

Complexes of Gilman Reagents with C–S and C–N Double Bonds: σ or π Bonding?

Steven H. Bertz,* Yasamin Moazami, Michael D. Murphy, Craig A. Ogle,* Joshua D. Richter, and Andy A. Thomas

Department of Chemistry, University of North Carolina–Charlotte, Charlotte, North Carolina 28223

Received April 12, 2010; E-mail: sbertz1@uncc.edu; cogle@uncc.edu

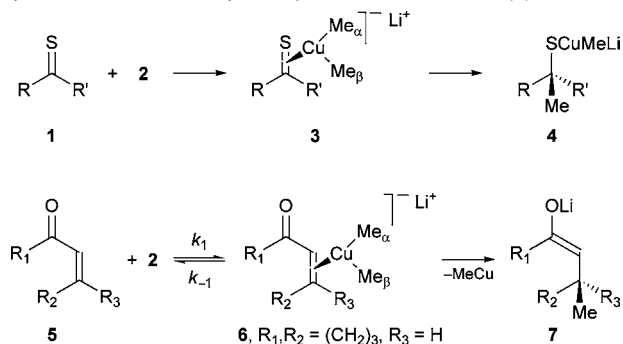
Abstract: Upon rapid injection, a variety of thiocarbonyl compounds react with the Gilman reagent Me_2CuLi at -100°C inside the probe of an NMR spectrometer to give high yields of complexes. Typical examples of substrates include carbon disulfide, methyl dithioacetate, methyl dithiobenzoate, thiobenzophenone, ethylene trithiocarbonate, and phenyl isothiocyanate. Evidence suggesting the formal oxidation state of copper in these complexes to be Cu^{III} is presented. The last example was particularly interesting, since it involved a transient intermediate that was identified as a complex with a C–N double bond. Methyl isothiocyanate gave a stable C–N double-bond complex.

In 1941, Kharasch and Tawney discovered that catalytic amounts of copper salts change the regioselectivity of the reaction between Grignard reagents and α -enones from 1,2- to 1,4-addition.¹ In 1966, House, Respass, and Whitesides demonstrated that stoichiometric organocuprate(I) reagents (Gilman reagents) also give 1,4-addition to α -enones.² In 1985, it was shown that Cu^{I} reagents, catalytic or stoichiometric, change the regioselectivity of addition to thiocarbonyl compounds from thiophilic to carbophilic.³ Is this analogy between α,β -unsaturated carbonyl compounds and thiocarbonyl compounds a superficial one, or is it a reflection of a deeper connection?

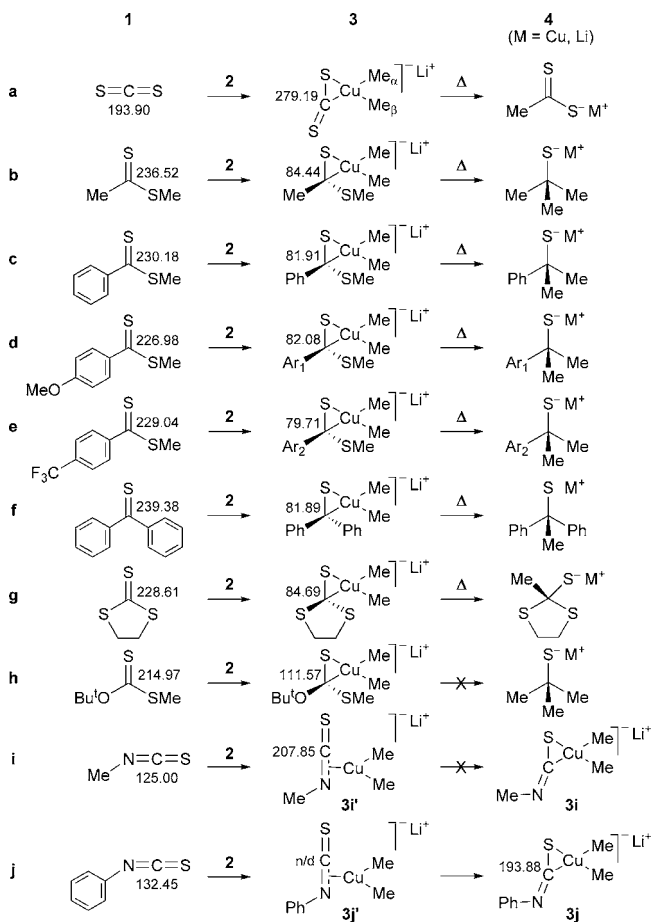
We investigated the reactions of a variety of substrates **1** containing C–S double bonds with the Gilman reagent Me_2CuLi (**2**) using rapid-injection NMR (RI-NMR) spectroscopy,^{4,5} and we can now report that the analogy between the thiocarbonyl group and the α -enone system is a deep one, as both functional groups form complexes with Gilman reagents on the reaction pathway, as illustrated in Scheme 1.

