1
Structures and Reactivities of Organocopper Compounds

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1.1
Introduction

1.1.1
Historical Perspective

The first attempts to prepare organocopper compounds date back to 1859, when the reaction between diethylzinc and CuCl was studied. That resulted in the formation of metallic mirrors [1], however, and it was therefore concluded that it was impossible to bind an organic group to copper. More than 60 years later, the isolation of phenylcopper, although still impure, from the reaction between a phenyl Grignard reagent and CuI was reported by Reich. This result should be regarded as the start of organocopper chemistry [2]. Pioneering work by Gilman in 1936 demonstrated the applicability of organocopper reagents in synthetic organic chemistry [3]. The observation that catalytic amounts of copper halides favored 1,4-addition over the more usually observed 1,2-addition in the reaction between Grignard reagents and \( \alpha,\beta \)-unsaturated ketones [4] (see Scheme 1.1) was of crucial importance for the further development of organocopper reagents as synthetic tools in organic chemistry.

The discovery of the Gilman cuprate Me₂CuLi [5–8], and House’s [6, 7] and Corey’s [8] demonstrations of its synthetic potential, produced a major breakthrough in this area of chemistry. A major disadvantage of the application of this type of cuprate reagents in stoichiometric amounts, especially from the point of view of ‘atom economy’, is the fact that one equivalent of the (potentially valuable) organic component is usually not used in the reaction and ends up as chemical
waste. This was already recognized at an early stage of this chemistry and was addressed by Posner et al. [9], who introduced the concept of cuprate reagents in which one of the groups is nontransferable. One example of such a nontransferable group is the PhS⁻ anion, introduced into the reaction mixture as CuSPh. Much later, this idea was to find application in the enantioselective 1,4-addition of Grignard reagents to \( z, \beta \)-unsaturated ketones, using catalytic amounts of the highly soluble amino-arenethiolates, possessing amine functionalities available for coordination to the magnesium or lithium cations in the cuprate reagents. In the case of an enantiopure amino-arenethiolate, the chiral thiolate anion both acts as the nontransferable group and induces enantioselectivity [10]. The development of the so-called higher-order cyanocuprates \([\text{CuLi}_2\text{R}_2(\text{CN})]\) by Lipshutz et al. also contributed much to the synthetic applicability of organocupper reagents in organic synthesis [11–13].

Nowadays, organocuprates are among the most frequently used reagents in synthetic organic chemistry. These reagents are usually prepared in situ, and it is only in the last decade that systematic studies – still ongoing – have begun to be carried out, using NMR, X-ray crystal structure determination, and computational methods to provide better insight into the actual mechanisms and species that play a role in these transformations.

Pioneering work directed towards the isolation and structural characterization of organocopper compounds began in the late 1960s and early 1970s. Important contributors to this field were (i) Cairncross and co-workers: \([\text{Cu}(\text{C}_6\text{F}_5)]\) and \([\text{Cu}(\text{C}_6\text{H}_4\text{CF}_3-3)]\) [14, 15], (ii) Camus: 2-, 3- and 4-tolycopper [16], (iii) Lappert: \([\text{CuCH}_2\text{SiMe}_3]_4\) [17], (iv) van Koten and co-workers, who introduced the concept of stabilization by intramolecular coordination in, for example, \([\text{Cu}(\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)_4]\) and other functionally substituted arylcopper compounds [18, 19], and (v) Power et al., on the topic of unsubstituted arylcopper compounds [20]. It was already being proposed at an early stage, on the basis of molecular weight determinations, that organocopper compounds exist as aggregated species. This was confirmed by the X-ray crystal structure determinations of \([\text{Cu}(\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2-\text{Me}-5)]_4\) [21], (see Fig. 1.1A) and \([\text{CuCH}_2\text{SiMe}_3]_4\) [17], (see Fig. 1.1B).

The overall structure of \([\text{Cu}(\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2-\text{Me}-5)]_4\) comprises four copper atoms in a butterfly arrangement. The short Cu–Cu distances (average 2.38 Å) are notable, being even shorter than those observed in metallic copper (2.56 Å). Another central structural feature is the bridge-bonding of the aryl groups to two copper atoms, involving electron-deficient, three-center, two-electron bonds. In those days, such bonding modes were only known from organoaluminium and boron chemistry [22], but since then it has become established as a common type of bonding in organocopper chemistry. Finally, each of the nitrogen atom-containing substituents is coordinated to one of the copper atoms, giving rise to three-coordinate copper. As a consequence of the rather small bite angle of the C–N bidentate monoanionic ligand, the coordination geometry around each copper atom is rather distorted and can best be described as intermediate between trigonal and T-shaped (vide infra). Similar structural features were found for \([\text{CuCH}_2\text{SiMe}_3]_4\). The trimethylsilylmethyl groups are bridge-bonded between two
adjacent copper atoms, but the copper atoms are digonally coordinated as a consequence of the lack of potential coordinating substituents.

More recently, structural studies have been increasingly directed towards better understanding of the mechanisms that play a role in copper-mediated reactions and towards the actual organocopper species involved. In particular, X-ray structural investigations of pure compounds, in combination with solution studies (NMR, IR), have contributed much to the understanding of the nature of bonding in aggregated organocopper species. With respect to the reactivity of such species, however, it should be noted that the crystallization of organocopper species out of frequently complicated reaction mixtures is governed mainly by thermodynamic parameters, and so it is often the less reactive species (resting-state species) that crystallize from solution. Elucidation of solution structures in conjunction with investigation into structure-activity relationships is therefore of prime importance. Modern multinuclear NMR spectroscopic techniques [23, 24], XAFS [25, 26], in situ XAFS [27], and computational methods [28] all represent powerful tools for such investigations.

To date, hundreds of organocopper species have been isolated and characterized. It is beyond the scope of this chapter to discuss the synthesis and structural characterization of these compounds in detail [29]. Here, general structural features, especially those associated with the reactivity of organocopper compounds, are discussed and illustrated by representative examples.

1.1.2 The Oxidation States of Copper

In the periodic table of the elements, copper is listed in group 11, together with silver and gold. Copper, as a late transition element, occurs in a range of oxidation states (Cu(0), Cu(I), Cu(II), Cu(III), and Cu(IV)), and the ions readily form complexes yielding a variety of coordination compounds. Oxidation states I, II, and III
are the most common; copper(0) and copper(IV) species are extremely rare. Cu(0)
species—such as monomeric \([\text{Cu(CO)}_3]\) and dimeric \([\text{CuCu(CO)}_3]\)—have only
been observed with the aid of matrix isolation techniques [30], while Cu(IV) only
exists in compounds with extremely electronegative ligands, such as Cs2[CuF6] [31].

In inorganic and coordination chemistry, the Cu(II) state is the most abundant
one, and is regarded as more stable than the Cu(I) state under normal conditions
[32]. Although numerous examples of Cu(I) coordination complexes are known,
their chemistry is rather limited and they are readily oxidized to Cu(II) species
[32]. Of the common oxidation states, compounds derived from copper(III) are
rare, with only 30–40 reported examples [32]. Despite the small number of isolated
Cu(III) compounds, however, organocopper(III) species have been proposed as im-
portant intermediates in copper-mediated organic reactions (Chaps. 4 and 10).

To date, the organometallic chemistry of copper, in terms of isolation and structural
characterization of compounds, is essentially limited to the Cu(I) oxidation
state. Only a very few examples of other oxidation states are known. The older lit-
erature offers a reported synthetic procedure for the synthesis of bis(aryl)copper(II)
compounds [33, 34] (see Scheme 1.2), but this result has never been reproduced by
others.

\[
\text{R} - \text{Cu}^{0} \text{Hg} \rightarrow \text{R} \text{Cu}^{0} \text{Hg}
\]

\( R = \text{Me}, \text{OMe}, \text{NH}_2 \)

Scheme 1.2.

The intrinsic instability of organocopper(II) compounds is most probably asso-
ciated with the redox properties of copper. Decomposition of organocopper(II)
compounds can occur by two different routes: (i) formation of an organocopper(I)
compound and an organic radical \( R' \) that can undergo further reactions, which
formally represents a one-electron reduction process, and (ii) direct formation of
\( R' \rightarrow \text{Cu}(0) \), which is formally a two-electron reduction process (reductive
elimination; cf. Eqns. 1 and 2 in Scheme 1.3).

\[
\text{R} \rightarrow \text{Cu}^{I} \text{R} \rightarrow \text{R} \rightarrow \text{Cu}^{I} \quad \text{(1)}
\]

\[
\text{R} \rightarrow \text{Cu}^{I} \text{R} \rightarrow \text{R} + \text{Cu}^{0} \quad \text{(2)}
\]

Scheme 1.3.

It is well established that copper in its divalent oxidation state should be regarded
as a strong oxidizing agent, used, for example, to oxidize arylcopper(I) compounds
to give the symmetric biaryls [35]. Moreover, it also has to be taken into account
that organolithium and organomagnesium compounds, common starting mate-
rials for the synthesis of organocopper compounds, can easily undergo one-
electron oxidation reactions. Consequently, a primary step in the reaction between
organolithium compounds and Cu(II) salts is reduction to Cu(I), with concomi-
tant oxidation of the organic ligands to be transferred (see Scheme 1.4).
The Cu$^{+}$ thus produced undergoes the usual transmetalation reaction with the organolithium compound to give an organocopper(I) species. At this stage, though, further complications may arise because the organocopper(I) compound can also be oxidized by Cu$^{2+}$. This reaction sequence has important implications from a synthetic point of view. If copper(II) salts are used as starting material for the synthesis of organocopper compounds, the yield can never exceed 50%, with considerable amounts (also 50%) of organic side-products also being formed and hampering the isolation and purification of the target organocopper compound.

On the other hand, an elegant synthetic pathway to macrocyclic molecules has been developed by taking advantage of these oxidizing properties of Cu$^{2+}$, affording these in quantitative yields (see Scheme 1.5) [36].

