Electronic Supplementary Material (ESI) for ChemComm.

Supplementary Information

Total synthesis of (+)-kopsihainanine A

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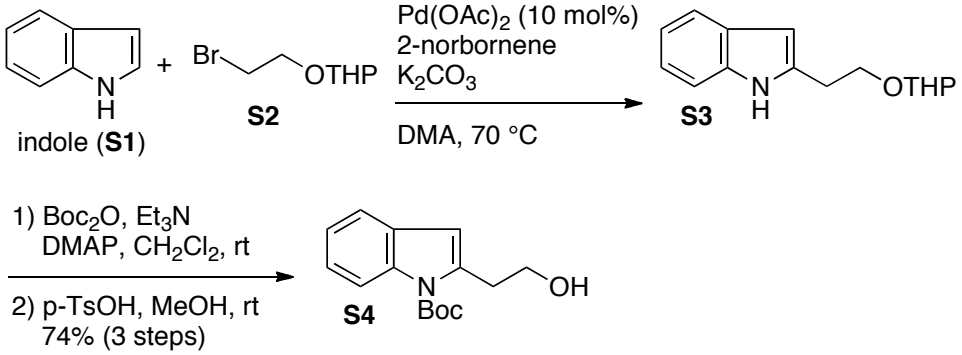
Experimental Section

General. Melting points were measured with YANAGIMOTO micro melting point apparatus, and were uncorrected. Optical rotations were measured on a JASCO P-2200. Infrared spectra were measured with a SHIMADZU FTIR-8700 spectrometer for samples in $CHCl_3$. ^1H NMR spectra were measured with JNM-ECS400 or JNM-ECA600 spectrometers for samples in $CDCl_3$. Tetramethylsilane (0.00 ppm) for compounds with a phenyl group or $CHCl_3$ (7.26 ppm) were used as an internal standard. ^{13}C NMR spectra were measured with JNM-ECS400 or JNM-ECA600 spectrometers for samples in $CDCl_3$. $CDCl_3$ (77.00 ppm) was used as an internal standard. High-resolution mass spectra and mass spectra were measured with JMS-SX102A (FAB) or JMS-T100TD (DART) mass spectrometers. Commercially available anhydrous THF, CH_2Cl_2, and toluene were employed for reactions. Et_3N was distilled from CaH_2. DMSO was distilled from $CaSO_4$. 3-Allyloxycarbonyl-1-benzoyl-2-oxopiperidine (**7**) was prepared by known method.[1] Other reagents were commercially available and used without further purification. All reactions were carried out under a nitrogen atmosphere. Silica gel (silica gel 60, 230–400 mesh) was used for chromatography. Organic extracts were dried over anhydrous Na_2SO_4.

1-*tert*-Butoxycarbonyl-2-(2-hydroxyethyl)-1*H*-indole (S4)



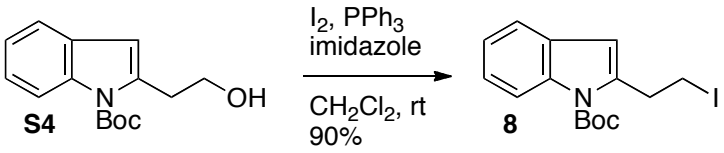
The coupling reaction of indole (**S1**) with **S2** was conducted by the method reported by Bach.[2]

To a solution of indole (**S1**, 3.50 g, 29.9 mmol) and bromide **S2** (12.5 g, 60.1 mmol) in DMA (reagent grade without purification, 150 mL) were added 2-norbornene (5.71 g, 60.7 mmol), K_2CO_3 (8.28 g, 60.0 mmol) and $Pd(OAc)_2$ (710 mg, 3.16 mmol). The resulting solution was briefly evacuated and then backfilled with argon (3 times). The mixture was then placed in an oil bath at 70 °C. Vigorous stirring was applied and the mixture was reacted under a balloon pressure of argon. After 16 h, the reaction mixture was cooled to room temperature, diluted with Et_2O and filtered. The filtrate was extracted with Et_2O, washed with water and brine, dried, concentrated to dryness. The residue was chromatographed with hexane-AcOEt (5:1) to afford the crude **S3** (7.41 g).

To a solution of the crude **S3** (7.41 g) in CH_2Cl_2 (90 mL) were added Boc_2O (8.00 mL, 34.9

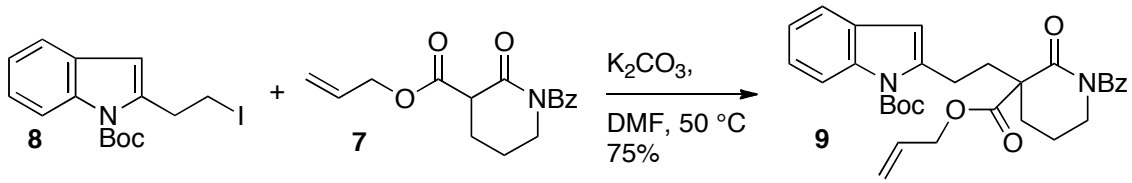
mmol), Et_3N (6.60 mL, 47.0 mmol) and DMAP (330 mg, 2.70 mmol) at room temperature. After stirring for 3 h at the same temperature, the mixture was quenched with water and extracted with CH_2Cl_2, washed with water and brine, dried, concentrated to dryness. The residue was dissolved in MeOH (110 mL) and to the solution was added *p*-TsOH (1.00 g, 5.26 mmol) at room temperature. After stirring for 14 h, the mixture was quenched with solid $NaHCO_3$ (1.2 g) and filtered, concentrated to dryness. The residue was chromatographed with hexane-AcOEt (4:1) to afford **S4** (5.81 g, 74% for 3 steps) as a yellow oil: R*f* = 0.2 (hexane-AcOEt = 3:1, UV, *p*-anisaldehyde); IR 3609, 3447, 1726 cm^{-1}; ^1H NMR δ 8.07 (d, 1H, *J* = 8.2 Hz), 7.46 (d, 1H, *J* = 6.9 Hz), 7.26–7.23 (m, 1H), 7.20 (td, 1H, *J* = 7.4, 1.0 Hz), 6.45 (s, 1H), 3.94 (t, 2H, *J* = 6.3 Hz), 3.31 (t, 2H, *J* = 6.3 Hz), 1.79 (brs, 1H), 1.69 (s, 9H); ^{13}C NMR δ 150.6, 138.1, 136.6, 129.1, 123.6, 122.8, 119.9, 115.6, 109.0, 84.1, 61.8, 33.3, 28.2; DART MS *m/z* 262 (M^++1, 75.4); DART HRMS calcd. for $C_{15}H_{20}NO_3$ 262.1443, found 262.1430.

1-*tert*-Butoxycarbonyl-2-(2-iodoethyl)-1*H*-indole (8)



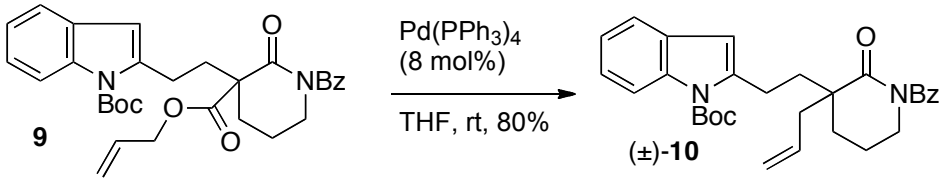
To a solution of **S4** (5.81 g, 22.3 mmol) in CH_2Cl_2 (90 mL) were added imidazole (2.34 g, 34.4 mmol), PPh_3 (7.00 g, 26.7 mmol) and I_2 (6.88 g, 27.0 mmol) at 0 °C. After stirring for 2 h at room temperature, the mixture was quenched with saturated aqueous $Na_2S_2O_3$, and the mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane-AcOEt (20:1) to give **8** (7.43 g, 90%) as a colorless oil: R*f* = 0.3 (hexane-AcOEt = 20:1, UV, *p*-anisaldehyde); IR 1732 cm^{-1}; ^1H NMR δ 8.09 (d, 1H, *J* = 8.7 Hz), 7.49 (d, 1H, *J* = 7.8 Hz), 7.29–7.18 (m, 2H), 6.45 (s, 1H), 3.56 (t, 2H, *J* = 7.4 Hz), 3.44 (t, 2H, *J* = 7.4 Hz), 1.70 (s, 9H); ^{13}C NMR δ 150.2, 139.6, 136.5, 128.9, 123.9, 122.9, 120.1, 115.8, 109.0, 84.2, 34.7, 28.3, 3.6; DART MS *m/z* 372 (M^++1, 71.7); DART HRMS calcd. for $C_{15}H_{19}INO_2$ 372.0460, found 372.0473.

2-{2-(3-Allyloxycarbonyl-1-benzoyl-2-oxopiperidin-3-yl)ethyl}-1-*tert*-butoxycarbonyl-1*H*-indole (9)



To a solution of **8** (7.43 g, 20.0 mmol) and lactam **7**[1] (4.10 g, 14.3 mmol) in distilled DMF (30 mL) was added K_2CO_3 (5.10 g, 37.0 mmol) at room temperature. The mixture was warmed to 50 °C and stirred at the same temperature for 3 h. After cooling to room temperature, the mixture was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane-AcOEt (4:1) to give **9** (5.68 g, 75%) as a pale yellow oil: R*f* = 0.4 (hexane-AcOEt = 3:1, UV, *p*-anisaldehyde); IR 1732, 1682 cm^{-1}; ^1H NMR δ 8.02 (d, 1H, *J* = 8.2 Hz), 7.73 (d, 2H, *J* = 7.3 Hz), 7.49–7.35 (m, 4H), 7.27–7.14 (m, 2H), 6.34 (s, 1H), 6.04–5.94 (m, 1H), 5.40 (dd, 1H, *J* = 16.9, 1.2 Hz), 5.33 (dd, 1H, *J* = 10.5, 1.2 Hz), 4.73 (d, 2H, *J* = 6.0 Hz), 3.86–3.74 (m, 2H), 3.20–3.12 (m, 1H), 3.01–2.91 (m, 1H), 2.57–2.53 (m, 1H), 2.39–2.27 (m, 2H), 2.08–1.98 (m, 3H), 1.66 (s, 9H); ^{13}C NMR δ 174.9, 171.8, 171.5, 150.4, 141.1, 136.3, 135.8, 131.6, 131.3, 129.1, 128.01, 127.99, 123.3, 122.5, 119.8, 119.7, 115.4, 107.0, 83.7, 66.6, 56.3, 46.4, 34.3, 30.4, 28.2, 25.1, 20.2; DART MS *m/z* 531 (M^++1, 41.4); DART HRMS calcd. for $C_{31}H_{35}N_2O_6$ 531.2495, found 531.2510.

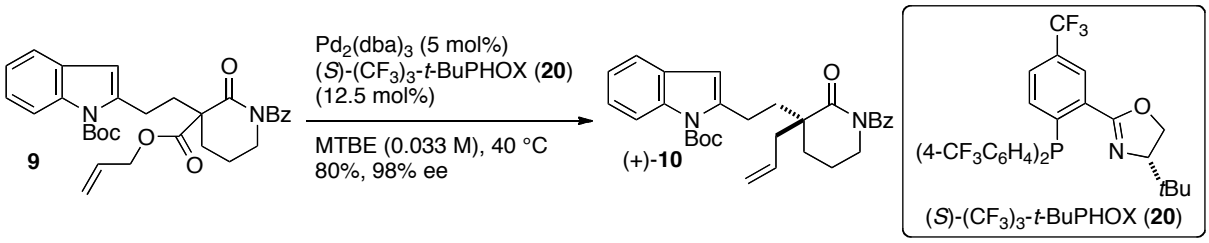
2-{2-(3-Allyl-1-benzoyl-2-oxopiperidin-3-yl)ethyl}-1-*tert*-butoxycarbonyl-1*H*-indole {(±)-10}



To a solution of **9** (1.10 g, 2.08 mmol) in dry THF (10 mL) was added $Pd(PPh_3)_4$ (192 mg, 0.166 mmol) at room temperature. The resulting solution was briefly evacuated and then backfilled with argon (10 times). After stirring for 12 h at the same temperature, the mixture was concentrated to dryness. The residue was chromatographed with hexane-AcOEt (6:1) to give (±)-**10** (810 mg, 80%) as a colorless oil: R*f* = 0.5 (hexane-AcOEt = 3:1, UV, *p*-anisaldehyde); IR 1734, 1695, 1680 cm^{-1}; ^1H NMR δ 8.05 (d, 1H, *J* = 8.2 Hz), 7.52 (d, 2H, *J* = 7.3 Hz), 7.44 (t, 2H, *J* = 7.6 Hz), 7.33 (t, 2H, *J* = 7.6 Hz), 7.23–7.17 (m, 2H) 6.36 (s, 1H), 5.84–5.74 (m, 1H), 5.16 (d, 1H, *J* = 11.4 Hz), 5.15 (d, 1H, *J* = 16.0 Hz), 3.81 (t, 2H, *J* = 5.7 Hz), 3.10–2.96 (m, 2H), 2.64 (dd, 1H, *J* = 13.9, 7.1 Hz), 2.42 (dd, 1H, *J* = 13.9, 7.8 Hz), 2.16–1.96 (m, 6H), 1.66 (s, 9H); ^{13}C NMR δ 177.7, 175.6, 150.4, 141.8, 136.7, 136.4, 133.3, 131.3, 129.2, 128.1, 127.4, 123.3, 122.6, 119.8, 119.1, 115.5, 106.8, 83.8, 47.2, 47.0, 41.6, 36.2, 31.0, 28.2, 24.6, 19.5; DART MS *m/z* 487 (M^++1, 98.6); DART HRMS calcd. for

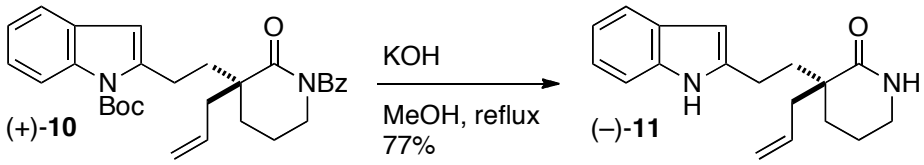
$C_{30}H_{35}N_2O_4$ 487.2597, found 487.2611.

(*R*)-2-{2-(3-Allyl-1-benzoyl-2-oxopiperidin-3-yl)ethyl}-1-*tert*-butoxycarbonyl-1*H*-indole {(+)-10}



$Pd_2(dba)_3$ (45.8 mg, 0.050 mmol) and a solution of **20** (73.9 mg, 0.125 mmol) in MTBE (20 mL) were added in a 200-mL reaction flask, and the resulting mixture was briefly evacuated and then backfilled with argon (10 times). After stirring for 30 min at room temperature, **9** (528 mg, 1.0 mmol) in MTBE (20 mL) was added to the resulting solution. The solution was briefly evacuated and then backfilled with argon (10 times). After stirring for 15 h at 40 °C, the mixture was cooled to room temperature and concentrated to dryness. The residue was chromatographed with hexane-AcOEt (6:1) to give (+)-**10** (398 mg, 82%) as a colorless oil: R*f* = 0.5 (hexane-AcOEt = 3:1, UV, *p*-anisaldehyde); $[\alpha]_D^{23}$ = +44.2 (c = 0.98, $CHCl_3$); IR 1734, 1695, 1680 cm^{-1}; ^1H NMR δ 8.05 (d, 1H, *J* = 8.2 Hz), 7.52 (d, 2H, *J* = 7.3 Hz), 7.44 (t, 2H, *J* = 7.6 Hz), 7.33 (t, 2H, *J* = 7.6 Hz), 7.23–7.17 (m, 2H) 6.36 (s, 1H), 5.84–5.74 (m, 1H), 5.16 (d, 1H, *J* = 11.4 Hz), 5.15 (d, 1H, *J* = 16.0 Hz), 3.81 (t, 2H, *J* = 5.7 Hz), 3.10–2.96 (m, 2H), 2.64 (dd, 1H, *J* = 13.9, 7.1 Hz), 2.42 (dd, 1H, *J* = 13.9, 7.8 Hz), 2.16–1.96 (m, 6H), 1.66 (s, 9H); ^{13}C NMR δ 177.7, 175.6, 150.4, 141.8, 136.7, 136.4, 133.3, 131.3, 129.2, 128.1, 127.4, 123.3, 122.6, 119.8, 119.1, 115.5, 106.8, 83.8, 47.2, 47.0, 41.6, 36.2, 31.0, 28.2, 24.6, 19.5; DART MS *m/z* 487 (M^++1, 98.6); DART HRMS calcd. for $C_{30}H_{35}N_2O_4$ 487.2597, found 487.2611; HPLC: OD-H column; λ = 254 nm; eluent: hexane/2-propanol = 97/3; flow rate: 1.0 mL/min; t_R = 16.8 min (minor), t_R = 21.0 min (major); ee = 98%.

