Catalytic Asymmetric Total Synthesis of (+)-Yohimbine

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SUPPORTING INFORMATION

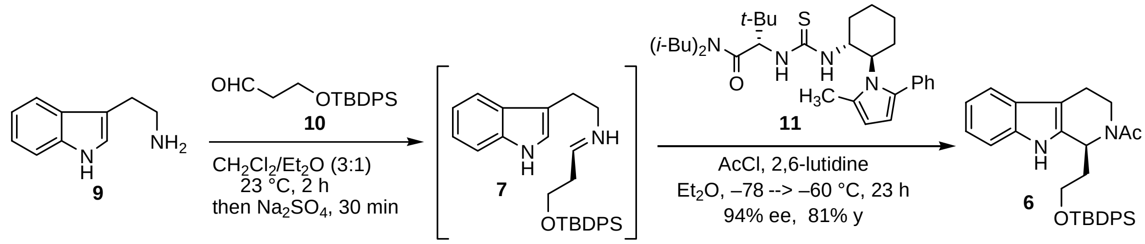
Experimental Methods: All reaction solvents were purified before use. Tetrahydrofuran and ether were purified by distillation from sodium benzophenone ketyl. Dichloromethane, acetonitrile, diisopropylamine, diisopropylethylamine, and dimethylsulfoxide were purified by distillation from calcium hydride. Methanol was purified by distillation from magnesium turnings. Acetyl chloride, 2,6-lutidine, borane-ammonia complex, *n*-butyllithium, sodium cyanoborohydride, benzoic acid, potassium bis(trimethylsilylamide), sulfurtrioxide-pyridine complex, methyl(triphenylphosphoranylidene) acetate, trifluoroethanol, scandium triflate, cesium carbonate, and 10% Pd/C were purchased from Aldrich and used as received. All reactions sensitive to moisture or oxygen were conducted under a nitrogen or argon atmosphere using flame-dried or oven-dried (150 °C, overnight) glassware. House nitrogen was passed through a column of anhydrous calcium sulfate prior to use. Removal of solvents was accomplished on a rotary evaporator at reduced pressure.

Physical Properties and Spectroscopic Measurements: Proton nuclear magnetic resonance (^1H NMR) spectra and carbon-13 (^{13}C) NMR spectra were recorded on a Varian Mercury-400 spectrometer at 400 MHz or on a Varian Inova-500 spectrometer at 500 MHz. The proton signal of residual, non-deuterated solvent (δ 7.26 ppm for $CHCl_3$) was used as an internal reference for ^1H spectra measured in these solvents. For ^{13}C spectra, chemical shifts are reported relative to the δ 77.0 ppm resonance of $CDCl_3$. Coupling constants are reported in Hz. Infrared (IR) spectra were recorded as thin films on a Mattson Galaxy Series FTIR 3000 spectrophotometer referenced to a polystyrene standard. Optical rotations were measured on a Jasco DIP 370 digital polarimeter using a quartz cell with 2 mL capacity and a 10 cm path length. Mass spectra were recorded at the Harvard University mass spectrometry facility.

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F_{254} glass plates precoated with a 0.25 mm thickness of silica gel (EM Science). The TLC plates were visualized with UV light and/or by staining with Hanessian solution (a mixture of ceric sulfate and ammonium molybdate in aqueous sulfuric acid). Column chromatography was generally performed according to the method of Still[1] using Kieselgel 60 (230-400 mesh) silica gel. Unless noted otherwise, all compounds isolated by chromatography were sufficiently pure by ^1H NMR analysis for use in

(1) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

subsequent reactions. The amount of silica gel used for purification was 50-100 : 1 weight ratio of silica : crude product.



1-((*S*)-3,4-dihydro-1-(2-(*tert*-butyl-diphenyl-silanyloxy)ethyl)-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)ethanone (6).[2] Tryptamine (**9**) (400 mg, 2.5 mmol) was dissolved in CH_2Cl_2 (62 mL) and Et_2O (31 mL) was added. Aldehyde **10**[3] was then added dropwise in CH_2Cl_2 (25 mL) over 10 min (Note: best results were achieved when aldehyde **10** was purified *immediately* prior to use). The flask containing **10** was rinsed three times with CH_2Cl_2 (3, 3, 1 mL). These rinses were added and the resulting reaction mixture was stirred for 1.5 h. Na_2SO_4 (5 g) was then added, and the heterogeneous mixture was stirred vigorously for 30 min. The stirring was then stopped, and the reaction mixture was filtered via cannula to a 200-mL round-bottom flask. The flask originally containing imine **7** was rinsed four times with CH_2Cl_2 (25 mL, then 3 x 6 mL). This mixture was concentrated yielding **7** as a dark yellow foam, which was used immediately in the acyl-Pictet–Spengler reaction.

Imine **7** was dissolved in Et_2O (50 mL). Thiourea catalyst **11**[2] (136 mg, 0.25 mmol, 10 mol%) was added, and the reaction mixture was cooled to –78 °C. 2,6-Lutidine (290 μL, 2.5 mmol) was added dropwise, followed by dropwise addition of acetyl chloride (179 μL, 2.5 mmol). The resulting mixture was stirred for 10 min at –78 °C and then transferred to a cryocool bath held at –60 °C. The mixture was then stirred under positive N_2 pressure (balloon) for 22 h (the reaction mixture became increasingly heterogeneous during this time) at which point the cryocool bath was allowed to warm slowy, over 4.5 h, to 5 °C. The resulting light yellow slurry was concentrated yielding a brownish yellow solid. Purification of this solid by column chromatography (gradient solvent system of 1 → 5 → 10% ethyl aceate in dichloromethane) provided **6** (1.0 g, 81%) as a white foam. This compound exists as a 1.6 : 1 mixture of amide rotamers. The enantiomeric excess was determined to be 94% by

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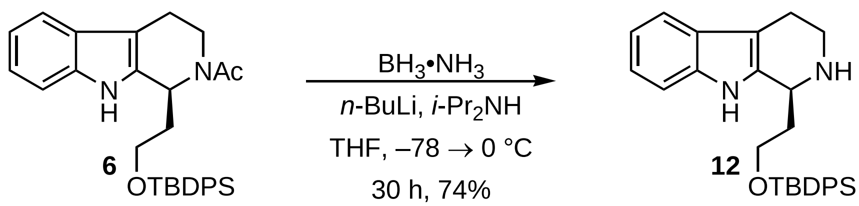
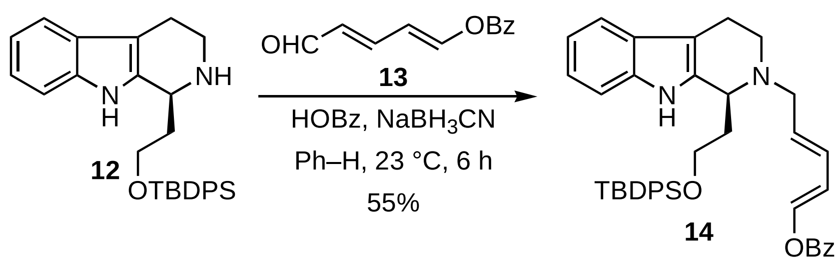
(2) Taylor, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 10558.

(3) Smith, A. B., III.; Safonov, I. G.; Corbett, R. M. *J. Am. Chem. Soc.* **2002**, *124*, 11102.

chiral HPLC according to the previous published method.[2] The spectroscopic properties of **6** were in agreement with the previously published data.[2]



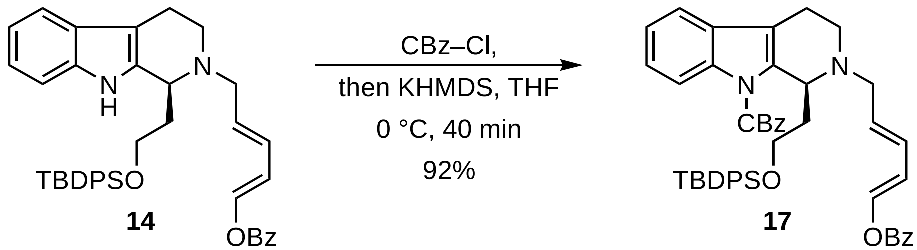
(*S*)-2,3,4,9-tetrahydro-1-(2-(*tert*-butyl-diphenyl-silanyloxy)ethyl)-1*H*-pyrido[3,4-*b*]indole (12). *i*-Pr_2NH (1.64 mL, 11.7 mmol) was dissolved in THF (3.9 mL) and cooled to –78 °C. *n*-BuLi (1.98 M solution in hexanes, 5.4 mL, 10.7 mmol) was added slowly. The resulting white slurry was stirred at –78 °C for 15 min and then warmed to 0 °C. After stirring at 0 °C for 25 min, BH_3•NH_3 (90%, 400 mg, 11.6 mmol) was added in one portion. The frothy white mixture was stirred for 20 min at 0 °C and then warmed to 23 °C. The resulting biphasic mixture was stirred vigorously until the viscous lower layer precluded further stirring, providing a solution of lithium amidotrihydroborate. In a separate flask, tetrahydro-β-carboline **6** was dried azeotropically with benzene. The dry residue was dissolved in THF (1.05 mL) and cooled to –78 °C. The top, homogeneous layer of the lithium amidotrihydroborate solution was then added slowly. The resulting light yellow, opaque reaction mixture was stirred at –78 °C for 10 min and warmed to 0 °C. The reaction mixture was transferred to a cold room and stirred in an ice bath at 0 °C under positive N_2 pressure (balloon) for 24 h at which point only a trace of **6** remained as judged by TLC analysis. Trifluoroethanol (1.2 mL) was added and the reaction was then diluted with CH_2Cl_2. $NaHSO_4$ (2 M, 10 mL) was added slowly (CAUTION! Gas evolution) and the biphasic mixture was stirred vigorously for 1 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic phases were washed with saturated $NaHCO_3$ (agitate at least 30 sec in separatory funnel). This aqueous layer was also extracted with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4, filtered, and concentrated yielding a yellow oil. Purification of this oil by column chromatography (25x155 mm silica, gradient solvent mixture of 1 → 3 → 4 → 5% methanol in dichloromethane) afforded amine **12** as a white foam (100 mg, 74%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (br s, 1 H), 7.72-7.68 (m, 4 H), 7.50-7.44 (m, 3 H), 7.42-7.37 (m, 4 H), 7.15-7.07 (m, 3 H), 4.32-4.28 (m, 1 H), 4.00-3.92 (m, 2 H), 3.33 (dt, J = 13.2, 4.4, 4.4 Hz, 1 H), 3.06 (ddd, J = 13.2, 8.3, 5.4 Hz, 1 H), 2.82-2.71 (m, 2 H), 2.47-2.25 (br s, 1 H), 2.17-2.09 (m, 1 H), 1.97-1.91 (m, 1 H), 1.15 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 135.5, 135.5, 135.4, 133.0, 132.9, 130.0, 129.9, 127.9, 127.9, 127.4, 121.3, 119.1, 118.0, 110.8, 108.3, 62.7, 52.1, 42.7, 37.6, 27.0, 22.5, 19.2; $[\alpha]_D^{28}$ –18.7 ° (c 1.4, $CHCl_3$); IR (thin film) 3070, 3051, 2931, 2894, 2858, 1471, 1453, 1428, 1111, 1086, 823, 739, 703, 613 cm^{-1}; HRMS (ES), calcd for $C_{29}H_{35}N_2OSi$ $[M + H]^+$ 455.2519, found 455.2515 *m/z*.



(1*E*,3*E*)-5-((*S*)-3,4-dihydro-1-(2-(*tert*-butyl-diphenyl-silanyloxy)ethyl)-1*H*-pyrido[3,4-*b*]indol-2(9*H*)-yl)penta-1,3-dienyl benzoate (14). Amine **12** (110 mg, 0.24 mmol) was dissolved in Ph–H (5.4 mL) and HOBz (191 mg, 1.6 mmol) was added followed by $NaBH_3CN$ (44 mg, 0.7 mmol). Aldehyde **13**[4] (72 mg, 0.36 mmol) was then added and the clear, heterogeneous reaction mixture turned bright yellow. This mixture was stirred for 6 h at which point TLC analysis indicated the consumption of aldehyde (the aldehyde co-spots with the product thus the reaction was allowed to proceed until all excess aldehyde had been reduced). Saturated $NaHCO_3$ (ca. 5 mL) was added and the biphasic mixture was stirred for 10 min. The biphasic mixture was further diluted with CH_2Cl_2 and saturated $NaHCO_3$. The layers were separated and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4, filterd, and concentrated giving a yellow oil. Purification of this material by column chromatography (25x155 mm silica, gradient solvent system of 3 $\rightarrow$ 5 $\rightarrow$ 10 $\rightarrow$ 15 $\rightarrow$ 20% ethyl acetate in hexanes) afforded **14** (85 mg, 55%) as a clear oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (br s, 1 H), 8.12-8.09 (m, 2 H), 7.74-7.69 (m, 4 H), 7.63-7.59 (m, 1 H), 7.58 (d, J = 11.7 Hz, 1 H), 7.51-7.39 (m, 9 H), 7.17-7.06 (m, 3 H), 6.22 (q, J = 11.2 Hz, 1 H), 6.18-6.13 (m, 1 H), 5.83 (ddd, 14.2, 6.8, 6.8 Hz, 1 H), 4.08-4.04 (m, 1 H), 3.99-3.94 (m, 1 H), 3.86 (ddd, 11.7, 7.8, 4.4 Hz, 1 H), 3.34-3.24 (m, 2 H), 3.17 (ddd, 13.2, 8.3, 4.9 Hz, 1 H), 3.00-2.94 (m, 1 H), 2.85 (ddd, 14.7, 9.3, 4.9 Hz, 1 H), 2.59 (dt, 15.1, 3.9, 3.9 Hz, 1 H), 2.11-2.04 (m, 1 H), 1.94-1.87 (m, 1 H), 1.14,

(4) Becher, J. *Org. Synth.* **1980**, *59*, 79

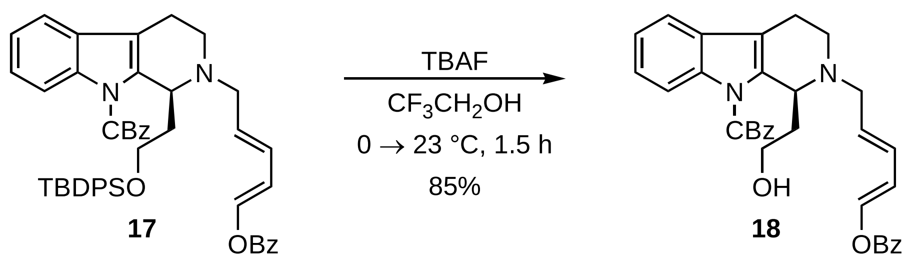
s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 138.1, 135.6, 135.6, 135.5, 134.8, 133.6, 133.5, 133.2, 132.0, 129.9, 128.9, 128.5, 127.9, 127.9, 127.3, 127.2, 121.2, 119.0, 118.0, 115.7, 110.7, 107.3, 62.1, 55.4, 54.0, 45.2, 36.8, 27.0, 19.3, 18.1; $[\alpha]_D^{28}$ –38.9° (*c* 1.5, $CHCl_3$); IR (thin film) 3423, 2932, 2890, 2858, 1733, 1465, 1452, 1428, 1315, 1298, 1264, 1157, 1114, 1091, 979, 740, 706, 506 cm^{-1}; HRMS (ES), calcd for $C_{41}H_{45}N_2O_3Si$ [M + H]$^+$ 641.3199, found 641.3201 m/z.



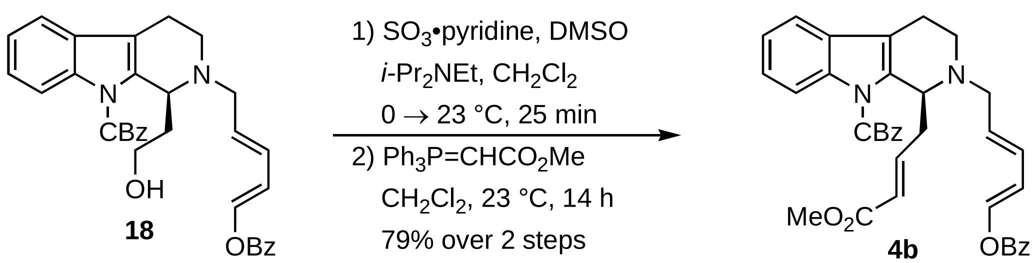
14 **17**

(1*E*,3*E*)-5-((*S*)-3,4-dihydro-1-(2-(*tert*-butyl-diphenyl-silanyloxy)ethyl)-1*H*-pyrido[3,4-*b*]indol-2(9-carbobenzyloxy)-yl)penta-1,3-dienyl benzoate (17). Amine **14** (115 mg, 0.18 mmol) was dried azeotropically by evaporation of a benzene solution. This dry material was dissolved in THF (3.6 mL) and cooled to 0 °C. CBz-Cl (36 µL, 0.26 mmol) was added, followed by KHMDS (1 M solution prepared by dissolving 1 mmol solid KHMDS in 1 mL THF, 210 µL, 0.21 mmol). The resulting light yellow reaction mixture was stirred for 15 min, at which point additional CBz-Cl (36 uL, 0.26 mmol) was added followed by KHMDS (1 M in THF, 210 µL, 0.21 mmol). The reaction mixture was stirred for an additional 25 min at which point only a trace of **13** remained as judged by TLC analysis. Saturated NH_4Cl was added, the ice bath was removed, and the biphasic mixture was stirred vigorously for 5 min. The reaction mixture was then diluted further with ethyl acetate and saturated NH_4Cl. The layers were separated, and the aqueous layer was extracted with ethyl acetate. The combined organic phases were washed with saturated $NaHCO_3$, dried over Na_2SO_4, and concentrated yielding a yellow oil. Purification of this oil by column chromatography (25x150 mm silica, gradient solvent system of 1 → 7 → 15% ethyl acetate in hexanes) afforded *N*-CBz indole **17** as a clear oil. This material was contaminated with an inseparable impurity derived from addition of KHMDS to CBz-Cl ($BnO_2CNH(TMS)$). The corrected yield of **15** was 129 mg (92%). Data for **15**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16-8.10 (m, 2 H), 7.75-7.68 (m, 3 H), 7.66-7.60 (m, 1 H), 7.54-7.48 (m, 2 H), 7.46-7.30 (m, 13 H), 7.29-7.21 (m, 3 H), 6.17 (t, *J* = 11.2 Hz, 1 H), 6.05 (dd, *J* = 15.1, 11.2 Hz, 1 H), 5.68 (ddd, *J* = 13.7, 6.4, 6.4 Hz, 1 H), 4.27 (br d, *J* = 8.8 Hz, 1 H), 3.90-3.80 (m, 2 H), 3.21 (dddd, *J* = 14.2, 14.2, 14.2, 6.4 Hz, 2 H), 3.10-3.02 (m 1 H), 2.91 (dd, *J* = 14.2, 6.4 Hz, 1 H), 2.76 (ddd, *J* = 17.1, 11.7, 5.9

Hz, 1 H), 2.41 (dd, J = 16.6, 4.9 Hz, 1 H), 2.18-2.11 (m, 1 H), 1.87-1.81 (m, 1 H), 1.07 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 151.3, 137.9, 136.7, 136.5, 135.8, 135.6, 135.0, 134.4, 134.3, 133.6, 132.6, 130.0, 129.6, 129.4, 129.4, 128.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.1, 128.0, 127.6, 127.5, 126.5, 124.1, 122.9, 117.8, 115.9, 115.8, 114.8, 77.2, 68.5, 66.9, 62.1, 55.3, 54.8, 41.0, 37.1, 26.9, 19.3, 16.6; $[\alpha]_D^{24}$ –17.4° (c 0.7, $CHCl_3$); IR (thin film) 3070, 3034, 2957, 2933, 2898, 2858, 1729, 1455, 1429, 1392, 1361, 1321, 1297, 1254, 1211, 1179, 1142, 1114, 1088, 1069, 1021, 978, 865, 849, 744, 703 cm^{-1}; HRMS (ES) calcd for $C_{49}H_{51}N_2O_5Si$ $[M + H]^+$ 775.3567, found 775.3553 m/z.

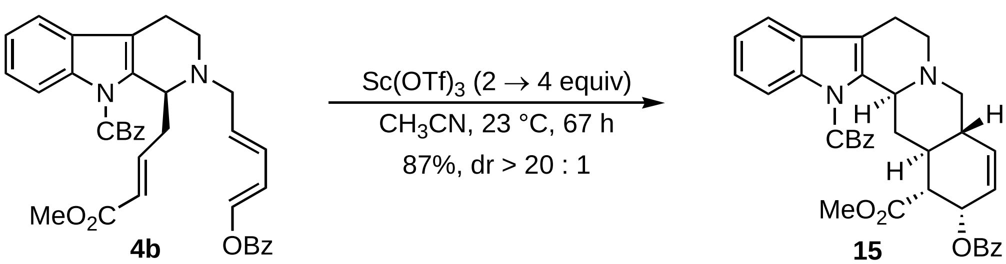


(1*E*,3*E*)-5-((*S*)-3,4-dihydro-1-(2-hydroxyethyl)-1*H*-pyrido[3,4-*b*]indol-2(9-carbobenzyloxy)-yl)penta-1,3-dienyl benzoate (18). Trifluoroethanol (4.7 mL) was added to a flask containing silyl ether **17** (105 mg, 0.14 mmol) and the mixture was stirred vigorously for ca. 15 min (**17** is only partially soluble in trifluoroethanol). The resulting suspension was cooled to 0 °C and TBAF (1 M solution in THF, 840 μL, 0.84 mmol) was added. The resulting mixture was alloed to warm to 23 °C and then stirred for 1.25 h at which point **17** was consumed as judged by TLC analysis. The reaction mixture was poured into saturated NH_4Cl and quickly diluted with ethyl acetate (Note: It was necessary to use saturated NH_4Cl for the aqueous workup. Complete decomposition was observed when saturated $NaHCO_3$ was used). This biphasic mixture was agitated in the separatory funnel, the layers were separated, and the aqueous layer was extracted with ethyl acetate. The combined organic phases were washed with saturated sodium chloride, dried over Na_2SO_4, filtered, and concentrated yielding a yellow oil contaminated with trifluoroethanol. Excess trifluoroethanol was removed via high vacuum. The resulting crude oil was purified by column chromatography (25x160mm silica, gradient solvent system of 1 → 7 → 15 → 20% acetone in hexanes) and alcohol 16 was isolated as a clear oil. This material was contaminated with $BnOC(O)NH_2$. The corrected yield of **18** was 64 mg (85%). Data for 17: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, J = 7.8 Hz, 1 H), 8.14-8.10 (m, 2 H), 7.64-7.59 (m, 2 H), 7.52-7.36 (m, 7 H), 7.32-7.25 (m, 3 H), 6.27 (t, J = 11.2 Hz, 1 H), 6.15 (dd, J = 15.1, 10.7 Hz, 1 H), 5.81 (ddd, J = 14.7, 6.8, 6.8 Hz, 1 H), 5.43 (d, J = 11.7 Hz, 1 H, A of AB system), 5.38 (d, J = 11.7 Hz, 1 H, B of AB system), 4.45 (br d, J = 9.78 Hz, 1 H), 3.64-3.54 (m, 2 H), 3.42-3.28 (m, 3 H), 3.07 (dd, J = 14.2, 6.4 Hz, 1 H), 2.82 (ddd, J = 16.6, 11.7, 6.4 Hz, 1 H), 2.57 (dd, J = 16.6, 4.9 Hz, 1 H), 2.02-1.91 (m, 1 H), 1.89-1.83 (m, 1 H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 151.2, 138.6, 135.8, 134.7, 134.5, 133.7, 130.6, 130.0, 129.3, 129.0, 129.0, 128.8, 128.7, 128.6, 128.5, 128.2, 128.1, 124.6, 123.2, 118.0, 115.9, 115,4, 114.9, 69.0, 63.5, 59.2, 55.1, 41.3, 34.3, 16.2; $[\alpha]_D$ (c , $CHCl_3$); IR (thin film) 3285, 3071, 3035, 2949, 2848, 1730, 1456, 1395, 1350, 1323, 1263, 1208, 1143, 1128, 1066, 1040, 1021, 979, 751, 709 cm^{-1}; HRMS (ES) calcd for $C_{33}H_{33}N_2O_5$ $[M + H]^+$ 537.2389, found 537.2386 *m/z*.



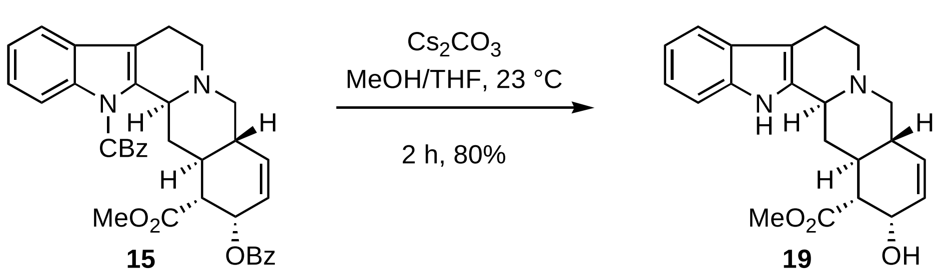
(1*E*,3*E*)-5-((*S*)-1-((*E*)-3-(methoxycarbonyl)allyl)-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2(9-carbobenzyloxy)-yl)penta-1,3-dienyl benzoate (4b). Alcohol **18** (57 mg, 0.11 mmol) was dried azeotropically by evaporation of a benzene solution. The solid residue was dissolved in CH_2Cl_2 (3.7 mL) and *i*-Pr_2NEt (160 μL, 0.92 mmol) was added followed by DMSO (130 μL, 1.83 mmol). The mixture was cooled to 0 °C and SO_3•pyridine (78 mg, 0.49 mmol) was added in one portion. The resulting mixture was stirred for 25 min at which point TLC analysis indicated the complete consumption of **18**. The reaction mixture was diluted with saturated $NaHCO_3$, the ice bath was removed, and the biphasic mixture was stirred vigorously for 10 min. The mixture was further diluted with saturated $NaHCO_3$ and ethyl acetate. The layers were separated and the aqueous layer was extracted with ethyl acetate. The combined organic phases were washed with saturated sodium chloride, dried over Na_2SO_4, filtered, and concentrated yielding a yellow, odorous oil. Excess pyridine was removed from this crude oil by coevaporation with benzene. The resulting pyridine-free residue was used immediately in the following olefination reaction.

The crude aldehyde (prepared above, theoretically 0.11 mmol) was dissolved in CH_2Cl_2 and methyl(triphenylphosphoranylidene)acetate (78 mg, 0.23 mmol) was added. The resulting orange reaction mixture was stirred for 1 h at which point additional methyl(triphenylphosphoranylidene)acetate (37 mg, 0.11 mmol) was added. The reaction mixture was stirred for 11.5 h, and the recharging process was repeated as above. The reaction mixture was stirred for an additional 2.5 h at which point all of the aldehyde had been consumed as judged by TLC analysis. This mixture was partially concentrated and the resulting maroon oil was purified by column chromatography (25x120mm silica, gradient solvent system of 5 10 15 20% acetone in hexanes), and triene **4b** (51 mg, 79% over 2 steps) was isolated as a white solid. An analytical sample of **4b** was prepared by preparative TLC (250 μM silica plate, 40% ethyl acetate in hexanes): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (br d, *J* = 7.8 Hz, 1 H), 8.13-8.10 (m, 2 H), 7.64-7.59 (m, 1 H) 7.58 (d, *J* = 12.2 Hz, 1 H), 7.51-7.36 (m, 7 H), 7.31-7.24 (m, 3 H), 6.94 (ddd, *J* = 15.6, 7.3, 7.3 Hz, 1 H), 6.26 (t, *J* = 11.2 Hz, 1 H), 6.15 (dd, *J* = 14.6, 10.7 Hz, 1 H), 5.79-5.72 (m, 1 H), 5.77 (t, *J* = 15.6 Hz, 1 H), 5.44 (d, *J* = 12.2 Hz, 1 H, A of AB system), 5.40 (d, *J* = 12.2 H, 1 H, B of AB system), 4.38 (br d, *J* = 7.8 Hz, 1 H), 3.77 (s, 3 H), 3.32 (dd, *J* = 14.2, 5.9 Hz, 1 H), 3.26-3.16 (m, 2 H), 3.04 (dd, *J* = 14.2, 5.9 Hz, 1 H), 2.86-2.76 (m, 1 H), 2.69-2.62 (m, 1 H), 2.53-2.45 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 163.4, 151.3, 147.4, 138.1, 135.8, 135.5, 134.6, 133.6, 131.9, 130.0, 129.4, 128.9, 128.8, 128.6, 127.0, 124.5, 123.1, 121.7, 118.1, 115.9, 115.8, 115.5, 69.0, 56.6, 55.3, 51.4, 41.5, 36.9, 16.8; $[\alpha]_D^{27}$ –2.2° (*c* 2.4 , $CHCl_3$); IR (thin film) 3072, 3034, 2996, 2948, 2846, 1728, 1658, 1456, 1436, 1394, 1351, 1323, 1264, 1208, 1158, 1143, 1120, 1021, 980, 751, 709 cm^{-1}; HRMS (ES) calcd for $C_{36}H_{35}N_2O_6$ $[M + H]^+$ 591.2495, found 591.2486 *m/z*.



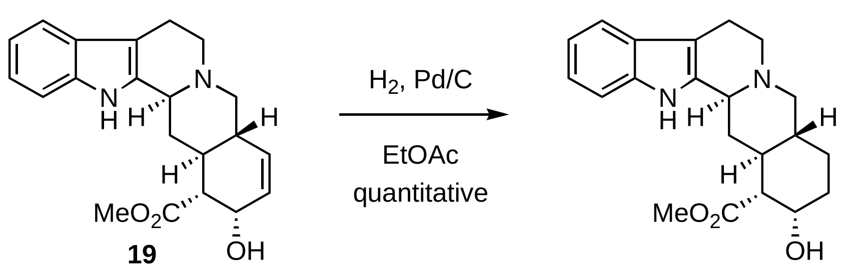
(3*E*,5*E*,8*S*,9*R*,10*Z*,12*E*)-11-bromo-9-(*tert*-butyl-dimethyl-silanyloxy)-14-hydroxy-8-[(6-Deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-tetradeca-3,5,10,12-tetraen-2-one (15). Triene **4b** (47 mg, 0.08 mmol) was dried azeotropically by evaporation of a benzene solution. The resulting solid residue was dissolved in CH_3CN (2.6 mL) and $Sc(OTf)_3$ (79 mg, 0.16 mmol) was added. The reaction mixture was stirred for 15 h at which point additional $Sc(OTf)_3$ (39 mg, 0.08

mmol) was added. The reaction mixture was then stirred an additional 13 h at which point $Sc(OTf)_3$ (39 mg, 0.08 mmol) was again added. This mixture was stirred for 15 h at which point **4b** had been consumed as judged by TLC analysis. The reaction mixture was poured into a biphasic mixture of saturated $NaHCO_3$ and CH_2Cl_2. This biphasic mixture was shaken in the separatory funnel, additional saturated $NaHCO_3$ was added, the mixture was further agitated, additional saturated $NaHCO_3$ was added, and the mixture was shaken again. The aqueous layer was then extracted three times with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4, filtered, and concentrated yielding a yellow oil. Purification of this oil by column chromatography (25x150mm silica, gradient solvent system of 5 → 10 → 15 → 20% acetone in hexanes) afforded **15** (41 mg, 87%) as a white solid: ^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (br d, 7.8 Hz, 1 H), 8.07-8.04 (m, 2 H), 7.60-7.57 (m, 2 H), 7.56-7.52 (m, 1 H), 7.42-7.33 (m, 5 H), 7.29-7.21 (m, 3 H), 6.02 (ddd, *J* = 9.8, 4.4, 2.9 Hz, 1 H), 5.83 (d, *J* = 9.8 Hz, 1 H), 5.75 (br t, *J* = 4.4 Hz, 1 H), 5.73 (d, *J* = 12.0 Hz, 1 H, A of AB system), 5.47 (d, *J* = 12.0 Hz, 1 H, B of AB system), 4.22 (br d, *J* = 9.8 Hz, 1 H), 3.58 (s, 3 H), 3.20-3.14 (m, 2 H), 2.86-2.70 (m, 5 H), 2.69-2.64 (m, 1 H), 2.29 (br t, *J* = 10.7 Hz, 1 H), 2.16 (dddd, *J* = 11.7, 11.7, 11.7, 2.9 Hz, 1 H), 1.30 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 165.8, 151.4, 136.8, 136.2, 135.3, 134.4, 133.1, 130.1, 129.7, 129.2, 129.0, 128.7, 128.6, 128.4, 124.7, 124.3, 122.9, 118.0, 116.5, 115.4, 68.7, 67.4, 59.6, 59.2, 51.7, 49.1, 47.2, 37.2, 36.4, 31.4, 22.4; $[\alpha]_D^{32}$ +139.0° (*c* 2.0 , $CHCl_3$); IR (thin film) 3064, 3033, 2995, 2949, 2916, 2848, 2809, 1730, 1457, 1436, 1394, 1350, 1315, 1269, 1212, 1162, 1112, 1070, 1026, 742, 712 cm^{-1}; HRMS (ES) calcd for $C_{36}H_{35}N_2O_6$ $[M + H]^+$ 591.2495, found 591.2480 *m/z*.



