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Some Observations on the Mechanism of Diorganocuprate 1,4-Addition Reactions with α,*β*-Unsaturated Ketones: Effects of Diethyl Ether in Reactions of Butylcoppers in Toluene

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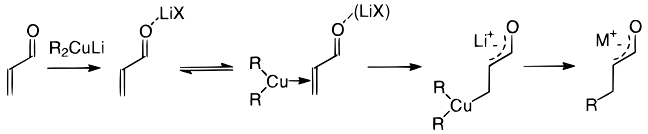
Mixtures of butyllithium and copper iodide prepared in toluene react with α,*β*-unsaturated ketones predominantly in a 1,2-fashion. Addition of 2 equiv of diethyl ether to the system results in a dramatic preference for the 1,4-product, as found normally with diorganocuprates in ethereal solvents. These results are in accordance with the theoretical predictions that a suitable ligand is required to facilitate the stabilization of a formally copper(III) reaction intermediate on the 1,4-addition mechanistic pathway.

Introduction

The 1,4-addition (conjugate) reaction of lithium diorganocuprates (R_2CuLi) with α,*β*-unsaturated ketones (enones) is a well established synthetic protocol[1] for creating a carbon−carbon *σ* bond relatively remote from the carbonyl group. Despite substantial efforts dating from 1965,[2] the detailed mechanism of the organocuprate 1,4-addition reaction remains uncertain. Indeed, a generalized reaction mechanism may not be possible as even slight modification of the reaction conditions (*e.g.* solvent, temperature, additives) can significantly influence the reaction outcome. Mechanistic investigations are made even more difficult by the absence of structural knowledge of the reacting species in solution. Nonetheless, the current belief is that the 1,4-addition reaction proceeds *via* a lithium-coordinated enone (**1**) to a cuprate(3d) → alkene(*π**) complex (**2**) and finally to an enolate (**4**),[3−7] as illustrated in Scheme 1.

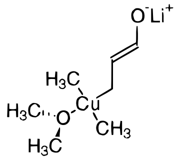
The intermediates **1**, **2**, and **4** have been directly observed and characterized by low temperature NMR studies.[4,5] The conversion of **2** to **4** has been proposed to proceed *via* a formal copper(III) intermediate species (**3**).[7−9] This situation arises from the incorporation of three covalently bound anionic organic groups about the copper center. To the best of our knowledge, direct observation of **3** has not been achieved and some skepticism has been expressed about the viability of a copper(III) intermediate.[10]

Scheme 1



1 2 3 4

Schleyer *et. al.*[11] have carried out *ab initio* calculations on trimethylcopper, $Cu(CH_3)_3$, as a simple model for **3**, and found a local energy minimum provided the copper center was stabilized by donors such as water or ammonia. These donors were used as model ligands for reactions performed in the presence of ethereal solvents and/or nitrogen ligands. The energy changes involved in the fragmentation of the oxygen-coordinated trimethylcopper species to methylcopper and ethane were also estimated, and a metallocyclopropane was found to be an energetically viable transition state. It was concluded that the oxygen-coordinated trimethylcopper species was kinetically stable although thermodynamically much less stable than the reaction products. Snyder[12] has recently modeled a series of similar compounds viewed as "key parts of the potential energy surface" for the 1,4-addition reaction. It was found that without solvent (*e.g.* dimethyl ether) stabilization, a trialkyl copper species had little or no independent existence and was therefore presumably unlikely to serve as an intermediate. However, with appropriate ligand support a viable intermediate was located. As a result of these studies an overall mechanism was proposed for the 1,4-addition reaction which involves, at one stage, solvent stabilization of the copper(III) species **3**, *e.g.* as **5**, which subsequently undergoes facile reductive elimination.



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The notion of considering intermediates **3** and **5** as formal copper(III) species has been discussed[13] and

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alternative views such as "copper(I) complexes whose bonds are dominated by ionic contributions, but whose structures are determined by a nonvanishing degree of covalent Cu($d_{x^2-y^2}$) ligand binding" have been expressed.[12]

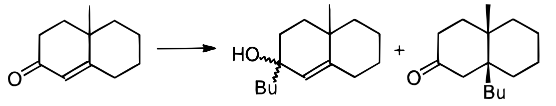
This paper reports experimental findings from some reactions which relate to this aspect of the mechanism. The focus of this research was to prepare an organocopper species in a hydrocarbon solvent and to investigate its reactivity with enones using stoichiometric amounts of the typical, heteroatom donor diethyl ether (Et_2O). The amount of 1,4-addition product was expected to be an indicator of cuprate activity. An alternative, (1,2-) addition, product was also anticipated and this could be derived from **1** and/or **2** without evoking a copper(III) intermediate.

