Models for the reactive states of homocuprates: syntheses, structures and reactivities of [Cu$_2$Li$_2$Mes$_4$] and [Cu$_3$LiMes$_4$]†

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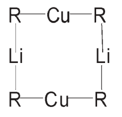
The synthesis and characterisation of two novel tetranuclear and thermally-stable lithium arylcuprates, [Cu$_2$Li$_2$Mes$_4$] and [Cu$_3$LiMes$_4$], are reported and [Cu$_3$LiMes$_4$] is shown to be a highly active promoter for the 1,4-addition of organolithiums to enones.

Lithium homocuprates, LiCuR$_2$ (R = alkyl, aryl), are one of the oldest and most commonly used reagents for the generation of carbon–carbon bonds *via* conjugate addition, and are thus key to many synthetic endeavours.[1] Although the structures and reaction mechanisms of these reagents has in the past been a subject of much debate, it is now generally accepted that their resting state (and probably the reactive species too) is the neutral dimeric form [R$_2$CuLi]$_2$ (**1**).[1] Fundamental to our current understanding of lithium homocuprates are the solid-state structural characterisations of [Cu$_2$Li$_2$Ph$_4$(OEt$_2$)$_2$] (**2**),[2] [Cu$_2$Li$_2$Ph$_4$(SMe$_2$)$_3$] (**3**),[3] [Cu$_2$Li$_2$(C$_6$H$_4$CH$_2$NMe$_2$-2)$_4$] (**4**),[4] [Cu$_2$Li$_2$(CH$_2$SiMe$_3$)$_4$(OEt$_2$)$_3$][5] and [Cu$_2$Li$_2$(CH$_2$SiMe$_3$)$_4$(SMe$_2$)$_2$]$_\infty$[6] which all contain dimeric structures of type **1** with the alkyl or aryl R group asymmetrically bridging the Cu and Li centres to form a 3 centre 2 electron (3c–2e) bond. In all of these structures the lithium is additionally coordinated by either a solvent donor molecule (Et$_2$O or Me$_2$S) or in the case of **4** an amino side-arm donor on the R group. Other solid-state structural studies of lithium homocuprates include a monomeric R$_2$CuLi homocuprate where R is the very bulky C$_6$H$_3$Mes$_2$-2,6 ligand,[7] and five ion-separated compounds containing [R$_2$Cu]$^-$ cuprate anions and Li$^+$ cations solvated by 12-crown-4 or other strongly coordinating ligands.[5,8,9] In addition several lithium homocuprate clusters with differing Cu to Li ratios have been reported: [Li$_3$Cu$_2$Ph$_5$(SMe$_2$)$_4$],[3,10] [Li$_5$Cu$_4$Ph$_9$(SMe$_2$)$_4$][3] and the anionic clusters [Li$_2$Cu$_3$Ph$_6$]$^-$[11] and [LiCu$_4$Ph$_6$]$^-$.[12] However, in contrast to the dimeric form **1**, at present there is no direct evidence to suggest that any of these non-stoichiometric species exist in any quantifiable amount in lithium diorganocuprate solutions.



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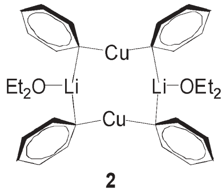

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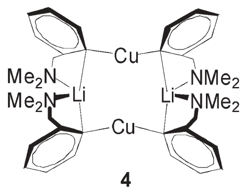

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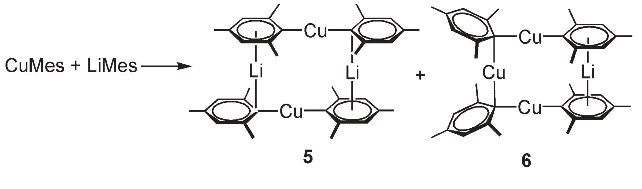
We now report on the synthesis, characterisation and reactivity of two novel lithium homocuprates, [Cu$_2$Li$_2$Mes$_4$] (**5**) and [Cu$_3$LiMes$_4$] (**6**), prepared from the 1 : 1 reaction of CuMes with LiMes (Mes = C$_6$H$_2$Me$_3$-2,4,6) in toluene (Scheme 1). The differing solubilities of **5** and **6** in hexane and toluene facilitated their separation and isolation as pure products in yields of 27 and 33% respectively (see ESI for experimental procedure†).

