CHEMISTRY
A EUROPEAN JOURNAL

Supporting Information

Tricycles by a New Ugi Variation and Pictet–Spengler Reaction in One Pot

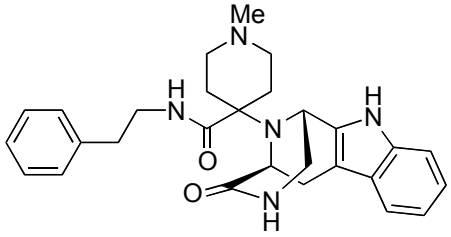
Mantosh K. Sinha,[b] Kareem Khoury,[b] Eberhardt Herdtweck,[c] and Alexander Dömling*[a, b]

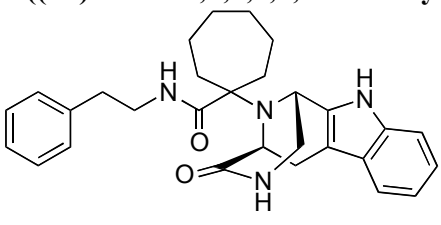
chem_201300962_sm_miscellaneous_information.pdf

List of Contents

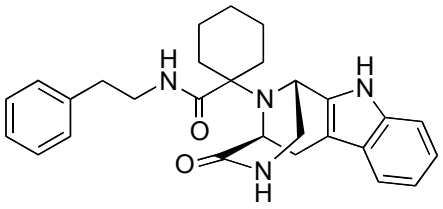
General information:
All reactions were carried out either under air or nitrogen. Solvents were purchased from Aldrich, Fisher Scientific, Acros Organics or Alfa Aesar and used as received. ^{1}H- and ^{13}C NMR spectra were recorded on a Bruker Ultrashield Plus 600. Chemical shift values are in ppm relative either to CDCl3 or DMSO-d_6. Abbreviations used are s = singlet, brs = broad singlet d = doublet, dd = double doublet, t = triplet, td = triple doublet, dt = double triplet q=quartet, m=multiplet; data in parenthesis are given in the following order: multiplicity, number of protons, and coupling constants in Hz. Column flash chromatography (ISCO) was performed using solvents Dichloromethane, Ethyl Acetate, Hexanes, and Methanol, and Preparative Waters Super Critical Fluid Chromatography (SFC) was performed using solvent system of Methanol and CO_2. MS spectra were recorded on a SFC with a 3100 MS Detector.

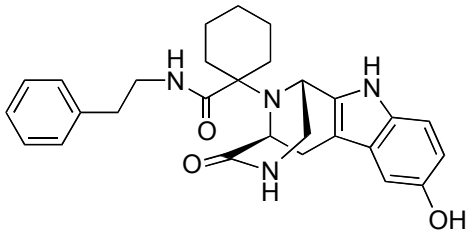
General procedure of Ugi-Pictet-Spengler reaction:
A mixture of L-amino acid (0.5 mmol), ketone (0.5 mmol), isocyanide (0.5 mmol) and Aminoacetaldehyde dimethyl acetal (0.5 mmol), in 0.1 M of MeOH/H_2O (4:1) were stirred for 24 – 72 hours at room temperature (In the case of 3,4-Dimethoxy phenylalanine, the reaction mixture was heated at 50 ºC for 72 hours). Solvents were evaporated under reduced pressure. The crude Ugi product was dissolved in formic acid (2 mL) and stirred for another 16 h at room temperature. Reaction mixture was diluted with DCM and solid K_2CO_3 was added slowly until the mixture was neutralized. The excess K_2CO_3 was filtered off on celite and solvents were evaporated to obtain crude product, which was purified to yield title compound.

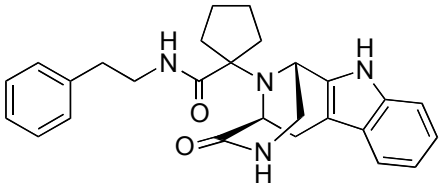
1-methyl-4-((5*S*)-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-*N*-phenethylpiperidine-4-carboxamide [19]: 
Purified by SFC (CO_2/MeOH); Yield 42% (99 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.56-1.62 (m, 1H), 1.78-1.85 (m, 2H), 1.92-1.99 (m, 2H), 2.04 (s, 3H), 2.04-2.09 (m, 1H), 2.39-2.43 (m, 1H), 2.50-2.59 (m, 3H), 2.69 (d, *J* = 15.6 Hz, 1H), 2.97 (dd, *J* = 15.0, 5.4 Hz, 1H), 3.02 (dd, *J* = 10.8, 3.0 Hz, 1H), 3.10-3.15 (m, 2H), 3.55 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.97 (d, *J* = 5.4 Hz, 1H), 4.35 (s, 1H), 6.93 (t, *J* = 7.8 Hz, 1H), 7.00-7.06 (m, 3H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.23 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 3.0 Hz, 1H), 7.85 (brs, 1H), 10.71 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 24.6, 30.4, 32.0, 34.6, 40.0, 40.3, 44.9, 45.6, 47.2, 51.9, 52.5, 54.2, 106.9, 111.1, 117.4, 118.4, 120.7, 126.0, 126.6, 128.2, 128.5, 134.3, 135.4, 139.5, 171.6, 172.3 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 472.59; found: 473.24.

1-((5*S*)-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-*N*-phenethylcycloheptanecarboxamide [20]: 
Purified by SFC (CO_2/MeOH); Yield 52% (122 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.25-1.55 (m, 9H), 1.73-178 (m, 1H), 1.95-2.04 (m, 2H), 2.68-2.75 (m, 3H), 2.93-2.98 (m, 2H), 3.28 (q, *J* = 13.8, 7.2 Hz, 2H), 3.49 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.85 (d, *J* = 5.4 Hz, 1H), 4.04 (d, *J* = 3.6 Hz, 1H), 6.94 (t, *J* = 7.2 Hz, 1H), 7.03 (t, *J* = 7.2 Hz, 1H), 7.16-7.21 (m, 3H), 7.26-7.31 (m, 3H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 3.6 Hz, 1H), 7.86 (t, *J* = 5.4 Hz, 1H), 10.73 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 23.0,

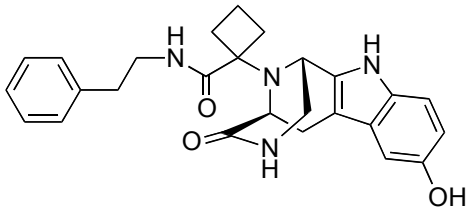
33.8, 24.8, 29.3, 29.5, 32.5, 35.1, 35.3, 40.5, 46.3, 47.2, 54.6, 68.6, 106.9, 111.2, 117.5, 118.5, 120.8, 126.0, 126.5, 128.3, 128.5, 134.3, 135.4, 139.5, 171.5, 175.4 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 471.61; found: 471.25.

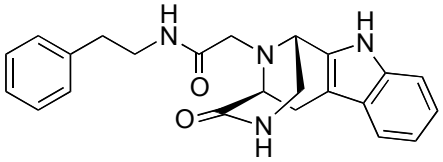
1-((5*S*)-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-*N*-phenethylcyclohexanecarboxamide [21]:  Purified by SFC (CO_2/MeOH); Yield 48% (109 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.07-1.16 (m, 2H), 1.34-1.46 (m, 4H), 1.53-1.57 (m, 1H), 1.62-1.67 (m, 1H), 1.87-1.94 (m,2H), 2.53-2.62 (m, 2H), 2.70 (d, *J* = 15.0 Hz, 1H), 2.97 (dd, *J* = 15.6, 5.4 Hz, 1H), 3.02 (dd, *J* = 10.8, 3.0 Hz, 1H), 3.15 (q, *J* = 13.2, 7.2 Hz, 2H), 3.54 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.99 (d, *J* = 5.4 Hz, 1H), 4.33 (d, *J* = 3.6 Hz, 1H), 6.93 (t, *J* = 7.8 Hz, 1H), 7.02 (t, *J* = 7.2 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.24 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 3.6 Hz, 1H), 7.81 (t, *J* = 6.0 Hz, 1H), 10.71 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 22.6, 22.8, 24.7, 25.1, 30.9, 32.6, 34.8, 40.4, 45.0, 47.2, 54.1, 63.4, 106.9, 111.1, 117.4, 118.4, 120.6, 126.0, 126.6, 128.2, 128.4, 134.6, 135.4, 139.5, 171.7, 173.1 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 457.58; found 457.25.

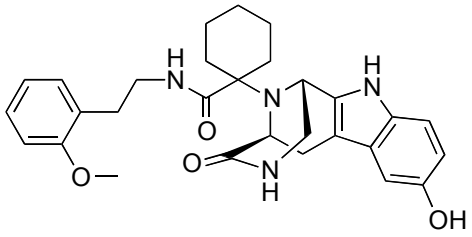
1-((5*S*)-8-hydroxy-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-*N*-phenethylcyclohexane-carboxamide [22]:  Purified by SFC (CO_2/MeOH); Yield 35% (82 mg) as a light brownish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.05-1.14 (m, 2H), 1.52-1.55 (m, 1H), 1.60-1.64 (m, 1H), 1.85-1.92 (m, 2H), 2.56-2.64 (m, 3H), 2.87 (dd, *J* = 21.0, 6.0 Hz, 1H), 2.98 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.17 (q, *J* = 13.8, 7.2 Hz, 2H), 3.51 (dd, *J* = 11.4, 4.8 Hz, 1H), 3.94 (d, *J* = 5.4 Hz, 1H), 4.25 (d, *J* = 4.2 Hz, 1H), 6.52 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.64 (d, *J* = 1.8 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 2H), 7.16 (t, *J* = 7.8 Hz, 1H), 7.25 (t, *J* = 7.8 Hz, 2H), 7.37 (d, *J* = 3.6 Hz, 1H), 7.79 (t, *J* = 5.4 Hz, 1H), 8.55 (s, 1H), 10.35 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 22.6, 22.8, 25.1, 30.9, 32.5, 34.8, 40.4, 45.1, 47.2, 54.2, 63.5, 101.7, 106.1, 110.5, 111.3, 126.0, 127.3, 128.3, 128.5, 129.9, 135.1, 139.6, 150.4, 171.8, 173.2 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 473.58; found: 473.24.

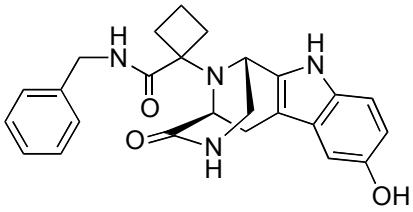
1-((5*S*)-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-*N*-phenethylcyclopentanecarboxamide [23]:  Purified by SFC (CO_2/MeOH); Yield 27% (60 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.34-1.40 (m, 1H), 1.44-1.52 (m, 2H), 1.53-1.59 (m, 2H), 1.77-1.83 (m, 1H), 1.88-193 (m, 1H), 1.97-2.02 (m, 1H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.72 (d, *J* = 15.6 Hz, 1H), 2.90 (dd, *J* = 15.0, 5.4 Hz, 1H), 3.01 (dd, *J* = 11.4, 3.0 Hz, 1H), 3.21 (q, *J* = 13.8, 6.6 Hz, 2H), 3.57 (dd, *J* = 11.4, 4.8 Hz, 1H), 3.85 (d, *J* = 5.4 Hz, 1H), 4.19 (d, *J* = 3.0 Hz, 1H), 6.94 (t, *J* = 7.2 Hz, 1H), 7.03 (t, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.25 (t, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 3.0 Hz, 1H), 7.85 (t, *J* = 5.4 Hz, 1H), 10.74 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 23.2, 23.3, 24.6, 31.6, 33.6, 34.9, 40.5, 46.9, 47.1,

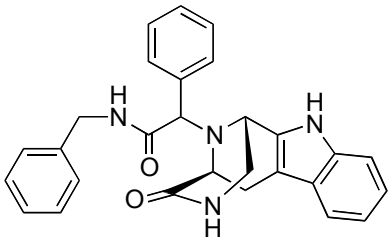
55.5, 73.4, 107.0, 111.2, 117.5, 118.5, 120.7, 126.0, 126.5, 128.3, 128.5, 134.1, 135.5, 139.5, 171.5, 174.4 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 443.55; found: 443.24.

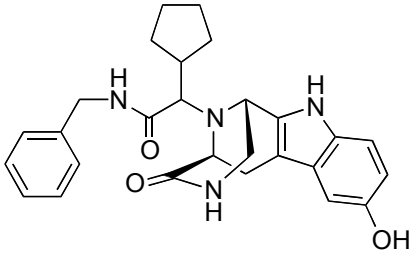
1-((5*S*)-8-hydroxy-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-*N*-phenethylcyclobutane-carboxamide [24]:  Purified by SFC (CO_2/MeOH); Yield 35% (77 mg) as a light brownish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.45-1.54 (m, 2H), 2.08-2.22 (m, 4H), 2.61-2.72 (m, 3H), 2.84 (dd, *J* = 15.0, 4.8 Hz, 1H), 3.01 (d, *J* = 8.4 Hz, 1H), 3.24-3.33 (m, 2H), 3.53 (dd, *J* = 11.4, 3.0 Hz, 1H), 3.79 (d, *J* = 4.8 Hz, 1H), 4.12 (s, 1H), 6.54 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.66 (s, 1H), 7.09 (dd, *J* = 9.0, 1.8 Hz, 1H), 7.14-7.19 (m, 3H), 7.25 (t, *J* = 7.2 Hz, 2H), 7.48 (s, 1H), 7.83 (t, *J* = 4.2 Hz, 1H), 8.62 (brs, 1H), 10.42 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 13.8, 24.8, 28.4, 29.0, 35.0, 40.5, 46.2, 46.8, 55.0, 66.6, 101.8, 106.2, 110.8, 111.5, 126.1, 127.1, 128.4, 128.6, 130.0, 134.2, 139.5, 150.5, 171.5, 174.0 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 445.53; found: 445.24.

2-((5*S*)-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-*N*-phenethylacetamide [25]:  Purified by SFC (CO_2/MeOH); Yield 28% (54 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.66 (d, *J* = 16.2 Hz, 1H), 2.76 (t, *J* = 7.2 Hz, 2H), 2.97 (dd, *J* = 15.6, 3.6 Hz, 2H), 3.07 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.29 (dd, *J* = 15.6, 8.4 Hz, 2H), 3.40-3.46 (m, 1H), 3.56 (d, *J* = 5.4 Hz, 1H), 3.67 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.95 (d, *J* = 4.2 Hz, 1H), 6.97 (t, *J* = 7.2 Hz, 1H), 7.03-7.09 (m, 2H), 7.22 (d, *J* = 7.2 Hz, 2H), 7.29-7.34 (m, 3H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 3.6 Hz, 1H), 7.91 (t, *J* = 6.0 Hz, 1H), 10.79 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 21.7, 35.1, 40.0, 46.0, 49.7, 54.8, 58.4, 106.0, 111.2, 117.7, 118.6, 121.1, 126.1, 126.3, 128.4, 128.7, 131.4, 135.8, 139.4, 169.1, 170.7 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 389.46; found: 389.19.

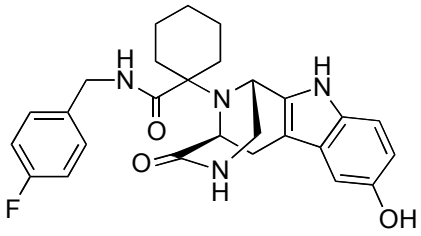
1-((5*S*)-8-hydroxy-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-*N*-phenethylcyclohexane-carboxamide [26]:  Purified by SFC (CO_2/MeOH); Yield 44% (110 mg) as a light brownish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.07-1.13 (m, 2H), 1.26-1.30 (m, 1H), 1.36-1.49 (m, 3H), 1.51-1.56 (m, 1H), 1.59-1.64 (m, 1H), 1.84-1.92 (m, 2H), 2.59 (d, *J* = 15.0 Hz, 1H), 2.61-2.69 (m, 2H), 2.85 (dd, *J* = 15.0, 5.4 Hz, 1H), 2.98 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.12-3.17 (m, 2H), 3.49 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.76 (s, 3H) 3.93 (d, *J* = 5.4 Hz, 1H), 4.21 (d, *J* = 3.6 Hz, 1H), 6.52 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.63 (d, *J* = 2.4 Hz, 1H), 6.84 (t, *J* = 7.2 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 7.17 (t, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 3.6 Hz, 1H), 7.77 (t, *J* = 5.4 Hz, 1H), 8.56 (s, 1H), 10.36 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 22.7, 22.9, 24.9, 25.1, 29.6, 30.9, 32.4, 45.2, 47.2, 54.2, 55.2, 63.7, 101.7, 106.1, 110.6, 111.4, 120.3, 127.5, 129.8, 130.0, 135.2, 150.4, 157.2, 171.8, 173.3 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 503.60; found: 503.28.

***N*-benzyl-1-((5*S*)-8-hydroxy-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]-indol-12-yl)cyclobutane-carboxamide [27]:**  Purified by SFC (CO_2/MeOH); Yield 29% (62 mg) as a light brownish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.47-1.59 (m, 2H), 2.16-2.19 (m, 3H), 2.23-2.29 (m, 1H), 2.64 (d, *J* = 15.0 Hz, 1H), 2.87 (dd, *J* = 15.6, 6.0 Hz, 1H), 3.02 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.57 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.82 (d, *J* = 5.4 Hz, 1H), 4.14 (d, *J* = 3.6 Hz, 1H), 4.24 (dd, *J* = 15.0, 6.0 Hz, 1H), 4.31 (dd, *J* = 15.0, 6.6 Hz, 1H), 6.54 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.66 (d, *J* = 1.8 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 7.20-7.24 (m, 3H), 7.29 (t, *J* = 7.2 Hz, 2H), 7.48 (d, *J* = 3.6 Hz, 1H), 8.38 (t, *J* = 6.0 Hz, 1H), 8.61 (s, 1H), 10.43 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 13.3, 24.6, 28.3, 29.0, 42.5, 46.3, 46.6, 55.2, 66.8, 101.8, 106.2, 110.8, 111.5, 126.7, 127.1, 127.2, 128.3, 130.0, 134.2, 140.1, 150.5, 171.5, 174.2 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 431.50; found: 431.20.

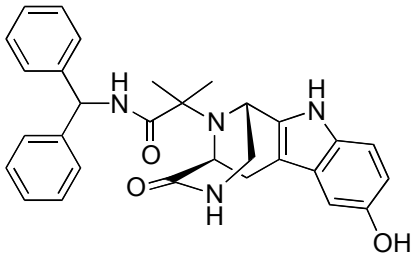
***N*-benzyl-2-((5*S*)-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-2-phenylacetamide [28]:**  Purified by column flash chromatography (CH_2Cl_2/MeOH); Yield 61% (137 mg) as a light yellowish solid; **Data for 1st diastereomer** (12.2% yield)**:** ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.56 (d, *J* = 15.6 Hz, 1H), 3.83 (dd, *J* = 16.2, 6.0 Hz, 1H), 3.15-3.17 (m, 1H), 3.28-3.31 (m, 1H), 3.77 (dd, *J* = 11.4, 4.8 Hz, 1H), 4.15 (d, *J* = 4.2 Hz, 1H), 4.21-4.25 (m, 3H), 6.97 (t, *J* = 7.8 Hz, 1H), 7.05-7.08 (m, 3H), 7.18-7.20 (m, 1H), 7.22-7.25 (m, 2H), 7.33-7.41 (m, 5H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.65 (d, *J* = 3.6 Hz, 1H), 8.72 (t, *J* = 6.0 Hz, 1H), 10.85 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 21.3, 41.9, 46.2, 48.3, 55.4, 68.9, 106.0, 111.3, 117.9, 118.7, 121.2, 126.4, 126.7, 126.9, 128.1, 128.3, 128.5, 128.6, 131.2, 135.8, 136.8, 139.4, 170.2, 170.6 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 451.53; found: 451.19. **Data for 2nd diastereomer** (48.8% yield)**:** ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.75 (d, *J* = 16.2 Hz, 1H), 3.07 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.11 (dd, *J* = 15.6, 5.4 Hz, 1H), 3.62 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.81 (d, *J* = 6.0 Hz, 1H), 3.86 (d, *J* = 4.2 Hz, 1H), 4.18 (dd, *J* = 15.6, 6.0 Hz, 1H), 4.30 (dd, *J* = 15.0, 6.0 Hz, 1H), 4.32 (s, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.2 Hz, 1H), 7.09 (*J* = 7.2 Hz, 1H), 7.19-7.22 (m, 1H), 7.24-7.29 (m, 3H), 7.30-7.37 (m, 3H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 6.6 Hz, 2H), 7.64 (d, *J* = 3.6 Hz, 1H), 8.89 (t, *J* = 6.0 Hz, 1H), 10.65 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 21.4, 42.0, 46.5, 46.6, 56.3, 67.5, 106.2, 111.3, 117.8, 118.6, 121.1, 126.3, 126.8, 126.9, 128.1, 128.2, 128.3, 128.6, 131.2, 135.7, 138.2, 139.3, 169.5, 170.8 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 451.53; found: 451.19.

***N*-benzyl-2-cyclopentyl-2-((5*S*)-8-hydroxy-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)acetamide [29]:**  Purified by SFC (CO_2/MeOH); Yield 38% (87 mg) as a brownish solid; **Data for 1st diastereomer** (7.6% yield)**:** ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.78-0.87 (m, 1H), 1.31-1.49 (m, 6H), 1.68-1.71 (m, 1H), 2.31-2.39 (m, 1H), 2.57 (d, *J* = 15.6 Hz, 1H), 2.92 (dd, *J* = 15.0, 5.4 Hz, 1H), 3.01-3.06 (m, 2H), 3.64 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.76 (d, *J* = 5.4 Hz, 1H), 4.07-4.14

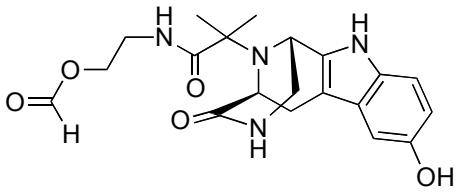
(m, 2H), 4.21 (d, *J* = 3.0 Hz, 1H), 6.54 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.67(d, *J* = 1.8 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 7.12-7.15 (m, 2H), 7.19-7.26 (m, 3H), 7.44 (d, *J* = 3.0 Hz, 1H), 8.37 (t, *J* = 5.4 Hz, 1H), 8.60 (s, 1H), 10.42 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 23.3, 24.7, 25.0, 27.6, 29.6, 42.1, 46.7, 48.0, 57.4, 67.5, 101.8, 105.5, 110.6, 111.4, 126.8, 127.3, 127.7, 128.2, 130.0, 133.7, 139.3, 150.4, 171.3, 171.5 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 459.55; found: 459.24. **Data for 2nd diastereomer** (30.4% yield)**:** ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.83-0.88 (m, 1H), 1.11-1.18 (m, 1H), 1.36-1.47 (m, 3H), 1.52-1.63 (m, 3H), 2.16-2.23 (m, 1H), 2.51 (d, 1H), 3.05-3.10 (m, 2H), 3.15 (d, *J* = 7.2 Hz, 1H), 3.62 (d, *J* = 5.4 Hz, 1H), 3.72 (dd, *J* = 12.0, 4.8 Hz, 1H), 4.20-4.29 (m, 2H), 4.31 (d, *J* = 3.6 Hz, 1H), 6.56 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.68 (d, *J* = 1.8 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.19-7.23 (m, 3H), 7.25-7.29 (m, 2H), 7.54 (d, *J* = 3.0 Hz, 1H), 8.50 (t, *J* = 5.4 Hz, 1H), 8.62 (s, 1H), 10.40 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 21.7, 24.7, 25.0, 27.5, 29.8, 42.1, 46.6, 46.8, 56.7, 66.2, 101.9, 105.6, 110.9, 111.5, 126.8, 127.2, 127.4, 128.3, 130.1, 132.8, 139.5, 150.5, 171.1, 171.2 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 459.55; found: 459.31.

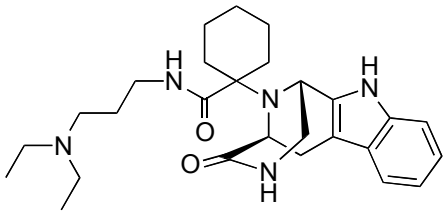
***N*-(4-fluorobenzyl)-1-((5*S*)-8-hydroxy-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5 epiminoazocino-[4,5-*b*]indol-12-yl)cyclohexane-carboxamide [30]:** 

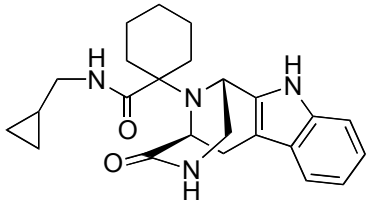
Purified by SFC (CO_2/MeOH); Yield 40% (95 mg) as a brownish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.10-1.14 (m, 2H), 1.24-1.28 (m, 1H), 1.38-1.51 (m, 3H), 1.57-1.60 (m, 1H), 1.63-1.68 (m, 1H), 1.86-1.89 (m, 1H), 1.98-2.02 (m, 1H), 2.59 (d, *J* = 15.0 Hz, 1H), 2.84 (dd, *J* = 15.0, 5.4 Hz, 1H), 2.94 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.38 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.93 (d, *J* = 5.4 Hz, 1H), 4.10-4.21 (m, 2H), 6.53 (d, *J* = 8.4 Hz, 1H), 6.64 (s, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 7.08 (t, *J* = 9.0 Hz, 2H), 7.25 (t, *J* = 5.4 Hz, 2H), 7.34 (d, *J* = 3.6 Hz, 1H), 8.30 (t, *J* = 6.0 Hz, 1H), 8.56 (s, 1H), 10.37 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 22.8, 23.0, 24.8, 25.0, 30.9, 32.2, 41.7, 45.2, 47.2, 54.2, 64.0, 101.7, 106.1, 110.6, 111.4, 114.7, 114.9, 127.3, 129.3, 129.4, 129.9, 135.1, 136.3, 136.4, 150.4, 171.7, 173.7 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 477.54; found: 477.23.

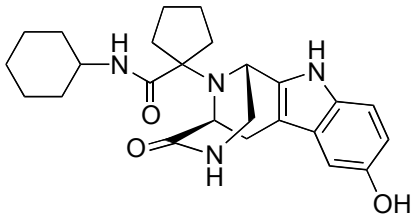
***N*-benzhydryl-2-((5*S*)-8-hydroxy-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-2-methylpropanamide [31]:** 

Purified by SFC (CO_2/MeOH); Yield 27% (66 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.96 (s, 3H), 1.34 (s, 3H), 2.61 (d, *J* = 15.0 Hz, 1H), 2.73 (dd, *J* = 15.6, 5.4 Hz, 1H), 2.88 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.22 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.84 (t, *J* = 4.8 Hz, 2H), 6.14 (d, *J* = 8.4 Hz, 1H), 6.53 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.62 (d, *J* = 2.4 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 7.21-7.25 (m, 1H), 7.28-7.34 (m, 10H), 8.59 (brs, 1H), 8.69 (d, *J* = 9.0 Hz, 1H), 10.36 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 20.4, 24.3, 24.6, 46.8, 54.8, 54.9, 56.3, 62.8, 101.8, 106.1, 110.8, 111.5, 126.8, 126.9, 127.2, 127.3, 127.8, 128.3, 128.6, 129.9, 134.4, 142.4, 142.6, 150.4, 171.7, 175.3 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 495.58; found: 495.23.

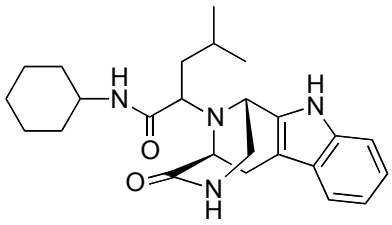
2-(2-((5*S*)-8-hydroxy-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)-2-methylpropanamido)ethyl formate [32]:  Purified by SFC (CO_2/MeOH); Yield 51% (102 mg) as a light brownish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.95 (s, 3H), 1.27 (s, 3H), 2.66 (d, *J* = 15.6 Hz, 1H), 2.87 (dd, *J* = 15.6, 6.0 Hz, 1H), 3.03 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.24-3.30 (m, 1H), 3.45-3.51 (m, 1H), 3.68 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.78 (d, *J* = 6.0 Hz, 1H), 3.87 (d, *J* = 3.6 Hz, 1H), 4.11-4.18 (m, 2H), 6.54 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.66 (d, *J* = 1.8 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H),7.50 (d, *J* = 3.6 Hz, 1H), 8.17 (t, *J* = 6.0 Hz, 1H), 8.22 (s, 1H), 10.40 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 20.3, 24.6, 24.7, 37.9, 46.9, 54.9, 59.7, 62.2, 62.7, 101.8, 106.1, 110.8, 111.5, 127.2, 130.0, 134.4, 150.5, 162.1, 171.6, 176.4 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 401.43; found 401.17.

***N*-(3-(diethylamino)propyl)-1-((5*S*)-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino-[4,5-*b*]indol-12-yl)cyclohexanecarboxamide [33]:**  Purified by SFC (CO_2/MeOH); Yield 25% (58 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.90 (t, *J* = 7.2 Hz, 6H), 1.14-1.19 (m, 2H), 1.35-1.46 (m, 6H), 1.57-1.64 (m, 2H), 1.86-1.94 (m, 2H), 2.28 (t, *J* = 7.2 Hz, 2H), 2.38 (q, *J* = 14.4, 7.2 Hz, 4H), 2.70 (d, *J* = 15.0 Hz, 1H), 2.93-2.97 (m, 3H), 3.04 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.57 (dd, *J* = 11.4, 4.8 Hz, 1H), 3.95 (d, *J* = 5.4 Hz, 1H), 4.31 (d, *J* = 4.2 Hz, 1H), 6.92 (t, *J* = 7.2 Hz, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 3.6 Hz, 1H), 7.80 (t, *J* = 5.4 Hz, 1H), 10.75 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 11.5, 22.8, 23.0, 24.8, 25.1, 26.3, 31.0, 32.5, 37.9, 45.0, 46.1, 47.3, 50.5, 54.2, 63.6, 101.5, 106.9, 111.1, 117.4, 118.3, 120.6, 126.6, 134.6, 135.4, 171.7, 172.9 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 466.63; found: 466.31.

***N*-(cyclopropylmethyl)-1-((5*S*)-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)cyclohexanecarboxamide [34]:**  Purified by SFC (CO_2/MeOH); Yield 19% (38 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.11-0.14 (m, 2H), 0.29-0.35 (m, 2H), 0.83-0.86 (m, 1H), 1.14-1.66 (m, 8H), 1.86-1.95 (m, 2H), 2.72 (d, *J* = 15.6 Hz, 1H), 2.80-2.88 (m, 2H), 2.96 (dd, *J* = 15.6, 5.4 Hz, 1H), 3.04 (d, *J* = 11.4 Hz, 1H), 3.63 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.99 (d, *J* = 4.8 Hz, 1H), 4.29 (s, 1H), 6.93 (t, *J* = 7.2 Hz, 1H), 7.01 (t, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 3.0 Hz, 1H), 7.82 (t, *J* = 5.4 Hz, 1H), 10.73 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 3.2, 3.2, 10.9, 22.7, 23.0, 24.9, 25.1, 31.0, 32.4, 43.1, 45.1, 47.2, 54.2, 63.8, 107.0, 111.1, 117.4, 118.3, 120.6, 126.6, 134.6, 135.4, 171.7, 173.2 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 407.52; found: 407.22.

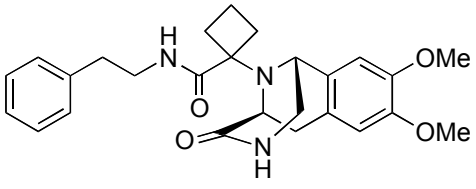
***N*-cyclohexyl-1-((5*S*)-8-hydroxy-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)cyclopentane-carboxamide [35]:**  Purified by SFC (CO_2/MeOH); Yield 24% (52 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.04-1.08 (m, 1H)

1.12-1.22 (m, 4H), 1.36-1.42 (m, 1H), 1.45-1.55 (m, 5H), 1.57-1.65 (m, 4H), 1.76-1.83 (m, 1H), 1.89-1.93 (m, 1H), 1.98-2.02 (m, 1H), 2.63 (d, *J* = 15.0 Hz, 1H), 2.83 (dd, *J* = 15.6, 5.4 Hz, 1H), 3.02 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.83 (d, *J* = 5.4 Hz, 1H), 4.11 (d, *J* = 3.6 Hz, 1H), 6.53 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.64 (d, *J* = 1.8 Hz, 1H), 7.07 (d, *J* = 9.0 Hz, 1H), 7.41 (d, *J* = 4.2 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 8.58 (s, 1H), 10.38 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 23.3, 23.4, 24.8, 24.9, 25.2, 31.4, 32.1, 32.2, 33.5, 47.0, 47.1, 47.8, 55.4, 73.5, 101.8, 106.2, 110.7, 111.4, 127.2, 129.9, 134.6, 150.4, 171.6, 173.5 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 437.55; found: 437.26.



***N*-cyclohexyl-4-methyl-2-((5*S*)-4-oxo-2,3,4,5,6,11-hexahydro-1*H*-1,5-epiminoazocino[4,5-*b*]indol-12-yl)pentanamide [36]:** Purified by SFC (CO_2/MeOH); Yield 52% (109 mg) as a light yellowish solid; **Data for 1st diastereomer** (11.3% yield)**:** ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.83-0.86 (m, 6H), 1.04-1.23 (m, 5H), 1.45-1.68 (m, 8H), 2.68 (d, *J* = 15.6 Hz, 1H), 2.92 (dd, *J* = 15.6, 5.4 Hz, 1H), 3.07-3.13 (m, 2H), 3.46-3.52 (m, 1H), 3.59 (dd, *J* = 15.6, 4.2 Hz, 1H), 3.78 (d, *J* = 4.8 Hz, 1H), 4.05 (d, *J* = 3.6 Hz, 1H), 6.95 (t, *J* = 7.8 Hz, 1H), 7.03 (t, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 3.6 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 10.78 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 21.8, 21.9, 24.0, 24.6, 24.7, 24.8, 25.2, 32.2, 32.3, 46.6, 47.2, 48.1, 55.9, 62.3, 106.3, 111.2, 117.7, 118.5, 120.9, 126.5, 132.2, 135.6, 170.9, 171.0 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 423.56; found: 423.32. **Data for 2nd diastereomer** (40.7% yield)**:** ^{1}H NMR (600 MHz, DMSO-d_6) δ: 0.77 (d, *J* = 6.0 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H), 1.06-1.19 (m, 3H), 1.20-1.29 (m, 2H), 1.33-1.41 (m, 2H), 1.53-1.61 (m, 2H), 1.64-1.72 (m, 4H), 2.63 (d, *J* = 15.0 Hz, 1H), 3.08-3.17 (m, 3H), 3.57-3.61 (m 1H), 3.63 (d, *J* = 6.0 Hz, 1H), 3.67 (dd, *J* = 11.4, 4.8 Hz, 1H), 4.31 (d, *J* = 4.2 Hz, 1H), 6.96 (t, *J* = 7.2 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 3.6 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 10.76 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 22.0, 22.1, 24.0, 24.7, 25.0, 25.2, 32.3, 32.4, 46.1, 46.7, 47.4, 48.7, 56.7, 61.4, 106.5, 111.3, 117.8, 118.5, 121.0, 126.5, 132.2, 135.7, 170.3, 171.1 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 423.56; found 423.32.

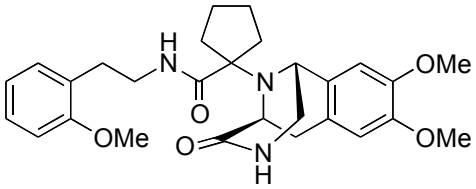
1-((5*S*)-8,9-dimethoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5-epiminobenzo[*d*]azocin-11-yl)-*N*-phenethylcyclobutanecarboxamide [40]: Purified by column flash chromatography (Hexanes/EtOAc); Yield 64% (143 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ:1.46-1.57 (m, 2H), 2.08-2.14 (m, 2H), 2.16-2.22 (m, 2H), 2.63-2.75 (m, 3H), 2.91-2.97 (m, 2H), 3.25-3.34 (m, 2H), 3.56 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.64 (d, *J* = 6.0 Hz, 1H), 3.69 (s, 3H), 3.71 (s, 3H), 4.08 (d, *J* = 3.6 Hz, 1H), 6.63 (s, 1H), 6.80 (s, 1H), 7.17-7.20 (m, 3H), 7.26 (t, *J* = 7.8 Hz, 2H), 7.50 (d, *J* = 3.0 Hz, 1H), 7.75 (t, *J* = 5.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 13.7, 28.3, 29.2, 30.8, 35.0, 40.4, 48.3, 49.6, 54.1, 55.4, 55.5, 66.7, 110.1, 111.4, 125.8, 126.1, 128.3, 128.6, 129.3, 139.5, 147.2, 147.7, 171.1, 173.9 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 450.54; found: 450.21.



4-((5*S*)-8,9-dimethoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5-epiminobenzo[*d*]azocin-11-yl)-*N*-phenethyltetrahydro-2*H*-pyran-4-carboxamide [41]: Purified by column flash chromatography

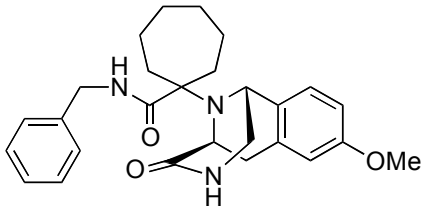
(Hexanes/EtOAc); Yield 59% (141 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.54-1.58 (m, 1H), 1.75-1.78 (m, 1H), 1.91-1.94 (m, 2H), 2.61-2,68 (m, 3H), 2.91-2.99 (m, 2H), 3.10 (t, *J* = 10.8 Hz, 1H), 3.13-3.25(m, 2H), 3.37 (t, *J* = 10.2 Hz, 1H), 3.61 (dd, *J* = 11.4, 4.8 Hz, 2H), 3.65-3.67 (m, 1H), 3.68 (s, 3H), 3.70 (s, 3H), 3.81 (d, *J* = 6.0 Hz, 1H), 4.21 (d, *J* = 3.6 Hz, 1H), 6.61 (s, 1H), 6.79 (s, 1H), 7.16-7.20 (m, 3H), 7.27 (t, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 3.6 Hz, 1H), 7.88 (t, *J* = 5.4Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 30.6, 31.9, 32.8, 34.7, 40.5, 48.4, 48.6, 53.2, 55.4, 55.5, 61.4, 63.7, 64.5, 110.1, 111.5, 125.7, 126.1, 128.3, 128.6, 129.8, 139.5, 147.1, 147.6, 171.1, 172.5 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 480.57; found: 480.21.

1-((5*S*)-8,9-dimethoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5-epiminobenzo[*d*]azocin-11-yl)-*N*-(2-methoxyphenethyl)cyclopentane-carboxamide [42]:



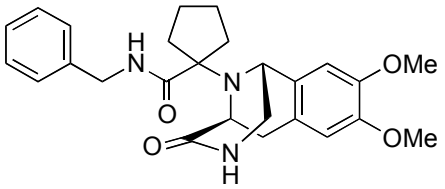
Purified by column flash chromatography (Hexanes/EtOAc); Yield 62% (153 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.36-1.42 (m, 1H), 1.46-1.53 (m, 3H), 1.54-1.59 (m, 1H), 1.71-1.76 (m, 1H), 1.85-1.90 (m, 1H), 1.99-2.04 (m, 1H), 2.59-2.71 (m, 3H), 2.89-2.93 (m, 2H), 3.20 (q, *J* = 14.4, 7.8 Hz, 2H), 3.57 (dd, *J* = 12.0, 4.8 Hz, 1H), 3.62 (d, *J* = 6.0 Hz, 1H), 3.68 (s, 3H), 3.70 (s, 3H), 3.75 (s, 3H), 4.04 (d, *J* = 3.6 Hz, 1H), 6.60 (s, 1H), 6.79 (s, 1H), 6.84 (t, *J* = 7.2 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 7.18 (t, *J* = 9.0 Hz, 1H), 7.43 (d, *J* = 3.6 Hz, 1H), 7.72 (t, *J* = 6.0 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 23.4, 33.6, 29.6, 30.8, 32.1, 33.4, 40.0, 48.5, 50.3, 54.8, 55.2, 55.4, 55.5, 73.3, 110.1, 110.6, 111.4, 120.3, 125.7, 127.3, 127.6, 129.7, 129.9, 147.1, 147.6, 157.2,171.2, 174.6 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 494.59; found: 494.25.

***N*-benzyl-1-((1*R*,5*S*)-8-methoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5-epiminobenzo[*d*]azocin-11-yl)cycloheptanecarboxamide [43]:**



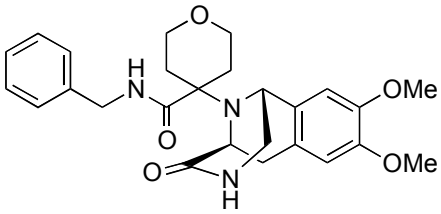
Purified by SFC (CO_2/MeOH); Yield 35% (78 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.34-1.48 (m, 3H), 1.55-1.75 (m, 6H), 1.90-1.98 (m, 2H), 2.24 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.85 (d, *J* = 16.8, Hz, 1H), 3.01 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.05 (dd, *J* = 17.4, 6.6 Hz, 1H), 3.60 (dd, *J* = 11.4, 4.8 Hz, 1H), 3.75 (s, 3H), 3.84 (d, *J* = 6.6 Hz, 1H), 3.97 (d, *J* = 4.2 Hz, 1H), 4.32 (d, *J* = 14.4 Hz, 1H), 4.46 (d, *J* = 14.4 Hz, 1H), 6.28 (s, 1H), 6.54 (d, *J* = 2.4 Hz, 1H), 6.72 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 7.23-7.33 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 24.2, 24.8, 30.3, 30.4, 31.8, 33.6, 36.5, 43.3, 49.8, 50.3, 54.4, 55.2, 70.1, 113.2, 127.1, 127.5, 127.8, 128.7, 129.3, 134.5, 138.8, 158.6, 172.7, 176.5 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 448.57; found: 448.25.

***N*-benzyl-1-((5*S*)-8,9-dimethoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5-epiminobenzo[*d*]azocin-11-yl)cyclopentanecarboxamide [44]:**



Purified by column flash chromatography (Hexanes/EtOAc); Yield 72% (161 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.39-1.46 (m, 1H), 1.48-1.56 (m, 2H), 1.58-1.63 (m, 2H), 1.74-1.79 (m, 1H), 1.97-2.02 (m, 1H), 2.04-2.09 (m, 1H), 2.63 (d, *J* = 16.2 Hz, 1H), 2.92-2.98 (m, 2H), 3.58-3.64 (m, 2H), 3.69 (s, 3H), 3.70 (s, 3H), 4.08 (d, *J* = 4.2 Hz, 1H), 4.16 (dd, *J* = 15.0, 6.0 Hz,

1H), 4.27 (dd, *J* = 14.4, 6.0 Hz, 1H), 6.61 (s, 1H), 6.77 (s, 1H), 7.20-7.23 (m, 3H), 7.27-7.31 (m, 2H), 7.42 (d, *J* = 3.6 Hz, 1H), 8.26 (t, *J* = 6.0 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 23.4, 23.7, 31.1, 32.5, 33.0, 42.5, 48.4, 50.4, 54.8, 55.4, 55.5, 73.8, 110.1, 111.4, 125.8, 126.7, 127.2, 128.2, 129.8, 140.1, 147.1, 147.6, 171.3, 174.9 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 450.54; found: 450.21.

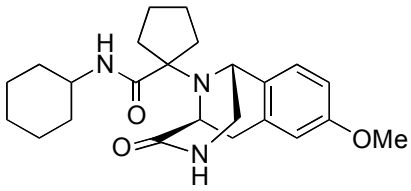


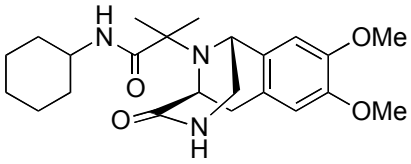
***N*-benzyl-4-((5*S*)-8,9-dimethoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5-epiminobenzo[*d*]azocin-11-yl)tetrahydro-2*H*-pyran-4-carboxamide [45]:** Purified by SFC (CO_2/MeOH); Yield 49% (114 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.55-1.60 (m, 1H), 1.81-1.86 (m, 1H), 1.96-1.99 (m, 1H), 2.01-2.05 (m, 1H), 2.63 (d, *J* = 16.2 Hz, 1H), 2.92-2.97 (m, 2H), 3.21 (t, *J* = 10.8 Hz, 1H), 3.43 (td, *J* = 11.4, 1.8 Hz, 1H), 3.57 (dd, *J* = 12.0, 4.8 Hz, 1H), 3.63-3.67 (m, 1H), 3.69 (s, 3H), 3.71 (s, 3H), 3.73-3.76 (m, 1H), 3.80 (d, *J* = 6.6 Hz, 1H), 4.11 (dd, *J* = 14.4, 5.4 Hz, 1H), 4.20 (d, *J* = 3.6 Hz, 1H), 4.25 (dd, *J* = 15.0, 6.0 Hz, 1H), 6.61 (s, 1H), 6.77 (s, 1H), 7.22-7.24 (m, 3H), 7.29-7.31 (m, 2H), 7.40 (d, *J* = 3.6 Hz, 1H), 8.35 (t, *J* = 6.0 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 30.7, 32.0, 32.6, 40.1, 42.5, 48.5, 53.2, 55.4, 55.5, 61.9, 63.9, 64.7, 110.0, 111.5, 125.6, 126.7, 127.4, 128.2, 129.8, 139.8, 147.1, 147.6, 171.1, 172.7 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 466.54; found: 466.24.

***N*-(4-fluorobenzyl)-2-((1*R*,5*S*)-8-methoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5-epiminobenzo[*d*]azocin-11-yl)-2-methylpropanamide [46]:** Purified by SFC (CO_2/MeOH); Yield 44% (90 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.25 (s, 3H), 1.39 (s, 3H), 2.87 (d, *J* = 16.8 Hz, 1H), 2.94 (dd, *J* = 16.8, 6.0 Hz, 1H), 3.12 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.63 (dd, *J* = 12.0, 4.8 Hz, 1H), 3.69 (d, *J* = 6.6 Hz, 1H), 3.73 (s, 3H), 4.01 (d, *J* = 3.6 Hz, 1H), 4.24 (dd, *J* = 15.0, 5.4 Hz, 1H), 4.47 (dd, *J* = 15.0, 6.6 Hz, 1H), 6.54 (d, *J* = 2.4 Hz, 1H), 6.73 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.98-7.02 (m, 3H), 7.21 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.61 (t, *J* = 6.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 20.5, 25.1, 31.7, 42.7, 49.3, 50.2, 54.7, 55.1, 63.7, 113.1, 113.2, 115.4, 115.6, 127.2, 128.9, 129.2, 129.3, 134.1, 134.4, 134.5, 158.6, 161.2, 162.9, 172.8, 176.2 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 412.47; found: 412.19.

diethyl-((1-((5*S*)-8,9-dimethoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5-epiminobenzo[*d*]azocin-11-yl)cyclohexanecarboxamido)-methyl)phosphonate [47]: Purified by column flash chromatography (Hexanes/EtOAc); Yield 76% (198 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.11-1.29 (m, 9H), 1.42-1.47 (m, 2H), 1.53-1.63 (m, 3H), 1.91-1.98 (m, 2H), 2.59 (d, *J* = 16.2 Hz, 1H), 2.93 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.01 (dd, *J* = 16.8, 6.6 Hz, 1H), 3.44 (q, *J* = 10.8, 6.0 Hz, 2H), 3.64 (dd, *J* = 12.0, 4.8 Hz, 1H), 3.69 (s, 3H), 3.70 (s, 3H), 3.73 (d, *J* = 6.0 Hz, 1H), 3.98-4.03 (m, 4H), 4.15 (d, *J* = 3.6 Hz, 1H), 6.60 (s, 1H), 6.73 (s, 1H), 7.38 (d, *J* = 3.6 Hz, 1H), 7.92 (t, *J* = 6.0 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 16.2 (q), 22.5, 22.9, 25.0, 30.6, 31.2, 32.3, 33.6, 34.6, 48.7, 48.8,

53.5, 55.4, 55.5, 61.4 (q), 64.3, 109.9, 111.5, 125.8, 130.1, 147.0, 147.5, 171.4, 173.5 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 524.56; found: 524.28.

***N*-cyclohexyl-1-((1*R*,5*S*)-8-methoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5epiminobenzo[*d*]azocin-11-yl)cyclopentanecarboxamide [48]:**  Purified by SFC (CO_2/MeOH); Yield 47% (96 mg) as a colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.97-1.12 (m, 3H), 1.26-1.35 (m, 2H), 1.55-1.73 (m, 8H), 1.78-1.85 (m, 3H), 1.94-1.99 (m, 1H), 2.07-2.10 (m, 1H), 2.92 (d, *J* = 16.8 Hz, 1H), 3.11 (d, *J* = 11.4 Hz, 1H), 3.65-3.70 (m, 1H), 3.74 (s, 3H), 3.76-3.80 (m, 1H), 3.82 (d, *J* = 6.6 Hz, 1H), 4.04 (*J* = 4.2 Hz, 1H), 6.58 (d, *J* = 1.8 Hz, 1H), 6.72 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 24.8, 24.9, 25.0, 25.4, 32.3, 32.9, 33.0, 33.1, 33.5, 47.8, 49.2, 50.9, 54.5, 55.1, 74.5, 74.6, 113.0, 113.2, 127.2, 129.2, 134.6, 158.5, 172.9, 174.9 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 412.54; found: 412.23.

***N*-cyclohexyl-2-((1*R*,5*S*)-8,9-dimethoxy-4-oxo-1,2,3,4,5,6-hexahydro-1,5-epiminobenzo[*d*]azocin-11-yl)-2-methylpropanamide [49]:**  Purified by SFC (CO_2/MeOH); Yield 52% (108 mg) as a light yellowish solid; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.01 (s, 3H), 1.09-1.30 (m, 8H), 1.54-1.76 (m, 5H), 2.68 (d, *J* = 16.8 Hz, 1H), 2.95 (dd, *J* = 16.8, 6.0 Hz, 1H), 3.00 (dd, *J* = 12.0, 4.2 Hz, 1H), 3.49-3.54 (m, 2H), 3.62 (dd, *J* = 12.0, 4.2 Hz, 1H), 3.70 (s, 3H), 3.71 (s, 3H), 3.95 (d, *J* = 3.6 Hz, 1H), 6.65 (s, 1H), 6.86 (s, 1H), 7.49 (d, *J* = 3.6 Hz, 1H), 7.62 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 20.4, 24.6, 24.7, 24.8, 25.2, 30.4, 32.2, 32.5, 47.6, 48.8, 49.9, 54.4, 55.4, 55.5, 62.5, 110.0, 111.5, 125.3, 129.7, 147.3, 147.6, 171.3, 174.6 ppm. SFCMS (APCI, *m/z*): $[M]^+$ calc.: 416.53; found: 416.22.