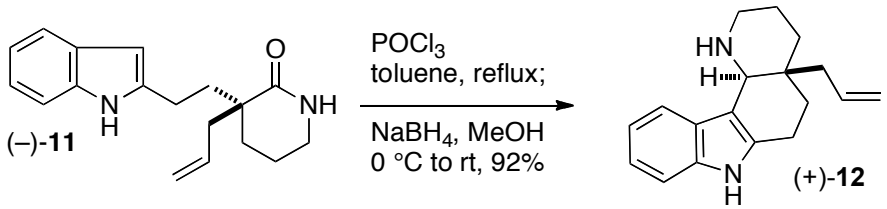
(*R*)-2-{2-(3-Allyl-2-oxo-piperidin-3-yl)ethyl}-1*H*-indole {(–)-11}



To a solution of (+)-**10** (98% ee, 1.39 g, 2.86 mmol) in MeOH (30 mL) was added KOH (770 mg, 13.3 mmol) at room temperature and the mixture was warmed to reflux. After stirring for 3.5 h, the mixture was cooled and concentrated to dryness. To the residue was added water and extracted with CH_2Cl_2, washed with water and brine, dried, concentrated to dryness. The residue was chromatographed with hexane-AcOEt (1:1 to 1:2) to give (–)-**11** (624mg, 77%) as a colorless powder:

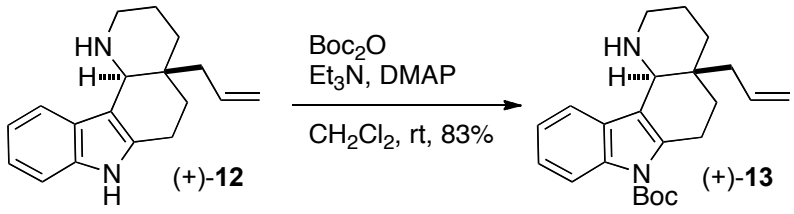
R*f* = 0.3 (hexane-AcOEt = 1:2, UV, *p*-anisaldehyde); mp 167–168 °C (from AcOEt); $[\alpha]_D^{23}$ = –11.0 (c = 1.46, $CHCl_3$); IR 3468, 3402, 3294, 3202, 1645 cm^{-1}; ^1H NMR δ 8.33 (brs, 1H), 7.48 (d, 1H, *J* = 7.8 Hz), 7.26 (d, 1H, *J* = 8.2 Hz), 7.10–7.01 (m, 2H), 6.20 (brs, 1H), 5.86–5.75 (m, 2H), 5.10 (d, 1H, *J* = 9.6 Hz), 5.09 (d, 1H, *J* = 17.4 Hz), 3.29 (brs, 2H), 2.91–2.83 (m, 1H), 2.76–2.68 (m, 1H), 2.54 (dd, 1H, *J* = 13.7, 6.4 Hz), 2.34 (dd, 1H, *J* = 13.6, 7.8 Hz), 2.16 (td, 1H, *J* = 17.7, 6.3 Hz), 1.89–1.76 (m, 5H); ^{13}C NMR δ 176.3, 139.7, 136.2, 133.8, 128.8, 121.0, 119.7, 119.5, 118.5, 110.5, 99.4, 45.0, 43.0, 42.8, 37.9, 29.7, 23.7, 19.6; DART MS *m/z* 283 (M^++1, 49.5); DART HRMS calcd. for $C_{18}H_{23}N_2O$ 283.1810, found 283.1806.

(4a*R*,11c*S*)-4a-Allyl-2,3,4,4a,5,6,7,11c-octahydro-1*H*-pyrido-[3,2-c]carbazole {(+)-12}



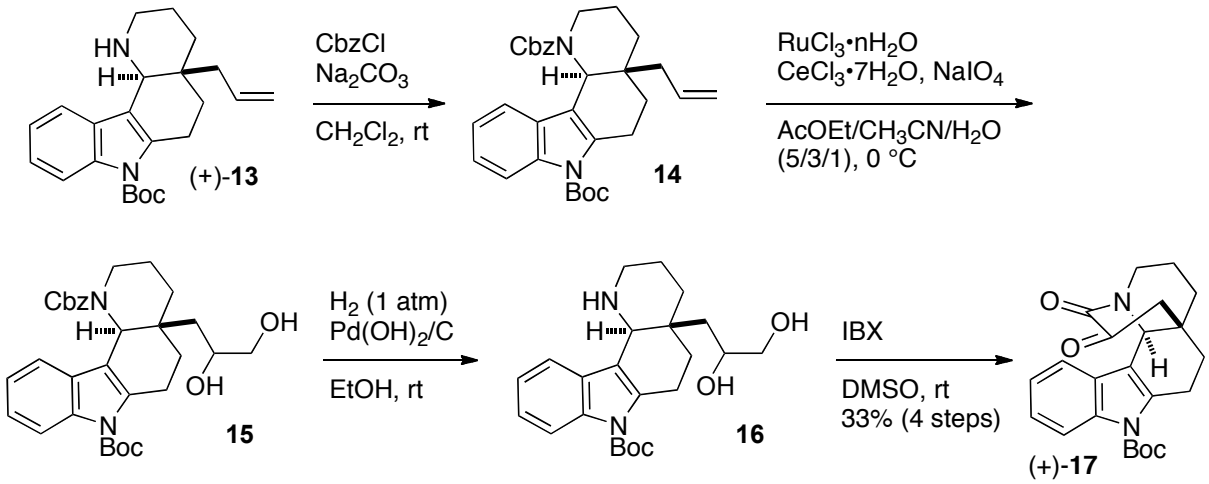
A solution of (–)-**11** (767 mg, 2.72 mmol) and $POCl_3$ (0.370 mL, 4.08 mmol) in toluene (15 mL) was heated under reflux for 30 min. The solvent was removed under reduced pressure. The crude product was dissolved in MeOH (30 mL) and treated with $NaBH_4$ (362 mg, 9.52 mmol) at 0 °C, stirred for 3 h. The reaction mixture was concentrated to dryness, chromatographed with AcOEt to give (+)-**12** (668 mg, 92%) as a colorless amorphous powder: R*f* = 0.3 (AcOEt, UV, *p*-anisaldehyde); $[\alpha]_D^{28}$ = +123 (c = 1.02, $CHCl_3$); IR 3472, 3402, 3327, 1637 cm^{-1}, ^1H NMR δ 7.87 (d, 1H, *J* = 7.8 Hz), 7.78 (brs, 1H), 7.23 (d, 1H, *J* = 7.3 Hz), 7.08–6.99 (m, 2H), 5.89–5.79 (m, 1H), 5.07 (d, 1H, *J* = 10.1 Hz), 5.06 (d, 1H, *J* = 16.5 Hz), 3.95 (s, 1H), 3.30 (dd, 1H, *J* = 12.4, 4.1 Hz), 2.91 (dd, 1H, *J* = 12.9, 3.5 Hz), 2.82–2.73 (m, 1H), 2.60 (dd, 1H, *J* = 16.9, 6.4 Hz), 2.40 (dd, 1H, *J* = 14.3, 7.3 Hz), 1.95 (dd, 1H, *J* = 14.3, 7.6 Hz), 1.86–1.74 (m, 4H), 1.53–1.43 (m, 2H), 1.28–1.21 (m, 1H); ^{13}C NMR δ 135.9, 135.3, 133.3, 127.1, 120.6, 120.2, 119.0, 117.0, 110.9, 110.3, 63.7, 47.2, 35.9, 33.6, 32.1, 29.6, 22.2, 20.0; DART MS *m/z* 267 (M^++1, 26.0), DART HRMS calcd. for $C_{18}H_{23}N_2$ 267.1861, found 267.1858; HPLC: IA column; λ = 254 nm; eluent: hexane/2-propanol/diethylamine = 80/20/0.2; flow rate: 1.0 mL/min; t_R = 5.3 min (major), t_R = 6.9 min (minor); ee = 98%.

(4a*R*,11c*S*)-4a-Allyl-7-(*tert*-butoxycarbonyl)-2,3,4,4a,5,6,7,11c-octahydro-1*H*-pyrido-[3,2-c]carbazole {(+)-13}



To a solution of (+)-**12** (500 mg, 1.88 mmol) in CH_2Cl_2 (20 mL) were added Boc_2O (0.517 mL, 2.26 mmol), Et_3N (0.450 mL, 3.21 mmol) and DMAP (23.0 mg, 0.189 mmol) at room temperature. After stirring for 12 h at the same temperature, the mixture was quenched with water and extracted with CH_2Cl_2. The extract was washed with water and brine, dried, concentrated to dryness. The residue was chromatographed with hexane-AcOEt (5:1) to give (+)-**13** (570 mg, 83%) as a colorless oil: R*f* = 0.4 (hexane-AcOEt = 3:1, UV, *p*-anisaldehyde); $[\alpha]_D^{29}$ = +53.2 (c = 1.18, $CHCl_3$); IR 3009, 2932, 1722, 1369 cm^{-1}; ^1H NMR δ 8.09 (t, 2H, *J* = 8.9 Hz), 7.22–7.12 (m, 2H), 5.90–5.80 (m, 1H), 5.10 (d, 1H, *J* = 16.0 Hz), 5.09 (d, 1H, *J* = 11.0 Hz), 3.88 (t, 1H, *J* = 2.5 Hz), 3.29 (dd, 1H, *J* = 13.5, 4.8 Hz), 3.07–2.84 (m, 3H), 2.35 (dd, 1H, *J* = 14.2, 7.8 Hz), 2.00 (dd, 1H, *J* = 14.2, 7.3 Hz), 1.88–1.79 (m, 2H), 1.77–1.70 (m, 1H), 1.67 (s, 9H), 1.51 (brs, 1H), 1.46–1.38 (m, 2H), 1.22 (td, 1H, *J* = 13.3, 3.2 Hz); ^{13}C NMR δ 150.6, 136.0, 135.0, 134.9, 129.1, 122.9, 122.1, 121.0, 117.2, 116.7, 115.1, 83.4, 63.3, 47.1, 34.8, 33.6, 32.5, 29.4, 28.3, 23.0, 22.3; DART MS *m/z* 367 (M^++1, 26.3); DART HRMS calcd. for $C_{23}H_{31}N_2O_2$ 367.2386, found 367.2386.

(1*S*,4a*R*,11c*S*)-7-*tert*-Butoxycarbonyl-2,3(1*H*,4*H*)-dioxo-1,4a-propano-4a*H*-5,6,7,11c-tetrahydropyrido[3,2-*c*]carbazole {(+)-17}



To a solution of (+)-**13** (783 mg, 2.14 mmol) in CH_2Cl_2 (25 mL) were added Na_2CO_3 (1.15 g, 10.8 mmol) and CbzCl (0.920 mL, 6.50 mmol) at room temperature. After stirring for 12 h at the

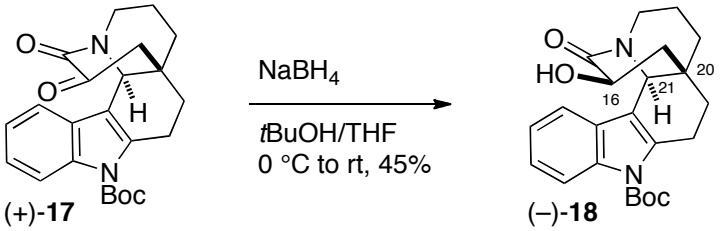
same temperature, the mixture was quenched with water and extracted with CH_2Cl_2, washed with water and brine, dried, concentrated to dryness. The residue was chromatographed with hexane-AcOEt (8:1 to 6:1) to give the crude **14** (1.00 g).

$CeCl_3$•$7H_2O$ (15.0 mg, 0.040 mmol), $NaIO_4$ (64.9 mg, 0.30 mmol), and water (0.16 mL) were added sequentially to a reaction flask. The resulting suspension was heated to 50 °C and stirred for 20 min. After cooling to 0°C, AcOEt (0.40 mL), CH_3CN (0.60 mL), and a 0.050 M aqueous solution of $RuCl_3$ (40 mL, 0.0020 mmol) were added sequentially to the suspension. After stirring for 5 min at 0 °C, a solution of the crude **14** (101 mg) in AcOEt (0.60 mL) was added to the suspension. After stirring for 15 min at the same temperature, AcOEt (2.0 mL) and solid Na_2SO_4 (100 mg) were added to the reaction mixture. The resulting mixture was filtered off and the filter cake was washed with AcOEt. The filtrate was washed with saturated aqueous Na_2SO_3, dried, concentrated to dryness. The residue was chromatographed with hexane-AcOEt (1:1 to 1:4) to give the crude **15** (75.3 mg).

To a solution of the crude **15** (292 mg) in EtOH (8.0 mL) was added 20% $Pd(OH)_2$/C (56 mg) at room temperature. The resulting mixture was stirred under H_2 atmosphere at the same temperature for 20 min. Then the mixture was filtered through Celite and the filtrate was concentrated to dryness. The residue was chromatographed with AcOEt-MeOH (10:1) to give the crude **16** (209 mg).

To a suspension of IBX (338 mg, 1.21 mmol) in DMSO (0.50 mL) was added a solution of the crude **16** (69.0 mg) in DMSO (1.1 mL) at room temperature. After stirring for 12 h, the mixture was quenched with saturated aqueous $Na_2S_2O_3$, extracted with AcOEt. The extract was washed with water and brine, dried and concentrated to dryness. The residue was chromatographed with CH_2Cl_2-MeOH (100:1) to give (+)-**17** (36.0 mg, 33% from (+)-**13**) as a colorless solid: R*f* = 0.3 (CH_2Cl_2, UV, *p*-anisaldehyde); mp 182–184 °C (from AcOEt); $[\alpha]_D^{30}$ = +174 (c = 1.13, $CHCl_3$); IR 1734, 1682, 1360, 1150 cm^{-1}; ^1H NMR δ 8.03 (d, 1H, *J* = 7.8 Hz), 7.61 (d, 1H, *J* = 7.8 Hz), 7.22 (dd, 1H, *J* = 7.8, 7.2 Hz), 7.15 (dd, 1H, *J* = 7.8, 7.2 Hz), 4.50 (dd, 1H, *J* = 13.2, 5.4 Hz), 4.28 (s, 1H), 3.34 (ddd, 1H, *J* = 13.2, 12.6, 3.0 Hz), 3.27 (dd, 1H, *J* = 19.2, 6.6 Hz), 3.16–3.09 (m, 1H), 2.77 (d, 1H, *J* = 17.5 Hz), 2.34 (d, 1H, *J* = 17.5 Hz), 2.13–2.05 (m, 1H), 1.95 (dd, 2H, *J* = 13.4, 5.8 Hz), 1.87–1.77 (m, 3H), 1.68 (s, 9H); ^{13}C NMR δ 195.9, 171.5, 150.1, 136.8, 136.1, 126.1, 124.3, 123.2, 120.0, 115.6, 114.1, 84.4, 61.7, 52.2, 42.3, 38.9, 37.6, 33.8, 28.2, 22.7, 22.4; DART MS *m/z* 395 (M^++1, 41.0), DART HRMS calcd. for $C_{23}H_{27}N_2O_4$ 395.1971 found 395.1988.

