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A new synthesis of bis(2-{pyrid-2-yl}ethyl)amine (L^H) from bis(2-{pyrid-2-yl}ethyl)hydroxylamine (L^{OH}), and the copper-dependent reduction of L^{OH} to L^H†

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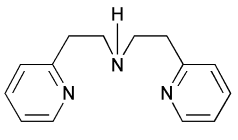
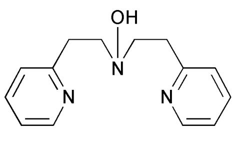
Solutions of [$CuCl_2L^{OH}$], and other reaction mixtures containing L^{OH} and Cu(II) or Cu(I) salts, degrade to yield dark green or brown residues containing the L^H ligand. In contrast, [MCl_2L^{OH}] (M = Zn, Ni, Co) are indefinitely stable in solution and the solid state.

Ligands derived from *N*-alkyl- or *N*-aryl-bis(2-{pyrid-2-yl}-ethyl)amines have played a central role in biomimetic coordination chemistry, particularly in delineating the mechanism of O_2 binding and activation by copper[1] and iron[2] centres. As part of our own studies of copper coordination chemistry, we wished to use bis(2-{pyrid-2-yl}ethyl)amine (L^H) as a precursor for some new *N*-alkyl-bis(2-{pyrid-2-yl}ethyl)amines. Previously, L^H has been synthesised by the Michael addition of an excess of 2-vinylpyridine with ammonium chloride.[3–5] This is a messy reaction that we have found to be unreliable, possibly because of the difficulty in distilling crude L^H, which decomposes at a temperature very close to its low-pressure boiling point.[4,5] We noted that L^{OH} is a convenient source of the bis(2-{pyrid-2-yl}ethyl)amino skeleton, since it can be prepared in a one-pot solvent-free reaction and, as a solid, it can be purified by recrystallisation.[6] Reduction of L^{OH} using zinc powder in dilute acid, followed by basification of the reaction mixture, solvent extraction and drying, cleanly affords a pale yellow oil in 90% yield (ESI†). This product analyses reproducibly as the hemihydrate of L^H, without further purification; recrystallisation of the product as its oxalate salt, followed by aqueous regeneration of the free base, gave an identical hemihydrate oil. The presence of half a mole-equivalent of water in the product was confirmed by ^1H NMR spectroscopy in predried $CDCl_3$, which showed broad singlets assignable to the NH (δ 5.21, 1H) and OH_2 (δ 1.94, 1H) protons. Although it requires two steps, this synthesis is higher yielding overall than the previous one-pot procedure.


L^H


L^{OH}

Complexation of hydrated $CuCl_2$, $Cu(O_2CMe)_2$, $Cu(NO_3)_2$ or $Cu(BF_4)_2$ by L^{OH} in water, MeOH or $MeNO_2$ initially affords blue or green solutions, which darken noticeably after a few tens of minutes. Intensely dark green solid products can only be isolated from the reactions carried out in aqueous solution; other solvents yield intractable oils upon evaporation of the solvent and/or addition of Et_2O, that are either dark green or brown depending on the solvent used. Since this colour change proceeds the most slowly when $CuCl_2$ is used as a reagent, the reaction of $CuCl_2$ with L^{OH} was examined in more detail. A turquoise solid analysing as [$CuCl_2L^{OH}$] (**1**) can sometimes be precipitated in low yield from a $MeNO_2$ solution of $CuCl_2$ and L^{OH}, if this is achieved as soon as the reactants have dissolved. Unfortunately, these crystals are not suitable for X-ray diffraction measurements. However, the X-band EPR spectra of powdered **1** at 120 K ($g_1 = 2.21$, $g_2 = 2.13$, $g_3 = 2.00$, no resolved hyperfine coupling) and [$CuCl_2L^H$] (**2**)[3,7] ($g_1 = 2.16$, $g_2 = 2.11$, $g_3 = 2.01$, no resolved hyperfine coupling) closely resemble those of other complexes [CuX_2L] (X = halide, L = a meridional tridentate ligand), that have a structure mid-way between the extremes of a trigonal bipyramid and square pyramid.[8] This is consistent with the crystal structure of **2** (see below)‡, and implies that solid **1** and **2** adopt similar coordination geometries.

Solutions of pure **1** decompose more slowly than those of the crude reaction mixtures mentioned earlier, the reaction taking 12–48 h to complete depending on the solvent. In CH_2Cl_2 the reaction is non-isosbestic, and results in a colour change from turquoise to dark green–brown, together with a small amount of dark brown precipitate (Fig. 1). The energies of the vis-NIR absorbance maxima of the final product solution bear some resemblance to those shown by **2**, notably in the ingrowth of two peaks near 21 000 cm^{-1} that are present in the spectrum of **2**, but not **1** (ESI†). However, the comparison is complicated by the possibility of scattering effects in the decomposition spectrum, from a small amount of fine suspension that formed during the reaction.

