Dearomative Indole (3 + 2) Cycloaddition Reactions

Hui Li, Russell P. Hughes*, and Jimmy Wu*

Department of Chemistry, Dartmouth College, Hanover
New Hampshire 03755, United States

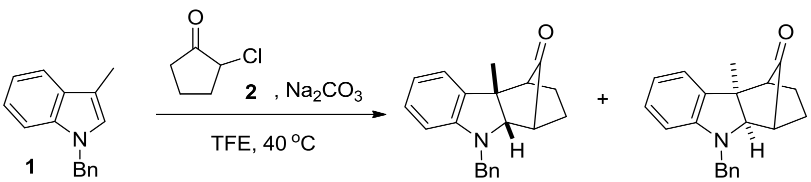
I. General Information

^{1}H NMR spectra were recorded on a Varian Unity Plus 300 (300 MHz) or 500 (500 MHz) FT spectrometer at ambient temperature. Chemical shift values (δ) are expressed in ppm downfield relative to internal standard (tetramethylsilane at 0 ppm). Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and brs (broad singlet). Coupling constants are reported in hertz (Hz). ^{13}C NMR spectra were recorded on a Varian Unity Plus 500 (125 MHz) FT spectrometer at ambient temperature, and are expressed in ppm using solvent as the internal standard ($CDCl_3$ at 77.0 ppm, CD_2Cl_2 at 54.0 ppm, CD_3OD at 48.0 ppm). IR spectra were recorded on a Jasco FT-IR 4100 Series spectrophotometer, ν_{max} (cm^{-1}) are partially reported. Analytical thin layer chromatography (TLC) was performed on SILICYCLE pre-coated TLC plates (silica gel 60 F-254, 0.25 mm). Flash column chromatography was performed on silica gel 60 (SILICYCLE 230-400 mesh). Visualization was accomplished with UV light and/or with ceric ammonium molybdate (CAM) or $KMnO_4$ staining solutions. High resolution mass spectra were acquired from the Mass Spectrometry Laboratory of the University of Illinois (Urbana-Champaign, IL).

All reactions were carried out in oven-dried glassware with magnetic stirring unless otherwise noted. All solvents were freshly distilled. All other reagents and starting materials, unless otherwise noted, were purchased from commercial vendors and used without further purification.

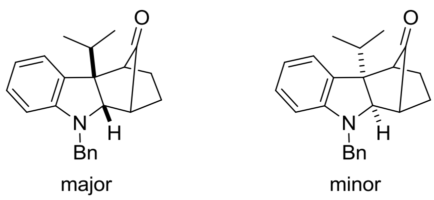
II. Experimental Procedures and Analytical Data

General procedure for the (3 + 2) cycloaddition of indoles

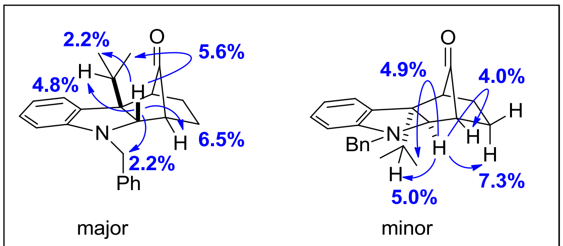


1 **3** (major) **3** (minor)

To a TFE (0.18 mL) solution of **1** (40 mg, 0.18 mmol) and **2** (30 mg, 0.252 mmol) was added Na_2CO_3 (28 mg, 0.27 mmol). The reaction mixture was stirred at 40 °C until the reaction was judged complete as determined by thin layer chromatographic analysis. The mixture was filtered through a short pad of Celite. The filtrate was concentrated *in vacuo* and the residue was purified *via* silica gel column chromatography (3% ethyl acetate/hexane) to afford 44 mg of major diastereomer and 7 mg of minor diastereomer as colorless solids, with a combined yield of 93%. For the ***major diastereomer***, **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.24-7.32 (m, 5H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 7 Hz, 1H), 6.66 (t, *J* = 7.5, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 4.44 (d, J = 15.5 Hz, 1H), 4.22 (d, J = 15.5 Hz, 1H), 3.67 (d, J = 5.0 Hz, 1H), 2.02 (t, J = 4.5 Hz, 1H), 1.96 (d, J = 4.5 Hz, 1H), 1.80 (m, 1H), 1.65 (m, 1H), 1.55 (m, 1H), 1.35 (m, 1H), 1.32 (s, 3H); **^{13}C-NMR** ($CDCl_3$, 500 MHz) δ 214.1, 153.4, 137.9, 131.8, 128.9, 128.8, 128.0, 127.6, 124.8, 117.4, 105.9, 69.6, 51.1, 49.9, 48.2, 44.8, 28.3, 20.1, 16.3; **IR** (film, cm^{-1}), 2951, 1766, 1603, 1488, 1452, 740, 699. **HRMS (ESI) calcd. for** $C_{21}H_{22}NO$ (*m/z* M+H$^+$): 304.1701, found: 304.1694. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.31-7.34 (m, 2H), 7.24-7.27 (m, 3H), 6.98 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 7.5 Hz, 1H), 6.61 (t, J = 7.5, 1H), 6.25 (d, J = 8.0 Hz, 1H), 4.48 (d, J = 16.5 Hz, 1H), 4.31 (d, J = 16.5 Hz, 1H), 3.37 (s, 1H), 2.10 (d, J = 5.5 Hz, 1H), 2.07 (d, J = 4.0 Hz, 1H), 1.95 (m, 1H), 1.88 (m, 1H), 1.81 (m, 1H), 1.47 (s, 3H), 1.43 (m, 1H); **^{13}C-NMR** ($CDCl_3$, 500 MHz) δ 213.9, 150.49, 138.5, 134.5, 128.9, 128.8, 127.4, 127.3, 123.5, 117.6, 105.9, 74.5, 50.2, 49.9, 47.8, 45.3, 24.0, 19.9, 18.5. **IR** (film, cm^{-1}), 2867, 2359, 1768, 1633, 1485, 735, 446. **HRMS (ESI) calcd. for** $C_{21}H_{22}NO$ (*m/z* M+H$^+$): 304.1701, found: 304.1694.



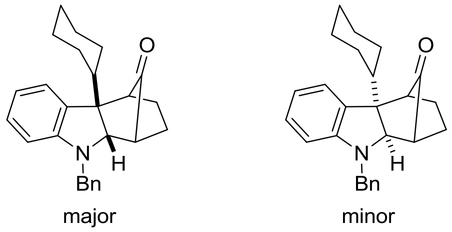
Entry 1, Table 2



observed nOe

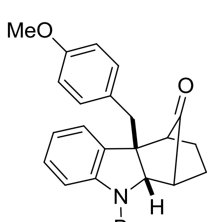
By following the general procedure described above, a mixture of *N*-benzyl-3-isopropylindole (200 mg, 0.80 mmol), **2** (133 mg, 1.12 mmol) and Na_2CO_3 (127 mg, 1.20 mmol) in TFE (0.80 mL) afforded 212 mg of major diastereomer as a colorless solid, and 19 mg of minor diastereomer as a colorless oil, with a combined yield of 87%. For the ***major diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.28-7.35 (m, 5H), 7.10 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 7 Hz, 1H), 6.62 (t, J = 7.0, 1H), 6.48 (d, J = 7.5 Hz, 1H), 4.87 (d, J = 15.5 Hz, 1H), 4.18 (d, J = 15.5 Hz, 1H), 3.84 (d, J = 4.5 Hz, 1H), 2.25 (d, J = 4.0 Hz, 1H), 2.04 (t, J = 4.5 Hz, 1H), 1.72-1.75 (m, 1H), 1.56-1.67 (m, 3H), 1.37-1.41 (m, 1H), 0.90 (d, J = 6.5 Hz, 3H), 0.75 (d, J = 7.0 Hz, 3H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.8, 154.4, 138.4, 129.2, 128.7, 128.5, 128.0, 127.5, 126.0, 116.6, 105.1, 65.4, 56.1, 50.7, 47.2, 44.7, 36.6, 20.7, 18.1, 17.2, 16.0; **IR** (film, cm^{-1}), 2961, 2359, 1768, 1600, 1488, 1461, 1358, 738. **HRMS (ESI) calcd.** for $C_{23}H_{26}NO$ (*m/z* M+H$^+$): 332.2014, found: 332.2015. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.26-7.36 (m, 5H), 6.99-7.03

(m, 2H), 6.58 (t, J = 7.5 Hz, 1H), 6.25 (d, J = 8.0, 1H), 4.44 (d, J = 16 Hz, 1H), 4.29 (d, J = 15.5 Hz, 1H), 3.39 (s, 1H), 2.23 (d, J = 4.0 Hz, 1H), 2.08 (d, J = 5.5 Hz, 1H), 1.96-2.06 (m, 2H), 1.39-1.44 (m, 2H), 1.08 (d, J = 6.5 Hz, 3H), 0.72 (d, J = 6.5 Hz, 3H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.0, 152.1, 138.7, 130.1, 128.9, 128.7, 127.6, 127.3, 125.4, 116.7, 105.5, 73.4, 55.3, 50.0, 48.4, 44.7, 33.7, 20.6, 17.7, 17.6, 16.7. **IR** (film, cm^{-1}), 2944, 1768, 1711, 1489, 744. **HRMS (ESI) calcd.** for $C_{23}H_{26}NO$ (*m/z* M+H$^+$): 332.2014, found: 332.2018.



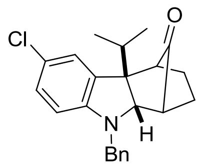
Entry 2, Table 2

By following the general procedure described above, a mixture of *N*-benzyl-3-cyclohexylindole (200 mg, 0.69 mmol), **2** (115 mg, 0.97 mmol) and Na_2CO_3 (109 mg, 1.04 mmol) in TFE (0.70 mL) afforded 203 mg of major diastereomer and 11.3 mg of minor diastereomer as colorless oils, with a combined yield of 84%. For the ***major diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.11-7.36 (m, 5H), 7.09 (t, J = 7.5 Hz, 1H), 6.91 (d, J = 7 Hz, 1H), 6.63 (t, J = 7.5, 1H), 6.46 (d, J = 7.5 Hz, 1H), 4.45 (d, J = 15.5 Hz, 1H), 4.21 (d, J = 15.5 Hz, 1H), 3.90 (d, J = 4.5 Hz, 1H), 2.27 (d, J = 4.0 Hz, 1H), 2.02 (t, J = 4.5 Hz, 1H), 1.70-1.76 (m, 3H), 1.53-1.68 (m, 5H), 1.36-1.41 (m, 2H), 1.14-1.20 (m, 3H), 1.03-1.08 (m, 1H), 0.60-0.68 (m, 1H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 214.0, 154.4, 138.5, 129.9, 128.7, 128.5, 128.0, 127.5, 125.9, 116.6, 105.2, 65.6, 56.1, 50.9, 47.2, 46.7, 44.7, 28.2, 27.6, 26.9, 26.8, 26.7, 20.7, 16.0; **IR** (film, cm^{-1}), 2929, 1767, 1644, 1453, 115, 471. **HRMS (ESI) calcd.** for $C_{26}H_{30}NO$ (*m/z* M+H$^+$): 372.2327, found: 372.2320. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.27-7.36 (m, 5H), 6.98-7.01 (m, 2H), 6.58 (t, J = 7.5 Hz, 1H), 6.23 (d, J = 8.0 Hz, 1H), 4.42 (d, J = 15.5 Hz, 1H), 4.29 (d, J = 15.5 Hz, 1H), 3.42 (d, J = 4.5 Hz, 1H), 2.22 (d, J = 5.0 Hz, 1H), 2.06 (d, J = 4.5 Hz, 1H), 1.63-1.99 (m, 9H), 1.41-1.49 (m, 2H), 1.04-1.11 (m, 1H), 0.55-0.61 (m, 1H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.2, 152.0, 138.7, 131.0, 128.7, 128.6, 127.6, 127.3, 125.5, 116.7, 105.6, 73.4, 55.0, 50.2, 47.8, 44.6, 44.5, 28.2, 27.2, 26.8, 26.7, 26.6, 20.6, 17.5. **HRMS (ESI) calcd.** for $C_{26}H_{30}NO$ (*m/z* M+H$^+$): 372.2327, found: 372.2320.



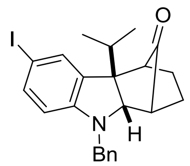
Entry 3, Table 2

By following the general procedure described above, a mixture of *N*-benzyl-3-(*p*-methoxybenzyl)indole (200 mg, 0.61 mmol), **2** (100 mg, 0.85 mmol) and Na_2CO_3 (97 mg, 0.92 mmol) in TFE (0.60 mL) afforded 168 mg of title compound as a yellow oil, with a yield of 67%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.13-7.20 (m, 2H), 7.05 (t, J = 8.0 Hz, 2H), 7.01 (t, J = 8.0 Hz, 1H), 6.67-6.74 (m, 8H), 6.22 (d, J = 8.0 Hz, 1H), 4.15 (d, J = 16.0 Hz, 1H), 3.98 (d, J = 16.0 Hz, 1H), 3.93 (d, J = 4.5 Hz, 1H), 3.78 (s, 3H), 3.15 (d, J = 13.5 Hz, 1H), 2.60 (d, J = 14.0 Hz, 1H), 2.13 (d, J = 4.0 Hz, 1H), 2.07 (t, J = 4.5 Hz, 1H), 1.63-1.75 (m, 3H), 1.41-1.46 (m, 1H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.2, 158.6, 154.3, 137.8, 131.8, 129.6, 128.7, 128.5, 127.2, 127.0, 125.6, 116.7, 113.5, 105.2, 65.1, 55.3, 53.0, 49.8, 49.7, 44.7, 44.4, 20.2, 16.3. **IR** (film, cm^{-1}), 2915, 1765, 1643, 1515, 1237, 738. **HRMS (ESI) calcd.** for $C_{28}H_{28}NO_2$ (*m/z* $M+H^+$): 410.2120, found: 410.2124.



Entry 4, Table 2

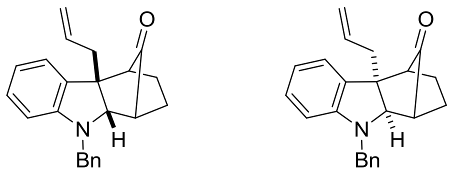
By following the general procedure described above, a mixture of *N*-benzyl-3-isopropyl-5-chloroindole (75 mg, 0.26 mmol), **2** (44 mg, 0.37 mmol) and Na_2CO_3 (42 mg, 0.40 mmol) in TFE (0.26 mL) afforded 85.3 mg of title compound as a colorless oil, with a yield of 91%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.30-7.37 (m, 5H), 7.07 (dd, J = 8.5 Hz, 2.5 Hz, 1H), 6.89 (d, J = 3.0 Hz, 1H), 6.40 (d, J = 8.5 Hz, 1H), 4.46 (d, J = 15.5 Hz, 1H), 4.17 (d, J = 15.5 Hz, 1H), 3.89 (d, J = 3.5 Hz, 1H), 2.25 (d, J = 4.5 Hz, 1H), 2.08 (t, J = 4.5 Hz, 1H), 1.60 (m, 4H), 1.42-1.46 (m, 1H), 0.91 (d, J = 7.0 Hz, 3H), 0.78 (d, J = 7.0 Hz, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.05, 153.02, 137.85, 131.53, 128.82, 128.31, 128.00, 127.69, 125.89, 120.79, 105.86, 65.65, 56.19, 50.73, 47.17, 44.52, 36.55, 20.74, 18.00, 17.15, 15.94. **IR** (film, cm^{-1}), 2962, 1769, 1598, 1488, 1357, 1268, 701. **HRMS (ESI) calcd.** for $C_{23}H_{25}NOCl$ (*m/z* $M+H^+$): 366.1625, found: 366.1629.



Entry 5, Table 2

By following the general procedure described above, a mixture of *N*-benzyl-3-isopropyl-5-iodoindole (100 mg, 0.27 mmol), **2** (44 mg, 0.37 mmol) and Na_2CO_3 (42 mg, 0.40 mmol) in TFE (0.27 mL) afforded 108 mg of title compound as a colorless oil, with a yield of 92%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.30-7.38 (m, 6H), 7.16 (d, J = 1.5 Hz, 1H), 6.29 (d, J = 8.5 Hz, 1H), 4.46 (d, J = 15.5 Hz, 1H), 4.14

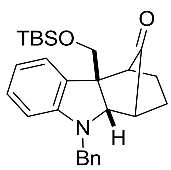
(d, *J* = 15.5 Hz, 1H), 3.86 (d, *J* = 4.5 Hz, 1H), 2.23 (d, *J* = 4.5 Hz, 1H), 2.06-2.08 (m, 1H), 1.59-1.75 (m, 5H), 1.40-1.45 (m, 1H), 0.88 (d, *J* = 6.5 Hz, 3H), 0.76 (d, *J* = 7.0 Hz, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.02, 153.95, 137.68, 137.23, 134.24, 132.63, 128.82, 127.98, 127.70, 107.36, 76.14, 65.32, 56.05, 50.39, 47.21, 44.41, 36.57, 20.76, 17.98, 17.11, 15.90. **IR** (film, cm^{-1}), 2968, 1768, 1592, 1484, 1266, 735, 360. **HRMS (ESI) calcd. for** $C_{23}H_{25}NOI$ (*m/z* M+H$^+$): 458.0981, found: 458.0992.



major minor

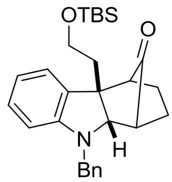
Entry 6, Table 2

By following the general procedure described above, a mixture of *N*-benzyl-3-allylindole (100 mg, 0.40 mmol), **2** (67 mg, 0.56 mmol) and Na_2CO_3 (64 mg, 0.60 mmol) in TFE (0.40 mL) afforded 101.8 mg of major diastereomer and 9.2 mg of minor diastereomer as colorless oils, with a combined yield of 83%. For the ***major diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.30-7.34 (m, 5H), 7.09-7.13 (m, 1H), 6.94-6.97 (m, 1H), 6.66-6.69 (m, 1H), 6.48-6.5 (m, 1H), 5.44-5.48 (m, 1H), 4.9-5.03 (m, 2H), 4.44 (d, *J* = 15.5 Hz, 1H), 4.20 (d, *J* = 15.5 Hz, 1H), 3.86 (s, 1H), 2.53-2.56 (m, 1H), 2.19-2.22 (m, 1H), 2.18 (s, 1H), 1.60-1.80 (m, 3H), 1.38-1.43 (m, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.3, 154.22, 138.16, 133.92, 129.61, 128.74, 128.66, 128.09, 127.48, 125.19, 118.68, 117.08, 105.60, 66.18, 51.81, 50.79, 49.21, 44.74, 44.49, 20.04, 16.40. **IR** (film, cm^{-1}), 2979, 1767, 1603, 1490, 920, 740, 700. **HRMS (ESI) calcd.** for $C_{23}H_{24}NO$ (*m/z* M+H$^+$): 330.1858, found: 330.1859. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.28-7.35 (m, 5H), 6.98-7.01 (m, 2H), 6.94-6.97 (m, 1H), 6.60 (d, *J* = 7.5 Hz, 1H), 6.24 (d, *J* = 8.0 Hz, 1H), 5.50-5.63 (m, 1H), 5.05-5.12 (m, 2H), 4.44 (d, *J* = 16.0 Hz, 1H), 4.30 (d, *J* = 16.5 Hz, 1H), 3.50 (s, 1H), 2.51-2.64 (m, 2H), 2.02-2.12 (m, 2H), 1.78-1.94 (m, 2H), 1.44-1.49 (m, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 212.81, 151.36, 138.56, 133.86, 132.30, 128.85, 128.67, 127.48, 127.29, 124.36, 118.40, 117.07, 105.56, 72.23, 51.17, 49.99, 49.42, 44.77, 40.97, 20.11, 18.10. **HRMS (ESI) calcd.** for $C_{23}H_{24}NO$ (*m/z* M+H$^+$): 330.1858, found: 330.1861.



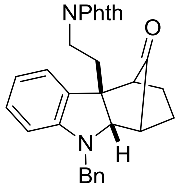
Entry 7, Table 2

By following the general procedure described above, a mixture of *N*-benzyl-3-(*t*-butyldimethylsilyl)oxymethylindole (100 mg, 0.29 mmol), **2** (47 mg, 0.56 mmol) and Na_2CO_3 (45 mg, 0.43 mmol) in TFE (0.29 mL) afforded 101.1 mg of title compound as colorless oil, with a yield of 82%. ^{1}**H-NMR** (500 MHz, CD_2Cl_2): δ 7.27-7.35 (m, 5H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.0 Hz, 1H), 6.63 (t, *J* = 7.5 Hz, 1H), 6.51 (d, *J* = 8.0 Hz, 1H), 4.45 (d, *J* = 15.5 Hz, 1H), 4.26 (d, *J* = 16.0 Hz, 1H), 3.98 (s,1H), 3.60-3.66 (q, *J* = 17.5 Hz, 10 Hz, 6.5 Hz, 1H), 2.14 (d, *J* = 4.5 Hz, 1H), 1.99 (t, *J* = 4.5 Hz, 1H), 1.77-1.81 (m, 1H), 1.63-1.76 (m, 1H), 1.56-1.59 (m, 1H), 1.37-1.42 (m, 1H), 0.86 (s, 9H), 0.02 (s, 9H), -0.03 (s, 9H). ^{13}**C-NMR** (CD_2Cl_2, 500 MHz) δ 212.64, 154.33, 138.36, 128.95, 128.78, 128.73, 127.98, 127.44, 125.69, 116.89, 105.79, 68.89, 64.94, 54.54, 51.08, 45.92, 44.54, 52.79, 19.84, 18.39, 16.28, -5.60, -5.78. **IR** (film, cm^{-1}), 2959, 2947, 1772, 1492, 838, 739. **HRMS (ESI) calcd.** for $C_{27}H_{36}NO_2Si$ (*m/z* $M+H^+$): 434.2515, found: 434.2506.



Entry 8, Table 2

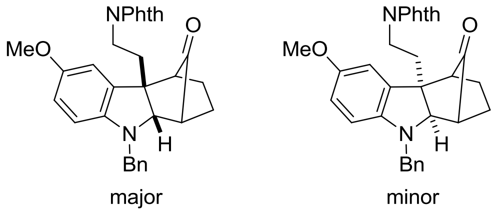
By following the general procedure described above, a mixture of *N*-benzyl-3-(*t*-butyldimethylsilyl)oxyethylindole (3.77 g, 10.36 mmol), **2** (1.6 g, 13.47 mmol) and Na_2CO_3 (1.54 g, 14.50 mmol) in TFE (10.4 mL) afforded 3.42 g of title compound as a colorless oil, with a yield of 74%. ^{1}**H-NMR** (500 MHz, CD_2Cl_2): δ 7.75-7.77 (m, 2H), 7.69-7.71 (m, 2H), 7.27-7.35 (m, 5H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 7.0 Hz, 1H), 6.65 (t, *J* = 7.5 Hz, 1H), 6.52 (d, *J* = 8.0 Hz, 1H), 4.48 (d, *J* = 15.0 Hz, 1H), 4.17 (d, *J* = 15.5 Hz, 1H), 3.94 (s, 1H), 3.48-3.53 (m, 1H), 3.36-3.41 (m, 1H), 1.76-2.05 (m, 3H), 1.58-1.74 (m, 4H), 1.34-1.39 (m, 1H), 0.85 (s, 9 H), -0.02 (s, 6H). ^{13}**C-NMR** (CD_2Cl_2, 500 MHz) δ 213.20, 153.78, 138.19, 129.26, 128.78, 128.73, 128.00, 127.56, 125.21, 117.06, 105.54, 66.79, 59.55, 50.67, 50.48, 49.60, 44.32, 43.00, 25.88, 19.87, 18.27, 16.39, -5.44. **IR** (film, cm^{-1}), 2954, 170, 1603, 1489, 1098, 837,739. **HRMS (ESI) calcd.** for $C_{28}H_{38}NO_2Si$ (*m/z* $M+H^+$): 448.2672, found: 448.2683.