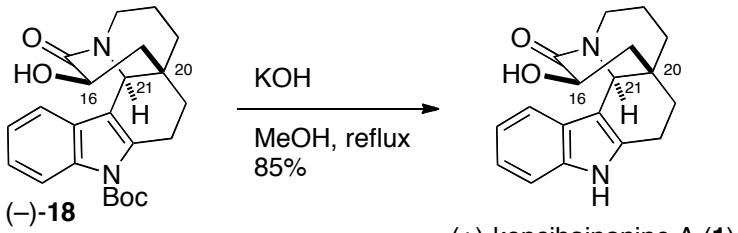
(1*S*,3*R*,4a*R*,11c*S*)-7-*tert*-Butoxycarbonyl-3,4,5,6,7,11c-hexahydro-3-hydroxy-1,4a-propano-4a*H*-pyrido-[3,2-*c*]carbazol-2(1*H*)-one {(–)-18}



(+)-**17** (–)-**18**

$NaBH_4$ (25.5 mg, 0.671 mmol) was added to *t*BuOH/THF (1:1, 4.0 mL) at 0 °C. To the resulting suspension was added (+)-**17** (33.1 mg, 0.0840 mmol) in *t*BuOH/THF (1:1, 4.0 mL) at 0 °C. After stirring for 1 h at the same temperature, the mixture was quenched with saturated aqueous NH_4Cl, extracted with AcOEt. The extract was washed with water and brine, dried and concentrated to dryness. The residue was chromatographed with hexane-AcOEt (2:1 to 1:1) to give (–)-**18** (15.0 mg, 45%) as a colorless oil: R*f* = 0.4 (hexane-AcOEt = 2:1, UV, PMA); $[\alpha]_D^{29}$ = –26.7 (c = 1.20, $CHCl_3$); IR 3466, 2934, 1728, 1670, 1456, 1360 cm^{-1}; ^1H NMR δ 8.09 (d, 1H, *J* = 8.4 Hz), 7.64 (d, 1H, *J* = 7.2 Hz), 7.24 (dd, 1H, *J* = 8.4, 7.2 Hz), 7.16 (dd, 1H, *J* = 7.2, 7.2 Hz), 4.43 (dd, 1H, *J* = 12.6, 5.4 Hz), 4.23 (s, 1H), 4.04 (ddd, 1H, *J* = 10.8, 9.0, 5.4 Hz), 3.57 (d, 1H, *J* = 6.0 Hz), 3.27–3.19 (m, 3H), 2.44 (dd, 1H, *J* = 13.8, 9.0 Hz), 2.00–1.90 (m, 2H), 1.75–1.64 (m, 12H), 1.63–1.58 (m, 1H), 1.27 (dd, 1H, *J* = 13.8, 10.8 Hz); ^{13}C NMR δ 185.6, 150.3, 136.2, 135.0, 126.1, 124.1, 122.7, 120.0, 115.5, 84.1, 68.6, 63.3, 53.8, 39.3, 37.1, 36.6, 34.7, 28.3, 22.3, 21.7; DART MS *m/z* 397 (M^++1, 100.0), DART HRMS calcd. for $C_{23}H_{29}N_2O_4$ 397.2127 found 397.2118; HPLC: AD-H column; λ = 254 nm; eluent: hexane/2-propanol = 97/3; flow rate: 1.0 mL/min; t_R = 26.9 min (minor), t_R = 29.5 min (major); ee = 99%.

(1*S*,3*R*,4a*R*,11c*S*)-3,4,5,6,7,11c-hexahydro-3-hydroxy-1,4a-propano-4a*H*-pyrido-[3,2-*c*]carbazol-2(1*H*)-one {(+)-kopsihainaine A} (1)



(–)-**18** (+)-kopsihainanine A (**1**)

To a solution of (–)-**18** (11.5 mg, 0.0290 mmol) in MeOH (4.5 mL) was added KOH (10.3 mg, 0.183 mmol) at room temperature and the mixture was warmed to reflux. After stirring for 3 h, the mixture was cooled and concentrated to dryness. To the residue was added water and extracted with CH_2Cl_2, washed with water and brine, dried, concentrated to dryness. The residue was chromatographed with hexane-AcOEt (1:1 to 1:2) to give (+)-kopsihainanine A (**1**) (7.3 mg, 85%) as a

colorless powder: R*f* = 0.2 (hexane-AcOEt = 1:1, UV, PMA); mp 168–170 °C (from AcOEt); $[\alpha]_D^{30}$ = +25.4 (c = 0.33, $CHCl_3$), $[\alpha]_D^{16}$ = +39.4 (c = 0.10, MeOH), $[\alpha]_D^{19}$ = +10.0 (c = 0.10, AcOEt) {lit.[3] $[\alpha]_D^{25}$ = 60 (c = 0.10, $CHCl_3$), lit.[4] $[\alpha]_D^{20}$ = 55.0 (c = 0.5, $CHCl_3$)}; IR 3470, 3013, 2930, 1668, 1466, 1095 cm^{-1}; ^1H NMR δ 7.86 (brs, 1H), 7.62 (d, 1H, *J* = 7.8 Hz), 7.27 (d, 1H, *J* = 7.8 Hz), 7.13 (dd, 1H, *J* = 7.8, 7.2 Hz), 7.04 (dd, 1H, *J* = 7.8, 7.2 Hz), 4.43 (dd, 1H, *J* = 12.6, 5.4 Hz), 4.36 (s, 1H), 4.02 (ddd, 1H, *J* = 10.8, 8.4, 5.4 Hz), 3.59 (d, 1H, *J* = 5.4 Hz), 3.26 (ddd, 1H, *J* = 12.6, 12.6, 3.0 Hz), 3.11–3.05 (m, 1H), 2.77 (dd, 1H, *J* = 17.2, 6.2 Hz), 2.38 (dd, 1H, *J* = 14.1, 8.6 Hz), 2.00–1.91 (m, 2H), 1.82 (ddd, 1H, *J* = 13.2, 12.0, 6.0 Hz), 1.72–1.69 (m, 2H), 1.62–1.57 (m, 1H), 1.27 (dd, 1H, *J* = 13.8, 10.8 Hz); ^{13}C NMR δ 185.8, 136.2, 133.0, 124.6, 122.0, 120.0, 119.8, 110.5, 109.9, 68.7, 63.8, 53.8, 39.4, 37.6, 37.4, 34.5, 21.8, 19.6; DART MS *m/z* 297 (M^++1, 29.0), DART HRMS calcd. for $C_{18}H_{21}N_2O_2$ 297.1603 found 297.1617; HPLC: IE column; λ = 280 nm; eluent: hexane/MeOH/CH_2Cl_2/ethylenediamine = 70/6/24/0.06; flow rate: 1.0 mL/min; t_R = 13.7 min (minor), t_R = 24.6 min (major); ee = 99%.

The obtained spectral data were identical with reported kopsihainanine A.[3,4]

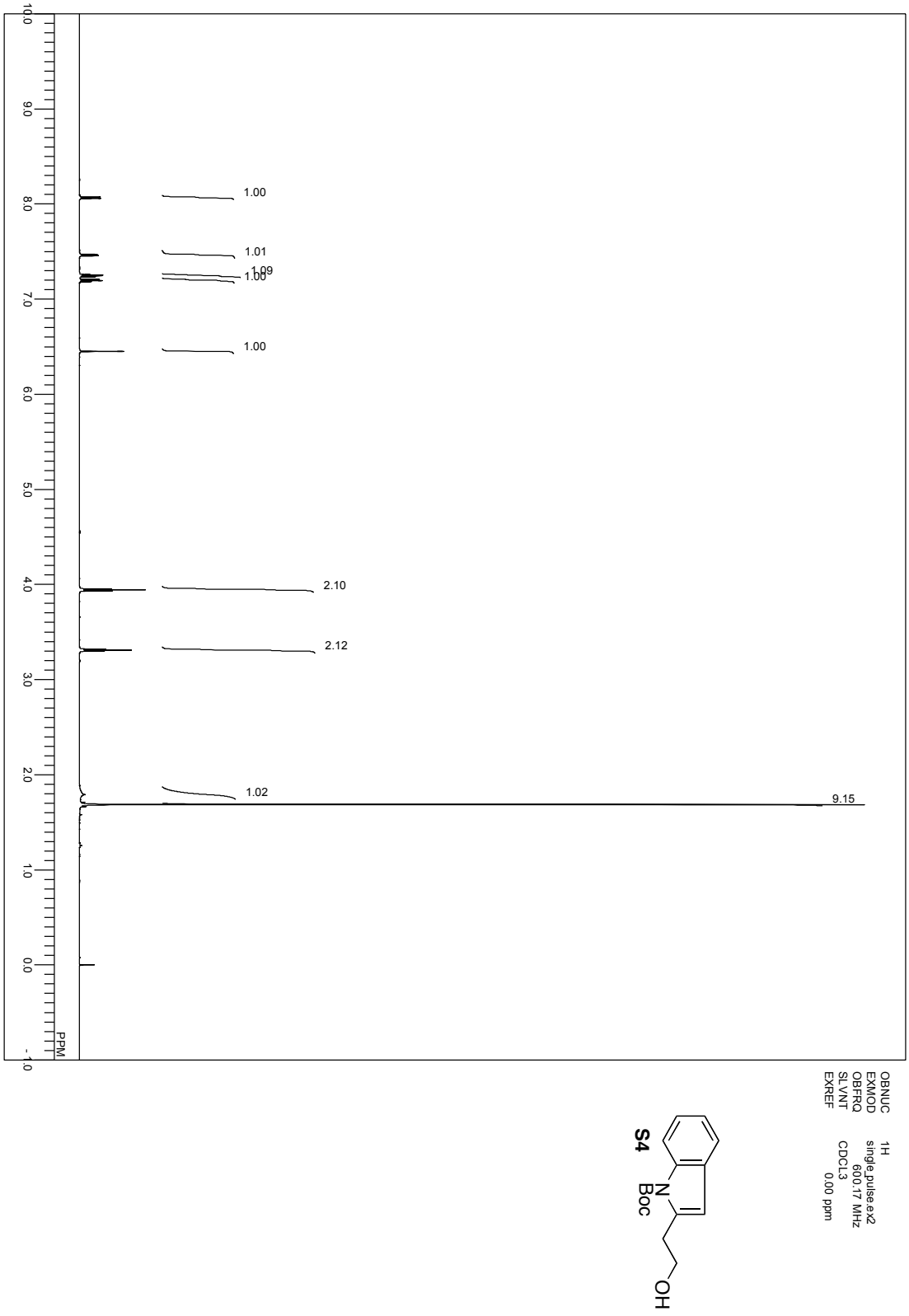
References

1) D. C. Behenna, Y. Liu, T. Yurino, J. Kim. D. E. White, S. C. Virgil and B. M. Stoltz, *Nature Chem*., 2012, **4**, 130–133.

2) L. Jiao and T. Bach, *J. Am. Chem. Soc*., 2011, **133**, 12990–12993.

3) J. Chen, J.-J. Chen, X. Yao and K. Gao, *Org. Biomol. Chem*., 2011, **9**, 5334–5336.

