Conjugate Addition Reactions of Allylic Copper Species Derived from Grignard Reagents: Synthetic and Spectroscopic Aspects

Bruce H. Lipshutz* and Claus Hackmann

Department of Chemistry, University of California, Santa Barbara, California 93106

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A general study on the 1,4-addition chemistry of allyl, methallyl, crotyl, and prenyl Grignard-derived organocopper reagents has been conducted. While diallylic cuprates formed from such species are not effective Michael donors, the 1:1:1 combination of an allylic Grignard, $CuBr{\cdot}SMe_2$, and Me_3SiCl leads to high yields of 1,4-adducts. The stereo- and regiochemistry associated with the allylic ligand, where appropriate, has also been examined. Low temperature ^{13}C NMR studies provide insight as to the nature of these complexes.

Introduction

Although the chemistry of organocopper reagents spans many types of valuable bond-forming processes,[1] few would argue that their ability to effect 1,4-additions to α,β-unsaturated carbonyl systems is the hallmark of these extensively utilized organometallics. One ligand which is conspicuously lacking in usage relative to the vast array of commonly relied upon reagents is the allylic copper system.[2] This notoriously problematic, ill-behaved,[2a] and until recently,[3b] poorly understood class of cuprates can now be appreciated as being among the most reactive organocopper reagents available.[4] Both experimental and spectroscopic data have been used to advantage in developing a chemoselective version of the potent cuprate forms **1** and **2** (Figure 1).[5] In most situations calling for Michael addition of **1** or **2**, useful levels of chemoselectivity are rare, as significant amounts of competing 1,2-adduct is routinely observed (Scheme 1).[2,6] It has previously been demonstrated that the allylic copper species prepared from an allylic *lithium* reagent and CuI,[7a] together with 1 equiv of Me_3SiCl, provides a highly effective means of delivering these otherwise troublesome ligands in the desired 1,4 sense.[5] In that account, we suggested that the more readily available Grignard reagents appeared to function akin to their lithium counterparts, however, only a single example for the simplest of cases (*i.e.*, allyl Grignard) was examined. We now describe a far more detailed study on the use of

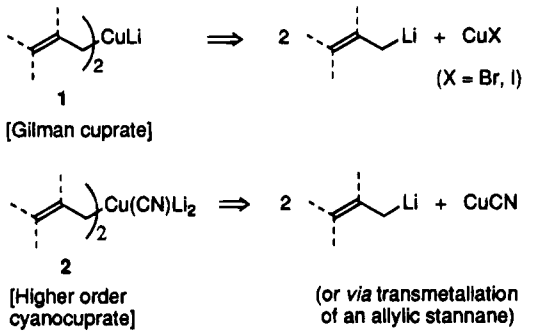
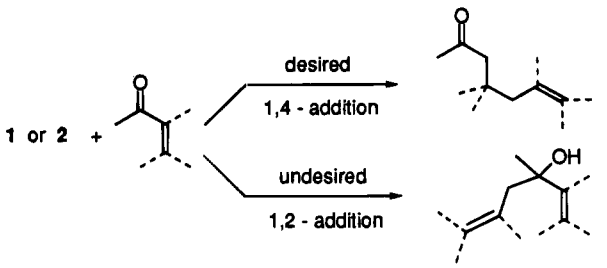


Figure 1.

Scheme 1



Grignard-derived allylic copper reagents which addresses the "scope and limitations" of this evolving methodology.

Results and Discussion

Synthetic Aspects. The combination of an allylmagnesium halide, $CuBr{\cdot}SMe_2$, and Me_3SiCl in THF at −78 °C leads to reagent mixtures which are of variable coloration and solubility at low temperatures (see Experimental Section for details). While they can be used as such without complications, the presence of 1 equiv of LiCl,[7b] together with $CuBr{\cdot}SMe_2$, leads to homogeneous solutions of reagent which do not appear to be altered upon introduction of the silyl chloride at −78 °C. Given the 1:1 correspondence of Grignard and Cu(I) source, tradition has it that a species "$RCu{\cdot}MgX_2$" is formed,[8] rather than the *ate* complex "R(X)CuMgX"; *i.e.*, the halocuprate analog of the generic cuprate "R_2CuM", M = Li or MgX. In light of work on the role of salts in cuprate activation,[9] together with the insightful com-

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(1) (a) Lipshutz, B. H.; Sengupta, S. *Org. React. (N. Y.)* **1992**, *41*, 135. (b) Posner, G. H. *Ibid.* **1975**, *22*, 253. (c) Posner, G. H. *Ibid.* **1972**, *19*, 1. (d) Posner, G. H. An Introduction to Synthesis Using Organocopper Reagents; Wiley: New York, 1980. (e) Normant, J. F. *Synthesis* **1972**, 63.

(2) Review on allylic organometallics: Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.

(3) (a) Hutchinson, D. K.; Fuchs, P. L. *Tetrahedron Lett.* **1986**, *27*, 1429. (b) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Smith. R. A. J. *J. Org. Chem.* **1989**, *54*, 4977.

(4) Lipshutz, B. H.; Crow, R.; Dimock, S. H.; Ellsworth, E. L.; Smith, R. A. J.; Behling, J. R. *J. Am. Chem. Soc.* **1990**, *112*, 4063.

(5) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Smith, R. A. J. *J. Am. Chem. Soc.* **1990**, *112*, 4404.

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(7) (a) For alternative modes of preparation of allylic copper reagents, see Stack, D. E.; Dawson, B. T.; Rieke, R. D. *J. Am. Chem. Soc.* **1992**, *114*, 5110. *Ibid.* **1991**, *113*, 4672. AchyuthaRao, S.; Knochel, P. *Ibid.* **1992**, *114*, 7579. Stack, D. E.; Rieke, R. D. *Tetrahedron Lett.* **1992**, *33*, 6575. Knochel, P.; Singer, R. D. *Chem. Rev.* **1993**, *93*, 2117. (b) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390. AchyuthaRao, S.; Rozema, M. J.; Knocha, P. *Ibid.* **1993**, *58*, 2694.

(8) Alexakis, A.; Commercon, A.; Coulentianos, C.; Normant, J. F. *Pure Appl. Chem.* **1983**, *55*, 1759.

(9) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H. *J. Am. Chem. Soc.* **1990**, *112*, 5869.

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Scheme 2

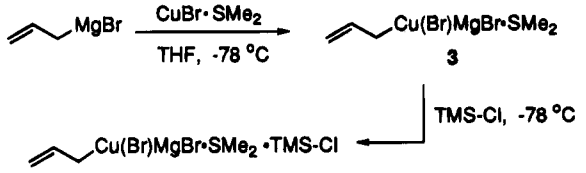
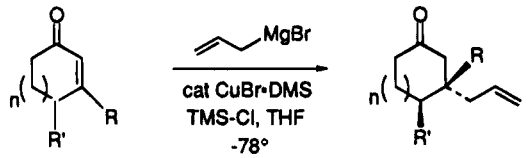


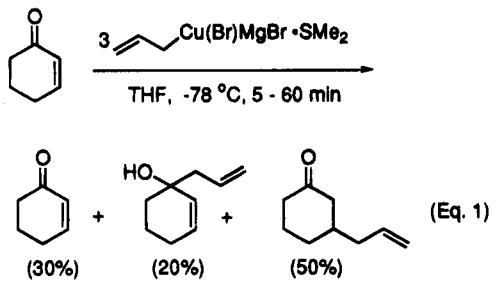
Table 1. Reactions with Allylcopper·$MgBr_2$·SMe_2 + TMS-Cl at −78 °C in THF



Entry	Educt / Adduct	Yield (%)[a]
1	n = 0, R = R' = H	86
2	n = 0, R = CH_3, R' = H	66[b]
3	n = 1, R = R' = H	86
4	n = 1, R = H, R' = *i*-Pr	75[c]

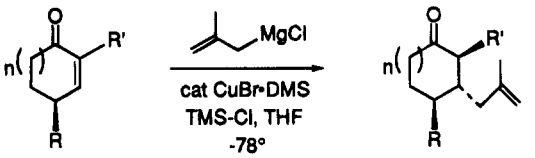
[a] Isolated. [b] The 1,2-adduct (21%) was also isolated. [c] Diastereoselectivity (9.3:1 *trans:cis*) determined by GLC.

ments of House close to three decades ago,[10] it seems quite reasonable to view these species as halocuprates **3** (Scheme 2). Moreover, with very recent information on the role of TMS-Cl in 1,4-addition reactions of lithiocuprates (R_2CuLi·LiI, from 2RLi + CuI),[11] it is also reasonable to include this additive as part of reagent make-up, although the presence of Lewis acidic $MgBr_2$ could be such that TMS-Cl serves to solely trap an equilibrium percentage of a β-carbon-Cu(III) intermediate, as previously suggested.[12] In the absence of this silyl halide, these allylic copper reagents are less reactive and nowhere near as chemoselective toward enones (*cf.* eq 1).



