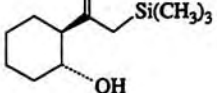
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.	
$C_5$ 	 (10% D)	THF, ether, $-25^\circ$	 + (n = 1) (87) (n = 2) (72)	619	
		$n-C_4H_9MgBr$ (10% D)	THF, ether, $-40^\circ$	 (n = 1) (13) (n = 2) (18)	
			THF, ether, $-40^\circ$	 (n = 1) (75) (n = 2) (72)	619
				 (n = 1) (13) (n = 2) (14)	
	$C_5$ 	 (10% D)	THF, $-30^\circ$ , 1.5 h	 (86)	111
		 (—% A)	—	 (—)	623
$C_6$ 	 (25% E)	THF, $-30^\circ$ , 24 h	 (26)	143	
	 [10% D (98% purity)]	THF, $0^\circ$ , 3 h	 55:45 <i>trans</i> : <i>cis</i> (—)	112	
	 (10% E)	THF, $0^\circ$ , 3 h	 (—)	112	
	$C_6H_5MgBr$ (10% D)	THF, $-30^\circ$ , 3 h	 (81)	568	
	 (10% D)	THF, $-30$ to $0^\circ$ , 3 h	 (85)	620	



TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

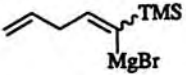
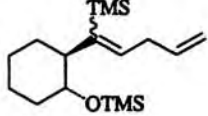
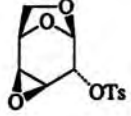
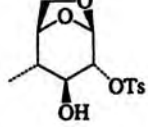
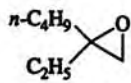
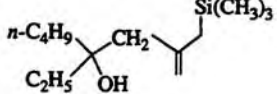
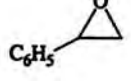
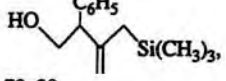
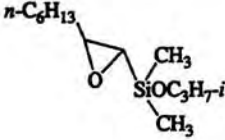
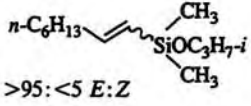
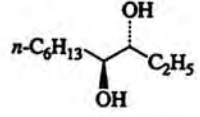
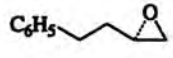
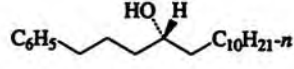
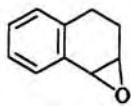
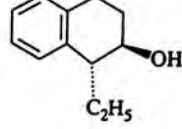
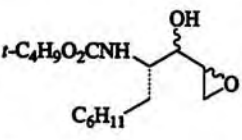
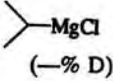
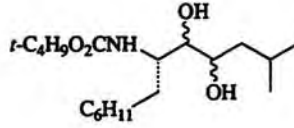
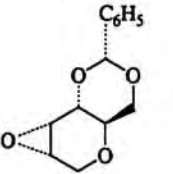
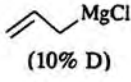
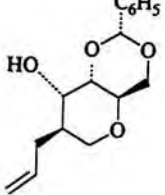
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
		THF, TMSCl, 0°, 2 h		(54) 624
	CH <sub>3</sub> MgCl (- % C)	—		(74) 625
	BrMg-CH=CH-Si(CH <sub>3</sub> ) <sub>3</sub> (10% D)	THF, -30 to 0°, 3 h		(93) 619
	BrMg-CH=CH-Si(CH <sub>3</sub> ) <sub>3</sub> (10% D)	THF, -30 to 0°, 3 h		(95) 619
	<i>i</i> -C <sub>2</sub> H <sub>5</sub> MgCl (10% G)	THF, -40 to -25°, 1.5 h		(>70) 626
	C <sub>2</sub> H <sub>5</sub> MgBr (10% G)	1. Ether, -50 to -20°, 4 h 2. H <sub>2</sub> O <sub>2</sub> , KF, KHCO <sub>3</sub> , THF, CH <sub>3</sub> OH, 25°, 12 h		(>45) 627
	<i>n</i> -C <sub>10</sub> H <sub>21</sub> MgBr, 1.7 eq (20% D)	THF, DMS (10:1), -20°		(83) 613
	C <sub>2</sub> H <sub>5</sub> MgI (5% D)	THF, 0°, 4 h		(53) 629
	 (- % D)	—		(55) 628
	 (10% D)	THF, -30°		(80-88) 113

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

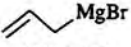
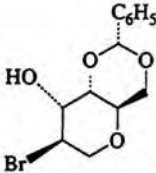
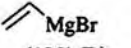
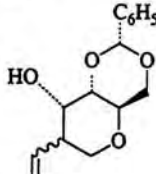
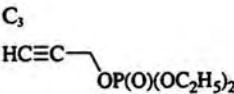
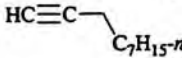
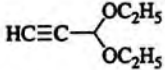
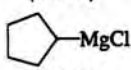
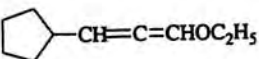
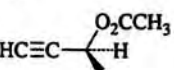
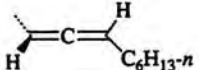
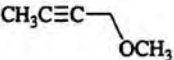
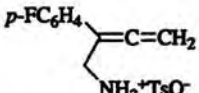
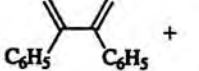
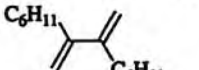
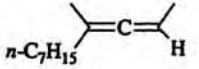
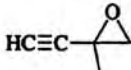
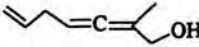
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$n\text{-C}_7\text{H}_{15}\text{MgBr}$ (10% D)	THF, $-30^\circ$		(90) 113
	$n\text{-C}_7\text{H}_{15}\text{MgBr}$ (10% D)	THF, $-30^\circ$		(75) 113
D. Reactions of Propargylic Substrates				
$\text{C}_3$ 	$n\text{-C}_7\text{H}_{15}\text{MgBr}$ (5% C)	Ether, $0^\circ$ , 12 h	$n\text{-C}_7\text{H}_{15}\text{CH}=\text{C}=\text{CH}_2$ + 	(68) 120
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (2% C)	Ether, $-15^\circ$ , 0.5 h	$n\text{-C}_4\text{H}_9\text{CH}=\text{C}=\text{CHOC}_2\text{H}_5$	(78) 136
	$i\text{-C}_4\text{H}_9\text{MgBr}$ (2% C)	Ether, $20^\circ$ , 0.5 h	$i\text{-C}_4\text{H}_9\text{CH}=\text{C}=\text{CHOC}_2\text{H}_5$	(79) 136
		Ether, $30^\circ$ , 0.5 h		(80) 136
$\text{C}_4$ 	$n\text{-C}_6\text{H}_{13}\text{MgBr}$ (2 eq) (10% C)	Ether, $-30^\circ$ , 12 min		(70) 128
	$n\text{-C}_7\text{H}_{15}\text{MgBr}$ (10% C)	Ether, $25^\circ$ , 2 h	$n\text{-C}_7\text{H}_{15}\text{CH}=\text{C}=\text{CH}_2$	(81) 133
	$i\text{-C}_5\text{H}_{11}\text{MgBr}$ (10% C)	Ether, $25^\circ$ , 2 h	$i\text{-C}_5\text{H}_{11}\text{CH}=\text{C}=\text{CH}_2$	(85) 133
$\text{CH}_3\text{OCH}_2\text{C}\equiv\text{CCH}_2\text{N}(\text{TMS})_2$	$p\text{-FC}_6\text{H}_4\text{MgBr}$ (5% E)	1. Ether, $-25$ to $25^\circ$ , 18 h 2. TsOH, $\text{C}_2\text{H}_5\text{OH}$		(86) 630
$\text{CH}_3\text{OCH}_2\text{C}\equiv\text{CCH}_2\text{OCH}_3$	$\text{C}_6\text{H}_5\text{MgBr}$ (2 eq) (10% C)	Ether, $0^\circ$		(66)
			$\text{C}_6\text{H}_5\text{CH}_2\text{CH}=\text{C}(\text{C}_6\text{H}_5)\text{CH}_2\text{OCH}_3$	(19) 631
$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{CH}_2\text{C}\equiv\text{CCH}_2\text{P}(\text{O})(\text{OC}_2\text{H}_5)_2$	$\text{C}_6\text{H}_{11}\text{MgBr}$ (3 eq) (10% D)	THF, $0$ – $20^\circ$ , 12 h		(88) 632
$\text{BrCH}_2\text{C}\equiv\text{CCH}_2\text{Br}$	$\text{THPOCH}_2\text{C}\equiv\text{CMgBr}$ (2 eq) (5% B)	1. THF, reflux, 16 h 2. DOWEX W50-X8, $\text{CH}_3\text{OH}$	$\text{HO}(\text{CH}_2\text{C}\equiv\text{C})_3\text{CH}_2\text{OH}$	(43) 633
$\text{C}_3$ $\text{HC}\equiv\text{CCH}(\text{CH}_3)\text{OCH}_3$	$n\text{-C}_7\text{H}_{15}\text{MgBr}$ (10% C)	Ether, $25^\circ$ , 2 h		(85) 133
	$n\text{-C}_7\text{H}_{15}\text{MgBr}$ (5% C)	Ether, $-20^\circ$ , 1 h		(80) 127

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.	
	CH <sub>3</sub> MgI (4 eq) (25% D)	Ether, -20°, 4 h		(80) 128	
	CH <sub>3</sub> MgI (4 eq) (25% D)	Ether, -20°, 4 h		(50) 128	
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N(CH <sub>3</sub> )CH <sub>2</sub> C≡CCH(OCH <sub>3</sub> )CH <sub>3</sub>	CH <sub>3</sub> MgI (10% D)	Ether, 25°, 12 h	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N(CH <sub>3</sub> )CH <sub>2</sub> -C=C(H)CH <sub>3</sub>	(70) 130, 138	
H <sub>2</sub> NCH <sub>2</sub> C≡CCH(CH <sub>3</sub> )OCH <sub>3</sub>	CH <sub>3</sub> MgI (5 eq) (10% D)	Ether, 25°, 12 h		(75) 130, 138	
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2% D)	THF, DMS (20:1), -78°, 1 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -C=C-CH <sub>2</sub> CO <sub>2</sub> H	(97) 137	
	<i>s</i> -C <sub>4</sub> H <sub>9</sub> MgCl (2% D)	THF, DMS (20:1), -78°, 1 h	<i>s</i> -C <sub>4</sub> H <sub>9</sub> -C=C-CH <sub>2</sub> CO <sub>2</sub> H	(90) 137	
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (2% D)	THF, DMS (20:1), -78°, 1 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -C=C-CH <sub>2</sub> CO <sub>2</sub> H	(85) 137	
		(2% D)	THF, DMS (20:1), -78°, 1 h		(72) 137
		(2% D)	THF, DMS (20:1), -78°, 1 h		(11) 137
C <sub>6</sub> C <sub>2</sub> H <sub>5</sub> C≡CCH(CH <sub>3</sub> )OCH <sub>3</sub>	<i>n</i> -C <sub>8</sub> H <sub>17</sub> MgBr (10% C)	Ether, 37°, 3 h		(46) 133	
	C <sub>6</sub> H <sub>5</sub> MgBr (10% C)	Ether, 25°, 2 h		(63) 133	
CH <sub>3</sub> C≡CC(CH <sub>3</sub> ) <sub>2</sub> OCH <sub>3</sub>	<i>n</i> -C <sub>8</sub> H <sub>17</sub> MgBr (10% C)	Ether, 25°, 2 h		(52) 133	
	C <sub>6</sub> H <sub>5</sub> MgBr (10% C)	Ether, 25°, 2 h		(94) 133	
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N(CH <sub>3</sub> )CH <sub>2</sub> C≡CC(CH <sub>3</sub> ) <sub>2</sub> OCH <sub>3</sub>	<i>n</i> -C <sub>8</sub> H <sub>17</sub> MgBr (20% D)	THF, 25°, 6 h		(70) 130, 138	
C <sub>7</sub> 	CH <sub>3</sub> MgBr (5% C)	Ether, 0°		(100) 135	
	CH <sub>3</sub> MgBr [5% C, 3P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ]	Ether, 0°		56% de <sup>b</sup> (100) 135	
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (5% C)	Ether, 0°		78% de <sup>b</sup> (100) 135	

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

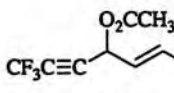
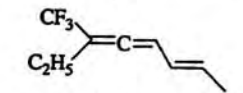
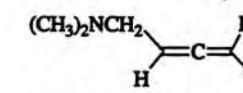
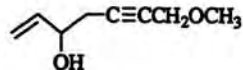
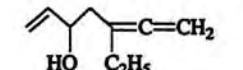
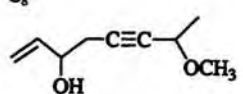
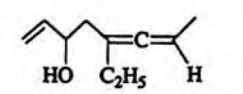
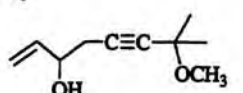
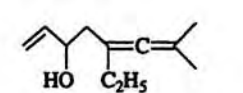
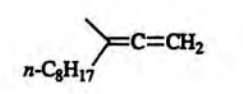
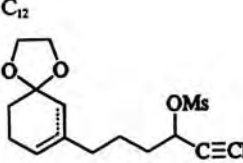
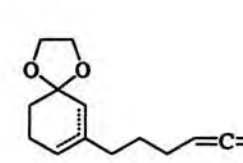
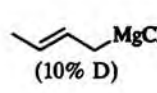
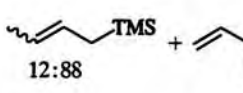
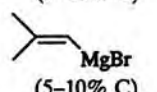
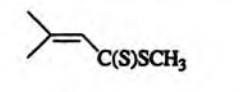
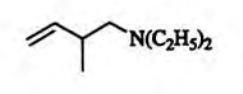
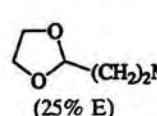
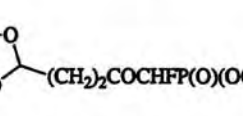

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
THPO(CH <sub>2</sub> ) <sub>4</sub> C≡CCH <sub>2</sub> OCH <sub>3</sub>	CH <sub>3</sub> MgBr (25% C)	1. Ether, reflux 2. C <sub>2</sub> H <sub>5</sub> OH, H <sup>+</sup>	HO(CH <sub>2</sub> ) <sub>4</sub> C=CH <sub>2</sub> (43)	634
	C <sub>2</sub> H <sub>5</sub> MgBr (—% A)	—	 (43)	635
(CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> C≡CCH(OCH <sub>3</sub> )C <sub>3</sub> H <sub>7-n</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (20% D)	THF, 25°, 6 h	 (63)	130, 138
	C <sub>2</sub> H <sub>5</sub> MgBr (5 eq) (10% C)	Ether	 (40)	134
<i>C</i> <sub>8</sub> 	C <sub>2</sub> H <sub>5</sub> MgBr (5 eq) (10% C)	Ether	 (45)	134
<i>C</i> <sub>9</sub> 	C <sub>2</sub> H <sub>5</sub> MgBr (5 eq) (10% C)	Ether	 (33)	134
<i>C</i> <sub>11</sub> <i>n</i> -C <sub>8</sub> H <sub>17</sub> C≡C—OCH <sub>3</sub>	CH <sub>3</sub> MgBr (10% C)	Ether, 37°, 3 h	 (44)	133
<i>C</i> <sub>12</sub> 	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (10% D)	Ether, 0–20°, 30 min	 (36)	636
<i>E. Miscellaneous Reactions</i>				
<i>C</i> <sub>6</sub> TMSCl	 (10% D)	Ether, –30°	 (92)	637
<i>C</i> <sub>1</sub> CS <sub>2</sub>	C <sub>6</sub> H <sub>11</sub> MgCl (5–10% C)	1. THF, –30°, 0.5 h 2. CH <sub>3</sub> I, 25°	C <sub>6</sub> H <sub>11</sub> C(S)SCH <sub>3</sub> (100)	142
	 (5–10% C)	"	 (93)	142
	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> NCH <sub>2</sub> — OC <sub>4</sub> H <sub>9-n</sub>	Ether, 0–20°, 15 h	 (60)	638
<i>C</i> <sub>2</sub> ( <i>i</i> -C <sub>3</sub> H <sub>7</sub> O) <sub>2</sub> — P(O)CHFCOCl	 (CH <sub>2</sub> ) <sub>2</sub> MgBr (25% E)	–78 to 0°, 3 h	 (69)	639
<i>C</i> <sub>3</sub> 	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (10% C)	THF, –5°, 1 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> CO <sub>2</sub> H + Br(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H (44)	167 (40)

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)


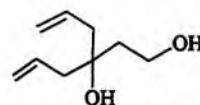
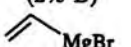
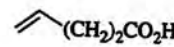





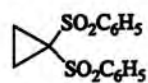
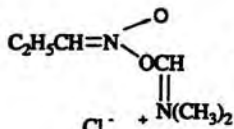
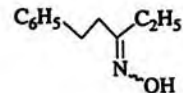
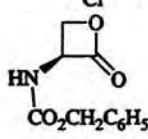
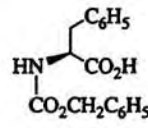
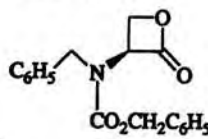
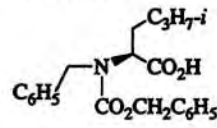


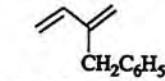
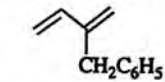
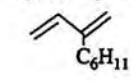

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2% B)	THF, 0°, 15 min	<i>n</i> -C <sub>6</sub> H <sub>13</sub> CO <sub>2</sub> H	(90) 166
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (10% C)	THF, -5°, 1 h	<i>i</i> -C <sub>3</sub> H <sub>7</sub> (CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	(82) 167
	 MgBr (10% C)	Ether, -5°, 1 h		(—) 167
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (2% B)	THF, 0°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> (CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	(85) 166
	 MgBr (2% B)	THF, 0°, 15 min	 (CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	(59) 166
 (2 eq)	BrMg(CH <sub>2</sub> ) <sub>8</sub> MgBr (10% A)	THF, 0°, 3 h	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>12</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> <sup>c</sup>	(68) 640
	BrMg(CH <sub>2</sub> ) <sub>9</sub> MgBr (10% A)	THF, 0°, 3 h	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>13</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> <sup>c</sup>	(63) 640
	ClMg(CH <sub>2</sub> ) <sub>5</sub> 	THF, 0°, 3 h	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>7</sub> 	(50) 640
	ClMg(CH <sub>2</sub> ) <sub>5</sub> 	THF, 0°, 3 h	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>7</sub> 	(50) 640
C <sub>3</sub> F <sub>7</sub> OCF(CF <sub>3</sub> )COF	C <sub>6</sub> F <sub>5</sub> MgBr (10% B)	THF, ether, -20°, 18 h	C <sub>6</sub> F <sub>5</sub> COCF(CF <sub>3</sub> )OC <sub>3</sub> F <sub>7</sub>	(92) 641
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (10% E)	Ether, THF, 0 to 10°	<i>n</i> -C <sub>6</sub> H <sub>13</sub> CH(SO <sub>2</sub> C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub>	(82) 642
	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> MgBr (10% E)	THF, -30°, 2 h		(99) 643
	C <sub>6</sub> H <sub>5</sub> MgCl (6 eq) (5% E)	THF, DMS (20:1), -23°, 2 h		(55) 644
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (5 eq) (4% E)	THF, DMS (20:1), -23°, 2 h		(83) 644
 	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> MgCl (5 eq) (10% D)	THF	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> CH=C=CH <sub>2</sub> + 	(72) (12) 645
	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> MgCl (5 eq) (20% E)	THF	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> CH=C=CH <sub>2</sub> + 	(<3) (50) 645
	C <sub>6</sub> H <sub>11</sub> MgBr (4 eq) (20% D)	THF	C <sub>6</sub> H <sub>11</sub> CH <sub>2</sub> CH=C=CH <sub>2</sub> + 	(23) (7) 645
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (2% B)	THF, 0°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> CH(CH <sub>3</sub> )CO <sub>2</sub> H (89)	166

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	MgBr (2% B)	THF, -30°, 2 h		(60) 166
	MgBr (2% D)	THF, DMS (30:1), -10°, 1.5 h		(87) 646
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2% B)	THF, 0°, 15 min	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CO <sub>2</sub> H	(81) 166
	C <sub>6</sub> H <sub>5</sub> MgBr (2% B)	THF, 0°, 15 min	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CO <sub>2</sub> H	(13) 166
	MgBr (2% D)	THF, DMS (20:1), -15 to -4°, 4 h		(90) 648
	MgBr (72:28 <i>E</i> : <i>Z</i> ) (2% D)	THF, DMS (20:1), -15 to -5°, 4 h	 78:28 <i>E</i> : <i>Z</i>	(80) 648
	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> MgCl (1% A)	1. THF, -78°, 2 h 2. 20% H <sub>2</sub> SO <sub>4</sub>		(73) 647
	RMgX (10% C) R = <i>n</i> -C <sub>4</sub> H <sub>9</sub> , C <sub>2</sub> H <sub>5</sub> , <i>i</i> -C <sub>3</sub> H <sub>7</sub> , CH <sub>3</sub> , C <sub>6</sub> H <sub>5</sub> , C <sub>6</sub> H <sub>11</sub>	THF or ether, 35°, 1 h		(80-90) 179
	CH <sub>3</sub> MgBr (2% B)	THF, 0°, 15 min	C <sub>2</sub> H <sub>5</sub> C(CH <sub>3</sub> ) <sub>2</sub> CO <sub>2</sub> H	(80) 166
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (2% B)	THF, 0°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> CO <sub>2</sub> H	(24) 166
	C <sub>6</sub> H <sub>11</sub> MgCl (5% D)	THF, ether, 0°, 15 min		(77) 140
<i>t</i> -C <sub>4</sub> H <sub>9</sub> CN	C <sub>6</sub> H <sub>11</sub> MgCl (2% C)	1. THF, reflux, 14 h 2. H <sup>+</sup> , H <sub>2</sub> O	<i>t</i> -C <sub>4</sub> H <sub>9</sub> COC <sub>6</sub> H <sub>11</sub>	(45) 649
	C <sub>2</sub> H <sub>5</sub> MgCl (5% D)	THF, ether, 0°, 15 min		(27) 140

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)


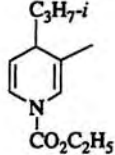
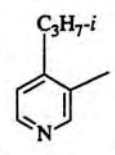

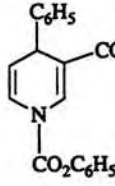
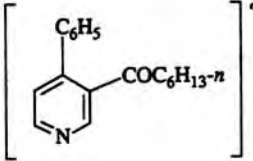
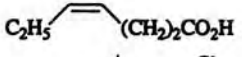
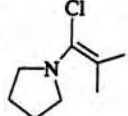
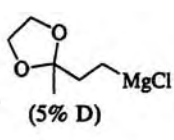
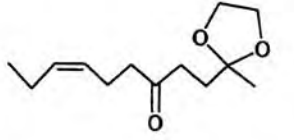
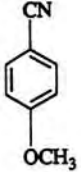
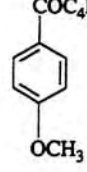

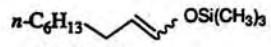
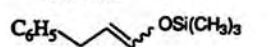
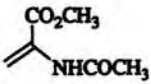
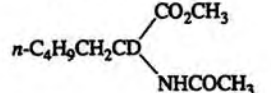
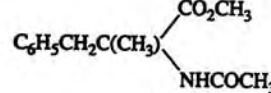
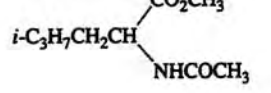
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
 , ClCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (5% D)	THF, ether, 0°, 15 min	 +  (60)	140
 , ClCO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub> MgBr (5% D)	THF, ether, 0°, 15 min	 +  (40)	141
 + 	 MgCl (5% D)	—	 (91)	650
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (2% C)	1. THF, reflux, 14 h 2. H <sup>+</sup> , H <sub>2</sub> O	 (99)	649
F. Conjugate Addition Reactions				
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> Br (3.5% E)	THF, HMPA, (CH <sub>3</sub> ) <sub>3</sub> SiCl (2 eq), -78°, 2 h	 (83)	157
	C <sub>6</sub> H <sub>5</sub> MgBr (3.5% E)	THF, HMPA, (CH <sub>3</sub> ) <sub>3</sub> SiCl (2 eq), -100°, 2 h	 (90)	157
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (2 eq) (5% D)	Ether, C <sub>6</sub> H <sub>6</sub> , 0°, 30 min, then D <sub>2</sub> O	 (65)	151
	C <sub>6</sub> H <sub>5</sub> MgBr (2 eq) (5% D)	Ether, C <sub>6</sub> H <sub>6</sub> , 0°, 30 min, then CH <sub>3</sub> I	 (62)	151
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (2 eq) (5% D)	THF, 0°, 30 min	 (61)	151

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

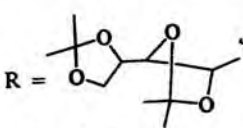
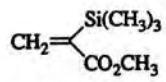
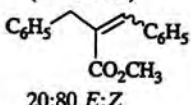
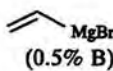
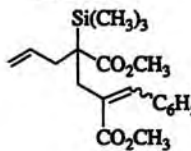
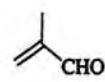
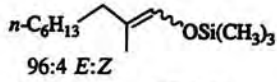
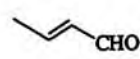
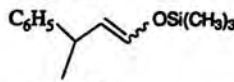
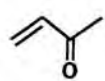
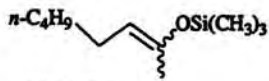
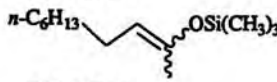
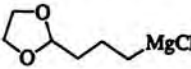
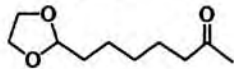
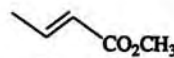
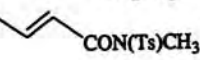
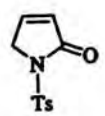
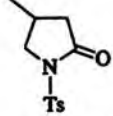
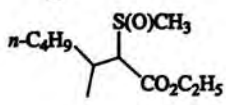
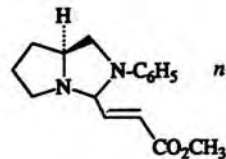
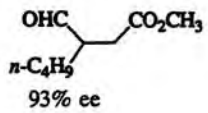
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$R-CH=CHCO_2C_2H_5$	$C_6H_5MgBr$ (5% D)	Ether, $-10^\circ$	$C_6H_5CHRCH_2CO_2C_2H_5$ (D-manno-)	(89) 153
$R =$ 	$C_6H_{11}MgBr$ (5% D)	Ether, $-70^\circ$ , 5 h	$C_6H_{11}CHRCH_2CO_2C_2H_5$ (mixture of D-manno- and D-arabino)	(60) 153
D-arabino-	$i-C_3H_7MgBr$ (5% D)	Ether, $-70^\circ$ , 5 h	$i-C_3H_7CHRCH_2CO_2C_2H_5$ (D-gluco)	(70) 153
	$t-C_4H_9MgCl$ (5% D)	Ether, $-70^\circ$ , 5 h	$t-C_4H_9CHRCH_2CO_2C_2H_5$ (D-manno-)	(37) 153
	$C_6H_5MgBr$ (0.5% B)	Ether, $-15^\circ$ , 1 h, then $C_6H_5CHO$ , $-25$ to $25^\circ$	 20:80 E:Z	(80) 651
	 (0.5% B)	Ether, $-15^\circ$ , 1 h, then $C_6H_5CHO$ , $-25$ to $25^\circ$	 20:80 E:Z	(84) 651
$C_4$				
	$n-C_6H_{13}MgBr$ (3.5% E)	THF, HMPA, $(CH_3)_3SiCl$ (2 eq), $-78^\circ$ , 2 h	 96:4 E:Z	(89) 157
	$C_6H_5MgBr$ (3.5% E)	THF, HMPA, $(CH_3)_3SiCl$ (2 eq), $-78^\circ$ ; 2 h	 87:13 E:Z	(89) 157
	$n-C_4H_9MgBr$ (3.5% E)	THF, HMPA, $(CH_3)_3SiCl$ (2 eq), $-78^\circ$ , 2 h	 28:72 E:Z	(96) 157
	$n-C_6H_{13}MgBr$ (3.5% E)	THF, HMPA, $(CH_3)_3SiCl$ (2 eq), $-78^\circ$ , 2 h	 23:77 E:Z	(91) 157
		THF, $-78^\circ$ , 2.5 h		(66) 143
	$C_6H_5MgBr$ (3.5% E)	THF, HMPA, $(CH_3)_3SiCl$ (2 eq), $-78^\circ$ , 3 h	$C_6H_5CH(CH_3)CH_2CO_2CH_3$	(76) 157
	$CH_3MgI$ (3% D)	Ether, $-20^\circ$ , 2.5 h	$i-C_4H_9CON(Ts)CH_3$	(79) 652
	$C_6H_5MgBr$ (3% D)	Ether, $-20^\circ$ , 2.5 h	$C_6H_5CH(CH_3)CH_2CON(Ts)CH_3$	(76) 652
	$CH_3MgI$ (3% D)	Ether, $-20^\circ$ , 2.5 h		(73) 652
$CH_3CH=CHCO_2C_2H_5$	$n-C_4H_9MgBr$ (2% B)	Ether, $-30^\circ$ , 40 min, then $CH_3S(O)Cl$ , $-78$ to $0^\circ$		(—) 653
	$n-C_4H_9MgBr$ (5% D)	1. Ether, $-78^\circ$ , 4 h 2. HCl, $H_2O$	 93% ee	(83) 654



TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)


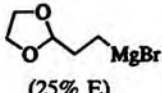
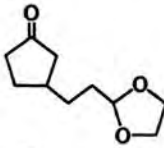
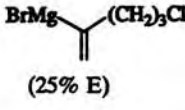
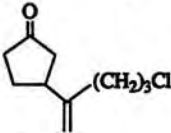
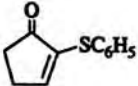
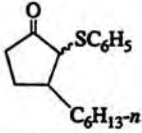
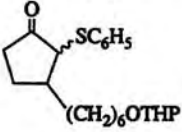
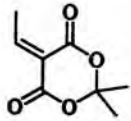
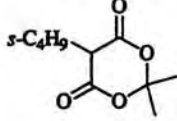
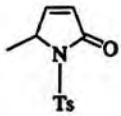
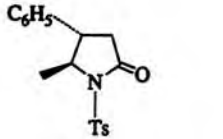
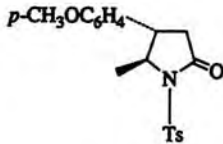
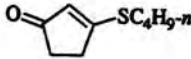
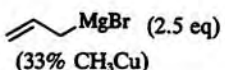
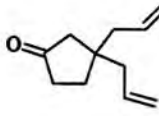
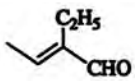
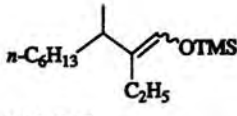
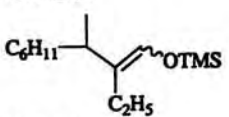

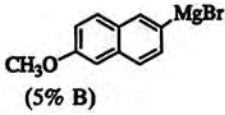
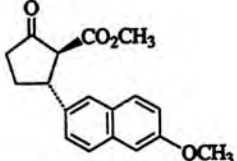
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
<b>C<sub>5</sub></b>				
	 (25% E)	THF, -78 to 0°, 16 h		(77) 143
	 (25% E)	THF, -78°, 2-3 h		(54) 655
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (5% B)	THF, 65°, 30 min		(95) 656
	BrMg(CH <sub>2</sub> ) <sub>6</sub> OTHP (5% B)	THF, 65°, 30 min		(41) 656
	C <sub>2</sub> H <sub>5</sub> MgBr (0.05% B)	Ether, 25°, 30 min		(83) 657
	C <sub>6</sub> H <sub>5</sub> MgBr (5% D)	Ether, -20°, 2.5 h		(70) 652
	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> MgBr (5% D)	Ether, -20°, 2.5 h		(74) 652
	 MgBr (2.5 eq) (33% CH <sub>3</sub> Cu)	Ether, 0°, 15 min		(64) 658
<b>C<sub>6</sub></b>				
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (3.5% E)	THF, HMPA, (CH <sub>3</sub> ) <sub>3</sub> SiCl (2 eq), -100°, 2 h		(89) 157
	C <sub>6</sub> H <sub>11</sub> MgBr (3.5% E)	THF, HMPA, (CH <sub>3</sub> ) <sub>3</sub> SiCl (2 eq), -100°, 2 h		(80) 157
	 (5% B)	THF, 0-25°, 1 h		(53) 659

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

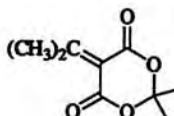
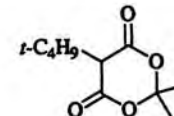
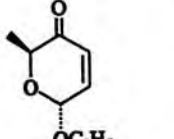
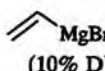
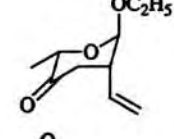
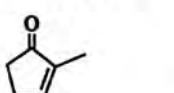
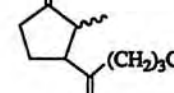

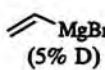
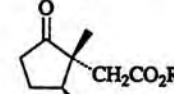

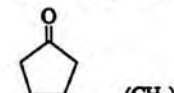


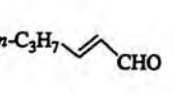
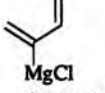
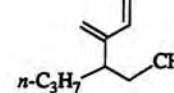
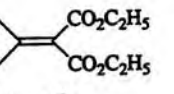
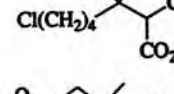
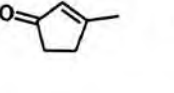
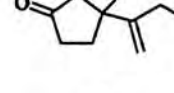
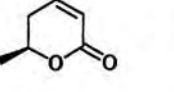
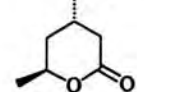
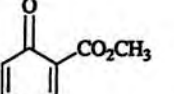
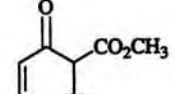

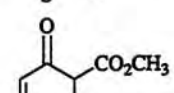
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	CH <sub>3</sub> MgI (0.05% B)	Ether, 25°, 30 min		(83) 657
	 (10% D)	THF, P(C <sub>4</sub> H <sub>9</sub> - <i>n</i> ) <sub>3</sub> , -40°, 3 h		(7) 154
	BrMg-CH=CH-(CH <sub>2</sub> ) <sub>3</sub> Cl (25% E)	THF, BF <sub>3</sub> · Et <sub>2</sub> O (1.2 eq), -78°, 2-3 h		(33) 655
	 (5% D)	1. THF, DMS, -60°, 1.5 h 2. BrCH <sub>2</sub> CO <sub>2</sub> R, HMPA, 25°, 18 h	 R = <i>t</i> -C <sub>4</sub> H <sub>9</sub> , 2:98 <i>cis:trans</i> R = CH <sub>3</sub> , 12:88 <i>cis:trans</i>	(78) 660
	BrMg-CH=CH-(CH <sub>2</sub> ) <sub>3</sub> Cl (25% E)	THF, BF <sub>3</sub> · Et <sub>2</sub> O (1.2 eq), -78°, 2-3 h		(54) 655
	<i>i</i> -C <sub>4</sub> H <sub>9</sub> MgBr (10% D)	Ether, P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> , 0°		(43) 661
	 (10% D)	THF, DMS, -25°, 2 h		(84) 662
	Cl(CH <sub>2</sub> ) <sub>4</sub> MgBr (5% D)	Ether, P(C <sub>4</sub> H <sub>9</sub> - <i>n</i> ) <sub>3</sub> , -10 to 20°, 3 h		(52) 663
	TMS-CH=CH-MgBr (5% D)	Ether		(88) 664
	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> MgCl (- % B)	Ether, -78 to 25°		(69) 665
	CH <sub>3</sub> MgBr (2.5% E)	THF, DMS, -78°, 1 h		(23) 666
	C <sub>2</sub> H <sub>5</sub> MgBr (2.5% E)	THF, DMS, -78°, 1 h		(64) 666

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

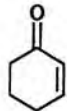
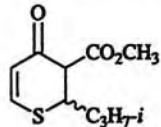
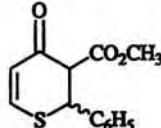
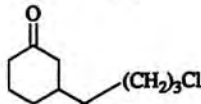
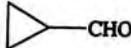
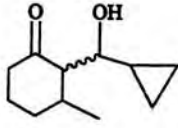
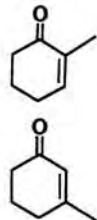
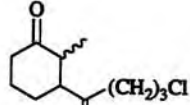
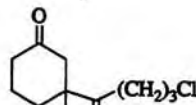
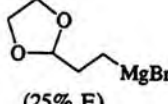
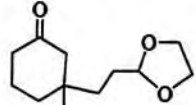
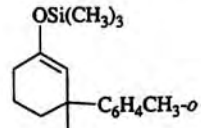
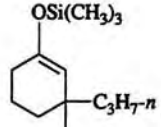
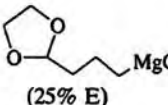
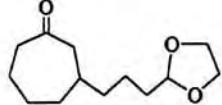
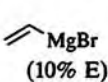
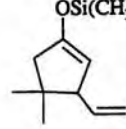
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$i\text{-C}_3\text{H}_7\text{MgBr}$ (2.5% E)	THF, DMS, $-78^\circ$ , 1 h		(57) 666
	$\text{C}_6\text{H}_5\text{MgBr}$ (2.5% E)	THF, DMS, $-78^\circ$ , 1 h		(68) 666
	$\text{BrMgC}(\text{CH}_2)_3\text{Cl}$ (25% E)	THF, $-78^\circ$ , 2-3 h		(81) 655
	$\text{CH}_3\text{MgI}$ (- % D)	1. Ether, $0^\circ$ , 30 min, then 2. 		(-) 667
	$\text{BrMgC}(\text{CH}_2)_3\text{Cl}$ (25% E)	THF, $\text{BF}_3 \cdot \text{Et}_2\text{O}$ , $-78^\circ$ , 2-3 h		(55) 655
	$\text{BrMgC}(\text{CH}_2)_3\text{Cl}$ (25% E)	THF, $\text{BF}_3 \cdot \text{Et}_2\text{O}$ , $-78^\circ$ , 2-3 h		(37) 655
		THF, $-78$ to $0^\circ$ , 16 h		(74) 143
	$o\text{-CH}_3\text{C}_6\text{H}_4\text{MgBr}$ (3.5% E)	THF, HMPA, $(\text{CH}_3)_3\text{SiCl}$ (2 eq), $-78^\circ$ , 3 h		(77) 157
Cycloheptenone	$n\text{-C}_3\text{H}_7\text{MgBr}$ (3.5% E)	THF, HMPA, $(\text{CH}_3)_3\text{SiCl}$ (2 eq), $-78^\circ$ , 3 h		(85) 157
		THF, $-78^\circ$ , 2.5 h		(76) 143
		1. THF, $-78^\circ$ 2. $(\text{CH}_3)_3\text{SiCl}$ , $(\text{C}_2\text{H}_5)_3\text{N}$ , HMPA, $-78$ to $25^\circ$		(81) 669

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

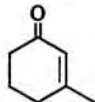
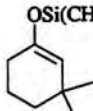
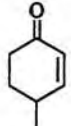
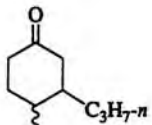
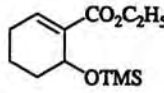
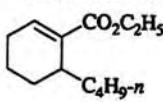
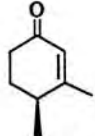
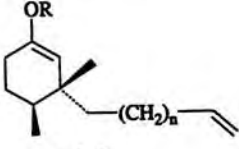
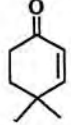
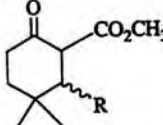
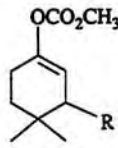
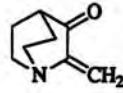
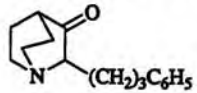
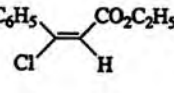
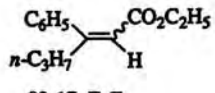
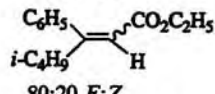
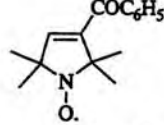
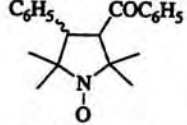
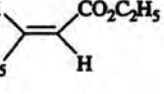
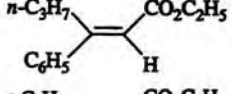
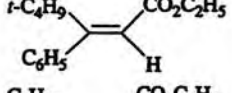
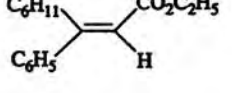
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	CH <sub>3</sub> MgI (- % D)	1. Ether, 0°, 1 h, 2. (CH <sub>3</sub> ) <sub>3</sub> SiCl, (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N, HMPA, 25°	 (76)	670
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgBr (10% D)	THF, -20 to 20°, 1 h	 (78)	671
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (2.5% CuX)	THF, ether, -78°	 (66)	672
	BrMg(CH <sub>2</sub> ) <sub>n</sub> (10% D)	1. Ether, DMS, 0 to 25° 2. RCl	 (~85-90)	673, 674
	RMgI (7% G)	1. Ether, -23°, 4 h, 2. CH <sub>3</sub> O <sub>2</sub> CCl, -23 to 25°	 (60)	675
			R = (CH <sub>2</sub> ) <sub>3</sub> C≡CSi(CH <sub>3</sub> ) <sub>3</sub>	
	RMgCl (6% G)	1. Ether, -23°, 1 h, 2. CH <sub>3</sub> O <sub>2</sub> CCl, -23 to 25°	 (—)	675
			R = (CH <sub>2</sub> ) <sub>3</sub> C≡CSi(CH <sub>3</sub> ) <sub>3</sub>	
	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub> MgBr (10% B)	Ether, reflux 2 h	 (40)	676
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgBr (10% D)	Ether, 20°, 2 h	 (68)	155
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (10% D)	Ether, 20°, 2 h	 (68)	155
	C <sub>6</sub> H <sub>5</sub> MgBr (33% D)	1. Ether, -30°, 3 h 2. PbO <sub>2</sub> , air	 (75)	677
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgBr (10% D)	Ether, 20°, 2 h	 (76)	155
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (10% D)	Ether, 0°, 2 h	 (70)	155
	C <sub>6</sub> H <sub>11</sub> MgCl (10% D)	Ether, 20°, 2 h	 (91)	155

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

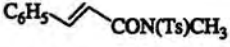
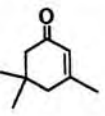
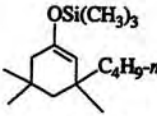
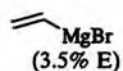
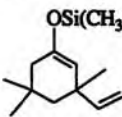
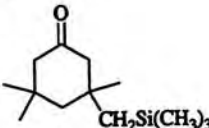
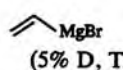
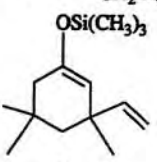
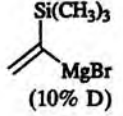
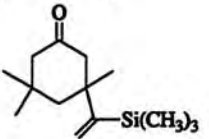
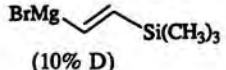
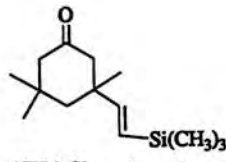
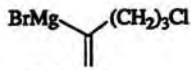
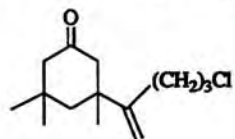
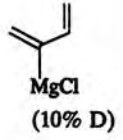
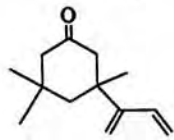
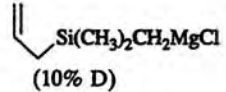
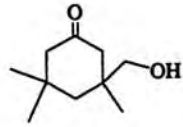
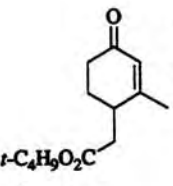
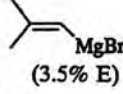
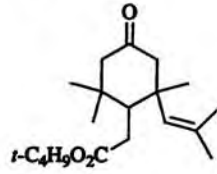
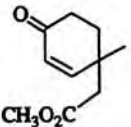
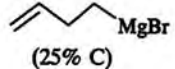
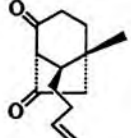
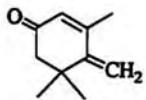
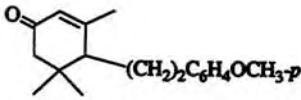
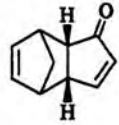
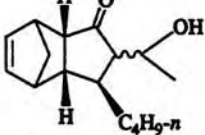
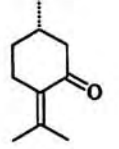
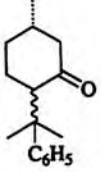
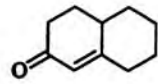
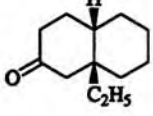
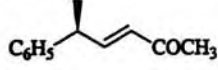
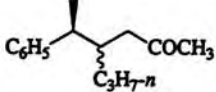
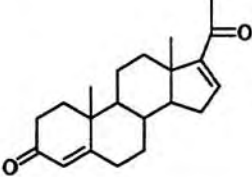
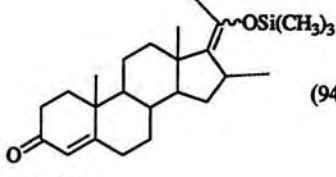
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	CH <sub>3</sub> MgI (3.5% D)	Ether, -25°, 2.5 h	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CON(Ts)CH <sub>3</sub> (81)	652
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (3.5% E)	THF, HMPA, (CH <sub>3</sub> ) <sub>3</sub> SiCl (2 eq), -78°, 2-4 h	 (89)	157
	 (3.5% E)	THF, HMPA, (CH <sub>3</sub> ) <sub>3</sub> SiCl (2 eq), -78°, 2-4 h	 (97)	157
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (2.5% C)	Ether, 0-25°, 30 min	 (77)	678
	 (5% D, TMEDA)	THF, TMEDA, (CH <sub>3</sub> ) <sub>3</sub> SiCl, -78°	 (80)	679
	 (10% D)	—	 (80)	577
	BrMg-  (10% D)	—	 (62)	577
	BrMg-  (25% E)	THF, BF <sub>3</sub> ·Et <sub>2</sub> O, -78°, 4.5 h	 (45)	655
	 (10% D)	THF, DMS, -60 to 0°, 18 h	 (52)	662
	 (10% D)	1. Ether, 20°, 1 h 2. KHF <sub>2</sub> , CF <sub>3</sub> CO <sub>2</sub> H 3. 30% H <sub>2</sub> O <sub>2</sub>	 (68)	680
	 (3.5% E)	THF, (CH <sub>3</sub> ) <sub>3</sub> SiCl (4 eq), -78°, 3 h	 (71)	157
	 (25% C)	THF, -28 to -12°, 3.5 h	 (60)	152

TABLE I. COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$p\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}_2\text{MgCl}$ (1% E)	Ether, DMS (1:1), 25°, 30 min	 (66)	156
	$n\text{-C}_4\text{H}_9\text{MgX}$ (—% B)	1. — 2. CH <sub>3</sub> CHO	 (—)	681
	$\text{C}_6\text{H}_5\text{MgBr}$ (10% D)	Ether, -15 to 20°, 12 h	 (70)	682
	$\text{C}_2\text{H}_5\text{MgBr}$ [cat. Cu(O <sub>2</sub> CCH <sub>3</sub> ) <sub>2</sub> ]	THF, reflux 12 h	 (—)	683
<b>C<sub>11</sub></b>				
	$n\text{-C}_3\text{H}_7\text{MgBr}$ (20% D)	THF, -20°, 1 h	 (41)	684
			<i>syn:anti</i> 1:4	
<b>C<sub>21</sub></b>				
	$\text{CH}_3\text{MgBr}$ (3.5% E)	THF, HMPA, (CH <sub>3</sub> ) <sub>3</sub> SiCl, 2 eq, -50°, 15 h	 (94)	157
			2:98 <i>E:Z</i>	

<sup>a</sup> The yield was estimated.

<sup>b</sup> The *de* was determined by <sup>13</sup>C NMR.

<sup>c</sup> The product was obtained by esterifying the crude diacid with ethanol.

<sup>d</sup> The product was obtained by treating the crude product with 3 N HCl.

<sup>e</sup> The yield is of the isolated pyridine after treatment with S<sub>8</sub>.

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS

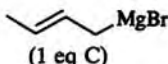
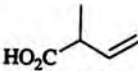
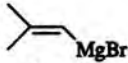
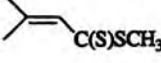

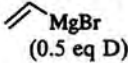
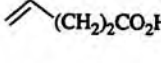
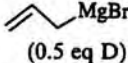
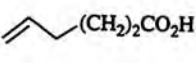
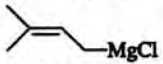
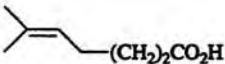

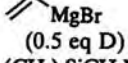
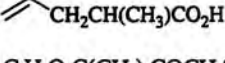

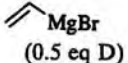
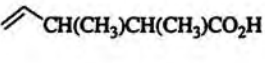
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
<i>A. Substitutions with Carbonyl-Containing Substrates</i>				
C <sub>1</sub>				
CO <sub>2</sub>	 (1 eq C)	THF, HMPA, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , 0.1 eq, -45°, 4 h		(90) 685
CS <sub>2</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (0.5 eq C)	THF, -50°, 30 min, then CH <sub>3</sub> I, 25°	<i>t</i> -C <sub>4</sub> H <sub>9</sub> C(S)SCH <sub>3</sub>	(81) 142
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq C)	THF, -50°, 30 min, then CH <sub>3</sub> I, 25°	"	(80) 142
	 (1 eq C)	THF, -50°, 30 min, then CH <sub>3</sub> I, 25°		(95) 142
C <sub>2</sub>				
CH <sub>3</sub> COCl	C <sub>6</sub> H <sub>5</sub> MgBr (0.5 eq D)	THF, -8 to 0°, 2 h	C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	(61) 686
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (1 eq CH <sub>3</sub> Cu)	THF, ether, 25°, 30 min	<i>n</i> -C <sub>6</sub> H <sub>13</sub> COCH <sub>3</sub>	(75) 163
C <sub>3</sub>				
C <sub>2</sub> H <sub>5</sub> C(S)SCH <sub>3</sub>	CH <sub>3</sub> MgBr (0.5 eq CuOTf)	Ether, 0°, 1 h	C <sub>2</sub> H <sub>5</sub> C(CH <sub>3</sub> ) <sub>2</sub> SH	(85) 164
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (0.5 eq CuOTf)	Ether, 0°, 1 h	C <sub>2</sub> H <sub>5</sub> C(C <sub>4</sub> H <sub>9</sub> - <i>n</i> ) <sub>2</sub> SH	(16) 164
	C <sub>6</sub> H <sub>5</sub> MgBr (0.5 eq CuOTf)	Ether, 0°, 1 h	C <sub>2</sub> H <sub>5</sub> C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> SH	(77) 164
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (0.5 eq B)	THF, DMS, -40°	<i>n</i> -C <sub>4</sub> H <sub>9</sub> (CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	(95) 167
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgBr (0.5 eq D)	THF, DMS, -30°, 2 h	<i>i</i> -C <sub>3</sub> H <sub>7</sub> (CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	(79) 168
	 (0.5 eq D)	THF, DMS, -30°, 2 h		(88) 168
	 (0.5 eq D)	THF, DMS, -30°, 2 h		(75) 168
	 (0.5 eq B)	THF, DMS, -50 to -10°, 2 h		(56) 167
C <sub>4</sub>				
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (0.5 eq D)	THF, DMS, -30 to 0°, 2 h	<i>n</i> -C <sub>3</sub> H <sub>11</sub> CH(CH <sub>3</sub> )CO <sub>2</sub> H	(85) 168
	 (0.5 eq D)	THF, DMS, -30 to 0°, 2 h		(72) 168
C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> - COCl	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl · (1 eq D)	Ether, -78 to 0°	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> COCH <sub>2</sub> Si(CH <sub>3</sub> ) <sub>3</sub>	(72) 687
<i>n</i> -C <sub>3</sub> H <sub>7</sub> COCl	TMSCH <sub>2</sub> MgCl (0.5 eq D)	Ether, -78 to 0°, 1 h	<i>n</i> -C <sub>3</sub> H <sub>7</sub> COCH <sub>2</sub> TMS	(83) 688
C <sub>5</sub>				
<i>t</i> -C <sub>4</sub> H <sub>9</sub> COCl	C <sub>6</sub> H <sub>5</sub> MgBr (1 eq CH <sub>3</sub> Cu)	THF, ether, 25°, 30 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> COC <sub>6</sub> H <sub>5</sub>	(93) 163
	 (0.5 eq D)	THF, DMS, -30 to 0°, 2 h		(17) 168

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

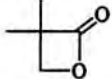
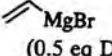

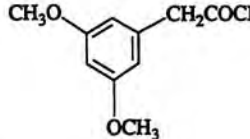
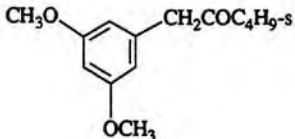
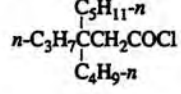
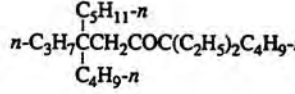
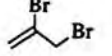

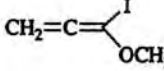
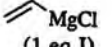
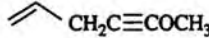
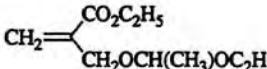
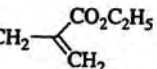
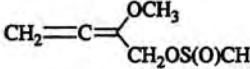
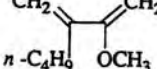
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (0.5 eq D)	THF, DMS, -30 to 0°, 2 h	<i>n</i> -C <sub>3</sub> H <sub>7</sub> C(CH <sub>3</sub> ) <sub>2</sub> CO <sub>2</sub> H (82)	168
	 MgBr (0.5 eq D)	THF, DMS, -30 to 0°, 2 h	 CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> CO <sub>2</sub> H (48)	168
C <sub>7</sub> C <sub>6</sub> H <sub>5</sub> COCl	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq CH <sub>3</sub> Cu)	THF, ether, 25°, 30 min	C <sub>6</sub> H <sub>5</sub> COC(C <sub>4</sub> H <sub>9</sub> )- <i>t</i> (93)	163
<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> COCl	C <sub>6</sub> H <sub>5</sub> MgBr (0.5 eq D)	THF, -8 to 0°, 2 h	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> COC <sub>6</sub> H <sub>5</sub> (76)	686
C <sub>6</sub> H <sub>5</sub> C(S)SCH <sub>3</sub>	CH <sub>3</sub> MgBr (0.5 eq CuOTf)	Ether, 0°, 1 h	C <sub>6</sub> H <sub>5</sub> C(CH <sub>3</sub> ) <sub>2</sub> SH (71)	164
C <sub>9</sub> ( <i>i</i> -C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> (CH <sub>3</sub> )- CCOCl	CH <sub>3</sub> MgI (1 eq B)	Ether, -5 to 0°	( <i>i</i> -C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> (CH <sub>3</sub> )CCOCH <sub>3</sub> (88)	162
C <sub>10</sub> ( <i>i</i> -C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> (C <sub>2</sub> H <sub>5</sub> )- CCOCl	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> MgCl (1 eq B)	Ether, -5 to 0°	( <i>i</i> -C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> (C <sub>2</sub> H <sub>5</sub> )CCOCH <sub>2</sub> C <sub>4</sub> H <sub>9</sub> - <i>t</i> (85)	162
	<i>s</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq C)	Ether		(72) 689
C <sub>11</sub> ( <i>t</i> -C <sub>4</sub> H <sub>9</sub> )( <i>i</i> -C <sub>3</sub> H <sub>7</sub> )CCOCl   C <sub>2</sub> H <sub>5</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq B)	Ether, -5 to 0°	( <i>t</i> -C <sub>4</sub> H <sub>9</sub> )( <i>i</i> -C <sub>3</sub> H <sub>7</sub> )CCOC <sub>4</sub> H <sub>9</sub> - <i>t</i>   C <sub>2</sub> H <sub>5</sub> (31)	162
C <sub>15</sub> 	<i>n</i> -C <sub>4</sub> H <sub>9</sub> (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CMgCl (1 eq B)	Ether, reflux		(65) 690
B. Substitution Reactions of Allylic Substrates				
C <sub>3</sub> 	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> MgBr (0.5 CuI · DMS)	Ether, -10 to 25°, 4 h	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> - 	(—) 691
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	THF, HMPT, -85°, 1 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> C≡COCH <sub>3</sub> (80)	177, 178
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (0.5 eq C, 1 eq LiBr)	THF, HMPT, -85°, 0.8 h	<i>i</i> -C <sub>3</sub> H <sub>7</sub> CH <sub>2</sub> C≡COCH <sub>3</sub> (65)	177, 178
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	THF, -85°, 1 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> C≡COCH <sub>3</sub> (70)	177, 178
	 MgCl (1 eq I)	THF, TMEDA, -50°, 1 h	 CH <sub>2</sub> C≡COCH <sub>3</sub> (67)	177, 178
	C <sub>6</sub> H <sub>5</sub> MgCl (1 eq I)	THF, -50°, 1 h	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C≡COCH <sub>3</sub> (77)	177, 178
C <sub>4</sub> 	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (0.5 eq D)	THF, -40°	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> - 	(61) 598
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	THF, 20°, 30 min		(70) 176



TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

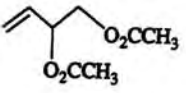
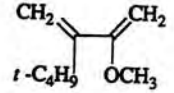
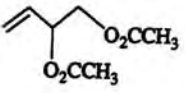
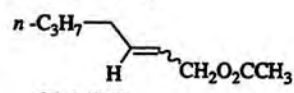
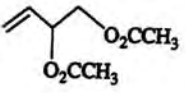
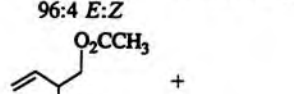
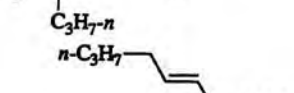
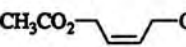
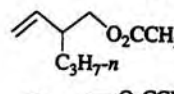
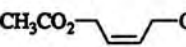
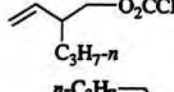
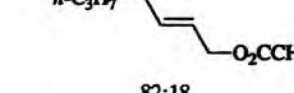

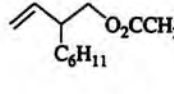
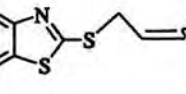
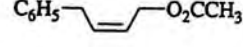
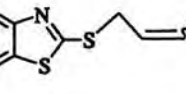
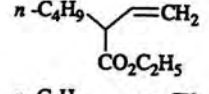
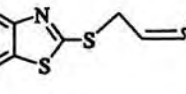
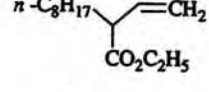
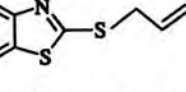
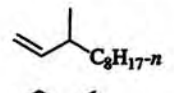
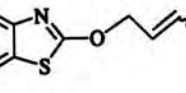
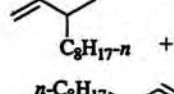
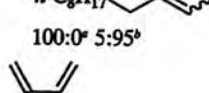
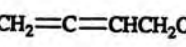
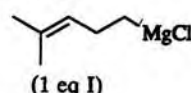
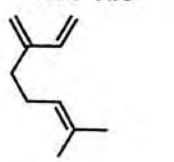
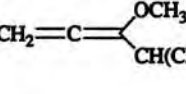
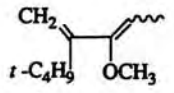
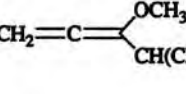
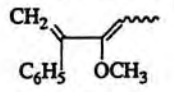
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	THF, 20°, 30 min	 (80)	176
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgCl (1 eq I)	THF, -70°, 12 h	 (47)	173
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgCl (1 eq I)	THF, -70°, 12 h	 +  (45)	173
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgCl (1 eq I)	THF, -70°, 12 h	 (75)	173
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgCl (1 eq I)	Ether, -70°, 12 h	 +  (37)	173
	C <sub>6</sub> H <sub>11</sub> MgCl (1 eq I)	THF, -70°, 12 h	 (68)	173
	C <sub>6</sub> H <sub>5</sub> MgBr (1 eq I)	THF, -70°, 12 h	 (31)	173
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1.5 eq C)	THF, -15°	 (83)	172b
	<i>n</i> -C <sub>8</sub> H <sub>17</sub> MgBr (1.5 eq C)	THF, -15°	 (88)	172b
	<i>n</i> -C <sub>8</sub> H <sub>17</sub> MgBr (3 eq C)	THF, 0°, 1.5 h	 (85)	172a
	<i>n</i> -C <sub>8</sub> H <sub>17</sub> MgBr (1 eq C)	THF, 0°, 30 min	 +  (87)	171a
	 MgCl (1 eq I)	THF, -50 to 20°, 30 min	 (90)	184
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	THF, 20°, 30 min	 (75)	176
	C <sub>6</sub> H <sub>5</sub> MgBr (1 eq I)	THF, 20°, 30 min	 (95)	176

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

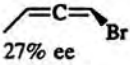
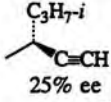
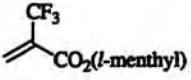
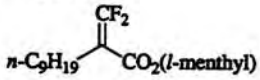
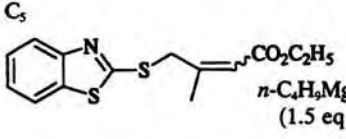
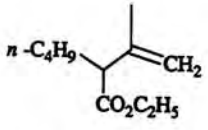
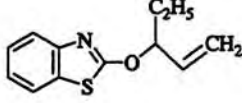

