Supporting Information (120 pages)

Asymmetric construction of densely functionalized three-dimensional aza-tetracyclic scaffolds for drug discovery

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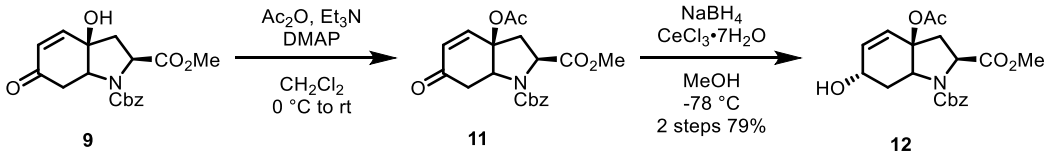
1. General techniques

NMR spectra were recorded on a Bruker biospin AVANCE II (400 MHz for ^{1}H, 100 MHz for ^{13}C, 376 MHz for ^{19}F) or a Bruker biospin AVANCE III (500 MHz for ^{1}H, 125 MHz for ^{13}C) instrument in the indicated solvent. Chemical shifts are reported in units parts per million (ppm) relative to $CDCl_3$ (7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C NMR) or CD_3OD (3.31 ppm for ^{1}H NMR, 49.00 ppm for ^{13}C NMR). Multiplicities are reported using the following abbreviations: s; singlet, d; doublet, dd; double doublets, ddd; double double doublets, dq; double quartet, t; triplet, q; quartet, m; multiplet, br; broad, *J*; coupling constants in Hertz (Hz). IR spectra were recorded on a JASCO FT/IR-4200 spectrometer. Only the strongest and/or structurally important peaks are reported as IR data given in cm^{-1}. High-resolution mass spectra (HRMS) were recorded on Bruker ESI-TOF-MS (micro TOF II). Analytical thin layer chromatography (TLC) was performed on a glass plate of silica gel 60 GF254 (Merck) with UV light (254 nm), visualized by an aqueous alkaline $KMnO_4$ solution. Column chromatography was performed using silica gel (Fuji Silysia, CHROMATREX PSQ 60B, 50-200 μm). Preparative thin-layer chromatography (PTLC) was performed using Wakogel B5-F silica coated plates (1.0 mm) prepared in our laboratory. Gel permeation chromatography (GPC) for purification was performed on Japan Analytical Industry Model LC- 9225 NEXT (recycling preparative HPLC) and a Japan Analytical Industry Model UV-600 NEXT ultraviolet detector with a polystyrene gel column (JAIGEL-1H, 20 mm × 600 mm), using chloroform as solvent (3.5 mL/min). Analytical HPLC was performed using JASCO PU-2080 Plus Intelligent HPLC pump system with a JASCO UV-2075 Plus Intelligent UV/VIS Detector, JASCO CO4060 Column Oven, JASCO LG-4580 Quaternary Gradient Unit, JASCO DG-2080-53 3-Line Degasser, JASCO AS-4550 Autosampler and JASCO LC-NetII/ADC Interface Box. Bicyclic scaffold **9**[1]and ally bromide **15b**[2] were prepared according to the literature.

2. Experimental procedures and compound characterizations

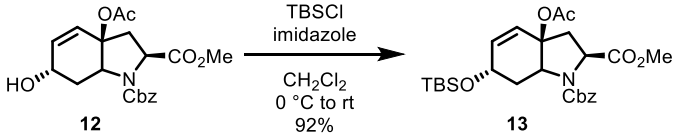
Preparation of alcohol 12:



To a solution of alcohol **S1**[1] (6.02 g, 17.4 mmol, 1.0 equiv.) in CH_2Cl_2 (90.0 mL) was added Et_3N (2.20 mL, 15.8 mmol, 3.0 equiv.), Ac_2O (3.29 mL, 34.8 mmol, 2.0 equiv.), and DMAP (213 mg, 1.74 mmol, 0.10 equiv.) at 0 ℃. After being stirred at room temperature for 5.5 h under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 60:40 to hexane:EtOAc = 45:55) to afford crude enone **11** (5.61 g) as a yellow amorphous solid.

To a solution of crude enone **11** (5.61 g) in MeOH (120 mL) was added $CeCl_3 \cdot 7H_2O$ (7.04 g, 18.9 mmol) at room temperature. The reaction mixture was cooled to -78 ℃, and $NaBH_4$ (605 mg, 16.0 mmol) was added. After being stirred at -78 ℃ for 10 min under an argon atmosphere, the reaction mixture was diluted with saturated aqueous NH_4Cl and passed through a pad of Celite®. The aqueous layer was extracted with CH_2Cl_2 for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 50:50 to hexane:EtOAc = 45:55) to afford alcohol **12** (5.34 g, 13.7 mmol, 2 steps 79%) as a white amorphous solid. $[\alpha]_{405}^{29.3}$ −524.2 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H), 5.97-5.90 (m, 1H), 5.82-5.74 (m, 1H), 5.27-5.02 (m, 2H), 4.61-4.45 (m, 3H), 3.72-3.58 (m, 3H), 2.86-2.62 (m, 2H), 2.46-2.02 (m, 2H), 1.93-1.91 (m, 3H), 1.46-1.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 171.2, 170.3, 170.0, 154.7, 154.2, 136.7, 136.4, 136.4, 136.2, 128.7, 128.6, 128.3, 128.2, 128.1, 125.2, 124.9, 85.4, 84.4, 67.6, 67.3, 66.0, 65.8, 61.0, 60.2, 58.6, 58.4, 52.4, 52.2, 39.6, 38.9, 38.8, 37.9, 22.0, 21.9; IR (neat): 3455, 3064, 3034, 2952, 1738, 1706, 1413, 1366, 1353, 1248, 1233, 1212, 1127, 1115, 1067, 1031, 970, 765, 753 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{23}NO_7Na^+$ [M + Na^+] 412.1367, found 412.1376.

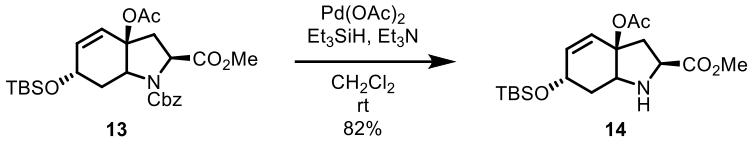
Preparation of silyl ether 13:



To a solution of alcohol **12** (1.58 g, 4.06 mmol, 1.0 equiv.) in CH_2Cl_2 (20 mL) was added TBSCl (918 mg, 6.09 mmol, 1.5 equiv.) and imidazole (831 mg, 12.2 mol, 3.0 equiv.) at 0 ℃. After being stirred at room temperature for 14 h under an argon atmosphere, the reaction mixture was diluted with water and the aqueous layer was extracted with CH_2Cl_2 for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 90:10 to hexane:EtOAc = 50:50) to afford silyl ether **13** (1.89 g, 3.75 mmol, 92%) as a colorless oil. $[\alpha]_{405}^{27.3}$ −370.6 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 5.87-5.69 (m, 2H), 5.34-5.01 (m, 2H),

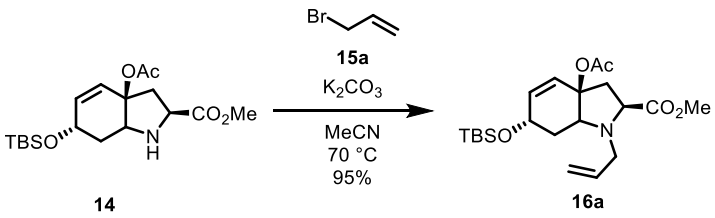
4.62-4.38 (m, 3H), 3.73-3.57 (m, 3H), 2.77-2.38 (m, 3H), 1.93-1.90 (m, 3H), 1.46-1.36 (m, 1H), 0.88-0.85 (m, 9H), 0.10-0.00 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 171.2, 170.3, 170.0, 154.5, 154.1, 137.8, 137.5, 128.7, 128.5, 128.34, 128.30, 128.2, 128.1, 124.4, 124.3, 85.7, 84.6, 67.6, 67.2, 66.7, 66.5, 61.2, 60.3, 58.53, 58.46, 52.3, 52.2, 39.7, 39.4, 38.8, 38.3, 25.94, 25.90, 22.0, 21.9, 18.21, 18.20, -4.45, -4,54, -4.63, -4.78; IR (neat): 3064, 3034, 2953, 2930, 2886, 2856, 1758, 1740, 1711, 1411, 1344, 1251, 1213, 1090, 1040, 836, 776, 698 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{37}NO_7SiNa^+$ [M + Na^+] 526.2231, found 526.2234.

Preparation of amine 14:



Following the slightly modified procedure reported in the literature,[3] to a solution of $Pd(OAc)_2$ (27.1 mg, 0.121 mmol, 0.05 equiv.) in CH_2Cl_2 (12 mL) was added Et_3N (33.7 µL, 0.242 mmol, 0.1 equiv.) and Et_3SiH (850 µL, 5.34 mmol, 2.2 equiv). After being stirred at room temperature for 15 min under an argon atmosphere, ester **13** (1.22 g, 2.42 mmol, 1.0 equiv.) dissolved in CH_2Cl_2 (12 mL) was added, and the reaction mixture was stirred for another 4.5 h. After this time, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 95:5 to hexane:EtOAc = 70:30) to afford amine **14** (735 mg, 1.99 mmol, 82%) as a pale yellow oil. $[\alpha]_{405}^{27.3}$ −353.7 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 (d, *J* = 10.2 Hz, 1H), 5.82 (dd, *J* = 10.2, 2.6 Hz, 1H), 4.32 (m, 1H), 3.87 (t, *J* = 7.02 Hz, 1H), 3.73-3.70 (m, 4H), 2.83 (brs, 1H), 2.55 (d, *J* = 6.8 Hz, 2H), 2.04 (dt, *J* = 13.3, 4.7 Hz, 1H), 1.92 (s, 3H), 1.77-1.70 (m, 1H), 0.86 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 170.3, 135.0, 126.2, 85.1, 65.8, 60.8, 58.4, 52.3, 41.4, 37.3, 25.9, 21.9, 18.2, -4.58, -4.63; IR (neat): 3456, 3356, 3037, 2953, 2930, 2886, 2857, 1740, 1461, 1387, 1367, 1320, 1252, 1084, 1017, 977, 936, 836, 777 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{32}NO_5Si^+$ [M + H^+] 370.2044, found 370.2054.

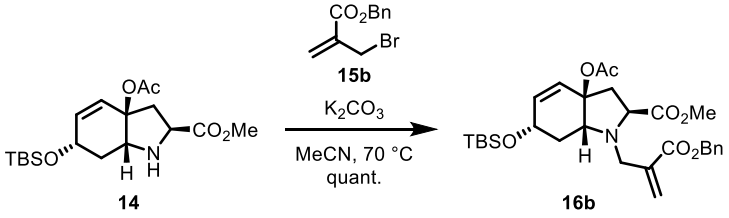
Preparation of allyl amine 16a:



To a mixture of amine **14** (2.22 g, 6.01 mmol, 1.0 equiv.) and K_2CO_3 (4.15 g, 30.0 mmol, 5.0 equiv.) in MeCN (18 mL) was added allyl bromide (**15a**) (1.52 mL, 18.0 mmol, 3.0 equiv.) and stirred at 70 °C for 1 h. After this time, ally bromide (500 µL, 5.91 mml, 0.98 equiv.) was further added and stirred at the same temperature for 1 h before another amount of ally bromide (500 µL, 5.91 mml, 0.98 equiv.) was added. After being stirred at 70 °C for another 1 h, the reaction mixture was passed through a pad of Celite®, and the filtrate was concentrated under reduced pressure. The

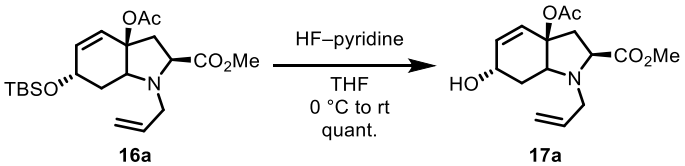
residue was purified by silica gel column chromatography (hexane:EtOAc = 95:5 to hexane:EtOAc = 80:20) to afford allyl amine **16a** (2.29 g, 5.59 mmol, 93%) as a colorless oil. $[\alpha]_{405}^{29.0}$ −434.3 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.96-5.85 (m, 2H), 5.79 (dt, *J* = 10.2, 1.3 Hz, 1H), 5.20 (dq, *J* = 17.1, 1.47 Hz, 1H), 5.09 (dd, *J* = 10.1, 0.8 Hz, 1H), 4.38-4.34 (m, 1H), 3.81 (dd, *J* = 12.3, 4.8 Hz, 1H), 3.68 (s, 3H), 3.58 (dd, *J* = 9.4, 4.9 Hz, 1H), 3.44 (ddt, *J* = 13.5, 5.3, 1.6 Hz, 1H), 3.34 (dd, *J* = 13.5, 5.3 Hz, 1H), 2.61 (dd, *J* = 14.5, 5.0 Hz, 1H), 2.40 (dd, *J* = 14.5, 9.4 Hz, 1H), 2.20-2.14 (m, 1H), 1.98 (s, 3H), 1.40-1.32 (m, 1H), 0.89 (s, 9H), 0.072 (s, 3H), 0.068 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 170.8, 136.6, 135.9, 126.3, 117.3, 85.8, 67.0, 63.8, 61.9, 52.1, 51.9, 41.1, 34.3, 26.0, 22.4, 18.3, -4.5, -4.6; IR (neat): 3074, 3034, 2952, 2930, 2886, 2857, 1738, 1471, 1366, 1251, 1193, 1175, 1084, 994, 836, 776, 665 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{36}NO_5Si^+$ [M + H^+] 410.2357, found 410.2362.

Preparation of allyl amine 16b:



A mixture of amine **14** (1.51 g, 4.08 mmol, 1.0 equiv.), allyl bromide **15b**[2] (3.04 g, 11.9 mmol, 2.9 equiv.), and K_2CO_3 (7.25 g, 52.5 mmol, 19.9 mmol, 4.9 equiv.) in MeCN (16.0 mL) was stirred at 70 °C for 4 h under an argon atmosphere. After this time, the reaction mixture was passed through a pad of Celite®, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 95:5 to hexane:EtOAc = 80:20) to afford allyl amine **16b** (2.17 g, 3.99 mmol, quant.) as a colorless oil. $[\alpha]_D^{24.0}$ −104.1 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 5H), 6.24 (s, 1H), 5.84-5.79 (m, 3H), 5.23 (d, *J* = 13.0 Hz, 1H), 5.17 (d, *J* = 12.5 Hz, 1H), 4.38 (dd, *J* = 10.3, 4.4 Hz, 1H), 3.88 (d, *J* = 15.8 Hz, 1H), 3.78-3.72 (m, 2H), 3.64-3.55 (m, 4H), 2.63 (dd, *J* = 14.4, 2.9 Hz, 1H), 2.31 (dd, *J* = 14.2, 9.1 Hz, 1H), 2.19-2.13 (m, 1H), 1.94 (s, 3H), 1.38-1.30 (m, 1H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 170.5, 166.7, 138.7, 137.2, 136.2, 128.7, 128.3, 128.2, 126.2, 125.8, 86.0, 67.0, 66.5, 63.8, 62.2, 51.6, 48.8, 40.6, 36.9, 26.0, 22.2, 18.3, -4.4, -4.6. IR (neat, cm^{-1}): 3065, 3033, 2951, 2930, 2886, 2856, 1734, 1456, 1253, 1141, 1083, 836, 777, 697; HRMS (ESI) calcd for $C_{29}H_{41}NO_7Si^+$ [M + H^+] 544.2725, found 544.2724.

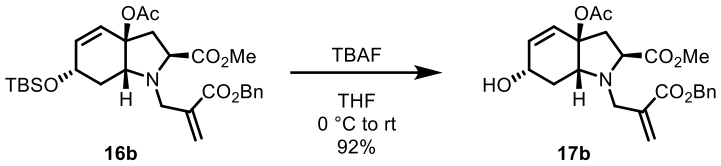
Preparation of alcohol 17a:



To a solution of allyl amine **16a** (252 mg, 0.627 mmol) in THF (3.1 mL) was added pyridinium poly(hydrogenfluoride) (630 μL) at 0 °C. After being stirred at room temperature for 50 min under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and

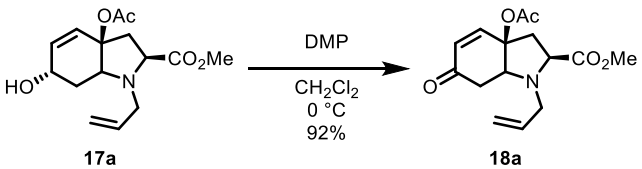
concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 80:20 to hexane:EtOAc = 40:60) to afford alcohol **17a** (188 mg, 0.637 mmol, quant.) as a pale yellow oil. $[\alpha]_{405}^{28.8}$ −501.9 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.07 (dd, *J* = 10.2, 0.5 Hz, 1H), 6.02 (dd, *J* = 10.2, 4.4 Hz, 1H), 5.81-5.71 (m, 1H), 5.14 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.09 (dq, *J* = 10.1, 0.8 Hz, 1H), 4.10 (dd, *J* = 8.1, 4.0 Hz, 1H), 3.78 (dd, *J* = 9.0, 3.4 Hz, 1H), 3.75 (t, *J* = 4.1 Hz, 1H), 3.67-3.62 (m, 4H), 3.30 (dd, *J* = 13.6, 8.3 Hz, 1H), 2.53 (dd, *J* = 14.6, 9.0 Hz, 1H), 2.42 (dd, *J* = 14.6, 3.4 Hz, 1H), 2.13-2.01 (m, 2H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 170.2, 134.6, 131.4, 129.4, 118.2, 82.6, 64.3, 63.5, 60.4, 51.5, 50.6, 41.9, 28.9, 21.8; IR (neat): 3438, 3076, 3033, 2951, 2927, 2859, 1736, 1435, 1369, 1245, 1202, 1174, 1117, 1061, 1032, 927, 789 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}NO_5^+$ [M + H$^+$] 296.1492, found 296.1493.

Preparation of alcohol 17b:



To a solution of allyl amine **16b** (10.9 g, 20.0 mmol, 1.0 equiv.) in THF (100 mL) was added tetrabutylammonium fluoride (TBAF) (ca. 1 mol/L in THF, 60 mL) at 0 °C. After being stirred for 1.5 h at room temperature under argon atmosphere, the reaction mixture was diluted with saturated aqueous NH_4Cl, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 70:30 to 50:50) to afford alcohol **17b** (7.88 g, 18.3 mmol, 92%) as a pale yellow oil. $[\alpha]_D^{24.0}$ – 145.30 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.32 (m, 5H), 6.27 (s, 1H), 6.09 (d, *J* = 10.2 Hz, 1H), 6.03 (dd, *J* = 10.1, 5.6 Hz, 1H), 5.69 (s, 1H), 5.22 (d, *J* = 12.3 Hz, 1H), 5.15 (d, *J* = 12.3 Hz, 1H), 4.09 (brs, 1H), 3.99 (d, *J* = 13.3 Hz, 1H), 3.81-3.75 (m, 2H), 3.65-3.60 (m, 5H), 2.55 (dd, *J* = 14.5, 9.3 Hz, 1H), 2.34 (dd, *J* = 14.6, 2.9 Hz, 1H), 2.23-2.18 (m, 1H), 2.07 (dt, *J* = 15.1, 4.0 Hz, 1H), 1.97 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 170.2, 166.1, 137.1, 135.9, 131.3, 129.2, 129.0, 128.7, 128.5, 128.4, 81.9, 66.9, 63.9, 62.5, 59.8, 51.5, 49.0, 41.6, 28.9, 21.8; IR (neat, cm^{-1}): 3463, 3091, 3065, 2950, 2890, 1734, 1455, 1435, 1368, 1255, 1201, 1168, 1124, 1063, 1036, 750, 699; HRMS (ESI) calcd for $C_{23}H_{28}NO_7^+$ [M + H$^+$] 430.1860, found 430.1867.

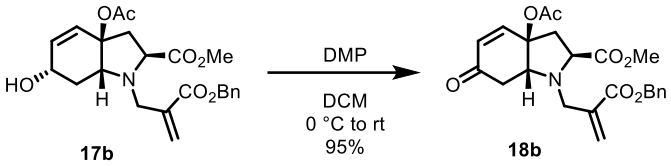
Representative procedure for preparation of enone 18a,b:



To a solution of alcohol **17a** (155 mg, 0.525 mmol, 1.0 equiv) in CH_2Cl_2 (2.6 mL) was added Dess-Martin periodinane (DMP) (274 mg, 0.646 mmol, 1.2 equiv) at 0 °C. After being stirred at the same temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and

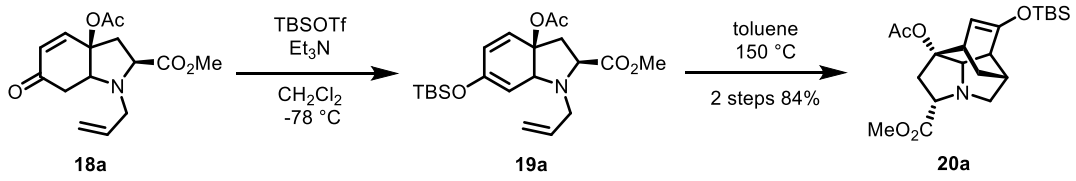
concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 80:20 to hexane:EtOAc = 70:30) to afford enone **18a** (142 mg, 0.483 mmol, 92%) as a pale yellow oil. $[\alpha]_D^{26.1}$ −343.9 (c 1.00 in $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (dd, *J* = 10.3, 1.5 Hz, 1H), 5.93 (d, *J* = 10.3 Hz, 1H), 5.75-5.65 (m, 1H), 5.09 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.03 (dd, *J* = 10.1, 0.8 Hz, 1H), 3.97-3.95 (m, 1H), 3.74 (dd, *J* = 9.31, 3.56 Hz, 1H), 3.65 (s, 3H), 3.40 (ddt, *J* = 13.9, 4.9 Hz, *J* = 1.7 Hz, 1H), 3.22 (dd, *J* = 13.9, 8.0 Hz, 1H), 2.84 (dd, *J* = 16.6, 5.0 Hz, 1H), 2.62-2.54 (m, 2H), 2.43 (dd, *J* = 14.6, 3.6 Hz, 1H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9, 173.5, 170.2, 145.8, 135.0, 128.4, 117.6, 81.4, 64.3, 60.6, 51.6, 50.6, 41.1, 37.6, 21.5. FT-IR (neat): 3077, 3005, 2978, 2952, 2907, 2852, 1736, 1688, 1434, 1369, 1239, 1200, 1170, 1111, 1038, 928, 763 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{20}NO_5^+$ [M + H$^+$] 294.1336, found 294.1342.

Preparation of enone 18b:



Following the representative procedure using alcohol **17b** (94.0 mg, 0.219 mmol, 1.0 equiv.), purified by silica gel column chromatography (hexane:EtOAc = 75:25 to hexane:EtOAc = 70:30) afforded enone **18b** (88.6 mg, 0.207 mmol, 95%) as a yellow oil. $[\alpha]_D^{23.3}$ – 61.80 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.31 (m, 5H), 6.93 (dd, *J* = 10.3, 1.5 Hz, 1H), 6.23 (d, *J* = 0.7 Hz, 1H), 5.96 (d, *J* = 10.4 Hz, 1H), 5.63 (d, *J* = 1.5 Hz, 1H), 5.21 (d, *J* = 12.5 Hz, 1H), 5.14 (d, *J* = 12.4 Hz, 1H), 4.03-4.01 (m, 1H), 3.79 (dd, *J* = 9.1, 3.3 Hz, 1H), 3.67 (s, 3H), 3.63 (d, *J* = 16.1 Hz, 1H), 3.56 (d, *J* = 16.0 Hz, 1H), 2.87 (dd, *J* = 16.8, 4.9 Hz, 1H), 2.63-2.57 (m, 2H), 2.47 (dd, *J* = 14.5, 3.4 Hz, 1H), 2.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.7, 173.6, 170.3, 166.3, 145.8, 137.5, 136.1, 128.7, 128.6, 128.33, 128.31, 127.0, 81.0, 66.5, 64.5, 60.6, 51.8, 47.9, 41.4, 37.8, 21.5; IR (neat, cm^{-1}): 3090, 3062, 3032, 2952, 2888, 1735, 1689, 1651, 1455, 1369, 1240, 1208, 1121, 1038, 981, 750, 699; HRMS (ESI) calcd for $C_{23}H_{26}NO_7^+$ [M + H$^+$] 428.1704, found 428.1712.

Preparation of tetracyclic amine 20a:

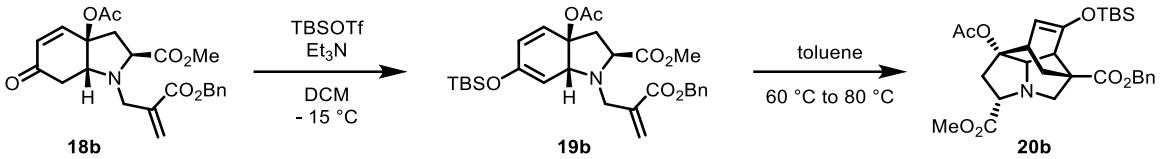


A solution of TBSOTf (1.40 mL) in DCM (4.6 mL) was prepared. To a solution of enone **18a** (1.10 g, 3.75 mmol, 1.0 equiv) in CH_2Cl_2 (19 mL) was added Et_3N (1.57 mL, 11.3 mmol, 3.0 equiv.) and the prepared solution of TBSOTf (4.9 mL) at -78 °C. After being stirred for 10 min at the same temperature under an argon atmosphere, the reaction mixture was again added the prepared solution of TBSOTf (1.0 mL) and stirred for another 10 min. The reaction mixture was diluted with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with CH_2Cl_2 for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 95:5 to hexane:EtOAc =

80:20) to afford crude silyl enol ether **19a** (1.43 g) as an orange oil.

Sealed tube was charged with the crude silyl enol ether **19a** (1.43 g) and then toluene (15 mL) was added. The reaction mixture was stirred at 150 °C for 3.5 h before being concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 70:30 to hexane:EtOAc = 30:70) to afford tetracyclic amines **20b** (291 mg, 0.714 mmol, 94%) as a pale yellow oil. $[\alpha]_{405}^{27.8}$ −52.6 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.02 (dd, *J* = 7.1, 2.2 Hz, 1H), 3.84 (dd, *J* = 9.8, 3.5 Hz, 1H), 3.72 (s, 3H), 3.45-3.41 (m, 2H), 3.28-3.26 (m, 1H), 2.92-2.89 (m, 1H), 2.65 (dd, *J* = 15.5, 9.9 Hz, 1H), 2.40 (dd, *J* = 15.5, 3.6 Hz, 1H), 2.4 (d, *J* = 11.3 Hz, 1H), 2.07-2.03 (m, 1H), 1.94 (s, 3H), 1.60-1.54 (m, 1H), 1.17 (dd, *J* = 13.9, 1.7 Hz, 1H), 0.91 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 170.4, 152.4, 104.6, 94.0, 73.1, 71.1, 64.3, 52.3, 49.0, 38.3, 36.0, 34.0, 32.7, 25.8, 21.7, 18.1, -4.2, -4.5; IR (neat): 3064, 2952, 2932, 2883, 2858, 1732, 1646, 1453, 1366, 1251, 1221, 1202, 1170, 1072, 931, 835, 781 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{34}NO_5Si^+$ [M + H^+] 408.2201, found 403.2208.

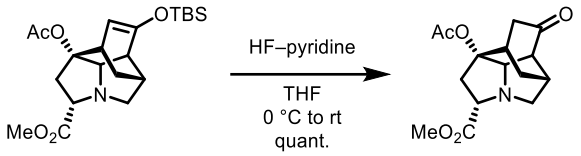
Preparation of tetracyclic amine 20b:



To a solution of enone **18b** (7.31 g, 17.1 mmol, 1.0 equiv.) and Et_3N (7.00 mL, 47.4 mmol, 2.8 equiv.) in CH_2Cl_2 (7.0 mL) was added TBSOTf (4.70 mmL, 20.4 mmol, 1.2 equiv.) at -15 °C under an argon atmosphere. After being stirred for 10 min at the same temperature, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure to afford crude silyl enol ether **19b**.

The crude silyl enol ether **19b** was dissolved in toluene (50 mL) and stirred for at 60 °C for 12.5 h under an argon atmosphere. After this time, the reaction mixture was heated to 80 °C and stirred for additional 30 min before being concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 70:30 to hexane:EtOAc = 50:50) to afford tetracyclic amine **20b** (7.42 g, 13.7 mmol, 2 steps 80%) as a red oil. $[\alpha]_D^{22.6}$ – 66.80 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 5.08 (s, 2H), 5.02 (dd, *J* = 7.13, 2.14, 1H), 3.82 (dd, *J* = 9.88, 3.84, 1Hz) 3.75-3.72 (m, 4H), 3.53-3.51 (m, 1H), 3.38-3.34 (m, 2H), 2.70 (dd, *J* = 15.5, 9.9 Hz, 1H), 2.58 (d, *J* = 11.3 Hz, 1H), 2.42 (dd, *J* = 15.5, 3.9 Hz, 1H), 2.14-2.10 (m, 1H), 1.95 (s, 3H), 1.46 (dd, *J* = 14.3, 2.9 Hz, 1H), 0.88 (s, 9H), 0.103 (s, 3H), 0.099 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 173.3, 170.4, 151.2, 135.9, 128.6, 128.3, 127.9, 103.8, 93.1, 73.3, 70.8, 67.0, 66.9, 52.4, 52.0, 50.1, 38.5, 36.7, 35.0, 25.7, 21.7, 18.1, -4.3, -4.6; IR (neat, cm^{-1}): 3066, 30332, 3004, 2953, 2931, 2886, 2856, 1731, 1646, 1455, 1435, 1367, 1253, 1207, 1085, 835, 763, 750, 698; HRMS (ESI) calcd for $C_{29}H_{40}NO_7Si^+$ [M + H^+] 542.2569, found 542.2574.

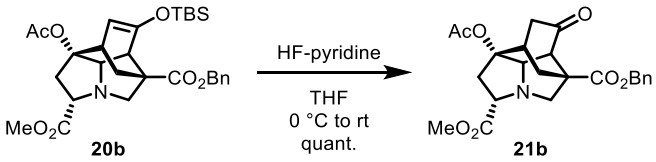
Representative procedure for preparation of ketone 21a,b:



20a **21a**

To a solution of tetracyclic amine **20a** (576 mg, 1.41 mmol) in THF (7.0 mL) was added pyridinium poly(hydrogenfluoride) (1.40 mL) at 0 °C. After being stirred at room temperature for 50 min under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 80:20 to hexane:EtOAc = 40:60) to afford ketone **21a** (188 mg, 0.637 mmol, quant.) as a yellow oil. $[\alpha]_{405}^{29.5}$ −16.7 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (dd, *J* = 9.8, 4.0 Hz, 1H), 3.73 (s, 3H), 3.64 (d, *J* = 4.8 Hz, 1H), 3.46 (dd, *J* = 11.3, 3.7 Hz, 1H), 2.80-2.94 (m, 1H), 2.87-2.85 (m, 1H), 2.77 (dd, *J* = 15.5, 9.8 Hz, 1H), 2.55 (dd, *J* = 15.5, 4.0 Hz, 1H), 2.45 (d, *J* = 11.3 Hz, 1H), 2.34-2.30 (m, 1H), 2.25 (dt, *J* = 19.3, 2.9 Hz, 1H), 2.00 (s, 3H), 1.98-1.93 (m, 2H), 1.43 (d, *J* = 14.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.4, 174.0, 170.3, 89.3, 72.0, 69.6, 65.6, 55.0, 52.5, 39.33, 39.32, 34.5, 33.0, 30.8, 21.5; FT-IR (neat): 2951, 2877, 1730, 1436, 1370, 1243, 1218, 1068, 1023 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{20}NO_5^+$ [M + H^+] 294.1336, found 294.1339.

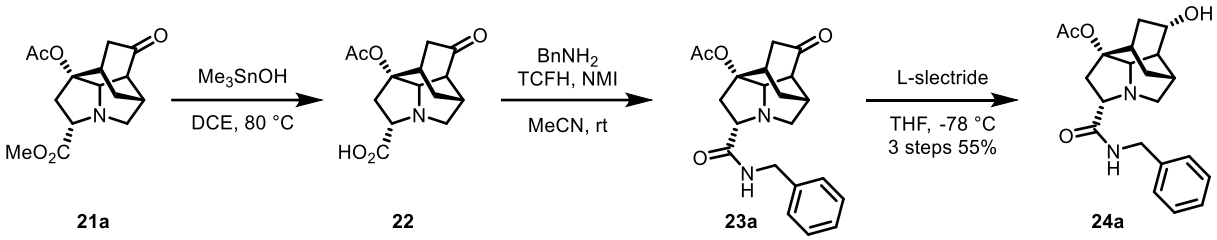
Preparation of ketone 21b:



20b **21b**

Following the representative procedure using **20b** (572.5 mg, 1.06 mmol, 1.0 equiv.), purified by silica gel column chromatography (hexane:acetone = 80:20 to hexane:EtOAc = 50:50) to afforded ketone **21b** (447 mg, 1.05 mmol, quant.) as an orange oil. $[\alpha]_D^{21.6}$ – 21.9 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.24 (m, 5H), 5.10 (d, *J* = 12.4 Hz, 1H), 5.06 (d, *J* = 12.4 Hz, 1H), 3.85 (dd, *J* = 10.0, 4.7 Hz, 1H), 3.73-3.69 (m, 5H), 3.14 (d, *J* = 5.28 Hz, 1H), 3.04 (brs, 1H), 2.83 (dd, *J* = 15.5, 9.8 Hz, 1H), 2.68 (d, *J* = 11.4 Hz, 1H), 2.53 (dd, *J* = 15.4, 4.7 Hz, 1H), 2.37 (d, *J* = 14.8 Hz, 1H), 2.26 (dt, *J* = 19.2, 2.9 Hz, 1H), 2.05-2.00 (m, 4H), 1.70 (dt, *J* = 15.0, 3.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.9, 173.8, 172.1, 170.2, 135.2, 128.7, 128.5, 128.1, 88.1, 72.5, 69.6, 67.4, 67.3, 56.9, 52.6, 49.8, 39.6, 38.8, 33.6, 33.5, 21.4; IR (neat, cm^{-1}): 3089, 3063, 3032, 2953, 2889, 2845, 1732, 1455, 1436, 1243, 1175, 1147, 1087, 749, 699; HRMS (ESI) calcd for $C_{23}H_{26}NO_7^+$ [M + H^+] 428.1704, found 428.1707.

Preparation of alcohol 24a:

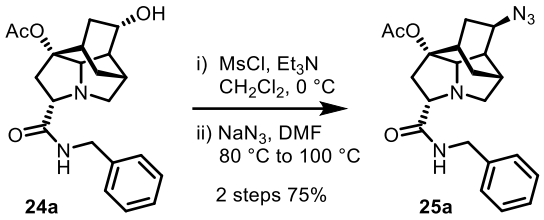


Following the slightly modified procedure reported in the literature,[4] to a solution of ketone **21a** (371 mg, 1.26 mmol, 1.0 equiv.) in DCE (6.0 mL) was added trimethyltin hydroxide (342 mg, 1.89 mmol, 1.5 equiv.). After being stirred at 80 ℃ for 50 min under an argon atmosphere, the reaction mixture was added another amount of trimethyltin hydroxide (114 mg, 0.631 mmol, 0.5 equiv.) and stirred for 1h. After this time, another amount of trimethyltin hydroxide (22.7 mg, 0.126 mmol, 0.1 equiv.) was added and stirred for 20 min. The reaction mixture was concentrated under reduced pressure and passed through a pad of silica eluting with MeOH to afford crude carboxylic acid **22** (345 mg) as a white solid.

Following the slightly modified procedure reported in the literature,[5] to a suspension of crude carboxylic acid **22** (345 mg), benzylamine (165 µL, 1.51 mmol, 1.2 equiv.), and *N*-methylimidazole (300 µL, 3.80 mmol, 3.0 equiv.) in MeCN (5.0 mL) was added TCFH (424 mg, 1.51 mmol, 1.2 equiv.). After being stirred for 40 min at room temperature under an argon atmosphere, the reaction mixture was diluted with water and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 10:90 to hexane:EtOAc = 5:95) to afford crude amide **23a** (504 mg) as a yellow oil.

To a solution of amide **23a** (504 mg) in THF (8.8 mL) was added L-selectride (1.4 mL, 1.0 M in THF, 1.1 equiv.) at -78 ℃. After being stirred for 20 min at the same temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous NH_4Cl, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 30:70 to EtOAc:MeOH = 90:10) to afford alcohol **24a** (258 mg, 0.696 mmol, 3 steps 55%) as a white amorphous solid. $[\alpha]_{405}^{27.3}$ + 80.0 (c 1.00 in $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (t, *J* = 5.3 Hz, 1H), 7.36-7.28 (m, 5H), 4.48 (dd, *J* = 14.9, 6.1 Hz, 1H), 4.43 (dd, *J* = 14.9, 5.9 Hz, 1H), 4.18 (d, *J* = 9.8 Hz, 1H), 3.62 (dd, *J* = 10.2, 4.4 Hz, 1H), 3.37 (d, *J* = 4.9 Hz, 1H), 3.32 (dd, *J* = 11.0, 3.6 Hz, 1H), 2.77 (dd, *J* = 15.5, 10.2 Hz, 1H), 2.67 (dd, *J* = 15.5, 4.4 Hz, 1H), 2.60 (brs, 1H), 2.42 (dd, *J* = 8.4, 4.0 Hz, 1H), 2.28 (d, *J* = 11.1 Hz, 1H), 2.04 (s, 3H), 1.99-1.96 (m, 1H), 1.84-1.79 (m, 1H), 1.70-1.65 (m, 2H), 1.51 (ddd, *J* = 14.7, 5.4, 2.7 Hz, 1H), 1.16 (d, *J* = 14.6, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 170.0, 138.7, 128.8, 127.8, 127.5, 90.1, 70.5, 67.7, 65.6, 64.8, 45.9, 43.4, 40.2, 33.7, 32.4, 31.0, 30.5, 21.7; IR (neat): 3421, 3339, 3086, 3060, 3028, 2932, 2869, 2359, 2341, 1727, 1653, 1518, 1454, 1367, 1224, 1055, 1036, 1022, 732, 699 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{27}N_2O_4^+$ [M + H^+] 371.1965, found 371.1965.

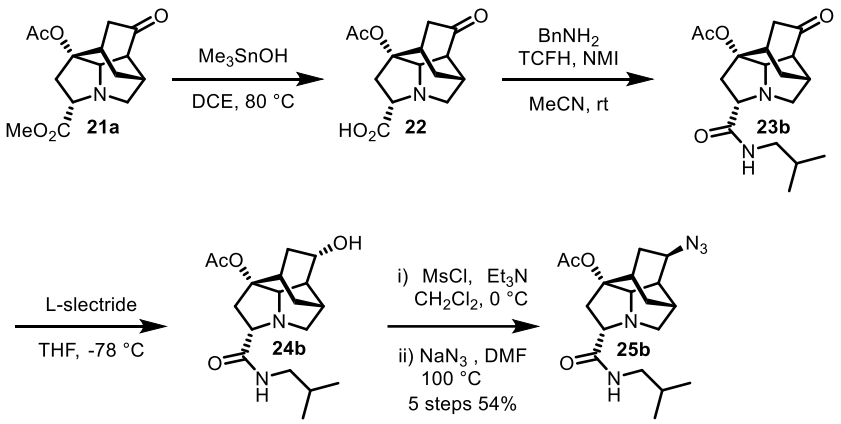
Preparation of azide 25a:



To a solution of alcohol **24a** (677 mg, 1.83 mmol, 1.0 equiv.) and Et_3N (765 µL, 5.46 mmol, 3.0 equiv.) in CH_2Cl_2 (7.3 mL) was added methanesulfonyl chloride (184 µL, 2.38 mmol, 1.3 equiv.) at 0 °C. After being stirred for 10 min under argon atmosphere at the same temperature, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure to afford curde mesylate (762 mg) as a white amorphous.

To a solution of crude mesylate (762 mg) in DMF (7.3 mL) was added NaN_3 (240 mg, 3.66 mmol, 2.0 equiv.) and stirred at 80 °C under argon atmosphere. After being stirred for 2 h, the reaction mixture was heated to 100 °C and further stirred for 40 min. After this time, the reaction mixture was diluted with ice cooled water, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 65:45 to hexane:EtOAc = 45:65) to afford azide **25a** (543 mg, 1.37 mmol, 2 steps 75%) as a colorless solid. $[\alpha]_{405}^{26.1}$ + 38.5 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (t, *J* = 5.5 Hz, 1 H), 7.37-7.26 (m, 5H), 4.51-4.41 (m, 2H), 3.94-3.89 (m, 1H), 3.64 (dd, *J* = 10.2, 4.4 Hz, 1H), 3.30 (dd, *J* = 11.2, 3.6 Hz, 1H), 3.17 (d, *J* = 5.0 Hz, 1H), 2.77 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.63 (dd, *J* = 15.5, 4.5 Hz, 1H), 2.57-2.55 (m, 1H), 2.35-2.32 (m, 1H), 2.27 (d, *J* = 11.2 Hz, 1H), 2.21-2.17 (m, 1H), 2.05-1.97 (m, 4H), 1.94-1.88 (m, 1H), 1.28-1.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 169.9, 138.7, 128.8, 127.8, 127.5, 89.8, 71.1, 70.7, 65.9, 54.0, 43.3, 43.2, 39.7, 30.8, 30.5, 30.2, 29.3, 21.6; IR (neat): 3343, 3086, 3062, 3028, 2936, 2872, 2099, 1733, 1670, 1511, 1454, 1367, 1243, 1227, 1076, 1024, 699 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{26}N_5O_3^+$ [M + H^+] 396.2030, found 396.2035.

Preparation of azide 25b:



To a solution of ketone **21a** (979 mg, 3.34 mmol, 1.0 equiv.) in DCE (16.0 mL) was added trimethyltin hydroxide (906 mg, 5.01 mmol, 1.5 equiv.). After being stirred at 80 °C for 1.5 h under an argon atmosphere, the reaction

mixture was added another amount of trimethyltin hydroxide (604 mg, 3.34 mmol, 1.0 equiv.) and stirred for 1 h. The reaction mixture was concentrated under reduced pressure and passed through a pad of silica eluting with MeOH to afford crude carboxylic acid **22** (893 mg) as a white solid.

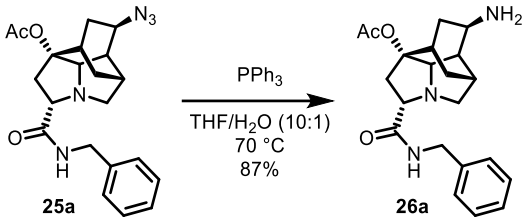
To a suspension of crude carboxylic acid **22** (893 mg), isobutylamine (400 μL, 4.03 mmol, 1.2 equiv.), and *N*-methylimidazole (790 μL, 10.0 mmol, 3.0 equiv.) in MeCN (13.0 mL) was added TCFH (1.13 mg, 4.01 mmol, 1.2 equiv.). After being stirred for 4 h at room temperature under an argon atmosphere, the reaction mixture was diluted with water and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 10:90 to EtOAc = 100%) to afford crude amide **23b** (1.83 g) as a yellow oil.

To a solution of the crude amide **23b** (1.83 g) in THF (23.0 mL) was added L-selectride (4.00 mL, 1.0 M in THF, 1.1 equiv.) at -78 ˚C。 After being stirred for 15 min at the same temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous NH_4Cl, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:acetone = 65:35 to hexane:acetone = 45:55) to afford crude alcohol **24b** (685 mg) as a white solid.

To a solution of the crude alcohol **24b** (685 mg, assumed as 2.04 mmol, 1.0 equiv.) and Et_3N (850 μL, 6.10 mmol, 3.0 equiv.) in CH_2Cl_2 (8.0 mL) was added methanesulfonyl chloride (20.5 μL, 2.65 mmol, 1.3 equiv.) at 0 ℃. After being stirred for 10 min under argon atmosphere at the same temperature, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure to afford curde mesylate (708 mg) as a white amorphous.

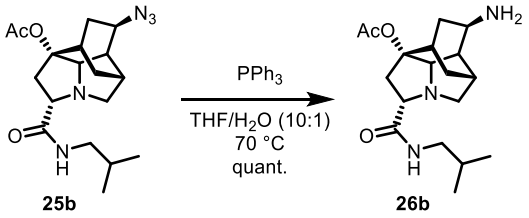
To a solution of crude mesylate (708 mg) in DMF (8.0 mL) was added NaN_3 (265 mg, 4.08 mmol, 2.0 equiv.) and stirred at 100 ℃ under argon atmosphere. After being stirred for 1 h, the reaction mixture was diluted with ice cooled water, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:acetone = 80:20) to afford azide **25b** (651 mg, 1.80 mmol, 5 steps 54%) as a colorless solid. $[\alpha]_{405}^{24.8}$ – 45.3 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (brs, 1H), 3.96-3.92 (m, 1H), 3.58 (dd, *J* = 10.4, 4.6 Hz, 1H), 3.34 (dd, *J* = 11.2, 3.5 Hz, 1H), 3.17 (d, *J* = 5.0 Hz, 1H), 3.16-3.09 (m, 1H), 3.06-3.00 (m, 1H), 2.76 (dd, *J* = 15.5, 10.2 Hz, 1H), 2.58-2.53 (m, 2H), 2.40-2.37 (m, 1H), 2.28 (d, *J* = 11.2 Hz, 1H), 2.23-2.20 (m, 1H), 2.04-1.97 (m, 4H), 1.94-1.88 (m, 1H), 1.85-1.75 (m, 1H), 1.28-1.21 (m, 2H), 0.93 (s, 3H), 0.91 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 169.9, 89.7, 71.1, 70.8, 65.9, 54.0, 46.5, 43.2, 39.8, 30.8, 30.4, 30.2, 29.3, 28.8, 21.6, 20.3, 20.2; IR (neat): 3343, 2956, 2935, 2871, 2100, 1734, 1671, 1517, 1465, 1368, 1242, 1227, 1178, 1073, 1023, 948 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{28}N_5O_3^+$ [M + H^+] 362.2187, found 362.2190.

Representative procedure for preparation of amine 26a,b:



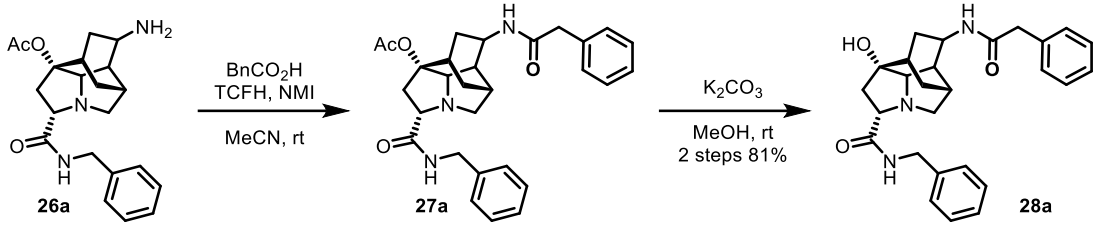
To a solution of azide **25a** (78.5 mg, 0.199 mmol, 1.0 equiv.) in a mixture of THF (1.0 mL) and H_2O (100 µL) was added PPh_3 (85.8 mg, 0.327 mmol, 1.6 equiv.). After being stirred for 2 h at 70 °C under an argon atmosphere, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc = 100% to CH_2Cl_2/MeOH/Et_3N = 90:10:1) to afford amine **26a** (64.4 mg, 0.174 mmol, 87%) as a colorless oil. $[\alpha]_{405}^{25.5}$ + 59.2 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (t, *J* = 5.46 Hz, 1H), 7.35-7.25 (m, 5H), 4.45 (d, *J* = 6.24 Hz, 2H), 3.63 (dd, *J* = 10.4, 4.5 Hz, 1H), 3.30-3.24 (m, 2H), 3.14 (d, *J* = 5.0 Hz, 1H), 2.79 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.58 (dd, *J* = 15.4, 4.6 Hz, 1H), 2.48 (brs, 1H), 2.25 (d, *J* = 11.1 Hz, 1H), 2.20-2.18 (m, 1H), 2.09-2.06 (m, 1H), 2.04-1.96 (m, 4H), 1.93-1.86 (m ,1H), 1.60 (brs, 2H), 1.18 (d, *J* = 14.4 Hz, 1H), 0.90 (ddd, *J* = 13.7, 5.2, 2.2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 169.9, 138.6, 128.6, 127.6, 127.2, 89.8, 71.0, 70.95, 66.1, 46.9, 43.1, 42.6, 39.8, 33.6, 31.03, 31.00, 29.4, 21.5; IR (neat): 3341, 3292, 3085, 3059, 3029, 2932, 2868, 1730, 1663, 1513, 1454, 1367, 1246, 1227, 1078, 1022, 732, 699 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{28}N_3O_3^+$ [M + H$^+$] 370.2125, found 370.2131.

preparation of amine 26b:



Following the representative procedure using azide **25b** (615 mg, 1.70 mmol, 1.0 equiv.), purification by silica gel column chromatography (EtOAc = 100% to CH_2Cl_2/MeOH/Et_3N = 90:10:1) afforded amine **26b** (599 mg, 1.78 mmol, quant.) as a yellow oil. $[\alpha]_{405}^{27.5}$ – 17.4 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (t, *J* = 5.6 Hz, 1H), 3.56 (dd, *J* = 10.4, 4.6 Hz, 1H), 3.31-3.28 (m, 2H), 3.15-3.09 (m, 2H), 3.05-3.00 (m, 1H), 2.77 (dd, *J* = 15.4, 10.4 Hz, 1H), 2.53-2.48 (m, 2H), 2.26 (d, *J* = 11.1 Hz, 1H), 2.14-2.19 (m, 1H), 2.14-2.11 (m, 1H), 2.03-1.96 (m, 4H), 1.93-1.86 (m, 1H), 1.85-1.75 (m, 1H), 1.41 (brs, 2H), 1.18 (d, *J* = 14.6 Hz, 1H), 0.92-0.87 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 170.0, 90.0, 71.3, 71.2, 66.3, 47.1, 46.5, 42.9, 40.0, 33.9, 31.2, 31.1, 29.6, 28.8, 21.6, 20.3, 20.2; FT-IR (neat): 3342, 2955, 2931, 2869, 1731, 1661, 1519, 1466, 1368, 1246, 1227, 1078, 1022, 750 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{30}N_3O_3^+$ [M + H$^+$] 336.2282, found 336.2287.

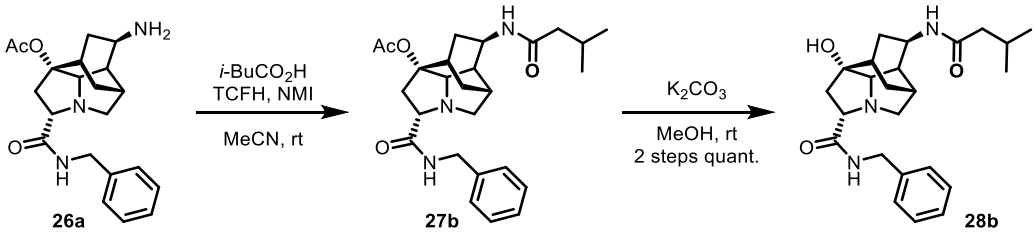
Representative procedure for preparation of alcohol 28a-d:



To a solution of amine **26a** (211 mg, 0.571 mmol, 10 equiv.), phenylacetic acid (93.3 mg, 0.685 mmol, 1.2 equiv.), and *N*-methylimidazole (192 µL, 1.71 mmol, 3.0 equiv.) in MeCN (2.3 mL) was added TCFH (192 mg, 0.685 mmol, 1.2 equiv.). After being stirred for 1 h at room temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 10:90 to EtOAc = 100%) to afford crude amide **27a** (314 mg) as a white amorphous solid.

To a solution of the crude amide **27a** (314 mg) in MeOH (2.3 mL) was added K_2CO_3 (315 mg, 2.28 mmol, 4.0 equiv.) and stirred at room temperature for 3 h under an argon atmosphere. After this time, another amount of MeOH (1.0 mL) and K_2CO_3 (78.9 mg, 0.571 mmol, 1.0 equiv.) and stirred for additional 15 h. The reaction mixture was diluted with saturated aqueous NH_4Cl and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 10:90 to EtOAc:MeOH = 90:10) to afford alcohol **28a** (207 mg, 0.465 mmol, 2 steps 81%) as a white amorphous solid. $[\alpha]_{405}^{26.4}$ - 31.3 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (t, *J* = 5.8 Hz, 1H), 7.36-7.23 (m, 10 H), 5.42 (d, *J* = 7.4 Hz, 1H), 4.46-4.36 (m, 2H), 4.32-4.25 (m, 1H), 3.54 (s, 2H), 3.50 (dd, *J* = 9.8, 4.4 Hz, 1H), 3.19 (dd, *J* = 11.2, 3.6 Hz, 1H), 2.96 (d, *J* = 5.0 Hz, 1H), 2.68 (brs, 1H), 2.54-2.40 (m, 2H), 2.34 (dd, *J* = 14.6, 4.5 Hz, 1H), 2.27-2.25 (m, 1H), 2.15 (d, *J* = 11.2 Hz, 1H), 1.79-1.77 (m, 1H), 1.70 (s, 1H), 1.65-1.59 (m, 1H), 1.17 (d, *J* = 14.4 Hz, 1H), 0.70 (ddd, *J* = 13.7, 4.9, 2.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 170.6, 138.4, 135.1, 129.4, 129.1, 128.8, 127.7, 127.5, 82.1, 72.3, 70.4, 65.7, 43.9, 43.3, 43.2, 42.9, 41.8, 34.3, 31.6, 31.0, 29.8; FT-IR (neat): 3409, 3307, 3078, 3061, 3028, 2929, 2870, 1644, 1454, 1357, 1309, 1264, 1177, 1099, 1029, 970, 930, 730, 697 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{32}N_3O_3^+$ [M + H$^+$] 446.2438, found 446.2443.

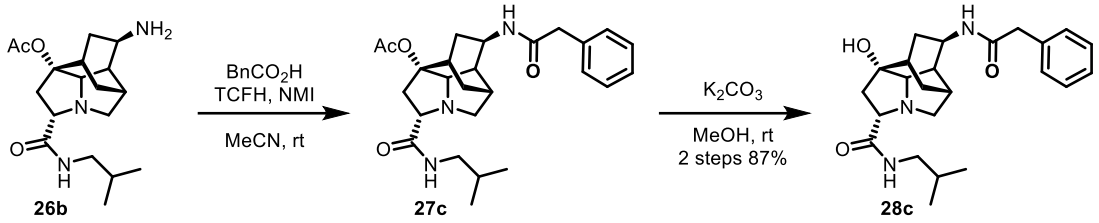
Preparation of alcohol 28b:



Following the representative procedure using amine **26a** (236 mg, 0.639 mmol, 1.0 equiv.) and isovaleric acid (84.7 µL, 0.767 mmol, 1.2 equiv.) purification by silica gel column chromatography (hexane:EtOAc = 10:90 to EtOAc:MeOH = 90:10) afforded alcohol **28b** (257 mg, 0.624 mmol, 2 steps quant.) as a white amorphous solid. $[\alpha]_{405}$

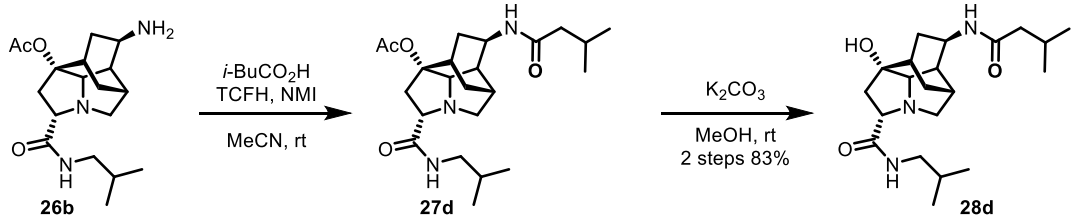
$^{26.0}$ + 16.6 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (t, *J* = 6.7 Hz, 1H), 7.35-7.25 (m, 5H), 5.51 (m, 1H), 4.47-4.30 (m, 3H), 3.54 (dd, *J* = 9.9, 4.4 Hz, 1H), 3.26-3.23 (m, 1H), 3.01 (d, *J* = 5.0 Hz, 1H), 2.73 (brs, 1H), 2.61-2.46 (m, 2H), 2.37 (dd, *J* = 14.6, 4.5 Hz, 1H), 2.32 (m, 1H), 2.22 (d, *J* = 11.2 Hz, 1H), 2.12-1.95 (m, 4H), 1.85-1.78 (m, 2H), 1.26 (d, *J* = 13.8 Hz, 1H), 0.94-0.91 (m, 6H), 0.89-0.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 172.2, 138.5, 128.8, 127.7, 127.5, 82.2, 72.4, 70.5, 65.9, 46.3, 43.5, 43.4, 43.1, 41.6, 34.5, 31.8, 31.3, 30.0, 26.4, 22.6, 22.5; FT-IR (neat): 3409, 3310, 3085, 3063, 3029, 2954, 2927, 2869, 1643, 1521, 1454, 1359, 1309, 1263, 1214, 1113, 734, 698, 669 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{34}N_3O_3^+$ [M + H$^+$] 412.2595, found 412.2599.

Preparation of alcohol 28c:



Following the representative procedure using amine **26b** (225 mg, 0.671 mmol, 1.0 equiv.) and phenylacetic acid (110 mg, 0.805 mmol, 1.2 equiv.), purification by silica gel column chromatography (hexane:EtOAc = 5:95 to EtOAc:MeOH = 90:10) afforded alcohol **28c** (241 mg, 0.586 mmol, 2 steps 87%) as a white amorphous solid. $[\alpha]_{405}^{27.0}$ – 49.0 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (t, *J* = 5.5 Hz, 1H), 7.38-7.24 (m, 5H), 5.34 (d, *J* = 7.6 Hz, 1H), 4.33-4.27 (m, 1H), 3.56 (s, 2H), 3.45 (dd, *J* = 9.9, 4.2 Hz, 1H), 3.24 (dd, *J* = 11.2, 3.6 Hz, 1H), 3.12-2.98 (m, 2H), 2.95 (d, *J* = 4.9 Hz, 1H), 2.55-2.48 (m, 1H), 2.45-2.39 (m, 1H), 2.35-2.30 (m, 1H), 2.29 (dd, *J* = 14.6, 4.3 Hz, 1H), 2.17 (d, *J* = 11.2 Hz, 1H), 1.81-1.71 (m, 3H), 1.65-1.59 (m, 1H), 1.20-1.17 (d, *J* = 14.2 Hz, 1H), 0.91 (s, 3H), 0.90 (s, 3H), 0.72-0.68 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 170.6, 135.2, 129.4, 129.2, 127.5, 82.2, 72.4, 70.4, 65.7, 46.6, 44.0, 43.2, 43.0, 41.9, 34.3, 31.7, 31.0, 29.9, 28.7, 20.31, 20.28; IR (neat): 3412, 3299, 3086, 3061, 3027, 2956, 2925, 2869, 1644, 1529, 1465, 1264, 1211, 1099, 1031, 729, 696 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{34}N_3O_3^+$ [M + H$^+$] 412.2595, found 412.2602.

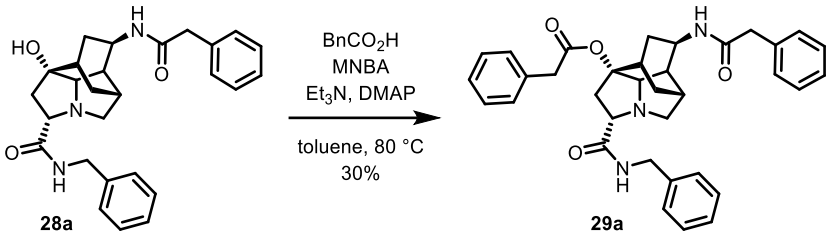
Preparation of alcohol 28d:



Following the representative procedure using amine **26b** (209 mg, 0.623 mmol, 1.0 equiv.) and isovaleric acid (83.0 µL, 0.752 mmol, 1.2 equiv.), purification by silica gel column chromatography (hexane:EtOAc = 5:95 to EtOAc:MeOH = 90:10) afforded alcohol **28d** (196 mg, 0.518 mmol, 2 steps 83%) as a white amorphous solid. $[\alpha]_{405}^{26.8}$ – 1.9 (c 0.756 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (t, *J* = 5.8 Hz, 1H), 5.44 (d, *J* = 7.5 Hz, 1H), 4.38-4.32 (m, 1H), 3.49 (dd, *J* = 10.0, 4.3 Hz, 1H), 3.29 (dd, *J* = 11.2, 3.6 Hz, 1H), 3.13-2.98 (m, 3H), 2.62-2.56 (m, 1H), 2.48 (dd, *J* = 14.6, 10.1 Hz, 1H), 2.41-2.38 (m, 1H), 2.31 (dd, *J* = 14.6, 4.4 Hz, 1H), 2.24 (d, *J* = 11.2 Hz, 1H), 2.15-

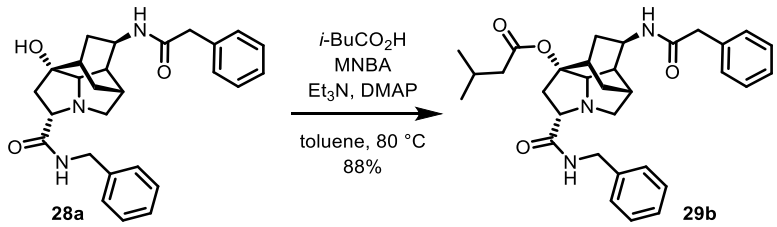
1.97 (m, 4H), 1.85-1.73 (m, 3H), 1.29-1.25 (m, 1H), 0.95-0.85 (m, 13H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2, 172.2, 82.3, 72.5, 70.5, 65.9, 46.6, 46.4, 43.5, 43.2, 41.6, 34.5, 31.8, 31.3, 30.0, 28.7, 26.4, 22.6, 22.5, 20.32, 20.29; IR (neat): 3307, 3064, 2956, 2926, 2869, 1642, 1530, 1465, 1367, 1214, 1096, 1032, 749 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{36}N_3O_3^+$ [M + H$^+$] 378.2751, found 378.2759.

Representative procedure for preparation of ester 29a-h:



Following the slightly modified procedure reported in the literature,[6] to a mixture of alcohol **28a** (41.9 mg, 0.0940 mmol, 1.0 equiv.), phenylacetic acid (25.6 mg, 0.188 mg, 2.0 equiv.) and DMAP (1.4 mg, 0.011 mmol, 0.12 equiv.) in toluene (500 μL) was added Et_3N (39.0 μL, 0.280 mmol, 3.0 equiv.) and MNBA (69.9 mg, 0.203 mmol, 2.0 equiv.). After being stirred for 1.5 h under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by GPC to afford ester **29a** (15.9 mg, 0.0282 mmol, 75%) as a colorless oil. $[\alpha]_{405}^{28.4}$ – 26.1 (c 1.00 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (t, *J* = 5.7 Hz, 1H), 7.37-7.23 (m, 15H), 5.22 (d, *J* = 7.6 Hz, 1H), 4.48 (dd, *J* = 14.8, 6.3 Hz, 1H), 4.40 (dd, *J* = 14.8, 5.7 Hz, 1H), 4.14-4.09 (m, 1H), 3.60-3.51 (m, 5H), 3.22-3.18 (m, 2H), 2.74 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.59 (dd, *J* = 15.5, 4.6 Hz, 1H), 2.42 (brs, 1H), 2.28-2.26 (m, 1H), 2.19 (d, *J* = 11.2 Hz, 1H), 1.79-1.73 (m, 2H), 1.66-1.59 (m, 2H), 1.14 (d, *J* = 14.7 Hz, 1H), 0.58 (ddd, *J* = 14.1, 5.6, 2.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 170.59, 170.58, 138.6, 135.1, 134.0, 129.3, 129.2, 128.82, 128.75, 127.7, 127.6, 127.5, 127.3, 90.0, 71.0, 70.6, 66.0, 44.0, 43.3, 42.8, 42.0, 41.5, 40.0, 31.2, 30.9, 30.6, 29.7; IR (neat): 3308, 3084, 3059, 3028, 2871, 1731, 1644, 1519, 1454, 1256, 1160, 1076, 1018, 728, 697 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{38}N_3O_4^+$ [M + H$^+$] 564.2857, found 564.2863.

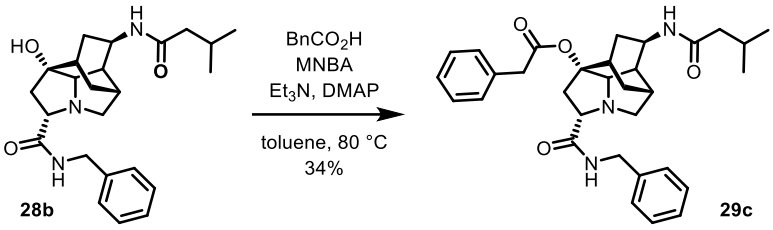
Preparation of ester 29b:



Following the representative procedure using alcohol **28a** (40.1 mg, 0.0900 mmol, 1.0 equiv.) and isovaleric acid (20.0 μL, 0.181 mmol, 2.0 equiv.), purification by PTLC (hexane:acetone = 65:35) to afford ester **29b** (41.8 mg, 0.0789 mmol, 88%) as a colorless oil. $[\alpha]_{405}^{27.5}$ + 32.4 (c 1.00 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (t, *J* = 5.3 Hz, 1H), 7.37-7.23 (m, 10H), 5.37 (d, *J* = 7.6 Hz, 1H), 4.53 (dd, *J* = 14.8, 6.7 Hz, 1H), 4.36 (dd, *J* = 14.9, 5.5 Hz,

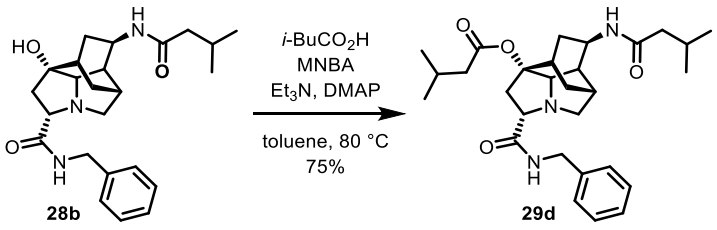
1H), 4.27-4.23 (m, 1H), 3.59 (dd, *J* = 10.2, 4.3 Hz, 1H), 3.55 (s, 2H), 3.22-3.20 (m, 2H), 2.75 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.57 (dd, *J* = 15.5, 4.4 Hz, 1H), 2.49 (brs, 1H), 2.29-2.27 (m, 1H), 2.20 (d, *J* = 11.2 Hz, 1H), 2.16-1.98 (m, 4H), 1.82-1.80 (m, 1H), 1.69-1.64 (m, 1H), 1.17 (d, *J* = 14.6 Hz, 1H), 097-0.92 (m, 6H), 0.74 (ddd, *J* = 14.0, 5.3, 2.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 172.2, 170.7, 138.7, 135.0, 129.4, 129.2, 128.8, 127.7, 127.6, 127.5, 89.4, 77.4, 71.0, 70.7, 65.9, 44.0, 43.8, 43.2, 42.9, 41.6, 40.0, 31.19, 31.15, 30.7, 29.7, 25.7, 22.60, 22.57; FT-IR (neat): 3299, 3084, 3060, 3028, 3005, 2956, 2930, 2870, 1729, 1644, 1519, 1519, 1454, 1361, 1296, 1255, 1167, 1077, 748, 729, 697 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{40}N_3O_6^+$ [M + H$^+$] 530.3013, found 530.3014.

Preparation of ester 29c:



Following the representative procedure using alcohol **28b** (42.3 mg, 0.103 mmol, 1.0 equiv.) and phenylacetic acid (28.0 mg, 0.206 mg, 2.0 equiv.), purificaton by GPC afforded ester **29c** (18.4 mg, 0.0347 mmol, 34%) as a colorless oil. $[\alpha]_{405}^{28.1}$ – 6.73 (c 0.728 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (t, *J* = 5.8 Hz, 1H), 7.37-7.22 (m, 10H), 5.30 (d, *J* = 7.6 Hz, 1H), 4.49 (dd, *J* = 14.9, 6.3 Hz, 1H), 4.41 (dd, *J* = 14.9, 5.7 Hz, 1H), 4.52-4.38 (m, 1H), 3.63-3.52 (m, 3H), 3.27-3.23 (m, 2H), 2.79 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.60 (dd, *J* = 15.5, 4.7 Hz, 1H), 2.48 (brs, 1H), 2.35-2.32 (m, 1H), 2.25 (d, *J* = 11.2 Hz, 1H), 2.13-1.95 (m, 4H), 1.85-1.76 (m, 2H), 1.22 (d, *J* = 14.7 Hz, 1H), 0.95 (d, *J* = 4.9 Hz, 3H), 0.93 (d, *J* = 4.9 Hz, 3H), 0.74 (ddd, *J* = 14.0, 5.8, 2.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 172.1, 170.6, 138.6, 134.1, 129.4, 128.83, 128.76, 127.8, 127.5, 127.3, 90.1, 71.1, 70.7, 66.1, 46.3, 43.3, 43.1, 42.0, 41.3, 40.1, 31.4, 31.1, 30.8, 29.8, 26.4, 22.6, 22.5; FT-IR (neat): 3310, 3085, 3062, 3029, 2954, 2928, 2869, 1732, 1644, 1519, 1455, 1255, 1219, 1159, 1128, 1076, 1018, 750, 726, 698 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{40}N_3O_4^+$ [M + H$^+$] 530.3013, found 530.3018.

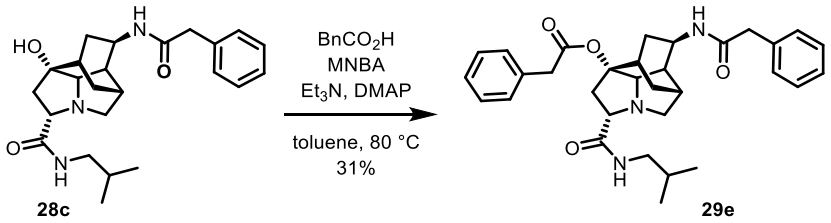
Preparation of ester 29d:



Following the representative procedure using alcohol **28b** (42.3 mg, 0.103 mmol, 1.0 equiv.) and isovaleric acid (23.0 μL, 0.208 mmol, 2.0 equiv.), purified by PTLC (hexane:acetone = 65:35) afforded ester **29d** (38.5 mg, 0.0777 mmol, 75%) as a white amorphous solid. $[\alpha]_{405}^{27.6}$ + 67.4 (c 1.00 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (t, *J* = 5.9 Hz, 1H), 7.35-7.27 (m, 5H), 5.49 (d, *J* = 7.6 Hz, 1H), 4.53 (dd, *J* = 14.9, 6.5 Hz, 1H), 4.36 (dd, *J* = 14.9, 5.6 Hz, 1H), 4.32-4.26 (m, 1H), 3.62 (dd, *J* = 10.3, 4.4 Hz, 1H), 3.28-3.24 (m, 2H), 2.79 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.60-2.56 (m, 2H), 2.34-2.33 (m, 1H), 2.26 (d, *J* = 11.2 Hz, 1H), 2.19-1.97 (m, 8H), 1.87-1.82 (m, 1H), 1.27-1.23 (m, 1H), 0.97-0.89 (m, 13H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 172.3, 172.2, 138.6, 128.8, 127.7, 127.5, 89.5, 71.0, 70.8,

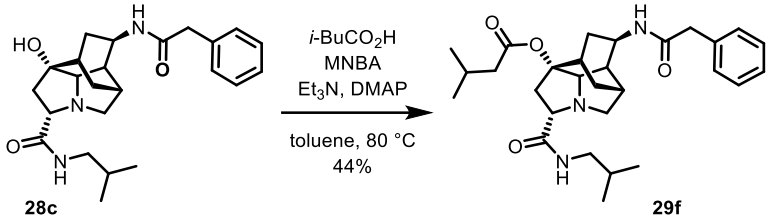
66.1, 46.3, 43.8, 43.2, 43.1, 41.3, 40.2, 31.3, 30.9, 29.9, 26.4, 25.7, 22.61, 22.57, 22.5; IR (neat): 3309, 3196, 3085, 3063, 3029, 2956, 2930, 2870, 1729, 1643, 1519, 1464, 1367, 1296, 1178, 1119, 1077, 1019, 730, 699 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{42}N_3O_4^+$ [M + H^+] 496.3170, found 496.3173.

