The Composition of Lithium Methylcuprates in Ether Solvents

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Abstract: Variable temperature ^1H NMR studies on the system CH_3Li–CH_3Cu in various stoichiometric ratios have been carried out in Me_2O, Et_2O, and THF. In Me_2O and THF, $LiCu_2(CH_3)_3$ and $LiCu(CH_3)_2$ have been found to exist as pure stoichiometric compounds when the $CH_3Li:CH_3Cu$ ratio is 1:2 and 1:1, respectively. When the $CH_3Li:CH_3Cu$ ratio is 2:1, $Li_2Cu(CH_3)_3$ is formed as an equilibrium mixture containing $LiCu(CH_3)_2$ and CH_3Li. In Et_2O, evidence is presented to indicate the existence of $Li_2Cu_3(CH_3)_5$, $LiCu(CH_3)_2$, and $Li_2Cu(CH_3)_3$. The first two compounds can be prepared stoichiometrically pure. However, the latter compound is part of an equilibrium mixture. The solution composition of these cuprates is presented based on variable temperature NMR and molecular association data.

Lithium dialkylcuprates have proven to be very versatile reagents in organic synthesis.[1] Several recent reports, however, have been concerned with unusual reactivity of reagents prepared by mixing lithium dialkl- or diarylcuprates with the corresponding organolithium compounds. For example, the reagent having the stoichiometry $LiCuPh_2 \cdot PhLi$ appears to be more reactive than $LiCuPh_2$ in metal–halogen exchange reactions and coupling with aryl bromides.[2] Also it has been recently found that a 3:2 mixture of $LiCu(CH_3)_2$ and CH_3Li is more stereoselective toward 4-*tert*-butylcyclohexanone than either $LiCu(CH_3)_2$ or CH_3Li.[3] In addition, mixtures of $LiCu(CH_3)_2$ and CH_3Li have been found to react with diaryl ketones as if a reducing agent more powerful than either $LiCu(CH_3)_2$ or CH_3Li were present.[4] These reports suggest that lithium diorganocuprates and organolithium compounds are capable of reacting to form complexes of the type $Li_2Cu(CH_3)_3$ and $Li_3Cu(CH_3)_4$. However, previous ^1H and natural abundance ^{13}C NMR studies on the system CH_3Li–$LiCu(CH_3)_2$ in diethyl ether at -60 °C failed to detect the existence of any complexes.[4,5,13] In view of the intense interest in this area and the obvious possibility of the existence of other cuprates in addition to $LiCu(CH_3)_2$, we decided to study the ^1H NMR of the CH_3Li–CH_3Cu mixture further.

Dimethyl ether was chosen as the initial solvent for this study since methyl group exchange rates should be significantly slower in dimethyl ether (owing to its greater basicity) than conventional ether solvents (e.g., diethyl ether). In addition, considerably lower solution temperatures can be reached with dimethyl ether (-136 vs. -100 °C) than with most other ethers. After the studies in dimethyl ether, the cuprates were studied in tetrahydrofuran and then finally in diethyl ether. It was our hope that the results obtained in the more basic solvents, dimethyl ether and THF, could be used to help explain the system in diethyl ether. In addition, various ligands were added to the cuprates in diethyl ether in an effort to clarify the situation in that solvent.

Experimental Section

Apparatus. Reactions were performed under nitrogen at the bench using Schlenk tube techniques.[6] Other manipulations were carried out in a glove box equipped with a recirculating system.[7] ^1H NMR spectra were obtained using a Varian A-60 NMR spectrometer. All chemical shift values are expressed in values (ppm) relative to $(CH_3)_4Si$. Calibrated syringes equipped with stainless steel needles were used for transfer of reagents. Deliveries could be reproduced to better than 0.5%.

Analytical. Active CH_3 group analysis was carried out by hydrolyzing samples with hydrochloric acid on a standard vacuum line and collecting the evolved methane with a Toepler pump.[6] Lithium was determined by flame photometry, halide was determined by the Volhard procedure, and copper was determined by electrolytic deposition on a Pt electrode.

Materials. Tetrahydrofuran (Fisher Certified Reagent Grade) was distilled under nitrogen over $NaAlH_4$ and diethyl ether (Fisher Reagent) over $LiAlH_4$ prior to use. Dimethyl ether was stored at -78 °C over $LiAlH_4$ and vapor transferred (by means of a vacuum line) just prior to use. Lithium metal was obtained as a 30% dispersion in petrolatum from Alfa-Ventron. Dimethylmercury, obtained from Org-Met, was found to be pure and therefore used without any further purification. Methyllithium in THF, Me_2O, and Et_2O was prepared halide-free by the reaction of $(CH_3)_2Hg$ with excess lithium metal. All solutions of CH_3Li were stored at -78 °C until ready to use. Analysis of the CH_3Li solutions gave CH_3:Li ratios of essentially 1:1 and the solutions were used within a week of preparation. Cuprous iodide (Fisher Reagent) was purified by precipitation from an aqueous solution of KI–CuI and the resulting solid washed with distilled water, ethanol, and diethyl ether prior to drying at room temperature under reduced pressure. Cuprous chloride was prepared by the reaction of copper(II) chloride dihydrate (Baker Purified) with sodium sulfite.[9] The resulting precipitated solid was washed with an aqueous solution of SO_2, glacial acetic acid, ethanol, and diethyl ether, then dried at room temperature under reduced pressure. Tri-*n*-butylphosphine (98%) was obtained from Aldrich chemical Co. and used without further purification. Solutions of tetrakis[chloro(tri-*n*-butylphosphine)copper(I)] in diethyl ether were prepared by adding tri-*n*-butylphosphine to a slurry of CuCl in 1:1 ratio. The resulting mixture was stirred overnight, then filtered the next day to remove traces of residual material that remained. An analysis of the resulting solution indicated that Cu and Cl were present in a 1.00:1.03 ratio.

