Supporting Information
Silver-promoted Friedel-Crafts Reaction: Concise Total Synthesis of (−)-Ardeemin, (−)-Formylardeemin and (−)-Acetylardeemin

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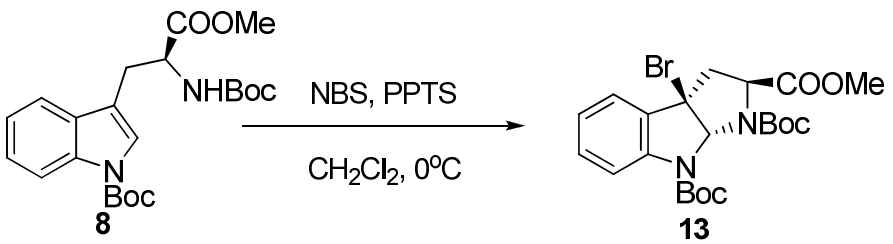
Contents of Supporting Information

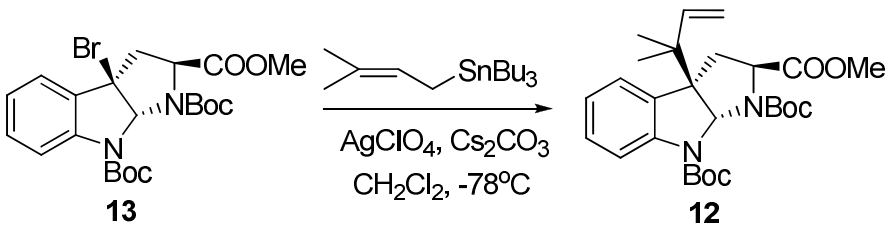
General methods

All commercially available reagents were used without further purification. All solvents were dried and distilled before use; toluene was distilled from sodium; THF was distilled from sodium/benzophenone ketyl; dichloromethane, acetonitrile and *N*, *N*-dimethylformamide were distilled from calcium hydride. Chromatography was conducted by using 200−300 mesh silica gel. All new compounds gave satisfactory spectroscopic analyses (IR, ^{1}H NMR, ^{13}C NMR, HRMS). IR spectra were recorded on a FT IR spectrometer. NMR spectra were recorded on a 400 MHz NMR spectrometer. HRMS spectra were obtained by the FAB method.



Procedure for the synthesis of 13[1]

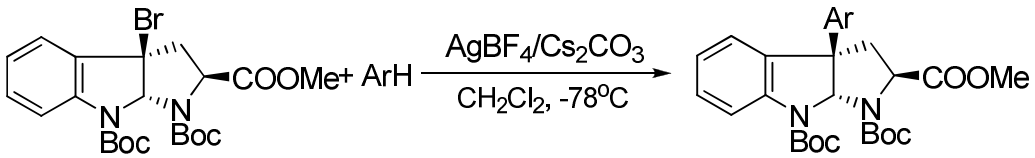
To a solution of the tryptophan derivative **8** (1.605 g, 3.8 mmol) and pyridinium *p*-toluenesulfonate (0.818 mg, 3.8 mmol) in CH_2Cl_2 (30 mL) under nitrogen was added *N*-bromosuccinimide (0.676 mg, 3.8 mmol) at 0 ℃. After stirring at 0 ℃ for 4 hours, the reaction mixture was treated with 10% $NaHCO_3$ solution (20 mL) and 10% $Na_2S_2O_4$ solution (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), the combined organic layers were dried over Na_2SO_4 and the solvents were removed under reduced pressure. The residue was purified by flash chromatography (ethyl acetate/petroleum 1:20) to afford compound **13** (1.612 g, 85%) as a white foam. An analytic sample was purified by recrystallization from hexane. $[\alpha]^{20}_{D}$ = + 181 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (s, 9H), 1.59 (s, 9H), 2.82 (dd, *J* = 12.4, 9.6 Hz, 1H), 3.21 (dd, *J* = 12.8, 6.4 Hz, 1H), 3.75 (s, 3H), 3.89 (dd, *J* = 10.4, 6.4 Hz, 1H), 6.40(s, 1H), 7.13(t, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.6Hz, 1H), 7.57 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0, 41.7, 52.1, 59.2, 59.5, 81.1, 81.9, 83.5, 118.5, 123.0, 124.2, 130.4, 132.4, 141.2, 151.9, 171.2 ppm; HRMS ($M+H^+$) calcd for $C_{22}H_{30}BrN_2O_6$ 497.1287, found 497.1295; IR (KBr) 2982, 2935, 1764, 1723, 1480, 1397, 1256, 1156, 1016 cm^{-1}.



Procedure for synthesis of 12[2]

To a solution of the bromopyrroloindoline **13** (10.0 g, 20.1 mmol), Cs_2CO_3 (9.8 g, 30.2 mmol) and prenyl tributylstannane (10.9 g, 30.2 mmol) in 300 mL of anhydrous CH_2Cl_2 at −78 ℃ under nitrogen was added

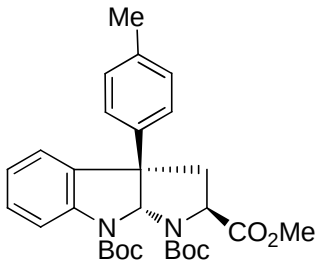
$AgClO_4$ (8.3 g, 40.2 mmol). After stirring at −78 ℃ for 16 h, the reaction was quenched with 150 mL of saturated NH_4Cl solution and then extracted with CH_2Cl_2 (3 × 200 mL), the combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by flash chromatography (ethyl acetate/petroleum 1:15) to afford compound **12** (8.8 g, 91%) as a white solid. Mp: 143−145 ℃; $[\alpha]^{20}_{D}$ = −72.1 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (s, 3H), 1.02 (s, 3H), 1.46 (broad s, 9H), 1.55 (s, 9H), 2.25-2.30 (m, 1H), 2.35-2.40 (m, 1H), 3.70(s, 3H), 3.80 (dd, *J* = 10, 6.8 Hz, 1H), 4.98-5.08 (m, 2H), 5.86 (dd, *J* = 17.2, 10.8 Hz, 1H), 6.16 (s, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.25 (t, *J* = 8.8 Hz, 1H), 7.38 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 22.5, 27.9, 34.9, 39.8, 51.5, 58.9, 61.3, 78.0, 80.7, 113.9, 117.0, 118.1, 123.0, 124.2, 128.1, 133.3, 142.7, 151.7, 172.0ppm; HRMS ($M+H^+$) calcd for $C_{27}H_{39}N_2O_6$ 487.2808, found 487.2816; IR (KBr) 2980, 2932, 1760, 1710, 1481, 1400, 1260, 1155, 1018 cm^{-1}.



13 **14** **15**

General procedure for preparation of 15

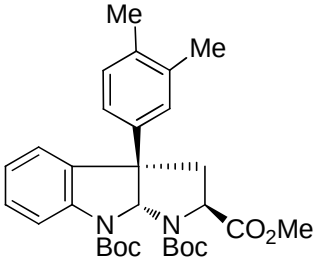
Bromopyrroloindoline **13** (1.007 g, 2.0 mmol), Cs_2CO_3 (0.977 g, 3.0 mmol) and **14** (6.0 mmol) were dissolved in 50 mL of anhydrous CH_2Cl_2 under N_2 at −78 ℃, then $AgBF_4$ (0.778 g, 4.0 mmol) was added. After complete consumption of **13**, 50 mL of saturated NH_4Cl solution was added to quench the reaction. The reaction mixture was extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were dried over Na_2SO_4, and the solvents were removed under reduced pressure. Purification by silica gel chromatography (ethyl acetate/petroleum) provided **15**.



15a

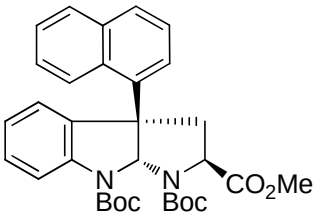
15a, purified by chromatography (ethyl acetate/petroleum 1:15) as a white solid (0.939 g, 92%). Mp: 58−61 ℃; $[\alpha]^{20}_{D}$ = −77.3 (c 0.85, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (broad s, 9H), 1.53 (s, 9H), 2.27 (s, 3H), 2.62 (t, *J* = 11.2 Hz, 1H), 2.94 (q, *J* = 6.0 Hz, 1H), 3.74 (s, 3H), 4.00 (dd, *J* = 10.4, 6.0 Hz, 1H), 6.40 (s, 1H), 7.05-7.07 (m, 5H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.48 (broad s, 1H)

ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 28.3, 39.0, 52.2, 59.7, 81.7, 82.3, 119.0, 123.3, 124.0, 125.4, 128.6, 129.4, 137.0, 137.3, 141.6, 147.2, 152.4, 172.4 ppm; HRMS ($M+H^+$) calcd for $C_{29}H_{37}N_2O_6$ 509.2652, found 509.2649; IR (KBr) 2977, 2927, 1754, 1714, 1601, 1480, 1398, 1259, 1159, 1020 cm^{-1}.



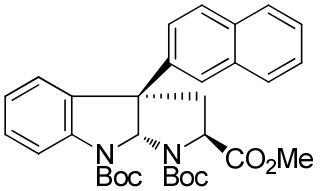
15b

15b, purified by chromatography (ethyl acetate/petroleum 1:15) as a white solid (0.935 g, 89%). Mp: 64−67 ℃; $[\alpha]^{20}_{D}$ = −136.4 (c 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (broad s, 9H), 1.55 (s, 9H), 2.18 (s, 6H), 2.61 (dd, *J* = 10.4, 12.0 Hz, 1H), 2.94 (q, *J* = 6.4 Hz, 1H), 3.74 (s, 3H), 3.99 (dd, *J* = 10.8, 6.4 Hz, 1H), 6.41 (s, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.97 (s, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 7.06(t, *J* = 7.2 Hz, 1H), 7.19 (d, *J* = 6.8 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 1H), 7.48 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 19.9, 28.3, 38.7, 52.2, 59.7, 81.6, 82.1, 119.0, 122.8, 123.3, 124.4, 126.6, 128.5, 129.9, 135.7, 137.0, 139.3, 147.4, 152.4, 172.7 ppm; HRMS ($M+Na^+$) calcd for $C_{30}H_{38}N_2NaO_6$ 545.2628, found 545.2674; IR (KBr) 2976, 2919, 2850, 1751, 1713, 1582, 1479, 1397, 1339, 1157 cm^{-1}.



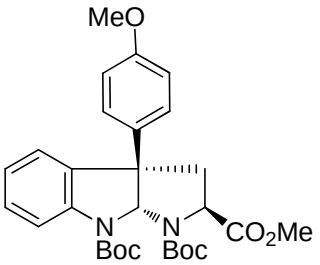
15c-α

15c-α, purified by chromatography (ethyl acetate/petroleum 1:12) as a white solid (0.218 g, 20%). Mp: 71−73 ℃; $[\alpha]^{20}_{D}$ = +204.5 (c, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (broad s, 9H), 1.48 (s, 9H), 2.82 (q, *J* = 6.8 Hz, 1H), 3.29 (dd, *J* = 10.0, 12.4 Hz, 1H), 3.80 (s, 3H), 4.18 (t, *J* = 8.4 Hz, 1H), 6.94 (s, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 7.19-7.26 (m, 2H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.52 (t, *J* = 7.6 Hz , 1H), 7.55-7.67 (m, 2H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 8.41 (d, *J* = 8.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0, 28.2, 38.7, 52.2, 60.4, 81.5, 82.1, 124.2, 124.5, 124.7, 125.4, 125.9, 126.5, 127.3, 129.0, 129.2, 129.8, 130.3, 131.3, 134.9, 141.8, 152.4, 172.9 ppm; HRMS ($M+Na^+$) calcd for $C_{32}H_{36}N_2NaO_6$ 567.2471, found 567.2469; IR (KBr) 3079, 2959, 2919, 2851, 1919, 1716, 1582, 1438, 1030 cm^{-1}.



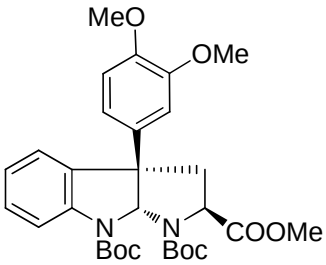
15c-β

15c-β, purified by chromatography (ethyl acetate/petroleum 1:12) as a white solid (0.659 g, 60%). Mp: 58−61 °C; $[\alpha]^{20}_{D}$ = +105.0 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (broad s, 9H), 1.57 (s, 9H), 2.77 (t, *J* = 11.2 Hz, 1H), 3.08 (q, *J* = 6.0 Hz, 1H), 3.77 (s, 3H), 4.11 (dd, *J* = 10.4, 6.0 Hz, 1H), 6.62 (s, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 2H), 7.38-7.56 (m, 4H), 7.62 (s, 1H), 7.70-7.77 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 38.7, 52.2, 59.7, 81.7, 82.2, 123.5, 123.7, 124.0, 126.1, 126.4, 127.4, 128.0, 128.8, 130.9, 132.4, 133.1, 138.5, 152.4, 171.7 ppm; HRMS ($M+Na^+$) calcd for $C_{32}H_{36}N_2NaO_6$ 567.2471, found 567.2469; IR (KBr) 3079, 2959, 2919, 2851, 1919, 1716, 1582, 1438, 1030 cm^{-1}.



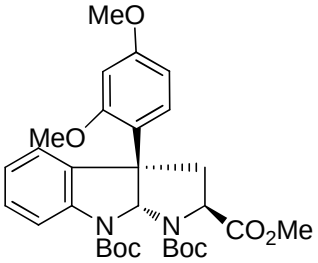
15d

15d, purified by chromatography (ethyl acetate/petroleum 1:10) as a white solid (0.762 g, 72%). Mp: 72−74 °C; $[\alpha]^{20}_{D}$ = −125.8 (c 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (broad s, 9H), 1.53 (s, 9H), 2.61 (dd, *J* = 11.2, 1.2 Hz, 1H), 2.91 (q, *J* = 6.4 Hz, 1H), 3.75 (s, 6H), 3.99 (dd, *J* = 10.4, 6.0 Hz, 1H), 6.35 (s, 1H), 6.79 (d, *J* = 8.8 Hz, 2H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 6.8 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.52 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2, 38.7, 52.2, 53.4, 55.8, 59.7, 81.6, 82.4, 114.0, 118.8, 120.4, 123.3, 124.0, 126.8, 128.6, 141.6, 152.4, 158.6, 172.7 ppm; HRMS ($M+Na^+$) calcd for $C_{29}H_{36}N_2NaO_7$ 547.2420, found 547.2413; IR (KBr) 2977, 2934, 2844, 1758, 1720, 1699, 1345, 1157, 757 cm^{-1}.



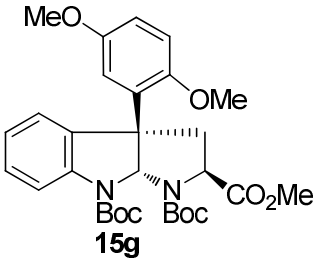
15e

15e, purified by chromatography (ethyl acetate/petroleum 1:7) as a white solid (0.757 g, 68%). Mp: 69–71 ℃; $[\alpha]^{20}_{D}$ = −142.1 (c 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (broad s, 9H), 1.54 (s, 9H), 2.60 (t, *J* = 11.2 Hz, 1H), 2.95 (q, *J* = 6.0 Hz, 1H), 3.74 (s, 3H), 3.80 (s, 3H), 3.82 (s, 3H), 3.99 (dd, *J* = 10.8, 6.0 Hz, 1H), 6.43 (s, 1H), 6.72 (s, 1H), 6.76 (d, *J* = 8.4 Hz, 2H), 7.07 (t, *J* = 7.2 Hz, 1H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.44 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 39.2, 52.2, 55.2, 55.8, 59.6, 81.6, 83.5, 108.8, 111.1, 117.7, 119.3, 123.2, 128.7, 134.1, 135.7, 141.4, 148.1, 149.0, 152.4, 172.8 ppm; HRMS ($M+Na^+$) calcd for $C_{30}H_{38}N_2NaO_8$ 577.2526, found 577.2518; IR (KBr) 2975, 2951, 2841, 1741, 1715, 1699, 1403, 1259, 1154, 1029 cm^{-1}.



15f

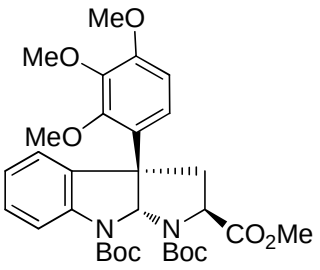
15f, purified by chromatography (ethyl acetate/petroleum 1:10) as a white solid (0.694 g, 62%). Mp: 55–58 ℃; $[\alpha]^{20}_{D}$ = −21.7 (c 10.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (broad s, 9H), 1.49 (s, 9H), 2.79 (t, *J* = 11.2 Hz, 1H), 2.89 (broad s , 1H), 3.73 (s, 3H), 3.75 (s, 3H), 3.87 (s, 3H), 4.00 (t, *J* = 8.4 Hz, 1H), 6.28 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.46 (d, *J* = 2.4 Hz, 1H), 6.55 (s, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.2 Hz, 1H), 7.60 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 38.4, 52.0, 55.2, 55.3, 59.7, 81.0, 81.3, 99.4, 103.6, 105.1, 123.1, 124.2, 124.7, 127.9, 128.8, 135.7, 141.6, 152.4, 158.1, 160.3, 172.9 ppm; HRMS ($M+Na^+$) calcd for $C_{30}H_{38}N_2NaO_8$ 577.2526, found 577.2527; IR (KBr) 2957, 2919, 2851, 1719, 1582, 1439, 1215, 754 cm^{-1}.



15g

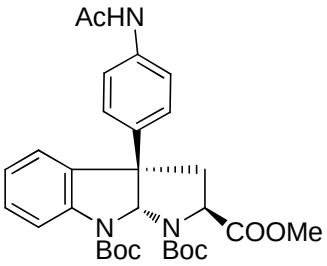
15g, purified by chromatography (ethyl acetate/petroleum 1:10) as a white solid (0.891 g, 80%). Mp: 61–63 ℃; $[\alpha]^{20}_{D}$ = −75.8 (c 1.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (broad s, 9H), 1.52 (s, 9H), 2.76 (t, *J* = 11.2 Hz, 1H), 3.01 (t, *J* = 7.2 Hz, 1H), 3.66 (s, 3H), 3.73 (s, 3H), 3.85 (s, 3H), 4.02 (dd, *J* = 10.0, 6.8 Hz, 1H), 6.58 (s, 1H), 6.63 (s, 1H), 6.72 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.60 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2, 38.5, 52.8, 55.6, 59.7, 81.6, 81.7, 112.2, 112.7, 116.0, 118.9, 123.4, 124.7,

128.6, 129.4, 141.7, 151.1, 152.3, 153.2, 172.6 ppm; HRMS (M+Na$^+$) calcd for $C_{30}H_{38}N_2NaO_8$ 577.2526, found 577.2536; IR (KBr) 2977, 2934, 2837, 1755, 1716, 1591, 1481, 1397, 1157, 1022 cm^{-1}.



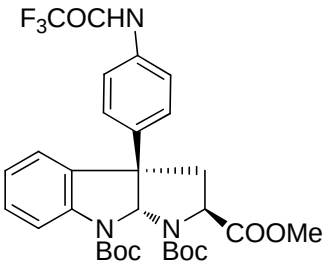
15h

15h, purified by chromatography (ethyl acetate/petroleum 1:5) as a white solid (1.102 g, 91%). Mp: 76−78 ℃; $[\alpha]^{20}_{D}$ = −55.6 (c 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (broad s, 9H), 1.52 (s, 9H), 2.75 (t, *J* = 11.2 Hz, 1H), 2.91 (broad s, 1H), 3.75 (s, 3H), 3.80 (s, 3H), 3.81 (s, 3H), 3.89 (s, 3H), 3.98 (dd, *J* = 10.0, 6.8 Hz, 1H), 6.44 (s, 1H), 6.47 (d, *J* = 5.6 Hz, 1H), 6.62 (s, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 6.8 Hz, 1H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.52 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 38.7, 52.1, 55.9, 59.6, 60.5, 60.6, 81.3, 81.7, 105.8, 115.8, 118.7, 121.4, 122.1, 124.5, 128.5, 134.5, 141.7, 152.1, 153.4, 157.9, 158.1, 159.0, 175.5 ppm; HRMS (M+Na$^+$) calcd for $C_{31}H_{40}N_2NaO_9$ 607.2632, found 607.2634; IR (KBr) 2958, 2918, 2849, 1714, 1583, 1439, 1259, 1157, 753 cm^{-1}.



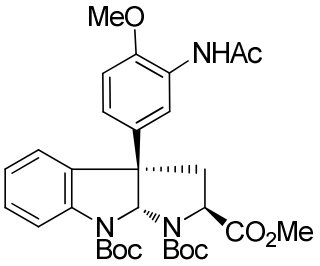
15i

15i, purified by chromatography (ethyl acetate/petroleum 1:2) as a white solid (1.008 g, 90%). Mp: 233−236 ℃; $[\alpha]^{20}_{D}$ = −103.6 (c 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (broad s, 9H), 1.51 (s, 9H), 2.08 (s, 3H), 2.56 (t, *J* = 11.2 Hz, 1H), 2.91 (q, *J* = 6.0 Hz, 1H), 3.72 (s, 3H), 3.98 (dd, *J* = 10.8, 6.4 Hz, 1H), 6.35 (s, 1H), 7.06 (d, *J* = 8.0 Hz, 3H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.58 (broad s, 1H), 8.16 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 28.1, 38.9, 52.2, 59.6, 81.8, 82.2, 117.9, 120.1, 123.4, 124.0, 126.0, 128.8, 135.2, 136.4, 137.4, 141.4, 152.4, 168.8, 172.7 ppm; HRMS (M+Na$^+$) calcd for $C_{30}H_{37}N_3NaO_7$ 574.2529, found 574.2514; IR (KBr) 3334, 2977, 2933, 1756, 1722, 1683, 1529, 1398, 1158 cm^{-1}.