Since isolable organocopper(II) compounds do not apparently exist, it is rather surprising that oxidation of the cuprate CdI$^+$/[Cu(I)]$_2$ (prepared in situ) with thiuram disulfide affords (CF$_3$)$_2$CuI$_2$S$_2$CNET$_2$ (see Eqn. 1 in Scheme 1.6), the first and so far only example of an organocopper compound with the copper atom in the trivalent oxidation state. The structure of this compound was unambiguously proven by an X-ray crystal structure determination (see Fig. 1.2) [37].

Another approach to the same compound involves treatment of Br$_2$CuI$_2$S$_2$CNET$_2$ with a mixture of Cd(CF$_3$)$_2$ and CF$_3$CdI (see Eqn. 2 in Scheme 1.6) [37]. In
this respect, it is interesting to note that treatment of \( \text{Br}_2\text{Cu}^{\text{III}}\text{S}_2\text{CNEt}_2 \) with alkyl- or aryl-Grignard or -lithium reagents invariably results in reductive elimination of the organocopper(III) intermediate (most probably) formed in situ, to furnish the coupling product \( R_a\overline{R} \) and a stable copper(I) dithiocarbamate (see Eqn. 3 in Scheme 1.6). Most probably, stabilization of the organocopper compound in its trivalent oxidation state is a consequence of the strongly electron-withdrawing properties of the CF₃ groups.

1.1.3 Thermal Stability and Bonding in Organocopper(I) Compounds

Earlier structural investigations into organocopper compounds were hampered by the intrinsic thermal instability of these compounds. Simple alkylcopper compounds decompose below 0 °C; methylcopper in the dry state explodes at temperatures above –15 °C. It is well established that the thermal stability of organocopper compounds increases in the order alkyl < aryl < alkenyl < alkynyl [29]. Attempts to increase the thermal stability of organocopper(I) compounds have included (i) substitution of hydrogen atoms by fluorine in the organic moiety, (ii) addition of external ligands such as phosphines and amines, and (iii) the presence of intramolecular coordinating substituents. An additional problem is the fact that trace amounts of impurities such as colloidal copper considerably reduce the decomposition temperature of organocopper compounds, most probably as a result of autocatalytic decomposition. It has been established that the decomposition of simple alkylcopper compounds and the corresponding phosphine complexes proceeds through a \( \beta \)-hydrogen elimination process [38]. It is therefore not surprising that the first well characterized alkylcopper(I) compound, \( \text{Cu}_4(\text{CH}_2\text{SiMe}_3)_4 \) [17, 39], features an organic moiety with no \( \beta \)-hydrogen atoms.

As a consequence of its electronic configuration, a variety of coordination numbers and geometries have been observed for copper(I) compounds, especially for inorganic representatives (see Fig. 1.3) [32]. In the organometallic chemistry of copper, the linear and trigonal coordination geometries in particular, though distorted towards T-shaped, are frequently encountered.

Today, there is ample evidence that organocopper compounds are usually highly
aggregated species. Simple $\eta^1$-bonding between copper(I) and a carbon ligand has not so far been documented, while coordination saturation at the copper(I) atom by external or internal donor molecules is rare. Most organocopper compounds, especially arylcopper compounds, are aggregated by means of electron-deficient, two-electron, three-center bonding, or in other words, through bridging organic groups (Fig. 1.4).

The lowest MO is a bonding combination of the filled sp$^2$–C(1) orbital with mutually bonding orbitals on the two copper atoms (see Fig. 1.4A). A higher-energy MO results from a combination of a $\pi$–C(1) orbital with an antibonding combination of copper orbitals (Fig. 1.4B). Back-donation from the copper atoms to the aryl bridging ligand occurs through overlap of filled antibonding orbitals of the copper atoms to a $\pi^*$–C(1) orbital (Fig. 1.4C). The contribution of the second MO to Cu–C bonding increases the electron density at C(1) and thus the kinetic stability of the Cu–C bond.

This simplified view can explain stability trends and differences between various organocopper(I) compounds, as well as the influence of bulky or coordinating substituents ortho to the copper-carbon bond on the stability of arylcopper compounds. This interpretation of the copper-carbon bond can also be applied to the binding of sp$^1$ (alkyl: e.g., CH$_2$SiMe$_3$), sp (C= C– R) [40], and other sp$^2$ (vinyl) groups [41, 42].

Recent theoretical developments such as DFT methods, can of course provide more advanced and precise understanding of these interactions. Hence, Nakamura et al. have recently used computational methods to explain and forecast structure-reactivity relationships in organocopper reagents (Chapt. 10) [28, 43].
1.2
Homoleptic Organocopper Compounds Cu₄R₄

In the early days of organocopper chemistry, synthesis and structural characterization of pure organocopper compounds were hampered by several factors. One of the problems was the tendency of organocopper compounds to associate with metal halides (even copper halides itself) to form highly aggregated species. Therefore, products containing both the organocopper compound and metal halides were regarded as impure, although they were in fact pure compounds in which metal halides constituted an integral part of the complex. Definite proof for this view was obtained as early as 1975 [44].

On the basis of this information, techniques for the synthesis of pure copper compounds were developed. The following parameters played an important role:

1. purity and nature of the starting materials,
2. the reaction temperature,
3. the nature of the solvent, and
4. the presence of co-solvents.

It is consequently not possible to give one general synthetic procedure (for a detailed discussion see refs. 29 and 45). It also became evident that the order of addition of the reagents can play a crucial role, which is nicely illustrated by the following examples.

When a suspension of \([\text{Li(C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)]\) is added in stoichiometric amounts to a suspension of \(\text{CuX} \quad (X = \text{Cl or Br})\) in \(\text{Et}_2\text{O}\) (see Scheme 1.7), an insoluble red compound with the composition \([\text{Cu(C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)\text{CuX}]\) is formed. This compound does not undergo any further reaction, even with an excess of the corresponding organolithium reagent [35].

When the order of addition is reversed (i.e., when a suspension of \(\text{CuBr}\) is gradually added to a suspension of \([\text{Li(C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)]\)), a pure, yellow-colored organocopper compound \([\text{Cu}_4(\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)]_4\) is isolated from the reaction mixture in about 40% yield [19]. This was the first organocopper compound to be fully structurally characterized by X-ray crystal structure determination (see Fig. 1.1 in the previous section). The latter reaction sequence proceeds through a “cuprate stage”, a stable, soluble intermediate with \([\text{Cu}_2\text{Li}_2(\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)]_4\) stoichio-
metry, which was also fully characterized and which is discussed later in this chapter. When the copper arenethiolate \([\text{Cu}_3(\text{SC}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)_3]\) was used in place of \(\text{CuBr}\), \([\text{Cu}_4(\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)_4]\) was formed and subsequently isolated in almost quantitative yield \([46]\).

An entirely different methodology is applied for the synthesis of the closely related organocopper compound \([\text{Cu}(\text{C}_6\text{H}_4\text{NMe}_2-2)]\). This proceeds by way of a stable organocopper-\(\text{CuBr}\) aggregate \([47]\) (see Scheme 1.8). Although structural characterization of \([\text{Cu}(\text{C}_6\text{H}_4\text{NMe}_2-2)]\) was hampered by its insolubility in all common solvents, it most probably has a polymeric structure.

![Scheme 1.8.](image)

A major problem that often complicates the structural characterization of simple organocopper compounds is their insolubility in common organic solvents, which precludes the application of NMR techniques or the growing of suitable single crystals for X-ray structure determination. Attempts have been made to solubilize these compounds by addition of additional donor molecules such as amines \([48]\) and phosphines \([48–50]\). It was expected that binding of additional donor molecules would increase the intrinsic thermal stability of simple organocopper compounds. However, the opposite result was often observed, whilst complexation of additional ligands also caused the breaking down of the original aggregated structures into mononuclear copper compounds.

The stabilizing effect of additional donor molecules is nicely illustrated by the increase in decomposition temperatures seen on going from \(\text{MeCu} < -15 \degree\text{C}\) to \(\text{CuMe}(\text{PPh}_3)_3\), which decomposes at about 75 \degree\text{C} \([49]\). The structure of the latter compound in the solid state (see Fig. 1.5) comprises a mononuclear complex with

![Fig. 1.5. Structure of \(\text{CuMe}(\text{PPh}_3)_3\) in the solid state.](image)
the methyl group and the three PPh₃ groups in a tetrahedral arrangement around
the copper atom [51].

Another illustration of the stabilizing effect of phosphines is supplied by cyclo-
pentadienylcopper triphenylphosphine, one of the very few examples in which a
cyclopentadienyl group is $\eta^5$-bonded to copper (see Fig. 1.6) [52].

An enhancement in the solubility of otherwise almost insoluble, and most
probably polymeric, phenylcopper species has been achieved by treatment with
a tridentate phosphine. The resulting soluble phenylcopper compound was fully
structurally characterized (see Scheme 1.9) [53].

![Fig. 1.6. Structure of CuCp(PPh₃) in the solid state.](image)

Scheme 1.9. Structure of CuPh(P₃) in the solid state (Ph groups at P are omitted for clarity).

A remarkably stable organocopper compound was obtained on treatment of
Me₃P=CH₂ with CuCl (see Scheme 1.10) [54, 55]. Formally, this product should be
regarded as an “ate” complex, with positive charges on the phosphorus atoms and
negative charges on the copper atoms.

![Scheme 1.10. Reaction between copper(I) chloride and Me₃P=CH₂.](image)

Complete degradation of organocopper aggregates may occur when they react with
tertiary phosphines. This is illustrated by treatment of arylcopper compounds with
bis-(diphenylphosphino)methane (DPPM) and with 1,2-bis-(diphenylphosphino)-
ethane (DPPE) (see Scheme 1.11).
Treatment of 2-, 3- or 4-MePhCu with DPPM affords the trimeric aggregate Cu₃[CH(PPh₂)₂] in quantitative yield [56]. This is in fact a simple acid-base reaction (Cu/H exchange). It should be noted that the latter compound is also accessible by means of a transmetalation reaction between Li[CH(PPh₂)₂] and CuCl. In contrast, treatment of [Cu₄(C₆H₄CH₂NMe₂-2)₄] with DPPE results in selective C–P bond cleavage and formation of Cu₂(PPh₂)₂(DPPE)₂ (see Scheme 1.11) [57].

