2-phenylbut-3-en-2-ol, 29290-99-1; 1-(3-heptyl)cyclohexanol, 84370-47-8; propylidenecyclohexane oxide, 28256-59-9; 2-chloropentane, 625-29-6; 2-bromoheptane, 1974-04-5; 2-iodoheptane, 18589-29-2; 4-methyl-1-nonene, 26741-20-8; 3-methyl-1-octene, 13151-08-1; 2-methylheptane, 592-27-8; 3-methyloctane, 2216-33-3; 4-methylnonane, 17301-94-9; 2-phenylheptane, 2132-84-5; 3,4-dimethylnonane, 17302-22-6; 1-*tert*-butylcyclohexene oxide, 7583-74-6.

Conjugate Addition Reactions of α,β-Unsaturated Ketones with Higher Order, Mixed Organocuprate Reagents, $R_2Cu(CN)Li_2$

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Conjugate addition reactions of mixed cuprates $R_2Cu(CN)Li_2$ with α,β-unsaturated ketones are reported. These reagents, in most cases, react extremely rapidly affording the corresponding alkylated ketones in high yields. Attempts at trapping the intermediate enolates appeared to be successful using MeI as electrophile; however, the method is not general and was, therefore, not pursued. The effects of solvent and ligand composition on $R_2Cu(CN)Li_2$ as well as on the more highly mixed species $R_TR_RCu(CN)Li_2$ have been examined. The selectivity of ligand transfer in these latter, second generation organocuprates is also discussed.

Introduction

The facility with which organocuprates R_2CuM, **1** (M = Li or MgX), add to α,β-unsaturated ketones[1] forming carbon–carbon bonds exclusively at the β-position has afforded them the distinction of being the reagents of choice for effecting such transformations. The original procedure, which dates back over forty years and relies upon a CuCl-catalyzed addition of a Grignard reagent (MeMgBr) to an enone,[2] has been modified and refined considerably over time. Indeed, today one has myriad literature examples from which to choose in deciding upon reaction parameters.[3] Most commonly sought are lithium-based cuprates **1**, M = Li, prepared stoichiometrically from CuX and 2 RLi, thus obviating use of (large) excesses of strong base in the reaction medium.[1,3] While lower order Gilman reagents R_2CuLi, **2**, continue to serve admirably, they are not without drawbacks, such as thermal instability which necessitates use of additional stabilizing and solubilizing ligands.[1] Hence, the continuing evolution of synthetic methodology, having made extraordinary gains over the past decade, encourages realization of new and improved reagents for molecular elaboration. In this paper we present an extensive accounting of our investigation on the development of novel higher order, mixed organocuprates $R_2Cu(CN)Li_2$, **3**. These species are highly reactive toward conjugated ketones transferring ligands very efficiently in a Michael sense.[4] The scope and limitations of the procedure have been examined, including the effects of variation in the substrate, ligands on copper, and solvent. Moreover, the selectivity of ligand transfer in still more highly mixed systems, $R_1R_2Cu(CN)Li_2$, has also been determined.

Results and Discussion

Although a variety of cuprates **3** are readily prepared, their efficient coupling with secondary halides[5,6] and epoxides[6,7] in no way guaranteed their successful application as formal Michael donors. Both chemical[8] and spectroscopic[9] evidence has accrued suggesting that higher order homocuprates, generalized by Me_3CuLi_2, **4**, may not be synthetically useful in this regard due to competing 1,2-addition. Our concurrent detailed studies on the more highly mixed reagents, $R(CH_3)Cu(CN)Li_2$, **5**, have revealed the presence of free MeLi in Et_2O solution,[10] as previously observed with **4**.[9] These concerns notwithstanding, a preliminary study, reported previously,[4] was undertaken which clearly demonstrated that a variety of substrates, both cyclic and acyclic, participate in the coupling. Moreover, cuprates derived from primary, secondary, tertiary, vinyl, and aryllithium reagents may be employed.

Of practical importance, it should be noted that it is a common occurrance for many lower order cuprate additions to enones[1] to rely on the presence of solubilizing or stabilizing ligands (e.g., HMPA,[12] $(EtO)_3P$,[13] Me_2S,[14] LiBr,[15] n-Bu_3P[16]). Such a requirement not only introduces another variable into an already complex scheme but also mandates care in handling (e.g., n-Bu_3P is pyrophoric) and chromatographic separation after workup. To date, we

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[†] A. P. Sloan Foundation Fellow, 1984–1986.

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[2] Kharasch, M. S.; Tawney, P. O. *J. Am. Chem. Soc.* **1941**, *63*, 2308.

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[4] Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. *Tetrahedron Lett.* **1982**, *23*, 3755. For the analogous reaction with unsaturated esters, see: Lipshutz, B. H. *Ibid.* **1983**, *24*, 123.

