scatter and give the most reproducible results. All other aspects of the kinetic and statistical analysis were carried out as described previously.[3]

X-ray Crystal Structure Determination of $[(LDA)_2TMEDA]_\infty$. A 40-mL, thick-walled centrifuge tube containing a stir bar, fitted with a septum, flushed with N_2, and cooled to 0 °C was charged sequentially with hexane (2.5 mL), diisopropylamine (1.4 mL), and 2.5 M *n*-BuLi in hexanes (4.0 mL). The resulting syrupy mixture was placed in a −30 °C freezer for 4 h, during which time a white precipitate of LDA formed. Excess solvent was removed via syringe and the precipitate was washed with 2 × 3 mL of fresh hexane by introduction and removal of the solvent with a syringe at 0 °C. The solid was redissolved by adding hexane (2.5 mL) and TMEDA (45 mL) while stirring. The solution was placed in a −40 °C freezer overnight, during which time needle-like crystals and amorphous solid deposited. The vessel was warmed to 0 °C to dissolve the crystals and the remaining undissolved solid was removed by filtration under N_2. The clear solution was placed in a −10 °C freezer overnight, affording substantially improved needle-like crystals. An additional recrystallization at −10 °C over 12 h provided superb crystals.

MNDO Calculations. MNDO[51] calculations were performed on an IBM 3090 supercomputer by using a modified version of the MOPAC[52] program. The lithium parameters were those of Clark and Theil.[53] The current lithium parameters appear to accurately reproduce lithium interactions with nitrogen and oxygen.[26,54] All structures were fully optimized under the more rigorous criteria of the keyword PRECISE with no constraints unless explicitly stated otherwise. The heats of formation result from extensive searches for the global minimum starting from several different initial geometries. Symmetrical structures were reoptimized from distorted geometries to ensure that the symmetry is not a computational artifact. The keyword GEO-OK was used with caution to override the small interatomic distance check. All energies quoted refer only to enthalpy to the exclusion of entropic effects other than those implicit in the parametric scheme.

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Supplementary Material Available: Table with details of the diffraction analysis, plots of atom labels, and tables of atomic coordinates, bond lengths and angles, and anisotropic thermal parameters for $[(LDA)_2TMEDA]_\infty$ (9 pages). Ordering information is given on any current masthead page.

(51) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899, 4907.
(52) Stewart, J. J. P. *QCPE 581*.
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(54) Kaufmann, E.; Clark, T.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1984**, *106*, 1856. Sapse, A.-M.; Kaufmann, E.; Schleyer, P. v. R.; Gleiter, R. *Inorg. Chem.* **1984**, *23*, 1569.

Direct Formation of Highly Functionalized Allylic Organocopper Reagents from Allylic Chlorides and Acetates

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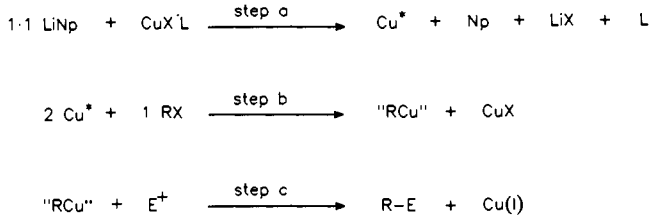
Abstract: The direct formation of highly functionalized allylic organocopper reagents has been carried out using a highly active form of zerovalent copper (Cu*). The cold-temperature reduction of CuCN·*n*LiX complexes by lithium naphthalenide in THF under an argon atmosphere produces the Cu* complex, which reacts rapidly with primary and secondary allyl chlorides at −100 °C with little homocoupling. Allyl, methallyl, and crotyl acetates also oxidatively add with Cu* at low temperatures to afford the corresponding organocopper reagent. Significantly, the allyl chlorides can contain a wide array of functional groups including ketones, α,β-unsaturated ketones, epoxides, alkyl acetates, esters, alkyl chlorides, nitriles, and carbamates. The cross-coupling of the highly functionalized allylic organocopper reagents with various electrophiles proceeds in excellent yields.

Introduction

Allylic organometallics have seen considerable use in organic synthesis for the formation of carbon–carbon bonds.[1] Although organocopper reagents have been used extensively in C–C bond formation,[2] their use in delivering an allylic ligand has been limited when compared to sp^3 and sp^2 ligands. The reasons for the confined use of allylic organocopper reagents lie in both the difficulty in their preparation and their limited thermal stability. Recently, significant progress has been made in both the understanding and the synthetic use of allylic organocopper reagents

Scheme I



(1) (A) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69* 1. (b) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. (c) Biellmann, J. F.; Ducep, J. B. *Org. React. (N.Y.)* **1982**, *27*, 1. (d) Benkeser, R. A. *Synthesis* **1971**, *347*. (e) Chan, T. H.; Fleming, I. *Synthesis* **1979**, 763. (f) Schlosser, M. *Pure Appl. Chem.* **1988**, *60*, 1627. (g) Yamamoto, Y. *Acc. Chem. Res.* **1987**, *20*, 243.
(2) Reviews: (a) Posner, G. H. *Org. React. (N.Y.)* **1972**, *19*, 1. (B) Posner, G. H. *Org. React. (N.Y.)* **1975**, *22*, 253. (c) Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; Wiley: New York, **1980**. (d) Lipshutz, B. H. *Synthesis* **1987**, 325. (e) Lipshutz, B. H. *Tetrahedron* **1984**, *40*, 5005. (f) Normant, J. F. *Synthesis* **1972**, 63.

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due to Lipshutz's development of higher order allylic cyanocuprates that possess both remarkable stability and reactivity.[3] While the higher order cyanocuprates have greatly enhanced the use of organocopper reagents in delivering allylic moieties, their preparation involves several transmetalations from other organometallic species. Also to date, the higher order cuprates have been used to deliver fairly simple allylic ligands such as allyl, methallyl, crotyl, and prenyl groups.

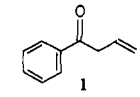
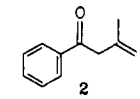
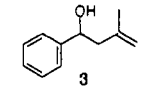
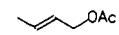
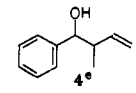
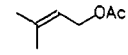
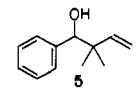
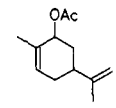
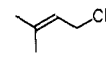
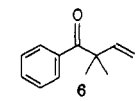
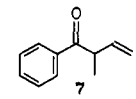
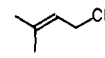
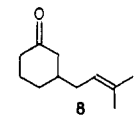
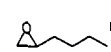
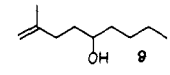
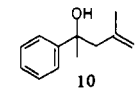
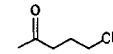
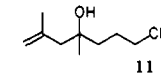
With the development in these laboratories of several highly reactive forms of zerovalent copper,[4] we sought to prepare allylic organocopper reagents directly from the corresponding allylic chlorides, thus bypassing the need of other organometallic species in the transmetalation processes. Moreover, it was hoped that the mild conditions in which the active copper oxidatively adds to allylic chlorides would allow for extensive functionality to be present in the allylic ligand. The preparation of functionalized allylic organocopper reagents and reactions with various electrophiles are discussed.

Results and Discussion

Production of the Active Copper Species. The preparation of highly reactive zerovalent copper (Cu*) by the reduction of copper(I) complexes has led in recent years to a new, straightforward method of preparing functionalized organocopper reagents.[4] The reactions (Scheme I) involve three steps: first, the reduction of a Cu(I) salt by preformed lithium naphthalenide (LiNp) to form the Cu*; second, the oxidative addition of Cu* to an appropriate organic halide; and finally, the cross-coupling of the newly formed organocopper reagent with an electrophile. The entire process is carried out under an atmosphere of purified argon using THF as a solvent. Initially, Cu* was made by the reduction of $CuI{\cdot}PR_3$ complexes. While Cu* produced from Cu(I) phosphine complexes was shown to be highly reactive, the separation of phosphines made product isolation difficult. Also, the reactivity of both the Cu* and the resulting organocopper reagent was dependent on the type of phosphine used. For example, while organocopper reagents made from $CuI{\cdot}PBu_3$ were found to be more nucleophilic and capable of epoxide opening and conjugate addition reactions (Scheme I, step c), the oxidative addition to alkyl bromides produced significant homocoupling (Scheme I, step b).[4c] Other phosphines, PPh_3 for example, oxidatively added to organic halides with diminished homocoupling; however, the resulting organocopper reagents showed reduced reactivity with electrophiles. Thus, it was hoped that a new type of Cu(I) complex could be found that circumvented these problems. In fact, the readily available CuCN salt, solubilized by either LiCl or LiBr, was shown to produce Cu* which not only oxidatively added with little homocoupling but also resulted in an organocopper reagent which reacted with a wide range of electrophiles.[5]