Preparation of Cuprates. Diethyl Ether Solvents. Solutions of the cuprates were prepared free of contaminants for NMR and molecular weight experiments. Cuprous iodide was allowed to react with CH_3Li in 1:1 ratio at -78 °C to produce CH_3Cu as a yellow solid slurry. The yellow solid was prepared free of LiI by centrifuging, decanting, and washing with several portions of dry diethyl ether. These manipulations were carried out under nitrogen at -78 °C. The resulting CH_3Cu was slurried with dry ether and used in this way as a reagent. A typical analysis of the slurry showed Li, Cu, CH_3, and I present in molar ratios of 0.02:1.00:0.97:0.01. The slurry was stored at -78 °C.

Methyllithium was then allowed to react with samples of the CH_3Cu slurry in ratios of 0.50, 0.75, 1.00, 2.00, 3.00, and 4.00 (CH_3Li/CH_3Cu) at -78 °C. NMR samples of the resulting solutions were prepared at -78 °C by transferring the solutions to NMR tubes equipped with rubber septum caps by means of a cannula. These solutions were also analyzed for Li, Cu, and CH_3. (See Table I for some representative data.)

Solutions of $Li_2Cu_3(CH_3)_5$, $LiCu(CH_3)_2$, and $Li_2Cu(CH_3)_3$ used in the molecular weight measurements were prepared in a similar way.

Tetrahydrofuran Solvent. Solutions of cuprates in this solvent were prepared in the same way as described above for diethyl ether. In

Table I. Chemical Shifts for the System CH_3Li-CH_3Cu in Diethyl Ether

Approximate ratio CH_3Li/CH_3Cu	Temp, °C	δ^a	Analysis of the solution		
			Li	Cu	CH_3
3	−51	1.09, 1.95	2.80	1.00	3.88
	−67	1.13, 2.01			
	−83	1.09, 1.98			
	−98	1.09, 1.98			
1	−83	1.09	1.02	1.00	1.96
	−98	1.10			
0.75	−67	0.95	2.18	3.00	5.09
	−83	0.99			
	−98	1.03			
0.50	−67	0.93	2.24	3.00	4.97
	−83	0.99			
	−98	0.94 (sh), 1.01			
	−106	0.88 (sh), 1.08			

^{a} Parts per million upfield from Me_4Si.

Table II. Chemical Shifts for the System CH_3Li-$CH_3Cu\cdot P(n$-$Bu)_3$ in Diethyl Ether

Approximate ratio CH_3Li/CH_3Cu	Temp, °C	δ^a	Analysis of the solution		
			Li	Cu	CH_3
4	−51	1.13, 1.97	4.06	1.00	4.87
	−67	1.10, 1.23, 1.98			
	−83	1.10, 1.25, 1.96			
	−98	1.09, 1.24, 1.98			
2	−36	1.11, 1.97	2.04	1.00	2.86
	−51	1.12, 1.97			
	−67	1.10, 1.25, 1.98			
	−83	1.11, 1.24, 1.99			
	−98	1.10, 1.24, 1.98			
1	−67	1.11	1.02	1.00	1.91
	−83	1.09			
	−98	1.10			
0.75	−51	0.85	1.97	3.00	4.87
	−67	0.85			
	−83	0.85			
	−98	0.85			
0.50	−51	0.69	0.98	2.00	2.86
	−67	0.68			
	−83	0.69			
	−98	0.68			
	−106	0.69			

^{a} Parts per million upfield from Me_4Si.

addition, the same cuprates were prepared in the presence of LiI in order to evaluate the effect of LiI on the solution composition.

Dimethyl Ether Solvent. Since LiI was found to be mostly insoluble in dimethyl ether, solutions of cuprates in this solvent were prepared by adding CH_3Li directly to CuI in 1.50, 1.75, 2.00, 3.00, and 4.00 ratios at −78 °C. For obtaining NMR spectra, samples of the supernatant solutions were transferred at −78 °C by means of a cannula to NMR tubes with rubber septum caps. The supernatant solutions were also analyzed for Li, Cu, and CH_3. Typically, the amount of LiI remaining in these solutions was equivalent to about 15% of the copper present. It is felt, however, that the presence of this halide did not influence the NMR spectra. This statement is based on the fact that the NMR spectra in THF were unchanged by the presence of halide and were essentially the same as the spectra observed in dimethyl ether.