[5] Lipshutz, B. H.; Wilhelm, R. S.; Floyd, D. M. *J. Am. Chem. Soc.* **1981**, *103*, 7672 and references therein.

[6] Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A.; Parker, D. *J. Org. Chem.*, preceding paper in this issue.

[7] Lipshutz, B. H.; Kozlowski, J. A.; Wilhelm, R. S. *J. Am. Chem. Soc.* **1982**, *104*, 2305.

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[9] Ashby, E. C.; Watkins, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 5312.

[10] Lipshutz, B. H.; Kozlowski, J. A.; Wilhelm, R. S. *J. Org. Chem.*, the following paper in this issue.

[11] 3-Vinylcyclopentanone derivatives themselves have been used in several steroid related synthetic endeavors: cf. Posner, G. H.; Mallamo, J. P.; Hulce, M.; Frye, L. L. *J. Am. Chem. Soc.* **1982**, *104*, 4180 and references therein.

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[13] House, H. O.; Fischer, W. F. *J. Org. Chem.* **1968**, *33*, 949.

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[16] Hooz, J.; Layton, R. B. *Can. J. Chem.* **1970**, *48*, 1626.

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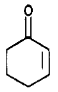
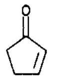
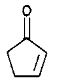
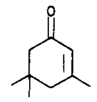
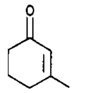
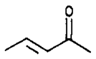
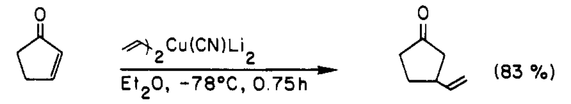
Table I. Selectivity of Ligand Transfer: Reactions of Enones

entry	substrate	reagent[a]	conditn	yield, %	ratio[b]
1		n-Bu(Me)Cu(CN)Li$_2$	Et$_2$O, −85 °C, 1 h	92[c]	11–21:1, n-Bu:Me
2		sec-Bu(Me)Cu(CN)Li$_2$	THF, −78 °C, 0.5 h	97[d,e]	1:0, sec-Bu:Me
3		H$_2$C=C(Me)Cu(CN)Li$_2$	THF, −78 °C, 1 h	>93[c]	142:1, H$_2$C=CHCH$_3$:Me
4		H$_2$C=C(Me)Cu(CN)Li$_2$	Et$_2$O, −50 °C, 3.5 h	>97[c]	37:1, H$_2$C=CHCH$_3$:Me
5		t-Bu(Me)Cu(CN)Li$_2$	Et$_2$O, −25 °C, 0.25 h	85[c]	1:0, t-Bu:Me
6		n-Bu(Me)Cu(CN)Li$_2$	Et$_2$O, −78 °C, 3 H	89[c]	12:1, n-Bu:Me

[a] 1.5–2.0 equiv used. [b] Determined by VPC analysis. [c] By quantitative VPC. [d] Isolated yield. [e] Product is an inseparable mixture of diastereomers, by capillary VPC.

have not encountered one substrate/reagent pair which has necessitated use of an additive in any form.

Although **3**, R = vinyl, adds readily to isophorone,[4] Ph$_2$Cu(CN)Li$_2$ could not be coaxed into following suit, even at elevated temperatures, where predominant 1,2-addition ensued. The ease with which (vinyl)$_2$Cu(CN)Li$_2$ forms 3-vinylcyclopentanone argues well for potential applications of more elaborate ligands in prostanoid related efforts,[11] in particular with a method now in hand for conserving valuable vinyl groups (vide infra).



Having completed this preliminary study, we recognized that a need for 1.5–2 equiv of reagent, which was routinely called upon, had not been established. Furthermore, while sterically more demanding cases[4] had been followed in terms of temperature and time, it was not clear that 0.5–1 h was actually necessary with the less encumbered examples. Hence, to gain a better feeling for both the quantity of cuprate needed and the time frame involved for consumption of enone, reactions involving 1.04–1.10 equiv of cuprate per substrate were carried out with mesityl oxide and cyclohexenone. Perhaps not surprisingly,[17] the former reacted to the extent of 42% in 75 s, while the latter had completely disappeared within 60 s of addition (92% yield). Thus, it appears that these conjugate addition reactions are quite rapid at very low temperatures, and mole quantities of **3** just slightly in excess of substrate are satisfactory without compromising efficiency.

Conjugate Addition/Alkylation. The successful trapping of enolates generated from organocuprate additions to enones is generally limited to the use of reactive electrophiles.[1,18] This tandem conjugate addition/alkylation process, which has not been looked at with higher order cuprates, was worth examining as the nature of the species in solution must necessarily be different from those formed via reactions of **2**. Treatment of cyclohexenone in DME with **3**, R = n-Bu, followed by addition of excess MeI at 0 °C led to a new product in ca. 80% (VPC) yield. In testing the generality of the process, similar experiments employing benzyl bromide as electrophile in various quantities and at numerous times and temperatures, unfortunately afforded little, if any, of the dialkylated ketone. Following this result, when coupled with the knowledge that a reactive lower order reagent (i.e., RCu(CN)Li) is formed by delivery of R from **3**,[6,10,19] which rapidly consumes an equivalent of E$^+$, our efforts along these lines were discontinued.