Entry 9, Table 2

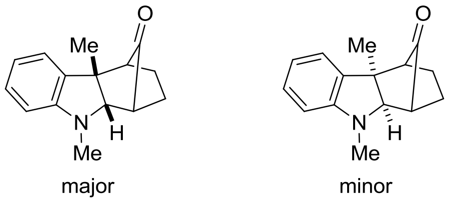
By following the general procedure described above, a mixture of 2-(2-(1-benzyl-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (100 mg, 0.263 mmol), **2** (44 mg, 0.37 mmol) and Na_2CO_3 (42 mg, 0.40 mmol) in TFE (0.26 mL) afforded 98.4 mg of title compound as yellow solid, with a yield of 87%. ^{1}**H-NMR** (500 MHz,

CD_2Cl_2): δ 7.75-7.77 (m, 2H), 7.69-7.71 (m, 2H), 7.27-7.38 (m, 3H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.60 (t, *J* = 7.5 Hz, 1H), 6.53 (d, *J* = 7.5 Hz, 1H), 4.48 (d, *J* = 15.5 Hz, 1H), 4.30 (d, *J* = 15.5 Hz, 1H), 4.04 (s, 1H), 3.36-3.48 (m, 2H), 2.21-2.28 (m, 1H), 2.03 (m, 1H), 1.97 (m, 1H), 1.54-1.79 (m, 5 H), 1.33-1.38 (m, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.04, 168.99, 154.04, 138.17, 133.96, 132.34, 128.94, 128.79, 128.33, 128.09, 127.60, 125.05, 123.06, 117.45, 106.08, 66.45, 51.42, 50.85, 49.76, 44.61, 37.57, 33.70, 19.65, 16.54. **IR** (film, cm^{-1}), 2952, 1771, 1492, 1399, 725, 369. **HRMS (ESI) calcd.** for $C_{30}H_{27}N_2O_3$ (*m/z* M+H$^+$): 463.2022, found: 463.2025.

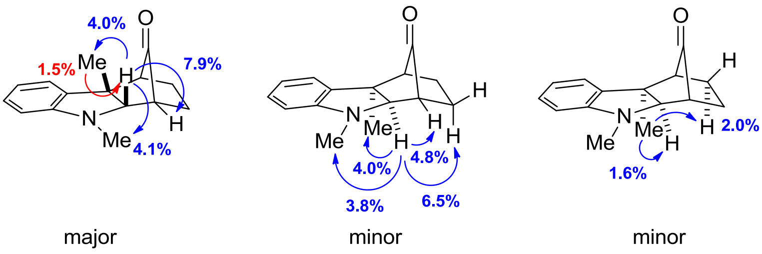


Entry 10, Table 2

By following the general procedure described above, a mixture of 2-(2-(1-benzyl-5-methoxy-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (200 mg, 0.49 mmol), **2** (81 mg, 0.68 mmol) and Na_2CO_3 (77 mg, 0.73 mmol) in TFE (0.50 mL) afforded 178 mg of major diastereomer and 27 mg of minor diastereomer as yellow solids, with a combined yield of 83%. For the ***major diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.69-7.77 (m, 4H), 7.27-7.40 (m, 5H), 6.52-6.56 (m, 2H), 6.66-6.69 (m, 1H), 6.43 (d, *J* = 8.5 Hz, 1H), 4.36 (s, 2H), 3.99 (d, *J* = 4.5 Hz, 1H), 3.66 (s, 3H), 3.47-3.51 (m, 2H), 2.28-2.34 (m, 1H), 1.84-1.94 (m, 3H), 1.53-1.68 (m, 3H), 1.33-1.38 (m, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.33. 167.99, 152.77, 148.63, 138.68, 133.93, 132.30, 129.57, 128.72, 128.50, 127.52, 123.00, 113.55, 111.71, 107.16, 67.2, 55.86, 53.25, 5.40, 49.76, 45.10, 37.13, 33.67, 19.49, 16.67. **IR** (film, cm^{-1}), 2950, 1769, 1711, 1590, 1493, 1218, 1048, 723. **HRMS (ESI) calcd.** for $C_{31}H_{29}N_2O$ (*m/z* M+H$^+$): 493.2127, found: 493.2127. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.71-7.81 (m, 4H), 7.25-7.35 (m, 5H), 6.69 (s, 1H), 6.54 (d, *J* = 8.5 Hz, 1H), 6.18 (d, *J* = 8.5 Hz, 1H), 4.42 (d, *J* = 15.5 Hz, 1H), 4.32 (d, *J* = 15.5 Hz, 1H), 3.71 (s, 3H), 3.61-3.66 (m, 2H), 3.50-3.56 (m, 1H), 2.22-2.28 (m, 1H), 1.97-2.10 (m, 4H), 1.44-1.50 (m, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 212.57, 168.13, 152.86, 145.59, 138.87, 134.08, 132.46, 132.36, 128.75, 127.63, 127.30, 123.13, 113.55, 111.43, 106.79, 73.23, 55.94, 51.66, 50.64, 49.58, 44.99, 34.15, 33.97, 20.01, 18.00. **HRMS (ESI) calcd.** for $C_{31}H_{29}N_2O$ (*m/z* M+H$^+$): 493.2127, found: 493.2127.

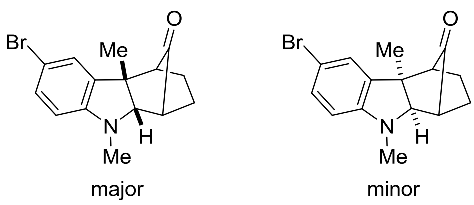


Entry 11, Table 2



observed nOe

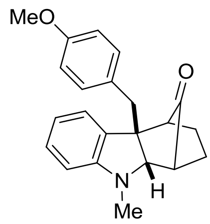
By following the general procedure described above, a mixture of *N*-methyl-3-cyclohexylindole (60 mg, 0.41 mmol), **2** (69 mg, 0.58 mmol) and Na_2CO_3 (66 mg, 0.62 mmol) in TFE (0.40 mL) afforded 71 mg of major diastereomer as a slightly yellow oil, and 14 mg of minor diastereomer as a colorless solid, with a combined yield of 91%. For the ***major diastereomer***, **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 7.10 (t, *J* = 7.8 Hz, 1H), 6.88 (d, *J*=7.2 Hz, 1H), 6.60 (t, *J* = 7.2 Hz, 1H), 6.36 (d, *J* = 7.8 Hz, 1H), 3.62 (d, *J* = 4.5 Hz, 1H), 2.77 (s, 3H), 2.29 (t, *J* = 4.5 Hz, 1H), 1.94 (d, *J* = 4.0 Hz, 1H), 1.60-1.77 (m, 3H), 1.34 (s, 3H), 1.31 (m, 1H); **^{13}C-NMR** ($CDCl_3$, 300 MHz) δ 214.1, 153.6, 131.6, 128.7, 124.5, 116.7, 104.9, 71.4, 49.9, 48.0, 44.4, 33.0, 27.9, 19.9, 16.2; **IR** (film, cm^{-1}), 2950, 2867, 1767, 1605, 1494, 1224, 1016, 741. **HRMS (ESI) calcd.** for $C_{15}H_{18}NO$ (*m/z* $M+H^+$): 228.1388, found: 228.1384. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.03 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.0 Hz, 1H), 6.58 (t, *J* = 7.5 Hz, 1H), 6.26 (d, *J* = 8.0 Hz, 1H), 3.29 (s, 1H), 2.81 (s, 3H), 2.21 (d, *J* = 4.0 Hz, 1H), 2.03 (d, *J* = 4.0 Hz, 1H), 1.93-1.99 (m, 2H), 1.79-1.84(m, 1H), 1.49-1.56 (m, 1H), 1.47 (s, 3H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.8, 150.9, 134.6, 128.9, 123.3, 117.3, 105.5, 76.1, 49.9, 47.6, 44.5, 32.7, 23.7, 20.0, 18.4. **IR** (film, cm^{-1}), 2918, 2874, 1769, 1604, 1494, 1019, 738. **HRMS (ESI) calcd.** for $C_{15}H_{18}NO$ (*m/z* $M+H^+$): 228.1393, found: 228.1384



Entry 12, Table 2

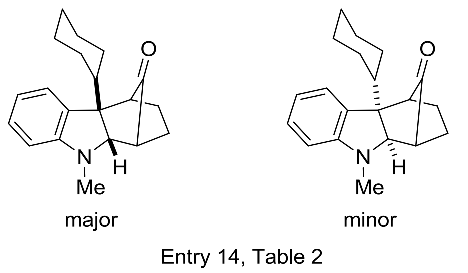
By following the general procedure described above, a mixture of *N*-methyl-3-methyl-5-bromoindole (60 mg, 0.27 mmol), **2** (45 mg, 0.37 mmol) and

Na_2CO_3 (43 mg, 0.40 mmol) in TFE (0.25 mL) afforded 59 mg of major diastereomer and 13 mg of minor diastereomer as colorless oils, with a combined yield of 88%. For the ***major diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.17 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.96 (d, *J* = 2.0 Hz, 1H), 6.24 (d, *J* = 8.0 Hz, 1H), 3.66 (d, , *J* = 4.5 Hz, 1H), 2.75 (s, 3H), 2.27 (t, *J* = 4.0 Hz, 1H), 1.91 (d, *J* = 4.5 Hz, 1H), 1.64-1.72 (m, 4H), 1.32 (s, 3H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 212.6, 152.8, 134.3, 131.1, 127.3, 107.3, 106.0, 71.6, 49.7, 47.8, 44.2, 32.6, 27.6, 19,9, 16.0; **IR** (film, cm^{-1}), 2880, 1769, 1645, 1490, 740, 445. **HRMS (ESI) calcd. for** $C_{15}H_{17}NOBr$ (*m/z* $M+H^+$): 306.0494, found: 306.0496. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.10 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.97 (d, *J* = 2.0 Hz, 1H), 6.13 (d, *J* = 8.5 Hz, 1H), 3.33 (s, 1H), 2.79 (s, 3H), 2.17 (d, *J* = 5.0 Hz, 1H), 1.95-2.00 (m, 3H), 1.81 (m, 1H), 1.46 (s, 3H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 212.9, 150.2, 137.4, 131.2, 126.3, 107.7, 106.4, 76.0, 49.9, 47.4, 44.5, 32.3, 23.5, 19.8, 18.3. **IR** (film, cm^{-1}), 2982, 1772, 1602, 1491, 739, 418. **HRMS (ESI) calcd.** for $C_{15}H_{17}NOBr$ (*m/z* $M+H^+$): 306.0494, found: 306.0495.



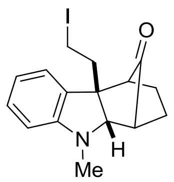
Entry 13, Table 2

By following the general procedure described above, a mixture of *N*-methyl-3-(*p*-methoxybenzyl)indole (180 mg, 0.72 mmol), **2** (120 mg, 1.02 mmol) and Na_2CO_3 (114 mg, 1.08 mmol) in TFE (0.7 mL) afforded 170 mg of title compound as a colorless solid, with a yield of 71%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.09 (t, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 8.5 Hz, 3H), 6.69 (d, *J* = 8.5 Hz, 2H), 6.61 (t, *J* = 7.0 Hz, 1H), 6.27 (d, *J* = 7.0 Hz, 1H), 3.76 (s, 3H), 3,68 (d, *J* = 4.0 Hz, 1H), 3.10 (d, *J* = 14.0 Hz, 1H), 2.67 (d, *J* = 14.0 Hz, 1H), 2.52 (s, 3H), 2.24 (t, *J* = 4.5 Hz, 1H), 2.18 (d, *J* = 4.0 Hz, 1H), 1.60-1.73 (m, 3H), 1.34-1.42 (m, 1H); **^{13}C-NMR** ($CDCl_3$, 500 MHz): δ 214.4, 158.4, 154.8, 131.8, 129.7, 128.9, 128.8, 125.9, 16.6, 113.4, 105.6, 67.9, 55.4, 53.1, 48.7, 45.3, 44.5, 33.4, 20,1, 16.1. **IR** (film, cm^{-1}), 2925, 1766, 1608, 1511, 1247. **HRMS (ESI) calcd.** for $C_{22}H_{24}NO_2$ (*m/z* $M+H^+$): 334.1807, found: 334.1812.



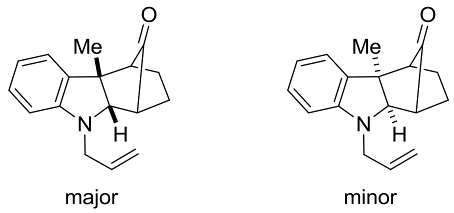
Entry 14, Table 2

By following the general procedure described above, a mixture of *N*-methyl-3-cyclohexylindole (90 mg, 0.42 mmol), **2** (70 mg, 0.59 mmol) and Na_2CO_3 (67 mg, 0.63 mmol) in TFE (0.42 mL) afforded 96 mg of major diastereomer as a colorless oil, and 6 mg of minor diastereomer as a colorless solid, with a combined yield of 82%. For the ***major diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.09 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.5 Hz, 1H), 6.57 (t, *J* = 7.5 Hz, 1H), 6.31 (d, *J* = 8.0 Hz, 1H), 3.84 (d, *J* = 4.5 Hz, 1H), 2.78 (s, 3H), 2.29 (d, *J* = 4.0 Hz, 1H), 2.23 (d, *J* = 4.5 Hz, 1H), 1.52-1.79 (m, 8H),1.34-1.42 (m, 2H), 1.14-1.19 (m, 3H), 1.02-1.05 (m, 1H), 0.64-0.67 (m, 1H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 214.9, 154.5, 129.7, 128.6, 125.7, 116.1, 104.5, 67.1, 56.1, 47.0, 46.6, 44.5, 32.5, 28.0, 27.6, 26.8, 26.7, 26.6, 20.6, 15.8; **IR** (film, cm^{-1}), 2959, 1715, 1491, 1247, 737. **HRMS (ESI) calcd.** for $C_{20}H_{26}NO$ (*m/z* $M+H^+$): 296.2014, found: 29.2021. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.03 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.56 (t, *J* = 7.5 Hz, 1H), 6.23 (d, *J* = 8.0 Hz, 1H), 3.34 (s, 1H), 2.78 (s, 3H), 2.25 (d, *J* = 4.0 Hz, 1H), 2.19 (d, *J* = 5.0 Hz, 1H), 1.92-1.97 (m, 2H), 1.78-1.83 (m, 2H), 1.63-1.70 (m, 5H), 1.48-1.56 (m, 3H), 1.42-1.45 (m, 2H), 1.05-1.08 (m, 1H), 0.60-0.62 (m, 1H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.4, 142.7, 130.9, 129.0, 125.3, 116.9, 110.0,105.6, 75.0, 5.1, 47.7, 44.6, 43.6, 32.3, 29.9, 28.2, 27.1, 26.9, 26.7, 26.6, 20.9, 17.5. **IR** (film, cm^{-1}), 2925, 1608, 1511, 1247, 740. **HRMS (ESI) calcd.** for $C_{20}H_{26}NO$ (*m/z* $M+H^+$): 296.2014, found: 29.2021.



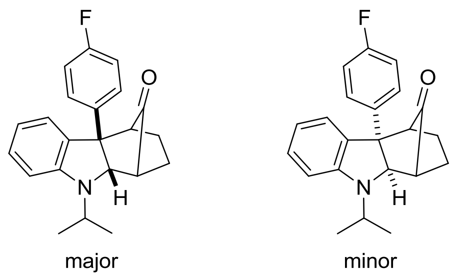
Entry 15, Table 2

By following the general procedure described above, a mixture of *N*-benzyl-3-(2-iodoethyl)indole (100 mg, 0.42 mmol), **2** (70 mg, 0.59 mmol) and Na_2CO_3 (67 mg, 0.63 mmol) in TFE (0.7 mL) afforded 121 mg of title compound as a colorless solid, with a yield of 90%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.12 (t, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 7.5 Hz, 1H), 6.61 (t, *J* = 7.5 Hz, 1H), 6.37 (d, *J* = 7.5 Hz, 1H), 3.79 (d, *J* = 4.5 Hz, 1H), 3.04-3.09 (m, 1H), 2.78 (s, 3H), 2.67-2.73 (m, 1H), 2.33-2.39 (m, 1H), 2.28 (s, 1H), 2.08-2.15 (m, 1H), 1.98 (s, 1H), 1.63-1.68 (m, 3H), 1.33-1.35 (m, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 212.80, 154.41, 129.17, 127.47, 124.74, 116.73, 104.97, 67.66, 49.13, 44.86, 44.16, 32.39, 19.90, 16.14, -1.43. **IR** (film, cm^{-1}), 2944, 1769, 1607, 1497, 1118, 454. **HRMS (ESI) calcd.** for $C_{16}H_{19}NOI$ (*m/z* $M+H^+$): 368.0511, found: 368.0519.



Entry 16, Table 2

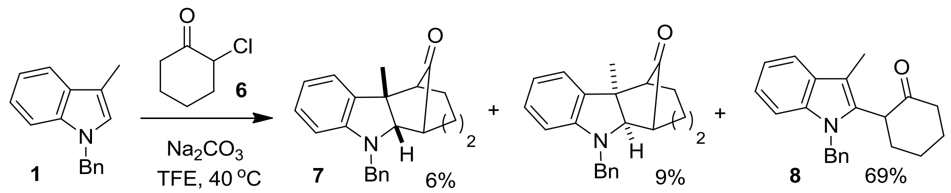
By following the general procedure described above, a mixture of *N*-allylskatole (100 mg, 0.58 mmol), **2** (97 mg, 0.82 mmol) and Na_2CO_3 (92 mg, 0.87 mmol) in TFE (0.58 mL) afforded 104 mg of major diastereomer and 13 mg of minor diastereomer as colorless oils, with a combined yield of 79%. For the ***major diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.09 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.63 (t, *J* = 7.5 Hz, 1H), 6.46 (d, *J* = 7.0 Hz, 1H), 5.80-5.87 (m, 1H), 5.26 (s, 1H), 5.20 (t, *J* = 11.5 Hz, 1H), 3.84-3.88 (dd, *J* = 16.0 Hz, 6.0 Hz, 1H), 3.73 (s, 1H), 3.65-3.69 (dd, *J* = 16.0 Hz, 6.0 Hz, 1H), 2.24 (t, *J* = 4.5 Hz, 1H), 2.24 (d, *J* = 4.5 Hz, 1H), 1.82-1.87 (m, 1H), 1.62-1.71 (m, 2H), 1.34 (s, 3H), 1.28-1.32 (m, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.45, 153.09, 133.81, 132.02, 128.52, 124.59, 117.28, 117.10, 105.99, 69.62, 49.77, 49.76, 48.10, 44.92, 28.03, 20.08, 16.33. **IR** (film, cm^{-1}), 2952, 1768, 1603, 1488, 1328, 1106, 923, 740. **HRMS (ESI) calcd.** for $C_{17}H_{20}NO$ (*m/z* $M+H^+$): 254.1545, found: 254.1545. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.01 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.59 (t, *J* = 7.5 Hz, 1H), 6.28 (d, *J* = 8.0 Hz, 1H), 5.80-5.87 (m, 1H), 5.24 (s, 1H), 5.19 (t, *J* = 10 Hz, 1H), 3.85-3.89 (dd, *J* = 16.5 Hz, 5.0 Hz, 1H), 3.71-3.76 (dd, *J* = 17.0 Hz, 5.5 Hz, 1H), 3.39 (s, 1H), 2.12 (d, *J* = 5.0 Hz, 1H), 1.90-2.03 (m, 3H), 1.78-1.84 (m, 1H), 1.50-1.56 (m, 1H), 1.46 (s, 3H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 213.69, 150.24, 135.06, 134.07, 128.59, 123.41, 117.19, 116.58, 105.88, 74.33, 49.93, 49.01, 47.62, 45.83, 23.84, 19.79, 18.50. **IR** (film, cm^{-1}), 2875, 1771, 1603, 1489, 738, 460. **HRMS (ESI) calcd.** for $C_{17}H_{20}NO$ (*m/z* $M+H^+$): 254.1545, found: 254.1552.



Entry 17, Table 2

By following the general procedure described above, a mixture of 3-(4-fluorophenyl)-1-isopropyl-1*H*-indole (100 mg, 0.39 mmol), **2** (65 mg, 0.55 mmol) and Na_2CO_3 (62 mg, 0.59 mmol) in TFE (0.39 mL) was stirred at 40 °C for 26 hours. Another 34 mg of **2** (0.28 mmol) was added and reaction was stirred for extra 17 hours to afford 58 mg of major diastereomer and 39 mg of minor diastereomer as colorless oils, with a combined yield of 73%. For the ***major diastereomer***, **^{1}H-NMR**

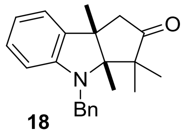
(500 MHz, CD_2Cl_2): δ 7.13-7.17 (m, 3H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.58-6.63 (m, 3H), 3.98-4.04 (m, 2H), 2.73 (d, *J* = 4.5 Hz, 1H), 2.18 (t, *J* = 4.5 Hz, 1H), 2.06-2.12 (m, 1H), 1.80-1.86 (m, 1H), 1.63-1.68 (m, 1H), 1.45-1.50 (m, 1H), 1.11-1.17 (dd, *J* = 19.0 Hz, 7.0 Hz, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 214.11, 162.46, 160.52, 153.52, 143.96, 143.94, 132.71, 128.93, 128.89, 128.40, 128.33, 126.25, 11.62, 11.7, 115.20, 107.59, 67.64, 67.63, 56.00, 46.95, 46.94, 45.85, 21.16, 20.48, 17.93, 15.98. **IR** (film, cm^{-1}), 2974, 1767, 1643, 1509, 1484, 1233, 738, 441. **HRMS (ESI) calcd.** for $C_{22}H_{23}NOF$ (*m/z* $M+H^+$): 336.1764, found: 336.1768. For the ***minor diastereomer***, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ7.32-7.35 (m, 2H), 7.07-7.10 (m, 2H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.76 (d, *J* = 7.5 Hz, 1H), 6.47 (t, *J* = 8.0 Hz, 1H), 6.38 (d, *J* = 8.0 Hz, 1H), 4.26 (s, 1H), 4.26 (m, 1H), 2.62-2.63 (d, *J* = 4.0 Hz, 1H), 2.19-2.20 (d, *J* = 4.5 Hz, 1H), 1.86-1.92 (m, 2H), 1.75-1.80 (m, 1H), 1.44-1.49 (m, 1H), 1.36 (d, *J* = 7.0 Hz, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 212.22, 162.67, 160.72, 148.81, 140.60, 140.57, 137.27, 128.91, 127.90, 12.83, 124.47, 117.05, 11.87, 115.70, 107.05, 70.07, 56.78, 48.35, 48.10, 46.92, 21.35, 20.20, 19.89, 19.20. **IR** (film, cm^{-1}), 2982, 1776, 1597, 1508, 826, 746. **HRMS (ESI) calcd.** for $C_{22}H_{23}NOF$ (*m/z* $M+H^+$): 336.1764, found: 336.1768.



