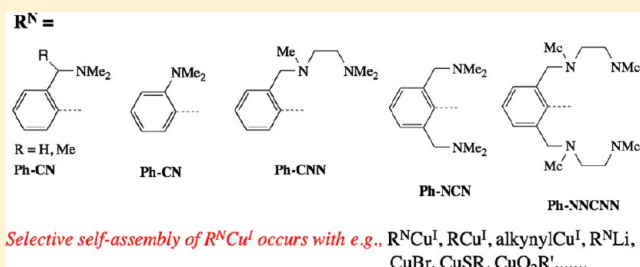# Organocopper Compounds: From Elusive to Isolable Species, from Early Supramolecular Chemistry with RCu^I Building Blocks to Mononuclear R$_{2-n}$Cu^{II} and R$_{3-m}$Cu^{III} Compounds. A Personal View†

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ABSTRACT: The first reports on copper-mediated organic reactions and speculations about the role of presumed organocopper compounds as intermediates or transient species date back to the early 20th century. Since that time, copper salt mediated and much later, copper-catalyzed C−X bond forming reactions (X = C, O, N) have been developed. Phenyl- and methylcopper(I) (highly explosive as a dry solid) were the first organocopper materials synthesized by Reich (1923) and Gilman (1952), respectively. However, it was not until the late 1960s and early 1970s that the first pure organocopper(I) compounds, which are also stable at room temperature, were isolated and structurally characterized. Recently, by the application of clever design and new synthetic approaches even organocopper(II) and -(III) compounds have been isolated, species that during the greater part of the last century were considered elusive. Significantly, these species had for some time been surmised, via kinetic and computational studies, to play a key role in copper-mediated and -catalyzed C−X bond forming reactions. In this personal account the various stages along which organocopper chemistry developed, with a steady pace, will be highlighted.

R^N =

R = H, Me
Ph-CN

Ph-CN

Ph-CNN

Ph-NCN

Ph-NNCNN

Selective self-assembly of R^{N}Cu^I occurs with e.g., R^{N}Cu^I, RCu^I, alkynylCu^I, R^{N}Li, CuBr, CuSR, CuO$_2$R',......

INTRODUCTION

Copper is the cheapest and most abundant metal of the Cu, Ag, and Au series and may occur in formal oxidation states ranging from 0 to 4+. The first uses of copper in organic synthesis comprised the pioneering work by Ullmann and, independently, Goldberg in the early 1900s, on copper-mediated aromatic nucleophilic substitution reactions.[1−4] In spite of the stoichiometric use of copper and the high reaction temperatures (≥200 °C) typically required, numerous industrial applications were developed from this chemistry and these involved the production of intermediates for pharmaceuticals, agrochemicals, and polymers.[4−7] Another important industrial use of copper was in the so-called "Ullmann" reaction for the production of biaryls from aryl halides.[8−11] In a recent review comments on the mechanistic aspects of the copper-mediated and -catalyzed C−C and C−X coupling reactions in organic synthesis can be found.[12] Modern, alternate versions of these Ullmann chemistries include palladium-catalyzed cross-coupling reactions between aryl halides and nucleophiles, of which the Buchwald−Hartwig amination reaction is an extremely successful example.[13−17] Whereas these novel palladium-catalyzed protocols alleviate many drawbacks of the classical Ullmann protocols (e.g., high reaction temperatures, high metal loadings, long reaction times, and narrow scope), these "modern" reactions have an obvious disadvantage with respect to the high price and low availability of the precious palladium metal. This has spurred renewed interest in copper-catalyzed versions of the Ullmann-type processes, and in recent years these have indeed been developed with great success.[18−25] In addition, more advantageous conditions for these copper-catalyzed protocols have now been realized. Interestingly, the palladium- and copper-catalyzed versions of C−C and C−X coupling reactions show different but complementary scopes. Recently, the various Pd and Cu protocols displayed by these two metals have been highlighted and compared by Hickman and Sanford in an excellent review. It highlights the differences and similarities of both the mechanisms and scope of reactions involving high-valent organometallic copper and palladium species in catalysis.[26]

In the early literature, there was already speculation about the possible role of organocopper species as key intermediates in the Ullmann biaryl synthesis: i.e., one that involves the reaction of aryl halides on copper metal over 200 °C.[8] Combined STM/XPS studies of the chemisorption and reaction of phenyl iodide at well-defined Cu(110) surfaces has revealed the dissociation and selective, structured binding of the iodine atom as well as that of the phenyl group prior to its desorption as biphenyl; this occurs with increased exposure to phenyl iodide at room temperature.[27] Using more recent mechanistic insights, the formation of phenylcopper(III) iodide intermediates in the reaction of phenyl iodide with excess copper metal using thiophene-2-carboxylatocopper(I) (CuTC) as a promotor have been proposed (see Scheme 1).[28]

Scheme 1. A More Recent Example of the Reductive "Ullmann Biaryl" Synthesis using CuTC as Promotor[28]
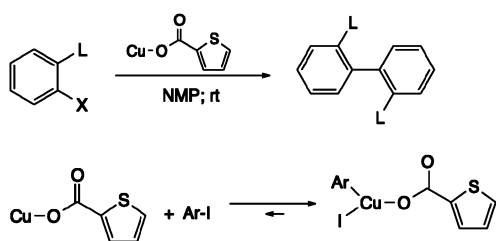
In the 1970s[29] various research groups (e.g., those of Cairncross,[30] Camus,[31] van Koten,[32] Lappert,[33] and later Floriani[34] and Power,[35] vide infra) started to explore the syntheses and structural features of pure organocopper compounds. In the beginning, structural elucidation of organocopper compounds had to rely on elemental analysis and molecular weight determinations of the species in solution, while by NMR spectroscopy some insight as to the composition of the organocopper in hand could be obtained.[36] However, in those days, very little awareness and knowledge about the aggregated structural aspects of organometallic complexes existed. For example, the existence and nature of electron-deficient bonding between metals and organyl anions as in organolithium and aluminum species, intra- and intermolecular exchange between organometallic species and metal salts, electron-transfer processes between metal species, etc. had just been realized or had yet to be discovered and formulated. During this period X-ray structure determination techniques and NMR spectroscopy started to become increasingly more powerful and it is through this development that the first, crucial insights in many of the aforementioned bonding and dynamic aspects of organocopper compounds were obtained: cf. full characterization of the structure of $R^N_4M_2Li_2$ (M = Cu, Ag; R^N = aryl anion with a coordinating o-amino substituent $[2\text{-}Me_2NCH_2C_6H_4]^-$) in solution.[36] Two recent reviews, "Structural Organocopper Chemistry"[37] and "The Structures of Lithium and Magnesium Organocuprates and Related Species",[38] provide excellent insight into the structural and bonding diversity encountered in the field of organocopper chemistry during the past few decades. These aspects form a key background to the discussions detailed below.

In this review, a somewhat personal view on the development of the organometallic aspects of organocopper chemistry will be presented. Speaking solely from my own perspective, at the onset of my first involvement with attempts to synthesize pure organocopper compounds I was both struck and fascinated by the apparent connection among the structural, bonding, and reactivity features of both organocopper(I) and lithium compounds and of their apparent magic combination, the cuprates. Molecular weight determinations clearly indicated that organocopper compounds exist as aggregated species in solution, while the first X-ray structure determinations unambiguously showed that this was also the case in the solid state.[30−36] From our early synthetic experiments onward, it became quickly obvious that unexpected aggregates could be created and isolated when distinct stoichiometric combinations of organocopper(I) and other organometallic fragments (e.g., organolithium) or metal salt (e.g., copper(I) halides) units were brought together in solution.[36,39] These findings were used to build aggregates with often very complex structural features

using a type of synthetic planning that nowadays is very common in both the fields of "Supramolecular Chemistry" and the "Self-Assembly of Species to Aggregates".[40] Apparently, concepts from these fields were already part of the thinking framework of many of the researchers in the organocopper field long before these ideas were formulated and formally labeled. Finally, for a long time, organocopper species with copper centers in a formal oxidation state different from 1+ were considered elusive. By the 1980s and 1990s, however, computational (e.g., Snyder[41] and Nakamura[42]) and mechanistic studies of both copper-mediated and -catalyzed reactions (e.g., Ullenius[43] and Bertz[44]) had pointed to the possible role of organocopper(III) species as key intermediates in the key turnover (i.e., rate-limiting) step(s). Nevertheless, any attempt to synthesize and isolate such species had proved fruitless except in the case of $(CF_3)_2CuS_2CNEt_2$.[45] Recently, this situation has fundamentally changed with the synthesis of a series of different organocopper(II) and -(III) compounds. These compounds commonly have the $[R_xCuL_n]X_{z-x}$ (X = anion) stoichiometry in which z is either 2 or 3 and x can be 1, 2, or 3. An excellent review by Ribas summarizes the recent findings involving the synthetic and structural aspects of mononuclear, high-valent copper organometallics.[46]

In fact, at the beginning of my career, I had been tantalizingly close to the isolation of the first example of a stable Cu(III) compound, but alas, I missed it, vide infra!