Diethyl Ether Solvent with P(n-Bu)₃ Present. The cuprates in this system were prepared by reacting CH_3Li with $[CuCl\cdot P(n$-$Bu)_3]_4$ in ratios of 1.50, 1.75, 2.00, 3.00, 4.00, and 5.00 in diethyl ether at room temperature. The resulting mixtures were stirred at this temperature
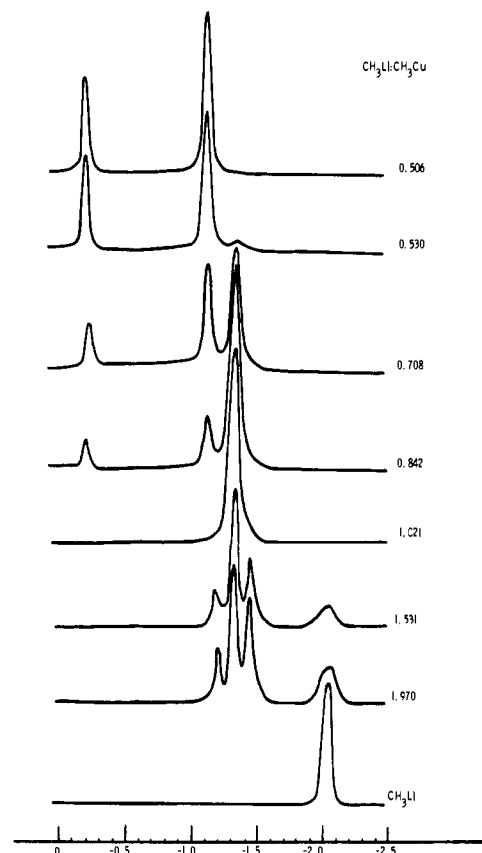

Figure 1. 60MHz ^{1}H NMR at −136 °C in dimethyl ether for solutions of CH_3Li-CH_3Cu.

for about 2 h in order to assure complete precipitation of LiCl. The mixtures were then cooled to −78 °C and the LiCl allowed to settle. The supernatant solutions were analyzed and prepared for obtaining NMR spectra in the way described above. (See Table II for representative data.)

Molecular Weight Measurements. The solutions of $LiCu_2(CH_3)_3$, $LiCu(CH_3)_2$, and $Li_2Cu(CH_3)_3$, used in the molecular weight measurements, were prepared as above except that the LiCl by-product was removed in order to obtain pure solutions.

The ebullioscopic technique reported earlier[10] was used for determining molecular weights of the cuprates in this study. The concentration of solute molecules is given approximately by

$$C = \frac{1000\rho}{M_1\left(1 + \dfrac{1000\,K_B}{M_1 T_B}\right)} \tag{1}$$

where ρ is the density of the solvent in g/cm^3, M_1 is the molecular weight of the solvent, K_B is the molal boiling point elevation constant, and ΔT_B is the boiling point elevation in °C. The concentration of solute molecules C is in units of molarity. Equation 1 was derived from eq 2 reported earlier[10]

$$i = \frac{W_2 M_1}{W_1 M_2}\left[\frac{1}{e^{\Delta T_B M_1/1000 K_B} - 1}\right] \tag{2}$$

where i is the molecular association. In this study the molecular association was determined by taking the ratio of the solution concentration (as determined by analysis) to the apparent solution concentration given by eq 1. The results of these molecular weight measurements are given in Figures 5-7. Molecular weight measurements in diethyl ether were carried out at 740.0 mmHg pressure of N_2 (K_B = 2.06). In THF the measurements were made at 240.0 mmHg pressure of N_2 (K_B = 1.79).

Results and Discussion

^{1}H NMR spectra for the system CH_3Li-CH_3Cu at −136 °C[1] in dimethyl ether solvent are shown in Figure 1 at molar ratios ranging from 0.51 to 1.97. When the ratio of CH_3Li:
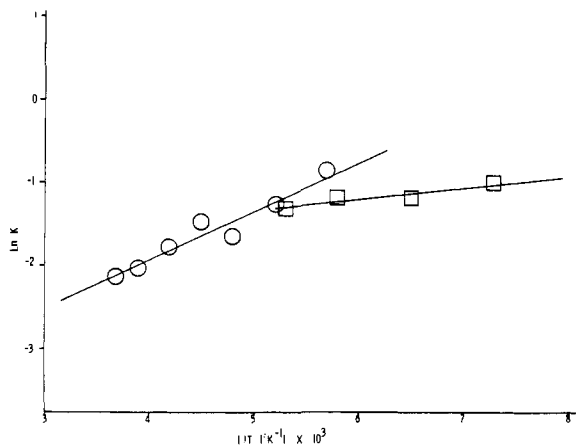
Figure 2. Plot of ln K vs. $1/T$ for the reaction $\frac{1}{4}(CH_3Li)_4 + \frac{1}{2}[LiCu(CH_3)_2] \rightleftharpoons Li_2Cu(CH_3)_3$ in the systems □, CH_3Li-CH_3Cu in dimethyl ether; O CH_3Li-CH_3Cu in THF.

CH_3Cu was less than 1, three signals were observed (δ −0.22, −1.17, and −1.38). The signal at δ −1.38 (assigned to $LiCu(CH_3)_2$) became more intense as the $CH_3Li:CH_3Cu$ ratio was increased from 0.53 to 1.02 and was the only one observed at the latter ratio. The signals at δ −0.22 and −1.17 integrated in approximately a 1:2 ratio (the range was 1:1.8–1:2.1) and were assigned to $LiCu_2(CH_3)_3$, since they were the only ones observed at a $CH_3Li:CH_3Cu$ ratio of 0.51. When the ratio of $CH_3Li:CH_3Cu$ was greater than 1, four signals were observed (δ −1.25, −1.38, −1.49, and −2.03). The signals at δ −2.03 and −1.38 were assigned to CH_3Li and $LiCu(CH_3)_2$, respectively, while the signals at δ −1.25 and −1.49, which integrated in an approximate ratio of 1:2 (the range was 1:1.7–1:2.1), were assigned to $Li_2Cu(CH_3)_3$. The presence of $Li_2Cu(CH_3)_3$ was indicated by integration of the NMR spectra, which allows a calculation of equilibrium constants for the reaction[11] described by eq 3.

