Supporting Information

Efficient and chemoselective alkylation of amines/amino acids using alcohols as alkylation reagents under mild conditions

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Contents (60 pages):

- General procedure for the alkylation of amines with alcohol. (pp. 2)
- Procedure for the recovery and recycle of 10%Pd/C. (pp. 2)
- A plausible mechanism for the N-alkylation of an amine with an alcohol (pp. 3)
- Experimental procedures for compounds 1, 2a-d, 3, 4, 5, 6, 8, 10, 14, 17, 18, 19, 20, 22, 24, 26 (pp. 4-11)
- 1H and 13C NMR spectra of compounds 1, 2a-d, 3, 4, 5, 6, 8, 10, 14, 17, 18, 19, 20, 22, 24, 26 (pp. 12-49)
- References (pp. 50)
General Methods

Melting points were uncorrected. Optical rotations were measured with Perkin-Elmer 341 automatic polarimeter. Infrared spectra were measured using KBr pellet techniques. $^1$H-NMR spectra were acquired at 400 or 500 MHz and $^{13}$C were acquired at 100 or 125 MHz. Mass spectra were recorded by a Bruker Dalton ESquire 3000 plus liquid chromatography-mass spectrum (direct injection). Silica gel (300-400 mesh) was used for flash column chromatography. The alcohols used are analytically pure grade.

General procedure for the alkylation of amines with alcohol.

After vacuum to remove air from the reaction tube, the stirred mixture of the amines/amino acids (0.1 mmol), 10% Pd/C (100 mg, 0.094 mmol) or 20% Pd(OH)$_2$/C (80 mg, 0.114 mmol) in an alcohol (5 mL) was hydrogenated under 1 atm of hydrogen (balloon) at room temperature. The reaction was vigorously stirred. When the reaction was judged to be complete by TLC monitoring, the mixture was filtered using a filter paper under a reduced pressure, and the filtrate was washed with the corresponding alcohol (5 mL) and the filtrate was concentrated under reduced pressure (about 80% of the solvent could be recovered by distillation). The crude product was purified by flash column chromatography on silica gel, if necessary. Yield and time are indicated in Table 1 and Table 2.

Procedure for the recovery and recycle of 10%Pd/C.

The catalyst (10%Pd/C) was recovered by filtration through a filter paper under reduced pressure, and reused following the general procedure. This procedure was repeated four times with the results indicated in Table 3. Caution: upon washing of 10%Pd/C, this catalyst might burned spontaneously when expose to air, and precautions should be taken (avoiding the excessively dryness of Pd/C during the vacuum filtration).

Table 1. N-Alkylation reaction of amine with recycled catalyst or solvent.
<table>
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<th>Entry</th>
<th>Cycle</th>
<th>T (h)</th>
<th>Yield (%)&lt;sup&gt;[c]&lt;/sup&gt;</th>
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<td>5&lt;sup&gt;[b]&lt;/sup&gt;</td>
<td>1</td>
<td>16</td>
<td>70</td>
</tr>
</tbody>
</table>

<sup>[a]</sup> Reaction with recycled catalyst.

<sup>[b]</sup> Reaction with recycled solvent.

<sup>[c]</sup> Isolated yield.

![Scheme 1](image-url)

**Scheme 1.** A plausible mechanism for the N-alkylation of an amine with an alcohol.
(4-Methylpiperazin-1-yl)(phenyl)methanone (2a)

Following the general procedure, the reaction of \(N\)-benzoylpiperazine (1) (0.1 mmol, 19 mg) in MeOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 2a\(^3\) as a colorless oil (17.3 mg, 85%). By using 20%Pd(OH)\(_2\)/C (80 mg) as the catalyst, 12.6 mg of 2a was obtained (yield: 62%). IR (film) \(\nu_{\text{max}}\): 2936, 2850, 2786, 1632, 1424, 1296, 1271, 1168, 1141, 1128, 1019, 1004 \text{cm}^{-1}; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 2.31 (s, 3H), 2.35 (br s, 2H), 2.48 (br s, 2H), 3.44 (br s, 2H), 3.79 (br s, 2H), 7.28-7.42 (s, 5H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 42.0, 46.0, 47.5, 55.0(2C), 127.0, 128.4, 129.6, 135.8, 170.3; MS (ESI): \(m/z\) 205.1 (M+H\(^+\), 100).