■ THE START OF MY JOURNEY IN ORGANOCOPPER CHEMISTRY

My first project as a researcher (1967 at the OCI-TNO) concerned the development of a copper-based material that would be more effective in fighting water-dwelling snails that are the natural reservoir of the disease Bilharzia (i.e., Schistosomiasis).[47] During those days, $CuSO_4$ was used for fighting these pesky snails. However, the copper ions rapidly deactivate in open waters (e.g., by reaction with sulfides), and therefore I got the task to develop a material that would ensure slow, continuous release of the copper ions. Note that this was the 1960s and these were the exciting days of organometallic chemistry as an emerging science. The idea of my supervisor (and later Ph.D. examiner), Prof. G. J. M. van der Kerk, was to use organocopper compounds as an effective depot for these copper ions. Slow hydrolysis and oxidation of the insoluble organocopper deposited in open waters would create the desired constant release of soluble copper ions. A shock for me, as a young starting researcher, was that a quick literature survey (which was undertaken, by the way, using hard copies, nonelectronic journals, and books!) revealed that only a few organocopper(I) compounds had been reported. Notably, there were no reports about organocopper(II) or -(III) compounds at all. It was revealing that, rather than being isolated as pure materials, these reported organocopper(I) compounds were comprised of undefined mixtures of organocopper(I) containing other metal salts originating from their preparation routes. Even more dramatically, it appeared that whereas almost all known compounds were reported to decompose rapidly in contact with water and air (a property that I was looking for indeed), these at the same time appeared to decompose above room temperature: to my chagrin, not a particularly useful property for enabling large-scale "real world" applications!

For the onset of my research, therefore, two novel approaches were then followed to arrive at stable organocopper materials. First, in analogy with earlier synthesized dialkylgold-

(III) *N,N*-dialkyldithiocarbamates,[48] we attempted to make the corresponding mono- or dialkyl copper(II) or copper(III) *N,N*-dialkyl dithiocarbamates. In a second approach we studied the synthesis of arylcopper(I) compounds bearing one or two ortho substituents with heteroatoms able to coordinate intramolecularly to the copper (see Scheme 2).

Scheme 2. Two Initially Chosen Approaches of the OCI-TNO Research To Arrive at Stable Organocopper Compounds in 1967
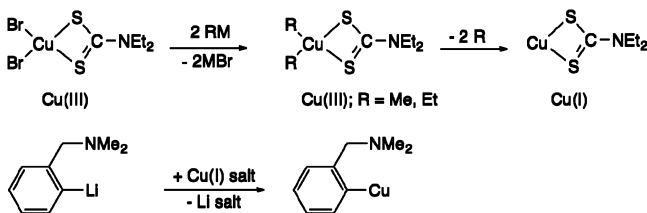
The first approach I had to abandon quickly, because the chance that this would lead to applicable materials was considered low. It appeared that, whereas the reaction was successful, the Cu(III) species formed with R = alkyl rapidly decomposed into the stable copper(I) dithiocarbamate and other products from R. What I missed indeed was the use of a Cd(CF$_3$)$_2$ reagent and a fluorous alkyl group as shown by Willert-Porada et al. in the late 1980s, because that would have resulted in the isolation of the stable diorganocopper(III) compound (CF$_3$)$_2$CuS$_2$CNEt$_2$.[45]

The second approach, based on the use of intramolecular coordination for the stabilization of the copper–carbon bond to form stable organocopper species, appeared in contrast to be extremely successful, however.[29a] It resulted in the synthesis of stable organocopper(I) materials that, moreover, could be produced with acceptable purity and in larger quantities and hence facilitated our biological testing. Even more satisfying was the fundamental research that emerged from this initial exploratory applied research in organocopper chemistry.[37,38,49,50]

In the next few paragraphs the synthesis and structural aspects of organocopper(I) chemistry with emphasis on protocols leading to the directed synthesis of pure organocopper(I) compounds with a well-defined (aggregated) structure will be highlighted. Examples of the in situ generation of organocopper(I) reagents and the directed synthesis of heteroleptic arylcopper aggregates with monoanionic dummy (nontransferable) groupings will also be discussed. Subsequently, the intrinsically different self-assembling properties of R^{Bulky}Cu and R^{L}Cu molecular units, having either large and bulky (R^{Bulky}) or coordinating (R^{L}Cu) substituents, L, in the position(s) ortho to the (aryl)C$_{ipso}$–Cu bond, will be evaluated. Finally, some comments about the novel developments in the field of isolable, high-valent organocopper(II) and -(III) compounds will be discussed.

◼ ORGANOCOPPER(I) COMPOUNDS AND SUPRAMOLECULAR CHEMISTRY WITH RCU^I BUILDING BLOCKS

1. General Synthetic Aspects. The first reports on the attempted syntheses of arylcoppers, from the reaction of a copper(I) halide with either aryl Grignard or lithium reagent, revealed the great tendency of organocopper compounds to form aggregates with all kinds of other metal salts, with

organometallic reagents used in their synthesis, and even with copper halides: i.e., in many instances organocopper materials were obtained from which the desired organocopper(I) could not be separated as a pure product. Contributors to these early studies were the groups of Camus (phenyl- and tolylcoppers),[30] Cairncross (fluoro and fluorous alkyl substituted arylcoppers),[31] Lappert (Me$_3$SiCH$_2$Cu),[33] and myself (arylcoppers with potentially coordinating *o*-amino substituents).[32] In fact, most compounds were obtained in low yields, while the first X-ray crystal structures were the result of selective crystal picking and hence did not necessarily reflect the composition of the bulk material(s). Nevertheless, these structures gave the first insight into the beautiful but complex structural features of organocopper(I) chemistry: for some examples see the various aggregates **1–8** in Schemes 3 and 4.

**Scheme 3. Examples of a Variety of Arylcopper(I) Compounds with R^N Groupings**[a]

1, Cu$_6$R$^N_4$Br$_2$

3, Cu$_4$R$^N_4$

2, Cu$_n$R^N_n

4, Cu$_2$Li$_2$R$^N_4$
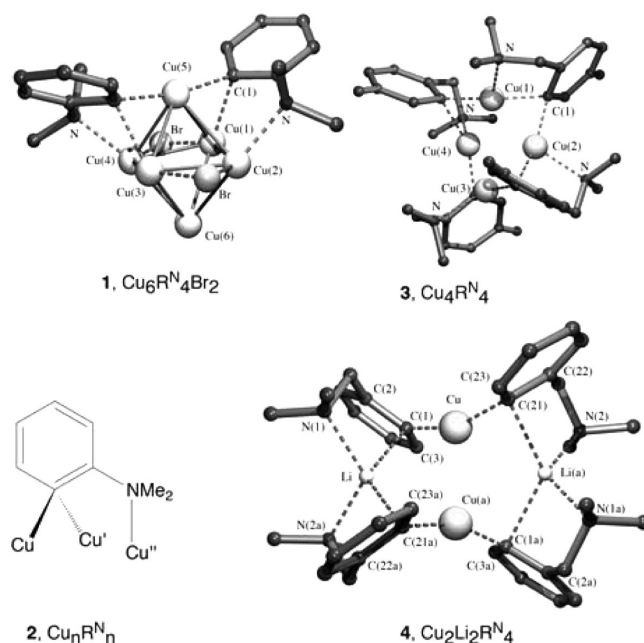
[a]Note that the structure of **1** shows the binding of only two of the four R^N groups. In the schematic structure of **2** Cu′ and Cu″ are the respective copper centers of a second and a third CuR^N unit in the polymeric chain. See ref 37; copyright 2009 by John Wiley & Sons, Inc. Reprinted by permission of John Wiley & Sons, Inc., via the Rightslink service of the CCC.

These initial studies pointed out that the thermal stability of organocopper(I) compounds, RCu, increases in the series R = alkyl (stable at low temperature) < alkenyl ≈ aryl < alkynyl, while the presence of fluorous substituents further improves the thermal stability of the resulting RCu species. A further stabilizing effect arises from the presence of either coordinating substituents L in R, i.e. R^L, that can potentially lead to C,L-chelate binding of the R^L group to copper (cf. Scheme 3) or of sterically bulky ortho substituents in arylcopper compounds R^{Bulky}Cu (vide infra).

These early studies indicated that the synthesis of pure organocopper materials of the type (RCu)$_n$, (R^{Bulky}Cu)$_n$, and (R^{L}Cu)$_n$ required the use of pure, well-defined starting materials (involving both the organometallic reagent and the copper salt) and the use of a solvent with a suitable polarity.

Scheme 4. Several Homoleptic Organocopper Compounds (5−7) and an Example of a Neutral Phenylmagnesium Cuprate (8)[a]
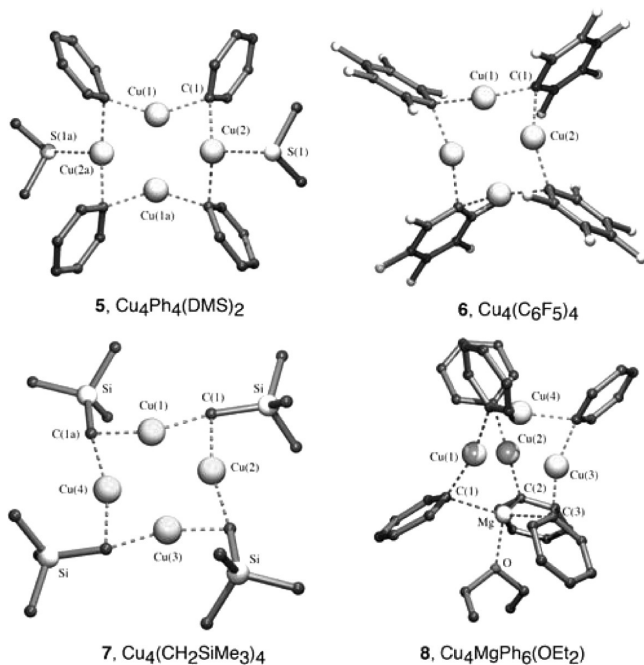
5, Cu₄Ph₄(DMS)₂

6, Cu₄(C₆F₅)₄

7, Cu₄(CH₂SiMe₃)₄

8, Cu₄MgPh₆(OEt₂)

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For me personally, the most fascinating observation was the finding that pure organocoppers $(R^LCu)_n$ could react in a *stoichiometric* fashion with other metal salts MX to yield $(R^LCu)_n(MX_z)_m$ complexes with well-defined values for n and m; see, for example, **1** in Scheme 3 for the formation of $R^N_4Cu_6Br_2$ ($R^N = [2\text{-}Me_2NC_6H_4]^-$) from the reaction of pure R^NCu **2** with CuBr.[51,52] Of course, from the cuprate chemistry it was already known that a 1:2 molar reaction of CuI with, for example, an organolithium reagent affords a very reactive cuprate species with an R_2CuLi stoichiometry (cf. Gilman, Kharasch, House, Whitesides, Corey, and Posner).[53−56] However, that such reactions could be possible between RCu itself and either a copper(I) halide or even another organocopper species had been a real surprise. It is through the use of the C,N-chelating aryl anions R^N that this finding could systematically be studied at a very early stage of our own organocopper chemistry projects.

Indeed at these early stages, the high-yield synthesis of either pure $(RCu)_n$ or pure $(RCu)_n(MX_z)_m$ type species meant that we had started to learn and understand how to manage equilibria existing in reaction mixtures between organometallics and copper salts: in other words, to produce quantitatively the various possible aggregates and thus to steer product formation into the direction of the thermodynamically most stable species, either $(RCu)_n$, $(RCu)_n(MX_z)_m$ (M = e.g. Li, Cu, Mg; X = e.g. halide, CN, SR′, O₂CR) or $(RCu)_n(MR′_z)_m$ (M = e.g., Li, Cu, Au; R = aryl, R′ = alkynyl).[29,37,50]

In summary, these systematic studies revealed that the following aspects are important for a high-yield synthesis of an organocopper(I) material that possesses a well-defined composition and unique structural features.

(a) Quality of the reagents: for both RCu and homocuprates R_2CuLi the organometallic reagents used have to also be well-defined; i.e., a freshly prepared copper(I) halide salt and an organolithium reagent free of its purely organic precursor should be used. The copper(I) source preferentially is copper bromide.[57] Preferably only one type of anion is present in solution. Note that Cu^IOTf can cause valence disproportionation of the newly formed organocopper; for example, catalytic amounts of Cu^IOTf cleanly decompose tetrameric tolylcopper into bitolyl and metallic copper.[58] The reagents should be used in the *correct* stoichiometry.

(b) Order of addition of the reagents: the copper(I) halides are typically insoluble in the commonly used organic solvents. This is not a problem when pure, freshly prepared copper(I) bromide is used. In most cases it is advisable not to use additional ligands for solubilizing the copper bromide, as these ligands may become incorporated in the final aggregated material: see e.g. $Cu_4Mes_4DMS_2$.[34b] Depending on the solubility of the organocopper compound (RCu) and stability of the intermediates two routes can be followed. (i) Addition of the organolithium to the copper(I) bromide slurry forms at the surface of the copper bromide $(RCu)_n(CuBr)_m$ intermediates; these latter materials may thermally be less stable than the corresponding RCu compound. In that case, the alternate way of addition (ii) of the reagent, i.e. addition of the copper bromide slurry to the organolithium solution, is preferred. Here, a *soluble* organocuprate of moderate stability is formed that on further addition of copper bromide is gradually converted into the organocopper RCu. However, in cases where the $(RCu)_n(CuBr)_m$ intermediate is very stable and soluble (e.g., $R^N_4Cu_6Br_2$ (**1**) decomposes at about 200 °C), method i is the preferred way of adding the reagents.[52] For the synthesis of homocuprates R_2CuLi requires (iii) one to mix the right amount of the pure RCu with a stoichiometric amount of the corresponding pure RLi: i.e., the reaction of **3** and $R^N_4Li_4$ affords pure **4** without the need for further purification.[51]

(c) Choice of solvent: the organocopper aggregate and the lithium salt formed can be easily separated in the absence of potentially coordinating substituents in the R anion of RCu. In these cases, both can be easily separated, making use of the different solubility properties of RCu and LiBr products. Ample evidence exists that the structures found for the organocopper species in the solid state is retained in solution.[37] However, in the case of the organocuprate compounds the polarity of the solvent plays a dominant role that often complicates the isolation of discrete complexes. Elegant NMR studies by Boche, Gschwind, et al. demonstrated that in polar solvents also having weakly coordinating properties (e.g., THF), organocuprates R_2CuLi, $RCuLiX$, and R_2CuLi_2X are present in solution as solvent-separated ion pairs (SSIP). In poorly solvating solvents (diethyl ether, benzene) these species are present as contact ion pairs (CIP).[59]

(d) Role of additives: strongly coordinating solvents or the presence of, for example, phosphines (R_3P), dimethyl sulphide, (DMS), or pyridine (py) originating from using XCu(I)−ligand complexes as starting materials can cause deaggregation of the organocopper and formation of an $(RCu)_n(ligand)_m$ end product (see ref 37 for examples).

Obviously, the comments a−d made above deal with the organometallic synthesis aspects with an emphasis on the isolation of pure, well-defined organocopper materials. However, in organic synthesis, rather than preformed organo-

Scheme 5. First Examples of Diorganocyanocuprates (9^{67} and 10^{68}) and a Diorganobromocuprate (11^{69})[a]
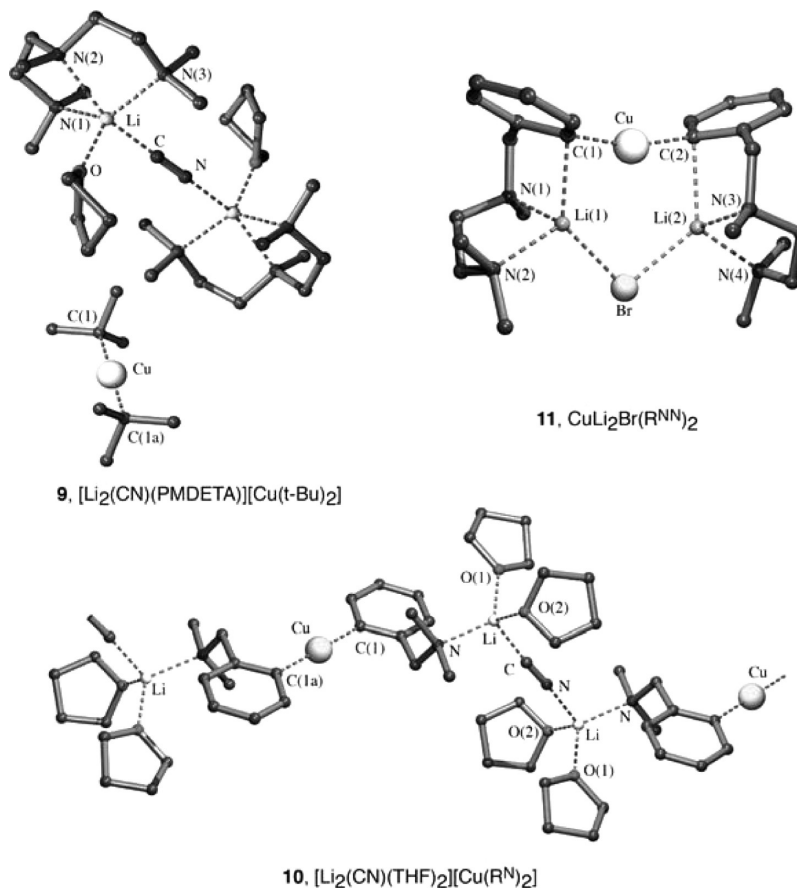
9, [Li$_2$(CN)(PMDETA)][Cu(t-Bu)$_2$]

11, CuLi$_2$Br(R^{NN})$_2$

10, [Li$_2$(CN)(THF)$_2$][Cu(R^N)$_2$]

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copper compounds, in situ generated organocuprate reagents are often used.

2. In Situ Chemistry and Organocopper Species Involved. During the past 40 years, organocuprates have gained the position of privileged reagents in organic synthesis. Numerous important reactions have been discovered, starting with the C−C cross-coupling reactions between organocoppers and organic halides in the 1930s. Since then, numerous other reactions were developed, ranging from the early discovery of 1,4-addition reactions of cuprate type reagents derived from Grignard reagents to α,β-unsaturated ketones, up to the directed ortho cupration reactions, which have become the subject of recent studies.[57,60−62] An important breakthrough has been the notion that the cuprate reagents can be divided into two classes: i.e., the homoleptic Gilman type, R$_4$Cu$_2$Li$_2$ and R$_4$Cu$_2$Li$_2$·2LiX, and the heteroleptic Lipshutz type, R$_2$CuLi·LiCN, lithium cyano cuprate species. An important structural feature of Lipshutz reagents is the presence of a transferable group R and a nontransferable (often called the dummy) CN group. A long debate preceded the classification of these reagents, and in the beginning it primarily was based on the observed difference in reactivity of the in situ formed organocuprate and its relation with the actual molar ratio RLi:CuX that was used for its generation.[63] For the neutral homoleptic lithium cuprates a series of different compounds were already known for a long time, e.g., Ph$_4$Cu$_2$Li$_2$·2Et$_2$O[64] and R$^N_4$Cu$_2$Li$_2$ (**4**)[65] (see Scheme 3), but examples of cuprates having either a RCuLiX or R$_2$CuLi·LiX stoichiometry in which X is the monoanionic dummy ligand, e.g., halide, alkynyl, cyano,

arylthio, amido, or phosphido, were reported much more recently.[37,38] It spurred the debate around the origin of the somewhat higher reactivity of the Lipshutz cyano cuprates that concentrated on a discussion about the role and the binding characteristics of the CN anion in the cuprate species.[66] The structural elucidation (in the solid state) of two cyano cuprates, **9**[67] and **10**,[68] shown in Scheme 5, provided the first answer, as both reveal a [LiCNLi]$^+$ cationic and [RCuR]$^−$ monoanionic arrangement as a common structural feature. Moreover, the structure of the diarylbromocuprate R$^{NN}_2$CuLi$_2$Br (**11**)[69] in the solid state has the cyanide analogue R$^{NN}_2$CuLi$_2$CN, ^{13}C NMR studies of which in solution convincingly showed that the CN anion is bridging between the two Li centers, thus forming a LiCNLi cation and RCuR anion pair;[69] i.e., a SSIP in which the nitrogen atoms can be seen as the solvent molecules (vide infra) and the [Li-(CN)-Li]$^+$ cation is captured in the cavity formed by these four nitrogen atoms.

Interestingly, additional spectroscopic studies of the diorganocyanocuprates confirmed the presence of a homoleptic [R$_2$Cu]$^−$ anionic structure in solution. The review by Davies[38] provides an excellent overview and critical discussion of the various species with RCuLiX and R$_2$CuLi·LiX stoichiometries reported in the literature as well as of the commonly accepted representations of some of these species in solution. The result of computational studies is currently of great importance for the further development of a mechanistic understanding of the reactivity of organocuprate reagents.[42] It must be recalled that the synthesis and isolation of organocopper materials can only provide information about thermodynamically stable aggregates

Scheme 6. Three Examples of Directed Assembly Yielding Neutral Aggregates: A Monoaryltricopper biscarboxylate (12[72]), a Diaryltetracopper bisarenethiolate (13[73]), and a Monoaryltricopper Triphenylphosphine Bis(arenethiolate) (14[73])[a]
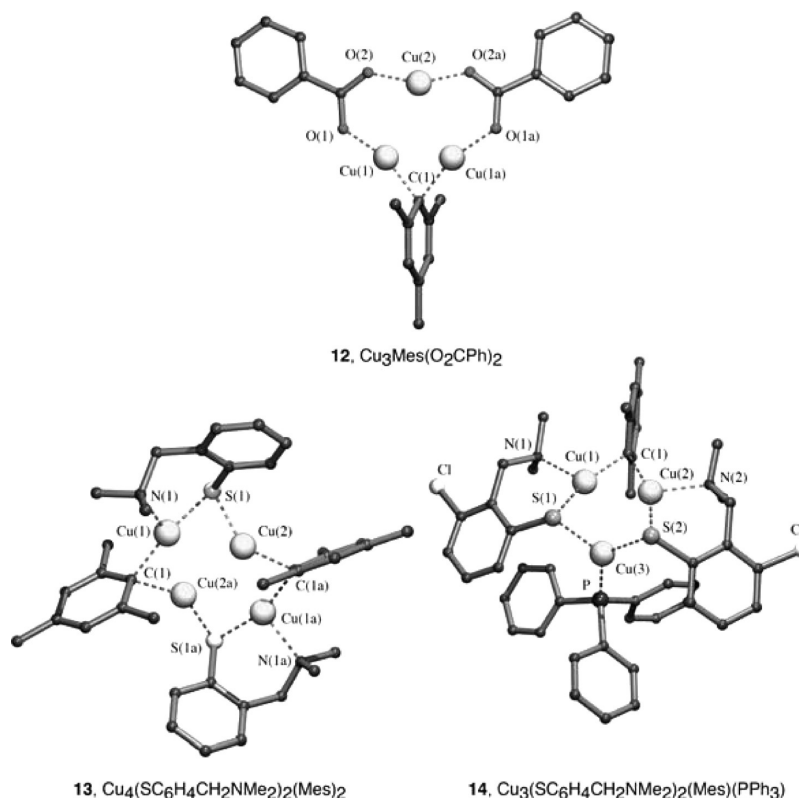
12, $Cu_3Mes(O_2CPh)_2$

13, $Cu_4(SC_6H_4CH_2NMe_2)_2(Mes)_2$ **14**, $Cu_3(SC_6H_4CH_2NMe_2)_2(Mes)(PPh_3)$

and model possible resting states of likely intermediates in organocuprate reactions. Therefore, a recent, fascinating development is the information emerging from novel experiments in which reactions of organocuprates are followed with rapid-injection NMR techniques at low temperature.[44] The first results convincingly demonstrate that key intermediates in the reactions studied are mononuclear organocopper(III) species, from which product formation occurs.[41,44]

RCu[I] Building Blocks and Self-Assembly. Obviously, reviews about the structural aspects of organocopper(I) chemistry comprise a large number of compounds showing an overwhelming degree of structural variety seemingly having no method in it. Many of the compounds have aggregated structures assembled from the various molecular units present in the reaction mixture from which they have been isolated and represent a thermodynamic minimum in this reaction mixture. In most cases these aggregates appear stable on resolution in a suitable solvent. Therefore, the question arises whether any systemization would be possible; it could support any process to arrive at protocols for the selective synthesis of materials and to synthesize structures that can be expected to represent specific resting states in copper-catalyzed organic synthesis (vide supra).

An important reason for the structural variety in organocopper(I) chemistry is the diversity of coordination geometries that can be attained by copper(I). Whereas the diagonal, linear coordination is the dominating geometry, not only in mononuclear but also in polynuclear (aggregated) copper complexes, a series of other geometries, e.g., trigonal, square planar and pyramidal, T-shaped, seesaw, and trigonal

pyramidal, are found in structures of organocopper aggregates in the solid state.[37,38]

In general, single, mononuclear species RCu do not exist either in the solid state or in solution. Only when the R anion provides extreme steric shielding of the copper coordination sphere, as pioneered by Power,[37] has evidence for the mononuclear species $R^{Bulky}Cu$ been found. However, in these structures intramolecular, close-contact interactions are also noted. In general, the neutral RCu unit does interact with ligands, providing the species $RCuL_n$, or they react with electrophiles (metal salts) or organometallic units, including RCu itself, to yield neutral or ionic materials (depending on the polarity of the solvent used). Neutral aggregates $(RCu)_n$ formed by mutual interaction of the RCu units via formation of electron-deficient species (featuring bridging interactions of the R anion between metal centers) lead either to polymeric structures, e.g. **2**, or afford discrete aggregates, e.g. **3**, **6**, and **8**. Aggregates can also result from a selective reaction with a metal salt, e.g. CuBr, affording the $R^N_4Cu_6Br_2$ aggregate (**1**) or result from the reaction with another organometallic unit (cf. $Ph_4Cu_2Li_2·2Et_2O$).[64]

The syntheses of $(RCu)_n(CuX)_m$ (X = dummy anion) aggregates **12−14** are further examples of the directed synthesis of organocopper materials (Scheme 6). The monoaryltricopper biscarboxylate **12** is formed quantitatively in the reaction of Cu_5Mes_5[34] with copper(I) benzoate in the proper molar ratio.[72] Two copper centers in the trinuclear copper core are 2e-3c bridged by a mesityl anion, while the carboxylato groupings are each O,O′-bridge-bonded to a Cu_2 edge. Each of the coppers is diagonally coordinated. Aggregates with structural motifs as found for **12** are possible models for intermediates that can play

a role during either the insertion reaction of CO_2 into Cu−C bonds of arylcopper compounds or the reverse reaction, i.e. the decarboxylation reaction of copper carboxylates to yield organocopper compounds.

The two other structures, **13**[73] and **14**[73] (see Scheme 6), originate from a study in which chiral (at the benzylic center) *o*-amino-substituted arenethiolates have been used as chiral, monoanionic dummy ligands. It resulted in the finding of the first examples[73,74] of, among others, enantioselective 1,4-[73] and 1,6-addition[74] reactions of Grignard reagents to unsaturated ketones, in addition to the regioselective cross-coupling of allylic derivatives with Grignard reagents.[50]

Both arylcopper arenethiolate aggregates were obtained by a selective synthesis route; $Cu_4(SAr)_2Mes_2$ (**13**) was obtained from the interaggregate exchange reaction of the parent arylcopper Cu_5Mes_5 with the copper arenethiolate $Cu_3(SAr)_3$. Most interesting was the observation that on addition of a Lewis base such as PPh_3 to $Cu_4(SAr)_2Mes_2$ deaggregation and reassembling occurs (quantitatively), yielding the three-component aggregate $Cu_3(SAr)_2Mes(PPh_3)$ (**14**) together with Cu_5Mes_5 as a requirement of the reaction stoichiometry. Obviously, it is the ArS-(dummy) anion in combination with the *o*-amino ligand that controls the assembling of the aggregates by a combination of *S*-bridging and *S,N*-chelate binding.

Inspection of the available structural information on arylcoppers indicates that for R groups providing no or little steric constraint near the C_{ipso}−Cu_n bond (n = 1, 2), neutral aggregates are formed in which assembly of the RCu units involves electron-deficient bridge-bonding through the C_{ipso} anion between copper centers. The bonding in these aggregates has the tendency to be asymmetric in nature, thus creating $[RCuR]^−$ anions and $[Cu-L]^+$ cations (L is often a weakly coordinating ligand [DMS] or solvent molecule $[Et_2O]$).[75] Structures that illustrate very nicely this point are the mono-organo cyano- and iodocuprates **15** and **16**, respectively (Scheme 7). The sterically encumbering ortho groups in the respective $R^{Bulky}Cu$ units in **15** and **16** hamper any self-assembly of these units. Alternately, these units assemble with including either a $CNLi(THF)_3$ or a $ILi(OEt_2)_2$ unit, respectively, to yield the thermodynamically stable aggregates **15** and **16**, respectively.[70,71] Of course, on interpretation from a

Scheme 7. Examples of (Aryl)cyanocuprates with Bis-Ortho-Substituted Aryl Groups R^{Bulky}: i.e., Cyanocuprate (15[70]) and Iodocuprate (16[71])[a]
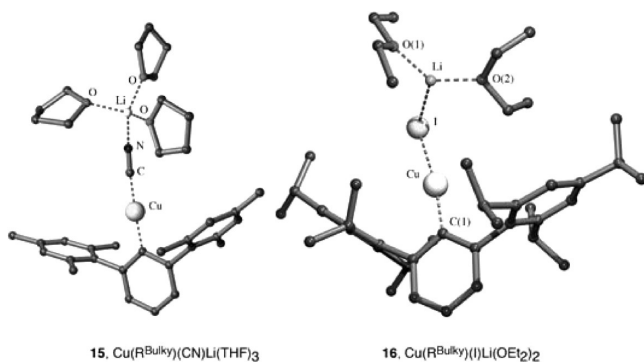
15. $Cu(R^{Bulky})(CN)Li(THF)_3$ **16.** $Cu(R^{Bulky})(I)Li(OEt_2)_2$

[a]See ref 37; copyright 2009 by John Wiley & Sons, Inc. Reprinted by permission of John Wiley & Sons, Inc., via the Rightslink service of the CCC.

binding point of view these structures can be seen as CIPs consisting of a $[R^{Bulky}Cu\text{-}X]^−$ anion and a $[Li\text{-solvent}_2]^+$ cation.

It can be concluded that organocopper(I) compounds $R^{Bulky}Cu$, i.e. compounds having aryl groups bearing bulky substituents at either one or both positions ortho to the C_{ipso}−Cu_n bonding, (self)assemble in processes that are strongly affected by the steric constraints arising from the bulky ortho groupings. The many wonderful examples in various reviews on organocopper and -cuprate species are a testimony of this.[37,38]

In fact and in hindsight, during our studies we have also chosen to influence the assembly process of RCu units but in a different manner, i.e., by using aryl anions, R^L, that have heteroatom-containing substituents, L, that can act as potential coordinating ligands in either one or both ortho position(s). Moreover, instead of choosing for a better match (with Cu(I)) heteroatoms with a "soft" character, we used dimethylamino groups having "hard" donor properties. Consequently, we expected that these amino substituent(s) would complement the primary assembly process through C_{ipso}−Cu_n bonding rather than determine the self-assembly process because of N−Cu coordination. In other words, this weak, additional N−Cu^I coordination would stabilize selected aggregates as the diethyl ether molecules are doing in, e.g., $Ph_4Cu_2Li_2·2Et_2O$ (vide supra) and in the way the four N atoms capture the [Li-(CN)-Li]$^+$ cation in the cyano analogue of aggregate **11** (Br replaced by CN). Finally, as turned out to be the case, these *o*-amino-substituted R^N anions are excellent for matching of a "soft−hard" dimetal combination as is the case, e.g., in $R^N_4Cu_2Li_2$ (**4**). Actually in the latter structure the amino substituents take the place of the ether molecules in $Ph_4Cu_2Li_2·2Et_2O$. Note that the N−Li coordination in **4** renders the C_{ipso} centers in the LiR^NCu unit stereogenic (either *S* or *R* configuration).[37,49,76] This affects the assembly process, providing an enantiomeric pair of one diastereoisomer, either *SSSS* or *RRRR*; the presence of the Me_2NCH_2 renders the assembly process stereoselective (^{13}C and ^7Li NMR and cryoscopy measurements). The use of a chiral (either *S* or *R* configuration) *o*-Me_2NCHMe grouping makes the LiR^NCu unit diastereoisomeric. Again ^{13}C and ^7Li NMR and cryoscopy measurements revealed that the assembly of four of these units to a homodimeric $R^N_4Cu_2Li_2$ occurs with high stereoselectivity (see refs 49 and 76 for a detailed discussion).

To study more systematically the way these *o*-amino ligands in R^N affect the aggregate formation, a series of *o*-amino-substituted aryl anions, comprising monoanionic, bidentate (Ph-CN, Ph-N′ and Vi-CN), tridentate (Ph-CNN, Naph-CNN, and Ph-NCN), or pentadentate (Ph-NNCNN) aryl ligands, were used (see Scheme 8). The corresponding pure aryllithium R^NLi compounds were reacted with copper bromide; the structures in the solid state of the isolated organocopper−copper halide aggregates are shown in Scheme 9. In conclusion, each of these species is the result of a high-yield synthesis process and represents the thermodynamically most stable aggregate in the reaction mixture. The composition of the aggregates is largely influenced by (i) the nature and the number of potentially coordinating substituents and (ii) the spatial orientation of these substituents.

In $Cu_4R^N_4$ (**3**), each of the $Ph\text{-}CH_2N$ anions is C,N-chelate bonded, involving formation of a five-membered chelate ring and thus defining a R^NCu building block; the C_{ipso} anion is electron deficiently (bridge) bonded to two copper(I) atoms, while N−Cu coordination renders each copper three-coordinate. In the case of the Ph-N anion, formation of a less

Scheme 8. Various *o*-Aminoaryl (R^N) Groupings Used in a Systematic Study^a

Ph-CN   **Ph-CN'**   **Ph-NCN**   **Ph-NNCNN**

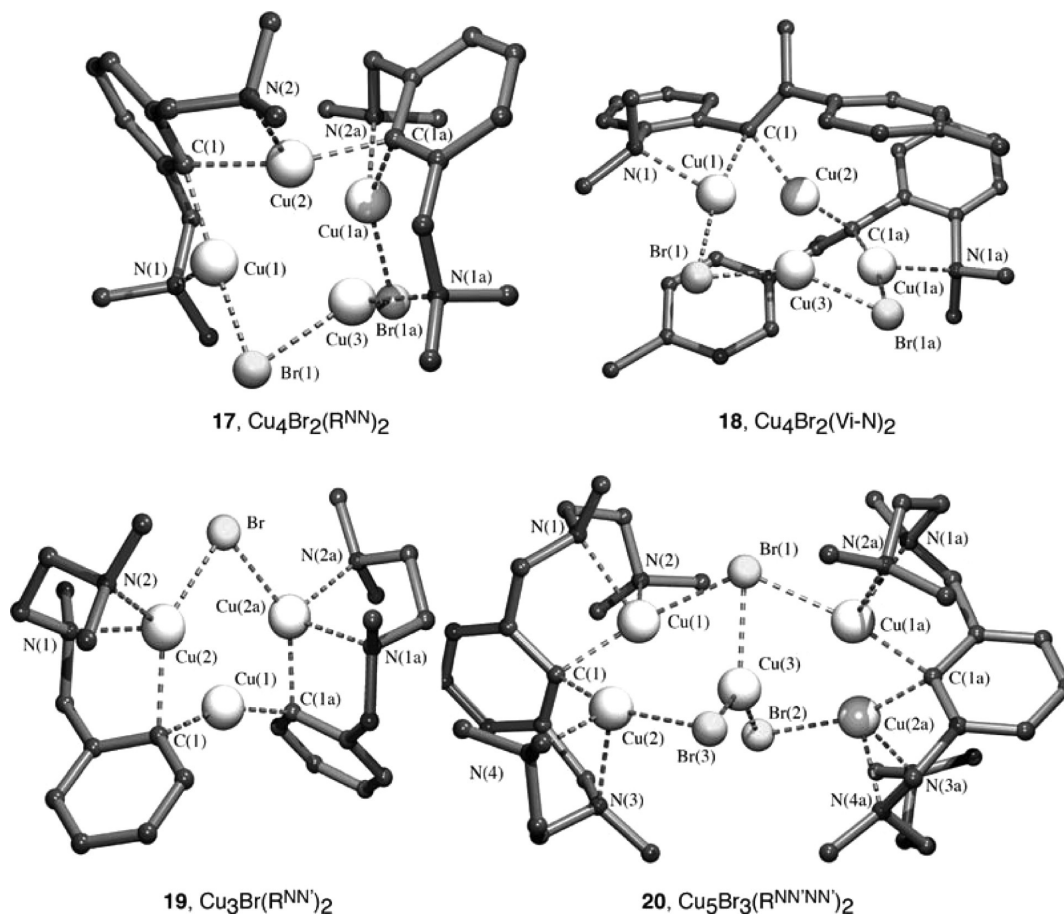**2-Naph-CNN**   **Vi-CN**   **Ph-CNN**
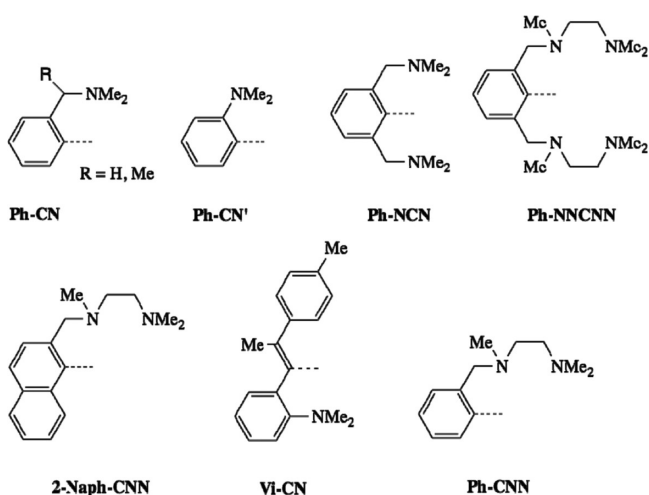
^{a}See Scheme 9 for the respective homo- and heteroleptic aggregates formed as a result of selective self-assembly processes.

favorable four-membered C,N-chelate bonding would have to occur. Instead, in both **1** and **2** coordination of the amino ligand necessarily involves a third Cu atom as well as C$_{ipso}$Cu$_2$

bonding as in **3**, thus defining a C$_{ipso}$Cu$_3$ unit. Apparently, for **2** this results in the formation of a (proposed) polymeric structure (see **2** in Scheme 3) or in self-assembly of an alternate aggregate by including next to four R^{N}Cu another two CuBr units, affording the stable Cu$_6$Br$_2$(R^N)$_4$ aggregate. It is interesting to recall that the Cu$_6$Br$_2$(R^N)$_4$ (**1**) aggregate is more stable than the parent organocopper **2**. The reaction of LiC$_6$H$_4$NMe$_2$-2 with CuBr in a 1:1 molar ratio in diethyl ether provides quantitatively soluble **1** (i.e., leaving still unreacted LiC$_6$H$_4$NMe$_2$-2); continued reaction in benzene is required to convert the R$_4$Cu$_6$Br$_2$ aggregate quantitatively into pure, insoluble (RCu)$_n$ (**2**). Interestingly, the two apical copper atoms of Cu$_6$Br$_2$(R^N)$_4$ are diagonally coordinated (taking the electron-deficient bridge bonding of the C$_6$H$_4$NMe$_2$-2 anion into account^{51}). Consequently, as the stability of the diagonal coordination increases down the series of the coinage metals, this allows the selective synthesis of the corresponding R$_4$M$_2$Cu$_6$Br$_2$ aggregates (M = Au(I), Ag(I)) having either the Au or Ag atoms specifically positioned at the two apical positions. Spectroscopic studies pointed to the stability of the [R$^L_4$Cu$_6$]$^{2+}$ core of **1**; i.e., the two Br anions can be substituted by alkynyl anions with retention of the core structure, leading to the formation of R$^N_4$Cu$_6$(alkynyl)$_2$. The latter heteroleptic (aryl)(alkynyl)copper aggregate is also accessible by reacting pure (RCu)$_n$ (**2**) and the respective Cu(alkynyl) compound in an equimolar ratio.^{77}

Scheme 9. Depending on the Number and Nature of the *o*-Amino Substituent, Different Self-Assembled Arylcopper–Copper Bromide Aggregates Are Obtained^a

17, Cu$_4$Br$_2$(R^{NN})$_2$ **18, Cu$_4$Br$_2$(Vi-N)$_2$**

19, Cu$_3$Br(R$^{NN'}$)$_2$ **20, Cu$_5$Br$_3$(R$^{NN'NN'}$)$_2$**

^{a}See ref 37; copyright 2009 by John Wiley & Sons, Inc. Reprinted by permission of John Wiley & Sons, Inc., via the Rightslink service of the CCC.