$$\frac{1}{4}(CH_3Li)_4 + \frac{1}{2}[LiCu(CH_3)_2]_2 \rightleftharpoons Li_2Cu(CH_3)_3 \quad (3)$$
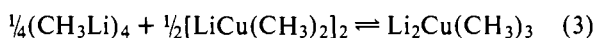
At the various ratios of $CH_3Li:CH_3Cu$ used in this study, the equilibrium constants were essentially the same. For example, the equilibrium constant at −136 °C for a $CH_3Li:CH_3Cu$ ratio of 1.53 was 0.36 and for a ratio of 1.97 at −136 °C was also 0.36. In addition to this evidence, a straight line was obtained when equilibrium constants were calculated at several different temperatures and plotted as ln K vs. $1/T$ (see Figure 2 and data in Table III). If any equilibrium mixture other than CH_3Li, $LiCu(CH_3)_2$, and $Li_2Cu(CH_3)_3$ is assumed, the calculated equilibrium constants do not have the consistency as those above. For example, if one assumes an equilibrium mixture of CH_3Li, $LiCu(CH_3)_2$, and $Li_3Cu(CH_3)_4$, then the equilibrium constants calculated at −136 °C for $CH_3Li:CH_3Cu$ ratios of 1.53 and 1.97 become 0.15 and 0.26. In addition, a linear curve fit to ln K vs. $1/T$ for this mixture yielded a correlation coefficient of 0.46. The correlation coefficient, assuming a mixture of CH_3Li, $LiCu(CH_3)_2$, and $Li_2Cu(CH_3)_3$, is 0.95. This leads us to conclude that the signals at δ −1.25 and 1.49 must be due to $Li_2Cu(CH_3)_3$. Increasing $CH_3Li:CH_3Cu$ ratio above 2 did not result in the appearance of any new signals.

The ^{1}H NMR spectra in THF at −98 °C were very similar to those observed in dimethyl ether, indicating that the solution composition in these two solvents should be similar. When the ratio of $CH_3Li:CH_3Cu$ was 0.51, two signals (which always integrated in an approximately 1:2 ratio) were observed at δ −0.24 and −1.24. These signals correspond very closely to those observed for $LiCu_2(CH_3)_3$ in dimethyl ether and were assigned to that compound. At $CH_3Li:CH_3Cu$ ratios intermediate between 0.5 and 1.0, three signals were observed (δ

Table III. Equilibrium Constants and Thermodynamic Parameters for the Reaction

$$\frac{1}{4}(CH_3Li)_4 + \frac{1}{2}(LiCu(CH_3)_2)_2 \overset{K}{\rightleftharpoons} Li_2Cu(CH_3)_3$$

System	Temp, °C	K	$\Delta H^{\circ a}$	$\Delta S^{\circ b}$
CH_3Li-CH_3Cu	−38	2.2	5.9	27
(Et_2O)	−51	0.76		
	−67	0.32		
	−83	0.19		
	−98	0.02		
$CH_3Li-CH_3Cu\cdot P(n-$	−51	1.8	3.3	16
$Bu)_3$				
(Et_2O)	−67	0.77		
	−83	0.53		
	−98	0.22		
	−106	0.12		
CH_3Li-CH_3Cu	−5	0.12	−1.2	−8.6
(THF)	−19	0.13		
	−36	0.17		
	−51	0.22		
	−67	0.19		
	−83	0.27		
	−98	0.42		
CH_3Li-CH_3Cu	−84	0.27	−0.25	−3.9
(Me_2O)	−102	0.30		
	−119	0.30		
	−136	0.36		

^{a} kcal/mol. ^{b} cal/K mol.

−0.24, −1.24, and −1.50). The signal at δ −1.50 (assigned to $LiCu(CH_3)_2$) became more intense as the $CH_3Li:CH_3Cu$ ratio was increased from 0.51 to 1.02 and was the only signal observed at the latter ratio. When the ratio of $CH_3Li:CH_3Cu$ was greater than 1, four signals were observed (δ −1.37, −1.50, −1.63, and −2.01). The signal at δ −2.01 was assigned to CH_3Li since CH_3Li alone gave a signal at this position. The signals at −1.37 and −1.63 (which integrated in an approximately 1:2 ratio) were assigned to $Li_2Cu(CH_3)_3$, since these signals were very similar to the signals observed for $Li_2Cu(CH_3)_3$ in dimethyl ether. This point was established by calculating equilibrium constants from the integration data for several equilibrium mixtures. The system CH_3Li, $LiCu(CH_3)_2$, $Li_2Cu(CH_3)_3$ (eq 3) yielded the most consistent equilibrium constants; therefore, the signals at δ −1.37 and −1.63 are attributed to $Li_2Cu(CH_3)_3$. A plot of ln K vs. $1/T$ for this system is shown in Figure 2 and the equilibrium constants are listed in Table III.