By following the general procedure described above, a mixture of *N*-benzylskatole (100 mg, 0.45 mmol), **6** (84 mg, 0.63 mmol) and Na_2CO_3 (72 mg, 0.68 mmol) in TFE (0.45 mL) afforded 10.1 mg of compound **7** and 12.8 mg of its diastereomer as colorless oils, 98.7 mg of compound **8** as a colorless solid, with a yield of 6% and 9%, 69% respectively. For compound **7**, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.27-7.35 (m, 5H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.72 (t, *J* = 7.5 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 4.77-4.80 (d, *J* = 16.5 Hz, 1H), 4.50-4.53 (d, *J* = 16.0 Hz, 1H), 3.93 (s, 1H), 2.51-2.54 (m, 2H), 2.13-2.14 (m, 1H), 1.91-1.96 (m, 2H), 1.60-1.64 (m, 1H), 1.24-1.28 (m, 2H), 1.23 (s, 3H).

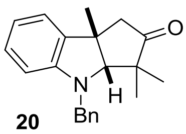
For the diastereomer of compound **7**, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.26-7.35 (m, 5H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 6.0 Hz, 1H), 6.68 (t, *J* = 7.5 Hz, 1H), 6.56 (d, *J* = 7.5 Hz, 1H), 4.52-4.55 (d, *J* = 16.0 Hz, 1H), 4.37-4.40 (d, *J* = 16.0 Hz, 1H), 3.77 (d, *J* = 6.5 Hz, 1H), 2.38-2.39 (m, 1H), 2.37 (s, 1H), 1.84-2.05 (m, 4H), 1.42-1.53 (m, 1H), 1.26 (s, 3H), 1.08-1.13 (m, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 219.86, 153.48, 138.46, 132.42, 128.74, 128.34, 128.07, 127.45, 125.05, 117.30, 106.83, 71.49, 56.52, 51.96, 51.14, 48.53, 34.32, 33.28, 31.91, 17.07. **IR** (film, cm^{-1}), 2944, 1747, 1643, 1490, 744. **HRMS (ESI) calcd. for** $C_{22}H_{24}NO$ (*m/z* $M+H^+$): 318.1858, found: 318.1855.

For compound **8**, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.56 (d, *J* = 8.0 Hz, 1H), 7.22-7.30 (m, 3H), 7.08-7.14 (m, 3H), 6.98 (d, *J* = 6.5 Hz, 2H), 5.26 (s, 2H), 3.85 (t, *J* = 8.0 Hz, 1H), 2.53-2.57 (m, 1H), 2.38-2.46 (m, 1H), 2.25 (s, 3H), 2.12-2.16 (m, 1H), 2.03-2.07 (m, 2H), 1.90-1.94 (m, 1H), 1.67-1.82 (m, 2H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 207.68, 138.56, 136.69, 134.03, 128.98, 128.84, 127.39, 126.20, 121.45, 119.11, 118.42, 109.58, 108.84, 49.19, 47.60, 42.34, 33.65, 26.93, 25.86, 9.78. **IR** (film, cm^{-1}), 2943, 2101, 1709, 1644, 1467, 739. **HRMS (ESI) calcd. for** $C_{22}H_{24}NO$ (*m/z* $M+H^+$): 318.1858, found: 318.1854.

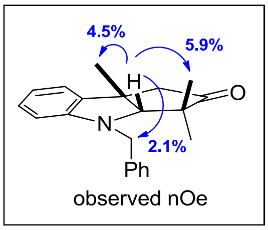


18

By following the general procedure described above, a mixture of *N*-benzyl-2,3-dimethylindole (80 mg, 0.34 mmol), 3-bromo-3-methylbutan-2-one **12** (112 mg, 0.68 mmol) and Na_2CO_3 (54 mg, 0.51 mmol) in TFE (0.40 mL) was stirred at 50 ^oC to afford 87.9 mg of title compound **18** as colorless solid, with a yield of 81%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.23-7.35 (m, 5H), 7.08 (d, *J* = 7.5 Hz, 1H), 6.92 (t, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.01 (d, *J* = 7.5 Hz, 1H), 4.47 (d, *J* = 17 Hz, 1H), 4.24 (d, *J* = 16.5 Hz, 1H), 2.79 (d, *J* = 19.5 Hz, 1H), 2.57 (d, *J* = 19 Hz, 1H), 1.52 (s, 3H), 1.30 (s, 3H), 1.13 (s, 3H), 0.95 (s, 3H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 219.24, 150.52, 139.43, 137.66, 128.74, 127.99, 126.89, 126.48, 121.57, 118.12, 107.12, 80.34, 55.00, 49.99, 49.05, 48.74, 24.78, 22.62, 22.29, 15.01. **IR** (film, cm^{-1}), 2969, 1737, 1604, 1487, 742, 480. **HRMS (ESI) calcd.** for $C_{22}H_{26}NO$ (m/z $M+H^+$): 320.2014, found: 320.2018.

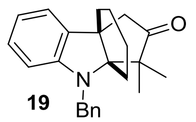


20



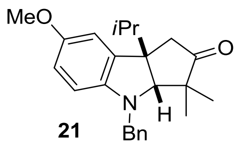
To a TFE (0.36 mL) solution of *N*-benzylskatole (80 mg, 0.36 mmol) and 3-bromo-3-methylbutan-2-one **12** (84 mg, 0.51 mmol) was added Na_2CO_3 (57 mg, 0.54 mmol). The reaction mixture was stirred at 40 ^oC for 67 hours. 36 mg of 3-bromo-3-methylbutan-2-one **12** was added and reaction was stirred at 50 ^oC for another 23 hours until the reaction was judged complete as determined by thin layer chromatographic analysis. The mixture was filtered through a short pad of Celite. The filtrate was concentrated *in vacuo* and the residue was purified *via* silica gel column chromatography (3% ethyl acetate/hexane) to afford 84.3 mg of title compound **20** as a colorless oil, with a yield of 76%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.27-7.35 (m, 5H), 7.00-7.06 (m, 2H), 6.65-6.58 (t, *J* = 7.5 Hz, 1H), 6.34 (d, *J* = 8.0 Hz, 1H), 4.62

(d, *J* = 16.5 Hz, 1H), 4.33 (d, *J* = 16.5 Hz, 1H), 4.39 (s, 1H), 2.80 (d, *J* = 18.5 Hz, 1H), 2.58 (d, *J* = 18.5 Hz, 1H), 1.47 (s, 1H), 1.16 (s, 1H), 1.00 (s, 1H). ^{13}**C-NMR** (CD_2Cl_2, 500 MHz) δ 220.33, 150.88, 138.62, 137.35, 128.79, 128.71, 128.33, 127.53, 127.27, 122.66, 117.90, 106.98, 82.43, 52.70, 51.36, 48.98, 45.88, 29.70, 25.84, 21.02. **IR** (film, cm^{-1}), 2968, 1720, 1644, 1497, 731. **HRMS (ESI) calcd.** for $C_{21}H_{24}NO$ (*m/z* $M+H^+$): 306.1858, found: 306.1853.



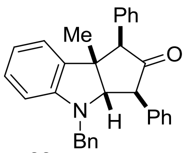
19

To a TFE (0.20 mL) solution of 9-benzyl-2,3,4,9-tetrahydro-1*H*-carbazole **10** (60 mg, 0.22 mmol) and 3-bromo-3-methylbutan-2-one **12** (50 mg, 0.31 mmol) was added Na_2CO_3 (36 mg, 0.33 mmol). The reaction mixture was stirred at 50 ^oC for 75 hours. The mixture was filtered through a short pad of Celite. The filtrate was concentrated *in vacuo* and the residue was purified *via* silica gel column chromatography (3% ethyl acetate/hexane) to recover 11.6 mg of starting material and to afford 61.3 mg of title compound **19** as a colorless oil, with a yield of 77% and a b.r.s.m. yield of 95%. ^{1}**H-NMR** (500 MHz, CD_2Cl_2): δ 7.26-7.37 (m, 5H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.12 (d, *J* = 8.0 Hz, 1H), 4.44 (d, *J* = 5.0 Hz, 1H), 2.94 (d, *J* = 19.5 Hz, 1H), 2.55 (d, *J* = 18 Hz, 1H), 1.98-2.02 (m, 1H), 1.86-1.90 (m, 1H), 1.72-1.77 (m, 1H), 1.33-1.56 (m, 5H), 1.15 (s, 3H), 0.75 (s, 3H). ^{13}**C-NMR** (CD_2Cl_2, 500 MHz) δ 219.04, 151.0, 139.47, 138.57, 128.68, 127.91, 126.91, 126.77, 120.52, 117.94, 106.75, 77.67, 56.89, 48.88, 47.92, 45.21, 37.17, 28.25, 23.80, 21.63, 21.06, 20.62. **IR** (film, cm^{-1}), 2933, 1736, 1605, 1482, 1354, 737. **HRMS (ESI) calcd**. for $C_{24}H_{28}NO$ (*m/z* $M+H^+$): 346.2171, found: 346.2171.

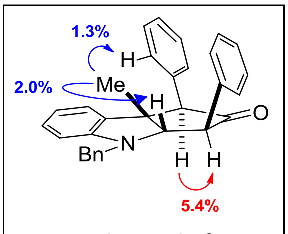


21

To a TFE (0.30 mL) solution of *N*-benzyl-3-isopropyl-5-methoxyindole **11** (85 mg, 0.22 mmol) and 3-bromo-3-methylbutan-2-one **12** (70 mg, 0.43 mmol) was added Na_2CO_3 (48 mg, 0.45 mmol). The reaction mixture was stirred at 75 ^oC for 45 hours. The mixture was filtered through a short pad of Celite. The filtrate was concentrated *in vacuo* and the residue was purified *via* silica gel column chromatography (3% ethyl acetate/hexane) to afford 79.3 mg of title compound **21** as a colorless oil, with a yield of 72%. ^{1}**H-NMR** (500 MHz, CD_2Cl_2): δ 7.29-7.38 (m, 5H), 6.62-6.65 (m, 2H), 6.33 (d, *J* = 5.5 Hz, 1H), 4.46-4.49 (d, *J* = 15.5 Hz, 1H), 4.34-4.37 (d, *J* = 15.5 Hz, 1H), 3.71-3.72 (m, 4H), 2.77-2.81 (d, *J* = 18.5 Hz, 1H), 2.61-2.64 (d, *J* = 18.0 Hz, 1H), 1.83-1.86 (m, 1H), 1.03 (s, 3H), 0.87 (s, 3H), 0.78-0.80 (dd, *J* = 6.5 Hz, 2.5 Hz, 1H). ^{13}**C-NMR** (CD_2Cl_2, 500 MHz) δ 220.14, 152.62, 146.13, 139.03, 136.13, 128.61, 128.43, 127.41, 112.85, 111.85, 106.72, 77.50, 56.07, 53.59, 51.46, 45.73, 37.43, 24.64, 21.51, 18.13, 17.56. **IR** (film, cm^{-1}), 2968, 2359, 1737, 1644, 1494, 1219. **HRMS (ESI) calcd.** for $C_{24}H_{30}NO_2$ (*m/z* $M+H^+$): 364.2277, found: 364.2271.

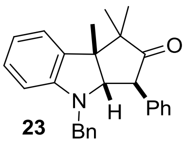


22

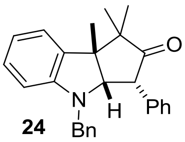


observed nOe

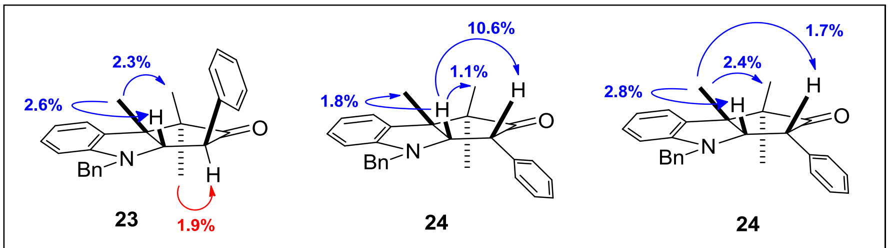
By following the general procedure described above, a mixture of *N*-benzylskatole (70 mg, 0.34 mmol), 1-chloro-1,3-diphenylpropan-2-one **13** (109 mg, 0.45 mmol)[1] and Na_2CO_3 (51 mg, 0.48 mmol) in TFE (0.30 mL) afforded 64 mg of title compound **22** as colorless oil, with a yield of 47%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.24-7.41 (m, 11H), δ 7.07-7.16 (m, 5H), 6.70-6.77 (m, 2H), 6.55 (d, *J* = 8.5 Hz, 1H), 4.39-4.50 (q, *J* = 36 Hz, 20.5 Hz, 16 Hz, 1H), 4.18 (d, *J* = 3.0 Hz, 1H), 4.16 (s, 1H), 4.05 (dd, *J* = 3.5 Hz, 1.0 Hz, 1H), 1.22 (s, 3H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 212.92, 150.59, 138.24, 137.87, 135.64, 134.16, 131.15, 129.04, 128.94, 128.76, 128.48, 128.17, 127.81, 127.49, 127.45, 127.35, 123.49, 118.27, 107.96, 79.47, 63.87, 59.44, 51.99, 51.16, 22.01. **IR** (film, cm^{-1}), 2923, 1746, 1642, 1446, 1160, 744. **HRMS (ESI) calcd.** for $C_{31}H_{28}NO$ (*m/z* $M+H^+$): 430.2171, found: 430.2162.



23



24



observed nOe

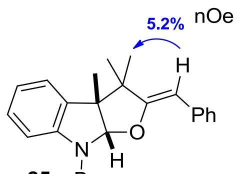
By following the general procedure described above, a mixture of *N*-benzylskatole (80 mg, 0.36 mmol), 3-chloro-3-methyl-1-phenylbutan-2-one **17** (99 mg, 0.51 mmol) and Na_2CO_3 (57 mg, 0.54 mmol) in TFE (0.36 mL) was stirred at 40 ^{o}C. After 28 hours, 35 mg of 3-chloro-3-methyl-1-phenylbutan-2-one **17** (0.19 mmol) and 26.7 mg (0.25 mmol) of Na_2CO_3 was added. Reaction was stirred for another 21 hours to afford 101.9 mg of compound **23** and 4.3 mg of compound **24** as colorless solids, with a combined yield of 74%. When starting with α-haloketone **14**, a mixture of

[1] Grein, F.; Chen, A. C.; Edwards, D.; Crudden, C. M. *J. Org. Chem.* **2006**, *71*, 861.

N-benzylskatole (80 mg, 0.36 mmol), **14** (173.5 mg, 0.72 mmol) and Na_2CO_3 (83.7 mg, 0.79 mmol) in TFE (0.36 mL) was stirred at 40 °C for 9 days to give 67.1 mg of compound **23** and 1.9 mg of compound **24**, with a combined yield of 50%. When starting with α-haloketone **15**, a mixture of *N*-benzylskatole (80 mg, 0.36 mmol), **15** (141.6 mg, 0.72 mmol) and Na_2CO_3 (83.7 mg, 0.79 mmol) in TFE (0.36 mL) was stirred at 40 °C for 9 days to give 61.1 mg of compound **23** and 2.5 mg of compound **24**, with a combined yield of 46%. When starting with α-haloketone **16**, a mixture of *N*-benzylskatole (80 mg, 0.36 mmol), **16** (173.5 mg, 0.72 mmol) and Na_2CO_3 (83.7 mg, 0.79 mmol) in TFE (0.36 mL) was stirred at 40 °C for 49 hours to give 93.7 mg of compound **23** and 4.2 mg of compound **24**, with a combined yield of 71%.

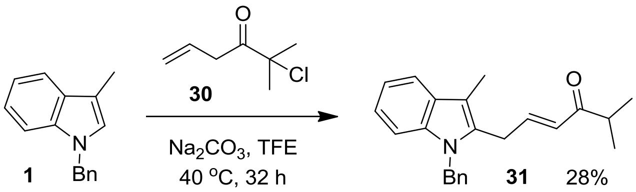
For compound **23**, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.25-7.34 (m, 6H), 7.10-7.16 (m, 4H), 6.96-6.98 (m, 2H), 6.77 (dt, *J* = 7.5 Hz, 1.0 Hz, 1H), 6.52 (dd, *J* = 8.0 Hz, 1.0 Hz, 1H), 4.34 (d, *J* = 3.5 Hz, 1H), 4.02 (d, *J* = 4.5 Hz, 1H), 3.93 (d, *J* = 4.0 Hz, 1H), 1.41 (s, 3H), 1.17 (s, 3H), 1.07 (s, 3H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 219.20, 152.51, 138.91, 138.50, 133.05, 129.11, 128.83, 128.68, 128.44, 127.80, 127.36, 127.14, 58.64, 52.82, 52.54, 24.67, 24.45, 18.97. **IR** (film, cm^{-1}), 2967, 1742, 1603, 1484, 1453, 741, 698. **HRMS (ESI) calcd.** For $C_{27}H_{28}NO$ (m/z $M+H^+$): 382.2171, found: 382.2169.

For compound **24**, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.01-7.21 (m, 9H), 7.02 (t, *J* = 7.5 Hz, 1H), 4.34 (d, *J* = 3.5 Hz, 1H), 4.02 (d, *J* = 4.5 Hz, 1H), 3.93 (d, *J* = 4.0 Hz, 1H), 1.48 (s, 3H), 1.22 (s, 3H), 1.03 (s, 3H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 220.51, 153.04, 138.28, 135.83, 134.51, 130.91, 128.50, 128.23, 128.22, 127.52, 127.44, 126.80 123.94, 118.63, 109.12, 76.46, 57.49, 52.90, 51.07, 23.23, 22.77, 22.29. **IR** (film, cm^{-1}), 2926, 1721, 1453, 740, 693. **HRMS (ESI) calcd.** for $C_{27}H_{28}NO$ (*m/z* $M+H^+$): 382.2171, found: 382.2179.

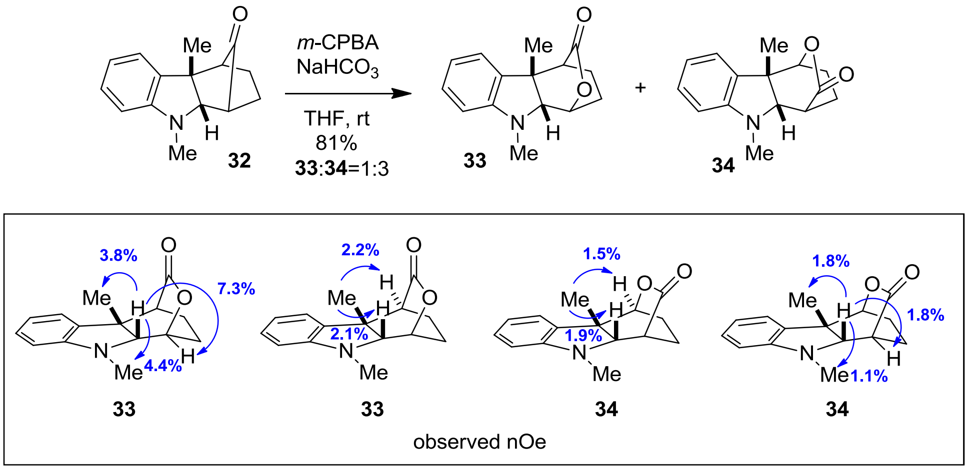


25

A mixture of *N*-benzylskatole (50 mg, 0.22 mmol), 3-bromo-3-methyl-1-phenylbutan -2-one **16** (108 mg, 0.45 mmol) and Na_2CO_3 (47 mg, 0.45 mmol) in TFE (0.22 mL) was stirred at 40 °C for 8.5 hours. Solvent was then removed *in vacuo* and the residue was subject to column chromatography (2% EtOAc/pentane) to give 25.3 mg of compound **25** as a colorless oil, with a yield of 29%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.46-7.48 (m, 4H), 7.30-7.39 (m, 3H), 7.24 (t, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 7.0 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1 Hz, 1H), 6.45 (d, *J* = 8.0 Hz, 1H), 5.52 (s, 1H), 4.99 (s, 1H), 4.65 (d, *J* = 4.5 Hz, 2H), 1.45 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 165.74, 148.65, 138.05, 137.0, 133.51, 128.81, 128.32, 128.27, 128.04, 127.59, 127.49, 125.73, 124.74, 118.62, 107.75, 104.07, 94.27, 55.99, 49.4, 48.32, 28.19, 22.45, 18.57. **IR** (film, cm^{-1}), 2964, 1665, 1605, 1485, 911, 695. **HRMS (ESI) calcd.** for $C_{27}H_{28}NO$ (*m/z* M+H$^+$): 382.2171, found: 382.2172.

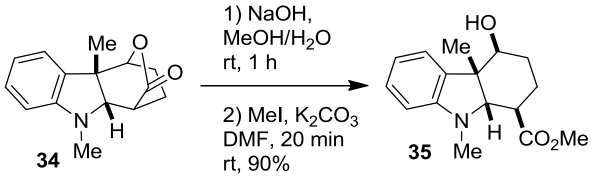


By following the general procedure described above, a mixture of *N*-benzylskatole (80 mg, 0.36 mmol), 2-chloro-2-methylhex-5-en-3-one **30** (74 mg, 0.50 mmol) and Na_2CO_3 (57 mg, 0.54 mmol) in TFE (0.36 mL) was stirred for 32 hours to afford 33.4 mg of compound **31** as colorless oil, with a yield of 28%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.57 (dd, *J* = 7.0 Hz, 1.5 Hz, 1H), 7.09-7.15 (m, 1H), 6.30 (dd, *J* = 7.0 Hz, 1.5 Hz, 1H), 6.79 (td, *J* = 16 Hz, 6 Hz, 1H), 5.97 (td, *J* = 15.5 Hz, 2.0 Hz, 1H), 5.30 (s, 1H), 3.64 (dd, *J* = 6.0 Hz, 1.5 Hz, 1H), 2.65 (sep, 1H), 2.30 (s, 1H), 0.99 (d, *J* = 7.0 Hz, 6H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 203.38, 142.41, 138.48, 136.97, 132.08, 129.40, 128.88, 128.74, 127.44, 126.13, 121.59, 119.23, 118.59, 109.39, 109.09, 46.80, 38.49, 27.72, 19.29, 8.73. **IR** (film, cm^{-1}), 2967, 1635, 1465, 1352, 1176, 732. **HRMS (ESI) calcd.** for $C_{23}H_{26}NO$ (*m/z* M+H$^+$): 332.2014, found: 332.2012.