4) Z. Li, S. Zhang, S. Wu, X. Shen, L. Zou, F. Wang, X. Li, F. Peng, H. Zhang and Z. Shao, *Angew. Chem., Int. Ed*., 2013, **52**, 4117–4121.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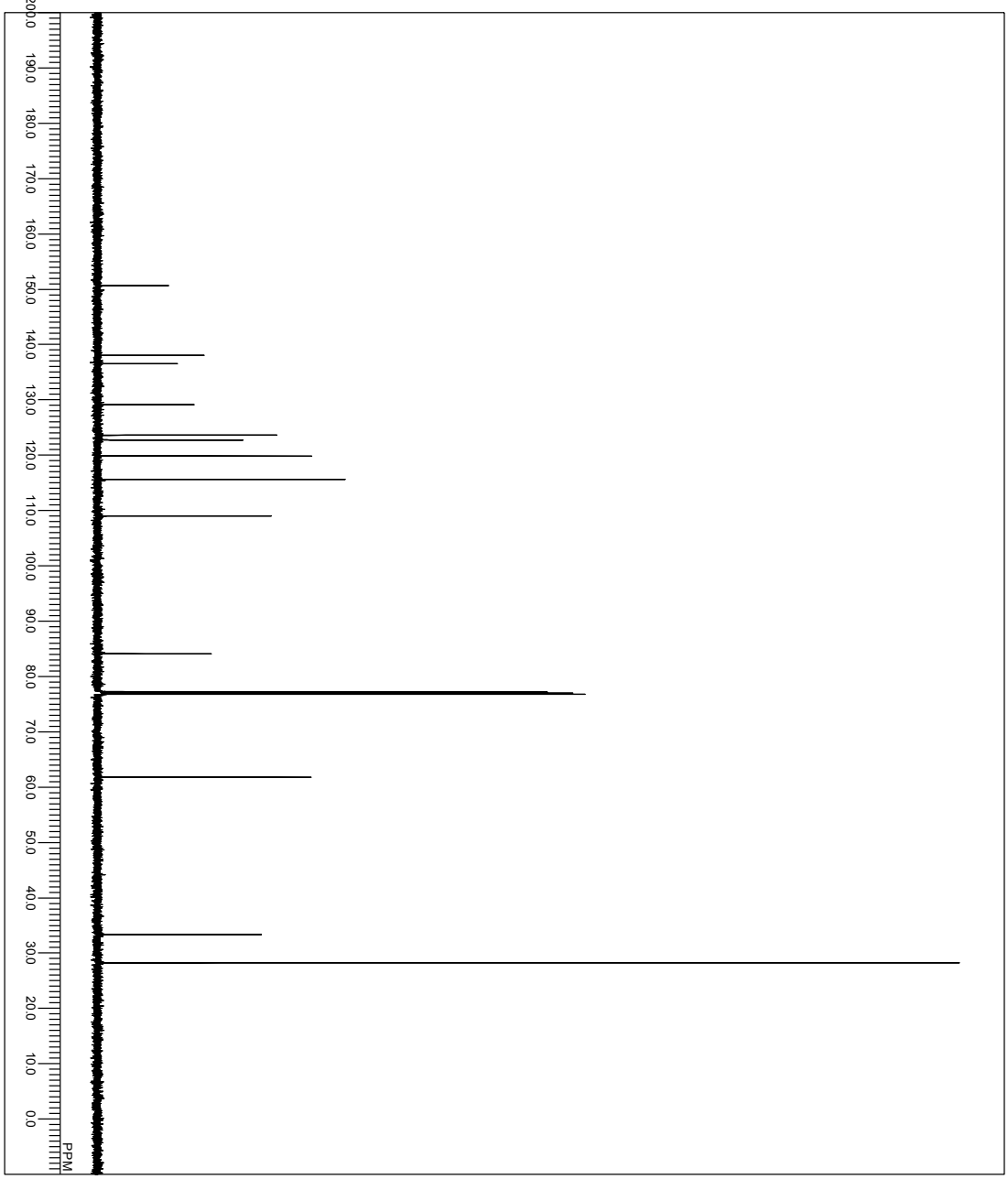
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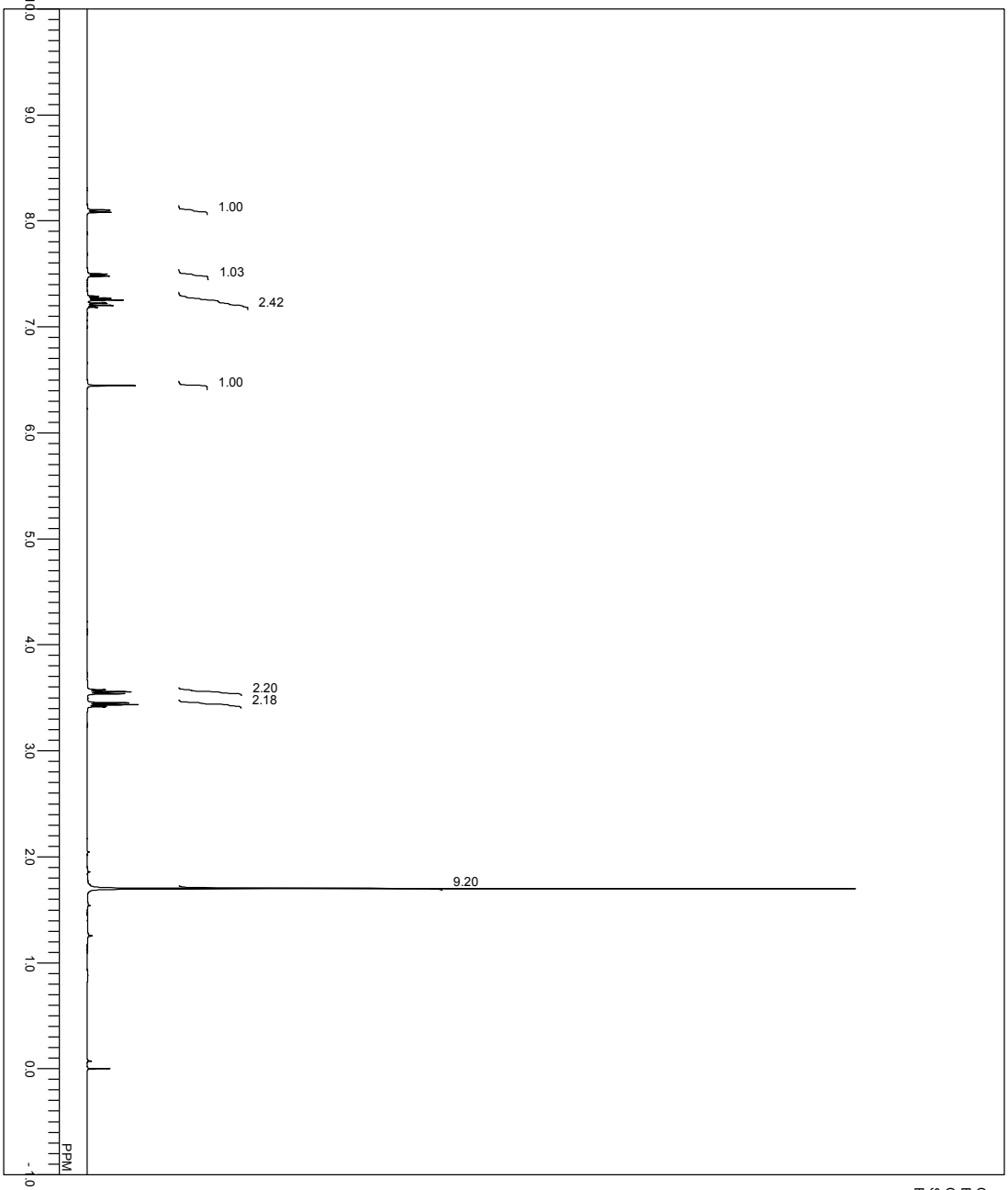
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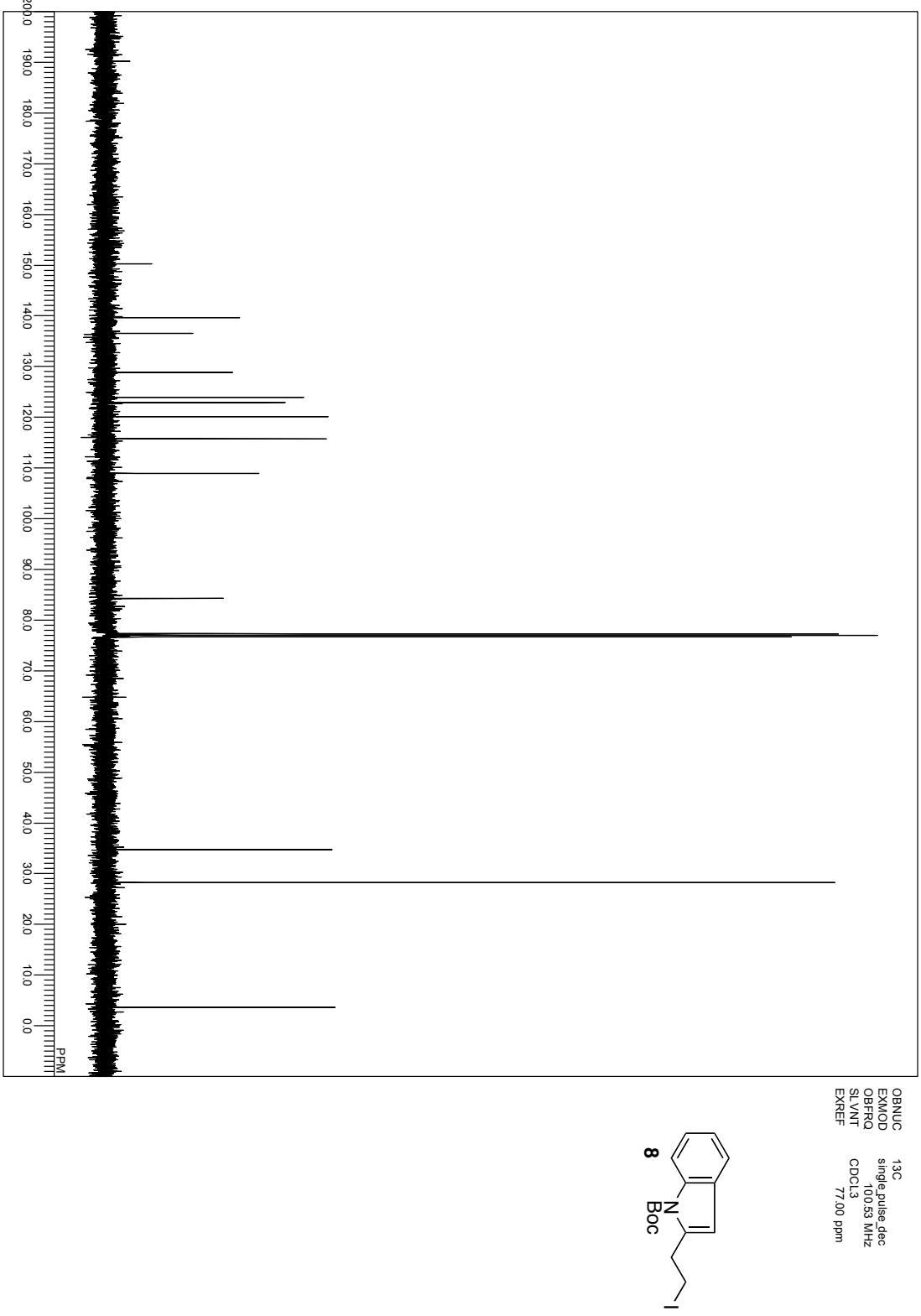
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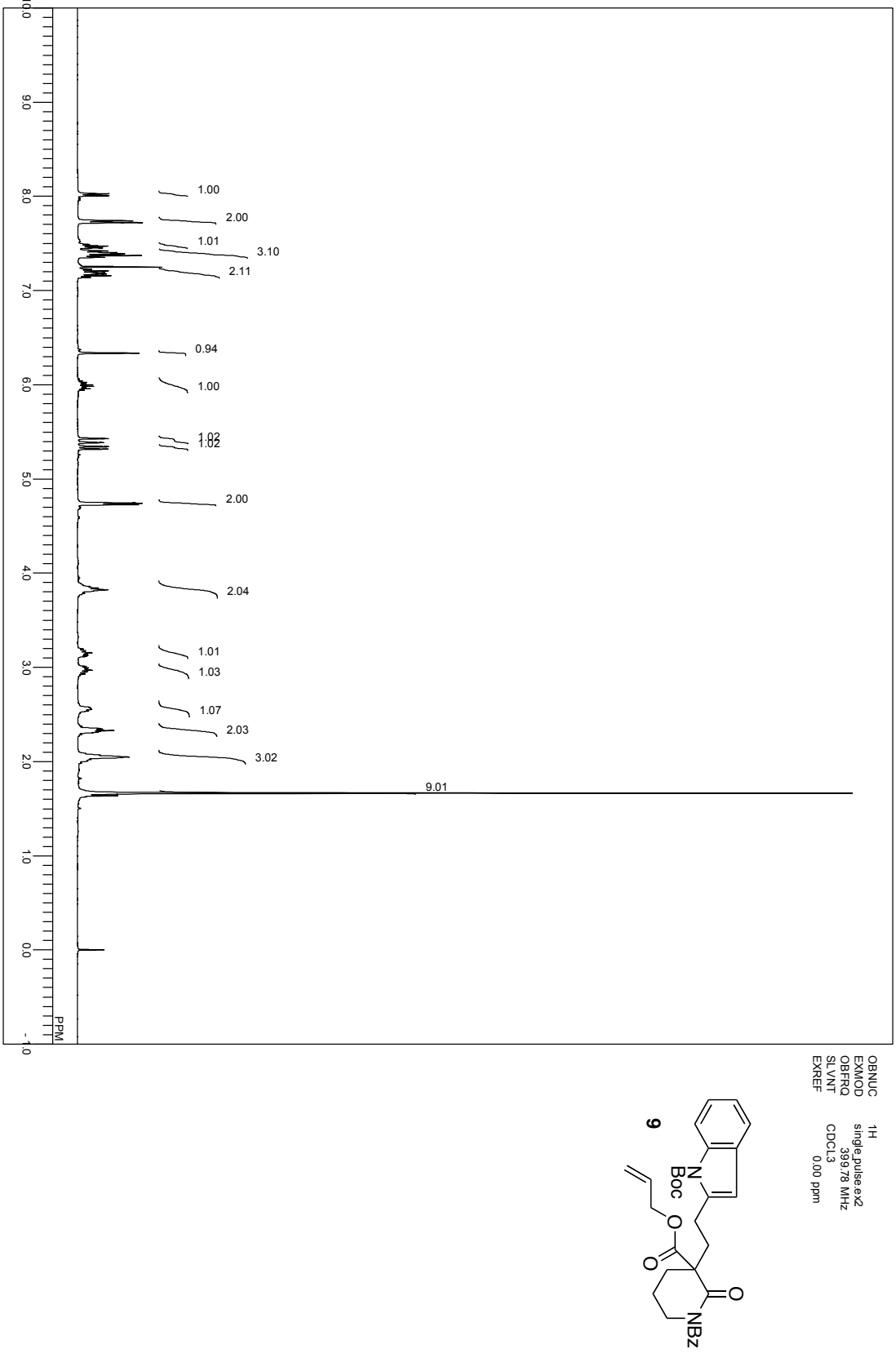
