Supporting Information

Synthetic studies on (–)-lemonomycin: An efficient asymmetric synthesis of lemonomycinone amide

Yan-Chao Wu, Guillaume Bernadat, Géraldine Masson,
Cédric Couturier, Thierry Schlama, Zhu Jieping*

Institut de Chimie des Substances Naturelles, CNRS, 91198 Gif-sur-Yvette, France
zhu@icsn.cnrs-gif.fr

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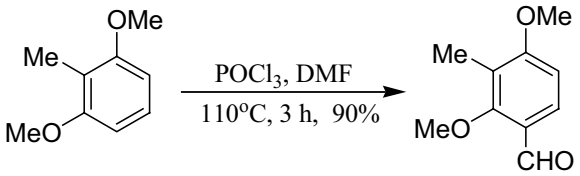
2. General Information

All reactions were performed in flame-dried flasks under a positive pressure of argon unless otherwise stated. Common reagents and materials were purchased from commercial sources and purified by recrystallization or distillation. Where necessary, organic solvents were routinely dried and/or distilled prior to use and stored over molecular sieves under argon. Other solvents were dried by distillation from the following: tetrahydrofuran (sodium); diethyl ether (sodium); toluene (sodium); 1,4-dioxane (sodium); dichloromethane (calcium hydride); acetonitrile (calcium hydride); triethylamine (calcium hydride); *N*,*N*-diisopropylethylamine (calcium hydride); methanol (magnesium/iodine); *N*,*N*-dimethyl formamide (calcium hydride). Organic extracts were, in general, dried over anhydrous sodium sulfate (Na_2SO_4). TLC plates were visualized by exposure to ultraviolet light (UV) and/or submersion in ethanolic phosphomolybdic acid (PMA), aqueous ceric ammonium molybdate solution (CAM), or solutions of ninhydrin in *n*-butanol, followed by brief heating on a hot plate (~200 °C, 10–15 s). Chemical shifts for protons are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvents ($CHCl_3$: δ 7.26). Chemical shifts for carbon resonances are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.0). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, and coupling constant in Hz. Coupling constants (*J*) are reported in Hertz (Hz).

3. Experimental Procedures

3a. Synthesis of Tetrahydroisoquinoline **8** and the Intermediates

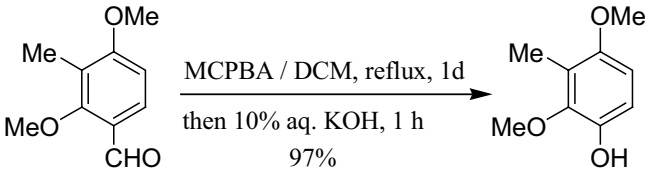
3aa. 2,4-Dimethoxy-3-methylbenzaldehyde (**32**)



31 **32**

To a solution of dry *N*,*N*-dimethylformamide (DMF, 5 mL) at 0°C, phosphoryl chloride ($POCl_3$, 2.8 mL, 30.0 mmol) were added dropwise. The obtained Vilsmeier complex was stirred at room temperature for 30 min, and was then added to a solution of 1,3-dimethoxy-2-methylbenzene (**31**, 3.9 g, 25.0 mmol) in DMF (5 mL) at 100°C. The mixture was stirred at 100°C for 4 h, and was then poured onto ice-water. The two layers were separated, and the aqueous layer was extracted with ethyl acetate (30 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 0% $\rightarrow$ 2% ethyl acetate in heptanes) to afford 2,4-dimethoxy-3-methylbenzaldehyde (**32**, 4.1 g) in 90% yield. Light yellow solids; mp = 53–54°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.22 (s, 1H), 7.73 (d, 1H, J = 8.7 Hz), 6.73 (d, 1H, J = 8.7 Hz), 3.89 (s, 3H), 3.85 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.1, 164.0, 162.5, 127.9, 122.8, 120.1, 106.5, 63.1, 55.8, 8.5 ppm; FTIR (film): 2940, 2840, 1673, 1587, 1485, 1455, 1415, 1386, 1373, 1310, 1273, 1252, 1234, 1214, 1163, 1100, 1000, 958, 861, 805, 779, 701 cm^{-1}. HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{10}H_{13}O_3$ $[M+H]^+$: 181.0865. Found: 181.0865.

3ab. 2,4-Dimethoxy-3-methylphenol (**33**)

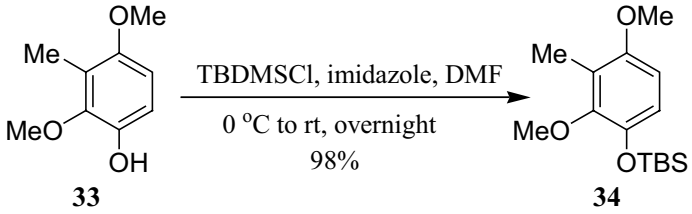


32 **33**

A solution of 2,4-dimethoxy-3-methylbenzaldehyde (**32**, 9.0 g, 50.0 mmol) and *m*-chloroperbenzoic acid (MCPBA, 70%, 18.5 g, 75.0 mmol) in 50 mL of dichloromethane (DCM) was stirred at reflux for 1 d, and concentrated to remove most of DCM. The resulted mixture was dissolved with ethyl acetate, and neutralized with aqueous sodium bicarbonate ($NaHCO_3$). The obtained mixture was washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was dissolved in methanol (MeOH, 5 mL), and was then added with 10% potassium hydroxide (KOH, 34 mL, 60.0 mmol). The mixture was stirred at room

temperature for 1 h, and neutralized with hydrochloric acid (HCl, 1 N). The obtained mixture was extracted ethyl acetate (50 mL x 3), washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 1% → 25% ethyl acetate in heptanes) to afford 2,4-dimethoxy-3-methylphenol (**33**, 8.1 g) in 97% yield. White solid; mp = 33–34°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.76 (d, 1H, *J* = 9.0 Hz), 6.54 (d, 1H, *J* = 9.0 Hz), 5.36 (s, 1H), 3.78 (s, 6H), 2.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.9, 145.9, 142.9, 119.9, 111.6, 106.7, 60.8, 56.0, 55.9, 9.3 ppm; FTIR (film): 3405, 2995, 2938, 2832, 1485, 1467, 1424, 1257, 1232, 1188, 1151, 1097, 1012, 976, 859, 796, 729, 674 cm^{-1}. HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_9H_{11}O_3$ $[M+H]^+$: 167.0708. Found: 167.0709.