Lithium dimethylcuprate could not be used for this work, as it is not possible to remove the final traces of ethereal solvents from the cuprate[14] nor the methyllithium precursor.[15] For these reasons the copper species examined was based on butyllithium, which is commercially available in a hexane solution. Toluene has been used previously as a solvent component in lithium dimethylcuprate reactions[16] (necessarily including Et_2O) and was utilized as the solvent in these studies. 4,4a,5,6,7,8-Hexahydro-4a-methyl-2(3*H*)-naphthalenone (**6**) was chosen as the primary reaction substrate as the organocuprate reactivity,[4,17] and electrochemistry[18] has been thoroughly examined previously in these laboratories.

Results and Discussion

Butyl addition to **6** gives the 1,2- and the 1,4-addition products, **7** and **8** (Scheme 2). Reference samples of **7** and **8** were prepared using standard procedures. Compound **7** was obtained by the addition of **6** to BuLi followed by careful isolation to avoid dehydration. The 1,4-addition product **8** was synthesized, in 89% isolated yield, by reaction of lithium dibutylcuprate (Bu_2CuLi) with **6** in Et_2O. At room temperature, the ^1H NMR and ^{13}C NMR spectra of **8** showed many broad resonances; however, spectra obtained at 90 °C showed significantly sharper resonances. This phenomenon is indicative of the conformational mobility associated with the labile, *cis*-fused, dialkyl ring junction.[19] Gas chromatography (GC) has been employed for determining the yields of methyl addition products from **6**,[20] and an adaptation of this methodology was used in this work. The GC chromatogram of **7** showed a series of up to five peaks assumed to be the various isomeric dehydration products. The relative amount of **7** was derived by the summation of the integrals of all these peaks.

Scheme 2



6 **7** **8**

Addition of 2 equiv of BuLi to a grey suspension of CuI in toluene at −78 °C gave no apparent reaction. On warming to −40 °C, the temperature at which Bu_2CuLi was formed in Et_2O solvent, no change was noted. It was found that reaction at −20 °C for 15 min was necessary to create a visible change in the toluene solvent system. Addition of **6** (1.0 equiv) to this black mixture recooled to −78 °C and reaction at −40 °C for 30 min resulted in complete consumption of the starting material. The product was predominantly **7** (98 mol %) with minor amounts (2 mol %) of **8**. Numerous repetitions of this experiment gave similar results and confirmed that the 1,4-/1,2-addition product ratio in toluene was completely different to that in Et_2O.

A series of experiments adding various amounts of Et_2O to the 1:2 CuI/BuLi mixture in toluene were then carried out using a standard protocol of stoichiometry, time, temperature, and order of addition (see Experimental Section). Only a slight excess (10%) of the organometallic over enone was required to consume all starting material. A slight excess of CuI to BuLi was used in these reactions to allow for all free BuLi to be reacted. The amount of Et_2O used in these studies is expressed in terms of molar equivalents (ME). The basic ME unit is equal to half the amount of BuLi used in each experiment. The results from varying the amount of Et_2O are presented in Figure 1.

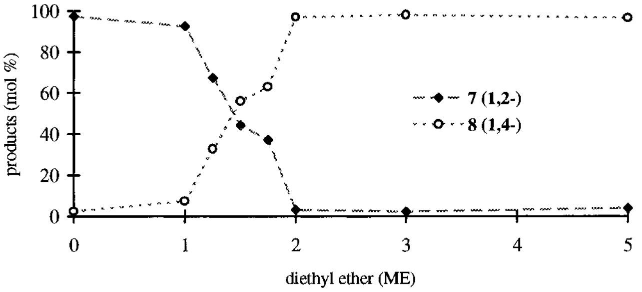


Figure 1. Effect of Et_2O on the amount of 1,4-/1,2-addition to **6** with 1:2 CuLi/BuLi.

Reaction of the 1:2:1 CuI/BuLi/Et_2O mixture in toluene with **6** consistently gave approximately 7 mol % **8**, *i.e.* comparable to that obtained without any Et_2O. However, reaction using 2 ME of Et_2O gave 97 mol % **8**, *i.e.* similar to that observed with Et_2O as the solvent. There was a dramatic, progressive increase in the amount of **8** produced from reactions carried out with between 1 and 2 ME of Et_2O. Increasing the amount of Et_2O above 2 ME had no deleterious effects on the amount of **8** produced.

Other enones were reacted with the 1:2 CuI/BuLi mixture in toluene to establish whether the Et_2O effect on the 1,4-/1,2-addition ratio was unique to the sterically and electronically demanding substrate **6**. The results with 2-cyclohexen-1-one (**9**), 3,5,5-trimethyl-2-cyclohexen-1-one (**10**), and *trans*-4-phenyl-3-buten-2-one (**11**) are presented in Table 1, together with those from similar reactions with **6** for comparison purposes.

