Extending motifs in lithiocuprate chemistry: unexpected structural diversity in thiocyanate complexes†

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The new area of lithio(thiocyanato)cuprates has been developed. Using inexpensive, stable and safe CuSCN for their preparation, these complexes revealed Lipshutz-type dimeric motifs with solvent-dependent point group identities; planar, boat-shaped and chair shaped conformers are seen in the solid state. In solution, both Lipshutz-type and Gilman structures are clearly seen. Since the advent in 2007 of directed ortho cupration, effort has gone into understanding the structure-reactivity effects of amide ligand variation in and alkali metal salt abstraction from Lipshutz-type cuprates such as (TMP)2Cu(CN)Li2(THF) 1 (TMP = 2,2,6,6-tetramethylpiperidide). The replacement of CN− with SCN− is investigated presently as a means of improving the safety of lithium cuprates. The synthesis and solid state structural characterization of reference cuprate (TMP)2Cu(CN)Li2(THF) 8 (THF = tetrahydrofuran) precedes that of the thiocyanate series (TMP)2Cu(SCN)Li2(L) (L = OEt2 9, THF 10, THP 11). For each of 9–11, preformed TMPLi was combined with CuSCN (2 : 1) in the presence of sub-stoichiometric Lewis base (0.5 eq. wrt Li). The avoidance of Lewis basic solvents incurs formation of the unsolvated Gilman cuprate (TMP)2CuLi 12, whilst multidimensional NMR spectroscopy has evidenced the abstraction of LiSCN from 9–11 in hydrocarbon solution and the in situ formation of Gilman reagents. The synthetic utility of 10 is established in the selective deprotonation of chloropyridine substrates, including effecting transition metal-free homocoupling in 51–69% yield.

Introduction

Enhanced methods for the regioselective functionalization of aromatics that avoid the complications associated with the use of traditional main group organometallic bases1 are of ongoing interest. This search led, in 1999,2 to the development of the first of what have become known as ‘synergic bases’3 of the type RmM(NR′)2nAM (R = alkyl; m = 0, 2, 3; M = less polarizing metal; NR′2 = amide; n = 1, 2, 3; AM = (more polarizing) alkali metal). These have, for example, previously incorporated M = Al,4 Cd,5 Mg,6 Mn7 and Zn8 and have shown hitherto unachievable potential in anionic activation9 and templated polymetalation.10 In a similar vein, new lithium cyanocuprates11 have been central to the development of directed ortho cupration (DoC)12 (Fig. 1).

Following the inception of lithium cuprate chemistry13 through the development of R2CuLi,14 attempts have focused on enhancing reactivity. Modifications have taken two major forms. Firstly, lithium amidocuprates have been developed, offering often unique reactivities as well as the potential of the amido group as a non-transferable ligand and as a chiral auxiliary.15 Secondly, there has been a focus on the incorporation of LiCN within lithium cuprates,16 the presumption being that the cyano group would be transferred to Cu to give a higher order (tricoordinate) copper centre.17 The issue of the Cu-sequestering of cyanide has been discussed at length in the literature, though calculations,18 spectroscopy19 and X-ray diffraction20 have increasingly pointed to the retention of lower order (dicoordinate) copper. This was noted too in the recently developed field of DoC transformations, with the 2 : 1 reaction of TMPLi (TMP = 2,2,6,6-tetramethylpiperidide) and CuCN giving complexes that could be characterized by X-ray diffraction. Results revealed that in the solid state such Lip-
shutz formulation cuprates were dimers based on \((\text{TMP})_2\text{Cu}-(\text{CN})\text{Li}_2(L)\) \((L = \text{OEt}_2, \text{THF})\) \(^{12,21}\) monomers that clearly lacked Cu–CN interactions (Scheme 1).

Finally, the reaction of CuCN, R\(\text{Li}\) and TMPLi established that the inclusion of cyanide in the cuprate structure was by no means guaranteed, by furnishing the externally solvated amido(organyl) monomers \(\text{RCu(TMP)Li(L)}_n\) \((R = \text{Ph}, L = \text{THF}, n = 3 3; R = \text{Me}, L = \text{TMEDA} = N,N,N',N'-\text{tetramethyl-}
\text{ethylenediamine}, n = 1 4)\).\(^{22}\) This observation took on added importance when recent DFT analysis suggested the in situ conversion of cyanide-incorporating cuprates to reactive Gilman reagents as the precursor to DoC reaction.\(^{23}\)

Recent studies have sought to extend the principles established by the isolation of \(1\) and \(2\) to the use of general inorganic anions. This has led to the isolation and full characterization of \((\text{TMP})_2\text{Cu}(X)\text{Li}_2(L)\) \((X = \text{Cl}, \text{Br}, \text{I}, L = \text{OEt}_2, \text{THF})\).\(^{23,24}\) These species have been viewed as being Lipshutz-type by virtue of their demonstrating essentially the same structural principles as \(1\) and \(2\). They have been successfully tested in the deprotonative metalation of halopyridines,\(^{25}\) notably in the course of azafluorenone synthesis.\(^{24}\) Herein we extend this principle further, introducing the use of the thiocyanate anion as a non-toxic but potentially synthetically useful analogue of the cyanide components in \(1\) and \(2\). Preliminary results reveal novel variations in thiocyanatocuprate structure as a function of solvent both in the solid state and in solution.

**Results and discussion**

**Solid state analysis**

With this study aiming to probe new thiocyanatocuprate bases solvated by THF, \(\text{OEt}_2\) and \(\text{THP} (=\text{tetrahydropyran})\) it was first necessary to complete the series of cyanocuprates \(1,12\) \(^2\) \(2\) \(^{21}\) and \((\text{TMP})_2\text{Cu}(\text{CN})\text{Li}_2(\text{THP})\) \(8\). To do this a hexane solution of TMPLi containing also THP \((0.5\text{ eq. wrt Li})\) was added to a suspension of CuCN \((0.5\text{ eq. wrt Li})\) in toluene. Following the addition of hexane the mixture was heated to reflux and then filtered to give a pale-straw coloured solution from which block-like crystals could be obtained (Scheme 2).

The product was shown by \(^1\text{H NMR spectroscopy to incorporate TMP and THP in a 2 : 1 ratio, suggesting a formulation analogous to that previously reported for} 1 \text{ and} 2\). Corroboration of this view came from X-ray diffraction, which established the product to be \(8\) and to be the analogue of \(1\) and \(2\) (Fig. 2). All three structures proved to be relatively flat. IR spectroscopy on \(8\) revealed a dominant \(\text{Cu-CN}\) stretching mode at \(\nu = 2104.3\text{ cm}^{-1}\), with a signal developing at \(2138.3\text{ cm}^{-1}\) upon air exposure (see ESI, Fig. S1\(^\dagger\)), which compared closely with prior work.\(^{22}\)

Moving to the employment of CuSCN in an attempt to render a safer analogue of \(\text{OEt}_2\)-solvate \(1\), a low temperature solution of TMPH in \(\text{Et}_2\text{O/toluene}\) was treated with \(^4\text{BuLi}\). The resulting solution was transferred to a suspension of CuSCN in toluene. The mixture was heated to reflux, turning from pale cream to grey-black, whereupon filtration gave a yellow solution. Storage at room temperature gave a low yield of needle-like crystals after 1 day, which dissolved with further standing, and after several days were replaced with crystals of pseudo-rhombic habit in low yield. \(^1\text{H NMR spectroscopy revealed these to comprise TMP and \(\text{OEt}_2\) in a 2 : 1 ratio. Though...
$^{13}$C NMR spectroscopy failed to suggest the presence of SCN, this ligand was obviously incorporated, with IR spectroscopy revealing peaks at 2064.6 (s) and 1996.6 (m) cm$^{-1}$ (Fig. S2†). Air exposure of the sample for 30 s incurred the growth of a signal at 2107.1 cm$^{-1}$, which compared with 2066 and 2070 cm$^{-1}$ for calculated free [SCN]$^-$ and LiSCN, respectively.26,27 Overall, these data suggest the presence of [S$^{−}$Li$_2$A]$_2$,2OEt$_2$ formulation was verified by X-ray diffraction, which established an essentially flat dimer (Scheme 3). NMR spectroscopy revealed that, contrast to the structure of 9$_2$, these crystals incorporated TMP and Lewis base in a 2:1 ratio and a SCN group (δ 141.5 ppm by $^{13}$C NMR spectroscopy). Corroboration of the last point came from IR spectroscopy, with two peaks seen at 2050.4 (s) and 1998.0 (m) cm$^{-1}$ (Fig. S3,† cf. 2064.6 and 1996.6 cm$^{-1}$ in 9$_2$), the signals being replaced by a peak at 2105.7 cm$^{-1}$ after air exposure for 30 s. X-ray diffraction was undertaken, with data revealing a dimer based on (TMP)$_2$Cu(SCN)Li$_2$(THF) 10. However, in contrast to the structure of 9$_2$, 10$_2$ exhibited a novel boat conformation (Fig. 4) based on the aggregation of two crystallographically independent monomers (of which one will be representatively discussed) and in which the geometry at
sulfur is fundamentally altered relative to that seen in 9₂. The result is that the two sulfur centres in 10₂ constitute the hinge about which deviation from planarity of the dimer operates. In spite of this, diffraction fails to reveal any significant difference in the bond lengths associated with sulfur (cf. S1–C19 1.631(3), S1–Li2A 2.518(4) Å in 9₂ and S2–Cu2 1.625(3), S2–Li1 2.500(6) Å in 10₂). This suggested equivalent thiocyanate anion structure to that seen in 9₂ even if the angle at sulfur now dramatically constricted on account of the dimer folding along the S⋯S vector (Li2 87.66(18), N1 Li1 87.45(18), Cu1 Li1 87.2 91.72(17)° in 10₂). The two 6-membered Cu-containing CuLi₂N₃ rings in 10₂ are essentially planar (angles at Li1 and N3 sum to 359.9° and 359.6°, respectively).

Having established significantly different geometries for 9₂ and 10₂, attention switched to use of the Lewis base THP. TMPLi in hexane/toluene and THP (0.5 eq. wrt Li) was reacted with CuSCN, leading to the isolation of a modest yield of colourless blocks (Scheme 3). NMR spectroscopy revealed the presence therein of TMP and THP in a 2:1 ratio. Meanwhile, IR spectroscopy demonstrated signals attributable to SCN at 2063.2 (s) and 2006.5 (w) cm⁻¹, these being replaced by peaks at 2173.7 and 2108.5 cm⁻¹ upon air exposure for 30 s. (Fig. S4†). X-ray diffraction confirmed the expected formulation of the product as the dimer of (TMP)₂Cu(SCN)Li₂(THP) 11 but revealed a structure (Fig. 5) that, in contrast to the structures of 9₂ and 10₂, exhibited a clear chair conformation ostensibly by virtue of the significant displacement (by ±0.43 Å) of Li2 and its symmetry equivalent from the mean plane described by the Li1–N3–C19–S1 fragment and its symmetry analogue. In order to allow this to occur not only S1 but also N3 necessarily deviate from planarity (in contrast to the geometry of N3 in 10₂), with angles at nitrogen now summing to 351.6°. This small deviation from planarity (presumably limited to maximize the electrostatic directionality of nitrogen) is reflected also in the geometry at S1 for which, at 96.09(12)°, the Li–S–C angle is intermediate between those seen in the two previous structures (103.92(13)° in 9₂, 91.72(17)° in 10₂).

**Fig. 4** (a) Molecular structure of 10₂. H-atoms omitted. Selected bond lengths (Å) and angles (°): N1–Cu1 1.908(2), N2–Cu1 1.906(2), N1–Li1 1.977(5), N2–Li2 1.995(6), S2–Li1 2.500(6), N3–Li1 2.071(6), N3–Li2 2.105(6), N3–C1 1.159(4), S1–C1 1.627(3), Cu1–N1–Li1 87.45(18), Cu1–N2–Li2 87.66(18), N1–Li1–N3 130.7(3), N2–Li2–N3 128.9(3), Li1–N3–C1 125.0(3), Li2–N3–C1 124.8(3), S2–Li1–N3 108.8(2), Li1–S2–C24 91.72(17); (b) view emphasising the boat-shaped dimer core.

**Fig. 5** (a) Molecular structure of 11₂. H-atoms omitted. Selected bond lengths (Å) and angles (°): N1–Cu1 1.9204(17), N2–Cu1 1.9148(17), N1–Li1 1.990(4), N2–Li2 1.968(4), S1A–Li2 2.464(4), N3–Li1 2.164(5), N3–Li2 2.005(4), N5–C19 1.162(3), S1–C19 1.632(3), Cu1–N1–Li1 110.75(19), Cu1–N2–Li2 88.84(13), N1–Li1–N3 123.42(1), N2–Li2–N3 128.5(2), Li1–N3–C19 106.7(2), Li2–N3–C19 134.5(2), S1A–Li2–N3 107.90(18), Li2A–S1–C19 96.09(12); (b) the chair-shaped dimer core.
Diffraction reveals bond lengths of S1–C19 1.632(3), S1–Li2A 2.464(4) Å associated with sulfur, which are essentially the same as those seen in 9 and 10 and point to a common thiocyanate ligand electronic structure.

The solvent sensitivity of thiocyanatocuprate formation was also investigated by eliminating external Lewis bases. As described above, reaction of TMPLi (4 mmol) with CuSCN (2 mmol) in bulk hydrocarbon doped with L (= OEt2, THF, TMP; 0.5 eq. wrt Li) gave (TMP)2Cu(SCN)Li2(L) 9–11. However, crystallographic analysis of the product revealed that the avoidance of donor solvent afforded a convenient and clean route to material which demonstrated a single signal at δ 0.90 ppm by 7Li NMR spectroscopy. Crystallography subsequently revealed previously reported (TMP)2CuLi 12,23 which was a dimer in the solid state, with IR spectroscopy corroborating the absence of SCN ligands (see ESI Fig. S5†). However, the suggestion from 7Li NMR spectroscopy that omitting Lewis base avoided contamination of the product with minor impurities23 led us to undertake further re-characterization, obtaining a simple 13C NMR spectrum of the Gilman cuprate (see below) which served to aid our interpretation of the more complex behaviour of 9–11 in solution.

**NMR spectroscopy**

The improved synthesis of 12 made available clean NMR spectra of the Gilman cuprate (TMP)2CuLi, with 13C and 7Li NMR spectra obtained in d6-benzene that could then be deployed in order to deconvolute the solution behaviour of thiocyanates 9–11. The 13C NMR spectrum revealed a simple set of signals attributable to [TMP]− with singlets due to the 2,6-, 3,5- and 4-positions of the rings seen at δ 54.2, 42.1 and 19.2 ppm, respectively, and two Me signals located at δ 40.1 and 34.5 ppm (Fig. 6d). Comparison with the analogous spectrum obtained for diethyl ether complex 9 (at a concentration of ~20 mg/0.7 mL d6-benzene, Fig. 6a) revealed it to be dominated by essentially identical signals, with a small amount of decomposition to give TMPH peaks, with minor traces of Lipshutz-type cuprate (see below) also manifest. These data strongly suggest ostensible conversion from the Lipshutz-type structure seen crystallographically for this system (Fig. 3a) to a Gilman formulation in solution.

Moving to the 13C NMR spectroscopic data for THF-solvate 10 at the same concentration, a more complicated system is revealed. (The SCN component itself can be located at δ 4.5 ppm, but this signal overlapped with the copper and lithium signals.) The 13C NMR spectrum of 10 showed a complex pattern of signals, with significant contributions from both the Gilman and Lipshutz-type structures. A detailed analysis of these signals revealed the presence of minor impurities, including a small amount of TMPH, which was also observed in the 7Li NMR spectrum (Fig. 6a).

**Fig. 6** 13C NMR spectroscopic data obtained in d6-benzene for (a) 9, (b) 10, (c) 11, (d) 12 (*TMPH, G = Gilman, L = Lipshutz-type). Sample concentrations for 9–11 were 20 mg/0.7 mL.
141.5 ppm for this system in a 50 mg/0.7 mL sample, Fig. S11†) It is immediately obvious that whilst signals attributable to the amide ligands in the Gilman cuprate remain, they no longer represent the dominant species in solution (Fig. 6b). Instead, major signals are now observed at the high-field side of each Gilman resonance (at \( \delta \) 53.5, 40.6, 38.3, 34.4 ppm) and, in one case (\( \delta \) 19.2 ppm), coincident with it. These are attributed to the corresponding carbon atoms in the Lipshutz-type structure, which appears to be substantially retained in solution, with an approximate Gilman : Lipshutz-type ratio of 1 : 3 suggested. Equivalently concentrated THP complex 11 (20 mg/0.7 mL in \( d_6 \)-benzene) revealed a similar picture to that demonstrated by 10, albeit the distribution of Gilman and Lipshutz-type species is approaching equivalence (Fig. 6c). Moreover, similar to 10, the analysis of a more concentrated sample (50 mg/0.7 mL in \( d_6 \)-benzene) located the thiocyanate resonance at \( \delta \) 141.7 ppm (Fig. S11†).

Coincident with the near-quantitative in situ conversion of Lipshutz-type crystalline 9 to a Gilman cuprate in \( d_6 \)-benzene (Fig. 6a) the deposition of a white powder was observed in the NMR tube to which 9 (20 mg/0.7 mL) had been added. Based on a control experiment in which pre-isolated Lipshutz-type cuprate was dissolved in benzene and the resulting white deposit analyzed by IR spectroscopy, we attribute this observation to LiSCN precipitation (Fig. S6†). \(^7\)Li NMR spectroscopy on this sample therefore accorded no signal attributable to LiSCN. Rather, it revealed a dominant peak precisely matching the \( \delta \) 0.90 ppm Gilman cuprate peak in 12 (Fig. 7d) accompanied by the development of a minor high-field signal at \( \delta \) 0.65 ppm (Fig. 7a). Consistent with the \(^{13}\)C NMR spectroscopic data, the high-field signal can be attributed to the retention of a small amount of Lipshutz-type cuprate in hydrocarbon solution, with the relative integrations (of 1 and 0.4) suggesting an approximate Gilman : Lipshutz-type ratio of 5 : 1.

Moving to 10 in solution it is immediately apparent that the \(^7\)Li NMR spectrum revealed a significant change in behaviour, with the high-field signal at \( \delta \) 0.71 ppm now dominant (Fig. 7b). Taken together with \(^{13}\)C NMR spectroscopic data, this confirms the attribution of the high-field signal as retained Lipshutz-type cuprate and emphasizes the solvent dependence of LiSCN abstraction, with a Gilman : Lipshutz-type ratio of 0.2 : 1 calculated based on the \(^7\)Li NMR data – which substantiates the \(^{13}\)C NMR spectrum in Fig. 6b. Fig. 7c reinforces this view, with the Gilman : Lipshutz-type ratio of 0.6 : 1 calculated from \(^7\)Li NMR data for 11 correlating with the appearance of Fig. 6c.

**Chloropyridine derivatization**

Based upon recent work on the use of halide-containing Lipshutz-type cuprates to facilitate the synthesis of azafluorenone frameworks\(^ {24}\) it was decided to test the reactivity of new thiocyanatocuprates in the selective elaboration of halopyridines. The in situ preparation of 10 was therefore undertaken using THF solvent and the resulting mixture was tested in the selective deprotonmetalation of both 2-chloropyridine 13 and 2,3-dichloropyridine 14. Under the conditions employed it was expected that reaction of 13 would occur at the aromatic 3-position, while the employment of two adjacent acidifying halogens would promote attack of the 4-position in the dichlorinated substrate.

Results of the use of in situ-generated 10 in the selective metalation of 13 are reported in Table 1. Under the conditions employed, reaction afforded the 3-substituted derivatives 15a–c in 46–71% yields after subsequent trapping with 4-methoxybenzoyl chloride, methyl iodide or phenyl disulfide, respectively (Table 1, entries 1–3 and Fig. S13†). In the light of cyanocuprate 2 having been shown to promote the quantitative homocoupling of \( N,N \)-diisopropylbenzamide in the presence of the oxidant PhNO\(_2\),\(^ {12}\) so obviating the need for the inclusion of an additional transition metal-based catalyst, it was decided to test the efficacy of 10 in this respect as a safer alternative to the cyanocuprate. Accordingly, the formation of 15d was observed in 69% yield (entry 4).

The response of 2,3-dichloropyridine 14 was tested next (Table 2). This is known to undergo lithiation at the 4-position...
The preparation of (TMP)$_2$Cu(CN)Li$_2$(THP) 8 served to extend the family of TMP-incorporating lithiocuprates based on the formulation (TMP)$_2$Cu(CN)Li$_2$(L) (L = OEt$_2$, 1, THF 2) and to establish the prevalence of approximately flat dimers for these complexes in the solid state. The use of thiocyanate instead of cyanide was then probed to investigate the former as a convenient, cheap and safe alternative that avoids redirecting reactivity in ways recently described when cyanide has been replaced by halide. The resulting complexes showed interesting structural variability; the use of Et$_2$O incurring an essentially planar dimer akin to those of 1, 2 and 8 but based on a [LiNCs]$_2$ core, while THF and TMP gave boat and chair conformers, respectively. These aggregates were best viewed as incorporating Li[S–C≡N] moieties. Consistent with recently developed theoretical views on cuprate reactivity, solid state structures were not necessarily retained in solution, with at least some Gilman cuprate formation noted for each thiocyanate system in benzene. Lastly, preliminary synthetic investigations successfully applied 10 to the selective deprotonation and homocoupling of halopyridines, with ongoing work seeking to establish the extent of the synthetic portfolio of these new reagents.

**Conclusions**

The preparation of (TMP)$_2$Cu(CN)Li$_2$(THP) 8 served to extend the family of TMP-incorporating lithiocuprates based on the formulation (TMP)$_2$Cu(CN)Li$_2$(L) (L = OEt$_2$, 1, THF 2) and to establish the prevalence of approximately flat dimers for these complexes in the solid state. The use of thiocyanate instead of cyanide was then probed to investigate the former as a convenient, cheap and safe alternative that avoids redirecting reactivity in ways recently described when cyanide has been replaced by halide. The resulting complexes showed interesting structural variability; the use of Et$_2$O incurring an essentially planar dimer akin to those of 1, 2 and 8 but based on a [LiNCs]$_2$ core, while THF and TMP gave boat and chair conformers, respectively. These aggregates were best viewed as incorporating Li[S–C≡N] moieties. Consistent with recently developed theoretical views on cuprate reactivity, solid state structures were not necessarily retained in solution, with at least some Gilman cuprate formation noted for each thiocyanate system in benzene. Lastly, preliminary synthetic investigations successfully applied 10 to the selective deprotonation and homocoupling of halopyridines, with ongoing work seeking to establish the extent of the synthetic portfolio of these new reagents.

**Experimental section**

**General synthetic and analytical details**

Reactions and manipulations were carried out under an inert atmosphere of dry nitrogen, using standard double manifold and glove-box techniques. Solvents were distilled off sodium (toluene) or sodium–potassium amalgam (Et$_2$O, THF, hexane) immediately prior to use. Copper(I) thiocyanate and tetrahydrodropyran (THP, Sureseal) were purchased from Aldrich and 2,2,6,6-tetramethylpiperidine (TMPH) was purchased from Alfa Aesar. The amine was stored over molecular sieve (4 Å) while the other chemicals were used as received. Isolated yield. — 55% yield by using CuCl instead of CuSCN. — Yield estimated by $^1$H NMR spectroscopy due to volatile nature of the product.

**Crystallographic details**

**Compounds 8–12.** For details of data collections see Table 3. Crystals were transferred directly from the mother liquor to a drop of perfluoropolyether oil mounted upon a microscope slide under a stream of cool nitrogen gas. Suitable crystals were selected and attached to the goniometer head via a MicroLoop™, which was then centred on the diffractometer. Data were collected on a Bruker D8 Quest equipped with an Oxford Cryosystems low-temperature device (Cu-Kα, $\lambda = 1.54184$ Å, $T = 180(2)$ K). Structures were solved using SHELXT, with refinement, based on $F^2$, by full-matrix least squares. Except when disordered, non-hydrogen atoms were

**Table 1** Results of the reaction of 10 with 2-chloropyridine 13 in THF and subsequent reaction with electrophiles or in the presence of PhNO$_2$

<table>
<thead>
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<th>Entry</th>
<th>Electrophile or PhNO$_2$</th>
<th>E</th>
<th>Product, yield (%)</th>
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<tr>
<td>1</td>
<td>4-MeOC$_6$H$_4$COCl</td>
<td>COC$_6$H$_4$-4-OMe</td>
<td>15a, 46$^a,b$</td>
</tr>
<tr>
<td>2</td>
<td>MeI</td>
<td>Me</td>
<td>15b, 65$^c$</td>
</tr>
<tr>
<td>3</td>
<td>PhSSPh</td>
<td>SPh</td>
<td>15c, 71$^a$</td>
</tr>
<tr>
<td>4</td>
<td>PhNO$_2$</td>
<td>—</td>
<td>15d, 69$^a$</td>
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</table>

$^a$ Isolated yield. $^b$ 55% yield by using CuCl instead of CuSCN. $^c$ Yield estimated by $^1$H NMR spectroscopy due to volatile nature of the product.

**Table 2** Results of the reaction of 10 with 2,3-dichloropyridine 14 in THF and subsequent reaction with electrophiles or in the presence of PhNO$_2$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Electrophile or PhNO$_2$</th>
<th>E</th>
<th>Product, yield (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>MeI</td>
<td>Me</td>
<td>16b, 58$^a$</td>
</tr>
<tr>
<td>2</td>
<td>PhSSPh</td>
<td>SPh</td>
<td>16c, 62$^b$</td>
</tr>
<tr>
<td>3</td>
<td>PhNO$_2$</td>
<td>—</td>
<td>16d, 51$^b$</td>
</tr>
</tbody>
</table>

$^a$ Yield estimated by $^1$H NMR spectroscopy due to volatile nature of the product. $^b$ Isolated yield.
refined anisotropically and a riding model with idealized geometry was employed for the refinement of H-atoms. Compound 12 was subjected to a crystallographic cell check that corresponded to previously reported data.\textsuperscript{23} Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications CCDC 1429486 (8\textsuperscript{a}), 1429485 (9\textsuperscript{a}), 1429483 (10\textsuperscript{a}) and 1429484 (11\textsuperscript{a}).

**Compounds 15c and 16c.** Samples were studied using graphite monochromated Mo-K\textsubscript{α} radiation (\(\lambda = 0.71073\) Å). X-ray diffraction data were collected using an APEXII, Bruker-AXS diffractometer at \(T = 150(2)\) K (15c) or a D8 VENTURE Bruker AXS diffractometer at 294(2) K (16c). The structures were solved by direct methods using the SIR97 program,\textsuperscript{33} and then refined with full-matrix least-square methods based on \(F^2\) (SHELX-97)\textsuperscript{34} with the aid of the WINGX program.\textsuperscript{35} Non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H-atoms were finally included in their calculated positions. Molecular diagrams (Fig. S13\textsuperscript{†}) were generated by ORTEP-3 (version 2.02).\textsuperscript{15}

**Synthesis and characterization of (TMP)\textsubscript{2}Cu(SCN)Li\textsubscript{2}(THP) 8.** To a stirred solution of TMPH (0.68 mL, 4 mmol) and THP (0.17 mL, 2 mmol) in hexane (4 mL) was added \(^{6}\text{BuLi}\) (2.5 mL, 1.6 M in hexanes, 4 mmol) at \(-78^\circ\text{C}\). The resulting solution was returned to room temperature to give a yellow solution that was transferred to a suspension of CuCN (0.179 g, 2 mmol) in toluene (6 mL) at \(-78^\circ\text{C}\). The mixture was warmed to room temperature to give a pale cream-coloured suspension. Hexane (4 mL) was added and the mixture heated to reflux until most solid had dissolved. Immediate filtration gave a pale-straw coloured solution. Storage at room temperature for 24 h gave colourless block-like crystals. Yield 20 mg (27%), melting point 185–187 °C. Elemental Analysis, \(\text{C}_{48}\text{H}_{92}\text{Cu}_{2}\text{Li}_{4}\text{N}_{6}\text{O}_{2}\text{S}_{2}\) requires (%) C 61.32, H 9.86, N 8.94; found (%) C 60.69, H 9.65, N 8.84. \(^{1}\text{H} \text{NMR spectroscopy (500 MHz, C}_{6}\text{D}_{6}\) \(\delta\) 3.50 (m, 8H, THP), 2.13–1.80 (br, m, 4H, TMP-4), 1.74 (s, 24H, TMP-Me), 1.71–1.39 (br, m, 24H, TMP-3,5,-Me), 1.39–1.23 (m, 18H, TMP-3,5,-Me), 1.23–1.15 (br, m, 4H, THP), 1.14 (m, 2H, TMP-3,5), 1.07 (s, 16H, TMP-Me), 0.32 (br, s, 0.13H, TMP-Me-NH). \(^{13}\text{C} \text{NMR (126 MHz, C}_{6}\text{D}_{6}\) \(\delta\) 69.0 (THP), 38.4 (TMP-Me, L), 38.2 (TMP-Me, G), 34.5 (TMP-Me, G), 34.0 (TMP-Me, L), 31.6 (TMP-Me, L), 25.7 (THP), 22.6 (THP), 19.4 (TMP-4, L), 19.2 (TMP-4, G), 18.4 (TMP-4). \(^{7}\text{Li} \text{NMR spectroscopy (nujol) \(\bar{\nu}\) 2104.3 cm\textsuperscript{-1} (m)).

**Synthesis and characterization of (TMP)\textsubscript{2}Cu(SCN)Li\textsubscript{2}(OEt\textsubscript{2}) 9.** To a stirred solution of TMPH (0.68 mL, 4 mmol) and Et\textsubscript{2}O (0.21 mL, 2 mmol) in toluene (2 mL) at \(-78^\circ\text{C}\) was added \(^{6}\text{BuLi}\) (2.5 mL, 1.6 M in hexanes, 4 mmol). The solution was returned to room temperature whereupon it was transferred to a suspension of CuSCN (0.243 g, 2 mmol), in toluene (2 mL), at \(-78^\circ\text{C}\). The mixture was warmed to room temperature to give a pale cream-coloured suspension which was then heated to reflux until it turned grey-black. The mixture was filtered immediately, giving a yellow solution. Storage at room temperature gave needle-like crystals after 1 day, which dissolved with further standing, to be replaced after several days with crystals of pseudo-rhombic habit. Yield 97 mg (10%), melting point 173–175 °C. Elemental Analysis, \(\text{C}_{46}\text{H}_{90}\text{Cu}_{2}\text{Li}_{4}\text{N}_{6}\text{O}_{2}\text{S}_{2}\) requires (%) C 56.63, H 9.46, N 8.57; found (%) C 55.58, H 9.34, N 8.46. \(^{1}\text{H} \text{NMR spectroscopy (500 MHz, C}_{6}\text{D}_{6}\) \(\delta\) 3.28 (q, \(J = 7\) Hz, 8H, Et\textsubscript{2}O), 1.89–1.76 (m, 4H, TMP-4), 1.66–1.61 (m, 8H, TMP-3,5), 1.60 (s, 24H, TMP-Me), 1.59–1.57 (m, 4H, TMP-Me).
was treated with \(-\)TMP-3,5, 1.15 (m, 10H, THF), 1.49 (s, 8H, TMP-3,5), 1.39 (s, 1Li, G), 0.71 (s, 1Li, L), Selected IR spectroscopy (nujol) \(\delta 2050.4 \text{ cm}^{-1}\) (s), 1998.0 cm\(^{-1}\) (m).