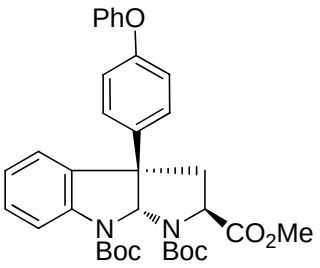
15j

15j, purified by chromatography (ethyl acetate/petroleum 1:3) as a white solid (0.813 g, 67%). Mp: 122−124 ℃; $[\alpha]^{20}_{D}$= −102.6 (c 6.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (broad s, 9H), 1.53 (s, 9H), 2.60 (t, *J* = 11.2 Hz, 1H), 2.94 (q, *J* = 6.0 Hz, 1H), 3.75 (s, 3H), 4.00 (dd, *J* = 10.8, 6.0 Hz, 1H), 6.38 (s, 1H), 7.08 (t, *J* = 7.2 Hz, 1H), 7.19 (t, *J* = 8.8 Hz, 3H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.57 (broad s, 1H), 8.03 (d, *J* = 12.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 39.1, 52.3, 59.6, 81.9, 82.2, 117.2, 118.5, 120.9, 123.4, 124.0, 126.7, 128.9, 134.3, 139.4, 141.6, 143.0, 152.3, 154.4, 172.8 ppm; HRMS ($M+Na^+$) calcd for $C_{30}H_{34}F_3N_3NaO_7$ 628.2247, found 628.2205; IR (KBr) 2958, 2925, 2853, 1717, 1478, 1398, 1157, 1020, 753 cm^{-1}.



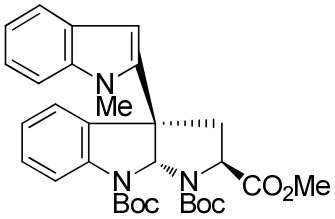
15k

15k, purified by chromatography (ethyl acetate/petroleum 1:1) as a white solid (0.616 g, 53%). Mp: 91−94 ℃; $[\alpha]^{20}_{D}$= −140.5 (c 12.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (broad s, 9H), 1.55 (s, 9H), 2.18 (s, 3H), 2.60 (t, *J* = 11.6 Hz, 1H), 3.00 (q, *J* = 6.0 Hz, 1H), 3.74 (s, 3H), 3.81 (s, 3H), 3.98 (dd, *J* = 10.4, 6.0 Hz, 1H), 6.44 (s, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.26 (d, *J* = 6.8 Hz, 1H), 7.45 (broad s, 1H), 7.72 (s, 1H), 8.44 (d, *J* = 2.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 28.3, 38.9, 52.1, 55.6, 59.6, 81.5, 81.7, 109.8, 116.9, 120.4, 123.3, 124.3, 127.9, 128.5, 134.1, 135.9, 139.0, 141.3, 146.6, 152.3, 168.2, 172.4 ppm; HRMS ($M+Na^+$) calcd for $C_{31}H_{39}N_3NaO_8$ 604.2635, found 604.2645; IR (KBr) 2958, 2926, 2852, 1750, 1714, 1586, 1531, 1257, 1029 cm^{-1}.



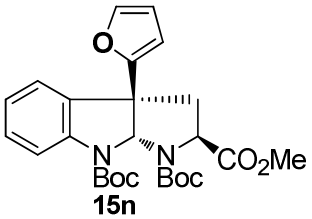
15l

15l, purified by chromatography (ethyl acetate/petroleum 1:9) as a white solid (0.519 g, 44%). Mp: 52−55 ℃; $[\alpha]^{20}_{D}$ = −57.5 (c 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (broad s, 9H), 1.53 (s, 9H), 2.63 (t, *J* = 11.2 Hz, 1H), 2.94 (q, *J* = 6.4 Hz, 1H), 3.75 (s, 3H), 4.00 (dd, *J* = 10.4, 6.4 Hz, 1H), 6.40 (s, 1H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 7.09 (t, *J* = 7.6 Hz, 2H), 7.14 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.25-7.33 (m, 3H), 7.51 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 38.8, 52.2, 59.7, 81.7, 82.4, 118.9, 123.4, 124.0, 127.1, 128.7, 129.7, 133.0, 135.6, 135.9, 141.7, 149.5, 152.4, 156.4, 156.8, 172.3 ppm; HRMS ($M+Na^+$) calcd for $C_{34}H_{38}N_2NaO_7$ 609.2577, found 609.2589; IR (KBr) 2973, 2930, 1754, 1715, 1485, 1398, 1252, 1158, 1020 cm^{-1}.



15m

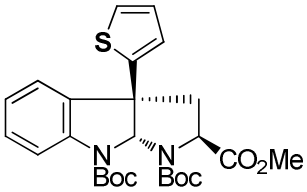
15m, purified by chromatography (ethyl acetate/petroleum 1:10) as a white solid (0.506 g, 46%). Mp: 69−71 ℃; $[\alpha]^{20}_{D}$ = +2.3 (c 7.0, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD) δ 1.41 (broad s, 18H), 2.90-2.94 (m, 2H), 3.63 (s, 3H), 3.77 (s, 3H), 3.96 (dd, *J* = 9.6, 7.2 Hz, 1H), 6.42 (s, 1H), 6.56 (s, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 7.16-7.21 (m, 2H), 7.31-7.36 (m, 2H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.51 (d, *J* = 6.4 Hz, 1H), 7.60 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 28.5, 32.7, 39.6, 52.9, 61.0, 82.5, 83.0, 101.8, 110.9, 118.8, 120.2, 120.4, 122.9, 125.2, 126.6, 128.9, 129.8, 136.6, 139.6, 142.9, 154.2, 175.0 ppm; HRMS ($M+Na^+$) calcd for $C_{31}H_{37}N_3NaO_6$ 570.2580, found 570.2590; IR (KBr) 2956, 2922, 2852, 1750, 1716, 1479, 1396, 1252, 1157 cm^{-1}.



15n

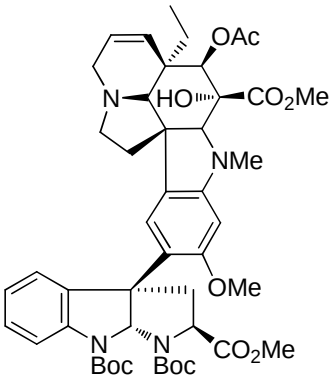
15n, purified by chromatography (ethyl acetate/petroleum 1:12) as a colorless solid (0.305 g, 31%). Mp: 46−51 ℃; $[\alpha]^{20}_{D}$ = −146.3 (c 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (broad s, 9H), 1.53 (s,

9H), 2.70 (t, J = 11.2 Hz, 1H), 2.82 (q, J = 6.4 Hz, 1H), 3.75 (s, 3H), 4.01 (dd, J = 10.4, 6.4 Hz, 1H), 5.86 (d, J = 2.8 Hz, 1H), 6.21 (dd, J = 3.2, 1.6 Hz, 1H), 6.36 (s, 1H), 7.10 (t, J = 7.6 Hz, 1H), 7.27 (t, J = 7.2 Hz, 2H), 7.32 (d, J = 5.6Hz, 1H), 7.52 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2, 38.9, 52.2, 59.4, 80.5, 81.7, 106.7, 110.2, 119.0, 123.4, 124.1, 129.1, 130.9, 142.2, 142.7, 152.9, 172.3 ppm; HRMS ($M+Na^+$) calcd for $C_{26}H_{32}N_2NaO_7$ 507.2107, found 507.2121; IR (KBr) 3079, 2957, 2921, 2850, 1752, 1718, 1397, 1336, 1161 cm^{-1}.



15o

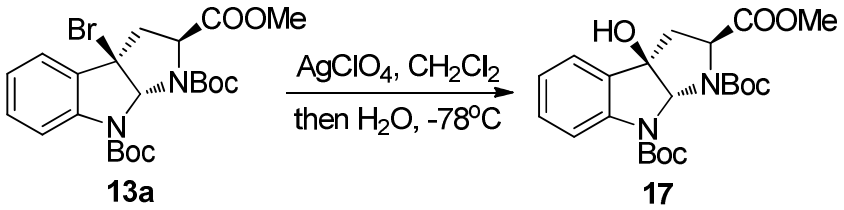
15o, purified by chromatography (ethyl acetate/petroleum 1:12) as a colorless white solid (0.946 g, 94%). Mp: 47−50 ℃; $[\alpha]^{20}_{D}$ = −112.5 (c 2.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (broad s, 9H), 1.53 (s, 9H), 2.68 (t, J = 11.6 Hz, 1H), 2.96 (q, J = 6.0 Hz, 1H), 3.75 (s, 3H), 4.00 (dd, J = 10.4, 6.4 Hz, 1H), 6.30 (s, 1H), 6.72 (d, J = 2.8 Hz, 1H), 6.86 (dd, J = 4.8, 3.6 Hz, 1H), 7.09 (t, J = 7.6 Hz, 1H), 7.16 (d, J = 4.4 Hz, 1H), 7.22 (d, J = 7.2 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.52 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 38.9, 52.3, 59.7, 81.8, 82.8, 123.1, 123.2, 124.0, 124.9, 125.4, 126.9, 128.8, 129.1, 130.9, 141.6, 152.7, 172.8 ppm; HRMS ($M+Na^+$) calcd for $C_{26}H_{32}N_2NaO_6S$ 523.1879, found 523.1877; IR (KBr) 2969, 2925, 2852, 1752, 1715, 1397, 1366, 1157 cm^{-1}.



15p

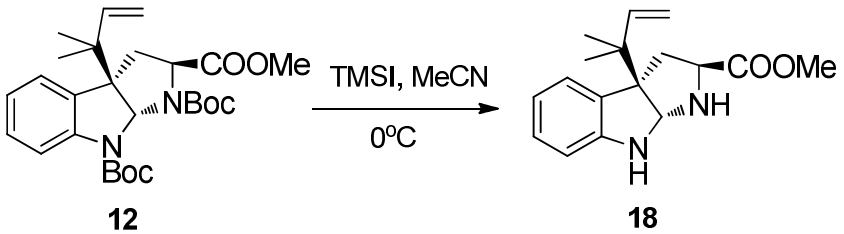
15p, purified by chromatography (ethyl acetate/petroleum 1:9) as a white solid (0.859 g, 49%). Mp: 129−132 ℃; $[\alpha]^{20}_{D}$ = −84.8 (c 2.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.16 (t, J = 7.2 Hz, 3H), 1.26-1.60 (m, 20H), 2.02 (s, 3H), 2.11-2.19 (m, 2H), 2.44-2.51 (m, 2H), 2.65 (s, 3H), 2.74 (d, J = 16.0 Hz, 1H), 3.10-3.18 (m, 1H), 3.30-3.35 (m, 2H), 3.41 (dd, J = 16.0, 4.0 Hz, 1H), 3.66 (s, 1H), 3.70 (s, 3H), 3.75 (s, 3H), 3.88 (s, 3H), 3.97 (t, J = 8.4 Hz, 1H), 5.15 (d, J = 8.8 Hz, 1H), 5.29 (s, 1H), 5.78 (dd, J = 10.0, 3.6 Hz, 1H), 6.05 (s, 1H), 6.56 (s, 1H), 6.64 (s, 1H), 6.96-7.15 (m, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.27-734 (m,

1H), 7.47 (broad s, 1H), 9.70 (broad s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.2, 21.0, 26.7, 28.1, 28.3, 30.6, 38.4, 42.5, 43.6, 50.6, 51.3, 51.9, 52.1, 52.9, 55.2, 59.6, 65.9, 76.3, 79.5, 81.0, 83.3, 94.0, 116.8, 121.0, 123.1, 124.1, 128.3, 130.2, 135.5, 139.9, 140.4, 152.7, 158.2, 170.7, 171.7, 173.0 ppm; HRMS ($M+H^+$) calcd for $C_{47}H_{61}N_4O_{12}$ 873.4286, found 873.4276; IR (KBr) 3455, 2969, 2932, 2878, 2850, 1746, 1720, 1618, 1397, 1250, 1159, 1041, 753 cm^{-1}.



Procedure for synthesis of 17

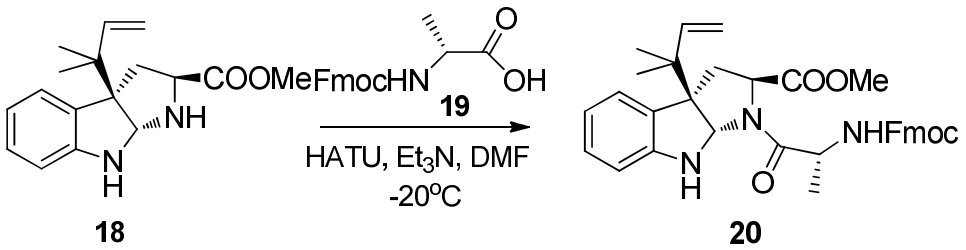
To a solution of the compound **13a** (1.005 g, 2.0 mmol) in 75 mL of dry CH_2Cl_2 at −78 ℃ under nitrogen was added $AgClO_4$ (0.829 g, 4.0 mmol). The reaction mixture was stirred at −78 ℃ 2 h. Then the reaction was quenched with saturated NH_4Cl solution (50 mL) and was extracted with CH_2Cl_2 (3 × 80 mL), the combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuum. The crude residue was purified by flash chromatography (ethyl acetate/petroleum 1:3) to afford **17** (0.151 g, 17%) as a white foam. Mp: 54−57 ℃; $[\alpha]^{20}_D$ = −80.6 (c 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 9H), 1.57 (s, 9H), 2.44 (dd, *J* = 9.6, 12.4 Hz, 1H), 2.75 (q, *J* = 6.8 Hz, 1H), 2.91 (s, 1H), 3.75 (s, 3H), 3.95 (dd, *J* = 9.6, 7.2 Hz, 1H), 6.04 (s, 1H), 7.10 (t, *J* = 7.2 Hz, 1H), 7.34 (m, 2H), 7.62 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 38.3, 52.3, 59.1, 81.2, 81.9, 83.4, 117.7, 123.0, 123.7, 130.5, 142.4, 152.5, 173.0 ppm; HRMS ($M+H^+$) calcd for $C_{22}H_{31}N_2O_7$ 435.2131, found 435.2138; IR (KBr) 3441, 2979, 2932, 1722, 1480, 1398, 1340, 1161, 1077 cm^{-1}.



Procedure for synthesis of 18

Trimethylsilyl iodide (5.9 mL, 41.2 mmol) was added dropwise to the solution of compound **12** (10.0 g, 20.6 mmol) in anhydrous MeCN (200 mL) at 0 °C. After stirring for 2 hours, the reaction was quenched with saturated $NaHCO_3$ solution (100 mL) and then extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by flash chromatography (ethyl acetate/petroleum 1:1) to afford **15** (5.3 g, 90%) as colorless oil. $[\alpha]^{20}_D$ = −82.3 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (s, 3H), 0.95 (s, 3H), 2.01 (t, *J* = 11.2 Hz, 1H),

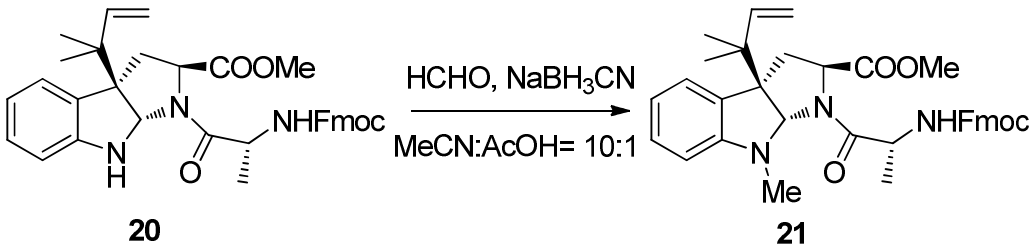
2.11 (q, J = 5.6 Hz, 1H), 2.73 (broad s, 1H), 3.44-3.48 (m, 4H), 4.86-4.94 (m, 3H), 5.88 (dd, J = 17.2, 10.8 Hz, 1H), 6.35 (d, J = 7.6 Hz, 1H), 6.52 (t, J = 7.2 Hz, 1H), 6.87 (t, J = 7.2 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 22.4, 40.2, 40.5, 51.1, 58.9, 64.6, 79.0, 107.6, 112.6, 117.0, 124.3, 127.4, 129.9, 143.8, 150.6, 173.3 ppm; HRMS ($M+H^+$) calcd for $C_{17}H_{23}N_2O_2$ 287.1760, found 287.1756; IR (KBr) 3081, 3051, 2964, 2873, 1738, 1606, 1468, 1316, 1252, 743 cm^{-1}.



Procedure for synthesis of 20

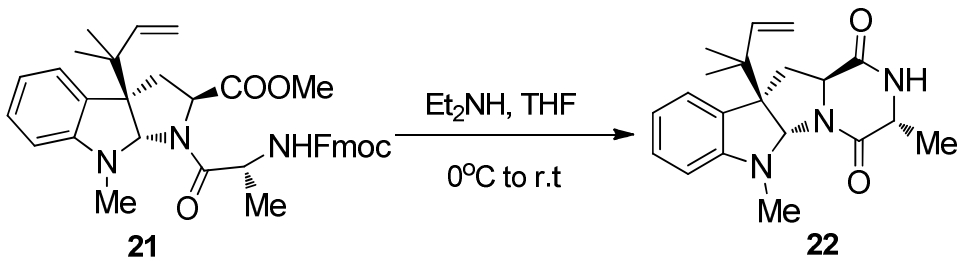
A mixture of **18** (5.0 g, 17.5 mmol) and *N*-Fmoc-D-alanine **19** (8.2 g, 26.2 mmol) was stirred in anhydrous DMF (300 mL) at −20 ℃ for 10 min, HATU (7.3 g, 19.2 mmol) and Et_3N (4.9 mL, 35.0 mmol) were added into the above solution at −20 ℃. After stirring for 10 hours, the reaction was quenched by brine (500 mL), and extracted with EtOAc (3 × 250 mL). The combined organic layers were dried over Na_2SO_4 and the solvents were removed under reduced pressure. The residue was purified by flash chromatography (ethyl acetate/petroleum 1:7) to afford a mixture of **20a/20b** as white foam (8.1 g, 80%). $[\alpha]^{20}_{D}$ = −152.8 (c 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, a mixture of two rotamers in a 1:1 ratio) δ 0.94 (rotamer A and B; s, 6H), 1.03-1.04 (rotamer A and B; m, 6H), 1.30 (rotamer A ; d, J = 6.4 Hz, 3H), 1.40 (rotamer B; d, J = 6.8 Hz, 3H), 2.33-2.47 (rotamer A and B; m, rotamer A 2H ; rotamer B 1H), 2.65 (rotamer B; dd, J = 12.6, 8.8 Hz, 1H), 3.71 (rotamer A; s, 3H), 3.78 (rotamer B; s, 3H), 4.00 (rotamer A; t, J = 6.8 Hz, 1H), 4.07-4.20 (rotamer A and B; m, 5H), 4.24 (rotamer A; t, J = 7.2 Hz, 1H), 4.60 (rotamer B; t, J = 8.4 Hz, 1H), 4.78-4.84 (rotamer A and B; m, 2H), 4.96-5.11 (rotamer A and B; m, 5H), 5.31(rotamer A; d, J = 8.8 Hz, 1H), 5.62 (rotamer B; d, J = 9.6 Hz, 1H), 5.83 (rotamer A ; dd, J = 17.2, 6.4 Hz, 1H), 5.94 (rotamer B; dd, J = 17.2, 6.4 Hz, 1H), 6.70-6.64 (rotamer A and B; m, 2H), 6.81 (rotamer A ; t, J = 7.6 Hz, 1H), 6.88 (rotamer B; t, J = 7.2 Hz, 1H), 7.08-7.17 (rotamer A and B; m, 4H), 7.28-7.34 (rotamer A and B; m, 5H), 7.41 (rotamer A and B; t, J = 6.8 Hz, 5H), 7.52 (rotamer A; d, J = 7.6 Hz, 2H), 7.62 (rotamer B; d, J = 7.2 Hz, 2H), 7.77 (rotamer A and B; d, J = 7.2 Hz, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) rotamer A: δ 16.9, 21.9, 22.7, 35.2, 40.9, 47.0, 48.3, 52.2, 59.2, 60.6, 67.1, 78.2, 109.0. 111.9, 114.3, 118.2, 120.0, 124.9, 127.1, 129.0, 129.6, 141.2, 143.4, 143.9, 148.9, 155.7, 172.3, 173.4 ppm; rotamer B: 18.5, 22.2 , 22.9, 38.1, 41.4, 47.0, 48.5, 52.8, 59.5, 64.5, 67.3, 80.8, 111.9, 114.3, 120.0, 120.3, 125.2, 127.7, 129.0, 131.7, 141.2, 143.7, 144.0, 149.6, 156.2, 172.5, 174.0 ppm; HRMS

($M+H^+$) calcd for $C_{35}H_{38}N_3O_5$ 580.2811, found 580.2813; IR (KBr) 2975, 1744, 1716, 1641, 1450, 1245, 1218, 1073, 1035, 879, 758, 741 cm^{-1}.