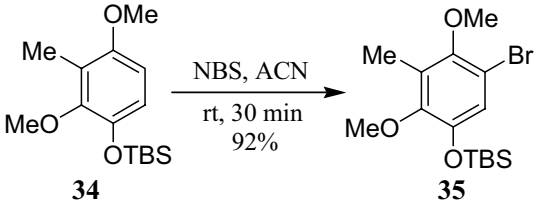
3ac. 1-*tert*-Butyldimethylsilyloxy-2,4-bimethoxy-3-methylbenzene (**34**)



33 **34**

To a solution of 2,4-dimethoxy-3-methylphenol (**33**, 1.3 g, 7.9 mmol) in 5 mL of dimethylformamide (DMF), imidazole (0.8 g, 11.8 mmol) and *tert*-butyldimethylsilyl chloride (TBDMSCl, 1.6 g, 10.2 mmol) were added sequentially at 0 °C. The mixture was stirred at 0 °C for 10 min, stirred at room temperature for overnight, and added with ethyl acetate (20 mL) and water (10 mL) at 0 °C. The two layers were separated, and the aqueous layer was extracted with a 1:1 mixture of ethyl acetate–hexanes (20 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 0% → 10% ethyl acetate in heptanes) to afford 1-*tert*-butyldimethylsilyloxy-2,4-bimethoxy-3-methylbenzene (**34**, 2.2 g) in 98%. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.75 (d, 1H, *J* = 8.7 Hz), 6.52 (d, 1H, *J* = 8.7 Hz), 3.84 (s, 3H), 3.81 (s, 3H), 2.27 (s, 3H), 1.15 (s, 9H), 0.29 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 150.0, 142.5, 120.6, 117.3, 105.2, 59.5, 55.3, 25.7, 18.1, 8.9, –4.8 ppm; FTIR (film): 2952, 2929, 2894, 2856, 1484, 1470, 1251, 1108, 1030, 996, 871, 838, 802, 780 cm^{-1}. HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{15}H_{26}NO_3NaSi$ $[M+Na]^+$: 305.1549. Found: 305.1548.

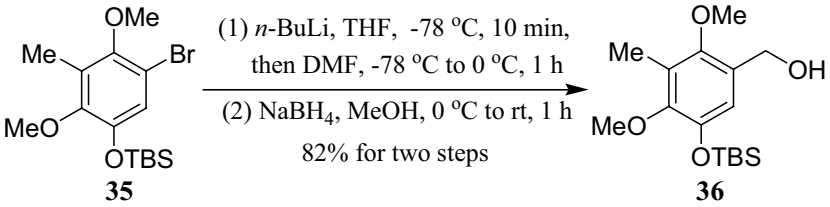
3ad. 5-Bromo-1-*tert*-butyldimethylsilyloxy-2,4-dimethoxy-3-methylbenzene (**35**)



34 **35**

To a solution of 1-*tert*-butyldimethylsilyloxy-2,4-bimethoxy-3-methylbenzene (**34**, 3.7 g, 13.1 mmol) in 26 mL of acetonitrile (ACN), *N*-bromosuccinimide (NBS, 2.6 g, 14.4 mmol) was added at room temperature. The mixture was stirred at room temperature for 30 min and concentrated, after which the residue was diluted with water (20 mL) and dichloromethane (20 mL). The two layers were separated, and the aqueous layer was extracted with dichloromethane (30 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 1% $\rightarrow$ 10% ethyl acetate in heptanes) to afford 5-bromo-1-*tert*-butyldimethylsilyloxy-2,4-dimethoxy-3-methylbenzene (**35**, 4.3 g) in 96% yield. Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (s, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 2.23 (s, 3H), 1.00 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 149.5, 145.7, 127.0, 121.8, 110.6, 60.3, 59.8, 25.6, 18.1, 10.1, –4.7 ppm; FTIR (film): 2954, 2930, 2895, 2858, 1470, 1417, 1401, 1315, 1252, 1234, 1205, 1171, 1097, 1049, 1001, 860, 837, 800, 781, 683 cm^{-1}; Anal. calcd for $C_{15}H_{25}BrO_3Si$: C, 49.86; H, 6.97. Found: C, 49.89; H, 6.87.

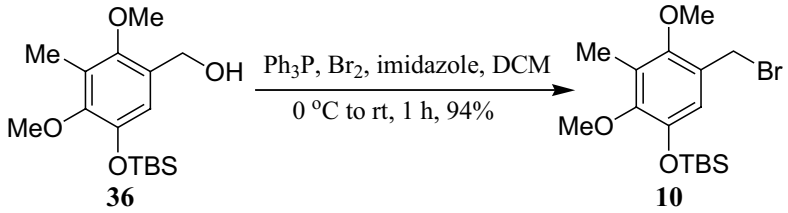
3ae. 5-*tert*-Butyldimethylsilyloxy-2,4-dimethoxy-3-methylphenyl alcohol (**36**)



To a solution of 5-bromo-1-*tert*-butyldimethylsilyloxy-2,4-dimethoxy-3-methylbenzene (**35**, 4.1 g, 11.2 mmol) in tetrahydrofuran (THF, 12 mmol), *n*-butyllithium (*n*-BuLi, 1.6 M, 7.7 mL, 12.3 mmol) was added at –78°C. The mixture was stirred at -78°C for 30 min, and was then added dropwise *N*,*N*-dimethylformamide (DMF, 1.0 mL, 12.4 mmol) at the same temperature. The mixture was stirred at –78°C for 10 min, and stirred at 0°C for 1 h. The mixture was diluted with ethyl acetate (50 mL) and water (50 mL), and the two layers were separated. The aqueous layer was extracted with ethyl acetate (50 mL x 3), and the combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was dissolved in absolute methanol (MeOH, 25 mL), and was then added with sodium borohydride ($NaBH_4$, 0.5 g, 12.3 mmol) at 0 °C. The mixture was stirred at 0 °C for 10 min, stirred at room temperature for 50 min, and concentrated. Water (10 mL) was added to the residue, and the mixture was extracted ethyl acetate (30 mL x 3). The extracts were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 1% $\rightarrow$ 20% ethyl acetate in heptanes) to afford 5-*tert*-butyldimethylsilyloxy-2,4-dimethoxy-3-methylphenyl alcohol (**36**, 2.9 g, 82% yield for two steps) as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.69 (s, 1H), 4.53 (d, 2H, J = 3.9 Hz), 3.70 (s,

3H), 3.65 (s, 3H), 3.03 (s, 1H), 2.15 (s, 3H), 0.98 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.5, 149.2, 144.9, 129.1, 125.1, 117.8, 60.8, 69.3, 59.5, 25.5, 18.0, 9.2, –4.8 ppm; FTIR (film): 3418, 2953, 2930, 2857, 1481, 1419, 1338, 1251, 1238, 1118, 1060, 1012, 863, 836, 827, 813, 780, 687 cm^{-1}; Anal. calcd for $C_{16}H_{28}O_4Si$: C, 61.50; H, 9.03. Found: C, 61.52; H, 8.82.