Upon injection of carbon disulfide (**1a**; 32 μmol) into a solution of $2\cdot\text{LiCl}$ (30 μmol) in $\text{THF-}d_8$ that was spinning in the probe of an NMR spectrometer at -100°C , a new species rapidly formed. In the ^{13}C NMR spectrum, peaks for **1a** (193.90 ppm) and $2\cdot\text{LiCl}$ (-9.07 ppm) disappeared, and new peaks at 279.19, 20.10, and -10.54 ppm appeared. The ^1H NMR peak for $2\cdot\text{LiCl}$ (-1.48 ppm) disappeared,

Scheme 1. Analogous Reactions of Thiocarbonyl Compounds and α,β -Unsaturated Carbonyl Compounds with Me_2CuLi (**2**)



Scheme 2. Structures of Substrates **1**, Complexes **3**, and Carbophilic Addition Products **4** ($2 = \text{Me}_2\text{CuLi}$; n/d = not detected)



and new peaks at 0.37 and -0.76 ppm appeared. The HMBC spectrum had cross-peaks between the methyl groups and also between the methyls and the thiocarbonyl carbon. Complex **3a** formed equally well with $2\cdot\text{LiX}$ ($\text{X} = \text{Cl}, \text{Br}, \text{I}, \text{CN}$).

The NMR data are consistent with the pseudo-square-planar structure **3a** (Scheme 2), which was confirmed by two-bond ^{13}C – ^{13}C coupling across Cu. In all previous examples, trans coupling was significantly larger in magnitude than cis.⁶ Using $^{13}\text{CS}_2$, we were able to measure $^2J_{\text{trans}} = 28.8$ Hz for coupling to the upfield methyl (Me_α) and $^2J_{\text{cis}} = 4.5$ Hz for coupling to the downfield methyl (Me_β). When $^{13}\text{CS}_2$ was added to **3a** at -100°C , no incorporation of the labeled ligand was observed.

When injected into solutions of $2\cdot\text{LiI}$ in $\text{THF-}d_8$ at -100°C , methyl dithioacetate (**1b**) and methyl dithiobenzoates **1c–e** formed **3b–e**, respectively. In all cases, the Gilman reagent was completely converted to complex with a small excess of substrate, although warming to -90

Table 1. ^1H and ^{13}C NMR Shifts for Methyl Groups Me_α and Me_β

complex (bond)	^1H shifts (ppm) ^a			^{13}C shifts (ppm) ^b		
	Me_α	Me_β	$\Delta(^1\text{H})$	Me_α	Me_β	$\Delta(^{13}\text{C})$
3a (C=S)	-0.76	0.37	1.13	-10.54	20.10	30.64
3b (C=S)	-0.96	-0.16	0.80	-8.58	7.17	15.75
3c (C=S)	-0.68	-0.29	0.39	-9.31	9.35	18.66
3d (C=S)	-0.74	-0.29	0.45	-9.46	9.19	18.65
3e (C=S)	-0.52	-0.27	0.25	-9.18	9.18	18.36
3f (C=S)	-0.55	-0.33	0.22	-9.02	9.13	18.15
3g (C=S)	-0.76	0.12	0.88	-9.51	8.84	18.35
3h (C=S)	-1.00	-0.03	0.97	-9.34	4.06	13.40
3i' (C=N)	-0.48	0.52	1.00	-1.48	-1.25	0.23
3j' (C=N)	-0.47	-0.03	0.44	-2.76	2.15	4.91
3j (C=S)	-0.79	0.43	1.22	-9.09	10.81	19.90
6 (C=C)	-1.12	-0.10	1.02	-5.04	-0.60	4.44

$$^a \Delta(^1\text{H}) = \delta_{\text{H}}(\text{Me}_\beta) - \delta_{\text{H}}(\text{Me}_\alpha). \quad ^b \Delta(^{13}\text{C}) = \delta_{\text{C}}(\text{Me}_\beta) - \delta_{\text{C}}(\text{Me}_\alpha).$$

$^\circ\text{C}$ was necessary to complete the reaction with **1b** in a reasonable time (<1 h). The colors of the solutions of these complexes were shades of yellow to red.

There were two salient features in the NMR spectra of these complexes: (i) a pair of ^1H peaks and the corresponding ^{13}C peaks (Table 1) for the methyl groups Me_α (upfield) and Me_β (downfield) attached to Cu and (ii) a characteristic ^{13}C peak at ca. 80 ppm for the C atom attached to Cu and S (Scheme 2). For the methyl groups on Cu, the upfield ^{13}C peak corresponded to the upfield ^1H peak (HMQC/HSQC) and likewise for the downfield peaks in these and the rest of the complexes reported herein. NOESY cross-peaks between the hydrogens of Me_β and those of the substituents were particularly prominent.