(2*Z*,4*E*,6*Z*,8*R*,9*S*,11*E*,13*E*)-6-bromo-8-(*tert*-butyl-dimethyl-silanyloxy)-15-oxo-9-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-hexadeca-2,4,6,11,13-pentaenoic acid methyl ester (19). Pentacycle **15** (9 mg, 0.015 mmol) was dried azeotropically by evaporation of a benzene solution. The resulting dry residue was dissolved in THF (220 μL) and MeOH (180 μL) added.

Cs_2CO_3 (12 mg, 0.037 mmol) was then added and the resulting heterogeneous mixture was stirred vigorously for 2 h at which point the mixture was homogeneous. TLC analysis of this mixture indicated the complete consumption of **15**. The reaction mixture was diluted with saturated NH_4Cl and transferred to a separatory funnel. The reaction flask was rinsed with ethyl acetate and these rinses were added to the separatory funnel. The mixture was shaken, the layers were separated, and the aqueous layer was extracted twice with ethyl acetate. The combined organic phases were washed with saturated $NaHCO_3$ (shaken ≥ 1 min) then washed with saturated NaCl, dried over Na_2SO_4, filtered, and concentrated yielding a yellow oil. Purification of this oil by preparative TLC (250 uM silica plate, 7 % MeOH in CH_2Cl_2) afforded **15** (4.3 mg, 80%) as a clear oil: ^1H NMR (500 MHz, $CDCl_3$) δ7.83 (br s, 1 H), 7.47 (d, *J* = 7.3 Hz, 1 H), 7.30 (d, *J* = 7.8 Hz, 1 H), 7.16-7.12 (m, 1 H), 7.11-7.07 (m, 1 H), 5.91 (ddd, *J* = 9.8, 4.9, 2.9 Hz, 1 H), 5.74 (d, *J* = 9.8 Hz, 1 H), 4.44 (br t, *J* = 3.9 Hz, 1 H), 3.81 (s, 3 H), 3.43, (br d, *J* = 9.8 Hz, 1 H), 3.15-3.09 (m, 2 H), 3.00 (dddd, *J* = 15.1, 8.8, 5.9, 2.4 Hz, 1 H), 2.77-2.65 (m, 2 H), 2.62 (dd, *J* = 11.7, 3.9, Hz, 1 H), 2.43 (dt, *J* = 12.2, 2.9 Hz, 1 H), 2.30 (ddd, *J* = 11.7, 11.7, 11.7, 1 H), 2.30-2.23 (m, 1 H), 1.93 (dddd, *J* = 11.7, 11.7, 11.7, 2.9 Hz, 1 H), 1.39 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 136.0, 134.3, 132.5, 127.9, 127.3, 121.4, 119.4, 118.1, 110.8, 108.1, 65.1, 60.1, 59.8, 52.9, 51.8, 50.5, 40.9, 34.9, 33.0, 21.8; $[\alpha]_D^{28}$+44.2 ° (*c* 0.21, $CHCl_3$); IR (thin film) 3377, 3360, 3054, 3024, 2948, 2916, 2851, 2811, 2759, 1727, 1452, 1438, 1378, 1353, 1323, 1293, 1265, 1219, 1201, 1176, 1156, 1082, 1046, 1004, 740 cm^{-1}; HRMS (ES) calcd for $C_{21}H_{25}N_2O_3$ $[M + H]^+$ 353.1865 found 353.1852 *m/z*.



(1*R*,2*S*,,3*aS*,4*S*,5*R*,7a*S*)-3-[7-bromo-1-(*tert*-butyl-dimethyl-silanyloxy)-4-(3-oxo-but-1-enyl)-2-[(6-Deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]--2,3,3a,4,5,7a-hexahydro-1*H*-inden-5-yl]-acrylic acid methyl ester (1). Olefin **17** was dissolved in ethyl acetate, transferred to a 5 mL round-bottom flask, and concentrated. The residue was redissolved in ethyl acetate (HPLC/GC grade, 600 μL) and 10% Pd/C was added. The reaction vessel containing **17** in ethyl acetate was then evacuated until gentle bumping of the solvent was observed, and then backfilled with H_2. This process was repeated eleven times. The reaction was then stirred under H_2 (balloon pressure) for 14 h at which point the reaction was diluted with ethyl acetate (ca. 1.5 mL), followed by saturated $NaHCO_3$ (ca. 1.5 mL). The biphasic mixture was stirred vigorously for 5 min, transferred to a separatory funnel, further dlited with ethyl acetate and saturated $NaHCO_3$ and shaken for 1 min. The layers were separated and the aqueous layer was extracted with ethyl acetate. The combined organic phases were washed with saturated NaCl, dried over a mixture of Na_2SO_4 and K_2CO_3, filtered, and concentrated yielding (+)-yohimbine (**1**) (4 mg, quantitative) as white solid. An analytical sample of **1** was prepared by preparative TLC (10% isopropanol in CH_2Cl_2): ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (br s, 1 H) 7.47 (d, J = 7.8 Hz, 1 H), 7.31 (d, J = 7.8 Hz, 1 H), 7.16-7.11 (m, 1 H), 7.11-7.06 (m, 1 H), 4.23 (br s, 1 H), 3.82 (s, 3 H), 3.35 (br d, J = 10.7 Hz, 1 H), 3.09 (dd, J = 10.7, 5.4 Hz, 1 H), 3.04-2.95 (m, 1 H), 2.96 (dd, J = 11.2, 2.9 Hz, 1 H), 2.91 (br s, 1 H), 2.75-2.69 (m, 1 H), 2.63 (ddd, J = 11.2, 11.2, 4.4 Hz, 1 H), 2.36 (dd, J = 11.7, 2.4 Hz, 1 H), 2.29-2.23 (m, 1 H), 2.08-1.96 (m, 3 H), 1.64-1.52 (m, 3 H), 1.47-1.42 (m, 1 H), 1.38 (ddd, J = 11.2, 11.2, 11.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 136.0, 134.3, 127.4, 121.4, 119.4, 118.1, 110.7, 108.3, 66.9, 61.3, 59.9, 52.9, 52.3, 52.0, 40.7, 36.7, 34.3, 31.4, 23.3, 21.7; $[\alpha]_D^{30}$ +40.0 ° (c 0.28, EtOH); IR (thin film) 3529, 2918, 2874, 2851, 1726, 1452, 1436, 1323, 1295, 1270, 1207, 1149, 1112, 1096, 1006, 969, 739, 720 cm^{-1}; HRMS (ES) calcd for $C_{21}H_{27}N_2O_3$ $[M + H]^+$ 355.2022 found 355.2014 *m/z*.

Comparison of ^{1}H NMR Spectral Data for Yohimbine (1)

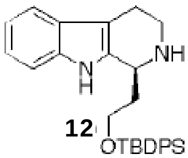
Aubé[a]	This Work	Natural[b]
7.77 (s, 1 H)	7.73 (br s, 1 H)	7.73 (br s, 1 H)
7.46 (d, *J* = 7.7 Hz, 1 H)	7.47 (d, *J* = 7.8 Hz, 1 H)	7.47 (d, *J* = 7.8 Hz, 1 H)
7.29 (dt, *J* = 7.9 Hz, 1 H)	7.31 (d, *J* = 7.8 Hz, 1 H)	7.30 (d, *J* = 7.8 Hz, 1 H)
7.14-7.06 (m, 2 H)	7.16-7.11 (m, 1 H)	7.16-7.11 (m, 1 H)
	7.11-7.06 (m, 1 H)	7.10-7.06 (m, 1 H)
4.22 (br s, 1 H)	4.23 (br s, 1 H)	4.23 (br s, 1 H)
3.81 (s, 3 H)	3.82 (s, 3 H)	3.81 (s, 3 H)
3.33 (br d, *J* = 11.3 Hz, 1 H)	3.35 (br d, *J* = 10.7 Hz, 1 H)	3.35 (br d, *J* = 11.2 Hz, 1 H)
3.07 (m, 1 H)	3.09 (dd, *J* = 10.7, 5.4 Hz, 1 H)	3.09 (dd, *J* = 11.2, 4.9 Hz, 1 H)
3.02-2.93 (m, 3 H)	3.04-2.95 (m, 1 H)	3.03-2.95 (m, 1 H)
	2.96 (dd, *J* = 11.2, 2.9 Hz, 1 H)	2.96 (dd, *J* = 11.2, 2.9 Hz, 1 H)
	2.91 (br s, 1 H)	2.95-2.89 (br s, 1 H)
2.72 (dd, *J* = 15.2, 4.2 Hz, 1 H)	2.75-2.69 (m, 1 H)	2.75-2.69 (m, 1 H)
2.62 (td, *J* = 11.3, 4.3 Hz, 1 H)	2.63 (ddd, *J* = 11.2, 11.2, 4.4 Hz, 1 H)	2.63 (ddd, *J* = 11.2, 11.2, 4.4 Hz, 1 H)
2.34 (dd, *J* = 11.5, 1.9 Hz, 1 H)	2.36 (dd, *J* = 11.7, 2.4 Hz, 1 H)	2.36 (dd, *J* = 11.2, 2.0, 1 H)
2.27-2.23 (m, 1 H)	2.29-2.23 (m, 1 H)	2.29-2.23 (m, 1 H)
2.04-1.98 (m, 3 H)	2.08-1.96 (m, 3 H)	2.07-1.96 (m, 3 H)
1.58 (m, 3 H)	1.64-1.52 (m, 3 H)	1.65-1.51 (m, 3 H)
1.43 (m, 1 H)	1.47-1.42 (m, 1 H)	1.46-1.42 (m, 1 H)
1.37 (q, *J* = 11.7 Hz 1 H)	1.38 (ddd, *J* = 11.2, 11.2, 11.2 Hz, 1 H)	1.38 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1 H)

a) Aubé, J.; Ghosh, S.; Tanol, M. *J. Am. Chem. Soc.* **1994**, *116*, 9009–9018. b) Data were obtained by measuring the ^{1}H NMR spectrum of natural **1**.

Comparison of ^{13}C NMR Spectral Data for (+)-Yohimbine (1)

Aubé[a]	This Work	Natural[b]
175.6	175.6	175.6
135.9	136.0	135.9
134.5	134.3	134.5
127.4	127.4	127.4
121.3	121.4	121.3
119.4	119.4	119.3
118.1	118.1	118.1
110.7	110.7	110.7
108.2	108.3	108.2
66.9	66.9	66.9
61.3	61.3	61.3
59.8	59.9	59.8
52.9	52.9	52.8
52.3	52.3	52.3
51.9	52.0	51.9
40.7	40.7	40.7
36.7	36.7	36.7
34.3	34.3	34.3
31.4	31.4	31.5
23.3	23.3	23.3
21.7	21.7	21.7

a) Aubé, J.; Ghosh, S.; Tanol, M. *J. Am. Chem. Soc.* **1994**, *116*, 9009–9018. b) Data were obtained by recording the ^{13}C NMR spectrum of **1** obtained commercially from Aldrich.



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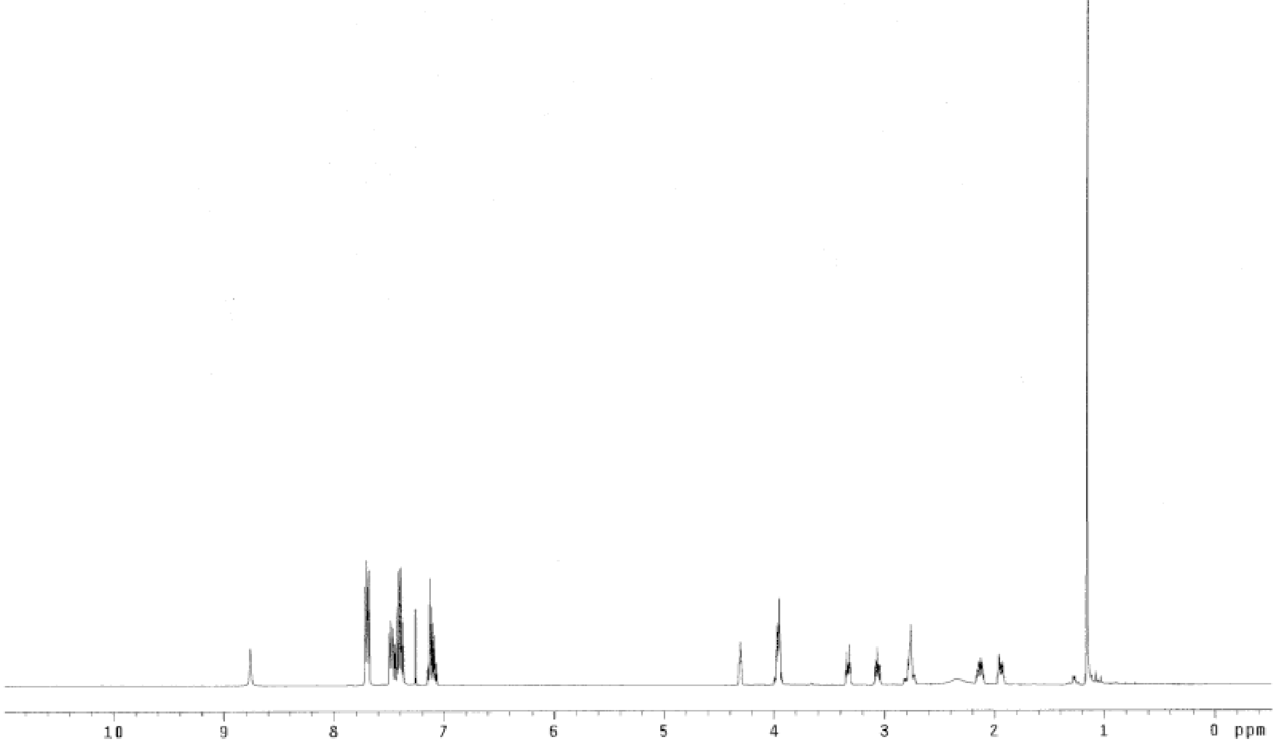

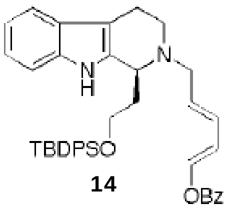

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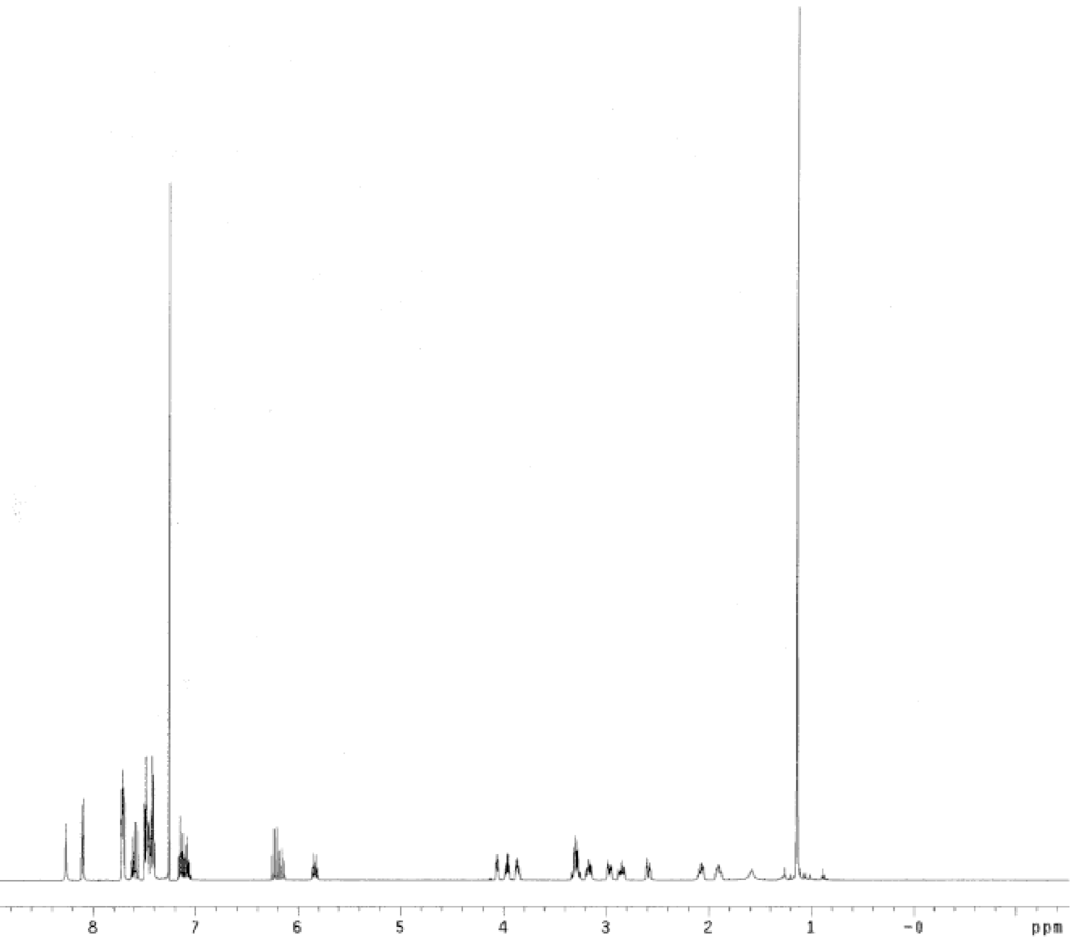