(4-Ethylpiperazin-1-yl)(phenyl)methanone (2b)

Following the general procedure, the reaction of \(N\)-benzoylpiperazine (1) (0.1 mmol, 19 mg) in EtOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 2b\(^4\) as a colorless oil (19.4 mg, 89%). By using 20%Pd(OH)\(_2\)/C (80 mg) as the catalyst, 16.1 mg of 2b was obtained (yield: 74%). IR (film) \(\nu_{\text{max}}\): 2970, 2924, 2805, 1632, 1577, 1427, 1290, 1260, 1165, 1119, 1013, \text{cm}^{-1}; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 1.08 (t, \(J = 7.2\ \text{Hz},\ 3\text{H})\), 2.38 (br s, 2H), 2.43 (q, \(J = 7.2\ \text{Hz},\ 2\text{H})\), 2.50 (br s, 2H), 3.43 (br s, 2H), 3.79 (br s, 2H), 7.36-7.40 (s, 5H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 11.8, 42.2, 47.7, 52.2, 52.4, 53.0, 127.0, 128.4, 129.6, 135.8, 170.2; MS (ESI): \(m/z\) 219.1 (M+H\(^+\), 100).

Phenyl(4-propylpiperazin-1-yl)methanone (2c)

Following the general procedure, the reaction of \(N\)-benzoylpiperazine (1) (0.1 mmol, 19 mg) in \(n\)-PrOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 2c\(^5\) as a
colorless oil (17.6 mg, 76%).

By using 20%Pd(OH)_2/C (80 mg) as the catalyst, 21.3 mg of 2c was obtained (yield: 92%). IR (film) \( \nu_{\text{max}} \): 2964, 2921, 2866, 2805, 2765, 1632, 1372, 1293, 1278, 1159, 1015, 1001 cm\(^{-1}\); \( ^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \): 0.91 (t, \( J = 7.4 \) Hz, 3H), 1.51 (tq apparent sextet, \( J = 7.7,7.4 \) Hz, 2H), 2.33 (t, \( J = 7.7 \) Hz, 2H), 2.38 (br s, 2H), 2.52 (br s, 2H), 3.44 (br s, 2H), 3.50 (br s, 2H), 7.39 (s, 5H); \( ^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \): 11.8, 19.9, 42.2, 47.7, 52.9, 53.4, 60.5, 127.0, 128.4, 129.6, 136.0, 170.2; MS (ESI): m/z 233.1 (M+H\(^+\), 100).

(4-Isopropylpiperazin-1-yl)(phenyl)methanone (2d)

Following the general procedure, the reaction was performed starting from \( N \)-benzoylpiperazine (1) (0.1 mmol, 19 mg), \( t \)-PrOH (5 mL) and 10% Pd/C (100 mg). The residue was purified by flash column chromatography on silica gel eluting with CH\(_2\)Cl\(_2\)–CH\(_3\)OH (60:1), gave 2d\(^{[6]}\) as a colorless oil (14.8 mg, 64%). IR (film) \( \nu_{\text{max}} \): 2969, 2924, 2853, 2811, 1631, 1576, 1424, 1283, 1262, 1177, 1012 cm\(^{-1}\); \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 1.04 (d, \( J = 6.6 \) Hz, 6H), 2.45 (br s, 2H), 2.58 (br s, 2H), 2.72 (h, \( J = 6.6 \) Hz, 1H), 3.42 (br s, 2H), 3.79 (br s, 2H), 7.39 (s, 5H); \( ^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \): 18.3, 42.3, 48.0, 48.3, 49.0, 54.6, 127.0, 128.4, 129.5, 135.9, 170.1; MS (ESI): m/z 233.1 (M+H\(^+\), 100).