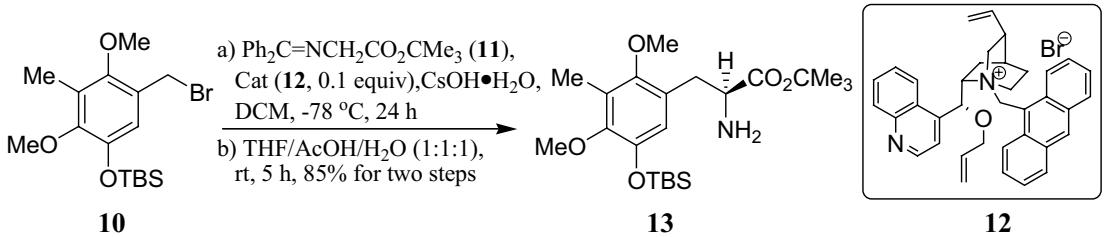
3af. 5-*tert*-Butyldimethylsilyloxy-2,4-dimethoxy-3-methylbenzyl bromide (**10**)



36 **10**

To a solution of triphenylphosphine (Ph_3P, 3.2 g, 12.3 mmol) and imidazole (0.9 g, 13.7 mmol) in 30 mL of dichloromethane (DCM), bromine (Br_2, 0.6 mL, 11.9 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 15 min, and added dropwise with a solution of 5-*tert*-butyldimethylsilyloxy-2,4-dimethoxy-3-methylphenyl alcohol (**36**, 2.9 g, 9.1 mmol) in 15 mL of dichloromethane at that temperature. The mixture was stirred at 0 °C for 1 h, and added with 10 mL of water. The two layers were separated, and the aqueous layer was extracted with dichloromethane (30 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 10% → 15% ethyl acetate in heptanes) to afford 5-*tert*-butyldimethylsilyloxy-2,4-dimethoxy-3-methylbenzyl bromide (**10**, 3.2 g) in 94% yield. Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.71 (s, 1H), 4.51 (s, 2H), 3.81 (s, 3H), 3.75 (s, 3H), 2.20 (s, 3H), 1.01 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3, 150.8, 145.2, 126.1, 125.9, 119.9, 61.0, 59.9, 28.8, 25.7, 18.2, 9.1, –4.6 ppm; FTIR (film): 2954, 2929, 2857, 1481, 1420, 1343, 1247, 1211, 1127, 1061, 1003, 860, 838, 825, 782 cm^{-1}; Anal. calcd for $C_{16}H_{27}BrO_3Si$: C, 51.19; H, 7.25. Found: C, 51.39; H, 7.55.

3ag. (*S*)-Amino ester **13**

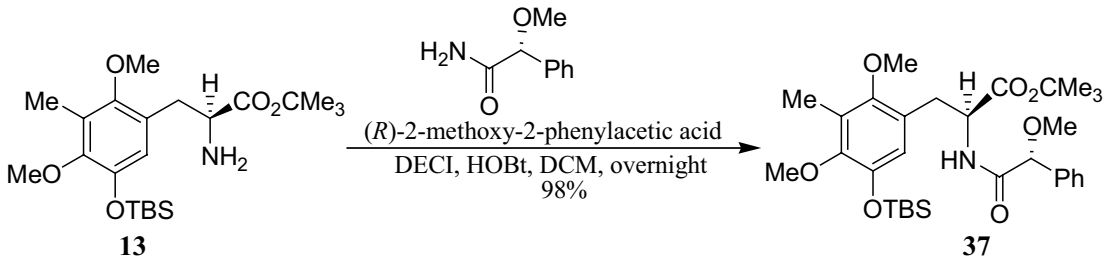


10 **13** **12**

To a solution of *tert*-butylglycinate benzophenone (**11**, 4.8 g, 16.4 mmol), O(9)-ally-N-9-anthracenylcynchonidium bromide (**12**, 0.9 g, 1.5 mmol) and cesium hydroxide monohydrate ($CsOH \cdot H_2O$, 26.4 g, 149.3 mmol) in 25 mL of dichloromethane (DCM), a solution of

5-*tert*-butyldimethylsilyloxy-2,4-dimethoxy-3-methylbenzyl bromide (**10**, 5.6 g, 14.9 mmol) in 25 mL of dichloromethane was added dropwise at –78 °C. The mixture was stirred at –78 °C for 24 h, and added with diethyl ether (100 mL) and water (50 mL). The two layers were separated, and the aqueous layer was extracted with diethyl ether (200 mL x 3), after which the aqueous layer can be further extracted with dichloromethane (30 mL x 3) to provide catalyst **12** for reuse. The combined diethyl ether layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was diluted in a mixture solvent of terahydrofuran (THF, 30 mL), acetic acid (AcOH, 30 mL) and water (H_2O, 30 mL). The mixture was stirred at room temperature for 6 h, diluted with 50 mL of water, neutralized with sodium carbonate (Na_2CO_3) at 0 °C until pH = 8, and extracted with ethyl acetate (100 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 20% → 50% ethyl acetate in heptanes) to afford (*S*)-amino ester **13** (5.4 g, 85% yield for two steps) as yellow oil. $[\alpha]_D^{26}$ +16.5° (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.52 (s, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 3.69 (dd, 1H, *J* = 8.4, 5.7 Hz), 2.97 (dd, 1H, *J* = 13.5, 5.7 Hz), 2.65 (dd, 1H, *J* = 13.5, 8.4 Hz), 2.18 (s, 3H), 1.52 (s, br, 2H), 1.41 (s, 9H), 0.99 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 151.6, 148.8, 144.7, 125.9, 125.3, 119.9, 80.8, 60.5, 59.8, 55.7, 35.9, 27.9, 25.7, 18.2, 9.7, –4.6 ppm; FTIR (film): 3381, 2954, 2930, 2857, 1728, 1481, 1453, 1420, 1391, 1366, 1346, 1250, 1237, 1215, 1153, 1119, 1061, 1014, 870, 838, 782 cm^{-1}; HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{22}H_{39}NO_5NaSi$ $[M+Na]^+$: 448.2495. Found: 448.2502.

3ah. Amino ester **37**

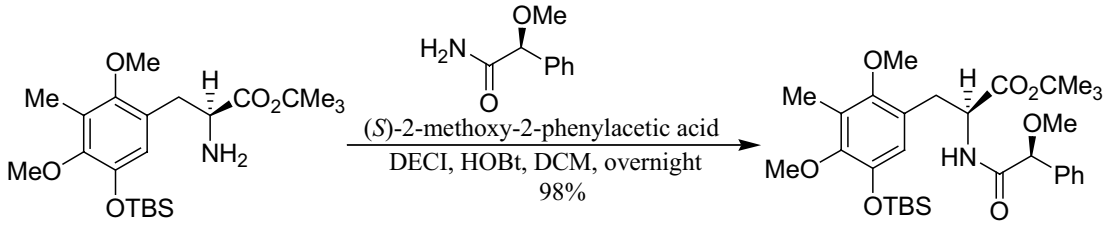


13 **37**

A solution of (*S*)-amino ester **13** (20.0 mg, 47.0 μmol), (*R*)-2-methoxy-2-phenylacetic acid (9.1 mg, 54.0 μmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (DECI, 11.4 mg, 58.7 μmol) and 1-hydroxybenzotriazole (HOBt, 7.4 mg, 54.0 μmol) in 1.2 mL of dichloromethane (DCM) was stirred at room temperature for overnight, and concentrated. The residue was purified by column chromatography (gradient elution 1% → 20% ethyl acetate in heptanes) to afford amino ester **37** (26.4 mg) in 98% yield. Colorless oil; $[\alpha]_D^{26}$ –29.3° (*c* = 3.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, 1H, *J* = 7.5 Hz), 7.44–7.26 (m, 5H), 6.55 (s, 1H), 4.63–4.56 (m, 1H), 4.55 (s, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.30 (s, 3H), 3.03 (d, 2H, *J* = 7.2 Hz), 2.22 (s, 3H), 1.33 (s, 9H), 1.02 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 170.3, 151.5, 149.1, 144.9, 137.2, 128.4, 128.3, 127.2, 125.2, 124.8, 119.9, 83.9, 81.7, 60.6, 59.8, 57.3, 53.7, 32.4, 27.8, 25.7, 18.2, 9.8, –4.6 ppm;

FTIR (film): 2930, 2857, 1730, 1682, 1511, 1482, 1454, 1421, 1366, 1349, 1239, 1155, 1116, 1100, 1063, 1012, 870, 839, 783, 697 cm^{-1}; HRMS (TOF MS ES^+) *m*/*z*: Calcd for $C_{31}H_{47}NO_7NaSi$ $[M+Na]^+$: 596.3020. Found: 596.3033.

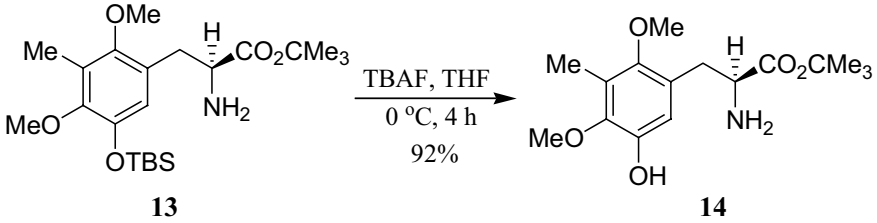
3ai. Amino ester **38**



A solution of (*S*)-amino ester **13** (20.0 mg, 47.0 μmol), (*S*)-2-methoxy-2-phenylacetic acid (9.1 mg, 54.0 μmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (DECI, 11.4 mg, 58.7 μmol) and 1-hydroxybenzotriazole (HOBt, 7.4 mg, 54.0 μmol) in 1.2 mL of dichloromethane (DCM) was stirred at room temperature for overnight, and concentrated. The residue was purified by column chromatography (gradient elution 1% → 20% ethyl acetate in heptanes) to afford amino ester **38** (26.4 mg) in 98% yield. Colorless oil; $[\alpha]_D^{27}$ +48.0° (*c* = 2.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, 1H, *J* = 7.5 Hz), 7.25–7.24 (m, 5H), 6.50 (s, 1H), 4.59–4.51 (m, 2H), 3.72 (s, 3H), 3.64 (s, 3H), 3.39 (s, 3H), 2.95 (d, 2H, *J* = 7.2 Hz), 2.20 (s, 3H), 1.39 (s, 9H), 0.99 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.5, 151.4, 149.1, 144.9, 137.1, 128.3, 128.2, 127.0, 125.3, 124.6, 119.8, 83.9, 81.8, 60.6, 59.8, 57.4, 53.5, 32.2, 27.9, 25.7, 18.1, 9.8, –4.6 ppm; FTIR (film): 2930, 2857, 1731, 1682, 1513, 1483, 1454, 1421, 1367, 1239, 1156, 1118, 1063, 1012, 872, 839, 784, 697 cm^{-1}; HRMS (TOF MS ES^+) *m*/*z*: Calcd for $C_{31}H_{47}NO_7NaSi$ $[M+Na]^+$: 596.3020. Found: 596.3040.

The absolute configuration of **13** was deduced on the basis of the Corey-Lygo's empiric model[1] and was confirmed by Trost's method.[2] Accordingly, both (*R*)- and (*S*)-*O*-methyl mandelic amides **37** and **38** were prepared by coupling of amine **13** with the respective mandelic acids. The calculated chemical shift differences (Δδ$ArCH_2$ (**38**–**37**) = –0.08 ppm; ΔδCO_2CMe_3 (**38**–**37**) = +0.06 ppm) are in accordance with the *S* configuration of the amino ester **13**.[2] In addition, analysis of ^1H NMR spectra of compounds **37** and **38** indicated that the *de* of **37** and **38**, and hence the *ee* of their precursor **13**, is higher than 95%.

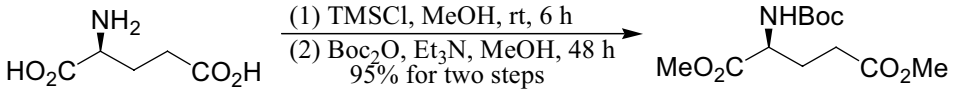
3aj. (*S*)-*tert*-Butyl 2-amino-3-(5-hydroxy-2,4-dimethoxy-3-methylphenyl)propanoate (**14**)



To a solution of (*S*)-amino ester **13** (1.3 g, 3.1 mmol) in terahydrofuran (THF, 30 mL), tetra-*n*-butylammonium fluoride (TBAF, 6.1 mL, 1.0 M solution in THF, 6.1 mmol) was added at 0°C. The mixture was stirred at 0 °C for 4 h, and added with 10 mL of water. The two layers were separated, and the aqueous layer was extracted with ethyl acetate (20 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 10% → 50% ethyl acetate in heptanes) to afford (*S*)-*tert*-butyl 2-amino-3-(5-hydroxy-2,4-dimethoxy-3-methylphenyl)propanoate (**14**, 8.7 g) in 91% yield. White solids; mp = 108–110°C; $[\alpha]_D^{27}$ +12.6° (*c* = 4.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.46 (s, 1H), 3.90 (br, 3H), 3.61 (s, 3H), 3.61–3.55 (m, 1H), 3.55 (s, 3H), 2.88 (dd, 1H, *J* = 13.5, 5.4 Hz), 2.62 (dd, 1H, *J* = 13.5, 8.4 Hz), 2.09 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 149.7, 145.6, 145.1, 125.5, 124.3, 115.1, 80.8, 60.1, 59.6, 55.0, 35.4, 27.5, 9.4 ppm; FTIR (film): 3358, 2976, 2934, 2830, 1726, 1591, 1482, 1455, 1418, 1367, 1233, 1154, 1113, 1049, 1011, 845 cm^{-1}; HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{16}H_{26}NO_5$ $[M+H]^+$: 312.1811. Found: 312.1794.

3b. Synthesis of *N*-Boc amino acid **9** and the Intermediates

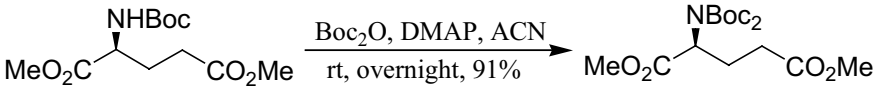
3ba. *tert*-Butyl (*S*)-1,3-di(methoxycarbonyl)propylcarbamate (**19**)



18 **19**

To a suspension of L-glutamic acid (**18**, 7.4 g, 50.0 mmol) in 100 mL of dry methanol (MeOH), chlorotrimethylsilane (TMSCl, 32 mL, 250.0 mmol) was added slowly at 0 °C. The mixture was stirred at room temperature for 6 h, and then was added sequentially with triethylamine (Et_3N, 49 mL, 350.0 mmol) and di-*tert*-butyldicarbonate (Boc_2O, 13.2 g, 60.0 mmol) at 0 °C. The obtained mixture was stirred at room temperature for 48 h, concentrated under reduced pressure, and added with 200 mL of ethyl acetate and 100 mL of water. The two layers were separated, and the aqueous layer was extracted with ethyl acetate (100 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 10% → 30% ethyl acetate in heptanes) to afford *tert*-butyl (*S*)-1,3-di(methoxycarbonyl)propylcarbamate (**19**, 13.1 g, 95% yield for two steps) as colorless oil. $[\alpha]_D^{28}$ +12.7° (*c* = 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.14 (s, br, 1H), 4.29 (s, br, 1H), 3.70 (s, 3H), 3.63 (s, 3H), 2.43–2.30 (m, 2H), 2.19–1.84 (s, 2H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 172.6, 155.3, 79.9, 52.8, 52.3, 51.6, 29.9, 28.2, 27.6 ppm; FTIR (film): 2977, 2953, 1736, 1711, 1697, 1513, 1437, 1365, 1248, 1208, 1160, 1049, 1027 cm^{-1}; HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{12}H_{21}NO_6Na$ $[M+Na]^+$: 298.1267. Found: 298.1273.

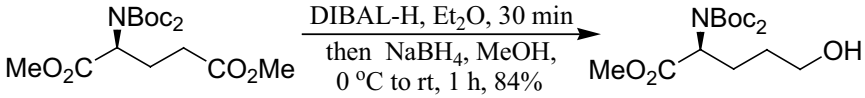
3bb. (*S*)-Dimethyl 2-(*N*,*N*-di-Boc-amino)pentanedioate (**40**)



19 **40**

To a solution of *tert*-butyl (*S*)-1,3-di(methoxycarbonyl)propylcarbamate (**19**, 11.0 g, 40.0 mmol) and *N,N*-dimethylpyridin-4-amine (DMAP, 1.0 g, 8.0 mmol) in dry acetonitrile (ACN, 133 mL), di-*tert*-butyldicarbonate (Boc_2O, 14.1 g, 64.0 mmol) was added at room temperature. The mixture was stirred at room temperature for overnight, and concentrated. The residue was purified by column chromatography (gradient elution 10% $\rightarrow$ 30% ethyl acetate in heptanes) to afford (*S*)-dimethyl 2-(*N*,*N*-di-Boc-amino)pentanedioate (**40**, 13.7 g) in 91% yield. Colorless oil; $[\alpha]_D^{27}$ –37.6 ° (*c* = 6.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.89–4.83 (s, 1H), 3.65 (s, 3H), 3.60 (s, 3H), 2.44–2.07 (s, 4H), 1.42 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 170.6, 151.7, 83.1, 57.2, 52.0, 51.4, 30.4, 27.8, 25.0 ppm; FTIR (film): 2980, 2953, 1738, 1698, 1436, 1366, 1302, 1271, 1250, 1223, 1166, 1137, 1112, 1012, 853, 782 cm^{-1}; HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{17}H_{29}NO_8Na$ $[M+Na]^+$: 398.1791. Found: 398.1789.

3bc. (*S*)-Methyl 2-(*N*,*N*-di-Boc-amino)-5-hydroxypentanoate (**20**)

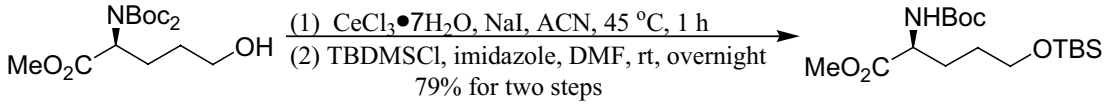


40 **20**

To a solution of (*S*)-dimethyl 2-(*N*,*N*-di-Boc-amino)pentanedioate (**40**, 19.9 g, 53.1 mmol) in 530 mL of diethyl ether (Et_2O), diisobutylaluminium hydride (DIBAL-H, 1 M in dichloromethane, 85 mL) was added dropwise at –78 °C. The mixture was stirred at that temperature for 30 min, and then was added with ethyl acetate (200 mL) and water (100 mL). The two layers were separated, and the aqueous layer was extracted with ethyl acetate (100 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was diluted in 133 mL of methanol (MeOH), and added with sodium borohydride ($NaBH_4$, 2.5 g, 63.7 mmol) at 0 °C. The mixture was stirred at room temperature for 1 h, concentrated, and added with ethyl acetate (100 mL) and water (50 mL). The two layers were separated, and the aqueous layer was extracted with ethyl acetate (100 mL x 3). The combined extracts was washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 10% $\rightarrow$ 60% ethyl acetate in heptanes) to afford (*S*)-methyl 2-(*N*,*N*-di-Boc-amino)-5-hydroxypentanoate (**20**, 15.5 g) in 84% yield. Colorless oil; $[\alpha]_D^{27}$ –37.9° (*c* = 4.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.76 (dd, 1H, *J* = 9.3, 5.4 Hz), 3.59 (s, 3H), 3.52 (t, 2H, *J* = 6.3 Hz), 2.54 (s, br, 1H), 2.17–1.74 (m, 2H), 1.59–1.47 (m, 2H), 1.38 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 151.9, 82.8, 61.7, 57.6, 51.9, 29.0, 27.7, 26.1 ppm; FTIR (film): 3473, 2979, 2935, 1738, 1697, 1366, 1248, 1227, 1167 1141, 1116, 852, 783 cm^{-1}; HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{16}H_{29}NO_7Na$ $[M+Na]^+$:

370.1842. Found: 370.1833.

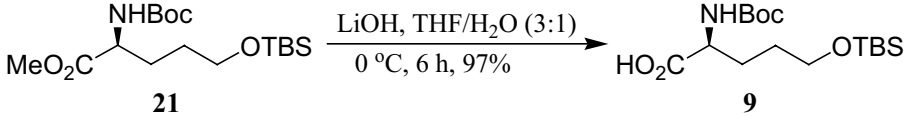
3bd. (*S*)-Methyl 5-*tert*-butyldimethylsilyloxy-2-(*N*-Boc-amino)pentanoate (**21**)