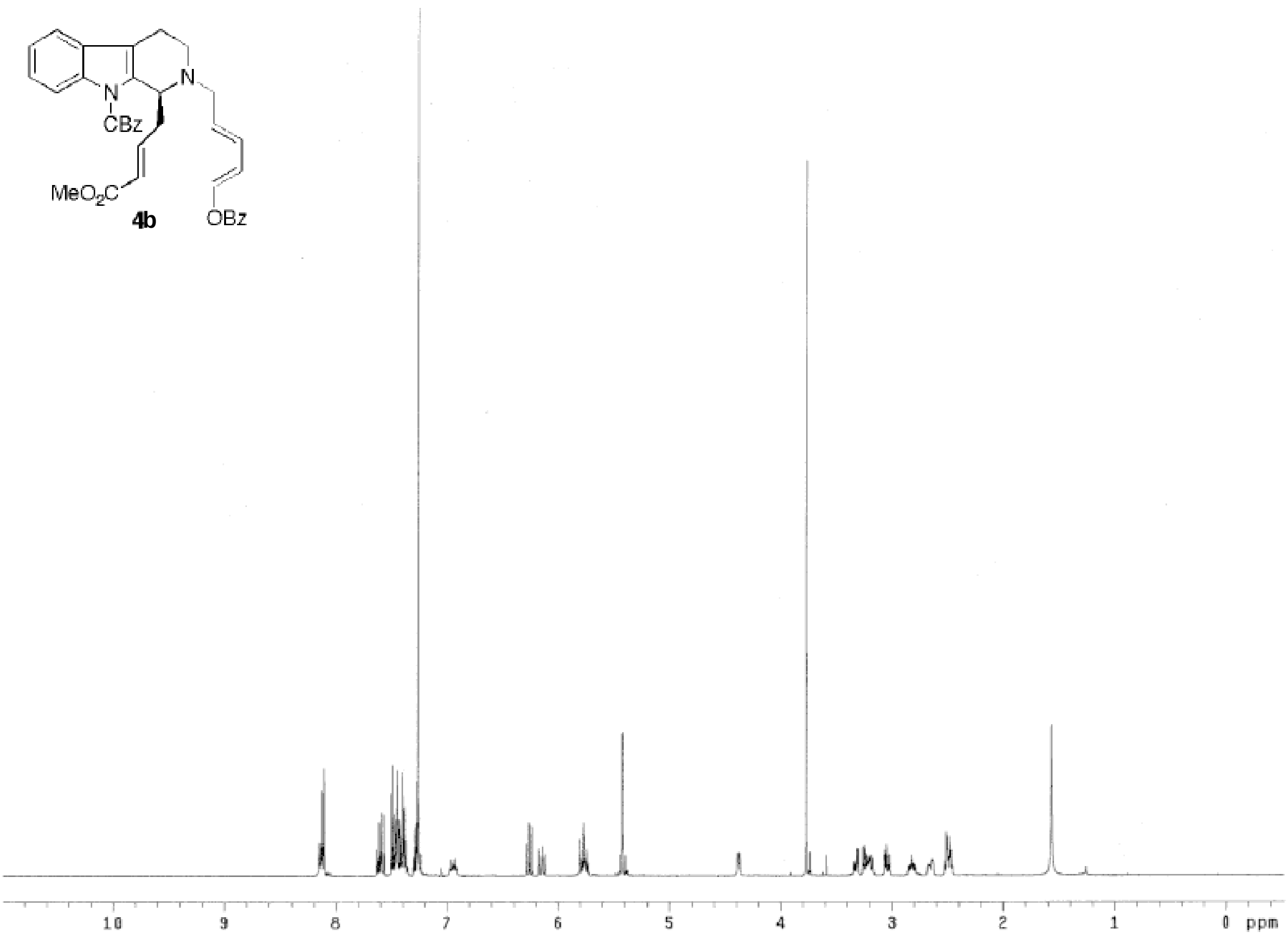
N
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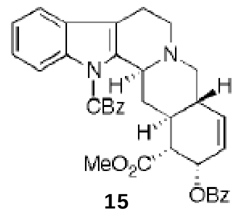
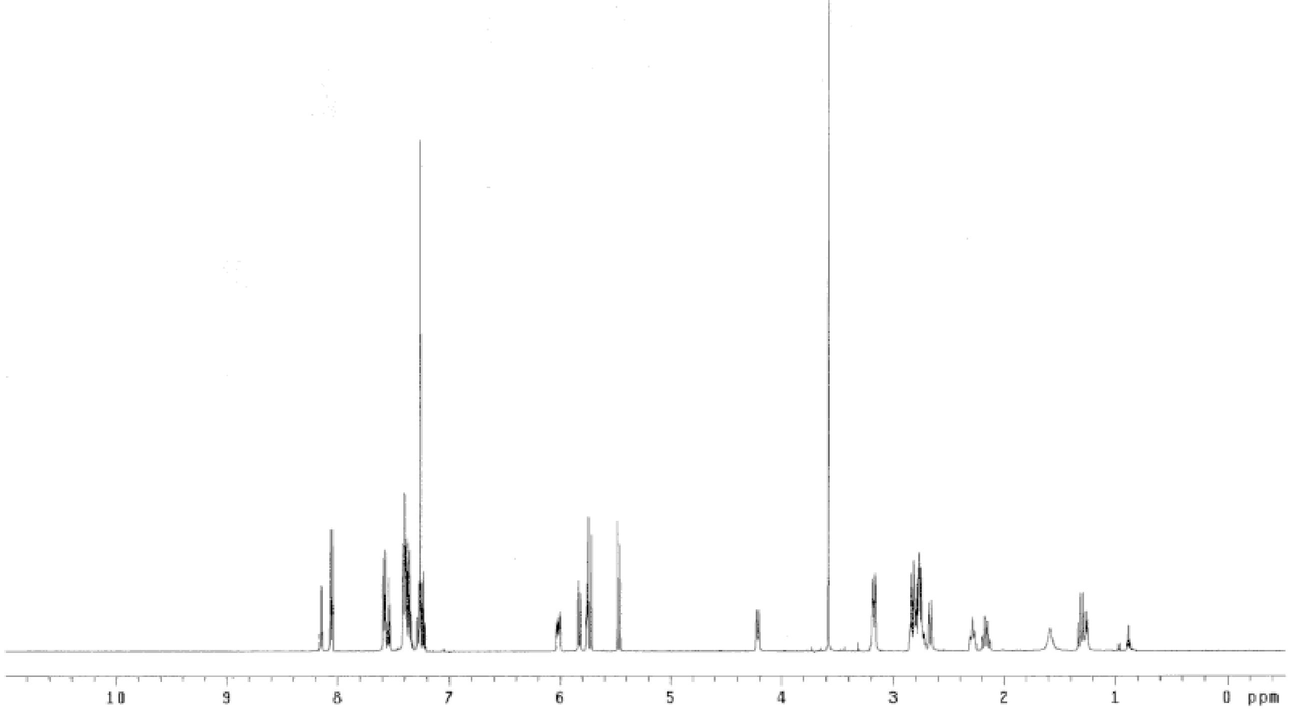
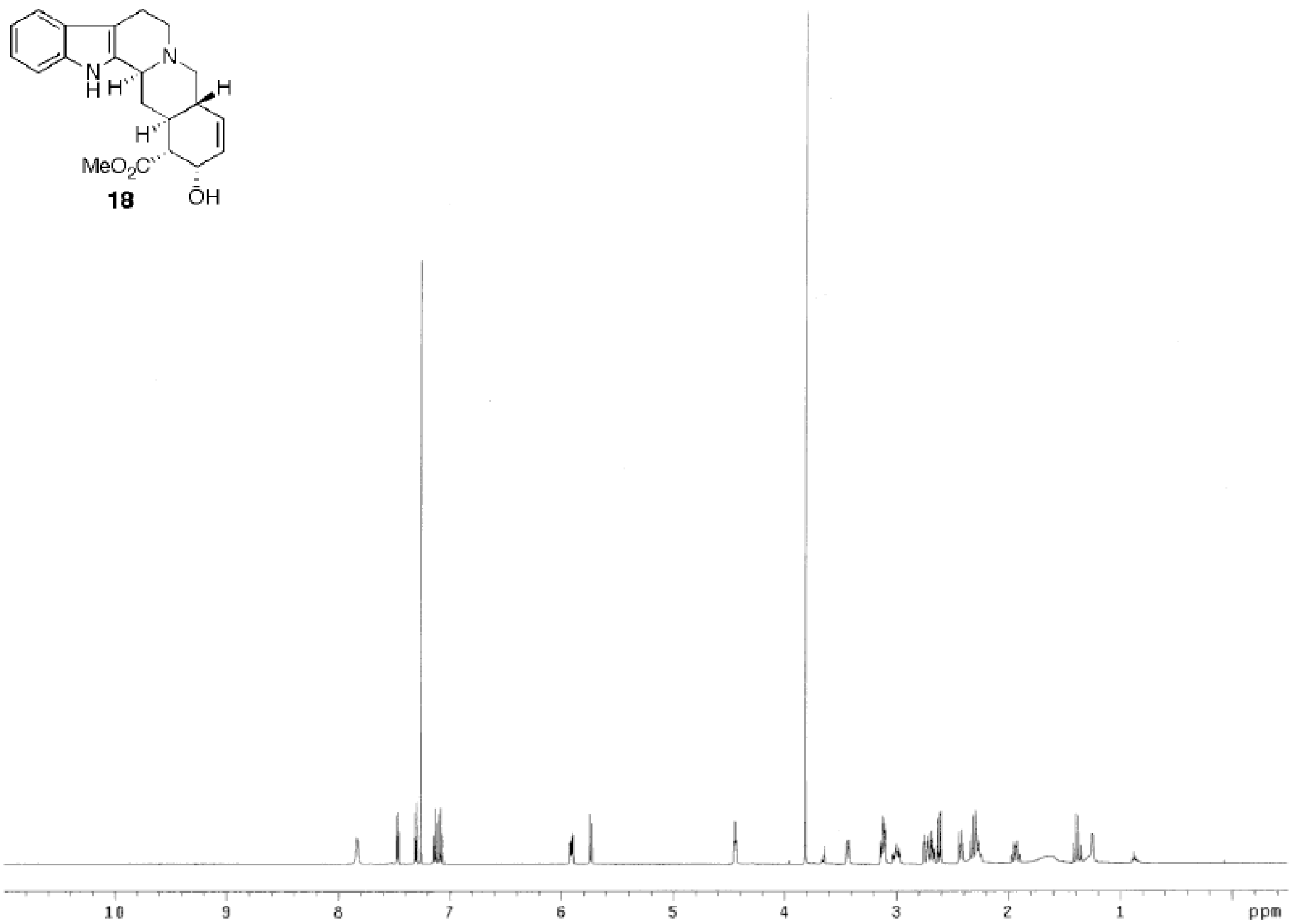
CBz
MeO2C
4b
OBz
10
9
8
7
6
5
4
3
2
1
0 ppm