Selectivity of Ligand Transfer. Our experience with displacement reactions[5-7] using more highly mixed organocuprates R$_T$R$_R$Cu(CN)Li$_2$, **6** (R$_T$ = a transferrable ligand, R$_R$ = a second "dummy" ligand) led us to evaluate R$_R$ = methyl, where MeLi serves as a substitute for the second equivalent of R$_T$Li. Table I lists the examples studied which suggest that a simple methyl residue serves rather nicely in this capacity. Primary alkyl ligands (entries 1,6) are delivered with a ca. 11–12:1 preference over CH$_3$, not an overly impressive ratio but certainly tolerable considering the normally excellent yields realized. Interestingly, crotonate derivatives, which are structurally related to, for example, 3-penten-2-one, react with **6**, R$_T$ = n-Bu, R$_R$ = Me to afford a somewhat greater selectivity (ca. 19:1) of n-butyl to methyl transfer.[4] As the steric bulk of R$_T$ in **6** increases, exclusive transfer occurs relative to a methyl group (compare 1,2,5).[6] Entry 5, which demonstrates formation of two adjacent quarternary centers is worthy of mention. This general preference for selective transfer presumably reflects the relative kinetic reactivities of **6**, as well as the stability of the resulting lower order reagent formed (R$_R$Cu(CN)Li)[10] following loss of R$_T$.

Perhaps the most unexpected finding concerns the total reversal in transferability of methyl vs. vinyl ligands on going from reactions of **6**, R$_T$ = vinyl, R$_R$ = CH$_3$, with secondary halides and oxiranes, to enones. In the former series, products of methyl over vinyl transfer predominated (ca. 2–6:1).[6] With enones, typified by entries 3 and 4, *ratios for the selective transfer of vinyl over methyl ranged from 37–142:1 with yields in excess of 90%*. There is precedent for this latter selectivity in Posner's work employing (vinyl)MeCuLi, where a 25:1 ratio is cited.[20] The corre-

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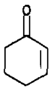
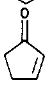
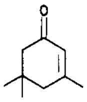
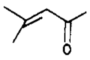
[17] Hallnemo, G.; Ullenius, C. *Tetrahedron* **1983**, *39*, 1621.

[18] Coates, R. M.; Sandefur, L. O. *J. Org. Chem.* **1974**, *39*, 275.

[19] The major product was n-pentylbenzene, resulting from displacement by n-BuCu(CN)Li. Also obtained was bibenzyl.

[20] Posner, G. H.; Sterling, J. J.; Whitten, C. E.; Lentz, C. M.; Brunelle, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 107. See also: Leyendecker, F.; Drouin, J.; Debesse, J. J.; Conia, J. M. *Tetrahedron Lett.* **1977**, 1591.

Table II. Effect of Solvent on Reactions of $R_2Cu(CN)Li_2$ with Enones

substrate	reagent	conditn	solvent	yield, %[a]
	n-$Bu_2Cu(CN)Li_2$	−78 °C, 0.5 h	Et_2O	>97
			DME	>97
			THF	>97
	$(H_2C{=}CH)_2Cu$-$(CN)Li^2$	−78 °C, 0.75 h[b]	Et_2O	83
			DME	74
			THF	93
	$(H_2C{=}CH)_2Cu$-$(CN)Li_2$	−50 °C, 2.5 h	Et_2O	98
			DME	11[c]
			THF	34[c]
	$Ph_2Cu(CN)Li_2$	−78 °C, 1 h	Et_2O	98
			DME	8[d,e]
			THF	1[f]

[a] Determined by VPC. [b] All of the enone was consumed. [c] The remainder of the material was isophorone. [d] Only 60% starting material was recovered. [e] Reaction run at −20 °C due to insolubility of reagent at −78 °C. [f] ca. 90% enone remained.