Preparation of ester 29e:



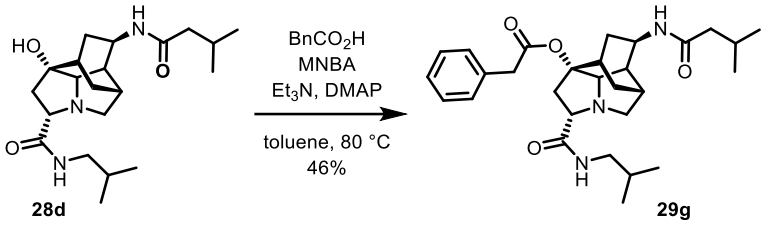
Following the representative procedure using alcohol **28c** (44.1 mg, 0.107 mmol, 1.0 equiv.) and phenylacetic acid (21.9 mg, 0.161 mg, 1.5 equiv.), purification by GPC afforde ester **29e** (17.6 mg, 0.0332 mmol, 31%) as a colorless oil. $[\alpha]_{405}^{25.4}$ – 66.9 (c 1.00 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (t, *J* = 6.1 Hz, 1H), 7.38-7.21 (m, 10H), 5.22 (d, *J* = 7.6 Hz, 1H), 4.16-4.11 (m, 1H), 3.56-3.51 (m, 5H), 3.25-3.21 (m, 2H), 3.16-3.12 (m, 1H), 3.00-2.95 (m, 1H), 2.73 (dd, *J* = 15.6, 10.3 Hz, 1H), 2.50 (dd, *J* = 15.4, 4.7 Hz, 1H), 2.43 (brs, 1H), 2.35-2.33 (m, 1H), 2.20 (d, *J* = 11.2 Hz, 1H), 1.82-1.71 (m, 3H), 1.64-1.59 (m, 1H), 1.13 (d, *J* = 14.7 Hz, 1H), 0.92 (s, 3H), 0.90 (s, 3H), 0.58 (ddd, *J* = 14.1, 5.7, 2.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 170.7, 170.6, 135.1, 134.0, 129.4, 129.3, 129.2, 128.7, 127.6, 127.2, 90.0, 71.1, 70.7, 65.9, 46.5, 44.0, 42.9, 42.0, 41.6, 40.2, 31.2, 30.9, 30.5, 29.7, 28.7, 20.3, 20.2; IR (neat): 3298, 3085, 3063, 3028, 2955, 2929, 2870, 1732, 1644, 1524, 1252, 1159, 1074, 728, 696, 669 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{40}N_3O_4^+$ [M + H^+] 530.3013, found 530.3021.

Preparation of ester 29f:



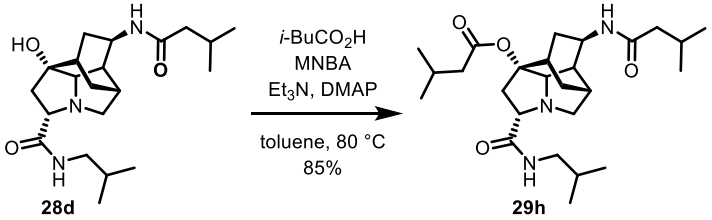
Following the representative procedure using alcohol **28c** (41.7 mg, 0.101 mmol, 1.0 equiv.) and isovaleric acid (17.0 μL, 0.154 mmol, 1.5 equiv.), purification by PTLC (hexane:acetone = 65:35) afforded ester **29f** (22.1 mg, 0.0446 mmol, 44%) as a colorless oil. $[\alpha]_{405}^{26.4}$ – 40.2 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (t, *J* = 5.8 Hz, 1H), 7.38-7.24 (m, 5H), 5.34 (d, *J* = 7.6 Hz, 1H), 4.30-4.24 (m, 1H), 3.57 (s, 2H), 3.53 (dd, *J* = 10.3, 4.5 Hz, 1H), 3.27-3.14 (m, 3H), 2.97-2.93 (m, 1H), 2.74 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.51-2.46 (m, 2H), 2.36-2.33 (m, 1H), 2.21 (d, *J* = 11.1 Hz, 1H), 2.13-1.96 (m, 4H), 1.84-1.73 (m, 2H), 1.70-1.63 (m, 1H), 1.17 (d, *J* = 14.6, 1H), 0.91-0.90 (m, 12H), 0.75-0.70 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 172.3, 170.7, 135.0, 129.4, 129.2, 127.6, 89.4, 71.1, 70.9, 65.9, 46.4, 44.0, 43.8, 42.9, 41.7, 40.3, 31.20, 31.16, 30.7, 29.7, 28.8, 25.7, 22.6, 22.5, 20.22, 20.15; IR (neat): 3297, 3082, 3062, 3028, 2957, 2927, 2870, 1730, 1644, 1527, 1465, 1367, 1296, 1167, 1121, 730, 697 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{42}N_3O_4^+$ [M + H^+] 496.3170, found 496.3178.

Preparation of ester 29g:



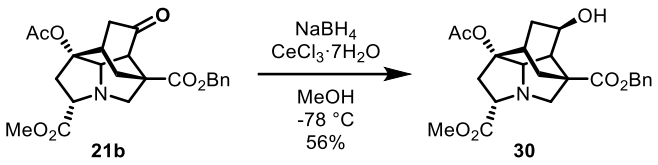
Following the representative procedure using alcohol **28d** (40.9 mg, 0.108 mmol, 1.0 equiv.) and phenylacetic acid (29.4 mg, 0.216 mg, 2.0 equiv.) purification by GPC afforded ester **29g** (24.8 mg, 0.0500 mmol, 46%) as a colorless oil. $[\alpha]_{405}^{25.3}$ – 70.0 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (t, *J* = 6.0 Hz, 1H), 7.31-7.20 (m, 5H), 5.34 (d, *J* = 7.6 Hz, 1H), 4.21-4.14 (m, 1H), 3.57-3.49 (m, 3H), 3.29-3.25 (m, 2H), 3.19-3.12 (m, 1H), 3.01-2.95 (m, 1H), 2.78 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.53-2.48 (m, 2H), 2.41-2.38 (m, 1H), 2,25 (d, *J* = 11.1 Hz, 1H), 2.16-1.96 (m, 4H), 1.81-1,74 (m, 3H), 1.20 (d, *J* = 14.8 Hz, 1H), 0.95 (d, *J* = 4.4 Hz, 3H), 0.94 (d, *J* = 4.4 Hz, 3H), 0.92 (s, 3H), 0.90 (s, 3H), 0.73 (ddd, *J* = 14.1, 5.8, 1.92 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 172.2, 170.6, 134.0, 129.3, 128.7, 127.2, 90.0, 77.4, 71.2, 70.8, 66.1, 46.3, 43.1, 42.0, 41.3, 40.3, 31.3, 31.1, 29.8, 28.7, 26.4, 26.3, 22.6, 22.5, 20.3, 20.2; IR (neat): 3306, 3089, 3064, 3030, 2955, 2929, 2869, 1732, 1643, 1527, 1455, 1253, 1219, 1159, 1075, 1018, 727, 695 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{42}N_3O_4^+$ [M + H$^+$] 496.3170, found 496.3177.

Preparation of ester 29h:



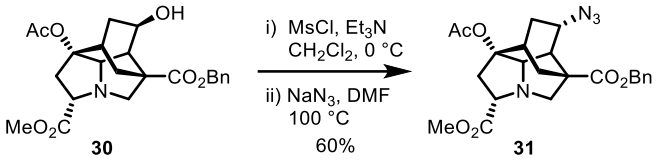
Following the representative procedure using alcohol **28d** (42.1 mg, 0.112 mmol, 1.0 equiv.) and isovaleric acid (25.0 μL, 0.226 mmol, 2.0 equiv.), purification by PTLC (hexane:acetone = 65:35) afforded ester **29h** (43.9 mg, 0.0951 mmol, 85%) as a colorless oil. $[\alpha]_{405}^{25.6}$ – 17.8 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (t, *J* = 6.1 Hz, 1H), 5.45 (d, *J* = 7.6 Hz, 1H), 4.35-4.28 (m, 1H), 3.56 (dd, *J* = 10.3, 4.6 Hz, 1H), 3.30 (dd, *J* = 11.1, 3.5 Hz, 1H), 3.26 (d, *J* = 5.1 Hz, 1H), 3.22-3.15 (m, 1H), 2.98-2.92 (m, 1H), 2.79 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.57 (brs, 1H), 2.50 (dd, *J* = 15.5, 4.6 Hz, 1H), 2.42-2.39 (m, 1H), 2.27 (d, *J* = 11.1 Hz, 1H), 2.17-1.96 (m, 8H), 1.88-1.73 (m, 2H), 1.27-1.23 (m, 1H), 0.96-0.87 (m, 19H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 172.31, 172.27, 89.5, 71.1, 71.0, 66.0, 46.4, 46.3, 43.8, 41.1, 40.4, 31.4, 30.8, 29.9, 28.8, 26.4, 25.7, 22.6, 25.7, 22.62, 22.55. 22.5, 20.23, 20.16; IR (neat): 3305, 3061, 2957, 2931, 2870, 1731, 1643, 1528, 1465, 1367, 1296, 1254, 1167, 1120, 1089, 1019, 750, 674 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{44}N_3O_4^+$ [M + H$^+$] 462.3326, found 496.3334.

Preparation of alcohol 30:



To a solution of ketone **21b** (328 mg, 0.767 mmol, 10 equiv.) and $CeCl_3 \cdot 7H_2O$ (765 mg, 2.05 mmol, 2.7 equiv.) in MeOH (6.0 mL) was added $NaBH_4$ (63.3 mg, 1.67 mmol, 2.2 equiv.) at -78 ℃ and stirred for 40 min under argon atmosphere. The reaction mixture was diluted with saturated aqueous NH_4Cl, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 30:70 to 25:75) to afford alcohol **30** (184 mg, 0.428 mmol, 56%) as a white amorphous solid. $[\alpha]_D^{19.5}$ – 1.5 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 5H), 5.24 (s, 2H), 4.15 (brs, 1H), 3.74-3.67 (m, 5H), 3.51 (d, *J* = 5.0 Hz, 1H), 2.89-2.83 (m, 2H), 2.74 (dd, *J* = 15.4, 9.9 Hz, 1H), 2.64 (brs, 1H), 2.50 (d, *J* = 11.2 Hz, 1H), 2.46-2.38 (m, 2H), 2.13-2.07 (m, 1H), 2.02 (s, 3H), 1.47 (d, *J* = 14.9 Hz, 1H), 1.21 (dd, *J* = 14.0, 3.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.7, 174.2, 170.4, 135.5, 128.8, 128.6, 128.2, 88.7, 72.0, 69.8, 69.2, 67.3, 63.7, 52.5, 48.3, 46.7, 39.8, 34.0, 33.7, 31.3, 21.5; IR (neat, cm^{-1}): 3493, 3091, 3067, 3033, 3003, 2951, 2884, 1731, 1455, 1435, 1371, 1247, 1092, 1040, 749, 699; HRMS (ESI) calcd for $C_{23}H_{28}NO_7^+$ [M + H^+] 430.1860, found 430.1861.

Preparation of azide 31

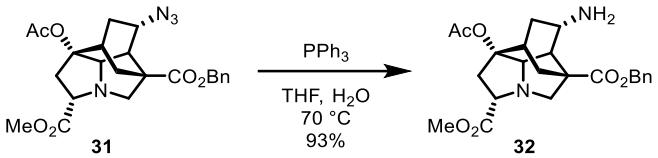


To a solution of alcohol **30** (2.79 g, 6.50 mmol, 1.0 equiv.) and Et_3N (2.70 mL, 19.4 mmol, 3.0 eqiv.) in CH_2Cl_2 (26.0 mL) was added methanesulfonyl chloride (1.00 mL, 12.9 mmol, 2.0 equiv.) at 0 ℃. After being stirred for 20 min under argon atmosphere at the same temperature, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure to afford curde mesylate (3.30 g) as a yellow amorphous solid.

To a solution of the crude mesylate (3.30 g) in DMF (20 mL) was added NaN_3 (1.27 g, 19.5 mmol, 3.0 equiv.) and stirred at 100 ℃ under argon atmosphere. After being stirred for 10.5 h, the reaction mixture was heated to 100 ℃ and further stirred for 40 min. After this time, the reaction mixture was diluted with ice cooled water, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 70:30 to hexane:EtOAc = 55:45) to afford azide **31** (1.77 g, 3.89 mmol, 2 steps 60%) as a yellow oil. $[\alpha]_D^{21.5}$ + 8.5 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 5.15-5.09 (m, 2H), 3.98 (dt, *J* = 10.1, 3.2 Hz, 1H), 3.76-3.67 (m, 6H), 2.87 (t, *J* = 4.1 Hz, 1H), 2.69-2.62 (m, 2H), 2.54 (dd, *J* =

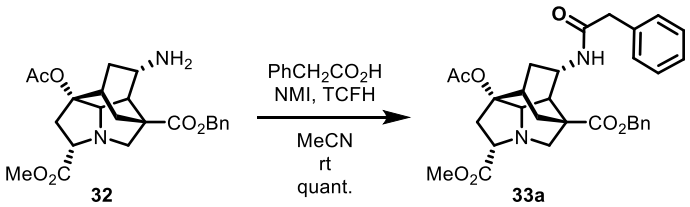
15.5, 3.7 Hz, 1H), 2.45 (d, J = 11.2 Hz, 1H), 2.19 (d, J = 14.8 Hz, 1H), 2.06 (s, 3H), 1.76-1.69 (m, 1H), 1.61 (dd, J = 14.7, 2.8 Hz, 1H), 1.43 (d, J = 14.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 173.0, 170.7, 135.5, 128.8, 128.6, 128.1, 88.2, 68.8, 68.6, 68.2, 67.1, 52.6, 52.0, 47.6, 45.4, 40.0, 33.1, 31.7, 27.5, 21.6; IR (neat, cm^{-1}): 3091, 3065, 3004, 2951, 2886, 2853, 2102, 1730, 1455, 1436, 1370, 1248, 1090, 749, 699; HRMS (ESI) calcd for $C_{23}H_{27}N_4O_6^+$ [M + H$^+$] 455.1925, found 455.1925.**:**

Preparation of amine 32:



To a solution of azide **31** (111 mg, 0.244 mmol, 1.0 equiv.) in THF (1.2 mL) and H_2O (120 µL) was added PPh_3 (96.0 mg, 0.366 mmol, 1.5 equiv.). The reaction mixture was stirred at 70 °C for 10.5 h under argon atmosphere before being concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc 100% to CH_2Cl_2:MeOH = 90:10) to afford amine **32** (97.1 mg, 0.227 mmol, 93%) as a yellow oil. $[\alpha]_D^{23.9}$ – 2.3 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.26 (m, 5H), 5.12 (d, J = 12.4 Hz), 5.08 (d, J = 12.4 Hz, 1H), 3.74-3.67 (m, 6H), 3.21 (dt, J = 10.7, 32 Hz, 1H), 2.75-2.67 (m, 3H), 2.50-2.44 (m, 2H), 2.24 (d, J = 14.0 Hz, 1H), 2.05 (s, 3H), 1.82-1.75 (m, 1H), 1.71 (brs, 2H), 1.37-1.26 (m, 2H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4, 173.6, 170.3, 135.7, 128.8, 128.5, 128.1, 89.0, 69.2, 68.9, 68.8, 66.9, 52.5, 50.0, 48.1, 41.9, 40.3, 32.8, 32.18, 32.15, 21.6; IR (neat, cm^{-1}): 3370, 3063, 3031, 2989, 1730, 1455, 1436, 1371, 1246, 1091, 763, 750, 699; HRMS (ESI) calcd for $C_{23}H_{29}N_2O_6^+$ [M + H$^+$] 429.2020, found 429.2022.

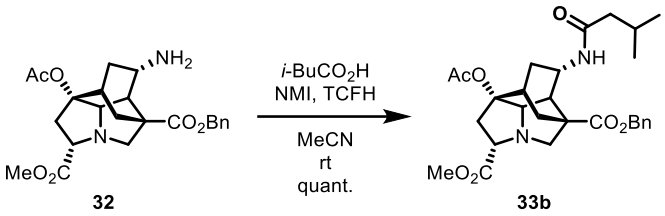
Representative procedure for preparation of amide 33a-c:



To a solution of amine **32** (344 mg, 0.803 mmol, 1.0 equiv.), phenylacetic acid (132 mg, 0.969 mmol, 1.2 equiv.), and *N*-methylimidazole (190 µL, 2.38 mmol, 3.0 equiv.) in MeCN (3.2 mL) was added TCFH (278 mg, 0.991 mmol, 1.2 equiv.). After being stirred for 3 h at room temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:acetone = 80:20 to 65:35) to afford amide **33a** (436 mg, 0.798 mmol, quant.) as a white amorphous solid. $[\alpha]_D^{23.3}$ – 29.9 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.21 (m, 10H), 5.52 (d, J = 9.1 Hz, 1H), 5.16 (d, J = 12.4 Hz, 1H), 5.11 (d, J = 12.4 Hz, 1H), 4.54-4.49 (m, 1H), 3.71 (s, 3H), 3.68-3.52 (m, 4H), 3.32 (d, J = 5.0 Hz, 1H), 2.84-2.82 (m, 1H), 2.69 (dd, J = 15.3, 10.0 Hz, 1H), 2.57 (brs, 1H), 2.44 (d, J = 11.1 Hz, 1H), 2.34 (dd, J = 15.4, 4.9 Hz, 1H), 2.23 (d, J = 14.7 Hz,

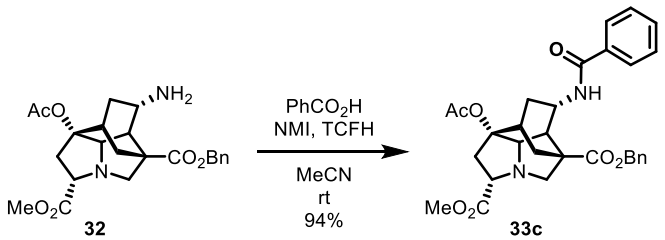
1H), 1.83-1.76 (m, 1H), 1.60 (s, 3H), 1.27 (d, *J* = 14.9 Hz, 1H), 1.85 (dd, J = 14.7, 2.69 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 172.9, 169.8, 169.6, 135.7, 134.9, 129.6, 129.3, 128.7, 128.3, 128.0, 127.6, 88.4, 69.2, 69.0, 68.6, 67.1, 52.4, 47.6, 45.5, 44.0, 40.2, 39.5, 32.4, 31.6, 30.1, 21.1; IR (neat, cm^{-1}): 3415, 3315, 3086, 3061, 3030, 2952, 1731, 1669, 1652, 1508, 1455, 1370, 1246, 1092, 763, 750, 699; HRMS (ESI) calcd for $C_{31}H_{35}N_2O_7^+$ [M + H^+] 547.2439, found 547.2448.

Preparation of amide 33b:



Following the representative procedure using amine **32** (767 mg, 1.79 mmol, 1.0 equiv.) and isovaleric acid (237 μL, 2.15 mmol, 1.2 equiv.), purification by silica gel column chromatography (hexane:acetone = 80:20 to 50:50) to afford amide **33b** (887 mg, 1.73 mmol, quant.) as a white amorphous solid. $[\alpha]_D^{23.3}$ – 31.1 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 5.60 (d, *J* = 8.7 Hz, 1H), 5.15 (d, *J* = 12.4 Hz, 1H), 5.11 (d, *J* = 12.4 Hz, 1H), 4.53-4.47 (m, 1H), 3.71-3.67 (m, 5H), 3.58 (d, *J* = 5.8 Hz, 1H), 2.85-2.84 (m, 1H), 2.75 (dd, *J* = 9.9, 15.4 Hz, 1H), 2.67 (brs, 1H), 2.49-2.44 (m, 2H), 2.30-2.26 (m, 1H), 2.09-1.87 (m, 7H), 1.34-1.24 (m, 2H), 0.94 (d, *J* = 6.5 Hz, 6H); ^{13}C NMR (100 MHz, MeOD) δ 174.3, 172.9, 171.1, 169.6, 135.7, 128.7, 128.3, 128, 89, 69.5, 68.9, 68.5, 67.1, 52.4, 47.7, 46.5, 45.5, 40.3, 39.4, 32.7, 31.7, 30.9, 26.3, 22.6, 22.6, 21.5; IR (neat, cm^{-1}): 3288, 3008, 2980, 2965, 2922, 2841, 2824, 1732, 1654, 1541, 1525, 1456, 1368, 1247, 1218, 1054, 1032, 1013, 796; HRMS (ESI) calcd for $C_{28}H_{37}N_2O_7^+$ [M + H^+] 513.2595, found 513.2602.

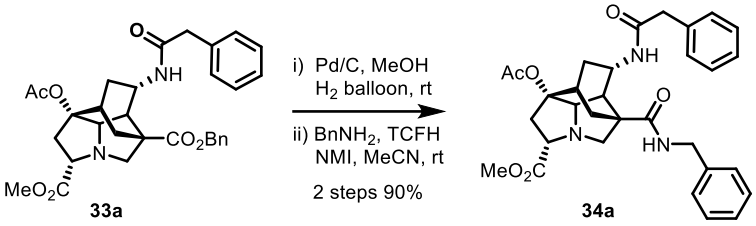
Preparation of amide 33c:



Following the representative procedure using amine **32** (108 mg, 0.252 mmol, 1.0 equiv.) and benzoic acid (37.1 mg, 0.303 mmol, 1.2 equiv.), purification by silica gel column chromatography (hexane:acetone = 80:20 to 70:30) to afford amide **33c** (126 mg, 0.237 mmol, 94%) as a white amorphous solid. $[\alpha]_D^{28.5}$ -43.0 (c 0.853 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.70 (m, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.36-7.29 (m, 5H), 6.39 (d, *J* = 8.6 Hz, 1H), 5.21 (d, *J* = 12.4 Hz, 1H), 5.16 (d, *J* = 12.4 Hz, 1H), 4.73-4.67 (m, 1H), 3.75-3.70 (m, 6H), 3.03 (t, *J* = 4.5 Hz, 1H), 2.81 (dd, *J* = 9.9, 15.4 Hz, 1H), 2.74 (brs, 1H), 2.54-2.48 (m, 2H), 2.34 (d, *J* = 14.6 Hz, 1H), 2.06 (s, 3H), 2.04-1.97 (m, 1H), 1.45-1.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 173, 169.6, 166.3, 135.7, 134.7, 131.7, 128.8, 128.8, 128.4, 128.1, 126.7, 89.2, 69.6, 69.1, 68.7, 67.2, 52.5, 47.6, 45.4, 40.5, 40.2, 32.9, 31.8,

30.9, 21.5; IR (neat, cm^{-1}): 3439, 3062, 3031, 2951, 2884, 1731, 1655, 1519, 1486, 1369, 1245, 1091, 912, 745, 697. HRMS (ESI) calcd for $C_{30}H_{33}N_2O_7^+$ [M + H^+] 533.2282, found 533.2278.

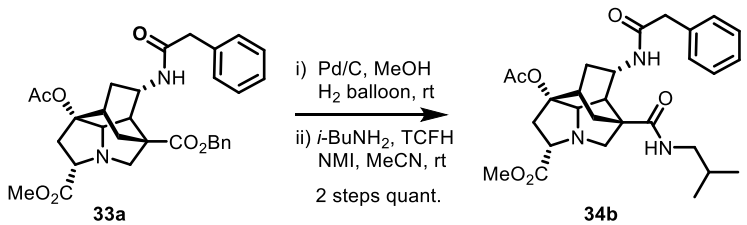
Representative procedure for preparation of amide 34a,b:



To a solution of amide **33a** (403 mg, 0.737 mmol, 1.0 equiv.) in MeOH (3.5 mL) was added Pd/C (46.6 mg, 12wt%) and stirred for 3.5 h at room temperature under H_2 atmosphere. The reaction mixture was passed through a pad of Celite®, and the filtrate was concentrated under reduced pressure to afford crude carboxylic acid.

To a solution of the crude carboxylic acid, *N*-methylimidazole (175 µL, 2.20 mmol, 3.0 equiv.), and benzylamine (100 µL, 0.915 mmol, 1.2 equiv.) in MeCN (3.8 mL) was added TCFH (255 mg, 0.909 mmol, 1.2 equiv.). After being stirred for 1 h at room temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:acetone = 70:30 to 40:60). Further purification with silica gel column chromatography (EtOAc:MeOH = 98:2) afforded amide **34a** (360 mg, 0.660 mmol, 2 steps 90%) as a white amorphous solid. $[\alpha]_D^{23.1}$ – 21.9 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.22 (m, 10H), 6.61 (brs, 1H), 5.37 (d, *J* = 7.6 Hz, 1H), 4.56 (dd, *J* = 14.8, 6.2 Hz, 1H), 4.39-4.34 (m, 2H), 3.72 (s, 3H), 3.68 (dd, *J* = 9.8, 4.2 Hz, 1H), 3.57 (s, 2H), 3.44 (d, J = 11.2 Hz, 1H), 3.38 (d, *J* = 4.9 Hz, 1H), 2.84-2.82 (m, 1H), 2.68 (dd, *J* = 15.6, 9.8 Hz, 1H), 2.62-2.60 (m, 1H), 2.53 (d, *J* = 1.2 Hz, 1H), 2.42 (dd, *J* = 15.4, 4.1 Hz, 1H), 2.18-2.14 (m, 1H), 1.83-1.75 (m, 1H), 1.68 (m, 3H), 1.49 (d, *J* = 15.2 Hz, 1H), 1.03 (dd, J = 14.7, 3.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2, 172.7, 171.2, 169.8, 138.3, 134.6, 129.7, 129.4, 128.8, 127.6, 127.5, 88.5, 69.6, 69.4, 68.7, 52.5, 48.1, 43.81, 43.75, 43.6, 40.5, 39.9, 33.2, 32.0, 28.8, 21.3; IR (neat, cm^{-1}): 3413, 3318, 3085, 3061, 3005, 2950, 2871, 1734, 1647, 1525, 1455, 1369, 1255, 1204, 1171, 843, 763, 749, 699; HRMS (ESI) calcd for $C_{31}H_{36}N_3O_6^+$ [M + H^+] 546.2599, found 546.2606.

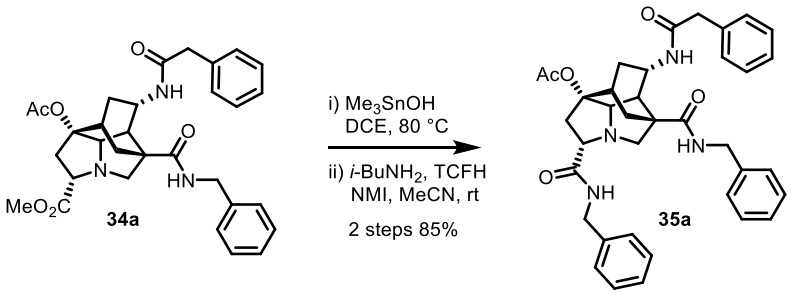
Preparation of amide 34b:



Following the representative procedure using amide **33a** (429 mg, 0.785 mmol, 1.0 equiv.) and isobutylamine (95.0 µL, 0.956 mmol, 1.2 equiv.), purification by silica gel column chromatography (hexane:acetone = 70:30 to EtOAc:MeOH = 97:3) afforded amide **34b** (415 mg, 0.811 mmol, 2 steps quant.) as a white amorphous solid. $[\alpha]_D$

$^{24.7}$ – 6.7 (c 1.00 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.25 (m, 5H), 6.27 (brs, 1H), 5.33 (d, *J* = 7.42 Hz, 1H), 4.34-4.31 (m, 1H), 3.74-3.72 (m, 4H), 3.66-3.57 (m, 2H), 3.39 (d, *J* = 5.5 Hz, 2H), 3.17-3.11 (m, 1H), 3.07-3.01 (m, 1H), 2.84 (m, 1H), 2.74 (dd, *J* = 15.3, 10.0 Hz, 1H), 2.60-2.57 (m, 2H), 2.41 (dd, *J* = 15.6, 4.4 Hz, 1H), 2.08 (d, *J* = 14.8 Hz, 1H), 1.83-1.75 (m, 2H), 1.66 (s, 3H), 1.59 (d, *J* = 15.3 Hz, 1H), 1.02 (dd, *J* = 14.4, 2.6 Hz, 1H), 0.90 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, MeOD) δ 175.5, 175.3, 173.7, 172.0, 136.9, 130.1, 129.8, 128.0, 90.0, 70.1, 68.8, 68.7, 52.7, 49.5, 48.2, 48.1, 45.0, 43.5, 42.0, 40.4, 34.0, 33.4, 30.0, 29.6, 21.4, 20.5; IR (neat, cm^{-1}): 3417, 3297, 3064, 3029, 3004, 2957, 2872, 2844, 1734, 1655, 1530, 1371, 1256, 1052, 1032, 842; HRMS (ESI) calcd for $C_{28}H_{38}N_3O_6^+$ [M + H^+] 512.2755, found 512.2757.

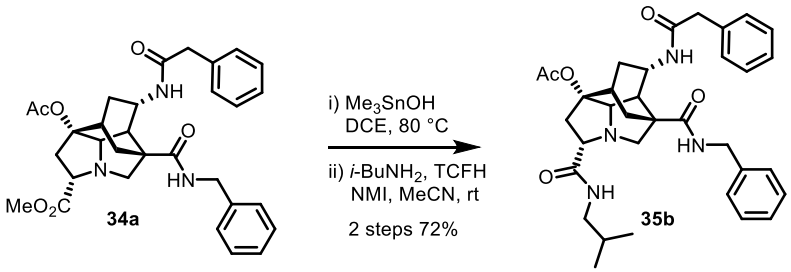
Representative procedure for preparation of amide 35a-d:



To a solution of amide **34a** (40.3 mg, 0.0739 mmol, 1.0 equiv.) in 1,2-dichroloethane (500 μL) was added trimethyltin hydroxide (23.5 mg, 0.130 mmol, 1.8 equiv.), and the reaction mixture was stirred for 45 min at 80 °C under an argon atmosphere. After this time, another amount of trimethyltin hydroxide (16.5 mg, 0.913 mmol, 1.3 equiv.) and stirred for additional 3 h. The reaction mixture was passed through a pad of silica gel with MeOH, and the filtrate was concentrated under reduced pressure to afford crude carboxylic acid (37.7 mg) as a white solid.

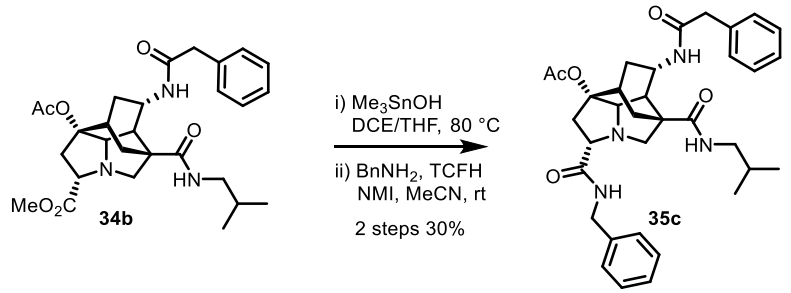
To a solution of the crude carboxylic acid (37.7 mg), *N*-methylimidazole (18.0 μL, 0.228 mmol, 3.1 equiv.), and benzyllamine (10.0 μL, 0.0915 mmol, 1.2 equiv.) in MeCN (500 μL) was added TCFH (30.4 mg, 0.108 mmol, 1.5 equiv.). After being stirred for 1 h at room temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:acetone = 70:30 to EtOAc:MeOH = 97:3) to afford amide **35a** (28.9 mg, 0.0466 mmol, 2 steps 85%) as a white amorphous solid. $[\alpha]_D$ $^{22.9}$ – 1.7 (c 1.00 in MeOH); ^{1}H NMR (400 MHz, MeOD) δ 7.37-7.21 (m, 15H), 4.49-4.30 (m, 5H), 3.71 (dd, *J* = 10.1, 3.8 Hz, 1H), 3.55 (s, 2H), 3.49-3.44 (m, 2H), 2.83 (dd, *J* = 4.9, 3.1 Hz, 1H), 2.74 (dd, *J* = 15.4, 10.2 Hz, 1H), 2.62-2.53 (m, 3H), 2.15 (d, *J* = 13.5 Hz, 1H), 1.89-1.82 (m, 4H), 1.63 (d, *J* = 14.8 Hz, 1H), 1.38-1.34 (m, 1H); ^{13}C NMR (100 MHz, MeOD) δ 176.4, 175.2, 173.5, 171.8, 140.1, 140.0, 136.9, 130.1, 129.8, 129.6, 129.5, 128.4, 128.3, 128.2, 128.1, 90.3, 70.6, 69.8, 69.0, 49.7, 45.3, 44.2, 43.9, 43.7, 42.0, 41.0, 33.7, 33.5, 30.3, 21.4; IR (neat, cm^{-1}): 3408, 3313, 3085, 3058, 3026, 3006, 2938, 2844, 1734, 1653, 1519, 1454, 1367, 1247, 1052, 1032, 843, 748, 697; HRMS (ESI) calcd for $C_{37}H_{41}N_4O_5^+$ [M + H^+] 621.3071, found 621.3079.

Preparation of amide 35b:



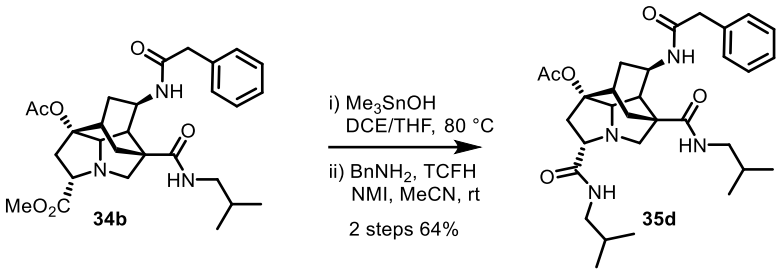
Following the representative procedure using amide **34a** and isobutylamine (11.0 μL, 0.110 mmol, 1.3 equiv.), purification by GPC to affordded amide **35b** (36.5 mg, 0.662 mmol, 2 steps 72%) as a white amorphous solid. $[\alpha]_D^{21.7}$ – 9.7 (c 0.58 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (t, *J* = 6.1 Hz, 1H), 7.37-7.21 (m, 10H), 6.53 (t, *J* = 5.6 Hz, 1H), 5.33 (d, *J* = 7.5 Hz, 1H), 4.56 (dd, *J* = 14.8, 6.0 Hz, 1H), 4.42-4.33 (m, 2H), 3.51 (dd, *J* = 10.3, 4.4 Hz, 1H), 3.39 (d, *J* = 11.0 Hz, 1H), 3.16-2.99 (m, 3H), 2.81 (dd, *J* = 5.1, 3.3 Hz, 1H), 2.73 (dd, *J* = 15.6, 10.3 Hz, 1H), 2.63 (brs, 1H), 2.56-2.50 (m, 2H), 2.17 (d, *J* = 14.0 Hz, 1H), 1.84-1.76 (m, 2H), 1.62 (s, 3H), 1.52 (dt, *J* = 15.2, 3.0 Hz, 1H), 1.04-1.00 (m, 1H), 0.93 (dd, *J* = 6.7, 0.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 172.4, 171.1, 169.4, 138.3, 134.6, 129.7, 129.4, 128.9, 127.9, 127.8, 127.6, 88.8, 70.1, 69.3, 69.1, 48.3, 46.6, 43.9, 43.8, 43.7, 40.6, 40.0, 33.2, 332.0, 28.7, 21.2, 20.3, 20.2; IR (neat, cm^{-1}): 3407, 3310, 3082, 3061, 3028, 2956, 2937, 2923, 2870, 2843, 1733, 1651, 1524, 1238, 1053, 1032, 699; HRMS (ESI) calcd for $C_{34}H_{43}N_4O_5^+$ [M + H^+] 587.3228, found 587.3236.

Preparation of amide 35c:



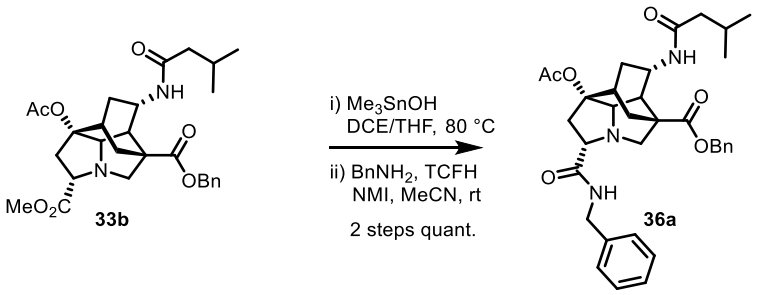
Following the representative procedure using amide **34b** (51.1 mg, 0.0999 mmol, 1.0 equiv.) and benylamine (14.0 μL, 0.128 mmol, 1.3 equiv.) purification by PTLC (EtOAc:MeOH = 97:3) afforded amide **35c** (17.4 mg, 0.0297 mmol, 2 steps 30%) as a white amorphous solid. $[\alpha]_D^{21.1}$ + 2.5 (c 1.00 in MeOH); ^{1}H NMR (400 MHz, MeOD) δ 7.36-7.20 (m, 10H), 4.46 (d, *J* = 14.9 Hz, 1H), 4.36 (d, *J* = 14.9 Hz, 1H), 4.27 (dt, *J* = 10.8, 3.4 Hz, 1H), 3.70 (dd, *J* = 10.1, 3.7 Hz, 1H), 3.53 (s, 2H), 3.45 (d, *J* = 5.0 Hz, 1H), 3.40 (d, *J* = 10.9 Hz, 1H), 3.05-2.96 (m, 2H), 2.78 (dd, *J* = 4.9, 3.1 Hz, 1H), 2.73 (dd, *J* = 15.6, 10.1, 1H), 2.60-2.52 (m, 3H), 2.10 (d, *J* = 14.4 Hz, 1H), 1.88-1.76 (m, 5H), 1.63 (d, *J* = 14.8 Hz, 1H), 1.35 (dd, *J* = 14.4, 3.2 Hz, 1H), 0.89 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, MeOD) δ 176.3, 175.3, 173.6, 171.8, 140.1, 136.9, 130.1, 129.8, 129.6, 128.5, 128.3, 128.1, 90.4, 70.5, 69.8, 69.1, 49.8, 48.1, 45.1, 44, 43.6, 42.1, 40.9, 33.9, 33.6, 30.1, 29.6, 21.4, 20.5; IR (neat, cm^{-1}): 3416, 3319, 3064, 3030, 3003, 2955, 2922, 2870, 2844, 2824, 1733, 1653, 1521, 1247, 1053, 1032, 1016, 843; HRMS (ESI) calcd for $C_{34}H_{43}N_4O_5^+$ [M + H^+] 587.3228, found 587.3217.

Preparation of amide 35d:



Following the representative procedure using amide **34b** (53.1 mg, 0.104 mmol, 1.0 equiv.) and benylamine (13.0 μL, 0.130 mmol, 1.2 equiv.), purification by silica gel column chromatography (hexane:acetone = 70:30 to EtOAc:MeOH = 97:3) afforded amide **35d** (37.0 mg, 0.0669 mmol, 2 steps 64%) as a white amorphous solid. $[\alpha]_D^{21.5}$ – 10.0 (c 1.00 in MeOH); ^{1}H NMR (400 MHz, MeOD) δ 7.67 (t, *J* = 5.7 Hz, 1H), 7.34-7.23 (m, 5H), 4.29 (dt, *J* = 10.9, 3.4 Hz, 1H), 3.64 (dd, *J* = 10.1, 3.8 Hz, 1H), 3.55 (s, 2H), 3.44 (d, *J* = 4.9 Hz, 1H), 3.41 (d, *J* = 11.0 Hz, 1H), 3.12-2.96 (m, 3H), 2.81-2.79 (m, 1H), 2.71 (dd, *J* = 15.3, 10.2 Hz, 1H), 2.59-2.57 (m, 2H), 2.49 (dd, *J* = 15.4, 3.9 Hz, 1H), 2.10 (d, *J* = 14.6 Hz, 1H), 1.87-1.77 (m, 6H), 1.62 (d, *J* = 14.9 Hz, 1H), 1.38-1.33 (m, 1H), 0.94-0.89 (m, 12H); ^{13}C NMR (100 MHz, MeOD) δ 176.2, 175.3, 173.6, 171.8, 136.9, 130.1, 129.8, 128.1, 90.3, 70.5, 69.8, 69.1, 49.8, 48.1, 47.6, 45.1, 43.6, 42.1, 41.0, 33.8, 33.5, 30.1, 29.8, 29.6, 21.4, 20.5, 20.4; IR (neat, cm^{-1}): 3407, 3328, 3061, 3026, 3003, 2957, 2937, 2870, 2842, 1734, 1650, 1523, 1455, 1237, 1053, 1032, 1017, 844; HRMS (ESI) calcd for $C_{31}H_{45}N_4O_5^+$ [M + H$^+$] 553.3384, found 553.3386.

Representative procedure for preparation of amide 36a-h:

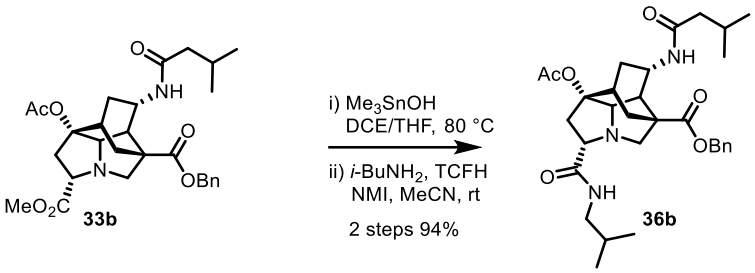


To a solution of amide **33b** (52.6 mg, 0.102 mmol. 1.0 equiv.) in 1,2-dichroloethane (1.0 mL) was added trimethyltin hydroxide (29.1 mg, 0.161 mmol, 1.6 equiv.), and the reaction mixture was stirred for 1 h at 80 °C under an argon atmosphere. After this time, another amount of trimethyltin hydroxide (31.0 mg, 0.171 mmol, 1.7 equiv.). After being stirred for 1 h, the reaction mixture was passed through a pad of silica gel with MeOH, and the filtrate was concentrated under reduced pressure to afford crude carboxylic acid (56.6 mg) as a white solid.

To a solution of the crude carboxylic acid (56.6 mg), *N*-methylimidazole (24.0 μL, 0.304 mmol, 3.0 equiv.), and benzylamine (13.0 μL, 0.119 mmol, 1.2 equiv.) in MeCN (500 μL) was added TCFH (46.9 mg, 0.175 mmol, 1.6 equiv.). After being stirred for 45 min at room temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:acetone = 75:25 to 60:40) to afford

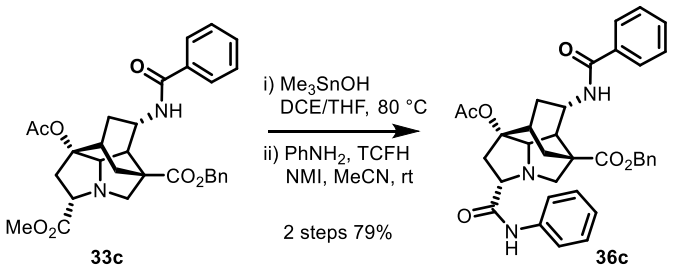
amide **36a** (61.4 mg, 0.104 mmol, 2 steps quant.) as a colorless oil. $[\alpha]_D^{21.7}$ -25.7 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (t, *J* = 5.8 Hz, 1H), 7.35-7.26 (m, 10H), 5.49 (d, *J* = 8.4 Hz, 1H), 5.15 (s, 2H), 4.51-4.38 (m, 3H), 3.63-3.59 (m, 2H), 3.33 (d, *J* = 5.0 Hz, 1H), 2.89 (dd, *J* = 10.4, 15.6 Hz, 1H), 2.83 (t, *J* = 4.4 Hz, 1H), 2.71 (brs, 1H), 2.61 (dd, *J* = 5.1, 15.5 Hz, 1H), 2.49 (d, *J* = 11.2 Hz, 1H), 2.31 (d, *J* = 13.6 Hz, 1H), 2.09-2.04 (m, 4H), 2.00-1.95 (m, 2H), 1.95-1.88 (m, 1H), 1.40 (d, *J* = 14.9 Hz, 1H), 1.28-1.24 (m, 1H), 0.95 (d, *J* = 2.4 Hz, 6H), 0.94 (d, *J* = 2.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 172.8, 171.3, 169.2, 138.5, 135.7, 128.8, 128.8, 128.5, 128.2, 127.9, 127.6, 89.3, 70.5, 69.1, 68.4, 67.2, 47.9, 46.6, 45.6, 43.4, 40.5, 39.6, 32.6, 31.8, 30.6, 26.3, 22.7, 21.5; IR (neat, cm^{-1}): 3316, 3061, 3031, 3008, 2954, 2923, 2867, 2842, 2825, 1731, 1653, 1519, 1508, 1454, 1368, 1094, 1054, 1032, 1014, 783, 731, 698; HRMS (ESI) calcd for $C_{34}H_{42}N_3O_6^+$ [M + H^+] 588.3068, found 588.3062.

Preparation of amide 36b:



Following the representative procedure using amide **33b** (64.9 mg, 0.127 mmol. 1.0 equiv.) and isobutylamine (15.0 μL, 0.150 mmol, 1.2 equiv.), purification by silica gel column chromatography (hexane:acetone = 75:25 to 60:40) afforded amide **36b** (65.9 mg, 0.119 mmol, 2 steps 94%) as a colorless oil. $[\alpha]_D^{22.2}$ -19.0 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (t, *J* = 6.0 Hz, 1H), 7.39-7.30 (m, 5H), 5.50 (d, *J* = 8.4 Hz, 1H), 5.17 (s, 2H), 4.53-4.48 (m, 1H), 3.66 (d, *J* = 11.0 Hz, 1H), 3.55 (dd, *J* = 5.1, 10.3 Hz, 1H), 3.34 (d, *J* = 5.1 Hz, 1H), 3.07 (t, *J* = 6.5 Hz, 2H), 2.91-2.84 (m, 2H), 2.71 (brs, 1H), 2.58-2.49 (m, 2H), 2.33-2.30 (m, 1H), 2.13-2.05 (m, 4H), 2.02-2.00 (m, 2H), 1.95-1.89 (m, 1H), 1.84-1.74 (m, 1H), 1.41-1.38 (m, 1H), 1.27-1.23 (m, 1H), 0.96 (d, *J* = 6.4 Hz, 6H), 0.91 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 172.9, 171.3, 169.2, 135.7, 128.8, 128.5, 128.3, 89.3, 70.5, 69.2, 68.4, 67.3, 47.8, 46.6, 46.6, 45.6, 40.6, 39.7, 32.6, 31.8, 30.6, 28.7, 26.4, 22.7, 22.7, 21.5, 20.3, 20.2; IR (neat, cm^{-1}): 3437, 3322, 3063, 3032, 3005, 2956, 2869, 1732, 1653, 1522, 1464, 1368, 1244, 1059, 1032, 733, 697; HRMS (ESI) calcd for $C_{31}H_{44}N_3O_6^+$ [M + H^+] 554.3225, found 554.3222.

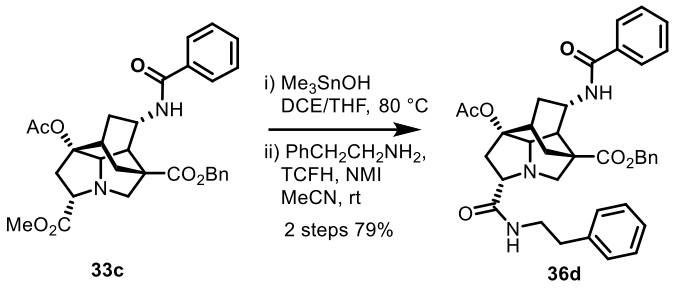
Preparation of amide 36c:



Following the representative procedure using amide **33c** (107 mg, 0.201 mmol. 1.0 equiv.) and aniline (22.0 μL, 0.241 mmol, 1.2 equiv.), purification by silica gel column chromatography (hexane:EtOAc = 60:40 to 50:50) to afford

amide **36c** (94.3 mg, 0.159 mmol, 2 steps 79%) as a white amorphous solid. $[\alpha]_D^{26.2}$ -28.2 (c 1.02 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 7.74-7.71 (m, 2H), 7.62-7.60 (m, 2H), 7.52-7.48 (m, 1H), 7.45-7.29 (m, 9H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.34 (d, *J* = 8.4 Hz, 1H), 5.23 (s, 2H), 4.76-4.70 (m, 1H), 3.79 (d, *J* = 11.2 Hz, 1H), 3.71 (dd, *J* = 5.2, 10.5 Hz, 1H), 3.56 (d, *J* = 5.4 Hz, 1H), 3.12 (t, *J* = 4.6 Hz, 1H), 2.99 (dd, *J* = 10.6, 15.7 Hz, 1H), 2.80 (brs, 1H), 2.69 (dd, *J* = 5.2, 15.6 Hz, 1H), 2.63 (d, *J* = 11.2 Hz, 1H), 2.42-2.39 (m, 1H), 2.07-2.03 (m, 4H), 1.49-1.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 171.6, 169.1, 166.3, 137.6, 135.6, 134.5, 131.8, 129.1, 128.9, 128.8, 128.5, 128.3, 126.7, 124.4, 119.3, 89.4, 70.9, 69.2, 68.5, 67.4, 47.7, 45.5, 40.6, 40.3, 32.7, 31.9, 30.4, 21.5; IR (neat, cm^{-1}): 3438, 3264, 3059, 3031, 2954, 2885, 1730, 1660, 1600, 1519, 1486, 1442, 1240, 1091, 1030, 911, 753, 731, 695; 383.1601; HRMS (ESI) calcd for $C_{35}H_{36}N_3O_6^+$ [M + H^+] 594.2599, found 594.2592.

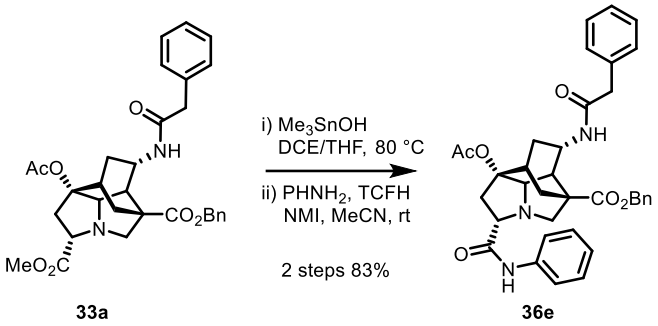
Preparation of amide 36d:



33c **36d**

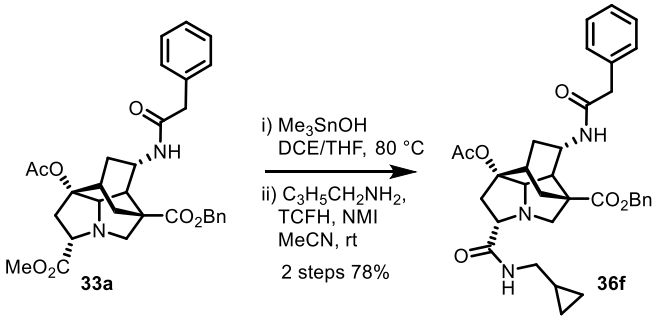
Following the representative procedure using amide **33c** (118 mg, 0.222 mmol. 1.0 equiv.) and 2-phenylethylamine (34.0 μL, 0.269 mmol, 1.2 equiv.), purification by silica gel column chromatography (hexane:acetone = 75:25 to hexane:EtOAc = 30:70) afforded amide **36d** (110 mg, 0.177 mmol, 2 steps 80%) as a white amorphous solid. $[\alpha]_D^{27.4}$ -8.51 (c 0.67 in MeOH); ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.0 Hz, 2H), 7.65 (t, *J* = 5.8 Hz, 1H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.41-7.32 (m, 5H), 7.18-7.12 (m, 4H), 7.01 (t, *J* = 7.3 Hz, 1H), 6.30 (d, *J* = 8.5 Hz, 1H), 5.20 (s, 2H), 4.71-4.67 (m, 1H), 3.58-3.41 (m, 4H), 3.27 (d, *J* = 4.6 Hz, 1H), 2.95-2.74 (m, 5H), 2.51-2.47 (m, 2H), 2.32 (d, *J* = 15.7 Hz, 1H), 2.09 (s, 3H)1.98 (t, *J* = 12.5 Hz, 1H), 1.42-1.38 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 172.9, 169, 166.3, 139, 135.7, 134.6, 131.9, 128.9, 128.9, 128.8, 128.5, 128.5, 128.2, 126.7, 126.5, 89.3, 70.5, 69, 68.3, 67.3, 47.6, 45.3, 40.8, 40.3, 40.3, 35.6, 32.7, 31.8, 30.5, 21.5; IR (neat, cm^{-1}): 3433, 3355, 3082, 3060, 3026, 1725, 1650, 1519, 1485, 1455, 1367, 1240, 1093, 1066, 1032, 842, 749, 699; HRMS (ESI) calcd for $C_{37}H_{39}N_3O_6Na^+$ [M + Na^+] 644.2731, found 644.2729.

Preparation of amide 36e:



Following the representative procedure using amide **33a** (130 mg, 0.238 mmol. 1.0 equiv.) and aniline (30 µL, 0.329 mmol, 1.4 equiv.), purification by silica gel column chromatography (hexane:acetone = 75:25 to hexane:EtOAc = 30:70) afforded amide **36e** (120 mg, 0.197 mmol, 2 steps 83%) as a white amorphous solid. $[\alpha]_D^{28.7}$ -8.7(c 0.904 in MeOH); ^{1}H NMR (400 MHz, MeOD) δ 7.61 (d, *J* = 7.6 Hz, 2H), 7.39-7.24 (m, 10H), 7.18-7.12 (m, 2H), 5.20 (d, *J* = 12.3 Hz, 1H), 5.16 (d, *J* = 12.3 Hz, 1H), 4.31 (td, *J* = 3.2, 10.9 Hz, 1H), 3.80 (dd, *J* = 3.9, 10.1 Hz, 1H), 3.73 (d, *J* = 11.1 Hz, 1H), 3.54 (s, 2H), 3.51 (d, *J* = 5.0 Hz, 1H), 2.86 (dd, *J* = 3.6, 4.8 Hz, 1H), 2.74 (dd, *J* = 10.1, 15.4 Hz, 1H), 2.66 (d, *J* = 11.1 Hz, 1H), 2.61 (dd, *J* = 4.0, 15.4 Hz, 1H), 2.56 (brs, 1H), 2.28 (d, *J* = 15.0 Hz, 1H), 1.90-1.82 (m, 4H), 1.59 (d, *J* = 14.9 Hz, 1H), 1.35 (dd, *J* = 2.9, 14.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 171.5, 170.1, 169.2, 137.6, 135.5, 134.7, 129.6, 129.3, 129.1, 128.7, 128.4, 128.2, 127.7, 124.3, 119.3, 88.7, 70.7, 68.8, 68.3, 67.3, 47.6, 45.4, 44, 40.2, 39.8, 32.4, 31.6, 29.5, 21.0; IR (neat, cm^{-1}): 3451, 3290, 3059, 3028, 2968, 2949, 2880, 1735, 1663, 1599, 1499, 1412, 1367, 1231, 1092, 753, 696; HRMS (ESI) calcd for $C_{36}H_{38}N_3O_6^+$ [M + H$^+$] 608.2755, found 608.2757.

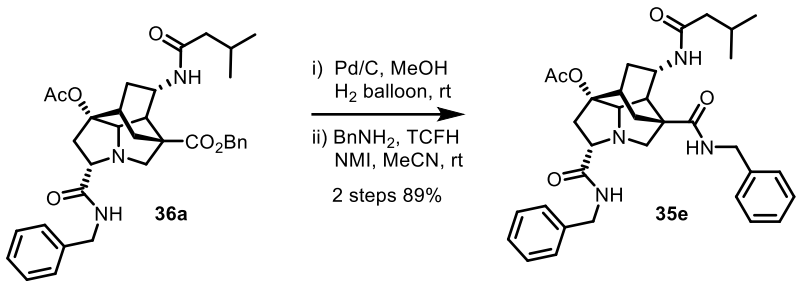
Preparation of amide 36f:



Following the representative procedure using amide **33a** (120 mg, 0.220 mmol. 1.0 equiv.) and cyclopropylmethylamine (100 µL, 1.17 mmol, 5.3 equiv.), purification by silica gel column chromatography (hexane:acetone = 75:25 to hexane:EtOAc = 25:75) afforded amide **36f** (101 mg, 0.172 mmol, 2 steps 78%) as a white amorphous solid. $[\alpha]_D^{27.8}$ -10.4 (c 1.00 in MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (t, *J* = 5.5 Hz, 1H), 7.40-7.31 (m, 7H), 7.29-7.27 (m, 1H), 7.24-7.23 (m, 2H), 5.43 (d, *J* = 8.6 Hz, 1H), 5.18 (d, *J* = 12.5 Hz, 1H), 5.15 (d, *J* = 12.4 Hz, 1H), 4.52-4.47 (m, 1H), 3.65 (d, *J* = 11.0 Hz, 1H), 3.61 (d, *J* = 16.8 Hz, 1H), 3.57 (d, *J* = 16.5 Hz, 1H), 3.49 (dd, *J* = 5.0, 10.3 Hz, 1H), 3.17-3.05 (m, 3H), 2.88 (t, *J* = 4.4 Hz, 1H), 2.77 (dd, *J* = 10.5, 15.7 Hz, 1H), 2.61 (brs, 1H), 2.48-2.41(m, 2H), 2.26 (dd, *J* = 1.3, 14.8 Hz, 1H), 1.83-1.77 (m, 1H), 1.58 (s, 3H), 1.35-1.32 (m, 1H), 1.05-1.02 (m, 1H), 1.00-0.93 (m, 1H), 0.55-0.53 (m, 2H), 0.24-0.21 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4,

173, 170.1, 169.3, 135.7, 134.9, 129.7, 129.3, 128.8, 128.5, 128.2, 127.7, 88.8, 70.3, 68.8, 68.4, 67.3, 47.7, 45.5, 44.1, 44, 40.4, 39.8, 32.5, 31.6, 29.7, 21.1, 10.8, 3.5, 3.4; IR (neat, cm^{-1}): 3325, 3082, 3061, 3026, 2969, 2933, 2872, 1736, 1717, 1644, 1576, 1525, 1487, 1455, 1363, 1277, 1108, 1076, 1044; HRMS (ESI) calcd for $C_{34}H_{40}N_3O_6^+$ [M + H^+] 586.2912, found 586.2919.

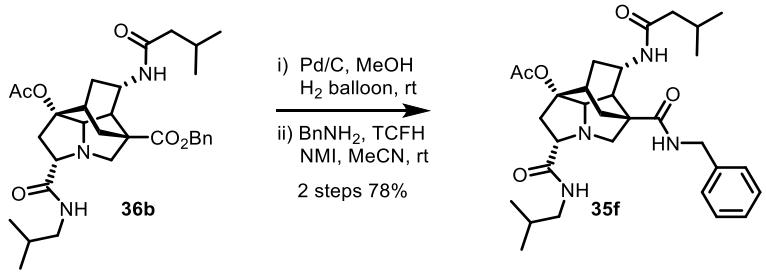
Representative procedure for preparation of amide 35e-p:



To a solution of amide **36a** (42.4 mg, 0.0721 mmol, 1.0 equiv.) in MeOH (700 µL) was added Pd/C (5.6 mg, 13wt%) and stirred for 3.5 h at room temperature under H_2 atmosphere. The reaction mixture was passed through a pad of Celite®, and the filtrate was concentrated under reduced pressure to afford crude carboxylic acid (43.5 mg).

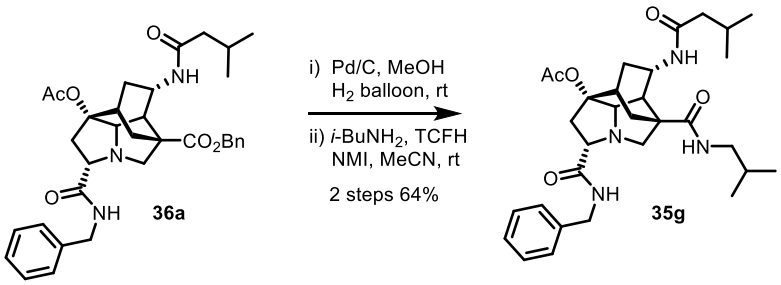
To a mixture of the crude carboxylic acid (43.5 mg), *N*-methylimidazole (17.0 µL, 0.215 mmol, 3.0 equiv.), and benzylamine (9.0 µL, 0.0823 mmol, 1.1 equiv.) in MeCN (500 µL) was added TCFH (43.8 mg, 0.156 mmol, 2.2 equiv.). After being stirred for 17 h at room temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:acetone = 70:30 to EtOAc:MeOH = 98:2) to afforded amide **35e** (37.8 mg, 0.0644 mmol, 2 steps 89%) as a white amorphous solid. $[\alpha]_D^{20.9}$ + 7.9 (c 1.00 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (t, *J* = 5.9 Hz, 1H), 7.34-7.22 (m, 10H), 6.77 (t, *J* = 5.2 Hz, 1H), 5.37 (d, *J* = 7.1 Hz, 1H), 4.54 (dd, *J* = 5.9, 14.7 Hz, 1H), 4.56-4.31 (m, 4H), 3.60 (dd, *J* = 4.8, 9.1 Hz, 1H), 3.38 (d, *J* = 11.1 Hz, 1H), 3.29 (d, *J* = 4.9 Hz, 1H), 2.81-2.70 (m, 4H), 2.55 (d, *J* = 11.2 Hz, 1H), 2.16 (d, *J* = 14.8 Hz, 1H), 2.07-1.99 (m, 6H), 1.93-1.86 (m, 1H), 1.61 (d, *J* = 15.0 Hz, 1H), 1.28-1.24 (m, 1H), 0.95-0.92 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 172.7, 172.6, 169.5, 138.5, 138.4, 128.8, 127.9, 127.8, 127.6, 127.5, 89.3, 69.9, 69.1, 69, 48.5, 46.2, 43.7, 43.5, 40.7, 39.7, 33.4, 32.2, 28.9, 26.3, 22.6, 22.6, 21.7; IR (neat, cm^{-1}): 3319, 3008, 2965, 2866, 2844, 2824, 1736, 1718, 1647, 1634, 1540, 1455, 1317, 1240, 1054, 1032, 1013783, 698; HRMS (ESI) calcd for $C_{34}H_{43}N_4O_5^+$ [M + H^+] 587.3228, found 587.3229.

Preparation of amide 35f:



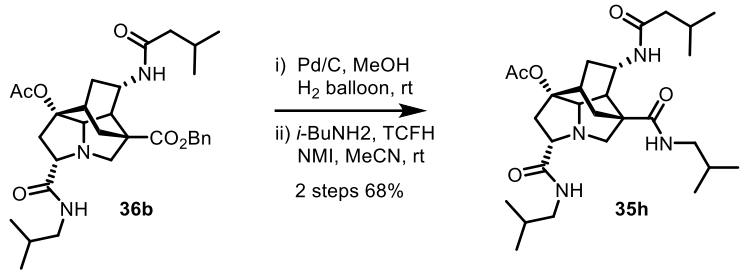
Following the representative procedure using amide **36b** (64.7 mg, 0.110 mmol, 1.0 equiv.) and benzylamine (13.0 μL, 0.119 mmol, 1.1 equiv.), purification by silica gel column chromatography (hexane:acetone = 75:25 to EtOAc:MeOH = 98:2) afforded amide **35f** (47.4 mg, 0.0858 mmol, 2 steps 89%) as a white amorphous solid. $[\alpha]_D^{21.1}$ – 21.7 (c 1.00 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (t, *J* = 6.0 Hz, 1H), 7.33-7.24 (m, 5H), 6.82 (t, *J* = 5.6 Hz, 1H), 5.42 (d, *J* = 7.0 Hz, 1H), 4.54 (dd, *J* = 6.0, 14.8 Hz, 1H), 4.41-4.32 (m, 2H), 3.53 (dd, *J* = 4.2, 9.7 Hz, 1H), 3.41 (d, *J* = 11.0 Hz, 1H), 3.31 (d, *J* = 4.9 Hz, 1H), 3.14-3.07 (m, 1H), 3.03-2.97 (m, 1H), 2.88 (dd, *J* = 3.1, 4.7 Hz, 1H), 2.77-2.63 (m, 3H), 2.55 (d, *J* = 11.1 Hz, 1H), 2.19-1.98 (m, 7H), 1.92-1.85 (m, 1H), 1.82-1.72 (m, 1H), 1.61 (d, *J* = 14.9 Hz, 1H), 1.27-1.24 (m, 1H), 0.95 (d, *J* = 4.4 Hz, 6H), 0.89 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 172.9, 172.8, 169.6, 138.4, 128.8, 127.9, 127.5, 89.3, 69.9, 69.2, 68.9, 48.4, 46.6, 46.2, 43.7, 43.6, 40.8, 39.8, 33.4, 32.2, 28.9, 28.7, 26.3, 22.6, 22.5, 21.6, 20.2, 20.2; IR (neat, cm^{-1}): 3423, 3317, 3062, 3026, 3005, 2956, 2923, 2869, 2826, 1733, 1652, 1524, 1464, 1369, 1248, 1054, 1032, 1017, 845: HRMS (ESI) calcd for $C_{31}H_{45}N_4O_5^+$ [M + H^+] 553.3384, found 553.3381.

Preparation of amide 35g:



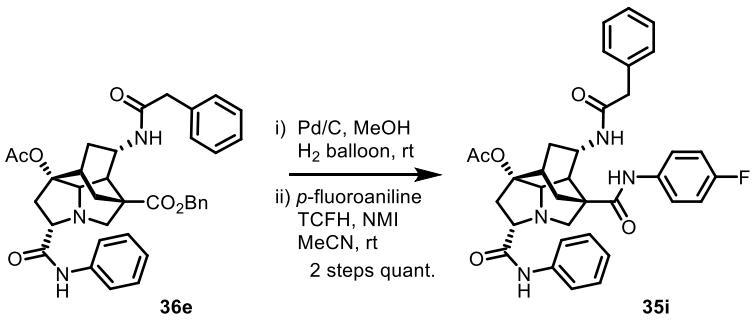
Following the representative procedure using amide **36a** (58.8 mg, 0.100 mmol, 1.0 equiv.) and isobutylamine (11.0 μL, 0.110 mmol, 1.1 equiv.), purification by silica gel column chromatography (hexane:acetone = 70:30 to EtOAc:MeOH = 98:2) afforded amide **35g** (35.3 mg, 0.0639 mmol, 2 steps 64%) as a white amorphous solid. $[\alpha]_D^{21.3}$ – 1.8 (c 1.00 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (t, *J* = 5.7 Hz, 1H), 7.35-7.28 (m, 5H), 6.44 (t, *J* = 5.3 Hz, 1H), 5.35 (d, *J* = 7.7 Hz, 1H), 4.50-4.39 (m, 2H), 4.33-4.29 (m, 1H), 3.62 (dd, *J* = 5.2, 8.6 Hz, 1H), 3.35 (d, *J* = 11.1 Hz, 1H), 3.30 (d, *J* = 4.8 Hz, 1H), 3.10 (t, *J* = 6.3 Hz, 2H), 2.82- 2.75 (m, 4H), 2.57 (d, *J* = 11.2 Hz, 1H), 2.14-2.00 (m, 7H), 1.92-1.78 (m, 2H), 1.65 (d, *J* = 15.2 Hz, 1H), 1.28-1.25 (m, 1H), 0.95-0.90 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 172.9, 172.8, 169.6, 138.6, 128.8, 127.9, 127.6, 89.4, 69.9, 69.2, 48.5, 47.1, 46.2, 43.5, 43.4, 40.8, 39.7, 33.6, 32.3, 28.8, 28.6, 26.4, 22.6, 22.6, 21.7, 20.3, 20.3; IR (neat, cm^{-1}): 3322, 2980, 2965, 2922, 2867, 2843, 1733, 1653, 1637, 1540, 1508, 1362, 1238, 1054, 1032, 1013; HRMS (ESI) calcd for $C_{31}H_{45}N_4O_5^+$ [M + H^+] 553.3384, found 553.3386.

Preparation of amide 35h:



Following the representative procedure using amide **36b** (50.8 mg, 0.0917 mmol, 1.0 equiv.) and isobutylamine (10.0 μL, 0.0998 mmol, 1.1 equiv.) purification by silica gel column chromatography (hexane:acetone = 70:30 to EtOAc:MeOH = 98:2) afforded amide **35h** (32.6 mg, 0.0628 mmol, 2 steps 68%) as a white amorphous solid. $[\alpha]_D^{21.7}$ – 9.4 (c 0.705 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (t, *J* = 6.0 Hz, 1H), 6.47 (t, *J* = 5.5 Hz, 1H), 5.39 (d, *J* = 6.8 Hz, 1H), 4.34-4.30 (m, 1H), 3.56 (dd, *J* = 4.6, 9.9 Hz, 1H), 3.39 (d, *J* = 11.1 Hz, 1H), 3.31 (d, *J* = 4.9 Hz, 1H), 3.16-3.06 (m, 3H), 3.04-2.97 (m, 1H), 2.85 (dd, *J* = 2.9, 4.9 Hz, 1H), 2.78-2.65 (m, 3H), 2.58 (d, *J* = 11.1 Hz, 1H), 2.13-2.01 (m, 7H), 1.92-1.75 (m, 3H), 1.65 (d, *J* = 14.9 Hz, 1H), 1.28-1.24 (m, 1H), 0.97-0.89 (m, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173, 173, 172.8, 169.5, 89.4, 69.9, 69.3, 69.2, 48.5, 47.1, 46.6, 46.2, 43.3, 40.9, 39.7, 33.6, 32.2, 28.8, 28.6, 26.4, 22.7, 22.5, 21.7, 20.3, 20.3, 20.2, 20.2; IR (neat, cm^{-1}): 3416, 3326, 2957, 2936, 2870, 2843, 1734, 1652, 1525, 1465, 1369, 1248, 1053, 1032, 1015, 846; HRMS (ESI) calcd for $C_{28}H_{47}N_4O_5^+$ [M + H^+] 519.3541, found 519.3538.

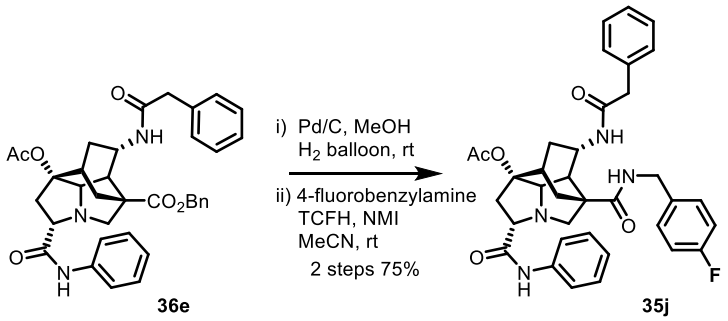
Preparation of amide 35i:



Following the representative procedure using amide **36e** (101 mg, 0.166 mmol, 1.0 equiv.) and *p*-fluoroaniline (25 μL, 0.264 mmol, 1.6 equiv.), purification with PTLC (hexane:EtOAc = 30:70) afforded amide **35i** (96.7 mg, 0.158 mmol, 2 steps quant.) as a white amorphous solid. $[\alpha]_D^{26.9}$ + 6.6 (c 0.90 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 8.37 (s, 1H), 7.73-7.63 (m, 2H), 7.64 (d, *J* = 7.8 Hz, 2H), 7.40-7.35 (m, 4H), 7.31-7.28 (m, 3H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.04 (t, *J* = 8.6 Hz, 2H), 5.33 (d, *J* = 6.6 Hz, 1H), 4.42-4.40 (m, 1H), 3.71 (dd, *J* = 5.0, 9.4 Hz, 1H), 3.67 (s, 2H), 3.59 (d, *J* = 11.1 Hz, 1H), 3.28 (d, *J* = 5.0 Hz, 1H), 3.05 (dd, *J* = 2.5, 4.9 Hz, 1H), 2.79-2.69 (m, 4H), 2.19 (d, *J* = 15.8 Hz, 1H), 1.88-1.81 (m, 1H), 1.76-1.71 (m, 4H), 1.10-1.07 (m,1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 171.2, 171, 169.4, 159.7 (d, *J* = 244 Hz), 137.8, 134.3, 134.1 (d, *J* = 2.3 Hz), 129.7, 129.5, 129.3, 128, 124.5, 121.9 (d, *J* = 7.7 Hz), 119.4, 115.8 (d, *J* = 22.5 Hz), 88.6, 70.5, 69, 68.9, 49.3, 43.8, 42.9, 41.1, 39.4, 33.5, 32.4, 27.8, 21.3 ； ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.7; IR (neat, cm^{-1}): 3289, 3028, 2969, 2945, 2873, 1736, 1663, 1600, 1509, 1443, 1367, 1232, 1162, 1092, 1034, 834, 755, 695; HRMS (ESI) calcd for $C_{35}H_{36}FN_4O_6^+$ [M + H^+] 611.2664, found

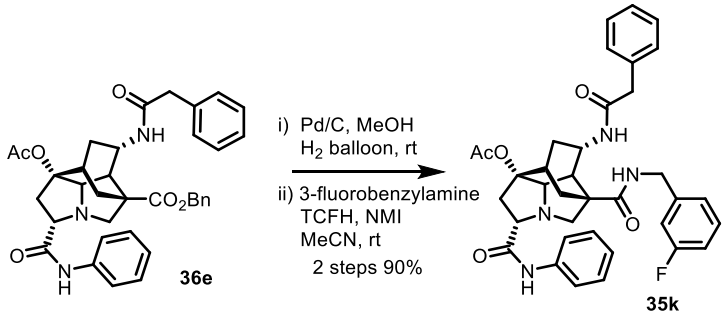
611.2652.