5. Single crystal X-Ray structure Determination of Product 32

General:

The data was collected on a X-ray single crystal diffractometer equipped with a CCD detector (Bruker, APEX II, κ–CCD), a rotating anode (Bruker AXS, FR591) with MoK_α radiation (λ = 0.71073 Å), and a graphite monochromator by using the SMART software package.[1] The measurement was performed on a single crystal coated with perfluorinated ether. The crystal was fixed on the top of a cactus brickle (Opuntia ficus-india), transferred to the diffractometer and frozen under a stream of cold nitrogen. A matrix scan, using three short runs, was used to determine the initial lattice parameters. Reflections were merged and corrected for Lorenz and polarization effects, scan speed, and background using SAINT.[2] Absorption corrections, including odd and even ordered spherical harmonics were performed using SADABS.[2] Space group assignments were based upon systematic absences, *E* statistics, and successful refinement of the structures. Structures were solved by direct methods with the aid of successive difference Fourier maps, and were refined against all data using WinGX[7] based on SIR-92.[3] Hydrogen atoms could be located in the difference Fourier maps and were allowed to refine freely. If not mentioned otherwise, non-hydrogen atoms were refined with anisotropic displacement parameters. Full-matrix least-squares refinements were carried out by minimizing $\Sigma w(F_o^2-F_c^2)^2$ with SHELXL-97[5] weighting scheme. Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from *International Tables for Crystallography*.[4] Images of the crystal structures were generated by PLATON[6]. CCDC 928118 (**32**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif or https://www.ccdc.cam.ac.uk/services/structure_deposit/

Single Crystal X-Ray Structure Determination of Product 32

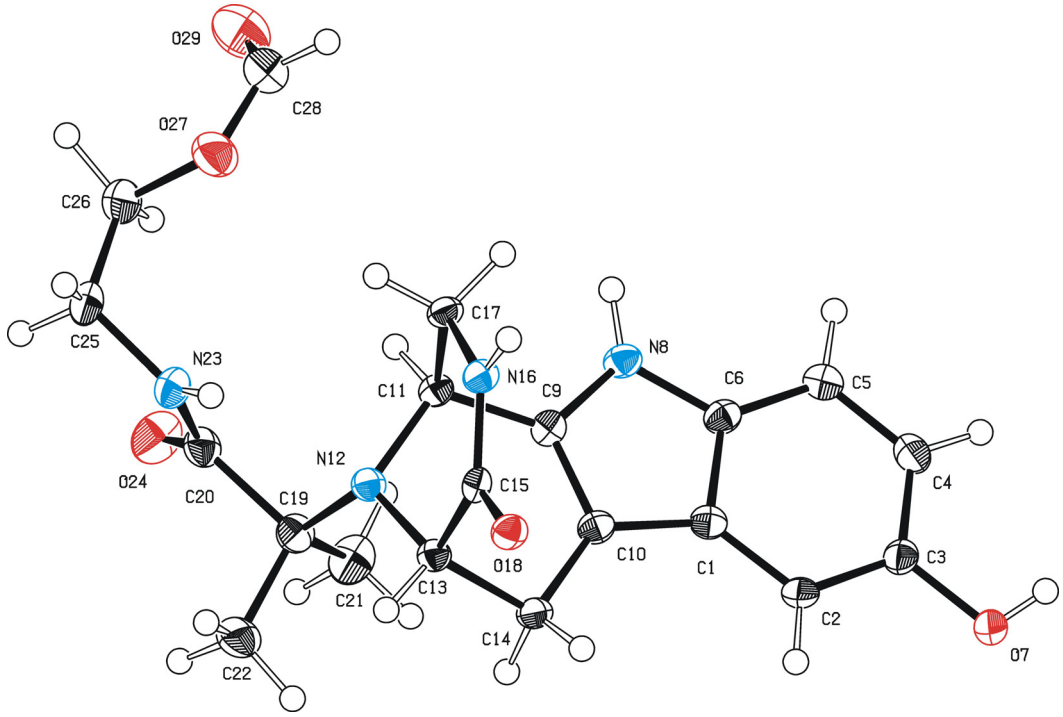


Figure 1 – Ortep drawing of product **32** with 50% ellipsoids.[6]

Operator:	*** Herdtweck ***
Molecular Formula:	$C_{20}\ H_{24}\ N_4\ O_5$
Crystal Color / Shape	Colorless needle
Crystal Size	Approximate size of crystal fragment used for data collection: $0.05 \times 0.10 \times 0.53$ mm
Molecular Weight:	400.43 a.m.u.
F_{000}:	848
Systematic Absences:	h00: h≠2n; 0k0: k≠2n, 00l: l≠2n
Space Group:	Orthorhombic $P\ 2_1 2_1 2_1$ (I.T.-No.: 19)
Cell Constants:	Least-squares refinement of 9717 reflections with the programs "APEX suite" and "SAINT" [1,2]; theta range 2.41° < θ < 25.39°; Mo($K\overline{\alpha}$); λ = 71.073 pm a = 674.49(2) pm b = 872.16(3) pm c = 3350.58(11) pm V = 1971.02(11)· 10^6 pm^3; Z = 4; D_{calc} = 1.349 g cm^{-3}; Mos. = 0.68
Diffractometer:	Kappa APEX II (Area Diffraction System; BRUKER AXS); rotating anode; graphite monochromator; 50 kV; 40 mA; λ = 71.073 pm; Mo($K\overline{\alpha}$)
Temperature:	(-150±1) °C; (123±1) K
Measurement Range:	2.41° < θ < 25.39°; h: -8/8, k: -10/10, l: -40/40

Measurement Time:	2×10 s per film
Measurement Mode:	measured: 11 runs; 4951 films / scaled: 11 runs; 4951 films φ– and ω–movement; Increment: $\Delta\varphi/\Delta\omega = 0.50°$; dx = 80.0 mm
LP - Correction:	Yes [2]
Intensity Correction	No/Yes; during scaling [2]
Absorption Correction:	Multi-scan; during scaling; $\mu = 0.099$ mm^{-1} [2] Correction Factors: T_{min} = 0.6499 T_{max} = 0.7452
Reflection Data:	35582 reflections were integrated and scaled 120 reflections systematic absent and rejected 35462 reflections to be merged 3635 independent reflections 0.029 R_{int}: (basis F_o^2) 3635 independent reflections (all) were used in refinements 3539 independent reflections with $I_o > 2\sigma(I_o)$ 100 % completeness of the data set 358 parameter full-matrix refinement 10.2 reflections per parameter
Solution:	Direct Methods [3]; Difference Fourier syntheses
Refinement Parameters:	In the asymmetric unit: 29 Non-hydrogen atoms with anisotropic displacement parameters 24 Hydrogen atoms with isotropic displacement parameters
Hydrogen Atoms:	All hydrogen atom positions were found in the difference map calculated from the model containing all non-hydrogen atoms. The hydrogen positions were refined with individual isotropic displacement parameters.
Atomic Form Factors:	For neutral atoms and anomalous dispersion [4]
Extinction Correction:	no
Weighting Scheme:	$w^{-1} = \sigma^2(F_o^2)+(a*P)^2+b*P$ with a: 0.0265; b: 0.4988; P: [Maximum(0 or F_o^2)+2$*F_c^2$]/3
Shift/Err:	Less than 0.001 in the last cycle of refinement:
Resid. Electron Density:	+0.15 e_0^-/Å^3; -0.16 e_0^-/Å^3
R1:	$\Sigma(\|\|F_o\|-\|F_c\|\|)/\Sigma\|F_o\|$
[$F_o > 4\sigma(F_o)$; N=3539]:	= 0.0246
[all reflctns;	N=3635]: = 0.0255
wR2:	$[\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$
[$F_o > 4\sigma(F_o)$; N=3539]:	= 0.0606
[all reflctns; N=3635]:	= 0.0612
Goodness of fit:	$[\Sigma w(F_o^2-F_c^2)^2/(NO-NV)]^{1/2}$ = 1.077
Flack's Parameter :	x =- 0.2(7)
Remarks:	Refinement expression $\Sigma w(F_o^2-F_c^2)^2$ The correct enantiomere could **not** be proved by Flack's Parameter.

References:

[1] APEX suite of crystallographic software. APEX 2 Version 2008.4. Bruker AXS Inc., Madison, Wisconsin, USA (2008).

[2] SAINT, Version 7.56a and SADABS Version 2008/1. Bruker AXS Inc., Madison, Wisconsin, USA (2008).

[3] Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli M. "**SIR92**", *J. Appl. Cryst.* **1994**, *27*, 435-436.

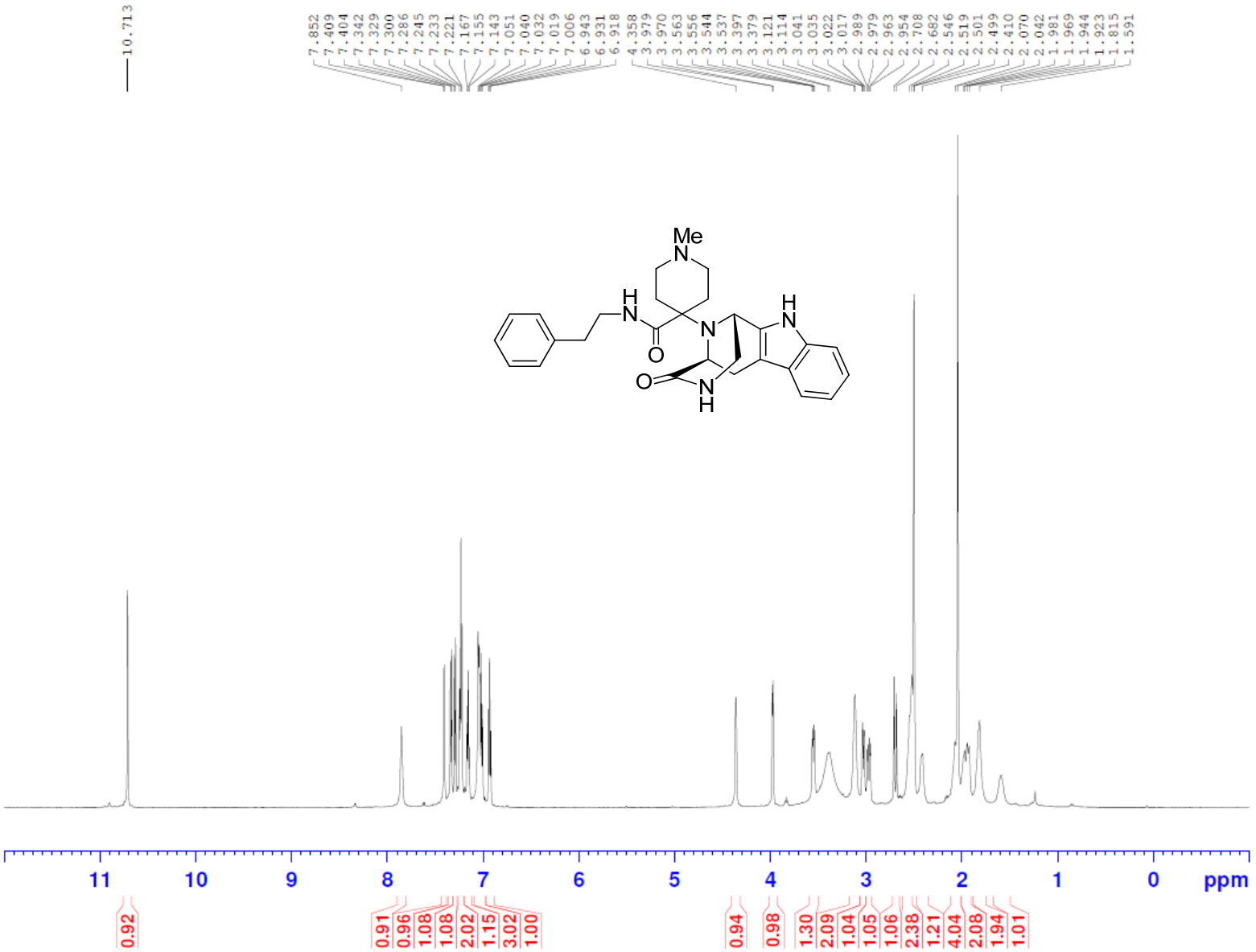
[4] International Tables for Crystallography, Vol. C, Tables 6.1.1.4 (pp. 500-502), 4.2.6.8 (pp. 219-222), and 4.2.4.2 (pp. 193-199), Wilson, A. J. C., Ed., Kluwer Academic Publishers, Dordrecht, The Netherlands, 1992.

[5] Sheldrick, G. M. "**SHELXL-97**", University of Göttingen, Göttingen, Germany, (1998).

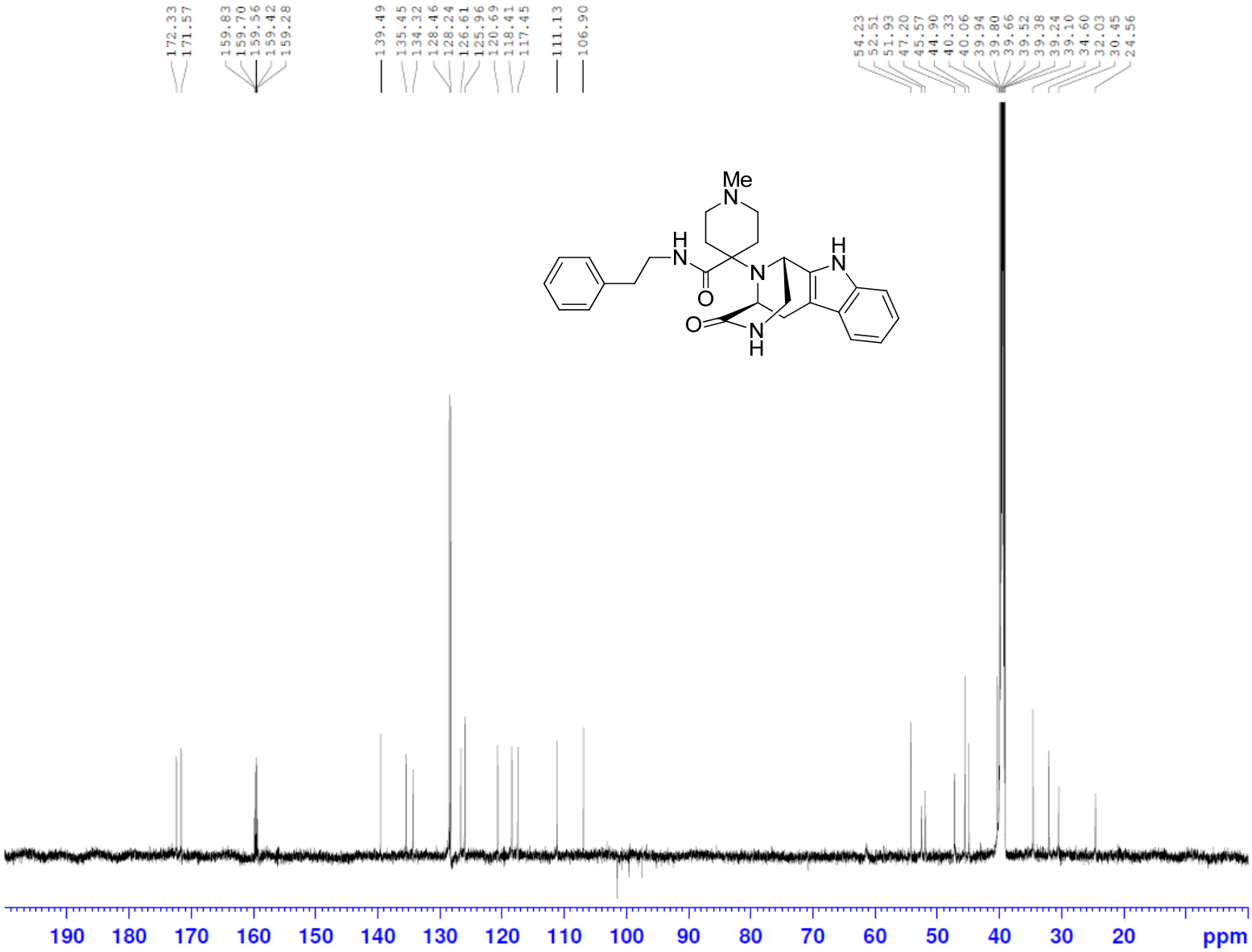
[6] Spek, A. L. "**PLATON**", A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands, (2010).

[7] L. J. Farrugia, "**WinGX** (Version 1.70.01 January 2005) ", *J. Appl. Cryst.* **1999**, *32*, 837-838.

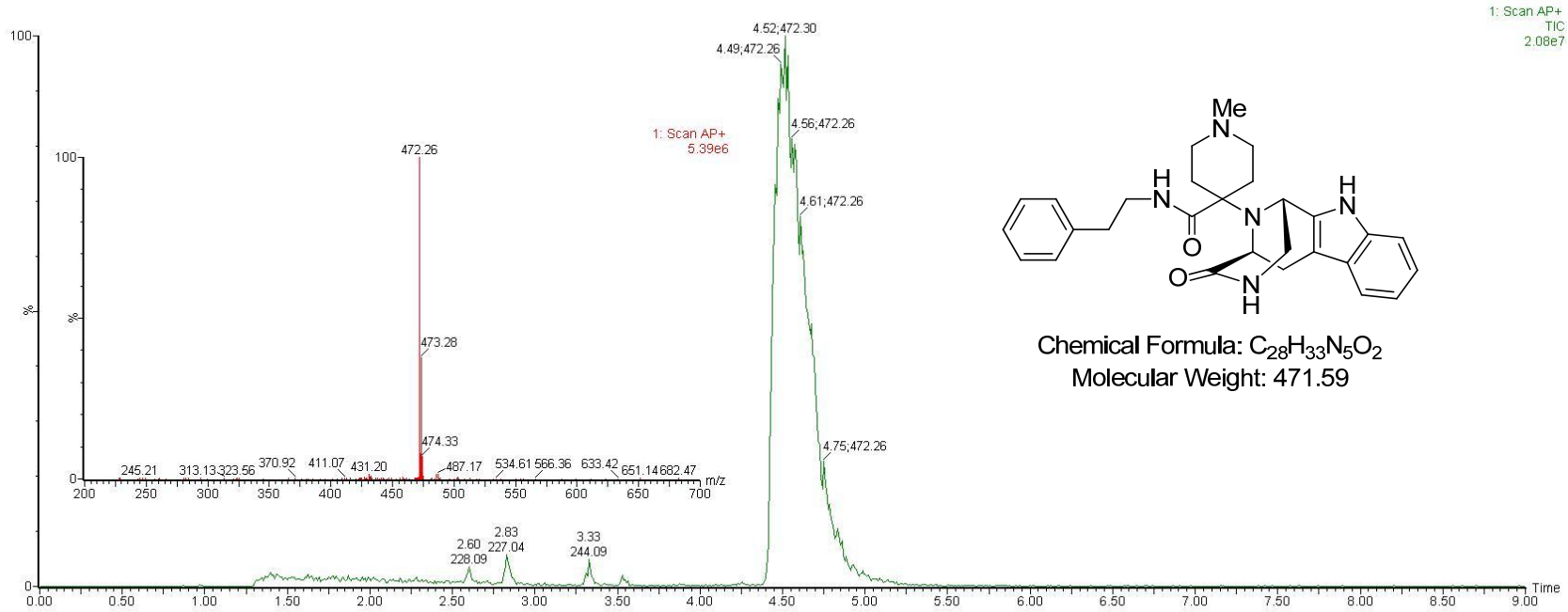
Compound-19


10.713
7.852
7.409
7.404
7.342
7.329
7.300
7.286
7.245
7.233
7.221
7.167
7.155
7.143
7.051
7.040
7.032
7.019
7.006
6.943
6.931
6.918
4.358
3.979
3.970
3.563
3.556
3.544
3.537
3.397
3.379
3.121
3.114
3.041
3.035
3.022
3.017
2.989
2.979
2.963
2.954
2.708
2.682
2.546
2.519
2.501
2.499
2.410
2.070
2.042
1.981
1.969
1.944
1.923
1.815
1.591
Me
N
H
N
O
N
H
N
O
N
H
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.92
0.91
0.96
1.08
1.08
2.02
1.15
3.02
1.00
0.94
0.98
1.30
2.09
1.04
1.05
1.06
2.38
1.21
4.04
2.08
1.94
1.01

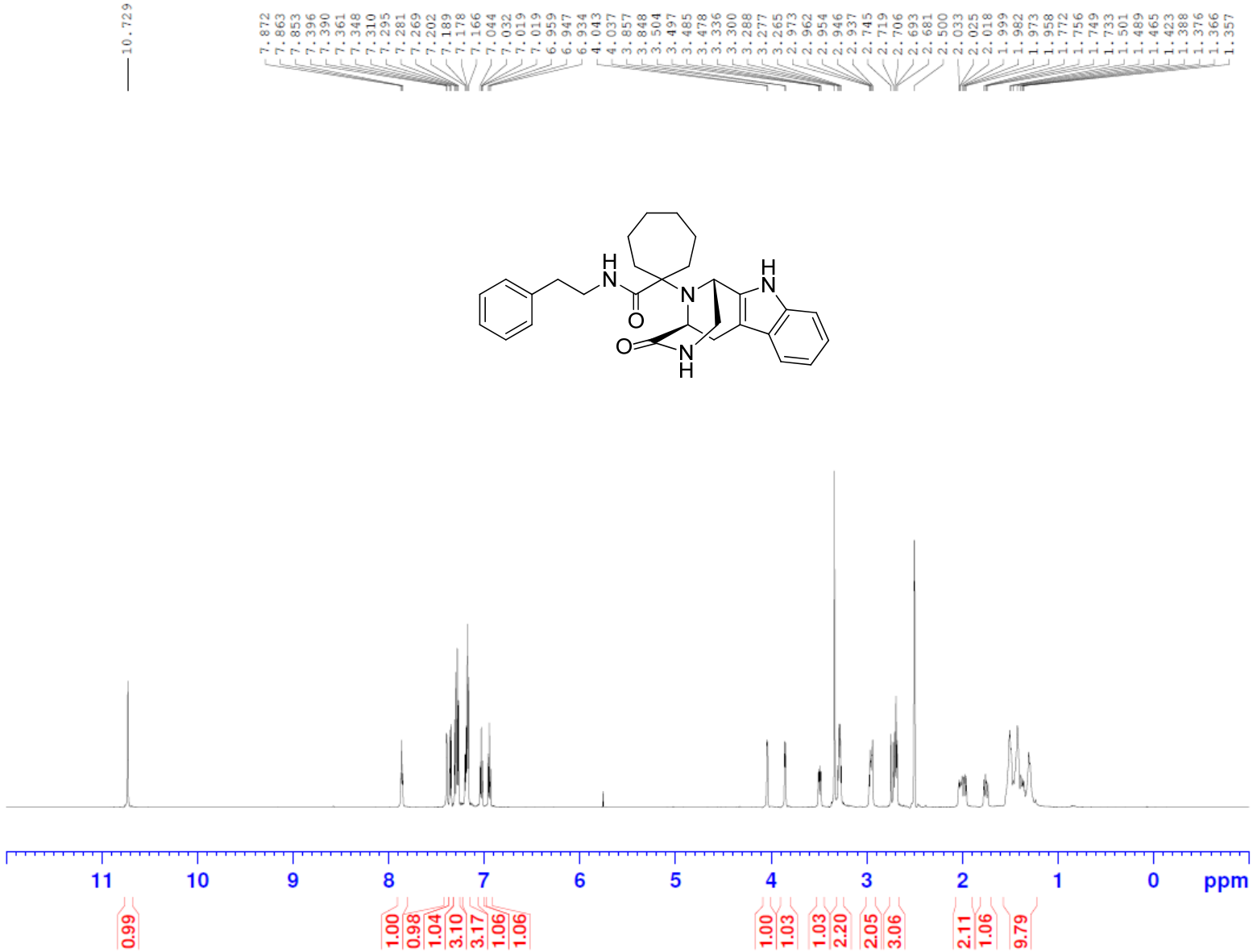
Compound-19


172.33
171.57
159.83
159.70
159.56
159.42
159.28
139.49
135.45
134.32
128.46
128.24
126.61
125.96
120.69
118.41
117.45
111.13
106.90
54.23
52.51
51.93
47.20
45.57
44.90
40.33
40.06
39.94
39.80
39.66
39.52
39.38
39.24
39.10
34.60
32.03
30.45
24.56
Me
N
H
N
N
H
N
O
O
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

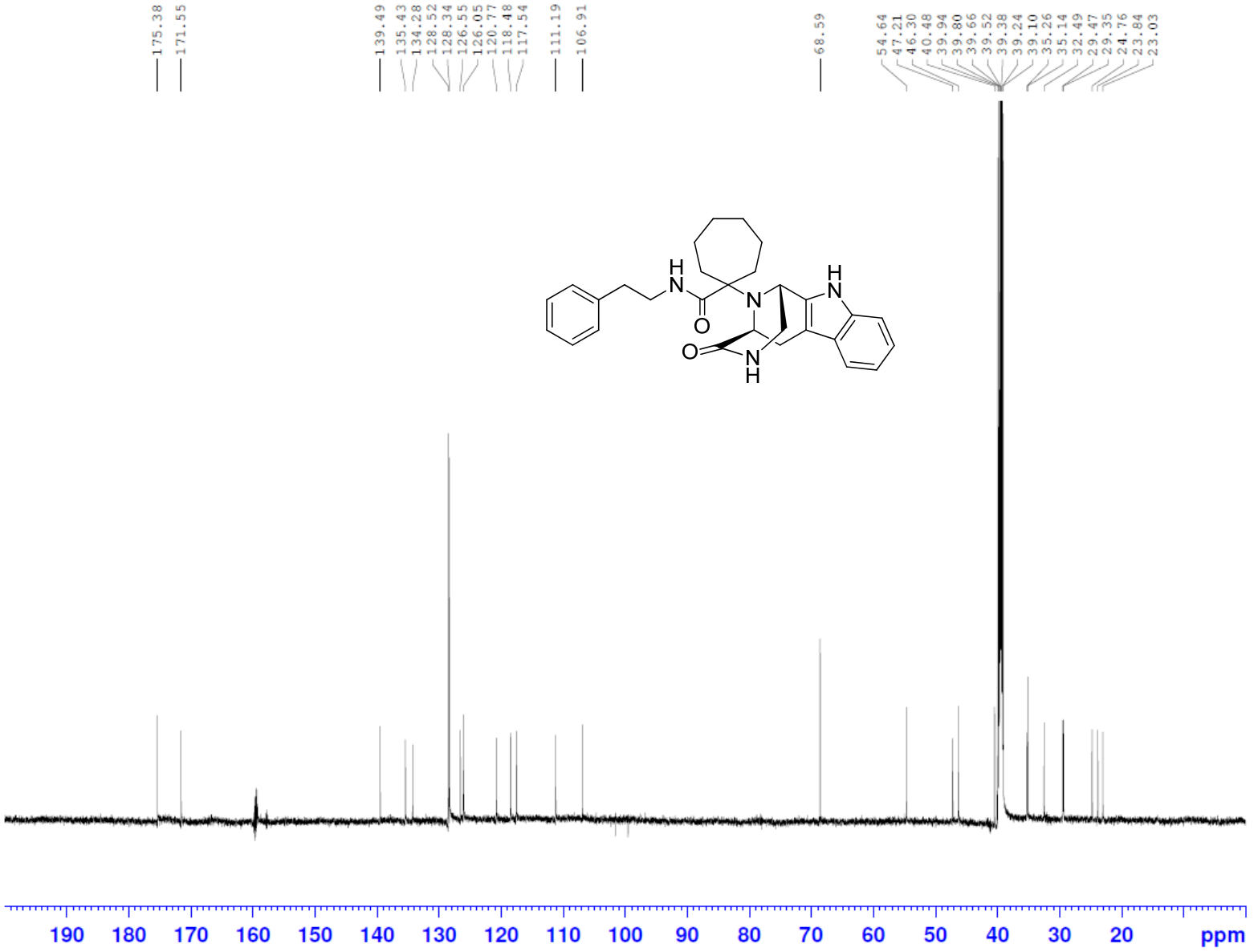
Compound-19


1: Scan AP+
TIC
2.08e7
4.52;472.30
4.49;472.26
4.56;472.26
4.61;472.26
4.75;472.26
1: Scan AP+
5.39e6
472.26
473.28
474.33
245.21
313.13
323.56
370.92
411.07
431.20
487.17
534.61
566.36
633.42
651.14
682.47
m/z
2.60
228.09
2.83
227.04
3.33
244.09
Time
Me
N
H
N
N
O
O
N
H
H
N
Chemical Formula: $C_{28}H_{33}N_5O_2$
Molecular Weight: 471.59

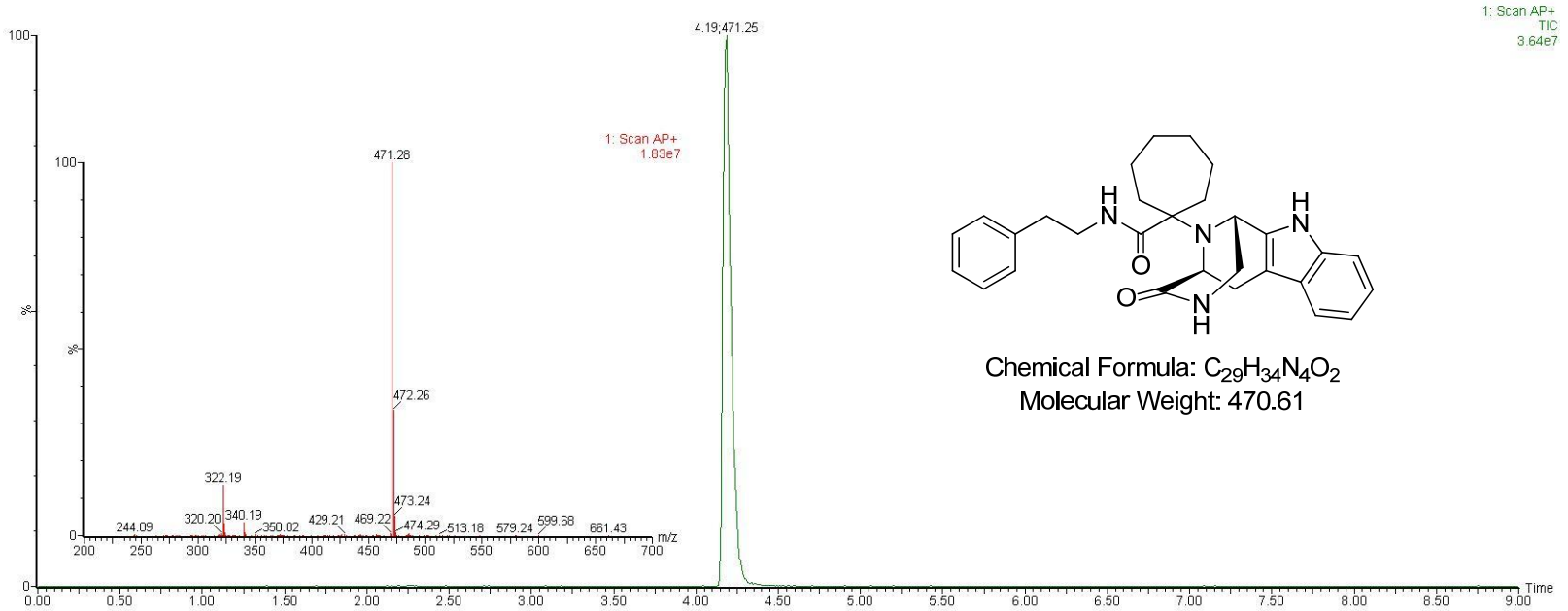
Compound-20


10.729
7.872
7.863
7.853
7.396
7.390
7.361
7.348
7.310
7.295
7.281
7.269
7.202
7.189
7.178
7.166
7.044
7.032
7.019
6.959
6.947
6.934
4.043
4.037
3.857
3.848
3.504
3.497
3.485
3.478
3.336
3.300
3.288
3.277
3.265
2.973
2.962
2.954
2.946
2.937
2.745
2.719
2.706
2.693
2.681
2.500
2.033
2.025
2.018
1.999
1.982
1.973
1.958
1.772
1.756
1.749
1.733
1.501
1.489
1.465
1.423
1.388
1.376
1.366
1.357
H
N
O
O
N
H
N
H
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.99
1.00
0.98
1.04
3.10
3.17
1.06
1.06
1.00
1.03
1.03
2.20
2.05
3.06
2.11
1.06
9.79

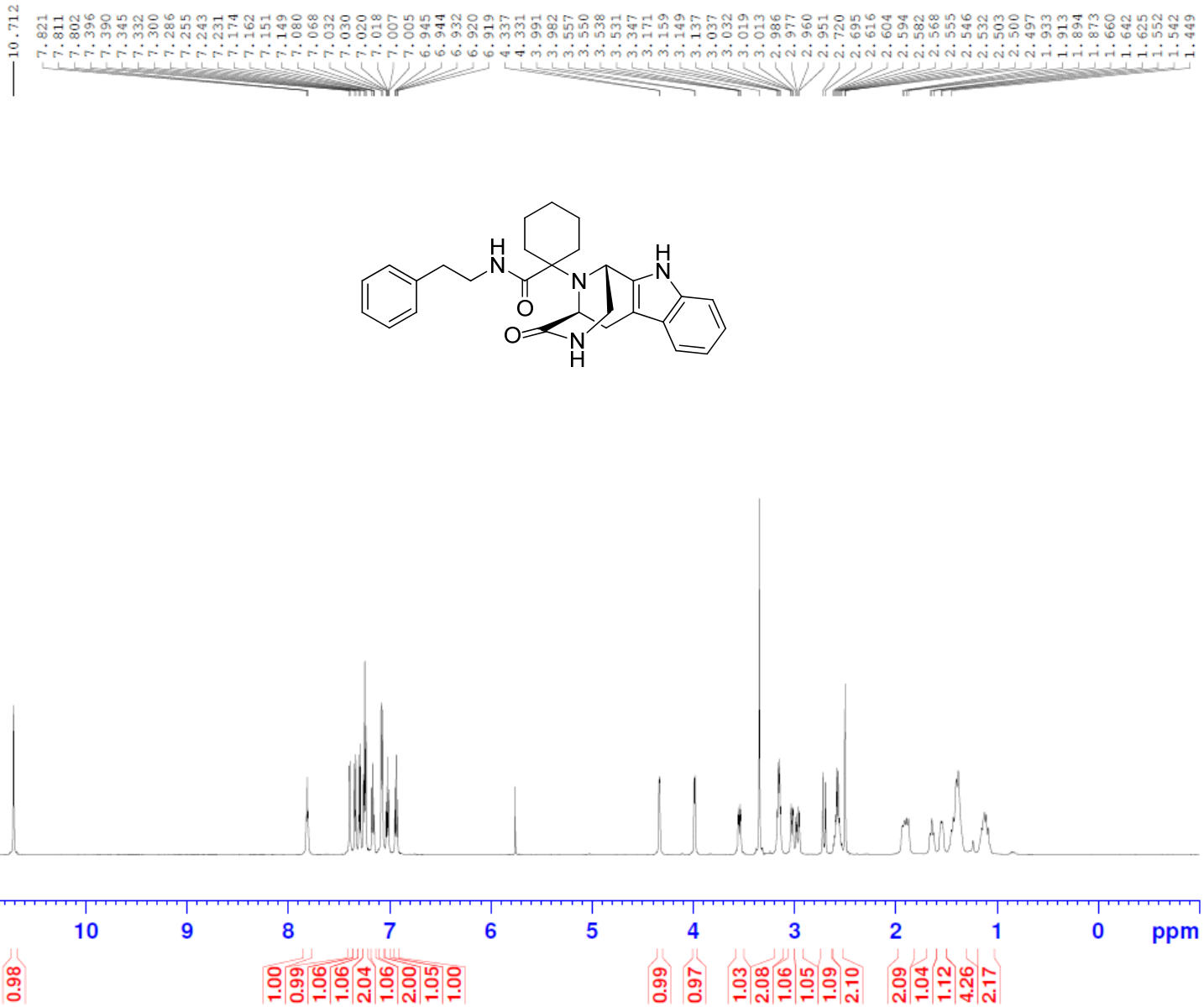
Compound-20


175.38
171.55
139.49
135.43
134.28
128.52
128.34
126.55
126.05
120.77
118.48
117.54
111.19
106.91
68.59
54.64
47.21
46.30
40.48
39.94
39.80
39.66
39.52
39.38
39.24
39.10
35.26
35.14
32.49
29.47
29.35
24.76
23.84
23.03
H
N
O
N
O
N
H
H
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

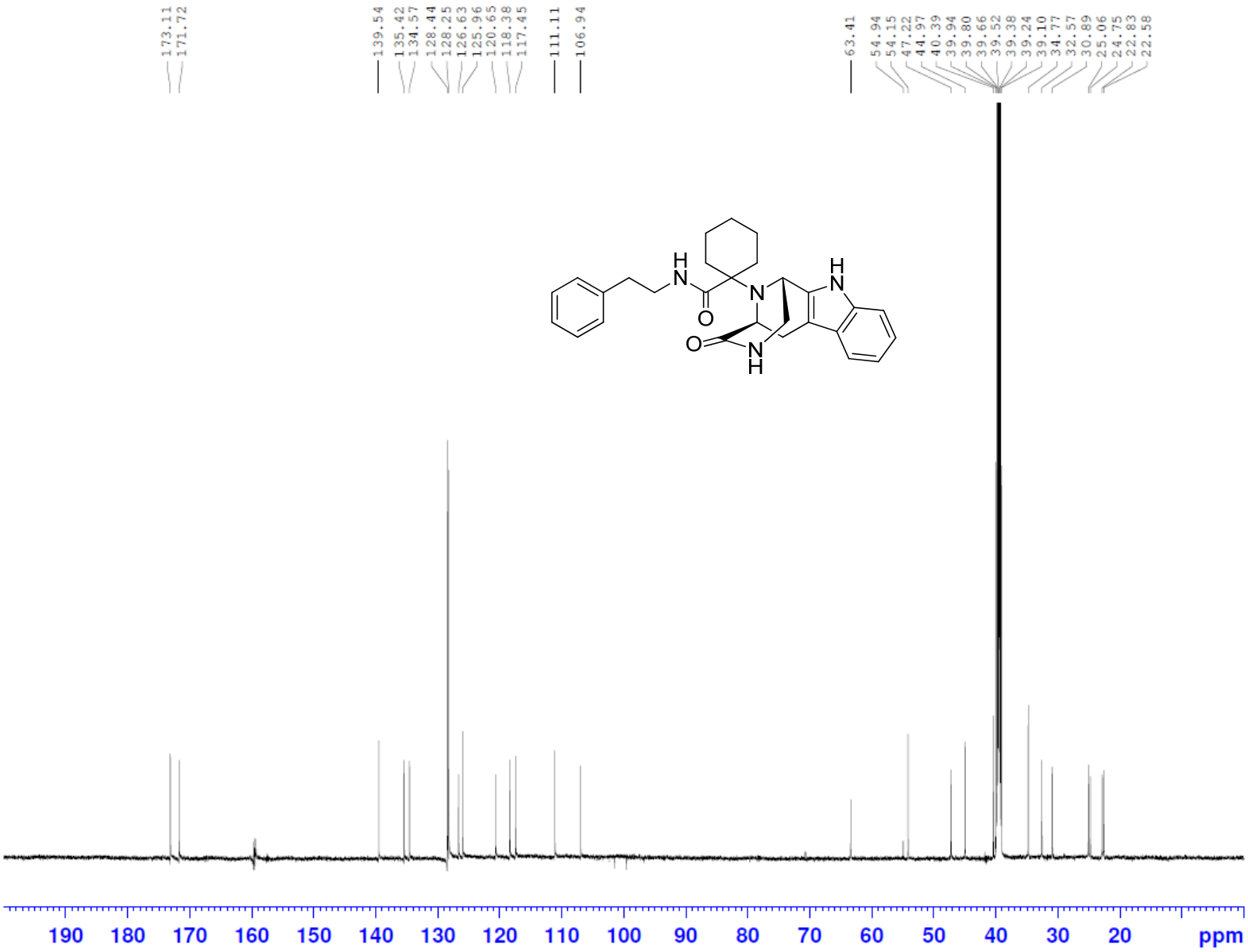
Compound-20


1: Scan AP+
TIC
3.64e7
4.19;471.25
1: Scan AP+
1.83e7
471.28
472.26
322.19
473.24
320.20
340.19
350.02
429.21
469.22
474.29
513.18
579.24
599.68
661.43
244.09
m/z
Time
Chemical Formula: $C_{29}H_{34}N_4O_2$
Molecular Weight: 470.61

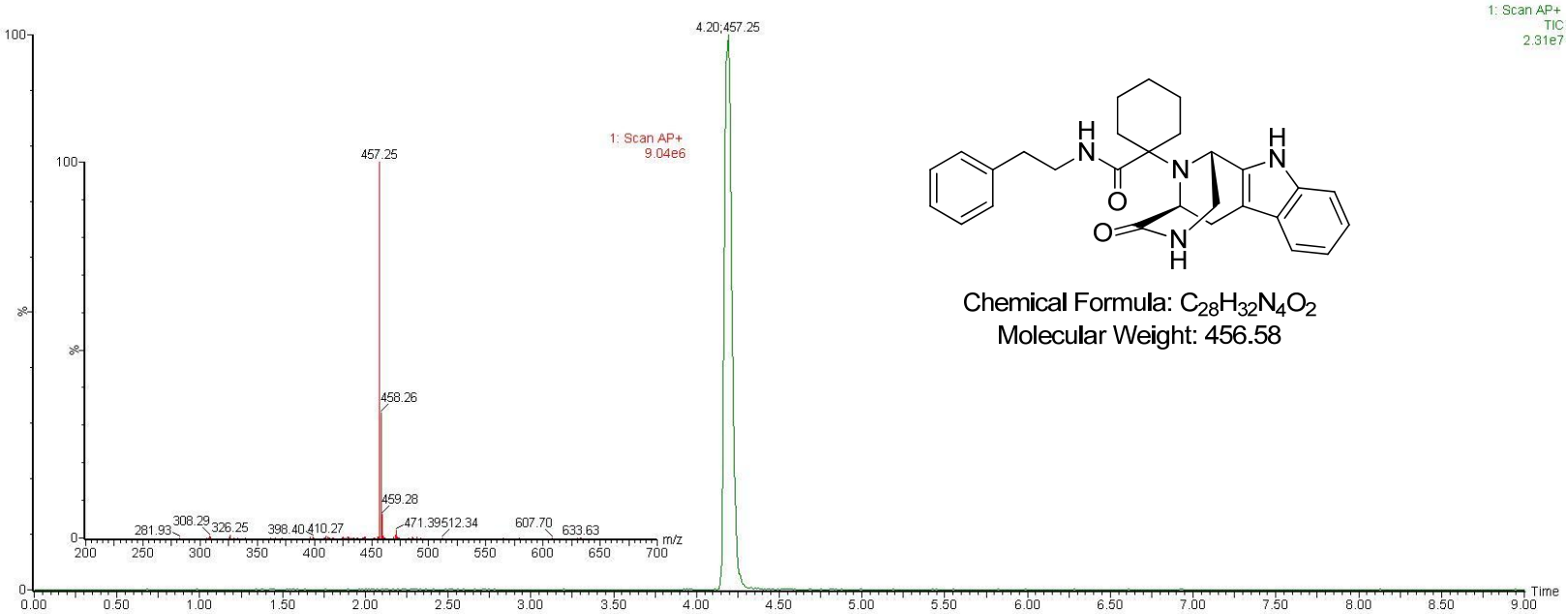
Compound-21


10.712
7.821
7.811
7.802
7.396
7.390
7.345
7.332
7.300
7.286
7.255
7.243
7.231
7.174
7.162
7.151
7.149
7.080
7.068
7.032
7.030
7.020
7.018
7.007
7.005
6.945
6.944
6.932
6.920
6.919
4.337
4.331
3.991
3.982
3.557
3.550
3.538
3.531
3.347
3.171
3.159
3.149
3.137
3.037
3.032
3.019
3.013
2.986
2.977
2.960
2.951
2.720
2.695
2.616
2.604
2.594
2.582
2.568
2.555
2.546
2.532
2.503
2.500
2.497
1.933
1.913
1.894
1.873
1.660
1.642
1.625
1.552
1.542
1.449
H
N
O
N
O
N
H
H
N
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
1.00
0.99
1.06
1.06
2.04
1.06
2.00
1.05
1.00
0.99
0.97
1.03
2.08
1.06
1.05
1.09
2.10
2.09
1.04
1.12
4.26
2.17

Compound-21

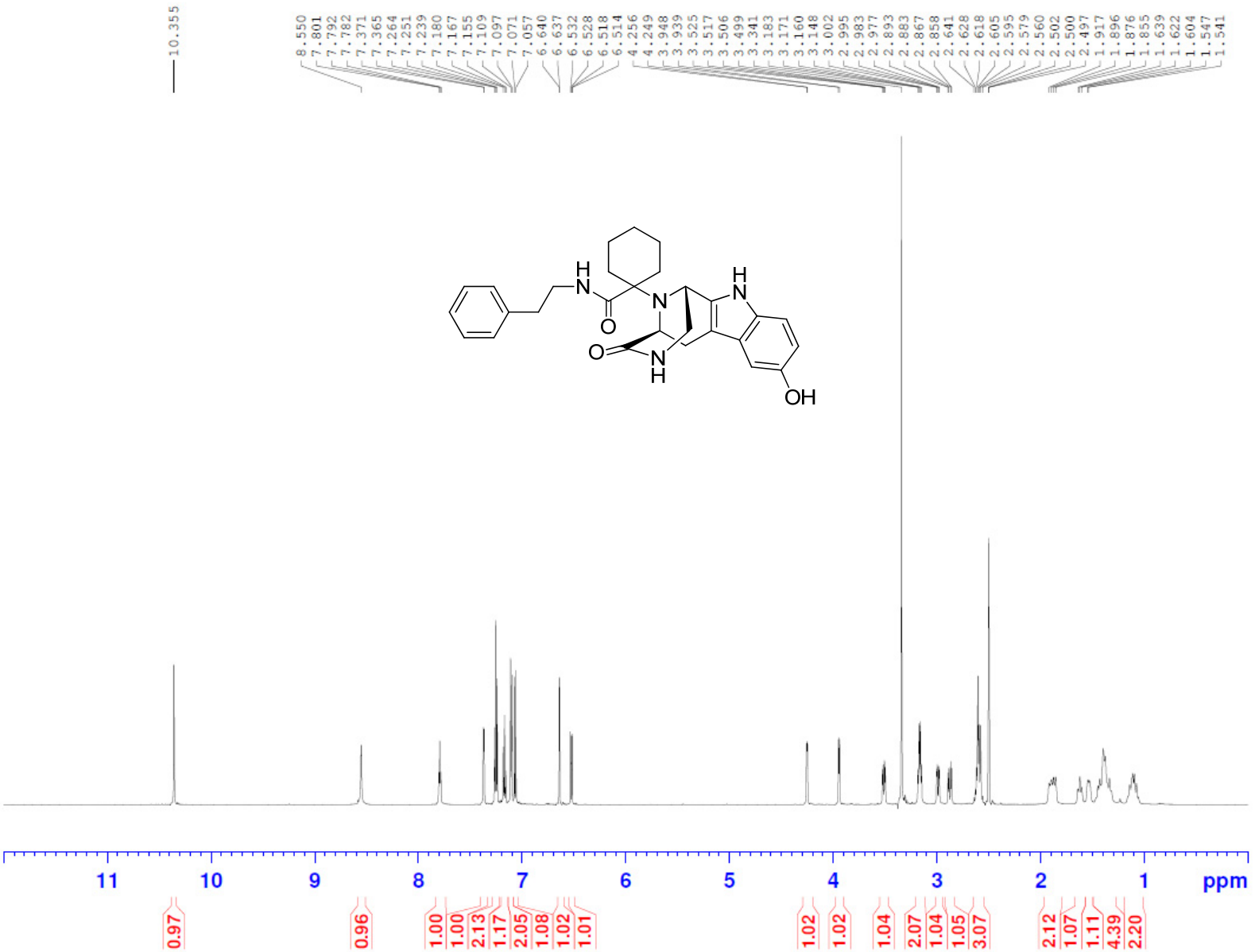

173.11
171.72
139.54
135.42
134.57
128.44
128.25
126.63
125.96
120.65
118.38
117.45
111.11
106.94
63.41
54.94
54.15
47.22
44.97
40.39
39.94
39.80
39.66
39.52
39.38
39.24
39.10
34.77
32.57
30.89
25.06
24.75
22.83
22.58
H
N
O
N
H
O
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

