Tetrahedron Vol. 45, No. 2, pp. 443 to 454, 1989
Printed in Great Britain.

0040-4020/89 $3.00+.00

NEW ORGANOCOPPER REAGENTS PREPARED UTILIZING HIGHLY REACTIVE COPPER

Reuben D. Rieke*, Richard M. Wehmeyer,
Tse-Chong Wu, and Greg W. Ebert

Department of Chemistry
University of Nebraska-Lincoln
Lincoln, Nebraska 68588-0304

(*Received in USA* 17 *June* 1988)

Abstract - Highly reactive copper solutions have been prepared by the lithium naphthalide reduction of copper(I) iodide/trialkylphosphine complexes. These activated copper solutions will react with organic halides under very mild conditions to form stable organocopper reagents. Significantly, the organocopper reagents can contain considerable functionalities such as ester, nitrile, chloride, epoxide, and ketone groups. These functionalized organocopper species undergo many reactions typical of other organocopper species. Intermolecular 1,4-additions, epoxide-opening reactions, and ketone formation with acid chlorides have been successfully achieved. In addition, this methodology has been applied to an intramolecular epoxide-cleavage reaction. The influence of the connecting chain length, substitution pattern, reaction solvent, and CuI/phosphine complex upon the regioselectivity of the intramolecular cyclization is described.

We have previously demonstrated that highly reactive metal powders can be prepared by the reduction of anhydrous metal salts with a variety of reducing agents.[1] Recently, we have reported the extension of this approach to copper. In this paper, we would like to report our most recent findings on the use of this highly reactive zerovalent copper to generate novel functionalized organocopper reagents.[2]

Organocopper and lithium cuprate reagents have seen increased usage in synthetic chemistry in recent years.[3] In general, however, these reagents are derived from the reaction of an organolithium[4] or Grignard reagent[5] with an appropriate copper(I) salt. This approach severely limits the types of functional groups that can be present.

Recently we have reported that the use of lithium or Grignard reagents can be circumvented by using a highly reactive zerovalent copper that rapidly undergoes oxidative addition to alkyl, vinyl, and aryl halides.[2] The oxidative addition to alkyl bromides, for example, occurs at temperatures as low as -78 °C. Aryl halides react within minutes at room temperature or below. The highly reactive zerovalent copper is readily prepared by the lithium naphthalide reduction of a CuI·L complex in THF under an argon atmosphere. The choice of ligand is critical in determining the degree of reactivity of the resulting copper. Amines are of limited value. Sulfides such as $S(CH_3)_2$ yield reactive copper but not nearly as reactive as that prepared using phosphines. The choice of the phosphine is quite significant not only in influencing the reactivity of the zerovalent copper, but also in influencing the resulting chemistry of the organocopper reagent. In general, the more electron donating the phosphine the more reactive towards oxidative addition is the copper.[2b,2f] Also, the resulting organocopper reagent is generally more nucleophilic. In some cases, a less reactive and less nucleophilic organocopper reagent gives better results. For example, formation of alkylcopper species at -78 °C is generally accompanied by some homocoupling (10 to 30%) when PBu_3, PEt_3, tris(dimethylamino)phosphine (HMPT), or tricyclohexylphosphine (PCy_3) is used as the ligand.[2b]

In contrast, the use of PPh_3 results in essentially no homocoupling. Although they are less nucleophilic, the PPh_3-derived organocopper species give high yields in certain cross-coupling reactions described below. The exact nature of the highly reactive zerovalent copper reagent has not yet been determined. However, the facts that the solutions appear to be homogeneous and the reactivity is highly dependent upon the ligand suggests that it is a zerovalent complex $(Cu)_n(L)_y$ rather than just copper powder. Efforts to determine the exact nature of the zerovalent copper are underway.

The ability to form organocopper reagents by oxidative addition to carbon-halogen bonds allows for the ready preparation of functionalized organocopper reagents. Ester, nitrile, chloride, nitro, epoxide, and ketone functionalities are all compatible to varying degrees depending upon the particular halide used.[2] In this paper, we discuss the use of these functionalized organocopper reagents in conjugate addition reactions, cross-coupling reactions with acid chlorides, intermolecular epoxide-opening reactions, and intramolecular cyclizations of epoxyalkylcopper reagents.

Functionalized Ketones

The lithium naphthalide reduction of a mixture of copper(I) iodide and triphenylphosphine in THF under an argon atmosphere gives a solution of highly reactive copper. The copper reacts very rapidly with functionalized alkyl bromides (<10 min, -35 °C) to give stable alkylcopper species. The alkylcopper species can be trapped with an acid chloride to give good yields of functionalized ketones (Table I).[2f] An excess of the acid chloride must be used to trap the organocopper reagent since unreacted active copper will also react with the acid chloride.

Table I. Reactions of Functionalized Organocopper Reagents With Acid Chlorides

Entry	Alkyl Halide (equiv.)[a]		Acid Chloride (equiv.)[a]		Product	% Yield[b]
1	$Br(CH_2)_7CH_3$	(0.20)	PhCOCl	(1.33)	$PhCO(CH_2)_7CH_3$	83
2	$Br(CH_2)_3CO_2Et$	(0.20)	PhCOCl	(0.55)	$PhCO(CH_2)_3CO_2Et$	93 (81)
3	$Br(CH_2)_3CN$	(0.20)	PhCOCl	(0.57)	$PhCO(CH_2)_3CN$	-- (79)
4	$Br(CH_2)_6Cl$	(0.20)	PhCOCl	(0.56)	$PhCO(CH_2)_6Cl$	83 (77)
5	$Br(CH_2)_6$	(0.21)	PhCOCl	(0.59)	$PhCO(CH_2)_6$ 	59 (58)[c]
6	p-$IC_6H_4CO_2Et$	(0.20)	PhCOCl	(1.01)	p-$EtO_2CC_6H_4COPh$	85
7		(0.20)		(0.58)		69
8	$Br(CH_2)_2CO_2Et$	(0.20)	PhCOCl	(0.53)	$PhCO(CH_2)_2CO_2Et$	79 (66)
9	$Br(CH_2)_3CO_2Et$	(0.21)	$MeO_2C(CH_2)_2COCl$	(0.64)	$MeO_2C(CH_2)_2CO(CH_2)_3CO_2Et$	49[c]
10	$Br(CH_2)_3CN$	(0.20)	$CH_3(CH_2)_2COCl$	(0.57)	$CH_3(CH_2)_2CO(CH_2)_3CN$	61
11	Iodobenzene	(0.50)	PhCOCl	(1.50)	PhCOPh	60[d]
12	o-BrC_6H_4CN	(0.50)	PhCOCl	(1.50)	o-CNC_6H_4COPh	-- (71)[d]
13	o-BrC_6H_4CN	(0.50)	CH_3COCl	(1.50)	o-$CNC_6H_4COCH_3$	-- (41)[d]

[a]Based on equivalents of CuI. [b]GC yields based on calibrated chromatographically pure isolated samples. Isolated yields (after column and usually preparative thin layer chromatography) are given in parentheses. [c]Approximately 10-15% of the starting alkyl halide was also observed in these reactions. [d]These aryl copper species were prepared using active copper prepared from the CuI/PEt_3 complex in DME.