To establish both a link with our prior efforts on this subject[5] and a standardized set of reaction conditions involving allylic Grignard reagents, four different enones were each treated with the reagent prepared from allylMgBr, CuBr·SMe_2, and TMS-Cl (Table 1). Reactions are rapid at −78 °C, being complete in *ca.* 5 min, although longer times were permitted to insure complete consumption of educt. Yields, all of which represent isolated, chromatographically purified materials, are generally quite good. β,β-Disubstituted systems are somewhat less responsive, an oftentimes common feature in most cuprate couplings.[1] Only 1.3 equiv of Grignard are needed relative to substrate, and an equal quantity of copper salt is required to achieve high yields. Catalytic amounts of CuBr·SMe_2 led to product yields corresponding to essentially the amount of catalyst present. Competitive 1,2-addition to any significant degree (*i.e.*, >5%) was observed only with 3-methylcyclopentenone (21%), the 1,4-adduct in this case still being the major product (66%).

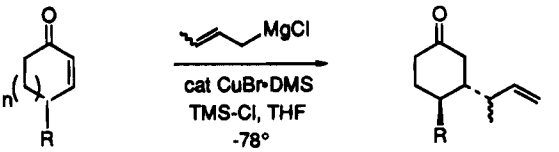
Table 2. Reactions with Methallylcopper·MgBrCl·SMe_2 + TMS-Cl at −78 °C in THF



Entry	Educt / Product	Yield (%)[a]
1	n = 1, R = R' = H	95
2	n = 1, R = *i*-Pr, R' = H	71[b]
3	n = 0, R = Et_3SiO, R' = $(CH_2)_6CO_2Me$ [4 / 5]	70[c]
4	2-hexen-4-one / 2,4-dimethylocten-6-one	86

[a] Isolated. [b] Selectivity 26.5:1 *trans:cis*. [c] Only one diastereomer detected by GLC, TLC, and NMR.

Table 3. Reactions with Crotylcopper·MgBrCl·SMe_2 + TMS-Cl at −78 °C in THF



Entry	Educt / Product	Yield (%)[a]	α : γ[b]
1	n = 0, R = H	82[c]	1 : 25.5
2a	n = 1, R = H	90[d]	11.3 : 1
2b[e]	n = 1, R = H	84	12.1 : 1
3	n = 1, R = *i*-Pr	77[f]	> 40 : 1

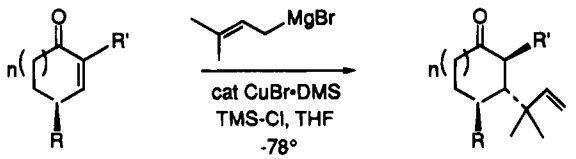
[a] Isolated. [b] Selectivity determined by GLC. [c] Two diastereomers: 3.2:1. [d] *E*:*Z* ratio = 3.0:1. [e] Reaction is carried out with crotylcopper·$MgBr_2$·SMe_2 + TMS-Cl, *E*:*Z* ratio = 3.0:1 by NMR. [f] *E*:*Z* ratio = 3.4:1 by NMR.

Similar tests were run using copper reagents containing the methallyl, crotyl, and prenyl ligands (Tables 2−4, respectively). With the former species, both cyclic enones and an acyclic example (Table 2, entry 4) afforded excellent results. The far more substantial cyclopentenone **4** (entry 3) led to the 1,4-adduct in moderate yield, only one diastereomer being detected by TLC, GC, and high field NMR. Note that the product isolated (*i.e.*, **5**) is fully desilylated material. This reflects the fact that the initial adduct, in general, from these couplings (*e.g.*, of **6**) is a silyl enol ether **7**, which is converted to product ketone upon treatment with commercially available Bu_4NF in THF (Scheme 3).

Both crotyl- and prenyl-type reagents raise issues not present in cuprate couplings of simple allyl or methallyl systems. That is, crotyl delivery can take place at either the α or γ site in **8** (eq 2). Moreover, should α-attack occur, geometrical isomers about the disubstituted alkene may result. In practice, the four examples illustrated in Table 3 reveal the beginnings of trends not only previ-

(10) House, H. O.; Fischer, W. F. *J. Org. Chem.* **1968**, *33*, 949.
(11) Lipshutz, B. H.; Dimock, S. H.; James, B. *J. Am. Chem. Soc.* **1993**, *115*, 9283. See also, Bergdahl, M.; Erilsson, M.; Nilsson, M.; Olsson, T. *J. Org. Chem.* **1993**, *58*, 7238.
(12) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6019.

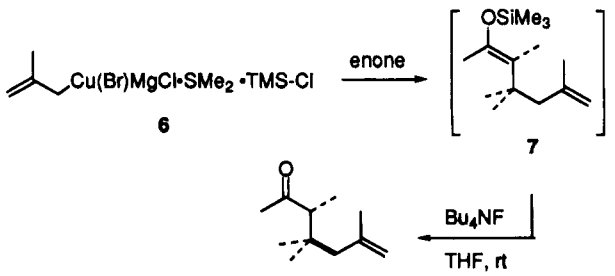
Table 4. Reactions with Prenylcopper·TMSCl·$MgBr_2$·SMe_2 at −78 °C in THF



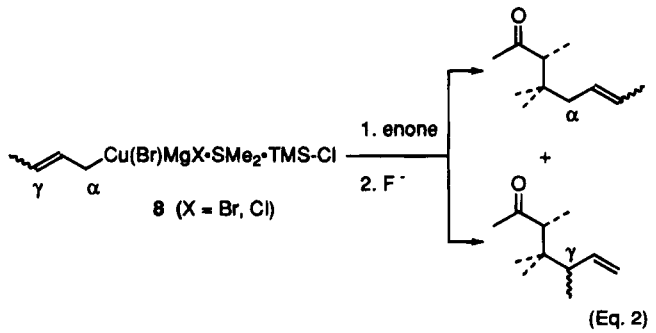
Entry	Educt / Adduct	Yield (%)[a]	α : γ[b]
1	n = 0, R = R' = H	70	1 : 75
2	n = 0, R = H, R' = CH_3	80	1 : 25
3	n = 0, R = Et_3SiO, R' = $(CH_2)_6CO_2Me$	76[c]	7.5 : 1
4	n = 1, R = R' = H	91	7.3 : 1
5	n = 1, R = *i*-Pr, R' = H	87[d]	16.1 : 1
6	n = 1, R = *t*-Bu, R' = H	86	48.0 : 1
7	2-hexen-4-one / 2,5-dimethylnon-2-en-7-one	85	>50 : 1

[a] Isolated. [b] Diastereoselectivity determined by GLC. [c] Only one diastereomer detected by TLC, GLC, and NMR. [d] Selectivity, *trans/cis* 13.1:1.