As mentioned above, one of the thermal decomposition pathways of alkylcopper compounds involves a β-hydrogen elimination process, and so it is not surprising that the first well characterized alkylcopper compounds lacked such β-hydrogens.

Treatment of LiCH₂SiMe₃ with CuI afforded a tetrameric aggregate, the structure of which was unambiguously proven by an X-ray crystal structure determination (see Fig. 1.1B in the previous section). This represented the first example of a well characterized alkylcopper compound [17].

On the basis of molecular weight determinations, simple arylcopper compounds such as 4-Me and 2-MePhCu are tetrameric [58] or (in the case of CuPhCF₃-3 [59]) octameric. Polymeric structures are implied for insoluble compounds such as CuPh [60]. It has been proposed that the tetrameric aggregates are isostructural with [Cu₄(C₆H₄CH₂NMe₂-2)₄], containing four copper atoms in a butterfly arrangement and with each of the aryl groups bridging between adjacent copper atoms (see Fig. 1.1 in the previous section).

More recently, several arylcopper compound syntheses that make use of a soluble form of a copper halide precursor, CuBr-DMS (DMS = dimethylsulfide) in DMS as the solvent have been reported. Some of these compounds, such as [Cu₄(C₆H₄)₄(DMS)₂] [61] and [Cu₄(C₆H₄Me-2)₄(DMS)₂] [62], appeared to be DMS adducts and were fully characterized by X-ray crystal structure determination (see Fig. 1.7). It is interesting to note that these structures contain two- and three-coordinate copper atoms in trans positions. These structures may be envisaged as ion-pairs comprising Cu(Aryl)₂ anions bound to Cu(DMS) cations through the Cipso atoms.

The overall structural motif of pure organocopper compounds can be changed dramatically by the addition or the presence of coordinating solvents such as DMS or THT (THT = tetrahydrothiophene). This is illustrated by comparison of the structures of [Cu₄Mes[Si(THF)₄]], and [Cu₃Mesil₃] (see Fig. 1.8) [63, 64].

Scheme 1.11. Reactions between arylcopper compounds and diphosphines.
There is also evidence for the influence of steric crowding exerted by large groups present near the Cu–C bond on the aggregation state of the organocopper compound. When methyl substituents, as present in [Cu₅Mes₅], are replaced by i-Pr groups, the corresponding organocopper compound [Cu₅C₆H₂(i-Pr)₅] becomes tetrameric [65]. If the even more sterically demanding t-Bu groups are subsequently introduced in the presence of DMS, a mononuclear copper compound [Cu₅C₆H₂(t-Bu)₅] is isolated [66]. Both compounds have been characterized by X-ray crystal structure determinations (see Fig. 1.9). The latter compound is one of the very few examples of a monomeric organocopper compound.

The triphenyl analogue of mesitylcopper, prepared from the corresponding lithium compound and CuBr-DMS, has a rather unexpected structure (see Fig. 1.10) [66]. Two 2,4,6-triphenyl groups are bound to one copper atom in an almost linear arrangement, while one of the aryl groups is bound to a Cu(DMS)₂ unit. Formally, this compound should be regarded as consisting of Ar₂Cu anions coordinated to a Cu(DMS)₂ cation (cf. the interpretation of the structure of [Cu₄(C₆H₄Me-2)₄(DMS)₂]).
The introduction, initiated by Van Koten et al. in the early 1970s [18, 19], of the concept of stabilization of organocopper compounds through the use of organic groups, thus permitting additional intramolecular coordination, provided more detailed insight into the factors determining the formation of specific aggregates. The first example of this approach was the synthesis and structural characterization of \([\text{Cu}_4(\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)\text{Cu}_2(\text{t-Bu})_2\text{Cu}_2(\text{2,4,6}-\text{DMS})_2]\) (vide supra). As the overall structural features found in this compound – bridging three-center, two-electron-bonded aryl groups – are comparable to those in simple aryl copper compounds, the influence of the coordinating \textit{ortho}-(dimethylamino)methyl substituent on the stability of the compound is twofold in nature. Firstly, the \textit{ortho} substituent stabilizes the rotamer with the aryl ring perpendicular to the \textit{Cu–Cu} vector, thus increasing the electron density between \textit{Cipso} and \textit{Cu}. Secondly, the Lewis base stabilizes the tetrameric aggregate relative to other possible aggregation states. This last point is illustrated by comparison of the features of closely related ligand systems. Whereas \(\text{CuC}_6\text{H}_4\text{NMe}_2-2\)
is insoluble, most probably pointing to a polymeric structure [47]. CuC₆H₄OMe-2 is soluble and exists as an octameric aggregate in the solid state [67].

That subtle variations in the ligand system can have a large influence on the overall structure of the copper compound is also attested to by the different structures of [Cu(Me₃SiCH(Py-2))]₄ (Py-2 = 2-pyridyl) and [Cu((Me₃Si)₂C(Py-2))]₂. In both compounds, the 2-methylpyridyl group is η¹-bonded to a copper atom, while a linear coordination geometry at the copper center is achieved through intermolecular coordination of the nitrogen atom of an adjacent pyridyl unit. However, [Cu(Me₃SiCH(Py-2))]₄ exists as a tetramer in solution and in the solid state [68], whereas [Cu((Me₃Si)₂C(Py-2))]₂ has a dimeric structure (see Fig. 1.11) [68, 69]. This difference is probably a consequence of the presence of a second bulky Me₃Si substituent at the carbon atom bound to copper in [Cu((Me₃Si)₂C(Py-2))]₂.

Finally, an important role is also played by the flexibility of the chelate ring formed upon coordination of a heteroatom-containing substituent. This is obvious when the structures of [Cu₄(C₆H₄CH₂NMe₂-2)]₄ and the corresponding arylocopper compound containing a 2-oxazoline ligand are compared. Although both ligand systems contain a potentially coordinating nitrogen atom in the γ-position (with respect to the copper atom), [Cu₄(C₆H₄CH₂NMe₂-2)]₄ is a tetramer while the latter compound (see Fig. 1.12, left) is a dimer [70].

The use of the more rigid 8-(dimethylamino)naphthyl group affords an organocopper compound with some remarkable features (see Fig. 1.12, right). It comprises a tetranuclear aggregate in which each of the naphthyl groups bridge between two adjacent copper atoms. However, the heteroatom-containing substituents are pairwise coordinated to two, mutually trans-positioned copper atoms [71], or in other words, the structure contains two CuAr₂ anions with two-coordinate copper atoms and two four-coordinate CuN₂ cations. Ion-pair formation involving coordination of Cipso to the CuN₂ cations affords the neutral tetranuclear aggregate seen in the solid state structure. This organocopper compound shows an unusual reactivity – usually observed only for cuprates – towards organic substrates. These observations provide a direct link between the structural features of this compound and its reactivity in organic synthesis.
When cuprates are used as reagents in organic chemistry, the compounds are usually prepared in situ from copper salts, starting either from a Grignard reagent or from an organolithium compound. Because of the presence of magnesium or lithium halides, these systems are not always suitable for mechanistic studies or structural characterization of the cuprate involved (see Sect. 1.3). An excellent synthetic pathway to pure organocuprates, free from additional metal halides or other impurities, involves treatment of the pure organocopper compound with the pure organolithium compound in the required stoichiometry [72] (see Eqn. 1 in Scheme 1.12).

Another application of pure organocopper compounds is as starting materials for the synthesis of other organocuprate compounds. Treatment of $[\text{Cu}C_6H_4(\text{oxazolyl})-2(\text{Me})-4]$ with $(\text{CF}_3)_3\text{Cu}$, for example, affords $\text{Cu}C(\text{CF}_3)_3$ through a halogen/metal exchange reaction [73] (Eqn. 2 in Scheme 1.12). A further demonstration of the applicability of pure organocopper compounds is the insertion reaction of an isocyanide into a copper-carbon bond [74], (Eqn. 3 in Scheme 1.12).

**Fig. 1.12.** Structures of $[\text{Cu}(\text{C}_6\text{H}_4(\text{oxazolyl})-2(\text{Me})-4)]_2$ and $[1-C\text{u}C_{10}H_6\text{NMe}_2-8]_4$ in the solid state.
Finally, some organocopper compounds undergo charge disproportionation under the influence of ligands that bind strongly to copper. Treatment of mesitylcopper with 1,2-bis-(diphenylphosphino)ethane (DPPE), for example, results in the formation of bis(mesityl)copper anions and a copper cation to which four phosphorus atoms of two DPPE molecules are coordinated [75].

The selective formation of symmetric biaryls in high yield through thermal or oxidative decomposition is a feature that can be directly associated with the structure of the compound involved. It has been shown that arylcopper compounds with a structure comprising three-center, two-electron-bonded bridging aryl groups undergo this selective reaction (see Scheme 1.13), while arylcopper compounds in which the Cu atom is σ2-bonded to the aryl group give a mixture of unidentified decomposition products, most probably by a radical pathway. In structures incorporating bridging aryl groups, the carbon atoms are already in close proximity [76], as shown schematically in Scheme 1.13. Therefore, only a slight further distortion of this geometry is needed to bring the ipso-carbon atoms even closer together, thus promoting the C–C bond formation.

Furthermore, it has been demonstrated that an increase in the electrophilicity of the copper centers in aggregate structures, by incorporation of Cu+ into such structures, for example, favors C–C bond formation to give biaryls. Treatment of various organocopper compounds with Cu+ (in the form of CuOTf, OTf=trifluoromethanesulfonate) has been studied [77]. For some compounds containing potential coordinating substituents, it was possible to isolate and study species such as \([\{\text{Cu}_4\text{R}_4\}^{2+}]\)[2 OTf−] [76], but addition of only catalytic amounts of CuOTf to simple arylcopper compounds such as Cu4(C6H4Me-2)4 and Cu4(C6H4Me-4)4 affords the corresponding biaryls in quantitative yield. This was explained in terms of a mechanism involving a valence disproportionation reaction of two Cu(I) into Cu(II) and Cu(0) [77].

Finally, pure organocopper compounds have found applications in one-step syntheses of tri- and diorganotin halides. Its has now become well established that treatment of Grignard and organolithium reagents with tin(IV) halides always gives a mixture of products (Eqn. 1 in Scheme 1.14) rather than the desired tri- or diorganotin halides.

In contrast, treatment of SnCl4 with excess CuPh affords SnPh3Cl as the only product [78] (Eqn. 2 in Scheme 1.14). Furthermore, it has been shown that reaction of functionally substituted arylcopper compounds with organotin halides proceeds very selectively to afford a novel type of pentacoordinate organotin compounds possessing interesting structural features [79]. Treatment of Cu4(C6H4CH2NMe-2)4 with four equivalents of SnMeCl3, for example, gives
SnMeCl$_2$(C$_6$H$_4$CH$_2$NMe-2) as the only product, in quantitative yield [80] (Eqn. 3 in Scheme 1.14).

1.3 Heteroleptic Organocopper Compounds Cu$_{n+m}$R$_n$X$_m$

As outlined previously, aggregation of organocopper compounds is a consequence of the fact that the carbon moieties in these compounds are capable of bridging between two copper atoms. It is therefore to be expected that other anionic ligands capable of bridging between metal centers – halides, for example – might easily become incorporated into such aggregates.

By the early 1970s it was already recognized that the excess CuBr in the red product obtained on treatment of LiC$_6$H$_4$NMe$_2$-2 with CuBr (for which the elemental analysis pointed to a Cu$_3$(C$_6$H$_4$NMe$_2$-2)$_2$Br stoichiometry) is not a contaminant but an integral part of an aggregated species [47]. An X-ray crystal structure determination of this compound showed a structure (see Fig. 1.13) of Cu$_6$(C$_6$H$_4$NMe$_2$-2)$_4$Br$_2$ stoichiometry, with the copper atoms in an octahedral arrangement [44].

Each of the four organic moieties bridges between an equatorial and an axial copper atom through its C(1) atom, while the nitrogen atom in the substituent is coordinated to an adjacent equatorial copper atom. The two bromine atoms bridge, at opposite sites, between two equatorial copper atoms. This structural arrangement has the consequence that the aggregate incorporates two distinct types of

\[ \text{Eqn. 3 in Scheme 1.14.} \]

\[ \begin{align*}
\text{SnX}_4 & \xrightarrow{\text{RMgX or RLi}} \text{R}_n\text{SnX}_{n-m} \\
\text{SnCl}_4 & \xrightarrow{\text{PhCu}} \text{Ph}_3\text{SnCl} \\
\frac{1}{4} \text{Cu}_3\text{(C}_6\text{H}_4\text{CH}_2\text{NMe}_2\text{-2})_2\text{Br} & \xrightarrow{\text{MeSnCl}_3} \end{align*} \]
copper atoms: four equatorial ones with distorted trigonal coordination geometries, and the two apical ones, with distorted digonal coordination geometries.

It should be noted that a combination of various bonding features – bridging organic groups, bridging anionic ligands such as halogen atoms, and also the presence of potentially coordinating substituents – might give rise to more diverse structural patterns, as has been observed for homoleptic organocopper compounds (vide supra). In addition, though, organocopper compounds that do not contain functional substituents can also aggregate with copper halides, as demonstrated by the following observation:

During the synthesis of \( \text{Cu(C}_6\text{H}_4\text{Me-4)} \), prepared by gradual addition of a solution of \( \text{LiC}_6\text{H}_4\text{Me-4} \) to a suspension of \( \text{CuBr} \) in Et_2O \[16\], a completely clear solution is obtained at the stage at which about half of the quantity of \( \text{LiC}_6\text{H}_4\text{Me-4} \) has been added. This indicates that at this point the excess \( \text{CuBr} \) has been solubilized, most probably as a consequence of aggregation with the \( \text{Cu(C}_6\text{H}_4\text{Me-4)} \) produced (see Scheme 1.15). It was impossible to isolate any well defined compound from this solution, due to the intrinsic low thermal stability of the species formed.

\[
\begin{align*}
2 \text{CuBr} & \rightarrow \text{LiC}_6\text{H}_4\text{Me-4} & \text{[CuC}_6\text{H}_4\text{Me-4} \text{CuBr]} & \rightarrow \text{LiC}_6\text{H}_4\text{Me-4} & \rightarrow 2 \text{[CuC}_6\text{H}_4\text{Me-4]} \\
\text{Scheme 1.15.}
\end{align*}
\]

To discuss all the structures elucidated for heteroleptic organocopper compounds to date \[29, 45\] is beyond the scope of this chapter, and so only some representative examples of the various kinds of structural motifs are discussed. As outlined in the previous section, the order of addition of the reagents can play an important role in the synthesis of homoleptic organocopper compounds, and might determine the structure of the final product. Similar observations have been made for the synthesis of organocopper-copper halide aggregates. In other cases, however, the same aggregated species is always formed, irrespective of the order of addition or the stoichiometry of the starting materials. This is most probably the result of a large difference in thermodynamic stability of the possible final products, the most stable one acting as a thermodynamic sink.

Organic moieties containing potentially coordinating substituents are largely responsible for the diversity of structures observed in heteroleptic organocopper compounds. The structures observed in compounds containing one of the ligands depicted in Fig. 1.14 demonstrate that important roles are played not only by

Fig. 1.14. Bidentate-, tridentate- and pentadentate monoanionic ligands applied in the synthesis of various organocopper aggregates.
the number of heteroatoms, but also by the spatial arrangement of the functional groups.

As outlined above, the aggregate Cu_6(C_6H_4NMe_2-2)_4Br_2, incorporating ligand A, comprises a structure with six copper atoms in an octahedral arrangement (see Fig. 1.13). It is interesting to note that the other group 11 metals, silver and gold, can also be incorporated into this metal framework. Compounds of compositions Ag_6(C_6H_4NMe_2-2)_4X_2, Ag_4Cu_2(C_6H_4NMe_2-2)_4X_2, Ag_2Cu_4(C_6H_4NMe_2-2)_4X_2, Au_2Cu_4(C_6H_4NMe_2-2)_4X_2, and Au_2Ag_4(C_6H_4NMe_2-2)_4X_2 (X = anionic ligand) [77, 81] have been isolated. On the basis of spectroscopic evidence, structures comparable to that observed for Cu_6(C_6H_4NMe_2-2)_4Br_2 have been proposed. For the latter two compounds it is most likely that the Au atoms occupy axial positions, as a consequence of the tendency of gold(I) to attain a linear digonal coordination geometry.

As mentioned in Section 1.2, the organocopper compound derived from ligand B is a discrete, tetranuclear species. Aggregation of this compound with CuCl or CuBr results in an insoluble material with the composition Cu(C_6H_4CH_2NMe_2-2)/CuX (X = Br, Cl) [35]. Because of its insolubility, which hampers structural characterization, a polymeric structure has been proposed for this compound.

When the (dimeric and structurally characterized [82]) organolithium compound derived from ligand C is treated with CuBr, either Cu_3Br[C_6H_4CH_2N(Me)CH=CH_2NMe_2-2]_2 or Cu_4Br_2[C_6H_4CH_2N(Me)CH=CH_2NMe_2-2]_2 is formed, depending on the RLi/CuBr molar ratio (see Scheme 1.16).

The structure of the first compound was unambiguously proven by X-ray crystal structure determination (see Fig. 1.15) [46]. It should be noted that an attempt to prepare and isolate the pure, copper halide-free organocopper compound (by application of less than three equivalents of CuBr) failed, with the 2:1 organocopper-copper bromide aggregate always being isolated, although in lower yield. An interesting structural feature of these compounds is that they may be regarded as
consisting of a cuprate anionic moiety \( \text{R}_2\text{Cu}^- \) and either a \([\text{Cu}_2\text{Br}]^+ \) (first compound) or a \([\text{Cu}_3\text{Br}_2]^+ \) (second compound) cationic unit.

Introduction of a second \( \text{o-} \)-(dimethylamino)methyl substituent, ligand \( \text{D} \) in Figure 1.14, affords an aggregated species with \( \text{Cu}_4\text{Br}_2\text{R}_2 \) stoichiometry, established by X-ray crystal structure determination \[83\]. The structure comprises two organic, monoanionic, terdentate ligands binding four copper atoms (arranged in a butterfly pattern) through \( \text{C}_{\text{ipso}} \) bridge bonding and \( \text{N}^-\text{Cu} \) coordination, as well as by two bridging bromine atoms (see Fig. 1.16). This compound may also be considered as consisting of a \( \text{R}_2\text{Cu}^- \) (cuprate) anionic unit and a \([\text{Cu}_3\text{Br}_2]^+ \) cationic moiety, held together as a consequence of the special spatial arrangement of the heteroatom-containing substituents.

On extension of the coordinating properties of the ligand system to a monoanionic pentadentate representative – ligand \( \text{E} \) in Fig. 1.14 – an even less expected structure was obtained. Treatment of the corresponding organolithium compound (which only exists as an aggregate with \( \text{LiBr} \) \[84\]) with \( \text{CuBr} \) afforded an aggregate, the X-ray structure of which is shown in Fig. 1.17. The structure consists of two monoanionic, pentadentate organic groups, five copper atoms, and three bromine

Fig. 1.15. Structure of \( \text{Cu}_3\text{Br}[\text{C}_6\text{H}_4\text{CH}_2\text{N}^-(\text{Me})\text{CH}_2\text{CH}_2\text{NMe}_2]_{2,6}\) in the solid state.

Fig. 1.16. Structure of \( \text{Cu}_4\text{Br}_2[\text{C}_6\text{H}_3(\text{CH}_2\text{NMe}_2)_{2,6}]_{2,6}\) in the solid state.
atoms, and can be described in terms of two $[\text{RCu}_2]^+$ cationic building blocks held together by a central $[\text{CuBr}_3]^-$ anionic unit [85].

Treatment of a functionalized vinyllithium compound with two equivalents of CuBr (see Scheme 1.17) afforded an aggregate, the structure of which was established by an X-ray crystal structure determination [41, 42] (see Fig. 1.18A).

![Scheme 1.17](image)

Fig. 1.18. Structures of $\text{Cu}_4\text{Br}_2[2\text{-Me}_2\text{NC}_6\text{H}_4\text{C}(\text{Me})=\text{C}(\text{C}_4\text{H}_4\text{Me}-4)]_2$ (A) and $\text{Cu}_4[2\text{-Me}_2\text{NC}_6\text{H}_4\text{C}(\text{Me})=\text{C}(\text{C}_4\text{H}_4\text{Me}-4)]_2[\text{C}_6\text{H}_4\text{NMe}_2-2], (B)$ in the solid state.
This structure represents the first of the very few examples of structurally characterized organocopper compounds containing vinlylic carbon-to-copper bonds. The four copper atoms are arranged in a rhombus-type pattern, while the propenyl groups and the two bromine atoms occupy adjoining edges. As a consequence, the copper atoms are alternately two- and three-coordinate. An interesting feature of this compound is that the two bromine atoms can be replaced by aryl groups on treatment with an aryllithium compound, with retention of the overall structural arrangement [41] (see Fig. 1.18B).

This latter compound represents an example of a heteroleptic organocopper compound containing two different organic moieties: aryl groups and vinyl groups. The existence of such heteroleptic organocopper compounds had been proposed earlier, on the basis of spectroscopic and chemical evidence [77]. Thus, it had been shown by NMR spectroscopic studies that organocopper species in solution undergo interaggregate exchange. Mixing of pure $[\text{CuC}_6\text{H}_4\text{CH}_2\text{NMe}_2-2]_4$ with $[\text{CuC}_6\text{H}_4\text{Me}-4]_4$, for example, affords an equilibrium mixture of all possible mixed aggregates (Scheme 1.18).

\[
\begin{align*}
[\text{CuC}_6\text{H}_4\text{CH}_2\text{NMe}_2]_4 &+ [\text{CuC}_6\text{H}_4\text{Me}-4]_4 &\overset{\text{CuOTf}}{\longrightarrow} [\text{Cu}_6(\text{C}_6\text{H}_4\text{NMe}_2)_n(\text{C}_6\text{H}_4\text{Me}-4)_{4-n}]_4 \\
\text{Me}_2\text{NCH}_2\text{C}_6\text{H}_4\text{C}_6\text{H}_4\text{Me}_2 &+ \text{MeC}_6\text{H}_4\text{C}_6\text{H}_4\text{Me} &+ \text{Me}_2\text{NCH}_2\text{C}_6\text{H}_4\text{C}_6\text{H}_4\text{Me}
\end{align*}
\]

Scheme 1.18.

Decomposition of this equilibrium mixture with catalytic amounts of CuOTf affords a mixture of all three possible biaryls. The formation of the unsymmetrical biaryl $2\text{Me}_2\text{NCH}_2\text{C}_6\text{H}_4\text{C}_6\text{H}_4\text{Me}$ can only be explained by the occurrence of aggregated copper species in which both the $\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2$ and the $\text{C}_6\text{H}_4\text{Me}$ groups are bound to the same copper core [77]. It was furthermore observed that the ratio of the formed biaryls is not statistical, which points to significant differences in the thermodynamic stabilities of the various mixed aggregates present in solution.

Treatment of $[\text{Cu}_6(\text{C}_6\text{H}_4\text{NMe}_2-2)]_4\text{Br}_2$ (Fig. 1.13) with two equivalents of a lithium acetylide resulted in selective replacement of the bromide anions with acetylide groups (see Scheme 1.19) [86]. The aggregate thus formed represents another example of a heteroleptic organocopper compound containing two different organic groups.

Two other synthetic approaches to this type of aggregates are available (Scheme 1.19). The first involves mixing of the pure arylocopper compound with an appropriate copper acetylide in a suitable solvent [87]. In this regard, it is interesting to note that the aggregate $[\text{Cu}_6(\text{C}_6\text{H}_4\text{NMe}_2-2)]_4(C=CR)_2$ is always obtained irrespective of the stoichiometry of the reagents, thus representing a nice example of selective self-assembly. The second approach involves treatment of a monosubstituted acet-
ylene with the pure organocopper compound. Partial protonolysis of the organocopper compound produces a copper acetylide, which is immediately trapped by unreacted organocopper compound. The structure of the obtained aggregate was unambiguously proven by an X-ray crystal structure determination (see Fig. 1.19) [88].

An interesting feature of these compounds is that, upon thermolysis in benzene at 80 °C, the unsymmetrical C–C coupling product 2-Me₂NCH₂CH₂C≡CR is formed exclusively. The selectivity of this reaction is probably directly related to the structural features of this heteroleptic aggregate [89].

There is ample evidence that anions other than halides can also become incorporated in aggregate structures. For example, interaggregate exchange between organocopper compounds and copper carboxylates has been observed in reactions between copper benzoate and mesitylcopper in the appropriate molar ratio [90]. In one reaction, a yellow, crystalline material was isolated in high yield. According to X-ray crystallography [90], it appeared to be a trinuclear aggregate with one mesityl group bridge-bonded between two copper atoms, and with the two benzoate anions each binding in a bridging fashion between one of these copper atoms and a third one (see Fig. 1.20).

Other examples are provided by structures with bridging arenethiolate anions. The application of functionally substituted copper arenethiolates as catalysts in...
copper-mediated C–C bond formation reactions is now well established [91, 92], and it has been argued that the formation of mixed arenethiolate alkyl- or aryl-copper aggregates might play a role in these reactions. This assumption is supported by the synthesis of Cu₄(Mes)₂(SC₆H₄CH₂NMe₂-2)₂, which was achieved by treatment of the appropriate copper arene thiolate with mesitylcopper in 1:1 molar ratio. The molecular geometry of this compound was established by X-ray crystal structure determination (Fig. 1.21) [93].

The structure of this compound consists of four copper atoms in a butterfly arrangement, in which the two mesityl groups bridge opposite edges. The remaining two edges are occupied by the arenethiolate ligands through bridging Cu–S bonds, while the nitrogen atoms of the substituents are coordinated to two opposite copper atoms. In this way, two of the copper atoms become three-coordinate and the other two copper atoms two-coordinate.
It is not only heteroatom-functionalized organocopper compounds that give rise to a large diversity of aggregates with copper halides. Organocopper compounds with olefinic substituents, which are also able to coordinate to copper, similarly form aggregates, such as \([\text{Cu}_5\text{Br}_4(\text{C}_6\text{H}_4\text{CH}–\text{CH}_2-2)_2]^–\) and \([\text{Cu}_5\text{Br}_2(\text{C}_6\text{H}_4\text{CH}–\text{CH}_2-2)_4]^–\) [94]. These anionic aggregates formally belong to an other class of compounds: the cuprates, discussed in the next section.

The ability of organocopper compounds to form various kinds of aggregated species with metal halides is a factor often overlooked when organocopper compounds are applied as reagents in organic synthesis. It needs to be taken into account that copper halides are often formed during reactions of pure organocopper reagents. It is obvious that these can form aggregates with the organocopper reagent, so that, at a certain stage in the reaction, the initial reagent is no longer present. The organocopper-copper halide aggregate produced probably has a reactivity different to that of the initial organocopper reagent. At the current state of knowledge, the consequences are unpredictable and may well be different for each specific organocopper compound. When an aggregate with much higher stability than the pure organocopper compound is formed, any further reaction may be prevented. If, on the other hand, the aggregate has a considerably reduced thermal stability, extensive decomposition might occur, giving rise to the formation of unwanted side products.

An illustrative example is the formation of the symmetric biaryl from the reaction between \(\text{CuC}_6\text{H}_4\text{NMe}_2-2\) and \(\text{IC}_6\text{H}_4\text{NMe}_2-2\), which has been studied in detail in the authors’ laboratory [95]. When this reaction is carried out in benzene as a solvent, the reaction stops when one third of the original organocopper compound has been consumed (Eqn. 1 in Scheme 1.20).

\[
\text{CuCl}_{2} + 2\text{IC}_6\text{H}_4\text{NMe}_2-2 \xrightarrow{\text{C}_6\text{H}_6} \text{Cu}_{6}(\text{C}_6\text{H}_4\text{NMe}_2-2)_4\text{I}_2 + 2(\text{C}_6\text{H}_4\text{NMe}_2-2)_2 \quad (1)
\]

\[
\text{CuCl}_{2} + 2\text{IC}_6\text{H}_4\text{NMe}_2-2 \xrightarrow{\text{DMF}} (\text{C}_6\text{H}_4\text{NMe}_2-2)_2 + \text{CuI} \quad (2)
\]

Scheme 1.20.

The CuI formed during the reaction is immediately trapped by the unreacted organocopper compound, resulting in the formation of \(\text{Cu}_6(\text{C}_6\text{H}_4\text{NMe}_2-2)_4\text{I}_2\). This aggregate has a structure similar to that of the corresponding bromine compound (Fig. 1.13). Compared to the parent organocopper compound, this aggregate has considerably greater kinetic stability and so blocks any further reaction even when excess of aryl iodide is present. When, however, the same reaction is carried out in DMF, quantitative formation of the biaryl is observed (Eqn. 2 in Scheme 1.20). It appears likely that the good donor DMF effectively cleaves the aggregated species into the parent organocopper compound and solvated CuI, so that the reaction goes to completion. This observation might also explain why co-solvents such as DMF, NMP, or HMPA are often required to produce high yields in reactions involving organocopper compounds.
1.4 Organocuprates

From the viewpoint of their synthetic potential in organic synthesis, the organocuprates are the most important of all organocopper compound types [13, 96–98]. Organocuprates are commonly obtained by addition of more than one equivalent of an organolithium or Grignard reagent to a copper halide [5] (Eqn. 1 in Scheme 1.21). The existence of such species was discovered after the observation that insoluble MeCu reacts with an additional equivalent of MeLi to afford a clear, colorless solution of a compound represented as “Me₂CuLi” (Eqn. 2 in Scheme 1.21) [6, 7].

\[
\text{CuX} + 2 \text{RMgX}_2 \text{ or } 2 \text{RLi} \rightarrow \text{R}_2\text{Cu(MgX)}_{\frac{1}{2}} \text{ or (Li)} \quad (1)
\]

\[
\text{CuX} + \text{MeLi} \rightarrow \text{MeCu} \quad \text{yellow, insoluble}
\]

\[
\text{CuX} \quad \text{MeLi} \rightarrow \text{MeCu} \quad \text{MeLi} \quad \text{“Me₂CuLi”} \quad \text{colorless solution} \quad (2)
\]

Scheme 1.21.

A large variety of cuprates are known nowadays. They include heteroleptic derivatives \( R(Y)\text{CuM} \) (\( Y \) = alkynyl, halide, amido, alkoxide, thiolato, phosphido; \( M = \text{Li or Mg} \)), and have found widespread application in organic chemistry. Their syntheses and applications are discussed in the other chapters of this book. In addition, compounds in which the copper to lithium (or magnesium) ratio differs from 1:1 are also known; examples are \( R_3\text{CuLi}_2 \) and the so-called higher order cyanocuprates introduced by Lipshutz et al. [99].

Studies of the structures of cuprate species were initiated to elucidate the mechanisms by which they interact with substrates and to understand their special reactivities. In the early days these investigations were restricted to solution studies by spectroscopic techniques. It was not until 1982 that the first example of a cuprate species – \( [(\text{Cu}_5\text{Ph}_6)(\text{Li(THF)}_4)] \) – was structurally characterized by X-ray crystal structure determination [100] (vide infra). It should be noted that most of these studies, reviewed previously [29, 45, 101], were limited to “simple” alkyl and aryl derivatives.

In principle, three different types of organocuprates need to be taken account of. These are:

1. the neutral homoleptic organocuprates, as initially discovered by Gilman,
2. ionic species, often obtained by adding strongly coordinating molecules such as crown ethers to neutral organocuprates, and
3. heteroleptic cuprates, of which the cyanocuprates are the most important and most extensively studied representatives.

However, these borderlines should not be taken too strictly.
It is beyond the scope of this chapter to discuss the special reactivities associated with each specific type of cuprate; these are covered in other chapters in this book. Here, we will concentrate on the various structural motifs of organocuprates in organic synthesis.

1.4.1 Neutral Homoleptic and Heteroleptic Organocuprates

Molecular weight determination – by vapor pressure depression, \(^1\)H NMR, and solution X-ray scattering data – made it evident that \(\text{CuLiMe}_2\) exists as a dimer in \(\text{Et}_2\text{O}\) solution \([102]\). A planar cyclic structure \(\text{Cu}_2\text{Li}_2\text{Me}_4\), shown schematically in Fig. 1.22A, has been proposed; it comprises alternating copper and lithium atoms with each of the Me groups bridging between one lithium and one copper atom. Similar conclusions were drawn from variable temperature \(^1\)H NMR studies of \(\text{LiCH}_2\text{SiMe}_3\) and \(\text{CuCH}_2\text{SiMe}_3\) in various ratios. It was shown that the only significant “mixed” species present in solution was the 1:1 aggregate, for which a similar dimeric planar structure was proposed (see Fig. 1.22B) \([39, 103]\). Furthermore, kinetic data relating to the reaction between \(\text{CuLiMe}_2\) and \(\text{MeI}\) implied that the rate-determining step involved the dimeric aggregate, \(\text{Cu}_2\text{Li}_2\text{Me}_4\) \([102]\).

The first example of an arylcuprate isolated as a pure compound and studied in detail was the compound of stoichiometry \(\text{CuLi(C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)_2\) \([104]\). The synthesis of the corresponding pure aurate, \(\text{AuLi(C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)_2\) \([105]\) and the pure argentate \(\text{AgLi(C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)_2\) \([106]\) were reported by the same authors. Molecular weight determinations by cryoscopy in benzene revealed that these compounds exist in apolar solvents as dimeric aggregates \(\text{M}_2\text{Li}_2\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2-2)_4\) (\(\text{M} = \text{Cu, Ag, Au}\)). The presence of four magnetically active nuclei (\(^1\)H, \(^{13}\)C, \(^{107, 109}\)Ag, and \(^{6, 7}\)Li) in the argentate allowed detailed structural characterization in solution to be carried out by NMR spectroscopy. \(^1\)H and \(^{13}\)C NMR spectroscopy showed the presence of four magnetically equivalent organic moieties over the whole temperature range studied (−70 to +100 °C). At the low exchange limit (< 10 °C), the nitrogen atoms of the substituents are coordinated in pairs to the same type of metal, most probably lithium. Furthermore, the \(^{13}\)C NMR spectrum
showed that each of the C_{ipso} atoms is coupled to one Li atom (^{1}J(^{13}C, ^{7}Li) = 7.2 Hz) and to one Ag atom (^{1}J(^{13}C, ^{109}Ag) = 136 Hz). The ^{6}Li, ^{7}Li, and ^{109}Ag NMR spectra pointed to the presence of one type of silver and one type of lithium atom, with each lithium atom being coupled to two silver atoms and each silver atom coupled to two lithium atoms (^{2}J(^{7}Li, ^{109}Ag) = 3.91 Hz) [107].

On the basis of these data and of spectroscopic similarities between the Cu, Ag, and Au compounds, a structure for these compounds was proposed. This is shown schematically in Fig. 1.23A. This dimeric aggregated structure is not a consequence of the ortho functionalization of the aryl anion with a coordinating heteroatom substituent, as became evident from studies of the structural features of the simple arylcuprate Cu_{2}Li_{2}(C_{6}H_{4}Me-4)(OEt)_{2} and the corresponding gold compound in solution [108]. For these aggregated species, a structure similar to that of M_{2}Li_{2}(C_{6}H_{4}CH_{2}NMe_{2})_{4} was proposed (see Fig. 1.23B). However, the lithium atoms are now trigonally coordinated.

The solid state structures of Cu_{2}Li_{2}(C_{6}H_{4}CH_{2}NMe_{2})_{4} (Fig. 1.24A) [72], Au_{2}Li_{2}(C_{6}H_{4}CH_{2}NMe_{2})_{4} [109], and Cu_{2}Li_{2}(C_{6}H_{5})_{4}(OEt)_{2} (Fig. 1.24B) [110],
were later established by X-ray crystal structure determination and appeared to be in full agreement with the corresponding structures in solution as deduced from spectroscopic data.

Cu$_2$Li$_2$(C$_6$H$_4$CH$_2$NMe$_2$-2)$_4$ was the first neutral cuprate for which the structure could be unambiguously established. A common feature of such structures is the bridging nature of the aryl group. As a consequence of the binding of C$_{ipso}$ to two different metal atoms, this bridging (in comparison with that in homoleptic organocupper compounds) is unsymmetrical (shorter Cu–C bond, longer Li–C bond). This asymmetry is even more pronounced in the corresponding gold compound [109], which is best described as consisting of two R$_2$Au$^-$ anionic units linked together by solvated lithium cations through contact ion-pair formation. Another consequence of the bridging between two different metal atoms is the fact that, if the aryl group is not symmetrically substituted, the bridging carbon atom becomes a center of chirality. This has important stereochemical consequences [111]. A particularly complicated situation arises if the benzylic group in, for example, Cu$_2$Li$_2$(C$_6$H$_4$CH$_2$NMe$_2$-2)$_4$ bears a substituent that gives rise to the presence of different diastereoisomeric units in one aggregate [111]. The pure organocupper compound Cu$_4$([C$_6$H$_4$CH(Me)NMe$_2$-2])$_4$, and the corresponding cuprate, Cu$_2$Li$_2$(C$_6$H$_4$CH(Me)NMe$_2$-2)$_4$, were prepared starting both from the enantiopure ligand and from the racemic ligand. It appeared that the organocupper compound Cu$_4$([C$_6$H$_4$CH(Me)NMe$_2$-2])$_4$ derived from the racemic ligand exists in solution as a mixture of all possible diastereoisomeric aggregates. This observation, however, contrasts with the situation found for the cuprate Cu$_2$Li$_2$(C$_6$H$_4$CH(Me)NMe$_2$-2)$_4$ derived from the racemic ligand. In this case, only aggregates in which all four bridging and benzylic carbon centers have the same relative stereochemical configuration are formed, in a nice example of diastereoselective self-assembly [112].

That the natures both of the organic group and of the additional donor-solvent molecules are factors that determine the actual cuprate aggregates formed is demonstrated by the structure of [Cu$_2$Li$_2$(CH$_2$SiMe$_3$)$_4$(DMS)$_2$]$\infty$ in the solid state [113] (see Fig. 1.25). In this structure, the basic framework consists of repeating central

![Fig. 1.25. Structure of [Cu$_2$Li$_2$(CH$_2$SiMe$_3$)$_4$(DMS)$_2$]$\infty$ in the solid state.](image)
Cu$_2$Li$_2$ cores with bridging Me$_3$SiCH$_2$ groups. These Cu$_2$Li$_2$ cores are interlinked to form linear chains through bridging Me$_2$S ligands between the lithium atoms of two adjacent Cu$_2$Li$_2$ cores.

The solid-state structure of Cu$_2$Li$_3$Ph$_4$(DMS)$_3$ is closely related to that observed for Cu$_2$Li$_2$Ph$_4$(OEt)$_2$, except that one of the lithium atoms here is now four-coordinate as a result of coordination of two DMS molecules [114]. This observation shows that even slight changes in the coordinating properties of donor solvent molecules may change the overall structure of the cuprate.

So far, only cuprates with a 1:1 copper/lithium ratio have been considered. Treatment of phenyllithium with various substoichiometric quantities of copper bromide in DMS as solvent afforded so-called higher order cuprates, of which two were characterizable by X-ray crystallography. These have the overall stoichiometries Cu$_2$Li$_3$Ph$_5$(DMS)$_4$ and Cu$_4$Li$_5$Ph$_9$(DMS)$_4$ [114, 115]. The structure of the former compound in the solid state is shown in Fig. 1.26.

The Cu$_4$Li$_5$Ph$_9$(DMS)$_4$ aggregate may be described as consisting of three linear CuPh$_2$ anions, triply bridged by two lithium cations, and of one trigonal Ph$_3$Cu$_2$ anion, which is associated with three lithium cations and coordinated by four DMS ligands. The two resulting units – [(CuPh$_2$)$_3$Li$_2$]$^-$ and [(CuPh$_3$)Li$_3$(DMS)$_4$]$^+$ – are linked together by a bridging phenyl group ipso carbon atom.

The only examples of cuprates in which copper and magnesium atoms are incorporated in one aggregate have the stoichiometries Cu$_2$MgPh$_4$(THF)$_n$ [60], Cu$_3$Mg$_2$Ph$_4$Br$_3$(THF)$_n$ [60], Cu$_4$Mg(PhMe-4)$_6$(OEt)$_2$ [116], and Cu$_4$MgPh$_6$(OEt)$_2$ [116]. The structure of Cu$_4$MgPh$_6$(OEt)$_2$ in the solid state (Fig. 1.27) was established by X-ray crystal structure determination [117].

The structure of Cu$_4$MgPh$_6$(OEt)$_2$ comprises a central core of five metal atoms in a trigonal bipyramidal arrangement, with the magnesium atom at an axial position. The six phenyl groups bridge across the axial–equatorial edges of the trigonal bipyramid. One diethyl ether molecule is coordinated to the magnesium atom,
to attain coordination saturation. A similar arrangement of the metal framework is observed in the anions \([\text{Cu}_5\text{Ph}_6]\) and \([\text{Cu}_3\text{Li}_2\text{Ph}_6]\), discussed in the next section.

For reasons outlined above, the neutral heteroleptic cuprates “RCuLiX” \((X = \text{heteroatom-containing ligand})\) are valuable reagents in organic synthesis. Despite this importance, however, only a very few have been structurally characterized. The structure of \(\text{CuLiMe}(t\text{-Bu}_2\text{P})(\text{THF})_3\) has been established by X-ray crystal structure determination [118] (Fig. 1.28A). The copper atom has a linear C–Cu–P geometry. In contrast to most other cuprates, in which lithium is involved in two-electron, three-center bonding with the organic group, the lithium atom is bound in this case to the heteroatom anion (P) and three THF molecules.

Another example of a neutral, heteroleptic cuprate is the arylcopper magnesium arenethiolate \([\text{Cu}_4\text{Mes}_4]\)[Mg(SC_6H_4CH(Me)NMe_2-2)]_2 (Fig. 1.28B), formed by self-assembly in solutions of \(\text{Cu}_3(\text{SC}_6\text{H}_4\text{CH(Me)NMe}_2-2)_3\) and Mes_2Mg [93]. This copper complex may be regarded as a model compound for a possible active species.
when Cu₃(SC₆H₄CH(Me)NMe₂-2)_₃ is used as a catalyst in enantioselective 1,4-
addition reactions of Grignard reagents to enones [91, 92].

The formation of heteroleptic organocuprates "CuLiRR" in solution has been 
proposed in, for example, the reaction in diethyl ether between enantiopure 
Cu₄(C₆H₄CH(Me)NMe₂-2)₄ and Li₄Me₄ (Eqn. 1 in Scheme 1.22) to afford a heter-
oleptic cuprate Cu₂Li₂(C₆H₄CH(Me)NMe₂-2)₂(Me)₂. These solutions were applied 
in 1,4-addition reactions. Although methyl transfer to the substrate occurs, no 
enantioselective induction is observed [119]. A possible explanation for this lack 
of stereoselectivity involves the occurrence of a disproportionation reaction of the 
heteroleptic cuprate into the corresponding homoleptic cuprates Cu₂Li₂(C₆H₄CH-
(Me)NMe₂-2)₄ and Cu₂Li₂Me₄. In the authors' laboratory, the reaction between 
the corresponding achiral organocopper compound Cu₄(C₆H₄CH₂NMe₂-2)₄ and 
Li₄Me₄ in various ratios has been studied. ¹H NMR spectroscopy has shown that 
such solutions are complicated equilibrium mixtures (Eqn. 2 in Scheme 1.22) of 
several aggregates, of which the homoleptic cuprates Cu₂Li₂(C₆H₄CH₂NMe₂-2)₄ 
and Cu₂Li₂Me₄ are the most abundant. It should be noted that species in which 
the Cu/Li ratio is different from 1:1 can also not be ruled out a priori.

\[
\begin{align*}
\text{Cu}_4(C_6H_4CH(Me)NMe}_22\text{Me}_4 + Li_4Me_4 & \rightarrow 2 \text{Cu}_2Li_2(C_6H_4CH(Me)NMe}_22\text{Me}_2 \\
\text{Cu}_2Li_2R_4 + Li_4Me_4 & \rightarrow \text{Cu}_2Li_2R_4Me + \text{Cu}_2Li_2R_2Me_2 + \text{Cu}_2Li_2RMe_3 + \text{Cu}_2Li_2Me_4
\end{align*}
\]

\text{Scheme 1.22.}

Such equilibria are governed by thermodynamics, and so the abundances of the 
different species in solution are dependent on their relative thermodynamic stabil-
ities. If, however, such a mixture of species is applied in, for example, a conjugate 
addition reaction, the product formation will be controlled by kinetics, and it is 
most likely that Cu₂Li₂Me₄ would be kinetically the most active species present.

1.4.2
Anionic Homoleptic and Heteroleptic Organocuprates

The first example of a cuprate structurally characterized by X-ray crystal structure 
determination was the ionic aggregate [Cu₅Ph₆][Li(THF)₄] [100] (Fig. 1.29A). The 
structural features of the anionic cuprate unit are closely related to those observed in 
[Cu₄LiPh₆]⁻ [117] and [Cu₃Li₂Ph₆]⁻ [20]. These aggregates have in common 
that the metal atoms are arranged in trigonal bipyramidal fashion, and the lithium 
atoms in the latter two compounds reside in axial positions. The six phenyl groups 
are bridge-bonded, spanning the axial–equatorial edges of the trigonal bipyramid.

Two peculiar examples of anionic aggregated cuprate species are [Cu₅Br₄(C₆H₄CH= 
CH₂-2)₂]⁻ and [Cu₃Br₂(C₆H₄CH=CH₂-2)₄]⁻ (Fig. 1.30). In the first compound,
both vinylic substituents are π-coordinated to two adjacent copper atoms, whilst in the second compound only one of the four available vinylic substituents is involved in π-coordination [94]. Bridge-bonding by the phenyl groups, however, as well as various types of Br-to-Cu bridging, is also clearly present in these structures.

Addition of the strongly coordinating 1,2-bis(diphenylphosphino)ethane (DPPE) ligand to a solution of Cu$_5$Mes$_5$ causes a disproportionation reaction, resulting in the formation of ionic [CuMes$_2$][Cu(DPPE)$_2$]. This was the first example of a mononuclear cuprate anion for which the structure was established by X-ray crystal structure determination (Fig. 1.31A) [75]. After this discovery, other ionic mononuclear cuprates were prepared by different approaches and structurally characterized. The first approach made use of bulky substituents in the organic groups bound to copper to prevent aggregation. This was achieved, for example, in the crystallization of CuLi[C(SiMe$_3$)$_3$]$_2$ from THF, which gave the ionic compound [Cu(C(SiMe$_3$)$_3$)$_2$][Li(THF)$_4$] [120]. Another approach used an additional ligand

![Fig. 1.29. Structures of [Cu$_5$Ph$_6$] (A) and [Cu$_5$Li$_2$Ph$_6$] (B) in the solid state.](image)

![Fig. 1.30. Structures of [Cu$_5$Br$_4$(C$_6$H$_4$CH=CH$_2$)$_2$] (A) and [Cu$_5$Br$_2$(C$_6$H$_4$CH=CH$_2$)$_4$] (B) in the solid state.](image)
(such as 12-crown-4 or PMDTA (PMDTA = pentamethyldiethylenetriamine)), capable of binding very strongly to the cation; these can break down the aggregated cuprate to form mononuclear ionic species. Examples of mononuclear ionic cuprates obtained in this way are \([\text{CuMe}_2][\text{Li}(12\text{-crown}-4)_2]\) \[121\] and \([\text{CuPh}_2][\text{Li}(12\text{-crown}-4)_2]\) \[121\] (Fig. 1.31B).

The reaction between equimolar quantities of \(\text{LiCH(SiMe}_3)_2\) and \(\text{CuBr}\) in the presence of 12-crown-4 afforded \([\text{Cu(CH(SiMe}_3)_2}\text{Br}][\text{Li}(12\text{-crown}-4)_2]\), the first example of an ionic mononuclear heteroleptic cuprate \[121\] for which the structure was established by X-ray crystal structure determination (Fig. 1.31C).

1.4.3 Lower- and Higher-order Cyanocuprates

The importance of cyanocuprates as a synthetic tool in organic chemistry is well established. Depending on the amount of organolithium reagent \(\text{LiR}\) (one or two equivalents) added to \(\text{CuCN}\), two different type of cyanocuprates are formed, with stoichiometries of \(\text{RCu(CN)}\text{Li}\) and \(\text{R}_2\text{Cu(CN)}\text{Li}_2\), respectively \[122\] (Scheme 1.23).

In order to distinguish between these two different types of cyanocuprates, the term “higher-order” cyanocuprates was introduced by Lipshutz et. al. for the second type of cyanocuprate, and the term “lower-order” cyanocuprate consequently

\[
\text{CuCN} + \text{L} + \text{R} \quad \rightarrow \quad \text{RCu(CN)Li} + \text{RLi} \quad (1)
\]

\[
\text{CuCN} + 2\text{L} + 2\text{R} \quad \rightarrow \quad \text{R}_2\text{Cu(CN)}\text{Li}_2 \quad (2)
\]

Scheme 1.23.
became established for the first type. The earliest report on cyanocuprates (with a 1:1 stoichiometry) dates from 1973 [123].

The discovery of these cyanocuprates and their application in organic synthesis – particularly of the higher-order cyanocuprates, to which a special reactivity was ascribed [97, 124, 125] – resulted in a scientific controversy concerning the actual structure of these compounds. For a number of years, a large number of reports with appealing titles such as “If the cyano ligand is not on copper, then where is it?” [126] and “It’s on Lithium” [127] appeared in the literature. Initially, two models to describe the structure of these cyanocuprates were put forward: (i) a bis-anionic species in which two organic groups and the cyanide were bound to the same copper atom (Fig. 1.32A), and (ii) a cyano-Gilman cuprate in which only the two organic groups were bound to copper (Fig. 1.32B). The controversy was resolved in 1999 [128], in favor of proposal B.