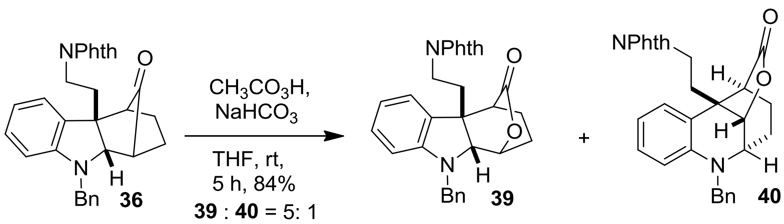


To a mixture of compound **32** (20 mg, 0.09 mmol) and $NaHCO_3$ (22 mg, 0.27 mmol) in THF (0.4 mL) at room temperature was added portionwise *m*-cpba (50-55%, cont. ca 10% *m*-cba, balance water; 76 mg, 0.22 mmol). The reaction was stirred for 30 min. Reaction was quenched with 1 mL of 15% Na_2SO_3 and was stirred for another 10 min. 5 mL of ethyl acetate was then added. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue underwent silica gel column chromatography (8 % ethyl acetate/pentane) to afford 4.4 mg of lactone **33** and 13.1mg of lactone **34**, with a combined yield of 81%. For lactone **33**, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.13 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 5.0 Hz, 1H), 6.67 (t, *J* =

7.5 Hz, 1H), 6.41 (d, *J* = 10 Hz, 1H), 4.75-4.77 (m, 1H), 3.57 (d, *J* = 4.5 Hz, 1H), 2.86 (s, 3H), 2.65 (t, *J* = 3.5 Hz, 1H), 1.73-1.77 (m, 2H), 1.61-1.70 (m, 1H), 1.51-1.58 (m, 1H), 1.37 (s, 3H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 175.29, 151.96, 131.22, 129.07, 123.37, 117.47, 106.09, 76.19, 71.91, 47.06, 45.17, 33.46, 29.58, 20.05, 19.44. **IR** (film, cm^{-1}) 2362, 2337, 1644, 776. **HRMS (ESI) calcd.** for $C_{15}H_{18}NO_2$ (m/z M+H$^+$): 244.1338, found: 244.1340. For lactone **34**, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.12 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.61 (t, *J* = 7.5 Hz, 1H), 6.41 (d, *J* = 8.0 Hz, 1H), 4.56 (d, *J* = 4.5 Hz, 1H), 3.58 (d, *J* = 4.0 Hz, 1H), 2.92 (m, 1H), 2.83 (s, 3H), 1.88-1.95 (m, 1H), 1.72-1.78 (m, 1H), 1.56-1.61 (m, 1H), 1.43-1.49 (m, 1H), 1.41 (s, 3H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 174.51, 151.93, 131.72, 129.03, 123.23, 116.89, 105.52, 82.36, 71.31, 48.80, 39.40, 32.28, 26.81, 22.67, 15.84. **IR** (film, cm^{-1}) 2870, 1640, 1494, 736. **HRMS (ESI) calcd.** for $C_{15}H_{18}NO_2$ (*m/z* M+H$^+$): 244.1338, found: 244.1332.

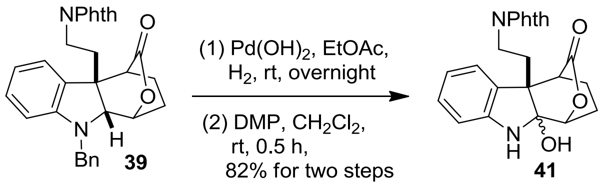


To a solution of compound **34** (20 mg, 0.08 mmol) in MeOH/H_2O (0.5 mL, v/v = 4:1) was added 5 mg (0.12 mmol) of NaOH. Reaction was quenched by 0.2 mL 1N HCl after being stirred at room temperature for 40 min. The mixture was then extracted with 5 mL of CHCl3 for six times (5 mL × 6). Organic portions were combined, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give 20 mg of colorless solid. The solid was dissolved in 0.5 mL of DMF, which was followed by the addition of K_2CO_3 (15.9 mg, 0.11 mmol) and MeI (15.6 mg, 0.11 mmol). The reaction was stirred at room temperature for 20 min. Then reaction was diluted with 15 mL of EtOAc and washed three times with 4 mL of brine/H_2O (v/v = 1:1). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (20% EtOAc/pentane) to give 20.3 mg of compound **35** as a colorless oil. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.14 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 7.0 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.59 (d, *J* = 7.5 Hz, 1H), 3.72 (s, 3H), 3.58 (d, *J* = 3.0 Hz, 1H), 3.53-3.57 (m, 1H), 2.86-2.88 (m, 1H), 2.70 (s, 3H), 2.10-2.16 (m, 1H), 1.70-1.82 (m, 2H), 1.61-1.65 (m, 1H), 1.25 (s, 3H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 174.70, 151.57, 137.36, 127.92, 122.25, 118.68, 108.85, 75.95, 73.34, 51.92, 47.64, 38.36, 34.13, 26.76, 22.16, 16.34. **IR** (film, cm^{-1}) 2950, 1726, 1643, 1447, 746. **HRMS (ESI) calcd.** for $C_{16}H_{22}NO_3$ (*m/z* M+H$^+$): 276.1600, found: 276.1592.

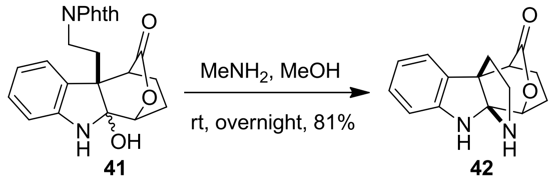


To a mixture of compound **36** (0.46 g, 1.2 mmol) and $NaHCO_3$ (0.93 g, 11.04 mmol) in THF (5.0 mL) at room temperature was added dropwise CH_3CO_3H (32 wt% in dilute acetic acid, 0.718 g, 3.0 mmol). The reaction was stirred for 5 hours. Reaction was quenched with 20 mL of 15% Na_2SO_3 and was stirred for another 20 min. 40 mL of ethyl acetate was then added. The organic layer was separated and washed sequentially with Sat. $NaHCO_3$ (10 mL) and brine (10 mL). After dried over anhydrous Na_2SO_4, the organic portion was concentrated *in vacuo*. The residue underwent silica gel column chromatography (15 % ethyl acetate/hexane) to afford 405 mg of lactone **39** and 79 mg of lactone **40** as yellow solids, with a combined yield of 84%. For lactone **39**, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.76 (d, J = 5.0 Hz, 2H), 7.70 (d, J = 8.5 Hz, 2H), 7.30-7.41 (m, 5 H), 7.10 (t, J = 7.5 Hz, 1H), 7.02 (d, J = 7.0 Hz), 6.70 (t, J = 7.5 Hz, 1H), 6.60 (d, J = 7.5 Hz), 4.45 (d, J = 7.0 Hz, 1H), 4.39 (s, 1H), 3.95 (s, 1H), 3.27-3.40 (m, 2H), 2.66 (s, 1H), 2.24-2.31 (m, 1H), 1.80-1.82 (m, 1H), 1.59-1.71 (m, 4H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 174.83, 167.94, 152.29, 138.26, 134.01, 132.31, 129.46, 128.99, 128.37, 127.91, 127.40, 124.03, 123.09, 118.61, 107.59, 76.43, 67.86, 52.63, 49.92, 44.79, 39.18, 33.55, 19.67, 19.46. **IR** (film, cm^{-1}) 2927,1756, 1711, 1374, 1242, 718. **HRMS (ESI) calcd.** for $C_{30}H_{27}N_2O_4$ (*m/z* $M+H^+$): 479.1971, found: 479.1974.

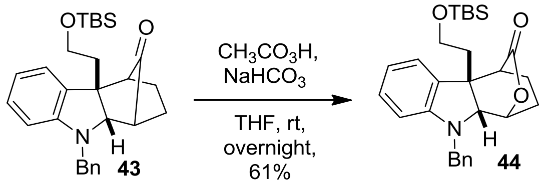
For lactone **40**, **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.62-7.68 (m, 4H), 7.39-7.44 (m, 4H), 7.31 (t, J = 7.0 Hz, 1H), 7.11 (d, J = 8.0 Hz, 1H), 6.73 (d, J = 8.5 Hz, 1H), 6.51 (d, J = 8.0 Hz, 1H), 6.44 (d, J = 8.5 Hz, 1H), 5.19 (d, J = 5.0 Hz, 1H), 4.57 (d, J = 16.5 Hz, 1H), 4.32 (d, J = 16.0 Hz, 1H), 3.76-3.83 (m, 1H), 3.75 (t, J = 5.0 Hz, 1H), 3.57-3.63 (m, 1H), 2.65-2.72 (m, 1H), 2.47 (s, 1H), 1.95-2.00 (m, 1H), 1.78-1.92 (m, 2H), 1.66-1.71 (m, 1H), 1.34-1.41 (m, 1H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 177.97, 168.00, 146.64, 138.72, 133.82, 132.24, 128.87, 127.89, 127.38, 127.07, 126.71, 123.02, 120.48, 117.86, 112.76, 75.64, 55.61, 55.00, 52.56, 46.16, 33.38, 32.17, 24.86, 22.23. **IR** (film, cm^{-1}) 2918, 1779, 1709, 1442, 1159, 1026. **HRMS (ESI) calcd.** for $C_{30}H_{27}N_2O_4$ (*m/z* $M+H^+$): 479.1968, found: 479.1974.



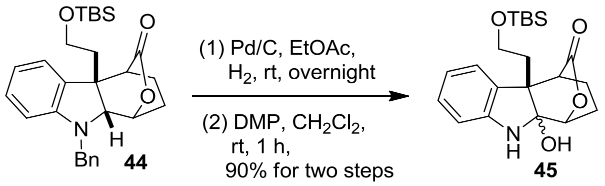
Compound **39** (300 mg, 0.64 mmol) was dissolved in 20 mL of ethyl acetate. $Pd(OH)_2$ (20% on carbon, 44.7 mg, 0.064 mmol) was added under hydrogen atmosphere. The reaction mixture was stirred at room temperature overnight and was then filtered through a short pad of Celite. The filtrate was concentrated in *vacuo* to give 218 mg of a yellow solid. To a DCM (15 mL) solution of this yellow solid was adde portionwise Dess-Martin Periodinane (332 mg, 0.78 mmol). Reaction was judged complete after 0.5 h as determined by thin layer chromatographic analysis. The reaction mixture was concentrated *in vacuo* and the residue was purified *via* silica gel column chromatography (45-55% ethyl acetate/hexane) to afford 210 mg of compound **41** as a yellow solid, with a yield of 82% for two consecutive steps. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.75-7.77 (m, 2H), 7.69-7.71 (m, 2H), 7.03-7.06 (m, 2 H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.63 (d, *J* = 8.5 Hz), 4.65 (s, 1H), 4.57 (d, *J* = 3.0 Hz), 4.24 (s, 1H), 3.50-3.58 (m, 2H), 2.74 (t, *J* = 3.0 Hz, 1H), 2.24-2.28 (m, 1H), 2.12-2.14 (m, 1H), 1.82-1.89 (m, 1H), 1.57-1.58 (m, 1H), 1.46-1.48 (m, 4H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 174.11, 168.44, 147.74, 134.15, 132.23, 129.31, 127.04, 124.45, 123.27, 119.73, 109.17, 93.35, 82.51, 54.31, 47.24, 35.27, 34.07, 21.33, 19.10. **IR** (film, cm^{-1}) 3466, 2092, 1643, 1102, 727. **HRMS (ESI) calcd.** for $C_{23}H_{20}N_2O_5Na$ (*m/z* M+Na$^+$): 427.1270, found: 427.1264.



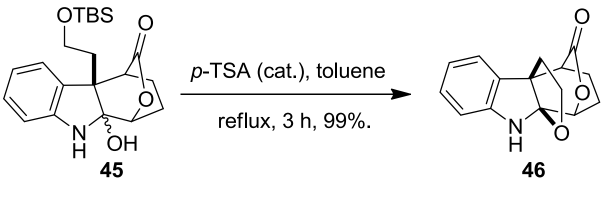
To a MeOH solution (2 mL) of compound **41** (70 mg, 0.17 mmol) was added $MeNH_2$ (108 μL, 0.87 mmol). Reaction was stirring overnight at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified *via* silica gel column chromatography (4% MeOH/DCM) to afford 36 mg of compound **42** as a pale yellow solid, with a yield of 81%. **^{1}H-NMR** (500 MHz, CD_3OD): δ 7.60 (d, *J* = 8.5 Hz, 1H), 7.42 (m, 2H), 7.30 (d, *J* = 8.5 Hz, 1H), 3.64-3.69 (m, 1H), 3.54-3.58 (m, 1H), 3.21-3.31 (m, 3H), 2.30-2.36 (m, 2H), 1.98-2.01 (m, 2H), 1.67 (t, J = 8.0 Hz, 1H), 1.28-1.32 (dd, J = 14.5 Hz, 5.0 Hz, 1H). **^{13}C-NMR** (CD_3OD, 500 MHz) δ 185.74, 173.83, 152.80, 142.93, 128.61, 126.39, 123.11, 129.86, 86.37, 55.55, 48.99, 48.67, 38.76, 35.00, 23.07, 21.78. **^{13}C-NMR** (CD_3OD, 500 MHz) δ 185.73, 173.33, 152.80, 142.93, 128.61, 126.38, 123.11, 120.85, 68.36, 55.54, 48.99, 38.76, 35.00, 23.06, 21.78. **IR** (film, cm^{-1}) 2929, 1640, 1498, 1341, 1011, 754. **HRMS (ESI) calcd.** for $C_{15}H_{17}N_2O_2$ (*m/z* M+H$^+$): 257.1290, found: 257.1280.



To a mixture of compound **43** (1.88 g, 4.2 mmol) and $NaHCO_3$ (3.2 g, 38.6 mmol) in THF (25.0 mL) at room temperature was added dropwise CH_3CO_3H (32 wt% in dilute acetic acid, 2.5 g, 10.5 mmol). The reaction was stirred for overnight. Reaction was quenched with 50 mL of 15% Na_2SO_3 and was stirred for another 20 min. 100 mL of ethyl acetate was then added. The organic layer was separated and washed sequentially with Sat. $NaHCO_3$ (20 mL) and brine (20 mL). After dried over anhydrous Na_2SO_4, the organic portion was concentrated *in vacuo*. The residue underwent silica gel column chromatography (5 % ethyl acetate/hexane) to afford 1.48 g of lactone **44**. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.30-7.38 (m, 5H), 7.16 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.0 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.57 (d, *J* = 8.0 Hz, 1H), 4.36-4.39 (m, 3H), 3.84 (d, *J* = 4.0 Hz, 1H), 3.40-3.44 (m, 1H), 3.31-3.34 (m, 1H), 2.73 (d, *J* = 3.0 Hz, 1H), 1.92-1.97 (m, 1H), 1.73-1.78 (m, 2H), 1.56-1.67 (m. 3H), 0.84 (s, 9H), -0.03 (s, 6H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 175.07, 152.20, 138.33, 129.23, 128.94, 128.91, 128.44, 128.11, 128.87, 124.20, 118.25, 107.20, 76.23, 68.21, 59.52, 52.21, 44.70, 44.31, 25.90, 19.93, 18.30, -5.40, -5.42. **IR** (film, cm^{-1}) 2955, 2863, 1760, 1603, 1487, 1251, 1088, 837. **HRMS (ESI) calcd.** for $C_{28}H_{38}NO_3Si$ (*m/z* $M+H^+$): 464.2621, found: 464.2617.

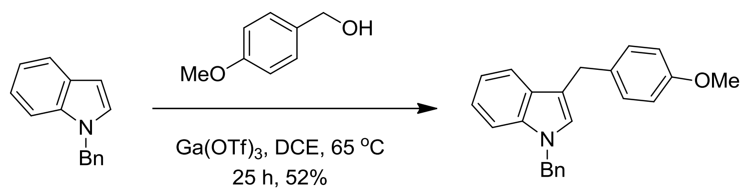


Compound **44** (620 mg, 1.34 mmol) was dissolved in 10 mL of ethyl acetate. Pd/C (10% on activated carbon, 142 mg, 0.134 mmol) was added under hydrogen atmosphere. The reaction mixture was stirred at room temperature overnight and was then filtered through a short pad of Celite. The filtrate was concentrated *in vacuo* to give 499 mg of a colorless oil. To a DCM (4 mL) solution of this yellow solid (80 mg, 0.21 mmol) was added portionwise Dess-Martin Periodinane (136 mg, 0.32 mmol). Reaction was judged complete after 1 h as determined by thin layer chromatographic analysis. The reaction mixture was concentrated *in vacuo* and the residue was purified *via* silica gel column chromatography (15% ethyl acetate/hexane) to afford 75 mg of compound **45** as a yellow solid, with a yield of 90% for two consecutive steps. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.12 (t, *J* = 8.0 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.76 (t, *J* = 8.0 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 6.24 (s, 1H), 4.53 (s, 1H), 4.23 (brs,1H), 3.61-3.64 (m, 1H), 3.28-3.32 (t, *J* = 10 Hz, 1H), 2.67 (s, 1H), 2.40-2.47 (m, 1H), 1.99 (t, *J* = 11 Hz, 1H), 1.75-1.84 (m, 2 H), 1.56-1.60 (m, 1H), 1.41-1.47 (m, 1H), 0.80 (s, 9H), -0.14 (s, 3H), -0.20 (s, 3 H). **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 174.36, 148.46, 129.14, 126.16, 124.44, 118.63, 108.74, 92.33, 81.89, 59.81, 55.51, 48.72, 36.17, 25.61, 21.98, 19.16, 18.22, -6.33, -6.44. **IR** (film, cm^{-1}) 3433, 2853, 2094, 1644, 1255, 1016. **HRMS (ESI) calcd.** for $C_{21}H_{31}NO_4NaSi$ (*m/z* $M+H^+$): 412.1920, found: 412.1914.

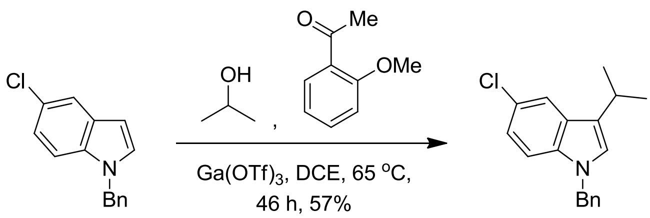


To a toluene solution (2 mL) of compound **45** (40 mg, 0.10 mmol) was added *p*-toluenesulfonic acid (1.9 mg, 0.01 mmol). Reaction was refluxed overnight. The reaction mixture was concentrated *in vacuo* and the residue was purified *via* silica gel column chromatography (25% ethyl acetate/hexane) to afford 26 mg of compound **46** as a colorless oil, with a yield of 99%. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.13 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.5 Hz, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 8.0 Hz, 1H), 4.74 (s, 1H), 4.35 (brs, 1H), 4.01 (t, *J* = 8.0 Hz, 1H), 3.53-3.58 (m, 1H), 3.10 (s, 1H), 2.17-2.21 (m, 1H), 1.85-2.11 (m, 3H), 1.66-1.72 (m, 1H), 1.38-1.43 (m, 1H); **^{13}C-NMR** (CD_2Cl_2, 500 MHz) δ 173.82, 150.50, 129.40, 128.13, 124.50, 119.76, 108.58, 101.99, 78.44, 66.02, 59.18, 45.14, 40.00, 22.53, 19.04; **IR** (film, cm^{-1}) 3398, 2946, 1748, 1612, 1469, 1023, 750. **HRMS (ESI) calcd.** for $C_{15}H_{16}NO_3$ (*m/z* $M+H^+$): 258.1130, found: 258.1131.

Preparation of 3-substituted indole substrates and α-haloketones



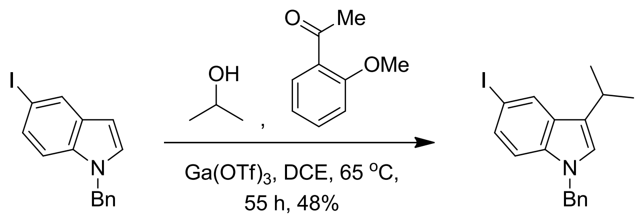
To a mixture of *N*-benzylindole (1 g, 4.82 mmol) and 4-methoxybenzyl alcohol (0.8 g, 5.78 mmol) in dichloroethane (10 mL) was added $Ga(OTf)_3$ (124 mg, 0.24 mml). Reaction was stirred at 65 ^{o}C for 25 hours. Solvent was then removed *in vacuo* and the residue underwent column chromatography (2% EtOAc/hexane) to afford 0.83 g of title compound as a colorless oil, with a yield of 52%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.0 Hz, 1H), 7.07-7.32 (m, 8H), 6.83-6.86 (m, 3H), 5.28 (s, 2H), 4.08 (s, 2H), 3.80 (s, 2H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) 158.04, 138.03, 137.11, 133.61, 129.81, 128.96, 128.35, 127.74, 126.94, 126.71, 122.00, 119.61, 119.25, 115.63, 113.98, 109.88, 55.50, 50.13, 30.91; **IR** (film, cm^{-1}), 1642, 1509, 1243, 740. **HRMS (ESI) calcd. for** $C_{23}H_{22}NO$ (*m/z* $M+H^+$): 328.1701, found: 328.1694.



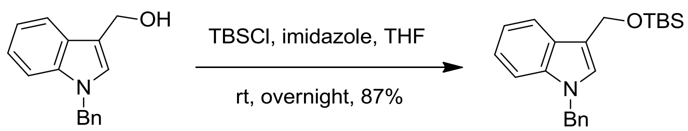
Compound was prepared with modification of a reported procedure.[2] To a mixture of *N*-benzyl-5-chloroindole (1.24 g, 5.1 mmol), 2-methoxyacetophenone (38 mg, 0.26 mmol) and isopropyl alcohol (0.618 g, 10.2 mmol) in dichloroethane (10 mL) was added 131 mg of $Ga(OTf)_3$. Reaction was stirred at 65 ^{o}C for 46 hours. Solvent was

[2] Han X.; Wu J. *Angew. Chem. Int. Ed.* **2013**, *52*, 4637.

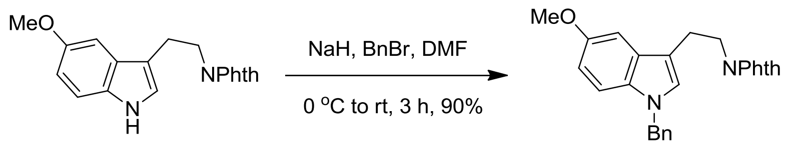
then removed *in vacuo* and the residue underwent column chromatography (2% EtOAc/hexane) to afford 0.82 g of title compound as a colorless oil, with a yield of 57%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.63 (s, 1H), 7.25-7.33 (m, 3H), 7.07-7.15 (m, 4H), 6.91 (s, 1H), 5.25 (s, 2H), 3.14-3.20 (sep, 1H), 1.35 (d, *J* = 4.5 Hz, 6H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) 137.67, 135.50, 129.02, 128.68, 127.87, 126.86, 12.23, 124.74, 123.15, 122.03, 11927, 110.92, 50.34, 25.61, 23.60; **IR** (film, cm^{-1}), 2959, 1642, 1471, 1177, 730. **HRMS (ESI) calcd. for** $C_{18}H_{19}NCl$ (*m/z* $M+H^+$): 284.1206, found: 284.1194.