As previously discussed, the choice of phosphine is quite significant in forming the organocopper species. Homocoupling of primary alkyl bromides does not occur when the active copper is prepared using triphenylphosphine as the ligand. The use of other ligands such as PBu_3, PEt_3, HMPT, or PCy_3 has been shown in previous results to give 10-30% of the homocoupled alkyl product. However, even the copper solutions prepared using PPh_3 will produce some homocoupled product in reactions with primary alkyl iodides. This suggests that the extent of homocoupling of the alkyl halide (and, in turn, the nucleophilicity of the organocopper reagent) is directly related to the electron donating ability of the phosphine.[6]

Although the PPh_3-derived primary alkylcopper reagents are less nucleophilic, they, nonetheless, give better yields in the cross-coupling reactions with acid chlorides since none of the primary alkyl bromide is lost as the homocoupled product. Since aryl halides do not homocouple as readily as alkyl halides, the choice of phosphine is less critical in their cross-coupling reactions with acid halides. As seen in Table I, PPh_3 as well as more highly donating phosphines (e.g. PEt_3) give good yields of the arylcopper species and of the cross-coupled products. In general, however, active copper solutions produced using the more highly donating ligands (PEt_3, PBu_3, PCy_3, HMPT, etc.) are somewhat more reactive toward organic halides and appear to give more reactive (nucleophilic) organocopper reagents.

The formation of stable (<-10 °C) primary alkylcopper species containing ester, nitrile, and chloride functionalities is readily accomplished using active copper. The compatibility of more highly reactive functionalities such as epoxide or ketone groups appears to be dependent upon the length of the alkyl chain between the copper and epoxide or ketone moieties.[2f] Previous results have shown that these groups can be tolerated to some degree, however, intramolecular epoxide opening[7] or 1,2-carbonyl addition[8] can occur if a favorable ring size is formed. The compatibility of other functional groups in the organocopper reagents and the reactions to form functionalized cross-coupled ketone products is currently under investigation.

Conjugate Addition

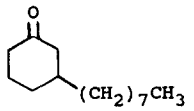
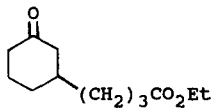
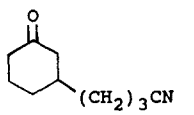
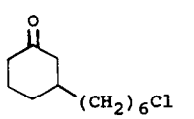
Alkylcopper species, derived from copper(I) iodide/trialkylphosphine complexes, are very reactive in conjugate addition reactions with 2-cyclohexenone giving 3-alkylated cyclohexanone products in generally good to excellent yields (Table II).[2b] The 1,4-addition proceeds to a large degree at -78 °C, with the enone being completely consumed (as observed by GC) upon reacting at -50 °C. Significantly, highly functionalized organocopper species can be derived from the reaction of the inexpensive and readily available alkyl bromides with active copper.

As noted in the previous sections, the choice of phosphine can be quite significant in determining the reactivity of the active copper and of the resultant organocopper species. PBu_3, PEt_3, HMPT, and PCy_3 have been used quite effectively in preparing organocopper species which undergo 1,4-addition reactions. However, organocopper species derived using triphenylphosphine have not (in preliminary studies) been sucessful in effecting conjugate additions to 2-cyclohexenone. These results agree well with the observed lower nucleophilicity of the PPh_3-derived organocopper species, as discussed earlier.

Chlorotrimethylsilane is compatible with the reaction conditions as well.[10] Low-temperature addition of chlorotrimethylsilane to the organocopper reagents followed by addition of the enone results in formation of the trimethylsilyl enol ether of the 1,4-adduct. The enol ether is readily hydrolyzed upon workup, giving the 3-alkylated cyclohexanone product in good yield. In accordance with the observations of Noyori,[11] the amount of phosphine present in the reaction also affects the yield of 1,4-adduct. Reaction of n-octylcopper prepared using 1 equiv. of PBu_3 gave 3-n-octylcyclohexanone in 62% yield while in a separate reaction using 2.3 equiv. of PBu_3, a 92% yield was obtained.

The use of $BF_3{\cdot}OEt_2$ has also been studied in these systems,[12] but does not appear to have any noticeable effect upon the reaction yields. As other, more sterically-demanding enones are

Table II. Reaction of 2-Cyclohexen-1-one With Organocopper Reagents

Product	Alkyl Halide	(equiv)[a]	Cu*[b]	Equiv. Enone[a]	% Yield[c]
	$CH_3(CH_2)_7Br$	(0.50)	B	0.21	94
		(0.40)	A	0.19	62
		(0.41)	C	0.15	64
		(0.41)	D	0.13	78
	$Br(CH_2)_3CO_2Et$	(0.41)	B	0.19	90
		(0.50)	E	0.19	90
	$Br(CH_2)_3CN$	(0.44)	B	0.15	71
	$Br(CH_2)_6Cl$	(0.40)	B	0.15	52

[a]Based on equivalents CuI. [b]Active copper prepared by reduction of one of the following CuI complexes. A: Preformed $CuIPBu_3$[9]. B: Preformed $CuIPBu_3$[9] plus excess PBu_3 (1.3-1.5 equiv.). C: Unpurified CuI[9] plus HMPT (2.3-2.5 equiv.). D: Unpurified CuI[9] plus $P(Cy)_3$ (2.3-2.5 equiv.). E: Unpurified CuI[9] plus PBu_3 (2.3-2.5 equiv.). [c]GC yields based on calibrated chromatographically pure isolated samples.

studied, the effects of $BF_3{\cdot}OEt_2$ may be more pronounced. In the case of the PPh_3-derived organocopper reagents, the 1,4-addition reaction does not appear to proceed in the presence of excess phosphine nor even in the presence of $BF_3{\cdot}OEt_2$.

The range of compatible functional groups which can be present in the organocopper species, the reactivity of more sterically-demanding enones, as well as the effects of solvent and additives upon the conjugate addition process are currently under investigation.

Intermolecular Epoxide-Opening Reactions

The functionalized organocopper reagents discussed above also readily undergo epoxide-opening reactions.[2a] Table III presents a summary of some of the intermolecular epoxide-opening reactions.

Reactions of the alkylcopper compounds with 1,2-epoxybutane produced a single regioisomer in high yields. The typical reaction temperature is around -15 °C or lower. The epoxides were found to be reasonably stable in the presence of activated copper under these conditions. The alkylcopper reagents decompose giving a mixture of reduced and elimination products above -10 °C.[13] Although THF was reported to retard the epoxide-cleavage reactions with organocuprate reagents,[14] we have successfully used THF as the solvent for these reactions.[15]

Nearly all the aryl halides formed arylcopper compounds at 25 °C or lower. These arylcopper species are generally quite stable at room temperature or even in refluxing THF. Arylcopper compounds underwent oxirane cleavage reaction with 1,2-epoxybutane to form β-hydroxyphenylbutanes in high yields at ambient temperature or with moderate heating. Also of note is the exclusive regioselective substitution at the less-hindered position.

Table III. Reactions of Alkylcoppers or Arylcoppers with 1,2-Epoxybutane

Entry	Halide	Product	% yield[a]
1	$CH_3(CH_2)_7Br$	3-Dodecanol	77
2	$Br(CH_2)_3COO^tBu$	$CH_3CH_2CH(OH)(CH_2)_4COO^tBu$	87
3	$Br(CH_2)_3CN$	$CH_3CH_2CH(OH)(CH_2)_4CN$	88
4	$Br(CH_2)_6Cl$	$CH_3CH_2CH(OH)(CH_2)_7Cl$	81 (78)
5	PhI	$CH_3CH_2CH(OH)CH_2Ph$	b (81)
6	(p-CH_3)PhI	$CH_3CH_2CH(OH)CH_2Ph$(p-CH_3)	76
7	(p-OCH_3)PhI	$CH_3CH_2CH(OH)CH_2Ph$(p-OCH_3)	71 (73)
8	(p-CH_3)PhBr	$CH_3CH_2CH(OH)CH_2Ph$(p-CH_3)	58

[a]Yields reported were mostly determined by gas chromatography analysis. Isolated yields are shown in parentheses. [b]The GC yield could not be determined due to overlap of the product peak with the naphthalene peak.