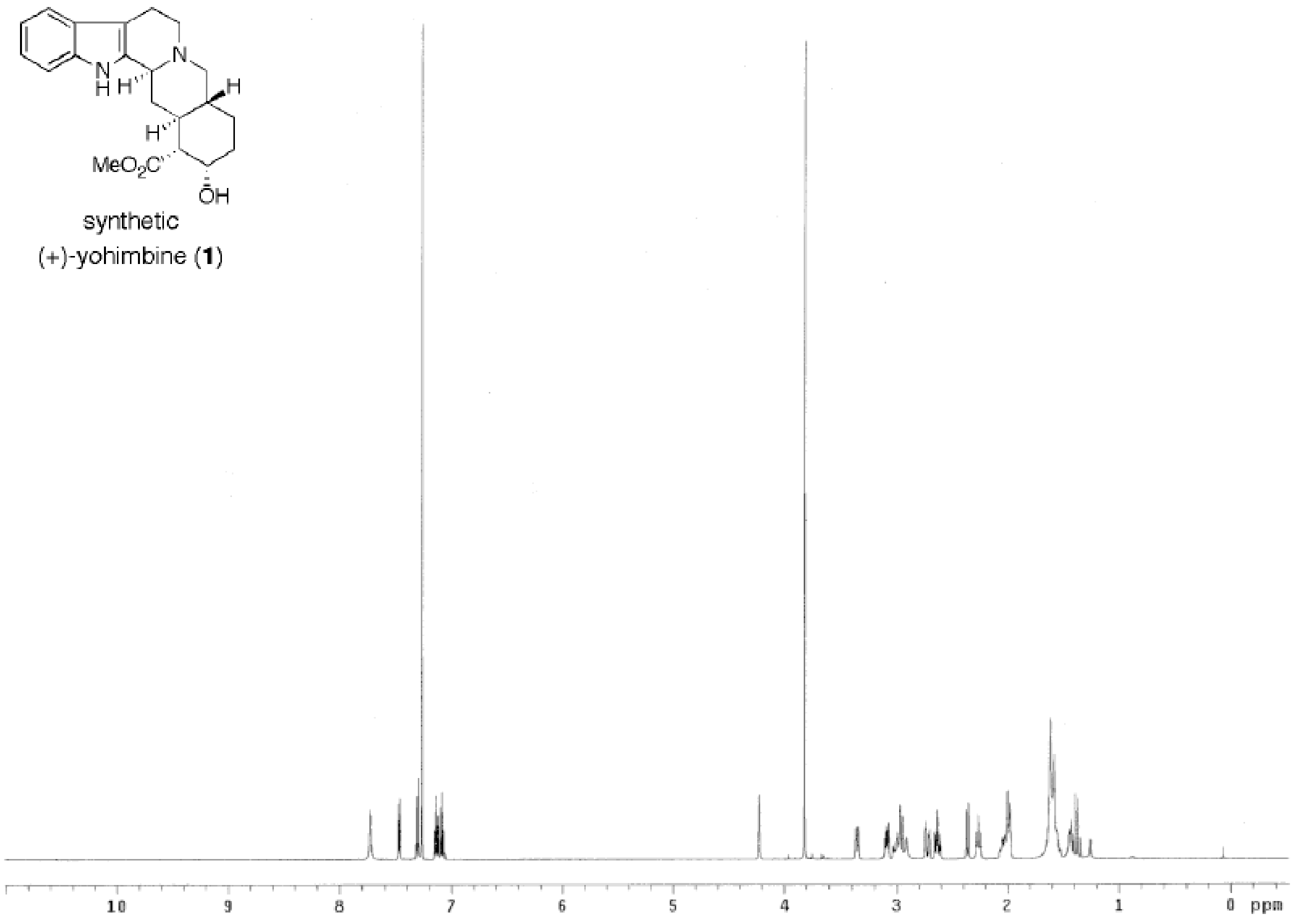


15

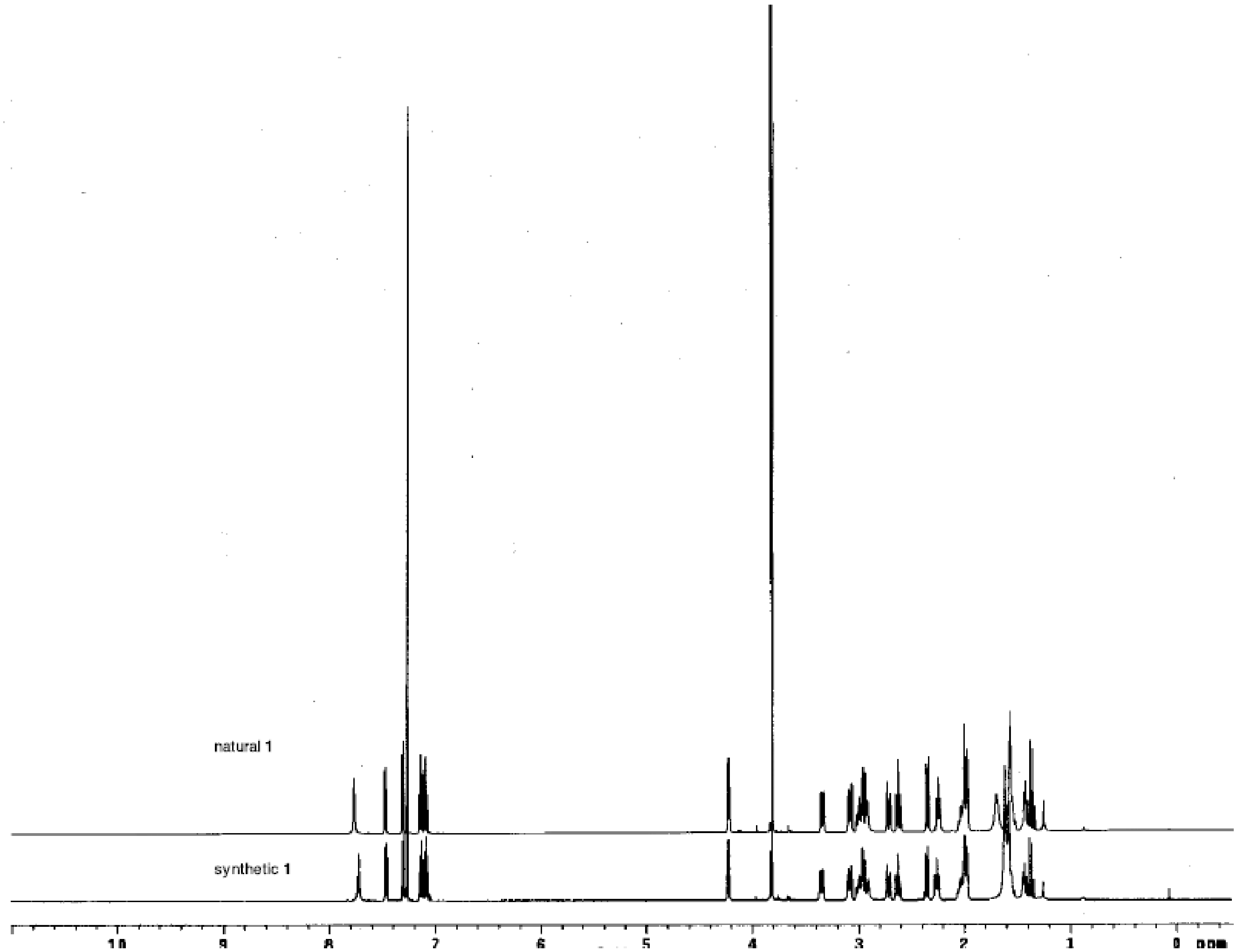




N
NH
H
H
H
MeO2C
OH
18
10
9
8
7
6
5
4
3
2
1
ppm



synthetic
(+)-yohimbine (**1**)


natural 1
synthetic 1
10
9
8
7
6
5
4
3
2
1
0 ppm

Calculations

A. Methods. Calculations were performed using the Gaussian 98 program[5] with the B3LYP[6] or MP2[7] methods, as specified. The 6-31G(d), 6-31+G(d), and 6-311+G(d,p) basis sets of Pople and coworkers were used, as specified.[8] All B3LYP/6-31G(d) transition structures were shown to be legitimate first-order saddle points by the existence of a single imaginary frequency. Single-point energy calculations at the B3LYP/6-31+G(d)// B3LYP/6-31G(d) and B3LYP/6-311+G(d,p)//B3LYP/6-31G(d) levels employed the keyword SCF=Tight. Unscaled zero-point vibrational energy corrections at the B3LYP/6-31G(d) level are included where specified. The following units are used: relative energy, kcal/mol; absolute energy, Hartree; distance, Å.

B. Model Study. A model study was conducted to evaluate the effect of level of theory and basis set on the geometries (i.e. length of forming C–C bonds) and relative energies of Diels-Alder transition structures.

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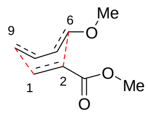
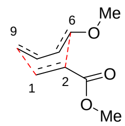
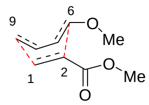
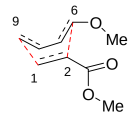
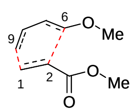
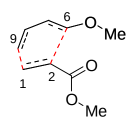
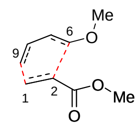
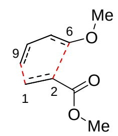
(5) Gaussian 98, Revision A.11.3, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, Jr., J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennuci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Rega, N.; Salvador, P.; Dannenberg, J. J.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Head-Gordon, M; Replogle, E. S.; Pople, J. A.; Gaussian, Inc., Pittsburgh PA, 2002.
(6) B3LYP = Becke-3-Lee-Yang-Parr density functional theory. (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372–1377. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789.
(7) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618–622.
(8) (a) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1971**, *54*, 724–728. (b) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257–2261. (c) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta.* **1973**, *28*, 213–223.

Endo transition structures:

				
Geometry				
B3LYP:	C1-C9/C2-C6	C1-C9/C2-C6	C1-C9/C2-C6	C1-C9/C2-C6
6-31G(d)	2.026/2.772	2.028/2.727	1.997/2.699	2.000/2.669
6-31G+G(d)	2.011/2.763	2.014/2.760	1.973/2.747	1.983/2.703
6-311G+G(d,p)	2.001/2.730	2.003/2.728	1.963/2.712	1.972/2.672
MP2:				
6-31G(d)	2.139/2.570	2.146/2.562	2.112/2.506	2.105/2.504
6-31+G(d)	2.134/2.579			
Relative Energy				
B3LYP:				
6-31G(d)	0.0 (def)	0.07	0.83	1.35
6-31G+G(d)		0.28	0.79	1.69
6-311G+G(d,p)		0.31	1.04	1.92
6-31G+G(d)//6-31G(d)		0.24	0.79	1.66
6-311G+G(d,p)//6-31G(d)		0.29	1.01	1.89
MP2//B3LYP				
6-31G(d)/6-31G(d)		0.65	0.62	0.89
MP2:				
6-31G(d)		0.61	0.45	0.95
6-31+G(d)				
6-31+G(d)//6-31G(d)				

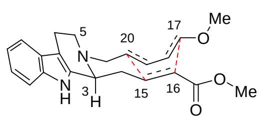
Exo transition structures:

				
Geometry				
B3LYP:	C1-C9/C2-C6	C1-C9/C2-C6	C1-C9/C2-C6	C1-C9/C2-C6
6-31G(d)	1.989/2.835	1.993/2.795	1.989/2.716	2.007/2.671
6-31G+G(d)	1.977/2.860	1.979/2.824	1.969/2.760	1.988/2.714
6-311G+G(d,p)	1.964/2.829	1.968/2.794	1.961/2.720	1.978/2.676
MP2:				
6-31G(d)	2.106/2.624		2.113/2.530	
6-31+G(d)	2.123/2.553		2.112/2.531	
Relative Energy				
B3LYP:				
6-31G(d)	–0.50	0.09	0.06	1.73
6-31G+G(d)	–0.09	0.46	0.24	1.85
6-311G+G(d,p)	0.07	0.55	0.46	2.01
6-31G+G(d)//6-31G(d)	–0.09	0.44	0.21	1.81
6-311G+G(d,p)//6-31G(d)	0.08	0.55	0.44	1.96
MP2//B3LYP:				
6-31G(d)//6-31G(d)	1.29	2.11	0.62	1.72
MP2:				
6-31G(d)	1.38		0.79	
6-31+G(d)	1.91		1.09	
6-31+G(d)//6-31G(d)	2.23		1.09	

Energies are electronic energies and do not include zero-point vibrational energy corrections.

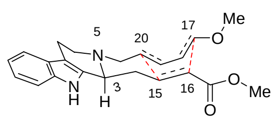
C. Relative energies and geometries of IMDA transition structures using substrate 4a.

Endo, C(3)-C(15) *cis*:



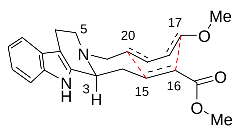
Geometry, B: 2.040/2.657
Geometry, M: 2.171/2.576

B/6-31G(d): 2.91
B/6-31+G(d): 2.96
B/6-311+G(d,p): 2.58
M/6-31G(d): 2.18



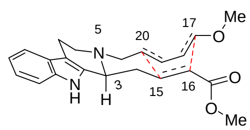
Geometry, B: 2.049/2.675
Geometry, M: 2.174/2.609

B/6-31G(d): 0.71
B/6-31+G(d):0.42
B/6-311+G(d,p): 0.06
M/6-31G(d): 0.46



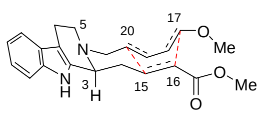
Geometry, B: 2.055/2.639

B/6-31G(d):3.47
B/6-31+G(d): 3.40
B/6-311+G(d,p): 3.27



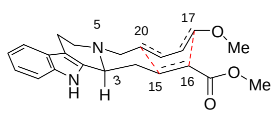
Geometry, B: 2.055/2.670

B/6-31G(d): 1.14
B/6-31+G(d): 0.94
B/6-311+G(d,p): 0.66



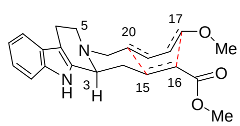
Geometry, B: 2.004/2.642

B/6-31G(d): 4.42
B/6-31+G(d): 4.31
B/6-311+G(d,p): 4.21



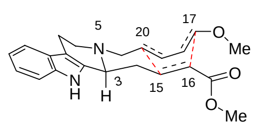
Geometry, B: 2.014/2.662

B/6-31G(d): 2.15
B/6-31+G(d): 1.76
B/6-311+G(d,p): 1.63



Geometry, B: 2.010/2.614

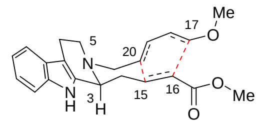
B/6-31G(d): 5.14
B/6-31+G(d): 5.32
B/6-311+G(d,p): 5.18



Geometry, B: 2.015/2.637

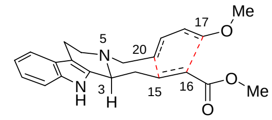
B/6-31G(d): 2.89
B/6-31+G(d): 2.86
B/6-311+G(d,p): 2.62

Exo, C(3)-C(15) *cis*:



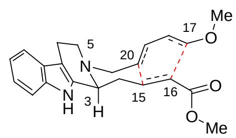
Geometry, B: 2.014/2.612
Geometry, M: 2.157/2.518

B/6-31G(d): 4.86
B/6-31+G(d): 5.00
B/6-311+G(d,p): 4.91
M/6-31G(d): 4.18



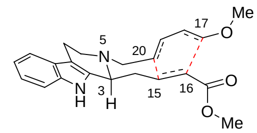
Geometry, B: 2.001/2.683
Geometry, M: 2.142/2.590

B/6-31G(d): 0.68
B/6-31+G(d): 0.77
B/6-311+G(d,p): 0.49
M/6-31G(d): 0.0 (def)



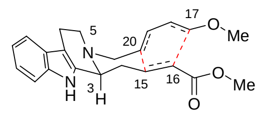
Geometry, B: 2.039/2.570

B/6-31G(d): 6.55
B/6-31+G(d): 6.48
B/6-311+G(d,p): 6.39



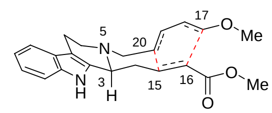
Geometry, B: 2.019/2.653

B/6-31G(d): 2.44
B/6-31+G(d): 2.39
B/6-311+G(d,p): 2.02



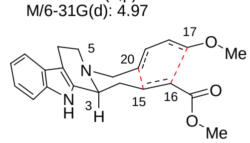
Geometry, B: 2.001/2.738
Geometry, M: 2.158/2.613

B/6-31G(d): 4.48
B/6-31+G(d): 5.02
B/6-311+G(d,p): 4.80
M/6-31G(d): 4.97



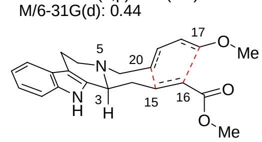
Geometry, B: 1.999/2.808
Geometry, M: 2.147/2.684

B/6-31G(d): 0.0 (def)
B/6-31+G(d): 0.0 (def)
B/6-311+G(d,p): 0.0 (def)
M/6-31G(d): 0.44



Geometry, B: 2.006/2.703

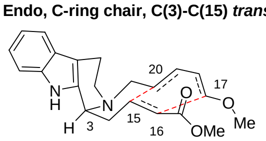
B/6-31G(d): 5.20
B/6-31+G(d): 5.72



Geometry, B: 2.005/2.768

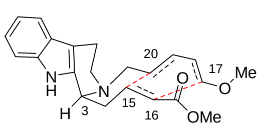
B/6-31G(d): 0.71
B/6-31+G(d): 0.67
B/6-311+G(d,p): 0.54

Endo, C-ring chair, C(3)-C(15) *trans*:



Geometry, B: 2.043/2.670

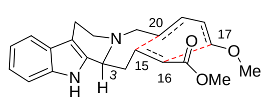
B/6-31G(d): 3.78
B/6-311+G(d,p): 3.18
M/6-31G(d): 0.77



Geometry, B: 2.008/2.655

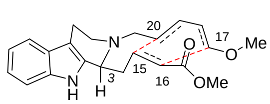
B/6-31G(d): 5.11
B/6-311+G(d,p): 4.71

Endo, C-ring boat, C(3)-C(15) *trans*:



Geometry, B: 2.014/2.617

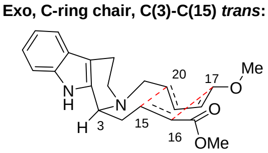
B/6-31G(d): 5.04
B/6-311+G(d,p): 4.55



Geometry, B: 1.980/2.604

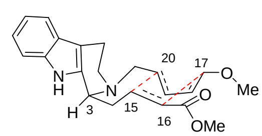
B/6-31G(d): 6.14
B/6-311+G(d,p): 5.84

Exo, C-ring chair, C(3)-C(15) *trans*:



Geometry, B: 1.991/2.797

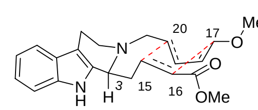
B/6-31G(d): 2.88
B/6-311+G(d,p): 3.04
M/6-31G(d): 0.72



Geometry, B: 1.994/2.679

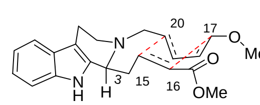
B/6-31G(d): 3.68
B/6-311+G(d,p): 3.63

Exo, C-ring boat, C(3)-C(15) *trans*:



Geometry, B: 1.970/2.703

B/6-31G(d): 5.02
B/6-311+G(d,p): 5.10



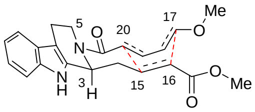
Geometry, B: 1.985/2.579

B/6-31G(d): 5.79
B/6-311+G(d,p): 5.72

Geometry = C15-C20/C16-C17; all geometries obtained using the 6-31G(d) basis set. B = B3LYP, M = MP2.
Energies are electronic energies and include unscaled B3LYP/6-31G(d) zero-point vibrational energy corrections.

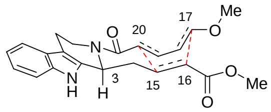
D. Relative energies and geometries of IMDA transition structures using substrate 5.