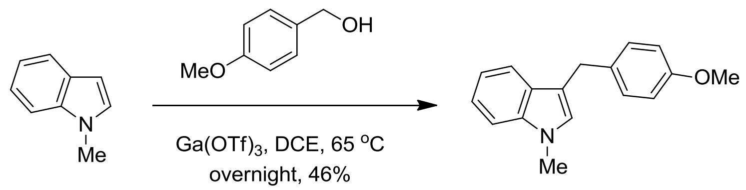
Compound was prepared with modification of a reported procedure.[2] To a mixture of *N*-benzyl-5-iodoindole (1.48 g, 4.44 mmol), 2-methoxyacetophenone (34 mg, 0.22 mmol) and isopropyl alcohol (0.53 g, 8.88 mmol) in dichloroethane (10 mL) was added 115 mg of $Ga(OTf)_3$. Reaction was stirred at 65 ^{o}C for 55 hours. Solvent was then removed *in vacuo* and the residue underwent column chromatography (2% EtOAc/hexane) to afford 0.79 g of title compound as a colorless oil, with a yield of 48%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.39 (dd, *J* = 8.5 Hz, 1.5 Hz, 1H) 7.25-7.32 (m, 3H), 7.06-7.08 (m, 2H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.85 (s, 1H), 5.28 (s, 2H), 3.11-3.20 (sep, 1H), 1.34 (d, *J* = 7.0 Hz, 6H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) 137.61, 136.17, 130.26, 130.04, 129.02, 128.67, 127.88, 126.85, 124.69, 122.92, 111.95, 82.49, 50.25, 25.57, 23.66; **IR** (film, cm^{-1}), 2961, 1643, 1470, 1174, 695. **HRMS (ESI) calcd. for** $C_{18}H_{19}NI$ (*m/z* $M+H^+$): 376.0562, found: 376.0552.



To a mixture of *N*-benzylindole-3-methanol (1 g, 4.2 mmol) and imidazole (371 mg, 5.46 mmol) in THF (10 mL) was added *t*-butyldimethylsilyl chloride (0.76 g, 5.1 mmo). Reaction was stirred at room temperature overnight. The mixture was diluted with 30 mL of EtOAc and then washed with H_2O and brine. The organic layer was dried over anhydrous Na_2SO_4. Solvent was removed *in vacuo*. The residue was subject to column chromatography (1% EtOAc) to give 1.30 g of title compound as a colorless oil, with a yield of 87%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.5 Hz, 1H), 7.24-7.32 (m, 4H), 7.10-7.19 (m, 4H), 7.07 (s, 1H), 5.30 (s, 1H), 4.95 (s, 2H), 0.94 (s, 9H), 0.11 (s, 6H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) 137.82, 137.17, 128.99, 127.83, 127.55, 127.11, 126.52, 122.13, 119.84, 119.53, 116.11, 110.00, 109.96, 58.48, 50.22, 26.34, 18.78, -4.82; **IR** (film, cm^{-1}) 2954, 2853, 1643, 1467, 1061, 737. **HRMS (ESI) calcd. for** $C_{22}H_{29}NOSiNa$ (*m/z* $M+Na^+$): 374.1916, found: 374.1912.



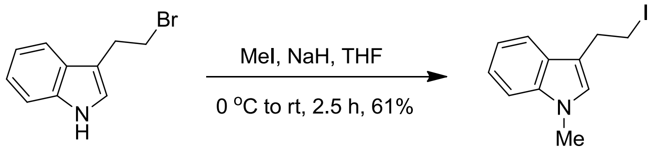
5-Methoxy-*N*-phthalyltryptamine (1.4 g, 4.37 mmol), which was prepared according to a reported procedure,[3] was dissolved in dry DMF (20 mL) and cooled to 0 °C in an ice-water bath. NaH (60% in oil, 0.35 g, 8.74 mmol) was added portionwise to the solution and stirring was continued for 30 min until the cease of gas evolution. A DMF solution (20 mL) of benzyl bromide was added dropwise over 5 min. After stirring at 0 °C for 30 min, reaction was warmed to room temperature. Two hours later, reaction was quenched with sat. NH_4Cl (20 mL) and diluted with EtOAc (100 mL). The organic layer was washed with brine/water (v/v = 1:1, 30 mL) for three times and then dried over anhydrous Na_2SO_4. Solvent was removed *in vacuo* and the residue underwent column chromatography (20% EtOAc/hexane) to give 1.61 g of title compound as a yellow solid, with a yield of 90%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.82-7.85 (m, 2H), 7.68-7.72 (m, 2H), 7.19-7.27 (m, 3H), 7.19 (d, *J* = 2.0 Hz, 1H), 7.11 (d, *J* = 9.0 Hz, 1H), 7.07 (d, *J* = 7.0 Hz, 2H), 7.00 (s, 1H), 6.81 (dd, *J* = 9.0 Hz, 2.0 Hz, 1H), 5.23 (s, 2H), 3.98-4.02 (m, 2H), 3.87 (s, 3H), 3.10-3.14 (m, 2H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) 168.5, 154.20, 137.90, 134.09, 132.44, 132.07, 128.94, 128.65, 127.75, 127.01, 126.94, 123.40, 112.52, 111.25, 110.80, 100.76, 56.06, 50.36, 38.75, 24.70; **IR** (film, cm^{-1}) 2939, 1709, 1487, 1396, 1226, 715. **HRMS (ESI) calcd.** for $C_{26}H_{23}N_2O_3$ (*m/z* $M+H^+$): 411.1709, found: 411.1703.



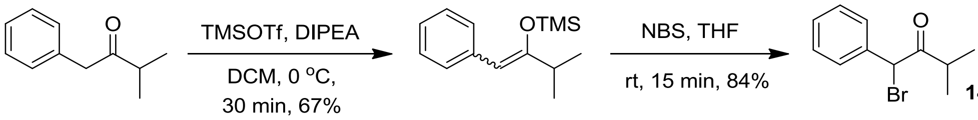
To a mixture of *N*-methylindole (200 mg, 1.50 mmol) and 4-methoxybenzyl alcohol (248 mg, 1.80 mmol) in dichloroethane (5 mL) was added $Ga(OTf)_3$ (77 mg, 0.15 mmol). Reaction was stirred overnight at 65 °C. Solvent was then removed *in vacuo* and the residue underwent column chromatography (2% EtOAc/hexane) to afford 175 mg of title compound as a colorless oil, with a yield of 46%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.56 (d, *J* = 7.5 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.23-7.27 (m, 3H), 7.11-7.13 (m, 1H), 6.86 (dd, *J* = 6.5 Hz, 2.0 Hz, 1H), 6.76 (s, 1H), 4.08 (s, 2H), 3.81 (s, 3H), 3.75 (s, 3H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) 158.06, 137.45, 13.78, 129.84, 129.82, 128.07, 127.28, 121.81, 119.48, 118.99, 115.03, 114.00, 109.39, 55.52, 32.84, 30.88; **IR** (film, cm^{-1}) 2932, 2832, 1612, 1510, 1244, 1034, 740. **HRMS (ESI) calcd.**

[3] Wang, S.; Yin, Q.; You. S. *Org. Lett.* **2013**, *15*, 2688.

for $C_{17}H_{18}NO$ (*m/z* $M+H^+$): 252.1388, found: 252.1383.

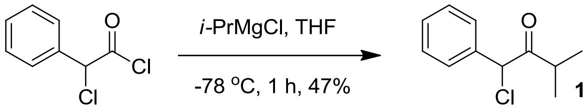


3-(2-Bromoethyl)indole (0.25 g, 1.11 mmol) was dissolved in dry THF (3 mL) and cooled to 0 °C in an ice-water bath. NaH (60% in oil, 88 mg, 2.22 mmol) was added portionwise to the solution and stirring was continued for 30 min until the cease of gas evolution. A THF solution (1 mL) of MeI was added dropwise. After stirring at 0 °C for 30 min, reaction was warmed to room temperature and stirred for another 1.5 hours. Reaction was quenched with sat. NH_4Cl (2 mL) and diluted with EtOAc (10mL). The organic layer was washed with brine (2 mL) and then dried over anhydrous Na_2SO_4. Solvent was removed *in vacuo* and the residue underwent column chromatography (2% EtOAc/hexane) to give 193 mg of title compound as a colorless oil, with a yield of 61%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.58 (dt, *J* = 8.0 Hz, 1.0 Hz, 1H), 7.32 (dt, *J* = 8.5 Hz, 1.0 Hz, 1H), 7.23-7.26 (m, 1H), 7.32 (td, *J* = 7.5 Hz, 1.0 Hz, 1H), 6.94 (s, 1H), 3.77 (s, 3H), 3.40-3.44 (m, 2H), 3.33-3.37 (m, 2H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) 137.184, 127.42, 126.92, 122.02, 119.28, 118.81, 114.23, 109.62, 32.96, 30.58, 6.62; **IR** (film, cm^{-1}) 2096, 1643, 1161, 732. **HRMS (ESI) calcd.** for $C_{11}H_{13}NI$ (*m/z* $M+H^+$): 286.0093, found: 286.0092.



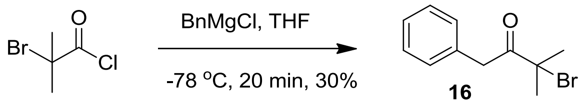
14

To a solution of diisopropylethylamine (205 μL, 1.24mmol) and starting ketone (100 mg, 0.62 mmol) in DCM (2 mL) at 0 °C was added dropwise a DCM (0.5 mL) solution of trimethylsilyl trifluoromethanesulfonate (164.4 mg, 0.74 mmol). Reaction was allowed to stir for 30 min at 0 °C. Solvent was removed and the residue underwent column chromatography (hexane) to give 97.2 mg of the corresponding silyl enol ether as a colorless oil, with a yield of 67%. The silyl enol ether (15 mg, 0.06 mmol) was dissolved in dry THF (0.5 mL), which was followed by the addition of *N*-bromosuccinimide (12.5 mg, 0.07 mmol). Reaction was stirred at room temperature for 15 min. The solvent was removed *in vacuo* and the residue was subject to column chromatography (2% EtOAc/hexane) to give 12.8 mg of title compound as a colorless oil, with a yield of 84%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.43-7.46 (m, 2H), 7.34-7.39 (m, 3H), 5.58 (s, 1H), 2.95 (sep, 1H), 1.12 (d, *J* = 6.5 Hz, 3H), 1.07 (d, *J* = 6.5 Hz, 3H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) 205.31, 135.56, 129.37, 129.20, 129.17, 54.18, 38.36, 19.51, 19.30; **IR** (film, cm^{-1}) 2970, 1722, 1640, 1450, 1033, 698. **HRMS (EI+) calcd.** for $C_{11}H_{13}OBr$ (*m/z* M^+): 240.0150, found: 240.0152.



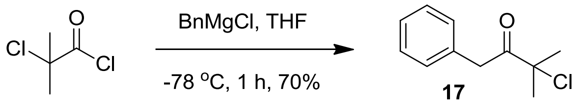
15

α-Chlorophenylacetyl chloride (~90%, 100 mg, 0.53mmol) was dissolved in dry THF (1 mL) and the mixture was cooled to -78 ^{o}C under N_2 atmosphere. Isopropylmagnesium chloride (2 M, 265 μL, 0.53 mmol) was added dropwise. Reaction was stirred for 1 hour before it was quenched by sat. NH_4Cl (1 mL). The resulting mixture was allowed to warm to room temperature over 20 min. EtOAc (5 mL) was added and the organic layer was separated and dried over anhydrous Na_2SO_4. Solvent was removed *in vacuo* and the residue underwent column chromatography (1% EtOAc/hexane) to give 49 mg of title compound as a colorless oil, with a yield of 47%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.34-7.42 (m, 5H), 5.50 (s, 1H), 2.89 (sep, 1H), 1.07 (d, J = 7.0 Hz, 3H), 1.03 (d, J = 7.0 Hz, 3H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) 206.09, 135.48 129.43, 129.29, 128.47, 64.97, 37.77, 19.62, 19.07; **IR** (film, cm^{-1}) 2971, 1727, 1643, 1453, 1030, 694. **HRMS (EI+) calcd.** for $C_{11}H_{13}OCl$ (*m/z* M^{+}): 196.0655, found: 196.0650.



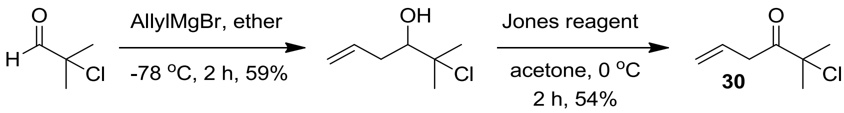
16

2-Bromo-2-methylpropanoyl chloride (100 mg, 0.54 mmol) was dissolved in dry THF (1 mL) and the mixture was cooled to -78 ^{o}C under N_2 atmosphere. Benzylmagnesium chloride (1.4 M, 0.38 mL, 0.54 mmol) was added dropwise. Reaction was stirred for 20 minutes before it was quenched by sat. NH_4Cl (1 mL). The resulting mixture was allowed to warm to room temperature over 20 min. EtOAc (5 mL) was added and the organic layer was separated and dried over anhydrous Na_2SO_4. Solvent was removed *in vacuo* and the residue underwent column chromatography (1% EtOAc/hexane) to give 38 mg of title compound as a colorless oil, with a yield of 30%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.25-7.35 (m, 5H), 4.13 (s, 2H), 1.91 (s, 6H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) δ 202.91, 134.71, 129.76, 128.74, 127.20, 64.44, 42.89, 29.74; **IR** (film, cm^{-1}) 2925, 1716, 1455, 1051, 730, 697. **HRMS (EI+) calcd.** for $C_{11}H_{13}OBr$ (*m/z* M^{+}): 240.0150, found: 240.0155.



17

2-Chloro-2-methylpropanoyl chloride (100 mg, 0.71 mmol) was dissolved in THF (1 mL) and the mixture was cooled to -78 ^{o}C under N_2 atmosphere. Benzylmagnesium chloride (1.4 M, 0.51 mL, 0.71 mmol) was added dropwise. Reaction was stirred for 1 hour before it was quenched by sat. NH_4Cl (1 mL). The resulting mixture was allowed to warm to room temperature over 20 min. EtOAc (5 mL) was added and the organic layer was separated and dried over anhydrous Na_2SO_4. Solvent was removed *in vacuo* and the residue underwent column chromatography (1% EtOAc/hexane) to give 97.1 mg of title compound as a colorless oil, with a yield of 70%. Analytical data are in accordance with what is reported.[4] **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.31-7.35 (m, 2H), 7.22-7.29 (m, 3H), 4.09 (s, 2H), 1.73 (s, 6H). **IR** (film, cm^{-1}) 2923, 1721, 1453, 693. **HRMS (EI+) calcd.** for $C_{11}H_{13}OCl$ (*m/z* M$^+$): 196.0655, found: 196.0657.



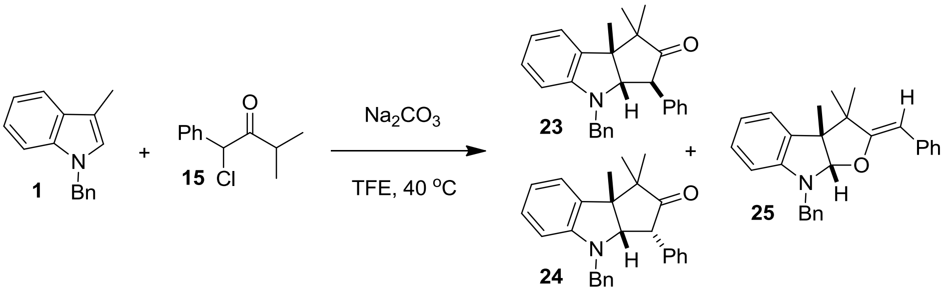
To an ether solution (0.5 mL) of 2-chloro-2-methylpropanal (150 mg, 1.41 mmol) pre-cooled to -78 °C was added dropwise allylmagnesium bromide (1 M, 0.47 mL, 0.47 mmol). Reaction was allowed to stir at -78 °C for 2 hours before it was quenched with sat. NH_4Cl (1 mL). The resulting mixture was allowed to warm to room temperature over 20 min and was diluted with EtOAc (5 mL). The organic layer was separated and dried over anhydrous Na_2SO_4. Solvent was removed *in vacuo* and the residue underwent column chromatography (8% EtOAc/hexane) to give 41.3 mg of corresponding alcohol as a colorless oil, with a yield of 59%. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 5.86-5.95 (m, 1H), 5.13-5.19 (m, 2H), 3.58-3.62 (m, 1H), 2.40-2.50 (m, 1H), 2.13-2.20 (m, 2H), 1.61 (s, 3H), 1.58 (s, 3H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) δ 135.42, 117.98, 78.22, 75.14, 36.64, 29.19, 27.90.

To an acetone solution (10 mL) of alcohol (803 mg, 5.4 mmol) pre-cooled to 0 °C was added dropwise freshly prepared Jones reagent till an orange color persisted. Acetone was removed *in vacuo* and the resulting residue was diluted with EtOAc (20 mL) and washed sequentially with H_2O (5 mL) and brine (5 mL). The The organic layer was separated and dried over anhydrous Na_2SO_4. Solvent was removed *in vacuo* and the residue underwent column chromatography (2% EtOAc/hexane) to give 428 mg of corresponding alcohol as a colorless oil, with a yield of 54%. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 5.86-6.00 (m, 1H), 5.11-5.21 (m, 2H), 3.56 (dt, J = 9.0 Hz, 2.0 Hz, 2H), 1.68 (s, 6H). **^{13}C-NMR** ($CDCl_3$, 500 MHz) δ 205.20, 131.02, 118.97, 70.81, 41.17, 28.92; **IR** (film, cm^{-1}) 2986, 1741, 1164, 501. **HRMS (EI+) calcd.** for $C_7H_{11}OCl$ (*m/z* M$^+$): 146.04985, found: 146.04964.

[4] Satoh, T.; Sugimoto, A.; Yamakawa, K. *Chem. Pharm. Bull.* **1987**, *35*, 4632.

III. Quantitative NMR Analysis

1. Procedure and data for quantitative NMR to track the reaction process of entry 7, Table 3:



To a mixture of *N*-benzylskatole **1** (100 mg, 0.45 mmol), **15** (177.8 mg, 0.90 mmol) and Na_2CO_3 (105.4 mg, 0.99 mmol) in TFE (0.45 mL) was added hexamethylbenzene (14.4 mg, 0.089 mmol) as an internal standard. Reaction was stirred at 40 ^{o}C and monitored by ^{1}H-NMR spectroscopy (500 MHz). Due to the partial overlap of the peaks of hexamethylbenzene (2.22 ppm in CD_2Cl_2) and trifluoroethanol (2.16 ppm in CD_2Cl_2), trifluoroethanol in each sample taken was removed *in vacuo* before NMR measurement. Relaxation time T1 was calculated for compound **1**, **23**, **24**, **25** and hexamethylbenzene, with hexamethylbenzene bearing the largest value, 8.0. Delay time d1 was set to 24 to allow adequate (T1) relaxation between repeated scans. As shown in the table below, results were reported as integration relative to hexamethylbenzene which has an intergral of 1800.

Table S1. Data for Kinetic Profile of Entry 7, Table 3

Relative Integration / Reaction Time (h)	1	23	24	25
1.5	522.6	4.0	0	0
5.5	509.0	7.1	0.4	0
24.0	447.8	24.3	17.5	0
36.0	453.7	21.5	28.4	0
49.5	435.6	25.6	40.4	0
59.0	413.7	36.0	52.1	0
73.0	394.7	26.3	68.0	0.7
106.5	327.0	30.9	105.9	3.4
120.5	280.	23.6	115.0	1.7
154.0	204.6	36.3	139.2	6.5
179.5	179.0	30.7	153.2	9.9
217.0	121.5	36.8	179.6	9.5
271.5	76.9	26.4	198.9	4.9
309.0	60.0	25.5	206.4	11.0

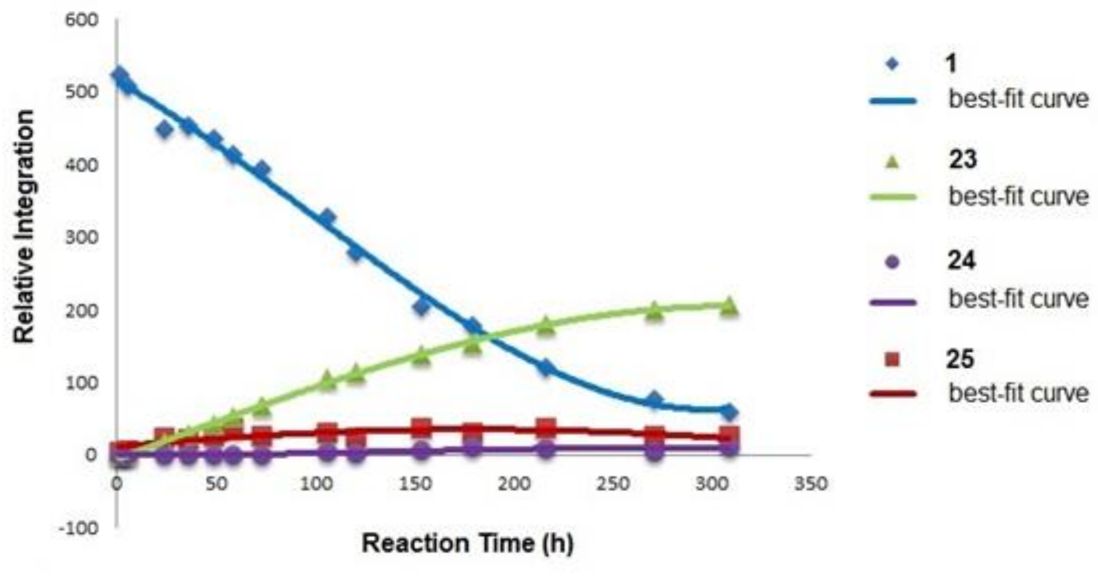
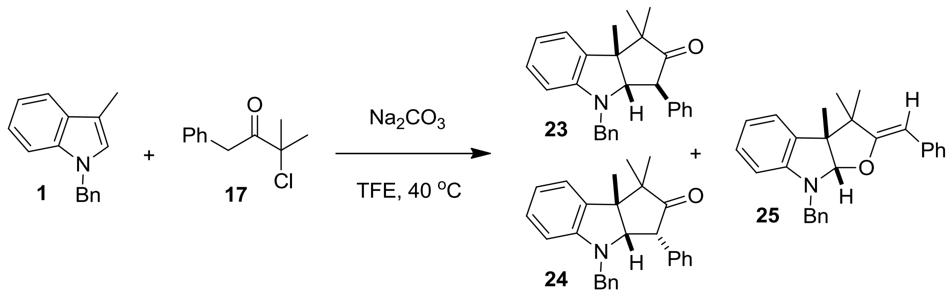


Figure S1. Kinetic profile of Entry 7, Table 3

2. **Procedure and data for quantitative NMR to track the reaction process of entry 9, Table 3:**



To a mixture of *N*-benzylskatole **1** (100 mg, 0.45 mmol), **17** (177.8 mg, 0.90 mmol) and Na_2CO_3 (105.4 mg, 0.99 mmol) in TFE (0.45 mL) was added hexamethylbenzene (14.4 mg, 0.089 mmol) as an internal standard. Reaction was stirred at 40 °C and monitored by ^{1}H-NMR spectroscopy (500 MHz). Due to the partial overlap of the peaks of hexamethylbenzene (2.22 ppm in CD_2Cl_2) and trifluoroethanol (2.16 ppm in CD_2Cl_2), trifluoroethanol in each sample taken was removed *in vacuo* before NMR measurement. Relaxation time T1 was calculated for compound **1**, **23**, **24**, **25** and hexamethylbenzene, with hexamethylbenzene bearing the largest value, 7.5. Delay time d1 was set to 23 to allow adequate (T1) relaxation between repeated scans. As shown in the table below, results were reported as integration relative to hexamethylbenzene which has an intergral of 1800.