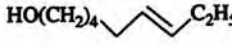
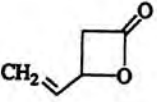
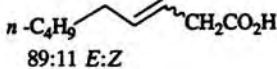
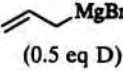
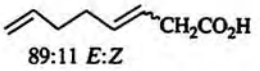
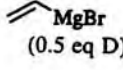
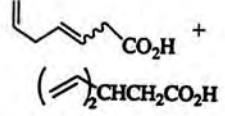
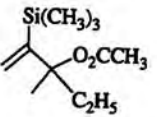
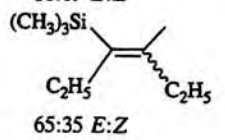
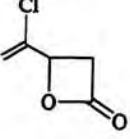
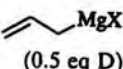
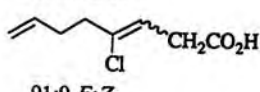
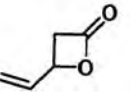
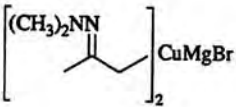
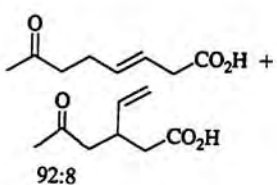
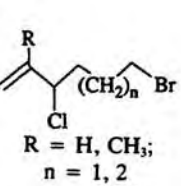
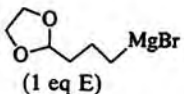
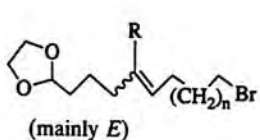
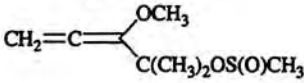
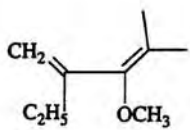
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
 27% ee	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgBr (1 eq I)	THF, -70°, 30 min	 25% ee	(—) 692
	<i>n</i> -C <sub>8</sub> H <sub>17</sub> MgBr (0.5 eq D)	Ether, (CH <sub>3</sub> ) <sub>3</sub> SiCl, 0°, 3 h		(84) 693
 C <sub>5</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1.5 eq C)	THF, -15°	 (78, 82°)	172b
	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> MgCl (1 eq C)	THF, 25°, 30 min		(73) 171a
	ClMgO(CH <sub>2</sub> ) <sub>4</sub> MgCl (1 eq C)	THF, 25°, 30 min		(90) 171a
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (0.5 eq D)	THF, -78°, 1 h	 89:11 <i>E</i> : <i>Z</i>	(92) 116
	 (0.5 eq D)	THF, -50°, 1 h	 89:11 <i>E</i> : <i>Z</i>	(88) 116
	 (0.5 eq D)	THF, -50°, 1 h	 81:19 <i>E</i> : <i>Z</i> (CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub> CO <sub>2</sub> H	(64) 116
	CH <sub>3</sub> MgI (0.5 eq D)	—	 65:35 <i>E</i> : <i>Z</i>	(80) 694
	 (0.5 eq D)	THF, DMS, -50°, 1 h	 91:9 <i>E</i> : <i>Z</i>	(77) 695
		1. THF, DMS, -100°, 2 h 2. 3 M aq. HCl	 92:8	(91) 696a
 R = H, CH <sub>3</sub> ; n = 1, 2	 (1 eq E)	—	 (mainly <i>E</i> )	(46-63) 697b
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq I)	THF, 20°, 30 min		(80) 176

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$n\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, $-50$ to $20^\circ$ , 30 min	 $\text{C}_2\text{H}_5$ $\text{C}_4\text{H}_9\text{-}n$	(83) 184
		THF, DMS (10:1), $-30$ to $0^\circ$ , 2.5 h	 69:31 <i>E:Z</i>	(49) 115
		THF, DMS (10:1), $-30$ to $0^\circ$ , 2.5 h	 76:24 <i>E:Z</i>	(57) 115
		THF, DMS (10:1), $-30$ to $0^\circ$ , 2.5 h	 75:25 <i>E:Z</i>	(89) 115
		THF, DMS (10:1), $-50$ to $-30^\circ$ , 2 h	 78:22 <i>E:Z</i>	(68) 115
		THF, DMS (10:1), $-30$ to $25^\circ$ , 1 h	 82:18 <i>E:Z</i>	(91) 117
		THF, DMS (10:1), $-30$ to $25^\circ$ , 1 h	 82:18 <i>E:Z</i>	(70) 117
		THF, DMS (10:1), $-30$ to $25^\circ$ , 1 h	 86:14 <i>E:Z</i>	(41) 117
	$\text{CH}_3\text{MgBr}$ (0.5 eq D)	THF, DMS, $-30^\circ$ , 1 h	 24:76 <i>E:Z</i> 8:92	(67) 650
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (0.5 eq D)	THF, DMS, $-30^\circ$ , 30 min	 3:97 <i>E:Z</i> 6:96	(84) 650
	$n\text{-C}_8\text{H}_{17}\text{MgBr}$ (3 eq C)	THF, $0^\circ$ , 1.5 h	 $\text{C}_8\text{H}_{17}\text{-}n$	(80) 172a
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (1.5 eq C)	THF, $-15^\circ$	 $n\text{-C}_4\text{H}_9$ $\text{CO}_2\text{C}_2\text{H}_5$	(85) 172b
	$\text{ClMgO}(\text{CH}_2)_4\text{MgCl}$ (1 eq D)	THF, $25^\circ$ , 30 min	 98:2 <i>E:Z</i>	(75) 170
	$\text{ClMgO}(\text{CH}_2)_6\text{MgCl}$ (1 eq D)	THF, $25^\circ$ , 5 h	 98:2 <i>E:Z</i>	(75) 170
	$i\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	Ether, $-70^\circ$ , 30 min	 $\text{C}_2\text{H}_5$ $\text{C}_4\text{H}_9\text{-}i$	(—) 692
	$\text{TMSCH}_2\text{MgCl}$ (1 eq I)	THF, $25^\circ$ , 30 min	 TMS	(95) 698

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

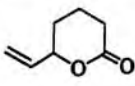
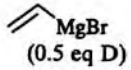
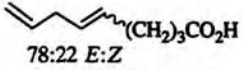
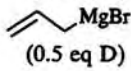
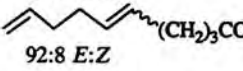
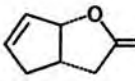
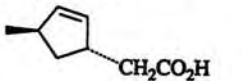
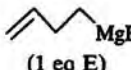
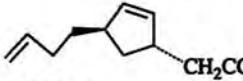
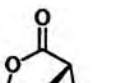
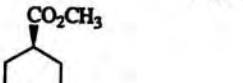

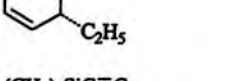
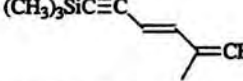
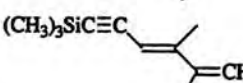
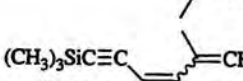
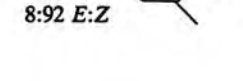
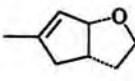
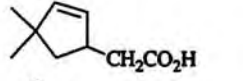
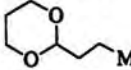

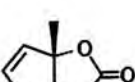
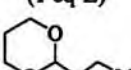

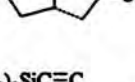
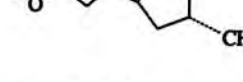
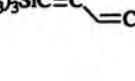
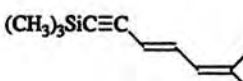
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.		
C <sub>7</sub>		 (0.5 eq D)	THF, DMS (20:1), -30°, 1 h	 78:22 E:Z	(67) 117	
		 (0.5 eq D)	THF, DMS (20:1), -30°, 1 h	 92:8 E:Z	(51) 117	
		CH <sub>3</sub> MgBr (1 eq E)	THF, -20°, 5 h		(97) <sup>r</sup> 174	
		 (1 eq E)	THF, DMS (7:3), -20°, 5 h		(94) <sup>r</sup> 174	
		C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	1. THF, -30 to 0°, 2 h 2. CH <sub>3</sub> COCl, CH <sub>3</sub> OH, 0°		(75) 699	
		<i>s</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	THF, -30°, 1 h		(—) 177	
		<i>s</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	1. THF, -30°, 1 h 2. CH <sub>3</sub> I		(85) 177	
		CH <sub>3</sub> MgCl (1 eq I)	THF, -30°, 1 h		(—) 177	
		C <sub>2</sub> H <sub>5</sub> MgCl (1 eq I)	THF, -30°, 1 h		(—) 177	
		<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	THF, -30°, 1 h		(—) 177	
	C <sub>4</sub>		CH <sub>3</sub> MgBr (1 eq E)	THF, DMS (7:3), -20°, 5 h		(73) <sup>r</sup> 174
			 (1 eq E)	THF, DMS (7:3), -20°, 5 h		(90) <sup>r</sup> 174
		 (1 eq E)	THF, DMS (7:3), -20°, 5 h		(83) <sup>r</sup> 174	
		<i>s</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	THF, -30°, 1 h		(—) 177	
		<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (1 eq I)	THF, -50 to 20°, 0.5 h		(80) 184	

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$n\text{-C}_3\text{H}_7\text{MgBr}$ (0.5 eq E)	THF, $-78^\circ$	$n\text{-C}_3\text{H}_7$ 85:15 E:Z	(80) 697a
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (0.5 eq D)	Ether, $0^\circ$ , 1 h	$n\text{-C}_4\text{H}_9$ 66:33 E:Z	(92) 169
C <sub>9</sub>				
	$\text{C}_2\text{H}_5\text{MgCl}$ (1 eq I)	THF, $-50$ to $20^\circ$ , 30 min		(70) 184
C <sub>10</sub>				
	$\text{CH}_3\text{MgCl}$ (1 eq I)	THF, $-10$ to $20^\circ$ , 30 min	 90:10 E:Z	(90) 176
	$i\text{-C}_3\text{H}_7\text{MgCl}$ (1 eq I)	THF, $20^\circ$ , 30 min	 95:5 E:Z	(90) 176
	$\text{C}_2\text{H}_5\text{MgCl}$ (1 eq I)	THF, $-30^\circ$ , 1 h	 98:2 E:Z	(—) 177
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (1 eq C)	THF, $0$ – $25^\circ$ , 30 min	 (88, 80 <sup>a</sup> )	171a
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (3 eq C)	THF, $0^\circ$ , 1.5 h		(90) 172a
	$i\text{-C}_3\text{H}_7\text{MgBr}$ (3 eq C)	THF, $0^\circ$ , 1.5 h		(83) 172a
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (0.5 eq D)	Ether, $0^\circ$ , 1 h	 + 94:6	(76) 169
C <sub>11</sub>				
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (0.5 eq D)	Ether, $0^\circ$ , 1.5 h	 40:60 E:Z	(86) 169
C <sub>12</sub>				
		THF, $-78^\circ$	 78:22 E:Z	(83) 697a

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

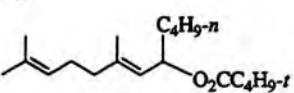
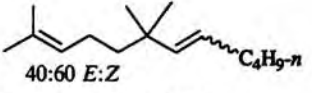
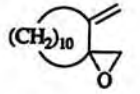
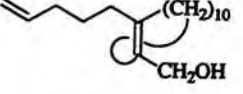
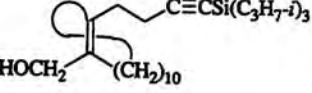
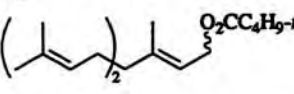
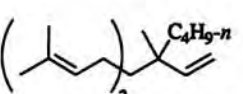
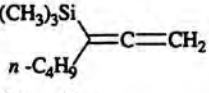
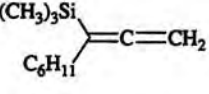
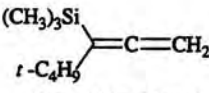
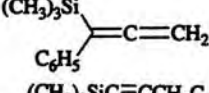
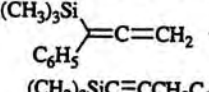
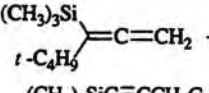
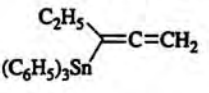
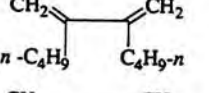
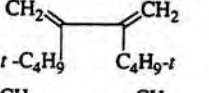
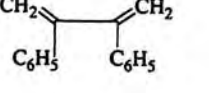
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{14}$ 	$CH_3MgI$ (0.5 eq D)	Ether, 0°, 3 h	 (62)	169
	$CH_3CH_2CH_2MgBr$ (1 eq D)	THF, DMS, -25°, 12 h	 (99)	700
	$(i-C_3H_7)_3SiC\equiv CCH_2MgBr$ (1 eq D)	THF, DMS, -78 to -20°, 12 h	 (79)	701
$C_{15}$ 	$n-C_4H_9MgBr$ (0.5 eq D)	Ether, 0°, 1 h	 (99)	169
<i>C. Reactions of Propargylic Substrates</i>				
$C_3$ $(CH_3)_3SiC\equiv CCH_2OS(O)CH_3$	$n-C_4H_9MgX$ (1 eq I)	THF, -60 to 20°, 1.5 h	 (88)	183
	$C_6H_{11}MgX$ (1 eq I)	THF, -60 to 20°, 1.5 h	 (90)	183
	$t-C_4H_9MgX$ (1 eq I)	THF, -60 to 20°, 1.5 h	 (30) (70)	183
	$C_6H_5MgX$ (1 eq I)	THF, -60 to 20°, 1.5 h	 (40) (60)	183
$(CH_3)_3SiC\equiv CCH_2OS(O)CH_3$	$C_6H_5MgX$ (1 eq I)	THF, -60 to 20°, 1.5 h	 (85) (15)	183
$(CH_3)_3SiC\equiv CCH_2OTs$	$t-C_4H_9MgX$ (1 eq I)	THF, -60 to 20°, 1.5 h	 (85) (15)	183
$(C_6H_5)_3SnC\equiv CCH_2Cl$	$C_2H_5MgBr$ (1 eq I)	THF, -60°, 1 h	 (90)	702
$C_4$ $CH_3(O)SOCH_2C\equiv CCH_2OS(O)CH_3$	$n-C_4H_9MgCl$ (2 eq) (2 eq I)	THF, -50 to 20°, 30 min	 (90)	29
	$t-C_4H_9MgCl$ (2 eq) (2 eq I)	THF, -50 to 20°, 30 min	 (90)	29
$p-CH_3C_6H_4SO_3CH_2C\equiv CCH_2OTs$	$C_6H_5MgBr$ (2 eq) (2 eq C)	THF, 25°, 30 min	 (95)	29

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

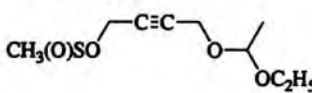
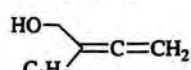
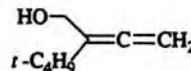
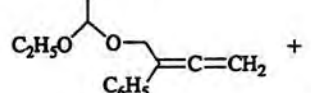
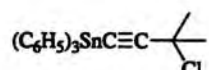
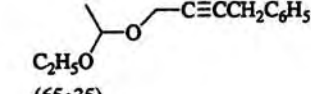
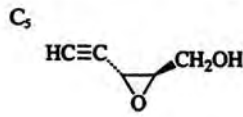
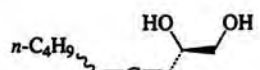
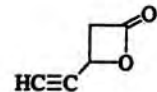
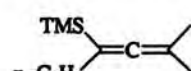
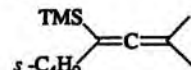
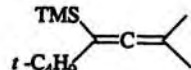
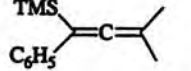
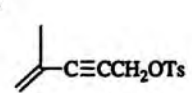
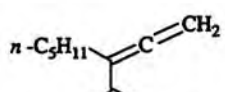
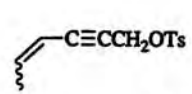
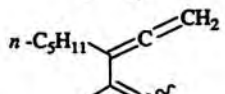
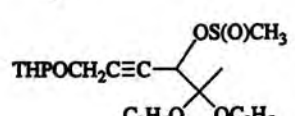
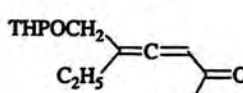
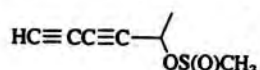
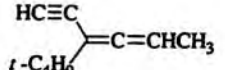
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$\text{CH}_3\text{CH}(\text{OSO}_2\text{C}_6\text{H}_4\text{CH}_3\text{-4})\text{-C}\equiv\text{CSi}(\text{CH}_3)_3$	$(\text{CH}_3)_3\text{SiCH}_2\text{MgCl}$ (1 eq I)	THF, 0°, 30 min	$\text{CH}_3\text{CH}=\text{C}=\text{C}(\text{Si}(\text{CH}_3)_3)\text{-CH}_2\text{Si}(\text{CH}_3)_3$	(70) 703
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq I)	THF, -50 to 20°, then TsOH/CH <sub>3</sub> OH, heat		(60) 188
	$t\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, -50 to 20°, then TsOH/CH <sub>3</sub> OH, heat		(73) 188
	$\text{C}_6\text{H}_5\text{MgBr}$ (1 eq I)	THF, -50 to 20°		(-) 188
	$t\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, -60°, 1 h		(>90) 704
		$n\text{-C}_4\text{H}_9\text{MgBr}$ (0.5 eq D)	Ether, -60°, 1.5 h	 <i>syn:anti</i> 1:99
	$\text{CH}_2=\text{CHMgBr}$ (0.5 eq D)	THF, DMS (10:1), -50°, 1 h	$\text{CH}_2=\text{CH}-\text{C}=\text{CHCH}_2\text{CO}_2\text{H}$	(54) 137
$\text{TMSC}\equiv\text{CC}(\text{CH}_3)_2\text{OS}(\text{O})\text{CH}_3$	$n\text{-C}_3\text{H}_7\text{MgX}$ (1 eq I)	THF, -60 to 20°, 1.5 h		(95) 183
	$s\text{-C}_4\text{H}_9\text{MgX}$ (1 eq I)	THF, -60 to 20°, 1.5 h		(94) 183
	$t\text{-C}_4\text{H}_9\text{MgX}$ (1 eq I)	THF, -60 to 20°, 1.5 h		(95) 183
	$\text{C}_6\text{H}_5\text{MgX}$ (1 eq I)	THF, -60 to 20°, 1.5 h		(91) 183
	$n\text{-C}_5\text{H}_{11}\text{MgBr}$ (1 eq C)	THF, 25°, 2 h		(76) 181
		$n\text{-C}_5\text{H}_{11}\text{MgBr}$ (1 eq C)	THF, 25°, 2 h	
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	THF, -30°, then dil. acid		(63) 189
	$t\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, -25°, 1 h		(60) 184

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

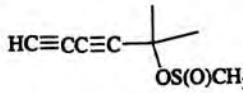
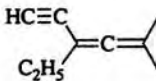
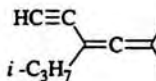
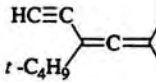
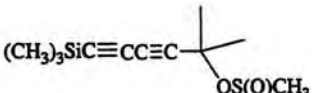
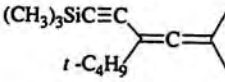
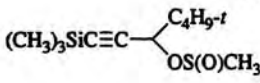
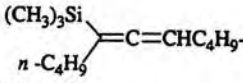
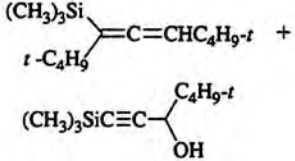
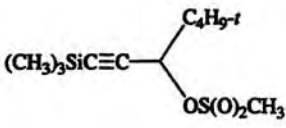
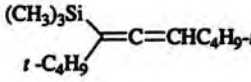
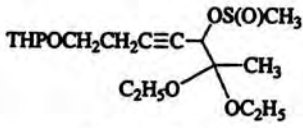
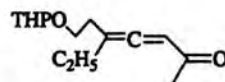
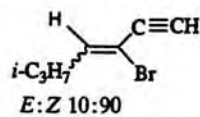
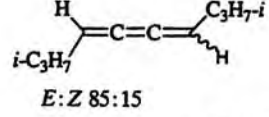
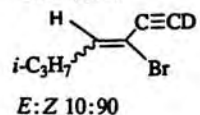
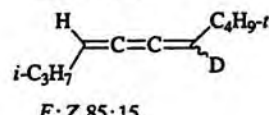
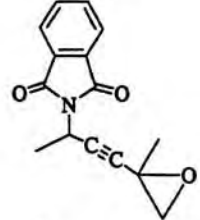
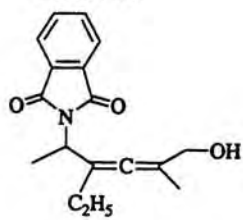
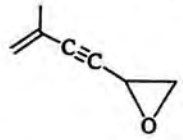
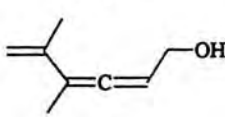
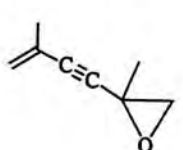
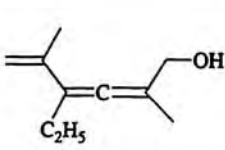
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$C_7$ 	$C_2H_5MgBr$ (1 eq I)	THF, 0°, 1 h	 (56)	184
	$i-C_3H_7MgCl$ (1 eq I)	THF, -25°, 1 h	 (25)	184
	$t-C_4H_9MgCl$ (1 eq I)	THF, -25°, 1 h	 (15)	184
	$t-C_4H_9MgCl$ (1 eq I)	THF, -25°, 1 h	 (90)	184
	$n-C_4H_9MgX$ (1 eq I)	THF, -60 to 20°, 1.5 h	 (91)	183
	$t-C_4H_9MgCl$ (1 eq I)	THF, -60 to 20°, 1.5 h	 (40)	183
	$t-C_4H_9MgX$ (1 eq I)	THF, -60 to 20°, 1.5 h	 (98)	183
	$C_2H_5MgBr$ (1 eq C)	THF, -30, then dil. acid	 (76)	189
 E:Z 10:90	$i-C_3H_7MgCl$ (1 eq I)	THF, -50 to 0°	 (90)	190
 E:Z 10:90	$t-C_4H_9MgCl$ (1 eq I)	THF, -50 to 0°	 (88)	190
	$C_2H_5MgBr$ (4 eq C)	THF	 (60)	706
	$CH_3MgCl$ (4 eq C)	THF, 20°, 2 h	 (60)	707
$C_8$ 	$C_2H_5MgBr$ (4 eq C)	THF, 20°, 2 h	 (50)	707



TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
 $n\text{-C}_4\text{H}_9$ <i>E:Z</i> 18:82	$t\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, -50 to 0°	 $n\text{-C}_4\text{H}_9$ <i>E:Z</i> 80:20	(95) 190
 $t\text{-C}_4\text{H}_9$ <i>E:Z</i> 7:93	$t\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, -50 to 0°	 $t\text{-C}_4\text{H}_9$ <i>E:Z</i> 97:3	(95) 190
 $t\text{-C}_4\text{H}_9$ <i>E:Z</i> 7:93	$i\text{-C}_3\text{H}_7\text{MgCl}$ (1 eq I)	THF, -50 to 0°	 $t\text{-C}_4\text{H}_9$ <i>E:Z</i> 90:10	(85) 190
	$\text{CH}_3\text{MgX}$ (1 eq I)	THF, -60 to 20°, 1.5 h		(91) 183
	$\text{C}_6\text{H}_5\text{MgX}$ (1 eq I)	THF, -60 to 20°, 1.5 h		(97) 183
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq I)	THF, -50 to 20°, then TsOH, CH <sub>3</sub> OH, heat		(75) 188
	$\text{C}_6\text{H}_5\text{MgBr}$ (1 eq I)	THF, -50 to 20°, then NaOH, CH <sub>3</sub> OH		(90) 188
	$\text{CH}_3\text{MgCl}$ (1 eq I)	THF, -50 to 20°, then NaOH, CH <sub>3</sub> OH		(70) 188
	$t\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, -25°, 1 h		(50) 184
	$t\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, -25°, 1 h		(90) 184
	$\text{C}_2\text{H}_5\text{MgBr}$ (1.3 eq C)	THF, -50 to 25°, 1 h		(85) 134
	$\text{C}_2\text{H}_5\text{MgBr}$ (excess) (1.3 eq C)	THF, -50 to 25°, 1 h		(62) 134
	$n\text{-C}_5\text{H}_{11}\text{MgBr}$ (4 eq) (1.3 eq C)	THF, -50 to 25°, 1 h		(74) 134
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (1 eq I)	THF, -60 to 0°, 15 min		(95) 708
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	THF, -30°, then dil. acid		(68) 189
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	THF, -30°, then dil. acid		(37) 189

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

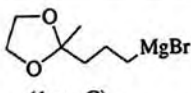
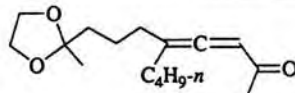
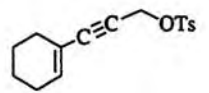
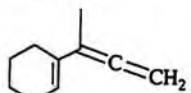
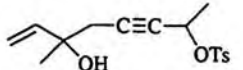
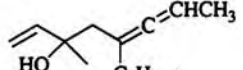
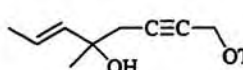
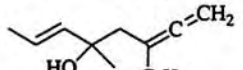
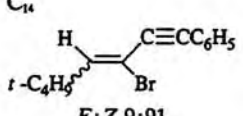
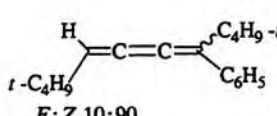
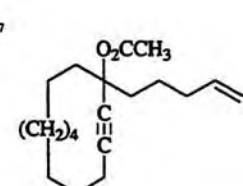
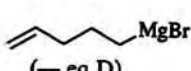
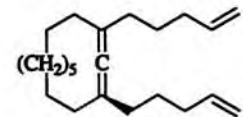
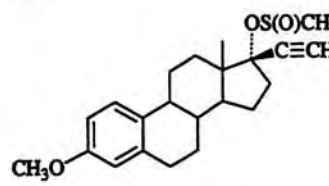
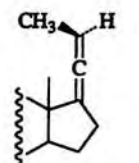
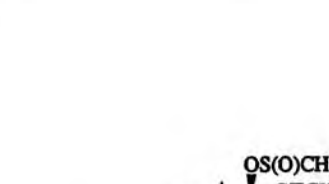
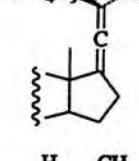
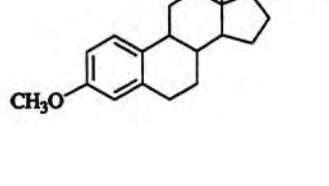
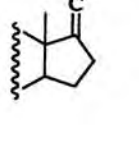
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	MgBr (1 eq C)	THF, -30°, then dil. acid		(70) 189
$(\text{CH}_3)_3\text{SiC}\equiv\text{CC}\equiv\text{C}-\text{C}(\text{OS}(\text{O})\text{CH}_3)(\text{C}_4\text{H}_9-t)$	$t\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, -25°, 1 h, then NaOH, CH <sub>3</sub> OH	$\text{HC}\equiv\text{C}-\text{C}(\text{C}_4\text{H}_9-t)=\text{C}=\text{CHC}_4\text{H}_9-t$	(80) 184
	$\text{CH}_3\text{MgCl}$ (3 eq C)	THF, 25°, 2 h		(80) 181
	$n\text{-C}_5\text{H}_{11}\text{MgBr}$ (4 eq) (1.3 eq C)	THF, -50 to 25°, 1 h		(74) 134
	$\text{C}_2\text{H}_5\text{MgBr}$ (4 eq) (1 eq C)	THF, -50 to 25, 1 h		(70) 134
$\text{C}_{14}$ 	$t\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq I)	THF, -50 to 0°		(95) 190
$\text{C}_{17}$ 	 (- eq D)	THF, DMS, -78 to 20°		(92) 709
$\text{C}_{21}$ 	$\text{CH}_3\text{MgBr}$ (1 eq I)	THF, 0°, 1 h		(>97) 192
	$t\text{-C}_4\text{H}_9\text{MgBr}$ (1 eq I)	THF, -50°, 1 h		(>97) 192
	$\text{CH}_3\text{MgCl}$ (1 eq I)	THF, 20°, 45 min		(98) 186

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

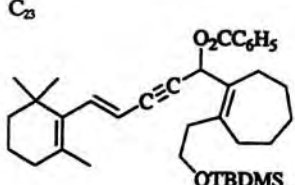
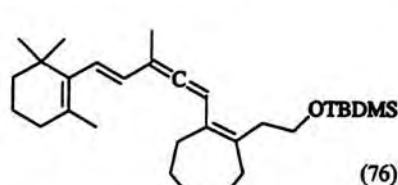
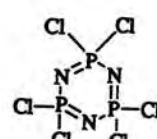
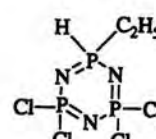
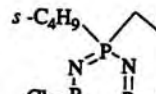
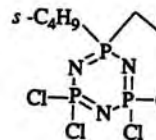
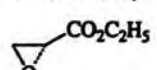
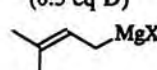
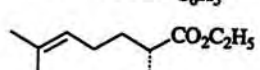
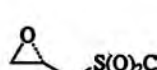
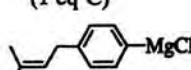
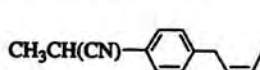
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{23}$ 	$CH_3MgBr$ (1 eq D · LiBr)	THF, 0°, 1 h	 (76)	710
D. Other Substitution Reactions				
$C_9$ $CpRe(NO)(CO)Cl$	$C_6H_5MgBr$ (excess D)	THF, 25°, 1 h	$CpRe(NO)(CO)C_6H_5$ (91)	711
	$p-CH_3C_6H_4MgBr$ (excess D)	THF, 25°, 1 h	$CpRe(NO)(CO)C_6H_4CH_3-p$ (90)	711
	$p-CF_3C_6H_4MgBr$ (excess D)	THF, 25°, 1 h	$CpRe(NO)(CO)C_6H_4CH_3-p$ (92)	711
$CpFe(CO)_2Br$	$C_6H_5MgBr$ (1 eq B)	—	$CpFe(CO)_2C_6H_5$ (55)	712
	$C_2H_5MgCl$ (0.5 eq[Cu·P(C <sub>4</sub> H <sub>7</sub> -n) <sub>3</sub> ])	1. THF, -30 to 25°, 16 h 2. <i>i</i> -C <sub>3</sub> H <sub>7</sub> OH	 (60)	713a
	$s-C_4H_9MgCl$ (0.5 eq[Cu·P(C <sub>4</sub> H <sub>7</sub> -n) <sub>3</sub> ])	1. THF, -30 to 25°, 16 h 2. 	 (65)	713b
$SO_2$	$n-C_4H_9$ $n-C_7H_{15}$ MgBr (1 eq C)	Ether, -40°	$n-C_4H_9$ $n-C_7H_{15}$ SO <sub>2</sub> H (100)	714
$C_2$ $(C_2H_5O)_2CHCH(OC_2H_5)$	$CH_3MgI$ (0.5 eq D)	—	$(C_2H_5O)_2CHCH(CH_3)OC_2H_5$ (85)	715
$(C_2H_5O)_2CHCH(OC_2H_5)$	$CH_3MgI$ (0.5 eq D)	Ether, 25°	$(C_2H_5O)_2CHCH(CH_3)OC_2H_5$ (85)	716
$C_3$ $n-C_4H_9O_2C-CH=CH_2$	$C_6H_5MgBr$ (0.5 eq D)	$CH_3CN$ , HMPA, PdCl <sub>2</sub> , LiCl, K <sub>2</sub> CO <sub>3</sub> , 0°, 20 h	$n-C_4H_9O_2C-CH=CH-C_6H_5$ (100) <sup>a</sup>	717
	 (0.5 eq CuX)	—	 (71)	718
	$n-C_8H_{17}MgBr$ (1.5 eq D)	Ether, THF, -60°, 1 min	$n-C_8H_{17}$ $S(O)_2C_6H_5$ (83)	719
$CH_3CH(CN)OSO_2CH_3$	$C_6H_5MgBr$ (1 eq C)	THF, 25°, 4 h	$CH_3CH(CN)C_6H_5$ (40)	720
	$1-C_{10}H_7MgCl$ (1 eq C)	THF, 25°, 4 h	$CH_3CH(CN)C_{10}H_7-1$ (37)	720
	 (1 eq C)	THF, 25°, 4 h	$CH_3CH(CN)-$  (56)	720
	$p-C_6H_5OC_6H_4MgCl$ (1 eq C)	THF, 25°, 4 h	$CH_3CH(CN)C_6H_4OC_6H_5-p$ (42)	720

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$n\text{-C}_8\text{H}_{17}\text{MgBr}$ (0.5 eq E)	THF	 $\text{C}_8\text{H}_{17}\text{-}n$ $n\text{-C}_8\text{H}_{17}\text{CH}_2\text{CH}=\text{C}=\text{CH}_2$	(6) (21) 645
	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{MgBr}$ (1 eq D) (1 eq $\text{BF}_3$ )	THF, 25°, 3 h		(81) 721
	$\text{CH}_3\text{MgX}$ (0.5 eq CuX)	—		(82) 722
$\text{C}_2\text{H}_5\text{CH}=\text{C}=\text{CHBr}$	$\text{C}_6\text{H}_5\text{MgBr}$ (1 eq I)	THF, -70 to 25°, 30 min	$\text{C}_6\text{H}_5\text{CH}(\text{C}_2\text{H}_5)\text{C}\equiv\text{CH}$	(79) 723
	$[t\text{-C}_4\text{H}_9\text{MgCl}]$ (0.5 eq G) (4 eq)	THF, -78 to 25°, 30 min		(52) 724
$n\text{-C}_4\text{H}_9\text{C}\equiv\text{CCl}$	$n\text{-C}_4\text{H}_9\text{MgBr}$ (1 eq D)	THF, ether, -40°, 2 h	$n\text{-C}_4\text{H}_9\text{C}\equiv\text{CC}_4\text{H}_9\text{-}n$	(72) 159
	$(\text{C}_6\text{H}_5\text{CH}_2)_2\text{CuMgCl}$	-78 to 0°		(73) 725
	$[n\text{-C}_4\text{H}_9\text{MgCl}]$ (0.5 eq B) (2 eq)	THF, -80°		(95) 726
	$\text{ClMg}(\text{CH}_2)_4\text{MgCl}$ (1 eq E, 1 eq $n\text{-C}_3\text{H}_7\text{C}\equiv\text{CLi}$ )	THF, -90 to 20°, 12 h		(40) 726
	$\text{CH}_2=\text{CHMgCl}$ (4 eq D)	Ether, -30°, 18 h		(45) 727
	$p\text{-CH}_3\text{C}_6\text{H}_4\text{MgBr}$ (0.5 eq C)	THF, -78 to 25°		(80) 728
	$\text{CH}_2=\text{CHMgBr}$ (0.5 eq D)	THF, HMPA, -23°		(83) 729
	$\text{CH}_3\text{O-C}_6\text{H}_4\text{-C}\equiv\text{CTMS}$ (1 eq E)	THF, -78 to 20°, 2 h		(31) 730

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>10</sub> 	 (0.5 eq C)	THF, -15°, 12 h	 C <sub>4</sub> H <sub>9</sub> -t	(68) 286
C <sub>13</sub> 	 (0.5 eq C)	THF, -30°		(86) 613
C <sub>20</sub> 	$\left[ \text{CH}_3\text{MgBr} \right]$ (0.5 eq C) (4 eq)	THF, -78 to 25°, 18 h		(75) 724
E. Conjugate Addition Reactions				
C <sub>3</sub> HC≡CCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq CH <sub>3</sub> Cu) <i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (1 eq CH <sub>3</sub> Cu)	Ether, -78°, 2 h Ether, -78°, 2 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> <i>i</i> -C <sub>3</sub> H <sub>7</sub>	(70) 249 (69) 249
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (0.5 eq E)	THF, (CH <sub>3</sub> ) <sub>3</sub> SiCl, (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N, -90°, 1 h	<i>n</i> -C <sub>5</sub> H <sub>11</sub>	(84) 240
	C <sub>6</sub> H <sub>5</sub> MgBr (0.5 eq C)	Ether, THF, DMS, -55°	 92% de	(92) 731
C <sub>1</sub> CH <sub>3</sub> O <sub>2</sub> CC≡CCO <sub>2</sub> CH <sub>3</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (1 eq E)	THF, -78°, 40 min	<i>n</i> -C <sub>6</sub> H <sub>13</sub>	(86) 235
	 (1 eq E)	THF, -78°, 40 min		(71) 235
	 (1 eq E)	THF, -78°, 40 min		(71) 235
	C <sub>6</sub> H <sub>5</sub> MgBr (1 eq D)	THF, -78°, 40 min	C <sub>6</sub> H <sub>5</sub>	(85) 235
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq D)	THF, -78°, 40 min	TMS	(97) 235

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

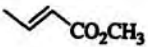
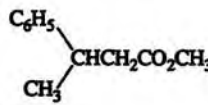
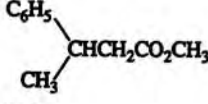

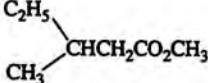
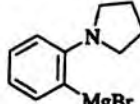
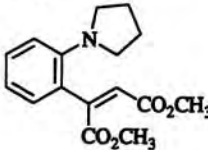
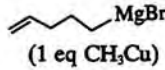
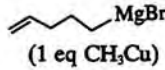


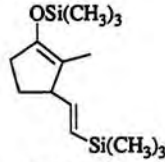
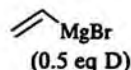
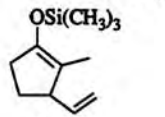

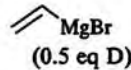
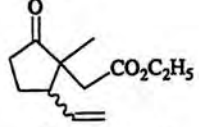
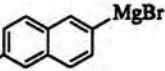
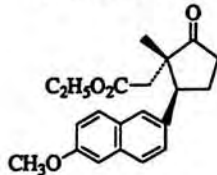
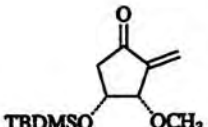
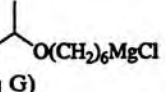
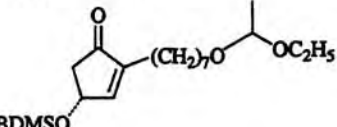
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	CH <sub>3</sub> MgI (0.5 eq D)	Ether, -10°, 2.5 h	<i>i</i> -C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> CH <sub>3</sub>	(25) 233
	CH <sub>3</sub> MgBr (1 eq C <sub>6</sub> H <sub>5</sub> SCu)	Ether, -70 to -10°, 2.5 h	<i>i</i> -C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> CH <sub>3</sub>	(33) 241
	C <sub>6</sub> H <sub>5</sub> MgBr (0.5 eq D)	Ether, -10°, 2.5 h		(70) 233
	C <sub>6</sub> H <sub>5</sub> MgCl (1 eq <i>o</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SCu)	Ether, -40°, 2 h		(100) 241
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C <sub>6</sub> H <sub>5</sub> SCu)	Ether, -70°C to -40°, 2 h		(41) 241
C <sub>2</sub> H <sub>5</sub> MgBr (1 eq <i>o</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SCu)	Ether, -70°C to -40°, 2 h		(94) 241	
CH <sub>3</sub> O <sub>2</sub> CC≡CCO <sub>2</sub> CH <sub>3</sub>	 (1 eq I)	THF, -50 to 0°, 2 h		(75) 732
C <sub>5</sub> (CH <sub>3</sub> ) <sub>2</sub> C=CHCOCH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> MgBr (0.5 eq D)	Ether, -10°, 2.5 h	(CH <sub>3</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> )CH <sub>2</sub> COCH <sub>3</sub>	(45-70) 233
	 (1 eq CH <sub>3</sub> Cu)			(79)(11) 246
	(CH <sub>3</sub> ) <sub>3</sub> Si-  (0.5 eq D)	THF, -70°, 30 min, then (CH <sub>3</sub> ) <sub>3</sub> SiCl, (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N, HMPA		(78) 238
	 (0.5 eq D)	THF, -40°, 45 min, then (CH <sub>3</sub> ) <sub>3</sub> SiCl, (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N, HMPA		(89) 253
	 (0.5 eq D)	THF, -30°, 45 min, then BrCH <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> , HMPA	 24:76 <i>cis:trans</i>	(81) 253
	CH <sub>3</sub> O-  <i>n</i> -C <sub>3</sub> H <sub>7</sub> C≡CCu	THF, 25°, 3 h, then ICH <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> , HMPA		(>95) 244
	 TBDMSO, OCH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub> O-  (1 eq G)	THF, -78 to 0°, 1 h	

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

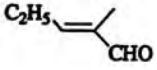
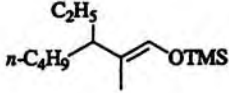
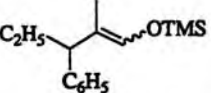
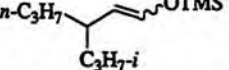
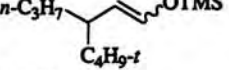
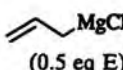
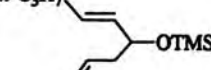
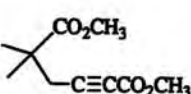
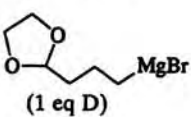
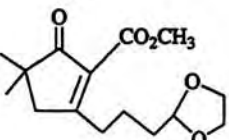
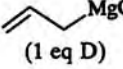
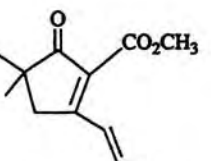
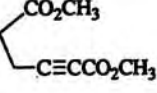
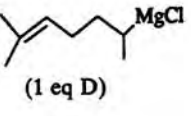
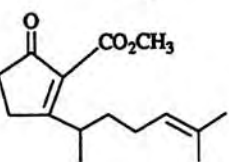
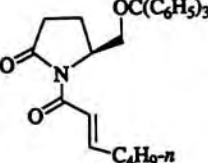
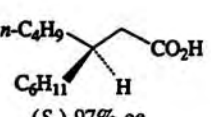
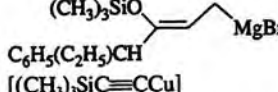
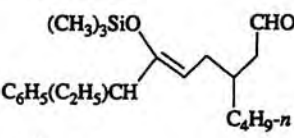

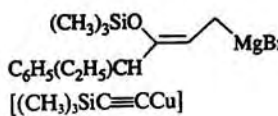
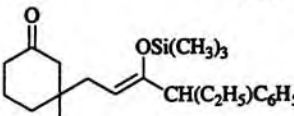
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$n\text{-C}_4\text{H}_9\text{MgCl}$ (0.5 eq E)	THF, TMSCl, $(\text{C}_2\text{H}_5)_3\text{N}$ , 90°, 1 h		(80)(4) <sup>i</sup> 240
	$\text{C}_6\text{H}_5\text{MgCl}$ (0.5 eq E)	"		(60)(12) <sup>i</sup> 240
$n\text{-C}_3\text{H}_7\text{CH=CHCHO}$	$i\text{-C}_3\text{H}_7\text{MgCl}$ (0.5 eq E)	"		(72) 240
	$t\text{-C}_4\text{H}_9\text{MgCl}$ (0.5 eq E)	"		(23)(21) <sup>i</sup> 240
	 (0.5 eq E)	"		(58) 240
	 (1 eq D)	THF, -78 to 25°, 5 h		(42) 236
	 (1 eq D)	THF, -78 to 25°, 5 h		(40) 236
	 (1 eq D)	THF, -78 to 25°, 5 h		(48) 236
	$\text{C}_6\text{H}_{11}\text{MgCl}$ (0.5 eq E)	1. THF, DMS, -23°, 1.5 h 2. HCl, CH <sub>3</sub> OH 3. KOH	 (S-) 97% ee	(76) 734
$n\text{-C}_4\text{H}_9\text{CH=CHCHO}$	 $\text{C}_6\text{H}_5(\text{C}_2\text{H}_5)\text{CH}$ [[ $(\text{CH}_3)_3\text{SiC}\equiv\text{CCu}$ ]]	Ether, THF, -20°, 2-12 h		(49) 735
	 $\text{C}_6\text{H}_5(\text{C}_2\text{H}_5)\text{CH}$ [[ $(\text{CH}_3)_3\text{SiC}\equiv\text{CCu}$ ]]	Ether, THF, -20°, 2-12 h		(74) 735

TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

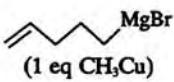
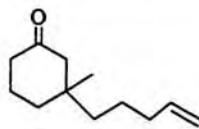
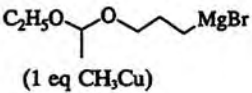
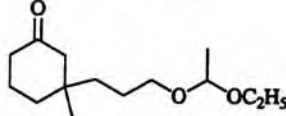
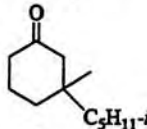
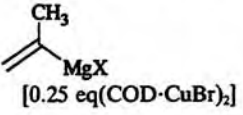
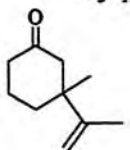
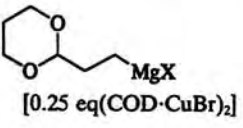
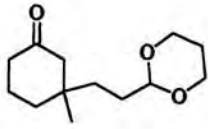
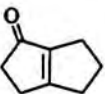
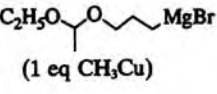
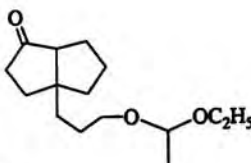
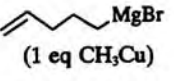
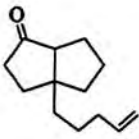
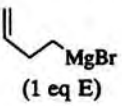
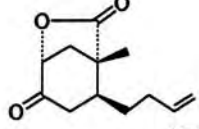
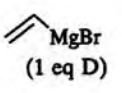
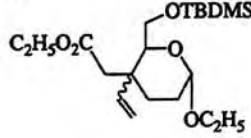
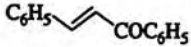
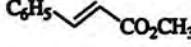

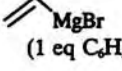
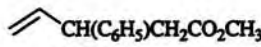
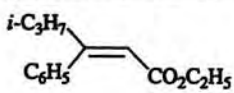
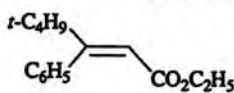
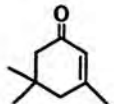
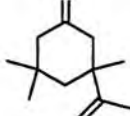
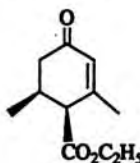
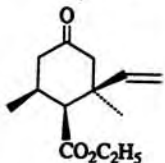
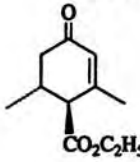
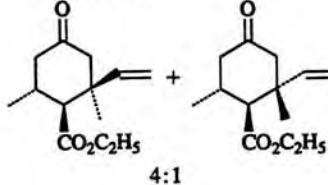
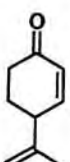
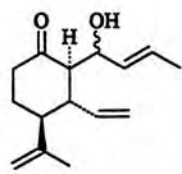
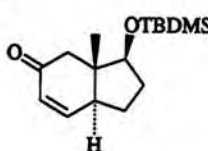
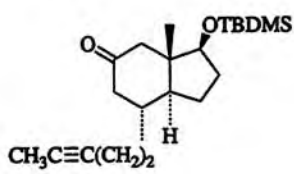
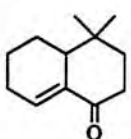
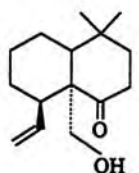
Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	 (1 eq CH <sub>3</sub> Cu)	THF		(76)(6) <sup>l</sup> 246
	 (1 eq CH <sub>3</sub> Cu)	THF		(56)(18) <sup>l</sup> 246
	<i>i</i> -C <sub>5</sub> H <sub>11</sub> MgX [0.25 eq(COD·CuBr) <sub>2</sub> ]	Ether, -30°, 1 h		(65) 251
	 [0.25 eq(COD·CuBr) <sub>2</sub> ]	Ether, -30°, 1 h		(58) 251
	 [0.25 eq(COD·CuBr) <sub>2</sub> ]	Ether, -30°, 1 h		(86) 251
C <sub>4</sub>				
	 (1 eq CH <sub>3</sub> Cu)	THF		(60) <sup>a</sup> (16) <sup>l</sup> 246
	 (1 eq CH <sub>3</sub> Cu)	THF		(80) <sup>a</sup> (3) <sup>l</sup> 246
	 (1 eq E)	THF, DMS, -10°		(74) 736
	 (1 eq D)	—		(—) 737
C <sub>5</sub>	 C <sub>6</sub> H <sub>5</sub> MgBr (0.5 eq D)	Ether, -10°, 2.5 h	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CHCH <sub>2</sub> COC <sub>6</sub> H <sub>5</sub>	(66) 233
	 CH <sub>3</sub> MgI (0.5 eq D)	Ether, -10°, 2.5 h	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	(46-58) 233
	 <i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq C <sub>6</sub> H <sub>5</sub> SCu)	THF, -10°, 1.5 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH(C <sub>6</sub> H <sub>5</sub> )CH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	(87) 241
	 (1 eq C <sub>6</sub> H <sub>5</sub> SCu)	Ether, -40°, 2.5 h		(90) 241



TABLE II. SUBSTITUTION AND CONJUGATE ADDITIONS OF STOICHIOMETRIC Cu(I)-RMgX REAGENTS (Continued)

Substrate	RMgX (mole % CuX)	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$C_6H_5C\equiv CCO_2C_2H_5$	$i-C_3H_7MgCl$ (1 eq $CH_3Cu$ )	Ether, $-10^\circ$		(65) 249
	$i-C_4H_9MgCl$ (1 eq $CH_3Cu$ )	Ether, $-10^\circ$		(47)(25) <sup>f</sup> 249
	$MgX$ [0.25 eq(COD-CuBr) <sub>2</sub> ] <sup>d</sup>	Ether, $-30^\circ$ , 1 h		(60) 251
	$MgBr$ (0.5 eq D)	THF, $-78$ to $-40^\circ$ , 1.5 h		(—) 237
	$MgBr$ (0.5 eq D)	THF, $-78$ to $-40^\circ$ , 1.5 h		(—) 237
	$MgBr$ (0.5 eq B)	1. Ether, $-75^\circ$ , 15 min 2. $CH_3CH=CHCHO$ , $ZnCl_2$		(88) 738
$C_{10}$ 	$CH_3C\equiv C-CH_2MgBr$ (1 eq D)	THF, $BF_3 \cdot Et_2O$ $-78$ to $25^\circ$ , 4 h		(55) 739
$C_{12}$ 	$MgX$ (0.5 eq CuX)	1. Ether, $-50^\circ$ 2. HCHO		(65) <sup>h</sup> 740

<sup>a</sup> The Grignard reagent was added immediately after mixing CuBr with the substrate.

<sup>b</sup> The Grignard reagent was added after stirring the CuBr with the substrates for 6 h.

<sup>c</sup> The substrate was the *E* isomer.

<sup>d</sup> The substrate was the *Z* isomer.

<sup>e</sup> There was also <2–5% of the *S<sub>N</sub>2* products.

<sup>f</sup> There was also 15% of the *S<sub>N</sub>2* product.

<sup>g</sup> The yield was based on PdCl<sub>2</sub>.

<sup>h</sup> The stereochemistry was not assigned.

<sup>i</sup> The values in parentheses are the percent of 1,2-addition product formed.

<sup>j</sup> The values in parentheses are the percent of methyl transfer product formed.

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
C <sub>2</sub> HC≡CH	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -50 to -20°, 15 min	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -50 to -20°, 15 min	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -50 to -15°	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -50 to -15°	
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgCl (1 eq C)	THF, -50 to -20°, 15 min	<i>i</i> -C <sub>3</sub> H <sub>7</sub> -Cu-MgBrCl
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -Cu-MgBr <sub>2</sub>
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -Cu-MgBr <sub>2</sub>
	(excess) <i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (0.5 eq D)	THF, DMS (20:1), -78 to -30°, 1 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -Cu <sub>2</sub> MgX
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq C)	THF, -50°, 10 min	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -Cu-MgBrCl
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq C)	THF, -50 to -20°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -Cu-MgBrCl
<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq C)	THF, -50 to -20°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -Cu-MgBrCl	
<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq C)	THF, -50 to -20°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -Cu-MgBrCl	
<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq C)	THF, -50 to -20°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -Cu-MgBrCl	
<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq C)	THF, -50 to -20°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -Cu-MgBr <sub>2</sub>	
<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (0.5 eq C)	THF, -50 to -20°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -Cu-MgX	
<i>n</i> -C <sub>5</sub> H <sub>11</sub> MgBr (0.5 eq D)	Ether, DMS (1:1), -23°, 2 h	<i>n</i> -C <sub>5</sub> H <sub>11</sub> -Cu-MgX	
<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (1 eq C)	THF, -50 to -20°, 15 min	<i>n</i> -C <sub>6</sub> H <sub>13</sub> -Cu-MgBr <sub>2</sub>	
<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (1 eq C)	Ether, DMS (1:1), -25°, 4 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> -Cu-MgBr <sub>2</sub>	
<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (1 eq C)	Ether, DMS (1:1), -25°, 4 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> -Cu-MgBr <sub>2</sub>	
(excess) <i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (0.5 eq D)	THF, DMS (20:1), -78 to -30°, 1 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> -Cu <sub>2</sub> MgX	
C <sub>6</sub> H <sub>11</sub> MgBr (1 eq C)	THF, -50 to -30°	C <sub>6</sub> H <sub>11</sub> -Cu-MgBr <sub>2</sub>	
C <sub>6</sub> H <sub>11</sub> MgCl (1 eq C)	THF, -50 to -20°	C <sub>6</sub> H <sub>11</sub> -Cu-MgBrCl	
(excess) <i>n</i> -C <sub>9</sub> H <sub>19</sub> MgBr (0.5 eq D)	THF, DMS (20:1), -78 to -30°, 1 h	<i>n</i> -C <sub>9</sub> H <sub>19</sub> -Cu <sub>2</sub> MgX	

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> PCl	THF, -40°, 1.5 h	C <sub>2</sub> H <sub>5</sub> -P(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> (—) <sup>a</sup>	209
(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> SnCl	THF, -40°, 1.5 h	C <sub>2</sub> H <sub>5</sub> -Sn(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> (—) <sup>a</sup>	209
<i>n</i> -C <sub>3</sub> H <sub>11</sub> C≡CBr	Ether, THF (1:1), TMEDA, -15°, 1 h	C <sub>2</sub> H <sub>5</sub> -C≡CC <sub>3</sub> H <sub>11</sub> - <i>n</i> (60)	159
(CH <sub>3</sub> ) <sub>3</sub> SiO-C≡CBr	Ether, THF (1:1), TMEDA, -15°, 1 h	C <sub>2</sub> H <sub>5</sub> -C≡C(CH <sub>2</sub> ) <sub>2</sub> OH (60)	159
O <sub>2</sub>	THF	<i>i</i> -C <sub>3</sub> H <sub>7</sub> -C≡C-C <sub>3</sub> H <sub>7</sub> - <i>i</i> (>95)	185
I <sub>2</sub>	Ether, -30°	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -I (64)	208
	Ether, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -CH=CH <sub>2</sub> (50)	208
	THF, DMS (20:1), -30°, 3 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -CH <sub>2</sub> CO <sub>2</sub> H (90)	228
1. CS <sub>2</sub> 2. CH <sub>3</sub> I	1. THF, -50°, 30 min 2. THF, -50 to 0°	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -C(S)SCH <sub>3</sub> ( <i>E</i> : <i>Z</i> 98:2) (75)	142
CH <sub>3</sub> SSO <sub>2</sub> CH <sub>3</sub>	THF, -40°, 10 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -SCH <sub>3</sub> (—) <sup>a</sup>	209
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH=CH <sub>2</sub> (>95) <sup>b</sup>	185
CICN	THF, -50 to -20°	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -CN (90)	227
C <sub>6</sub> H <sub>5</sub> S(O) <sub>2</sub> CN	THF, -50 to -20°	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -CN (92)	227
I <sub>2</sub>	THF, HMPT, -50 to 20°, 15 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -I (>90)	207
CICN (2 eq)	THF, -50 to -20°	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -CN (94)	227
	THF, ether, DMS, -30°, 3 h	<i>n</i> -C <sub>5</sub> H <sub>11</sub> -CH <sub>2</sub> CO <sub>2</sub> H (87)	117
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	<i>n</i> -C <sub>6</sub> H <sub>13</sub> CH=CH <sub>2</sub> (~90) <sup>b</sup>	185
NCS	Ether, DMS, THF, -25°, 1 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> -Cl (50)	206
NBS	Ether, DMS, THF, -25°, 1 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> -Br (52)	206
	THF, DMS (20:1), -30°, 3 h	<i>n</i> -C <sub>6</sub> H <sub>13</sub> -CH <sub>2</sub> CO <sub>2</sub> H (87)	228
BrCN	THF, HMPT, -50 to 20°	C <sub>6</sub> H <sub>11</sub> -Br (>90)	207
(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> SnCl	THF, -40°, 1.5 h	C <sub>6</sub> H <sub>11</sub> -Sn(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> (—) <sup>a</sup>	209
	THF, DMS (20:1), -30°, 3 h	<i>n</i> -C <sub>9</sub> H <sub>19</sub> -CH <sub>2</sub> CO <sub>2</sub> H (81)	228

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq CuBr·LiI)	Ether, 10°	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu·MgBrCl
	(CH <sub>3</sub> ) <sub>3</sub> SiCH-(C <sub>3</sub> H <sub>7-n</sub> )MgCl (1 eq [CuBr·2 LiCl])	THF, -20°, 2 h	(CH <sub>3</sub> ) <sub>3</sub> SiCH(C <sub>3</sub> H <sub>7-n</sub> )-CH=Cu·MgBrCl
	(CH <sub>3</sub> ) <sub>3</sub> SiCH-(C <sub>3</sub> H <sub>11-n</sub> )MgCl (3 eq [CuBr·2 LiCl])	THF, -30 to -20°, 2 h	(CH <sub>3</sub> ) <sub>3</sub> SiCH(C <sub>3</sub> H <sub>11-n</sub> )-CH=Cu·MgBrCl
(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> SiC≡CH	C <sub>2</sub> H <sub>5</sub> MgX <sup>c</sup> (CuY)	THF, -50°, 10 min	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>2</sub> H <sub>5</sub>
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgX <sup>c</sup> (CuY)	THF, -50°, 10 min	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>3</sub> H <sub>7-i</sub>
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgX <sup>c</sup> (CuY)	THF, -50°, 10 min	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>4</sub> H <sub>9-t</sub>
	C <sub>6</sub> H <sub>11</sub> MgX <sup>c</sup> (CuY)	THF, -50°, 10 min	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>6</sub> H <sub>11</sub>
C <sub>2</sub> H <sub>5</sub> OC≡CH	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgX <sup>c</sup> (CuY)	—	C <sub>2</sub> H <sub>5</sub> O-CH=Cu-CH <sub>2</sub> -C <sub>4</sub> H <sub>9</sub>
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq C)	Ether, -40°, 3 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>2</sub> H <sub>5</sub> O
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq C)	Ether, -40°, 3 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>2</sub> H <sub>5</sub> O
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq C)	Ether, -40°, 3 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>2</sub> H <sub>5</sub> O
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq C)	Ether, -40°, 3 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>2</sub> H <sub>5</sub> O
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq C)	Ether, -40°, 3 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>2</sub> H <sub>5</sub> O
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq C)	Ether, -40°, 3 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>2</sub> H <sub>5</sub> O
	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq C)	Ether, -40°, 3 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>2</sub> H <sub>5</sub> O

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)


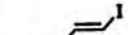


Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
Li <sub>2</sub> CuCl <sub>4</sub>	THF, 20°, 2 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -Si(CH <sub>3</sub> ) <sub>3</sub> (42)	222c
I <sub>2</sub>	THF, 10°, 1 h	(CH <sub>3</sub> ) <sub>3</sub> SiCH(C <sub>3</sub> H <sub>7-n</sub> )-CH=I (38)	222c
NH <sub>4</sub> Cl/NH <sub>4</sub> OH	—	(CH <sub>3</sub> ) <sub>3</sub> SiCH(C <sub>3</sub> H <sub>11-n</sub> )-CH= (56)	222b
NBS or BrCN	THF, 20°	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -Br (—) <sup>a</sup>	203
CH <sub>3</sub> I	THF, 20°	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -CH <sub>3</sub> (—) <sup>a</sup>	203
NCS	THF, 20°	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -Cl (—) <sup>a</sup>	203
NH <sub>4</sub> Cl/H <sub>2</sub> O	THF, 20°	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>6</sub> H <sub>11</sub> (—) <sup>a</sup>	203
CH <sub>3</sub> COCl	THF, 3% Pd-[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub>	C <sub>2</sub> H <sub>5</sub> O-CH=Cu-CH <sub>2</sub> -COCH <sub>3</sub> (74)	221
NH <sub>4</sub> Cl/NH <sub>4</sub> OH	THF, 3% Pd-[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub>	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -CH=O (68)	222b
Li <sub>2</sub> CuCl <sub>4</sub>	THF, -10°, 2 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -OC <sub>2</sub> H <sub>5</sub> (55)	222c
I <sub>2</sub>	THF, -10°, 1 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -I (54)	222c
	THF, ether, LiI, 20°, 3 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -CH=CH <sub>2</sub> (41)	222c
	THF, ether, 5% Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub> , 20°, 2 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -C <sub>4</sub> H <sub>9-n</sub> (78)	222c
	THF, ether, 5% Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub> , 20°, 2 h	(CH <sub>3</sub> ) <sub>3</sub> Si-CH=Cu-CH <sub>2</sub> -COC <sub>6</sub> H <sub>13-n</sub> (65)	222c
CH <sub>3</sub> COCl	THF, 5% Pd [P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub> , -10°, 2 h	C <sub>2</sub> H <sub>5</sub> O-CH=Cu-CH <sub>2</sub> -OSi(CH <sub>3</sub> ) <sub>3</sub> (59)	222c
	THF, 5% Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub> , -10°, 2 h	C <sub>2</sub> H <sub>5</sub> O-CH=Cu-CH <sub>2</sub> -OSi(CH <sub>3</sub> ) <sub>3</sub> (76)	222c

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
C <sub>3</sub> CH <sub>3</sub> C≡CH	(CH <sub>3</sub> ) <sub>3</sub> SiCH-(C <sub>3</sub> H <sub>7-n</sub> )MgCl (1 eq CuBr·LiI)	Ether, 10°, 18 h	
	(CH <sub>3</sub> ) <sub>3</sub> SiCH-(C <sub>3</sub> H <sub>6-n</sub> )MgCl (1 eq CuBr·LiI)	Ether, 10°, 18 h	
		THF, -20°, 2 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -50 to -20°, 15 min	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -50 to -20°, 15 min	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -15°, 1.5 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -50 to -15°	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -50 to -15°	