Compound-21

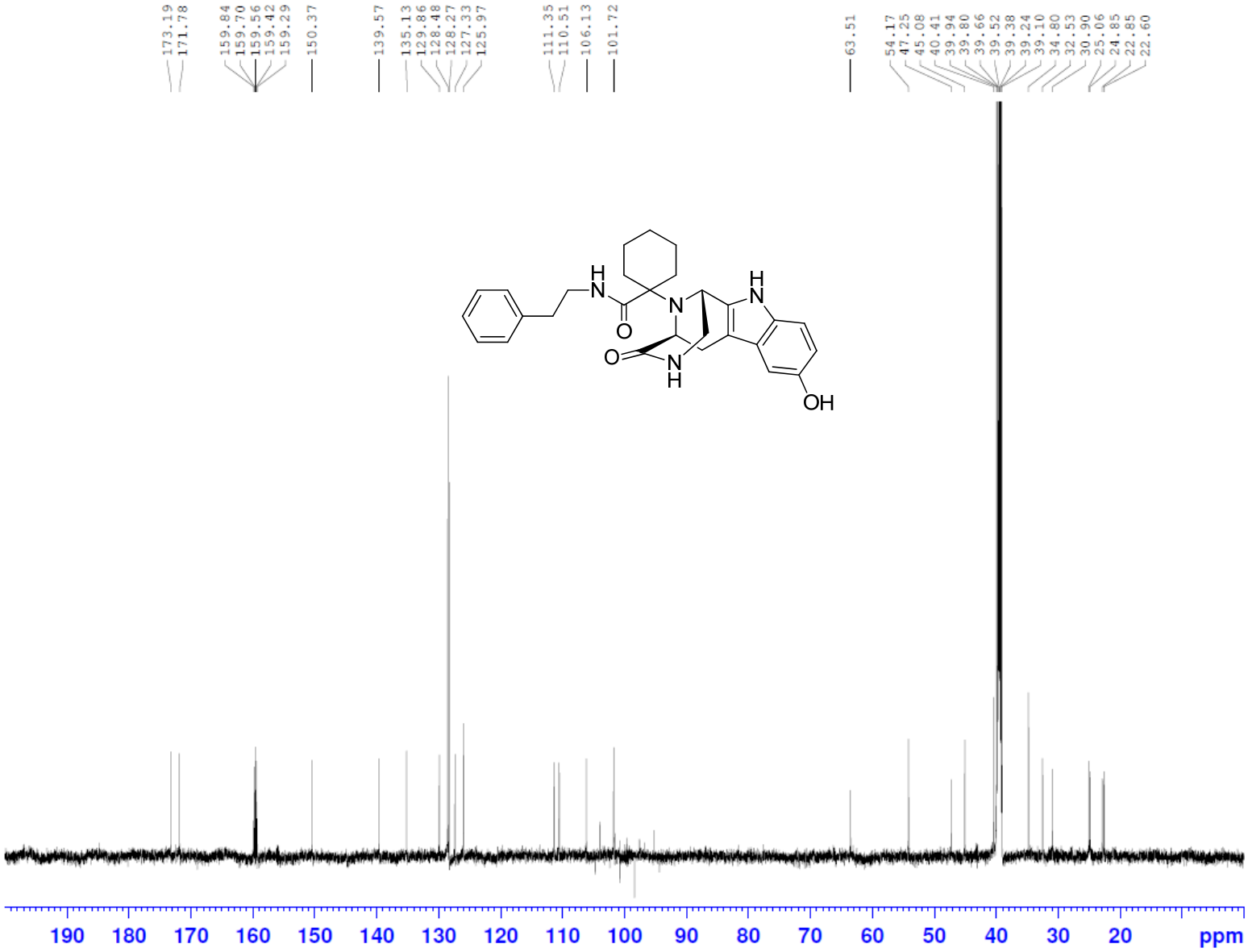


Chemical Formula: $C_{28}H_{32}N_4O_2$
Molecular Weight: 456.58

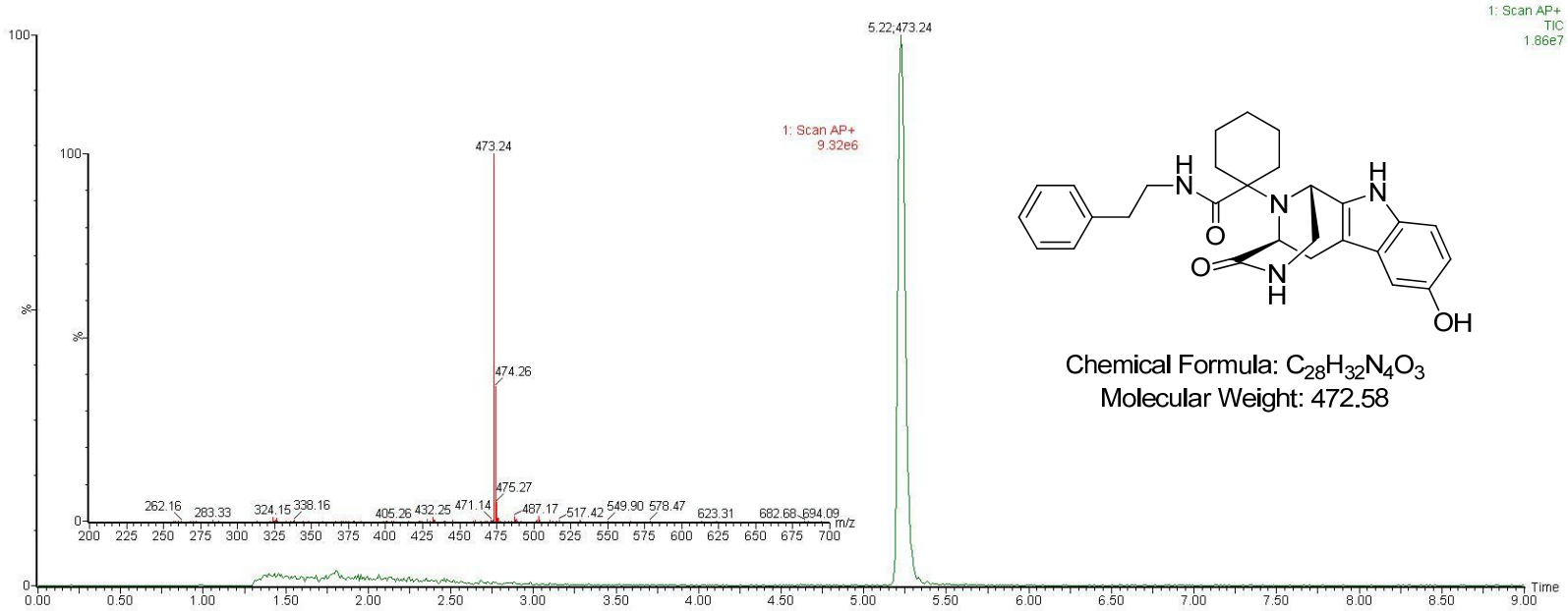
Compound-22


10.355
8.550
7.801
7.792
7.782
7.371
7.365
7.264
7.251
7.239
7.180
7.167
7.155
7.109
7.097
7.071
7.057
6.640
6.637
6.532
6.528
6.518
6.514
4.256
4.249
3.948
3.939
3.525
3.517
3.506
3.499
3.341
3.183
3.171
3.160
3.148
3.002
2.995
2.983
2.977
2.893
2.883
2.867
2.858
2.641
2.628
2.618
2.605
2.595
2.579
2.560
2.502
2.500
2.497
1.917
1.896
1.876
1.855
1.639
1.622
1.604
1.547
1.541
H
N
O
O
N
H
N
H
OH
11
10
9
8
7
6
5
4
3
2
1
ppm
0.97
0.96
1.00
1.00
2.13
1.17
2.05
1.08
1.02
1.01
1.02
1.02
1.04
2.07
1.04
1.05
3.07
2.12
1.07
1.11
4.39
2.20

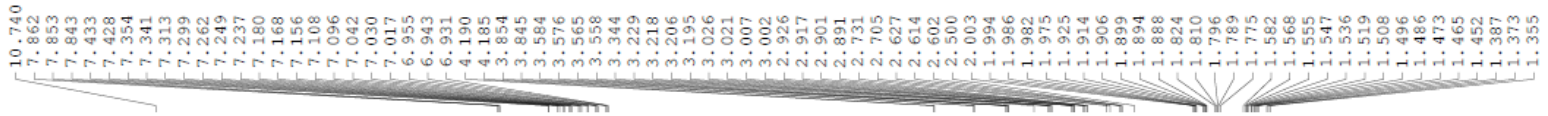
Compound-22

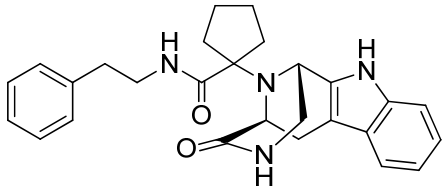

173.19
171.78
159.84
159.70
159.56
159.42
159.29
150.37
139.57
135.13
129.86
128.48
128.27
127.33
125.97
111.35
110.51
106.13
101.72
63.51
54.17
47.25
45.08
40.41
39.94
39.80
39.66
39.52
39.38
39.24
39.10
34.80
32.53
30.90
25.06
24.85
22.85
22.60
H
N
O
N
O
N
H
H
N
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

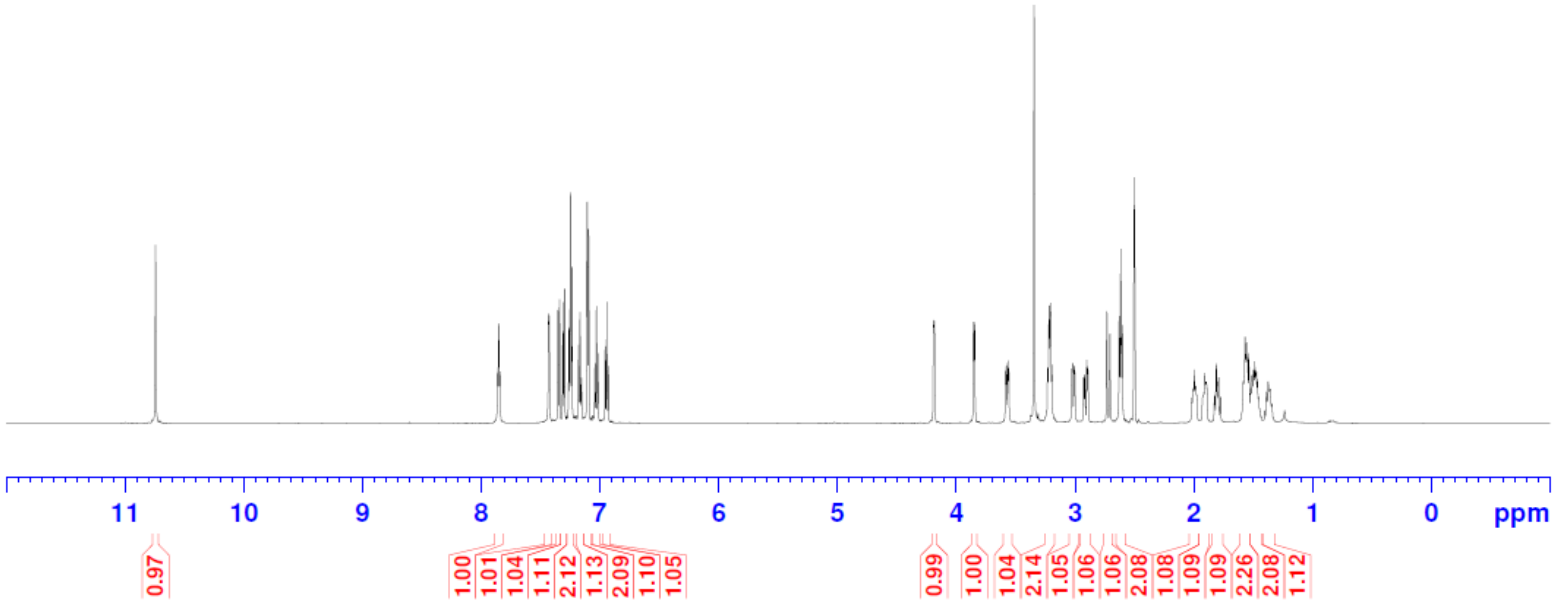
Compound-22


1: Scan AP+
TIC
1.86e7
5.22,473.24
1: Scan AP+
9.32e6
473.24
474.26
475.27
262.16
283.33
324.15
338.16
405.26
432.25
471.14
487.17
517.42
549.90
578.47
623.31
682.68
694.09
m/z
Time
Chemical Formula: C28H32N4O3
Molecular Weight: 472.58

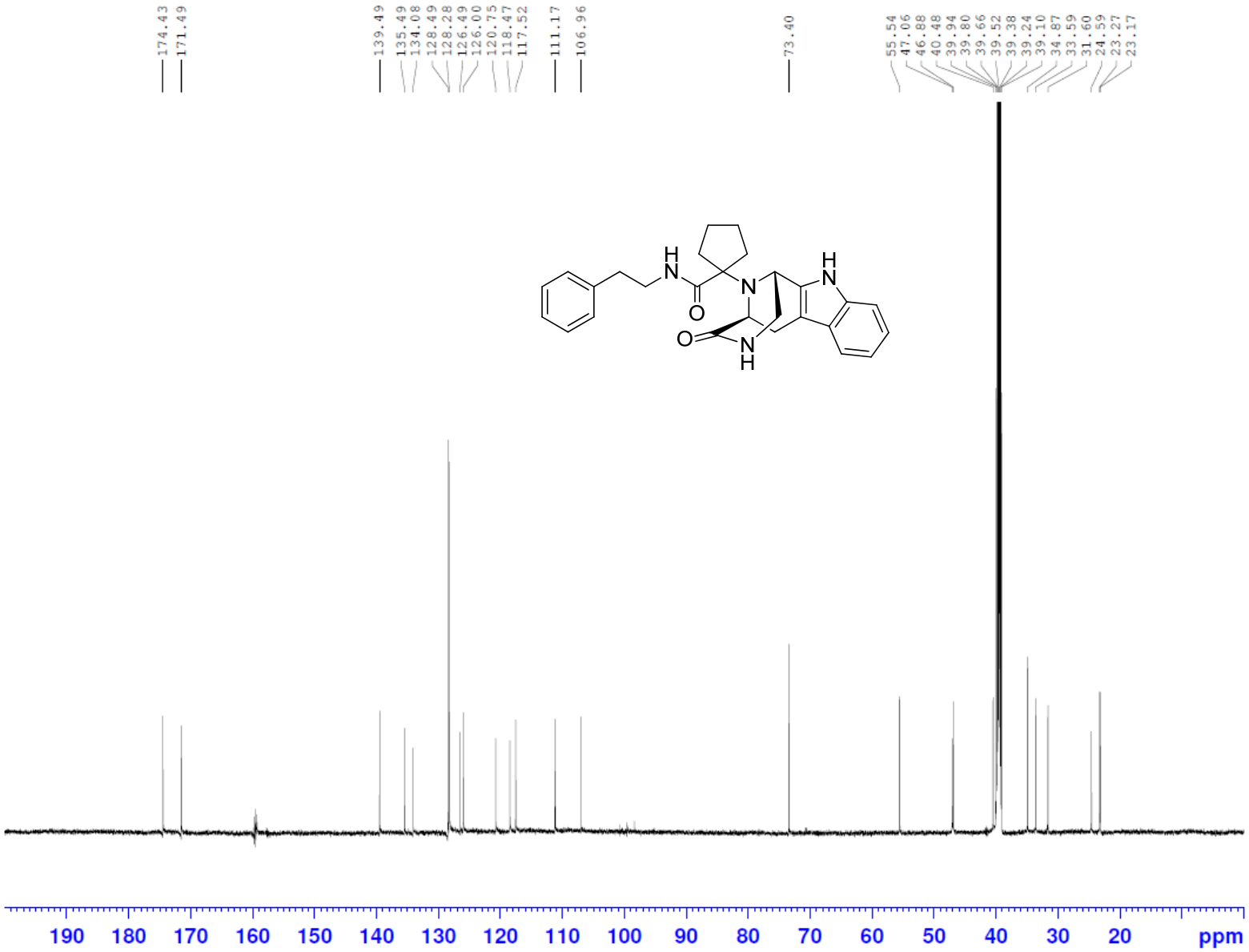
Compound-23


10.740
7.862
7.853
7.843
7.433
7.428
7.354
7.341
7.313
7.299
7.262
7.249
7.237
7.180
7.168
7.156
7.108
7.096
7.042
7.030
7.017
6.955
6.943
6.931
4.190
4.185
3.854
3.845
3.584
3.576
3.565
3.558
3.344
3.229
3.218
3.206
3.195
3.026
3.021
3.007
3.002
2.926
2.917
2.901
2.891
2.731
2.705
2.627
2.614
2.602
2.500
2.003
1.994
1.986
1.982
1.975
1.925
1.914
1.906
1.899
1.894
1.888
1.824
1.810
1.796
1.789
1.775
1.582
1.568
1.555
1.547
1.536
1.519
1.508
1.496
1.486
1.473
1.465
1.452
1.387
1.373
1.355

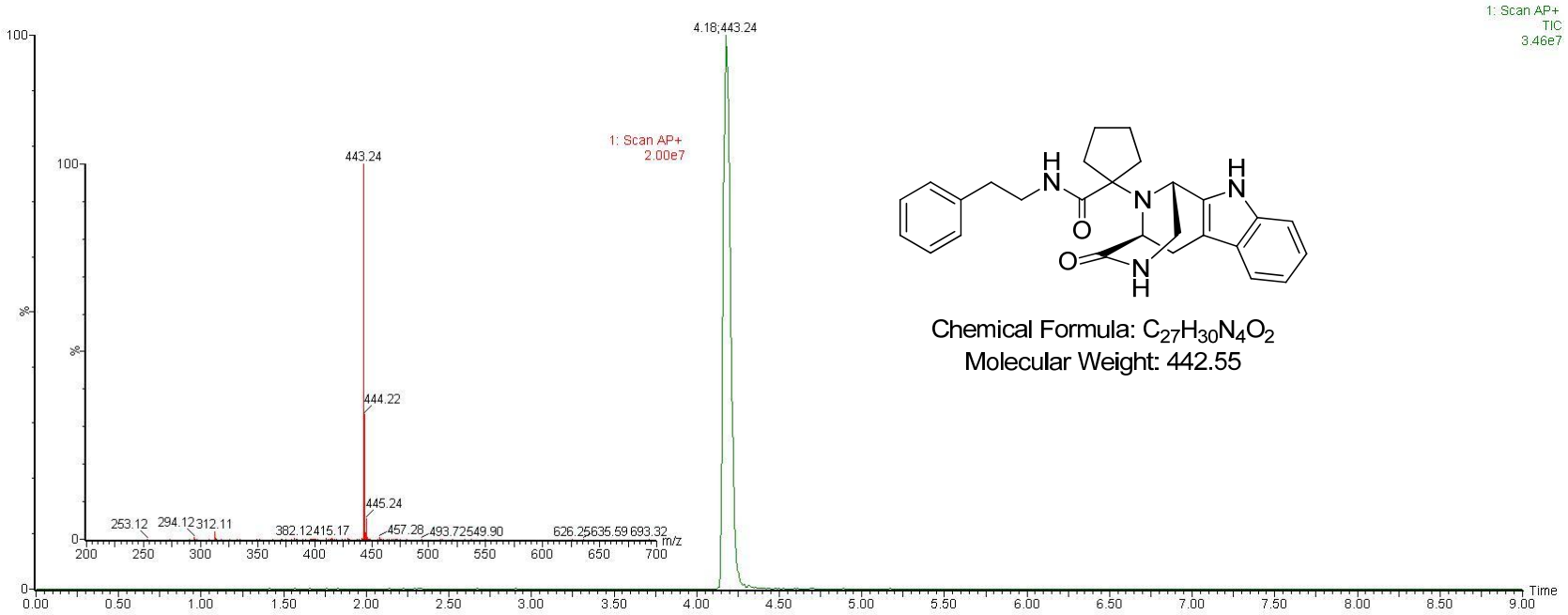

H
N
O
N
O
N
H
H
N


11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.97
1.00
1.01
1.04
1.11
2.12
1.13
2.09
1.10
1.05
0.99
1.00
1.04
2.14
1.05
1.06
1.06
2.08
1.08
1.09
1.09
2.26
2.08
1.12

Compound-23

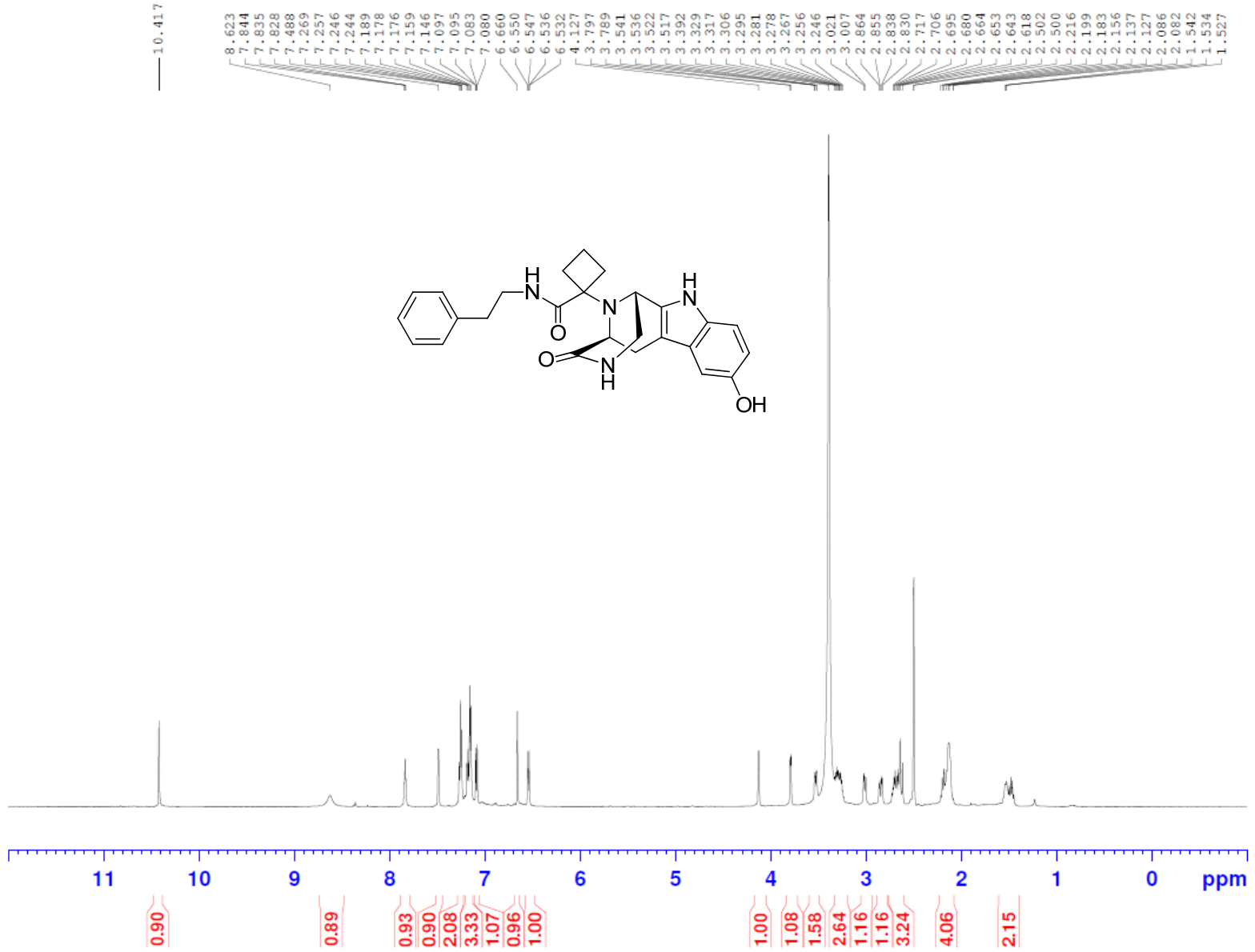

174.43
171.49
139.49
135.49
134.08
128.49
128.28
126.49
126.00
120.75
118.47
117.52
111.17
106.96
73.40
55.54
47.06
46.88
40.48
39.94
39.80
39.66
39.52
39.38
39.24
39.10
34.87
33.59
31.60
24.59
23.27
23.17
H
N
O
N
O
N
H
H
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

Compound-23

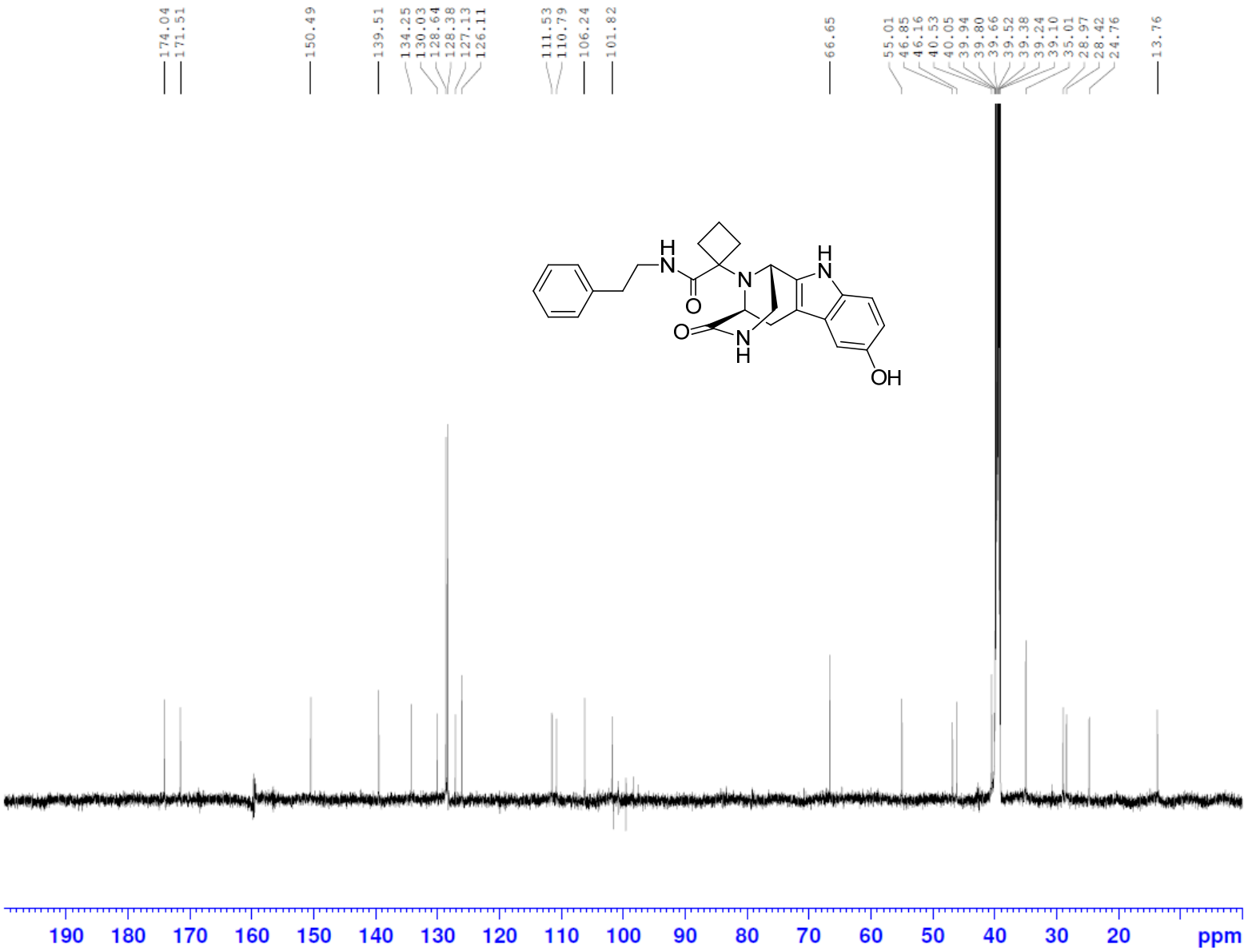


Chemical Formula: $C_{27}H_{30}N_4O_2$
Molecular Weight: 442.55

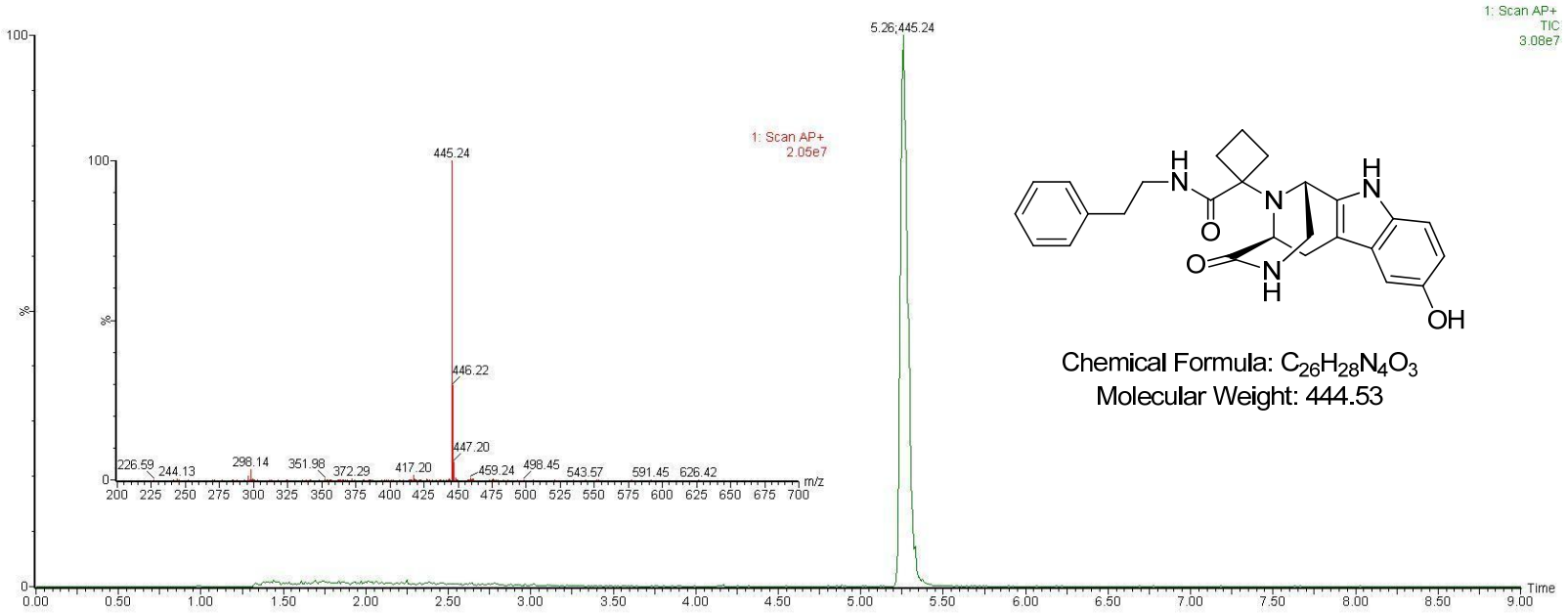
Compound-24


10.417
8.623
7.844
7.835
7.828
7.488
7.269
7.257
7.246
7.244
7.189
7.178
7.176
7.159
7.146
7.097
7.095
7.083
7.080
6.660
6.550
6.547
6.536
6.532
4.127
3.797
3.789
3.541
3.536
3.522
3.517
3.392
3.329
3.317
3.306
3.295
3.281
3.278
3.267
3.256
3.246
3.021
3.007
2.864
2.855
2.838
2.830
2.717
2.706
2.695
2.680
2.664
2.653
2.643
2.618
2.502
2.500
2.216
2.199
2.183
2.156
2.137
2.127
2.086
2.082
1.542
1.534
1.527
H
N
O
O
N
H
N
H
OH
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.90
0.89
0.93
0.90
2.08
3.33
1.07
0.96
1.00
1.00
1.08
1.58
2.64
1.16
1.16
3.24
4.06
2.15

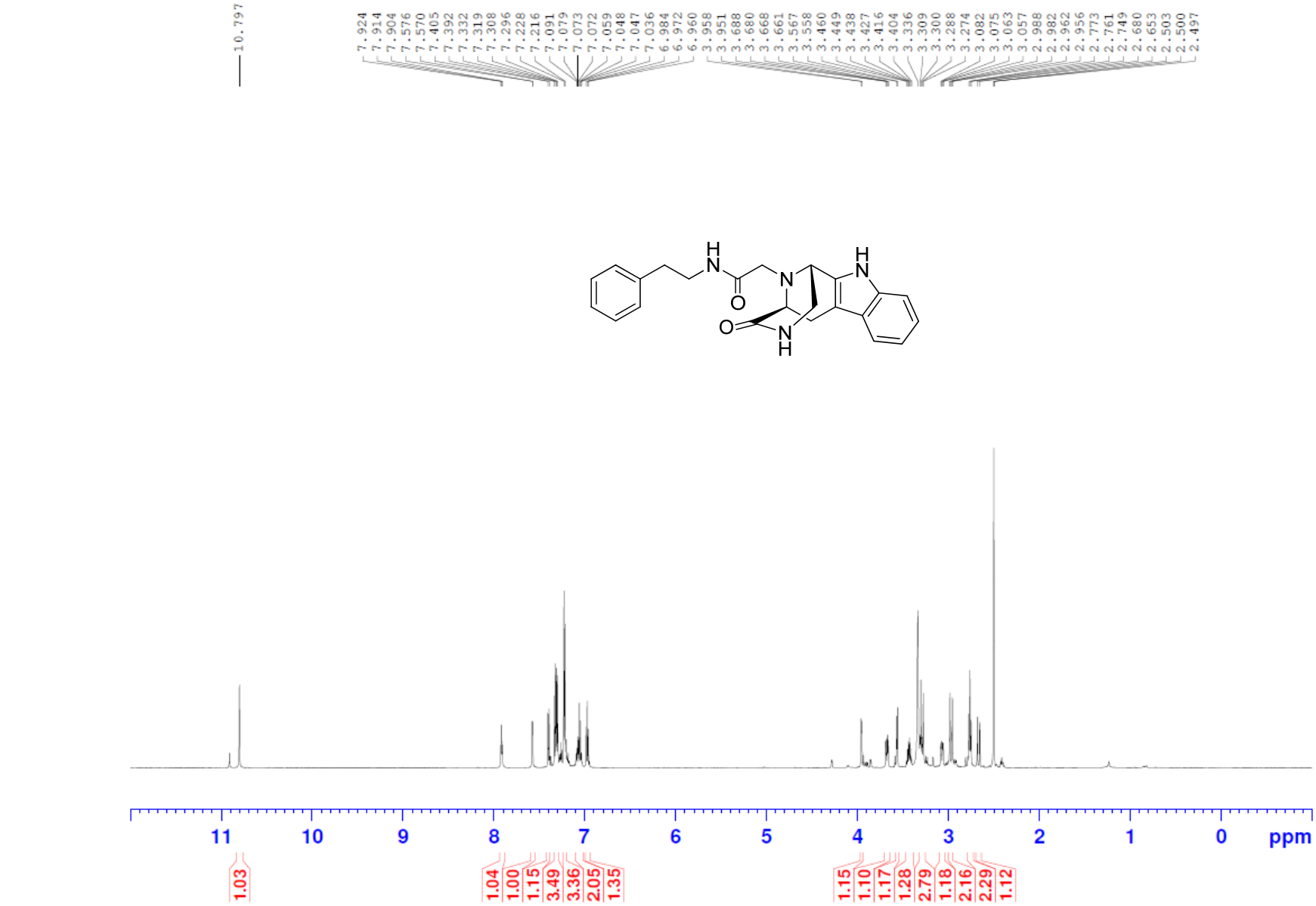
Compound-24


174.04
171.51
150.49
139.51
134.25
130.03
128.64
128.38
127.13
126.11
111.53
110.79
106.24
101.82
66.65
55.01
46.85
46.16
40.53
40.05
39.94
39.80
39.66
39.52
39.38
39.24
39.10
35.01
28.97
28.42
24.76
13.76
H
N
O
N
H
N
H
O
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

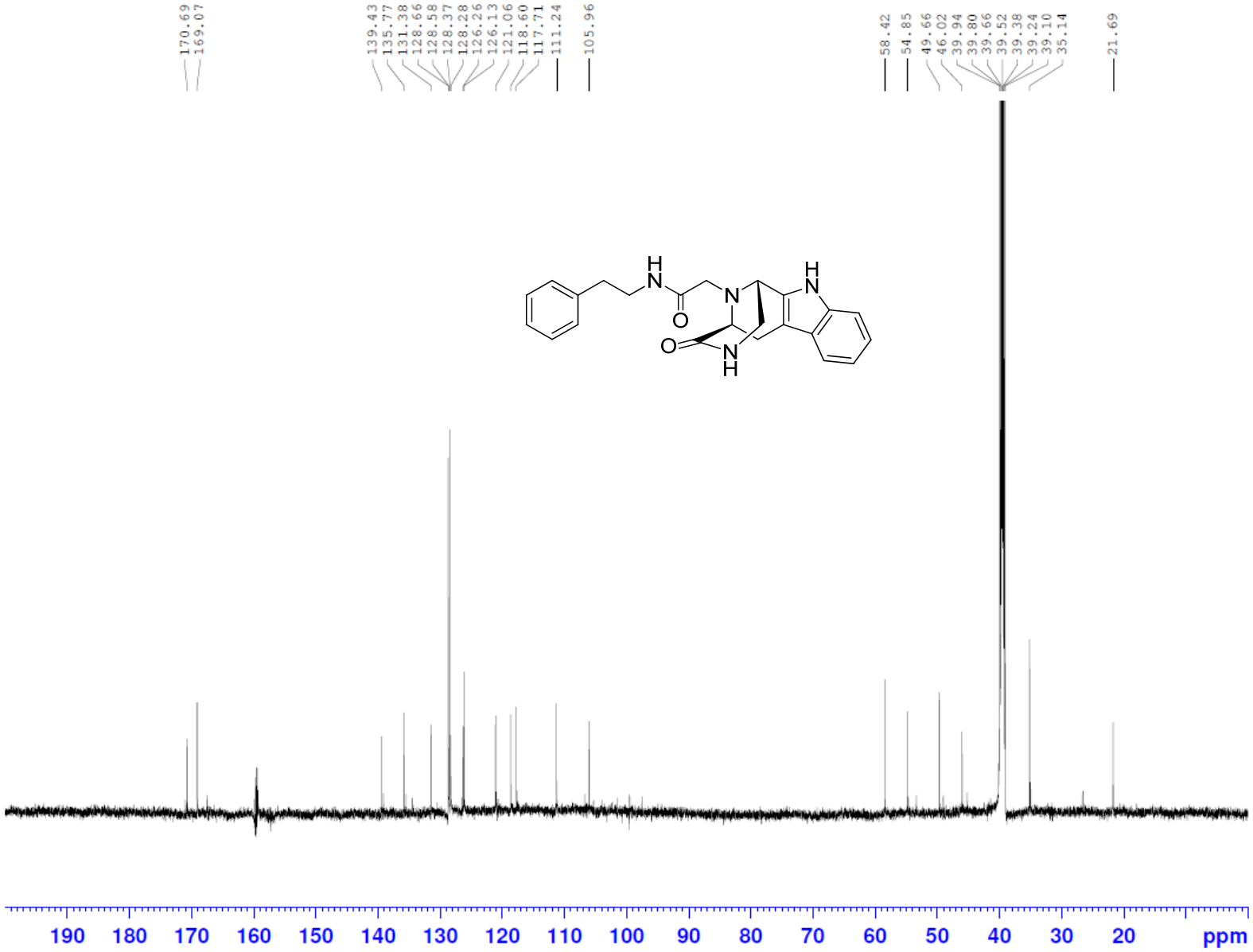
Compound-24


1: Scan AP+
TIC
3.08e7
5.26;445.24
1: Scan AP+
2.05e7
445.24
446.22
447.20
226.59
244.13
298.14
351.98
372.29
417.20
459.24
498.45
543.57
591.45
626.42
m/z
Time
Chemical Formula: C26H28N4O3
Molecular Weight: 444.53

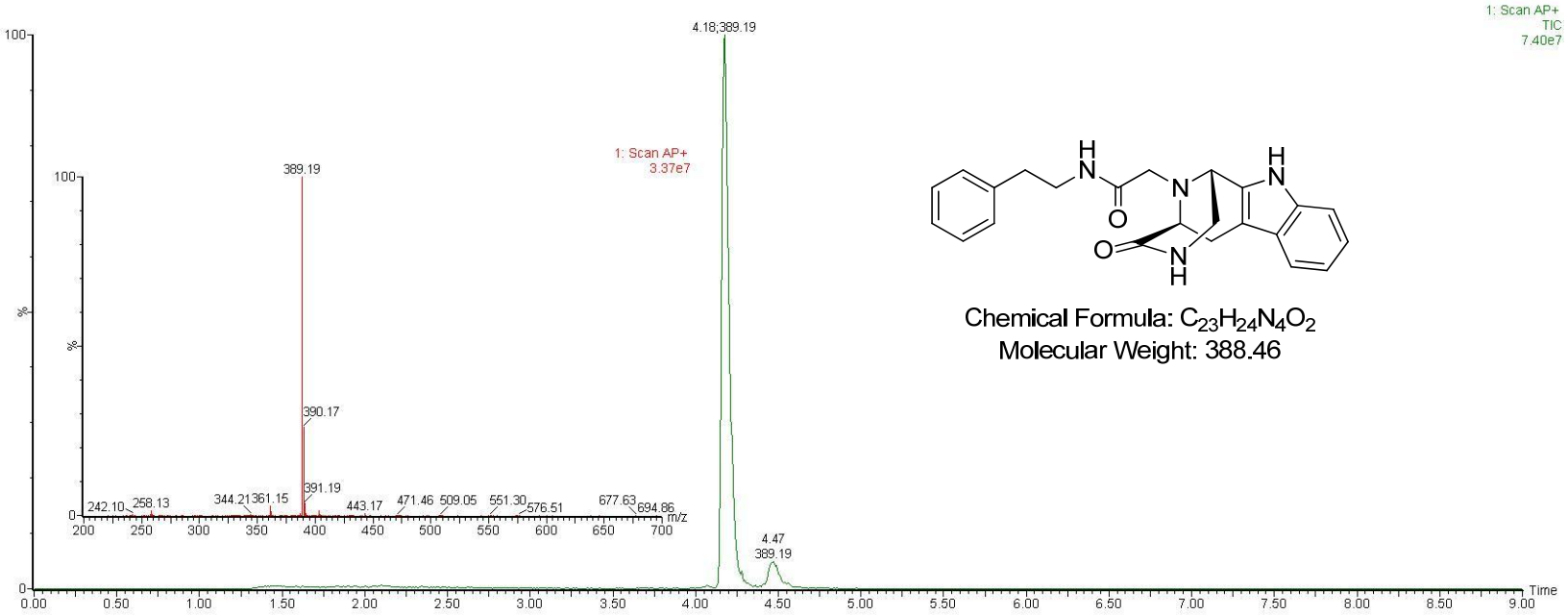
Compound-25


10.797
7.924
7.914
7.904
7.576
7.570
7.405
7.392
7.332
7.319
7.308
7.296
7.228
7.216
7.091
7.079
7.073
7.072
7.059
7.048
7.047
7.036
6.984
6.972
6.960
3.958
3.951
3.688
3.680
3.668
3.661
3.567
3.558
3.460
3.449
3.438
3.427
3.416
3.404
3.336
3.309
3.300
3.288
3.274
3.082
3.075
3.063
3.057
2.988
2.982
2.962
2.956
2.773
2.761
2.749
2.680
2.653
2.503
2.500
2.497
H
N
O
N
O
N
H
N
H
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.03
1.04
1.00
1.15
3.49
3.36
2.05
1.35
1.15
1.10
1.17
1.28
2.79
1.18
2.16
2.29
1.12

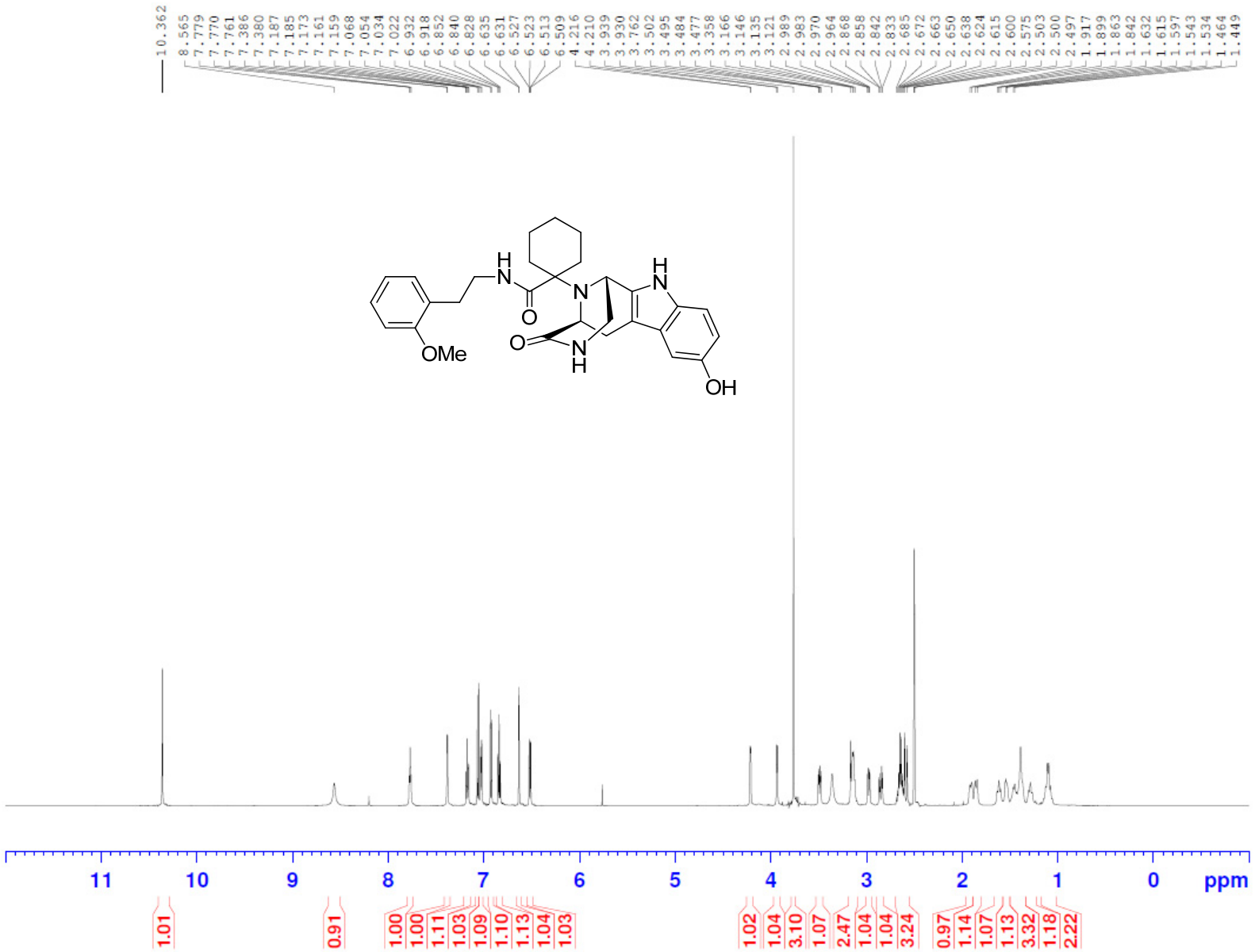
Compound-25


170.69
169.07
139.43
135.77
131.38
128.66
128.58
128.37
128.28
126.26
126.13
121.06
118.60
117.71
111.24
105.96
58.42
54.85
49.66
46.02
39.94
39.80
39.66
39.52
39.38
39.24
39.10
35.14
21.69
H
N
O
N
O
N
H
H
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

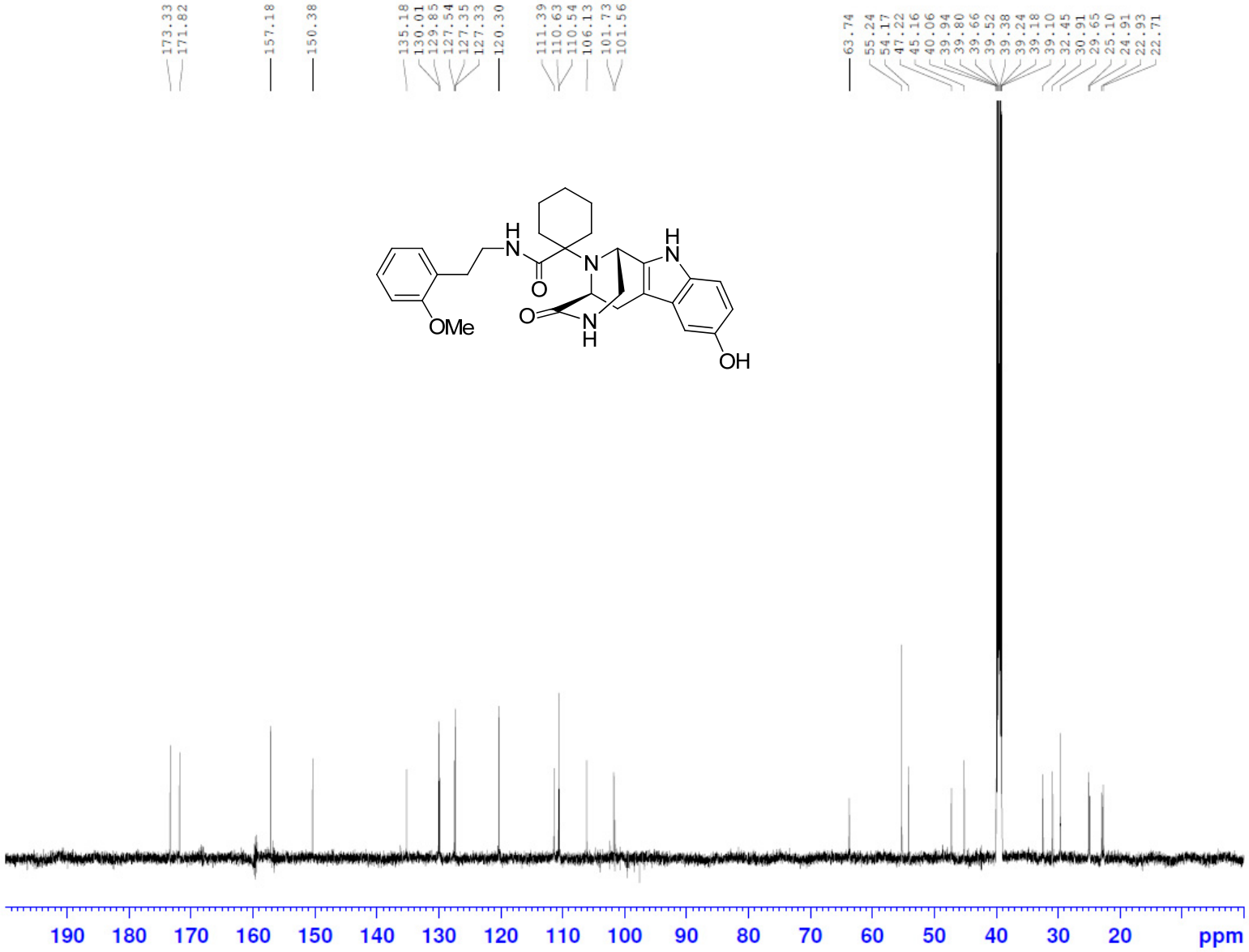
Compound-25


1: Scan AP+
TIC
7.40e7
4.18;389.19
1: Scan AP+
3.37e7
389.19
390.17
391.19
242.10
258.13
344.21
361.15
443.17
471.46
509.05
551.30
576.51
677.63
694.86
m/z
4.47
389.19
Time
%
Chemical Formula: $C_{23}H_{24}N_4O_2$
Molecular Weight: 388.46

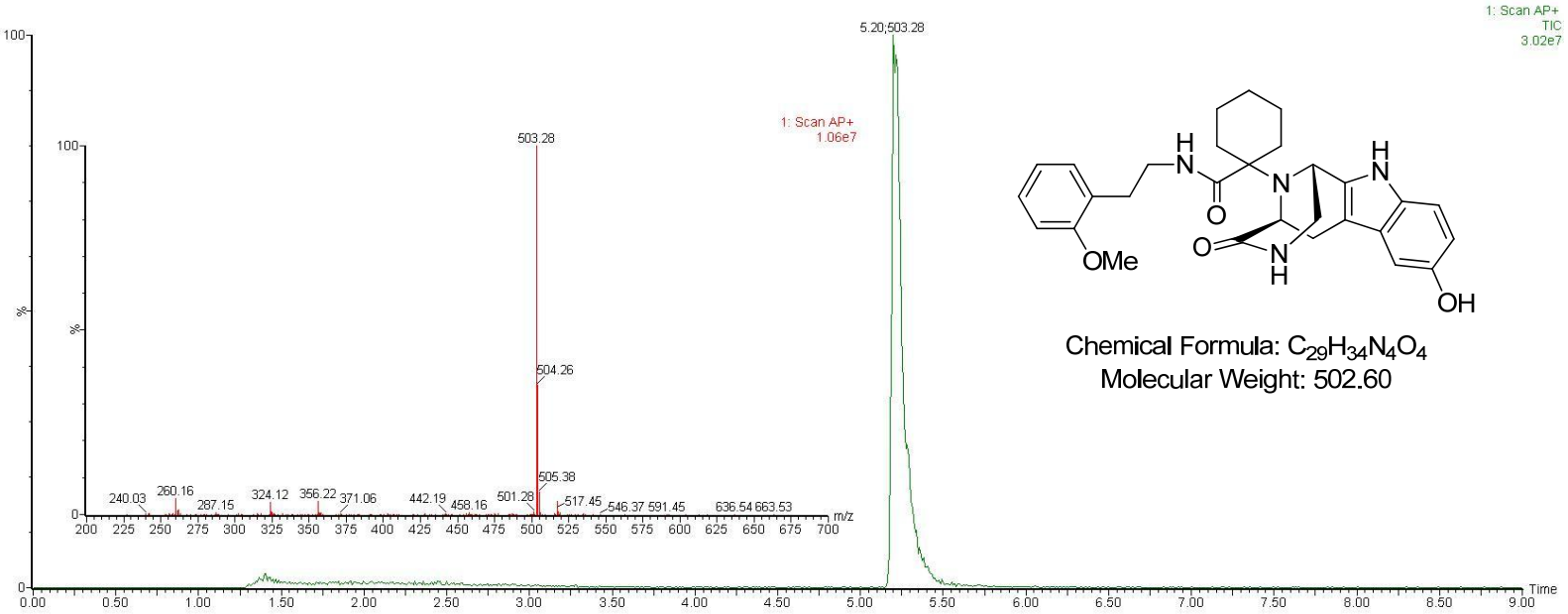
Compound-26


10.362
8.565
7.779
7.770
7.761
7.386
7.380
7.187
7.185
7.173
7.161
7.159
7.068
7.054
7.034
7.022
6.932
6.918
6.852
6.840
6.828
6.635
6.631
6.527
6.523
6.513
6.509
4.216
4.210
3.939
3.930
3.762
3.502
3.495
3.484
3.477
3.358
3.166
3.146
3.135
3.121
2.989
2.983
2.970
2.964
2.868
2.858
2.842
2.833
2.685
2.672
2.663
2.650
2.638
2.624
2.615
2.600
2.575
2.503
2.500
2.497
1.917
1.899
1.863
1.842
1.632
1.615
1.597
1.543
1.534
1.464
1.449
H
N
O
O
N
H
N
H
OMe
OH
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.01
0.91
1.00
1.00
1.11
1.03
1.09
1.10
1.13
1.04
1.03
1.02
1.04
3.10
1.07
2.47
1.04
1.04
3.24
0.97
1.14
1.07
1.13
3.32
1.18
2.22