The strongly donating group (e.g. -OCH_3) was observed to accelerate the substitution reaction, presumably due to the enhanced nucleophilicity of the resulting arylcopper reagents. In contrast, arylcopper species with strongly withdrawing groups in the ortho or para position were observed to be very unreactive toward the epoxides even in refluxing THF because of their poor nucleophilicities. Ethyl 3-iodobenzoate, with a strongly withdrawing group in the meta position, gave a low yield of coupled product.

Aryl bromides underwent oxidative addition somewhat less rapidly than the corresponding iodides. The resulting arylcopper reagents also showed less reactivity toward the epoxide substitutions and gave relatively lower yields compared to those derived from aryl iodides.

Intramolecular Epoxide-Opening Reactions

Molecules containing both an epoxide and a nucleophile which can undergo an intramolecular cyclization have been found to be synthetically useful.[16] In our laboratories, we have been investigating the intramolecular cyclizations via an epoxide-cleavage process[7] using activated copper (Scheme I).[2g] Table IV presents a summary of some of the intramolecular epoxide-opening reactions using the activated copper.

Scheme I

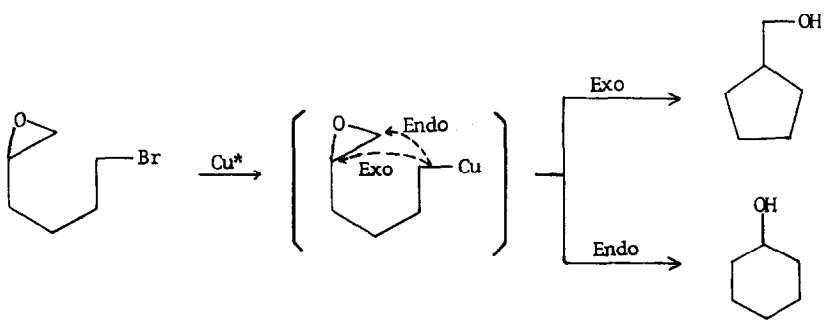
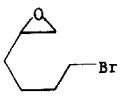
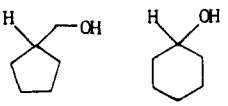
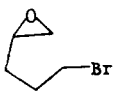
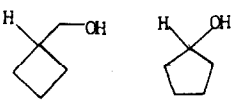
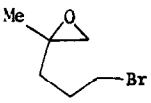
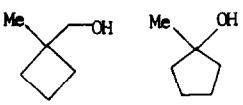
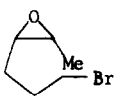
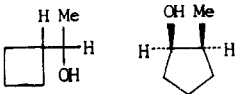
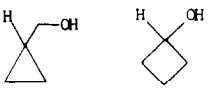
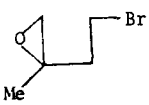
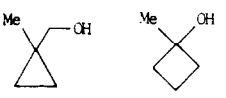
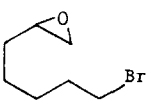
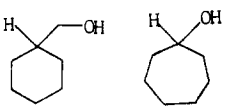
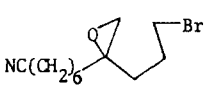
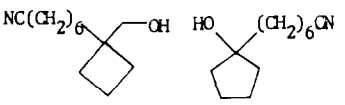
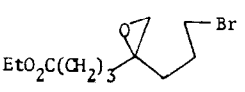
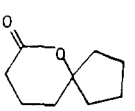


Table IV. Intramolecular Cyclizations of Bromoepoxides with Activated Copper

Entry	Haloepoxides	PR_3[a]	Solvent	Products	% Yield[b]
					
1		PBu_3	THF	1 : 6	56
2		PBu_3	Toluene	1 : 0	45
3		PPh_3	THF	1 : 4	37
4		PPh_3	Toluene	1 : 1.5	62
					
5		PPh_3	THF	1 : 37	87
					
6		PPh_3	THF	0 : 1	95
					
7		PPh_3	THF	25 : 1	41
8		PPh_3	Toluene	29 : 1	61
					
9		PPh_3	THF	1 : 0	89
					
10		PPn_3	THF	1 : 0	96
					
11		PBu_3	Toluene	0 : 1	12[c]
					
12		PPh_3	THF	0 : 1	83[c]
					
13		PPh_3	THF		50[c]

[a] PBu_3 (2.3 equiv) or PPh_3 (2.0 equiv) was used. [b] Yields reported were mostly determined by gas chromatography analysis. [c] Isolated yields.

Cyclization of 6-bromo-1,2-epoxyhexane with activated copper in THF gave cyclohexanol and cyclopentylmethanol in a ratio of 6:1 in a 56% combined yield. Solvent effects were found to be drastic for this reaction. The regiochemistry of this reaction was reversed by carrying out the reaction in toluene.

It should be pointed out that the homocoupling of alkyl halides could be completely eliminated when the CuI/PPh_3 complex was used. The cycloalkylation of 5-bromo-1,2-epoxypentane with highly reactive copper, which was generated from lithium naphthalide and CuI/PPh_3, gave a 37:1 mixture of cyclopentanol and cyclobutylmethanol in excellent yield (87%) with no evidence of any homocoupling reaction.

Methyl substitution at the internal position of the epoxides gave only the endo-mode cyclized products for the medium-sized connecting chains.[17,18] Cis-6-bromo-2,3-epoxyhexane, with a methyl substituent at the external position of the epoxide, surprisingly reversed the regioselectivity to undergo preferential exo-mode ring closure to furnish 1-cyclobutylethanol and cis-2-methylcyclopentanol in a 29:1 ratio in a 61% combined yield. For these medium-sized ring closures, ring strain imposed by the connecting chain and nonbonding interactions arising from the substitution are both equally important.[17,18] Therefore, the exo-mode ring closure will be favored when both termini of the epoxide are equally substituted.

Surprisingly, 7-bromo-1,2-epoxyheptane gave only cycloheptanol in 12% yield. Conversely, Cooke, Jr. and Houpis reported that only 6-membered ring formation was observed with no evidence of any 7-membered ring formation.[7a]

Reactions of 4-bromo-1,2-epoxybutane and 4-bromo-2-methyl-1,2-epoxybutane with the activated copper gave only the 3-membered ring alcohols cyclopropylmethanol and 1-methyl-1-(hydroxymethyl)cyclopropane in 89% and 96% yields, respectively. For the small-sized ring closure, ring strain imposed by the connecting chain becomes crucial. The geometry of endo-mode ring closure is more difficult to reach for these cycloalkylation reactions with a shorter connecting chain and the exo-mode cyclization is consequently preferred.[17]

As most of the products were volatile with relatively low boiling points, the isolated yields were usually low. Trapping the cyclized alkoxide with an acid chloride to form a higher boiling point derivative helps prevent the evaporation of volatile cycloproducts and facilitates the isolation. For example, cyclopropylmethyl benzoate was isolated in 77% yield by this method.[2f]

A bromoepoxide containing a remote cyano group gave only the 5-membered ring alcohol in 83% isolated yield (Table IV, entry 12). With an appropriate linkage between epoxide and ester groups, 4-bromo-2-(3-carboethoxypropyl)-1,2-epoxybutane underwent tandem epoxide-opening and lactonization reactions to form the spirolactone in 50% yield (Table IV, entry 13).