20 **21**

To a solution of (*S*)-methyl 2-(*N*,*N*-di-Boc-amino)-5-hydroxypentanoate (**20**, 9.1 g, 26.5 mmol) in 132 mL of dry acetonitrile (ACN), sodium iodide (NaI, 4.8 g, 31.8 mmol) and Cerium(III) chloride heptahydrate ($CeCl_3 \cdot 7H_2O$, 11.8 g, 31.8 mmol) were added at room temperature. The mixture was stirred at 45°C for 1 h, and added with ethyl acetate (50 mL) and water (30 mL) at 0 °C. The two layers were separated, and the aqueous layer was extracted with ethyl acetate (50 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was diluted with 20 mL of *N*,*N*-dimethylformamide (DMF), imidazole (1.4 g, 21.2 mmol) and *tert*-butyldimethylsilyl chloride (TBDMSCl, 2.8 g, 18.4 mmol) were added sequentially at 0 °C. The mixture was stirred at 0 °C for 10 min, stirred at room temperature for overnight, and added with ethyl acetate (20 mL) and water (10 mL) at 0 °C. The two layers were separated, and the aqueous layer was extracted with a 1:1 mixture of ethyl acetate–hexanes (20 mL x 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 1% $\rightarrow$ 10% ethyl acetate in heptanes) to afford (*S*)-methyl 5-*tert*-butyldimethylsilyloxy-2-(*N*-Boc-amino)pentanoate (**21**, 7.6 g, 79% yield for two steps) as colorless oil. $[\alpha]_D^{27}$ +5.4° (*c* = 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.22 (s, br, 1H), 4.22 (s, 1H), 3.65 (s, 3H), 3.55 (t, 2H, *J* = 5.5 Hz), 1.88–1.58 (m, 2H), 1.57–1.44 (m, 2H), 1.36 (s, 9H), 0.81 (s, 9H), -0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 155.3, 79.5, 62.1, 53.1, 28.9, 28.3, 28.2, 25.8, 18.1, –5.5 ppm; FTIR (film): 2954, 2930, 2858, 1746, 1716, 1504, 1366, 1253, 1171, 1099, 836 cm^{-1}; HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{17}H_{35}NO_5NaSi$ $[M+Na]^+$: 384.2182. Found: 384.2181.

3be. (*S*)-5-*tert*-Butyldimethylsilyloxy-2-(*N*-Boc-amino)pentanoic acid (**9**)



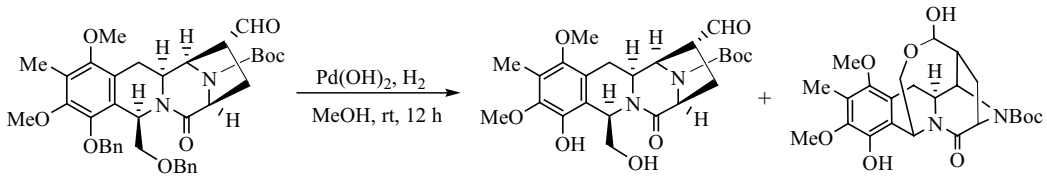
21 **9**

To a solution of (*S*)-methyl 5-*tert*-butyldimethylsilyloxy-2-(*N*-Boc-amino)pentanoate (**21**, 1.3 g, 3.6 mmol) in the mixture of tetrahydrofuran (THF, 60 mL) and water (H_2O, 20 mL), lithium hydroxide monohydrate ($LiOH \cdot H_2O$, 0.6 g, 14.4 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 6 h, and added with 20 mL of water. The obtained mixture was neutralized with 2 N hydrochloric acid until pH = 6, and then was extracted with ethyl acetate (100 mL x 3). The

combined organic layers were washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (gradient elution 1% → 20% methanol in dichloromethanes) to afford (*S*)-5-*tert*-butyldimethylsilyloxy-2-(*N*-Boc-amino)pentanoic acid (**9**, 1.2 g) in 97% yield. Colorless oil; $[\alpha]_D^{26}$ +8.7° (*c* = 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.41 (s, br, 1H), 6.49 & 5.39 (s, br, 1H), 4.23 & 4.05 (s, 1H), 3.64–3.58 (m, 2H), 1.92–1.62 (m, 2H), 1.55–1.47 (m, 2H), 1.37 (s, 9H), 0.82 (s, 9H), –0.01 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 155.6 (156.8), 79.7 (81.4), 62.4, 53.2 (54.4), 28.8, 28.2, 25.9, 25.8, 18.2, –5.5 ppm; FTIR (film): 3732, 2930, 1717, 1699, 1506, 1255, 1164, 1099, 836, 668 cm^{-1}; HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{16}H_{33}NO_5NaSi$ $[M+Na]^+$: 370.2026. Found: 370.2023.

3c. Studies on Synthesis of (–)-Lemonomycinone amide (**2**) and the Intermediates

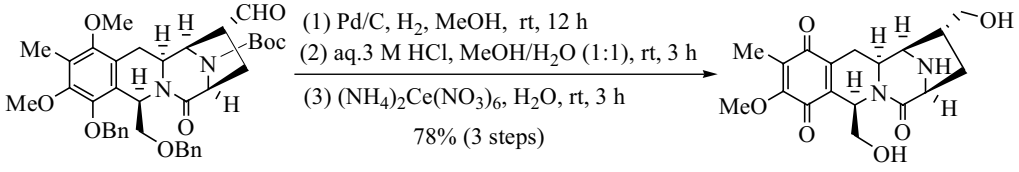
3ca. Hemi-acetal **28**



27 **3** (trace) **28** (85%)

To a solution of tetracyclic aldehyde **27** (24.6 mg, 37.5 μmol) in 2 mL of methanol (MeOH), Palladium hydroxide [$Pd(OH)_2$, moist, Pd content 20%, 8 mg] was added at room temperature. The mixture was stirred at room temperature under an atmosphere of hydrogen (H_2) for 12 h, filtered through a plug of Celite, washed with MeOH, and concentrated. The residue was purified by column chromatography (gradient elution 50% → 100% ethyl acetate in heptanes) to afford tetracyclic alcohol **3** (trace), together with hemi-acetal **28** (15.2 mg) in 85%. Foam; $[\alpha]_D^{25}$ +176.5° (*c* = 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.12 (s, 1H, t, 1H, *J* = 3.9 Hz), 5.99 (s, br, 1H), 4.99–4.61 (m, 2H), 3.92–3.78 (m, 3H), 3.77 (s, 3H), 3.69 (s, 3H), 2.21 (s, 3H), 2.20–2.07 (m, 3H), 1.97–1.82 (m, 2H), 1.82–1.70 (m, 1H), 1.44–1.43 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 167.2, 146.9, 145.2, 141.5, 124.0, 120.3, 113.1, 104.6, 81.1, 77.2, 65.2, 61.6, 61.0, 60.4, 50.3, 29.7, 28.3, 27.9, 21.0, 14.2, 9.5 ppm; FTIR (film): 3396, 2937, 1701, 1634, 1470, 1419, 1367, 1310, 1258, 1164, 1071, 1005 cm^{-1}; HRMS (TOF MS ES$^+$) *m*/*z*: Calcd for $C_{24}H_{32}N_2O_8Na$ $[M+Na]^+$ 499.2056. Found 499.2065.