Scheme 3

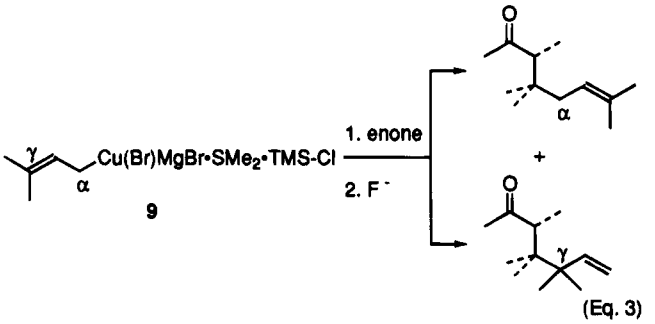


ously unappreciated, but rather unexpected. Thus, while the simple cyclopentenone system (entry 1) reacts to afford an overwhelming preference for γ-attack, the one carbon homolog educt reverses the crotyl ligand regiochemistry to strongly favor α-attack. As the steric congestion in the cyclohexenone increases, so does α-site selectivity. The geometrical preference of the resulting olefin, however, remains at *ca.* 3:1 *E:Z*, precisely the ratio seen previously with allyllithium-derived reagents.[5]



(Eq. 2)

Although the prenyl unit has no geometrical isomerism associated with its additions, it shares in the α vs γ regiochemical questions posed by the crotyl moiety (eq 3). The educt-sensitive reversal in regiochemistry, foreshadowed by the cyclopentenone vs cyclohexenone cases in Table 3, was indeed substantiated by the prenyl cuprate couplings shown in Table 4. Hence, simple cyclopentenones afforded products strongly favoring γ-site attack (entries 1, 2). As the degree of steric congestion increases, however, a shift to α-attack occurs, even in the cyclopentenone system (entry 3). Cyclohexenones appear to favor α-attack in unhindered cases to the extent of *ca.* 7−8:1, although as complexity builds near the β-position, the preference goes up rapidly (compare entries 4−6).



(Eq. 3)

As is generally true in cuprate additions to γ-substituted enones,[1a] all allylic ligands were found to add to a cyclic enone, *e.g.*, cryptone, predominantly in a *trans* rather than *cis* fashion, ratios being on the order of >9:1. The trend is such that again, as the steric demands of the allylic group increase, the ratio of *trans:cis* addition increases.

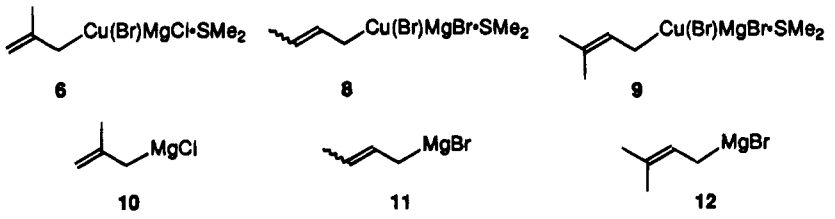
Several other variables were investigated concerning these conjugate additions. While CuBr·SMe_2 was used in all cases discussed thus far, it was found that CuI is an acceptable alternative, as alluded to previously.[5] No other sources of Cu(I) were tested in this study.

The role of the halide ion in allyl-MgX was briefly addressed in a comparison between crotyl magnesium chloride and bromide (Table 3, entries 2a,b, respectively). That the results from each are basically the same comes as no surprise, given the multitude of halide ions present in the medium. Furthermore, it should be recalled that while in this study, allyl and prenyl ligands on copper derive from the precursor *bromides*, both crotyl and methallyl reagents were prepared from the precursor *chlorides*. We conclude, therefore, that although effects of halides have been observed in magnesio cuprate reactions,[13] in these couplings there is little impact due to halide ion(s) in solution.

Spectroscopic Aspects. ^1H and ^{13}C NMR spectra were recorded in THF at −78 °C for copper reagents **6**, **8**, and **9**, in the absense of TMS-Cl in each case. The signals observed are listed in Table 5, as are those for the precursor Grignard reagents. Particularly revealing is the spectrum associated with the prenyl reagent, where only four discrete lines are observable and might lead to the proposal that this species is best represented by the γ-bound cuprate **9′**, as **9** would give rise to a five-line spectrum (eq 4). That the lacking fifth signal in the spectrum lies under solvent peaks could be deduced from the corresponding sample prepared in ether which is quite similar to that seen in THF, but shows this additional resonance at 25.6 ppm. Interestingly, the chemical shifts in the ^{13}C NMR spectrum in THF for the β (δ 133.8) and γ (δ 107.8) carbons in **9** are virtually identical to those noted previously for the prenyllithium-derived analog (δ 133.6 and 107.9).[5]

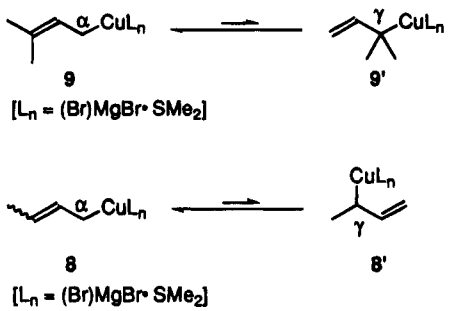
(13) Alexakis, A. *Pure Appl. Chem.* **1992**, *64*, 387. Alexakis, A.; Marek, I.; Mangeney, P.; Normant, J. F. *Tetrahedron Lett.* **1989**, *30*, 2387. Marek, I.; Mangeney P.; Alexakis, A.; Normant, J. F. *Ibid.* **1986**, *27*, 5499.

Table 5. Selected ^1H and ^{13}C NMR Data of Allylic Cuprates in THF (Ether) Obtained at −78 °C in the Absence of TMS-Cl



Reagent	Chemical shifts, δ
6	^{13}C NMR (THF) 171.2, 95.6, 23.4, 21.8
10	^{13}C NMR (THF) 156.8, 57.8, 26.7
8	^{13}C NMR (THF) 139.6, 101.6, 23.7, 12.3 ^1H NMR (THF) 5.70 (q), 4.77 (quin), 1.34 (d), 0.80 (d)
11	^{13}C NMR (THF) 141.5, 97.2, 17.6, 12.5
9	^{13}C NMR (THF) 133.8, 107.8, -, 16.8, 13.7 ^{13}C NMR (Ether) 133.1, 105.9, 25.6, 16.7, 16.4 ^1H NMR (THF) 5.37 (t), 1.43 (s), 1.34 (s), 0.72 (d)
12	^{13}C NMR (THF) 135.7, 103.3, -, 17.0, 16.2 ^{13}C NMR (Ether) 131.8, 108.4, 25.4, 16.7,16.4

Related observations have been made with respect to the crotyl reagent, suggesting that **8′**, a γ-bound species, is *not* in line with experiment which shows the presence of mainly four resonances in the ^1H and ^{13}C NMR spectra. The chemical shifts and couplings in the ^1H NMR spectra are similar to those observed for the α-bonded crotyl Grignard.[14] Thus, as for the prenyl case, an α-bound species **8** is the major cuprate in solution (eq 4). Here



too, the chemical shifts for the β (139.6 ppm) and γ (101.6 ppm) carbons are strikingly similar to those recorded for the crotyllithium derivative (139.2 and 101.7 ppm).[5]

Mechanistic Interpretations. Two intriguing issues raised by the synthetic studies above include (1) the α- versus γ-attack by allylic cuprates **8** and **9** as a function of enone; and (2) the α-versus γ-attack on an enone as a function of the allylic ligand on copper (*cf.* Tables 3 and 4). Insofar as the prenyl reagent **9** is concerned (the discussion of which applies as well to cuprate **8**), an initial π-complex **13** is likely (Scheme 4).[15] Oxidation at copper[16] assisted by TMS enol ether formation[12] to **14** followed by reductive elimination[17] leads to the observed product **15**. This route (path A) presupposes that any α vs γ equilibrium between **9** and **9′** (or **8** and **8′**) lies heavily on the side of **9** (or **8**). Nonetheless, **9′** (and **8′**) could well be present in small quantities not detectable by NMR. Depending upon educt, **9′** (or **8′**) could be the more reactive component leading analogously *via* **13′** and **14′** to γ-adduct **16** (path B). Species **9′** (and **8′**) is clearly more sensitive to steric encumberance in the educt, and hence it follows from data in Tables 3 and 4 that the least hindered substrates (*i.e.*, cyclopentenones) would afford the greatest proportion of γ-attack by **9′** (or **8′**). Conversely, increasing steric bulk in the enone favors approach by **9** (or **8**; path A). Thus, formation of π-complex **13** or **13′** is likely to be the regiocontrolling step in the overall process. It is conceivable that an equlibrium between **14** and **14′** comes into play (path C); however, it is unlikely that a fleeting Cu(III) intermediate[16] would be present long enough to allow for this 1,3-metallo shift to occur.