The 1,2-addition product was predominant in all reactions without Et_2O present. Only in the case with the very reactive enone, **9**, was a significant amount of 1,4-addition observed. In contrast to **6**, reactions with **9**, **10**, or **11** and the 1:2:1 CuI/BuLi/Et_2O mixture gave signifi-

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Table 1. Effect of Et_2O on 1,4-/1,2-Addition Ratios with Various Enones

$$\mathrm{CuI} + 2\mathrm{BuLi} \xrightarrow{\text{toluene}} [\ \ ] \xrightarrow{w\,\mathrm{Et_2O}} [\ \ ] \xrightarrow{\text{enone}} \text{products}$$

		products (%)[a]	
enone	*w* (ME)	1,2-addition	1,4-addition
6	0	98[b]	2[b]
9	0	66	34
10	0	95	5
11	0	90	10
6	1	93[b]	7[b]
9	1	27	73
10	1	78	22
11	1	73	27
6	2	3[b]	97[b]
9	2	1	99
10	2	5	95
11	2	5	95

[a] Obtained by ^1H NMR unless stated otherwise. [b] From GC analysis.

cant amounts of 1,4-addition, particularly with **9**. The variation of 1,4-/1,2-addition ratio with enone using 1 ME of Et_2O is consistent with the enone/methylcuprate relative reactivity series reported previously.[5] Overwhelming preference for the 1,4-addition product was observed in all reactions containing 2 ME of Et_2O. These results clearly indicate the generality of the stoichiometric effect of Et_2O on the butylcopper system in toluene.

There are two possible segments in the proposed reaction where the presence of Et_2O could be influential on the 1,4-addition proclivity. The ligand may be necessary to allow the formation of the cuprate reagent and also, as discussed above, be required for intermediate stabilization. The large amounts of 1,2-addition observed in the toluene system with small amounts of Et_2O may indicate that, under these reaction conditions, either the cuprate species was formed but was 1,2-directing or, alternatively, free BuLi was present. In a typical ethereal diorganocuprate reaction system only one of the alkyl groups is transferred to the organic substrate and the second alkyl group is generally unavailable, presumably as an alkylcopper(RCu) species. Alkylcoppers are considered to be unreactive, particularly in Et_2O, and even in THF require the assistance of Lewis acids to become effective alkyl donors.[21] Hence, normally the addition of 2 ME of enone to a cuprate gives equal amounts of the 1,4-addition product and recovered starting material. In order to establish the amount of active butyl group in CuI/BuLi mixtures in toluene a series of experiments with different ratios of BuLi, CuI, and **6** were carried out, and the results are presented in Table 2.

Table 2. Reaction of Various CuI/BuLi Mixtures with 6 in Toluene

$$x\,\mathrm{CuI} + y\,\mathrm{BuLi} \xrightarrow{\text{toluene}} [\ \ ] \xrightarrow{z\,\mathbf{6}} \text{products}$$

	amount (mmol)			products (mol %)		
entry	*x*	*y*	*z*	**6**	**7**	**8**
1	0.0	1.0	1.0	3	97	0
2	1.0	1.0	1.0	14	79	7
3	1.0	2.0	1.0	1	98	1
4	1.0	2.0	2.0	12 (0.24 mmol)	86 (1.72 mmol)	2 (0.04 mmol)

Reaction of BuLi with **6** (entry 1) was included as a reference experiment, and a large amount of **7** was obtained. This result eliminates the possiblity of significant direct reaction between BuLi and toluene under these reaction conditions. The small amount of recovered starting material **6** may be the result of enolate formation or simply reflect the precision of BuLi delivery. Examination of the 1:1 CuI/BuLi system was undertaken to allow for the formation of butylcopper (BuCu) and resulted in a dark mixture indicating at least some interaction between the two reagents. Reaction of this material with **6** (entry 2) gave predominantly **7** together with **6** and a small amount of **8**. By comparison with the BuLi reaction (entry 1) it appeared that some modification of the BuLi by the CuI had occurred which manifested itself in the form of less **7** and some, albeit minor, 1,4-addition. Reaction of the 1:2 CuI/BuLi mixture with **6** (entry 3) gave a product distribution comparable to that obtained with BuLi, except a detectable amount of **8** was evident. This reaction was repeated but with 2 equiv of **6**. The result (entry 4) indicated that at least 88% of the butyl units were active, with a strong 1,2-addition preference. These reactivity experiments indicate that the black CuI/2BuLi/toluene mixture reacts as if it consists of varying amounts of BuCu and BuLi.

A similar set of reactions were run but with fixed amounts of Et_2O and are summarized in Table 3.

Table 3. Reaction of Various CuI/BuLi/Et_2O Mixtures with 6 in Toluene

$$x\,\mathrm{CuI} + y\,\mathrm{BuLi} \xrightarrow{\text{toluene}} [\ \ ] \xrightarrow{w\,\mathrm{Et_2O}} [\ \ ] \xrightarrow{z\,\mathbf{6}} \text{products}$$

	amount (mmol)			*w*	products (mol %)		
entry	*x*	*y*	*z*	(ME)	**6**	**7**	**8**
1	1.0	1.0	1.0	5	95	4	1
2	1.0	2.0	1.0	1	0	95	5
3	1.0	2.0	1.5	1	2 (0.03 mmol)	85 (1.28 mmol)	13 (0.19 mmol)
4	1.0	2.0	1.0	5	1	3	96
5	1.0	2.0	1.5	5	33 (0.49 mmol)	6 (0.09 mmol)	61 (0.92 mmol)

Reaction of **6** with 1:1:5 CuI/BuLi/Et_2O gave predominantly starting material, together with small amounts of both **7** and **8** (entry 1). This result is in concordance with established alkylcopper reactivity without Lewis acid activation and contrasts to the previous result in toluene alone (Table 2, entry 2). Two experiments were conducted using the 1:2:1 CuI/BuLi/Et_2O mixture. As shown in Figure 1, reaction with 1 equiv of **6** gave predominantly **7** (entry 2). The addition of 1.5 equiv of **6** (entry 3) gave a product distribution comparable to that obtained without Et_2O (Table 2, entry 4) with *ca.* 74% of the butyl groups being transferred. A substantial amount of **8** was observed from the reaction of **6** with the 1:2:5 CuI/BuLi/Et_2O mixture (entry 4). This result was anticipated based on the previous work (cf. Figure 1) which showed high 1,4-selectivity with these amounts of Et_2O. The total amount of active butyl groups available in this reaction was determined by using 1.5 equiv of **6** (entry 5). The recovery of 0.5 equiv of **6** along with high amounts of **8** is consistent with a "normal" cuprate. From these studies it can be concluded that traditional butylcopper (BuCu, Bu_2CuLi) properties can be established in toluene provided a certain minimum amount of Et_2O is also present.

It became clearly important to establish the nature of the species obtained by mixing CuI and BuLi in toluene, and a method for distinguishing organolithium from organocopper reactivity was required to clarify this issue.

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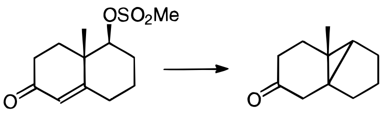
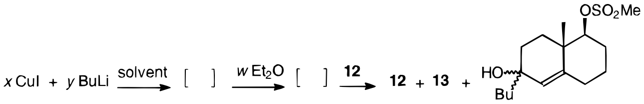
Early mechanistic research on the 1,4-addition reaction tended to focus on an electron transfer process, and molecules similar to those previously utilized for mechanistic studies of metal/ammonia reductions[22] were used to demonstrate the electron transfer potential of organocuprates toward enones. These molecules were designed to trap any increase in electron density at the β-carbon by an internal alkylation process.[23] Specifically, the establishment of organocopper properties in a variety of systems was related to the isolation of **13** from reaction with **12**.[24] Increased electron density on the alkenyl carbons has been demonstrated[4] by NMR techniques in the Cu(3d)$\rightarrow$alkene(π^*) complex from **6** so, even in the current mechanistic scenario which does not involve electron transfer, the use of internal trapping experiments remains valid.



12 **13**

This probe/trap sequence was applied to the system of interest in this work in order to gain evidence for organocuprate activity. Experiments were carried out using a variety of BuLi/CuI ratios in both toluene and Et$_2$O with a 10% excess of organometallic reagent relative to the amount of **12**. The reaction mixtures were analyzed by ^{1}H NMR and ratios of products determined by comparing the diagnostic resonances of **12** (5.84 ppm, 1H) and **13** (2.64 ppm, 2H). The amount of the 1,2-addition product **14** in reaction mixtures containing **12** was calculated by difference. The results from these experiments are depicted in Table 4.

Table 4. Reaction of Various CuI/BuLi/Et$_2$O Mixtures with 12 in Toluene



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entry	amount (mmol) x	y	solvent	w (ME)	products (mmol) 12	13	14
1	0.0	1.1	toluene	0	0.51	0.00	0.34
2	1.2	1.1	toluene	0	0.37	0.09	0.46
3	1.2	1.1	toluene	2	>0.95	<0.05	0.00
4	1.2	2.2	Et$_2$O	0	0.45	0.47	0.00
5	1.2	2.2	toluene	0	0.20	0.16	0.50
6	1.2	2.2	toluene	2	0.59	0.40	0.00

Reaction of **12** with BuLi did not yield any **13** (entry 1); however, the amount of **14** obtained did give an indication of the maximum yield attainable under these reaction conditions. Reaction of **12** with a 1:1 CuI/BuLi mixture (entry 2) gave some **13**, but once again the major products were **14** and **12**. These results confirm that copper is indeed required to obtain at least some **13**. Reaction of **12** with a 1:1:2 CuI/BuLi/Et$_2$O mixture gave nearly complete recovery of the starting material (entry 3). This provides further evidence that BuCu, formed in an ethereal environment, is unreactive even toward **12**. Reaction of Bu$_2$CuLi prepared in Et$_2$O solvent with **12** (entry 4) was included as a reference experiment, and the detection of 0.47 mmol of **13** indicated a typical baseline result for a "normal" cuprate. Reaction of the 1:2 CuI/BuLi mixture with **12** in the absence of Et$_2$O (entry 5) gave a significant amount of **13**, but the predominant species was **14**. The occurrence of **13** indicated that an organocopper species was formed, at least to some extent in toluene alone. Reaction of **12** with a 1:2:2 CuI/BuLi/Et$_2$O mixture (entry 6) gave a product distribution comparable to that obtained from reaction in Et$_2$O solvent (entry 4) and is fully consistent with traditional diorganocuprate activity.