(\( S \))-2-(Dimethylamino)-3-methylbutanoic acid (Dov, 3)

Following the general procedure, the reaction of L-valine (15) (0.1 mmol, 11.7 mg) in MeOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 3 as a white solid (13.5 mg, 93%). \( [\alpha]_D^{20} +45.4 \) (c 0.80, H\(_2\)O) \{lit.\( ^{[13]}\) [\( \alpha \]D\(^{14} \) +40.6 (c 2, H\(_2\)O)\}; M.p. 154-156 °C (EtOH/CH\(_3\)COCH\(_3\)) \{lit.\( ^{[13]}\) 154 °C\}. IR (KBr) \( \nu_{\text{max}} \): 3436, 2961, 2765, 1604, 1461, 1421, 1372, 1351 cm\(^{-1}\); \( ^1\)H NMR (400 MHz, D\(_2\)O) \( \delta \): 0.96 (d, \( J = 6.8 \) Hz,
3H), 1.09 (d, J = 6.8 Hz, 3H), 2.29-2.42 (m, 1H), 2.89 (d, J = 7.4 Hz, 6H), 3.43 (d, J = 5.1 Hz, 1H); $^{13}$C NMR (100 MHz, D$_2$O) δ: 15.8, 19.3, 26.0, 40.0, 43.0, 76.1, 171.6; MS (ESI): m/z 146.0 (M+H$^+$, 100).

**(R/S)**-2-(Dimethylamino)-4-methylpentanoic acid (4)

Following the general procedure, the reaction of (±)-leucine (13) (0.1 mmol, 13.1 mg) in MeOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 4 as a white solid (13.6 mg, 94%). M.p. 192-194 °C (EtOH) (lit.$^{[12]}$ 194 °C). IR (KBr) $\nu_{\text{max}}$: 3436, 2960, 2869, 1625, 1472, 1378, 1341, 1323, 1146, 1119 cm$^{-1}$; $^1$H NMR (400 MHz, D$_2$O) δ: 0.95-1.01 (t, 6H), 1.60-1.80 (m, 3H), 2.90 (br s, 6H), 3.58 (dd, J = 9.7, 4.1 Hz, 1H); $^{13}$C NMR (100 MHz, D$_2$O) δ: 20.7, 22.7, 25.1, 36.8, 40.1, 42.3, 70.3, 173.5; MS (ESI): m/z 160.1 (M+H$^+$, 100).

**(2S,3S)**-2-(Dimethylamino)-3-methylpentanoic acid (2S,3S)-N,N-diMe-Ile) (5)

Following the general procedure, the reaction of L-isoleucine (16) (0.1 mmol, 13.1 mg) in MeOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 5 as a white solid (14.5 mg, 91%). $[\alpha]_D^{20}$ +53.3 (c 1.13, H$_2$O) {lit.$^{[14]}$ $[\alpha]_D^{20}$ +48 (c 1, H$_2$O)}; M.p. 174-175 °C (CH$_3$COCH$_3$) (lit.$^{[14]}$ 173-174 °C). IR (KBr) $\nu_{\text{max}}$: 3433, 2970, 2869, 1622, 1470, 1385, 1311, 1144, 1064 cm$^{-1}$; $^1$H NMR (400 MHz, D$_2$O) δ: 0.93-1.02 (m, 6H), 1.28-1.41 (m, 1H), 1.48-1.61 (m, 1H), 2.03-2.14 (m, 1H), 2.88 (s, 3H), 2.91 (s, 3H), 3.52 (d, J = 4.4 Hz, 1H); $^{13}$C NMR (100 MHz, D$_2$O) δ: 11.2, 13.1, 26.6, 32.7, 39.7, 43.5, 74.9, 171.7; MS (ESI): m/z 160.0 (M+H$^+$, 100).