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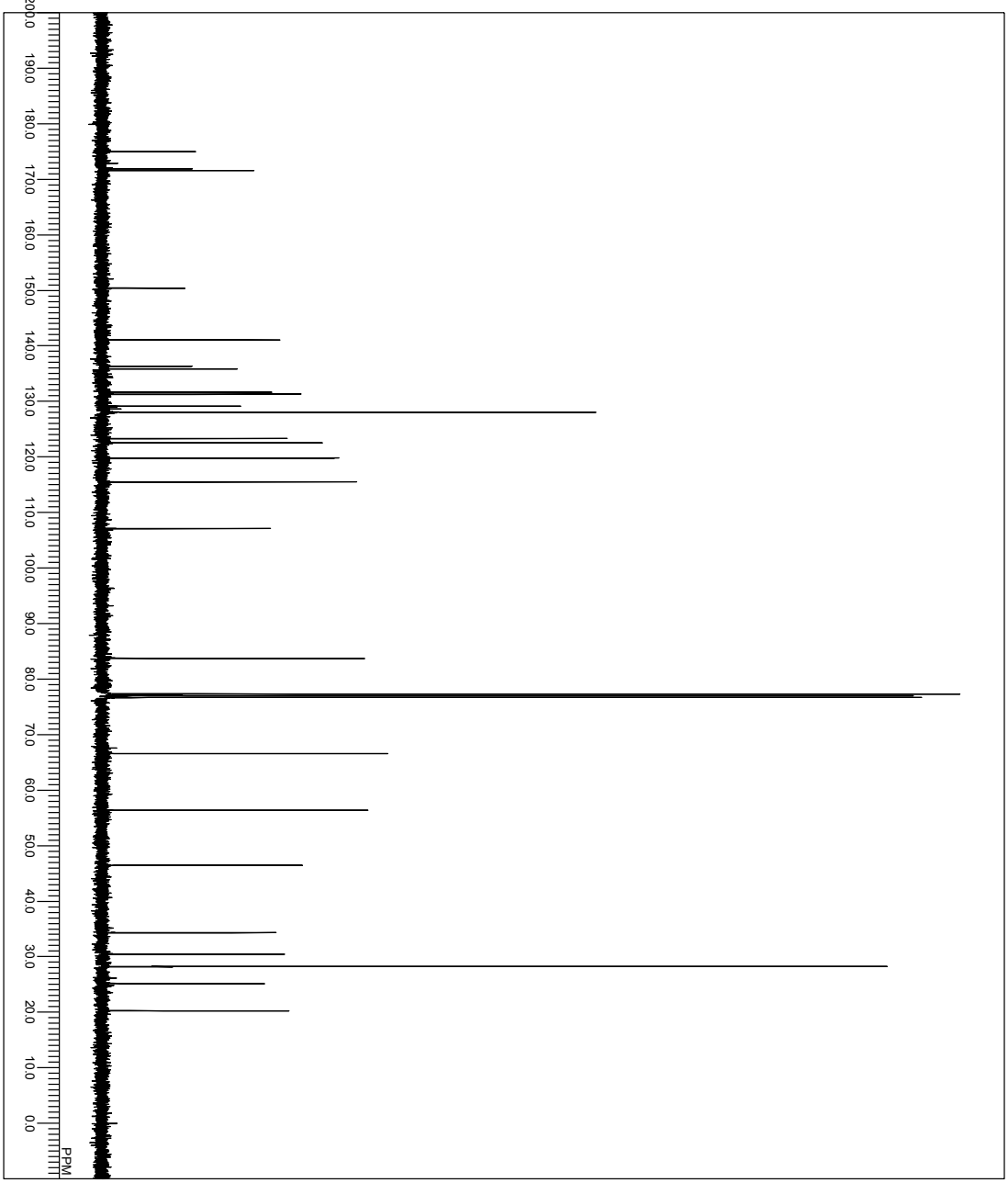
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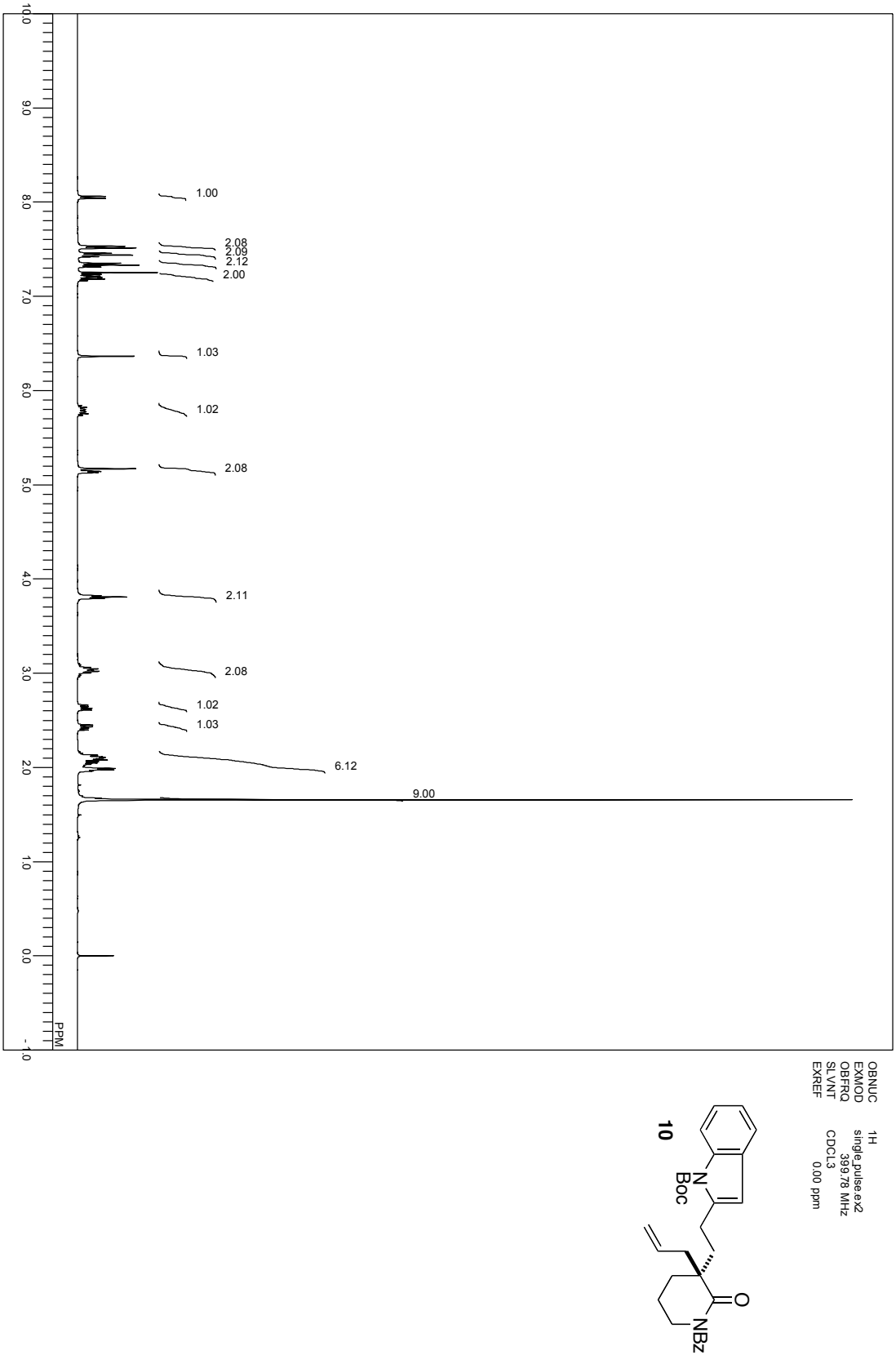
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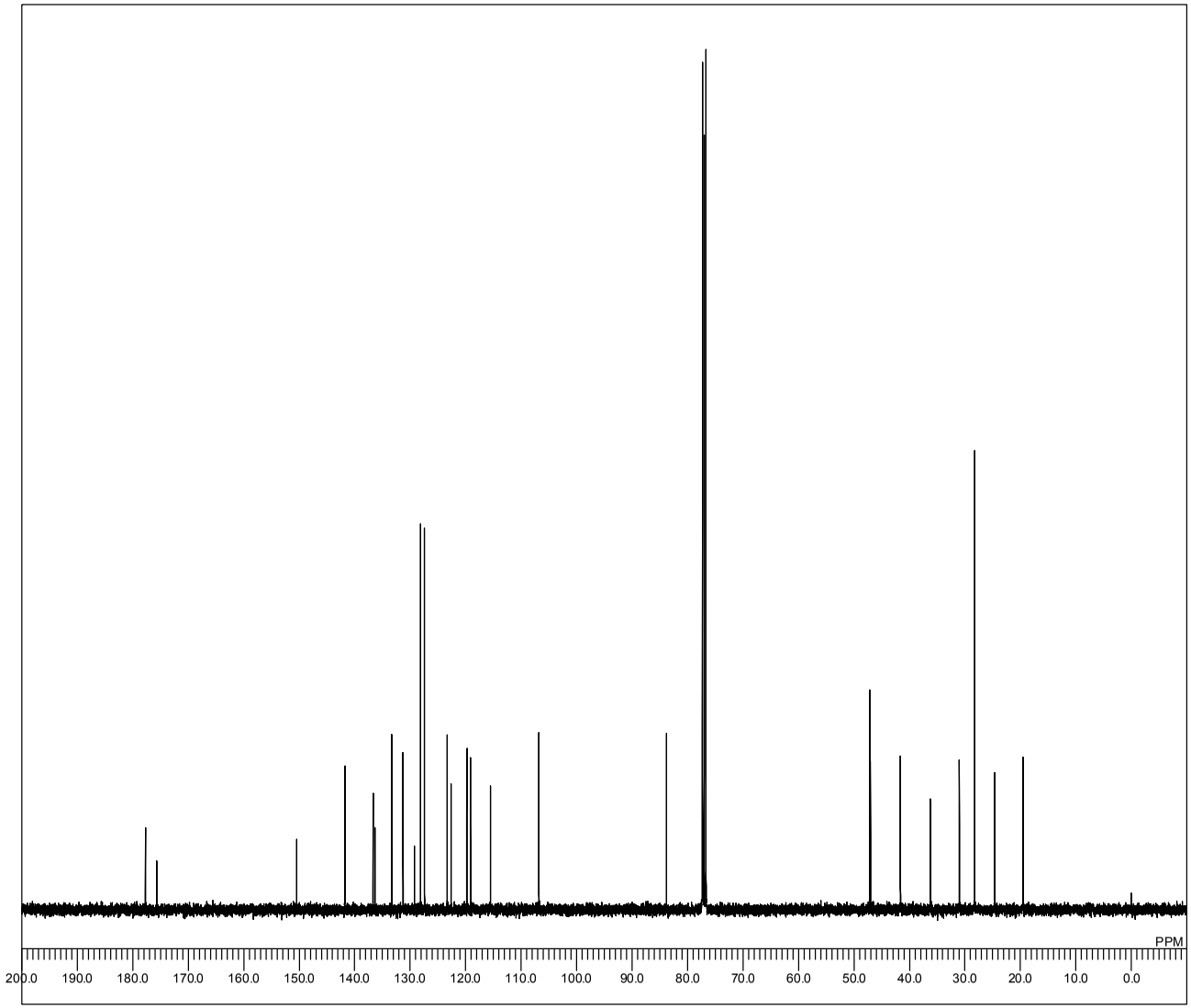
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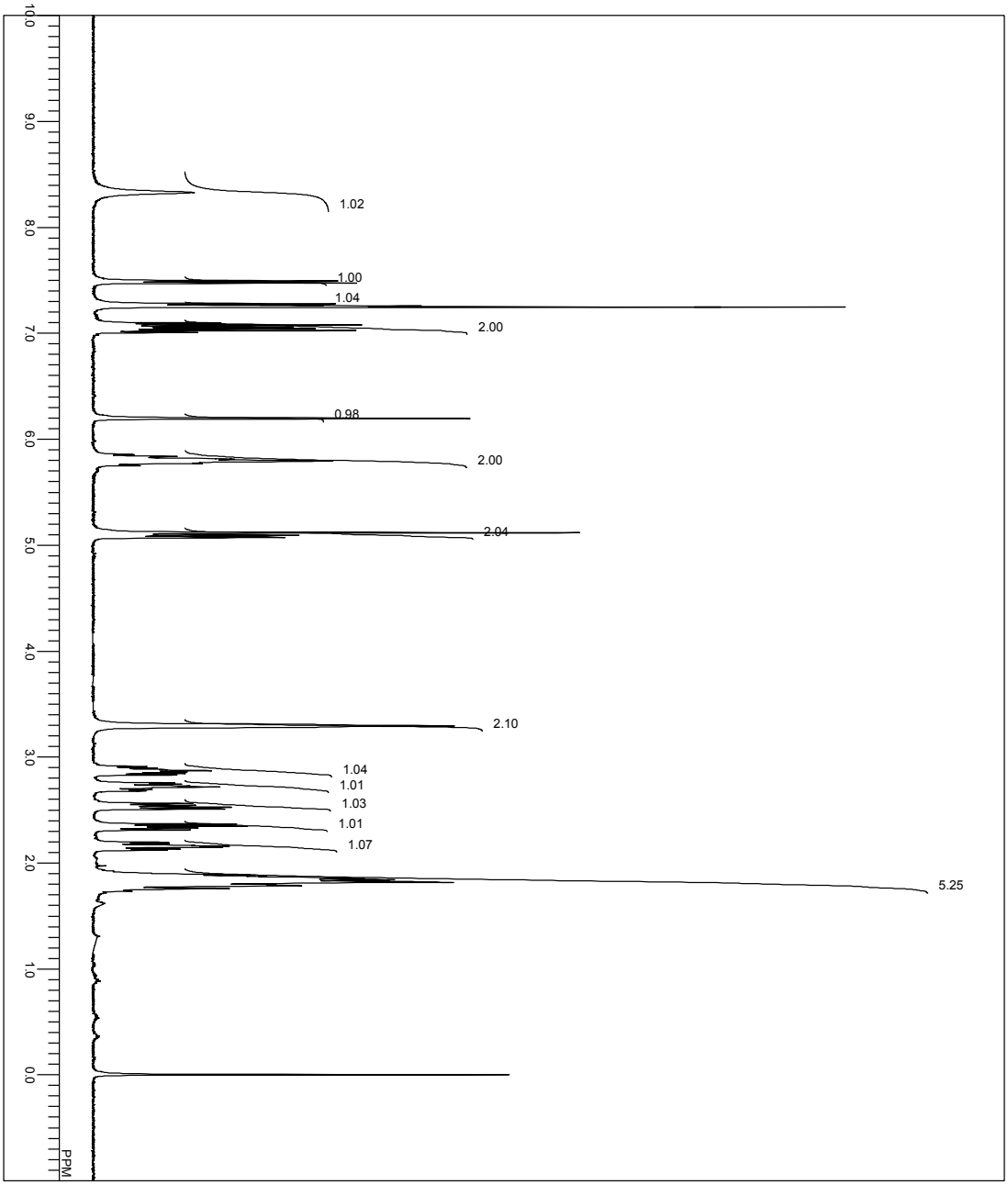
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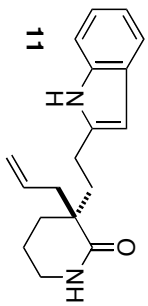