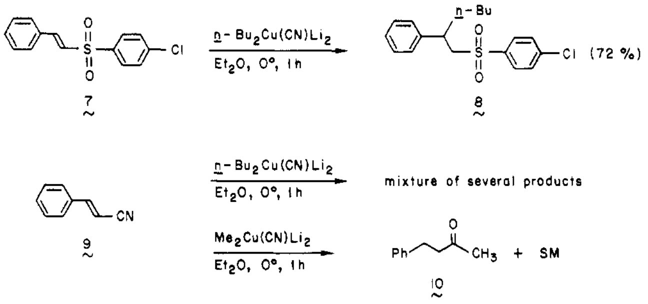
sponding selectivity with secondary halides, to our knowledge, has not been reported, most likely due to the limited synthetic utility of vinyl ligand-containing Gilman reagents in substitution reactions.[5,21]

What makes our results above all the more intriguing is that vinyl over methyl transfer is encouraged in both THF (entry 3) and Et_2O (entry 4). Our detailed NMR studies on higher order reagents **3** and **6** have unequivocally demonstrated that reagent constitution varies markedly from THF to Et_2O.[10] It has been shown that THF is the preferred solvent for substitution reactions of **3** and **4**.[5] Moreover, THF is well-known to decrease the rate of cuprate reactions with enones relative to Et_2O, presumably a result of competitive complexation with lithium ions.[22] Hence, Et_2O, which also leads to a higher aggregation state for **3** and **6**,[10] is the expected solvent of choice. While this is generally true, there are occasions (e.g., Table I, entries 2 and 3) when a change in reaction medium can be used to advantage (vide infra). Such phenomena pointed to the important role which solvent(s) can play, thereby engendering the following study.

Solvent Effects. In addition to THF and Et_2O, DME was also included as this solvent is reported to permit subsequent alkylation of the initially formed enolate.[18] Table II illustrates four cases, two being unhindered enones (entries 1,2) and the others β,β-disubstituted examples. The results indicate that, in the former situation, good yields of adduct are seen regardless of the choice of medium. In more sterically challenging molecules (entries 3,4), however, Et_2O is by far superior to THF and DME.

Recalling entries 2 and 3 in Table I, addition of a ligand to educt cyclopentenone is best achieved in THF. Attempted reactions of *sec*-$Bu(Me)Cu(CN)Li_2$ in Et_2O at −78 °C instantaneously led to a multitude of products, according to TLC. By switching to THF, the process could be sufficiently slowed thereby affording an excellent yield of ketone upon workup. The mixed species vinyl(Me)-$Cu(CN)Li_2$ was also used in THF. This modification was induced by both the reagent's limited solubility in Et_2O, in which a two-phase mixture is present, and the numerous byproducts which formed (noticeable by TLC) after the addition of the first drop of substrate. In THF, complete solubilization occurs and, following introduction of the enone, a handsome outcome to the coupling was realized both in terms of yield and selectivity of transfer. Thus, insofar as solvent effects are concerned, Et_2O is usually the wise choice; however, there is considerable flexibility inherent in this protocol for "fine tuning" via increasing percentages of, e.g., THF, so as to maximize solubility and efficiency.

Additions to Unsaturated Sulfones and Nitriles. In House's account on the role of lower order Gilman reagents in electron-transfer processes,[23] complexation of a cuprate cluster with a doubly bonded oxygen atom is invoked as a necessary (but not sufficient) first step prior to radical anion formation. Thus, conjugated esters and sulfones, in addition to enones, with the appropriate reduction potentials ($E_{red} > -2.4$ V) readily enter into coupling reactions. Unsaturated nitriles, however, which lack this functional group array, their E_{red} notwithstanding, do not participate. To determine whether this trend applies to higher order cuprate chemistry, we briefly examined the reactions of **3** with sulfone **7** ($E_{red} = -1.70$ V)[24] and cinnamonitrile, **9** ($E_{red} = -1.84$ V),[25] under conditions similar to those used previously by Posner.[24] Treatment of **7** with **3**, R = n-Bu, afforded **8** in 72% yield, which compares favorably with the literature result (75%) using n-Bu_2CuLi. Under identical conditions, **9** reacts to give a multitude of products. When the less reactive species **3**, R = Me, is involved, a clean reaction occurs, albeit slowly at 0 °C, and leads unexpectedly to methyl ketone **10**. These results again point to the highly reactive nature of cuprates **3**, as House found that no reaction between **9** and Me_2CuLi took place.[23] Hence, it appears that higher order mixed cuprates follow guidelines similar to those of lower order reagents with respect to the structural requirements of the substrates with which they will couple.



Summary

The data presented in this report serve to illustrate the emerging value of CuCN based higher order cuprate technology. In cases where conjugate addition reactions lead to results comparable to those obtained using lower order reagents, derived from copper halides, the experimental simplicity and economic benefits associated with CuCN encourage its use.[5] The dispensing of added ligands for solubilizing and/or stabilizing purposes significantly facilitate the overall sequence. While these reagents are usually prepared between −78 and 0 °C, some R_TLi may not be stable at these higher temperatures. To circumvent this potential problem, more highly mixed reagents $R_TR_RCu(CN)Li_2$ have been developed, which also allow for conservation of R_TLi. With these cuprates, MeLi is used first to preform (when necessary) a solution of MeCu-(CN)Li to which is added R_TLi at low temperatures (i.e., **6**, R_R = Me). The selectivity of transfer for alkyl and vinyl groups, R_T, examined is between 11–142:1, the ratio being a function of both the substrate and cuprate involved. Yields received with these second generation mixed reag-

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(21) Posner, G. H. *Org. React. (N.Y.)* **1975**, *22*, 253.

