Rearrangement of 3,3-Disubstituted Indolenines and Synthesis of 2,3-Substituted Indoles

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Supporting information

General Experimental

All solvents and reagents were obtained commercially and used as received. ¹H and ¹³C NMR spectra were recorded on a Varian instrument in the cited deuterated solvents. Chemical shifts are given in ppm, and coupling constants are in hertz. All final compounds were purified by flash chromatography using 220-400 mesh silica gel. Thin-layer chromatography was done on silica gel 60 F-254 (0.25-mm thickness) plates. Visualization was accomplished with UV light and/or 10% phosphomolybdic acid in ethanol. Mass spectra were recorded on either a Finnigan or a Hewlett-Packard spectrometer. LC-MS was run on an Agilent system with a Hewlett-Packard mass spectrometer.

General procedure for rearrangement of 3,3-disubstituted indolenines and synthesis of 2,3-substituted indoles: A mixture of phenylhydrazine **1** (1.68 mmol) and the aldehyde **2** (1.68 mmol) in AcOH (16.8 mL) was stirred at 60 °C for 30 min followed by addition of 4 M HCl in dioxane (0.42 mL, 1.68 mmol). The mixture was then stirred at 110 °C for 6 h, concentrated, and purified by chromatography with EtOAc/Hexane to provide the indole product.

5,6,7,8,9,10-Hexahydro-cyclohepta[b]indole (4a)

55% yield. ^1H NMR (400 MHz, CDCl_3) δ ppm 1.64 - 2.05 (m, 6 H) 2.59 - 3.02 (m, 4 H) 7.02 - 7.16 (m, 2 H) 7.22 - 7.33 (m, $J=4.4$, 4.4 Hz, 1 H) 7.45 - 7.53 (m, 1 H) 7.56 - 7.78 (m, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 24.6, 27.5, 28.7, 29.6, 31.8, 110.1, 113.8, 117.6, 119.0, 120.6, 129.3, 134.2, 137.4. HRMS Calcd for $(\text{M}-\text{H})^-$ $\text{C}_{12}\text{H}_{14}\text{FNO}^-$: 218.0981, Found: 218.0979. HRMS Calcd for $(\text{M}+\text{H})^+$: $\text{C}_{13}\text{H}_{16}\text{N}^+$: 186.1282, Found: 186.1277.

2,3,4,9-Tetrahydro-1H-carbazole (4b)

54% yield. ^1H NMR (400 MHz, CDCl_3) δ ppm 1.84 - 2.01 (m, 4 H) 2.60 - 2.82 (m, $J=4.3$ Hz, 4 H) 7.07 - 7.17 (m, 2 H) 7.29 (d, $J=7.9$ Hz, 1 H) 7.49 (d, $J=7.0$ Hz, 1 H) 7.56 - 7.75 (m, $J=7.6$ Hz, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 20.9, 23.2, 23.3, 110.1, 110.3, 117.7, 119.1, 121.0, 127.8, 134.0, 135.6. HRMS Calcd for $(\text{M}+\text{H})^+$: $\text{C}_{12}\text{H}_{14}\text{N}^+$: 172.1121, Found: 172.1120.

2,3-Dimethyl-1H-indole (4c)

50% yield. ^1H NMR (400 MHz, CDCl_3) δ ppm 2.24 (s, 3 H) 2.37 (s, 3 H) 7.04 - 7.19 (m, 2 H) 7.23 - 7.34 (m, 1 H) 7.49 (d, $J=7.3$ Hz, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 8.4, 11.5, 107.1, 110.0, 117.9, 119.0, 120.9, 129.4, 130.7, 135.2. HRMS Calcd for $(\text{M}+\text{H})^+$: $\text{C}_{10}\text{H}_{12}\text{N}^+$: 146.0964, Found: 146.0959.

2,3-Diphenyl-1H-indole (4d)

31% yield. ^1H NMR (400 MHz, CDCl_3) δ ppm 7.15 - 7.21 (m, 1 H) 7.23 - 7.51 (m, 12 H) 7.71 (d, 1 H) 8.19 - 8.30 (m, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 110.8, 110.9, 115.2, 119.7, 120.4, 122.7, 126.2, 127.7, 128.2,

128.5, 128.7, 130.2, 132.7, 134.1, 135.0, 135.9. HRMS Calcd for (M+H)⁺: C₂₀H₁₆N⁺: 270.1277, Found: 270.1274.

3-Methyl-2-phenyl-1H-indole (4e)

60% yield. ¹H NMR (400 MHz, CDCl₃) δ ppm 2.5 (s, 3 H) 7.1 - 7.2 (m, 1 H) 7.2 - 7.3 (m, 1 H) 7.3 - 7.4 (m, *J*=7.4, 7.4 Hz, 2 H) 7.5 (t, *J*=7.7 Hz, 2 H) 7.6 (s, 3 H) 8.0 (br. s., 1 H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 9.6, 108.7, 110.6, 119.0, 119.5, 122.3, 127.3, 127.7, 128.8, 130.0, 133.3, 134.0, 135.8. HRMS Calcd for (M+H)⁺: C₁₅H₁₄N⁺: 208.1126, Found: 208.1127.

3-Methyl-1H-indole-2-carboxylic acid ethyl ester (4f)

56% yield (with 25% being hydrolyzed acid). ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 1.4 (t, *J*=7.2 Hz, 3 H) 2.6 (s, 3 H) 4.4 (q, *J*=7.1 Hz, 2 H) 7.2 (t, *J*=7.5 Hz, 1 H) 7.3 (t, *J*=7.6 Hz, 1 H) 7.4 (d, *J*=8.2 Hz, 1 H) 7.7 (d, *J*=7.9 Hz, 1 H) 8.7 (br. s., 1 H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 10.0, 14.5, 60.7, 111.8, 120.1 (2C), 120.9, 123.5, 125.6, 128.6, 135.8, 162.7. HRMS Calcd for (M-H)⁻: C₁₂H₁₂NO₂⁻: 202.0868, Found: 202.0874.

NMR spectra follow below

(4a), ^1H NMR

(4a), ^{13}C NMR

CHLOROFORM-d

(4b), ^1H NMR

(4b), ^{13}C NMR

(4c), ^{13}C NMR

(4d), ^1H NMR

(4d), ^{13}C NMR

CHLOROFORM- d

(4e), ^1H NMR

06-2720-PNH

(4e), ^{13}C NMR

06-2839-PNC

06-2656-PNH

06-2838-PNC

L31699-5-5 Kevin Liu
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Run Date: June 12, 2008 15:35:02
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L37263-5-6A Kevin Liu
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 5866 v5a3 1D_NOE difference
 Run Date: June 09, 2006 07:59:41