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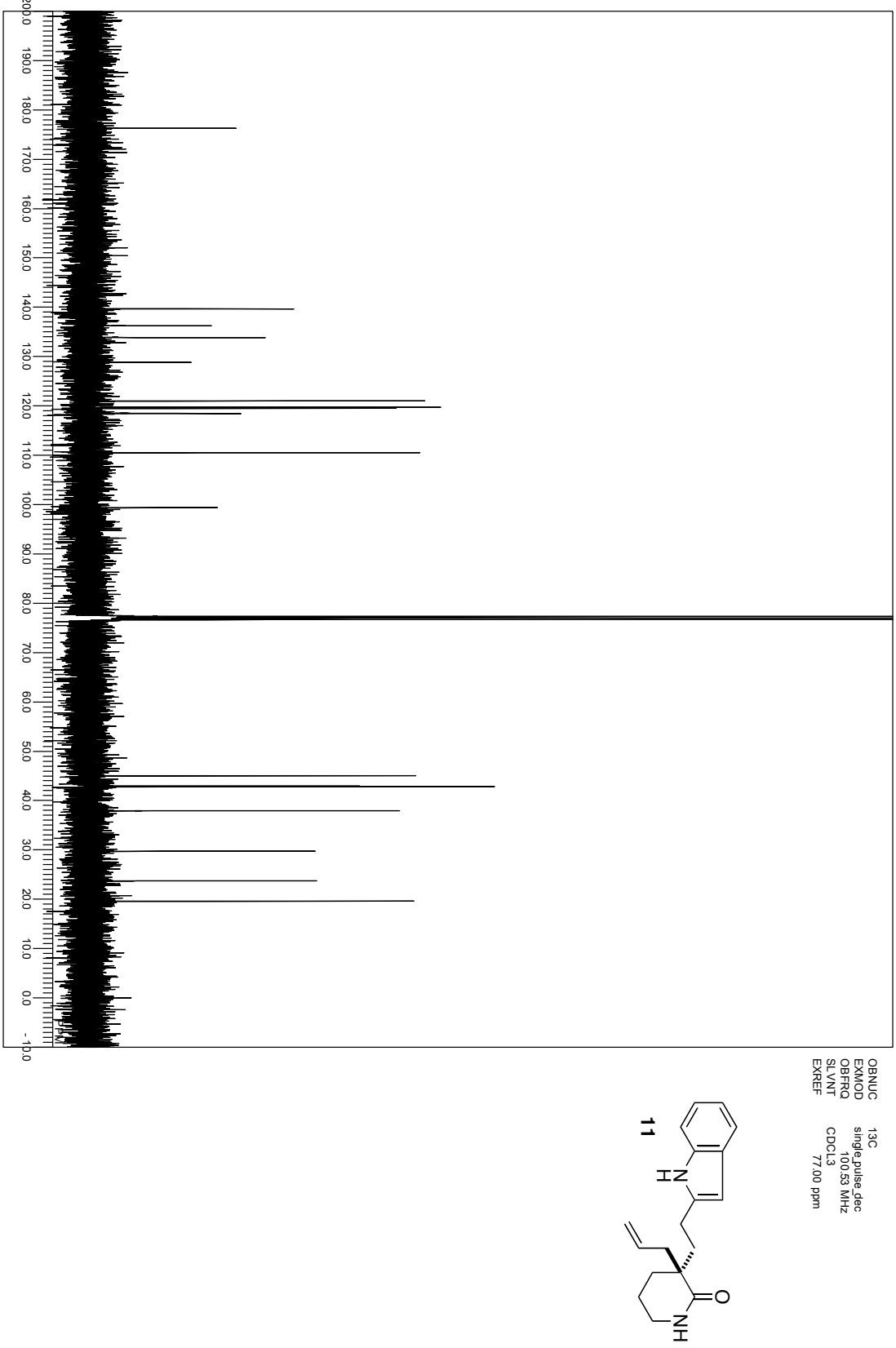
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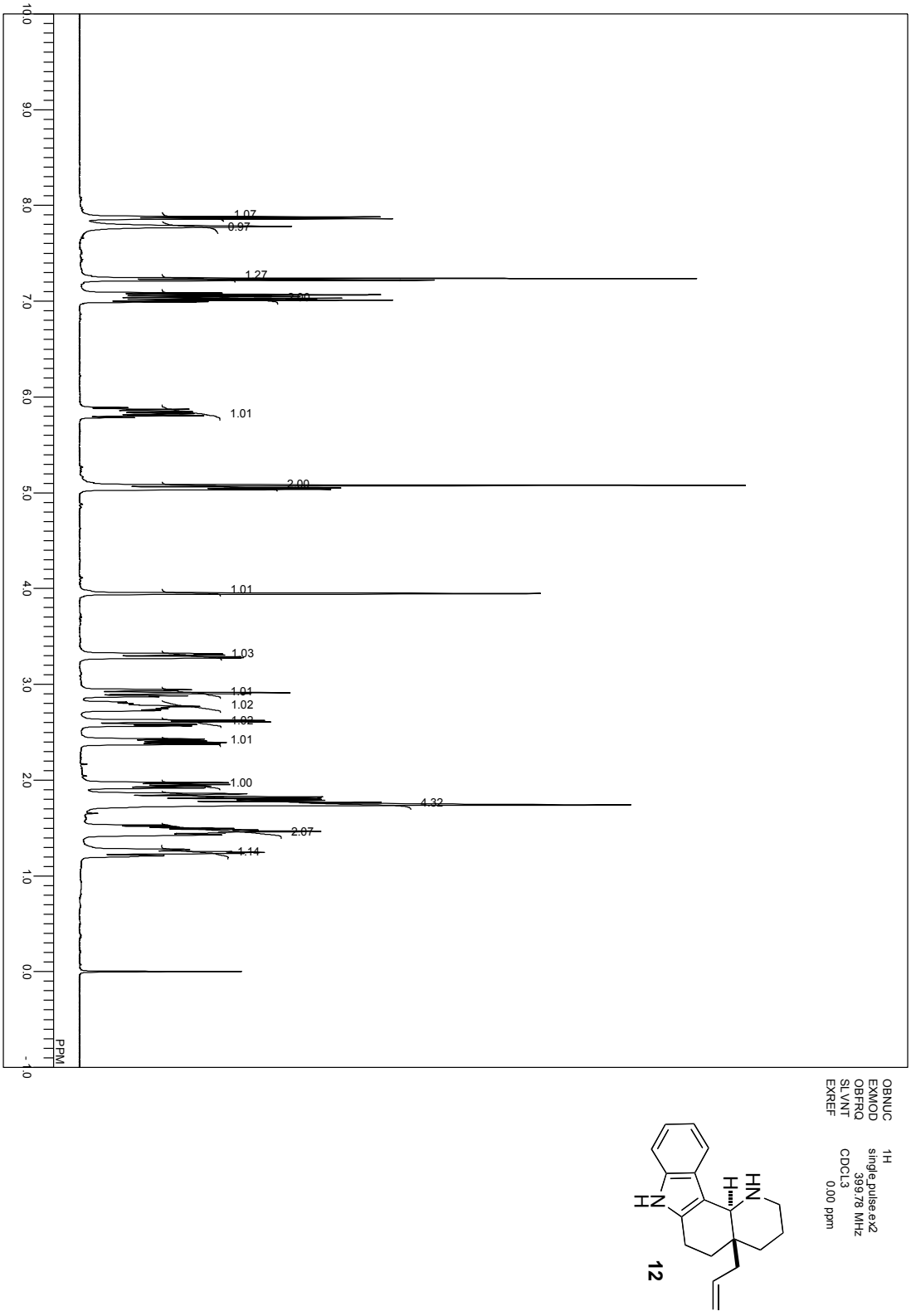
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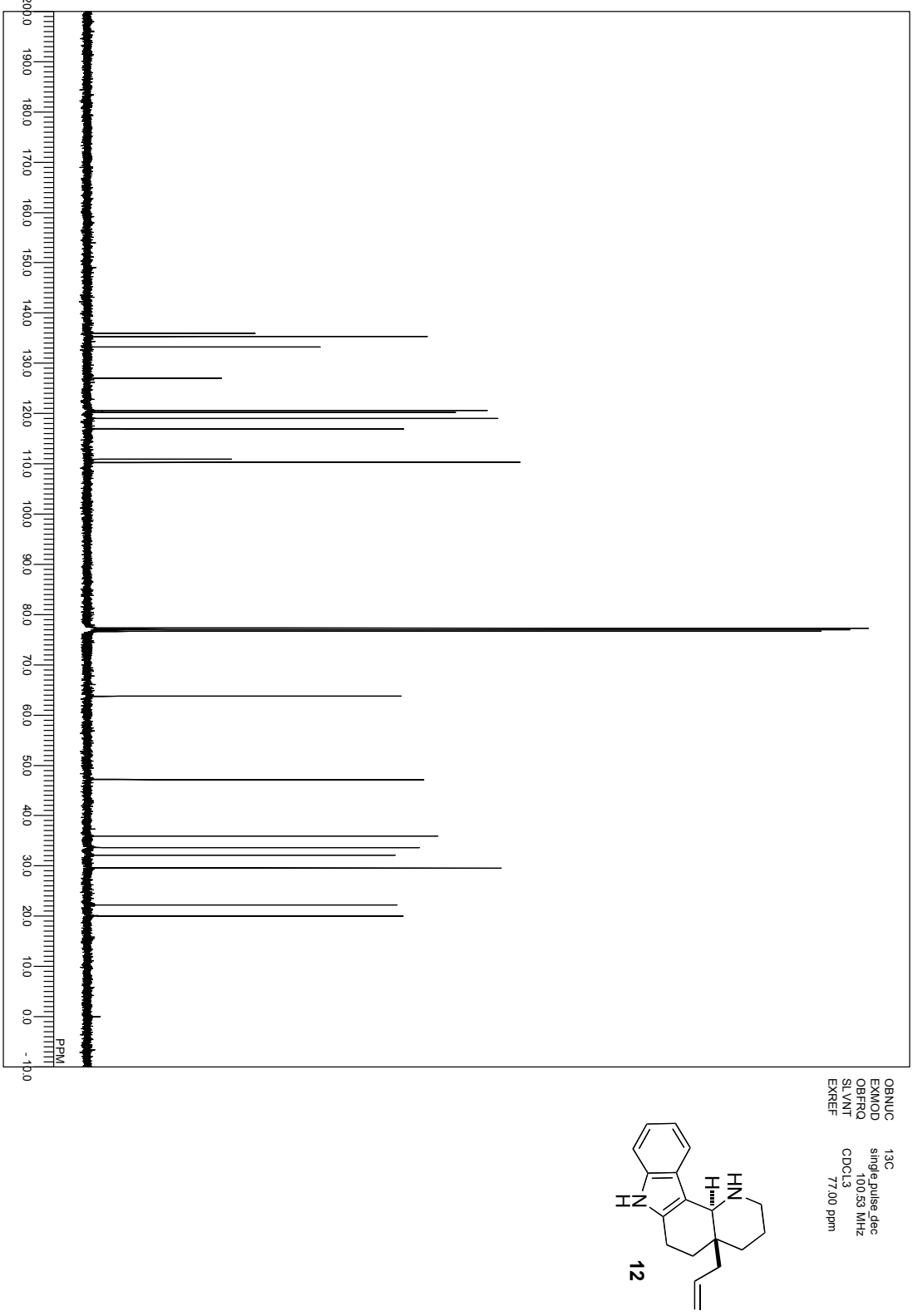
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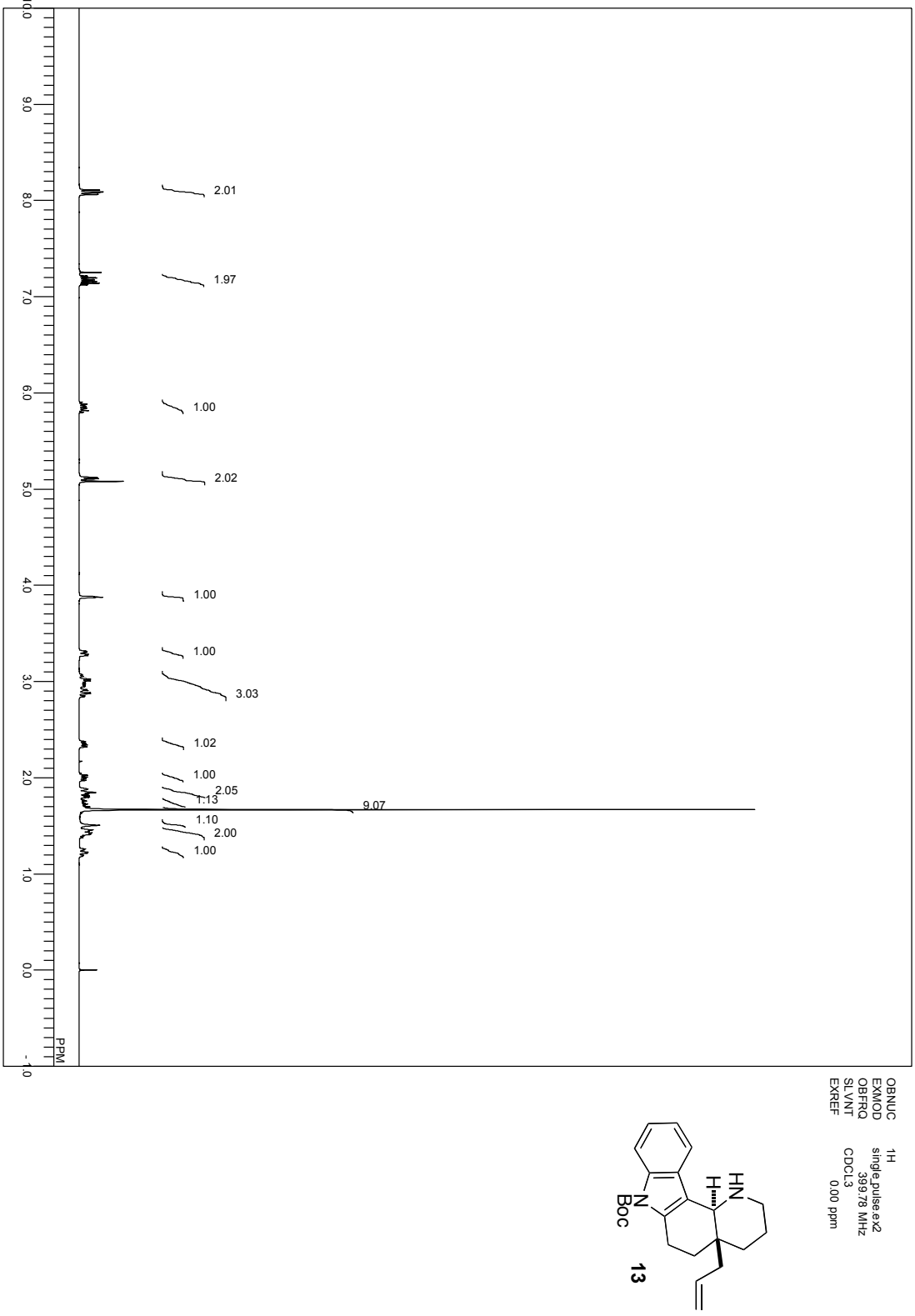
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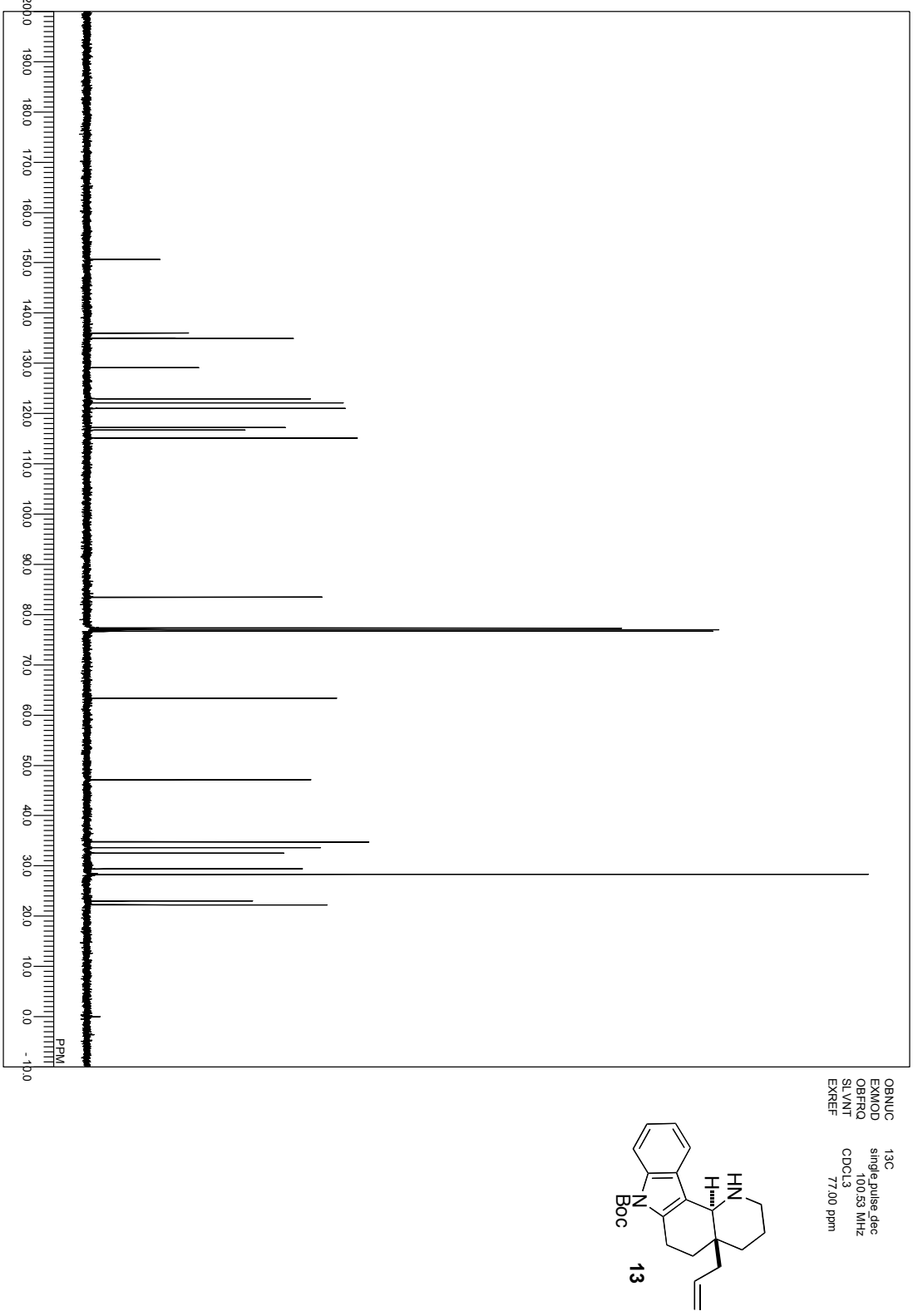
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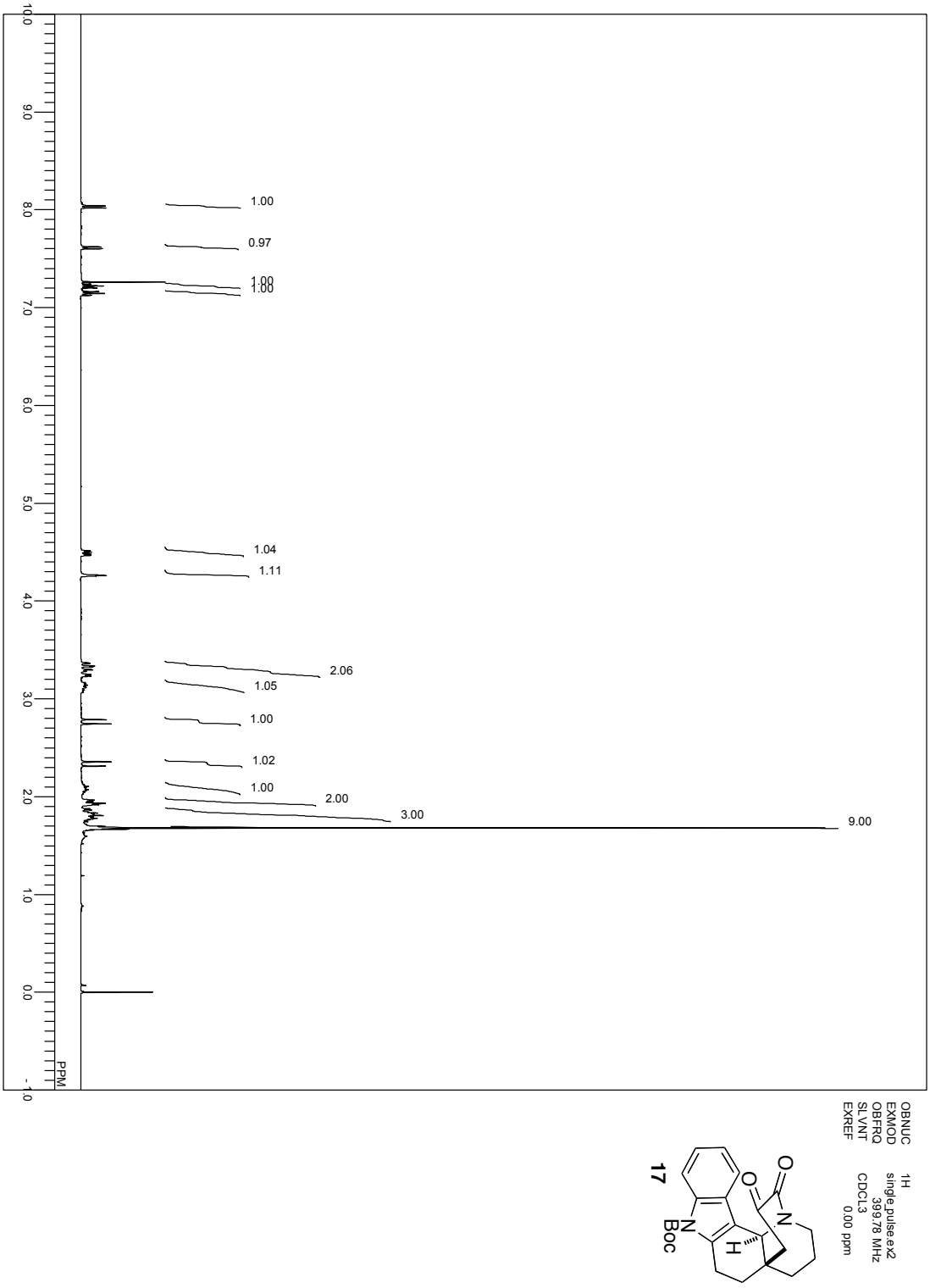