A feature of this work was that with 1 equiv of Et$_2$O relatively small amounts of 1,4-addition were evident, especially with the relatively unreactive enones. A reasonable explanation is that 1 equiv of Et$_2$O was being consumed preferentially and any additional Et$_2$O was then effective in enhancing cuprate-like reactivity. If reactions with CuI/BuLi proceed to completion then 1 equiv of LiI is produced which would be expected to be highly attracted to the Et$_2$O. Thus it seemed possible that the first equivalent of Et$_2$O was required to sequester the LiI and the additional amounts affected the 1,4-reactivity by Cu(III) intermediate stabilization. To test this idea, reactions were carried out with additional LiI in 1:2 CuI/BuLi mixtures containing various amounts of Et$_2$O, and the results are presented in Table 5.

Table 5. Reaction of 1:2:w CuI/BuLi/Et$_2$O and LiI Mixtures with 6

entry	amount (ME) LiI	(w)Et$_2$O	products (mol %) 6	7	8
1	0.0	2	0	3	97
2	1.0	2	0	35	65
3	1.0	3	5	3	92
4[a]	1.0	2	0	42	58
5[b]	1.0	2	4	2	94

[a] LiI added with CuI. [b] LiI added after Et$_2$O.

In contrast to the reaction of 1:2:2 CuI/2BuLi/Et$_2$O which gives predominantly **8** (entry 1), the presence of 1 ME of LiI resulted in the formation of significant amounts of **7** (entry 2). A high 1,4-/1,2-addition product ratio was reestablished by increasing the amount of Et$_2$O (entry 3). These observations are in complete accordance with the idea that the LiI removes some Et$_2$O from the reaction scene, but once this is complete then 1,4-activation can be achieved by any residual Et$_2$O. In the reactions, summarized in entries 2 and 3 of Table 5, LiI was added in the reaction sequence before Et$_2$O. It was established that addition of LiI to CuI at the initial stage of the reaction had the same effect (entry 4). Curiously, addition of the LiI *after* the Et$_2$O did not influence the reaction product distribution (entry 5) using reaction times comparable to the rest of this work.

Conclusion

These results indicate that the reactivity of the CuI/BuLi mixtures in toluene closely resembles that of a mixture of various amounts of BuLi and BuCu. The addition of only 2 ME of Et$_2$O to this mixture is sufficient to produce reactivity similar to that observed from a normal cuprate. The method by which Et$_2$O affects CuI/BuLi mixtures in toluene cannot be ascertained with absolute confidence from these results. Et$_2$O may activate an existing species already present in the toluene

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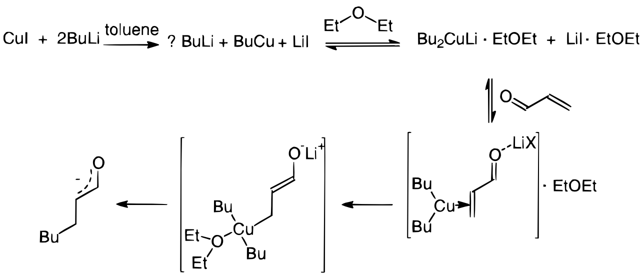
mixture or create an entirely new species and, in either event, influence 1,4-reactivity. Either scenario is possible but the clear indication from this work is that at least some reactive organocopper is created in toluene without Et_2O. A second area of influence is in the facilitation of collapse of the π-complex by stabilization involving coordination of the copper(III) intermediate as predicted by the theoretical results. The observations reported in this paper are totally in accord with this feature.

Illustrated in Scheme 3 is a summary of the possible effects of Et_2O on the reactivity of the 1:2 CuI/BuLi mixture in toluene.

Scheme 3



In the absence of Et_2O, the system reacts as a mixture of BuLi and BuCu, which may be 1,2-addition reactive under these conditions. The addition of appropriate amounts of Et_2O shifts the equilibrium toward a cuprate. Reaction of this material with an enone is reversible[5] and leads eventually to the π-complex. The Et_2O then stabilizes the trialkylcopper intermediate species to give the ultimate enolate product.

Direct, spectroscopic observation of the reagent(s) and intermediates in the presence of stoichiometric amounts of Et_2O may further resolve the nature of these species, and these studies are currently being pursued in these laboratories.