Initial attempts to make Cu* from $CuCN{\cdot}n$LiX did not seem promising since Cu* derived from this Cu(I) complex showed a reduction in reactivity toward oxidative addition with organic halides as compared to the $CuI{\cdot}PR_3$ complex. Also, reactions with alkyl bromides were accompanied by significant amounts of eliminated byproducts. These problems were overcome by carrying out the reduction at very low temperatures, ca. −100 °C. The Cu* species produced by this low-temperature reduction showed

Table I. Reaction of Nonfunctionalized Allyl Chlorides and Acetates with Cu* and Cross-Coupling with Various Electrophiles

Entry	RX[a]	Electrophile	Product	% Yield[b,c]
1		PhCOCl	 1	65
2		PhCOCl	1	63
3		PhCOCl	 2	75
4		PhCHO	 3	79
5		PhCHO	 4[e]	81
6		PhCHO	 5	27
7		PhCHO	--[f]	--
8		PhCOCl	 6	74
9		PhCOCl	 7	72
10		$C_6H_8(=O)$[g]	 8	81
11		 [h]	 9	67
12		$PhCOCH_3$	 10	91
13			 11	77

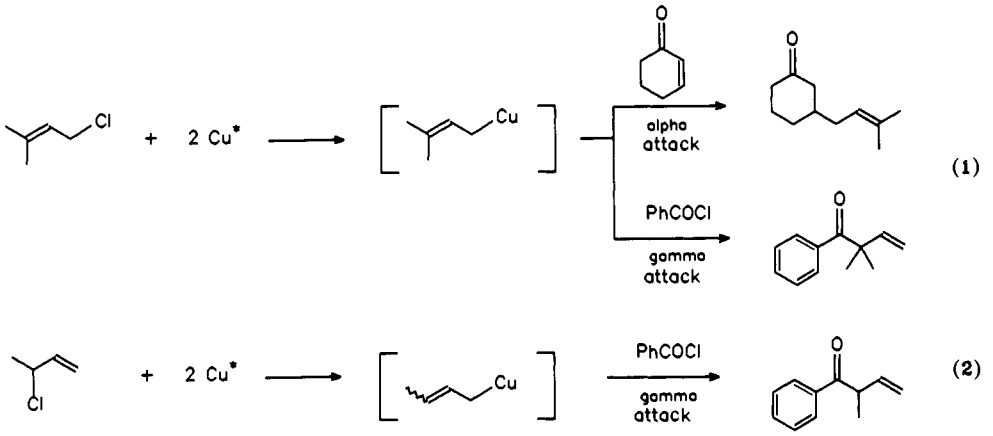
[a] The ratio between allyl chloride and Cu* was 0.4:1, respectively. The ratio between allyl acetate and Cu was 0.25:1, respectively. [b] Isolated yields. [c] For reactions with PhCOCl as the electrophile, the yields are based on RCl or ROAc with a 3:1 excess (based on RCl or ROAc) of the acid chloride used. For reactions using all other electrophiles, the yields are based on the final electrophile with the ratio of RCl or ROAc to electrophile being between 2.5:1 and 2:1, respectively. [d] Ninety-eight percent trans isomer. [e] A 70:30 mixture of syn and anti diastereomers was observed by NMR spectroscopy. [f] No desired product was isolated; instead 45% of carvol and 15% of starting material were recovered. [g] A 3-fold excess of TMSCl with respect to 2-cyclohexenone was added prior to enone addition. [h] Two equivalents of MeLi with respect to RCl was added to the mixture prior to the addition of the epoxide.

(3) (a) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Smith, R. A. *J. Org. Chem.* **1989**, *54*, 4977. (b) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Smith, R. A.; Crow, R.; Behling, J. R. *J. Am. Chem. Soc.* **1990**, *112*, 4063. (c) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Smith, R. A. *J. Am. Chem. Soc.* **1990**, *112*, 4404. (d) Lipshutz, B. H.; Elworthy, T. R. *J. Org. Chem.* **1990**, *55*, 1696. (e) Lipshutz, B. H.; Elworthy, T. R. *Tetrahedron Lett.* **1990**, *31*, 477.

(4) (a) Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1984**, *49*, 5280. (b) Wu, T.-C.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1987**, *52*, 5057. (c) Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1987**, 52, 5056. (d) Wu, T.-C.; Rieke, R. D. *Tetrahedron Lett.* **1988**, *29*, 6753. (e) Wehmeyer, R. M.; Rieke, R. D. *Tetrahedron Lett.* **1988**, *29*, 4513. (f) Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1988**, *53*, 4482. (g) Rieke, R. D.; Wehmeyer, R. M.; Wu, T.-C.; Ebert, G. W. *Tetrahedron* **1989**, *45*, 443. (h) Rieke, R. D.; Dawson, B. T.; Stack, D. E.; Stinn, D. E. *Synth. Commun.* **1990**, *20*, 2711.

(5) Stack, D. E.; Dawson, B. T.; Rieke, R. D. *J. Am. Chem. Soc.* **1991**, *113*, 4672.

Scheme II



reactivity comparable to that of Cu* derived from CuI·PR_3 as well as diminished side reactions. Since Cu* formed from CuCN·*n*LiX showed a low proclivity toward homocoupling of alkyl bromides, it was thought that this new form of Cu* may be used to produce *allyl* organocopper reagents without significant Wurtz-type homocoupled side products.

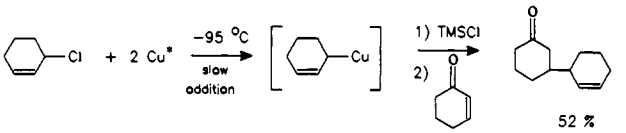
Reaction of Cu* with Nonfunctionalized Allylic Chlorides and Acetates. Table I shows the reaction of several nonfunctionalized allyl chlorides and acetates with Cu* derived from either CuCN·2LiBr or CuCN·*n*LiCl (where n = 1 or 2) and their cross-coupling with various electrophiles. While either CuCN·2LiBr or CuCN·*n*LiCl gave comparable results,[6] CuCN·*n*LiCl was used more often due to the smaller amount of lithium salt required. The allyl chloride or acetate is added to Cu* at −100 °C to avoid Wurtz-type byproducts. Also, the Cu* is more reactive toward oxidative addition with allyl chlorides and acetates at −100 °C than at warmer temperatures, such as −78 °C. To further diminish homocoupling, the allyl chlorides are cooled to −78 °C prior to addition to Cu*. The oxidative additions between Cu* and the allyl chlorides occur rapidly with 0.4 equiv of RCl (relative to Cu*) being consumed in less than 5 min. GC analysis showed that less than 10% of the homocoupled byproduct was formed. The electrophile is added to the allyl organocopper reagent at −90 °C, and the mixture is allowed to warm typically to −20 °C for an appropriate amount of time. After workup, the products are easily isolated via flash silica gel chromatography.

The reaction of allyl acetates is limited since disubstitution in either the α or γ positions renders them inactive toward oxidative addition with Cu* (Table I, entries 6 and 7). The addition of various Lewis acids to the substituted allyl acetates did not prove fruitful. The reaction of crotyl acetate with benzaldehyde produced a 70:30 syn to anti mixture of the resulting homoallyl alcohol (entry 5).[7] Later discussion will show how close proximity of a functional group can increase diastereoselectivity.

Addition of ketones was also carried out (Table I, entries 12 and 13) with chemoselective reaction to the carbonyl in the presence of a nitrile functionality (entry 13). Thus, the formation of homoallyl alcohols containing nitrile groups is possible from the appropriate ketone or aldehyde (vide infra).

The addition of MeLi increases the nucleophilicity of the allylic organocopper reagents and allows substitution reactions with epoxides (Table I, entry 11). Without the addition of MeLi, only 6% of the alcohol product is isolated. With addition of MeLi, the yield is increased to 67%. The MeLi is believed to act as a "dummy" nontransferable ligand, presumably forming a higher order cuprate.

