

ORGANOMETALLICS

Volume 18, Number 9, April 26, 1999

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American Chemical Society

Communications

An Electrospray Ionization Mass Spectrometry Study of the Aggregation States of Organocopper Complexes in Solution

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Received January 26, 1999

Summary: Using the technique of ESMS, a number of carbon-bound organocuprate species derived from copper(I) halides and CuCN have been examined. The data obtained indicate the presence of several anionic aggregates in solution.

Recent advances in electrospray ionization mass spectrometry (ESMS)^{1a} have provided an especially powerful tool for observing in the gas phase the solution composition of charged species. While extensive usage continues to routinely address questions in biochemistry, the ESMS technique has also been very successfully applied to inorganic and organometallic complexes of various metals, including Pd,^{2a} Ag,^{2b} Na,^{2c} K,^{2c} Zn,^{2d} and others.^{1,2c,e} Accurate determinations of metal complex compositions have been realized due to the mildness of the ionization process. The method of ESMS delivers ionic components to the detector by aerosolizing the solution while concomitantly applying a static charge to the surface of solvent droplets. The static charge buildup then causes a series of "Coulombic explosions",

resulting in complete desolvation of the solute without the possibility of recombination of individual charged fragments.³

On the basis of our long-standing interest in organocopper chemistry,⁴ and the stream of new and valuable methodologies based on Cu(I) which continue to be developed,⁵ we have come to appreciate the challenges posed for securing information on the aggregation state(s) of various Gilman⁶ homo (R₂CuLi) and mixed (RR'-CuLi) cuprates in solution. Many NMR studies, of course, have contributed greatly over the years,⁷ as have more recent theoretical treatments⁸ and solid-state (*i.e.*, X-ray) determinations.⁹ Cryoscopic measurements have also been reported which provide interesting comparisons among the various cuprate types,^{10a} and X-ray absorption spectroscopy (XAS) has uncovered new evidence that the Gilman cuprate structure appears to be (ethereal) solvent-dependent.^{10b} In this report we present our preliminary findings on the composition of repre-

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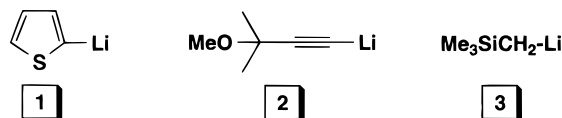
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sentative, synthetically valued mixed lithioorganocuprates in THF and/or Et₂O as revealed by ESMS, the first such study on anionic Cu(I) complexes containing carbon ligands bound to copper.¹¹

Homogeneous solutions of the traditional cuprates "RR'CuLi", derived from CuI, CuBr·SMe₂, and CuCN, were prepared mainly in THF at concentrations on the order of 10⁻³ M. Three different sources of organolithium reagents were used as ligand precursors, including the readily available and heavily utilized^{4,12} 2-lithiothiophene (2-ThLi; **1**)^{13a} and lithiated terminal alkyne **2**,^{13b} as well as the more recently introduced ((trimethylsilyl)methyl)lithium (TMSCH₂Li; **3**).^{13a,c}



In arriving at conditions for these ESMS experiments, several variables required assessment, including cone voltage, capillary voltage, HV lens voltage, source temperature, solution concentration, and sample injection flow rate. These were all systematically examined using ThCu(CN)Li as test substrate. To avoid exposure to either oxygen or moisture, gastight syringes in conjunction with a syringe pump were used to deliver the samples. Injection rates of between 20 and 75 μ L/min were examined¹⁴ but did not lead to changes in the observed spectra. Samples were introduced into the spectrometer at -78 °C and data acquired over a 3 min period. The source temperature, also varied from 25 to 70 °C, had no impact on the observed spectra. Likewise, data acquired for this cuprate solution at 10⁻³ M were identical with those obtained at 10⁻⁴ M. Typically, experiments were run using a capillary voltage of 3.75 kV and the HV lens voltage varied from 0.10 to 0.75 kV. Reducing (one or both) voltages gave decreased signal intensities, but no other changes in the observed spectra were noted. Variation of the cone voltage had a far more pronounced effect, as expected (*vide infra*).¹

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(14) The optimal flow rate is 20 μ L/min on our instrument as per manufacturer specifications.

(15) The selected parameters are as follows: sample temperature, -78 °C; source temperature, 25–35 °C; flow rate, 25 μ L/min; cone voltage, 20 V; HV lens, 0.75 kV; capillary, 3.75 kV.