**(R/S)**-2-(Dimethylamino)-3-phenylpropanoic acid (6)
Following the general procedure, the reaction of (±)-phenylalanine (14) (0.1 mmol, 16.5 mg) in MeOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 6 as a white solid (17.8 mg, 92%). M.p. 229-230 °C (MeOH) (lit.\(^{[13]}\) 228 °C). IR (KBr) \(\nu_{\text{max}}\): 3430, 3031, 2921, 1616, 1418, 1348, 1335, 1287, 1177, 1144, 1089, 1025 cm\(^{-1}\); \(^1\)H NMR (400 MHz, D\(_2\)O) \(\delta\): 2.94 (br s, 6H), 3.13 (dd, \(J = 13.7, 9.2\) Hz, 1H), 3.35 (dd, \(J = 13.7, 5.7\) Hz, 1H), 3.85 (dd, \(J = 9.2, 5.7\) Hz, 1H); \(^{13}\)C NMR (100 MHz, D\(_2\)O) \(\delta\): 34.0, 41.5, 42.4, 72.2, 127.5, 129.0, 129.2, 135.4, 172.2; MS (ESI): m/z 194.0 (M+H\(^+\), 100).

**\((2S,4R)\)-4-Hydroxy-1-methylpyrrolidine-2-carboxylic acid (7)**

Following the general procedure, the reaction of \((2S,4R)\)-4-hydroxy-1-methylpyrrolidine-2-carboxylic acid (11) (0.1 mmol, 13.1 mg) in MeOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 7 as a white solid (12.6 mg, 87%). \([\alpha]_D^{20} -90.0\) (c 0.13, CH\(_3\)OH) \{lit.\(^{[15]}\) \([\alpha]_D^{20} -95.0\) (c 0.1, CH\(_3\)OH)\}; M.p. 238-240 °C (MeOH) (lit.\(^{[16]}\) 237-241 °C). IR (KBr) \(\nu_{\text{max}}\): 3418, 1625, 1403, 1339, 1208, 1071 cm\(^{-1}\); \(^1\)H NMR (400 MHz, D\(_2\)O) \(\delta\): 2.20-2.31 (m, 1H), 2.44-2.55 (m, 1H), 3.06 (s, 3H), 3.21 (d, \(J = 13.0\) Hz, 1H), 3.97 (dd, \(J = 13.0, 4.6\) Hz, 1H), 4.21 (dd, \(J = 11.0, 7.5\) Hz, 1H), 4.62-4.67 (m, 1H); \(^{13}\)C NMR (100 MHz, D\(_2\)O) \(\delta\): 38.3, 43.2, 62.7, 69.5, 70.1, 172.9; MS (ESI): m/z 145.9 (M+H\(^+\), 100).

**\((R/S)\)-1-Methylpiperidine-2-carboxylic acid (8)**

Following the general procedure, the reaction of \((R/S)\)-piperidine-2-carboxylic acid (12) (0.1 mmol, 12.9 mg) in MeOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 8 as a white solid (12.9 mg, 90%).

By using 20%Pd(OH)\(_2\)/C (80 mg) as the catalyst, 13.4 mg of 8 was obtained (yield: 94%). M.p. 208-209 °C (EtOH) (lit.\(^{[10]}\) 208-210 °C). IR (KBr) \(\nu_{\text{max}}\): 3401, 3026, 2959,
2933, 2860, 1614, 1393, 1354, 1322, 1284, 1114 cm\(^{-1}\); \(^1\)H NMR (400 MHz, D\(_2\)O) \(\delta\): 1.53-1.66 (m, 1H), 1.70-1.84 (m, 2H), 1.87-2.03 (m, 2H), 2.22-2.31 (m, 1H), 2.91 (s, 3H), 3.04-3.13 (m, 1H), 3.50-3.58 (m, 2H); \(^{13}\)C NMR (100 MHz, D\(_2\)O) \(\delta\): 16.9, 21.0, 22.6, 28.0, 42.4, 54.5, 69.0, 174.1; MS (ESI): \(m/z\) 144.1 (M+H\(^+\), 100).

\((R/S)-1\)-Methylpyrrolidine-2-carboxylic acid (10)

Following the general procedure, the reaction of \((\pm)-proline\) (9) (0.1 mmol, 11.5 mg) in MeOH (5 mL) and in the presence of 10\% Pd/C (100 mg) gave 10 as a white solid (11.5 mg, 89%). By using 20\%Pd(OH)\(_2\)/C (80 mg) as the catalyst, 10.7 mg of 10 was obtained (yield: 83\%). M.p. 168-169 °C (EtOH) (lit.[8] 168-170 °C). IR (KBr) \(\nu_{\text{max}}\): 3430, 3064, 2857, 1628, 1473, 1455, 1400, 1321 cm\(^{-1}\); \(^1\)H NMR (400 MHz, D\(_2\)O) \(\delta\): 2.00-2.11 (m, 1H), 2.11-2.29 (m, 2H), 2.52-2.65 (m, 1H), 3.00 (s, 3H), 3.18-3.28 (m, 1H), 3.77-3.85 (m, 1H), 3.97-4.04 (m, 1H); \(^{13}\)C NMR (100 MHz, D\(_2\)O) \(\delta\): 22.8, 28.8, 40.8, 56.5, 70.5, 173.3; MS (ESI): \(m/z\) 152.0 (M+Na\(^+\), 100).

\((S)-4-(3\)-Hydroxy-2-(methylamino)propyl\)phenol (17)

To a mixture of \((S)-3-(4-(benzyloxy)phenyl)-2-(methylamino)propan-1-ol\)\(^{17}\) (68 mg, 0.25 mmol) and 10\% Pd/C (20 mg) was added MeOH (5 mL). The mixture was stirred at room temperature under an atmosphere of H\(_2\) for 1.5 hours. The mixture was filtered and concentrated under reduced pressure to give 17 (44.5 mg, 98\%) as a white solid. \([\alpha]_D^{20} +11.2\ (c\ 0.5,\ MeOH)\); M.p. 152-153 °C (MeOH). IR (KBr) \(\nu_{\text{max}}\): 3430, 3305, 3143, 2912, 1616, 1592, 1519, 1467, 1443, 1363, 1269, 1238, 1107, 1065, 1031 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CD\(_3\)OD) \(\delta\): 2.35 (s, 3H), 2.51 (dd, \(J = 15.1,\ 9.7\ Hz,\ 1H\)), 2.59-2.67 (m, 2H), 3.34 (dd, \(J = 11.2,\ 5.6\ Hz,\ 1H\)), 3.47 (dd, \(J = 11.2,\ 4.0\ Hz,\ 1H\)), 6.66 (d, \(J = 8.4\ Hz,\ 2H\)), 6.97 (d, \(J = 8.4\ Hz,\ 2H\)); \(^{13}\)C NMR (100 MHz, CD\(_3\)OD) \(\delta\):
(S)-4-(2-(Dimethylamino)-3-hydroxypropyl)phenol (18)

Following the general procedure, the reaction of (S)-4-(3-hydroxy-2-(methylamino)propyl)phenol (17) (0.1 mmol, 18.1 mg) in MeOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 18 as a white solid (14 mg, 72%). \([\alpha]_D^{20} +7.3\) (c 0.55, MeOH); M.p. 153-155 °C (MeOH). IR (KBr) \(\nu_{\text{max}}\): 3168, 2933, 2869, 2835, 2799, 1613, 1589, 1516, 1461, 1384, 1275, 1247, 1235, 1165, 1061, 1037, 1010 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CD\(_3\)OD) \(\delta\): 2.37 (s, 6H), 2.43 (dd, \(J = 13.2, 9.3\) Hz, 1H), 2.68-2.82 (m, 2H), 3.49 (d, \(J = 5.6\) Hz, 2H), 6.68-6.74 (m, 2H), 6.99-7.04 (m, 2H); \(^{13}\)C NMR (100 MHz, CD\(_3\)OD) \(\delta\): 32.1, 41.4, 61.2, 68.9, 116.3, 131.0, 131.8, 156.8; MS (ESI): \(m/z\) 196.0 (M+H\(^+\), 100).

1-Ethylpyrrolidine-2-carboxylic acid (19)

Following the general procedure, the reaction of (±)-proline (9) (0.1 mmol, 11.5 mg) in EtOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 19 as a white solid (12.2 mg, 85%). By using 20%Pd(OH)\(_2\)/C (80 mg) as the catalyst, 10.7 mg of 19 was obtained (yield: 75%). M.p. 168-169 °C (CHCl\(_3\)) (lit.\(^9\) 170 °C). IR (KBr) \(\nu_{\text{max}}\): 3433, 3055, 2985, 2881, 1628, 1461, 1400, 1327, 1235, 1171, 1043 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CD\(_3\)OD) \(\delta\): 1.34 (t, \(J = 7.2\) Hz, 3H), 1.88-2.02 (m, 1H), 2.04-2.19 (m, 2H), 2.38-2.50 (m, 1H), 3.05-3.14 (m, 1H), 3.15-3.26 (m, 1H), 3.27-3.38 (m, 1H), 3.69-3.78 (m, 1H), 3.83-3.90 (m, 1H); \(^{13}\)C NMR (100 MHz, CD\(_3\)OD) \(\delta\): 11.3, 24.4, 30.3, 51.6, 55.5, 70.1, 173.3; MS (ESI): \(m/z\) 144.1 (M+H\(^+\), 100).
1-Ethylpiperidine-2-carboxylic acid (20)

Following the general procedure, the reaction of (±)-piperidine-2-carboxylic acid (12) (0.1 mmol, 12.9 mg) in EtOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave 20 as a white solid (13.5 mg, 86%).

By using 20%Pd(OH)2/C (80 mg) as the catalyst, 15.1 mg of 20 was obtained (yield: 96%). M.p. 200-201 °C (EtOH). IR (KBr) νmax: 3427, 2975, 2940, 2927, 2863, 1617, 1457, 1377, 1322, 1274, 1175, 1085, 1018 cm⁻¹; 1H NMR (400 MHz, D2O) δ: 1.34 (t, J = 7.4 Hz, 3H), 1.50-1.63 (m, 1H), 1.63-1.82 (m, 2H), 1.82-2.00 (m, 1H), 2.16-2.26 (m, 1H), 2.90-3.01 (m, 1H), 3.06-3.18 (m, 1H), 3.26-3.37 (m, 1H), 3.51-3.58 (m, 1H), 3.59-3.67 (m, 1H); 13C NMR (100 MHz, D2O) δ: 8.6, 21.1, 22.3, 27.9, 50.6, 51.3, 67.6, 174.4; MS (ESI): m/z 180.1 (M+Na⁺, 100).

(2R,3R,4R,5R)-2,5-Bis(hydroxymethyl)-1-methylpyrrolidine-3,4-diol (22)

To 4.2 mg of 10% Pd/C was added a solution of compound (2R,3R,4R,5R)-21 (14.0 mg, 0.032 mmol) in 2 mL of dry methanol. The mixture was stirred under 1 atm of hydrogen for two days at rt and then filtered through filter paper under reduced pressure. After concentration under reduced pressure, the resulting residue afforded compound 22 (5.0 mg, 89%). [α]D²⁰ –8.0 (c 0.4, H2O) [lit.¹⁹] [α]D²⁰ –8.5 (c 1.0, H2O); IR (film): νmax : 3350, 2922, 1423, 1252, 1120 cm⁻¹; 1H NMR (400 MHz, D2O): δ : 2.59 (s, 3H), 3.03–3.10 (m, 2H), 3.85 (dd, J = 1.4, 4.6 Hz, 4H), 4.00 (td, J = 2.8, 4.6 Hz, 2H); 13C NMR (100 MHz, D2O) δ : 37.8, 61.6, 72.5, 80.0; MS (ESI) m/z 178 (M+H⁺, 100).