Preparation of amide 35j:



Following the representative procedure using amide **36e** (33.1 mg, 0.0545 mmol, 1.0 equiv.) and 4-fluorobenzyleamine (10.0 μL, 0.0879 mmol, 1.6 equiv.) purification by silica gel column chromatography (hexane:acetone = 75:25 to EtOAc:MeOH = 95:5) afforded amide **35j** (25.4 mg, 0.0407 mmol, 2 steps 75%) as a white amorphous solid. $[\alpha]_D^{28.4}$ – 2.6 (c 0.99 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.63 (d, *J* = 7.7 Hz, 2H), 7.38-7.27 (m, 6H), 7.24-7.22 (m, 3H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.02 (t, *J* = 8.7 Hz, 2H), 6.65 (t, *J* = 5.4 Hz, 1H), 5.33 (d, *J* = 7.2 Hz, 1H), 4.50 (dd, *J* = 5.9, 14.7 Hz, 1H), 4.42-4.32 (m, 2H), 3.66 (dd, *J* = 4.3, 10.2 Hz, 1H), 3.58 (s, 2H), 3.47 (d, *J* = 11.1 Hz, 1H), 3.20 (d, *J* = 5.0 Hz, 1H), 2.89 (dd, *J* = 3.2, 4.9 Hz, 1H), 2.79 (dd, *J* = 10.3, 15.7 Hz, 1H), 2.67-2.61 (m, 3H), 2.18 (d, *J* = 14.2 Hz, 1H), 1.84-1.77 (m, 2H), 1.64 (m, 3H), 1.57 (d, *J* = 15.0 Hz, 1H), 1.04 (dd, *J* = 3.0, 14.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 171.6, 171.4, 162.4 (d, *J* = 245.9 Hz), 161.1, 137.8, 134.5, 134.1 (d, *J* = 3.2 Hz), 129.7, 129.6 (d, *J* = 8.2 Hz), 129.5, 129.2, 127.9, 124.5, 119.4, 115.8 (d, *J* = 21.6 Hz), 88.8, 70.6, 69.3, 68.9, 48.3, 43.9, 43.7, 43.1, 40.7, 39.8, 33.2, 32.2, 28.6, 21.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.0; IR (neat, cm^{-1}): 3414, 3297, 3059, 3028, 3005, 2968, 2943, 2875, 1735, 1654, 1600, 1519, 1443, 1368, 1229, 846, 756, 695; HRMS (ESI) calcd for $C_{36}H_{38}FN_4O_5^+$ [M + H$^+$] 625.2821, found 625.2823.

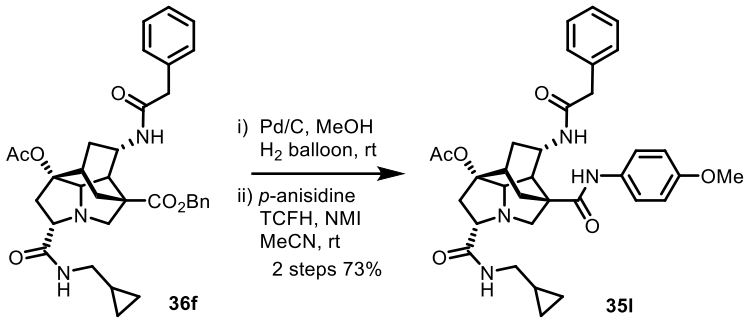
Preparation of amide 35k:



Following the representative procedure using amide **36e** (36.9 mg, 0.0607 mmol, 1.0 equiv.) and 3-fluorobenzyleamine (10.0 μL, 0.0887 mmol, 1.5 equiv.), purification by GPC afforded amide **35k** (34.2 mg, 0.0547 mmol, 2 steps 90%) as a white amorphous solid. $[\alpha]_D^{28.4}$ – 2.45 (c 1.02 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.63 (d, *J* = 7.7 Hz, 2H), 7.38-7.28 (m, 5H), 7.24-7.22 (m, 3H), 7.15-7.09 (m, 2H), 7.03-6.94 (m, 2H), 6.81 (t, *J* = 5.7 Hz, 1H), 5.34 (d, *J* = 7.2 Hz, 1H), 4.57 (dd, *J* = 6.1, 15.0 Hz, 1H), 4.43-4.33 (m, 2H), 3.66 (dd, *J* = 4.4, 10.2 Hz, 1H), 3.58 (s, 2H), 3.48 (d, *J* = 11.0 Hz, 1H), 3.20 (d, *J* = 5.0 Hz, 1H), 2.90 (dd, *J* = 3.2, 4.9 Hz, 1H),

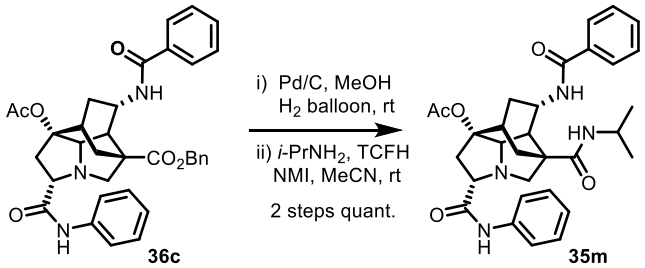
2.79 (dd, J = 10.3, 15.6 Hz, 1H), 2.68-2.63 (m, 3H), 2.19 (d, J = 15.1 Hz, 1H), 1.85-1.78 (m, 1H), 1.65 (s, 3H), 1.59 (d, J = 15.2 Hz, 1H), 1.05 (dd, J = 2.9, 14.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 171.6, 171.4, 169.4, 163.1 (d, J = 246.2 Hz), 140.9 (d, J = 6.9 Hz), 137.7, 134.4, 130.4 (d, J = 8.0 Hz), 129.6, 129.4, 129.2, 127.9, 124.4, 123.3 (d, J = 2.8 Hz), 119.4, 114.6 (d, J = 12.4 Hz), 114.5 (d, J = 11.9 Hz), 88.7, 70.5, 69.3, 68.9, 48.3, 43.8, 43.5, 43.2 (d, J = 1.9 Hz), 40.8, 39.7, 33.1, 32.1, 28.5, 21.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.7; IR (neat, cm^{-1}): 3409, 3289, 3082, 3059, 3028, 2936, 2875, 1734, 1652, 1599, 1519, 1443, 1368, 1233, 1030, 754, 696; HRMS (ESI) calcd for $C_{36}H_{38}FN_4O_5^+$ [M + H$^+$] 625.2821, found 625.2824.

Preparation of amide 35l:



Following the representative procedure using amide **36f** and *p*-anisidine (31.6 mg, 0.257 mmol, 1.9 equiv.), purification by PTLC (EtOAc = 100%) afforded amide **35l** (58.5 mg, 0.0974 mmol, 2 steps 73%) as a white amorphous solid $[\alpha]_D^{28.8}$ + 2.4 (c 0.83 in MeOH); ^{1}H NMR (500 MHz, MeOD) δ 7.43 (d, J = 9.1 Hz, 2H), 7.33-7.32 (m, 4H), 7.27-7.23 (m, 1H), 6.87 (d, J = 9.0 Hz, 2H), 4.38 (td, J = 3.5, 11.0 Hz, 1H), 3.77 (s, 3H), 3.67 (dd, J = 3.8, 10.1 Hz, 1H), 3.57 (s, 2H), 3.52 (d, J = 11.0 Hz, 1H), 3.49 (d, J = 5.0 Hz, 1H), 3.10 (d, J = 6.9 Hz, 1H), 2.93 (dd, J = 3.1, 5.0 Hz, 1H), 2.75-2.68 (m, 2H), 2.61 (brs, 1H), 2.53 (dd, J = 3.8, 15.4 Hz, 1H), 2.20 (d, J = 14.5 Hz, 1H), 1.89-1.86 (m, 4H), 1.72 (d, J = 14.7 Hz, 1H), 1.38 (dd, J = 3.3, 14.4 Hz, 1H), 1.05-0.99 (m, 1H), 0.52-0.49 (m, 2H), 0.26-0.23 (m, 2H); ^{13}C NMR (125 MHz, MeOD) δ 176.1, 173.7, 173.7, 171.8, 158.3, 136.9, 132.3, 130.2, 129.8, 128.1, 124.2, 114.9, 90.4, 70.5, 69.7, 68.8, 55.8, 50.3, 45, 44.8, 43.6, 42.1, 40.9, 33.8, 33.7, 30, 21.4, 11.7, 3.8, 3.6; IR (neat, cm^{-1}): 3406, 3312, 3059, 3030, 3003, 2936, 2873, 2836, 1735, 1653, 1510, 1242, 1027, 833; HRMS (ESI) calcd for $C_{34}H_{41}N_4O_6^+$ [M + H$^+$] 601.3021, found 601.3022.

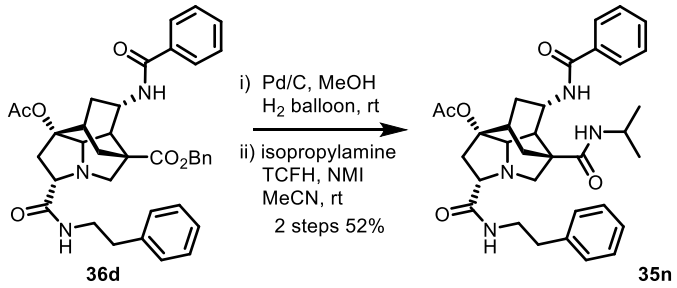
Preparation of amide 35m:



Following the representative procedure using amide **36c** (77.2 mg, 0.130 mmol, 1.0 equiv.) and isopropylamine (100 μL, 1.17 mmol, 9.0 equiv.), purification by silica gel column chromatography (hexane:acetone = 70:30 to EtOAc:MeOH = 95:5) afforded amide **35m** (70.5 mg, 0.129 mmol, 2 steps quant.) as a white amorphous solid. $[\alpha]_D$

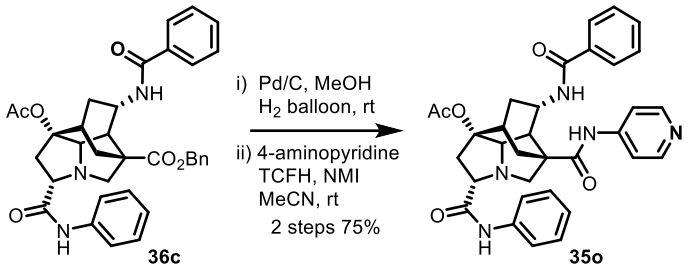
$^{26.8}$ – 14.5 (c 0.994 in MeCN); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (brs, 1H), 7.74-7.71 (m, 2H), 7.61-7.59 (m, 2H), 7.54-7.51 (m, 1H), 7.47-7.43 (m, 2H), 7.33-7.29 (m, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.30 (d, *J* = 7.6 Hz, 1H), 6.11 (d, *J* = 7.2 Hz, 1H), 4.58-4.51 (m, 1H), 4.19-4.09 (m, 2H), 3.72 (dd, *J* = 4.3, 9.8 Hz, 1H), 3.53-3.50 (m, 2H), 3.03 (dd, *J* = 3.1, 5.0 Hz, 1H), 2.89 (dd, *J* = 9.9, 15.7 Hz, 1H), 2.83-2.78 (m, 2H), 2.68 (d, *J* = 11.2 Hz, 1H), 2.25 (d, *J* = 14.3 Hz, 1H), 2.08-1.99 (m, 4H), 1.70-1.66 (m, 2H), 1.43 (dd, *J* = 3.2, 14.7 Hz, 1H), 1.28-1.22 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 171.3, 169.5, 167.8, 137.8, 134.1, 132.1, 129.2, 129, 126.8, 124.4, 119.4, 89.5, 70.5, 69.2, 48.4, 43.7, 41.9, 41.3, 39.8, 33.5, 32.4, 29, 22.8, 22.8, 21.7; IR (neat, cm^{-1}): 3547, 3474, 3412, 2965, 2939, 2844, 2827, 1732, 1646, 1522, 1444, 1370, 1053, 1032, 1014, 841; HRMS (ESI) calcd for $C_{31}H_{37}N_4O_5^+$ [M + H$^+$] 545.2758, found 545.2757.

Preparation of amide 35n:



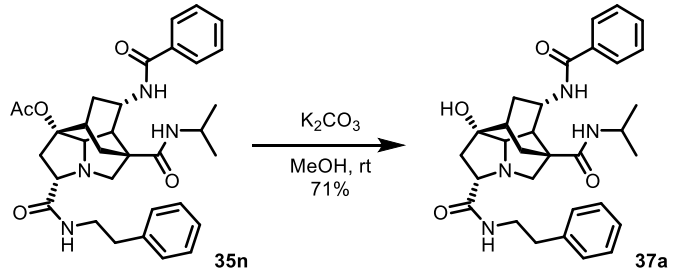
Following the representative procedure using amide **36d** and isopropylamine (100 μL, 1.17 mmol, 10.5 equiv.), purification by silica gel column chromatography (hexane:acetone = 70:30 to EtOAc:MeOH = 97:3) afforded amide **35n** (33.1 mg, 0.0578 mmol, 2 steps 52%) as a white amorphous solid $[\alpha]_D^{30.3}$ + 14.2 (c 0.720 in MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76-7.75 (m, 2H), 7.62-7.55 (m, 2H), 751-7.42 (m, 2H), 7.17-7.12 (m, 4H), 6.98-6.94 (m, 1H), 6.21 (d, *J* = 7.7 Hz, 1H), 6.11 (d, *J* = 7.3 Hz, 1H), 4.53-4.48 (m, 1H), 4.14-4.08 (m, 1H), 3.56-3.49 (m, 2H), 3.45-3.38 (m, 1H), 3.30 (d, *J* = 11.2 Hz, 1H), 3.20 (d, *J* = 5.0 Hz, 1H), 2.87-2.74 (m, 5H), 2.62 (dd, *J* = 15.6, 4.3 Hz, 1H), 2.53 (d, *J* = 11.1 Hz, 1H), 2.18 (d, *J* = 14.0 Hz, 1H), 2.10 (s, 3H), 2.01-1.95 (m, 1H), 1.59 (d, *J* = 15.1 Hz, 1H), 1.40 (dd, *J* = 3.1, 14.6 Hz, 1H), 1.25 (d, *J* = 7.3 Hz, 3H), 1.20 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ173.3, 171.8, 169.4, 167.6, 139.1, 134.2, 132.1, 129, 129, 128.5, 126.8, 126.5, 89.4, 70, 69.2, 69, 48.2, 43.5, 41.8, 41.2, 40.4, 40, 35.6, 33.3, 32.3, 29, 22.8, 22.7, 21.7; IR (neat, cm^{-1}): 3423, 3337, 3064, 3027, 2968, 2938, 2875, 1730, 1650, 1523, 1484, 1462, 1371, 1248, 1174, 1028, 842, 751, 702; HRMS (ESI) calcd for $C_{33}H_{41}N_4O_5^+$ [M + H$^+$] 573.3071, found 573.3077.

Preparation of amide 35o:



Following the representative procedure using amide **36c** (74.1 mg, 0.125 mmol, 1.0 equiv.) and 4-aminopyridine (18.5 mg, 0.197 mmol, 1.6 equiv.), purification by PTLC (EtOAc:MeOH = 90:10) to afforded amide **35o** (55.4 mg, 0.0933 mmol, 2 steps 75%.) as a white amorphous solid. $[\alpha]_D^{24.3}$ + 9.25 (c 0.984 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H), 9.19 (s, 1H), 8.55 (d, *J* = 5.7 Hz, 2H), 7.83-77.79 (m, 4H), 7.59-7.56 (m, 3H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.22 (d, *J* = 6.1 Hz, 1H), 4.61-4.60 (m, 1H), 3.74 (dd, *J* = 2.5, 9.6 Hz, 1H), 3.65 (d, *J* = 11.2 Hz, 1H), 3.55 (d, *J* = 4.8 Hz, 1H), 3.25 (d, *J* = 3.2 Hz, 1H), 2.96-2.90 (m, 2H), 2.81-2.73 (m, 2H), 2.24 (d, *J* = 14.9 Hz, 1H), 2.08-2.03 (m, 4H), 1.89 (d, *J* = 15.5 Hz, 1H), 1.53 (d, *J* = 13.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 170.8, 169.8, 168.9, 150.9, 145.4, 137.7, 133.4, 132.5, 129.2, 129, 127, 124.4, 119.5, 114.3, 89.1, 69.9, 69.1, 67.9, 49.9, 42.7, 42, 38.8, 33.6, 32.4, 27.5, 21.8; IR (neat, cm^{-1}): 3435, 3273, 3085, 3058, 3032, 2948, 2875, 1733, 1681, 1592, 1518, 1443, 1330, 1287, 1241, 911, 830, 730; HRMS (ESI) calcd for $C_{33}H_{34}N_5O_5^+$ [M + H^+] 580.2554, found 580.2555.

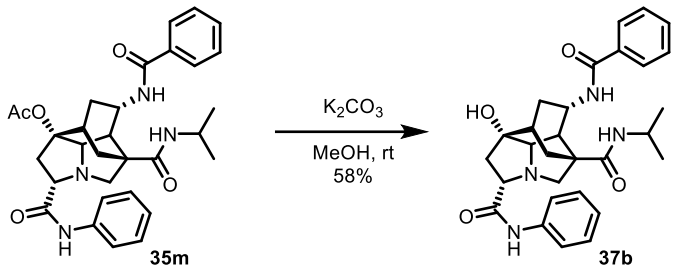
Representative procedure for preparation of alcohol 37a-e:



To a solution of amide **35n** (19.6 mg, 0.0342 mmol, 1.0 equiv.) in MeOH (500 μL) was added K_2CO_3 (19.7 mg, 0.143 mmol, 4.2 equiv.), and the reaction mixture was being stirred for 2 h at room temperature under an argon atmosphere. The reaction mixture was diluted with saturated aqueous NH_4Cl, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by PTLC (EtOAc 100%) to afford alcohol **37a** (12.9 mg, 0.0243 mmol, 71%) as a colorless oil. $[\alpha]_D^{28.0}$ + 27.4 (c 0.420 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.77 (m, 2H), 7.58-7.42 (m, 2H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.16-7.09 (m, 4H), 7.02-6.98 (m, 1H), 6.66 (d, *J* = 7.3 Hz, 1H), 6.37 (d, *J* = 7.7 Hz, 1H), 4.48-4.42 (m, 1H), 4.15-4.06 (m, 1H), 3.52-3.36 (m, 3H), 3.28 (d, *J* = 11.2 Hz, 1H), 2.95 (d, *J* = 5.0 Hz, 1H), 2.84-2.69 (m, 3H), 2.53-2.47 (m, 2H), 2.31 (dd, *J* = 4.0, 14.7 Hz, 1H), 2.12 (d, *J* = 14.5 Hz, 1H), 1.99-1.88 (m, 3H), 1.62 (d, *J* = 14.9 Hz, 1H), 1.25 (d, *J* = 6.5 Hz, 3H), 1.20 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 172.5, 167.6, 138.9, 134.2, 131.8, 128.9, 128.8, 128.6, 127.1, 126.6, 81.4, 70.7, 69.5, 69, 48.2, 43.8, 42.9, 41.7, 41.6, 40.4, 35.9, 35.6, 34.1, 28.3, 22.8, 22.7; IR (neat, cm^{-1}): 3325, 3082, 3061, 3026, 2969, 2933, 2872,

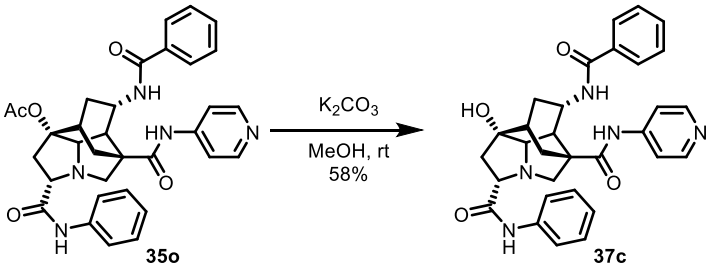
1736, 1644, 1525, 1363, 1277, 1227, 1108, 1044, 700; HRMS (ESI) calcd for $C_{31}H_{39}N_4O_4^+$ [M + H$^+$] 531.2966, found 531.2960.

Preparation of alcohol 37b:



Following the representative procedure using amide **35m** (26.6 mg, 0.0488 mmol, 1.0 equiv.), purification by silica gel column chromatography (EtOAC 100% to EtOAc:MeOH = 95:5) to afforded alcohol **37b** (14.1 mg, 0.0281 mmol, 58%) as a white amorphous solid. $[\alpha]_D^{28.9}$ – 4.48 (c 0.580 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (brs, 1H), 7.73 (d, *J* = 7.8 Hz, 2H), 7.49-7.44 (m, 3H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.02 (t, *J* = 7.9 Hz, 1H), 6.73 (d, *J* = 7.4 Hz, 1H), 6.42 (d, *J* = 7.7 Hz, 1H), 4.51-4.46 (s, 1H), 4.16-4.08 (s, 1H), 3.64 (dd, *J* = 4.3, 9.7 Hz, 1H), 3.43 (d, *J* = 11.2 Hz, 1H), 3.23 (d, *J* = 5.1 Hz, 1H), 2.96-2.94 (m, 1H), 2.64-2.56 (m, 2H), 2.50 (dd, *J* = 4.4, 14.7 Hz, 1H), 2.18 (d, *J* = 15.0 Hz, 1H), 2.04-1.96 (m, 2H), 1.92-1.86 (m, 1H), 1.66 (d, *J* = 15.0 Hz, 1H), 1.28-1.21 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 172, 167.7, 137.6, 134, 131.8, 129.1, 128.8, 127, 124.4, 119.5, 81.6, 70.7, 70.1, 69.2, 48.3, 44, 42.8, 41.8, 41.6, 36, 34, 28.4, 22.8, 22.8. IR (neat, cm^{-1}): 3285, 3053, 3031, 3008, 2966, 2936, 2921, 2869, 1646, 1522, 1444, 1360, 1317, 1277, 1051, 1032, 1010, 754, 691; HRMS (ESI) calcd for $C_{29}H_{35}N_4O_4^+$ [M + H$^+$] 503.2653, found 503.2654.

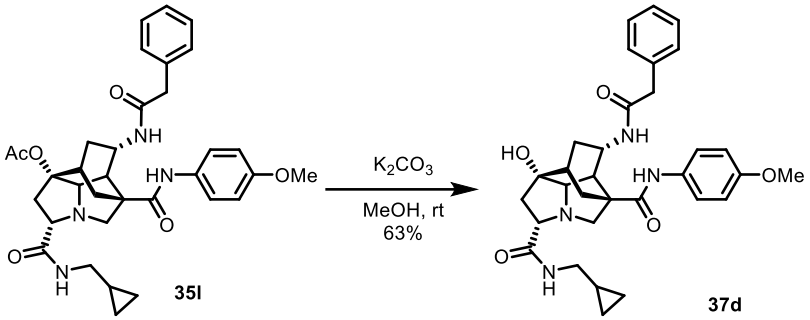
Preparation of alcohol 37c:



Following the representative procedure using amide **35o** (37.5 mg, 0.0647 mmol, 1.0 equiv.), purification by PTLC (EtOAc:MeOH = 90:10) afforded alcohol **37c** (14.1 mg, 0.0454 mmol, 70%) as a white amorphous solid. $[\alpha]_D^{25.5}$ – 14.3 (c 0.580 in MeOH); ^{1}H NMR (400 MHz, CD_3CN) δ 9.84 (s, 1H), 8.72 (s, 1H), 8.45 (d, *J* = 6.0 Hz, 1H), 7.80-7.77 (m, 2H), 7.71-7.69 (m, 2H), 7.62 (d, *J* = 7.6 Hz, 2H), 7.53-7.49 (m, 1H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.29 (t, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 4.63-4.58 (m, 1H), 3.69 (dd, *J* = 4.3, 10.3 Hz, 1H), 3.51 (d, *J* = 11.1 Hz, 1H), 3.36 (d, *J* = 5.2 Hz, 1H), 3.03 (dd, *J* = 3.6, 5.0 Hz, 1H), 2.78 (d, *J* = 11.0 Hz, 1H), 2.61 (dd, *J* = 10.3, 14.5 Hz, 1H), 2.36 (dd, *J* = 4.6, 14.6 Hz, 1H), 2.10 (d, *J* = 14.4 Hz, 1H), 2.02-1.98 (m, 2H), 1.87-1.77 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 173.5, 167.6, 151.5, 146.9, 139.6, 135.6, 132.4, 129.8, 129.5, 127.9, 124.7, 120.5, 114.9, 82.3, 71, 70.7, 68.5, 50.3, 45.1, 44, 42.4, 36.9, 34.4, 29.2; IR (neat, cm^{-1}): 3367, 3255, 3033,

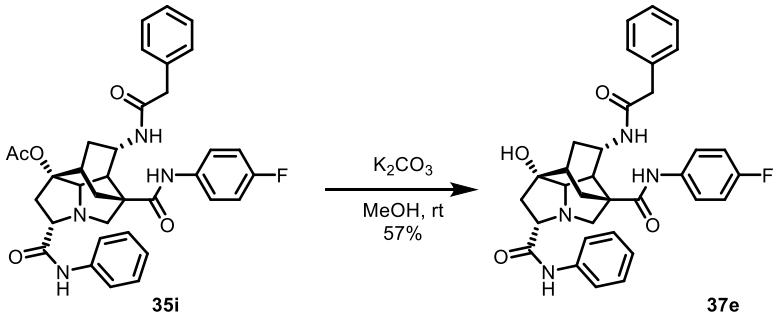
3005, 2938, 2869, 1646, 1592, 1519, 1444, 1417, 1329, 1284, 1051, 1032, 832, 754, 693; HRMS (ESI) calcd for $C_{31}H_{32}N_5O_4^+$ [M + H$^+$] 538.2449, found 580. 538.2441.

Preparation of alcohol 37d:



Following the representative procedure using amide **35l** (37.9 mg, 0.0631 mmol, 1.0 equiv.), purification by PTLC (EtOAc:MeOH = 95:5) afforded alcohol **37d** (22.2 mg, 0.0397 mmol, 63%) as a white amorphous solid. $[\alpha]_D^{28.8}$ – 12.8 (c 0.99 in MeOH); ^{1}H NMR (400 MHz, MeOD) δ 7.43 (d, *J* = 9.0 Hz, 2H), 7.33-7.21 (m, 5H), 6.86 (d, *J* = 9.0 Hz, 2H), 4.39 (td, *J* = 3.8, 10.2 Hz, 1H), 3.76 (s, 3H), 3.59 (dd, *J* = 4.5, 10.1 Hz, 1H), 3.56-3.47 (m, 3H), 3.17 (d, *J* = 5.1 Hz, 1H), 3.10 (d, *J* = 7.0 Hz, 2H), 2.85 (dd, *J* = 3.6, 5.0 Hz, 1H), 2.66 (d, *J* = 11.0 Hz, 1H), 2.52 (dd, *J* = 10.6, 14.2 Hz, 1H), 2.24 (dd, *J* = 4.6, 14.3 Hz, 1H), 2.18 (d, *J* = 14.5 Hz, 1H), 1.90 (brs, 1H), 1.85-1.74 (m, 2H), 1.66 (d, *J* = 14.6 Hz, 1H), 1.06-0.97 (m, 1H), 0.53-0.48 (m, 2H), 0.26-0.23 (m, 2H); ^{13}C NMR (100 MHz, MeOD) δ 176.7, 174.1, 173.3, 158.3, 136.8, 132.4, 130.2, 129.7, 128, 124.3, 114.9, 81.8, 71, 70.7, 69.2, 55.9, 50.2, 46, 44.8, 44.4, 44, 42.2, 37.3, 34.4, 29.8, 11.6, 3.8, 3.7; IR (neat, cm^{-1}): 3449, 3026, 3018, 3001, 2967, 2941, 1737, 1643, 1511, 1441, 1366, 1216, 1111, 1030, 900, 827, 726; HRMS (ESI) calcd for $C_{32}H_{39}N_4O_5^+$ [M + H$^+$] 559.2915, found 559.2911.

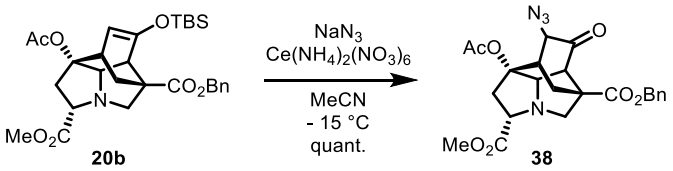
Preparation of alcohol 37e:



Following the representative procedure using amide **37i** (44.3 mg, 0.0725 mmol, 1.0 equiv.), purification by PTLC (hexane:EtOAc = 20:80) afforded alcohol **39e** (23.3 mg, 0.0410 mmol, 57%) as a white amorphous solid. $[\alpha]_D^{28.8}$ – 36.8 (c 1.10 in MeOH); ^{1}H NMR (400 MHz, MeOD) δ 7.62-7.55 (m, 4H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 2H), 7.30-7.24 (m, 4H),7.19-7.12 (m, 2H), 7.04 (t, *J* = 8.8 Hz, 2H), 4.42-4.38 (m, 1H), 3.77 (dd, *J* = 4.2, 10.1 Hz, 1H), 3.58 (d, *J* = 11.2 Hz, 1H), 3.53 (d, *J* = 14.4 Hz, 1H), 3.48 (d, *J* = 14.4 Hz, 1H), 3.26 (d, *J* = 5.0 Hz, 1H), 2.93 (dd, *J* = 3.5, 4.9 Hz, 1H), 2.76 (d, *J* = 11.2 Hz, 1H), 2.59 (dd, *J* = 10.3, 14.4 Hz, 1H), 2.38 (dd, *J* = 4.3, 14.4 Hz, 1H), 2.21 (d, *J* = 14.2 Hz, 1H), 1.94 (brs, 1H), 1.86-1.71 (m, 3H); ^{13}C NMR (100 MHz, MeOD) δ 174.7, 174, 173.4, 161.0 (d, *J* = 242.2 Hz), 139.1, 136.8, 135.7 (d, *J* = 3.1 Hz), 130.1, 129.9, 129.7, 128, 125.6, 124.4 (d, *J* = 7.7 Hz),

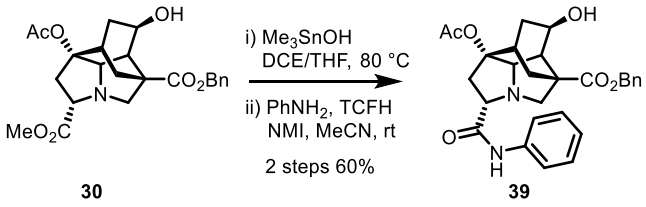
121.3, 116.1 (d, J = 22.5 Hz), 81.9, 71.1, 71, 68.8, 50.3, 45.8, 44.1, 44, 42.1, 37.2, 34.4, 29.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.9; IR (neat, cm^{-1}): 3463, 3027, 3015, 3003, 2967, 2946, 2924, 1737, 1441, 1366, 1216, 912, 846; HRMS (ESI) calcd for $C_{33}H_{34}FN_4O_4^+$ [M + H$^+$] 569.2559, found 569.2552

Preparation of azide 38:



Following the slightly modified procedure reported in the literature,[7] to a solution of silyl enol ether **20b** (162 mg, 0.299 mmol, 1.0 equiv.) in MeCN (1.2 mL) was added ammonium cerium(IV) nitrate (509 mg, 0.928 mmol, 3.1 equiv.) dissolved in MeCN (3.6 mL). After being stirred for 20 min at - 15 °C under an argon atomosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 60:40 to hexane:EtOAc = 30:70) to afford azide **38** (139 mg, 0.297 mmol, quant.) as a white amorphous solid. $[\alpha]_D^{21.5}$ + 96.2 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H), 5.14 (d, J = 12.2 Hz, 1H), 5.09 (d, J = 12.2 Hz, 1H), 3.86 (dd, J = 3.9, 9.8 Hz, 1H), 3.88-3.68 (m, 6H), 3.24 (d, J = 5.0 Hz, 1H), 2.97 (d, J = 2.8 Hz, 1H), 2.78 (dd, J = 9.8, 15.6 Hz, 1H), 2.72-2.65 (m, 2H), 2.60 (dd, J = 3.9, 15.6 Hz, 1H), 2.05 (2, 3H), 1.52-1.48 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.6, 173.4, 171.3, 170.1, 135.1, 128.7, 128.6, 128.2, 87.8, 72, 69.1, 67.6, 67.5, 58.1, 55.8, 52.6, 50.8, 39.9, 38.4, 27.1, 21.5; IR (neat, cm^{-1}): 3090, 3065, 3033, 2953, 2890, 2106, 1734, 1455, 1436, 1371, 1275, 1240, 1078, 1035, 749, 698; HRMS (ESI) calcd for $C_{23}H_{25}N_4O_7^+$ [M + H$^+$] 469.1718, found 469.1705.

Preparation of amide 39:

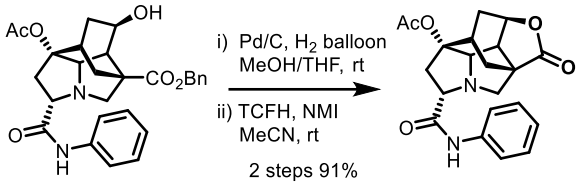


To a solution of alcohol **30** (76.7 mg, 0.179 mmol. 1.0 equiv.) in 1,2-dichroloethane (700 µL) was added trimethyltin hydroxide (49.3 mg, 0.273 mmol, 1.5 equiv.), and the reaction mixture was stirred for 1 h at 80 °C under an argon atmosphere. After this time, another amount of trimethyltin hydroxide (51.1 mg, 0.284 mmol, 1.6 equiv.). After being stirred for 1 h, the reaction mixture was passed through a pad of silica gel with MeOH, and the filtrate was concentrated under reduced pressure to afford crude carboxylic acid (60.8 mg) as a white solid.

To a solution of crude carboxylic acid (60.8 mg), *N*-methylimidazole (35.0 µL, 0.439 mmol, 2.5 equiv.), and aniline (16.0 µL, 0.175 mmol, 0.98 equiv.) in MeCN (500 µL) was added TCFH (125 mg, 0.445 mmol, 2.5 equiv.). After being stirred for 30 min at room temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic

layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:EtOAc = 60:40 to 55:45) to afford amide **39** (52.4 mg, 0.107 mmol, 2 steps 60%) as a white solid. $[\alpha]_D^{22.3}$ -25.9 (c 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.41-7.32 (m, 7H), 7.11 (t, *J* = 7.4 Hz, 1H), 5.20 (d, *J* = 12.2 Hz, 1H), 5.16 (d, *J* = 12.2 Hz, 1H), 4.18-4.12 (m, 1H), 3.73-3.70 (m, 2H), 3.46 (dd, *J* = 5.3, 28.3 Hz, 1H), 2.93-2.87 (m, 2H), 2.83 (dd, *J* = 2.5, 5.1 Hz, 1H), 2.67-2.59 (m, 3H), 2.48-2.44 (m, 1H), 2.18-2.12 (m, 1H), 1.98 (s, 3H), 1.59 (m, 1H), 1.26-1.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 171.7, 170, 137.7, 135.4, 129.2, 128.9, 128.8, 128.4, 124.4, 119.6, 88.9, 71.6, 71.4, 69, 67.6, 63.7, 48.5, 46.9, 39.9, 33.8, 33.6, 31.6, 21.5; IR (neat, cm^{-1}): 3446, 3273, 3089, 3060, 3032, 2953, 2888, 1730, 1674, 1599, 1519, 1443, 1246, 1091, 1079, 912, 753, 732, 696; HRMS (ESI) calcd for $C_{28}H_{31}N_3O_6^+$ [M + H^+] 491.2177, found 491.2182.

Preparation of lactone 40:



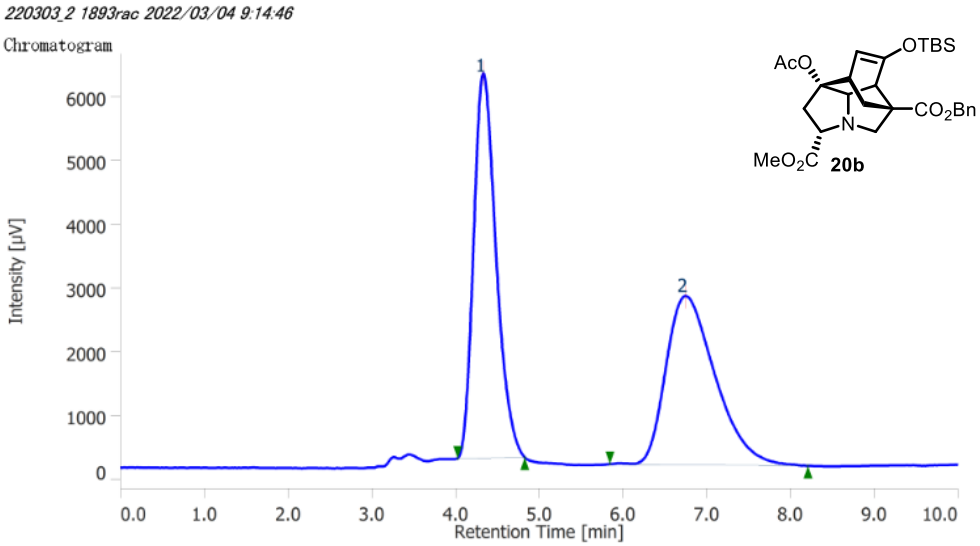
39 **40**

To a solution of amide **39** (63.8 mg, 0.130 mmol, 1.0 equiv.) in MeOH (1.0 mL) and THF (500 μL) was added Pd/C (11.1 mg, 17wt%) and stirred for 3 h at room temperature under H_2 atmosphere. The reaction mixture was passed through a pad of Celite®, and the filtrate was concentrated under reduced pressure to afford crude carboxylic acid (57.4 mg) as a white amorphous solid.

To a mixture of crude carboxylic acid (57.4 mg) and *N*-methylimidazole (31.0 μL, 0.393 mmol, 3.0 equiv.) in MeCN (1.0 mL) was added TCFH (76.2 mg, 0.272 mmol, 2.1 equiv.). After being stirred for 20 min at room temperature under an argon atmosphere, the reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by PTLC (hexane:EtOAc = 75:25) to afforded lactone **40** (45.0 mg, 0.118 mmol, 2 steps 91%) as a white amorphous solid. $[\alpha]_D^{25.5}$ – 12.9 (c 0.945 in MeOH); ^1H NMR (400 MHz, $CDCl_3$) δ 9.55 (brs, 1H), 7.62 (d, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 4.78 (t, *J* = 5.5 Hz, 1H), 3.75 (dd, *J* = 5.6, 10.6 Hz, 1H), 3.48 (d, *J* = 5.2 Hz, 1H), 3.41 (d, *J* = 10.8 Hz, 1H), 3.18 (t, *J* = 5.3 Hz, 1H), 3.08 (dd, *J* = 10.7, 15.6 Hz, 1H), 2.82 (brs, 1H), 2.68 (dd, *J* = 5.6, 15.5 Hz, 1H), 2.50 (d, *J* = 10.9 Hz, 1H), 2.22 (dd, *J* = 2.7, 15.1 Hz, 1H), 2.01 (s, 3H), 1.93-1.82 (m, 2H), 1.56 (d, *J* = 15.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 171.5, 169.7, 137.5, 129.2, 124.5, 119.6, 86.1, 74.7, 71.5, 63.6, 59.6, 49.1, 47, 41.8, 32, 30.8, 26.7, 21.5; IR (neat, cm^{-1}): 3270, 2955, 2935, 1780, 1732, 1681, 1599, 1520, 1443, 1371, 1235, 1070, 1052, 907, 845, 755, 695; HRMS (ESI) calcd for $C_{21}H_{23}N_2O_5^+$ [M + H^+] 383.1601, found 383.1603.

3. HPLC analysis of 20b

HPLC analysis of 22b on Daicel CHIRALCEL® OD (*i*-PrOH/hexane = 80:20, flow rate = 1.0 mL/min, 254 nm) indicated 97% ee: tR (major) = 4.30 min., tR (minor) = 6.47 min



Peak Information

#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
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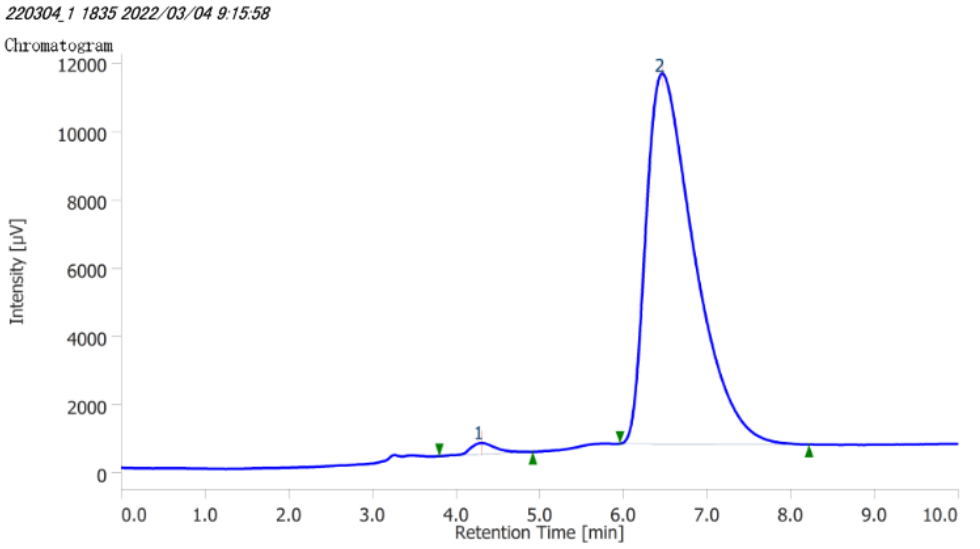
2	6.742	108116	2645	49.079	30.480



Peak Information

#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	4.300	7005	327	1.585	2.924
2	6.467	434955	10859	98.415	97.076

Figure S1. HPLC analysis of **20b**

4. X-ray structural analysis of 28a

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) crl41-1740_autored

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: crl41-1740_autored

```
Bond precision:   C-C = 0.0098 A          Wavelength=1.54184

Cell:             a=6.1843(1)      b=11.5565(1)      c=34.6069(3)
                  alpha=90         beta=90           gamma=90
Temperature:      90 K
```

	Calculated	Reported
Volume	2473.32(5)	2473.32(5)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C27 H31 N3 O3, Cl	Cl, C27 H31 N3 O3
Sum formula	C27 H31 Cl N3 O3	C27 H31 Cl N3 O3
Mr	481.00	481.00
Dx,g cm-3	1.292	1.292
Z	4	4
Mu (mm-1)	1.636	1.636
F000	1020.0	1020.0
F000'	1024.22	
h,k,lmax	7,14,43	7,14,43
Nref	5235[3029]	5034
Tmin,Tmax	0.851,0.926	0.529,1.000
Tmin'	0.729	

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Correction method= # Reported T Limits: Tmin=0.529 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.66/0.96        Theta(max)= 76.681

R(reflections)= 0.0934( 4922)                wR2(reflections)=
                                             0.2563( 5034)
S = 1.054                  Npar= 384
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The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

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PLAT035_ALERT_1_B _chemical_absolute_configuration Info  Not Given     Please Do !
PLAT094_ALERT_2_B Ratio of Maximum / Minimum Residual Density ....       4.57 Report
PLAT097_ALERT_2_B Large Reported Max.  (Positive) Residual Density       1.92 eA-3
PLAT971_ALERT_2_B Check Calcd Resid. Dens.  0.80Ang From N7              2.82 eA-3
```

Alert level C

```
DIFMX02_ALERT_1_C  The maximum difference density is > 0.1*ZMAX*0.75
           The relevant atom site should be identified.
PLAT042_ALERT_1_C Calc. and Reported MoietyFormula Strings  Differ      Please Check
PLAT084_ALERT_3_C High wR2 Value (i.e. > 0.25) ....................       0.26 Report
PLAT213_ALERT_2_C Atom O6              has ADP max/min Ratio .....        3.1 prolat
PLAT234_ALERT_4_C Large Hirshfeld Difference N005     --C32      .       0.17 Ang.
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ................    0.00984 Ang.
PLAT431_ALERT_2_C Short Inter HL..A Contact  C101     ..N005     .       3.06 Ang.
                                                    x,y,z  =      1_555 Check
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ......      2.281 Check
PLAT918_ALERT_3_C Reflection(s) with I(obs) much Smaller I(calc) .          3 Check
PLAT975_ALERT_2_C Check Calcd Resid. Dens.  1.09Ang From N005    .       0.45 eA-3
```

Alert level G

```
PLAT003_ALERT_2_G Number of Uiso or Uij Restrained non-H Atoms ...         45 Report
PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ...............         4 Report
PLAT072_ALERT_2_G SHELXL First  Parameter in WGHT  Unusually Large       0.15 Report
PLAT083_ALERT_2_G SHELXL Second Parameter in WGHT  Unusually Large       6.47 Why ?
PLAT142_ALERT_4_G s.u. on b - Axis Small or Missing ...............    0.00010 Ang.
PLAT143_ALERT_4_G s.u. on c - Axis Small or Missing ...............    0.00030 Ang.
PLAT178_ALERT_4_G The CIF-Embedded .res File Contains SIMU Records         2 Report
PLAT186_ALERT_4_G The CIF-Embedded .res File Contains ISOR Records         2 Report
PLAT301_ALERT_3_G Main Residue  Disorder ..............(Resd  1  )        33% Note
PLAT410_ALERT_2_G Short Intra H...H Contact  H00F     ..H32      .       1.92 Ang.
                                                    x,y,z  =      1_555 Check
PLAT720_ALERT_4_G Number of Unusual/Non-Standard Labels ..........         45 Note
PLAT791_ALERT_4_G Model has Chirality at C008        (Sohnke SpGr)         R Verify
PLAT791_ALERT_4_G Model has Chirality at C009        (Sohnke SpGr)         R Verify
PLAT791_ALERT_4_G Model has Chirality at C00B        (Sohnke SpGr)         R Verify
PLAT791_ALERT_4_G Model has Chirality at C00D        (Sohnke SpGr)         R Verify
PLAT791_ALERT_4_G Model has Chirality at C00F        (Sohnke SpGr)         S Verify
PLAT811_ALERT_5_G No ADDSYM Analysis: Too Many Excluded Atoms ....         ! Info
PLAT860_ALERT_3_G Number of Least-Squares Restraints .............       738 Note
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600         54 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.         1 Info
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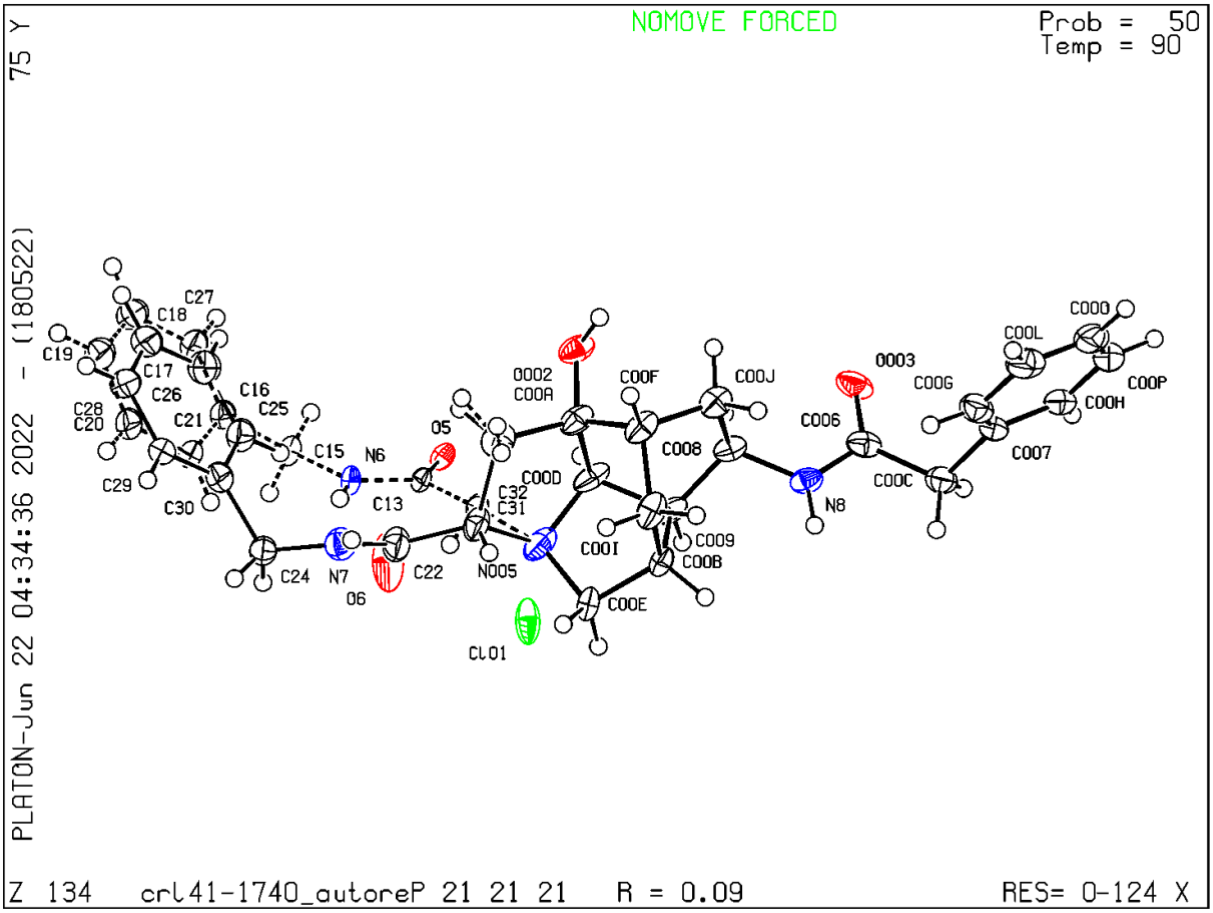
0 **ALERT level A** = Most likely a serious problem - resolve or explain
4 **ALERT level B** = A potentially serious problem, consider carefully
10 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
20 **ALERT level G** = General information/check it is not something unexpected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C18
C19
C17
C26
C16
C28
C20
C21
C25
C15
N6
C29
C30
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C32
C31
N005
C01
O002
C00A
C00F
C00J
C008
C00D
C00I
C009
C00B
C00E
C01
0003
C006
C00G
C00C
N8
C007
C00L
C00O
C00P
C00H

5. Materials and methods for biological assays

Cell culture

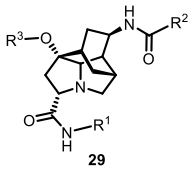
Human epithelioid cervical carcinoma (HeLa) cells were incubated with DMEM medium (FUJIFILM Wako Pure Chemical) containing 10% fetal bovine serum (Gibco; Thermo Fisher Scientific) and 1% peniciline/streptomycine (Gibco, 15070063). Cells were incubated in a cell incubator with 5% CO_2 at 37 ℃.

MTT assay

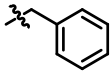
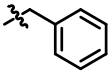
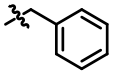
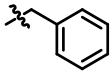
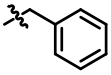
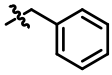
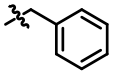
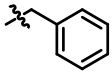
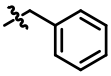
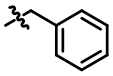
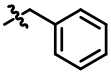
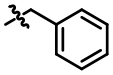
HeLa cells (1.0×10^3 cells/dish) were seeded in a 96-well plate and incubated at 37°C for 24 h in 5% CO_2. The medium was replaced with new medium containing indicated concentration compounds. After incubation at 37°C for 72 h in 5% CO_2, the medium was replaced with new medium containing 0.5 mg/mL thiazolyl blue tetrazolium bromide (MTT). After incubation for 3 h at 37 °C, the medium was removed, and 150 μL of dimethyl sulfoxide (DMSO) was added. Absorbance at 590 nm were measured using a microplate reader.

6. Antiproliferative activity of compounds

Table S1. Cell proliferation inhibitory activities of amides **29a-h**

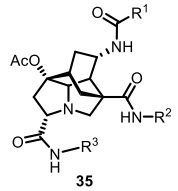


29

entry	R^1	R^2	R^3	[a]Growth inhibition rate (%) at 100 μM	[a]Growth inhibition rate (%) at 10 μM
29a				83±3	43±15
29b				87±1	43±4
29c				73±6	34±16
29d				60±3	25±22
29e				83±3	35±22
29f				75±6	40±9
29g				68±4	40±12
29h				57±6	22±7

[a]Growth inhibition rate of HeLa cells shown as the mean±SD of triplicated samples.

Table S2. Cell proliferation inhibitory activities of amides **35a-o**



35

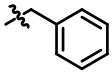
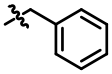
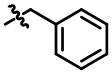
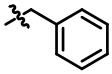
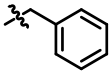
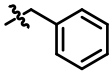
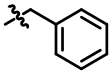
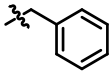
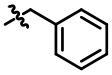
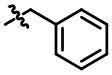
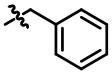
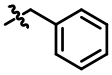
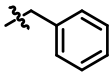
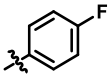
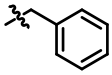
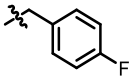
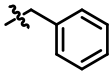
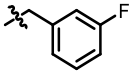
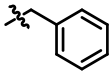
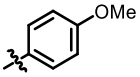
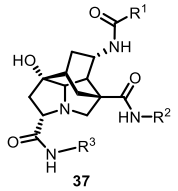
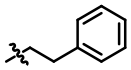
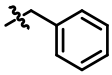
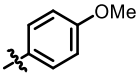
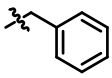
entry	R^1	R^2	R^3	[a]Growth inhibition rate (%) at 100 μM	[a]Growth inhibition rate (%) at 10 μM
35a				85±2	20±18
35b				75±1	42±10
35c				63±5	15±7
35d				19±11	-[b]
35e				57±6	30±5
35f				7±19	-[b]
35g				42±7	19±10
35h				50±7	36±16
35i				94±1	43±6
35j				93±1	37±6
35k				93±1	58±5
35l				49±2	-[b]
35m				93±1	33±6
35n				28±5	-[b]
35o				93±1	33±6

Table S3. Cell proliferation inhibitory activities of amides **37a-e**



37

entry	R^1	R^2	R^3	[a]Growth inhibition rate (%) at 100 μM	[a]Growth inhibition rate (%) at 10 μM
37a				41±6	-[b]
37b				70±4	26±2
37c				94±1	49±5
37d				60±3	25±22
37e				97±0	51±7

[a]Growth inhibition rate of HeLa cells shown as the mean±SD of triplicated samples. [b]No inhibitory activity was observed.

7. References

1. J. G. Pierce, D. Kasi, M. Fushimi, A. Cuzzupe, P. Wipf, *J. Org. Chem.* **2008**, *73*, 7807–7810.
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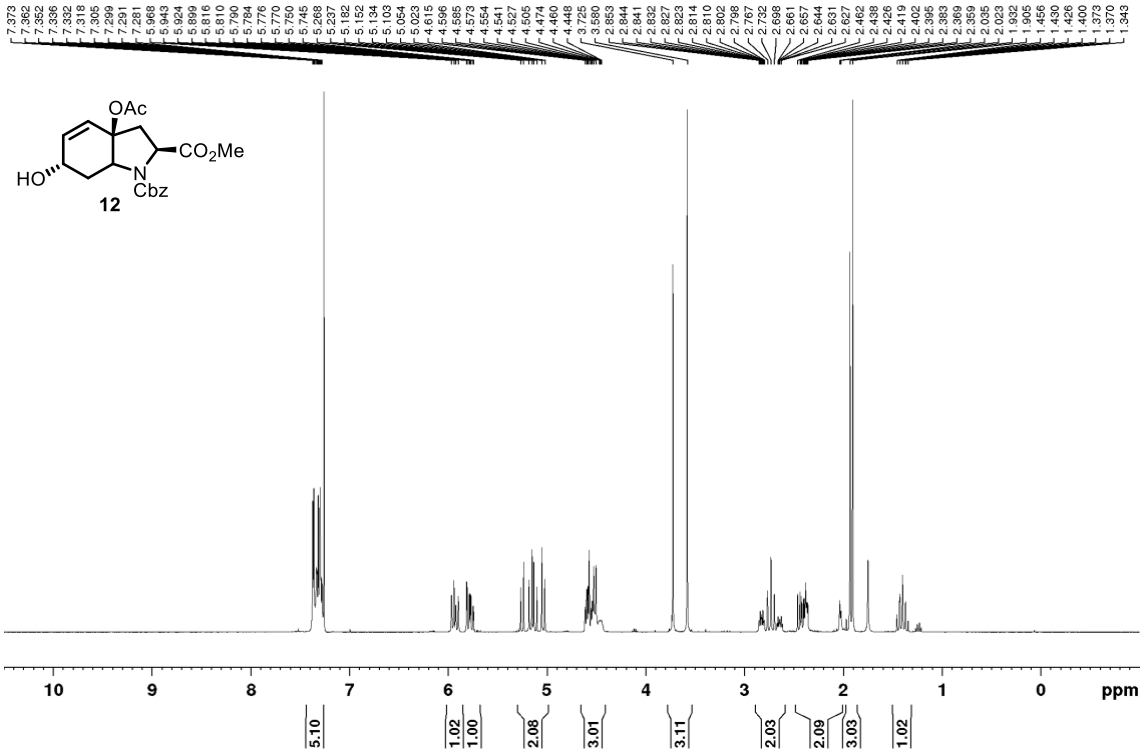
7. P. Magnus, L. Barth, *Tetrahedron Lett.* **1992**, *33*, 2777–2780.

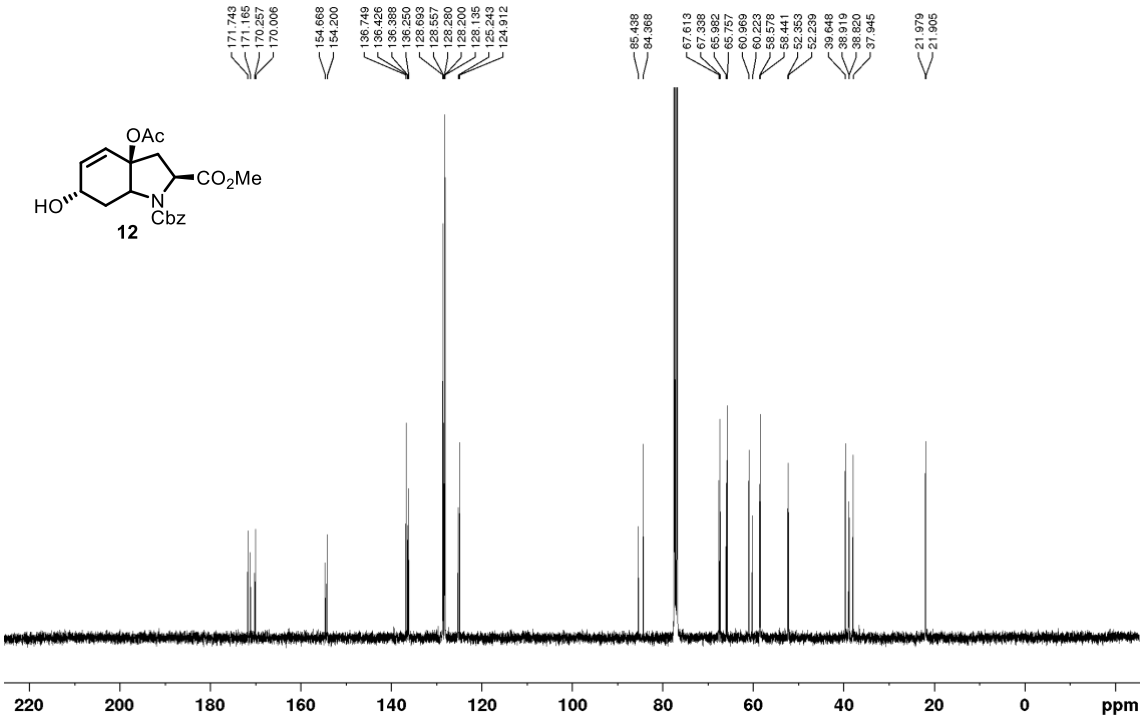
8. NMR spectra

Alcohol **12**

^{1}H NMR (400 MHz, $CDCl_3$)

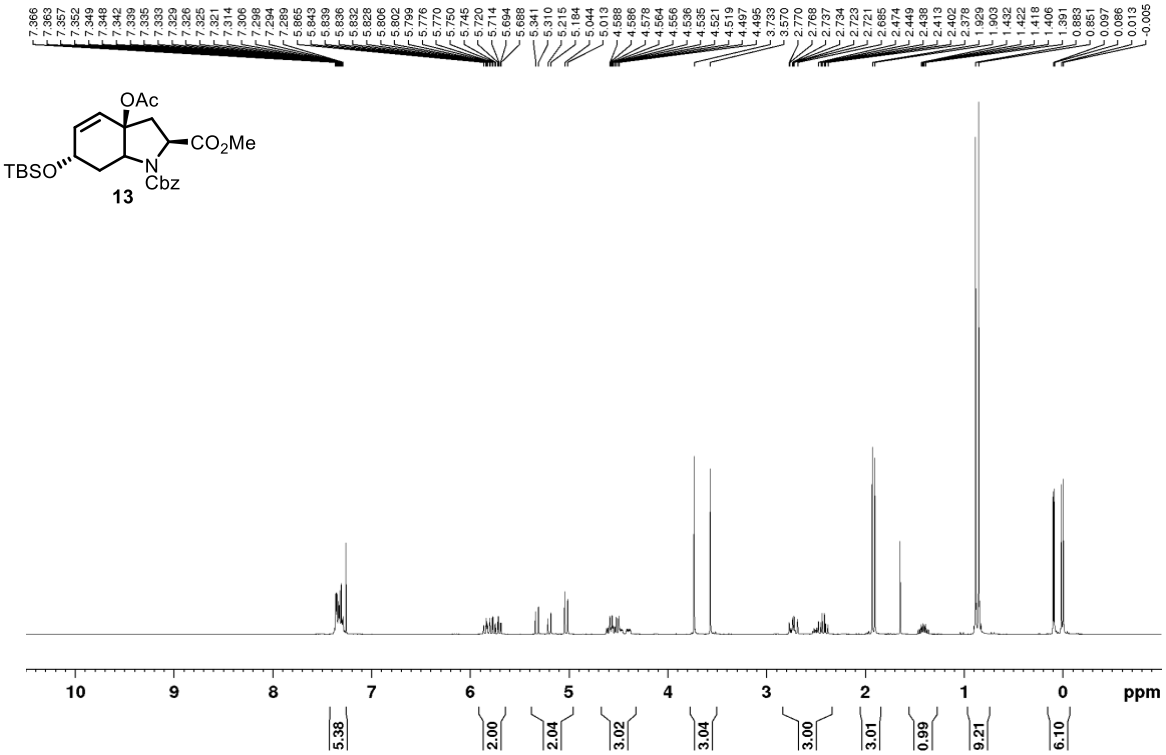


^{13}C NMR (100 MHz, $CDCl_3$)

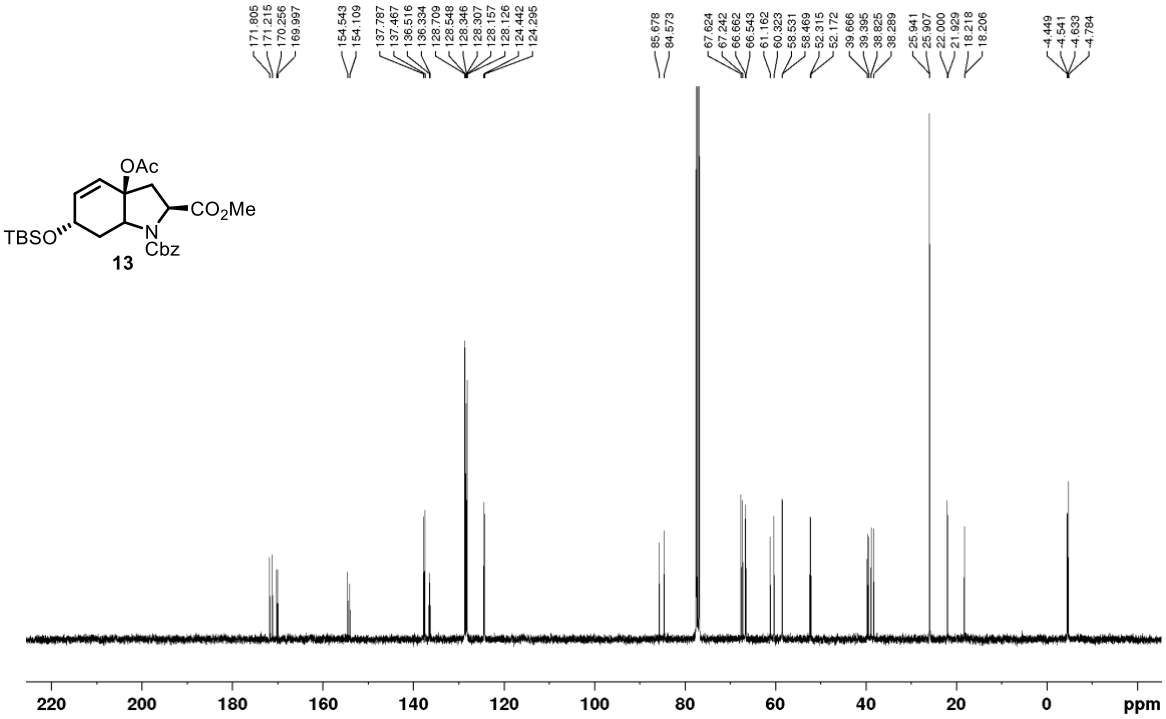


Silyl ether **13**

^{1}H NMR (400 MHz, $CDCl_3$)

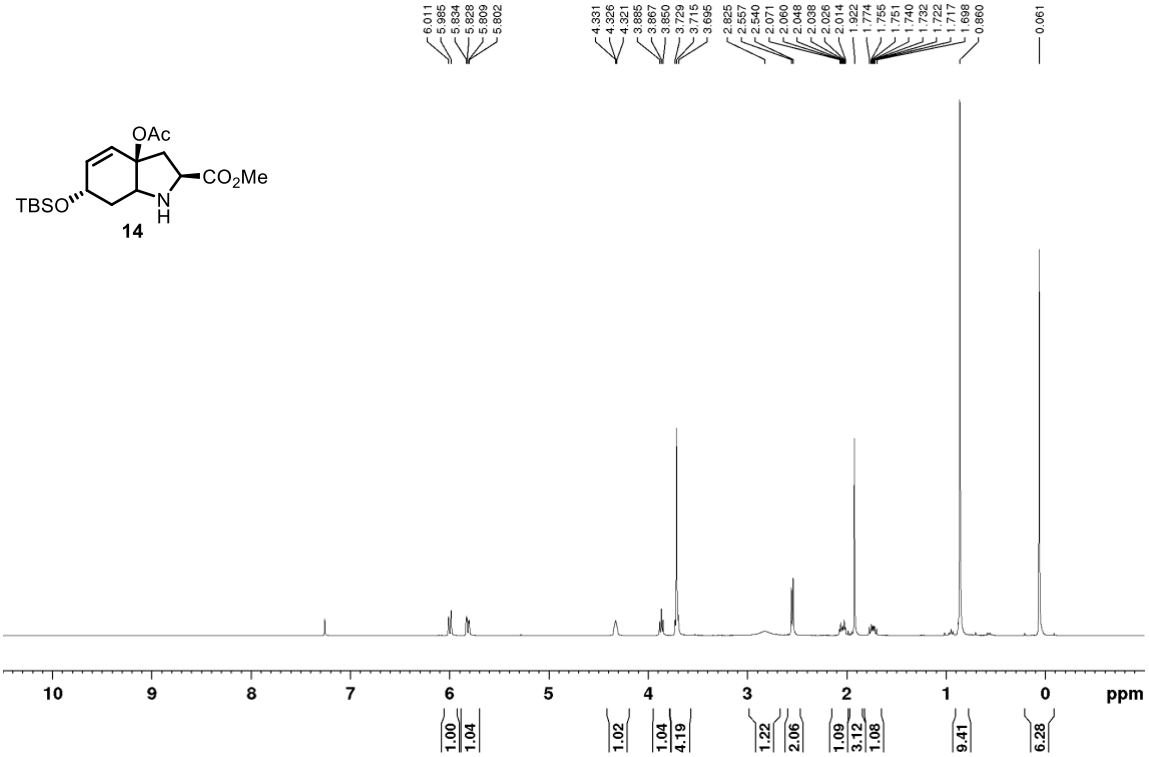


^{13}C NMR (100 MHz, $CDCl_3$)

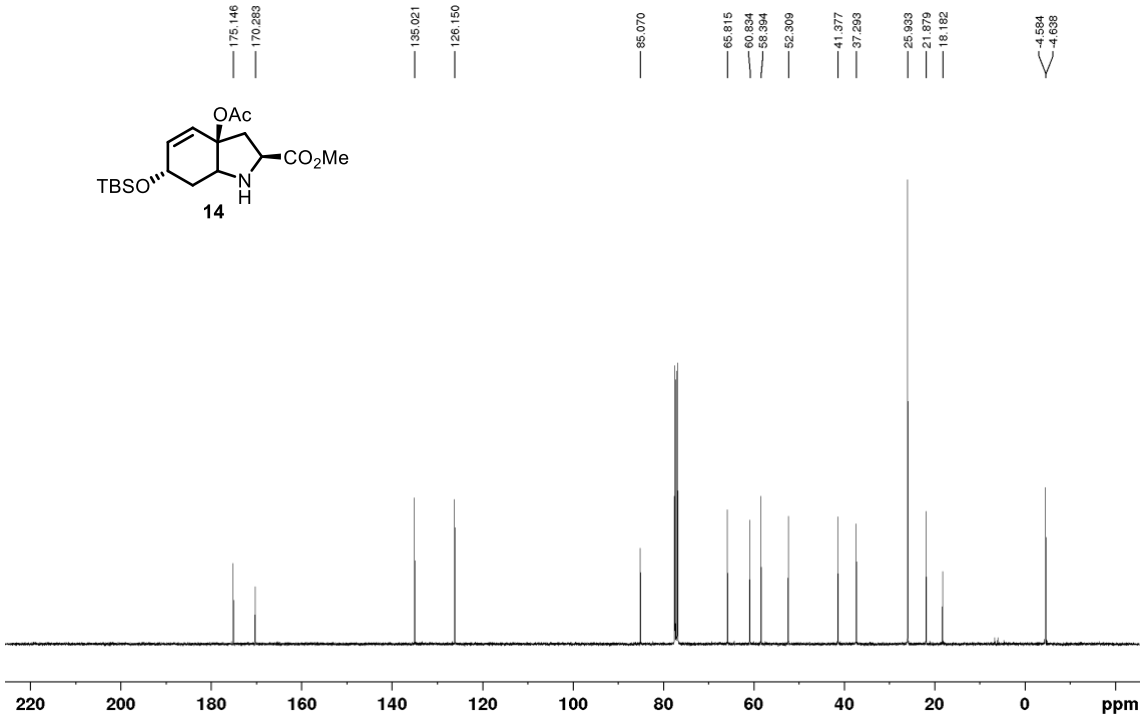


Amine **14**

^{1}H NMR (400 MHz, $CDCl_3$)