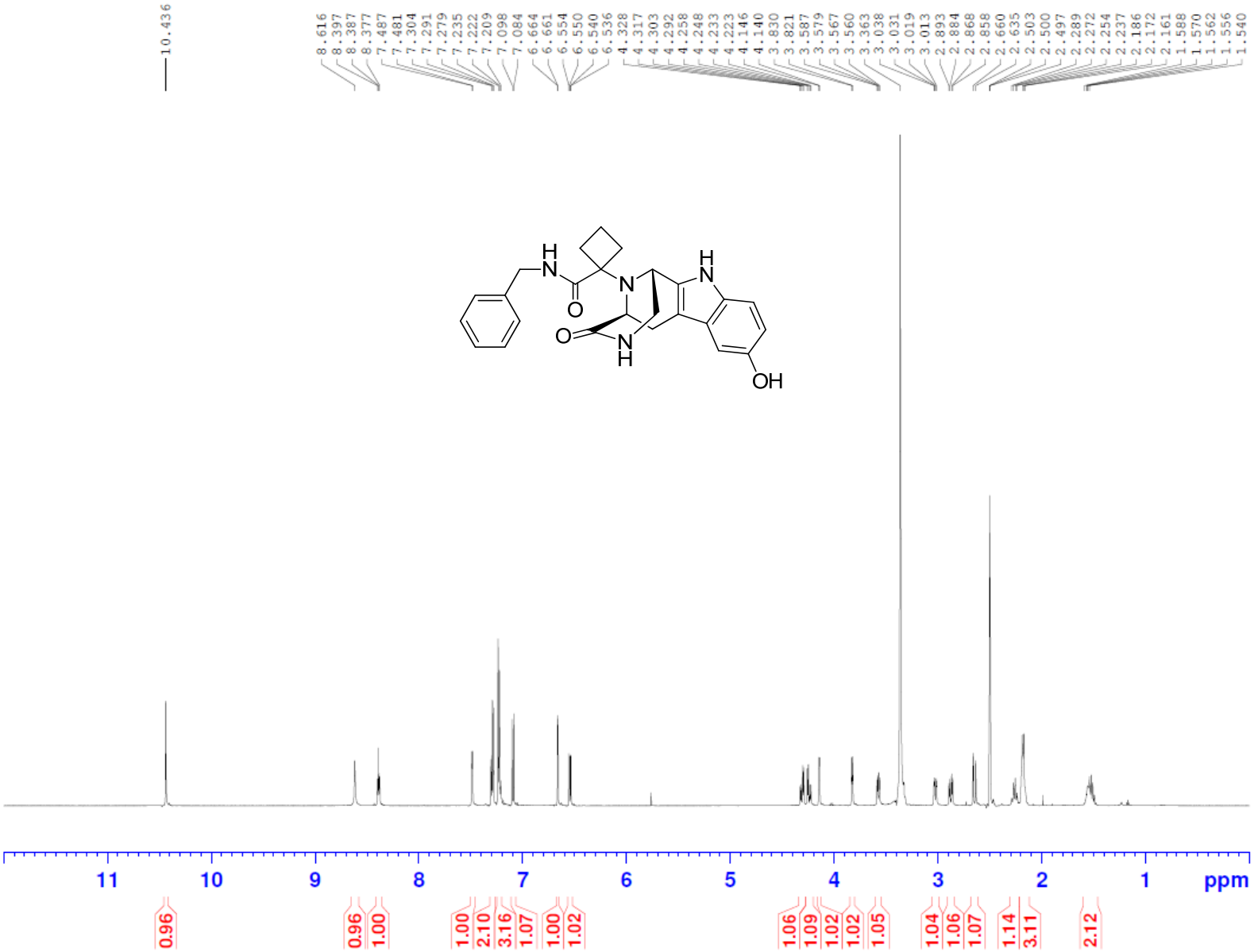
Compound-26


173.33
171.82
157.18
150.38
135.18
130.01
129.85
127.54
127.35
127.33
120.30
111.39
110.63
110.54
106.13
101.73
101.56
63.74
55.24
54.17
47.22
45.16
40.06
39.94
39.80
39.66
39.52
39.38
39.24
39.18
39.10
32.45
30.91
29.65
25.10
24.91
22.93
22.71
H
N
O
N
O
N
H
H
N
OMe
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

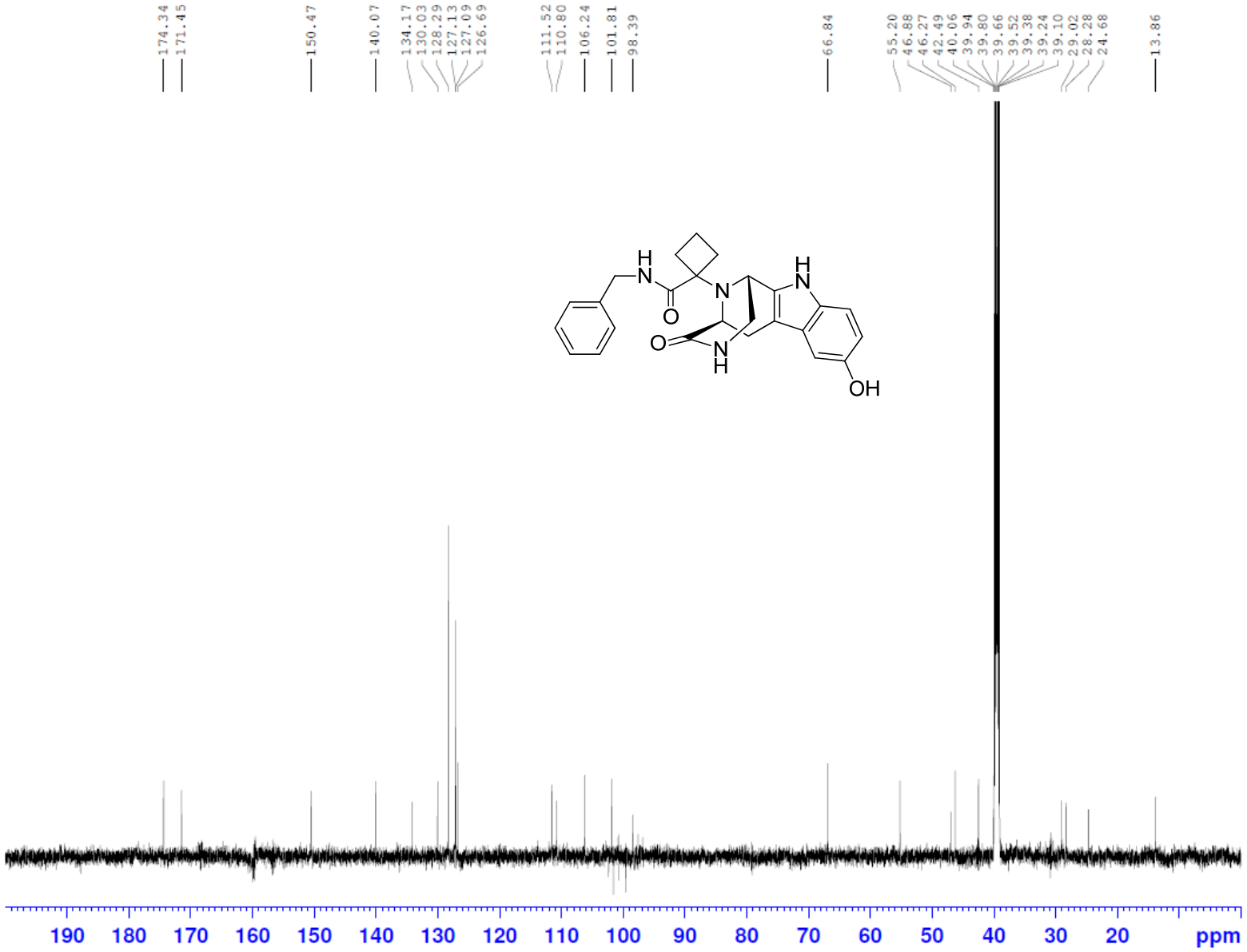
Compound-26


1: Scan AP+
TIC
3.02e7
5.20;503.28
1: Scan AP+
1.06e7
503.28
504.26
505.38
240.03
260.16
287.15
324.12
356.22
371.06
442.19
458.16
501.28
517.45
546.37
591.45
636.54
663.53
m/z
Time
OMe
OH
Chemical Formula: C29H34N4O4
Molecular Weight: 502.60

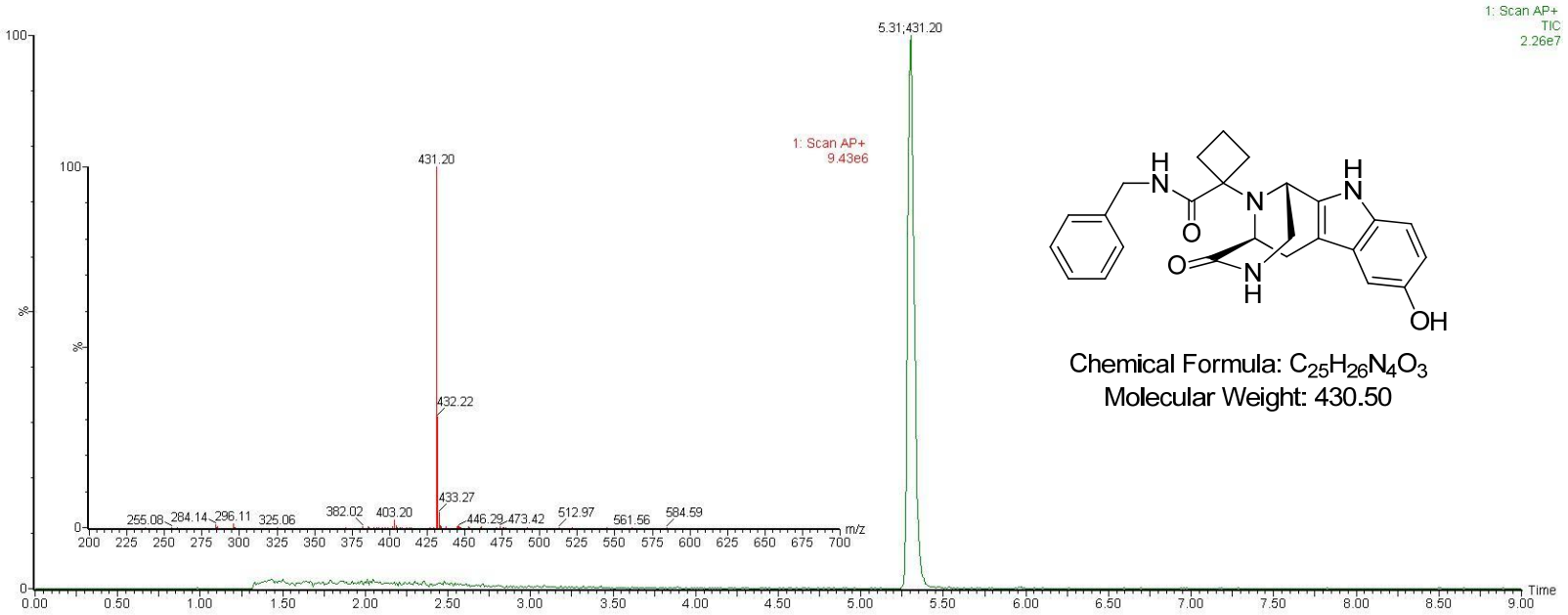
Compound-27


10.436
8.616
8.397
8.387
8.377
7.487
7.481
7.304
7.291
7.279
7.235
7.222
7.209
7.098
7.084
6.664
6.661
6.554
6.550
6.540
6.536
4.328
4.317
4.303
4.292
4.258
4.248
4.233
4.223
4.146
4.140
3.830
3.821
3.587
3.579
3.567
3.560
3.363
3.038
3.031
3.019
3.013
2.893
2.884
2.868
2.858
2.660
2.635
2.503
2.500
2.497
2.289
2.272
2.254
2.237
2.186
2.172
2.161
1.588
1.570
1.562
1.556
1.540
H
N
O
N
O
N
H
H
N
OH
11
10
9
8
7
6
5
4
3
2
1
ppm
0.96
0.96
1.00
1.00
2.10
3.16
1.07
1.00
1.02
1.06
1.09
1.02
1.02
1.05
1.04
1.06
1.07
1.14
3.11
2.12

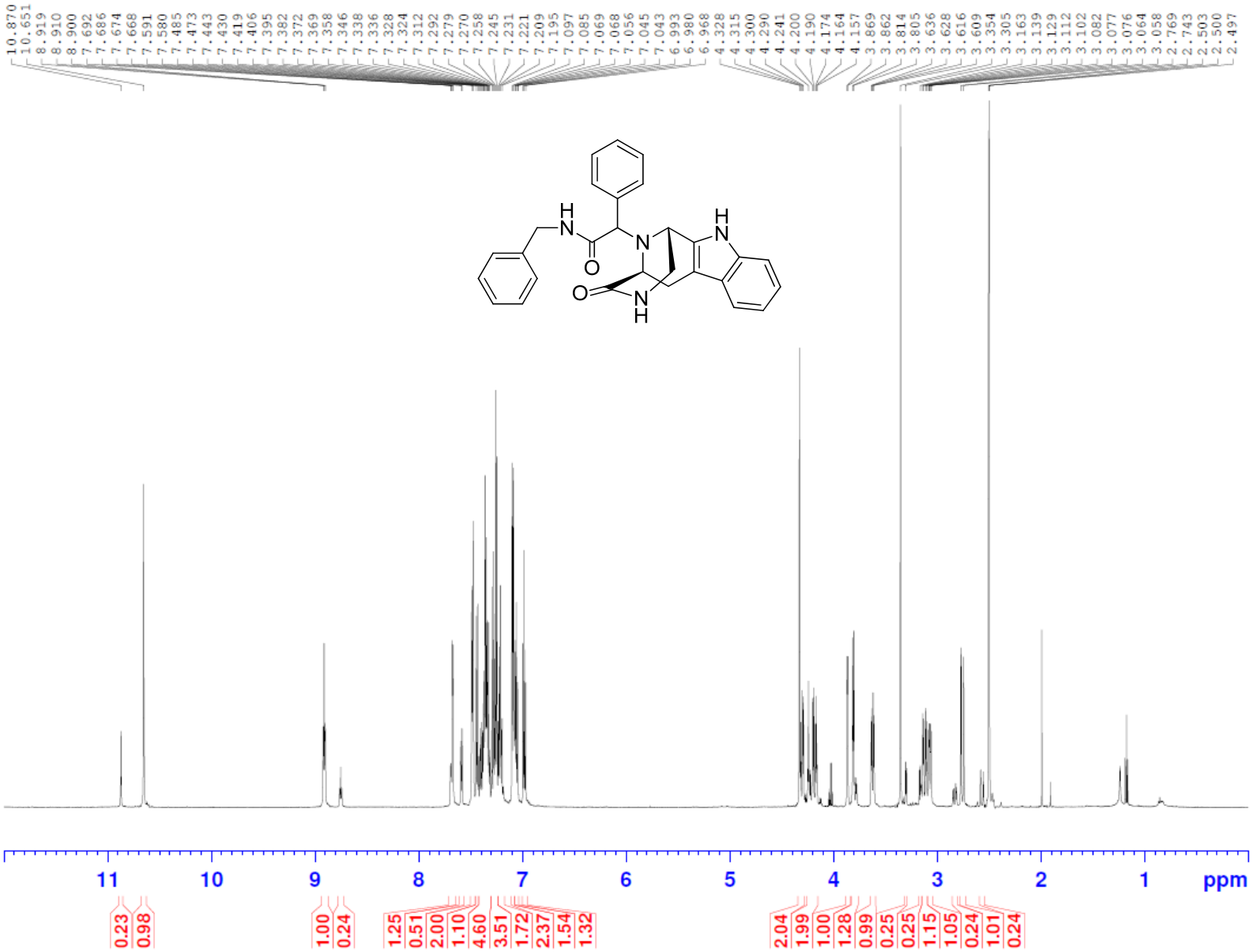
Compound-27


174.34
171.45
150.47
140.07
134.17
130.03
128.29
127.13
127.09
126.69
111.52
110.80
106.24
101.81
98.39
66.84
55.20
46.88
46.27
42.49
40.06
39.94
39.80
39.66
39.52
39.38
39.24
39.10
29.02
28.28
24.68
13.86
H
N
O
N
O
N
H
H
N
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

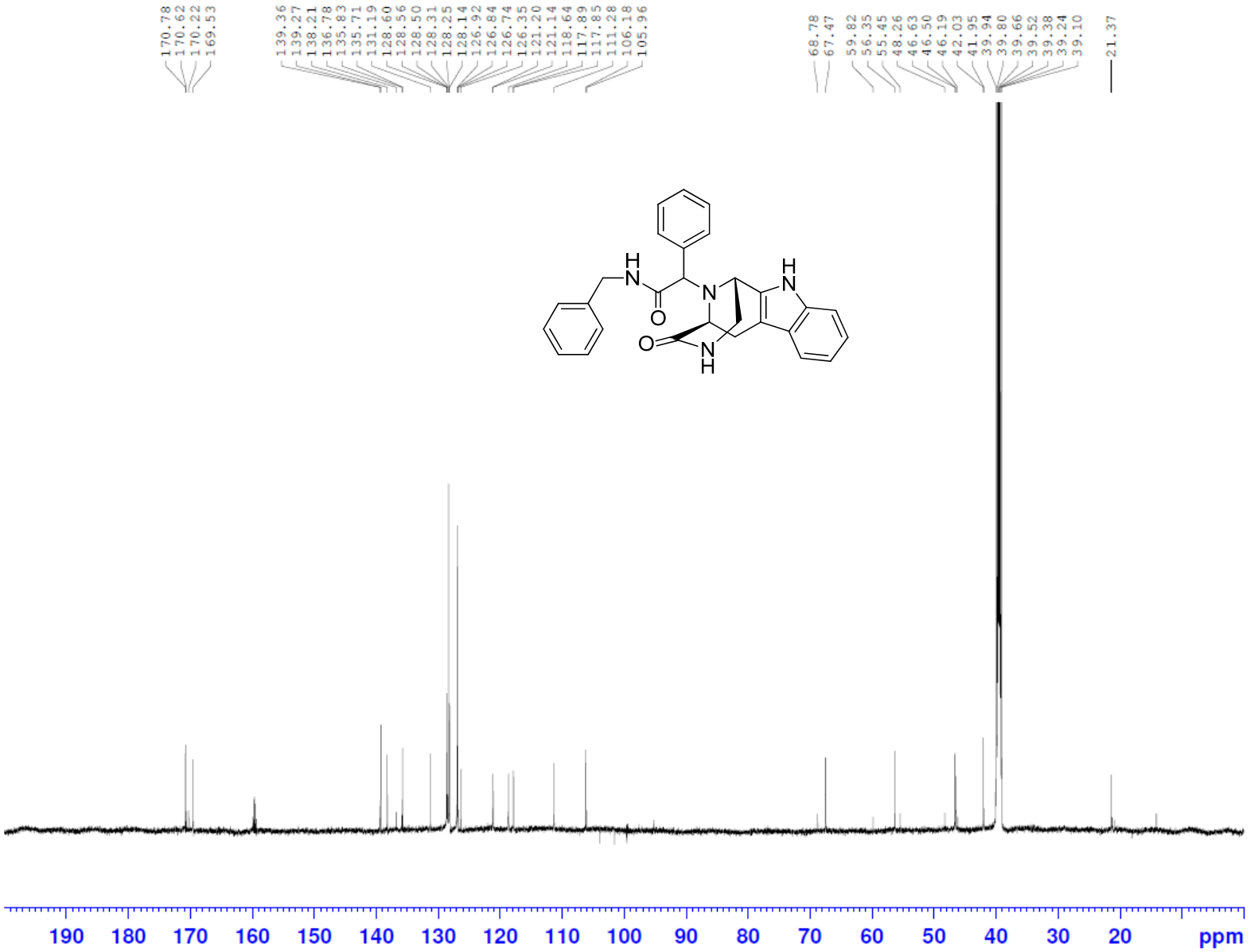
Compound-27

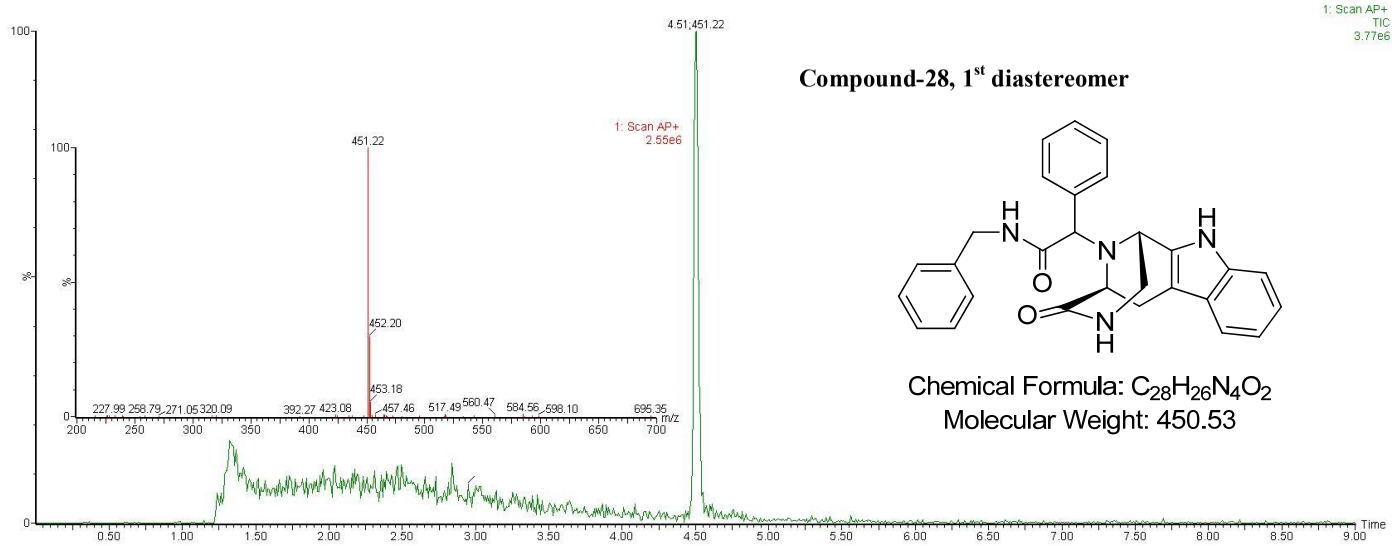

1: Scan AP+
TIC
2.26e7
5.31;431.20
1: Scan AP+
9.43e6
431.20
432.22
433.27
255.08
284.14
296.11
325.06
382.02
403.20
446.29
473.42
512.97
561.56
584.59
m/z
Time
Chemical Formula: C25H26N4O3
Molecular Weight: 430.50

Compound-28, mixture of both diastereomers



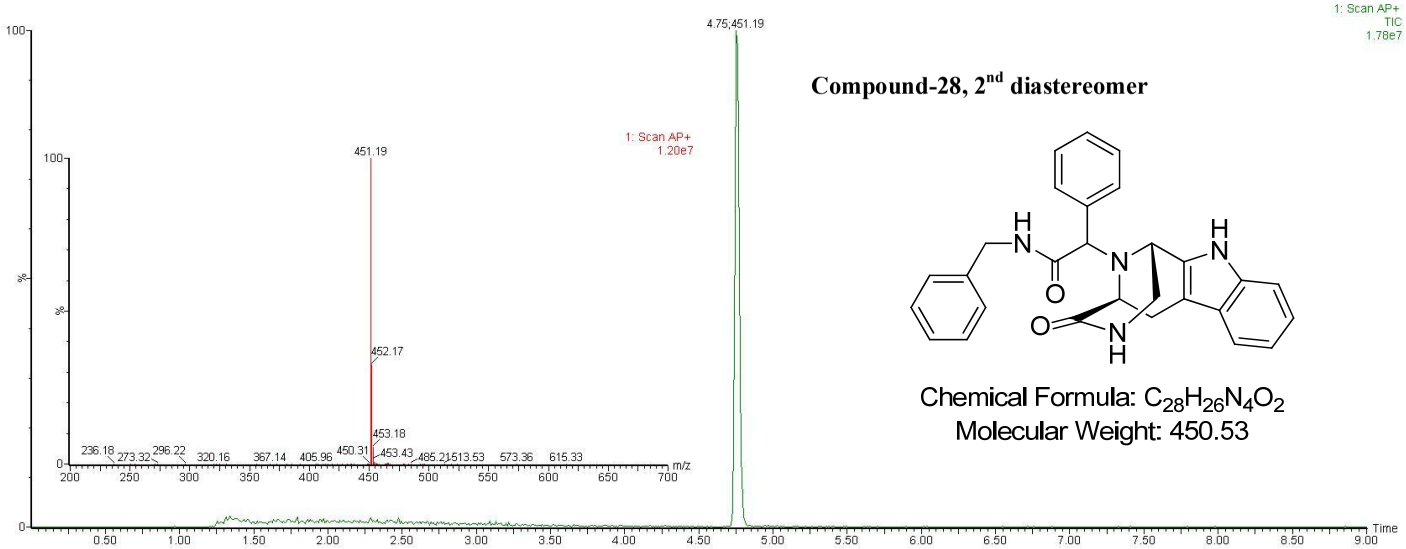
Compound-28, mixture of both diastereomers





Compound-28, 1st diastereomer

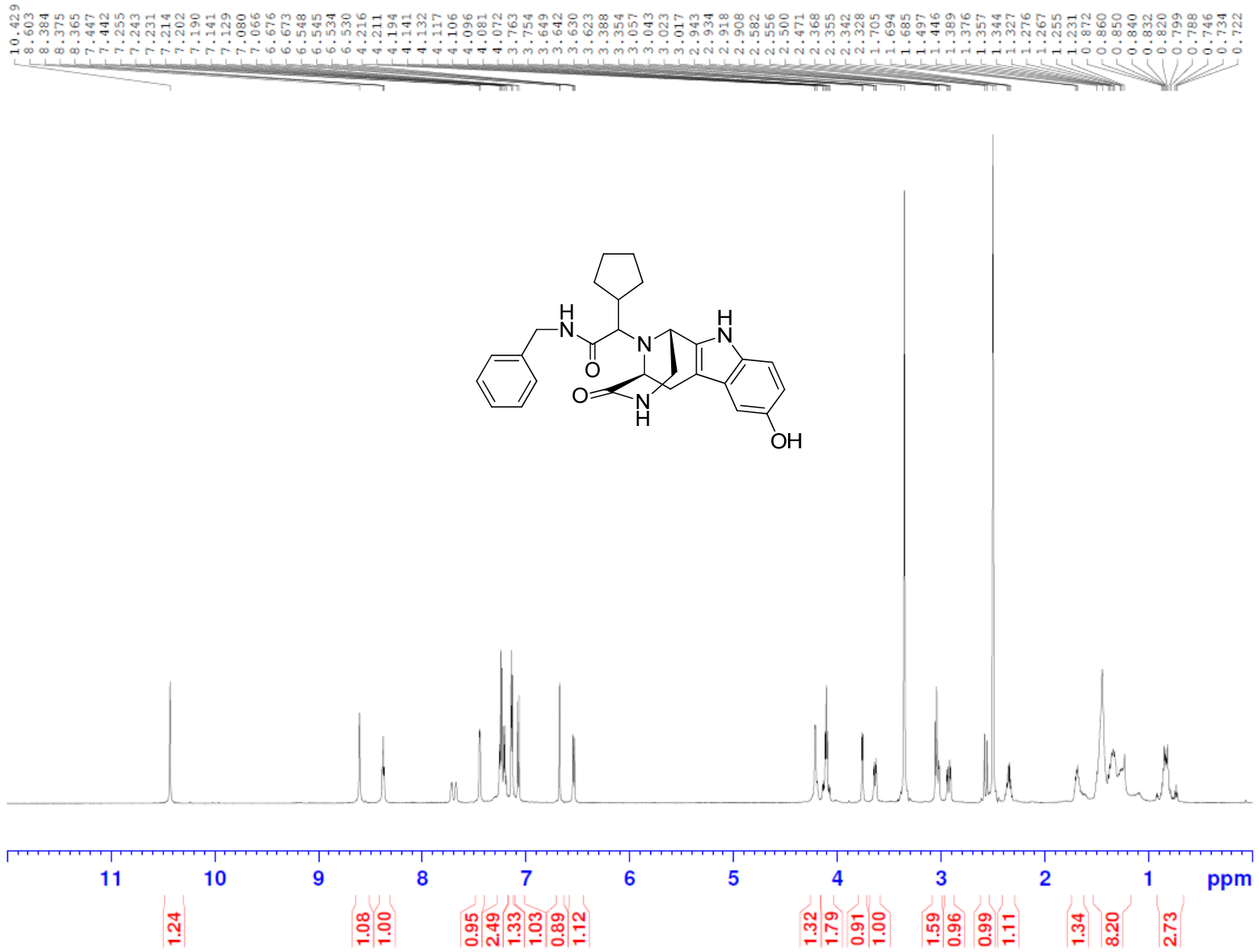
Chemical Formula: $C_{28}H_{26}N_4O_2$
Molecular Weight: 450.53



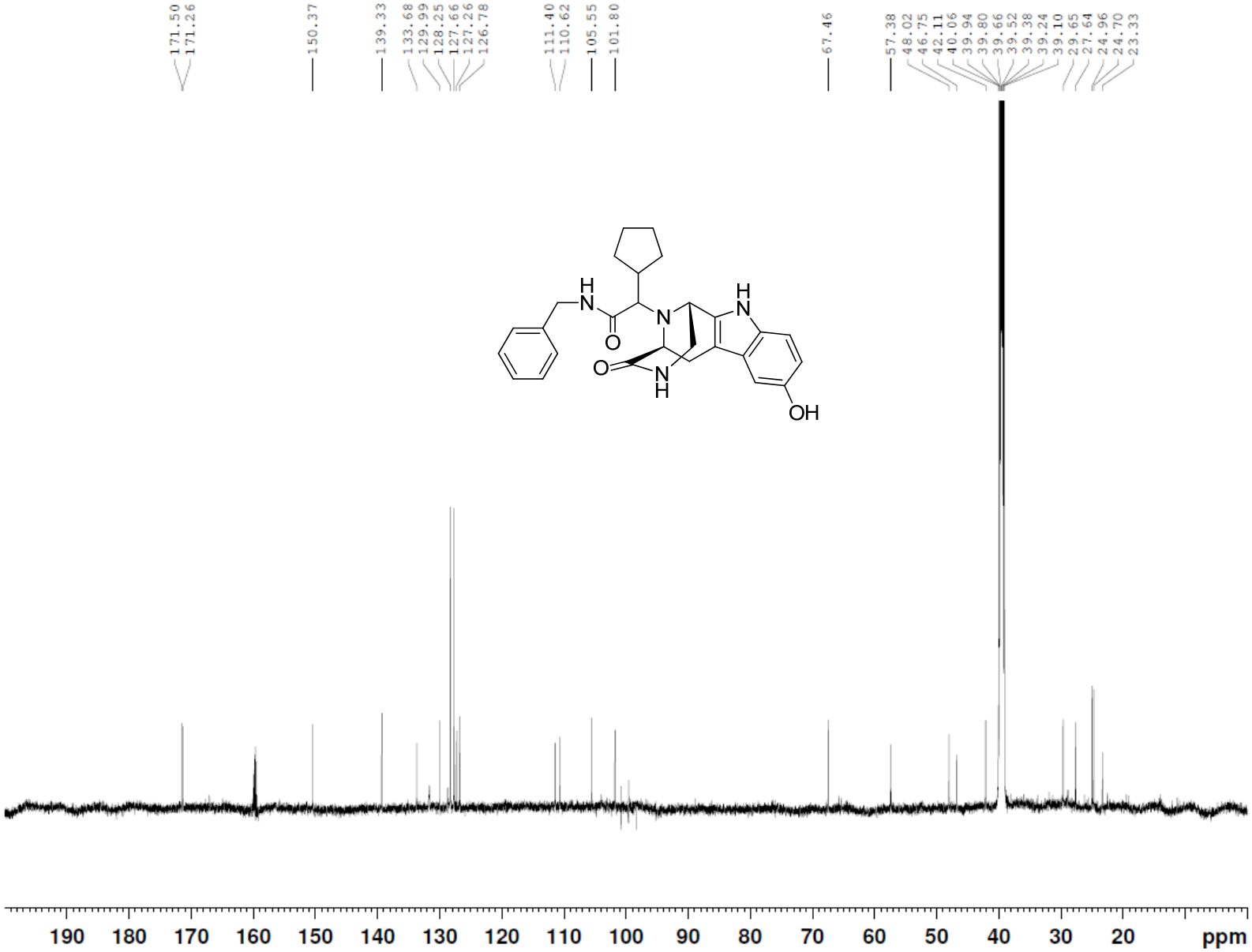
Compound-28, 2nd diastereomer

Chemical Formula: $C_{28}H_{26}N_4O_2$
Molecular Weight: 450.53

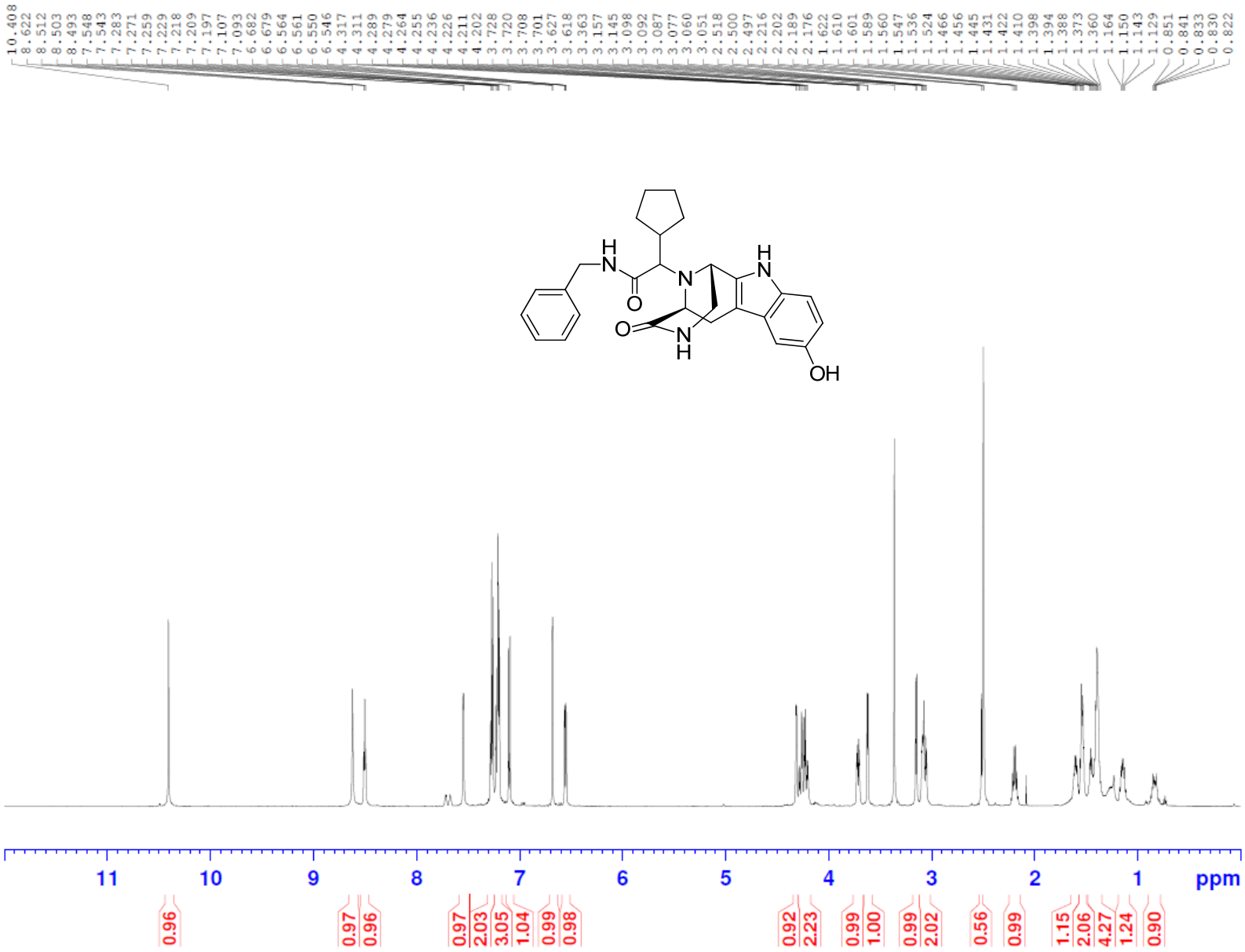
Compound-29, 1st diastereomer



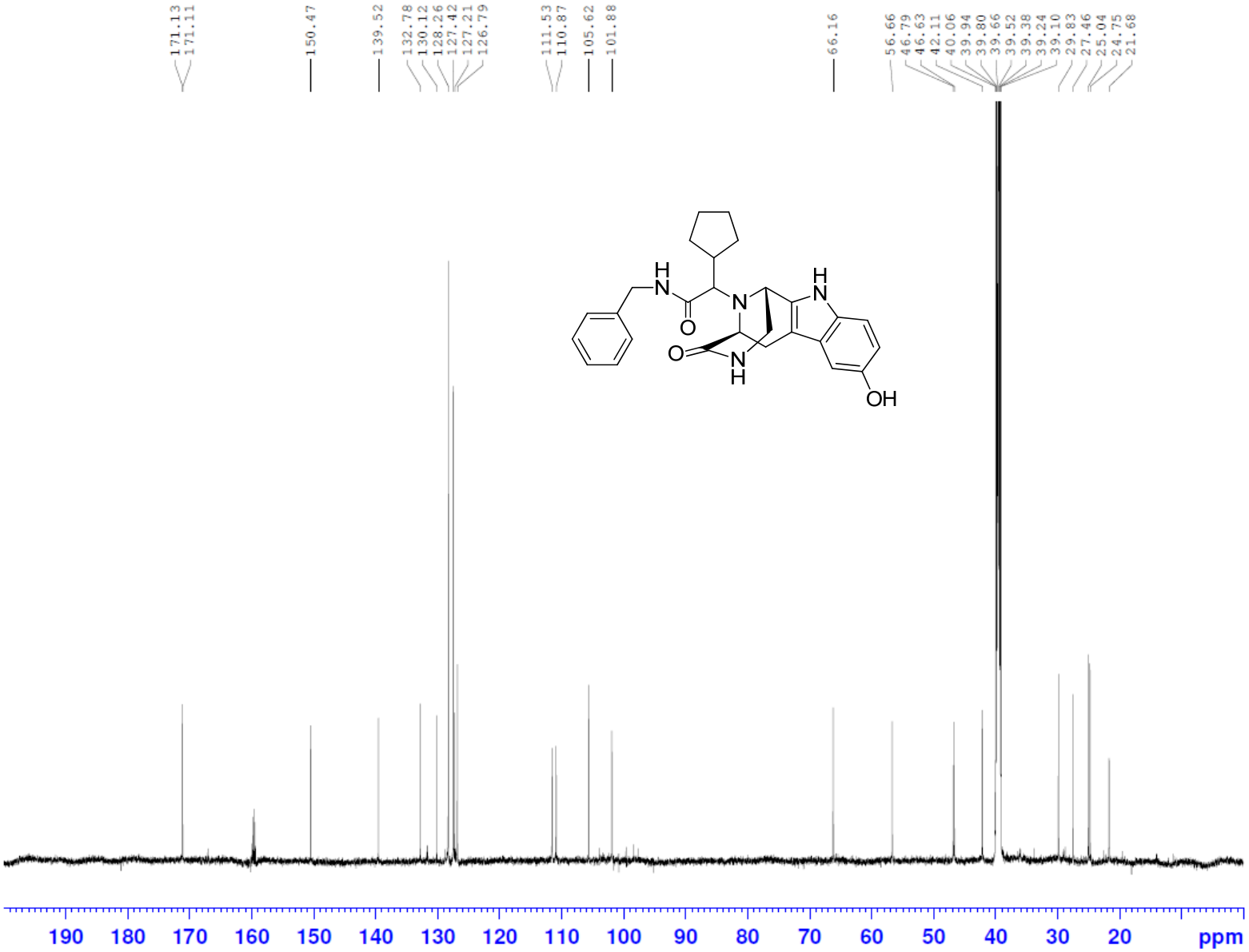
Compound-29, 1st diastereomer

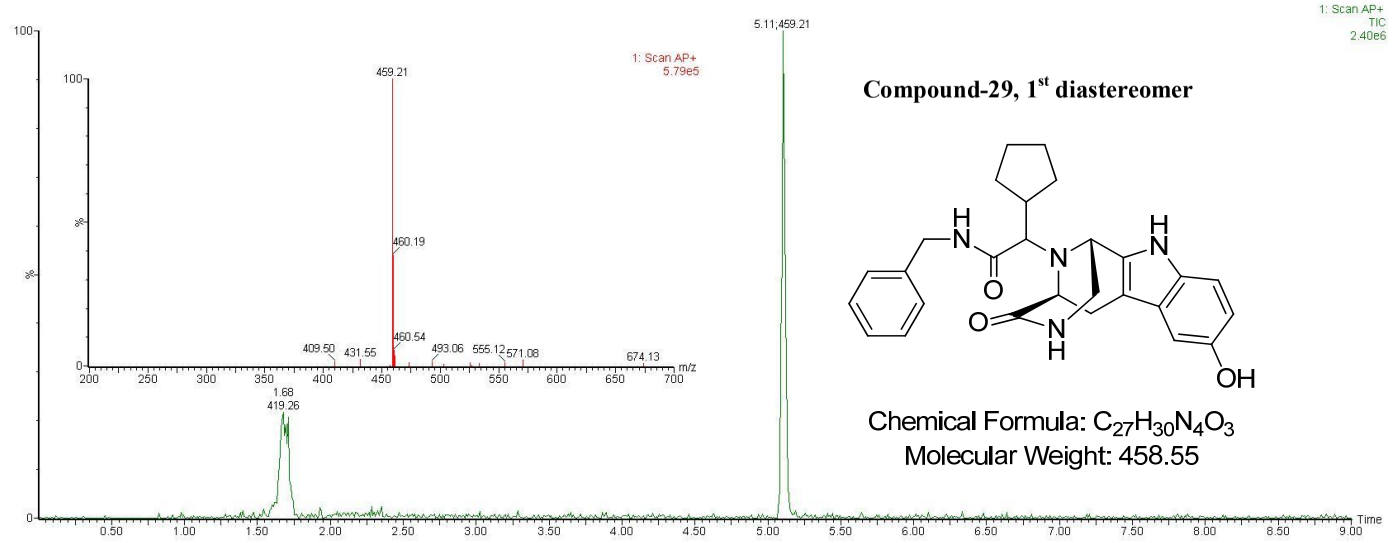


Compound-29, 2nd diastereomer



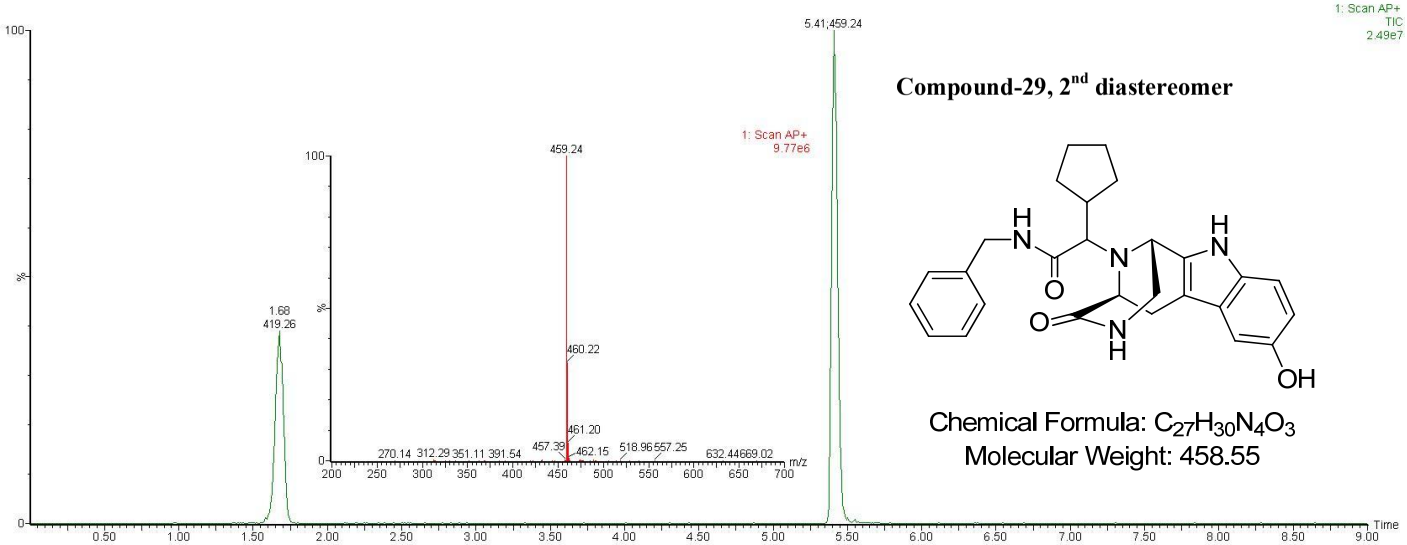
Compound-29, 2nd diastereomer





Compound-29, 1st diastereomer

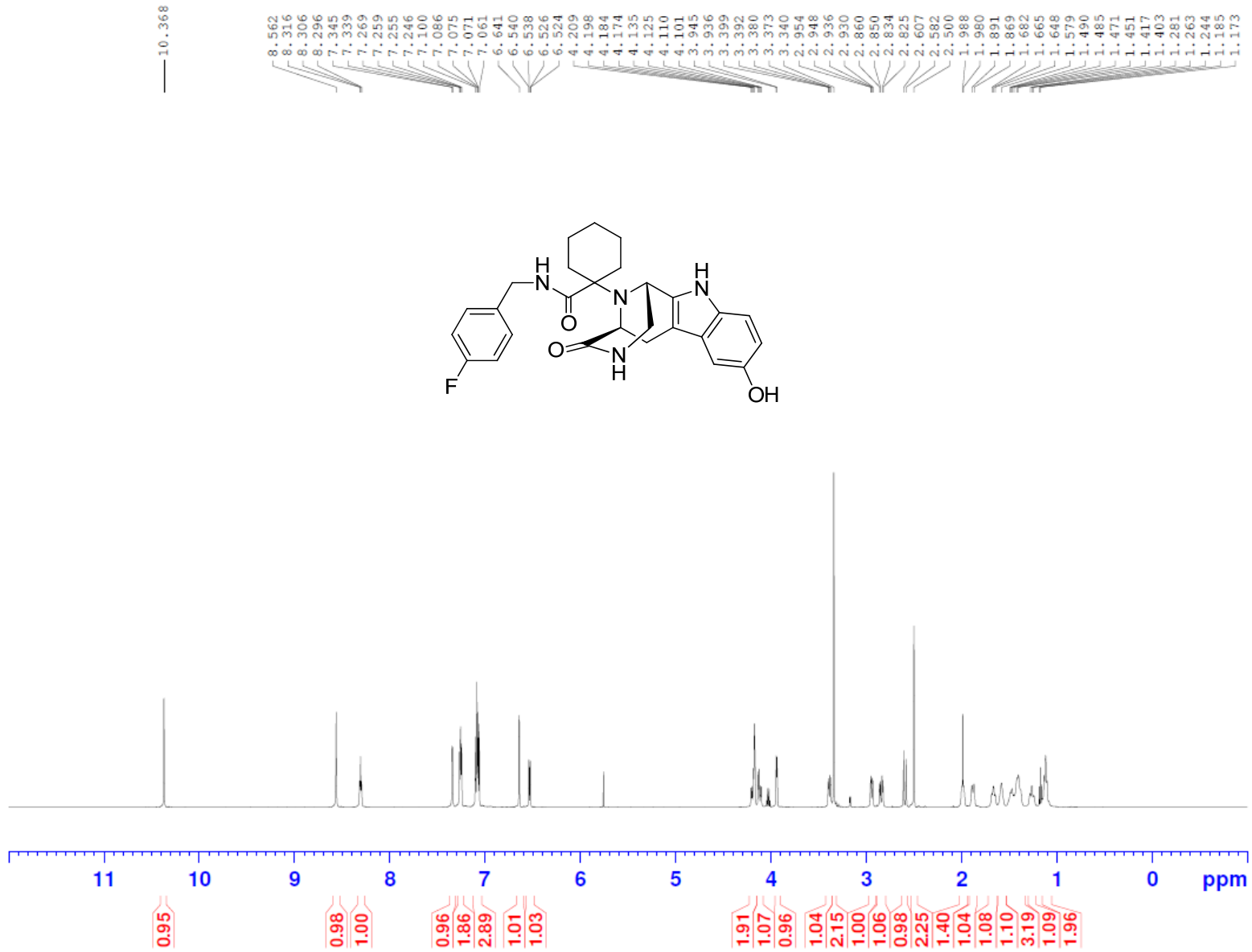
Chemical Formula: $C_{27}H_{30}N_4O_3$
Molecular Weight: 458.55



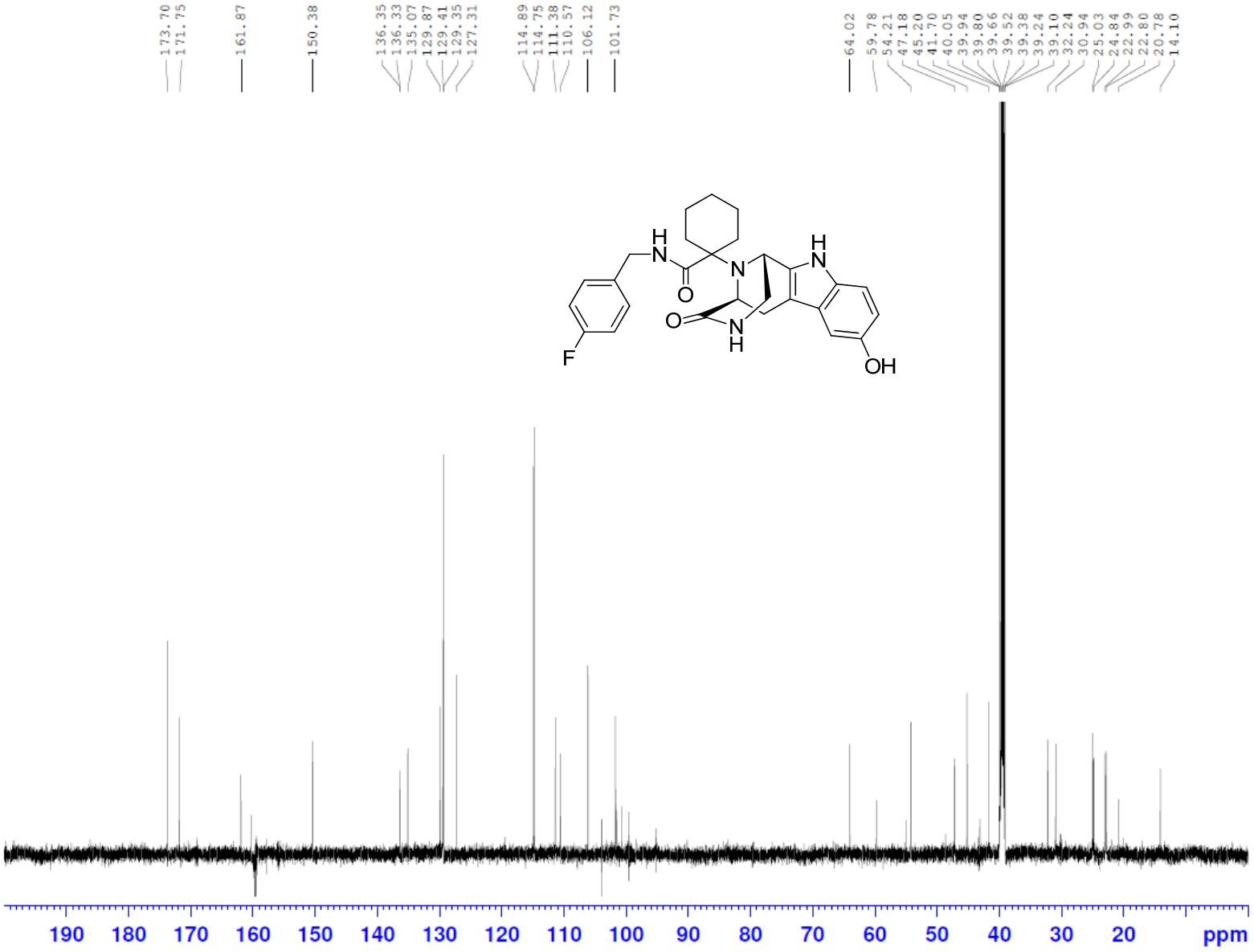
Compound-29, 2nd diastereomer

Chemical Formula: $C_{27}H_{30}N_4O_3$
Molecular Weight: 458.55

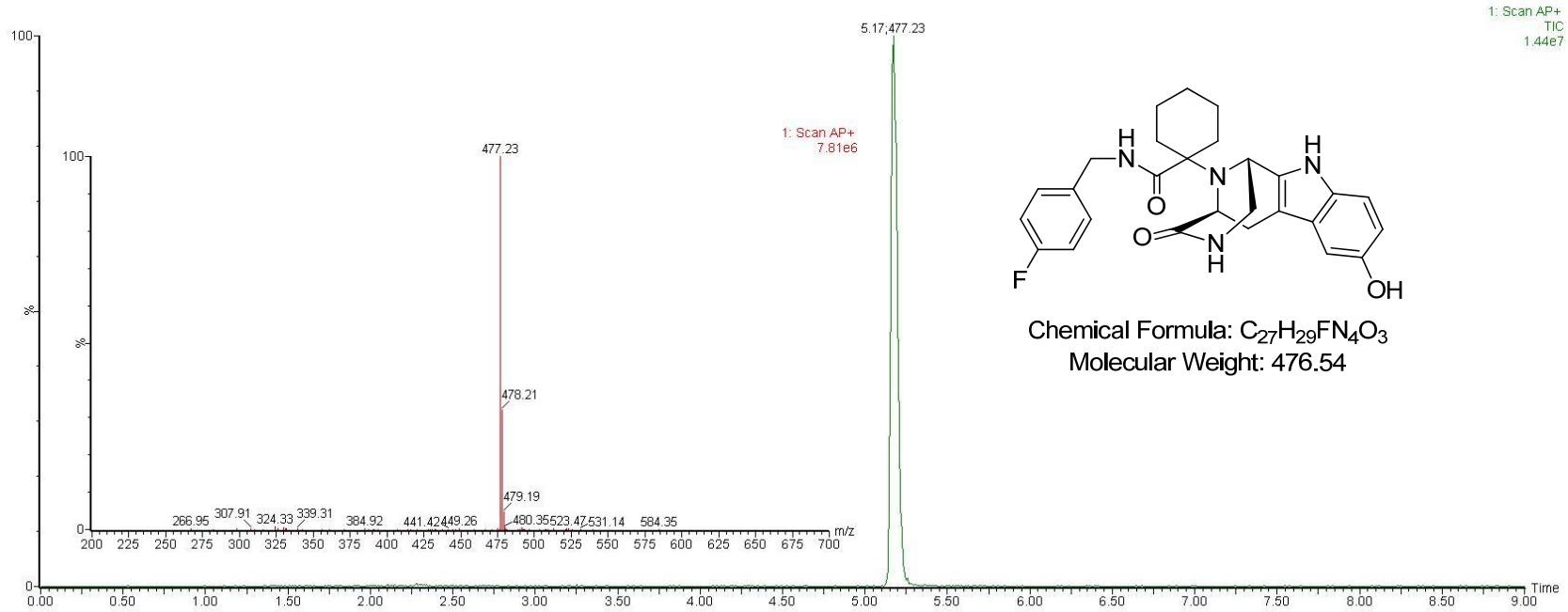
Compound-30


10.368
8.562
8.316
8.306
8.296
7.345
7.339
7.269
7.259
7.255
7.246
7.100
7.086
7.075
7.071
7.061
6.641
6.540
6.538
6.526
6.524
4.209
4.198
4.184
4.174
4.135
4.125
4.110
4.101
3.945
3.936
3.399
3.392
3.380
3.373
3.340
2.954
2.948
2.936
2.930
2.860
2.850
2.834
2.825
2.607
2.582
2.500
1.988
1.980
1.891
1.869
1.682
1.665
1.648
1.579
1.490
1.485
1.471
1.451
1.417
1.403
1.281
1.263
1.244
1.185
1.173
H
N
O
N
H
N
O
N
H
F
OH
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.95
0.98
1.00
0.96
1.86
2.89
1.01
1.03
1.91
1.07
0.96
1.04
2.15
1.00
1.06
0.98
2.25
1.40
1.04
1.08
1.10
3.19
1.09
1.96

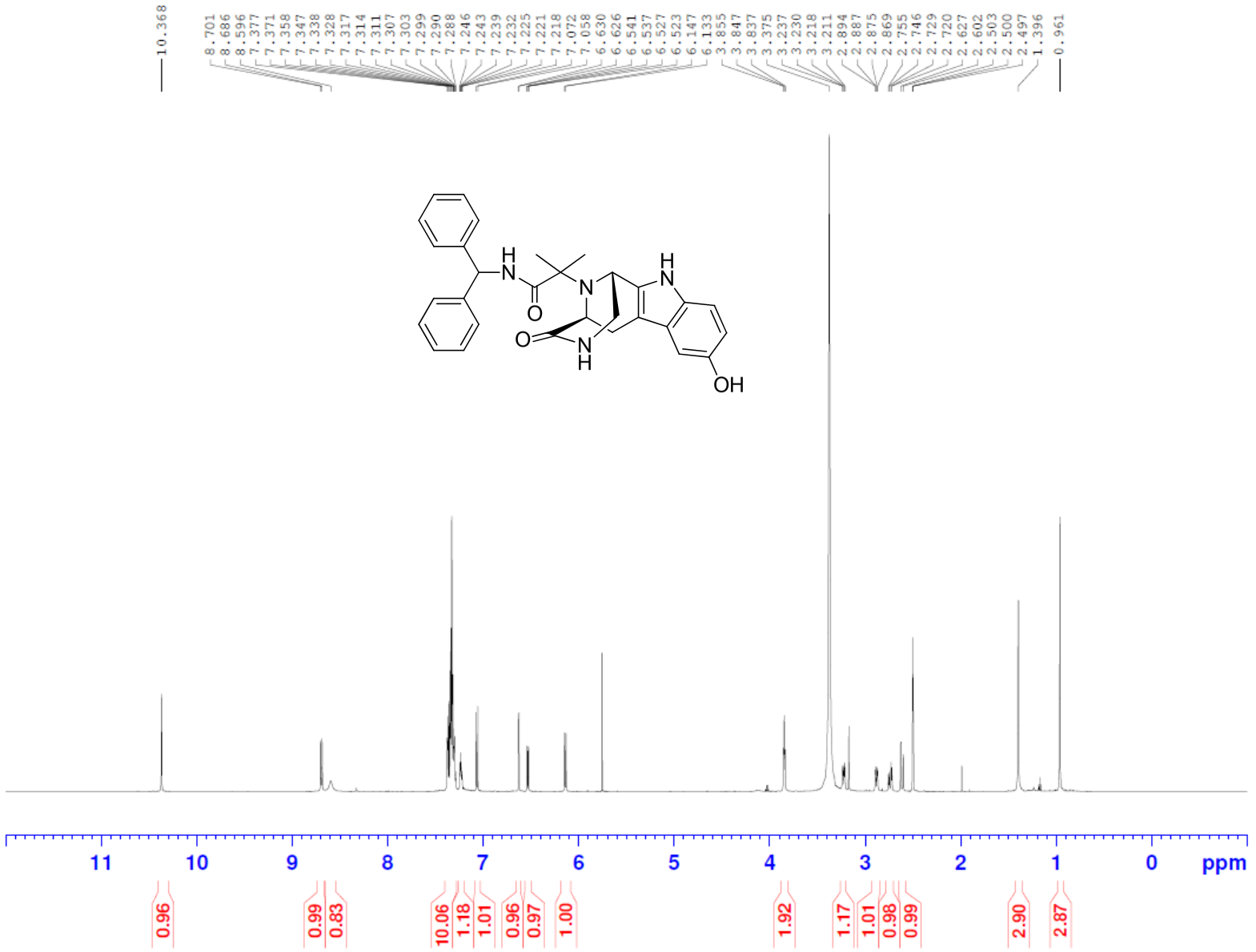
Compound-30


173.70
171.75
161.87
150.38
136.35
136.33
135.07
129.87
129.41
129.35
127.31
114.89
114.75
111.38
110.57
106.12
101.73
64.02
59.78
54.21
47.18
45.20
41.70
40.05
39.94
39.80
39.66
39.52
39.38
39.24
39.10
32.24
30.94
25.03
24.84
22.99
22.80
20.78
14.10
H
N
O
N
O
N
H
H
N
F
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

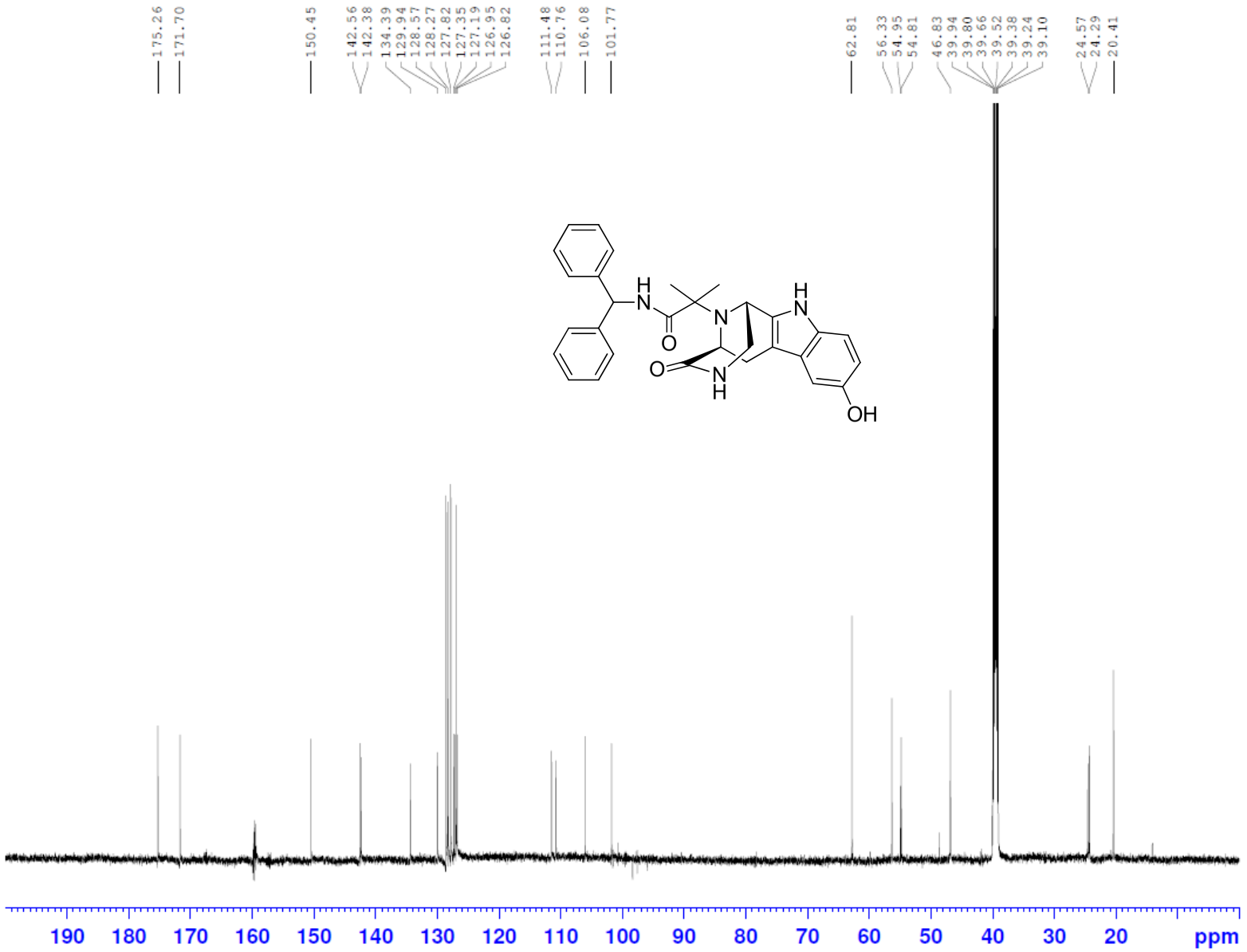
Compound-30


1: Scan AP+
TIC
1.44e7
5.17;477.23
1: Scan AP+
7.81e6
477.23
478.21
479.19
266.95
307.91
324.33
339.31
384.92
441.42
449.26
480.35
523.47
531.14
584.35
m/z
Time
Chemical Formula: C27H29FN4O3
Molecular Weight: 476.54

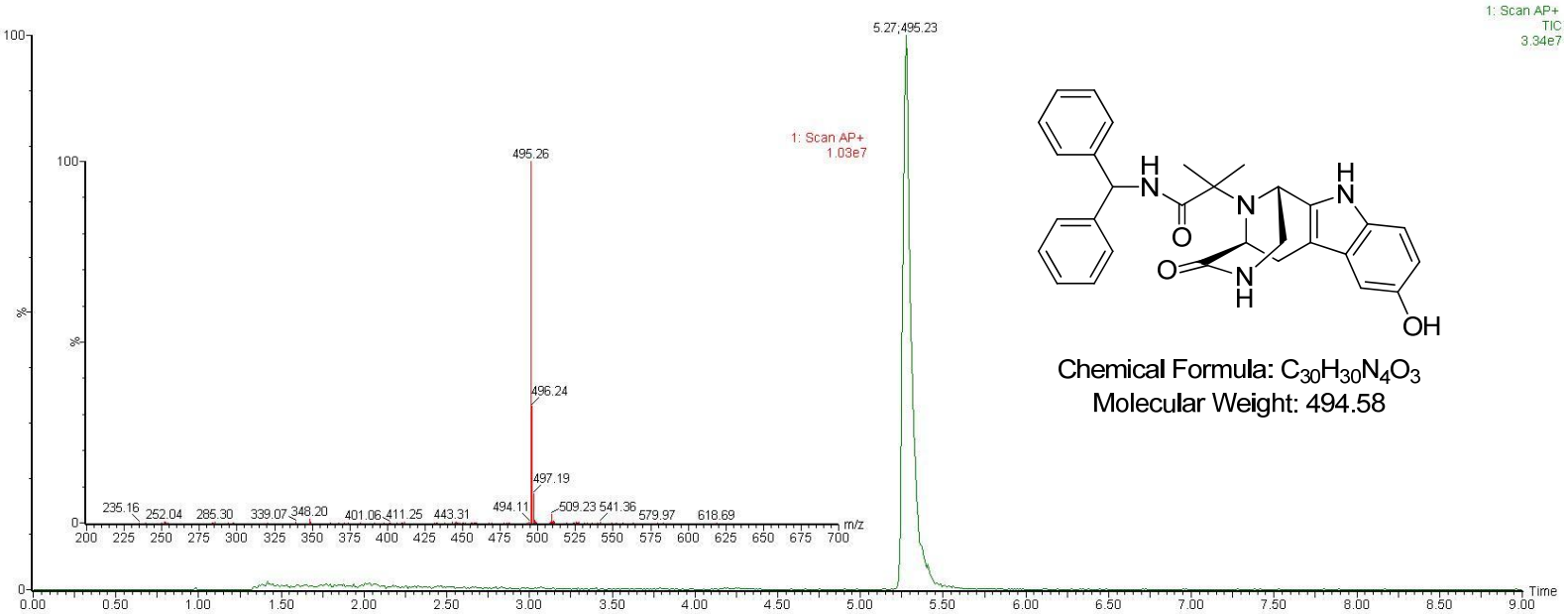
Compound-31


10.368
8.701
8.686
8.596
7.377
7.371
7.358
7.347
7.338
7.328
7.317
7.314
7.311
7.307
7.303
7.299
7.290
7.288
7.246
7.243
7.239
7.232
7.225
7.221
7.218
7.072
7.058
6.630
6.626
6.541
6.537
6.527
6.523
6.147
6.133
3.855
3.847
3.837
3.375
3.237
3.230
3.218
3.211
2.894
2.887
2.875
2.869
2.755
2.746
2.729
2.720
2.627
2.602
2.503
2.500
2.497
1.396
0.961
H
N
O
N
H
O
N
H
OH
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.96
0.99
0.83
10.06
1.18
1.01
0.96
0.97
1.00
1.92
1.17
1.01
0.98
0.99
2.90
2.87

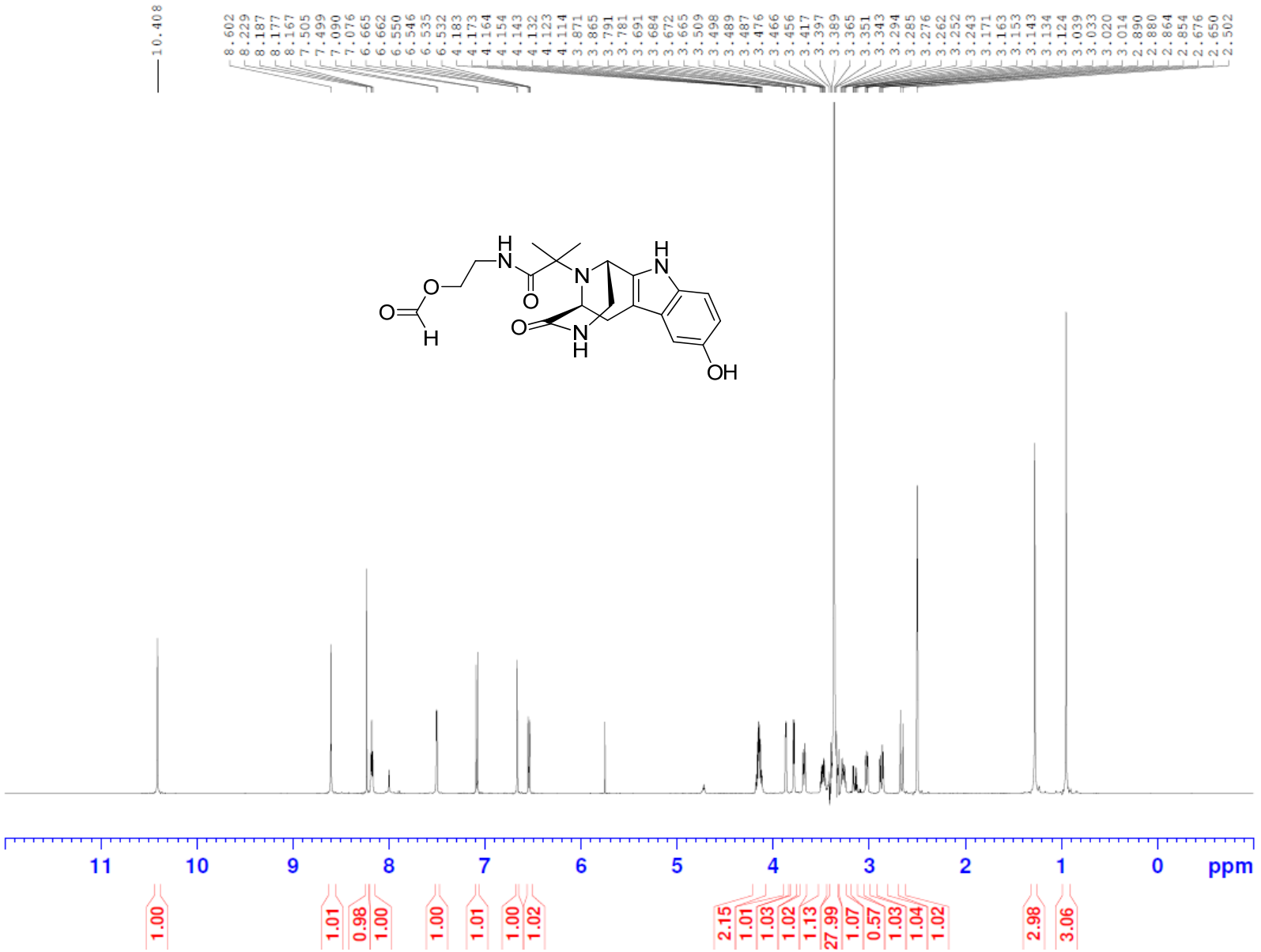
Compound-31


175.26
171.70
150.45
142.56
142.38
134.39
129.94
128.57
128.27
127.82
127.35
127.19
126.95
126.82
111.48
110.76
106.08
101.77
62.81
56.33
54.95
54.81
46.83
39.94
39.80
39.66
39.52
39.38
39.24
39.10
24.57
24.29
20.41
H
N
O
N
O
N
H
H
N
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

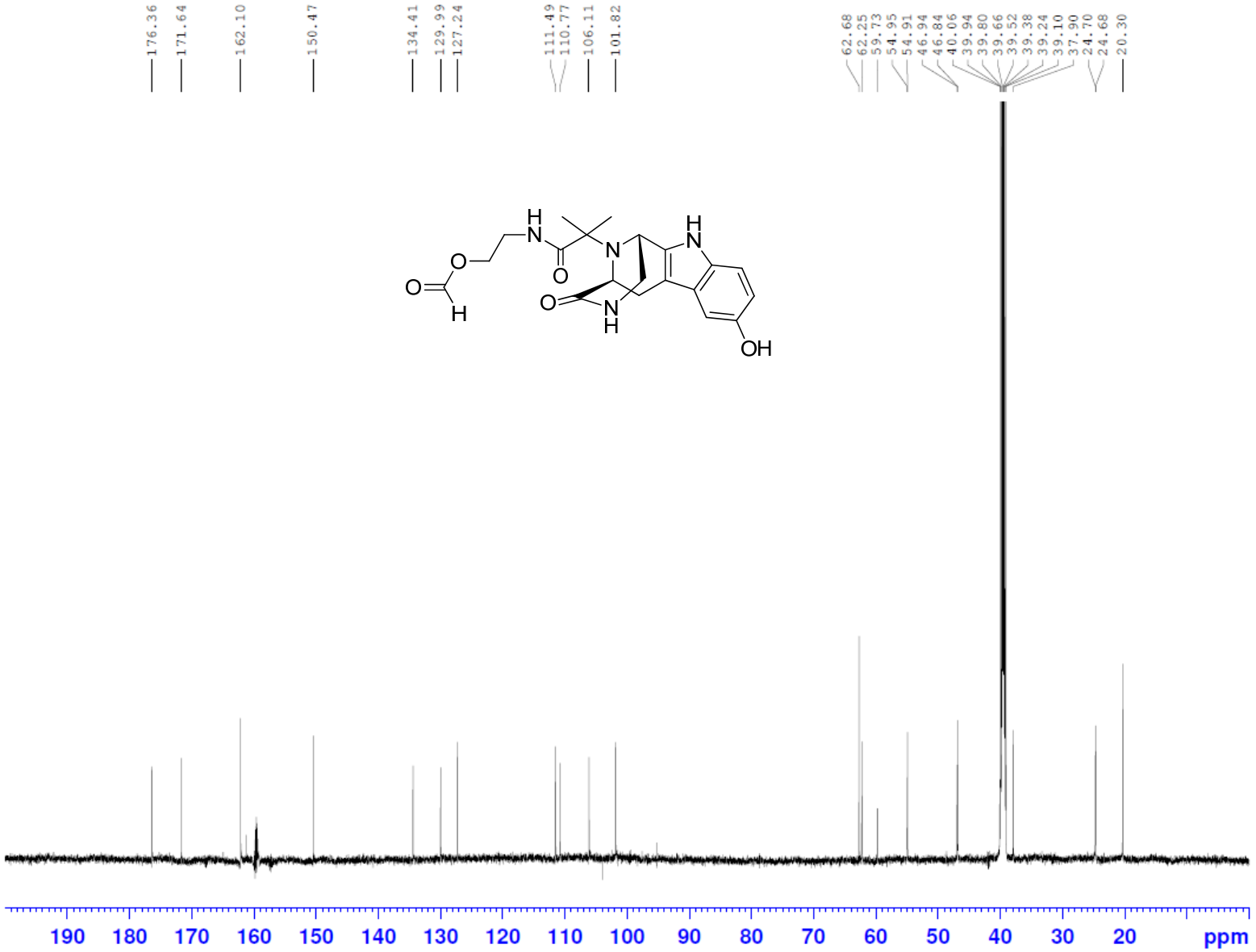
Compound-31


1: Scan AP+
TIC
3.34e7
5.27;495.23
1: Scan AP+
1.03e7
495.26
496.24
497.19
235.16
252.04
285.30
339.07
348.20
401.06
411.25
443.31
494.11
509.23
541.36
579.97
618.69
m/z
Time
Chemical Formula: $C_{30}H_{30}N_4O_3$
Molecular Weight: 494.58

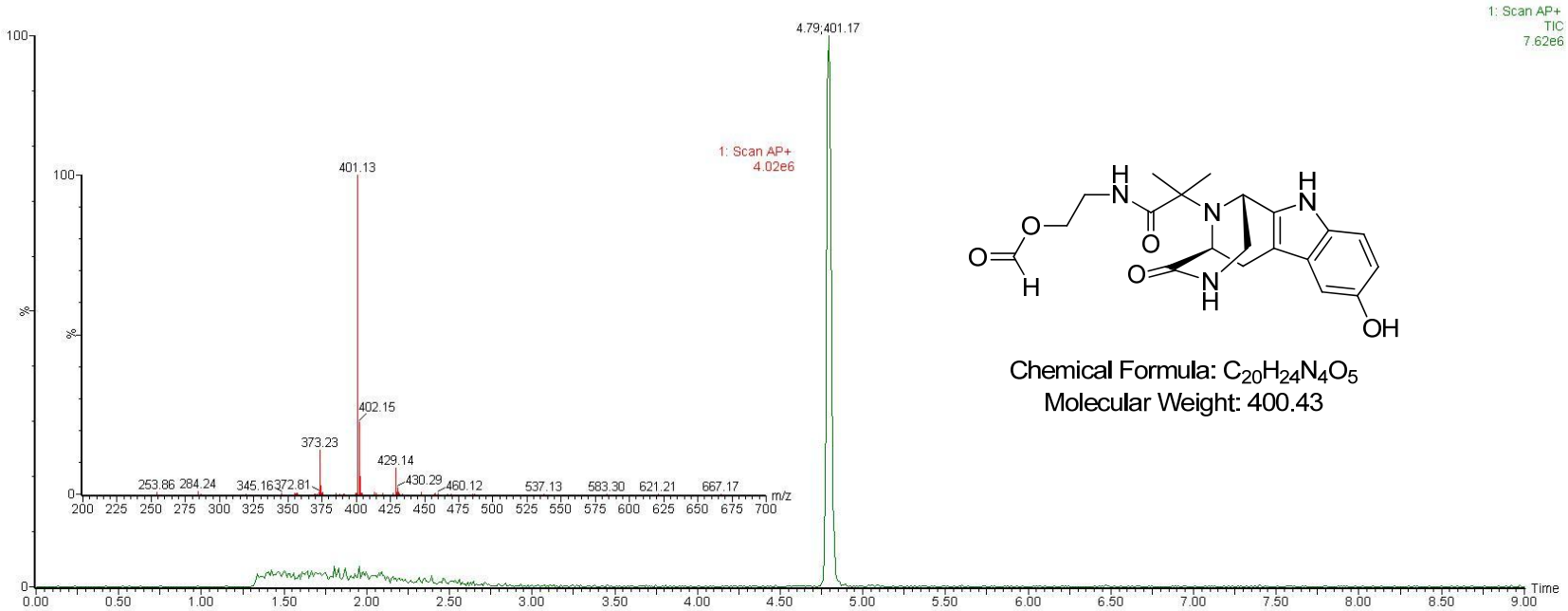
Compound-32


10.408
8.602
8.229
8.187
8.177
8.167
7.505
7.499
7.090
7.076
6.665
6.662
6.550
6.546
6.535
6.532
4.183
4.173
4.164
4.154
4.143
4.132
4.123
4.114
3.871
3.865
3.791
3.781
3.691
3.684
3.672
3.665
3.509
3.498
3.489
3.487
3.476
3.466
3.456
3.417
3.397
3.389
3.365
3.351
3.343
3.294
3.285
3.276
3.262
3.252
3.243
3.171
3.163
3.153
3.143
3.134
3.124
3.039
3.033
3.020
3.014
2.890
2.880
2.864
2.854
2.676
2.650
2.502
H
N
O
O
O
H
N
H
N
O
N
H
OH
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.01
0.98
1.00
1.00
1.01
1.00
1.02
2.15
1.01
1.03
1.02
1.13
27.99
1.07
0.57
1.03
1.04
1.02
2.98
3.06

Compound-32

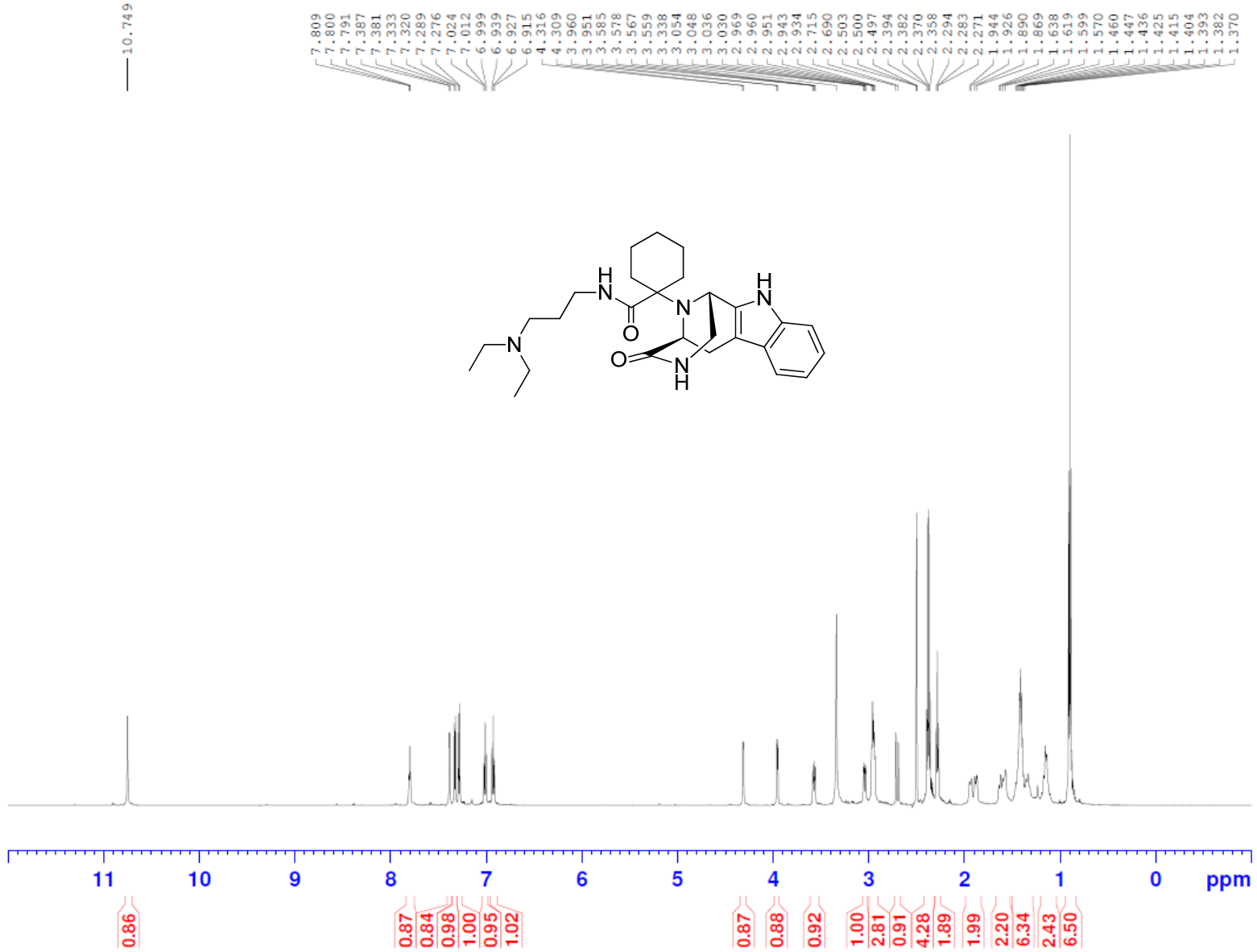

176.36
171.64
162.10
150.47
134.41
129.99
127.24
111.49
110.77
106.11
101.82
62.68
62.25
59.73
54.95
54.91
46.94
46.84
40.06
39.94
39.80
39.66
39.52
39.38
39.24
39.10
37.90
24.70
24.68
20.30
H
N
O
O
O
H
N
H
N
O
N
H
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

Compound-32

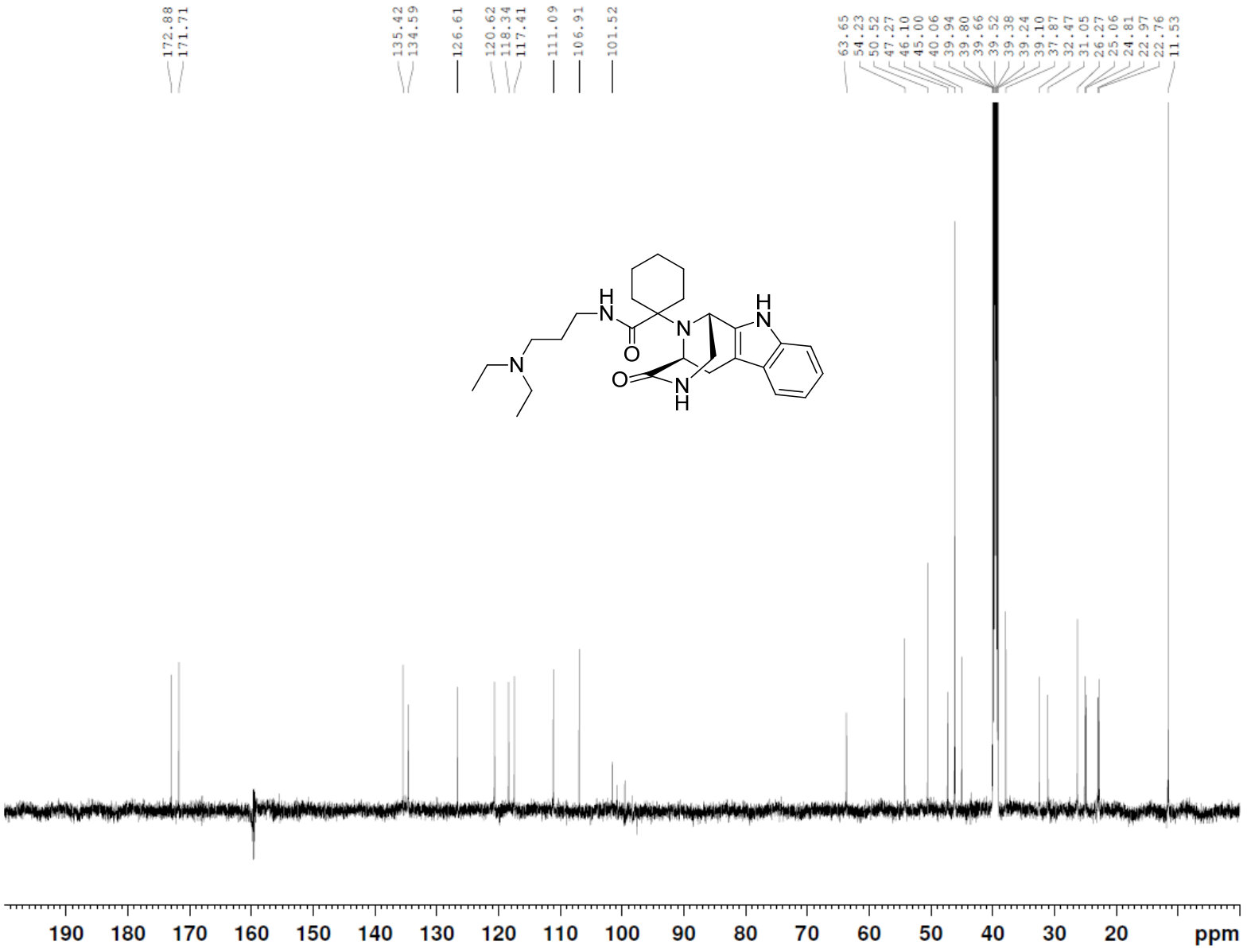


Chemical Formula: $C_{20}H_{24}N_4O_5$
Molecular Weight: 400.43

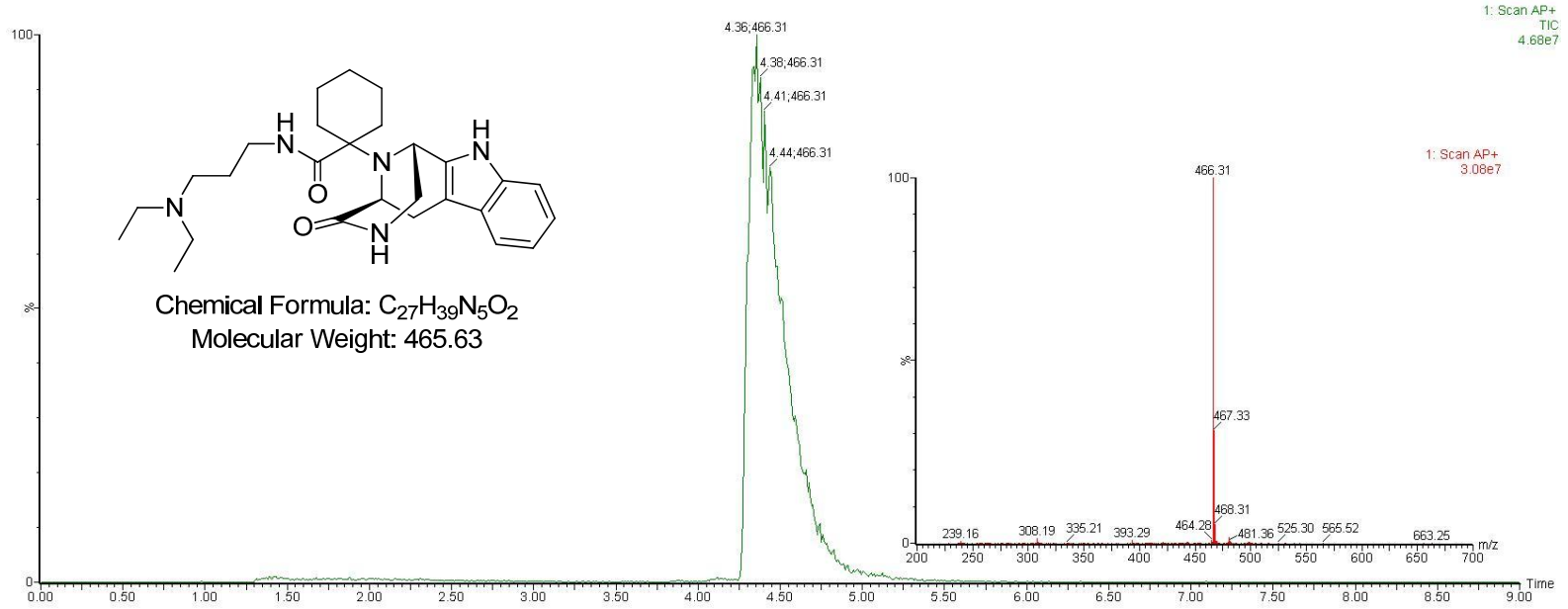
Compound-33


10.749
7.809
7.800
7.791
7.387
7.381
7.333
7.320
7.289
7.276
7.024
7.012
6.999
6.939
6.927
6.915
4.316
4.309
3.960
3.951
3.585
3.578
3.567
3.559
3.338
3.054
3.048
3.036
3.030
2.969
2.960
2.951
2.943
2.934
2.715
2.690
2.503
2.500
2.497
2.394
2.382
2.370
2.358
2.294
2.283
2.271
1.944
1.926
1.890
1.869
1.638
1.619
1.599
1.570
1.460
1.447
1.436
1.425
1.415
1.404
1.393
1.382
1.370
H
N
O
N
O
N
H
N
H
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.86
0.87
0.84
0.98
1.00
0.95
1.02
0.87
0.88
0.92
1.00
2.81
0.91
4.28
1.89
1.99
2.20
6.34
2.43
6.50

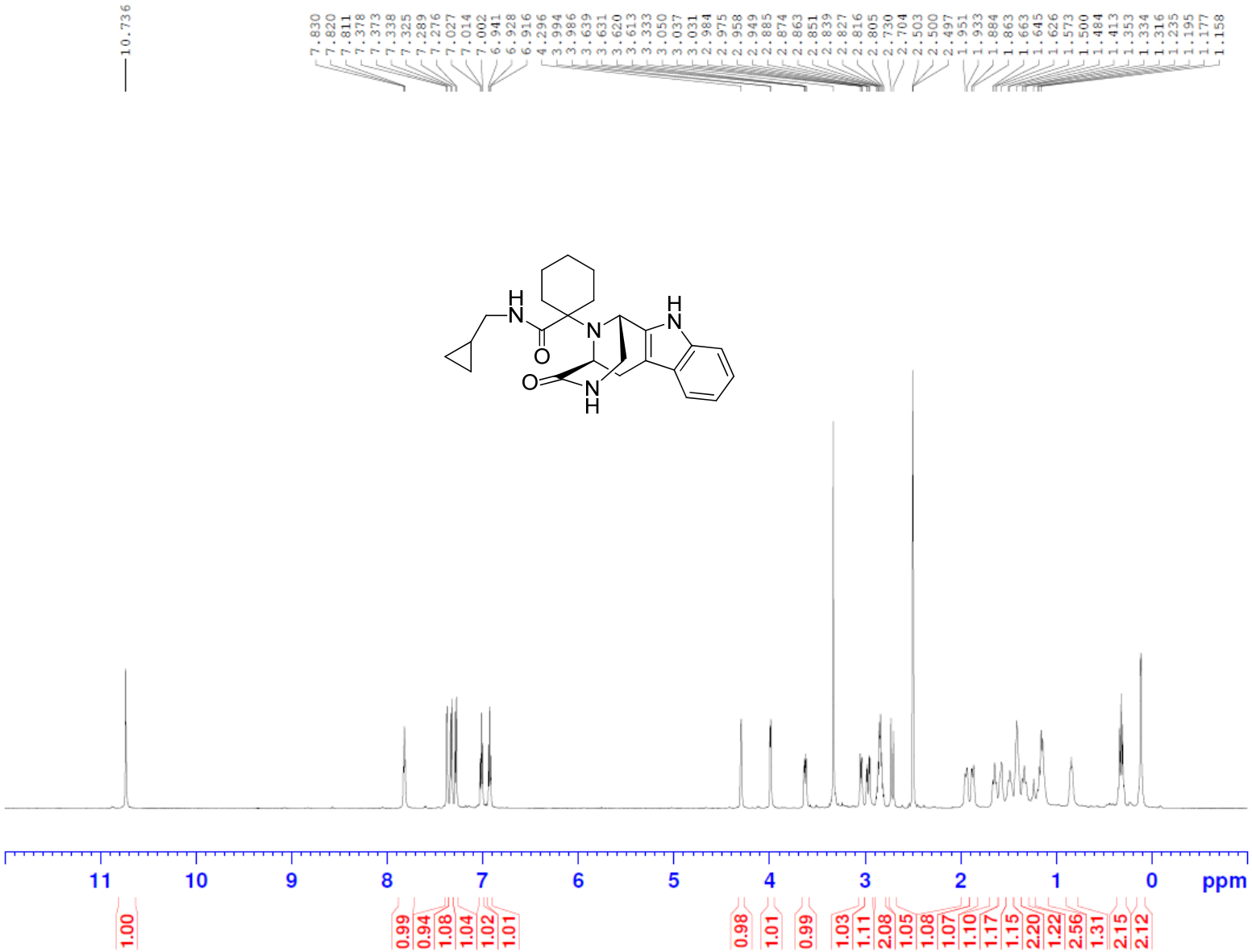
Compound-33


172.88
171.71
135.42
134.59
126.61
120.62
118.34
117.41
111.09
106.91
101.52
63.65
54.23
50.52
47.27
46.10
45.00
40.06
39.94
39.80
39.66
39.52
39.38
39.24
39.10
37.87
32.47
31.05
26.27
25.06
24.81
22.97
22.76
11.53
H
N
O
N
H
N
O
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

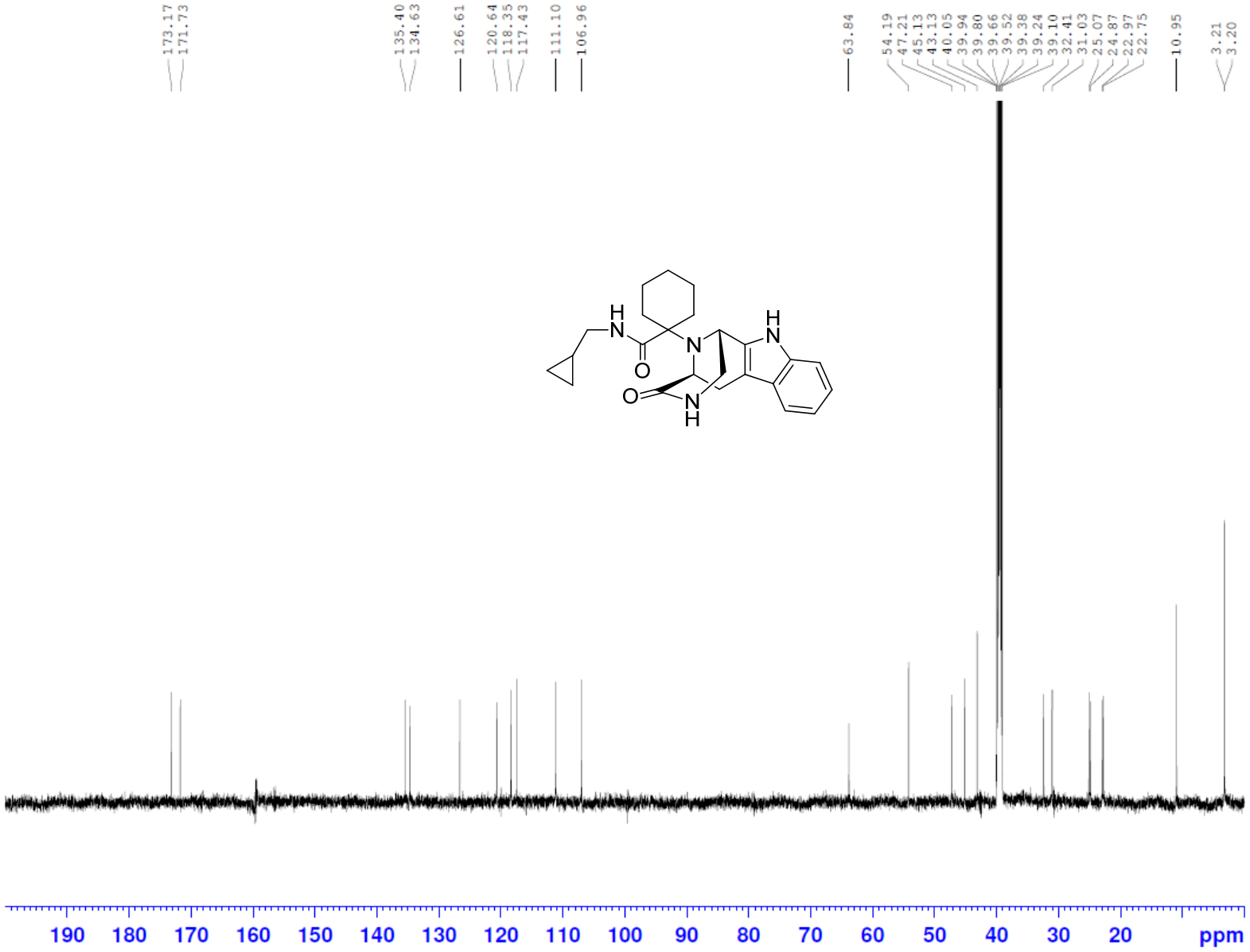
Compound-33


Chemical Formula: $C_{27}H_{39}N_5O_2$
Molecular Weight: 465.63
4.36;466.31
4.38;466.31
4.41;466.31
4.44;466.31
1: Scan AP+
TIC
4.68e7
1: Scan AP+
3.08e7
466.31
467.33
468.31
239.16
308.19
335.21
393.29
464.28
481.36
525.30
565.52
663.25
m/z
Time

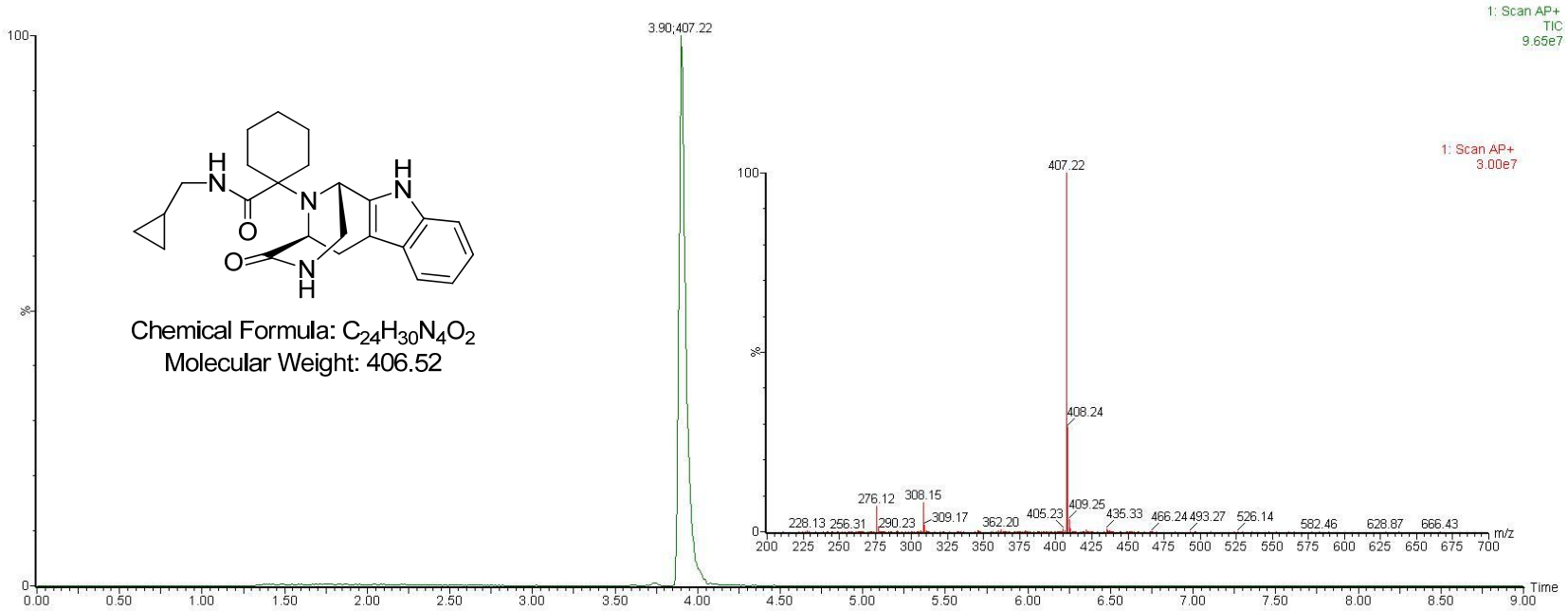
Compound-34


10.736
7.830
7.820
7.811
7.378
7.373
7.338
7.325
7.289
7.276
7.027
7.014
7.002
6.941
6.928
6.916
4.296
3.994
3.986
3.639
3.631
3.620
3.613
3.333
3.050
3.037
3.031
2.984
2.975
2.958
2.949
2.885
2.874
2.863
2.851
2.839
2.827
2.816
2.805
2.730
2.704
2.503
2.500
2.497
1.951
1.933
1.884
1.863
1.663
1.645
1.626
1.573
1.500
1.484
1.413
1.353
1.334
1.316
1.235
1.195
1.177
1.158
H
N
O
N
H
N
O
N
H
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.99
0.94
1.08
1.04
1.02
1.01
0.98
1.01
0.99
1.03
1.11
2.08
1.05
1.08
1.07
1.10
1.17
1.15
2.20
1.22
2.56
1.31
2.15
2.12