(2R,4S,5R)-1-Methyl-4-hydroxy-5-hydroxymethyl pyrrolidine-2-carboxylic acid (24)
To 50 mg of 20% Pd(OH)\textsubscript{2}/C was added a solution of compound \((2R,4S,5R)-23\) (16 mg, 0.047 mmol) in 5 mL of MeOH. The mixture was hydrogenated under 1 atm hydrogen pressure and stirred at room temperature for 15 h. The mixture was filtered through celite and the filtrate was evaporated in \textit{vacuo} to afford \(24\) (8.1 mg, 99%) as a colorless oil. \([\alpha]_D^{20} +55.2\) (c 0.63, MeOH), IR (film): 1024, 1093, 1334, 1383, 1629, 3317 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, D\textsubscript{2}O) \(\delta\) 2.40 (ddd, \(J = 5.4, 8.5, 13.9\) Hz, 1H), 2.49 (ddd, \(J = 5.4, 8.5, 13.9\) Hz, 1H), 3.13 (s, 3H), 3.55 (dd, \(J = 4.6, 9.2\) Hz, 1H), 3.92 (dd, \(J = 4.6, 12.9\) Hz, 1H), 4.03 (dd, \(J = 4.6, 12.9\) Hz, 1H), 4.25 (t, \(J = 8.5\) Hz, 1H), 4.39 (dd, \(J = 5.4, 9.2\) Hz, 1H); \(^{13}\)C-NMR (100 MHz, D\textsubscript{2}O) \(\delta\): 36.5, 42.4, 56.7, 69.9, 70.2, 76.3, 172.7; MS (ESI): 198 \(m/z\) (M+Na\(^+\), 100). ESI-HRMS: calcd for [C\textsubscript{7}H\textsubscript{13}NO\textsubscript{4} + H\(^+\)]: 176.0923; found: 176.0937.

\textbf{1-(3,4-Dimethylphenyl)-4-methylpiperazine (26)}

Following the general procedure, the reaction of 1-(3,4-dimethylphenyl)piperazine (\(25\)) (0.1 mmol, 19 mg) in MeOH (5 mL) and in the presence of 10% Pd/C (100 mg) gave \(26\) as a yellow oil (14.9 mg, 73%). IR (film) \(\nu_{\text{max}}\): 2967, 2936, 2793, 1622, 1507, 1449, 1375, 1293, 1244, 1153, 1000 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\): 2.18 (s, 3H), 2.23 (s, 3H), 2.36 (s, 3H), 2.59 (t, \(J = 5.0\) Hz, 4H), 3.17 (t, \(J = 5.0\) Hz, 4H), 6.69 (dd, \(J = 8.0, 2.5\) Hz, 1H), 6.76 (d, \(J = 2.5\) Hz, 1H), 7.02 (d, \(J = 8.0\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\): 18.7, 20.1, 46.1, 49.7, 55.2, 113.8, 118.1, 128.0, 130.2, 137.1, 149.6; MS (ESI): \(m/z\) 205.1 (M+H\(^+\), 100). ESI-HRMS: calcd for [C\textsubscript{13}H\textsubscript{20}N\textsubscript{2}+H\(^+\)]: 205.1705; found: 205.1696.
100 MHz, Methanol-d4
XCPB94T-H
CDCl₃

400MHz, CDCl₃
$\text{CDCl}_3$

500 MHz
Supplementary Material (ESI) for Chemical Communications

$\text{XCPB146T-C}$

$\text{D}_2\text{O}$

$100\text{MHz, D}_2\text{O}$
XCPB152 T-H
D2O

400MHz, D2O
Supplementary Material (ESI) for Chemical Communications

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$400\text{MHz, D}_2\text{O}$
Supplementary Material (ESI) for Chemical Communications

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400MHz, Methanol-d4
400MHz, D$_2$O
100MHz, D$_2$O
References:


