Supporting Information

Total Synthesis of (±)-Hirsutine: Application of Phosphine-Catalyzed Imine–Allene [4 + 2]-Annulation

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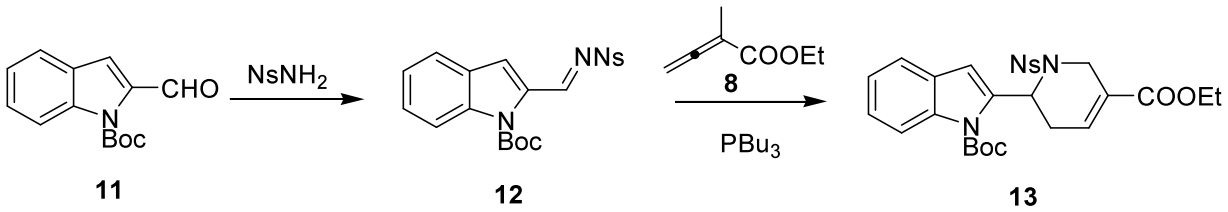
Contents

General Information

All reactions were performed in flame- or oven-dried round-bottom flasks or Schlenk flasks. All reactions were performed under positive pressure of Ar and anhydrous conditions with dry solvents, unless otherwise noted. Tetrahydrofuran (THF) and diethyl ether were distilled over sodium benzophenone-ketyl; dichloromethane (DCM), toluene, and benzene were distilled from CaH_2. Methanol was distilled from Mg turnings. Pyridine and triethylamine were both distilled from CaH_2 and diisopropylamine from NaOH. Reactions were monitored through thin layer chromatography (TLC) on 0.25-mm SiliCycle silica gel plates. Plates were visualized under UV light or through staining with *p*-anisaldehyde, potassium permanganate, or ceric ammonium molybdate (CAM), followed by heating (<1 min) with a heat gun. Flash column chromatography (FCC) was performed using SiliCycle Silica-P Flash silica gel (pore size: 60 Å; 40–63 μm). Organic solutions were concentrated in rotary evaporators under reduced pressure. NMR spectra were recorded using Bruker ARX-400, AV-300, and AV-500 instruments calibrated to signals from the solvent as internal references [7.26 (residual $CHCl_3$) and 77.00 ($CDCl_3$) ppm for ^{1}H and ^{13}C NMR spectra, respectively]. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ /ppm), multiplicity, coupling constant (Hz), and integration. Data for ^{13}C NMR spectra are reported in terms of chemical shift. The following abbreviations are used to denote multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; ddd, doublet of doublets of doublets; td, triplet of doublets; m, multiplet; app, apparent; br, broad. High-resolution mass spectra (HRMS) and low-resolution mass spectra (LRMS) were recorded after matrix-assisted laser desorption/ionization (MALDI) using an Applied Biosystems Voyager-DE STR [matrix: dihydroxybenzoic acid (DHB) or anthracene] operated in reflector mode, with internal or external calibration, at an accelerating potential of 25 kV. FTIR spectra of liquid films (neat) on NaCl plates were recorded using a PerkinElmer pargon 1600 FTIR spectrometer.

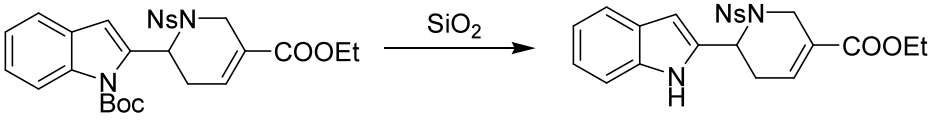
Imine formation and [4 + 2] annulation giving compound 13



11 **12** **13**

Et_3N (0.341 mL, 2.446 mmol) and $TiCl_4$ (1.0 M in DCM, 0.306 mL, 0.306 mmol) were added sequentially to a solution of the aldehyde **11** [1] (150 mg, 0.612 mmol) and *o*-nitrobenzenesulfonamide (124 mg, 0.612 mmol) in dry DCM (10 mL) at 0 °C. The mixture was stirred for 5 min before warming to room temperature and stirring for 1 h. Bu_3P (0.091 mL, 0.367 mmol) and α-methyl allenoate **8**[2] (0.088 mL, 0.734 mmol) were then added dropwise successively. The deep-red mixture was stirred overnight and then the mixture was filtered through a pad of Celite and washed with DCM; the filtrate was concentrated in vacuo to give a dark-red residue, which was purified through FCC (SiO_2; hexanes/EtOAc, 2:1) to give an orange foam (249 mg, 73.3%). ^{1}H NMR (400 MHz, $CDCl_3$) 7.98 (d, 2H, J = 8.0 Hz), 7.60 (d, J = 8.0 Hz, 2H), 7.57–7.51 (m, 1H), 7.42 (d, J = 7.4 Hz, 1H), 7.26 (dt, J = 8.5, 1.2 Hz, 1H), 7.19 (dt, J = 7.6 Hz, 1.2 Hz, 1H), 7.02–7.04 (m, 1H), 6.55 (s, 1H), 6.18 (d, J = 6.1 Hz, 1H), 4.35 (br s, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.08–3.00 (m, 1H), 2.84–2.78 (m, 1H), 1.70 (s, 9H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 164.4, 149.9, 147.6, 138.8, 136.4, 135.4, 133.5, 132.5, 131.6, 131.1, 128.3, 126.2, 124.4, 124.3, 122.8, 120.4, 115.4, 108.5, 84.8, 60.8, 48.5, 41.7, 30.7, 28.1, 14.1; FTIR (neat, cm^{-1}) 2980, 1731, 1544, 1369, 1326, 1165; MS (MALDl) Calculated [M + Na]$^+$ *m*/*z* 578.15, found 578.15.

Boc-Deprotection giving compound 14

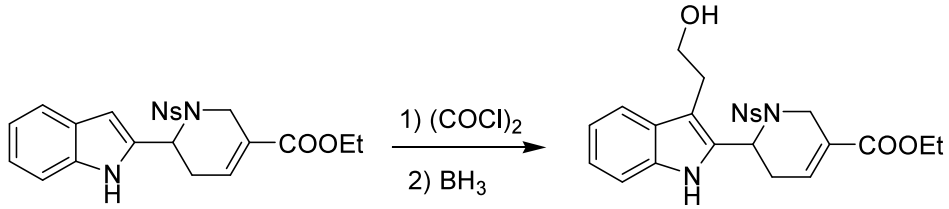


13 **14**

[1] Jeught, S. V.; Vos, N. D.; Masschelein, K.; Ghiviriga, I.; Stevens, C. V. *Eur. J. Org. Chem.* **2010**, 5444–5453.
[2] Lu, K.; Kwon, O. *Org. Synth.* **2009**, *86*, 212–224.