At $-100\text{ }^\circ\text{C}$, trifluoromethyl derivative **1e** completely displaced **1c** from complex **3c** to give complex **3e**, but it did not react with methoxy complex **3d**. At $-60\text{ }^\circ\text{C}$, **1e** converted complex **3d** to **3e** (plus free **1d**). Likewise, **1c** converted complex **3d** to **3c** (plus free **1d**) at $-60\text{ }^\circ\text{C}$. Consequently, the order of stability is **3e** > **3c** > **3d**, i.e., electron-poor ligands form more stable complexes than electron-rich ones. This observation suggests a "push-pull" interaction between the methyl and thiocarbonyl ligands.

Injection of a deep-blue solution of thiobenzophenone (**1f**) into a colorless solution of **2**·LiCl (both in THF- d_8) at $-100\text{ }^\circ\text{C}$ gave an emerald-green solution of **3f**. The ^{13}C NMR shift of the C bonded to Cu and S was 81.89 ppm. A number of transition-metal complexes of thiobenzophenone are known,⁷ and the ^{13}C shifts for the C=S groups are in the range 150–180 ppm. We attribute the large upfield displacement in our case to significantly higher sp^3 character. (For comparison, it should be noted that the ^{13}C shift of the methine in diphenylmethanethiol is 48 ppm.⁸)

Ethylene trithiocarbonate (**1g**) reacted with **2**·LiI at $-100\text{ }^\circ\text{C}$ to afford complex **3g** quantitatively. NOESY confirmed the methyl group nearest the ethylene bridge to be Me_β .

Alkoxy derivative **1h** reacted with **2**·LiI at $-100\text{ }^\circ\text{C}$ to yield complex **3h**, which was significantly less stable than the previous ones ($t_{1/2} \approx 1\text{ h}$); nevertheless, it was fully characterized over several runs.

While oxygen substitution was tolerated, sp^3 nitrogen was not: methyl pyrrolidine-1-carbodithioate, *N,N*-dimethylthioformamide, and *N,N,N',N'*-tetramethylthiourea were unreactive toward **2**·LiI.

In contrast, injection of methyl isothiocyanate (**1i**), which contains an sp^2 nitrogen, into **2**·LiI (both in THF- d_8 at $-100\text{ }^\circ\text{C}$) gave a relatively stable complex with methyl ^{13}C shifts that were far removed from those of **3a–h**. The ^{13}C peak at 207.85 ppm was 83 ppm downfield from the corresponding peak in the substrate, essentially the same effect that was observed upon complexation of carbon disulfide (85 ppm). Consequently, we assign structure **3i'** to this new product, which also has an uncomplexed C–S double bond. Finally, a strong NOE between the NMe group and Me_β was observed, which is consistent with the assigned structure.

Phenyl isothiocyanate (**1j**) reacted rapidly with **2**·LiI at $-100\text{ }^\circ\text{C}$ to afford a fleeting intermediate **3j'** ($t_{1/2} = 40\text{ s}$) and a final, stable complex **3j**. The methyl ^{13}C shifts for **3j** were very similar to those for **3a–h**, and therefore, we assign a structure that also has a complexed C–S double bond. The methyl ^{13}C shifts (obtained by using ^{13}C -labeled **2**·LiI) for intermediate **3j'** were far outside the range for **3a–h**. The difference, $\Delta(^{13}\text{C}) = 4.91\text{ ppm}$, is close to the $\Delta(^{13}\text{C})$ value of 4.44 ppm for C–C double-bond complex **6**. It is interesting to note that the difference $\Delta(^1\text{H}) = 0.44\text{ ppm}$ for **3j'** is in the range $\Delta(^1\text{H}) = 0.22\text{--}0.45\text{ ppm}$ for complexes **3c–f**, which have at least one phenyl group attached to a C bonded to Cu.

Are the double-bond complexes discussed above best described as trigonal $\text{d}^{10}\text{ Cu}^{\text{I}} \pi$ complexes, as shown in Scheme 1, or are they pseudo-square-planar $\text{d}^8\text{ Cu}^{\text{III}} \sigma$ bonded structures, as shown in Scheme 2? Calculations support the view that the charges on the ligands in Cu^{III} complexes are significantly smaller than they are in Cu^{I} complexes.⁹ This difference is reflected in the ^{13}C NMR shifts of lithium dimethylcuprate(I) (ca. -10 ppm) and lithium tetramethylcuprate(III) (ca. 15 ppm).⁵ Similarly, the ^{13}C NMR data summarized in Table 1 show a clear difference between the complexes involving C–C and C–N double bonds on one hand and those involving C–S double bonds on the other.