Scheme 10. Mononuclear High-Valent Organocopper(II) and -(III) Compounds[a]
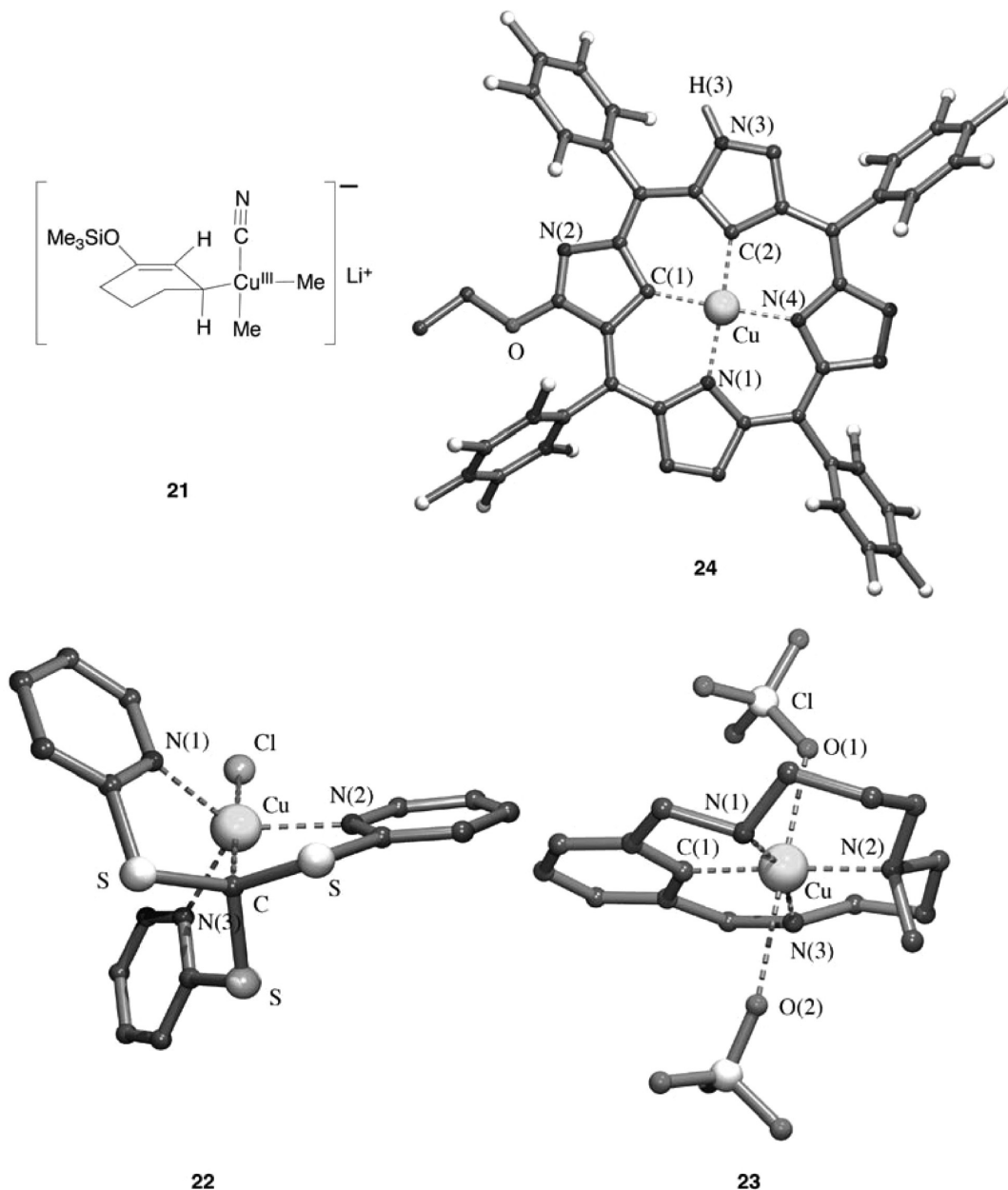
[a]See ref 37; copyright 2009 by John Wiley & Sons, Inc. Reprinted by permission of John Wiley & Sons, Inc., via the Rightslink service of the CCC.

Apparently, self-assembly of the specific R^NCu units with R^N = Vi-CN, Ph-NCN, Ph-CNN, Ph-NNCNN to neutral homoaggregates $(R^NCu)_n$ is not occurring. Instead, during the reaction of the corresponding R^NLi reagent with CuBr specific self-assembly of $(R^NCu)_n$ with unreacted CuBr occurs. Obviously, the formation of $(R^NCu)_n(CuBr)_m$ aggregates with a distinct composition is energetically more favorable, as is observed in the case of aggregates **17–20** (see Scheme 9).

The Vi-CN ligand in $Cu_4Br_2(R^N)_2$ compound **18**, shown in Scheme 9, is η^2-C,N-bonded (five-membered chelate ring), thus creating a R^NCu_2 building block. Alternately, the structure can be seen as consisting of two diagonally coordinated $[(R^N)_2Cu]^-$ and $[Br_2Cu]^-$ anions kept together by $[Cu-N]^+$ cations.[78] It is interesting to note that in a fashion similar to the formation of the heteroleptic (aryl)(alkynyl)copper aggregate derived from **1** (vide supra), the two Br anions in **17** likewise can be

substituted; in this case for two $2\text{-Me}_2\text{NC}_6\text{H}_4$ anions (=Ar) to the effect that a stable $Cu_4(R^{NN'})_2Ar_2$ heteroleptic aggregate is formed with retention of the $[Cu_4(R^{NN'})_2]^{2+}$ core.[79]

The triangular arrangement of the three copper atoms in aggregate **19** comprises a $[Cu(R^{NN'})_2]^-$ anionic building block to the effect that the two o-diamino ligands together form a N_4 cavity capturing a $[Cu_2Br]^+$ cation, a situation that is very similar to the structural features of the diorganobromocuprate **11** (cf. Scheme 5) discussed above.[80] When the same reaction was carried out with 2-Naph-CNN, an aggregate with $Cu_4Br_2(R^{NN'})_2$ stoichiometry was isolated; i.e., the N_4 cavity has become enlarged because of the steric requirements of the larger 2-Naph groups in the $[Cu(R^{NN'})_2]^-$ anion. As a result of this situation, this effect is balanced by incorporation of a larger $[Cu_3Br_2]^+$ cation; i.e., during the self-assembly process an extra CuBr equivalent becomes incorporated in the $[Cu_{n+1}Br_n]^+$

cation in comparison with the formation of **19**. The self-assembly process to these trinuclear copper aggregates has been studied in greater detail: during the self-assembly process both benzylic NMe centers become stereogenic. This induction of chirotopicity on self-assembly is not restricted to these NMe centers but simultaneously also renders both C_{ipso} centers stereogenic.[80]

Finally, it is interesting to compare the different effects that the R^NCu units (R^N is either Ph-NCN or Ph-NNCNN) have on the self-assembly process of the R^NCu fragments with CuBr. These reactions result in the formation of the unique self-assembled aggregates **17** and **20**, respectively, with either $Cu_4Br_2(R^{NN})_2$[81] or $Cu_5Br_3(R^{NN'/NN'})_2$[82] stoichiometry. Obviously, conversion of the monodentate o-amino substituent into a bidentate diamino one creates the two $[(R^{NN'/NN'})Cu_2]^+$ cations present in **20**. In these dinuclear copper units, the C_{ipso} atom is bridging two coppers, while each of these copper centers is C,N,N'-chelate coordinated by the N,N' o-diamino substituents. These two $[R^{NN'/NN'}Cu_2]^+$ cations then combine with a central $[CuBr_3]^{2-}$ dianion to provide the neutral $(R^{NN'/NN'})_2Cu_5Br_3$ aggregate.

It is obvious from the few known examples that R^{Bulky}- and R^L-type aryl anions have different but complementary influences on the self-assembly properties of the resulting RCu^I molecular units. In general, the use of R^{Bulky} groups restricts interactions with metal salts and external ligands, resulting in aggregates with smaller size, whereas R^L groups tend to regulate the self-assembly process. By including in this process Lewis acidic metal salts and organometallic reagents, this leads to organocopper(I) materials in high yield and with high selectivity. Most importantly, the majority of the organocopper materials with R^{Bulky}- and R^L-type aryl anions, discussed above, show improved thermal stability (as compared with phenylcopper itself), while many of the materials derived from R^NCu molecular units display superior stability toward decomposition with oxygen or water.