(22) Johnson, C. R.; Herr, R. W.; Wieland, D. M. *J. Org. Chem.* **1973**, *38*, 4263. House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59.

(23) House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59.

(24) Posner, G. H.; Brunelle, D. J. *J. Org. Chem.* **1973**, *38*, 2747.

ents are as good as those realized using $R_2Cu(CN)Li_2$. For unhindered enones, Et_2O, THF, or DME may be employed as solvent, although for more sterically demanding cases, Et_2O in the medium seems to be essential.

Experimental Section

Chemicals. Cyclohexenone, 5-methylcyclohexenone, isophorone, 3-penten-2-one, cyclopentenone, and mesityl oxide are commercially available from Aldrich. Octalone 11 was prepared according to Marshall and Fanta.[25] Methyllithium was purchased from Aldrich, *n*-butyllithium and phenyllithium from Ventron, and vinyllithium from Organometallics. Ethyllithium was prepared from ethyl chloride, while *n*-propyllithium was made from *n*-propyl chloride. Titration of all lithium reagents followed the procedure of Watson and Eastham.[26] Copper cyanide was obtained from MCB and stored in an Abderhalden at 56 °C over KOH.

Instrumentation. Infrared data were recorded on a Perkin-Elmer Model 283 spectrophotometer. NMR spectra were obtained in $CDCl_3$ by using a Varian T-60, FT-80, XL-100, or a Nicolet NT-300 instrument. Mass Spectral data were obtained on a ZAB-2F spectrometer. VPC analyses were conducted on a Hewlett-Packard Model 5880A by using a 6 ft × $^1/_8$ in. column packed with 20% SE-30 on Chromosorb W.

Materials. TLC analyses employed glass plates (0.25 mm) precoated with silica gel as supplied by Baker. Gravity filtrations used silica gel 60 obtained from Merck, 70–230 mesh. All glassware and syringes were oven-dried at 120 °C overnight prior to use.

Typical Preparation of Reagents 3. CuCN (89 mg, 1 mmol) is placed in a dry two-neck flask containing a serum cap and a T joint with access to Ar and a vacuum. The CuCN is flushed and evacuated with Ar 4–5 times and left under a static Ar pressure. Dry Et_2O (1 mL) is introduced and the slurry is cooled to −78 °C, to which is then added the RLi (2 mmol) via syringe. With gentle stirring, the pot is warmed slowly to between −30 and 0 °C until complete dissolution of CuCN results. The solution is then recooled to −78 °C followed by addition of the enone (0.5–0.95 mmol, neat or in Et_2O). The solution, which usually has taken on a different color from that of the cuprate itself, is permitted to stir at the necessary temperature and for the time needed to consume starting material, which is a function of both reagent and substrate. Upon completion, the reaction is quenched by the addition of a 10% NH_4OH/saturated aqueous NH_4Cl solution and worked up, after stirring at room temperature for 10–30 min, via Et_2O extraction. The crude product is then purified by standard techniques.

4-Methyl-4-phenylpentan-2-one.[27] $Ph_2Cu(CN)Li_2$ was prepared by the addition of PhLi (0.65 mL, 1.44 mmol) to CuCN (66 mg, 0.74 mmol) in 0.95 mL of Et_2O at −78 °C. Warming of this mixture to 0 °C produced a yellowish but not quite homogeneous solution. The temperature was returned to −78 °C at which point mesityl oxide (57 μL, 0.5 mmol) was added neat via syringe. Stirring was continued at −78 °C. After 45 min the solution became viscous and further stirring was difficult. Quenching after 1 h and workup in the usual manner were followed by column chromatography on SiO_2 with 3:1 pentane/Et_2O, yielding 72.6 mg (83%) of product R_f (3:1 pentane–Et_2O) 0.43; IR(neat) cm^{-1} 3060, 3025, 1722, 1705, 763, 698; ^1H NMR δ 1.45 (6 H, s), 1.80 (3 H, s), 2.70 (2 H, s), 7.10–7.45 (5 H, m), mass spectrum, *m*/*e* (relative intensity) 176 (M^+, 11.8), 119 (100), 91 (45.5), 43 (52.7); high-resolution MS calcd for $C_{12}H_{16}O$ 176.1201, found 176.1178.

3-Vinylcyclopentanone. To CuCN (89.6 mg, 1.0 mmol) in 2.0 mL of cold (−78 °C) Et_2O was added vinyllithium (0.90 mL, 2.0 mmol) and the mixture was warmed to 0 °C. Recooling to −78 °C and addition of cyclopentenone (75 μL, 0.9 mmol) was followed by stirring for 45 min and quenching. VPC analysis indicated formation of 3-vinylcyclopentanone in 82.7% vs. 3-methylcyclopentanone as internal standard: IR (neat) cm^{-1} 1740, 990, 910; ^1H NMR δ 1.5–3.0 (7 H, m), 5.1 (2 H, m), 5.8 (1 H, m); mass spectrum, *m*/*e* (relative intensity) 110 (M^+, 45.3), 82 (48.9), 68 (23.1), 67 (55.9), 54 (100), 41 (31.4); high-resolution MS calcd for $C_7H_{10}O$ 110.0732, found 110.0733.

Typical Procedure for the Preparation of R(Me)Cu(CN)Li$_2$. Methyllithium (1 mmol) was added to a slurry of CuCN (89 mg, 1 mmol) in Et_2O (1–1.5 mL) at −78 °C under argon. Warming to 0 °C resulted in a light tan solution which was recooled to −78 °C and RLi (1 mmol) was then added producing no color change. Dropwise introduction of the enone (neat or in Et_2O) initially affords a reaction solution of a different color relative to the cuprate but often will dissipate upon consumption of starting material. Following completion of the reaction, quenching with 10% NH_4OH/saturated aqueous NH_4Cl solution and workup give the crude product which is purified in the usual way.

3-*n*-Butylcyclohexanone.[28] To CuCN (49.6 mg, 0.55 mmol) in 1.0 mL of Et_2O at −78 °C was added MeLi (0.27 mL, 0.55 mmol) and the mixture was warmed to 0 °C. The solution was recooled to −78 °C and *n*-BuLi (0.23 mL, 0.54 mmol) was added, again followed by warming to 0 °C for 2–3 min. The temperature was lowered to −85 °C and cyclohex-2-enone (48.5 μL, 0.5 mmol) was added neat via syringe. Stirring was continued at −85 °C for 1 h, followed by quenching and workup. VPC analysis indicated formation of 3-*n*-butylcyclohexanone and 3-methylcyclohexanone in an 11.5:1 ratio. The identity of both products was established by coinjection with authentic samples.

3-*sec*-Butylcyclopentanone. To CuCN (67.2 mg, 0.75 mmol) in 1.25 mL of cold (−78 °C) THF was added MeLi (0.47 mL, 0.75 mmol) and the mixture was warmed to 0 °C. Recooling to −78 °C and addition of *sec*-BuLi (0.61 mL, 0.75 mmol) was followed by injection, via syringe, of cyclopentenone (42 μL, 0.5 mmol) and stirring for 0.5 h. Quenching and extractive (Et_2O) workup followed by chromatography on silica gel (40% Et_2O/pentane) afforded 67 mg (97%) of the product as a light oil: R_f (1:1 Et_2O–pentane) 0.69; IR (neat) cm^{-1} 1740; ^1H NMR δ 0.8–1.0 (6 H, m), 1.1–2.5 (10 H, m); mass spectrum, *m*/*e* (relative intensity) 140.0 (5.4), 125 (20.3), 111.0 (17.9), 83.0 (47.4), 69.9 (14.9), 55.2 (100); high-resolution MS calcd for $C_9H_{16}O$ 140.1200, found 140.1199.

3-Vinylcyclopentanone. To CuCN (89.0 mg, 1.0 mmol) in 2.0 mL of cold (−78 °C) THF was added MeLi (0.48 mL, 1.0 mmol) and the mixture was warmed to 0 °C. Recooling to −78 °C and addition of vinyllithium (0.48 mL, 1.0 mmol) was followed by injection, via syringe, of cyclopentenone (70 μL, 0.84 mmol) and stirring for 1.0 h. Quenching and VPC analysis indicated formation of 3-vinylcyclopentanone and 3-methylcyclopentanone (authentic sample) in a ratio of 142:1, in >93% yield.

3,5,5-Trimethyl-3-vinylcyclohexanone.[16] To CuCN (89.6 mg, 1.0 mmol) in 1.0 mL of cold (−78 °C) Et_2O was added MeLi (0.47 mL, 1.0 mmol) and the mixture was warmed to 0 °C. Recooling to −78 °C and addition of vinyllithium (0.48 mL, 1.0 mmol) was followed by addition of isophorone (75μL, 0.5 mmol) and warming to −50 °C. Stirring for 3.5 h and quenching were followed by VPC analysis which indicated formation of 3,5,5-trimethyl-3-vinylcyclohexanone and 3,3,5,5-tetramethylcyclohexanone in a 37:1 ratio, 97% yield vs. cyclohexanone. The identity of the latter compound was established by coinjection with an authentic sample.