Although moisture sensitive, compounds **5** and **6** are unusually thermally stable for lithium cuprates (decomp. 189, 174 °C respectively). This can, at least in part, be attributed to their lack of β-hydrogens, thus avoiding decomposition by β-hydride elimination pathways. Both **5** and **6** were fully characterised in the solid-state using single-crystal X-ray diffraction‡ and in solution using multinuclear NMR spectroscopy.†

The solid-state structure of **5** (Fig. 1) is comparable in stoichiometry to other previously reported neutral homocuprates (**1**). However, the coordination mode of the Li cation differs from that observed in previously reported diarylcuprates (**2–4**), which all contain 3c–2e Li–C–Cu bonds centred upon the aryl *ipso*-carbons. In **5** each Li is effectively sandwiched between two co-planar mesityl groups, being η^6 coordinated to one (mean Li–C = 2.316(4) Å; range 2.271(4) to 2.365(4) Å) and sitting almost directly above (η^1) the *ipso*-carbon of the other (Li–C11 = 2.129(4) Å). The Ar$_2$Cu units in **5** are close to planar, C–Cu–C = 178.34(7)°, although the mesityl rings are twisted by approximately 9.6° to one another. This contrasts with the less obtuse C–Cu–C bond angles in **2–4** (range 157.7(1) to 168.0(2)°),[2–4] and is closer in magnitude to the C–Cu–C bond angles in the ion-separate species [Mes$_2$Cu]$^-$ (180.0(7)°)[13] and [Ph$_2$Cu]$^-$ (178.5(4)°[8] and 174.8(4)°[14]). Hence, in **5** the *ipso*-carbon sp^2 lone pairs are almost exclusively bonded to the Cu atoms giving 2c–2e Cu–C bonds, in preference to the 3c–2e bonds observed in **2–4**. This also results in a shortening of the Cu–C bond lengths (1.925(2), 1.936(2) Å in **5**) compared to those in **2–4** (range 1.936(3) to 1.948(3) Å):[2–4] *cf.* [CuMes$_2$]$^-$ (1.915(9) Å);[13] [CuPh$_2$]$^-$ (range 1.900(11) to 1.931(11) Å).[8,14] One possible explanation for the differing Cu–C bonding modes in



Scheme 1

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† Electronic supplementary information (ESI) available: Full experimental details and characterizations of **5** and **6**, details of the experimental protocol for measuring the addition reaction yields, additional information on the theoretical calculations including pictures of the 3D optimised structures, and additional crystallographic details. See DOI: 10.1039/b612554a

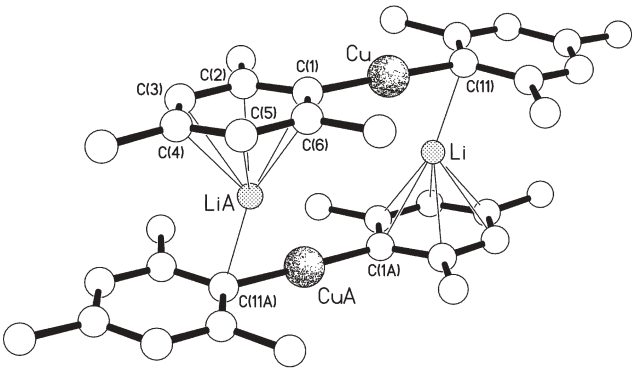


Fig. 1 The molecular structure of the C_i-symmetric complex **5**.

5 and **2–4** is that the additional Li-coordinating Lewis-basic donor ligands in **2–4** prevent the parallel stacking of the aryl groups due to steric considerations, hence forcing them to adopt a more orthogonal placement and favouring the formation of asymmetric 3c–2e Cu–C–Li bonds. Note however that Au–C 2c–2e bonds have been reported in the related gold complex $[Au_2Li_2(C_6H_4CH_2NMe_2\text{-}2)_4]$,[15] and similar aryl bridging modes have also been observed in heterobimetallic Li/Na/K–Mg/Zn systems.[16]

In order to further examine the nature of the bonding in **5**, we carried out density functional calculations (B3LYP) on the three possible conformers of $[Cu_2Li_2Mes_4]$ (Fig. 2).† In agreement with the structure obtained from X-ray crystallography, these calculations showed the optimised η^6,η^1 conformer **I** to be lower in energy than either the optimised η^6,η^6 (**II**) or η^1,η^1 (**III**) conformers. In addition, natural population analysis revealed a high positive natural charge on the Li centre in **I** (+0.945), which reflects the highly electrostatic nature of the Li-aryl interactions in this conformer. This compares to Li charges of +0.885 in **II** and +0.831 in **III**. The lower natural charge on Li in **III** can be accounted for by the additional participation of this atom in asymmetric 3c–2e Cu–C–Li bonds.

