Cu(I)-promoted one-pot “S_NAr-click reaction” of nitrobenzaldehydes

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EXPERIMENTAL

General

Melting points were recorded on a Fischer–Johns micro hot-stage apparatus and were uncorrected. IR spectra were recorded on a Nexus FT-IR spectrophotometer. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AV400 MHz spectrometer by using tetramethylsilane as internal standard and DMSO-*d*₆ or CDCl₃ as solvent at room temperature. Elemental analyses were performed using a Perkin–Elmer 2400 CHNS elemental analyzer. Mass spectra were obtained using a Finnigan MAT-95 mass spectrometer. All reactions were monitored by TLC equipped with Huanghai GF 254 silica gel-coated plates. Column chromatography was performed using 100–200 mesh silica gel under medium pressure. All the reagents for the synthesis were commercially available and used as received or purified via standard methods prior to use.

General procedure

A solution of *o*- or *p*-nitrobenzaldehyde (151 mg, 1 mmol), NaN₃ (78 mg, 1.2 mmol), alkyne (1.1 mmol), CuI (38 mg, 0.2 mmol), and Na ascorbate (79 mg, 0.4 mmol) in HMPT (3 mL) in a round-bottom flask was stirred under N₂. The mixture was heated to the temperature indicated in Table 2, until the starting *o/p*-nitrobenzaldehyde had been completely consumed (monitored by TLC). The mixture was diluted with H₂O and then extracted with EtOAc or CH₂Cl₂ (3 × 20 mL). The combined organic layers were washed with sat. brine (3 × 30 mL), dried with anhyd. Na₂SO₄, and concentrated under reduced pressure to afford the crude product which was purified by flash chromatography (silica gel, particle size 100-200 mesh, *n*-hexane-EtOAc) or crystallized by EtOAc.

Spectral data of the synthesized compounds:

4-(4-Phenyl-1H-1,2,3-triazol-1-yl)benzaldehyde (3a)^[1]: Yellow solid, mp: 219.2-220.3 °C. IR (KBr): 3112, 1686, 1598, 1498, 1455 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 10.12 (s, 1H), 8.32 (s, 1H), 8.12 (d, *J* = 8.5 Hz, 2H), 8.06 (d, *J* = 8.5 Hz, 2H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.43 (t, 1H). MS (ESI): *m/z* 250 (M+H)⁺.

2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzaldehyde (3b): Yellow solid, mp: 236.5-238.1 °C. IR (KBr): 3145, 1598, 1521, 1348, 1215 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 9.99 (s, 1H), 8.22 (s,

1H), 8.12 (d, $J = 7.5$ Hz, 1H), 7.93 (d, $J = 7.3$ Hz, 2H), 7.83-7.74 (m, 1H), 7.72-7.62 (m, 1H), 7.58 (d, $J = 7.7$ Hz, 1H), 7.53-7.44 (m, 2H), 7.41 (d, $J = 7.0$ Hz, 1H). MS (ESI): m/z 250 ($M+H$)⁺.

4-(4-(4-ethylphenyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3c)^[2]: White solid, mp: 193.5-196.0 °C. IR (KBr): 3137, 2961, 1691, 1604, 1591, 1411, 1230 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 10.10 (s, 1H), 8.27 (s, 1H), 8.10 (d, $J = 8.6$ Hz, 2H), 8.04 (d, $J = 8.6$ Hz, 2H), 7.85 (d, $J = 8.1$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 2.72 (q, $J = 7.6$ Hz, 2H), 1.30 (t, $J = 7.6$ Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 190.66, 149.08, 145.14, 141.06, 135.94, 131.40, 128.54, 127.13, 125.96, 120.38, 116.84, 28.74, 15.49. MS (ESI): m/z 278 ($M+H$)⁺. Anal. Calcd. for C₁₇H₁₅N₃O: C, 73.63; H, 5.45; N, 15.15. Found: C, 73.59; H, 5.46; N, 15.19.