The chemical shifts observed upfield from Me_4Si in diethyl ether at various temperatures and selected ratios of $CH_3Li:CH_3Cu$ are given in Table I. Selected NMR spectra are shown in Figure 3. In this solvent the direct observation of signals assignable to any complexes other than $LiCu(CH_3)_2$ was not possible. However, indirect evidence can be presented for the existence of the complexes $Li_2Cu_3(CH_3)_5$ and $Li_2Cu(CH_3)_3$. The addition of CH_3Li to a slurry of CH_3Cu in diethyl ether yielded a clear solution when the ratio of $CH_3Li:CH_3Cu$ reached 0.67. In both dimethyl ether and THF, this happened when the ratio was 0.50. Since $LiCu_2(CH_3)_3$ was observed in both of those solvents, the above observation indicated that $Li_2Cu_3(CH_3)_5$ was formed in diethyl ether. The addition of CH_3Li to a slurry of CH_3Cu in diethyl ether such that the ratio was 1:2 did not result in a clear solution. An analysis of the supernatant solution resulting from this mixture showed that Li, Cu, and CH_3 were present in an approximately 2:3:5 ratio (see Table I). This again indicates that 2:3 is the lowest ratio of Li:Cu that can be obtained in a cuprate complex.
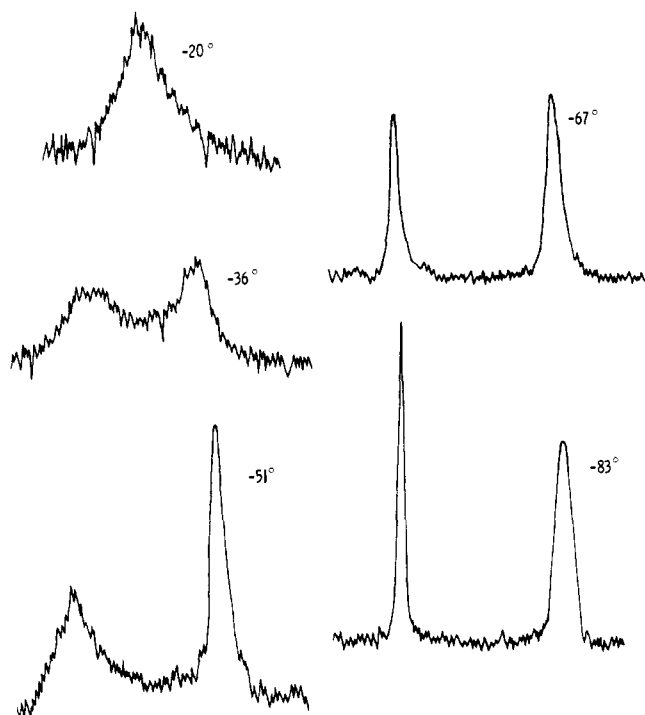
Figure 3. Representative ^{1}H spectra of the $CH_3Li-LiCu(CH_3)_2$ system in diethyl ether.

The integration of NMR spectra recorded for diethyl ether solutions where the ratio of $CH_3Li:CH_3Cu$ was greater than 1 always showed less area under the CH_3Li signal than would have been expected based on an analysis of the solution. This type of behavior is consistent with the formation of a complex between CH_3Li and $LiCu(CH_3)_2$. Using the integration data, equilibrium constants were calculated for several mixtures which contained CH_3Li, $LiCu(CH_3)_2$, and complexes between these two reagents. The equilibrium shown in eq 3 yielded the most consistent set of equilibrium constants (see Table III and Figure 4). For example, a linear curve fit to the data ln K vs. $1/T$ yielded a correlation coefficient of 0.25 when an equilibrium mixture of CH_3Li, $LiCu(CH_3)_2$, and $Li_3Cu(CH_3)_4$ was assumed. On the other hand, when an equilibrium mixture of CH_3Li, $LiCu(CH_3)_2$, and $Li_2Cu(CH_3)_3$ was assumed, the correlation coefficient became 0.91. The assumption of mixtures containing other complexes or combination of complexes gives correlation coefficients much lower than 0.91. This result indicated that the complex between CH_3Li and $LiCu(CH_3)_2$ is $Li_2Cu(CH_3)_3$.

The chemical shifts observed upfield from Me_4Si in diethyl ether when the ligand $P(n\text{-}Bu)_3$ is present are given in Table II. The addition of CH_3Li to a solution of $CuCl\cdot P(n\text{-}Bu)_3$ yielded slurries of CH_3Cu until the ratio of $CH_3Li:CuCl$ reached 1.50. At that point all the CH_3Cu dissolved and only a slurry of $LiCl$ remained. This result indicated that the complex $LiCu_2(CH_3)_3$ was formed. Evidently, the presence of $P(n\text{-}Bu)_3$ favors the formation of $LiCu_2(CH_3)_3$ over $Li_2Cu_3(CH_3)_5$ in diethyl ether. When the ratio of $CH_3Li:CuCl$ was greater than 2, three signals were observed (δ -1.10, -1.24, and -1.97). The signals at δ -1.10 and -1.97 were assigned to $LiCu(CH_3)_2$ and CH_3Li since these compounds alone gave rise to the same signals. The signal at δ -1.24 was assigned to $Li_2Cu(CH_3)_3$. This point was established in the same way as was done in the three previous cases.

The cuprate complexes that exist in the three solvents studied here are listed in Table IV. In dimethyl ether and THF, the NMR data suggest that the reactions as shown in eq 4-6 are taking place.
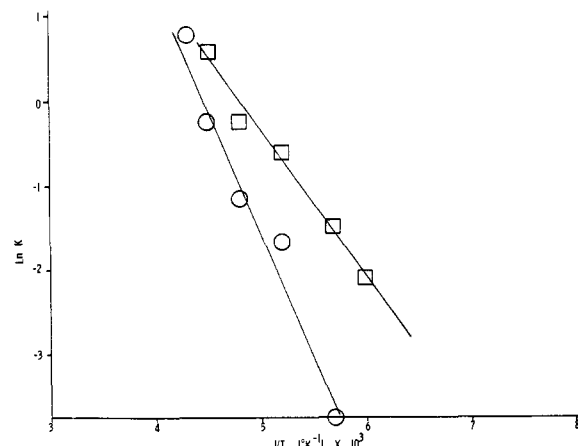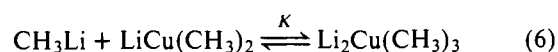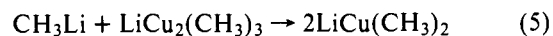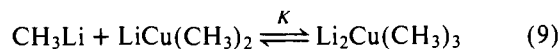
$$CH_3Li + 2CH_3Cu \rightarrow LiCu_2(CH_3)_3 \qquad (4)$$