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
CH <sub>3</sub> COCl	THF, 5% Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub> , -10°, 2 h		(48) 222c
NH <sub>4</sub> Cl/NH <sub>4</sub> OH	—		(62) 222b
NH <sub>4</sub> Cl/NH <sub>4</sub> OH	—		(66) 222b
I <sub>2</sub>	Ether, -30°		(76) 208
CH <sub>3</sub> SSO <sub>2</sub> CH <sub>3</sub>	THF, -40°, 10 min		(—) <sup>a</sup> 209
(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> SnCl	THF, -40°, 1.5 h		(—) <sup>a</sup> 209
n-C <sub>4</sub> H <sub>9</sub> I	Ether, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h		(58) 208
	Ether, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h		(73) 208
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Br	Ether, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h		(85) 208
	Ether, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h		(83) 208
	Ether, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h		(38) 208
Cl(CH <sub>2</sub> ) <sub>3</sub> I	Ether, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h		(48) 208
CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> I	Ether, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h		(56) 208
C <sub>6</sub> H <sub>5</sub> C≡CCH <sub>2</sub> Br	Ether, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h		(10) 208
CH <sub>3</sub> O <sub>2</sub> CC≡CBr	Ether, THF, TMEDA, -15°, 1 h		(78) 159
(CH <sub>3</sub> ) <sub>3</sub> SiO(CH <sub>2</sub> ) <sub>n</sub> C≡CBr	Ether, THF, TMEDA, -15°, 1 h, then 2 N H <sub>2</sub> SO <sub>4</sub>		(82) (n = 1) (84) (n = 2) 159

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	Ether, -15°, 1 h	
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgBr (1 eq E)	Ether, DMS (1:1), -25°, 4 h	
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgX <sup>c</sup> (1 eq CuY)	—	
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgX <sup>c</sup> (1 eq CuY)	—	
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgX <sup>c</sup> (1 eq CuY)	—	
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgX (1 eq CuY)	—	
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgCl (1 eq C)	THF, -15°, 30 min	
	<i>n</i> -C <sub>6</sub> H <sub>13</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2.2 h	
	MgBr (1 eq C)	Ether, -15°, 1.5 h	
(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> C≡CH	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq [CuBr·1.5 Lil])	Ether, -10°, 10 h	
C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CC≡CH	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq C)	Ether, -50°, 2 h	
(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CHC≡CH	(CH <sub>3</sub> ) <sub>3</sub> SiCH <sub>2</sub> MgCl (1 eq C)	THF, -10°, 6 h	
C <sub>4</sub>			
C <sub>2</sub> H <sub>5</sub> C≡CH	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgBr (1 eq E)	Ether, DMS (1:1), -25°, 4 h	
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2 h	

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	Ether, -20°, 1 h		(96) 127
NBS	Ether, DMS, THF, -25°, 1 h		(72) 206
<i>i</i> -C <sub>4</sub> H <sub>9</sub> COCl	THF, 3% Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub>		(84) 221
C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCl	THF, 3% Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub>		(56) 221
	THF, 3% Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub>		(58) 221
	THF, 3% Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub>		(85) 221
NH <sub>4</sub> Cl/H <sub>2</sub> O	—		(~90) <sup>b</sup> 185
	Ether, DMS (1:1), -23 to 0°, 14 h		(73) 218b
CH <sub>3</sub> I	Ether, HMPA, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -10°, 1.5 h		(68) 208
NH <sub>4</sub> Cl/NH <sub>4</sub> OH	—		(56) 222b
NH <sub>4</sub> Cl/NH <sub>4</sub> OH	—		(55) 222a,b
NH <sub>4</sub> Cl/NH <sub>4</sub> OH	—	<i>E:Z</i> 75:25 	(25) 222a,b
NCS	Ether, DMS, THF, -25°, 1 h		(98) 206
	Ether, DMS, HMPA, -33°, 24 h <sup>d</sup>		(75) 218b

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (1 eq E)	Ether, DMS (1:1), $-23^\circ$ , 2 h	
	$n\text{-C}_3\text{H}_7\text{MgBr}$ (1 eq E)	Ether, DMS (1:1), $-23^\circ$ , 2 h	
	$n\text{-C}_6\text{H}_{13}\text{MgBr}$ (1 eq E)	Ether, DMS (1:1), $-23^\circ$ , 2 h	
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (1 eq C)	Ether, $-15^\circ$ , 1 h	
	$s\text{-C}_4\text{H}_9\text{MgBr}$ (1 eq C)	Ether, $-15^\circ$ , 1 h	
$\text{HC}\equiv\text{CC}\equiv\text{CH}$	$n\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq C)	THF, $-60^\circ$ , 30 min	
$\text{CH}_3\text{C}\equiv\text{CCN}$	$\text{C}_6\text{H}_5\text{MgBr}$ (1 eq C)	THF, $0^\circ$ , 30 min	
$\text{C}_5$ $\text{C}_2\text{H}_5\text{C}\equiv\text{CCN}$	$\text{C}_6\text{H}_5\text{MgBr}$ (1 eq C)	THF, $-50^\circ$ , 30 min	
	(1 eq B)	THF, $-10^\circ$ , 2.5 h	
$n\text{-C}_3\text{H}_7\text{C}\equiv\text{CH}$	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq E)	Ether, DMS (1:1), $-23^\circ$ , 2 h	

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	Ether, DMS, HMPA, $-33^\circ$ , 24 h	(82)	218b
	Ether, DMS (1:1), $-23$ to $0^\circ$ , 14 h	(50)	218b
	Ether, DMS (1:1), $-23$ to $0^\circ$ , 14 h	(68)	218b
$(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{SC}_6\text{H}_5$ (0.75 eq)	THF, ether (1:1), $25^\circ$ , 3-4 h	(87)	225
$\text{I}_2$	Ether, $-30^\circ$	(73)	208
$\text{NH}_4\text{Cl}/\text{H}_2\text{O}$	—	(>80)	201
$\text{NH}_4\text{Cl}/\text{H}_2\text{O}$	—	66:34 E:Z (94)	741a
$\text{NH}_4\text{Cl}/\text{H}_2\text{O}$	—	(92)	741a
$\text{NH}_4\text{Cl}/\text{H}_2\text{O}$	—	(88)	741a
	Ether, DMS (1:1), $-23$ to $0^\circ$ , 14 h	(50)	218b

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
$n\text{-C}_4\text{H}_9\text{C}\equiv\text{CH}$	$\text{CH}_3\text{MgBr}$ (1 eq E)	Ether, DMS (1:), $-25^\circ$ , 65 h	
	$\text{C}_2\text{H}_5\text{MgBr}$ (0.5 eq C)	THF, $0^\circ$ , 1 h	
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	Ether, $-50$ to $-15^\circ$	
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	Ether, $-50$ to $-15^\circ$	
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	Ether, $-50$ to $-15^\circ$	
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	Ether, $-15^\circ$ , 1 h	
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	Ether, $-15^\circ$ , 1 h	
	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	Ether, $-15^\circ$ , 1 h	
	$n\text{-C}_3\text{H}_7\text{MgBr}$ (1 eq E)	Ether, DMS (1:1), $-25^\circ$ , 2 h	
	$n\text{-C}_3\text{H}_7\text{MgBr}$ (1 eq E)	Ether, DMS (1:1), $-25^\circ$ , 2 h	
	$i\text{-C}_3\text{H}_7\text{MgBr}$ (0.5 eq C)	THF, $-50$ to $-30^\circ$	
	$i\text{-C}_3\text{H}_7\text{MgCl}$ (1 eq C)	THF, $-50$ to $-30^\circ$	
	$i\text{-C}_3\text{H}_7\text{MgBr}$ (1 eq C)	THF, $-50$ to $-30^\circ$	
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (1 eq C)	Ether, $-15^\circ$ , 1.5 h	

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	Ether, DMS, HMPT, $-30^\circ$ , 12 h	(84)	218a
$\text{CH}_3\text{SSO}_2\text{CH}_3$ (2 eq)	THF, $-40^\circ$ , 10 min	(—) <sup>a</sup>	209
$n\text{-C}_3\text{H}_7\text{C}\equiv\text{CBr}$	Ether, THF, TMEDA, $-15^\circ$ , 2 h	(78)	159
$(\text{CH}_3)_3\text{SiC}\equiv\text{Cl}$	Ether, THF, TMEDA, $-15^\circ$ , 2 h, then $\text{NaOCH}_3$ , $\text{CH}_3\text{OH}$	(82)	159
$\text{THPOCH}_2\text{C}\equiv\text{CBr}$	Ether, THF, TMEDA, $-15^\circ$ , 1 h, then 2 N $\text{H}_2\text{SO}_4$	(80)	159
$(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{SC}_6\text{H}_5$ (0.75 eq)	Ether, THF (1:1), $25^\circ$ , 3-4 h	(71)	225
	Ether, $-20^\circ$ , 2 h	(78)	127
$\text{CO}_2$	Ether, HMPT, 10% $\text{P}(\text{OC}_2\text{H}_5)_3$ , $-45^\circ$ , 4 h	(95)	224
	Ether, DMS, HMPA, $-33^\circ$ , 24 h <sup>d</sup>	(95)	218b
	Ether, DMS, HMPA, $-33^\circ$ , 24 h <sup>d</sup>	(26)	218b
$\text{BrCN}$ (2 eq)	THF, HMPT, $-50^\circ$ , $20^\circ$ , 15 min	(>90)	207
$\text{CH}_3\text{SSO}_2\text{CH}_3$	THF, $-40^\circ$ , 10 min	(—) <sup>a</sup>	209
$\text{ClCN}$	THF, $-50$ to $-20^\circ$	(92)	227
$\text{CH}_3\text{I}$	Ether, HMPT, $\text{P}(\text{OC}_2\text{H}_5)_3$ , $-10^\circ$ , 1.5 h	(63)	208

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
$n\text{-C}_4\text{H}_9\text{C}\equiv\text{CH}$	$\text{C}_2\text{H}_5\text{MgBr}$ (1 eq C)	Ether, $-15^\circ$ , 1.5 h	
	$n\text{-C}_4\text{H}_9\text{MgCl}$ (1 eq C)	THF, $-50^\circ$ , 10 min	
	$n\text{-C}_5\text{H}_{11}\text{MgCl}$ (0.5 eq C)	THF, $0^\circ$ , 45 min	
	$\text{C}_6\text{H}_{11}\text{MgCl}$ (0.5 eq C)	THF, $0^\circ$ , 45 min	
	$(\text{CH}_3)_3\text{SiCH}_2\text{MgCl}$ (1 eq CuBr·LiI)	Ether, $10^\circ$ , 18 h	
	$(\text{CH}_3)_3\text{SiCH}_2\text{MgCl}$ (1 eq CuBr·LiI)	Ether, $10^\circ$ , 18 h	
	$(\text{CH}_3)_3\text{SiCH}_2\text{MgCl}$ (1 eq CuBr·LiI)	Ether, $10^\circ$ , 18 h	
$t\text{-C}_4\text{H}_9\text{C}\equiv\text{CH}$	$t\text{-C}_4\text{H}_9\text{MgCl}$ (0.5 eq C)	THF, $0^\circ$ , 45 min	
	$n\text{-C}_5\text{H}_{11}\text{C}\equiv\text{CH}$	1. Ether, $-45$ to $-25^\circ$ 2. HMPT, $\text{P}(\text{OC}_2\text{H}_5)_3$ , $-25^\circ$ , 2 h	
$\text{C}_7$	$(\text{CH}_3)_3\text{SiCH}_2\text{MgCl}$ (1 eq C)	Ether, $30^\circ$ , 48 h	
	$n\text{-C}_6\text{H}_{13}\text{C}\equiv\text{CH}$	$\left[ \begin{array}{l} \text{CH}_3\text{MgCl} \\ (0.5 \text{ eq CuBr}\cdot\text{LiBr}) \\ (5 \text{ eq}) \end{array} \right]$	
$\text{C}_8$	$\text{CH}_3\text{MgBr}$ (1 eq E)	Ether, DMS (1:1), $-25^\circ$ , 65 h	

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$i\text{-C}_3\text{H}_7\text{I}$	Ether, HMPT, $\text{P}(\text{OC}_2\text{H}_5)_3$ , $-10^\circ$ , 1.5 h		(15) 208
1. $\text{CS}_2$ 2. $\text{CH}_3\text{I}$	1. THF, $-50^\circ$ , 30 min 2. THF, $-50$ to $0^\circ$		(80) 142
$\text{NH}_4\text{Cl}/\text{H}_2\text{O}$	—		(>95) <sup>b</sup> 741b
$\text{NH}_4\text{Cl}/\text{H}_2\text{O}$	—		(>95) <sup>b</sup> 741b
$\text{NH}_4\text{Cl}/\text{NH}_4\text{OH}$	—		94:6 (78) 222b
$\text{Li}_2\text{CuCl}_4$	THF, $20^\circ$ , 2 h		(52) 222c
$\text{I}_2$	THF, $20^\circ$ , 1 h		(45) 222c
$\text{CH}_3\text{COCl}$	THF, 5% $\text{Pd}[\text{P}(\text{C}_6\text{H}_5)_3]_4$ , $-10^\circ$ , 2 h		(42) 222c
$\text{NH}_4\text{Cl}/\text{H}_2\text{O}$	—		(~30) <sup>b</sup> 741b
$\text{P}(\text{O})(\text{OC}_2\text{H}_5)_2$	Ether, $-25$ to $20^\circ$ , 3 h		(70) 742
$\text{NH}_4\text{Cl}/\text{NH}_4\text{OH}$	—		(78) 222a
$\text{NH}_4\text{Cl}/\text{H}_2\text{O}$	—		(>95) <sup>b</sup> 741b
$\text{CH}_2=\text{CHBr}$	Ether, DMS, HMPT, $-30^\circ$ , 12 h		(81) 218a



TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

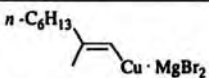
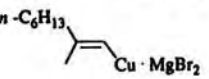
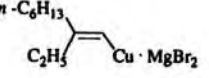
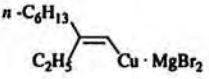
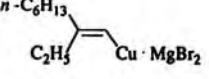
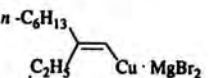
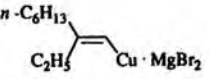
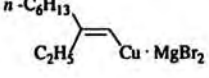
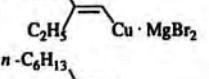
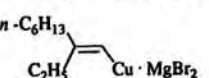
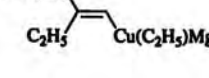

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
	CH <sub>3</sub> MgBr (1 eq E)	Ether, DMS (1:1), -25°, 65 h	
	CH <sub>3</sub> MgBr (1 eq E)	Ether, DMS (1:1), -25°, 5 d	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2.25 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2.25 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2.25 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2.25 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2.25 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2.25 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2.25 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	Ether, DMS (1:1), -23°, 2.25 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -15°, 1 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (0.5 eq C)	THF, 0°, 45 min	

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

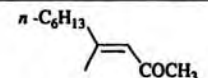



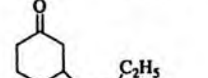
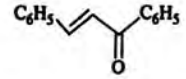
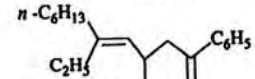
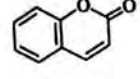
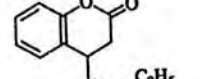

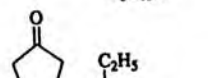
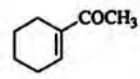
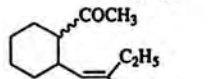
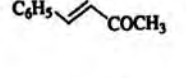
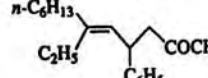
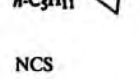
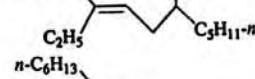
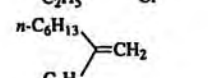
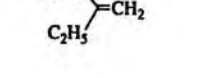

Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
CH <sub>3</sub> COCl	Ether, DMS, HMPT, -30°, 12 h	 (65)	218a
	Ether, DMS (1:1), -23 to 0°, 14 h	 (63)	218b
	Ether, DMS (1:1), -23 to 0°, 14 h	 (70)	218b
	Ether, DMS (1:1), -23 to 0°, 14 h	 (52)	218b
	Ether, THF, DMS, <sup>d</sup> HMPA, 4°, 60 h	 (62)	218b
	Ether, DMS, HMPA, <sup>d</sup> -78°, 4 h	 (30)	218b
	Ether, DMS, HMPA, <sup>d</sup> -23°, 12 h	 (69)	218b
	Ether, DMS, HMPA, <sup>d</sup> 4°, 12 h	 (53)	218b
	Ether, DMS, HMPA, <sup>d</sup> -33°, 24 h	 (94)	218b
NCS	Ether, DMS, THF, -25°, 1 h	 (61)	206
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	 (10-15) <sup>b</sup>	185
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	 (>95) <sup>b</sup>	741b

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
C <sub>6</sub> H <sub>11</sub> C≡CH	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq CuOC <sub>4</sub> H <sub>9</sub> - <i>t</i> )	THF, -10°, 20 min	
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgCl (0.5 eq C)	THF, 0°, 45 min	
C <sub>6</sub> H <sub>5</sub> C≡CH	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -50 to -30°, 10 min	
	<i>n</i> -C <sub>3</sub> H <sub>7</sub> MgBr (1 eq C)	THF, -20°, 30 min	
C <sub>6</sub> H <sub>5</sub> C≡CH	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgBr (1 eq C)	THF, -20°, 30 min	
	<i>i</i> -C <sub>3</sub> H <sub>7</sub> MgBr (0.5 eq C)	THF, -20°, 1 h	
C <sub>6</sub> H <sub>5</sub> C≡CH	[CH <sub>3</sub> MgCl (0.5 eq I)] (2 eq)	THF, 0°, 1 h	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -50 to -30°	
C <sub>6</sub> H <sub>5</sub> C≡CH	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -50 to -30°	
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq E)	Ether, DMS (1:1), -25°, 4 h	
C <sub>6</sub> H <sub>5</sub> C≡CSCH <sub>3</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq C)	THF, -50 to -20°, 30 min	
	C <sub>6</sub> H <sub>5</sub> MgBr (0.5 eq C)	THF, 30°, 1 h	
C <sub>6</sub> H <sub>5</sub> C≡CCN	CH <sub>3</sub> MgCl (1 eq C)	THF, -50°, 15 min	
	CH <sub>3</sub> MgCl (0.5 eq C)	THF, -50 to 30°, 1 h	

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(>95) <sup>b</sup>	185
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(>95) <sup>b</sup>	741b
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(>95) <sup>b</sup>	185
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(>95) <sup>b</sup>	185
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(>95) <sup>b</sup>	185
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(>95) <sup>b</sup>	741b
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(>90) <sup>b</sup>	741b
BrCN	THF, HMPT, -50°, 20°, 15 min	(>90)	207
(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> SnCl	THF, -40°, 1.5 h	(—) <sup>a</sup>	209
NCS	Ether, THF, DMS, -25°, 1 h	(63)	206
(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> NCH <sub>2</sub> SC <sub>6</sub> H <sub>5</sub> (0.75 eq)	THF, ether (1:1), 25°, 3 h	(66)	225
1. CS <sub>2</sub> 2. CH <sub>3</sub> I	1. THF, 30°, 1 h 2. THF, 30°, 1 h	(98)	142
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(95)	741a
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(93)	741a

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Acetylene Derivative	RMgX (Eq. of CuX)	Carbometallation Conditions	Adduct
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -50°, 30 min	
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq C)	THF, -50°, 10 min	
	CH <sub>3</sub> MgCl (1 eq C)	THF, 0°, 30 min	
C <sub>10</sub> C <sub>6</sub> H <sub>5</sub> C≡CC≡CH	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgCl (1 eq I)	THF, -60°, 30 min	
C <sub>13</sub> 	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq C)	THF, -50°, 15 min	

<sup>a</sup> Yields are in the range 80–95%.

<sup>b</sup> The yield was not reported; the number represents the percent conversion of the alkyne.

<sup>c</sup> The preparation of the reagent was not specified.

<sup>d</sup> 1-Lithio-1-pentyne (1 eq) was added to the alkenylcopper prior to addition of the electrophile.

TABLE III. CARBOCUPRATION REACTIONS OF STOICHIOMETRIC Cu(I)/RMgX REAGENTS (Continued)

Electrophile	Substitution Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(92)	741a
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(96)	741a
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(90)	741a
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(>80)	201
NH <sub>4</sub> Cl/H <sub>2</sub> O	—	(98)	741a

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES

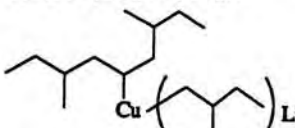
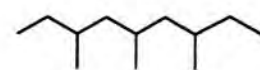
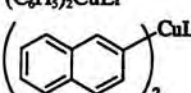
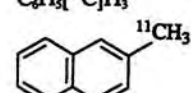
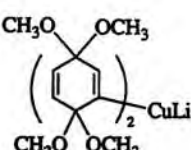
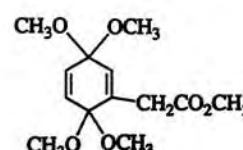


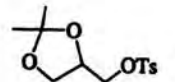
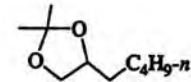
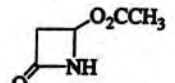
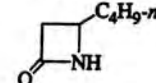
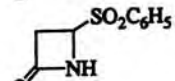
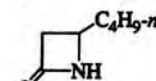
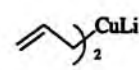
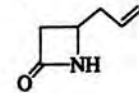
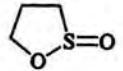
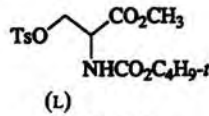
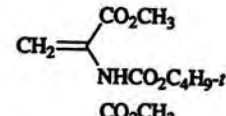
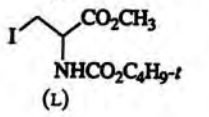
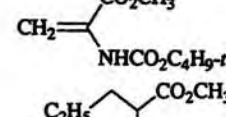
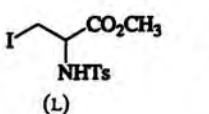
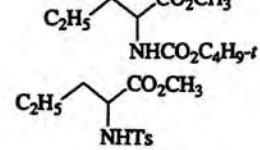
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
<i>A. Reactions of Alkyl, Alkenyl, and Aryl Halides and Sulfonates</i>				
C <sub>1</sub>				
CH <sub>3</sub> I	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH(CH <sub>3</sub> )Cu(CH <sub>3</sub> )Li <i>t</i> -C <sub>4</sub> H <sub>9</sub> CH( <i>n</i> -C <sub>4</sub> H <sub>9</sub> )Cu( <i>n</i> -C <sub>4</sub> H <sub>9</sub> )Li C <sub>6</sub> H <sub>11</sub> CH(CH <sub>3</sub> )Cu(CH <sub>3</sub> )Li	Ether, -70 to 0°, 30 min Ether, -70 to 0°, 30 min Ether, -70 to 0°, 30 min	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH(CH <sub>3</sub> ) <sub>2</sub> <i>t</i> -C <sub>4</sub> H <sub>9</sub> CH(CH <sub>3</sub> )C <sub>4</sub> H <sub>9</sub> - <i>n</i> C <sub>6</sub> H <sub>11</sub> CH(CH <sub>3</sub> ) <sub>2</sub>	(89) 743 (86) 743 (75) 743
		Ether, -70 to 0°, 30 min		(23) 743
<sup>11</sup> CH <sub>3</sub> I	( <i>n</i> -C <sub>8</sub> H <sub>17</sub> ) <sub>2</sub> CuLi (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CuLi 	Ether, 30°, 10 min Ether, 30°, 30 min Ether, 30°, 15 min	<i>n</i> -C <sub>8</sub> H <sub>17</sub> [ <sup>11</sup> C]H <sub>3</sub> C <sub>6</sub> H <sub>5</sub> [ <sup>11</sup> C]H <sub>3</sub> 	(95) <sup>a</sup> 278 (99) <sup>a</sup> 278 (95) <sup>a</sup> 278
C <sub>2</sub>				
BrCH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>		THF, -60 to 25°, 1.5 h		(32) 310
C <sub>6</sub> H <sub>5</sub> (O) <sub>2</sub> S-CH=CH-F	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, 0°, 30-45 s	C <sub>6</sub> H <sub>5</sub> (O) <sub>2</sub> S-CH=CH- 	(75-95) <sup>b</sup> 291
C <sub>6</sub> H <sub>5</sub> (O) <sub>2</sub> S-CH=CH-F	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, 0°, 30-45 s	C <sub>6</sub> H <sub>5</sub> (O) <sub>2</sub> S-CH=CH-  50:50 <i>E</i> : <i>Z</i>	(75-95) <sup>b</sup> 291
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	Ether, 20°, 2 h		(80) 280
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	THF, -78 to 0°, 1.5 h		(89) 744
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	THF, -78 to 0°, 1.5 h		(94) 744
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	THF, -78 to 0°, 1.5 h		(100) 744
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	Ether, 0°, 15 min Ether, 0°, 15 min	CH <sub>3</sub> S(O)(CH <sub>2</sub> ) <sub>3</sub> OH C <sub>6</sub> H <sub>5</sub> S(O)(CH <sub>2</sub> ) <sub>3</sub> OH	(59) 293 (32) 293
C <sub>3</sub>				
	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi (4 eq)	Ether, -60°, 3 h		(90) 282
	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi (4 eq)	Ether, -60°, 3 h	 + (42)	282
	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi (4 eq)	Ether, -60°, 3 h		(48) (70) 282

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(n\text{-C}_3\text{H}_7)_2\text{CuLi}$ (4 eq)	Ether, $-60^\circ$ , 3 h		(74) 282
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$ (4 eq)	Ether, $-10^\circ$ , 5 h		(65) 282
	 (4 eq)	Ether, $-60^\circ$ , 18 h		(69) 282
	$n\text{-C}_4\text{H}_9\text{Li}$ + 0.6 eq CuI	THF, TMEDA, $-78^\circ$ , 15 min		(65) 745
	$s\text{-C}_4\text{H}_9(\text{C}_6\text{H}_5\text{S})\text{CuLi}$ , 2.5 eq	THF		(65) 746
	$[\text{TBDMSO}(\text{CH}_2)_3]_2\text{CuLi}$ , 2 eq	Ether, DMS, $-50^\circ$ , 30 min		(98) 747
	$(\text{allyl})_2\text{CuLi}$	Ether, THF, $-78^\circ$ , 20 min	 <i>cis:trans</i> 5:95	(75) 748
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (3 eq)	Ether, $-80$ to $-20^\circ$ , 1 h		(71) 749
$\text{Br}(\text{CH}_2)_3\text{Cl}$		THF, $-20^\circ$		(76) 750
$n\text{-C}_4\text{H}_9\text{Br}$	$t\text{-C}_4\text{H}_9\text{CH}(\text{CH}_3)\text{Cu}(\text{CH}_3)\text{Li}$	Ether, $-70$ to $0^\circ$ , 30 min	$t\text{-C}_4\text{H}_9\text{CH}(\text{C}_6\text{H}_9\text{-}n)\text{CH}_3$	(83) 743
$\text{Br}(\text{CH}_2)_4\text{Cl}$		THF, $-35^\circ$ , 1.5 h		(90) 281
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	Ether, THF, $25^\circ$ , 2 h		(47) 751
$\text{C}_6\text{H}_5\text{CH}_2\text{OCH}_2$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	1. THF, $-48^\circ$ , 30 min 2.		(65) 284a
	$(t\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	Ether, $(n\text{-C}_4\text{H}_9)_2\text{S}$ , $-60^\circ$ , 18 h		(74) 282
	$(n\text{-C}_3\text{H}_7)_2\text{CuLi}$ (4 eq)	Ether, $-60^\circ$ , 3 h		(75) 282
	 (4 eq)	Ether, $(n\text{-C}_4\text{H}_9)_2\text{S}$ , $-60^\circ$ , 18 h		(69) 282
	 (4 eq)	Ether, $(n\text{-C}_4\text{H}_9)_2\text{S}$ , $-60^\circ$ , 18 h		(65) 282
	 (4 eq)	Ether, $(n\text{-C}_4\text{H}_9)_2\text{S}$ , $-60^\circ$ , 3 h		(71) 282

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

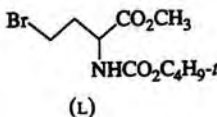
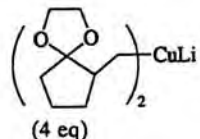
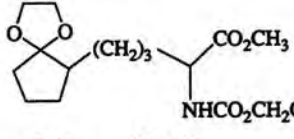
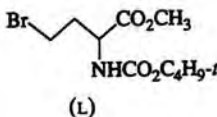
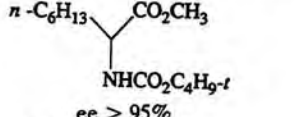
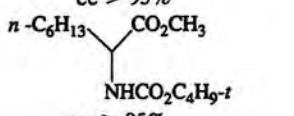
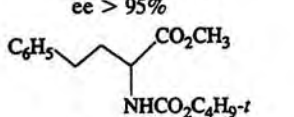
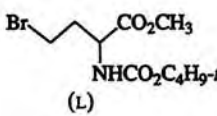
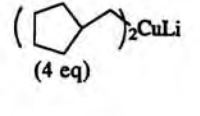
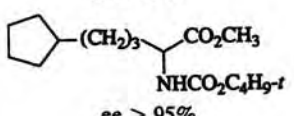
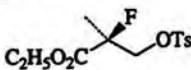
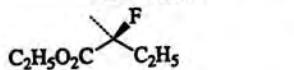
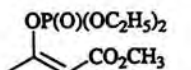
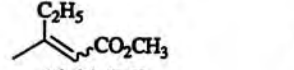
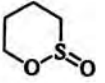
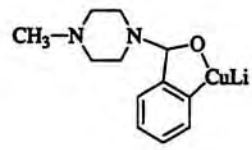
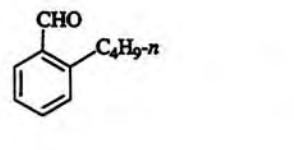
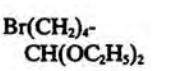

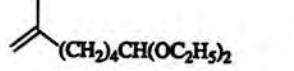
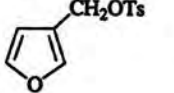
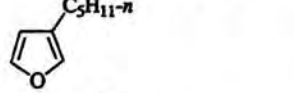
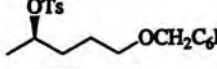
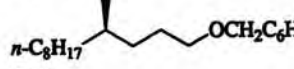
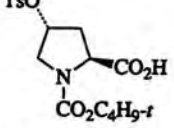
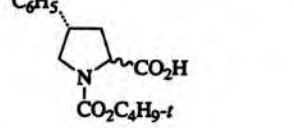
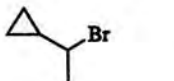
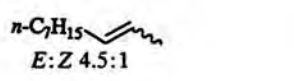
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
		Ether, ( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> S, -60°, 3 h	 (22)	282
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi (4 eq)	THF, -10°, 7 h	 (74)	282
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi (4 eq)	Ether, -5°, 14 h	 ee > 95% (51)	282
	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CuLi (4 eq)	Ether, -5°, 14 h	 ee > 95% (71)	282
		Ether, -5°, 14 h	 ee > 95% (44)	282
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, 0-5°, 15 h	 (50)	752
	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi (2 eq)	Ether, -90 to -45°, 1-4 h	 16:84 E:Z (>90)	288
	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	Ether, 0°, 15 min	C <sub>6</sub> H <sub>5</sub> S(O)(CH <sub>2</sub> ) <sub>4</sub> OH (52)	293
<i>n</i> -C <sub>4</sub> H <sub>9</sub> I		C <sub>6</sub> H <sub>6</sub> , THF, -42 to 0°, 5 h	 (47)	753
C <sub>5</sub> 		THF, -35°, 1.5 h	 (72)	281
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	Ether, -20°, 4 h	 (45)	754
	( <i>n</i> -C <sub>8</sub> H <sub>17</sub> ) <sub>2</sub> CuLi	Ether, -45°, 2 h	 (73)	755
	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CuLi (2 eq)	Ether, THF, DMS 0°	 (90)	756
	( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub> CuLi	Ether, -20°, 4 h	 (71)	757
C <sub>6</sub> I(CH <sub>2</sub> ) <sub>4</sub>	([ <sup>13</sup> C]H <sub>3</sub> ) <sub>2</sub> CuLi	Ether, 25°, 12 h	<sup>13</sup> CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> (—)	279

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

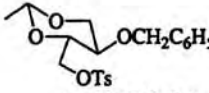
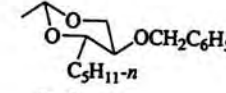
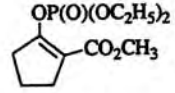
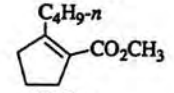
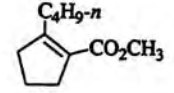
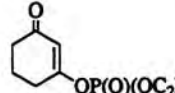
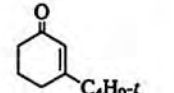
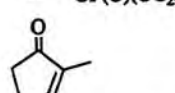
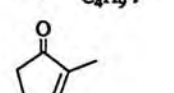
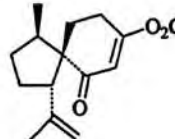
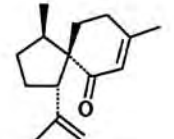
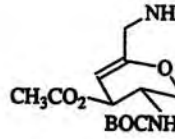
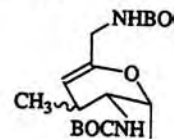
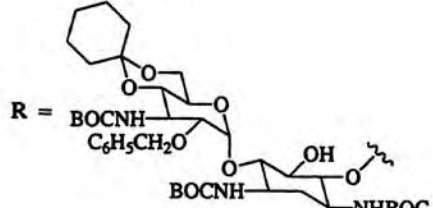
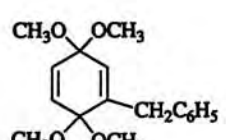
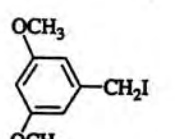
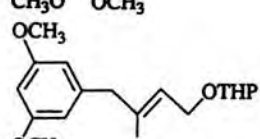
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$C_6H_{11}I$	$n-C_4H_9Cu(-C\equiv C-\langle OCH_3 \rangle Li)$	THF, $-20^\circ$	$C_6H_{11}C_4H_9-n$ (40)	266
	$(n-C_4H_9)_2CuLi$ (2 eq)	Ether, $CH_2Cl_2$ , $-20^\circ$ , 2 h		(80) 280
	$n-C_4H_9)_2CuLi$ (2 eq)	Ether, $-90$ to $-45^\circ$ , 1-4 h		(67) 288
	$(n-C_4H_9)_2CuLi$ (2 eq)	Ether, $n-C_4H_9Br$ , $-90$ to $-45^\circ$ , 1-4 h		(80) 288
	$(t-C_4H_9)_2CuLi$ (2 eq)	Ether, $-90$ to $-45^\circ$ , 1-4 h		(83) 288
	$(CH_3)_2CuLi$ (2 eq)	Ether, $-90$ to $-45^\circ$ , 1-4 h		(74) 288
$C_6H_5I$	$\left( \begin{array}{c} CH_3O \\ C_6H_5S \end{array} \right)_2 CuLi$	THF, $-78^\circ$ , 3 h	$\begin{array}{c} CH_3O \\ C_6H_5S \end{array} - C_6H_5$ (—)	758
	$(CH_3)_2CuLi$	Ether, $-78^\circ$ , 1 h		(80) 759
$C_6H_5SO_2CH_3$	$(CH_3)_2CuLi$	Ether, $0^\circ$ , 15 min	$C_6H_5S(O)CH_3$ (59)	293
	$(n-C_4H_9)_2CuLi$	Ether, $-40^\circ$ , 15 min	$C_6H_5SC_4H_9-n$ (36)	293
	$(C_6H_5)_2CuLi$	Ether, $0^\circ$ , 15 min	$(C_6H_5)_2S=O$ (50)	293
$C_6H_5SO_2C_6H_4CH_3-p$	$(CH_3)_2CuLi$	Ether, $0^\circ$ , 15 min	$C_6H_5S(O)CH_3$ + $(C_6H_5)SCH_3$ (22) (53)	293
$p-CH_3C_6H_4SO_2R^{*d}$ (S) <sup>r</sup>	$(CH_3)_2CuLi$	Ether, $0^\circ$ , 1 h	$p-CH_3C_6H_4S(O)CH_3$ (55)	293
	$(C_6H_5)_2CuLi$	Ether, $0^\circ$ , 1 h	$p-CH_3C_6H_4S(O)C_6H_5$ (59)	293
	$(CH_3)_2CuLi$	Ether, $-15$ to $0^\circ$		(51) 863
$R =$ 				
$C_6H_5CH_2Br$	$\left( \begin{array}{c} CH_3O \\ OCH_3 \end{array} \right)_2 CuLi$	THF, $-60$ to $25^\circ$ , 1.5 h		(67) 310
	$Cu(-C\equiv C-\langle OCH_3 \rangle Li)$	THF, $-20^\circ$		(92) 266

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (2 eq)	Ether, $-20^\circ$ , 2 h	$(n\text{-C}_5\text{H}_{11})_2\text{CHOTBDMS}$ (90)	280
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	Ether, $-48^\circ$ , 1 h, then $\text{CH}_3\text{I}$ , $-48$ to $25^\circ$ , 3 h		(82) 284b
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	Ether, $-48$ to $0^\circ$ , 1 h, then $\text{CH}_3\text{I}$ , $0$ to $25^\circ$ , 16 h		(78) 284b
	$(\text{CH}_2\text{=CH-CH}_2\text{CH}_2)_2\text{CuLi}$ (2 eq)	Ether, $-70$ to $-20^\circ$ , 1 h, then $\text{CH}_3\text{I}$ , $-20$ to $25^\circ$ , 16 h		(44) 284b
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (2 eq)	Ether, $n\text{-C}_4\text{H}_9\text{Br}$ , $-90$ to $-45^\circ$ , 1-4 h		(73) 288
	$(s\text{-C}_4\text{H}_9)_2\text{CuLi}$ (2 eq)	Ether, $-90$ to $-45^\circ$ , 1-4 h		(20) 288
	$(t\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	Ether, $-90$ to $-45^\circ$ , 1-4 h		(80) 288
	$(\text{C}_2\text{H}_5)_2\text{CuLi}$ (1 eq $\text{C}_2\text{H}_5\text{Li}$ )	Ether, $0-10^\circ$ , 24 h		(74) 760
	$(\text{CH}_3)_2\text{CuLi}$ (10 eq)	—		(97) 761
$n\text{-C}_6\text{H}_{13}\text{CH}(\text{I})\text{OTMS}$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ $\text{CuI}$ (1 eq)	Ether, $-20$ to $25^\circ$ , 1 d	$n\text{-C}_6\text{H}_{13}\text{CH}(\text{OH})\text{C}_4\text{H}_9\text{-}n$ (77)	762
	$\text{CH}_3(\text{OC}_4\text{H}_9\text{-}t)\text{CuLi}$	THF, $-78^\circ$ , 15 min		(55) 763
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	Ether, $0^\circ$ , 3 d		(84) 51
	$t\text{-C}_4\text{H}_9(\text{SC}_6\text{H}_5)\text{CuLi}$ (5 eq)	Ether, $0^\circ$ , 3 d		(91) 51
$n\text{-C}_8\text{H}_{17}\text{Br}$	$(\text{C}=\text{C})_2\text{CuLi}$	THF, $0^\circ$ , 45 min		(91) 764
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	1. THF, $-48$ to $0^\circ$ , 30 min 2.  Br, $0^\circ$ , 30 min		(65) 284a



TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

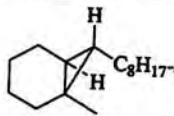
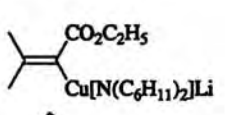
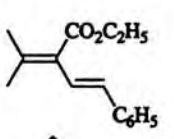
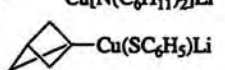
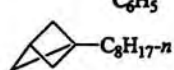
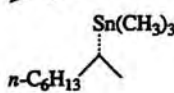
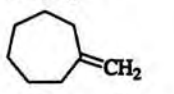
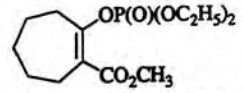
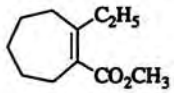
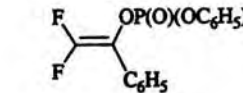
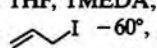
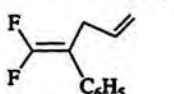
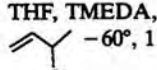
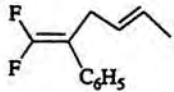
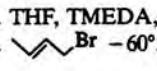
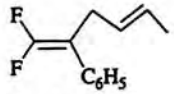
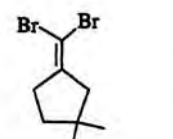
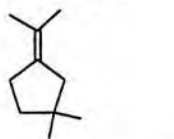
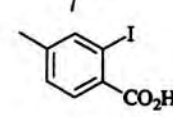
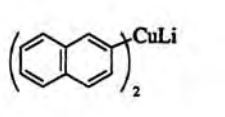
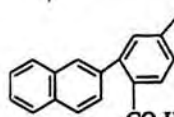

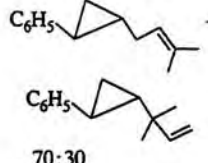
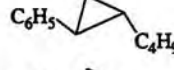

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	THF, $-48$ to $0^\circ$ , 30 min, then $n\text{-C}_8\text{H}_{17}\text{Br}$ , $0^\circ$ , 30 min		(50) 284a
$n\text{-C}_7\text{H}_{15}\text{C}(\text{Cl})=\text{NC}_6\text{H}_{13-n}$	$\text{CH}_3(t\text{-C}_4\text{H}_9\text{O})\text{CuLi}$	1. THF, $-78^\circ$ , 15 min 2. $\text{H}^+/\text{H}_2\text{O}$	$n\text{-C}_7\text{H}_{15}\text{COCH}_3$	(63) 763
$\text{C}_6\text{H}_5\text{CH}=\text{CHBr}$		Ether, THF, $\text{Pd}[\text{PC}_6\text{H}_5]_4$ (cat.), $20^\circ$ , 2 h		(59) 765
$n\text{-C}_8\text{H}_{17}\text{I}$		—		(—) 766
$n\text{-C}_6\text{H}_{13}\text{C}(\text{Br})\text{CH}_3$	$[(\text{CH}_3)_3\text{Sn}]_2\text{CuLi}$	THF, $-50^\circ$		(—) 767
$\text{Cl}(\text{CH}_2)_6\text{C}(\text{Li})=\text{CH}_2$	$\text{Li}_2\text{CuCl}_4$ (cat.)	THF, $0^\circ$		(72) 768
	$(\text{C}_2\text{H}_5)_2\text{CuLi}$ (2 eq)	Ether, $-90$ to $-45^\circ$ , 1–4 h		(79) 288
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	1. THF, TMEDA, $-60^\circ$ , 1 h 2.  $-60^\circ$ , 1 h		(88) 289
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	1. THF, TMEDA, $-60^\circ$ , 1 h 2.  $-60^\circ$ , 1 h		(44) 289
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	1. THF, TMEDA, $-60^\circ$ , 1 h 2.  $-60^\circ$ , 1 h		(90) 289
	$(\text{CH}_3)_2\text{CuLi}$ (10 eq)	Ether, $25^\circ$ , 15 h		(82) 769
		Ether, $25^\circ$ , 16 h		(38) 770
$\text{C}_6\text{H}_5\text{CH}_2\text{C}(\text{CO}_2\text{H})(\text{OTs})\text{H}$ (S)	$(\text{CH}_3)_2\text{CuLi}$ (4 eq)	Ether, $0^\circ$ , 3 h	$\text{C}_6\text{H}_5\text{CH}_2\text{C}(\text{CO}_2\text{H})\text{H}$ (R) ee = 78%	(55–63) 283
$\text{C}_6\text{H}_5\text{C}(\text{Br})\text{C}(\text{C}_6\text{H}_5)_2$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	THF, $-48^\circ$ , 30 min, then, $-48^\circ$ ,  $30$ min		284a (97)
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	THF, $-48^\circ$ , 30 min, then $\text{O}_2$		(60) 284a
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	THF, $-48^\circ$ , 30 min, then $\text{C}_6\text{H}_5\text{COCl}$		(95) 284a

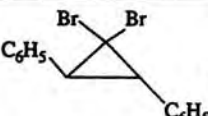
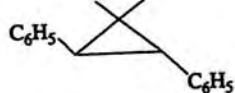
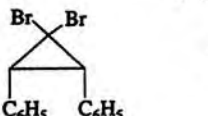
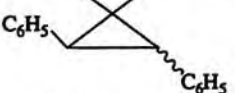
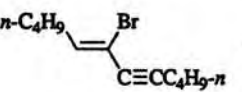
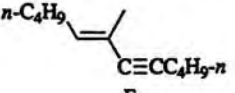
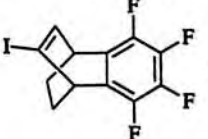
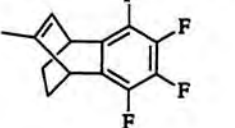
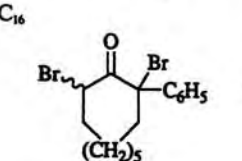
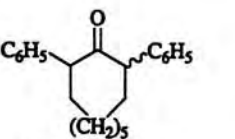
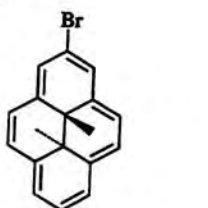
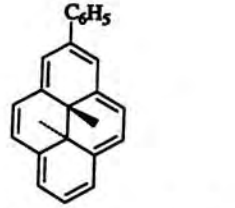
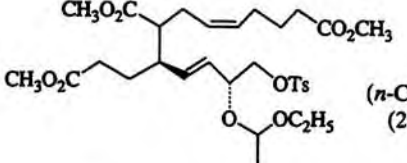
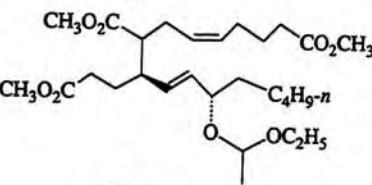
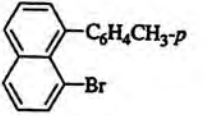
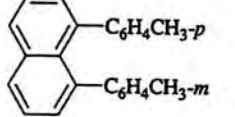
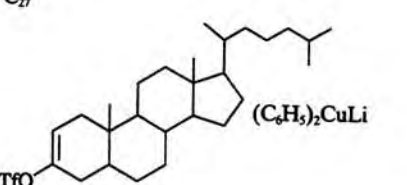
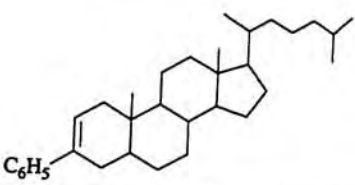
TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	THF, $-48^\circ$ , 30 min, then $\text{BrCH}_2\text{CO}_2\text{CH}_3$ , $-48^\circ$ , 30 min		(75) 284a
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	THF, $-48$ to $0^\circ$ , 30 min, then $\text{CH}_3\text{I}$ , $-48^\circ$ , 30 min		(96) 284a
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	Ether, $-48$ to $-20^\circ$ , 1 h, then $\text{CH}_3\text{COBr}$ , $-78$ to $25^\circ$ , 15 h	 + 	(34) 284b
	$(s\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	Ether, $-78$ to $-20^\circ$ , 3 h, then $\text{CH}_3\text{I}$ , $-20$ to $25^\circ$ , 5 h	 + 	80:20 (43) 284b
	$(t\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	Ether, $-55$ to $-20^\circ$ , 3 h, then $\text{CH}_3\text{I}$ , $-20$ to $25^\circ$ , 15 h		(20) 284b
	$(\text{CH}_3)_2\text{CuLi}$ (3 eq)	THF, $-78$ to $25^\circ$ , 15 h		(48) 284b
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$ (3 eq)	Ether, $-48$ to $0^\circ$ , 3 h		(47) 284b
	$(\text{CH}_3)_2\text{CuLi}$	Ether, DME, $50^\circ$ , 2 h		(85) 285
	$(\text{CH}_3)_2\text{CuLi}$	Ether, DME, $50^\circ$ , 2 h		(88) 285
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$ (4 eq)	Ether, $-78^\circ$ , 2 h		(18) 771
	$(\text{CH}_3)_2\text{CuLi}$ (excess)	Ether, hexane		(50-60) 772
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	THF, $-15^\circ$ , 12 h		(100) 286
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, $-15^\circ$ , 12 h		(75) 286
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	THF, $-30^\circ$ , 12 h		(59) 287
	$(\text{CH}_3)_2\text{CuLi}$	THF, $-30^\circ$ , 12 h		(11) 287
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, $-90$ to $-45^\circ$ , 1-4 h		(92) 288

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	—		(80) 773
	( <i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> ) <sub>2</sub> CuLi	—		(—) 774
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	Ether, -78°, 3 h		(84) 775
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi (2 eq)	Ether, -40°, 1 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> SC <sub>6</sub> H <sub>5</sub>	(80) 293
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (2 eq)	Ether, CH <sub>3</sub> I, 0°, 2 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> COC(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CH <sub>3</sub>	(68) 776
	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi (2 eq)	Ether, C <sub>2</sub> H <sub>5</sub> I, 0°, 2 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> COC(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub>	(22) 776
	CH <sub>3</sub> Cu(SeC <sub>6</sub> H <sub>5</sub> )Li	THF, 0°, 3 h		(86) 777
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (2 eq)	Ether, CH <sub>3</sub> I, 0°, 2 h	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> CCOC <sub>4</sub> H <sub>9</sub> - <i>t</i>	(79) 776
	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi (2 eq)	Ether, C <sub>2</sub> H <sub>5</sub> I, 0°, 2 h	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> CCOC(CH <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	(51) 776
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	THF, -15°, 12 h		(76) 286
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, THF, 20°, 12 h		(50) 778
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (10 eq)	Ether, -20°, 4 d		(29) 779
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	THF, -30°, 12 h		(52) 287
	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	Ether, 0°, 4.5 h		(60) 571
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (2 eq)	Ether, -90 to -45°, 1-4 h		(91) 288

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$ (excess)	Ether, $-15^\circ$ , 3 d, then $\text{CH}_3\text{I}$ , $-15^\circ$ , 3 h	 (82)	780
	$(\text{CH}_3)_2\text{CuLi}$ (excess)	Ether, $-15^\circ$ , 3 d, then $\text{CH}_3\text{I}$ , $-15^\circ$ , 3 h	 (57)	780
	$(\text{CH}_3)_2\text{CuLi}$	Diglyme, $-30$ to $25^\circ$	 87:13 <i>cis:trans</i>	(72) 781
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0-20^\circ$ , 22 h	 (61)	782
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$ (3-6 eq)	Ether, $-78$ to $20^\circ$	 <i>cis:trans</i> 95:5	(83) 783
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	Ether, $20^\circ$ , 8 d	 (16)	784
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (2 eq)	Ether, $-40^\circ$ , 2 h	 (70)	280
	$(m\text{-CH}_3\text{C}_6\text{H}_4)_2\text{CuLi}$	Ether, $0^\circ$	 (34)	774b
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, $-15^\circ$ , 12 h	 (100)	286

<sup>a</sup> The yield refers to the radiochemical yield.

<sup>b</sup> The yield was not specified.

<sup>c</sup> The ee was not reported.

<sup>d</sup> OR\* = (-)-menthyl.

<sup>e</sup> The configuration is at sulfur.

<sup>f</sup> The product was obtained by hydrolysis of the primary product.

<sup>g</sup> The product was obtained by esterification of the crude product with  $\text{SOCl}_2$  and then  $\text{C}_2\text{H}_5\text{OH}$ .

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

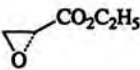
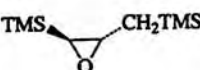
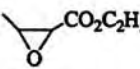

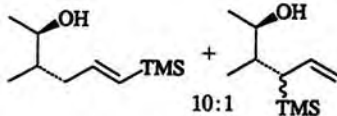
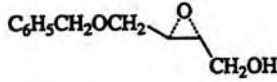
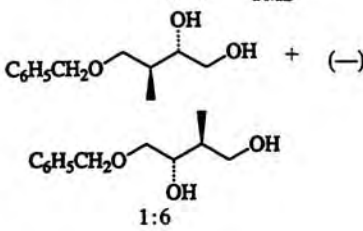
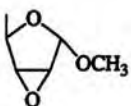
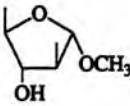
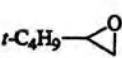
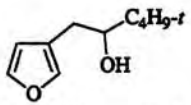

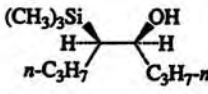
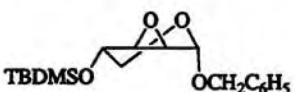
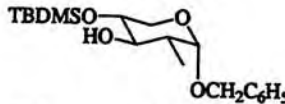
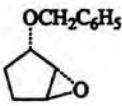
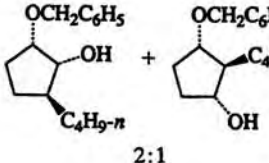
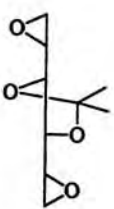
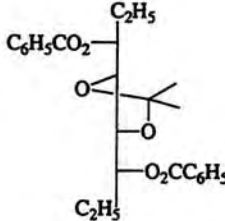
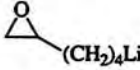
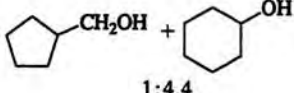
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
<i>B. Reactions of Saturated Epoxides</i>				
C <sub>3</sub>		$(\text{CH}_2=\text{CH})_2\text{CuLi}$	—	(90) 718
		$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, -40°, 24 h	(75) 785
C <sub>4</sub>		$n\text{-C}_4\text{H}_9\text{Cu}(\text{CN})\text{Li}$	Ether, -78 to 0°, 7 h	$\text{CH}_3\text{CHOHCH}(\text{C}_4\text{H}_9\text{-}n)\text{CO}_2\text{C}_2\text{H}_5$ (48) 317
		$\text{TMS}-\text{CH}=\text{CH}-\text{CH}_2)_2\text{CuLi}$	THF, DMS, -78 to 20°, 12 h	 (68) 786
		$(\text{CH}_3)_2\text{CuLi}$ (1.2 eq)	Ether, -20°, 1 h	 (—) 787
C <sub>5</sub>		$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, 0°, 3 h	 (54) 788
		$(\text{furyl})_2\text{CuLi}$ (3 eq)	Ether, -20°, 10 h	 (75) 789
		$(n\text{-C}_3\text{H}_7)_2\text{CuLi}$	Ether, -78 to 5°, 4 h	 (70) 790
		$(\text{CH}_3)_2\text{CuLi}$ (5 eq)	Ether, 20°, 30 h	 (70) 791
		$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, -78°, 3 h	 (45–50) 792
C <sub>6</sub>		$(\text{CH}_3)_2\text{CuLi}$ (excess)	1. Ether, -40° 2. $\text{C}_6\text{H}_5\text{COCl}$ , HMPT, 0°	 (95) 793
		$\text{CuBr}\cdot\text{DMS}$ (0.5 eq)	Ether, pentane, 30–50°	 (59) 794

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

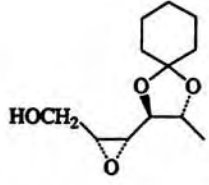
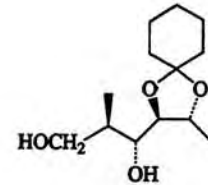

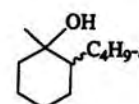
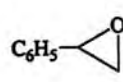
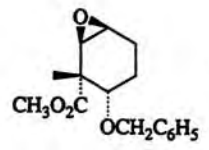
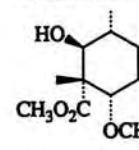
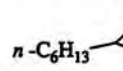
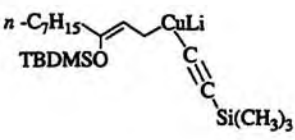
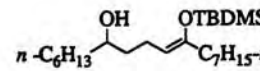
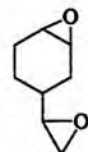
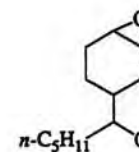
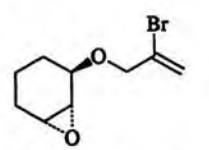
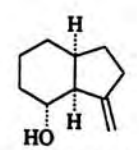
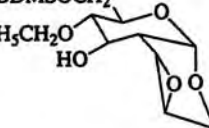
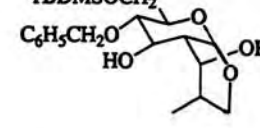
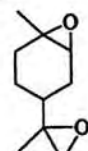
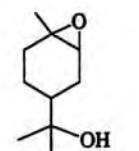
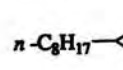

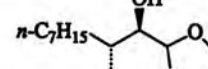
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$ (2.5 eq)	1. Ether, $-40^\circ$ , 4.5 h 2. $\text{NaIO}_4$ , THF, $\text{H}_2\text{O}$		(55) 795
$\text{C}_7$ 	$n\text{-C}_4\text{H}_9\text{Cu}(\text{CN})\text{Li}$ (2 eq)	Ether, $-78$ to $0^\circ$		(63) 317
$\text{C}_8$ 	$[\text{C}_6\text{H}_5\text{N}(\text{CH}_3)\text{CO}]_2\text{CuLi}$ $\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	Ether, $-78$ to $25^\circ$ , 12 h Ether, $-78$ to $0^\circ$ , 7 h	$\text{C}_6\text{H}_5\text{N}(\text{CH}_3)\text{-COCH}_2\text{CHOHC}_6\text{H}_5$ (52) $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{CH}_2\text{OH}$ (81) $\text{C}_6\text{H}_5\text{CHOHC}_2\text{H}_5$ (18)	296 317 (18)
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $20^\circ$ , 18 h		(85) 796
$n\text{-C}_6\text{H}_{13}$ 	$n\text{-C}_7\text{H}_{15}\text{-CH=CH-CuLi}$ TBDMMSO 	—		(74) 735
	$n\text{-C}_4\text{H}_9\text{Cu}(\text{CN})\text{Li}$	—		(81) 318
$\text{C}_9$ 	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	Ether, $-78^\circ$ , 2 h		(89) 797
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0\text{-}20^\circ$ , 18 h		(97) 798
$\text{C}_{10}$ 	$n\text{-C}_4\text{H}_9\text{Cu}(\text{CN})\text{Li}$	—		(84) 318
$n\text{-C}_8\text{H}_{17}$ 	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	Ether, $-78$ to $0^\circ$ , 7 h	$n\text{-C}_8\text{H}_{17}\text{CHOHC}_2\text{H}_5$ (71)	317
$n\text{-C}_7\text{H}_{15}$ 	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-40^\circ$ , 70 min		(81) 799

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$\text{Cu(CN)Li}$	Ether, $-60$ to $-40^\circ$ , 1.5 h		(61) 800
$\text{C}_{12}$ 	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	Ether, THF, $-45$ to $25^\circ$		(73) 801
	$(\text{CH}_3)_2\text{CuLi}$ (excess)	THF, reflux 48 h		(36) 802
C. Reactions of Allylic Substrates				
$\text{C}_3$ 	$(\text{O} \begin{array}{c} \diagup \text{NCO} \diagdown \\ \text{---} \end{array})_2\text{CuLi}$	THF, HMPA, $\text{CO}$ , 50 kg/cm <sup>2</sup> , $25^\circ$ , 12 h		(93) 297
	$[\text{C}_6\text{H}_5(\text{CH}_3)\text{NCO}]_2\text{CuLi}$	Ether, $25^\circ$ , 1 h		(88) 296
	$[\text{C}_6\text{H}_5\text{SeCH}(\text{C}_6\text{H}_{13-n})]_2\text{CuLi}$	THF, DMS, $-100^\circ$ , 30 min		(78) 803
		Ether, THF, $-20^\circ$ , 4 h		(87) 804
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	Ether, $0^\circ$ , 5.5 h		(78) 805
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $-40^\circ$ , 30 min		(74) 805
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$ (5 eq)	Ether, $-25^\circ$ , 30 min		(73) 806
$\text{C}_4$ 	$(\text{CH}_3)_2\text{CuLi}$	THF, $-78^\circ$ , 2 h		(87) 808
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, $-78^\circ$ , 2 h		(64) 808
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	—		(71) 810
	$n\text{-C}_6\text{H}_{13}\text{Cu(CN)Li}$ ( $\text{BF}_3 \cdot \text{Et}_2\text{O}$ )	Ether, THF, $-15^\circ$ , 1.5 h		(78) 809
	$n\text{-C}_4\text{H}_9\text{Cu(CN)Li}$	Ether, $-30^\circ$ , 20 min		(70) 807
$\text{C}_5$ 	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	Ether, $0$ – $25^\circ$ , 7 h		(71) 805

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

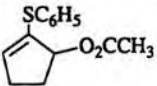
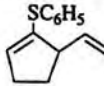
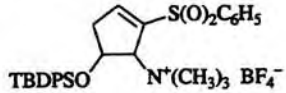
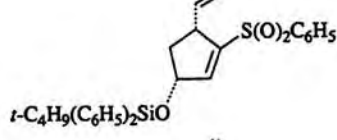
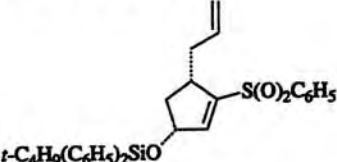
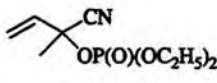
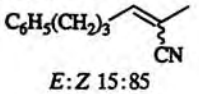

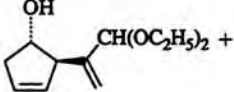
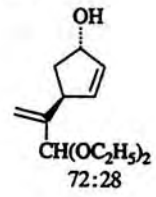

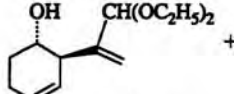
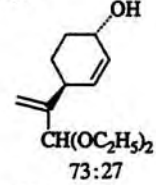
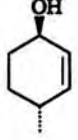
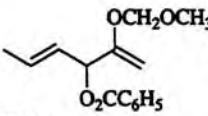
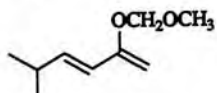
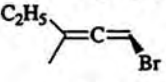
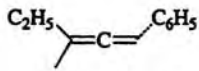
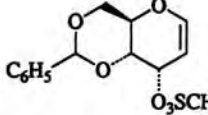
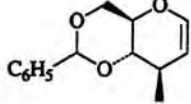
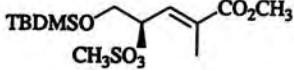
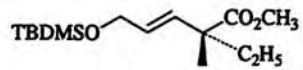
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	THF, $-78^\circ$	 (76)	811
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	THF, $-78^\circ$ , 20 min	 (78)	812
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	THF, $-78^\circ$ , 20 min	 (91)	812
	$[\text{C}_6\text{H}_5(\text{CH}_2)_2]_2\text{CuLi}$	THF, $-78^\circ$ , 30 min	 (96) <i>E:Z</i> 15:85	813
	$[(\text{C}_2\text{H}_5\text{O})_2\text{CH}-\text{CH}=\text{CH}]_2\text{CuLi}$	THF, $-40^\circ$ , 5-6 h	 +  (87)	330
$\text{C}_6$ 	$[(\text{C}_2\text{H}_5\text{O})_2\text{CH}-\text{CH}=\text{CH}]_2\text{CuLi}$	Ether, $-40^\circ$ , 5-6 h	 +  (94)	330
	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	Ether, $-78^\circ$	 (—)	331
	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	—	 (—)	872
	$\text{C}_6\text{H}_5\text{Cu}(\text{CN})\text{Li}$	Ether, $-70$ to $20^\circ$	 (—)	828
	$(\text{CH}_3)_2\text{CuLi}$	THF, ether, $-80$ to $0^\circ$ , 4 h	 (30)	815, 816
	$\text{C}_2\text{H}_5\text{Cu}(\text{CN})\text{Li}$	THF, $\text{BF}_3\cdot\text{Et}_2\text{O}$ , $-78^\circ$ , 30 min	 (92)	817



TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

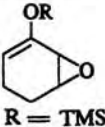
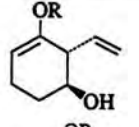
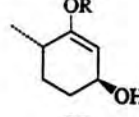
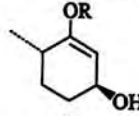
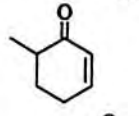
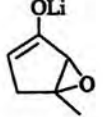
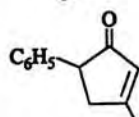
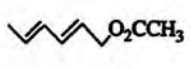
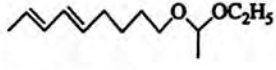
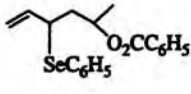
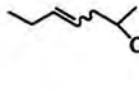
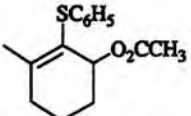
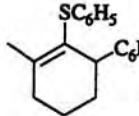
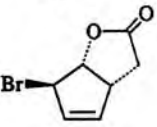
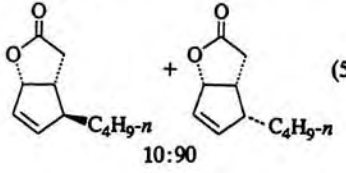
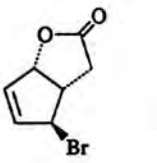
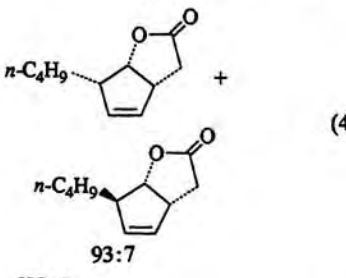
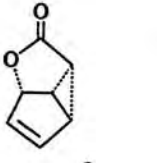
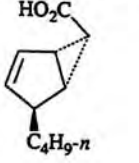
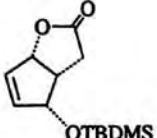
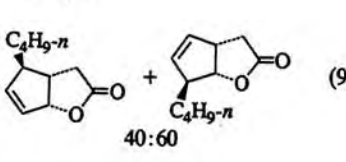
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
 R = TMS	$\text{CH}_2=\text{CHCu}(\text{CN})\text{Li}$	Ether, $-78$ to $25^\circ$ , 5 h		(80) 332
	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}$	Ether, $-78$ to $25^\circ$ , 5 h		(75) 332
R = $\text{P}(\text{O})(\text{OC}_2\text{H}_5)_2$	$(\text{CH}_3)_2\text{CuLi}$ (2.5 eq)	THF, $-23^\circ$ , 2 h		(83) 333
R = Li	$(\text{CH}_3)_2\text{CuLi}$ (2.5 eq)	THF, $-23^\circ$ , 2 h, then TsOH, $\text{C}_6\text{H}_6$		(65) 333
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, $-23^\circ$ , 2 h, then TsOH, $\text{C}_6\text{H}_6$		(40) 333
	$(\text{C}_2\text{H}_5\text{O})_2\text{CuLi}$	THF, $-55$ to $25^\circ$		(60) 594
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0$ – $25^\circ$		(—) 819
C <sub>1</sub>				
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, $0^\circ$		(77) 811
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, DMS, $-78^\circ$ , 2.5 h		(51) 328, 329
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, DMS, $-78^\circ$ , 4 h		(40) 328, 329
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	—		(75) 329
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, DMS, $-78$ to $-20^\circ$ , 6 h, then HF, $\text{CH}_3\text{CN}$		(90) 329

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

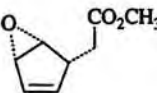
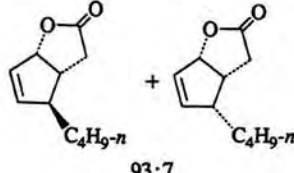

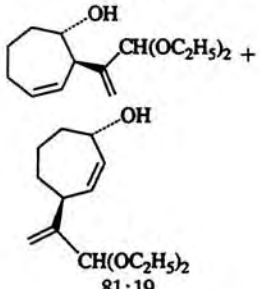
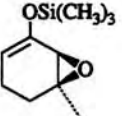
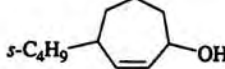
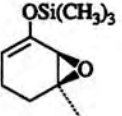
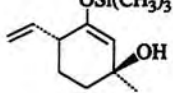
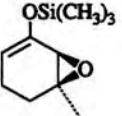
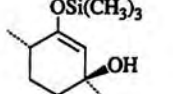
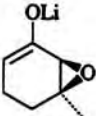
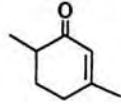
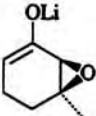
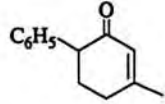
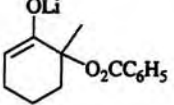
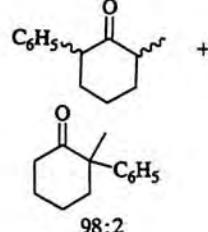
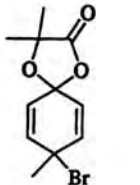
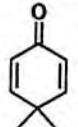
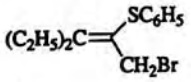
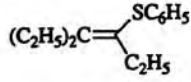
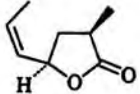
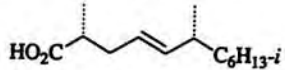
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, DMS, $-78^\circ$ , 3.5 h	 93:7	(48) 328, 329
	$[(\text{C}_2\text{H}_5\text{O})_2\text{CHCH}=\text{CH}]_2\text{CuLi}$	Ether, $-40^\circ$ , 5–6 h	 81:19	(98) 330
	$(s\text{-C}_4\text{H}_9)\text{Cu}(\text{CN})\text{Li}$	Ether, $-78^\circ$ , 1–3 h		(—) 331
	$\text{CH}_2=\text{CHCu}(\text{CN})\text{Li}$	Ether, $-78$ to $25^\circ$ , 5 h		(80) 332
	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	Ether, $-78$ to $25^\circ$ , 5 h		(95) 332
	$(\text{CH}_3)_2\text{CuLi}$	THF, $-23^\circ$ , 2 h, then TsOH, $\text{C}_6\text{H}_6$		(80) 333
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, $-23^\circ$ , 2 h, then 3 N HCl, $\text{C}_2\text{H}_5\text{OH}$		(72) 333
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, $-23^\circ$ , 2 h	 98:2	(65) 333
	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	1. — 2. KOH		(—) 820
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, DMS, $-78$ to $20^\circ$ , 10 h		(61) 821
	$i\text{-C}_6\text{H}_{13}\text{Cu}(\text{CN})\text{Li}$	Ether, $-20$ to $0^\circ$		(95) 822

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, 0°	 (88)	823
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, 0°	 (72)	823
	$\text{CuI}$ (1 eq), $\text{P}(\text{C}_6\text{H}_5)_3$ (2 eq), $\text{C}_6\text{H}_5(\text{CH}_3)_2\text{SiLi}$ (1 eq)	Ether, THF, 0°, 2 h	 (87)	824
	"	Ether, THF, 0°, 2 h	 (87)	824
	 MPTP* (1 eq)	THF, DMF, -70 to 25°, 8 h, then 2 N HCl, 25°	 (49)	825
$n\text{-C}_5\text{H}_{11}\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$	$(\text{CH}_3)_2\text{CuLi}$ 25:75 E:Z	Ether, DMS, -78°, 5 min	 25:75 E,E:Z,E (95)	826
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -20°, 30 min	 93:7 E:Z (74)	827
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{CuLi}$	THF, 25°, 12 h	 (87)	325a
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{CuLi}$	THF, 25°, 12 h	 (93)	325a
	$n\text{-C}_4\text{H}_9\text{Cu}(\text{CN})\text{Li}$	Ether, -78°, 1 h	 (85)	828
	$\text{Cu}(\text{CN})\text{Li}$	Ether, -78°, 1 h	 (75)	828

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(C_6H_5)_2Cu(CN)Li$	Ether, $-78^\circ$ , 1 h		(85) 828
	$CH_2=CH-Cu(CN)Li$	Ether, $-78^\circ$ , 1 h		(75) 828
	$(n-C_4H_9)_2Cu(CN)Li$	Ether, $-78$ to $25^\circ$ , 5 h		(70) 332
	$(n-C_4H_9)_2Cu(CN)Li$	Ether, $-78$ to $25^\circ$ , 5 h		(85) 828
	$(n-C_4H_9)_2Cu(CN)Li$	Ether, $-78$ to $25^\circ$ , 5 h		(74) 332
	$(n-C_4H_9)_2CuLi$	Ether, $-15$ to $25^\circ$ , 15 h		(60) 829
	$(n-C_4H_9)_2CuLi$	Ether, $-60$ to $-10^\circ$ , 1 h		(57) 830
	$(C_6H_5)_2CuLi$	THF, DMS, $-78^\circ$ , 20 min		(79) 831
	$(n-C_4H_9)_2CuLi$ (10 eq)	Ether, HMPT, $-35^\circ$ , 2 h		(95) 832
	$(C_6H_5)_2CuLi$ (1.5 eq)	Ether, $0^\circ$ , 7 h		(70) 327
	$(CH_3)_2CuLi$	Ether, $0^\circ$ , 5 h		(90) 327
	$CH_3Cu(CN)Li$	Ether, $-78^\circ$ , 1 h		(90) 828

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

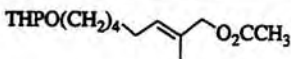
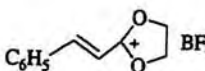
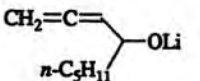
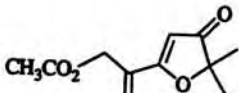
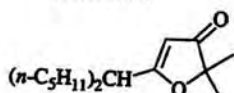
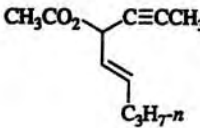
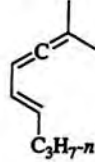
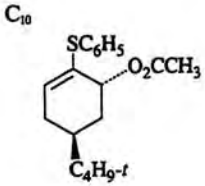
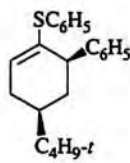
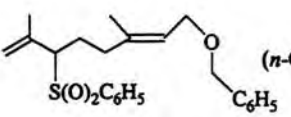
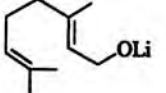
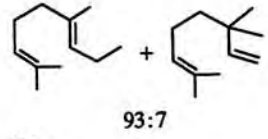
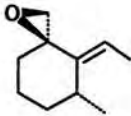
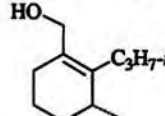
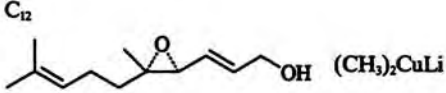
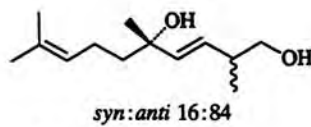
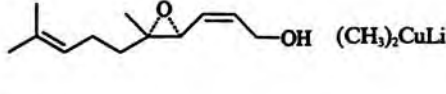
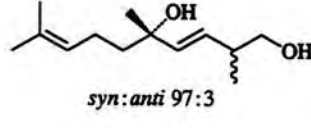
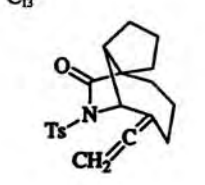
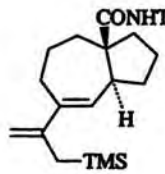
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(n\text{-C}_5\text{H}_{11})_2\text{CuLi}$	1. — 2. TsOH, CH <sub>3</sub> OH	HO(CH <sub>2</sub> ) <sub>4</sub> -CH=CH-C <sub>6</sub> H <sub>13-n</sub> 98:2 E:Z	(—) 833
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -78°, 1 h, 0°, 6 h	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )-CH <sub>2</sub> CO <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> OH	(92) 834
	CH <sub>3</sub> Li, CuI, MPTP <sup>a</sup> (1 eq)	THF, -78 to 20°, 3 h	CH <sub>2</sub> =C(CH <sub>3</sub> )-CH=C-C <sub>5</sub> H <sub>11-n</sub> E:Z 50:50	(55) 835
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (excess)	Ether, 0°, 2 h		(40) 836
	$(\text{CH}_3)_2\text{CuLi}$	THF, -30 to 20°, 1.5 h		(65) 837
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, 0°		(71) 811
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, -20°, 30 min	$n\text{-C}_4\text{H}_9\text{-CH=C(CH}_3\text{)-CH}_2\text{-CH}_2\text{-CH=C(O)-C}_6\text{H}_5$ E:Z 86:14 (73)	827
	$(\text{CH}_3)_2\text{CuLi}$ , CH <sub>3</sub> Li, MPTP <sup>a</sup>	THF, ether, DMF, -78 to 25°, 3 h		(90) 838
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°, 30 min		(86) 573
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, -15°, 16 h		(81) 839
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, -23°		(75) 839
	$(\text{TMSCH}_2)_2\text{CuLi}$	Ether, -78 to 0°, 4.5 h		(100) 840

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

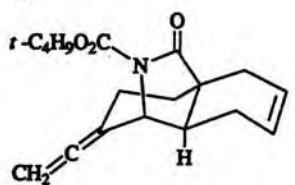
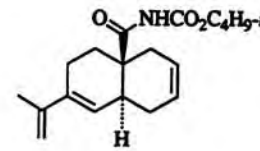
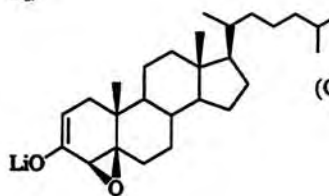
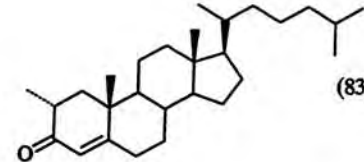
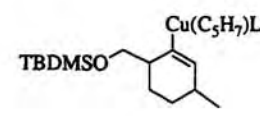
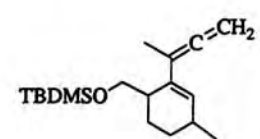
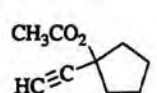
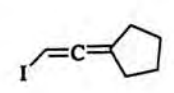
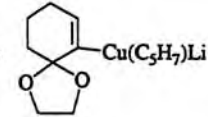
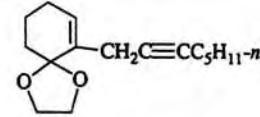
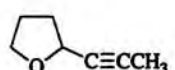
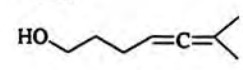
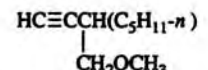
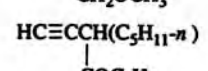
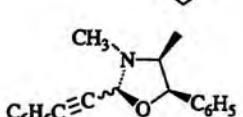
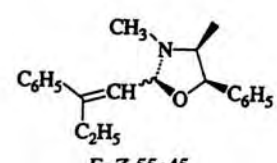
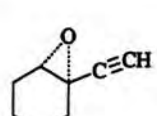
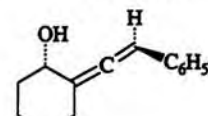
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{14}$ 	$(CH_3)_2CuLi$	Ether, $-78$ to $-40^\circ$ , 1.5 h	 (75)	841
$C_{27}$ 	$(CH_3)_2CuLi$	THF, $-23^\circ$ , 2 h, then TsOH, $C_6H_6$	 (83)	333
D. Reactions of Propargylic Substrates				
$C_4$ $CH_3C\equiv CCH_2OTs$		THF, $P[N(CH_3)_2]_3$ , $-78^\circ$	 (82)	337
$C_5$ $HC\equiv C(C_6H_5)_2Cl$	$(n-C_4H_9)_2CuLi$ (2 eq)	Ether, $0^\circ$ , 30 min	$n-C_4H_9CH=C(C_6H_5)_2$ (60)	28
$C_7$ 	$(CH_3)_2CuLi$ (2 eq)	Ether, $-78^\circ$ , 2 h, then $I_2/DME$	 (70)	339
$n-C_5H_{11}C\equiv CCH_2OTs$		THF, $P[N(CH_3)_2]_3$ , $-78^\circ$	 (80)	337
	$(CH_3)_2CuLi$	Ether, $-10$ to $20^\circ$ , 4 h	 (95)	842
$C_n$ $HC\equiv CCH(C_5H_{11-n})O_2CCH_3$	$(CH_3)_2CuLi$ (2 eq)	1. Ether, $-78^\circ$ , 2 h 2. $ClCH_2OCH_3$	 (75)	339
	$(CH_3)_2CuLi$ (2 eq)	1. Ether, $-78^\circ$ , 2 h 2. $(C_6H_5CO)_2O$	 (60)	339
$CH_3C\equiv C$	$(CH_3)_2CuLi$ (2 eq)	Ether, $0^\circ$ , 30 min	$(CH_3)_2C=C$ (50)	28
	$(C_2H_5)_2CuLi$	Ether, $-70$ to $-40^\circ$	 (—)	843
	$C_6H_5(CH_2SOCH_2)CuLi$ (2 eq)	THF, $-78$ to $0^\circ$ , 2 h	 (80)	273

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

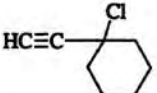



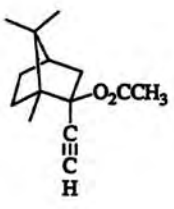

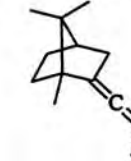
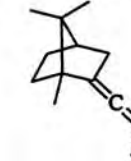
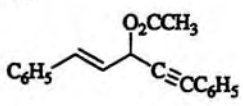
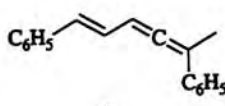
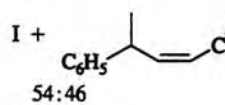
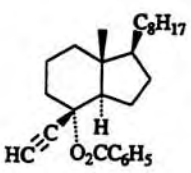
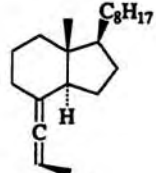
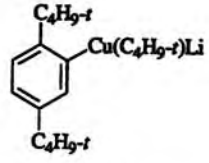
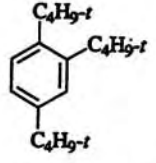
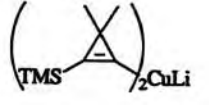
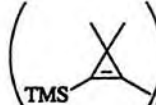
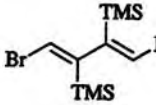
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (2 eq)	Ether, 0°, 30 min	$n\text{-C}_4\text{H}_9\text{CH}=\text{C}$  (90)	28
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, 0°, 30 min	$\text{CH}_3\text{CH}=\text{C}$  (70)	28
			$\text{CH}_2=\text{C}$  (20)	
C <sub>12</sub> 	$(\text{CH}_3)_2\text{CuLi}$	Ether, -10 to 20°	 +  (78)	844
			 (18)	
C <sub>17</sub> 	$(\text{CH}_3)_2\text{CuLi}$	Ether, 20°, 12 h	 (75)	845
	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	Ether, 20°, 12 h	I +  (96)	845
C <sub>20</sub> 	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0-25°, 5 h	 (85)	846
<i>E. Miscellaneous Couplings</i>				
C <sub>0</sub> O <sub>2</sub>	 -Cu(C <sub>4</sub> H <sub>9</sub> -t)Li	THF, -78°	 (18)	847
	 -CuLi	Ether, -78°	 (30)	848
	$(\text{CHBr}=\text{CTMS})_2\text{CuLi}$	Ether pentane, -83 to 20°, 45 min	 (62)	849

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

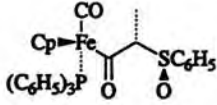
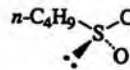
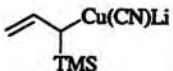
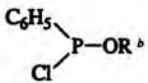
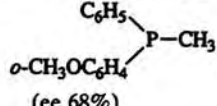
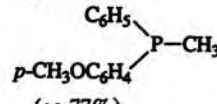
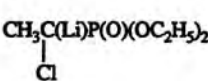
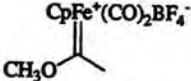
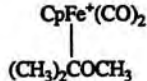
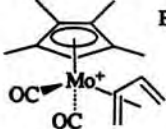
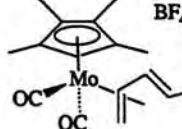


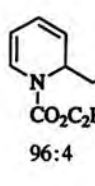
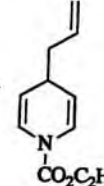
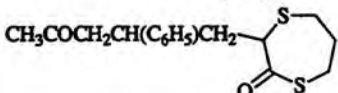
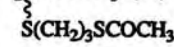
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$C_6H_5(CO)_3Mn^+$	$(CH_3)_2CuLi$ $(CH_3)_2CuLi$	Ether, 0° Ether, -78°	$C_6H_5(CO)_2MnCH_3$ (42) $C_6H_5Mn(CO)_2COCH_3$ (45)	307 307
	$(n-C_4H_9)_2CuLi$	—		(96) 850
$(SeCN)_2$		THF, -78 to 20°, 1 h	$TMS-CH=CH-CH_2-SeCN$	(70) 851
$(CH_3)_2NOP(O)(C_6H_5)_2$ (3 eq)	$(n-C_6H_{13}C\equiv C)_2CuLi$	Ether	$n-C_6H_{13}C\equiv CN(CH_3)_2$	(67) 295
	$(i-C_6H_{13}C\equiv C)_2CuLi$	Ether	$i-C_6H_{13}C\equiv CN(CH_3)_2$	(75) 295
	$[(CH_3)_3SiC\equiv C]_2CuLi$	Ether	$(CH_3)_3SiC\equiv CN(CH_3)_2$	(67) 295
	$o-CH_3OC_6H_4Cu(CN)Li$	1. Ether, THF 2. KCN 3. $CH_3Li$		(60) <sup>c</sup> 294
	$p-CH_3OC_6H_4Cu(CN)Li$	1. Ether, THF 2. KCN 3. $CH_3Li$		(40) <sup>c</sup> 294
9-Borabicyclo-[3.3.1]nonane (9-BBN)	$n-C_4H_9Cu(SC_6H_5)Li$	1. THF, -80 to 25° 2. $H_2O_2$ , NaOH, 60°	$n-C_4H_9OH$	(86) 852
$C_2$ 	$(n-C_4H_9)_2CuLi$	THF, ether, -90 to -20°	$n-C_4H_9CH(CH_3)P(O)(OC_2H_5)_2$	(81) 305
	$s-C_4H_9Cu(OC_4H_9-t)Li$	THF, ether, -90 to -35°	$s-C_4H_9CH(CH_3)P(O)(OC_2H_5)_2$	(62) 305
$C_3$ 	$(CH_3)_2CuLi$	Ether, $CH_2Cl_2$ , -78°		(50) 308
$C_4$ 	$(n-C_5H_{11})_2CuLi$	THF, -78°		(—) 853
$C_5$ 	$(C_6H_5)_2CuLi$	THF, ether, -90 to -13°	$n-C_4H_9CH(C_6H_5)P(O)(OC_2H_5)_2$	(77) 305
	$ClCO_2C_2H_5$ $(CH_2)_2CuLi$	THF, -78 to 0°, 45 min	 + 	(80) 843
	$(CH_3)_2CuLi$	1. Ether, DMS, -78°, 2 h 2. $H_2S$ (g) 3. $(CH_3CO)_2O$ , $C_5H_5N$	$CH_3COCH_2CH(C_6H_5)CH_2CHCOCH_3$ (58) 	855



TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)



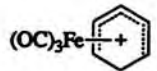
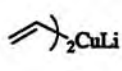
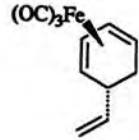
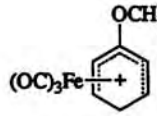
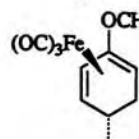
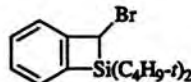
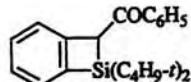
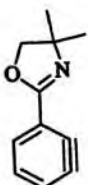
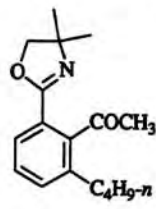
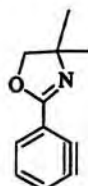
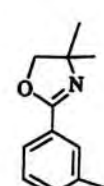


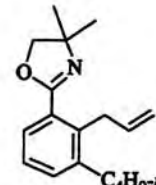

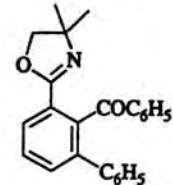
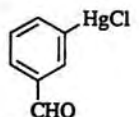
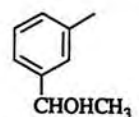
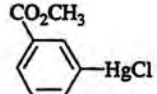
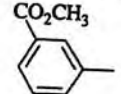
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>6</sub> C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	 $(\text{C}_{10}\text{H}_{15})_2\text{CuLi}$	Ether, -78°		(45) 856
	$(\text{OC})_3\text{Fe}$ 	THF, -78°, 2 min		(63) 857
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°		(63) 858
C <sub>7</sub> 	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	1. THF -48° 2. C <sub>6</sub> H <sub>5</sub> COCl		(57) 859
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	1. Ether, -78 to 20°, 40 min 2. CH <sub>3</sub> COCl, 20°, 16 h		(67) 860
	$(\text{CH}_3)_2\text{CuLi}$ (3 eq)	Ether, -78 to 25°		(66) 304
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (3 eq)	1. Ether, -78 to 25° 2.  Br (10 eq)		(88) 304
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$ (3 eq)	1. Ether, -78 to 25° 2. C <sub>6</sub> H <sub>5</sub> COCl (10 eq)		(66) 304
C <sub>6</sub> H <sub>5</sub> NHCH <sub>3</sub>	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	Ether, -20°, 2 h, then O <sub>2</sub> , -78°	C <sub>6</sub> H <sub>5</sub> N(CH <sub>3</sub> )C <sub>4</sub> H <sub>9-n</sub>	(57) 303
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$ (5 eq)	THF, reflux, 6 h, then O <sub>2</sub> , -20°	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> NCH <sub>3</sub>	(72) 303
	$[(\text{CH}_3)_2\text{CuLi} + \text{CH}_3\text{Li}]$ (5 eq)	Ether, -78 to 0°, 2 h, then CH <sub>3</sub> I, O <sub>2</sub>		(86) 306
	$[(\text{CH}_3)_2\text{CuLi} + \text{CH}_3\text{Li}]$ (5 eq)	Ether -78 to 0°, 2 h, then CH <sub>3</sub> I, O <sub>2</sub>		(82) 306

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

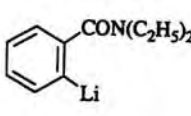
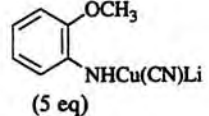
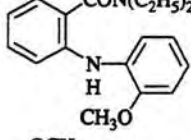
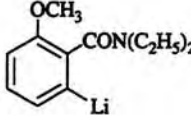
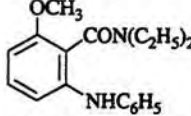
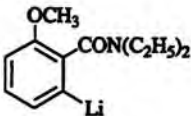
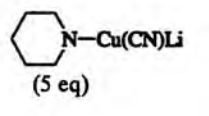
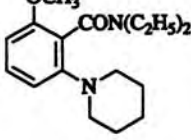
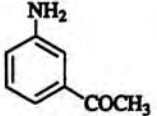
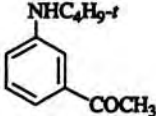
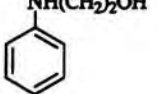
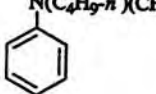
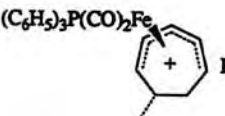
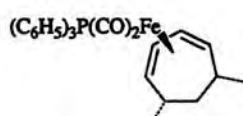
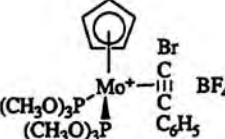
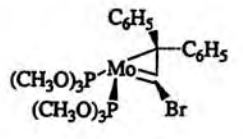
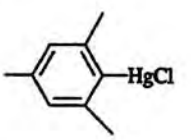
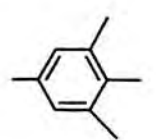
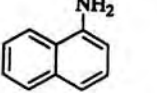
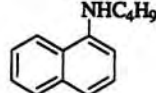
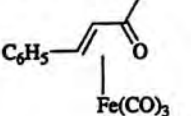
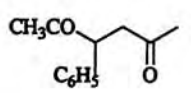
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$C_6H_5CH_2N(Tf)_2$	$(CH_3)_2CuLi$ (5 eq)	Ether, $-25^\circ$ , 2 h - 3 d	$C_6H_5C_2H_5$ (60-70)	806
	 (5 eq)	THF, $-10^\circ$ , 2 h, then $O_2$ , $-78^\circ$	 (50)	302
	$C_6H_5NHCu(CN)Li$ (5 eq)	THF, $-10^\circ$ , 2 h, then $O_2$ , $-78^\circ$	 (63)	302
	 (5 eq)	1. THF, $-10^\circ$ , 2 h 2. $O_2$ , $-78^\circ$	 (33)	302
$C_6$				
	$(t-C_4H_9)_2CuLi$ (5 eq)	1. THF, $-20^\circ$ , 2 h 2. $O_2$ , $-20^\circ$	 (32)	303
	$(n-C_4H_9)_2CuLi$ (5 eq)	1. Ether, $-20^\circ$ , 2 h 2. $O_2$ , $-20^\circ$	 (37)	303
	$(CH_3)_2CuLi$ $PF_6^-$	Ether, $0^\circ$	 (83)	861
	$(C_6H_5)_2CuLi$ $BF_4^-$	THF	 (—)	862
$C_9$				
	$[(CH_3)_2CuLi + CH_3Li]$ (5 eq)	1. Ether, $-78$ to $0^\circ$ , 2 h 2. $CH_3I$ , $O_2$	 (75)	306
$C_{10}$				
$n-C_{10}H_{21}NH_2$	$(t-C_4H_9)_2CuLi$ (5 eq)	1. THF, $-20^\circ$ , 2 h 2. $O_2$ , $-20^\circ$	$n-C_{10}H_{21}NHC_4H_9-t$ (23)	303
	$(t-C_4H_9)_2CuLi$ (5 eq)	1. THF, $-20^\circ$ , 2 h 2. $O_2$ , $-20^\circ$	 (35)	303
	$(CH_3)_2CuLi$	1. Ether, $-23^\circ$ , 30 min 2. $t-C_4H_9Br$ , $-78$ to $20^\circ$	 (26)	863
$C_{11}$				
$n-C_7H_{15}NHC_4H_9-n$	$(C_6H_5)_2CuLi$ (5 eq)	1. Ether, $-37^\circ$ , 6 h 2. $O_2$ , $-78^\circ$	$n-C_7H_{15}N(C_6H_5)C_4H_9-n$ (64)	303

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

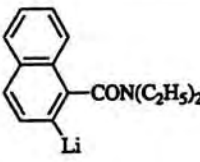
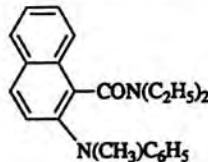
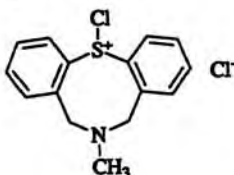
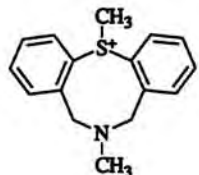
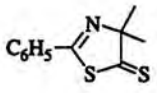
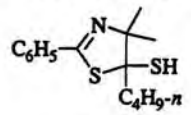
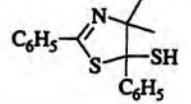
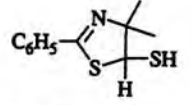
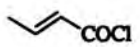
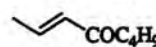
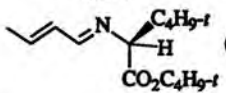
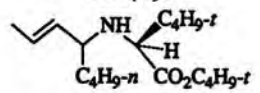
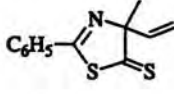
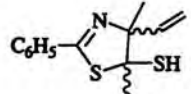
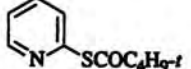
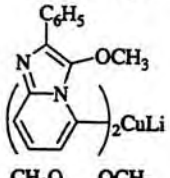
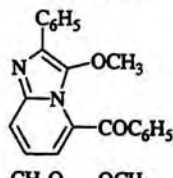
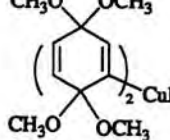
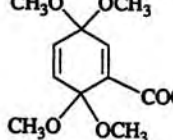
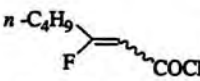
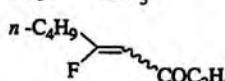
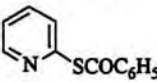
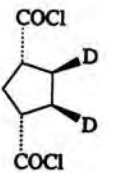
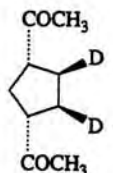
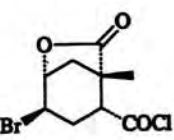
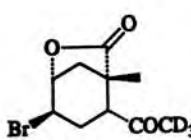
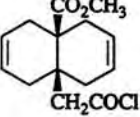
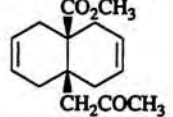
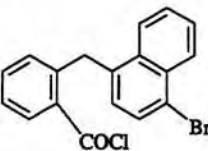
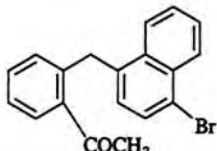
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$\text{C}_6\text{H}_5\text{N}(\text{CH}_3)\text{Cu}(\text{CN})\text{Li}$ (5 eq)	THF, $-10^\circ$ , 2 h, then $\text{O}_2$ , $-78^\circ$	 (61)	302
$\text{C}_{12}$ $(\text{C}_6\text{H}_{11})_2\text{NH}$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	Ether, $-20^\circ$ , 2 h, then $\text{O}_2$ , $-78^\circ$	$(\text{C}_6\text{H}_{11})_2\text{NC}_4\text{H}_9\text{-}n$ (38)	303
$(\text{C}_6\text{H}_5)_2\text{NH}$	$(\text{C}_6\text{H}_5)_2\text{CuLi}$ (5 eq)	Ether, $-37^\circ$ , 6 h, then $\text{O}_2$ , $-78^\circ$	$(\text{C}_6\text{H}_5)_3\text{N}$ (94)	303
$\text{C}_{14}$ 	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, THF, $-78^\circ$ , 4 h 2. $\text{KPF}_6$ , $\text{H}_2\text{O}$ , $0^\circ$	 $\text{PF}_6^-$ (16)	864
<i>F. Reactions with Carbonyl-Containing Substrates</i>				
$\text{C}_2$ $\text{CH}_3\text{COBr}$ $(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{-CH}(\text{SC}_6\text{H}_5)\text{COCl}$	$[\text{C}_6\text{H}_5(\text{CH}_3)\text{NCO}]_2\text{CuLi}$ $(\text{C}_2\text{H}_5)_2\text{CuLi}$	Ether, 1 h Ether, THF, $-78$ to $-40^\circ$ , 1.5 h	$\text{C}_6\text{H}_5(\text{CH}_3)\text{NCOCOCH}_3$ (72) $(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{CH}(\text{SC}_6\text{H}_5)\text{COC}_2\text{H}_5$ (100)	296 865
$\text{C}_3$ $\text{C}_2\text{H}_5\text{CS}_2\text{CH}_3$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ $(\text{C}_6\text{H}_5)_2\text{CuLi}$	Ether, $0^\circ$ , 1 h Ether, $0^\circ$ , 1 h	$(n\text{-C}_4\text{H}_9)_2\text{C}(\text{SH})\text{C}_2\text{H}_5$ (87-93) $(\text{C}_6\text{H}_5)_2\text{C}(\text{SH})\text{C}_2\text{H}_5$ (44-97)	164 164
$\text{C}_4$ $\text{Br}(\text{CH}_2)_3\text{COCl}$ $\text{CH}_3\text{O}_2\text{C}(\text{CH}_2)_2\text{COCl}$	$(\text{C}_2\text{H}_5)_2\text{CuLi}$ $[(\text{C}_6\text{H}_5)_2\text{P}(\text{O})\text{CH}(\text{CH}_3)]_2\text{CuLi}$	Ether, $-70^\circ$ , 5 min —	$\text{Br}(\text{CH}_2)_3\text{COC}_2\text{H}_5$ (88) $(\text{C}_6\text{H}_5)_2\text{P}(\text{O})\text{CH}(\text{CH}_3)\text{-CO}(\text{CH}_2)_3\text{CO}_2\text{CH}_3$ (60)	282 866
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	THF, 0 to $25^\circ$ , 2 h	 (93)	316
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, 0 to $25^\circ$ , 2 h	 (75)	316
	$(t\text{-C}_4\text{H}_9)_2\text{CuLi}$	THF, 0 to $25^\circ$ , 2 h	 (76)	316
	$(t\text{-C}_4\text{H}_9)(\text{CH}_3\text{SOCH}_2)\text{CuLi}$	THF, $-78^\circ$ , 1 h	 (78)	273
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	THF, $-55^\circ$ , 1 h	 (72)	867
$\text{C}_5$ 	$(\text{CH}_3)_2\text{CuLi}$	THF, 0 to $25^\circ$ , 2 h	 (96)	316
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $\text{O}_2$ , $-78$ to $25^\circ$ , 3 h	$t\text{-C}_4\text{H}_9\text{CO}_2\text{C}_4\text{H}_9\text{-}n$ (57)	315
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $-78$ to $25^\circ$ , 3 h	$t\text{-C}_4\text{H}_9\text{COC}_4\text{H}_9\text{-}n$ (70)	315

TABLE IV. SUBSTITUTION REACTIONS OF LOWER-ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>7</sub> C <sub>6</sub> H <sub>5</sub> COCl	[(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> NCO] <sub>2</sub> CuLi <i>t</i> -C <sub>4</sub> H <sub>9</sub> (C <sub>6</sub> H <sub>5</sub> )CuLi	THF, HMPA, CO, 80°, 30 min THF, 60°, 20 min	(CH <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> NCOCOC <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>5</sub> COC <sub>4</sub> H <sub>9</sub> - <i>t</i>	(61) 297 (87) 309
C <sub>6</sub> H <sub>5</sub> COCl	 $(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CuLi}$	THF, -70°		(30) 868
C <sub>6</sub> H <sub>5</sub> COCl	 $(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CuLi}$	THF, DMS, -60°, 30 min		(65) 310
 77:13 <i>E:Z</i>	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	Ether, THF, HMPT, -110 to -70°	 73:27 <i>E:Z</i>	(70) 312
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	Ether, O <sub>2</sub> , -78 to 25°, 3 h	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> C <sub>4</sub> H <sub>9</sub> - <i>n</i>	(99) 315
C <sub>6</sub> H <sub>5</sub> CS <sub>2</sub> CH <sub>3</sub>	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	Ether, -78 to 25°, 3 h	C <sub>6</sub> H <sub>5</sub> COC <sub>4</sub> H <sub>9</sub> - <i>n</i>	(99) 315
	( <i>t</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	Ether, O <sub>2</sub> , -78 to 25°, 2 h	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> C <sub>4</sub> H <sub>9</sub> - <i>t</i>	(43) 315
	( <i>i</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	Ether, -78 to 25°, 3 h	C <sub>6</sub> H <sub>5</sub> COC <sub>4</sub> H <sub>9</sub> - <i>t</i>	(96) 315
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, 0°, 1 h	(CH <sub>3</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> )SH	(88) 164
	CH <sub>3</sub> Cu(SCH <sub>3</sub> )Li (2 eq)	Ether, 0°, 1 h	(CH <sub>3</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> )SH	(99) 164
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (3 eq)	Ether, -78°, 15 min		(55) 869
C <sub>8</sub> <i>n</i> -C <sub>7</sub> H <sub>15</sub> COSeCH <sub>3</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub> (SC <sub>6</sub> H <sub>5</sub> )CuLi	-78°, 1 h	<i>n</i> -C <sub>7</sub> H <sub>15</sub> COC <sub>4</sub> H <sub>9</sub> - <i>t</i>	(89) 312
C <sub>9</sub> 	(CD <sub>3</sub> ) <sub>2</sub> CuLi	Ether, THF, -78°, 30 min		(78) 870
C <sub>13</sub> (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C=S	C <sub>2</sub> H <sub>5</sub> Cu(SCH <sub>3</sub> )Li	Ether, 0°, 1 h	C <sub>2</sub> H <sub>5</sub> C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> SH	(95) 164
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, -70°, 30 min		(92) 871
C <sub>18</sub> 	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, -78°, 15 min		(74) 872

<sup>a</sup> MPTP is C<sub>6</sub>H<sub>5</sub>N(CH<sub>3</sub>)P<sup>+</sup>(C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>I<sup>-</sup>.

<sup>b</sup> R\* = cinchonyl.

<sup>c</sup> The yield is overall after (1) KCN, (2) CH<sub>3</sub>Li, and (3) H<sub>2</sub>O<sub>2</sub>.

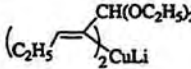
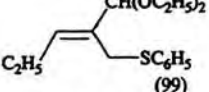
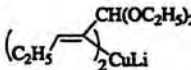
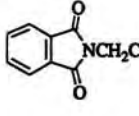
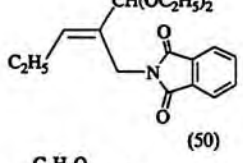
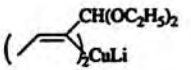
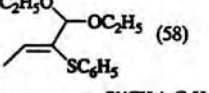
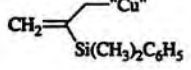
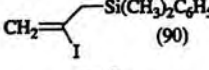
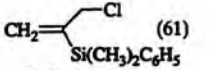
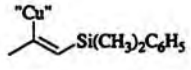
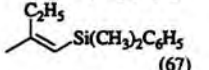

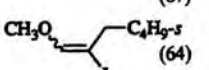

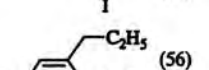
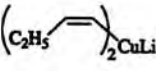
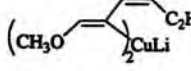
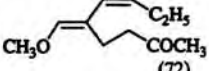
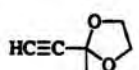
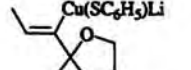
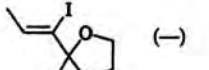
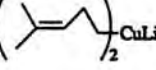
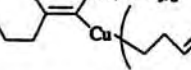
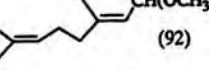
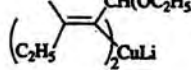
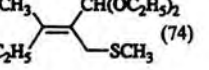
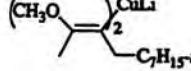
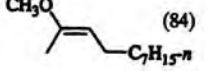
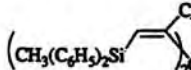
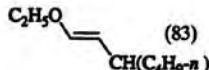
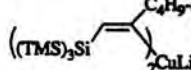
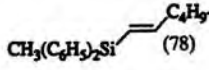
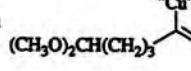
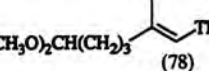
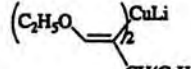
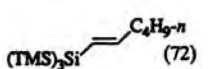
TABLE V. CARBOCUPRATION REACTIONS OF LOWER ORDER LITHIO ORGANOCUPRATES

Acetylene Derivative	Organocuprate	Carbometallation Conditions	Adduct	Electrophile	Substitution Conditions	Product(s) and Yield(s) (%)	Refs.	
C <sub>2</sub>	H <sub>2</sub> C=CH <sub>2</sub> (2 eq)				Et <sub>2</sub> O, -60 to 10°		345	
		(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	Et <sub>2</sub> O, -20°, 30 min					
		(n-C <sub>7</sub> H <sub>15</sub> ) <sub>2</sub> CuLi	"			THF, HMPA (2 eq), -30 to 25°, 1 h		346
		(n-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	"			"		346
		(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	"			THF, HMPA (1 eq), -30 to 20°, 5-12 h		346
		"	"			THF, HMPA (2 eq), P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> (1.5 eq), -30 to 20°, 5-12 h		346
		"	"			THF, TMEDA, (1.2 eq), -15°, 1 h		346
		(n-C <sub>7</sub> H <sub>15</sub> ) <sub>2</sub> CuLi	"			THF, HMPA (2 eq), P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> (1.5 eq), -30 to 20°, 5-12 h		346
		(n-C <sub>5</sub> H <sub>11</sub> ) <sub>2</sub> CuLi	"			Et <sub>2</sub> O, THF, ZnBr <sub>2</sub> (1 eq), 5% Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub> , -25 to 10°, 2 h		347
		(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	"			"		347
		"	"			"		348
			"		CH <sub>3</sub> I	THF, HMPA (1 eq), P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> (1.5 eq), -30 to 20°, 5-12 h		349
		(THPO(CH <sub>2</sub> ) <sub>8</sub> ) <sub>2</sub> CuLi	Et <sub>2</sub> O, DMS, -25°, 30 min		1. NH <sub>4</sub> Cl, H <sub>2</sub> SO <sub>4</sub> 2. CH <sub>3</sub> COCl, CH <sub>3</sub> CO <sub>2</sub> H	-		350a
			"		I <sub>2</sub>	Et <sub>2</sub> O, -50 to -10°, 30 min		350a
		(C <sub>2</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>8</sub> ) <sub>2</sub> CuLi	"		n-C <sub>4</sub> H <sub>9</sub> I (2 eq)	THF, HMPT (1 eq), P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> (3 eq), 20°, 3-4 h		350a
	(C <sub>2</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>8</sub> ) <sub>2</sub> CuLi	"			1. THF, HMPA (1 eq) 2. H <sub>2</sub> SO <sub>4</sub>		350a	
	(n-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	Et <sub>2</sub> O, -25°, 30 min		CH <sub>3</sub> SCH <sub>2</sub> Cl	THF, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> (3 eq), 25°, 4 h		350b	

TABLE V. CARBOCUPRATION REACTIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Acetylene Derivative	Organocuprate	Carbometallation Conditions	Adduct	Electrophile	Substitution Conditions	Product(s) and Yield(s) (%)	Refs.
"	"	"		OHCN(CH <sub>3</sub> )CH <sub>2</sub> Cl	THF, 20°, 3 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH=CHN(CH <sub>3</sub> )CHO (83)	350b
(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi		Et <sub>2</sub> O, -30°, 30 min			1. <i>n</i> -C <sub>4</sub> H <sub>9</sub> C≡CLi 2. Et <sub>2</sub> O, -30 to -15°, 2 h	C <sub>2</sub> H <sub>5</sub> CH=CHCH(OH)CH <sub>3</sub> (82)	873
( <i>n</i> -C <sub>5</sub> H <sub>11</sub> ) <sub>2</sub> CuLi		"			Et <sub>2</sub> O, -30 to -10°, 2 h	<i>n</i> -C <sub>5</sub> H <sub>11</sub> CH=CHCH <sub>2</sub> CH <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> (88)	873
( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi		"		CO <sub>2</sub> (excess)	Et <sub>2</sub> O, HMPA (2 eq), P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> (0.01 eq), -40 to -20°	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH=CHCO <sub>2</sub> H (98)	973
		Et <sub>2</sub> O, 15°, 30 min		CO <sub>2</sub> (excess)	"		349
( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi		Et <sub>2</sub> O, -25°, 30 min		<i>i</i> -C <sub>3</sub> H <sub>7</sub> CHO	Et <sub>2</sub> O, -40 to -10°	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH=CHCH(OH)C <sub>3</sub> H <sub>7</sub> - <i>i</i> (68)	873
(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi		"			Et <sub>2</sub> O, -30 to -15°, 1 h	C <sub>2</sub> H <sub>5</sub> CH=CHCH(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> (92)	873
( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi		"		HC≡COC <sub>2</sub> H <sub>5</sub> (2 eq)	1. THF, -15°, 2 h 2. 20% HCl	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH=CHCOCH <sub>3</sub> (75)	873
( <i>n</i> -C <sub>5</sub> H <sub>11</sub> ) <sub>2</sub> CuLi		"		HC≡CCH(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	Et <sub>2</sub> O, -25°, 2 h	<i>n</i> -C <sub>5</sub> H <sub>11</sub> CH=CHCH(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (76)	873
( <i>n</i> -C <sub>7</sub> H <sub>15</sub> ) <sub>2</sub> CuLi		"			1. <i>n</i> -C <sub>4</sub> H <sub>9</sub> C≡CLi 2. Et <sub>2</sub> O, -70 to -10°, 1 h	<i>n</i> -C <sub>7</sub> H <sub>15</sub> CH=CHC <sub>6</sub> H <sub>10</sub> O (82)	873
(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi		"			Et <sub>2</sub> O, -30 to -15°	C <sub>2</sub> H <sub>5</sub> CH=CHCH(CH <sub>3</sub> )CHO (95)	873
C <sub>2</sub> H <sub>5</sub> OCH(CH <sub>3</sub> )O(CH <sub>2</sub> ) <sub>4</sub> Cu(SC <sub>6</sub> H <sub>5</sub> )Li		"	C <sub>2</sub> H <sub>5</sub> OCH(CH <sub>3</sub> )O(CH <sub>2</sub> ) <sub>4</sub> Cu(SC <sub>6</sub> H <sub>5</sub> )Li	HC≡CCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	THF, -50 to -20°	CH <sub>3</sub> CO <sub>2</sub> (CH <sub>2</sub> ) <sub>4</sub> CH=CHCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> (74)	350a
(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi		"			Et <sub>2</sub> O, -20°, 1 h	C <sub>2</sub> H <sub>5</sub> CH=CHCH(OH)CH <sub>3</sub> (82) <i>E:Z</i> 86:14	127
[(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Sn] <sub>2</sub> CuLi		THF, HMPA (3 eq), -55°, 15 min		CH <sub>3</sub> OD, D <sub>2</sub> SO <sub>4</sub>	—	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> SnCH=CHD (~90)	874
( <i>t</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi		Ether, DMS, -40°		C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> CH=CH <sub>2</sub>	Ether, DMS, -40°, 1 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH=CHSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub> (87)	875
( <i>n</i> -C <sub>7</sub> H <sub>15</sub> ) <sub>2</sub> CuLi		Et <sub>2</sub> O, -30°, 30 min		TMSCl	THF, HMPA (1 eq), -30 to 20°, 5 h	<i>n</i> -C <sub>7</sub> H <sub>15</sub> CH=CHTMS (80)	346
( <i>t</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi		Et <sub>2</sub> O, DMS, -40°		C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub>	Ether, DMS, -40°, 1 h	<i>t</i> -C <sub>4</sub> H <sub>9</sub> CH=CHSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub> (87)	856
HC≡COC <sub>2</sub> H <sub>5</sub> (2 eq)	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	THF		CH <sub>3</sub> SCH <sub>2</sub> Cl	THF, 25°, 4 h	C <sub>2</sub> H <sub>5</sub> OCH=CHSCH <sub>3</sub> (76)	350b
C <sub>3</sub> HC≡CCH(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	(TMSCH <sub>2</sub> ) <sub>2</sub> CuLi	Et <sub>2</sub> O, -10°, 6 h	TMSCH <sub>2</sub> CH=Cu(CH <sub>2</sub> TMS)Li CH(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	NH <sub>4</sub> Cl, H <sub>2</sub> O	—	TMSCH <sub>2</sub> CH=CHCH(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (80)	222b
HC≡CCH(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (2 eq)	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	Et <sub>2</sub> O, -60°		C <sub>6</sub> H <sub>5</sub> SCH <sub>2</sub> N(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (2 eq)	THF, 25°, 3-4 h	C <sub>2</sub> H <sub>5</sub> CH=CHCH(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> N(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (79)	225

TABLE V. CARBOCUPRATION REACTIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Acetylene Derivative	Organocuprate	Carbometallation Conditions	Adduct	Electrophile	Substitution Conditions	Product(s) and Yield(s) (%)	Refs.	
"	"	"		$C_6H_5SCH_2Cl$ (2 eq)	THF, 25°, 4 h	 (99)	350b	
"	"	"			THF, 25°, 4 h	 (50)	350a	
"	$(CH_3)_2CuLi$	$Et_2O$		$(C_6H_5S)_2$ (2 eq)	Ether, THF, HMPT, 20°, 3 h	 (58)	876	
$CH_2=C=CH_2$	$[C_6H_5(CH_3)_2Si]_2Cu(CN)Li_2$	THF, -78°, 1 h		$I_2$	THF, -70°, 1 h	 (90)	507	
"	"	"	"	$Cl_2$	THF, -70°, 1 h	 (61)	507	
$CH_3C\equiv CH$	$[C_6H_5(CH_3)_2Si]_2CuLi$	THF, 0°, 20 min		1. $n-C_4H_9C\equiv CLi$ 2. $C_2H_5I$	THF, -78°, 30 min, 0°, 40 h	 (67)	877	
$CH_2=C=CHOCH_3$ (2 eq)	$(s-C_4H_9)_2CuLi$	$Et_2O$ , -40°, 30 min		$I_2$ (2 eq)	$Et_2O$ , -20°, 1 h	 (64)	354	
"	$(C_2H_5)_2CuLi$	"		$CH_3SCH_2Cl$ (2 eq)	THF, 20°, 15 min	 (56)	354	
"		"		$CH_2=COCH_3$	$Et_2O$ , -60°, 30 min	 (72)	354	
$C_4$		$C_6H_5S(CH_3)CuLi$	—		$I_2$	—	 (—)	878
$CH_3C\equiv CCH(OCH_3)_2$		—		$NH_4Cl, H_2O$	—	 (92)	878	
$CH_3C\equiv CCH(OC_2H_5)_2$	$(C_2H_5)_2CuLi$	$Et_2O$ , -50 to 25°		$CH_3SCH_2Cl$ (2 eq)	THF, 25°, 4 h	 (74)	350b	
$CH_2=C=CH(OCH_3)$ (2 eq)	$(n-C_7H_{15})_2CuLi$	$Et_2O$ , -20°, 1 h		$NH_4Cl, H_2O$	—	 (84)	354	
$C_5$	$n-C_4H_9C\equiv CH$	$[CH_3(C_6H_5)_2Si]_2CuLi$	THF, 0°, 30 min		$NH_4Cl, H_2O$	—	 (83)	354
$t-C_4H_9C\equiv CH$	$[(TMS)_2Si]_2CuLi$	THF, 0°, 30 min		$NH_4Cl, H_2O$	—	 (78)	879	
$(CH_3O)_2CH(CH_2)_3C\equiv CH$	$(TMS)_2CuLi$	THF, -23°, 45 min		$CH_3I$	THF, -23°, 2 h	 (78)	880	
$C_7$	$n-C_4H_9CH=C=CHOC_2H_5$ (2 eq)	$(n-C_4H_9)_2CuLi$	$Et_2O$ , 5°, 1 h		$NH_4Cl, H_2O$	—	 (72)	879

\* The product was obtained after hydrolysis with 5 N HCl.

\* This product was obtained after hydrolysis and acetylation of the initial product.