A mixture of **13** (8.10 g, 14.6 mmol) and silica gel (8.10 g) in toluene was heated under reflux for 5 h. After cooling to room temperature, the solid was removed through a plug of silica gel, which was eluted with hexanes/EtOAc (1:1) to give a yellow solid (6.0 g, 90.4%). ^{1}H NMR (400 MHz, $CDCl_3$) 8.74 (br s, 1H), 8.13 (d, J = 7.0 Hz, 1H), 7.74–7.68 (m, 3H), 7.53 (d, J = 7.8 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.22–7.18 (m, 2H), 7.08 (t, J = 8.0 Hz, 1H), 6.31 (s, 1H), 5.50 (s, 1H), 4.26 (d, J = 17.8 Hz, 1H), 4.17 (q, J = 7.2 Hz, 2H), 3.54 (dd, J = 17.8, 2.5 Hz, 1H), 2.91 (s, 2H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 164.3, 147.5, 136.4, 135.7, 134.2, 134.0, 132.8, 132.2, 131.0, 127.5, 126.8, 124.7, 122.5, 120.4, 119.9, 111.2, 101.9, 60.9, 48.1, 40.2, 27.9, 14.0; IR (neat, cm^{-1}) 2938, 1708, 1543, 1297, 1164; HRMS (EI) Calculated $[M]^+$ m/z 455.1151, found 455.1154.

Synthesis of compound 15

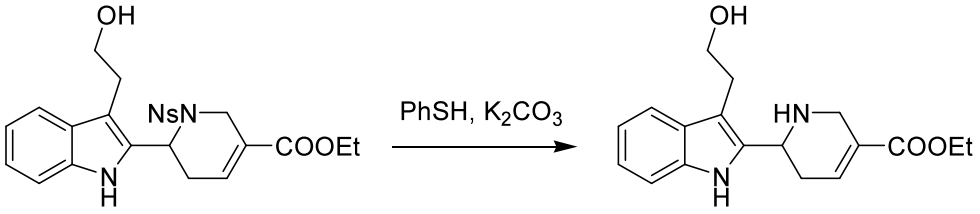


14 **15**

Oxalyl chloride (0.532 mL, 6.10 mmol) was added dropwise to a solution of **14** (1.39 g, 3.05 mmol) in dry THF (35 mL) at 0 °C and then the mixture was stirred at 23 °C overnight. The solvent was concentrated in vacuo and the residue placed under high vacuum overnight to give a light-green foam. The foam was dissolved in dry THF (35 mL) and then BH_3·DMS (1.16 mL, 12.2 mmol) was added via syringe; the mixture was stirred at 23 °C for 2 h before water (25 mL) was added carefully. Solid Na_2CO_3 was then added until no bubbles were formed. The aqueous layer was extracted with EtOAc; the combined organic phases were washed with saturated $NaHCO_3$, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified through FCC (SiO_2; hexanes/EtOAc, 1:1) to give a yellow solid (1.46 g, 96.0% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) 8.13 (br s, 1H), 7.93 (d, J = 7.5 Hz, 1H), 7.68–7.64 (m, 2H), 7.56–7.53 (m, 2H), 7.31 (d, J = 8.0 Hz, 1H), 7.26 (app s, 1H), 7.22 (t, J = 8.0 Hz, 1H), 7.12 (t, J = 8.0 Hz, 1H), 5.67 (d, J = 5.5 Hz, 1H), 4.44 (d, J = 18.5 Hz, 1H), 4.28 (q, J = 7.5 Hz, 2H), 3.98 (app d, J = 18.5 Hz, 1H), 3.87–3.77 (m, 2H), 3.08–2.94 (m, 3H), 2.82 (app d, J =19.5 Hz, 1H), 1.33 (t, J = 7.5 Hz,

3H); ^{13}C NMR (125 MHz, $CDCl_3$) 164.4, 147.8, 136.7, 135.5, 133.8, 132.9, 131.9, 131.7, 130.8, 128.3, 127.9, 124.6, 123.0, 119.9, 119.2, 111.6, 111.1, 62.9, 61.3, 46.8, 41.4, 29.1, 27.5, 14.2; IR (neat, cm^{-1}) 3404, 2940, 1707, 1544, 1368, 1164; HRMS (EI) Calculated $[M]^+$ *m*/*z* 499.1413, found 499.1412.

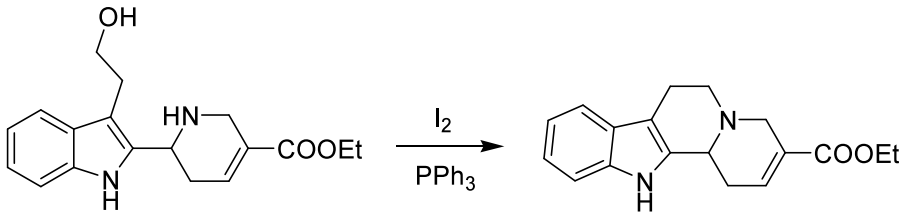
Synthesis of compound 16



15 **16**

Thiophenol (2.59 mL, 25.2 mmol) and dry K_2CO_3 (8.72 g, 63.0 mmol) were added sequentially to a solution of **15** (10.5 g, 21.0 mmol) in dry MeCN (250 mL) and then the mixture was heated at 50 °C for 5 h. After cooling to room temperature, the mixture was filtered through a pad of Celite. The filtrate was concentrated to give an orange residue, which was purified through FCC (SiO_2; DCM/MeOH, 15:1) to give a white solid (6.6 g, 99.9%). ^{1}H NMR (500 MHz, $CDCl_3$) 8.65 (br s, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.17 (dt, *J* = 7.1, 1.0 Hz, 1H), 7.13–7.09 (m, 2H), 4.24–4.20 (m, 3H), 3.90–3.85 (m, 1H), 3.81–3.77 (m, 1H), 3.67 (br s, 2H), 3.07–2.94 (m, 2H), 2.69–2.66 (m, 1H), 2.56–2.51 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 165.5, 136.7, 136.4, 135.3, 129.8, 127.9, 122.0, 119.4, 118.4, 110.9, 109.2, 62.4, 60.4, 47.9, 44.1, 31.8, 27.6, 14.1; IR (neat, cm^{-1}) 3407, 1711, 1542, 1363, 1160; HRMS (EI) Calculated $[M]^+$ *m*/*z* 314.1630, found 314.1622.

