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POLYNUCLEAR ARYL-COPPER SPECIES AND NEUTRAL ARYL-CUPRATES WITH A CHIRAL-CH(Me)NMe$_2$ ORTHO SUBSTITUENT

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At present, there are still few structurally characterized examples of pure organocopper species. Moreover, of the many compounds known that are related to diorganocopper lithium ("cuprate") reagents there has been only one report of a structurally elucidated neutral cuprate, i.e. $Cu_2Li_2(C_6H_4CH_2NMe_2\text{-}2)_4$, **1**.[2-4] As shown schematically in Fig. 1a, this molecule has a planar tetranuclear structure in which each aryl group asymmetrically bridges a copper lithium pair (*vide infra*). It is also the only neutral cuprate species for which the polynuclear structure in solution could be unequivocally established by NMR (observation of $^1J(^7Li\text{-}^{13}C)$ as well as $^1J(^{107}Ag\text{-}^{13}C_{ipso})$ and $^1J(^7Li\text{-}^{13}C_{ipso})$ in the isostructural argentate compound). Other polynuclear cuprates whose structures are known from X-ray structure determinations, are the anionic species (with solvated lithium cations) $[Li_2Cu_3Ph_6]^-$,[5] $[Cu_5Ph_6]^-$,[6] and $[LiCu_4Ph_6]^-$,[7] in which the polyhedral cage structure is held together by bridging phenyl groups.

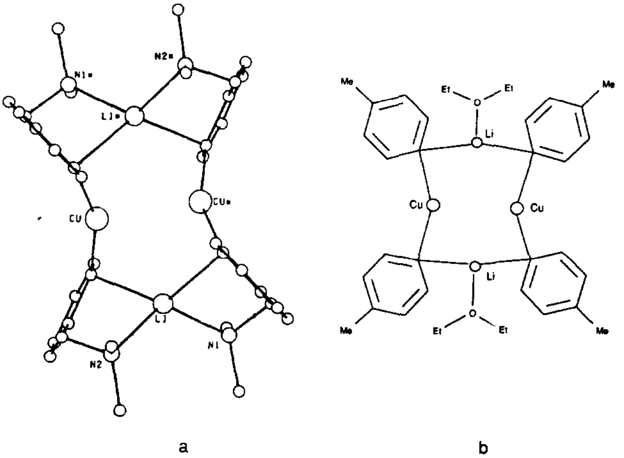


Fig. 1a: Structure of the neutral cuprate **1** (aryl groups viewed from the side) Fig. 1b: Proposed structure of $Cu_2Li_2(p\text{-}Tol)_4.Et_2O$ (see ref. 8)

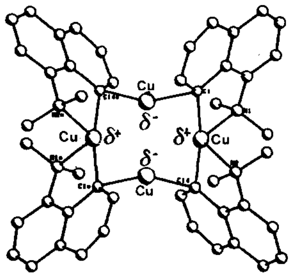
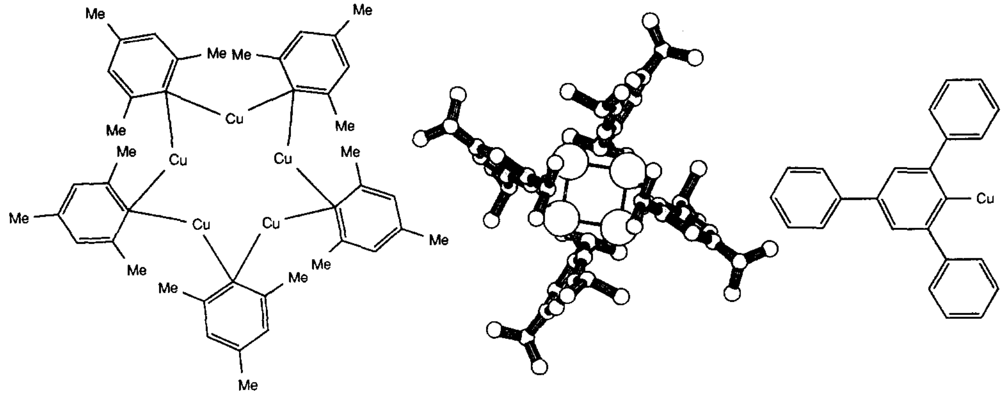


Fig. 2. Structure of $Cu_4(naphthylNMe_2\text{-}8)_4$ with four- and two-coordinate Cu sites (ref. 18)

The structural features of **1**, especially the square-planar Cu_2Li_2 core, are frequently used as a key model in many mechanistic discussions of cuprate reactions, for instance for the conjugate addition of related neutral alkylcuprate species to enones.[10-13] It must be noted, however, that the actual core in **1** is not square-planar but is distorted with Cu-Li-Cu and Li-Cu-Li angles of 57.9(1) and 122.1(2)°, respectively.[3] Particularly interesting is the asymmetry of the bridge-bonding mode of aryl groups to the Cu_2Li_2-core which suggests that the aryl groups are mainly bonded to copper atoms and are only weakly coordinated to the Li atoms.[2,4] This suggestion seems to be corroborated by the results of computational studies for $Cu_2Li_2Me_4$.[10] The amine ligand in **1** functions as an intramolecularly positioned "solvent molecule" which does not affect the basic structural features of the cuprate. This is supported by results of previous[8] and recent[9] studies on di-p-tolylcopperlithium that have revealed that this cuprate has a similar tetranuclear structure: i.e. $Cu_2Li_2(p\text{-}Tol)_4.2Et_2O$ (**2**) with one Et_2O molecule coordinating to each Li atom, see Fig. 1b.

In a recent paper[4] we pointed out that for both **1** and **2** the copper centres should be considered as the nucleophilic sites which are, for example, particularly suited for alkene-copper π-bonding in reactions with enones,[3,13] while the lithium centres function as electrophilic sites which interact with either solvent or substrate heteroatoms. The stronger the latter interactions become the more favourable it is for the occurrence of lithium cation solvation which results in formation of anionic cuprate species with Cu/Li-ratios higher than one. The knowledge that a neutral cuprate species may convert into an anionic one, be it polynuclear (*vide supra*) or mononuclear (e.g. $[Me_2Cu][Li(12\text{-crown-}4)_2])$[14], by solvent or ligand interaction is important for an understanding of the influence of solvents or additional ligands on the reactivity of cuprates in organic synthesis.[4]

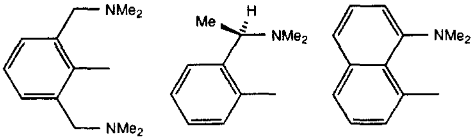
One of the factors that can highly affect the bonding mode of the organo groups in organocopper chemistry, has a steric origin. This is clearly demonstrated by the change of the aryl-group to copper bonding mode in a series of three 2,4,6-trisubstituted phenylcopper compounds: **3**, $Cu_5(C_6H_2Me_3\text{-}2,4\text{-}6)_5$, [15]; **4**, $Cu_4(C_6H_2Pr^i_3\text{-}2,4,6)_4$ [16]; and **5**, $Cu(C_6H_2Ph_3\text{-}2,4,6)$,[17]see Fig. 3. Most probably due to the increasing steric bulk of the ortho-substituents in this series (Me < Pr^i < Ph) the symmetric 3c-2e (three centre-two electron) binding of the aryl to two copper atoms found in **3** changes into an asymmetric bridging mode involving a 2c-2e (two centre-two electron) aryl-Cu interaction with C_{ipso} π-bonding to a second copper atom in **4**. Finally, in **5** the ortho-phenyl substituents lead to a mononuclear copper compound with a 2c-2e C_{ipso}-copper bonding mode; this compound is monomeric because the C_{ipso}-Cu region is effectively shielded by the ortho-substituents from further interaction with other mononuclear units.[16]



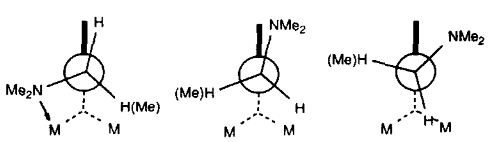
3 4 5

Fig. 3. Structures showing the effect of steric ortho-substituents on the (aryl)C_{ipso}-copper binding.

Currently we are studying the effect that a further α–substitution has on the structure and reactivity of aryl copper and cuprate compounds when one proton in the ortho alkyl substituent is already replaced by an NMe_2 group. The ligands **6**, **7**, and **8**, respectively (see Fig. 4) containing CH_2NMe_2, $CHMeNMe_2$, and NMe_2-substituted aryl groups are representative examples of those used in our study. In complexes of **8** the N-atom always resides close to the metal site, even when no N-M coordination occurs and hence, this gives rise to cuprate behaviour of the resulting $Cu_4(naphthylNMe_2\text{-}8)_4$ compound, see Fig. 2.[18]



6 7 8



A B C

Fig. 4. Heteroatom substituted aryl groups for the study of the interplay between chelation and steric hindrance.

Fig. 5 Newman projection along the C_{aryl}-C_{α}-bond in **7** when 3c-2e bridge bonded to two Cu^I atoms.

In **6** and **7** there is a considerable chelation and conformational flexibility in the bonds of ortho-substituents and consequently rotation around the C_{aryl}-C_{α}-bond leads to removal of the N-donor atom from the coordination sphete of the metal(s) bound to C_{ipso}.[4] Considering an aryl bridged species of **6**(**7**) there are various rotamers possible as shown by Newman projections along the C_{aryl}-C_{benzyl}-axis (Fig. 5). Rotamer A is the situation when the ortho substituent coordinates to one of the metal centres. In rotamer B M-N coordination is impossible and the Me_2NCH_2 group now has a large steric effect. Moreover, when not bonded the NMe_2 group will prefer to be in an anti-planar position with respect to the aromatic ring as shown by rotamer C. The latter conformation is in line with what we observed for the $-CH(CH_3)_2$ group in **4** (see Fig. 3). In the absence of M-N coordination this conformation can also be expected[19] for the -CH(Me)NMe_2 substituent of 7.

We already reported briefly[19] on the synthesis of copper compounds derived from the latter ligand, i.e. Cu{$C_6H_4CH(Me)NMe_2$-2-(*R*)} (**9**) and CuLi{$C_6H_4CH(Me)NMe_2$-2-(*R*)}$_2$ (**10**). One aim of our study was to investigate the suitability of these compounds for selective syntheses of triorganotin compounds. With minor success, mixed cuprates derived from **9** and RLi were also used for the stereoselective cuprate addition reactions to enones in which the chiral ligand **7** was meant to behave as a non-transferable group.[13]

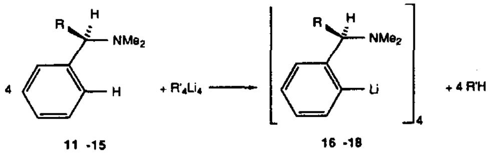
In this report we focus our attention on the synthetic and structural aspects of the chiral aryl copper **9** and the arylcuprate **10** with special emphasis on some of the stereochemical aspects of these compounds.

Synthetic aspects

The synthesis and isolation of pure arylcopper compounds is not a trivial affair,[20,21] and in fact, standard conditions for a successful synthesis cannot be given. Some general requirements for the successful synthesis and isolation of pure arylcoppers are[4]: i. the use of pure, halide free aryllithium compounds and preferably copper bromide with diethyl ether or dimethyl sulfide as the reaction solvent,[20,22] ii. the correct order and rate of addition,[20] iii. the correct temperature [23,24] and, iv. the use of exact 1/1 molar ratios of the reagents. Concerning requirement iv. excess copper(I) halide should, in most cases, be avoided in order to prevent the formation of organocopper-copper halide adducts. Examples of such adducts in which copper(I) halides are integral parts of the polynuclear structures are: $Cu_6Br_2(C_6H_4NMe_2\text{-}2)_4$,[25] Cu_4Br_2-{$C_6H_3(CH_2NMe_2)_2$-2,6}$_2$,[26] and Cu_4Br_2{(Z)-(2-$Me_2NC_6H_4$)C=C(Me)(C_6H_4Me-4)}$_2$.[27] Furthermore the presence of an excess of aryllithium could lead to cuprate formation which is undesirable since these species often have a solubility in hydrocarbon and ether solvents comparabe to that of the parent arylcoppers.[20]

The procedure we reported on some years ago[19] for the synthesis of 2-{(1-dimethylamino)ethyl}phenylcopper had a low yield (37%). Recent reinvestigation of the lithiation reaction of α-substituted N,N-dimethylbenzylamines[4] (**12-13**) with butyllithium revealed that, in contrast to the virtually quantitative ortho-lithiation reaction of the parent amine **11** (R = H) with butyllithium in diethyl ether (which is complete in about 48 h), the reaction of **12** (R = Me) was complete after 48 h but only afforded the lithiated product in a 50% yield (see Table 1). Most probably this is due to the formation of stable mixed butyl-aryllithium species [Li_4Bu_{4-n}{$C_6H_4CH(Me)NMe_2$-2}$_n$($C_6H_5CH(Me)NMe_2$)$_{4-n}$] (butyl:aryl ratio is 1:1). Accordingly, use of these reaction mixtures for the synthesis of corresponding arylcopper leads to concomitant formation of butylcopper, that decomposes immediately under the reaction conditions (-20°C) employed, and thereby limits the yield of Cu_4{$C_6H_4CH(Me)NMe_2$-2}$_4$ to 50%. For **12** it appeared that even prolonged reaction times (> 100 h) with BuLi did not increase the yield of lithiated product.

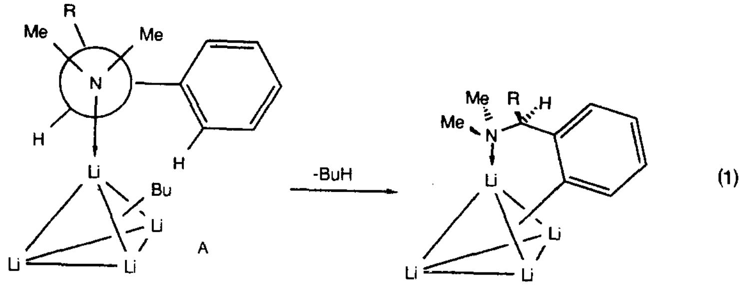
Table I.



R'Li	% of ortho-lithiation (reaction time)		
	11, R=H	**12**, Me	**13**,Et
BuLi[a]	~ 95 (48h)	~50 (48h)	~50 (48h)
t-BuLi[b]	~95 (**16**) (10 min)	~95 (**17**) (~1 h)	~95(**18**) ~(5h)

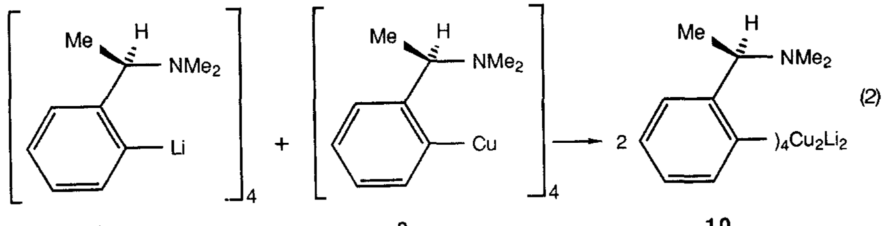
[a] In Et_2O/hexane 60/40. [b] In pentane. [c]. No reaction for **14**,i-Pr and **15**, t-Bu was observed with BuLi and t-BuLi

Moreover, lithiation of the amines **14** and **15** where R = i-Pr or R = t-Bu respectively, with the same reagent did not occur at all. Interestingly, the ortho-lithiation reactions of **11-13** with tert-butyllithium are much faster and even proceed in pentane. In this case the pure Li product **17** (R = Me) is formed quantitatively from **12** in 1 h. Although, as with BuLi, there is no lithiation of the benzylamines in which R is i-Pr and t-Bu , the route via t-butyllithium is highly preferable for the synthesis of the aryllithium compounds **16, 17,** and **18** with R = H , Me and Et, respectively. The lithiation of dimethylbenzylamines (eq. 1) can be perceived to occur in the following way: the initial step is the coordination of the amine function to the butyllithium polynuclear species which thus brings the butyl group into close proximity of the ortho C-H bond which will be metalated (situation A). Based on the X-ray data of 2-{dimethylamino)methyl}phenyllithium, situation A, as shown schematically in



eqn. 1, can promote intramolecular Li-H exchange and formation of the tetranuclear products **16-18**. The size of the R group then must be expected to have a large influence on the lithiation reaction because of its effect on the distribution of the C_{aryl}-C_{α} bond rotamers. The lack of reactivity of **14** and **15** indicates that for large R groups, the lone pair of the NMe_2 group, through which the initial coordination to the BuLi-aggregate occurs, is turned away from the ortho-C-H region. (Compare the formation of incompletely metalated products $Li_4Bu_{4-n}\{C_6H_4CH(Me)NMe_2\text{-}2\}_n\{C_6H_5CH(Me)NMe_2\}_{4-n}$, containing still unmetalated N-coordinated dimethylethylbenzylamine, from reaction of Bu_4Li_4 with $C_6H_5CH(Me)NMe_2$-2.)

From the 1:1 molar reaction of pure (*R*)-2-{1-(dimethylamino)methyl}phenyllithium **17** with copper(I) bromide at -20°C the arylcopper **9** was obtained as a yellow solid in 95% yield. The corresponding homocuprate **10** was obtained by mixing arylcopper **9** and aryllithium **17** in a 1:1 molar ratio in benzene at room temperature (eqn.2).



17 **9** **10**

Structural features

An X-ray crystal structure determination of $Cu(C_6H_3CH_2NMe_2\text{-}2\text{-}Me\text{-}5)$ **19** has shown this compound to be a tetramer in the solid state.[22,25] The four copper atoms are positioned in a butterfly arrangement, see Fig. 6A. The aryl groups are 3c-

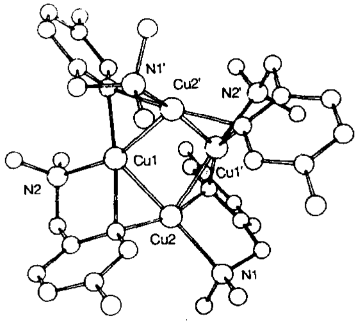
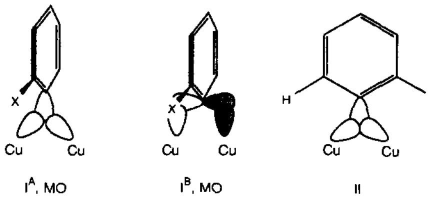


Fig. 6A. Structure of $Cu_4\{C_6H_3(CH_2NMe_2\text{-}2\text{-}Me\text{-}5\}_4$, **19**. (Cu..Cu 2.38 Å, Cu-N 2.12 Å, Cu1..Cu2'..Cu1' 76.1°, Cu2..Cu1..Cu2' 95.1°).



B. Rotamers I and II with aryl-to-Cu..Cu angles of 90° and 0°, respectively. Filled MO^A is bonding between C_{ipso} and Cu and between the two Cu atoms mutually; MO^B is the next higher MO representing back-donation from Cu to π^* aryl.

2e bonded to two copper atoms, while each NMe_2 group coordinates via its nitrogen lone pair to one of the copper atoms. Cryoscopic molecular weight determinations in benzene showed **19** to be also tetrameric in solution. The structure in the solid state of the related α-methyl substituted **9** is not yet known, but in view of its molecular weight in benzene we propose it to have a tetrameric structure similar to that established for **19**. It is interesting to note that of both ^1H and ^{13}C NMR spectra of **19** in tolulene-d_8 solution, in the temperature range 80 to -90 °C, show a single line for the NCH_2 protons as well as for the NMe_2 groups; this does not reflect the $\bar{4}$-axis symmetry that was found in the solid state structure of **19**. If in solution the solid state structure is retained and Cu-N coordination is stable on the NMR timescale, then the CH_2 protons and NMe_2 methyl groups would be diastereotopic and anisochronous. The seemingly simple NMR patterns could be due to the occurrence of various dynamic processes such as interaggregate exchange, an inversion process of the Cu_4 butterfly with retention of the Cu-N coordination (*vide infra*), or a Cu-N dissociation-association process with concomitant rotation of the aryl group around the C_{ipso}-C_{para} axis.

Before elaborating on the structural features of **19** and its α-methyl analogue **9**, it is essential to discuss the unique properties of 3c-2e copper-carbon bonding and its stereochemical consequences. As can be seen in the structure of **19** (Fig. 6A) each aryl group is almost perpendicularly orientated to the Cu--Cu vector. This can be explained by the minimal steric interference of the ortho substituent (also in the absence of Cu-N coordination) and the ortho H atom with the copper atoms (see Fig. 6B). Accordingly, rotation of the aryl ring around the C_{ipso}-C_{para} axis has a minimum energy rotamer I^A when the ring is perpendicular to the Cu--Cu vector and a maximum energy rotamer IB when this vector is coplanar with the aryl ring. From an molecular orbital point of view (see Fig. 6B) this rotation does not affect overlap of the C_{ipso} sp^2-hybrid orbital with the combination of empty orbitals on the Cu atoms. It is however, only in rotamer type I that the copper core can π-backdonate to the aryl ring; this will lead to enhanced kinetic stability of the aryl-copper bond.

An interesting point is that C_{ipso} is a chiral centre, provided that Cu-N coordination is stable on the NMR timescale (see Fig. 5A). In I, C_{ipso} is tetrahedrally surrounded by two dissimilar aryl-C atoms and two dissimilar Cu atoms. Assemblage of four of these units, as is realized in the tetranuclear butterfly structure of **19**, results in a stereochemistry at the bridging C_{ipso} centres where neighbouring centres have opposite configurations (denoted in this discussion as R^M and S^M); i.e. structure **19** contains alternate $(2\text{-}NMe_2CH_2C_6H_4)Cu_2$ units that are enantiomers of each other, see Fig. 7A.

Inversion of the Cu_4 butterfly with retention of the Cu-N coordination does not affect the configuration of the C_{ipso} centres. Only when Cu-N dissociation followed by recoordination with the other bridged Cu-atom occurs does this configuration also invert. Provided that each Cu atom remains three-coordinate, this is by necessity a cooperative process in which all four $(2\text{-}NMe_2CH_2C_6H_4)Cu_2$ units must participate. It must be noted that there is an alternative process involving intermediate C of Fig. 7A. In C, that contains two four-coordinate and two two-coordinate Cu atoms, all C_{ipso} centers will have the same configuration. Whereas for **19** this diastereoisomer is a possible intermediate it is for $Cu_4(naphthylNMe_2\text{-}8)_4$ a groundstate structure which results from the rigid arrangement of the chelating C and N donor atoms in monoanionic **7**. From the unique cuprate-like reactivity of the latter pure naphthyl copper compound it can be deduced that in a diastereomer of type C the electronic properties of the Cu^I centre have changed, i.e. in this structure the four-coordinate Cu centres are electrophilic sites whereas the two-coordinate ones are the nucleophilic sites, see Fig. 2. As soon as the NMe_2 grouping in **19**, on the NMR timescale, is not coordinated any discussion of the stereochemistry of the C_{ipso} centres is irrelevant because in this situation the Cu atoms will become equivalent.

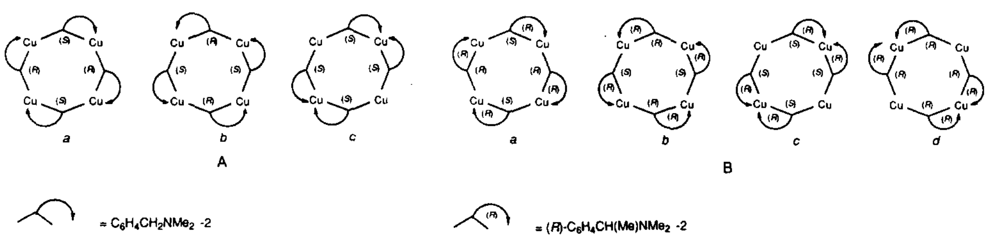


Fig. 7A. Stereochemistry at C_{ipso} in the slow exchange limit (a and b0 of $Cu_4\{C_6H_4(CH_2NMe_2)\text{-}2\}_4$; c shows a possible intermediate in the process a ↔b cf. the structure of $Cu_4(naphthylNMe_2\text{-}8)_4$ in Fig. 2.

B. Stereochemistry at C_{ipso} and the benzylic C atom in the slow exchange limit (a and b) of $Cu_4\{C_6H_4(CH(Me)NMe_2)\text{-}2\text{-}(R)\}_4$; c and d are intermediates in the process a ↔b.

Introduction of chiral information into the bridging aryl group by substituting the CH_2NMe_2 group in **19** for a $CH(Me)NMe_2$ group (i.e. **9**) with a chosen configuration (R^C) at the benzylic carbon atom, allows substantiation of the aforementioned concepts. Firstly this chirality can unambiguously establish the occurrence of Cu-N coordination, and secondly in case of stable Cu-N coordination, it can provide evidence for the stereochemistry at the C_{ipso} centres in the tetranuclear aggregate. The basis for the first supposition is that stable Cu-N coordination causes the N donor atom to take on a stable pyramidal arrangement, and thus, owing to the presence of the chiral benzylic C-centre in this situation, the coordinated NMe_2 methyl groups will be diastereotopic. The second supposition can be drawn because the stable configuration at the C_{ipso} centres is now accompanied by a chosen configuration at the benzylic centres. Consequently the [(*R*)-2-$NMe_2CH(Me)C_6H_4]Cu_2$ units are either R^CS^M or R^CR^M diastereometric units (R^C is the configuration at the benzylic C-centre and either S^M or R^M is that at the bridging C_{ipso} centre). Assemblage of the diastereomeric units, on the condition that each Cu-atom is three-coordinate, leads to a structure with alternating R^CS^M and R^CR^M diastereomeric units, Fig. 7B).

The ^{13}C NMR spectrum (see Table 2) of **9** at low temperature shows two distinctly different resonance patterns for the aryl groups. Furthermore, both NMe_2 resonances are split into two lines. This points to Cu-N coordination that is inert on the NMR timescale at this temperature (cf. ref. 19).The observation of two resonance patterns in a 1:1 intensity ratio can be explained by the presence of alternating R^CR^M and R^CS^M diastereoisomerically bridged units in a tetranuclear structure (see Fig. 7B). At T_{coal} ~ 0°C the two resonance patterns coalesce into one with concomitant coalescence of the four NMe resonances into one single line. This indicates that at higher temperatures the "Cu-N dissociation /N-inversion/C_α-N rotation/Cu-N"-association process is fast on the NMR timescale and thus renders the NMe_2 methyl groups homotopic and the Cu atoms equivalent thus leading to loss of the chiral information at the bridging C_{ipso} centres

When a racemic (*R*)/(*S*) mixture of $Me_2NCH(Me)C_6H_5$ is used for preparing **9** (**9'** in Table 2) the NMR spectra are much more complicated because in this case tetrameric diastereoisomers consisting of different combinations of R^C- and S^C-enantiomers of the dimethylaminoethylphenyl group are formed. This is clearly indicated by the patterns observed for the $^{13}C_{ipso}$ of **9'** at room temperature (see Figure 8) which shows the 7 lines originating from the 7 possible diastereoisomers that can be formed.

Table 2. Relevant ^{13}C NMR data for Cu_4R_4, **9** and $Cu_2Li_2R_4$, **10**.[a]

Compound	Temp.(°C)	$\delta^{13}C$						
		C1	C2	C6	α-c	α-CH_3	NCH	
9[b]	+30	153.1	159.2	145.6	71.3	16.5	42.8	
	-30	156.8	161.6	145.1	72.8	25.4	44.1	42.7
		150.2	157.2	146.1	69.5	78.1	41.4	35.1
9'[c]	+30	see text and Fig. 8 for C(1)						
	- 30	see text and Fig. 8 for C(1)						
10[b]	+30	169.2[d]	144.1	152.0	69.5	6.5	41.1[e]	
10'[c]	+30	169.2[d]	144.0	152.0	69.5	6.4	41.1[e]	

[a] In toluene-d_8 at 50.32 MHz on a Bruker AC 200 spectrometer; δ ppm with $SiMe_4$ as internal standard. [b] R = pure (*R*)-$Me_2NCH(Me)C_6H_4$. [c] R = racemic mixture of (*R*) and (*S*)-$MeNCH(Me)C_6H_4$. Several resonance are found for each of the ^{13}C atoms. [d] Four line pattern, See Fig. 9, ^1J ^7Li-^{13}C 7 Hz. [e] T_{coal} + 10°C. At -10°C NCH_3 appears as two singlets at 45.1 and 36.5 ppm.

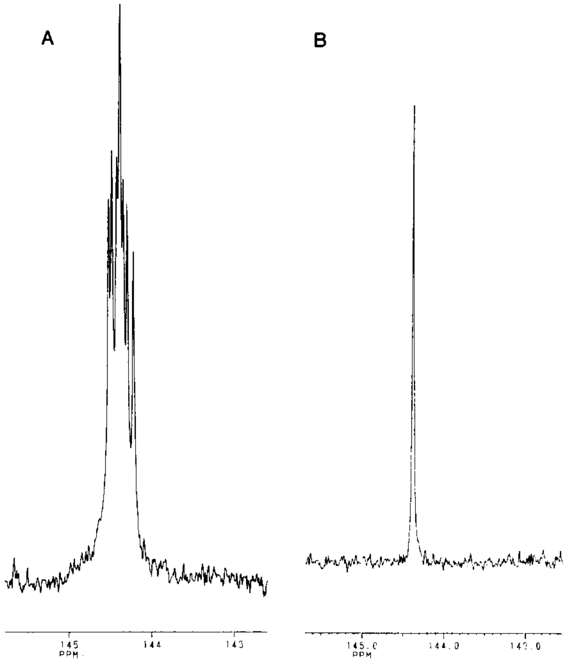


Figure 8A. $^{13}C_{ipso}$ resonances observed at 90° C in racemic $Cu_4\{C_6H_4CH(Me)NMe_2\text{-}2\}_4$, **9'**.

B. Same $^{13}C_{ipso}$ resonances observed at 90° C for $Cu_4\{C_6H_4CH(Me)NMe_2\text{-}2\text{-}(R)\}_4$ (see text).

It is of interest to find that this pattern does not coalesce until a temperature of 90°C is reached, since this indicates that at ambient temperatures interaggregate exchange is slow on the NMR time scale. The occurrence of this exchange on the laboratory timescale was established by a separate experiment in which the pure enantiomer $Cu_4\{C_6H_4CH(Me)NMe_2\text{-}2\text{-}(S)\}_4$ was mixed with $Cu_4\{C_6H_4CH(Me)NMe_2\text{-}2\text{-}(R)\}_4$ in a 1:1 molar ratio. After several hours the ^{13}C NMR spectrum of this solution was identical to that observed for **9'** obtained directly from the racemic aryllithium compound. Owing to the fairly low solublity of **9'** (and **9**) and the large number of diastereoisomeric species, the ^{13}C NMR spectra of 9' in the slow exchange limit of the Cu-N dissociation/association process did not prove informative.