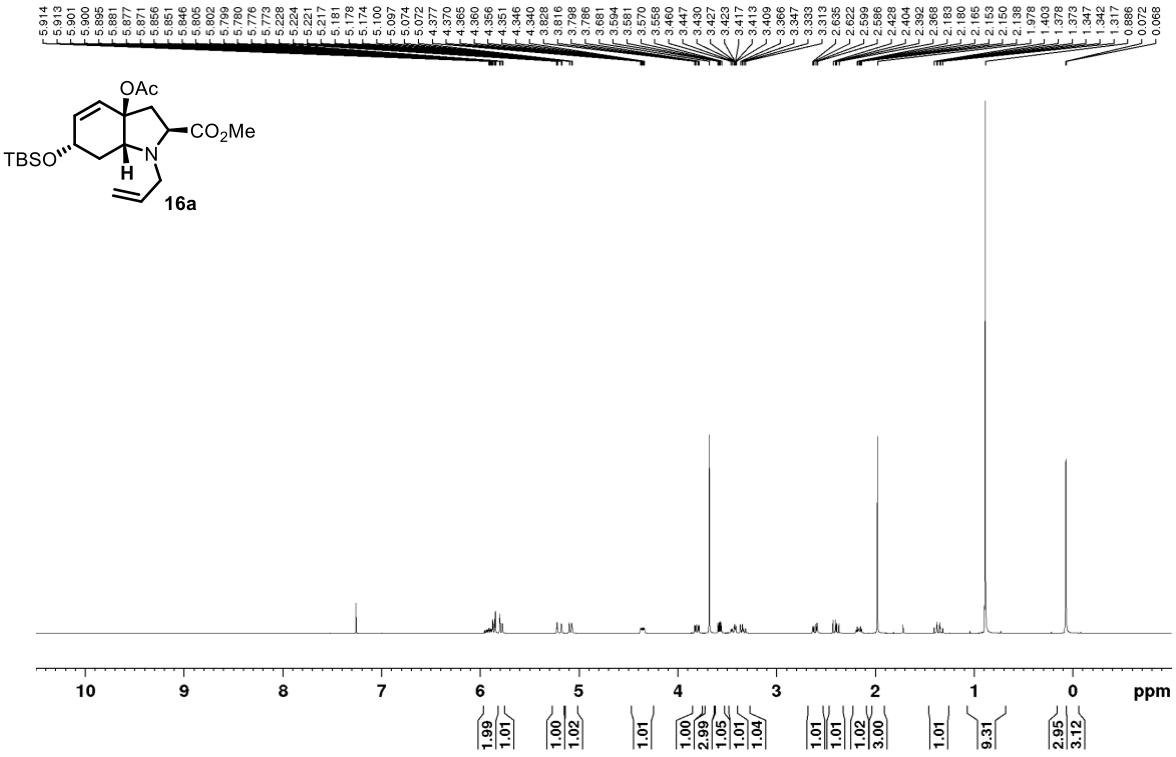


^{13}C NMR (100 MHz, $CDCl_3$)

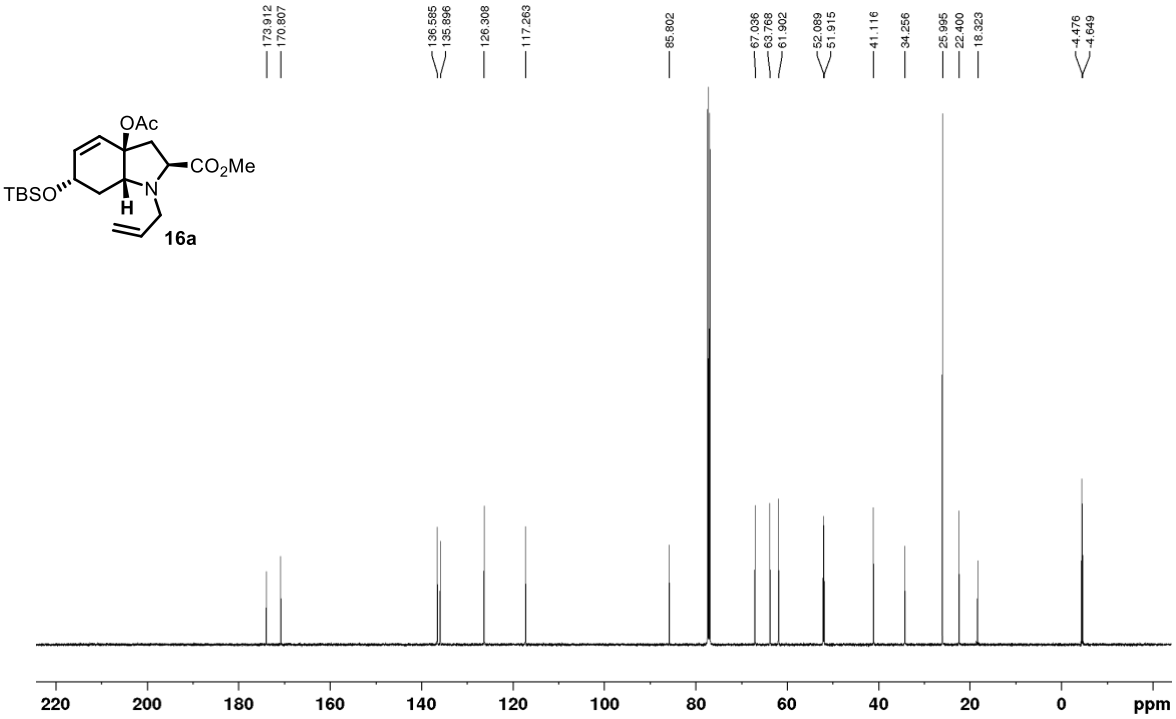


Allyl amine **16a**

^{1}H NMR (400 MHz, $CDCl_3$)

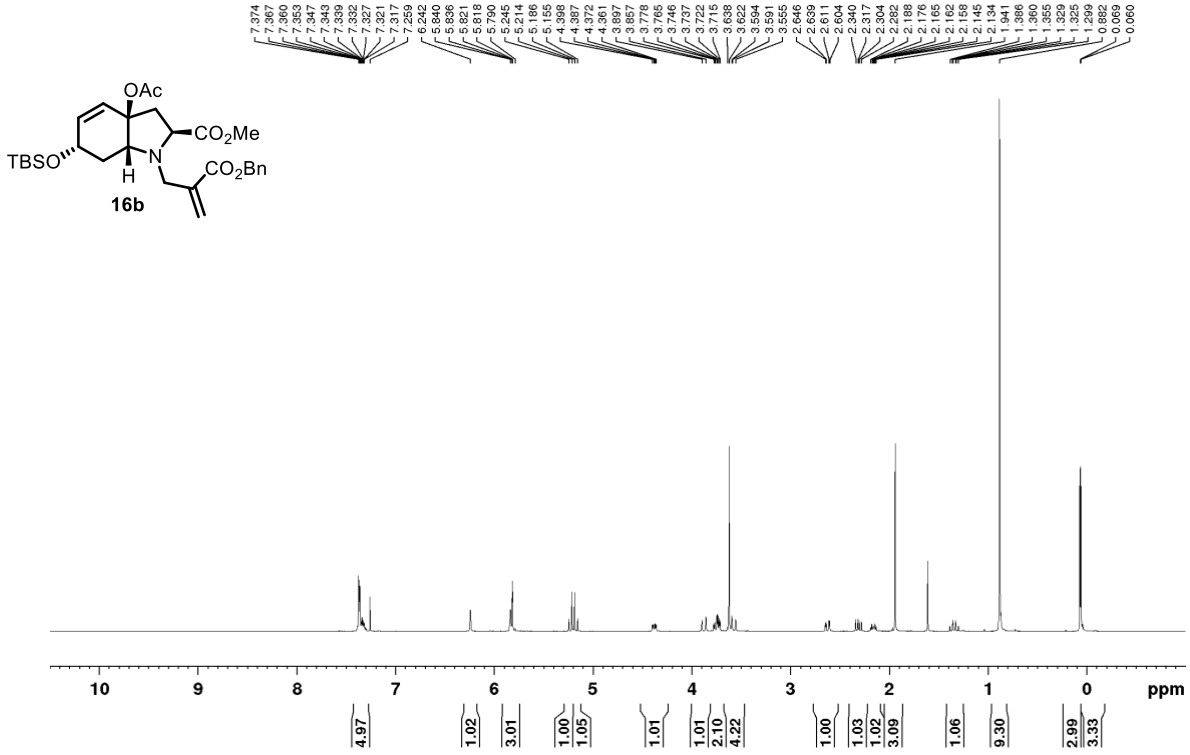


^{13}C NMR (125 MHz, $CDCl_3$)

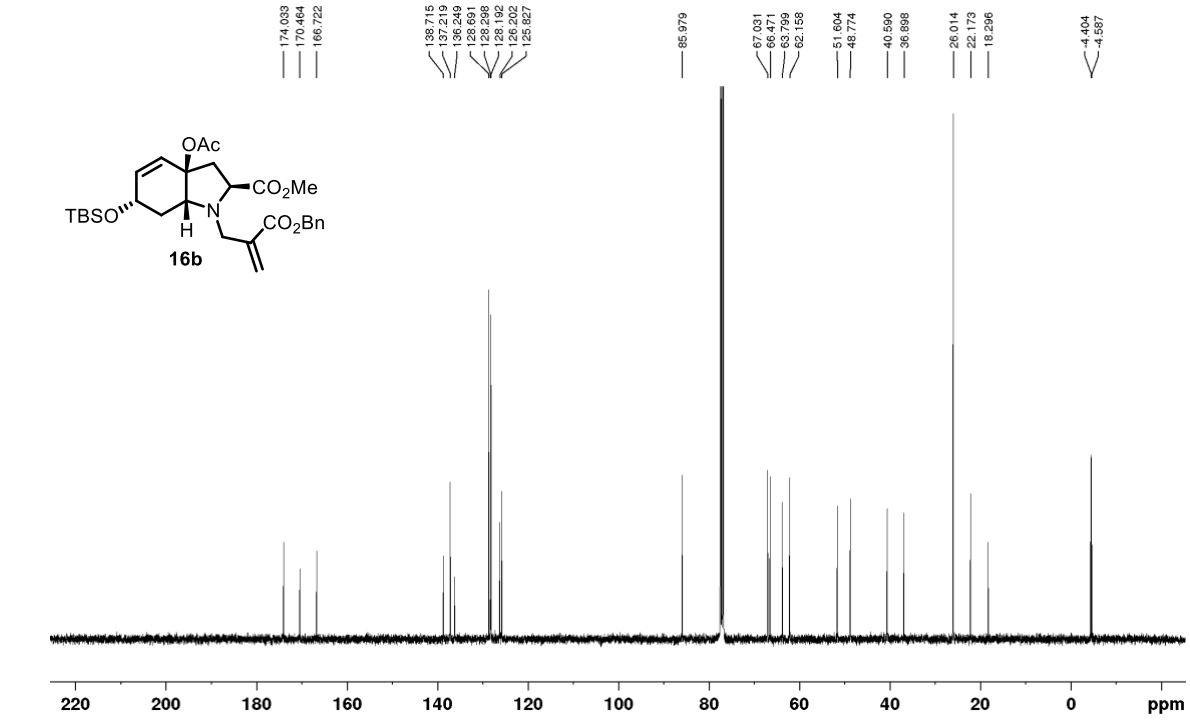


Allyl amine **16b**

^{1}H NMR (400 MHz, $CDCl_3$)

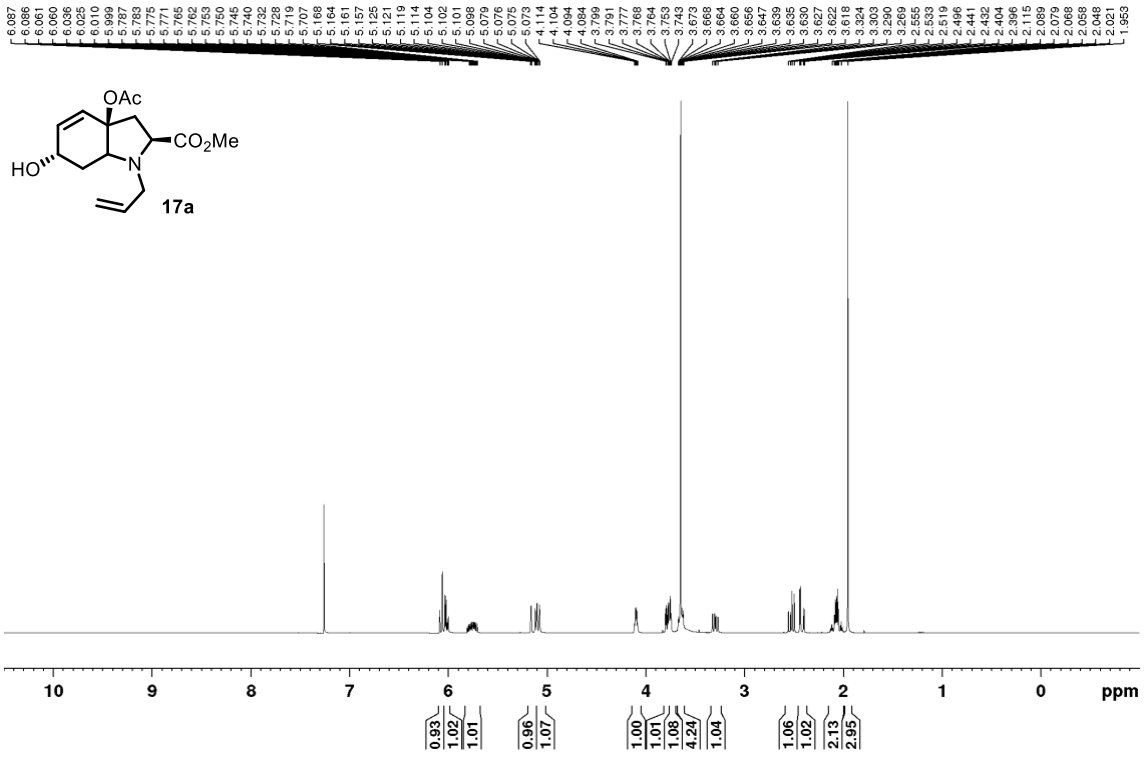


^{13}C NMR (100 MHz, $CDCl_3$)

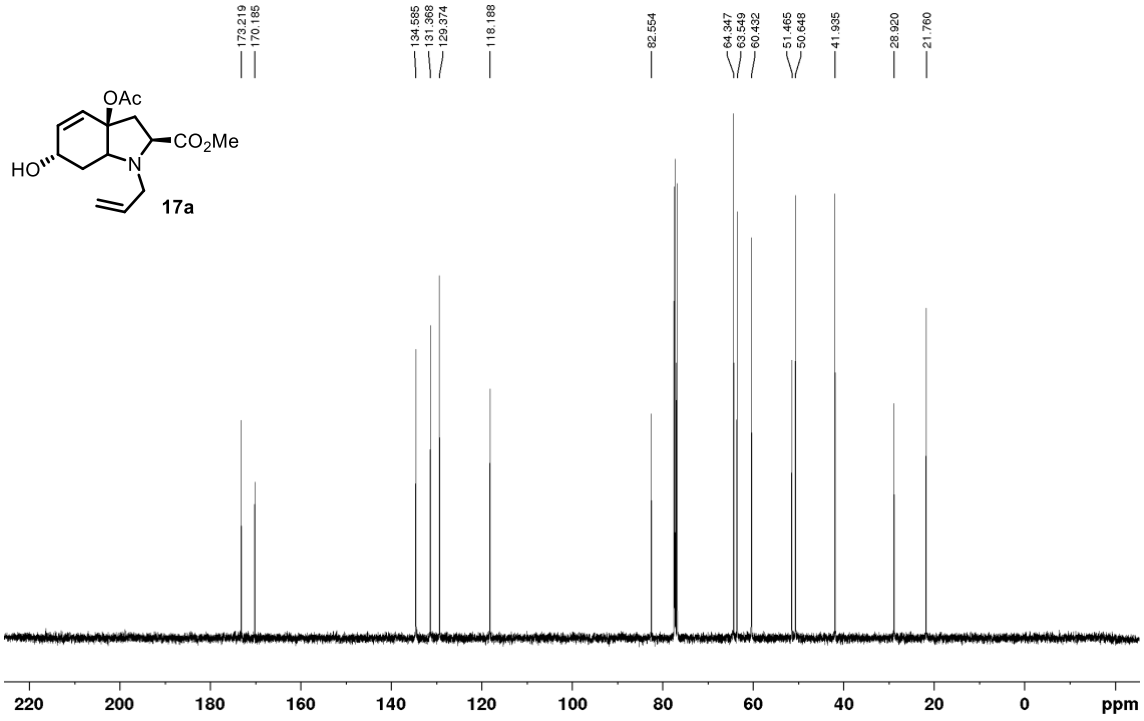


Alcohol **17a**

^{1}H NMR (400 MHz, $CDCl_3$)

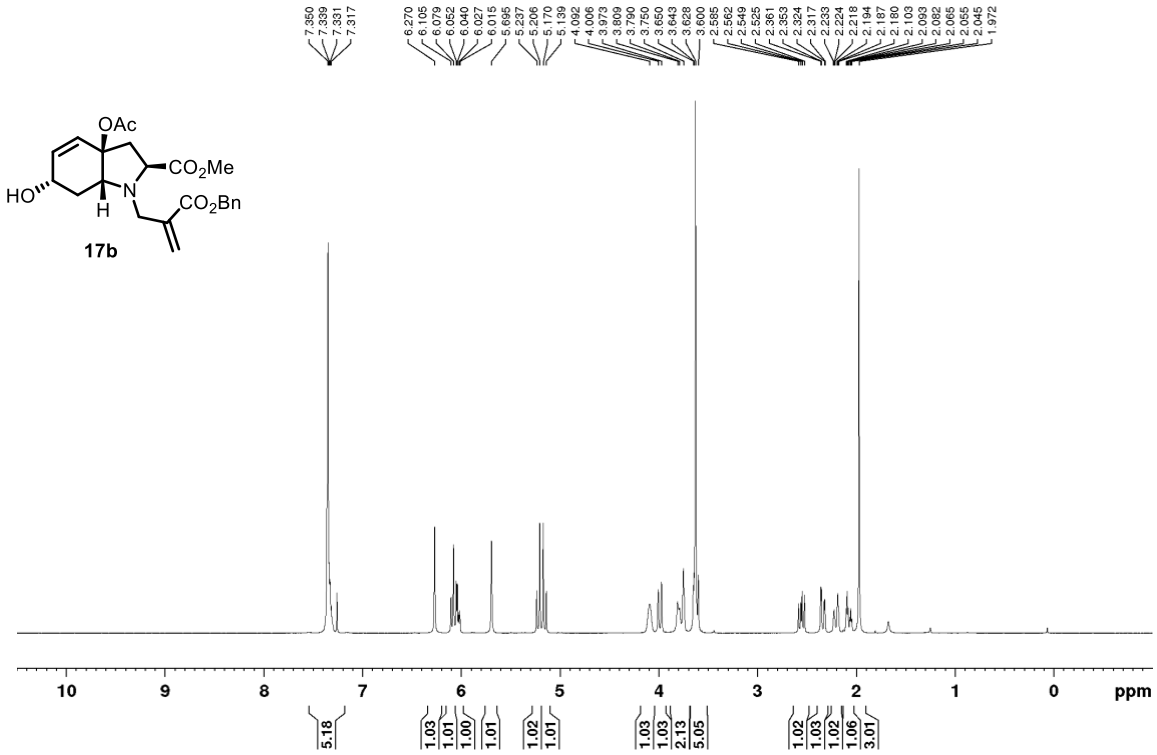


^{13}C NMR (100 MHz, $CDCl_3$)

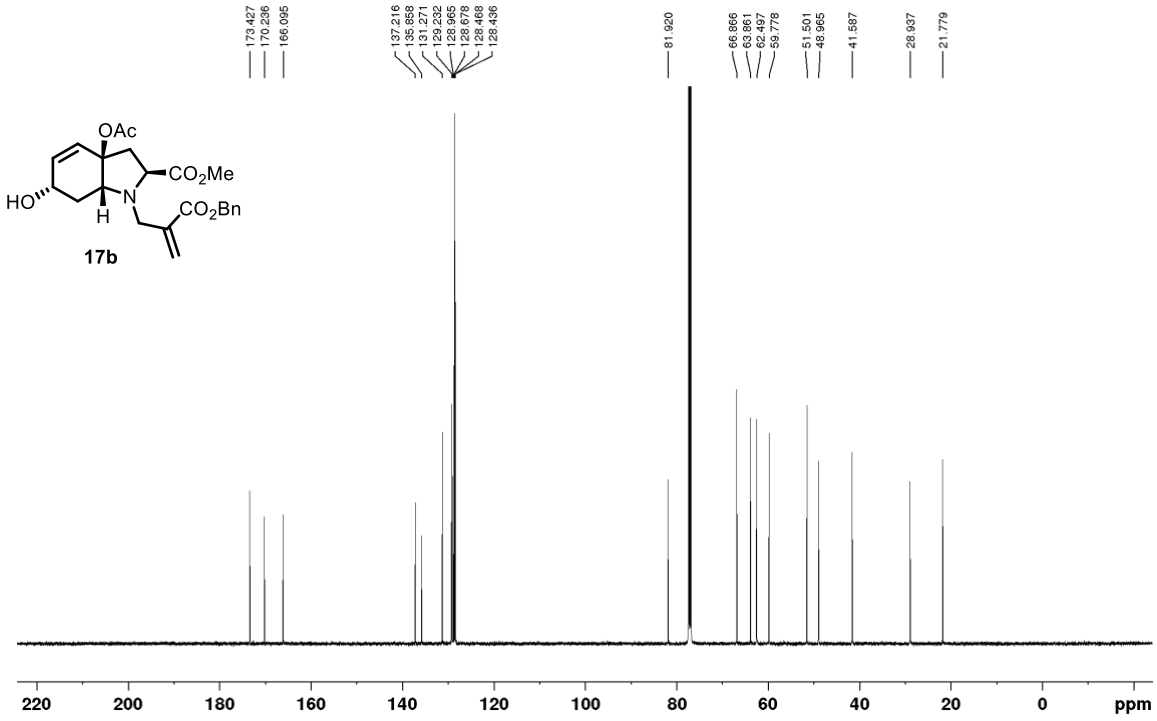


Alcohol **17b**

^{1}H NMR (400 MHz, $CDCl_3$)

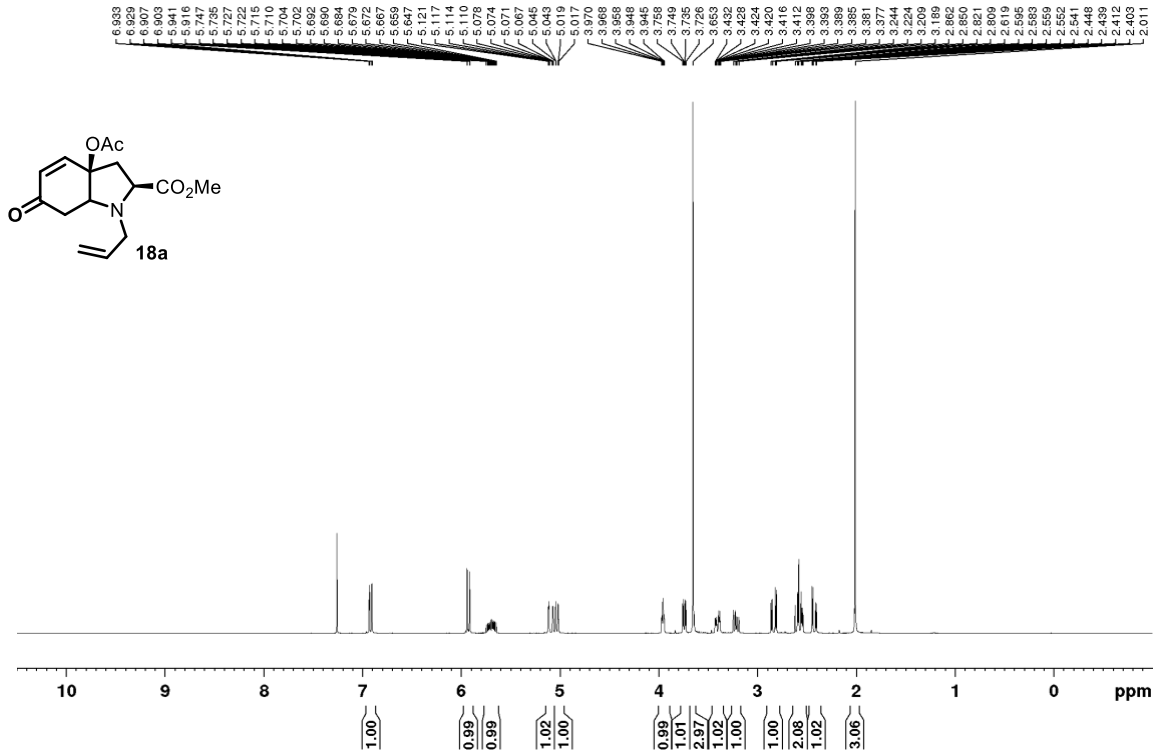


^{13}C NMR (125 MHz, $CDCl_3$)

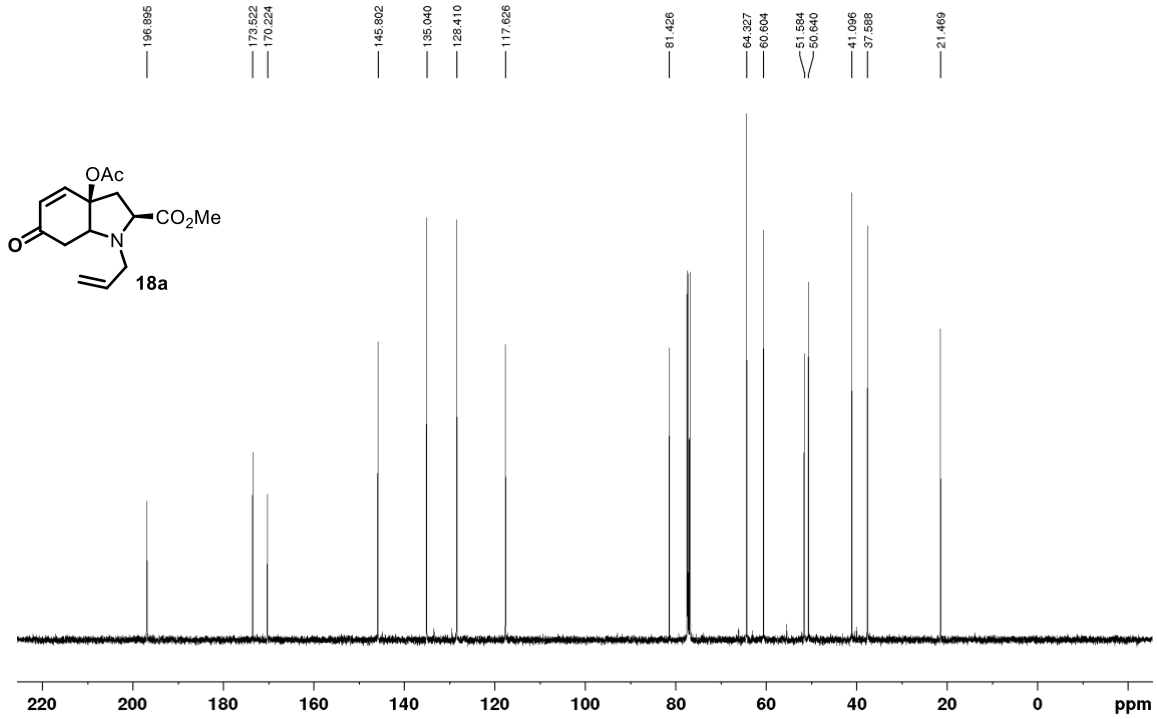


Enone **18a**

^{1}H NMR (400 MHz, $CDCl_3$)

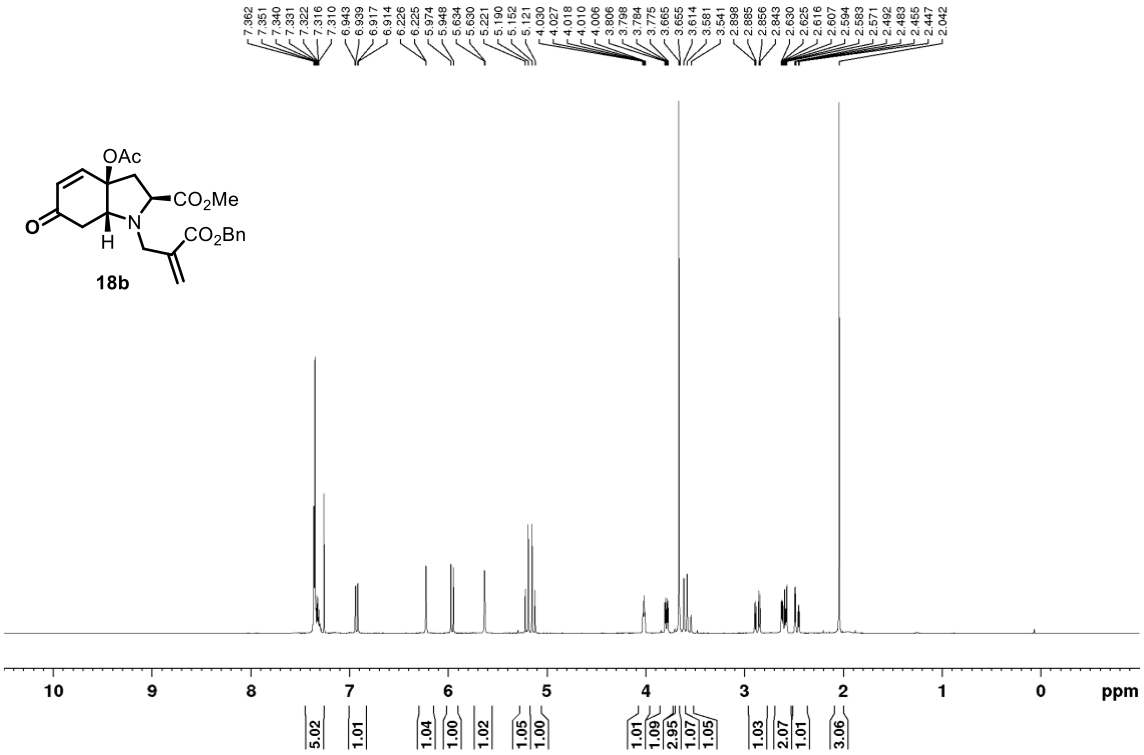


^{13}C NMR (100 MHz, $CDCl_3$)

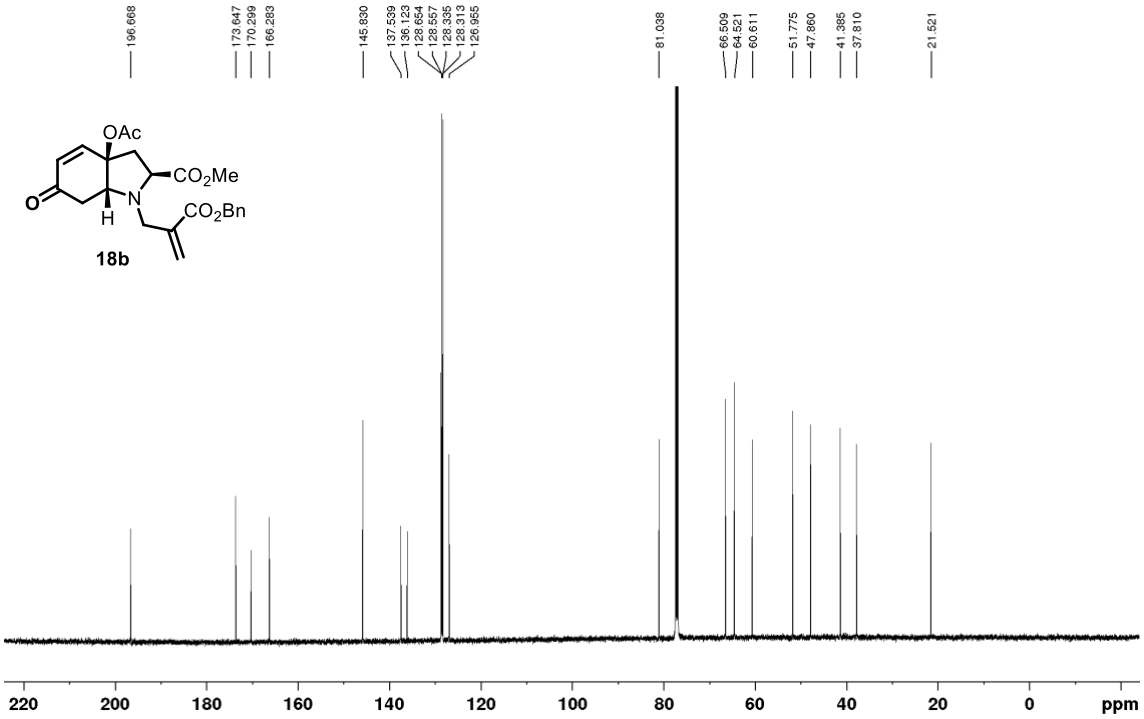


Enone **18b**

^{1}H NMR (400 MHz, $CDCl_3$)

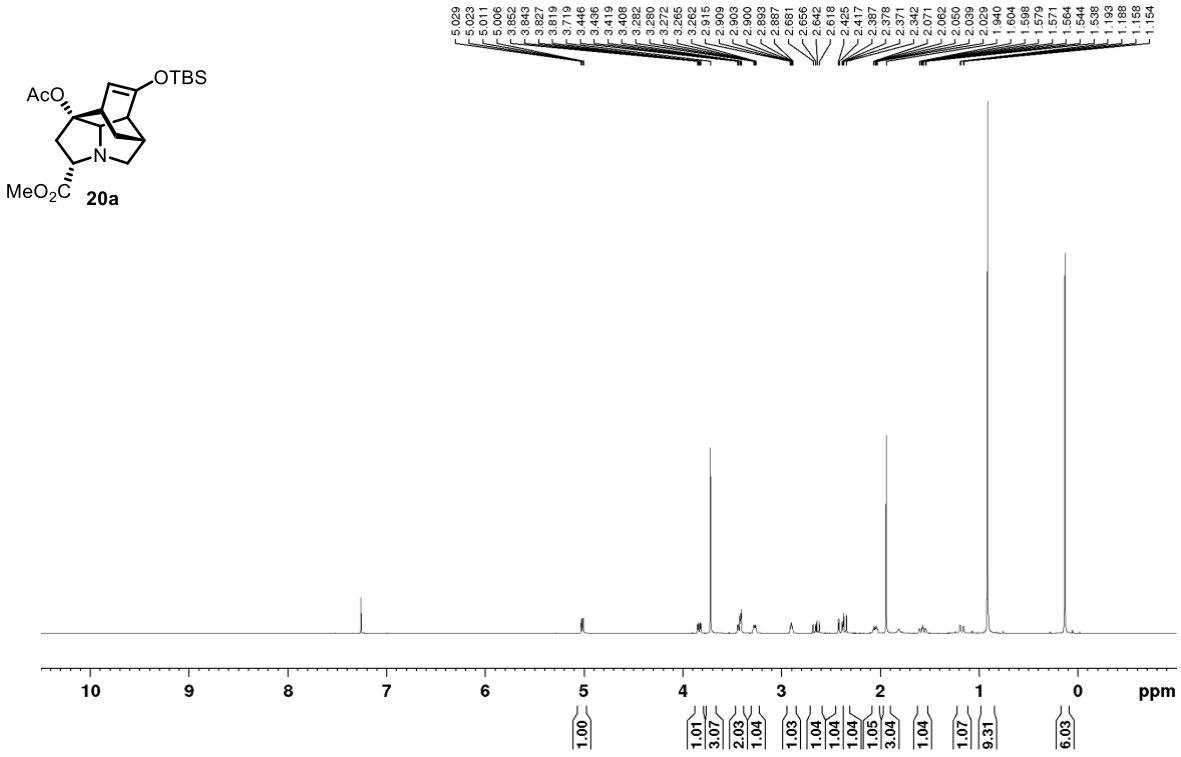


^{13}C NMR (125 MHz, $CDCl_3$)

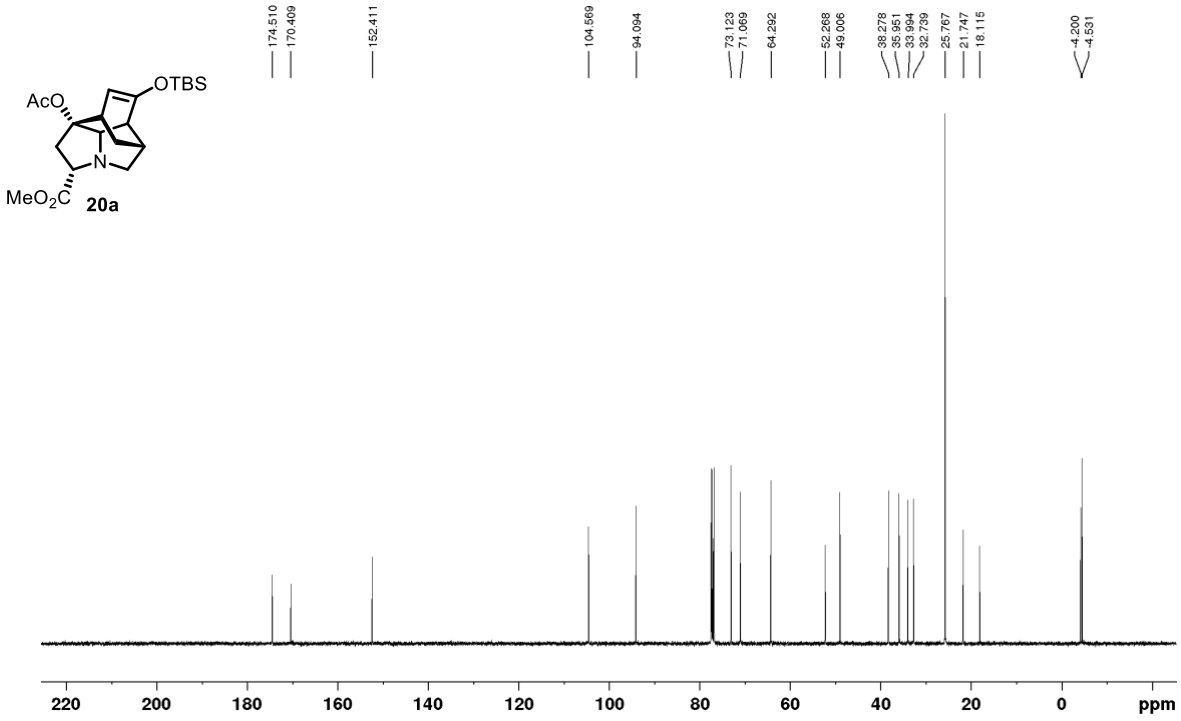


Tetracyclic amine 20a

^{1}H NMR (400 MHz, $CDCl_3$)

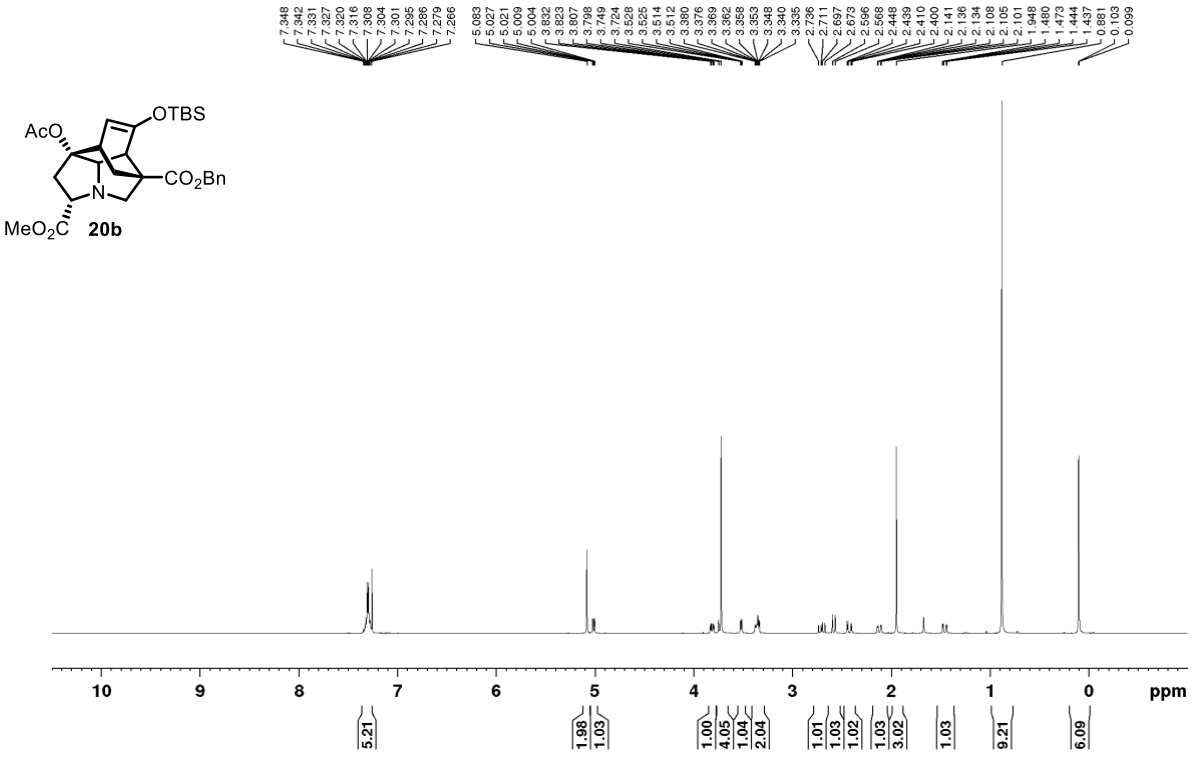


^{13}C NMR (100 MHz, $CDCl_3$)

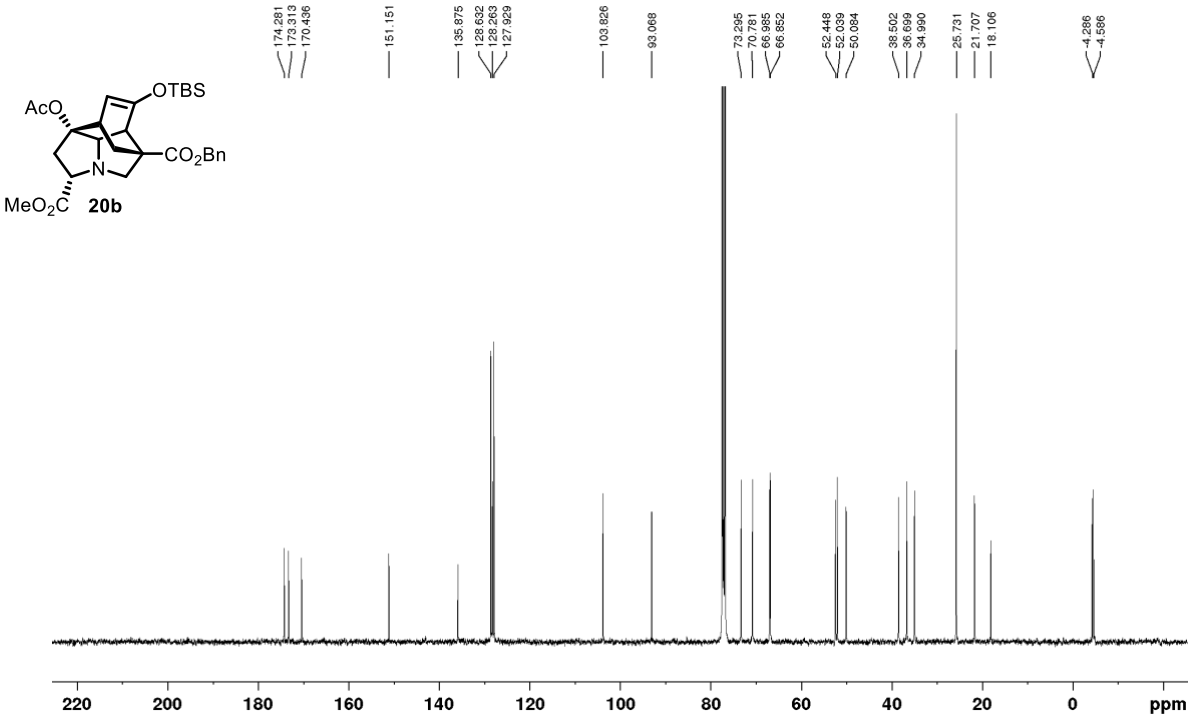


Tetracyclic amine 20b

^{1}H NMR (400 MHz, $CDCl_3$)

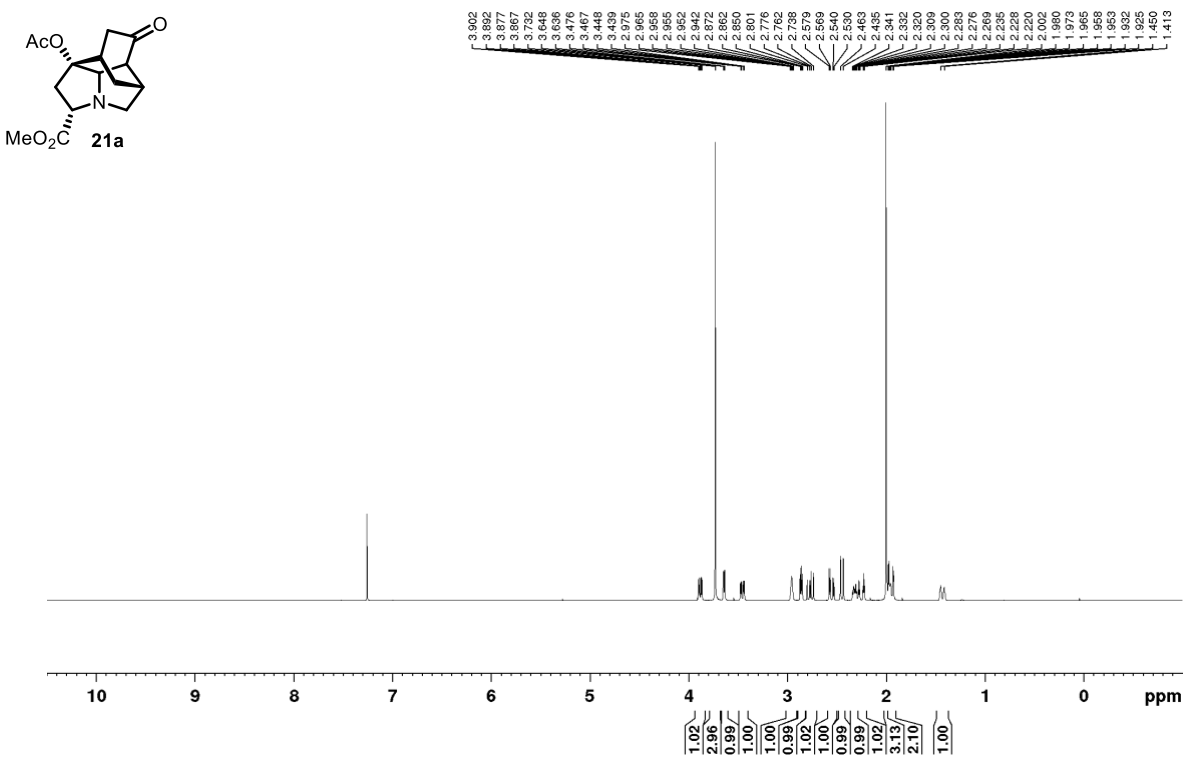


^{13}C NMR (100 MHz, $CDCl_3$)

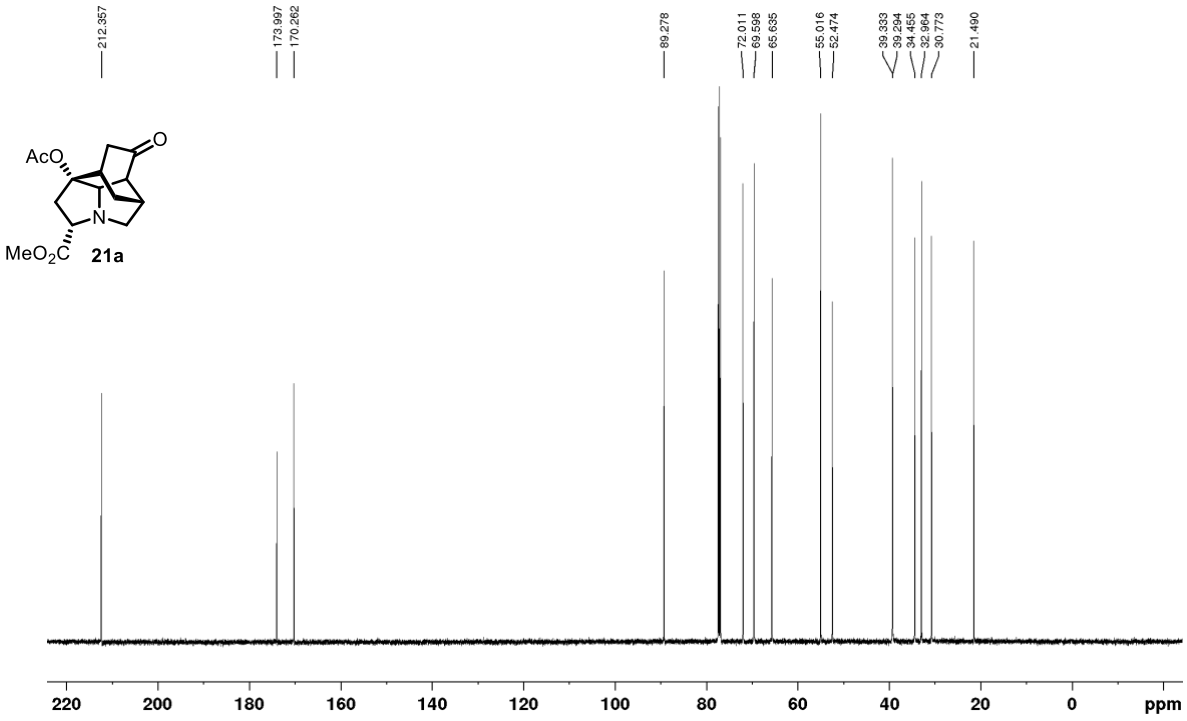


Ketone 21a

^{1}H NMR (400 MHz, $CDCl_3$)

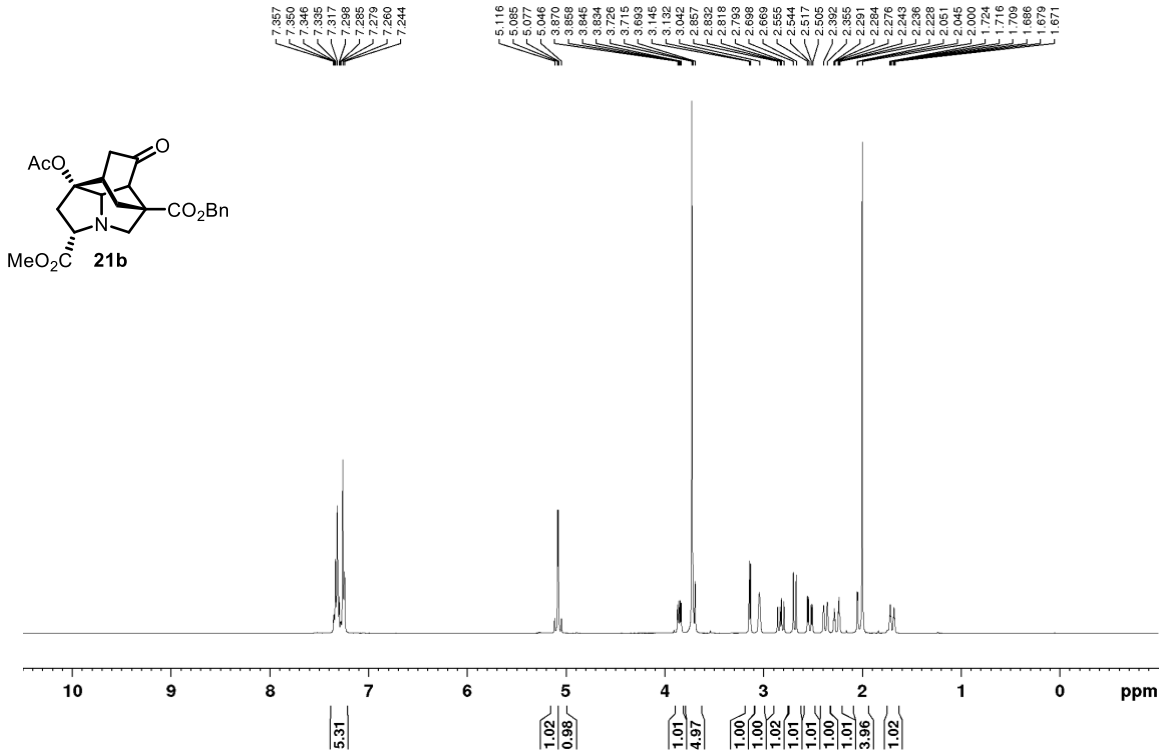


^{13}C NMR (125 MHz, $CDCl_3$)

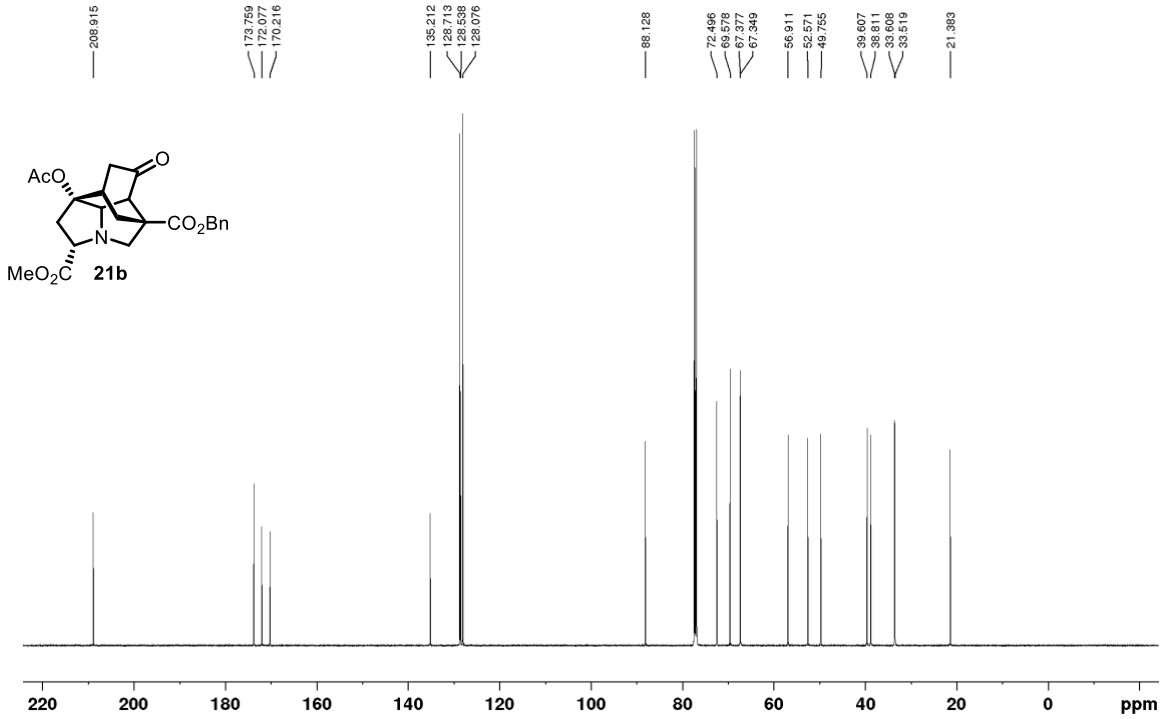


Ketone **21b**

^{1}H NMR (400 MHz, $CDCl_3$)

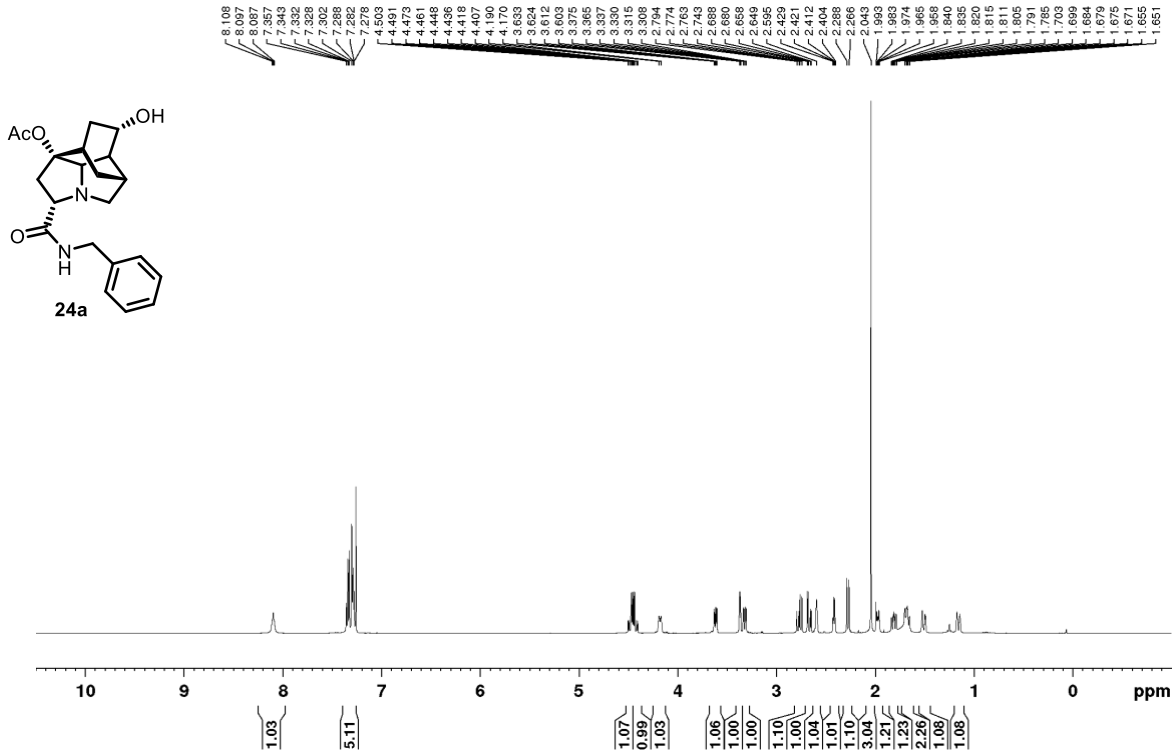


^{13}C NMR (125 MHz, $CDCl_3$)

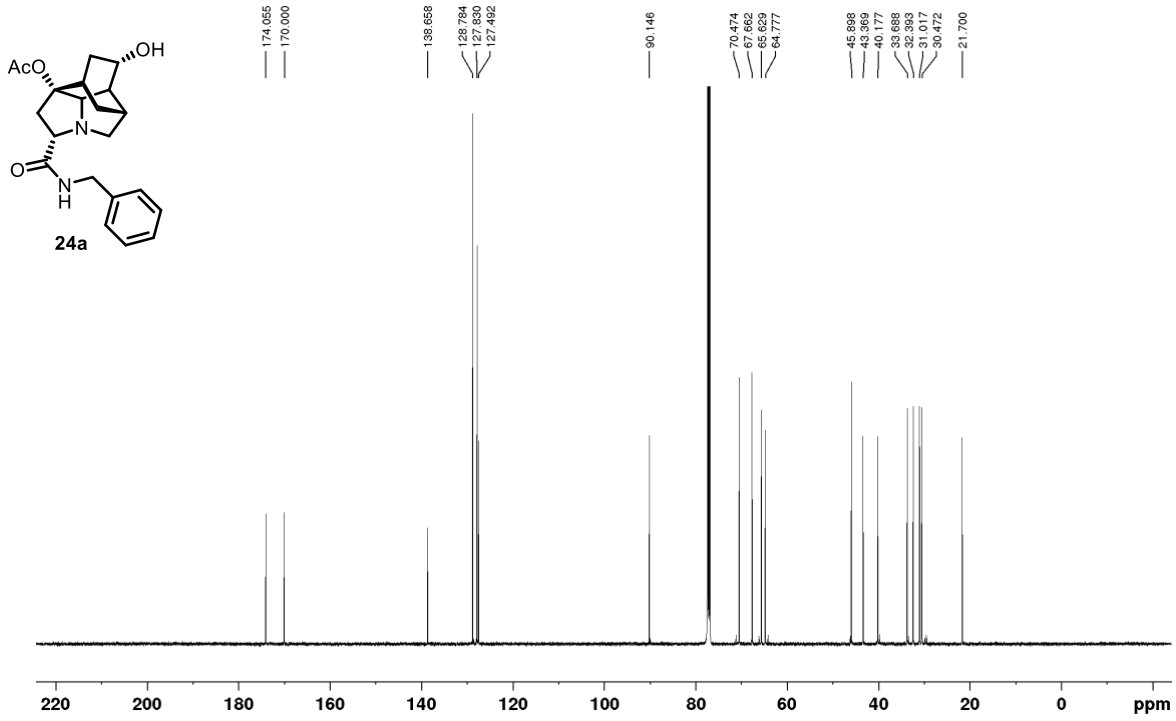


Alcohol **24a**

^{1}H NMR (500 MHz, $CDCl_3$)

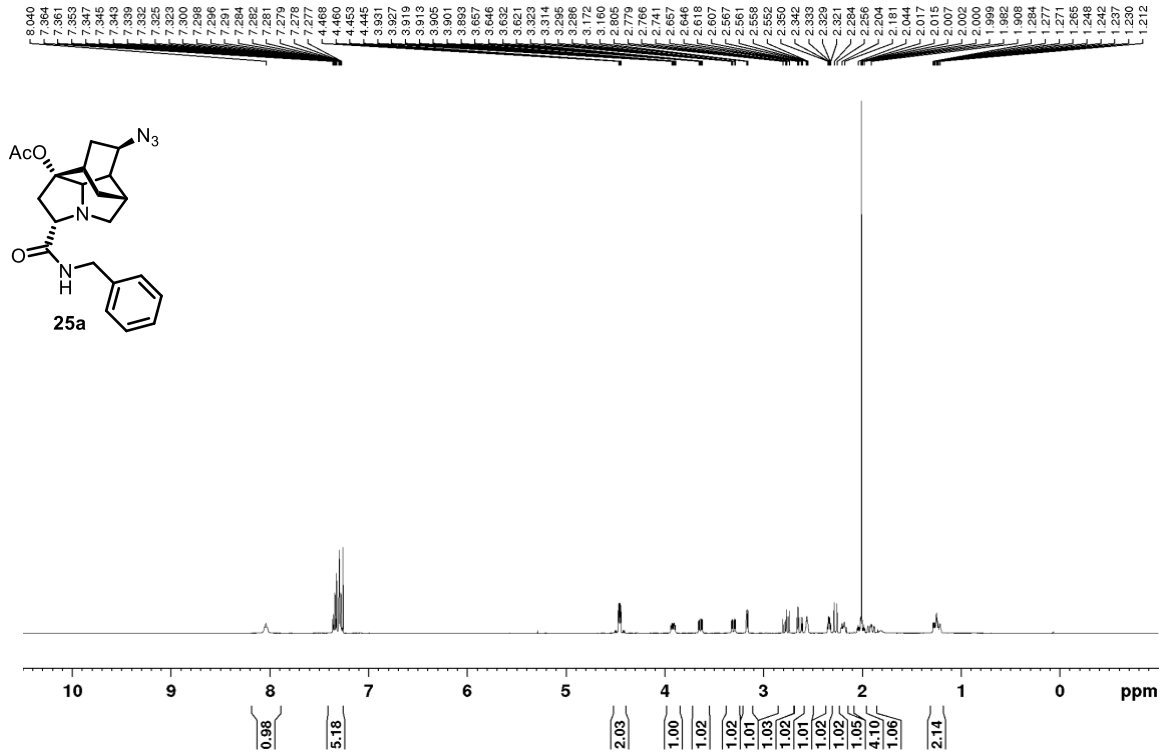


^{13}C NMR (125 MHz, $CDCl_3$)

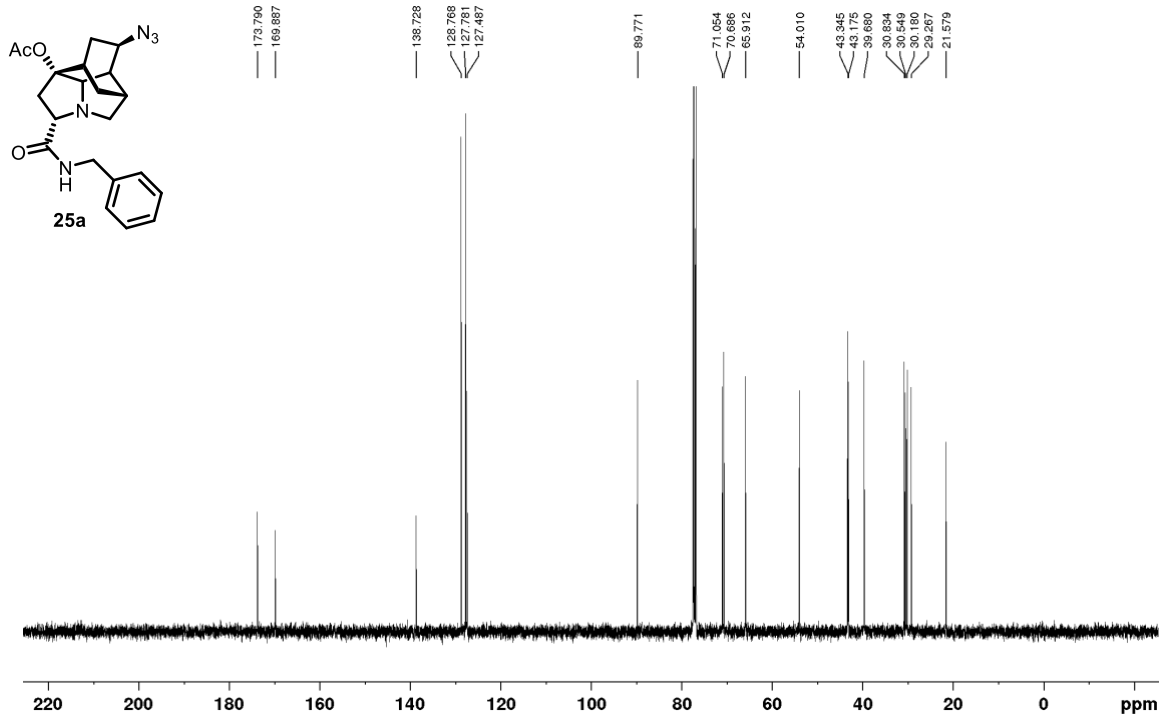


Azide **25a**

^{1}H NMR (400 MHz, $CDCl_3$)

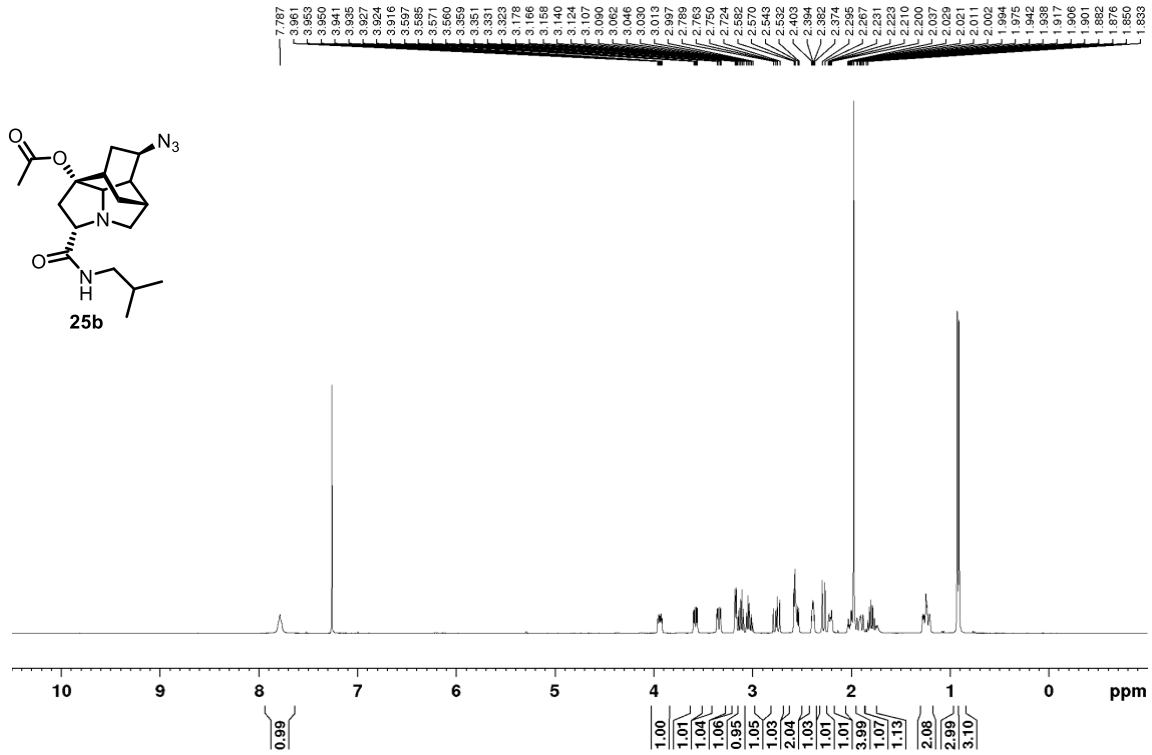


^{13}C NMR (100 MHz, $CDCl_3$)

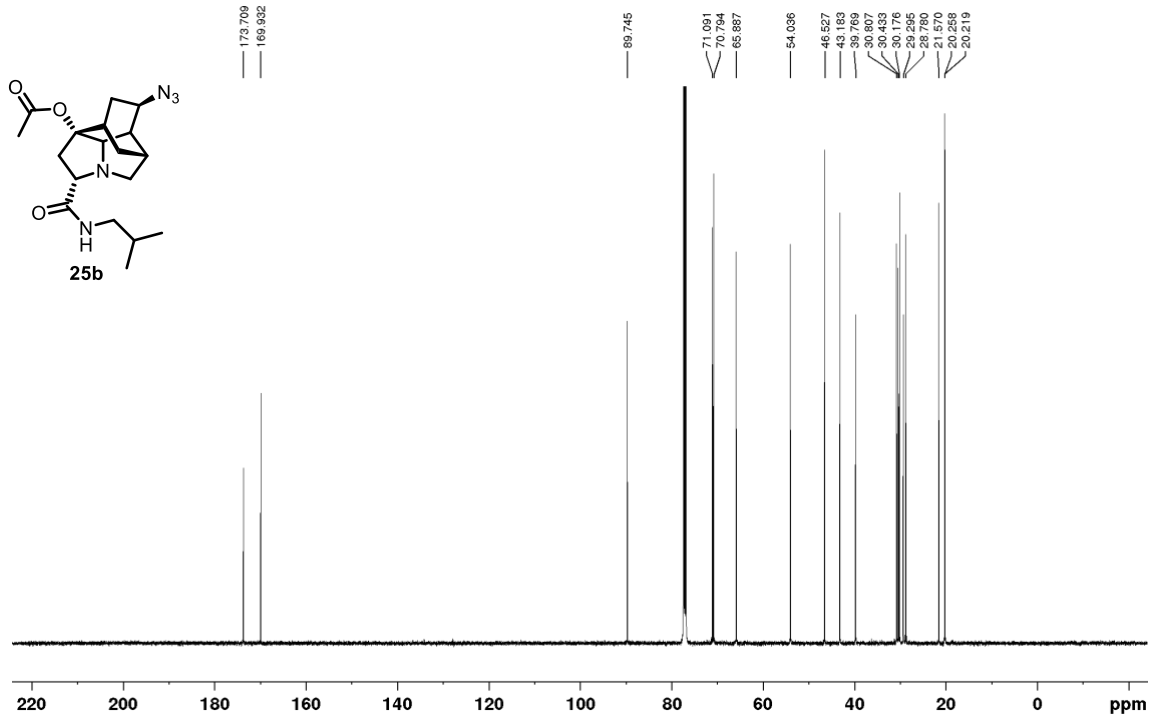


Azide **25b**

^{1}H NMR (400 MHz, $CDCl_3$)

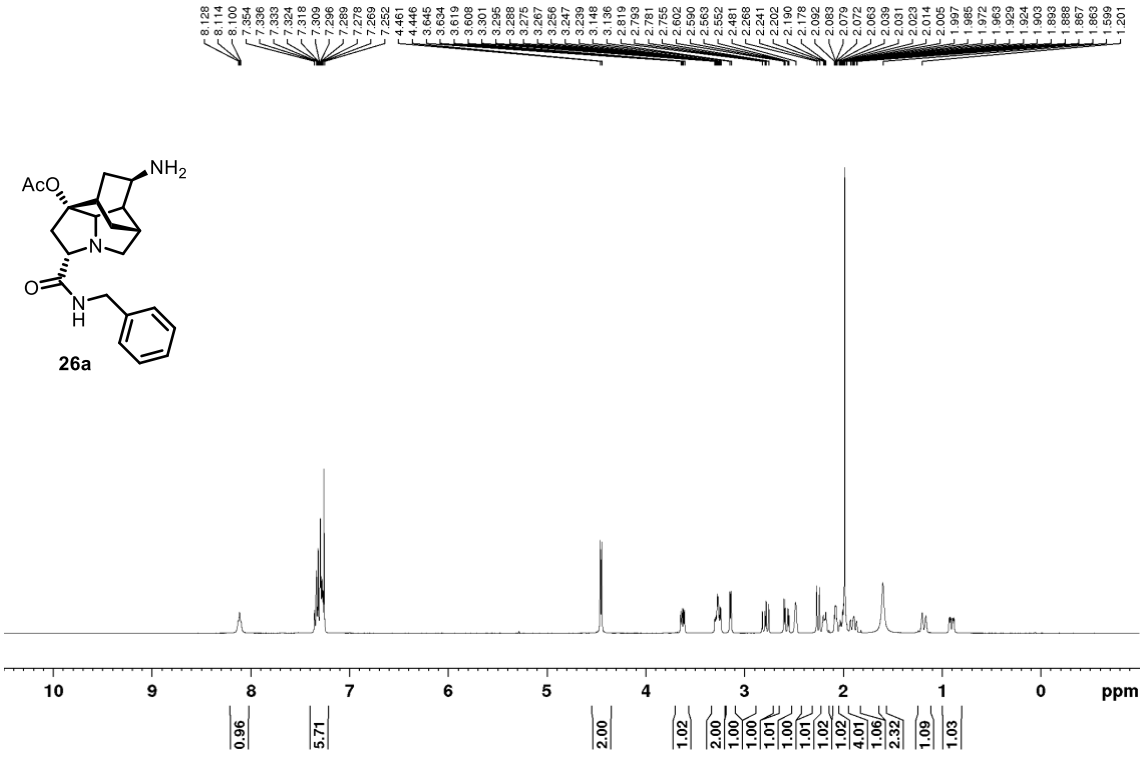


^{13}C NMR (125 MHz, $CDCl_3$)