Endo, C(3)-C(15) *cis*:



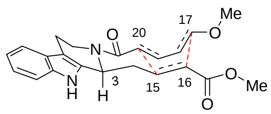
Geometry, B: 2.049/2.654

B/6-31G(d): 6.88
B/6-311+G(d,p): 6.38



Geometry, B: 2.047/2.634

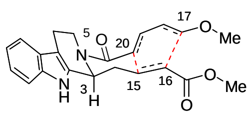
B/6-31G(d): 0.98
B/6-311+G(d,p): 0.58



Geometry, B: 2.012/2.618

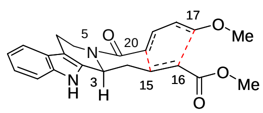
B/6-31G(d): 2.13
B/6-311+G(d,p): 1.86

Exo, C(3)-C(15) *cis*:



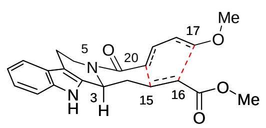
Geometry, B: 2.003/2.654

B/6-31G(d): 7.55
B/6-311+G(d,p): 6.83



Geometry, B: 1.993/2.803

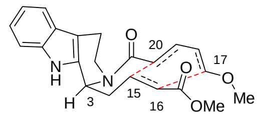
B/6-31G(d): 1.72
B/6-311+G(d,p): 0.91



Geometry, B: 2.003/2.675

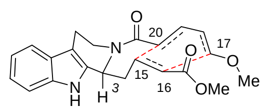
B/6-31G(d): 2.50
B/6-311+G(d,p): 1.78

Endo, C-ring chair, C(3)-C(15) *trans*:



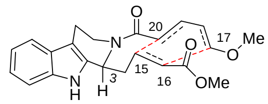
Geometry, B: 2.039/2.618

B/6-31G(d): 1.70
B/6-311+G(d,p): 1.28



Geometry, B: 2.022/2.584

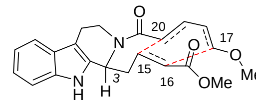
B/6-31G(d): 0.25
B/6-311+G(d,p): 0.25



Geometry, B: 1.987/2.568

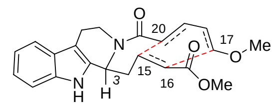
B/6-31G(d): 1.41
B/6-311+G(d,p): 1.54

Endo, C-ring boat, C(3)-C(15) *trans*:



Geometry, B: 2.034/2.524

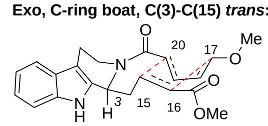
B/6-31G(d): 0.0 (def.)
B/6-311+G(d,p): 0.0 (def.)



Geometry, B: 1.998/2.506

B/6-31G(d): 1.32
B/6-311+G(d,p): 1.49

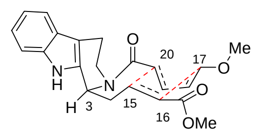
Exo, C-ring boat, C(3)-C(15) *trans*:



Geometry, B: 1.963/2.788

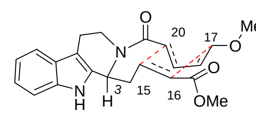
B/6-31G(d): 2.80
B/6-311+G(d,p): 2.56

Exo, C-ring chair, C(3)-C(15) *trans*:



Geometry, B: 1.986/2.779

B/6-31G(d): 2.60
B/6-311+G(d,p): 2.14



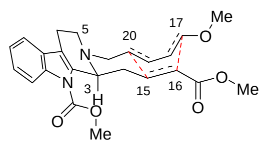
Geometry, B: 1.959/2.719

B/6-31G(d): 3.24
B/6-311+G(d,p): 3.15

Geometry = C15-C20/C16-C17; all geometries obtained using the 6-31G(d) basis set. B = B3LYP.
Energies are electronic energies and include unscaled B3LYP/6-31G(d) zero-point vibrational energy corrections.

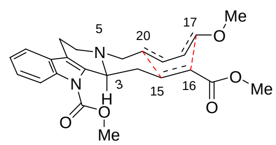
E. Relative energies and geometries of IMDA transition structures using substrate <u>4c</u>.

Endo, C(3)-C(15) *cis*:



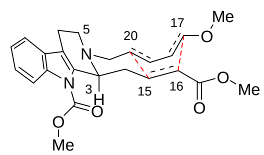
Geometry, B: 2.043/2.649

B/6-31G(d): 0.78
B/6-311+G(d,p): 0.82



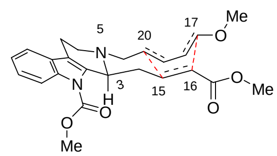
Geometry, B: 2.045/2.664

B/6-31G(d): 0.15
B/6-311+G(d,p): 0.0 (def)



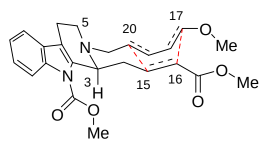
Geometry, B: 2.040/2.649

B/6-31G(d): 0.88
B/6-311+G(d,p): 0.91



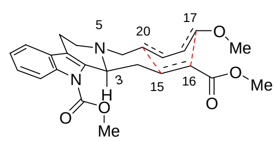
Geometry, B: 2.044/2.669

B/6-31G(d): 0.54
B/6-311+G(d,p):0.31



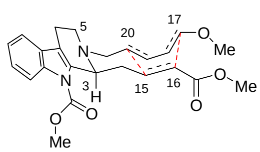
Geometry, B: 2.007/2.639

B/6-31G(d): 2.29
B/6-311+G(d,p): 2.24



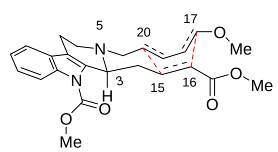
Geometry, B: 2.013/2.652

B/6-31G(d): 1.70
B/6-311+G(d,p):1.66



Geometry, B: 2.004/2.640

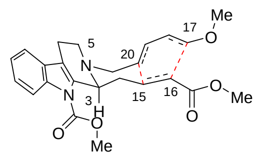
B/6-31G(d): 2.34
B/6-311+G(d,p): 2.53



Geometry, B: 2.011/2.660

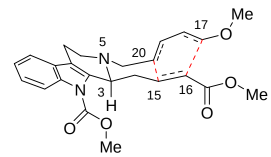
B/6-31G(d): 1.98
B/6-311+G(d,p):1.89

Exo, C(3)-C(15) *cis*:



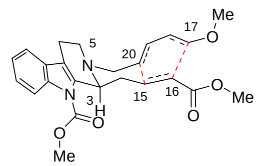
Geometry, B: 2.024/2.593

B/6-31G(d): 3.24
B/6-311+G(d,p):4.29



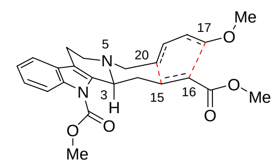
Geometry, B: 2.003/2.673

B/6-31G(d): 0.58
B/6-311+G(d,p):0.77



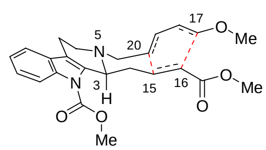
Geometry, B: 2.022/2.591

B/6-31G(d): 3.23
B/6-311+G(d,p):3.76



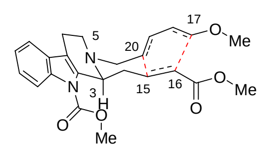
Geometry, B: 2.000/2.678

B/6-31G(d): 0.71
B/6-311+G(d,p):0.98



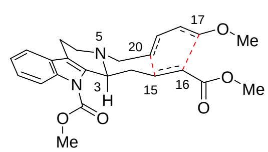
Geometry, B: 1.996/2.804

B/6-31G(d): 0.01
B/6-311+G(d,p):0.35



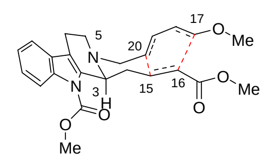
Geometry, B: 2.003/2.731

B/6-31G(d): 2.96
B/6-311+G(d,p):3.41



Geometry, B: 1.997/2.796

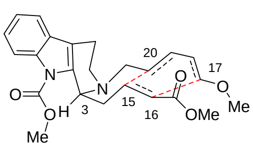
B/6-31G(d): 0.0 (def)
B/6-311+G(d,p): 0.41



Geometry, B: 2.002/2.726

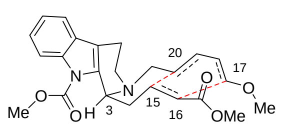
B/6-31G(d): 2.84
B/6-311+G(d,p):3.46

Endo, C-ring chair, C(3)-C(15) *trans*:



Geometry, B: 2.037/2.699

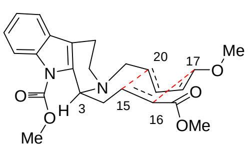
B/6-31G(d): 6.19
B/6-311+G(d,p): 5.75



Geometry, B: 2.036/2.688

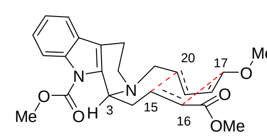
B/6-31G(d): 5.33
B/6-311+G(d,p): 4.95

Exo, C-ring chair, C(3)-C(15) *trans*:



Geometry, B: 1.990/2.823

B/6-31G(d): 5.25
B/6-311+G(d,p): 5.42

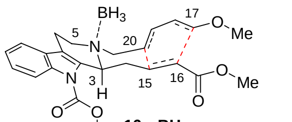


Geometry, B: 1.985/2.823

B/6-31G(d): 4.79
B/6-311+G(d,p): 5.16

Geometry = C15-C20/C16-C17; all geometries obtained using the 6-31G(d) basis set. B = B3LYP, M = MP2.
Energies are electronic energies and include unscaled B3LYP/6-31G(d) zero-point vibrational energy corrections.

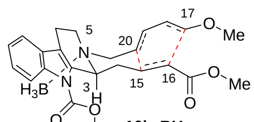
F. Relative energies and geometries of IMDA transition structures using substrate <u>4c</u>•BH_3.



16a•BH_3

Geometry, B: 2.081/2.563

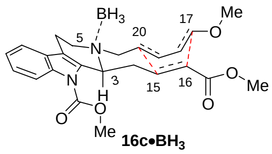
B/6-31G(d): 8.96
B/6-311+G(d,p): 10.0



16b•BH_3

Geometry, B: 2.010/2.766

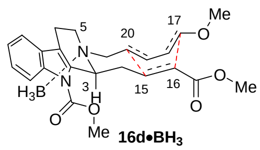
B/6-31G(d): 3.24
B/6-311+G(d,p): 3.79



16c•BH_3

Geometry, B: 2.051/2.626

B/6-31G(d): 2.81
B/6-311+G(d,p): 3.61

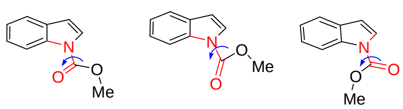


16d•BH_3

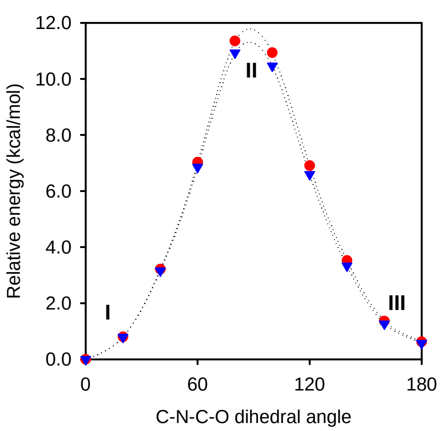
Geometry, B: 2.044/2.699

B/6-31G(d): 0.0 (def)
B/6-311+G(d,p): 0.0 (def)

G. Torsional energy profile for the rotation of a carbamate C=O relative to the indole aromatic plane. Two stationary points (**I** and **III**) were located at the B3LYP/6-31G(d) level and shown to be local minima by the existence of no imaginary frequencies. The C-N-C-O dihedral angle shown in red was then fixed and varied in 20° increments and all other coordinates fully relaxed. The relative energies of the resulting structures at the B3LYP/6-31G(d)//B3LYP/6-31G(d) (●) and B3LYP/6-311+G(d,p)//B3LYP/6-31G(d) (▼) are plotted below. The C-N-C-O dihedral angles of local minima **I** and **III** are 0.01° and 179.97°.



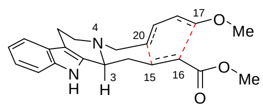
I **II** **III**



H. N(1)-C(2)-C(3)-C(14) dihedral angle in TSs <u>8a–8d</u> and <u>16a–16d</u>

TS	N(1)-C(2)-C(3)-C(14) dihedral angle	TS	N(1)-C(2)-C(3)-C(14) dihedral angle
8a	45.3	**16a**	51.9
8b	59.9	**16b**	65.6
8c	47.6	**16c**	54.8
8d	64.8	**16d**	69.2

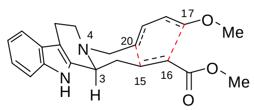
I. Complete geometries and absolute energies of transition structures depicted in Figures 1–3.



8a: 0.0 kcal/mol

E (B3LYP/6-31G(d)): –1189.082081
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –1189.402627
ZPE (B3LYP/6-31G(d)): 0.446225
Imaginary frequencies: 1

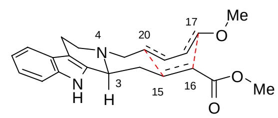
C	4.57482600	0.01296600	0.22966800
C	4.18762600	1.38339800	0.20993900
C	5.06654900	2.41199900	0.55979100
C	6.35794200	2.05538700	0.93521400
C	6.76418300	0.70609800	0.96044300
C	5.88671300	-0.31411200	0.61213700
C	3.42729400	-0.74758700	-0.18830400
C	2.41541900	0.14352500	-0.43026300
H	4.75484600	3.45339300	0.53975600
H	7.06536400	2.83204300	1.21292600
H	7.78063600	0.46295200	1.25817700
H	6.21054100	-1.35166800	0.63653600
C	1.03036000	-0.19998600	-0.90459200
C	-0.05300000	0.58550500	-0.13248600
H	0.93847000	0.10033500	-1.97350100
C	-0.42032800	-2.08449700	-1.38865200
H	0.01249900	0.34970200	0.93527700
H	0.17046900	1.65782800	-0.23388600
H	-0.40788000	-3.17960000	-1.45598300
H	-0.53458700	-1.71030200	-2.42533200
N	0.84357800	-1.65770800	-0.78941800
C	3.22579900	-2.21707800	-0.39698500
C	1.99468500	-2.42169200	-1.29032300
H	4.10048400	-2.67665600	-0.87648200
H	1.71127600	-3.47948900	-1.30069800
H	2.24633500	-2.14089100	-2.33172700
H	3.07635500	-2.74031900	0.55838300
N	2.86774300	1.43329600	-0.19889400
H	2.32003400	2.27391500	-0.29214700
C	-1.46116700	0.35515200	-0.65142200
H	-1.53562700	0.30480900	-1.73923400
C	-1.61013800	-1.63542800	-0.55408500
H	-2.55761000	-1.63417100	-1.09021500
C	-1.61606500	-1.94912500	0.81104600
H	-0.67869700	-2.29882800	1.23777800
C	-2.54674700	1.01647900	-0.05395700
H	-2.45134200	1.53183400	0.89515900
C	-3.83914300	-1.05060300	1.33942100
C	-2.64773400	-1.63506200	1.70705900
H	-2.48144600	-1.77227900	2.77324400
C	-3.74446400	1.22363300	-0.83771100
O	-4.04477100	0.61652100	-1.86262900
O	-4.56297100	2.19545000	-0.31353100
C	-5.72962000	2.48176000	-1.09120100
H	-6.38093200	1.60506800	-1.16757600
H	-6.24212300	3.29055100	-0.56708000
H	-5.45705500	2.79692000	-2.10250000
H	-4.19160300	-1.00563300	0.31375200
O	-4.71276400	-0.70160200	2.29853400
C	-5.94645400	-0.12595400	1.86050400
H	-6.56704400	-0.02329400	2.75201700
H	-5.76663700	0.85505100	1.41222400
H	-6.44915000	-0.78200600	1.13887600



8b: + 4.8

E (B3LYP/6-31G(d)): –1189.074916
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –1189.395371
ZPE (B3LYP/6-31G(d)): 0.446201
Imaginary frequencies: 1

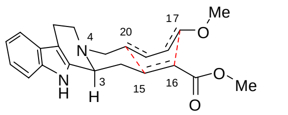
C	-4.59515000	-0.06093000	-0.20744600
C	-4.29865800	1.33229000	-0.19446100
C	-5.24347200	2.29902500	-0.54855700
C	-6.50863300	1.85656200	-0.92260700
C	-6.82413200	0.48337900	-0.94520000
C	-5.88130700	-0.47523200	-0.59229900
C	-3.39865600	-0.74478900	0.20833500
C	-2.45081400	0.21362800	0.45450000
H	-5.00125400	3.35882500	-0.53286900
H	-7.26586700	2.58391100	-1.20253400
H	-7.82195800	0.17237800	-1.24283600
H	-6.13626000	-1.53194100	-0.61165100
C	-1.04950500	-0.02944900	0.93287300
C	0.01863100	0.51971600	-0.05541400
H	-0.90133100	0.52170300	1.87891400
C	0.39826400	-1.80520200	1.78856300
H	-0.04740600	-0.00093900	-1.01792000
H	-0.21208000	1.57560700	-0.26079600
H	0.37253900	-2.86799000	2.06281500
H	0.53759400	-1.24946300	2.72714900
N	-0.91519700	-1.45136300	1.26346600
C	-3.09215300	-2.20189500	0.38130600
C	-1.56633500	-2.38591500	0.34250200
H	-3.48389700	-2.57924900	1.33665300
H	-1.23428800	-2.26920700	-0.70521300
H	-1.29707500	-3.40057500	0.65601200
H	-3.55171500	-2.80461100	-0.41377000
N	-2.98282800	1.46987800	0.20799000
H	-2.50430200	2.34659100	0.34409400
C	1.42544400	0.43464300	0.51440500
H	1.48175600	0.65609300	1.58225000
C	1.61042300	-1.52093700	0.89470400
H	2.52985200	-1.35228100	1.45502500
C	1.73362400	-2.14951200	-0.35489600
H	0.87004100	-2.67259100	-0.75642500
C	2.51660900	0.95746100	-0.20439400
H	2.43330700	1.22538500	-1.25166100
C	3.94860300	-1.25927200	-0.93558200
C	2.81413700	-1.98742400	-1.22974900
H	2.73824300	-2.37782500	-2.24218800
C	3.66079200	1.43939300	0.54131000
O	3.94837700	1.12754500	1.69369900
O	4.43686100	2.31192600	-0.18185200
C	5.54174300	2.87103700	0.53602300
H	6.24543100	2.09322600	0.84964700
H	6.02422300	3.56213600	-0.15748600
H	5.19836300	3.40423800	1.42710600
H	4.23610700	-0.98003400	0.07322300
O	4.87292200	-1.09988900	-1.89808400
C	6.06020000	-0.38848800	-1.53942200
H	6.75652200	-0.52132900	-2.36897100
H	5.83559100	0.67254700	-1.40328100
H	6.50083100	-0.79940100	-0.62255300



8c: + 0.1

E (B3LYP/6-31G(d)): –1189.080582
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –1189.402175
ZPE (B3LYP/6-31G(d)): 0.445861
Imaginary frequencies: 1

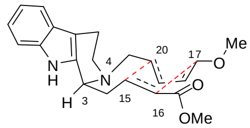
C	-4.65935500	-0.04350100	0.29060700
C	-4.26497200	-1.36158100	-0.07712400
C	-5.14446800	-2.44615200	-0.02023000
C	-6.44314100	-2.19981800	0.41430000
C	-6.85586900	-0.90374500	0.78303900
C	-5.97800700	0.17234100	0.72516300
C	-3.51052100	0.80108000	0.09895100
C	-2.49061900	0.00486100	-0.35072700
H	-4.82795300	-3.44659100	-0.30481900
H	-7.15107200	-3.02232500	0.46968600
H	-7.87767100	-0.74680400	1.11804300
H	-6.30700700	1.16781000	1.01292400
C	-1.09891100	0.45967900	-0.69558400
C	-0.02964700	-0.46409700	-0.07775800
H	-0.97358400	0.40801800	-1.80101600
C	0.32160100	2.42908000	-0.71109600
C	1.38869100	-0.21675500	-0.56908400
H	-0.09083600	-0.39406500	1.01485700
H	-0.28313600	-1.50180800	-0.33732100
C	1.54197100	1.77109300	-0.09618500
H	0.31197400	3.48861000	-0.42284200
H	0.40266400	2.40608800	-1.81748000
H	1.47594900	-0.07272200	-1.64519700
H	1.41324600	1.58025400	0.96790100
N	-0.92920100	1.84692800	-0.23502200
C	-3.31690400	2.27597000	0.27086700
C	-2.08468900	2.70324200	-0.53707400
H	-4.19283100	2.83681400	-0.08176300
H	-1.80935700	3.73233300	-0.28271700
H	-2.33086800	2.68932600	-1.61694000
H	-3.17359600	2.54248100	1.32775600
N	-2.93823500	-1.30286600	-0.46206800
H	-2.39543600	-2.08464100	-0.79324500
C	2.44393500	-0.94922200	-0.00839700
H	2.32845500	-1.45620700	0.94496500
C	2.81812400	2.13795600	-0.53695400
H	2.90260300	2.66055200	-1.48882700
C	4.04135300	0.85945600	1.14655100
H	3.19829500	0.73468200	1.81814000
C	4.00921300	1.68842400	0.04608400
H	4.95189300	1.87096200	-0.46239100
O	5.21731200	0.35743500	1.56492300
C	5.15673700	-0.54902400	2.66599200
H	4.69924200	-1.49214500	2.35132000
H	6.18847900	-0.72420200	2.97524500
H	4.59575300	-0.11382800	3.50327800
C	3.59741400	-1.28504900	-0.82270700
O	3.82086700	-0.88426900	-1.95698400
O	4.44897300	-2.14186200	-0.17004800
C	5.61924200	-2.50342600	-0.90896100
H	6.23484200	-1.62362100	-1.11856300
H	6.16500100	-3.20471600	-0.27470800
H	5.35272500	-2.97799000	-1.85780800



8d: + 2.6

E (B3LYP/6-31G(d)): –1189.077085
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –1189.398144
ZPE (B3LYP/6-31G(d)): 0.44586
Imaginary frequencies: 1

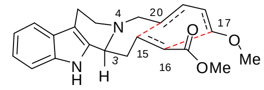
C	-4.60762600	0.05151300	0.33834700
C	-4.38038600	-1.26484100	-0.15647100
C	-5.35393000	-2.26493600	-0.08979400
C	-6.57692200	-1.93595300	0.48678200
C	-6.82304700	-0.64172800	0.98675500
C	-5.85205400	0.35070100	0.91784200
C	-3.40155900	0.80029500	0.09865100
C	-2.51704800	-0.04655300	-0.51524000
H	-5.16506200	-3.26428300	-0.47408400
H	-7.35500200	-2.69162500	0.55252000
H	-7.78924200	-0.41880200	1.43141400
H	-6.05397200	1.34656100	1.30453400
C	-1.12199600	0.30069200	-0.94569600
C	-0.06508900	-0.49186400	-0.12745600
H	-0.98716400	0.01466500	-2.00262800
C	0.33072400	2.22394100	-1.31100200
C	1.36825900	-0.32302000	-0.61350200
H	-0.15022300	-0.23250300	0.93563100
H	-0.32119700	-1.55924300	-0.19387900
C	1.51830500	1.70838100	-0.50084300
H	0.31273700	3.32190500	-1.28246500
H	0.47413900	1.94473000	-2.36547700
H	1.48917900	-0.37314700	-1.69543500
H	1.34910700	1.71658400	0.57530200
N	-0.98422000	1.76133300	-0.89225300
C	-3.04214500	2.22620500	0.39059700
C	-1.51355300	2.38233100	0.32650500
H	-3.50805900	2.90390400	-0.33895700
H	-1.07253900	1.96543500	1.25147900
H	-1.24632300	3.44435900	0.29870100
H	-3.39802900	2.53482400	1.38293700
N	-3.09309900	-1.29887900	-0.66165000
H	-2.67354600	-2.08505700	-1.13327500
C	2.40625200	-0.94670400	0.09737500
H	2.25490500	-1.29383000	1.11508500
C	2.81847800	1.99680000	-0.93600900
H	2.94947300	2.34735200	-1.95936300
C	3.95774500	1.01762900	0.98964600
H	3.09044900	1.01316200	1.64173300
C	3.97843100	1.65429900	-0.23397100
H	4.94410000	1.74982700	-0.72294900
O	5.11363300	0.59499000	1.53398800
C	5.00285800	-0.12359600	2.76215000
H	4.55477800	-1.10573400	2.58276900
H	6.01979000	-0.24460400	3.13900700
H	4.40891000	0.43843400	3.49478700
C	3.58185600	-1.41534700	-0.61223200
O	3.84603300	-1.20302000	-1.78808100
O	4.40368700	-2.15892800	0.19841700
C	5.59473100	-2.63828200	-0.43225800
H	6.22655700	-1.80564200	-0.75568900
H	6.11101800	-3.23347300	0.32346100
H	5.35592600	-3.25508600	-1.30348200



8e:+ 3.0

E (B3LYP/6-31G(d)): –1189.07800807
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –1189.39829972
ZPE (B3LYP/6-31G(d)): 0.446749
Imaginary frequencies: 1

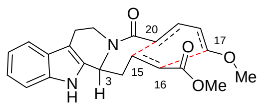
C	0.26956900	-0.63389200	1.58206100
C	1.02201400	0.03488000	0.44593600
C	1.32197100	-1.50825500	-0.77528100
C	-0.10139500	-1.95663300	-1.05947000
C	-1.00955600	-1.38976500	1.17218300
H	0.39255100	0.51217000	-0.30616200
H	0.93716000	-1.32956200	2.10161100
H	-0.01051500	0.12117900	2.33225400
H	-0.64319000	-1.12906600	-1.54810600
H	-0.09631700	-2.79112500	-1.77383200
H	-1.33453000	-1.92985300	2.07540000
H	1.74473600	-0.86964300	-1.54888600
C	2.19927700	0.74978700	0.72716000
H	2.68201500	0.69794200	1.69679000
C	2.63653000	1.76033000	-0.21100000
C	2.18115900	-2.37873600	-0.09123900
H	1.72767600	-3.24383600	0.38766200
C	3.52082400	-2.10461500	0.21741100
H	4.05292300	-2.76448900	0.89923400
C	4.19451800	-0.97728600	-0.19974200
H	3.84648900	-0.33649400	-1.00372100
O	2.27707900	1.85389300	-1.38151800
O	3.53830000	2.64200100	0.33630600
N	-0.77280700	-2.43726900	0.15523900
C	-2.15740300	-0.50762000	0.72803200
C	-2.02954200	-3.13798000	-0.15067200
H	-2.41574300	-3.53716700	0.79572600
H	-1.79558500	-3.99576900	-0.79213600
C	-3.11583500	-2.25171400	-0.81202600
H	-2.91952200	-2.14924100	-1.88997300
H	-4.08856800	-2.75658600	-0.73183000
C	-3.13943500	-0.90493200	-0.14723700
N	-2.44193300	0.76651600	1.19410900
C	-3.60442900	1.21944400	0.59746100
C	-4.27633100	2.43731500	0.73322800
C	-4.07637800	0.18183000	-0.25617500
C	-5.44659200	2.61239600	0.00154100
H	-3.90007900	3.22067900	1.38653900
C	-5.26331600	0.38885500	-0.97991100
C	-5.93595400	1.59756300	-0.84530700
H	-5.99265100	3.54806300	0.08581900
H	-5.64955700	-0.38593300	-1.63758800
H	-6.85385300	1.76692200	-1.40189200
H	-1.84706700	1.31664700	1.79347600
C	3.95368800	3.69602300	-0.53828000
H	3.09551400	4.28404500	-0.87617300
H	4.63118900	4.31763600	0.05003200
H	4.46851500	3.30042900	-1.41968900
O	5.44356100	-0.76636000	0.24871500
C	6.11056200	0.39727100	-0.24782400
H	5.61438300	1.30068300	0.11738000
H	7.13134700	0.34852300	0.13436000
H	6.13066200	0.39725500	-1.34485900



8f: + 4.6

E (B3LYP/6-31G(d)): –1189.07391095
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –1189.39523459
ZPE (B3LYP/6-31G(d)): 0.446079
Imaginary frequencies: 1

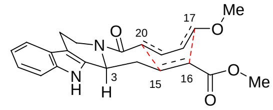
C	-4.60277500	-0.09779900	0.25646900
C	-4.27010200	-1.24048600	-0.52621200
C	-5.19010000	-2.25921900	-0.78678300
C	-6.46673700	-2.12742400	-0.24877900
C	-6.81846800	-1.00613400	0.52854000
C	-5.90049900	0.00601400	0.78441900
C	-3.42506700	0.72859300	0.30563200
C	-2.45222900	0.08984300	-0.41484600
H	-4.92032200	-3.12511200	-1.38643200
H	-7.20448300	-2.90388900	-0.43207300
H	-7.82413000	-0.93506200	0.93408300
H	-6.18222900	0.86573900	1.38725100
C	-1.03985700	0.55416400	-0.60776100
C	-0.03274700	-0.52270600	-0.10662200
H	-0.87386900	0.71659100	-1.69501400
C	0.34311800	2.51967000	-0.41860000
C	1.30509300	-0.01214700	0.41543700
H	-0.50599700	-1.06169800	0.72378600
H	0.13397200	-1.25889600	-0.90569300
C	1.55175500	1.64300600	-0.70605600
H	0.62086900	3.30449500	0.29559800
H	0.05891500	3.03120600	-1.36385800
H	1.23419300	0.54378400	1.34540000
H	1.46925800	1.07778000	-1.63385000
N	-0.81341800	1.80457500	0.13271300
C	-3.15280400	2.05740000	0.94030100
C	-1.96825800	2.70555500	0.21393200
H	-4.02431200	2.72127500	0.86856500
H	-1.64065100	3.60281000	0.75204500
H	-2.29531700	3.03380100	-0.79303300
H	-2.91915800	1.95370200	2.00929800
N	-2.95184500	-1.10008300	-0.92180800
H	-2.43997800	-1.76070500	-1.48513600
C	2.41423100	-0.87252700	0.33410100
H	2.39011500	-1.75209400	-0.30200600
C	2.82953700	2.14213700	-0.40866900
H	2.90182300	3.00311700	0.25326500
C	4.06015700	0.25847400	-1.35782200
H	3.24565400	-0.11587700	-1.96949700
C	4.02044100	1.47867900	-0.71341800
H	4.95265100	1.84078200	-0.28862900
O	5.23860000	-0.38149000	-1.48019100
C	5.18842100	-1.69057700	-2.04413200
H	4.62628600	-1.69281400	-2.98755000
H	6.22211000	-1.98041300	-2.24027800
H	4.73665800	-2.38782400	-1.33160400
C	3.46937200	-0.78818600	1.32758700
O	3.58570100	0.08026500	2.18060500
O	4.36528800	-1.82134600	1.20689600
C	5.45209200	-1.78479300	2.13639700
H	5.08643000	-1.79106400	3.16725100
H	6.04254600	-2.68124800	1.93760800
H	6.06166300	-0.88848100	1.98699500



0.0 kcal/mol

E (B3LYP/6-31G(d)): –1263.12050391
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –1263.46397885
ZPE (B3LYP/6-31G(d)): 0.428200
Imaginary frequencies: 1

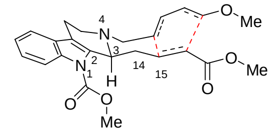
C	4.67464600	-0.14691500	0.01255500
C	4.21605500	-1.48703500	0.15435500
C	5.09102200	-2.57653900	0.17590100
C	6.45142800	-2.31056600	0.05859800
C	6.92878500	-0.99157200	-0.07855300
C	6.05502400	0.08873000	-0.10270100
C	3.50739100	0.69531500	0.01732700
C	2.41943200	-0.12524600	0.15552100
H	4.72484300	-3.59463100	0.28190100
H	7.15821500	-3.13564700	0.07362200
H	7.99811600	-0.82020800	-0.16648400
H	6.43395500	1.10206100	-0.20853600
C	0.99053700	0.30671600	0.29371300
C	0.01169100	-0.50501800	-0.60287900
H	0.70123900	0.11869400	1.33811600
C	-0.33191600	2.37442000	0.21420800
C	-1.41971500	0.02761700	-0.69537200
H	0.42704400	-0.54710500	-1.61730700
H	-0.00793800	-1.53722300	-0.22752800
C	-1.42839900	1.48721600	0.72099200
H	-1.58483600	0.72725900	-1.51049500
H	-1.15914400	0.78848100	1.50771800
N	0.89259100	1.75482400	0.06389600
C	3.34165700	2.17901400	-0.10652000
C	1.94679700	2.47178100	-0.67022800
N	2.83654900	-1.44432500	0.25254500
H	2.23389600	-2.25033300	0.30525300
C	-2.49329400	-0.86969300	-0.50624900
H	-2.32162000	-1.84014000	-0.05001400
C	-2.73221000	2.01678700	0.75704000
H	-2.88148200	2.99350300	0.30611600
C	-3.74410200	-0.06087600	1.53173700
H	-2.83834900	-0.48491900	1.95326300
C	-3.83769900	1.26912200	1.13688200
H	-4.83634300	1.66629600	0.97738500
O	-4.87702600	-0.75024400	1.74640400
C	-4.72800100	-2.11797800	2.12666900
H	-4.01364400	-2.22040700	2.95393800
H	-5.71269700	-2.45300200	2.45630900
H	-4.40363800	-2.71123500	1.26650600
C	-3.71048000	-0.70690800	-1.28826500
O	-3.99263400	0.25463400	-1.98613800
O	-4.54297000	-1.78732900	-1.15331900
C	-5.77678700	-1.68969400	-1.87344400
H	-5.59459400	-1.55769400	-2.94366300
H	-6.30117700	-2.62926300	-1.69014200
H	-6.37148700	-0.84570200	-1.51210100
O	-0.52681100	3.54356800	-0.11176300
H	1.69226800	3.52955500	-0.60901600
H	1.91868900	2.18142100	-1.73086300
H	3.46720900	2.68051200	0.86388500
H	4.09187100	2.60911600	-0.78215800