4-(4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3d): White solid, mp: 197.3-199.2 °C. IR (KBr): 3123, 2954, 1696, 1601, 1408, 1437, 1372 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 10.11 (s, 1H), 8.23 (s, 1H), 8.11 (d, $J = 8.6$ Hz, 2H), 8.04 (d, $J = 8.6$ Hz, 2H), 7.88 (d, $J = 8.8$ Hz, 2H), 7.04 (d, $J = 8.8$ Hz, 2H), 3.90 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 190.67, 160.10, 148.69, 135.91, 131.41, 127.30, 122.39, 120.35, 116.30, 114.45, 99.99, 55.39. MS (ESI): m/z 280 ($M+H$)⁺. Anal. Calcd. for C₁₆H₁₃N₃O₂: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.80; H, 4.72; N, 15.09.

4-(4-(4-chlorophenyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3e): Light-yellow solid, mp: 213.8-215.4 °C. IR (KBr): 3119, 3090, 1706, 1604, 1484, 1405, 1207 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 10.12 (s, 1H), 8.31 (s, 1H), 8.12 (d, $J = 8.0$ Hz, 2H), 8.04 (d, $J = 8.0$ Hz, 2H), 7.88 (d, $J = 8.1$ Hz, 2H), 7.48 (d, $J = 8.1$ Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 190.62, 147.94, 136.11, 131.44, 129.93, 129.54, 129.28, 127.19, 125.39, 120.47, 117.33. MS (ESI): m/z 284 ($M+H$)⁺. Anal. Calcd. for C₁₅H₁₀ClN₃O: C, 63.50; H, 3.55; N, 14.81. Found: C, 63.53; H, 3.59; N, 14.78.

4-(4-(4-fluorophenyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3f): White solid, mp: 215.7-219.3 °C. IR (KBr): 3137, 1689, 1605, 1591, 1498, 1409, 1242 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 10.11 (s, 1H), 8.27 (s, 1H), 8.11 (d, $J = 8.4$ Hz, 2H), 8.04 (d, $J = 8.4$ Hz, 2H), 7.91 (dd, $J = 8.4$, 5.4 Hz, 2H), 7.19 (t, $J = 8.6$ Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 190.61, 164.28, 161.81, 140.94, 136.07, 131.43, 127.75, 126.00, 120.44, 117.00, 115.99. MS (ESI): m/z 268 ($M+H$)⁺. Anal. Calcd. for C₁₅H₁₀FN₃O: C, 67.41; H, 3.77; N, 15.72. Found: C, 67.38; H, 3.79; N, 15.70.

4-(4-(pyridin-3-yl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3g): Yellow solid, mp: 230.6-231.8 °C. IR (KBr): 3139, 2959, 1693, 1606, 1500, 1452 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 10.12 (s, 1H), 9.13 (s, 1H), 8.66 (d, $J = 8.0$ Hz, 1H), 8.42 (s, 1H), 8.33 (d, $J = 8.0$ Hz, 1H), 8.13 (d, $J = 8.5$ Hz, 2H), 8.06 (d, 2H), 7.46 (m, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 190.58, 149.79, 147.14, 145.97, 140.76, 136.24, 133.34, 131.46, 126.04, 123.95, 120.58, 117.71. MS (ESI): m/z 251 ($M+H$)⁺. Anal. Calcd. for C₁₄H₁₀N₄O: C, 67.19; H, 4.03; N, 22.39. Found: C, 67.18; H, 4.06; N, 22.35.

4-(4-(chloromethyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3h): White solid, mp: 119.5-120.3 °C. IR (KBr): 3129, 2959, 1693, 1609, 1507, 1455 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 10.08 (s, 1H), 8.14 (s, 1H), 8.07 (d, $J = 8.4$ Hz, 2H), 7.96 (d, $J = 8.4$ Hz, 2H), 4.80 (s, 2H). ¹³C NMR (CDCl₃, 75 MHz): δ 190.19, 145.73, 140.35, 135.82, 131.01, 120.45, 119.13, 35.47. MS (ESI): m/z 244

(M+Na)⁺. Anal. Calcd. for C₁₀H₈ClN₃O: C, 54.19; H, 3.64; N, 18.96. Found: C, 54.22; H, 3.63; N, 18.92.