3cb. Lemonomycinone alcohol **30**



27 **30**

To a solution of tetracyclic aldehyde **27** (39.4 mg, 60.0 μmol) in 5 mL of methanol (MeOH), Pd/C (10 mg) was added at room temperature. The mixture was stirred at room temperature under an atmosphere of hydrogen (H_2) for 12 h, filtered through a plug of Celite, washed with MeOH, and concentrated. The residue was dissolved in 1.8 mL of methanol (MeOH), and added with hydrochloric acid (HCl, 12 M, 0.6 mL) at 0 °C. The mixture was stirred at room temperature for 3 h, and concentrated. The residue was diluted with H_2O (1.0 mL), and added with ammonium cerium(IV) nitrate (131.6 mg, 240.0 μmol) at room temperature. The mixture was stirred at room temperature for 3 h, purified on reverse phase HPLC, and lyophilized to afford Lemonomycinone alcohol **30** (17.0 mg) in 78% overall yield. Orange form; UV = 268.3; $[\alpha]_D^{25}$ –78.1° (*c* = 1.7, MeOH); ^{1}H NMR (300 MHz, D_2O) δ 7.26–6.49 (m, 2H), 4.95 (s, br, 1H), 4.23 (dd, 1H, *J* = 7.5, 1.2 Hz), 4.21 (s, br, 1H), 4.04–3.99 (m, 1H), 3.80 (s, br, 1H), 3.76 (s, 3H), 3.59–3.41 (m, 4H), 2.89–2.83 (m, 1H), 2.83–2.70 (m, 1H), 2.48–2.35 (m, 2H), 2.03 (s, br, 1H), 2.02–1.95 (m, 1H), 1.83 (s, 3H) ppm; ^{13}C NMR (75 MHz, D_2O) δ 186.7, 181.2, 166.9, 162.6, 155.5, 142.4, 136.2, 130.9, 62.0, 61.2, 60.7, 59.6, 59.4, 54.8, 51.9, 36.6, 32.2, 23.1, 8.4 ppm; ; FTIR (film): 3347, 1678, 1440, 1203, 1140, 942, 845, 798, 721 cm^{-1}; HRMS (TOF MS ES^+) *m*/*z*: Calcd for $C_{18}H_{22}N_2O_6Na$ $[M+Na]^+$ 385.1376. Found 385.1385.

Reference

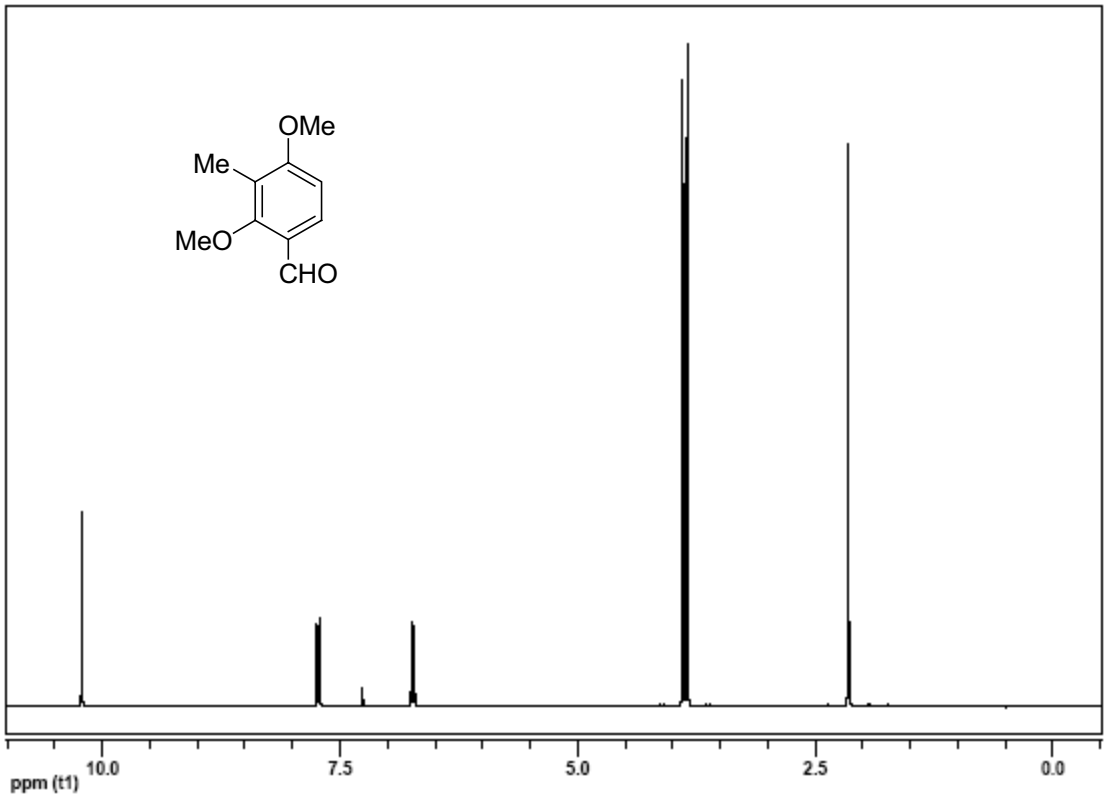
1. Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119,* 12414–12415.
2. (a) Ott, R.; Sauber, K. *Tetrahedron Lett.* **1972**, 3873–3878. (b) Trost, B. M.; Bunt, R. C.; Pulley, S. R. *J. Org. Chem.* **1994**, *59*, 4202–4205.

4. ^{1}H NMR and ^{13}C NMR Spectra

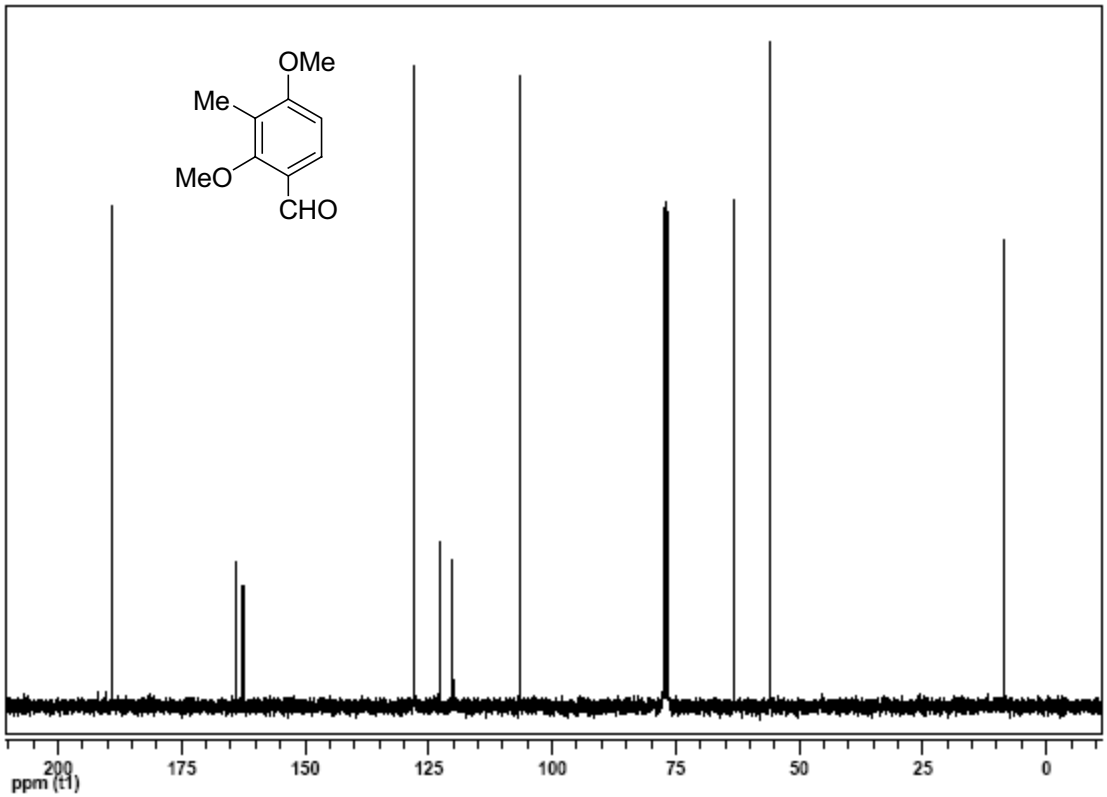
4a. Tetrahydroisoquinoline **8** and the Intermediates