NMR spectroscopic studies† are consistent with retention of the η^6,η^1 dimeric structure of **5** in benzene solution. In particular, only one singlet peak is observed in the ^7Li spectra at −9.99 ppm. The high chemical shift of this peak can be attributed to ring current phenomena, whereby the Li sits in the magnetically anisotropic environment of the two aryl rings.[17]

The X-ray crystal structure‡ of **6** contains two very similar $[Cu_3LiMes_4]$ cuprate complexes (one of which is shown in Fig. 3, and the other in Fig. S5 in the ESI†) and a molecule of hexane. This tetranuclear cuprate complex can best be considered as either a dimer similar to **1** with one of the Li cations replaced by a Cu(I) centre, or alternatively as a $[Cu_4Mes_4]$ tetramer with one of the Cu(I) centres replaced by Li. Although it has previously been postulated that Cu_3LiR_4 species are present in small quantities in lithium diorganocuprate solutions,[18] as far as we are aware this is the first characterised example of such a species in either the solid state or solution. The Li cation in **6** is sandwiched directly between two aromatic rings with η^6,η^6 coordination (mean C–Li = 2.393(8) Å; range 2.304(7) to 2.531(8) Å). The Mes_2Cu_3 'half' of **6** is similar in structure to that of Cu_4Mes_4[19] with the Mes groups arranged approximately orthogonal to the Cu–Cu axes and coordinated to two Cu centres *via* their *ipso*-carbon to give 3c–2e Cu–C–Cu bonds. The C–Cu–C angle at Cu(3) is 159.60(16)/159.53(15)° whereas the mean C–Cu–C angle at Cu1/2 is 171.07(16)°. The average Cu–C bond distance in **6** for these 3c–2e bonds (Cu1–C1, Cu2–C21, Cu3–C1 and Cu3–C21) is 2.007(4) Å (range 1.999(4) to 2.016(4) Å): this is longer than the Cu–C bonds in **5** and comparable with Cu–C distances in Cu_4Mes_4[19] (mean 1.993(10) Å) and Cu_5Mes_5[20] (mean 1.96(3) Å). The remaining Cu–C bonds in **6** (Cu1–C11, Cu2–C31) are shorter (mean 1.936(4) Å), and are therefore similar in length to the Cu–C bonds in **5** and can likewise be considered 2c–2e bonds.

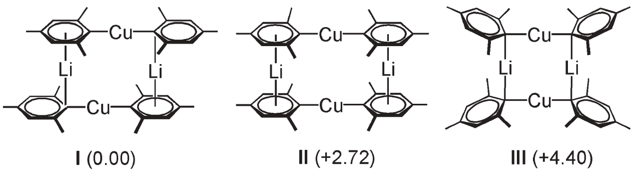


Fig. 2 Schematic diagram of the optimised structural conformers of $[Cu_2Li_2Mes_4]$ at the B3LYP/631AS level† (relative energies, kcal mol^{-1}).

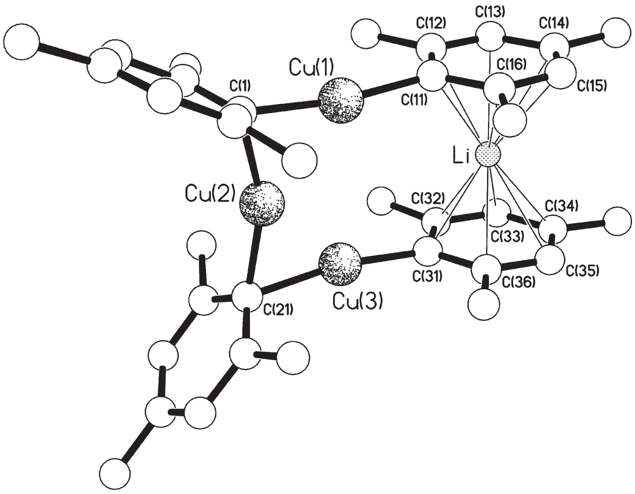
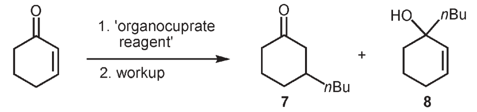


Fig. 3 The molecular structure of one of the two independent complexes present in the crystals of **6**.

Similar to **5**, **6** is highly stable in benzene giving just one peak in its ^7Li NMR spectrum at −11.02 ppm. The chemical shift for the Li centre in **6** is further upfield than that in **5** since the Li is now directly sandwiched in the middle of two eclipsed aromatic rings and therefore experiences the maximum effect of the two ring currents. Further NMR spectroscopic studies on separate samples of **5** and **6** in toluene showed no signs of any solution equilibria occurring, with both complexes retaining their respective tetranuclear structures even after heating at 80 °C for 48 h. It was previously postulated by van Koten and Noltes[21] that Cu_3LiAr_4 species (such as **6**) are present in lithium diarylcuprate solutions due to interaggregate exchange between $Cu_2Li_2Ar_4$ and Cu_4Ar_4 species (possibly *via* octanuclear intermediates). In agreement with this hypothesis, reaction of **5** with Cu_4Mes_4 (monitored *in situ* using ^7Li NMR spectroscopy) was observed to result in the formation of the Cu_3LiAr_4 species **6**. It is noteworthy that this reaction sits, as far as is detectable, on the side of **6** with no evidence of formation of **5** and Cu_4Mes_4 from the back reaction.