+ 0.6

E (B3LYP/6-31G(d)): –1263.11857263999
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –1263.46268937
ZPE (B3LYP/6-31G(d)): 0.427835
Imaginary frequencies: 1

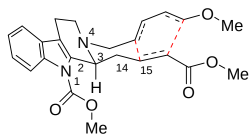
C	-4.63148800	-0.17898800	0.21722500
C	-4.21918100	-1.50138200	-0.11052300
C	-5.08082300	-2.59760800	-0.01356700
C	-6.38080400	-2.35680200	0.41901300
C	-6.81219500	-1.05556700	0.74689500
C	-5.95182200	0.03134500	0.65016900
C	-3.49734800	0.67850600	-0.00528700
C	-2.46683000	-0.11846100	-0.43233200
H	-4.75028600	-3.60165700	-0.26769600
H	-7.07591100	-3.18755500	0.50429800
H	-7.83499900	-0.90366100	1.08077800
H	-6.29489600	1.03045700	0.90657400
C	-1.08402700	0.34994200	-0.81062000
C	0.00517400	-0.61863400	-0.32706000
H	-1.01077000	0.36937400	-1.91533100
C	0.25956400	2.37490200	-0.08683800
C	1.41843300	-0.19334700	-0.68430600
H	-0.09482500	-0.79410600	0.75117700
H	-0.19336200	-1.58311800	-0.81556900
C	1.39652500	1.52874500	0.42177800
H	1.53114700	0.29791000	-1.64901400
H	1.14095100	0.94344000	1.30133700
N	-0.94668800	1.74346600	-0.33870100
C	-3.33829700	2.16475900	0.11616900
C	-2.09648000	2.59766400	-0.67693600
H	-4.21721200	2.69084800	-0.27995800
H	-1.80868500	3.62564900	-0.46359700
H	-2.30131400	2.52158900	-1.75563100
H	-3.23490800	2.47423200	1.16604900
N	-2.89574200	-1.43521800	-0.50656600
H	-2.33733000	-2.22333000	-0.79314500
C	2.49328500	-1.01837600	-0.33074900
H	2.36374100	-1.83095500	0.37793700
C	2.68072500	2.08832500	0.35227200
H	2.79894900	2.97758700	-0.25967100
C	3.80565000	0.28068900	1.54772300
H	2.91158500	-0.10868700	2.02441800
C	3.82791000	1.47777900	0.85816300
H	4.80345300	1.87993800	0.59909100
O	4.96398400	-0.30407000	1.88705400
C	4.87022800	-1.56493600	2.55239300
H	4.55752000	-2.33738300	1.84338100
H	5.87066800	-1.78827900	2.92597400
H	4.17019500	-1.51263800	3.39590800
C	3.70956100	-0.99531300	-1.12548500
O	3.96296500	-0.21014900	-2.02707900
O	4.58176400	-1.98295200	-0.74511300
C	5.81685500	-2.00506900	-1.46884100
H	6.37382700	-1.07625900	-1.31501600
H	6.37720600	-2.85347900	-1.07177900
H	5.63971000	-2.13407600	-2.54035400
O	0.38689700	3.59184600	-0.20096700



16a: + 0.4

E (B3LYP/6-31G(d)): –1416.95763282
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –1417.34130529
ZPE (B3LYP/6-31G(d)): 0.489784
Imaginary frequencies: 1

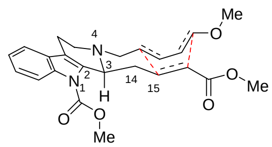
C	-4.21433300	-0.86578600	-0.38000400
C	-4.04774300	0.51460000	-0.63220400
C	-5.03481200	1.27187800	-1.26461800
C	-6.20115100	0.61003000	-1.64964600
C	-6.38308300	-0.76160600	-1.41011200
C	-5.39516400	-1.50760600	-0.77475300
C	-3.01904000	-1.32782800	0.28300300
C	-2.16533800	-0.27587500	0.41544500
H	-4.89366600	2.32702700	-1.45294000
H	-6.98295700	1.17360100	-2.15141000
H	-7.30378500	-1.24400100	-1.72691700
H	-5.53419400	-2.56933900	-0.58876600
C	-0.74246100	-0.38810100	0.91078300
C	0.27982000	0.13032400	-0.13209200
H	-0.62539700	0.22906400	1.82137100
C	0.82144100	-1.93373600	1.93482200
H	0.23404900	-0.50433500	-1.02342200
H	-0.01014200	1.13915700	-0.43824100
H	0.87651500	-2.94986600	2.34481600
H	0.88673200	-1.24443700	2.79905400
N	-0.44901600	-1.80289200	1.22452900
C	-2.69384000	-2.68413200	0.82602400
C	-1.55624400	-2.53354400	1.84023000
H	-3.57520900	-3.12307800	1.31243100
H	-1.18324300	-3.51839800	2.14019200
H	-1.93874900	-2.03570500	2.75237800
H	-2.38909100	-3.37566400	0.02841500
N	-2.78280300	0.89343000	-0.11545700
C	1.69499800	0.19199100	0.41805400
H	1.75343100	0.52254600	1.45685100
C	2.00192000	-1.69184400	1.00345500
H	2.92920000	-1.43192500	1.51109200
C	2.07628400	-2.44832200	-0.17305800
H	1.18211000	-2.99656900	-0.46147600
C	2.74141900	0.69323800	-0.37510600
H	2.62904400	0.84401000	-1.44285300
C	4.24015200	-1.60162200	-0.96603400
C	3.10914300	-2.37264200	-1.11769900
H	2.98811600	-2.87563500	-2.07455400
C	3.89717100	1.25761500	0.28514400
O	4.21905900	1.06951200	1.45615300
O	4.64821700	2.05610000	-0.54496300
C	5.76671300	2.69059600	0.08180100
H	6.48624300	1.95295100	0.45179600
H	6.22414800	3.31211000	-0.69029000
H	5.44403500	3.30852800	0.92476600
H	4.55708300	-1.18391500	-0.01544900
O	5.11529700	-1.53022300	-1.98312700
C	6.28766200	-0.74132600	-1.76415400
H	6.93131900	-0.90710600	-2.62945000
H	6.02174700	0.31668500	-1.69029600
H	6.80966600	-1.06141100	-0.85363500
C	-2.45300700	2.23229600	0.09393700
O	-2.98842800	3.16555100	-0.46698900
O	-1.47576100	2.36811500	1.01420100
C	-1.04934000	3.72275600	1.24586600
H	-0.67260400	4.16981100	0.32277300
H	-1.88005100	4.32279600	1.62427500
H	-0.25569000	3.64875800	1.98928900



16b: + 3.4

E (B3LYP/6-31G(d)): – 1416.95318247
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –
1417.33667775
ZPE (B3LYP/6-31G(d)): 0.490043
Imaginary frequencies: 1

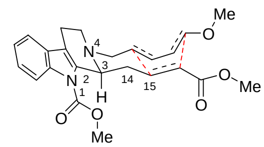
C	-4.26177100	-0.90531300	-0.31186000
C	-4.17652100	0.49752000	-0.45850800
C	-5.24285200	1.24961200	-0.95535500
C	-6.40480200	0.56147800	-1.30589000
C	-6.50619400	-0.83212600	-1.16798600
C	-5.43888300	-1.57376400	-0.67150300
C	-2.99797600	-1.36181000	0.21341600
C	-2.18710100	-0.28160800	0.38141400
H	-5.16636300	2.32196500	-1.06485600
H	-7.24835900	1.12303300	-1.69797600
H	-7.42682200	-1.33428200	-1.45280400
H	-5.51470700	-2.65240200	-0.56225400
C	-0.75776800	-0.36339100	0.85603500
C	0.27046000	0.01018400	-0.25069500
H	-0.61312100	0.34992500	1.67582600
C	0.78112900	-1.84505600	2.03964000
H	0.25234400	-0.73506300	-1.05446100
H	-0.02473900	0.96393300	-0.70033400
H	0.82091500	-2.83693100	2.50919700
H	0.84469500	-1.11378700	2.85704400
N	-0.54097700	-1.69873900	1.43397000
C	-2.56796600	-2.75686400	0.54995400
C	-1.03691700	-2.81030900	0.62393600
H	-2.99775700	-3.06338700	1.51379400
H	-0.64096700	-2.81240000	-0.40772000
H	-0.71172200	-3.74426400	1.09534500
H	-2.92885100	-3.47101300	-0.20235000
N	-2.88923700	0.89422000	-0.01608200
C	1.67041300	0.15864400	0.32511400
H	1.68523500	0.61543700	1.31660500
C	2.00214700	-1.64363400	1.13306900
H	2.87704100	-1.26833000	1.66390500
C	2.24064400	-2.52263300	0.06349700
H	1.45232000	-3.21311300	-0.22275600
C	2.73577000	0.59923200	-0.48307100
H	2.66196900	0.61640500	-1.56466700
C	4.38586500	-1.56932700	-0.66549800
C	3.33590500	-2.45386800	-0.80428300
H	3.33873400	-3.06969500	-1.70097600
C	3.80625900	1.34475800	0.14619300
O	4.07848000	1.33650100	1.34386500
O	4.52905400	2.09618000	-0.74846700
C	5.55266500	2.90745500	-0.16343100
H	6.30514100	2.29379200	0.34210900
H	6.00390300	3.45579600	-0.99233900
H	5.12963600	3.60353300	0.56669200
H	4.61025500	-1.04526800	0.25805000
O	5.32663800	-1.54376100	-1.62495500
C	6.43637300	-0.66637800	-1.41783500
H	7.16711000	-0.91337600	-2.18964700
H	6.11727400	0.37381300	-1.52152400
H	6.88208200	-0.82563600	-0.42802600
C	-2.54289800	2.23405100	0.14156700
O	-1.37931500	2.38053100	0.80933400
O	-3.20601200	3.16581700	-0.26522900
C	-0.95297600	3.74338800	0.98505400
H	-0.83024800	4.23452400	0.01699600
H	-1.68345500	4.29688900	1.57972400
H	0.00116500	3.67794000	1.50795500



16c: 0.0

E (B3LYP/6-31G(d)): –1416.95703747
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –
1417.34149748
ZPE (B3LYP/6-31G(d)): 0.489421
Imaginary frequencies: 1

C	4.33363800	-0.76799500	0.54893200
C	4.12896800	0.62919300	0.49010900
C	5.11649500	1.53410200	0.88308900
C	6.32187300	1.00583300	1.34630400
C	6.54160100	-0.37940900	1.41438700
C	5.55303400	-1.27411700	1.01671500
C	3.12861700	-1.39871600	0.06791800
C	2.23341500	-0.42636800	-0.25617500
H	4.94746100	2.60059600	0.83365200
H	7.10540700	1.68789600	1.66486400
H	7.49245100	-0.75437900	1.78328500
H	5.72078400	-2.34666700	1.06828100
C	0.80365500	-0.68335600	-0.66485300
C	-0.20590900	-0.02210100	0.30310900
H	0.63487700	-0.25744200	-1.67049000
C	-0.70205500	-2.44419700	-1.36689100
C	-1.61726000	0.05053500	-0.26095400
H	-0.17971300	-0.56948200	1.25251800
H	0.11466500	1.00145600	0.51482900
C	-1.92180900	-1.94076800	-0.61536900
H	-0.76858100	-3.53795800	-1.44223800
H	-0.71836500	-2.05585100	-2.40578800
H	-1.66267800	0.36261100	-1.30347700
H	-1.87451500	-2.18341000	0.44478200
N	0.54805400	-2.13816800	-0.68100400
C	2.82894400	-2.84955700	-0.14588500
C	1.66954300	-2.95734800	-1.14047100
H	3.71164800	-3.36903500	-0.54192200
H	1.32185700	-3.99406400	-1.20420400
H	2.02161200	-2.66763900	-2.14980900
H	2.55722700	-3.34897200	0.79422200
N	2.82906200	0.84875800	-0.03129600
C	-2.65435200	0.57594600	0.52449600
H	-2.56418600	0.63176200	1.60533600
C	-3.17664100	-1.99273000	-1.23453000
H	-3.20970000	-2.09995000	-2.31800600
C	-4.45978800	-1.37002500	0.74771500
H	-3.67943800	-1.61206100	1.46162100
C	-4.38262100	-1.69587000	-0.59007400
H	-5.28631300	-1.57451700	-1.18106000
O	-5.63311200	-0.96150700	1.26367500
C	-5.62002500	-0.60604400	2.64644800
H	-5.05460200	0.31959200	2.79083800
H	-6.66172800	-0.45097900	2.93214000
H	-5.19307800	-1.41335600	3.25557200
C	-3.71309500	1.34129000	-0.10752600
O	-3.88100600	1.48698800	-1.31113800
O	-4.54207900	1.92478900	0.81906000
C	-5.62366100	2.67955900	0.26575400
H	-6.28871400	2.03576000	-0.31751300
H	-6.15790200	3.10107200	1.11949200
H	-5.25318300	3.47899600	-0.38247400
C	2.42093800	2.10450500	-0.48187900
O	2.96323400	3.14804100	-0.18270600
O	1.35535400	2.01866800	-1.30349600
C	0.84110600	3.28156600	-1.76523100
H	0.57700800	3.92014300	-0.91927600
H	1.58513900	3.79008100	-2.38292900
H	-0.04404600	3.03226000	-2.35013500



16d: + 0.8

E (B3LYP/6-31G(d)): –1416.95623266
E (B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)): –
1417.34038914
ZPE (B3LYP/6-31G(d)): 0.48962
Imaginary frequencies: 1

C	4.25668600	-0.95447800	0.48171600
C	4.22633400	0.45775700	0.43485900
C	5.31294600	1.22912000	0.85221400
C	6.43843500	0.55121700	1.32146500
C	6.48520300	-0.85098700	1.37571800
C	5.39823000	-1.61208200	0.95756300
C	2.98641800	-1.43011100	-0.00995800
C	2.22611700	-0.35236600	-0.34540400
H	5.27937500	2.30849000	0.81279300
H	7.29689200	1.12833700	1.65409900
H	7.37894700	-1.34440700	1.74798800
H	5.43207300	-2.69767300	0.99705500
C	0.80651400	-0.45120800	-0.84465300
C	-0.21581400	0.02363200	0.22503700
H	0.68212000	0.19149100	-1.72266400
C	-0.73036100	-2.01196800	-1.90531700
C	-1.63409000	0.17192800	-0.31052400
H	-0.19211500	-0.65363100	1.08814200
H	0.10606900	1.00216000	0.59675500
C	-1.93003100	-1.72654400	-1.00450100
H	-0.78124000	-3.04837100	-2.26687100
H	-0.79473300	-1.37005100	-2.79595600
H	-1.69667200	0.65351200	-1.28592000
H	-1.84126300	-2.15951400	-0.00892200
N	0.58673700	-1.83019600	-1.30980700
C	2.51389800	-2.84239800	-0.17797000
C	0.98991600	-2.86511500	-0.35780200
H	2.99477200	-3.29433000	-1.05684300
H	0.50892900	-2.76121900	0.63292400
H	0.67507800	-3.83392100	-0.76064100
H	2.79581300	-3.45639200	0.68791200
N	2.96436900	0.83906000	-0.08617500
C	-2.66499800	0.54870300	0.56548900
H	-2.54910900	0.44624200	1.64043200
C	-3.21329400	-1.70187800	-1.56657900
H	-3.29598400	-1.61750000	-2.64982600
C	-4.40952000	-1.44445000	0.54611500
H	-3.59389600	-1.78253700	1.17675100
C	-4.39189900	-1.54944700	-0.82954900
H	-5.32516300	-1.35400100	-1.35064900
O	-5.56588300	-1.15763400	1.17188200
C	-5.49262700	-1.01220200	2.58978800
H	-4.95404700	-0.09472500	2.84607100
H	-6.52257100	-0.94714000	2.94447700
H	-5.00484300	-1.88173400	3.04953100
C	-3.75324400	1.37521000	0.07674700
O	-3.95490900	1.68739400	-1.08937700
O	-4.56859200	1.79964200	1.09657000
C	-5.67983500	2.59977800	0.68334600
H	-6.34439600	2.03220700	0.02522300
H	-6.20239100	2.87740300	1.60082800
H	-5.34288100	3.49507800	0.15280800
C	2.65484000	2.16286500	-0.38989000
O	3.35870500	3.11198000	-0.11254000
O	1.47357900	2.27028300	-1.03290300
C	1.08148300	3.61690000	-1.35637900
H	1.01775500	4.22476900	-0.45103300
H	1.80157400	4.06776000	-2.04329500
H	0.10312700	3.52307500	-1.82751500