Not only does interaggregate exchange occur between arylcopper species, it also takes place between arylcopper and aryllithium aggregates. In the case of ortho-Me_2NCH_2 and -(*R*)-$Me_2NCH(Me)$ substituted phenylcopper and phenyllithium compounds interaggregate exchange results in selective formation of 1:1 cuprates $Cu_2Li_2(C_6H_4CH_2NMe_2\text{-}2)_4$, (**1**) and $Cu_2Li_2\{C_6H_4CH(Me)NMe_2\text{-}2\text{-}(R)\}$, (**10**), see eqn. 2.

The tetranuclear structure of **1** has been confirmed in solution and in the solid state. Notable aspects of these tetranuclear Cu_2Li_2 species is their exclusive formation and surprising stability; in aromatic solvents no indication for the presence of "higher order" cuprates could be found. The ortho-CH_2NMe_2 group functions as a suitably positioned intramolecular solvent molecule that coordinates to lithium and so mimics the role of the ether molecule in simple neutral arylcuprate lithium species. Since the C_{ipso} atoms now bridge dissimilar metal atoms and again the aryl ring is ortho-substituted, the C_{ipso} atoms are chiral centres which can either have an S^M or R^M configuration. Structural information for **1**(see Fig. 1) revealed that all four C_{ipso} centres have the same configuration; see ref. 3 for an extensive discussion of the NMR spectra.

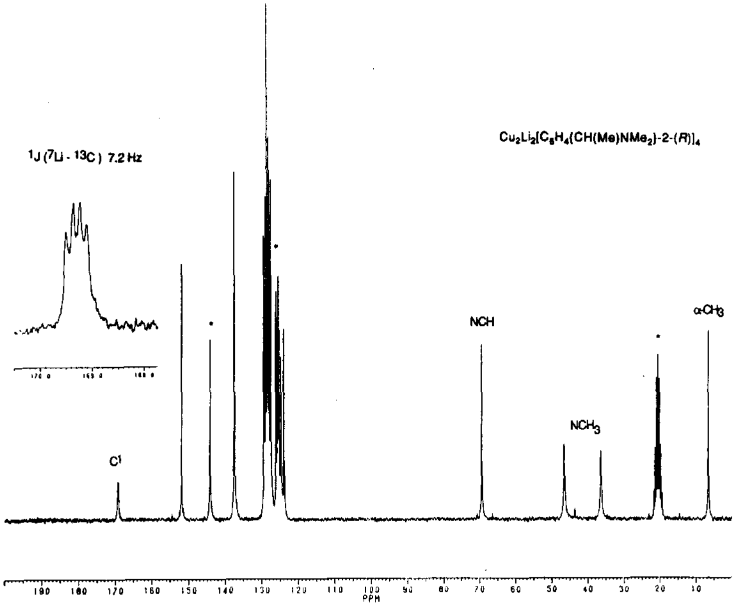


Fig. 9 ^{13}C NMR spectrum in toluene-d$_8$ (see *) at 10 °C of the neutral cuprate **10**.

Cryoscopic molecular weight determinations of **10** in benzene have shown that this homo (aryl)cuprate exists as a $Cu_2Li_2(aryl)_4$ aggregate in solution. Based on this fact and the data of ^{13}C NMR spectra recorded at various temperatures, (see Table 2) a structure for **10** is proposed that is similar to that established for **1**. This new cuprate has a structure that comprises eight chiral centra (the benzylic carbon atoms and the ipso carbon atoms of the four organo groups, cf. situation c or d (see Fig. 7B) in which the four-coordinate Cu centres are replaced by Li). Provided that there is no rotation of the aryl ring around the C_{ipso}-C_{para} axis, the configuration at C_{ipso} is now theoretically independent of Li-N coordination. The asymmetric bridging by C_{ipso} is unique, i.e. the aryl ring bridging the Cu--Li pair is primarily σ-bonded to copper. However, the bonding to lithium is not exclusively of a π-type but still contains some σ-character as is indicated by the $^1J(^7Li$-$^{13}C)$ of 7 Hz, see Fig. 9. The ^{13}C NMR spectra of **10** show only one resonance pattern for the aryl groups in the whole temperature range (-80°C - +100°C) studied. Below +10°C two resonances are observed for the NMe_2 groups, see Table 2, which indicates that Li-N coordination at this temperature is inert on the NMR time scale. It, moreover, establishes that in **10** neighbouring C_{ipso} centres have the same configuration as a consequence of coordination of $CH(Me)NMe_2$ substituents of neighbouring aryl units to the same type of metal atom; i.e. to Li as in **1**; in contrast, in **19** and **9** these substituents are each coordinated to a different metal atom site.