Experimental Section

General Methods and Materials. Column chromatography was performed using Merck 9385 silica gel or Riedel-de Haën basic alumina S (modified to activity II by addition of 3% H_2O). A 1:60 ratio of crude material to adsorbent was used. NMR spectra were recorded in $CDCl_3$ solution, unless otherwise indicated. Numbers in brackets directly after chemical shift values reflect the relative isomeric ratio. Gas chromatographic (GC) analyses were carried out using a 10 m, 0.25 mm internal diameter, 0.25 μm film thickness, DB1 fused silica column. Helium was used as the carrier gas at a flow rate of 1.5 mL min^{-1} with a 50:1 split.

Toluene was distilled from sodium and stored over sodium wire. Anhydrous diethyl ether (Et_2O) (Aldrich, 99+%) was stored over sodium wire. For organometallic reactions, the solvents were deoxygenated by alternate application of vacuum and argon. *n*-Butyllithium (BuLi) was obtained (Aldrich) as a 1.6 mol L^{-1} hexane solution and analyzed by the Gilman double titration method.[25] Free alkali was determined by adding BuLi (1.00 mL) to a solution of 3-bromo-1-propene (0.5 mL) at −40 °C, in either Et_2O (10 mL) or toluene (10 mL). The toluene reaction was quenched with ethanol. Commercial copper iodide (CuI) (Aldrich, 99.999%) was finely ground and purified by continuous extraction with THF.[26] Anhydrous lithium iodide was prepared according to the literature method.[27]

2-Cyclohexenone (**9**), 3,5,5-trimethyl-2-cyclohexenone (**10**), and *trans*-4-phenyl-3-buten-2-one (**11**) were commercial samples. 1-Butyl-2-cyclohexen-1-ol,[28] 3-butylcyclohexanone,[28] 3-butyl-3,5,5-trimethylcyclohexanone,[29] *trans*-3-methyl-1-phenyl-1-hepten-3-ol,[30] and 4-phenyl-2-octanone[31] were identified from authentic samples or spectra. 4,4a,5,6,7,8-Hexahydro-4a-methyl-2(3*H*)-naphthalenone (**6**)[32] and *cis*-4,4a,5,6,7,8-hexahydro-5-(mesyloxy)-4a-methyl-2(3*H*)-naphthalenone (**12**)[26] were prepared as described previously.

Reactions involving the use of moisture and/or oxygen sensitive compounds were performed on a double manifold system under an atmosphere of argon. Manipulations of all sensitive materials and dry solvents were carried out using double-ended needle techniques. Cooling baths were obtained by the addition of liquid nitrogen to appropriate solvent mixtures. The −78 °C bath was prepared from a mixture of ethanol and acetone, and the warmer baths were prepared from mixtures of ethanol and water. Organometallic reactions were routinely quenched at −40 °C with an aqueous mixture of ammonium chloride/ammonia (NH_4^+/NH_3), prepared by mixing saturated ammonium chloride and 25% ammonia in a ratio of 25:4.

General Methods for Organometallic Reactions. (*Note: details of solvent, enone, and Et_2O are given with each example.*)

Method A. BuLi (1.1 mmol) was added to dry degassed solvent (10 mL) in a dry Schlenk tube at −78 °C. The solution was stirred for 10 min, and then enone (1.0 mmol) was added by syringe over 5−10 s. The mixture was stirred at −40 °C for 30 min and then quenched and worked up as described below.

Method B. CuI (0.228 g, 1.2 mmol) was weighed into a dry Schlenk tube, evacuated for 5 min, and then filled with argon. Dry, degassed Et_2O (10 mL) was added, and the resulting white suspension was cooled to −78 °C, with stirring. BuLi (2.2 mmol) was added, and the mixture was stirred for 30 min. Over this time period the mixture darkened to a grey suspension. The mixture was then transferred to a −40 °C cold bath and stirred for 5 min, resulting in a black mixture. This mixture was recooled to −78 °C before enone (1.0 mmol) was added by syringe over 5−10 s, resulting in a slight khaki hue. The mixture was stirred for 30 min at −40 °C and then worked up as below.

Method C. CuI (0.228 g, 1.2 mmol) was weighed into a dry Schlenk tube, evacuated for 5 min, and then filled with argon. Dry, degassed toluene (10 mL) was added and the resulting white suspension was cooled to −78 °C, with stirring. BuLi (2.2 mmol) was added, and the mixture was stirred for 30 min, transferred to a −20 °C cold bath, and stirred for 15 min. Over this time period the suspension darkened through grey to a black color. The mixture was again cooled to −40 °C, inoculated with various amounts of Et_2O, and stirred for 10 min. This mixture was recooled to −78 °C before enone (1.0 mmol) was added by syringe over 5−10 s. The mixture was stirred for 30 min at −40 °C and then quenched and worked up as below.

Method D. As for Method C, except using BuLi (1.1 mmol).

In reactions that were analyzed by GC an internal standard (1.0 mmol) was added by syringe after the enone addition at −78 °C.