Figure 4. Plot of ln K vs. $1/T$ for the reaction $\frac{1}{4}(CH_3Li)_4 + \frac{1}{2}[LiCu(CH_3)_2]_2 \rightleftharpoons Li_2Cu(CH_3)_3$ in the systems O, CH_3Li-CH_3Cu in diethyl ether; $\square$, $CH_3Li-CH_3Cu\cdot P(n\text{-}Bu)_3$ in diethyl ether.

Table IV. Cuprate Complexes That Exist in Various Ether Solvents

Dimethyl ether	Tetrahydrofuran	Diethyl ether Without $P(n\text{-}Bu)_3$	With $P(n\text{-}Bu)_3$
$LiCu_2(CH_3)_3$	$LiCu_2(CH_3)_3$	$Li_2Cu_3(CH_3)_5$	$LiCu_2(CH_3)_3$
$LiCu(CH_3)_2$	$LiCu(CH_3)_2$	$LiCu(CH_3)_2$	$LiCu(CH_3)_2$
$Li_2Cu(CH_3)_3$	$Li_2Cu(CH_3)_3$	$Li_2Cu(CH_3)_3$	$Li_2Cu(CH_3)_3$

$$CH_3Li + LiCu_2(CH_3)_3 \rightarrow 2LiCu(CH_3)_2 \qquad (5)$$

$$CH_3Li + LiCu(CH_3)_2 \overset{K}{\rightleftharpoons} Li_2Cu(CH_3)_3 \qquad (6)$$

In diethyl ether alone, the reactions are shown in eq 7-9.

$$2CH_3Li + 3CH_3Cu \rightarrow Li_2Cu_3(CH_3)_5 \qquad (7)$$

$$CH_3Li + Li_2Cu_3(CH_3)_5 \rightarrow 3LiCu(CH_3)_2 \qquad (8)$$

$$CH_3Li + LiCu(CH_3)_2 \overset{K}{\rightleftharpoons} Li_2Cu(CH_3)_3 \qquad (9)$$
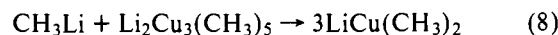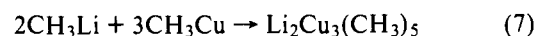
All four systems yield $Li_2Cu(CH_3)_3$ when the ratio $CH_3Li:CH_3Cu$ is greater than 1; and they all yield $LiCu(CH_3)_2$ when the ratio is 1. When the ratio is less than 1, all of the systems except diethyl ether without $P(n\text{-}Bu)_3$ yield $LiCu_2(CH_3)_3$.

Using the NMR integration data for the above systems, equilibrium constants can be calculated for reaction 3. The equilibrium constants at various temperatures for these systems are listed in Table III. Plots of ln K as a function of $1/T$ for these systems are shown in Figures 2 and 3. It can be seen that these plots give rise to straight lines, from which the thermodynamic parameters ΔH and ΔS can be calculated (Table III). It is readily seen that both ΔH and ΔS decrease from positive to negative values as the solvent is changed from diethyl ether to dimethyl ether to THF. This order of solvents also reflects increasing basicity. So it is seen, then, that ΔH and ΔS decrease as the basicity of the solvent is increased, a result which would be expected from increased specific solvation.

Ebullioscopic molecular weight measurements have been carried out on the systems CH_3Li-CH_3Cu in THF, CH_3Li-CH_3Cu in diethyl ether, and $CH_3Li-CH_3Cu\cdot P(n\text{-}Bu)_3$ in diethyl ether. The results of these studies are shown in Figures 5-7. For $LiCu(CH_3)_2$ in THF, the association values varied from 1.81 to 1.91 over a concentration range of 0.071-0.142 M. These results indicate that $LiCu(CH_3)_2$ is dimeric in THF. For $LiCu_2(CH_3)_3$ the association values varied from 1.83 to 2.11 over a concentration range of 0.065-0.095 M, indicating
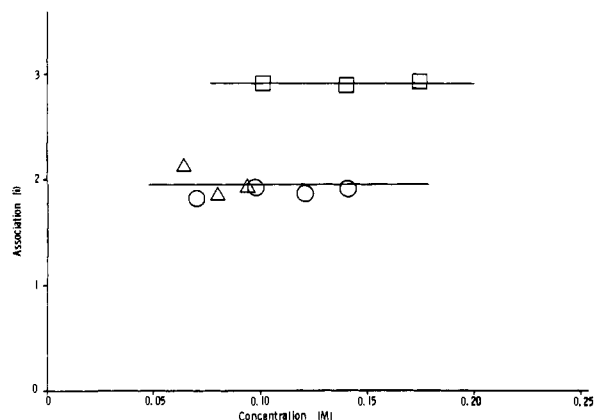
Figure 5. Molecular association data for the system CH₃Li–CH₃Cu in THF. Ratio CH₃Li:CH₃Cu: □, 2.89; O, 1.02; △, 0.52.

Figure 7. Molecular association data for the system CH₃Li–CH₃Cu· P(n-Bu)₃ in diethyl ether. Ratio CH₃Li:CH₃Cu: □, 2.93; O, 1.02; △, 0.52.

