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Solution Composition of the Normant Reagent. Identification of New THF-Soluble Magnesium Methylcuprates $Cu_nMg_mMe_{2m+n}$[1]

E. C. Ashby* and A. B. Goel[1b]

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

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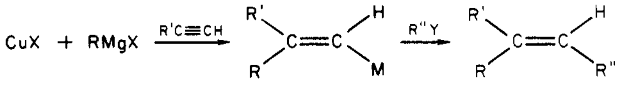
The composition of the Normant reagent (MeMgX + CuX) in THF was studied by variable-temperature ^1H NMR. The formation of various magnesium methylcuprates, $Cu_nMg_mMe_{2m+n}$ (where $m = 1$, $n = 1$–4 and 6 and where $m = 2$, $n = 3$), in solution was demonstrated where the reactions of methyl Grignard reagents and cuprous halides were carried out at various temperatures ranging from −78 to −30 °C for different lengths of time. The same complexes were prepared in THF solution by the reactions of Me_2Mg with CuX or MeCu in various stoichiometric ratios. Molecular association studies carried out at reduced pressure in THF for $CuMgMe_3$ and Cu_2MgMe_4 showed these compounds to be monomeric and dimeric, respectively, in solution.

Applications of lithium organocuprate reagents in organic synthesis over the past few years have been the subject of numerous reports.[2,3] Recently, organomagnesium cuprate reagents (Normant reagents) derived from the reactions of Grignard reagents with cuprous halides have attracted a great deal of interest and have been utilized very imaginatively in organic synthesis.[3-7] For example, a stoichiometric mixture of Grignard reagent and cuprous halide is a versatile reagent for the stereoselective synthesis of trisubstituted alkenes from terminal alkynes (eq 1). Although the precise composition of this reagent or the identification of the reactive species present in the mixture has not been determined, the Normant reagent has been represented by the formula $RCu{\cdot}MgX_2$ and sometimes R_2CuMgX.



(1)

More recently, Rahman et al.[8] reported the preparation of iodomagnesium dimethylcuprate by the reaction of MeMgI with CuI according to eq 2. In this reaction these

$$2RMgI + CuI \xrightarrow{\text{THF, ether}} R_2CuMgI + MgI_2 \qquad (2)$$

workers observed the formation of a brown solid suspended in THF. However, this complex was never isolated in pure form and was used as such in further reactions. We have been involved, for some time, in the isolation and characterization of various types of organocuprate and copper hydride complexes.[9] Due to our continuing interest in the chemistry of organocuprates, we decided to perform a detailed investigation of the composition of the Normant reagent, particularly the reaction of MeMgBr and Me_2Mg with CuX (where X = Cl, Br, I, and Me). During our investigation, we observed the formation of several methylmagnesium copper(1)ate complexes, depending upon the reaction conditions. Surprisingly, we have noticed no halide component in any of these methylcuprates, contrary to earlier suggestions. A detailed account of our studies is presented here.

Experimental Section

Apparatus. Reactions were performed under dry nitrogen at the bench by using Schlenk tube techniques.[10] Other manipu-

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[1] (a) Presented in part at the Annual Meeting of the Southeast and Southwest Regional American Chemical Society, New Orleans, LA, Dec, 1980. (b) Present address: Ashland Chemical Co., 5200 Paul G. Blaser Memorial Parkway, Dublin, OH 43017.

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lations were carried out in a glovebox equipped with a recirculating system.[11] ^{1}H NMR spectra were obtained on a Varian T-60 NMR spectrometer. All chemical shift values are expressed in values (ppm) relative to the upfield multiplet signal of THF. Values are also reported with respect to Me_4Si as an external standard. Calibrated syringes with stainless steel needles were used for transfer of reagents. Deliveries could be reproduced to better than 0.5%.

Analytical. Active methyl (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.[10] Magnesium was analyzed by titration with EDTA, 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 $NaAlH_4$ or over sodium benzophenone ketyl just 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. Magnesium metal was obtained from Alpha-Ventron (99.995% pure). Dimethylmercury, obtained from Org-Met, was found to be pure and therefore used without any further purification. Methylmagnesium bromide was prepared in THF by reacting magnesium metal with methyl bromide. Me_2Mg was prepared by the reaction of magnesium metal (2–3-fold excess) with dimethylmercury at room temperature.[12] Magnesium chloride and magnesium bromide solutions in THF were prepared by reacting magnesium metal with the corresponding mercuric halides. Methylmagnesium chloride in THF was prepared by mixing equimolar solutions of Me_2Mg and $MgCl_2$ in THF. Methyllithium in Et_2O was freshly prepared halide free by the reaction of Me_2Hg with excess lithium metal (Alfa-Ventron). Solutions of MeLi were stored at −78 °C until ready to use. Analysis of MeLi 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 was washed with distilled water, ethanol, and diethyl ether followed by drying under reduced pressure at room temperature for about 2 days. Cuprous chloride and cuprous bromide were prepared by the reaction of copper(II) chloride or copper(II) bromide with sodium sulfite.[13] The resulting precipitated solids were washed with an aqueous solution of SO_2, glacial acetic acid, ethanol, and diethyl ether, and then dried at room temperature under reduced pressure.

