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SUPPORTING INFORMATION

Brønsted-Acid Catalyzed Condensation-Michael Reaction-Pictet-Spengler Cyclization – Highly Diastereoselective Synthesis of Indoloquinolizidines

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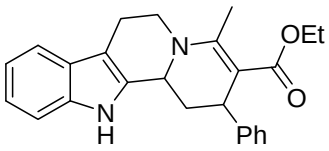
Methods: Unless otherwise stated, reactions were conducted in flame-dried glassware under vacuum. Solvents after reactions and extractions were evaporated in a rotatory evaporator under vacuum. TLC for reaction monitoring was performed on 60 F_{254} (Merck) with detection by UV light and charring with $KMnO_4$ or Pancaldi reagent. ^{1}H and ^{13}C NMR spectra were recorded by using Varian Inova 400 spectrometer at 400 MHz and 100.6 MHz respectively and are reported relative to Me_4Si (δ 0.0) or to the solvents residual ^{1}H-signal ($CH\text{-}Cl_3$, δ(H) 7.27). 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 reported in terms of chemical shift. IR spectra were recorded on a Perkin-Elmer-100 spectrometer and are reported in frequency of absorption (cm^{-1}). High Resolution ESI-TOF mass spectra were obtained from the Institute of Organic Chemistry, RWTH Aachen University. Diastereoselective ratios were determined by 1H NMR of the crude reaction mixtures.

Typical Experimental Procedure: In a screw-cap tube were placed 50 mg of tryptamine (0.31 mmol, 1 equiv.), 8 mg of DPP (0.03 mmol, 10 mol%) and 200 mg of 4Å molecular sieves. 1.0 mL of dry DCM was added to the tube and heated slightly with a heat gun to dissolve the tryptamine. Activated methylene compound (1.5 equiv.) was added at once to the reaction and stirred at room temperature. After 2h, the corresponding aldehyde (2 equiv.) was added to the reaction and continued stirring for overnight. Reaction was quenched with water and extracted with DCM (3 times, 20 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated under reduced pressure (rotatory evaporator). The residue was purified by chromatography on silica gel with a 9 : 1 cyclohexane to ethylacetate mixture.

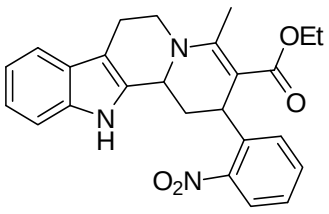
Ethyl-4-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4a):



Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 80 µL of cinnamaldehyde (0.62 mmol, 2 equiv.), 99 mg (0.26 mmol, 83%) of product was obtained as light yellow solid. This compound was known and has shown the same spectral data reported for the compound.[1]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, 3H, *J* = 7.1 Hz, Me), 2.04 (td, 1H, *J* = 12.6 Hz, 5.5 Hz), 2.27 (ddd, 1H, *J* = 12.6 Hz, 3.6 Hz, 2.7 Hz), 2.63 (s, 3H, Me), 2.69 – 2.89 (m, 2H), 3.14 (ddd, 1H, *J* = 13.7 Hz. 11.3 Hz, 3.6 Hz), 3.92 (qd, 2H, *J* = 7.1 Hz, 2.2 Hz, CH_2), 4.23 – 4.34 (m, 3H), 7.04 – 7.14 (m, 2H, Arom.), 7.18 (tt, 1H, *J* = 6.6 Hz, 1.4 Hz, Arom.), 7.20 – 7.25 (m, 3H, Arom.), 7.26 – 7.32 (m, 2 H, Arom.), 7.45 (d, 1H, *J* = 7.8 Hz, Arom.), 7.66 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 14.35, 17.64, 22.51, 36.11, 38.21, 44.85, 49.57, 58.97, 96.90, 109.04, 110.84, 117.97, 119.58, 121,74, 125.91, 126,75, 127.78, 128.17, 133.94, 135.94, 146.95, 154.65, 168.87. **IR (film):** 3288, 3060, 1730, 1646, 1619, 1541, 1493, 1442, 1371, 1353, 1212, 1168, 986, 921, 886, 855, 809 cm^{-1}. **HRMS (ESI-TOF):** ($C_{25}H_{27}N_2O_2$), calcd: 387.2067; found: 387.2068. de >95%.

Ethyl-4-methyl-2-(2-nitrophenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate



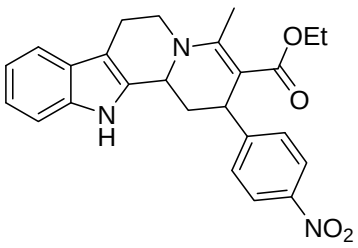
(4b): Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 110 mg of *p*-nitrocinnamaldehyde (0.62 mmol, 2 equiv.), 107 mg (0.25 mmol, 80%) of product was obtained as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, 3H, *J* = 7.1 Hz, Me), 2.20 (ddd, 1H, *J* = 13.5 Hz, 11.8 Hz, 6.0 Hz), 2.51 (dt, 1H, *J* = 13.5 Hz, 3.5 Hz), 2.66 (s, 3H, Me), 2.76 – 2.95 (m, 2H), 3.25 (ddd, 1H, *J* = 13.5 Hz. 11.5 Hz, 3.8 Hz), 3.79 (qd, 2H, *J* = 7.17 Hz, 5.5 Hz, CH_2), 4.38 (ddd, 1H, *J* = 13.5 Hz, 4.7 Hz, 1.7 Hz),

[1] Wu, X.; Dai, X.; Nie, L.; Fang, H.; Chen, J.; Ren, Z.; Cao, W.; Zhao, G. *Chem. Comm.* **2010**, *46*, 2733 – 2735.

4.49 (d, 1H, *J* = 9.9 Hz), 4.61 (dd, 1H, *J* = 5.5 Hz, 1.7 Hz), 7.08 (td, 1H, *J* = 7.1 Hz, 1.3 Hz, Arom.), 7.13 (td, 1H, *J* = 7.4 Hz, 1.3 Hz, Arom.), 7.27 (d, 1H, 7.7 Hz, Arom.), 7.30 – 7.39 (m, 2H, Arom.), 7.44 – 7.52 (m, 2H, Arom.), 7.79 (s, 1H, NH), 7.82 (dd, 1H, *J* = 8.2 Hz, 1.3 Hz, Arom.). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 13.97, 17.27, 22.37, 34.00, 34.18, 45.10, 49.99, 58.98, 96.92, 109.22, 111.00, 118.00, 119.71, 121.99, 124.15, 126.69, 126.87, 130.31, 132.27, 133.19, 136.03, 141.50, 149.57, 155.69, 167.93. **IR (film):** 3289, 2922, 2849, 1652, 1549, 1521, 1425, 1350, 1300, 1215, 1121, 1094, 1029, 923, 886, 857, 781, 740, 708, 674 cm^{-1}. **HRMS (ESI-TOF):** ($C_{25}H_{26}N_3O_4$), calcd: 432.1918; found: 432.1918. de >95%.

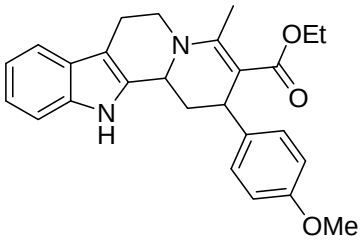
Ethyl-4-methyl-2-(4-nitrophenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate



(4c): Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 110 mg of *p*-nitrocinnamaldehyde (0.62 mmol, 2 equiv.), 106 mg (0.25 mmol, 79%) of product was obtained as light yellow solid. This compound was known and has shown the same spectral data reported for the compound.[1]

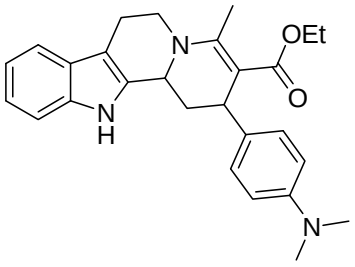
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, 3H, *J* = 7.2 Hz, Me), 2.05 (td, 1H, *J* = 12.9 Hz, 5.5 Hz), 2.31 (ddd, 1H, *J* = 16.0 Hz, 6.3 Hz, 3.0 Hz), 2.61 (s, 3H, Me), 2.68 – 2.86 (m, 2H), 3.14 (ddd, 1H, *J* = 13.0 Hz. 11.3 Hz, 3.8 Hz), 3.85 (q, 2H, *J* = 7.1 Hz, CH_2), 4.18 (d, 1H, *J* = 11.0 Hz), 4.23 – 4.33 (m, 2H), 6.99 – 7.08 (m, 2H, Arom.), 7.17 (d, 1H, *J* = 7.4 Hz, Arom.), 7.32 (d, 2H, *J* = 8.8 Hz, Arom.), 7.40 (d, 1H, *J* = 7.1 Hz, Arom.), 8.01 (s, 1H, NH), 8.02 (d, 2H, *J* = 8.8 Hz, Arom.). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 14.39, 17.63, 22.43, 35.68, 38.62, 44.99, 49.56, 59.14, 95.38, 109.16, 110.95, 118.03, 119.64, 121.91, 123.47, 126.60, 128.59, 133.24, 136.10, 146.14, 155.29, 155.67, 168.41. **IR (film):** 3306, 2924, 2853, 1726, 1673, 1596, 1549, 1514, 1428, 1341, 1301, 1210, 1092, 1028, 984, 961, 856, 741, 700 cm^{-1}. **HRMS (ESI-TOF):** ($C_{25}H_{26}N_3O_4$), calcd: 432.1918; found: 432.1914. de >95%.

Ethyl-2-(4-methoxyphenyl)-4-methyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4d): Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 100 mg of *p*-methoxycinnamaldehyde (0.62 mmol, 2 equiv.), 107 mg (0.26 mmol, 82%) of product was obtained as light yellow solid.



^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, 3H, *J* = 7.2 Hz, Me), 2.03 (td, 1H, *J* = 12.6 Hz, 5.2 Hz), 2.27 (ddd, 1H, *J* = 13.0 Hz, 3.7 Hz, 2.7 Hz), 2.64 (s, 3H, Me), 2.70 – 2.94 (m, 2H), 3.16 (ddd, 1H, *J* = 15.1 Hz. 11.1 Hz, 4.2 Hz), 3.79 (s, 3H, OMe), 3.96 (q, 2H, *J* = 7.2 Hz, CH_2), 4.22 – 4.36 (m, 3H), 6.85 (d, 2H, *J* = 8.9Hz, Arom.), 7.05 – 7.18 (m, 2H, Arom.), 7.16 (d, 2H, *J* = 8.9 Hz, Arom.), 7.24 (d, 1H, *J* = 8.4 Hz, Arom.), 7.46 (d, 1H, *J* = 6.9 Hz, Arom.), 7.77 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 14.29, 17.54, 22.40, 36.14, 37.24, 44.78, 49.52, 55.24, 58.93, 97.30, 108.98, 110.87, 113.60, 117.97, 119.58, 121.73, 126.82, 128.73, 134.13, 136.03, 139.11, 154.48, 157.85, 169.08. **IR (film):** 3317, 2958, 2919, 1729, 1639, 1543, 1508, 1440, 1423, 1351, 1299, 1246, 1213, 1177, 1096, 1031, 986, 922, 886, 834, 738, 673 cm^{-1}. **HRMS (ESI-TOF):** ($C_{25}H_{29}N_2O_3$), calcd: 417.2173; found: 417.2171. de >95%.

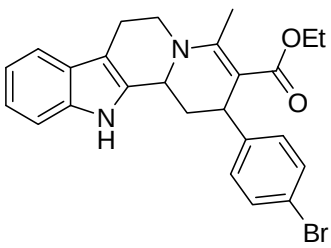
Ethyl-2-(4-(dimethylamino)phenyl)-4-methyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4e): Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 108 mg of *p*-dimethylaminocinnamaldehyde (0.62 mmol, 2 equiv.), 103 mg (0.24 mmol, 77%) of product was obtained as light yellow solid.



^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (t, 3H, *J* = 7.0 Hz, Me), 2.01 (td, 1H, *J* = 12.6 Hz, 5.0 Hz), 2.25 (ddd, 1H, *J* = 12.5 Hz, 3.5 Hz, 2.5 Hz), 2.63 (s, 3H, Me), 2.69 – 2.90 (m, 2H), 2.93 (s, 6H, NMe_2), 3.16 (ddd, 1H, *J* = 13.4 Hz. 10.9 Hz, 3.9 Hz), 3.79 (qd, 2H, *J* = 7.0 Hz, 1.2 Hz, CH_2), 4.21 – 4.36 (m, 3H), 6.72 (d, 2H, *J* = 8.7 Hz, Arom.), 7.02 – 7.18 (m, 4H, Arom.), 7.25 (d, 1H, *J* = 7.8 Hz, Arom.), 7.47 (d, 1H, *J* = 7.12 Hz), 7.64 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 14.34, 17.55, 22.45, 36.23, 37.04, 40.89, 44.75, 49.60, 58.90, 97.65, 108.96, 110.83, 112.79, 117.95, 119.56,

121.68, 126.86, 128.47, 134.36, 135.98, 154.12, 169.19. **IR (film):** 3297, 2922, 2852, 1730, 1649, 1548, 1517, 1438, 1350, 1299, 12122, 1114, 1091, 1027, 945, 885, 822, 775, 738 cm^{-1}. **HRMS (ESI-TOF):** ($C_{27}H_{32}N_3O_2$), calcd: 430.2489; found: 430.2486. de >95%.

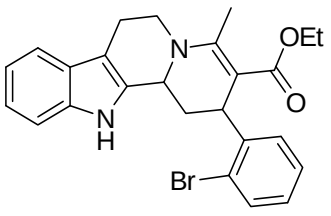
Ethyl-2-(4-bromophenyl)-4-methyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate



(4f): Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 131 mg of *p*-bromocinnamaldehyde (0.62 mmol, 2 equiv.), 123 mg (0.27 mmol, 85%) of product was obtained as light yellow solid. This compound was known and has shown the same spectral data reported for the compound.[1]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, 3H, *J* = 7.0 Hz, Me), 2.05 (td, 1H, *J* = 12.6 Hz, 5.5 Hz), 2.28 (ddd, 1H, *J* = 12.6 Hz, 3.5 Hz, 2.7 Hz), 2.64 (s, 3H, Me), 2.71 – 2.94 (m, 2H), 3.14 (ddd, 1H, *J* = 13.1 Hz. 11.1 Hz, 3.9 Hz), 3.95 (q, 2H, *J* = 7.2 Hz, CH_2), 4.18 – 4.37 (m, 3H), 7.06 – 7.17 (m, 4H, Arom.), 7.24 (d, 1H, *J* = 9.4 Hz, Arom.), 7.42 (d, 2H, *J* = 8.2 Hz, Arom.), 7.47 (d, 1H, *J* = 6.9 Hz, Arom.), 7.92 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 14.29, 17.52, 22.36, 35.79, 37.72, 44.85, 49.48, 59.04, 96.29, 109.05, 110.92, 118.02, 119.62, 119.71, 121,83, 126.75, 129,59, 131.27, 133.71, 136.10, 146.15, 155.10, 168.84. **IR (film):** 3298, 2922, 2853, 1729, 1648, 1545, 1457, 1422, 1352, 1300, 1210, 1121, 1094, 1028, 1008, 986, 886, 831, 798, 739, 672 cm^{-1}. **HRMS (ESI-TOF):** ($C_{25}H_{26}BrN_2O_2$), calcd: 467.1151; found: 467.1155. de >95%.

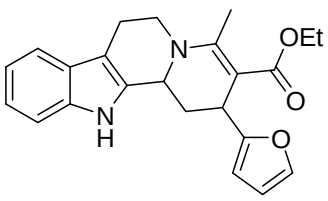
Ethyl-2-(2-bromophenyl)-4-methyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate



(4g): Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 131 mg of *p*-methoxycinnamaldehyde (0.62 mmol, 2 equiv.), 118 mg (0.26 mmol, 84%) of product was obtained as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, 3H, *J* = 7.2 Hz, Me), 2.02 (td, 1H, *J* = 12.9 Hz, 5.7 Hz), 2.38 (ddd, 1H, *J* = 13.4 Hz, 3.7 Hz, 2.3 Hz), 2.67 (s, 3H, Me), 2.71 – 2.95 (m, 2H), 3.19 (ddd, 1H, *J* = 13.6 Hz. 11.1 Hz, 4.0 Hz), 3.91 (q, 2H, *J* = 7.2 Hz, CH_2), 4.24 – 4.40 (m, 2H), 4.67 (d, 1H, *J* = 4.2 Hz), 7.05 – 7.16 (m, 3H, Arom.), 7.17 – 7.28 (m, 3H, Arom.), 7.48 (d, 1H, *J* = 6.9 Hz, Arom.), 7.61 (dd, 1H, *J* = 7.9 Hz, 1.2 Hz, Arom.), 7.80 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 14.08, 17.38, 22.35, 33.15, 38.02, 44.75, 49.58, 58.94, 96.80, 109.04, 110.96, 117.99, 119.61, 121.82, 124.05, 126.75, 127.05, 127.70, 129.79, 132.95, 133.71, 136.07, 145.43, 155.44, 168.63. **IR (film):** 3391, 3202, 2974, 2921, 2846, 1676, 1645, 1556, 1459, 1432, 1351, 1296, 1217, 1169, 1129, 1110, 1091, 1027, 919, 886, 804, 779, 743 cm^{-1}. **HRMS (ESI-TOF):** ($C_{25}H_{26}BrN_2O_2$), calcd: 465.1172; found: 465.1173. de >95%.

Ethyl-2-(furan-2-yl)-4-methyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4h):

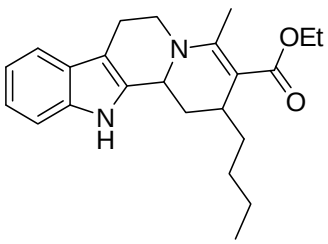


Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 76 mg of 3-(2-furyl)-acrolein (0.62 mmol, 2 equiv.), 103 mg (0.27 mmol, 88%) of product was obtained as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 (t, 3H, *J* = 7.0 Hz, Me), 1.87 (td, 1H, *J* = 12.6 Hz, 4.8 Hz), 2.55 (ddd, 1H, *J* = 12.6 Hz, 3.8 Hz, 2.5 Hz), 2.56 (s, 3H, Me), 2.68 – 2.88 (m, 2H), 3.11 (ddd, 1H, *J* = 13.4 Hz. 11.3 Hz, 3.8 Hz), 3.96 – 4.15 (m, 2H, CH_2), 4.20 – 4.36 (m, 3H), 5.96 (d, 1H, *J* = 3.0 Hz, Arom.), 6.27 (dd, 1H, *J* = 3.0 Hz, 2.0 Hz), 7.08 (td, 1H, *J* = 7.7 Hz, 1.2 Hz, Arom.), 7.13 (td, 1H, *J* = 7.1 Hz, 1.3 Hz), 7.23 – 7.28 (m, 1H, Arom.), 7.33 (d, 1H, *J* = 2.0 Hz), 7.46 (d, 1H, *J* = 8.2 Hz, Arom.), 7.87 (s, 1H, NH).

^{13}C NMR (100.6 MHz, $CDCl_3$): 14.54, 17.74, 22.47, 32.43, 32.60, 44.86, 50.54, 59.13, 95.30, 106.41, 108.93, 110.18, 110.92, 118.00, 119.60, 121.79, 126.71, 133.83, 136.03, 140.92, 154.71, 159.02, 168.79. **IR (film):** 3397, 3298, 2924, 2851, 1726, 1649, 1547, 1428, 1352, 1299, 1215, 1168, 1117, 1091, 1028, 1007, 918, 884, 735, 688 cm^{-1}. **HRMS (ESI-TOF):** ($C_{23}H_{25}N_2O_3$), calcd: 377.1860; found: 377.1858. de >95%.

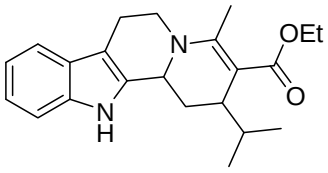
Ethyl-2-butyl-4-methyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4i):



Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 80 µL of hept-2-enal (0.62 mmol, 2 equiv.), 89 mg (0.24 mmol, 78%) of product was obtained as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, 3H, *J* = 6.9 Hz, Me), 1.26 (t, 3H, *J* = 7.1 Hz, Me), 1.29 – 1.40 (m, 5 H, aliphatic), 1.51 – 1.60 (m, 1H, aliphatic), 1.67 (td, 1H, *J* = 12.6 Hz, 4.9 Hz), 2.24 (ddd, 1H, *J* = 12.6 Hz, 4.1 Hz, 2.2 Hz), 2.46 (s, 3H, Me), 2.68 – 2.88 (m, 2H), 2.88 – 2.95 (m, 1H), 3.13 (ddd, 1H, *J* = 13.5 Hz, 11.3 Hz, 3.9 Hz), 4.02 – 4.26 (m, 3H, CH_2 + CH), 4.50 (d, 1H, *J* = 12.6 Hz), 7.05 – 7.17 (m, 2H, Arom.), 7.31 (d, 1H, *J* = 7.9 Hz, Arom.), 7.46 (d, 1H, *J* = 7.7 Hz, Arom.), 8.00 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 14.30, 14.70, 17.67, 22.56, 22.89, 29.60, 31.29, 35.59, 45.04, 50.07, 59.03, 100.32, 108.87, 110.88, 118.00, 119.58, 121.70, 126.88, 134.58, 135.99, 152.59, 169.44. **IR (film):** 3313, 2955, 2928, 2860, 1729, 1622, 1545, 1458, 1369, 1302, 1219, 1128, 1096, 1025, 859, 742 cm^{-1}. **HRMS (ESI-TOF):** ($C_{23}H_{31}N_2O_2$), calcd: 367.2380; found: 367.2381. de >95%.

Ethyl=-2-isopropyl-4-methyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4j):

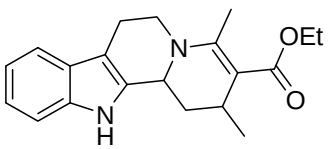


Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 71 µL of 4-methyl-2-pent-enal (0.62 mmol, 2 equiv.), 81 mg (0.23 mmol, 74%) of product was obtained as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (d, 3H, *J* = 6.7 Hz, Me), 0.96 (d, 3H, *J* = 6.9 Hz, Me), 1.19 (t, 3H, *J* = 7.2 Hz, Me), 1.49 – 1.63 (m, 2H), 2.37 (ddd, 1H, *J* = 13.1 Hz, 5.2 Hz, 3.0 Hz), 2.40 (s, 3H, Me), 2.60 – 2.86 (m, 3H), 3.10 (ddd, 1H, *J* = 13.6 Hz, 11.4 Hz, 3.9 Hz), 4.04 (qd, 2H, *J* = 12.1 Hz, 7.2 Hz, CH_2), 4.18 (dd, 1H, *J* = 13.9 Hz, 4.7 Hz), 4.48 (d, 1H, 12.9 Hz), 6.99 – 7.12 (m, 2H, Arom.), 7.26 (d, 1H, *J* = 7.2 Hz, Arom.), 7.41 (d, 1H, *J* = 7.2 Hz, Arom.), 7.89 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 14.56, 17.34, 20.65, 21.08, 22.53, 30.29, 31.99, 37.34, 45.34, 50.68, 58.90, 99.01, 108.67, 110.89, 118.04,

119.63, 121.75, 126.95, 134.93, 135.97, 151.91, 169.99. **IR (film):** 3303, 2959, 2870, 1728, 1642, 1544, 1458, 1353, 1302, 1220, 1094, 1024, 921, 858, 775, 741, 698 cm^{-1}. **HRMS (ESI-TOF):** ($C_{22}H_{29}N_2O_2$), calcd: 353.2223; found: 353.2221. de >95%.

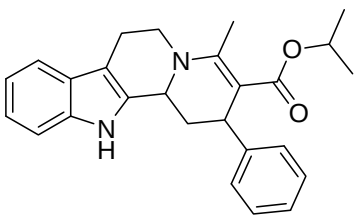
Ethyl-2,4-dimethyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4k):



Following the Typical Experimental Procedure using 60 µL of ethylacetoacetate (0.46 mmol, 1.5 equiv.), 45 µL of crotonaldehyde (0.62 mmol, 2 equiv.), 72 mg (0.22 mmol, 71%) of product was obtained as light yellow solid. This compound was known and has shown the same spectral data reported for the compound.[1]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (d, 3H, *J* = 6.9 Hz, Me), 1.26 (t, 3H, *J* = 7.1 Hz, Me), 1.78 (td, 1H, *J* = 12.6 Hz, 5.2 Hz), 2.06 (ddd, 1H, *J* = 12.9 Hz, 3.8 Hz, 2.5 Hz), 2.46 (s, 3H, Me), 2.69 – 2.88 (m, 2H), 3.08 (qn, 1H, *J* = 6.3 Hz), 3.16 (ddd, 1H, *J* = 13.2 Hz, 11.3 Hz, 4.1 Hz), 4.13 (qd, 2H, *J* = 21.9 Hz, 7.1 Hz), 4.18 – 4.25 (m, 1H), 4.53 (d, 1H, *J* = 12.0 Hz), 7.06 – 7.17 (m, 2H, Arom.), 7.31 (d, 1H, *J* = 7.9 Hz, Arom.), 7.47 (d, 1H, *J* = 7.7 Hz, Arom.), 7.96 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 14.71, 17.73, 22.23, 22.51, 26.53, 34.79, 44.90, 49.75, 59.03, 100.93, 108.94, 110.88, 118.01, 119.60, 121.73, 126.86, 134.45, 136.02, 152.91, 169.30. **IR (film):** 3330, 2925, 2856, 1727, 1620, 1544, 1452, 1368, 1299, 1222, 1128, 1090, 1016, 923, 858, 743, 678 cm^{-1}. **HRMS (ESI-TOF):** ($C_{20}H_{25}BrN_2O_2$), calcd: 325.1911; found: 325.1910. de >95%.

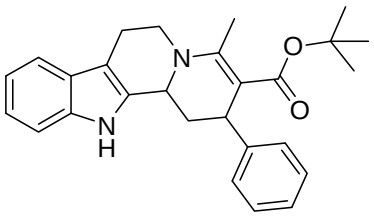
Isopropyl-4-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4l):



Following the Typical Experimental Procedure using 68 µL of *i*-propylacetoacetate (0.46 mmol, 1.5 equiv.), 80 µL of cinnamaldehyde (0.62 mmol, 2 equiv.), 97 mg (0.24 mmol, 78%) of product was obtained as light yellow solid. This compound was known and has shown the same spectral data reported for the compound.[1]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.68 (d, 3H, *J* = 6.0 Hz, Me), 1.04 (d, 3H, *J* = 6.0 Hz, Me), 1.97 (td, 1H, *J* = 12.36 Hz, 5.5 Hz), 2.19 (ddd, 1H, *J* = 12.9 Hz, 3.6 Hz, 2.2 Hz), 2.54 (s, 3H, Me), 2.62 – 2.82 (m, 2H), 3.07 (ddd, 1H, *J* = 13.2 Hz. 11.1 Hz, 3.6 Hz), 4.15 – 4.24 (m, 3H), 4.75 (sept, 1H, *J* = 6.0 Hz, CH), 6.97 – 7.07 (m, 2H, Arom.), 7.09 – 7.25 (m, 6H, Arom.), 7.38 (d, 1H, *J* = 7.2 Hz, Arom.), 7.61 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 17.73, 21.53, 22.32, 22.49, 36.09, 38.45, 44.73, 49.47, 65.79, 97.67, 109.01, 110.87, 117.95, 119.54, 121.69, 125.84, 126.74, 127.87, 128.12, 133.96, 135.96, 147.37, 154.56, 168.44. **IR (film):** 3397, 3187, 2926, 1732, 1674, 1635, 1550, 1453, 1410, 1295, 1215, 1133, 1091, 1029, 931, 882, 779, 744, 698 cm^{-1}. **HRMS (ESI-TOF):** ($C_{26}H_{29}N_2O_2$), calcd: 401.2223; found: 401.2220. de >95%.

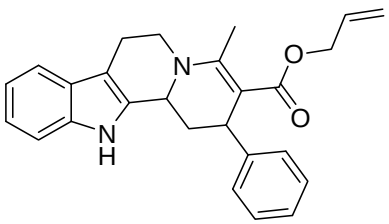
tert-Butyl-4-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4m):



Following the Typical Experimental Procedure using 74 mg of *t*-butylacetoacetate (0.46 mmol, 1.5 equiv.), 80 μL of cinnamaldehyde (0.62 mmol, 2 equiv.), 104 mg (0.25 mmol, 81%) of product was obtained as light yellow solid. This compound was known and has shown the same spectral data reported for the compound.[1]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 (s, 9H, *t*-Bu), 1.99 (td, 1H, *J* = 12.6 Hz, 5.8 Hz), 2.16 (ddd, 1H, *J* = 12.9 Hz, 2.8 Hz, 2.5 Hz), 2.52 (s, 3H, Me), 2.63 – 2.82 (m, 2H), 3.09 (ddd, 1H, *J* = 13.2 Hz. 11.0 Hz, 3.8 Hz), 4.09 – 4.24 (m, 3H), 6.98 – 7.08 (m, 2H, Arom.), 7.10 – 7.27 (m, 6H, Arom.), 7.39 (d, 1H, *J* = 7.7 Hz, Arom.), 7.56 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 17.77, 22.50, 28.25, 36.21, 39.04, 44.58, 49.33, 78.23, 99.30, 109.09, 110.82, 117.95, 119.54, 121.68, 125.82, 126.78, 127.96, 128.08, 133.99, 135.94, 147.66, 154.03, 168.51. **IR (film):** 3397, 3229, 2975, 2924, 2850, 1717, 1677, 1637, 1554, 1452, 1365, 1300, 1227, 1166, 1124, 1092, 1029, 778, 746, 699 cm^{-1}. **HRMS (ESI-TOF):** ($C_{27}H_{31}N_2O_2$), calcd: 415.2380; found: 415.2378. de >95%.

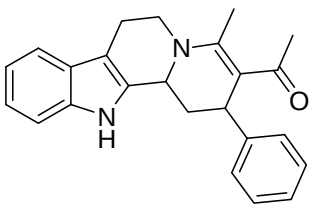
Allyl-4-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4n):



Following the Typical Experimental Procedure using 66 mg of allylacetoacetate (0.46 mmol, 1.5 equiv.), 80 µL of cinnamaldehyde (0.62 mmol, 2 equiv.), 106 mg (0.26 mmol, 85%) of product was obtained as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.95 (td, 1H, *J* = 12.6 Hz, 5.2 Hz), 2.22 (ddd, 1H, *J* = 12.9 Hz, 3.85 Hz, 2.47 Hz), 2.57 (s, 3H, Me), 2.60 – 2.68 (m, 1H), 2.71 – 2.81 (m, 1H), 3.05 (ddd, 1H, *J* = 13.4 Hz. 11.5 Hz, 3.6 Hz), 4.14 – 4.28 (m, 3H), 4.33 (qt, 1H, *J* = 14.0 Hz, 1.64 Hz), 4.34 (qt, 1H, *J* = 14.0 Hz, 1.65 Hz), 4.86 (dq, 1H, *J* = 8.7 Hz, 1.65 Hz), 4.90 (q, 1H, *J* = 1.64 Hz), 5.55 – 5.67 (m, 1H), 6.96 – 7.06 (m, 2H, Arom.), 7.09 – 7.26 (m, 6H, Arom.), 7.37 (d, 1H, *J* = 6.9 Hz, Arom.), 7.69 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 17.65, 22.51, 36.05, 38.08, 45.00, 49.70, 63.66, 96.09, 108.92, 110.91, 115.89, 117.96, 119.55, 121.72, 126.03, 126.71, 127.82, 128.25, 133.34, 133.90, 135.97, 146.70, 155.31, 168.38. **IR (film):** 3399, 3301, 2922, 2851, 1733, 1645, 1543, 1425, 1351, 1300, 1209, 1117, 1088, 1028, 990, 919, 882, 776, 739, 700 cm^{-1}. **HRMS (ESI-TOF):** ($C_{26}H_{27}N_2O_2$), calcd: 399.2067; found: 399.2064. de >95%.

1-(4-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizin-3-yl)ethanone (4o):

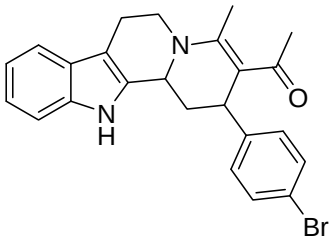


Following the Typical Experimental Procedure using 47 mg of acetylacetone (0.46 mmol, 1.5 equiv.), 80 µL of cinnamaldehyde (0.62 mmol, 2 equiv.), 93 mg (0.26 mmol, 84%) of product was obtained as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.97 (s, 3H, Me), 2.08 (td, 1H, *J* = 12.6 Hz, 4.8 Hz), 2.40 (ddd, 1H, *J* = 12.6 Hz, 3.57 Hz, 2.75 Hz), 2.57 (s, 3H, Me), 2.70 – 2.78 (m, 1H), 2.79 – 2.91 (m, 1H), 3.14 (ddd, 1H, *J* = 13.5 Hz. 11.8 Hz, 3.8 Hz), 4.11 – 4.16 (m, 1H), 4.24 (d, 1H, *J* = 12.4 Hz), 4.36 (dd, 1H, *J* = 13.5 Hz, 4.4 Hz), 7.04 – 7.14 (m, 2H, Arom.), 7.19 – 7.26 (m, 4H, Arom.), 7.28 – 7.35 (m, 2H, Arom.), 7.45 (d, 1H, *J* = 7.7 Hz, Arom.), 7.98 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 18.22, 22.38, 29.56, 36.40,

39.77, 45.10, 49.89, 106.10, 109.00, 110.91, 117.99, 119.61, 121.82, 126.49, 126.65, 127.93, 128.60, 133.61, 136.04, 145.53, 155.64, 196.90. **IR (film):** 3258, 2919, 2848, 1601, 1505, 1450, 1416, 1349, 1303, 1227, 1119, 1096, 1021, 961, 883, 811, 740, 700 cm^{-1}. **HRMS (ESI-TOF):** ($C_{24}H_{25}N_2O$), calcd: 357.1961; found: 357.1958. de >95%.

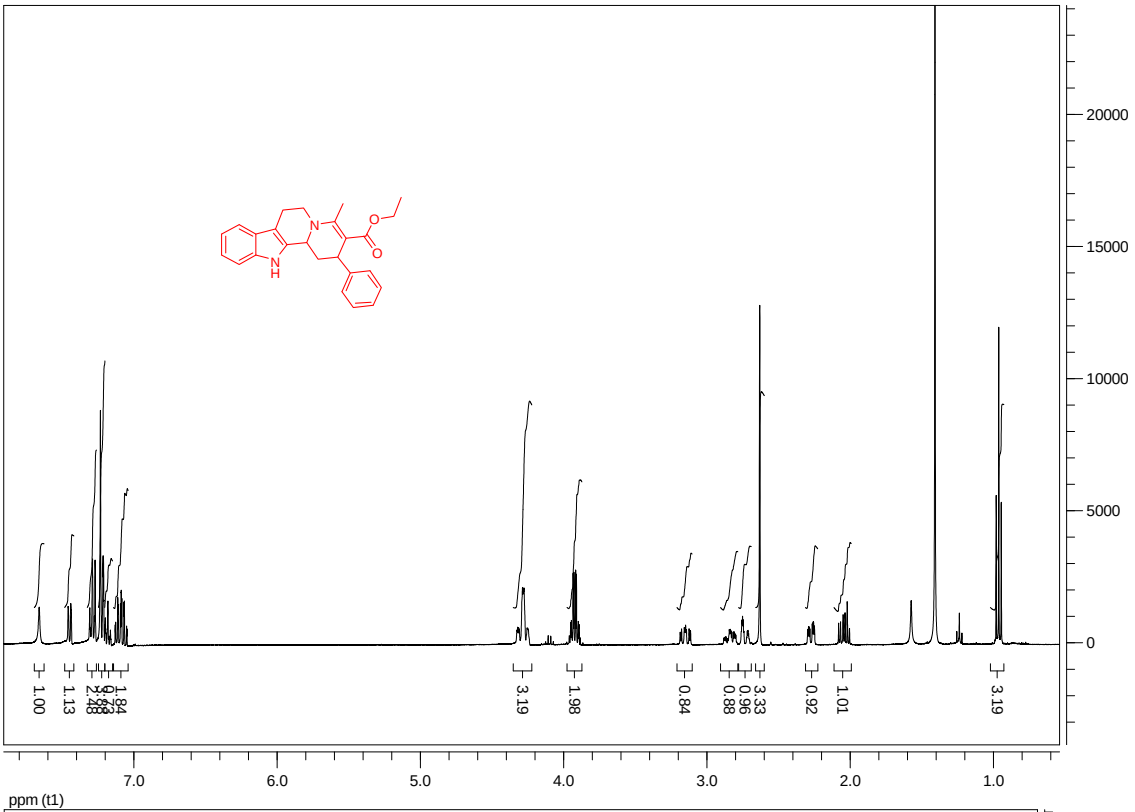
1-(2-(4-Bromophenyl)-4-methyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizin-3-yl)ethanone

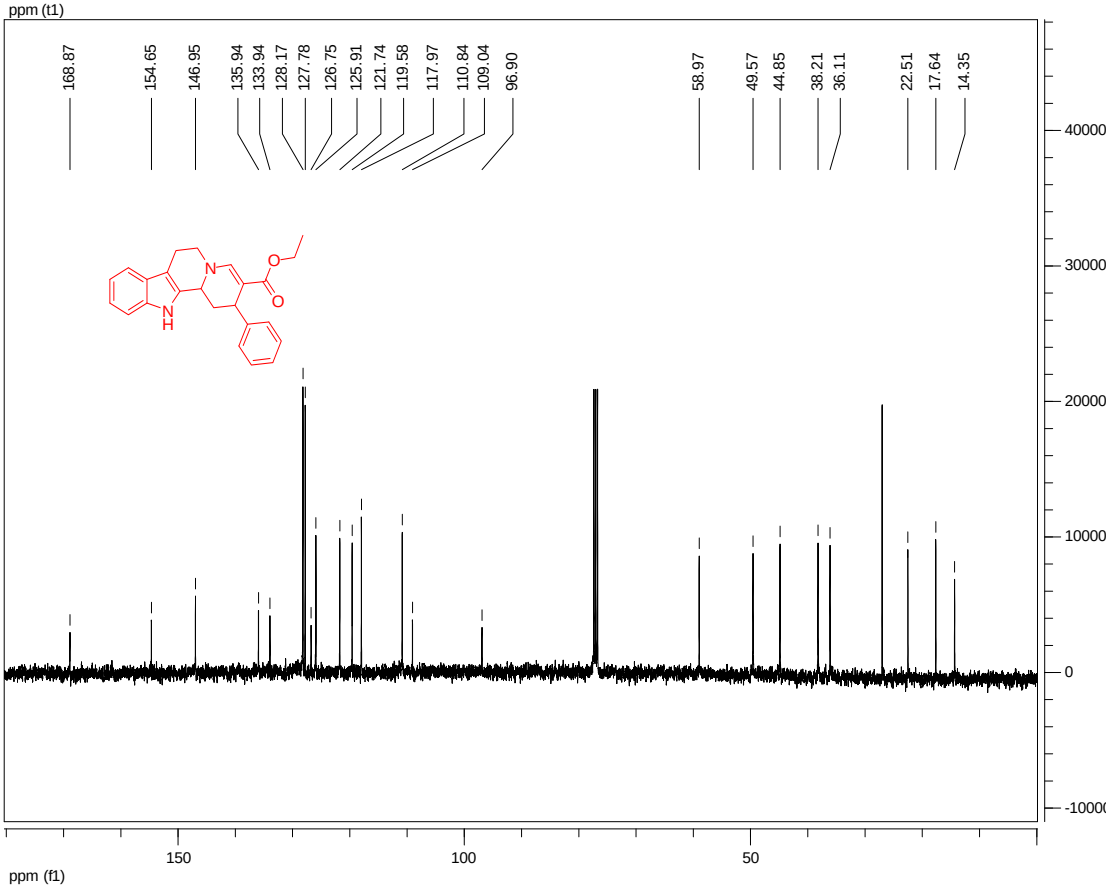


(4p): Following the Typical Experimental Procedure using 47 mg of acetylacetone (0.46 mmol, 1.5 equiv.), 130 mg of *p*-bromocinnamaldehyde (0.62 mmol, 2 equiv.), 111 mg (0.25 mmol, 82%) of product was obtained as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.97 (s, 3H, Me), 2.06 (td, 1H, *J* = 12.6 Hz, 4.7 Hz), 2.45 (ddd, 1H, *J* = 12.9 Hz, 3.95 Hz, 2.7 Hz), 2.65 (s, 3H, Me), 2.73 – 2.95 (m, 2H), 3.17 (ddd, 1H, *J* = 13.3 Hz. 11.1 Hz, 3.95 Hz), 4.07 – 4.12 (m, 2H), 4.22 (d, 1H, *J* = 11.6 Hz), 4.37 (d, 1H, *J* = 11.6 Hz), 7.05 – 7.17 (m, 4H, Arom.), 7.24 – 7.29 (m, 1H, Arom.), 7.40 – 7.51 (m, 3H, Arom.), 8.42 (s, 1H, NH). **^{13}C NMR (100.6 MHz, $CDCl_3$):** 18.24, 22.21, 29.28, 36.02, 39.12, 45.24, 49.96, 105.76, 108.89, 111.03, 118.02, 119.62, 120.37, 121.89, 126.61, 129.72, 131.72, 133.36, 136.22, 144.55, 156.49, 196.48. **IR (film):** 3392, 2919, 2851, 1723, 1581, 1541, 1506, 1431, 1308, 1226, 1110, 1015, 832, 753 cm^{-1}. **HRMS (ESI-TOF):** ($C_{24}H_{24}BrN_2O$), calcd: 435.1066; found: 435.1062. de >95%.

13





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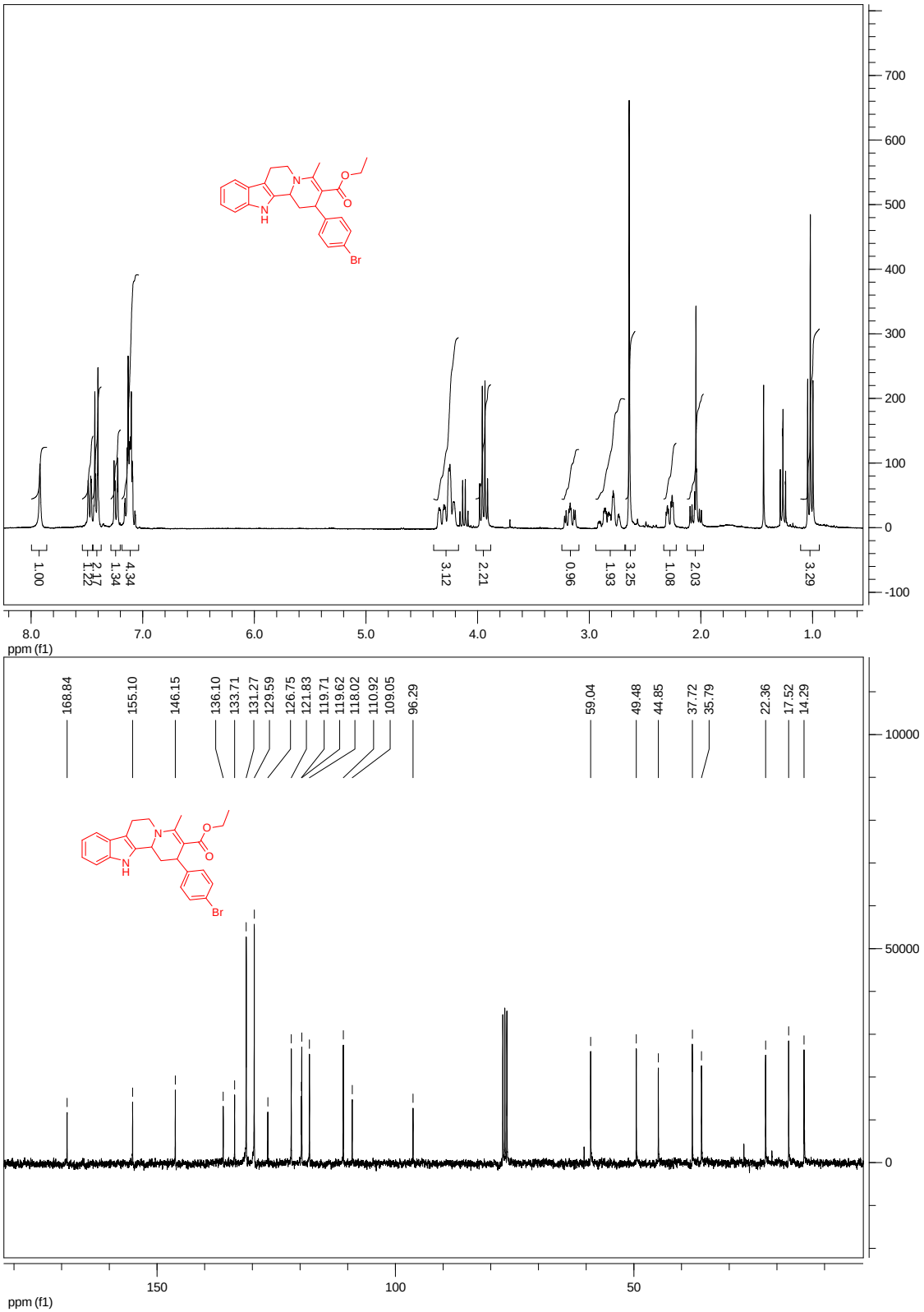
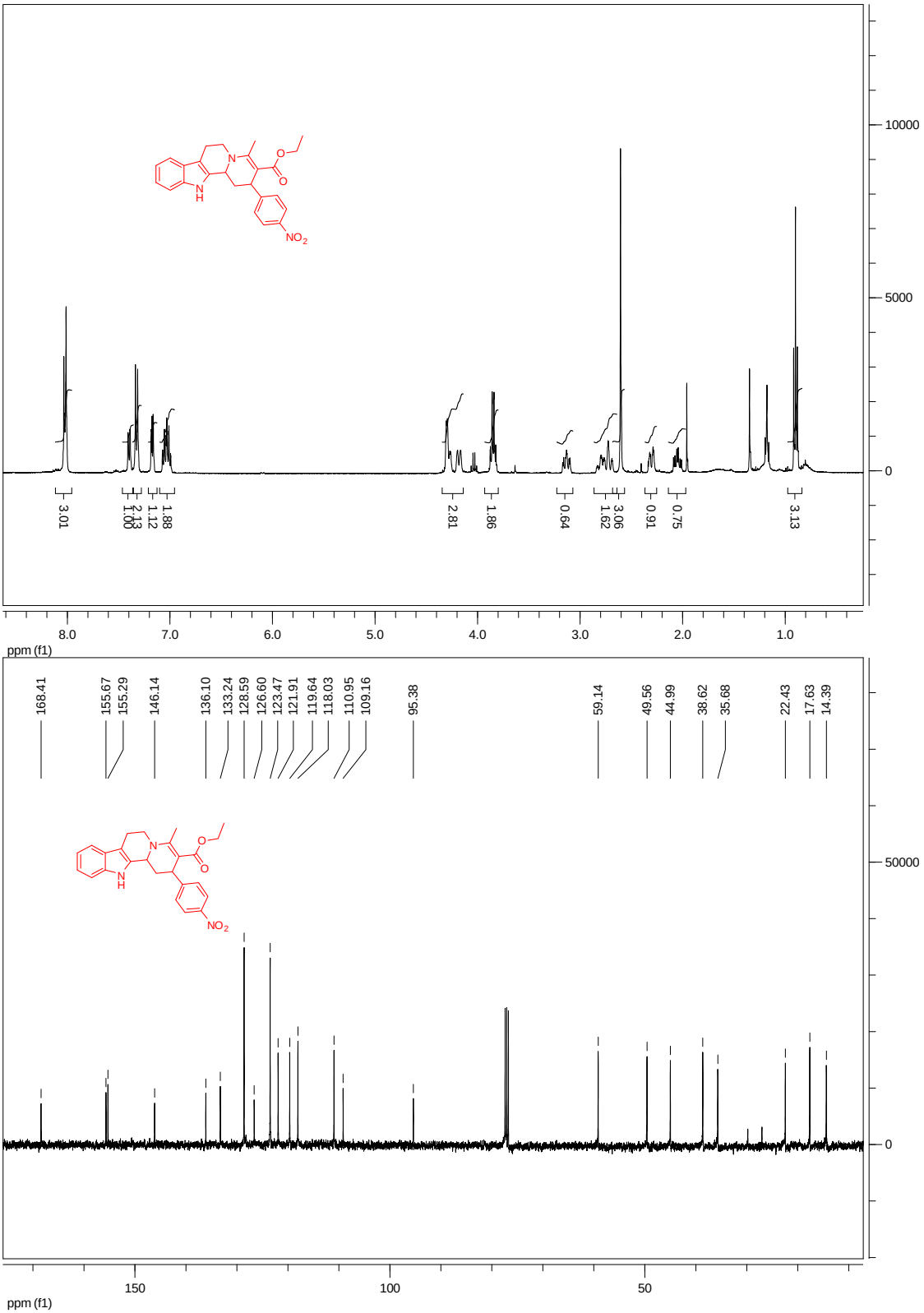


15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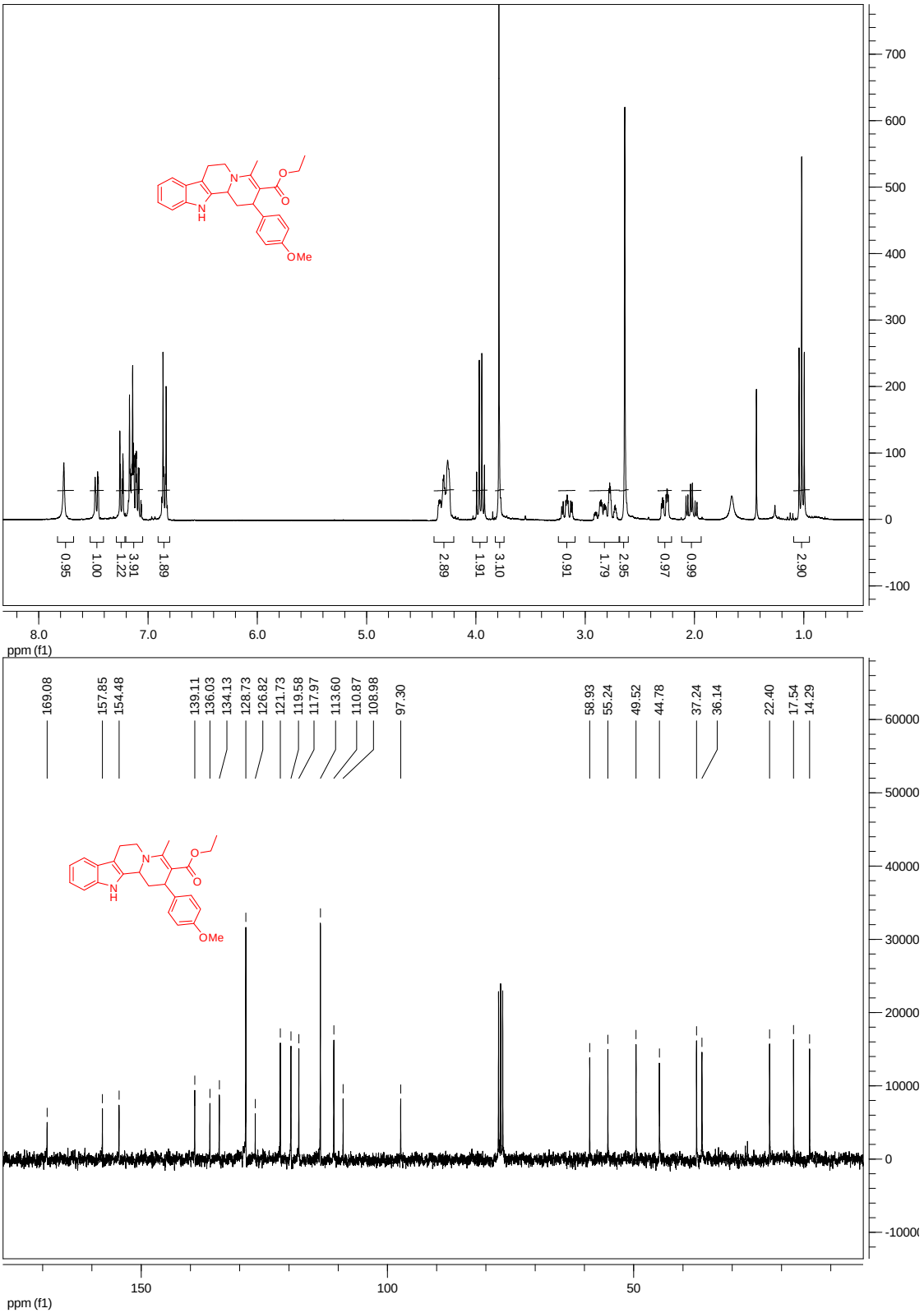
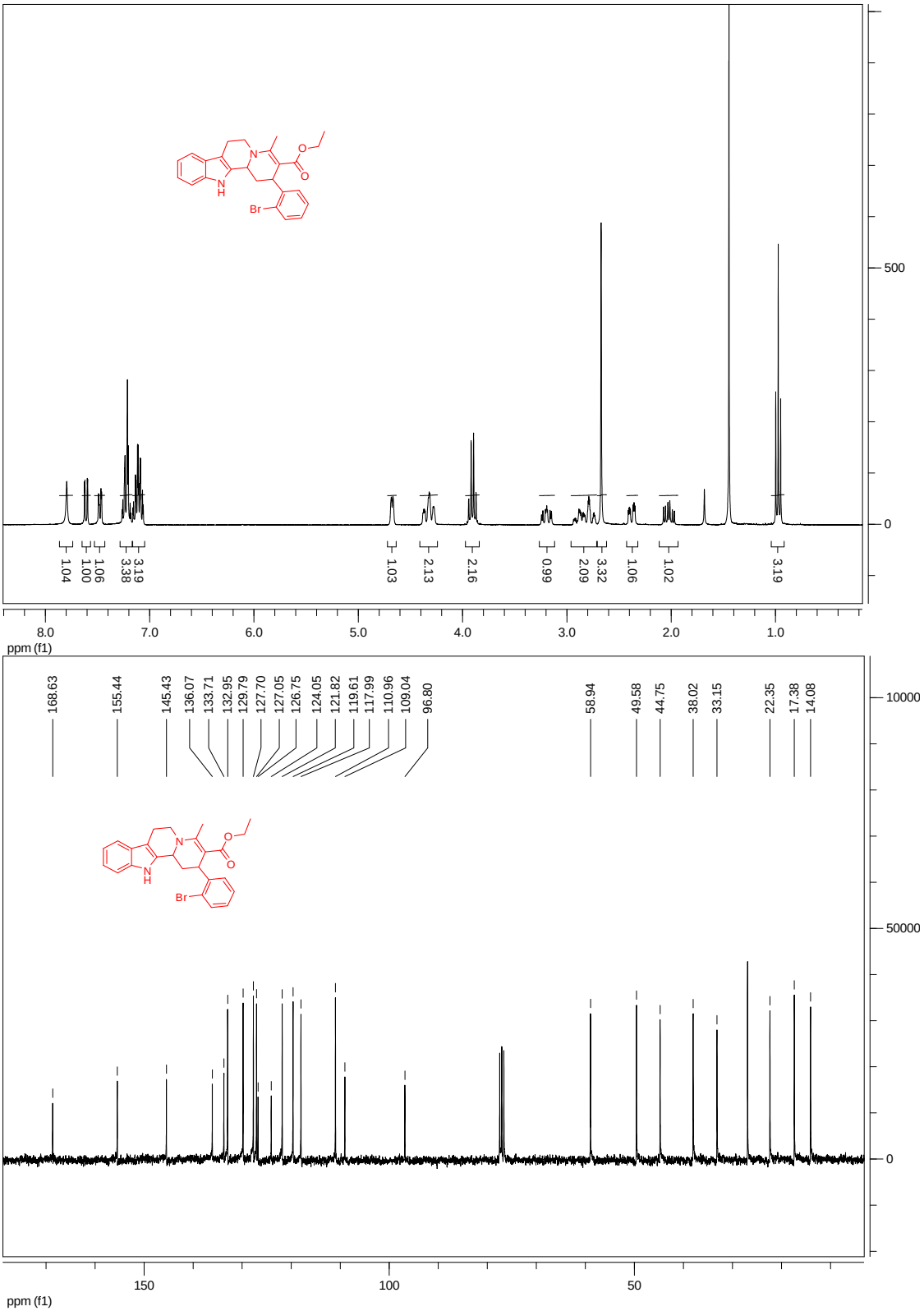
50
ppm (f1)

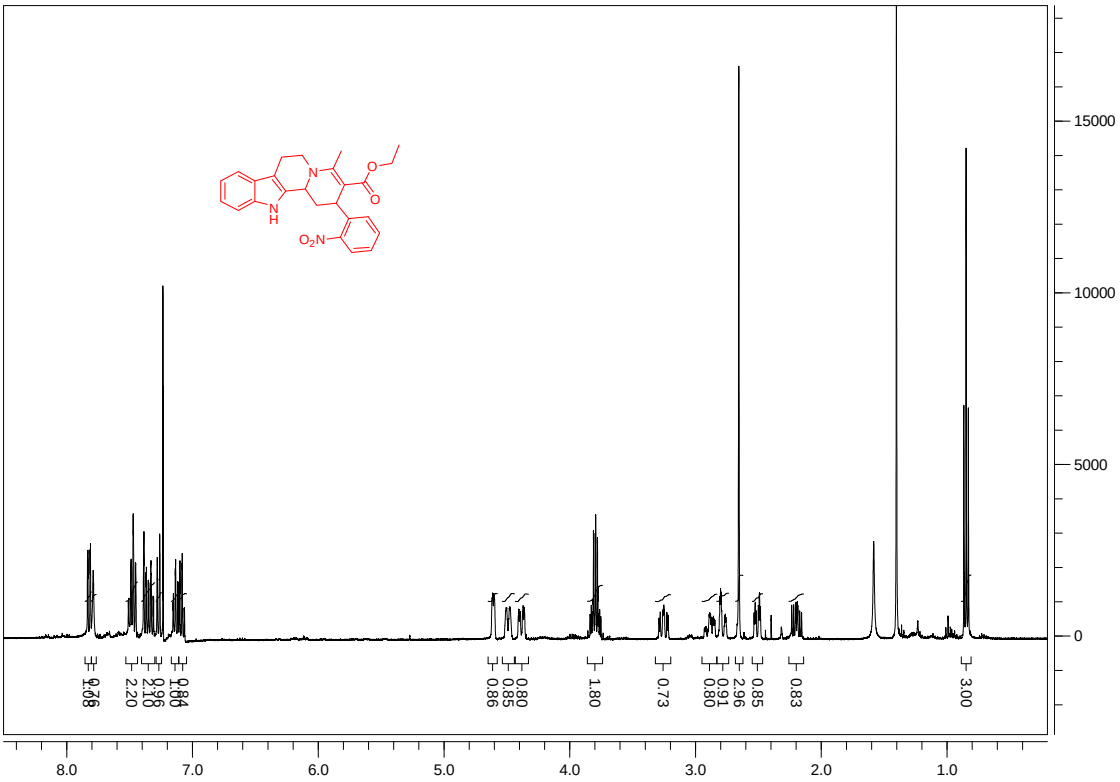
16

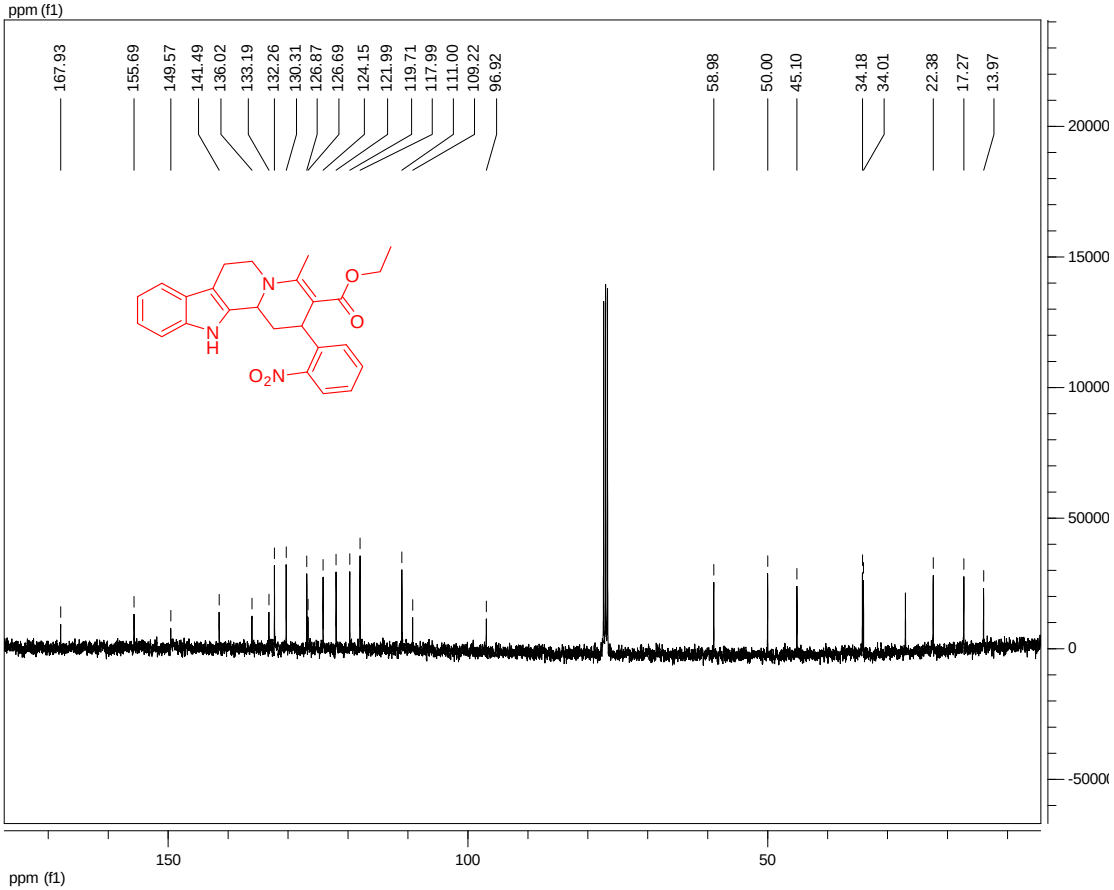


17

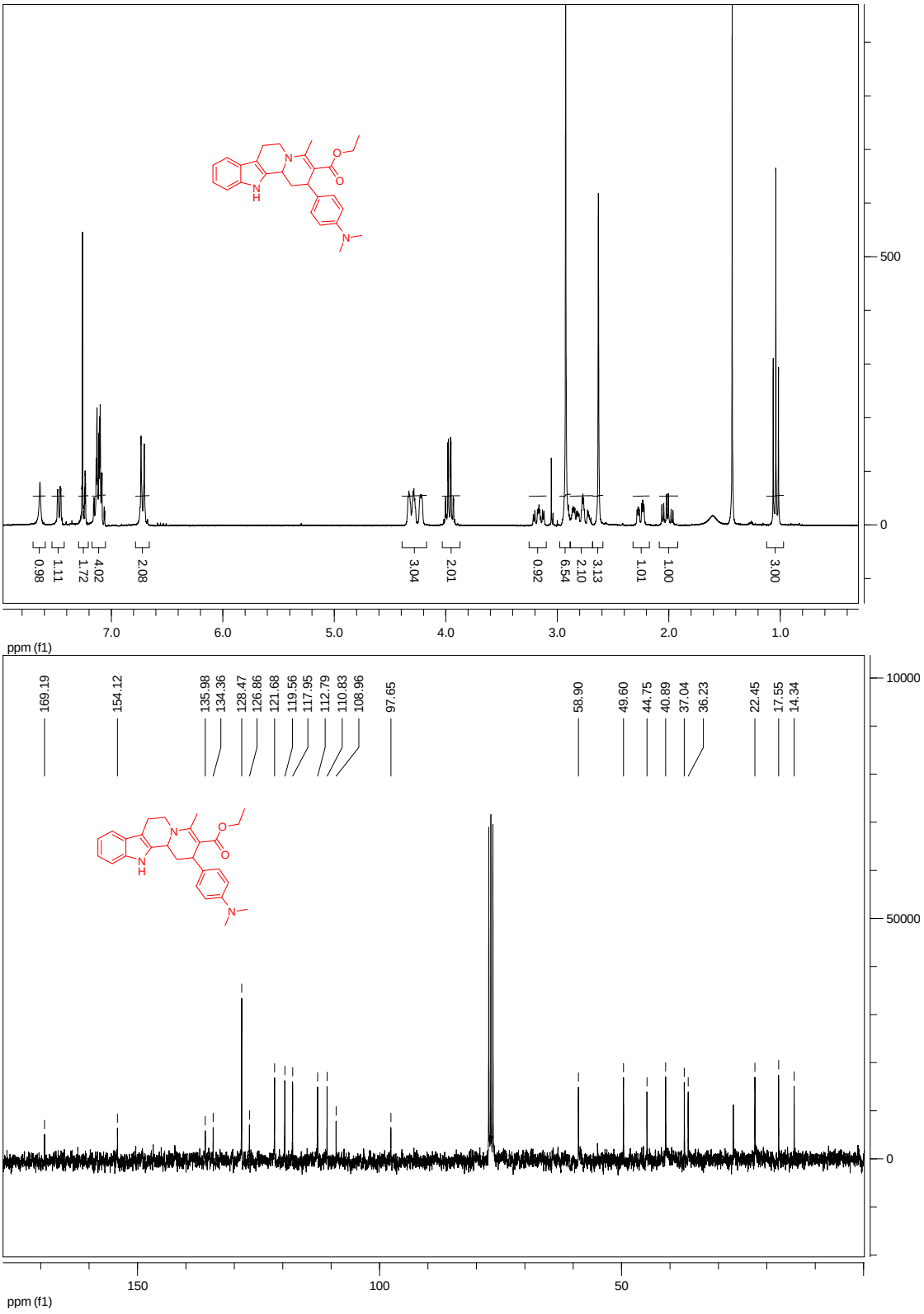


18

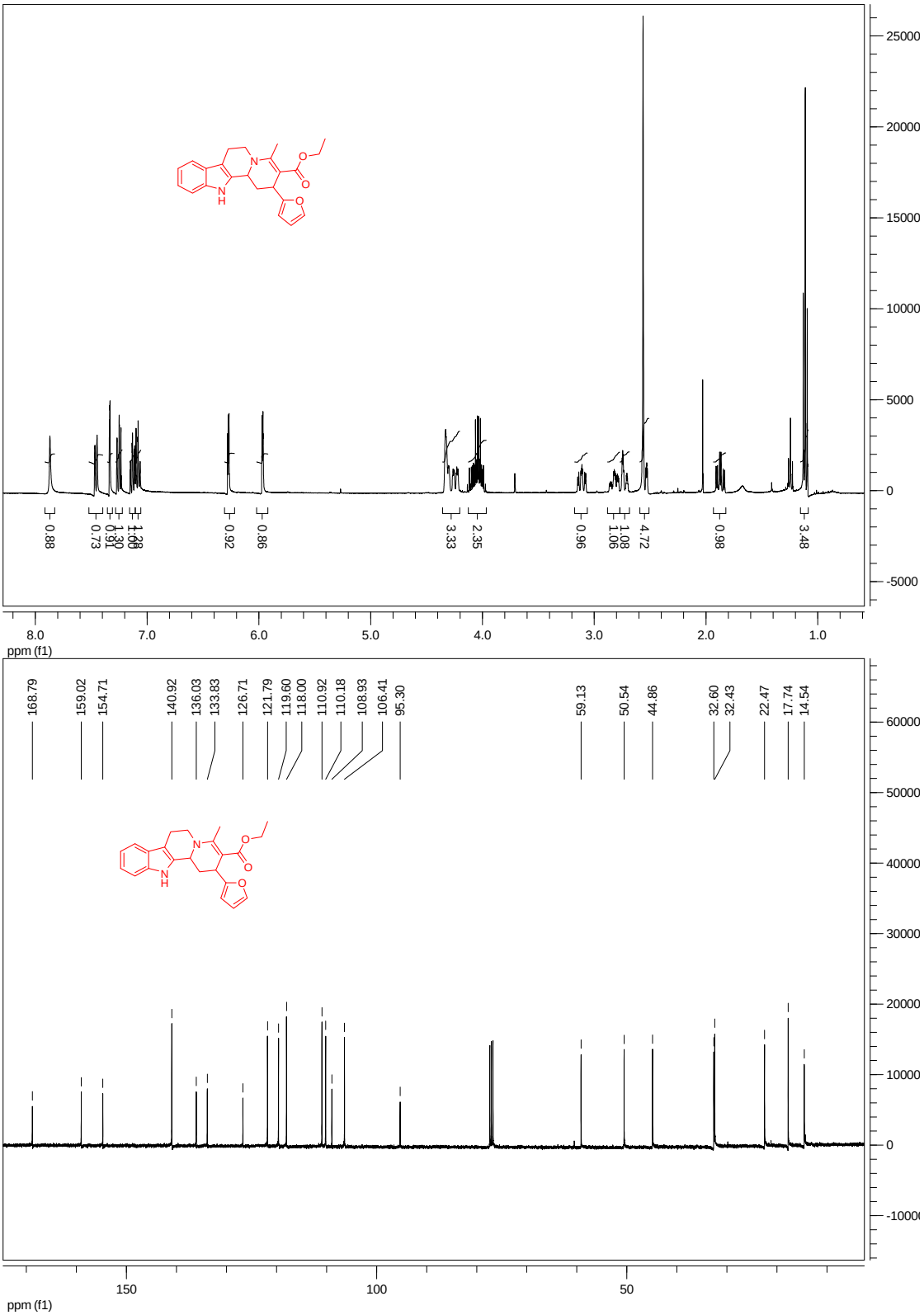




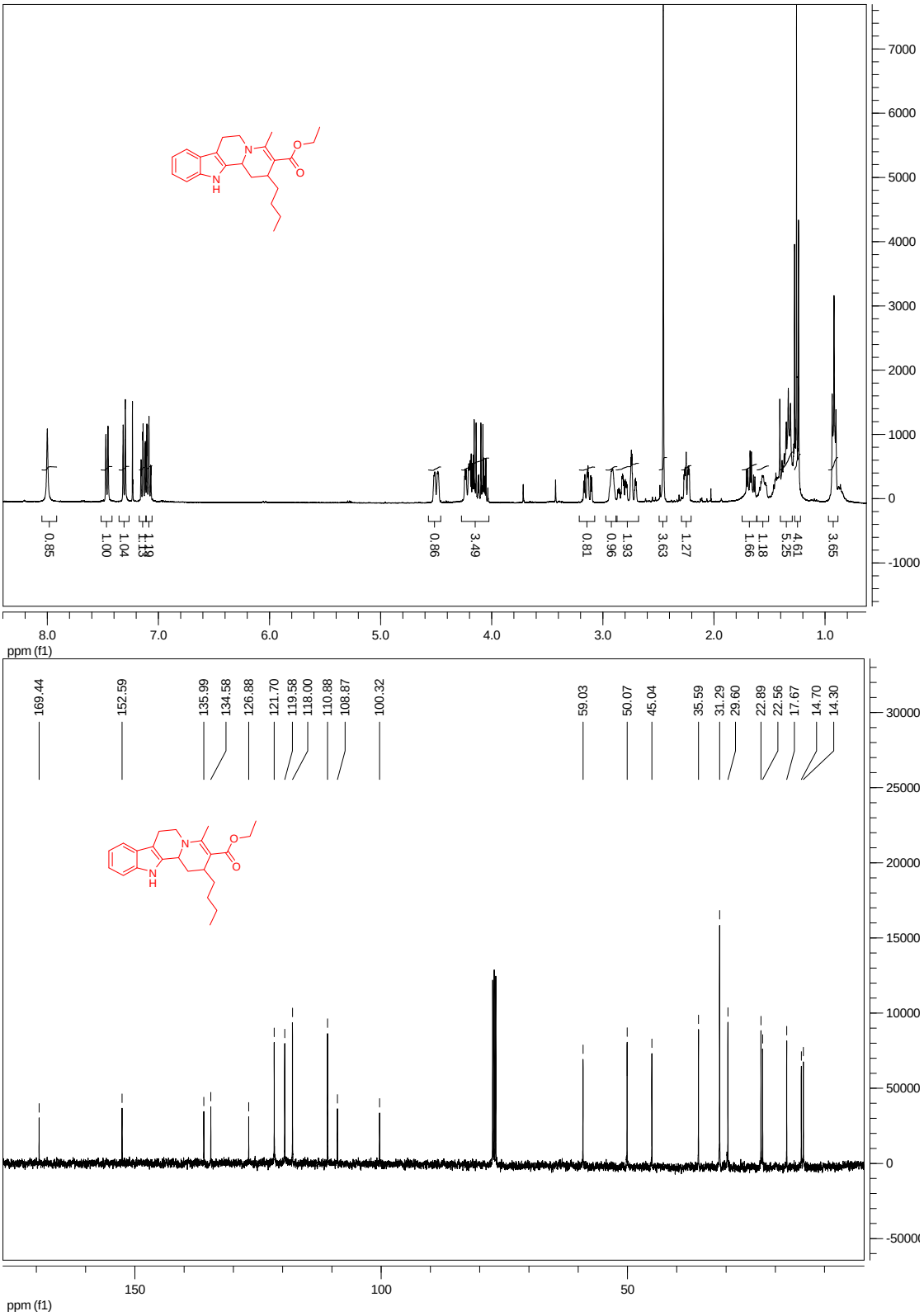
19

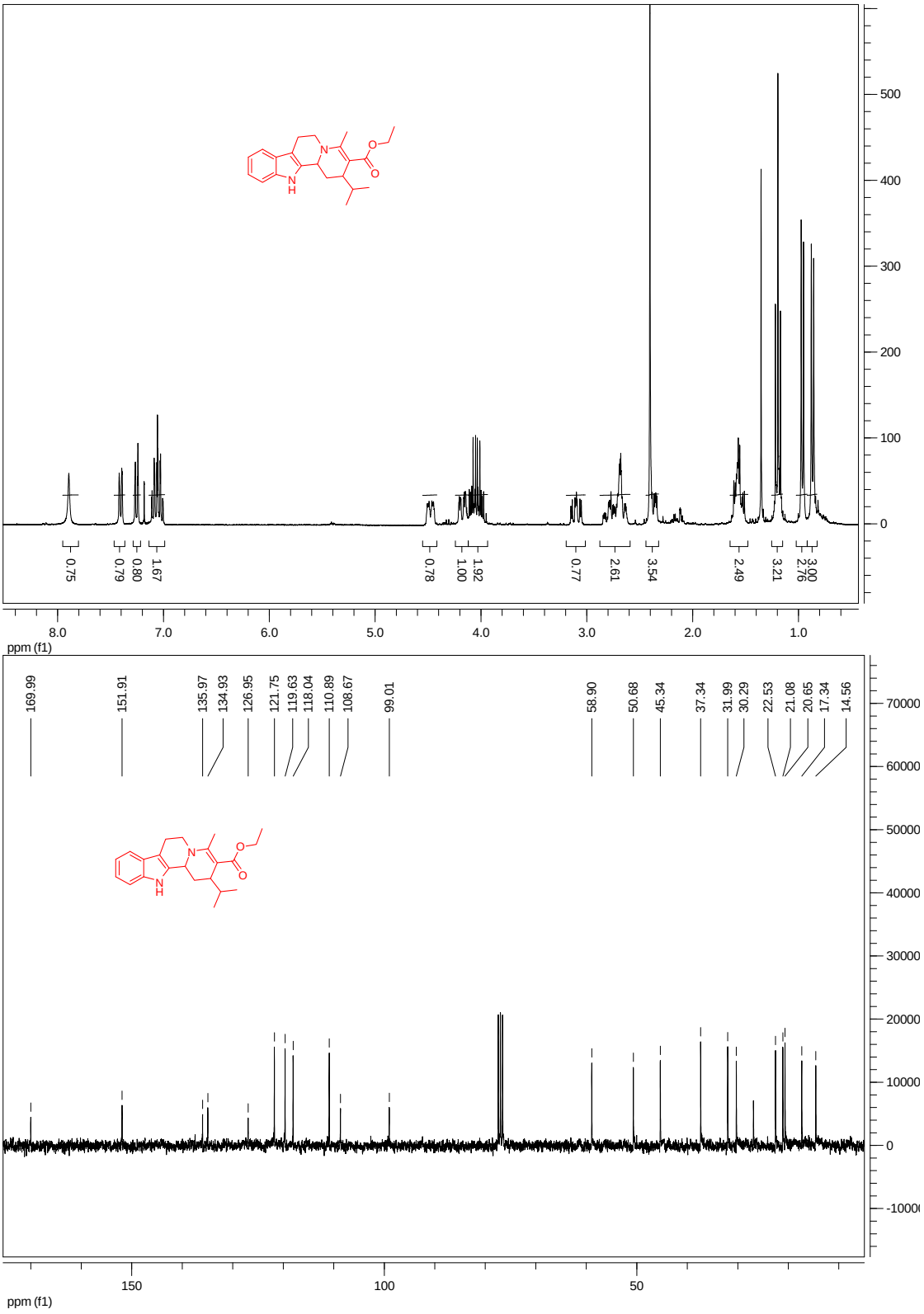


20

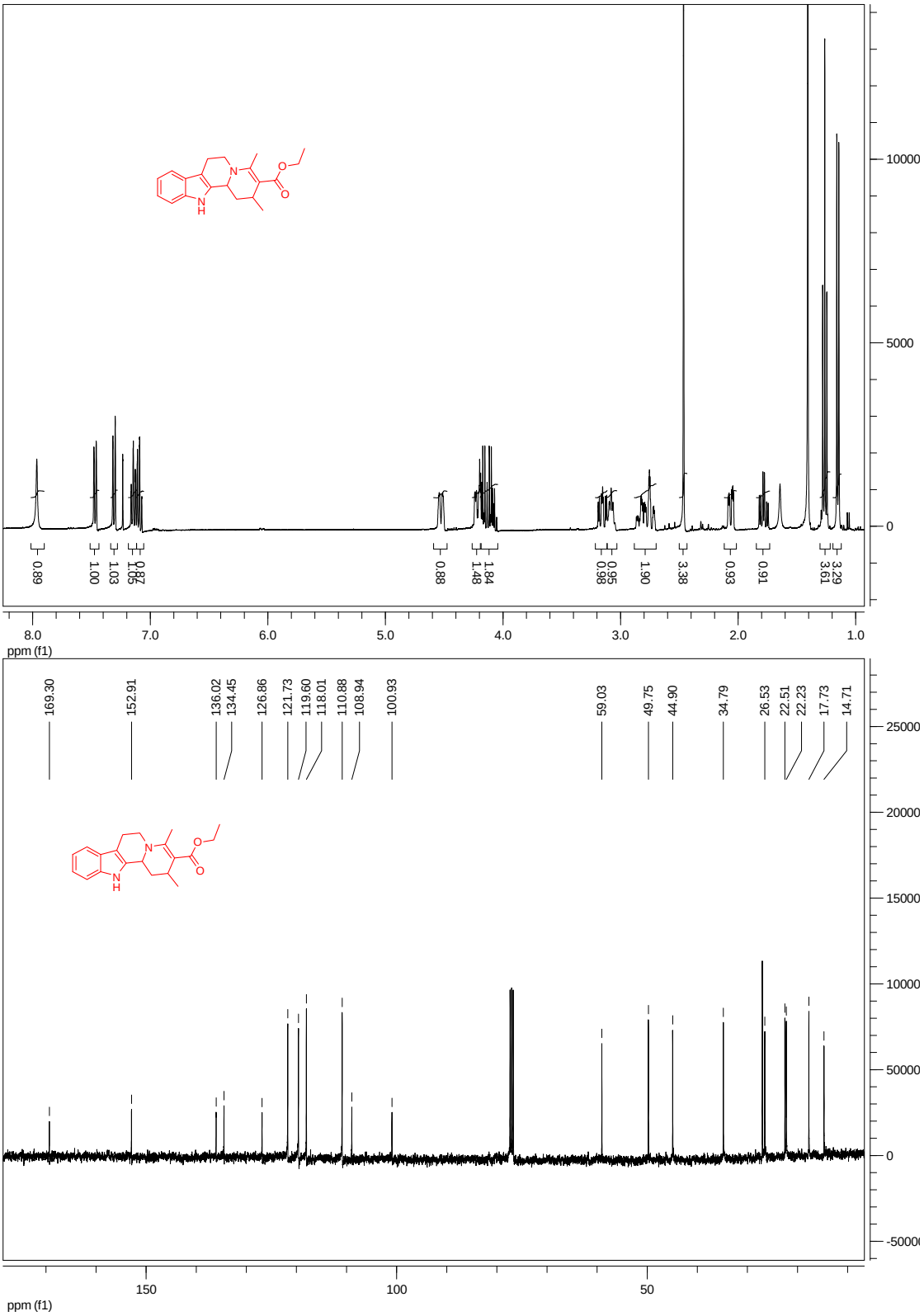


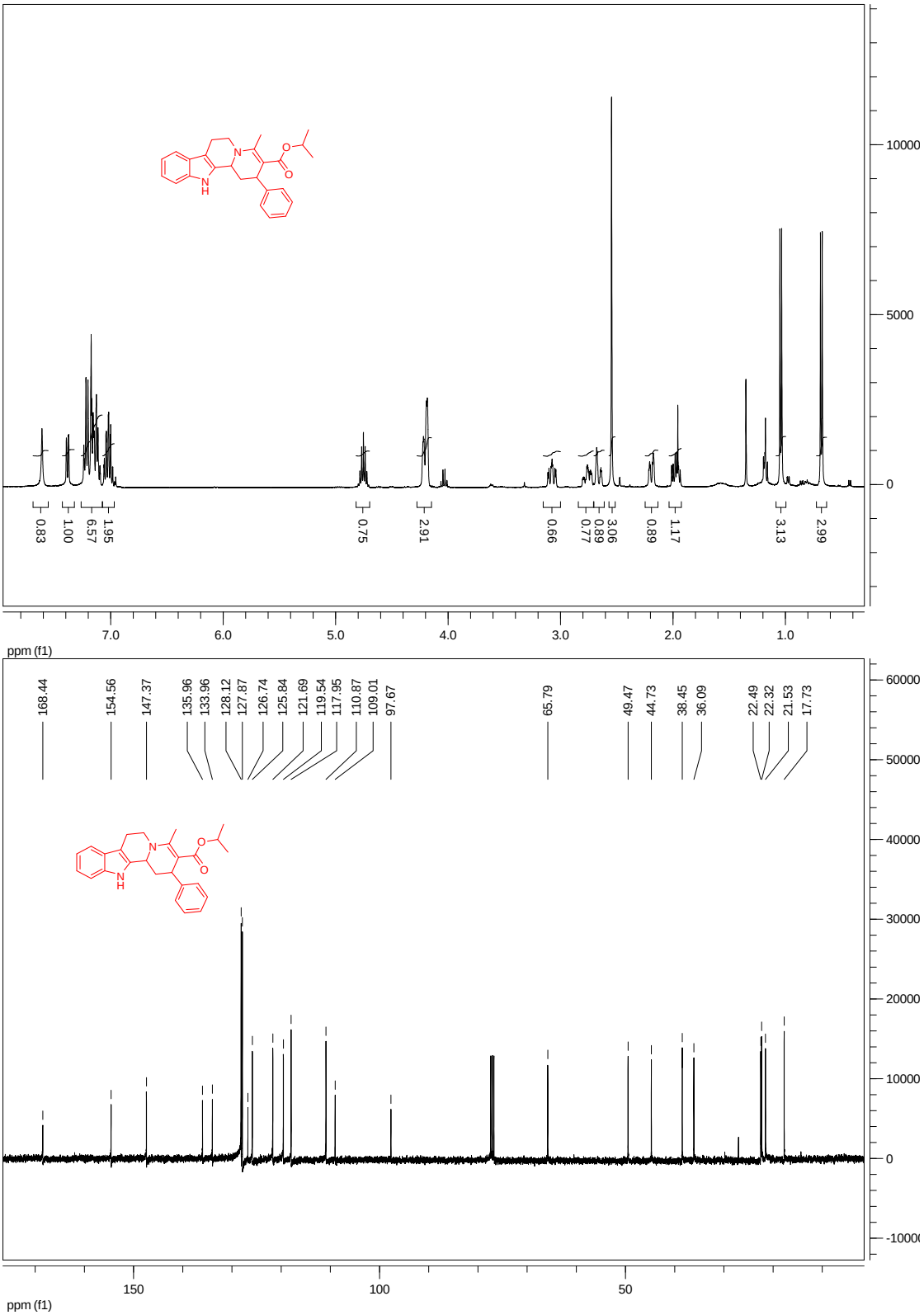
21



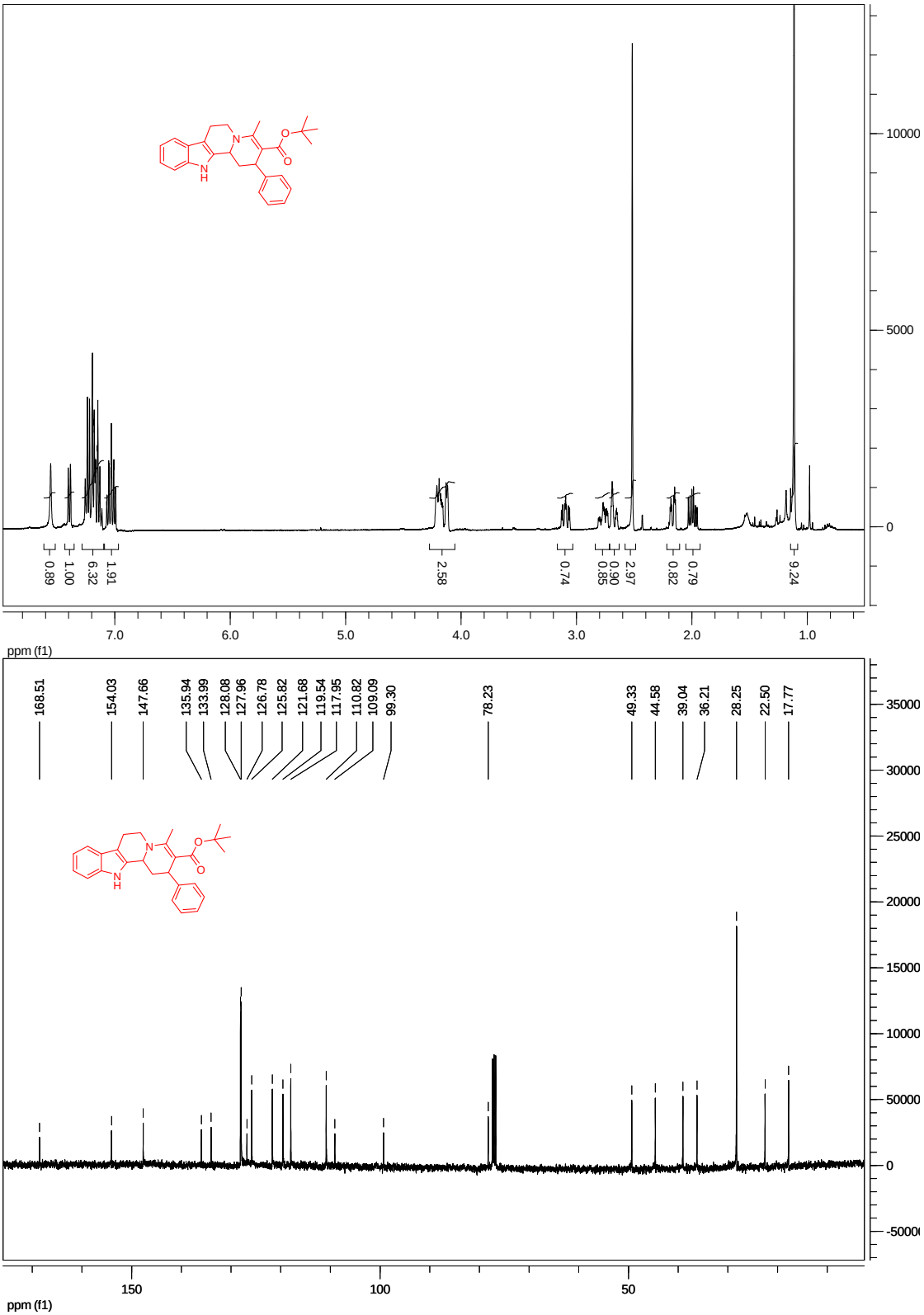


23





25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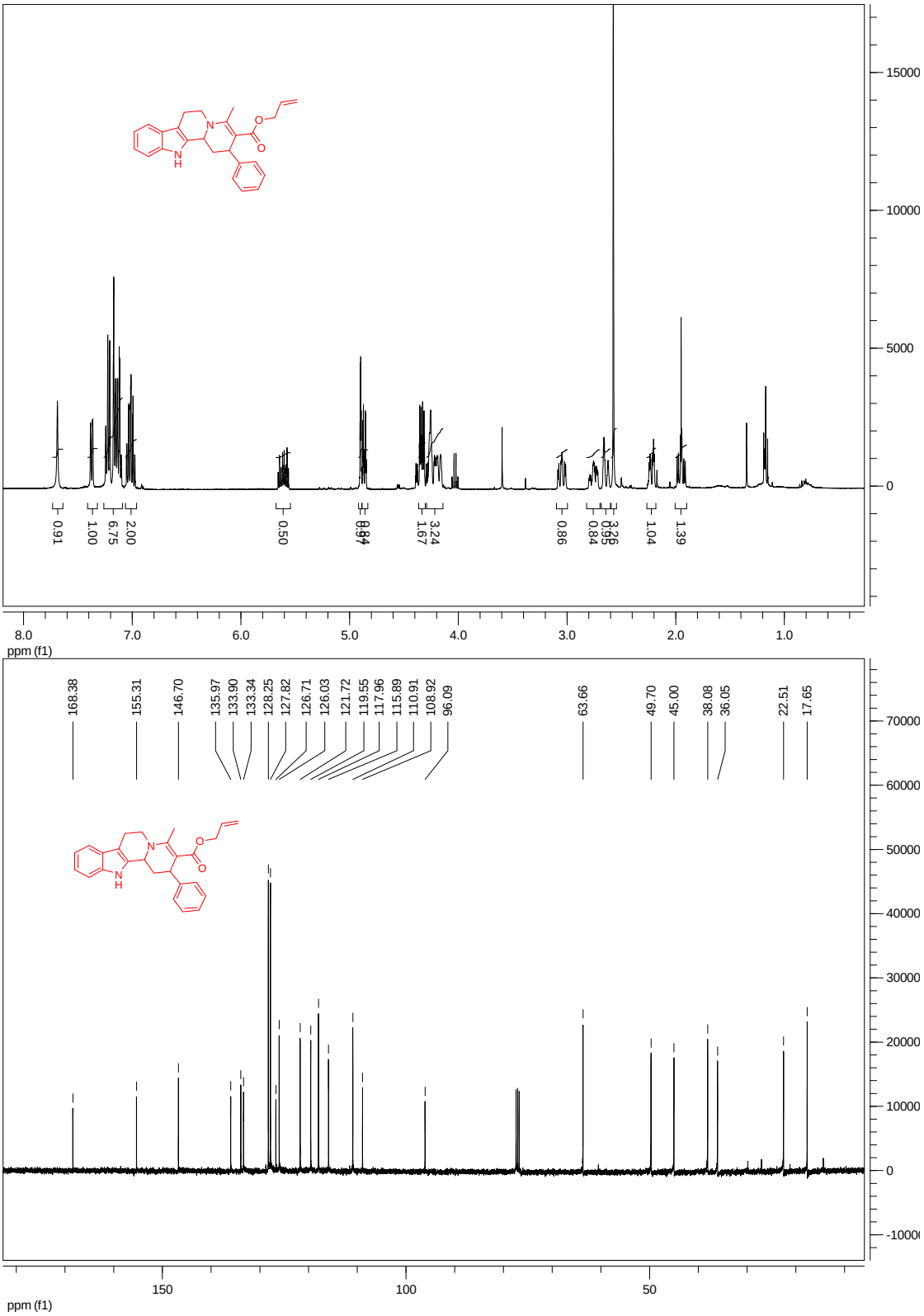
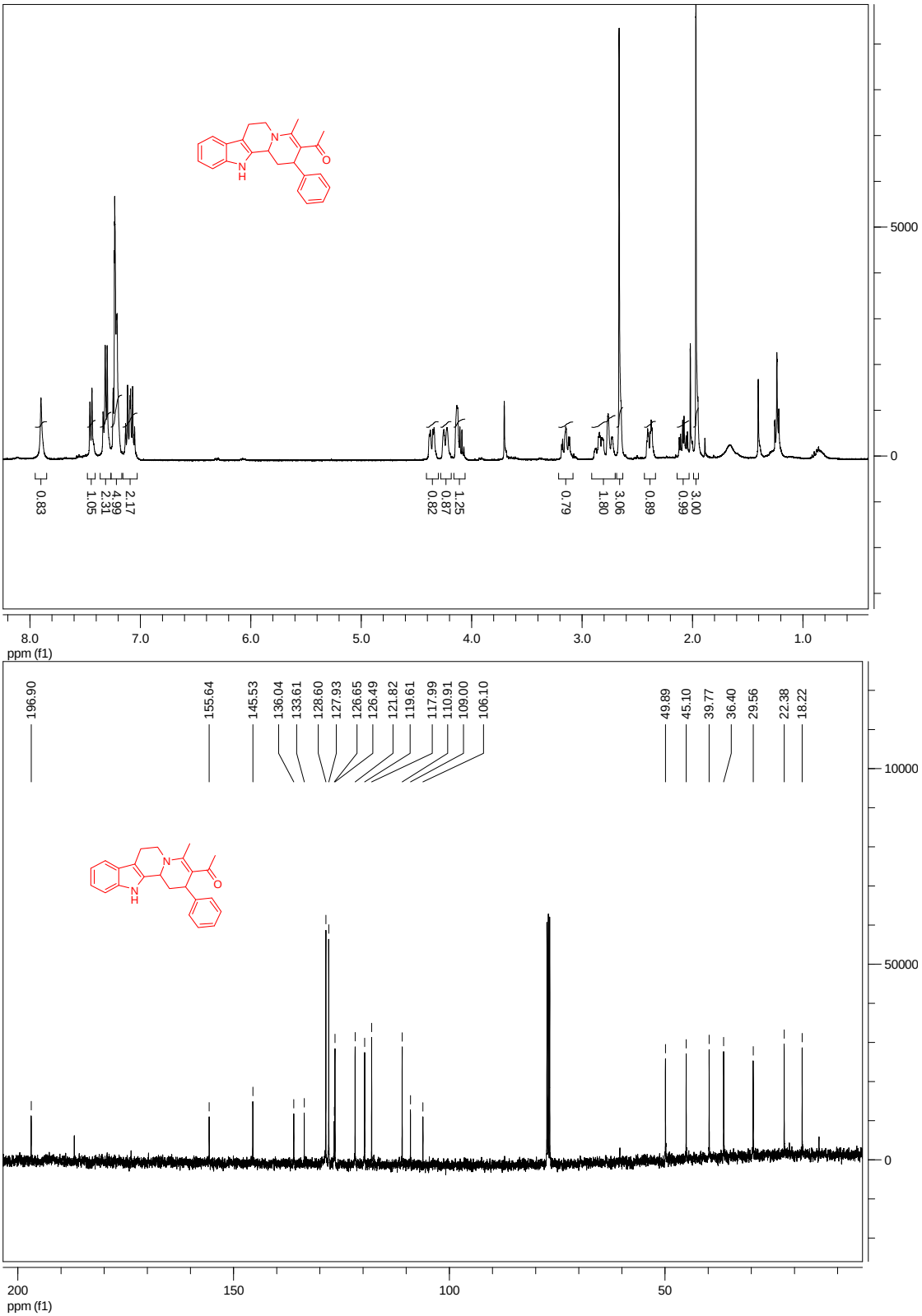
ppm (f1)

26



27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3.00
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0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
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126.65
126.49
121.82
119.61
117.99
110.91
109.00
106.10
49.89
45.10
39.77
36.40
29.56
22.38
18.22
10000
50000
0
200
150
100
50
ppm (f1)

28