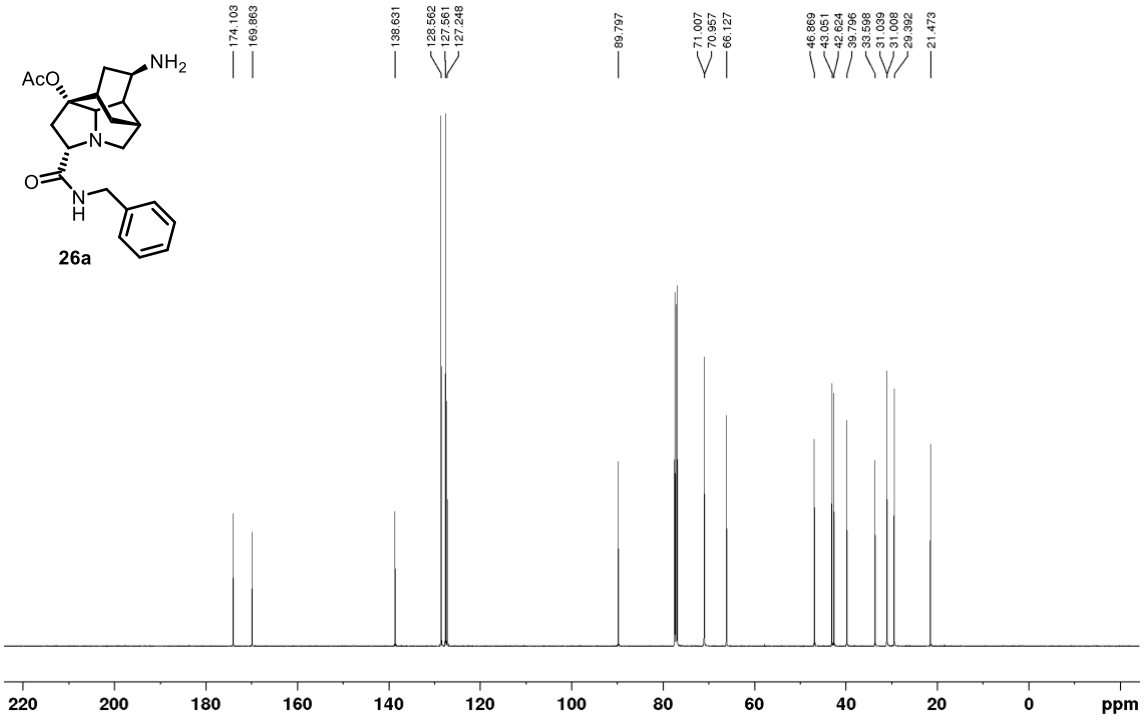


Amine **26a**

^{1}H NMR (400 MHz, $CDCl_3$)

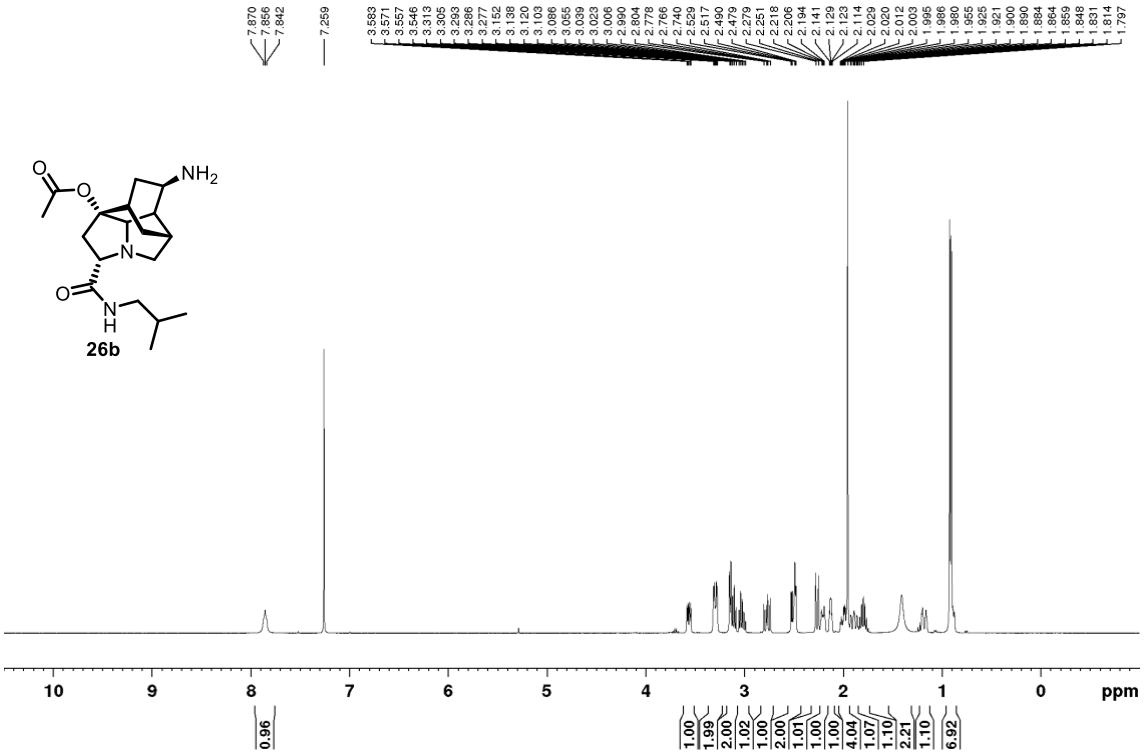


^{13}C NMR (125 MHz, $CDCl_3$)

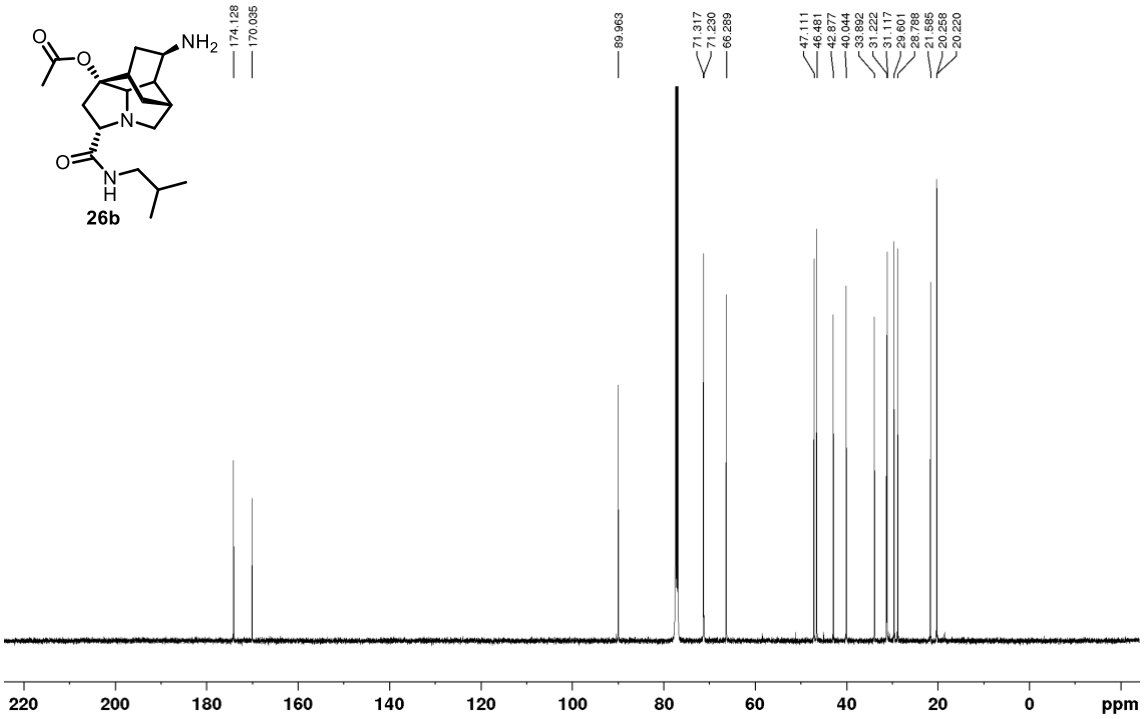


Amine **26b**

^{1}H NMR (400 MHz, $CDCl_3$)

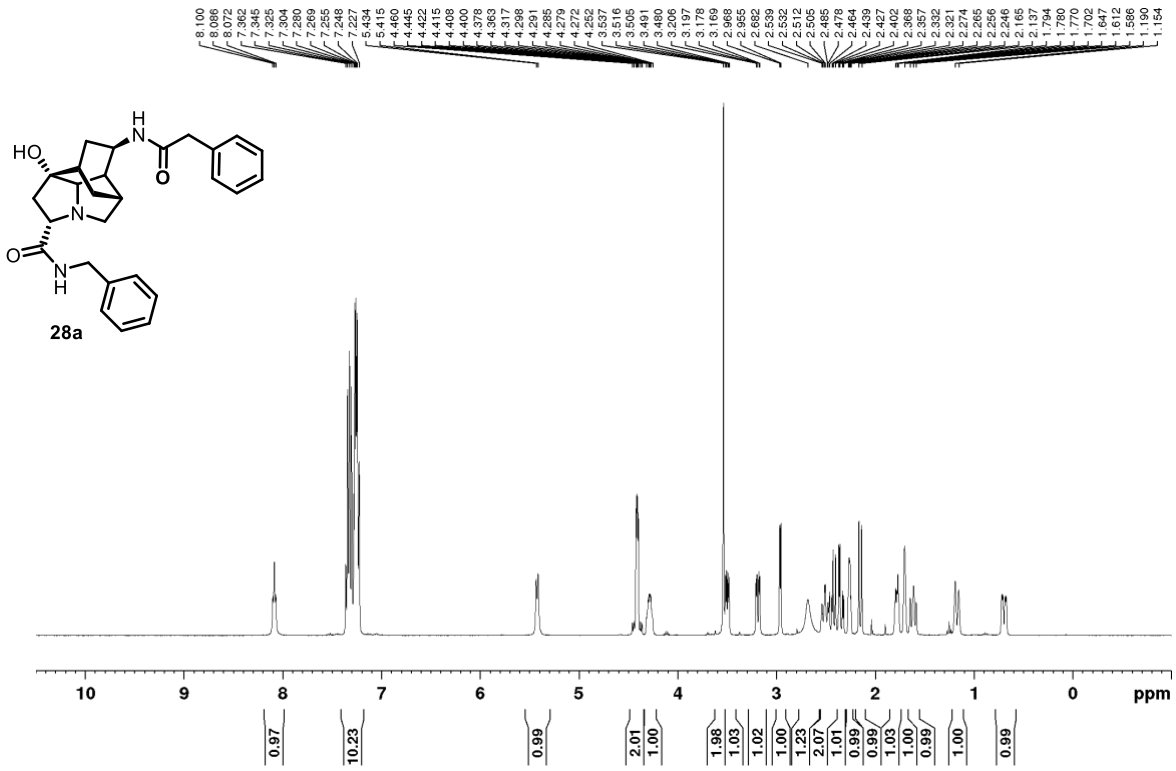


^{13}C NMR (125 MHz, $CDCl_3$)

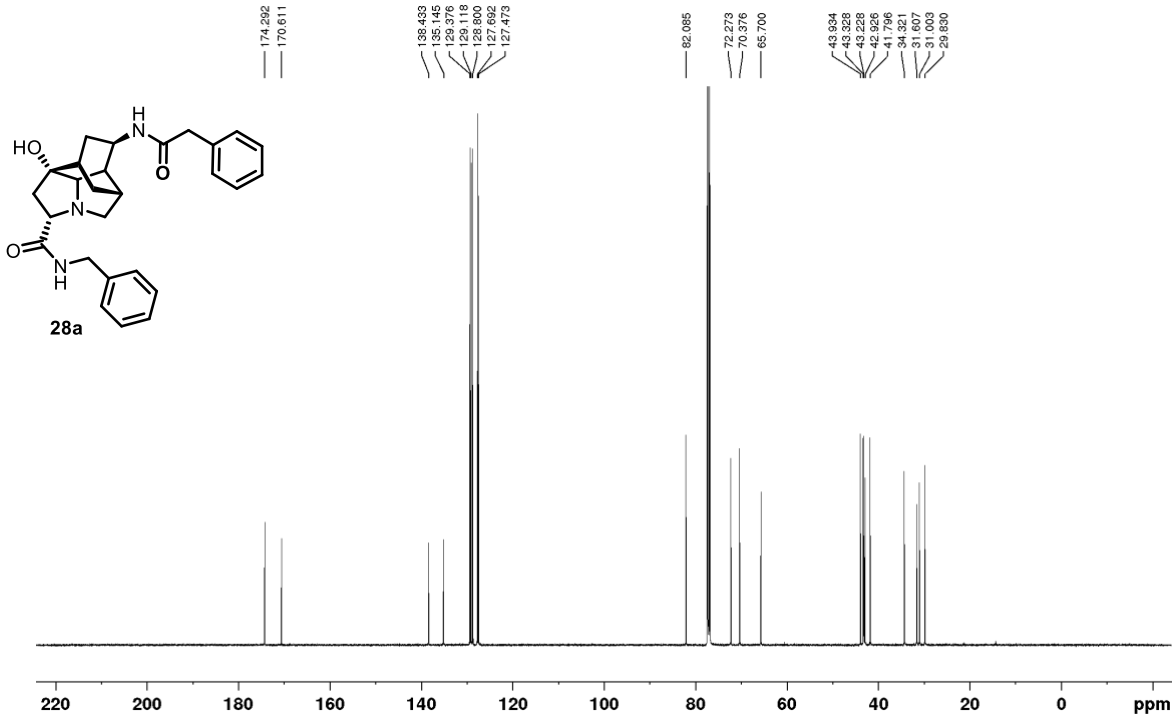


Alcohol **28a**

^{1}H NMR (400 MHz, $CDCl_3$)

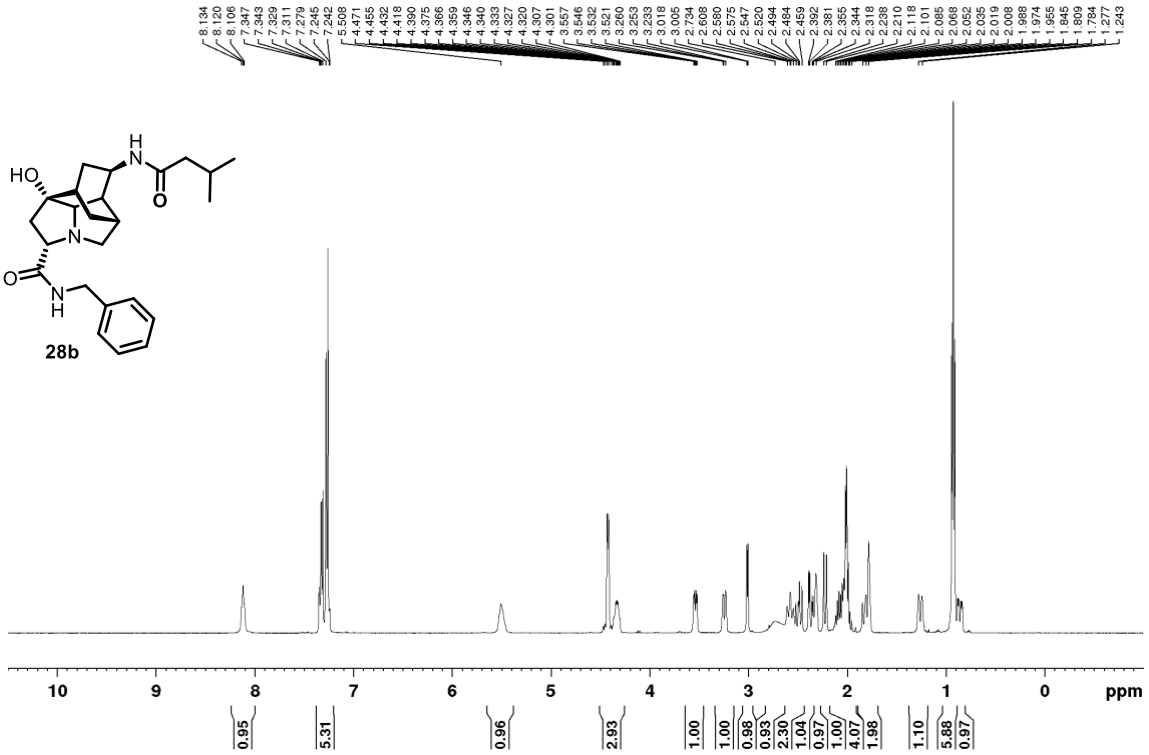


^{13}C NMR (125 MHz, $CDCl_3$)

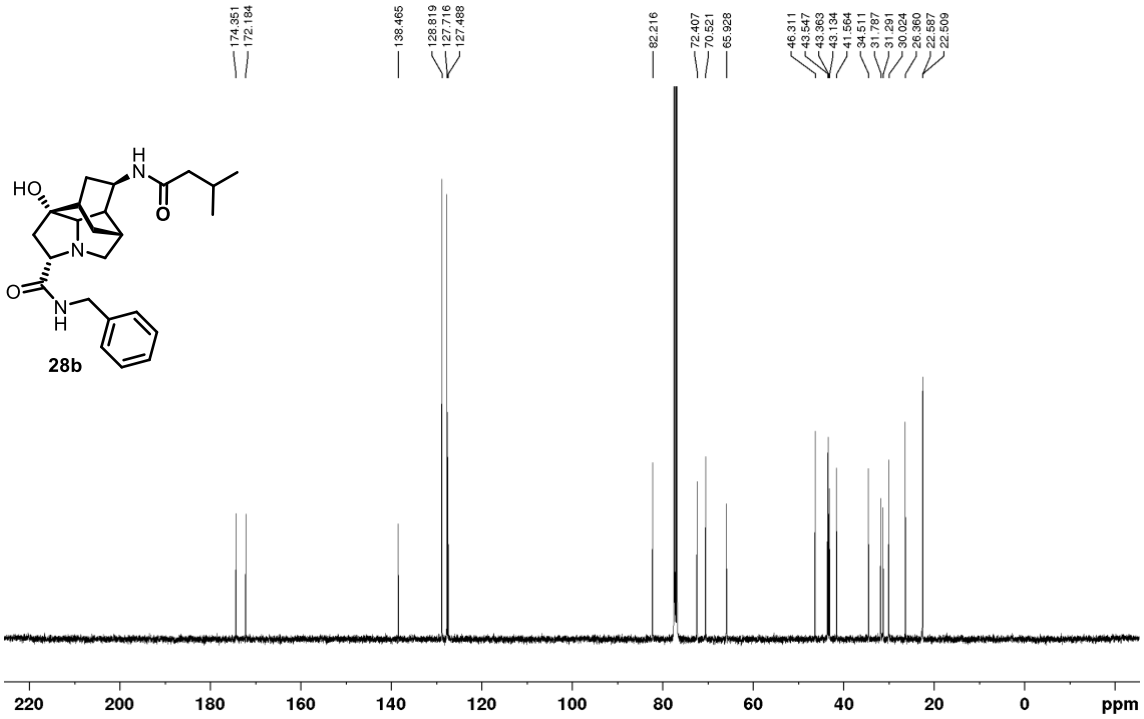


Alcohol **28b**

^{1}H NMR (400 MHz, $CDCl_3$)

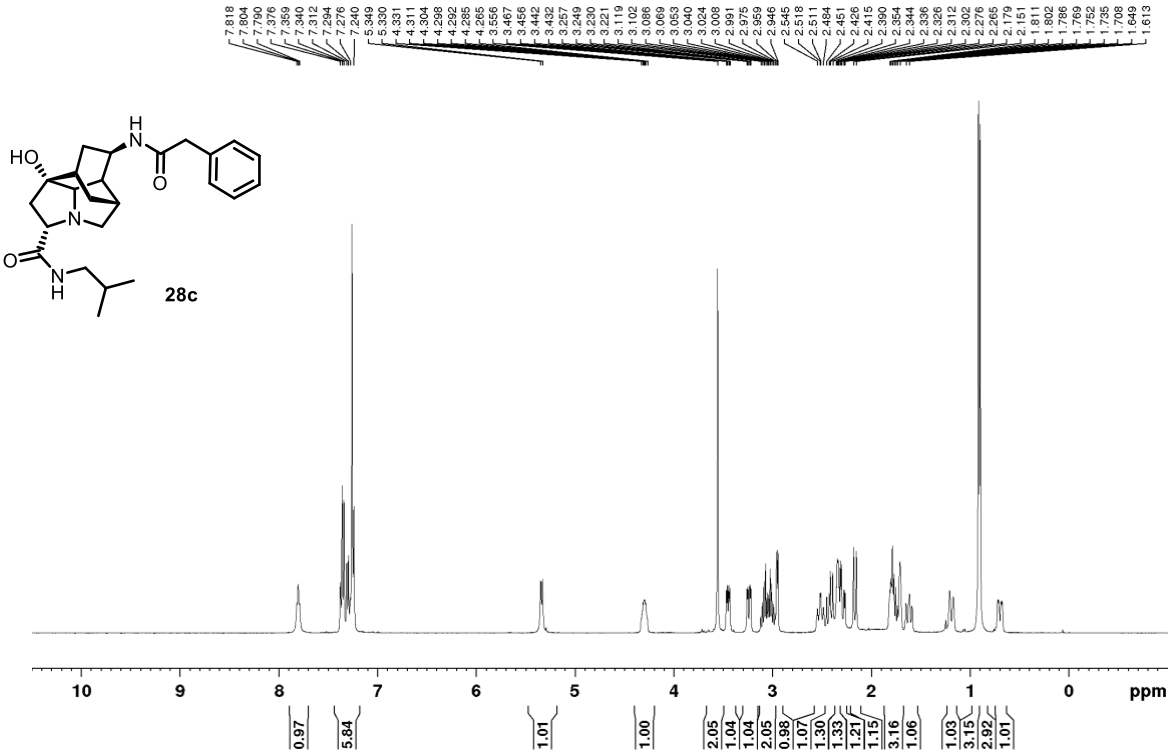


^{13}C NMR (100 MHz, $CDCl_3$)

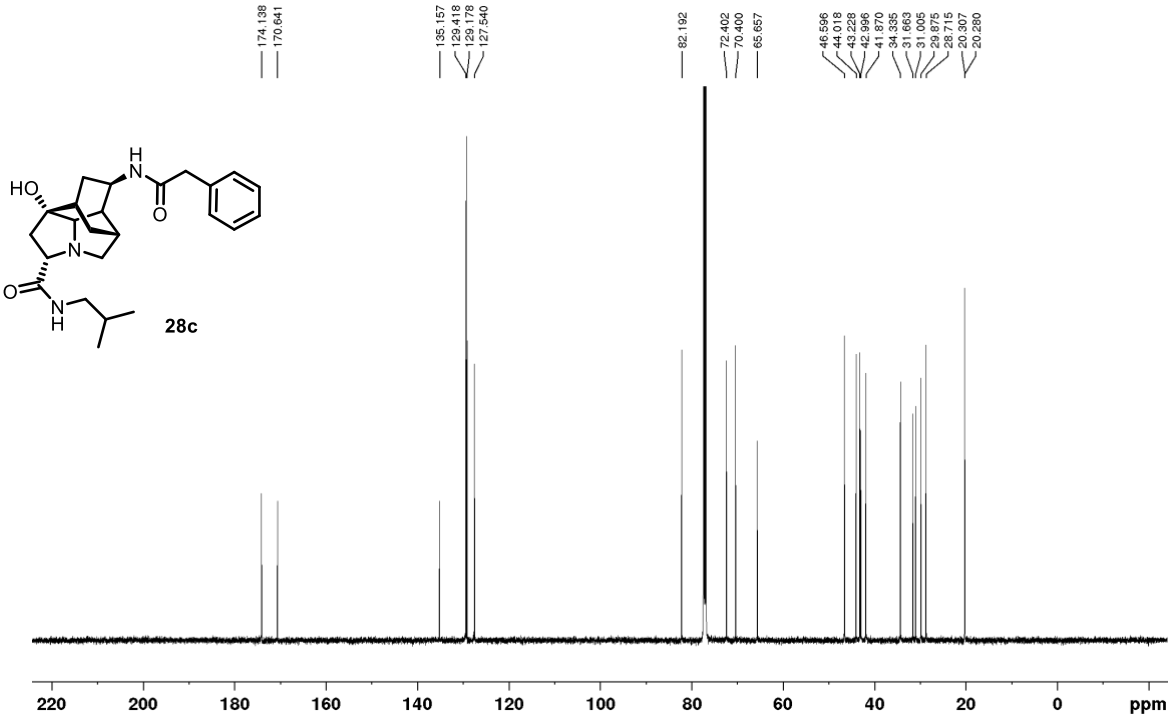


Alcohol **28c**

^{1}H NMR (400 MHz, $CDCl_3$)

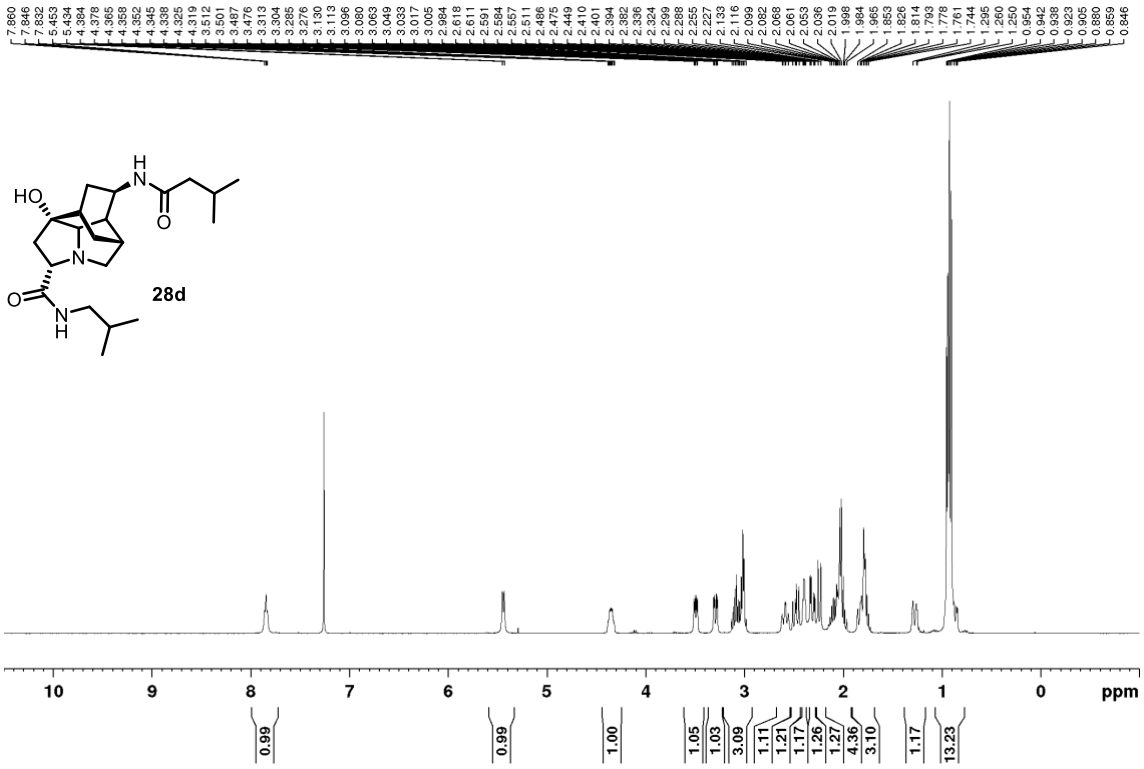


^{13}C NMR (125 MHz, $CDCl_3$)

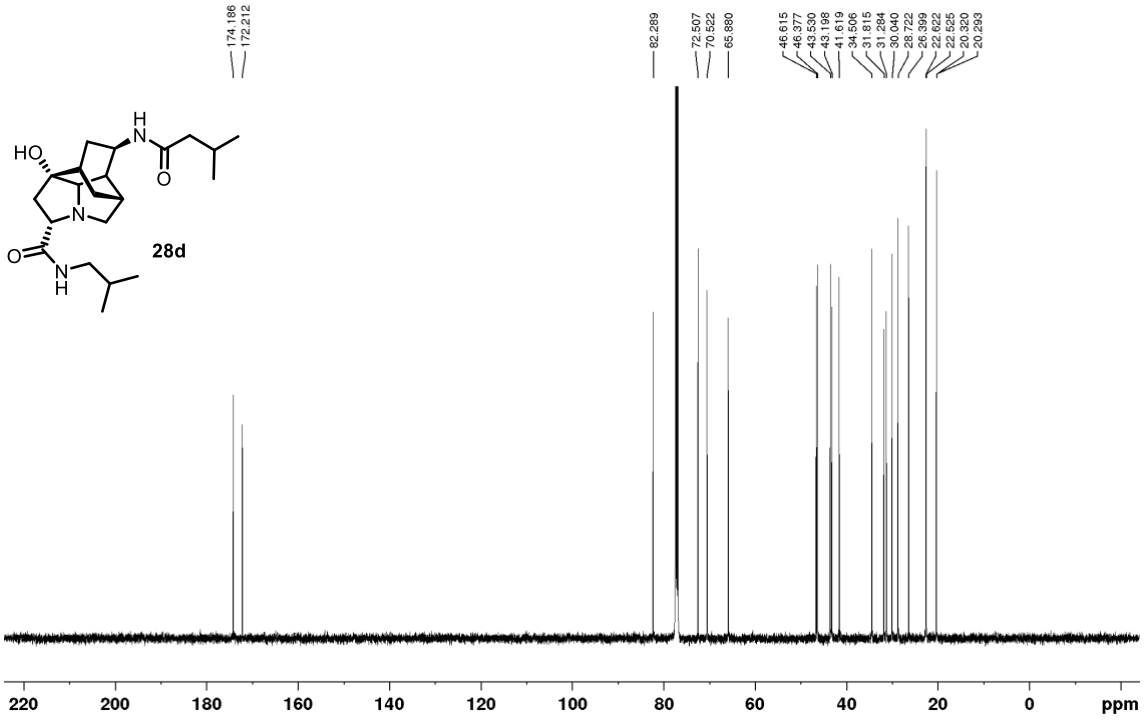


Alcohol **28d**

^{1}H NMR (400 MHz, $CDCl_3$)

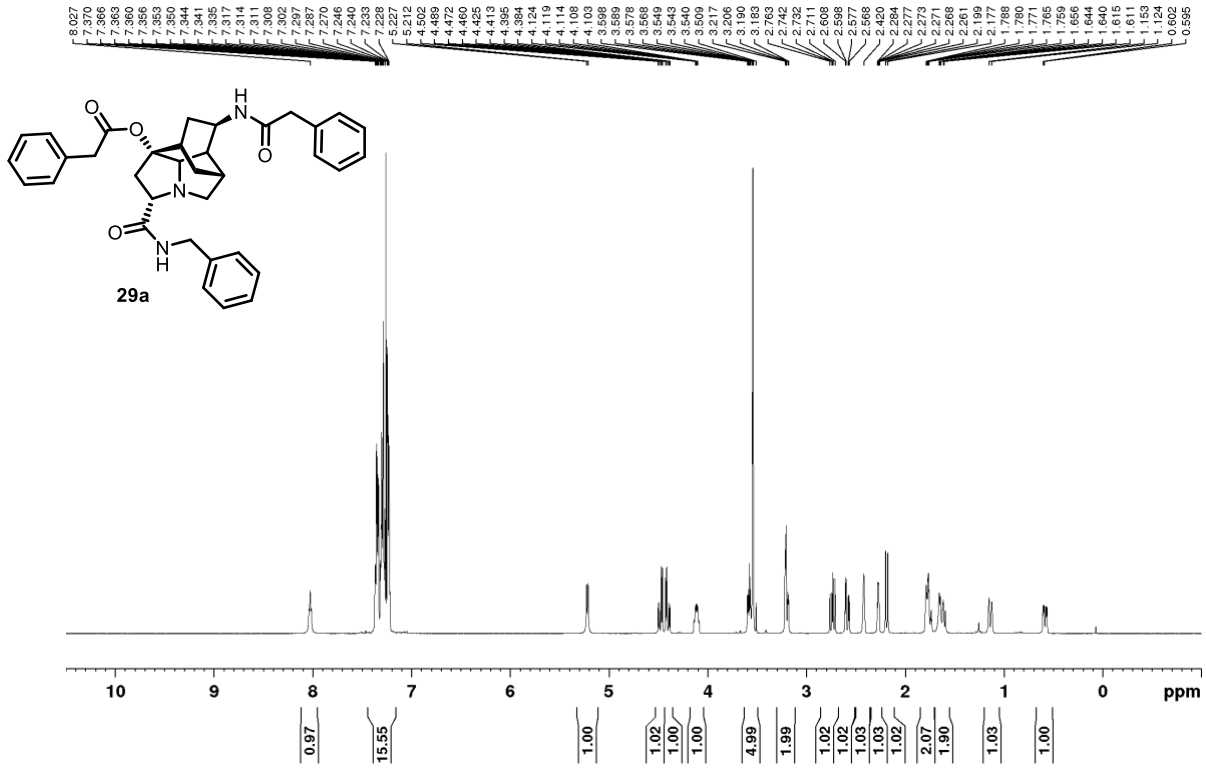


^{13}C NMR (125 MHz, $CDCl_3$)

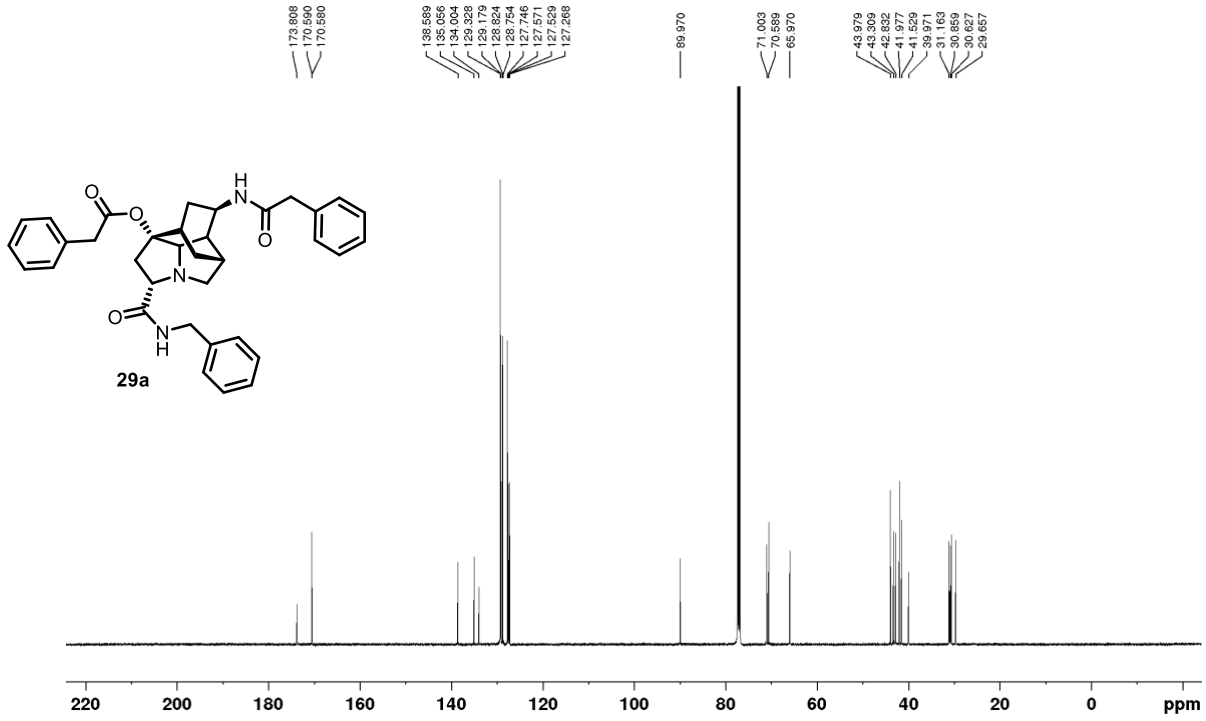


Ester **29a**

^{1}H NMR (500 MHz, $CDCl_3$)

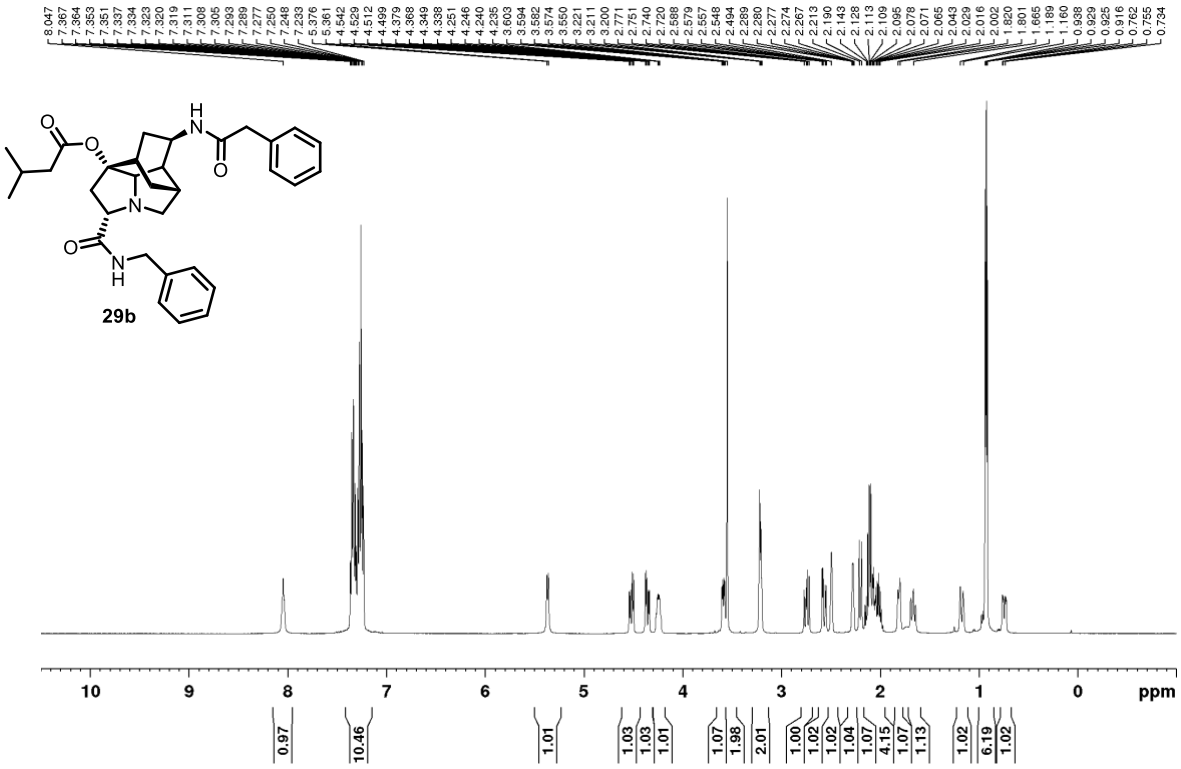


^{13}C NMR (125 MHz, $CDCl_3$)

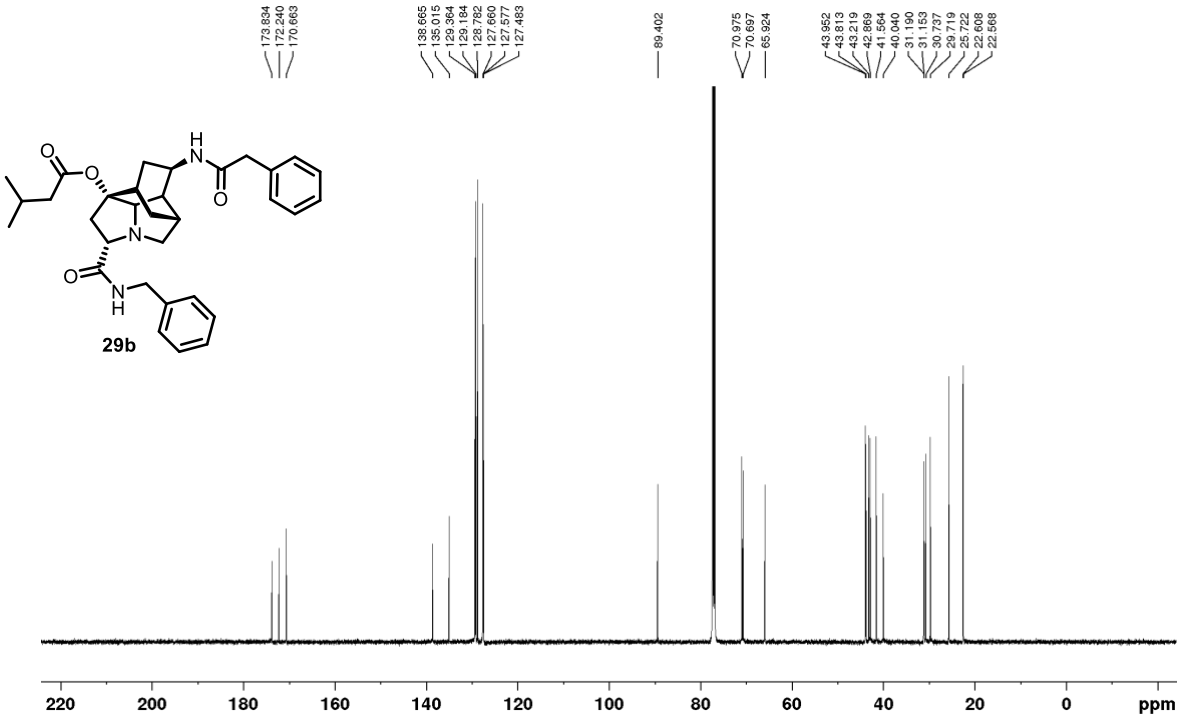


Ester **29b**

^{1}H NMR (500 MHz, $CDCl_3$)

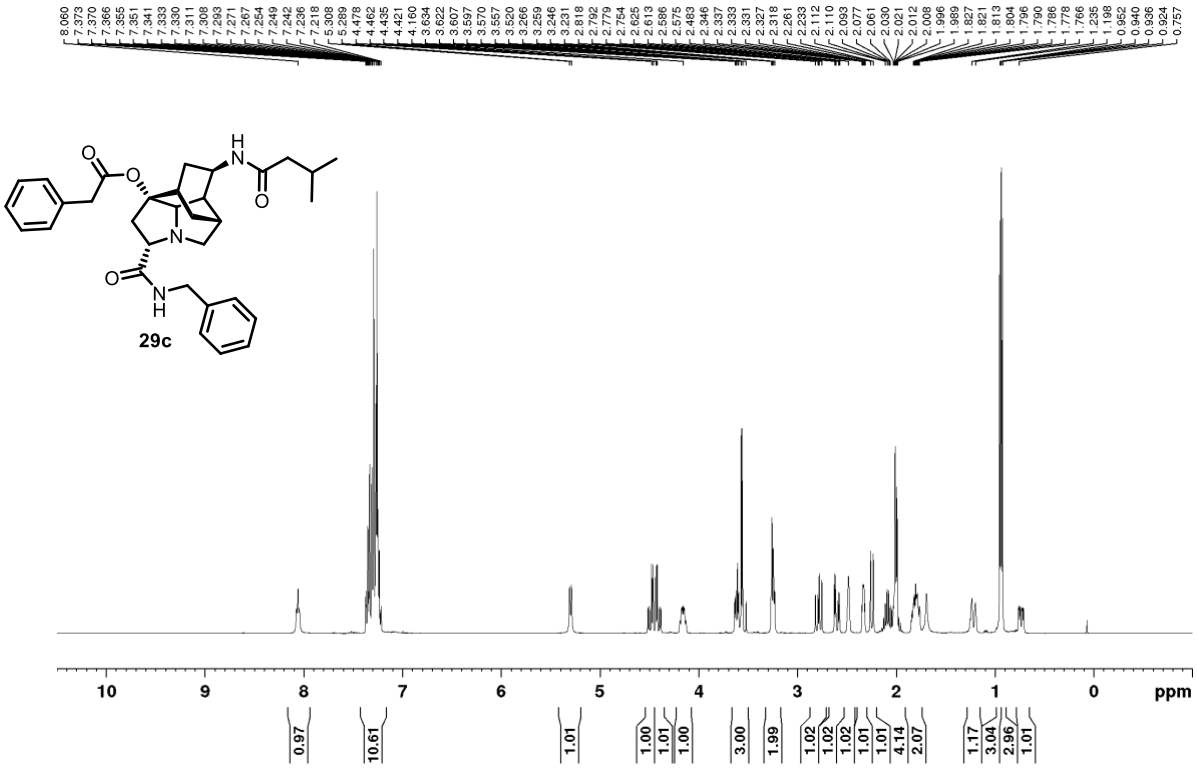


^{13}C NMR (125 MHz, $CDCl_3$)

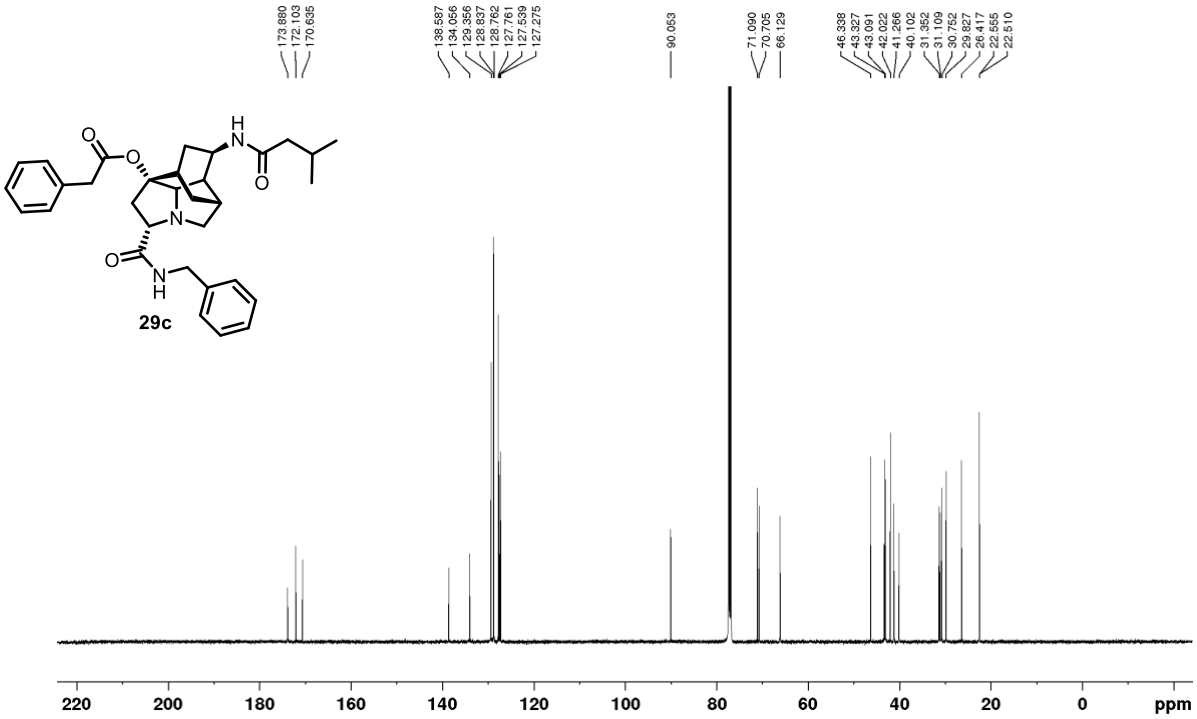


Ester **29c**

^{1}H NMR (400 MHz, $CDCl_3$)

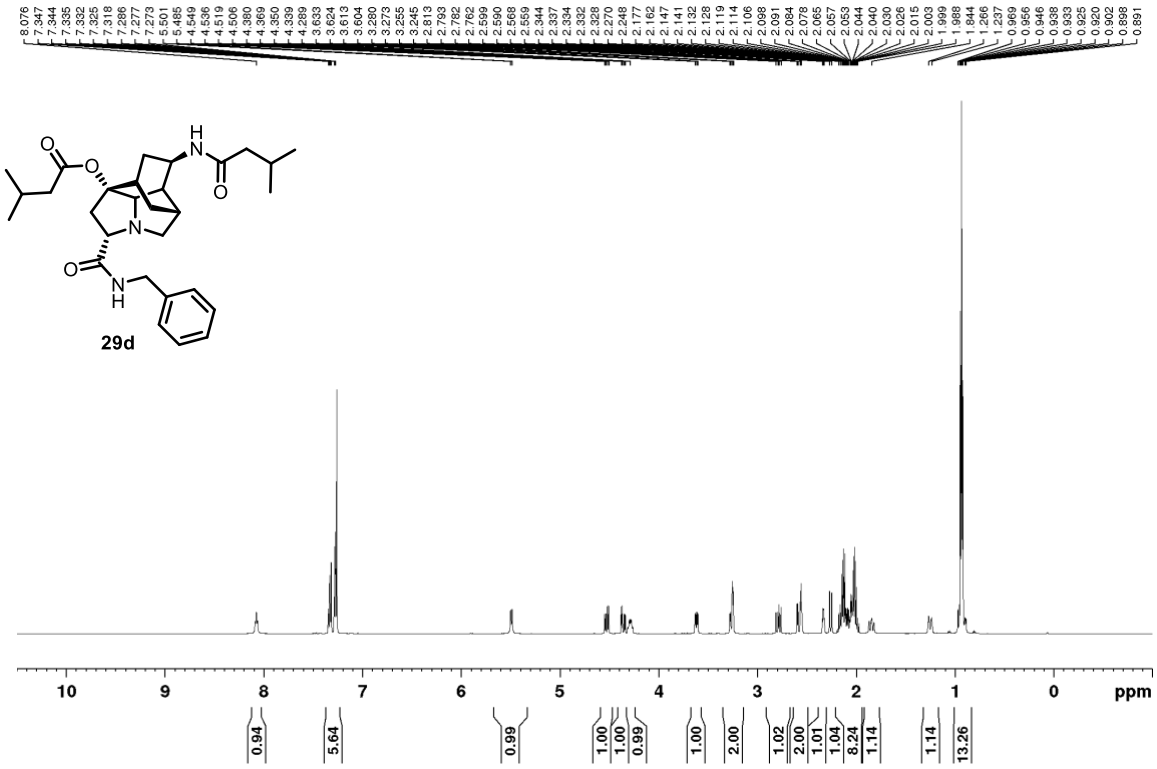


^{13}C NMR (125 MHz, $CDCl_3$)

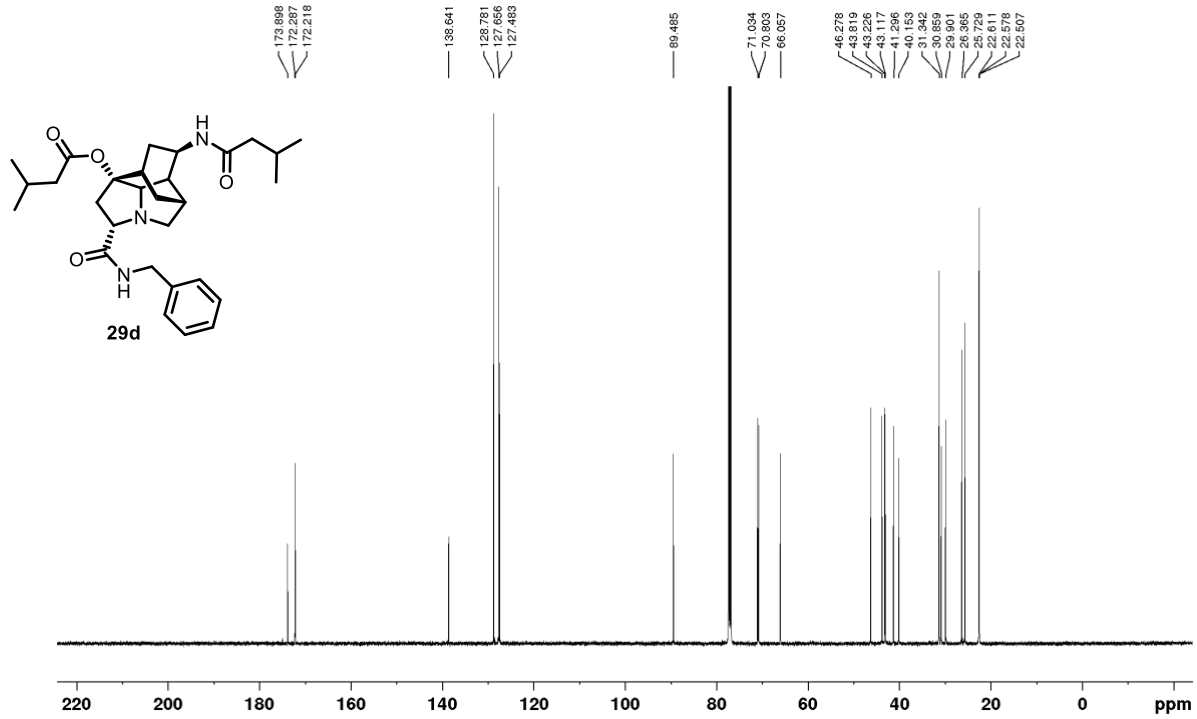


Ester **29d**

^{1}H NMR (500 MHz, $CDCl_3$)

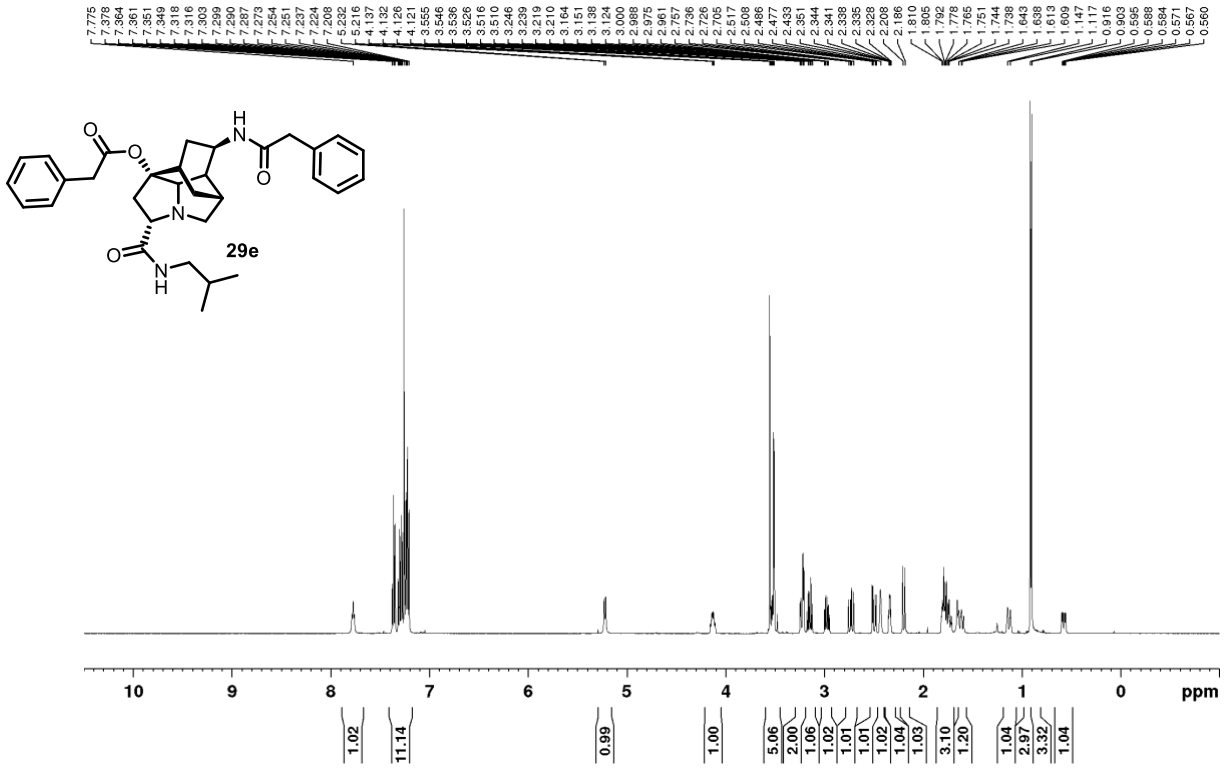


^{13}C NMR (125 MHz, $CDCl_3$)

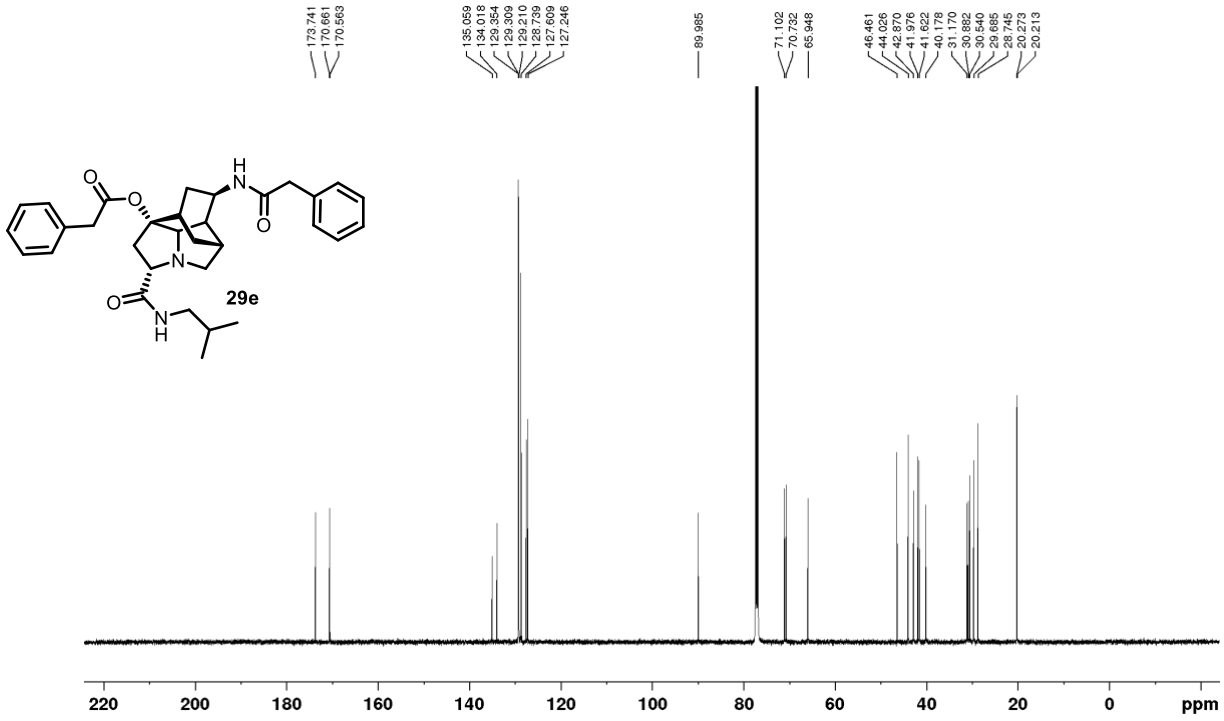


Ester **29e**

^{1}H NMR (500 MHz, $CDCl_3$)

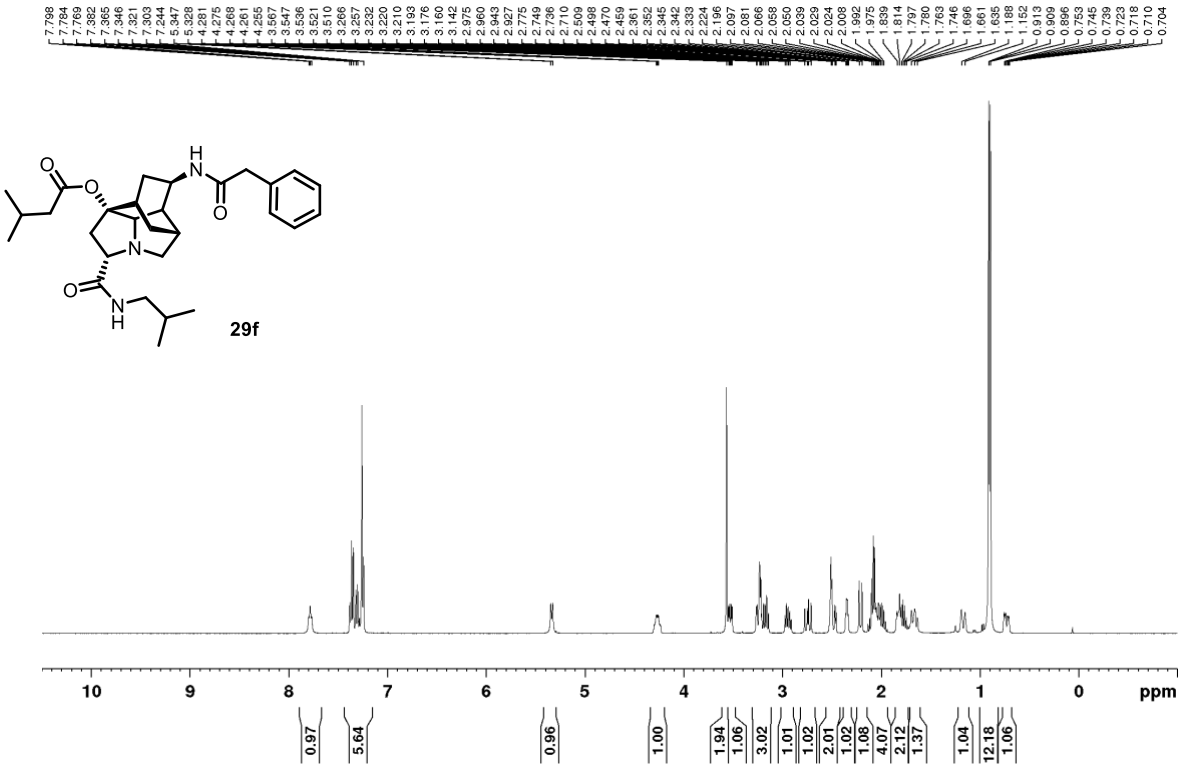


^{13}C NMR (125 MHz, $CDCl_3$)

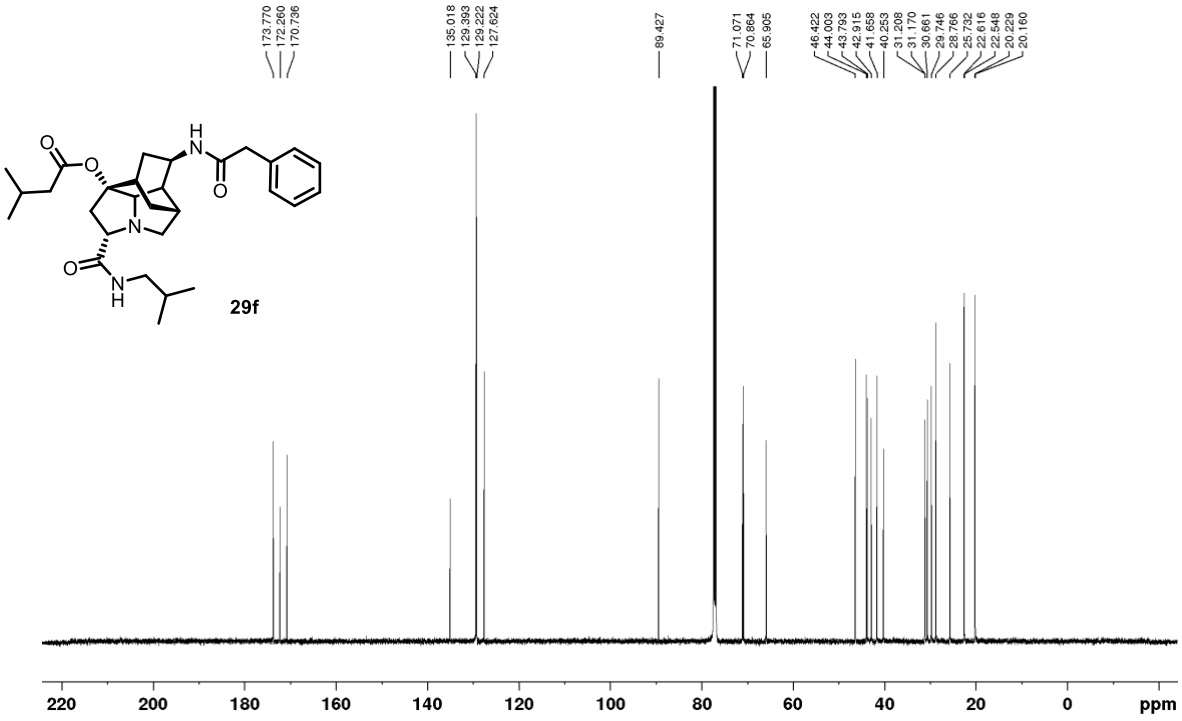


Ester **29f**

^{1}H NMR (400 MHz, $CDCl_3$)

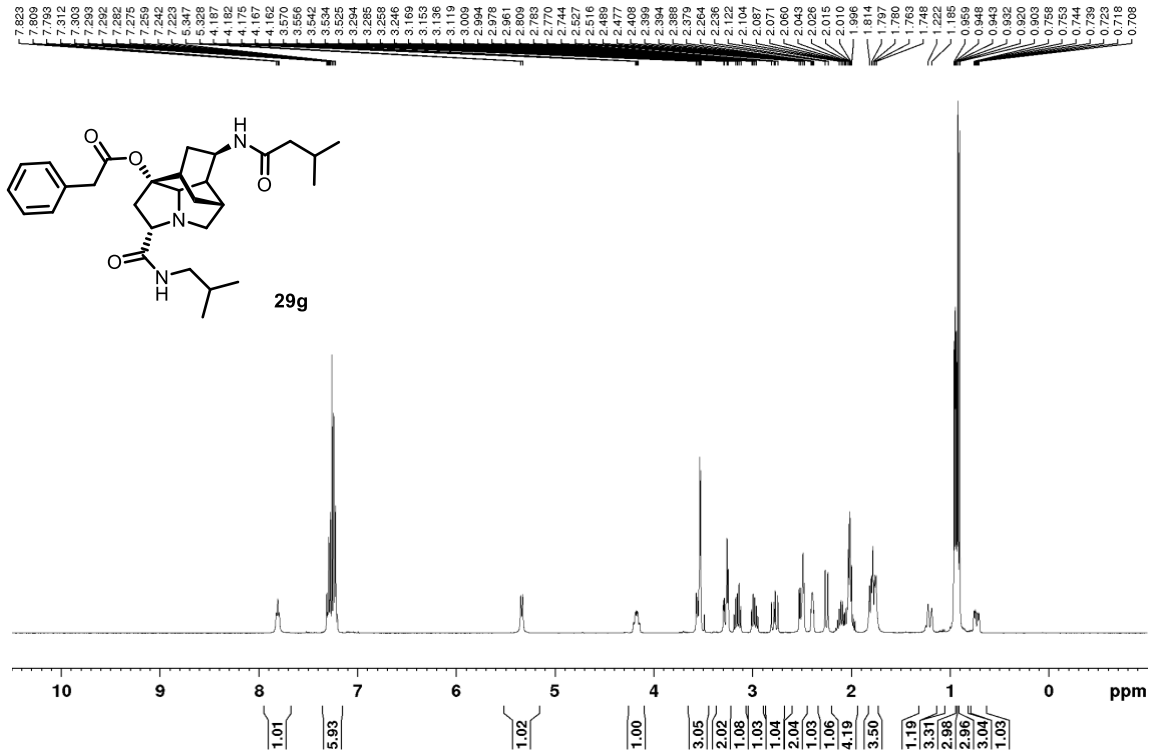


^{13}C NMR (125 MHz, $CDCl_3$)

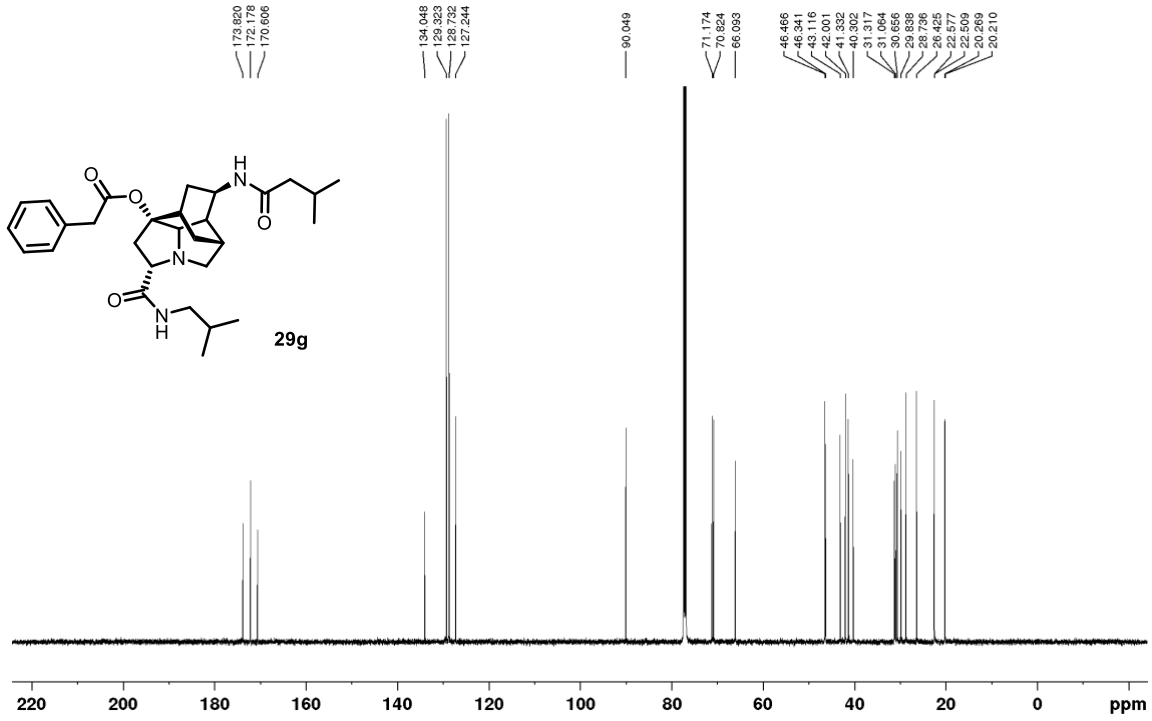


Ester **29g**

^{1}H NMR (400 MHz, $CDCl_3$)

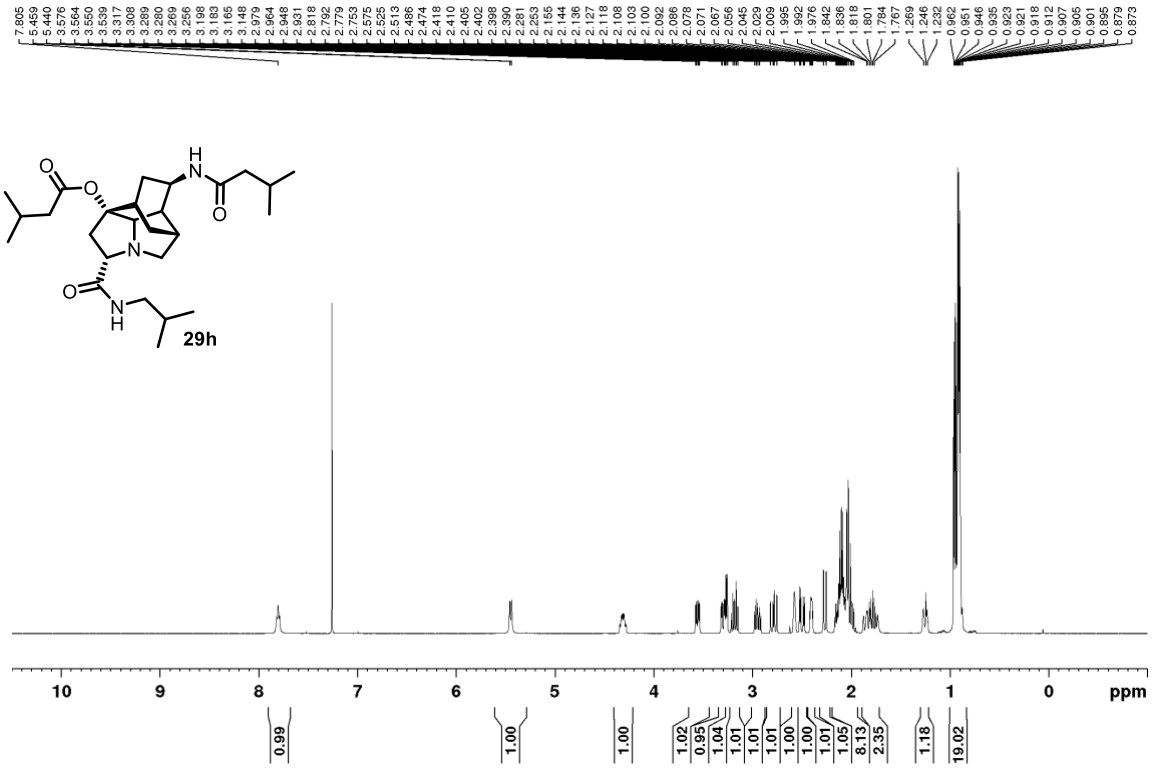


^{13}C NMR (125 MHz, $CDCl_3$)

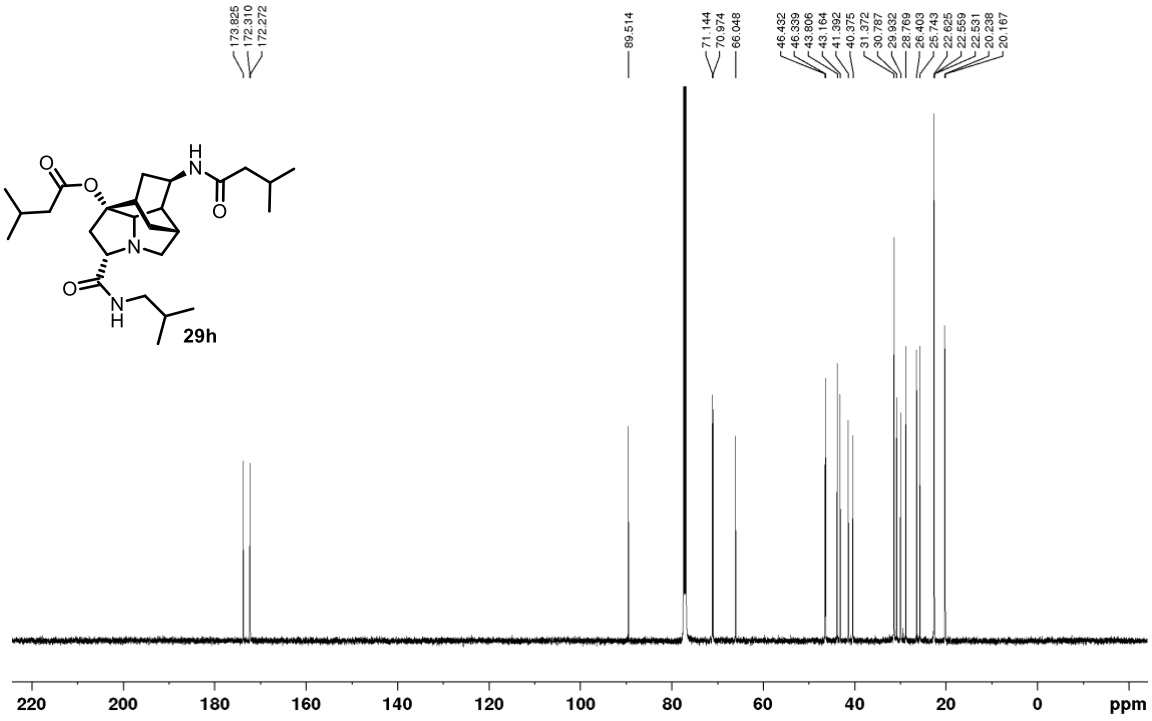


Ester **29h**

^{1}H NMR (400 MHz, $CDCl_3$)

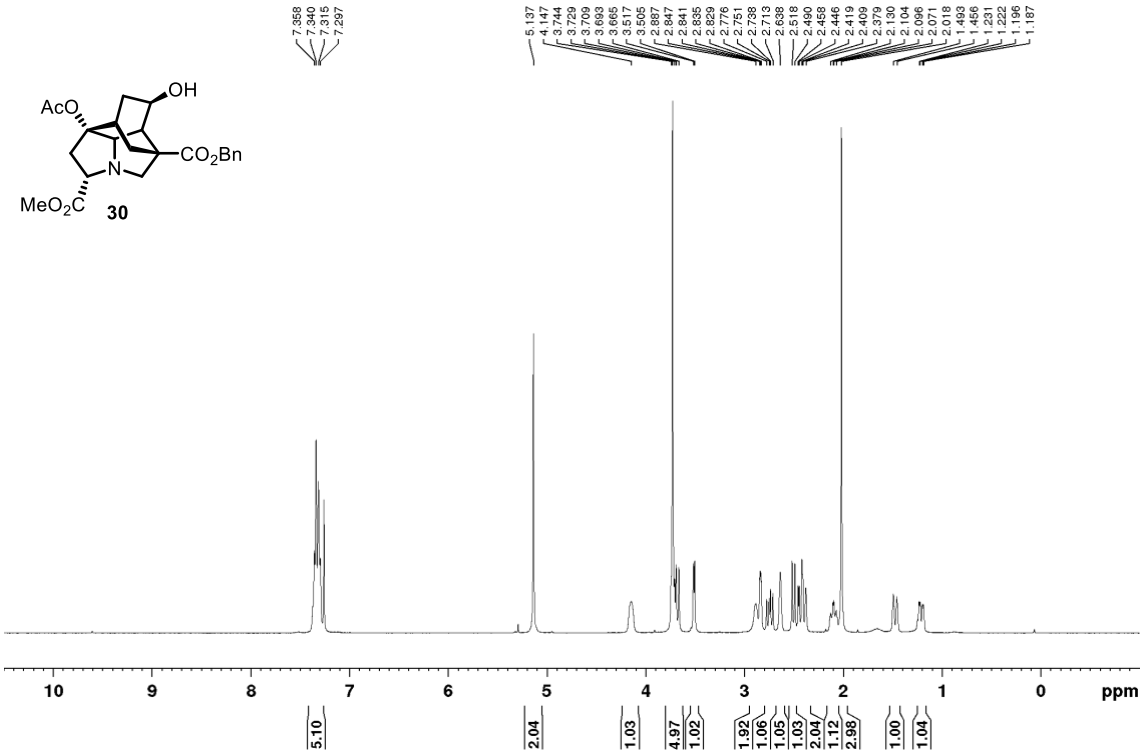


^{13}C NMR (125 MHz, $CDCl_3$)

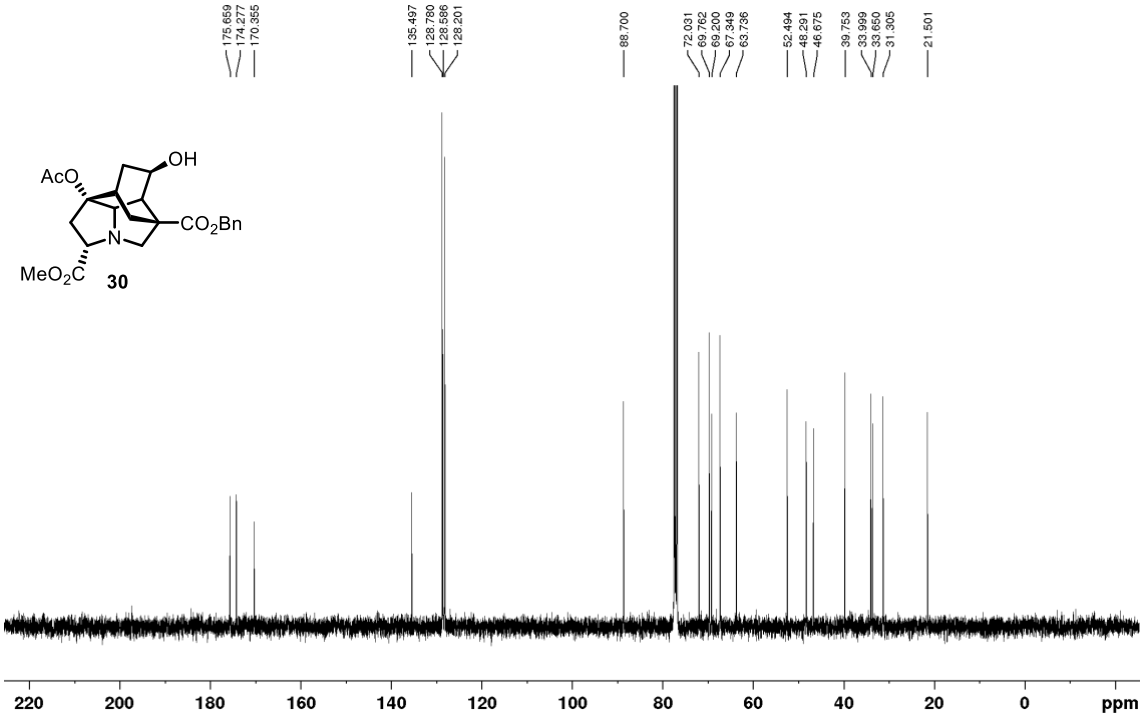


Alcohol **30**

^{1}H NMR (400 MHz, $CDCl_3$)

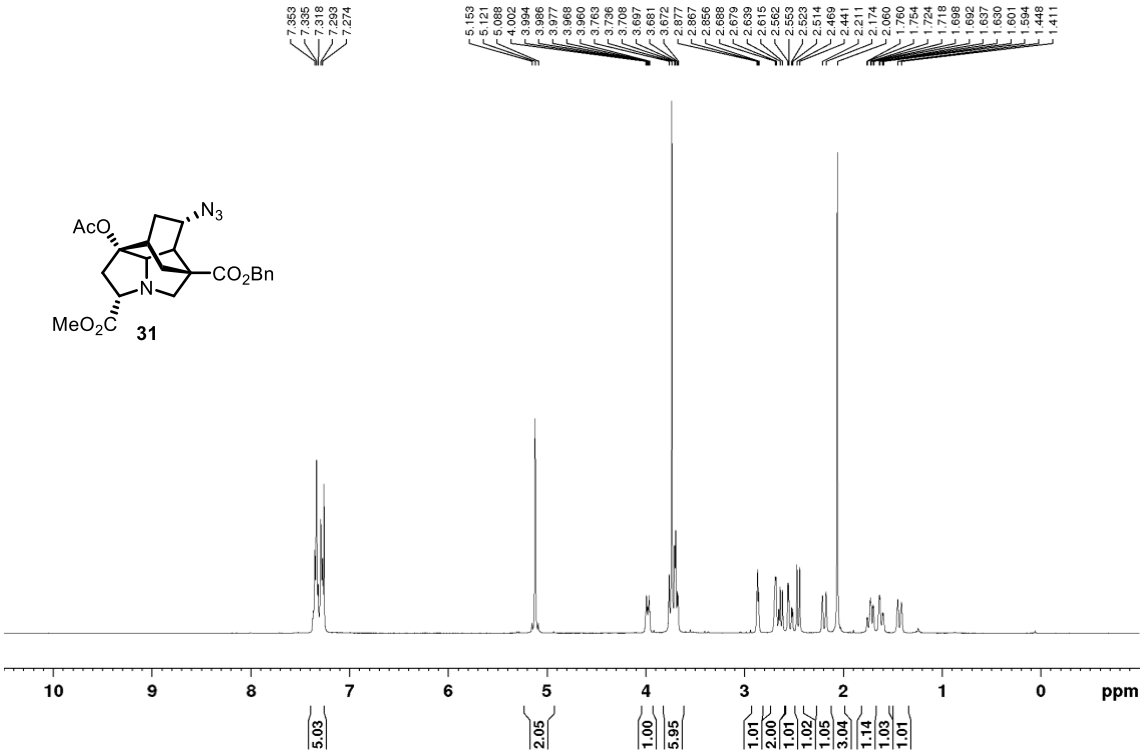


^{13}C NMR (100 MHz, $CDCl_3$)

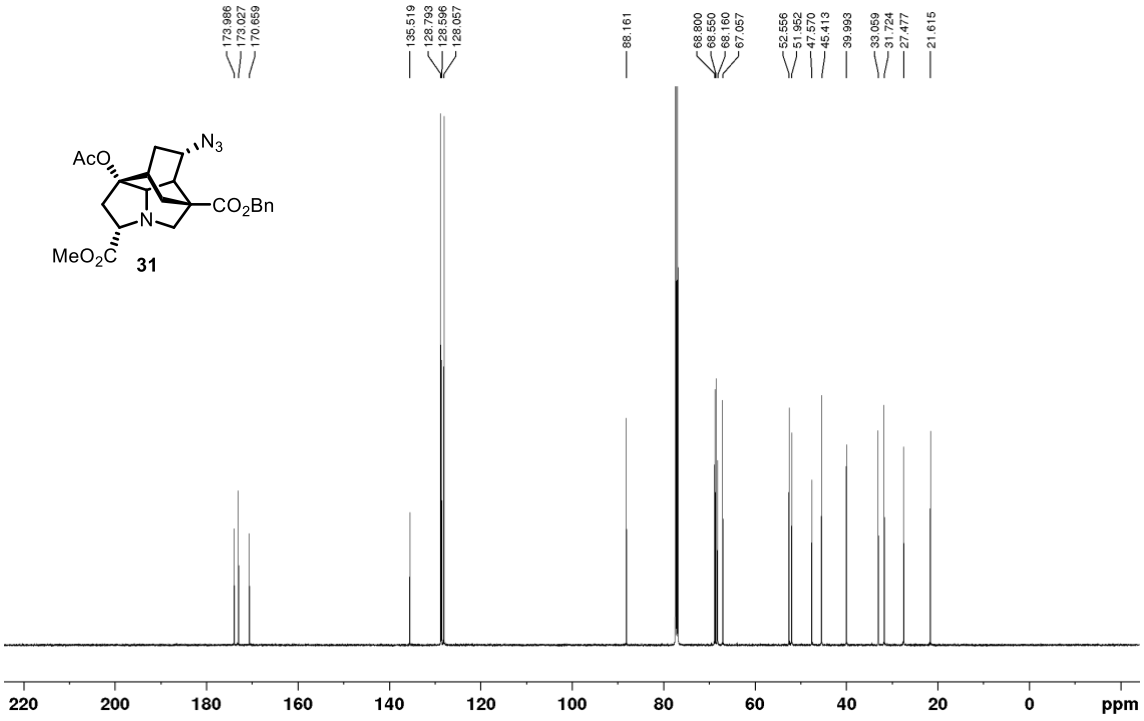


Azide **31**

^{1}H NMR (400 MHz, $CDCl_3$)

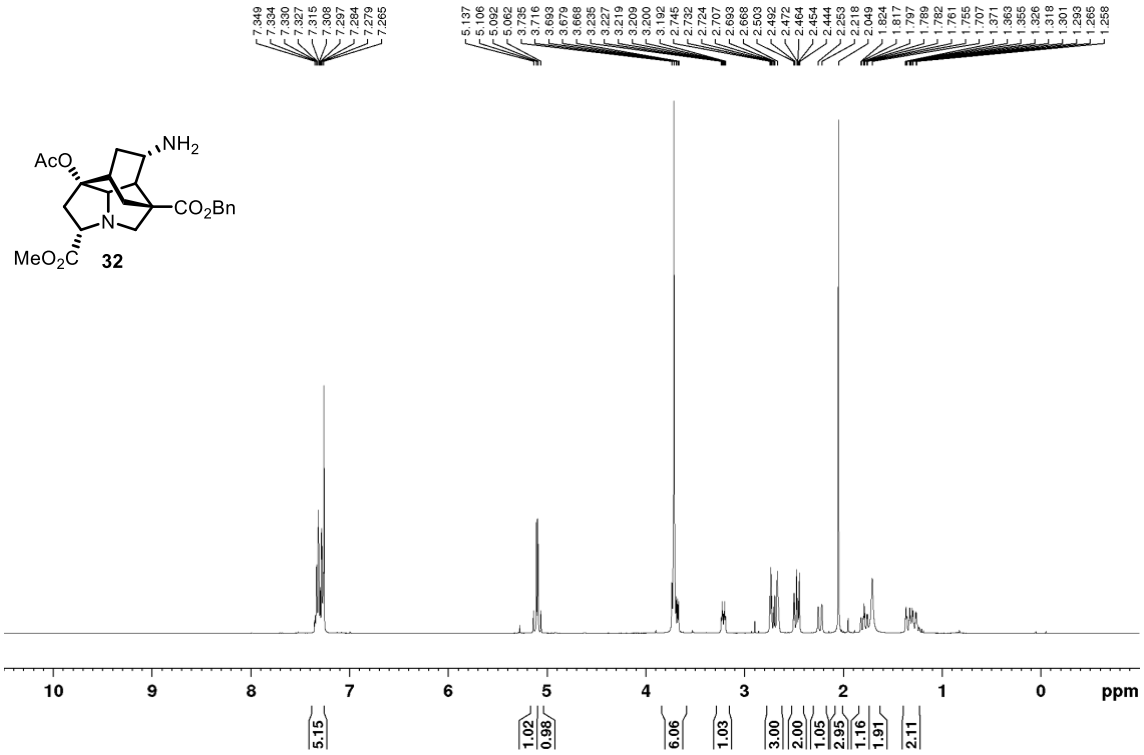


^{13}C NMR (125 MHz, $CDCl_3$)

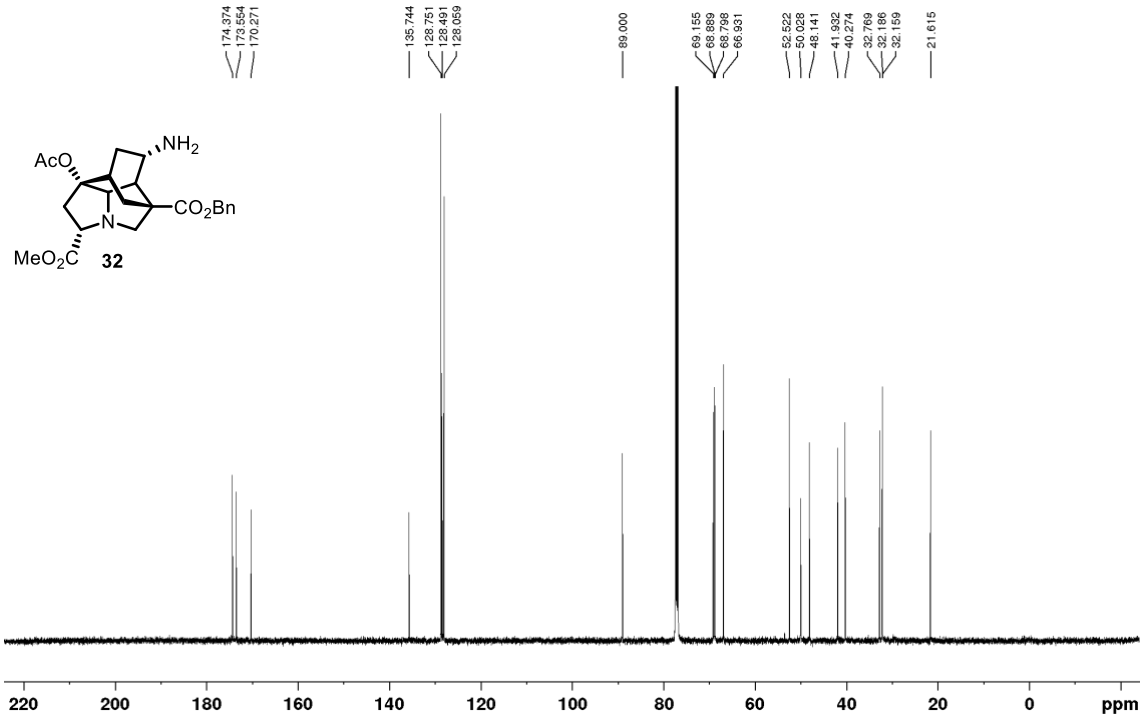


Amine **32**

^{1}H NMR (400 MHz, $CDCl_3$)

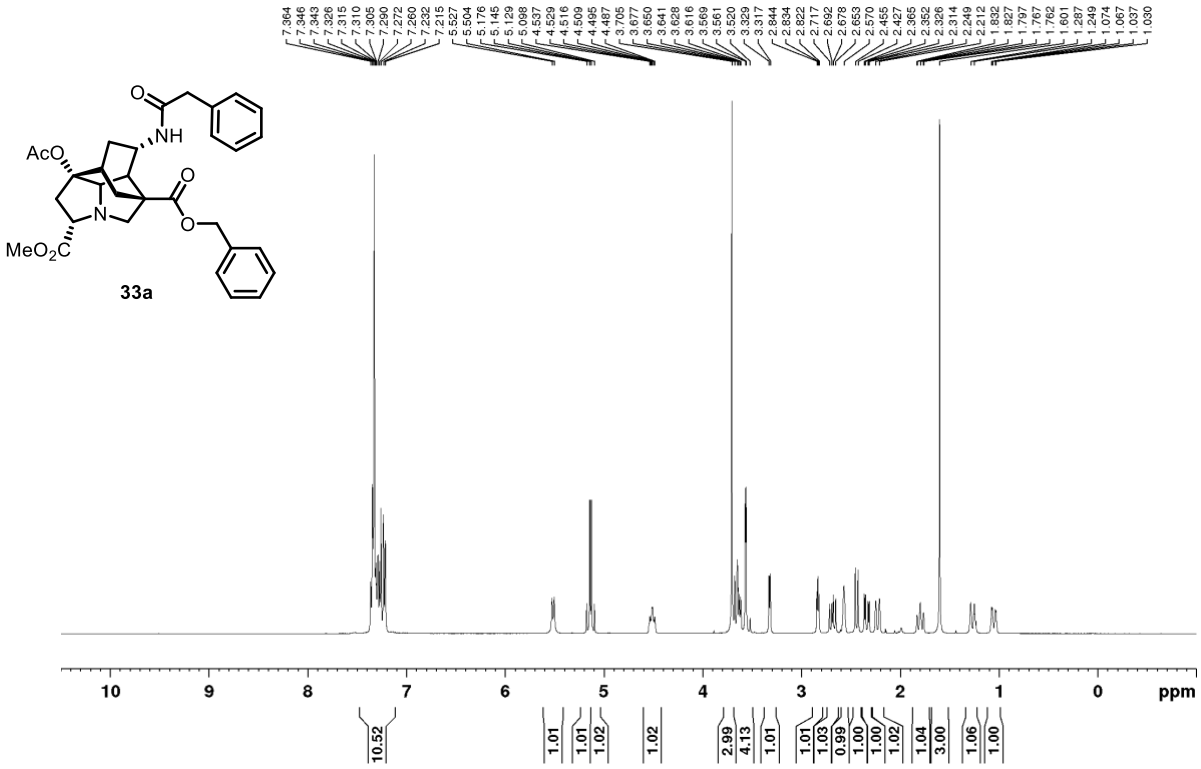


^{13}C NMR (125 MHz, $CDCl_3$)

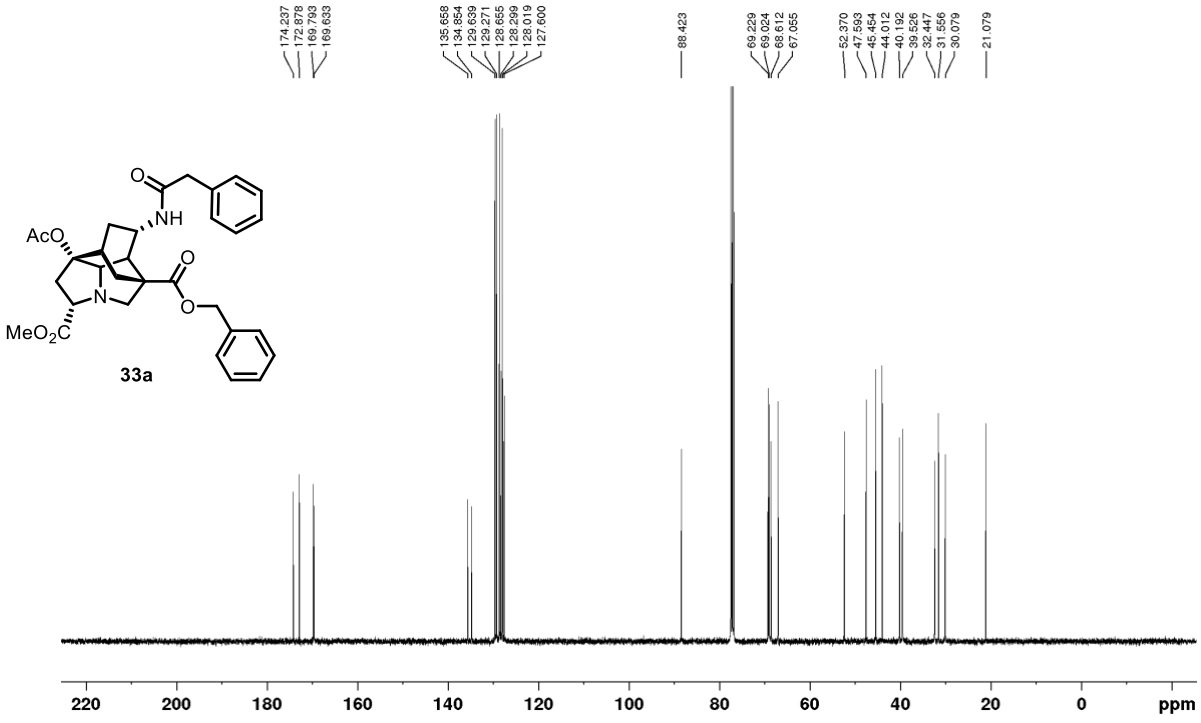


Amide **33a**

^{1}H NMR (400 MHz, $CDCl_3$)

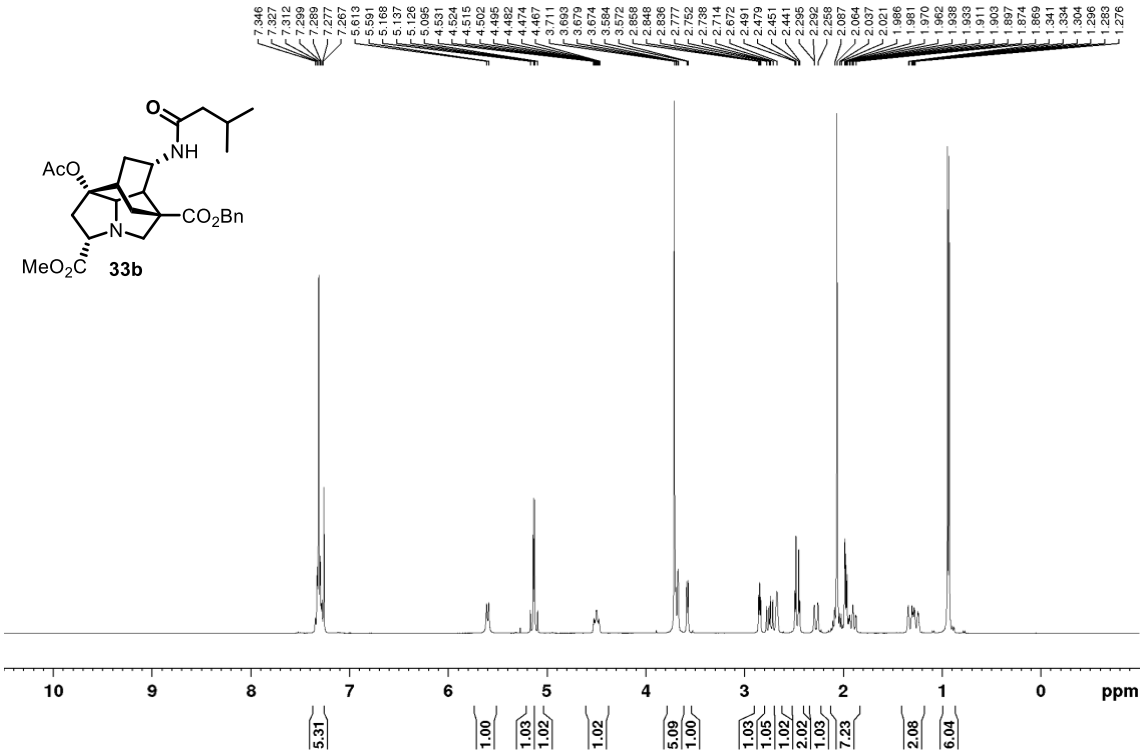


^{13}C NMR (100 MHz, $CDCl_3$)

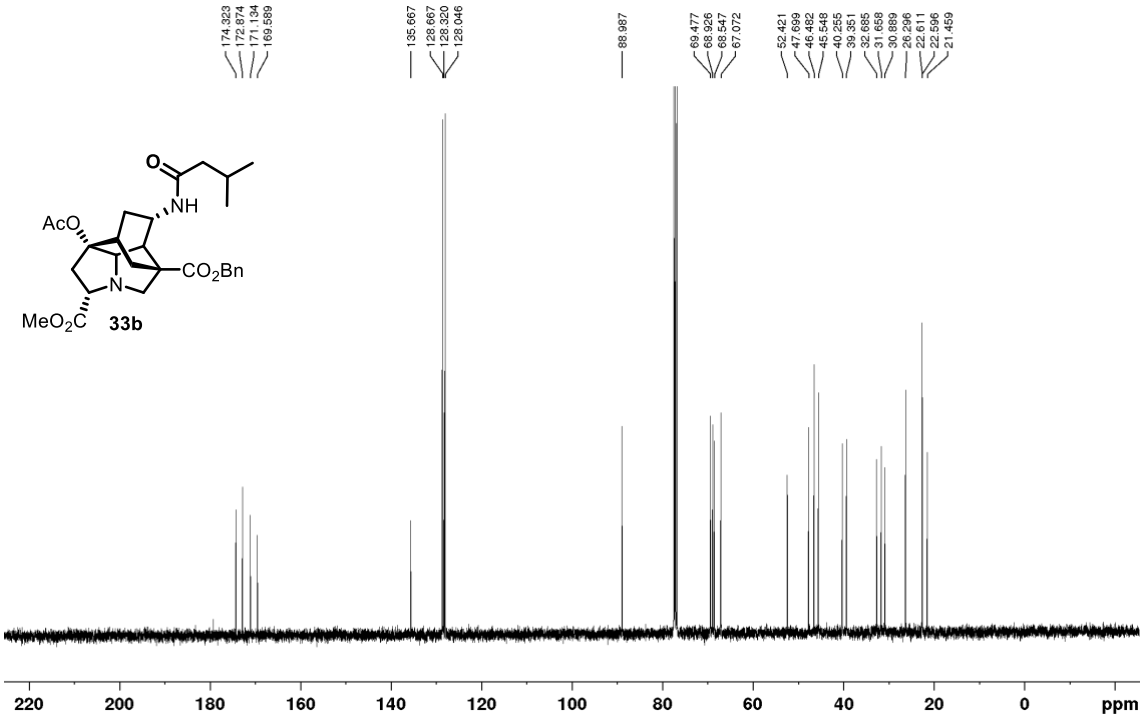


Amide **33b**

^{1}H NMR (400 MHz, $CDCl_3$)

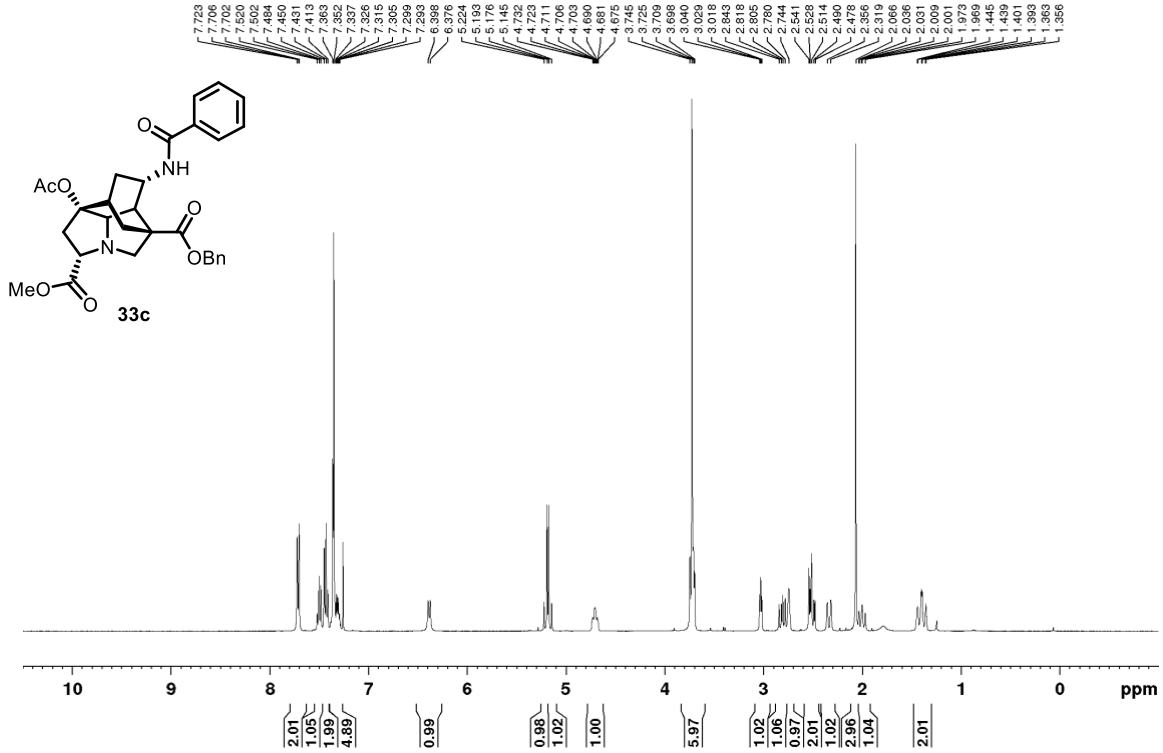


^{13}C NMR (100 MHz, $CDCl_3$)

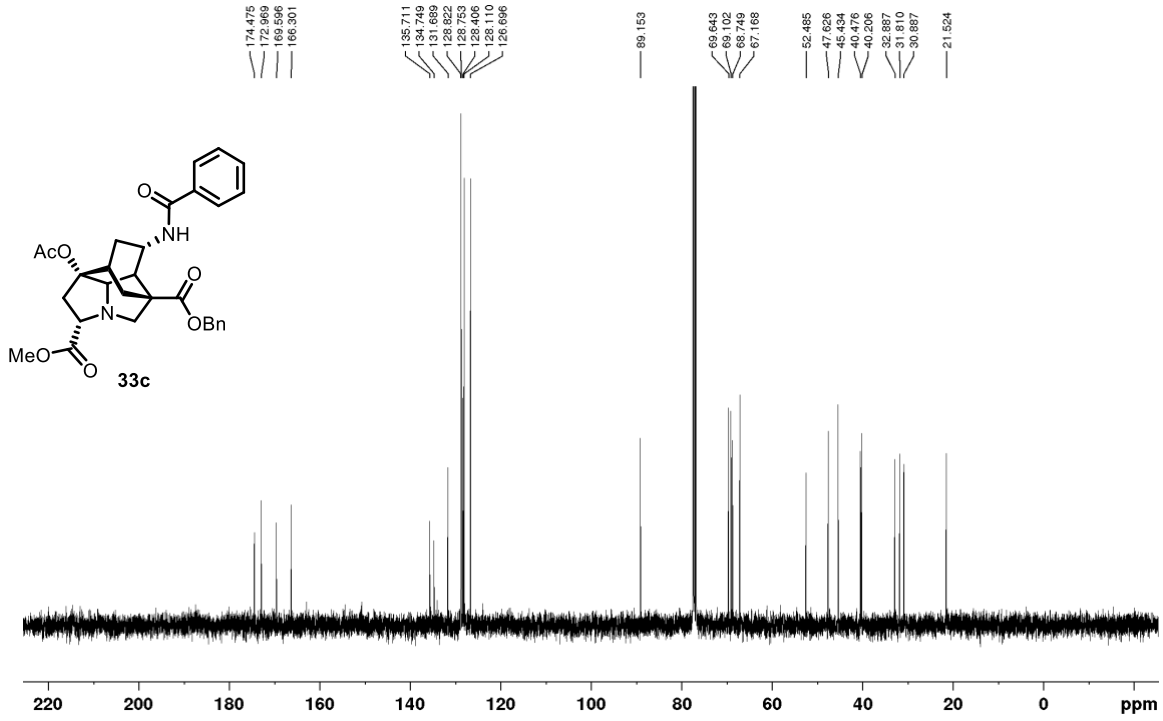


Amide **33c**

^{1}H NMR (400 MHz, $CDCl_3$)

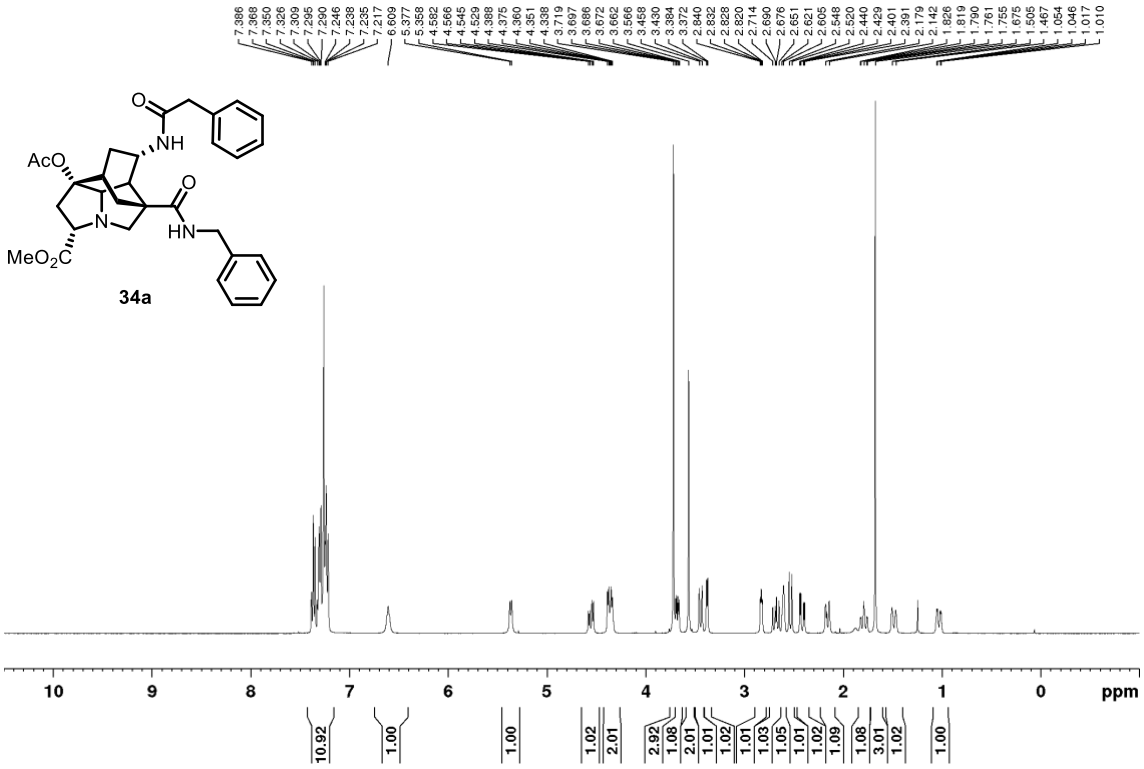


^{13}C NMR (100 MHz, $CDCl_3$)

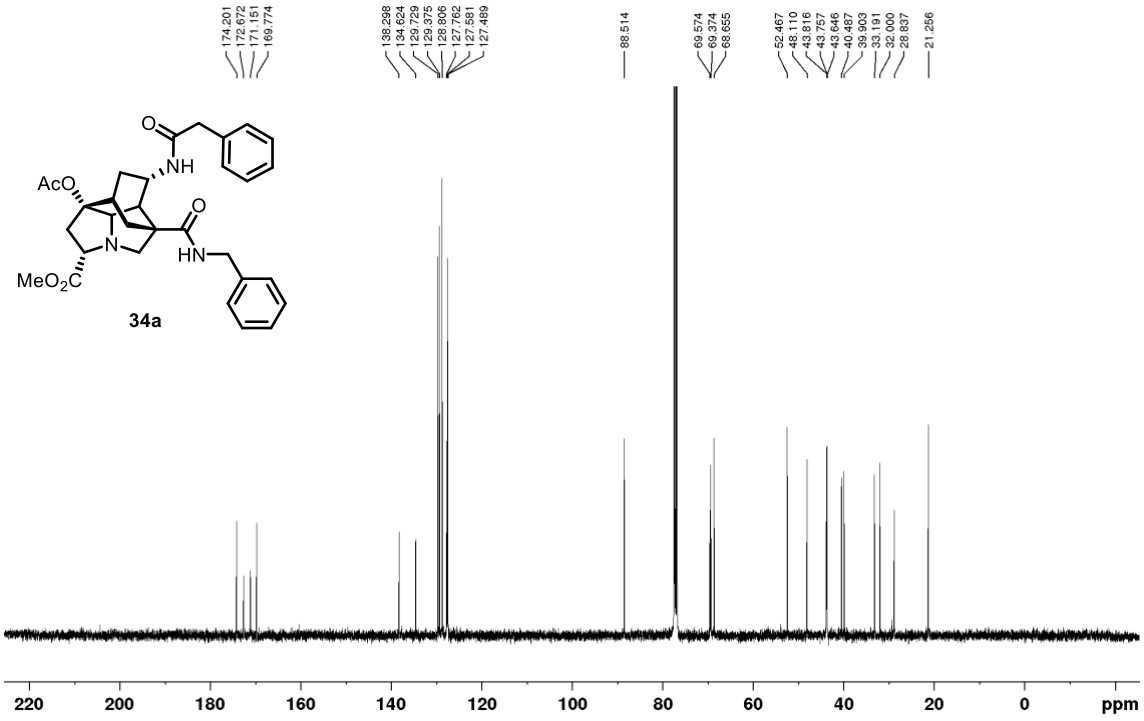


Amide **34a**

^{1}H NMR (400 MHz, $CDCl_3$)

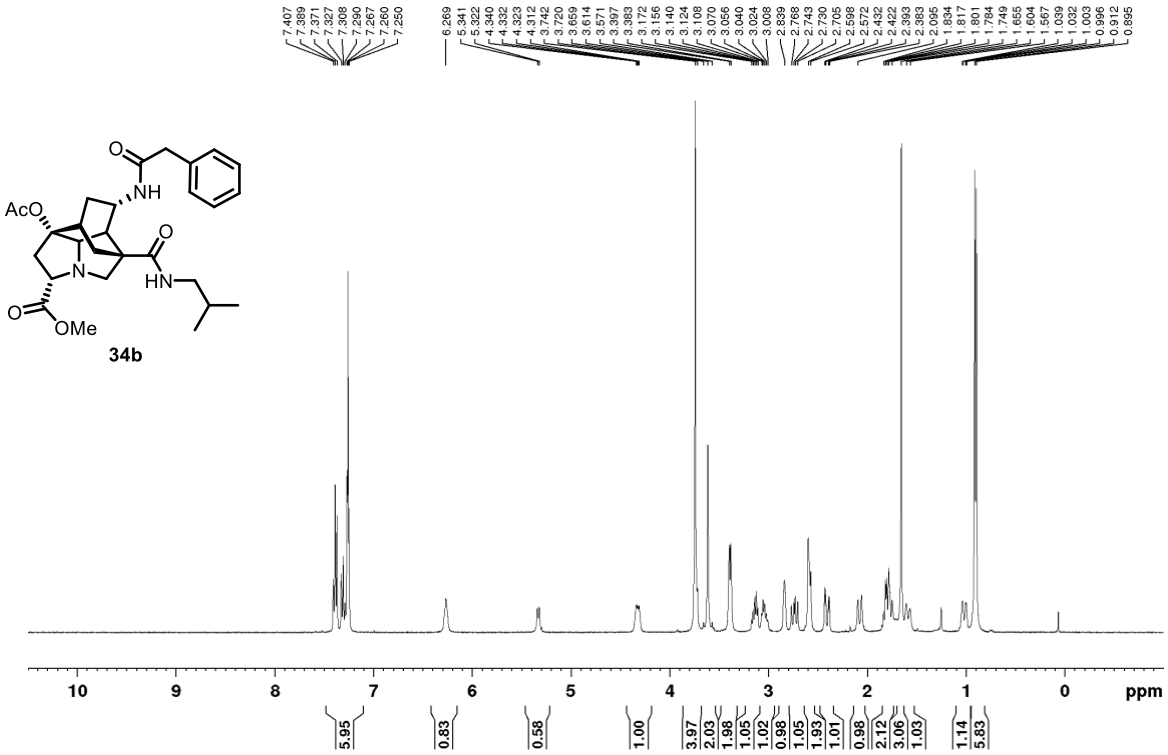


^{13}C NMR (100 MHz, $CDCl_3$)

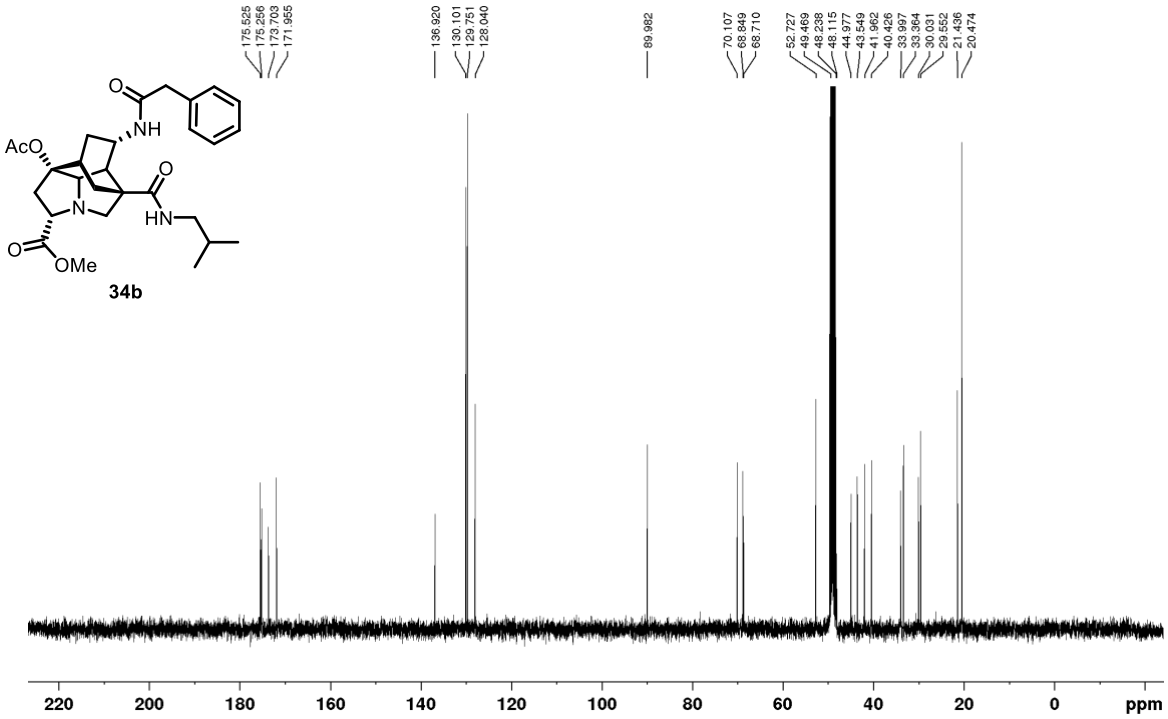


Amide **34b**

^{1}H NMR (400 MHz, $CDCl_3$)

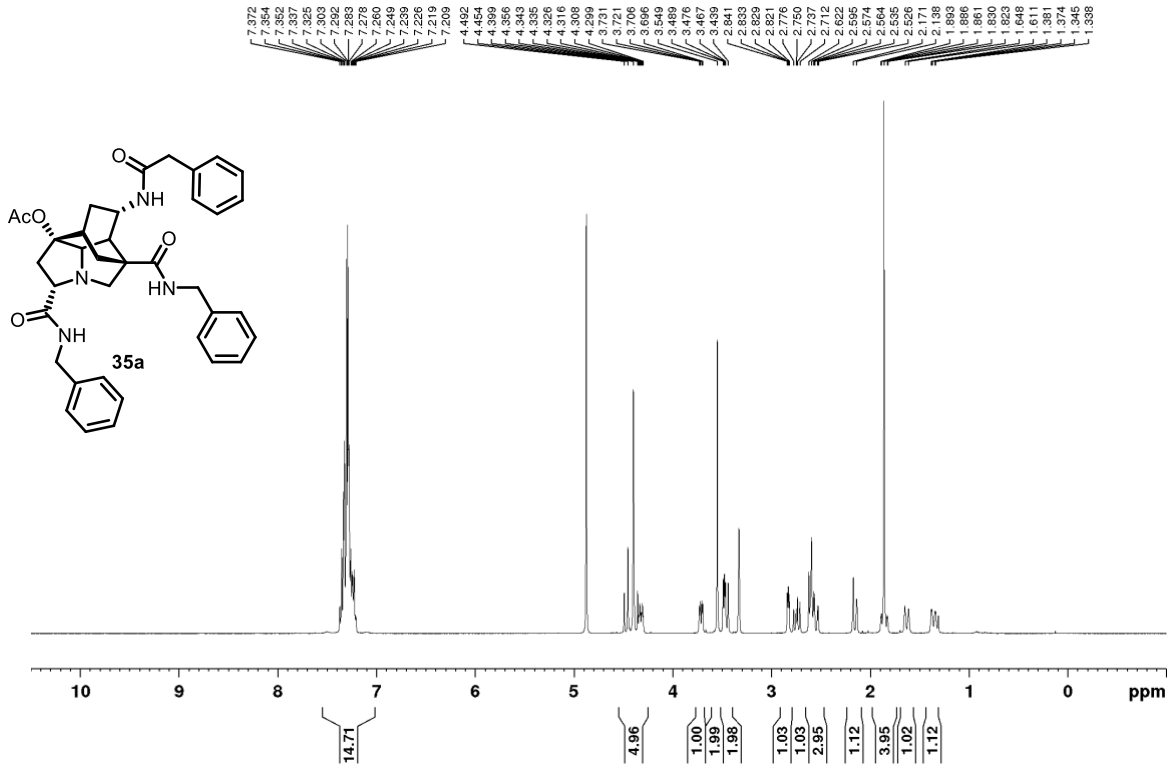


^{13}C NMR (100 MHz, CD_3OD)

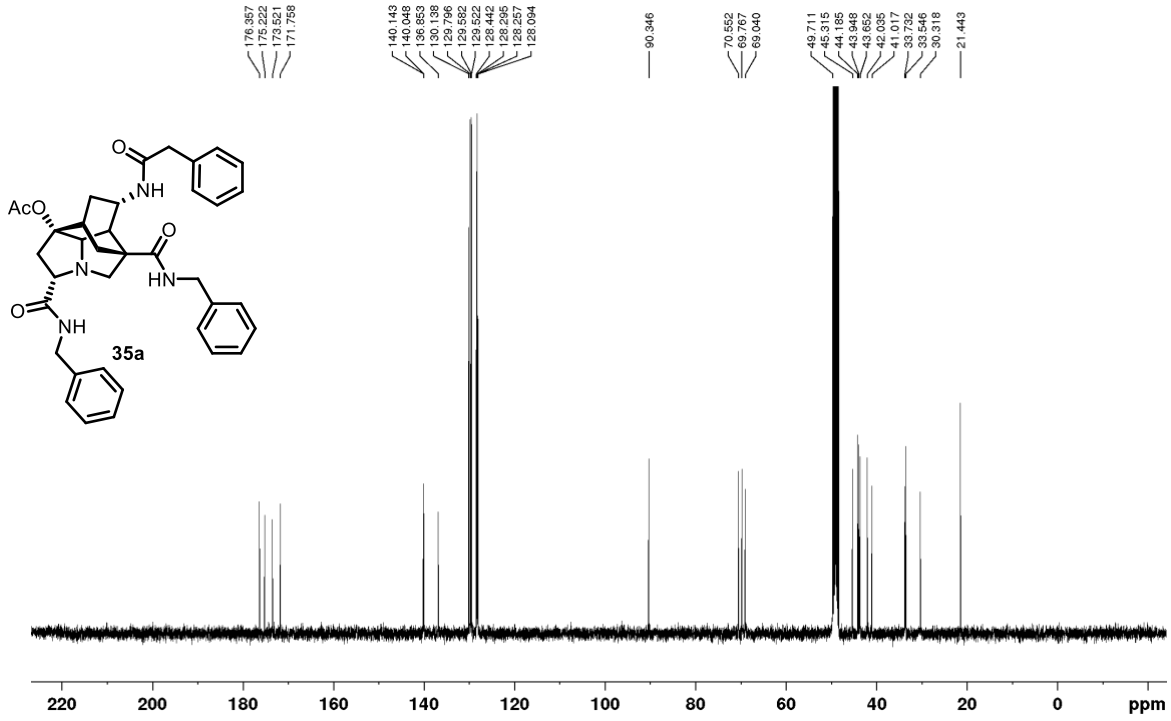


Amide **35a**

^{1}H NMR (400 MHz, CD_3OD)

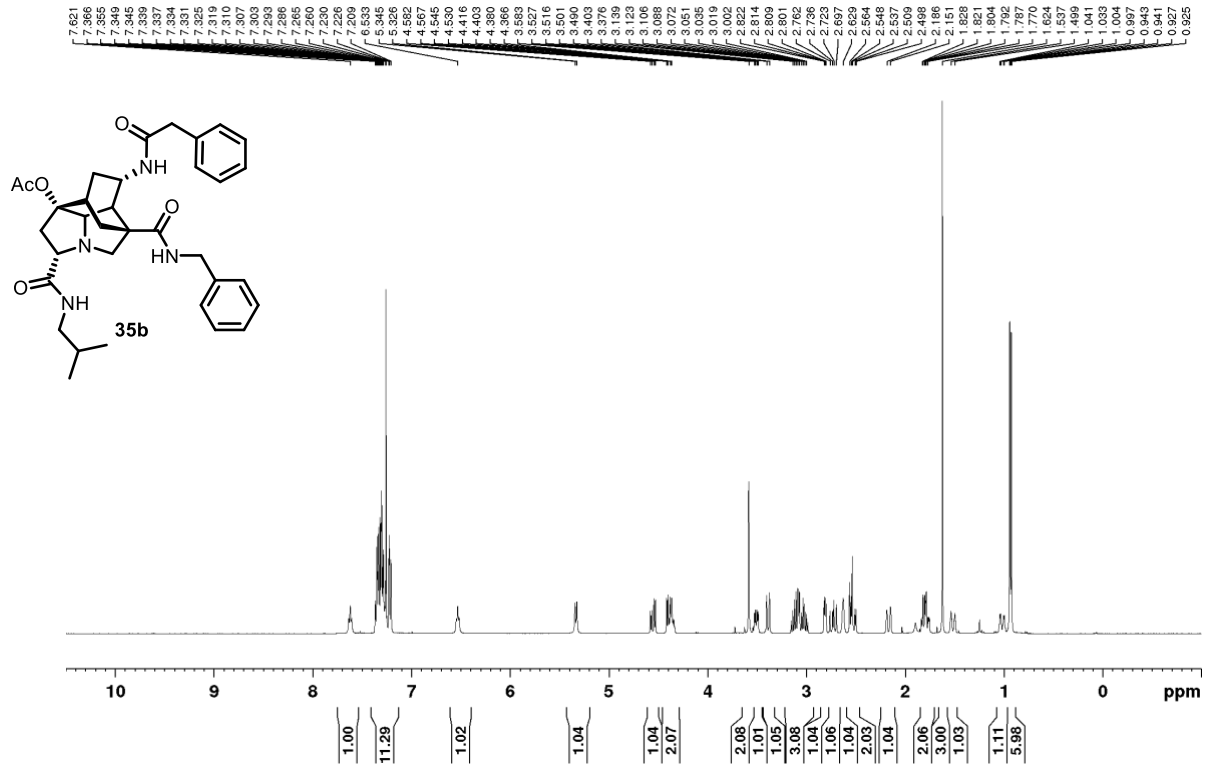


^{13}C NMR (100 MHz, CD_3OD)

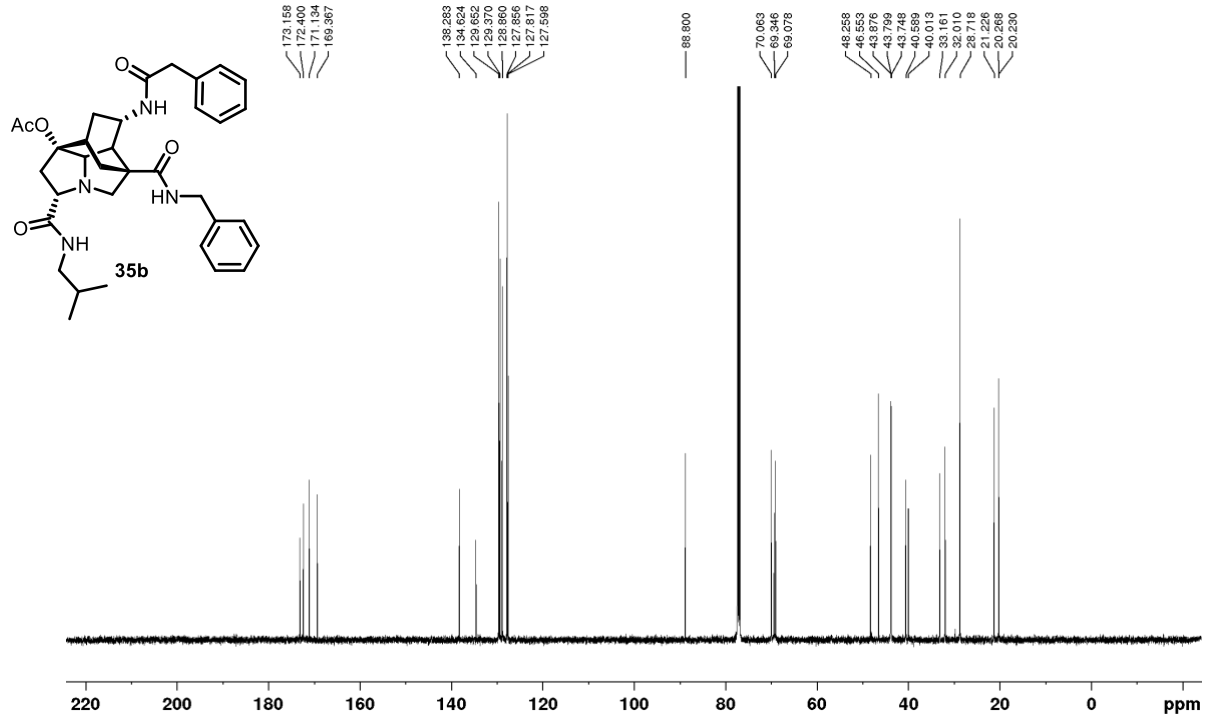


Amide **35b**

^{1}H NMR (400 MHz, $CDCl_3$)

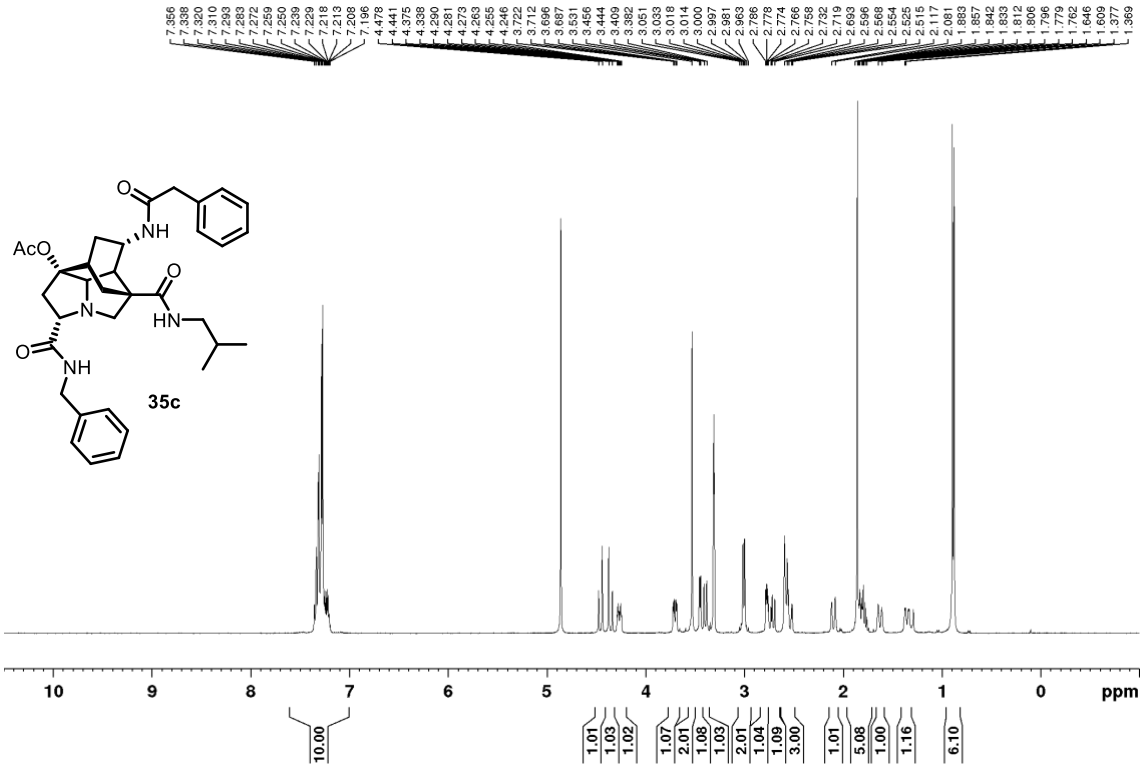


^{13}C NMR (125 MHz, $CDCl_3$)

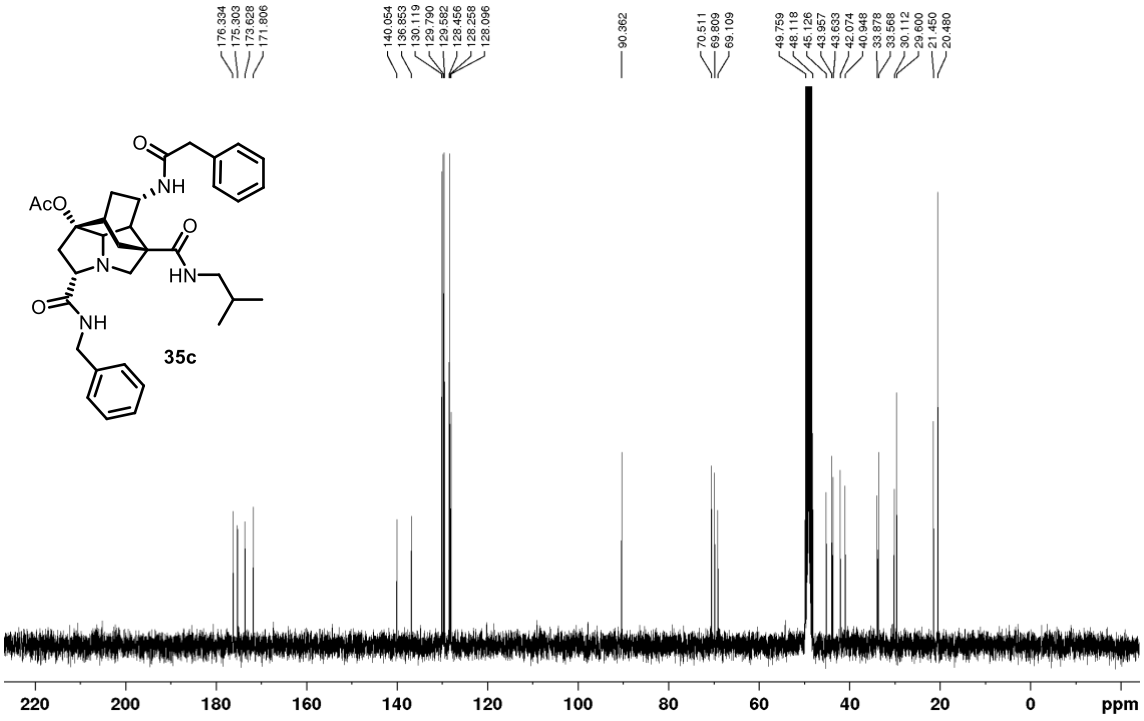


Amide **35c**

^{1}H NMR (400 MHz, CD_3OD)

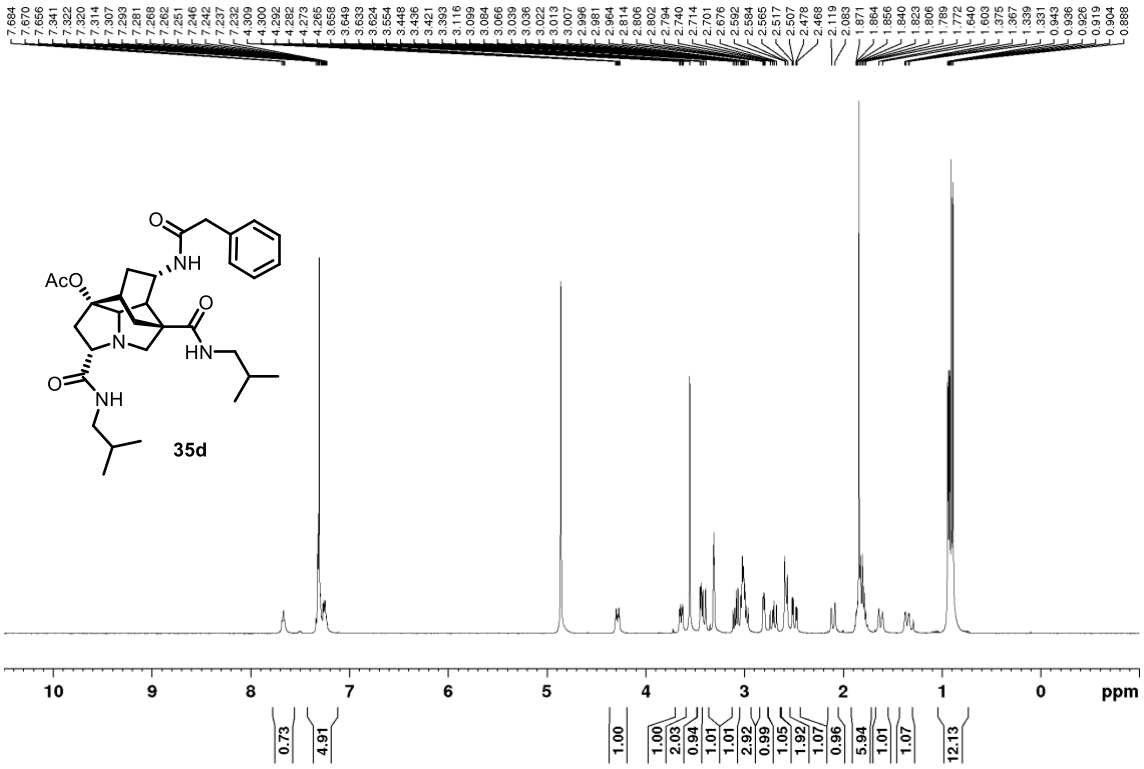


^{13}C NMR (100 MHz, CD_3OD)

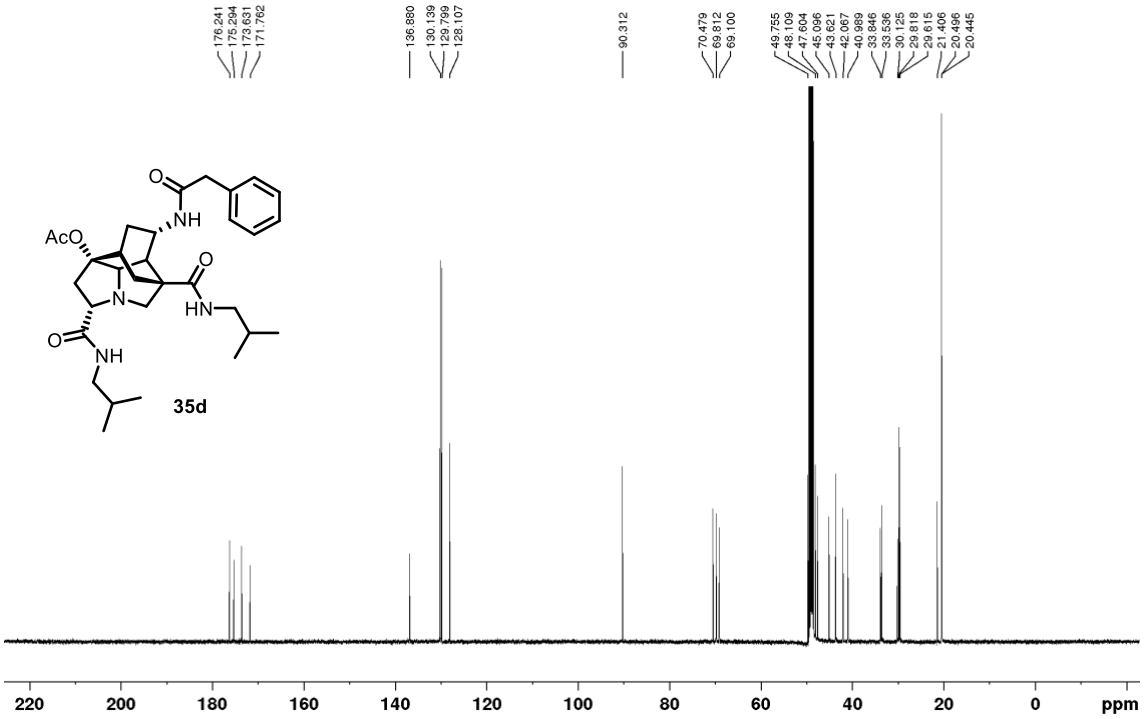


Amide **35d**

^{1}H NMR (400 MHz, CD_3OD)

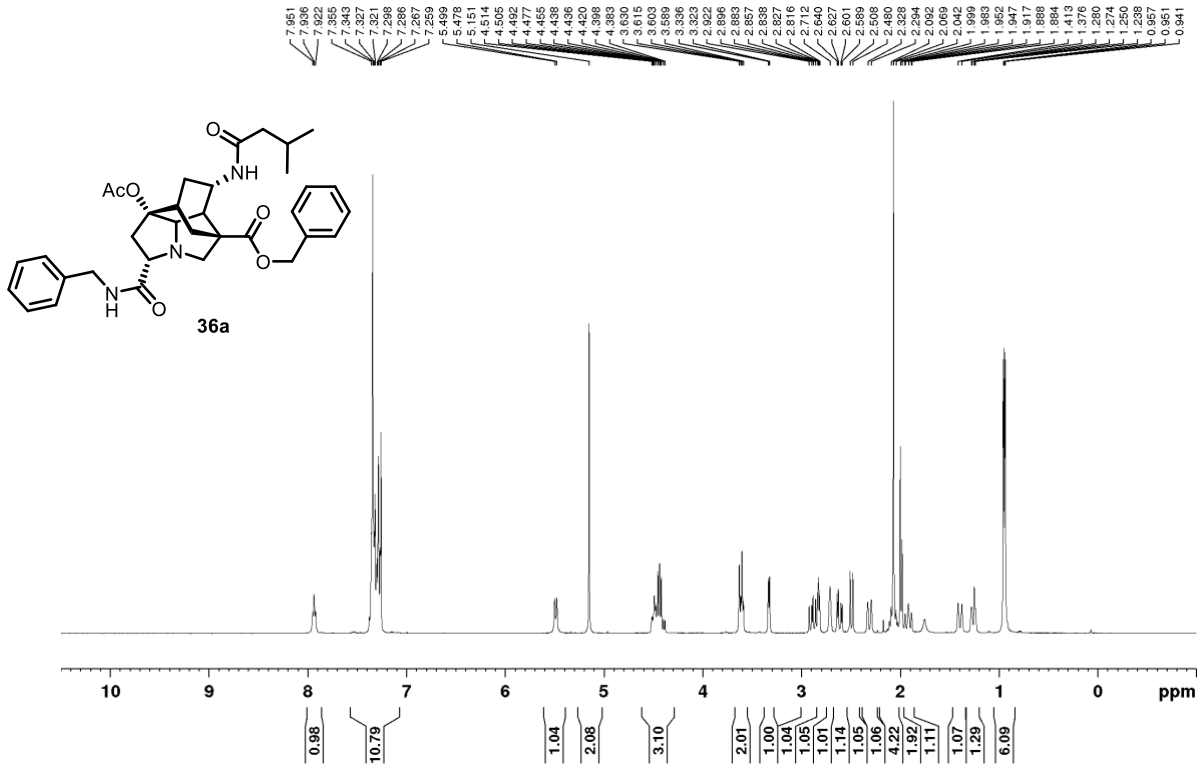


^{13}C NMR (125 MHz, CD_3OD)

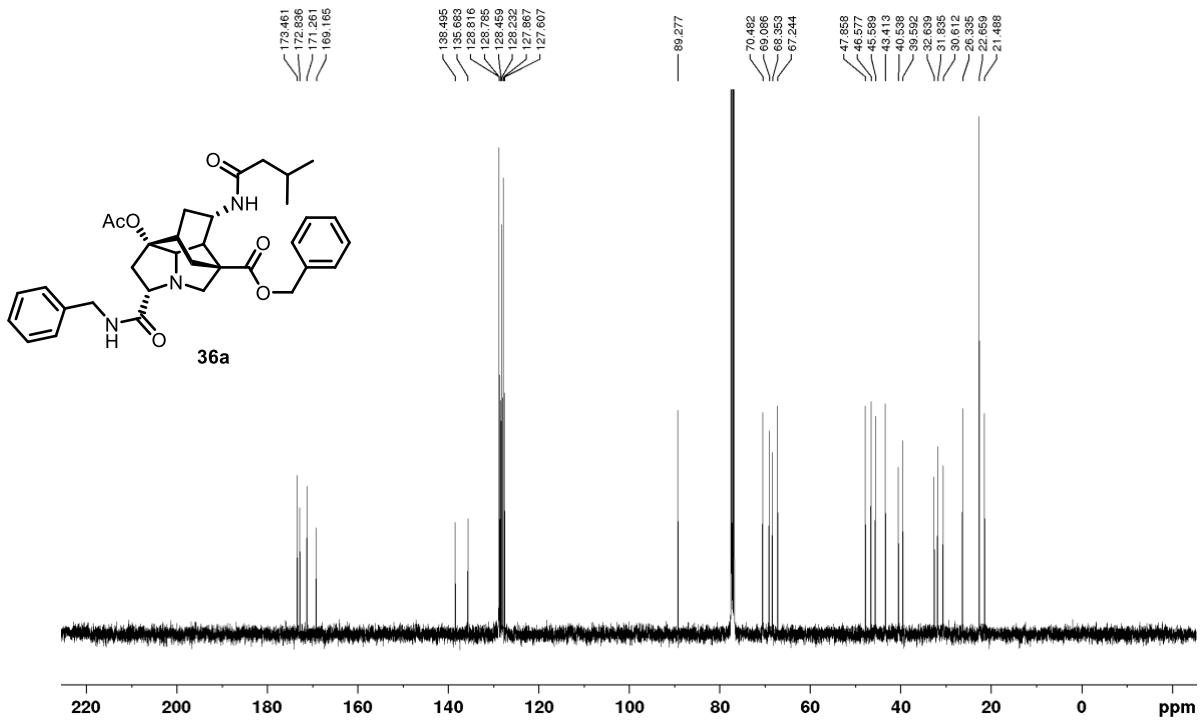


Amide **36a**

^{1}H NMR (400 MHz, $CDCl_3$)

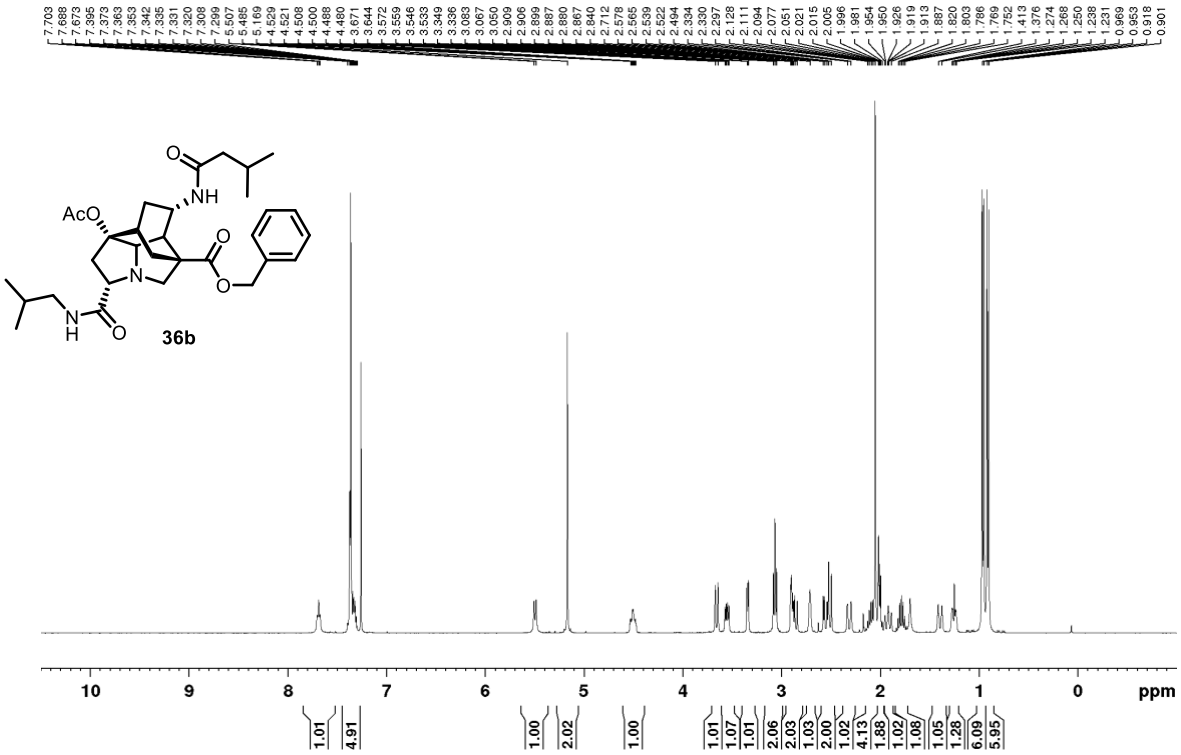


^{13}C NMR (100 MHz, $CDCl_3$)

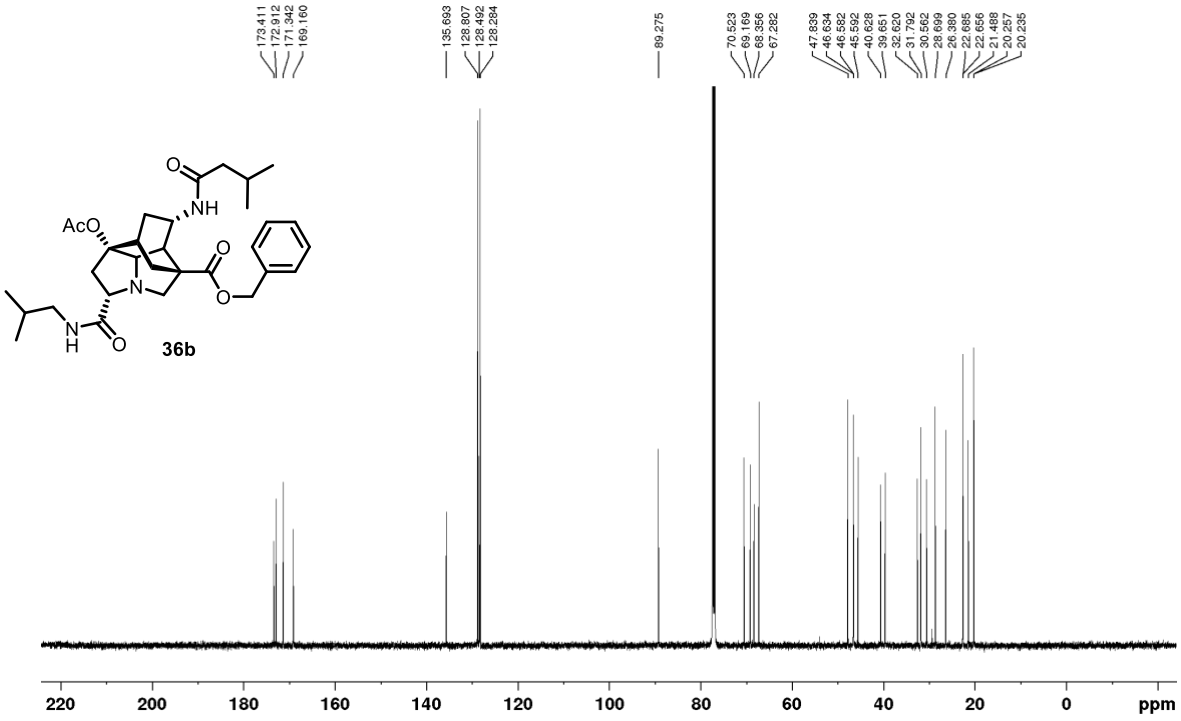


Amide **36b**

^{1}H NMR (400 MHz, $CDCl_3$)

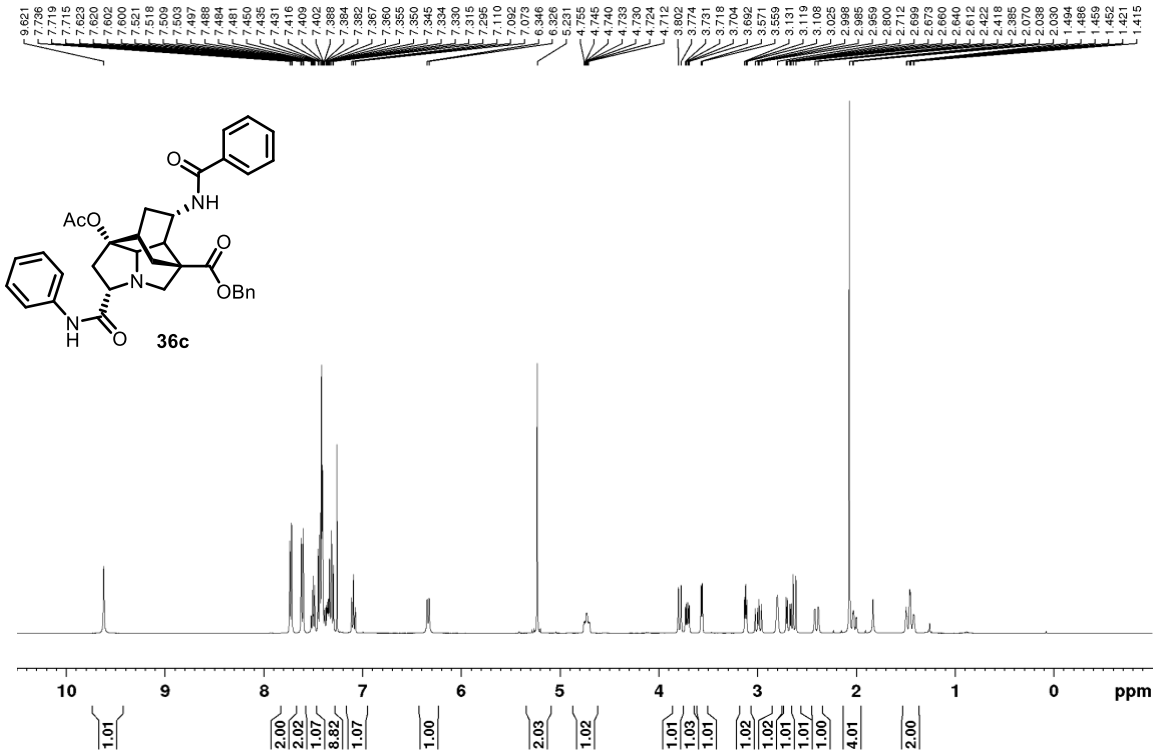


^{13}C NMR (125 MHz, $CDCl_3$)

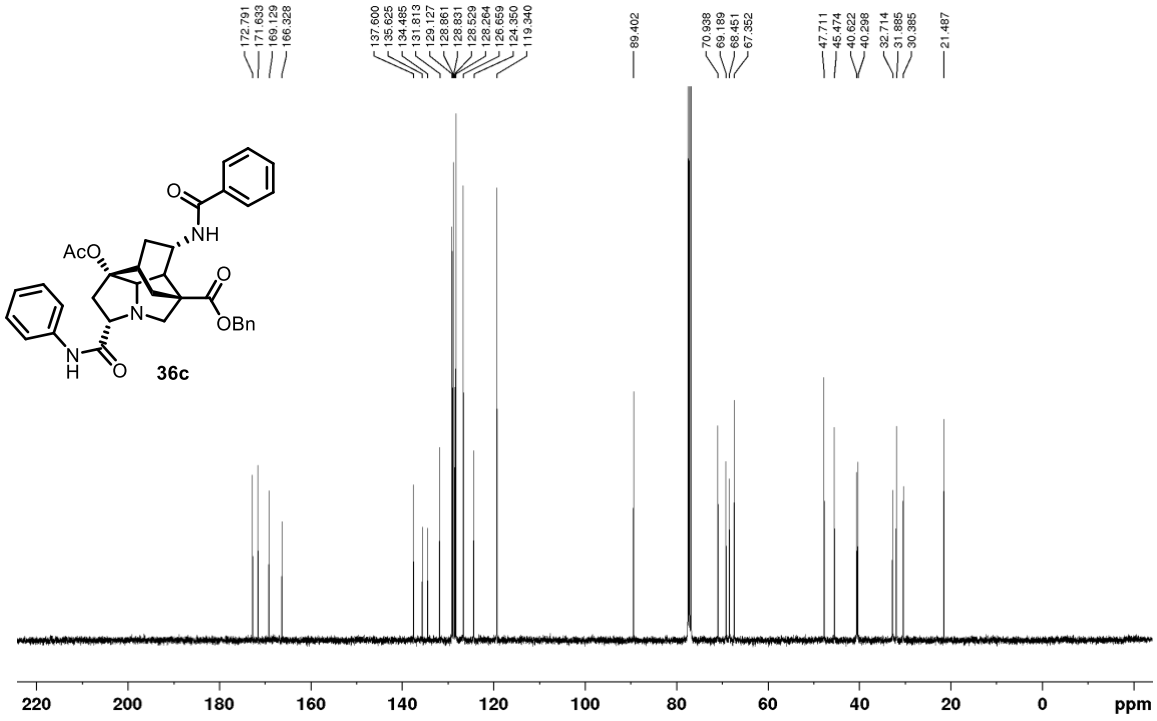


Amide **36c**

^{1}H NMR (400 MHz, $CDCl_3$)

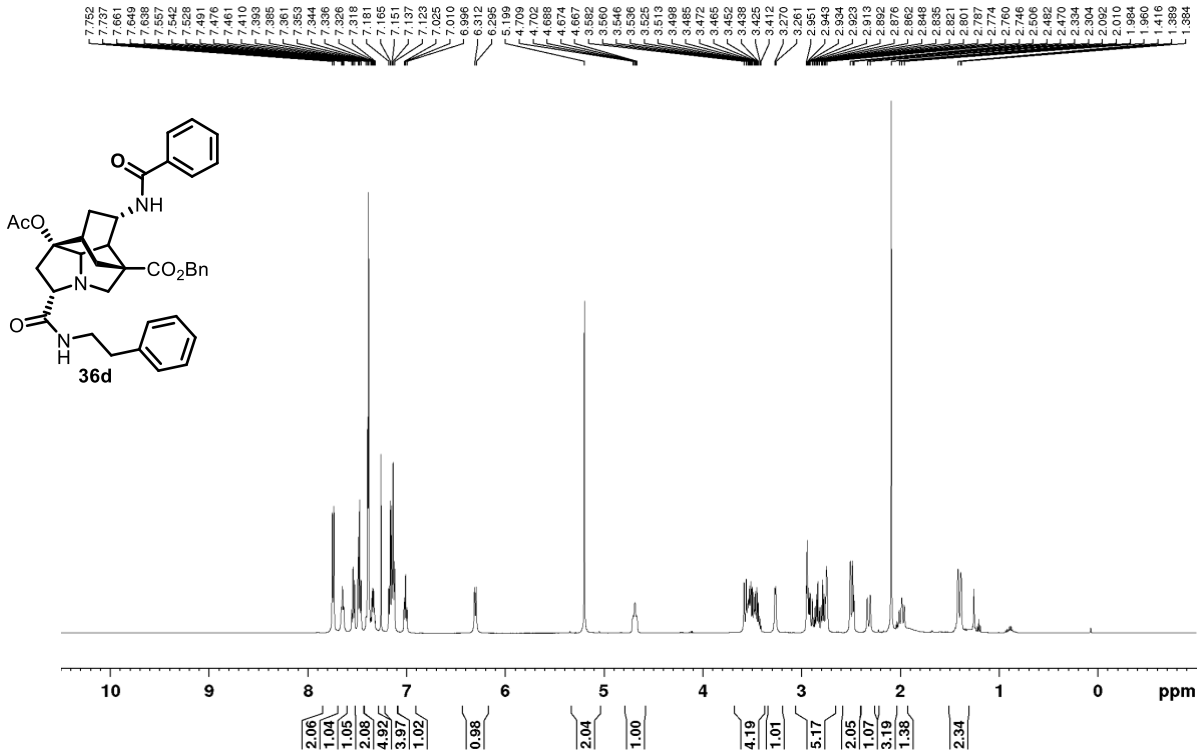


^{13}C NMR (100 MHz, $CDCl_3$)

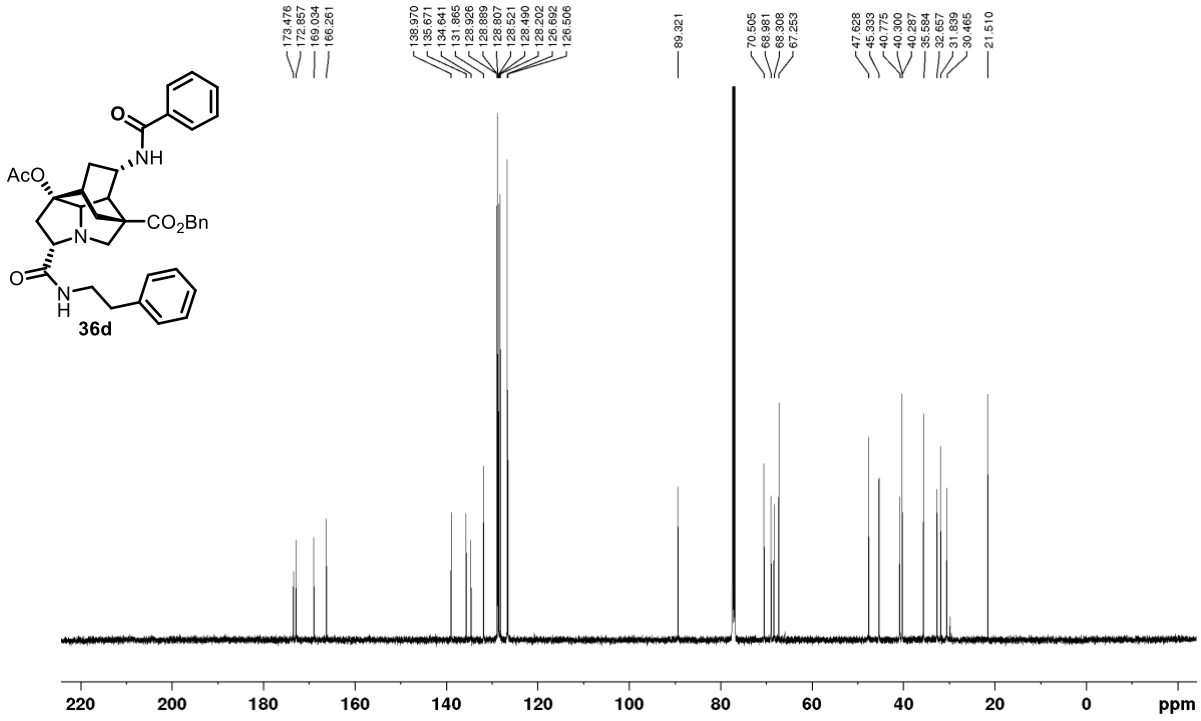


Amide **36d**

^{1}H NMR (500 MHz, $CDCl_3$)

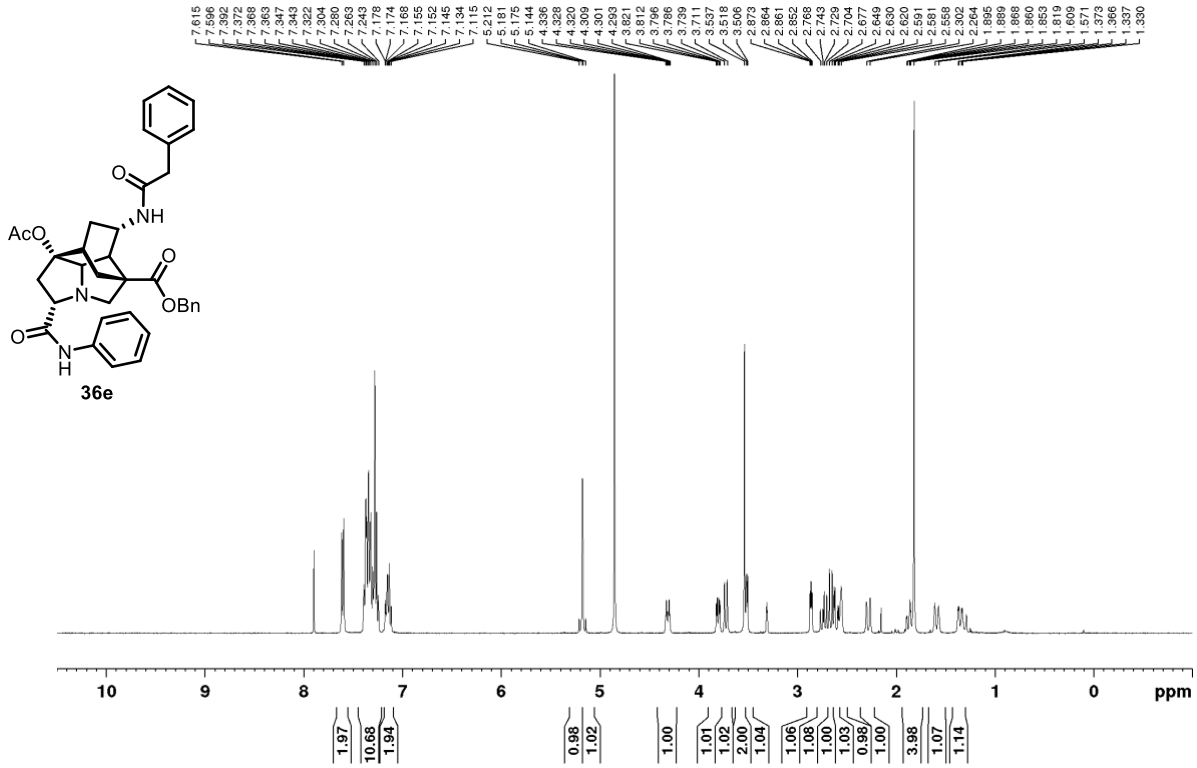


^{13}C NMR (125 MHz, $CDCl_3$)

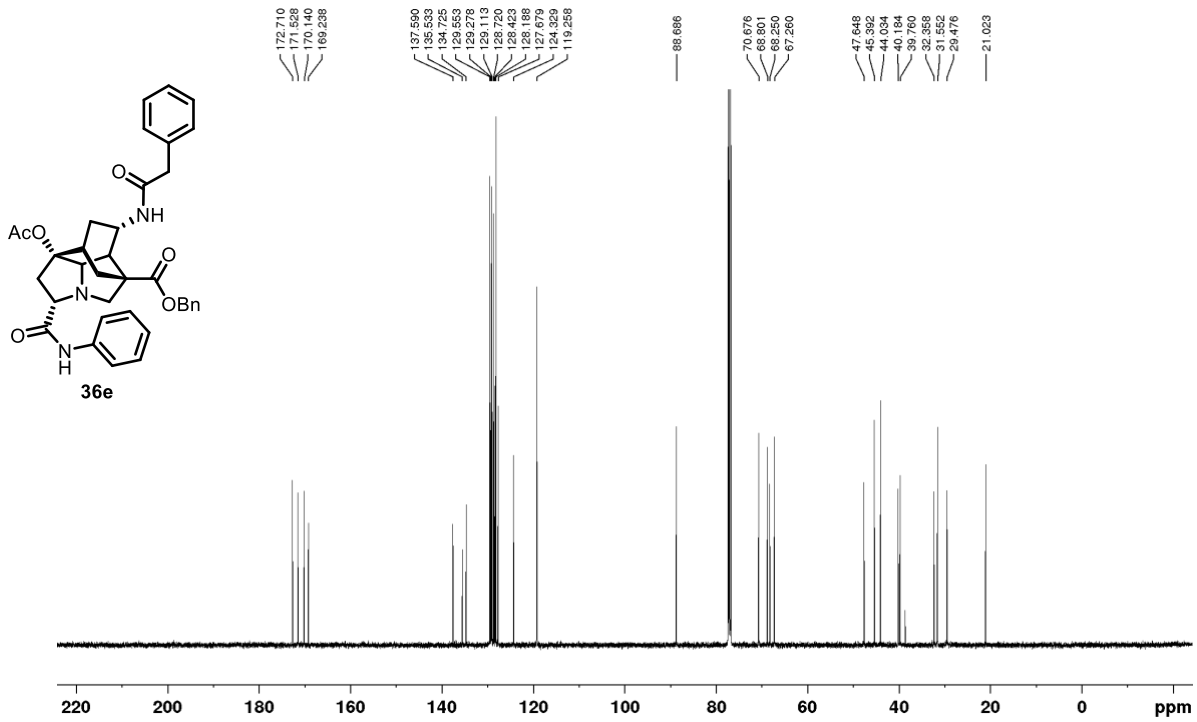


Amide **36e**

^{1}H NMR (400 MHz, CD_3OD)

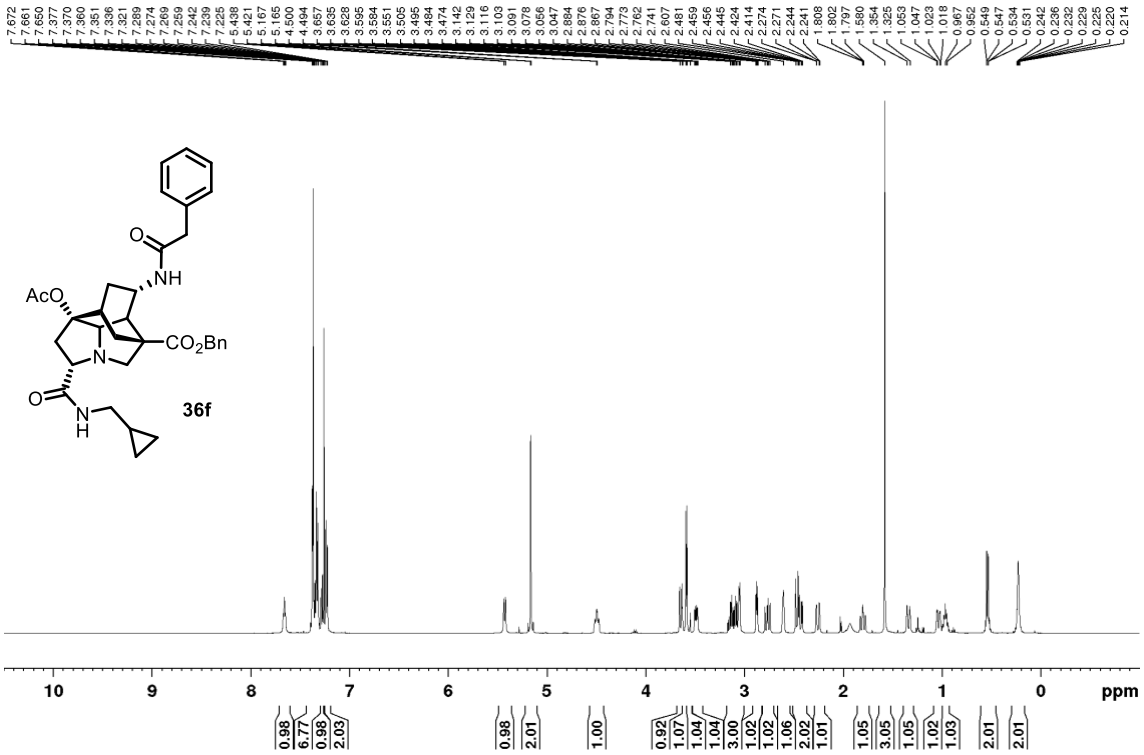


^{13}C NMR (125 MHz, $CDCl_3$)

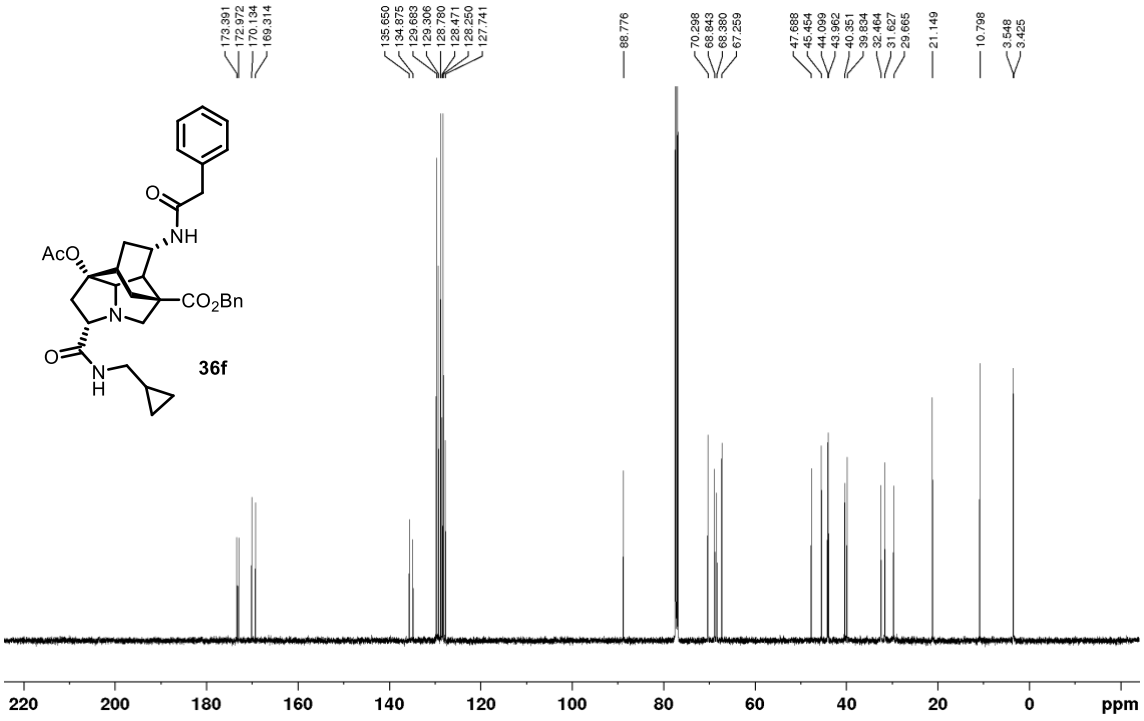


Amide **36f**

^{1}H NMR (500 MHz, $CDCl_3$)

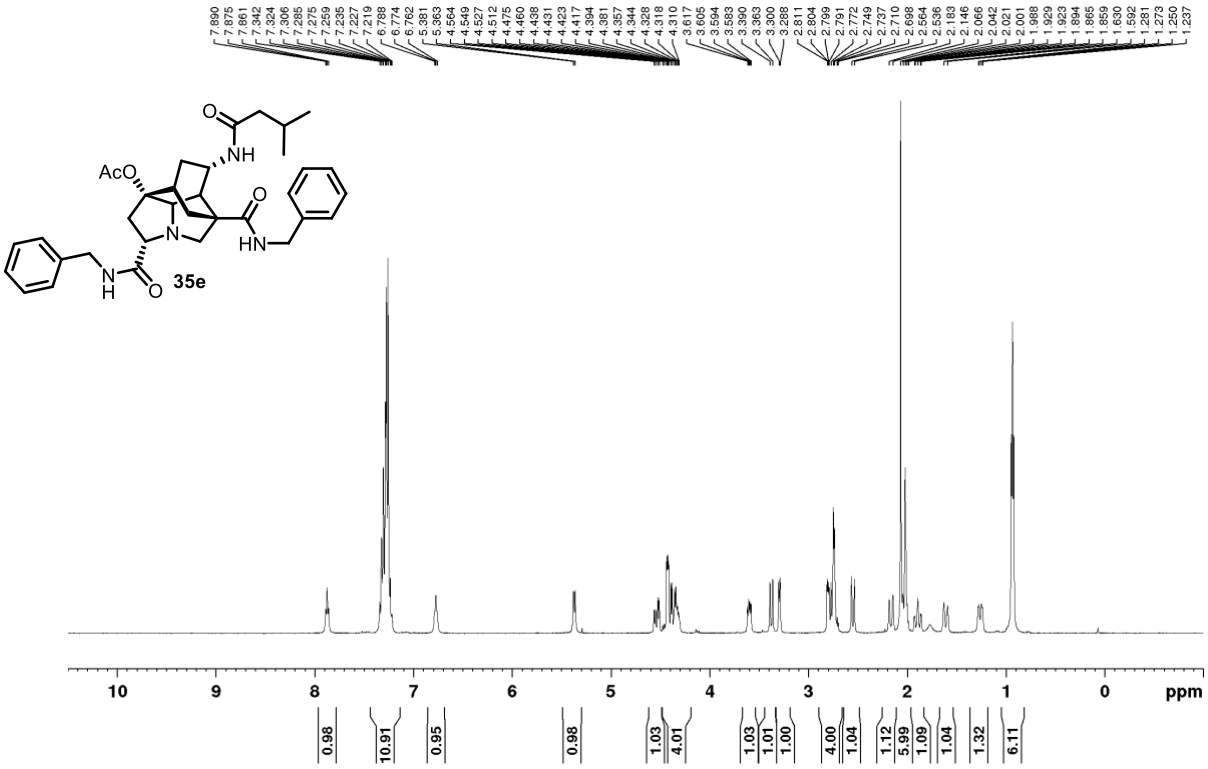


^{13}C NMR (125 MHz, $CDCl_3$)

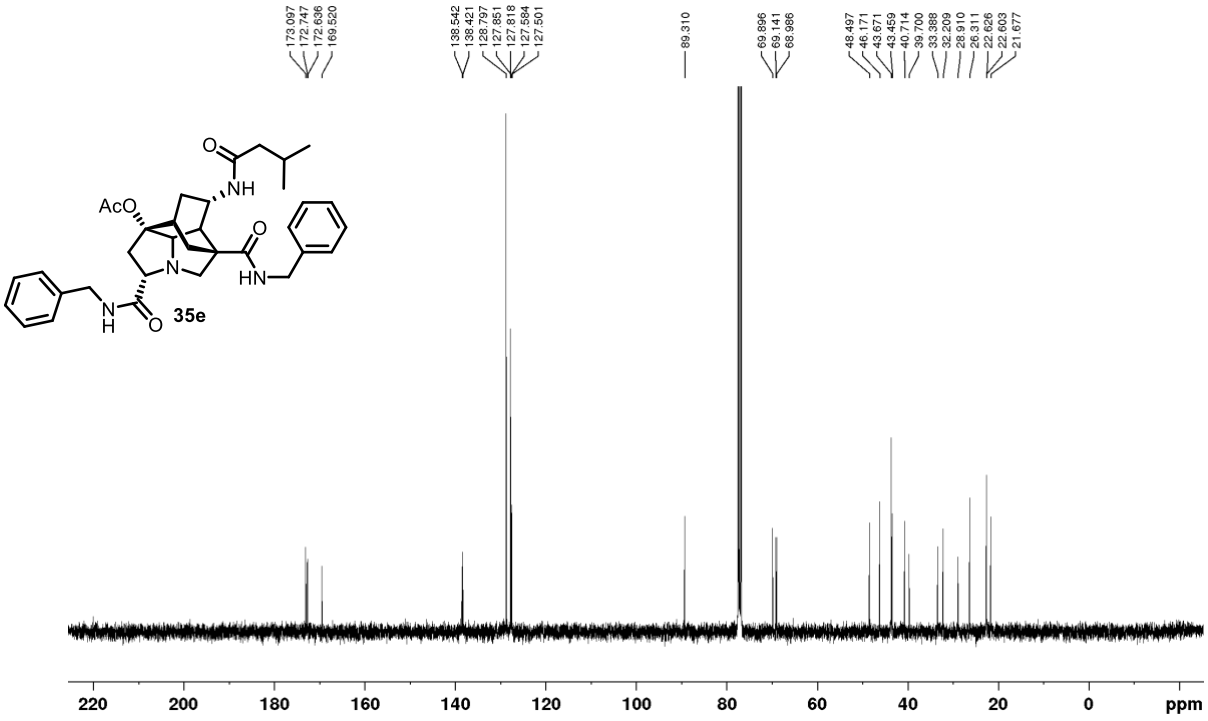


Amide **35e**

^{1}H NMR (400 MHz, $CDCl_3$)

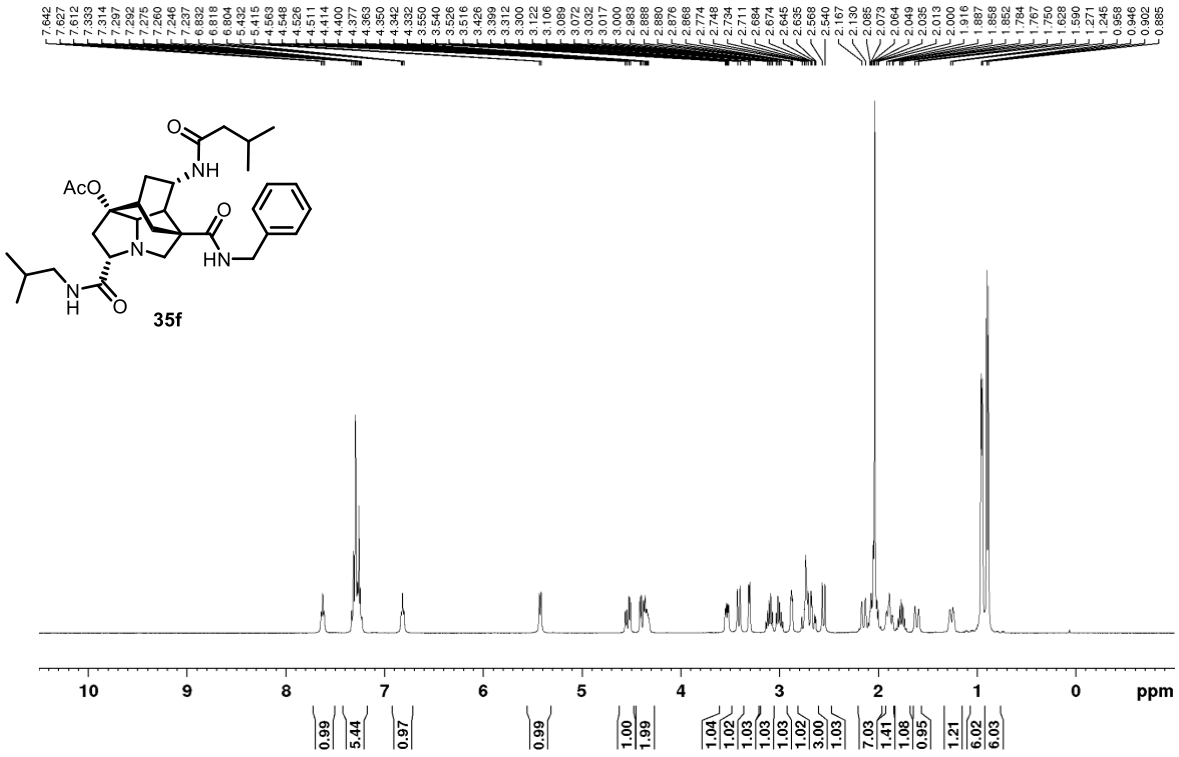


^{13}C NMR (100 MHz, $CDCl_3$)

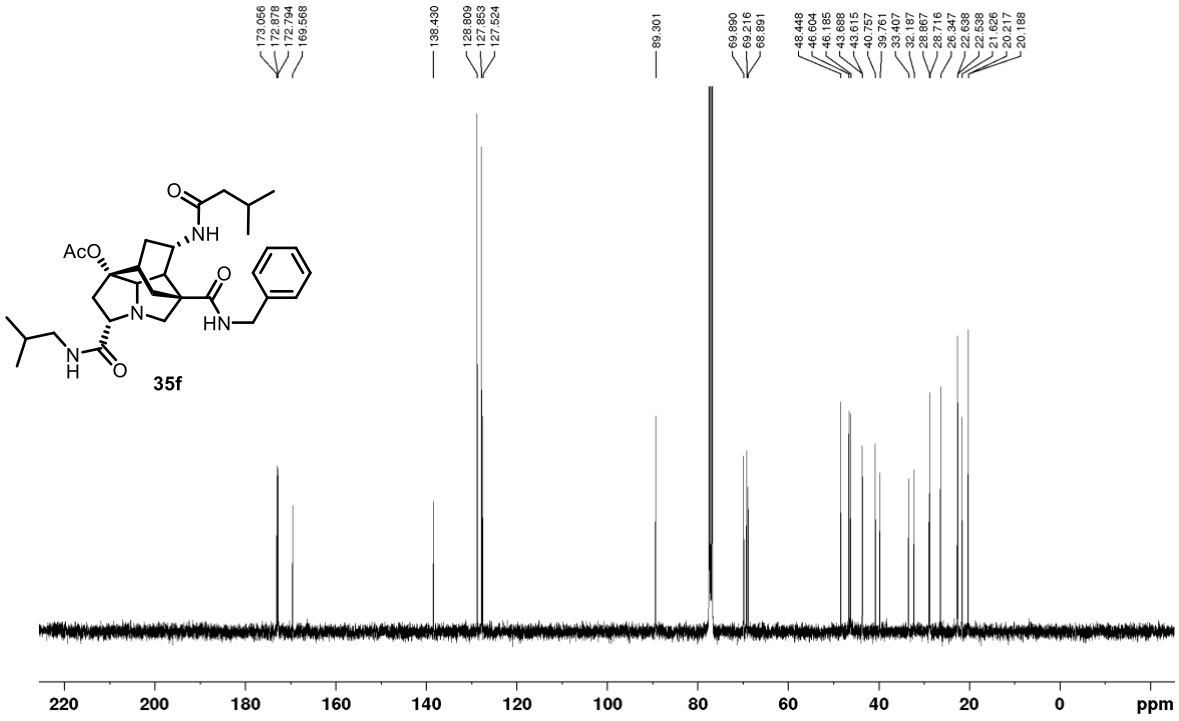


Amide **35f**

^{1}H NMR (400 MHz, $CDCl_3$)

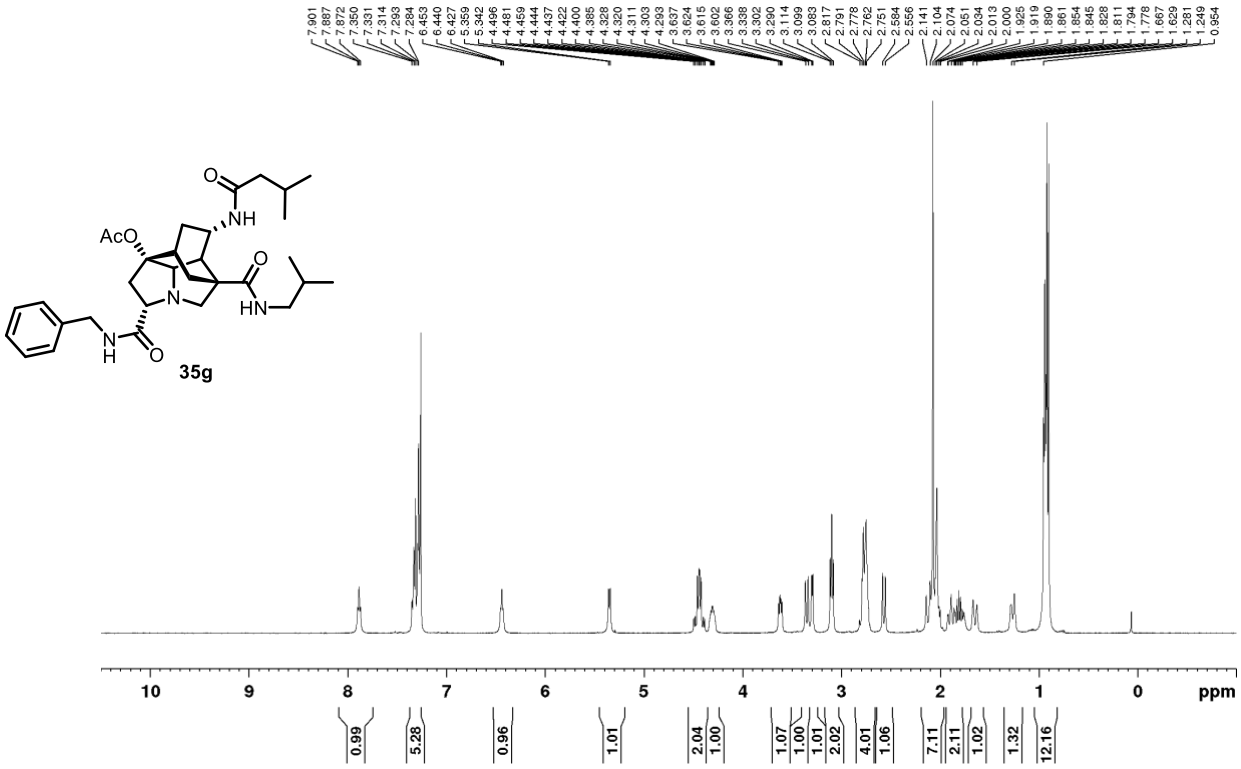


^{13}C NMR (100 MHz, $CDCl_3$)

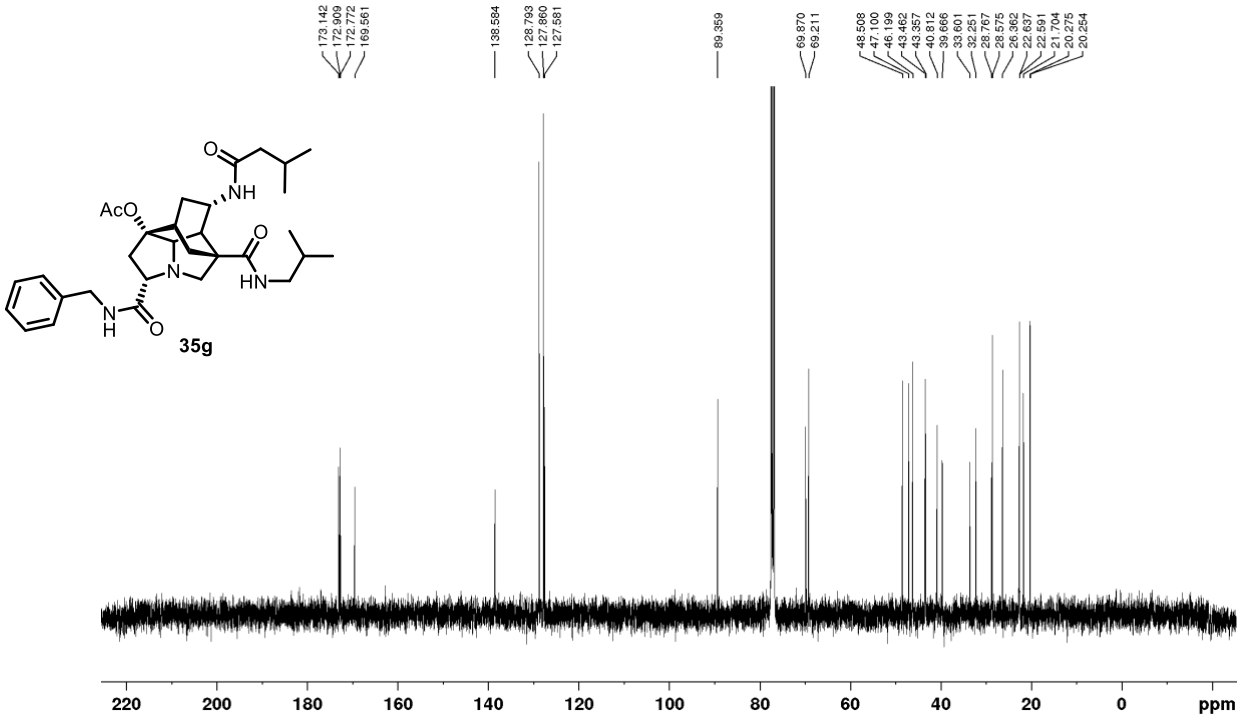


Amide **35g**

^{1}H NMR (400 MHz, $CDCl_3$)

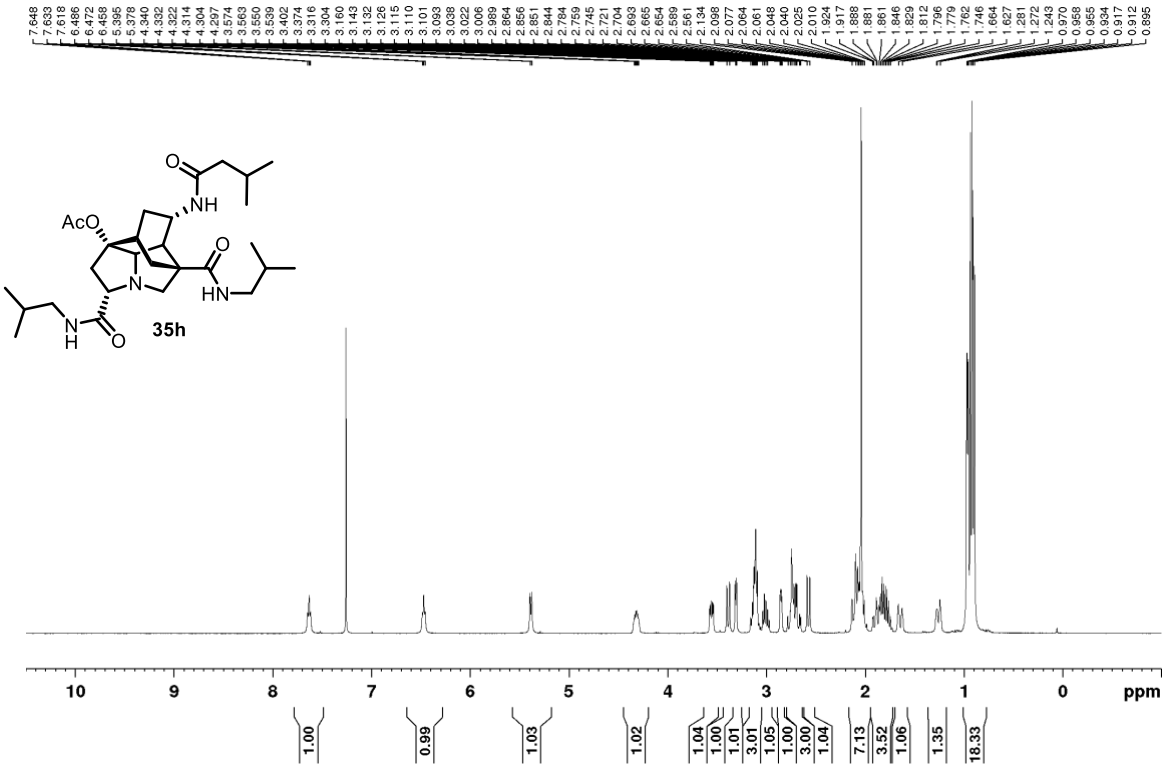


^{13}C NMR (100 MHz, $CDCl_3$)

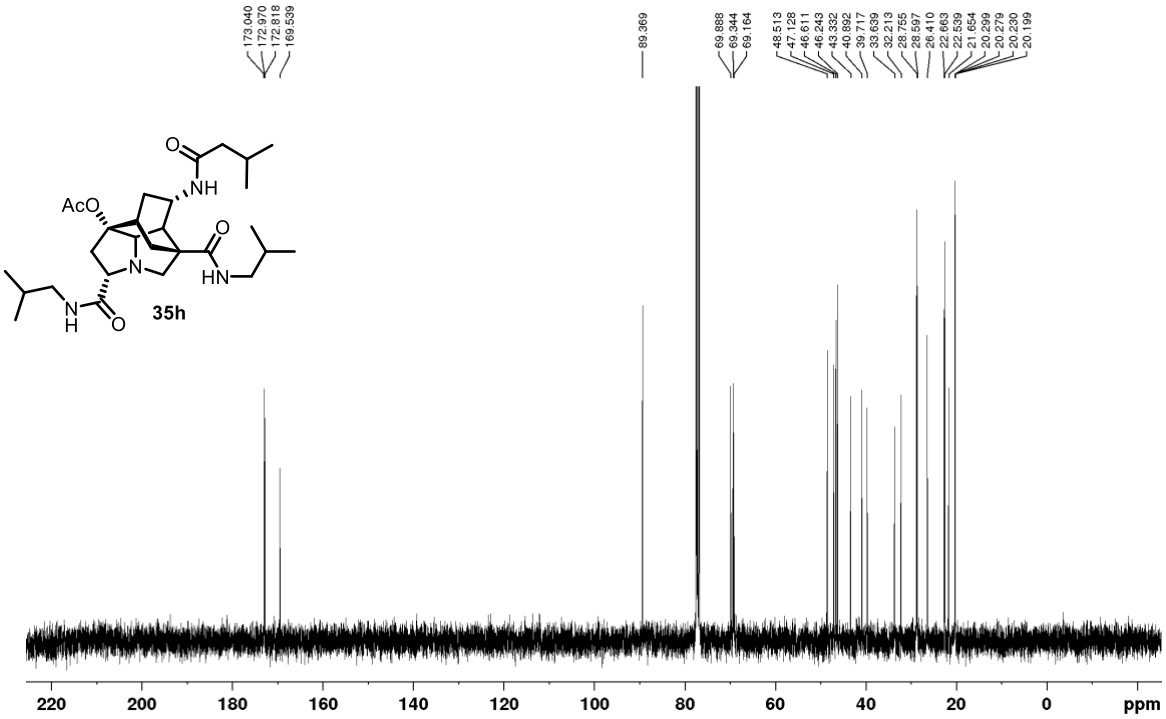


Amide **35h**

^{1}H NMR (400 MHz, $CDCl_3$)

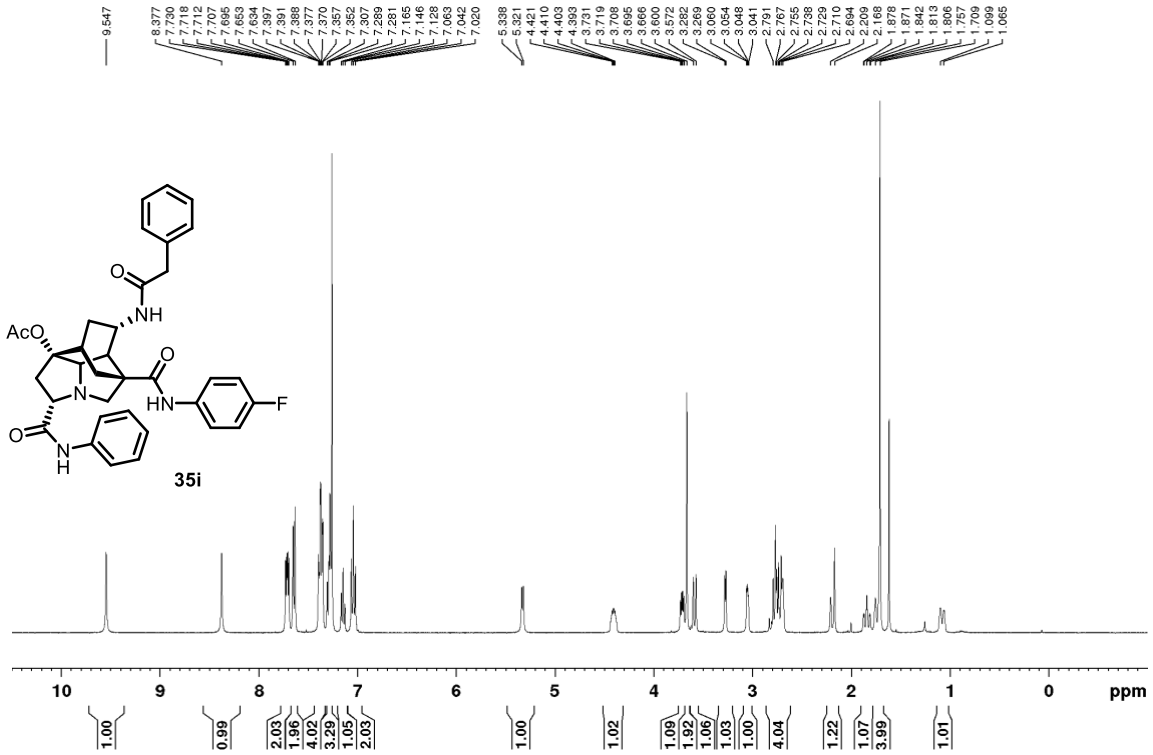


^{13}C NMR (100 MHz, $CDCl_3$)

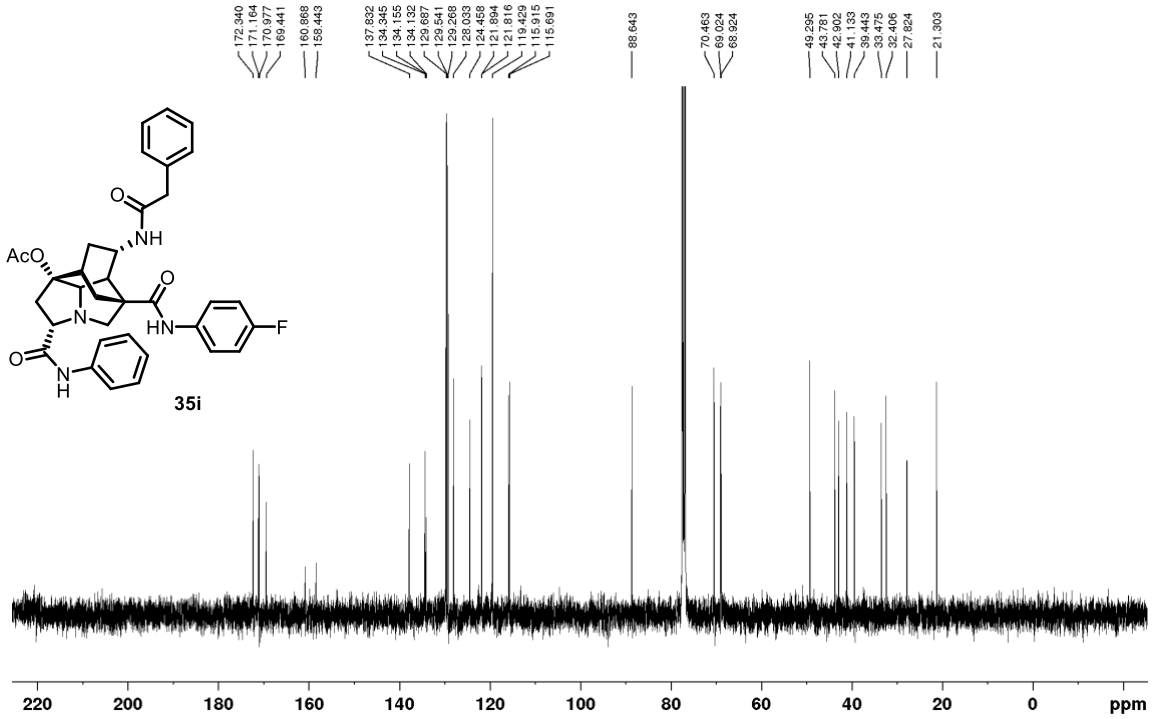


Amide **35i**

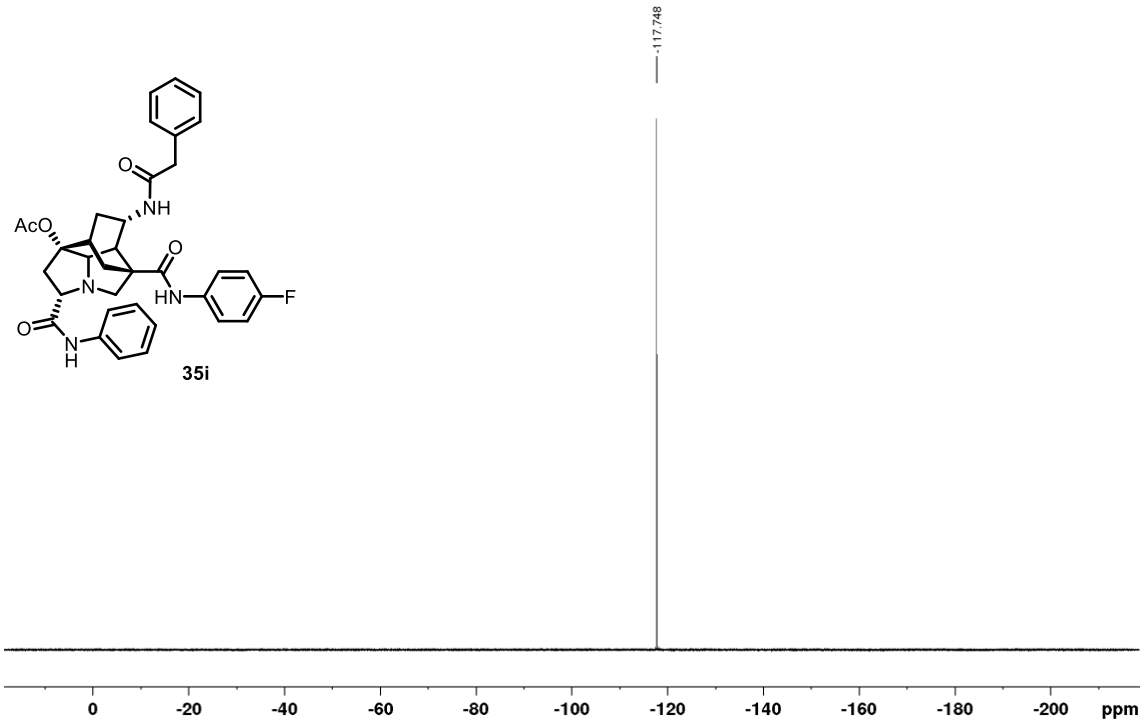
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

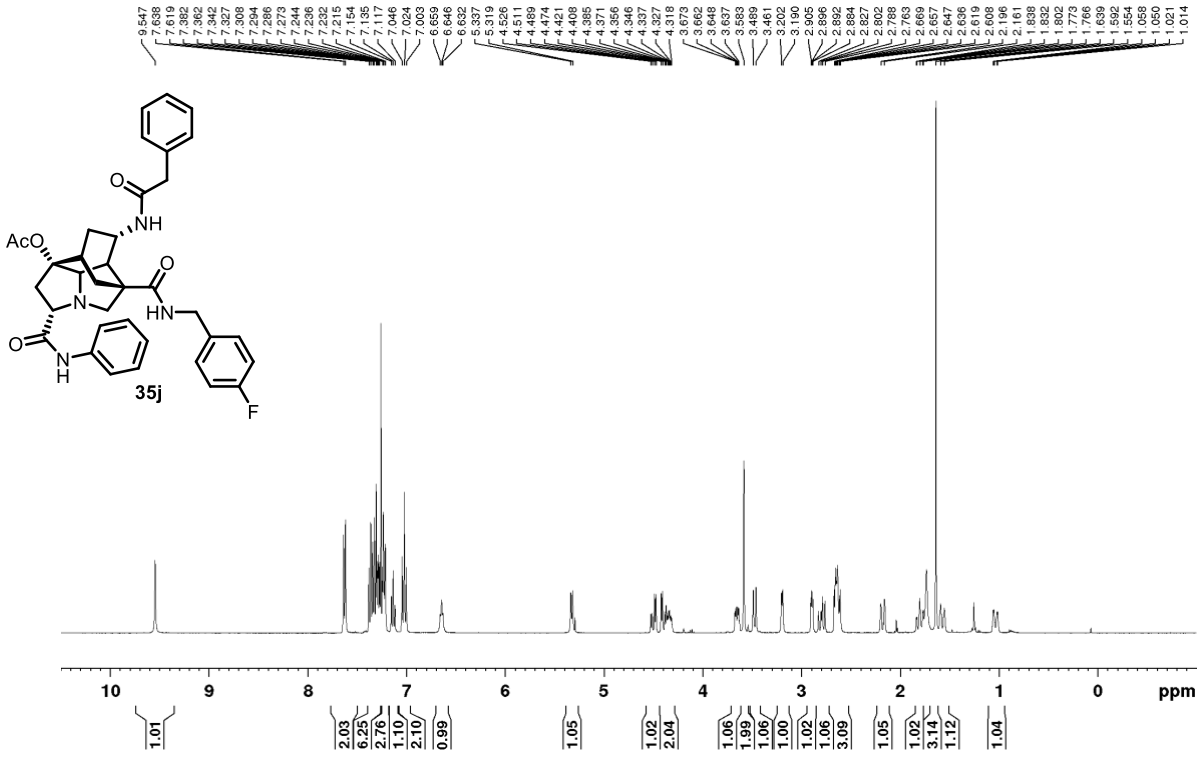


^{19}F NMR (376 MHz, $CDCl_3$)

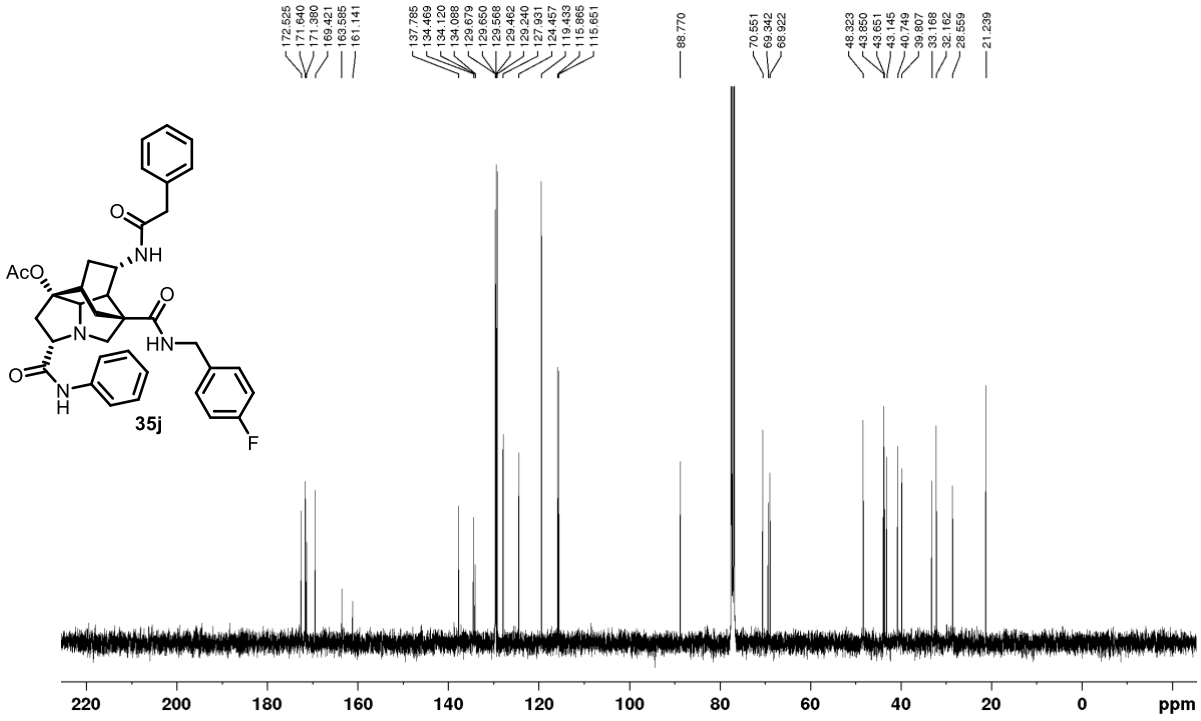


Amide **35j**

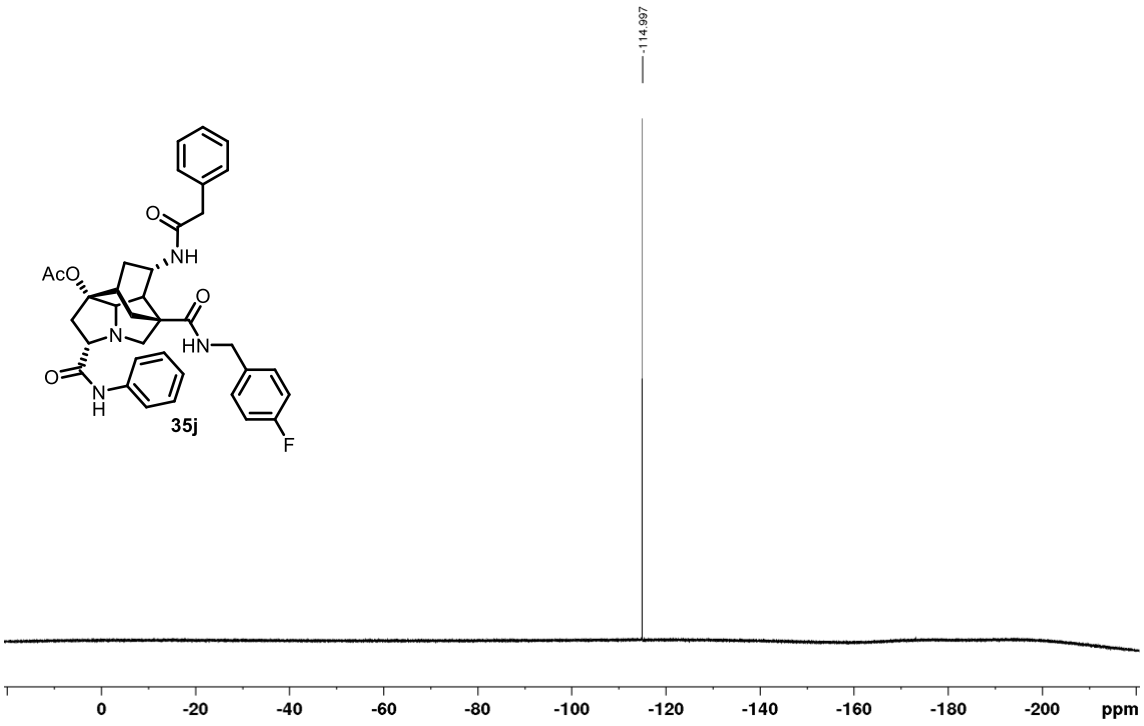
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

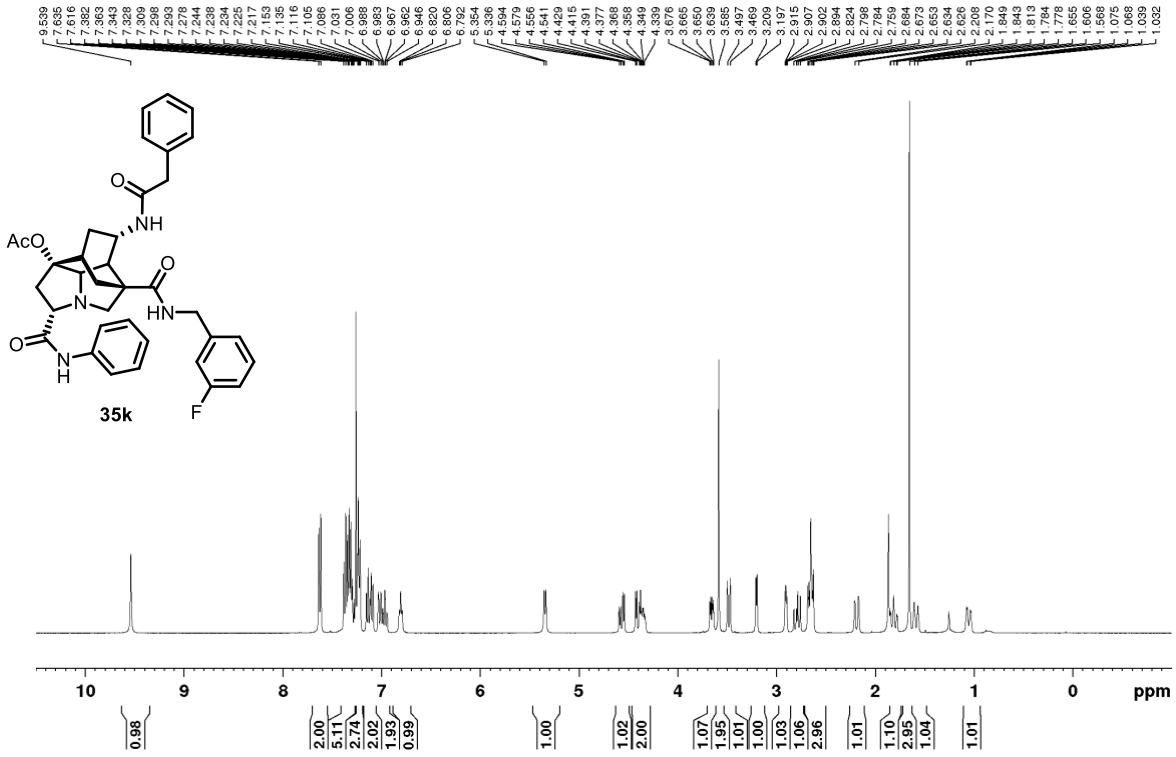


^{19}F (376 MHz, $CDCl_3$)