3-*tert*-Butyl-3-methylcyclohexanone. To CuCN (89.6 mg, 1.0 mmol) in 1.5 mL of cold (−78 °C) Et_2O was added MeLi (0.48 mL, 1.0 mmol) and the mixture was warmed to 0 °C. Recooling to −78 °C and addition of *t*-BuLi (0.61 mL, 1.0 mL) was followed by 3-methylcyclohex-2-enone (85 μL, 0.75 mmol). Stirring for 0.25 h and quenching was followed by VPC analysis which indicated formation of 3-methyl-3-*tert*-butylcyclohexanone in 85% yield vs. cyclohexanone: IR (neat) cm^{-1} 1710; ^1H NMR δ 1.0 (12 H, s), 1.5–2.0 (4 H, m), 2.19 (2 H, s), 2.2–2.3 (2 H, m); mass spectrum, *m*/*e* (relative intensity) 112.0 (10.1), 110.9 (100), 83.0 (31.3), 57.3 (92.5); high-resolution MS calcd for $C_{11}H_{21}O - C_4H_9$ 111.0808, found 111.0780.

4-Methyloctan-2-one. To CuCN (89.6 mg, 1.0 mmol) in 1.2 mL of cold (−78 °C) Et_2O was added MeLi (0.48 mL, 1.0 mmol) and the mixture warmed to 0 °C. Recooling to −78 °C and addition of *n*-BuLi (0.41 mL, 1.0 mmol) were followed by 3-

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penten-2-one (64 μL, 0.66 mmol) and stirring for 3 h. Quenching was followed by VPC analysis which indicated formation of 4-methyloctan-2-one and 4-methylpentan-2-one in a ratio of 12:1, 89% yield vs. 2-heptanone. The presence of isobutyl methyl ketone was established by coinjection with an authentic sample.

Solvent Effects. Cyclohexenone. To CuCN (89.6 mg, 1.0 mmol) in 1.5 mL of cold (−78 °C) THF was added *n*-BuLi (0.86 mL, 2.0 mmol) and the mixture was warmed to 0 °C. Recooling to −78 °C, addition of cyclohexenone (72.6 μL, 0.75 mmol), and stirring for 1 h were followed by quenching. VPC analysis indicated formation of 3-*n*-butylcyclohexanone in >97% vs. cyclohexanone.

The procedure above was duplicated, substituting Et_2O (1.5 mL) for THF. VPC analysis indicated formation of 3-*n*-butylcyclohexanone in >97% yield.

The procedure above was duplicated, substituting DME (1.5 mL) for THF. VPC analysis indicated formation of 3-*n*-butylcyclohexanone in >97%.

Cyclopentenone. To CuCN (89.0 mg, 1.0 mmol) in 2.0 mL of cold (−78 °C) THF was added vinyllithium (0.96 mL, 2.0 mmol) and the mixture was warmed to 0 °C. Recooling to −78 °C, addition of cyclopentenone (75 μL, 0.90 mmol), and stirring for 0.75 h were followed by quenching. VPC analysis indicated formation of 3-vinylcyclopentanone in 93% yield vs. 3-methylcyclohexanone as internal standard.

The procedure above was duplicated, substituting Et_2O (2.0 mL) for THF. VPC analysis indicated formation of 3-vinylcyclopentanone to the extent of 83%.

The procedure above was duplicated, substituting DME (2.0 mL) for THF. VPC analysis indicated formation of 3-vinylcyclopentanone in 74% yield.

Isophorone. To CuCN (89.6 mg, 1.0 mmol) in 1.0 mL of cold (−78 °C) THF was added vinyllithium (0.96 mL, 2.0 mmol) and the mixture was warmed to 0 °C. Recooling to −78 °C, addition of isophorone (75 μL, 0.5 mmol), and warming to −50 °C was followed by stirring for 2.5 h and quenching. VPC analysis indicated formation of 3,5,5-trimethyl-3-vinylcyclohexanone in 34% yield vs. cyclohexanone.

The procedure above was duplicated substituting Et_2O (1.0 mL) for THF. VPC analysis indicated formation of 3,5,5-trimethyl-3-vinylcyclohexanone to the extent of 98%.

The procedure above was duplicated, substituting DME (1.0 mL) for THF. VPC analysis indicated formation of 3,5,5-trimethyl-3-vinylcyclohexanone in 11% yield.

Mesityl Oxide. To CuCN (89.6 mg, 1.0 mmol) in 1.5 mL of cold (−78 °C) THF was added PhLi (0.92 mL, 2.0 mmol) and the mixture was warmed to 0 °C. Recooling to −78 °C, addition of mesityl oxide (76 μL, 0.66 mmol), and stirring for 1 h were followed by quenching. VPC analysis indicated formation of 4-methyl-4-phenylpentan-2-one in 1% yield vs. phenylacetone as standard.

The procedure above was duplicated, substituting Et_2O (1.5 mL) for THF. VPC analysis indicated formation of 4-methyl-4-phenylpentan-2-one in 98% yield.