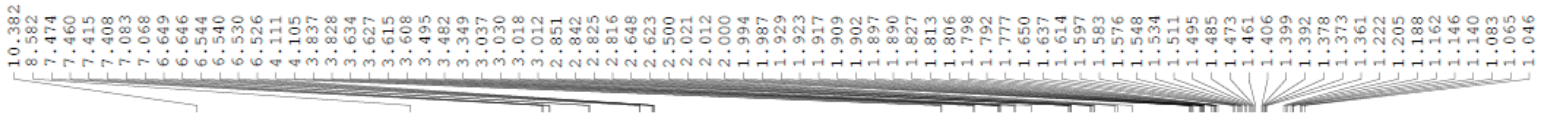
Compound-34

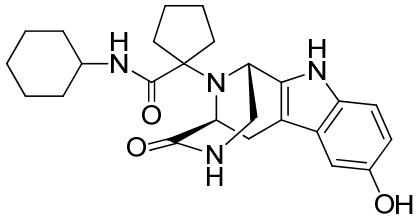

173.17
171.73
135.40
134.63
126.61
120.64
118.35
117.43
111.10
106.96
63.84
54.19
47.21
45.13
43.13
40.05
39.94
39.80
39.66
39.52
39.38
39.24
39.10
32.41
31.03
25.07
24.87
22.97
22.75
10.95
3.21
3.20
H
N
O
N
O
N
H
H
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

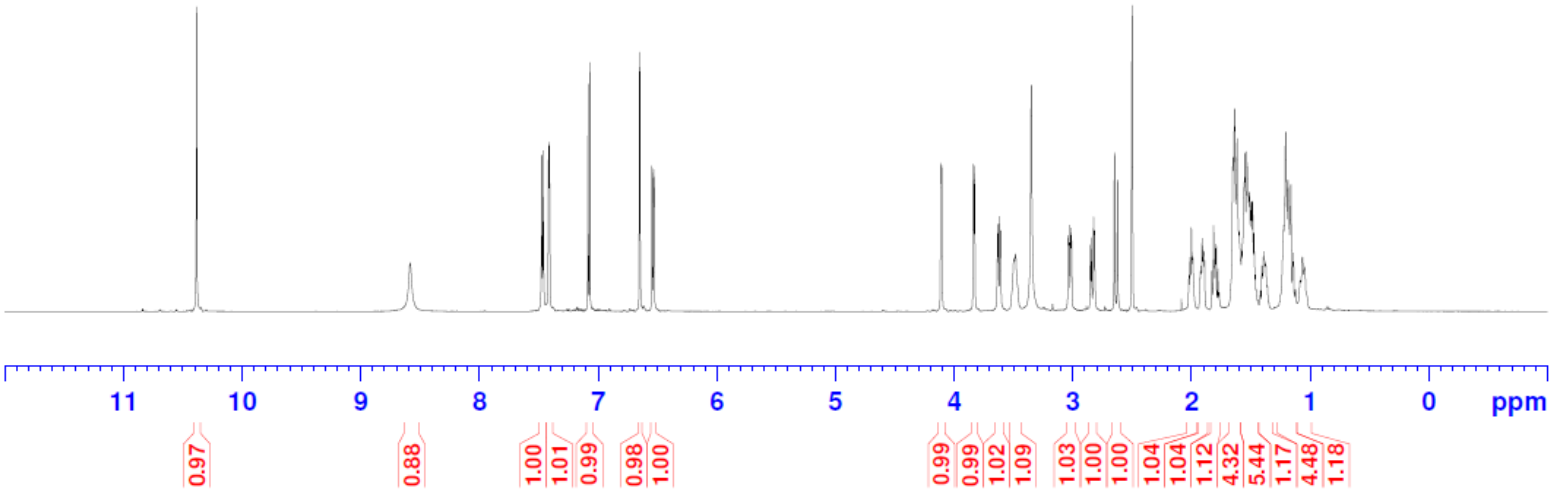
Compound-34


1: Scan AP+
TIC
9.65e7
3.90;407.22
100
%
0
0.00 0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00 8.50 9.00
Time
Chemical Formula: C24H30N4O2
Molecular Weight: 406.52
1: Scan AP+
3.00e7
407.22
408.24
276.12
308.15
228.13 256.31 290.23 309.17 362.20 405.23 409.25 435.33 466.24 493.27 526.14 582.46 628.87 666.43
200 225 250 275 300 325 350 375 400 425 450 475 500 525 550 575 600 625 650 675 700
m/z

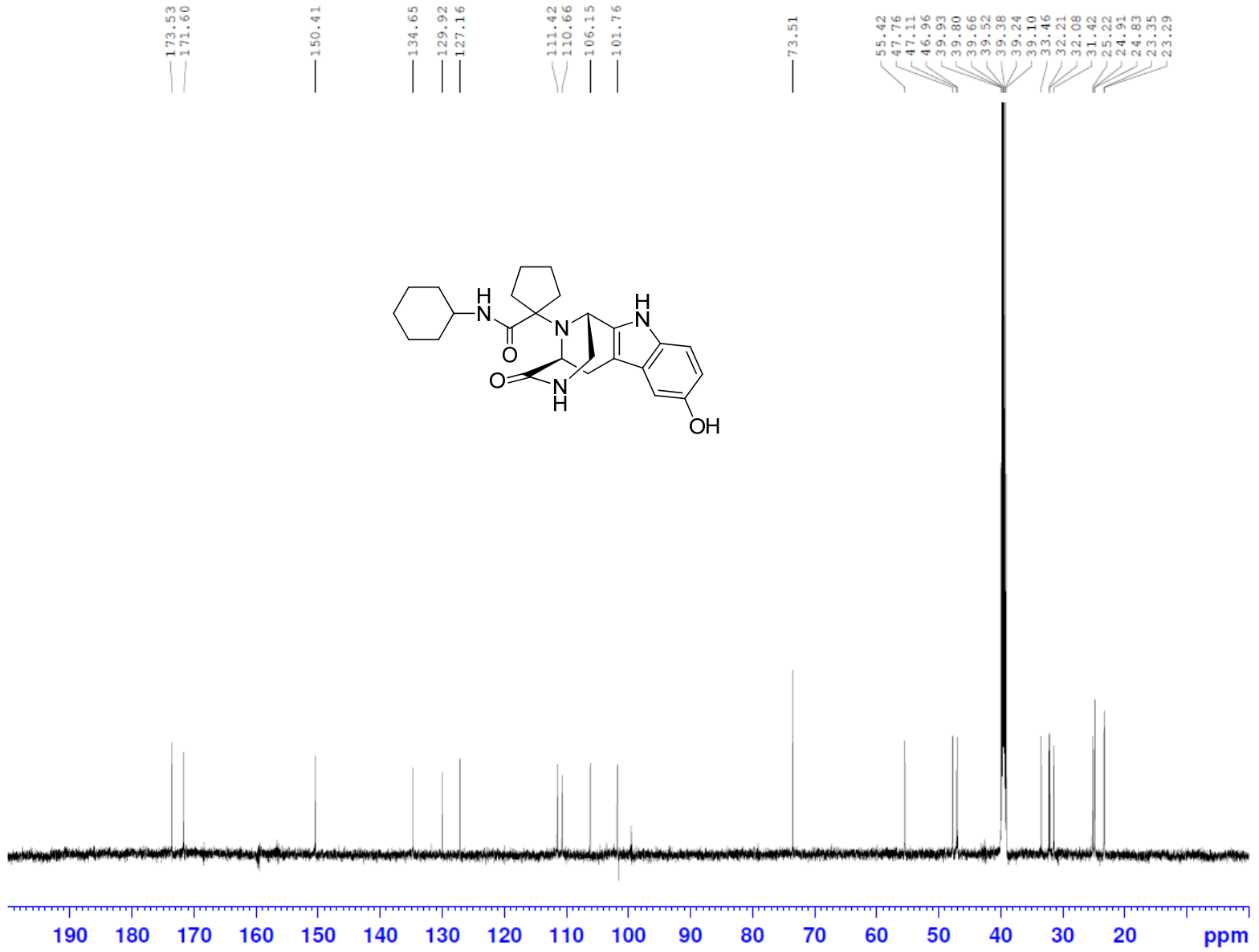
Compound-35


10.382
8.582
7.474
7.460
7.415
7.408
7.083
7.068
6.649
6.646
6.544
6.540
6.530
6.526
4.111
4.105
3.837
3.828
3.634
3.627
3.615
3.608
3.495
3.482
3.349
3.037
3.030
3.018
3.012
2.851
2.842
2.825
2.816
2.648
2.623
2.500
2.021
2.012
2.000
1.994
1.987
1.929
1.923
1.917
1.909
1.902
1.897
1.890
1.827
1.813
1.806
1.798
1.792
1.777
1.650
1.637
1.614
1.597
1.583
1.576
1.548
1.534
1.511
1.495
1.485
1.473
1.461
1.406
1.399
1.392
1.378
1.373
1.361
1.222
1.205
1.188
1.162
1.146
1.140
1.083
1.065
1.046

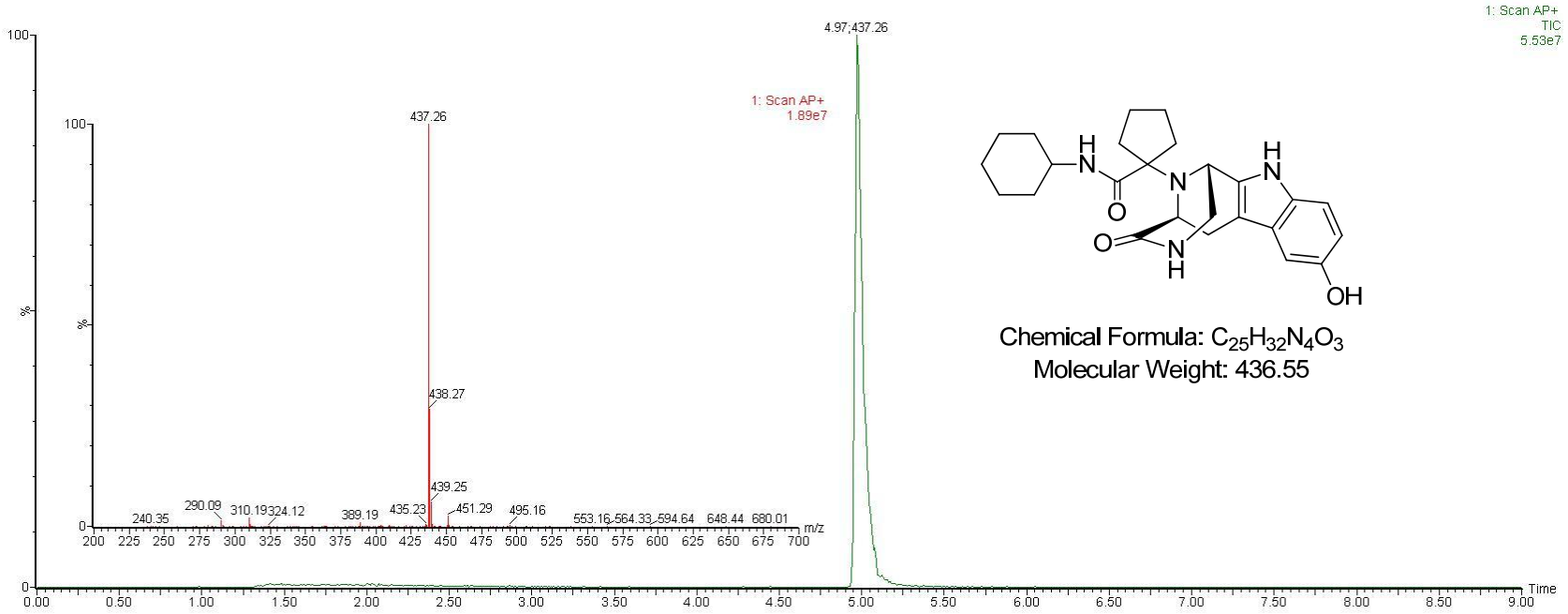

H
N
O
N
O
N
H
H
N
OH


11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.97
0.88
1.00
1.01
0.99
0.98
1.00
0.99
0.99
1.02
1.09
1.03
1.00
1.00
1.04
1.04
1.12
4.32
5.44
1.17
4.48
1.18

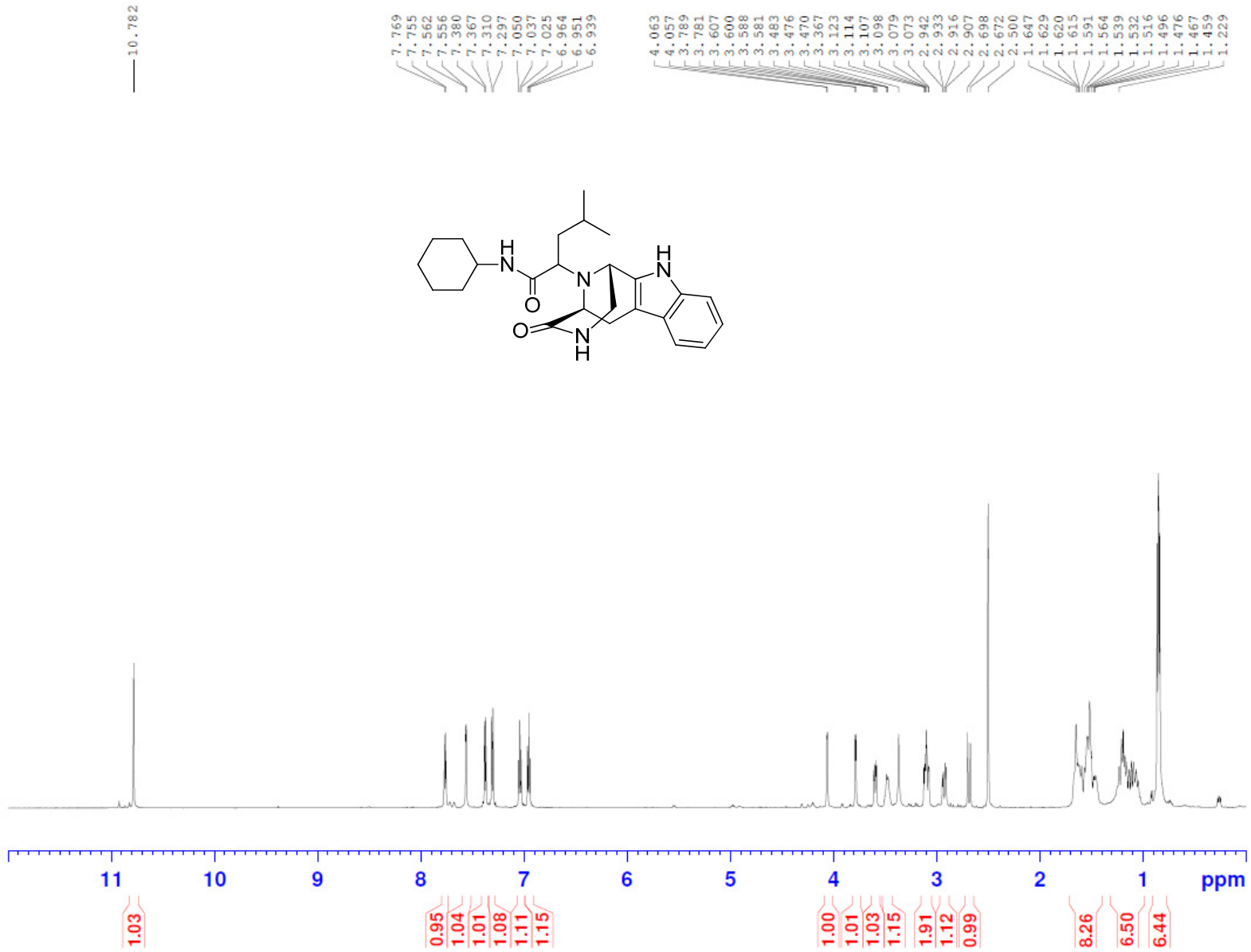
Compound-35


173.53
171.60
150.41
134.65
129.92
127.16
111.42
110.66
106.15
101.76
73.51
55.42
47.76
47.11
46.96
39.93
39.80
39.66
39.52
39.38
39.24
39.10
33.46
32.21
32.08
31.42
25.22
24.91
24.83
23.35
23.29
H
N
O
O
N
H
N
H
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

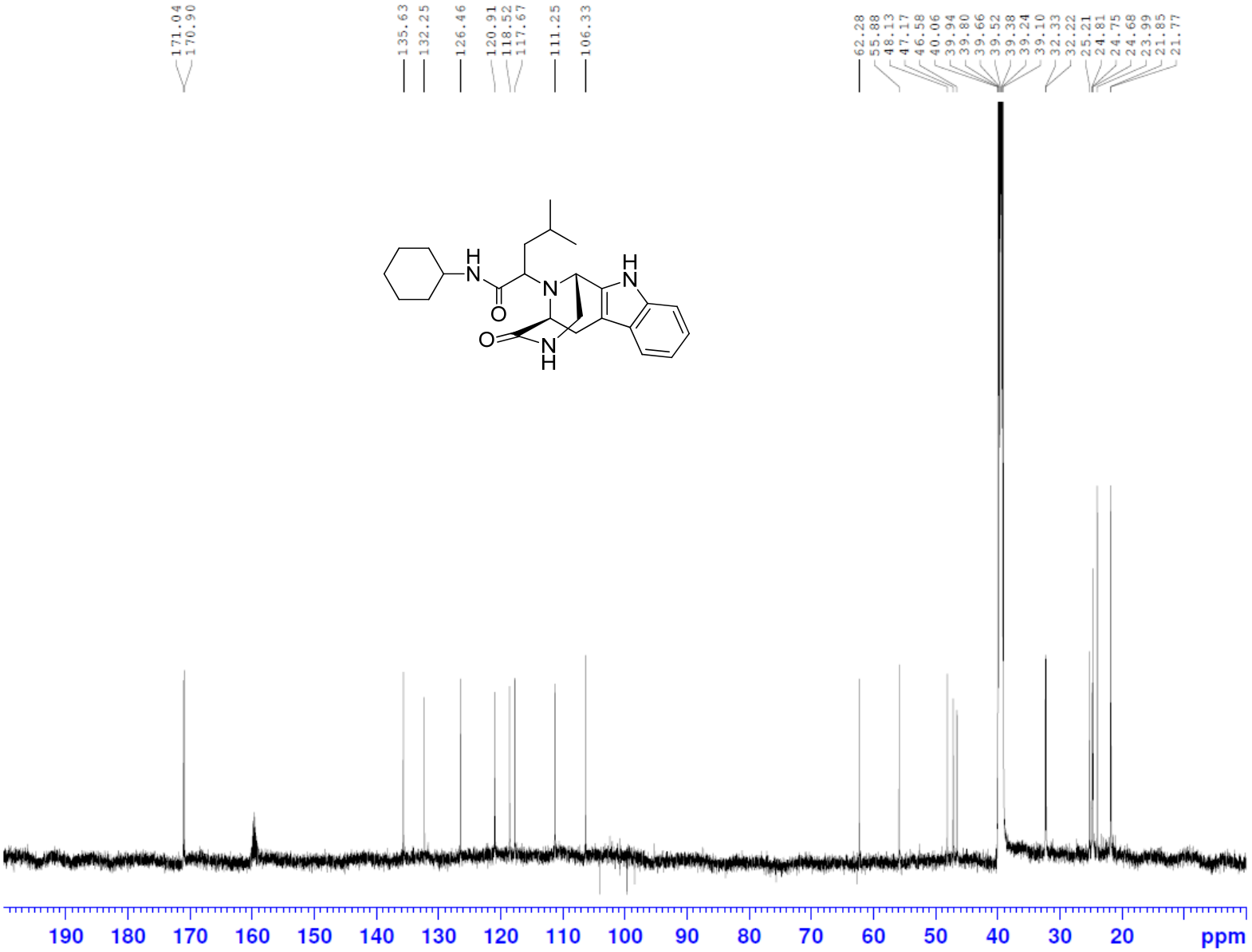
Compound-35


1: Scan AP+
TIC
5.53e7
4.97;437.26
1: Scan AP+
1.89e7
437.26
438.27
439.25
240.35
290.09
310.19
324.12
389.19
435.23
451.29
495.16
553.16
564.33
594.64
648.44
680.01
m/z
Time
Chemical Formula: C25H32N4O3
Molecular Weight: 436.55

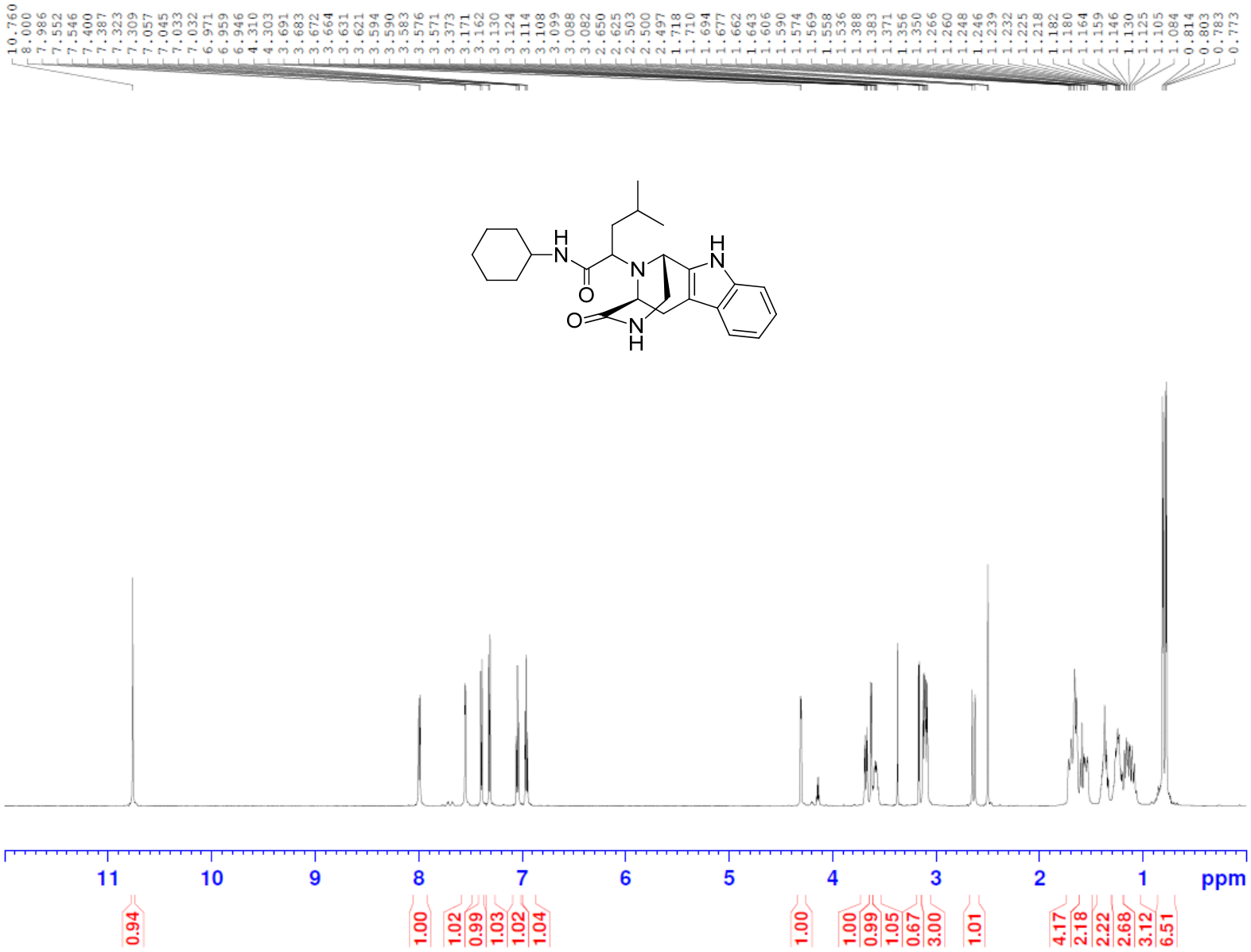
Compound-36, 1st diastereomer



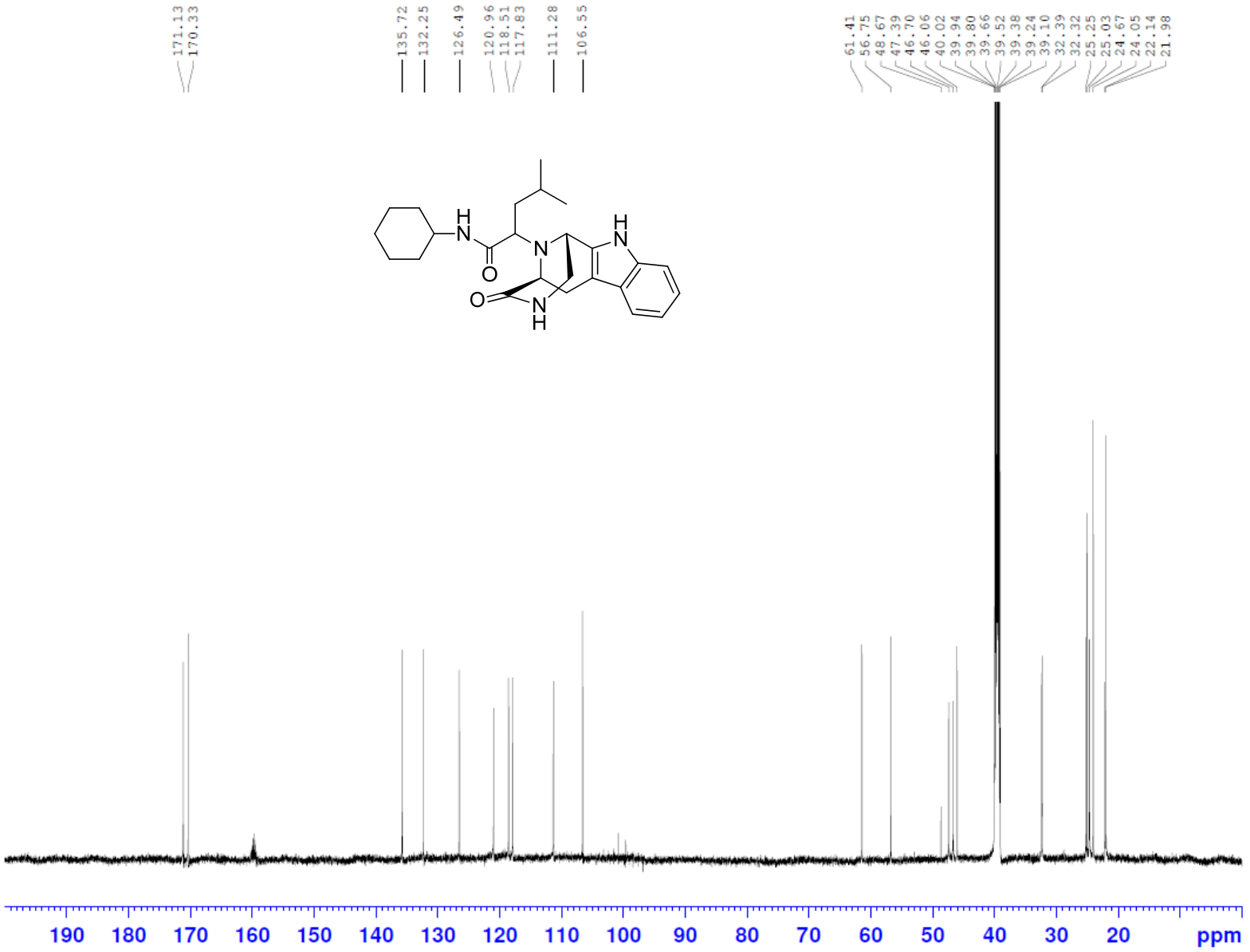
Compound-36, 1st diastereomer

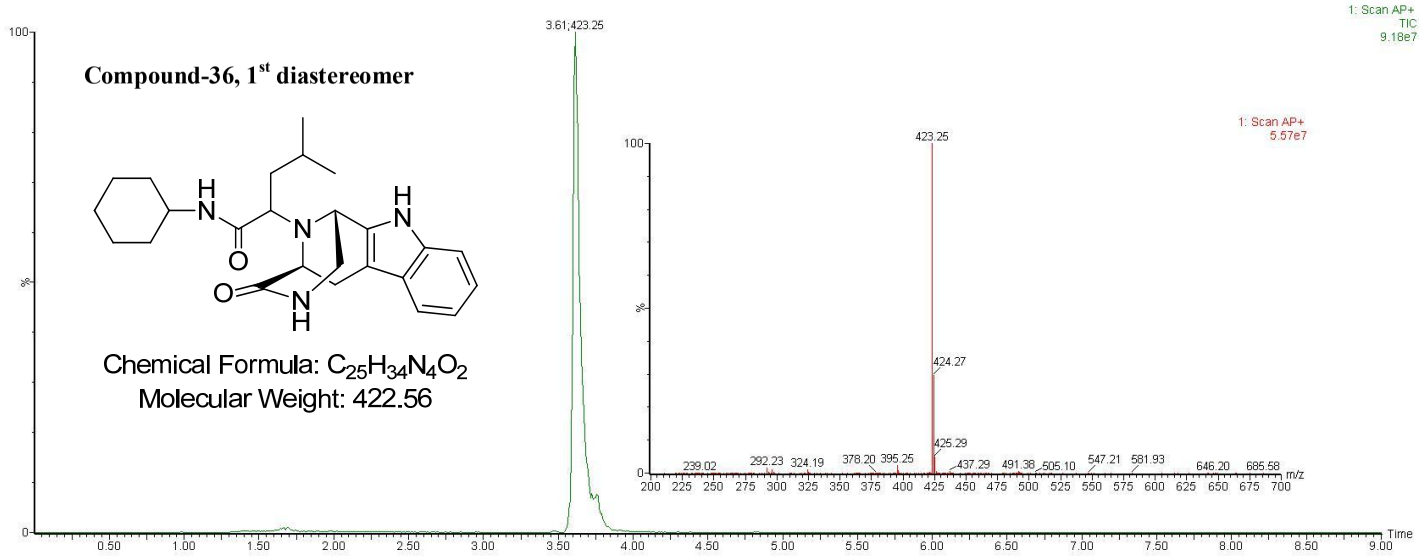


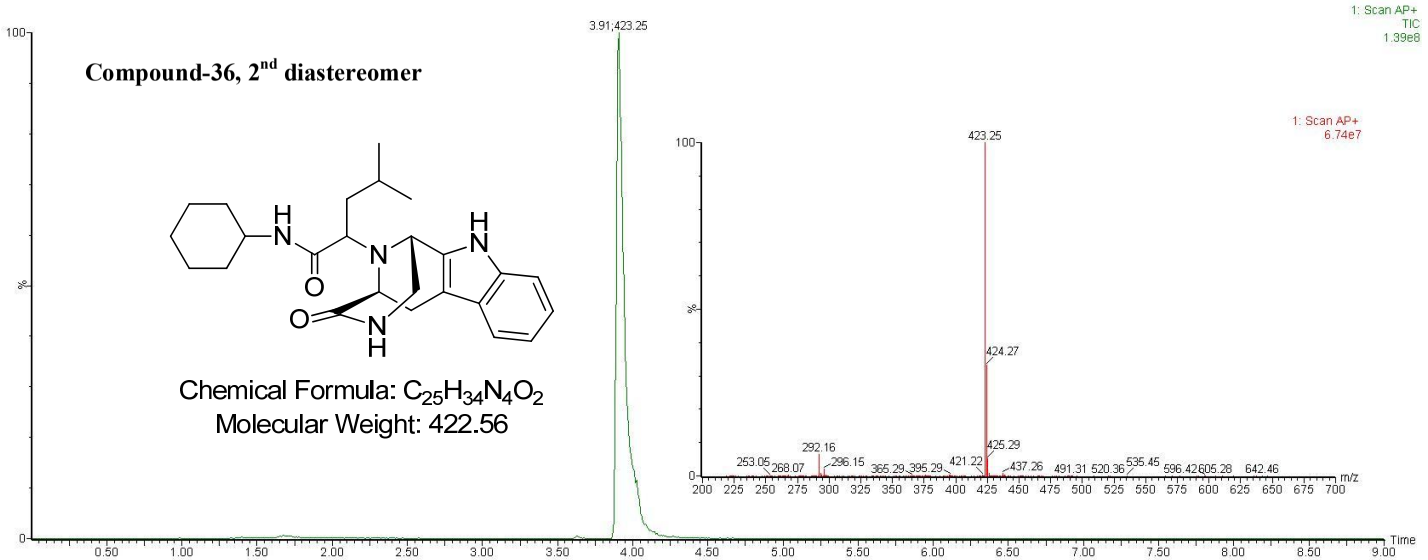
Compound-36, 2nd diastereomer



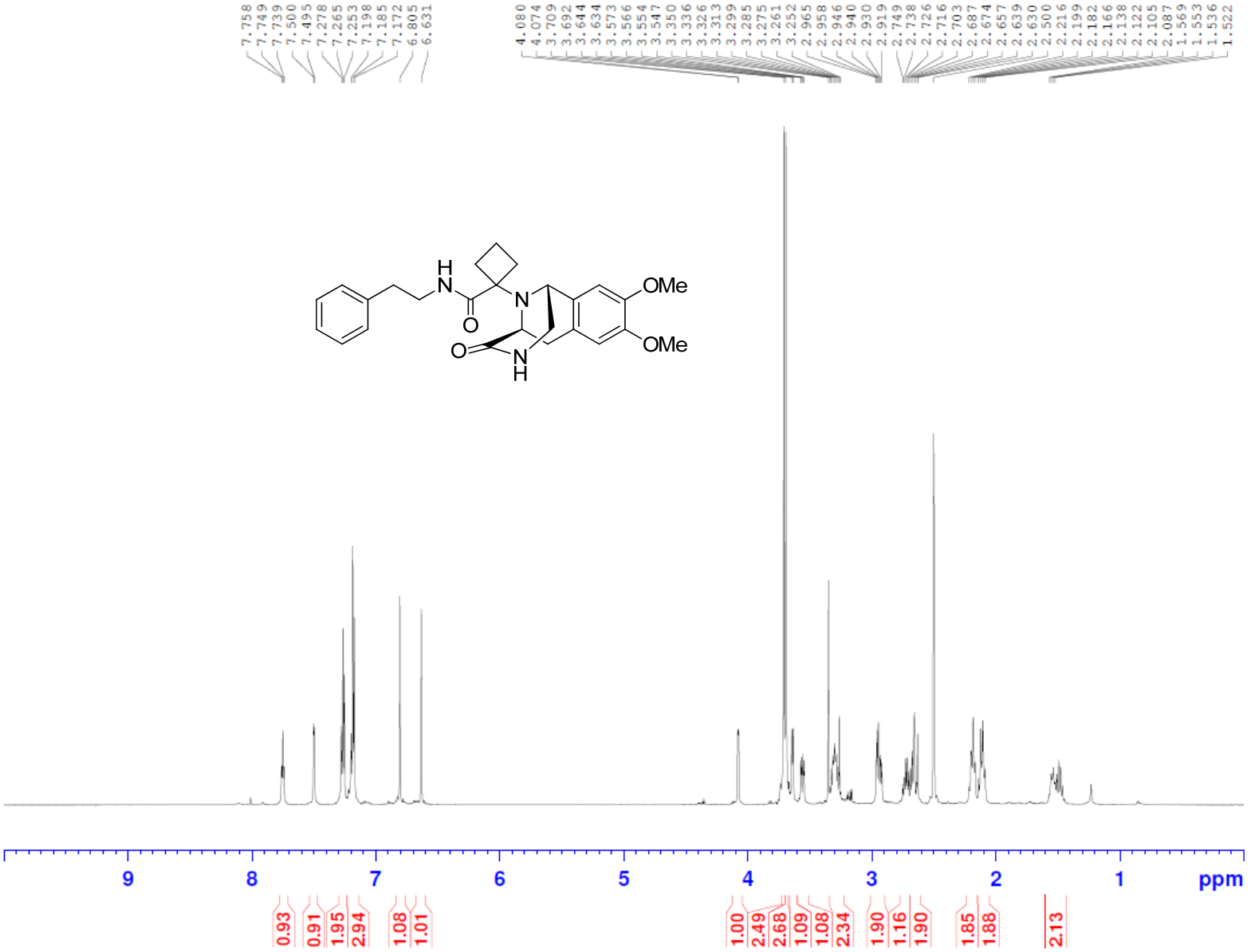
Compound-36, 2nd diastereomer



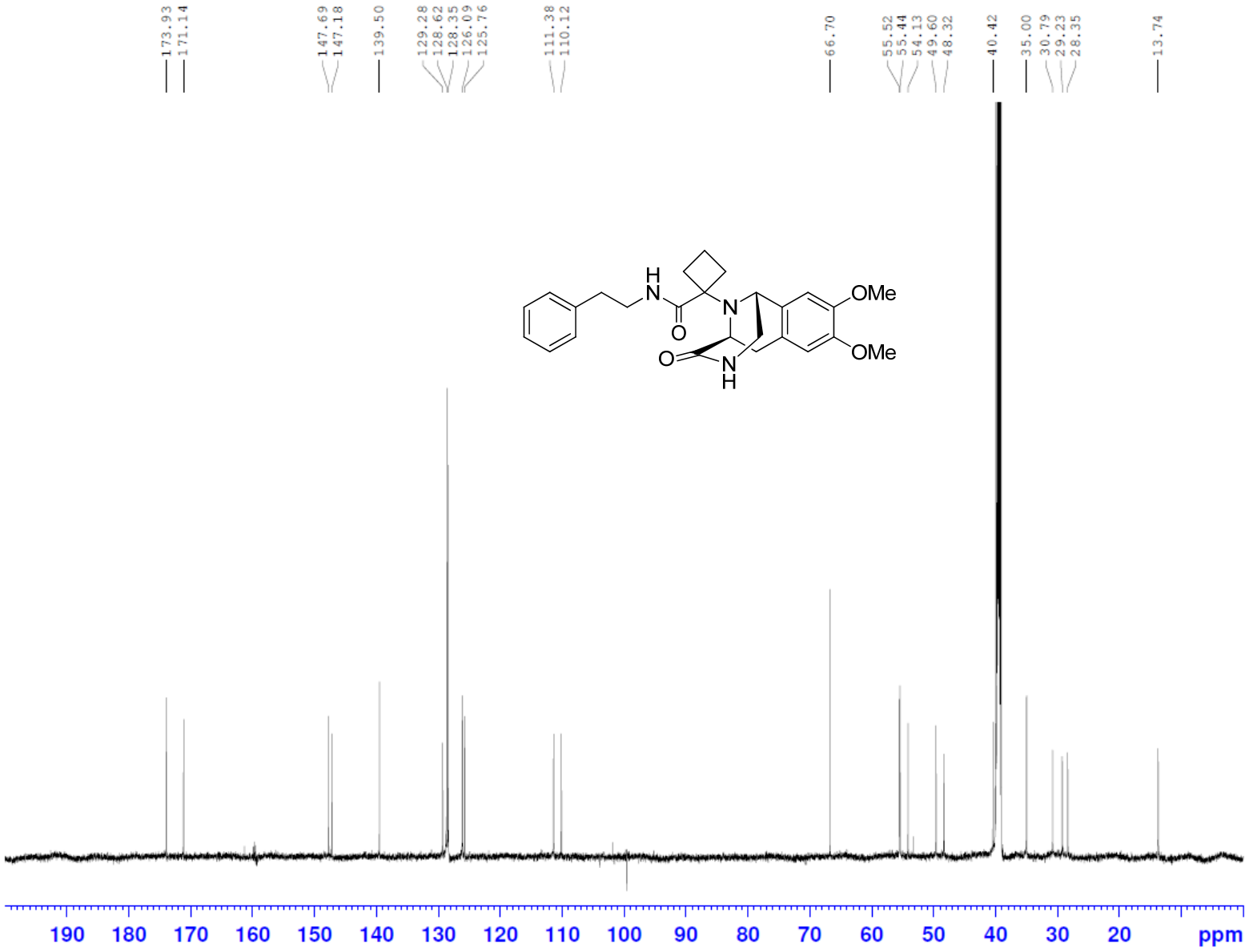

Compound-36, 1st diastereomer
Chemical Formula: C25H34N4O2
Molecular Weight: 422.56
3.61;423.25
1: Scan AP+
TIC
9.18e7
1: Scan AP+
5.57e7
423.25
424.27
425.29
Time
m/z


Compound-36, 2nd diastereomer
Chemical Formula: C25H34N4O2
Molecular Weight: 422.56
3.91;423.25
1: Scan AP+
TIC
1.39e8
1: Scan AP+
6.74e7
423.25
424.27
425.29
Time
m/z

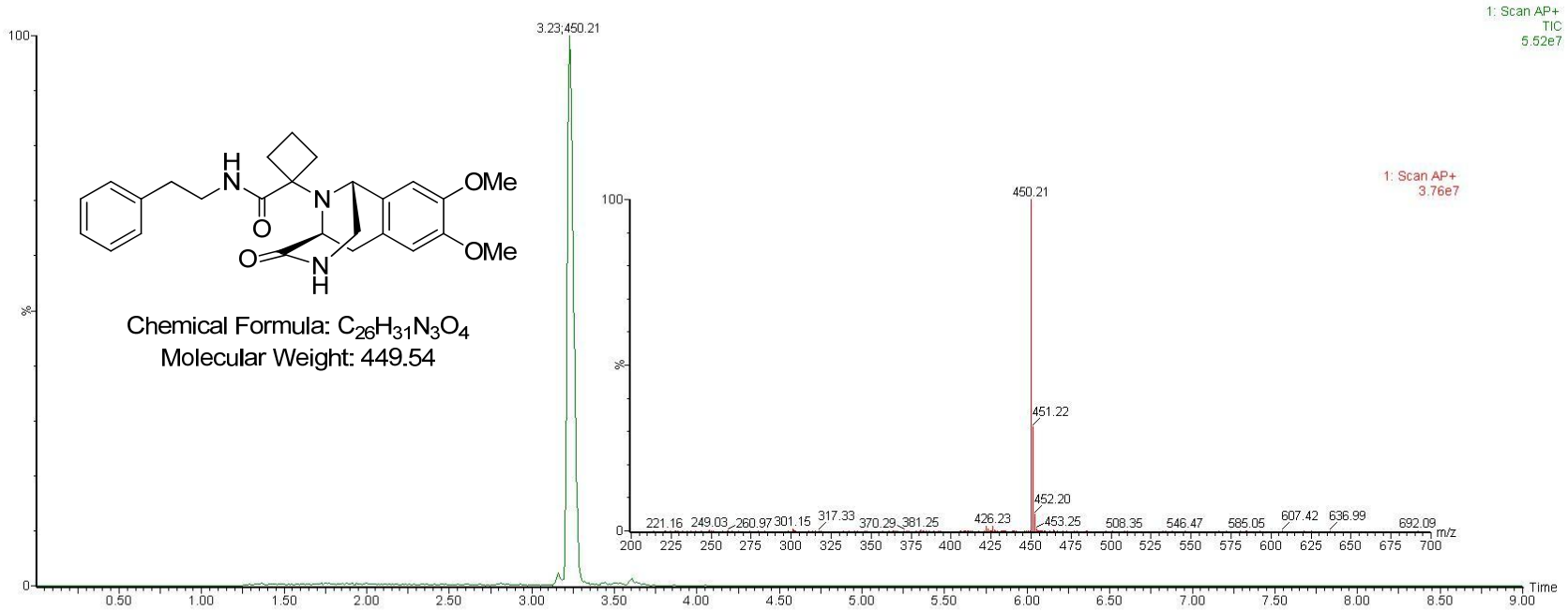
Compound-40


7.758
7.749
7.739
7.500
7.495
7.278
7.265
7.253
7.198
7.185
7.172
6.805
6.631
4.080
4.074
3.709
3.692
3.644
3.634
3.573
3.566
3.554
3.547
3.350
3.336
3.326
3.313
3.299
3.285
3.275
3.261
3.252
2.965
2.958
2.946
2.940
2.930
2.919
2.749
2.738
2.726
2.716
2.703
2.687
2.674
2.657
2.639
2.630
2.500
2.216
2.199
2.182
2.166
2.138
2.122
2.105
2.087
1.569
1.553
1.536
1.522
H
N
O
O
N
N
H
OMe
OMe
9
8
7
6
5
4
3
2
1
ppm
0.93
0.91
1.95
2.94
1.08
1.01
1.00
2.49
2.68
1.09
1.08
2.34
1.90
1.16
1.90
1.85
1.88
2.13

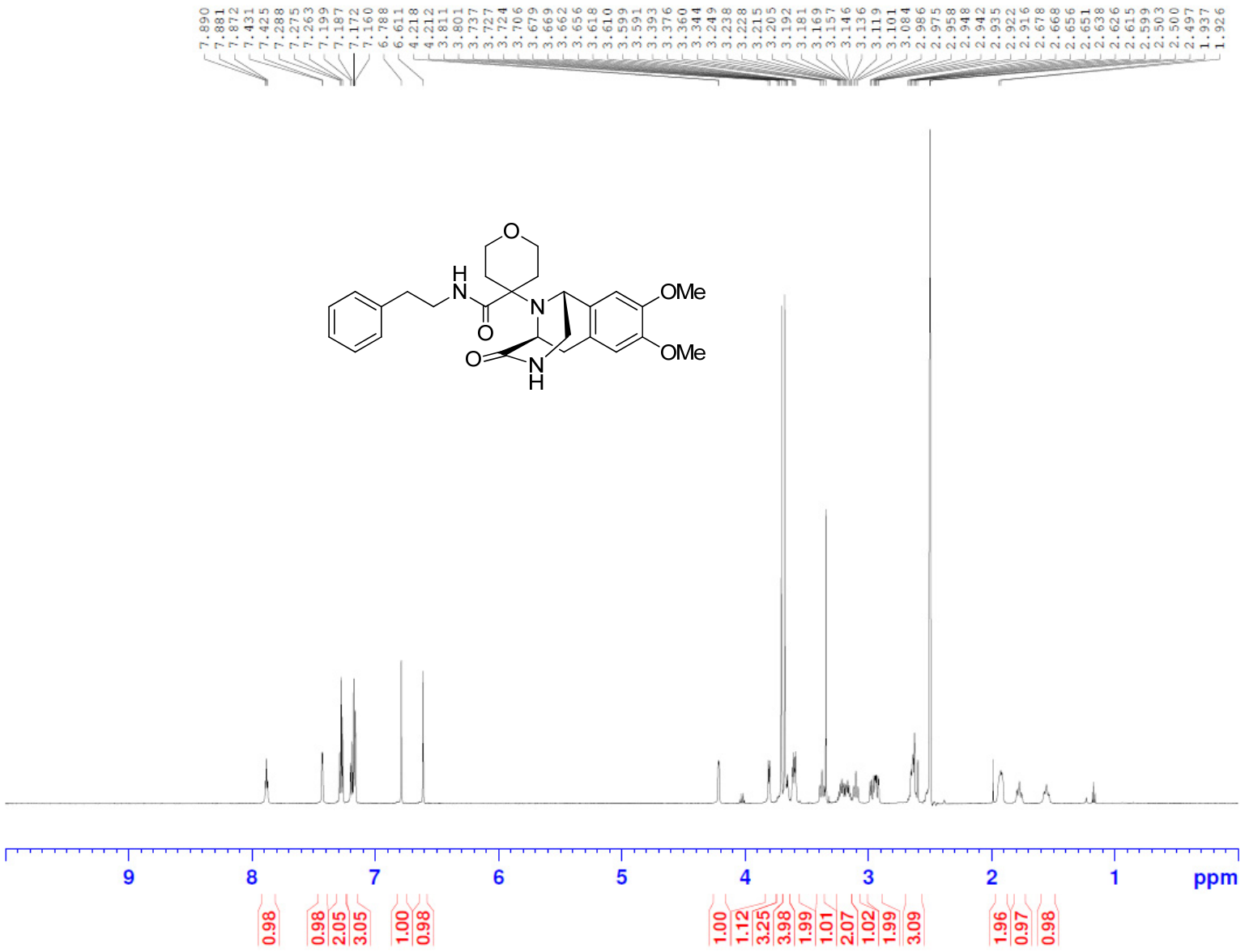
Compound-40


173.93
171.14
147.69
147.18
139.50
129.28
128.62
128.35
126.09
125.76
111.38
110.12
66.70
55.52
55.44
54.13
49.60
48.32
40.42
35.00
30.79
29.23
28.35
13.74
H
N
O
N
O
N
H
OMe
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

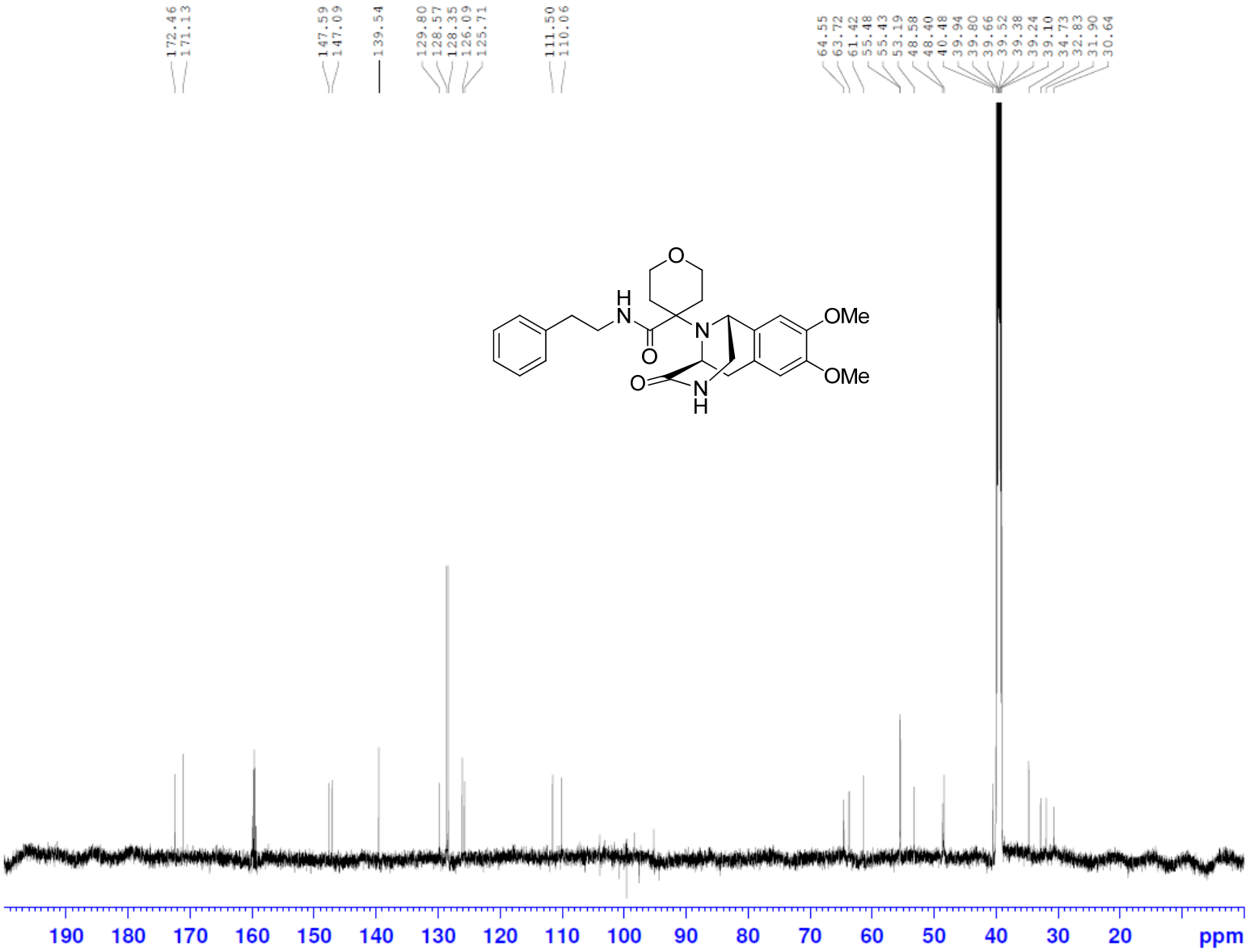
Compound-40


1: Scan AP+
TIC
5.52e7
3.23;450.21
100
%
0
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
Time
H
N
O
O
N
N
H
OMe
OMe
Chemical Formula: C26H31N3O4
Molecular Weight: 449.54
1: Scan AP+
3.76e7
450.21
451.22
452.20
221.16
249.03
260.97
301.15
317.33
370.29
381.25
426.23
453.25
508.35
546.47
585.05
607.42
636.99
692.09
m/z
200
225
250
275
300
325
350
375
400
425
450
475
500
525
550
575
600
625
650
675
700

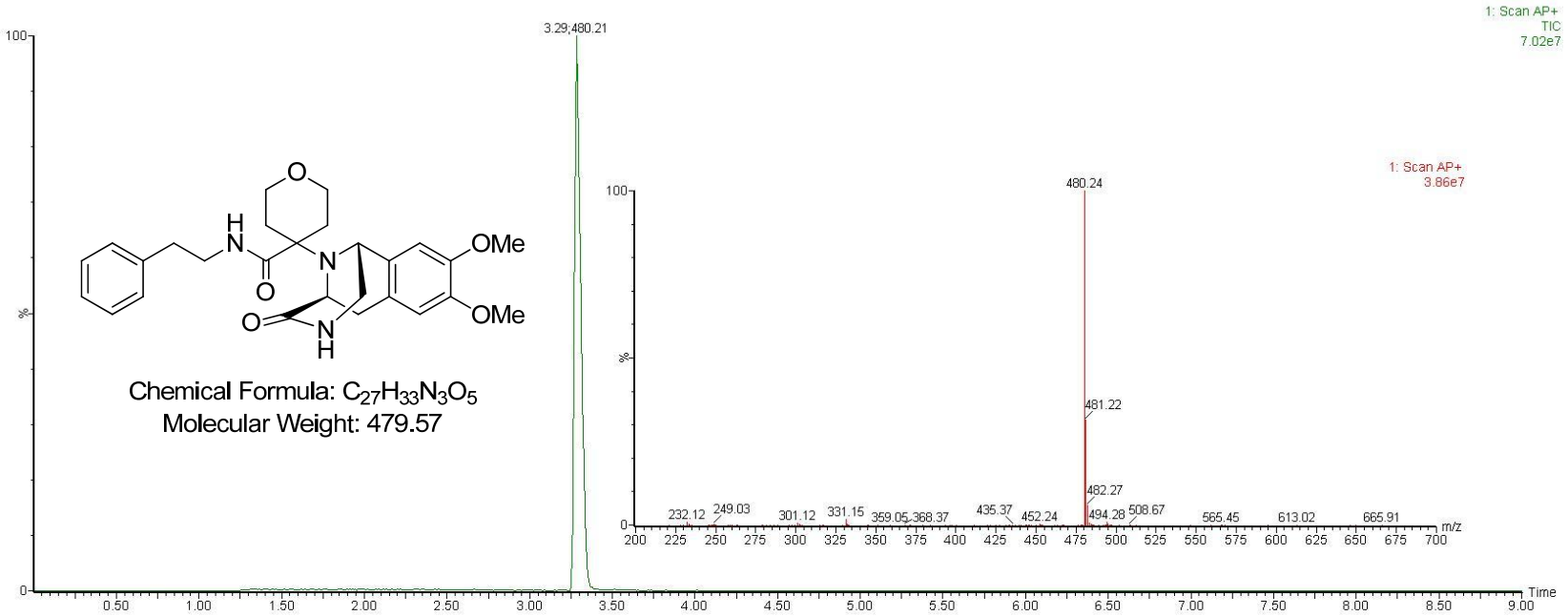
Compound-41


7.890
7.881
7.872
7.431
7.425
7.288
7.275
7.263
7.199
7.187
7.172
7.160
6.788
6.611
4.218
4.212
3.811
3.801
3.737
3.727
3.724
3.706
3.679
3.669
3.662
3.656
3.618
3.610
3.599
3.591
3.393
3.376
3.360
3.344
3.249
3.238
3.228
3.215
3.205
3.192
3.181
3.169
3.157
3.146
3.136
3.119
3.101
3.084
2.986
2.975
2.958
2.948
2.942
2.935
2.922
2.916
2.678
2.668
2.656
2.651
2.638
2.626
2.615
2.599
2.503
2.500
2.497
1.937
1.926
O
H
N
O
N
OMe
OMe
O
N
H
9
8
7
6
5
4
3
2
1
ppm
0.98
0.98
2.05
3.05
1.00
0.98
1.00
1.12
3.25
3.98
1.99
1.01
2.07
1.02
1.99
3.09
1.96
0.97
0.98

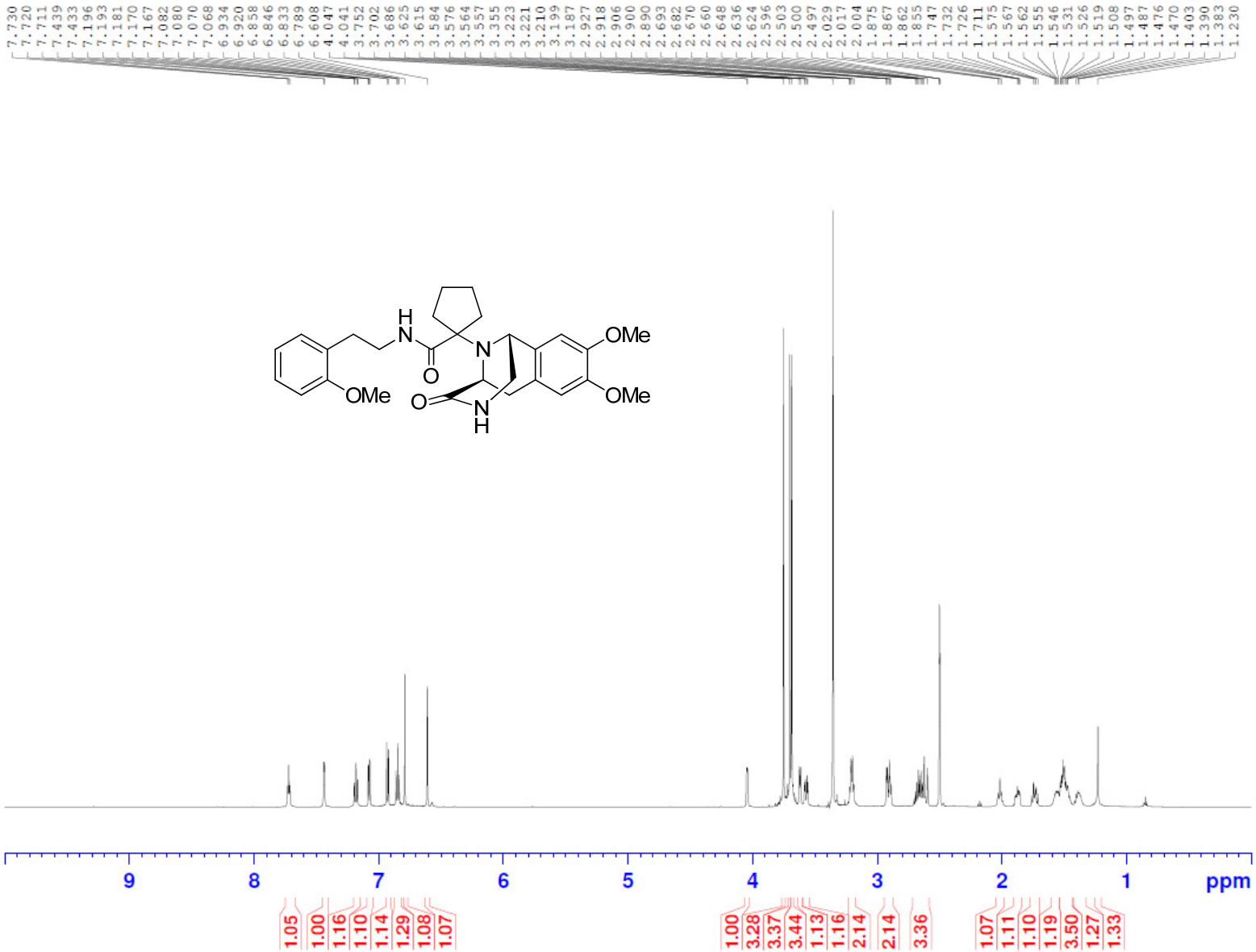
Compound-41


172.46
171.13
147.59
147.09
139.54
129.80
128.57
128.35
126.09
125.71
111.50
110.06
64.55
63.72
61.42
55.48
55.43
53.19
48.58
48.40
40.48
39.94
39.80
39.66
39.52
39.38
39.24
39.10
34.73
32.83
31.90
30.64
O
H
N
O
N
OMe
OMe
O
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

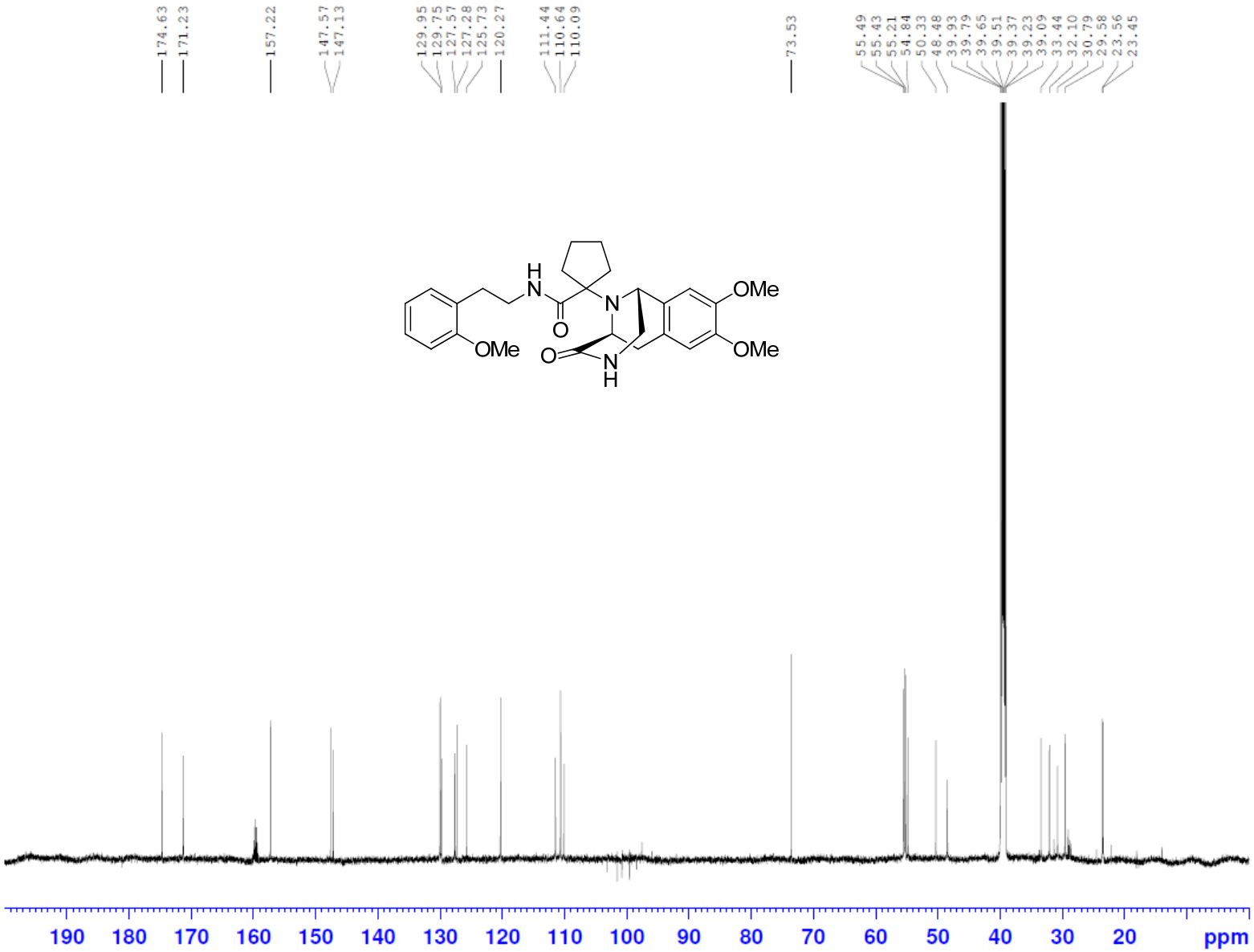
Compound-41


1: Scan AP+
TIC
7.02e7
3.29;480.21
100
%
0
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
Time
O
H
N
O
N
OMe
OMe
O
N
H
Chemical Formula: C27H33N3O5
Molecular Weight: 479.57
1: Scan AP+
3.86e7
480.24
481.22
482.27
232.12
249.03
301.12
331.15
359.05
368.37
435.37
452.24
494.28
508.67
565.45
613.02
665.91
m/z

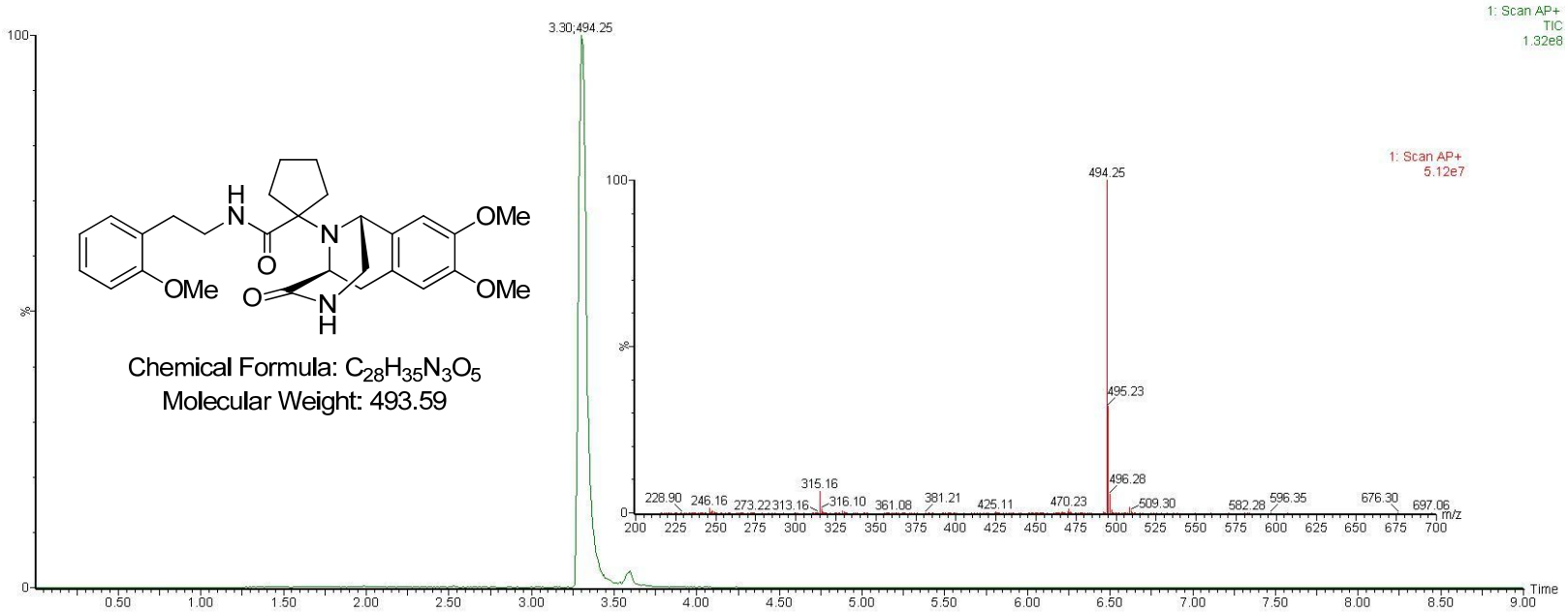
Compound-42


7.730
7.720
7.711
7.439
7.433
7.196
7.193
7.181
7.170
7.167
7.082
7.080
7.070
7.068
6.934
6.920
6.858
6.846
6.833
6.789
6.608
4.047
4.041
3.752
3.702
3.686
3.625
3.615
3.584
3.576
3.564
3.557
3.355
3.223
3.221
3.210
3.199
3.187
2.927
2.918
2.906
2.900
2.890
2.693
2.682
2.670
2.660
2.648
2.636
2.624
2.596
2.503
2.500
2.497
2.029
2.017
2.004
1.875
1.867
1.862
1.855
1.747
1.732
1.726
1.711
1.575
1.567
1.562
1.555
1.546
1.531
1.526
1.519
1.508
1.497
1.487
1.476
1.470
1.403
1.390
1.383
1.230
H
N
O
N
OMe
OMe
O
N
H
OMe
9
8
7
6
5
4
3
2
1
ppm
1.05
1.00
1.16
1.10
1.14
1.29
1.08
1.07
1.00
3.28
3.37
3.44
1.13
1.16
2.14
2.14
3.36
1.07
1.11
1.10
1.19
3.50
1.27
1.33

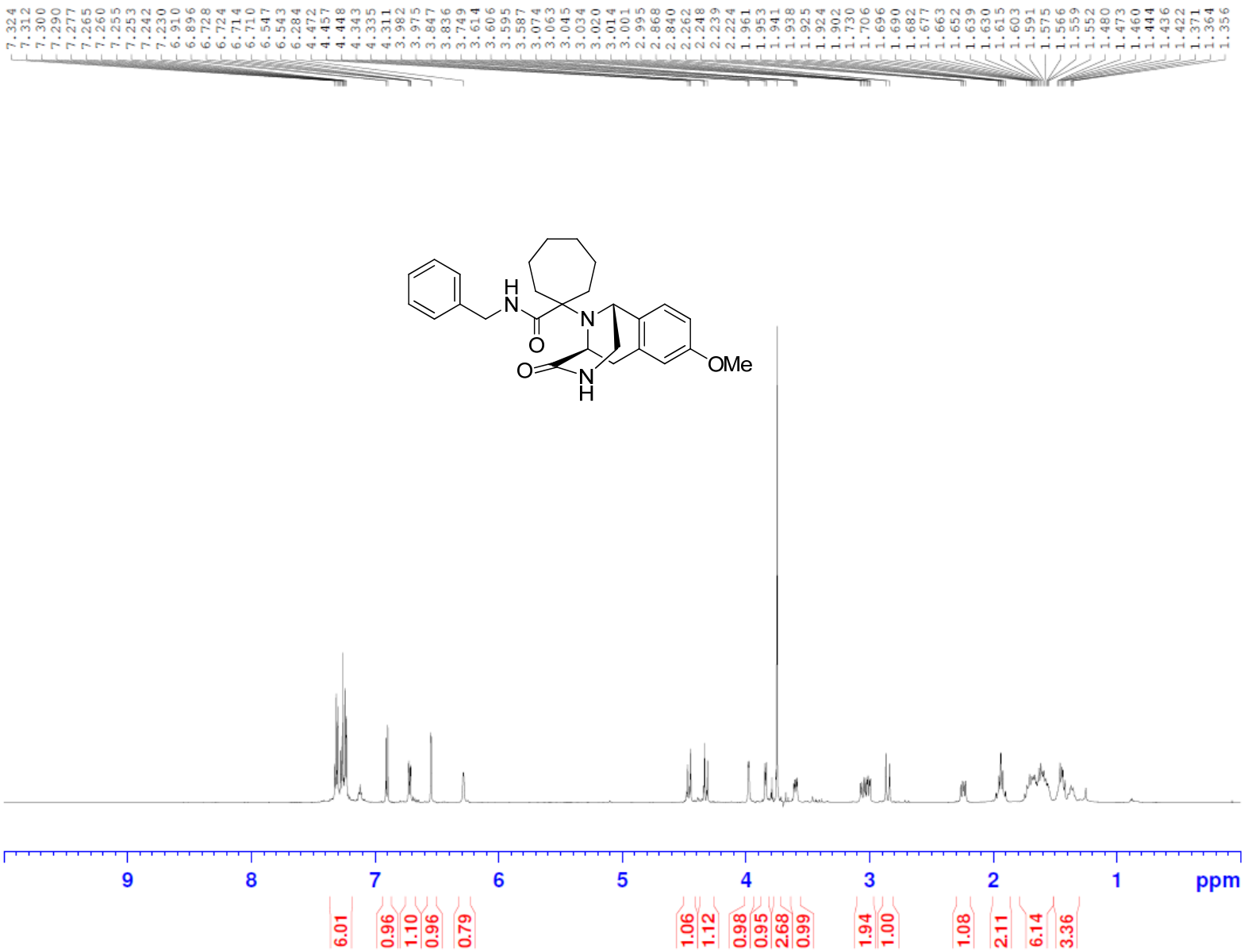
Compound-42


174.63
171.23
157.22
147.57
147.13
129.95
129.75
127.57
127.28
125.73
120.27
111.44
110.64
110.09
73.53
55.49
55.43
55.21
54.84
50.33
48.48
39.93
39.79
39.65
39.51
39.37
39.23
39.09
33.44
32.10
30.79
29.58
23.56
23.45
H
N
O
N
OMe
OMe
O
N
H
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

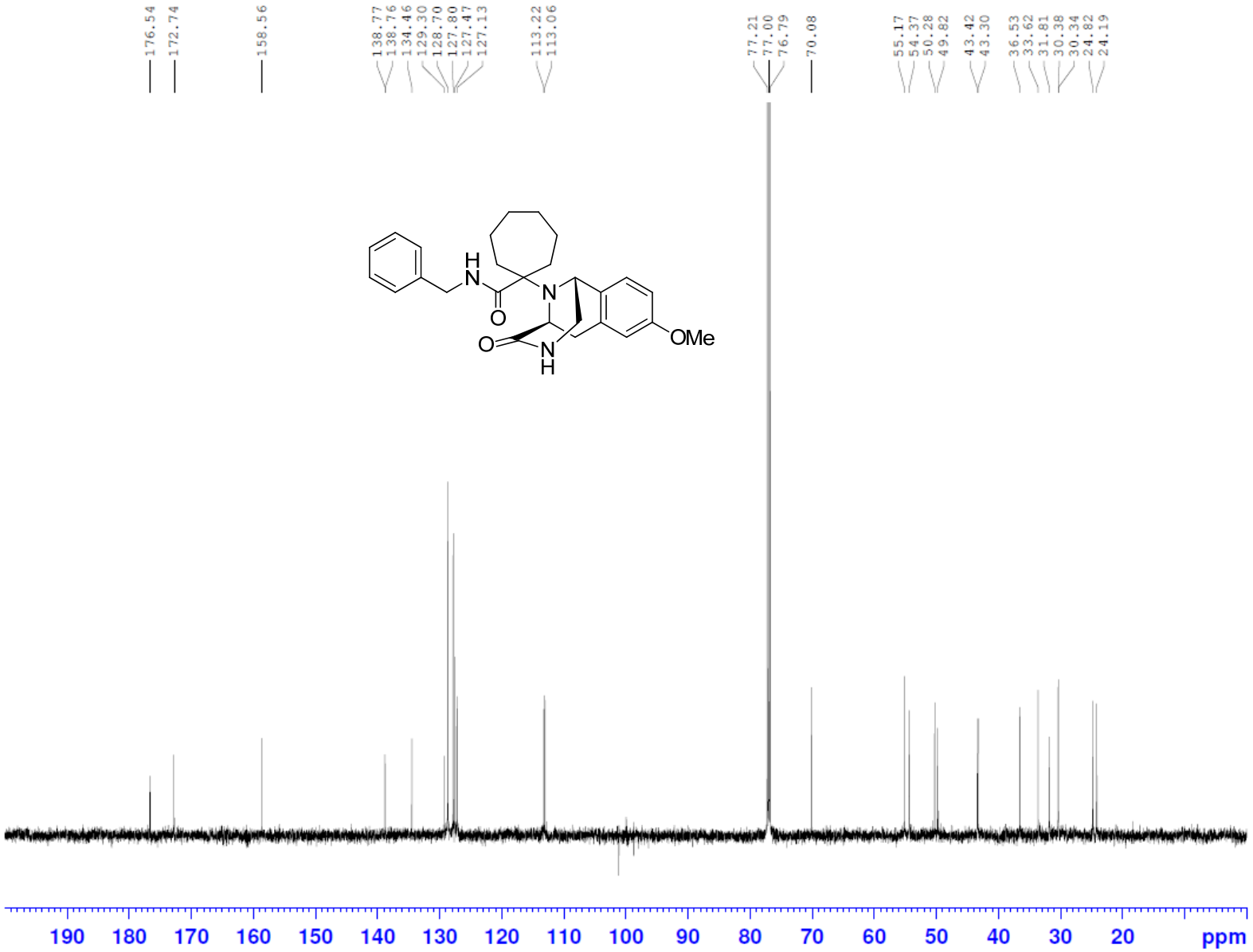
Compound-42


1: Scan AP+
TIC
1.32e8
3.30;494.25
100
%
0
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
Time
H
N
O
N
OMe
OMe
O
N
H
OMe
Chemical Formula: C28H35N3O5
Molecular Weight: 493.59
1: Scan AP+
5.12e7
494.25
495.23
496.28
315.16
316.10
228.90
246.16
273.22
313.16
361.08
381.21
425.11
470.23
509.30
582.28
596.35
676.30
697.06
m/z
200
225
250
275
300
325
350
375
400
425
450
475
500
525
550
575
600
625
650
675
700

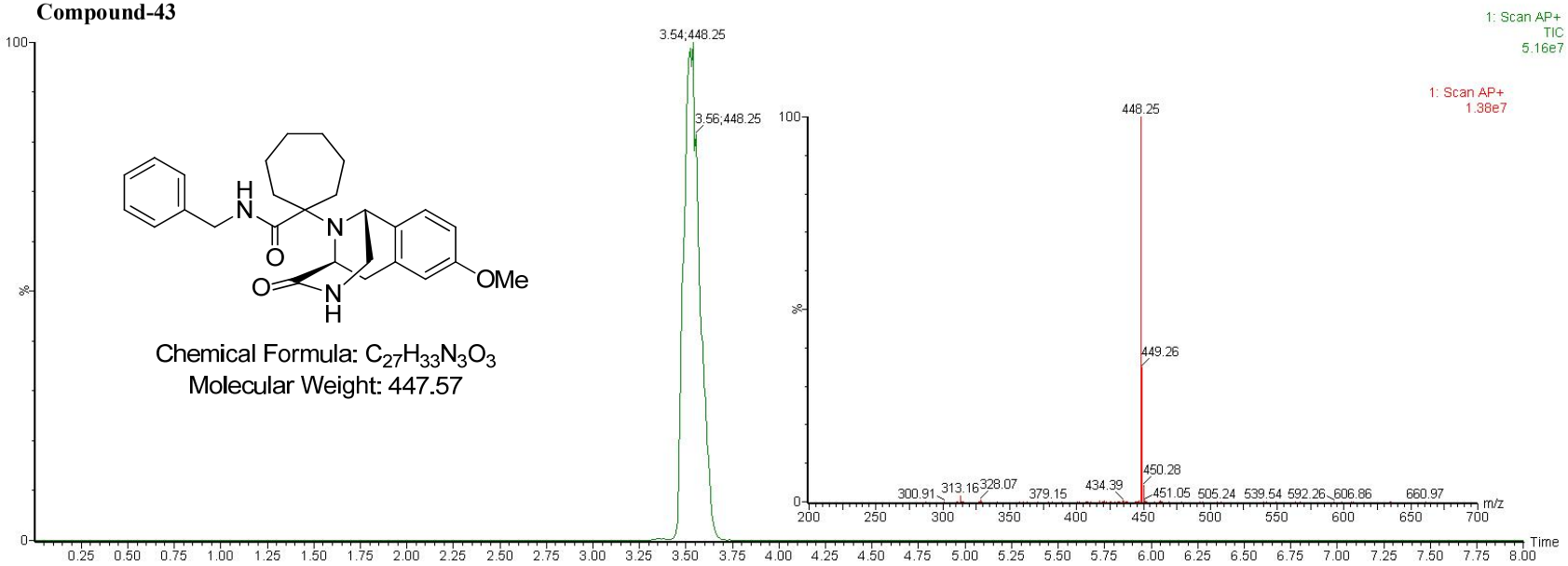
Compound-43


7.324
7.312
7.300
7.290
7.277
7.265
7.260
7.255
7.253
7.242
7.230
6.910
6.896
6.728
6.724
6.714
6.710
6.547
6.543
6.284
4.472
4.457
4.448
4.343
4.335
4.311
3.982
3.975
3.847
3.836
3.749
3.614
3.606
3.595
3.587
3.074
3.063
3.045
3.034
3.020
3.014
3.001
2.995
2.868
2.840
2.262
2.248
2.239
2.224
1.961
1.953
1.941
1.938
1.925
1.924
1.902
1.730
1.706
1.696
1.690
1.682
1.677
1.663
1.652
1.639
1.630
1.615
1.603
1.591
1.575
1.566
1.559
1.552
1.480
1.473
1.460
1.444
1.436
1.422
1.371
1.364
1.356
H
N
O
N
O
N
H
OMe
9
8
7
6
5
4
3
2
1
ppm
6.01
0.96
1.10
0.96
0.79
1.06
1.12
0.98
0.95
2.68
0.99
1.94
1.00
1.08
2.11
6.14
3.36

Compound-43

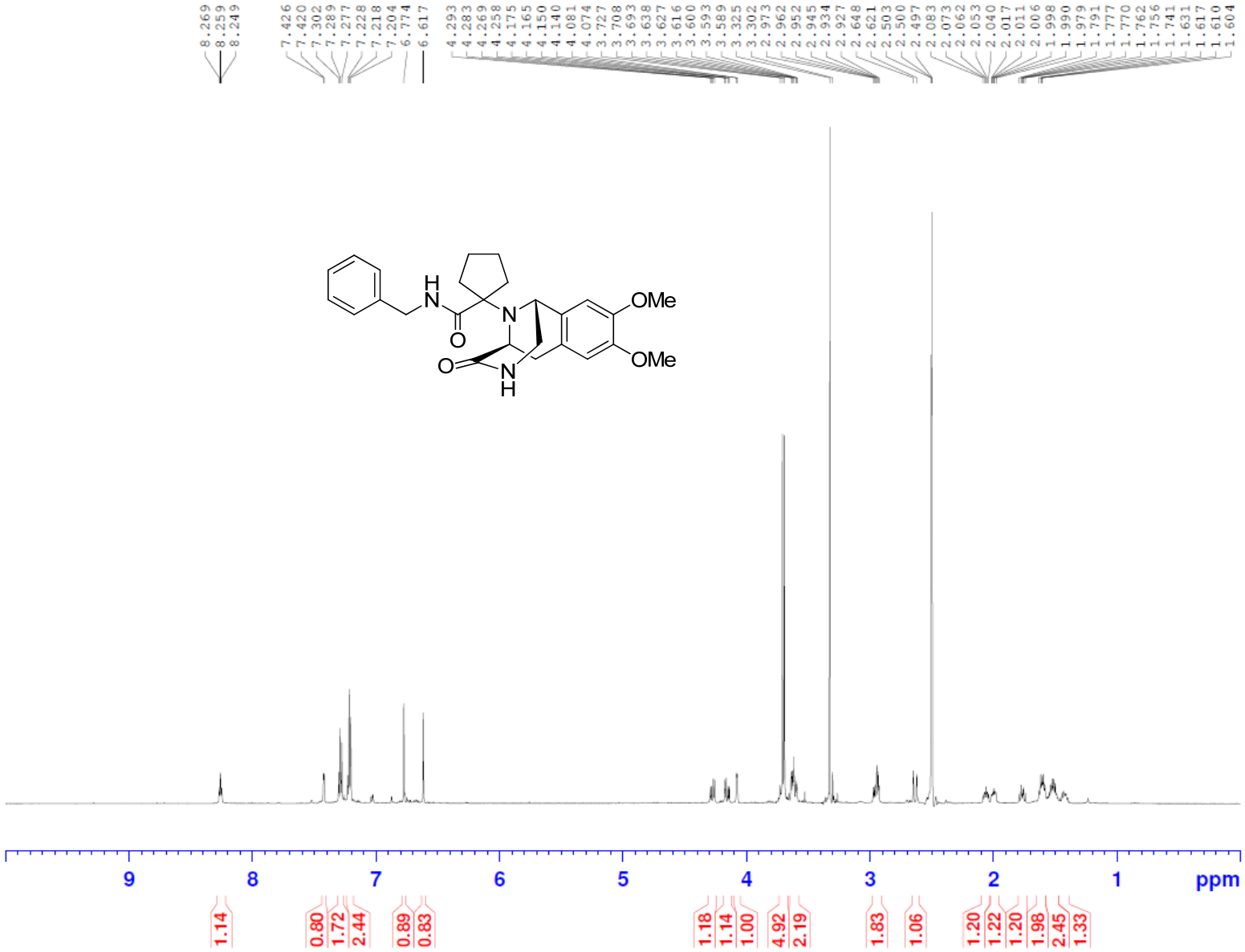

176.54
172.74
158.56
138.77
138.76
134.46
129.30
128.70
127.80
127.47
127.13
113.22
113.06
77.21
77.00
76.79
70.08
55.17
54.37
50.28
49.82
43.42
43.30
36.53
33.62
31.81
30.38
30.34
24.82
24.19
H
N
O
N
O
N
H
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

Compound-43

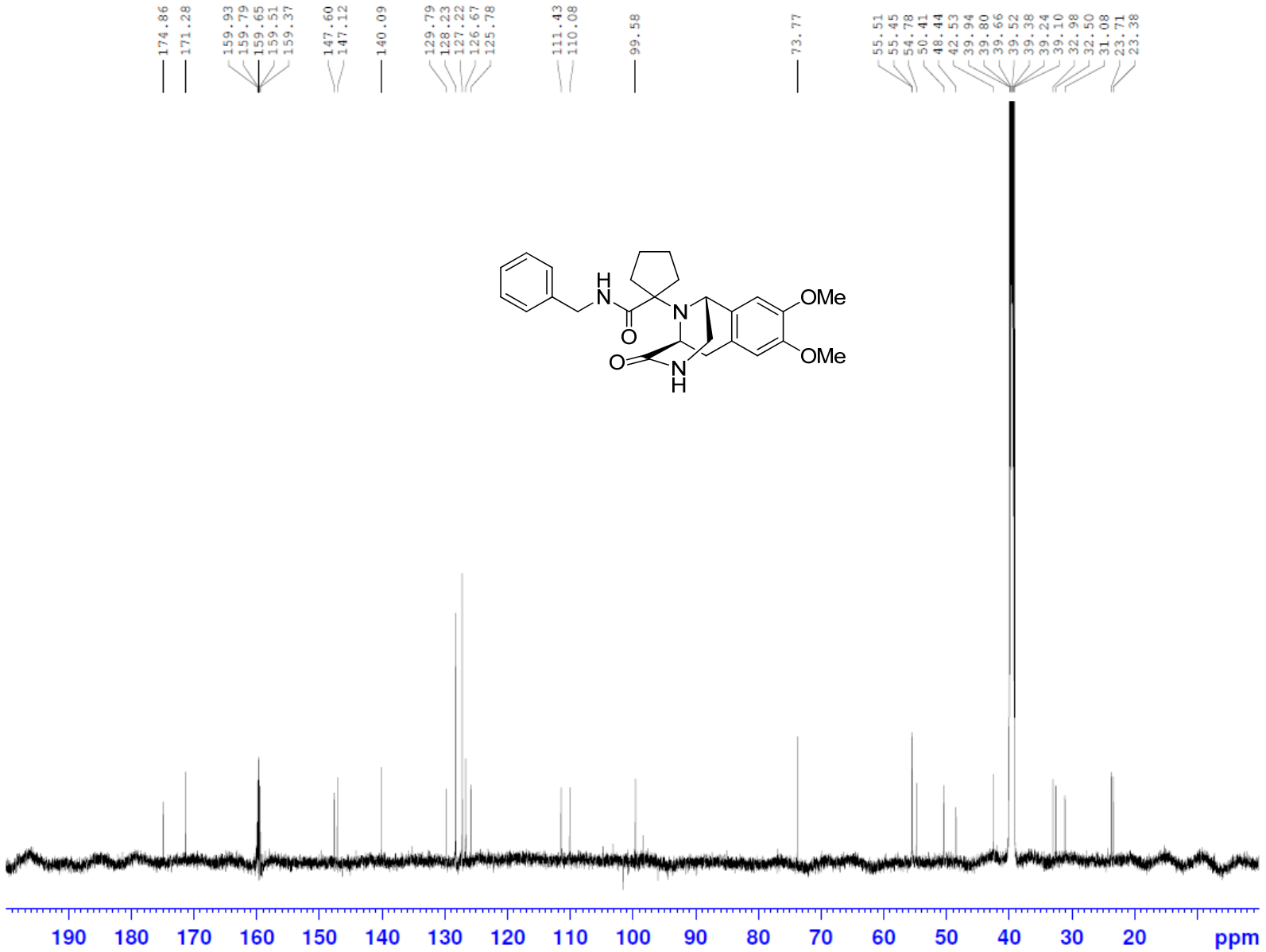


Chemical Formula: $C_{27}H_{33}N_3O_3$
Molecular Weight: 447.57

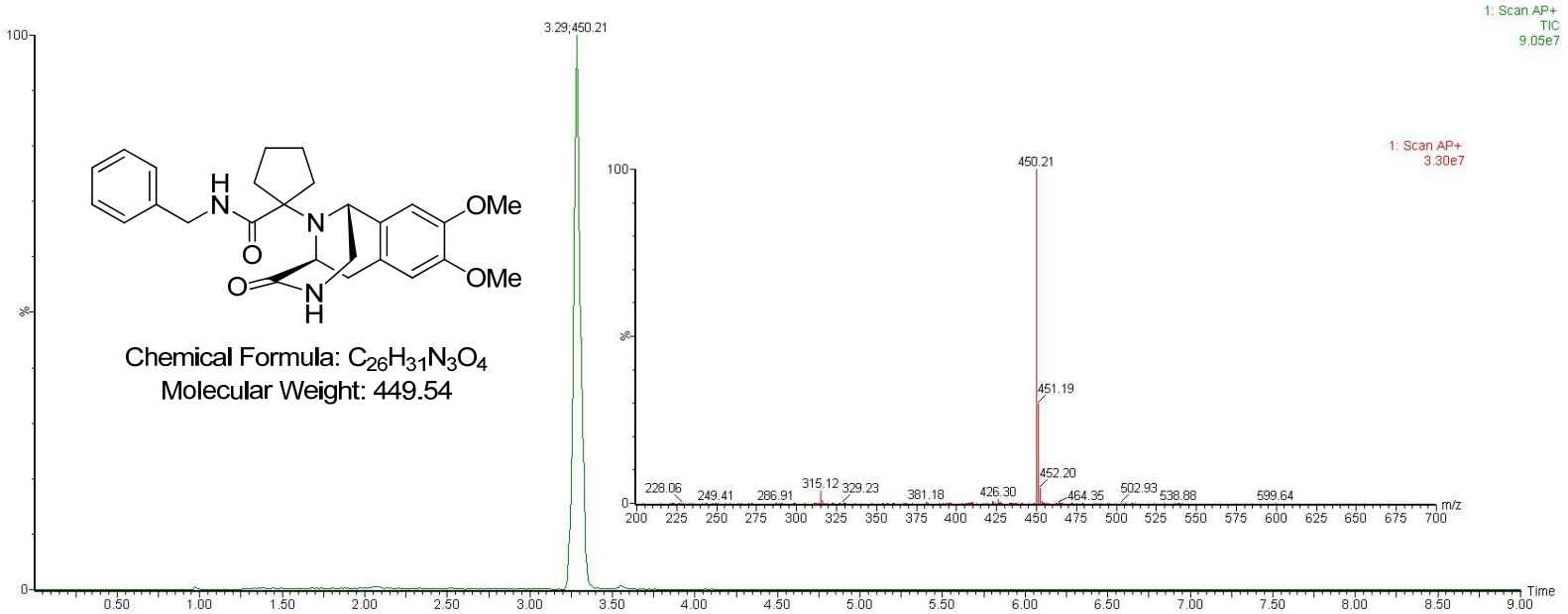
Compound-44


8.269
8.259
8.249
7.426
7.420
7.302
7.289
7.277
7.228
7.218
7.204
6.774
6.617
4.293
4.283
4.269
4.258
4.175
4.165
4.150
4.140
4.081
4.074
3.727
3.708
3.693
3.638
3.627
3.616
3.600
3.593
3.589
3.325
3.302
2.973
2.962
2.952
2.945
2.934
2.927
2.648
2.621
2.503
2.500
2.497
2.083
2.073
2.062
2.053
2.040
2.017
2.011
2.006
1.998
1.990
1.979
1.791
1.777
1.770
1.762
1.756
1.741
1.631
1.617
1.610
1.604
H
N
O
O
N
H
OMe
OMe
9
8
7
6
5
4
3
2
1
ppm
1.14
0.80
1.72
2.44
0.89
0.83
1.18
1.14
1.00
4.92
2.19
1.83
1.06
1.20
1.22
1.20
1.98
2.45
1.33

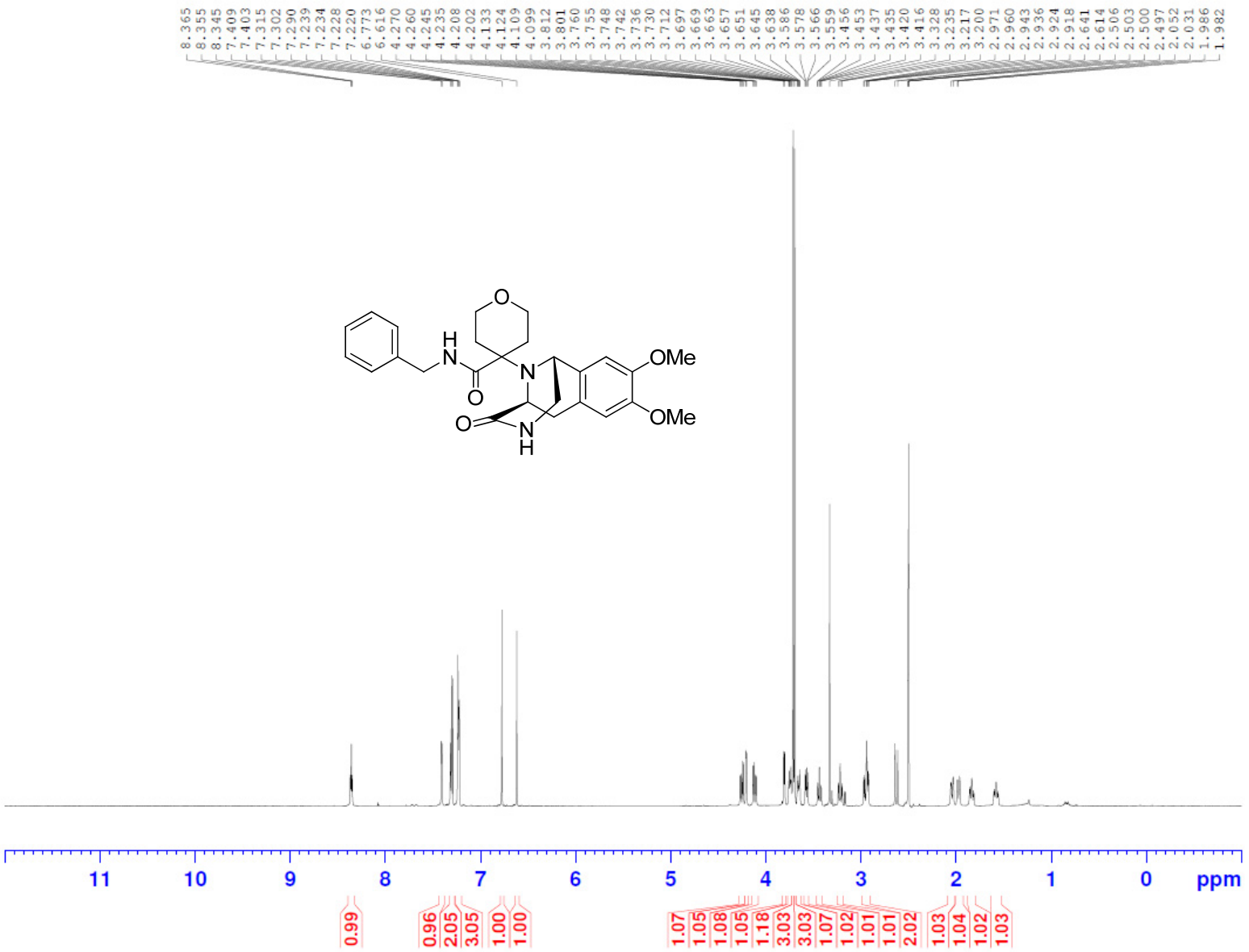
Compound-44


174.86
171.28
159.93
159.79
159.65
159.51
159.37
147.60
147.12
140.09
129.79
128.23
127.22
126.67
125.78
111.43
110.08
99.58
73.77
55.51
55.45
54.78
50.41
48.44
42.53
39.94
39.80
39.66
39.52
39.38
39.24
39.10
32.98
32.50
31.08
23.71
23.38
H
N
O
N
O
N
H
OMe
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

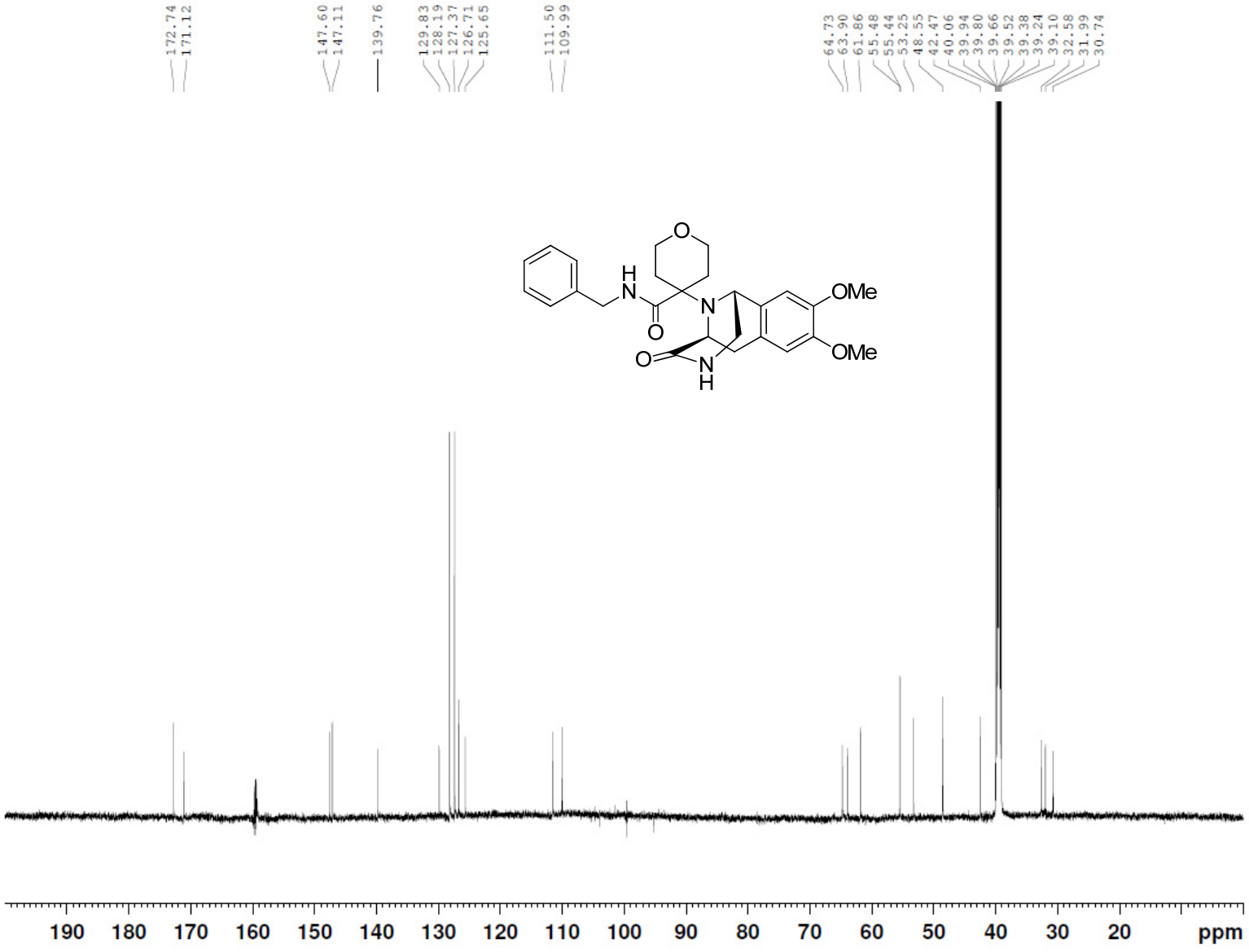
Compound-44


1: Scan AP+
TIC
9.05e7
3.29;450.21
100
%
0
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
Time
H
N
O
N
O
N
H
OMe
OMe
Chemical Formula: C26H31N3O4
Molecular Weight: 449.54
1: Scan AP+
3.30e7
450.21
451.19
452.20
228.06
249.41
286.91
315.12
329.23
381.18
426.30
464.35
502.93
538.88
599.64
200
225
250
275
300
325
350
375
400
425
450
475
500
525
550
575
600
625
650
675
700
m/z