Table S2. Data for Kinetic Profile of Entry 9, Table 3

Relative Integration / Reaction Time (h)	**1**	**23**	**24**	**25**
1.5	443.0	58.9	10.2	0
3.0	323.0	105.3	17.7	3.5
5.5	203.5	146.7	29.5	5.8
7.0	171.1	161.9	32.7	4.5
9.0	123.6	179.5	41.2	6.4
17.0	33.3	189.1	75.3	13.2
20.0	24.5	181.4	82.3	13.3
24.0	16.4	168.7	93.0	13.3
27.5	9.8	149.9	113.0	12.7
32.0	9.7	137.3	119.0	13.6
37.5	11.2	122.2	136.3	8.7
44.5	12.6	98.7	156.0	10.3
50.5	10.4	90.6	161.3	12.7
61.0	10.0	53.9	224.2	8.9
73.5	7.1	30.6	240.1	8.0
86.5	14.1	16.3	256.0	7.7
94.0	14.3	16.3	254.0	8.5

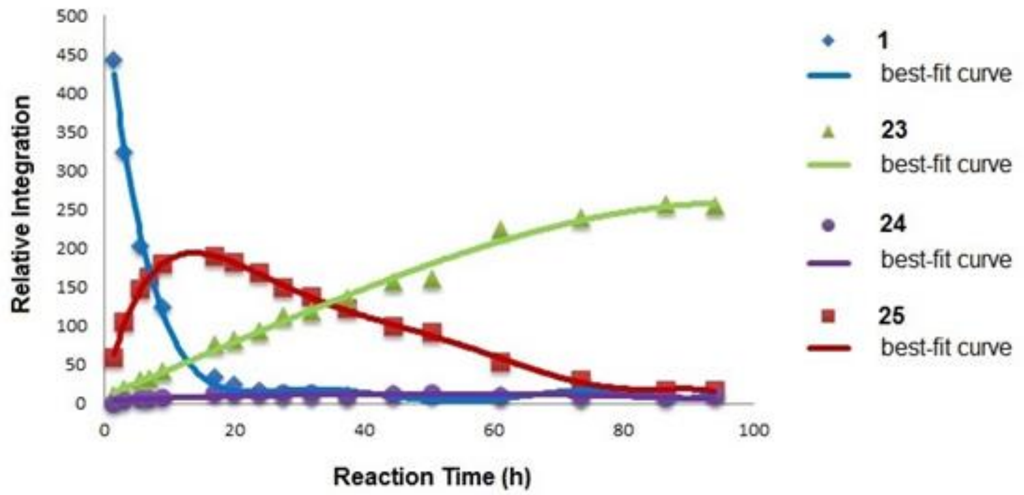


Figure S2. Kinetic profile of Entry 9, Table 3

Supporting Information for DFT

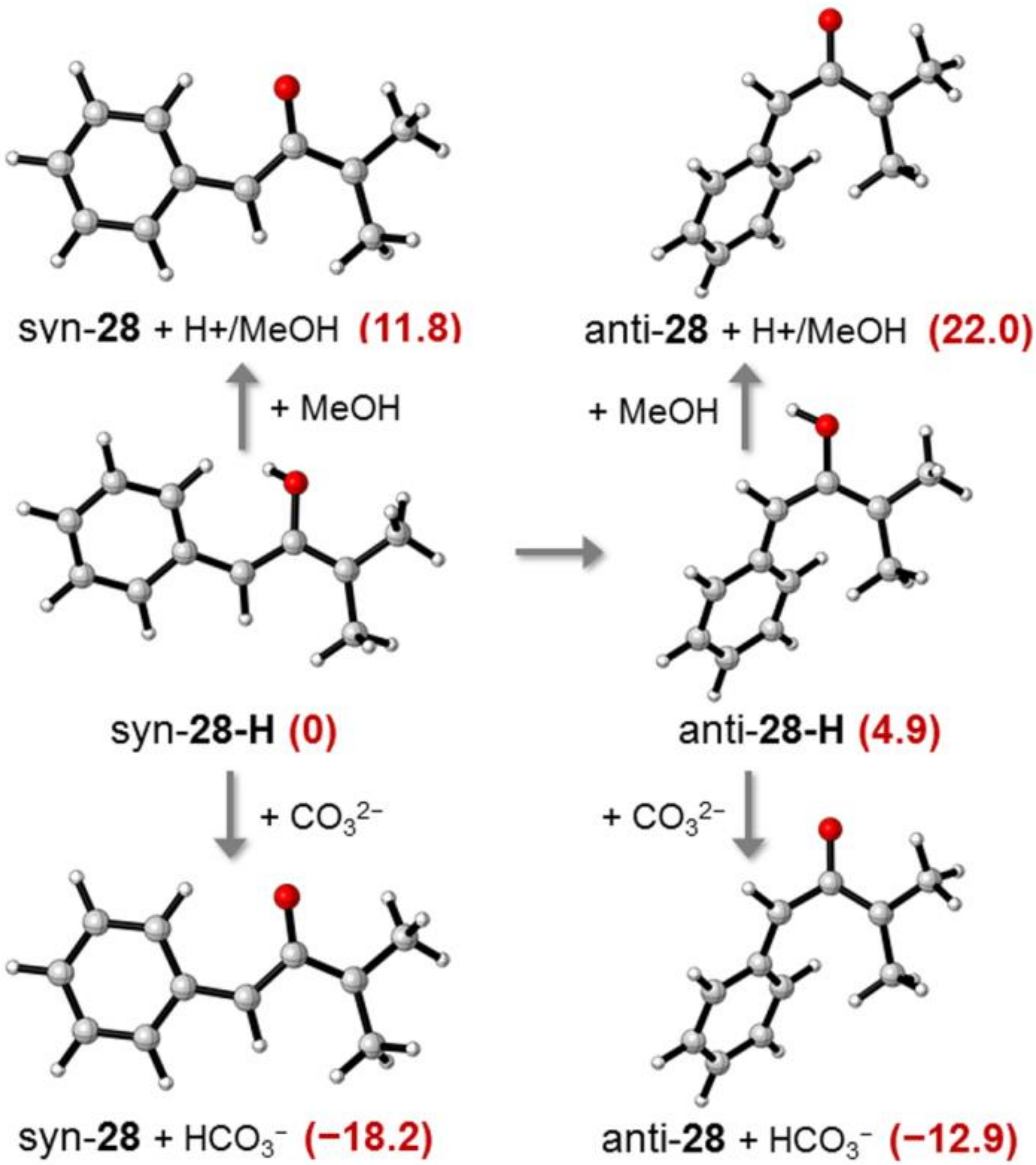


Figure S3. Enlarged graphic of Figure 7 from manuscript

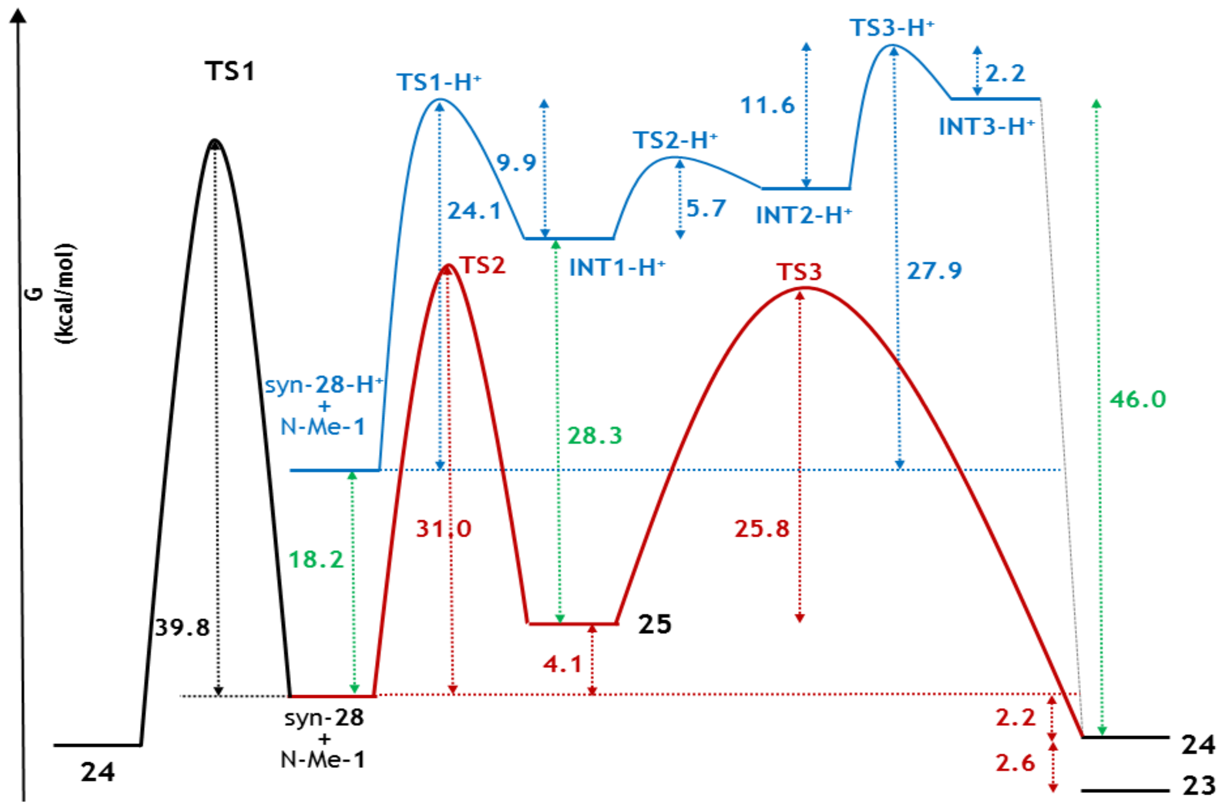


Figure S4. Enlarged graphic of reaction profile in Figure 8 from manuscript

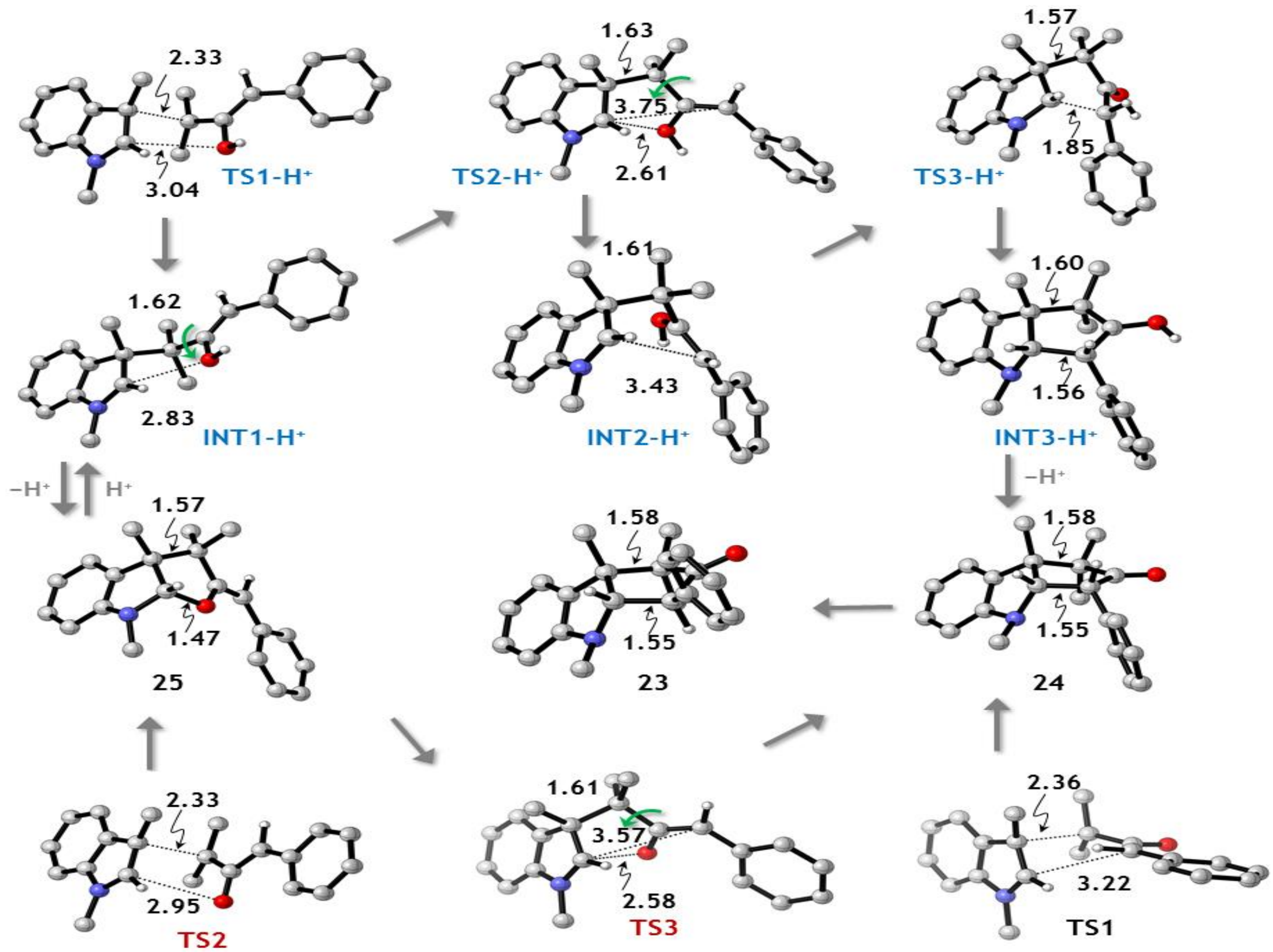


Figure S5. Enlarged graphic of transition states, intermediates, and products in Figure 8 from manuscript

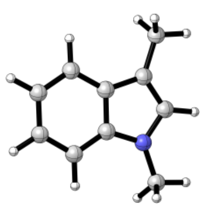
DFT Calculation Details.

Full-molecule calculations were carried out using the hybrid B3LYP-D3 functional[1] with the zero-damping, two-body only D3 correction of Grimme et al.,[2] and the 6-311++G** basis,[3] as implemented in the Jaguar[4] suite of programs. All computations were carried out in a methanol solvent model using the Poisson-Boltzmann solver[5] implemented as part of the Jaguar suite. Computed structures were confirmed as energy minima by calculating the vibrational frequencies using second derivative analytic methods, and confirming the absence of imaginary frequencies for minima, and the presence of a single imaginary frequency for transition states. Thermodynamic quantities were calculated assuming an ideal gas, and are zero point energy corrected.

Material Relevant to all DFT output

```
+-------------------------------------------------------------------+
|  Jaguar version 7.9, release  23                                  |
|  Copyright Schrodinger, LLC                                       |
|  All Rights Reserved.                                             |
|                                                                   |
|  Use of this program should be acknowledged in publications as:   |
|  Jaguar, version 7.9, Schrodinger, LLC, New York, NY, 2011.       |

Non-default options chosen:
   SCF calculation type: DFT(b3lyp-d3)
   DFT=Becke_3_Parameter/HF+Slater+Becke88+VWN+LYP (B3LYP)
   Solvation energy will be computed using PBF
   Vibrational frequencies and related properties will be computed from
    analytic second derivatives
   Molecular symmetry not used
   Energy convergence criterion:  1.00E-05 hartrees
   RMS density matrix convergence criterion:  1.00E-06
   Highest accuracy cutoffs used in SCF
```

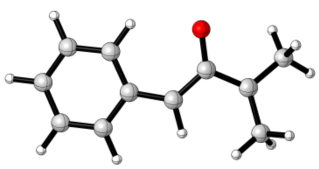


N-Me-**1**

```
final geometry:
                               angstroms
  atom              x                 y                 z
  C1          -1.5434730000      1.7894190000     -0.0487840000
  C2          -2.7962540000      2.1768450000     -0.5459350000
  C3          -3.6398430000      1.2097900000     -1.0759260000
  C4          -3.2552220000     -0.1442060000     -1.1196630000
  C5          -2.0202460000     -0.5590460000     -0.6358910000
  C6          -1.1739640000      0.4175340000     -0.1045560000
  C7          -0.4486150000      2.5015520000      0.5540150000
  C8           0.5095230000      1.5616520000      0.8306310000
```

N9	0.0879060000	0.3003540000	0.4356540000
H10	-3.1009740000	3.2173630000	-0.5156750000
H11	-4.6109870000	1.4969200000	-1.4628260000
H12	-3.9355660000	-0.8769170000	-1.5385860000
H13	-1.7284210000	-1.6023890000	-0.6704590000
H15	1.4814860000	1.6890780000	1.2836140000
C16	0.8208740000	-0.9384420000	0.5892360000
H17	1.8041820000	-0.7232870000	1.0068490000
H18	0.2975540000	-1.6242560000	1.2633060000
H19	0.9550610000	-1.4321220000	-0.3779950000
C19	-0.3813390000	3.9730790000	0.8194000000
H20	0.5653660000	4.2467810000	1.2912500000
H21	-0.4722200000	4.5512100000	-0.1065900000
H22	-1.1907310000	4.2970260000	1.4826210000

SCF energy: -442.57549028228 hartrees
Total internal energy, Utot (SCFE + ZPE + U): -442.375481 hartrees
Total enthalpy, Htot (Utot + pV): -442.374537 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -442.420685 hartrees



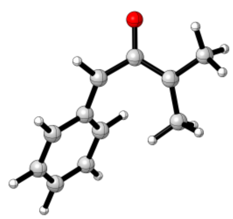
syn - **28**

final geometry:

atom	x (angstroms)	y (angstroms)	z (angstroms)
C1	0.2463730000	1.3162760000	-0.8232910000
O2	-0.0077610000	2.3156620000	-1.5396490000
C4	1.5646170000	1.1170220000	-0.2656630000
C7	-0.5795940000	0.1565450000	-0.6723540000
H8	-0.3104800000	-0.5690170000	0.0832820000
C10	1.9338480000	0.2860540000	0.9168790000
H11	2.7104840000	-0.4436030000	0.6548020000
H12	2.3862790000	0.9424140000	1.6734110000
H13	1.1004300000	-0.2304510000	1.3881140000
C13	2.6499420000	1.9348520000	-0.8648190000
H14	3.6387960000	1.4986300000	-0.7042520000
H15	2.4547360000	2.1190070000	-1.9234430000
H16	2.6369700000	2.9292220000	-0.3929240000
C16	-3.9059650000	-0.9747210000	-3.0478070000
C17	-3.4004070000	-1.8412000000	-2.0722410000
C18	-2.3187910000	-1.4538700000	-1.3005370000
C19	-1.7082470000	-0.1858790000	-1.4789940000
C20	-2.2427150000	0.6837030000	-2.4639940000
C21	-3.3226600000	0.2793310000	-3.2372880000

H22	-4.7554190000	-1.2760140000	-3.6506320000
H23	-3.8548910000	-2.8137840000	-1.9215550000
H24	-1.9228400000	-2.1289700000	-0.5486470000
H25	-1.7896930000	1.6584140000	-2.5825720000
H26	-3.7223150000	0.9513420000	-3.9883800000

SCF energy: -501.70678740922 hartrees
Total internal energy, Utot (SCFE + ZPE + U): -501.504126 hartrees
Total enthalpy, Htot (Utot + pV): -501.503182 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -501.553693 hartrees



anti - **28**

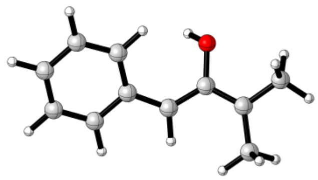
final geometry:

angstroms

atom	x	y	z
C1	0.9468808923	0.7347536453	-1.2925838254
O2	1.0167106655	1.1637477050	-2.5007490575
C4	1.6873144867	1.3452107417	-0.2280249505
C7	-0.1537890667	-0.0932378913	-0.9022784135
H8	-1.0682144662	0.1520803413	-1.4445833252
C10	1.9756334725	0.8167646331	1.1406869806
H11	2.9768865939	0.3605356452	1.1483620292
H12	2.0040005240	1.6391297703	1.8627578346
H13	1.2790596913	0.0586698193	1.4921845032
C13	2.2770062643	2.6871259894	-0.5175231189
H14	3.3396135015	2.5530495703	-0.7762857475
H15	1.8026343162	3.1691696331	-1.3727874959
H16	2.2468512237	3.3338856481	0.3642575900
C16	-0.4857080158	-3.4654232680	1.6589305689
C17	-1.6203382575	-2.7162857488	1.3204427405
C18	-1.5033678272	-1.6172429743	0.4810470437
C19	-0.2371412825	-1.2203778557	-0.0210673041
C20	0.8923053926	-2.0091618495	0.3108028178
C21	0.7665327807	-3.1135175631	1.1442139873
H22	-0.5816840571	-4.3306161558	2.3076461264
H23	-2.5927981928	-3.0008503265	1.7095237316
H24	-2.3838671607	-1.0408324481	0.2122250205
H25	1.8574265857	-1.7618772599	-0.1170692577
H26	1.6402678336	-3.7105332413	1.3855224242

SCF energy: -501.69792299244 hartrees

Total internal energy, Utot (SCFE + ZPE + U): -501.490635 hartrees
Total enthalpy, Htot (Utot + pV): -501.489691 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -501.537410 hartrees



syn-**28**-**H+**

final geometry:

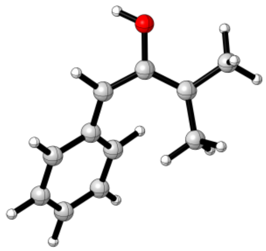
atom	x (angstroms)	y (angstroms)	z (angstroms)
C1	0.5636810000	0.8950160000	-1.0911380000
O2	0.5822010000	1.6919230000	-2.1997190000
C3	1.6260950000	1.1030210000	-0.2006820000
C4	-0.4458870000	-0.0368960000	-0.8434860000
H5	-0.2662520000	-0.7038090000	-0.0103570000
C6	1.7803210000	0.4398310000	1.1185440000
H7	2.7661150000	-0.0380260000	1.1606180000
H8	1.7983880000	1.2141690000	1.8963420000
H9	1.0167370000	-0.2869160000	1.3818590000
C10	2.6579880000	2.1041260000	-0.5736410000
H11	3.0499110000	1.8900370000	-1.5739500000
H12	2.1945450000	3.0953220000	-0.6646580000
H13	3.4692670000	2.1509240000	0.1501980000
C14	-4.0481880000	-0.9111850000	-2.8684590000
C15	-3.5014510000	-1.8186970000	-1.9562050000
C16	-2.3294210000	-1.5018480000	-1.2951760000
C17	-1.6521240000	-0.2799550000	-1.5585940000
C18	-2.2364070000	0.6341260000	-2.4793370000
C19	-3.4227190000	0.3177690000	-3.1140000000
H20	-4.9723520000	-1.1538290000	-3.3799350000
H21	-3.9993250000	-2.7600990000	-1.7605500000
H22	-1.9088090000	-2.1982390000	-0.5783640000
H23	-1.7981050000	1.6103760000	-2.6383050000
H24	-3.8744870000	1.0261520000	-3.7972420000
H25	0.1822680000	1.2497460000	-2.9581760000