Another distinct possibility involves the action of TMS-Cl as a Lewis *base*,[11] complexing *via* chloride ion to metal M (M = Li or MgX) in **9** and **9′**, thereby leading to the Me_3Si-activated enone π-complexes **18** and **18′**, respectively (Scheme 4). Presumably, the cuprate approaches from the accessible α-face (as shown) relative to γ-substituent R in a cyclic enone. Slippage of Cu(I) to the β-carbon with oxidation to the Cu(III) state arrives at **17** and **17′**. The α-bound prenyl ligand in **17**, as well as the γ-bound ligand in **17′**, can reductively eliminate *via* their γ- and α-carbon centers, respectively, as an alternative to the usual bonding between the two carbon atoms directly attached to the metal (*i.e.*, an allylic or "1,3-reductive elimination"). Species **17** would experience intrinsic steric hindrance due to the γ-dimethyl-substituted carbon leading to a quarternary carbon in product **16**. More influential, however, are the γ-R and γ-H

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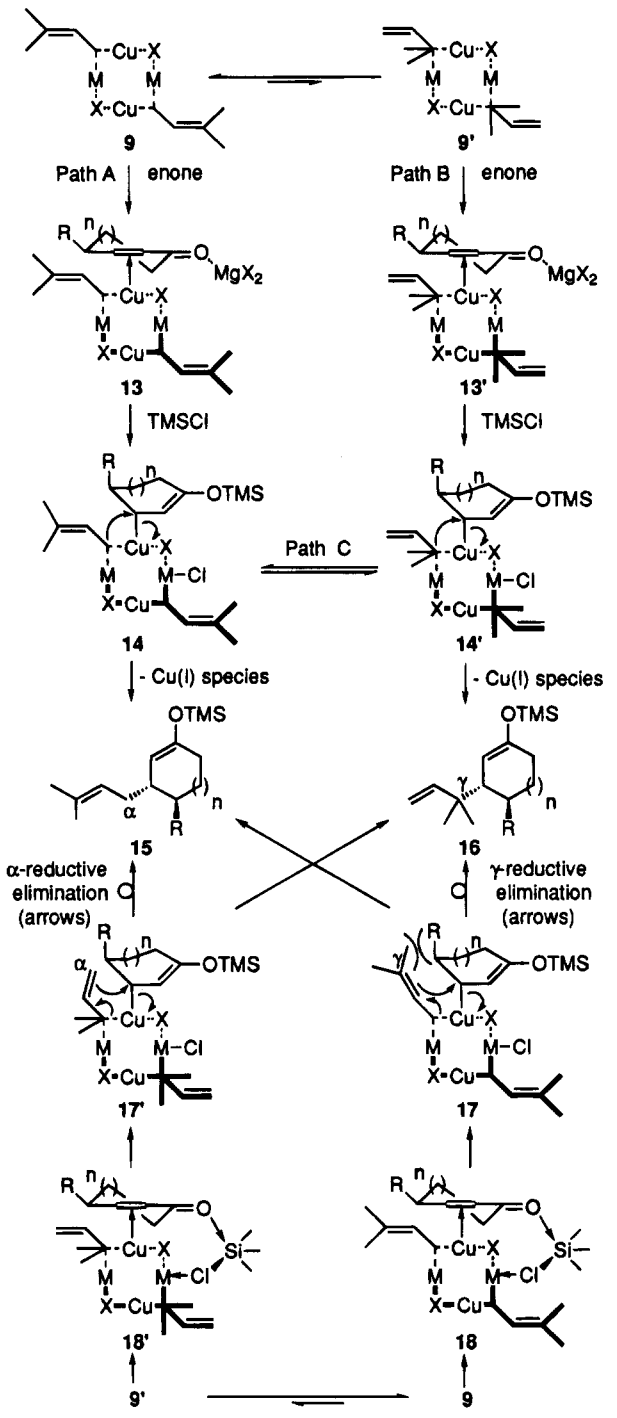
(15) Ullenius, C.; Christenson, B. *Pure Appl. Chem.* **1988**, *60*, 57. Vellekoop, A. S.; Smith, R. A. J. *J. Am. Chem. Soc.* **1994**, *116*, 2902.

(16) Smith, R. A. J.; Vellekoop, A. S. In *Advances in Detailed Reaction Mechanisms*; Coxon, J. M., Ed., JAI Press: Connecticut; Vol. 3, pp 79−130. Krauss, S. R.; Smith, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 141.

(17) Johnson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7783. Whitesides, G. M.; Filippo, J. S.; Stredronsky, E. R.; Casey, C. P. *Ibid.* **1969**, *91*, 6542.

Scheme 4



substituents on the ring (*cf.* **19**) giving rise to two significant interactions (Figure 2). The first is due to the γ hydrogen which protrudes directly toward the incoming π bond. The second interaction of consequence is between the R group and the *E*-methyl moiety on the olefin, both interactions favoring the α- over γ-product (*e.g.*, *cf.* Table 4, entry 1 vs 3 and 4 vs 6). In the unsubstituted five-membered ring case (**20**), the γ-methylene group is positioned away from the *E*-methyl appendage on the olefin, and a γ-hydrogen is no longer facing the π network. As the γ-substitution pattern changes on the cyclopentenone, steric congestion begins to accrue and the same interaction as noted in the cyclohexenone system (*i.e.*, **19**) controls the regiochemistry of reductive elimination. The acyclic example in Table 4 (entry 7), where the best α:γ ratio is observed, also supports this

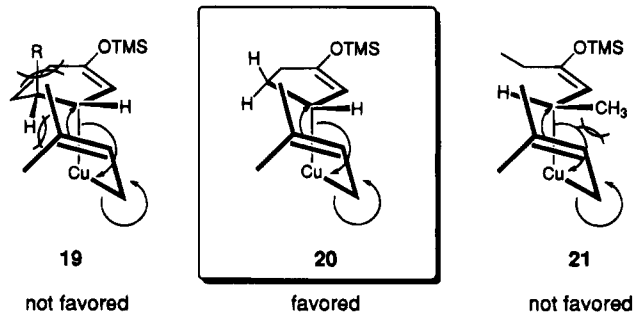


Figure 2.

analysis. In this case, reductive elimination in **21** is directly influenced, irrespective of conformation, by the β-methyl moiety in the enone, and therefore strongly favors α-attack.

Insight regarding this latter mechanism might be realized *via* low temperature heteronuclear NMR studies on the $RMgX{\cdot}CuBr{\cdot}SMe_2$ + TMS-Cl mixture looking to assess the presence of a Lewis acid–Lewis base interaction between the cuprate and silyl halide.[11] While possible, NMR experiments on Grignard-derived cuprates have proven to be notoriously difficult and oftentimes inconclusive due to solubility problems as well as opportunities for Schlenk equilibria which complicate these systems.[18,19]

Summary. The conjugate addition chemistry of four different allylic cuprates prepared from Grignard precursors has been studied in the presence of additive TMS-Cl. An appreciation has been developed for the various levels of selectivity to be expected in their (1) α vs γ-attack; (2) *cis* vs *trans* addition; and (3) *E* vs *Z* ligand stereochemistry, in both cyclic and acyclic systems. Low temperature ^{1}H NMR spectroscopy has shown that crotyl and prenyl cuprates are mainly α-bound to copper, although 1,3-metallotropic shifts to what are likely to be more reactive, γ-bound species occur. Mechanistic discussion is offerred to account for these observations.

Experimental Section

Materials. All chemicals were purchased from the Aldrich Chemical Co. All solvents, as well as chlorotrimethylsilane, were distilled under a dry nitrogen atmosphere. THF was distilled from sodium benzophenone ketyl prior to use. $CuBr{\cdot}SMe_2$ and LiCl were dried for one day under high vacuum at room temperature. Magnesium turnings (98%) were extensively ground prior to use. Methyl 5-oxo-3-[(triethylsilyl)-oxy]-1-cylopenteneheptanoate was generously supplied by G. D. Searle. All reactions were carried out under an inert atmosphere of argon. All glassware and stirring bars were dried overnight at *ca.* 140 °C prior to use. Flash chromatography was performed on ICN BioMedical's, ICN Silica, 32–63, 60 Å. Thin layer chromatography was carried out on precoated silica gel 60 F_{254} plates (EMx Science), 0.25 mm layer thickness.

Instrumentation. NMR spectra were obtained on either a General Electric GN-500 or Varian Gemini-200 spectrometer at 500 and 200 MHz, respectively. IR spectra were run on a 2020 Galaxy FTIR spectrometer. Mass spectra were run on either a VG-Autospec. at the UCLA campus or an analytical

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(19) Nahar, S. K.; Nur, H. P.; Rahman, M. T.; Nilsson, M.; Olsson,T. *J. Orgomet. Chem.* **1991**, *408*, 261. Ashby, E. C.; Goel, A. B. *J. Org. Chem.* **1983**, *48*, 2125. Westmijze, H.; George, A. V. E.; Vermeer, P. *Rec. Trav. Chim. Pays-Bas* **1983**, *102*, 322.

VG 70−250 HF instrument. Gas chromatographic analyses were performed on a Hewlett-Packard 5890A gas chromatograph equipped with a 60 m fused silica J&W DB-5 capillary column. Flame ionization detection was employed with H_2 as the carrier gas.

Preparation of Allyl Grignard Reagents. All Grignard solutions (methallyl-, crotyl-, and prenyl Grignard) were prepared using the same general procedure: Magnesium (10.1 g) was placed in a 100 mL round bottom Schlenk-flask equipped with a stir bar and a septum-sealed dropping funnel. The whole apparatus was then evacuated with a vacuum pump and purged with argon. This process was repeated three times. THF (25.0 mL) was injected and the suspension was cooled to 0 °C. Then 20.0 mmol of the allylic halide (methallyl chloride, crotyl chloride, or prenyl bromide) was added *via* syringe into an additional 25.0 mL of THF present in the dropping funnel. In order to start the reaction, 2.00 mL of this solution were dropped onto the magnesium slurry. After the THF went slightly dark, the slurry was cooled to −13 °C and the remaining solution of the allyl halide was added over 100 min. The reaction was then allowed to warm to room temperature over 30 min. The excess Mg was then removed by filtration. The grey allyl Grignard reagents were titrated from red to yellow against a standard benzyl alcohol solution (0.50 M in toluene) using 1,10-phenanthroline as indicator. The Grignard solutions are stable for weeks at +4 °C.

Reactions of Allylic Cuprates. Most of the reactions were carried out using the following typical procedure: CuBr·SMe_2 (411 mg, 2.00 mmol) and dry LiCl (84.6 mg, 2.0 mmol) were placed in a two-neck 25 mL round-bottom flask equipped with a stir bar and sealed with two septa. The flask was evacuated with a vacuum pump and then purged with argon while drying with a heat gun, this process being repeated three times. THF (3.00 mL) was injected and the mixture stirred for 3 min to yield a yellow, homogeneous solution which was then cooled to −78 °C. Concurrently, the Grignard solution was warmed to room temperature and then transferred *via* syringe (1.80 mmol) dropwise to the copper complex. TMS-Cl (253 μL, 2.00 mmol) was added followed immediately by the neat addition of the enone (0.90 mmol). The reaction was allowed to proceed for ≥5 min before being quenched at −78 °C with a saturated aqueous NH_4OH/NH_4Cl solution (1:9). Extraction with 4 × 25 mL of ether was followed by combining the organic layers and drying over Na_2SO_4. The solvent was removed *in vacuo* and the resulting liquid was treated with THF (3.00 mL) and TBAF (2.00 mL, 2.00 mmol) for 10 min. The solvent was again removed *in vacuo*, and the oil was subjected to flash chromatography (pentane/ether, 8:1). Any modifications to this procedure are mentioned in the specific examples below.

Reaction of (Allyl)Cu·TMS-Cl·$MgBr_2$·SMe_2 with 2-Cyclopentenone (Table 1, entry 1). The organocopper reagent (allyl)Cu·TMS-Cl·$MgBr_2$·SMe_2, was prepared as a tan slurry according to the above procedure. The following amounts of reagents were used: CuBr·SMe_2 (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), allylmagnesium bromide (1.80 mL, 1.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2-cyclopentenone (75.4 μL, 0.90 mmol); Yield 85.1 mg (86%) of 3-(1-propen-3-yl)cyclopentanone as a colorless oil; TLC R_f 0.23 (pentane/ether, 8:1); ^1H (200 MHz, $CDCl_3$) δ 5.83−5.66 (m, 1 H), 5.06−4.97 (m, 2 H), 2.39−2.08 (m, 7 H), 1.85−1.79 (m, 1 H), 1.58−1.46 (m, 1 H); IR (neat) 3075, 2960, 2902, 1743, 1641, 1157, 997, 914 cm^{-1}; mass spectrum (EI), *m/z* (rel intensity) 124 (68), 96 (5), 83 (73), 80 (60), 67 (55), 55 (100); exact mass calcd for $C_8H_{12}O$ 124.0888, found 124.0887.

Reaction of (Allyl)Cu·TMS-Cl·gBr$_2$·SMe_2 with 3-Methyl-2-cyclopentenone (Table 1, entry 2). The following amounts of reagents were used: CuBr·SMe_2 (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), allylmagnesium bromide (1.80 mL, 1.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2-cyclopentenone (59.4 μL, 0.60 mmol); yield 54.1 mg (66%) of 3-methyl-3-(1-propen-3-yl)cyclopentanone as a colorless oil; TLC R_f 0.24 (pentane/ether, 8:1); ^1H (200 MHz, $CDCl_3$) δ 5.84−5.68 (m, 1 H), 5.08−4.97 (m, 2 H), 2.23 (dd, 1 H, *J* = 7.0, 15.3 Hz), 2.12−2.00 (m, 5 H), 1.89−1.66 (m, 2 H), 1.04 (s, 3 H); IR (neat) 3076, 2956, 2925, 1743, 1639, 1438, 991, 912 cm^{-1}; mass spectrum (EI), *m/z* (rel intensity) 138 (10), 123 (5), 110 (12), 97 (43), 95 (11), 69 (100), 55 (31); exact mass calcd for $C_9H_{14}O$ 138.1045, found 138.1041.

Reaction of (Allyl)Cu·TMS-Cl·$MgBr_2$·SMe_2 with 2-Cyclohexenone (Table 1, entry 3). The following amounts of reagents were used: CuBr·SMe_2 (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), allylmagnesium bromide (1.80 mL, 1.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2-cyclohexenone (86.7 μL, 0.90 mmol); yield 107 mg (86%) of 3-(1-propen-3-yl)cyclohexanone as a colorless oil; TLC R_f 0.18 (pentane/ether, 8:1); ^1H (200 MHz, $CDCl_3$) δ 5.83−5.64 (m, 1 H), 5.05 (dd, 1 H, *J* = 1.1, 2.2 Hz), 5.01−4.97 (m, 1 H), 2.45−2.14 (m, 3 H), 2.10−1.80 (m, 6 H), 1.75−1.50 (m, 1 H), 1.49−1.19 (m, 1 H); IR (neat) 3076, 2931, 2866, 1711, 1641, 1157, 996, 913 cm^{-1}; mass spectrum (EI), *m/z* (rel intensity) 138 (65), 123 (35), 110 (5), 97 (100), 79 (21), 69 (99), 55 (48); exact mass calcd for $C_9H_{14}O$ 138.1045, found 138.1046.

Reaction of (Allyl)Cu·TMS-Cl·$MgBr_2$·SMe_2 with 4-Isopropyl-2-cyclohexenone (Table 1, entry 4). The following amounts of reagents were used: CuBr·SMe_2 (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), allylmagnesium bromide (1.80 mL, 1.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2-cyclohexenone (132 μL, 0.90 mmol); yield 126 mg (75%) of 4-isoprenyl-3-(1-propen-3-yl)cyclohexanone[5] as a colorless oil; TLC R_f 0.28 (pentane/ether, 8:1); ^1H (200 MHz, $CDCl_3$) δ 5.80−5.60 (m, 1 H), 5.16−4.96 (m, 2 H), 2.42−2.34 (m, 2 H), 2.26−1.80 (m, 5 H), 1.65−1.22 (m, 4 H), 0.97 (d, 3 H, *J* = 7.0 Hz), 0.79 (d, 3 H, *J* = 7.0 Hz); IR (neat) 3076, 2958, 2873, 1716, 1465, 995, 912 cm^{-1}.

Reaction of (Methallyl)Cu·TMS-Cl·$MgBrCl$·SMe_2 with 2-Cyclohexenone (Table 2, entry 1). The organocopper reagent (methallyl)Cu·TMS-Cl·$MgBrCl$·SMe_2 was prepared as an orange solution according to the above procedure. The following amounts of reagents were used: CuBr·SMe_2 (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), methallylmagnesium chloride (6.43 mL, 1.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2−cyclohexenone (86.7 μL, 0.90 mmol). Yield 130 mg (95%) of 3-(2-methyl-1-propen-3-yl)-cyclohexanone[5] as a colorless oil: TLC R_f 0.22 (pentane/ether, 8:1); ^1H (200 MHz, $CDCl_3$) δ 4.73 (d, 1 H, *J* = 1.8 Hz), 4.64 (d, 1 H, *J* = 1.8 Hz), 2.38−2.21 (m, 3 H), 2.10−1.94 (m, 5 H), 1.93−1.86 (m, 1 H), 1.66 (s, 3 H), 1.65−1.55 (m, 1 H) 1.35−1.20 (m, 1 H); IR (neat) 3072, 2933, 2869, 1714, 1646, 1448, 1224, 889 cm^{-1}.

Reaction of (Methallyl)Cu·TMS-Cl·$MgBrCl$·SMe_2 with 4-Isopropyl-2-cyclohexenone (Table 2, entry 2). The following amounts of reagents were used: CuBr·SMe_2 (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), methallylmagnesium chloride (6.43 mL, 1.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 4-isopropyl-2-cyclohexenone (95.2 μL, 0.65 mmol). Yield 123 mg (71%) of 4-isopropyl-3-(2-methyl-1-propen-3-yl)cyclohexanone as a colorless oil: TLC R_f 0.21 (pentane/ether, 8:1); ^1H (200 MHz, $CDCl_3$) δ 4.73 (s, 1 H), 4.63 (s, 1 H), 2.39−2.15 (m, 4 H), 2.10−1.80 (m, 5 H), 1.63 (s, 3 H), 1.59−1.40 (m, 1 H), 1.35−1.25 (m, 1H), 0.98 (d, 3 H, *J* = 6.8 Hz), 0.78 (d, 3 H, *J* = 6.8 Hz); IR (neat) 3072, 2603, 2873, 1718, 1646, 1450, 1290, 889 cm^{-1}; mass spectrum (EI), *m/z* (rel intensity) 194 (40), 153 (20), 151 (73), 139 (100), 121 (20), 109 (15), 96 (49), 83 (48), 69 (35), 55 (48); exact mass calcd for $C_{13}H_{22}O$ 194.1671, found 194.1671.

Reaction of (Methallyl)Cu·TMS-Cl·$MgBrCl$·SMe_2 with Methyl 5-Oxo-3−[(triethylsilyl)oxy]-1-cylopentene-heptanoate (Table 2, entry 3). The following amounts of reagents were used: CuBr·SMe_2 (514 mg, 2.50 mmol), LiCl (106 mg, 2.5 mmol), methallylmagnesium chloride (7.12 mL, 2.00 mmol), TMS-Cl (253 μL, 2.00 mmol), methyl 5-oxo-3-[(triethylsilyl)oxy]-1-cylopenteneheptanoate (197 mg, 0.56 mmol). The reaction was allowed to proceed for 15 min at −78 °C before being quenched with 15 mL of aqueous NH_4Cl. The solvent was removed *in vacuo* and 3 mL of THF and TBAF (4.00 mL, 4.00 mmol) were added. After 30 min the solvent was removed again *in vacuo* and the resulting residue was subjected to flash chromatography (pentane/ether, 3:1): yield 116 mg (70%) of methyl 3-hydroxy-2-(2-methyl-1-propen-3-yl)-5-oxo-1-cylopenteneheptanoate as a colorless oil; TLC R_f 0.28 (pentane/acetone, 3:1); ^1H (200 MHz, $CDCl_3$) δ 4.87 (s, 1 H),

4.84 (s, 1 H), 4.01 (s, 1 H), 3.63 (s, 3 H), 2.75–2.60 (dd, 1 H), 2.52–2.02 (m, 7 H), 1.98–1.70 (m, 2 H), 1.79 (s, 3 H), 1.69–1.45 (m, 3 H), 1.40–1.15 (m, 6 H); IR (neat) 3444, 3072, 2933, 2858, 1739, 1438, 1172, 1020, 891 cm^{-1}; mass spectrum (EI), *m/z* (rel intensity) 296 (8), 278 (5), 223 (10), 143 (48), 99 (100), 55 (48); exact mass calcd for $C_{17}H_{28}O_4$ 296.1987, found 296.1985.

Reaction of (Methallyl)Cu·TMS-Cl·MgBrCl·SMe$_2$ with 4-Hexen-3-one (Table 2, entry 4). The following amounts of reagents were used: CuBr·SMe$_2$ (514 mg, 2.50 mmol), LiCl (106 mg, 2.50 mmol), methallylmagnesium chloride (7.12 mL, 2.00 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 4-hexen-3-one (102 μL, 0.90 mmol): yield 84.7 mg (61%) of 5,7-dimethyl-7-octene-3-one as a colorless liquid; TLC R_f 0.40 (pentane/ether, 8:1); ^{1}H (200 MHz, $CDCl_3$) δ 4.72 (d, 1 H, *J* = 2.2 Hz), 4.63 (d, 1 H, *J* = 2.2 Hz), 2.38 (q, 2 H), 2.20–2.10 (m, 3 H), 1.89–1.86 (m, 2 H), 1.67 (s, 3 H), 1.01 (t, 3 H, *J* = 7.3 Hz), 0.86 (t, 3 H, *J* = 6.2 Hz); IR (neat) 3075, 2970, 2931, 1714, 1456, 1116, 889 cm^{-1}; mass spectrum (EI), *m/z* (rel intensity) 154 (4), 139 (17), 125 (40), 107 (50), 99 (35), 97 (10), 83 (48), 82 (100), 67 (60), 57, (56), 55 (52); exact mass calcd for $C_{10}H_{18}O$ 154.1357, found 154.1353.

Reaction of (Crotyl)Cu·TMS-Cl·MgBrCl·SMe$_2$ with 2-Cyclopentenone (Table 3, entry 1). The organocopper reagent (crotyl)Cu·TMS-Cl·MgBrCl·SMe$_2$ was prepared as a tan slurry according to the above procedure. The following amounts of reagents were used: CuBr·SMe$_2$ (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.00 mmol), crotylmagnesium chloride (4.15 mL, 1.50 mmol) TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2-cyclopentenone (50.2 μL, 0.60 mmol). Yield 76.5 mg (82%) of 3-(3-methyl-1-propen-3-yl)cyclopentanone as a colorless oil: TLC R_f 0.18 (pentane/ether, 8:1). Mixture (3.2:1) of *trans*/*cis*-γ-diastereomers: ^{1}H (200 MHz, $CDCl_3$) δ 5.79–5.58 (m, 1 H), 5.02–4.91 (m, 2 H), 2.38–1.95 (m, 6 H), 1.88–1.79 (m , 1 H), 1.65–1.40 (m, 1 H), 1.03 (d, 3 H, *J* = 6.2 Hz); IR (neat) 3075, 2964, 2929, 2879, 1743, 1639, 1456, 1159, 914 cm^{-1}; mass spectrum (EI), *m/z* (rel intensity) 138 (48), 123 (6), 110 (75), 96 (21), 83 (58), 67 (45), 55 (100); exact mass calcd for $C_9H_{14}O$ 138.1045, found 138.1046.

Reaction of (Crotyl)Cu·TMS-Cl·MgBrCl·SMe$_2$ with 2-Cyclohexenone (Table 3, entry 2). The following amounts of reagents were used: CuBr·SMe$_2$ (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.00 mmol), crotylmagnesium chloride (5.55 mL, 2.00 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2-cyclohexenone (86.7 μL, 0.90 mmol). Yield 123 mg (90%) of a mixture (3.0:1) of *trans*- and *cis*-3-(3-methyl-1-propen-3-yl)cyclopentanone[5] as a colorless oil: TLC R_f 0.34 (pentane/ether, 8:1). Mixture of α- and γ-diastereomers: ^{1}H (500 MHz, $CDCl_3$) δ 5.85–5.76 (m, vinyl H, γ-product), 5.58–5.52 (m, vinyl H *cis*; minor α-product), 5.46–5.38 (m, vinyl H *trans*+*cis*; *cis* minor α-product, 1 H), 5.35–5.27 (m, vinyl H *trans*; major α-product, 1 H), 5.05–4.95 (m, vinyl H, γ-product), 2.41–2.30 (m, 3 H), 2.25–2.16 (m, 1 H), 2.04–1.88 (m, 3 H), 1.90–1.81 (m , 1 H), 1.80–1.75 (m, 1 H), 1.64 (dd, 3 H, *J* = 1.0, 6.5 Hz, *trans*,*trans*-α-product), 1.38–1.23 (m, 2 H), 0.99 (d, γ-product); IR (neat) 3014, 2933, 2863, 1712, 1448, 1124, 968, 730 cm^{-1}.

Reaction of (Crotyl)Cu·TMS-Cl·MgBrCl·SMe$_2$ with 4-Isopropyl-2-cyclohexenone (Table 3, entry 4). The following amounts of reagents were used: CuBr·SMe$_2$ (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), crotylmagnesium chloride (5.55 mL, 2.00 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 4-isopropyl-2-cyclohexenone (132 μL, 0.90 mmol). Yield 135 mg (77%) of a mixture (3.4:1) of 4-isopropyl-*trans*- and *cis* -3-(2-buten-4-yl)cyclohexanone[5] as a colorless oil: TLC R_f 0.39 (pentane/ether, 8:1). Mixture of α-diastereomers: ^{1}H (500 MHz, $CDCl_3$) δ 5.58–5.52 (m, vinyl H *cis*; minor product), 5.46–5.38 (m, vinyl H *trans* +*cis*; *cis* minor product, 1 H), 5.35–5.27 (m, vinyl H *trans*; major product, 1 H), 2.38–2.30 (m, 2 H), 2.25–2.15 (m, 1 H), 2.14–2.05 (m, 1 H), 2.04–1.88 (m, 3 H), 1.85–1.79 (m , 2 H), 1.64 (dd, 3 H, *J* = 1.0, 6.5 Hz), 1.50–1.38 (m, 2 H), 0.96 (d, 3 H, *J* = 7.0 Hz), 0.78 (d, *J* = 7.0 Hz, 3 H); IR (neat) 3015, 2958, 2875, 1720, 1639, 1463, 1182, 968, 730 cm^{-1}.

Reaction of (Prenyl)Cu·TMS-Cl·MgBr$_2$·SMe$_2$ with 2-Cyclopentenone (Table 4, entry 1). The organocopper reagent (prenyl)Cu·TMS-Cl·MgBr$_2$·SMe$_2$ was prepared as a dark green slurry according to the above procedure. The following amounts of reagents were used: CuBr·SMe$_2$ (206 mg, 1.00 mmol), LiCl (42.3 mg, 1.00 mmol), prenylmagnesium bromide (3.15 mL, 0.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2-cyclopentenone (33.5 μL, 0.40 mmol). Yield 42.7 mg (70%) of 3-(3,3-dimethyl-1-propen-3-yl)cyclopentanone as a colorless oil: TLC R_f 0.27 (pentane/ether, 8:1). γ-Diastereomer: ^{1}H (200 MHz, $CDCl_3$) δ 5.79 (dd, 1 H, *J* = 10.6, 18.0 Hz), 5.10 (dd, 1 H, *J* = 2.0, 10.6 Hz), 4.96 (dd, 1 H, *J* = 2.0, 18.0 Hz), 2.38–1.90 (m, 6 H), 1.03 (s, 3 H) 1.02 (s, 3 H); IR (neat) 3083, 2966, 2873, 1743, 1637, 1461, 1160, 914 cm^{-1}, mass spectrum (EI), *m/z* (rel intensity) 152 (20), 137 (5), 123 (4), 109 (10), 96 (21), 83 (30), 69 (100), 55 (45); exact mass calcd for $C_{10}H_{16}O$ 152.1201, found 152.1194.

Reaction of (Prenyl)Cu·TMS-Cl·MgBr$_2$·SMe$_2$ with 2-Methyl-2-cyclopentenone (Table 4, entry 2). The following amounts of reagents were used: CuBr·SMe$_2$ (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), prenylmagnesium bromide (7.08 mL, 1.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2-methyl-2-cyclopentenone (89.1 μL, 0.90 mmol). Yield 109 mg (73%) of 3-(3,3-dimethyl-1-propen-3-yl)-2-methylcyclopentanone as a colorless oil: TLC R_f 0.29 (pentane/ether, 8:1). γ-Diastereomer: ^{1}H (200 MHz, $CDCl_3$) δ 5.81 (dd, 1 H, *J* = 11.5, 16.9 Hz), 4.99 (d, 1 H, *J* = 16.9 Hz), 4.95 (dd, 1 H, *J* = 11.6 Hz), 2.38–2.05 (m, 2 H), 2.00–1.80 (m, 2 H), 1.79–1.50 (m, 2 H), 1.14–0.97 (m, 9 H); IR (neat) 3081, 2966, 2933, 2873, 1741, 1637, 1460, 1161, 912 cm^{-1}; mass spectrum (EI), *m/z* (rel intensity) 166 (17), 151 (2), 137 (2), 123 (5), 97 (59), 83 (15), 69 (100), 55 (30); exact mass calcd for $C_{11}H_{16}O$ 166.1357, found 166.1357.

Reaction of (Prenyl)Cu·TMS-Cl·MgBr$_2$·SMe$_2$ with Methyl 5-Oxo-3-[(triethylsilyl)oxy]-1-cylopenteneheptanoate (Table 4, entry 3). The following amounts of reagents were used: CuBr·SMe$_2$ (309 mg, 1.50 mmol), LiCl (63.4 mg, 1.5 mmol), prenylmagnesium bromide (5.12 mL, 1.30 mmol), TMS-Cl (190 μL, 1.50 mmol), methyl 5-oxo-3-[(triethylsilyl)oxy]-1-cylopenteneheptanoate (172 mg, 0.48 mmol). The reaction was allowed to proceed for 15 min at −78 °C before being quenched with 15 mL of saturated aqueous NH_4Cl. The solvent was removed *in vacuo* and 3.00 mL of THF and TBAF (3.00 mL, 3.00 mmol) were added. After 30 min the solvent was removed again and the resulting residue was subjected to flash chromatography (pentane/ether, 3:1). Yield 114 mg (76%) of methyl 3-hydroxy-2-(2-methyl-2-buten-4-yl)-5-oxo-1-cyclopenteneheptanoate as a colorless oil: TLC R_f 0.25 (pentane/acetone, 3:1). α-Diastereomer: ^{1}H (200 MHz, $CDCl_3$) δ 5.20 (dd, 1 H, *J* = 6.9 Hz), 4.07 (dd, 1 H, *J* = 7.2 Hz), 3.61 (s, 3 H), 2.67 (dd, 1 H, *J* = 6.4, 18.5 Hz), 2.50–2.10 (m, 7 H), 1.88–1.80 (m, 2 H), 1.63 (s, 3 H), 1.60 (s, 3 H), 1.59–1.45 (m, 3 H), 1.40–1.15 (m, 6 H); IR (neat) 3432, 2929, 2858, 1739, 1639, 1438, 1166, 1074 cm^{-1}; *m/z* (rel intensity) 310 (2), 293 (19), 292 (43), 274 (6), 260 (76), 241 (15), 224 (34), 207 (20), 192 (57), 167 (8), 164 (21), 143 (13), 111 (33), 69 (100), 59 (12), 55 (26); exact mass calcd for $C_{18}H_{30}O_4$ 310.2144, found 310.2144.