Workup Protocols. Workup 1. The total reaction mixture was poured into a separatory funnel, and the reaction Schlenk tube was washed consecutively with NH_4^+/NH_3 (10 mL) and solvent (10 mL). Reactions containing copper were

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vigorously shaken until a deep blue color developed and all solids had dissolved. The layers were then separated. The aqueous layer was solvent extracted (2 × 20 mL), and the combined organic extracts were washed with water (50 mL) and then dried over anhydrous magnesium sulfate ($MgSO_4$). The mixture was filtered after approximately 15 min, and solvents were evaporated under reduced pressure.

Workup 2. After quenching, two aliquots (≈0.5 mL) were removed from the organic phase and were added to separate sample tubes, each containing NH_4^+/NH_3 (≈0.5 mL), and diluted with hexane (2 mL). The mixtures were shaken until all solid had dissolved and then allowed to settle, and the organic phase was analyzed by GC.

2-Butyl-2,3,4,4a,5,6,7,8-octahydro-4a-methyl-2-naphthalenol (7). Method A (three times scale), Et_2O (30 mL), **6** (465 μL, 3.0 mmol), workup 1, hexane, but dried over anhydrous sodium sulfate (Na_2SO_4). The ^{1}H NMR of the crude product indicated a small amount of **6** still remained, and this material was chromatographed on basic alumina (activity II). Elution with 15% Et_2O/hexane gave **7** (0.526 g, 2.37 mmol, 79%) of a colorless oil, as an inseparable mixture of isomeric allylic alcohols. Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79%. Found: C, 80.71; H, 11.48%. IR ν_{max} (cm^{-1}) (film) 3354 (OH), 1657 (C=C). ^{1}H NMR δ (ppm) 5.22 (1H, broad s, H-1), 2.3−1.1 (19H, m) 1.10 (2), 1.02 (1) (3H, s, H-9), 0.92 (3H, t, J = 6.9 Hz, H-13). Workup by standing over anhydrous magnesium sulfate or chromatography on silica gel or basic alumina (activity I) resulted in dehydration of **7**.

***cis*-8a-Butyl-3,4,4a,5,6,7,8,8a-octahydro-4a-methyl-2(1*H*)-naphthalenone (8).** Method B, **6** (155 μL, 1.0 mmol), workup 1, hexane. The ^{1}H NMR of the crude product showed a small amount of **7**. The product was chromatographed on silica gel, and elution with dichloromethane (CH_2Cl_2) gave **8** (0.179 g, 89%) as a colorless oil. Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79%. Found: C, 80.78; H,12.07%. IR ν_{max} (cm^{-1}) (film) 1715 (C=O). ^{1}H NMR (300 MHz) δ (ppm) 2.4−2.1 (4H, m), 1.6−1.1 (16H, m), 1.05 (3H, s, H-9), 0.89 (3H, t, J = 6.9 Hz, H-13). ^{1}H NMR (300 MHz) (90 °C) (toluene-d_8) δ (ppm) 2.17 (1H, d, J = 14.1 Hz, H-1), 2.09 (2H, d, J = 14.2 Hz, H-3), 1.91 (1H, d, J = 14.1 Hz, H-1), 1.69 (1H, m, H-3), 1.4−0.9 (15H, m), 0.85 (3H, t, J = 6.9 Hz, H-13), 0.80 (3H, s, H-9). ^{13}C NMR (75MHz) δ (ppm) 213.0 (C-2), ≈47 (very broad) 42.8, 38.1, 35.6 (broad), 34.2, 33.9 (broad), 30.1 (broad), 24.9, 23.6, 22.7, 21.6, 21.2, 14.1. ^{13}C NMR (75 MHz) (90 °C) (toluene-d_8) δ (ppm) 208.6 (C-2), 47.0 (CH_2), 42.9 (C), 38.1 (CH_2), 36.2 (CH_2), 36.0 (C), 34.7 (CH_2), 34.5 (CH_2), 30.8 (CH_2), 25.5 (CH_2), 24.1 (CH_2), 22.8 (CH_3), 22.1 (CH_2), 21.7 (CH_2), 14.1 (CH_3).

1-Butyl-3,5,5-trimethyl-2-cyclohexen-1-ol. Method C, **10** (150 μL, 1.0 mmol), workup 1, hexane, dried over anhydrous Na_2SO_4. The ^{1}H NMR analysis gave 1-butyl-3,5,5-trimethyl-2-cyclohexen-1-ol (95%), ^{1}H NMR δ (ppm) 5.32 (1H, broad s, H-2), and 3-butyl-3,5,5-trimethylcyclohexanone (5%), from the integrated areas. The crude material was chromatographed on alumina, and elution with 25% Et_2O/hexane gave the alcohol (0.161 g, 82%) as a colorless oil. Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32%. Found: C, 79.23; H, 12.46%. IR ν_{max} (cm^{-1}) (film) 3386 (OH) 1670 (C=C). ^{1}H NMR δ (ppm) 5.32 (1H, broad s, H-2), 1.8−1.6 (5H, m), 1.5−1.2 (9H, m), 1.04 (3H, s), 0.97 (3H, s), 0.90 (3H, t, J = 7.1 Hz). ^{13}C NMR (50 MHz) δ (ppm) 135.2 (C-3), 126.0 (C-2), 71.4 (C-1), 47.6, 44.4, 44.0, 31.7, 29.9, 27.4, 25.7, 24.0, 23.2, 14.1.