Scheme III



The reaction of the allylic organocopper reagents with carbonyls and acid chlorides occurs exclusively at the γ position (Table I, entries 5, 6, and 8). The reaction of a secondary allyl choride (entry 9) with benzoyl chloride, at first, appears to involve α attack, yet it is believed that the organocopper reagent equilibrates to the more favorable primary allyl structure (Scheme II). The reaction of prenylcopper to cyclohexenone is known to occur at the α position;[3c,8] thus the product in entry 8 must result from γ attack with the acid chloride. Therefore, the reaction of 3-chloro-1-butene must also involve δ attack of the primary allylic organocopper. Other zerovalent metals have been shown to react with secondary allyl chlorides and equilibrate predominantly to the primary structure.[9]

Recently, Lipshutz reported the preparation and reactions of *cyclic* allylic higher order cyanocuprates.[10] Transmetalation of acyclic allylic stannanes with $Me_2Cu(CN)Li_2$ affords the corresponding $(H_2C{=}CHCH_2)_2Cu(CN)Li_2$ reagent.[3b] The cyclic allylic stannanes, however, failed to transmetalate with complete conversion in forming the respective higher order cuprate. An alternative procedure involved the lithiation of the cyclic allylstannane prior to complexation with CuCN·LiCl. 3-Chlorocyclohexene likewise displayed atypical behavior in the reaction with active copper. Unlike the acyclic allyl chlorides, 3-chlorocyclohexene suffered from significant homocoupling when added to Cu*.[11] Homocoupling, however, was reduced by the slow addition of cyclic allyl chloride (diluted in THF) to the zerovalent copper. Subsequent reaction with 2-cyclohexenone resulted in the conjugate addition product in fair yield (Scheme III).

Reaction of Cu* with Functionalized Allyl Chlorides. Primary and secondary allyl chlorides containing diverse functionality were readily prepared by a method developed by Wolinsky.[12] Table

(6) For the first report of solubilized CuCN with LiX, see: Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390. For CuCn·*n*LiX's use as a transmetalating agent with organozinc reagents and subsequent reactions, see, for example: (a) Rao, S. A.; Knochel, P. *J. Am. Chem. Soc.* **1991**, *113*, 5735. (b) Knochel, P. *J. Am. Chem. Soc.* **1990**, *112*, 7431. (c) Knochel, P.; Chou, T.-S.; Chen, H. G.; Rozema, M. J. *J. Org. Chem.* **1989**, *54*, 5202. (d) Yeh, M. C. P.; Knochel, P.; Santa, L. E. *Tetrahedron Lett.* **1988**, *29*, 3887. (e) Berk, S. C.; Knochel, P.; Yeh, M. C. P. *J. Org. Chem.* **1988**, *53*, 5789.

(7) Ratio determined by ^{1}H NMR.

(8) The presence of TMSCl was essential for the conjugate addition reactions involving the organocopper reagents derived from the CuCN·*n*LiX active copper. The addition of BF_3·OEt_2 as the Lewis acid provided a diminished yield of 1,4-adduct (≈60%) by comparison and offered no additional advantage in a reaction where BF_3 and TMSCl were both added.

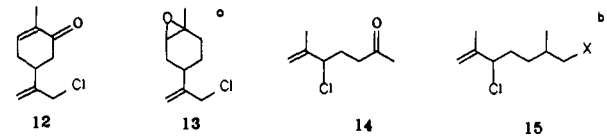
(9) (a) Nordlander, J. E.; Young, W. G.; Roberts, J. D. *J. Am. Chem. Soc.* **1961**, *83*, 494. (b) Whitesides, G. M.; Nordlander, J. E.; Roberts, J. D. *J. Am. Chem. Soc.* **1962**, *84*, 2010.

(10) Lipshutz, B. H.; Ung, C.; Elworthy, T. R; Reuter, D. C. *Tetrahedron Lett.* **1990**, *31*, 4539.

(11) Homocoupling byproduct was estimated to range from 50 to 75%.

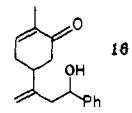
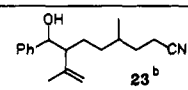
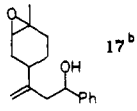
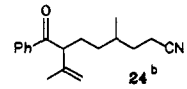
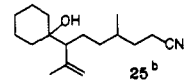
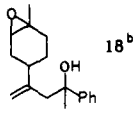
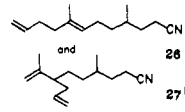
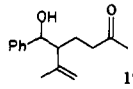
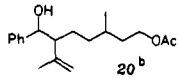
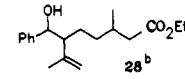
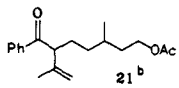
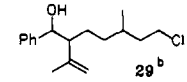
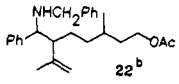
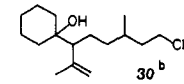
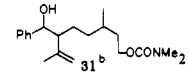
(12) (a) Hegde, S. G.; Vogel, M. K.; Saddler, J.; Hrinyo, T.; Rockwell, N.; Haynes, R.; Oliver, M.; Wolinsky, J. *Tetrahedron Lett.* **1980**, *21*, 441. (b) Hegde, S. G.; Wolinsky, J. *Tetrahedron Lett.* **1981**, *22*, 5019. (c) Hegde, S. G.; Beckwith, D.; Doti, R.; Wolinsky, J. *J. Org. Chem.* **1985**, *50*, 894.

Table II. Reaction of Functionalized Allyl Chlorides with Cu* and Cross-Coupling with Various Electrophiles



12 **13** **14** **15**

X = CH_2OAc **15a**
CH_2CN **15b**
CO_2Et **15c**
CH_2Cl **15d**
$CH_2OCON(CH_3)_2$ **15e**

Entry	RCl[c]	Electrophile	Product	% Yield[d,e]	Entry	RCl[c]	Electrophile	Product	% Yield[d,e]
1	**12**	PhCHO	 **16**	67	9	**15b**	PhCHO	 **23**[b]	89
2	**13**	PhCHO	 **17**[b]	94	10	**15b**	PhCOCl	 **24**[b]	70
3	**13**	PhCHO	**17**	89[f]	11	**15b**	$C_6H_{10}(=O)$	 **25**[b]	65
4	**13**	$PhCOCH_3$	 **18**[b]	90	12	**15b**	$CH_2=CHCH_2Br$	 **26** and **27**[h]	61
5	**14**	PhCHO	 **19**[g]	62	13	**15b**	$CH_2=CHCH_2Br$	—[i]	100
6	**15a**	PhCHO	 **20**[b]	83	14	**15c**	PhCHO	 **28**[b]	73
7	**15a**	PhCOCl	 **21**[b]	70	15	**15d**	PhCHO	 **29**[b]	65
8	**15a**	$PhCH=NCH_2Ph$	 **22**[b]	79	16	**15d**	$C_6H_{10}(=O)$	 **30**[b]	51
					17	**15e**	PhCHO	 **31**[b]	96

[a] Mixture of cis and trans isomers. [b] Mixture of diastereomers. [c] Ratio of RCl to Cu* is 0.4:1, respectively. [d] Isolated yields. [e] Yields involving acid chlorides are based on RCl with a 3-fold excess of acid chloride used. With other electrophiles, the yields are based on the final electrophile with the RCl to electrophile ratio being 2:1, respectively. [f] The organocopper solution was warmed to 0 °C for 1 h prior to addition of PhCHO. [g] The syn isomer was assigned on the basis of the large coupling constant observed for the proton attached to the hydroxyl carbon, J = 9.4 Hz. [h] The allyl bromide was used in excess. The isomers were separated via preparative TLC. The ratio of **26** to **27** equaled 67:33, respectively. [i] The allyl bromide was used as the limiting reagent. The ratio of **26** to **27** equaled 83:17, respectively.

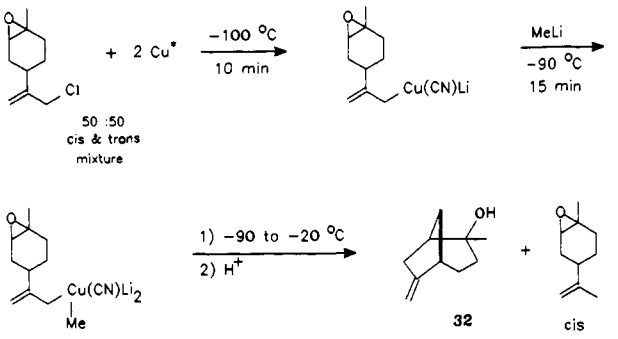
II shows that a wide range of functionalities are tolerated by Cu* oxidative addition to allyl chlorides. To date, allyl organocopper reagents containing ketone, α,β-unsaturated ketone, epoxide, nitrile, alkyl acetate, ester, alkyl chloride, and carbamate functionalities have been prepared. The ability of Cu* to tolerate a wide range of functionalities allows the facile formation of highly functionalized homoallyl alcohols, β,γ-unsaturated ketones, and amines as shown in Table II. The organocopper reagents derived from primary allyl chlorides show remarkable thermostability with little decomposition even at 0 °C (Table II, entries 2 and 3). Allyl organocopper reagents made from secondary allyl chlorides decompose at a significant rate (within 1 h) at 0 °C.