Reaction of (Prenyl)Cu·TMS-Cl·MgBr$_2$·SMe$_2$ with 2-Cyclohexenone (Table 4, entry 4). The following amounts of reagents were used: CuBr·SMe$_2$ (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), prenylmagnesium bromide (7.80 mL, 1.98 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 2-cyclopentenone (86.7 μL, 0.90 mmol). Yield 140 mg (91%) of 3-(2-methyl-2-buten-4-yl)cyclohexanone[5] as a colorless oil: TLC R_f 0.28 (pentane/ether, 8:1). α-Diastereomer: ^{1}H (200 MHz, $CDCl_3$) δ 5.07 (dd, 1 H, *J* = 7.5 Hz), 2.39–2.15 (m, 3 H), 2.10–1.75 (m, 6 H), 1.67 (s, 3 H), 1.66–1.57 (m, 1 H), 1.56 (s, 3 H), 1.38–1.28 (s, 1 H); IR (neat) 2927, 2865, 1712, 1448, 1376, 1099, 830 cm^{-1}.

Reaction of (Prenyl)Cu·TMS-Cl·MgBr$_2$·SMe$_2$ with 4-Isopropyl-2-cyclohexenone (Table 4, entry 5). The following amounts of reagents were used: CuBr·SMe$_2$ (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), prenylmagnesium bromide (6.12 mL, 1.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 4-isopropyl-2-cyclohexenone (122 μL, 0.90 mmol). Yield 163 mg (87%) of 4-isopropyl-3-(2-methyl-2-buten-4-yl)cyclohexanone as a colorless oil: TLC R_f 0.15 (pentane/ether, 8:1). α-Diastereomer: ^{1}H (200 MHz, $CDCl_3$)

δ 5.04 (dd, 1 H, J = 7.2 Hz), 2.39–2.15 (m, 4 H), 2.10–1.75 (m, 7 H), 1.68 (s, 3 H), 1.55 (s, 3 H), 1.47–1.37 (m, 2 H), 0.96 (d, 3 H, J = 6.8 Hz), 0.78 (d, 3 H, J = 6.8 Hz); IR (neat) 2967, 2873, 1718, 1454, 1384, 831 cm^{-1}; mass spectrum (EI), m/z (rel intensity) 208 (60), 193 (4), 165 (43), 139 (100), 137 (64), 109 (15), 97 (59), 83 (68), 69 (85), 55 (62); exact mass calcd for $C_{14}H_{24}O$ 208.1827, found 208.1822.

Reaction of (Prenyl)Cu·TMS-Cl·$MgBr_2$·SMe_2 with 4-*tert*-Butyl-2-cyclohexenone (Table 4, entry 6). The following amounts of reagents were used: CuBr·SMe_2 (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.0 mmol), prenylmagnesium bromide (6.12 mL, 1.80 mmol), TMS-Cl (253 μL, 2.00 mmol), TBAF (2.00 mL, 2.00 mmol), 4-*tert*-butyl-2-cyclohexenone (128 mg, 0.90 mmol). Yield 162 mg (86%) of 4-*t*ert-butyl-3-(2-methyl-2-buten-4-yl)cyclohexanone as a colorless oil; TLC R_f 0.16 (pentane/ether, 8:1). α-Diastereomer: ^1H (200 MHz, $CDCl_3$) δ 5.02 (dd, 1 H, J = 7.2 Hz), 2.39–2.15 (m, 3 H), 2.10–1.75 (m, 5 H), 1.63 (s, 3 H), 1.48 (s, 3 H), 1.25–1.15 (m, 2 H), 0.87 (s, 9 H); IR (neat) 2962, 2869, 1712, 1461, 1367, 1159, 1106 cm^{-1}; mass spectrum (EI), m/z (rel intensity) 222 (73), 207 (7), 179 (3), 165 (62), 153 (60), 97 (42), 69 (84), 55 (100); exact mass calcd for $C_{15}H_{26}O$ 222.2017, found 222.1977.

Reaction of (Prenyl)Cu·TMS-Cl·$MgBr_2$·SMe_2 with 4-Hexen-3-one (Table 4, entry 7). The following amounts of reagents were used: CuBr·SMe_2 (411 mg, 2.00 mmol), LiCl (84.6 mg, 2.00 mmol), prenylmagnesium bromide (5.10 mL, 1.50 mmol), TMS-Cl (190 μL, 1.50 mmol), TBAF (1.50 mL, 1.50 mmol), 4-hexen-3-one (68.6 μL, 0.60 mmol). Yield 86.1 mg (85%) of 5,8-dimethyl-7-nonene-3-one as a colorless liquid: TLC R_f 0.55 (pentane/ether, 8:1); ^1H (200 MHz, $CDCl_3$) δ 5.73 (d, 1 H, J = 7.3 Hz), 2.37 (q, 2 H), 2.20–1.94 (m, 3 H), 1.91–1.80 (m, 2 H), 1.67 (s, 3 H), 1.56 (t, 3 H), 1.01 (t, 3 H, J = 7.3 Hz), 0.86 (t, 3 H, J = 6.2 Hz); IR (neat) 2966, 2927, 2881, 1713, 1456, 1376, 1110, 844 cm^{-1}; mass spectrum (EI), m/z (rel intensity) 168 (26), 153 (20), 149 (28), 96 (100); exact mass calcd for $C_{11}H_{20}O$ 168.1514; found 168.1514.

NMR Sample Preparation of (Prenyl)Cu·$MgBr_2$·SMe_2. CuBr·SMe_2 (206 mg, 1.00 mmol) and LiCl (42.3 mg, 1.00 mmol) were placed in a dry three-necked flask sealed with two septa. The flask was then evacuated with a vacuum pump and purged with argon while drying with a heat gun. This process was repeated three times. THF (1.00 mL) was injected, and after 3 min the slurry was cooled to −78 °C. Concurrently, the Grignard solution was warmed to room temperature and then transferred *via* syringe (2.55 mL, 0.75 mmol) dropwise to the copper complex. An aliquot of the solution (0.75 mL) was then transferred *via* cannula under argon to a dry NMR tube (−78 °C). Prior to the addition of the cuprate, the NMR tube was fitted with a Teflon plug and a capillary insert (acetone-d_6), and purged thoroughly with argon. The NMR experiment was carried out at −78 °C; ^1H NMR (200 MHz) δ 5.37 (t), 1.43 (s), 1.34 (s), 0.72 (d); ^{13}C NMR (50 MHz) δ 133.8, 107.8, 16.8, 13.7.

Preparation of (Crotyl)Cu·$MgBr_2$·SMe_2. The cuprate (crotyl)Cu·$MgBr_2$·SMe_2 was prepared in the same manner as was (prenyl)Cu·$MgBr_2$·SMe_2. The following amounts of reagents were used: CuBr·SMe_2 (206 mg, 1.00 mmol), LiCl (42.3 mg, 1.00 mmol), THF (1.00 mL), and crotyl Grignard solution (2.43 mL, 0.75 mmol). The NMR experiment was carried out at −78 °C: ^1H NMR (200 MHz), δ 5.70 (q), 4.77 (quin), 1.34 (d), 0.80 (d); ^{13}C NMR (50 MHz) δ 139.6, 101.6, 23.7, 12.3.

Preparation of (Methallyl)Cu·$MgBrCl$·SMe_2. The cuprate (methallyl)Cu·$MgBrCl$·SMe_2 was prepared in the same manner as (prenyl)Cu·$MgBr_2$·SMe_2. The following amounts of reagents were used: CuBr·SMe_2 (206 mg, 1.00 mmol), LiCl (42.3 mg, 1.00 mmol), THF (1.00 mL), and methallyl Grignard solution (2.70 mL, 0.75 mmol). The NMR experiment was carried out at −78 °C: ^{13}C NMR (50 MHz) δ 171.2, 95.6, 23.4, 21.8.

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Supplementary Material Available: ^1H NMR spectra for all new compounds (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.