In conclusion, we have demonstrated that difunctional molecules, containing both an epoxide and a halide, can undergo intramolecular cyclization mediated by the activated copper to generate new carbocycles. Significantly, the haloepoxides can contain other functional groups leading to highly functionalized carbocycles.

Acknowledgment: The financial support provided by the National Institutes of Health (Grant GM35153) is gratefully acknowledged.

Experimental Section

Melting points were determined on a Thomas Hoover melting point apparatus and are corrected. IR spectra were taken on a Perkin-Elmer 283 spectrophotometer neat between NaCl or KBr plates or as KBr disks. ^1H NMR spectra were recorded on a Nicolet NT-360 (360 MHz) or on a Varian VXR-200 (200 MHz) spectrometer. All chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. Fully decoupled ^{13}C NMR spectra were recorded on a Varian VXR-200 (50 MHz) spectrometer. The central peak of $CDCl_3$ (77.0 ppm) was used as the internal reference. High resolution mass spectra were performed by the Midwest Center for Mass Spectrometry at the University of Nebraska-Lincoln using a Kratos MS-80 mass spectrometer. Gas chromatography analysis was done on a Hewlett-Packard 5890A chromatograph using stainless steel columns packed with OV-17 (3%) on 100/120 Chromosorb G.

All manipulations were carried out on a dual manifold vacuum/argon system. The Linde prepurified grade argon was further purified by passing it through a 150 °C catalyst column (BASF R3-11), a phosphorous pentoxide column, and a column of granular potassium hydroxide. Tetrahydrofuran, 1,2-dimethoxyethane (DME) and toluene were freshly distilled under argon from sodium/potassium alloy. Anhydrous copper(I) iodide was purchased from Cerac, Inc. Lithium and naphthalene were weighed out and charged into reaction flasks under argon in a Vacuum Atmospheres Company dry box. Other commercially available reagents were used as received.

Typical Reaction with Acid Chlorides to Form Ketones. Lithium (70.8 mg, 10.2 mmol) and naphthalene (1.588 g, 12.39 mmol) in freshly distilled THF (10 mL) were stirred under argon until the Li was consumed (approx. 2 h). CuI (1.751 g, 9.194 mmol) and PPh_3 (2.919 g, 11.13 mmol) in THF (15 mL) were stirred for 30 min giving a thick white slurry which was transferred via cannula to the dark green solution of lithium naphthalide at 0 °C. (Later experiments showed that slightly better results were obtained if the lithium naphthalide solution was added to the CuI/PPh_3 mixture.) The resultant reddish-black solution of active copper was stirred for 20 min at 0 °C. Ethyl 4-bromobutyrate (0.3663 g, 1.888 mmol) and GC internal standard n-decane (0.1566 g, 1.101 mmol) were added neat via syringe to the active copper solution at -35 °C. The solution was allow to stir for 10-15 min at -35 °C followed by addition of benzoyl chloride (0.7120 g, 5.065 mmol) neat to the organocopper solution at -35 °C. The reaction was allowed to stir 1 h 30 min at -35 °C followed by warming to room temperature for 30 min. (GC analysis showed the reaction to be essentially complete after stirring at -35 °C.) The reaction was then worked-up by pouring into saturated aqueous ammonium chloride, extracting with diethyl ether, and drying over anhydrous sodium sulfate. (For compounds not sensitive to base, the ether layer was also washed with 5% aqueous sodium hydroxide solution.) Silica gel chromatography (hexanes followed by mixtures of hexanes/ ethyl acetate) and further purification by preparative thin-layer chromatography (2 mm plate) provided 4-carboethoxy-1-phenyl-1-butanone in 81% isolated yield (93% GC yield after quantitation using the isolated product for the preparation of GC standards). IR (neat) 3060, 2960, 1735, 1690, 1600, 1580, 1450, 1375, 1240, 1205 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.90-8.04 (m, 2H), 7.36-7.64 (m, 3H), 4.14 (q, J= 7.2 Hz, 2H), 3.05 (t, J= 7.2 Hz, 2H), 2.43 (t, J= 7.2 Hz, 2H), 2.07 (tt, J= 7.2, 7.2 Hz, 2H), 1.25 (t, J= 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 199.2, 173.0, 136.9, 132.9, 128.5, 127.9, 60.2, 37.4, 33.4, 19.4, 14.1. MS (EI) m/e (relative intensity) 220 (M^+, 1.0), 175 (8.5), 147 (10.8), 133 (2.7), 120 (9.1), 105 (100.0), 77 (47.3), 55 (7.1). Calcd for $C_{13}H_{16}O_3$ m/e 220.1100, found m/e 220.1092.

1-Phenyl-1-nonanone. IR (neat) 3060, 2930, 2860, 1690, 1600, 1585, 1450, 1260, 1215 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.90-8.02 (m, 2H), 7.38-7.62 (m, 3H), 2.96 (t, J= 7.4 Hz, 2H), 1.74 (app. quintet, J= 7.3 Hz, 2H), 1.14-1.50 (m, 10H), 0.88 (app. t, J= 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 200.5, 137.2, 132.7, 128.5, 128.0, 38.6, 31.8, 29.4, 29.4, 29.1, 24.4, 22.6, 14.0. MS (EI) m/e (relative intensity) 218 (M^+, 3.0), 133 (12.2), 120 (92.5), 105 (100.0), 77 (30.7), 55 (2.8). Calcd for $C_{15}H_{22}O$ m/e 218.1671, found m/e 218.1676.

4-Cyano-1-phenyl-1-butanone. IR (neat) 3060, 2940, 2240, 1690, 1600, 1580, 1450, 1235, 1205 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.90-8.04 (m, 2H), 7.36-7.66 (m, 3H), 3.16 (t, J= 6.8 Hz, 2H), 2.51 (t, J= 7.0 Hz, 2H), 2.10 (tt, J= 7.0, 6.8 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 198.0, 136.5, 133.3, 128.6, 127.9, 119.2, 36.3, 19.8, 16.5. MS (EI) m/e (relative intensity) 173 (M^+, 10.4), 147 (0.1), 133 (0.8), 120 (2.6), 105 (100.0), 77 (33.1), 55 (0.9). Calcd for $C_{11}H_{11}NO$ m/e 173.0841, found m/e 173.0839.

7-Chloro-1-phenyl-1-heptanone. IR (neat) 3060, 2960, 2860, 1690, 1600, 1580, 1450, 1410, 1260 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.90-8.02 (m, 2H), 7.38-7.62 (m, 3H), 3.53 (t, J= 6.6 Hz, 2H), 2.98 (t, J= 7.2 Hz, 2H), 1.65-1.90 (m, 4H), 1.31-1.60 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 200.1, 137.1, 132.8, 128.5, 127.9, 44.8, 38.3, 32.4, 28.5, 26.7, 24.0. MS (EI) m/e (relative intensity) 226 (1.8), 224 (M^+, 5.2), 189 (1.6), 133 (2.8), 120 (40.5), 105 (100.0), 77 (75.5), 55 (8.2). Calcd for $C_{13}H_{17}ClO$ m/e 224.0968, found m/e 224.0967.

