

Click Chemistry from Organic Halides, Diazonium Salts and Anilines in Water Catalysed by Copper Nanoparticles on Activated Carbon

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Supplementary Information

General

Anhydrous copper(II) chloride (Aldrich), lithium powder (MEDALCHEMY S. L.), DTBB (4,4'-di-*tert*-butylbiphenyl, Aldrich), activated charcoal (Norit CA1, Aldrich), and sodium azide (Across) are commercially available. All the starting organic halides, anilines, diazonium salts **4a** and **4e**, and *tert*-butyl nitrite were commercially available of the best grade (Aldrich, Acros, Alfa Aesar) and were used without further purification. Alkyne **2e** was obtained as a white crystalline solid (90% yield) by dropwise addition of propargyl bromide (312 μ L, 2.8 mmol) to a solution of phthalimide (368 mg, 2.5 mmol) and K_2CO_3 (345 mg, 2.5 mmol) in MeCN (4 mL), followed by heating at 80 °C (24 h), work-up with water (10 mL) and NH_4Cl (10 mL), extraction with EtOAc, washing of the organic phase with water (2×10 mL) and brine (2×10 mL), and drying with $MgSO_4$. The diazonium salts **4b-4d** were prepared following a literature procedure.¹ THF was dried in a Sharlab PS-400-3MD solvent purification system using an alumina column. Melting points were obtained with a Reichert Thermovar apparatus. Infrared analysis was performed with a FT-IR Nicolet Impact 400D (transmission) and FT-IR-4100 (ATR) spectrophotometers; wavenumbers are given in cm^{-1} . NMR spectra were recorded on Bruker Avance 300 and 400 spectrometers (300 and 400 MHz for 1H NMR; 75 and 100 MHz for ^{13}C NMR); chemical shifts are given in (δ) parts per million and coupling constants (J) in hertz. Mass spectra (EI) were obtained at 70 eV on an Agilent 5973 spectrometer; fragment ions in m/z with relative intensities (%) in parenthesis. HRMS analyses were carried out on a Finnigan MAT95S spectrometer. The purity of volatile compounds and the chromatographic analyses (GLC) were determined with a Hewlett Packard HP-6890 instrument equipped with a flame ionization detector and a 30 m

capillary column (0.32 mm diameter, 0.25 μm film thickness), using nitrogen (2 mL/min) as carrier gas, $T_{\text{injector}} = 270\text{ }^{\circ}\text{C}$, $T_{\text{column}} = 60\text{ }^{\circ}\text{C}$ (3 min) and 60–270 $^{\circ}\text{C}$ (15 $^{\circ}\text{C}/\text{min}$); retention times (t_r) are given in min. Thin layer chromatography was carried out on TLC plastic sheets with silica gel 60 F₂₅₄ (Merck). Column chromatography was performed using silica gel 60 of 40–60 microns (hexane/EtOAc as eluent).

The TEM image was recorded using a JEOLJEM2010 microscope, equipped with a lanthanum hexaboride filament, operated at an acceleration voltage of 200 kV. For their observation, the samples were mounted on holey-carbon coated gold grid. X-EDS analyses were carried out with an Oxford Inca Energy TEM100 attachment. The XRD diffractogram was collected in the θ - θ mode using a Bruker D8 Advance X-ray diffractometer: Cu $K\alpha_1$ irradiation, $\lambda = 1.5406\text{ \AA}$; room temperature (25 $^{\circ}\text{C}$); $2\theta = 4$ –80. The XPS spectra were measured with a VG-Microtech Multilab 3000 electron spectrometer using a non-monochromatized Mg- $K\alpha$ (1253.6 eV) radiation source of 300 W and a hemispheric electron analyzer equipped with 9 channeltron electron multipliers. The pressure inside the analysis chamber during the scans was about $5 \cdot 10^{-7}\text{ N}\cdot\text{m}^{-2}$. After the survey spectra were obtained, higher resolution survey scans were performed at pass energy of 50 eV. The intensities of the different contributions were obtained by means of the calculation of the integral of each peak, after having eliminated the baseline with S form and adjusting the experimental curves to a combination of Lorentz (30%) and Gaussian (70%) lines. All the bond energies were referred to the line of the C 1s to 284.4 eV, obtaining values with a precision of $\pm 0.2\text{ eV}$. Inductively coupled plasma mass spectrometry (ICP-MS) analyses were carried out on a Thermo Elemental VG PQ Excell according to the following parameters: Gas flows, cool (14.00 bar), auxiliar (0.95 bar), nebulizer (0.90 bar), liquid flow (1 mL/min), dwell time (10000 μs), sweeps (40), channels per mass (3), channel spacing (0.02), main runs (3), forward power (1350 w).

All reactions at 0.5 M and 0.1 M concentration were performed using tubes in a multi-reactor system, whereas reactions at 0.01 M concentration were performed in a round-bottom flask equipped with a condenser.

Typical procedure for the preparation of CuNPs/C

Anhydrous copper(II) chloride (135 mg, 1 mmol) was added to a suspension of lithium powder (14 mg, 2 mmol) and 4,4'-di-*tert*-butylbiphenyl (DTBB, 27 mg, 0.1 mmol) in THF (2 mL) at room temperature under an argon atmosphere. The reaction mixture, which was initially dark blue, rapidly changed to black (ca. 5–10 min), indicating that the suspension of copper nanoparticles was formed. This suspension was diluted with THF (18 mL) followed by the addition of the activated carbon (1.28 g). The resulting mixture was stirred for 1 h at room

temperature, filtered, and the solid successively washed with water (20 mL), THF (20 mL), and dried under vacuum (15 Torr). When the copper nanoparticles were generated in the presence of the active carbon, the resulting catalyst was shown to be less effective in the click reaction.

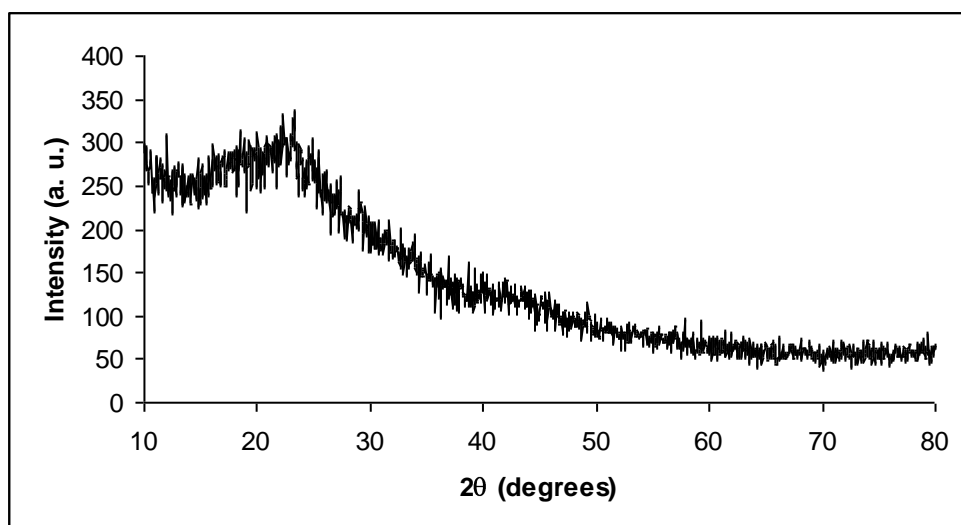
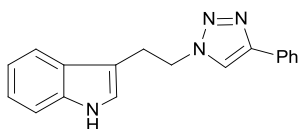


Figure 1. XRD spectrum of CuNPs/C.

General procedure for the CuNPs/C-catalysed click reaction in water using organic halides or diazonium salts as the azide precursors

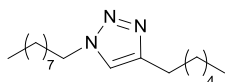
NaN₃ (72 mg, 1.1 mmol), the azide precursor (organic halide, or diazonium salt, 1 mmol) and the alkyne (1 mmol) were added to a suspension of CuNPs/C (20 mg, 0.5 mol% Cu) in H₂O (2 mL). The reaction mixture was warmed to 70 °C and monitored by TLC until total conversion of the starting materials. Water (30 mL) was added to the resulting mixture, followed by extraction with EtOAc (3 × 10 mL). The collected organic phases were dried with anhydrous MgSO₄ and the solvent was removed in vacuo to give the corresponding triazoles. Compound **3ka** was purified by column chromatography. We must point out that in some reactions with aryldiazonium salts (different from those shown in Table 3) a mixture of the regioisomeric triazoles was obtained. This fact could be due to the initial exothermicity observed for the heat of dissolution of the diazonium salt.

The triazoles derived from organic halides **3aa**,² **3ba**,³ **3ca**,⁴ **3da**,⁵ **3fa**,² **3ga**,⁶ **3ha**,² **3ia**,⁷ **3ja**,² **3ab**,⁸ **3ac**,⁹ **3ad**,⁹ **3ae**,¹⁰ **3af**,¹¹ **3lh**,² **3ai**,¹² **3aj**,² and **3m**¹³ were characterised by comparison of their physical and spectroscopic data with those described in the literature. Data for the new compounds, follow:



3-[2-(4-Phenyl-1H-1,2,3-triazol-1-yl)ethyl]-1H-indole (3ka)