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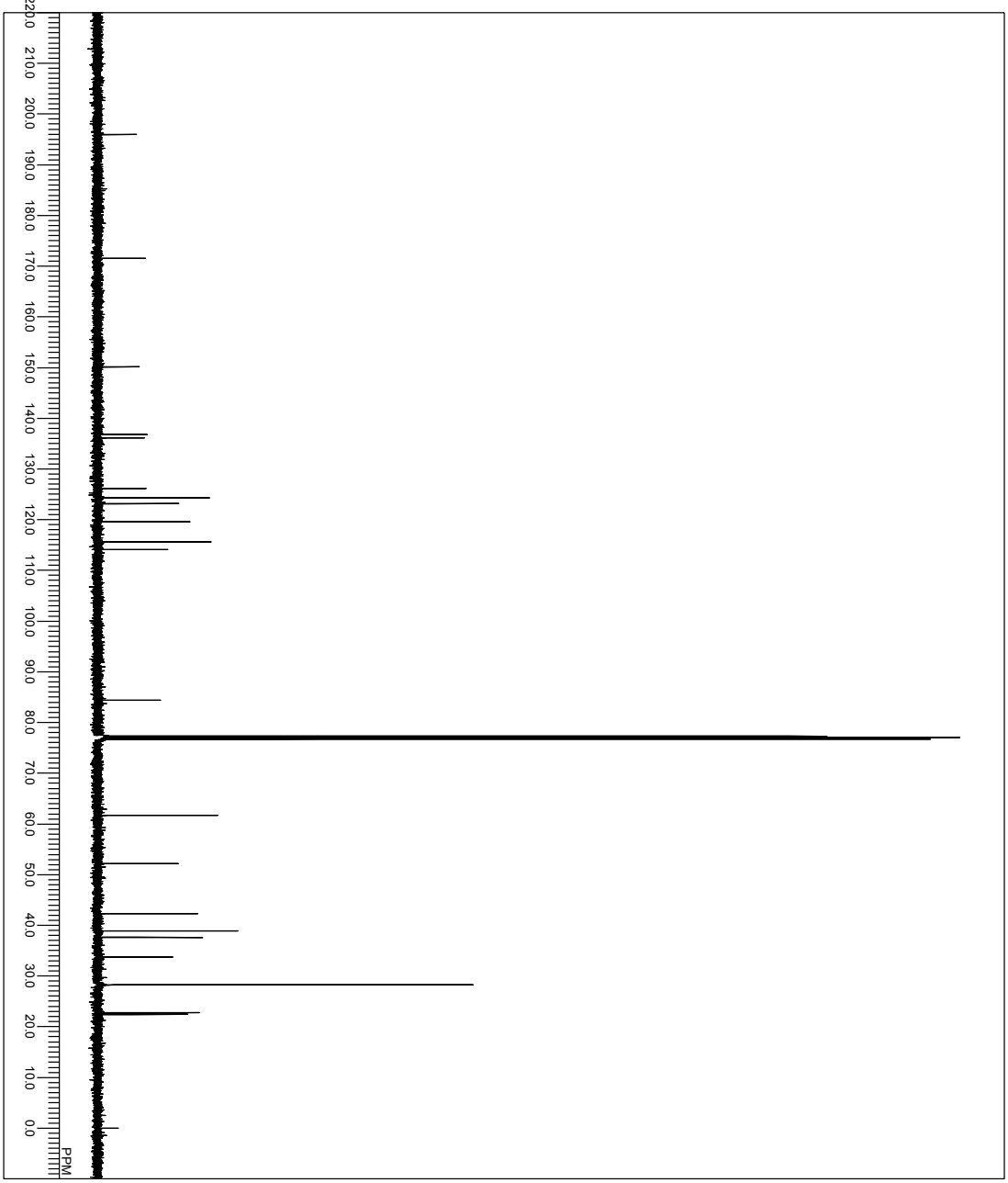
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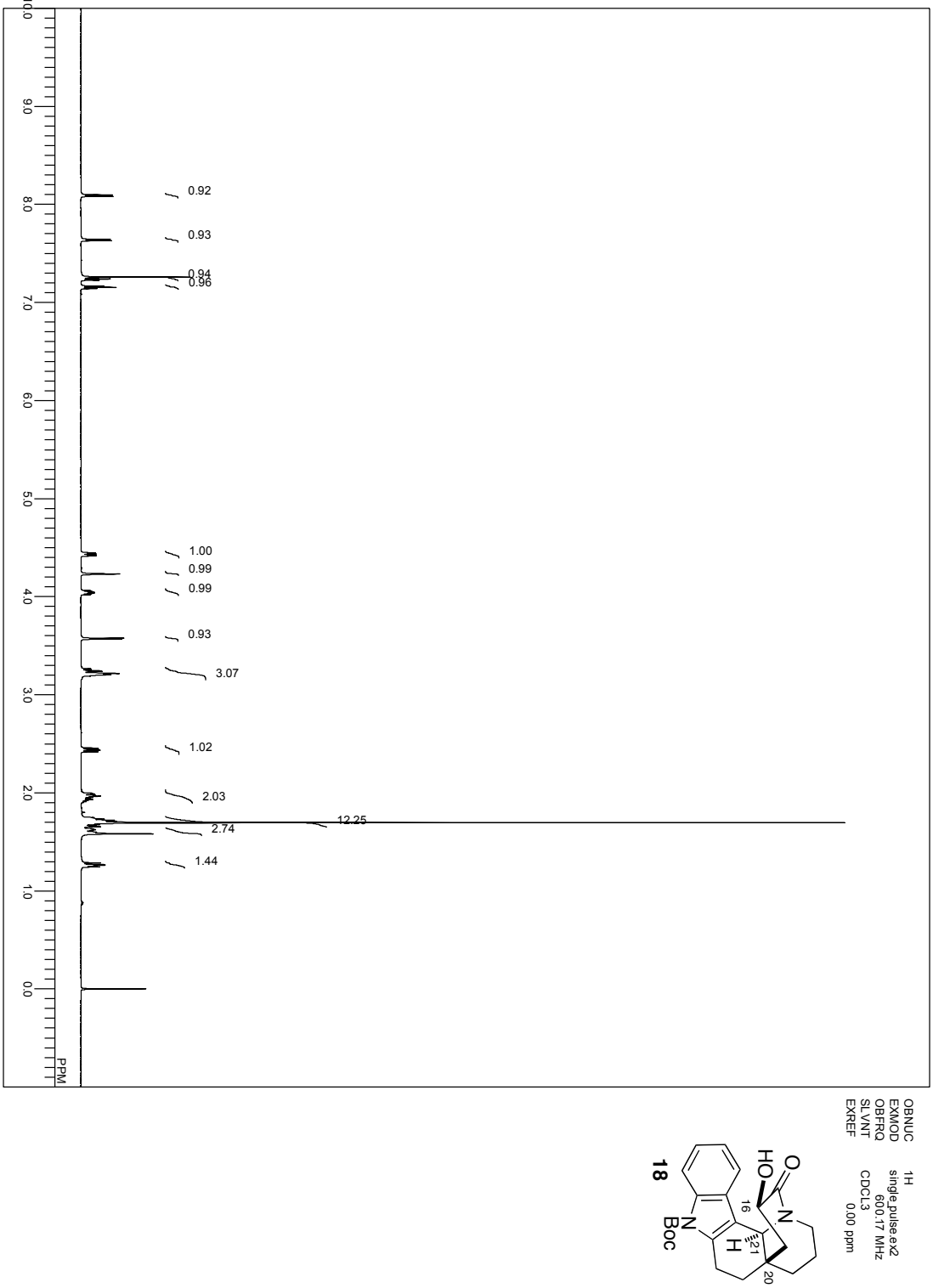
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PPM
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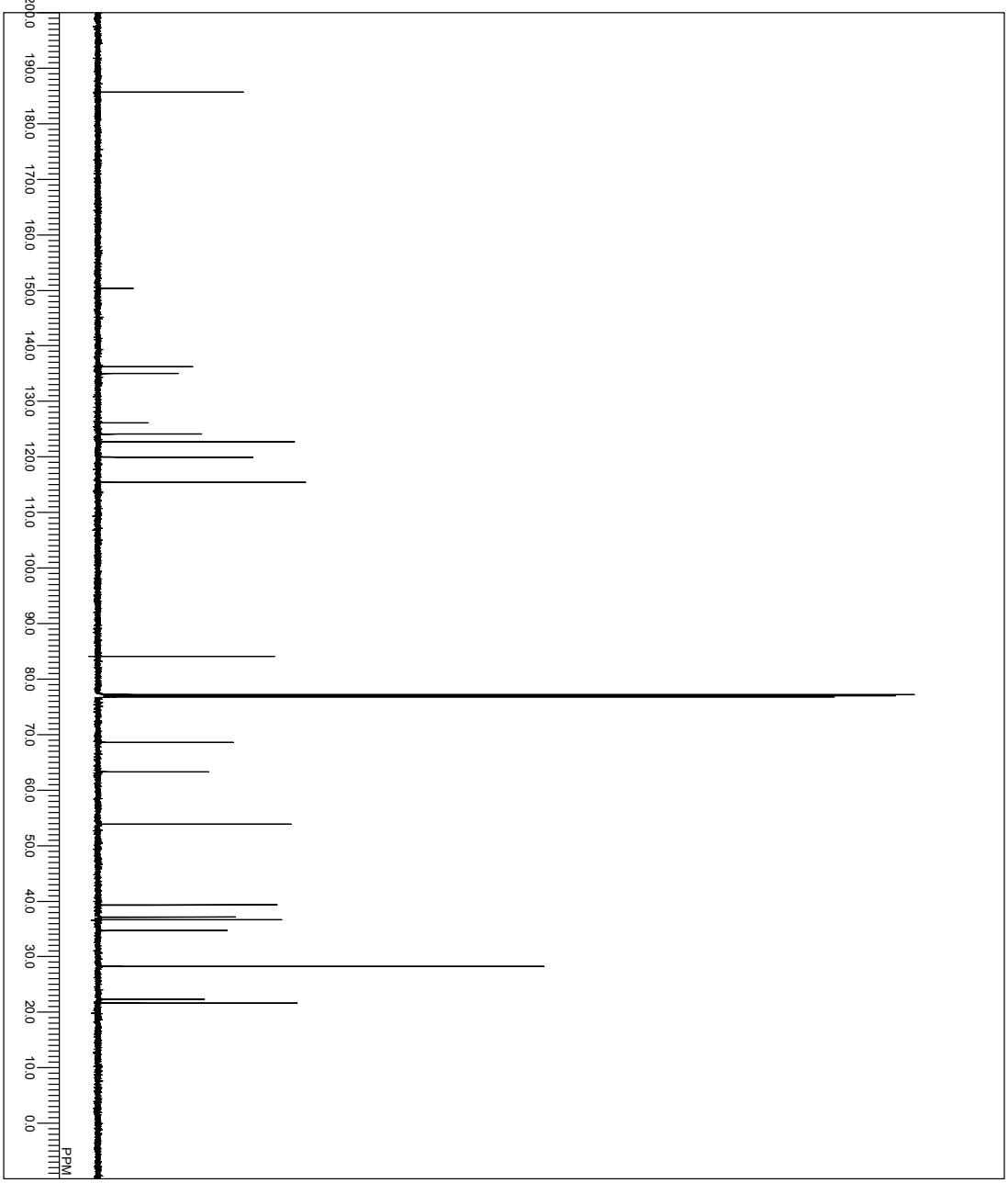
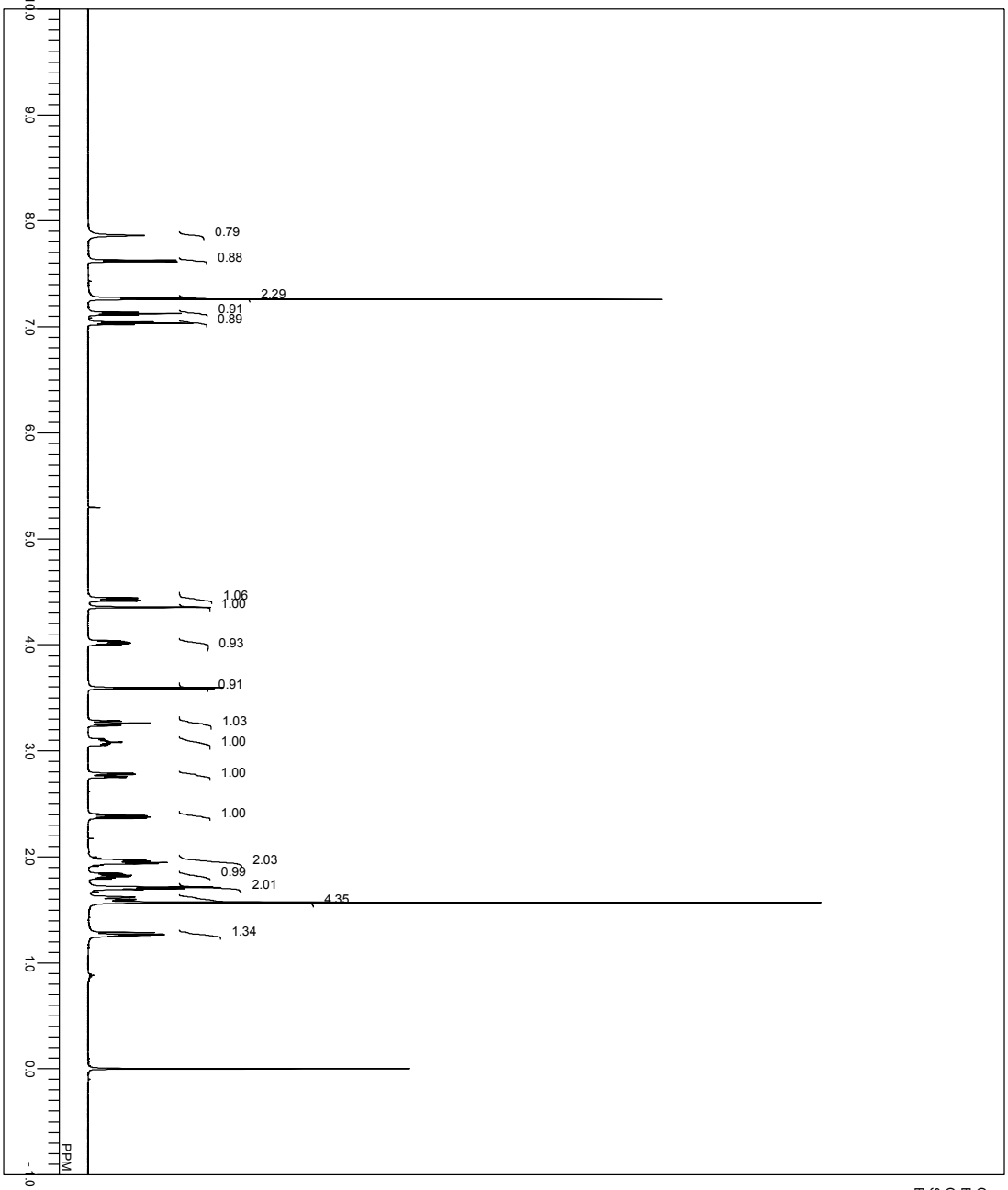
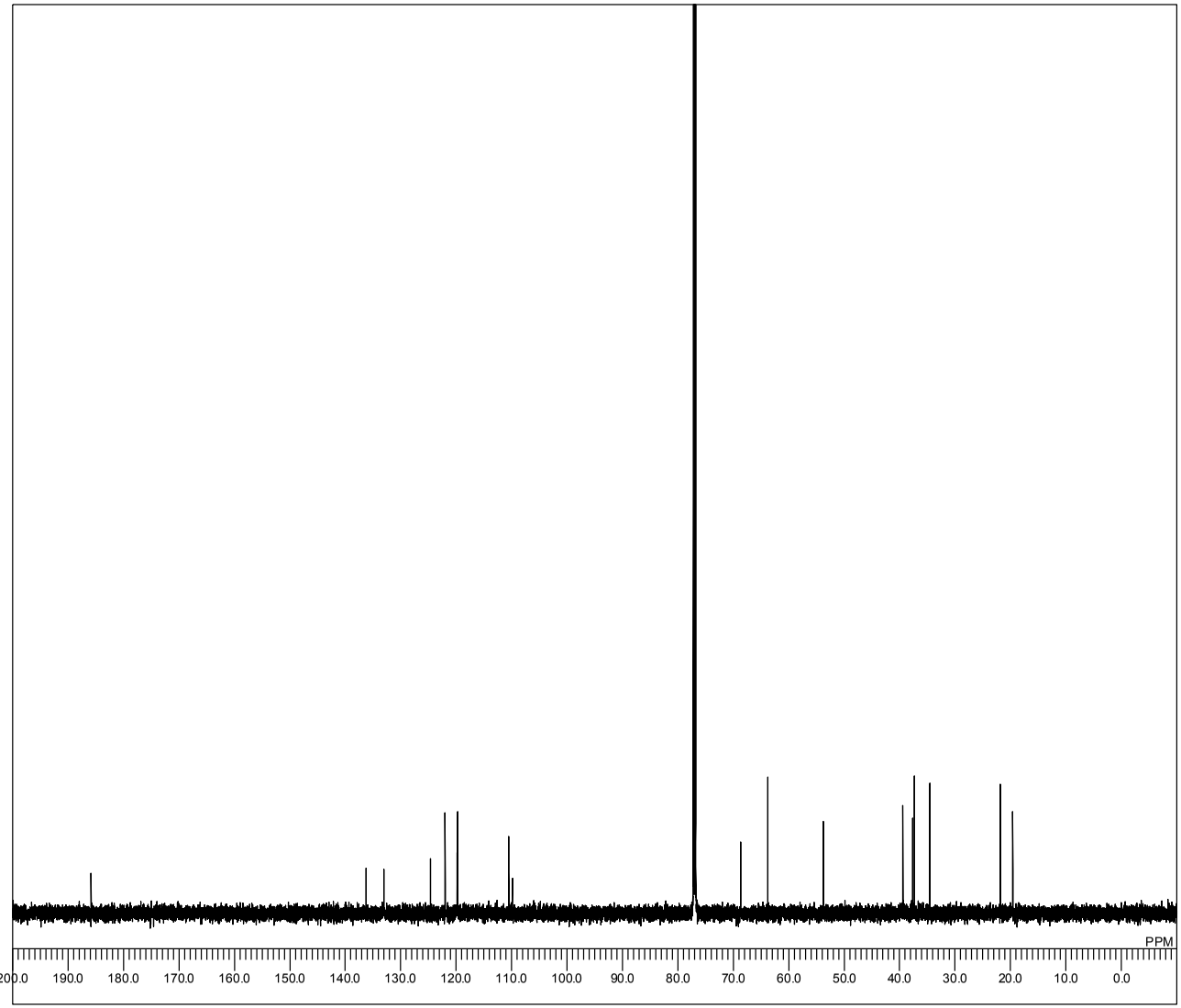
EXMOD single_pulse.ex2
OBFRQ 600.17 MHz
SLVNT CDCL3
EXREF 0.00 ppm
18
HO
O
N
Boc
H
16
21
20

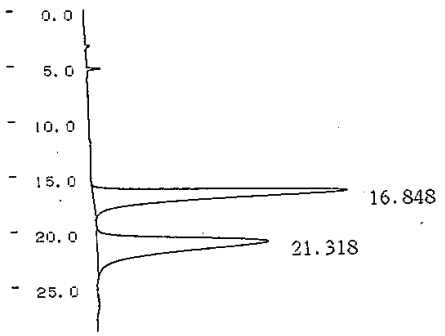

OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 150.92 MHz
SLVNT CDCL3
EXREF 77.00 ppm
18
HO
O
N
16
21
H
20
N
Boc
PPM
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0


0.79
0.88
2.29
0.91
0.89
1.06
1.00
0.93
0.91
1.03
1.00
1.00
1.00
2.03
0.99
2.01
4.35
1.34
PPM
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 600.17 MHz
SLVNT CDCL3
EXREF 0.00 ppm
kopsihainanine A (1)
HO
O
N
H
N
16
21
20

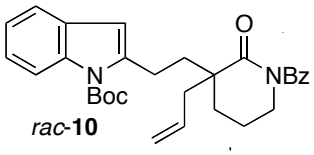


kopsihainanine A (**1**)

CHROMATOPAC C-R7A CH=1 REPORT No.=2 ｸﾛﾏﾄ=1:@CHRM1.C00 13/02/22 22:01:06



scheme 4



rac-**10**

** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	16.848	594838	10448			50.2624	
	2	21.318	588628	7071			49.7376	
		TOTAL	1183465	17518			100	

CHROMATOPAC C-R7A CH=1 REPORT No.=4 ｸﾛﾏﾄ=1:@CHRM1.C00 13/02/22 22:35:46

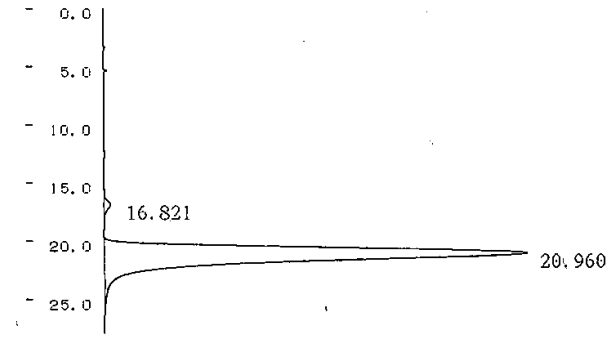
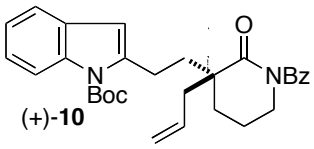


Table 1, entry 8

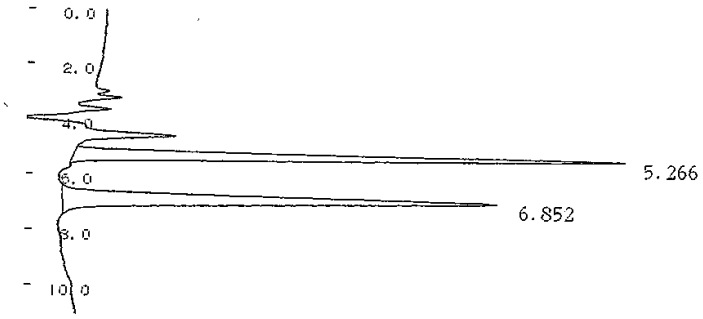


(+)-**10**

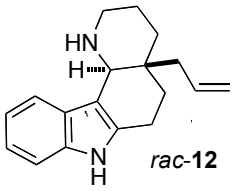
** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	16.821	55222	1062			0.9876	
	2	20.96	5536168	69415			99.0124	
		TOTAL	5591389	70477			100	

CHROMATOPAC C-R7A CH=1 REPORT No.=3 ｸﾛﾏﾄ=1:@CHRM1.C00 13/06/25 15:56:56



scheme 4

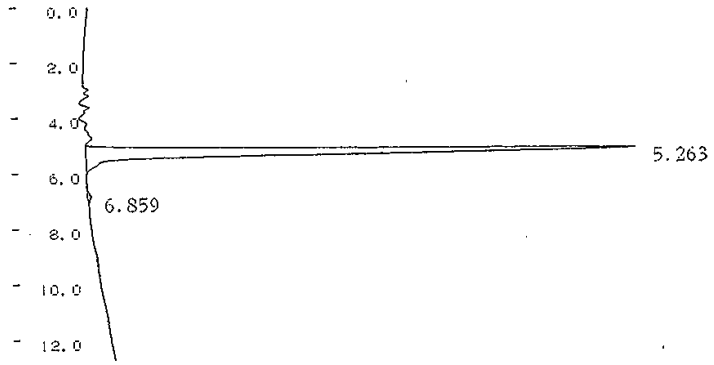


rac-**12**

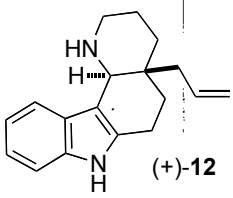
** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	5.266	39207	2818			47.5858	
	2	6.852	43185	2227			52.4141	
		TOTAL	82391	5045			100	

CHROMATOPAC C-R7A CH=1 REPORT No.=8 ｸﾛﾏﾄ=1:@CHRM1.C00 13/06/25 16:40:24



scheme 5

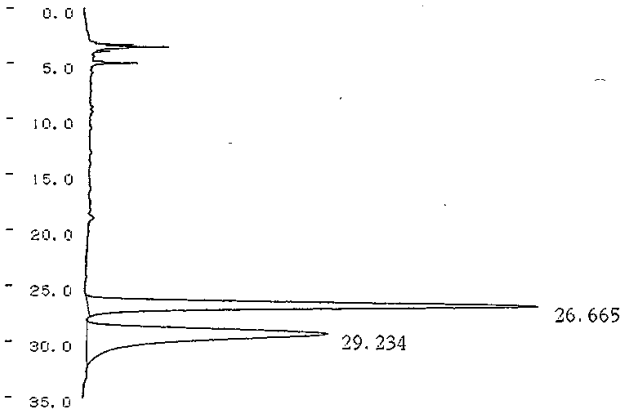


(+)-**12**

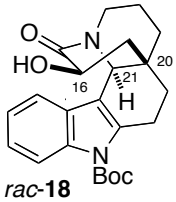
** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	5.263	164838	11230			99.1868	
	2	6.859	1351	71			0.8132	
		TOTAL	166190	11301			100	

CHROMATOPAC C-R7A CH=1 REPORT No.=10 ｸﾛﾏﾄ=1:@CHRM1.C00 13/07/01 19:35:10



scheme 4

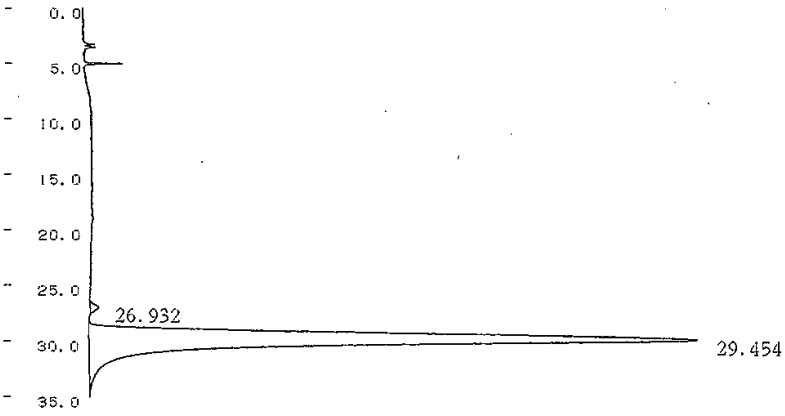


rac-**18**

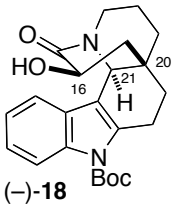
** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	26.665	186162	4624			50.9416	
	2	29.234	179279	2474			49.0583	
		TOTAL	365441	7098			100	

CHROMATOPAC C-R7A CH=1 REPORT No.=13 ｸﾛﾏﾄ=1:@CHRM1.C00 13/07/01 20:40:40



scheme 5

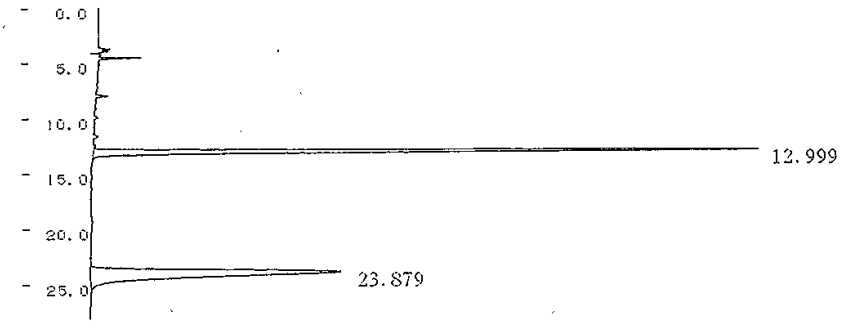


(–)-**18**

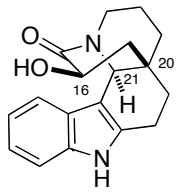
** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	26.932	2850	82			0.6131	
	2	29.454	461993	6253			99.3869	
		TOTAL	464843	6336			100	

CHROMATOPAC C-R7A CH=1 REPORT No.=4 ﾌｧｲﾙ=1:@CHRM1.C00 13/07/01 11:24:30



scheme 4

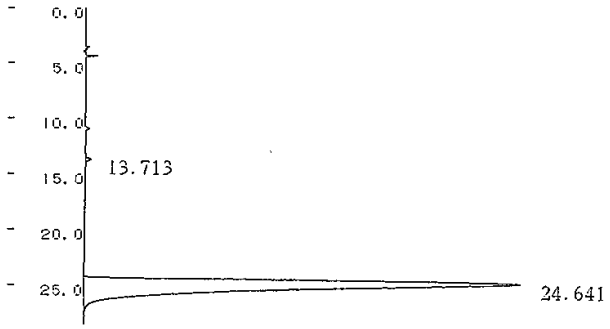


rac-kopsihainanine A (**1**)

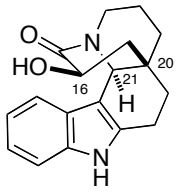
** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	12.999	445950	27232			50.761	
	2	23.879	432579	10332			49.239	
		TOTAL	878529	37563			100	

CHROMATOPAC C-R7A CH=1 REPORT No.=6 ﾌｧｲﾙ=1:@CHRM1.C00 13/07/01 12:03:58



scheme 5



(+)-kopsihainanine A (**1**)

** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	13.713	14229	922			0.3498	
	2	24.641	4053794	72006	S		99.6502	
		TOTAL	4068022	72929			100	