3-Carboethoxy-1-phenyl-1-propanone. IR (neat) 3060, 2970, 1735, 1690, 1600, 1580, 1450, 1365, 1350, 1265 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.92-8.04 (m, 2H), 7.37-7.62 (m, 3H), 4.14, (q, J= 7.2 Hz, 2H), 3.29 (t, J= 6.6 Hz, 2H), 2.74 (t, J= 6.6 Hz, 2H), 1.25 (t, J= 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 197.8, 172.6, 136.4, 132.9, 128.3, 127.7, 60.3, 33.1, 28.0, 14.0. MS (EI) m/e (relative intensity) 206 (M^+, 13.7), 161 (19.8), 133 (1.6), 105 (100.0), 77 (30.4). Calcd for $C_{12}H_{14}O_3$ m/e 206.0943, found m/e 206.0942.

4-Carboethoxybenzophenone. IR (neat) 3060, 2980, 1725, 1665, 1600, 1580, 1450, 1405, 1370, 1270, 1100, 1020 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 8.08-8.20 (m, 2H), 7.40-7.90 (m, 7H), 4.42 (q, J= 7.2 Hz, 2H), 1.42 (t, J= 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 195.8, 165.6, 141.0, 136.8, 133.4, 132.8, 129.9, 129.6, 129.3, 128.3, 61.3, 14.2. MS (EI) m/e (relative intensity) 254 (M^+, 0.2), 226 (4.9), 209 (35.2), 177 (51.0), 149 (10.6), 105 (100.0), 77 (32.8). Calcd for $C_{16}H_{14}O_3$ m/e 254.0943, found m/e 254.0938.

8,9-Epoxy-1-phenyl-1-nonanone. IR (neat) 3060, 2940, 2860, 1690, 1600, 1580, 1450, 1255, 1210 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.90-8.04 (m, 2H), 7.38-7.64 (m, 3H), 2.97 (t, J= 7.3 Hz, 2H), 2.83-2.98 (m, 1H), 2.74 (dd, J= 5.0, 4.0 Hz, 1H), 2.45 (dd, J= 5.0, 2.6 Hz, 1H), 1.75 (app. quintet, J= 7.1 Hz, 2H), 1.31-1.63 (m, 8H). ^{13}C NMR ($CDCl_3$) δ 200.3, 137.0, 132.8, 128.4, 127.9, 52.2, 47.0, 38.4, 32.3, 29.2, 29.1, 25.7, 24.1. MS (EI) m/e (relative intensity) 232 (M^+, 0.2), 231 (0.3), 133 (5.2), 120 (68.4), 112 (0.8), 105 (100.0), 77 (36.6). Calcd for $C_{15}H_{20}O_2$ m/e 232.1463, found m/e 232.1456.

6-Carboethoxy-1-Carbomethoxy-3-hexanone. IR (neat) 2940, 1735 (br), 1435, 1360, 1165 (br), 1095, 1020 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 4.13 (q, J= 7.1 Hz, 2H), 3.68 (s, 3H), 2.44-2.84 (m, 6H), 2.33 (t, J= 7.1 Hz, 2H), 1.91 (app. quintet, J= 7.0 Hz, 2H), 1.26 (t, J= 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 208.0, 173.1, 173.1, 60.3, 51.7, 41.5, 37.0, 33.2, 27.6, 18.8, 14.2. MS (EI) m/e (relative intensity) 230 (M^+, 0.5), 185 (3.7), 153 (17.5), 143 (19.9), 115 (100.0), 87 (24.8), 59 (17.8), 56 (6.6). Calcd for $C_{11}H_{18}O_5$ m/e 230.1154, found m/e 230.1160.

1-Cyano-4-heptanone. IR (neat) 2950, 2870, 2240, 1715, 1410, 1375, 1125 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 2.61 (t, J= 6.8 Hz, 2H), 2.43 (t, J= 6.9 Hz, 2H), 2.41 (t, J= 7.3 Hz, 2H), 1.92 (app. quintet, J= 7.0 Hz, 2H), 1.62 (app. sextet, J= 7.4 Hz, 2H), 0.92 (t, J= 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 209.1, 119.2, 44.8, 40.2, 19.2, 17.2, 16.4, 13.6. MS (EI) m/e (relative intensity) 139 (M^+, 5.8), 111 (1.3), 96 (42.5), 86 (0.4), 71 (100.0), 68 (29.6), 55 (11.5). Calcd for $C_8H_{13}NO$ m/e 139.0997, found m/e 139.1001.

o-Cyanobenzophenone. mp 83-84 °C (lit.[19] mp 83.5 °C). IR 1665, 2230 cm^{-1}.

o-Cyanoacetophenone. mp 39-42 °C (lit.[20] mp 48 °C). IR 1690, 2218 cm^{-1}. The phenylhydrazone derivative was prepared: mp 198-200 °C (lit.[20] mp 205-207 °C.)

Typical 1,4-Addition Reaction with 2-Cyclohexen-1-one. Lithium (71.2 mg, 10.3 mmol) and naphthalene (1.592 g, 12.42 mmol) in freshly distilled THF (10 mL) were stirred under argon until the Li was consumed (approx. 2 h). A solution of $CuIPBu_3$[9] (3.666 g, 9.333 mmol) and PBu_3 (2.89 g, 14.3 mmol) in THF (5 mL) was added via cannula to the dark green lithium naphthalide solution at 0 °C and the resultant reddish-black active copper solution was stirred for 20 min. 1-Bromooctane (0.9032g, 4.677 mmol) and GC internal standard n-decane (0.1725 g, 1.212 mmol) in THF (5 mL) were added rapidly via cannula to the active copper solution at -78 °C. The organocopper formation was typically complete within 20 min at -78 °C. 2-Cyclohexen-1-one (0.1875 g, 1.950 mmol) in THF (10 mL) was added slowly dropwise over 20 min to the organocopper species at -78 °C. The reaction was allowed to react at -78 °C, -50 °C, -30 °C, and room temperature for 1 h each. The reaction was then worked-up by pouring into saturated aqueous ammonium chloride, extracting with diethyl ether, and drying over anhydrous sodium sulfate. Silica gel chromatography (hexanes followed by mixtures of hexanes/ethyl acetate) and further purification by preparative thin-layer chromatography provided 3-n-octylcyclohexanone (93% GC yield after quantitation using the isolated product for the preparation of GC standards). IR (neat) 2930, 2860, 1715, 1465, 1425, 1225 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 1.50-2.50 (m, 9H), 1.15-1.45 (very broad app. s, 14H) 0.88 (app. t, J= 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 211.8, 48.2, 41.5, 39.1, 36.6, 31.9, 31.4, 29.7, 29.5, 29.2, 26.6, 25.3, 22.6, 14.0. MS (EI) m/e (relative intensity) 210 (M^+, 1.4), 167 (2.4), 97 (100.0), 83 (3.1), 69 (9.0), 55 (11.5). Calcd for $C_{14}H_{26}O$ m/e 210.1984, found m/e 210.1992.