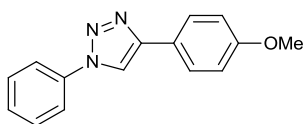
Yellow solid; m.p. 165.5–169.0 °C; t_r 27.13 min; R_f 0.55 (hexane/EtOAc 1:1). IR (KBr) ν = 3394, 3116, 3089, 1458, 1258, 1226, 1193, 743, 765, 694 cm^{-1} . ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ = 3.34 (t, J = 7.2 Hz, 2H), 4.68 (t, J = 7.2 Hz, 2H), 7.20–6.92 (m, 3H), 7.52–7.33 (m, 4H), 7.70–7.53 (m, 1H), 7.90–7.75 (m, 2H), 8.58 (s, 1H), 10.88 (s, 1H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$): δ = 26.2, 50.5, 110.2, 111.9, 118.6, 118.9, 121.6, 121.8, 123.7, 125.5, 127.2, 128.2, 129.4, 131.2, 136.4, 146.4. GC-MS (EI): m/z (%) = 288 (18) $[\text{M}]^+$, 259 (13), 156 (21), 144 (35), 143 (100), 131 (11), 130 (86), 115 (13), 103 (15), 102 (11), 77 (14). HRMS (EI): m/z calcd. for $\text{C}_{18}\text{H}_{16}\text{N}_4$ 288.1375; found 288.1384.



4-(*n*-Hexyl)-1-(*n*-nonyl)-1H-1,2,3-triazole (3ig)

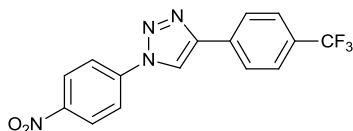
Palid yellow solid; m.p. 48.2–50.1 °C; t_r 16.44 min; R_f 0.26 (hexane/EtOAc 8:2). IR (neat) ν = 3121, 3073, 2952, 2913, 2869, 2847, 1555, 1468, 1333, 1212, 1154, 1061, 853, 719 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 0.93–0.84 (m, 6H), 1.41–1.21 (m, 18H), 1.66 (quintet, J = 7.4 Hz, 2H), 1.87 (quintet, J = 6.9 Hz, 2H), 2.71 (t, J = 7.6 Hz, 2H), 4.30 (t, J = 7.2 Hz, 2H), 7.24 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ = 14.0, 22.5, 22.6, 25.7, 26.5, 28.8, 28.9, 29.1, 29.3, 29.4, 30.3, 31.6, 31.7, 50.1, 120.3, 148.4. GC-MS (EI): m/z (%) = 279 (31) $[\text{M}]^+$, 250 (16), 236 (35), 223 (11), 222 (62), 209 (44), 208 (100), 195 (12), 194 (77), 181 (15), 180 (96), 166 (38), 154 (37), 152 (42), 139 (11), 138 (50), 125 (17), 124 (47), 111 (33), 110 (47), 109 (12), 97 (32), 96 (48), 94 (12), 85 (17), 84 (10), 83 (19), 82 (53), 81 (14), 80 (18), 71 (27), 70 (17), 69 (24), 68 (32), 67 (23), 57 (34), 56 (18), 55 (49), 54 (22). HRMS (EI) calcd. for $\text{C}_{17}\text{H}_{33}\text{N}_3$ 279.2674, found 279.2660.

The triazoles derived from the diazonium salts **5aa**,² **5ba**,¹⁴ **5ca**,¹⁵ **5da**,¹⁵ **5ea**,¹⁶ and **5bd**¹⁷ were characterised by comparison of their physical and spectroscopic data with those described in the literature. Data for the new compounds or for known compounds whose data are not reported in the literature, follow:



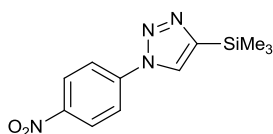
4-(4-Methoxyphenyl)-1-phenyl-1H-1,2,3-triazole (5ac)¹⁸

Palid yellow solid; m.p. 152.5–154.5 °C; t_r 18.48 min; R_f 0.50 (hexane/EtOAc 7:3). IR (neat) ν = 3134, 3076, 3004, 2956, 1617, 1561, 1491, 1463, 1242, 1231, 1177, 1043, 1028, 832, 814, 757, 686, 611 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 3.86 (s, 3H), 6.99, 7.84 (AA'XX' system, J = 9.0, 8.7 Hz, 4H), 7.44 (tt, J = 7.2, 1.2 Hz, 1H), 7.54 (td, J = 7.2, 1.8 Hz, 2H), 7.79 (dt, J = 7.2, 1.5 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ = 55.3, 114.3, 116.7, 120.4, 122.9, 127.1, 128.6, 129.7, 137.1, 148.2, 159.8. GC-MS (EI): m/z (%) = 251 (5) $[\text{M}]^+$, 223 (43), 209 (16), 208 (100), 180 (19), 152 (11), 77 (32), 51 (11). HRMS (EI) calcd. for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}$ 251.1059, found 251.1054.



1-(4-Nitrophenyl)-4-[4-(trifluoromethyl)phenyl]-1H-1,2,3-triazole (5ek)

Palid yellow solid; m.p. 214.9–217.9 °C; t_r 19.83 min; R_f 0.74 (hexane/EtOAc 7:3). IR (neat) ν = 3157, 2924, 2854, 1596, 1516, 1340, 1320, 1232, 1163, 1106, 1062, 1025, 1010, 852, 838, 807, 748, 684 cm^{-1} . ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ = 7.90 (d, J = 8.4 Hz, 2H), 8.17 (d, J = 8.4 Hz, 2H), 8.28 (d, J = 9.2 Hz, 2H), 8.52 (d, J = 9.2 Hz, 2H), 9.70 (s, 1H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$): δ = 120.6, 121.4, 125.5, 125.7, 126.0, 126.1 (q, J = 12 Hz), 128.6 (q, J = 125 Hz), 133.8, 140.7, 146.4, 146.9. GC-MS (EI): m/z (%) = 334 (1) $[\text{M}]^+$, 307 (12), 306 (69), 261 (17), 260 (100), 259 (24), 233 (19), 191 (37), 190 (17), 184 (12), 134 (12), 76 (18), 50 (10). HRMS (EI) calcd. for $\text{C}_{15}\text{H}_9\text{F}_3\text{N}_4\text{O}_2$ 334.0678, found 334.0688.



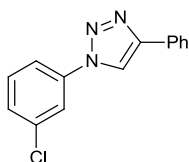
1-(4-Nitrophenyl)-4-(trimethylsilyl)-1H-1,2,3-triazole (5ef)

Yellow solid; m.p. 172.4–174.3 °C; t_r 16.03 min; R_f 0.53 (hexane/EtOAc 8:2). IR (neat) ν = 3135, 2953, 1594, 1519, 1504, 1341, 1249, 1203, 1109, 1033, 981, 840, 805, 759, 747, 633 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 0.40 (s, 3H), 7.99 (d, J = 9.3 Hz, 2H), 8.04 (s, 1H), 8.42 (d, J = 9.3 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ = -1.2, 120.6, 125.5, 126.8, 141.3, 146.9, 148.8. GC-MS (EI): m/z (%) = 262 (1) $[\text{M}]^+$, 220 (17), 219 (100), 173 (30). HRMS (EI) calcd. for $\text{C}_{11}\text{H}_{14}\text{N}_4\text{O}_2\text{Si}$ 262.0886, ($\text{M}^+ - \text{N}_2$) 234.0825, found 234.0832.

General procedure for the CuNPs/C-catalysed click reaction in water using anilines as the azide precursors

NaN₃ (72 mg, 1.1 mmol), aromatic amine (1.0 mmol.), *t*-BuONO (190 μL, 1.6 mmol) and the alkyne (1.0 mmol) were added to a suspension of CuNPs/C (20 mg, 0.5 mol% Cu) in H₂O (2 mL). The reaction mixture was warmed to 70 °C and monitored by TLC until total conversion of the starting materials. Water (30 mL) was added to the resulting mixture, followed by extraction with EtOAc (3 × 10 mL). The collected organic phases were dried with anhydrous MgSO₄, and the solvent was removed in vacuo to give the corresponding triazoles **5**, which did not require any further purification.

Triazoles **5aa**,² **5ba**,¹⁴ **5fa**,¹⁹ **5ha**,¹⁴ **5ia**,¹⁴ **5ja**,²⁰ **5ka**,¹⁴ **5ah**,² and **5ak**² were characterised by comparison of their physical and spectroscopic data with those described in the literature. Data for the new compound follow:



1-(3-Chlorophenyl)-4-phenyl-1H-1,2,3-triazole (**5ga**)

Orange solid; m.p. 158.0–161.1 °C; *t*_r 17.91 min; *R*_f 0.50 (hexane/EtOAc 7:3). IR (KBr) ν = 3127, 3103, 2919, 1594, 1480, 1455, 1227, 1076, 1040, 885, 795, 758, 693, 685 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 7.34–7.53 (m, 5H), 7.67–7.74 (m, 1H), 7.84 (t, *J* = 1.8 Hz, 1H), 7.84–7.94 (m, 2H), 8.19 (s, 1 H). ¹³C NMR (75 MHz, CDCl₃): δ = 117.7, 118.7, 121.0, 126.2, 128.9, 129.1, 129.3, 130.2, 131.1, 135.9, 138.2, 148.9. GC-MS (EI): *m/z* (%) = 255 (3) [M]⁺, 229 (32), 228 (17), 227 (100), 192 (45), 191 (10), 165 (42), 116 (48), 111 (13), 90 (26), 89 (36), 75 (24), 63 (12). HRMS (EI) calcd. for C₁₄H₁₀N₃Cl 255.0561, found 255.0563.

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