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
<b>C<sub>2</sub></b>				
CH <sub>2</sub> =CHS(O)C <sub>6</sub> H <sub>4</sub> Cl- <i>p</i>	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	1. Ether, -60°, 30 min 2. C <sub>6</sub> H <sub>5</sub> CHO, 25°		(67) 881
CH <sub>2</sub> =CHN(CH <sub>3</sub> )NO	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	0°	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> -CH <sub>2</sub> -N(CH <sub>3</sub> )NO	(88) 388
CH <sub>2</sub> =CHP(O)(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	1. Ether, -70° 2. CH <sub>2</sub> =CHCH <sub>2</sub> Br	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> -CH(CH <sub>2</sub> CH=CH <sub>2</sub> )-P(O)(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	(68) 387
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	1. Ether, -70° 2. C <sub>6</sub> H <sub>5</sub> CHO	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> -CH(OH)C <sub>6</sub> H <sub>5</sub>	(90) 387
CH <sub>2</sub> =CHP <sup>+</sup> (C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> Br <sup>-</sup>	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi (2 eq)	1. THF, HMPA, -50°, 9 h 2. C <sub>6</sub> H <sub>5</sub> CHO, 20°, 3 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> -CH=C(C <sub>6</sub> H <sub>5</sub> )H <i>E:Z</i> 3:97	(80) 882
HC≡CSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	(CH <sub>3</sub> ) <sub>2</sub> CuLi (1 eq)	Ether, 0°, 30 min	CH <sub>3</sub> CH=CHSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	(—) 383
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> S(O)CH=CH <sub>2</sub>	[TBDMSOCH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> CH <sub>2</sub> ] <sub>2</sub> CuLi	Ether, -35°, 2 h	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> S(O)(CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>3</sub> ) <sub>2</sub> -CH <sub>2</sub> OTBDMS	(75) 883
TMSC≡CSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	(CH <sub>3</sub> ) <sub>2</sub> CuLi	THF, -78°, 1.5 h		(95) 884
<b>C<sub>3</sub></b>				
CH <sub>2</sub> =C=CHP(O)(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub>	(CH <sub>3</sub> ) <sub>2</sub> CuLi	1. Ether, THF, -23°, 30 min 2. C <sub>6</sub> H <sub>5</sub> CH=CHCOC <sub>6</sub> H <sub>5</sub>		(66) 885
CH <sub>2</sub> =C=CHSO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> - <i>p</i>	CH <sub>3</sub> Cu(CN)Li	Ether, THF, -23°, 30 min	CH <sub>2</sub> =C(CH <sub>3</sub> )CH <sub>2</sub> SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> - <i>p</i>	(80) 886
CH <sub>2</sub> =C=CHS(O)-C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> - <i>p</i>	(CH <sub>3</sub> ) <sub>2</sub> CuLi	1. THF, ether, -23°, 30 min 2. CH <sub>2</sub> =CHCH <sub>2</sub> Br, -23°, 30 min	CH <sub>2</sub> =C(CH <sub>3</sub> )CH(CH <sub>2</sub> CH=CH <sub>2</sub> )-S(O)C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> - <i>p</i>	(70) 887
HC≡CCO <sub>2</sub> CH <sub>3</sub>	[(CH <sub>3</sub> ) <sub>2</sub> C=C=CH] <sub>2</sub> CuLi	Ether, -10°, 30 min		(91) 764
		THF, -78 to -10°, 5 h		(65) 574
		1. THF, ether, -78°, 1 h 2. 140°		(>90) 888
		—		(83) 642
HC≡CCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub> Cu(C≡CC <sub>4</sub> H <sub>9</sub> - <i>n</i> )Li	1. Ether, -78° 2.		(61) 362
CH <sub>2</sub> =C(CO <sub>2</sub> CH <sub>3</sub> )-N=CHC <sub>6</sub> H <sub>5</sub>	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, -15°, 1.5 h	C <sub>2</sub> H <sub>5</sub> CH(CO <sub>2</sub> CH <sub>3</sub> )N=CHC <sub>6</sub> H <sub>5</sub>	(61) 889
<b>C<sub>4</sub></b>				
CH <sub>3</sub> CH=CHCHO	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	1. Ether, -75°, 15 min 2. TMSCl, TEA, HMPA		(77) 890
( <i>E</i> )-CH <sub>3</sub> CH=CHCON(CH <sub>3</sub> )Ts	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	Ether, -78°	<i>E:Z</i> 75:25 <i>n</i> -C <sub>4</sub> H <sub>9</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CON(CH <sub>3</sub> )Ts	(74) 652
( <i>E</i> )-CH <sub>3</sub> CH=CHCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	[C <sub>6</sub> H <sub>5</sub> (CH <sub>3</sub> ) <sub>2</sub> Si] <sub>2</sub> CuLi	1. — 2. CH <sub>3</sub> I		(82) 891
			<i>syn:anti</i> 1:99	



TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

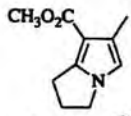
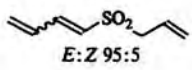
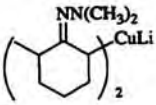
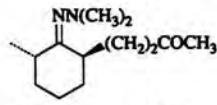
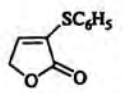
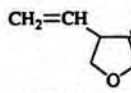
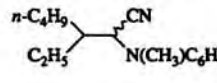
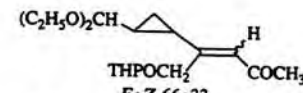
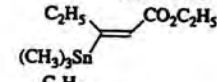
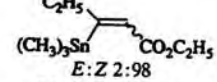
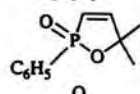
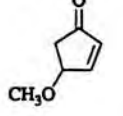
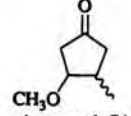
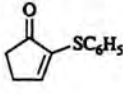
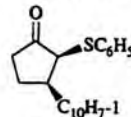
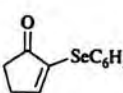
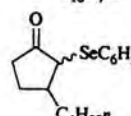
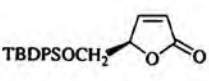
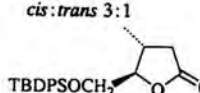
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$\text{CH}_2=\text{CHCOCH}_3$	$(n\text{-C}_7\text{H}_{15}\text{C}(\text{OTBDMS})=\text{C}=\text{CHCu})\text{Li}$ $(\text{CH}_3)_2\text{CuLi}$	1. THF 2. $\text{H}^+$ , $\text{H}_2\text{O}$	$(E)\text{-}n\text{-C}_7\text{H}_{15}\text{COCH}=\text{CH}(\text{CH}_2)_2\text{COCH}_3$ (96)	892
$\text{CH}_2=\text{C}=\text{CHCOC}_6\text{H}_5$	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-23^\circ$ , 30 min 2. $\text{C}_6\text{H}_5\text{CH}=\text{CHCOC}_6\text{H}_5$ , $-23^\circ$ , 30 min	$\text{C}_6\text{H}_5\text{COCH}=\text{C}(\text{CH}_3)\text{CH}_2\text{CH}(\text{C}_6\text{H}_5)\text{CH}_2$ $\text{C}_6\text{H}_5\text{C}=\text{O}$ (25) + $\text{CH}_2=\text{C}(\text{CH}_3)\text{CHCOC}_6\text{H}_5$ $\text{CH}(\text{C}_6\text{H}_5)\text{CH}_2\text{COC}_6\text{H}_5$ (25)	893
$\text{CH}_3\text{O}_2\text{C}\equiv\text{CCH}_2\text{N}(\text{TMS})_2$	$\text{CH}_3(n\text{-C}_4\text{H}_9\text{C}\equiv\text{C})\text{CuLi}$	1. THF, Ether, $-50^\circ$ 2. $\text{Br}(\text{CH}_2)_3\text{COCl}$ 3. KOH	 (65)	894
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $-40$ to $0^\circ$ , 3 h	$n\text{-C}_4\text{H}_9\text{CH}_2\text{CH}=\text{CHCH}_2\text{SO}_2\text{CH}_2\text{CH}=\text{CH}_2$ $E:Z$ 14:79 (46)	816
$\text{CH}_2=\text{CHCOCH}_3$		THF, $(i\text{-C}_3\text{H}_7)_2\text{S}$ , $-78$ to $20^\circ$ , 14 h	 (85)	357b
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	Ether, $-60^\circ$ , 2 h	$\text{CH}_2=\text{CH}$  (—) <sup>a</sup>	895
$\text{CH}_3\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$	$[(\text{CH}_3)_2\text{C}_6\text{H}_5\text{Si}]_2\text{CuLi}$	THF, $-23^\circ$ , 4 h	$(\text{CH}_3)_2\text{C}_6\text{H}_5\text{SiCH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (81)	575
$\text{C}_2\text{H}_5\text{C}(\text{CN})=\text{C}(\text{N}(\text{CH}_3)\text{C}_6\text{H}_5)$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $20^\circ$ , 24 h	$n\text{-C}_4\text{H}_9$  (52)	896
$\text{THPOCH}_2\text{C}\equiv\text{CCOCH}_3$	$[(\text{C}_2\text{H}_5\text{O})_2\text{CH}]_2\text{CuLi}$	—	$(\text{C}_2\text{H}_5\text{O})_2\text{CH}$  (81)	888
$\text{C}_2\text{H}_5\text{C}\equiv\text{CCO}_2\text{C}_2\text{H}_5$	$(\text{CH}_3)_3\text{SnCu}(\text{SC}_6\text{H}_5)\text{Li}$ (2 eq)	THF, $\text{CH}_3\text{OH}$ , $-100$ to $-78^\circ$ , 3 h	$\text{C}_2\text{H}_5$  (79)	897 898
	$(\text{CH}_3)_3\text{SnCu}(\text{SC}_6\text{H}_5)\text{Li}$ (1.2 eq)	THF, $-48^\circ$ , 4 h	$\text{C}_2\text{H}_5$  (76)	897 898
$\text{CF}_3\text{CH}=\text{CHCOCH}_3$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $20^\circ$ , 1 h	$n\text{-C}_4\text{H}_9\text{CH}(\text{CF}_3)\text{CH}_2\text{COCH}_3$ (44)	899
$(E)\text{-CH}_3\text{CH}=\text{CHC}(\text{=CH}_2)\text{SO}_2\text{C}_6\text{H}_5$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $-60$ to $-10^\circ$ , 1 h	$\text{CH}_3\text{CH}=\text{CH}(\text{C}_3\text{H}_{11}\text{-}n)\text{SO}_2\text{C}_6\text{H}_5$ (79)	830
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $0^\circ$ , 3.5 h 2. $\text{CH}_2\text{N}_2$ , ether	$\text{C}_6\text{H}_5\text{P}(\text{O})(\text{OCH}_3)\text{CH}_2\text{CH}=\text{C}(\text{CH}_3)_2$ (65)	900
	$(\text{CH}_3)_2\text{CuLi}$	THF, $\text{TMSCl}$ (5 eq), $-78^\circ$ , 30 min	 (61)	901
			$\text{cis:trans}$ 1:74	
	$(1\text{-C}_{10}\text{H}_7)_2\text{CuLi}$	THF, $-78^\circ$ , 1 h	 (95)	902
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $-20^\circ$ , 30 min	 (97)	903 904
			$\text{cis:trans}$ 3:1	
$\text{TBDPSoCH}_2$ 	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-20^\circ$ , 40 min	 (85)	905

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-70^\circ$		(61) 906
$\text{CH}_3\text{CH}=\text{CHCOCH}_3$	$n\text{-C}_6\text{H}_{13}\text{C}(\text{=CH}_2)\text{Cu}(\text{SC}_6\text{H}_5)_2\text{Li}$	THF, $-78$ to $20^\circ$ , 1 h	$n\text{-C}_6\text{H}_{13}\text{C}(\text{=CH}_2)\text{CH}(\text{CH}_3)\text{CH}_2\text{COCH}_3$	(82) 907
$(E)\text{-ClC}(\text{CH}_3)=\text{CHCOCH}_3$	$(\text{TMSCH}_2)_2\text{CuLi}$	THF, $-5^\circ$ , 1.5 h	$(E)\text{-TMSCH}_2\text{C}(\text{CH}_3)=\text{CHCOCH}_3$	(51) 908
$(E)\text{-TMSC}(\text{CH}_3)=\text{CHCOCH}_3$	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78$ to $0^\circ$	$(\text{CH}_3)_2\text{C}(\text{TMS})\text{CH}_2\text{COCH}_3$	(89) 909
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	1. Ether, $-78^\circ$ , 15 min 2. TBDMSCl, TEA, THF, HMPA		(54) 910
	$\text{CH}_2=\text{C}(\text{Cu}(\text{SC}_6\text{H}_5)_2\text{Li})(\text{CH}_2)_2\text{Cl}$	1. THF, $-78^\circ$ , 3 h 2. HMPA (1.5 eq), $20^\circ$		(—) <sup>b</sup> 911
	$[(n\text{-C}_4\text{H}_9)_3\text{Sn}]_2\text{CuLi}$	THF, DMS, $-25^\circ$		(84) 912
$t\text{-C}_4\text{H}_9(\text{CH}_3)_2\text{SiO}$	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78$ to $0^\circ$	$(E)\text{-TMSCH}=\text{CHCOC}_3\text{H}_7\text{-}n$	(79) 909
$(E)\text{-TMSCH}=\text{CHCOCH}=\text{CH}_2$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	—	$(n\text{-C}_3\text{H}_{11})_2\text{CHCOCH}_3$	(90) 913
$\text{C}_6\text{H}_5\text{SCH}_2\text{C}(\text{=CH}_2)\text{COCH}_3$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (3 eq)	—	—	—
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	1. Ether, $0^\circ$ , 1.5 h 2. $\text{CH}_2=\text{CHCH}_2\text{Br}$		(72) 914
			<i>cis:trans</i> 93:7	
	$(\text{C}_6\text{H}_5\text{S})\text{CuLi}$	THF, ether, $-20$ to $0^\circ$ , 4 h		(83) 915
	$\text{H}-\text{CH}=\text{CH}_2$ $\text{Cu}(\text{SC}_6\text{H}_5)_2\text{Li}$	1. THF, ether, $-78$ to $0^\circ$ , 3 h 2. $180^\circ$ , 30 min		(80) 916
$(\text{CH}_3)_2\text{C}=\text{C}(\text{CN})\text{-P}(\text{O})(\text{OC}_2\text{H}_5)_2$	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, hexane, $-30$ to $20^\circ$	$n\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)_2\text{CH}(\text{CN})\text{P}(\text{O})(\text{OC}_2\text{H}_5)_2$	(80) 917
	$\text{CH}_2=\text{CHCu}(\text{CN})\text{Li}$	1. Ether, $-78^\circ$ , 40 min 2. $(\text{CH}_3\text{CO})_2\text{O}$ , $25^\circ$		(79) 918
	$n\text{-C}_4\text{H}_9\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	Ether, $-78^\circ$ , 2 h		(52) 919
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-78^\circ$ 2. $\text{ICH}_2\text{C}\equiv\text{CC}_2\text{H}_5$ , glyme, $25^\circ$ , 2 h		(65) 920
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, DMS, $0^\circ$ , 1 h		(90) 921
	$(\text{CH}_3)_2\text{CuLi}$	THF, $-70^\circ$		(70) 922

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	THF, $-60$ to $-10^\circ$ , 2-3 h		(60) 929
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78^\circ$ , 1 h		(84) 923
	$(\text{CH}_3)_2\text{CuLi}$	—		(60) 924
$\text{Cl}(\text{CH}_2)_3\text{C}\equiv\text{CCO}_2\text{CH}_3$	$[\text{EEO}(\text{CH}_2)_3]_2\text{CuLi}$	THF, $-78^\circ$		(—) 925
	$[\text{EEO}(\text{CH}_2)_3]_2\text{CuLi}$	THF, $-78^\circ$		(—) 925
$(E)\text{-CH}_3\text{O}_2\text{CCH}=\text{CH}(\text{CH}_2)_2\text{CO}_2\text{CH}_3$	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-25^\circ$ , 30 min		(76) 659
	$(n\text{-C}_3\text{H}_7)_2\text{CuLi}$ (2.5 eq)	Ether, $-25^\circ$ , 12 h		(80) 926
$(E)\text{-}i\text{-C}_2\text{H}_5\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$	$\text{C}_2\text{H}_5\text{C}(\text{C}_6\text{H}_5)_2\text{CH}_2\text{CuLi}$ $(\text{C}_6\text{H}_5\text{S})$	THF, $-78$ to $0^\circ$ , 2.5 h	$\text{C}_2\text{H}_5\text{C}(\text{C}_6\text{H}_5)_2\text{CH}_2\text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$ <i>syn:anti</i> 6:1	927
	$(\text{CH}_3)_2\text{CuLi}$	Ether, DMS, $0^\circ$ , 2.5 h		(51) 928
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	Ether, $-78^\circ$		(84) 930
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-78^\circ$ , 10 min 2. $\text{CH}_3(\text{C}_6\text{H}_5)_2\text{SiCl}$ , TEA, HMPA, $-78$ to $20^\circ$		(76) 931
	$t\text{-C}_4\text{H}_9\text{Cu}(\text{SC}_6\text{H}_5)\text{Li}$	1. THF, $-78$ to $-10^\circ$ 2. TMSCl, TEA, HMPA, $0^\circ$		(89) 932
$\text{TMSCH}=\text{CHCH}_2\text{Cu}(\text{CN})\text{Li}$		Ether, TMEDA, $-78^\circ$ , 3 h		(65) 933
	$\text{Cu}(\text{C}\equiv\text{CC}(\text{CH}_3)_2\text{OCH}_3)\text{Li}$ $\text{Si}(\text{CH}_3)_2\text{C}_4\text{H}_9\text{-}t$	THF, $-78$ to $20^\circ$ , 3 h		(83) 934
$\text{LiCu}(\text{C}_4\text{H}_9\text{-}t)$ 		THF, $-80$ to $20^\circ$ , 2 h		(94) 935
R = $\text{CH}_2\text{OCH}_3$				
$\text{TBDMSOC}(\text{C}_2\text{H}_5)=\text{CHCH}_2\text{CuLi}$ $\text{TMSC}\equiv\text{C}$		Ether, THF, $-70^\circ$ , 3 h		(88) 735

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

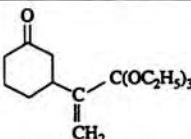
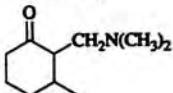
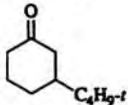
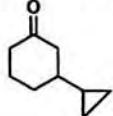
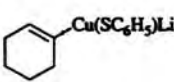
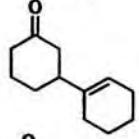
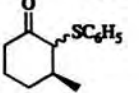
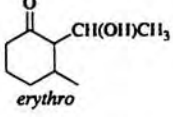
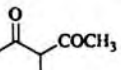
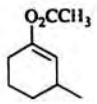
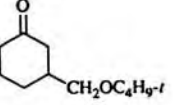
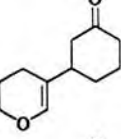
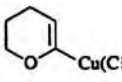
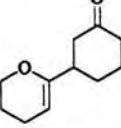
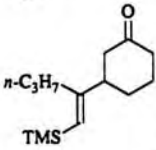
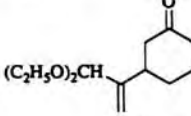
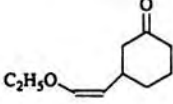
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(C_2H_5O)_3CC(=CH_2)Cu(CN)Li$	THF, $-50^\circ$ , 1.5 h		(68) 362b
	$(CH_3)_2CuLi$	1. — 2. $(CH_3)_2N^+=CH_2 CF_3CO_2^-$		(80) 945
	$t-C_4H_9Cu(C\equiv CC(CH_3)_2OCH_3)Li$	THF, $-20^\circ$		(95) 266
	$(\triangle)_2CuLi$	Ether, $-50^\circ$ , 15 min		(83) 944
	 $Cu(SC_6H_5)Li$	THF, $-78$ to $20^\circ$ , 2 h		(52) 907
	$(CH_3)_2CuLi$	1. Ether, $0^\circ$ , 1 h 2. $C_6H_5SCl$ , $-78$ to $20^\circ$		(55) 946
	$(CH_3)_2CuLi$	1. Ether, $0^\circ$ , 30 min 2. $CH_3CHO$ , $ZnCl_2$ , $0^\circ$		(97) 947
	$(CH_3)_2CuLi$	1. $(i-C_3H_7)_2O$ , $-25^\circ$ , 1 h 2. $CH_3COCl$ , $20^\circ$ , 1 h	 	(87) 948
	$(t-C_4H_9OCH_2)_2CuLi$	$t-C_4H_9OCH_3$ , $(i-C_3H_7)_2S$ , $-30^\circ$ , 45 min		(88) 949
	$(\text{piperidine})_2CuLi$	THF, DMS, $-80^\circ$ , 3 h		(90) 356
	 $Cu(C\equiv CC_3H_7-n)Li$	—		(91) 356c
	$\left[ \begin{array}{c} n-C_3H_7 \\   \\ \text{C} \\   \\ \text{TMS} \end{array} \right]_2CuLi$	—		(70) 356b
	$(C_2H_5O)_2CH-Cu(SC_6H_5)Li$	Ether, $-78$ to $-40^\circ$ , 3 h		(88) 358
	$(C_2H_5O)_2CH-CuLi$	THF, $-78$ to $-40^\circ$ , 1.5 h		(82) 574

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$\text{CH}_2=\text{CHCu}(\text{SC}_6\text{H}_5)_2\text{Li}$ (3 eq)	THF, $-78^\circ$		(70) 936
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78$ to $20^\circ$		(72) 937
	$(\text{CH}_3)_2\text{CuLi}$	THF, $-78$ to $0^\circ$		(100) 938
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0^\circ$ , 2 h		(90) 939
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	1. Ether, $0^\circ$ , 1 h 2. $\text{CH}_3\text{I}$ , HMPA, $0$ – $20^\circ$		(70) 914
	$\text{C}_6\text{H}_5(n\text{-C}_3\text{H}_7\text{C}\equiv\text{C})\text{CuLi}$	1. Ether, $0^\circ$ , 2.5 h 2. $\text{BrCH}_2\text{CO}_2\text{CH}_3$ , HMPA, $20^\circ$		(51) 914
	$(\text{N}(\text{C}_4\text{H}_9)_2\text{OCH}_3)_2\text{CuLi}$ (3 eq)	1. THF, $-60$ to $-20^\circ$ 2. TMSCl 3. $\text{NH}_3/\text{NH}_4\text{Cl}$ , $\text{H}_2\text{O}$		(—) 940
	$(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2)_2\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	1. Ether, $-78$ to $-25^\circ$ , 2 h 2. $\text{TMSC}(\text{=CH}_2)\text{COCH}_3$ , $-25^\circ$ , 1 h		(67) 941
	$(\text{Cyclopropyl})_2\text{Cu}(\text{SC}_6\text{H}_5)_2\text{Li}$	3. $\text{KOH}$ , $\text{CH}_3\text{OH}$ Ether, THF, $0^\circ$ , 2.5 h		(86) 942
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$ (3 eq)	—		(80) 913
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, $-78^\circ$ , 1.5 h		(99) 943
	$(\text{Cyclopropyl})_2\text{CuLi}$	Ether, $-78^\circ$ , 3 h		(75) 944
	$(\text{C}_2\text{H}_5\text{O})_2\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{Cu}[\text{C}\equiv\text{CC}_4\text{H}_9\text{-}t]\text{Li}$	Ether, $-78$ to $0^\circ$ , 16 h		(93) 356a

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

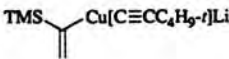
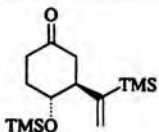
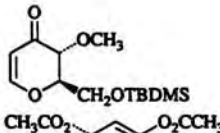
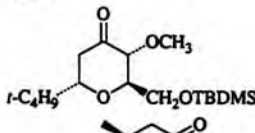
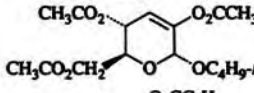
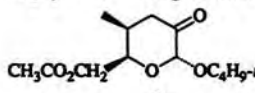
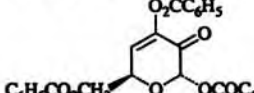
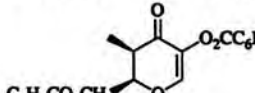
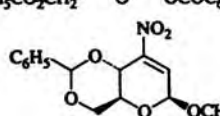
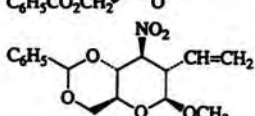
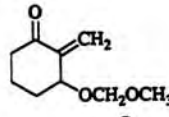
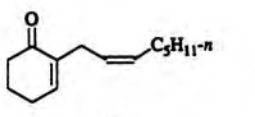
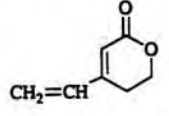
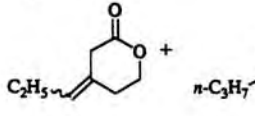
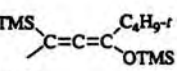
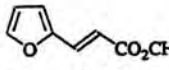
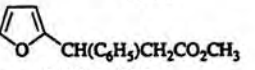
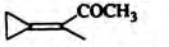
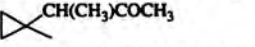
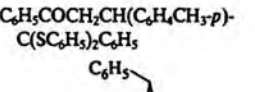
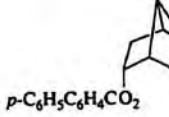
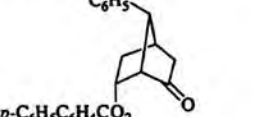
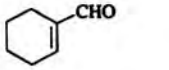
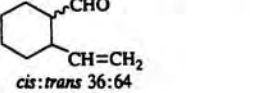
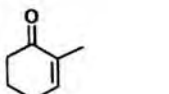


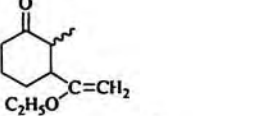
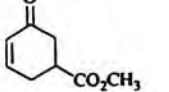
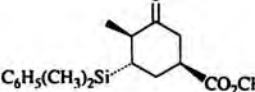
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield (%)	Refs.
		Ether, -78 to 0°, 16 h		(97) 356a
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> (C <sub>6</sub> H <sub>5</sub> S)CuLi	THF, 0°, 2 h		(64) 950
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (2 eq)	THF, 0°, 30 min		(60) 951
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	THF, 0°, 2 h		(—) 951
	(CH <sub>2</sub> =CH) <sub>2</sub> CuLi	Ether, THF, 0°, 1 h		(68) 952
C <sub>7</sub> 	( <i>n</i> -C <sub>5</sub> H <sub>11</sub> ) <sub>2</sub> CuLi	Ether, -78°, 20 min		(67) 953
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, DMS, -30°, 25 min		(51) 954 (8)
TMSC≡CCOC <sub>4</sub> H <sub>9</sub> - <i>t</i>	(CH <sub>3</sub> ) <sub>2</sub> CuLi	1. Ether, -78 to 0° 2. TMSCl, TEA		(86) 909
	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	Ether, 0°, 1 h		(64) 955
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	—		(67) 956
C <sub>6</sub> H <sub>5</sub> COCH=CHC <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> - <i>p</i>	[(C <sub>6</sub> H <sub>5</sub> S) <sub>2</sub> CC <sub>6</sub> H <sub>5</sub> ] <sub>2</sub> CuLi	THF, -70°, 2 h		(50) 957
	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	Ether, 0°, 2 h		(80) 958
	(CH <sub>2</sub> =CH) <sub>2</sub> CuLi	THF, DMS, -78 to -20°, 2.5 h		(50) 959
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	1. — 2. C <sub>6</sub> H <sub>5</sub> N(O <sub>2</sub> SCF <sub>3</sub> ) <sub>2</sub>		(72) 960
	[C <sub>2</sub> H <sub>5</sub> OC(=CH <sub>2</sub> ) <sub>2</sub> CuLi (2 eq)]	Ether, -78 to 0°, 1 h		(80) 357b
	[C <sub>6</sub> H <sub>5</sub> (CH <sub>3</sub> ) <sub>2</sub> Si] <sub>2</sub> CuLi	1. THF, -23°, 45 min 2. CH <sub>3</sub> I, HMPA, -23°, 2 h		(92) 575

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$\text{CH}_2=\text{CH}-\text{C}(\text{CH}_3)_2-\text{Cu}(\text{SC}_6\text{H}_5)\text{Li}$	Ether, THF, 25°	 (76)	961
	$(\text{CH}_3)_3\text{SnCu}(\text{SC}_6\text{H}_5)\text{Li}$	THF, -20 to 20°, 45 min	 (77)	962 963
	$(\text{CH}_3)_2\text{CuLi}$ (3 eq)	—	 <i>cis:trans</i> 11:89 (77)	913
	$\text{NN}(\text{CH}_3)_2$ $(\text{CH}_2=\text{CH}-\text{C}(\text{CH}_3)_2-\text{CuLi})$	1. THF, ( <i>i</i> -C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> S, -30 to 0°, 12 h 2. NaIO <sub>4</sub> , CH <sub>3</sub> OH	 (80)	357b
	$\text{NN}(\text{CH}_3)_2$ $(\text{CH}_2=\text{CH}-\text{C}(\text{CH}_3)_2-\text{CuLi})$	1. THF, ( <i>i</i> -C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> S, -78 to 0°, 5 h 2. CuCl <sub>2</sub> , H <sub>2</sub> O	 (89)	357b
$\text{CH}_3(\text{CH}=\text{CH})_2\text{COCH}_3$	$(E)-(\text{CH}_3\text{CH}=\text{CHCH}_2)_2\text{CuLi}$	Ether, -60°	$\text{CH}_2=\text{CHCH}(\text{CH}_3)\text{C}(\text{CH}_3)=\text{CHCH}_2\text{COCH}_3$ (60)	385
	$n\text{-C}_4\text{H}_9\text{Cu}(\text{SC}_6\text{H}_5)\text{Li}$	THF, -78°	 <i>E:Z</i> 90:10 (70)	517
	$\text{CH}_3\text{Cu}(\text{SC}_6\text{H}_5)\text{Li}$	THF, -78°	 <i>E:Z</i> 93:7 (84)	517
	$(\text{CH}_3)_2\text{CuLi}$	1. THF, -20° 2. TMSCl, TEA, HMPA, -78 to 20°	 (93)	964
$n\text{-C}_3\text{H}_7\text{CH}=\text{CClCOC}_2\text{H}_5$	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, -70°, 30 min	$n\text{-C}_3\text{H}_7\text{CH}(\text{CH}_3)\text{CHClCOC}_2\text{H}_5$ (79)	965
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -50°, 30 min	 (73)	965
	$[\text{CH}_2=\text{C}(\text{CH}_3)]_2\text{CuLi}$	1. Ether, DMS 2. NaOC <sub>2</sub> H <sub>5</sub> , C <sub>2</sub> H <sub>5</sub> OH	 (—)	966
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	THF, ether, DMS	 (—)	967
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -5°, 3 h	 (—)	967
	$(\text{CH}_3)_2\text{CuLi}$	1. ( <i>i</i> -C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> O, -25°, 1 h 2. CH <sub>3</sub> COCl, 25°	 (87)	968
	$(E)-(\text{TMSCH}=\text{CH})_2\text{CuLi}$	Ether, -78°, 5 h	 (53)	969

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$ (3 eq)	Ether, 0°, 2 h		(62) 970
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°		(54) 971
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -23°, 30 min		(95) 972
	$\triangle\text{-Cu}(\text{SC}_6\text{H}_5)\text{Li}$	THF, ether, 0°, 2.5 h	 <i>E:Z</i> 50:50	(91) 942
	$(\text{CH}_3)_2\text{C}=\text{CH}(\text{CH}_2)_2\text{Cu}(\text{SC}_6\text{H}_5)\text{Li}$	THF, -78°	 <i>E:Z</i> 96:4	(75) 517
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -23 to 0°, 25 min		(59) 973
	$(\text{CH}_3)_2\text{CuLi}$	THF, -78°, 45 min		(67) 517
	$(t\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, DMS, -70°	 <i>cis:trans</i> 82:18	(88) 974
	$(\text{CH}_3)_2\text{CuLi}$	THF, -15°	 <i>cis:trans</i> 10:90	(74) 974
	$(t\text{-C}_4\text{H}_9)_2\text{CuLi}$	THF, -15°	 <i>cis:trans</i> 2:98	(38) 974
$(\text{C}_2\text{H}_5)_2\text{C}=\text{C}(\text{CH}_3)\text{CHO}$	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, pentane, 0° 2. TMSCl, TEA, HMPA	$(\text{C}_2\text{H}_5)_2\text{C}(\text{CH}_3)\text{C}(\text{CH}_3)=\text{CHOTMS}$ + $(\text{C}_2\text{H}_5)_2\text{C}=\text{C}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{OTMS}$	(70) 890 (16)
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	THF, -70 to 20°		(77) 975
	$\text{Cl}(\text{CH}_2)_2\text{C}(\text{=CH}_2)\text{Cu}(\text{CN})\text{Li}$	THF, -78 to -48°, 2.5 h		(72) 911



TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{CH}_3)_3\text{SnCu}(\text{SC}_6\text{H}_5)\text{Li}$	THF, HMPA, $-20$ to $0^\circ$ , 2 h		(—) 976
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$ (2 eq)	Ether, DMS, $-35^\circ$ , 5 h		(78) 977
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (4 eq)	1. THF, ether, $-35^\circ$ , 2.5 h 2. 10% $\text{H}_2\text{SO}_4$ , THF, $25^\circ$ , 18 h		(88) 978
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-15$ to $25^\circ$ 2. $\text{Al}(\text{Hg})$ , $\text{C}_6\text{H}_5\text{OH}$ , $\text{H}_2\text{O}$ 3. $\text{NaOH}$ , $\text{H}_2\text{O}$		(53) 979
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0^\circ$ , 1 h		(—) 980
$(E)\text{-C}_6\text{H}_5\text{CH}=\text{CHCO}_2\text{C}_6\text{H}_5$	$(\text{CH}_2=\text{CHCH}_2)_2\text{CuLi}$	Ether, $0$ to $20^\circ$ , 1 h	$\text{C}_6\text{H}_5\text{CH}(\text{CH}_2\text{CH}=\text{CH}_2)\text{CH}_2\text{COC}_6\text{H}_5$ + $\text{C}_6\text{H}_5\text{CH}=\text{CH}(\text{CH}_2\text{CH}=\text{CH}_2)\text{-}(\text{C}_6\text{H}_5\text{-}t)\text{OH}$	(45) 981 (43)
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-15$ to $25^\circ$		(86) 982
$(E)\text{-C}_6\text{H}_5\text{CH}=\text{CHCO}_2\text{C}_6\text{H}_5$	$\left[ (\text{CH}_3)_3\text{Sn} \begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{CuLi} \right]_2$	—	$(\text{CH}_3)_3\text{Sn} \begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{CH}(\text{C}_6\text{H}_5)\text{CH}_2\text{COC}_6\text{H}_5$	(52) 983
	$(\text{CH}_3)_3\text{SnCu}(\text{SC}_6\text{H}_5)\text{Li}$	THF, $-20$ to $20^\circ$ , 75 min		(69) 963
	$[\text{C}_6\text{H}_5\text{SCH}(\text{TMS})]_2\text{CuLi}$	THF, $-78$ to $20^\circ$ , 12 h		(52) 984
	$(\text{CH}_3)_2\text{CuLi}$ (5 eq)	Ether, THF, $-78$ to $0^\circ$ , 3 h		(—) 985
$(E)\text{-C}_6\text{H}_5\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$	$(2\text{-C}_5\text{H}_4\text{N})_2\text{CuLi}$	Ether, $0^\circ$ , 20 min	$2\text{-C}_5\text{H}_4\text{NCH}(\text{C}_6\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	(82) 987
	$[\text{TMSC}(\text{=CH}_2)]_2\text{CuLi}$ (4 eq)	Ether, THF, $-20^\circ$ , 10 h		(61) 357b
	$(E)\text{-}(\text{TMSCH}=\text{CH})_2\text{CuLi}$	Ether, $-78$ to $0^\circ$ , 1 h		(64) 357b

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

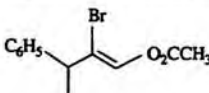
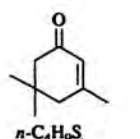
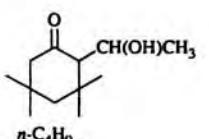
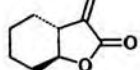
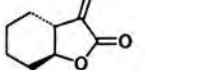
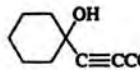
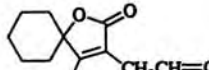
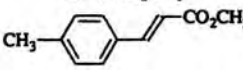
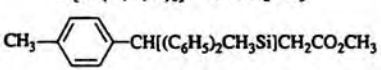
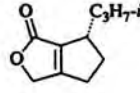
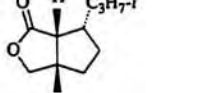
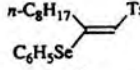
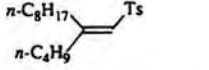
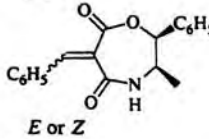
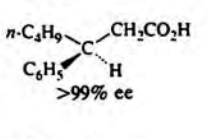
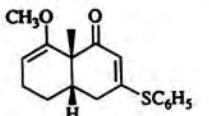
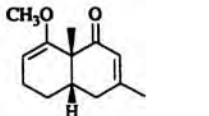
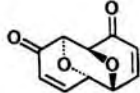
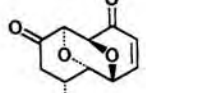
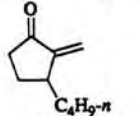
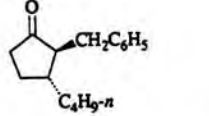
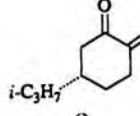
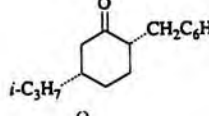
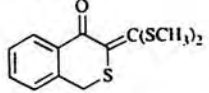
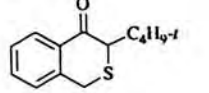
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$(Z)\text{-C}_6\text{H}_5\text{CH}=\text{CBrCHO}$	$(\text{CH}_3)_2\text{CuLi}$ (4 eq)	1. Ether, $0^\circ$ 2. $(\text{CH}_3\text{CO})_2\text{O}$ , $-78$ to $20^\circ$		(39) 918
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $0^\circ$ , 30 min 2. $\text{CH}_3\text{CHO}$ , $\text{ZnCl}_2$ , $0^\circ$		(82) 947
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $-78^\circ$ , 30 min		(88) 988
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	1. Ether, $-78$ to $25^\circ$ 2. $\text{CH}_2=\text{CHCH}_2\text{Br}$ , HMPA, $0^\circ$ 3. $\text{H}^+$ , $\text{H}_2\text{O}$		(71) 989
$\text{C}_{10}$ $\text{THPOCH}_2\text{C}(\text{CH}_3)_2(\text{CH}_2)_3\text{C}\equiv\text{CCO}_2\text{CH}_3$	$(n\text{-C}_4\text{H}_9)_3\text{SnCu}(\text{SC}_6\text{H}_5)\text{Li}$	THF, $-40^\circ$	$\text{THPOCH}_2\text{C}(\text{CH}_3)_2(\text{CH}_2)_3\text{C}[\text{Sn}(\text{C}_4\text{H}_9)_3]\text{CHCO}_2\text{CH}_3$	(86) 990
	$[(\text{C}_6\text{H}_5)_2\text{CH}_3\text{Si}]_2\text{CuLi}$	THF		(—) 991
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78^\circ$ , 4 h		(71) 992
	$n\text{-C}_4\text{H}_9\text{Cu}(\text{SeC}_6\text{H}_5)\text{Li}$	THF, $0^\circ$ , 2 h		(62) 993
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	1. THF, diglyme, $-78^\circ$ , 2 h 2. $\text{HOAc}$ , $\text{H}_2\text{SO}_4$ , $\text{H}_2\text{O}$		(64-76) 377
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78^\circ$ , 1 h		(89) 994
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, DMS, $-70^\circ$ , 1.5 h		(42) 995
$n\text{-C}_3\text{H}_7\text{CH}=\text{CFCOC}_4\text{H}_9\text{-}n$	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, $-30^\circ$ , 1.5 h	$n\text{-C}_3\text{H}_7\text{CH}(\text{CH}_3)\text{CHFCOC}_4\text{H}_9\text{-}n$	(80) 965
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	—		(57) 913
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	THF, $-78$ to $20^\circ$ , 3 h		(30) 996
	$(\text{CH}_3)_2\text{CuLi}$ (xs)	Ether, $0^\circ$ , 5 h		(20) 997

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

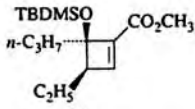
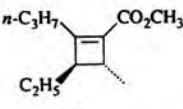
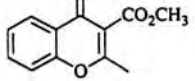
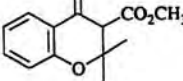
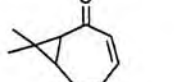
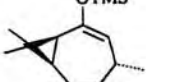
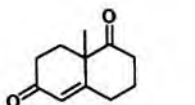
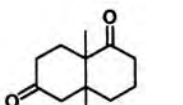
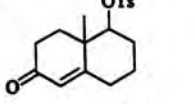
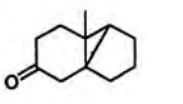
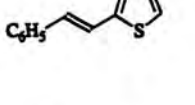
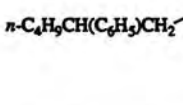
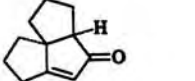
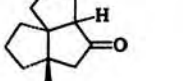
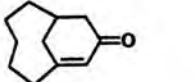
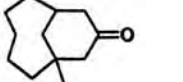

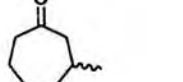
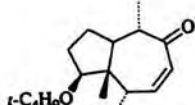
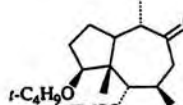
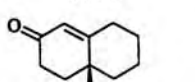
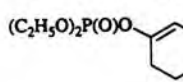
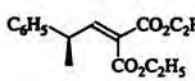
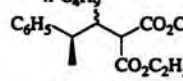
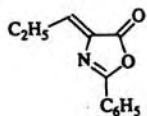
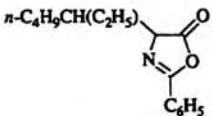
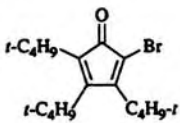
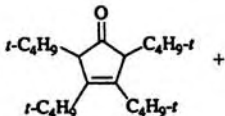
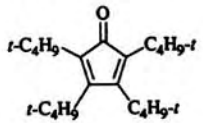
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$(E)\text{-C}_6\text{H}_5\text{CH=CHCOCH}_3$	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	1. Ether, 0°, 30 min 2. $\text{HCO}_2\text{C}_2\text{H}_5$ , 0° 3. $\text{BF}_3\cdot\text{CH}_3\text{OH}$ , 20°	$\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{CH}_2\text{COCH}_2\text{CH}(\text{OCH}_3)_2$ (65)	947
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	THF, -70 to 20°		(60) 975
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, -10°, 30 min		(74) 998
	$(\text{CH}_3)_2\text{CuLi}$	1. THF, -78° 2. TMSCl		(—) 999
C <sub>11</sub>				
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°, 30 min		(83) 68a
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°, 15 min		(70) 68a
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, -20°, 2 h		(33) 1000
$(E,E)\text{-C}_6\text{H}_5(\text{CH=CH})_2\text{CN}$	$(\text{CH}_2=\text{CHCH}_2)_2\text{CuLi}$	Ether, 0 to 20°, 1 h	$(E)\text{-C}_6\text{H}_5\text{CH}(\text{CH}_2\text{CH=CH}_2)\text{-CH=CHCH}_2\text{CN}$ (80)	981
	$(\text{CH}_3)_2\text{CuLi}$ (5 eq)	Ether, 0°, 2 h		(89) 1001
	$(\text{CH}_3)_2\text{CuLi}$	Ether, DMS, 0-25°, 4 h		(67) 1002
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -15°		(70) 974
			<i>cis:trans</i> 3:97	
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	Ether, 0°, 2 h		(71) 1003
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, 0°, 1 h 2. $(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{Cl}$ , ether, HMPT		(84) 1004
C <sub>12</sub>				
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	DME, -78 to -20°		(87) 1005
			<i>syn:anti</i> 92:8	

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yields (%)	Refs.	
	$(C_6H_5)_2CuLi$	Ether, $-78^\circ$		(—) 1006	
	$(CH_3)_2CuLi$	Ether, DMS, $20^\circ$ , 1 h		(84) 1007	
	$[CH_2=C(CH_3)]_2CuLi$	Ether, $-60$ to $0^\circ$ , 4 h		(81) 1008	
	$(CH_3)_2CuLi$ (2 eq)	Ether, $-30$ to $25^\circ$		(88) 1009	
	$(n-C_4H_9)_2CuLi$ (3 eq)	Ether, $0^\circ$		(79) 1010 <i>cis:trans</i> 1:20	
C <sub>13</sub>	$(E)-Br(CH_2)_3C(CH_3)_2CH=CHCO_2C_4H_9-t$	$(CH_3)_2CuLi$	Ether, DMS, $0^\circ$ , 1.5 h	$Br(CH_2)_3C(CH_3)_2CH(CH_3)CH_2CO_2C_4H_9-t$	1011 (82-92)
	$(E)-n-C_4H_9C(CH_3)_2CH=CHCO_2C_4H_9-t$	$(CH_3)_2CuLi$	Ether, DMS, HMPT, $25^\circ$ , 7.5 h	$(E)-n-C_4H_9C(CH_3)_2CH=CHCO_2C_4H_9-t$	1011 (72-97)
	$(CH_3)_2CuLi$	Ether, $0^\circ$ , 2 h		(85) 1012	
	$CH_3Cu(SC_6H_5)Li$ (1.2 eq)	THF, $-78$ to $0^\circ$ , 45 min		(82) <sup>d</sup> 517 <i>E:Z</i> 67:33	
C <sub>14</sub>		$(CH_3)_2CuLi$	Ether, $25^\circ$ , 45 min		(95) 1013
		$t-C_4H_9Cu(C\equiv CC_3H_7-n)Li$	Ether, HMPA, $-25^\circ$		(95) 1014
		$(CH_3)_2CuLi$	Ether, $-78^\circ$ , 1 h		(40) 1015
C <sub>15</sub>		$(CH_3)_2CuLi$	1. Ether, $0^\circ$ , 10 min 2. $(C_6H_5)_2Se_2$ 3. $H_2O_2$		(55) 1016

TABLE VI. CONJUGATE ADDITIONS OF LOWER ORDER LITHIO ORGANOCUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
C <sub>16</sub> 	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu(SC <sub>6</sub> H <sub>5</sub> )Li	THF, -10°	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH(C <sub>2</sub> H <sub>5</sub> ) 	(95) 1017
C <sub>17</sub> 	( <i>t</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi	THF, -78°, 4 h	 + 	(22) 1018  (2)

<sup>a</sup> The yield was reported in the 75–100% range.

<sup>b</sup> The yield was reported in the 55–60% range.

<sup>c</sup> BT = benzothiazol-2-yl.

<sup>d</sup> The dimethylated product was also formed in 4% yield.

TABLE VII. SUBSTITUTION REACTIONS OF ORGANOCOPPER REAGENTS, R<sub>2</sub>Cu

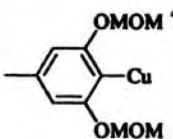
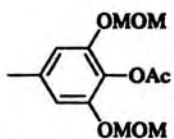
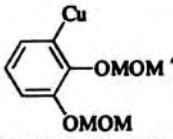
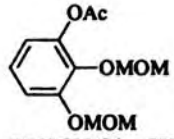
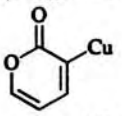
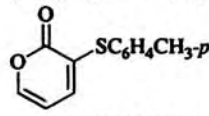
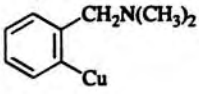
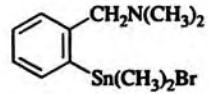
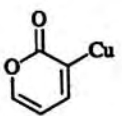
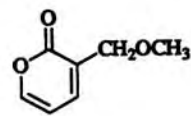
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
O <sub>2</sub>		1. THF, 0°, 45 min 2. Ac <sub>2</sub> O, 25°, 12 h		(67) 300
		"		(58) 300
CuCl <sub>2</sub>	TMSCH <sub>2</sub> C(=CH <sub>2</sub> )Cu	Ether, -23°, 1 h; 25°, 15 h	TMSCH <sub>2</sub> C(=CH <sub>2</sub> )- C(=CH <sub>2</sub> )CH <sub>2</sub> TMS (70-88)	1019
C <sub>6</sub> H <sub>5</sub> N=S=O	(CH <sub>3</sub> ) <sub>2</sub> C=C=CHCu	THF, -60°, 3 h	(CH <sub>3</sub> ) <sub>2</sub> C(C≡CH)S(O)NHC <sub>6</sub> H <sub>5</sub> (85)	1020
	(CH <sub>3</sub> ) <sub>2</sub> C=C=C(C <sub>6</sub> H <sub>5</sub> )Cu	THF, -60°, 3 h	(CH <sub>3</sub> ) <sub>2</sub> C(C≡CC <sub>6</sub> H <sub>5</sub> )S(O)NHC <sub>6</sub> H <sub>5</sub> (72)	1020
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> STs		Ether, THF, -78 to 25°, 4 h		(67) 1021
(CH <sub>3</sub> ) <sub>2</sub> SnBr <sub>2</sub>		C <sub>6</sub> H <sub>6</sub> , 25°		(81) 1022
CH <sub>3</sub> OCH <sub>2</sub> Br		Ether, 25°, 3 h		(54) 1021

TABLE VII. SUBSTITUTION REACTIONS OF ORGANOCOPPER REAGENTS, RCu (Continued)

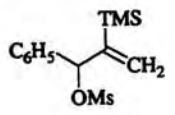
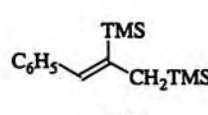
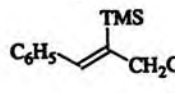
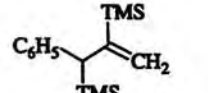
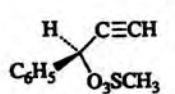
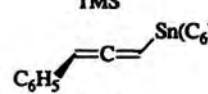
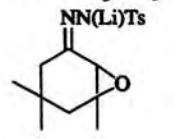
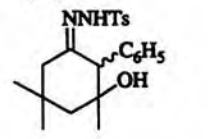
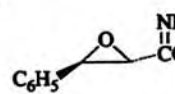
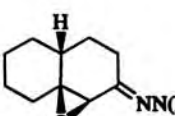
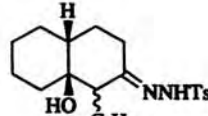
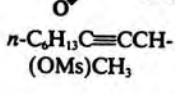
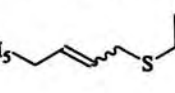
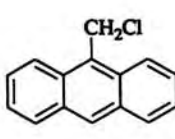
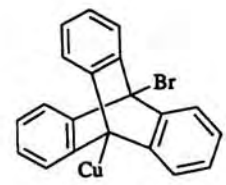
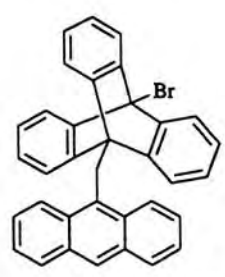
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$C_6H_5CH_2OCH_2Cl$		Ether, 25°, 3 h		(65) 1021
$(C_2H_5O)_2P(O)CH_2Cl$		THF, reflux 12 h		(64) 1023
$C_2$ TMSC≡Cl	$CH_2=C=CHCu$	THF, -40 to 0°, 30 min	$CH_2=C=CHC≡TMS$	(85) 1024
$C_3$ $C_6H_5O_2SCH=CHI$	$C_6H_5C≡CCu$	Py, 25°, 24 h	$C_6H_5O_2SCH=C=CHC≡CC_6H_5$	(63) 290
$BrC(=CH_2)CH_2OTMS$		THF, DMS, 20°, 16 h		(76) 1025
$C_6H_5(O_2)S$ 	$C_6H_5C≡CCu$	Py, 25°, 3 d		(62) 290
$CH_3C≡Cl$	$t-C_4H_9CH=C=CHCu$	THF, -40 to 0°, 30 min	$t-C_4H_9CH=C=CHC≡CCH_3$	(75) 1024
$HC≡CCH_2Br$	$(C_2H_5O)_2P(O)CH_2Cu$	THF, -35 to 25°, 16 h	$(C_2H_5O)_2P(O)CH_2CH=C=CH_2$	(72) 1026
	$(C_2H_5O)_2P(O)CH(CH_3)Cu$	THF, -35 to 25°, 16 h	$(C_2H_5O)_2P(O)CH(CH_3)CH=C=CH_2$	(60) 1026
	$CH_3CH=CHCH_2Cu$	Ether, $(n-C_4H_9)_2S$ , THF, -35 to 0°		(66) 1027
			<i>cis:trans</i> 45:55	
$C_4$ $t-C_4H_9N=CHC(CH_3)_2Cl$	$CH_3Cu$	Ether, reflux, 15 h	$[t-C_4H_9N=CHC(CH_3)_2]_2$	(85-89) 1028
$CH_2=C(CH_3)COCl$	$C_6H_5C≡CCu$ (1 eq LiI)	Ether, HMPA, 20°, 12 h	$C_6H_5C≡CCOC(CH_3)=CH_2$	(85) 1029
$C_5$ $CH_2=C(CH_3)C≡Cl$	$t-C_4H_9CH=C=CHCu$	THF, -40 to 0°, 30 min	$CH_2=C(CH_3)C≡CCH=C=CHC_4H_9-t$	(85) 1024
		THF, -40 to 0°, 30 min		(85) 1024
$CH_3C≡CCl$	$t-C_4H_9CH=C=CHCu$	THF, -40 to 0°, 30 min	$CH_3(C≡C)_2CH=C=CHC_4H_9-t$	(75) 1024
$HC≡CC(CH_3)_2Br$	$(C_2H_5O)_2P(O)CH_2Cu$	THF, -35 to 25°, 16 h	$(C_2H_5O)_2P(O)CH_2CH=C=C(CH_3)_2$	(69) 1026
$C_5$ 	$(CH_3)_3SnCu$	THF, DMS, HMPA, -48 to 20°, 4 h		(82) 963
$C_6H_5I$		—		(56) 1030
		Neat, 130°, 1 h		(70) 1031
		THF, DMS, -78 to 20°, 16 h		(84) 1032

TABLE VII. SUBSTITUTION REACTIONS OF ORGANOCOPPER REAGENTS, R<sub>2</sub>Cu (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
HC≡CCH(OMs)- C <sub>3</sub> H <sub>7-n</sub>	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C=NCH <sub>2</sub> Cu·DMS	THF, -50°, 45 min	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C=N-CH <sub>2</sub> -C≡C-C <sub>3</sub> H <sub>7-n</sub>	(49) 1033
	CH <sub>3</sub> Cu	THF, 0°, 10 min		(96) 290
	CH <sub>3</sub> Cu	THF, 0°, 10 min		(47) 290
ClCO(CH <sub>2</sub> ) <sub>4</sub> COCl		THF, 25°, 1.5 h		(39) 1031
		1. THF, hexane, reflux 2 h 2. O <sub>2</sub> , -78°		(51) 303
	C <sub>6</sub> H <sub>5</sub> Cu·S(C <sub>3</sub> H <sub>7-i</sub> ) <sub>2</sub>	THF, -20 to 0°, 1.5 h		(78) 1034
	(CH <sub>3</sub> ) <sub>3</sub> SnCu	THF, DMS, -48°, 2 h		(75) 963
	C <sub>6</sub> H <sub>5</sub> N(CH <sub>3</sub> )Cu (5 eq)	1. THF, 10°, 2 h 2. O <sub>2</sub> , -78°		(48) 302
<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> COCl		THF, 25°, 1.5 h		(79) 1031
<i>n</i> -C <sub>4</sub> H <sub>9</sub> -C≡C-CH <sub>2</sub> Br TMS	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (2 eq)	Ether, -70 to -40°, 2 h	TMS(C <sub>4</sub> H <sub>9-n</sub> ) <sub>2</sub> C≡C-	(100) 1035
	<i>s</i> -C <sub>4</sub> H <sub>9</sub> Cu (3 eq)	Ether, -70 to -40°, 2 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> -C≡C-CH <sub>2</sub> -C <sub>4</sub> H <sub>9-s</sub>	(100) 1035
<i>n</i> -C <sub>4</sub> H <sub>9</sub> C≡CCH <sub>2</sub> Br	(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> P(O)CH <sub>2</sub> Cu	THF, -35 to 25°, 16 h	(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> P(O)CH <sub>2</sub> -C≡C-C <sub>4</sub> H <sub>9-n</sub>	(70) 1026
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu	THF, 0°, 10 min		(90) 290
	C <sub>6</sub> H <sub>5</sub> C≡CCu	Py, 100°, 11 h		(76) 290
C <sub>6</sub> H <sub>5</sub> C≡Cl	(CH <sub>3</sub> ) <sub>2</sub> C=C=CHCu	THF, -40 to 0°, 30 min	(CH <sub>3</sub> ) <sub>2</sub> C=C=CHC≡CC <sub>6</sub> H <sub>5</sub>	(90) 1024
		THF, Pd[P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub> (cat.), -78 to 20°, 5 h		(61) 1036



TABLE VII. SUBSTITUTION REACTIONS OF ORGANOCOPPER REAGENTS, RCu (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
<b>C<sub>9</sub></b>				
	TMSCu	Ether, HMPA, -60°, 1 h		(47) 1037
	TMSCu	Ether, HMPA, -60°, 1 h		(77) 1037
	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> SnCu	THF, LiBr, -60°, 3 min		(—) 1038
	C <sub>6</sub> H <sub>5</sub> Cu-(i-C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> S	THF, -20 to 0°, 1.5 h		(80) 1034
<b>C<sub>10</sub></b>				
	C <sub>6</sub> H <sub>5</sub> Cu-(i-C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> S	THF, -20 to 0°, 1.5 h	C <sub>6</sub> H <sub>5</sub> CH(OH)CH(C <sub>6</sub> H <sub>5</sub> )- C(CH <sub>3</sub> )=NNHTs <i>erythro:threo</i> 7:1	(60) 1034
	C <sub>6</sub> H <sub>5</sub> Cu-(i-C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> S	THF, -20 to 0°, 1.5 h		(79) 1034
	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C=NCH <sub>2</sub> Cu-DMS	THF, -50°, 45 min	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C=NCH <sub>2</sub> C- (C <sub>6</sub> H <sub>13</sub> - <i>n</i> )=C=CHCH <sub>3</sub>	(54) 1033
	(n-C <sub>4</sub> H <sub>9</sub> ) <sub>3</sub> SnCu	THF, HMPA, 0°, 4.3 h	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> Sn(C <sub>4</sub> H <sub>9</sub> - <i>n</i> ) <sub>3</sub>	(54) 1039
<b>C<sub>15</sub></b>				
		Ether, C <sub>6</sub> H <sub>6</sub> , 20°, 12 h		(64) 1040

<sup>a</sup> MOM = CH<sub>3</sub>OCH<sub>2</sub>.

TABLE VIII. REACTIONS OF RCu IN THE PRESENCE OF ADDITIVES

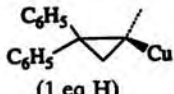
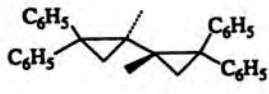
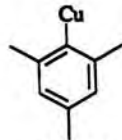
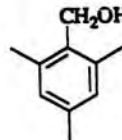
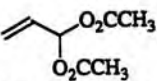
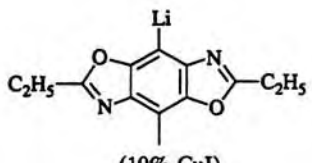
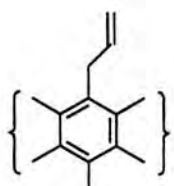
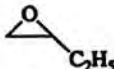

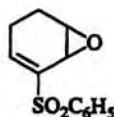
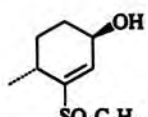
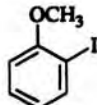
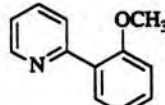
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
A. Substitution Reactions				
C <sub>0</sub> O <sub>2</sub>	 (1 eq H)	THF, -42°, 4 h	 (61)	1041
C <sub>1</sub> (HCHO) <sub>n</sub>	 (2 eq H)	THF, 20°	 (60)	457
C <sub>3</sub>  (CH <sub>3</sub> ) <sub>2</sub> C(OCH <sub>3</sub> ) <sub>2</sub> CH <sub>2</sub> =CHCH <sub>2</sub> Br	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq A) <i>n</i> -C <sub>7</sub> H <sub>15</sub> Cu (1 eq A) C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Cu (4 eq I)	Ether, -10 to 25° Ether, -30°, 30 min THF, 0°, 10 min	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> CH=CH <sub>2</sub> O <sub>2</sub> CCH <sub>3</sub> (70) <i>E</i> : <i>Z</i> 70:30 <i>n</i> -C <sub>7</sub> H <sub>15</sub> C(CH <sub>3</sub> ) <sub>2</sub> OCH <sub>3</sub> (70) C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub> CH=CH <sub>2</sub> (50)	397 395 480
C <sub>4</sub>	 (10% CuI)	THF, 50°, 18 h	 (90)	1042
C <sub>4</sub> CH <sub>3</sub> CH=CHCH <sub>2</sub> OH	[ <i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq A)] (3 eq)	Ether, -70 to 20°	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH(CH <sub>3</sub> )CH=CH <sub>2</sub> + CH <sub>3</sub> CH=CHC <sub>5</sub> H <sub>11</sub> - <i>n</i> (99) 86:14	464
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> Cu (2 eq) (xs B)	THF, -78 to -15°	<i>t</i> -C <sub>4</sub> H <sub>9</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>4</sub> CHOHC <sub>2</sub> H <sub>5</sub> (87)	482
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Li (5 eq) (20% CuI)	Ether, DMS, 0°, 3 h	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> OH (91)	1043
C <sub>5</sub> CH <sub>3</sub> C≡CCl	EEO(CH <sub>2</sub> ) <sub>2</sub> CH=C=CHCu (1 eq LiBr)	THF, -50 to 0°, 1 h	CH <sub>3</sub> (C≡C) <sub>2</sub> CH=C=CH(CH <sub>2</sub> ) <sub>2</sub> OEE (95)	1044
C <sub>6</sub> 	CH <sub>3</sub> Cu (1 eq G)	THF, -78°	 (70)	1045
CH <sub>3</sub> (CH=CH) <sub>2</sub> -CH <sub>2</sub> OH	[ <i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq A)] (3 eq)	Ether, -70 to 20°	CH <sub>3</sub> CH=CHCH(C <sub>4</sub> H <sub>9</sub> - <i>n</i> )CH=CH <sub>2</sub> (70)	464
	2-C <sub>5</sub> H <sub>4</sub> NCu (1 eq H)	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> , 100°, 1 h	 (76)	1046

TABLE VIII. REACTIONS OF RCU IN THE PRESENCE OF ADDITIVES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq A)	1. — 2. CH <sub>3</sub> OH, H <sub>2</sub> O, HCl		(54) 1047
	[ <i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq C)] (7.5 eq)	Ether, -70°		(98) 463
C <sub>6</sub> H <sub>5</sub> COCl	<i>o</i> -NCC <sub>6</sub> H <sub>4</sub> Cu (4 eq I)	THF, 0°, 10 min	<i>o</i> -NCC <sub>6</sub> H <sub>4</sub> COC <sub>6</sub> H <sub>5</sub>	(95) 480b
C <sub>4</sub>				
	Li-Naphthalene, CuI (2 eq H)	THF, -45 to 20°, 3 h		(50) 482b
	[ <i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq A)] (3 eq)	THF, -78°, 30 min		(78) 813
C <sub>10</sub>				
	CH <sub>3</sub> Cu (1 eq A)	1. Ether 2. HCl, THF, H <sub>2</sub> O		(—) 1048
B. Conjugate Addition Reactions				
C <sub>4</sub>				
CH <sub>3</sub> O <sub>2</sub> CC≡CCO <sub>2</sub> CH <sub>3</sub>	CH <sub>3</sub> Cu (1 eq D)	Ether, -60°, 30 min		(88) 1049
HC≡CCOCH <sub>3</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq D)	Ether, -70°, 30 min		(78) 1049
	[ <i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq A)] (2 eq)	Ether, -70 to 20°	<i>n</i> -C <sub>4</sub> H <sub>9</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	(95) 455
	[C <sub>6</sub> H <sub>5</sub> Cu (1 eq A)] (5 eq)	1. Ether, -80 to -20° 2. NaOH		(>90) 472
Ar =				
	[ <i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq A)] (2 eq)	1. Ether, -78 to 25° 2. NaOCH <sub>3</sub> , CH <sub>3</sub> OH, H <sub>2</sub> O		(~75) 473

TABLE VIII. REACTIONS OF RCu IN THE PRESENCE OF ADDITIVES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
$\text{CH}_3\text{CH}=\text{CHCO}_2\text{H}$	$\left[ n\text{-C}_4\text{H}_9\text{Cu} \right]$ (3 eq)	Ether, $-78$ to $20^\circ$	$n\text{-C}_4\text{H}_9\text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{H}$	(86) 465
	$\left[ \text{CH}_2=\text{CHCu} \right]$ (10 eq) (1 eq A, 1 eq B)	1. Ether, THF, $-78$ to $-40^\circ$ 2. NaOH, $\text{C}_2\text{H}_5\text{OH}$	 98% ee	(~80) 475
	$n\text{-C}_4\text{H}_9\text{Cu}$ (3 eq B)	Ether, $-70$ to $-40^\circ$ , 5 h		(93) 1050
	THPO- $n\text{-C}_5\text{H}_{11}$ (3 eq B)	THF, $-78^\circ$ , 1 h		(84) 468
	$t\text{-C}_4\text{H}_9\text{Cu}$ (F)	THF, $-78^\circ$ , 20 min		(93) 679
	$\text{C}_6\text{H}_5\text{Cu}$ (2 eq B)	Ether, $-78^\circ$ , 1.5 h		(71) 1051
$(\text{CH}_3)_2\text{C}=\text{CHCO}_2\text{C}_2\text{H}_5$	$\left[ n\text{-C}_4\text{H}_9\text{Cu} \right]$ (3 eq) (1 eq A)	Ether, $-78$ to $20^\circ$	$n\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	(94) 465
	$n\text{-C}_4\text{H}_9\text{Cu}$ (1 eq A)	THF, $-78$ to $-10^\circ$ , 16 h		(76) 1052, 1053
	$\text{Cl}(\text{CH}_2)_3\text{C}(\text{=CH}_2)\text{Cu}$ (2 eq B, 1 eq A)	Ether, $-78$ to $-40^\circ$ , 3 h		(67) 655
	$\left[ n\text{-C}_4\text{H}_9\text{Cu} \right]$ (2 eq) (1 eq A)	Ether, $-70$ to $20^\circ$	 +  93:7	455 (44)
	$t\text{-C}_4\text{H}_9\text{N}=\text{C}(\text{Cu})\text{C}_4\text{H}_9\text{-s}$ (1 eq A)	Ether, $-78$ to $0^\circ$		(65) 1054

TABLE VIII. REACTIONS OF RCU IN THE PRESENCE OF ADDITIVES (Continued)

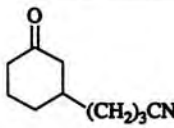
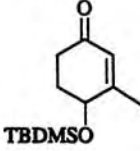
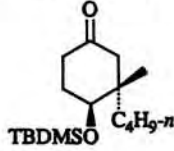
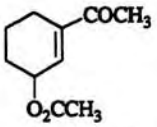
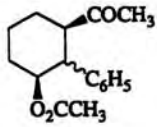
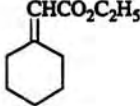
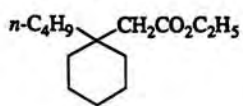
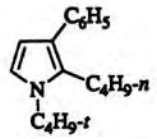
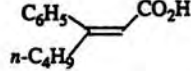
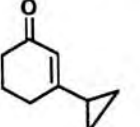
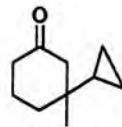
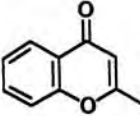
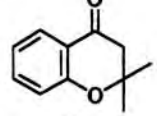
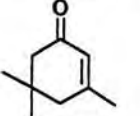
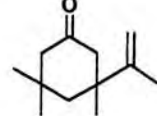
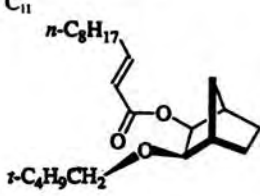
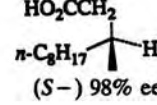
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$[\text{NC}(\text{CH}_2)_3\text{Cu}]$ (3 eq) (xs B)	THF, -78 to 20°, 4 h		(71) 481
C <sub>7</sub> HO(CH <sub>2</sub> ) <sub>4</sub> - CH=CHCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	$[n\text{-C}_4\text{H}_9\text{Cu}]$ (1 eq A) (xs)	—	HO(CH <sub>2</sub> ) <sub>4</sub> CH(C <sub>4</sub> H <sub>9</sub> - <i>n</i> ) CH <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	(75) 1055
	$n\text{-C}_4\text{H}_9\text{Cu}$ (1 eq C)	Ether, -70 to -25°		(81) 1056
C <sub>8</sub> 	$\text{C}_6\text{H}_5\text{Cu}$ (1 eq C)	Ether, -25°, 30 min		(87) 1057
	$[n\text{-C}_4\text{H}_9\text{Cu}]$ (2 eq) (1 eq A)	Ether, -70 to 20°		(51) 455
C <sub>9</sub> C <sub>6</sub> H <sub>5</sub> CH=CHCHO	$t\text{-C}_4\text{H}_9\text{N}=\text{C}(\text{Cu})\text{C}_4\text{H}_9\text{-}n$ (1 eq A)	Ether, -78 to 0°		(93) 1054
C <sub>6</sub> H <sub>5</sub> C≡CCO <sub>2</sub> H	$[n\text{-C}_4\text{H}_9\text{Cu}]$ (2 eq) (1 eq E)	Ether, 20°, 12 h		(85) 1049
	$[\text{CH}_3\text{Cu}]$ (1 eq C) (5 eq)	Ether, -70 to -40°		(98) 471
	$[\text{CH}_3\text{Cu}]$ (1 eq A) (6 eq)	Ether, -70 to 20°, 14 h		(76) 448
	$\text{CH}_2=\text{C}(\text{CH}_3)\text{Cu}$ (3 eq B)	Ether, -78 to 40°, 1.5 h		(100) 468, 469
C <sub>11</sub> 	$[\text{CH}_3\text{Cu}]$ (1 eq A, 1 eq B) (10 eq)	1. Ether, -78° to -35°, 18 h 2. NaOCH <sub>3</sub> , CH <sub>3</sub> OH, H <sub>2</sub> O	HO <sub>2</sub> CCH <sub>2</sub>  (S-) 98% ee	(>90) 1058