3-(3-Cyanopropyl)cyclohexanone. IR (neat) 2915, 2860, 2240, 1715, 1455, 1425, 1225 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 2.36 (t, J= 6.9 Hz, 2H), 1.22-2.50 (m, 13H). ^{13}C NMR ($CDCl_3$) δ 210.5, 119.2, 47.6, 41.2, 38.2, 35.3, 31.0, 24.9, 22.6, 17.2. MS (EI) m/e (relative intensity) 165 (M^+, 18.9), 122 (62.3), 97 (100.0), 81 (13.0), 69 (41.7), 55 (48.4). Calcd for $C_{10}H_{15}NO$ m/e 165.1154, found m/e 165.1157.

3-(3-Carboethoxypropyl)cyclohexanone. IR (neat) 2940, 2865, 1740, 1720, 1455, 1420, 1195 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 4.13 (q, J= 7.2 Hz, 2H), 1.26-2.50 (m, 15H including 2.29 (t, J= 7.2 Hz)), 1.26 (t, J= 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 211.1, 173.0, 60.0, 47.7, 41.2, 38.5, 35.6, 34.0, 30.8, 24.9, 21.8, 14.0. MS (EI) m/e (relative intensity) 212 (M^+, 0.4), 194 (0.5), 184 (0.4), 167 (1.9), 149 (2.7), 123 (4.4), 121 (9.4), 97 (100.0), 88 (11.3), 69 (10.9), 55 (19.2). Calcd for $C_{12}H_{20}O_3$ m/e 212.1413 found m/e 212.1411.

3-(6-Chlorohexyl)cyclohexanone. IR (neat) 2930, 2860, 1715, 1450, 1430, 1225 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 3.53 (t, J= 6.7 Hz, 2H), 1.18-2.50 (m, 19H). ^{13}C NMR ($CDCl_3$) δ 211.5, 48.2, 45.0, 41.5, 39.0, 36.4, 32.6, 31.3, 28.9, 26.8, 26.5, 25.2. MS (EI) m/e 216 (M^+, 1.4), 173 (1.0), 97 (100.0), 81 (5.4), 69 (9.4), 55 (11.4). Calcd for $C_{12}H_{21}ClO$ m/e 216.1281, found m/e 216.1285.

Typical Procedure for Intermolecular Epoxide-Opening Reaction. Lithium (69.0 mg, 9.9 mmol) and naphthalene (1.418 g, 11.1 mmol) in freshly distilled THF (10 mL) were stirred at ambient temperature for 3 h under argon. Then a solution of $CuIPBu_3$[9] (3.592 g, 9.2 mmol) and PBu_3 (2.790 g, 13.8 mmol) in THF (7 mL) was transferred via a cannula into the lithium naphthalide at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and was then cooled to -78 °C. A solution of GC internal standard (n-decane) and t-butyl 4-bromobutyrate (808.0 mg, 3.6 mmol) in THF (7 mL) was rapidly added to the activated copper at -78 °C. After stirring at -78 °C for 1 h, 1,2-epoxybutane (117.0 mg, 1.6 mmol) in THF (5 mL) was then added at -78 °C. The reaction mixture was stirred at -78 °C for 1 h and was gradually warmed to -10 °C. Aliquots were withdrawn and quenched with saturated aqueous NH_4Cl solution at -78 °C, -50 °C, -20 °C, and -10 °C. The organic solution of each aliquot was dried over $MgSO_4$ and was subjected to GC analysis (12'x1/8" stainless steel column packed with OV-17 (3%) on 100/120 Chromosorb G-NAW). The maximum yield was achieved at around -20 °C. The organocopper and coupled product decomposed when the reaction temperature was raised above -20 °C. The reaction solution was cooled to -60 °C and was then quenched with saturated $NH_4Cl_{(aq)}$ solution (20 mL). The reaction mixture was allowed to warm to room temperature and was extracted twice with diethyl ether (75 mL each). The combined ether layers were washed with H_2O and were dried over anhydrous $MgSO_4$. Solvent was removed under reduced pressure and the resulting residue was chromatographed on silica gel to give a colorless liquid. The coupled products were usually purified by preparative TLC or preparative GC. t-Butyl 6-hydroxyoctanoate: IR (neat) 3100-3650, 2975, 2935, 2870, 1735, 1465,

1365, 1150, 1255 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 3.49-3.60 (m, 1H), 2.23 (t, J= 7.4 Hz, 2H), 1.30-1.70 (m, 18H including 1.44 (s, 9H)), 0.94 (t, J= 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 173.1, 80.0, 72.9, 36.6, 35.5, 30.2, 28.1, 25.1, 25.1, 9.8.

3-Dodecanol.[21] IR (neat) 3100-3600, 2965, 2930, 2860, 1465 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 3.48-3.57 (m, 1H), 1.20-1.60 (m, 19H), 0.94 (t, J= 7.3 Hz, 3H), 0.88 (t, J= 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 73.5, 37.1, 32.0, 30.3, 29.8, 29.7, 29.7, 29.4, 25.8, 22.8, 14.1, 9.9.

6-Hydroxyoctanenitrile. IR (neat) 3150-3650, 2940, 2860, 2240, 1460 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 3.50-3.60 (m, 1H), 2.37 (t, J= 7.0 Hz, 2H), 1.38-1.80 (m, 9H), 0.95 (t, J= 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 121.3 (weak), 73.0, 36.0, 30.4, 25.6, 25.0, 17.2, 9.8. MS (EI) m/e (relative intensity) 142 ($[M+1]^+$, 4.5), 140 (3.8), 124 (100.0), 112 (13.8), 94 (7.3), 84 (80.6), 67 (21.3), 59 (37.3), 54 (65.6).

1-Chloro-8-decanol. IR (neat) 3100-3650, 2940, 2860, 1465, 1120, 965 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 3.53 (t, J= 6.7 Hz, 2H), 3.52 (m, 1H), 1.72-1.83 (m, 2H), 1.20-1.60 (m, 13H), 0.94 (t, J= 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 73.3, 45.0, 36.9, 32.7, 30.2, 29.6, 28.9, 26.9, 25.6, 9.8. MS (EI) m/e (relative intensity) 192 (M^+, 0.1), 175 (8.6), 163 (28.3), 145 (5.6), 109 (87.4), 97 (7.1), 83 (14.9), 67 (18.8), 59 (100.0), 55 (35.1). Calcd for $C_{10}H_{21}ClO$ m/e 192.1281, found m/e 192.1281.

1-Phenyl-2-butanol.[22] IR (neat) 3120-3650, 3015, 3055, 2970, 2940, 2880, 1495, 1455, 1110, 1080, 1015, 975, 740, 695 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 7.20-7.35 (m, 5H), 3.70-3.78 (m, 1H), 2.83 (dd, J= 13.5, 4.3 Hz, 1H), 2.64 (dd, J= 13.5, 8.4 Hz, 1H), 1.44-1.68 (m, 3H), 0.99 (t, J= 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 138.8, 129.5, 128.5, 126.4, 74.0, 43.7, 29.7, 10.0.

1-(4-Methylphenyl)-2-butanol. IR (neat) 3120-3650, 3055, 3015, 2970, 2930, 2880, 1535, 1465, 1120, 1040, 975, 800 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 7.12 (m, 4H), 3.65-3.76 (m, 1H), 2.80 (dd, J= 13.6, 4.3 Hz, 1H), 2.60 (dd, J= 13.6, 8.4 Hz, 1H), 2.33 (s, 3H), 1.45-1.65 (m, 3H), 0.99 (t, J= 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 135.9, 135.6, 129.4, 129.3, 74.1, 43.2, 29.6, 21.0, 10.0. MS (EI) m/e (relative intensity) 164 (M^+, 0.6), 135 (5.2), 106 (100.0), 91 (53.3), 77 (12.2). Calcd for $C_{11}H_{16}O$ m/e 164.1201, found m/e 164.1196.