Figure 6. Molecular association data for the system CH₃Li–CH₃Cu in diethyl ether. Ratio CH₃Li:CH₃Cu: □, 2.91; O, 1.04; △, 0.68.

Solutions of LiCu(CH₃)₂ prepared by reacting CH₃Li with CuCl·p)n-Bu)₃ in diethyl ether gave association values varying from 0.63 to 0.71 over the concentration range 0.043–0.087 M. If it is assumed that a mixture of dimeric LiCu(CH₃)₂ and free uncoordinated P(n-Bu)₃ is present, then an association value of 0.67 can be calculated. This value agrees very well with the data. Solutions of LiCu₂(CH₃)₃ gave association values varying from 0.49 to 0.53 over the concentration range 0.050–0.099 M. A mixture of monomeric LiCu₂(CH₃)₃ with 1 equiv of P(n-Bu)₃ coordinated and another 1 equiv of P(n-Bu)₃ uncoordinated gives a calculated association value of 0.50, which agrees very well with the observed values. A solution prepared by reacting CH₃Li with CuCl·P(n-Bu)₃ in 4:1 ratio gave association values varying from 2.35 to 2.42 over the concentration range 0.075–0.149 (concentration of lithium). If it is assumed that Li₂Cu(CH₃)₃ is present as a monomer with the P(n-Bu)₃ coordinated to it, then, with the aid of the equilibrium data in Table III, an association value of 2.38 can be calculated. This agrees very well with the experimentally determined values.

In diethyl ether, when P(n-Bu)₃ is present, the NMR and molecular association data suggests that the reactions represented by eq 10–12 occur.

$$3CH_3Li + 2CuCl \cdot P(n\text{-}Bu)_3 \rightarrow LiCu_2(CH_3)_3 \cdot P(n\text{-}Bu)_3$$
$$+ P(n\text{-}Bu)_3 + 2LiCl \quad (10)$$

$$CH_3Li + LiCu_2(CH_3)_3 \cdot P(n\text{-}Bu)_3 + P(n\text{-}Bu)_3$$
$$\rightarrow [LiCu(CH_3)_2] + 2P(n\text{-}Bu)_3 \quad (11)$$

$$CH_3Li + LiCu(CH_3)_2 + P(n\text{-}Bu)_3$$
$$\overset{K}{\rightleftharpoons} Li_2Cu(CH_3)_3 \cdot P(n\text{-}Bu)_3 \quad (12)$$

that LiCu₂(CH₃)₃ is also dimeric in THF. In order to determine the association of Li₂Cu(CH₃)₃, an approximately 3:1 mixture of CH₃Li and CH₃Cu was prepared. This mixture of CH₃Li and CH₃Cu yielded association values which varied from 2.85 to 2.90 over the concentration range 0.102–0.175 M (concentration of lithium). Using the equilibrium data from Table III, the amounts of CH₃Li, LiCu(CH₃)₂, and Li₂Cu(CH₃)₃ present in the mixture can be calculated. With this data, two association values were calculated—one assuming that Li₂Cu(CH₃)₃ is a monomer, the other assuming it is a dimer. The calculated association value, assuming that Li₂Cu(CH₃)₃ is a monomer, is 2.84. Assuming Li₂Cu(CH₃)₃ as a dimer, this becomes 3.12. The data are more consistent with Li₂Cu(CH₃)₃ as a monomer.

For LiCu(CH₃)₂ in diethyl ether, the association values varied from 1.78 to 1.90 over a concentration range of 0.086–0.172 M, indicating that LiCu(CH₃)₂ is dimeric in this solvent. For Li₂Cu₃(CH₃)₅ the association values varied from 1.04 to 0.96 over a concentration range of 0.047–0.093 M, indicating that Li₂Cu₃(CH₃)₅ is monomeric. A 3:1 mixture of CH₃Li and CH₃Cu gave association values which varied from 2.44 to 2.29 over the concentration range 0.107–0.214 M (concentration of lithium). Again, by using the equilibrium data in Table III, it is possible to calculate the amounts of CH₃Li, LiCu(CH₃)₂, and Li₂Cu(CH₃)₃ present. With this data, two association values were calculated—again one for monomer and one for dimer Li₂Cu(CH₃)₃. The calculated association value based on monomer is 2.37. Based on dimer the association is 4.00. The assignment of Li₂Cu(CH₃)₃ as a monomer is more consistent with the data.

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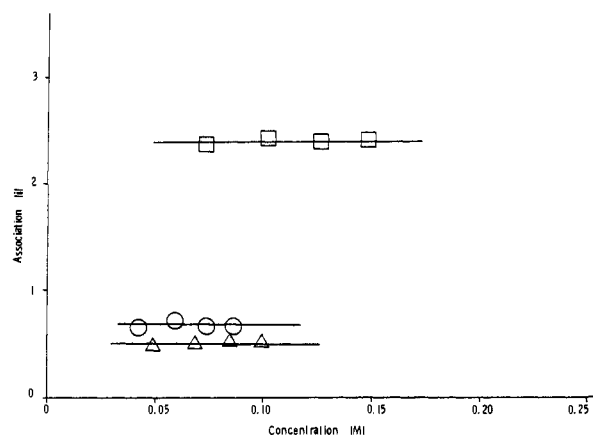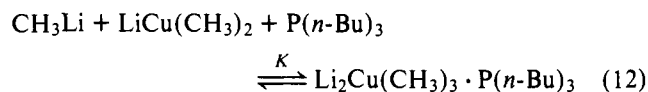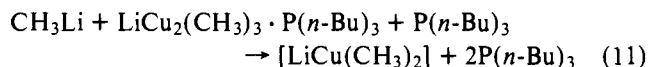
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(11) Methyllithium has been found to be a tetramer in both diethyl ether and THF.[12] Lithium dimethylcuprate has been found to be dimeric in diethyl ether.[13] The results of this work show that LiCu(CH₃)₂ is dimeric in THF; and, in addition, that Li₂Cu(CH₃)₃ is monomeric in THF. Since dimethyl ether