The difference in charge is also responsible for the dramatic difference in the reactivity of these complexes toward methanol (4 equiv), as observed using RI-NMR spectroscopy. At $-100\text{ }^\circ\text{C}$, lithium dimethylcuprate(I) reacted completely before the first spectrum was obtained (<1 s). In contrast, lithium tetramethylcuprate(III) reacted very slowly at $-100\text{ }^\circ\text{C}$ but gave a quantitative yield of methane upon warming to $-60\text{ }^\circ\text{C}$.¹⁰

A mixture of α -enone complexes **6** and **6**·LiI⁴ reacted rapidly at $-100\text{ }^\circ\text{C}$. In fact, the rate of methanolysis was much higher than the rate of dissociation of the complexes (k_{-1} ; see Scheme 1).⁴ Complex **3i'** reacted slowly at $-100\text{ }^\circ\text{C}$. Complex **3e** gave no reaction at $-100\text{ }^\circ\text{C}$; however, methane was generated upon warming to $-60\text{ }^\circ\text{C}$. The results, C–C > C–N \gg C–S, are indicative of their positions on the π – σ continuum, with C–C double bonds close to π and C–S double bonds close to σ .

Facile ligand exchange is typical of square-planar d^8 complexes, and it usually proceeds via an associative mechanism, either pseudorotation or an $\text{S}_{\text{N}}2$ -like reaction. For ligands such as ours with low-lying LUMOs, we posit initial coordination of the new ligand by a filled d orbital followed by the pseudorotation pathway. In contrast, on the basis of theoretical calculations, Gärtner et al.¹¹ have proposed an $\text{S}_{\text{N}}2$ mechanism for the displacement of chloride by methyl in $\text{d}^8\text{ Cu}^{\text{III}}$ complexes.

η^2 -Complexes of Gilman reagents with C–C double bonds are well-known, and we have now prepared and identified the first such complexes of these valuable synthetic reagents with C–N and C–S double bonds, which also have considerable potential.

Acknowledgment. We thank the NSF for Grants 0353061 and 0321056 and Tom DuBois for helpful discussions.

Note Added after ASAP Publication. Due to a production error, the uncorrected proof version was published ASAP on June 11, 2010. Typographical corrections have now been made and ref 9b has been added. Corrections were also made to Scheme 2 and Table 1. The corrected version was published on June 28, 2010.

Supporting Information Available: Typical NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) Kharasch, M. S.; Tawney, P. O. *J. Am. Chem. Soc.* **1941**, *63*, 2308.
- (2) House, H. O.; Respass, W. L.; Whitesides, G. M. *J. Org. Chem.* **1966**, *31*, 3128.

- (3) Bertz, S. H.; Dabbagh, G.; Williams, L. M. *J. Org. Chem.* **1985**, *50*, 4415.
- (4) Background: Bertz, S. H.; Carlin, C. M.; Deadwyler, D. A.; Murphy, M. D.; Ogle, C. A.; Seagle, P. H. *J. Am. Chem. Soc.* **2002**, *124*, 13650.
- (5) Procedure: Bartholomew, E. R.; Bertz, S. H.; Cope, S. K.; Murphy, M. D.; Ogle, C. A.; Thomas, A. A. *Chem. Commun.* **2010**, *46*, 1253.
- (6) (a) Bertz, S. H.; Cope, S.; Murphy, M.; Ogle, C. A.; Taylor, B. J. *J. Am. Chem. Soc.* **2007**, *129*, 7208. (b) Bertz, S. H.; Cope, S.; Dorton, D.; Murphy, M.; Ogle, C. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 7082. (c) Bartholomew, E. R.; Bertz, S. H.; Cope, S.; Dorton, D. C.; Murphy, M.; Ogle, C. A. *Chem. Commun.* **2008**, 1176. (d) Bartholomew, E. R.; Bertz, S. H.; Cope, S.; Murphy, M.; Ogle, C. A. *J. Am. Chem. Soc.* **2008**, *130*, 11244.
- (7) Beck, R.; Sun, H.; Li, X.; Camadanli, S.; Klein, H.-F. *Eur. J. Inorg. Chem.* **2008**, 3253 and refs 7 and 8 cited therein.
- (8) Makioka, Y.; Uebori, S.; Tsuno, M.; Taniguchi, Y.; Takaki, K.; Fujiwara, Y. *J. Org. Chem.* **1996**, *61*, 372.
- (9) (a) Hu, H.; Snyder, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 7210. (b) Snyder, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 11025.
- (10) Bertz, S. H.; Murphy, M. D.; Ogle, C. A.; Thomas, A. A. *Chem. Commun.* **2010**, *46*, 1255.
- (11) Gärtner, T.; Yoshikai, N.; Neumeier, M.; Nakamura, E.; Gschwind, R. M. *Chem. Commun.* **2010**, *46*, 4625.

JA103068H