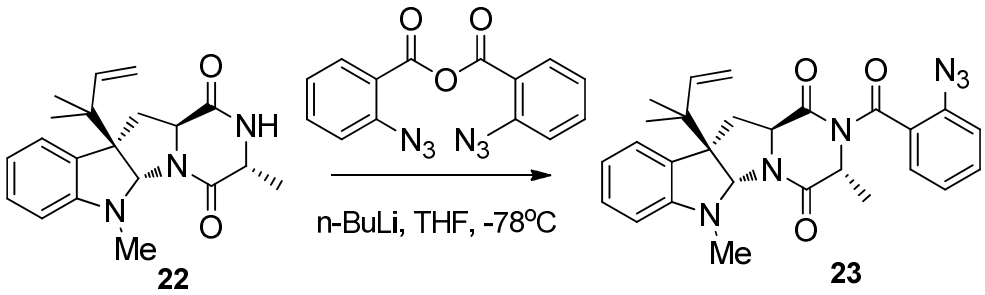
Procedure for synthesis of 21

Compound **20** (5.0 g, 8.6 mmol) was dissolved in a 1:10 mixture of AcOH/MeCN (300 mL). HCHO (37% solution in water, 152 mL) and $NaBH_3CN$ (1.6 g, 25.8 mmol) were added into the reaction mixture sequentially at room temperature. After stirring for 30 min, the mixture was quenched by saturated $NaHCO_3$ solution (70 mL). The resulting mixture was extracted with EtOAc (3 × 100 mL). The combined extracts were washed with brine (3 × 150 mL), dried over Na_2SO_4 and concentrated. The crude residue was purified by column chromatography (ethyl acetate/petroleum 1:9) to afford a mixture of **21a/21b** (4.6 g, 90%) as a white solid. Mp: 76–77 ℃; $[\alpha]^{20}_{D}$ = −59.3 (c 1.65, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, a mixture of two rotamers in a 1:4 ratio) δ 0.74 (rotamer A; s, 3H), 0.86 (rotamer B; s, 3H), 0.98 (rotamer A; s, 3H), 1.02 (rotamer B; s, 3H), 1.28 (rotamer A; d, *J* = 7.6 Hz, 0.7H), 1.37 (rotamer B; d, *J* = 6.8 Hz, 3H), 2.32-2.43 (rotamer A and B; m, 2H), 3.05 (rotamer A; s, 3H), 3.10 (rotamer B; s, 3H), 3.70 (rotamer A and B; s, 3H), 4.01 (rotamer A and B; dd, *J* = 10, 7.2 Hz, 1H), 4.24 (rotamer A and B; t, *J* = 8.0 Hz, 1H), 4.35-4.45 (rotamer A and B; m, 2H), 4.77-4.84 (rotamer A and B; m, 1H), 4.98-5.08 (rotamer A and B; m, 2H), 5.44 (rotamer A and B; s, 1H), 5.50 (rotamer B; s, 1H), 5.76 (rotamer A and B; dd, *J* = 17.2, 6.4 Hz, 1H), 6.53 (rotamer A and B; d, *J* = 8.0 Hz, 1H), 6.63 (rotamer A; t, *J* = 7.6 Hz, 1H), 6.81 (rotamer A and B; t, *J* = 7.6 Hz, 1H), 6.90 (rotamer A and B; t, *J* = 7.6 Hz, 1H), 7.04 (rotamer A; d, *J* = 7.6 Hz,1H), 7.07 (rotamer B; d, *J* = 7.6 Hz, 1H), 7.19 (rotamer A and B; t, *J* = 8.0 Hz, 1H), 7.33 (rotamer A and B; t, *J* = 7.6 Hz, 2H), 7.41 (rotamer A and B; t, *J* = 7.2 Hz, 2H), 7.51 (rotamer A; t, *J* = 6.8 Hz, 1H), 7.63 (rotamer A and B; d, *J* = 7.6 Hz, 2H), 7.77 (rotamer A and B; d, *J* = 7.2 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) rotamer A: δ 17.4, 21.5, 22.7, 34.9, 37.1, 40.3, 40.4, 46.5, 47.6, 48.1, 52.2, 52.7, 59.4, 64.1, 66.9, 86.2, 86.5, 88.5, 109.6, 113.9, 118.2, 119.3, 119.7, 124.2, 124.8, 126.8, 127.5, 128.9, 130.4, 140.9, 143.3, 143.4, 151.2, 155.9, 172.3, 172.9 ppm; rotamer B: δ 17.4, 21.7, 23.2, 34.9, 37.1, 40.3, 40.4, 46.5, 46.6, 47.6, 48.1, 52.2, 52.7, 59.4, 64.1, 66.9, 86.2, 86.5, 88.5, 109.6, 113.9, 118.2, 119.3, 119.7, 124.2, 124.8, 126.8, 127.5, 128.9, 130.4, 140.9, 143.3, 143.4, 151.2, 155.9, 172.3, 172.9 ppm; HRMS ($M+H^+$) calcd for $C_{36}H_{39}N_3O_5$, 594.2968, found 594.2666; IR (KBr) 2953, 1745, 1716, 1655, 1451, 1289, 1080, 740 cm^{-1}.



Procedure for synthesis of 22

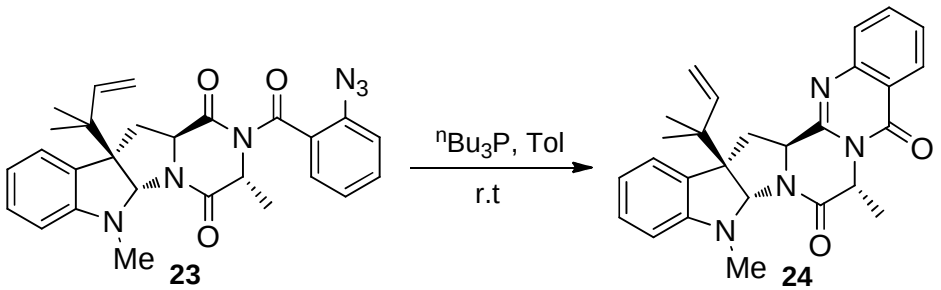
Diethylamine (31.0 mL) was added to a solution of **21a/21b** (5.0 g, 8.4 mmol) in anhydrous THF (400 mL) at 0 ℃, the mixture was allowed to warm to room temperature and stirred overnight. The solvents were removed under reduced pressure and the residue was purified by chromatography (ethyl acetate/petroleum 1:1) to afford **22** (2.7 g, 93%) as a white solid. Mp: 67−69 ℃; $[\alpha]^{20}_{D}$ = −384.4 (c 1.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (s, 3H), 1.10 (s, 3H), 1.46 (d, *J* = 7.2 Hz, 3H), 2.31 (t, *J* = 12.0 Hz, 1H), 2.54 (dd, *J* = 12.4, 6.0 Hz, 1H), 2.98 (s, 3H), 3.93 (dd, *J* = 11.6, 5.6 Hz, 1H), 3.99-4.05 (m, 1H), 5.05-5.13 (m, 2H), 5.70 (s, 1H), 5.91 (dd, *J* = 17.2, 6.4 Hz, 1H), 6.38 (d, *J* = 7.6 Hz, 1H), 6.45 (broad s, 1H), 6.69 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.2 Hz, 1H),7.18 (d, *J* = 7.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 22.1, 22.9, 32.0, 38.6, 40.7, 52.9, 57.7, 59.8, 82.3, 105.5, 114.4, 117.1, 124.7, 128.8, 129.1, 143.2, 151.5, 166.1, 169.0 ppm; HRMS ($M+H^+$) calcd for $C_{20}H_{26}N_3O_2$ 340.2025, found 340.2032; IR (KBr) 2974, 2932, 2875,1674, 1605, 1493, 1442, 1303, 1130, 746 cm^{-1}.



Procedure for synthesis of 23

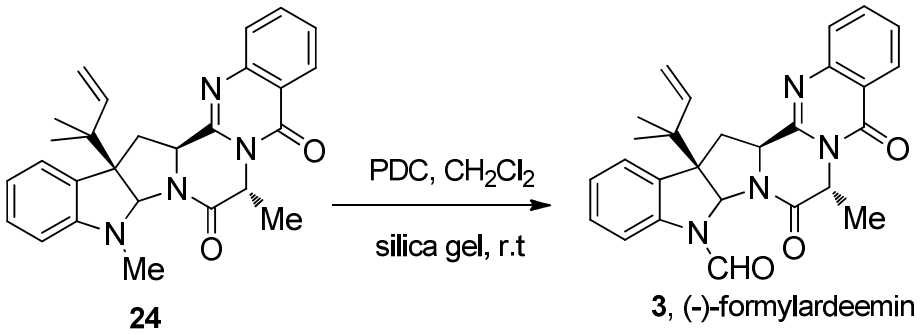
To a solution of compound **22** (5.0 g**,** 14.7 mmoL) in anhydrous THF (250 mL) at −78 ℃ under nitrogen was added a solution of *n*-BuLi (12 mL, 2.5 M in THF, 30 mmol). After stirring for 20 min at −78 ℃, a solution of *o*-azidobenzoic anhydride (9.1 g, 29.5 mmol) in THF (50 mL) was added dropwise. After stirring for 30 minutes at −78 ℃, the reaction was poured into a biphasic mixture (300 mL) of saturated $NaHCO_3$ solution and EtOAc. The aqueous layer was separated and extracted with EtOAc (3 × 150 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by chromatography (ethyl acetate/petroleum 1:15) to give **23** as a white foam (6.6 g, 92%). Mp: 55−56 ℃; $[\alpha]^{20}_{D}$ = −112.6 (c 1.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (s, 3H), 1.10 (s, 3H), 1.56 (d, *J* = 7.2 Hz, 3H), 2.43-2.54 (m, 2H), 3.04 (s, 3H), 4.06 (dd, *J* = 10.8, 6.4

Hz, 1H), 5.03 (q, *J* = 6.8 Hz, 1H), 5.09-5.17 (m, 2H), 5.73 (s, 1H), 5.94 (dd, *J* = 17.2, 10.8 Hz, 1H), 6.41 (d, *J* = 8.0 Hz, 1H) 6.70 (t, *J* = 7.2 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 7.14-7.17 (m, 2H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.40 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.50 (dt, *J* = 8.0, 1.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.7, 21.8, 22.9, 32.5, 38.5, 40.7, 55.3, 58.9, 60.0, 82.2, 105.7, 114.6, 117.2, 117.9, 124.4, 124.9, 128.2, 128.7, 129.0, 129.1, 131.6, 135.9, 142.9, 151.3, 165.8, 167.5, 168.8 ppm; HRMS ($M+H^+$) calcd for $C_{27}H_{29}N_6O_3$ 485.2301, found 485.2300; IR (KBr) 2964, 2927, 2871, 2128, 1721, 1679, 1602, 1491, 1451, 1300 cm^{-1}.



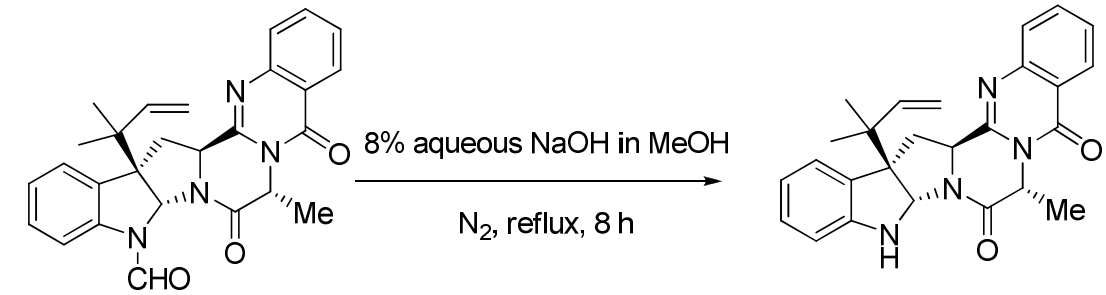
Procedure for synthesis of 24

Tri(*n*-butyl)phosphine (5.2 mL, 20.6 mmol) was added to a solution of compound **23** (5.0 g, 10.3 mmol) in anhydrous toluene (150 mL) under nitrogen. The yellow solution was stirred for 1 h, concentrated and then chromatographed (ethyl acetate/petroleum 1:10) to give compound **24** (3.9 g, 86%) as a white solid. Mp: 103−106 ℃; $[\alpha]^{20}_{D}$ = −310.0 (c 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (s, 3H), 1.14 (s, 3H), 1.58 (d, *J* = 6.8 Hz, 3H), 2.60 (dd, *J* = 11.6, 10.8 Hz, 1H), 2.93 (dd, *J* = 12.4, 5.6 Hz, 1H), 3.11 (s, 3H), 4.58 (dd, *J* = 10.4, 6.0 Hz, 1H), 5.07 (s, 1H), 5.12 (t, *J* = 8.4 Hz, 1H), 5.40 (q, 6.8 Hz, 1H), 5.72 (s, 1H), 5.94 (dd, *J* = 17.6 , 7.2 Hz, 1H), 6.42 (d, *J* = 7.8 Hz, 1H), 6.72 (t, *J* = 7.2 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.64 (d, *J* = 8 Hz, 1H), 7.75 (t, *J* = 7.2 Hz, 1H), 8.26 (d, *J* = 8.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 22.1, 22.9, 33.0, 40.1, 40.9, 53.1, 58.1, 60.4, 82.6, 105.8, 114.3, 117.9, 120.3, 124.7, 126.7, 126.9, 127.0, 129.0, 129.4, 134.5, 143.3, 147.1, 150.6, 151.4, 159.7, 165.8 ppm; HRMS ($M+H^+$) calcd for $C_{27}H_{29}N_4O_2$ 441.2291, found 441.2283; IR (KBr) 2968, 2931, 2875, 1679, 1602, 1466, 1403, 1160, 775, 747 cm^{-1}.



Procedure for synthesis of 3 [3]

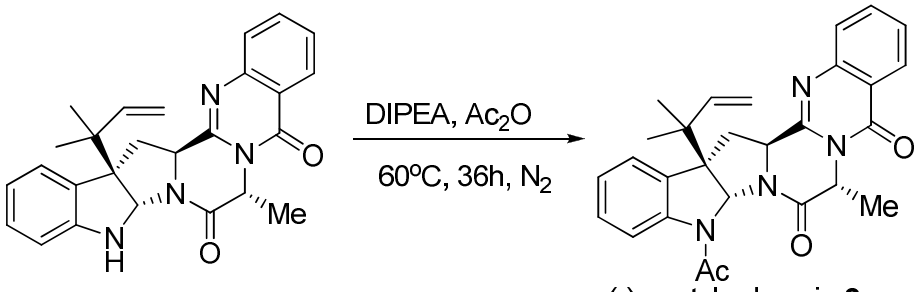
To the solution of compound **24** (5.03 g, 11.4 mmol) and silica gel (21.4 g) in anhydrous CH_2Cl_2, PDC (10.71 g, 28.4 mmol) was added. After being stirred for 7 hours, the mixture was poured onto a pad of silica gel and the filter cake was washed with ethyl acetate. The combined organic phases were concentrated in vacuum, and purified by chromatography (ethyl acetate/petroleum 1:6) to yield **3** (4.13 g, 80%) as a white solid. Mp: 133−135 ℃; $[\alpha]^{20}_{D}$= −127 (c 1.6, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (s, 3H), 1.21 (s, 3H), 1.48 (d, *J* = 7.2 Hz, 3H), 2.73 (dd, *J* =12.8, 10.8 Hz, 1H), 3.03 (dd, *J* = 12.8, 6.0 Hz, 1H), 4.54 (dd, *J* = 10.4, 6.0 Hz, 1H), 5.17-5.11 (m, 2H), 5.46 (q, *J* = 7.2 Hz, 1H), 5.88 (dd, *J* = 17.2, 10.8 Hz, 1H), 6.13 (s, 1H), 7.20 (t, *J* =7.6 Hz, 1H), 7.36 (t, *J* =7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.50 (t, *J* =7.6 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* =6.8 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 9.08 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.2, 22.1, 22.8, 38.3, 40.9, 53.0, 57.8, 60.4, 76.8, 115.2, 116.9, 120.2, 124.7, 124.9, 126.7, 126.9, 127.1, 129.3, 132.1, 134.5, 140.9, 142.3, 146.8, 149.9, 159.5, 161.5, 166.0 ppm; HRMS ($M+H^+$) calcd for $C_{27}H_{27}N_4O_3$ 455.2083, found 455.2081; IR (KBr) 2973, 2932, 1688, 1603, 1465, 1403, 1162, 769 cm^{-1}.



(-)-formylardeemin **3** (-)-ardeemin **2b**

Procedure for synthesis of 2b [3, 4]

To a solution of compound **3** (1.208 g, 2.6 mmol) in MeOH (20 mL) under N_2, 10 mL of 8% NaOH solution (13.2 mmol) was added. After being heated at reflux for 8 hours, the mixture was concentrated in vacuum. The mixture was concentrated. The residue was dissolved in CH_2Cl_2 (100 mL), washed by brine (50 mL) and dried over Na_2SO_4. Concentrated and chromatography (ethyl acetate/petroleum 1:4) afforded (−)-ardeemin **2b** as a white foam (0.955 g, 85 %). $[\alpha]^{20}_{D}$ = −204.0 (c 7.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (s, 3H), 1.18 (s, 3H), 1.49 (d, *J* = 7.2 Hz, 3H), 2.75 (dd, *J* = 13.2, 10.8 Hz, 1H), 2.93 (dd, *J* = 12.8, 6 Hz, 1H), 4.52 (dd, *J* = 10.8, 6.4 Hz, 1H), 5.09-5.17 (m, 3H), 5.45 (q, *J* = 7.2 Hz, 1H), 5.60 (s, 1H), 6.03 (dd, *J* = 13.2, 11.2 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 6.80 (t, 7.6 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 6.0 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.76 (t, *J* = 8.4 Hz, 1H), 8.26 (d, *J* = 7.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.7, 22.4, 22.7, 37.9, 40.8, 53.0, 57.9, 61.6, 77.6, 109.1, 114.5, 118.6, 120.4, 124.9, 126.7, 127.0, 128.9, 134.5, 143.3, 146.9, 149.6, 150.6, 159.8, 166.4 ppm



Procedure for synthesis of 2a [3, 4]

To a solution of compound **2b** (1.106 g, 2.6 mmol) in acetic anhydride (60.0 mL) DIPEA (0.78 mL, 7.7 mmol) was added under N_2. Then the reaction mixture was warmed to 60 ℃ and stirred for 36 h. The mixture was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (50 mL), washed with saturated $NaHCO_3$ solution (50 mL) and brine (50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by chromatography (ethyl acetate/petroleum 1:5) to give (−)-acetylardeemin **2a** (0.806 g, 75%). $[\alpha]^{20}_{D}$ = −47.0 (c 3.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (s, 3H), 1.21 (s, 3H), 1.42 (d, *J* = 6.8 Hz, 3H), 2.66-2.71 (m, 4H), 3.02 (dd, *J* = 13.2, 6 Hz, 1H), 4.40-4.43 (m, 1H), 5.11-5.16 (m, 2H), 5.40 (q, *J* = 6.8 Hz, 1H), 5.84 (dd, *J* = 13.6, 10.8 Hz, 1H), 6.03 (s br, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.33-7.40 (m, 2H), 7.50 (t, 7.6 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 8.0 Hz, 1H), 8.02 (s br, 1H), 8.22 (d, *J* = 7.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.9, 22.3, 23.0, 23.4, 37.1, 40.3, 53.4, 58.2, 60.9, 79.3, 114.5, 119.4, 120.3, 124.4, 124.5, 126.7, 127.0, 127.2, 129.0, 134.6, 142.8, 143.0, 146.9, 159.6, 165.8, 169.9 ppm.

References

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[3] B. He, H. Song, Y. Du and Y. Qin, *J. Org. Chem.*, **2009**, *74*, 298.

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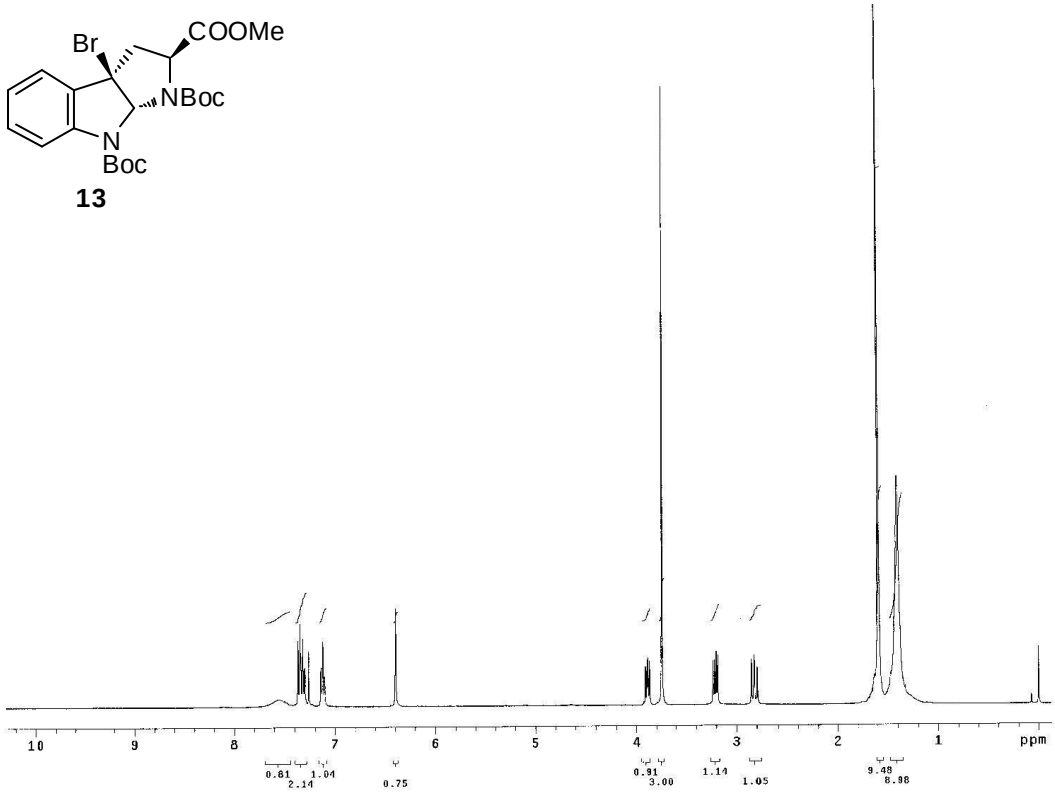
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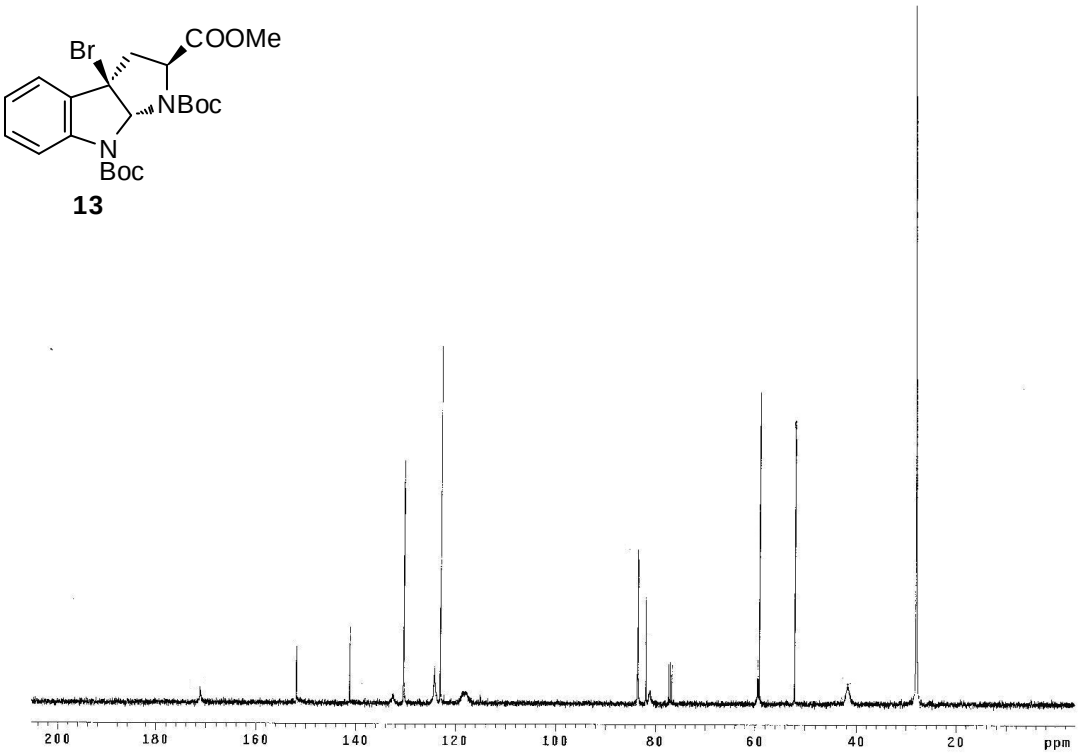
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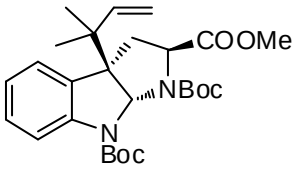
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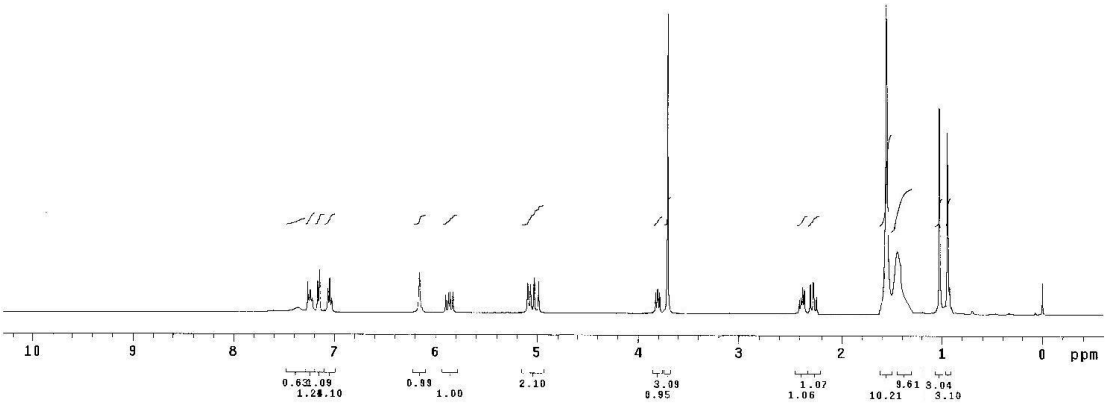
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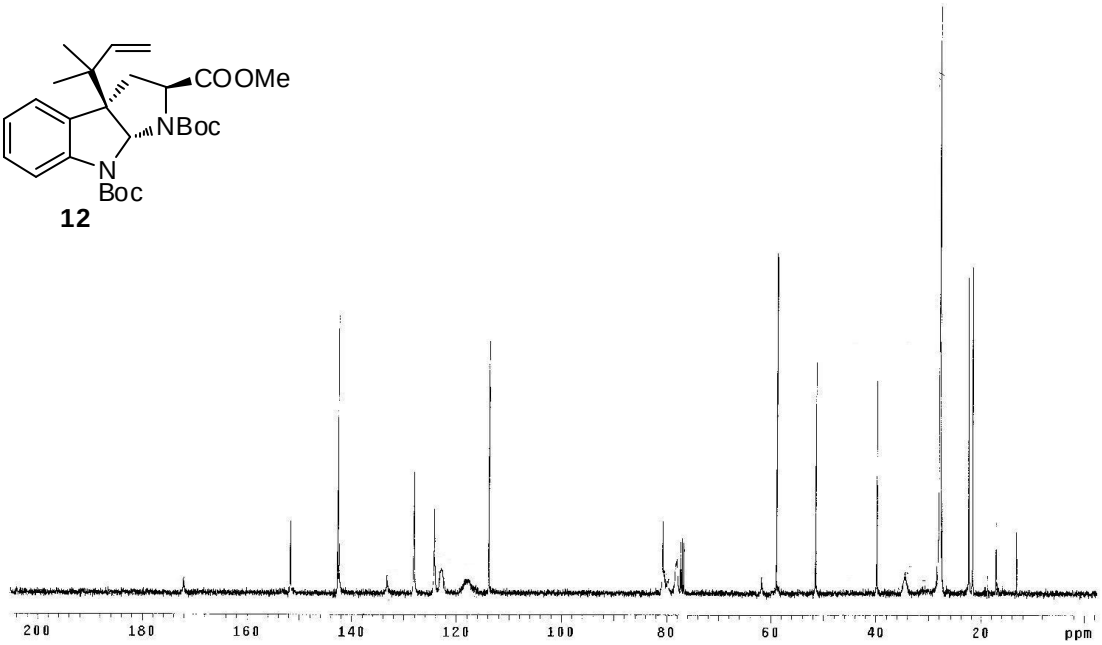
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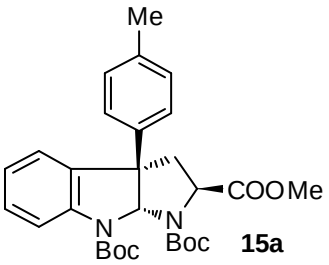
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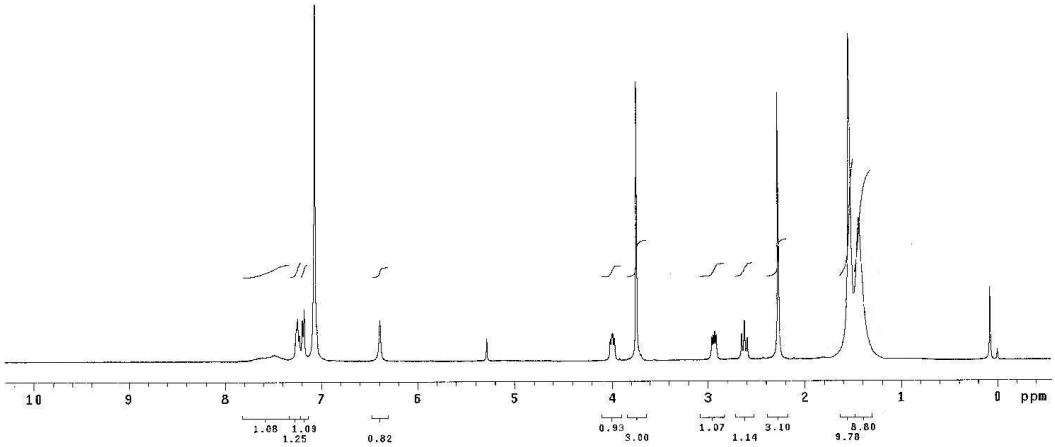
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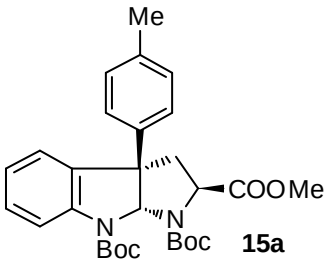
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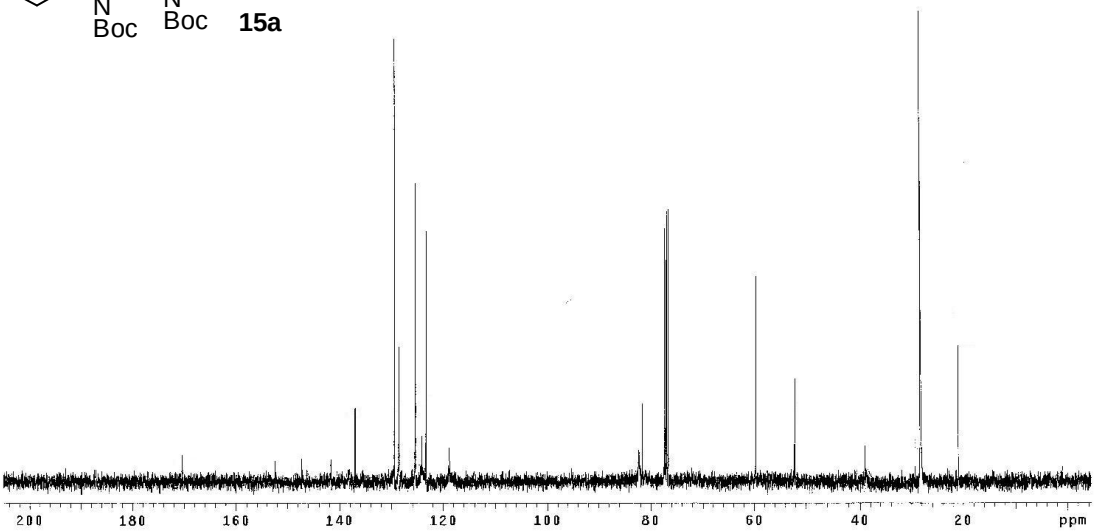
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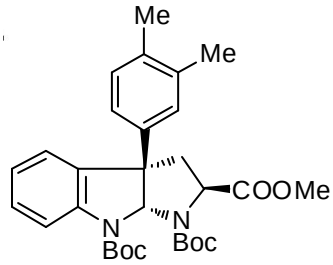
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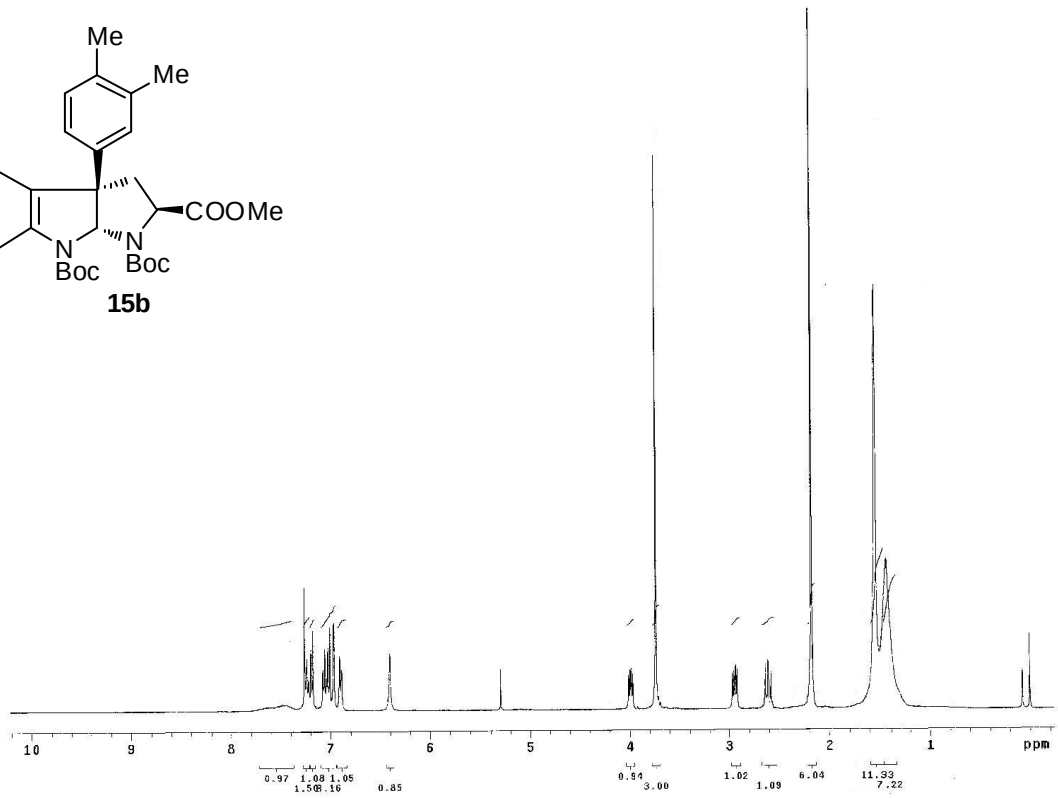
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5
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2
1
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1.50
8.16
0.85
0.94
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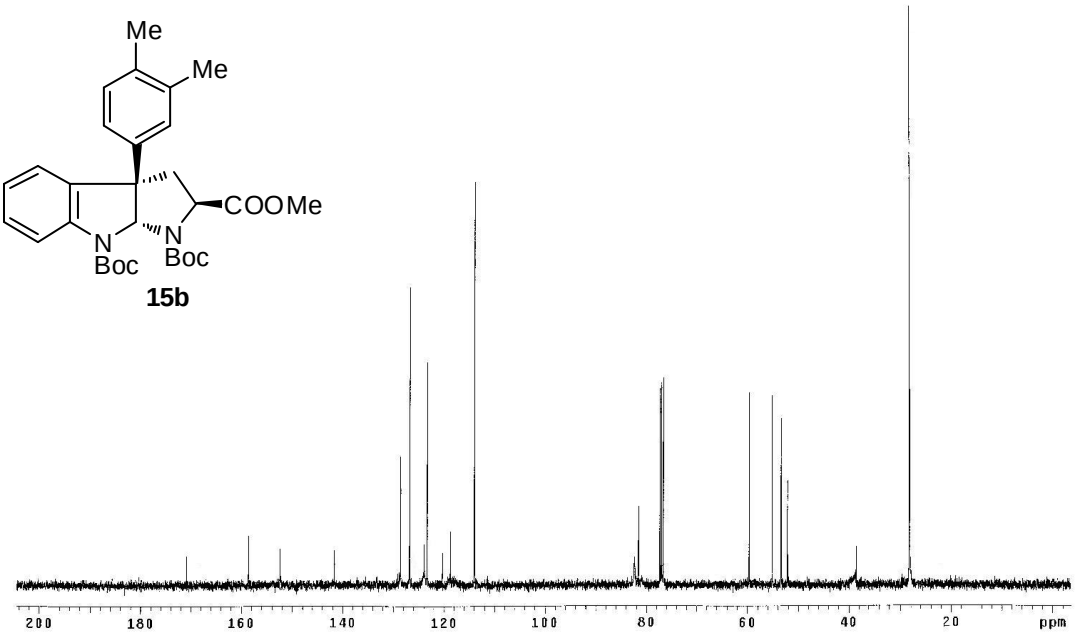
1.09
6.04
11.93
7.22

Me
Me
COOMe
N
Boc
N
Boc

15b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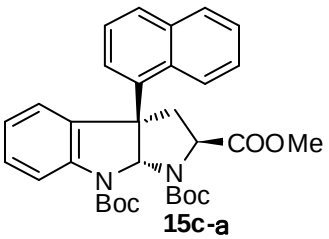
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Boc
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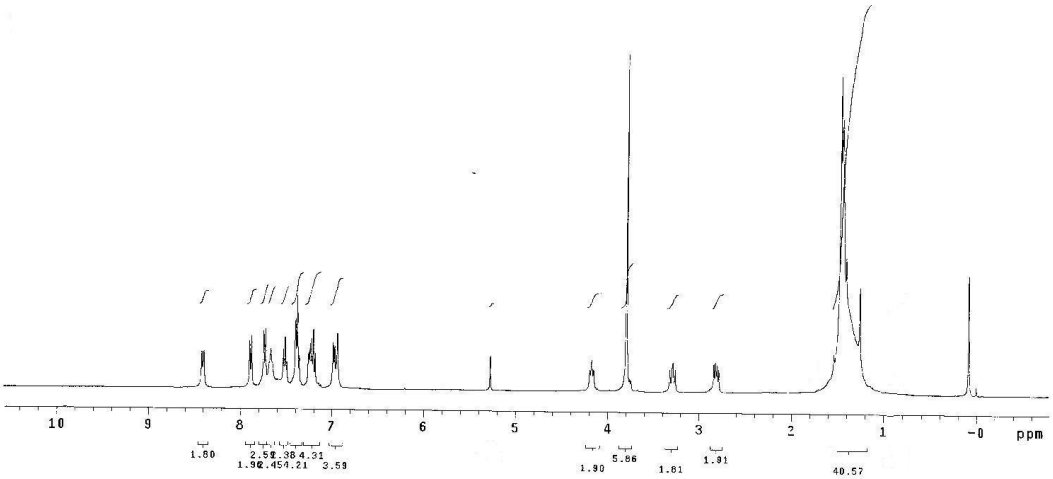
Boc
15c-a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1.91
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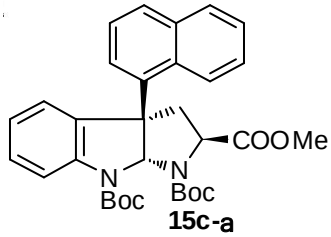
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N
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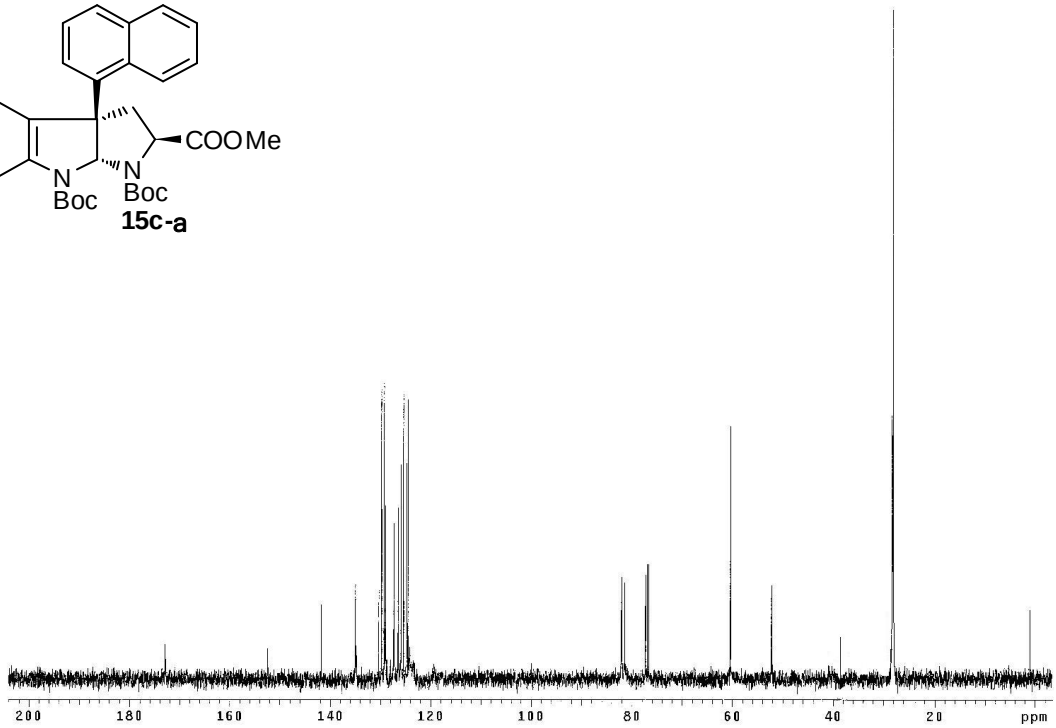
15c-a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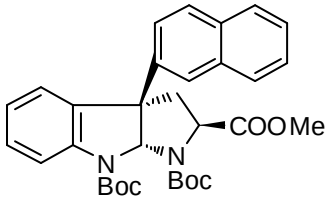
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Boc
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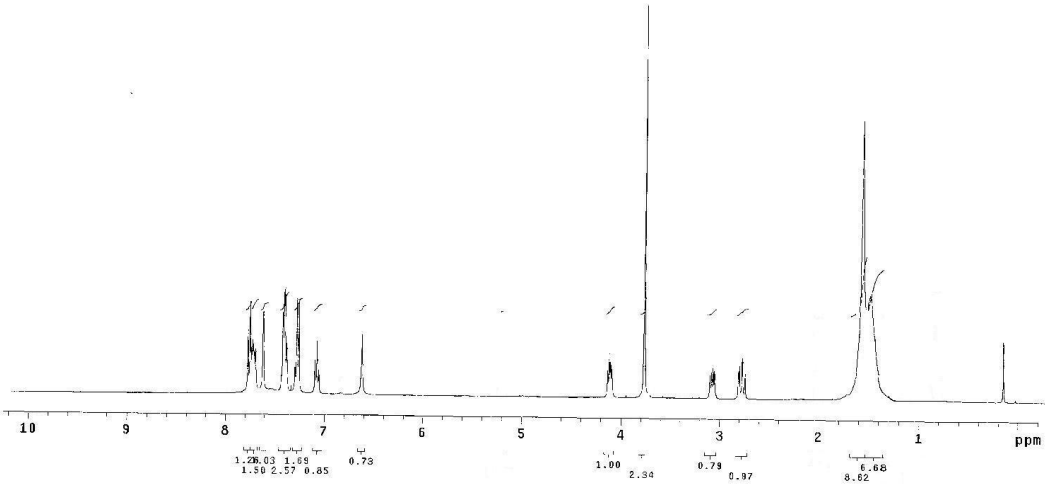
Boc

15c-ß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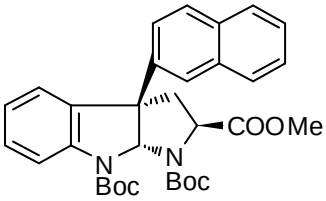
8.82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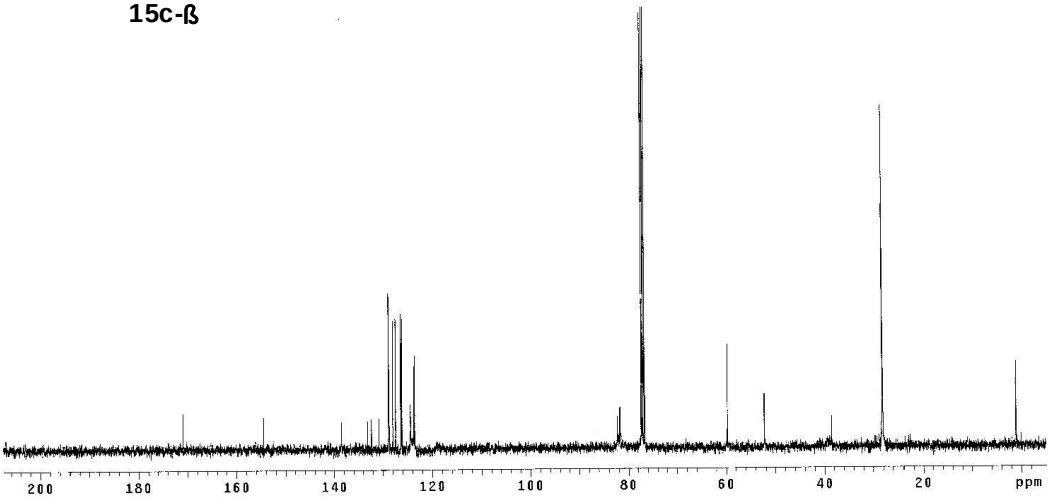
Boc
N
Boc

15c-ß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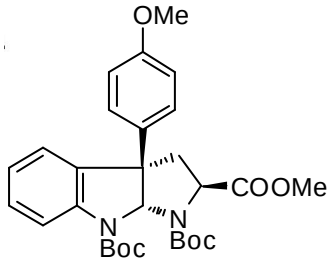
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COOMe
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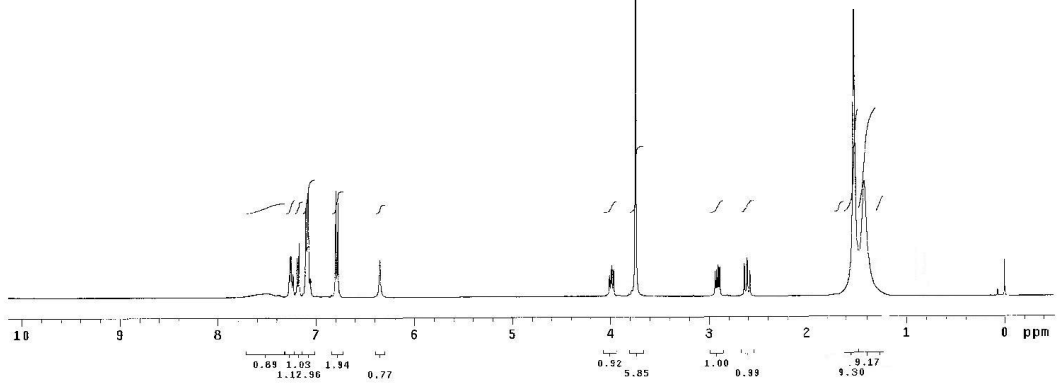
Boc
N
Boc

15d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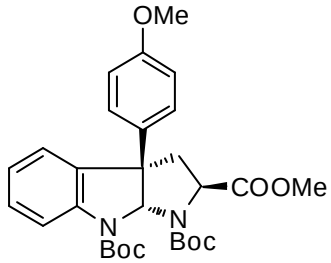
9.30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COOMe
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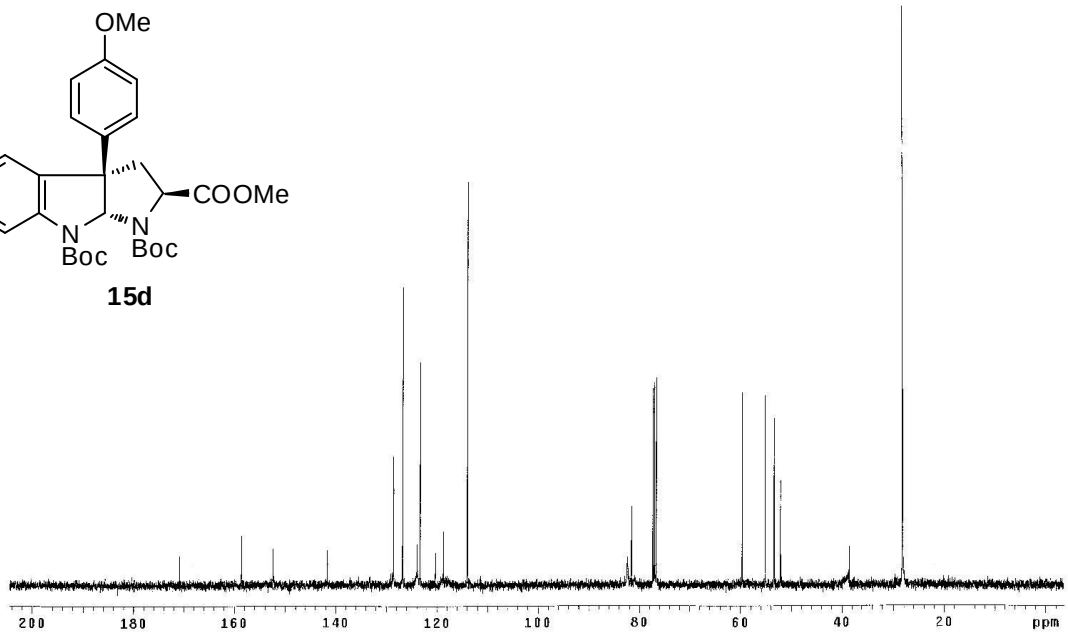
N
Boc

15d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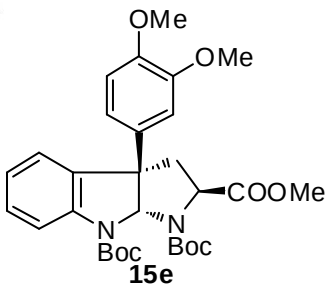
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OMe
COOMe
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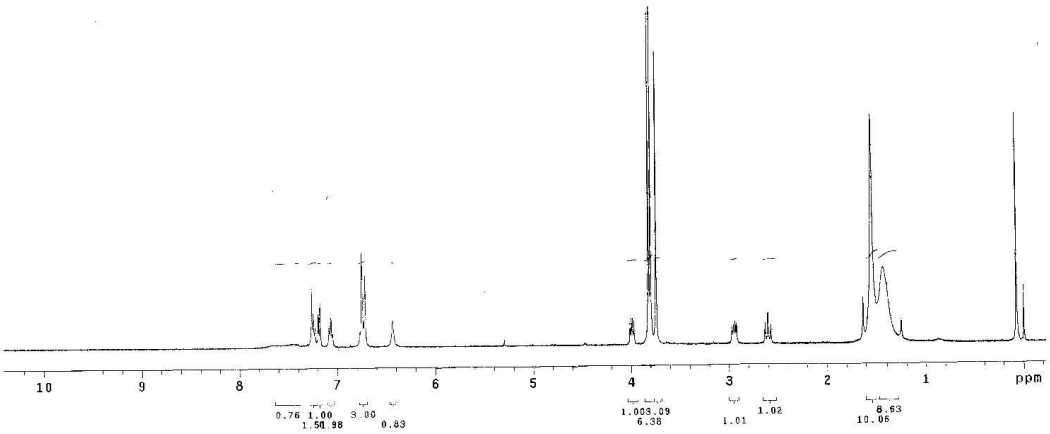
Boc
N
Boc

15e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2
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1.50 0.98 0.83
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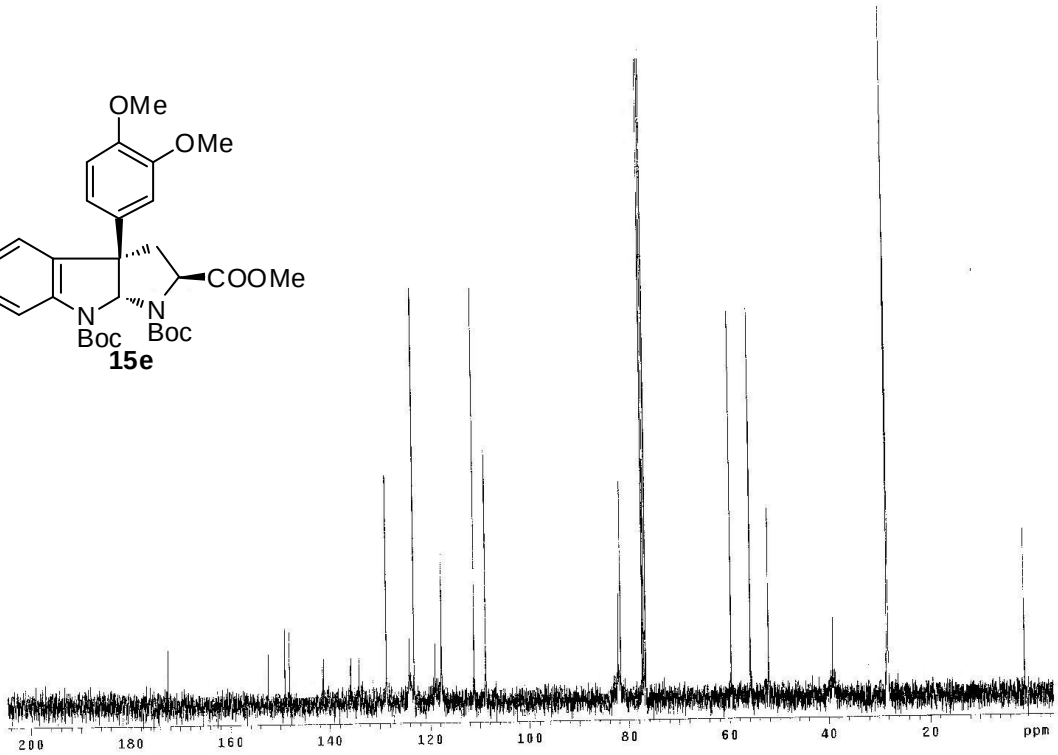
1.02
8.63
10.05

OMe
OMe
COOMe
N
Boc
N
Boc

15e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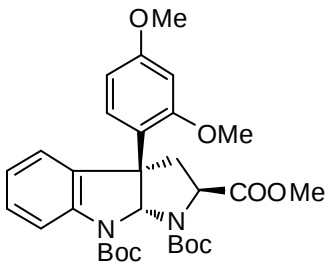
ppm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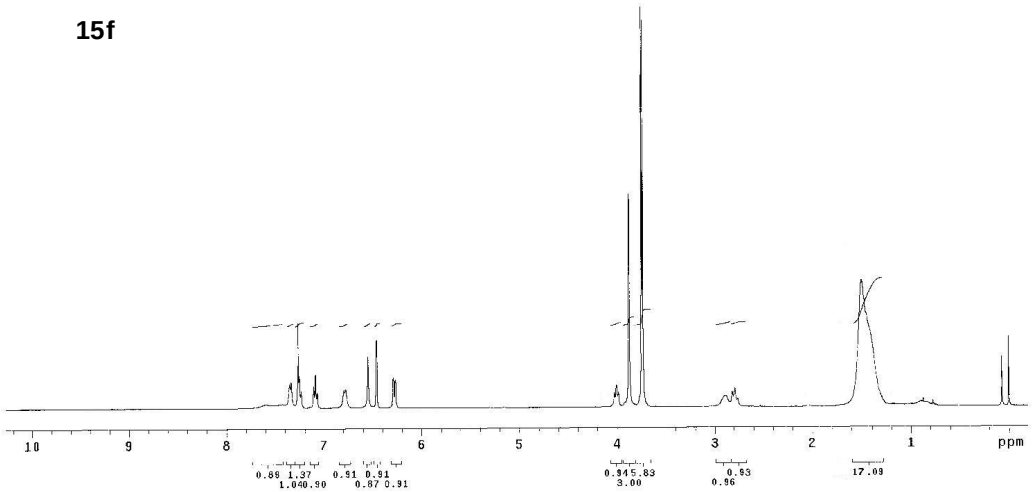
OMe
COOMe
N
Boc
N
Boc

15f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5
4
3
2
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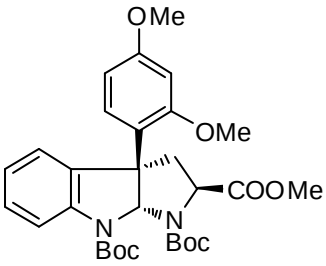
ppm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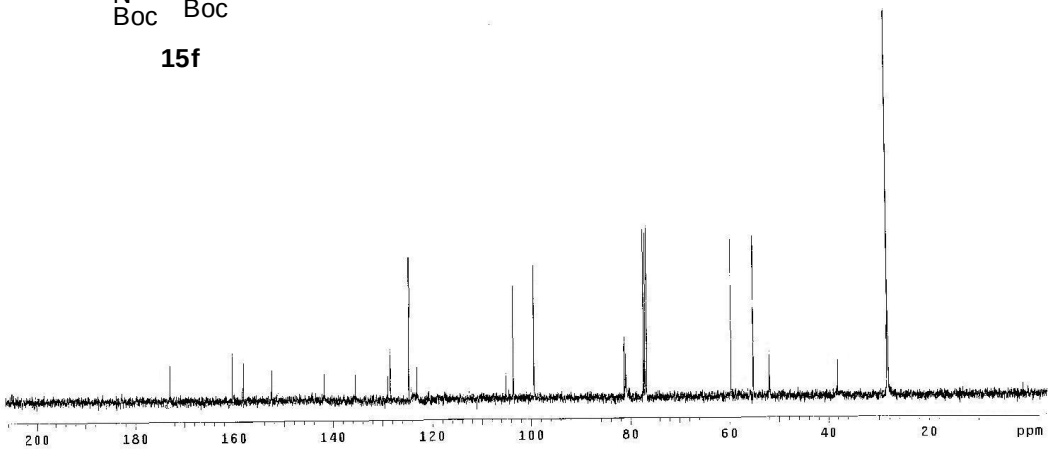
OMe
COOMe
N
Boc
N
Boc

15f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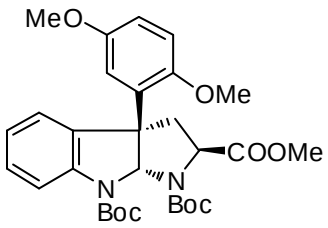
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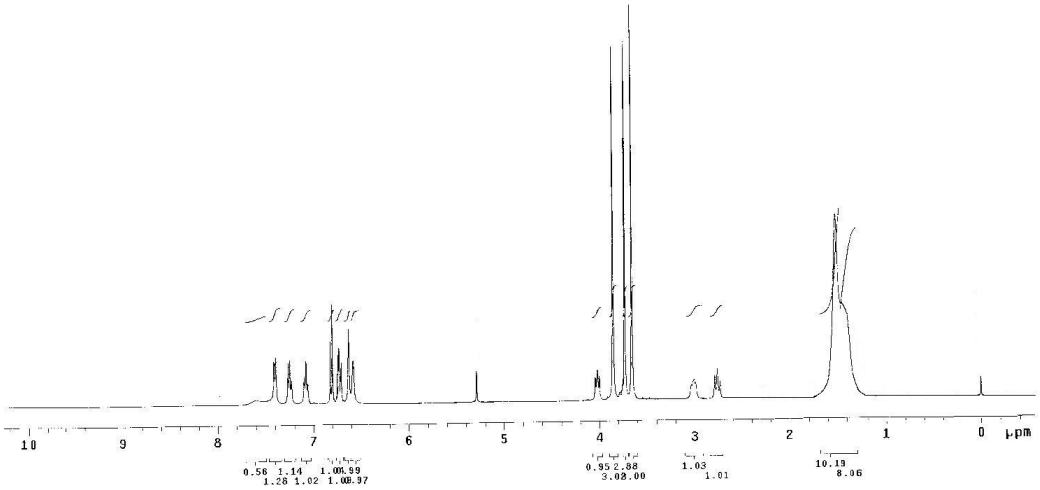
OMe
COOMe
N
Boc
N
Boc

15g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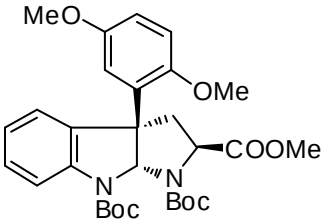
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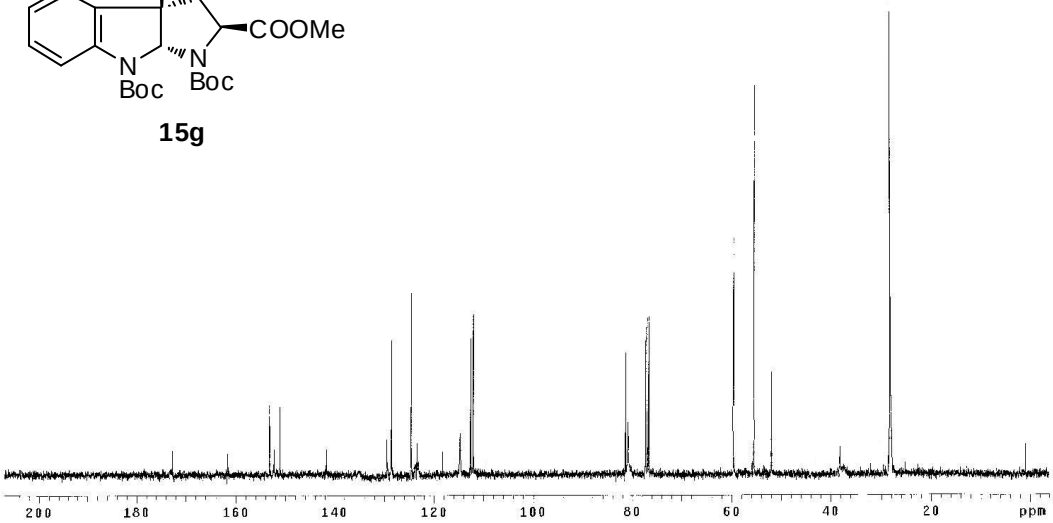
OMe
COOMe
N
Boc
N
Boc

15g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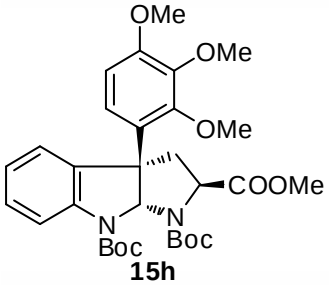
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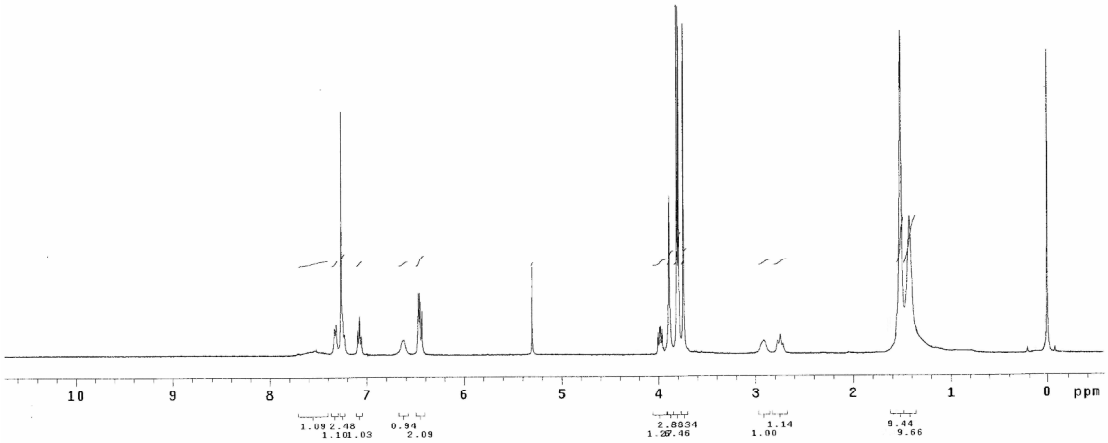
OMe
OMe
COOMe
N
Boc
N
Boc

15h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6
5
4
3
2
1
0
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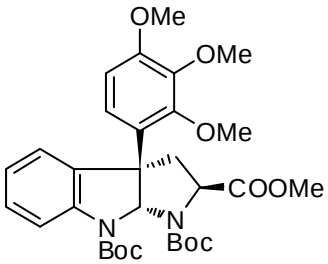
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OMe
OMe
COOMe
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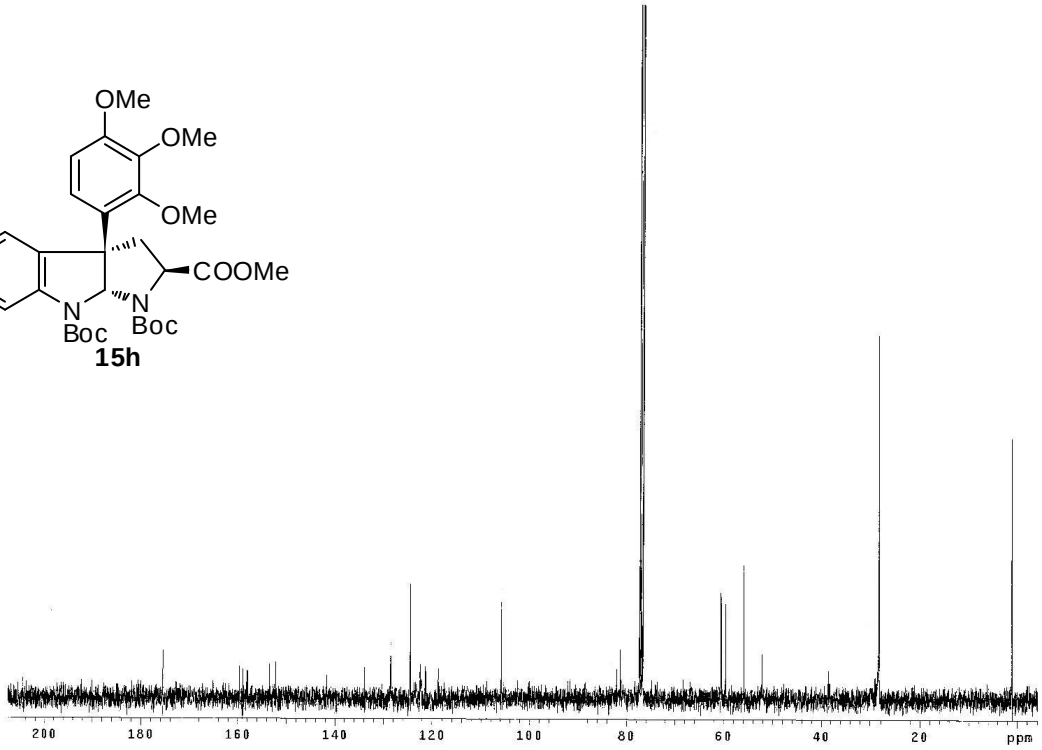
Boc
N
Boc

15h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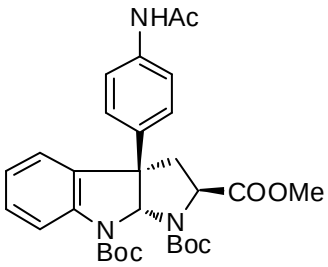
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COOMe
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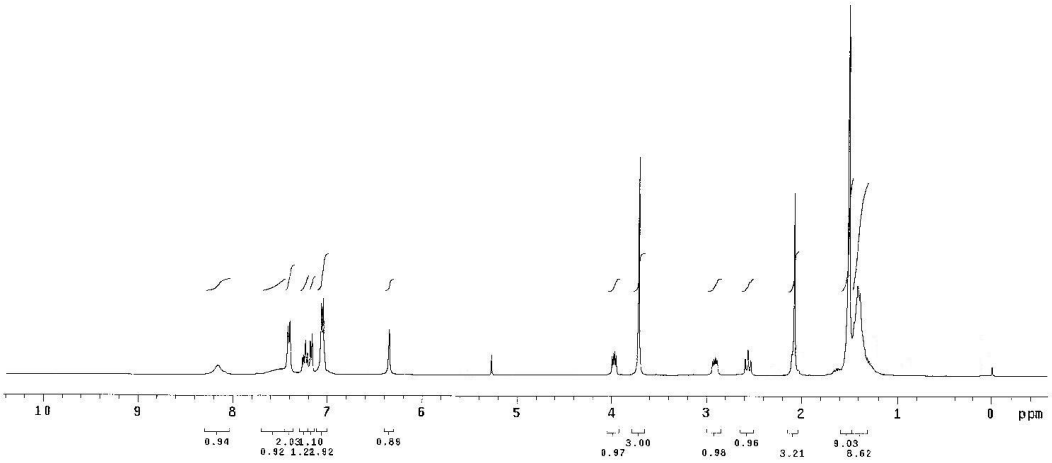
Boc
N
Boc

15i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6
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1.10
0.92 1.22
0.92
0.88
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9.03
8.62

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COOMe
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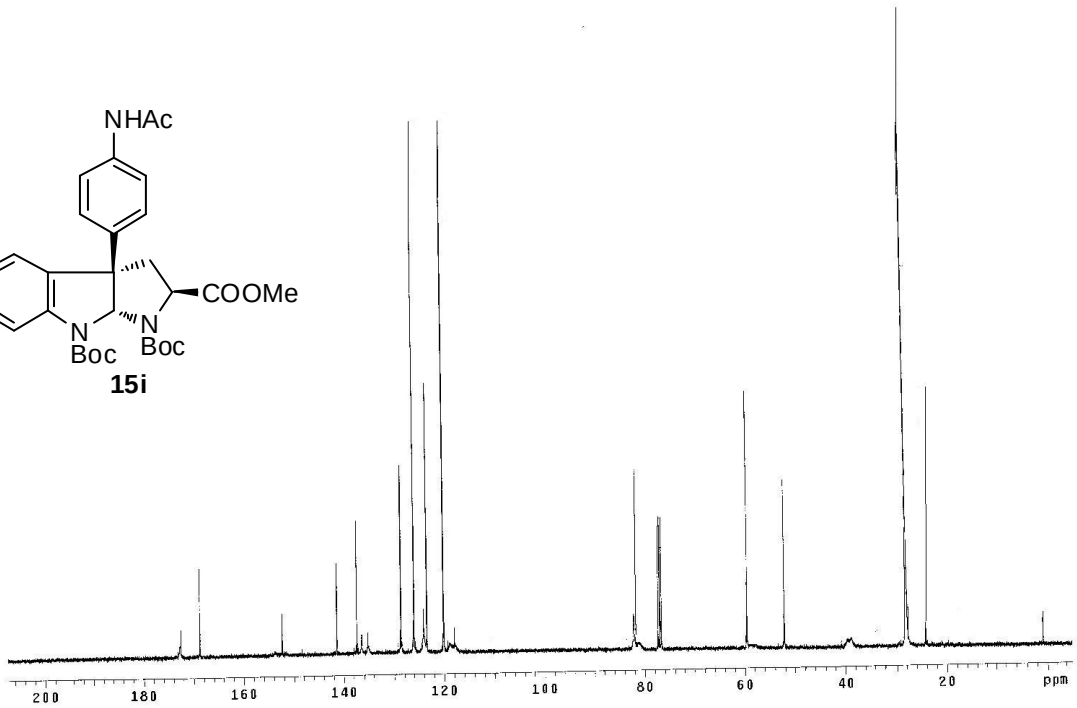
Boc
N
Boc

15i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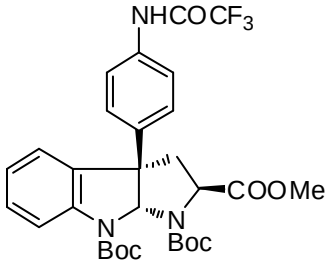
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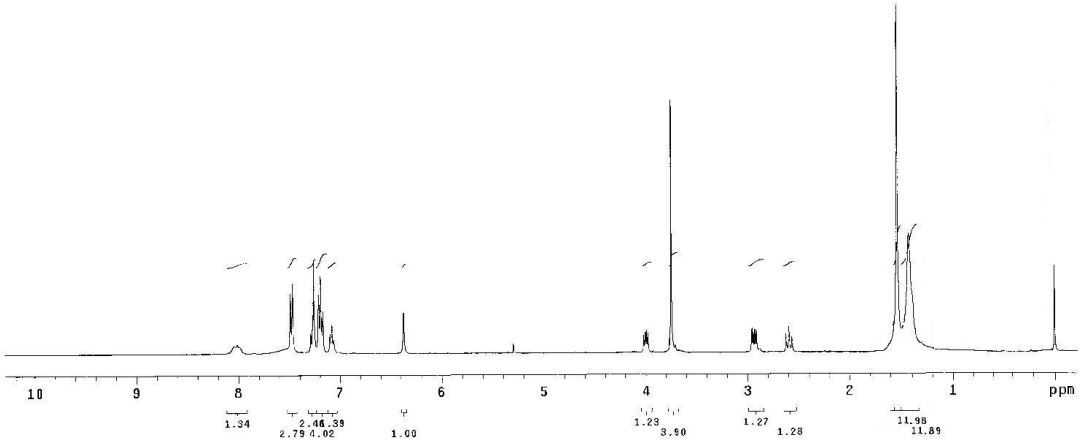
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1.00
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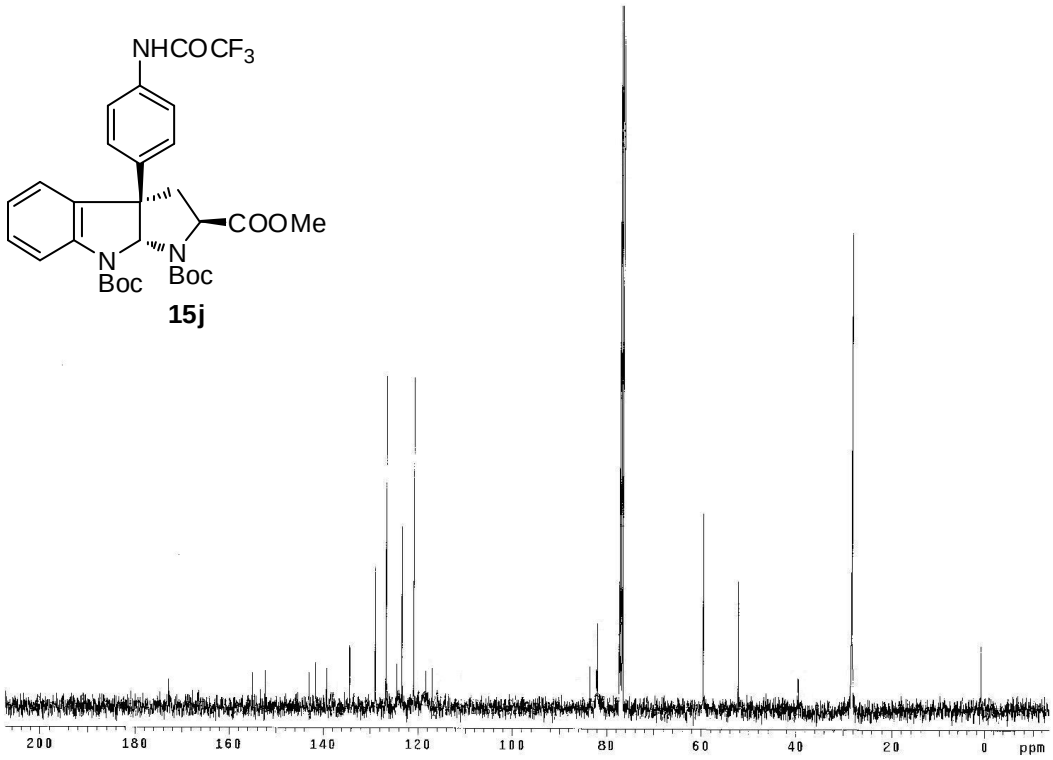
Boc

15j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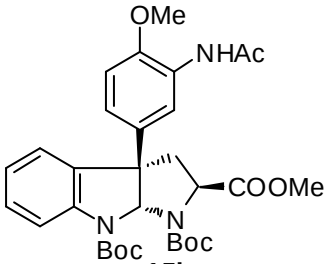
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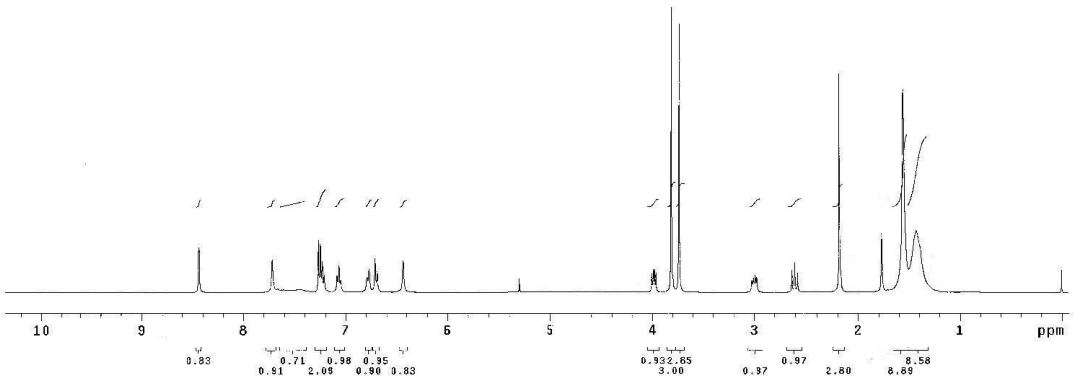
COOMe
N
Boc
N
Boc

15k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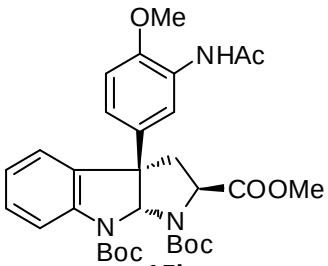
ppm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COOMe
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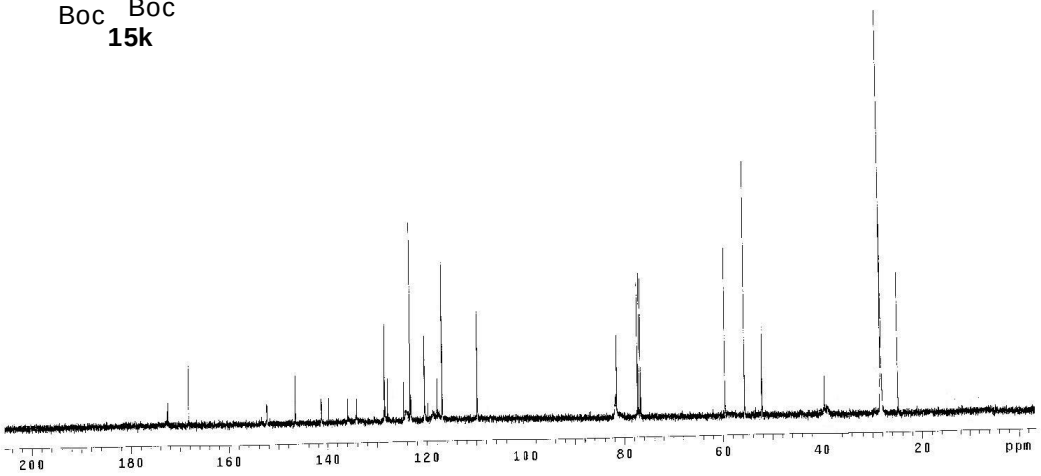
Boc
N
Boc

15k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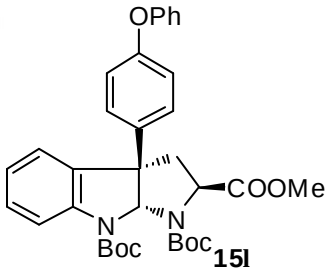
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COOMe
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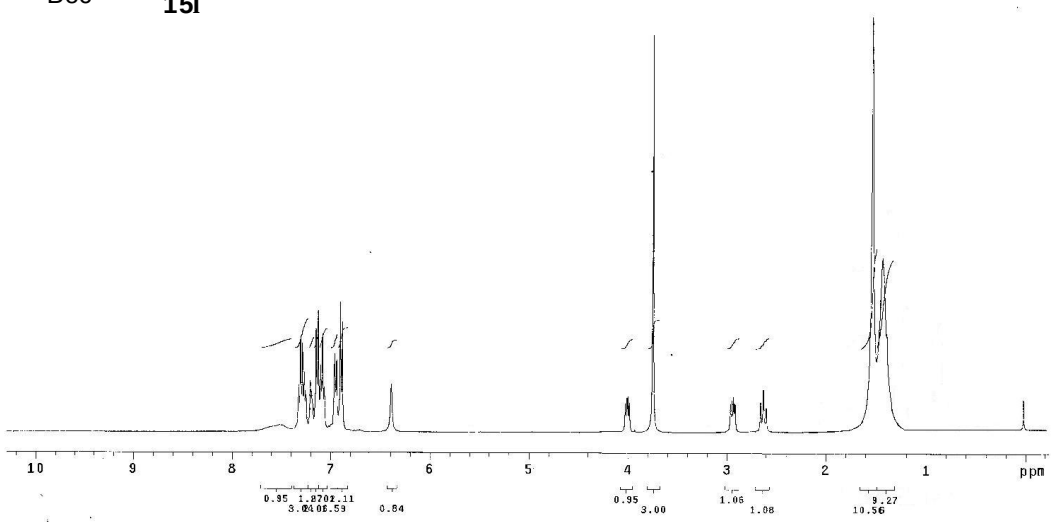
Boc
N
Boc

15l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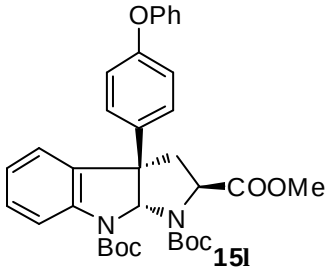
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Boc

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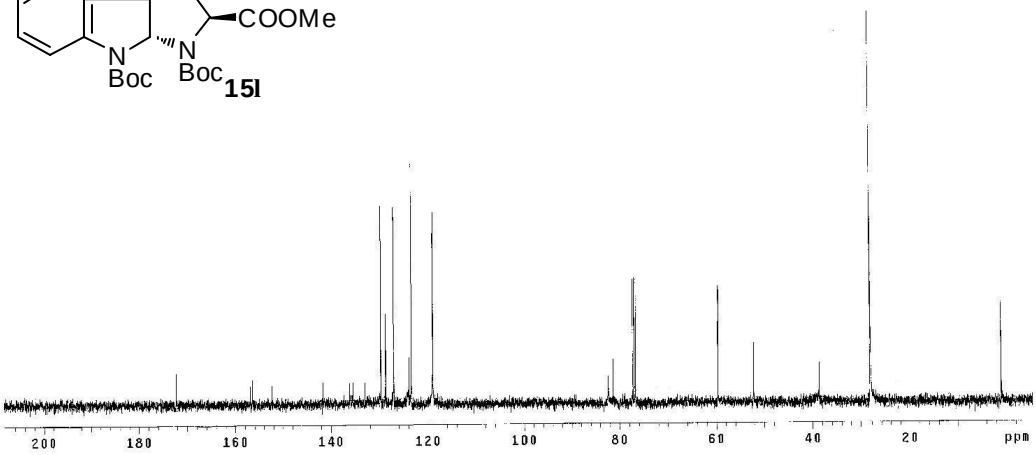
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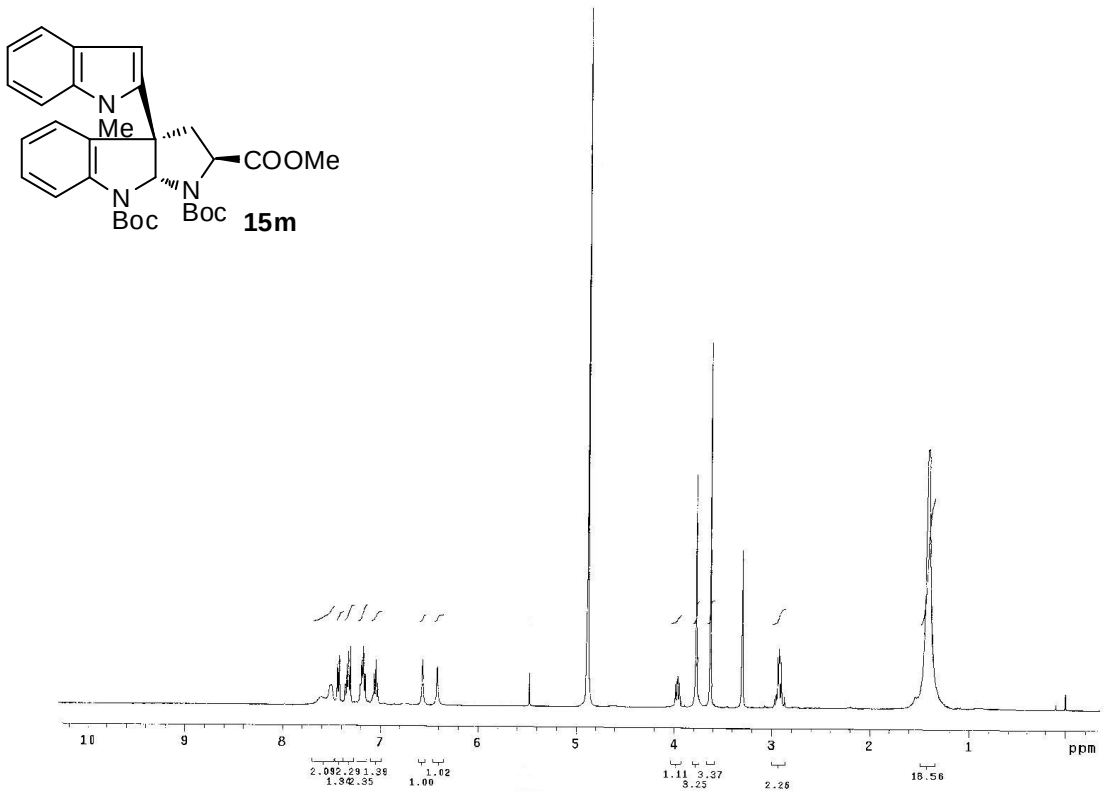
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Me
COOMe
N
Boc
N
Boc
15m
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5
4
3
2
1
ppm
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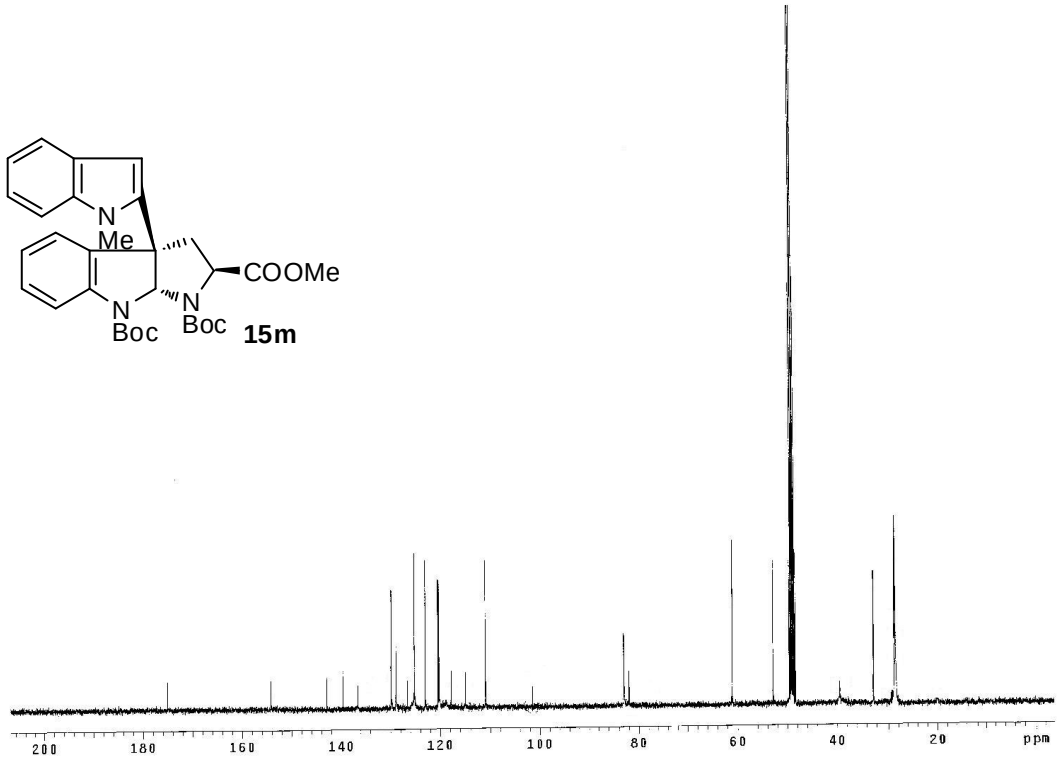
1.02
1.00
1.11
3.37
3.25
2.26
18.56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COOMe
N
Boc
N
Boc
15m
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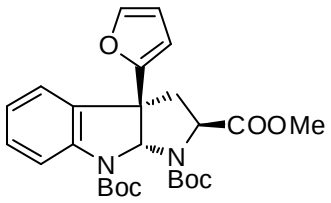
20
ppm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COOMe
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Boc
N
Boc

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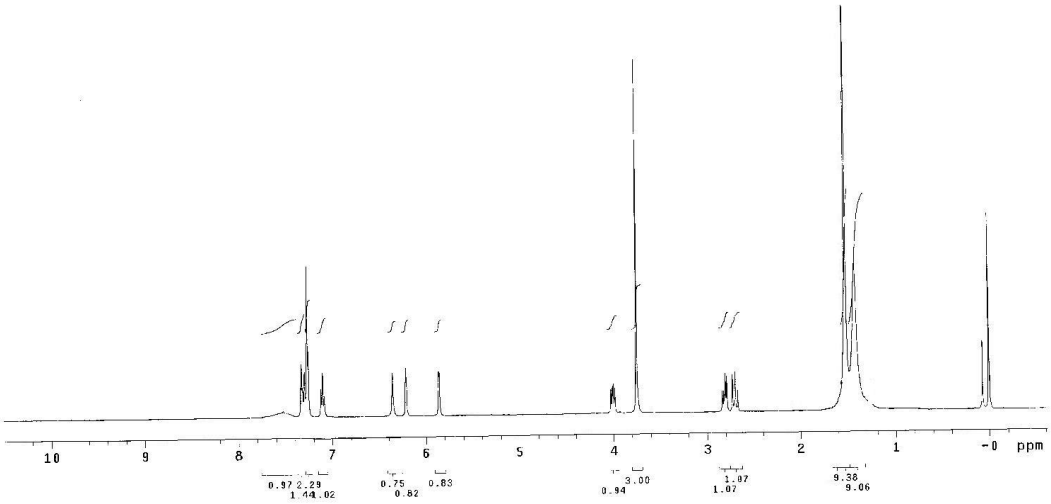
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-0
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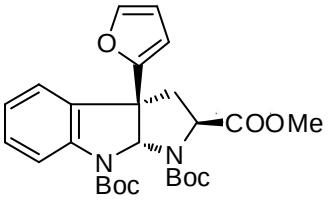
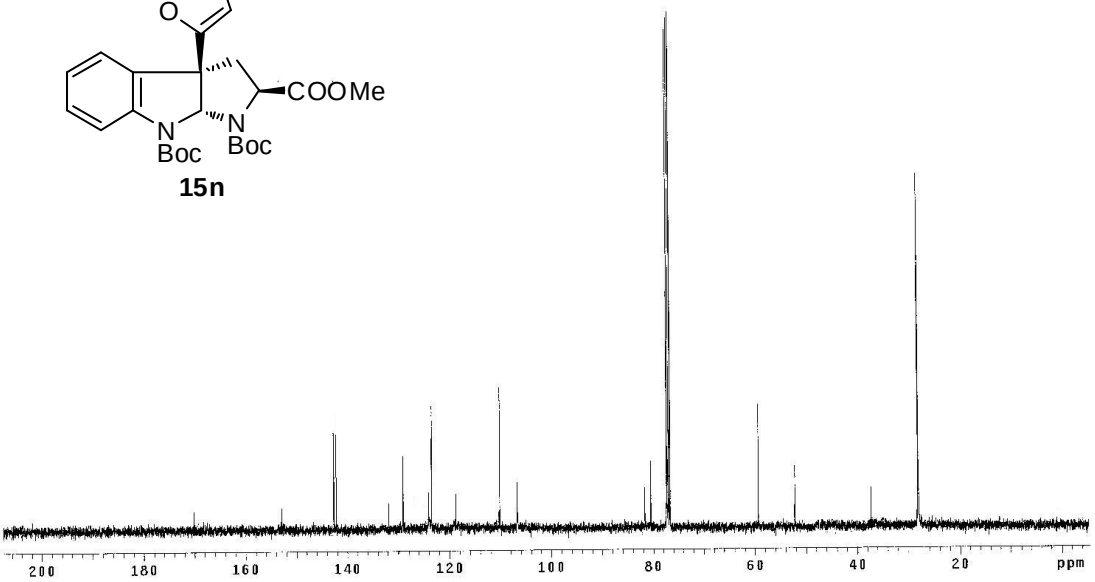

O
COOMe
N
Boc
N
Boc

15n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60
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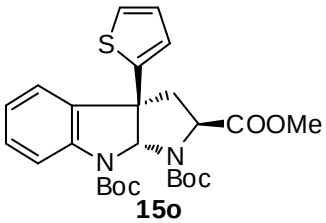
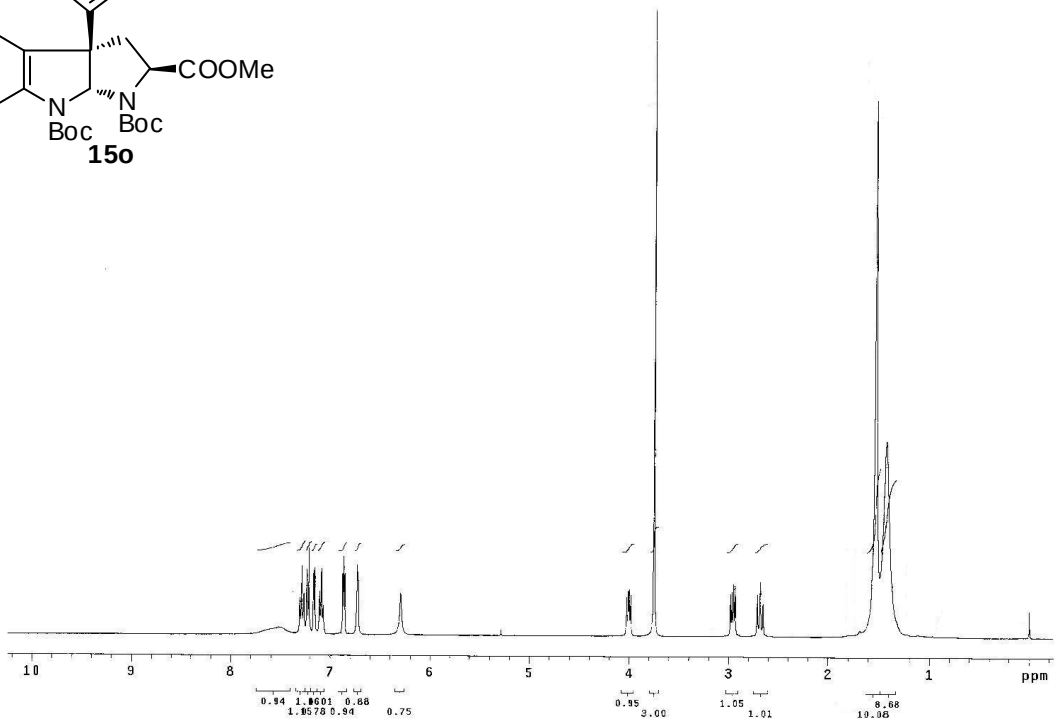

S
COOMe
N
Boc
N
Boc

15o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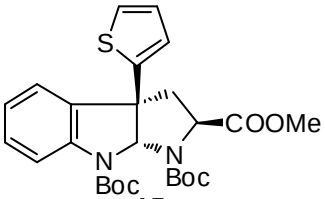
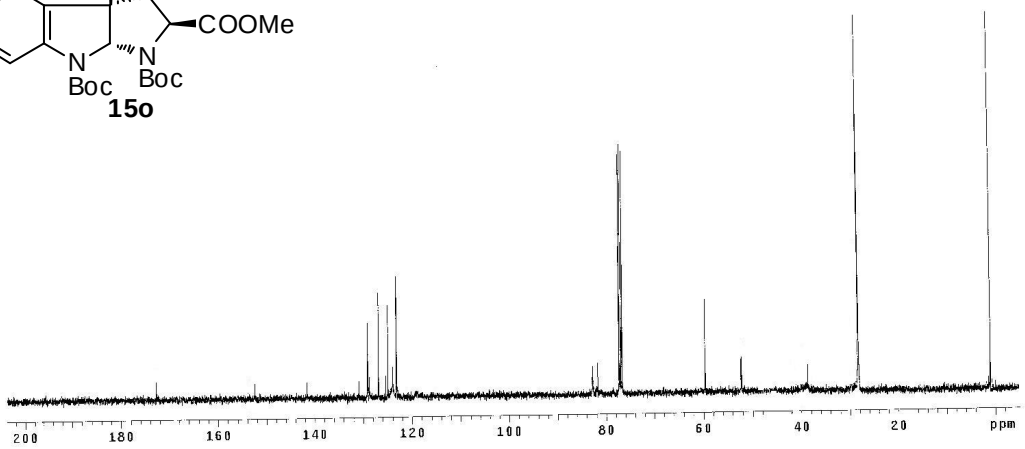
ppm


S
COOMe
N
Boc
N
Boc

15o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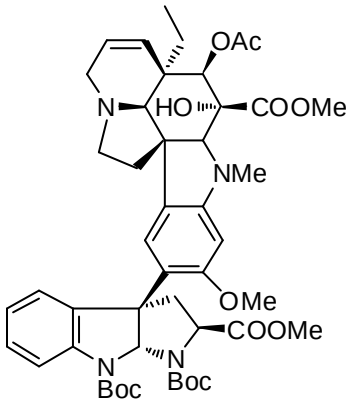
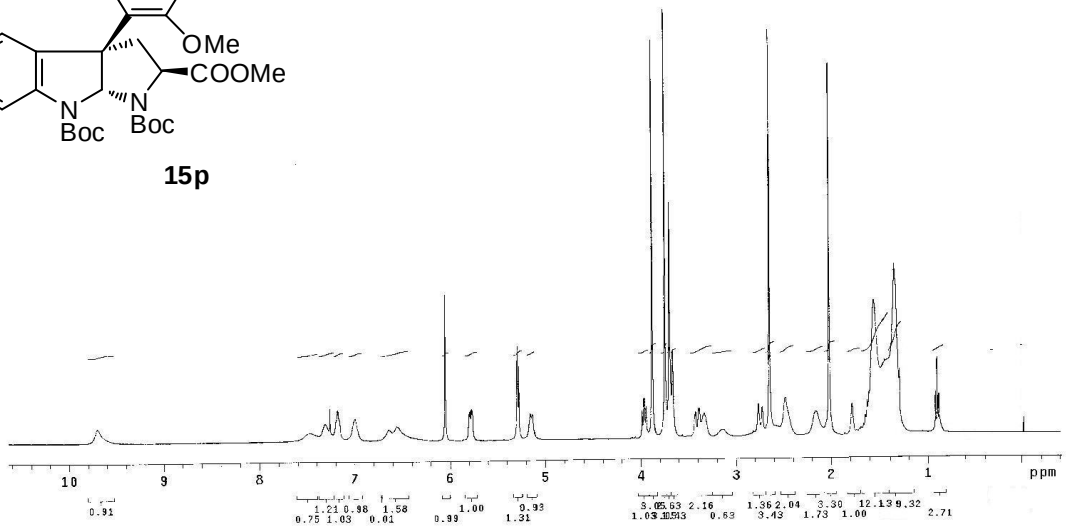

OAc
N
HO
COOMe
NMe
OMe
COOMe
N
Boc
N
Boc

15p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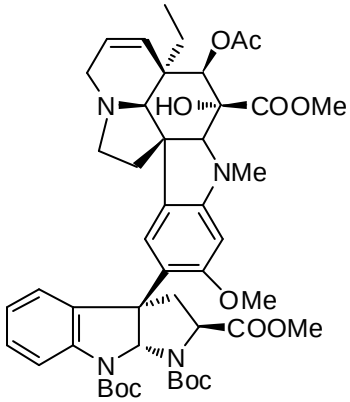
6
5
4
3
2
1
ppm


OAc
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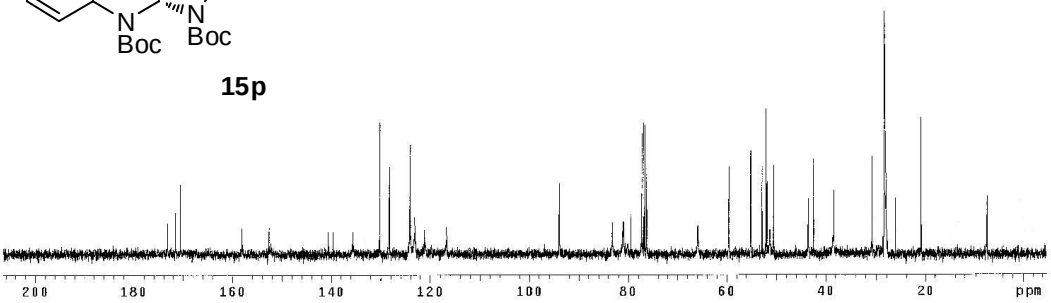
HO
COOMe
NMe
OMe
COOMe
N
Boc
N
Boc

15p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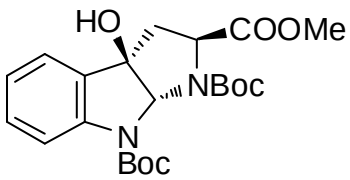
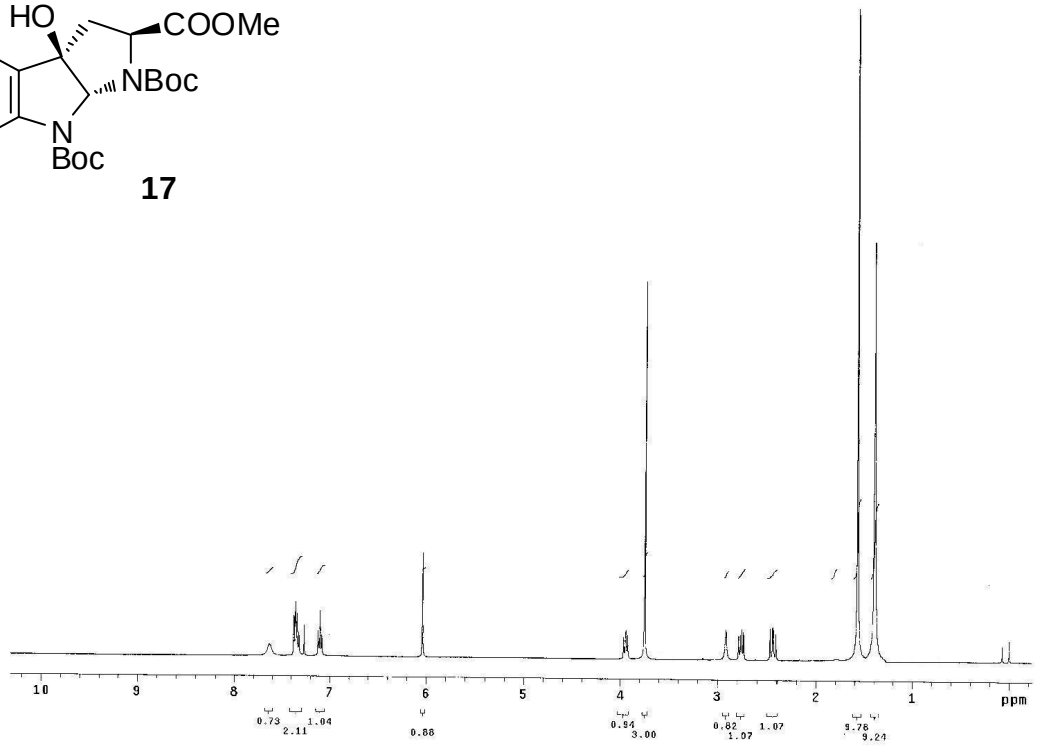
20
ppm


HO
COOMe
NBoc
N
Boc

17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6
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4
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2
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ppm
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0.88
0.94
3.00
0.82
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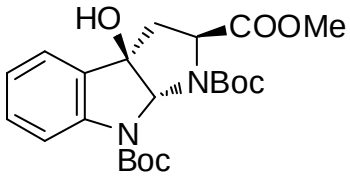
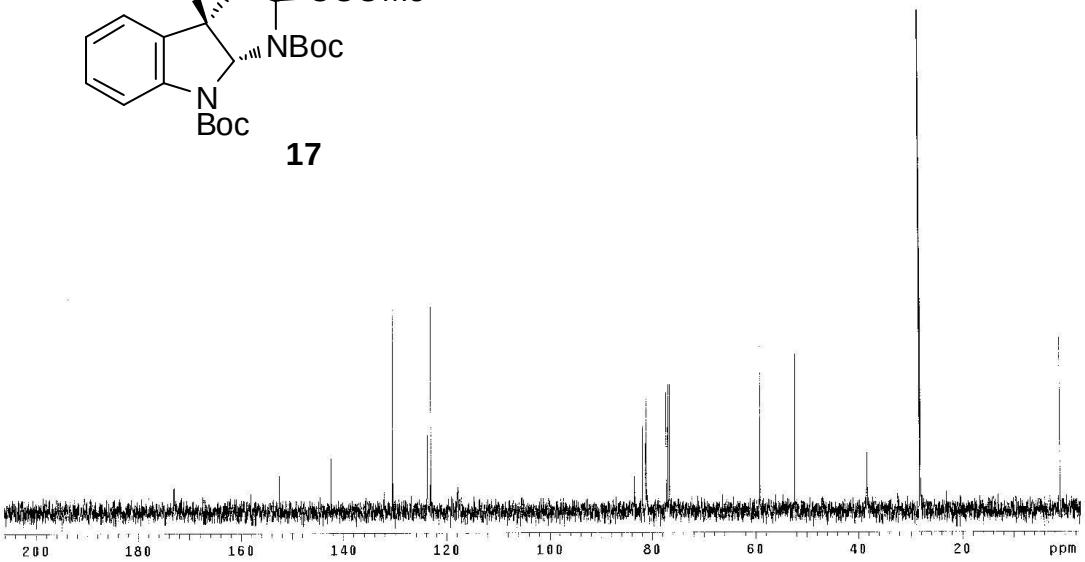
1.07
9.76
9.24


HO
COOMe
NBoc
N
Boc

17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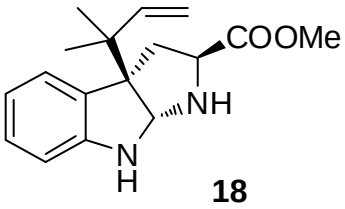
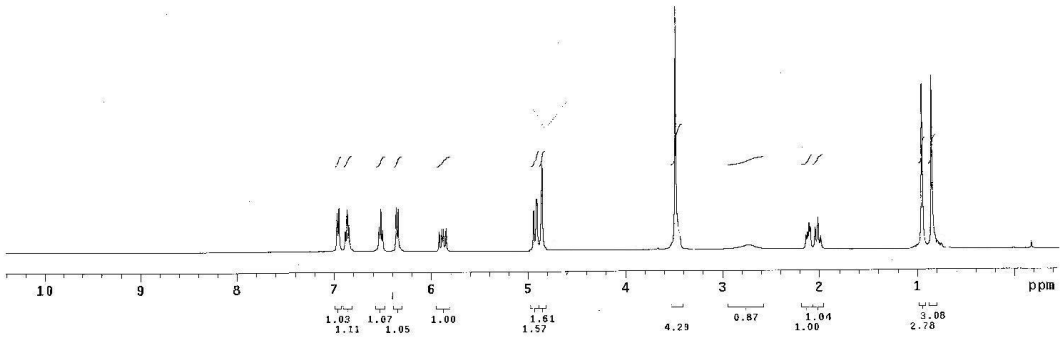
120
100
80
60
40
20
ppm


COOMe
NH
N
H

18


10
9
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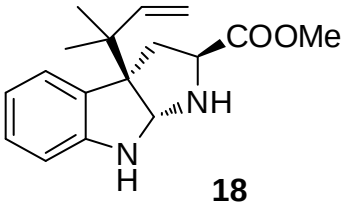
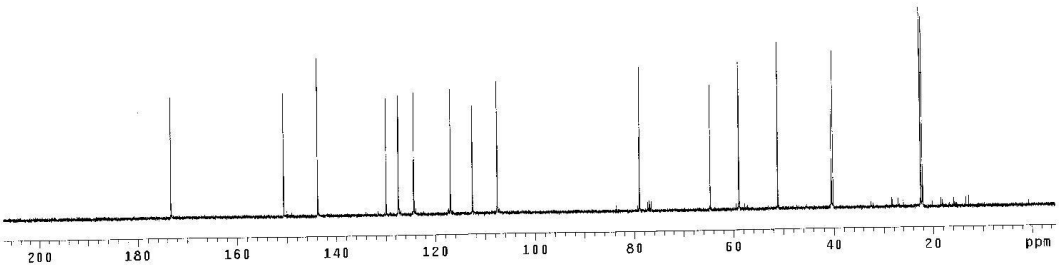
7
6
5
4
3
2
1
ppm
1.03
1.11
1.07
1.05
1.00
1.61
1.57
4.29
0.87
1.04
1.00
3.08
2.78


COOMe
NH
N
H

18


200
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100
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60
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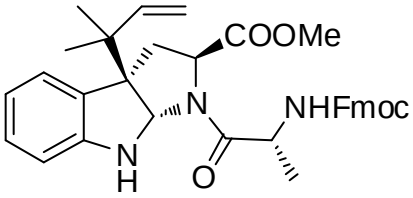
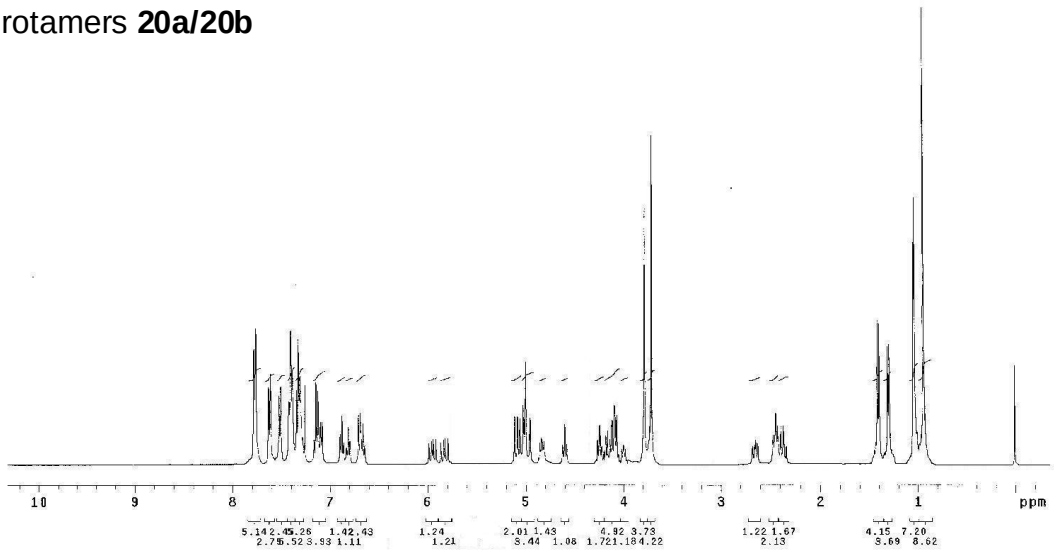
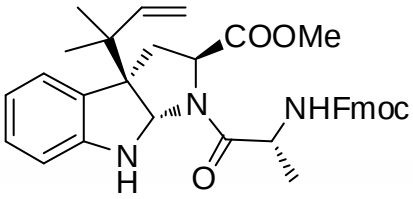
20
ppm

