Electronic Supplementary Information

The Influence of Tetrahydrofuran on the Structures and Reactivities of Lithium Organo-Amidocuprates

Roberta Bomparola, Robert P. Davies*****, Stefan Hornauer
and Andrew J. P. White

Department of Chemistry
Imperial College London
South Kensington
London
UK SW7 2AZ

E-mail: r.davies@imperial.ac.uk
*Fax: +44 870 1300438*
Tel: +44 207 5945754

Experimental Procedures

General Remarks:

Decane (Aldrich, anhydrous 99+%), *n*-butyllithium (Sigma-Aldrich, 2.5M in hexanes) and 2-cyclohexene-1-one (Sigma-Aldrich 95+%) were used without further purification. CuMes was prepared according to literature procedures.[1] THF and diethylether were dried by distillation over sodium/benzophenone. Toluene was distilled from over sodium. Unless otherwise stated, all manipulations were carried out under nitrogen using either a glove box or double-manifold vacuum line. Dry ice 2-propanol baths were used for reactions at -78 °C. GC analyses were performed with an HP GC 5890 gas chromatograph equipped with FID detector and a 25m SGE BP1 capillary column (0.22 mm i.d., 0.25 micron film, dimethyl polysiloxane). The GC was calibrated with authentic product (3-butylcyclohexan-1-one, 1-butyl-cyclohexan-1-ol) and decane (Aldrich 99+%) as an internal standard. NMR spectra were recorded on a Bruker AV-400 spectrometer. External standards used were TMS (^{1}H) and LiCl/D$_2$O (^{7}Li).

Synthesis of [Cu$_2$Li$_2$Mes$_2$(N(CH$_2$Ph)$_2$)$_2$] (3):

s-BuLi in hexanes (1.3 M, 1.53 ml, 2 mmol) was added to a solution of dibenzylamine (340 mg, 2 mmol) in 5 ml toluene at 0 ˚C. The solution was allowed to warm to room temperature and stirred for 1 h to give a light red precipitate. A solution of CuMes (365 mg, 2 mmol) in 5 ml toluene was added drop wise to give a clear red solution which was filtered through celite and reduced under vacuum to approximately 2 ml. Storage at 4 °C for two days yielded colourless crystals (431 mg, 56%). M.p. 89 °C (decomp). ^{7}Li NMR – see Figure 1. See ref [2] for full spectroscopic analysis.

(a)

(b)
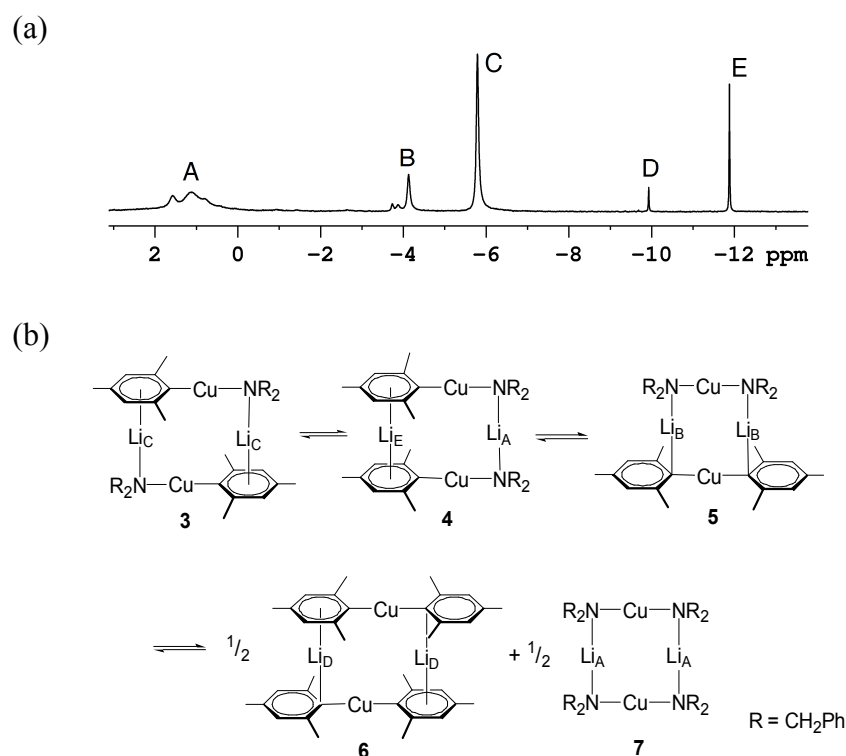
Fig. S1. (a) ^{7}Li NMR spectrum of **3** in [D$_8$]toluene (298K); (b) Assignment of peaks to structural isomers – see ref [2] for full details
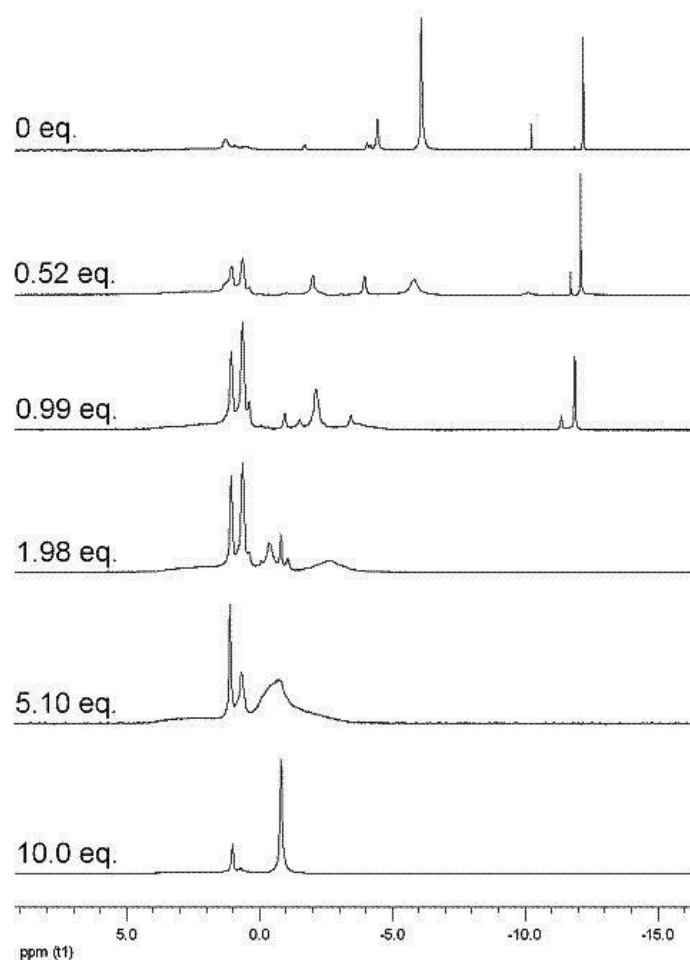
Fig. S2. The influence of thf on the solution-state structures of **3**: ^{7}Li NMR in [D$_8$]toluene + specified thf equivs (298K).

Synthesis of [MesCuN(Et)(CH$_2$Ph)Li(thf)$_3$] (9):

A solution of 2 mmol *N*-benzylethylamide (271 mg) in 3 ml toluene was treated at 0 °C with 2 mmol *s*BuLi (1.4 ml, 1.4 M solution in cyclohexane). The resultant light pink solution was warmed to room temperature and stirred for 1h. A solution of 2 mmol (365 mg) CuMes in 5 ml toluene was added slowly and the reaction mixture stirred for 15 min. The mixture was reduced in volume under vacuum to yield 1 ml of a viscous solution to which 0.5 ml of thf was added. After one week at -20 °C, light pink crystals of **9** suitable for X-ray crystal structure analysis were formed. Yield = 113 mg (22 %). Collection of elemental analysis data on **9** was precluded by its high air and temperature sensitivity. ^{1}H NMR (500.1 MHz, [D$_8$]thf, 298 K): δ = 8.03–6.60 (m, 7H, NCH$_2$C$_6$*H$_5$* and C$_6$*H$_2$*(CH$_3$)$_3$), 4.24-3.91 (m, 2H, NC*H$_2$*C$_6$H$_5$), 3.43 (s, 12H, thf), 2.91–2.70 (m, 9H, *o*-C*H$_3$*, *p*-C*H$_3$*), 2.24-1.81(m, 5H, C*H$_2$CH$_3$*), 1.39 (s, 12H, thf) – note that solution decomposition to give [CuMes]$_n$ and [PhCH$_2$(Et)NLi(thf)$_x$]$_{n'}$ (see manuscript) results in more than one peak for each assignment. ^{7}Li NMR (194.37 MHz, [D$_8$]thf, 298 K): δ = 2.00 ([PhCH$_2$(Et)NLi(thf)$_x$]$_{n'}$), -0.59 (**9**).

Logarithmic Reactivity Profiles: Cuprate preparation and reaction

The procedure used was an adaptation of that reported by Bertz, Ogle and Rastogi for 1,4-addition of *N*-silylamidocuprates to Chalcone [3]. 4 mmol of *n*-BuLi (1.6 ml, 2.5 M in hexanes) was added to a solution of 4 mmol dibenzylamine (0.77 ml) in Et_2O or thf (40 ml) at -78 ℃. The solution was warmed to room temperature and stirred for 0.5 h to give a solution of lithium dibenzylamide. Meanwhile a suspension of CuI (4 mmol, 0.76 g) in the same solvent (40 ml) was cooled to -78 ℃ and 4 mmol *n*-BuLi (1.6 ml, 2.5 M in hexane) was added. The reaction mixture was stirred at -78 ℃ for 6 min, annealed at 0 ℃ for 3 min and cooled to -78 ℃ for 6 mins to give a suspension of *n*BuCu. The chilled solution of lithium dibenzylamide was transferred *via* cannula to the *n*BuCu suspension and the reaction mixture was stirred at -78 ℃ for 6 min, 0 ℃ for 6 min, and -78 ℃ for 6 min. The resultant solution was divided in 4 equal parts. Each one of the four portions was treated with 1 mmol of 2-cyclohexen-1-one (0.11 ml) at -78 ℃. The reactions were quenched with the 6 ml of a saturated solution of NH_4Cl after 4, 36, 360 and 3600 seconds respectively. The organic layer was then separated and the aqueous layer was washed with Et_2O (2 x 5 ml). The combined organic layers were dried over anhydrous $MgSO_4$. After filtration, 1 mmol of decane (0.2 ml) was added and the solutions were analysed via GC.

[1] T. Tsuda, T. Yazawa, K. Watanabe, T. Fujii and T. Saegusa, *J. Org. Chem.*, 1981, **46**, 192.

[2] R. P. Davies, S. Hornauer and P. B. Hitchcock, *Angew. Chem. Int. Ed.*, 2007, **46**, 5191.

[3] S. H. Bertz, C. A. Ogle and A. Rastogi, *J. Am. Chem. Soc.*, 2005, **127**, 1372-1373

Theoretical Calculations

All calculations were carried out with a Gaussian 03 package.[1] The density functional theory method was employed using the B3LYP hybrid functional.[2] Structures were optimised with a basis set consisting of the all electron SVP basis set by Horn and Ahlrichs[3] for copper and 6-31G(d)[4] for the other atoms in neutral species, 6-31+G(d)[4] in anionic species. The method and basis set used here (denoted as B3LYP/631AS) have been applied to the optimisation of other lithium cuprates and are known to give reliable results.[5] Natural charges were calculated by natural population analysis at the same level used for geometry optimization.[6] Frequency analysis was carried out after geometry optimization to confirm the models were true energy minima with no imaginary frequencies.
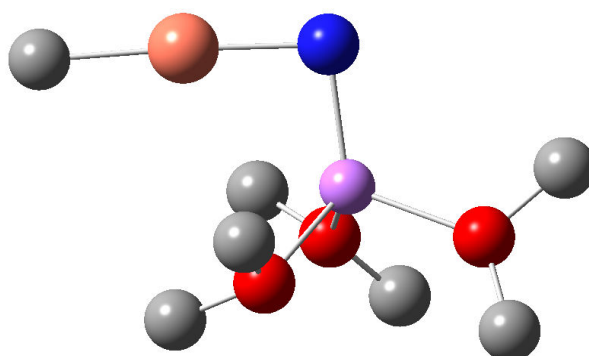
Figure S3. 3D optimised structure of $CH_3CuNH_2Li(OMe_2)_3$ (orange = Cu; purple = Li; grey = carbon; blue = nitrogen; hydrogen atoms not shown for clarity). C_1-symmetry. E = -2208.91355846 au. Cu-C = 1.934 Å; Cu-N 1.942 Å; Cu-Li = 2.879 Å; Li-N = 1.945 Å; Li-O = 2.047, 2.035, 2.037 Å; C-Cu-N = 177.00°; Cu-N-Li = 95.57° Natural charges: Li +0.844, Cu +0.490, C -1.209, N -1.479, O -0.621, -0.626, -0.633.
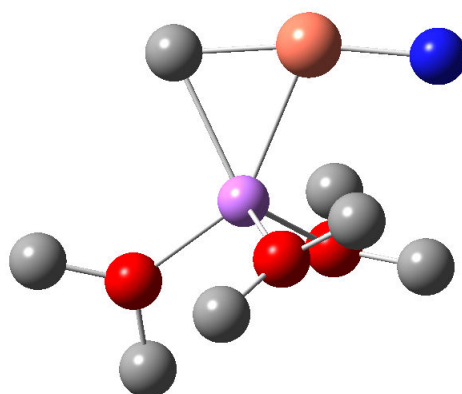
Figure S4. 3D optimised structure of $(Me_2O)_3LiCH_3CuNH_2$ (orange = Cu; purple = Li; grey = carbon; blue = nitrogen; hydrogen atoms not shown for clarity). C_1-symmetry. E = -2208.89105273 au. Cu-C = 1.963 Å; Cu-N 1.887 Å; Cu-Li = 2.455 Å; Li-C = 2.370 Å; Li-O = 2.015, 2.046, 2.037Å; C-Cu-N = 171.75°; Cu-C-Li = 68.28° Natural charges: Li +0.823, Cu +0.519, C -1.303, N -1.386, O -0.630, -0.637, -0.644
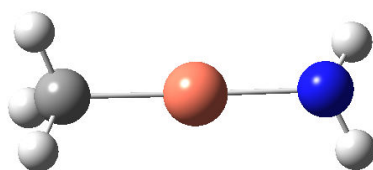
Figure S5. 3D optimised structure of $[CH_3CuNH_2]^-$ (orange = Cu; grey = carbon; blue = nitrogen; white = hydrogen). C_1-symmetry. E = -1736.23457680 au. Cu-C = 1.960 Å; Cu-N 1.914 Å; C-Cu-N = 176.28°; Natural charges: Cu +0.544, C -1.293, N -1.504

[1] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople, *Gaussian 03, revision C.02*, Gaussian Inc., Wallingford CT, 2004.

[2] A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648.

[3] A. Schaefer, H. Horn, and R. Ahlrichs, *J. Chem. Phys.*, 1992, **97**, 2571; A. Schaefer, C. Huber and R. Ahlrichs, *J. Chem. Phys.*, 1994, **100**, 5829.

[4] See W. J. Hehre, L. Radom, P. con Ragué Schleyer and J. A. Pople, *Ab Initio Molecular Orbital Theory*, Wiley, New York, 1986 and references therein.

[5] M. Yamanaka, A. Inagaki and E. Nakamura, *J. Comput. Chem.*, 2003, **24**, 1401.

[6] E. D. Glendening, A. E. Reed, J. E. Carpenter and F. Weinhold, *NBO Version 3.1*.

X-Ray Crystallography Supporting Information

Indexing of the diffraction images, and indeed observation of the images themselves, revealed the crystal of **9** used for the experiment to suffer from some minor twinning. Various different approaches to the handling of this twinning were attempted, with the best results coming from the simplest approach of just using the diffraction peaks from the major component. It is the presence of this twinning in the crystal studied that we believe is responsible for the residual electron density peaks around the copper centre.

Table S1. Selected bond lengths (Å) and angles (°) for **9**.

Cu–N(1)	1.912(3)	Cu–C(11)	1.907(4)
Li–N(1)	2.041(8)	Li–O(20)	1.992(8)
Li–O(25)	1.962(8)	Li–O(30)	1.972(8)
Cu···Li	3.170(7)		
N(1)–Cu–C(11)	171.98(16)	N(1)–Li–O(20)	116.2(4)
N(1)–Li–O(25)	113.1(4)	N(1)–Li–O(30)	119.2(4)
O(20)–Li–O(25)	100.2(3)	O(20)–Li–O(30)	103.2(4)
O(25)–Li–O(30)	102.4(4)		
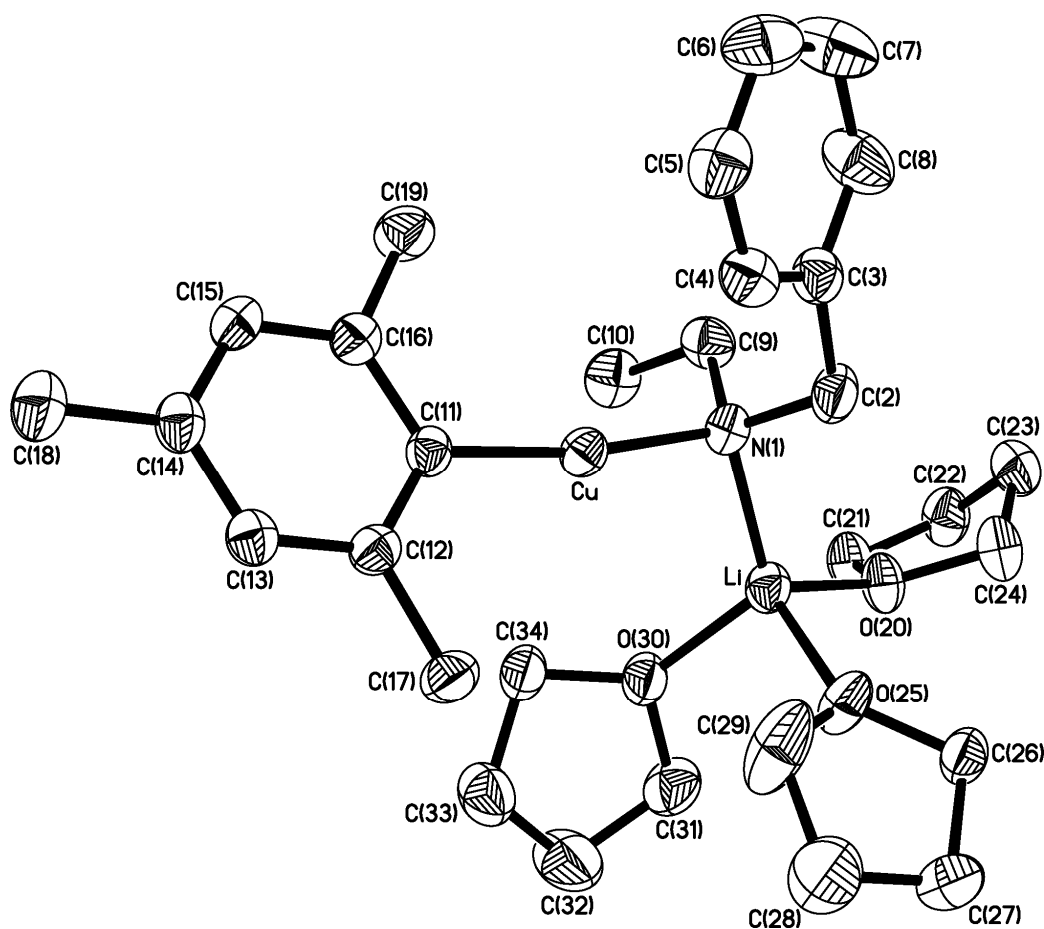
Fig. S6 The molecular structure of **9** (50% probability ellipsoids)