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“Click” Cycloaddition Catalysts: Copper(I) and Copper(II) *tris*-(Triazolylmethyl)amine Complexes

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Preparation of complexes 1 and 2

General. Melting points were obtained using a Reichert-Jung hotstage microscope (corrected). ^{1}H and ^{13}C NMR spectra were recorded using Unity Plus 400 or Inova 400 or 500 instruments (Melbourne, Australia). Elemental analyses were conducted by C.M.A.S. (Belmont, Victoria). Low resolution mass spectrometry was performed by Sioe See Volaric (Melbourne University, Australia). High resolution mass spectrometry was performed by Mr Chris Barlow on a Finnigan hybrid LTQ-FT mass spectrometer (Thermo Electron Corp.). IR spectra were obtained using a Perkin–Elmer Spectrum One FTIR spectrometer, with a zinc selenide/diamond universal ATR sampling accessory, as a thin film. Standard Schlenk techniques were used for the synthesis of the Cu(I) complex.

Cu(II) complex.

Method 1. $CuCl_2.2H_2O$ (72 mg, 0.42 mmol) was partially dissolved in CH_3CN (5 mL) and the dark green mixture was added to a solution of TBTA (203 mg, 0.38 mmol) dissolved in warm CH_3CN (5 mL). Upon mixing an immediate colour change occurred to lime green. The mixture was heated at reflux for 30 min, then was allowed to cool to room temperature and concentrated by evaporation at ambient temperature. After 48 h a green solid had precipitated. Water (1 mL) was added and the lime green solid was collected by filtration and washed with diethyl ether to give [CuCl(TBTA)]Cl as a green solid (74 mg, 0.10 mmol, 27%). Anal. Found C, 50.37; H, 4.67; N, 20.20. $CuCl(C_{30}H_{30}N_{10})]Cl\cdot2.5H_2O$ requires C, 50.74; H, 4.97; N, 19.72; HRMS (ESI$^+$) *m/z* 593.1944 (calcd. for $[C_{30}H_{30}Cu^IN_{10}]^+$ 593.1951). Note: reduction of the metal centre is observed in the electrospray source.

Method 2. TBTA (42 mg, 0.08 mmol) was dissolved in CH_2Cl_2 (5 mL), $CuCl_2.2H_2O$ (13 mg, 0.08 mmol) was added and the mixture was heated at reflux for 3 h. The green mixture was filtered whilst hot to remove unreacted $CuCl_2.2H_2O$ and the green filtrate was allowed to cool to ambient temperature. A green precipitate was collected by filtration, washed with CH_2Cl_2 and pentane to give $[Cu(Cl(TBTA)]Cl\cdot1.5H_2O$ (33 mg, 0.053 mmol, 67%). Anal. Found C, 51.92; H: 4.64; N: 20.29. $[CuCl(C_{30}H_{30}N_{10})]Cl\cdot1.5H_2O$ requires C, 52.06; H, 4.81; N, 20.24; HRMS (ESI$^+$) *m/z*

628.1650 (calcd. for $[C_{30}H_{30}ClCu^{II}N_{10}]^+$ 628.1634); HRMS (ESI$^+$) *m*/*z* 593.1943 (calcd. for $[C_{30}H_{30}Cu^{I}N_{10}]^+$ 593.1951).

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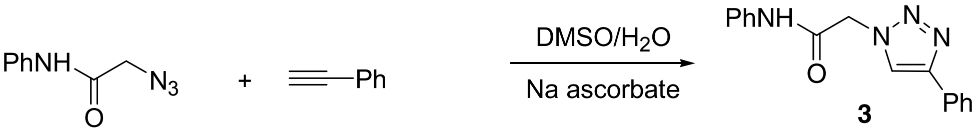
Cu(I) complex.

[Cu(CH_3CN)$_4$]BF_4 (0.120 g, 0.38 mmol) was dissolved in deoxygenated CH_3CN (2 mL) and added to a solution of TBTA (0.201 g, 0.38 mmol) dissolved in deoxygenated CH_2Cl_2 (3 mL). The mixture was stirred at room temperature for 30 min. Deoxygenated diethyl ether (5 mL) was added and the mixture stored at –20 ºC for 1 week, during which time a precipitate was formed. A colourless sticky solid was collected by filtration under nitrogen and washed with a copious quantity of diethyl ether to give **2** as a fine colourless powder (0.240 g, 0.176 mmol, 93%). ^{1}H NMR (500 MHz, CD_3CN) δ 3.74 (6H, br s, C**H**$_2$N), 5.55 (6H, br s, C**H**$_2$Ph), 7.30-7.45 (15H, m), 7.81 (3H, br s); Anal. Found: C, 52.98; H, 4.37; N, 20.61. $C_{60}H_{60}B_2Cu_2F_8N_{20}$ requires C, 52.91; H, 4.44; N, 20.57; HRMS (ESI$^+$) *m/z* 593.1944 (calcd. for $[C_{30}H_{30}Cu^IN_{10}]^+$ 593.1945).

Procedure for cycloaddition reactions

General description. Cycloaddition reactions were conducted in stoppered round bottom flasks (15 mL) in 2:1 DMSO:water with stirring for 24 h at room temperature. Reactions were carried out using the indicated Cu source (1 mol%) and with the addition or omission of TBTA (1 mol%) and/or sodium ascorbate (10 mol%), as shown in Table 1. The isolated mixtures were analysed by ^{1}H NMR spectroscopy. For incomplete reactions the triazole **3** was isolated as a mixture with unreacted azidoacetanilide; the yield of **3** was determined by integration of the amide proton of the triazole product at δ_H 10.50 ppm and the amide proton of azidoacetanilide at δ_H 10.11 ppm.