Methylcopper(I) was prepared by the reaction of methyllithium with cuprous iodide in diethyl ether in a 1:1 molar ratio at −78 °C as a yellow solid slurry. The yellow solid (MeCu) was prepared free of LiI by centrifuging, syringing out the supernatant solutions, and washing the resulting yellow solid with several portions of dry diethyl ether. All these manipulations were carried out under nitrogen at −78 °C. The resulting MeCu was slurried in dry ether and used in this way as a reagent. A typical analysis of the slurry showed Li, Cu, Me, and I present in molar ratios of 0.03:1.00:0.98:0.02. The slurry was stored at −78 °C and used within 1 day of preparation.

Reaction of Cuprous Bromide with Methylmagnesium Bromide in THF in 1:1 Molar Ratio. Solutions for NMR were obtained from a large-scale reaction of methylmagnesium bromide with cuprous bromide in THF. CuBr (30 mmol) was placed in a 500-mL round-bottom flask equipped with a magnetic stirring bar and rubber septum cap. THF (400 mL) was introduced and the flask was kept at −78 °C and stirred vigorously. To this suspension of CuBr in THF was added a THF solution of MeMgBr (0.5 M) dropwise (60 mL, 30 mmol) by syringe. The reaction mixture was stirred for variable lengths of time at various temperatures by raising or lowering a dry ice–acetone bath. Typically, samples for NMR were withdrawn at temperatures (−78, −65, −50, −45, −40, −35 °C) after stirring the reaction mixture at these temperatures for 5 min (−78 °C), 15 min (−65 °C), 20 min (−60 °C), 20 min (−50 °C), 40 min (−50 °C), 10 min (−40 °C), 10 min (−35 °C). These samples were transferred to cooled NMR tubes equipped with rubber septum caps. Proton NMR spectra were recorded at −85 °C.

Seven other reactions were carried out on a much smaller scale (2 mmol). In these reactions CuBr (2 mmol) and MeMgBr (2 mmol) were mixed in THF (50 mL) at −78 °C and the temperatures of these reactions raised to the above-mentioned temperatures (ranging from −78 to −35 °C) and allowed to react for the same lengths of time as given above. After the appropriate reaction times, the supernatant solutions were separated from the insoluble solids by use of a cannula. Both the solutions and the solids were analyzed for Mg, Cu, Me, and Br. The analyses obtained for the solutions and the solids are given below.

(a) Reaction of CuBr (2.0 mmol) with MeMgBr (2.0 mmol) at −78 °C for 5 min. Supernatant solution: Found: Mg:Cu:Me:Br = 1.00:0.02:1.01:1.03. Total amount of Mg = 2.0 mmol, Cu = 0.04 mmol, Me = 2.02 mmol, Br = 2.06 mmol. Proton NMR showed a peak at 3.67 ppm upfield from THF. **Insoluble solid**: Found: Mg:Cu:Me:Br = 0.00:1.00:0.00:1.02. Total amount of Mg = 0.0 mmol, Cu = 2.0 mmol, Me = 0.0 mmol, Br = 2.04 mmol.

(b) Reaction of CuBr (2.0 mmol) with MeMgBr (2.0 mmol) at −65 °C for 15 min. Supernatant solution: Found: Mg:Cu:Me:Br = 1.00:0.22:1.01:1.24. Total amount of Mg = 2.0 mmol, Cu = 0.44 mmol, Me = 2.02 mmol, Br = 2.48 mmol. ^{1}H NMR: peaks at 3.67 and 3.34 ppm in ratios of approximately 1:2. **Insoluble solid**: Found: Mg:Cu:Me:Br = 0.03:1.00:0.00:1.06. Total amounts of Mg = 0.05 mmol, Cu = 1.56 mmol, Me = 0.00 mmol, Br = 1.65 mmol.

(c) Reaction of CuBr (2.0 mmol) with MeMgBr (2.0 mmol) at −60 °C for 20 min. Supernatant solution: Found: Mg:Cu:Me:Br = 1.00:0.35:1.02:1.32. Total amount of Mg = 1.98 mmol, Cu = 0.69 mmol, Me = 2.01 mmol, Br = 2.63 mmol. Proton NMR spectrum showed a peak at 3.34 ppm upfield from the THF multiplet. **Insoluble solid**: Found: Mg:Cu:Me:Br = 0.03:1.00:0.00:1.05. Total amount of Mg = 0.04 mmol, Cu = 1.31 mmol, Me = 0.00 mmol, Br = 1.39 mmol.

(d) Reaction of CuBr (2.0 mmol) with MeMgBr (2.0 mmol) at −60 °C for 20 min and at −50 °C for 20 min. Supernatant solution: Found: Mg:Cu:Me:Br = 1.00:0.45:0.98:1.40. Total amount of Mg = 1.97 mmols, Cu = 0.89 mmols, Me = 1.96 mmol, Br = 2.76 mmol. ^{1}H NMR spectrum showed peaks at 3.33 (s) and 2.21 (s) ppm in 3:1 ratio upfield from the THF multiplet. **Insoluble solid**: Found: Mg:Cu:Me:Br = 0.07:1.00:0.00:1.09. Total amount of Mg = 0.08 mmol, Cu = 1.11 mmol, Me = 0.00 mmol, Br = 1.10 mmol.