4-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3i): Light-yellow solid, mp: 135.3-136.1 °C. IR (KBr): 3123, 2963, 1700, 1614, 1513, 1432 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 10.08(s, 1H), 7.95-8.08 (m, 5H), 4.93 (s, 2H). ¹³C NMR (CDCl₃, 75 MHz): δ 192.18, 149.68, 140.64, 135.59, 131.33, 121.26, 120.13, 54.99. MS (ESI): m/z 204 (M+H)⁺. MS (ESI): m/z 204 (M+H)⁺. Anal. Calcd. for C₁₀H₉N₃O₂: C, 59.11; H, 4.46; N, 20.68. Found: C, 59.15; H, 4.50; N, 20.71.

4-(4-pentyl-1H-1,2,3-triazol-1-yl)benzaldehyde (3j): White solid, mp: 123.3-125.1 °C. IR (KBr): 3117, 2964, 1702, 1601, 1500, 1451 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 10.09 (s, 1H), 8.07 (d, *J* = 8.5 Hz, 2H), 7.97 (d, *J* = 8.5 Hz, 2H), 7.83 (s, 1H), 2.83 (t, 2H), 1.40-1.79 (m, 6H), 0.94 (t, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 190.71, 149.87, 141.25, 135.72, 131.34, 120.24, 118.52, 31.41, 28.99, 25.60, 22.42, 13.99. MS (ESI): m/z 244 (M+H)⁺. Anal. Calcd. for C₁₄H₁₇N₃O: C, 69.11; H, 7.04; N, 17.27. Found: C, 69.16; H, 7.05; N, 17.23.

1-(4-formylphenyl)-1H-1,2,3-triazole-4-carboxylic acid (3k): Light-yellow solid, mp: 194.7-195.4 °C. IR (KBr): 3409, 3137, 1729, 1659, 1603, 1586, 1447, 1231 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆): δ 13.43 (s, 1H), 10.09 (s, 1H), 9.56 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 192.67, 161.83, 141.43, 140.49, 136.51, 131.68, 127.89, 121.30. MS (ESI): m/z 216 (M-H)⁺. Anal. Calcd. for C₁₀H₇N₃O₃: C, 55.36; H, 3.31; N, 19.33. Found: C, 55.30; H, 3.25; N, 19.35.

4-(1H-1,2,3-triazol-1-yl)benzaldehyde (3l)^[3]: Yellow solid, mp: 121.6-125.8 °C. IR(KBr): 3209, 2972, 2818, 1696, 1604, 1518, 1304 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 10.10 (s, 1H), 8.13 (s, 1H), 8.09 (d, *J* = 8.6 Hz, 2H), 8.00 (d, *J* = 8.6 Hz, 2H), 7.92 (s, 1H). MS (ESI): m/z 174 (M+H)⁺.

2-(1H-1,2,3-triazol-1-yl)benzaldehyde (3m)^[3]: Yellow solid, mp: 126.1-128.2 °C. IR(KBr): 3118, 2985, 2820, 1697, 1609, 1215. ¹H NMR (300 MHz, CDCl₃): δ 9.90 (s, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 8.00 (s, 1H), 7.95 (s, 1H), 7.80 (t, *J* = 7.5 Hz, 1H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H). MS (ESI): m/z 174 (M+H)⁺.

References

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4-(4-Phenyl-1H-1,2,3-triazol-1-yl)benzaldehyde (3a)

2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzaldehyde (3b)

4-(4-(4-ethylphenyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3c)

4-(4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3d)

4-(4-(4-fluorophenyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3f)

4-(4-(pyridin-3-yl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3g)

4-(4-(chloromethyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3h)

4-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)benzaldehyde (3i)

4-(4-pentyl-1H-1,2,3-triazol-1-yl)benzaldehyde (3j)

1-(4-formylphenyl)-1H-1,2,3-triazole-4-carboxylic acid (3k)

4-(1H-1,2,3-triazol-1-yl)benzaldehyde (3l)

2-(1H-1,2,3-triazol-1-yl)benzaldehyde (3m)