is similar in many respects to THF, one would expect CH₃Li, LiCu(CH₃)₂, and Li₂Cu(CH₃)₃ to have the same association in dimethyl ether as in THF.
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Reaction of *gem*-Dichloroallyllithium with Aldehydes, Ketones, and Other Organic Substrates. An Example of Electronic Control of Regioselectivity in the Reactions of an Ambident Nucleophile[1]

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Abstract: The reactions of *gem*-dichloroallyllithium, obtained by the action of *n*-butyllithium on 3,3-dichloroallyltriphenyllead in THF at −95 °C, with a variety of organic substrates have been investigated. Hydrolysis gives HCCl₂CH=CH₂ and alkylation of the reagent with organic halides and acylation using esters occurred with formation of the new C–C bond at the CCl₂ terminus of the reagent. The addition of this reagent to the C=O bond of aldehydes and ketones proceeded with C–C bond formation at either terminus. Dialkyl ketones gave alcohols (after hydrolysis) of type RR′C(OH)CCl₂CH=CH₂, while PhCHO, Ph₂CO, (CF₃)₂CO, and RC(O)CF₃ (R = Me, Ph) reacted to give products of type RR′C(OH)CH₂CH=CCl₂. Aliphatic aldehydes, acetophenone, and substituted acetophenones gave both types of products. In the case of substituted acetophenones, the ratio of the CH₂=CHCCl₂- and CCl₂=CHCH₂-substituted products appeared to depend on electronic factors; the regioselectivity observed in Li(CCl₂CHCH₂) additions to other carbonyl systems also can be rationalized in terms of electronic factors in the substrate.

Unsymmetrically substituted allylic metal reagents react readily with aldehydes and ketones to form products which are characteristic of reaction at either or both termini of the propenylic system. In the cases studied to date[4] the major emphasis has been on alkyl-substituted reagents of type I and II,

I (M = Li, Na)

II (M = MgX, Mg/2, ZnX, Zn/2)
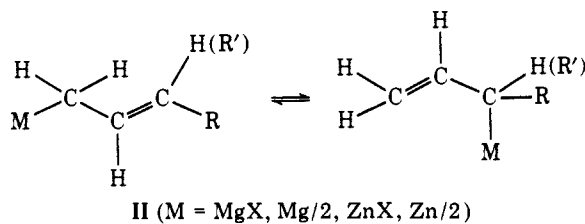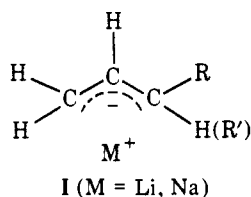
although such reactions of a few organofunctional allylic lithium reagents (e.g., R = alkoxy or thioalkoxy) have been reported.[5]

For purposes not related to the present study, we required such an unsymmetrical allylic lithium reagent, *gem*-dichloroallyllithium. Initially it was prepared by the reaction of 3,3,3-trichloropropene with *n*-butyllithium in tetrahydrofuran/diethyl ether medium at −115 to −100 °C.[6,7] Among the reactions of this reagent which we studied was that with benzaldehyde which gave the alcohol C₆H₅CH(OH)-CH₂CH=CCl₂ in 52% yield after hydrolysis.[7] In subsequent work,[6,8] a much better synthesis of *gem*-dichloroallyllithium was developed, as shown in eq 1. Although our interests were

directed more toward the organometallic applications of this novel reagent, we felt that it would be of interest to examine more thoroughly its reactions with aldehydes and ketones. It was by no means certain that the result obtained with benzaldehyde, C–C bond formation exclusively at the CH₂ terminus, would be observed with every other carbonyl compound.

The results of this study are of considerable interest since they provide the first example of exclusive electronic control of regioselectivity in the reactions of unsymmetrically substituted allyl anions.

Results and Discussion

The first carbonyl substrate examined using the new route (eq 1) to *gem*-dichloroallyllithium was acetone, and we were

$$Ph_3PbCH_2CH=CCl_2 + n\text{-}BuLi \xrightarrow[-95\,°C]{THF/hexane} Ph_3PbBu\text{-}n$$

(1)
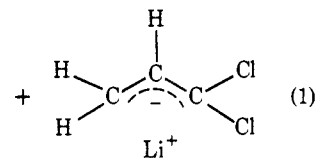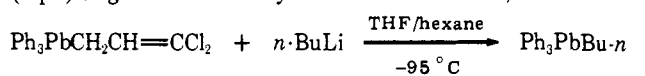
surprised to find that in this reaction C–C bond formation occurred exclusively at the CCl₂ end of the *gem*-dichloroallyl anion, giving the alcohol Me₂C(OH)CCl₂CH=CH₂ after hydrolysis of the reaction mixture. Since the two carbonyl compounds examined had given completely opposite results in their reactions with *gem*-dichloroallyllithium, we carried out *gem*-dichloroallyllithium addition reactions to a fairly large number of other carbonyl substrates in order to identify the factors which are important in determining the regioselectivity of addition. In all of these reactions the *gem*-dichloroallyllithium was prepared at −90 °C in THF by the transmetalation