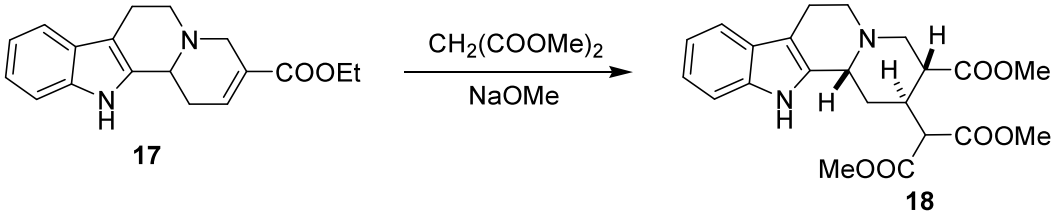
Synthesis of the tetracycle 17



16 **17**

I_2 (6.30 g, 24.8 mmol) and PPh_3 (8.134 g, 31.013 mmol) were added sequentially to a solution of the alcohol **16** (6.50 g, 20.7 mmol) in dry DCM (150 mL) and then the mixture was stirred for 30 min. Et_3N (14.4 mL, 103 mmol) was added and then the solution was concentrated in vacuo to give a black residue, which was purified through FCC (SiO_2; hexanes/EtOAc, 3:1) to give a white foam (5.90 g, 96.3%).[3] ^{1}H NMR (400 MHz, $CDCl_3$) 7.76 (br s, 1H), 7.51 (d, J = 7.7 Hz, 1H), 7.32 (d, J =7.7 Hz, 1H), 7.19–7.10 (m, 2H), 7.07 (br s, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.83 (d, J = 16.5 Hz, 1H), 3.54 (d, J = 10.4 Hz, 1H), 3.30–3.19 (m, 2 H), 3.07–2.99 (m, 1H), 2.82–2.67 (m, 3H), 2.51–2.43 (m, 1H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 165.6, 136.3, 136.2, 133.8, 129.4, 126.9, 121.4, 119.3, 118.0, 110.8, 108.4, 60.5, 54.5, 53.2, 52.0, 31.5, 21.3, 14.1; IR (neat, cm^{-1}) 3368, 2905, 1706, 1254, 1094; HRMS (EI) Calculated $[M]^+$ m/z 296.1524, found 296.1526.

Synthesis of the triester 18

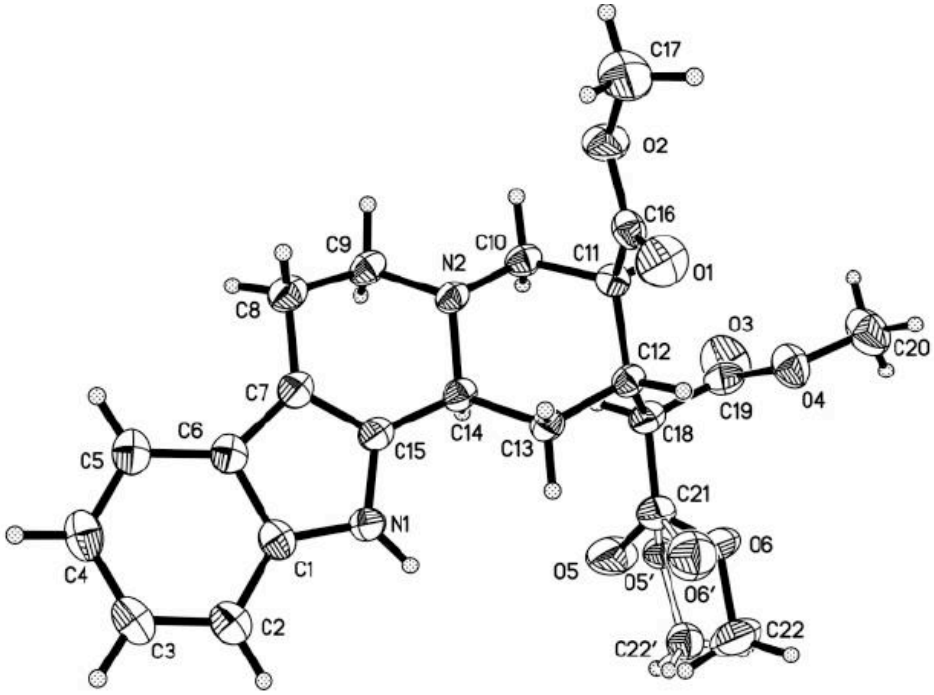


Sodium methoxide, prepared from MeOH (13.6 mL) and Na (0.309 g, 13.443 mmol), was added to a suspension of the enoate **17** (1.39 g, 4.70 mmol) in dimethyl malonate (4.07 mL, 35.2 mmol). The solution was stirred for 10 min then it was left to stand for 7 days. The solid was collected by filtration and washed with MeOH to give **18** as beautiful crystals (1.41 g). The filtrate was concentrated and the residue partitioned between EtOAc and saturated aqueous NH_4Cl. The organic phase was dried ($MgSO_4$) and concentrated. The residue was purified through FCC (SiO_2; hexanes/EtOAc, 1:1) to give **18** as a white solid (0.330 g). Overall, the yield of the triester **18** was 1.735 g (89.1%).[4] ^{1}H NMR (400 MHz, $CDCl_3$) 8.13 (br s, 1H), 7.46 (d, J = 7.7 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.10 (t, J = 7.8 Hz, 1H), 4.25 (br s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.75 (d, J = 5.3 Hz, 1H), 3.66 (s, 3H), 3.26–3.14 (m, 2H), 3.02–2.87 (m, 3H), 2.69 (dt, J = 9.1, 3.9 Hz, 1H), 2.60 (dd, J = 15.9, 3.9 Hz, 1H), 2.55–2.48 (m, 2H), 1.83–1.76 (m,

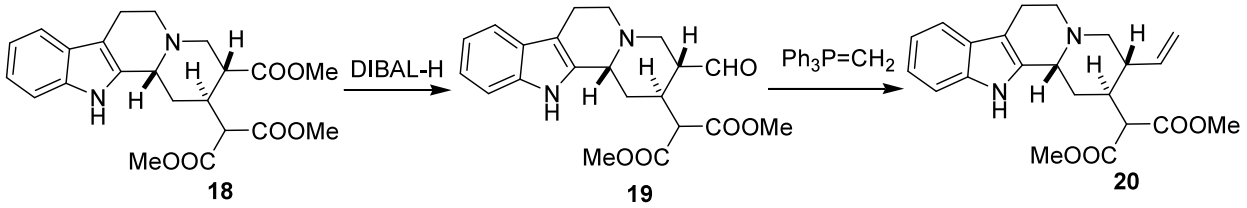
[3] Rosenmund, P.; Casutt, M. *Tetrahedron Lett.* **1983**, *24*, 1771–1774.
[4] Rosenmund, P.; Casutt, M.; Wittich, M. *Liebigs Ann. Chem.* **1990**, 233–238.

1H); ^{13}C NMR (125 MHz, $CDCl_3$) 172.9, 169.2, 168.5, 136.0 132.4, 127.5, 121.4, 119.3, 117.9, 111.1, 107.9, 53.9, 52.6, 52.4, 51.9, 51.8, 51.3, 49.5, 44.8, 32.8, 28.9, 18.1; IR (neat, cm^{-1}) 3397, 2952, 1732, 1435, 1166; HRMS (EI) Calculated $[M - H]^+$ *m*/*z* 413.1713, found 413.1713.

Single crystals suitable for X-ray diffraction were prepared through slow evaporation of a solution of **18** in EtOAc/hexanes. An ORTEP image of **18** is provided below:



Selective reduction of the triester 18 and Wittig olefination giving the alkene 20



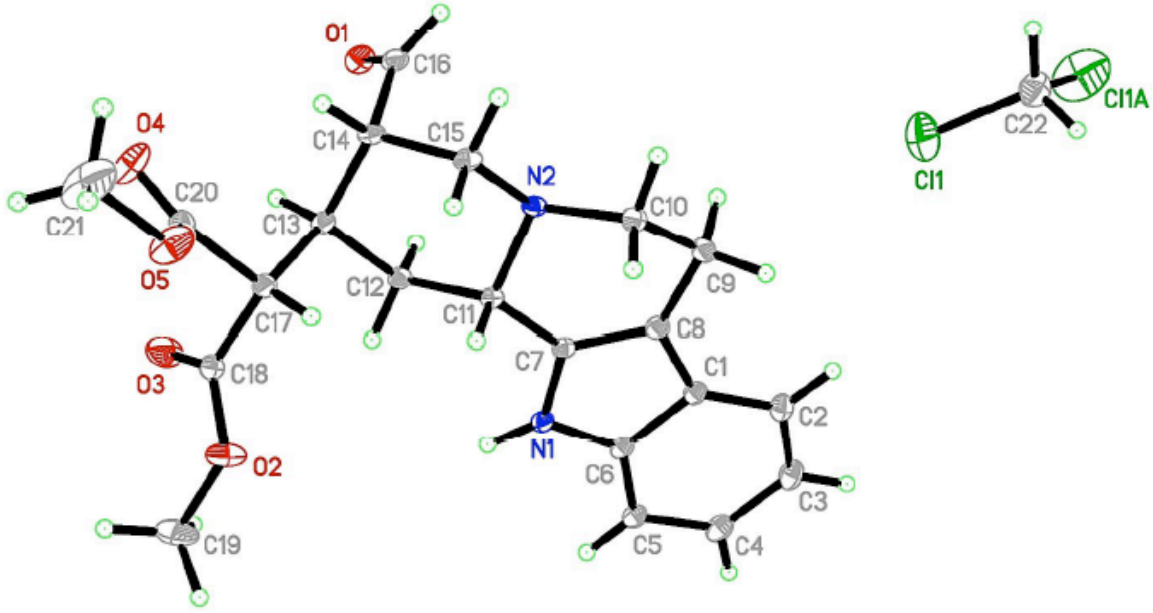
DIBAL-H (1.0 M in DCM, 7.69 mL, 7.69 mmol) was added to a solution of the triester **18** (1.14 g, 2.75 mmol) in DCM (30 mL) at –78 °C. The reaction was quenched after 1 h through the slow addition of MeOH (5 mL). The mixture was brought to room temperature, stirred for 1 h, and then concentrated and dried in vacuo; the residue was used directly for the next step. In another flask, NaHMDS (1.0 M in THF, 11.0 mL, 11.0 mmol) was added to a solution of $Ph_3P^+MeBr^-$ (3.92 g, 11.0 mmol) in DMSO (0.5 mL) and THF (50 mL). The mixture was stirred at room

temperature for 1 h before being transferred to the flask containing the crude aldehyde **19** at –78 °C. After stirred overnight at room temperature, the reaction was quenched through addition of saturated NH_4Cl. The organic phase was separated, dried, and concentrated. The residue was purified through FCC (SiO_2; hexanes/EtOAc, 1:1) to give **20** as a light-yellow solid (0.435 g, 41.2%). ^{1}H NMR (400 MHz, $CDCl_3$) 8.27 (br s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.17 (dt, J = 1.2, 7.2 Hz, 1H), 7.11 (dt, J = 1.2, 8.0 Hz, 1H), 5.42–5.31 (m, 1H), 5.16 (dd, J = 2.0, 17.2 Hz, 1H), 5.08 (dd, J = 2.0, 10.1 Hz, 1H), 4.47 (br s, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.66 (app d, J = 3.2 Hz, 1H), 3.28 (dd, J = 3.2, 6.9 Hz, 2H), 3.31–3.28 (m, 2H), 3.07–2.98 (m, 1H), 2.71–2.63 (m, 3 H), 2.53 (dd, J = 11.2, 3.6 Hz, 1H), 2.49–2.40 (m, 1H), 1.85 (app d, J = 9.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.0, 168.9, 138.0, 136.0, 132.7, 127.7, 121.5, 119.4, 118.2, 118.0, 111.4, 107.8, 53.9, 52.5, 52.3, 51.8, 51.3, 50.9, 44.4, 35.9, 29.4, 17.2; IR (neat, cm^{-1}) 3394, 2951, 1736; MS (MALDI) calcd for $C_{22}H_{26}N_2O_4Na$ $[M + Na]^+$ m/z 405.2, found 405.2.

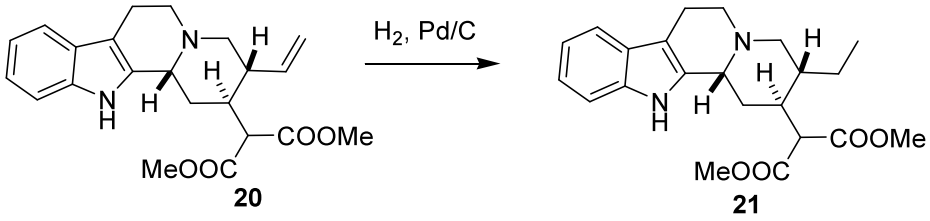
For the characterization of the aldehyde **19**, the following procedure was enacted: DIBAL-H (1.0 M in DCM, 0.531 mL, 0.531 mmol) was added to a solution of the triester **18** (100 mg, 0.265 mmol) in DCM (18 mL) at –78 °C. The reaction was quenched after 3 h through slow addition of MeOH (0.1 mL), followed by H_2O (0.1 mL). The mixture was warmed to room temperature, stirred for 1 h, and then concentrated. The residue was washed thoroughly with DCM. The DCM extracts were concentrated and the residue purified through FCC (SiO_2; hexanes/EtOAc, 1:1) to give a light-yellow solid (21 mg, 20.6%). ^{1}H NMR (500 MHz, $CDCl_3$) 9.68 (s, 1H), 7.86 (br s, 1H), 7.46 (d, J = 7.5 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 3.88 (d, J = 9.5 Hz, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 3.16–3.12 (m, 2H), 2.99–2.88 (m, 4H), 2.69 (d, J = 12.5 Hz, 1H), 2.51 (br s, 1H), 2.10 (br s, 1H), 1.84 (br d, J = 13.9 Hz, 1H), 1.64 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 201.8, 168.8, 168.6, 136.0, 132.9, 127.2, 122.0, 119.6, 118.1, 111.0, 108.4, 54.3, 52.88, 52.87, 52.6, 51.9, 49.5, 31.0, 29.7, 29.3, 20.1; IR (neat, cm^{-1}) 3319, 2820, 1758, 1732, 1712, 1437, 1255, 1224, 1013, 744; HRMS (ESI) Calculated $[M + MeOH + H]^+$ m/z 417.2026, found 417.2013.

Single crystals suitable for X-ray diffraction were prepared through slow evaporation of a solution of **19** in DCM/hexanes. X-ray crystallography confirmed that the CHO group was appended to C20, with the stereochemistry at C20 remaining unchanged. An ORTEP image of

19 is provided below:



Hydrogenation of the alkene 20 giving the diester 21

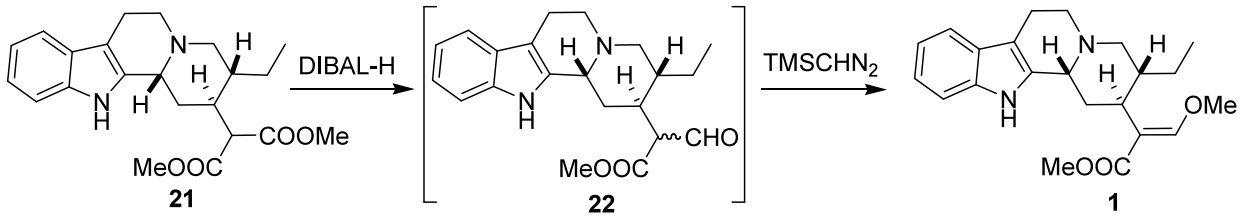


Palladium on carbon (10%, 5 wt%, 13.3 mg) was added to a solution of **20** (267 mg, 0.698 mmol) in MeOH (20 mL). The mixture was stirred under H_2 (balloon) at room temperature overnight and then filtered through a pad of Celite. The filtrate was concentrated and the residue purified through FCC (SiO_2; hexanes/EtOAc, 1:1) to give a light-yellow solid (265 mg, 98.7%).[5] ^{1}H NMR (400 MHz, $CDCl_3$) 8.13 (br s, 1H), 7.47 (d, J = 7.6 Hz, 1 H), 7.38 (d, J = 7.6 Hz, 1H), 7.14 (dt, J = 1.2, 7.2 Hz, 1H), 7.09 (dt, J = 1.2, 8.0 Hz, 1H), 4.12 (br s, 1 H), 3.80 (s, 3H), 3.79 (s, 3H), 3.22–3.17 (m, 1 H), 3.10–2.96 (m, 2 H), 2.74 (dd, J = 11.6, 3.6 Hz, 1 H), 2.63 (app d, J = 11.6 Hz, 1 H), 2.51 (dd, J = 11.6, 8.0 Hz, 1 H), 2.41–2.33 (m, 1 H), 2.05–1.96 (m, 1 H), 1.87–1.81 (m, 1 H), 1.67–1.56 (m, 1 H), 1.55–1.47 (m, 1 H), 1.33–1.18 (m, 1 H), 0.99–0.92 (m, 1 H), 0.87 (t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 169.8, 168.9, 136.0, 129.9, 127.6, 121.4, 119.4,

[5] (a) Wenkert, E.; Vankar, Y. D.; Yadav, J. S. *J. Am. Chem. Soc.* **1980**, *102*, 7971–7972. (b) Lounasmaa, M.; Miettinen, J.; Hanhinen, P.; Jokela, R. *Tetrahedron Lett.*, **1997**, *38*, 1455–1458.

118.0, 111.2, 108.0, 54.4, 52.6, 52.4, 51.8, 51.5, 39.1, 36.2, 29.7, 29.2, 23.9, 18.5, 11.3; IR (neat, cm^{-1}) 3425, 1739; MS (MALDI) calcd for $C_{22}H_{28}N_2O_4Na$ $[M + Na]^+$ *m*/*z* 407.2, found 407.0.

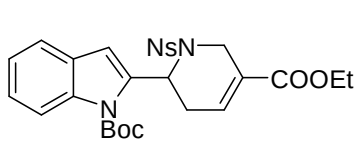
Synthesis of hirsutine (1)



DIBAL-H (1.0 M in DCM, 0.655 mL, 0.655 mmol) was added to a solution of **21** (105 mg, 0.273 mmol) in DCM (6 mL) at –78 °C. The reaction was quenched after 1 h through slow addition of 10% aqueous HCl (10 mL). The aqueous phase was extracted thoroughly with DCM. The combined organic phases were washed with brine, dried, and concentrated. The crude aldehyde **22** (79 mg, ca. 82%; ^{1}H NMR spectroscopy revealed a tautomeric mixture) was used directly in the next step. *i*Pr_2NEt (0.054 mL, 0.312 mmol) and $TMSCHN_2$ (2.0 M in hexane, 0.156 mL, 0.312 mmol) were added sequentially at room temperature to a solution of the crude aldehyde **22** in dry MeOH (0.5 mL) and MeCN (4.5 mL). The mixture was stirred overnight, then concentrated. The residue was purified through FCC [SiO_2; hexanes/acetone, 2:1 (with 1% Et_3N)] to give a glass (31 mg, 30.8% from the diester **21** over two steps).[6] ^{1}H NMR (500 MHz, $CDCl_3$) 7.95 (br s, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.32 (s, 1H), 7.16 (t, *J* = 7.0 Hz, 1H), 7.10 (t, *J* = 7.0 Hz, 1H), 4.51 (br s, 1H), 3.77 (s, 3H), 3.69 (s, 3H), 3.38–3.28 (m, 1H), 3.07–3.00 (m, 1H), 2.81 (d, *J* = 10.0 Hz, 1H), 2.59 (d, *J* = 18.0 Hz, 1H), 2.49 (br s, 1H), 2.37 (t, *J* = 10.0 Hz, 1H), 2.17 (d, *J* = 9.5 Hz, 2H), 1.98 (d, *J* = 13.5 Hz, 1H), 1.34–1.26 (m, 1H), 0.95–0.82 (m, 1H), 0.76 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 169.0, 159.8, 135.9, 133.1, 127.9, 122.6, 121.3, 119.3, 118.0, 111.7, 111.2, 107.8, 61.5, 54.2, 51.4, 51.3, 50.7, 39.0, 34.9, 31.7, 24.3, 17.0, 11.4; IR (neat, cm^{-1}) 3399, 1712; HRMS (EI) Calculated for $[M + Na]^+$, $C_{22}H_{28}N_2O_3Na$: *m*/*z* 391.1998, found 391.1990.

[6] (a) Lounasmaa, M.; Jokela, R.; Laine, C.; Hanhinen, P. *Heterocycles* **1998**, *49*, 445–450. (b) Xin, W.; Gui, X.; Wang, Z. *Chin. Traditional and Herbal Drugs* **2009**, *40*, 204–207.

Selected copies of ^{1}H and ^{13}C NMR spectra



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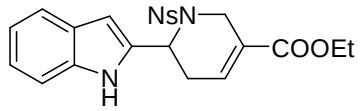
NsN
COOEt
N
H

14

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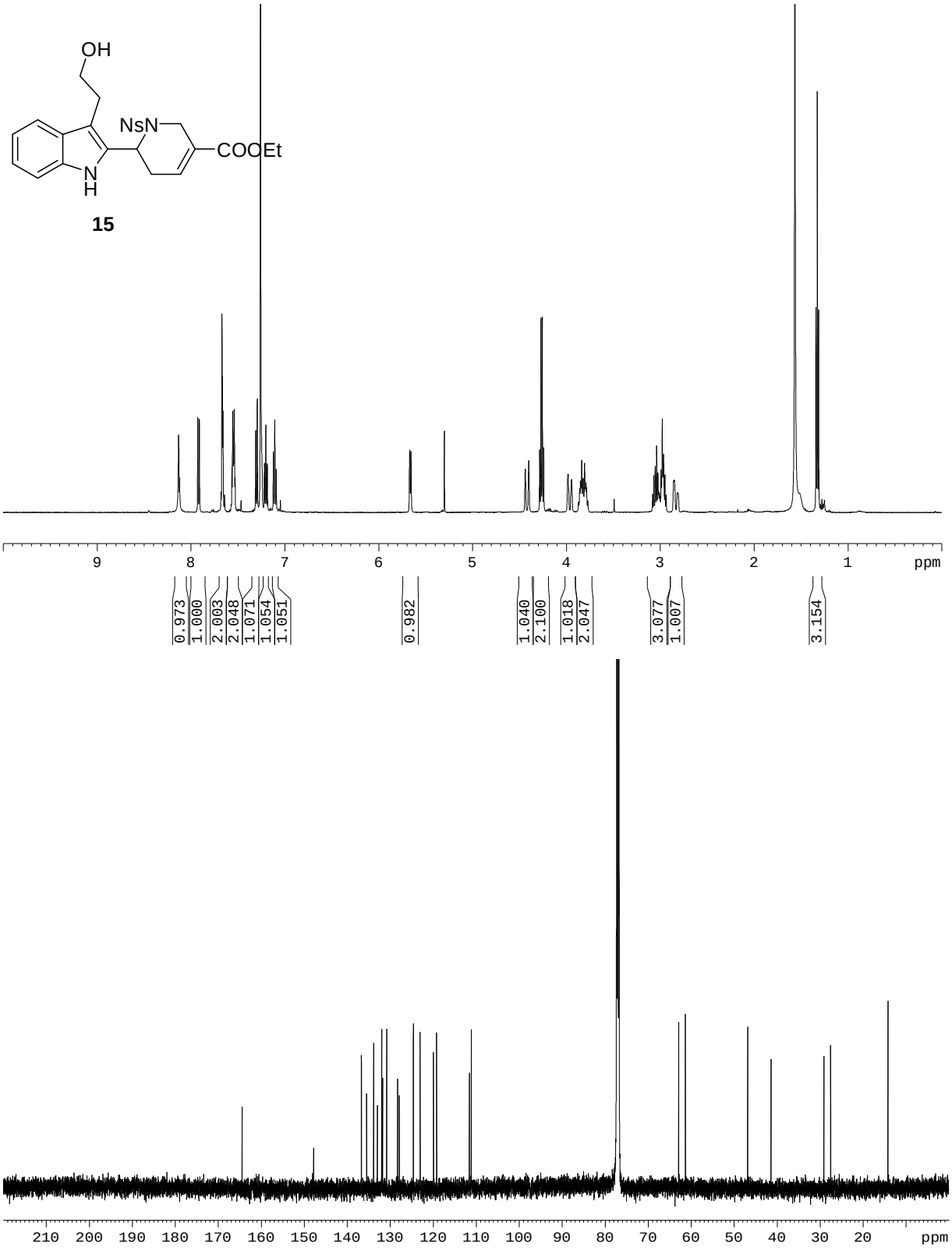
0.987
1.032
3.152
1.086
1.038
2.056
1.073
1.003
1.000
1.019
2.156
0.999
2.008
3.336

240 220 200 180 160 140 120 100 80 60 40 20 ppm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COOEt
N
H
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8
7
6
5
4
3
2
1
ppm
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2.003
2.048
1.071
1.054
1.051
0.982
1.040
2.100
1.018
2.047
3.077
1.007
3.154
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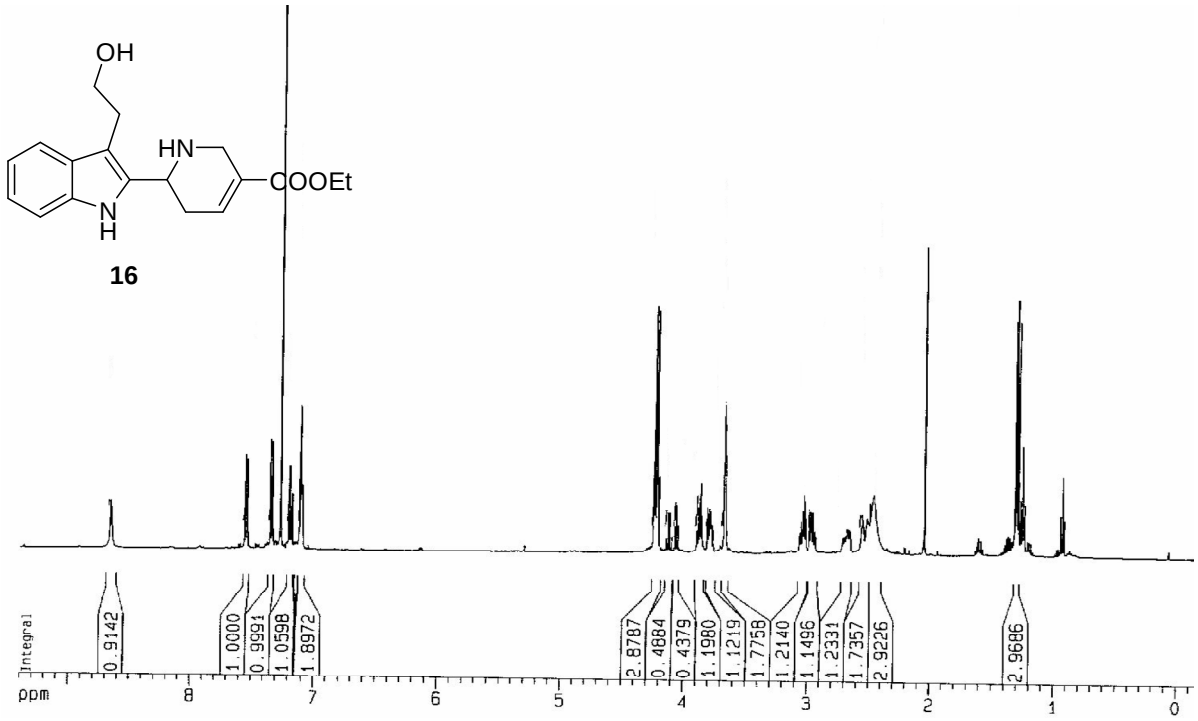
80
70
60
50
40
30
20
ppm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0.4379
1.1980
1.1219
1.7758
1.2140
1.1496
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2.9686
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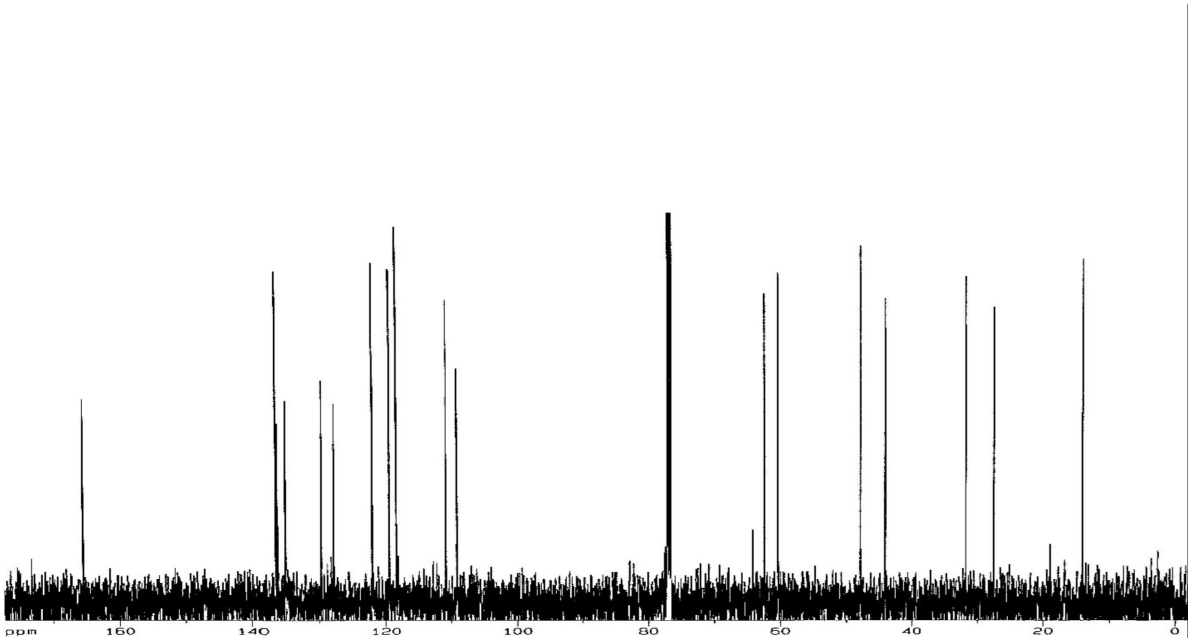
8
7
6
5
4
3
2
1
0

16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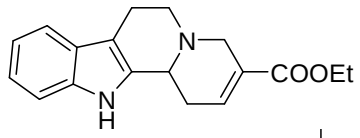
140
120
100
80
60
40
20
0


N
COOEt
N
H

17

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1.027
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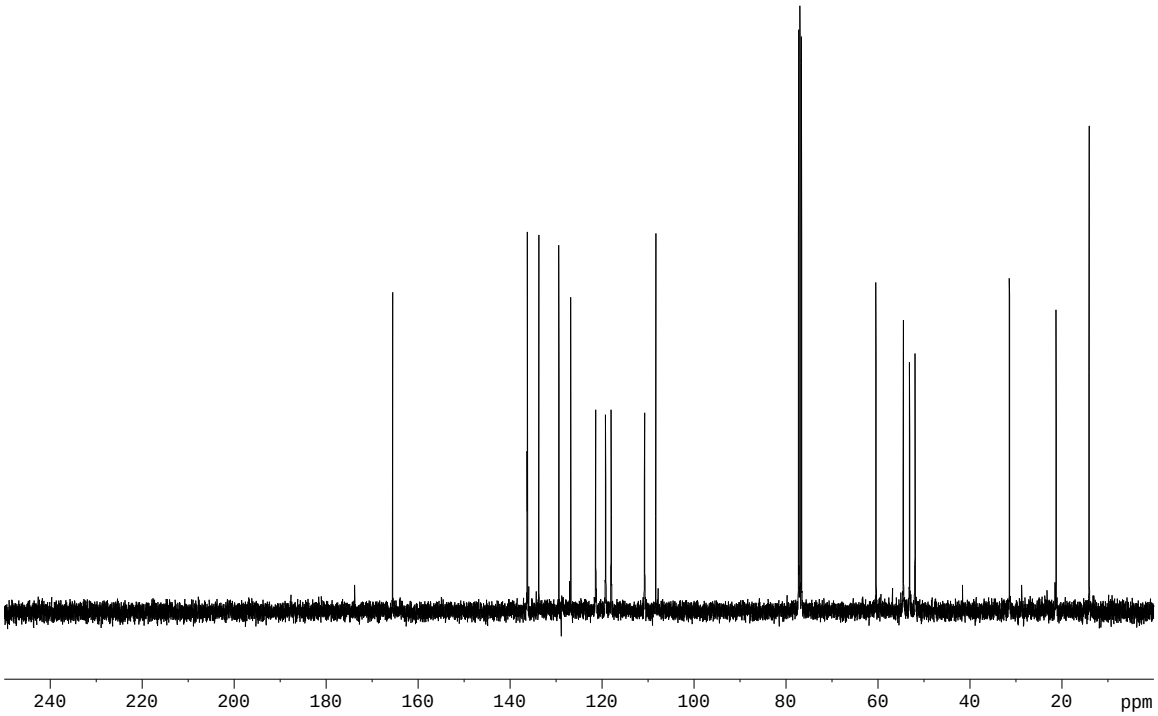
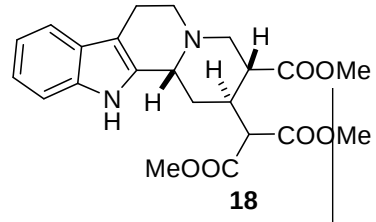
1.000
1.001
2.070
1.052
3.047
1.026
3.083