Finally it has previously been reported that CuMes can act as a reagent for promoting the 1,4-addition reactions of organolithium

Table 1 Addition reactions of lithium organocuprate reagents



Reagent	Solvent	Yield **7** (%)[a]	Yield **8** (%)[a]
CuMes + *n*BuLi	Toluene	61	3
	THF	66	8
	Et_2O	81	4
5 + 2*n*BuLi	Toluene	29	53
	THF	12	66
	Et_2O	52	7
6 + 2*n*BuLi	Toluene	82	0
	THF	96	1
	Et_2O	95	0

[a] Yields were determined by GC against an internal standard of decane and are based on *n*BuLi.

reagents (RLi) to enones.[22] The reactive organocuprate reagent responsible for the conjugate addition of the R group is thought to be a heteroleptic complex of general formula $[(MesCuR)Li]_n$, in which the Mes group acts as a non-transferable holding group.[22] A comparison of the application of the new lithium organocuprates **5** and **6** with CuMes in the promotion of 1,4-addition is given in Table 1 for the reaction of *n*BuLi with cyclohexen-2-one. Note that no transfer of the Mes group to the cyclic enone was observed in any of the reactions.

The reactivity results (Table 1) show **6** to be highly active and regioselective in promoting the conjugate addition reaction of *n*BuLi, giving yields in excess of those achieved for CuMes, with virtually zero contamination from 1,2-addition products. Possible explanations for the improved reactivity of **6** over CuMes include: the equilibrium reaction of **6** with *n*BuLi lies further on the side of the reactive heterocuprate [MesCu(*n*Bu)Li] than the reaction of CuMes with *n*BuLi does; or alternatively the higher Mes:*n*Bu ratio results in the formation of more reactive species with different stoichiometries, for example $[Cu_2Li_2Mes_3(n\text{Bu})]$.

Regioselectivities for the addition reactions using **5** are significantly worse than for **6** or CuMes, with a high degree of 1,2-addition suggesting incomplete heterocuprate formation and direct addition of unreacted *n*BuLi with the cyclohexenone. This is perhaps not surprising given this is the only one of the three reagents in which the Li : Cu ratio is greater than 1 : 1, therefore increasing the likelihood of excess *n*BuLi being present in solution. The regioselectivity of **5** is also extremely solvent dependent, giving predominately 1,2-addition in toluene or THF and 1,4-addition in Et_2O. Recent studies have shown organocuprates to be far more reactive in Et_2O than THF due to the formation of contact ion-pairs,[5] and this increased reactivity in Et_2O can perhaps explain the higher 1,4-selectivity in this solvent. Further studies on the structures and solution equilibria of **5** and **6** and their heteroleptic derivatives in different solvent systems are currently ongoing.

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Notes and references

‡ Crystal data for **5**: $C_{36}H_{44}Cu_2Li_2$, M = 617.67, $P2_1/n$ (no. 14), a = 13.3359(7), b = 8.6156(5), c = 14.4588(7) Å, β = 106.459(5)°, V = 1593.19(15) $Å^3$, Z = 2 (C_i symmetry), D_c = 1.288 g cm^{-3}, μ(Mo-Kα) = 1.357 mm^{-1}, T = 173 K, colourless plates; 5507 independent measured reflections, R_1 = 0.044, wR_2 = 0.106, 3405 independent observed absorption corrected reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta_{max}$ = 65°], 187 parameters. **6**: $C_{39}H_{51}Cu_3Li_2$, M = 717.36, $P2_1/c$ (no. 14), a = 17.3561(18), b = 28.142(2), c = 15.7048(11) Å, β = 111.095(8)°, V = 7156.6(10) $Å^3$, Z = 8 (2 independent complexes and one *n*-hexane in the asymmetric unit), D_c = 1.332 g cm^{-3}, μ(Cu-Kα) = 2.231 mm^{-1}, T = 173(2) K, colourless needles; 13781 independent measured reflections, R_1 = 0.036, wR_2 = 0.050, 4347 independent observed absorption corrected reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta_{max}$ = 143°], 800 parameters. CCDC 619872 and 691873. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b612554a

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