Supporting Information for

Total Synthesis and Absolute Configuration Determination of (+)-Subincanadine F

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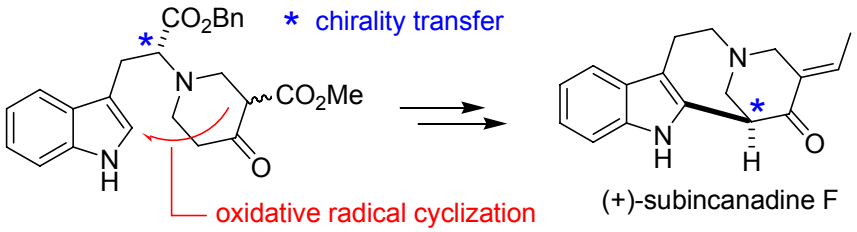

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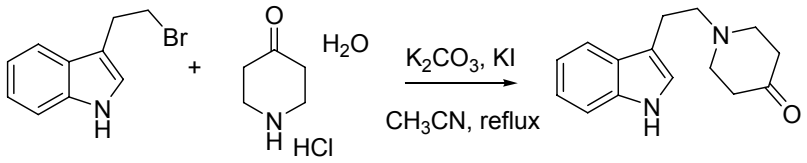
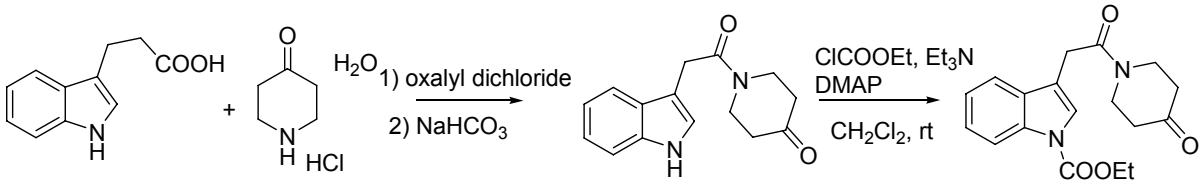
1. Experimental Details.



4

1-(2-(1*H*-Indol-3-yl)ethyl)piperidin-4-one (4). A mixture of piperidin-4-one monohydrate hydrochloride (184 mg, 1.2 mmol), potassium carbonate (208 mg, 1.5 mmol), 3-(2-bromo-ethyl)indole (246 mg, 1.1 mmol) and potassium iodide (50 mg, 0.3 mmol) in acetonitrile (5 mL) was heated at reflux for 12 h. The resulting mixture was cooled to rt, diluted with ethyl acetate and filtered. The filtrate was dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane-acetone (3:1, v:v) as the eluent to give the pure **4** as a white solid. Yield: 190 mg (70%); mp 126-127 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 2.50 (4 H, t, J = 6.0 Hz), 2.81-2.88 (4 H, m), 2.99-3.03 (2 H, t, J = 6.3 Hz), 7.05 (1 H, s), 7.12 (1 H, t, J = 7.2 Hz), 7.19 (1 H, t, J = 7.2 Hz), 7.35 (1 H, d, J = 8.0 Hz), 7.60 (1 H, d, J = 8.0 Hz), 8.02 (1 H, br); ^3C NMR (100 MHz, $CDCl_3$) δ 23.6, 41.3, 53.2, 58.1, 111.3, 114.0, 118.8, 119.3, 121.7, 122.0, 127.5, 136.4, 209.5.

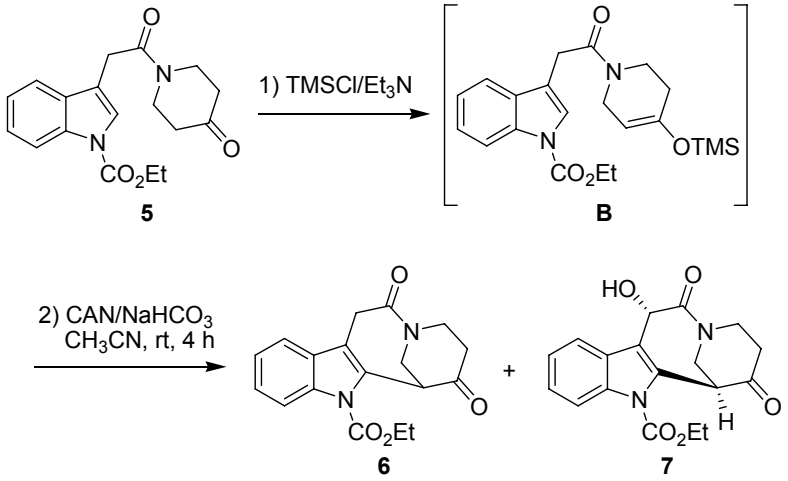


5

Ethyl 3-(2-oxo-2-(4-oxopiperidin-1-yl)ethyl)-1*H*-indole-1-carboxylate (5). The solution of oxalyl dichloride (0.94 mL, 10.8 mmol) in CH_2Cl_2 (15 mL) was added dropwise into the slurry of indole-3-acetic acid (0.95 g, 5.4 mmol) and two drops of DMF in CH_2Cl_2 (15 mL). The reaction mixture was stirred at rt for 2 h. The solvent was then evaporated under reduced pressure and the brown residue was dissolved in CH_2Cl_2 (15 mL). The resulting solution was added dropwise into the solution of piperidin-4-one monohydrate hydrochloride (830 mg, 5.4 mmol) and sodium bicarbonate (1.26 g, 16.2 mmol) in H_2O (15 mL). The reaction mixture was stirred at rt for 3 h and then quenched with H_2O. The two layers were separated and the aqueous phase was extracted with

CH_2Cl_2 (3 × 15 mL). The combined organic phase was washed with brine and then dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the product 1-(2-(1*H*-indol-3-yl)acetyl)piperidin-4-one was obtained as a yellow solid. Yield 1.27 g (93%); mp 45-46 ^oC; IR (KBr): *v* (cm^{-1}) 3280, 2923, 1717, 1635, 1458, 1228, 1093, 983, 747; ^1H NMR (300 MHz, $CDCl_3$) δ 2.10 (2 H, t, *J* = 6.0 Hz), 2.40 (2 H, t, *J* = 6.0 Hz), 3.75 (2 H, t, *J* = 6.0 Hz), 3.91 (2 H, t, *J* = 6.0 Hz), 3.95 (3 H, s), 7.10 (1 H, s), 7.10-7.19 (2 H, m), 7.36 (1 H, d, *J* = 7.8 Hz), 7.65 (1 H, d, *J* = 7.5 Hz), 8.32 (1 H, br); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.5, 40.6, 40.7, 40.9, 44.6, 108.3, 111.4, 118.4, 119.6, 122.2, 122.5, 126.7, 136.2, 170.5, 206.9; EIMS: *m/z* (rel intensity) 256 (M^+, 13), 191 (0.7), 158 (2), 130 (100), 98 (11), 77 (9), 58 (17), 43 (48); Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29, N, 10.93. Found: C, 70.11; H, 6.29; N, 10.92.

The solution of ethyl chloroformate (0.24 mL, 2.5 mmol) in CH_2Cl_2 (5 mL) was added dropwise into the solution of 1-(2-(1*H*-indol-3-yl)acetyl)piperidin-4-one (256 mg, 1.0 mmol), Et_3N (0.35 mL, 2.5 mmol) and DMAP (32 mg, 0.25 mmol) in CH_2Cl_2 (7 mL) at 0 ^oC. The mixture was stirred at rt for 24 h, then quenched with H_2O (10 mL), stirred for another 5 min. The two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic phase was washed with brine and then dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane-acetone (3:1, v:v) as the eluent to give the pure **5** as a yellow solid. Yield: 302 mg (89%); mp 81-82 ^oC; IR (KBr): *v* (cm^{-1}) 2989, 2862, 1734, 1644, 1458, 1381, 1259, 1085, 765, 747; ^1H NMR (300 MHz, $CDCl_3$) δ 1.46 (3 H, t, *J* = 7.2 Hz), 2.30 (2 H, t, *J* = 6.0 Hz), 2.45 (2 H, t, *J* = 6.0 Hz), 3.79 (2 H, t, *J* = 6.0 Hz), 3.88 (2 H, s), 3.92 (2 H, t, *J* = 6.0 Hz), 4.49 (2 H, q, *J* = 7.2 Hz), 7.25 (1 H, t, *J* = 7.5 Hz), 7.36 (1 H, t, *J* = 7.5 Hz), 7.57 (1 H, d, *J* = 7.8 Hz), 7.62 (1 H, d, *J* = 8.1 Hz), 8.17 (1 H, d, *J* = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 31.1, 40.6, 40.9, 41.1, 44.6, 63.2, 114.4, 115.3, 119.0, 123.0, 123.3, 124.9, 129.8, 135.4, 150.7, 168.9, 206.3; EIMS: *m/z* (rel intensity) 328 (M^+, 28), 283 (1), 229 (1), 202 (64), 158 (26), 130 (100), 98 (16), 56 (12); Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14, N, 8.53. Found: C, 65.66; H, 6.06; N, 8.30.



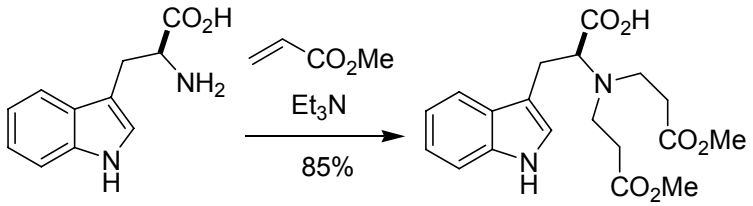
A sealed tube was filled with compound **5** (164 mg, 0.5 mmol), TMSCl (0.12 mL, 1.0 mmol), triethylamine (0.17 mL, 1.0 mmol) and DMF (0.6 mL) under N_2 atmosphere. The mixture was stirred at 80 ^{o}C for 20 h and then cooled down to rt. Saturated aqueous $NaHCO_3$ (10 mL) and hexane (10 mL) was then added. The two layers were separated and the aqueous phase was extracted with hexane (3 × 15 mL). The combined organic phase was washed with brine and then dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the expected silyl enol ether **B** was obtained as a yellow oil. Yield: 156 mg (78%).

The mixture of silyl enol ether **B** (156 mg, 0.39 mmol), ammonium ceric nitrate (427 mg, 0.78 mmol) and sodium bicarbonate (98 mg, 1.17 mmol) in acetonitrile (2 mL) was stirred at rt for 4 h. The resulting mixture was concentrated under reduced pressure. The residue was diluted with CH_2Cl_2 (10 mL) and then filtered. The filtrate was dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane- acetone (3:1, v:v) as the eluent to give the pure **6** and **7** both as white solids.

Ethyl 2,6-dioxo-1,2,4,5,6,7-hexahydro-3,7-methano-8*H*-azonino[5,4-*b*]indole-8-carboxylate (6): Yield: 32 mg (25%); mp 138-140 ^{o}C; IR (KBr): ν (cm^{-1}) 2918, 2848, 1743, 1636, 1493, 1444, 1126, 872; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50 (3 H, t, J = 7.2 Hz), 2.32-2.36 (1 H, m), 2.56-2.61 (1 H, m), 3.05-3.15 (1 H, m), 3.72 (1 H, dd, J = 15.0, 3.6 Hz), 3.83 (1 H, d, J = 15.0 Hz), 4.13 (1 H, d, J = 15.0 Hz), 4.50-4.65 (5 H, m), 7.26-7.36 (2 H, m), 7.55 (1 H, d, J = 7.5 Hz), 8.05 (1 H, d, J = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 32.4, 40.1, 45.4, 49.7, 51.0, 63.7, 113.2, 115.3, 118.3, 123.2, 125.4, 128.7, 130.5, 135.7, 151.5, 173.9, 204.3; EIMS: *m/z* (rel intensity) 326 (M^+, 16), 298 (7), 284 (11), 255 (15), 228 (52), 156 (41), 128 (27), 44 (100); Anal. Calcd for $C_{18}H_{18}N_2O_4$: C,

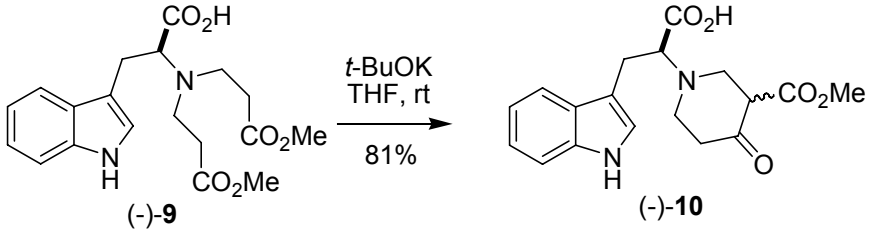
66.25; H, 5.56, N, 8.58. Found: C, 65.99; H, 5.72; N, 8.35.

Ethyl (1*S, 7*R**)-1-hydroxy-2,6-dioxo-1,2,4,5,6,7-hexahydro-3,7-methano-8*H*-azonino[5,4-*b*]-indole-8-carboxylate (7)**: Yield: 27 mg (20%); mp 179-180 ^{o}C; IR (KBr): ν (cm^{-1}) 3227, 1746, 1724, 1639, 1456, 1399, 1290, 1147, 1020, 755; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.51 (3 H, t, J = 7.2 Hz), 2.41-2.45 (1 H, m), 2.55-2.70 (1 H, m), 3.15-3.24 (2 H, m), 3.68 (1 H, dd, J = 15.0, 3.9 Hz), 4.49-4.72 (3 H, m), 3.77 (1 H, d, J = 3.9 Hz), 5.64 (1 H, d, J = 15.0 Hz), 5.79 (1 H, d, J = 3.6 Hz), 7.31-7.37 (2 H, m), 7.60 (1 H, d, J = 7.8 Hz), 8.04 (1 H, d, J = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 39.9, 45.6, 47.4, 50.7, 64.0, 69.5, 115.3, 116.2, 117.9, 123.4, 125.4, 128.4, 134.9, 135.7, 151.5, 173.8, 203.7; EIMS: *m/z* (rel intensity) 342 (M^+, 59), 297 (12), 284 (5), 255 (13), 244 (100), 228 (19), 144 (43), 115 (37); HRMS Calcd for $C_{18}H_{18}N_2O_5$ 342.1216, found 342.1215.

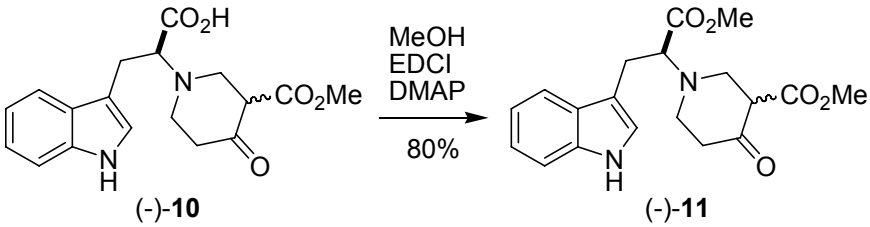


(-)-**8** (-)-**9**

(*S*)-2-(Bis(3-methoxy-3-oxopropyl)amino)-3-(1*H*-indol-3-yl)propanoic acid ((-)-9). To the solution of natural L-tryptophan (5.1 g, 25 mmol) and triethylamine (3.8 mL, 27.5 mmol) in MeOH (80 mL) and H_2O (40 mL) was added dropwise fresh distilled methyl acrylate (22 mL, 200 mmol) at rt. The mixture was stirred at rt for another 48 h and then acidified with dilute hydrochloric acid (27 mL, 1 N) until the pH was close to 6. The volatiles were removed under reduced pressure and the aqueous solution was extracted with ethyl acetate (3 × 100 mL). The combined organic phase was washed with brine and then dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane-ethyl acetate (1:1 to 0:1, v:v) as the eluent to give the pure (-)-**9** as a yellowish solid. Yield: 8.4 g (85%); $[\alpha]_D^{26}$ = -45.6 (*c* 1.66, MeOH); mp 56-58 ^{o}C; IR (KBr): ν (cm^{-1}) 3398, 1745, 1630, 1459, 1438, 1209, 1178, 746; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.42-2.16 (4 H, m), 2.90-2.99 (4 H, m), 3.07 (1 H, dd, J = 15.0, 6.9 Hz), 3.45 (1 H, dd, J = 15.0, 6.9Hz), 3.66 (6 H, s), 3.87 (1 H, t, J = 6.9 Hz), 7.10 (1 H, s), 7.12-7.21 (2 H, m), 7.35 (1 H, d, J = 8.1 Hz), 7.59 (1 H, d, J = 7.5 Hz), 8.21 (1 H, br); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9, 32.7, 47.0, 51.8, 64.5, 111.3, 111.4, 118.2, 119.3, 121.9, 123.4, 127.0, 136.2, 172.6, 174.3. ESI-MS *m/z* 377 (M^+ + H); HRMS calcd for $C_{19}H_{25}N_2O_6$ (M + H) 377.1707, found 377.1707.

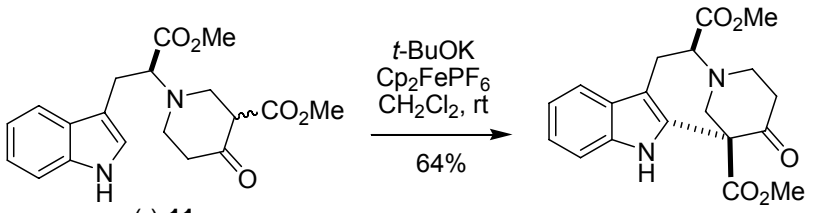


(2*S*)-3-(1*H*-Indol-3-yl)-2-(3-(methoxycarbonyl)-4-oxopiperidin-1-yl)propanoic acid ((-)-10). Potassium tert-butoxide (8.15 g, 72.7 mmol) was added into the solution of (-)-**9** (9.11 g, 24.2 mmol) in anhydrous THF (200 mL) at rt under argon atmosphere. The white slurry was stirred for about 3 h. TLC monitoring indicated that the reaction was complete. Dilute hydrochloric acid (36 mL, 2 N) was added and the resulting solution was extracted with ethyl acetate (3 × 100 mL). The combined organic phase was dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with acetone as the eluent to give the pure (-)-**10** as a white solid. Yield: 6.74 g (81%); $[\alpha]_D^{26}$ = -2.3 (*c* 0.94, MeOH); mp 115-120 ^oC; IR (KBr): *v* (cm^{-1}) 3399, 1708, 1672, 1629, 1445, 1226, 746; ^1H NMR (300 MHz, d_6-Acetone) δ 2.35-3.87 (13 H, m), 6.99-7.11 (2 H, m), 7.22 (1 H, d, *J* = 7.8 Hz), 7.35-7.39 (1 H, m), 7.59 (1 H, d, *J* = 7.8 Hz), 10.00 (1 H, br).; ^{13}C NMR (75 MHz, d_6-Acetone) δ 25.5, 33.4, 45.8, 46.5, 47.6, 51.6, 67.8, 97.3, 111.7, 111.9, 118.9, 119.3, 121.8, 123.9, 128.3, 137.3, 172.5, 173.0; ESI-MS *m/z* 345 (M^+ + H); HRMS calcd for $C_{18}H_{21}N_2O_5$ (M+H) 345.1436, found 345.1445.



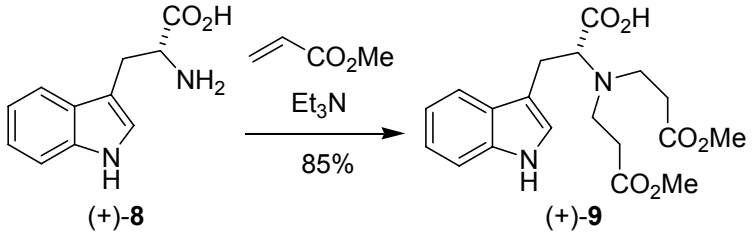
Methyl 1-((*S*)-3-(1*H*-indol-3-yl)-1-methoxy-1-oxopropan-2-yl)-4-oxopiperidine-3-carboxylate ((-)-11). The mixture of compound (-)-**10** (2.68 g, 7.8 mmol), EDCI (1.80 g, 9.4 mmol), DMAP (1.15 g, 9.4 mmol) and MeOH (6 mL) in anhydrous CH_2Cl_2 (80 mL) was stirred at rt for 24 h under argon atmosphere. The mixture was quenched with saturated aqueous NH_4Cl (30 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane-ethyl acetate (1:1,

v:v) as the eluent to give the pure (-)-**11** as a yellowish solid. Yield: 2.23 g (80%); $[\alpha]_D^{26}$ = -14.2 (*c* 2.0, $CHCl_3$); mp 62-63 ^oC; IR (film): *v* (cm^1) 3411, 1731, 1665, 1622, 1457, 1443, 743; ^1H NMR (300 MHz, $CDCl_3$) δ 2.43-3.76 (16 H, m), 7.04 (1 H, s), 7.12-7.19 (2 H, m), 7.33 (1 H, d, *J* = 7.5 Hz), 7.60 (1 H, d, *J* = 7.5 Hz), 8.10 (1 H, br); ^{13}C NMR (75 MHz, $CDCl_3$) (enol form) δ 25.3, 34.0, 45.6, 46.1, 51.2, 51.4, 67.2, 96.9, 111.1, 111.6, 118.5, 119.4, 121.8, 122.5, 127.3, 136.0, 170.2, 172.1; ESI-MS: *m/z* 359 (M^+ + H); HRMS calcd for $C_{19}H_{23}N_2O_5$ (M+H) 359.1607, found 359.1602.



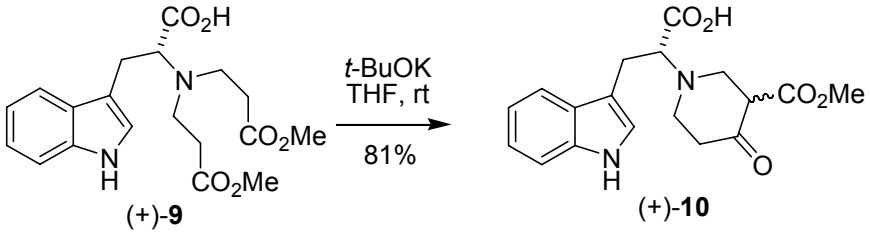
(-)-**11** (-)-**12**

(2*S*, 7*R*)-2,7-Bis(methoxycarbonyl)-6-oxo-1,2,4,5,6,7-hexahydro-3,7-methano-8*H*-azonino-[5,4-*b*]- indole ((-)-12). Potassium *tert*-butoxide (180 mg, 1.60 mmol) was added into the solution of (-)-**11** (250 mg, 0.70 mmol) in anhydrous CH_2Cl_2 (20 mL) at rt under argon atmosphere. The mixture was stirred at rt for 30 min. $FeCp_2PF_6$ (509 mg, 1.54 mmol) was then added in one portion. The color of the reaction mixture changed from yellow to green. After stirring for 15 min, the mixture was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane-ethyl acetate (1:1, v:v) as the eluent to give the pure (-)-**12** as a white solid. Yield: 160 mg (64%); $[\alpha]_D^{26}$ = -331.1 (*c* 1.05, $CHCl_3$); mp 168-169 ^oC. IR (KBr): *v* (cm^{-1}) 3348, 1752, 1738, 1693, 1461, 1435, 1257, 1199, 1040, 748; ^1H NMR (300 MHz, $CDCl_3$) δ 2.12 (1 H, d, *J* = 13.8 Hz), 2.45 (1 H, dt, *J* = 12.0, 6.9 Hz), 3.30-3.41 (4 H, m), 3.65 (1 H, dd, *J* = 7.5, 6.0 Hz), 3.79-3.84 (7 H, m), 4.41 (1 H, dd, *J* = 15.6, 2.7 Hz), 7.11-7.26 (2 H, m), 7.34 (1 H, d, *J* = 8.1 Hz), 7.57 (1 H, d, *J* = 8.1 Hz), 8.75 (1 H, br); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 35.4, 51.8, 52.3, 52.9, 54.2, 65.0, 65.3, 111.2, 112.2, 118.2, 119.8, 123.1, 127.3, 128.6, 136.2, 169.5, 173.9, 204.5; ESI-MS: *m/z* 357 (M^++H); Anal. cacld for $C_{19}H_{20}N_2O_5$: C, 64.04; H, 5.66; N, 7.86. Found: C, 64.08; H, 5.55; N, 7.78; The structure was further confirmed by its X-ray diffraction analysis.



(+)-**8** (+)-**9**

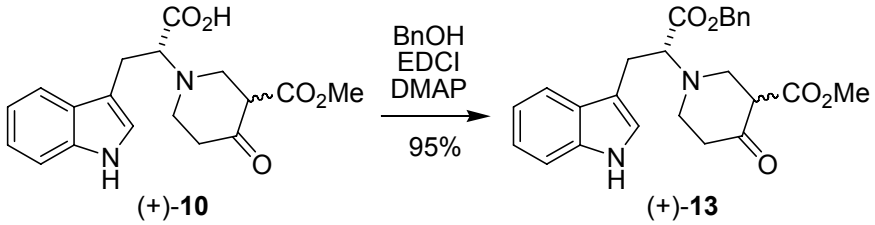
(*R*)-2-(Bis(3-methoxy-3-oxopropyl)amino)-3-(1*H*-indol-3-yl)propanoic acid ((+)-9). To the solution of natural D-tryptophan (5.1 g, 25 mmol) and triethylamine (3.8 mL, 27.5 mmol) in MeOH (80 mL) and H_2O (40 mL) was added dropwise fresh distilled methyl acrylate (22 mL, 200 mmol) at rt. The mixture was stirred at rt for another 48 h and then acidified with dilute hydrochloric acid (27 mL, 1 N) until the pH was close to 6. The volatiles were removed under reduced pressure and the aqueous solution was extracted with ethyl acetate (3 × 100 mL). The combined organic phase was washed with brine and then dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane-ethyl acetate (1:1 to 0:1, v:v) as the eluent to give the pure (+)-**9** as a yellowish solid. Yield: 85%; $[\alpha]_D^{26}$ = 47.1 (*c* 1.65, MeOH); mp 56-58 ^oC; IR (KBr): *v* (cm^{-1}) 3398, 1745, 1630, 1459, 1438, 1209, 1178, 746; ^1H NMR (400 MHz, $CDCl_3$) δ 2.40-2.47 (4 H, m), 2.88-2.97 (4 H, m), 3.07 (1 H, dd, *J* = 14.8, 7.2 Hz), 3.44 (1 H, dd, *J* = 14.8, 6.8 Hz), 3.66 (6 H, s), 3.87 (1 H, t, *J* = 6.8 Hz), 7.10 (1 H, s), 7.12-7.21 (2 H, m), 7.35 (1 H, d, *J* = 8.0 Hz), 7.59 (1 H, d, *J* = 8.0 Hz), 8.12 (1 H, br); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 32.4, 47.3, 51.8, 64.9, 110.8, 111.6, 118.2, 119.3, 121.8, 123.7, 127.1, 136.4, 172.5, 173.9. ESI-MS: *m/z* 377 (M^+ + H). HRMS calcd for $C_{19}H_{25}N_2O_6$ (M+H) 377.1707, found 377.1712.



(+)-**9** (+)-**10**

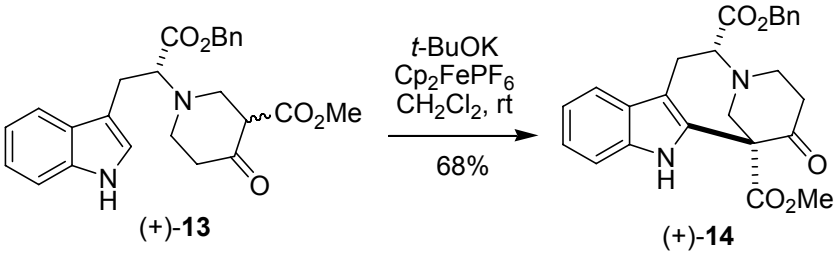
(2*R*)-3-(1*H*-Indol-3-yl)-2-(3-(methoxycarbonyl)-4-oxopiperidin-1-yl)propanoic acid ((+)-10). Potassium *tert*-butoxide (8.15 g, 72.7 mmol) was added into the solution of (+)-**9** (9.11 g, 24.2 mmol) in anhydrous THF (200 mL) at rt under argon atmosphere. The white slurry was stirred for about 3 h. TLC monitoring indicated that the reaction was complete. Dilute hydrochloric acid (36 mL, 2 N) was added and the resulting solution was extracted with ethyl acetate (3 × 100 mL). The combined organic phase was dried over anhydrous Na_2SO_4. After the

removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with acetone as the eluent to give the pure (+)-**10** as a white solid. Yield: 81%; $[\alpha]_D^{26}$ = 7.9 (*c* 1.09, MeOH); mp 115-120 ^oC; IR (KBr): *v* (cm^{-1}) 3399, 1708, 1672, 1629, 1445, 1226, 746; ^1H NMR (300 MHz, d_6-Acetone) δ 2.35-3.87 (13 H, m), 6.99-7.11 (2 H, m), 7.22 (1 H, d, *J* = 7.8 Hz), 7.35-7.39 (1 H, m), 7.59 (1 H, d, *J* = 7.8 Hz), 10.00 (1 H, br); ^{13}C NMR (100 MHz, d_6-DMSO) (enol form) δ 25.2, 31.1, 41.4, 45.4, 46.2, 51.9, 67.6, 97.1, 110.9, 111.8, 118.7, 118.8, 121.3, 123.8, 127.8, 136.6, 169.6, 172.9; ESI-MS: *m/z* 345 (M^+ + H). HRMS calcd for $C_{18}H_{21}N_2O_5$ (M+H) 345.1445, found 345.1460.

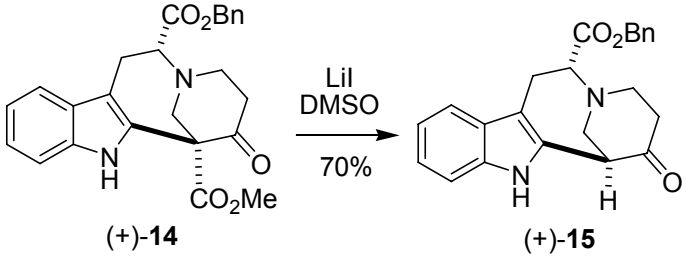


(+)-**10** (+)-**13**

Methyl 1-((*S*)-3-(1*H*-indol-3-yl)-1-benzyloxy-1-oxopropan-2-yl)-4-oxopiperidine-3-carboxylate ((+)-13). The mixture of compound (+)-**10** (1.72 g, 5.0 mmol), EDCI (1.15 g, 6 mmol), DMAP (0.76 g, 6 mmol) and BnOH (1.0 mL, 10 mmol) in anhydrous CH_2Cl_2 (50 mL) was stirred at rt for 24 h under argon atmosphere. The resulting mixture was quenched with saturated aqueous NH_4Cl (30 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane-ethyl acetate (1:1, v:v) as the eluent to give the pure (+)-**13** as a white solid. Yield: 2.06 g (95%); $[\alpha]_D^{26}$ = 15.7 (*c* 1.47, $CHCl_3$); mp 72-73 ^oC; IR (film): *v* (cm^1) 3410, 2952, 1729, 1665, 1622, 1456, 1443, 1224, 743; ^1H NMR (400 MHz, $CDCl_3$) δ 2.43-3.81 (13 H, m), 5.00-5.04 (2 H, m), 6.88 (1 H, s), 7.05-7.29 (8 H, m), 7.58 (1 H, d, *J* = 7.6 Hz), 8.06 (1 H, br); ^{13}C NMR (100 MHz, $CDCl_3$) (enol form) δ 25.6, 30.2, 45.7, 46.3, 51.4, 66.1, 67.8, 97.0, 111.3, 111.5, 118.7, 119.5, 122.0, 122.8, 127.5, 128.2, 128.3, 128.5, 135.8, 136.2, 170.4, 171.4; ESI-MS: *m/z* 435 (M^+ + H); HRMS calcd for $C_{25}H_{27}N_2O_5$ (M+H) 435.1920, found 435.1914.

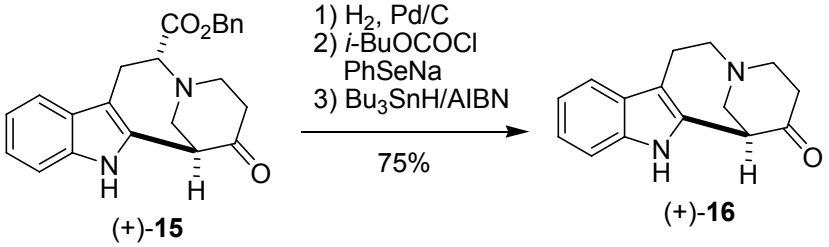


1,2,4,5,6,7-hexahydro-3,7-methano-8*H*-azonino[5,4-*b*]-indole ((+)-14). Potassium *tert*-butoxide (180 mg, 1.60 mmol) was added into the solution of (+)-**13** (304 mg, 0.70 mmol) in anhydrous CH_2Cl_2 (20 mL) at rt under argon atmosphere. The mixture was stirred at rt for 30 min. Cp_2FePF_6 (509 mg, 1.54 mmol) was then added in one portion. The color of the reaction mixture changed from yellow to green. After stirring for 15 min, the mixture was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane-ethyl acetate (1:1, v:v) as the eluent to give the pure (+)-**14** as a white solid. Yield: 205 mg (68%); $[\alpha]_D^{26}$ = 331.0 (*c* 0.85, $CHCl_3$); mp 176-177 ^oC. IR (KBr): *v* (cm^{-1}) 3397, 2953, 1736, 1706, 1458, 1260, 1172, 1039, 744; ^1H NMR (400 MHz, $CDCl_3$) δ 2.08 (1 H, d, *J* = 13.6 Hz), 2.45 (1 H, dd, *J* = 11.6, 7.2 Hz), 3.35-3.39 (4 H, m), 3.65 (1 H, t, *J* = 8.0), 3.79-3.83 (4 H, m), 4.40 (1 H, dd, *J* = 15.6, 2.4 Hz), 5.20 (1 H, d, *J* = 12.0 Hz), 5.25 (1 H, d, *J* = 12.8 Hz), 7.12 (1 H, t, *J* = 7.6 Hz), 7.20 (1 H, t, *J* = 7.6 Hz), 7.31-7.40 (6 H, m), 7.53 (1 H, d, *J* = 8.0 Hz), 8.74 (1 H, br); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 35.5, 51.8, 52.9, 54.3, 65.1, 65.4, 66.8, 111.3, 112.2, 118.2, 119.8, 123.1, 127.4, 128.1, 128.4, 128.7, 135.9, 136.3, 169.6, 173.2, 204.5; ESI-MS: *m/z* 433 (M^++H); HRMS calcd for $C_{25}H_{25}N_2O_5$ (M+H) 433.1763, found 433.1758.



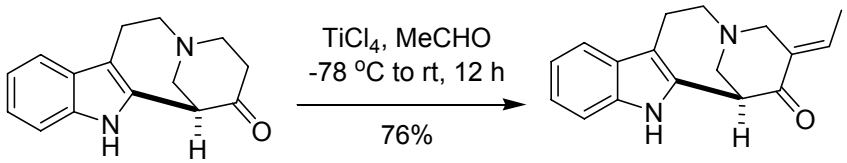
(2*R*, 7*R*)-2-Benzyloxycarbonyl-6-oxo-1,2,4,5,6,7-hexahydro-3,7-methano-8*H*-azonino-[5,4-*b*]-indole ((+)-15). A mixture of compound (+)-**14** (200 mg, 0.46 mmol) and LiI (310 mg, 2.3 mmol) in anhydrous DMSO (10 mL) was stirred at 180 ^oC for 1 h under argon atmosphere. The

resulting mixture was cooled to rt, added with water (20 mL), and extracted with ethyl acetate (3 × 20 mL). The combined organic phase was dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane-ethyl acetate (1:1, v:v) as the eluent to give pure (+)-**15** as a white solid. Yield: 118 mg (70%); $[\alpha]_D^{26}$ = 221.8 (*c* 2.05, $CHCl_3$); mp 143-144 °C. IR (KBr): *v* (cm^{-1}) 3363, 2924, 1736, 1705, 1460, 1339, 1283, 1173, 1028, 741; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (1 H, d, *J* = 14.8 Hz), 2.58-2.66 (1 H, m), 3.27-3.43 (5 H, m), 3.77-3.83 (2 H, m), 4.24 (1 H, d, *J* = 13.6Hz), 5.21 (1 H, d, *J* = 12.4 Hz), 5.25 (1 H, d, *J* = 12.4 Hz), 7.10 (1 H, t, *J* = 7.6 Hz), 7.17 (1 H, t, *J* = 7.6 Hz), 7.26 (1 H, d, *J* = 8.0 Hz), 7.35-7.40 (5 H, m), 7.53 (1 H, d, *J* = 8.0 Hz), 8.02 (1 H, br); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 35.6, 49.9, 53.1, 53.6, 65.9, 66.8, 110.8, 110.9, 117.9, 119.7, 122.4, 127.9, 128.1, 128.3, 128.5, 128.6, 130.7, 135.8, 135.9, 173.4, 208.8; ESI-MS: *m/z* 397 (M^++Na); HRMS calcd for $C_{23}H_{23}N_2O_3$ (M+H) 375.1708, found 375.1703.



(*R*)-6-Oxo-1,2,4,5,6,7-hexahydro-3,7-methano-8*H*-azonino-[5,4-*b*]-indole ((+)-16). The solution of compound (+)-**15** (42 mg, 0.112 mmol) in MeOH (5 mL) was hydrogenated with H_2 (1 atmosphere) over Pd/C (18 mg, 10%) at rt for 24 h. The catalyst was removed by filtration and the solvent was removed under reduced pressure to give 32 mg crude acid as an amorphous soild**.** The acid was then added into the THF (2 mL) solution of isobutyl chloroformate (26 μL, 0.20 mmol) and *N*-methylmorpholine (22 μL, 0.20 mmol) at -10 °C. The mixture was stirred at -10 °C for 15 min and at rt for another 15 min. The solution was again cooled to -10 °C. The THF solution of sodium phenylselenide, which was prepared by reaction of benzeneselenol (22 μL, 0.20 mmol) and sodium hydride (9 mg, 0.22 mmol) in anhydrous THF (2 mL) at 0 °C, was then added through a cannula. The resulting mixture was stirred at -10 °C for 20 min and at rt for another 2 h. The volatiles were removed under reduced pressure, and the residue was purified by column chromatography on silica gel with hexane-ethyl acetate (3:1, v:v) as the eluent to give the phenylselenyl ether as a yellowish solid. Yield: 35 mg (75%).

To the solution of the phenylselenyl ether (63 mg, 0.15 mmol) in anhydrous benzene (5 mL) at reflux was added the solution of Bu_3SnH (75 μL, 0.3 mmol) and AIBN (16 mg, 0.10 mmol) in anhydrous benzene (5 mL). The mixture was refluxed for 8 h. The solvent was then removed under reduced pressure, and the residue was purified by column chromatography on silica gel with CH_2Cl_2-MeOH (10:1, v:v) as the eluent to give pure (+)-**16** as a yellowish solid. Yield: 35 mg (99%); $[\alpha]^{23}_D$ = 158.7 (*c* 1.0, $CHCl_3$); mp 122-123 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18 (1 H, dd, *J* = 15.0, 3.3 Hz), 2.27-2.82 (1 H, m), 3.06-3.26 (2 H, m), 3.36-3.58 (5 H, m), 3.63 (1 H, s), 3.71 (1 H, d, *J* = 14.1 Hz), 7.09-7.19 (m, 2 H), 7.25 (d, *J* = 7.8 Hz, 1 H), 7.49 (d, *J* = 7.8 Hz, 1 H), 8.18 (1 H, br). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6, 39.3, 50.9, 54.9, 55.3, 55.7, 110.7, 113.1, 118.1, 119.6, 122.2, 128.9, 132.2, 135.4, 208.0. ESI-MS: *m/z* 241 (M^++H). HRMS calcd for $C_{15}H_{17}N_2O$ (M+H) 241.1341, found 241.1336.



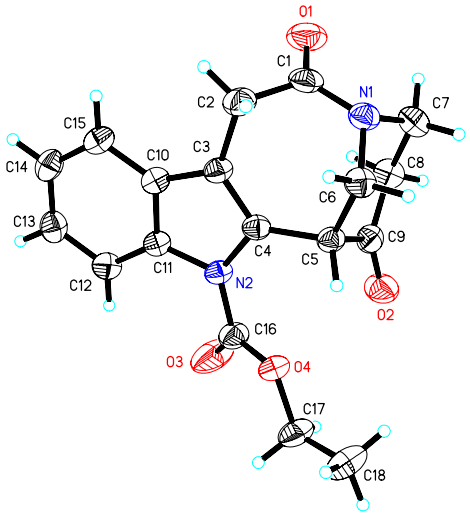
(+)-Subincanadine F ((+)-1). The solution of (+)-**16** (36 mg, 0.15 mmol) in anhydrous CH_2Cl_2 (2 mL) was cooled to -78 °C and $TiCl_4$ (0.18 mL, 0.18 mmol, 1.0 M solution in CH_2Cl_2) was added. The mixture was stirred at -78 °C for 5 min and diisopropylethylamine (33 μL, 0.20 mmol) was added slowly. The mixture was stirred at -78 °C for an additional 30 min and anhydrous acetaldehyde (0.23 mL, 0.50 mmol, 2.2 M solution in CH_2Cl_2) was added dropwise. The resulting mixture was stirred at -78 °C for 2 h and then at rt for 12 h. The reaction was then quenched with saturated aqueous $NaHCO_3$ (2 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phase was dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with CH_2Cl_2-MeOH (10:1, v:v) as the eluent to give the pure product (+)-**1** as a yellow solid. Yield: 30 mg (76%). $[\alpha]^{23}_D$ = 198.4 (*c* 0.25, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (3 H, d, *J* = 7.2 Hz), 2.84-2.90 (1 H, m), 2.97-3.06 (1 H, m), 3.31-3.45 (2 H, m), 3.58-3.77 (3 H, m), 3.86 (1 H, d, *J* = 16.8 Hz), 4.06 (1 H, d, *J* = 16.8 Hz), 6.69 (1 H, q, *J* = 7.2 Hz), 7.05-7.15 (2 H, m), 7.25 (1 H, d, *J* = 7.5 Hz), 7.42 (1 H, d, *J* = 7.5 Hz), 8.52 (1 H, br). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 23.4, 49.7, 50.7, 52.1, 55.9, 110.8, 114.3, 117.9, 119.5, 121.9, 128.5,

132.8, 135.2, 135.5, 135.9, 194.8.

2. References for known compounds.

4	Kuehne, M. E.; Muth, R. S. *J. Org. Chem.* **1991**, *56*, 2701.

3. X-Ray Structures of compounds 6 and 7.



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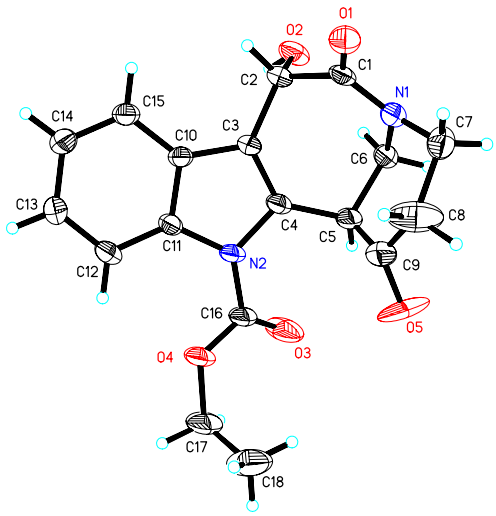
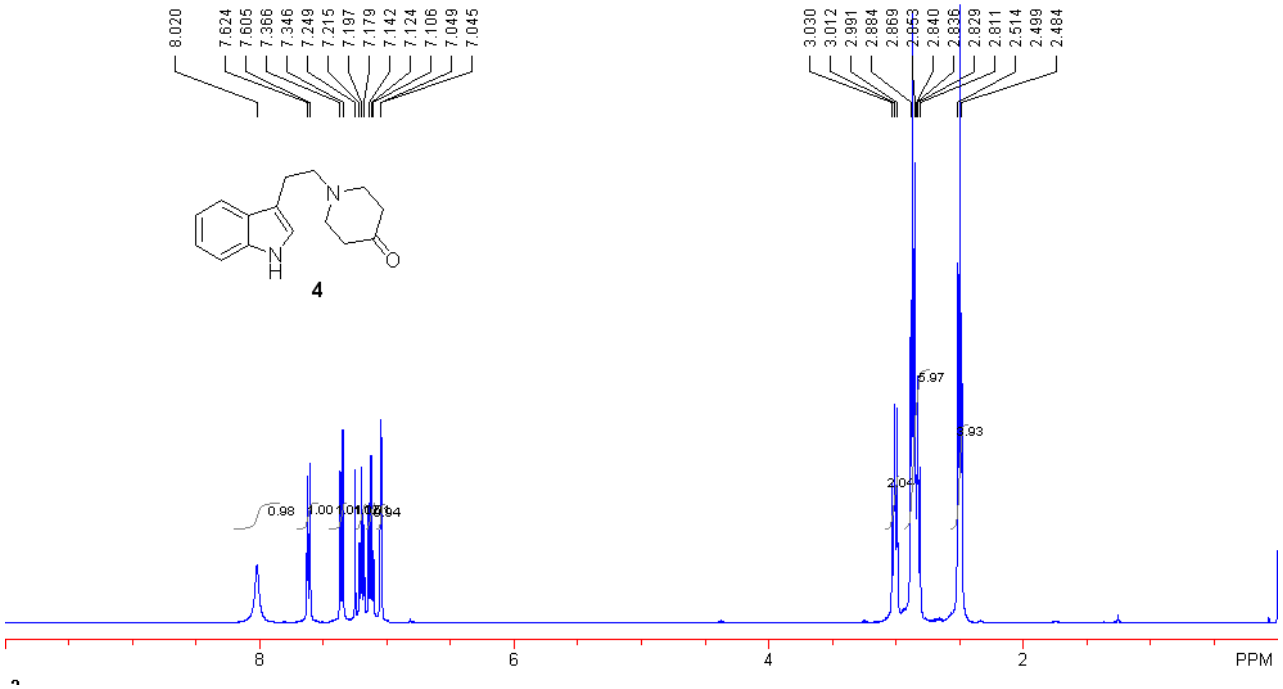
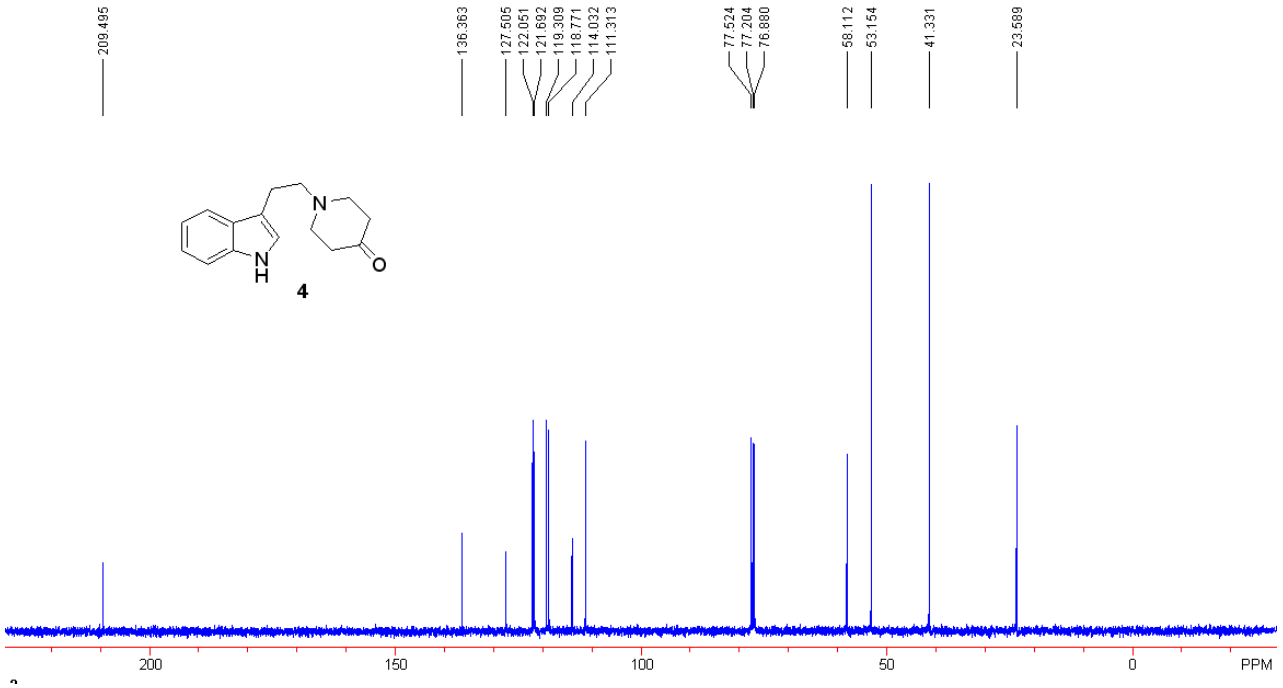
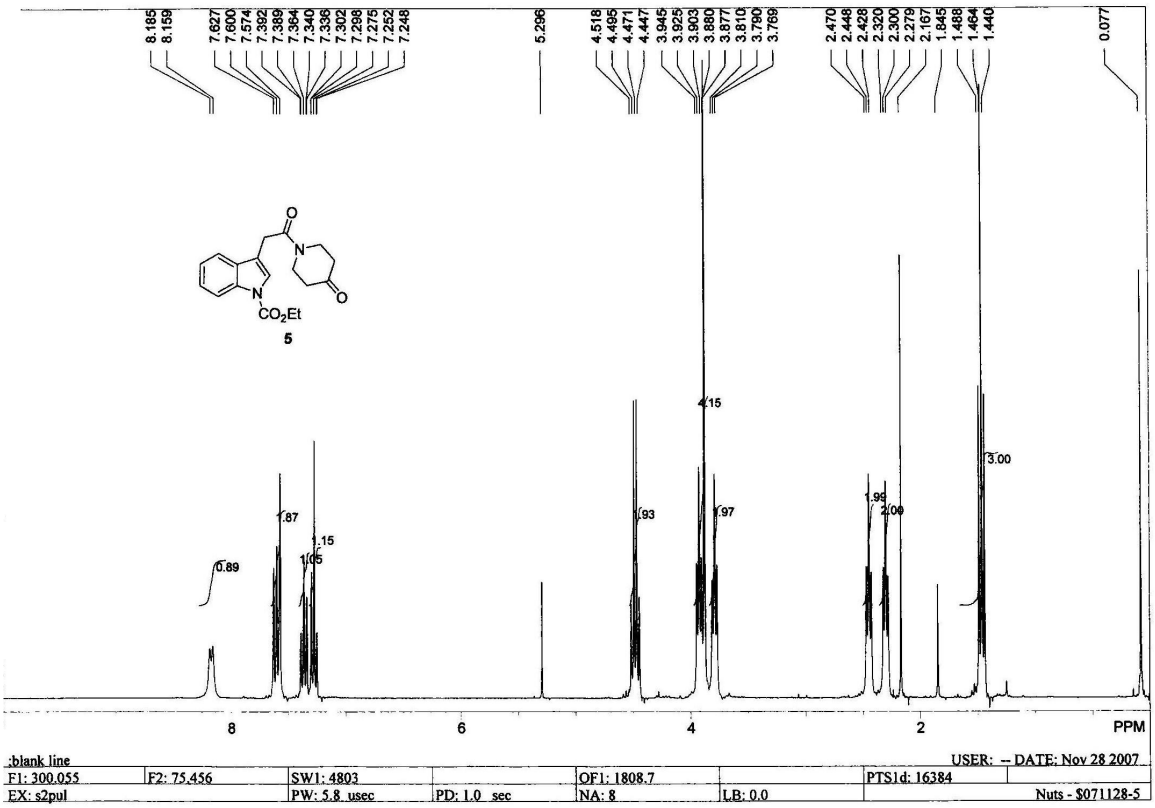


7

4. ^{1}H and ^{13}C spectra of all compounds.



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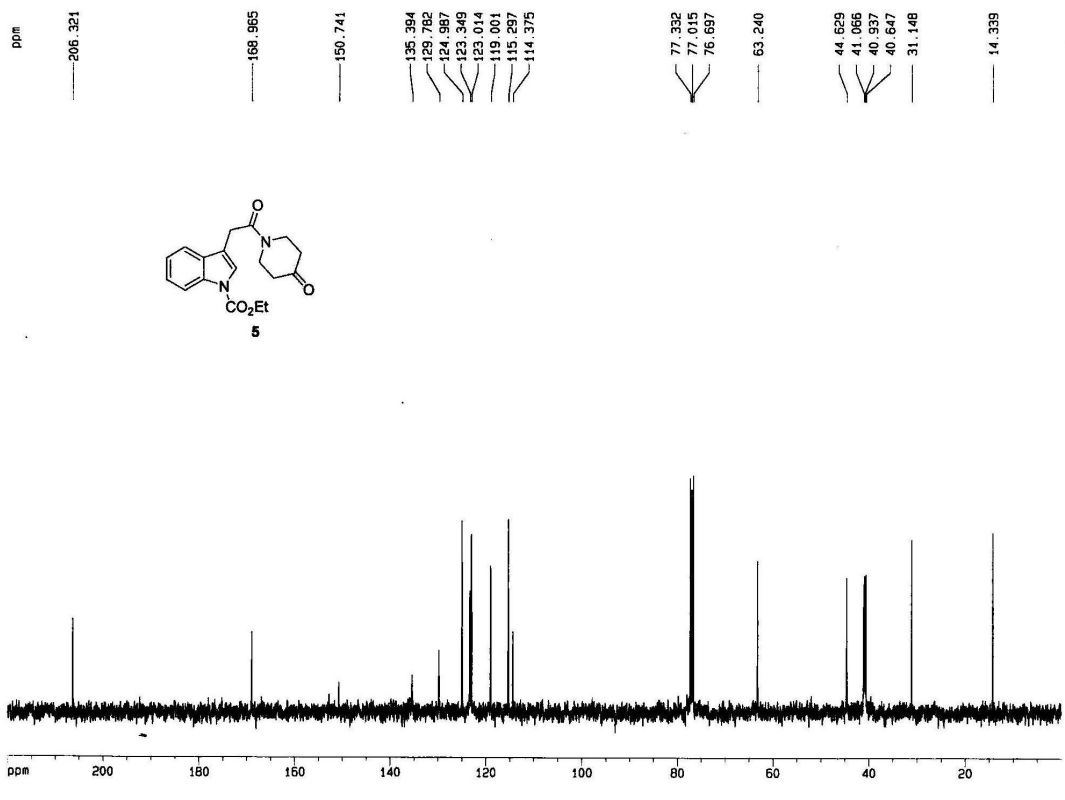
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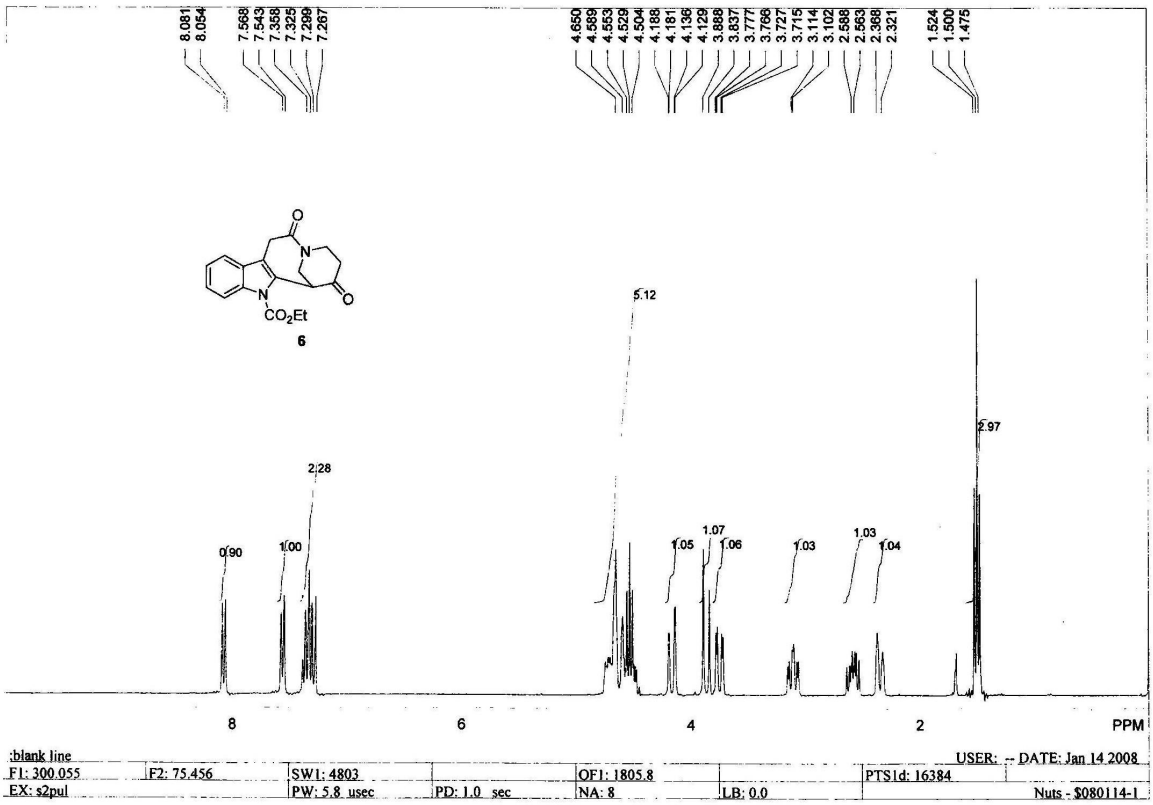
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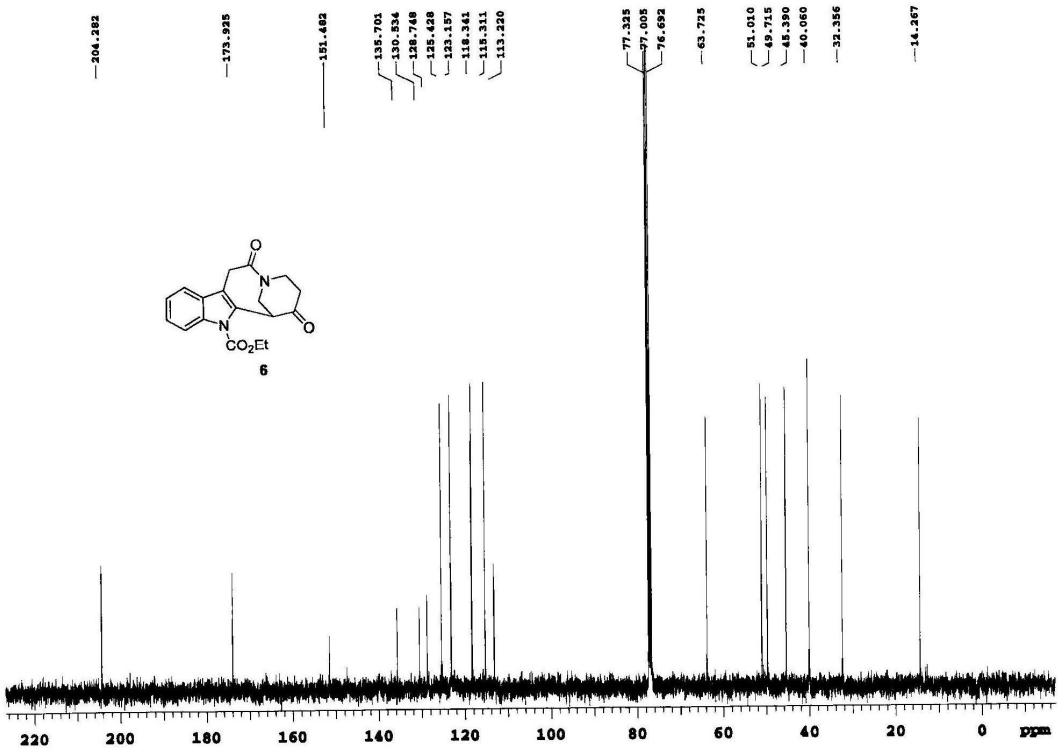
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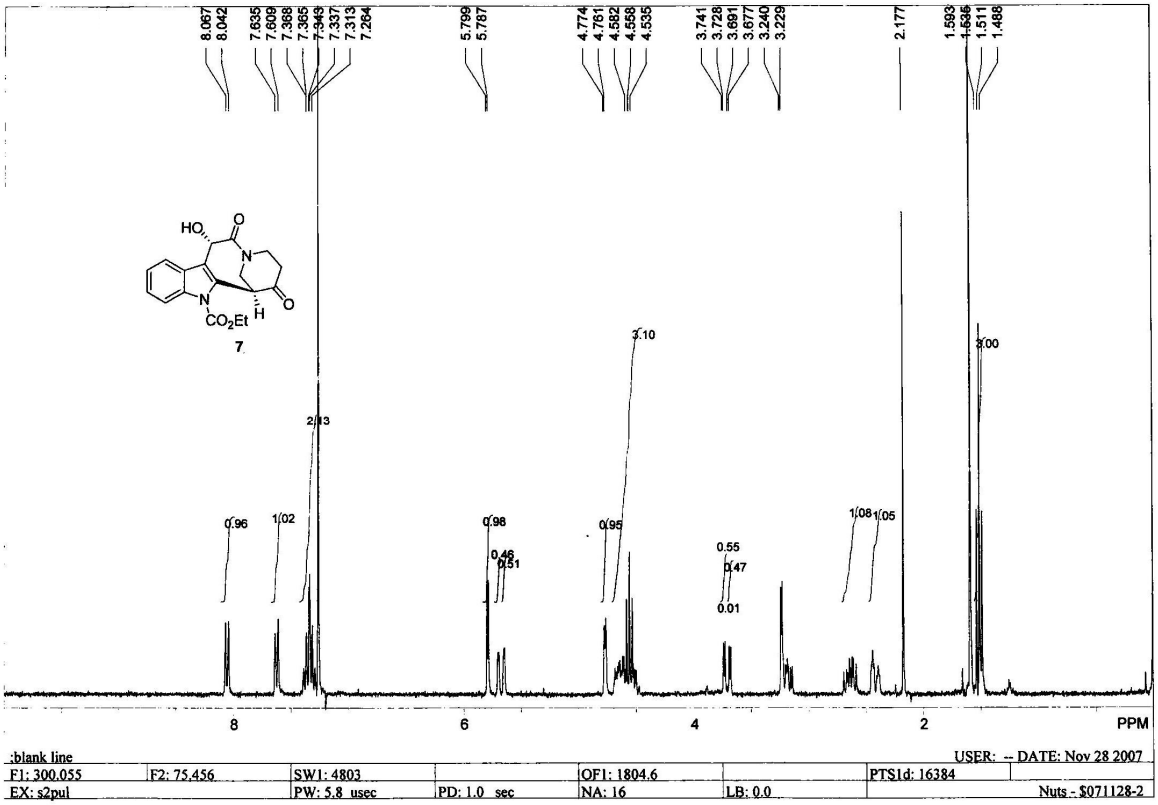
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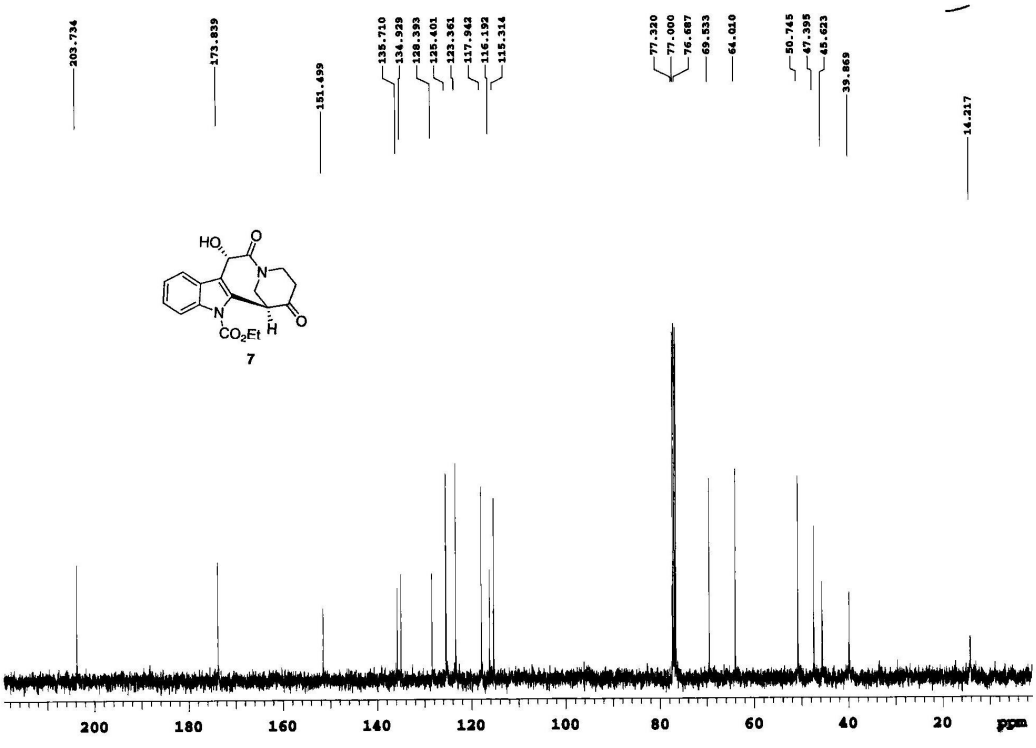
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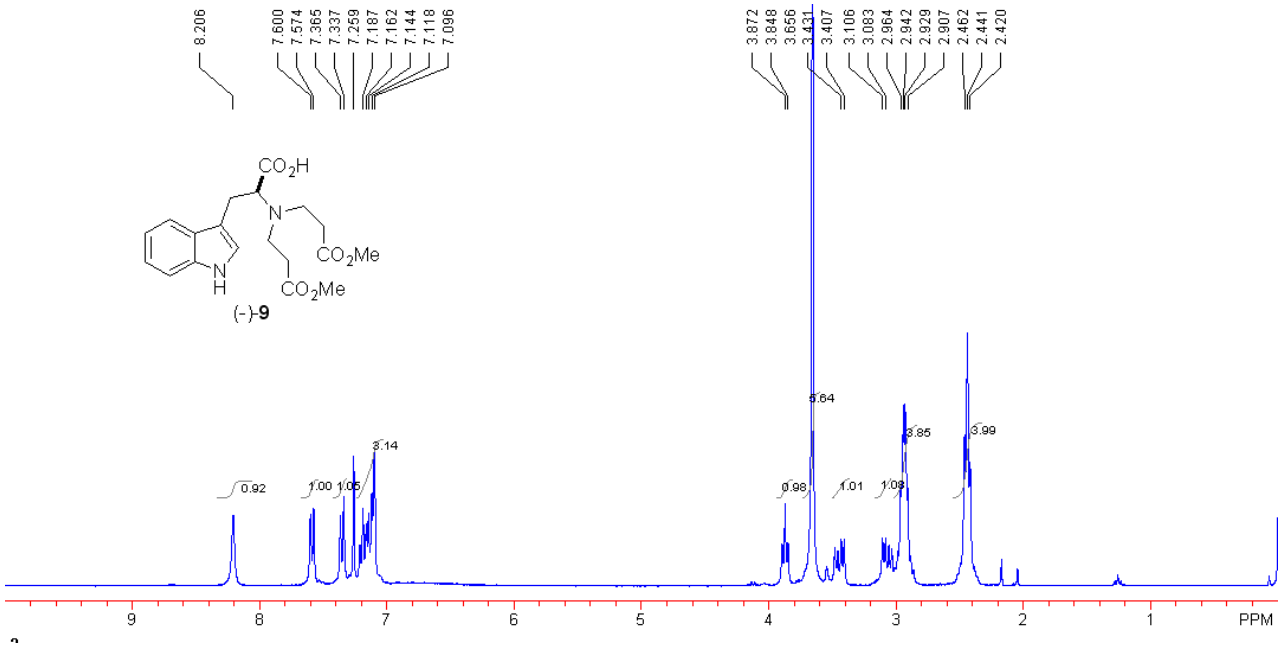
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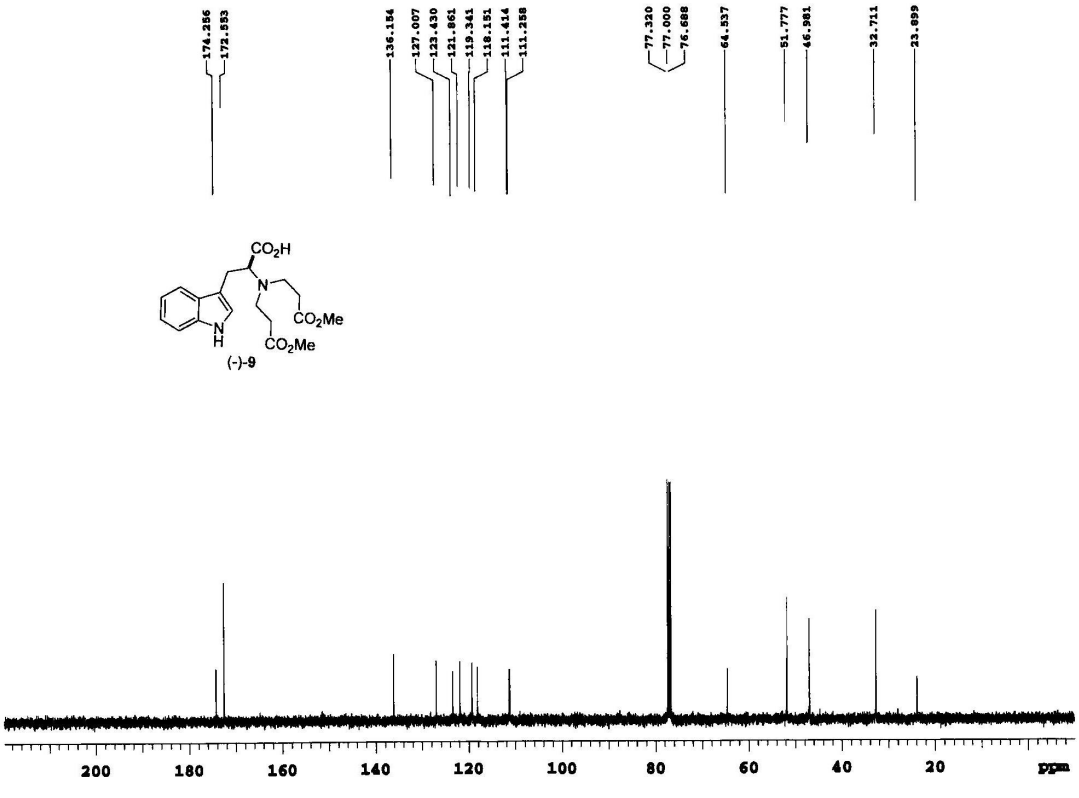
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CO2Me
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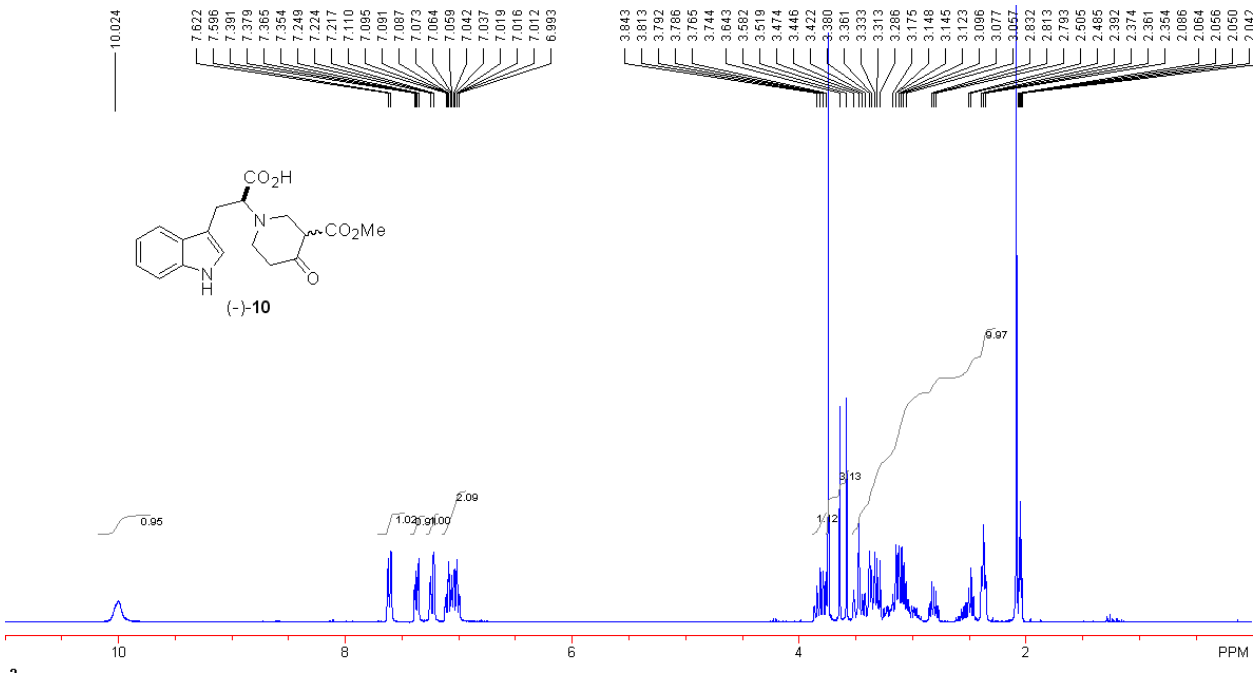
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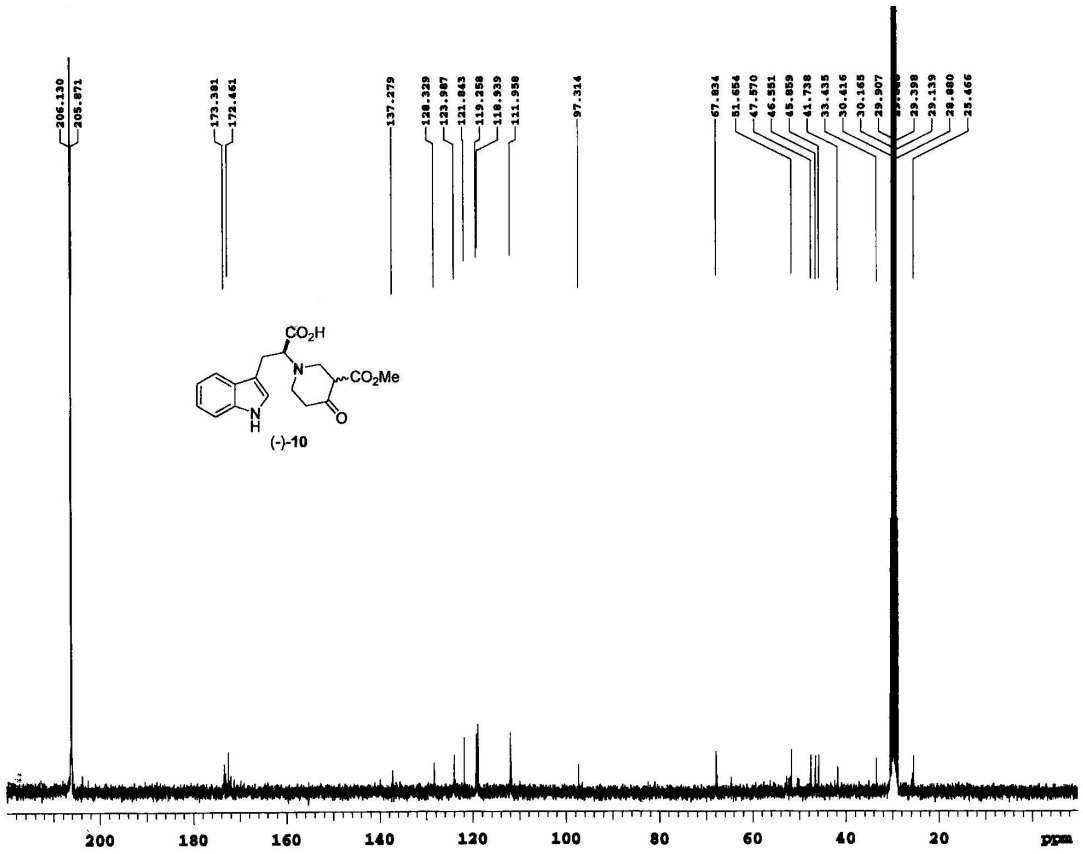
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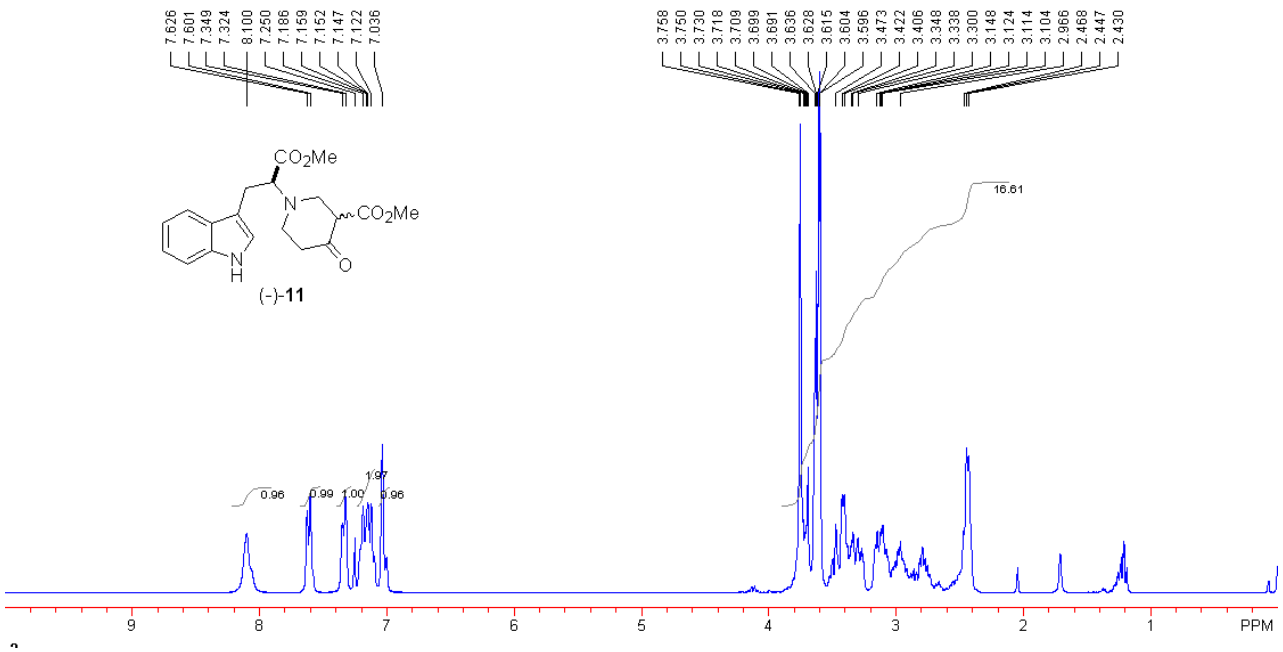
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CO2Me
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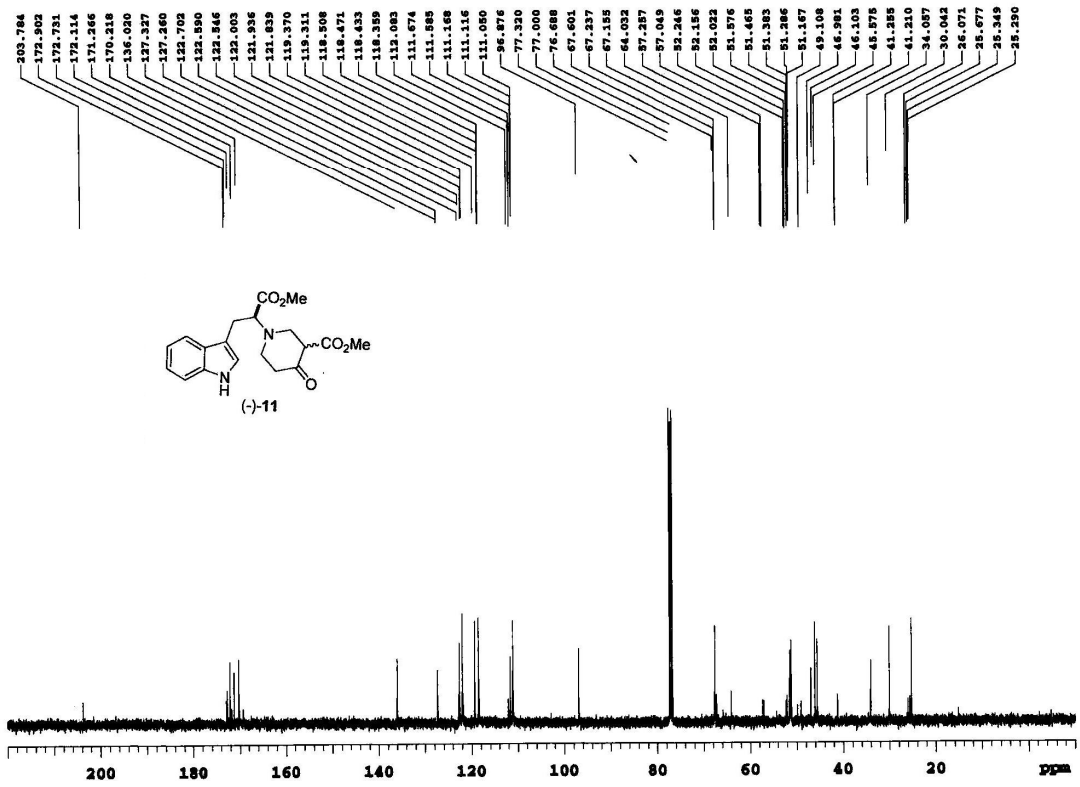
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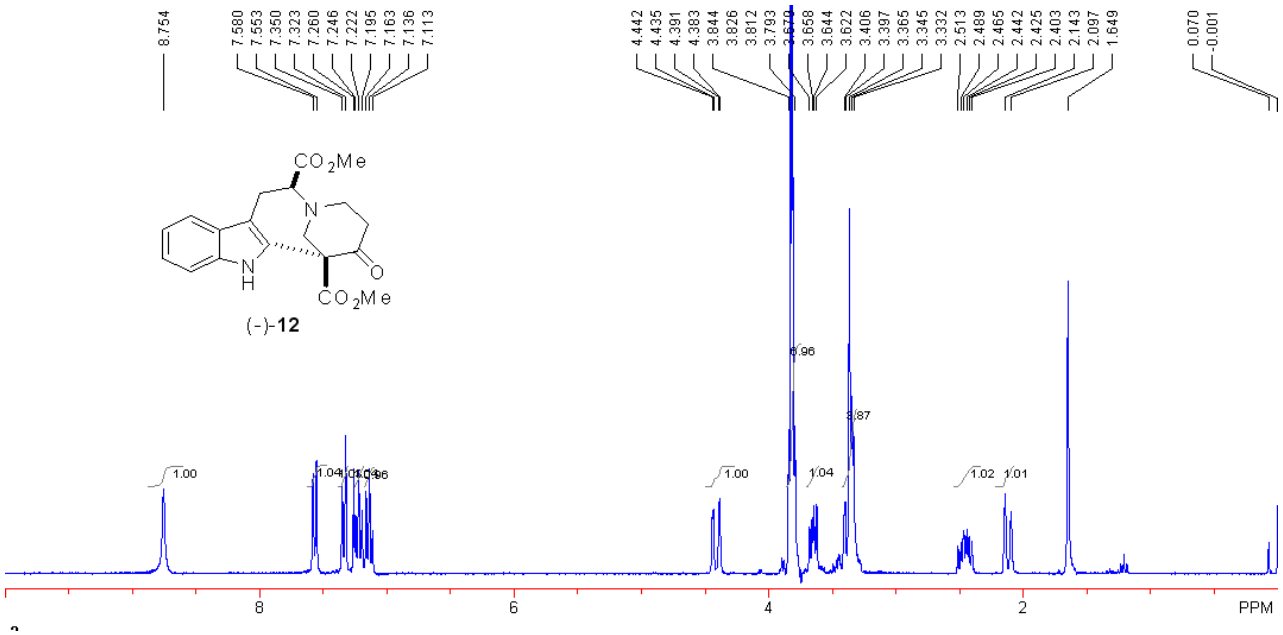
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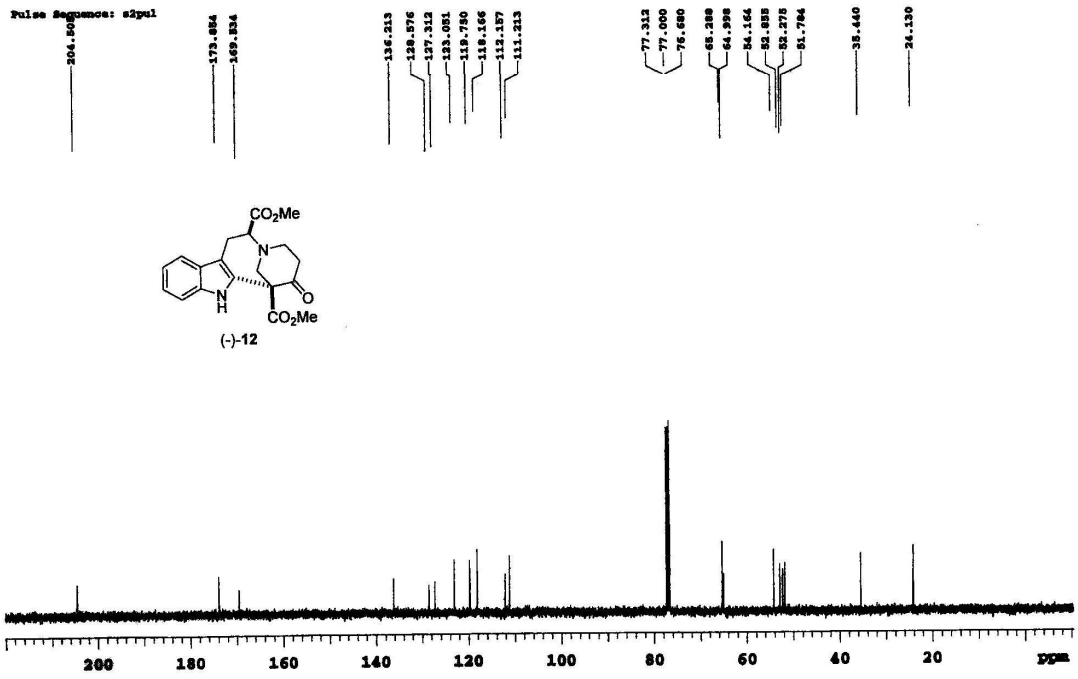
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64.998
54.164
52.685
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35.440
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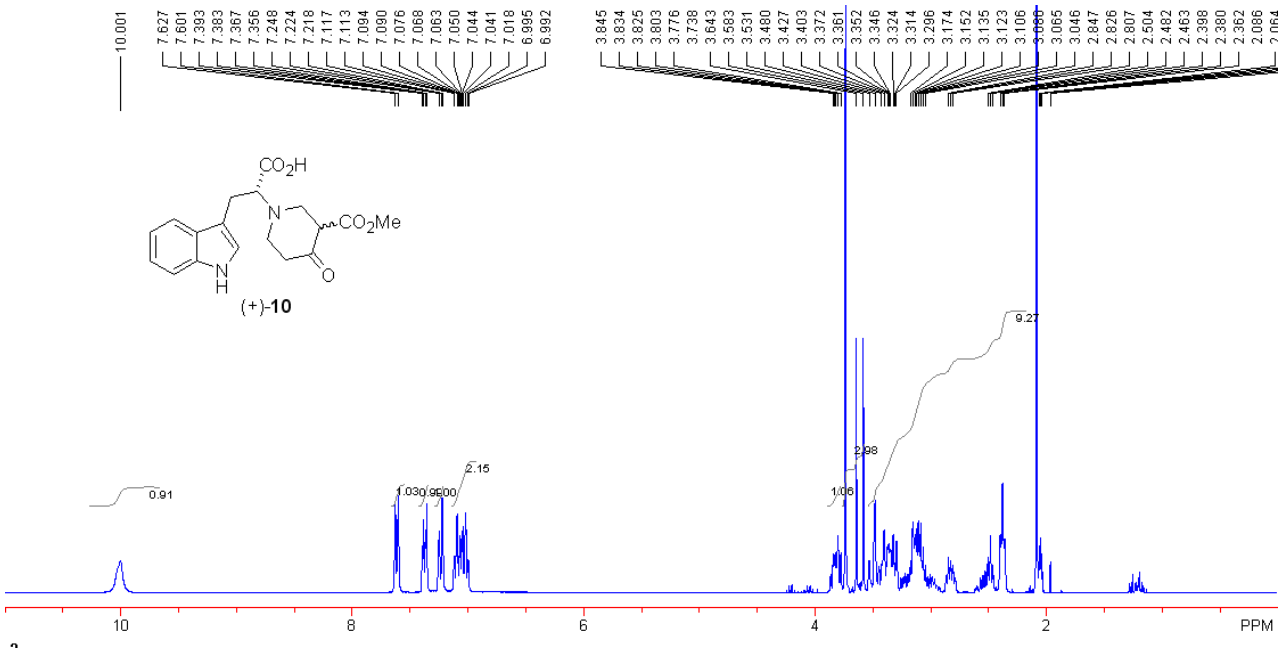
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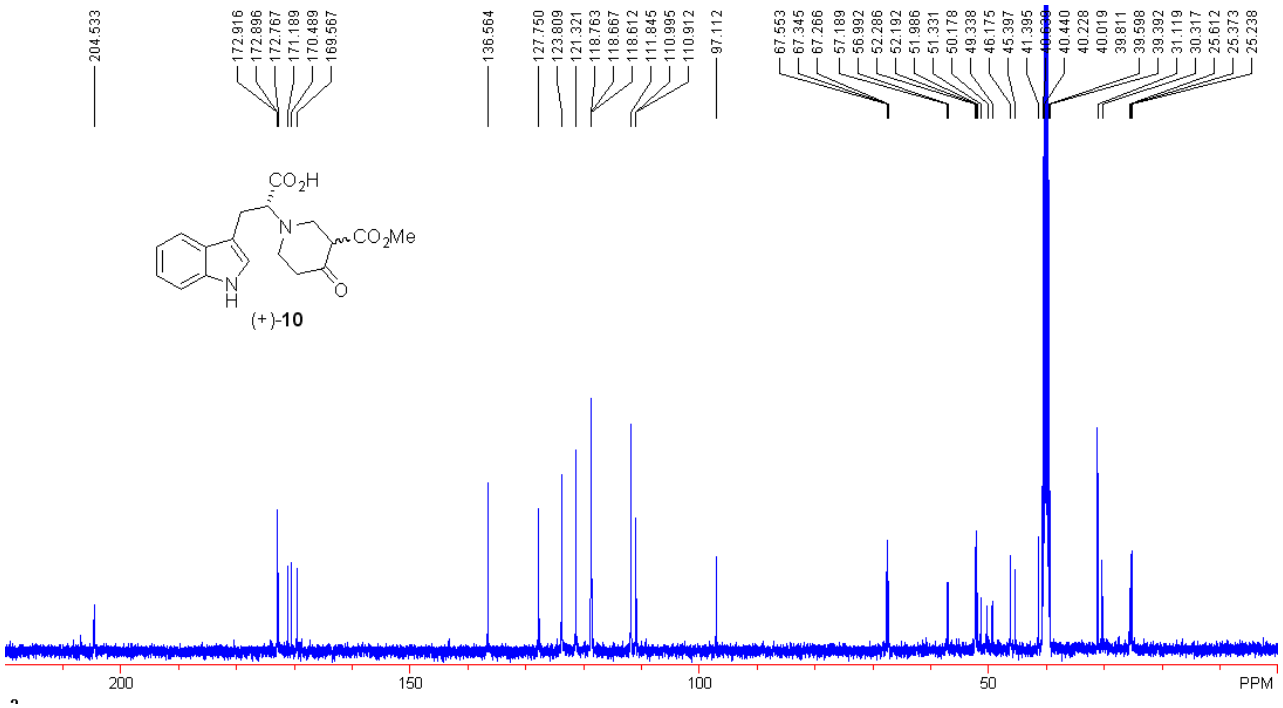
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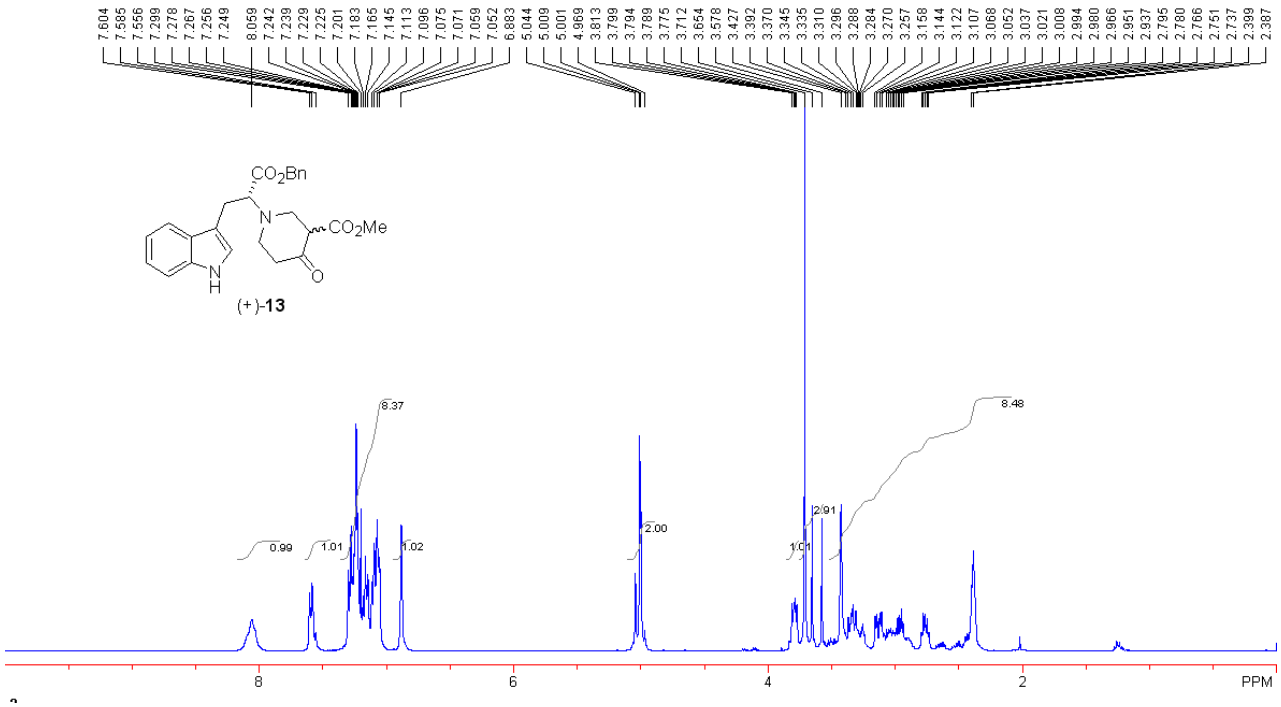
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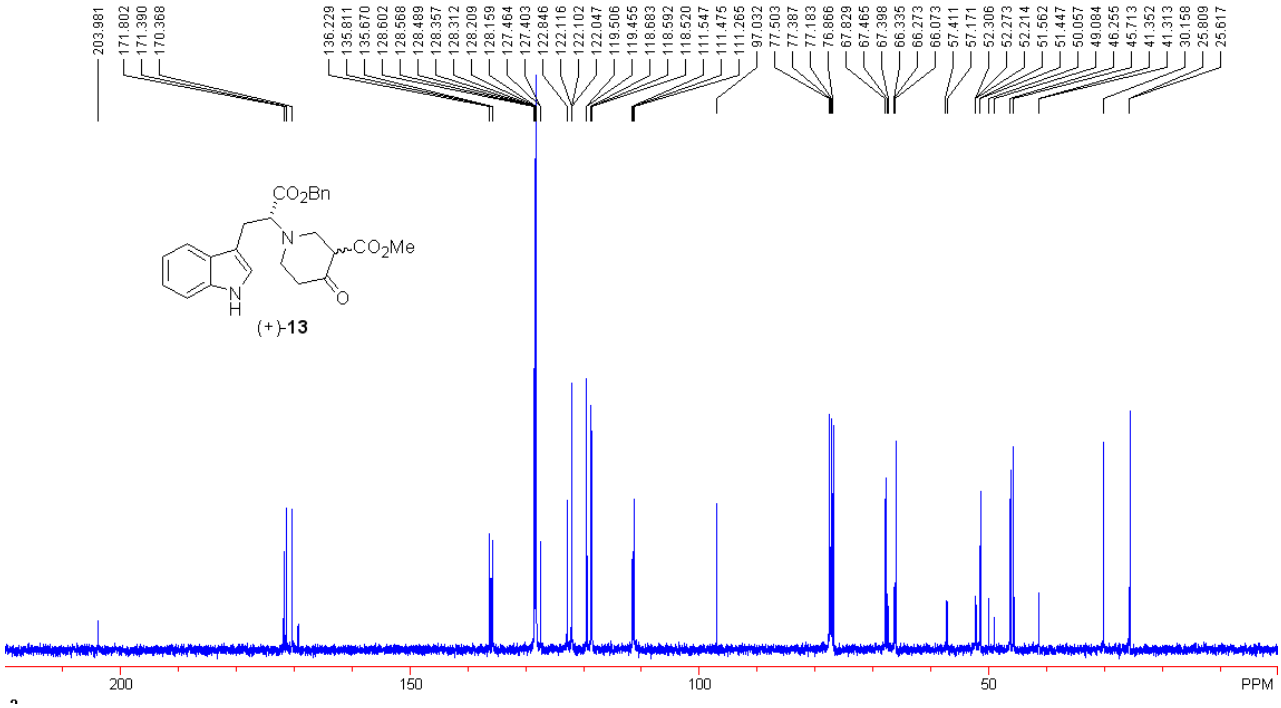
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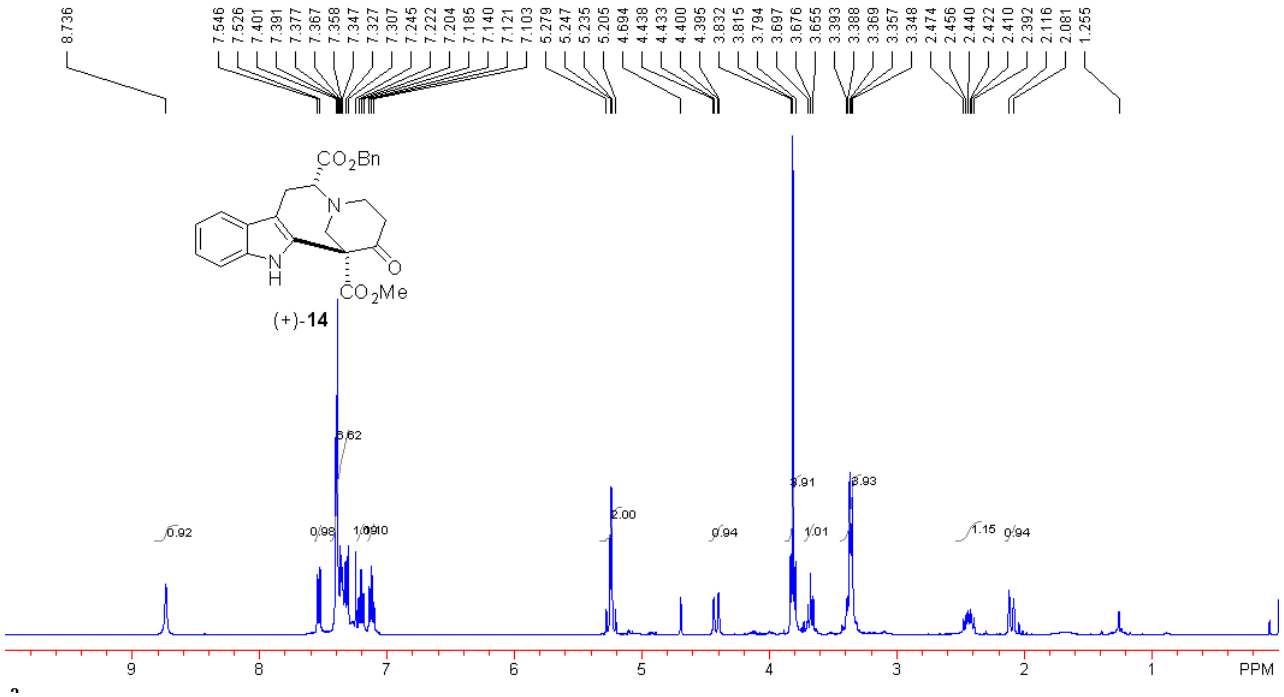
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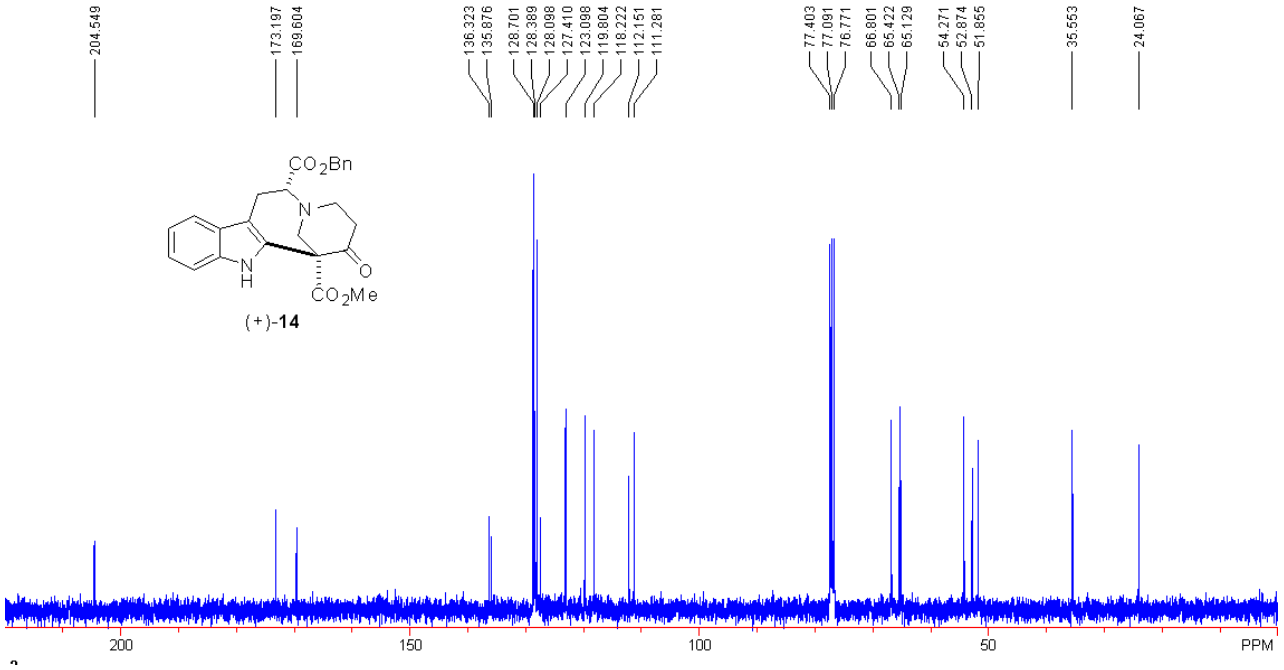
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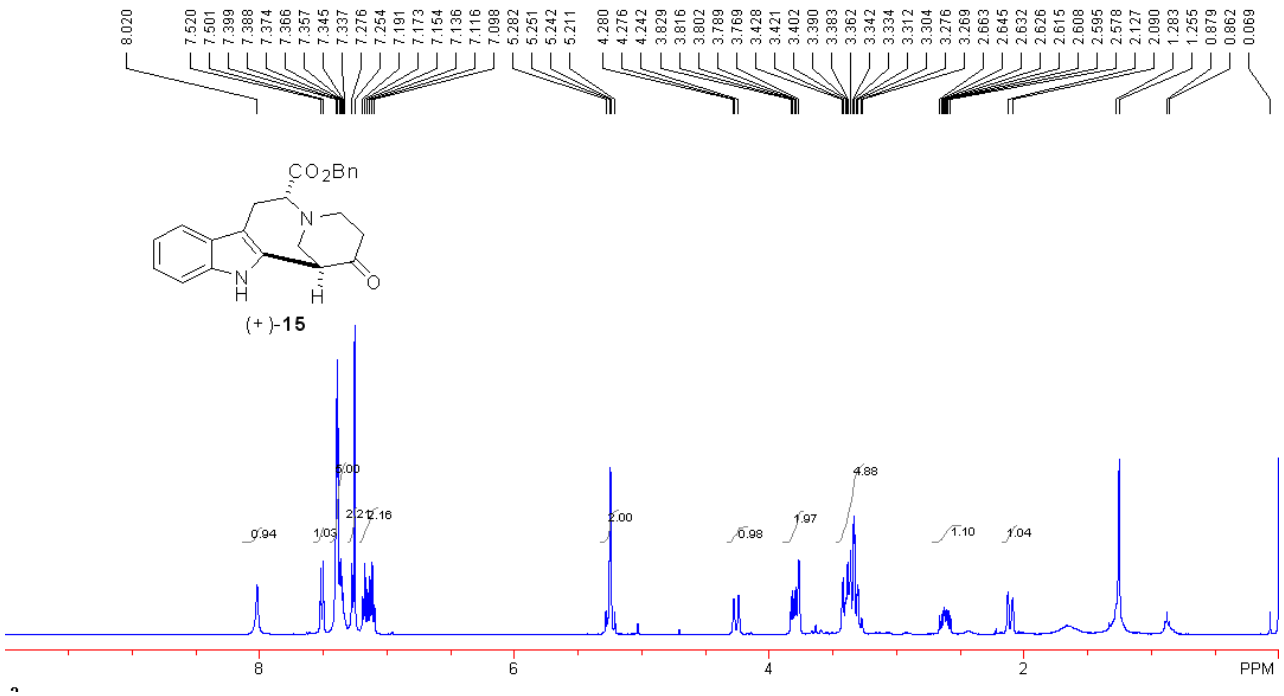
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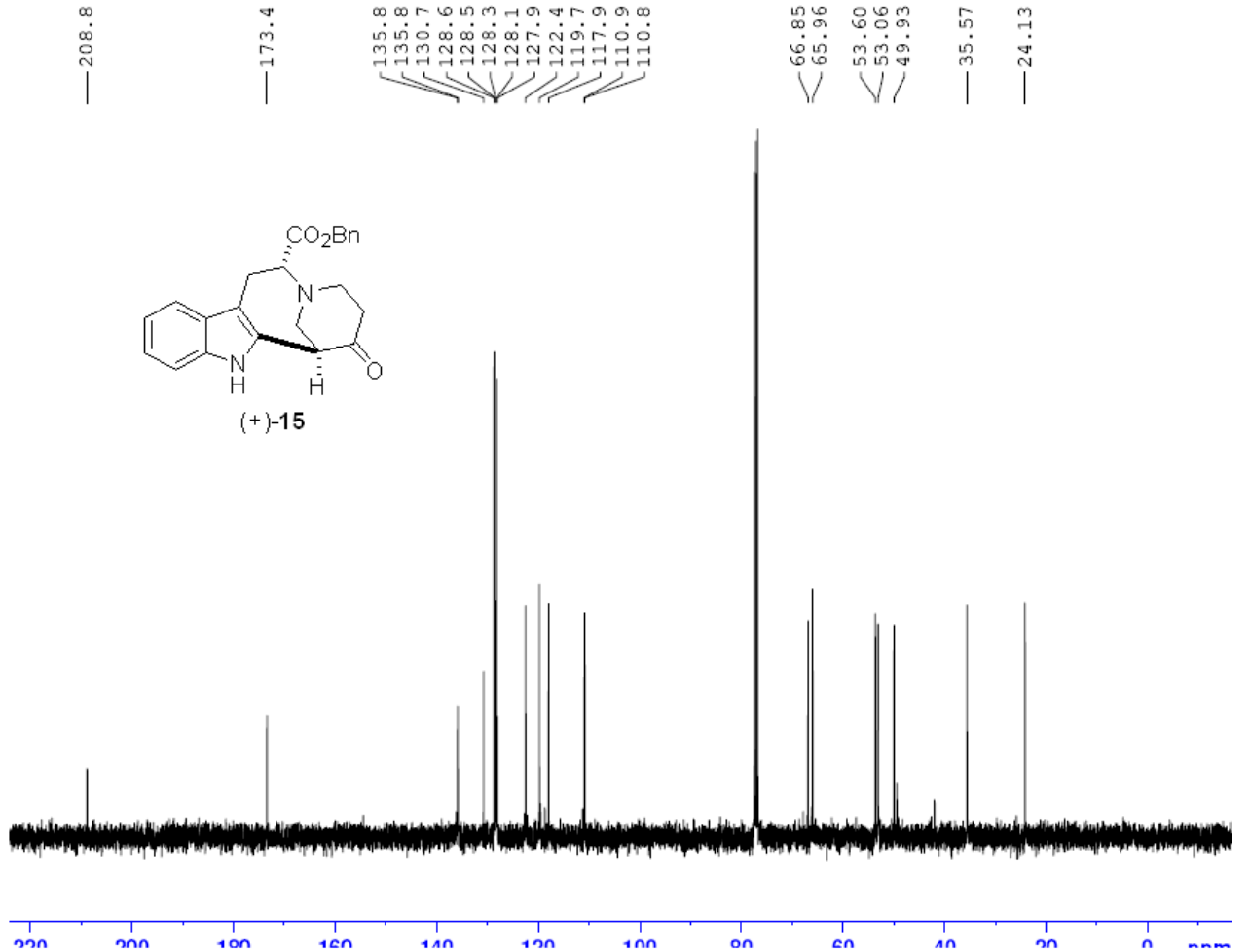
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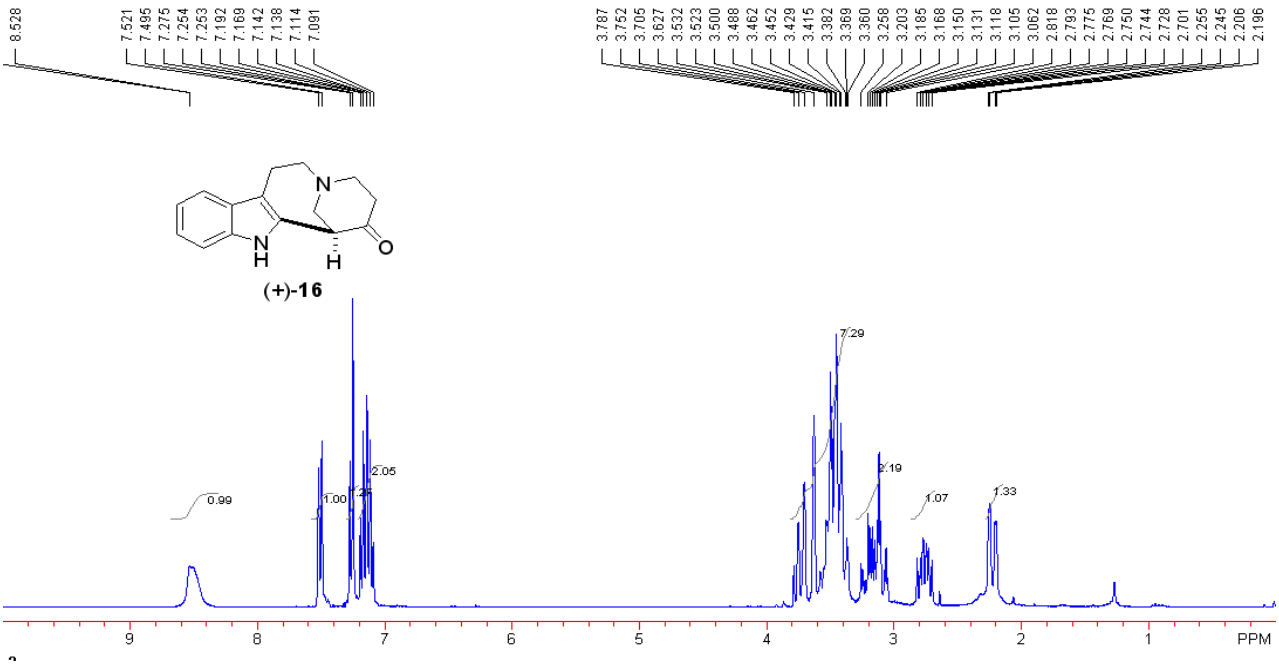
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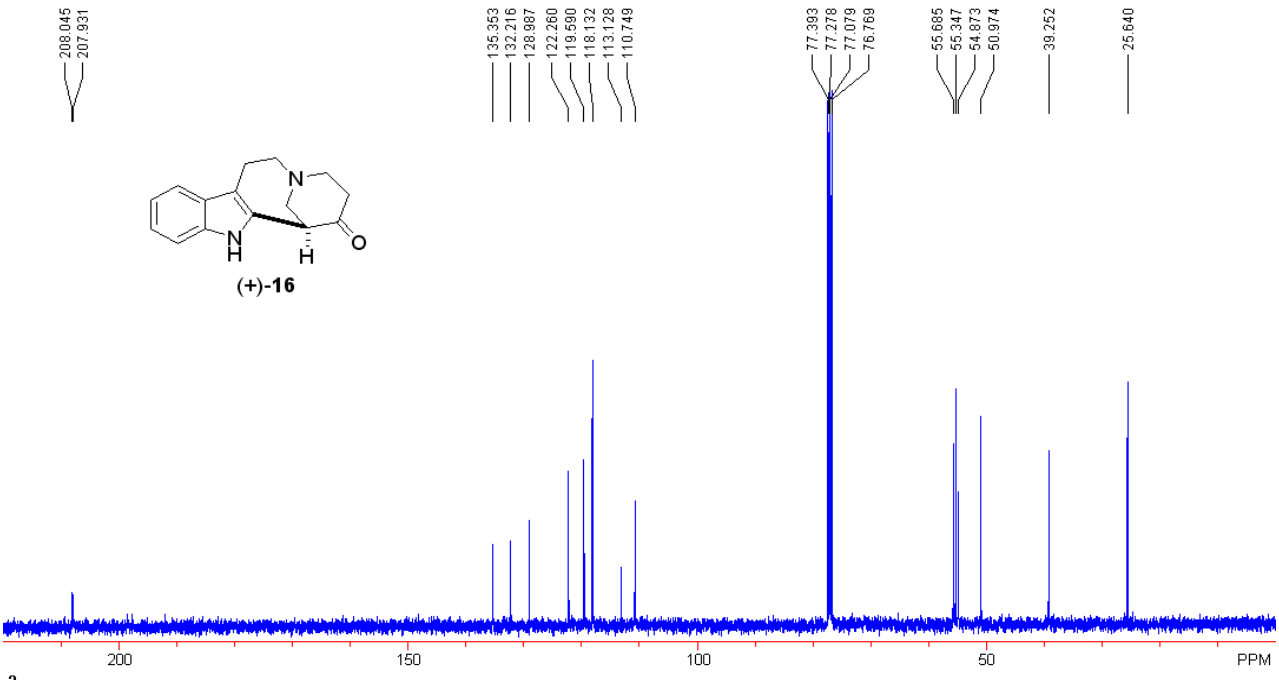
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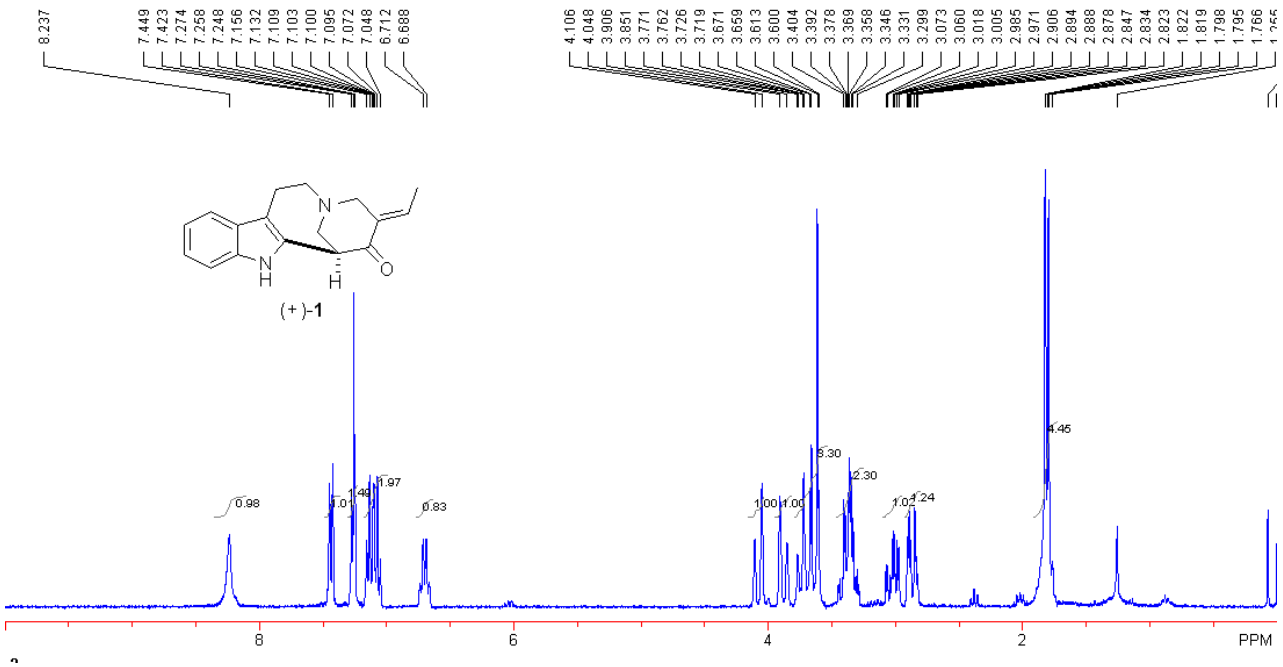
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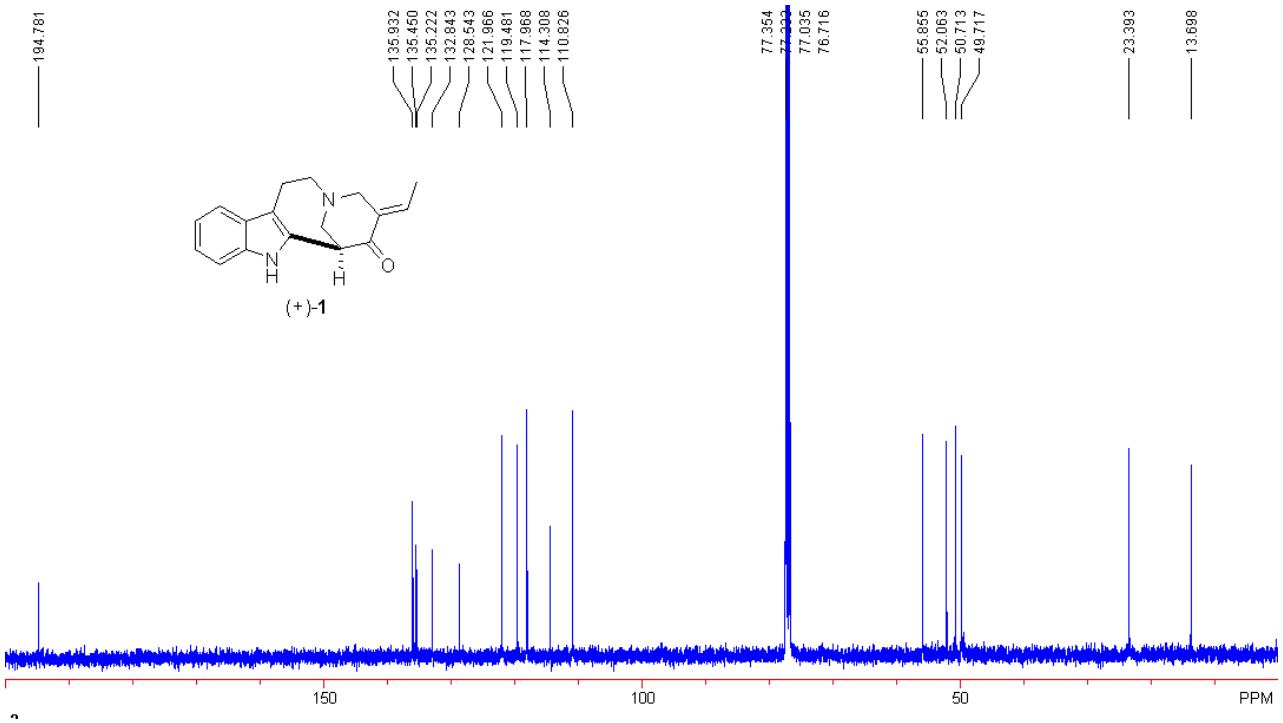
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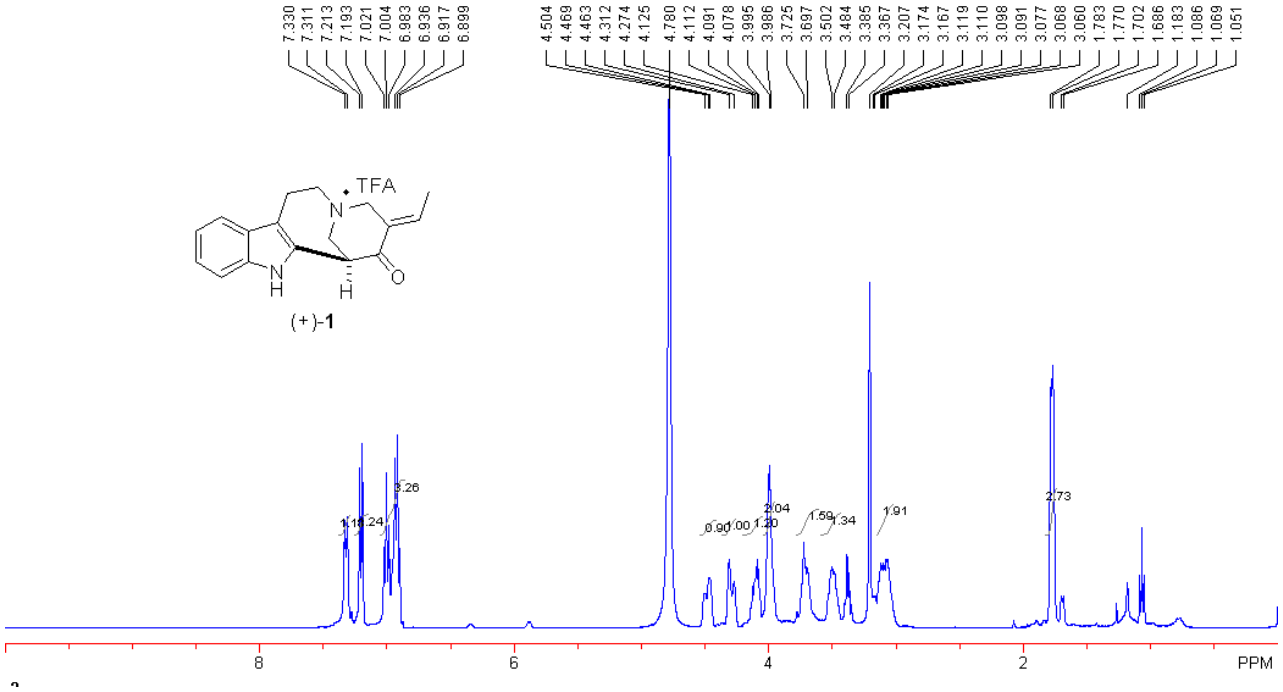
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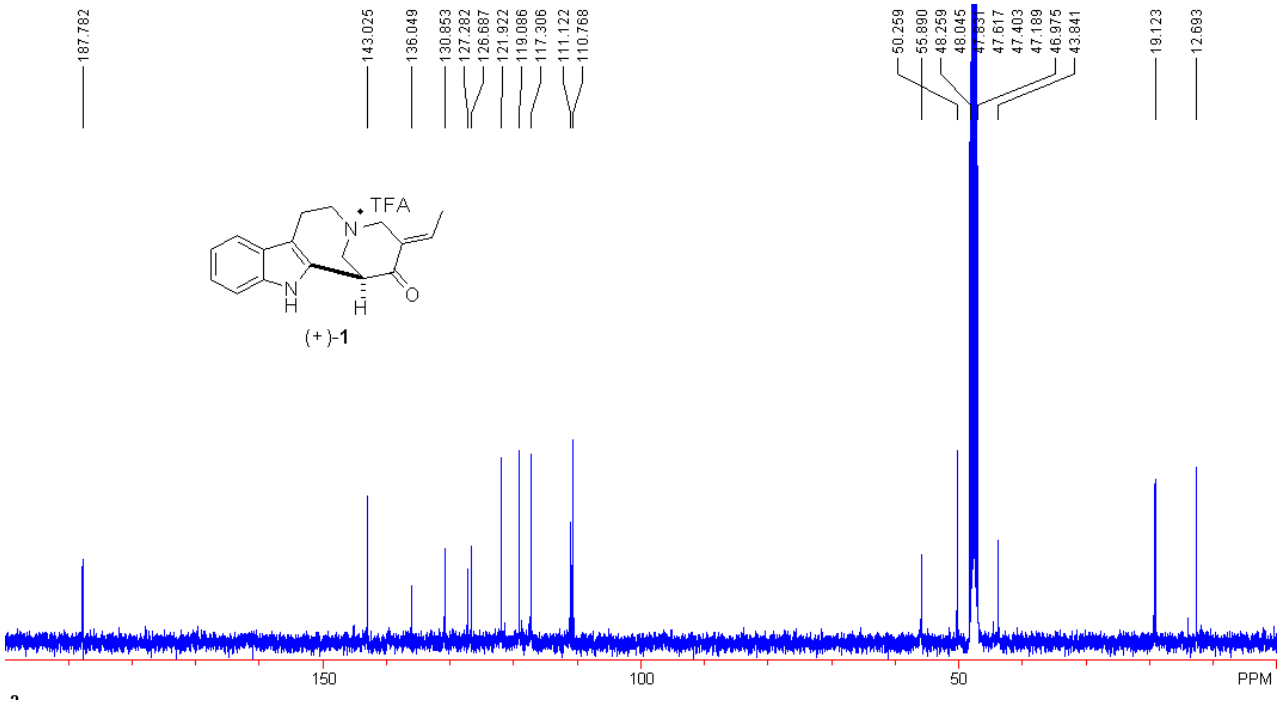
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121.922
119.086
117.306
111.122
110.768
50.259
55.890
48.259
48.045
47.831
47.617
47.403
47.189
46.975
43.841
19.123
12.693
TFA
N
H
O
(+)-1
150
100
50
PPM

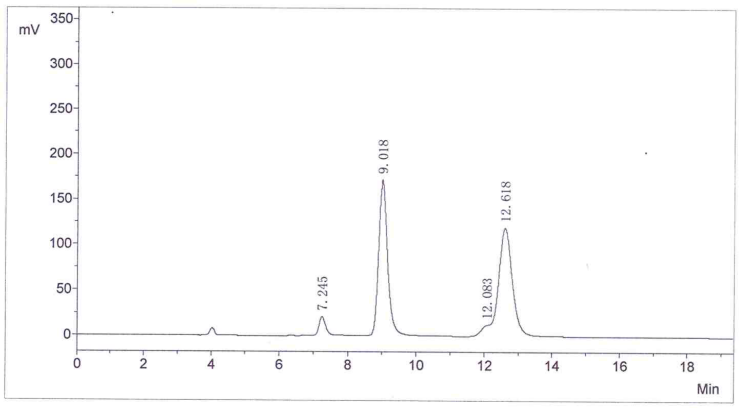
5. Chiral HPLC analyses of (±)-**1** and (+)-**1**.

(a) Chiral HPLC analyses of (±)-**1**.

色谱分析报告

样品名称:
样品批号:
分析日期:2010-04-10

样品文件名:CPH-15-73+- PC-2 55 214 0.7.che
分析者:
分析时间:09:26



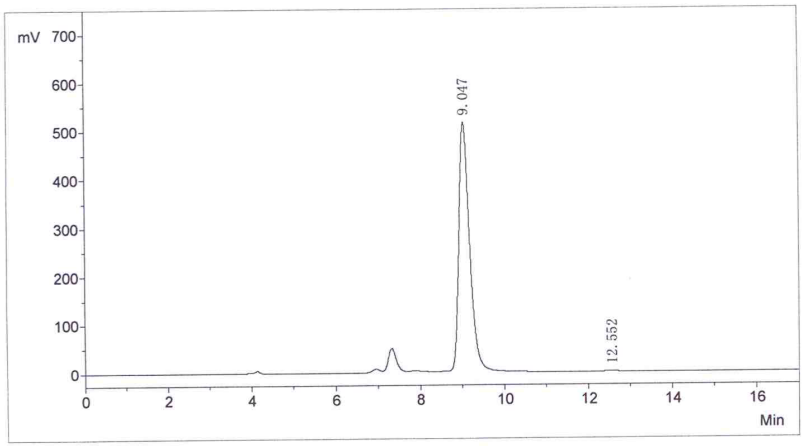
序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		7.245	20782.7	276976.3	3.9898
2	2		9.018	171494.9	3102568.1	44.6925
3	3		12.083	12494.7	212763.9	3.0649
4	4		12.618	119076.1	3349725.7	48.2528
合计:				323848.3	6942034.0	100.0000

(b) Chiral HPLC analyses of (+)-**1**.

HPLC REPORT

Data File:CPH-+.che
Date:2010-05-11
Operator:

Sample Name:
Time:14:16



No.	PeakNo	ID.Name	R.Time	PeakHeight	PeakArea	PerCent
1	1		9.047	513866.3	9096923.5	99.7443
2	2		12.552	1036.2	23316.4	0.2557
Total				514902.5	9120239.8	100.0000