For lower-order cyanocuprates, it was already clear at an early stage that the organic group and the cyanide were bound to the same copper atom. An elegant NMR study by Bertz [129] on 13C-labeled MeCu(13CN)Li showed that a coupling of 22 Hz was present between the cyanide carbon atom and the methyl group, which could only be the case if both groups were bound to the same copper atom. This spectroscopic evidence was later confirmed by X-ray crystal structure determinations of [t-BuCu(CN)Li(OEt)2] [130] (Fig. 1.33) and [2,6-Trip2C6H3Cu(CN)Li] (Trip = 2,4,6-(i-C3H7)3C6H3) [131], which appeared in the literature at practically the same time.

It appeared that [t-BuCu(CN)Li(OEt)2] exists in the solid state as a dimer [t-BuCu(CN)Li(OEt)2]2. Two anionic t-BuCu(CN) units, with almost linear geom-

Fig. 1.32. Proposed structures for higher-order cyanocuprates.

Fig. 1.33. Structure of [t-BuCu(CN)Li(OEt)2] in the solid state.
etries, are linked together through bridging cyanide group nitrogen atoms to two lithium cations. Each lithium cation adopts a tetrahedral coordination geometry as a result of coordination of two diethyl ether molecules. The overall structural features of \([2,6\text{-Trip}_2C_6H_3Cu(CN)Li(OEt)}_2\)] are very similar to those of \([t\text{-BuCu(CN)Li(OEt)}_2]\).

NMR investigations \([129, 132, 133]\), EXAFS and XANES studies \([134–136]\), and theoretical calculations \([127, 137, 138]\) performed on higher-order cyanocuprates strongly suggested that the cyanide anion was not bound to copper in these \(R_2Cu(CN)Li_2\) species. Additional evidence was provided by the first X-ray crystal structure determinations of “higher-order” cyanocuprates: \([[(C_6H_4CH_2NMe_2-2)_2Cu(CN)Li_2][139] (Fig. 1.34) and \([[(tBu)_2Cu(CN)Li_2][130] (Fig. 1.35).\]

The molecular structure of the first compound comprises a polymeric chain, consisting of alternating \([(C_6H_4CH_2NMe_2-2)_2Cu] anionic and \([Li_2(CN)(THF)_4] cationic units. In the cationic unit, two lithium atoms are end-on bridged by the cyanide group, and two additional THF molecules are coordinated to each lithium atom. The fourth coordination site is occupied by the nitrogen atom of the adjacent \((\text{dimethylamino})\text{methylphenyl} group of the \([(C_6H_4CH_2NMe_2-2)_2Cu] anionic unit.

On the basis of molecular weight determinations by cryoscopy in THF and conductivity measurements, it was concluded that the polymeric chain breaks up in solution to form smaller aggregates, probably giving rise to solvent-separated

Fig. 1.34. Structure of polymeric \([(C_6H_4CH_2NMe_2-2)_2Cu(CN)Li_2(THF)_4]\), in the solid state.

Fig. 1.35. Structure of \([t\text{-Bu}_2Cu][Li_2CN(THF)_4(PMDTA)_2]\) in the solid state.
ion-pairs. The presence of donor solvents, THF in this case, may greatly contribute to the (thermodynamic) stability of a particular structure. This may be inferred from the observation that the use of a less polar solvent such as benzene induces a disproportionation reaction, giving the neutral homoleptic cuprate $[\text{Cu}_2\text{Li}_2\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2\text{-2}]_4$ (discussed previously) and LiCN.

The structure of $[\text{t-Bu}_2\text{Cu(CN)Li}]$ in the solid state consists of isolated $[\text{t-Bu}_2\text{Cu}]$ anionic units and $[\text{Li}_2\text{CN(THF)}_2(\text{PMDTA})_2]$ cationic units (Fig. 1.35). The structural features of the linear $\text{R-Cu-R}$ arrangement are identical to those observed for other $[\text{R}_x\text{Cu}]$ anionic units discussed previously (cf. Fig. 1.31). The $[\text{Li}_2\text{CN(THF)}_2(\text{PMDTA})_2]$ cationic unit consists of a central cyanide moiety, to which two lithium atoms are bound in end-on fashion. Coordination saturation at each lithium atom is achieved by coordination of the three nitrogen atoms of the PMDTA molecule and one THF molecule, rendering each lithium atom pentacoordinate. Recent $^1\text{H}, ~^6\text{Li}$ HOESY experiments showed that this ionic structure found in the solid state is probably retained in polar solvents such as THF [140].

The solution structures of cyano-Gilman cuprates and lower-order cyanocuprates have been studied by cryoscopic measurements in THF [141]. The results of this study have in several cases shown ways to obtain useful single crystals of several higher- and lower-order cyanocuprates and consequently to determine their structures in the solid state. It appears that a number of these cyanocuprates retain their observed solid-state structure when dissolved in THF.

1.5 Concluding Remarks

This review substantiates the earlier opinion [29, 45] that the various types of organocopper compounds known today are almost always highly aggregated species. In spite of this structural information, it remains very difficult (and often also incorrect) to correlate a given structural feature of an organocopper or cuprate reagent with its specific reactivity. It always has to be kept in mind that X-ray crystal structural information is generally obtained from crystalline material that selectively crystallized out of a solution existing as a complicated equilibrium mixture of a number of aggregates, rather than as a solution of one pure compound. The aggregate that crystallizes from solution is the thermodynamically most stable one, and this is often the kinetically less reactive species. Indeed, there are only a very few examples of compounds for which it has been proven that the structure as observed in the solid state is retained in solution. One such is $[\text{Cu}_2\text{Li}_2\text{C}_6\text{H}_4\text{CH}_2\text{NMe}_2\text{-2}]_4$ in apolar solvents such as benzene.

Another factor that complicates understanding of reaction mechanisms and of the actual species involved in reactions of organocopper compounds is the strong tendency of organocopper compounds and cuprates to aggregate with metal halides. These metal halides are often formed as unavoidable co-products when an organocopper compound or an organocuprate is applied as a reagent in organic synthesis. This means that, during a reaction, the initial reagent is gradually con-
verted into another aggregate with different structural features and, consequently, often a different reactivity (cf. Eqns. 1 and 2 in Scheme 1.24) [95].

\[ 5 \text{Cu} \text{C}_6\text{H}_4\text{NMe}_2\cdot\text{Li} + 2 \text{IC}_{6}\text{H}_4\text{NMe}_2\cdot\text{Li} \rightarrow \text{Cu}_5\text{C}_6\text{H}_4\text{NMe}_2\cdot\text{Li}_2 + 2 \text{IC}_{6}\text{H}_4\text{NMe}_2\cdot\text{Li}_2 \]  

Scheme 1.24.

To correlate the structural features of a specific copper or cuprate reagent with its reactivity, a better understanding of the interaction of such species with metal halides, ligands, solvents, and, last but not least, substrates is required. Such investigations have already begun and seem to have a promising future. In an elegant NMR study by Krause et. al. [23] it was demonstrated that the reaction between \( t\)-BuCu(CN)Li and methyl propiolate (see Scheme 1.25) could be monitored by \( ^{13}\text{C} \) NMR. At \(-100^\circ\text{C}\), resonances attributable to the presence of a \( \pi \)-complex between the organocuprate and the substrate were observed. After the temperature had been raised to \(-40^\circ\text{C}\), the \( ^{13}\text{C} \) NMR spectrum of a vinylcupper intermediate was observed. Finally, hydrolysis afforded the final product.

More recently, \( ^1\text{H}, \text{^6Li} \) HOESY studies of the structures of cuprates in solution have been undertaken [24, 140]. As outlined in the previous section, the solid-state structures of neutral cuprates such as \( \text{Cu}_2\text{Li}_2\text{Ph}_4(\text{OEt}_2)_2 \) may be described in terms of contact ion-pairs (CIPs) of \( [\text{CuPh}_2]^– \) and \( [\text{Li}(\text{OEt}_2)]^+ \). These studies show that such “simple” cuprates exist in solution in equilibrium between the CIPs and solvent-separated ion-pairs (SSIPs), shown schematically for CuLiMe₂ in Fig. 1.36.
It has become evident that essentially only the CIP is present in less polar solvents such as diethyl ether, whereas in solvents with a strong affinity for Li\(^+\), such as THF, the major species in the equilibrium is the SSIP. Moreover, this difference in the structural features of the species present in solution could be directly related to its reactivity. In the Michael addition reaction it is most likely that the reactive species is the CIP, as shown by the following experiments. No reaction was observed when CuLiMe\(_2\) was treated with 2-cyclohexenone in the presence of two equivalents of 12-crown-4; the pure SSIP is present \[142\]. Furthermore, it has been observed that the rate of the reaction between CuLiMe\(_2\) and 2-cyclohexenone in THF is considerably slower than that of the same reaction in diethyl ether. Again, this solvent dependence can be explained by a CIP/SSIP equilibrium, which in the case of THF as the solvent lies predominantly on the SSIP side. These data are in perfect agreement with the logarithmic reactivity profiles of reactions between CuLiR\(_2\) and enones in diethyl ether and THF as reported by Bertz \[143, 144\].

Moreover, recent theoretical calculations for this type of reactions \[145\] point to a transition state involving a CIP type of structure for the cuprate moiety (see Fig. 1.37).

The present challenge for scientists is to use modern spectroscopic techniques (such as NMR, in situ IR, in situ EXAFS, and others already available, or which will become available in the near future) in combination with advanced theoretical calculations to obtain new insights into the actual mechanisms and species that play roles in reactions of well known organocopper and cuprate compounds.

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**Fig. 1.36.** Equilibrium between CIP and SSIP structures.

**Fig. 1.37.** Calculated structure of the transition state in the reaction between CuLiMe\(_2\) and 2-cyclohexenone.
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