(e) Reaction of CuBr (2.0 mmol) with MeMgBr (2.0 mmol) at −60 °C for 20 min and at −50 °C for 35 min. Solution: Found: Mg:Cu:Me:Br = 1.00:0.52:0.96:1.45. Total amount of Mg = 1.93 mmol, Cu = 1.00 mmol, Me = 1.85 mmol, Br = 2.80 mmol. Proton NMR spectrum showed peaks at 3.04 and 2.08 ppm in 3:1 ratio upfield from the THF multiplet. **Insoluble solid**: Found: Mg:Cu:Me:Br = 0.07:1.00:0.03:1.12. Total amount of Mg = 0.09 mmol, Cu = 0.97 mmol, Me = 0.03 mmol, Br = 1.11 mmol.

(f) Reaction of CuBr (2.0 mmol) with MeMgBr (2.0 mmol) at −50 °C for 30 min and then at −40 °C for 20 min. Solution: Found: Mg:Cu:Me:Br = 1.00:0.64:0.97:1.63. Total amount of Mg = 1.94 mmol, Cu = 1.24 mmol, Me = 1.88 mmol, Br = 3.16 mmol. Proton NMR showed peaks at 3.03 and 2.06 ppm in 2:1 ratio upfield from the THF multiplet. **Insoluble solid**: Found: Mg:Cu:Me:Br = 0.05:1.00:0.05:1.10. Total amount of Mg = 0.04 mmol, Cu = 0.72 mmol, Me = 0.04 mmol, Br = 0.79 mmol.

(g) Reaction of CuBr (2.0 mmol) with MeMgBr (2.0 mmol) at −40 °C for 40 min and then at −35 °C for 40 min. When "MeMgBr" in THF solution was added to a slurry of CuBr in THF at −78 °C and the reaction mixture allowed to react at −40 °C for about 40 min and then at −35 °C for 40 min, most of the CuBr gradually dissolved and a light yellow solution formed, which, in time, produced a yellow solid. Both the solution and the solid were analyzed. **Solution**: Found: Mg:Cu:Me:Br = 1.00:0.70:0.84:1.72. Total amount of Mg = 1.94 mmol, Cu = 1.36 mmol, Me = 1.63 mmol, Br = 3.34 mmol. Proton NMR showed peaks at 3.03, 2.18, and 2.06 ppm in 2:0.7:1 ratio upfield from THF. **Insoluble solid**: Found: Mg:Cu:Me:Br = 0.06:1.00:0.45:0.57. Total amount of Mg = 0.04 mmol, Cu = 0.62 mmol, Me = 0.28 mmol, Br = 0.35 mmol.

(h) Reaction of CuX (where X = Cl, Br, I, or Me) with MeMgX (where X = Cl or Br) and Me_2Mg in Variable Molar Ratios. Methylmagnesium halide or diemthylmagnesium solution in THF was introduced to a magnetically stirred slurry of CuX

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kept at −78 °C (dry ice–acetone bath) in the appropriate molar ratio and the reaction mixture allowed to react at various temperatures for various lengths of time. The resulting solutions were analyzed and the proton NMR spectra were recorded at −85 °C. The details of the reactions are given in Table I.

Molecular Weight Measurements[14]

The solutions of $CuMgMe_3$ and Cu_2MgMe_3 in THF, used in the molecular weight measurements were prepared by the reactions of Me_2Mg and MeCu in THF.

The ebullioscopic technique reported earlier[14] was used in this study for determination of molecular weights of the magnesium cuprates in THF solution. The concentration of solute molecules is given approximately by eq 3 where

$$C = \frac{1000P}{M_2\left(1 + \frac{1000}{M_1 \Delta T_B} K_B\right)} \tag{3}$$

P 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 3 was derived from eq 4 reported earlier[14] where

$$i = \frac{W_2 M_1}{W_1 M_2}\left[\frac{1}{e^{\Delta T_B M_1}/(100K_B - 1)}\right] \tag{4}$$

i is the molecular association. In the present 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 3. The results of these molecular weight measurements determined at reduced pressure (240.0 mmHg pressure of N_2; $K_B = 1.79$) are given in Figure 2.

Results and Discussion

Prior to the present studies, the isolation of any methylmagnesium cuprate complexes had not been reported in the literature. Such studies have been delayed probably due to the complex nature of organometallic compounds in solution, the extremely air-sensitive nature of organocopper compounds, and the generally unstable nature of the predicted copper complexes. In the present investigations we have carried out several series of reactions involving the interaction of MeMgX (where X = Cl or Br) and Me_2Mg with cuprous halides, CuX (where X = Cl, Br, or I), and methylcopper in various molar ratios under varying conditions of temperature and reaction time. In all these reactions the supernatant solutions formed where analyzed by complete elemental analysis and low-temperature proton NMR spectroscopy. The respective insoluble solids were also subjected to complete elemental analysis. On the basis of these results, the formation of a series of methylmagnesium cuprates is suggested.

When MeMgBr was allowed to react with CuBr in THF at temperatures ranging from −78 to −30 °C, several THF soluble complexes, i.e., $CuMgMe_3$, $Cu_3Mg_2Me_7$, Cu_2MgMe_4, Cu_3MgMe_5, Cu_4MgMe_6, and Cu_6MgMe_8, were suggested by NMR spectroscopy. At the same time unreacted cuprous bromide and/or MeCu were observed as insoluble solids. The characterization of these complexes was established by complete elemental analysis of both the solution phase and the solid phase of the reaction mixture at selected time intervals and at certain reaction temperatures. The analytical results were then used to compliment the low-temperature NMR data obtained for the soluble complexes in a comparison with authentic samples prepared independently by the reactions of cuprous halides or MeCu with Me_2Mg in the appropriate stoichiometry as shown in Schemes I–III. The spectrum of each complex, $Cu_nMg_mMe_{(2m+n)}$ (where n = 1–4 and 6 and m = 1, 2), matched perfectly with the product prepared by the reaction of Me_2Mg and MeCu in the proper stoichiometry (Scheme I).

Scheme I

$$MeCu + Me_2Mg \rightarrow CuMgMe_3$$

$$3MeCu + 2Me_2Mg \rightarrow Cu_3Mg_2Me_7$$

$$2MeCu + Me_2Mg \rightarrow Cu_2MgMe_4$$

$$3MeCu + Me_2Mg \rightarrow Cu_3MgMe_5$$

$$4MeCu + Me_2Mg \rightarrow Cu_4MgMe_6$$

$$6MeCu + Me_2Mg \rightarrow Cu_6MgMe_8 \rightleftharpoons Cu_4MgMe_6 + 2MeCu$$

Thus, when equimolar amounts of "MeMgBr" and CuBr in THF were mixed at −78 °C and the reaction mixture

$$CuBr + MeMgBr \rightarrow products \tag{5}$$

was allowed to react at −60 °C for about 25–20 min, about one-third of the CuBr dissolved, resulting in the formation of soluble $CuMgMe_3$ in addition to free $MgBr_2$. The low-temperature NMR spectrum (at −85 °C) of this solution showed a singlet at 3.34 ppm upfield to the THF multiplet that was found to be identical with the spectrum of the complex prepared from the reaction of CuX (where X = Cl, Br, or I) or MeCu with Me_2Mg in the ratio 2:3 or 1:1, respectively.

Alternatively, when CuBr and MeMgBr in THF were mixed in 1:3 ratio (Scheme II) and allowed to react at −30 °C for about 5 min, all the CuBr dissolved and $CuMgMe_3$ was formed. When the reaction mixture from eq 5 was allowed to stand for approximately 0.5 h at −60 °C, about 30% more CuBr dissolved. The stoichiometry and the NMR spectrum of the solution were found to be consistent with the formation of $Cu_3Mg_2Me_7$. Similarly, when this reaction mixture was allowed to react further by warming to −50 and −40 °C, in time other complexes, i.e., Cu_2MgMe_4, Cu_3MgMe_5 and Cu_4MgMe_6, formed as more CuBr dissolved. It is important to mention here that, at certain times, in solution one may find a mixture of two complexes observable by NMR. By intergration of the NMR spectrum and elemental analysis of the solution and the solid, the relative amounts of each complex could be determined.

Scheme II

$$CuX + 3MeMgX \rightarrow CuMgMe_3 + 2MgX_2$$

$$3CuX + 7MeMgX_2 \rightarrow Cu_3Mg_2Me_7 + 5MgX_2$$

$$2CuX + 4MeMgX \rightarrow Cu_2MgMe_4 + 3MgX_2$$

$$3CuX + 5MeMgX \rightarrow Cu_3MgMe_5 + 4MgX_2$$

$$4CuX + 6MeMgX \rightarrow Cu_4MgMe_6 + 5MgX_2$$

$$6CuX + 8MeMgX \rightarrow Cu_6MgMe_8 + 7MgX_2$$

X = Cl or Br

In the course of reaction 5 at −30 °C, there is a time when over 75% of the CuBr is in solution, giving a clear, very light yellow solution of Cu_6MgMe_8. However, this complex at −30 °C persists only a few minutes and then MeCu precipitates from solution. After 15 min, the solution contained Cu_4MgMe_6 and Cu_6MgMe_8 in about 6:1 ratio. This observation was better understood when we examined the nature of Cu_6MgMe_8 prepared separately by

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(14) The procedure used for the ebulliosciplc molecular weight studies can be found in: Ashby, E. C.; Walker, F. *J. Chem. Ed.* **1968**, *45*, 654.

