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Towards molecular diversity: Dealkylation of *tert*-butyl amine in Ugi-type multicomponent reaction product establishes *tert*-butyl isocyanide as useful convertible isonitrile

Sankar K. Guchhait,*[a] and Chetna Madaan [a]

[a] Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), S. A. S. Nagar (Mohali) - 160062, Punjab, India. Fax: 91 (0)172 2214692; Tel: 91 (0)172 2214683; Email: skguchhait@niper.ac.in

Experimental

General considerations: All reactants and reagents were obtained from commercial source and used without further purification. The NMR spectra were recorded in DMSO-d_6 solvents in 400 MHz spectrometer. The IR spectra were recorded as KBr pellets for solid samples and neat for liquid samples. High-resolution mass spectra were measured on HRMS-TOF (Maxis-Bruker). Melting points determined are uncorrected.

Representative experimental procedure (Table 2, Entry 1): To a mixture of 2-aminopyridine (0.09 g, 1mmol) and 4-chlorobenzaldehyde (0.14 g, 1 mmol) in *n*-BuOH (1 mL) taken in a microwave vial, were added *tert*-butyl isocyanide (0.08 g, 0.11 mL, 1 mmol) and $ZrCl_4$ (0.023 g, 10 mol%). The vessel was sealed with a cap and the mixture was then irradiated in a monomode microwave synthesizer (Biotage Initiator^{TM} EXP) at 140 °C for 7 min. After cooling to r.t. in the microwave cavity, the vial cap was removed and to the reaction mixture was added 40 % aqueous HBF_4 (0.2 mL, 1 mmol). The vial was resealed and then irradiated at 160 °C for 20 min. To the resultant mixture was added aqueous ammonia solution (10%) to basify (pH = 8). The mixture was then extracted with EtOAc (60 mL) and the solution was washed with H_2O (3 x 10 mL). The organic layer was dried (anhy. Na_2SO_4), filtered, and concentrated under reduced pressure. The column chromatographic purification of the crude product over silica gel (mesh size: 60-120) with EtOAc-hexane as eluent afforded 2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-amine in 90% yield. This experimental procedure was followed for all compounds (Table 1).

General procedure for synthesis of compunds (Table 3): The resultant mixture obtained after reaction following the above procedure was made basic (pH = 8) with addition of aqueous ammonia solution (10 mol%). The precipitated solids were then filtered and washed

with water and EtOAc. The pure products were obtained by crystallization from EtOH-EtOAc.

The structures of products were identified by ^{1}H and ^{13}C NMR, Mass and IR spectrocopies, and confirmed by elemental analysis or HRMS. The compounds, which were reported in literature, showed identical spectroscopic data.

2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-amine (Table 2, Entry 1): Yellow solid; mp = 146-148 °C; IR (KBr) ν_{max} = 3310, 2932, 1646, 1492, 1270, 1091, 767 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): 5.22 (br s, NH_2), 6.85 (t, J = 6.7 Hz, 1H), 7.08 (dd, J = 7.2, 8.3 Hz, 1H), 7.41 (d, J = 9.0 Hz, 1H), 7.46 (d, J = 8.4 Hz, 2H), 8.06 (d, J = 8.4 Hz, 2H), 8.25 (d, J = 6.9 Hz, 1H): ^{13}C NMR (100 MHz, DMSO-d_6): 111.5, 116.9, 122.9, 123.0, 126.6, 127.2, 128.1 (2CH), 128.7 (2CH), 130.7, 134.3, 139.3; MS (APCI) m/z: 244 (M+1). Anal. found: C, 63.8; H, 4.05; N, 17.4. Calcd. for $C_{13}H_{10}ClN_3$: C, 64.1; H, 4.1; N, 17.2%. HRMS (m/z) calcd. for $C_{13}H_{10}ClN_3$ 243.0563, found 243.0566.

2-(4-Chlorophenyl)-8-methylimidazo[1,2-*a*]pyridin-3-amine (Table 2, Entry 2): Yellow solid; mp = 140-143 °C; IR (KBr) ν_{max} = 3290, 2919, 1659, 1493, 1387, 1275, 1089, 750 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): 2.58 (s, 3H), 7.04 (t, J = 6.8 Hz, 1H), 7.26 (d, J = 6.6 Hz, 1H), 7.49 (d, J = 7.3 Hz, 2H), 7.87 (d, J = 7.1 Hz, 2H), 8.21 (d, J = 6.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 16.5, 115.0, 122.2, 125.9, 127.4, 129.7, 129.9 (2CH), 130.0 (2CH), 130.1, 130.2, 131.6, 134.6; MS (APCI) m/z: 258 (M+1). HRMS (m/z) calcd. for $C_{14}H_{12}ClN_3$ 257.0720, found 257.0721.