Reactions of Organocopper Reagents with 6. Products from organometallic reactions with **6** were analyzed by GC with n-dodecane (n-C_{12}) (227 μL, 1.0 mmol) as the internal standard (workup 2). The column was heated from 90 to 190 °C at a rate of 15 °C min^{-1}. Retention times (t_R) and response factors (R_f) for **6**−**8** are given in the following table.

compound	t_R (min)	R_f
n-C_{12}	2.0	−
6	3.7	1.30
7	4.2−5.4	0.98
8	6.1	0.92

Reaction of the 1:2:*w* CuI/BuLi/Et_2O Mixtures with 6. All reactions were run using method C, Et_2O (w(ME)), **6** (155 μL, 1.0 mmol), and workup 2, and products were analyzed by GC. The results, graphically presented in Figure 1:

(w)Et_2O (ME)	products (mol %) **7**	**8**
0.00	98	2
1.00	93	7
1.25	67	33
1.50	44	56
1.75	37	63
2.00	3	97
3.00	2	98
5.00	4	96

Reactions of 1:2:*w* CuI/BuLi/Et_2O Mixtures with 9−11. All reactions were run using method C, Et_2O (w(ME)), enone (1.0 mmol). Reactions were worked up *via* workup 1, dried over Na_2SO_4, and analyzed by ^{1}H NMR. Product percentages from mixtures were ascertained from diagnostic ^{1}H NMR resonances or from integrated area excesses. The results are given in Table 3.

Stoichiometric Studies on CuI/BuLi Mixtures with 6. All reactions were adjusted to 1.0 mmol scale and worked up as for workup 2. The results are given in Tables 2 and 3.

BuLi. Method A, toluene, and **6** (155 μL, 1.0 mmol).

1:1 CuI/BuLi. Method D and **6** (155 μL, 1.0 mmol).

1:2 CuI/BuLi. (a) Method C and **6** (155 μL, 1.0 mmol). (b) Method C and **6** (310 μL, 2.0 mmol).

1:1:5 CuI/BuLi/Et_2O. Method D, Et_2O (523 μL, 5.0 mmol), and **6** (155 μL, 1.0 mmol).

1:2:1 CuI/BuLi/Et_2O. (a) Method C, Et_2O (105 μL, 1.0 mmol), and **6** (155 μL, 1.0 mmol). (b) Method C, Et_2O (105 μL, 1.0 mmol), and **6** (233 μL, 1.5 mmol).

1:2:5 CuI/BuLi/Et_2O. (a) Method C, Et_2O (523 μL, 5.0 mmol), and **6** (155 μL, 1.0 mmol). (b) Method C, Et_2O (523 μL, 5.0 mmol), and **6** (233 μL, 1.5 mmol).

Reaction of CuI/BuLi Mixtures with 12. All reactions were carried out in toluene with **12** (0.258 g, 1.0 mmol) added as a CH_2Cl_2 solution (2 mL). Addition of **12** caused a yellow/orange precipitate to appear, which stopped stirring. Workup 1, CH_2Cl_2, was followed by analysis using ^{1}H NMR. The results are listed in Table 4.

BuLi. Method A gave **12** (0.131 g, 0.51 mmol) and *cis*-2-butyl-2,3,4,4a,5,6,7,8-octahydro-5-(mesyloxy)-4a-methyl-2-naphthalenol (**14**) (0.116 g, 0.34 mmol) as an inseparable mixture of isomers, ^{1}H NMR δ (ppm) 3.1−3.0 (3H, s, OMs), 0.90 (3H, t, J = 7.0 Hz, H-13).

1:1 CuI/BuLi. Method D gave **12** (0.095 g, 0.37 mmol) and 6-methyltricyclo[4.4.0.0^{1,5}]-9-decanone (**13**) (0.015 g, 0.09 mmol), ^{1}H NMR δ (ppm) 2.64, 2.63, (2H, AB system, J_{AB} = 18.6 Hz, H-1), 1.06 (3H, s, H-11), in agreement with an authentic sample,[17] and **14** (0.147 g, 0.46 mmol).

1:1:2 CuI/BuLi/Et_2O. Method D, Et_2O (230 μL, 2.2 mmol).

Bu_2CuLi/Et_2O. Method B.

1:2 CuI/BuLi. Method C.

1:2:2 CuI/BuLi/Et_2O. Method C, Et_2O (230 μL, 2.2 mmol).

Reactions of 1:2:*w* CuI/BuLi/Et_2O with 6 Containing LiI. All reactions were run using method C, Et_2O (w(ME)), LiI (0.147 g, 1.0 ME), and **6** (155 μL, 1.0 mmol), and the reactions were worked up *via* workup 2. The results are given in Table 5.

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