Similar to the allyl organocopper reagents containing no functionality (Table I, entry 5), the functionalized allyl organocopper reagents, where the functional group is removed from the carbon–copper bond, show limited diastereoselectivity in the reaction with aldehydes. However, the presence of a carbonyl group two carbons from the γ position increases the syn isomer above 97%[13] (Table II, entry 5).[14] Since diastereoselectivity in acyclic systems is a prominent goal in organic chemistry,[1g,15] we are investigating the directing effects of other functional groups having similar proximity.

As mentioned previously, the addition of MeLi to the allyl organocopper species increases the reactivity of the allyl organocopper reagent such that reactions with epoxides occur (Table I, entry 11). When MeLi was added to the functionalized or-

(13) Only the syn isomer was seen by ^1H and ^{13}C NMR.
(14) The same diastereoselectivity was observed with the reaction of **14** with *trans*-cinnamaldehyde, yielding the syn isomer in 63% yield.
(15) Reviews: (a) Heathcock, C. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, **1984**; Vol. 3, 111. (b) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1. (c) Seebach, D.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654. (d) Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.

Scheme IV



ganocopper species derived from allyl chloride **13** (see Scheme IV), an intramolecular opening of the epoxide produced the bicyclic product **32**. Since the starting allyl chloride **13** is a 50:50 mixture of cis and trans epoxides, only half of the available organocopper reagent (the one derived from the trans isomer) has the proper conformation to undergo addition to the epoxide.[16] The diaxial relationship between the newly formed C–C bond and the carbon–hydroxyl bond leads to a stereogenic center at C-2 in the bicyclic product. Moreover, the unreacted epoxide (protonated after the reaction was quenched with NH_4Cl_{sat}) was enriched by over 90% in the cis isomer.

^{13}C NMR Studies of Cu* and Organocopper Reagents. The first two steps of an active copper reaction involve the reduction of the CuCN·*n*LiX complex with 1 equiv of lithium naphthalenide and the formation of the organocopper reagent. The relative simplicity of the first steps encouraged further investigation of the reaction mixtures with ^{13}C NMR. Indeed, the ^{13}C NMR spectrum of CuCN solubilized with LiBr resulted in an observable signal at 145.0 ppm for the copper(I) nitrile. Reduction of CuCN·2LiBr at −100 °C with lithium naphthalenide provided a sample of Cu*, which in turn was probed by ^{13}C NMR at temperatures ranging from −90 to −20 °C. Notably, a peak associated with LiCN (166.9 ppm) was not observed. Furthermore, the peaks associated with naphthalene were absent.

Organocopper reagents oftentimes are soluble in THF, and the NMR studies of higher order lithium cyanocuprates have proved controversial.[17] Oxidative addition involving MeI, EtBr, or methallyl chloride with Cu* presumably resulted in an insoluble organocopper complex which disallowed characterization. Nitrile signals were not observed, either complexed to copper or in the form of free LiCN. As the zerovalent active copper is a one-electron reagent, the maximum ratio for oxidative addition of RX with Cu* is 1:2, respectively. Therefore, since LiCN was not observed, all nitrile ligands must be incorporated in some insoluble RCu structure. Also, addition of RX to active copper resulted in a reappearance of the naphthalene signals not observed in the Cu* spectrum. While the disappearance of the naphthalene peaks may be due to a paramagnetic Cu* species, other ^{13}C NMR signals of small amounts of additives (*n*-butyl ether) were observed at low concentrations, ca 0.02 M.[18] The possibility of a zerovalent copper–naphthalene complex, insoluble in THF, could account for the disappearance of the naphthalene peaks. Further investigations into the nature of the Cu* species are under way.

Conclusions

A phosphine-free highly reactive zerovalent copper reagent has been developed which will rapidly undergo oxidative addition to a variety of carbon–halogen bonds at low temperatures. Significantly, this copper reagent will react with allylic halides and some allylic acetates to produce high yields of the corresponding allylic copper reagent. It is of special note that the allylic halides can contain a wide range of functionality including ketones, α,β-unsaturated ketones, epoxides, alkyl acetates, esters, alkyl chlorides, nitriles, and carbamates. These allylic organocopper reagents can be cross-coupled with a wide variety of electrophiles in excellent yield. The ability to generate highly functionalized allylic organocopper reagents provides a novel route to a wide range of intramolecular additions and cross-coupling reactions. Current efforts are being directed toward a more comprehensive understanding of the chemistry of the highly functionalized organocopper reagents as well as second-generation zerovalent copper reagents.

Experimental Section

All manipulations were carried out in a Schlenk apparatus connected to a dual manifold providing vacuum and argon. The Linde prepurified grade argon was further purified with a BASF R3-11 catalyst column at 150 °C, a phosphorus pentoxide column, and a granular potassium hydroxide column. Lithium, naphthalene, CuCN, LiCl, and LiBr were weighed as needed in an argon Vacuum Atmosphere Co. drybox. All chemicals were purchased from Aldrich Chemical Co. and used without further purification unless otherwise specified. LiCl and LiBr were dried at 120 °C, 0.5 Torr, overnight before being transferred to the drybox. Tetrahydrofuran was distilled from a Na/K alloy under an argon atmosphere immeditely before use. Low-temperature conditions were maintained by utilizing a Neslab Endocal ULT-80 refrigerated circulating bath or by utilizing dry ice/acetone baths.

NMR spectra were obtained from a Nicolet NT-360, Varian VXR-200, G.E. Omega-500, or G.E. Omega-300. All NMR samples were dissolved in $CDCl_3$. ^1H NMR spectral chemical shifts are reported in parts per million (δ) downfield from TMSCl as an internal standard. ^{13}C NMR chemical shifts (δ) were reported in reference to the 77.00 ppm peak for $CDCl_3$. Infrared spectra were recorded on an Analect RFX-65 FTIR spectrophotometer. Analytical GC was performed on a Hewlett-Packard 5890A gas chromatograph equipped with 12-ft lengths of $^1/_8$-in. stainless steel tubing packed with 5% SP 2100 or SP 2250 on a Supelco support, and interfaced with a Perkin-Elmer LCI-100 integrator. GC yields were quantified by determining response factors for pure samples and calculating the yield relative to an internal standard.

Product purification was typically performed by column chromatography with use of Merck flash silica gel 60 (230–400 mesh). Fractions were monitored with analytical thin-layer aluminum-backed Merck 5735 indicating plates precoated with silica gel 60 F_{254} (layer thickness 0.2 mm). If the product was not UV active, the thin-layer plates were typically developed with a vanillin solution.[19] Elemental analyses were performed by Galbraith Labs, Knoxville, TN. High-resolution mass spectra were obtained from the Midwest Regional Center of Mass Spectrometry, University of Nebraska—Lincoln.

Typical Procedure for the Formation of Cu*. Lithium (5.43 mmol) and naphthalene (6.45 mmol) were weighed into a 100-mL, two-neck round-bottom flask equipped with an elliptical Teflon stir bar in an argon drybox, and the flask was sealed with a septum and stopcock outlet. Similarly, CuCN (5.03 mmol) and LiCl (6.17 mmol) were weighed into a 50-mL, two-neck round-bottom flash, equipped with a stir bar, and the flask was sealed with a septum and stopcock. The lithium and naphthalene were dissolved in 15 mL of THF, and the solution was stirred for 2–3 h until the lithium was consumed. The CuCN·LiCl complex was dissolved in 5 mL of THF, and after 30 min, the solution was cooled to 0 °C. The CuCN·LiCl solution was transferred via a cannula to the lithium naphthalenide, which had previously been cooled to −100 °C in a bath of liquid N_2 and a 4:1 (v/v) mixture of hexane and Et_2O, respectively. The solution was stirred for 5–10 min at −100 °C and was then ready for immediate use.

Typical Procedure for the Formation of Allyl Organocopper Reagents from Allyl Acetates. Methally acetate (2.00 mmol) was weighed into an 8-mL vial, and the vial was sealed with a septum. Using a freeze–pump–thaw technique, air was removed from the vial and replaced with argon. THF (4 mL) was added to the vial, and the methally acetate was transferred via a cannula to a suspension of Cu* (8.00 mmol) cooled at −100 °C. The solution was allowed to warm from −100 to −78 °C for 10 min, and a temperature of −78 °C was maintained for an additional 10 min. The allyl organocopper was then ready for use with an appropriate electrophile.

Typical Procedure for the Cross-Coupling of Allyl Organocopper Reagents with Acid Chlorides. Prenyl chloride (1.97 mmol) was weighed

(16) Johnson, C. R.; Herr, R. W.; Wieland, D. M. *J. Org. Chem.* **1973**, *38*, 4263.

(17) (b) Bertz, S. H. *J. Am. Chem. Soc.* **1990** *112*, 4031. (b) Lipshutz, B. H.; Sharma, S.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 4032. (c) Bertz, S. H. *J. Am. Chem. Soc.* **1991**, *113*, 5470.

(18) A conservative estimate for the concentration of the organocopper reagent would be greater than 0.06 M.

(19) *Dyeing Reagents for Thin Layer and Paper Chromatography*; E. Merck: Darmstadt, Germany, 1980.

into an 8-mL vial, and the vial was sealed with a septum. Using a freeze–pump–thaw technique, air was removed from the via and replaced with argon. THF (4 mL) was added to the vial, and the prenyl chloride was cooled to −78 °C (dry ice and acetone). The allyl chloride was transferred via a cannula to a suspension of Cu* (8.03 mmol) at −100 °C. The solution was stirred at −100 °C for 10 min and warmed to −90 °C. Benzoyl chloride (6.00 mmol), admixed with 2–4 mL of THF in a vial, was transferred via a cannula to the organocopper solution at −90 °C. The reaction mixture was immediately warmed to −78 °C and held at −78 °C for 30 min. The solution was quenched with NH_4Cl_{sat} and extracted with Et_2O (2 × 50 mL), 0.5 M NaOH (50 mL), and brine (2 × 50 mL), and the organic layer was dried over $MgSO_4$. Flash silica gel chromatography using gradient mixtures of hexane and ethyl acetate afforded 2,2-dimethyl-1-phenyl-3-buten-1-one (**6**, 1.46 mmol) in 74% yield.

Typical Procedure for Intermolecular Epoxide Openings. Methallyl chloride (3.16 mmol) was weighed into an 8-mL vial, and the vial was sealed with a septum and placed under argon as stated previously. THF (2–4 mL) was added to the vial, and the allyl chloride solution was cooled to −78 °C. The allyl chloride was added rapidly via a cannula to a suspension of Cu* (7.96 mmol) at −100 °C, and the resulting mixture was stirred for 10 min. MeLi (6.30 mmol) was added to the newly formed organocopper solution at −90 °C, and the mixture was stirred for 15 min. 1,2-Epoxyhexane (1.01 mmol) was added from a vial to the new organocopper solution at −90 °C, and the mixture was warmed to 0 °C over 3 h and held at 0 °C for 12 h. The reaction was quenched with NH_4Cl_{sat}, extracted with Et_2O (2 × 50 mL), and washed with brine (2 × 50 mL), and the organic layer was dried over $MgSO_4$. Flash silica gel chromatography, using gradient mixtures of hexane and ethyl acetate, afforded 2-methyl-1-nonen-5-ol (0.68 mmol, **9**): R_f = 0.23 in 9:1 (v/v) hexane and ethyl acetate, respectively (67% yield); IR (neat) 3317, 3070, 3016, 2954, 2931, 2869, 2854, 1647, 1452, 1375, 1126, 1084, 1053, 1036, 1003, 885 cm^{-1}; ^1H NMR (360 MHz) 4.72 (br s, 2 H), 3.63–3.58 (m, 1 H), 2.20–2.05 (m, 2 H), 1.74 (s, 3 H), 1.68–1.30 (m, 8 H), 0.91 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (50 MHz) 145.9, 110,0, 71.7, 37.2, 35.2, 34.0, 27.8, 22.7, 22.4, 14.0.

Procedure for the Conjugate Addition of a Cyclic Allyl Organocopper Reagent. In an effort to diminish homocoupling, 3-chlorocyclohexene (3.20 mmol) was weighed in a large vial, and the vial was capped with a septum. Under an argon atmosphere, THF (10 mL) was added to the via. To a stirring active copper solution (8.23 mmol in 23 mL of THF) at −95 °C, the allyl chloride was delivered dropwise from a cannula, over 30 min. After 5 min; TMSCl (2.84 mmol) was injected neat prior to the neat, dropwise injection of 2-cyclohexenone (0.82 mmol). The reaction flask was placed in a −78 °C bath and allowed to gradually warm to room temperature. The reaction mixture was quenched with NH_4Cl_{sat} (50 mL), and Et_2O (25 mL) was added prior to further extraction of the organic layer with 0.5 M HCl (50 mL), water (50 mL), and brine (50 mL). The combined aqueous layers were back extracted with Et_2O (30 mL). The combined organic layers were dried with $MgSO_4$ and reduced in volume for column chromatography. 3-(2-Cyclohexenyl)cyclohexanone (0.43 mmol) was isolated in 52% yield: R_f = 0.31 in 9:1 (v/v) hexane and ethyl acetate, respectively; ^1H NMR (300 MHz), 5.73–5.67 (m, 1 H), 5.53–5.50 (m, 1 H), 2.37–1.16 (m, 16 H); ^{13}C NMR (75 MHz) 212.50, 212.47, 129.1, 128.8, 128.7, 128.5, 45.2, 45.0, 43.6, 41.4, 40.0, 39.9, 28.4, 28.1, 25.52, 25.46, 25.41, 25.3, 25.2, 25.1, 21.8, 21.7; mass spectrum calcd for $C_{12}H_{18}O$ 178.1358, found 178.1354.

Typical Procedure for Additions of Allyl Organocopper Reagents to Aldehydes, Ketones, Imines, and Allyl Bromides. The functionalized allyl chloride **15e** (2.01 mmol) was weighed into an 8-mL vial, and the vial was sealed with a septum and placed under argon. THF (4 mL) was added to the vial, and the vial was cooled to −78 °C. The allyl chloride was added rapidly to a suspension of Cu* (5.02 mmol) at −100 °C, and the resulting mixture was mixed for 10 min. Benzaldehyde (1.02 mmol) was delivered from a vial in 2 mL of THF to the organocopper solution at −90 °C. The reaction mixture was allowed to warm to −20 °C for 3 h.[20] The solution was quenched with NH_4Cl_{sat}, extracted with Et_2O (2 × 50 mL), and washed with brine (2 × 50 mL), and the organic layer was dried over $MgSO_4$. Flash silica gel chromatography, utilizing gradient mixtures of hexane and ethyl acetate, afforded 6-(hydroxyphenylmethyl)-3,7-dimethyl-7-octenyl *N,N*-dimethylcarbamate (**31**, 0.98 mmol): R_f = 0.26 in 7:3 (v/v) hexane and ethyl acetate, respectively (96% yield); IR (neat) 3442, 3066, 3028, 2954, 2929, 2871, 1707, 1689, 1645, 1495, 1454, 1406, 1373, 1275, 1196, 1063, 1028, 889, 769, 702 cm^{-1}; ^1H NMR (360 MHz) 7.35–7.27 (m, 5 H), 5.04 ((s, 1 H), and a singlet at 4.73 for a diastereomer), 4.94 ((s, 1 H) and a singlet at 4.60 for a diastereomer), 4.54 ((d, J = 7.32 Hz, 1 H) and a doublet, J = 9.34 Hz at 4.38 for a diastereomer), 4.11–3.94 (m, 2 H), 2.89–2.39 (m, 6 H), 2.28–2.22 (m, 1 H), 1.99 (s, 1 H), 1.72 ((s, 3 H) and a singlet at 1.54 for a diastereomer), 1.55–0.77 (m, 10 H); ^{13}C NMR (50 MHz) 156.5, 144.8, 144.6, 143.5, 142.7, 128.0, 127.7, 127.4, 126.9, 126.8, 126.6, 126.3, 115.5, 115.4, 112.0, 76.1, 75.1, 63.7, 63.6, 63.5, 63.4, 56.0, 55.7, 54.7, 54.6, 36.2, 36.1, 35.9, 35.8, 35.7, 35.6, 35.3, 35.1, 34.5, 34.3, 34.0, 30.0, 29.6, 29.1, 25.9, 25.7, 25.4, 25.3, 20.8, 20.7, 19.6, 19.5, 19.0, 18.7, 18.1, 17.9. Anal. Calcd ($C_{20}H_{31}NO_3$): C, 72.03; H. 9.37; N, 4.20. Found: C, 71.86; H, 9.22; N, 4.48.

5-Hydroxy-5,7-dimethyl-7-octenenitrile (11): R_f = 0.11 in 4:1 (v/v) hexane and ethyl acetate, respectively (77% yield); IR (neat) 3477, 3074, 2970, 2929, 2247, 1714, 1643, 1458, 1427, 1375, 1319, 1236, 1151, 1109, 929, 893, 787 cm^{-1}; ^1H NMR (360 MHz) 4.97–4.91 (m, 1 H), 4.79–4.72 (m, 1 H), 2.38 (t, J = 6.9 Hz, 2 H), 2.25–2.15 (m, 2 H), 1.85–1.83 (m, 3 H), 1.82–1.74 (m, 2 H), 1.62–1.57 (m, 2 H), 1.19 (s, 3 H); ^{13}C NMR (50 MHz) 142.1, 119.6, 115.1, 71.7, 49.6, 40.9, 26.8, 24.9, 20.1, 17.4

5-(1-Methylene-3-hydroxy-3-phenylpropyl)-2-methyl-2-cyclohexenone (16): 67% yield; IR (neat) 3438, 3084, 3062, 3028, 2887, 1670, 1493, 1452, 1433, 1383, 1367, 1250, 1109, 1053, 760, 731, 702 cm^{-1}; ^1H NMR (360 MHz) 7.35–7.25 (m, 5 H), 6.77–6.72 (m, 1 H), 5.02–4.97 (m, 2 H), 4.80 (t, J = 6.7 Hz, 1 H), 2.72–2.57 (m, 2 H), 2.49–2.44 (m, 3 H), 2.42–2.23 (m, 3 H), 1.78 (s, 3 H); ^{13}C NMR (50 MHz) 199.5, 147.6, 147.5, 144.6, 144.3, 143.9, 135.4, 135.3, 128.4, 127.6, 125.7, 112.5, 72.5, 72.4, 44.6, 43.3, 43.1, 40.8, 40.6, 31.6, 31.4; mass spectrum calcd for $C_{17}H_{20}O_2$ [M − H_2O]$^{\cdot+}$ 238.1358, found 238.1367.

3-(3,4-Epoxy-4-methylcyclohexyl)-1-phenyl-3-buten-1-ol (17): R_f = 0.32 in 4:1 (v/v) hexane and ethyl acetate, respectively (94% yield); IR (neat) 3424, 3083, 3062, 3027, 2973, 2929, 2863 cm^{-1}; ^1H NMR (200 MHz) 7.35–7.25 (m, 5 H), 4.96–4.89 (m, 2 H), 4.78–4.75 (m, 1 H), 3.06 ((m, 1 H) multiplets also seen at 3.04, 2.98, 2.97), 2.46–2.32 (m, 3 H), 2.19–2.01 (m, 2 H), 1.86–1.55 (m, 4 H), 1.43–1.24 ((m, 4 H) including singlets at 1.313, 1.309, 1.30, 1.29); ^{13}C NMR (125 MHz) 150.04, 150.01, 149.9, 149.6, 144.0, 128.3, 127.4, 125.8, 125.7, 111.7, 111.5, 111.4, 111.3, 72.1, 72.0, 71.9, 71.7, 60.4, 60.3, 59.13, 59.10, 57.6, 57.5, 57.4, 57.3, 45.7, 45.6, 45.3, 45.0, 39.4, 38.7, 34.5, 34.4, 31.5, 30.8, 30.73, 30.68, 30.6, 30.3, 28.7, 28.4, 26.4, 26.1, 24.8, 24.5, 24.2, 24.1, 22.9. Anal. Calcd ($C_{17}H_{22}O_2$): C, 79.03; H, 8.58. Found: C, 78.63; H, 8.49.

3-(3,4-Epoxy-4-methylcyclohexyl)-1-methyl-1-phenyl-3-buten-1-ol (18): R_f = 0.25 in 4:1 (v/v) hexane and ethyl acetate, respectively (90% yield); ^1H NMR (500 MHz) 7.42–7.39 (m, 2 H), 7.32–7.29 (m, 2 H), 7.23–7.20 (m, 1 H), 4.85–4.74 (m, 2 H), 2.94–2.85 (m, 1 H), 2.65–2.59 (m, 1 H), 2.47–2.44 (m, 1 H), 2.36 (t, J = 15.8 Hz, 1 H), 2.20–1.81 (m, 2 H), 1.71–1.64 (m, 1 H), 1.57–1.02 ((m, 10 H) includes four singlets at ca. 1.55 and four singlets at ca 1.22); ^{13}C NMR (125 MHz) 150.7, 150.4, 150.0, 149.97, 147.91, 147.88, 147.8, 147.7, 127.97, 127.94, 126.5, 126.47, 126.42, 126.4, 124.72, 124.69, 124.6, 112.9, 112.8, 112.77, 112.5, 73.5, 73.4, 73.2, 60.3, 60.0, 59.2, 57.33, 57.30, 57.0, 50.0, 49.7, 49.6, 49.5, 39.1, 38.9, 35.3, 35.0, 31.7, 31.2, 30.9, 30.8, 30.7, 30.33, 30.30, 30.27, 30.2, 30.18, 28.6, 28.4, 26.3, 25.9, 25.1, 24.6, 24.1, 24.0, 22.9, 22.8. Anal. Calcd ($C_{18}H_{24}O_2$): C, 79.37; H, 8.88. Found: C, 78.91; H, 8.88.

***syn*-5-(Hydroxyphenylmethyl)-6-methyl-6-hepten-2-one (19)**: R_f = 0.10 in 4:1 (v/v) hexane and ethyl acetate, respectively (62% yield); IR (neat) 3456, 3066, 3030, 2964, 2933, 2891, 1716, 1645, 1454, 1409, 1028, 893, 726, 702 cm^{-1}; ^1H NMR (360 MHz) 7.38–7.26 (m, 5 H), 5.06 (s, 1 H), 4.95 (s, 1 H), 4.41 (d, J = 9.4 Hz, 1 H), 2.34–2.12 (m, 4 H), 2.00 (s, 3 H), 1.73 (s, 3 H), 1.51–1.43 (m, 2 H); ^{13}C NMR (50 MHz) 208.3, 144.4, 142.3, 128.4, 127.9, 127.1, 116.3, 75.3, 55.2, 41.3, 29.8, 22.6, 18.1. Anal. Calcd ($C_{15}H_{20}O_2$): C, 77.55; H, 8.68. Found: C, 77.69; H, 8.86.

6-(Hydroxyphenylmethyl)-3,7-dimethyl-7-octenyl ethanoate (20): R_f = 0.22 in 4:1 (v/v) hexane and ethyl acetate, respectively (83% yield); IR (neat) 3471, 3068, 3030, 2966, 2933, 2873, 1743, 1645, 1454, 1369, 1244, 1051, 1034, 891, 764, 702 cm^{-1}; ^1H NMR (360 MHz) 7.37–7.28 (m, 5 H), 5.06–5.05 ((m, 1 H) and 4.76 (brs), 4.96 ((s, 1 H) and singlet at 4.82 for diastereomer), 4.37 ((d, J = 9.4 Hz, 1 H) and doublets at 4.56 and 4.38, J = 7.2 and 9.3 Hz, respectively, for diastereomers), 4.10–3.94 (m, 2 H), 2.32–2.22 (m, 1 H), 2.02 ((s, 3 H) and singlets at 2.01, 1.99, 1.98 for diastereomers), 1.73 ((s, 3 H) and singlets at 1.56, 1.55 for diastereomers), 1.70–0.72 (m, 10 H); ^{13}C NMR (50 MHz) 171.0, 170.9, 144.9, 144.8, 144.6, 143.4, 142.6, 128.1, 127.8, 127.5, 127.0, 129.9, 129.8, 126.3, 115.7, 115.6, 113.1, 76.2, 75.2, 67.7, 62.9, 62.8, 62.7, 62.6, 56.1, 55.8, 54.8, 54.6, 35.7, 35.6, 34.8, 34.6, 34.5, 34.3, 34.2, 34.0, 30.0, 29.6, 29.1, 25.8, 25.6, 25.4, 25.3, 25.2, 20.9, 20.8, 20.7, 19.6, 19.5, 19.0, 18.7, 18.1, 17.9.

3,7-Dimethyl-6-(oxophenylmethyl)-7-octenyl ethanoate (21): R_f = 0.33 in 4:1 (v/v) hexane and ethyl acetate, respectively (70% yield); IR (neat) 3072, 3026, 2954, 2927, 2871, 1738, 1681, 1641, 1597, 1581, 1448, 1367, 1313, 1273, 1242, 1178, 1111, 1051, 1028, 1003, 955, 899, 771 739, 714 cm^{-1}; ^1H NMR (360 MHz) 8.05–7.95 (m, 2 H), 7.56–7.49 (m, 1 H), 7.46–7.40 (m, 2 H), 4.92 (s, 2 H), 4.11–4.05 (m, 2 H), 4.01

(20) Ketones and imines were allowed to react at −20 °C for 12 h.

(t, J = 7.3 Hz, 1 H), 2.03 ((s, 3 H) and a singlet at 2.01 for a diastereomer), 1.71–1.70 (m, 3 H), 1.62–1.08 (m, 7 H). 0.95–0.91 (m, 3 H); ^{13}C NMR (50 MHz) 200.1, 171.0, 143.3, 143.2, 137.0, 132.7, 129.4, 128.4, 128.3, 128.2, 114.8, 114.7, 62.8, 55.3, 35.3, 35.2, 34.7, 29.9, 29.8, 27.5, 27.3, 20.9, 20.0, 19.9, 19.3, 19.2. Anal. Calcd ($C_{19}H_{26}O_3$): C, 75.46; H, 8.67. Found: C, 75.32; H, 8.81.

3,7-Dimethyl-6-[[(phenylmethyl)amino]phenylmethyl]-7-octenyl ethanoate (22): R_f = 0.35 in 4:1 (v/v) hexane and ethyl acetate, respectively (79% yield); IR (neat) 3062, 3026, 2956, 2929, 2871, 1739, 1495, 1454, 1365, 1242, 1053, 1028, 893, 766, 737, 700 cm^{-1}; ^{1}H NMR (360 MHz) 7.33–7.18 (m, 10 H), 4.96 ((d, J = 1.5 Hz, 1 H) and a doublet at 4.68, J = 1.5 Hz, for a diastereomer), 4.92 ((s, 1 H) and a singlet at 4.55 for a diastereomer), 4.07–4.00 (m, 2 H), 3.66–3.62 (m, 1 H), 3.56 (d, J = 7.5 Hz, 1 H), 3.45–3.41 (m, 1 H), 2.27–2.18 (m, 1 H), 2.11–2.01 (m, 3 H), 1.90–1.52 (m, 4 H), 1.47 (s, 3 H), 1.44–1.05 (m, 4 H), 0.86 (t, J = 6.7 Hz, 3 H); ^{13}C NMR (50 MHz) 171.1, 145.1, 145.0, 142.9, 140.7, 128.2, 128.0, 127.9, 127.8, 126.7, 126.6, 113.1, 113.0, 64.6, 63.0, 54.2, 54.0, 51.5, 35.8, 34.9, 34.6, 30.1, 29.7, 25.8, 25.7, 20.9, 20.7, 20.6, 19.7, 19.1. Anal. Calcd ($C_{26}H_{35}NO_2$): C, 78.70; H, 9.25; N, 3.67. Found: C, 78.73; H, 9.08; N, 3.51.

7-(Hydroxyphenylmethyl)-4,8-dimethyl-8-nonenenitrile (23): R_f = 0.13 in 4:1 (v/v) hexane and ethyl acetate, respectively (89% yield); IR (neat) 3485, 3066, 3027, 2956, 2929, 2871, 2245, 1735, 1643, 1495, 1454, 1425, 1375, 1243, 1047, 1028, 893 cm^{-1}; ^{1}H NMR (500 MHz) 7.35–7.22 (m, 5 H), 5.04 (m, 1 H), 4.95–4.61 (m, 1 H), 4.53–4.36 (m, 1 H), 2.31–2.14 (m, 4 H), 1.72 (s, 3 H), 1.69–0.93 ((m, 7 H) including a singlet at 1.54), 0.87 ((d, J = 6.45 Hz, 3 H) also doublets for diastereomers at 0.85 (J = 6.44 Hz), 0.74 (J = 6.85 Hz), and 0.72 (J = 6.44 Hz)); ^{13}C NMR (125 MHz) 144.8, 144.7, 144.6, 144.5, 143.2, 142.5, 142.4, 128.2, 127.9, 127.6, 127.1, 126.9, 126.3, 119.8, 119.7, 119.6, 116.0, 115.8, 113.2, 113.1, 77.3, 77.0, 76.8, 76.0, 75.2, 56.0, 55.8, 54.6, 54.4, 33.8, 33.6, 33.5, 33.4, 32.4, 32.3, 32.0, 31.8, 31.6, 31.4, 31.3, 25.6, 25.5, 25.0, 24.9, 21.0, 20.9, 18.9, 18.7, 18.4, 18.1, 17.9, 14.7, 14.6, 14.5. Anal. Calcd ($C_{18}H_{25}NO$): C, 79.66; H, 9.28; N, 5.16. Found: C, 79.48; H, 9.03; N, 5.50.

4,8-Dimethyl-7-(oxophenylmethyl)-8-nonenenitrile (24): R_f = 0.10 in 9:1 (v/v) hexane and ethyl acetate, respectively (70% yield); IR (neat) 3070, 2956, 2931, 2871, 2245, 1682, 1641, 1597, 1448, 1378, 1269, 1234, 1203, 901 cm^{-1}; ^{1}H NMR (200 MHz) 8.00–7.96 (m, 2 H), 7.58–7.39 (m, 3 H), 4.93 (m, 2 H), 4.03 ((t, J = 7.2 Hz, 1 H) also a triplet at 4.02), 2.34 ((t, J = 7.2 Hz, 2 H) also a triplet at 2.32), 2.03–1.12 (m, 10 H), 0.94 ((d, J = 6.3 Hz, 3 H) also a doublet at 0.92); ^{13}C NMR (50 MHz) 199.9, 143.1, 142.9, 136.80, 136.76, 132.7, 128.3, 128.2, 119.74, 119.71, 114.9, 114.7, 55.0, 33.8, 33.7, 31.9, 31.8, 31.7, 27.1, 27.0, 20.0, 19.8, 18.6, 14.6, 14.59. Anal. Calcd ($C_{18}H_{23}NO$): C, 80.26; H, 8.61; N, 5.20. Found: C, 80.07; H, 8.70; N, 5.17.

7-(1-Hydroxycyclohexyl)-4,8-dimethyl-8-nonenenitrile (25): R_f = 0.23 in 4:1 (v/v) hexane and ethyl acetate, respectively (65% yield); ^{1}H NMR (300 MHz) 4.93 (m, 1 H), 4.75–4.74 (m, 1 H), 2.36–2.29 (m, 2 H), 1.95–1.91 (m, 1 H), 1.75 ((s, 3 H) also a singlet at 1.74 for other diastereomer), 1.72–1.12 (m, 18 H), 0.92 ((d, J = 6.44 Hz, 3 H) and a doublet at 0.92, J = 6.43 Hz, for the other diastereomer); ^{13}C NMR (75 MHz) 145.7, 145.6, 119.9, 114.2, 114.1, 72.6, 72.5, 57.3, 56.8, 36.2, 36.0, 35.9, 34.6, 34.2, 32.6, 32.3, 31.9, 31.8, 25.8, 23.9, 23.6, 22.1, 22.0, 21.9, 19.1, 18.6, 14.9, 14.8.

4,8-Dimethyl-7,11-dodecadienenitrile (26): R_f = 0.42 in 9:1 (v/v) hexane and ethyl acetate, respectively; ^{1}H NMR (500 MHz) 5.84–5.77 (m, 1 H), 5.11 (m, 1 H). 5.04–5.01 (m, 1 H), 4.96–4.94 (m, 1 H), 2.39–2.29 (m, 2 H), 2.17–1.94 (m, 5 H), 1.71–1.68 (m, 3 H), 1.67–1.56 (m, 2 H), 1.51–1.44 (m, 2 H), 1.38–1.31 (m, 1 H), 1.22–1.16 (m, 1 H), 0.92 (d, J = 6.45 Hz, 3 H); ^{13}C NMR (125 MHz) 138.4, 134.9, 125.0, 119.8, 114.5, 36.5, 32.2, 32.1, 31.6, 31.2, 24.9, 23.2, 18.6, 14.8; mass spectrum for $C_{14}H_{23}N$ calcd 205.1831, found 205.1825.

4-Methyl-7-(1-methylethenyl)-9-decenenitrile (27): R_f = 0.55 in 9:1 (v/v) hexane and ethyl acetate, respectively; ^{1}H NMR (500 MHz) 5.85–5.80 (m, 1 H), 5.21–5.20 (m, 1 H), 5.17 (s, 1 H), 4.70 (s, 1 H), 4.67 (s, 1 H), 2.67–2.64 (m, 1 H), 2.36–2.31 (m, 2 H), 2.12–1.99 (m, 2 H), 1.71 ((s, 3 H) also a singlet at 1.69), 1.54–1.23 (m, 7 H), 0.95 ((d, J = 6.85 Hz, 3 H) also a doublet at 0.92, J = 6.45 Hz, for the other diastereomer); ^{13}C NMR (125 MHz) 145.7, 145.6, 133.2, 133.1, 121.9, 121.6, 118.8, 118.7, 110.0, 109.9, 39.1, 39.0, 38.9, 37.8, 36.9, 36.8, 36.4, 35.3, 30.8, 30.6, 29.5, 29.3, 24.7, 24.5, 22.2, 19.7, 18.8.

Ethyl 6-(hydroxyphenylmethyl)-3,7-dimethyl-7-octenoate (28): R_f = 0.31 in 4:1 (v/v) hexane and ethyl acetate, respectively (73% yield); ^{1}H NMR (300 MHz) 7.36–7.21 (m, 5 H), 5.04 (m, 1 H), 4.94 ((m, 1 H) also sharp multiplets at 4.75 and 4.60 for other diastereomers), 4.36 ((dd, J = 9.29, 1.66 Hz, 1 H) also a dd at 4.53 (J = 7.15, 1.67 Hz)), 4.06 ((q, J = 7.15 Hz, 2 H) amid quartets for other diastereomers), 2.41–1.88 (m, 5 H), 1.71 (s, 3 H), 1.54 (s, 1 H), 1.28–0.96 (m, 6 H), 0.78 ((d, J = 6.43 Hz, 3 H) doublets also at 0.93, 0.88, 0.75, with J coupling 7.15, 6.91, and 6.68 Hz, respectively; ^{13}C NMR (75 MHz) 173.2, 173.1, 173.0, 172.9, 146.03, 146.0, 144.8, 144.7, 144.6, 144.5, 143.3, 142.5, 128.2, 128.1, 127.9, 127.6, 127.3, 127.1, 126.9, 126.3, 125.6, 116.0, 115.9, 113.2, 113.1, 112.7, 112.6, 76.1, 76.0, 75.2, 75.1, 71.6, 71.5, 59.9, 56.1, 55.9, 54.6, 54.4, 46.5, 41.9, 41.7, 41.6, 41.3, 41.0, 36.1, 36.0, 35.7, 35.6, 34.3, 34.1, 33.9, 30.5, 30.2, 30.1, 30.08, 30.03, 29.8, 25.8, 25.6, 25.3, 25.0, 24.8, 24.7, 21.0, 20.9, 19.9, 19.8, 19.6, 19.5, 19.3, 19.0, 18.0, 17.9, 14.1. Anal. Calcd ($C_{19}H_{28}O_3$): C, 74.96; H, 9.27. Found: C, 74.74; H, 9.56.

1-Chloro-6-(hydroxyphenylmethyl)-3,7-dimethyl-7-octene (29): R_f = 0.41 in 4:1 (v/v) hexane and ethyl acetate, respectively (65% yield); ^{1}H NMR (500 MHz) 7.35–7.23 (m, 5 H), 5.05 (m, 1 H), 4.96 ((m, 1 H) also multiplets for diastereomers at 4.74, 4.61), 4.36 (d, J = 8.46, 1 H), 3.49–3.37 (m, 2 H), 2.31–2.25 (m, 2 H), 1.72 (s, 3 H), 1.69–0.90 (m, 7 H), 0.73 ((d, J = 6.85 Hz, 3 H) doublets for other diastereomers at 0.71, 0.87, 0.85 with J values 6.05, 6.44, 6.45 Hz, respectively); ratios from integration of diastereomers equal 4.3, 3.2, 1, 1; ^{13}C NMR (125 MHz) 144.8, 144.6, 142.5, 128.2, 128.0, 127.7, 127.2, 127.0, 126.3, 116.1, 116.0, 76.1, 75.2, 75.1, 56.1, 55.9, 43.1, 39.9, 38.9, 34.0, 33.9, 33.8, 30.0, 29.6, 25.7, 25.6, 19.2, 19.1, 18.4, 18.0, 17.9. Anal. Calcd ($C_{17}H_{25}OCl$): C, 72.71; H, 8.97; Cl, 12.62. Found: C, 72.47; H, 9.14; Cl, 12.63.

1-Chloro-6-(1-hydroxycyclohexyl)-3,7-dimethyl-7-octene (30): R_f = 0.52 in 4:1 (v/v) hexane and ethyl acetate, respectively (51% yield); ^{1}H NMR (200 MHz) 4.92 (m, 1 H), 4.74 (m, 1 H), 3.56–3.50 (m, 2 H), 1.99–1.07 ((m, 18 H) including a singlet at 1.75 (3 H)), 0.90 ((d, J = 6.15 Hz, 3 H) also a doublet at 0.89 (J = 6.02) for the other diastereomer); ^{13}C NMR (50 MHz) 145.7, 145.6, 114.1, 72.6, 72.5, 57.9, 56.9, 43.2, 40.0, 39.3, 36.2, 36.1, 35.8, 35.0, 34.6, 30.7, 30.2, 25.8, 23.9, 23.7, 22.6, 22.1, 22.0, 19.4, 18.8. Anal. Calcd ($C_{16}H_{29}OCl$): C, 70.43; H, 10.71; Cl, 12.99. Found: C, 70.39; H, 10.85; Cl, 13.23.

Intramolecular Epoxide Opening Reaction. The procedure for the intramolecular epoxide opening reaction was the same as that for the intermolecular epoxide opening reaction already described. 6-Ethyl-2-hydroxy-2-methylbicyclo[3.2.1]octane (**32**): R_f = 0.22 in 4:1 (v/v) hexane and ethyl acetate, respectively (97% yield based on available isomer); mp 85.5–88.0 °C uncorrected; ^{1}H NMR (360 MHz) 4.89 (s, 1 H), 4.83 (s, 1 H), 2.56 (s, 1 H), 2.41–2.32 (m, 1 H), 2.17–2.12 (m, 1 H), 2.07–2.03 (m, 2 H), 1.80–1.71 (m, 1 H), 1.57–1.30 (m, 5 H), 1.18 (s, 3 H); ^{13}C NMR (50 MHz) 154.2, 104.4, 72.7, 46.5, 41.3, 35.5, 33.7, 32.3, 30.2, 29.2. Anal. Calcd ($C_{10}H_{16}O$): C, 78.91; H, 10.59. Found: C, 78.77; H, 10.80.

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Registry No. 1, 6249-80-5; **2**, 52813-35-1; **3**, 23092-23-1; **4** (isomer 1), 52922-19-7; **4** (isomer 2), 52922-10-8; **5**, 27644-02-6; **6**, 62894-04-6; **7**, 50599-02-5; **8**, 29843-83-2; **9**, 141063-40-3; **10**, 71370-05-3; **11**, 141088-16-6; **12**, 74514-31-1; *cis*-**13**, 141194-04-9; *trans*-**13**, 141194-05-0; **14**, 105737-83-5; **15a** (isomer 1), 141063-41-4; **15a** (isomer 2), 141063-62-9; **15b** (isomer 1), 141063-58-3; **15b** (isomer 2), 141063-63-0; **15c** (isomer 1), 141063-59-4; **15c** (isomer 2), 141063-64-1; **15d** (isomer 1), 141063-60-7; **15d** (isomer 2), 141063-65-2; **15e** (isomer 1), 141063-61-8; **15e** (isomer 2), 141063-66-3; **16**, 141063-42-5; **17**, 141063-43-6; **18**, 141063-44-7; **19**, 141063-45-8; **20**, 141063-46-9; **21** (isomer 1), 141063-47-0; **21** (isomer 2), 141063-67-4; **22**, 141063-48-1; **23**, 141063-49-2; **24** (isomer 1), 141063-50-5; **24** (isomer 2), 141063-68-5; **25** (isomer 1), 141063-51-6; **25** (isomer 2), 141088-17-7; **26**, 141063-52-7; **27** (isomer 1), 141063-53-8; **27** (isomer 2), 141063-71-0; **28**, 141063-54-9; **29**, 141063-55-0; **30** (isomer 1), 141063-56-1; **30** (isomer 2), 141063-70-9; **31**, 141063-57-2; **32**, 141088-18-8; $(CH_3)_2C{=}CHCH_2Cl$, 503-60-6; $H_3CCHClCH{=}CH_2$, 563-52-0; $H_2C{=}CHCH_2Cl$, 107-05-1; $H_2C{=}CHCH_2OAc$, 591-87-7; $H_2C{=}C(CH_3)CH_2Cl$, 563-47-3; $H_2C{=}C(CH_3)CH_2OAc$, 820-71-3; (*E*)-$H_3CCH{=}CHCH_2OAc$, 7204-29-7; $(CH_3)_2C{=}CHCH_2OAc$, 1191-16-8; PhCOCl, 98-88-4; c-$C_6H_8(=O)$, 25512-62-3; PhAc, 98-86-2; $CH_3CO(CH_2)_3CN$, 10412-98-3; PhCHO, 100-52-7; $PhCH{=}NCH_2Ph$, 780-25-6; $H_2C{=}CHCH_2Br$, 106-95-6; CuCN, 544-92-3; carval, 99-48-9; 3-acetoxy-2-methyl-4α-methylvinylcyclohexene, 97-42-7; 1,2-epoxyhexane, 1436-34-6; 3-chlorocyclohexene, 2441-97-6; 3-(2-cyclohexenyl)cyclohexanone, 141063-69-6.