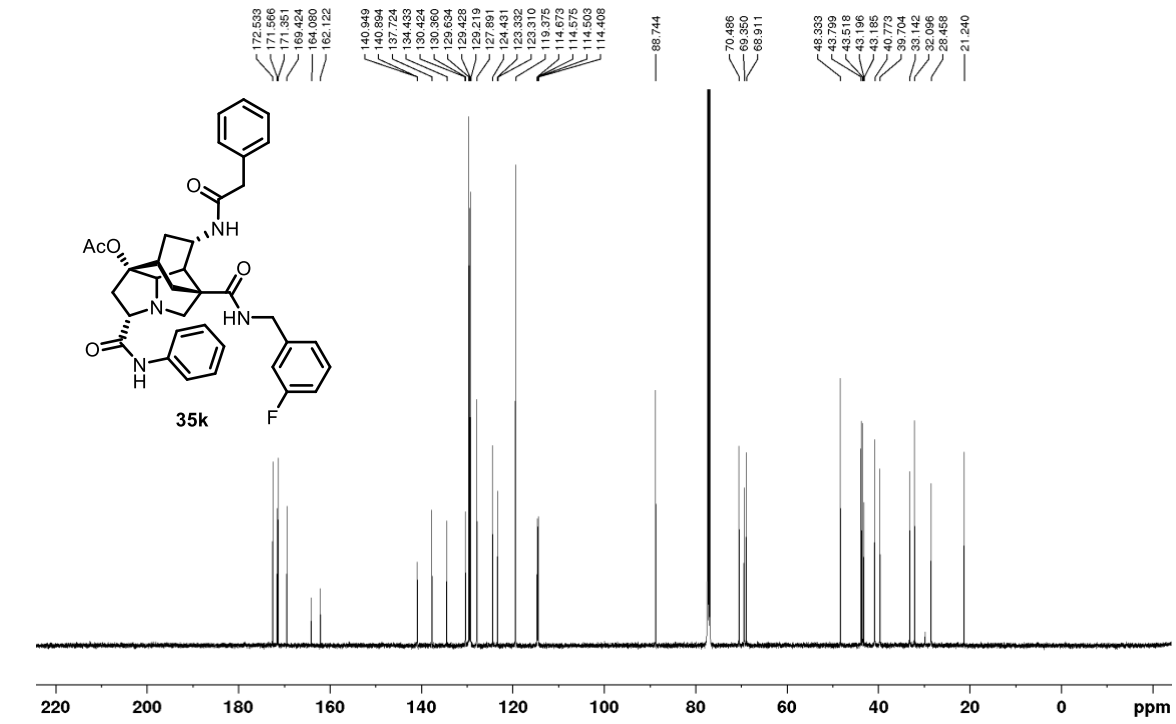


Amide **35k**

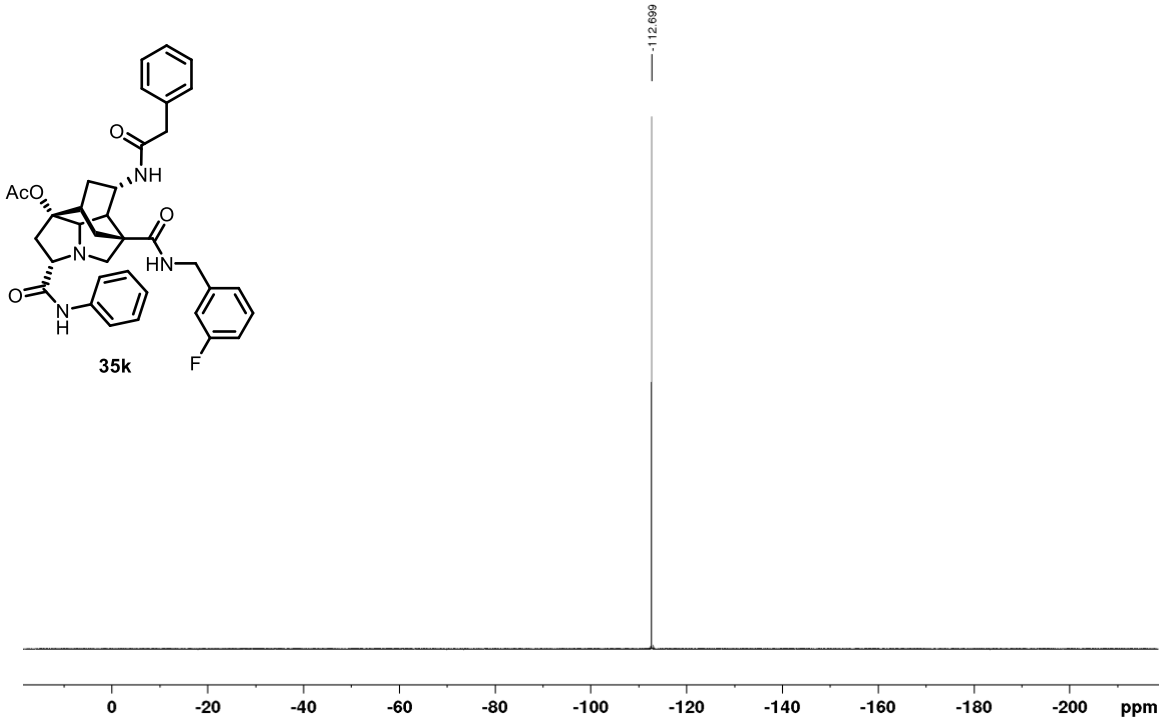
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)

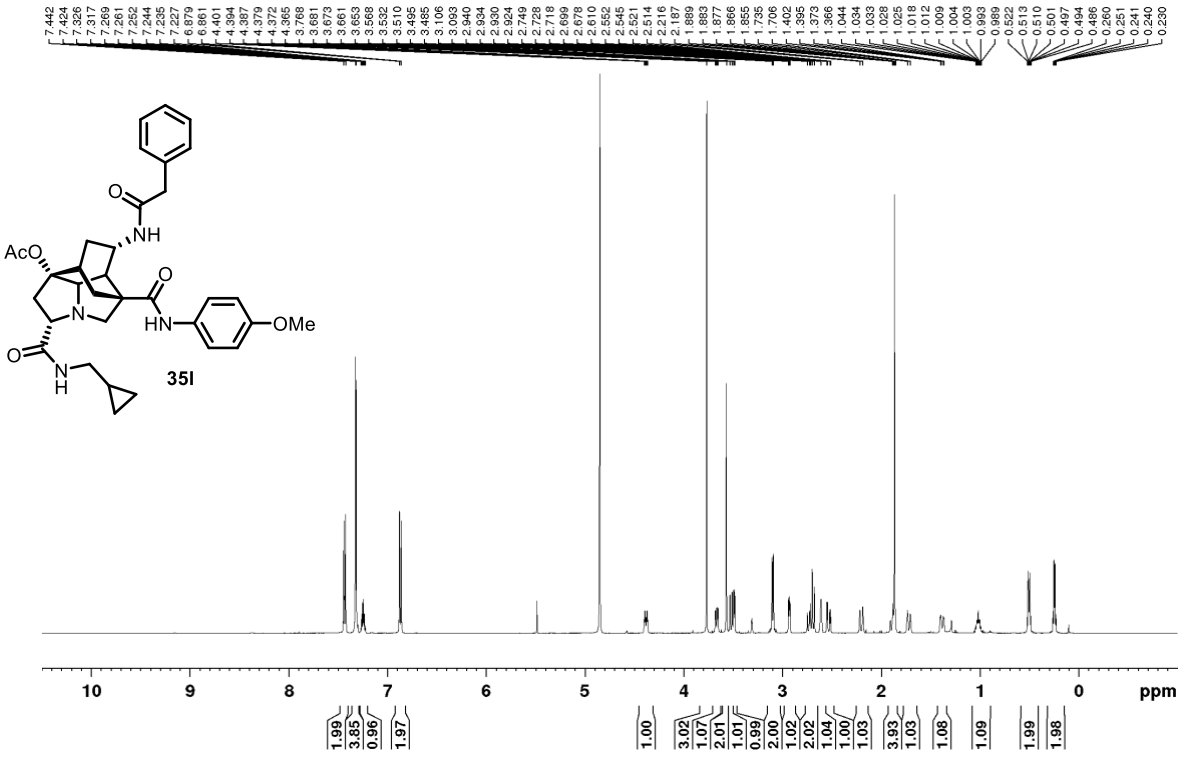


^{19}F (376 MHz, $CDCl_3$)

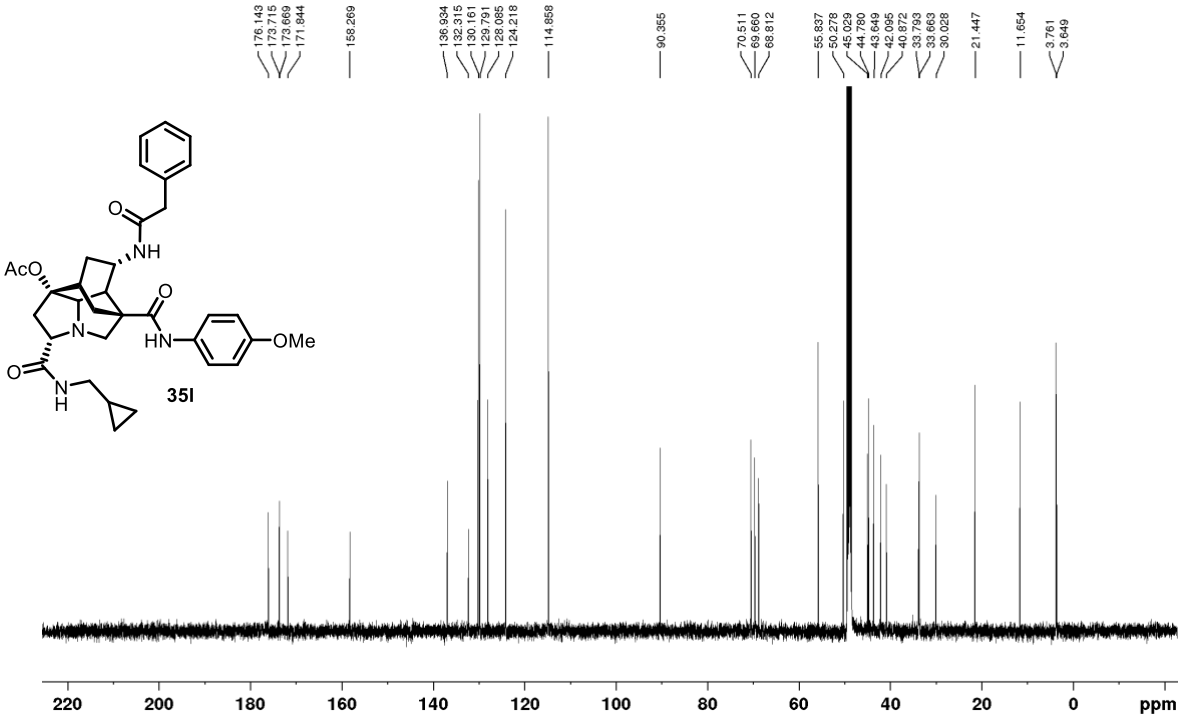


Amide **35l**

^{1}H NMR (500 MHz, MeOD)

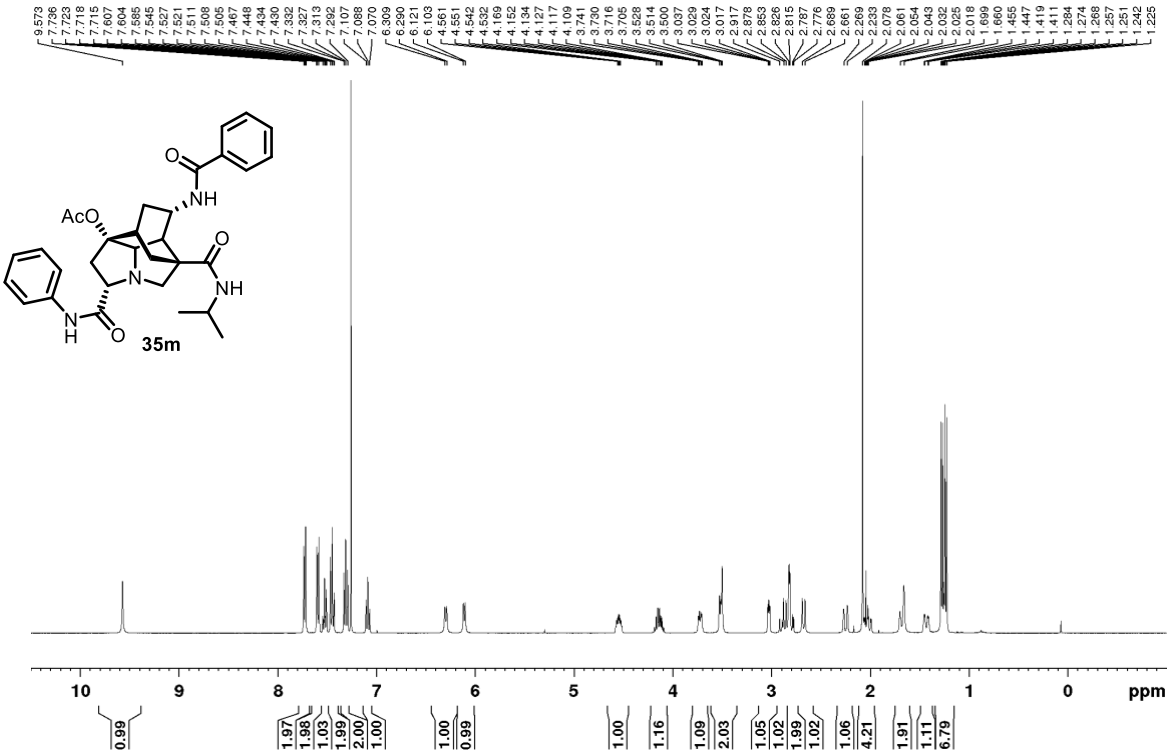


^{13}C NMR (125 MHz, MeOD)

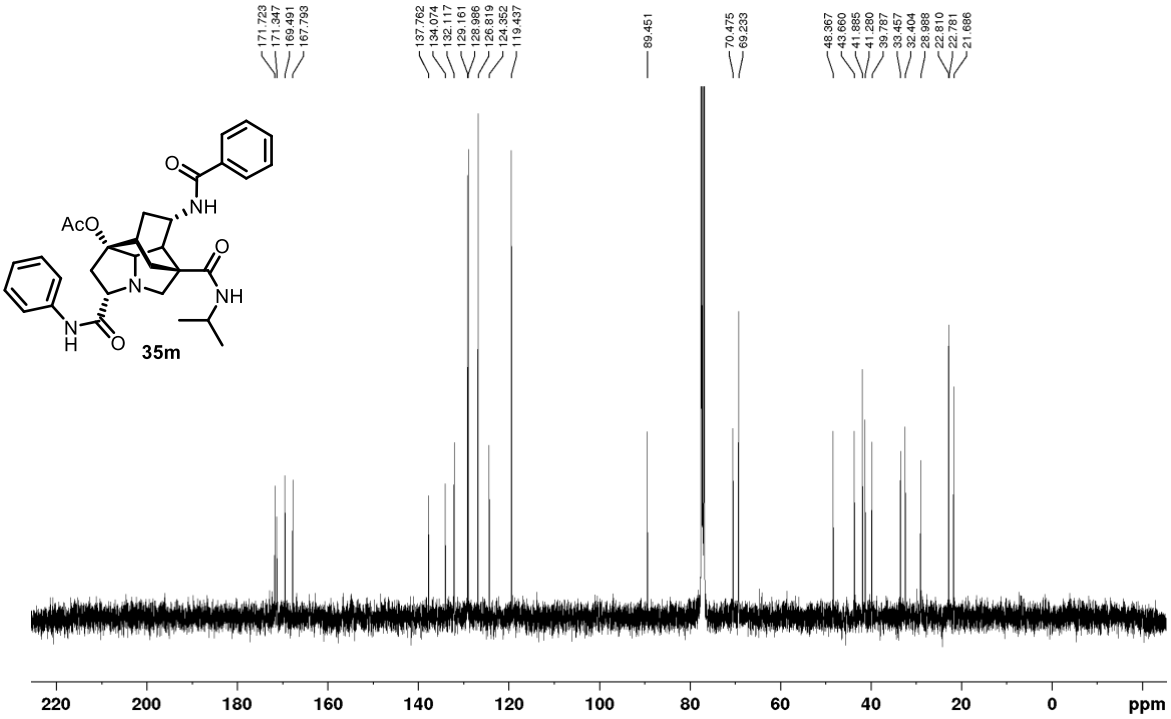


Amide **35m**

^{1}H NMR (400 MHz, $CDCl_3$)

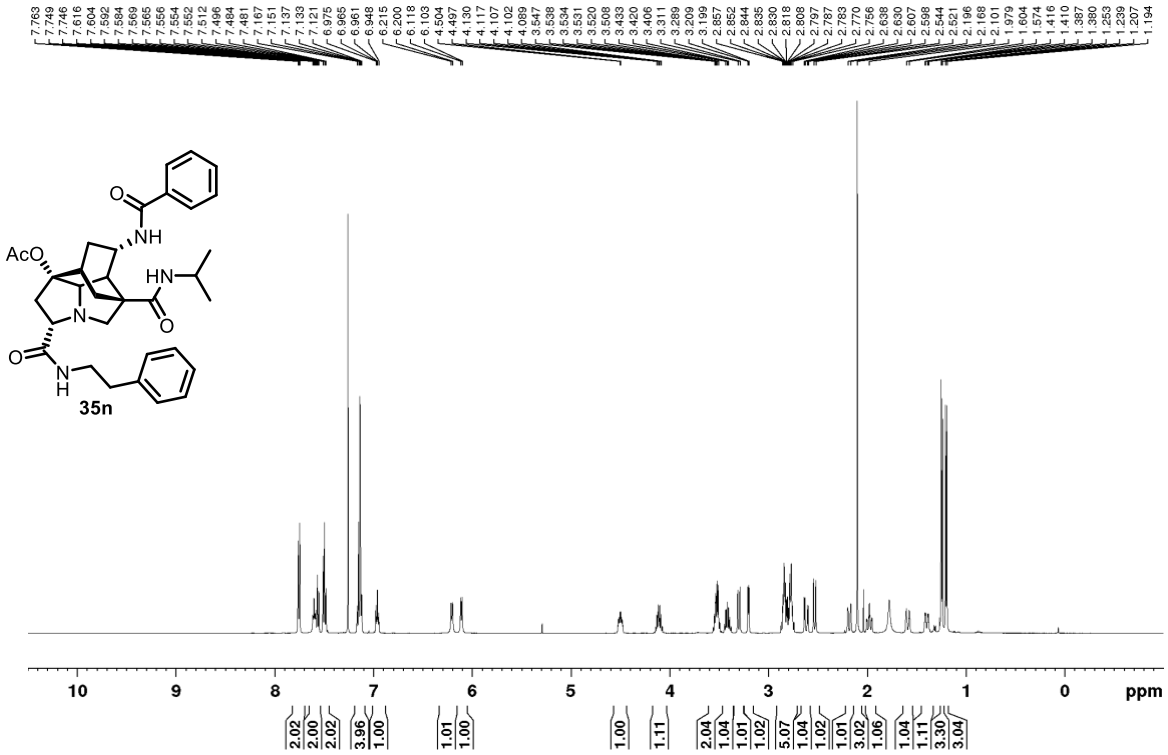


^{13}C NMR (100 MHz, $CDCl_3$)

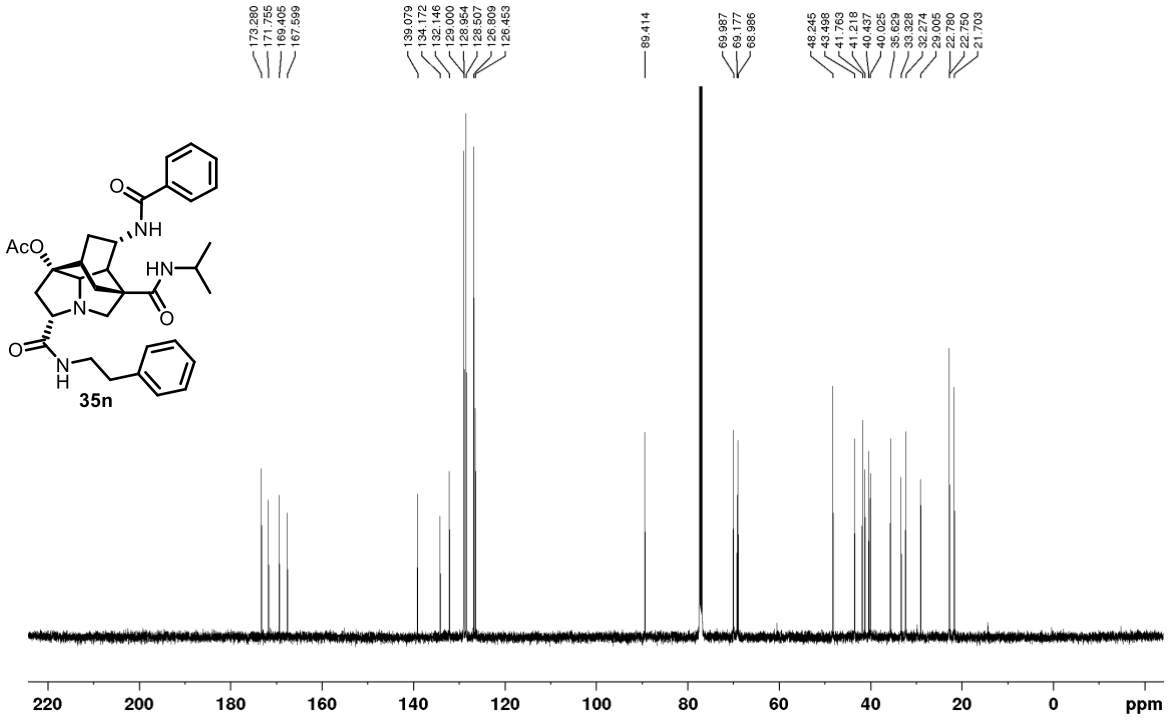


Amide **35n**

^{1}H NMR (500 MHz, $CDCl_3$)

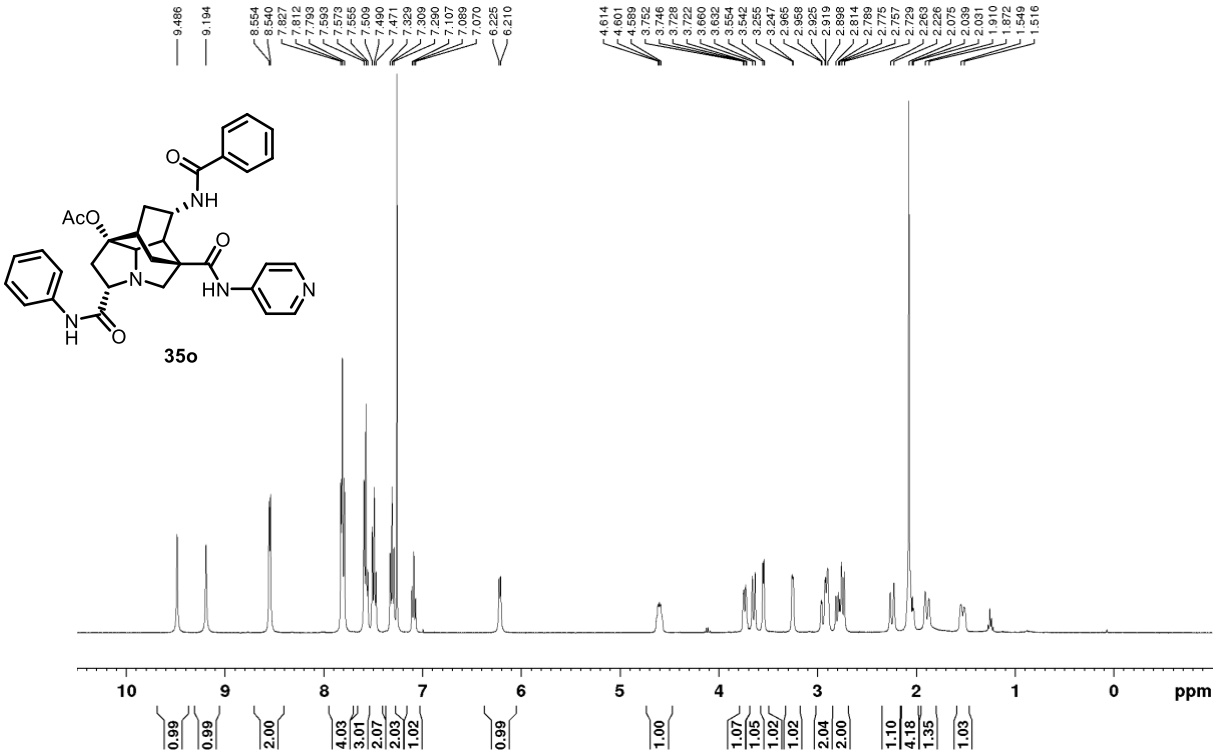


^{13}C NMR (125 MHz, $CDCl_3$)

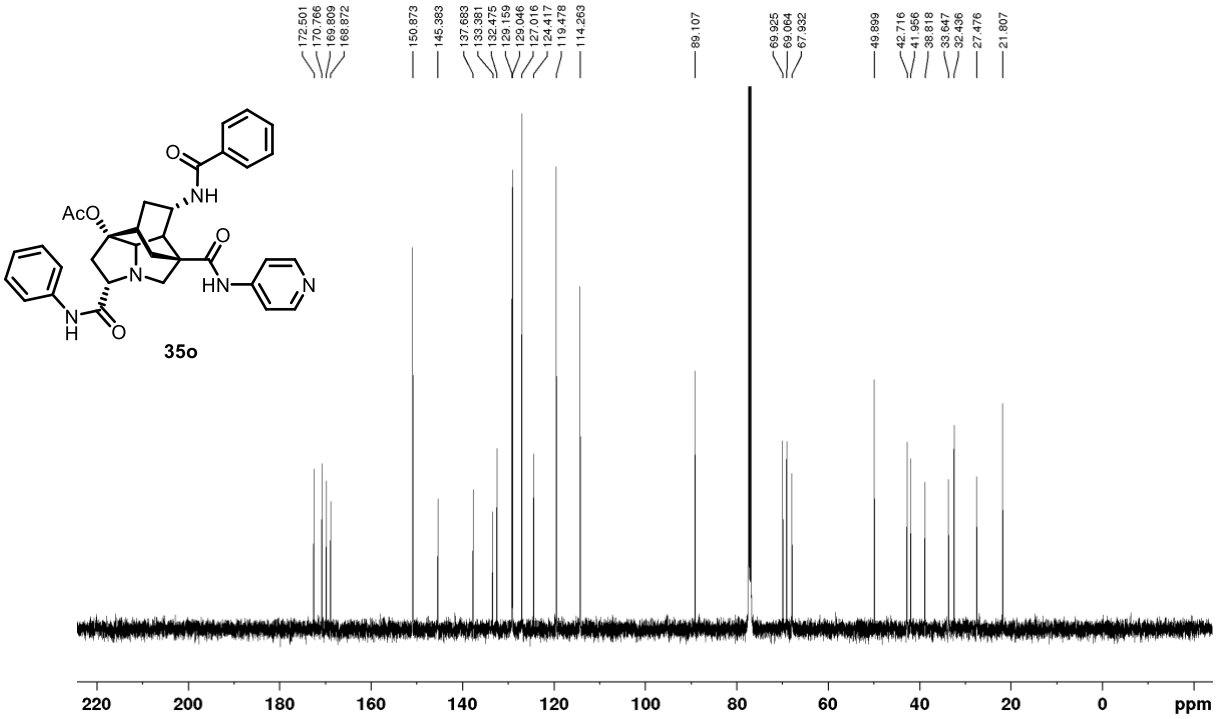


Amide **35o**

^{1}H NMR (400 MHz, $CDCl_3$)

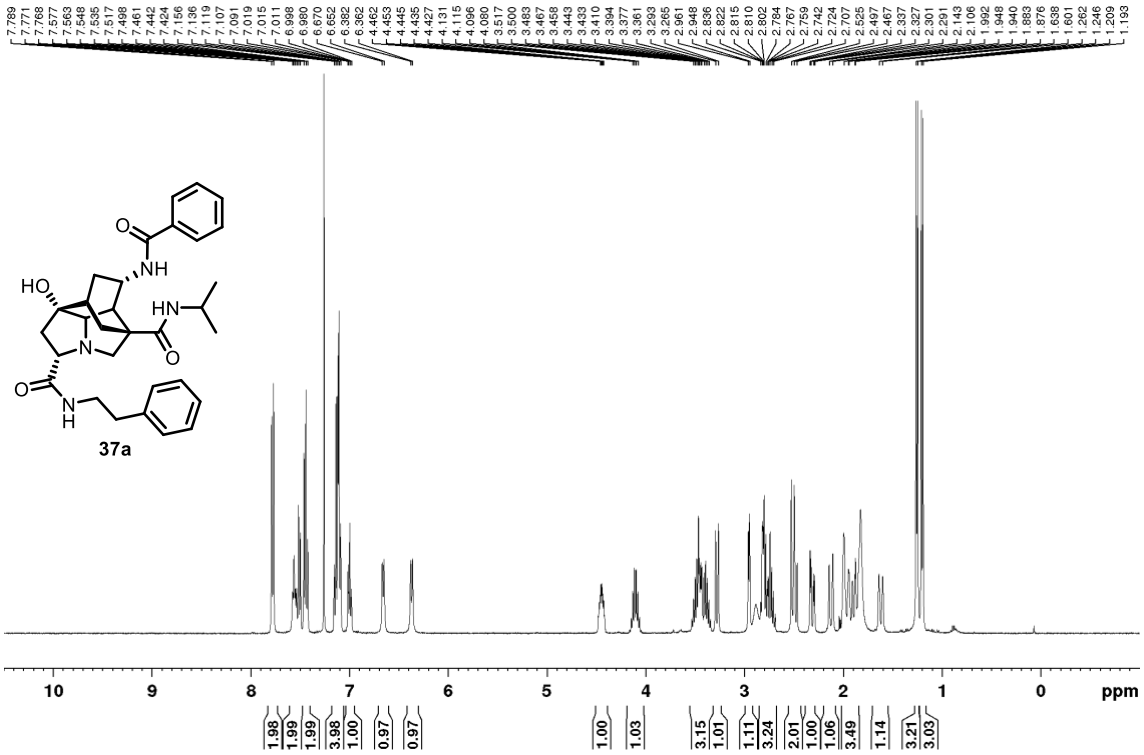


^{13}C NMR (125 MHz, $CDCl_3$)

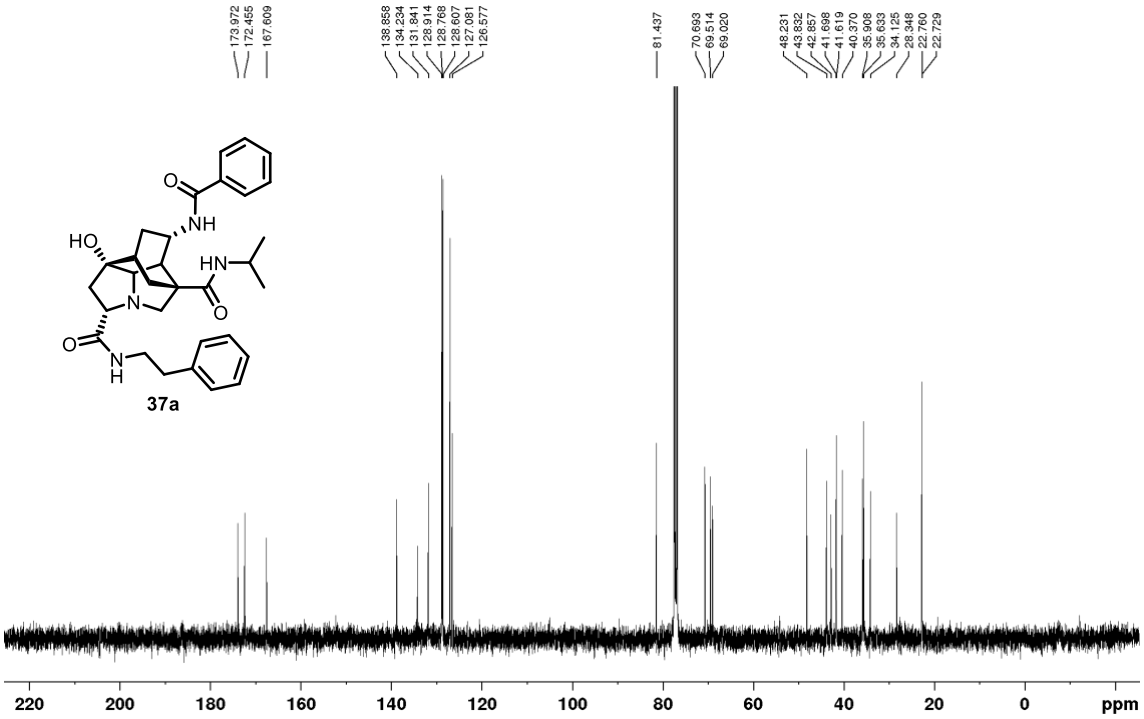


Alcohol **37a**

^{1}H NMR (400 MHz, $CDCl_3$)

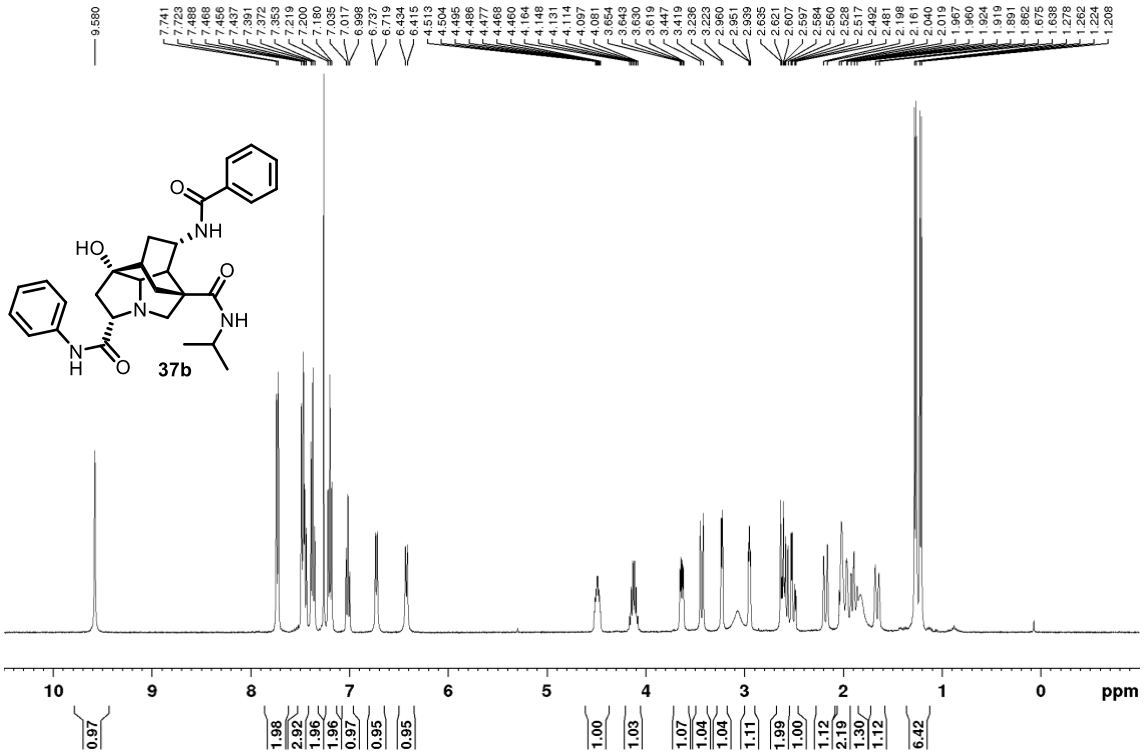


^{13}C NMR (100 MHz, $CDCl_3$)

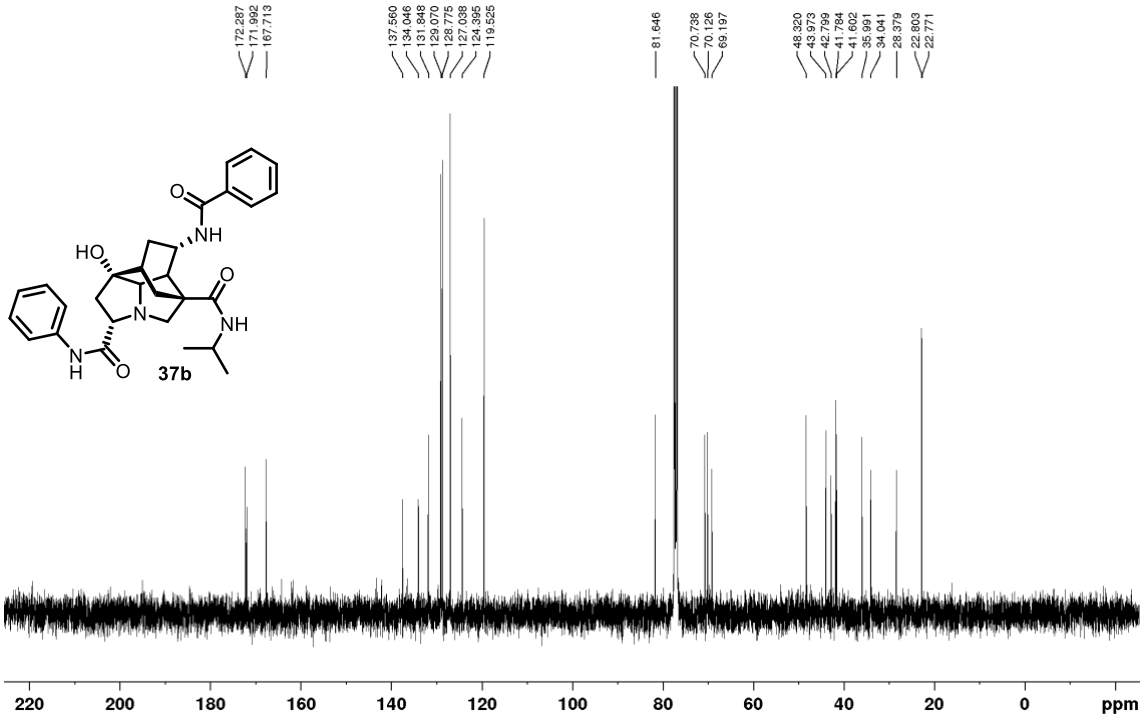


Alcohol **37b**

^{1}H NMR (400 MHz, $CDCl_3$)

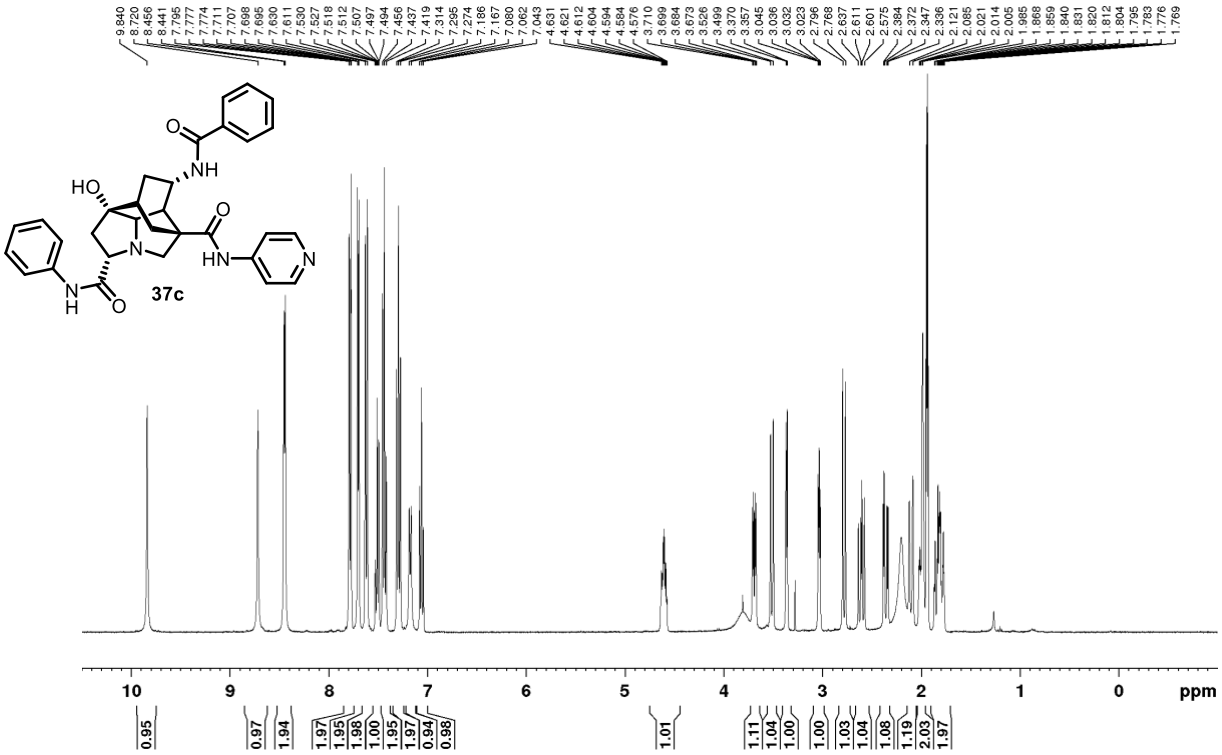


^{13}C NMR (100 MHz, $CDCl_3$)

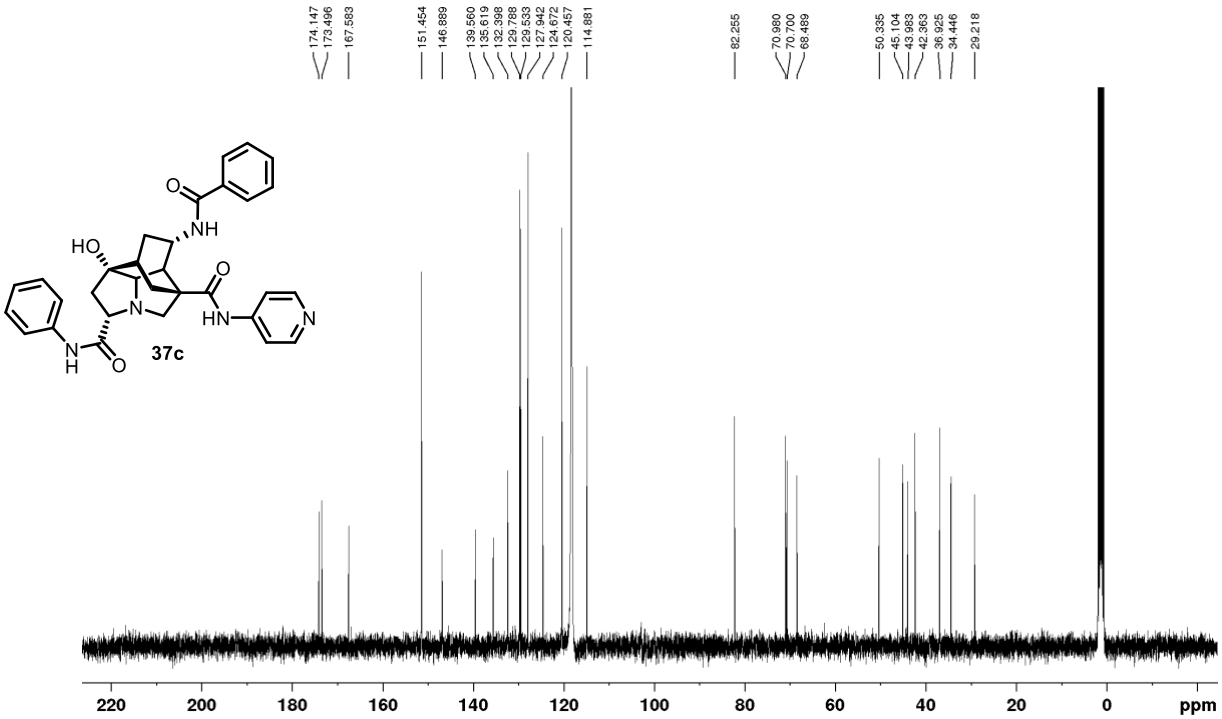


Alcohol **37c**

^{1}H NMR (400 MHz, CD_3CN)

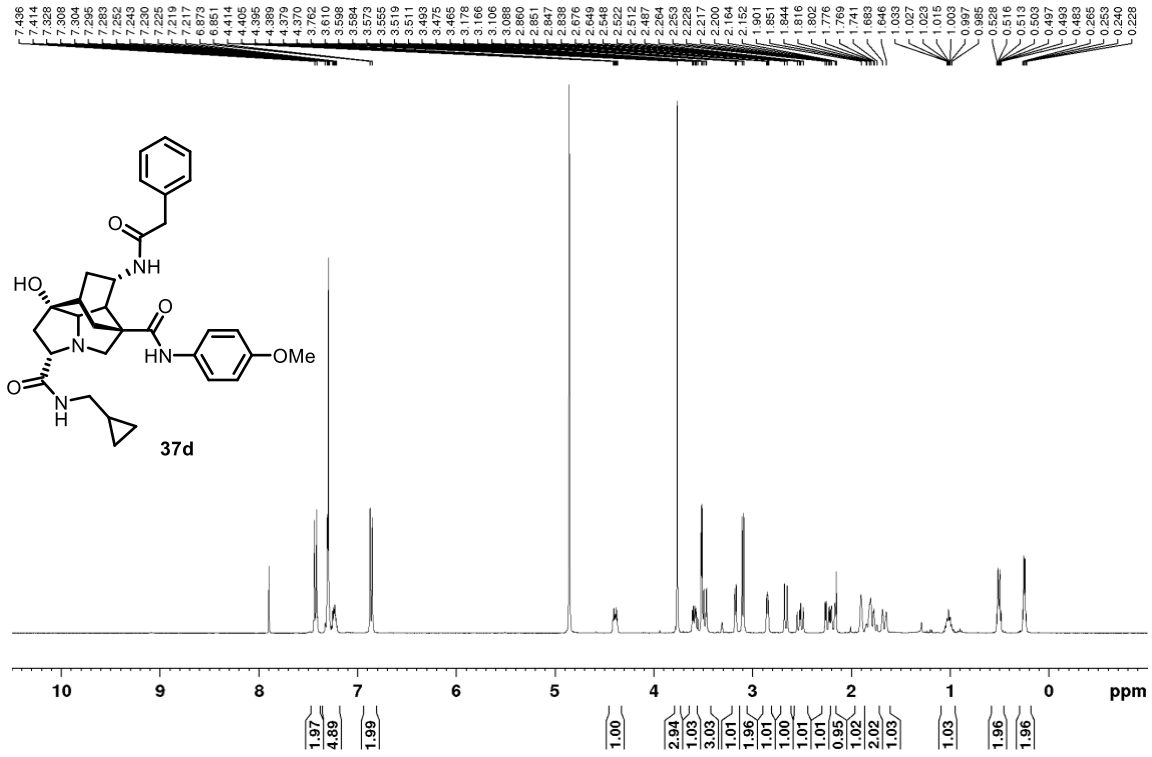


^{13}C NMR (100 MHz, CD_3CN)

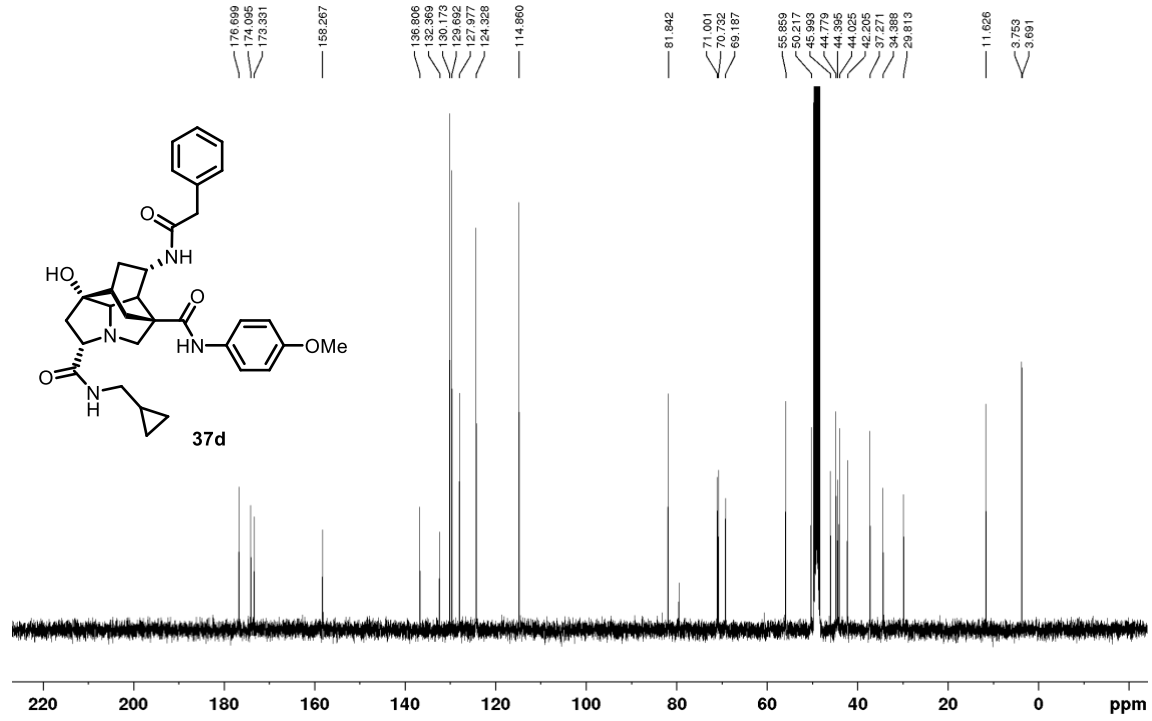


Alcohol **37d**

^{1}H NMR (400 MHz, CD_3OD)

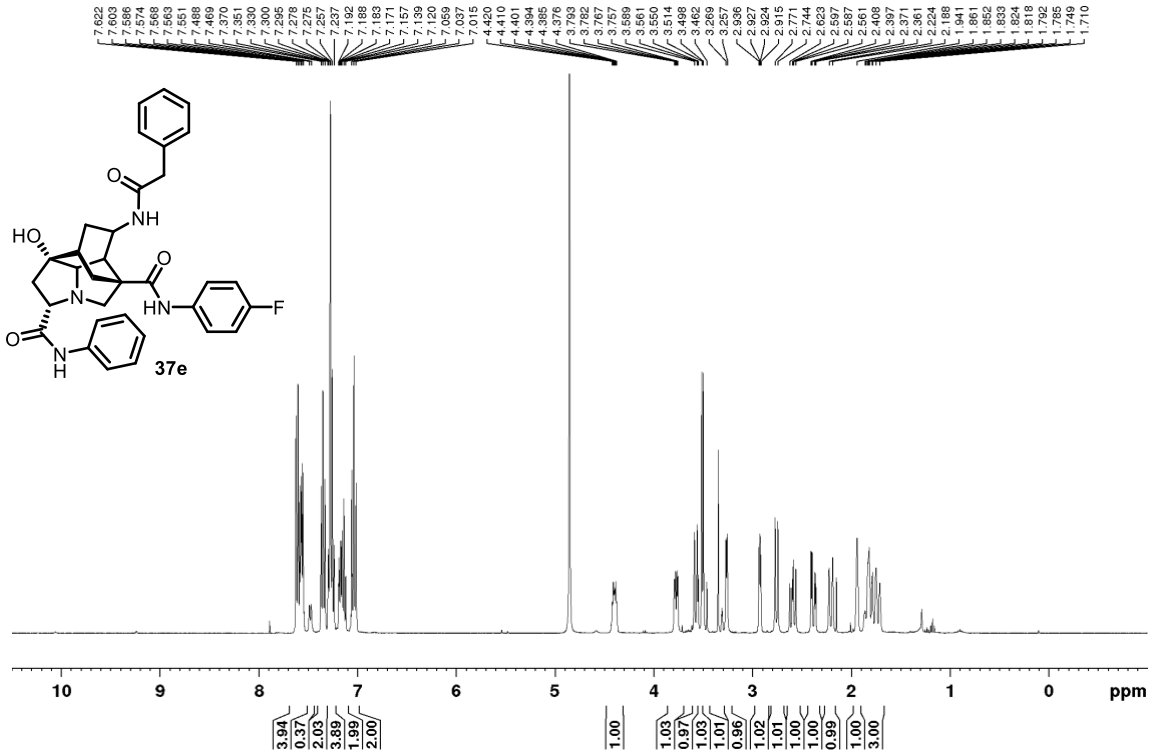


^{13}C NMR (100 MHz, CD_3OD)

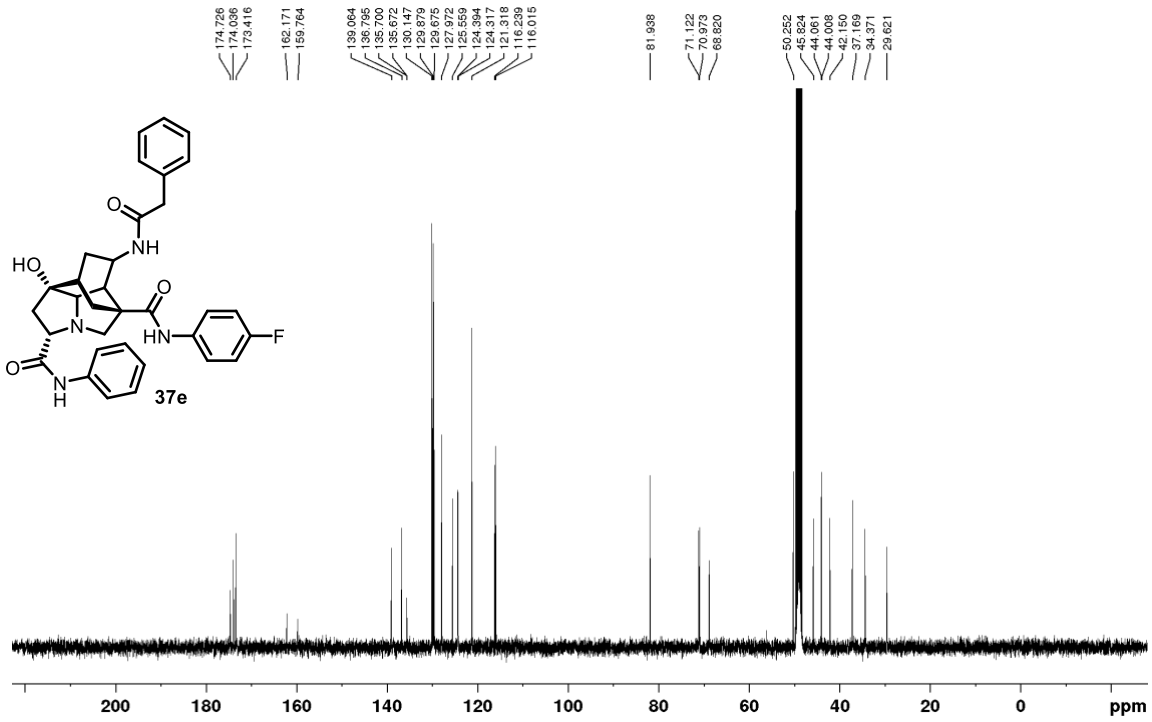


Alcohol **37e**

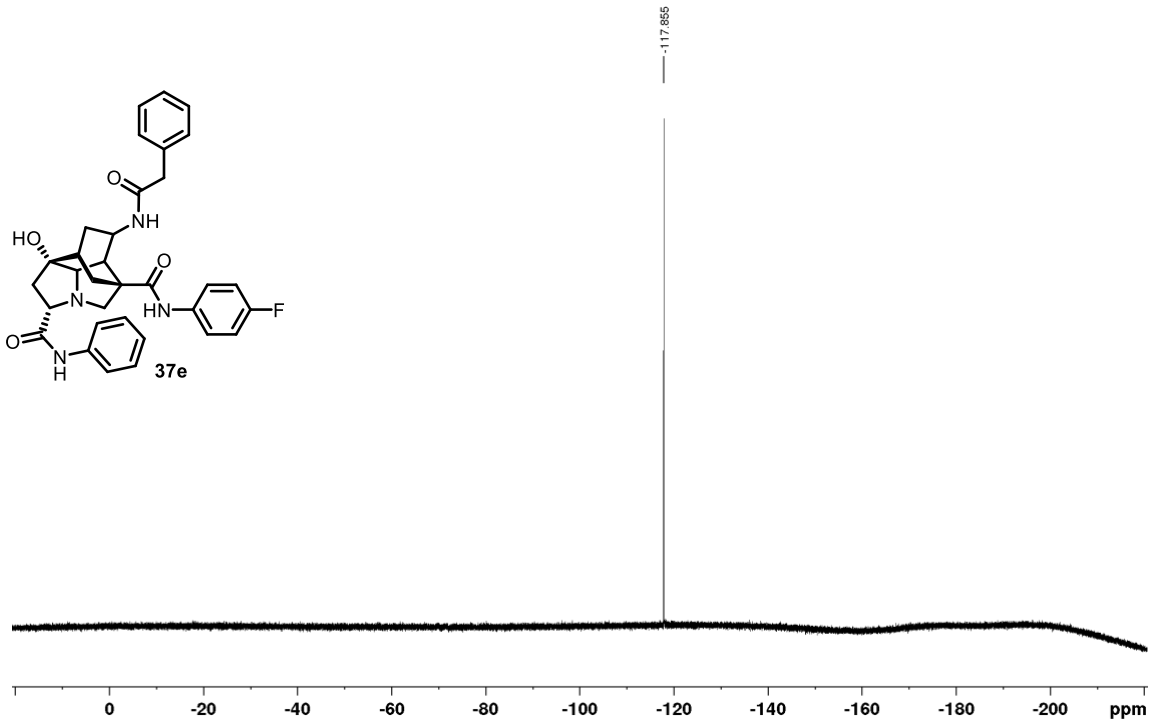
^{1}H NMR (400 MHz, MeOD)



^{13}C NMR (100 MHz, MeOD)

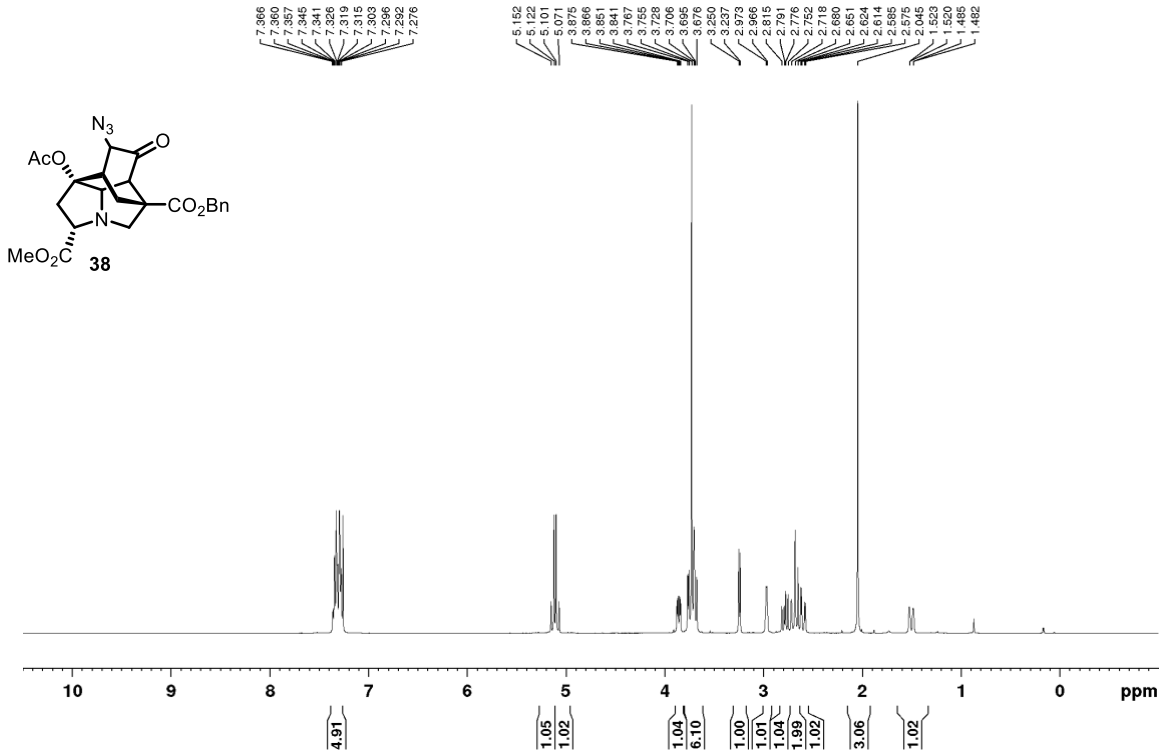


^{19}F (376 MHz, $CDCl_3$)

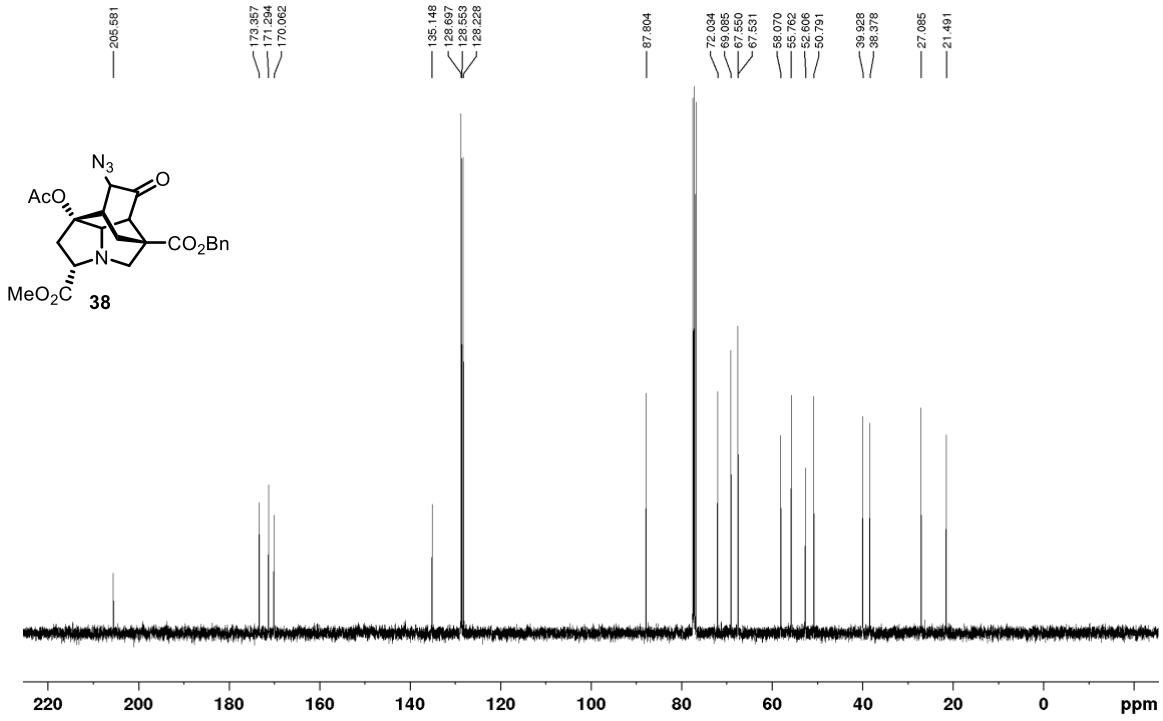


Azide **38**

^{1}H NMR (400 MHz, $CDCl_3$)

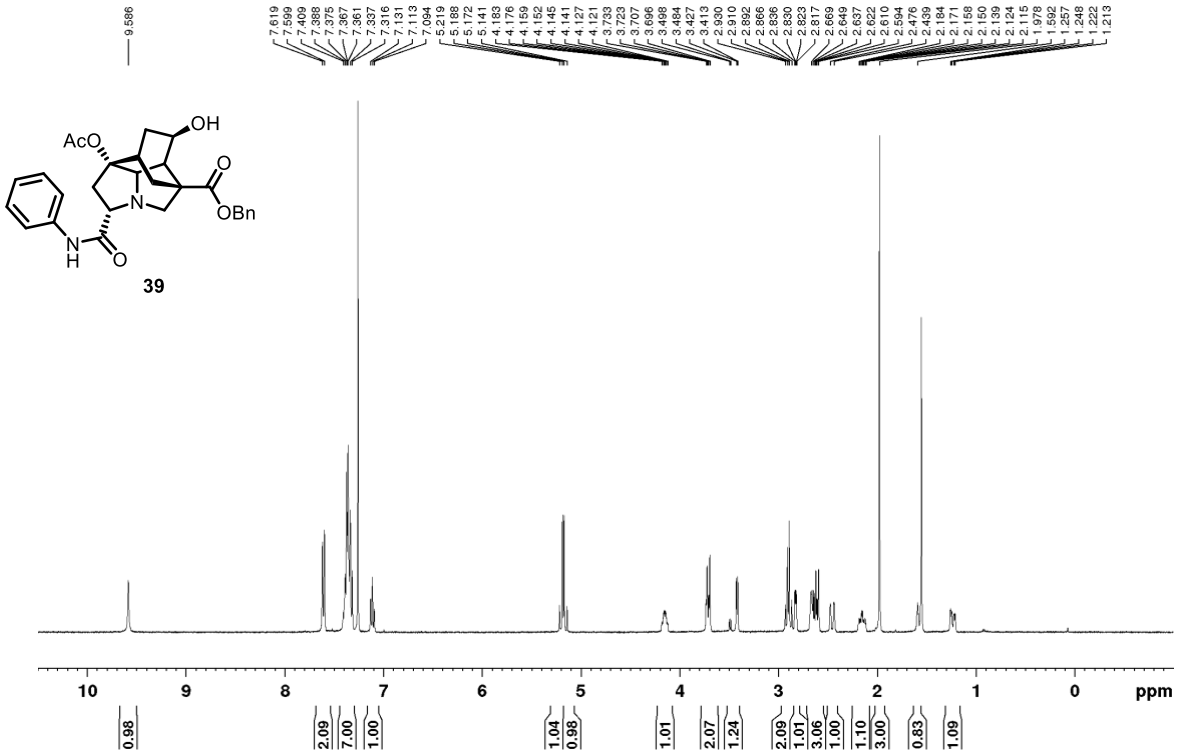


^{13}C NMR (100 MHz, $CDCl_3$)

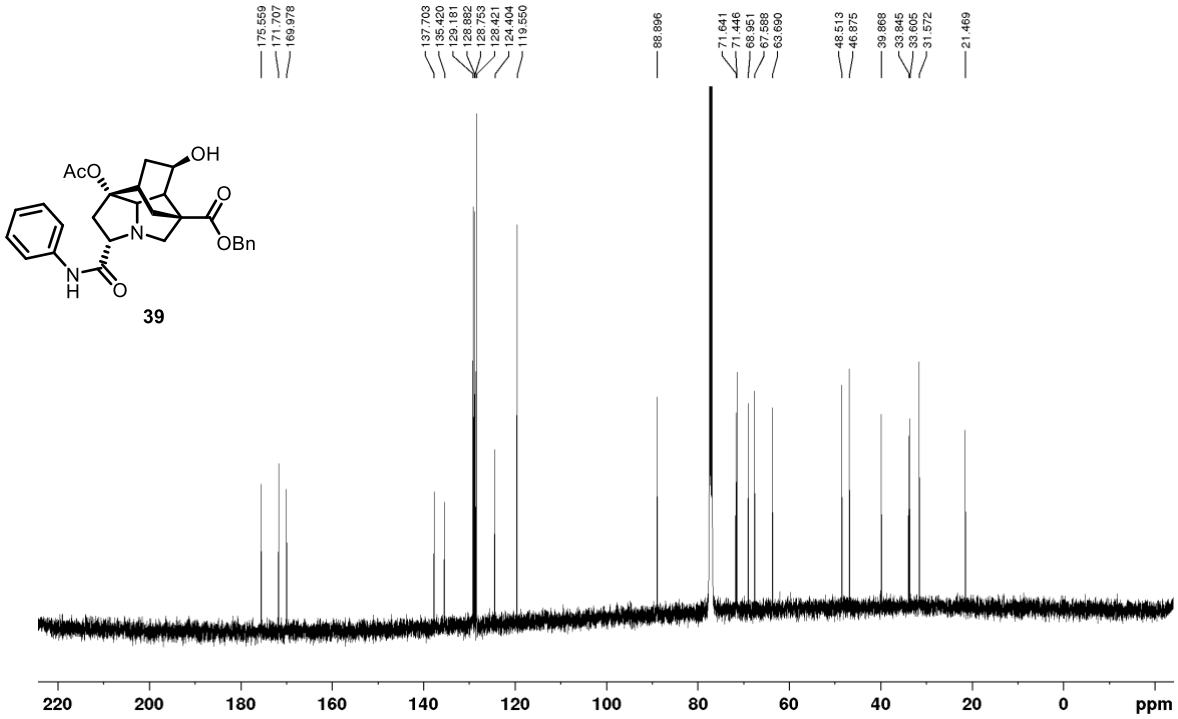


Amide **39**

^{1}H NMR (400 MHz, $CDCl_3$)

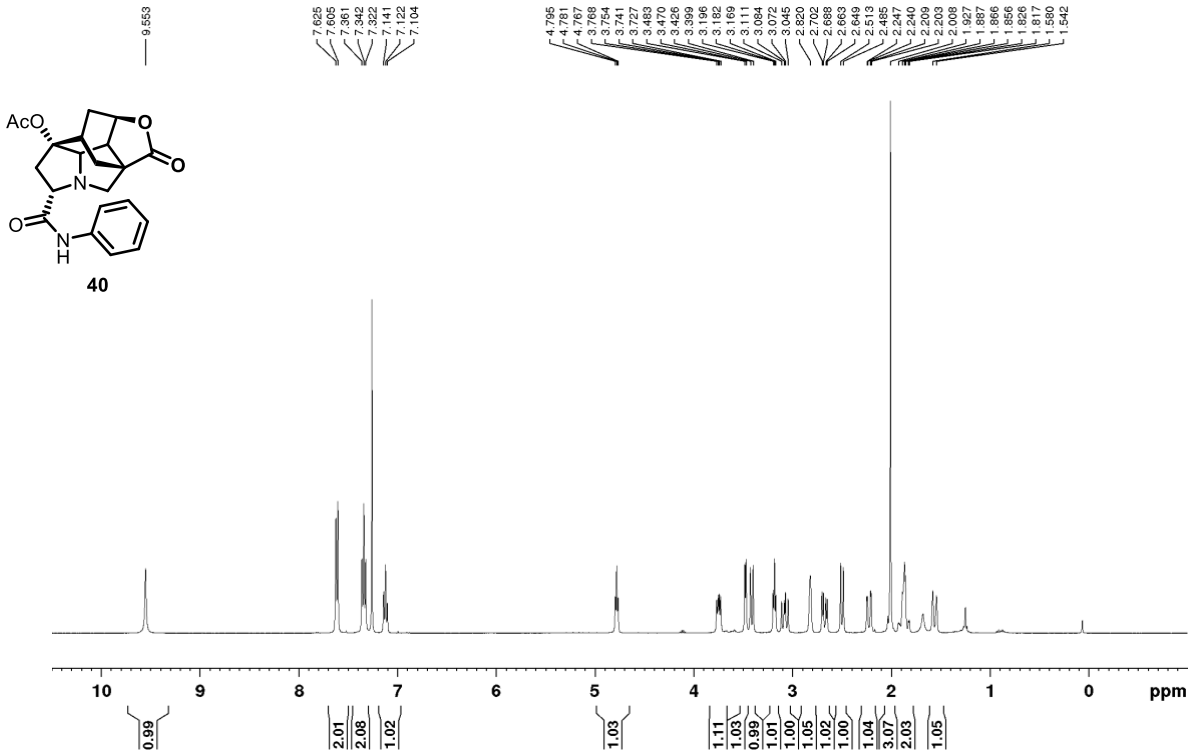


^{13}C NMR (125 MHz, $CDCl_3$)



Lactone **40**

^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)