New Results Regarding the Structure and Reactivity of Cyanocuprates—The End of an Old Controversy

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History

Organocopper reagents play a prominent role among the many organometallic compounds which can be used for the selective formation of C–C bonds.[1] Monoorganocopper compounds RCu and cuprates R_2CuLi are usually prepared by transmetalation of organolithium or Grignard reagents with copper(I) salts. In 1981, Lipshutz et al.[2] described for the first time cyanocuprates which were formed by reaction of copper(I) cyanide with one or two equivalents of RLi. These reagents seemed to differ considerably in terms of stability and reactivity (in Michael additions and substitution reactions) from the so-called Gilman cuprates $R_2CuLi \cdot LiX$ (X = Cl, Br, I) which are prepared from copper(I) halides. Lipshutz et al. explained these findings by postulating that the cyano group is bound to the copper center. Accordingly, the reaction of CuCN with one equivalent of RLi would lead to the copper species RCu(CN)Li (**1**) which was designated as a "lower-order" cyanocuprate; after addition of a second equivalent of RLi, the cyanocuprate $R_2Cu(CN)Li_2$ (**2**) would be formed [Eq. (1)]. In contrast to the monoanionic cuprates R_2CuLi, which can be described in ionic form as $[R_2Cu]^- + Li^+$, the latter species would exist as an dianionic cuprate ($[R_2Cu(CN)]^{2-} + 2\,Li^+$) with three organic groups bound to the copper. Lipshutz designated these reagents as "higher-order" cyanocuprates.[2, 3]

$$\mathrm{CuCN} \xrightarrow{\mathrm{RLi}} \underset{\mathbf{1}}{\mathrm{RCu(CN)Li}} \xrightarrow{\mathrm{RLi}} \underset{\mathbf{2}}{\mathrm{R_2Cu(CN)Li_2}} \text{ or } \underset{\mathbf{3}}{\mathrm{R_2CuLi \cdot LiCN}} \qquad (1)$$

The structural assigment for the "lower-order" species **1** was confirmed by different spectroscopic experiments. The most convincing proof is the coupling between the cyanide ligand and methyl group ($^2J \approx 22$ Hz) observed by Bertz[4] in the ^{13}C NMR spectrum of the labeled cuprate $MeCu(^{13}CN)Li$; of course, such a coupling can only be observed when *both* groups are bound to the copper atom. In contrast to this, the question whether cyanocuprates with a 2:1 stoichiometry exist as "higher-order" species **2** or rather as "cyano-Gilman" cuprates **3** in their thermodynamically most stable form has been a matter of controversy since 1990, the protagonists being B. H. Lipshutz ("If the cyano ligand is not on copper, then where is it?") and S. H. Bertz ("It's on lithium!"). The controversy started with different interpretations of the ^{13}C NMR data of several cuprates prepared from CuI or CuCN[5, 6] and the observation that no coupling occurs between the alkyl groups and the cyanide ligand in cyanocuprates with 2:1 stoichiometry which had been prepared from $Cu^{13}CN$.[4] Other arguments for and against "higher-order" cyanocuprates have already been summarized.[1] Here, it should only be mentioned that EXAFS and XANES spectra[7] as well as ab initio calculations[8] all point towards "cyano-Gilman" reagents **3** as most stable species wherein the cyanide is not bound to copper but rather to the lithium ions. This interpretation is also in accordance with recent NMR-spectroscopical studies of Bertz et al.[9] and Berger et al.[10]

Still, the most convincing structural proof is the determination of solid-state structures by X-ray analysis. The groups of Boche[11] and van Koten[12] now independently report the crystal structures of cyanocuprates with 2:1 stoichiometry which settle the question of the thermodynamically most stable form of these reagents unambiguously. Additionally, new results concerning the reactivity of these organocopper compounds also allow conclusions about the kinetically active species.

Structure

Based on their experience with C,N-chelating aminoaryl ligands, Kronenburg, Jastrzebski, Spek, and van Koten[12] solved the X-ray crystal structure of the cyanocuprate $[(2\text{-}(Me_2NCH_2)C_6H_4CH_2)_2CuLi_2(CN)(THF)_4]_\infty$ (**4**). In the solid state, the cuprate exists as a polymeric zigzag chain with alternating Ar_2Cu^- and Li-CN-Li^+ ions (Figure 1); the lithium ions reach the ideal coordination number 4 by additional coordination to two THF molecules and an amino group. The carbon and nitrogen atoms of the cyano groups cannot be differentiated in the X-ray analysis; the Li–C and Li–N bond lengths are 204.5 pm. As found frequently in solid-state structures of organocuprates,[13] also **4** contains a linear arrangement of the anionic Ar_2Cu^- fragements.

At first glance, the X-ray crystal structure of the alkylcyanocuprate $[tBu_2CuLi_2(CN)(THF)(pmdeta)]$ (**5**;

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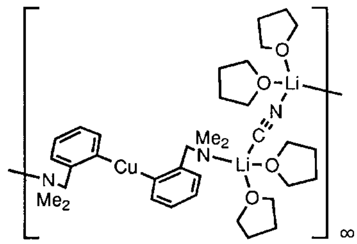

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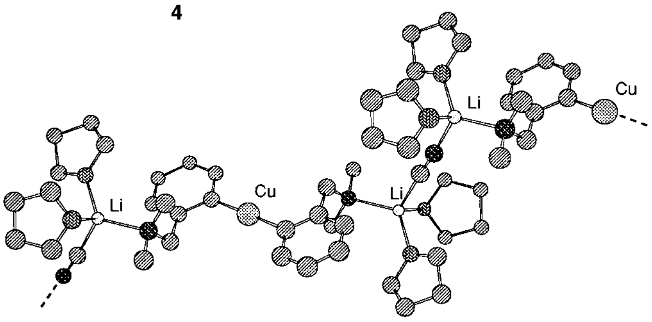
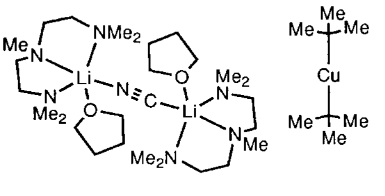


Figure 1. Part of the solid-state structure of the "cyano-Gilman" cuprate **4** (hydrogen atoms omitted for clarity).[12]

pmdeta = pentamethyldiethylenetriamine) (Figure 2) obtained by Boche, Bosold, Marsch, and Harms[11] seems to be rather different with respect to that of **4**, but it does indeed bear the *same structural features.* Also here, a linear cuprate anion and an almost linear Li-CN-Li$^+$ ion are found which, however, are completely separated from each other. The reason is that the lithium ions in **5** are coordinated to pmdeta ligands instead of the covalently bound amino groups of **4**; additionally, each lithium ion is coordinated to a THF molecule. Again, it is not possible to differentiate the carbon and nitrogen atoms of the cyanide; the length of the Li–C and Li–N bonds (210.5 pm) is very similar to that found for **4**. Both structures exhibit a high affinity of CN$^-$ for lithium ions; in the case of **5**, the cyanide is still attached to the Li$^+$ ions although the latter has already reached the coordination number 4 by binding to pmdeta and THF.



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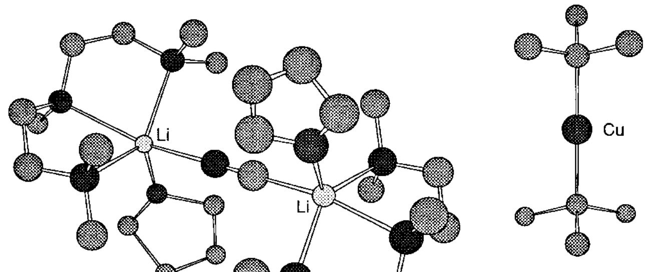
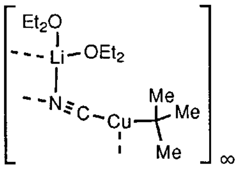


Figure 2. Solid-state structure of the "cyano-Gilman" cuprate **5** (hydrogen atoms and a disorder of the *tert*-butyl groups omitted).[11]

Based on these structures, the question of the thermodynamically most stable form of the reagents prepared from two equivalents of RLi and one equivalent of CuCN can be answered clearly in favor of the "cyano-Gilman" cuprates; the resemblence of structural details of **4** and **5** is particularly striking. This statement applies apriori only for the structure in the solid state. However, several experimental findings indicate that the cyanocuprates exist also in solution mainly as "cyano-Gilman" cuprates **3** and not as "higher-order" species **2**. In addition to the numerous spectroscopical studies mentioned above, this notion is also supported by additional investigations carried out by van Koten et al.[12] with **4**. This cuprate is highly soluble in THF, and the determination of the aggregation state by cryoscopy revealed that it exists as a monomeric species in this solvent. The analogous observation had already been made for the cyanocuprates $R_2CuLi \cdot LiCN$ with R = Me and Ph, and this can be explained in terms of contact-ion pairs with "cyano-Gilman" structure (linear R-Cu-R unit with Li-CN-Li bridge).[14] In the case of the *tert*-butyl cuprate $t\mathrm{Bu}_2CuLi \cdot LiCN$, the cryoscopic determination of the aggregation state hinted at the existence of equilibria between different species.[14a]

At this point it should be mentioned that Boche et al. did not only determine the solid-state structure of the "cyano-Gilman" cuprate **5**, but also the first structure of a "lower-order" cyanocuprate of type **1**, that is the *tert*-butyl cuprate $[t\mathrm{Bu}Cu(CN)Li(OEt_2)_2]_\infty$ (**6**; Figure 3).[11] In accordance with the solution studies mentioned above, a Cu–CN bond was found also in the solid state.[15]



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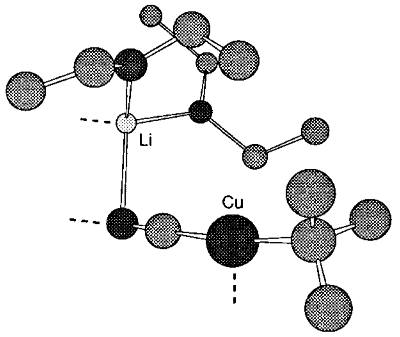

Figure 3. Part of the solid-state structure of the "lower-order" cyanocuprate **6** (hydrogen atoms omitted for clarity).[11]

Reactivity

In organometallic chemistry one often finds that the thermodynamically most stable species of a given reagent is not the kinetically active one. Of course, this can only occur if there is a fast equilibrium between different species, and the existence of such equilibria has indeed been proven spectroscopically for several organocuprates.[1] In the case of the cyanocuprates of 2:1 stoichiometry there might be an equilibrium between the thermodynamically more stable "cyano-Gilman" reagent **3** and the "higher-order" cuprate **2**; because of its (formal) dianionic character, the latter should be much more reactive towards electrophiles. The actual existence of such an equilibrium, however, has not been proven to date. Therefore, one may ask if there is really a noticeable difference in reactivity between cyanocuprates and classical monoanionic Gilman cuprates prepared from copper(I) halides.

The original postulate of the "higher-order" cyanocuprate structure was based on the observance of much higher yields in substitution reactions when CuCN was used instead of other copper sources for the preparation of the cuprate.[2, 3] Conclusions from yields on reactivities, however, can only be made when the reactions are carried out under identical conditions (solvent, temperature, concentrations etc.). Recent studies of this kind were reported by Bertz et al.;[8c] they revealed only small differences in reactivity between classical cuprates and "cyano-Gilman" reagents. This finding is in accordance with new kinetic measurements; for example, the 1,4-addition of $Me_2CuLi \cdot LiI$ to 4,4-dimethyl-2-cyclohexenone at −59 °C in diethyl ether takes place about five times faster than that of $Me_2CuLi \cdot LiCN$.[16]

Even these results do not allow an unambiguous decision for "cyano-Gilman" cuprates **3** or "higher-order" cyanocuprates **2** as reactive species. However, it seems reasonable to assume that the "cyano-Gilman" species is the kinetically active one for those transformations which show only a small reactivity difference since a dianionic cuprate should exhibit a drastically increased reactivity. The only difference between the Gilman reagents $R_2CuLi \cdot LiX$ (X = Cl, Br, I) and $R_2CuLi \cdot LiCN$ would then be the cation ($(Li\text{-}X\text{-}Li)^+$ vs. $(Li\text{-}CN\text{-}Li)^+$), whereas the cuprate anion $[R_2Cu]^-$ would be identical. The experimentally observed small reactivity differences could then be explained in terms of a (slightly) different electrophilic activation of the substrate[1] by the respective cation. Here, it may also be important whether the reactive cuprate species exists as a solvent-separated ion pair (such as **4** and **5**) or rather as a contact ion pair, consisting of $[R_2Cu]^-$ and $(Li_2X)^+$ ions. The former assumption would be in accordance with the observation that enantioselective 1,4-additions of chirally modified cuprates $RCu(L^*)Li$ take place with high stereoselectivities only when "soft" sulfur or phosphorus nucleophiles (which are bound to the copper center) are used as chiral ligands L*.[17] In contrast to this, "hard" amide or alcoholate ligands which bind to the lithium ions give only low enantioselectivities in most cases, presumably because the chiral ligand is too far away from the reaction center in these cases (cf. **5**).

Is there still a "chance" for "higher-order" cyanocuprates? In spite of the overwhelming evidence in favor of "cyano-Gilman" reagents as thermodynamically most stable and kinetically most active species, it is still impossible to answer the question definitely with "no". After all, the final product of all reactions of "cyano-Gilman" reagents is the "lower-order" cyanocuprate $RCu(CN)Li$, that is a Cu−CN bond is indeed formed at some point during the transformation! Moreover, there are certain reactions which can only be carried out with the cyanocuprates $R_2CuLi \cdot LiCN$ formed from CuCN, but not with classical Gilman reagents $R_2CuLi \cdot LiX$ (X = Br, I).[18] Therefore, the final answer to the question has to await further kinetic and spectroscopic studies.

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[1] Recent review: N. Krause, A. Gerold, *Angew. Chem.* **1997**, *109*, 194–213; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 186–204.

[2] B. H. Lipshutz, R. S. Wilhelm, D. M. Floyd, *J. Am. Chem. Soc.* **1981**, *103*, 7672–7674. The first cyanocuprate with 1:1 stoichiometry was reported by: J.-P. Gorlier, L. Hamon, J. Levisalles, J. Wagnon, *J. Chem. Soc. Chem. Commun.* **1973**, 88.

[3] Reviews: a) B. H. Lipshutz, *Synthesis* **1987**, 325–341; b) B. H. Lipshutz, *Synlett* **1990**, 119–128; c) B. H. Lipshutz, S. Sengupta, *Org. React.* **1992**, *41*, 135–631; d) B. H. Lipshutz in *Organometallics in Synthesis* (Ed.: M. Schlosser), Wiley, Chichester, **1994**, pp. 283–382; e) B. H. Lipshutz in *Advances in Metal-Organic Chemistry* (Ed.: L. S. Liebeskind), JAI Press, Greenwich, **1995**, Vol. 4, pp. 1–64.

[4] S. H. Bertz, *J. Am. Chem. Soc.* **1991**, *113*, 5470–5471.

[5] S. H. Bertz, *J. Am. Chem. Soc.* **1990**, *112*, 4031–4032.

[6] B. H. Lipshutz, S. Sharma, E. L. Ellsworth, *J. Am. Chem. Soc.* **1990**, *112*, 4032–4034.

[7] a) T. Stemmler, J. E. Penner-Hahn, P. Knochel, *J. Am. Chem. Soc.* **1993**, *115*, 348–350; b) T. M. Barnhart, H. Huang, J. E. Penner-Hahn, *J. Org. Chem.* **1995**, *60*, 4310–4311; c) T. L. Stemmler, T. M. Barnhart, J. E. Penner-Hahn, C. E. Tucker, P. Knochel, M. Böhme, G. Frenking, *J. Am. Chem. Soc.* **1995**, *117*, 12489–12497.

[8] a) J. P. Snyder, D. P. Spangler, J. R. Behling, B. E. Rossiter, *J. Org. Chem.* **1994**, *59*, 2665–2667; b) J. P. Snyder, S. H. Bertz, *J. Org. Chem.* **1995**, *60*, 4312–4313; c) S. H. Bertz, G. Miao, M. Eriksson, *Chem. Commun.* **1996**, 815–816.

[9] S. H. Bertz, J. P. Snyder, K. Nilsson, Ö. Davidsson, *Angew. Chem.* **1998**, *110*, 327–331; *Angew. Chem. Int. Ed.* **1998**, *37*, 314–317.

[10] T. A. Mobley, F. Müller, S. Berger, *J. Am. Chem. Soc.* **1998**, *120*, 1333–1334.

[11] G. Boche, F. Bosold, M. Marsch, K. Harms, *Angew. Chem.* **1998**, *110*, 1779–1781; *Angew. Chem. Int. Ed.* **1998**, *37*, 1684–1686.

[12] C. M. P. Kronenburg, J. T. B. H. Jastrzebski, A. L. Spek, G. van Koten, *J. Am. Chem. Soc.* **1998**, *120*, 9688–9689.

[13] G. van Koten, S. L. James, J. T. B. H. Jastrzebski in *Comprehensive Organometallic Chemistry II, Vol. 3* (Ed.: E. W.Abel, F. G. A. Stone, G. Wilkinson), Pergamon, Oxford, **1995**, pp. 57–133.

[14] a) A. Gerold, J. T. B. H. Jastrzebski, C. M. P. Kronenburg, G. van Koten, N. Krause, *Angew. Chem.* **1997**, 109, 778–780; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 755–757; b) H. Huang, C. H. Liang, J. E. Penner-Hahn, *Angew. Chem.* **1998**, 110, 1628–1630; *Angew. Chem. Int. Ed.* **1998**, *37*, 1564–1566.

[15] Recently, another solid state structure of a "lower-order" cyanocuprate with similar structural features was reported: C.-S. Hwang, P. P. Power, *J. Am. Chem. Soc.* **1998**, *120*, 6409–6410.

[16] N. Krause, J. Canisius, unpublished results.

[17] a) B. L. Feringa, M. Pineschi, L. A. Arnold, R. Imbos, A. H. M. de Vries, *Angew. Chem.* **1997**, *109*, 2733–2736; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2620–2623; b) N. Krause, *Angew. Chem.* **1998**, *110*, 295–297; *Angew. Chem. Int. Ed.* **1998**, *37*, 283–285.

[18] B. H. Lipshutz, K. Siegmann, E. Garcia, F. Kayser, *J. Am. Chem. Soc.* **1993**, *115*, 9276–9282, and references therein.