From the racemic cuprate, **10'**, obtained from the racemic aryllithium and copper compounds a complicated mixture of diastereoisomers is expected. At first sight, it was surprising to find that the ^{13}C NMR spectrum of **10'** is identical to that of **10** in the whole temperature range studied (-80°C + 100°C) (see Table 2). However, on the basis of the above discussion a likely explanation is that **10'** exists as an enantiomeric pair of diastereoisomers in which the C_{ipso} atoms and the benzylic carbon atoms have the same configuration (all (*R*) or all (*S*)). The explanation that the sole resonance pattern observed for the organo groups in the ^{13}C NMR spectra of **10'** is the result of fast interaggregate exchange, can be excluded since a scalar coupling ^7Li -$^{13}C_{ipso}$ of 7 Hz is observed in **10'** up to a temperature of 110°C. These results for **10** and **10'** suggests that the configuration of the benzylic carbon atom of one of the organo groups determines the configuration of the other seven chiral centra that come together to form the tetranuclear species of **10**; a process that could be identified as chiral assembling. As a consequence of puckering of the five atom chelate ring, the position of the α-methyl group will either be planar or anti-planar with respect to the aryl ring plane; one can thus conclude that of the $4R^{C}4S^{M}$ and $4R^{C}4R^{M}$ diastereomers the latter will be more stable, see ref. 16. These conclusions for the stereochemistry of chiral homocuprates are rather surprising and distinctly different from those drawn for the parent chiral arylcopper compound **9'**, for which a mixture of diastereoisomers was indeed observed (*vide supra*). These results demonstrate the profound influence that intramolecular coordination of chiral substituents can have on the stereochemistry of homo(aryl)cuprates.

Conclusions

Much research effort in organocopper chemistry is directed to the synthesis of natural products. Since the copper reagents used in these studies often possess heteroatom containing substituents, knowledge about the influence that potentially coordinating groups built into organocopper or cuprate molecules have on their structure-reactivity relationship is very relevant. The present results show that ortho-substitution of phenylcopper with the chiral $CH(R)NMe_2$ grouping has a distinct influence on the sterochemistry of the resulting organocopper aggregate. In both $Cu_4\{C_6H_4CH(Me)NMe_2\text{-}2\text{-}(R)$ or $(S)\}_4$, **9**, and the corresponding neutral aryl cuprate **10** this leads to selective formation of diastereomeric aggregates. In the case of **9** this is only apparent in the temperature range where Cu-N coordination results in a stable conformation at each copper centre. In the neutral cuprate **10**, heteroatom coordination occurs exclusively to Li. In this case the presence of a chiral $CH(Me)NMe_2$ ortho-substituent leads to diastereoselective cuprate aggregate formation (chiral assembling). Currently we are using these general findings to study the rational development of cuprate reagents for the purpose of asymmetric syntheses.

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Experimental.

Reactions were carried out under an atmosphere of dry nitrogen in vacuo, using standard Schlenk techniques. All solvents were dried and distilled under nitrogen prior to use. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 200 NMR spectrometer.

Synthesis of (*R*)-2-[1-(dimethylamino)ethyl]phenyllithium 12

To a solution of 30 mmol of (*R*)-[1-(dimethylamino)ethyl]benzene in 30 ml of pentane was added 30 ml of *t*-butyllithium in 20 ml of pentane. This solution was stirred for 12 h at room temperature, resulting in the formation of a cream coloured suspension. The solid material was then filtered off, washed three times with 10 ml portions of pentane and dried in vacuo. The resulting pure (*R*)-2-[1-(dimethylamino)ethyl]phenyllithium (**12**)was obtained as a white solid in 60% yield. In the same way racemic 2-[1-dimethylamino)ethyl]phenyllithium (**12'**) was prepared starting from racemic [1-dimethylamino)ethyl]- benzene.

Synthesis of 2-[1-(dimethylamino)ethyl]phenylcopper 9

To a stirred solution of pure **12** (20 mmol) in 25 ml of diethyl ether was added portionwise 20 mmol of solid CuBr in 30 min at -20°C. The resulting greenish-yellow suspension was stirred for 1 h at -20°C and then for a further hour at room temperature. The solvent was removed in vacuo and the remaining yellow solid was extracted with two 30 ml portions of warm (50°C) benzene. The combined benzene extracts were evaporated, and the yellow residue was washed two times with 20 ml portions of pentane and dried in vacuo. Pure (*R*)-2-[1-dimethylamino)ethyl]phenylcopper (**9**) was obtained as a yellow solid in 90% yield. The physical and spectroscopic properties were in accordance with those given in the literature.

Pure racemic 2-[1-(dimethylamino)ethyl]phenylcopper (**9'**) was prepared in the same way, starting from the racemic lithium compound **12'**.

Synthesis of the homocuprate $Cu_2Li_2\{(R)\text{-}2\text{-}Me_2NCH(Me)C_6H_4\}_4$ 10 and racemic $Cu_2Li_2\{2\text{-}Me_2NCH(Me)C_6H_4\}_4$ (10')

Equimolar amounts of the corresponding copper- (**9**, **9'**) and lithium- (**12** and **12'**) aryls were dissolved in benzene, giving a clear, almost colourless solution. The solvent was removed in vacuo and the remaining white solid was washed with pentane and dried in vacuo. The homocuprates **10** and **10'** were obtained as white solids in an almost quantitative yield.

Mol.wt. (by cryoscopy in benzene): found (calcd), 705 (753)

^1H NMR (toluene-d_8): δ 0.82 (d, α-CH_3, 3H), 1.81 (s, $N(CH_3)_2$, 6H) (at 20°C two resonances at 1.60 and 2.43, T_{coal} ~ 10°C), 4.10 (q, α-H, 1H), 6.95 (d, H_3, 1H), 7.18 (t, H_4 or H_5, 1H), 7.39 (t, H_4 or H_5, 1H), 8.85 (d, H_6, 1H). For ^{13}C NMR data see Table II and Fig.9.

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