Tetrahedron Letters 51 (2010) 5226–5229

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Copper(I) thiophenolate in copper N-heterocyclic carbene preparation

Federico Cisnetti [a,b], Pascale Lemoine [c], Malika El-Ghozzi [d,e], Daniel Avignant [d,e], Arnaud Gautier [a,b,*]

[a] *Clermont Université, Université Blaise Pascal, Laboratoire SEESIB, BP 10448, F-63000 Clermont-Ferrand, France*
[b] *CNRS, UMR 6504, SEESIB, F-63177 Aubiere, France*
[c] *Université Paris Descartes, Laboratoire de Cristallographie et RMN biologiques UMR 8015, Faculté de Pharmacie, 4 avenue de l'Observatoire, 75006 Paris, France*
[d] *Clermont Université, Université Blaise Pascal, Laboratoire des Matériaux Inorganiques, BP 10448, F-63000 Clermont-Ferrand, France*
[e] *CNRS, UMR 6002, LMI, F-63177 Aubiere, France*

ARTICLE INFO

Article history:
Received 11 May 2010
Revised 15 July 2010
Accepted 21 July 2010
Available online 30 July 2010

Keywords:
N-Heterocyclic carbenes
Transmetallation
Copper
Thiophenolate

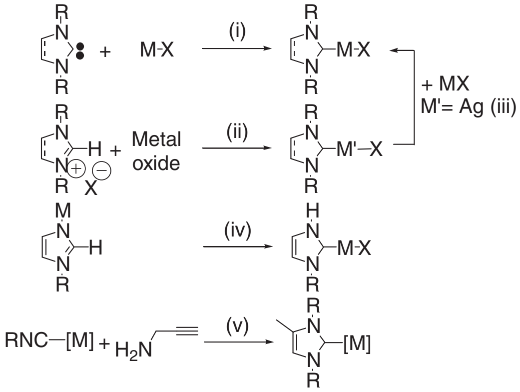
ABSTRACT

Copper(I) thiophenolate was considered as a copper source for the synthesis of Cu(I)-N-heterocyclic carbenes (Cu(I)-NHCs). It displayed a dual mode of reactivity allowing the synthesis of both thiophenolato-Cu(I)-NHCs via the free carbene in a one-pot procedure starting from imidazolium chlorides and chloro-Cu(I)-NHCs by a salt metathesis reaction starting from chloro-Ag(I)-NHCs.

Several methods are extensively used to generate metal-NHCs (NHCs: N-heterocyclic carbenes).[1] Besides the method reported by Lappert based on Wanzlick equilibrium, synthetic routes can be casted as follows: (i) the direct addition of free NHCs—isolated or prepared in situ—onto a metal precursor,[2] (ii) in situ deprotonation of imidazol(in)ium salts by metal oxides[3] (most frequently Ag_2O) that may be followed by (iii) carbene transfer[4] (iv) tautomerization of N-coordinated imidazoles[5], and (v) addition of propargylamine to isocyanide metal complexes[6] (Scheme 1).

Among the above-mentioned routes, methods (i) and (ii) + (iii) are probably the most widely used. The direct addition method—most frequently performed with carbenes prepared in situ—normally requires that reactions are conducted with exclusion of O_2, H_2O, and CO_2. The carbene transfer method is usually performed with silver NHCs as starting materials.[4] A drawback of method (iii)—particularly in the case of a transfer from a silver carbene—is the possibility of a redox side reaction between Ag(I) and a species containing the other metallic element. Indeed, several copper(I) complexes have been reported to be oxidized by silver triflate.[7a,7b] A similar redox reaction between Cu(I) and Ag(I) giving copper(II) compounds and silver metal is probably one of the reasons for the unsuccessful syntheses of some Cu(I)-NHCs using method (iii). In addition, oxidation by Ag(I) as an undesired reaction in carbene transfer with oxidizable metal centers (Ru(II), Rh(I)) has been described.[7c]

During a program devoted to the synthesis of anticancer Cu(I)-NHCs including chelating N-donor groups, we experienced unsuccessful NHC transfer to copper(I) chloride (silver transfer method) due presumably to metal-centered oxidation.[8] To circumvolve this problem, we hypothesized that copper(I) thiolates could replace CuCl as thiolato-copper species that are hardly oxidizable. For this purpose, we selected commercially available or easily prepared polymeric copper(I) thiophenolate.[9] However, by subjection of [AgCl(NHC)] complexes to carbene transfer reactions with CuSPh, we evidenced an unexpected conversion to [CuCl(NHC)] adducts (Scheme 2A). The reaction implies thus formally a carbene transfer

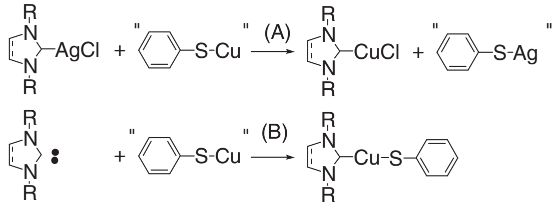


Scheme 1. General methods for the preparation of metal-NHCs.

---

* Corresponding author. Tel.: +33 4 73 40 76 46; fax: +33 4 73 40 77 17.
E-mail address: arnaud.gautier@univ-bpclermont.fr (A. Gautier).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.07.124



Scheme 2. Copper(I) thiophenolate reactions described herein.

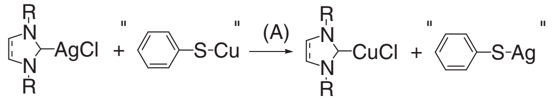
concomitant with an anion metathesis. A very recent literature report mentions a similar reaction with copper(I) iodide.[10] The reaction outcome may be influenced by a favorable balance of the solubilities of CuSPh and AgSPh and the strength of the thiolato and NHC bonds to Ag and Cu (increased softness of Ag^+ in comparison with Cu^+). Moreover, it could be argued that AgSPh possesses a lesser oxidizing power than AgCl (from extrapolation of reference data on the redox potential of Ag_nX, X = halides, sulphide, and n = 1, 2).[11] The application of this synthetic method to the selected Cu(I)-NHCs is reported in this letter. In addition, we report that CuSPh can be used efficiently in the direct addition of NHCs to form [Cu(SPh)(NHC)] (Scheme 2B). The latter products have been reported to have applications in the catalytic addition of S–H bonds to electron-deficient olefins.[12] CuSPh may thus be synthetically useful in both routes A and B in Cu(I)-NHC synthesis.

To evaluate the potential of copper(I) thiophenolate in both reactions we selected a range of usual NHCs—SIMes, IMes, SIPr, and IPr—that we reacted by both route A (transfer from silver chloride-NHCs) and route B (reaction with a free carbene generated in situ).[13] The reactions were conducted under the following conditions: (A) transmetallation in refluxing dichloromethane for 2 h and (B) direct addition by generating the carbene with ^{t}BuONa in dry THF in the presence of CuSPh. Results for route A are compiled in Table 1. All the complexes reported in this table were already reported in similar yields by direct addition of CuCl on the free carbene or by silver transfer (Scheme 1, route (i) or (ii) + (iii)).[14]

In all cases, inspection of the ^{1}H NMR of the crude reaction mixtures (see Supplementary data) revealed a clean and total conversion to the desired copper N-heterocyclic carbene core and only trace impurities of thiophenol. $Cu(NHC)_2$ species were detected (0–15%) in the crude mixture as in the transfer protocol onto CuCl. Analytically pure chloro-Cu(I)-NHCs were easily obtained after recrystallization and structures were confirmed by comparison with the literature data.

Metal-NHC thiolates have been reported previously by Gunnoe's group.[12] Although the [Cu(SPh)(SIMes)] complex was not described and [Cu(SPh)(IMes)] was reported to be unstable, [Cu(SPh)(IPr)] and [Cu(SPh)(SIPr)] have been synthesized in good yields by the acid–base reaction between [CuMe(NHC)] and thiophenol. To the best of our knowledge, no report relates the conceptually simpler addition of the free carbene directly onto copper thiophenolate.[15] The results of route B are compiled in Table 2.

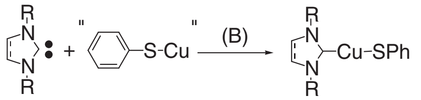
Table 1
Synthesis of [CuCl(NHC)] using copper(I) thiophenolate



Entry	[AgCl(NHC)]	[CuCl(NHC)]	Yield[a] (%)
1	[AgCl(IMes)]	[CuCl(IMes)]	75
2	[AgCl(SIMes)]	[CuCl(SIMes)]	76
3	[AgCl(IPr)]	[CuCl(IPr)]	87
4	[AgCl(SIPr)]	[CuCl(SIPr)]	90

[a] Refers to pure isolated product by crystallization.

Table 2
Addition of in situ-prepared free NHC onto copper(I) thiophenolate



Entry	NHC	[Cu(SPh)(NHC)]	Isolated yield (%)
1	IMes	[Cu(SPh)(IMes)]	0[a]
2	SIMes	[Cu(SPh)(SIMes)]	0[a]
3	IPr	[Cu(SPh)(IPr)]	89
4	SIPr	[Cu(SPh)(SIPr)]	90

[a] Unstable products.

All attempts to isolate cleanly the copper(I)-NHCs containing SIMes and IMes ligands failed, a feature reminiscent with Gunnoe's group report.[16] On the other hand, the two more hindered carbenes IPr and SIPr allow an easy synthesis in good yield.

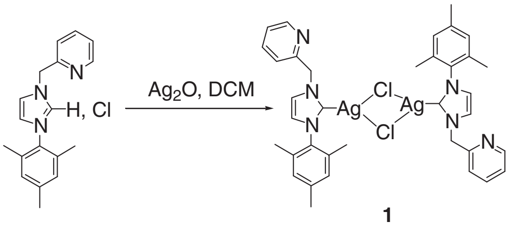
We were interested in synthesizing [CuCl(IMesPic)] for its potential biological activity.[13e] All attempts to synthesize this Cu(I)-NHC by methods (i), (ii) (Cu_2O), and (ii) + (iii) (Ag_2O, then CuCl) failed. Therefore, we used route A method. The starting silver(I)-NHC (**1**) was easily obtained with the classical silver oxide route starting from an imidazolium chloride as depicted in Scheme 3.

Complex **1** is of highly crystalline nature and suitable samples for X-ray diffraction are straightforwardly obtained. Figure 1 depicts an ellipsoid plot of **1**.[17]

The silver NHC **1** crystallizes in the centrosymmetrical $\bar{P}2_1/n$ space group. The crystal structure of **1** highlights a symmetrical dimeric structure bridged solely by two chlorides without participation of the picolyl moiety in the metal bonding. The carbon–silver bond length falls into the usual range reported in the literature.[18] This dimeric arrangement was already observed by Danopoulos and co-workers in the bromide series.[19] The crystal packing is supported by π–π stacking interactions between aromatic moieties. Structural features of interest are collected in Table 3.

Despite a number of variations of the experimental conditions (introduction of an inert atmosphere, variation of solvents, and temperature), the method (iii) from **1** onto CuCl invariably fails to furnish cleanly the Cu(I) carbene and yields unidentified greenish solids, presumably containing Cu(II). For that reason, we were pleased to observe a clean and efficient formation of compound **2** using our copper(I) thiophenolate transfer method (Scheme 4).

The transmetallation occurs in boiling dichloromethane and the product is obtained after a simple filtration over Celite. Crystals suitable for X-ray diffraction are obtained in 65% yield by a slow diffusion of pentane vapors to a saturated solution of **2** in dichloromethane. X-ray diffraction highlights an almost symmetrical



1

Scheme 3. Synthesis of the starting silver(I) NHC **1**.

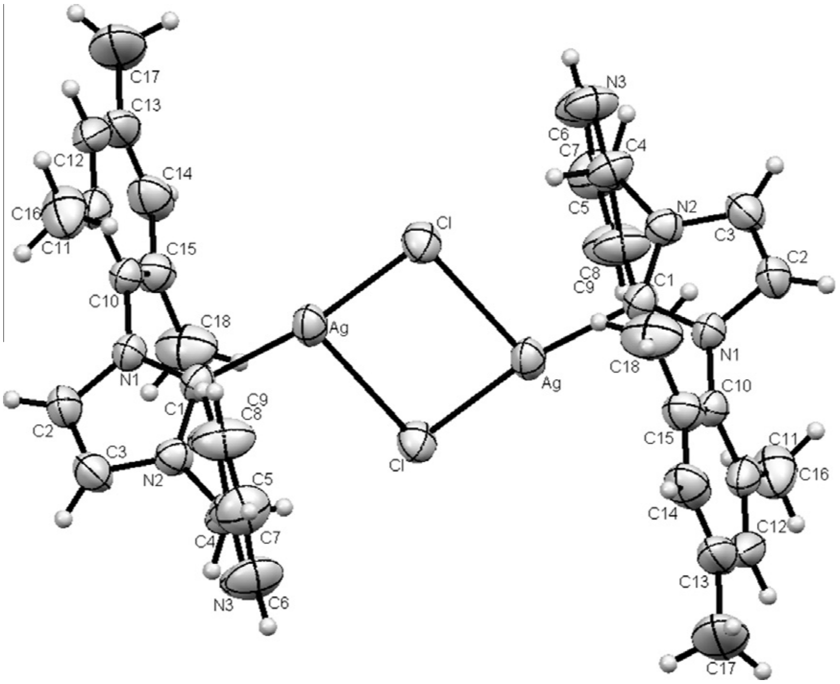
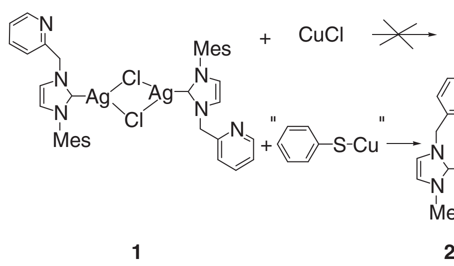


Figure 1. Thermal ellipsoid plot (50% probability) of Ag(I)-NHC (**1**).

Table 3
Lengths, angles, and torsions of interest for complex **1**

Lengths (Å)				
C1–Ag	Ag–Cl	Ag–Cl′	Ag· · ·Ag′	Cl· · ·Cl′
2.0762(19)	2.0763(19)	2.9916(6)	3.7027(4)	3.914
Angles (°)		Torsions (°)		
C1–Ag–Cl	C1–Ag–Cl′	C2–N1–C1–Ag	C3–N2–C1–Ag	
166.81(5)	99.57(5)	176.28(14)	−175.86(14)	



Scheme 4. Transmetallation using ‘Cu-SPh’ to obtain **2**.

dimeric structure in which the picolyl moieties now participate to the metal binding and bridge the copper(I) atoms (Fig. 2). In addition, the crystal lattice contains two molecules of dichloromethane.

Structural features of interest of **2**, which crystallizes in the noncentrosymmetric $P\bar{1}$ space group are collected in Table 4.[20] The complex displays a C–Cu· · ·C–Cu core adopting a distorted diamond shape. Each Cu atom is bound to the C1 NHC carbon, a pyridine nitrogen and a chloride. The Cu–C bond falls in the normal range.[21] A similar dimeric structure with a weak copper–copper interaction has been reported in the bromide series (synthesized by the Cu_2O route).[22] In comparison with that structure, the presence of chloride instead of bromide as the Cu(I) ligand induces some structural modifications—viz. the lengthening of the Cu–N bond (+0.04 Å) and an interesting shortening of the Cu–Cu distance (−0.08 Å).

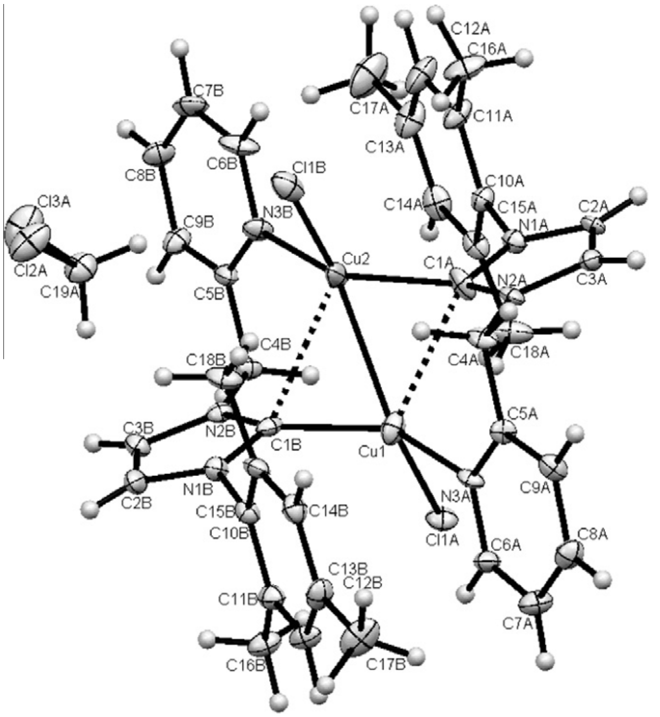


Figure 2. Thermal ellipsoid plot (50% probability) of $[Cu_2Cl_2(IMesPic)_2]\cdot 2CH_2Cl_2$ (**2**).

In conclusion, we have reported that copper(I) thiophenolate possesses a dual behavior by reacting with free N-heterocyclic carbenes to form [Cu(SPh)(NHC)] or by participating in a transmetallation reaction followed by a salt metathesis to form [CuCl(NHC)] even in the case of a complex unreachable by the usual transmetallation of a silver precursor. These methods add to the synthetic arsenal employed to generate copper(I) NHCs that possess catalytic and biological applications.

Table 4
Lengths, angles, and torsion of interest for complex **2**

		Lengths (Å)		
Cu–C	Cu–N	Cu–Cu	Cu–Cl	Cu···C
1.945(5); 1.981(5)	2.060(5); 2.083(5)	2.5637(17)	2.3642(19); 2.336(2)	2.518(5); 2.606(5)
		Angles (°)		
Cl–Cu–Cu	N–Cu–Cu	C–Cu–Cu	N–Cu–Cl	Cu–C···Cu
134.02(4); 133.86(4)	122.90(12); 120.50(12)	65.83(15); 69.06(14)	95.64(13); 97.71(12)	68.29(14); 66.75(15)
C–Cu–N	C–Cu–Cl			
130.08(19); 130.63(18)	109.40(15); 106.48(13)			
		Torsions (°)		
Cl–Cu–Cu–Cl	N–Cu–Cu–N	N–Cu–Cu–Cl		
179.6	179.6	38.1–38.5		

Supplementary data

Supplementary data (experimental procedures, compound characterizations and selected NMR spectra) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.07.124.

References and notes

1. For general and historical references: (a) Crabtree, R. H.; Bourissou, D.; Guerret, O.; Gabai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39–92; (b) Herrmann, W. A.; Kröcher, C. *Angew. Chem., Int. Ed.* **1997**, *36*, 2162–2187; (c) Wanzlick, H. W.; Schikora, E. *Angew. Chem.* **1960**, *72*, 494–495; (d) Lappert, M. F. *J. Organomet. Chem.* **1988**, *358*, 185–214.
2. (a) Hahn, F. E.; Jahnke, M. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 3122–3172; (b) Díez-González, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3162–3676.
3. Silver oxide, see: (a) Wang, H. M. J.; Lin, I. J. B. *Organometallics* **1998**, *17*, 972–975; Copper(I) oxide, see: (b) Arnold, P. L. *Heteroat. Chem.* **2002**, *13*, 534–539; (c) Simonovic, S.; Whitwood, A. C.; Clegg, W.; Harrington, R. W.; Hursthouse, M. B.; Male, L.; Douthwaite, R. E. *Eur. J. Inorg. Chem.* **2009**, 1786–1795.
4. (a) See Ref. 3a.; (b) Lin, I. J. B.; Vasam, C. S. *Coord. Chem. Rev.* **2007**, *251*, 642–670.
5. Sini, G.; Eisenstein, O.; Crabtree, R. H. *Inorg. Chem.* **2002**, *41*, 602–604.
6. (a) Ruiz, J.; Garcia, G.; Mosquera, M. E. G.; Perandones, B.; Gonzalo, M. P.; Vivanco, M. *J. Am. Chem. Soc.* **2005**, *127*, 8584–8585; (b) Ruiz, J.; Perandones, B.; Garcia, G.; Mosquera, M. E. G. *Organometallics* **2007**, *26*, 5687–5695.
7. Deliberate use of AgOTf as oxidant towards Cu(I)-NHCs (a) Hu, X.; Castro-Rodriguez, I.; Meyer, K. *J. Am. Chem. Soc.* **2003**, *125*, 12237–12245; (b) Goj, L. A.; Blue, E. D.; Delp, S. A.; Gunnoe, T. B.; Cundari, T. R.; Petersen, J. L. *Organometallics* **2006**, *25*, 4097–4104; General review on Ag(I)-NHCs reporting undesired redox side reactions: (c) Lin, I. J. B.; Vasam, C. S. *Coord. Chem. Rev.* **2007**, *251*, 642–670 (and references therein).
8. Teyssot, M. L.; Jarrousse, A. S.; Chevry, A.; De Haze, A.; Beaudoin, C.; Manin, M.; Nolan, S. P.; Díez-González, S.; Morel, L.; Gautier, A. *Chem. Eur. J.* **2009**, *15*, 314–318.
9. We also synthetized 'CuSPh' according to Nguyen, L. M.; Dellinger, M. E.; Lee, J. T.; Quinlan, R. A.; Rheingold, A. L.; Pike, R. D. *Inorg. Chim. Acta* **2005**, *358*, 1331–1336.
10. Badaj, A. C.; Dastgir, S.; Lough, A. J.; Lavoie, G. G. *Dalton Trans.* **2010**, *39*, 3361–3365.
11. Vanýsek, P. In *CRC Handbook of Chemistry and Physics*; Lide, R. D., Ed.; CRC Press: Boca Raton, 2001; pp 8–21.
12. Delp, S. A.; Munro-Leighton, C.; Goj, L. A.; Ramírez, M. A.; Gunnoe, T. B.; Petersen, J. L.; Boyle, P. D. *Inorg. Chem.* **2007**, *46*, 2365–2367.
13. (a) SIMes: 1,3-bis-(2,4,6-trimethylphenyl)imidazolin-2-ylidene.; (b) IMes: 1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene.; (c) SIPr: 1,3-bis-(2,6-diisopropylphenyl)imidazolin-2-ylidene.; (d) IPr: 1,3-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene.; (e) IMesPic: 1-(2,4,6-triphenylmethyl)-3-(2-picolyl)-imidazol-2-ylidene.
14. (a) Winkelmann, O.; Nather, C.; Luning, U. I. *J. Organomet. Chem.* **2008**, *693*, 923–932; (b) Seo, H.; Hirsch-Weil, D.; Abboud, K. A.; Hong, S. *J. Org. Chem.* **2008**, *73*, 1983–1986; (c) Park, K. H.; Ku, I.; Kim, H. J.; Son, S. U. *Chem. Mater.* **2008**, *20*, 1673–1675.
15. The synthesis of a bulky aromatic thiolate adduct of a Cu(I) NHC by a one-pot procedure (free carbene + NaSAr + CuBr(SMe)$_2$) was recently reported: Groysman, S.; Holm, R. H. *Inorg. Chem.* **2009**, *48*, 621–627.
16. [Cu(SPh)(IMes)] was reported in 75% yield by Gunnoe et al.[12] as an unstable product. The reported procedure relied on the direct precipitation of the desired compound from the reaction medium (benzene). In our case, the product instability in CH_2Cl_2 precluded the isolation of [Cu(SPh)(IMes)].
17. *Crystallographic data for* **1**: $C_{18}H_{19}AgClN_3$, monoclinic, space group $\bar{P}2_1/n$, colorless, $a = 9.8230(8)$ Å, $b = 16.6940(13)$ Å, $c = 10.9792(8)$ Å, $\beta = 94.503(2)$ Å, $V = 1794.9(2)$ Å^3, $T = 296(2)$ K, $Z = 4$, Final R $(I > 2\sigma(I))$: $R_1 = 0.0285$, $wR_2 = 0.0684$, GOF = 1.028. Structural information for **1** has been deposited with CCDC as 771502, available free of charge from www.ccdc.cam.ac.uk/conts/retreiving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033).
18. For selected examples, see (a) de Frémont, P.; Scott, N. M.; Steven, E. D.; Ramnial, T.; Lightbody, O. C.; Macdonald, C. L. B.; Clyburne, J. A. C.; Abernethy, C. D.; Nolan, S. P. *Organometallics* **2005**, *24*, 6301–6309; (b) Ramnial, T.; Abernethy, C. D.; Spicer, M. D.; McKenzie, I. D.; Gay, I. D.; Clyburne, J. A. C. *Inorg. Chem.* **2003**, *42*, 1391–1393.
19. Tulloch, A. A. D.; Danopoulos, A. A.; Winston, S.; Kleinhenz, S.; Eastham, G. *J. Chem. Soc., Dalton Trans.* **2000**, 4499–4506.
20. The dinuclear complex unit is almost centrosymmetric but the lattice symmetry is broken by the two CH_2Cl_2 present in the lattice. Crystallographic data for **2**: $C_{38}H_{42}Cl_6CuN_6$, triclinic, space group $\bar{P}1$, $a = 8.188(5)$ Å, $b = 10.933(5)$ Å, $c = 11.360(5)$ Å, $\alpha = 85.088(5)$ Å, $\beta = 85.235(5)$ Å, $\gamma = 77.498(5)$ Å, $V = 987.0(9)$ Å^3, $T = 293(2)$ K, $Z = 1$, Final R $(I > 2\sigma(I))$: $R_1 = 0.0388$, $wR_2 = 0.0979$, GOF = 1.032. Structural information for **2** has been deposited with CCDC as 771503.
21. (a) Kaur, H.; Zinn, F. K.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2004**, *23*, 1157–1160; (b) Díez-González, S.; Kaur, H.; Zinn, F. K.; Stevens, E. D.; Nolan, S. P. *J. Org. Chem.* **2005**, *70*, 4784–4796; (c) Díez-González, S.; Stevens, E. D.; Nolan, S. P. *Chem. Commun.* **2008**, 4747–4749; (d) Mankad, N. P.; Gray, T. G.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 1191–1193.
22. Tulloch, A. A. D.; Danopoulos, A. A.; Winston, S.; Light, M. E.; Hursthouse, M. B.; Eastham, G. *Organometallics* **2001**, *20*, 2027–2031.