2-(4-Bromophenyl)imidazo[1,2-*a*]pyridin-3-amine (Table 2, Entry 3): Yellow solid; mp = 144-146 °C; IR (KBr) ν_{max} = 3325, 2925, 1727, 1602, 1489, 1389, 1275, 1255, 1073, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 3.33 (br s, NH_2), 6.81 (t, J = 6.8 Hz, 1H), 7.11 (t, J = 8.0 Hz, 1H), 7.52 (d, J = 9.0 Hz, 1H), 7.55 (d, J = 6.8 Hz, 2H), 7.88 (d, J = 6.8 Hz, 2H), 7.97 (d, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 111.9, 117.3, 121.1, 121.8, 122.5, 123.6, 128.5 (2CH), 131.7 (2CH), 132.4, 133.3, 141.1; MS (APCI) m/z: 288 (M). HRMS (m/z) calcd. for $C_{13}H_{10}BrN_3$, 287.0058, found 287.0051.

6-Bromo-2-(3,4,5-trimethoxyphenyl)imidazo[1,2-*a*]pyridin-3-amine (Table 2, Entry 4): Fluorescent green solid; mp = 197-200 °C; IR (KBr) ν_{max} = 3317, 2945, 1602, 1504, 1406, 1241, 1124, 751 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): 3.70 (s, 3H), 3.87 (s, 6H), 7.23 (s, 2H), 7.36 (d, J = 9.4 Hz, 1H), 7.52 (d, J = 9.2 Hz, 1H), 8.70 (s, 1H); ^{13}C NMR (100 MHz,

DMSO-d_6): 56.3 ($2CH_3$), 60.5, 104.2 (2CH), 107.0, 116.5, 123.3, 125.0, 127.4, 127.6, 128.4, 136.3, 137.1, 153.4 (2C); MS (APCI) m/z: 380 (M+2). HRMS (m/z) calcd. for $C_{16}H_{16}BrN_3O_3$ 377.0375, found 377.0378.

6-Bromo-2-(4-cyanophenyl)imidazo[1,2-*a*]pyridin-3-amine (Table 2, Entry 5): Yellow solid; mp = 214-216 °C; IR (KBr) ν_{max} = 3337, 2221, 1604, 1504, 1406, 1257, 1074, 787 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 7.18 (d, J = 9.4 Hz, 1H), 7.42 (d, J = 9.3 Hz, 1H), 7.84 (d, J = 8.0 Hz, 2H), 8.17 (d, J = 8.0 Hz, 2H), 8.61 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 105.7, 107.7, 117.7, 119.2, 122.7, 124.0, 125.7, 126.0 (2CH), 129.5, 132.2 (2CH), 137.0, 138.9; MS (APCI) m/z: 315 (M+2). HRMS (m/z) calcd. for $C_{14}H_9BrN_4$, 312.0011, found 312.0010.

6-Chloro-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (Table 2, Entry 6): Yellow solid; mp = 220-222 °C; IR (KBr) ν_{max} = 3429, 1633, 1588, 1480, 1258, 1093, 1047, 772 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 6.53 (br s, NH_2), 7.04 (d, J = 9.6 Hz, 1H), 7.18 (dd, J = 6.5, 5.6 Hz, 1H), 7.46 (d, J = 9.6 Hz, 1H), 7.83 (t, J = 7.6 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 8.40 (s, 1H), 8.57 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 118.3, 118.7, 119.2, 120.64, 120.69, 122.8, 122.9, 132.7, 136.6, 137.2, 149.0, 155.5; MS (APCI) m/z: 245 (M+1). HRMS (m/z) calcd. for $C_{12}H_9ClN_4$, 244.0516, found 244.0519.

2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyrazin-3-amine (Table 2, Entry 7): Brownish yellow solid; mp = 175-177 °C; IR (KBr) ν_{max} = 3365, 2939, 1606, 1560, 1254, 1182, 1029, 765 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 3.72 (s, 3H), 5.62 (br s, NH_2), 7.02 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 4.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 2H), 8.22 (d, J = 4.0 Hz, 1H), 8.75 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 55.3, 114.2 (2CH), 114.9, 126.6, 127.6, 127.7 (3CH), 129.2, 133.9, 141.4, 158.3; MS (APCI) m/z: 241 (M+1). HRMS (m/z) calcd. for $C_{13}H_{12}N_4O$ 240.1011, found 240.1018.

6-(4-Bromophenyl)imidazo[2,1-*b*]thiazol-5-amine (Table 2, Entry 8): Dark green solid; mp = 170 °C (decomposed); IR (KBr) ν_{max} = 3098, 1540, 1487, 1381, 1281, 1076, 1009, 753 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 5.25 (s, NH_2), 7.13 (d, J = 4.4 Hz, 1H), 7.50 (d, J = 7.8 Hz, 2H), 7.66 (d, J = 4.4 Hz, 1H), 7.81 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 112.4, 117.6, 117.9, 126.2, 126.9 (2CH), 129.8, 131.4 (2CH), 135.2, 141.3; MS (APCI) m/z: 296 (M+2). %. HRMS (m/z) calcd. for $C_{11}H_8BrN_3S$ 292.9622, found 292.9620.

2-Isopropylimidazo[1,2-*a*]pyridin-3-amine (Table 2, Entry 9)[1]: Yellowish brown viscous liquid; IR (neat) ν_{max} = 3310, 2927, 1727, 1580, 1450, 1275, 1259, 1071, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 1.36 (d, *J* = 7.0 Hz, 6H), 3.18 (quintet, *J* = 7.0 Hz, 1H),), 6.72 (dt, *J* = 6.8, 1.0 Hz, 1H), 7.01 (dt, *J* = 6.8, 1.2 Hz, 1H),), 7.46 (d, *J* = 8.0 Hz, 1H),), 7.96 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 22.3 ($2CH_3$), 26.3, 111.1, 116.7, 121.6, 122.2, 137.8, 138.3, 141.6; MS (APCI) m/z: 176 (M+1).

Pyrido[2´,1´:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one[2] (Table 3, Entry 1):: Yellow solid; mp > 250 °C; IR (KBr) ν_{max} = 3365, 1657, 1622, 1561, 1384, 1261, 1129, 1056, 743 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 7.00 (t, *J* = 6.6 Hz, 1H), 7.29 (dd, *J* = 8.6, 6.8 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.63 (d, *J* = 9.0 Hz, 1H), 7.85 (t, *J* = 7.3 Hz, 1H), 8.27 (d, *J* = 7.8 Hz, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 8.63 (d, *J* = 6.6 Hz, 1H); MS (APCI) m/z: 236 (M+1).

9-Bromo-6*H*-pyrido[2´,1´:1,2]imidazo[5,4-*c*]isoquinolin-5-one[2] (Table 3, Entry 2): Yellow solid; mp > 250°C; IR (KBr) ν_{max} = 3423, 2919, 1646, 1602, 1513, 1387, 1235, 1040 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 7.37 (d, *J* = 8.0 Hz, 1H), 7.58-7.64 (m, 2H), 7.86 (t, *J* = 8.0 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 8.92 (s, 1H); MS (APCI) m/z: 314 (M), 316 (M+2).

Pyrazino[2´,1´:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one[2,3] (Table 3, Entry 3): Yellow solid; mp > 250 °C; IR (KBr) ν_{max} = 3078, 2361, 1699, 1645, 1541, 1295, 1123, 791 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 7.69 (t, *J* = 8.0 Hz, 1H), 7.93 (t, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 4.8 Hz, 1H), 8.35 (t, *J* = 8.0 Hz, 2H), 8.68 (d, *J* = 4.8 Hz, 1H), 9.25 (s, 1H); MS (APCI) m/z: 237 (M+1).

Thiazolo[2´,3´:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one[3] (Table 3, Entry 4): Yellowish cream solid; mp > 250 °C; IR (KBr) ν_{max} = 3100, 2866, 1670, 1623, 1574, `1290, 1136, 1099, 764 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 7.33 (d, *J* = 4.3 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.79 (t, *J* = 7.5 Hz, 1H), 7.95 (d, *J* = 4.3 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H); MS (APCI) m/z: 242 (M+1).

8,10-Dimethoxy-6*H*-pyrido[2´,1´:1,2]imidazo[5,4-*c*]isoquinolin-5-one (Table 3, Entry 5): Yellow solid; mp > 250 °C; IR (KBr) ν_{max} = 3356, 2952, 1650, 1610, 1586, 1447, 1374, 1275, 1149, 1036, 751 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 3.92 (s, 3H), 4.01 (s, 3H), 7.01-7.04 (m, 2H), 7.29-7.31 (m, 1H), 7.40 (s, 1H), 7.69 (d, *J* = 9.1 Hz, 1H), 8.63 (d, *J* = 6.8 Hz, 1H);

^{13}C NMR (100 MHz, DMSO-d_6 + 2 drops of THF): 55.6, 56.2, 88.1, 97.6, 100.4, 103.8, 112.0, 117.6 (2CH), 122.8 (2CH), 124.5, 141.9, 157.5, 158.9, 162.2; MS (APCI) m/z: 296 (M+1). HRMS (m/z) calcd. for $C_{16}H_{13}N_3O_3$, 295.0957, found 295.0950.

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