Table I. Elemental Analyses and ^1H NMR Spectral Data of the Products of the Reactions of CuX (where *X* = Cl, Br, I, or Me) with RMgX (where *X* = Cl, Br, or Me) in THF[a]

expt no.	reactants CuX	RMgX, mmol	ratio of CuX: RMgX	reactn temp, 0 °C	reactn time, min	anal. of solution	amounts, mmol	^1H NMR (ppm) with the multiplet	ratio of NMR signal	probable complexes in solution
						Mg:Cu:Me:X	MgCuMeX			
1	CuCl 2.0	MeMgCl 6.0	1:3	−30	40	1.00:0.32:1.02:1.32	6.00 1.97 6.12 7.12	3.34 (s)		$CuMgMe_3$ (+ 2 $MgCl_2$)
2	2.0	4.7	3:7	−35	40	1.00:0.43:0.97:1.42	4.65 2.00 4.56 6.67	3.33 (s) 2.21 (s)	3:1	$Cu_3Mg_2Me_7$ (+ 5$MgCl_2$)
3	2.0	4.0	1:2	−30	45	1.00:0.49:9.98:1.52	4.02 1.97 3.94 6.11	3.04 (s) 2.08 (s)	3:1	Cu_2MgMe_4 (+ 3$MgCl_2$)
4	2.5	4.2	3:5	−35	50	1.00:0.58:1.03:1.60	4.16 2.31 4.28 6.66	3.03 (s) 2.07 (s)	5:2	Cu_3MgMe_5 (+ 4$MgCl_2$)
5	2.5	3.8	2:3	−35	50	1.00:0.63:0.96:1.60	3.85 2.43 3.70 6.47	3.03 (s)	2:1	Cu_4MgMe_6 (+ 5$MgCl_2$)
6	2.3	3.1	3:4	−40	60	1.00:0.71:0.95:1.77	3.07 2.17 3.93 5.43	3.03 (s) 2.18 (s) 2.06 (s)	2:1:1	Cu_6MgMe_8 (+ 7$MgCl_2$)
7	CuBr 1.5	MeMgBr 4.5	1:3	−25	30	1.00:0.33:1.00:1.34	4.50 1.49 4.50 6.03	3.34		$CuMgMe_3$ (+ 2$MgBr_2$)
8	2.0	4.7	3:7	−38	45	1.00:0.43:0.99:1.41	4.65 2.00 4.60 6.64	3.33	3:1	$Cu_3Mg_2Me_7$ (+ 5$MgBr_2$)
9	1.5	3.0	1:2	−30	40	1.00:0.50:0.97:1.53	3.07 1.54 2.98 4.70	3.04, 2.08	3:1	Cu_2MgMe_4 (+ 3$MgBr_2$)
10	2.0	3.3	3:5	−36	50	1.00:0.59:9.98:1.62	3.35 1.98 3.28 5.43	3.03, 2.07	5:2	Cu_3MgMe_5 (+ 4$MgBr_2$)
11	2.5	3.8	2:3	−37	55	1.00:0.69:0.96:1.69	3.74 2.32 3.59 6.32	3.03, 2.06	2:1	Cu_4MgMe_6 (+ 5$MgBr_2$)
12	2.0	2.7	3:4	−41	60	1.00:0.70:0.95:1.76	2.71 1.90 2.57 4.77	3.03, 2.18, 2.06	2:1:1	Cu_6MgMe_8 (+ 7$MgBr_2$)
13	CuBr 2.0	Me_2Mg 3.0	2:3	−20	30	1.00:0.68:2.04:0.68	2.98 2.03 6.08 2.03	3.34		$CuMgMe_3$ (+ 0.5$MgBr_2$)
14	2.0	2.3	6:7	−40	50	1.00:0.98:2.00:0.85	2.34 2.04 4.68 1.99	3.33	3:1	$Cu_3Mg_2Me_7$ (+ 1.5$MgBr_2$)
15	2.0	2.0	1:1	−25	35	1.00:1.01:2.04:0.98	1.98 2.00 4.02 1.95	3.04, 2.08	3:1	Cu_2MgMe_4 (+ $MgBr_2$)
16	2.6	2.2	6:5	−38	50	1.00:1.18:1.94:1.24	2.23 2.64 4.33 2.77	3.03, 2.07	5:2	Cu_3MgMe_5 (+ 1.5$MgBr_2$)
17	3.0	2.25	4:3	−38	55	1.00:1.29:1.97:1.35	2.27 2.93 4.47 3.06	3.03, 2.06	2:1	Cu_4MgMe_6 (+ 2$MgBr_2$)
18	3.0	2.0	3:2	−40	60	1.00:1.59:2.06:1.55	1.95 3.10 4.03 3.02	3.03, 2.18, 2.06	2:1:1	Cu_6MgMe_8 (+ 3$MgBr_2$)
19	CuCl 1.5	Me_2Mg 2.3	2:3	−10	20	1.00:0.65:2.01:0.67	2.35 1.46 4.52 1.51	3.34		$CuMgMe_3$ (+ 0.5$MgCl_2$)
20	2.0	2.3	6:7	−35	40	1.00:0.84:1.95:0.87	2.28 1.92 4.45 1.98	3.33, 2.21	3:1	$Cu_3Mg_2Me_7$ (+ 1.5$MgCl_2$)
21	1.6	1.6	1:1	−20	30	1.00:0.96:1.97:1.07	1.64 1.57 3.23 1.75	3.04, 2.08	3:1	Cu_2MgMe_4 (+ $MgCl_2$)
22	2.0	1.7	6:5	−35	50	1.00:1.14:1.94:1.19	1.75 2.00 3.40 2.08	3.03, 2.07	5:2	Cu_3MgMe_5 (+ 1.5$MgCl_2$)
23	2.2	1.65	4:3	−36	50	1.00:1.29:1.95:1.37	1.70 2.19 3.32 2.33	3.03, 2.06	2:1	Cu_4MgMe_6 (+ 2$MgCl_2$)
24	2.0	1.3	3:2	−40	50	1.00:1.56:1.97:1.53	1.35 2.11 2.66 2.07	3.03, 2.18, 2.06	2:1:1	Cu_6MgMe_8 (+ 3$MgCl_2$)
25	MeCu 1.8	Me_2Mg 1.8	1:1	−35	40	1.00:0.94:2.91:—	1.82 1.71 5.30 —	3.34		$CuMgMe_3$
26	2.0	1.35	3:2	−35	45	1.00:1.45:3.41:—	1.32 1.91 4.50 —	3.33, 2.21	3:1	$Cu_3Mg_2Me_7$
27	2.6	1.3	2:1	−35	50	1.00:1.89:3.88:—	1.33 2.51 5.16 —	3.04, 2.08	3:1	Cu_2MgMe_4
28	3.6	1.2	3:1	−37	60	1.00:2.80:4.80:—	1.00 2.80 4.80 —	3.03, 2.07	5:2	Cu_3MgMe_5
29	3.0	0.75	4:1	−38	60	1.00:3.76:5.75:—	0.78 2.93 4.49 —	3.03, 2.06	2:2:1	Cu_4MgMe_6 (+ Cu_3MgMe_5)
30	CuI 2.0	Me_2Mg 3.0	2:3	−10	50	1.00:0.98:2.94:0.03	2.03 1.99 5.97 0.06	3.34		$CuMgMe_3$
31	2.0	2.3	6:7	−15	55	1.00:1.45:3.43:0.03	1.32 1.91 4.53 0.04	3.33, 2.21	3:1	$Cu_3Mg_2Me_7$
32	2.5	2.5	1:1	−15	50	1.00:1.98:3.92:0.05	1.26 2.53 4.63 0.06	3.04, 2.08	3:1	Cu_2MgMe_4
33	2.0	1.5	4:3	−35	95	1.00:3.89:5.78:0.06	0.54 2.10 3.12 0.03	3.03, 2.06	2:1:1	Cu_4MgMe_6

[a] Reactions were carried out under dry nitrogen atmosphere. In experiments 6, 12, 18, 24, some insoluble yellow solid (MeCu) formed slowly and the amount increased with time. It is probably due to disproportionation of Cu_6MgMe_8 to Cu_4MgMe_6 + 2MeCu.

Table II. Properties of Solutions of "ate" Complexes in THF

		^{1}H NMR spectral data (-85 °C)[a]			
probable complex	method of preparation[d]	δ(ppm) upfield from THF (with respect to Me_4Si)[b]	approx ratio of signals	approx temp of signal exchange,[c] °C	stability
Me_2Mg	A	3.66 (s) (−1.92)			stable at rt indefinitely
MeMgBr	B, C	3.65 (s) (−1.91)			stable at rt indefinitely
$CuMgMe_3$	D, E, F	3.34 (s) (−1.60)			stable at rt over 2 days; at 0 °C more than 4 weeks
$Cu_3Mg_2Me_7$	D, E, F	3.33 (s) (−1.59), 2.21 (s) (−0.47)	3:1	−35	stable at rt over 1 day; at 0 °C more than 1 week
Cu_2MgMe_4	D, E, F	3.04 (s) (−1.30), 2.08 (s) (−0.34)	3:1	−35	stable at rt for a few h; at −10 °C for 2 days
Cu_3MgMe_5	D, F	3.03 (s) (−1.29), 2.07 (s) (−0.33)	5:2	−45 to −50	stable at −25 °C for 1 day
Cu_4MgMe_6	D, F	3.03 (s) (−1.29), 2.06 (s) (−0.32)	2:1	−55	stable at −25 °C for ≈10 h
Cu_6MgMe_8	F	3.03 (s) (−1.29), 2.18 (s) (−0.44), 2.06 (s) (−0.32)	2:1:1	−55	stable below −40 °C for a few h with dissociation into MeCu and Cu_4MgMe_6

[a] Values are within ±0.01 ppm experimental error. [b] Values in parentheses are with respect to Me_4Si as external standard. [c] Temperature above which an exchange of signals takes place to give a single peak. [d] (A) Reaction of Me_2Hg with Mg; (B) $Me_2Mg + MgBr_2$; (C) reaction of Mg with MeBr; (D) reaction of Me_2Mg with MeCu in appropriate ratios; (E) reaction of Me_2Mg with CuI (halide-free solution); (F) reaction of Me_2Mg with CuBr or CuCl.

the reaction of CuBr with Me_2Mg in 3:2 ratio. We found that Cu_6MgMe_8 has a tendency to disproportionate in the presence of a small amount of CuBr or alone on dilution to give insoluble MeCu and leave Cu_4MgMe_6 in solution (eq 6). The amount of insoluble MeCu builds up slowly

$$\mathrm{Cu_6MgMe_8 \rightleftharpoons 2MeCu + Cu_4MgMe_6} \qquad (6)$$

as the reaction proceeds. This observation can be explained on the basis of the reaction of Cu_4MgMe_6 with the remaining unreacted CuBr, giving Cu_6MgMe_8, which in turn disproportionates to give MeCu and Cu_4MgMe_6. After the reaction of CuBr with "MeMgBr" proceeded for 1 h at −30 °C, only about 30% of the copper as Cu_4MgMe_6 and Cu_6MgMe_8 (in 6:1 ratio) was found in solution and the insoluble solid contained mainly MeCu contaminated with magnesium (≥10%) and the remaining unreacted CuBr. After approximately 2 h of reaction, it appears that equilibrium is reached and approximately 20% of the copper is in solution. However, on addition of a small amount of MeMgBr or Me_2Mg, more copper dissolves.

Thus, the Normant reagent, i.e., the reaction of MeMgBr with CuBr in THF at −35 °C for about 2 h, can best be represented by a mixture of Cu_4MgMe_6, Cu_6MgMe_8, MeCu, CuBr, and $MgBr_2$ as shown in Scheme II and eq 6.

When this reaction was carried out in diethyl ether, the equilibrium of eq 6 was far to the side of formation of MeCu and $MgBr_2$ with only a small amount of (~10%) methylmagnesium cuprate formation. We have not been able to determine the exact composition of the methylmagnesium cuprate formed in diethyl ether; however, it appears to have a magnesium:copper ratio of 1:8.

In the reactions of CuBr with either MeMgBr or Me_2Mg in THF, we have found in solution the same complexes, $Cu_nMg_mMe_{2m+n}$ (Scheme III). The only observable difference between the Me_2Mg and MeMgBr reactions is that Me_2Mg reacted at a faster rate than MeMgBr. The above complexes were prepared halide free by the reaction of MeCu with Me_2Mg; however, the reactions for the preparation of halide-free Cu_3MgMe_5 and higher copper-containing complexes were slow probably because of the loss of the reactivity of MeCu once isolated. The reactivity among the cuprous halides followed the trend CuCl > CuBr > CuI.

Scheme III

$$\mathrm{2CuX + 3Me_2Mg \rightarrow 2CuMgMe_3 + MgX_2}$$
$$\mathrm{6CuX + 7Me_2Mg \rightarrow 2Cu_3Mg_2M_7 + 3MgX_2}$$
$$\mathrm{2CuX + 2Me_2Mg \rightarrow Cu_2MgMe_4 + MgX_2}$$
$$\mathrm{6CuX + 5Me_2Mg \rightarrow 2Cu_3MgMe_5 + 3MgX_2}$$
$$\mathrm{4CuX + 3Me_2Mg \rightarrow Cu_4MgMe_6 + 2MgX_2}$$
$$\mathrm{6CuX + 4Me_2Mg \rightarrow Cu_6MgMe_8 + 3MgX_2}$$

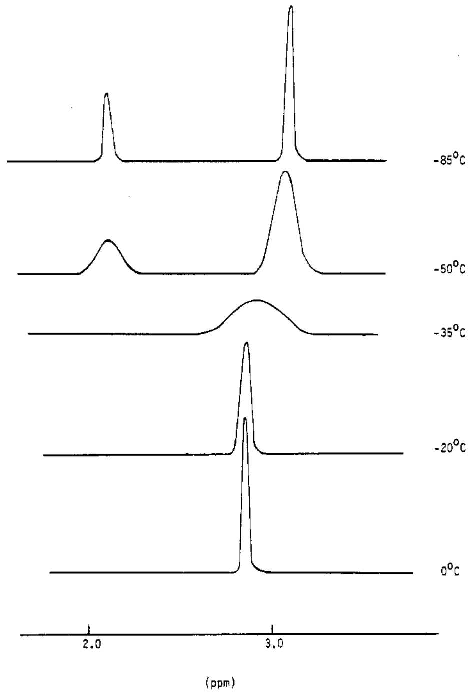

Figure 1. Variable-temperature proton NMR study of Cu_2MgMe_4 in THF obtained by the reactions of CuX (where X = Cl, Br, or Me) with MeMgX (where X = Cl or Br) and Me_2Mg.

All the cuprates reported here are soluble in THF and reasonably stable at low temperatures. The solubility and the stability in solution decreases as the Cu:Mg ratio increases and follows the sequence: $CuMgMe_3 > Cu_3Mg_2Me_7 > Cu_2MgMe_4 > Cu_3MgMe_5 > Cu_4MgMe_6 > Cu_6MgMe_8$. NMR spectra of all the complexes show only one peak at the highest temperature of their stability indicating a rapid methyl group exchange; however, upon cooling to ap-

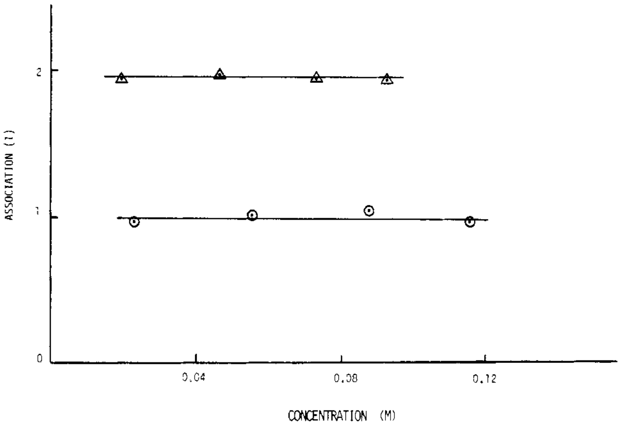

Figure 2. Molecular association studies for $CuMgMe_3$ (⊙) and Cu_2MgMe_4 (△) in THF.

proximately −50 °C, this exchange can be stopped where splitting of the signals is observed (Table II). The spectra at −85 °C show sharp signals. A variable-temperature spectral study on Cu_2MgMe_4 is shown in Figure 1. Addition of magnesium halide ($MgCl_2$ or $MgBr_2$) solution in THF to these reaction mixtures did not affect the proton NMR, indicating no possible interaction of MgX_2 with methylmagnesium cuprates.

In order to ascertain the absence of an exchange process, dimethyl ether was introduced at −120 °C where no further splitting in the signals was observed.

Upon analysis of the variable-temperature proton NMR data, it appears that the solutions containing higher amounts of organocopper in solution show signals at lower positions than that of higher organomagnesium species. This may be due to the probable formation of bridging methyl groups in the higher copper-containing complexes. This is consistent with the similar behavior observed by us in the system of methyllithium with methylcopper.[15] Although these variable-temperature NMR studies indicate the formation of various complexes in the reactions of methylmagnesium complexes with methylcopper(I) or cuprous halides in various stoichiometries, on the basis of this information it would be very risky to propose structures for these complexes. It is due to the fact that these magnesiummethyl cuprates may exist in ionic form or may be in the form of copper clusters as proposed earlier in the case of Cu_4MgPh_6[16] and recently determined by X-ray crystallography.[17]

In order to learn more about these complexes, molecular association studies in dilute THF solutions were carried out. Ebullioscopic molecular association studies performed under reduced pressure in THF reveals that $CuMgMe_3$ is monomeric whereas Cu_2MgMe_4 is dimeric (Figure 2). Molecular weights of the other complexes could not be carried out successfully due to their thermal instability above 0 °C.[14]

In conclusion, we have shown that various THF-soluble magnesium methylcuprates are formed when methylmagnesium compounds are allowed to react with methylcopper or cuprous halides in THF at temperatures ranging from −78 to −30 °C. Proton NMR spectral studies indicate no involvement of halides in these complexes. Some of these magnesium methylcuprates $Cu_nMg_mMe_{2m+n}$ (where $n = 1$ or 2 and $m = 1$) are stable even at room temperature for some time. Although, no interaction of halides has been observed in our studies, we do not imply that solutions of these complexes with and without halides would react with organic substrates such as alkenes and alkynes in exactly the same way and at the same rate, since the halides may have some interaction with the organic substrates under the reaction conditions.

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Registry No. CuBr, 7787-70-4; CuCl, 7758-89-6; MeCu, 1184-53-8; CuI, 7681-65-4; MeMgCl, 676-58-4; MeMgBr, 75-16-1; Me_2Mg, 2999-74-8.

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Selectivity in the Metalation of Polymethylpyrazines

Ronald L. Bassfield and Yoram Houminer*

Philip Morris U.S.A. Research Center, Richmond, Virginia 23261

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The selectivity in the LDA-promoted lithiation of 2,3,5-trimethylpyrazine was studied by using the perdeuterated substrate 1-d_9. Quenching of the lithium salts of the latter with H_2O gave a 1-d_8 isomer mixture which was analyzed by NMR. The order of reactivity of the three CH_3 groups in 1-d_9 was found to be 3 > 2 > 5. The metalation studies were extended also to isomeric dimethylpyrazines. It was established that the two ortho CH_3 groups in 2,3-dimethylpyrazine are more easily metalated than either of the CH_3 groups in the other isomeric dimethylpyrazines.

Alkylpyrazines are easily metalated by lithium amides such as lithium diisopropylamide (LDA), and the resulting anions are useful intermediates in the syntheses of a variety of pyrazine derivatives.[1] When 2,3,5-trimethylpyrazine (1) is reacted with an organolithium reagent, three different anions can be formed (**1a–c**, Scheme I). Hence, when such a mixture is treated with a reagent, the formation of three different products could be expected. A few reported examples, however, suggest that this assumption is incorrect. Rizzi[2] reported that the reaction

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(2) Rizzi, G. P. *J. Org. Chem.* **1968**, *33* 1333. In this case, methyllithium leads exclusively to side-chain metalation.

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