To CuCN (89.6 mg, 1.0 mL) in 1.5 mL of cold (−78 °C) DME was added PhLi (0.92 mL, 2.0 mmol) and the mixture was warmed to ambient temperature for 5 min. Recooling to −25 °C (colder temperatures precipitate the cuprate), addition of mesityl oxide (76 μL, 0.66 mmol), and stirring for 1 h were followed by quenching. VPC analysis indicated formation of 4-methyl-4-phenylpentan-2-one to the extent of 8%.

Diethyl [[(*p*-Chlorophenyl)sulfonyl]methyl]phosphonate. Chloromethyl *p*-chlorophenyl sulfide was refluxed with triethyl phosphite to give the phosphonate [bp 165–170 °C (5 mtorr), 87% yield].[29] To this sulfide phosphonate (2.70 g, 9.18 mmol) in 30 mL of MeOH at 0 °C was added oxone[30] (12 g, 19.5 mmol) in 30 mL of H_2O.[31] The resulting white slurry was warmed to room temperature and stirred for 4 h. The reaction was then diluted with H_2O, extracted with $CHCl_3$, washed with brine, and dried over $MgSO_4$. Removal of the solvent yielded 2.87 g (96%) of diethyl[[(*p*-chlorophenyl)sulfonyl]methyl]phosphonate: IR (KBr) cm^{-1} 2990, 2970, 1318, 1258, 1165, 1090; ^1H NMR ($CO(CD_3)_2$) 7.94 (d, 2 H, *J* = 8.4 Hz, aromatic protons), 7.50 (d, 2 H, *J* = 8.4 Hz, aromatic protons), 4.17 (q, 4 H), 3.75 (d, 2 H, *J* = 16.8 Hz), 1.31 (t, 6 H); mass spectrum, *m/e* (relative intensity) 327 (100, M^+).

The α,β-unsaturated sulfone *p*-chlorophenyl *trans*-styryl sulfone was prepared from this sulfone phosphonate via the Posner procedure.[29]

Preparation of *p*-Chlorophenyl 2-Phenylhexyl Sulfone. To a solution of *n*-$Bu_2Cu(CN)Li_2$ at 0 °C, prepared from CuCN (89.7 mg, 1 mmol) and *n*-BuLi (0.73 mL, 1.98 mmol) in 1.5 mL of Et_2O, was added *p*-chlorophenyl *trans*-styryl sulfone (53 mg, 0.19 mmol) in 1.0 mL of Et_2O via cannula. The flask was rinsed with an additional 0.7 mL of Et_2O. An immediate color change to a burnt orange is noted upon addition. The reaction is stirred for 1 h at 0 °C followed by inverse quenching into saturated, aqueous NH_4Cl. Workup involved Et_2O extraction and drying over $MgSO_4$. Column chromatography on SiO_2 with 35% Et_2O/65% Skelly Solve provided 46 mg (72%) of the known[24] 1,4-adduct (R_f 0.34) as a white solid, mp 71–73 °C (lit.[24] mp 69–72 °C).

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Registry No. $Bu(Me)Cu(CN)Li_2$, 86250-96-6; *sec*-$Bu(Me)Cu(CN)Li_2$, 91328-61-9; $H_2C{=}CH(Me)Cu(CN)Li_2$, 91328-63-1; *t*-$Bu(Me)Cu(CN)Li_2$, 91549-30-3; $Ph_2Cu(CN)Li_2$, 80473-66-1; $CH_3CH{=}CHCOCH_3$, 625-33-2; $(CH_3)_2C{=}CHCOCH_3$, 141-79-7; $C_6H_4C(CH_3)_2CH_2COCH_3$, 7403-42-1; $(H_2C{=}CH)_2Cu(CN)Li_2$, 80473-65-0; 2-cyclohexenone, 930-68-7; 2-cyclopentenone, 930-30-3; 3,5,5-trimethyl-2-cyclohexen-1-one, 78-59-1; 3-methyl-2-cyclohexen-1-one, 1193-18-6; 3-vinylcyclopentanone, 50337-14-9; 3-butylcyclohexanone, 39178-69-3; 3-methylcyclohexanone, 591-24-2; 3-*sec*-butylcyclopentanone, 91523-76-1; 3-methylcyclopentanone, 1757-42-2; 3,5,5-trimethyl-3-vinylcyclohexanone, 27749-07-1; 3,5,5-trimethylcyclohexanone, 14376-79-5; 3-methyl-3-*tert*-butylcyclohexanone, 91523-77-2; 4-methyloctan-2-one, 27608-01-1; 4-methylpentan-2-one, 108-10-1.

Supplementary Material Available: Experimental and spectral details associated with compounds prepared in ref 4 (3 pages). Ordering information is given on any current masthead page.

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