1-(4-Methoxyphenyl)-2-butanol. IR (neat) 3130-3660, 3060, 3035, 2970, 2935, 2875, 1610, 1510, 1465, 1250, 1180, 1110, 1035, 970, 800 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 7.12 (d, J= 8.5 Hz, 2H), 6.84 (d, J= 8.5 Hz, 2H), 3.77 (s, 3H), 3.63-3.72 (m, 1H), 2.75 (dd, J= 13.7, 4.4 Hz, 1H), 2.57 (dd, J= 13.7, 8.3 Hz, 1H), 1.72 (br s, 1H), 1.40-1.61 (m, 2H), 0.97 (t, J= 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 158.2, 130.7, 130.2, 113.9, 73.9, 55.1, 42.6, 29.4, 9.9. MS (EI) m/e (relative intensity) 180 (M^+, 30.1), 163 (0.6), 151 (0.3), 122 (100.0), 121 (70.7), 107 (16.9), 91 (6.9), 77 (6.4), 59 (5.2). Calcd for $C_{11}H_{16}O_2$ m/e 180.1150, found m/e 180.1150.

Typical Procedure for Intramolecular Epoxide-Opening Reaction. Lithium (70.5 mg, 10.2 mmol) and naphthalene (1.437 g, 11.2 mmol) in freshly distilled THF (10 mL) were stirred at ambient temperature for 2 h under argon. The dark green preformed lithium naphthalide solution was then transferred via a cannula into a 0 °C solution of CuI/PPh_3, which was prepared *in situ* by stirring CuI (1.769 g, 9.3 mmol) and PPh_3 (4.870 g, 18.6 mmol) in freshly distilled THF (10 mL) at room temperature for 1 h. After stirring at 0 °C for 0.5 h, the reaction mixture was then cooled to -45 °C (dry ice-CH_3CN bath). A solution of GC internal standard (n-undecane) and 5-bromo-1,2-epoxypentane (362.0 mg, 2.2 mmol) in THF (10 mL) was rapidly added to the activated copper at -45 °C. The reaction mixture was stirred at -45 °C for an additional 5 min, and was then allowed to warm to -23 °C (dry ice-CCl_4 bath). The reaction mixture was stirred at -23 °C for 3 h and was gradually warmed to room temperature. Aliquots were withdrawn and quenched with saturated aqueous NH_4Cl solution at -45 °C, -23 °C, 0 °C, and room temperature. The organic solution of each aliquot was dried over $MgSO_4$ and was subject to GC analysis (12'x1/8" stainless steel column packed with OV-17 (3%) on 100/120 Chromosorb G-NAW). The maximum yield was usually achieved around 0 °C. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$ solution (15 mL) at room temperature. After stirring at room temperature for 20 min, the reaction mixture was then transferred into a separatory funnel and was extracted twice with diethyl ether (100 mL each). The combined ether layers were dried over anhydrous $MgSO_4$ and were carefully concentrated under reduced pressure at 5 °C. The resulting residue was filtered and washed with hexanes-Et_2O (1:1, v/v). The combined washings were concentrated and chromatographed on silica gel to give a mixture of cyclopentanol and cyclobutylmethanol (37:1) as a colorless liquid. The product was further purified by preparative GC (12'x1/4" stainless steel column packed with SP-2100 (10%) on 100/120 Supelcoport). Cyclopentanol:[21] IR (neat) 3050-3650, 2960, 2870, 1340, 1165, 990 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 4.28-4.40 (m, 1H), 1.98 (s, 1H), 1.66-1.86 (m, 4H), 1.40-1.66 (m,4H). ^{13}C NMR ($CDCl_3$) δ 74.2, 35.8, 23.4. The proton resonances at 3.61 (d, J= 7.2 Hz) and 2.52 (m) were tentatively assigned to cyclobutylmethanol.

Cyclohexanol.[21] ^1H NMR (360 MHz, $CDCl_3$) δ 3.63 (m, 1H), 1.10-1.95 (m, 11H). ^{13}C NMR ($CDCl_3$) δ 70.3, 35.6, 25.6, 24.2.

Cyclopentylmethanol.[21] IR (neat) 3050-3620, 2950, 2865, 1455, 1030 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 3.45 (d, J= 7.1 Hz, 2H), 1.98-2.12 (m, 1H), 1.65-1.77 (m, 2H), 1.45-1.65 (m, 4H), 1.13-1.27 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 67.3, 42.1, 29.1, 25.4.

1-Methylcyclopentanol.[21] IR (neat) 3050-3650, 2960, 2870, 1445, 1370, 1320, 1205, 1115, 1030, 930, 900 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 1.50-1.90 (m, 8H), 1.46 (s, 1H), 1.36 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 80.2, 41.4, 28.3, 24.1.

1-Cyclobutylethanol.[23] IR (neat) 3050-3700, 2960, 2860, 1445, 1375, 1090, 1015, cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 3.64-3.74 (m, 1H), 2.20-2.33 (m, 1H), 1.70-2.10 (m, 6H), 1.48 (s, 1H), 1.08 (d, J= 6.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 72.2, 42.9, 24.4, 24.3, 20.3, 17.8.

Cyclopropylmethanol.[21] IR (neat) 3100-3680, 3080, 3010, 2870, 1430, 1030 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 3.44 (d, J= 7.1 Hz, 2H), 1.04-1.17 (m, 1H), 0.53 (m, 2H), 0.21 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 67.9, 13.7, 2.8.

Cyclopropylmethyl benzoate. IR (neat) 3070, 3010, 2950, 2890, 1720, 1605, 1585, 1270, 1105, 960, 705 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 8.00-8.15 (m, 2H), 7.35-7.60 (m, 3H), 4.15 (d, J= 7.2 Hz, 2H), 1.15-1.40 (m, 1H), 0.54-0.67 (m, 2H), 0.31-0.42 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 166.6, 132.7, 130.4, 129.5, 128.2, 69.5, 9.8, 3.2. MS (EI) m/e (relative intensity) 176 (M^+, 1.5), 158 (0.3), 148 (1.2), 120 (4.0), 105 (100.0), 77 (26.7), 55 (11.6). Calcd for $C_{11}H_{12}O_2$ m/e 176.0837, found m/e 176.0833.

1-Methylcyclopropylmethanol.[24] ^1H NMR (360 MHz, $CDCl_3$) δ 3.38 (s, 2H), 3.22 (br s, 1H), 1.15 (d, 3H), 0.28-0.45 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 71.2, 20.5, 18.3, 10.9.

Cycloheptanol.[21] IR (neat) 3010-3600, 2910, 2850, 1445, 1020 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) δ 3.80-3.90 (m, 1H), 1.86-1.97 (m, 2H), 1.35-1.70 (m, 11H). ^{13}C NMR ($CDCl_3$) δ 72.9, 37.7, 28.2, 22.7.

1-(6-Cyanohex-1-yl)-1-cyclopentanol. IR (neat) 3100-3600, 2920, 2850, 2235, 1460, 1175, 1110 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 2.34 (t, J= 7.0 Hz, 2H), 1.30-1.90 (m, 18H), 1.14 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 119.7, 82.3, 41.3, 39.6, 29.2, 28.6, 25.2, 24.3, 23.7, 17.0.

