A Facile Route to Indolo[2,1-\(a\)]isoquinolines and Dibenzopyrrocoline Alkaloids

Supporting Information

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Characterization data for products 3, 8, 10, and 16

General Procedure for Preparation of Indolo[2,1-\(a\)]isoquinolines 3a-3j (from 2a-2j, 6a, 6b), 8 (from 7), 10 (from 9), and 16 (from 15a,b). A solution of an appropriate 1-(2'-halobenzyl)isoquinoline (0.5 mmol) and \(\text{K}_2\text{CO}_3\) (1 mmol) in DMF (10 mL) was refluxed under nitrogen for 3, 2 or 1.5 days as described in the text. The solvent was removed by distillation under reduced pressure. The residue was dissolved in water (10 mL) and extracted with \(\text{CH}_2\text{Cl}_2\) (10 mL \(\times\) 3). The combined extracts were washed with water (30 mL \(\times\) 2), dried (\(\text{Na}_2\text{SO}_4\)), and evaporated. The crude product was crystallized from the proper solvent system or purified by preparative TLC (\(\text{CH}_2\text{Cl}_2\); \(R_f\) 0.9) prior to crystallization.

2,3,8,9-Tetramethoxy-5,6-dihydroindolo[2,1-\(a\)]isoquinoline (3a): dark green crystals; mp 193-195 °C (MeOH-Et\(_2\)O) (lit.\(^1\) mp 193-195 °C); IR (Nujol) 1609, 1575, 1556, 1508 cm\(^{-1}\); \(^1\)H NMR (270 MHz, CDCl\(_3\)) \(\delta\) 3.09, 4.63 (each t, \(J = 6.6\) Hz, each 2H), 3.92, 3.93, 3.95, 3.97 (each s, each 3H), 6.67, 6.75 (each s, each 1H), 6.81, 7.24 (AB type, \(J = 8.6\) Hz, each 1H), 7.18 (s, 1H); EI-MS \(m/z\) (rel. int.) 339 (M\(^+\), 100), 324 [(M - CH\(_3\))\(^+\), 68.7], 170 (23.5); FD-MS \(m/z\) (rel. int.) 340 [(M + H\(^+\), 24.1], 339 (M\(^+\), 100).

2,3-Dimethoxy-8,9-(methylenedioxy)-5,6-dihydroindolo[2,1-\(a\)]isoquinoline (3b);* dark green crystals; mp 195-198 °C (MeOH-Et\(_2\)O) (lit.\(^1\) 198-200 °C); \(^1\)H NMR (270 MHz, CDCl\(_3\)) \(\delta\) 3.11, 4.39 (each t, \(J = 6.6\) Hz, each 2H), 3.91, 3.95 (each s, each 3H), 6.00 (s, 2H), 6.68, 6.75 (each s, each 1H), 6.75, 7.07 (AB type, \(J = 8.3\) Hz, each 1H), 7.19 (s, 1H); EI-MS \(m/z\) (rel. int.) 323 (M\(^+\), 100), 308 [(M - CH\(_3\))\(^+\), 17.5].

* The word of "methylenedioxy" is conveniently used for "benzodioxolo" or "dioxolo" in this manuscript.
8,9-Dimethoxy-2,3-(methylenedioxy)-5,6-dihydroindolo[2,1-a]isoquinoline (3c): gray crystals; mp 180.5-182 °C (MeOH-Et₂O) (lit.¹ 177-180 °C); IR (Nujol) 1623, 1576, 1502 cm⁻¹;¹ ¹H NMR (270 MHz, CDCl₃) δ 3.06, 4.58 (each t, J = 6.3 Hz, each 2H), 3.93, 3.96 (each s, each 3H), 5.97 (s, 2H), 6.62, 6.71 (each s, each 1H), 6.81, 7.24 (AB type, J = 8.6 Hz, each 1H), 7.15 (s, 1H); EI-MS m/z (rel. int.) 323 (M⁺, 100), 308 [(M – CH₃)⁺, 93.0], 265 (35.2), 162 (20.5).