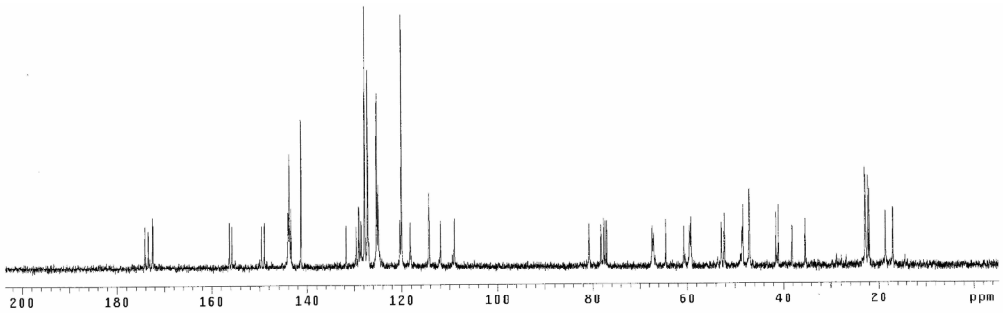


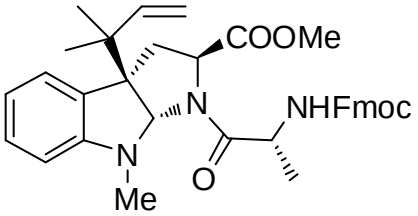
rotamers **20a/20b**



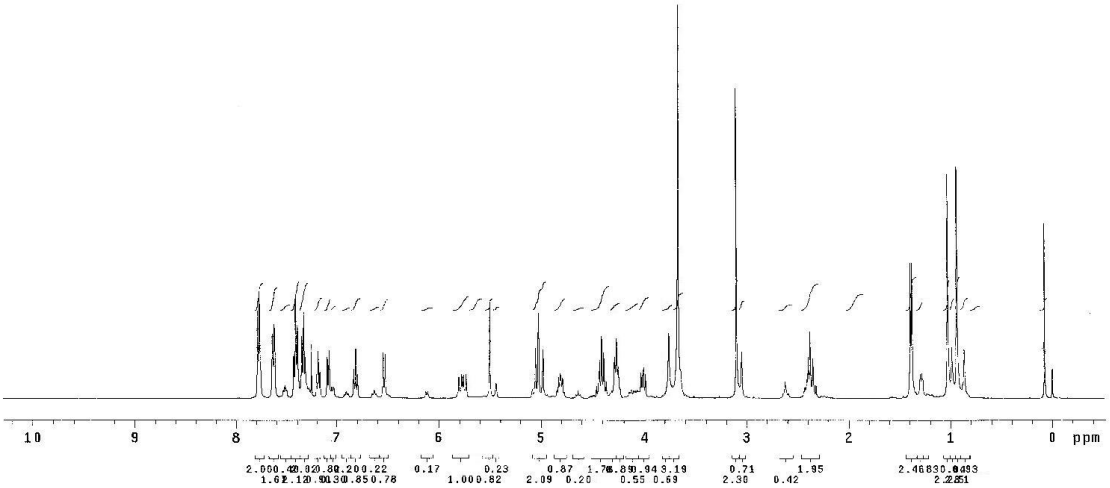


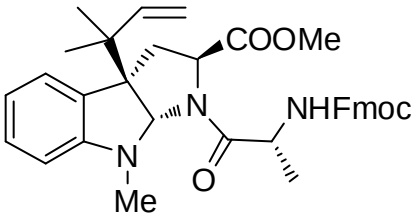
rotamers **20a/20b**



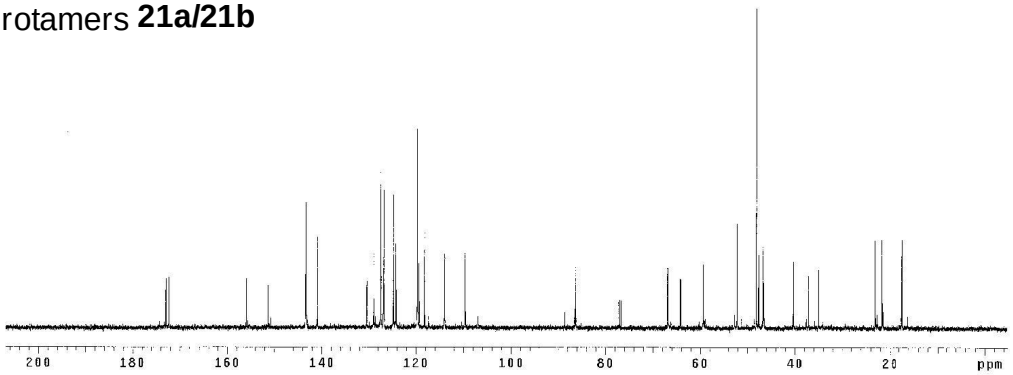


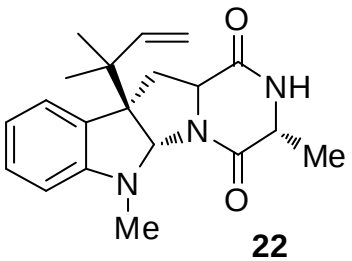
rotamers **21a/21b**



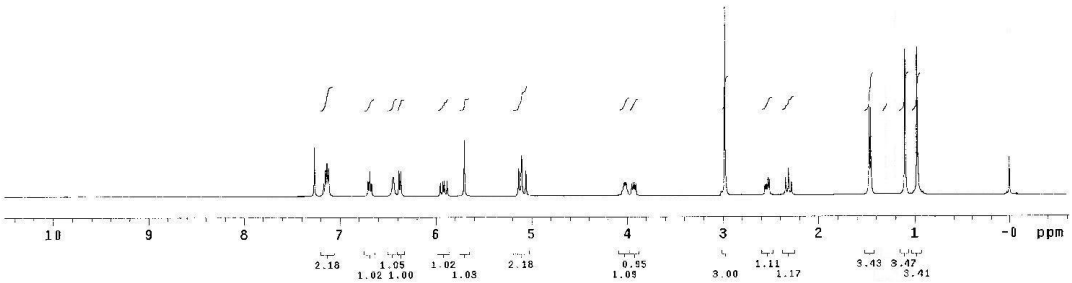


rotamers **21a/21b**




O
NH
N
Me
N
Me
O

22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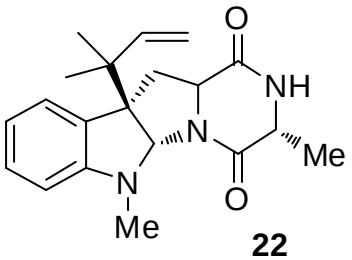
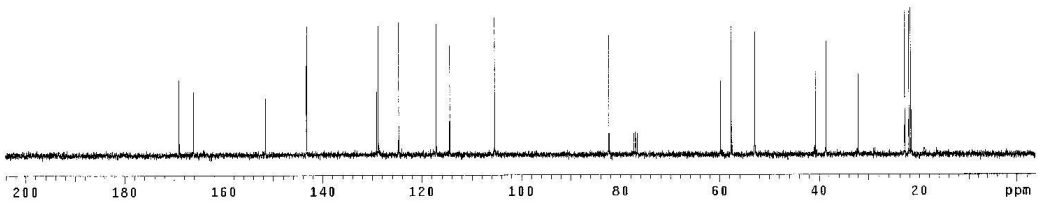
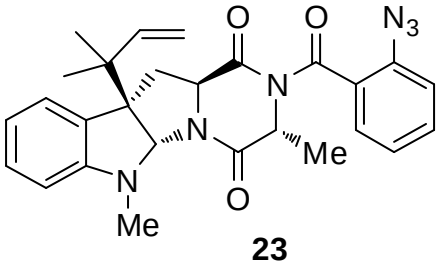
9
8
7
6
5
4
3
2
1
-0
ppm
2.18
1.05
1.02 1.00
1.02
1.03
2.18
0.95
1.09
3.00
1.11
1.17
3.43
3.47
3.41

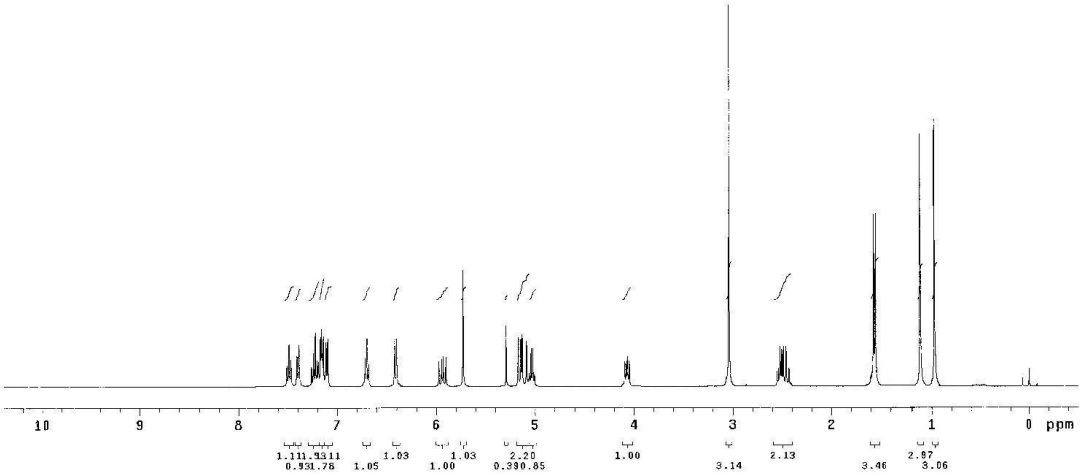

O
NH
N
Me
N
Me
O

22


200
180
160
140
120
100
80
60
40
20
ppm


O
O
N3
N
N
Me
O
N
Me

23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9
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6
5
4
3
2
1
0 ppm
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0.931.78
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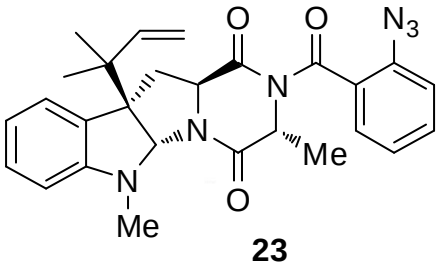
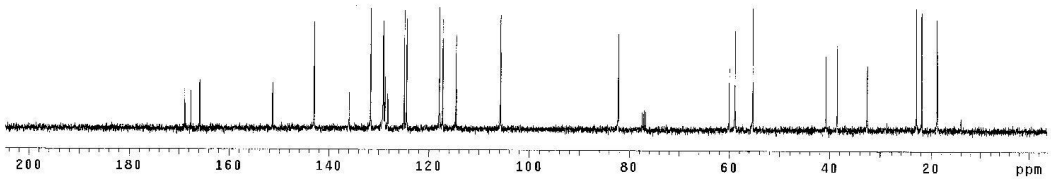
1.03
1.00
1.03
2.20
0.390.85
1.00
3.14
2.13
3.46
2.87
3.06


O
O
N3
N
N
Me
O
N
Me

23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100
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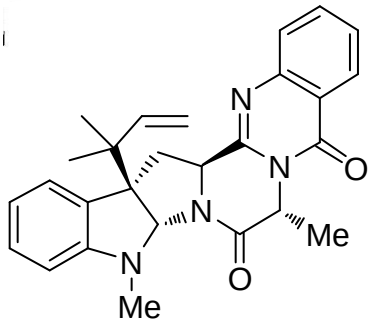
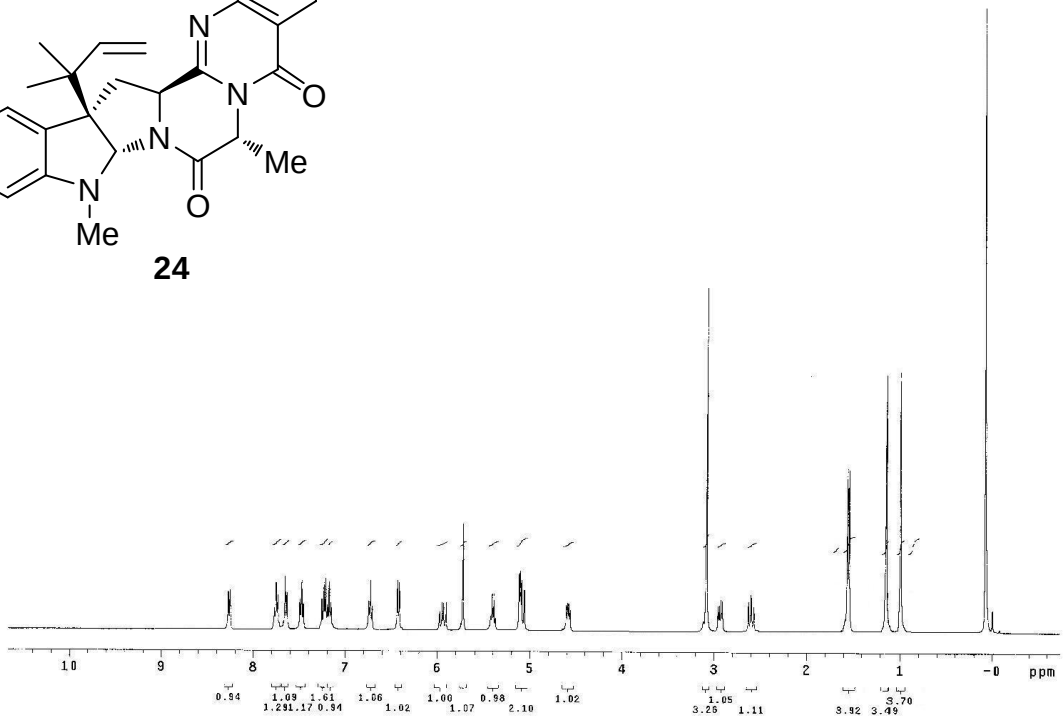
60
40
20
ppm


N
N
O
N
Me
N
O
Me

24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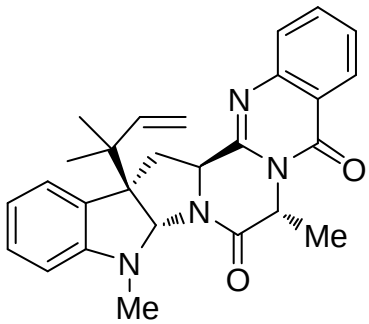
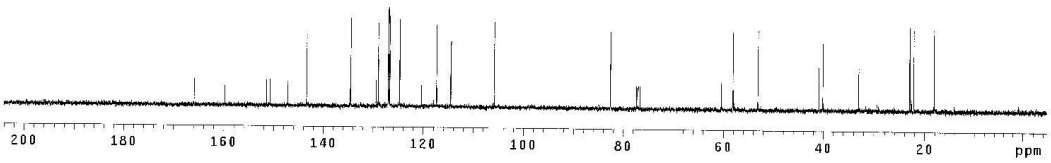
7
6
5
4
3
2
1
-0
ppm
0.94
1.09 1.61
1.29 1.17 0.94
1.06
1.02
1.00
1.07
0.98
2.10
1.02
1.05
3.26
1.11
3.92
3.70
3.49


N
N
O
N
Me
N
O
Me

24


200
180
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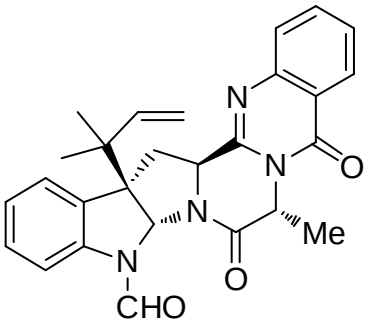
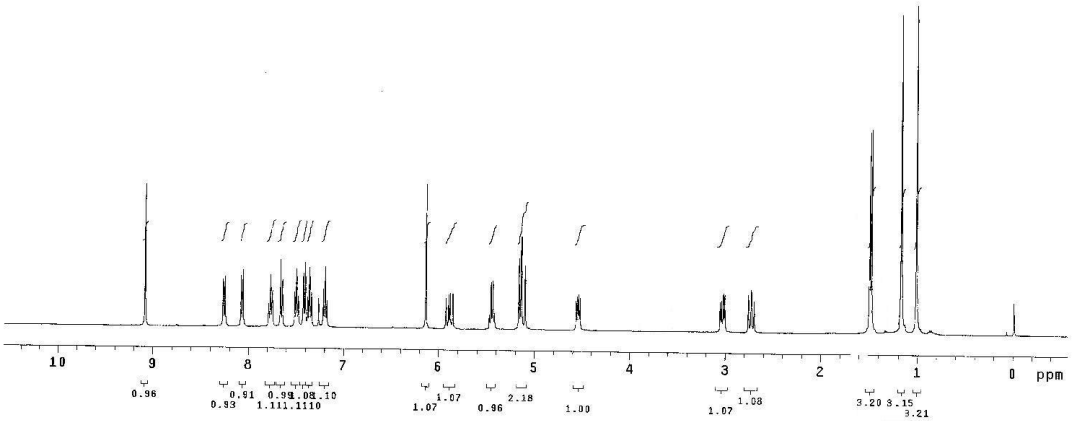
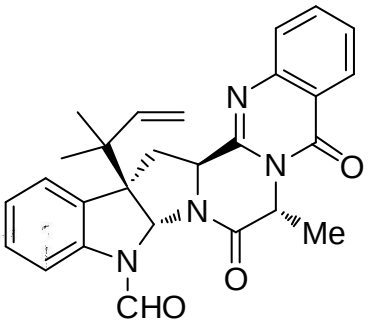
140
120
100
80
60
40
20
ppm

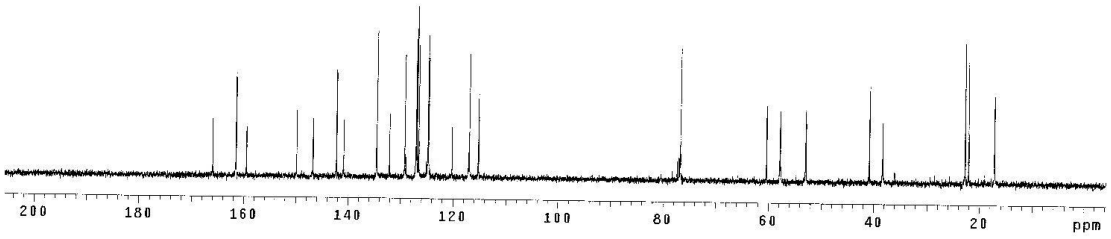


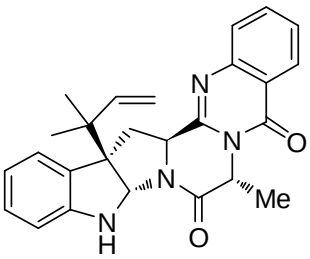
(-)-formylardeemin **3**



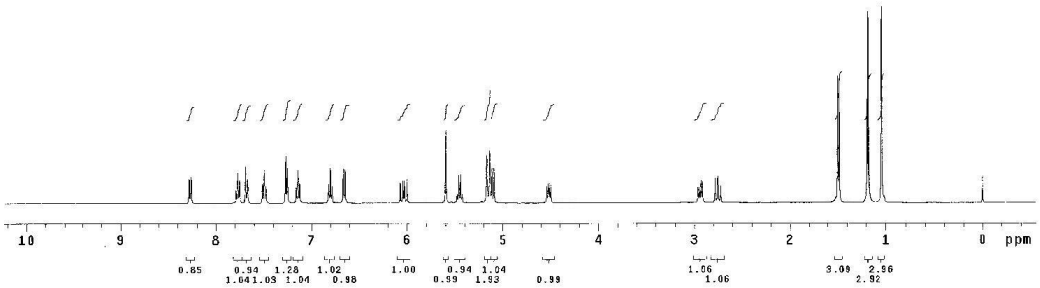


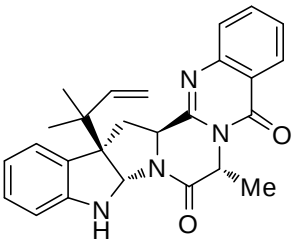
(-)-formylardeemin **3**



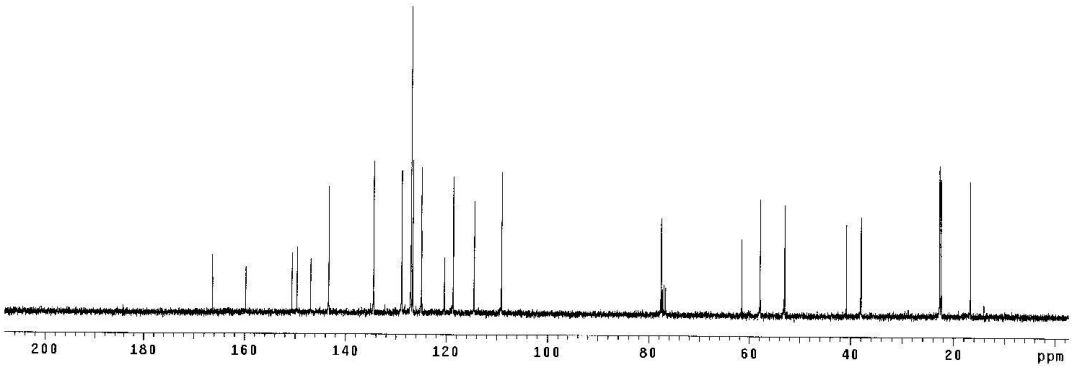


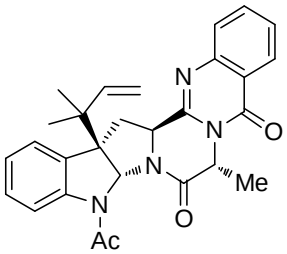
(-)-ardeemin **2b**



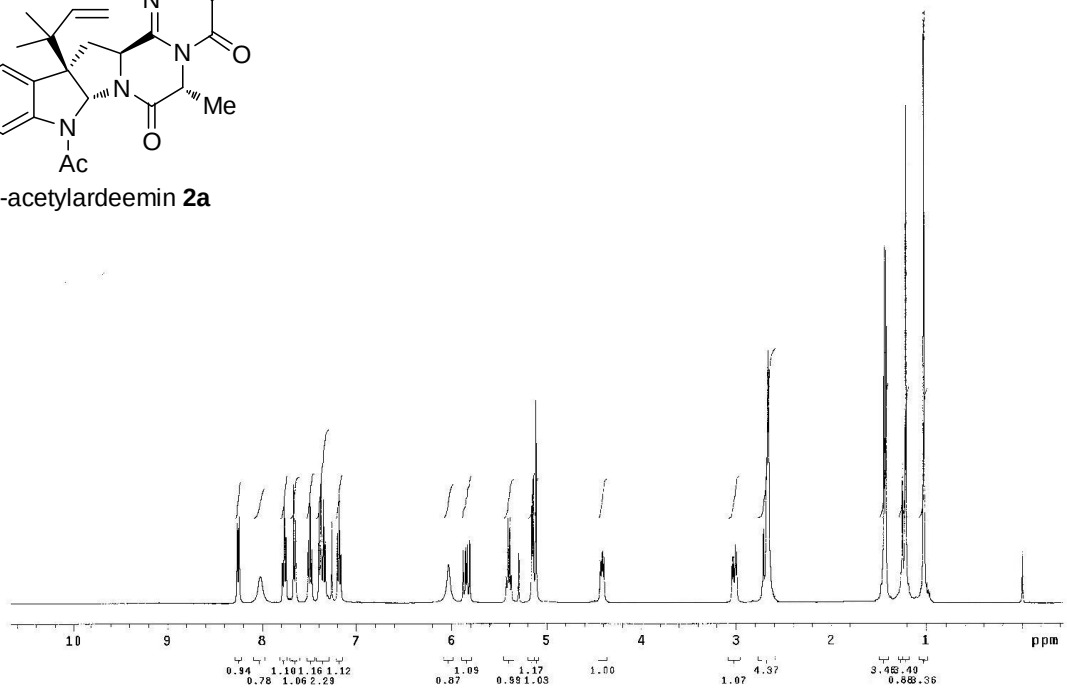


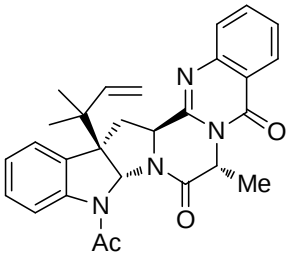
(-)-ardeemin **2b**





(-)-acetylardeemin **2a**





(-)-acetylardeemin **2a**