5-Oxaspiro[4.5]decan-6-one.[25] IR (neat) 2950, 2870, 1730, 1440, 1340, 1250, 1155, 1020 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 2.52 (m, 2H), 1.55-2.05 (m, 12H). ^{13}C NMR ($CDCl_3$) δ 171.4, 93.1, 39.4, 32.2, 29.3, 23.7, 17.7.

References and Footnotes

1. Rieke, R. D.; Burns, T. P.; Wehmeyer, R. M.; Kahn, B. E. "High-Energy Processes in Organometallic Chemistry", ACS Symposium Series No. 333; American Chemical Society: Washington, D.C., 1987; Chapter 14, p 223.

2. (a) Wu, T.-C.; Wehmeyer, R. M.; Rieke, R. D. J. Org. Chem. 1987, 52, 5057, (b) Wehmeyer, R. M.; Rieke, R. D. J. Org. Chem. 1987, 52, 5056, (c) Ebert, G. W.; Rieke, R. D. J. Org. Chem. 1984, 49, 5280, (d) Rieke, R. D.; Rhyne, L. D. J. Org. Chem. 1979, 44, 3445, (e) Ebert, G. W.; Rieke, R. D. J. Org. Chem. in press, (f) Wehmeyer, R. M.; Rieke, R. D., submitted for publication, (g) Wu, T.-C.; Rieke, R. D., submitted for publication.

3. Among the numerous excellent reviews in Cu chemistry are: (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. (g) "Comprehensive Organic Chemistry", Barton, D. and Ollis, W.D., Ed.; Pergamon Press: Oxford, 1979, Vol. 3, Chapter 15. (h) "Gmelin Handbook of Inorganic Chemistry: Organocopper Compounds", Springer-Verlag: Berlin, Part 1, 1985; Part 2, 1983. (i) "Comprehensive Organometallic Chemistry", Wilkinson, G; Stone, F.G.A., Abel, E.W., Ed.; Pergamon Press: Oxford, 1982; Vol. 2, pp 709-763; Vol. 7, pp 685-722.

4. Gilman, H.; Jones, R. G.; Woods, L. A. J. Org. Chem. 1952, 17, 1630.

5. Kharasch, M. S.; Tawney, P. O. J. Am. Chem. Soc. 1941, 63, 2308.

6. Background for the steric and electronic effects of phosphine ligands in transition-metal catalyzed reactions has been summarized in several papers and references included therein. (a) Tolman, C.A. J. Am. Chem. Soc. 1970, 92, 2953, 2956. (b) Tolman, C.A. Chem. Reviews 1977, 313. (c) "Comprehensive Organic Chemistry", Barton, D. and Ollis, W.D., Ed.; Pergamon Press: Oxford, 1979, Vol 2, Chapter 10.(9) Corey, E.J.; Boaz, N.W. Tetrahedron Lett. 1985, 26, 6015.

7. Many examples of similar intramolecular epoxide-opening reactions have been reported using other metals. (a) Cooke, Jr., M. P. and Houpis, I. N. Tet. Lett. 1985, 26, 3643, (b) Babler, J. H. and Bauta, W. E. Tet. Lett. 1984, 25, 4323, (c) Last, L. A.; Fretz, E. R.; Coates, R. M. J. Org. Chem. 1982, 47, 3211, (d) Dhawan, K. L.; Gowland, B. D.; Durst, T. J. Org. Chem. 1980, 45, 922, (e) Bradsher, C. K.; Reames, D. C. J. Org. Chem. 1978, 43, 3800.

8. Many examples of similar intramolecular 1,2-carbonyl addition reactions have been reported using other metals. (a) Cooke, M.P.; Houpis, I.N. Tetrahedron Lett. 1985, 26, 4987, (b) Molander, G.A.; Etter, J.B. Tetrahedron Lett. 1984, 25, 3281 and references included therein. Intramolecular cyclization has also been reported for a vinylcopper species. (c) Corey, E.J.; Kuwajima, I. J. Am. Chem. Soc. 1970, 92, 395.

9. Kauffman, G.; Teter, L. Inorg. Synth. 1963, 7. The preparation of $CuIPBu_3$ as well as a method for purification of CuI is given. $CuIPEt_3$ was prepared using the same procedure. $CuIPR_3$ complexes prepared *in situ* from unpurified CuI are very dark in solution while those prepared *in situ* from purified CuI give clear solutions.

10. (a) Corey, E.J.; Boaz, N.W. Tetrahedron Lett. 1985, 26, 6019, (b) Corey, E.J.; Boaz, N.W. Tetrahedron Lett. 1985, 26, 6019, (c) Alexakis, A.; Berlan, J.; Besace, Y. Tetrahedron Lett. 1986, 27, 1047.

11. Suzuki, M.; Suzuki, T.; Kawagishi, T.; Noyori, R. Tetrahedron Lett. 1980, 1247.

12. Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Ishihara, Y.; Maruyama, K. J. Org. Chem. 1982, 47, 119 and references cited therein.

13. Whitesides, G. M.; Stedronsky, E. R.; Casey, C. P.; Filippo, J. S., Jr. J. Am. Chem. Soc. 1970, 92, 1426.

14. Herr, R. W.; Wieland, D. M.; Johnson, C. R. J. Am. Chem. Soc. 1970, 92, 3813.

15. The use of THF as solvent for the epoxide opening reactions by higher order organocuprates has been reported by Lipshutz *et al*. (a) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A.; Parker, D. J. Org. Chem. 1984, 49, 3928, (b) Lipshutz, B. H.; Kozlowski, J.; Wilhelm, R. S. J. Am. Chem. Soc. 1982, 104, 2305.

16. A number of examples of the intramolecular epoxide-opening reactions involving attack of stabilized carbanions have been reviewed by Smith, J. G. Synthesis 1984, 635.

17. Baldwin, in his "rules for ring closure", discribed that "the rules for opening three-membered rings to form cyclic structures, seem to lie between those for tetrahedral and trigonal systems, generally preferring *exo*-modes", Baldwin, J. E. J. Chem. Soc., Chem. Commun. 1976, 734.

18. Baldwin's rules do not consider the substituent effects. Upon substitution at reactive sites of a molecule, the regiochemistry is often changed to sterically minimize the nonbonding interactions involved in the transition state.

19. Diesbach, H.; Bulliard, P. Helvetica Chim. Acta. 1924, 7, 618.

20. Helberger, J.H.; Rebay, A. Ann. 1937, 531, 279.

21. The spectral data of synthesized products are identical to those obtained from authentic samples.

22. The ^{13}C NMR spectral data are identical to those reported by Zushi, S.; Kodama, Y.; Fukuda, Y.; Nishihata, K.; Nishio, M.; Hirota, M.; Uzawa, J. Bull. Chem. Soc. Jpn. 1981, 54, 2113.

23. 1-Cyclobutylethanol was also synthesized by $LiAlH_4$ reduction of cyclobutyl methyl ketone. The spectral data of this synthesized alcohol are identical to those obtained from the cyclized product.

24. ^1H NMR spectral data: see House, H. O.; Weeks, P. D. J. Am. Chem. Soc. 1975, 97, 2778. ^{13}C NMR spectral data: see Burton, J. T.; Puddephatt, R. J. Organometallics 1983, 2(11), 1487.

25. Canonne, P.; Foscolos, G. B.; Belanger, D. J. Org. Chem. 1980, 45, 1828.