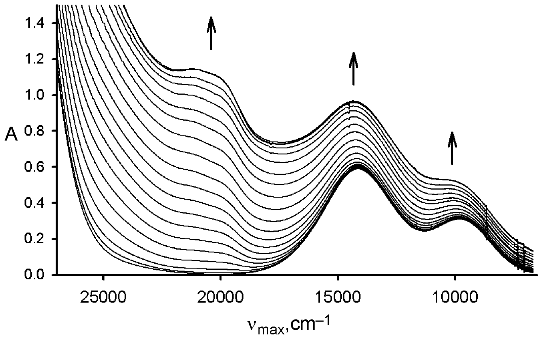


Fig. 1 Vis-NIR spectra following the decomposition of **1** in CH_2Cl_2 solution. Spectra were obtained at 2 h intervals. Some of the right-to-left upward slope of the spectrum may reflect scattering from a small amount of precipitation that took place inside the cuvette after *ca.* 10 h.

Evaporation of the solution of decomposed **1** affords a dark brown–green solid. Although different in appearance, the IR, EPR and FAB mass spectra of this product were almost identical to those of **2**.[3,7] These data support the contention that **2** is one of the major products of the decomposition of **1**. In order to confirm this, the copper content of the solid was removed with aqueous ammonia, leaving an oily organic residue. The ^1H NMR spectrum of this oil showed that it contained $L^H\cdot\frac{1}{2}H_2O$

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† Electronic supplementary information (ESI) available: Full synthetic procedures and analytical data for the compounds in this study. See http://www.rsc.org/suppdata/dt/b3/b310144d/

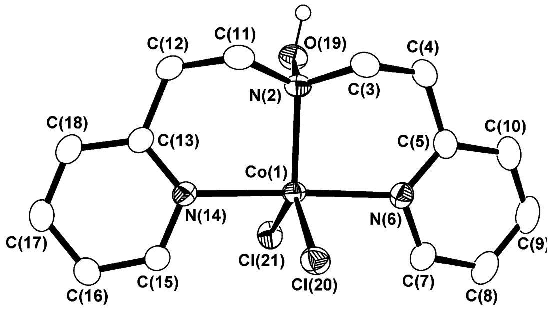

Fig. 2 View of the [$CoCl_2L^{OH}$] molecule in the crystal structure of **5**. For clarity, all C-bound H atoms have been omitted. Thermal ellipsoids are at the 50% probability level. Selected bond lengths (Å) and angles (°): Co(1)–N(2) 2.0982(12), Co(1)–N(6) 2.1751(13), Co(1)–N(14) 2.1731(12), Co(1)–Cl(19) 2.2999(4), Co(1)–Cl(20) 2.3435(4); N(2)–Co(1)–N(6) 91.01(5), N(2)–Co(1)–N(14) 90.93(5), N(2)–Co(1)–Cl(20) 113.54(3), N(2)–Co(1)–Cl(21) 121.78(3), N(6)–Co(1)–N(14) 176.61(5), N(6)–Co(1)–Cl(20) 87.55(3), N(6)–Co(1)–Cl(21) 93.30(3), N(14)–Co(1)–Cl(20) 89.13(3), N(14)–Co(1)–Cl(21) 88.04(3), Cl(20)–Co(1)–Cl(21) 124.640(15).

in *ca.* 80% purity, together with one or more unidentified contaminents. Hence, coordination of L^{OH} to Cu(II) results in its metal-promoted reduction to L^{H}. Very similar dark green or brown product mixtures, containing L^{H}, are obtained when decomposing **1** in MeCN in air or under N_2, and when reacting L^{OH} with [$Cu(NCMe)_4$]BF_4 in MeCN in air or under N_2. Finally, L^{OH} is recovered unchanged when washed with aqueous ammonia, showing that the transformation is copper-effected.

In order to gain more insight into this reaction, the complexation of L^{OH} with $ZnCl_2$, $NiCl_2$ and $CoCl_2$ was examined. All of these salts yield crystalline compounds of formula [MCl_2L^{OH}] (M = Zn, **3**; M = Ni, **4**; M = Co, **5**) from MeOH solution, in up to 56% yield. Importantly, **3**–**5** are indefinitely stable under ambient conditions in solution and the solid state. The d–d spectra of **4** and **5** in CH_2Cl_2 (ESI †). resemble those of [MCl_2L^{H}] (M = Ni,[4] Co[9]), which have been previously proposed to adopt trigonal bipyramidal stereochemistries. The similarity of the spectra of **4** and **5** to those of their L^{H}-containing congeners strongly suggests that the hydroxyl group of L^{OH} does not interact directly with the coordinated metal centre in these compounds. This is borne out by the crystal structure of **5** (see later). The ^1H NMR spectra of **3**–**5** in CD_2Cl_2 all show a single C_2 or *m*-symmetric L^{OH} environment (ESI †). Importantly, for the paramagnetic compounds **4** and **5**, eight contact-shifted peaks of approximately equal integral are observed. That is the number of C-bound H environments expected if the CH_2 groups in the ligand are diastereotopic. This demonstrates that the L^{OH} ligand remains tridentate in this solvent.

To compare the metal-binding modes of L^{H} and L^{OH}, single crystal X-ray analyses of **2** and **5** were undertaken. ‡ Both compounds show mononuclear, five-coordinate metal centres with MCl_2N_3 (M = Cu or Co) donor sets (Fig. 2). The bond angles at the metal ions in the two structures show some differences, however. The τ indices for the two independent molecules in the structure of **2** are 0.53 and 0.46, showing that this compound adopts a geometry that is intermediate between a square-pyramid ($\tau = 0$) and a trigonal bipyramid ($\tau = 1$).[10] This irregular five-coordinate geometry is consistent with the very rhombic *g*-values, with $g_3 \approx 2.00$, shown by solid **2** (and **1**).[8] In contrast, the Co ion in **5** exhibits $\tau = 0.91$, showing that this has a more regular trigonal bipyramidal structure (Fig. 1).[10] Despite these differences, it is clear that L^{OH} and L^{H} coordinate to the metal ions in **2** and **5** in the same way. Taken together, the EPR and structural data from **1**, **2** and **5** strongly imply that the coordination geometries of **1** and **2** will be very similar.

The decomposition of **1** is an unusual example of an N-deoxygenation reaction effected by copper centre, and as such it has some biological relevance.[11] Although we achieved only limited characterisation of **1**, it seems clear that **1** contains a L^{OH} ligand coordinated in a similar fashion as in **5** (Fig. 2). The reaction appears to be copper-specific, in that **3**–**5** do not decompose in this way. It does not require O_2, and it is effected by Cu(I) as well as by Cu(II). We have been unable to obtain any other mechanistic data relating to the transformation. However, there is literature precedent for one mechanism of N-deoxygenation of a Cu-bound substrate, namely O-atom transfer from a Cu(I) complex of the substrate to another acceptor, followed by an intramolecular electron transfer to yield a Cu(II) complex of the final product.[12] It is unclear what the O-atom acceptor could be in this reaction, however, while such a mechanism would also require pre-reduction of **1** to a Cu(I) species before the O-atom transfer step.

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Notes and references

‡ Crystal data for **2**. $C_{14}H_{17}Cl_2CuN_3$, $M_r = 361.75$, monoclinic, $P2_1/c$, $a = 28.1563(4)$, $b = 7.7451(2)$, $c = 14.2271(2)$ Å, $\beta = 104.4294(5)°$, $V = 3004.69(7)$ Å^3, $Z = 8$, μ(Mo-Kα) = 1.802 mm^{-1}, $T = 150(2)$ K; 45081 measured reflections, 5887 independent, $R_{int} = 0.107$; $R(F) = 0.068$, $wR(F^2) = 0.166$. CCDC reference number 202131.

Crystal data for **5**. $C_{14}H_{17}Cl_2CoN_3O$, $M_r = 373.14$, monoclinic, $P2_1/c$, $a = 7.3446(1)$, $b = 15.4679(2)$, $c = 15.2653(2)$ Å, $\beta = 118.1960(5)°$, $V = 1528.43(3)$ Å^3, $Z = 4$, μ(Mo-Kα) = 1.473 mm^{-1}, $T = 150(2)$ K; 29114 measured reflections, 3483 independent, $R_{int} = 0.070$; $R(F) = 0.027$, $wR(F^2) = 0.071$. CCDC reference number 218093.

Crystals of **2** were small, and had a high mosaicity of 0.60 (a strongly diffracting crystal would give a mosaicity of *ca.* 0.45 under our conditions). The asymmetric unit of **2** contains two molecules of the complex lying on general positions, while **5** contains a single molecule per asymmetric unit. No disorder was detected during refinement of either structure. All non-H atoms were modeled anisotropically, and no restraints were applied. All C- and (in **2**) N-bound H atoms were placed in calculated positions and refined using a riding model. The hydroxyl H atom in **5** was located in the Fourier difference map and allowed to refine freely.

See http://www.rsc.org/suppdata/dt/b3/b310144d/ for crystallographic data in CIF or other electronic format.

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