MONONUCLEAR ORGANOCOPPER(II) AND COPPER(III) COMPLEXES

For decades organocopper(II) and -(III) remained elusive species. However, in 1989 $(CF_3)_2CuS_2CNEt_2$ was isolated and characterized (vide infra) as the first example of an organocopper(III) species.[45] Later homoleptic tetra-organocuprate(III) anions were reported: i.e., a $[Cu(CF_3)_4]^-$ anion with a bulky PNP cation.[83] In the meantime mechanistic studies of copper-catalyzed and -mediated reactions showed direct evidence that organocopper(III) intermediates were playing a crucial role in the product-forming step of many of these reactions. These conclusions received further credence by the results of in silico experiments spurred by the ever-increasing power of computational methods. Compelling evidence for the existence of organocopper(III) intermediates in synthetic organic protocols involving organocopper and -cuprate reagents were thereafter obtained. Finally, by using ^{13}C-labeled CN-lithium salts and ^{13}C NMR, Bertz[84] and, independently, Gschwind proved the existence of the square-planar $[Me_3Cu(CN)]^-$ anion in solution.[85] In the presence of coordinating ligands (PPh$_3$, amines, etc.), neutral triorganocopper(III) complexes, e.g., $Cu^{III}EtMe_2L$, were also observed.[84] (Note that compounds with either d^{10} Cu(I) or (square planar) d^8 Cu(III) are diamagnetic species and hence observable by NMR). Recently, the intermediacy of the

trialkylcopper species **21** (see Scheme 10) in the reaction of $[CuMe_2Li\cdot Li^{13}CN]$ with 2-cyclohexenone in the presence of SiMe$_3$Cl was established by making use of rapid-injection NMR spectroscopy.[44]

To finish, three examples of one alkylcopper(II) and two arylcopper(III) compounds are presented in Scheme 10. The copper(II) compound **22** has a trigonal-bipyramidal structure with one chloride and a σ-bonded alkyl grouping in the respective apical positions.[86] The two arylcopper(III) compounds **23** and **24** contain a four-coordinate copper(III) center that is σ-bonded to the aryl grouping and to three N ligands; all four ligands are arranged in a square-planar geometry. Compound **23**[87] is a dication with the two ClO$_4$ anions arranged along the axis perpendicular to the coordination plane and featuring rather long $Cu\cdots O(ClO_3)$ distances. In **24**, the copper is σ-bonded to the C anion that is part of a doubly confused porphyrin ring.[88]

CONCLUSIONS

In this personal account, my primary focus has been on a discussion of the selective synthesis and structural features of arylcopper(I) materials (R^NCu) bearing in one or both ortho position(s) a potentially coordinating amino substituent. What not has been discussed in detail thus far is that, to gain access to these arylcopper(I) compounds in reasonably pure form, we had to develop, in parallel, methods to arrive at the corresponding, pure aryllithium compounds R^NLi, as these materials represent our most commonly used starting materials.[89] It was extremely rewarding that the structural features of these R^NLi compounds were as fascinating as those of the R^NCu compounds: indeed, the self-assembly properties of the R^NLi compounds have many characteristics in common with those encountered for the homo- and heteroleptic R^NCu compounds but also showed distinct differences. These contrasting elements are due to the polar Li–C vs the more covalent Cu–C bonding, the differences in the M–N bond strengths, and the difference in size of the respective Cu(I) and Li cations.[89] From an applied organometallic point of view, it was an important consequence that, in comparison with phenylcopper itself, the thermal stability of the R^NCu compounds was increased by at least 100 °C. This higher kinetic and thermal stability of the R^NCu compounds may arise from the fact that all rotamers (i.e., rotation of the aryl group along the C_{para}–C_{ipso} axis) of the 2e-3c binding in an (Aryl)CuM (M = e.g. Cu, Li) unit do not have the same stability; rotamers having the aryl ring plane perpendicularly orientated to the CuM vector will be more stable, because in these latter rotamers the interaction of the ortho groupings with the bridged metal atom unit will be minimal. In these rotamers, the σ-type C_{ipso}–CuM interaction can be complemented by increased participation of the aryl π electron density with an antibonding combination of orbitals of the CuM unit.[37] The resulting difference in rotamer stability is also the origin of the induction of chirotopicity on self-assembly of the R^NCu units because of the stereogenity (S or R configuration) of C_{ipso}. The fact that the o-amino substituents contained prochiral (e.g., CH$_2$ and NMe$_2$ when coordinated) or even chiral groupings (CHMe-N) facilitated detailed studies of these aspects for the various compounds in solution by NMR.[37,49,76,80]

The intrinsic instability of organocoppers is most probably associated with the redox properties of copper in addition to the stability of the R radical. In the case of Cu^I it is the diagonal, linear coordination that thermodynamically is, by far, the most

stable configuration. The organocuprate(III) species detected at low temperature (<100 °C) are mononuclear copper compounds having a square-planar copper center.[44,84] Well-defined and thermally stable aryl-Cu[III] species are likewise mononuclear, square-planar copper species. The stabilization of the σ-(aryl)C$_{ipso}$−copper(III) bond arises from three additional Cu−N interactions from amino-N atoms as present in, for example, the triaazaalkanediyl tether spanning the ortho positions of the aryl-Cu[III] unit (cf. **23**,[87] Scheme 10). In other words, the resulting macrocyclic ligand system provides the rigid C,N,N′,N-ligand environment required to ensure a stable d^8-Cu[III] electronic configuration. Other examples, providing rigid environments and thus stable σ-arylcopper(III) species, are the doubly confused porphyrin ring system used to make **24**[88] (Scheme 10). Disturbance of this configuration by attack of the Cu[III] center by a fifth ligand (i.e., a nucleophile) induces the occurrence of reductive elimination processes, leading to C−X bond formation[90,92] (i.e., in the case of **23** to C$_{ipso}$−N bond formation).[90] Likewise, the azacalix[1]arene[3]-pyridine macrocycle can stabilize the σ-C$_{ipso}$−Cu bond,[91] and this observation provides convincing evidence that, following this approach, inclusion of the σ-C$_{ipso}$−Cu[III] bond in a rigid, planar coordination environment can lead to the discovery of many more stable arylcopper(III) species that formerly were considered elusive. A similar approach, that is to say one involving the choice for a ligand which allows for the synthesis of a σ-C$_{ipso}$−Cu bond and, moreover, ensuring a rigid coordination environment, thus stabilizing this time a trigonal-bipyramidal, d^9-Cu[II] electronic configuration, afforded the well-defined organocopper(II) species **22** (Scheme 10).[87] In this context, it is interesting to note that the monoanionic Ph-NCN "pincer" ligand shown in Scheme 8 has a NC$_{ipso}$N arrangement similar to that present in both **23** and **24**. The use of Ph-NCN allowed for the synthesis of the corresponding (rare at the time) organo-Ni(III) compounds. These NCN-pincer-d^7-Ni[III] compounds have a low Ni[II]/Ni[III] redox potential[93,94] and could be a further inspiration to make the (aryl)-d^8-Cu[III] compounds: e.g. by proper choice of the amino substituents in Cu$_4$Br$_2$(R^{NN})$_2$ (**18**).[81]

Finally, the stable organocopper(II) and -(III) compounds are the direct result of a selective C−H activation process starting from the corresponding arene compound interacting with the appropriate copper salt. The reactivity of the Cu[III] compounds is currently undergoing extensive study aimed at increasing our mechanistic understanding of copper-catalyzed C−C and C−X bond forming processes using the stable arylcopper(III) compounds as models.[90,92]

The starting point of my travel was the need to find a novel source for the slow release of copper in natural waters (vide supra). In fact, we succeeded in making stable compounds and indeed could test these in a variety of applications.[95] No one could have anticipated that this direction of organometallic chemistry would lead to the present diversity and richness of compounds as well as provide deep insights into the mechanistic aspects of copper-catalyzed organic synthetic processes and the fact that next to organocopper(I) are novel organocopper(II) and -(III) compounds, which are no longer elusive. This situation will invariably create opportunities for studying the application of these compounds, not only in organic synthesis but also as important components in functional materials.

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Notes

The authors declare no competing financial interest.

Biography

Gerard van Koten (born 1942) is a Distinguished University Professor of the Utrecht University and Honorary Distinguished Professor (2011−) at Cardiff University U.K. He is well-known for his fundamental and applied organometallic research comprising organo-copper and XCX-pincer metal complexes. The preparation and use of the first examples of homogeneous metallodendrimer catalysts demonstrate his interest for supramolecular systems with (organo-metallic) catalytically active functionalities. He is a member of the Royal Netherlands Academy of Arts and Sciences and the governmental Foresight Group Chemistry that is responsible for the coordination and initiation of innovation in Industry and Academia in The Netherlands. During the period 2002−2012 he was Chairman of the Governmental committee that is responsible for the renewal of the Chemistry Educational Program at the preuniversity level.

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