TABLE VIII. REACTIONS OF RCU IN THE PRESENCE OF ADDITIVES (*Continued*)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	CH <sub>3</sub> Cu (1 eq A)	Ether, 0°		(98) 1059
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq A)	Ether, -78 to 20°		(83) 465
	[CH <sub>3</sub> Cu (1 eq C)] (5 eq)	Ether, -70 to -40°		(75) 471
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (1 eq A)	Ether, -78 to -20°	 <i>syn:anti</i> 12:88	(82) 1005
<sup>C<sub>13</sub></sup> 	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Cu (2 eq B)	Ether, -78 to -25°, 4.5 h		(89) 1060
	CH <sub>3</sub> Cu (1 eq A)	—		(79) 1061
<sup>C<sub>18</sub></sup> 	CH <sub>3</sub> Cu (1 eq A)	—	[( <i>t</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CH] <sub>2</sub> CO	(—) 1062

- A: BF<sub>3</sub>  
 B: P(C<sub>4</sub>H<sub>9</sub>-*n*)<sub>3</sub>  
 C: AlCl<sub>3</sub>  
 D: B(C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>  
 E: *n*-butyl-9-borabicyclo[3.3.1]nonane  
 F: TMEDA-(CH<sub>3</sub>)<sub>3</sub>SiCl  
 G: Al(CH<sub>3</sub>)<sub>3</sub>  
 H: P(C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>  
 I: P(C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>

TABLE IX. REACTIONS OF HIGHER-ORDER CUPRATES

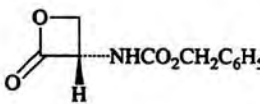
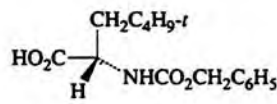
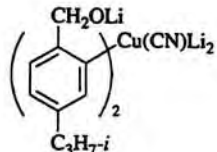
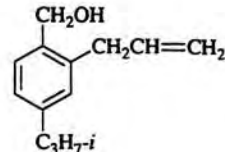
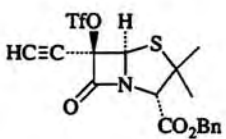
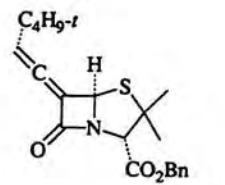
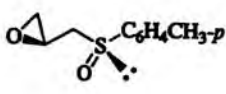
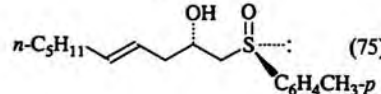

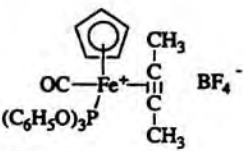
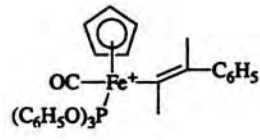
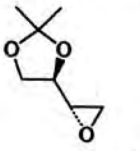
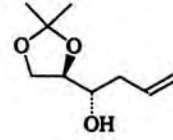
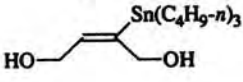
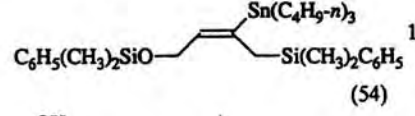
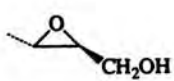
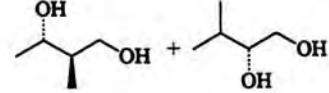
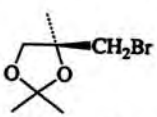
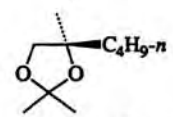
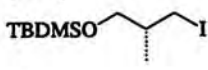
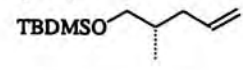
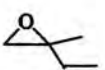
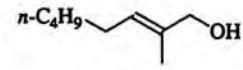
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
<i>A. Substitution Reactions</i>				
C <sub>2</sub> (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C=NCH(OAc)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> C <sub>6</sub> H <sub>5</sub> CONHCHBrCO <sub>2</sub> CH <sub>3</sub>	(C <sub>6</sub> H <sub>5</sub> S) <sub>2</sub> Cu(CN)Li <sub>2</sub> (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> Cu(CN)Li <sub>2</sub> (2 eq)	THF, -5°, 6 h THF, -78 to 20°	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C=NCH(C <sub>6</sub> H <sub>5</sub> S)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> C <sub>6</sub> H <sub>5</sub> CONHCH(C <sub>6</sub> H <sub>5</sub> )CO <sub>2</sub> CH <sub>3</sub>	(71) 1063 (83) 1064
C <sub>3</sub> 	<i>t</i> -C <sub>4</sub> H <sub>9</sub> (CH <sub>3</sub> )Cu(CN)Li <sub>2</sub> (3 eq)	THF, -23°, 1 h		(48) 644
CH <sub>2</sub> =CHCH <sub>2</sub> Cl		THF, TMEDA, 0°, 10 min		(67) 1065
	( <i>t</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> Cu(CN)Li <sub>2</sub>	THF, -78°, 3 min		(60) 1066
	( <i>E</i> )-(n-C <sub>5</sub> H <sub>11</sub> CH=CH) <sub>2</sub> - Cu(CN)Li <sub>2</sub>	—		(75) 1067
C <sub>4</sub> 	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> Cu(CN)Li <sub>2</sub>	1. Ether, BF <sub>3</sub> , -78 to -50° 2. AcCl, Py	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>3</sub> OAc	(87) 498
	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> Cu(CN)Li <sub>2</sub>	THF, -78 to 20°		(93) 1068
	(CH <sub>2</sub> =CH) <sub>2</sub> Cu(CN)Li <sub>2</sub>	THF, -78 to 20°		(46) 1069
	[C <sub>6</sub> H <sub>5</sub> (CH <sub>3</sub> ) <sub>2</sub> Si] <sub>2</sub> Cu(CN)Li <sub>2</sub> (1.5 eq)	THF, 0°, 4 h		1070 (54)
	(CH <sub>3</sub> ) <sub>2</sub> Cu(CN)Li <sub>2</sub>	THF, -20°, 2 h		(92) 1071
	(n-C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> Cu(CN)Li <sub>2</sub> (3 eq)	Ether, 0°, 1 h		(65) 1072
TBDMSO- 	(CH <sub>2</sub> =CH) <sub>2</sub> Cu(CN)Li <sub>2</sub>	THF, -78 to -13°		(—) 1073
C <sub>5</sub> 	(n-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> Cu(CN)Li <sub>2</sub>	Ether, BF <sub>3</sub> , -78 to -70°		(100) 498

TABLE IX. REACTIONS OF HIGHER-ORDER CUPRATES (Continued)

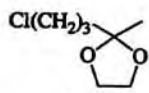
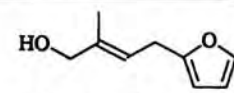
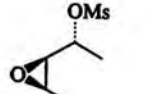
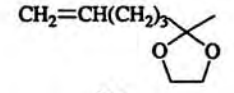
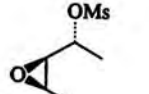
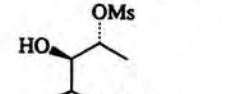
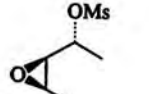
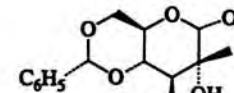
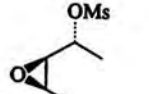
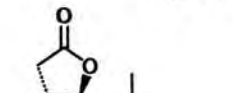
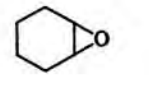
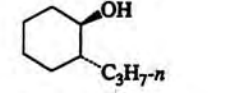
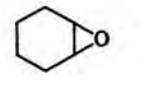
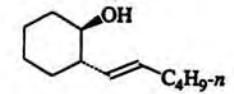
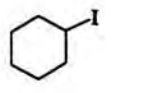
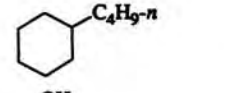
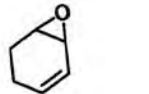

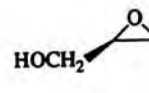
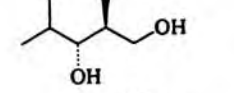
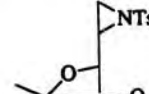
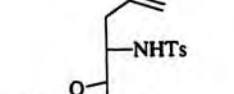
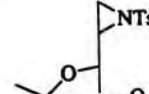
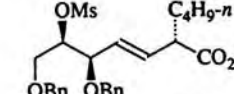
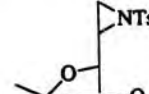
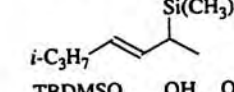
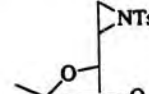
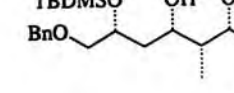
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(C_4H_9O)_2Cu(CN)Li_2$ ( $BF_3 \cdot Et_2O$ )	THF, $-78^\circ$ , 2 h		(90) 1074
	$(CH_2=CH)_2Cu(CN)Li_2$ (4 eq)	THF, $20^\circ$ , 24 h		(58) 1075
	$(n-C_4H_9)_2Cu(CN)Li_2$ (1 eq $BF_3 \cdot Et_2O$ )	THF, $-78^\circ$ , 2 h		(70) 1076
	$(CH_3)_2Cu(CN)Li_2$	—		(84) 1077
	$[CH_2=C(CH_3)]_2Cu(CN)Li_2$	Ether, $-40$ to $0^\circ$ , 5 h		(81) 800
	$n-C_3H_7(C_4H_9S)Cu(CN)Li_2$	THF, ether, $0^\circ$ , 1 h		(55) 496b
	$(E)-(n-C_4H_9CH=CH)_2Cu(CN)Li_2$	Ether, $-78$ to $-50^\circ$ , 1 h		(81) 498
	$(n-C_4H_9)_2Cu(CN)Li_2$	THF, $-78^\circ$ 1 h		(90) 494
	$[C_6H_5(CH_3)_2Si]_2Cu(CN)Li_2$	THF		(>75) 1078
	$(CH_3)_2Cu(CN)Li_2$ (4 eq)	1. Ether, $-30^\circ$ 2. $NaIO_4$ , $H^+$		(82) 1079
	$(CH_2=CH)_2Cu(CN)Li_2$ (4 eq)	THF, $-78$ to $0^\circ$ , 1 h		(80) 1080
	$(n-C_4H_9)_2Cu(CN)Li_2$ (3 eq)	THF, hexane, $BF_3 \cdot Et_2O$ , $-78^\circ$ , 30 min		(94) 497
	$[C_6H_5(CH_3)_2Si]_2Cu(CN)Li_2$ (3 eq $P(C_6H_5)_3$ )	THF, ether, $0^\circ$ , 3 h		(87) 823
	$(CH_2=CH)_2Cu(CN)Li_2$ (10 eq)	Ether, THF, $0^\circ$ , 4 h		(93) 1081



TABLE IX. REACTIONS OF HIGHER-ORDER CUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$ (3 eq $\text{P}(\text{C}_6\text{H}_5)_3$ )	THF, ether, 0°, 3 h	+ 1:9	824 (87)
	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, -78 to 20°, 15 h		(80) 1082
	$(\text{CH}_3)_2\text{Cu}(\text{SCN})\text{Li}_2$	1. Ether, HMPA, -20°, 1 h 2. $\text{CH}_3\text{I}$ , -50°		(71) 1083
	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	1. THF, hexane, $\text{BF}_3\cdot\text{Et}_2\text{O}$ , -78°, 2 h 2. $\text{H}_2\text{O}_2$ , KF, $\text{KHCO}_3$ , $\text{CH}_3\text{OH}$ , THF, 25°, 12 h		(>62) 627
	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$ (1.7 eq)	THF, 0°, 3.5 h		(91) 1075
$\text{CH}_3\text{CON}=\text{C}(\text{C}_6\text{H}_5)\text{CONHOCH}_3$	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$ (2.5 eq)	THF, -78°, 30 min	$\text{CH}_3\text{CONHC}(\text{C}_4\text{H}_9\text{-}n)\text{-}(\text{C}_6\text{H}_5)\text{CONHOCH}_3$	1084 (75)
	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, -20°, 40 h		(70) 1085
	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}_2$ (4 eq)	THF, TMEDA, 0°, 6 h		1086 (-)
	$t\text{-C}_4\text{H}_9[\text{CH}_2\text{S}(\text{O})\text{CH}_2]\text{Cu}(\text{CN})\text{Li}_2$ (1.1 eq)	THF, -78 to 0°, 1.5 h		(97) 273
	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, -30°, 20 h		(74) 1075
	$(n\text{-C}_5\text{H}_{11}\text{C}\equiv\text{C})_2\text{Cu}(\text{CN})\text{Li}_2$	THF, 0°, 30 min		(85) 1035
	$[(n\text{-C}_4\text{H}_9)_3\text{Sn}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF, -20°, 2 h		(91) 1087

 C<sub>4</sub>

 C<sub>3</sub>

TABLE IX. REACTIONS OF HIGHER-ORDER CUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-70$ to $20^\circ$ , 12 h		(92) 1088
	$(\text{pyridine-2-ylmethyl})_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-50^\circ$ , 3 h		(93) 1075
	$(\text{TMS})_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-23$ to $20^\circ$ , 1 h		(70) 1089
	$(\text{C}_2\text{H}_5)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78$ to $0^\circ$ , 6 h		(98) 494
	$(t\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-78^\circ$		(89) 1090
	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78^\circ$ , 1 h		(90) 1091
	$(t\text{-C}_4\text{H}_9)_2\text{C}(\text{CN})\text{Li}_2$ (2 eq)	Ether, $-78$ to $20^\circ$		(79) 1092
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-50^\circ$ , 3 h		(56) 1093
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-50^\circ$ , 3 h		(39) 1093
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	—		(86) 1094
	$(t\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-78^\circ$		(94) 1095

TABLE IX. REACTIONS OF HIGHER-ORDER CUPRATES (Continued)

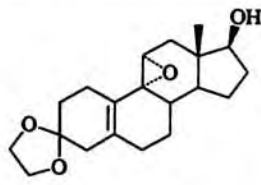
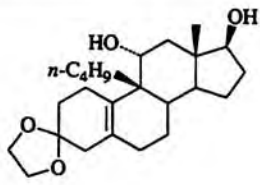
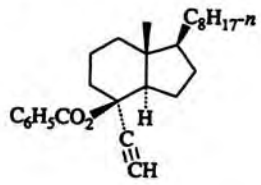
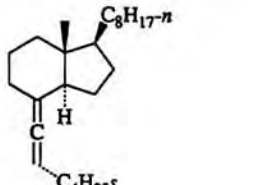
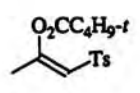
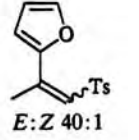
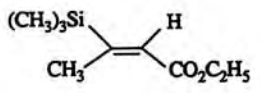
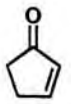
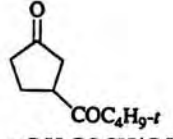
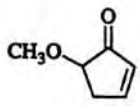
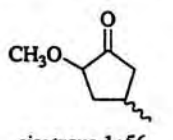
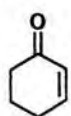
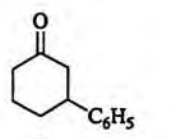
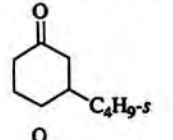
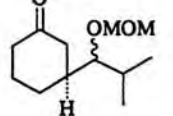
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-20^\circ$		(89) 1096
$\text{C}_{20}$ 	$(s\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-78^\circ$ , 6 h		(70) 1097
<i>B. Conjugate Addition Reactions</i>				
$\text{C}_2$ [2,4,6-( $\text{CH}_3$ ) $_3$ , $\text{C}_6\text{H}_5$ ] $_2\text{BC}=\text{CH}_2$   TMS	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-78$ to $20^\circ$	[2,4,6-( $\text{CH}_3$ ) $_3$ , $\text{C}_6\text{H}_5$ ] $_2\text{BCHC}_5\text{H}_{11-n}$   TMS	(66) 1098
$\text{C}_3$ 	$(\text{C}_4\text{H}_9\text{O})_2\text{Cu}(\text{CN})\text{Li}_2$ (2 eq)	THF, $-78^\circ$ , 30 min	 <i>E:Z</i> 40:1	(62) 1099
$\text{C}_4$ $\text{CH}_3\text{C}\equiv\text{CCO}_2\text{C}_2\text{H}_5$	$(\text{TMS})_2\text{Cu}(\text{CN})\text{Li}_2$	THF, HMPA, $-78^\circ$ , 24 h		(91) 1100
$\text{C}_5$ 	$(t\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$ , CO	THF, ether, pentane, $-110$ to $25^\circ$		(82) 1101
$\text{C}_2\text{H}_5\text{CH}=\text{CHCHO}$	$(s\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$ , CO	THF, ether, pentane, $-110$ to $25^\circ$	$s\text{-C}_4\text{H}_9\text{COCH}(\text{C}_2\text{H}_5)\text{CH}_2\text{CHO}$	(76) 1101
	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78^\circ$ , 30 min	 <i>cis:trans</i> 1:56	(76) 901
$\text{C}_6$ 	$\text{C}_6\text{H}_5(\text{C}_4\text{H}_9\text{S})\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-78^\circ$ , 20 min		(80) 496b
	$(s\text{-C}_4\text{H}_9)(\text{CH}_3)\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78^\circ$ , 30 min		(97) 499
	$i\text{-C}_3\text{H}_7\text{CH}(\text{OMOM})\text{Cu}(\text{CN})\text{Li}_2^d$	THF, TMSCl, $-78^\circ$ , 5 h		(96) 361

TABLE IX. REACTIONS OF HIGHER-ORDER CUPRATES (Continued)

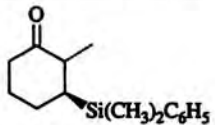
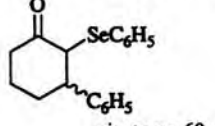
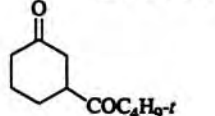
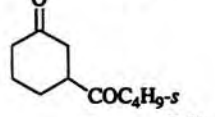
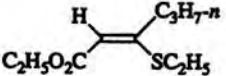
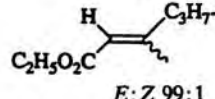
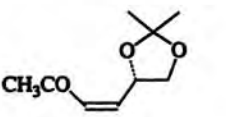
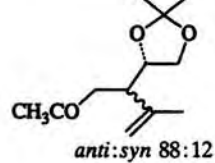
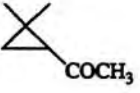
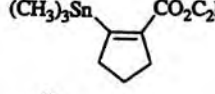
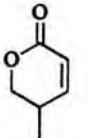
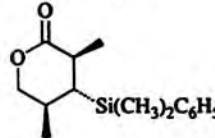
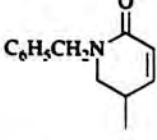
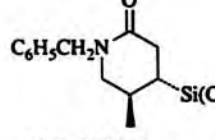
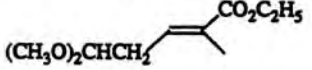
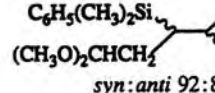
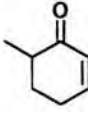
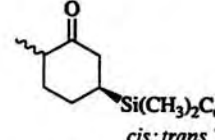
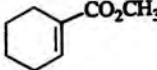
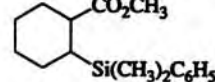
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	1. THF, $-78^\circ$ , 2 h 2. $\text{CH}_3\text{I}$ , $-78^\circ$ , 4 h		(64) 1102
	$(\text{C}_6\text{H}_5)_2\text{Cu}(\text{CN})\text{Li}_2$ (2 eq)	1. Ether, $-60^\circ$ , 1 h 2. $\text{C}_6\text{H}_5\text{SeBr}$ , THF, $-60^\circ$ , 30 min	 <i>cis:trans</i> 60:40	(65) 1103
	$(t\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$ , CO	THF, $0^\circ$ , 30 min		(94) 1104
	$(s\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$ , CO	THF, $-110^\circ$ , 30 min		(94) 1104
	$(\text{CH}_3)_2\text{Cu}(\text{SCN})\text{Li}_2$	Ether, $-78^\circ$	 <i>E:Z</i> 99:1	(99) 519
	$(\text{C}_6\text{H}_5)_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-100^\circ$	 <i>anti:syn</i> 88:12	(73) 1105
	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$ (2 eq)	Ether, $\text{BF}_3\cdot\text{Et}_2\text{O}$ , $-70^\circ$ , 1 h	$n\text{-C}_3\text{H}_7\text{C}(\text{CH}_3)_2\text{CH}_2\text{COCH}_3$	(55) 1106
$\text{I}(\text{CH}_2)_3\text{C}\equiv\text{CCO}_2\text{C}_2\text{H}_5$	$(\text{CH}_3)_3\text{Sn}(\text{C}_6\text{H}_5)\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78$ to $-48^\circ$ , 3 h		(62) 1107
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	1. THF, $-78^\circ$ , 2 h 2. $\text{CH}_3\text{I}$ , $-78^\circ$ , 2 h		(62) 1108
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78^\circ$ , 14 h		(73) 1108
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	—	 <i>syn:anti</i> 92:8	(89) 1094
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78^\circ$ , 2 h	 <i>cis:trans</i> 75:25	(85) 1102
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-23^\circ$ , 3 h		(—) 1109

TABLE IX. REACTIONS OF HIGHER-ORDER CUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(C_6H_5)_2Cu(CN)Li_2$	Ether, $-78^\circ$ , 1 h	+ 98.5:1.5 (82)	499
	$(n-C_4H_9)_2Cu(CN)Li_2$	THF, $BF_3 \cdot Et_2O$ , $-78^\circ$ , 30 min		(70) 817
	$(CH_3)_2Cu(CN)Li_2$	Ether, $-78^\circ$ , 4 h		(93) 1110
	$(C_4H_9O)_2Cu(CN)Li_2$ (2 eq)	THF, $BF_3 \cdot Et_2O$ (2 eq), $-78$ to $35^\circ$ , 2 h		(70) 1074
$C_6$ 	$[C_6H_5(CH_3)_2Si]_2Cu(CN)Li_2$	THF, $-23^\circ$ , 3 h		(70) 1109
	$(n-C_4H_9)_2Cu(CN)Li_2$	Ether, $0^\circ$ , 1 h		(72) 499
	$(n-C_4H_9)_2Cu(SCN)Li_2$	Ether, $-60^\circ$		(100) 519
$n-C_4H_9C \equiv CCOCF_3$	$(n-C_4H_9)_2Cu(CN)Li_2$	Ether, $-78^\circ$ , 2 h	$(n-C_4H_9)_2C=CHCOCF_3$	(55) 1111
$n-C_5H_{11}CH=CHCHO$	$(i-C_3H_7)_2Cu(CN)Li_2^d$	THF, $TMSCl$ , $-78$ to $20^\circ$	$i-C_3H_7CH(OMOM)CH_2CH_2CHO$ + $C_5H_{11-n}CH_2CH_2CHO$ <i>syn:anti</i> 92:9 (44) 1112	
			$i-C_3H_7CH(OMOM)CH(OH)CH_2CH_2CHO$ + $C_5H_{11-n}CH_2CH_2CHO$ <i>syn:anti</i> 50:50 (27)	
$C_5$ 	$CH_2=CH(C_4H_9S)Cu(CN)Li_2$	Ether, THF, $BF_3$ , $-78$ to $0^\circ$ , 2 h		(98) 496a
	$(C_6H_5)_2Cu(CN)Li_2$	Ether, THF, $BF_3$ , $-50$ to $15^\circ$ , 45 min		(95) 496a
	$n-C_4H_9(CH_2SOCH_2)Cu(CN)Li_2$ (2.2 eq)	Ether, $-78$ to $0^\circ$ , 4 h		(95) 273

TABLE IX. REACTIONS OF HIGHER-ORDER CUPRATES (Continued)

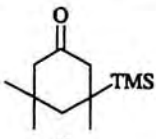
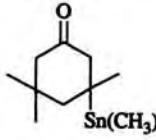
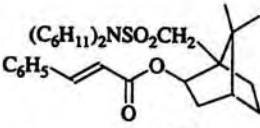
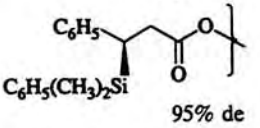
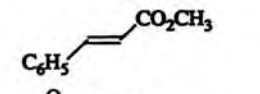
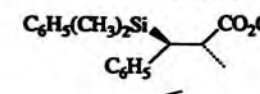
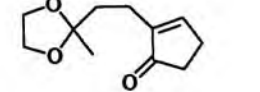
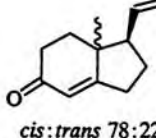
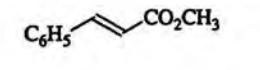
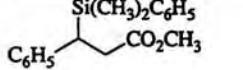
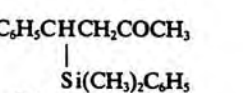
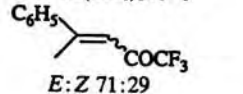
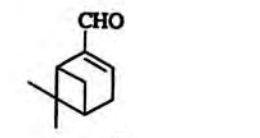
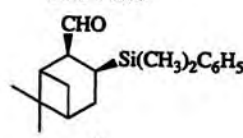
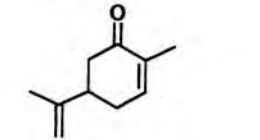
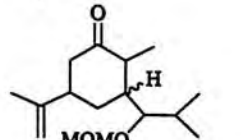
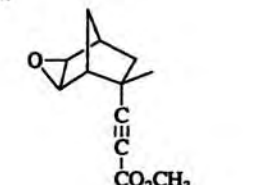
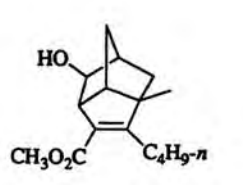
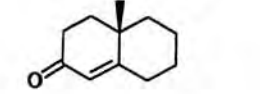

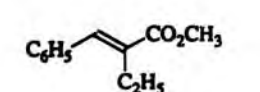
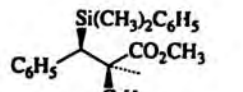
Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(\text{TMS})_2\text{Cu}(\text{CN})\text{Li}_2$	THF, ether, HMPA, $-23$ to $0^\circ$ , 1.5 h		(91) 1115
	$(\text{CH}_3)_3\text{Sn}(\text{C}_4\text{H}_9\text{S})\text{Cu}(\text{CN})\text{Li}_2$ (1.5 eq)	THF, $-20^\circ$ , 4 h		(87) 1107
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78^\circ$	 95% de	(67) 731
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	1. THF, $-23^\circ$ 2. $\text{CH}_3\text{I}$ , $-23^\circ$ , 1 h		(88) 1113
	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$	1. Ether 2. $\text{CH}_3\text{I}$ , HMPA 3. $\text{CuSO}_4$ , $\text{H}_2\text{O}$ , $\text{CH}_3\text{OH}$ 4. $\text{NaOCH}_3$ , $\text{CH}_3\text{OH}$	 <i>cis:trans</i> 78:22	(60) 1114
	$\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}(\text{CH}_3)\text{Cu}(\text{CN})\text{Li}_2$	THF, $-23$ to $0^\circ$ , 2 h		(73) 1115
$\text{C}_6\text{H}_5\text{CH}=\text{CHCOCH}_3$	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$ $[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{SiCl}]$	THF, $-75^\circ$		(65) 1116
$\text{C}_6\text{H}_5\text{C}\equiv\text{CCOCF}_3$	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}_2$	—	 <i>E:Z</i> 71:29	(51) 1117
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF		(70) 1118
	$(\text{MOMO})_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $\text{TMSCl}$ , $-78$ to $20^\circ$		(94) 502
	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $0^\circ$ , 1 min		(66) 1119
	$(n\text{-C}_3\text{H}_7)_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-25^\circ$ , 2 h		(85) 499
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	1. — 2. $\text{CH}_3\text{I}$		(95) 1120

TABLE IX. REACTIONS OF HIGHER-ORDER CUPRATES (Continued)

Substrate	Organocuprate	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$ (2 eq) (TBDMSCl)	THF, $-75$ to $-40^\circ$		(71) 1121
$\text{C}_{12}$ 	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-78$ to $-25^\circ$ , 1 h		(95) 1122
$\text{C}_{13}$ 	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}_2$ (1.2 eq)	$\text{C}_6\text{H}_5\text{CH}_3$ , $-78$ to $0^\circ$ , 45 min	 75:9	(91) 517
	$(\text{C}_6\text{H}_5)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-23^\circ$ , 10 min	 <i>syn:anti</i> 1:2.7	(66) 1123
$\text{C}_{18}$ 	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$ (3.5 eq)	Ether, $0^\circ$ , 10 min		(80) 1124

<sup>a</sup> Ms =  $\text{CH}_3\text{SO}_2\text{-}$ .

<sup>b</sup> Tf =  $\text{CF}_3\text{SO}_2\text{-}$ .

<sup>c</sup> The yield was reported in the 85–95% range.

<sup>d</sup> MOM = methoxymethyl.

TABLE X. REACTIONS OF OTHER ORGANOCOPPER SPECIES

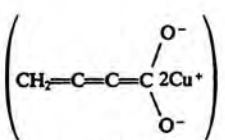
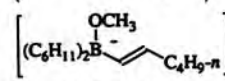
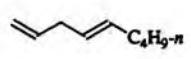
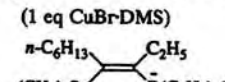
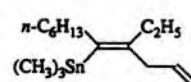
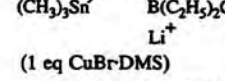
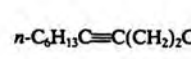
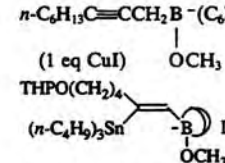
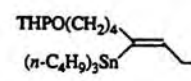
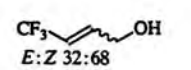
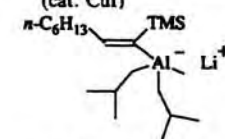
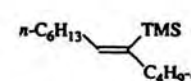

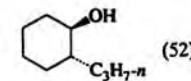

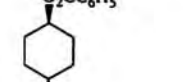
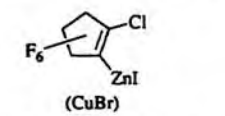
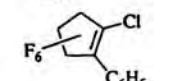
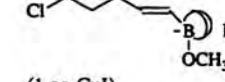

Substrate	Copper Reagent	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.		
<i>A. Substitution Reactions</i>						
C <sub>3</sub> CH <sub>2</sub> =CHCH <sub>2</sub> Br		1. THF, -78°, 1 h 2. TMSCl, (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N	CH <sub>2</sub> =C=C(CO <sub>2</sub> TMS)CH <sub>2</sub> CH=CH <sub>2</sub> (60)	1125		
		(1 eq CuBr-DMS) THF, -15 to 25°		(92)	527	
		1. THF, HMPA, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , -80 to 20° 2. NaOH, H <sub>2</sub> O <sub>2</sub>		(80)	1126	
		(1 eq CuBr-DMS) THF, -78 to 20°		(62)	1127	
		(1 eq CuI) THF, -78°, 1 h		(62)	1128	
HC≡CCH <sub>2</sub> OH	(1 eq CuBr-DMS) (CF <sub>3</sub> ) <sub>2</sub> CuZnI	THF, ultrasound, 2 h		(61)	1129	
C <sub>4</sub> THPOCH <sub>2</sub> -CH=CH-CH <sub>2</sub> Br	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> C≡CLi (cat. CuI)	THF, -60 to 20°, 12 h	THPOCH <sub>2</sub> -CH=CH-C≡C(CH <sub>2</sub> ) <sub>2</sub> OBn	(75)	1130	
		(1 eq CuI-P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ) THF, -78 to 20°, 18 h		(82)	1131	
C <sub>5</sub> Br(CH <sub>2</sub> ) <sub>3</sub> Br	C <sub>6</sub> H <sub>5</sub> CH=NCH(CH <sub>3</sub> )CO <sub>2</sub> CH <sub>3</sub> (LDA, cat. Li <sub>2</sub> CuCl <sub>4</sub> )	THF, 20°, 16 h	C <sub>6</sub> H <sub>5</sub> CH=NC(CH <sub>3</sub> )(CO <sub>2</sub> CH <sub>3</sub> )(CH <sub>2</sub> ) <sub>3</sub> Br	(90)	1132	
	(CH <sub>3</sub> ) <sub>2</sub> C=CHCH <sub>2</sub> Br	IZn(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> (15% CuCN)	THF, CH <sub>3</sub> CON(CH <sub>3</sub> ) <sub>2</sub> , 25°	(CH <sub>3</sub> ) <sub>2</sub> C=CH(CH <sub>2</sub> ) <sub>4</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> + CH <sub>2</sub> =CHC(CH <sub>3</sub> ) <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	(15) (76)	539
C <sub>6</sub>		<i>n</i> -C <sub>3</sub> H <sub>7</sub> (C <sub>6</sub> H <sub>5</sub> S)Cu(CN)LiMgBr		(52) + (26)	(78)	535
		C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> Na (1 eq CuCN)	THF, -78 to 20°, 14 h		(83)	1133
	C <sub>6</sub> H <sub>5</sub> I		DMF, 20°		(52)	1134
	<i>n</i> -C <sub>4</sub> H <sub>9</sub> C≡CBr		(1 eq CuI) THF, -40 to 25°, 1 h		(75)	1135



TABLE X. REACTIONS OF OTHER ORGANOCOPPER SPECIES (Continued)

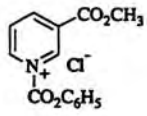
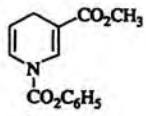
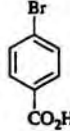
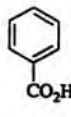
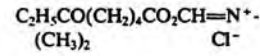
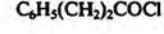

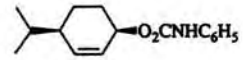
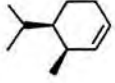

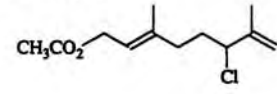
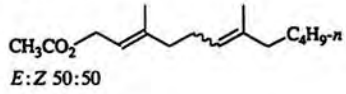
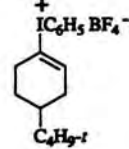
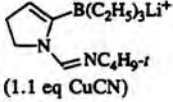
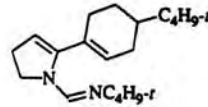
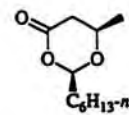
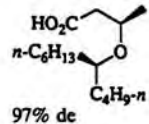
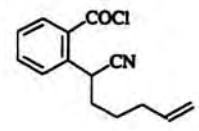
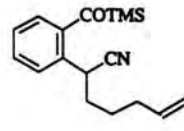

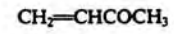
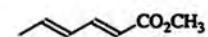


Substrate	Copper Reagent	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
	$(t\text{-C}_4\text{H}_9\text{O})_3\text{LiAlH}$ (1.5 eq CuBr)	THF, $-23^\circ$ , 1.5 h		(45) 1136
	$(t\text{-C}_4\text{H}_9\text{O})_3\text{LiAlH}$ (3 eq) (4.4 eq CuBr)	THF, $-23^\circ$ , 1.5 h	"	(45) 850
	$\text{K}(s\text{-C}_4\text{H}_9\text{O})_3\text{BH}$ (0.5 eq CuI)	THF, $-50^\circ$ , 2 h, $20^\circ$ , 3 h		(86) 1137
	$\text{Li}(t\text{-C}_4\text{H}_9\text{O})_3\text{AlH}$ (10% CuI)	THF, CH <sub>3</sub> CN, $-78^\circ$ , 10 min	$\text{C}_2\text{H}_5\text{CO}(\text{CH}_2)_4\text{CHO}$	(71) 1138
	 (ZnCl <sub>2</sub> , CuI)	Ether, HMPA	$\text{C}_6\text{H}_5(\text{CH}_2)_2\text{CO}(\text{CH}_2)_2\text{CO}_2\text{C}_2\text{H}_5$	(89) 541
	$(\text{CH}_3)_5\text{Cu}_3\text{Li}_2$	Ether		(82) 1139
	$\text{Li}_4\text{CuH}_5$	THF, $25^\circ$ , 24 h	$n\text{-C}_{10}\text{H}_{22}$	(99) 542
	$n\text{-C}_4\text{H}_9\text{ZnCl}$ (5% CuBr/DMS)	THF, $20^\circ$	 <i>E:Z</i> 50:50	(65) 1140
	 (1.1 eq CuCN)	THF, $-20$ to $20^\circ$ , 12 h		(61) 1141
	$(n\text{-C}_4\text{H}_9)_3\text{Cu}_2\text{Li}$	Ether, DMS, $-25^\circ$ , 1 h	 97% <i>dc</i>	(68) 1142
	$[\text{CH}_3(\text{TMS})_2\text{AlLi}]$ 0.5 eq (10% CuCN)	THF, ether, pentane, $0^\circ$ ,		(52) 1143
<i>B. Conjugate Addition Reactions</i>				
	$[(\text{C}_6\text{H}_5)_3\text{P-CuH}]_6$ (0.24 eq)	$\text{C}_6\text{H}_6$ , H <sub>2</sub> O (0.24 eq), $25^\circ$ , 30 min	$n\text{-C}_3\text{H}_7\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5$	(95) 553
	$t\text{-C}_4\text{H}_9\text{Zn}(\eta^5\text{-C}_5\text{H}_5)_2\text{Cl}$ (LiI, CuO <sub>3</sub> SCF <sub>3</sub> )	THF, $-78$ to $20^\circ$ , 16 h	$t\text{-C}_4\text{H}_9\text{CH}_2\text{CH}_2\text{CH}_2\text{COCH}_3$	(73) 1144
	$(i\text{-C}_4\text{H}_9)_2\text{AlH}$ (10% CH <sub>3</sub> Cu)	THF, HMPA, $-50^\circ$ , 1.5 h	$\text{C}_2\text{H}_5\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$	(80) 542
	$\text{LiAlD}_4$ (1 eq CuI)	1. THF, HMPA, $-78^\circ$ , 1 h 2. $(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{Cl}$		(67) 1145

TABLE X. REACTIONS OF OTHER ORGANOCOPPER SPECIES (Continued)

Substrate	Copper Reagent	Reaction Conditions	Product(s) and Yield(s) (%)	Refs.
		THF, -78°, 2.25 h		(85) 535
		THF, -70 to -20°, 15 h		(95) 1146
	$n\text{-C}_3\text{H}_7\text{C}\equiv\text{CCu}(\text{H})\text{Li}$	THF, -78°, 30 min		(86) 544
$n\text{-C}_3\text{H}_7\text{CH}=\text{CHCHO}$	$\text{LiAlH}_4$ (10% CuI)	THF, HMPA, -78°, 1 h	$n\text{-C}_3\text{H}_7\text{CHO}$ (63) + $n\text{-C}_3\text{H}_7\text{CH}=\text{CHCH}_2\text{OH}$ (12)	(75) 1147
$\text{C}_7$ 	$(i\text{-C}_4\text{H}_9)_2\text{AlH}$ (10% $\text{CH}_3\text{Cu}$ )	THF, HMPA, -50°, 30 min		(73) 547
		Ether, HMPA, 20°, 4 h		(92) 541
$\text{C}_9$ 	$(\text{CH}_3)_3\text{Cu}_3\text{Li}_2$	1. Ether-pentane (1:1), -75 to 0° 2. TMSCl		(88) 425
	$\text{NC}(\text{CH}_2)_3\text{Cu}(\text{CN})\text{ZnI}$ (3 eq $\text{BF}_3\cdot\text{Et}_2\text{O}$ )	THF, -78 to -30°		(79) 1148
	$\text{NaAl}[\text{O}(\text{CH}_2)_2\text{O}]_2\text{H}$ $\text{OC}_4\text{H}_9\text{-s}$ (0.5 eq CuBr)	THF, $\text{C}_6\text{H}_6$ , -78 to 20°, 6 h		(92) 1067
$\text{C}_{10}$ $\text{CH}_3\text{C}\equiv\text{C}(\text{CH}_2)_4\text{C}\equiv\text{CCOC}_3\text{H}_7\text{-}i$	$(i\text{-C}_4\text{H}_9)_2\text{AlH}$ (2 eq) (0.1 eq $\text{CH}_3\text{Cu}$ )	THF, HMPA (6 eq), -50°, 3.5 h	$\text{CH}_3\text{C}\equiv\text{C}(\text{CH}_2)_4\text{CH}=\text{CHCOC}_3\text{H}_7\text{-}i$ 40:60 <i>E:Z</i>	(63) 1149
$\text{C}_{11}$ $(E)\text{-}i\text{-C}_4\text{H}_9\text{CH}=\text{CH}_2\text{COC}_4\text{H}_9\text{-}t$ $i\text{-C}_4\text{H}_9\text{-CH}=\text{CHCOC}_4\text{H}_9\text{-}t$	$\text{Li}_2\text{CuH}_3$ $\text{Li}_4\text{CuH}_5$	Ether, 25°, 48 h THF, 25°, 24 h	$i\text{-C}_4\text{H}_9(\text{CH}_2)_2\text{COC}_4\text{H}_9\text{-}t^a$ $i\text{-C}_4\text{H}_9\text{-CH}=\text{CHC}_4\text{H}_9\text{-}t^b$ OH	(93) 543 (95) 543
$\text{C}_{13}$ 	$(\text{CH}_3)_3\text{Cu}_3\text{Li}_2$	1. Ether, -75 to -20° 2. $\text{H}^+$ , $\text{H}_2\text{O}$		(86) 425

<sup>a</sup>The 1,2-addition product (6%) was also obtained.

<sup>b</sup>The 1,4-addition product (5%) was also obtained.

<sup>c</sup>The 1,2-addition product (2%) was also obtained.

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS

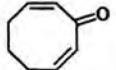
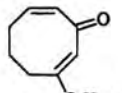
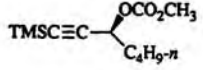
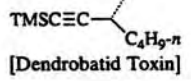
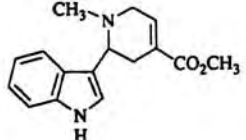
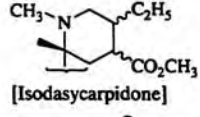
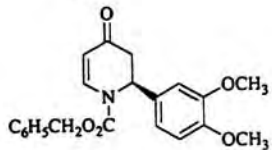
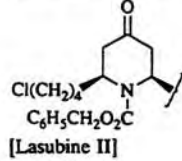
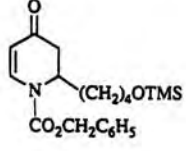
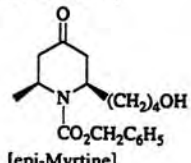
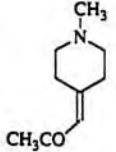
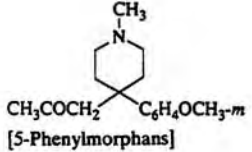

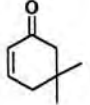
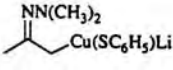
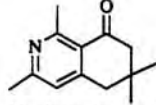
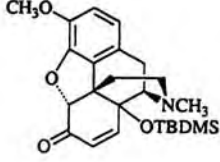
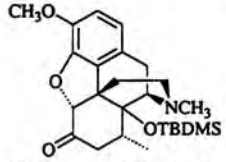
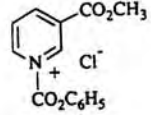
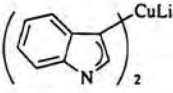
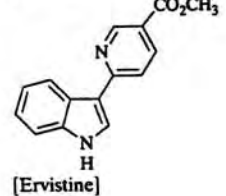
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
A. Alkaloids				
a. Grignard-Based Couplings				
	$n\text{-C}_5\text{H}_{11}\text{MgBr}$ (1% CuI)	1. Ether, 0°, 30 min 2. $\text{C}_6\text{H}_5\text{SeBr}$ , 10°, 10 min 3. $\text{H}_2\text{O}_2$ , Py, $\text{CH}_2\text{Cl}_2$ , 25°	 [(−)-Adaline]	(58–64) 1150
	$(\text{CH}_3)_2\text{CuMgX}$	THF, 25°	 [Dendrobatid Toxin]	(80) 1151
	$(\text{C}_2\text{H}_5)_2\text{CuMgBr}$ (xs)	THF, −30°, 6 h	 [Isodasycarpidone]	(89) 1152
	$\text{Cl}(\text{CH}_2)_4\text{MgBr}$ (1 eq CuBr·DMS) ( $\text{BF}_3\cdot\text{Et}_2\text{O}$ )	THF, −78°, 4 h	 [Lasubine II]	(56) 1153
	$\text{CH}_3\text{MgX}$ (5% CuI)	THF, −23°	 [epi-Myrtine]	(85) 1154
	$(m\text{-CH}_3\text{OC}_6\text{H}_4)_2\text{CuMgBr}$	THF, −70°, 1 h	 [5-Phenylmorphans]	(58) 1155
$\text{HC}\equiv\text{CCH}(\text{CH}_3)\text{OTs}$	$\text{BrMg}(\text{CH}_2)_3$  (CuBr)	1. THF, −60 to 25° 2. $\text{H}^+$ , $\text{H}_2\text{O}$ , $\text{CH}_3\text{OH}$	$\text{CH}_3\text{CO}(\text{CH}_2)_3\text{CH}=\text{C}=\text{CHCH}_3$ [Pinidine]	(85) 1156
b. Lithiocuprate Couplings				
	$\text{NN}(\text{CH}_3)_2$  $\text{Cu}(\text{SC}_6\text{H}_5)_2\text{Li}$	1. THF, −70 to 0°, 20 h 2. $\text{CH}_3\text{COCN}$ , −78°, 30 min 3. AcOH, reflux 4 h	 [Burley tobacco alkaloid]	(16) 1157
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $\text{CH}_2\text{Cl}_2$ , 0°, 1 h	 [Codeinone derivative]	(72) 1158
	 $\text{CuLi}$	Ether, $\text{CH}_2\text{Cl}_2$ , −40°, 2 h	 [Ervistine]	(16) 1159

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

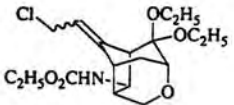
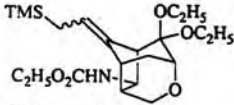
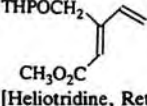
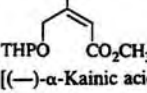
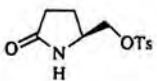
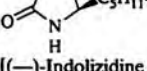
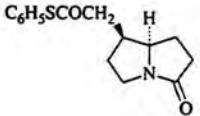
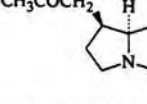
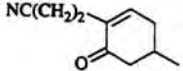
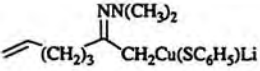
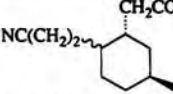
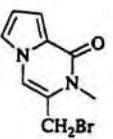
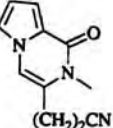
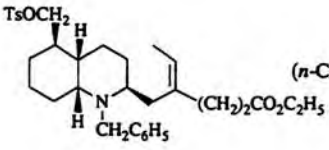
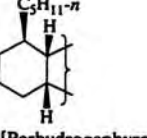
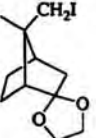
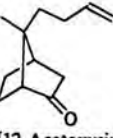
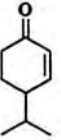
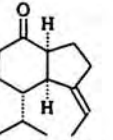
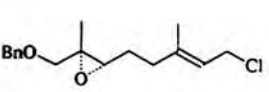
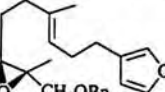
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{TMS})_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, THF, HMPA, $-78^\circ$ , 12 min		(84) 1160
$\text{THPOCH}_2\text{C}\equiv\text{CCO}_2\text{CH}_3$	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	THF, $-78^\circ$ , 4.25 h		(100) 1161
	$(\text{CH}_3)_2\text{CuLi}$	THF, $-78^\circ$		(90) 1162
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, DME, $-40^\circ$ , 16 h		(88) 1163
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, $-20^\circ$ , 5 min		(84) 1164
		1. THF 2. $\text{CuCl}_2$ , THF, $\text{H}_2\text{O}$ , $25^\circ$		(65) 1165
	$\text{NCCH}_2\text{Cu}$ (5 eq)	THF, $-40$ to $-20^\circ$ , 1 h		(—) 751
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $-20^\circ$		(91) 554
<b>B. Terpenes</b>				
<b>a. Grignard Couplings</b>				
	$\text{CH}_2=\text{CHCH}_2\text{MgBr}$ (3 eq) (25% CuI)	1. Ether, reflux 3 h 2. $\text{C}_2\text{H}_5\text{O}_4$ , $\text{H}_2\text{O}$ , $\text{SiO}_2$ , $\text{CH}_2\text{Cl}_2$ , $25^\circ$ , 14 h		(82) 1166
	$\text{BrMg}-\text{C}(\text{CH}_2)_2\text{Cl}$ (30% CuBr-DMS)	1. THF, ether, $\text{BF}_3 \cdot \text{Et}_2\text{O}$ , $-78^\circ$ , 2 h 2. KH, THF, $25^\circ$		(64) 1167
	$\text{CH}_2\text{MgCl}$ ( $\text{Li}_2\text{CuCl}_4$ )	THF, $0^\circ$ , 0.5 h		(79) 1168

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
$\text{HOCH}_2\text{C}\equiv\text{CCO}_2\text{H}$	$(\text{CH}_2)_2\text{MgBr}$ (excess) (cat. $\text{Li}_2\text{CuCl}_4$ )	THF, $-78$ to $25^\circ$	 [Asperdid] (75)	1169
	$\text{CH}_3(i\text{-C}_3\text{H}_7\text{O})_2\text{SiCH}_2\text{MgCl}$ (0.6% $\text{Li}_2\text{CuCl}_4$ )	1. — 2. $\text{KHF}_2$ , $\text{H}_2\text{O}_2$ , DMF	 [(-)-Asperdiol] (52)	1170
	$\text{CH}_2\text{MgCl}$ (10% CuI)	THF, $0^\circ$ , 1 h	 [Bifloratriene] (63)	1171
	$(\text{CuI})$ (2 eq)	THF, $20^\circ$ , 5 d	 [(-)-Botryococcene] (33-42)	1172
	$\text{CH}_2=\text{CHMgBr}$ [cat. $\text{CuI}\cdot\text{P}(\text{C}_4\text{H}_7\text{-}n)_3$ ]	THF, $-45$ to $-20^\circ$ , 4 h	 [Bruceantin] (80)	1173
	$\text{CH}_2=\text{CHMgBr}$ (~% CuI)	THF, $-78^\circ$	 [(±)- $\Delta^{9(12)}$ -Capnellene] (55)	1174
	$(\text{CH}_2)_2\text{MgBr}$ (1 eq CuBr-DMS)	1. THF, $-20^\circ$ 2. $\text{LiAlH}_4$	 [ $\Delta^{9(12)}$ -Capnellene] (80)	1175
$\text{ICH}_2\text{C}\equiv\text{CH}$	$(\text{C}_2\text{H}_5)_2\text{CuMgBr}\cdot\text{LiBr}$	THF, HMPT, $(\text{CH}_3\text{O})_3\text{P}$ , $25^\circ$ , 16 h	$(\text{CH}_2)_2\text{C}\equiv\text{CH}$ [Cecropia juvenile hormones] (70)	1176
$\text{CH}_3\text{C}\equiv\text{CCO}_2\text{CH}_3$	$\text{ClMgO}(\text{CH}_2)_3\text{MgCl}$ (1 eq CuI)	THF, DMS, $-78^\circ$ , 3 h	$\text{HO}(\text{CH}_2)_3\text{C}\equiv\text{CH}$ [Cembranolide precursors] (90)	1177a
	$(i\text{-C}_3\text{H}_7)_2\text{SiC}\equiv\text{CCH}_2\text{MgCl}$ (0.5 eq CuI)	THF, $-78$ to $-20^\circ$ , 7 h	$\text{C}\equiv\text{CSi}(\text{C}_3\text{H}_7)_2$ $\text{C}\equiv\text{CCH}_2\text{OH}$ [Cembranolides] (70)	1178
	$\text{BrMg}(\text{CH}_2)_2$ (10% CuI)	THF, $-25^\circ$ , 1 h	$\text{CH}_2\text{OH}$ [(±)-Chiloscyphone] (72)	1179
$n\text{-C}_3\text{H}_7\text{C}\equiv\text{CH}$	$n\text{-C}_3\text{H}_7\text{C}\equiv\text{C}(\text{CH}_2)_2\text{MgI}$ (1 eq CuBr-DMS)	1. Ether, DMS, $-23^\circ$ , 2.5 h 2. HMPA, $(\text{C}_2\text{H}_5\text{O})_3\text{P}$ , $\text{CO}_2$ , $-23^\circ$ , 6 h	$n\text{-C}_3\text{H}_7\text{C}\equiv\text{C}(\text{CH}_2)_2\text{CO}_2\text{H}$ [Codling moth constituent] (50)	1180
$n\text{-C}_3\text{H}_7\text{C}\equiv\text{CH}$	$(\text{CH}_2)_2\text{MgBr}$ (~% CuBr)	1. THF 2. $\text{CH}_3\text{I}$ , $\text{P}(\text{OC}_2\text{H}_5)_3$ , HMPA, $-30^\circ$	 [Natural Rubber] (32)	1181

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$\text{CH}_2=\text{C}(\text{CH}_3)\text{MgBr}$ (CuI)	1. THF 2. $\text{C}_6\text{H}_5\text{SeCH}_2\text{CHO}$	 [Confertin]	(—) 1182
	$\text{MgBr}$ (—% CuI)	THF, $-50^\circ$ , 2 h	 4:3 mixture of (84) <i>trans</i> isomers [(±)-Coriamyrtin]	1183
	$(\text{CH}_2)_2\text{MgBr}$ (0.25 eq CuBr-DMS)	THF, DMS, $-78$ to $0^\circ$ , 2.5 h	 [dl-Coriolin]	(92) 1184
	$\text{CH}_2=\text{CH}(\text{CH}_3)\text{MgBr}$ (—% CuBr-DMS)	THF, DMS, $-78^\circ$ , 2 h	 [Crinipellin]	(90) 1185
	$p\text{-CH}_3\text{C}_6\text{H}_4\text{MgBr}$ (—% CuBr-DMS)	THF, HMPA, TMSCl	 TMS $\text{C}_6\text{H}_4\text{CH}_3$ - <i>p</i> [(+)-α-Curcumene]	(96) 1186
	$\text{CH}_2\text{MgBr}$ (10% CuI)	THF	 [Dendrolasin]	(81) 1187
	$\text{CH}_2\text{MgBr}$ (cat. CuBr)	THF, $-78^\circ$	 [Dendrolasin]	(86) 1188
	$\text{MgBr}$ (10% CuI)	1. Ether, DMS, $0$ – $20^\circ$ , 1 h 2. $\text{ClCO}_2\text{CH}_3$ , $0$ – $20^\circ$ , 5 h	 OCO <sub>2</sub> CH <sub>3</sub> [Desmethylflavinine]	(75) 1189
	$(i\text{-C}_3\text{H}_7)_3\text{SiC}\equiv\text{CCH}_2\text{MgBr}$ (CuI)	1. THF, $-20^\circ$ , 3 h 2. $(n\text{-C}_4\text{H}_9)_4\text{NF}$ , THF	 CSi(C <sub>3</sub> H <sub>7</sub> - <i>i</i> ) <sub>3</sub> [Desoxyasperdiol]	(62) 1190
	$\text{CH}_2=\text{C}(\text{CH}_3)\text{MgBr}$ (10% CuI)	THF, $-45$ to $25^\circ$ , 12 h	 [7(8)-Desoxyasperdiol]	(89) 1177b
	$(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{MgCl}$ ( $n\text{-C}_3\text{H}_7\text{C}=\text{CCu}$ )	1. Ether, $-20^\circ$ , 2.5 h 2. THF, H <sub>2</sub> O, AcOH	 [(-)-Dictyolene]	(38) 1191

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
		THF, -30 to 25°, 2 h	 [Dihydrojasnone] (86)	1192
		1. THF, 0°, 2 h 2. H <sup>+</sup> , CH <sub>3</sub> OH, H <sub>2</sub> O	 [Mammalian dolichols] (85)	1193
		THF, -78°, 2 h	 [Elemanolides] (61)	1194
		—	 [β-Elemenone] (71)	1195
		THF	 [β-Elemenone] (20–30)	1196
		THF, 20°, 11 h	 [Furopergorgone A] (25)	1197
		1. THF, ether, DMS, -78°, 20 h 2. CH <sub>3</sub> I, HMPA, 25°, 24 h	 [(±)-Gymnomitrol] (66)	1198
		THF, -30°, 1 h	 [(+)-Hernandulcin] (84)	1199
		THF, α,α'-dipyridyl, 0°, 1 h	 [β-Ionone] (95)	1200
		Ether, 20°, 24 h	 [(±)-Iridodial] (70)	1201
		THF, ether, DMS, -78 to -5°, 15 h	 [(±)-Isocomene] (68)	1202
		Ether, 0–20°, 20 h	 [Isomarrubiin] (40)	802

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

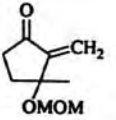
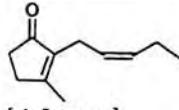
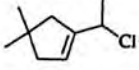
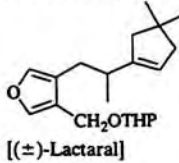
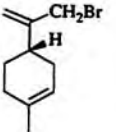
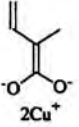
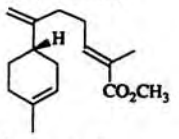
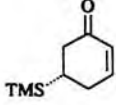
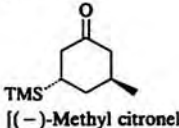
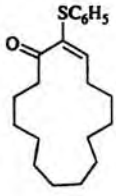
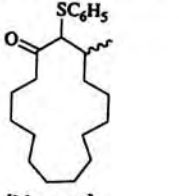
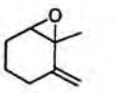
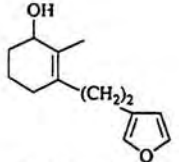
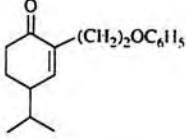
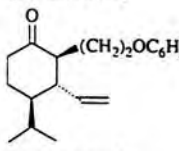
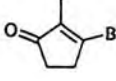
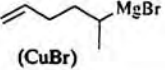
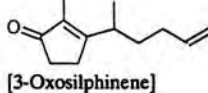
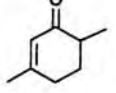
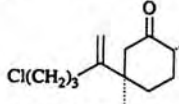
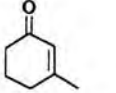
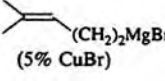
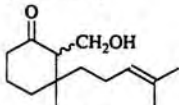
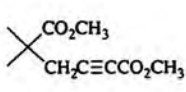
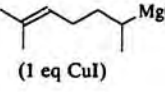
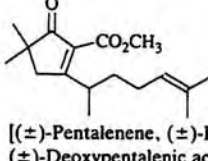
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{C}_2\text{H}_5\text{CH}=\text{CH})_2\text{CuMgBr}$	1. THF, $-70^\circ$ 2. 3 N HCl, $0^\circ$	 [cis-Jasmone]	(73) 1203
	$\text{CH}_2\text{MgCl}$ $\text{CH}_2\text{OTHP}$ ( $-\% \text{Li}_2\text{CuCl}_4$ )	(—)	 [(±)-Lactaral]	(75) 1204
	 $2\text{Cu}^+$	1. THF 2. $\text{CH}_2\text{N}_2$	 [dl-Lanceol]	(61) 1205
	$\text{CH}_3\text{MgI}$ (cat. CuBr·DMS)	THF, HMPA, TMSCl, $-78^\circ$ , 30 min	 [(-)-Methyl citronellate]	(92) 1206
	$\text{CH}_3\text{MgBr}$ (CuCl)	Ether	 [Muscone]	(67) 1207
	$\text{CH}_2\text{MgCl}$ (1 eq CuCN)	THF, $-78$ to $20^\circ$ , 4 h	 [Nakafuran 9]	(62) 1208
	$\text{CH}_2=\text{CHMgBr}$ (0.55 eq CuBr·DMS)	THF, DMS, $-30^\circ$ , 1 h	 [Oplopanone]	(52) 1209
	 (CuBr)	Ether, THF, $-20$ to $20^\circ$	 [3-Oxosilphinene]	(100) 1210
	$\text{Cl}(\text{CH}_2)_3\text{MgBr}$ (CuBr·DMS)	THF, $\text{BF}_3\cdot\text{Et}_2\text{O}$ , $-78^\circ$ , 3 h	 [Palauolide]	(77) 1211
	 (5% CuBr)	1. THF, DMS, $0^\circ$ , 45 min 2. $\text{H}_2\text{CO}$ (g), $0^\circ$ , 1 h	 [(+), (-)-Panasinsene]	(90) 1212
	 (1 eq CuI)	THF, TMEDA, $-78$ to $25^\circ$	 [(±)-Pentalene, (±)-Pentalenic acid, (±)-Deoxypentalenic acid]	(48) 1213



TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$\text{Cl}(\text{CH}_2)_2\text{MgBr}$ (30% CuBr-DMS)	THF, $-78^\circ$ , 1.5 h	 [Pentalenene] (83)	1214
	 (~% CuI)	THF, TMEDA, $-78$ to $25^\circ$	 [(±)-Pentalenic acid] (48)	1215
502	$\text{CH}_2=\text{C}(\text{CH}_3)\text{MgBr}$ (10% CuI)	THF, $-15^\circ$ , 1 h	 [Photocitral A] (75)	1216
	 (5% CuI)	THF, DMS, $-20$ to $0^\circ$ , 2 h	 [R,R-Phytol] 97: 3 E:Z (95)	1217
	 (cat. $\text{Li}_2\text{CuCl}_4$ )	THF, $-78$ to $25^\circ$ , 15 h	 [Phytol] (72)	1218
	 (1 eq CuI)	THF, TMEDA, $-78^\circ$	 [(±)-Protoilludine] (76)	1219
	$\text{CH}_3\text{MgCl}$ (0.5 eq CuBr-DMS)	THF, $0^\circ$	 [Pseudoguaianes] (25)	1220
	 (0.5 eq CuBr-DMS)	Ether, THF, DMS, $-78$ to $-10^\circ$ , 14 h	 [(-)-Ptilocaulin] (61)	1221
503	 (5-10% CuBr)	THF, $30^\circ$ , 8 h	 [Pyrocin] (60-75)	1222
	$\text{CH}_2\text{MgBr}$ (1 eq CuBr-DMS)	1. THF, $-78^\circ$ , 12 h TMSCl, $(\text{C}_2\text{H}_5)_3\text{N}$ 2. $\text{LiNH}_2$ , $\text{NH}_3$ (l), THF, $\text{BrCH}_2\text{C}(\text{OCH}_3)=\text{CHCO}_2\text{C}_2\text{H}_5$ 3. 30% $\text{HClO}_4$	 [Quadrone] [Quadrone] see ref. 1224 [dl-Quadrone] see ref. 1225 [Silphinene] see ref. 1226 (62)	1223
	$\text{CH}_2=\text{CHMgBr}$ (cat. $\text{CuI-P}(\text{C}_4\text{H}_7\text{-}n)_3$ )	THF, $-45^\circ$ , 2 h	 [Quassinoids] (80)	1227

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$\text{CH}_2\text{MgCl}$ (10% CuI)	Ether, $-10$ to $0^\circ$ , 15 h	 [Selinadiene]	(—) 1228
	 $(\text{CH}_2)_2\text{MgBr}$ (10% CuI)	THF, DMS, $20^\circ$ , 15 h	 [Senoxydene]	(100) 1229
	$\text{BrMg}(\text{CH}_2)_2$ (33% CuBr-DMS)	1. THF, $-78$ to $0^\circ$ , 16 h 2. HCl, THF, $\text{H}_2\text{O}$	 [(±)-Silphinene]	(48) 1230
	$\text{CH}_2=\text{CH}(\text{CH}_2)_2\text{MgBr}$ [( <i>n</i> - $\text{C}_4\text{H}_9$ ) $_3\text{P-CuI}$ ] $_4$	1. THF, $-50^\circ$ , 2 h 2. $\text{ICH}_2\text{C}(\text{OCH}_3)=\text{CHCO}_2\text{CH}_3$ , HMPA, $25^\circ$	 [Silphinene, laurenene]	(58) 1231
	$\text{CH}_2\text{MgCl}$ ( $\text{Li}_2\text{CuCl}_4$ )	1. THF 2. PPTS, $\text{C}_2\text{H}_5\text{OH}$	 [Taonianone]	(70) 1232
	$\text{CH}_2=\text{CH}(\text{CH}_2)_2\text{MgBr}$ (cat. $\text{Li}_2\text{CuCl}_4$ )	THF	 Tetrahydrocannabinol	(50) 1233
	$\text{BrMgO}(\text{CH}_2)_6\text{MgBr}$ (2.5% CuBr-DMS)	—	 [Tetrahydrodicranenone B]	(—) 1234
	 $[\text{Cu}(\text{acac})_2]$	THF, $25^\circ$ , 24 h	 [α-Tocopherol side chain]	(48) 1235
	$\text{CF}_3\text{CH}(\text{CH}_2)_3\text{MgBr}$ OTBDMS [( <i>n</i> - $\text{C}_4\text{H}_9$ ) $_3\text{P-CuI}$ ] $_4$	THF	 [Trifluorocyclocitral]	(86) 1236
	 $(\text{C}_6\text{H}_5)_2\text{CuMgBr}$	THF, DMS, $-30$ to $0^\circ$ , 1 h	 [(+)-ar-Turmerone] [ <i>cis</i> -Jasmone] see ref. 1238 [Aplysistatine] see ref. 1239	(60) 1237
	$\text{CH}_2=\text{CHMgBr}$ (0.5 eq CuI)	1. THF, $-70$ to $0^\circ$ 2. 10% $\text{H}_2\text{SO}_4$ , glyme, heat	 [Vernolepin]	(86) 1240
	 $(2.5\% \text{Li}_2\text{CuCl}_4)$	THF, $-78$ to $20^\circ$ , 31 h	 [Vitamin E side chain]	(93) 1241

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	THPOCH <sub>2</sub> -CH(CH <sub>3</sub> )-(CH <sub>2</sub> ) <sub>2</sub> MgBr (3.3 eq) (cat. Li <sub>2</sub> CuCl <sub>4</sub> )	1. THF, -20 to 0°, 4 h 2. Ac <sub>2</sub> O (excess)	 [(±)-Zoapatanol] (35)	1242
b. Lithocuprate Couplings, Substitutions				
CH <sub>2</sub> =CHCH <sub>2</sub> Br		THF, P(OCH <sub>3</sub> ) <sub>3</sub> , -78°, 2.5 h	 [Aromatin] (43)	1243
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, -78 to -47°, 4 h	 [Ascofuranone] (83)	1244
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (3 eq)	Ether, 0-20°, 48 h	 [(+)-Bakkenolide-A] (90)	1245
	[(CH <sub>3</sub> ) <sub>2</sub> C=CH] <sub>2</sub> CuLi	Ether, -10°, 12 h	 [α-Bisabolene] [Ubiquinone 2] see ref. 1247 (70)	1246
	(CH <sub>3</sub> ) <sub>2</sub> Cu(CN)Li <sub>2</sub> (2.5 eq)	Ether, -40°, 1.5 h	 [Bisabolenes, aromatic] (73)	1248
	(n-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi (excess)	Ether, -26°, 2 h	 [Cecropia juvenile hormones] (—)	1249
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	THF, 0°, 4 d	 [Cembranolide] (85)	1250
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (5 eq)	1. Ether, 0°, 12 h 2. CH <sub>3</sub> I, 0°, 6 h	 [Cembranolide] (91)	1177a
	[(CH <sub>3</sub> ) <sub>2</sub> C=CH(CH <sub>2</sub> ) <sub>2</sub> ] <sub>2</sub> CuLi	Ether, -70°, 12 h	 [(S-(-)-Citronellol] (47)	1251
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, 25°, 2 h	 [Dehydroiridodiol] (75) [Dehydroiridodiol] (64) [β-Damascenone] (70) [Germacrone] (70) [Mokupalide] (87)	1252 1253 1254 1255 1256

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	—	 [(+)-Dehydroiridodiol]	(66) 1257
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	THF, $-78$ to $0^\circ$ , 1 h	 [Eriolanin]	(85) 1258
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0^\circ$ , 4 h	 [(+)-Faranal]	(63) 1259
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (11 eq)	Ether, hexane, $-78^\circ$ , 2.5 h	 [Gibberellic acid]	(67) 1260
	$(\text{TBDMSO})_2\text{CuLi}$	1. Ether, THF, DMS, $-78^\circ$ , 1 h 2. $\text{LiAlH}_4$ , THF, $20^\circ$	 [Hypnophilin]	(90) 1261
	$(\text{CH}_3)_2\text{CuLi}$ (2.4 eq)	1. Ether, HMPA, $-25^\circ$ 2. $\text{CH}_2=\text{CHCH}_2\text{I}$ , HMPA, $-20^\circ$	 [Isabelin]	(70-80) 1262
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0^\circ$ , 12 h	 [JH-2]	(>81) 1263
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78$ to $0^\circ$ , 1 h	 [Juvenoid analog]	(68) 1264
	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78$ to $-13^\circ$	 [Kijanamicin]	(—) 1265
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0^\circ$ , 12 h	 [p-Menthenes]	(84) 1266
	$(i\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $-40^\circ$	 [Myodesmone]	(53) 1267
	$(n\text{-C}_4\text{H}_9)_3\text{Sn}-\text{Cu}(\text{C}\equiv\text{CC}_4\text{H}_9\text{-}n)\text{Li}$	THF, $-78$ to $20^\circ$	 [Plenaplyssillin 1]	(73) 1268
	$(\text{P}(\text{C}_4\text{H}_7\text{-}n)_2)_2\text{CuLi}$	Ether, $-40$ to $0^\circ$ , 1.1 h	 [(-)-Pulo'upone]	(—) 1269

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

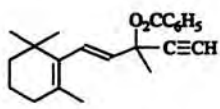
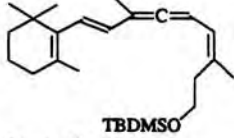
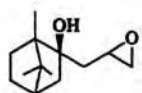
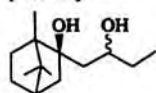
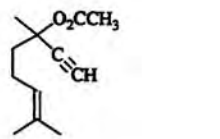
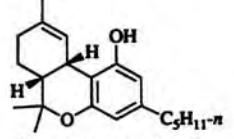
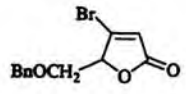
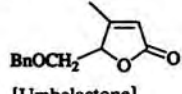
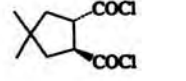
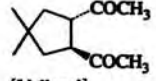
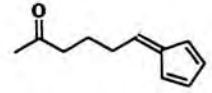
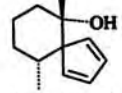
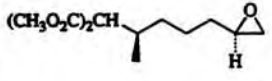
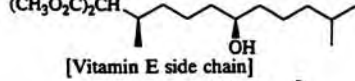
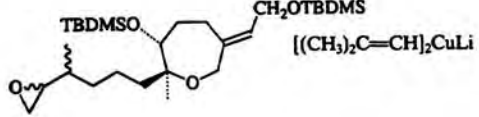
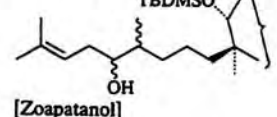
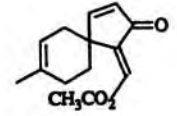
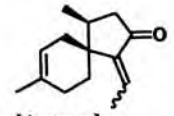
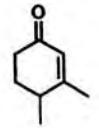
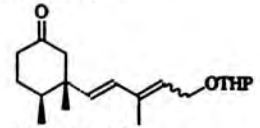
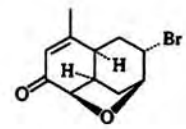
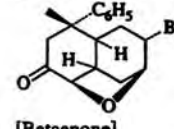
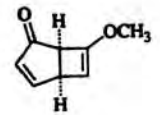
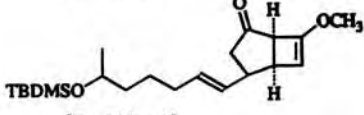
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$\text{Cu}(\text{C}\equiv\text{CC}(\text{CH}_3)_2\text{OCH}_3)\text{Li}$ $(\text{CH}_2)_2\text{OTBDMS}$	—	 TBDMSO	(50) 1270
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°, 20 h	 [Taximine]	(89) 1271
	$(\text{OTHP})_2\text{CuLi}$ $n\text{-C}_3\text{H}_{11}$	1. THF, 0–25° 2. $(\text{CO}_2\text{H})_2$ , $\text{C}_2\text{H}_5\text{OH}$	 [Tetrahydrocannabinol]	(20) 1272
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, DMS, –78 to –30°, 4 h	 [Umbelactone]	(28) 1273
	$(\text{CH}_3)_2\text{CuLi}$	Ether, –75°, 20 min	 [Vellaral]	(88) 1274
	$(\text{CH}_3)_2\text{CuLi}$	Ether, –20°	 [β-Vetivone]	(80–90) 1275
	$i\text{-C}_3\text{H}_7\text{Cu}(\text{CN})\text{Li}$	Ether, –10°	 [Vitamin E side chain]	(64) 1276
	$[(\text{CH}_3)_2\text{C}=\text{CH}]_2\text{CuLi}$	Ether, –10°	 [Zoapatanol]	(64) 1277
c. Lithocuprate Couplings, Conjugate Addition				
	$(\text{CH}_3)_2\text{CuLi}$ (6 eq)	Ether, –70°, 1 h	 [Acorone]	(—) 1278
	$\text{THPO}-\text{CH}_2-\text{CH}=\text{CH}-\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	Ether, HMPT, –78°, 1.5 h	 [Ascochlorin] [Eremophilone] see ref. 1281 [Ishwarone] see ref. 1282	(60) 1279 1280
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	Ether, THF, –40°	 [Betaenone]	(60) 1283
	$\text{OTBDMS}-\text{CH}_2-\text{CH}=\text{CH}-\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	THF, –78°	 [Brefeldin A]	(82) 1284

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
		THF, HMPA, -78°	 [Brefeldin-A]	(72) 1285
	$(C_6H_5)_2CuLi$	Ether, -25°	 [Bullatenone]	(57) 1286
	$(CH_3)_2CuLi$ ( $BF_3 \cdot Et_2O$ )	Ether, 20°, 1 h	 [Capnellene]	(88) 1287
	$(CH_3)_2CuLi$	—	 [Capnellene]	(96) 1288
	$(CH_3)_2CuLi$ (4 eq)	Ether, -20°, 30 min	 [Capnellene]	(88) 1289
	$(CH_2=CH)_2Cu(CN)Li_2$ ( $BF_3 \cdot Et_2O$ )	Ether, THF, -50°	 [Capnellols]	(86) 555
	$(CH_3)_2CuLi$	THF, 0°	 [Cembranolide]	(86) 1290
	$(CH_3)_2CuLi$	1. Ether, THF, 0°, 15 min 2. $LiSC_3H_7$ , THF, 20°	 [Cembranolide]	(90) 1291
	$(TBDM SO(CH_2)_3)_2CuLi$	1. Ether, DMS 2. $CH_3I$ , HMPA	 [Chokol A]	(52) 1292
	$(CH_3)_2CuLi$	1. Ether, pentane, DMS, -25°, 1.5 h 2. $H_2CO$ (g)	 [Clerodane diterpenes]	(46) 1293

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

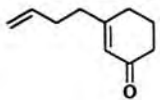
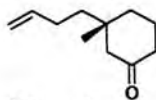

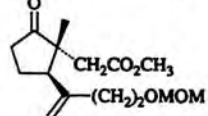
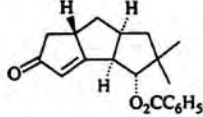
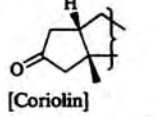
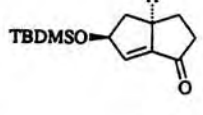
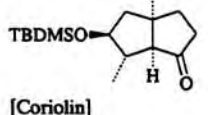
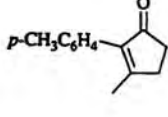
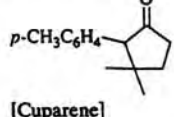
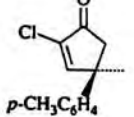
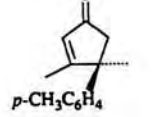
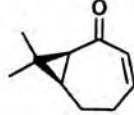
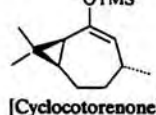
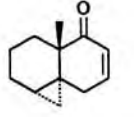
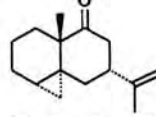
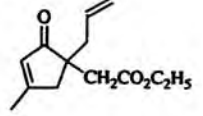
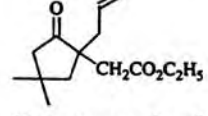
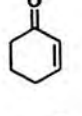
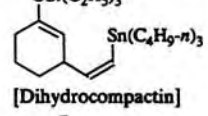
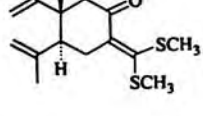
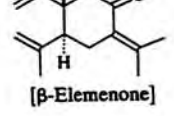
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	THF	 [Clovene] [Dehydroabietic acid] see ref. 1295	(90) 1294
	$\text{MOMO}(\text{CH}_2)_2\text{C}(\text{CH}_3)=\text{CH}-\text{Cu}(\text{C}\equiv\text{CC}_4\text{H}_9)\text{Li}$	1. Ether, THF, $-45^\circ$ 2. $\text{BrCH}_2\text{CO}_2\text{CH}_3$ , HMPA, ether, $-20^\circ$	 [Confertin]	(85) 1296
	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}_2$ $(\text{BF}_3 \cdot \text{Et}_2\text{O})$	THF, $-50^\circ$ , 3 h	 [Coriolin]	(80) 1297
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78^\circ$	 [Coriolin]	(95) 1298
	$(\text{CH}_3)_2\text{CuLi}$	THF, DMS, $0^\circ$ , 1 h	 [Cuparene]	(65) 1299
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-78^\circ$ 2. $\text{Li}_2\text{CO}_3$ , LiBr, DMF, $80^\circ$	 [ (+)- $\beta$ -Cuparenone]	(85) 1300
	$(\text{CH}_3)_2\text{CuLi}$	1. THF, $-78^\circ$ 2. TMSCl, $-78$ to $0^\circ$	 [Cyclototorenone]	(-) 1301
	$[\text{CH}_2=\text{C}(\text{CH}_3)]_2\text{CuLi}$	—	 [Cycloeudesmol]	(81) 1302
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-45^\circ$	 [Descarboxyquadrone]	(89) 1303
	$(n\text{-C}_4\text{H}_9)_3\text{Sn}-\text{C}(\text{CH}_3)=\text{CH}-\text{Cu}(\text{CN})\text{Li}$ $[(\text{C}_2\text{H}_5)_3\text{SiCl}]$	THF, $(\text{C}_2\text{H}_5)_3\text{N}$ , $-78$ to $0^\circ$ , 2 h	 [Dihydrocompactin]	(83) 1304
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether	 [ $\beta$ -Elemenone]	(90) 1305

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

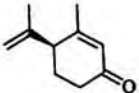
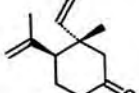
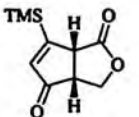
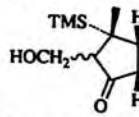
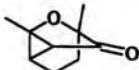
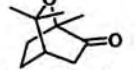
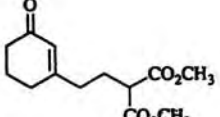
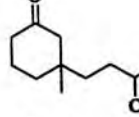
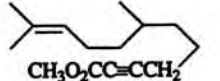
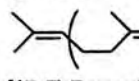
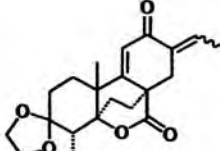
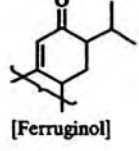
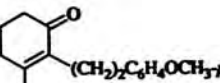
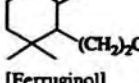
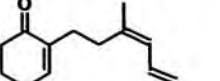
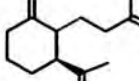
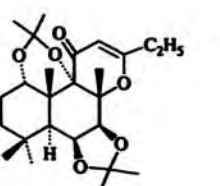
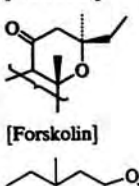
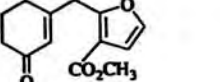
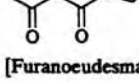
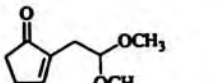
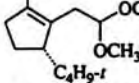
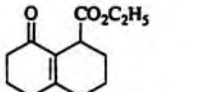
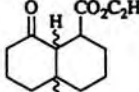
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-70$ to $-50^\circ$ , 2 h	 [β-Elemenone]	(78) 1306
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-10$ to $0^\circ$ , 4 h 2. $\text{H}_2\text{CO}$ , $-40$ to $20^\circ$ , 10 min	 [Enomycin A]	(57) 1307
	$(\text{CH}_3)_2\text{CuLi}$ $(\text{BF}_3 \cdot \text{Et}_2\text{O})$	Ether, $-78$ to $0^\circ$ , 75 min	 [Eucalyptol]	(—) 1308
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0^\circ$	 [β-Eudesmol]	(88) 1309
	$(\text{CH}_3)_2\text{CuLi}$ $(\text{CH}_3\text{Cu})$	THF, $-70^\circ$ , 6 h	 [(Z,Z)-Farnesol]	(62) 1310
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $\text{C}_6\text{H}_6$ , $0$ – $25^\circ$ , 4 h	 [Ferruginol]	(>54) 1311
	$(\text{CH}_3)_2\text{CuLi}$ $(\text{BF}_3 \cdot \text{Et}_2\text{O})$	Ether, $-25^\circ$ , 1h	 [Ferruginol]	(93) 1312
	$[\text{CH}_2=\text{C}(\text{CH}_3)]_2\text{CuLi}$	THF, DMS, $-40^\circ$	 [Fitchelite]	(84) 1313
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $\text{BF}_3 \cdot \text{Et}_2\text{O}$ , $-78$ to $25^\circ$	 [Forskolin]	(80) 1314
	$(\text{CH}_3)_2\text{CuLi}$ (3 eq)	Ether, $0^\circ$ , 45 h	 [Furanoeudesmane]	(73) 1315
	$(t\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	1. THF, $-78$ to $-45^\circ$ 2. $\text{TMSCl}$ , $(\text{C}_2\text{H}_5)_3\text{N}$	 [Ginkgolide B]	(93) 1316
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0$ – $5^\circ$ , 5h	 [epi-β-Gorgonene]	(90) 1317



TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-25^\circ$ , 70 min 2. $\text{Ac}_2\text{O}$ , DME	 [Grandisol] (81)	1318
	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78$ to $0^\circ$	 [Grandisol] (91)	1319
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, TMSCl, $-78^\circ$ , 5 min	 [Guajanolides] (95)	1320
	$(\text{CH}_3)_2\text{CuLi}$	1. THF, $-78^\circ$ 2. $\text{CH}_2=\text{CHCH}_2\text{Cl}$ , HMPA, $25^\circ$	 [Gymnomitrol] (74)	1321
	$(\text{C}_2\text{H}_5\text{O})_2\text{CH}(\text{CH}=\text{CH}_2)_2\text{CuLi}$	1. Ether 2. $\text{H}_2\text{CO}$	 [(+)-Hanegokedial] (84)	1322
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, $-25$ to $0^\circ$ , 9 h	 [Helminthosporal] (80)	1323
	 $\text{Cu}(\text{SC}_6\text{H}_5)\text{Li}$	Ether, THF, $-78$ to $23^\circ$ , 2 h	 [β-Himachalene] [(Z)-Jasmone] see ref. 1325 (100)	1324
	$(\text{TBDMSO})_2\text{CuLi}$	Ether, $-30^\circ$ , 1 h	 [(+)-Hirsutene] (88)	1326
$\text{CH}_2=\text{CHCOCH}_3$	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	Ether, $-65$ to $25^\circ$ , 1 h	 [Isocomene] (56)	1327
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $0^\circ$ , 2 h 2. $\text{CH}_3\text{I}$ , HMPA, $25^\circ$	 [Laurene] (66)	1328

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

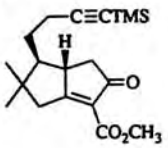
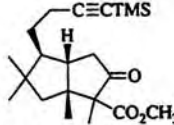
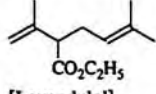
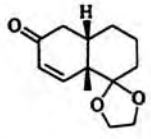
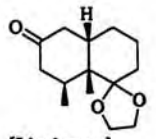

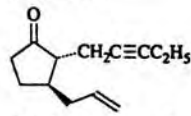
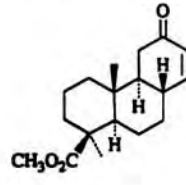
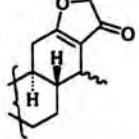
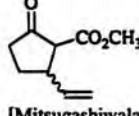
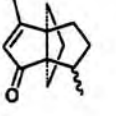

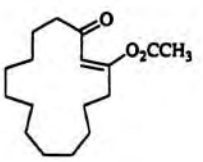
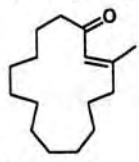
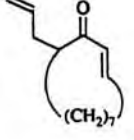
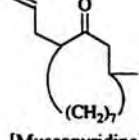
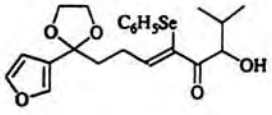
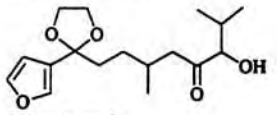
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78^\circ$ , 30 min	 [Laurenene]	(—) 1329
$\text{CH}_2=\text{C}=\text{CHCO}_2\text{C}_2\text{H}_5$	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-90^\circ$ 2. $(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{Br}$ , DME, $-30^\circ$	 [Lavandulol]	(—) 1330
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-5^\circ$ , 2 h	 [Ligularone]	(87) 1331
	$(\text{CH}_2=\text{CHCH}_2)_2\text{CuLi}$	1. THF, $-78^\circ$ 2. $\text{ICH}_2\text{C}\equiv\text{CC}_2\text{H}_5$ , HMPA, TMEDA	 [Methyl jasmonate]	(60) 1332
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-25^\circ$ , 1 h 2. $\text{ClCH}_2\text{COCl}$ , $25^\circ$ , 1.5 h	 [(+)-Methyl vouacapenate]	(76) 1333
$(E)\text{-CH}_3\text{O}_2\text{C}(\text{CH}_2)_7\text{-CH}=\text{CHCO}_2\text{CH}_3$	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-30^\circ$ , 30 min	 [Mitsugashiwalactone]	(77-85) 1334
	$(\text{CH}_3)_2\text{CuLi}$ $(\text{BF}_3 \cdot \text{Et}_2\text{O})$	Ether, $-78$ to $25^\circ$	 [Modhephene]	(70) 1335
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78^\circ$ , 30 min	 [Muscone]	(—) 1336
	$(\text{CH}_3)_2\text{CuLi}$	—	 [Muscopyridine]	(—) 1337
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, DMS, $-78^\circ$ , 2 h 2. $\text{C}_6\text{H}_5\text{SH}$ , $\text{CH}_3\text{OH}$	 [Myoporone]	(66) 1338

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

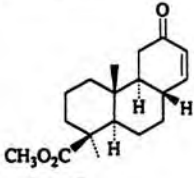
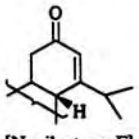
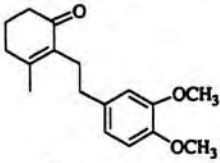
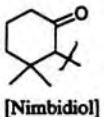
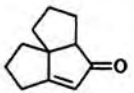
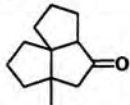
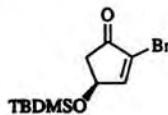
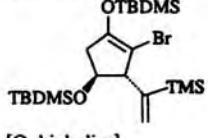
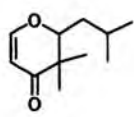
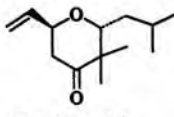
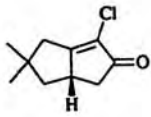
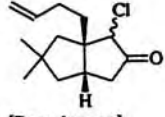
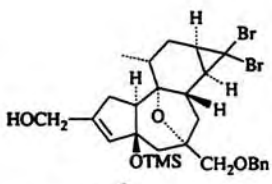
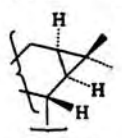
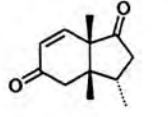
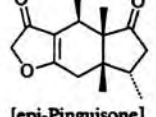
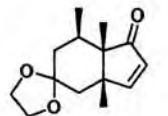
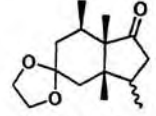
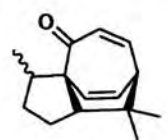
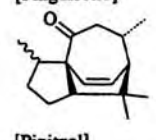
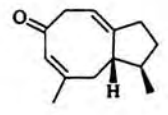
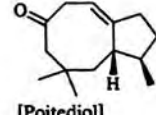
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(i-C_3H_7)_2CuLi$	1. THF, DMS, $-78$ to $-30^\circ$ , 1 h 2. $C_6H_5SeCl$ 3. 30% $H_2O_2$ , THF	 [Nagilactone F]	(75) 1339
	$(CH_3)_2CuLi$ ( $BF_3 \cdot Et_2O$ )	Ether, $-30$ to $-25^\circ$ , 1 h	 [Nimbidiol]	(90) 1340
	$(CH_3)_2CuLi$	Ether, $0$ – $25^\circ$ , 2.5 h	 [bis(Norisocomene)]	(90) 1341
	$TMS-Cu(C\equiv CC_3H_7-n)Li$	1. — 2. TBDMSOTf	 [Ophiobolins]	(86) 1342
	$(CH_2=CH)_2CuLi$	—	 [Pedaldehyde]	(—) 1343
	$(CH_2=CHCH_2)_2CuLi$	THF, DMS	 [Pentalenene]	(76) 1344
	$(CH_3)_2Cu(CN)Li_2$	1. Ether, $-20^\circ$ 2. $CH_3I$	 [Phorboid]	(—) 1345
	$(CH_3)_2CuLi$ (3 eq)	1. Ether, $-25^\circ$ , 1 h 2. $ClCH_2COCl$ , $25^\circ$	 [epi-Pinguisone]	(73) 1346
	$(CH_3)_2CuLi$	Ether, $0^\circ$	 [Pinguisone]	(76) 1347
	$(CH_3)_2CuLi$	—	 [Pipitzol]	(90) 1348
	$(CH_3)_2CuLi$	Ether	 [Poitediol]	(—) 1349

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

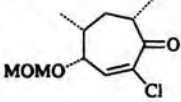
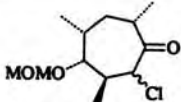
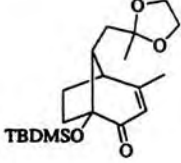
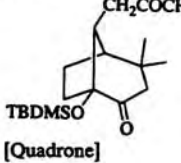
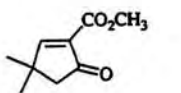
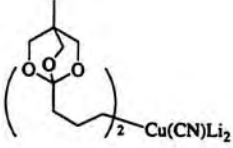
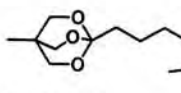
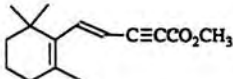
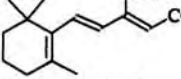
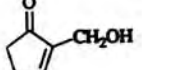
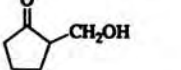
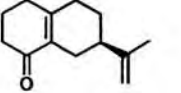
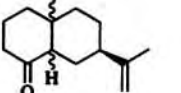
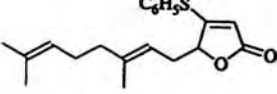
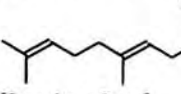
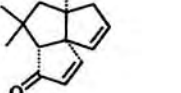
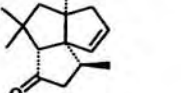
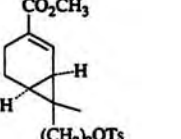
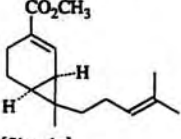
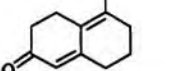
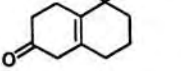
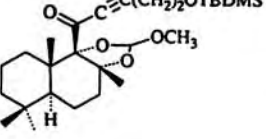
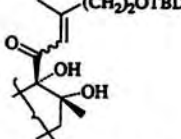
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°, 1.5 h	 [Prelog-Djerassi lactic acid]	(97) 1350
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether 2. $\text{CF}_3\text{SO}_3\text{H}$ (cat.), acetone	 [Quadrone]	(95) 1351
		—	 [Quadrone]	(85) 1352
	$(t\text{-C}_4\text{H}_9)_2\text{CuLi}$	THF, -20°, 2 h	 [Retinal analogs]	(87) 1353
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$ (2 eq)	Ether, THF, DMS, -78°, 30 min	 [Sarkomycin]	(73) 1354
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°, 12 h	 [(+)-β-Selinene]	(79) 1355
	$(\text{CH}_3)_2\text{CuLi}$	—	 [Sesquirose furan]	(70) 1356
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -78 to -20°	 [Silphinene] [Pentalenene] see ref. 1358 [Subergorgic acid] see ref. 1359	(89) 1357
	$[(\text{CH}_3)_2\text{C}=\text{CH}]_2\text{CuLi}$	Ether	 [Sirenin]	(87) 1360
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°, 30 min	 [Spiniferin-1]	(85) 1361
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, -78° 2. $\text{H}^+$ , $\text{H}_2\text{O}$	 [Trideoxyforskolin]	(82) 1180

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

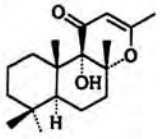
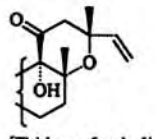
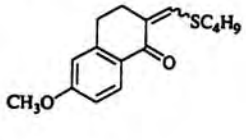
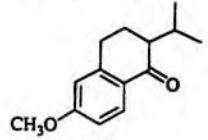
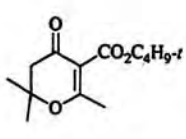
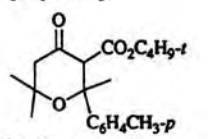
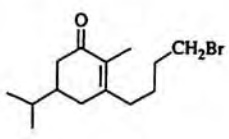
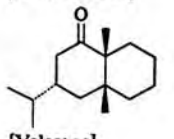
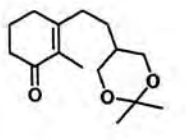
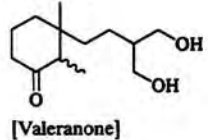
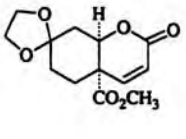
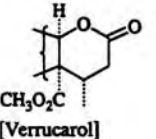
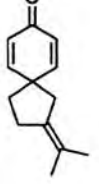
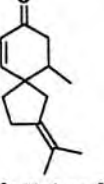
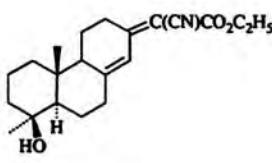
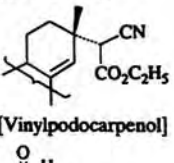
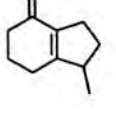

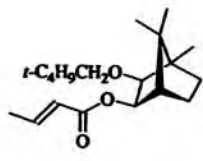
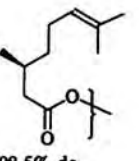
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, 0°, 10 min	 [Trideoxyforskolin]	(80) 1180
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°, 30 min	 [Triptolide]	(93) 1363
	$(p\text{-CH}_3\text{C}_6\text{H}_4)_2\text{CuLi}$	Ether, -50 to 0°, 6 h, 25°, 14 h	 [ar-Turmerone]	(83) 1364
	$(\text{CH}_3)_2\text{CuLi}$	HMPA, $\text{C}_6\text{H}_6$ , 0-5°, 4 h	 [Valerane]	(25-30) 1365
	$(\text{CH}_3)_2\text{CuLi}$	1. THF, TMSCl, -78 to 20°, 3h 2. THF, 1 M HCl 20°	 [Valeranone]	(77) 1366
	$(\text{CH}_3)_2\text{CuLi}$	THF, -10 to 0°, 1 h	 [Verrucarol]	(74) 1367
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°, 15 min	 [β-Vetivone]	(75) 1368
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -10 to 25°, 12 h	 [Vinylpodocarpene]	(28) 1369
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	Ether, DMS, -50 to 25°, 1 h	 [Zizaene]	(72) 1370
d. Reactions of $\text{RCu}$ , $\text{RCu}\cdot$ -Ligand				
	$(\text{CH}_3)_2\text{C}=\text{CH}(\text{CH}_2)_2\text{Cu}$ $(\text{BF}_3\cdot\text{Et}_2\text{O})$ $[\text{P}(\text{C}_6\text{H}_5)_3]$	Ether, -78 to -10°, 6 h	 98.5% de [(S)-(-)-Citronellic acid]	(81) 1371

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$\text{RO}(\text{CH}_2)_2\text{C}(\text{CH}_3)=\text{CH}_2\text{Cu}$ R = TBDMS (P[N(CH <sub>3</sub> ) <sub>2</sub> ] <sub>3</sub> ) (BF <sub>3</sub> ·Et <sub>2</sub> O)	Ether	 (70) 1372 [Hirsutene]	
	$\text{CH}_3\text{O}-\text{Cyclopropane}-\text{Cu}$	Ether, P(C <sub>4</sub> H <sub>9</sub> ) <sub>3</sub> , -78°	 (77) 1373 [Juvabione]	
	$\text{CH}_3\text{Cu}$ (BF <sub>3</sub> ·Et <sub>2</sub> O)	—	 (88) 1374 [Modhephene]	
	$\text{TMSC}\equiv\text{C}(\text{CH}_2)_2\text{Cu}$ (BF <sub>3</sub> ·Et <sub>2</sub> O)	THF, -78 to 20°	 (52) 1375 [Modhephene]	
	$\text{CH}_2=\text{CH}(\text{CH}_2)_2\text{Cu}$ (BF <sub>3</sub> ·Et <sub>2</sub> O)	THF, -78°, 2 h	 (59) 1376 [Parthenin]	
	$\text{CH}_3\text{Cu}$ (BF <sub>3</sub> ·Et <sub>2</sub> O)	Ether, -78 to 0°, 4 h	 (77) 1377 [Quadrone]	
	$\text{CH}_3\text{Cu}$ (BF <sub>3</sub> ·Et <sub>2</sub> O)	Ether, -70 to 20°	 (46) 1378 [(-)-β-Selinene]	
$\text{Cl}-\text{CH}_2-\text{CH}(\text{CH}_3)-\text{CH}(\text{CH}_3)-\text{CH}_2-\text{CH}(\text{CH}_3)-\text{CH}_2-\text{OTBDPS}$ R = Si(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>4</sub> H <sub>9</sub> t	$\text{TMSCu}$	Ether, HMPA, -60°, 1 h	 (81) 1379 [Tricyclohexaprenol]	
	$\text{CH}_3\text{Cu}$ [(i-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> NH]	1. Ether, -75 to 0° 2. CH <sub>3</sub> OH, H <sub>2</sub> O, 195°	 (75) 1380 [β-Vetivone]	
e. Miscellaneous Couplings				
$\text{CH}_2=\text{CHCH}_2\text{Br}$	 [CuI·P(OCH <sub>3</sub> ) <sub>3</sub> ]	THF, -78°, 2.5 h	 (50) 1381 [Aromatin]	
$(\text{CH}_3\text{O})_2\text{HC}-\text{Cyclopropane}-\text{C}(\text{CH}_3)_2\text{C}\equiv\text{CH}$	$(\text{CH}_3)_3\text{Cu}_2\text{MgCl}\cdot\text{LiBr}$	1. THF, DMS, 0°, 44 h 2. ICN, -45 to 20°	 (60) 1382 [Casbene]	

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

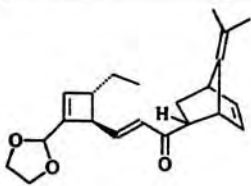
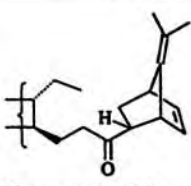
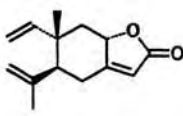
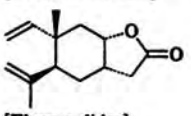
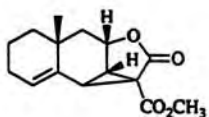
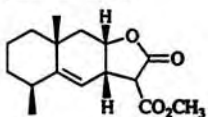
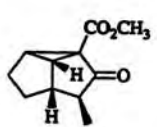
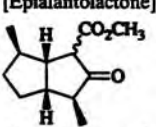
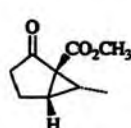
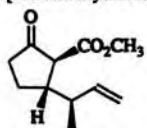
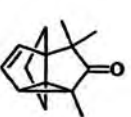
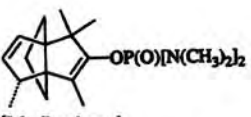
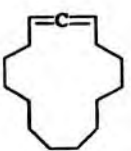

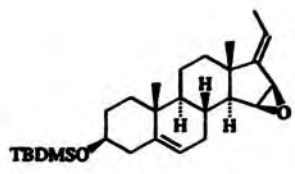
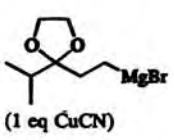
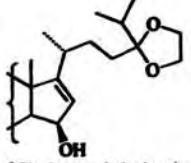
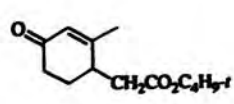
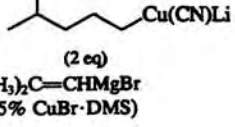
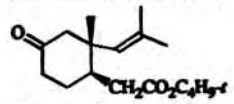
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	NaAl[O(CH <sub>2</sub> ) <sub>2</sub> O] <sub>2</sub> H <sub>2</sub> (CuI)	C <sub>6</sub> H <sub>6</sub> , THF, -45 to -10°, 2 h	 [Coronafacic acid]	(-) 1383
	( <i>i</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> AlH (1 eq CH <sub>3</sub> Cu)	Ether, toluene, HMPA, -30°, 4 h	 [Elemanolides]	(100) 1194
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, -20 to -5°, 40 min	 [Epilantolactone]	(75) 1384
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, -30°, 1.5 h	 [Isoiridomyrmecin]	(100) 1385
	(CH <sub>2</sub> =CH) <sub>2</sub> CuLi	Ether, DMS, -20 to 0°, 2 h	 [(+)-Isononepetalactone]	(76) 1386
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (5 eq)	1. THF, -78° 2. Cl <sub>2</sub> P(O)N(CH <sub>3</sub> ) <sub>2</sub> 3. (CH <sub>3</sub> ) <sub>2</sub> NH	 [Modhephene] [Isoiridomyrmecin] see ref. 1388	(76) 1387
	C <sub>6</sub> H <sub>5</sub> (CH <sub>3</sub> ) <sub>2</sub> SiMgCH <sub>3</sub> (5% CuI)	1. Ether, THF, 0°, 10 min 2. CH <sub>3</sub> I	 [Muscone]	(77) 1389
C. Steroids				
a. Grignard Couplings				
	 (1 eq CuCN)	THF, 20°, 12 h	 [Cholesterol derivative] [Cholesterol] see ref. 1391	(80) 1390
	 (2 eq) (CH <sub>3</sub> ) <sub>2</sub> C=CHMgBr (5% CuBr·DMS)	Ether, -78°  THF, TMSCl, -78°, 30 min	 [Cortisone]	(78) 1392

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(C_2H_5)_3SiOC(CH_3)_2(CH_2)_2MgBr$ (1.5 eq CuI)	1. THF, 20°, 40 min 2. ( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>4</sub> NF, THF, reflux	 [Dehydrovitamin D <sub>3</sub> ] [Hydroxyvitamin D <sub>3</sub> ] see ref. 1393	(780) 1403
	$CH_3C\equiv C(CH_2)_2MgBr$ (1 eq CuI)	THF, BF <sub>3</sub> ·Et <sub>2</sub> O, -78 to 25°, 4 h	 [11-Oxosteroids]	(53) 1394
	<i>i</i> -C <sub>3</sub> H <sub>11</sub> MgBr	THF, 30°, 5 h	 [(20 <i>S</i> )-Steroids]	(81) 1395
	<i>i</i> -C <sub>6</sub> H <sub>13</sub> MgBr (cat. CuI)	THF, -20°, 30 min	 [Vitamin D <sub>3</sub> ]	(43) 1396
b. Lithiocuprates, Substitutions				
	$(i-C_3H_7)_2Cu(CN)Li_2$	—	 [Brassinolide side chain]	(63) 1397
	$(CH_3)_2CuLi$ (1 eq CH <sub>3</sub> Li)	THF, -20°, 2 h	 [Cholestane triol]	(—) 1398
	$(CH_3)_2CuLi_2$	Ether, 20°, 48 h	 [Hydroxyvitamin D <sub>2</sub> ]	(78) 1399
	$(CH_3)_2CuLi$	Ether, -20°	 [Hydroxyvitamin D <sub>2</sub> ]	(93) 1400

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TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

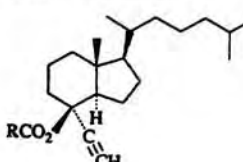
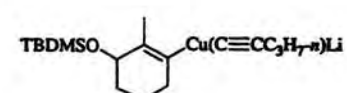
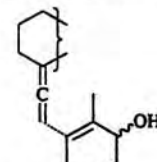
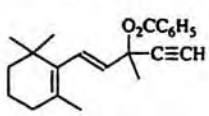
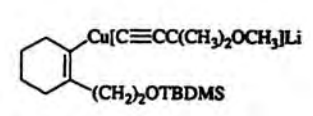
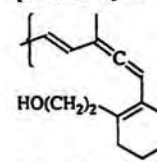
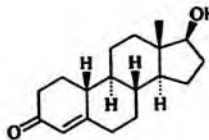
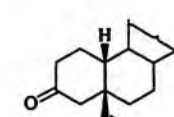
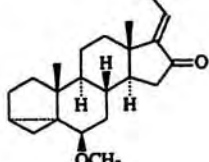
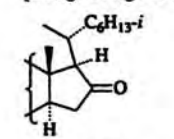
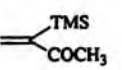
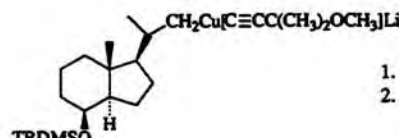
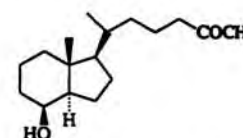
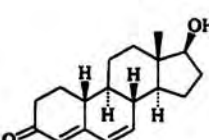
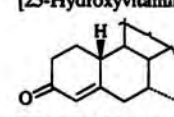
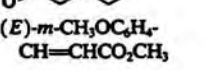
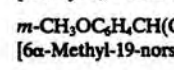
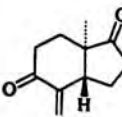
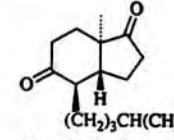

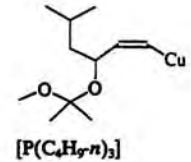
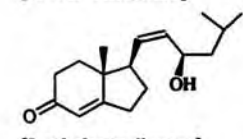
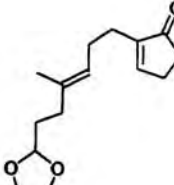
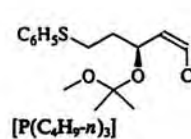
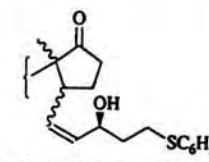
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
		1. -78°, 5 h 2. (n-C4H9)4NF, THF, 25°, 4 h		R = CH3 (37) 1401 R = C6H5 (87) 1402
R = CH3, C6H5			[1-Hydroxyvitamin D] [Vitamin D3 analog] see ref. 1404	
		1. Ether 2. (n-C4H9)4NF, THF, 20°, 4.5 h		(43) 1405
			[Retinal analogs]	
c. Lithiocuprates, Conjugate Additions				
	(CH2=CH)2CuLi [(n-C4H9)3P]	THF, -78 to 0°, 4 h		(85) 1406
			[Bridged-ring steroids]	
	(i-C6H13)2CuLi	Ether, -78 to -10°, 3.5 h		(73) 1407
			[Cholesterol]	
		1. Ether, -80°, 15 min 2. CH3CN, 48% HF		(65) 1408
			[25-Hydroxyvitamin D3]	
	(CH3)2CuLi	Ether, 0°, 3 h		(-) 1409
			[Methyl 7,14-isoestrones]	
	(CH3)2CuLi	Ether, 0°, 1 h		(68) 1410
			[6α-Methyl-19-norsteroids]	
d. Reactions of RCu, RCu·Ligand				
	i-C5H11Cu (BF3·Et2O)	THF, -78°, 10 min		(73) 1411
			[de-AB-Cholestane]	
		1. Ether, -70 to -20° 2. CH3COC(TMS)=CH2, -20° 3. NaOCH3, CH3OH 4. 1 N HCl		(56) 1412
			[Isocholestandienone] [(+)-Estratriendione] see ref. 1413	
		1. Ether, -70°, 1.5 h 2. HMPA, CH3I, -40 to -30° 3. THF, 0.1 N HCl		(64) 1414
			[Steroid skeleton]	

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

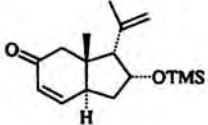

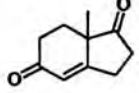
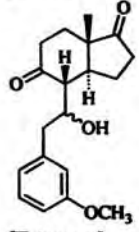
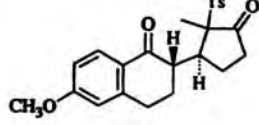
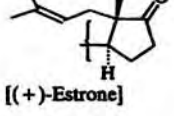

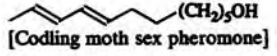
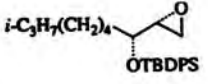
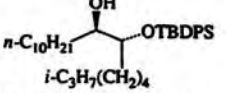
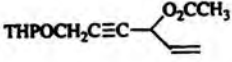
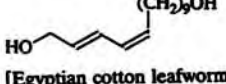
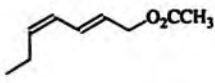
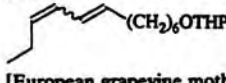
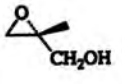
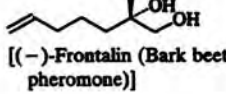
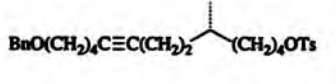
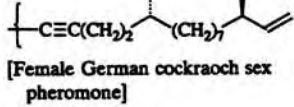
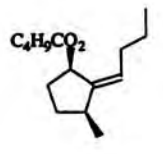
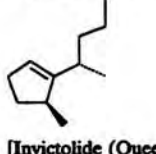
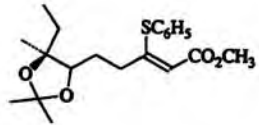
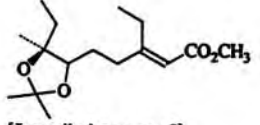
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
e. Miscellaneous Couplings				
	Zn[(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>3</sub> H <sub>7</sub> -i] <sub>2</sub> (15% CuBr·DMS) (4.8 eq BF <sub>3</sub> ·Et <sub>2</sub> O)	THF, HMPA	 (CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>3</sub> H <sub>7</sub> -i [Cortisone]	(>80) 1392
	(i-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> AlH (i-C <sub>4</sub> H <sub>9</sub> Cu)	1. HMPA 2. m-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CHO	 [Estrogens]	(72) 1415
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (4 eq)	1. Ether, THF, 0°, 1.25 h 2. (CH <sub>3</sub> ) <sub>2</sub> C=CHCH <sub>2</sub> Br, -20°, 1.25 h	 [(+)-Estrone]	(71) 1416
D. Pheromones				
a. Grignard Couplings				
	ClMg(CH <sub>2</sub> ) <sub>3</sub> OTMS (0.5% Li <sub>2</sub> CuCl <sub>4</sub> )	1. THF, 20°, 12 h 2. H <sup>+</sup> , H <sub>2</sub> O	 (CH <sub>2</sub> ) <sub>5</sub> OH [Codling moth sex pheromone]	(80) 1417
	n-C <sub>9</sub> H <sub>19</sub> MgBr (CuI)	THF, -20 to 25°	 n-C <sub>10</sub> H <sub>21</sub> i-C <sub>3</sub> H <sub>7</sub> (CH <sub>2</sub> ) <sub>4</sub> [(+)-Disparlure (Gypsy moth sex pheromone)]	(70) 1418
	ClMg(CH <sub>2</sub> ) <sub>7</sub> OTHP (2.5% Li <sub>2</sub> CuCl <sub>4</sub> )	1. THF, -10°, 1 h 2. H <sup>+</sup> , H <sub>2</sub> O 3. LiAlH <sub>4</sub> , DME, 80°	 (CH <sub>2</sub> ) <sub>9</sub> OH [Egyptian cotton leafworm pheromone]	(45) 1419
	THPO(CH <sub>2</sub> ) <sub>3</sub> MgCl (cat. Li <sub>2</sub> CuCl <sub>4</sub> )	THF, 5°, 18 h	 (CH <sub>2</sub> ) <sub>6</sub> OTHP [European grapevine moth sex pheromone]	(-) 1420
	CH <sub>2</sub> =CH(CH <sub>2</sub> ) <sub>2</sub> MgBr (10% Li <sub>2</sub> CuCl <sub>4</sub> )	THF, -78°	 [(-)-Frontalin (Bark beetle aggregation pheromone)]	(85) 1421
	BrMg(CH <sub>2</sub> ) <sub>7</sub> CH=CH <sub>2</sub> (cat. Li <sub>2</sub> CuCl <sub>4</sub> )	Ether, THF, 20°, 12 h	 [Female German cockroach sex pheromone]	(64) 1422
	CH <sub>3</sub> MgBr (5% CuCN)	Ether, 0°	 [Invictolide (Queen recognition pheromone of Solenopsis imicta)]	(74) 1423
	C <sub>2</sub> H <sub>5</sub> MgBr (CuI)	THF, -65°	 [Juvenile hormone-I]	(80) 1424

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
$\text{Br}(\text{CH}_2)_4\text{Br}$	$\text{THPO}(\text{CH}_2)_4\text{MgBr}$ (1% $\text{Li}_2\text{CuCl}_4$ )	THF, 0°, 2 h	$\text{THPO}(\text{CH}_2)_8\text{Br}$ [Lepidopteran sex pheromone]	(62) 1425
	$n\text{-C}_7\text{H}_{15}\text{CH}=\text{CHMgBr}$ (10% $\text{CuI}$ )	THF, HMPA, -23°, 30 min	 [Lepidopteran sex pheromone]	(50) 1426
	$\text{ClMg}(\text{CH}_2)_7\text{OTHP}$ (cat. $\text{Li}_2\text{CuCl}_4$ )	1. THF, -30°, 4 h 2. $\text{TsOH}$ , $\text{CH}_3\text{OH}$ 3. $\text{Ac}_2\text{O}$ , Py	$\text{CH}_3\text{CO}_2(\text{CH}_2)_8$ [Lepidopteran sex pheromone]	(74) 1427
$(E)\text{-CH}_3\text{CH}=\text{CHCOCH}_3$	$(\text{C}_2\text{H}_5)_2\text{CuMgBr}$	1. Ether, -60° 2. $\text{TMSCl}$ , HMPA, 20°	 [Manicone (ant alarm pheromone)]	(78) 1428
	$(n\text{-C}_8\text{H}_{17})_2\text{CuMgBr}\cdot\text{LiBr}$	THF, -60°, 1.5 h	$n\text{-C}_8\text{H}_{17}\text{CH}=\text{C}=\text{CH}$ [Mole dried bean beetle sex attractant]	(90) 1429
	$n\text{-C}_{10}\text{H}_{21}\text{MgBr}$ (15% $\text{Li}_2\text{CuCl}_4$ )	Ether, THF, -78°, 2 h	$\text{CH}(\text{OCH}_3)_2$ $\text{C}_{10}\text{H}_{21}\text{-n}$ [Muscalure (housefly sex pheromone)]	(75) 1430
$t\text{-C}_4\text{H}_9\text{O}_2\text{C}$	$n\text{-C}_{10}\text{H}_{21}\text{MgBr}$ ( $\text{CuI}\cdot\text{DMS}$ )	1. THF 2. $\text{TsOH}$ , $\text{C}_6\text{H}_6$	 $\text{C}_{11}\text{H}_{23}\text{-n}$	(64) 1431
$\text{Br}(\text{CH}_2)_3\text{-CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{OBn}$	$n\text{-C}_8\text{H}_{17}\text{CH}(\text{CH}_3)\text{MgBr}$ (1% $\text{Li}_2\text{CuCl}_4$ )	THF, 0-25°, 15 h	$n\text{-C}_8\text{H}_{17}\text{CH}(\text{CH}_3)(\text{CH}_2)_3\text{-CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{OBn}$ [Pine sawfly sex pheromone]	(40) 1432
	$(n\text{-C}_8\text{H}_{17})_2\text{CuMgBr}$	THF, -25°, 7 d	$n\text{-C}_8\text{H}_{17}\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{OBn}$ [Pine sawfly sex pheromone]	(82) 1433
	$n\text{-C}_8\text{H}_{13}\text{MgCl}$ ( $\text{CuI}$ )	—	$\text{C}_8\text{H}_{17}\text{-n}$ [Pine sawfly sex pheromone]	(80) 696b
	$(n\text{-C}_5\text{H}_{11})_2\text{MgBr}$	—	$n\text{-C}_6\text{H}_{13}\text{CH}(\text{OH})\text{CO}_2\text{C}_2\text{H}_5$ [Pine sawfly sex pheromone]	(—) 755
	$\text{ClMg}(\text{CH}_2)_5\text{OTBDMS}$ (10% $\text{CuI}$ )	THF, 0°, 3 h	$\text{CH}(\text{OH})(\text{CH}_2)_6\text{OTBDMS}$ [Queen honeybee pheromone]	(92) 1434
	$(\text{CH}_2)_3\text{MgCl}$ (cat. $\text{Li}_2\text{CuBr}_4$ )	THF, -10 to -5°, 1 h	$(\text{CH}_2)_4\text{CH}(\text{OC}_2\text{H}_5)$ [Queen substance of honeybee]	(—) 1435
	$\text{MgBr}$ (10% $\text{Li}_2\text{CuCl}_4$ )	Ether, THF, 20°, 5 h	 [Red flour beetle pheromone]	(59) 1436
	$\text{CH}_3\text{MgCl}$ (cat. $\text{CH}_3\text{Cu}$ )	—	$\text{CO}_2\text{CH}_3$ [San José scale pheromone]	(68) 1437
	$\text{CH}_2=\text{CH}(\text{CH}_2)_5\text{MgBr}$ (cat. $\text{Li}_2\text{CuCl}_4$ )	THF, -25 to 0°, 12 h	$(\text{CH}_2)_5$ [Southern corn rootworm sex pheromone]	(78) 1438

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{MgBr}$ (cat. CuI)	THF, -30 to 20°	 [(+)-Sulcatol (Ambrosia beetle aggregation pheromone)] [Square-necked grain beetle aggregation pheromone] see ref 1440	(81) 1439
	$(\text{CH}_3)_2\text{C}=\text{CHMgBr}$ (CuI)	THF, 0-40°, 16 h	 [(+)-Sulcatol (Ambrosia beetle aggregation pheromone)]	(100) 1441
	$\text{ClMg}(\text{CH}_2)_6\text{CH}=\text{CH}(\text{CH}_2)_6\text{O}(\text{CH}_2)_2\text{O}$ (5% CuI)	THF, DMS, -45°	 [Trogodermal (Khapra beetle pheromone)]	(77) 1442
$\text{THPO}(\text{CH}_2)_2\text{C}\equiv\text{CCH}_2\text{OTs}$	$n\text{-C}_9\text{H}_{17}(\text{CH}_2\text{C}\equiv\text{C})_2\text{MgBr}$ (CuBr-DMS)	1. THF, 0-20° 2. H <sup>+</sup> , CH <sub>3</sub> OH	$\text{HOCH}_2(\text{CH}_2\text{C}\equiv\text{C})_3\text{C}_9\text{H}_{17-n}$ [Female winter moth sex pheromone]	(75) 1443
b. Lithocuprates, Substitutions				
	$(n\text{-C}_5\text{H}_{11})_2\text{CuLi}$ (5 eq)	Ether, CH <sub>2</sub> Cl <sub>2</sub> , -30°, 2 h	 [Black-tailed deer pheromone]	(12) 1444
	$(n\text{-C}_3\text{H}_7)_2\text{CuLi}$ (BF <sub>3</sub> ·Et <sub>2</sub> O)	Ether, -60°, 30 min	 [Bombykol]	(—) 1445
	$(n\text{-C}_3\text{H}_7)_2\text{CuLi}$	THF, ether, ZnBr <sub>2</sub> , [PdP(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> ] <sub>4</sub> (5%), -40 to 10°, 1 h	 [Bombykol]	(—) 1446
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 5°, 16 h	 [(-)-exo-Brevicomin (Bark beetle aggregation pheromone)]	(74) 1447
	$(\text{CH}_3)_2\text{CuLi}$	Ether, HMPA, 20°, 24 h	 [(+),(-)-exo-Brevicomin]	(62) 1448
	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$ (3 eq)	THF, LiCl, 0 to 25°, 4 d	 [(+)-exo-Brevicomin]	(—) 1449
$\text{I}(\text{CH}_2)_3\text{CO}_2\text{C}_2\text{H}_5$	$(n\text{-C}_5\text{H}_{11})_2\text{CuLi}$	THF, HMPT, P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> , 25°, 3 h	$n\text{-C}_5\text{H}_{11}(\text{CH}_2)_3\text{CO}_2\text{C}_2\text{H}_5$ [Douglas fir tussock moth sex pheromone]	(87) 1450
	$(n\text{-C}_8\text{H}_{17})_2\text{CuLi}$	Ether, -78°, 7 h	$n\text{-C}_8\text{H}_{17}(\text{CH}_2)_2\text{CO}_2\text{CH}_3$ [Dried bean beetle sex attractant]	(62) 1451
	$[(\text{CH}_3)_2\text{C}=\text{CH}]_2\text{CuLi}$	Ether, -15°, 2 h	 [(+)-Eldanolide (Wing gland pheromone of sugar cane borer)]	(64) 1452