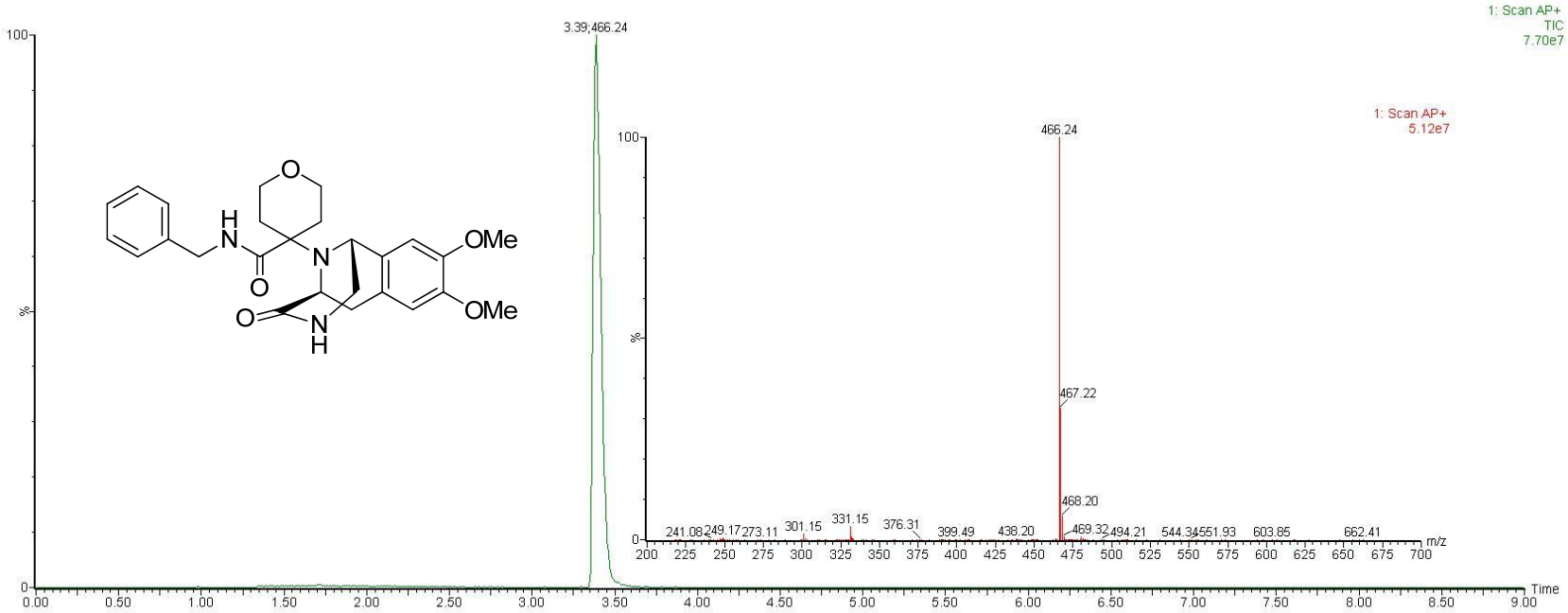
Compound-45


8.365
8.355
8.345
7.409
7.403
7.315
7.302
7.290
7.239
7.234
7.228
7.220
6.773
6.616
4.270
4.260
4.245
4.235
4.208
4.202
4.133
4.124
4.109
4.099
3.812
3.801
3.760
3.755
3.748
3.742
3.736
3.730
3.712
3.697
3.669
3.663
3.657
3.651
3.645
3.638
3.586
3.578
3.566
3.559
3.456
3.453
3.437
3.435
3.420
3.416
3.328
3.235
3.217
3.200
2.971
2.960
2.943
2.936
2.924
2.918
2.641
2.614
2.506
2.503
2.500
2.497
2.052
2.031
1.986
1.982
H
N
O
O
N
O
N
H
OMe
OMe
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.99
0.96
2.05
3.05
1.00
1.00
1.07
1.05
1.08
1.05
1.18
3.03
3.03
1.07
1.02
1.01
1.01
2.02
1.03
1.04
1.02
1.03

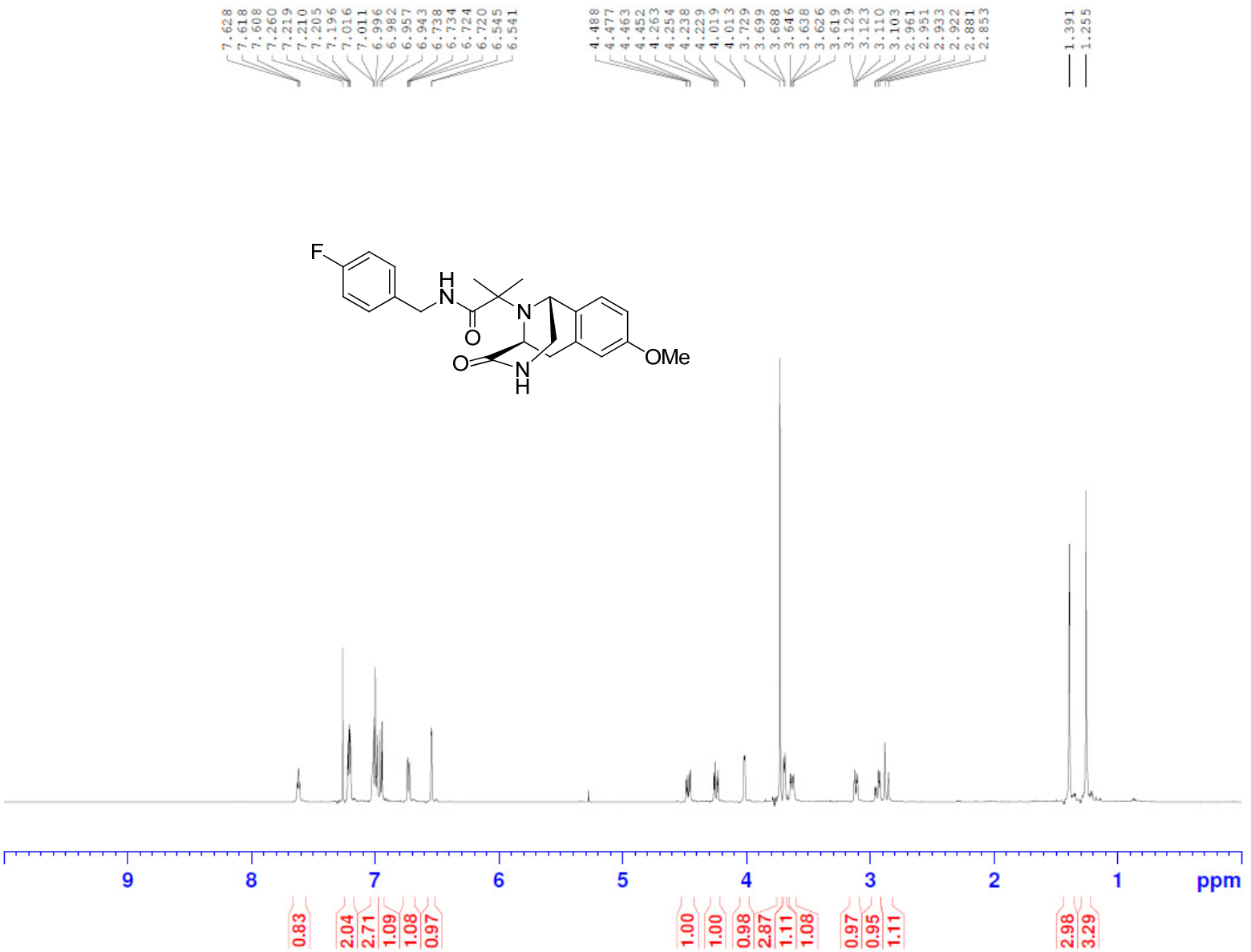
Compound-45


172.74
171.12
147.60
147.11
139.76
129.83
128.19
127.37
126.71
125.65
111.50
109.99
64.73
63.90
61.86
55.48
55.44
53.25
48.55
42.47
40.06
39.94
39.80
39.66
39.52
39.38
39.24
39.10
32.58
31.99
30.74
O
H
N
O
N
OMe
OMe
O
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

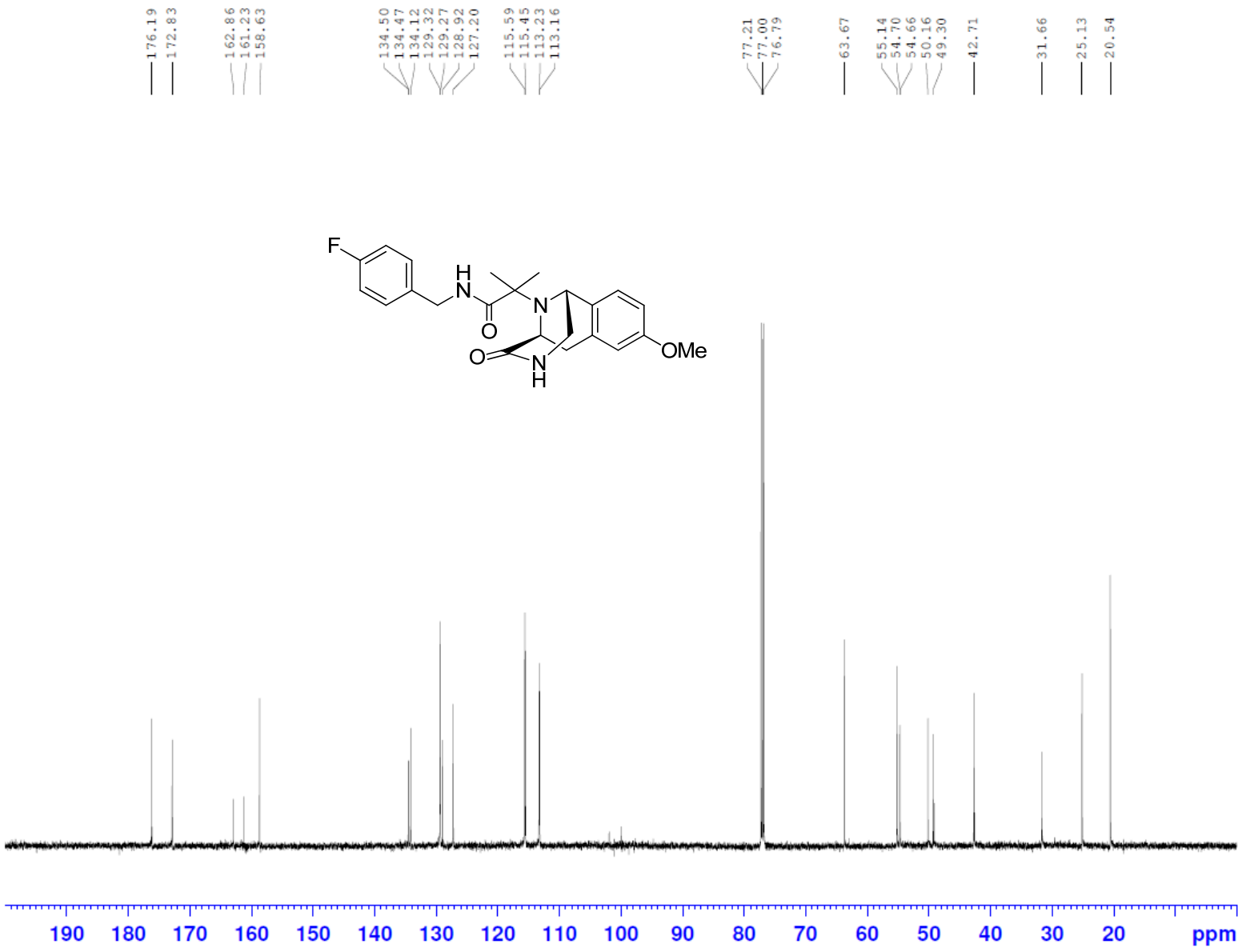
Compound-45


1: Scan AP+
TIC
7.70e7
3.39;466.24
1: Scan AP+
5.12e7
466.24
467.22
468.20
469.32
241.08
249.17
273.11
301.15
331.15
376.31
399.49
438.20
494.21
544.34
551.93
603.85
662.41
m/z
Time
%

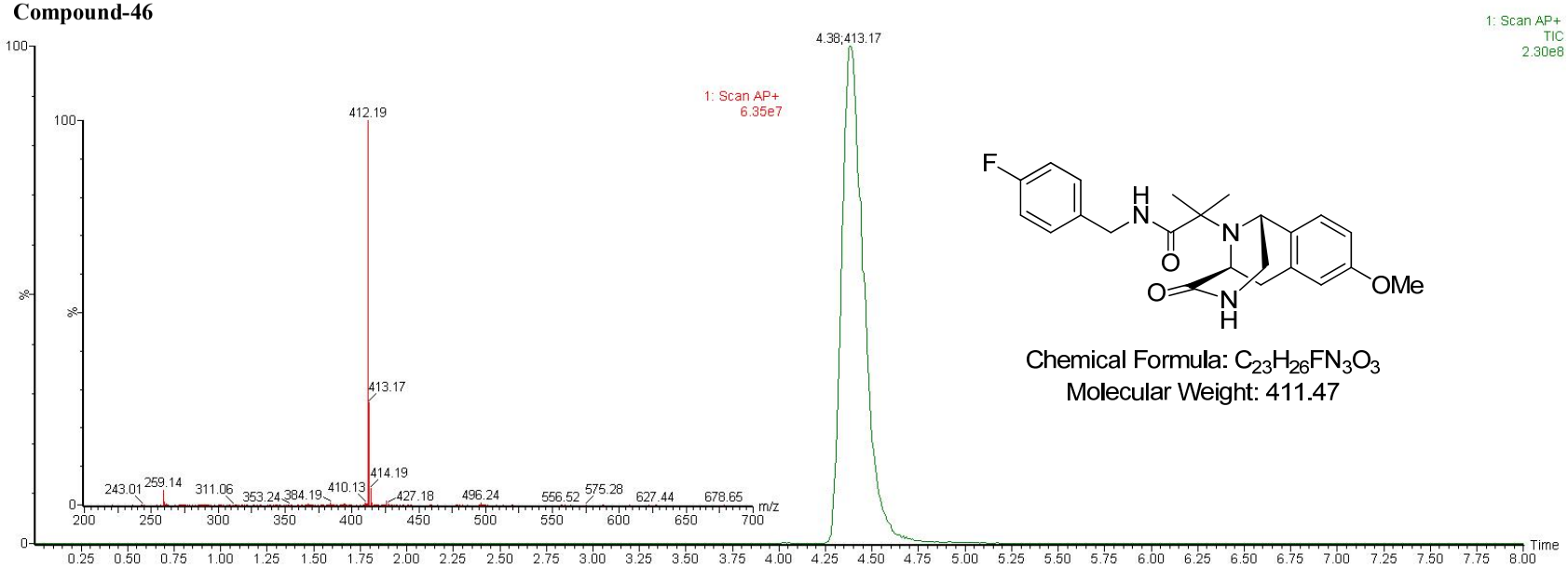
Compound-46


7.628
7.618
7.608
7.260
7.219
7.210
7.205
7.196
7.016
7.011
6.996
6.982
6.957
6.943
6.738
6.734
6.724
6.720
6.545
6.541
4.488
4.477
4.463
4.452
4.263
4.254
4.238
4.229
4.019
4.013
3.729
3.699
3.688
3.646
3.638
3.626
3.619
3.129
3.123
3.110
3.103
2.961
2.951
2.933
2.922
2.881
2.853
1.391
1.255
F
H
N
O
N
O
N
H
OMe
9
8
7
6
5
4
3
2
1
ppm
0.83
2.04
2.71
1.09
1.08
0.97
1.00
1.00
0.98
2.87
1.11
1.08
0.97
0.95
1.11
2.98
3.29

Compound-46

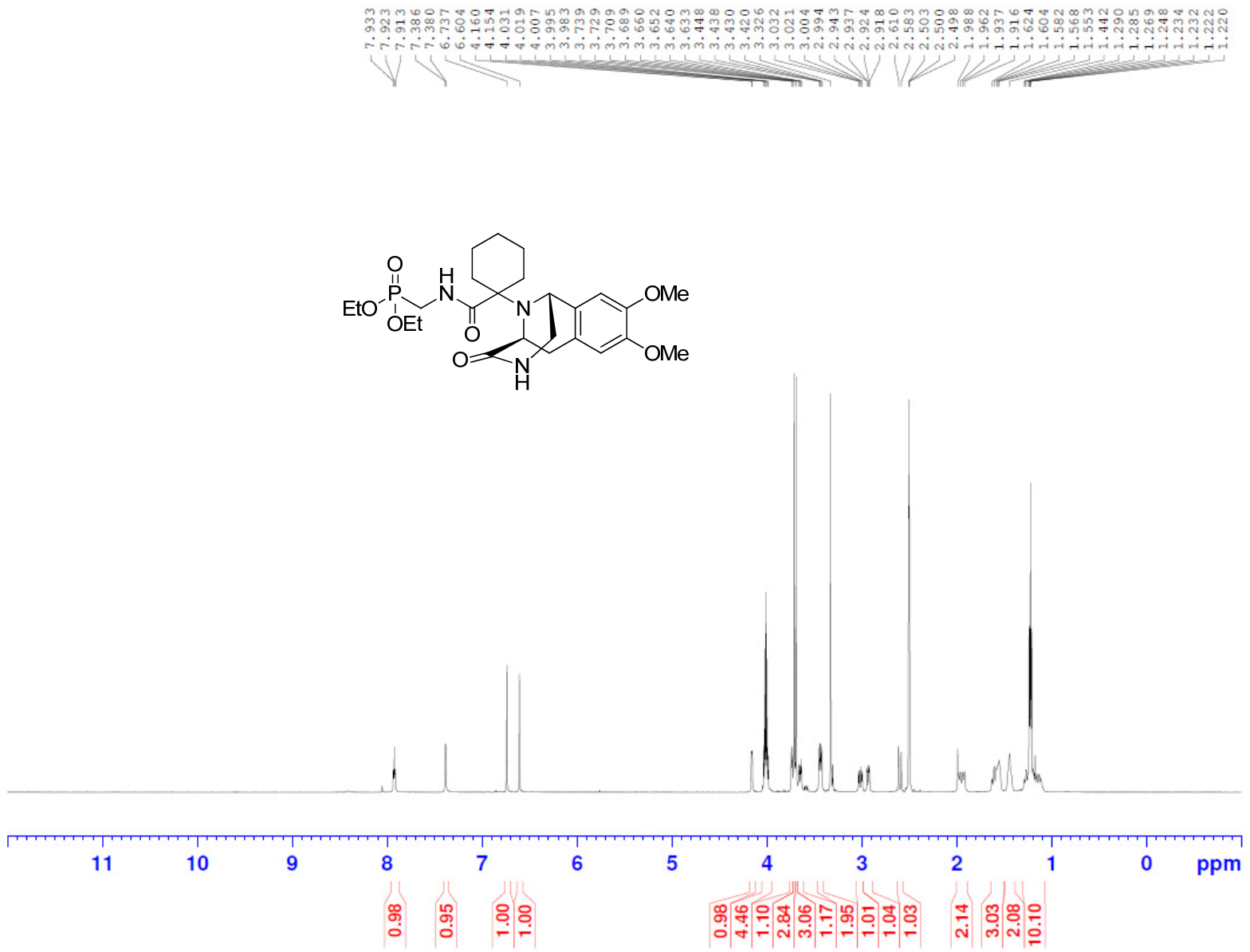

176.19
172.83
162.86
161.23
158.63
134.50
134.47
134.12
129.32
129.27
128.92
127.20
115.59
115.45
113.23
113.16
77.21
77.00
76.79
63.67
55.14
54.70
54.66
50.16
49.30
42.71
31.66
25.13
20.54
F
H
N
O
N
O
N
H
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

Compound-46

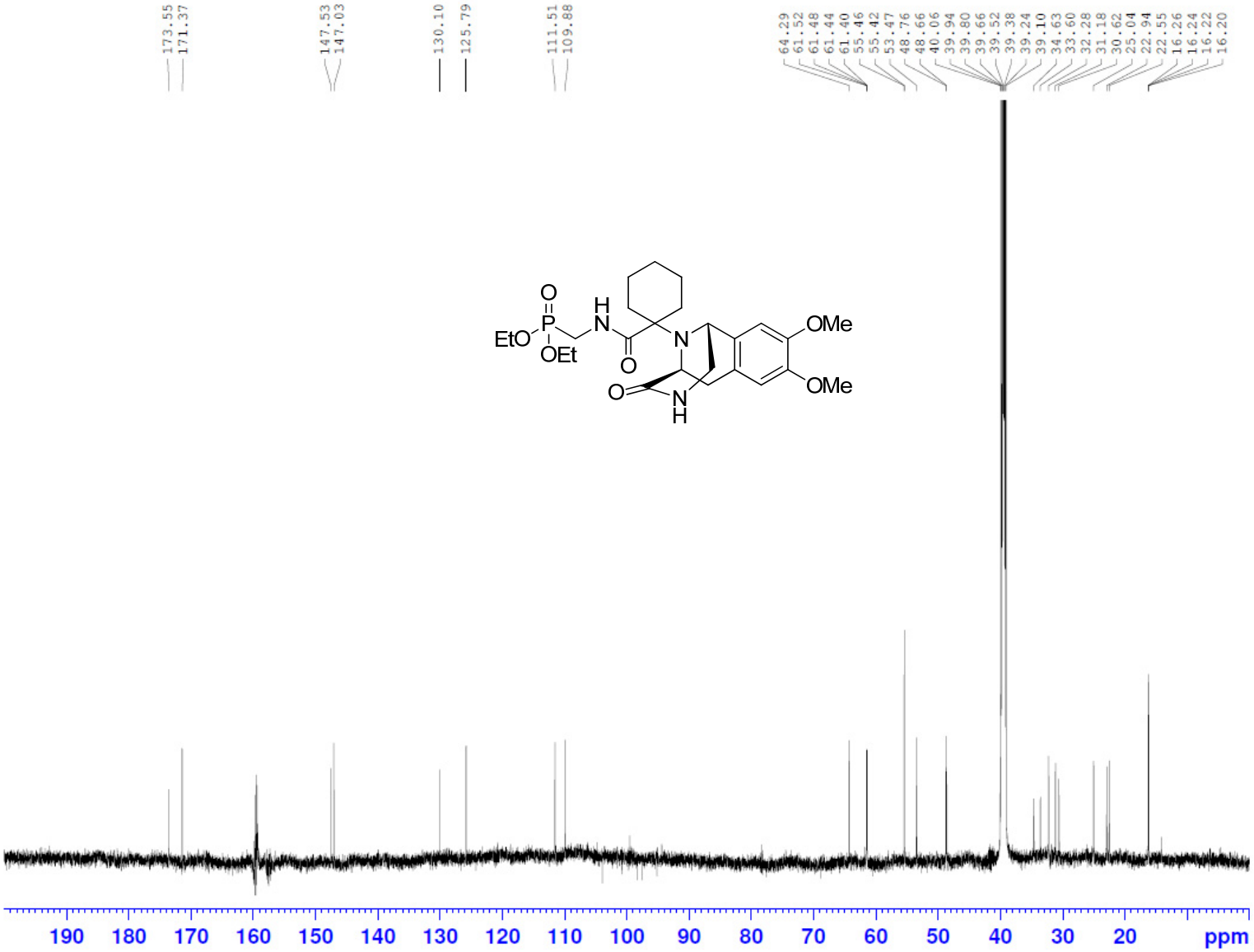


Chemical Formula: $C_{23}H_{26}FN_3O_3$
Molecular Weight: 411.47

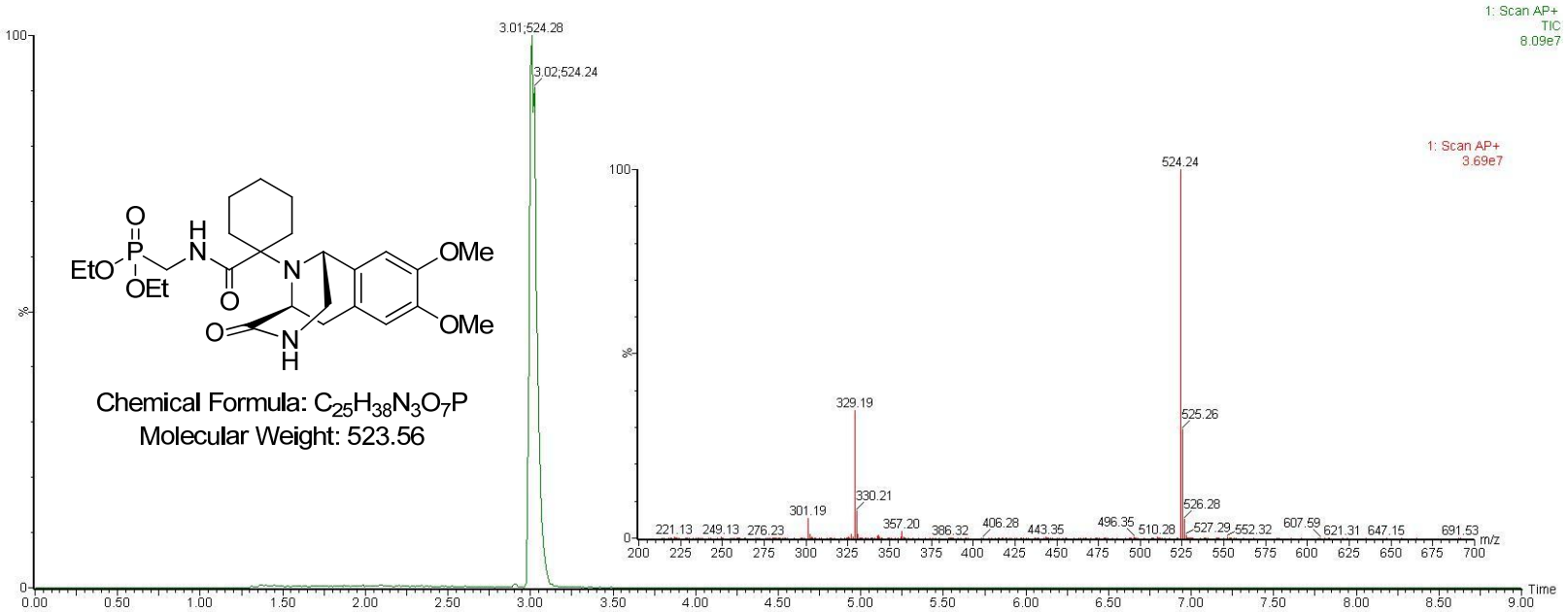
Compound-47


7.933
7.923
7.913
7.386
7.380
6.737
6.604
4.160
4.154
4.031
4.019
4.007
3.995
3.983
3.739
3.729
3.709
3.689
3.660
3.652
3.640
3.633
3.448
3.438
3.430
3.420
3.326
3.032
3.021
3.004
2.994
2.943
2.937
2.924
2.918
2.610
2.583
2.503
2.500
2.498
1.988
1.962
1.937
1.916
1.624
1.604
1.582
1.568
1.553
1.442
1.290
1.285
1.269
1.248
1.234
1.232
1.222
1.220
O
P
EtO
OEt
H
N
O
N
O
N
H
OMe
OMe
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
0.95
1.00
1.00
0.98
4.46
1.10
2.84
3.06
1.17
1.95
1.01
1.04
1.03
2.14
3.03
2.08
10.10

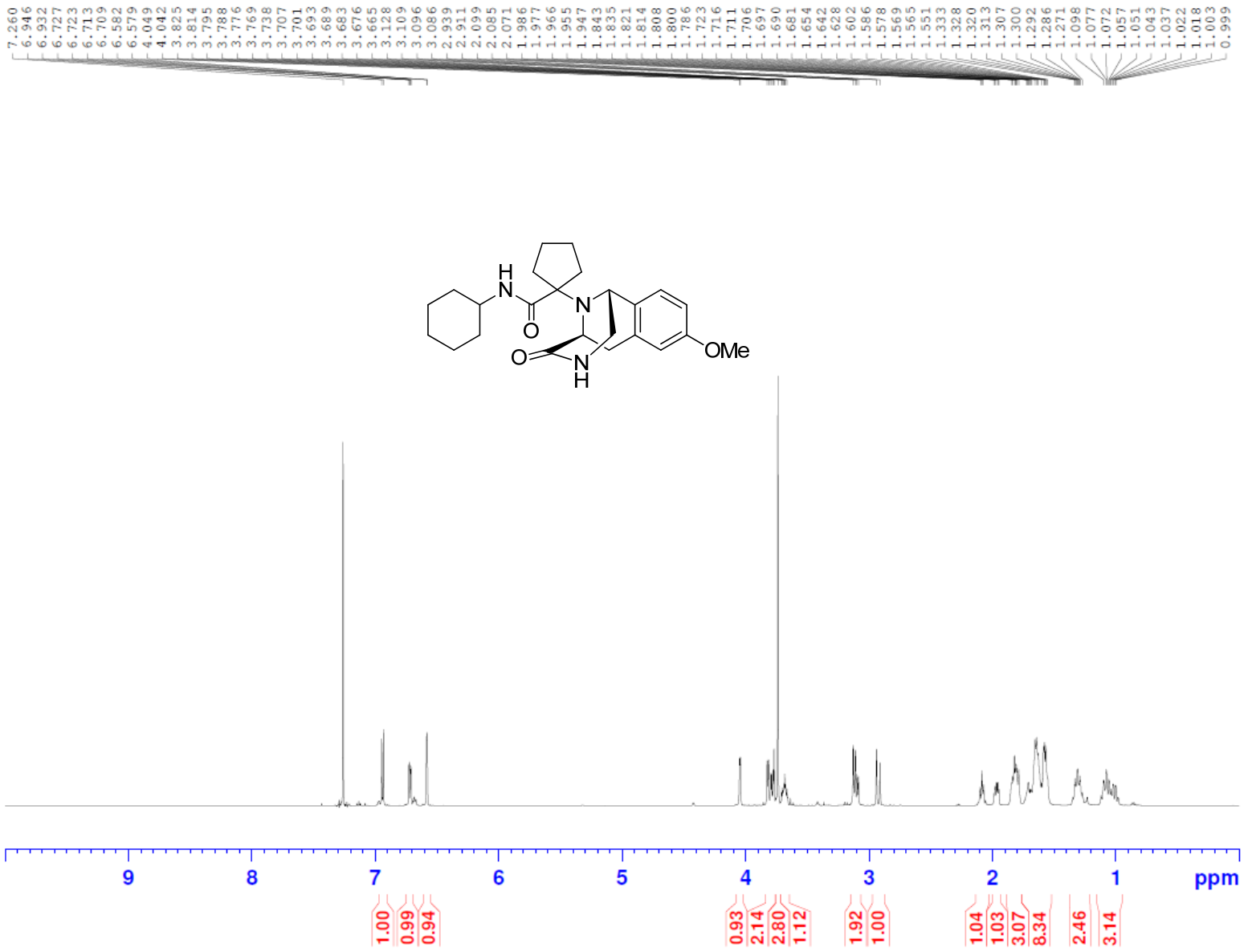
Compound-47


173.55
171.37
147.53
147.03
130.10
125.79
111.51
109.88
64.29
61.52
61.48
61.44
61.40
55.46
55.42
53.47
48.76
48.66
40.06
39.94
39.80
39.66
39.52
39.38
39.24
39.10
34.63
33.60
32.28
31.18
30.62
25.04
22.94
22.55
16.26
16.24
16.22
16.20
O
P
EtO
OEt
H
N
O
N
OMe
OMe
O
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

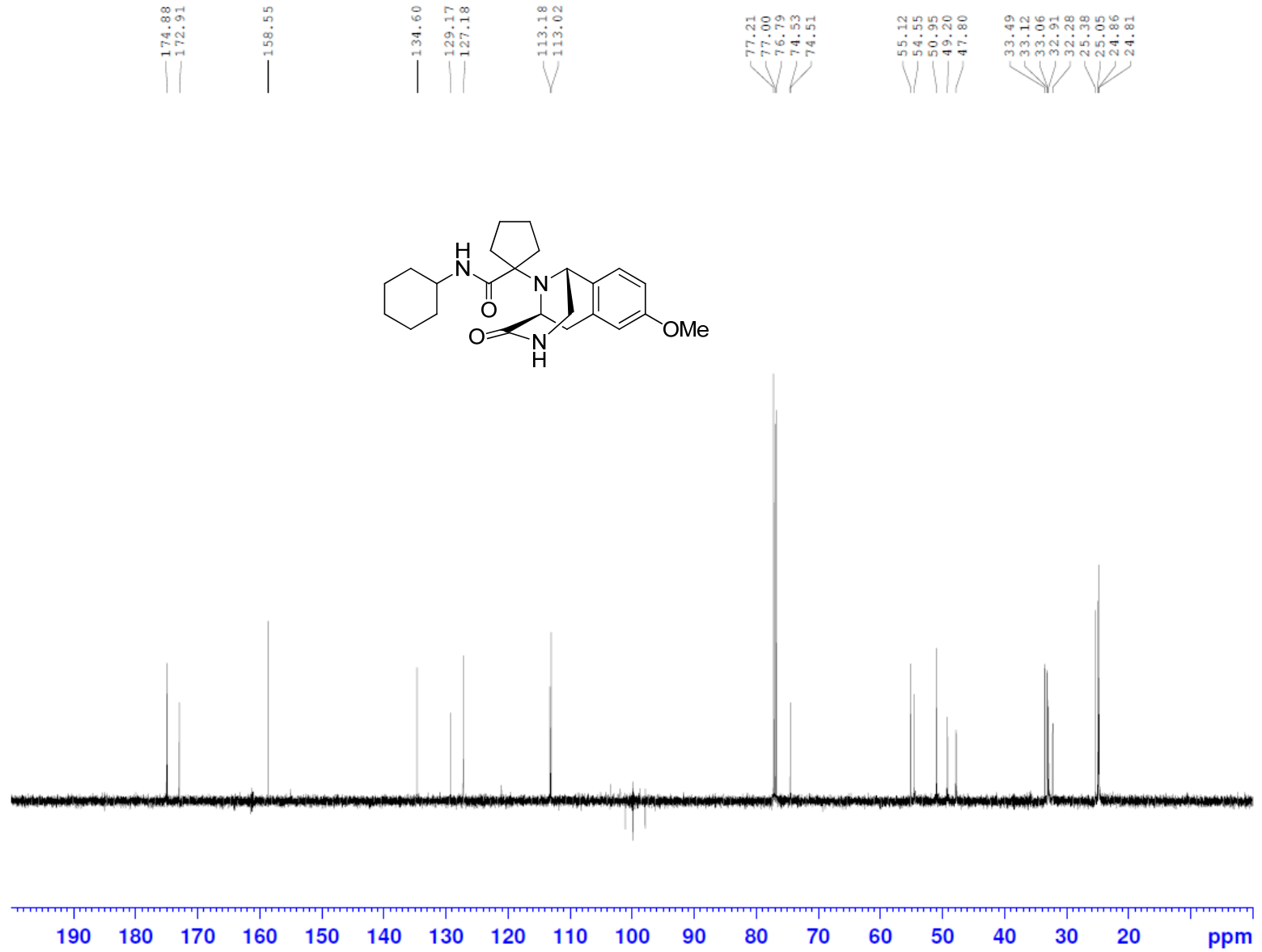
Compound-47


1: Scan AP+
TIC
8.09e7
3.01;524.28
3.02;524.24
Chemical Formula: C25H38N3O7P
Molecular Weight: 523.56
1: Scan AP+
3.69e7
524.24
329.19
525.26
330.21
526.28
301.19
357.20
386.32
406.28
443.35
496.35
510.28
527.29
552.32
607.59
621.31
647.15
691.53
m/z
Time

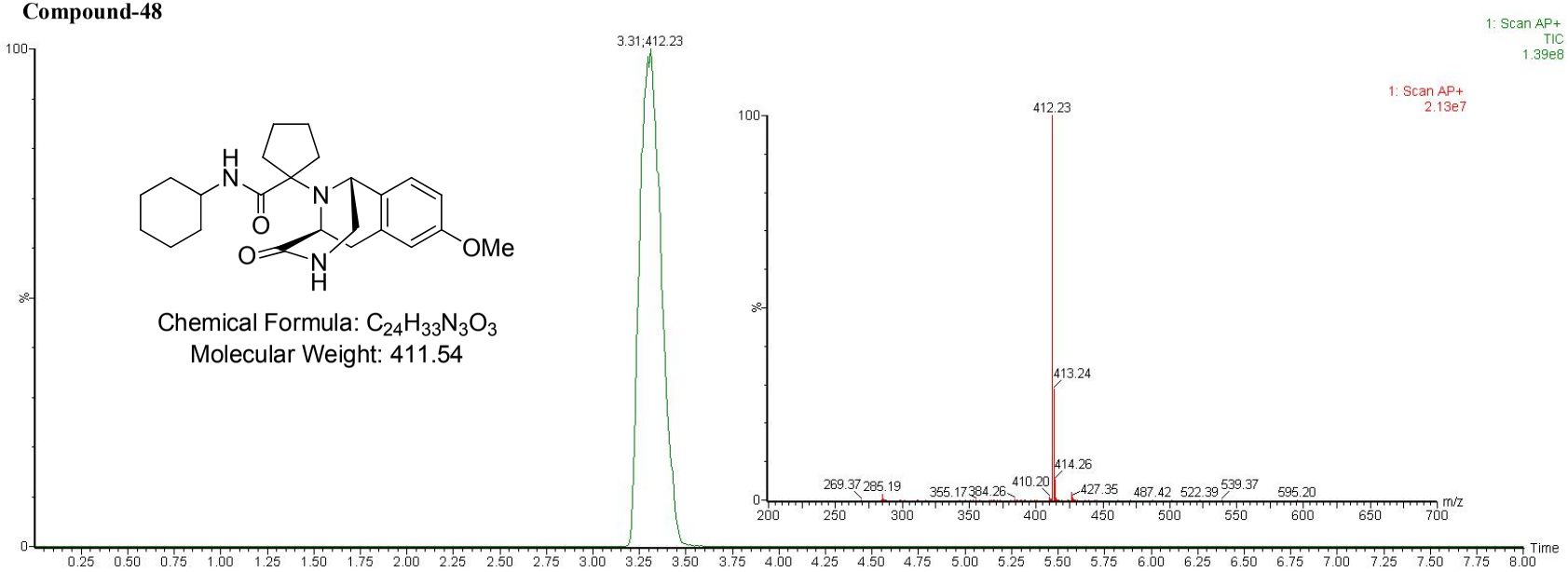
Compound-48


7.260
6.946
6.932
6.727
6.723
6.713
6.709
6.582
6.579
4.049
4.042
3.825
3.814
3.795
3.788
3.776
3.769
3.738
3.707
3.701
3.693
3.689
3.683
3.676
3.665
3.128
3.109
3.096
3.086
2.939
2.911
2.099
2.085
2.071
1.986
1.977
1.966
1.955
1.947
1.843
1.835
1.821
1.814
1.808
1.800
1.786
1.723
1.716
1.711
1.706
1.697
1.690
1.681
1.654
1.642
1.628
1.602
1.586
1.578
1.569
1.565
1.551
1.333
1.328
1.320
1.313
1.307
1.300
1.292
1.286
1.271
1.098
1.077
1.072
1.057
1.051
1.043
1.037
1.022
1.018
1.003
0.999
H
N
O
N
O
N
H
OMe
9
8
7
6
5
4
3
2
1
ppm
1.00
0.99
0.94
0.93
2.14
2.80
1.12
1.92
1.00
1.04
1.03
3.07
8.34
2.46
3.14

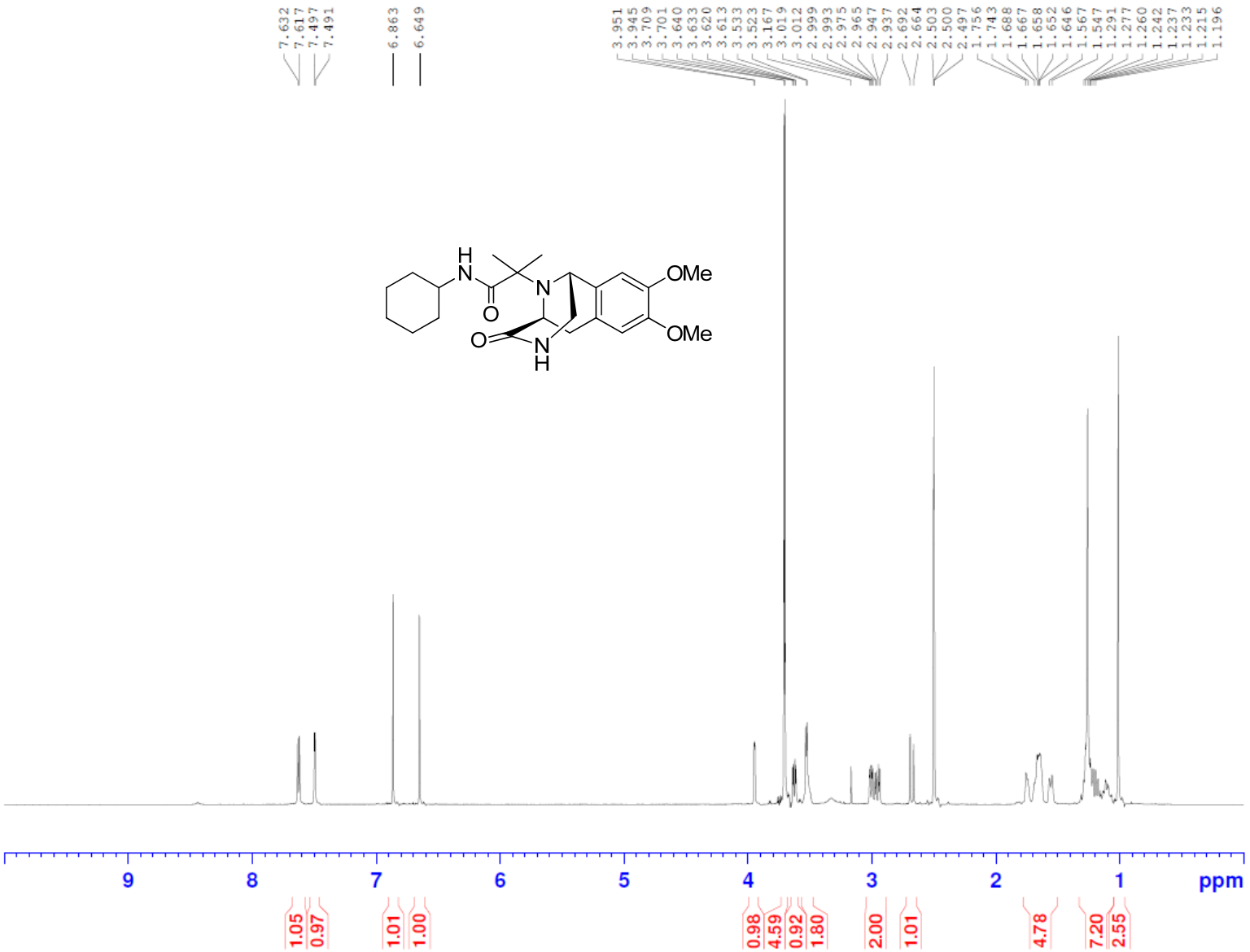
Compound-48


174.88
172.91
158.55
134.60
129.17
127.18
113.18
113.02
77.21
77.00
76.79
74.53
74.51
55.12
54.55
50.95
49.20
47.80
33.49
33.12
33.06
32.91
32.28
25.38
25.05
24.86
24.81
H
N
O
N
O
N
H
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

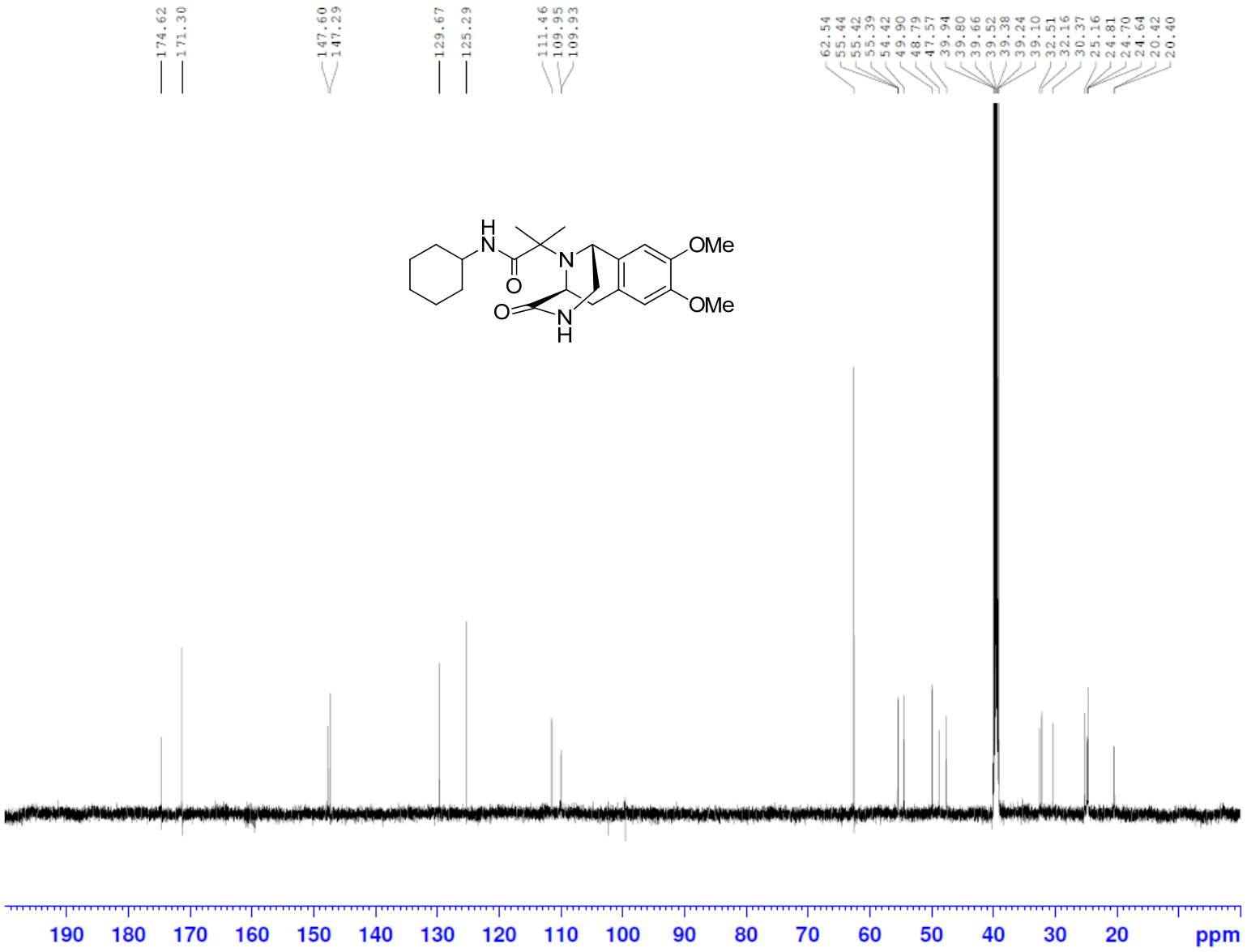
Compound-48


3.31;412.23
1: Scan AP+
TIC
1.39e8
1: Scan AP+
2.13e7
412.23
413.24
414.26
410.20
269.37
285.19
355.17
384.26
427.35
487.42
522.39
539.37
595.20
m/z
Time
Chemical Formula: C24H33N3O3
Molecular Weight: 411.54
OMe

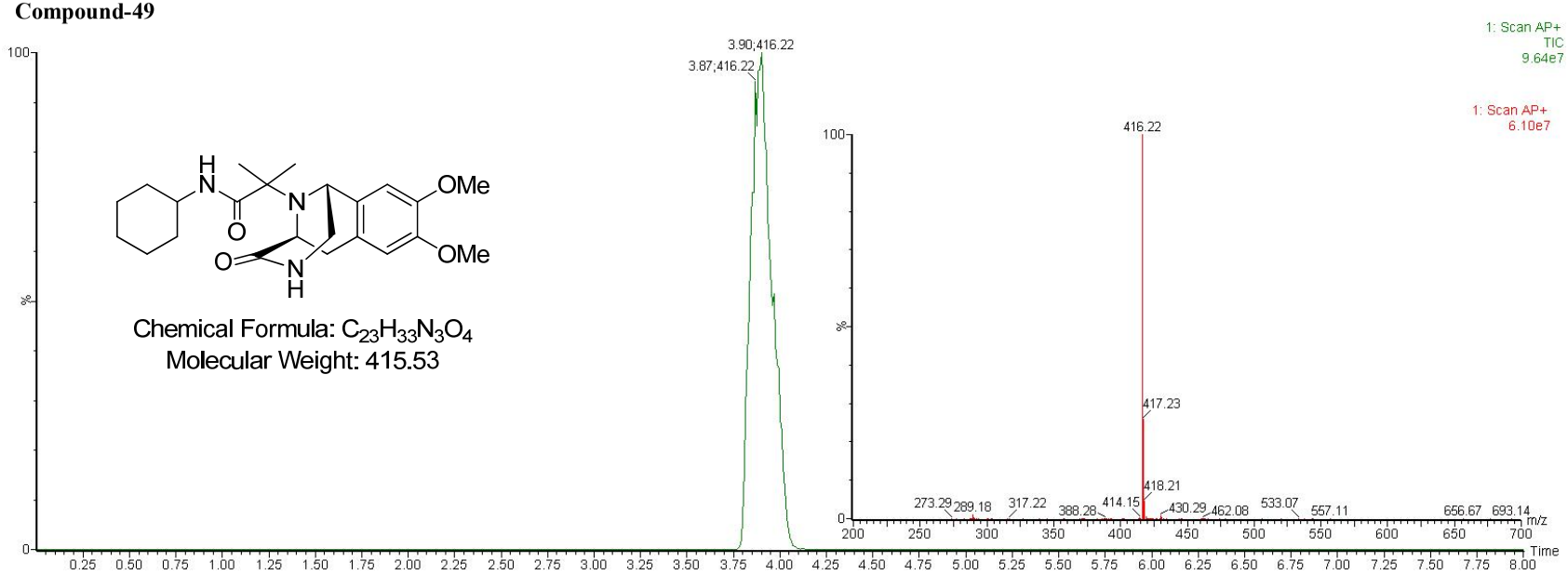
Compound-49


7.632
7.617
7.497
7.491
6.863
6.649
3.951
3.945
3.709
3.701
3.640
3.633
3.620
3.613
3.533
3.523
3.167
3.019
3.012
2.999
2.993
2.975
2.965
2.947
2.937
2.692
2.664
2.503
2.500
2.497
1.756
1.743
1.688
1.667
1.658
1.652
1.646
1.567
1.547
1.291
1.277
1.260
1.242
1.237
1.233
1.215
1.196
H
N
O
O
N
H
N
OMe
OMe
9
8
7
6
5
4
3
2
1
ppm
1.05
0.97
1.01
1.00
0.98
4.59
0.92
1.80
2.00
1.01
4.78
7.20
2.55

Compound-49


174.62
171.30
147.60
147.29
129.67
125.29
111.46
109.95
109.93
62.54
55.44
55.42
55.39
54.42
49.90
48.79
47.57
39.94
39.80
39.66
39.52
39.38
39.24
39.10
32.51
32.16
30.37
25.16
24.81
24.70
24.64
20.42
20.40
H
N
O
N
O
N
H
OMe
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

Compound-49


3.90;416.22
3.87;416.22
1: Scan AP+
TIC
9.64e7
1: Scan AP+
6.10e7
416.22
417.23
418.21
273.29
289.18
317.22
388.28
414.15
430.29
462.08
533.07
557.11
656.67
693.14
m/z
Time
OMe
OMe
Chemical Formula: $C_{23}H_{33}N_3O_4$
Molecular Weight: 415.53