Table 1. Cuprates Analyzed by ESMS

Cu(I) Source	Cuprate	Solvent	Figure 1
CuCN		THF	A
		THF	B
CuI		THF	C
		THF	D
CuBr·SMe ₂		THF	E
		Et ₂ O	F

These control studies allowed us to settle on the parameters which seemed most appropriate for maximizing information on organocuprate complexes.¹⁵

Of the many permutations possible using these three ligands (**1–3**) and three copper salts (above), those listed in Table 1 were prepared for analysis, their negative ion mass spectra being illustrated by cuprates **A–F** in Figure 1.¹⁶ Perhaps most striking, in general, is the complexity of each spectrum. Anionic species ranging from monomers to trimers are prevalent, while tetramers and pentamers can also on occasion be seen (Figure 1, cuprate **F**). Contributing to the complexity of the spectra may in part be the tendency for *larger* anions present in solution to fragment during the ionization process, giving rise to smaller aggregates. At low cone voltages (5–20 V) the base peak is typically of dimeric constitution. When the cone voltage was increased to 40–80 V, a gradual decrease occurred in signal intensities for the aggregates observed at lower cone voltages, while an increase was noted in the signal intensity for monomeric species.

Within each aggregation state can usually be found two or three combinations of the anionic ligands present. Those cuprates from CuCN (*i.e.*, "RCu(CN)Li"; Figure 1, cuprates **A** and **B**) afford relatively much cleaner, simpler spectra, uncomplicated by the presence of halide ions. On the other hand, cuprates generated in standard fashion^{12a} from either CuI or CuBr·SMe₂ reveal peaks characteristic not only of aggregates of copper but also of lithium halide salts (Li_nX_{n+1})⁻. Intriguing is the observation that for both cuprates **C** and **D** derived from CuI, and one of two derived from CuBr (**E**), most of the observed aggregates in each contain at least one halide ion. Implied in these data is the notion that halide ion may well be an integral part of the cuprate complex, as occasionally noted in the past¹⁷ and bolstering prior claims¹⁸ regarding, *e.g.*, the nature of Yamamoto's reagent ("RCu·BF₃", from RLi + CuI + BF₃·OEt₂).^{19,20}

(16) No identifiable copper-containing species were observed in the *positive* ion ESIMS data on these, or any other, cuprate samples examined.

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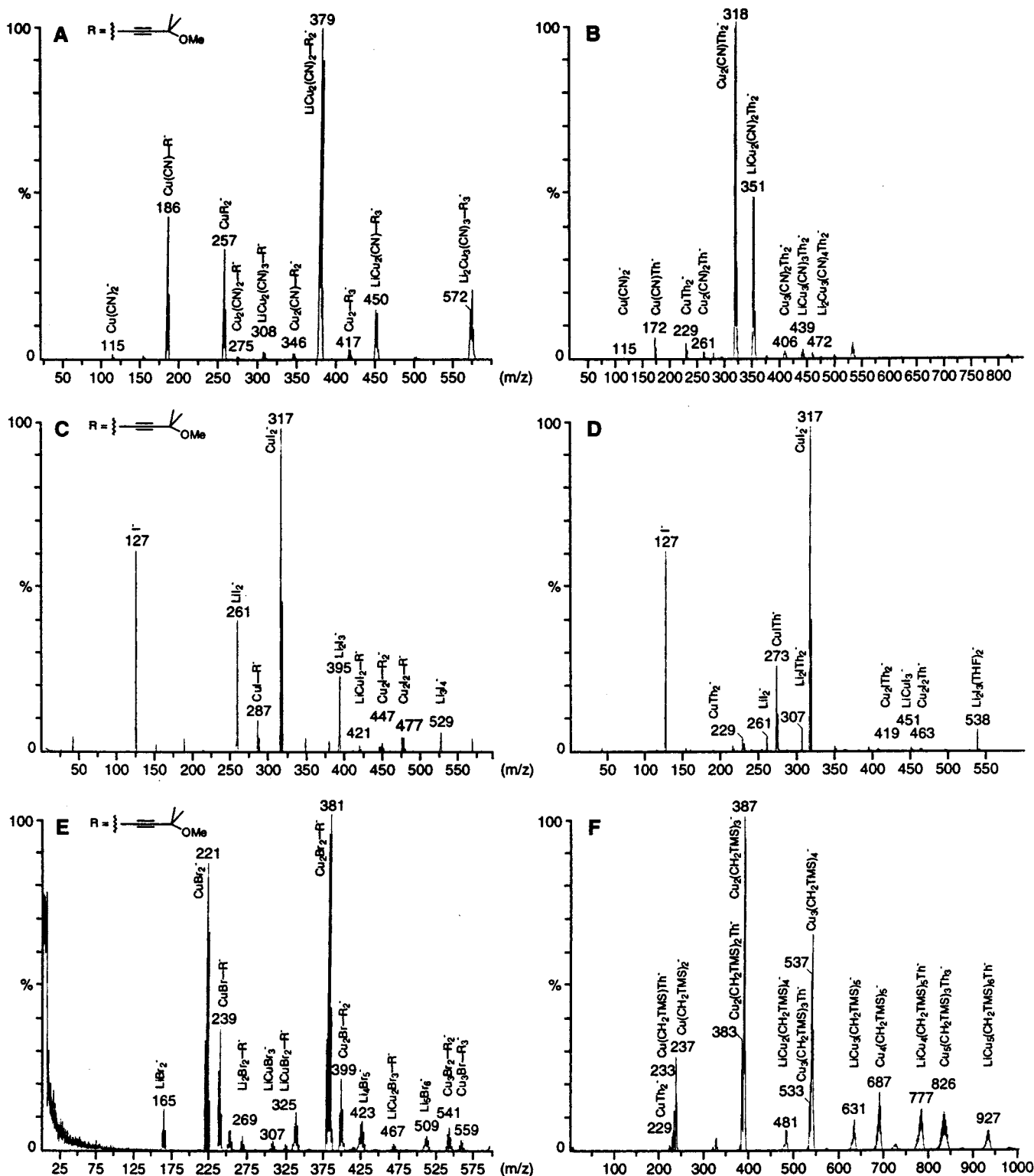


Figure 1. Negative ion mass spectra. For identification of parent cuprates A–F, see Tables 1 and 2.

The data shown in Figure 1 and summarized in Table 2, at first glance, may be unsettling. They present a case for cuprates in solution which is seemingly far more complex than either existing NMR⁷ or cryoscopic data^{10a} would suggest. However, while the electrospray experiment provides an alternative look at solution composi-

tion, it does so under high dilution conditions well outside the normal range for NMR samples⁷ and coupling reactions¹² with most organic substrates (ca. 0.1 M). At 10^2 – 10^3 higher reaction concentrations, known ligand exchange between cuprates may be fast on the NMR time scale, giving rise to time-averaged signals. Such signals could be interpreted as, or assigned to, one

(20) Presumably due to the known¹² thermal sensitivity and apparent instability under ESMS conditions, attempts to obtain spectra on the far more basic homocuprates Me_2CuLi and $n\text{-Bu}_2\text{CuLi}$ have thus far not been successful.

(21) Lipshutz, B. H.; Kozlowski, J. A.; Breneman, C. M. *Tetrahedron Lett.* **1985**, 26, 5911.

or perhaps (in mixed cuprates $RR'CuLi$) two species,²¹ whereas several discrete complexes appear to be present in varying amounts. It is also important to note that copper species present in solution that remain neutral will not be observed by ESMS. Although the ESMS technique itself does not allow for quantitative assessments, the spectra do implicate dimeric species as prominent components in all but one of these cuprates, in good agreement with several X-ray determinations.⁹ Moreover, the presence of halide ion ostensibly within the sphere of Cu(I) helps to explain the oftentimes frustrating and poorly understood role(s) which lithium salts can play in affecting both theoretical^{8a} as well as experimental reaction outcomes.²² Finally, that so many species may be involved in rapid ligand exchanges among several aggregates may shed light on the difficulty in finding a stoichiometric, nonracemic reagent capable of inducing chirality in cuprate 1,4-additions to enones that is independent of the transferrable ligand on the metal, as well as the nature of the substrate.²³

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In summary, the potential for negative ion electrospray ionization mass spectrometry to provide a new level of appreciation for the solution composition (but not structure!) of organocuprates has been documented. Several Cu(I) complexes, normally denoted as " $RR'CuLi$ " and " $RCu(CN)Li$ ", have been examined using different metal salts (*i.e.*, CuX ; $X = I, Br, CN$) and various organolithiums (**1–3**) as precursors. The spectra are quite complex, although most reveal the major species in solution to be of dimeric constitution. Further applications of ESMS as a potential tool for analysis of Grignard-based cuprates, as well as other organometallic reagents of general interest, will be reported in due course.

Acknowledgment. We are pleased to warmly thank the NSF (Grant No. CHE 97-34813) for its continued support of our programs.

Supporting Information Available: Table 2, giving ESMS data for cuprates in Table 1. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OM990048P