Typical procedure. Sodium ascorbate (22 mg, 10 mol%), TBTA (6.0 mg, 1 mol%), and $CuSO_4$ **2** (1.8 mg, 1 mol%) were added to a solution of phenyl acetylene (125 µL, 116 mg, 1.14 mmol) and azidoacetanilide[1] (200 mg, 1.14 mmol) in DMSO (2.0 mL) and water (1.0 mL). The mixture was stoppered and stirred at rt for 24 h. The suspension was diluted with water (10 mL), cooled to 0 ºC and the precipitate filtered and dried (263 mg, 83%); mp 243-245 °C; lit.[2] 164-165 °C; ^{1}H NMR (400 MHz, d_6-DMSO) δ 5.38 (2H, s, CH_2), 7.09 (1H, t, J = 7.6 Hz, Ph), 7.33 (3H, t, J = 7.6 Hz, Ph), 7.45 (2H, t, J = 7.6 Hz, Ph), 7.59 (2H, d, J = 7.6 Hz, Ph), 7.88 (2H, d, J = 7.6 Hz, Ph), 8.59 (1H, s, CH), 10.50 (1H, s, NH); ^{13}C NMR (100 MHz, d_6-DMSO) δ 52.4, 119.2, 123.1, 123.8, 125.1, 127.8, 128.9, 130.7, 138.4, 146.2, 164.2 (C=O); IR 3261, 2935, 1670, 1596, 1539, 1443 cm^{-1}; HRMS $[M+H]^+$ = found 279.1240, requires 279.1240 $C_{16}H_{15}N_4O$.

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Electrochemistry

Cyclic voltammograms were recorded on an AUTOLAB PGSTAT100 using GPES V4.9 software employing a glassy carbon working electrode, a platinum counter electrode and a Ag/Ag^+ reference electrode. The measurements were carried out in DMSO. The solutions were approximately 1.5 mM of analyte in 0.1 M tetraethylammonium hexafluorophosphate solution. The DMSO was dried over 3 Å molecular sieves under an atmosphere of N_2 before use. Each solution was purged with N_2 prior to analysis and measured at ambient temperatures under a N_2 atmosphere. Each sample was referenced to an internal reference of ferrocene and potentials are quoted versus (Fc/Fc^+).

Crystallography experimental

Intensity data for the Cu(II) complex were collected with an Oxford XCalibur X-ray diffractometer with Sapphire CCD detector using Cu-Kα radiation (graphite crystal monochromator λ = 1.54184 Å). Data were reduced and corrected for absorption.[3] Intensity data for the Cu(I) complex were collected with a Bruker SMART Apex CCD detector using Mo-Kα radiation (graphite crystal monochromator λ = 0.71073). Data were reduced using the program SAINT.[4] The structures were solved by direct methods and difference Fourier synthesis using the SHELX suite of programs[5] as implemented within the WINGX[6] software. Thermal ellipsoid plots were generated using the program ORTEP-3 integrated within the WINGX suite of programs.

Crystal data for Cu(II) complex. Very small crystals of **1** adequate for X-ray crystallography were grown by vapour diffusion of diethyl ether into a solution of the complex in CH_3CN. Repeated attempts at recrystallisation of this sample did not yield superior crystals. The structure is mixed charge complex with LCu(I)Cl and LCu(II)Cl sharing a single Cl^- counterion. Initial solution in space group P2(1)-3 revealed two complexes and a Cl^- ion which was found to be disordered over two sites consistent with the symmetry of the Pa-3 space group, therefore refinement was performed in the centrosymmetric space group with the chloride assigned half the occupancy required to fulfill overall stoichiometry. $[C_{30}H_{24}N_{10}ClCu].[Cl_{0.5}]$, M = 641.31, T = 130.0(1) K, 1 = 1.54184, cubic, space group *Pa-3*, *a*,*b*,*c* =17.6375(2) *Å,* 5486.7(1) *Å*^{3}, Z = 8, D_c = 1.572

mg M^{-3} m(Cu-Kα) 2.832 mm^{-1}, F(000) = 424, crystal size 0.04 × 0.035 × 0.03 mm. 8136 reflections measured, 1524 independent reflections (R_{int} = 0.077) the final R was 0.0919 [I > 2s(I)] and *w*R(F^2) was 0.3260 (all data).

Crystal data for Cu(I) complex. Crystals suitable for X-ray crystallography were grown from a deoxygenated solution of DMF/diethyl ether. [C_{30} H_{30} N_{10}Cu].[BF_4].[0.5 DMF], *M* = 717.54, *T* = 130.0(1) K, λ = 1.54184, monoclinic, space group C 2/c, *a* =16.306(1), *b* = 15.788(1), *c* = 25.425(2) *Å*, *b* = 96.785(1)° V = 6499.4(1) *Å*^{3}, Z = 8, D_c = 1.467 mg M^{-3} μ(Mo-Kα) 0.738 mm^{-1}, F(000) = 2960, crystal size 0.15 × 0.15 × 0.14 mm. 16902 reflections measured, 5746 independent reflections (R_{int} = 0.0507) the final R was 0.0375 [I > 2σ(I)] and *w*R(F^2) was 0.0913 (all data).

References for Supporting Information

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