2,3:8,9-Bis(methylenedioxy)-5,6-dihydroindolo[2,1-a]isoquinoline (3d): gray crystals; mp 205-206 °C (EtOH) (lit.¹ mp 205-206 °C); IR (Nujol) 1598, 1562, 1544, 1502 cm⁻¹;¹ ¹H NMR (270 MHz, CDCl₃) δ 3.08, 4.37 (each t, J = 6.3 Hz, each 2H), 5.97, 5.99 (each s, each 2H), 6.64, 6.72 (each s, each 1H), 6.75, 7.06 (AB type, J = 8.3 Hz, each 1H), 7.16 (s, 1H); EI-MS m/z (rel. int.) 308 [(M + H)⁺, 3.2], 307 (M⁺, 100), 248 (24.0), 153 (24.6).

2,3,9,10-Tetramethoxy-5,6-dihydroindolo[2,1-a]isoquinoline (3e): deep green crystals, mp 207-208°C (MeOH-Et₂O) (lit.² mp 199 °C; ³ 201-203 °C; ⁴ 202-203 °C; ⁵ 202-204 °C; ⁶ 204-205 °C; ¹ 207-208 °C; ⁷ 8 209-210 °C): IR (Nujol) 1623, 1609, 1547, 1503 cm⁻¹;¹ ¹H NMR (270 MHz, CDCl₃) δ 3.12 (t, J = 6.6 Hz, 2H), 3.91, 2.93, 3.96 (each s, each 3H), 4.17 (t, J = 6.6 Hz, 2H), 6.64 (s, 1H), 6.75 (s, 1H), 6.80 (s, 1H), 7.07 (s, 1H), 7.17 (s, 1H).

2,3-Dimethoxy-9,10-(methylenedioxy)-5,6-dihydroindolo[2,1-a]isoquinoline (3f): dark green crystals; mp 241-242.5 °C (MeOH-Et₂O); IR (Nujol) 1610, 1549, 1502 cm⁻¹;¹ ¹H NMR (270 MHz, CDCl₃) δ 3.10 (t, J = 6.6 Hz, 2H), 4.12 (t, J = 6.6 Hz, 2H), 3.91, 3.95 (each s, each 3H), 5.93 (s, 2H), 6.63 (s, 1H), 6.74 (s, 1H), 6.78 (s, 1H), 6.99 (s, 1H), 7.15 (s, 1H). Anal. Calcd for C₁₉H₁₇NO₄: C, 70.57; H, 5.30; N, 4.33. Found: C, 70.45; H, 5.44; N, 4.37.

9,10-Dimethoxy-2,3-(methylenedioxy)-5,6-dihydroindolo[2,1-a]isoquinoline (3g): dark green crystals; mp 215.5-219.0 °C (MeOH-Et₂O); IR (Nujol) 1599, 1550, 1503 cm⁻¹;¹ ¹H NMR (270 MHz, CDCl₃) δ 3.09 (t, J = 6.3 Hz, 2H), 4.14 (t, J = 6.3 Hz, 2H), 3.93, 3.96 (each s, each 3H), 5.96 (s, 2H), 6.60 (s, 1H), 6.72 (s, 1H), 6.79 (s, 1H), 7.06 (s, 1H),
7.15 (s, 1H); EI-MS m/z (rel. int.) 324 [(M + 1)+, 24.09], 323 (M+, 100), 308 [(M - CH3)+, 64.7], 280 (16.0), 162 (27.4). Anal. Calcd for C10H17NO4: C, 70.57; H, 5.30; N, 4.33. Found: C, 70.66; H, 5.38; N, 4.38.

2,3,9,10-Bis(methyleneedioxy)-5,6-dihydroindolo[2,1-a]isoquinoline (3h): deep green crystals; mp 214.5-217.5 °C (MeOH-Et2O) (lit.1 mp 219.5-222.5 °C); IR (Nujol) 1619, 1541, 1499 cm⁻¹; ¹H NMR (270 MHz, CDCl3) δ 3.07 (t, J = 6.6 Hz, 2H), 4.09 (t, J = 6.6 Hz, 2H), 5.93, 5.96 (each s, each 2H), 6.59 (s, 1H), 6.71 (s, 1H), 6.77 (s, 1H), 6.98 (s, 1H), 7.12 (s, 1H); EI-MS m/z (rel. int.) 308 [(M + H)+, 24.91], 307 (M+, 100), 248 (17.91), 154 (23.60).