240 220 200 180 160 140 120 100 80 60 40 20 ppm


N
H
H
COOMe
N
H
H
COOMe
MeOOC

18

9
8
7
6
5
4
3
2
1
ppm
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1.090
0.974
1.084
0.969
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5.948
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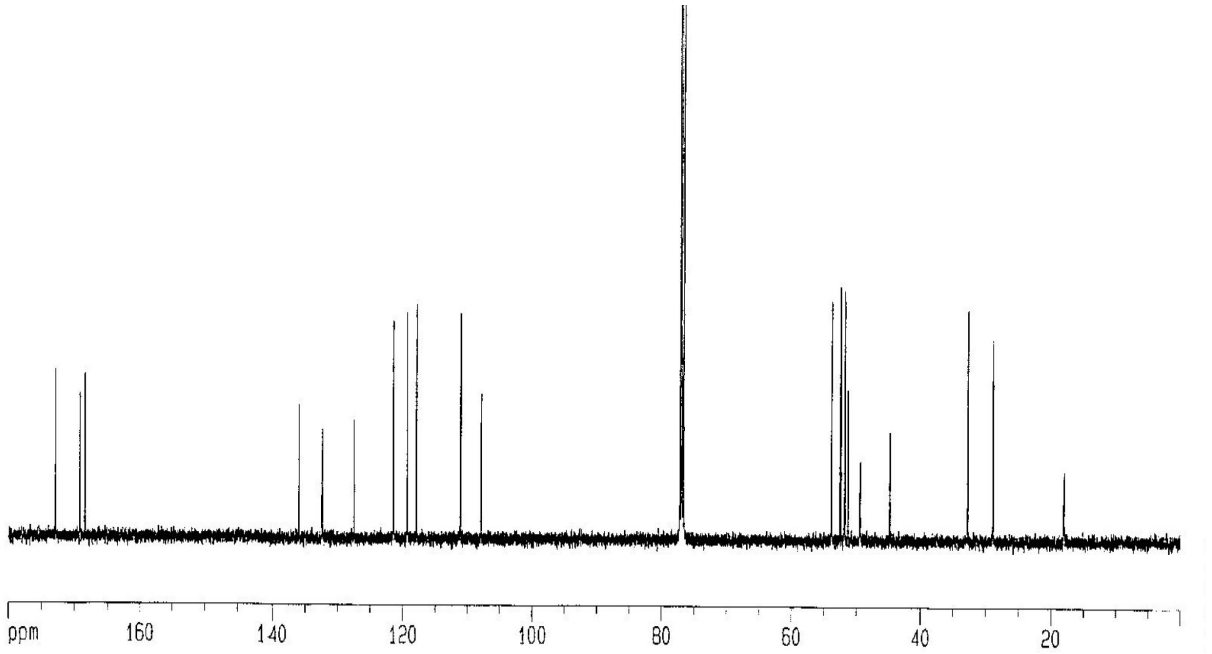
2.948
2.043
3.103
1.088
1.052
1.991
1.023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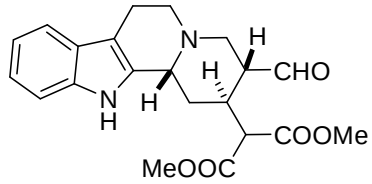
140
120
100
80
60
40
20


N
H
H
CHO
N
H
H
COOMe
MeOOC

19

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8
7
6
5
4
3
2
1
ppm
1.064
1.031
1.250
1.166
2.502
1.170
3.509
3.912
2.376
4.510
1.150
1.041
1.125
1.291
3.115
210
200
190
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160
150
140
130
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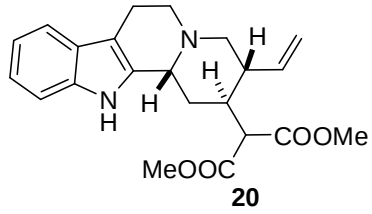
70
60
50
40
30
20
ppm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H
H
N
H
COOMe
MeOOC

20

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2.181
1.072
2.000
0.886
6.727
1.237
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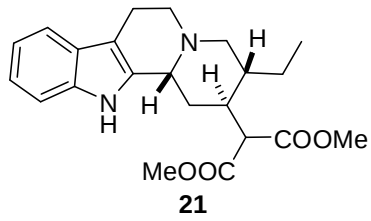
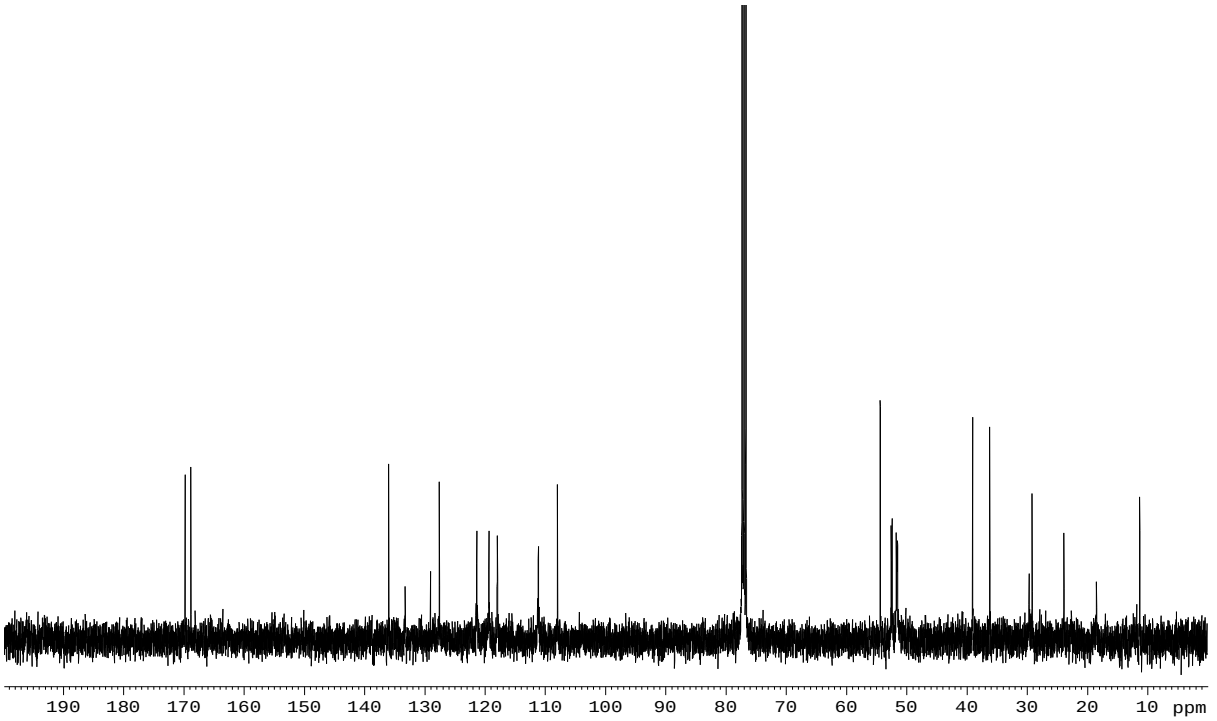
3.149
1.149
1.179
2.099
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


N
H
H
N
H
H
COOMe
MeOOC

21

9
8
7
6
5
4
3
2
1
ppm
0.67
1.01
0.86
2.00
0.63
5.42
0.93
1.88
0.89
1.20
1.10
1.06
1.16
0.99
1.15
0.99
1.06
1.17
2.43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80
70
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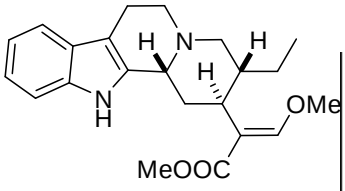
40
30
20
10
ppm


H
N
H
H
N
H
OMe
MeOOC

Hirsutine (1)

9
8
7
6
5
4
3
2
1
ppm
0.827
0.934
0.897
0.923
2.000
0.799
2.734
2.774
1.943
1.029
0.878
1.033
1.073
0.943
2.179
1.116
1.286
1.046
3.759
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm