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Modular syntheses of multidentate ligands with variable *N*-donors: applications to tri- and tetracopper(I) complexes†‡

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A general method for the preparation of multidentate ligands comprised of a multi-imine platform derived from 1,1,1-tris(aminomethyl)ethane or tris(aminoethyl)amine connected to bi- and tridentate *N*-donor chelates has been developed. The feasibility of the method has been demonstrated through the synthesis and characterization of a large set of these ligand types. Complexation to Cu(I) was accomplished for several cases, yielding tri- and tetracopper(I) complexes that have been characterized in solution by NMR spectroscopy and conductivity, and in the solid state by elemental analysis, mass spectrometry, and/or X-ray crystallography. These complexes are potentially useful for modeling multicopper protein active sites.

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Introduction

Among the diverse range of copper protein active sites found in biology, those comprising histidine-rich tri- and tetracopper clusters have attracted special interest as a result of their structural novelty and functional/mechanistic features.[1] Illustrative examples are the $[(His)_8Cu_3]$ and $[(His)_7Cu_4(\mu\text{-}S)]$ clusters in the multicopper blue oxidases[1,2] and nitrous oxide reductase (N_2OR),[3] respectively, for which intriguing mechanistic hypotheses have been proposed involving intermediates such as those derived from theory shown in Fig. 1.[4,5] Important aspects of the fundamental chemistry underlying the properties and catalytic behavior of such clusters, as well as related ones with different metal ions (*e.g.* Zn),[6,7] may be obtained through studies of synthetic analogs.[8] One strategy for constructing these analogs is to use appropriately designed multinucleating ligands to position the copper ions in the targeted arrangement. Some success in applying this strategy has been reported, mostly aimed at modeling the multicopper blue oxidases.[9] While several different ligand platforms have been used in these studies, they are typically designed to bind three copper ions and feature *N*-donor ligand sets of narrow scope (typically one type). In view of the absence of any reports of $[Cu_4(\mu\text{-}S)]$ models of the N_2OR active site and the demonstrated effects of supporting ligand structural variation on the course of Cu/O_2[10] and Cu/S[11] reactivity, it would be advantageous to develop a more general ligand synthesis protocol that would enable incorporation of a variety of *N*-donor types for generating structurally diverse 3- and 4-copper clusters. Herein we report such a method, and demonstrate its utility by preparing multiple ligand examples with variable *N*-donors and characterizing several potentially useful Cu^I_3 and Cu^I_4 complexes.

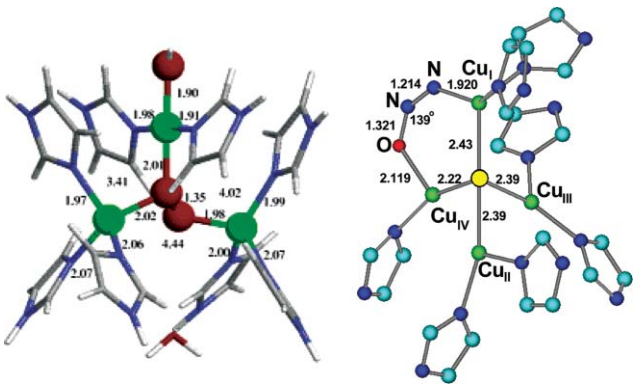

Fig. 1 Intermediates proposed on the basis of theory for (left) O_2 reduction by a multicopper oxidase (green, Cu; red, O), and (right) N_2O reduction by nitrous oxide reductase. Reproduced with permission from ref. 4 and 5*b*. © 2003 and 2007 American Chemical Society.

Experimental

General considerations

All solvents and reagents were obtained from commercial sources and used as received unless noted otherwise. The solvents toluene, tetrahydrofuran (THF), diethyl ether (Et_2O), and CH_2Cl_2 were passed through solvent purification columns (Glass Contour, Laguna, CA) prior to use. CH_3CN was dried over CaH_2 and distilled prior to use. All metal complexes were prepared and stored in a Vacuum Atmospheres inert atmosphere glove box under a dry nitrogen atmosphere or were manipulated using standard Schlenk line techniques. *N*-Isopropyl-*N*-(2-methylpyridine) was prepared according to a previously reported procedure.[9h] The syntheses of the ligands used in this study are shown in Scheme 1 and Scheme 2, and the derived copper(I) compounds are presented in Scheme 3.

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‡ Electronic supplementary information (ESI) available: Drawing of the X-ray structure of **19** and some representative ^{1}H NMR spectra. See DOI: 10.1039/b705806c

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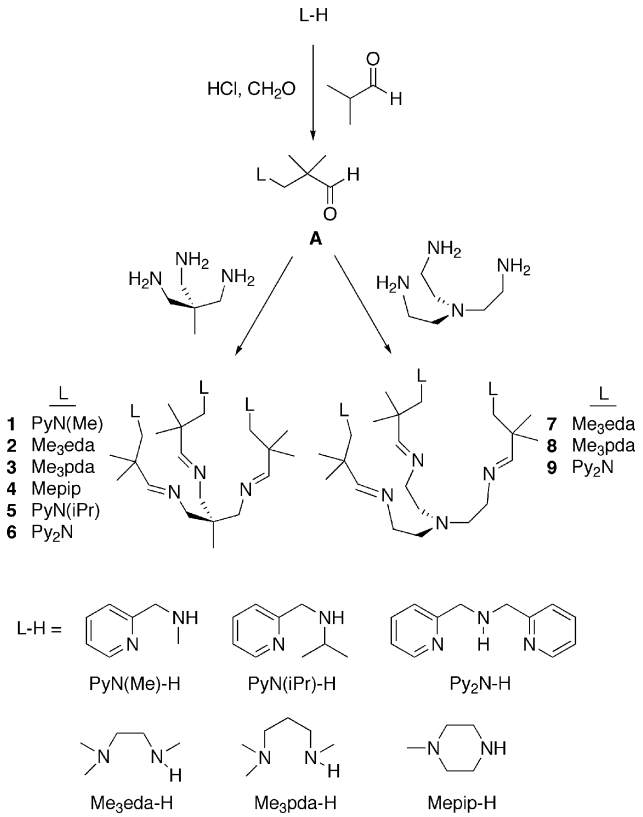
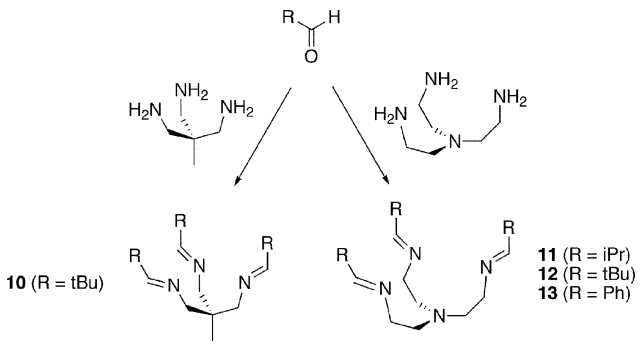


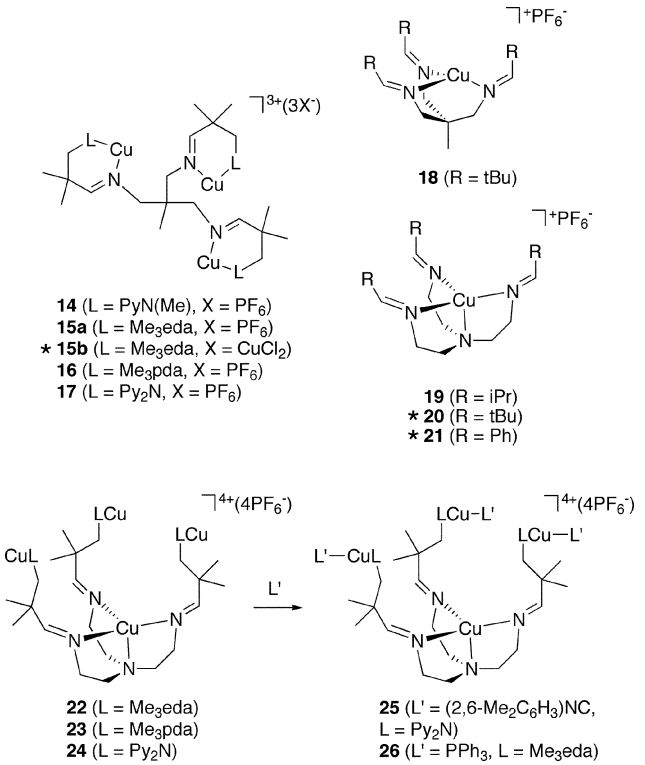
Scheme 1



Scheme 2

Physical methods

NMR spectra were recorded on a Varian VI-300 or VXR-300 spectrometer. Chemical shifts (δ) for ^{1}H or ^{13}C NMR spectra were referenced to residual protium in the deuterated solvent. UV-vis spectra were recorded on a HP8453 (190–1100 nm) diode array spectrophotometer. Low temperature spectra were acquired through the use of a Unisoko low temperature UV-vis cell holder. When necessary, UV-vis spectra were corrected for drifting baselines due to minimal frosting of the UV cells caused by the low-temperature device. This was achieved by subtracting the average of a region with no absorbance (*i.e.*, baseline, typically 950–1000 nm) from the entire spectrum. Resonance Raman spectra were recorded on an Acton 506 spectrometer using a Princeton Instruments LN/CCD-11100-PB/UVAR detector and ST-1385 controller interfaced with Winspec software. A Spectra-Physics Beamlok 2065-7S Ar Laser provided excitation at 568.2 nm. The



Scheme 3 Copper(I) compounds prepared in this work. Asterisks indicate those complexes characterized by X-ray diffraction.

spectra were obtained at −196 °C using a backscattering geometry; samples were frozen onto a cold-plated copper coldfinger in thermal contact with a Dewar flask containing liquid nitrogen. Raman shifts were externally referenced to liquid indene. High-resolution mass spectra were obtained on a Bruker BioTOF II ESI-TOF/MS spectrometer. Elemental analyses were performed by Robertson Microlit (Madison, NJ).

X-Ray crystallography. In each case, a crystal was placed onto the tip of a 0.1 mm diameter glass capillary and mounted on a Bruker SMART Platform CCD diffractometer for a data collection at 173(2) K. Data collections were carried out using MoKα radiation (graphite monochromator) with a detector distance of ~4.9 cm. A randomly oriented region of reciprocal space was surveyed to the extent of one sphere and to a resolution of 0.84 Å. Four major sections of frames were collected with 0.30° steps in ω at four different ϕ settings and a detector position of −28° in 2θ. The intensity data were corrected for absorption and decay (SADABS).[12] Final cell constants were calculated from the *xyz* centroids of strong reflections from the actual data collection after integration (SAINT).[13] See ESI† for full crystal and refinement details in the form of CIFs.

Conductivity measurements. Electrical conductivity measurements were carried out in acetonitrile using a Fischer Scientific Accumet Portable AP65 model conductivity bridge with a cell having a cell constant of 1.0 cm^{-1}. The equivalent conductance, Λ_e, was calculated from the conductance measurements and plotted against the square root of the concentration for each sample. Extrapolation of the linear portion to zero concentration resulted in the determination of the equivalent conductance at infinite dilution, Λ_o. A plot of ($\Lambda_o - \Lambda_e$) *versus* the square root of the

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concentration gave Onsager plots[14] with straight lines that enabled 1 : 1, 2 : 1,[15] 3 : 1, and 4 : 1 electrolytes to be distinguished.

1,1,1-Tris(aminomethyl)ethane (tame). This compound was prepared by a modification of a literature procedure.[16] Sodium azide (10.8 g, 166.4 mmol) was added to a mixture containing tris(benzenesulfonyloxymethyl)ethane (15.0 g, 27.8 mmol) and diethylene glycol (350 mL). The mixture was heated to 135 °C for 24 h under an atmosphere of dry nitrogen. The resulting brown solution was allowed to cool to room temperature and 300 mL of water was added. The mixture was stirred for 15 min, then extracted with CH_2Cl_2 (3 × 100 mL). Triphenylphosphine (36.4 g, 139 mmol) was then added to the organic phase and stirred for 3.5 h. The mixture was hydrolyzed by adding NaOH (3.3 g) in 10 mL of water. The mixture was stirred for 48 h, evaporated to a white semisolid and distilled at 100 °C (50 mTorr) to yield a colorless liquid. The colorless liquid was then added to a 200 mL flask equipped with a magnetic stirring bar and a Dean–Stark condenser. Dry toluene (100 mL) was added and the solution heated to reflux. Toluene (90 mL) was distilled and removed before the mixture was concentrated to give the product as a colorless oil (2.0 g, 17.1 mmol, 62%).

General procedure for synthesis of aldehydes A. The aldehydes can be synthesized by two methods. **Method 1**. Concentrated HCl (6.60 mL) was added dropwise to the appropriate diamine (typically 40.0 mmol) in CH_3CN or ethanol (60 mL) at 0 °C. The solution was stirred at room temperature for 15 min before *para*formaldehyde (1.47 g, 49.0 mmol) and isobutyraldehyde (3.10 g, 43.0 mmol) were added and refluxed for 1.5 h. After cooling to room temperature, additional *para*formaldehyde (1.47 g, 49.0 mmol) was added and the solution refluxed for another 1.5 h. To this solution, was added 200 mL of water which was extracted with diethyl ether (2 × 125 mL) to remove unreacted *para*formaldehyde and isobutyraldehyde. The aqueous solution was made strongly alkaline with 10% NaOH and added to 250 mL of diethyl ether. The organic layer was separated, dried with $MgSO_4$ and the solvent removed under reduced pressure. The resulting clear liquid was purified by distillation. **Method 2**. The appropriate diamine or triamine (typically 50.0 mmol) was added to 50 mL of dry methanol at 0 °C. HCl gas was bubbled through the solution for 5 min, causing the formation of a white precipitate. The cold solution was filtered, washed with diethyl ether (2 × 75 mL) and dried under reduced pressure for 3 h. The resulting dihydrochloride or trihydrochloride of the appropriate diamine or triamine (45 mmol) was added to *para*formaldehyde (1.58 g, 52.5 mmol) in CH_3CN (150 mL) and heated to reflux for 15 min. After cooling to room temperature, isobutyraldehyde (3.60 g, 50 mmol) was added and the solution was refluxed for 1 h. Upon cooling to ambient temperature, additional *para*formaldehyde (1.58 g, 52.5 mmol) was added and the solution refluxed for 1.5 h. To this solution, was added 200 mL of water which was extracted with diethyl ether (2 × 125 mL) to remove unreacted *para*formaldehyde and isobutyraldehyde. The aqueous solution was made strongly alkaline with 10% NaOH and added to 250 mL of diethyl ether. The organic layer was separated, dried with $MgSO_4$ and the solvent removed under reduced pressure. The resulting clear liquid was purified by distillation.

2,2-Dimethyl-3-((methyl)(pyridin-2-ylmethyl)amino)-propanal (A, L = PyN(Me)). Method 1 (32%), distilled at 0.05 Torr and 65 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 (s, 6H), 2.18 (s, 3H), 2.63 (s, 2H), 3.65 (s, 2H), 7.10 (m, 1H), 7.39 (m, 1H), 7.61 (m, 1H), 8.46 (m, 1H), 9.47 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3, 44.4, 47.8, 64.7, 65.5, 121.9, 122.7, 136.3, 148.7, 159.5, 206.2. IR (KBr): 2967, 2844, 2701, 1725, 1589, 1570, 1473, 1434, 1362, 1259, 1045, 995, 882, 863, 762 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{12}H_{18}N_2O + Na]^+$: 229.1312, found 229.1313. HRMS (ESI, Pos) calculated for $[C_{12}H_{18}N_2O + H]^+$: 207.1492, found 207.1477.

3-((2-(Dimethylamino)ethyl)(methyl)amino)-2,2-dimethyl-propanal (A, L = Me_3eda). Method 1 (35%), Method 2 (80%), distilled at 0.05 Torr and 38 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 (s, 6H), 2.17 (s, 6H), 2.18 (s, 3H), 2.30 (m, 2H), 2.45 (m, 2H), 2.49 (s, 2H), 9.51 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.4, 44.5, 45.8, 47.5, 57.5, 57.7, 65.5, 206.5. IR (KBr): 2966, 2816, 2771, 1725, 1464, 1261, 1118, 1038, 880 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{10}H_{22}N_2O + Na]^+$: 209.1625, found 209.1615.

3-((3-(Dimethylamino)propyl)(methyl)amino)-2,2-dimethylpropanal (A, L = Me_3pda). Method 1 (34%), Method 2 (54%), distilled at 0.05 Torr and 51 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 (s, 6H), 1.53 (dt, J = 7.2, 7.5 Hz, 2H), 2.14 (s, 3H), 2.16 (s, 6H), 2.19 (t, J = 7.2 Hz, 2H), 2.32 (t, J = 7.5 Hz, 2H), 2.45 (s, 2H), 9.50 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.4, 25.7, 44.0, 45.4, 47.5, 57.4, 57.5, 65.2, 206.5. IR (KBr): 2951, 2813, 2781, 1726, 1461, 1098, 1042 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{11}H_{24}N_2O + Na]^+$: 223.1781, found 223.1787. HRMS (ESI, Pos) calculated for $[C_{11}H_{24}N_2O + H]^+$: 201.1961, found 201.1958.

2,2-Dimethyl-3-(4-methyl-piperazin-1-yl)propanal (A, L = Mepip). Method 1 (27%), Method 2 (47%), distilled at 0.05 Torr and 50 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.99 (s, 6H), 2.19 (m, 4H), 2.31 (s, 3H), 2.40 (s, 2H), 2.43 (m, 4H), 9.49 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3, 45.8, 47.4, 54.6, 55.0, 64.9, 206.4. IR (ATR): 2934, 2792, 1667, 1456, 1373, 1280, 1163, 1123, 1016, 822 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{10}H_{20}N_2O + Na]^+$: 207.1457, found 207.1468.

3-((Isopropyl)(pyridin-2-ylmethyl)amino)-2,2-dimethyl-propanal (A, L = PyN(iPr)). Method 1 (18%), distilled at 0.05 Torr and 95 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.96 (s, 6H), 0.96 (d, J = 6.6 Hz, 6H), 2.63 (s, 2H), 2.64 (m, J = 6.6 Hz, 1H), 3.68 (s, 2H), 7.08 (m, 1H), 7.46 (m, 1H), 7.61 (m, 1H), 8.42 (m, 1H), 9.37 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.8, 20.3, 47.6, 51.6, 57.2, 58.1, 121.6, 122.4, 136.4, 148.5, 161.0, 206.3. IR (KBr): 2965, 2870, 2834, 2701, 1724, 1590, 1469, 1433, 1365 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{14}H_{22}N_2O + Na]^+$: 257.1625, found 257.1616.

Bis(3-((methyl)(pyridine-2-ylmethyl)amino)-2,2-dimethyl-propanal (A, L = Py_2N). Method 2 (52%); purification by distillation was not required. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.02 (s, 6H), 2.94 (s, 2H), 3.81 (s, 4H), 7.20 (m, 2H), 7.47 (d, J = 7.8 Hz, 2H), 7.70 (m, 2H), 8.56 (d, J = 4.8 Hz, 2H), 9.28 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.1, 48.1, 61.1, 61.6, 122.1, 123.3, 136.5, 148.8, 159.0, 206.1. IR (ATR): 2965, 2931, 2825, 1723, 1589, 1569, 1473, 1434, 1361, 1120, 1085, 1047, 995, 881, 766, 614 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{17}H_{21}N_3O + H]^+$: 284.1757, found 284.1765.

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General procedure for synthesis of ligands 1–13. To a 100 mL roundbottom flask equipped with a Dean–Stark condenser, 1,1,1-tris(aminomethyl)ethane (**1–6**) or tris(2-aminoethyl)amine (**7–9**) (1 equiv) was added to the appropriate aldehyde **A** (3.3 equiv) in 80 mL of dry toluene. The solution was heated to reflux and 75 mL of toluene was distilled and removed. The remaining solvent was removed under reduced pressure and unreacted aldehyde was removed by distillation (see below for conditions) leaving the product as a yellow oil.

Compound 1. Unreacted aldehyde **A** (L = PyN(Me)) was removed by distillation (80 °C at 0.05 Torr). Yield from 186 mg of 1,1,1-tris(aminomethyl)ethane: 0.87 g (1.3 mmol, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.823 (s, 3H), 1.03 (s, 18H), 2.20 (s, 9H), 2.51 (s, 6H), 3.23 (s, 6H), 3.68 (s, 6H), 7.10 (m, 3H), 7.48 (m, 3H), 7.50 (s, 3H), 7.61 (m, 3H), 8.47 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.40, 23.86, 40.25, 41.57, 44.98, 66.05, 66.82, 67.16, 121.8, 122.7, 136.3, 148.8, 160.4, 171.5. IR (ATR): 2957, 2924, 2838, 2812, 1667, 1589, 1456, 1433, 1360, 1044 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{41}H_{63}N_9 + Na]^+$: 704.5099, found 704.5088.

Compound 2. Unreacted aldehyde **A** (L = Me_3eda) was removed by distillation (55 °C at 0.05 Torr). Yield from 207 mg of 1,1,1-tris(aminomethyl)ethane: 0.88 g (1.4 mmol, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.898 (s, 3H), 1.06 (s, 18H), 2.24 (s, 18H), 2.26 (s, 9H), 2.35 (m, 6H), 2.40 (s, 6H), 2.52 (m, 6H), 3.30 (s, 6H), 7.55 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.31, 23.81, 40.13, 41.20, 45.19, 45.88, 57.65, 58.17, 66.79, 67.70, 171.6. IR (KBr): 2953, 2815, 2765, 1669, 1465, 1118, 1035 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{35}H_{75}N_9 + Na]^+$: 644.6038, found 644.6023.

Compound 3. Unreacted aldehyde **A** (L = Me_3pda) was removed by distillation (100 °C at 0.05 Torr). Yield from 411 mg of 1,1,1-tris(aminomethyl)ethane: 1.40 g (2.1 mmol, 60%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.842 (s, 3H), 1.02 (s, 18H), 1.56 (m, 6H), 2.18 (s, 9H), 2.19 (s, 18H), 2.23 (m, 6H), 2.32 (s, 6H), 2.35 (m, 6H), 3.25 (s, 6H), 7.51 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.45, 23.94, 26.03, 40.28, 41.27, 44.77, 45.57, 57.79, 58.18, 66.88, 67.44, 171.83. IR (ATR): 2949, 2812, 2763, 1667, 1458, 1383, 1042 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{38}H_{81}N_9 + Na]^+$: 686.6507, found 686.6503. HRMS (ESI, Pos) calculated for $[C_{38}H_{81}N_9 + H]^+$: 664.6688, found 664.6673.

Compound 4. Unreacted aldehyde **A** (L = Mepip) was removed by distillation (125 °C at 0.05 Torr). Yield from 64 mg of 1,1,1-tris(aminomethyl)ethane: 0.29 g (1.43 mmol, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.853 (s, 3H), 1.02 (s, 18H), 2.22 (s, 9H), 2.32 (m, 12H), 2.33 (s, 6H), 2.47 (m, 12H), 3.25 (s, 6H), 7.51 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.44, 23.82, 40.33, 41.32, 46.10, 55.23, 55.44, 66.96, 67.13, 171.7. IR (ATR): 2935, 2792, 1667, 1456, 1373, 1280, 1163, 1123, 1016, 822 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{35}H_{69}N_9 + Na]^+$: 638.5568, found 638.5574. HRMS (ESI, Pos) calculated for $[C_{35}H_{69}N_9 + H]^+$: 616.5749, found 616.5745.

Compound 5. Unreacted aldehyde **A** (L = PyN(iPr)) was removed by distillation (125 °C at 0.05 Torr). Yield from 255 mg of 1,1,1-tris(aminomethyl)ethane: 1.4 g (1.8 mmol, 84%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.795 (s, 3H), 0.968 (d, 18H, J = 6.6 Hz), 0.995 (s, 18H), 2.50 (s, 6H), 2.73 (m, 3H, J = 6.6 Hz), 3.14 (s, 6H), 3.75 (s, 6H), 7.10 (m, 3H), 7.47 (m, 3H), 7.60 (s, 3H), 7.62 (m, 3H), 8.46 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.86, 19.38, 20.23, 23.84, 39.98, 41.04, 51.44, 58.87, 66.66, 121.4, 122.2, 136.2, 148.5, 161.8, 171.5. IR (ATR): 2963, 2869, 2829, 1667, 1589, 1463, 1432, 1387, 1364, 1165, 1045, 781, 752. HRMS (ESI, Pos) calculated for $[C_{47}H_{75}N_9 + Na]^+$: 788.6038, found 788.6054. HRMS (ESI, Pos) calculated for $[C_{47}H_{75}N_9 + H]^+$: 766.6218, found 766.6242.

Compound 6. Unreacted aldehyde **A** (L = Py_2N) was removed by distillation (160 °C at 0.05 Torr). Yield from 160 mg of 1,1,1-tris(aminomethyl)ethane: 0.99 g (1.08 mmol, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.73 (s, 3H), 0.92 (s, 18H), 2.73 (s, 6H), 3.04 (s, 6H), 3.75(s, 12H), 7.20 (m, 6H), 7.37(s, 3H), 7.51(d, J = 8.0 Hz, 6H), 7.71(m, 6H), 8.49 (d, J = 5.0 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.29, 23.83, 40.22, 41.63, 61.24, 62.04, 63.49, 121.8, 123.2, 136.3, 148.9, 159.9, 171.2. IR (KBr): 2957, 2939, 2828, 1666, 1589, 1472, 1433, 1361, 1047 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{56}H_{72}N_{12} + Na]^+$: 935.5895, found 935.5927.

Compound 7. Unreacted aldehyde **A** (L = Me_3eda) was removed by distillation (160 °C at 0.05 Torr). Yield from 337 mg of tris(2-aminoethyl)amine: 1.212 g (1.86 mmol, 82%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.996 (s, 18H), 2.18 (s, 18H), 2.20 (s, 9H), 2.29 (t, J = 5.9 Hz, 6H), 2.33 (s, 6H), 2.47 (t, J = 5.9, 6H), 2.67 (t, J = 7.5 Hz, 6H), 3.40 (t, J = 7.1 Hz, 6H), 7.53 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.78, 41.05, 45.24, 46.01, 55.54, 57.75, 58.22, 59.87, 67.93, 172.7. IR (KBr): 2948, 2814, 2765, 1665, 1463, 1119, 1036 cm^{-1}. Anal. Calcd for $C_{36}H_{78}N_{10}$: C, 66.41; H, 12.08; N, 21.51. Found: C, 66.22; H, 12.18; N, 21.90.

Compound 8. Unreacted aldehyde **A** (L = Me_3pda) was removed by distillation (165 °C at 0.05 Torr). Yield from 262 mg of tris(2-aminoethyl)amine: 1.19 g (1.7 mmol, 96%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.00 (s, 18H), 1.55 (q, J = 7.1, 6H), 2.17 (s, 18H), 2.21 (t, J = 7.0 Hz, 6H), 2.30 (t, J = 7.0, 6H), 2.68 (t, J = 7.4 Hz, 6H), 3.42 (t, J = 6.8 Hz, 6H), 7.53 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.79, 26.03, 41.02, 44.75, 45.60, 55.55, 57.78, 58.14, 59.87, 67.53, 172.8. IR (KBr): 2948, 2812, 1666, 1459, 1153, 1041 cm^{-1}. Anal. Calcd for $C_{39}H_{84}N_{10}$: C, 67.58; H, 12.21; N, 20.21. Found: C, 67.43; H, 11.99; N, 20.45.

Compound 9. Unreacted aldehyde **A** (L = Py_2N) was removed by distillation (125 °C at 0.05 Torr). Yield from 230 mg of tris(2-aminoethyl)amine: 0.95 g (1.01 mmol, 64%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (s, 18H), 2.44 (t, J = 7.7 Hz, 6H), 2.73 (s, 6H), 3.16 (t, J = 7.4 Hz, 6H), 3.75 (s, 12H), 7.21 (m, 6H), 7.40 (s, 3H), 7.52 (d, J = 8.1 Hz, 6H), 7.72 (m, 6H), 8.49 (d, J = 4.2 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.66, 41.56, 55.41, 59.72, 62.19, 63.66, 122.1, 123.4, 136.4, 149.0, 159.8, 172.8. IR (KBr): 2957, 2939, 2828, 1666, 1589, 1472, 1433, 1361, 1047, cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{57}H_{75}N_{13} + Na]^+$: 964.6161, found 964.6201.

Compound 10. Unreacted aldehyde was removed by distillation (80 °C at 0.05 Torr). Yield from 133 mg of 1,1,1-tris(aminomethyl)ethane: 0.240 g (0.75 mmol, 66%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (s, 3H), 1.06 (s, 27H), 3.22 (s, 6H), 7.52 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.21, 23.74, 36.31, 40.17, 55.10, 172.3. IR (KBr): 2962, 2832, 1675, 1465, 1362, 1065, 954 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{20}H_{39}N_3 + H]^+$: 322.3217, found 322.3222.

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Compound 11. Unreacted aldehyde was removed by distillation (80 °C at 0.05 Torr). Yield from 467 mg of tris(2-aminoethyl)amine: 0.91 g (2.94 mmol, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (d, 18H), 2.35 (m, J = 6.7 Hz, 3H), 2.68 (t, J = 7.2 Hz, 6H), 3.37 (t, J = 7.0 Hz, 6H), 7.57 (d, J = 4.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.23, 33.91, 55.41, 59.48, 170.5. IR (KBr): 2962, 2833, 1671, 1465, 1364, 1067, 953 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{18}H_{36}N_4 + Na]^+$: 331.2832, found 331.2839.

Compound 12. Unreacted aldehyde was removed by distillation (80 °C at 0.05 Torr). Yield from 1.01 g of tris(2-aminoethyl)amine: 2.19 g (6.25 mmol, 90.6%) ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (s, 27H), 2.73 (t, J = 7.3 Hz, 6H), 3.42 (t, J = 7.0 Hz, 6H), 7.52 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.90, 36.00, 55.63, 59.75, 172.8. IR (KBr): 2956, 2930, 2814, 1667, 1475, 1362, 1071, 919 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{21}H_{42}N_4 + H]^+$: 351.3482, found 351.3491.

Compound 13. Unreacted aldehyde was removed by distillation (80 °C at 0.05 Torr). Yield from 538 mg of tris(2-aminoethyl)amine: 1.16 g (2.83 mmol, 77%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.94 (t, J = 6.5 Hz, 6H), 3.70 (t, J = 5.85 Hz, 6H), 7.38 (m, 9H), 7.52 (d, J = 6.6 Hz, 6H), 8.10 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.78, 60.20, 128.1, 128.6, 130.5, 136.3, 161.9. IR (KBr): 2952, 2848, 2795, 1647, 1064, 1034 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{27}H_{30}N_4 + Na]^+$: 433.2363, found 433.2382.

General procedure for the preparation of Cu(I) complexes. To a slurry of $[Cu(CH_3CN)_4]PF_6$ (1.0, 3.0, or 4.0 equiv, depending on the ligand used) or, for the case of **15b**, CuCl (6.0 equiv), in CH_3CN (3 mL), was added a 5 mL solution of the appropriate ligand (1.0 equiv) in CH_3CN. The solution was stirred for 15 min and the volume reduced to 2 mL under reduced pressure. Addition of diethyl ether (7 mL) resulted in the formation of a white-yellow solid which was collected, washed with diethyl ether (3 × 5 mL) and dried under reduced pressure.

Compound 14. Yield from 101 mg of **1**: 169 mg (0.13 mmol, 87%). Drying under vacuum resulted in the loss of coordinated CH_3CN. ^{1}H NMR (300 MHz, CD_3CN): δ 1.30 (s, 18H), 1.36 (s, 3H), 2.38 (s, 9H), 2.71 (s, 6H), 3.65 (s, 6H), 3.72 (s, 6H), 7.35 (m, 6H), 7.71 (s, 3H), 7.83 (t, J = 8.1 Hz, 3H), 8.44 (d, J = 4.8 Hz, 3H). ^{13}C NMR (75 MHz, CD_3CN): δ 20.2, 24.2, 38.8, 39.8, 46.5, 65.4, 65.8, 69.9, 123.7, 124.2, 138.0, 148.6, 156.8, 178.1. IR (KBr): 2966, 2871, 1667, 1630, 1608, 1463, 1446, 1381, 1307, 1159, 1108, 1033, 840, 764, 738, 558 cm^{-1}. Anal. Calcd for $C_{41}H_{63}N_9Cu_3P_3F_{18}$: C, 37.66; H, 4.86; N, 9.64. Found: C, 37.25; H, 4.67; N, 9.68.

Compound 15. (a) Yield from 154 mg of **2**: 285 mg (0.23 mmol, 92%). Drying under vacuum resulted in the loss of coordinated CH_3CN. ^{1}H NMR (300 MHz, CD_3CN): δ 1.28 (s, 18H), 1.39 (s, 3H), 2.43 (s, 18H), 2.50 (m, 6H), 2.52 (s, 9H), 2.56 (s, 6H), 2.62 (m, 6H), 3.55 (s, 6H), 7.75 (s, 3H). IR (KBr): 2969, 2875, 1633, 1470, 1288, 1038, 949, 840, 558 cm^{-1}. Anal. Calcd for $C_{35}H_{75}N_9Cu_3P_3F_{18}$: C, 33.70: H, 6.06; N, 10.10. Found: C, 33.66; H, 5.52; N, 10.58. (b) Yield from 68.6 mg of **2**: 130 mg (0.109 mmol, 94%). Drying under vacuum resulted in the loss of coordinated CH_3CN. ^{1}H NMR (300 MHz, CD_3CN): δ 1.19 (s, 3H), 1.26 (s, 18H), 2.39 (s, 18H), 2.45 (m, 6H), 2.48 (s, 9H), 2.53 (s, 6H), 2.58 (m, 6H), 3.63 (s, 6H), 7.78 (s, 3H). (KBr): 2969, 2875, 1633, 1470, 1288, 1106, 1038, 949, 840, 558 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{35}H_{75}N_9Cu_3Cl]^{2+}$: 880.3405, found 880.3741.

Compound 16. Yield from 459 mg of **3**: 742 mg (0.58 mmol, 83%). Drying under vacuum resulted in the loss of coordinated CH_3CN. ^{1}H NMR (300 MHz, CD_3CN): δ 1.19 (s, 3H), 1.23 (s, 18H), 2.37 (s, 18H), 2.42 (m, 6H), 2.50 (s, 9H), 2.57 (s, 6H), 2.61 (m, 6H), 2.78 (m, 6H), 3.53 (s, 6H), 7.70 (s, 3H). IR (KBr): 2969, 2874, 1634, 1468, 1389, 1026, 1004, 839, 751, 559 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{38}H_{81}N_9Cu_3]^{3+}$: 284.8158, found 284.8071.

Compound 17. Yield from 72 mg of **6**: 120.4 mg (0.078 mmol, 98%). Drying under vacuum resulted in the loss of coordinated CH_3CN. ^{1}H NMR (300 MHz, CD_3CN): δ 1.18 (s, 18H), 1.59 (s, 3H), 2.95 (s, 6H), 3.68 (s, 6H), 4.00 (s, 12H), 7.32 (m, 12H), 7.68 (s, 3H), 7.85 (t, J = 7.7 Hz, 6H), 8.52 (d, J = 5.1 Hz, 6H). IR (KBr): 2967, 2926, 2871, 1669, 1604, 1479, 1442, 1097, 1054, 840, 763, 558 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{56}H_{72}N_{12}Cu_3]^{3+}$: 367.1291, found 367.1206.

Compound 18. Yield from 123 mg of **10**: 191 mg (0.36 mmol, 87%). ^{1}H NMR (300 MHz, CD_3CN): δ 0.76 (s, 3H), 1.16 (s, 27H), 3.39 (s, 6H), 7.58 (s, 3H). IR (KBr): 2693, 2929, 2391, 1654, 1476, 1054, 927, 738, 555 cm^{-1}. Anal. Calcd for $C_{20}H_{39}N_3CuPF_6$: C, 45.32; H, 7.42; N, 7.93. Found: C, 45.01; H, 7.38; N, 8.21.

Compound 19. Yield from 127 mg of **11**: 200 mg (0.39 mmol, 87%). ^{1}H NMR (300 MHz, CD_3CN): δ 1.10 (s, 18H), 2.54 (m, J = 6.6 Hz, 3H), 2.87 (t, J = 5.9 Hz, 6H), 3.48 (t, J = 5.2 Hz, 6H), 7.56 (d, J = 0.6 Hz, 2H). IR (KBr): 2975, 2915, 2342 1665, 1409, 1235, 1065, 958, 763, 556 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{18}H_{36}N_4Cu]^+$: 371.2230, found 371.3155.

Compound 20. Yield from 96.5 mg of **12**: 136.8 mg (0.245 mmol, 89%). ^{1}H NMR (300 MHz, CD_3CN): δ 1.18 (s, 27H), 2.84 (dt, J = 5.0 Hz, 6H), 3.47 (dt, J = 5.4 Hz, 6H), 7.77 (s, 3H). IR (KBr): cm^{-1}: 2966, 2929, 2348, 1670, 1405, 1210, 1071, 930, 773, 559. Anal. Calcd for $C_{21}H_{42}N_4CuPF_6$: C, 45.11; H, 7.57; N, 10.02. Found: C, 44.70; H, 7.40; N, 10.01.

Compound 21. Yield from 22 mg of **13**: 29.3 mg (0.05 mmol, 83%). ^{1}H NMR (300 MHz, CD_3CN): δ 3.15 (t, J = 5.6 Hz, 6H), 3.87 (t, J = 5.1 Hz, 6H), 6.93 (t, J = 7.8 Hz, 6H), 7.42 (t, J = 7.4, 3H), 8.08 (d, J = 7.8, 6H), 8.52 (s, 3H). IR (KBr): 2976, 2918, 2342 1665, 1403, 1230, 1065, 956, 763, 559 cm^{-1}. HRMS (ESI, Pos) calculated for $[C_{27}H_{30}N_4Cu]^+$: 473.1761, found 473.1978.

Compound 22. Yield from 63 mg of **7**: 144 mg (0.0873 mmol, 91%). Drying under vacuum resulted in the loss of coordinated CH_3CN. ^{1}H NMR (300 MHz, CD_3CN): δ 1.25 (s, 18H), 2.46 (s, 18H), 2.49 (m, 6H), 2.51 (s, 9H), 2.58 (s, 6H), 2.64 (m, 6H), 2.88 (m, 6H), 3.53 (m, 6H), 7.74 (s, 3H). IR (KBr): 2695, 2873, 1629, 1469, 1285, 1036, 945, 836, 555 cm^{-1}. Anal. Calcd for $C_{44}H_{90}N_{14}Cu_4P_4F_{24}$: C, 32.04; H, 5.50; N, 11.89. Found: C, 31.92; H, 5.25; N, 11.48.

Compound 23. Yield from 60 mg of **8**: 129 mg (0.0763 mmol, 88%). Drying under vacuum resulted in the loss of coordinated CH_3CN. ^{1}H NMR (300 MHz, CD_3CN): δ 1.20 (s, 18H), 1.60 (quintet, J = 6.7 Hz, 6H), 2.22 (s, 18H), 2.24 (m, 6H), 2.26 (s, 9H), 2.45 (s, 6H), 2.49 (m, 6H), 2.85 (t, J = 6.0 Hz, 6H), 3.55 (t, J = 6.0 Hz, 6H), 7.80 (s, 3H). IR (KBr): 2965, 2875, 1629, 1465, 1283,

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1036, 940, 834, 557. Anal. Calcd for $C_{47}H_{96}N_{14}Cu_4P_4F_{24}$: C, 33.38; H, 5.72; N, 11.59. Found: C, 33.05; H, 5.55; N, 11.59.

Compound 24. Yield from 96.5 mg of **9**: 176.7 mg (0.091 mmol, 89%, assuming a molecular weight that included CH_3CN coligands). ^{1}H NMR (300 MHz, CD_3CN): δ 1.15 (s, 18H), 2.94 (s, 6H), 3.08 (m, 6H), 3.56 (m, 6H), 4.00 (s, 12H), 7.30 (m, 12H), 7.64 (s, 3H), 7.79 (m, 6H), 8.59 (d, J = 4.5 Hz, 6H). IR (KBr): 2965, 1658, 1604, 1479, 1443, 1095, 840, 766, 558 cm^{-1}. While high quality elemental analysis or HRMS data for this compound was not obtained, its identity is supported by the full characterization of its isocyanide derivative (**25**, see below).

Compound 25. A 3 mL solution of xylyl isocyanide (4.0 equiv) in CH_3CN was added to **24** (47.2 mg, 0.027 mmol) in 2 mL of CH_3CN. The solution was stirred for 20 min, filtered through Celite and the volume reduced to 2 mL under reduced pressure. Diethyl ether (7 mL) was added, causing the formation of a white-yellow solid. The solid was collected, washed with diethyl ether (2 × 4 mL) and dried under vacuum. Yield: 35.5 mg (0.015 mmol, 63%). ^{1}H NMR (300 MHz, CD_3CN): δ 1.30 (s, 18H), 2.31 (s, 24H), 2.71 (m, 6H), 3.09 (s, 6H), 3.43 (m, 6H), 3.92 (s, 12H), 7.13 (d, J = 7.3 Hz, 8H), 7.27 (t, J = 6.6 Hz, 4H), 7.38 (d, J = 6.6 Hz, 6H), 7.47 (t, J = 7.9 Hz, 6H), 7.86 (m, 9H), 8.70 (d, J = 4.6 Hz, 6H). IR (KBr): 2967, 1650, 1471, 1387, 1105, 840, 558 cm^{-1}. Anal. Calcd for $C_{93}H_{111}N_{17}Cu_4P_4F_{24}$: C, 48.54; H, 4.86; N, 10.35. Found: C, 48.53; H, 5.07; N, 10.08.

Compound 26. A 3 mL solution of triphenylphosphine (4.0 equiv) in CH_3CN was added to **22** (37.9 mg, 0.015 mmol) in 2 mL of CH_3CN. The solution was stirred for 20 min, filtered through Celite and the volume reduced to 2 mL under reduced pressure. Diethyl ether (7 mL) was added, causing the formation of a white solid. The solid was collected, washed with diethyl ether (2 × 4 mL) and dried under vacuum. Yield: 52.0 mg (0.023 mmol, 90%). Anal. Calcd for $C_{108}H_{138}N_{10}Cu_4P_8F_{24}$: C, 51.18; H, 5.49; N, 5.53; P, 9.78. Found: C, 51.15; H, 5.33; N, 5.53; P, 9.72 (for P: ICP emission).

Low temperature reaction of 24 with O_2. Solutions of **24** in propionitrile were cooled to −78 °C and exposed to dry O_2, causing a color change from yellow to intense purple. A sample for resonance Raman (15 mM) was prepared by removing an aliquot of the purple solution in propionitrile by frozen pipet. Solutions of the purple species decomposed at −78 °C in propionitrile to yield a green colored solution. Counterion metathesis with 4 equiv $NaB(3,5\text{-}(CF_3)_2C_6H_3)_4$ (4.2 mg, 0.0047 mmol) in THF (4 mL) and oxygenation at −78 °C produced a more stable purple species (no decomposition after 2 h at −78 °C). UV-vis (propionitrile) [λ_{max}/nm]: 535, 610; resonance Raman (λ_{ex} 568.2 nm, 77 K, propionitrile): 832 ($^{18}O_2$ 786), 544 ($^{18}O_2$ 516) cm^{-1}.

Results and discussion

Design and synthesis of ligands

We designed two types of multidentate ligands with the initial aim of preparing tetranuclear complexes, the specific goal being to bind one metal ion to a tris-imine platform and another three to tethered bi- or tridentate *N*-donor chelates "L" (**1–9**, Scheme 1). One ligand set was derived from 1,1,1-tris(aminomethyl)ethane (**1–6**) and the other from tris(2-aminoethyl)amine (**7–9**) to provide tri- and tetradentate ligation, respectively, to the metal ion envisioned to reside in the unique, basal "platform" position. Mononucleating ligands **10–13** (Scheme 2) were prepared as models of the platform portions of **1–9**, in order to test the ability of these fragments to coordinate a Cu(I) ion.

The syntheses of **1–9** involved condensation of the platform polyamine with amino-2,2-dimethylpropanals (**A**), which were prepared from the appropriate secondary amine L–H, isobutyraldehyde, and formaldehyde (Scheme 1). The products were obtained after distillation and obtained in purity suitable for complex preparation without the need for chromatography. The general utility of this relatively straightforward and high-yielding protocol is illustrated by its application toward ligands with a range of potentially bi- and tridentate *N*-donors L (**1–9**); further derivatives may be readily envisioned. In principle, the synthetic schemes could also be applied to obtain ligands with higher denticity, and complexes with higher nuclearity. Similar condensations with simpler aldehydes were used to prepare **10–13**. All of the ligands were fully characterized by ^{1}H and ^{13}C NMR and IR spectroscopy and either CHN analysis or high resolution mass spectrometry (HRMS). A particularly diagnostic property of the ligands is a single peak at ~7.5 ppm in the ^{1}H NMR spectrum due to the presence of 3 equivalent imine groups (C_3-symmetry).

Synthesis and characterization of Cu(I) complexes

Treatment of ligands **1–3** or **6** in CH_3CN with 3 or more equivalents of $[Cu(CH_3CN)_4]PF_6$ or, in one case, CuCl (preparation of **15b**) yielded trinuclear complexes **14–17** (Scheme 3). The anticipated binding of a fourth Cu(I) ion was not observed, as indicated by CHN analysis, HRMS, and/or X-ray crystallography (**15b**). Coordination of Cu(I) to the imine portion of the ligands was evident from a downfield shift of ~0.2 ppm of the imine proton peak. Most of the signals of the other protons of the ligands undergo downfield shifts to variable extent upon Cu(I) binding. The NMR data indicated C_3-symmetry in the complexes in solution.

The X-ray crystal structure of the tris-acetonitrile adduct of **15b** is shown in Fig. 2. The close similarities between the spectroscopic properties for **15b** and those for **14**, **15a**, **16**, and **17**, for which X-ray diffraction data are not available, implicate analogous structures for the set. Complex **15b** is comprised of a trication with three $[CuCl_2]^-$ counteranions (not shown). Each Cu(I) ion in the tricationic portion shown is coordinated by a bidentate Me_3eda fragment, an imine *N*-donor, and an acetonitrile solvent molecule in a distorted tetrahedral geometry. The Cu–N bond distances to the imine and CH_3CN donors (Cu–N ~ 1.9–2.0 Å) are shorter than those to the Me_3eda amine *N*-atoms (Cu–N ~ 2.1–2.2 Å). Most significantly, instead of the three imine *N*-donors acting as a tridentate platform to bind a fourth Cu(I) ion, they act independently to complete the coordination sphere of each of the three metal ions. That this platform can coordinate a single Cu(I) ion was shown by the successful synthesis and characterization of **18** (Scheme 3), in which the 1,1,1-tris(iminomethyl)ethane portion of the ligands **1–6** is capped by *tert*-butyl groups. Evidently, particular thermodynamic stability is conferred by the tridentate binding with two fused chelate rings of three Cu(I) ions observed in **14–17**.

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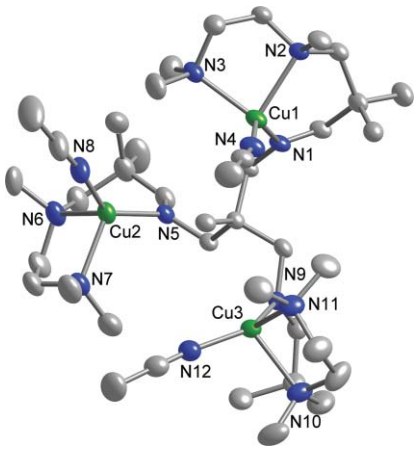

Fig. 2 Representation of the tricationic portion of the X-ray crystal structure of **15b** as its tris-acetonitrile adduct, showing all nonhydrogen atoms as 50% thermal ellipsoids. Selected bond distances (Å) and angles (°) are as follows: Cu1–N4, 1.931(4); Cu1–N1, 1.990(4); Cu1–N3, 2.163(4); Cu1–N2, 2.214(4); Cu2–N8, 1.930(4); Cu2–N5, 1.977(4); Cu2–N7, 2.155(4); Cu2–N6, 2.197(4); Cu3–N12, 1.925(4); Cu3–N9, 1.972(4); Cu3–N11, 2.161(4); Cu3–N10, 2.224(4); N4–Cu1–N1, 133.47(16); N4–Cu1–N3, 102.56(17); N1–Cu1–N3, 116.41(16); N4–Cu1–N2, 112.26(15); N1–Cu1–N2, 95.82(14); N3–Cu1–N2, 85.57(14); N8–Cu2–N5, 135.71(16); N8–Cu2–N7, 106.54(18); N5–Cu2–N7, 112.81(16); N8–Cu2–N6, 106.91(18); N5–Cu2–N6, 95.56(15); N7–Cu2–N6, 85.96(16); N12–Cu3–N9, 137.82(17); N12–Cu3–N11, 105.89(17); N9–Cu3–N11, 111.81(15); N12–Cu3–N10, 106.09(17); N9–Cu3–N10, 95.78(15); N11–Cu3–N10, 84.60(16).

To offset this undesired propensity, we examined the Cu(I) complexes of ligands **7–9** and the model fragments **11–13**, which contain an additional *N*-donor in the basal platform. Treatment of **11–13** with $[Cu(CH_3CN)_4]PF_6$ yielded **19–21**, respectively, of which the complexes with iPr (**19**) and Ph (**21**) substituents were defined structurally by X-ray crystallography (Fig. 3 and Fig. S1‡). These structures resemble others reported for related tetradentate tripodal ligands[17] and demonstrate the capability of the tris(2-iminoethyl)amine moiety to bind a single Cu(I) ion.

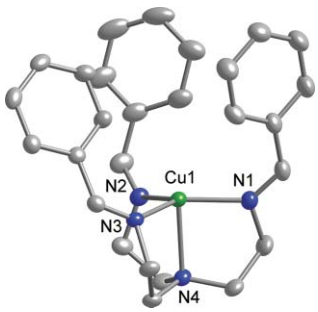

Fig. 3 Representation of the cationic portion of the X-ray crystal structure of **21**, showing all nonhydrogen atoms as 50% thermal ellipsoids. Selected bond distances (Å) and angles (°) are as follows: Cu1–N1, 1.9746(18); Cu1–N3, 2.0027(17); Cu1–N2, 2.0097(18); Cu1–N4, 2.2231(17); N1–Cu1–N3, 128.64(7); N1–Cu1–N2, 120.37(8); N3–Cu1–N2, 108.47(7); N1–Cu1–N4, 85.85(7); N3–Cu1–N4, 83.71(7); N2–Cu1–N4, 84.58(7).

Reaction of **7–9** with 4 equivalents of $[Cu(CH_3CN)_4]PF_6$ resulted in the formation of **22–24** (Scheme 3), which were identified on the basis of NMR spectroscopy (for representative data, see ESI‡), conductivity measurements (see below), and, for **22** and **23**, CHN analysis data. Crystals suitable for X-ray crystallography have yet to be obtained. Although analytical purity was not established for **24**, its tris(xylyl-isocyanide) adduct **25** was fully characterized. In addition, a tris(triphenyl-phosphine) adduct of **22** was isolated and characterized by elemental analysis (**26**, Scheme 3).

Conductivity data was useful for assaying the nature of the various Cu(I) complexes in solution and verifying their metal ion content. Onsager plots[14] were determined for a subset of the compounds prepared in this work, as well as an example of a 2 : 1 electrolyte reported previously[15] (Fig. 4). Good linear fits to the data were obtained, and each class of electrolyte (anion : cation ratio) is readily distinguished. Importantly, the clear separation of the lines for **22–24** from those for the 3 : 1 electrolytes **14**, **15a**, and **16** provide strong support for the tetracopper(I) (4 : 1) formulations for **22–24**.

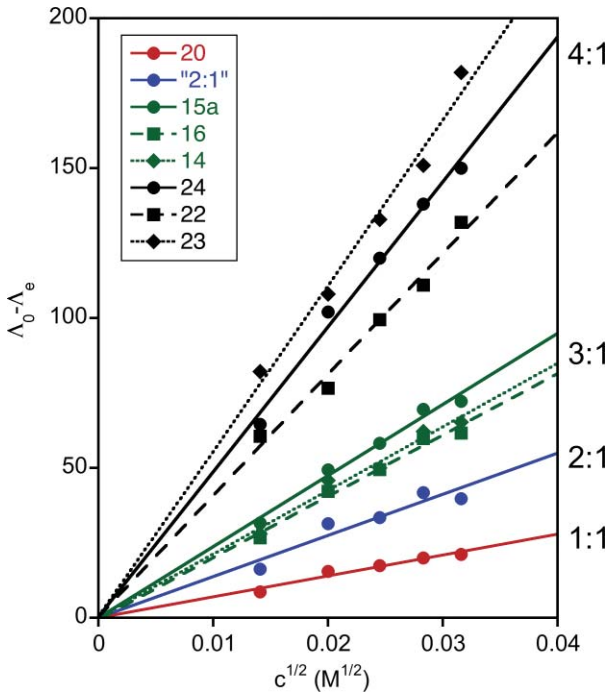

Fig. 4 Onsager conductivity plot (c = concentration) with the various electrolytes grouped by color (labeled on right as anion : cation ratios). Each data set corresponds to the compounds listed in the legend, where "2 : 1" in the legend refers to a dicopper(I) complex (2 : 1 electrolyte) reported in ref. 15.

Dioxygen reactivity of 24

With the viable synthetic procedures in hand for the aforementioned multicopper(I) clusters supported by variable *N*-donor ligands, reactivity studies can begin. In preliminary studies, we examined the reaction of **24** with O_2 at low temperature. These studies were motivated by literature reports of the O_2 reactivity of [bis(pyridylmethyl)amine]Cu(I) complexes, which yield μ-η^2:η^2-peroxo and/or bis(μ-oxo)dicopper complexes.[18] In contrast, bubbling O_2 through solutions of **24** in propionitrile at −78 °C resulted in the formation of a deep purple species readily identified

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as a *trans*-1,2-peroxo species through comparison of UV-vis and resonance Raman spectroscopic data to those of known examples. In particular, absorption features with λ_{max} values at 535 and 610 nm and a resonance enhanced peak at 832 cm^{-1} that shifted by 46 cm^{-1} with $^{18}O_2$ in the Raman spectrum (λ_{ex} = 568.2 nm) were observed, and these closely match data reported previously for (*trans*-1,2-peroxo)dicopper(II) complexes (see Table 5 in ref. 19). Multiple structures are possible for this species derived from **24**, including intramolecular and intermolecular (oligomeric) adducts, but we are unable to unambiguously identify it with the data currently available.

Conclusions

A versatile synthetic method for preparing multidentate ligands with variable *N*-donor sets has been developed, and Cu(I) complexes of a subset of these ligands have been prepared and characterized by spectroscopic, analytical, and, in several cases, X-ray crystallographic and conductivity measurements. The ligands derived from 1,1,1-tris(aminomethyl)ethane (**1–6**) bind three copper ions, each of which is coordinated to one of the imines in the lower platform of the ligand (*cf.* Fig. 4). Incorporation of an additional *N*-donor into the lower platform (ligands **7–9** derived from tris(aminoethyl)amine) results instead in the binding of four Cu(I) ions. Future explorations of reactivity relevant to multicopper enzyme active site chemistry are now enabled, with feasibility being supported by the finding of *trans*-1,2-peroxo species in preliminary studies of the oxygenation of **24**.

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References

1 Lead references: E. I. Solomon, U. M. Sundaram and T. E. Machonkin, *Chem. Rev.*, 1996, **96**, 2563; *Multi-Copper Oxidases*, ed. A. Messerschmidt, World Scientific, Singapore, 1997; E. I. Solomon, P. Chen, M. Metz, S.-K. Lee and A. E. Palmer, *Angew. Chem., Int. Ed.*, 2001, **40**, 4570.
2 I. Bento, L. O. Martins, G. G. Lopes, M. A. Carrondo and P. F. Lindley, *Dalton Trans.*, 2005, 3507.
3 K. Brown, M. Tegoni, M. Prudencio, A. S. Pereira, S. Besson, J. J. Moura, I. Moura and C. Cambillau, *Nat. Struct. Biol.*, 2000, **7**, 191; T. Rasmussen, B. C. Berks, J. Sanders-Loehr, D. M. Dooley, W. G. Zumft and A. J. Thomson, *Biochemistry*, 2000, **39**, 12753; T. Haltia, K. Brown, M. Tegoni, C. Cambillau, M. Saraste, K. Mattila and K. Djinovic-Carugo, *Biochem. J.*, 2003, **369**, 77.
4 U. Ryde, Y. W. Hsiao, L. Rulisek and E. I. Solomon, *J. Am. Chem. Soc.*, 2007, **129**, 726.
5 (*a*) P. Chen, S. I. Gorelsky, S. Ghosh and E. I. Solomon, *Angew. Chem., Int. Ed.*, 2004, **43**, 4132; (*b*) S. Ghosh, S. I. Gorelsky, P. Chen, I. Cabrito, J. J. G. Moura, I. Moura and E. I. Solomon, *J. Am. Chem. Soc.*, 2003, **125**, 15708; (*c*) J. M. Chan, J. A. Bollinger, C. L. Grewell and D. M. Dooley, *J. Am. Chem. Soc.*, 2004, **126**, 3030; (*d*) S. I. Gorelsky, S. Ghosh and E. I. Solomon, *J. Am. Chem. Soc.*, 2006, **128**, 278; (*e*) K. Fujita and D. M. Dooley, *Inorg. Chem.*, 2007, **46**, 613; S. Ghosh, S. I. Gorelsky, S. DeBeer, George, J. M. Chan, I. Cabrito, D. M. Dooley, J. J. G. Moura, I. Moura and E. I. Solomon, *J. Am. Chem. Soc.*, 2007, **129**, 3955.
6 N. Sträter, W. N. Lipscomb, T. Klabunde and B. Krebs, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 2024; W. N. Lipscomb and N. Sträter, *Chem. Rev.*, 1996, **96**, 2375; J. A. Cowan, *Chem. Rev.*, 1998, **98**, 1067.
7 L. Santagostini, M. Gullotti, L. D. Gioia, P. Fantucci, E. Franzini, A. Marchesini, E. Monzani and L. Casella, *Int. J. Biochem. Cell Biol.*, 2004, **36**, 881.
8 K. D. Karlin, *Science*, 1993, **261**, 701.
9 (*a*) K. D. Karlin, Q. Gan, A. Farooq, S. Liu and J. Zubieta, *Inorg. Chim. Acta*, 1989, **165**, 37; (*b*) E. Monzani, L. Casella, G. Zoppellaro, M. Gullotti, R. Pagliarin, R. P. Bonomo, G. Tabbi, G. Nardin and L. Randaccio, *Inorg. Chim. Acta*, 1998, **282**, 180; (*c*) L. Santagostini, M. Gullotti, R. Pagliarin, E. Monzani and L. Casella, *Chem. Commun.*, 2003, 2186; (*d*) M. C. Mimmi, M. Gullotti, L. Santagostini, G. Battaini, E. Monzani, R. Pagliarin, G. Zoppellaro and L. Casella, *Dalton Trans.*, 2004, 2192; (*e*) G. Battaini, A. Granata, E. Monzani, M. Gullotti and L. Casella, *Adv. Inorg. Chem.*, 2006, **58**, 185; (*f*) C. Walsdorff, S. Par, J. Kim, J. Heo, K. M. Park, J. Oh and K. Kim, *J. Chem. Soc., Dalton Trans.*, 1999, 923; (*g*) K. D. Karlin, Q.-f. Gan and Z. Tyeklár, *Chem. Commun.*, 1999, 2295; (*h*) D. J. E. Spencer, B. J. Johnson, B. J. Johnson and W. B. Tolman, *Org. Lett.*, 2002, **4**, 1391; (*i*) H. Ohi, Y. Tachi and S. Itoh, *Inorg. Chem.*, 2006, **45**, 10825.
10 L. M. Mirica, X. Ottenwaelder and T. D. P. Stack, *Chem. Rev.*, 2004, **104**, 1013; E. A. Lewis and W. B. Tolman, *Chem. Rev.*, 2004, **104**, 1047.
11 E. C. Brown, N. W. Aboelella, A. M. Reynolds, G. Aullón, S. Alvarez and W. B. Tolman, *Inorg. Chem.*, 2004, **43**, 3335; E. C. Brown, J. T. York, W. E. Antholine, E. Ruiz, S. Alvarez and W. B. Tolman, *J. Am. Chem. Soc.*, 2005, **127**, 13752; J. T. York, E. C. Brown and W. B. Tolman, *Angew. Chem., Int. Ed.*, 2005, **44**, 7745; E. C. Brown, I. Bar-Nahum, J. T. York, N. W. Aboelella and W. B. Tolman, *Inorg. Chem.*, 2007, **46**, 486.
12 An empirical correction for absorption anisotropy. R. H. Blessing, *Acta Crystallogr., Sect. A*, 1995, **A51**, 33.
13 *SAINT + V6.45*, Bruker Analytical X-Ray Systems, Madison, WI, 2003.
14 W. J. Geary, *Coord. Chem. Rev.*, 1971, **7**, 81; L. Casella and J. A. Ibers, *Inorg. Chem.*, 1981, **20**, 2438.
15 K. D. Karlin, P. L. Dahlstrom, S. N. Cozzette, P. M. Scensny and J. Zubieta, *J. Chem. Soc., Chem. Commun.*, 1981, 881.
16 E. B. Fleischer, A. E. Gebala, A. Levey and P. A. Tasker, *J. Org. Chem.*, 1971, **36**, 3042.
17 Z. Tyeklar, R. R. Jacobson, N. Wei, N. N. Murthy, J. Zubieta and K. D. Karlin, *J. Am. Chem. Soc.*, 1993, **115**, 2677; B. S. Lim and R. H. Holm, *Inorg. Chem.*, 1998, **37**, 4898; M. Becker, F. W. Heinemann and S. Schindler, *Chem.–Eur. J.*, 1999, **5**, 3124.
18 S. Itoh and Y. Tachi, *Dalton Trans.*, 2006, 4531, and references cited therein.
19 L. M. Mirica, X. Ottenwaelder and T. D. P. Stack, *Chem. Rev.*, 2004, **104**, 1013.

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