SCF energy: -502.10650103316 hartrees

Total internal energy, Utot (SCFE + ZPE + U): -501.944105 hartrees

Total enthalpy, Htot (Utot + pV): -501.943161 hartrees

Total Gibbs free energy, Gtot (Htot - T*S): -501.992475 hartrees



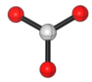
anti- **28-H+**

final geometry:

atom	x	y	z
		angstroms	
C1	0.8683488680	0.5478350552	-1.1290884940
O2	1.1034178543	0.9229133435	-2.4324926367
C3	1.5700437300	1.2525051423	-0.1425469934
C4	-0.2258801281	-0.3063990824	-0.9009352140
H5	-0.9948680813	-0.2737073915	-1.6764579197
C6	1.3641433795	1.1521832337	1.3343351369
H7	2.2183233011	0.6255545569	1.7821765560
H8	1.3783162148	2.1629866139	1.7580551579
H9	0.4509539898	0.6467494263	1.6400913810
C10	2.5142675516	2.3329745602	-0.5483670794
H11	2.9415292628	2.1925736717	-1.5387883500
H12	1.9621061153	3.2872797643	-0.5421593936
H13	3.3045038734	2.4369369038	0.2024042215
C14	-0.9300781541	-3.0995468469	2.1814729870
C15	-2.0060689174	-2.5412036194	1.4771476468
C16	-1.7670381084	-1.6373835249	0.4546097950
C17	-0.4373697689	-1.2340565179	0.1558139630
C18	0.6404157504	-1.8262835820	0.8668935258
C19	0.3911268726	-2.7516081692	1.8654798258
H20	-1.1206059882	-3.8272179525	2.9645663814
H21	-3.0225698068	-2.8288204503	1.7232477476
H22	-2.5922261326	-1.2088732975	-0.1067497905
H23	1.6602883630	-1.5844392291	0.5896222830
H24	1.2170751271	-3.2182997673	2.3920082882
H25	0.8153538049	0.2377683445	-3.0591968036

SCF energy: -502.15579677408 hartrees

Total internal energy, Utot (SCFE + ZPE + U): -501.934262 hartrees
Total enthalpy, Htot (Utot + pV): -501.933318 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -501.984610 hartrees



CO_3^{2-} DIANION

final geometry:

atom	x	y	z
C1	0.4652945967	0.3619629820	0.2034950924
O2	-0.6029910781	0.8956919031	0.7372429467
O3	0.9990202466	-0.7063245254	0.7372480427
O5	0.9998160910	0.8964928434	-0.8639266428

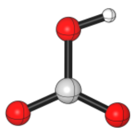
(coordinates in angstroms)

SCF energy: -263.77147452169 hartrees

Total internal energy, Utot (SCFE + ZPE + U): -264.176630 hartrees

Total enthalpy, Htot (Utot + pV): -264.175686 hartrees

Total Gibbs free energy, Gtot (Htot - T*S): -264.203681 hartrees



HCO_3^{-} ANION

final geometry:

atom	x	y	z
C1	0.4118644867	0.3154613902	0.3032984271
O2	-0.5905375311	0.9059783340	0.7146278471
O3	1.0242730860	-0.6987702894	0.7045363730
O4	1.0017174236	0.9150253059	-0.8844886935
H5	1.7545326433	0.3402697228	-1.0620413742

(coordinates in angstroms)

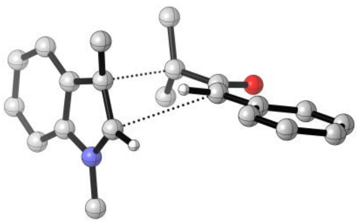
SCF energy: -264.55202282943 hartrees

Total internal energy, Utot (SCFE + ZPE + U): -264.642288 hartrees

Total enthalpy, Htot (Utot + pV): -264.641344 hartrees

Total Gibbs free energy, Gtot (Htot - T*S): -264.671401 hartrees

TS1



final geometry:

atom	x	y	z
C1	-1.5322093550	1.8606502135	0.3241941105
C2	-2.3768358488	2.5188458440	1.2165838165
C3	-3.6891497634	2.0684107211	1.3509225112
C4	-4.1619351327	0.9762516302	0.6099245100
C5	-3.3302578539	0.2952043115	-0.2774815652
C6	-2.0226595465	0.7498743838	-0.3871675311

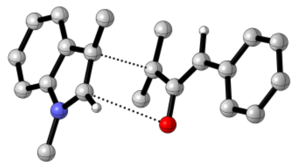
(coordinates in angstroms)

C7	-0.1535224593	2.1057831839	-0.1158346245
C8	0.1227068815	1.0106774267	-0.9863485702
N9	-0.9721161221	0.2644142823	-1.1840526038
H10	-2.0246759423	3.3661343889	1.7923990284
H11	-4.3585886217	2.5705054053	2.0393205104
H12	-5.1889341827	0.6533105082	0.7307391582
H13	-3.6934179698	-0.5479494899	-0.8520590534
H14	1.0389664236	0.7883090734	-1.5077800461
C15	-1.1047594138	-0.8196696543	-2.1477118299
H16	-0.1341767915	-1.0166298632	-2.5988489983
H17	-1.4614969072	-1.7199747592	-1.6441895968
H18	-1.8126176444	-0.5394759955	-2.9311665078
C19	0.8556802965	2.6927946445	0.8469116277
H20	1.7769304628	2.9976349615	0.3551568510
H21	0.4349868148	3.5662377040	1.3460500487
H22	1.0990008648	1.9590457955	1.6212712739
C23	-0.3663925981	3.5311738833	-1.7072014062
C24	2.0492866508	2.9133829289	-2.4340603918
C25	-1.6792071083	3.1428812136	-2.3538094918
H26	-2.5200731729	3.2246226584	-1.6658462933
H27	-1.6498326787	2.1433750196	-2.7890766422
C28	0.8307562975	3.5119569719	-2.6848223402
O29	0.4778420093	4.2287037643	-3.6656776509
C30	-0.4546141572	4.8087758253	-0.9022271381
H31	-0.6946196072	5.6075819884	-1.6100660664
H32	-1.2513230919	4.7690315975	-0.1559595371
H33	0.4934529998	5.0639234439	-0.4310707550
H34	-1.8300569531	3.8380783203	-3.1806686920
C35	5.5566811204	2.9065259784	-4.9044235812
C36	4.3846508862	3.5118722502	-5.3609315044
C37	3.2321125746	3.5316794377	-4.5818357074
C38	3.2144484670	2.9383818654	-3.2987393945
C39	4.4120766108	2.3317526003	-2.8556382261
C40	5.5589987751	2.3153368939	-3.6397079681
H41	6.4496137745	2.8964676312	-5.5193539582
H42	4.3671192575	3.9782928440	-6.3410079690
H43	2.3323353502	4.0086624818	-4.9448548308
H44	4.4353566411	1.8706587391	-1.8714970926
H45	6.4600766218	1.8417056419	-3.2628806250
H46	2.2056698331	2.4490652201	-1.4733273154

Total internal energy, Utot (SCFE + ZPE + U): -943.839406 hartrees
Total enthalpy, Htot (Utot + pV): -943.838462 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -943.911017 hartrees

υ(imaginary) = -173.79 cm-1

TS2



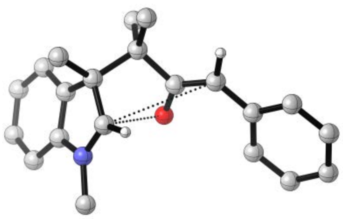
```
final geometry:
                                    angstroms
  atom            x                     y                   z
  C1          -1.3331042673       2.1411060149       0.2078226104
  C2          -2.1439324873       3.2713037251       0.1202987180
  C3          -3.5248491740       3.1211940796       0.2497007766
  C4          -4.0990371543       1.8605406279       0.4619438017
  C5          -3.3060178050       0.7180962265       0.5684675491
  C6          -1.9322607531       0.8875222735       0.4533256851
  C7           0.1047054322       1.9178058105       0.0328421705
  C8           0.2825706414       0.5385640474       0.3478273225
  N9          -0.9057041681      -0.0628446115       0.5416878216
  H10         -1.7113515935       4.2515173236      -0.0422764246
  H11         -4.1659695613       3.9926636744       0.1865154886
  H12         -5.1751505352       1.7713697955       0.5518167606
  H13         -3.7477855906      -0.2567700090       0.7355196728
  H14          1.2026662615      -0.0115623167       0.4319752666
  C15         -1.1134914954      -1.4943310854       0.6812240122
  H16         -0.1456236716      -1.9860885601       0.7537857125
  H17         -1.7003957598      -1.7038065257       1.5781258204
  H18         -1.6392130360      -1.8839487066      -0.1942121366
  C19          1.1527217577       2.9456048193       0.3794090990
  H20          2.1132620569       2.6873571408      -0.0726952371
  H21          0.8616713572       3.9362746807       0.0264263410
  H22          1.2845220867       3.0101833357       1.4636591870
  C23          0.2854394492       1.7454696733      -2.1295386370
  C24          2.7039715117       1.6752875464      -2.6039604815
  C25         -0.9033595121       0.9148277779      -2.5395294447
  H26         -1.8525932649       1.4095339638      -2.3304996522
  H27         -0.8733911764      -0.0746428357      -2.0891603260
  C28          1.5743928646       0.9914788353      -2.1512337494
  O29          1.5324802092      -0.2249046739      -1.7727882146
  C30          0.1663174676       3.1834706278      -2.5716545127
  H31          0.1289515864       3.2191690326      -3.6664333217
  H32         -0.7716540430       3.6120883647      -2.2109517211
  H33          0.9891558320       3.8134272540      -2.2414538082
  H34         -0.8313636691       0.7670159018      -3.6247856642
  C35          6.6729188937       0.1995829477      -3.1715633166
  C36          5.6721861039      -0.6649402972      -2.7249472856
  C37          4.3682058655      -0.2181160772      -2.5430235774
  C38          4.0267617886       1.1304224026      -2.8014723033
  C39          5.0541648263       1.9870364864      -3.2627524544
  C40          6.3528077533       1.5323549713      -3.4416796208
```

H41	7.6863296689	-0.1592707808	-3.3129587313
H42	5.9107527768	-1.7036788314	-2.5208591829
H43	3.5886711619	-0.8869739611	-2.2070608860
H44	4.8171229546	3.0250926143	-3.4759561505
H45	7.1192468885	2.2144910832	-3.7940250261
H46	2.5886970999	2.7093690126	-2.9004910747

Total internal energy, Utot (SCFE + ZPE + U): -943.882633 hartrees
Total enthalpy, Htot (Utot + pV): -943.881689 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -943.953824 hartrees

υ(imaginary) = -260.74 cm-1

TS3



final geometry:

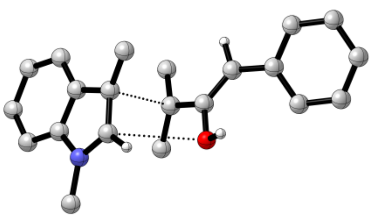
atom	x (angstroms)	y (angstroms)	z (angstroms)
C1	-1.3448354083	1.8663642502	-0.2941193333
C2	-2.6412799180	2.1839054702	-0.6721505416
C3	-3.6461030022	1.2252813763	-0.5076939738
C4	-3.3737714729	-0.0237479553	0.0526976901
C5	-2.0834322951	-0.3428970390	0.4806106539
C6	-1.1111833213	0.6238381052	0.2999121319
C7	-0.0594743998	2.6801113709	-0.2631978082
C8	0.8683460563	1.6523054011	0.3082810175
N9	0.2660452019	0.5579475933	0.6607323637
H10	-2.8750888286	3.1455363435	-1.1082876922
H11	-4.6560969958	1.4558048661	-0.8258596221
H12	-4.1686789200	-0.7511654899	0.1624516317
H13	-1.8619066056	-1.3051655448	0.9243276500
H14	1.9394518748	1.7656204830	0.4126058426
C15	0.9398812021	-0.6894346910	1.0111918773
H16	1.9674174442	-0.4746082669	1.2964653457
H17	0.4176956971	-1.1721405052	1.8367951918
H18	0.9351075832	-1.3265520278	0.1246703189
C19	-0.2546043401	3.8477080123	0.7414229416
H20	0.6849846564	4.3432718308	0.9819590111
H21	-0.9316539195	4.5839408452	0.3045752555
H22	-0.7066420527	3.4838685362	1.6673035161
C23	0.5826840046	3.1386615108	-1.6765349300
C24	2.7051682591	1.9625963982	-2.4883406053
C25	-0.5214486805	3.4382648764	-2.6997553055
H26	-1.2016484352	4.2251223261	-2.3544691480
H27	-1.0881239798	2.5360052025	-2.9258550420
C28	1.3689876122	1.8702996951	-2.1535763829
O29	0.6644371562	0.8004476929	-2.0851295635

C30	1.4438335834	4.3964206952	-1.5026691249
H31	1.9135536980	4.6383370326	-2.4571009662
H32	0.8426121031	5.2617628812	-1.2114843534
H33	2.2437261430	4.2635474639	-0.7699067481
H34	-0.0543906678	3.7861411389	-3.6244568986
C35	5.4292509138	-1.2307444793	-3.4062391408
C36	4.0735548046	-1.5045075621	-3.2212565487
C37	3.1642338738	-0.4899828666	-2.9328861600
C38	3.5873388034	0.8555126702	-2.8145859511
C39	4.9646060896	1.1097730068	-3.0155942012
C40	5.8653963572	0.0924481387	-3.3032140809
H41	6.1297368511	-2.0267777524	-3.6332302815
H42	3.7148509399	-2.5256419786	-3.3122490003
H43	2.1131421869	-0.7079269681	-2.8055821116
H44	5.3244574324	2.1322707018	-2.9411746925
H45	6.9141427651	0.3311418943	-3.4505639043
H46	3.1766070658	2.9360804874	-2.4828969397

Total internal energy, Utot (SCFE + ZPE + U): -943.862922 hartrees
Total enthalpy, Htot (Utot + pV): -943.861978 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -943.926647 hartrees

υ(imaginary) = -73.61 cm-1

TS1-H+



final geometry:

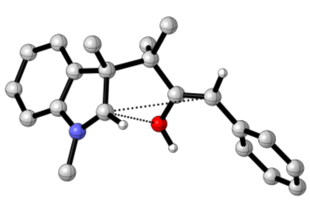
atom	x (angstroms)	y (angstroms)	z (angstroms)
C1	-1.1215908473	2.2141515390	0.3266596951
C2	-1.7348966648	3.4680492920	0.2765417360
C3	-3.1048042140	3.5482555360	0.5150835717
C4	-3.8618679234	2.4023449547	0.8034463119
C5	-3.2686848358	1.1436453338	0.8743368792
C6	-1.8999397464	1.0817286913	0.6404484218
C7	0.2467737698	1.7588285923	0.1109439818
C8	0.2105457957	0.3714463050	0.4072542825
N9	-1.0373842181	-0.0303264413	0.6744336302
H10	-1.1595507653	4.3612556487	0.0639334079
H11	-3.5972002522	4.5125893229	0.4843140143
H12	-4.9257335612	2.4983091534	0.9843744519
H13	-3.8517343290	0.2617001084	1.1092154070
H14	1.0296316672	-0.3297036716	0.3931283124
C15	-1.4706694216	-1.4004070160	0.9278516819
H16	-0.6055564005	-2.0602229087	0.9006418108
H17	-1.9413512466	-1.4617556132	1.9106695541

H18	-2.1871408173	-1.7124490132	0.1651998244
C19	1.4614247572	2.6164829015	0.3068828270
H20	2.3711306628	2.1170782898	-0.0280021795
H21	1.3715560902	3.5653921857	-0.2250454080
H22	1.5791241972	2.8546288355	1.3681746019
C23	0.2785907597	1.3730558953	-2.1890769278
C24	2.6652160631	1.7109582872	-2.7484511179
C25	-0.8132354388	0.3635138847	-2.4026888421
H26	-1.7410428554	0.6749489933	-1.9202381509
H27	-0.5396625269	-0.6391664728	-2.0871825198
C28	1.6445992872	0.9117485449	-2.3297595453
O29	1.8157112927	-0.4042209737	-1.9859864332
C30	-0.0863817288	2.7606306979	-2.6395754649
H31	-0.0670751677	2.7866447021	-3.7351172729
H32	-1.1000550085	3.0059944356	-2.3253154676
H33	0.5867328431	3.5362791511	-2.2784360052
H34	-1.0156856778	0.3309894623	-3.4813178679
C35	6.7652571008	0.6665049978	-3.3226134471
C36	5.7748407433	-0.2735145030	-3.6120382294
C37	4.4314846102	0.0465106428	-3.4410800153
C38	4.0517454889	1.3227948019	-2.9760381285
C39	5.0643145602	2.2721548320	-2.7293072178
C40	6.4046817489	1.9425359561	-2.8874105051
H41	7.8110586222	0.4130388829	-3.4535734190
H42	6.0486726795	-1.2518708468	-3.9885399319
H43	3.6777999584	-0.6720147943	-3.7492222199
H44	4.7909849755	3.2675770728	-2.3963376745
H45	7.1705155557	2.6818691468	-2.6794779495
H46	2.4387786216	2.7577894142	-2.8974819790
H47	2.7541864782	-0.6335480959	-2.0165459951

SCF energy -944.654124 hartrees
Total internal energy, Utot (SCFE + ZPE + U): -944.307583 hartrees
Total enthalpy, Htot (Utot + pV): -944.306639 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -944.374693 hartrees

υ(imaginary) = -170.14 cm-1

TS2-H+



final geometry:

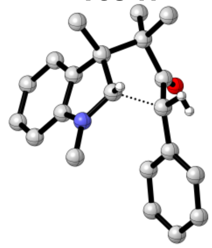
angstroms

atom	x	y	z
C1	-1.4655557836	1.7984516422	-0.2574447553
C2	-2.7371086229	2.2297631940	-0.6075281059

C3	-3.8354880612	1.4426745464	-0.2497533329
C4	-3.6770149042	0.2530860565	0.4658179949
C5	-2.4104270729	-0.1747971189	0.8635763912
C6	-1.3435351103	0.6248105961	0.4870971255
C7	-0.0878919667	2.4301257685	-0.4135069749
C8	0.7456694137	1.4083209182	0.3010733749
N9	0.0384884482	0.4513706906	0.8107069954
H10	-2.8884809282	3.1540047646	-1.1489261577
H11	-4.8312000485	1.7636886204	-0.5304661929
H12	-4.5461851620	-0.3369258625	0.7279239949
H13	-2.2795476241	-1.0812608762	1.4407134927
H14	1.8200039233	1.4457091351	0.4224429451
C15	0.5502312518	-0.7020909492	1.5535264986
H16	1.6250650787	-0.5989006951	1.6843774225
H17	0.0599488388	-0.7491091630	2.5260548746
H18	0.3296748624	-1.6076392821	0.9869122758
C19	-0.0527745778	3.7143019144	0.4718756573
H20	0.9473577956	4.1411089809	0.5328760825
H21	-0.7294768607	4.4597720514	0.0555676450
H22	-0.3975901690	3.4831737864	1.4821970708
C23	0.4638173795	2.6692241678	-1.9374537445
C24	2.8352246181	1.8999730466	-2.5400123372
C25	-0.6564976262	2.4234178313	-2.9745096170
H26	-1.4499520768	3.1659114436	-2.8797113881
H27	-1.0875091818	1.4282047665	-2.8861750736
C28	1.5587366590	1.6509346788	-2.2147920103
O29	1.0645100377	0.3729278583	-2.0471500398
C30	0.9783733641	4.1023843463	-2.1402281838
H31	1.3148993765	4.2190750792	-3.1714077343
H32	0.1797212248	4.8268902543	-1.9807319273
H33	1.8115444376	4.3608526753	-1.4859588747
H34	-0.2302601154	2.5235150639	-3.9750718114
C35	5.7848482504	-1.1347324593	-3.2420575393
C36	4.5408050267	-1.2238463918	-3.8616448869
C37	3.5804212343	-0.2352612715	-3.6502117831
C38	3.8460466936	0.8550686560	-2.8040878291
C39	5.1120908137	0.9418328253	-2.2049297894
C40	6.0701019587	-0.0438176702	-2.4201968196
H41	6.5339382356	-1.8988478481	-3.4116857175
H42	4.3231898257	-2.0499111554	-4.5286584510
H43	2.6419140429	-0.2787274436	-4.1944042402
H44	5.3444825968	1.7904168638	-1.5700366231
H45	7.0434978406	0.0409271727	-1.9511229351
H46	3.1696658216	2.9274824064	-2.5785489206
H47	1.7643707982	-0.2700524611	-2.2363916725

SCF energy: -944.658382 hartrees
Total internal energy, Utot (SCFE + ZPE + U): -944.315606 hartrees
Total enthalpy, Htot (Utot + pV): -944.314662 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -944.381439 hartrees
υ(imaginary) = -64.33 cm-1

TS3-H+



final geometry:

atom	x	y	z
C1	-1.2004971619	2.1009351466	-0.6137595506
C2	-2.5743492127	2.2155053555	-0.7718189743
C3	-3.2798070540	1.1739204440	-1.3849245483
C4	-2.6231384021	0.0190267467	-1.8102357280
C5	-1.2478311226	-0.1314940772	-1.6244639478
C6	-0.5673587226	0.9184398263	-1.0214687950
C7	-0.1718277361	2.9963651175	0.0938326731
C8	1.1237028752	2.2419542858	-0.3065289562
N9	0.7989123989	0.9823654939	-0.6963718535
H10	-3.1102945810	3.0844639842	-0.4155413886
H11	-4.3507755503	1.2622289546	-1.5191806073
H12	-3.1871102309	-0.7781481718	-2.2790277073
H13	-0.7373348818	-1.0352811862	-1.9320817377
H14	2.0156410452	2.3353708539	0.3007916065
C15	1.7435748153	-0.1031982191	-0.9257626022
H16	2.7103663994	0.1707263972	-0.5068408298
H17	1.3864366778	-1.0089499913	-0.4314600750
H18	1.8639475897	-0.2937665937	-1.9943848183
C19	-0.3971790518	2.9519082719	1.6135761735
H20	0.4130350921	3.4361404754	2.1608942923
H21	-1.3353630708	3.4488609295	1.8687243399
H22	-0.4728322709	1.9164645243	1.9520551487
C23	-0.0473535236	4.4540220260	-0.5014774328
C24	1.7187479861	3.3361108652	-1.8550227791
C25	-1.3657398430	5.2274015214	-0.6071733357
H26	-1.8419297940	5.2878307457	0.3730760368
H27	-2.0590588370	4.7753820088	-1.3117397957
C28	0.5370594155	4.1024286857	-1.8550098238
O29	-0.1938940924	4.3443188639	-2.9114054564
C30	0.9580467441	5.3128147458	0.3063439568
H31	1.2321356196	6.2042422631	-0.2621208071
H32	0.4901789405	5.6432028628	1.2343095577
H33	1.8739047639	4.7801269005	0.5678706023
H34	-1.1725064485	6.2479221402	-0.9436528674
C35	3.0609172474	1.1356162726	-5.2805866434
C36	1.7156565679	1.1033196234	-4.9185757080
C37	1.2704787648	1.8247644779	-3.8129613438
C38	2.1689878196	2.5985880554	-3.0567183564
C39	3.5203197688	2.6188823069	-3.4307560700
C40	3.9619490733	1.8938301428	-4.5324410639

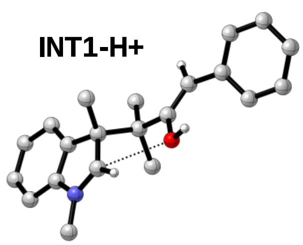
H41	3.4067390040	0.5725890660	-6.1390640031
H42	1.0123898673	0.5095307455	-5.4904714872
H43	0.2295978470	1.7475291599	-3.5169029774
H44	4.2273631734	3.2078591026	-2.8561517165
H45	5.0089864041	1.9214484816	-4.8096905221
H46	2.5141079920	3.7796344378	-1.2657516553
H47	0.2521912298	4.0391771597	-3.7231857060

SCF energy = -944.647029 hartrees

Total internal energy, Utot (SCFE + ZPE + U): -944.301613 hartrees
Total enthalpy, Htot (Utot + pV): -944.300669 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -944.368749 hartrees

υ(imaginary) = -316.38 cm-1

INT1-H+



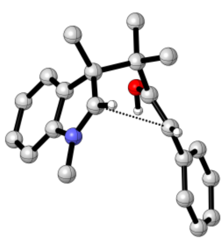
final geometry:

atom	x	y (angstroms)	z
C1	-1.3303126056	2.0728048077	0.0891765141
C2	-1.9144180998	3.3284508580	-0.0355336672
C3	-3.2722780724	3.4701898745	0.2774691166
C4	-4.0359359559	2.3833195803	0.7174731176
C5	-3.4544430387	1.1233498085	0.8889025736
C6	-2.1071902298	1.0197837677	0.5751409388
C7	0.0891799898	1.5671936963	-0.1489386448
C8	-0.0393939136	0.1617205932	0.3786251585
N9	-1.2531089362	-0.1200679584	0.7339585808
H10	-1.3430273617	4.1910758708	-0.3575490917
H11	-3.7396649290	4.4447899317	0.1790491313
H12	-5.0879659432	2.5214974670	0.9449349245
H13	-4.0320649710	0.2820071803	1.2558577459
H14	0.7575133853	-0.5649786382	0.4677927051
C15	-1.7287821162	-1.4084450754	1.2581936532
H16	-0.8934139846	-2.1059309844	1.2913255065
H17	-2.1357062065	-1.2514195063	2.2594641022
H18	-2.5109727244	-1.7855946364	0.5947611744
C19	1.1287753331	2.3502909578	0.6864830047
H20	2.1188647196	1.9003111401	0.5992868662
H21	1.1813879971	3.3811917121	0.3322910102
H22	0.8369803475	2.3666820526	1.7394434747
C23	0.4851053647	1.5301848180	-1.7226389740
C24	2.8732450714	1.8154082528	-2.5607382177
C25	-0.4053682654	0.5031055344	-2.4680924257
H26	-1.4627150457	0.7366100993	-2.3189790634
H27	-0.2209222727	-0.5222528001	-2.1437910568

C28	1.9425164132	1.1055984563	-1.8981354791
O29	2.1784561098	-0.1397539015	-1.3592536414
C30	0.2224981860	2.9081164399	-2.3583942009
H31	0.5442607476	2.8963219778	-3.4015557695
H32	-0.8451101873	3.1235746970	-2.3609592327
H33	0.7434028740	3.7233987614	-1.8513496991
H34	-0.1981358793	0.5566882321	-3.5396444794
C35	6.7548589078	0.6389306495	-3.9706927959
C36	5.7255068453	-0.3033571417	-3.9073186252
C37	4.4698547635	0.0558095582	-3.4179788985
C38	4.2145597476	1.3694080026	-2.9786701048
C39	5.2589160364	2.3096702887	-3.0599399691
C40	6.5143663054	1.9485915458	-3.5455019132
H41	7.7286914400	0.3603278972	-4.3607894207
H42	5.8925919619	-1.3174348062	-4.2581094355
H43	3.6712480924	-0.6793146796	-3.4227965743
H44	5.0755980011	3.3349588802	-2.7503197145
H45	7.3041893340	2.6919941964	-3.6014532160
H46	2.6212476752	2.8279284883	-2.8470941089
H47	3.1277290591	-0.3019697847	-1.2421342213

SCF energy: -944.669030 hartrees
Total internal energy, Utot (SCFE + ZPE + U): -944.322508 hartrees
Total enthalpy, Htot (Utot + pV): -944.321563 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -944.390532 hartrees

INT2-H+



final geometry:

atom	x (angstroms)	y (angstroms)	z (angstroms)
C1	-0.9800995584	1.9109179015	-0.8561927339
C2	-1.7089941560	2.2338810514	-1.9935211132
C3	-2.3929429713	1.2111291119	-2.6597228655
C4	-2.3615527819	-0.1100117937	-2.1967680564
C5	-1.6558970104	-0.4470238514	-1.0383676987
C6	-0.9887029566	0.5910232199	-0.4033301987
C7	-0.1357726277	2.7479232949	0.0951336926
C8	0.2670976199	1.6967486194	1.0968397316
N9	-0.2211185563	0.5329688752	0.8065031080
H10	-1.7521303595	3.2474711662	-2.3727553645
H11	-2.9576381779	1.4477661019	-3.5559880888
H12	-2.8980123114	-0.8818765816	-2.7386856463

H13	-1.6392524334	-1.4644402893	-0.6631006802
H14	0.8412505101	1.8487441837	2.0054603436
C15	-0.0856315985	-0.6897084649	1.6130346775
H16	0.5681048060	-0.4836000749	2.4592185163
H17	-1.0777948315	-0.9872343016	1.9601475498
H18	0.3368385997	-1.4791620851	0.9884836208
C19	-1.0365455220	3.7710208193	0.8512838370
H20	-0.4635356721	4.3541594802	1.5741727985
H21	-1.4976441229	4.4466638085	0.1300479911
H22	-1.8379471826	3.2486220908	1.3803850789
C23	1.1520281778	3.4297889241	-0.5820692830
C24	2.7251307424	1.5453348531	-1.2938993041
C25	0.7497920432	4.7261981570	-1.3215001700
H26	0.4479672518	5.4946830590	-0.6079617189
H27	-0.0542699396	4.5757575205	-2.0395748123
C28	1.7699851630	2.4468867637	-1.5902094501
O29	1.2224615258	2.5835631663	-2.8378908487
C30	2.1773262930	3.8293180208	0.5018646492
H31	3.0154054693	4.3452572129	0.0280635378
H32	1.7247984512	4.5153107341	1.2214693147
H33	2.5841645176	2.9839170028	1.0580365106
H34	1.6172879406	5.1028812516	-1.8697132483
C35	4.7411252639	-1.1482108577	-3.9700325732
C36	4.4008501831	0.1341987200	-4.4037065756
C37	3.7393473354	1.0158387494	-3.5483487695
C38	3.3928107003	0.6303088368	-2.2384896704
C39	3.7610732715	-0.6588219576	-1.8115331524
C40	4.4230495981	-1.5382020437	-2.6659268653
H41	5.2594636351	-1.8316962011	-4.6349345356
H42	4.6648009642	0.4587838053	-5.4057801673
H43	3.5332246335	2.0250003726	-3.8914157710
H44	3.5287844966	-0.9683571509	-0.7966062644
H45	4.6952142567	-2.5285385922	-2.3135718650
H46	3.0373560991	1.4612214361	-0.2598122380
H47	1.4454283503	1.8291424208	-3.4051411335

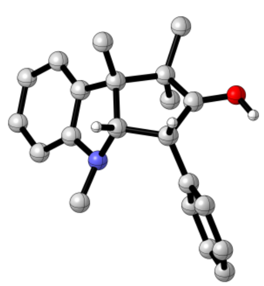
SCF energy = -944.639030

Total internal energy, Utot (SCFE + ZPE + U): -944.319295 hartrees

Total enthalpy, Htot (Utot + pV): -944.318351 hartrees

Total Gibbs free energy, Gtot (Htot - T*S): -944.387236 hartrees

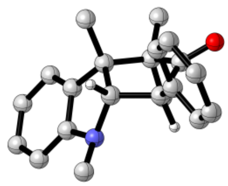
INT3-H+



final geometry:

atom	x	y	z
		angstroms	
C1	-1.3447377752	2.0269912062	-0.1389065943
C2	-2.5696446879	2.1701182031	0.4959150907
C3	-3.5749939881	1.2180796972	0.2668766016
C4	-3.3321325956	0.1407929346	-0.5873865486
C5	-2.0987113090	-0.0130430504	-1.2323026231
C6	-1.1095396684	0.9473667857	-1.0047642127
C7	-0.0922953353	2.8780282380	-0.0557095108
C8	0.9641808148	1.9485831562	-0.7544531106
N9	0.1784735745	1.0015437616	-1.5574147554
H10	-2.7518219734	2.9967521309	1.1758577325
H11	-4.5351104454	1.3099244261	0.7642175590
H12	-4.1081125609	-0.6018846806	-0.7486374979
H13	-1.9260495156	-0.8637207751	-1.8816037846
H14	1.5508651134	1.3978523600	-0.0091043532
C15	0.8284038158	-0.2565081023	-1.9206911037
H16	1.8168314026	-0.0540247018	-2.3309114298
H17	0.9343255691	-0.9216127066	-1.0504272446
H18	0.2483582461	-0.7685905198	-2.6908860804
C19	0.3116859779	3.1994877830	1.3894704539
H20	1.2561835527	3.7520913668	1.4355484881
H21	-0.4531700111	3.7945728897	1.8933701368
H22	0.4330003977	2.2673581140	1.9456526270
C23	-0.1389012988	4.1908358628	-0.9650071808
C24	1.9275618435	2.8964039307	-1.5360213825
C25	-1.1182242879	4.0200512737	-2.1867744641
H26	-2.1322476606	4.0533389272	-1.7826647012
H27	-0.9944896762	3.0697112791	-2.7018270222
C28	1.2178746930	4.2070488859	-1.5700318287
O29	1.7116444953	5.2758570769	-2.0562698459
C30	-0.5153205368	5.4955134783	-0.2446618719
H31	-0.5839357116	6.3169883697	-0.9608489035
H32	-1.4962839510	5.3708810858	0.2206004917
H33	0.2074673441	5.7658795004	0.5256683424
H34	-0.9892527173	4.8425974653	-2.8926558767
C35	3.4831252013	1.6476373408	-5.3710355896
C36	2.1117881974	1.8568788760	-5.2102898719
C37	1.6082764247	2.2713343537	-3.9798221519
C38	2.4717535664	2.4768631190	-2.8930847657
C39	3.8453579425	2.2754185147	-3.0619108291
C40	4.3484801173	1.8600960792	-4.2965033230
H41	3.8736020992	1.3219105828	-6.3299231469
H42	1.4307897683	1.6931042456	-6.0399327655
H43	0.5412121089	2.4044474589	-3.8658394226
H44	4.5204391626	2.4340926114	-2.2260104213
H45	5.4151232629	1.7009189180	-4.4160603655
H46	2.7849599625	3.0978973929	-0.8695009211
H47	2.6064505955	5.1932324189	-2.4650739127

Total internal energy, Utot (SCFE + ZPE + U): -944.307378 hartrees
Total enthalpy, Htot (Utot + pV): -944.306434 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -944.372314 hartrees



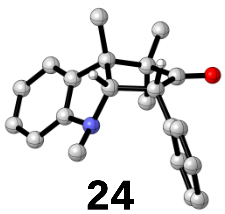
23

final geometry:

atom	x	y	z
		angstroms	
C1	-1.1340650000	1.9285110000	-0.3085210000
C2	-2.1403270000	2.6817080000	0.2698920000
C3	-3.4339190000	2.1506620000	0.3596820000
C4	-3.6909530000	0.8700600000	-0.1263550000
C5	-2.6828530000	0.0982950000	-0.7127270000
C6	-1.4029060000	0.6444020000	-0.8099550000
C7	0.3243330000	2.2613490000	-0.5289990000
C8	0.9042820000	0.8789370000	-1.0023440000
N9	-0.2692130000	0.0927380000	-1.4090640000
H10	-1.9285120000	3.6718410000	0.6593230000
H11	-4.2291440000	2.7292110000	0.8143480000
H12	-4.6905560000	0.4573120000	-0.0458380000
H13	-2.9002940000	-0.8969320000	-1.0804010000
H14	1.4111640000	0.3770620000	-0.1669830000
C15	-0.0985380000	-1.3431950000	-1.5122610000
H16	0.7891500000	-1.5573040000	-2.1104640000
H17	0.0234240000	-1.8218630000	-0.5273540000
H18	-0.9565930000	-1.7914590000	-2.0154530000
C19	1.0156750000	2.7272930000	0.7597490000
H20	2.0819610000	2.9155500000	0.5999070000
H21	0.5705460000	3.6491420000	1.1378740000
H22	0.9128240000	1.9633100000	1.5333040000
C23	0.6059850000	3.2356340000	-1.7338120000
C24	1.9066470000	1.1410040000	-2.1511970000
C25	-0.4394260000	3.0751770000	-2.8670720000
H26	-1.3981450000	3.4829740000	-2.5408310000
H27	-0.6016780000	2.0324420000	-3.1419280000
C28	1.9327760000	2.6809770000	-2.2714330000
O29	2.8441080000	3.3324880000	-2.7109370000
C30	0.7167830000	4.7168000000	-1.3701550000
H31	0.9117880000	5.3035920000	-2.2698040000
H32	-0.2180550000	5.0700600000	-0.9260990000
H33	1.5331360000	4.9127530000	-0.6746480000
H34	-0.1115960000	3.6256340000	-3.7526480000
C35	5.7830680000	-0.7272360000	-1.8173320000
C36	5.3140850000	0.1023140000	-0.7989240000
C37	4.0654060000	0.7066220000	-0.9085610000
C38	3.2609780000	0.4927280000	-2.0336010000
C39	3.7449480000	-0.3342660000	-3.0500370000
C40	4.9950650000	-0.9422610000	-2.9452010000
H41	6.7557510000	-1.1981650000	-1.7327330000

H42	5.9242070000	0.2823180000	0.0791650000
H43	3.7170860000	1.3570940000	-0.1139020000
H44	3.1390060000	-0.5028660000	-3.9344260000
H45	5.3518900000	-1.5817250000	-3.7448330000
H46	1.4335240000	0.8029920000	-3.0795450000

Total internal energy, Utot (SCFE + ZPE + U): -943.915073 hartrees
Total enthalpy, Htot (Utot + pV): -943.914129 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -943.982006 hartrees



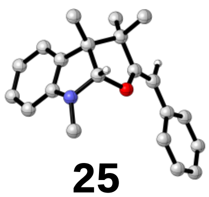
24

final geometry:

atom	x (angstroms)	y (angstroms)	z (angstroms)
C1	-1.2970330000	2.0000750000	-0.0767460000
C2	-2.4825800000	2.0922120000	0.6308400000
C3	-3.4886920000	1.1428110000	0.4107110000
C4	-3.2836590000	0.1179460000	-0.5112250000
C5	-2.0881680000	0.0142860000	-1.2294120000
C6	-1.0987290000	0.9722930000	-1.0103790000
C7	-0.0839580000	2.9001090000	-0.0706690000
C8	0.9614110000	2.0140800000	-0.8343480000
N9	0.1476800000	1.0894410000	-1.6446450000
H10	-2.6303970000	2.8880150000	1.3531740000
H11	-4.4200390000	1.1998250000	0.9613890000
H12	-4.0609420000	-0.6207070000	-0.6727600000
H13	-1.9445530000	-0.7935910000	-1.9357510000
H14	1.5557860000	1.4260090000	-0.1190070000
C15	0.7938970000	-0.1339930000	-2.1032400000
H16	1.7443170000	0.1052600000	-2.5741650000
H17	0.9700600000	-0.8366730000	-1.2733180000
H18	0.1709130000	-0.6252490000	-2.8520190000
C19	0.4125200000	3.2284840000	1.3428760000
H20	1.3404150000	3.8085250000	1.3202540000
H21	-0.3255310000	3.8050980000	1.9030470000
H22	0.6012120000	2.3036880000	1.8921330000
C23	-0.2599690000	4.1854340000	-0.9737480000
C24	1.8803320000	2.9952350000	-1.5988990000
C25	-1.3167100000	3.9981110000	-2.0946560000
H26	-2.3148470000	3.9275210000	-1.6589630000
H27	-1.1437350000	3.0947570000	-2.6801660000
C28	1.0791600000	4.3023870000	-1.7103870000
O29	1.4582800000	5.2859650000	-2.2955180000
C30	-0.5901090000	5.4763410000	-0.2162450000
H31	-0.6520720000	6.3051200000	-0.9236440000

H32	-1.5535320000	5.3834430000	0.2928630000
H33	0.1699230000	5.7333310000	0.5228900000
H34	-1.2812660000	4.8611600000	-2.7628820000
C35	3.6274870000	1.4937100000	-5.2469120000
C36	2.3217170000	1.9840080000	-5.2454610000
C37	1.7646490000	2.4932050000	-4.0764150000
C38	2.5011880000	2.5171900000	-2.8875600000
C39	3.8142240000	2.0391620000	-2.9034670000
C40	4.3753420000	1.5269660000	-4.0720910000
H41	4.0602580000	1.0971570000	-6.1582700000
H42	1.7364640000	1.9715630000	-6.1580550000
H43	0.7484110000	2.8663150000	-4.0851830000
H44	4.4014060000	2.0607700000	-1.9909900000
H45	5.3949530000	1.1583730000	-4.0643160000
H46	2.6931770000	3.2527690000	-0.9079200000

Total internal energy, Utot (SCFE + ZPE + U): -943.911643 hartrees
Total enthalpy, Htot (Utot + pV): -943.910698 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -943.977855 hartrees



25

final geometry:

atom	x (angstroms)	y (angstroms)	z (angstroms)
C1	-1.1907410000	1.7943770000	-0.5303160000
C2	-2.3032070000	1.9720020000	-1.3366180000
C3	-3.1743730000	0.8975150000	-1.5590130000
C4	-2.9263820000	-0.3364700000	-0.9622220000
C5	-1.8299790000	-0.5212420000	-0.1154140000
C6	-0.9845310000	0.5622300000	0.1092550000
C7	-0.1163900000	2.7790520000	-0.0709680000
C8	0.8555230000	1.8167900000	0.6701250000
N9	0.0981210000	0.6433610000	0.9894200000
H10	-2.5046170000	2.9299090000	-1.7996880000
H11	-4.0370760000	1.0263060000	-2.2016920000
H12	-3.5952400000	-1.1687750000	-1.1508180000
H13	-1.6520420000	-1.4804880000	0.3543380000
H14	1.3452600000	2.2260740000	1.5552650000
C15	0.7875600000	-0.5385600000	1.4732440000
H16	1.5363830000	-0.2367010000	2.2078160000
H17	0.0782270000	-1.2049870000	1.9679260000
H18	1.2900000000	-1.0848140000	0.6648390000
C19	-0.7425270000	3.8279330000	0.8576040000
H20	0.0103630000	4.4330610000	1.3654780000

H21	-1.3960520000	4.4951740000	0.2896140000
H22	-1.3529790000	3.3331760000	1.6162200000
C23	0.8023870000	3.3545040000	-1.2106390000
C24	2.2830670000	1.7950420000	-2.6186960000
C25	0.0529370000	3.8389410000	-2.4527710000
H26	-0.6906650000	4.5930550000	-2.1801200000
H27	-0.4460010000	3.0198580000	-2.9690710000
C28	1.7105200000	2.1647810000	-1.4630070000
O29	1.9150030000	1.5046880000	-0.2820050000
C30	1.6810860000	4.5147000000	-0.6779790000
H31	2.4216370000	4.7816670000	-1.4344190000
H32	1.0769970000	5.3999920000	-0.4650120000
H33	2.2195840000	4.2364580000	0.2306940000
H34	0.7476580000	4.3096480000	-3.1529020000
C35	4.8472590000	-1.4997020000	-3.5997830000
C36	4.4672850000	-1.2971870000	-2.2734480000
C37	3.6413310000	-0.2338980000	-1.9215980000
C38	3.1648900000	0.6623100000	-2.8987260000
C39	3.5624810000	0.4432280000	-4.2317430000
C40	4.3892090000	-0.6190000000	-4.5790500000
H41	5.4922030000	-2.3293310000	-3.8660450000
H42	4.8208300000	-1.9729130000	-1.5018430000
H43	3.3634770000	-0.0884810000	-0.8883360000
H44	3.2112830000	1.1196720000	-5.0045500000
H45	4.6759190000	-0.7603400000	-5.6154580000
H46	2.0487190000	2.4214600000	-3.4717100000

Total internal energy, Utot (SCFE + ZPE + U): -943.901294 hartrees
Total enthalpy, Htot (Utot + pV): -943.900350 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -943.967837 hartrees

References.

1. (a) Becke, A. D., Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **1993,** *98* (7), 5648-52; (b) Becke, A. D., A new mixing of Hartree-Fock and local-density-functional theories. *J. Chem. Phys.* **1993,** *98* (2), 1372-7; (c) Lee, C.; Yang, W.; Parr, R. G., Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B* **1988,** *37* (2), 785-9; (d) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J., Ab Initio Calculation of Vibrational Absorption and Circular Dichroism Spectra Using Density Functional Force Fields. *J. Phys. Chem.* **1994,** *98* (45), 11623-7.

2. (a) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H., A consistent and accurate ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H-Pu. *J. Chem. Phys.* **2010,** *132* (15), 154104; (b) Goerigk, L.; Grimme, S., A thorough benchmark of density functional methods for general main group thermochemistry, kinetics, and noncovalent interactions. *Phys. Chem. Chem. Phys.* **2011,** *13* (14), 6670-6688.

3. (a) Frisch, M. J.; Pople, J. A.; Binkley, J. S., Self-consistent molecular orbital methods. 25. Supplementary functions for Gaussian basis sets. *J. Chem. Phys.* **1984,** *80* (7), 3265-9; (b) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R., Efficient diffuse function-augmented basis sets for anion calculations. III. The 3-21 + G basis set for first-row elements, lithium to fluorine. *J. Comput. Chem.* **1983,** *4*, 294-301; (c) McLean, A. D.; Chandler, G. S., Contracted Gaussian basis sets for molecular calculations. I. Second row atoms, Z = 11-18. *J, Chem. Phys.* **1980,** *72*, 5639-48; (d) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A., Self-

consistent molecular orbital methods. XX. A basis set for correlated wave functions. *J. Chem. Phys.* **1980,** *72* (1), 650-4.

4. *Jaguar, versions 7.0-7.9*, Schrödinger, LLC, New York, NY: 2007-2012.

5. (a) Marten, B.; Kim, K.; Cortis, C.; Friesner, R. A.; Murphy, R. B.; Ringnalda, M. N.; Sitkoff, D.; Honig, B., A New Model For Calculation of Solvation Free Energies: Correction of Self-Consistent Reaction Field Continuum Dielectric Theory for Short Range Hydrogen-Bonding Effects. *J. Phys. Chem.* **1996,** *100* (28), 11775-11788; (b) Tannor, D. J.; Marten, B.; Murphy, R.; Friesner, R. A.; Sitkoff, D.; Nicholls, A.; Honig, B.; Ringnalda, M.; Goddard, W. A., III, Accurate First Principles Calculation of Molecular Charge Distributions and Solvation Energies from Ab Initio Quantum Mechanics and Continuum Dielectric Theory. *J. Am. Chem. Soc.* **1994,** *116* (26), 11875-82.