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$[(\text{CH}_3)_2\text{C}=\text{CH}]_2\text{CuLi}$	Ether, $-40$ to $-25^\circ$ , 2 h	 [(+)-Eldanolide]	(67) 1453
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78$ to $0^\circ$	 [European elm bark beetle aggregation pheromone]	(—) 1454
	$(n\text{-C}_4\text{H}_9\text{---}(\text{CH}_2)_8\text{---})_2\text{CuLi}$ (0.5 eq $\text{LiC}\equiv\text{CC}_4\text{H}_9$ )	1. Ether, $-25$ to $20^\circ$ , 1 h 2. $\text{CH}_3\text{COCl}$ , Py, $20^\circ$ , 2 h	 [Lesser peachtree borer pheromone]	(63) 681
	$(\text{CH}_3)_2\text{CuLi}$	1. THF, $-15^\circ$ , 4 h 2. TsOH, $\text{CH}_3\text{OH}$ 3. $\text{Ac}_2\text{O}$ , Py	$\text{CH}_3\text{CO}_2(\text{CH}_2)_6\text{---}$ [ <i>Lobesia botrana</i> sex pheromone]	(68) 1455
$\text{CH}_3\text{I}$		THF, HMPT, $-60$ to $20^\circ$ , 16 h	 [Manicone (ant alarm pheromone)]	(81) 1456
	$(\text{C}_2\text{H}_5)_2\text{CuLi}$	Ether, $-78^\circ$ , 15 min	 [Manicone (ant alarm pheromone)]	(84) 1457
	$(\text{CH}_3)_2\text{CuLi}$ (3 eq)	Ether, $-55$ to $-20^\circ$ , 4 h	 [ $\delta$ -Multistriatin]	(78) 1458
	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	Ether, $-78^\circ$ , 1 h	 [ $\alpha$ -Multistriatin (smaller European elm bark beetle aggregation pheromone)]	(91) 1459
$\text{I}(\text{CH}_2)_9\text{CH}(\text{OC}_2\text{H}_5)_2$	$(\text{---}(\text{CH}_2)_8\text{---})_2\text{CuLi}$	1. Ether, HMPA, $-40$ to $0^\circ$ , 3 h 2. $(\text{CO}_2\text{H})_2$ , THF, $\text{H}_2\text{O}$ , $60^\circ$	$(\text{CH}_2)_9\text{CHO}$ [Naval orange worm sex pheromone]	(33) 1460a
		1. THF, $0$ – $20^\circ$ 2. $\text{H}^+$ , $\text{H}_2\text{O}$	 [Olive fly sex pheromone]	(64) 1461
	$(n\text{-C}_5\text{H}_{11}\text{---})_2\text{CuLi}$	Ether, $-20^\circ$ , 1 h	$n\text{-C}_5\text{H}_{11}\text{---}$ [Phtorimaea opercubilla pheromone]	(—) 559
	$(n\text{-C}_8\text{H}_{17}\text{---})_2\text{CuLi}$	Ether, $-50$ to $-40^\circ$ , 3 h	$n\text{-C}_8\text{H}_{17}\text{---}$ [Pine sawfly sex pheromone]	(53) 1462
	$(n\text{-C}_{10}\text{H}_{21})_2\text{CuLi}$	—	$\text{C}_{10}\text{H}_{21}\text{---}$ [Saltmarsh caterpillar moth sex pheromone]	(34) 1463
	$(n\text{-C}_{10}\text{H}_{21})_2\text{Cu}(\text{SCN})\text{Li}_2$	THF, $-30^\circ$	$\text{C}_{10}\text{H}_{21}\text{---}$ [Saltmarsh caterpillar moth sex pheromone]	(81) 1464

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (2 eq)	Ether, -40 to 25°, 12 h	 [Serricornin (Cigarette beetle aggregation pheromone)]	(-) 1465
$n\text{-C}_5\text{H}_{11}\text{CH=CH(CH}_2)_8\text{OTs}$	$(n\text{-C}_3\text{H}_7)_2\text{CuLi}$ (2 eq)	Ether, -30°, 6 h	$n\text{-C}_5\text{H}_{11}\text{CH=CH(CH}_2)_8\text{C}_{11}\text{H}_{23}\text{-n}$ [ <i>U. ornatrix</i> pheromone]	(99) 1466
c. Lithiocuprates, Conjugate Additions				
$\text{CH}_2=\text{CHP}^+(\text{C}_6\text{H}_5)_3\text{Br}^-$	$(n\text{-C}_5\text{H}_{11})_2\text{CuLi}$	1. THF, HMPA, -50°, 20 h 2. $n\text{-C}_{11}\text{H}_{23}\text{CHO}$ , 25°, 3 h	$n\text{-C}_5\text{H}_{11}\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{C}_{11}\text{H}_{23}\text{-n}$ [Arctiid moth pheromone]	(40) 1460b
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	—	 [Eldanolide (wing gland pheromone of sugarcane borer)] [(±)-Eldanolide] see ref. 1468 [European marshfly sex pheromone] see ref. 1469	(70) 1467
$\text{CH}_2=\text{CHCOCH}_3$	$\text{C}_2\text{H}_5\text{CH=CHCu}(\text{C}\equiv\text{CC}_6\text{H}_9\text{-n})\text{Li}$	—	$\text{C}_2\text{H}_5\text{CH}_2\text{CH}_2\text{COCH}_3$ [Faranal (Pharaoh ant trail pheromone)]	(30) 1470
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	Ether, DMS, -78 to -40°, 1 h	 [(-)-α-Multistriatin (Smaller European elm bark beetle aggregation pheromone)] [Serricornin (Cigarette beetle aggregation pheromone)] see ref. 1472	(94) 1471
$n\text{-C}_9\text{H}_{17}\text{COCH=CH-TMS}$	$(n\text{-C}_6\text{H}_{13})_2\text{CuLi}$	1. Ether, -78°, 5 min 2. KF, CH <sub>3</sub> OH	$n\text{-C}_9\text{H}_{17}\text{CO(CH}_2)_2\text{CH=CH-C}_6\text{H}_{13}\text{-n}$ [Peach fruit moth sex pheromone]	(>98) 1473
d. Reactions of RCu, RCu·Ligand				
	$\text{CH}_2=\text{C}(\text{CH}_3)\text{Cu}\cdot\text{LiBr}$	1. Ether, BF <sub>3</sub> ·Et <sub>2</sub> O, P(C <sub>4</sub> H <sub>9</sub> -n) <sub>3</sub> , -78° 2. Ac <sub>2</sub> O, Py	 [California red scale pheromone]	(-) 1474
$\text{CH}_3\text{O}_2\text{C}(\text{CH}_2)_2\text{COCl}$	$n\text{-C}_6\text{H}_{17}\text{C}\equiv\text{CCu}$	—	$\text{CH}_3\text{O}_2\text{C}(\text{CH}_2)_2\text{COC}\equiv\text{CC}_6\text{H}_{17}\text{-n}$ [Japanese beetle aggregation pheromone]	(85) 1475
$\text{CH}_3\text{CO}_2(\text{CH}_2)_{10}\text{C}\equiv\text{Cl}$	$\text{C}_2\text{H}_5\text{CH=CHCu}\cdot\text{LiI}$	Ether, THF, TMEDA, -30 to 0°, 30 min	$\text{C}_2\text{H}_5\text{CH}_2\text{CH}_2\text{C}\equiv\text{C}(\text{CH}_2)_{10}\text{O}_2\text{CCH}_3$ [Processionary moth pheromone]	(76) 1476
e. Miscellaneous Couplings				
$\text{THPO}(\text{CH}_2)_9\text{C}\equiv\text{CH}$	(CH <sub>3</sub> ) <sub>3</sub> SnMgCH <sub>3</sub> (5% CuCN)	1. THF, 0°, 1 h 2. I <sub>2</sub> , CH <sub>2</sub> Cl <sub>2</sub>	$\text{THPO}(\text{CH}_2)_9\text{CH=CHI}$ [Bombykol]	(82) 1477
$\text{C}_2\text{H}_5\text{C}\equiv\text{C-CH=CH(CH}_2)_8\text{Br}$	EEO(CH <sub>2</sub> ) <sub>3</sub> Li (10% Li <sub>2</sub> CuCl <sub>4</sub> )	1. THF, -5°, 1 h 2. Cl <sub>3</sub> CCO <sub>2</sub> H, THF, H <sub>2</sub> O	$\text{C}_2\text{H}_5\text{C}\equiv\text{C-CH=CH(CH}_2)_8\text{OH}$ [European grapevine moth sex pheromone]	(50) 1478

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)



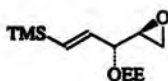
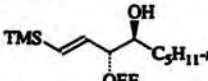
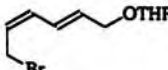
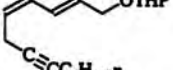
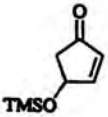
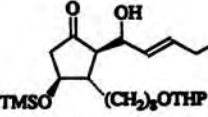
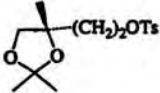
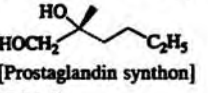
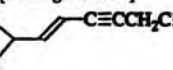
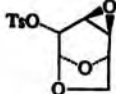
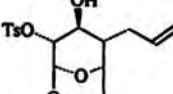
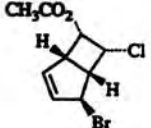
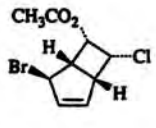
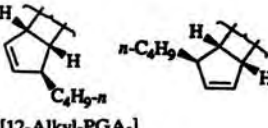
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
<i>E. Prostanoids</i>				
a. Grignard Couplings				
$\text{CH}_2=\text{CHCH}_2\text{Br}$ $\text{TMSC}\equiv\text{CCH}_2\text{OTs}$	$\text{BrMgC}\equiv\text{C}(\text{CH}_2)_3\text{CO}_2\text{MgBr}$ (5% CuBr) $(\text{CH}_3\text{O})_3\text{C}(\text{CH}_2)_3\text{C}\equiv\text{CMgBr}$ (10% CuI)	1. THF, reflux 8 h 2. $\text{CH}_2\text{N}_2$ , ether THF, $-78$ to $25^\circ$	$\text{CH}_2=\text{CHCH}_2\text{C}\equiv\text{C}(\text{CH}_2)_3\text{CO}_2\text{CH}_3$ (88) [Arachidonic acid metabolite] $\text{TMSC}\equiv\text{CCH}_2\text{C}\equiv\text{C}(\text{CH}_2)_3\text{CO}_2\text{CH}_3$ (84) [12(S)-HETE]	1479 1480
	$\text{BrMg}(\text{CH}_2)_3\text{OTHP}$ (cat. CuCN)	THF, $-20$ to $0^\circ$ , 2 h	 [12(S)-HETE metabolite]	(-) 1481
	$n\text{-C}_4\text{H}_9\text{MgBr}$ (CuI)	THF, ether	 [Lipoxin B]	(89) 1067
	$n\text{-C}_5\text{H}_{11}\text{C}\equiv\text{CMgBr}$ (0.5 eq CuCl)	THF, $60^\circ$ , 1 h	 [LTA <sub>4</sub> Methyl ester]	(65-71) 1482
$p\text{-BrC}_6\text{H}_4\text{CH}_2\text{Br}$	$\text{BrMg}(\text{CH}_2)_4\text{C}\equiv\text{C}(\text{CH}_2)_2\text{OTBDMS}$ (1 eq $\text{Li}_2\text{CuCl}_4$ )	THF, $-15^\circ$ , 18 h	$p\text{-BrC}_6\text{H}_4(\text{CH}_2)_5\text{C}\equiv\text{C}(\text{CH}_2)_2\text{OTBDMS}$ (50) [LTA <sub>4</sub> -20-Aryl]	1483
$n\text{-C}_5\text{H}_{11}\text{C}\equiv\text{CCH}_2\text{Br}$	$\text{EBOCH}_2\text{C}\equiv\text{C}\text{MgBr}$ (CuBr)	1. THF, $60^\circ$ , 45 min 2. Acetone, 0.5 $\text{NH}_4\text{SO}_4$ , $20^\circ$ , 3 h	$\text{HOCH}_2\text{C}\equiv\text{CCH}_2\text{C}\equiv\text{CC}_5\text{H}_{11-n}$ (-) [LTA <sub>4</sub> , diacetylenic]	1484, 1485
	$\text{ClMg}(\text{CH}_2)_8\text{OTHP}$ (CuI)	1. THF, $-45^\circ$ , 4 h 2. ( <i>E</i> )- $\text{C}_2\text{H}_5\text{CH}=\text{CHCHO}$ , $-78^\circ$ , 15 h	 [Prostaglandin analogs]	(-) 1486
	$\text{C}_2\text{H}_5\text{MgBr}$ (cat. $\text{Li}_2\text{CuCl}_4$ )	1. THF 2. $\text{H}^+$ , $\text{H}_2\text{O}$	 [Prostaglandin synthon]	(69) 1487
$(\text{CH}_3)_3\text{SnC}\equiv\text{CCH}_2\text{Cl}$	$n\text{-C}_5\text{H}_{11}\text{MgBr}$ (5% CuCN)	THF, $-25$ to $-18^\circ$ , 15 min	$(\text{CH}_3)_3\text{SnC}\equiv\text{C}=\text{CH}_2$ $n\text{-C}_5\text{H}_{11}\text{C}\equiv\text{C}=\text{CH}_2$ (74) [Pumaglandin 4]	1488
$\text{BrCH}_2\text{C}\equiv\text{C}(\text{CH}_2)_7\text{CO}_2\text{H}$	$\text{BrMgOCH}_2\text{C}\equiv\text{C}(\text{CH}_2)_7\text{CO}_2\text{MgBr}$ $\text{C}_2\text{H}_5$ (5% CuCl)	THF, $55^\circ$ , 12 h	 [Rice blast defensive agent]	(55) 1489
	$\text{CH}_2=\text{CHCH}_2\text{MgCl}$ (6 eq) (10% CuI)	THF, $0^\circ$ , 20 h	 [Thromboxane B <sub>2</sub> synthon]	(88) 1490
b. Lithiocuprates, Substitutions				
	 $(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	THF, $-78^\circ$	 [12-Alkyl-PGA <sub>2</sub> ]	(90-95) 1491

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$ (4 eq)	Ether, 0°	 [Allene carbacyclin] (97)	1492
	$n\text{-C}_4\text{H}_9\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	Ether, -78°, 6 min	 [Allenic prostanoids] (56)	1493
	$(n\text{-C}_{11}\text{H}_{23}\text{CH=CH-OTBDMS})_2\text{CuLi}$	Ether, -78°	 [Deoxadepro-PGD <sub>2</sub> ] (65)	1494
	$(n\text{-C}_{11}\text{H}_{23}\text{CH=CH})_2\text{CuLi}$	THF, HMPA, -110°, 30 min	 [Eicosenynoic acid] (26)	1495
		THF, HMPA, -20 to 23°, 60 h	 [11(R)-HETE] (89)	1496
	 + $[(\text{C}_6\text{H}_5)_3\text{PN}(\text{CH}_3)\text{-C}_6\text{H}_5]^+\text{I}^-$	—	 [Isocarbacyclin] see also ref. 1498 (—)	1497
	$n\text{-C}_3\text{H}_7\text{CH=CH-Cu}(\text{C}\equiv\text{CC}_4\text{H}_9\text{-}n)\text{Li}$	Ether, DMS, -25°, 16 h	 [Leukotriene B <sub>4</sub> ] (36)	1499
	$\text{TMS}(\text{CH}_2)_7\text{Cu}(\text{CN})\text{Li}$	Ether, -80 to -40°, 2 h	 [PGA, PGB] (60)	1500
	$\text{Li}(n\text{-C}_3\text{H}_7\text{C}\equiv\text{C})\text{Cu-CH=CH-C}_3\text{H}_{11}\text{-}n\text{OTBDMS}$	Ether, -78°	 [PGA <sub>2</sub> ] (43)	1501



TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (5 eq)	Ether, $-40^\circ$ , 2 h	 [(+)-15-(S)-PGA <sub>2</sub> ]	(67) 1502
	$\text{Li}(n\text{-C}_3\text{H}_7\text{C}\equiv\text{C})\text{Cu}$ 	$-30^\circ$ , 16 h	 [PGE <sub>2</sub> , PGF <sub>2α</sub> ]	(65-70) 1503
	$(\text{CH}_3)_3\text{SiO}(\text{CH}_2)_7\text{Cu}(\text{CN})\text{Li}$	1. Ether, $-78$ to $-35^\circ$ , 7 h; $-10^\circ$ , 12 h 2. KF, C <sub>2</sub> H <sub>5</sub> OH, pH 7	 [PGE <sub>1</sub> , PGF <sub>1α</sub> ]	(80) 1504
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (10 eq)	Ether, $-40^\circ$ , 2 h	 [PGF <sub>2α</sub> ]	(—) 1505
	$(n\text{-C}_3\text{H}_7\text{C}\equiv\text{C})_2\text{CuLi}$ 	Ether, $-78^\circ$	 [PGI <sub>2</sub> ]	(65) 1506
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-50^\circ$ , 30 min	 [Prostaglandin intermediates]	(29) 1507
	 $\text{Cu}(\text{CN})\text{Li}$	THF, $-78$ to $-45^\circ$ , 15 h	 [Pyridino prostanoids]	(44) 1508
	$(\text{C}_6\text{H}_5)_2\text{CuLi}$	Ether	 [Secoprostaglandin analog]	(80) 1509

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)


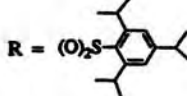
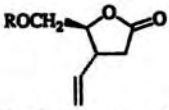

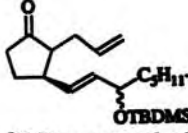

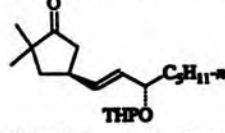
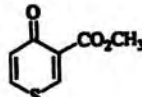
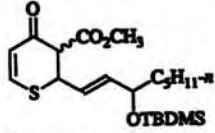
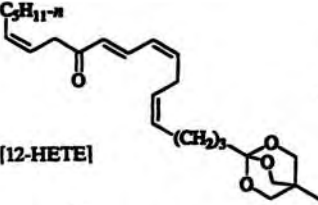
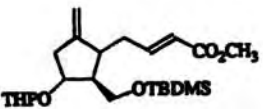
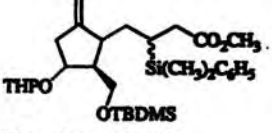

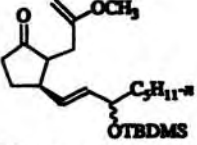
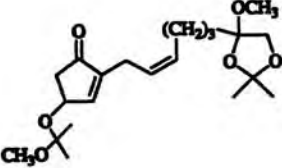
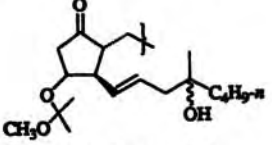
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
c. Lithiocuprates, Conjugate Additions				
 R = 	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, $-78^\circ$ , 1 h	 [6a-Carbacyclin analog]	(64) 1510
552 	$n\text{-C}_5\text{H}_{11}\text{CH}(\text{OTBDMS})\text{CH}=\text{CH}\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	1. Ether, HMPA, $-78^\circ$ , 1 h 2. $\text{CH}_2=\text{CHCH}_2\text{Br}$ , $\text{NH}_3$ (1)	 [11-Deoxyprostaglandins]	(24) 1511
	$(n\text{-C}_5\text{H}_{11}\text{CH}(\text{THPO})\text{CH}=\text{CH})_2\text{CuLi}$	Ether, $\text{P}(\text{C}_4\text{H}_9\text{-}n)_3$ , $-78$ to $-15^\circ$	 [Dimethylprostaglandins]	(84) 1512
	$(n\text{-C}_5\text{H}_{11}\text{CH}(\text{OTBDMS})\text{CH}=\text{CH})_2\text{CuLi}$	—	 [Dithiathromboxane A <sub>2</sub> ]	(82) 1513
$n\text{-C}_5\text{H}_{11}\text{CH}=\text{CH}\text{C}(=\text{O})\text{C}\equiv\text{CH}$	$(\text{THPO})_2\text{CH}(\text{CH}_2)_2\text{CH}=\text{CH}\text{CuLi}$	Ether, DMS, $-50^\circ$ , 1 min	 [12-HETE]	(68) 536
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $0^\circ$ , 20 min	 [Homoisocarbacyclin]	(99) 1514
553 	$n\text{-C}_5\text{H}_{11}\text{CH}(\text{OTBDMS})\text{CH}=\text{CH}\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	1. Ether, $-78^\circ$ 2. $\text{BrCH}_2\text{C}(\text{OCH}_3)=\text{CH}_2$ , $\text{NH}_3$ (1)	 [Homoprostacyclin analogs]	(16) 1515
	$n\text{-C}_4\text{H}_9\text{CH}(\text{OTMS})\text{CH}=\text{CH}\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	—	 [Ketoprostaglandins, hydroxymethyl]	(—) 1516

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	 P(C <sub>4</sub> H <sub>7-n</sub> ) <sub>3</sub>	1. THF, -40 to -78° 2. BF <sub>3</sub> ·Et <sub>2</sub> O, CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> C≡CCHO, -78°	 [5,6-Didehydro-PGE <sub>2</sub> ] (83)	1555
	 n-C <sub>3</sub> H <sub>11</sub>	Ether, -78 to 20°	 [Levuglandin D <sub>2</sub> ] (70)	1517
	 n-C <sub>3</sub> H <sub>11</sub> (MgBr <sub>2</sub> )	—	 [Levuglandin E <sub>2</sub> ] (—)	415
	 n-C <sub>4</sub> H <sub>9</sub> CH <sub>3</sub> O OTMS	Ether	 [Methoxyprostaglandins] (—)	1518
	 C <sub>4</sub> H <sub>9-n</sub> OTMS	1. THF, -60°, 1 h 2. TBDMSCl	 [Misoprostol analog] (60)	1519
	 C <sub>4</sub> H <sub>9-n</sub> OTMS	1. THF, HMPT, -60°, 45 min 2. Ether, HMPA, TBDMSCl	 [Misoprostol diene] (76)	1520
	 (n-C <sub>3</sub> H <sub>11</sub> ) <sub>2</sub> OTBDMS	—	 [6-Oxoprostaglandin E <sub>1</sub> ] (79)	1521
	 (n-C <sub>3</sub> H <sub>11</sub> ) <sub>2</sub> OTBDMS	—	 [PGD <sub>1</sub> ] (56)	1522
	 Li <sub>2</sub> (NC)Cu TBDMSO	THF, ether, pentane, -78 to 0°, 1 h	 [PGE <sub>1</sub> ] (92)	733

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_2=\text{CH})\text{Cu}(\text{CN})\text{Li}$ [2 eq $\text{P}(\text{OC}_2\text{H}_5)_3$ ]	Ether, THF, $-78^\circ$		(46) 1523
		1. Ether, $-78$ to $-15^\circ$ , 30 min 2. AcOH, ether, THF, $25^\circ$ , 4 h		(78) 1524
	$n\text{-C}_5\text{H}_{11}\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$ $\text{OC}(\text{C}_6\text{H}_5)_3$	Ether, HMPT, $-30^\circ$ , 1 h		(31) 1525
	$n\text{-C}_5\text{H}_{11}\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$ OTBDMS	—		(70) 1526
	$n\text{-C}_5\text{H}_{11}\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$ OTBDMS	1. Ether, $-78^\circ$ 2. $\text{H}^+$ , $\text{H}_2\text{O}$		(10) 1527
	$n\text{-C}_5\text{H}_{11}\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$ OTBDMS	1. THF, HMPA 2.		(41) 1528
	$(n\text{-C}_5\text{H}_{11})_2\text{Cu}(\text{CN})\text{Li}_2$ TBDMSO	1. THF, $\text{BF}_3\cdot\text{Et}_2\text{O}$ , $-78$ to $-50^\circ$ , 45 min 2.		(60) 1529
	$n\text{-C}_4\text{H}_9\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$ OTMS	1. THF 2. AcOH		(60) 1530
	$(n\text{-C}_5\text{H}_{11})_2\text{CuLi}$ TBDMSO	1. Ether, $\text{P}(\text{C}_4\text{H}_9\text{-}n)_3$ , $-78$ to $-20^\circ$ , 1.5 h 2. TMSCl		(73) 1531
2-Cyclohexenone	$(t\text{-C}_4\text{H}_9\text{OCH}_2)_2\text{CuLi}$	1. THF, DMS, $-30^\circ$ , 1 h 2. $t\text{-C}_4\text{H}_9(\text{CH}_3)_2\text{SiO}_3\text{SCF}_3$		(74) 1532

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(n\text{-C}_5\text{H}_{11}\text{CH}_2\text{CH}=\text{CH})_2\text{CuLi}$ BnOCH <sub>2</sub> O [1 eq P(C <sub>4</sub> H <sub>7</sub> -n) <sub>3</sub> ]	1. Ether, -78 to -20°, 1 h 2. HCHO, ether	 [PGF <sub>2a</sub> ]	1533
	$(\text{EEO}(\text{CH}_2)_4\text{CH}=\text{CH})_2\text{CuLi}$ [1 eq P(C <sub>4</sub> H <sub>7</sub> -n) <sub>3</sub> ]	Ether, -45 to -10°, 1.5 h	 [PGF <sub>2a</sub> ]	(-) 1534
	$(n\text{-C}_5\text{H}_{11}\text{CH}_2\text{CH}=\text{CH})_2\text{CuLi}$ [2 eq P(OCH <sub>3</sub> ) <sub>3</sub> ]	1. Ether, -78°, 30 min 2. CH <sub>3</sub> SC(SOCH <sub>3</sub> )=CH <sub>2</sub> , -78 to 0° 3. AcOH (30%)	 [PGF <sub>2a</sub> ]	(53) 1537
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	—	 [PGI <sub>2</sub> analog]	(66) 1538
	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CuLi	Ether, -10°, 30 min	 [11-PhenyldeoxyPGE <sub>1</sub> ]	(75) 1539
	$(\text{TBDMSO}-\text{C}_6\text{H}_4)_2\text{CuLi}$ [1 eq P(C <sub>4</sub> H <sub>7</sub> -n) <sub>3</sub> ]	Ether, -78°, 45 min	 [Phenylene prostaglandin]	(76) 1535
	$(\text{THPO}(\text{CH}_2)_3-\text{C}_6\text{H}_4-\text{OCH}_3)_2\text{CuLi}$ [1 eq P(C <sub>4</sub> H <sub>7</sub> -n) <sub>3</sub> ]	Ether, -78°	 [Benzopyran prostacyclin]	(77) 1536
	$n\text{-C}_5\text{H}_{11}\text{CH}_2\text{CH}=\text{CH}-\text{C}_6\text{H}_5\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-n})\text{Li}$	Ether, -40°, 2 h	 [14-Phenyl PGE]	(-) 1540
	$n\text{-C}_5\text{H}_{11}\text{CH}_2\text{CH}=\text{CH}-\text{OTBDMSCu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-n})\text{Li}$	Ether, HMPT, -78°, 4 h	 [Pinane thromboxane A <sub>2</sub> ]	(80) 1541
	$n\text{-C}_5\text{H}_{11}\text{CH}_2\text{CH}=\text{CH}-\text{OTBDMSCu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-n})\text{Li}$	1. Ether, -78° 2. ClCH <sub>2</sub> C(OCH <sub>3</sub> )=CH <sub>2</sub> , NH <sub>3</sub> (1)	 [Prostaglandin analogs]	(16) 1542

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
		THF, P(C4H9-n)3, -78 to -35°, 2 h	 R' = CH3 (60), R' = CF3 (45) [Prostaglandin analogs]	1543, 1544
		1. Ether, P(C4H9-n)3, -78 to -40°, 1 h 2. ClCO2CH3, THF, HMPA	 [Prostaglandin analogs]	(29) 1545
		1. Ether, P(OCH3)3, -78 to -20°, 2 h 2. H+, H2O, THF	 [Prostaglandin analogs]	(50) 1546
		Ether, P(OCH3)3	 [Prostaglandin analogs]	(44) 1547
		—	 [Thiaprostaglandin I1]	(50) 1548
		Ether, HMPA, -10°, 1.5 h	 [Thiaprostaglandins]	(40) 1549
		Ether, THF, HMPT, -78 to -20°, 4 h	 [Prostanoids, chiral]	(51) 1550
d. Reactions of RCu, RCu-Ligand				
		THF, DMS, -55°, 30 min	 [d-(+)-Carbacyclin]	(74) 1551
		THF, DMS, 50°, 8 h	 [11,12-Dehydroarachidonic acid] [5,6-Dehydroarachidonic acid] see ref. 1552	(65) 1552

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$n\text{-C}_3\text{H}_{11}\text{C}\equiv\text{CCH}_2\text{C}\equiv\text{CCu}$	THF, HMPA, 0°		(60-70) 1553
	$n\text{-C}_3\text{H}_{11}\text{CH}(\text{THPO})\text{CH}=\text{CHCu}$ [2.6 eq P(C <sub>4</sub> H <sub>7-n</sub> ) <sub>3</sub> ]	1. Ether, -78°, 50 min 2. OHC(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> CH <sub>3</sub>		(60) 1554
	$n\text{-C}_3\text{H}_{11}\text{CH}(\text{THPO})\text{CH}=\text{CHCu}$ [2.6 eq P(C <sub>4</sub> H <sub>7-n</sub> ) <sub>3</sub> ]	1. Ether, -78°, 50 min 2. CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> C≡CCHO		(65) 1556
	$n\text{-C}_3\text{H}_{11}\text{CH}(\text{TBDMSO})\text{CH}=\text{CHCu}$ [3 eq P(C <sub>4</sub> H <sub>7-n</sub> ) <sub>3</sub> ]	1. Ether, -78 to -40°, 1 h 2. CH <sub>2</sub> =C(NO <sub>2</sub> )(CH <sub>2</sub> ) <sub>4</sub> CO <sub>2</sub> CH <sub>3</sub>		(42) 1557
	$n\text{-C}_3\text{H}_{11}\text{CH}(\text{TBDMSO})\text{CH}=\text{CHCu}$ [2.6 eq P(C <sub>4</sub> H <sub>7-n</sub> ) <sub>3</sub> ]	1. Ether, THF, -78°, 1 h 2. HMPA, (C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> SnCl 3. ICH <sub>2</sub> CH=CH(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> CH <sub>3</sub>		(78) 561
	$n\text{-C}_3\text{H}_{11}\text{CH}(\text{OTBDMS})\text{CH}=\text{CHCu}$ [1 eq P(C <sub>4</sub> H <sub>7-n</sub> ) <sub>3</sub> ]	1. THF, -78° 2. HMPA, ICH <sub>2</sub> CH=CH(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> CH <sub>3</sub>		(46) 1558
	$n\text{-C}_3\text{H}_{11}\text{CH}(\text{TBDMSO})\text{CH}=\text{CHCu}$	Ether, P(C <sub>4</sub> H <sub>7-n</sub> ) <sub>3</sub> , -78 to -20°, 40 min		(48) 1559
	$n\text{-C}_3\text{H}_{11}\text{CH}(\text{TBDMSO})\text{CH}=\text{CHCu}$	Ether, DMS, -78°		(89) 1560
c. Miscellaneous Couplings				
	$n\text{-C}_3\text{H}_{11}\text{CH}(\text{OTBDMS})\text{CH}=\text{CHCu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-n})\text{Li}$	Ether, -60°, 2 h		(60) 1561
	$n\text{-C}_3\text{H}_{11}\text{CH}(\text{OTBDMS})\text{CH}=\text{CHCu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-n})\text{Li}$	Ether, CH <sub>2</sub> Cl <sub>2</sub> , -60°, 2 h		(61) 1562

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

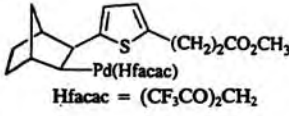
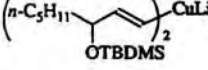
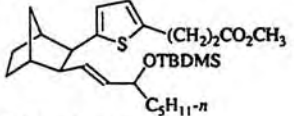
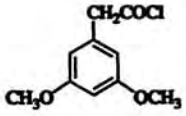
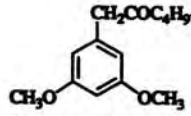
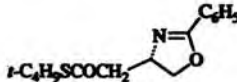
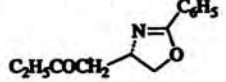
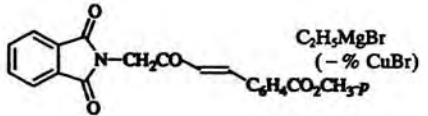


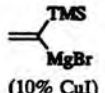
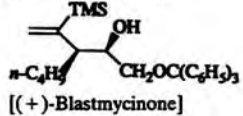
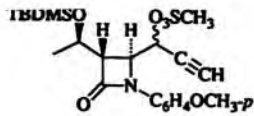
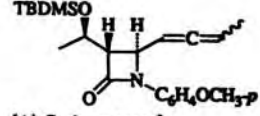
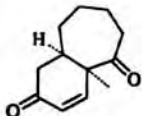
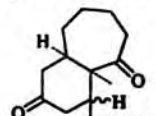
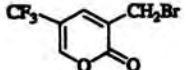
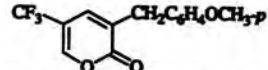
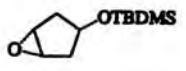
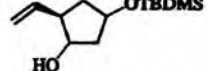
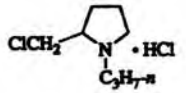
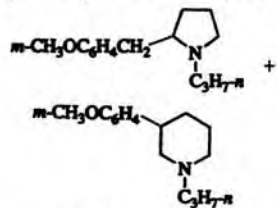
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
 Hfacac = (CF <sub>3</sub> CO) <sub>2</sub> CH <sub>2</sub>		THF, P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> , -78 to 25°	 [Thienylprostaglandins]	(30) 1563
<i>F. Miscellaneous</i>				
a. Grignard Couplings				
	<i>s</i> -C <sub>4</sub> H <sub>9</sub> MgBr (1 eq CuBr)	Ether, -50 to 25°	 [Acetogenin]	(70) 1564
	C <sub>2</sub> H <sub>5</sub> MgBr (1 eq CuBr·DMS)	THF, -23°, 4 h	 [Amphotericin B]	(90) 1565
	C <sub>2</sub> H <sub>5</sub> MgBr (-% CuBr)	THF, -15°	 [Antifolate agents]	(65) 1566
	 (10% CuI)	THF, DMS, 0°, 24 h	 [(+)-Blastmycinone]	(—) 1567
	CH <sub>3</sub> MgBr (CuBr·LiBr)	—	 [Δ <sup>1</sup> -Carbapenems]	(77) 1568
	BnO(CH <sub>2</sub> ) <sub>4</sub> MgBr [8% Cu(OAc) <sub>2</sub> ]	THF, 20°, 2.5 h	 [Chlorothricolide]	(88) 1569
	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> MgBr (1 eq CuBr·DMS)	THF, 50°, 4 h	 [α-Chymotripsin inhibitors]	(66) 1571
	CH <sub>2</sub> =CHMgBr (cat. CuI)	THF, -30°, 2 h, 0° 2 h	 [2'-Deoxyuridines, carbocyclic]	(79) 1572
	<i>m</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> MgBr (2 eq) (10% CuI)	THF, -10 to 20°, 3 h	 [Dopamine autoreceptor agonist]	(82) 1573



TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

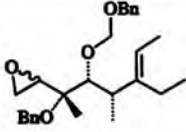
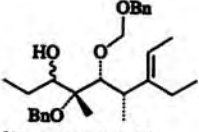
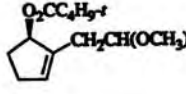
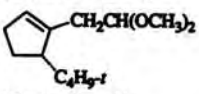
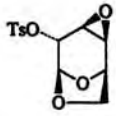
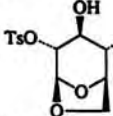
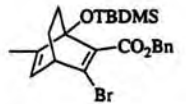

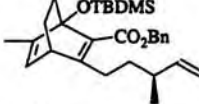

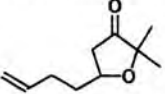
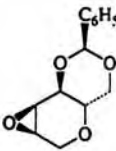
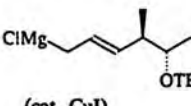
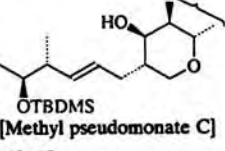
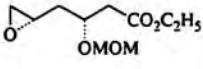
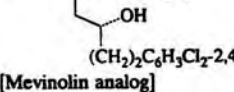
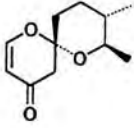
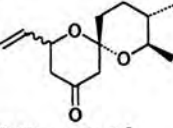
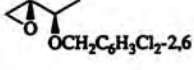
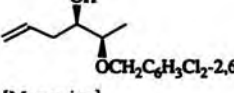

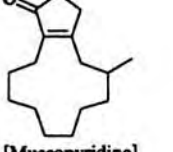
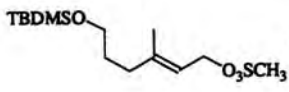
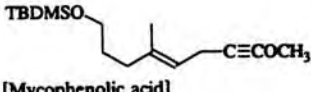
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	CH <sub>3</sub> MgBr (6% CuI)	THF, 0°, 3 h	 [Erythronolide A]	(60) 1574
	<i>t</i> -C <sub>4</sub> H <sub>9</sub> MgBr (3% CuCN)	Ether, -20°, 2 h	 [Ginkgolide B]	(87) 1575
	CH <sub>3</sub> MgCl (0.5 eq CuBr·DMS)	THF, -10°, 4 d	 [Indanamycin, Ionophore X-14547 A]	(86) 1576, 1577
	 [cat. Cu(OAc) <sub>2</sub> ]	Ether, 0°	 [ <i>ent</i> -Lasalocid A]	(90) 1578
C <sub>2</sub> H <sub>5</sub> C≡CCH <sub>2</sub> C≡CCH <sub>2</sub> Br	BrMgC≡C(CH <sub>2</sub> ) <sub>2</sub> OTHP (20% CuCl)	THF, reflux 4 h	C <sub>2</sub> H <sub>5</sub> (C≡CCH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub> OTHP [Laurencenyne]	(67) 1579
	CH <sub>2</sub> =CH(CH <sub>2</sub> ) <sub>2</sub> MgBr (CuBr·DMS)	THF, -78°	 [(±)-Methyl nonactate]	(97) 1580
	ClMg-  (cat. CuI)	THF, -30°, 10 min	 [Methyl pseudomonate C]	(43) 565
	(2,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> CuMgBr	Ether, DMS, -78°, 15 min	 [Mevinolin analog]	(100) 1581
	CH <sub>2</sub> =CHMgBr [CuI·P(C <sub>4</sub> H <sub>7</sub> - <i>n</i> ) <sub>3</sub> ] <sub>4</sub>	Ether, THF, -45 to -55°, 15 min	 [Milbemycin β <sub>3</sub> ]	(60) 1582
	CH <sub>2</sub> =CHMgBr (10% CuI)	THF, -30°	 [Muscarine]	(85) 1583, 1584
	CH <sub>3</sub> MgI (- % CuCl)	Ether, THF, 0°	 [Muscopyridine]	(74) 1585
	CH <sub>3</sub> OC≡CMgBr (cat. Li <sub>2</sub> CuCl <sub>4</sub> )	THF, -78 to 25°, 5.5 h	 [Mycophenolic acid]	(85) 1586

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
		THF, 25°, 2.5 d	 [Palytoxin] (90–95)	1587
$\text{CH}_3\text{C}\equiv\text{CH}$	$\text{CH}_2=\text{CH}(\text{CH}_2)_2\text{MgBr}$ (cat. CuX)	1. — 2.	 [Palytoxin] (75)	1588
	$n\text{-C}_{15}\text{H}_{31}\text{MgBr}$ (10% CuI)	THF, -40 to 20°, 14 h	 [Poison ivy allergen analog] (—)	1589
	$\text{CH}_2=\text{CHMgBr}$ (3 eq) (cat. CuI)	1. THF, HMPA (3 eq), TMSCl, -78°, 10 h 2. DMAP, -78 to -45°	 [Secoxyloganin aglucone] (75–100)	1590
	$\text{BrMg}(\text{CH}_2)_3\text{CH}(\text{OC}_2\text{H}_5)_2$ (cat. $\text{Li}_2\text{CuCl}_4$ )	THF, -15°, 2 h	 [(±)-Solanapyrone A] (62)	1591
	$\text{CH}_2=\text{C}(\text{CH}_3)(\text{CH}_2)_2\text{MgI}$ (cat. CuI)	—	 [(-)-Sydowic acid] (52)	1592
	$n\text{-C}_8\text{H}_{17}\text{MgBr}$ (cat. $\text{Li}_2\text{CuCl}_4$ )	THF	 [(+)-Tetrahydrocerulenin] (—)	1593
	$(\text{C}_6\text{H}_5)_2\text{CuMgX}$ (2 eq)	Ether, THF, -15 to 0°, 45 min	 [Thienamycin analogs] (66)	1594
	$n\text{-C}_6\text{H}_{13}\text{MgBr}$ (0.2% $\text{Li}_2\text{CuCl}_4$ )	THF, 0–20°, 4 h	 [Tuberculostearic acid] (86)	1595
	$\text{CH}_3\text{MgBr}$ (cat. $\text{Li}_2\text{CuCl}_4$ )	THF, 50°, 4 h	 [Tylonolide] (99)	1596
	$n\text{-C}_7\text{H}_7\text{MgBr}$ (- % CuI)	THF	 [Zincophorin] (—)	1597

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
b. Lithiocuprates, Substitutions				
	$(p\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}_2\text{OCH}_2)_2\text{CuLi}$	THF, 0°, 3 h		(60) 1598
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -78 to -40°		(100) 1599
	$\text{Li}_2(\text{CN})\text{Cu}$	THF, -35 to -15°, 50 h		(75) 1600
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -5°, 4 h		(56) 1601
Ar = <i>o</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>				
	$\text{CH}_3\text{Li}$ (30 eq), $\text{CuCN}$ (20 eq)	THF, -4°, 38 h		(50) 1602
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -78 to -47°		(85) 1603
	$(\text{CH}_3)_2\text{CuLi}$	Ether, -40 to 20°		(64) 1604
	$(n\text{-C}_5\text{H}_{11})_2\text{CuLi}$	THF, 12 h		(100) 1605
[Cannabidiol pyrolysis component]				
	$(\text{CH}_2=\text{CHCH}_2)_2\text{CuLi}$ (3 eq)	THF, -70 to 0°, 2.5 h		(32) 1606
[Carbapenem]				
	$(\text{C}_2\text{H}_5)_2\text{CuLi}$ (3 eq)	Ether, -78°, 1 h		(80) 1607
[Carbapenem (+)-PS-5]				

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

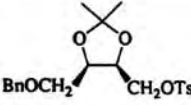
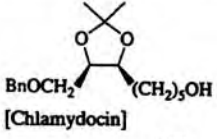
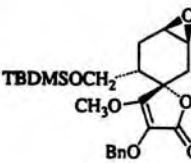
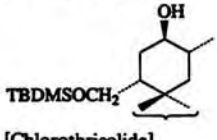
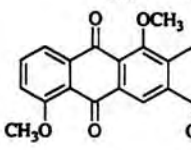

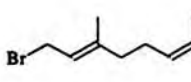
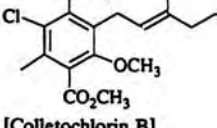
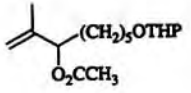
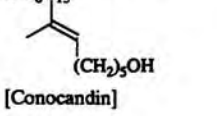
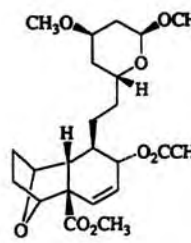
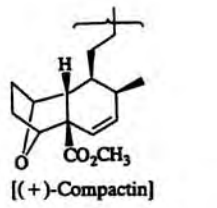
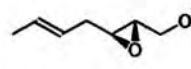
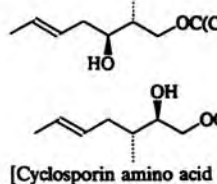
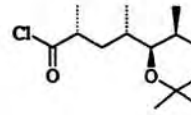
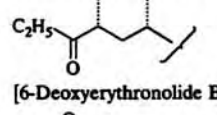
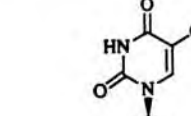
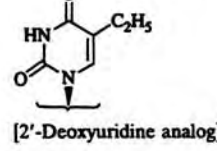
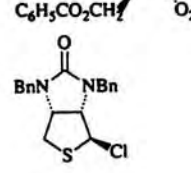
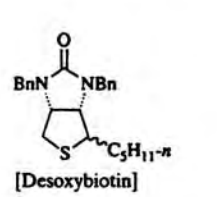
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$[\text{TMSO}(\text{CH}_2)_4]_2\text{CuLi}$	Ether, $-70$ to $20^\circ$ , 12 h	 [Chlamydocin]	(—) 1608
	$(\text{CH}_3)_2\text{CuLi}$ (10 eq)	Ether, hexane, $0-20^\circ$ , 5 h	 [Chlorothricolide]	(62) 1609
	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $0^\circ$	 [ $\gamma$ -Citromycinone]	(84) 1610
	$\text{Cu}[\text{C}\equiv\text{C}(\text{CH}_2)_2\text{OCH}_3]\text{Li}$	THF, HMPA, $-78^\circ$ , 7 h	 [Colletochlorin B]	(70) 1611
	$(n\text{-C}_6\text{H}_{11})_2\text{CuLi}$	1. Ether, $-25^\circ$ 2. TsOH, $\text{CH}_3\text{OH}$	 [Conocandin]	(84) 1612
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-10^\circ$	 [(+)-Compactin]	(86) 1613
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, $\text{BF}_3\cdot\text{Et}_2\text{O}$ (2 eq), $-75^\circ$ , 30 min	 [Cyclosporin amino acid "MeBMT"]	(14) 1614 (80)
	$(\text{C}_2\text{H}_5)_2\text{CuLi}$	Ether, $-78^\circ$ , 15 min	 [6-Deoxyerythronolide B]	(84) 1615
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, $-15$ to $3^\circ$ , 14 h	 [2'-Deoxyuridine analog]	(44) 1616
	$n\text{-C}_5\text{H}_{11}\text{Cu}(\text{CH}_3)\text{Li}$	Ether, $-60$ to $-55^\circ$ , 12 h	 [Desoxybiotin]	(42) 1617

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	Ether, THF, $-78$ to $0^\circ$ , 3 h	 [7,9-Dideoxydaunomycinone]	(80) 1618
	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$ (1 eq $\text{BF}_3 \cdot \text{Et}_2\text{O}$ )	1. THF, $-78^\circ$ 2. $(n\text{-C}_4\text{H}_9)_4\text{NF}$ , THF	 [2,6-Dideoxyhexoses]	(75) 1619
	$[\text{C}_6\text{H}_5(\text{CH}_3)_2\text{Si}]_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-50^\circ$ , 2 h	 [Dihydronepetalactone]	(74) 1620
	$(\text{TBDMSO}-\text{C}_6\text{H}_4)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78$ to $0^\circ$ , 5 h	 [Echinocandin D]	(65) 1621
	$(\text{CH}_3)_2\text{CuLi}$	THF, $0^\circ$	 [Erythronolide B]	(41) 1622
	$(\text{CH}_3)_2\text{CuLi}$ (excess)	Ether, $-20^\circ$ , 20 h	 [Erythronolide B]	(—) 1623
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (3.5 eq)	Ether, $\text{C}_6\text{H}_6$ , $-78$ to $-5^\circ$ , 3 h	 [(+)-L-Factor]	(40) 1624
	$(\text{CH}_3)_2\text{CuLi}$	Ether, DME, $0^\circ$ , 12 h	 [5-Fluorouracil prodrug]	(85) 1625
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0^\circ$ , 2.5 h	 [GABA-T inhibitor]	(75) 1626
	$(\text{TBDMSO}-\text{C}_6\text{H}_4)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78$ to $0^\circ$ , 15 h	 [(+)-Galantic acid]	(51) 1627

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.	
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$ (1.2 eq)	THF, $-70^\circ$	 [(-)-Gloeosporone] (40)	1628	
	$(n\text{-C}_4\text{H}_9)_2\text{Cu(CN)Li}_2$	THF, $-20^\circ$	 [(+)-Gloeosporone] (—)	1629	
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-20^\circ$ , 75 min	 [Iridomyrmecin] (84)	1630	
	$(\text{C}_6\text{H}_5)_2\text{CO}$	$(\text{BF}_3 \cdot \text{Et}_2\text{O})_2\text{CuLi}$	Ether, $-65^\circ$	 [Irumamycin degradation product] (72)	1631
		THF, $\text{P}(\text{C}_4\text{H}_9\text{-}n)_3$ , $-78$ to $20^\circ$ , 12 h	 [Islandicin] (82)	1632	
	$n\text{-C}_7\text{H}_{15}\text{Cu(CN)Li}$	Ether, $-23$ to $0^\circ$	 [(-)-Isoavenaciolide] (85)	1633	
	$(\text{CH}_3)_2\text{CuLi}$	Ether, pentane, DMS, $0^\circ$ , 3 h	 [Lasalocid A] (90)	1634	
	$\text{Li}_2(\text{CN})\text{Cu}$	Ether, $-40$ to $-20^\circ$ , 28 h	 [Macbecins] (35)	1635	
	 $\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	THF, HMPA, $-78^\circ$ , 4.5 h	 [(-)-Maysine] (62)	1636	
	$(\text{CH}_3)_2\text{CuLi}$ (2 eq)	Ether, $0^\circ$ , 5 h	 [Maytansine] (65)	1637	
	 $\text{Cu}(\text{C}\equiv\text{CC}_3\text{H}_7\text{-}n)\text{Li}$	THF, $-30$ to $20^\circ$ , 6 h	 [(+)-Milbemycin $\beta_3$ ] (—)	1638	

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

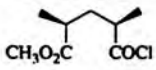
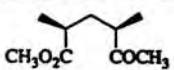
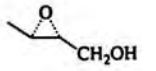
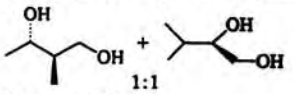
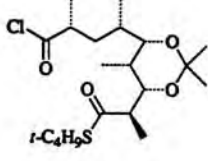
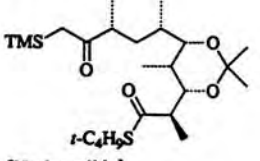
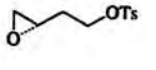
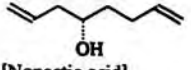
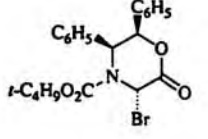
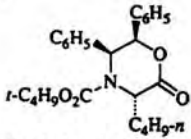
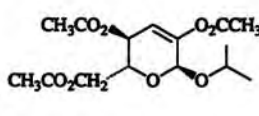
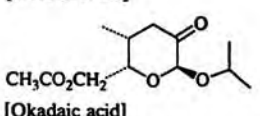
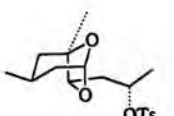
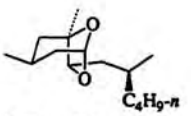

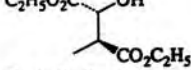
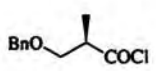
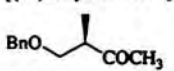
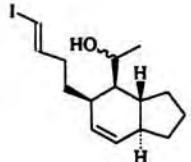
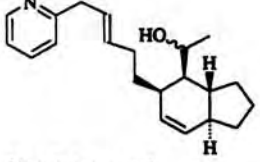
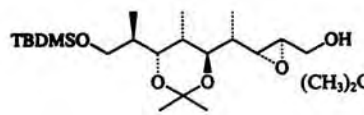
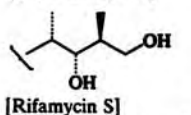
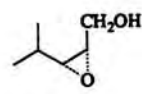
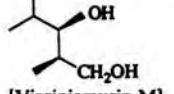
Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	THF, $-78^\circ$ , 30 min	 (92) 1639 [Monensin A biosynthetic intermediate]	
	$(\text{CH}_3)_2\text{Cu}(\text{CN})\text{Li}_2$	—	 (92) 1640 [Monic acid C]	
	$(\text{TMSCH}_2)_2\text{CuLi}$	Ether, $-78^\circ$ , 25 min	 (100) 1641 [Narbonolide]	
	$(\text{CH}_2=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$ (3 eq)	THF, $-40$ to $0^\circ$ , 6 h	 (92) 1642 [Nonactic acid]	
	$(n\text{-C}_4\text{H}_9)_2\text{Cu}(\text{CN})\text{Li}_2$	Ether, THF, $-78^\circ$	 (48) 1643 [L-Norleucine]	
	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	THF, $-20^\circ$	 (80) 1644 [Okadaic acid]	
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	Ether, $-20^\circ$	 (47) 1588 [Palytoxin]	
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-78^\circ$	 (—) 1645 [(+)-Phyllanthocin]	
	$(\text{CH}_3)_2\text{CuLi}$ (3 eq)	Ether, $-78^\circ$	 (75-80) 1646 [(+)-Phyllanthocin]	
	$(2\text{-C}_5\text{H}_4\text{NCH}_2)_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $-78^\circ$	 (—) 1647 [(±)-Pulo'upone]	
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-40$ to $-23^\circ$ , 5.5 h —	 (96) 1648 [Rifamycin S] [Roflamycin] see ref. 1650	
	$(\text{CH}_3)_2\text{CuLi}$ (5 eq)	Ether, $-20$ to $0^\circ$	 (87) 1649 [Virginiamycin M]	

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-20^\circ$	 1:1 [Protomycinolide IV]	(88) 1651
	$(n\text{-C}_{10}\text{H}_{21})_2\text{Cu}(\text{CN})\text{Li}_2$	THF, $0^\circ$ , 1 h	 [Protomycinolide IV] +	(46) 1652
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	—	 [Spiculisporic acid]	(52) 1653
	$(n\text{-C}_4\text{H}_9)_2\text{CuLi}$	—	 [(+)-Statine]	(83) 1653
	$(\text{CH}_3)_2\text{CuLi}$ (10 eq)	1. Ether, DMS, $0^\circ$ , 4h 2. TsOH, $\text{CHCl}_3$ , $20^\circ$	 [(+)-Streptolic acid]	(68) 1654
	$\text{Cu}(\text{C}\equiv\text{CC}_2\text{H}_5)_n\text{Li}$	Ether, $-78^\circ$ , 18 h	 [Swazincic acid]	(85) 1655
	$(\text{CH}_3)_2\text{CuLi}$	Ether	 [(+)-Talaromycin] [Talaromycin A] see ref. 1657	(91) 1656
	$(\text{C}_2\text{H}_5)_2\text{CuLi}$	1. THF, 0 to $20^\circ$ 2. aq HCl	 [Talaromycin B]	(—) 1658
	$(n\text{-C}_6\text{H}_{13})_2(\text{CH}_2)_6\text{CuLi}$	Ether, HMPT	 [Thermozymocidin]	(26) 1659
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 11 h	 [Tirandamycic acid]	(—) 1660
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-20^\circ$	 [Tirandamycin A]	(96) 1661



TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $0^\circ$ , 1 h	 [Tylosin]	(40) 1662
c. Lithiocuprates, Conjugate Additions				
$\text{C}_2\text{H}_5\text{C}\equiv\text{CCO}_2\text{CH}_3$	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	THF, DMS, $-78^\circ$ , 3 h	 [Aklavinone]	(—) 1663
		THF, $\text{BF}_3\cdot\text{Et}_2\text{O}$ , $\text{P}(\text{C}_4\text{H}_9\text{-}n)_3$ , $-78^\circ$ , 2 h	 [Analgesic analog]	(58) 1664
	$n\text{-C}_3\text{H}_7\text{C}\equiv\text{C}-\text{CuLi}$ $[\text{P}(\text{C}_6\text{H}_5)_3]$	THF, $-78$ to $-40^\circ$ , 20 min	 [Betaenone B]	(—) 1665
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-40^\circ$ , 30 min 2. $\text{TMSCl}$ , $\text{HMPA}$ , $(\text{C}_2\text{H}_5)_3\text{N}$ , $-40$ to $25^\circ$	 [Boromycin degradation product]	(100) 1666
	$\text{CH}_3\text{Cu}(\text{CN})\text{Li}$	THF, $\text{TBDMSCl}$ , $-78$ to $23^\circ$	 [(-)-Botryodiplodin]	(87) 1667
	$\text{EEO}(\text{CH}_2)_3(\text{C}_6\text{H}_5\text{S})\text{CuLi}$	1. THF, $-20^\circ$ , 30 min 2. $\text{CH}_3\text{I}$ , $\text{DME}$ , $-20^\circ$ , 15 min	 [(+)-Compactin]	(80) 1668
	$\text{EEO}(\text{CH}_2)_3\text{Cu}(\text{CN})\text{Li}_2$	1. THF, $-78^\circ$ 2. $[(\text{CH}_3)_2\text{N}]_2\text{POCl}$ 3. $\text{Li}$ , $\text{NH}_3$ (l), THF, $t\text{-C}_4\text{H}_9\text{OH}$ , $-30$ to $0^\circ$	 [(+)-18-Deoxynargenicin A <sub>1</sub> ]	(29) 1669
	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, $-78^\circ$ 2. $\text{TMSCl}$ , $(\text{C}_2\text{H}_5)_3\text{N}$	 [Erythronolide A]	(88) 1670
	$(\text{CH}_3)_2\text{CuLi}$	Ether, $-5^\circ$	 [Erythronolide A]	(~100) 1671

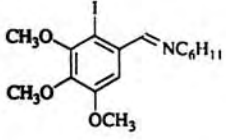
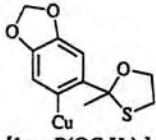
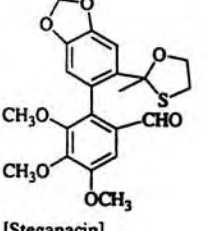
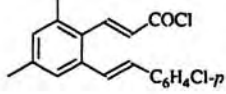
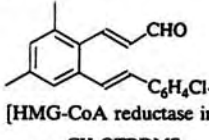
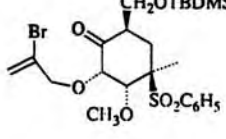
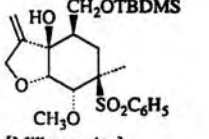
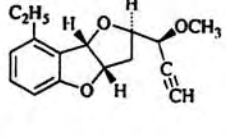
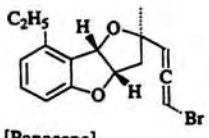
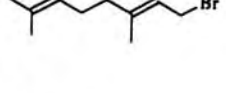
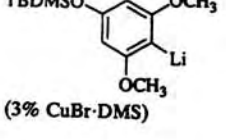
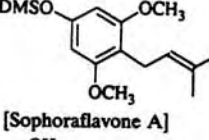
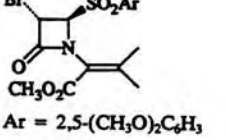
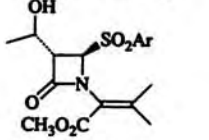
TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (*Continued*)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	1. Ether, 0° 2. F <sup>-</sup> , THF	 [(−)-Gilmicolin] (55)	1672
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	—	 [Lasalocid acid] (—)	1673
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°	 [Methymycin] (73)	1674
$\text{EEO}(\text{CH}_2)_2\text{C}\equiv\text{CCO}_2\text{C}_2\text{H}_5$	$(\text{CH}_3)_2\text{CuLi}$	1. Ether, −78°, 5 min 2. D <sub>2</sub> O	 [(−)-Mevalonic-2-d acid] (96)	1675
	$(\text{CH}_3)_2\text{CuLi}$	Ether, 0°	 [Mevinolin] (91)	1676
$(\text{C}_2\text{H}_5\text{O})_2\text{CH}(\text{CH}_2)_2\text{C}(\text{CH}_3)=\text{C}(\text{CH}_2)_2\text{C}\equiv\text{CCO}_2\text{CH}_3$	$(\text{C}_2\text{H}_5)_2\text{CuLi}$	—	 [Monensin] (60)	1677
	$[\text{CH}_2=\text{C}(\text{CH}_3)\text{CH}_2]_2\text{CuLi}$ (4 eq)	THF, −40°, 4 h	 [O-Mycinosyltylonolide] (84)	1678
	$\text{CH}_3\text{Li}$ (CuI)	Ether, 0°	 [Mycoticin B, Amphotericin B] (87)	1682
	$(\text{CH}_3)_2\text{CuLi}$	Ether	 [Okadaic acid] (98)	1679
	$(\text{CH}_2=\text{CH})_2\text{CuLi}$	Ether, THF, TMSCl, −78°	 [(+)-Olivin] (84–91)	1680

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs.
		THF, DMS, -70°	 [ $\delta$ -Oxoamino acids]	(71) 1681
	(CH <sub>3</sub> ) <sub>2</sub> CuLi (BF <sub>3</sub> ·Et <sub>2</sub> O)	—	 [Palytoxin] [Quercus lactone] see ref. 1683	(92) 1588
	[3,4,5-(CH <sub>3</sub> O) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> ] <sub>2</sub> CuLi	—	 3,4,5-(CH <sub>3</sub> O) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> [Podophyllotoxin]	(80) 1684
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	1. Ether, -20°, 1 h 2. TMSCl 3. Pd(OAc) <sub>2</sub> , CH <sub>3</sub> CN, 20°, 92 h	 [Prelog-Djerassi lactone]	(62) 1685
	(CH <sub>3</sub> ) <sub>2</sub> CuLi	THF, -78°	 [Rifamycin ansa chain]	(—) 1686
HC≡CCO <sub>2</sub> CH <sub>3</sub>		THF, DMS, -78°, 1 h	 [Tirandamycin A]	(—) 1687
	CH <sub>2</sub> =CH(CH <sub>2</sub> ) <sub>3</sub> Li (1.8 eq) (1 eq CuI·DMS)	1. Ether, THF, -78°, 14 h 2. TMSCl, -78°, 2 h 3. 10% HCl	 [Chlorothricin degradation product]	(91) 1688
	CH <sub>3</sub> Cu·P(C <sub>4</sub> H <sub>7</sub> - <i>n</i> ) <sub>3</sub> (10 eq) S(O) <sub>2</sub> N(C <sub>6</sub> H <sub>11</sub> ) <sub>2</sub>	Ether, toluene, BF <sub>3</sub> ·Et <sub>2</sub> O, -78 to -30°	 96.7% de [Norpeckinatone]	(83) 1689
	C <sub>2</sub> H <sub>5</sub> -CH=CH-Cu OBn [2 eq P(C <sub>4</sub> H <sub>7</sub> - <i>n</i> ) <sub>3</sub> ]	1. Ether, -35°, 1.5 h 2. <i>n</i> -C <sub>4</sub> H <sub>9</sub> Li 3. ClP(O)(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	 [Quassinoids]	(87) 1690

TABLE XI. ORGANOCOPPER COMPOUNDS IN SYNTHESIS OF NATURAL PRODUCTS (Continued)

Substrate	Organocopper Reagent	Reaction Conditions	Product(s) and Yield(s) (%) (Target Molecule)	Refs
	 [1 eq P(OC <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ]	1. THF, 25°, 20 h 2. 15% AcOH	 [Steganacin]	(82) 566
	[(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> P] <sub>2</sub> CuBH <sub>4</sub>	Acetone, P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> , 20°, 1 h	 [HMG-CoA reductase inhibitor]	(84) 1691
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi (excess)	Ether, pentane	 [Milbemycins]	(74) 1692
	Br <sub>2</sub> CuLi	THF	 [Panacene]	(—) 1693
	 (3% CuBr·DMS)	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> , -78°, 1 h; -15°, 15 h	 [Sophoraflavone A]	(72) 1694
	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> CuLi (10 eq)	1. THF, -78°, 40 min 2. CH <sub>3</sub> CHO, -78°, 1 h	 [Thienamycin]	(46) 1297

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