**Synthesis and characterization of \((\text{TMP})_2\text{Cu(SCN)Li}_2(\text{THF})\) 10.** \(\text{BuLi}\) (2.5 mL, 1.6 M in hexanes, 4 mmol) was added to a stirred solution of TMPH (0.68 mL, 4 mmol) and THF (0.16 mL, 2 mmol) in hexane (4 mL) at \(-78^\circ\text{C}\). The resulting solution was returned to room temperature and transferred to a suspension of CuSCN (0.243 g, 2 mmol), in hexane (2 mL), at \(-78^\circ\text{C}\). The mixture was warmed to room temperature to give a pale cream-coloured suspension which was heated to reflux until it turned grey-black. Immediate filtration gave a pale yellow solution. Storage at \(-27^\circ\text{C}\) for 24 h gave colourless prismatic crystals. Yield 516 mg (53%), melting point 143–145 \(^\circ\text{C}\). Elemental Analysis, C\(_{48}\)H\(_{92}\)Cu\(2\)Li\(4\)N\(6\)O\(2\)S\(2\) requires (\%) C 57.41, H 9.23, N 8.37; (27%), melting point 176 °C. This gave a yellow solution, the storage of which at room temperature for 24 h gave very large blade-shaped crystals. Yield 201 mg (40%), melting point 198–200 °C. Elemental Analysis, C\(_{36}\)H\(_{72}\)Cu\(2\)Li\(2\)N\(4\) requires (\%) C 61.60, H 10.34, N 7.98; found (\%) C 60.83, H 10.30, N 7.89. 3\(^1\)H NMR spectroscopy (500 MHz, C\(_6\)D\(_6\)) \(\delta 1.89–1.77\) (m, 4H, TMP-4), 1.67–1.61 (m, 8H, TMP-3,5), 1.60 (s, 24H, TMP-Me), 1.59–1.57 (m, 4H, TMP-4), 1.56 (s, 24H, TMP-Me), 1.14–1.06 (m, 8H, TMP-3,5). 3\(^1\)C NMR (126 MHz, C\(_6\)D\(_6\)) \(\delta 54.2\) (TMP-2,6, THF), 42.1 (TMP-3,5), 40.8 (TMP-3,5, L), 39.7 (TMP-Me, L), 32.0 (THF), 19.2 (TMP-4, G + L), 18.4 (TMP-FH). \(^{7}\)Li NMR (194 MHz, 27 °C, C\(_6\)D\(_6\)) \(\delta 0.90\) (s, 0.3Li, G), 0.60 (s, 1Li, L). Selected IR spectroscopy (nujol) \(\delta 2063.2 \text{ cm}^{-1}\) (s), 2006.5 cm\(^{-1}\) (w).

**Synthesis and characterization of \((\text{TMP})_2\text{CuLi}_2(\text{THF})\) 11.** A stirred solution of LiTMP was prepared at 0 °C by sequentially treating THF (5 mL) with 2,2,6,6-tetramethylpiperidine (0.68 mL, 4 mmol) and \(^{7}\)BuLi (2.5 mL, 1.6 M hexanes solution, 4 mmol). This reagent was then treated with copper(I) thiocyanate (0.24 g, 2 mmol). The mixture was stirred for 15 min at 0 °C before the introduction of 2-chloropyridine (13, 0.19 mL, 2 mmol) or 2,3-dichloropyridine (14, 0.30 g, 2 mmol). After 2 h. at RT, the electrophile (4 mmol) was added either as a neat liquid or as a solution in THF (5 mL). The mixture was stirred overnight at RT before addition of a 1 M aqueous solution of NaOH (20 mL) and extraction with Et\(_2\)O (2 × 20 mL). After washing the organic phase with an aqueous saturated solution of NH\(_4\)Cl (10 mL) and drying over anhydrous Na\(_2\)SO\(_4\), the solvent was evaporated under reduced pressure and the product isolated after purification by flash chromatography on silica gel (the eluent is given in the product description).

2-Chloro-3-pyridyl 4-methoxyphenyl ketone 15a was prepared from 13 by using 4-methoxybenzyl chloride as the electrophile and was isolated (eluent: 8:2 heptane/AcOEt) in 46% yield as a yellow powder: mp 79 °C. The product was identified from a previous report.\(^{24}\)

2-Chloro-3-(phenylsulfanyl)pyridine 15c (see Fig. S14) was
prepared from 13 by using phenyl disulfide as the electrophile and was isolated (elucent: 9 : 1 heptane/AcOEt) in 71% yield as a greenish powder: mp 70–72 °C; IR(ATR): 695, 725, 745, 795, 909, 1021, 1029, 1066, 1146, 1382, 1447, 1547, 1736, 2927, 3062 cm⁻¹;¹ H NMR (300 MHz, CDCl₃) δ 7.02 (dd, J = 7.8 and 4.5 Hz, 1H), 7.08 (dd, J = 7.8 and 1.8 Hz, 1H), 7.41–7.56 (m, 3H), 7.48–7.54 (m, 2H), 8.13 (dd, J = 4.5 and 1.8 Hz, 1H);¹³C NMR (75 MHz, CDCl₃) δ 122.8 (CH), 129.6 (CH), 130.1 (2CH), 130.3 (C), 134.8 (2CH), 136.1 (C), 136.3 (CH), 145.7 (CH), 149.1 (C), 153.3 (C); X-ray di

References