2,3-(Methylenedioxy)-5,6-dihydroindolo[2,1-a]isoquinoline (3j): pale green crystals; mp 189.5-193.5 °C (MeOH-CHCl3): IR (Nujol) 1620 cm⁻¹; ¹H NMR (270 MHz) δ 3.07 (t, J = 6.6 Hz, 2H), 4.18 (t, J = 6.6 Hz, 2H), 5.95 (s, 2H), 6.70 (s, 1H), 6.71 (s, 1H), 7.05-7.18 (m, 2H), 7.19 (s, 1H), 7.29 (d, J = 7.9 Hz, 1H), 7.59 (d, J = 7.6Hz, 1H); EI-MS m/z (rel. int.) 264 [(M + H)+, 22.8], 236 (23.7), 221 (10.5), 204 (8.4), 192 (12.0), 140 (14.3). Anal. Calcd for C17H13NO2: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.32; H, 5.18; N, 5.28.

2,3,9,10-Tetramethoxyindolo[2,1-a]isoquinoline (8): pale green crystals; mp 225.5-228 °C (MeOH, lit.8 mp 210 °C); IR (Nujol) 1620, 1534, 1504 cm⁻¹; ¹H NMR (270 MHz, CDCl3) δ 3.99, 4.00, 4.03, 4.06 (each s, each 3H), 6.64, 7.94 (AB type, J = 7.6 Hz, each 1H), 6.93 (s, 1H), 7.01 (s, 1H), 7.21 (s, 1H), 7.26 (s, 1H), 7.49 (s, 1H); EI-MS m/z (rel. int.) 338 [(M + H)+, 24.0], 337 (M+, 100), 322 [(M - CH3)+, 88.8]. Anal. Calcd for C20H19NO4: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.00; H, 5.81; N, 4.15.
2,3,9,10-Tetramethoxy-12-methyl-5,6-dihydroindolo[2,1-a]isoquinoline (10): white crystals; mp 224-226 °C (MeOH-CH₂Cl₂) (lit.⁹ mp 216-217 °C); IR (Nujol) 1609, 1546 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 2.59 (s, 3H), 3.08 (t, J = 6.3 Hz, 2H), 3.93 (s, 3H), 3.97 (s, 9H), 4.14 (t, J = 6.3 Hz, 2H), 6.78 (s, 1H), 6.80 (s, 1H), 7.02 (s, 1H), 7.35 (s, 1H); EI-MS m/z (rel. int.) 354 [(M + H)⁺, 24.2], 353 (M⁺, 100), 338 [(M - CH₃)⁺, 60.2].

2-Benzyloxy-3,9,10-trimethoxy-5,6-dihydroindolo[2,1-a]isoquinoline (16a): pale yellow crystals; mp 146.0-148.0 °C (MeOH); IR (Nujol) 1606, 1547, 1500 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 3.10 (t, J = 6.6 Hz, 2H), 3.91, 3.92, 3.95 (each s, each 3H), 4.14 (t, J = 6.6 Hz, 2H), 5.20 (s, 2H), 6.53 (s, 1H), 6.76 (s, 1H), 6.79 (s, 1H), 7.05 (s, 1H), 7.21 (s, 1H), 7.30-7.51 (m, 5H); EI-MS m/z (rel. int.) 416 [(M + H)⁺, 29.3], 415 (M⁺, 100), 400 [(M - CH₃)⁺, 15.4], 324 [(M - Bn)⁺, 10.0], 91 (PhCH₂⁺, 6.9). Anal. Calcd for C₂₆H₂₅NO₄: C, 75.16; H, 6.07; N, 3.37. Found: C, 75.43; H, 5.85; N, 3.11.

2-Benzyloxy-3-methoxy-9,10-(methylenedioxy)-5,6-dihydroindolo[2,1-a]isoquinoline (12b): pale gray crystals; mp 159.0-161.0 °C (MeOH); IR (Nujol) 1610, 1549, 1503 cm⁻¹; ¹H NMR (270MHz, CDCl₃) δ 3.82 (t, J = 6.6 Hz, 2H), 3.91 (s, 3H), 4.09 (t, J = 6.6 Hz, 2H), 5.19 (s, 2H), 5.92 (s, 2H), 6.51 (s, 1H), 6.75 (s, 1H), 6.76 (s, 1H), 6.96 (s, 1H), 7.19 (s, 1H), 7.31-7.51 (m, 5H); EI-MS m/z (rel. int.) 400 [(M + H)⁺, 30.6], 399 (M⁺, 100), 308 [(M - PhCH₂)⁺, 13.6], 91 (PhCH₂⁺, 34.2). Anal. Calcd for C₂₅H₂₁NO₄: C, 75.17; H, 5.30; N, 3.51. Found: C, 74.88; H, 5.51; N, 3.53.

References
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