4aa. 2,4-Dimethoxy-3-methylbenzaldehyde (**32**)

^{1}H NMR (300 MHz, $CDCl_3$)

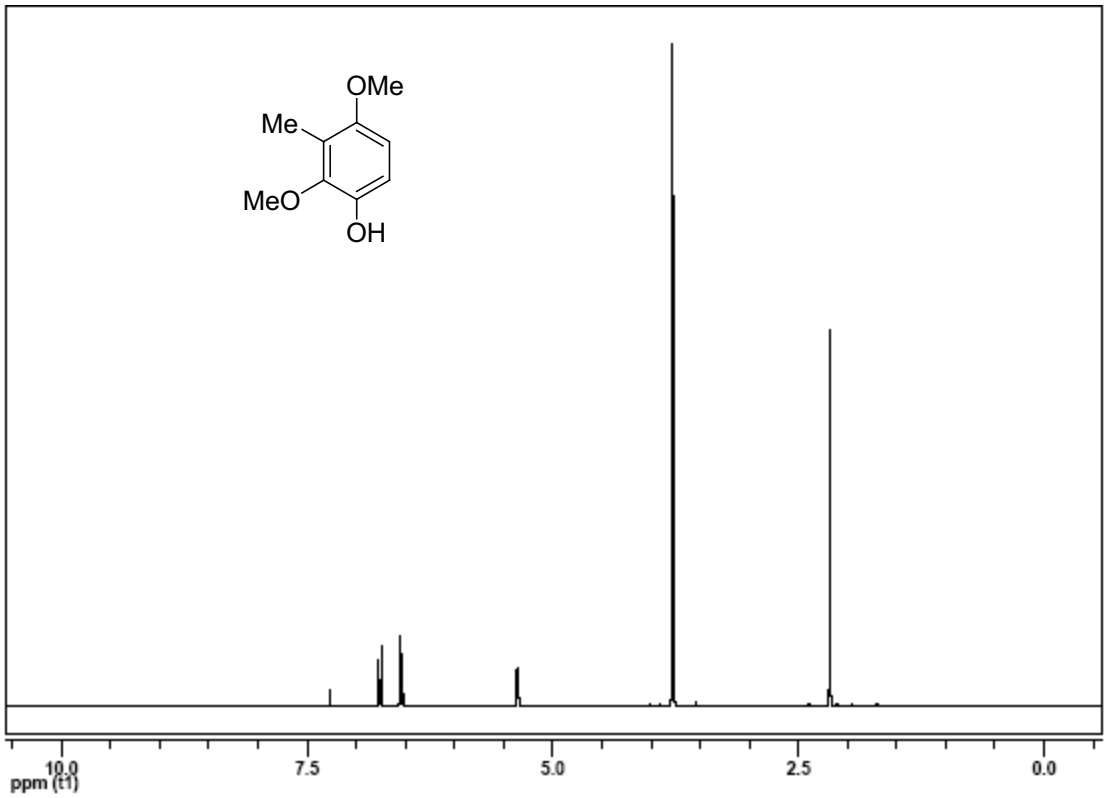


^{13}C NMR (75 MHz, $CDCl_3$)

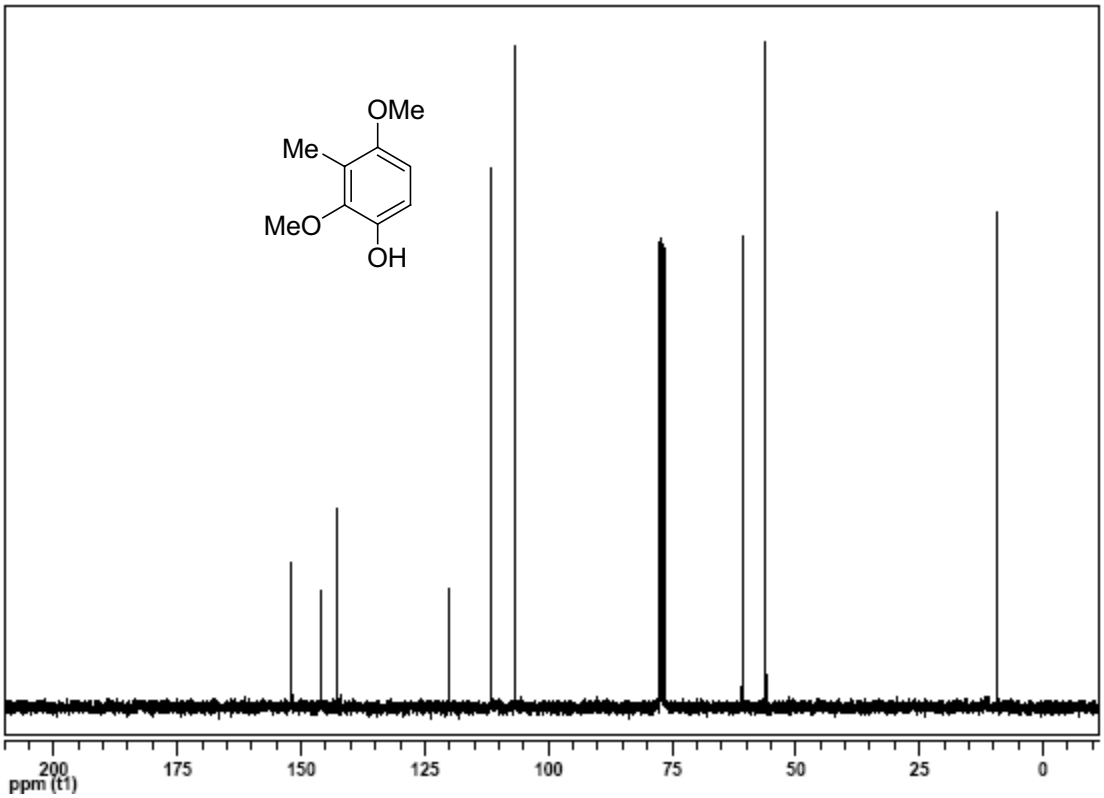


4ab. 2,4-Dimethoxy-3-methylphenol (**33**)

^{1}H NMR (300 MHz, $CDCl_3$)

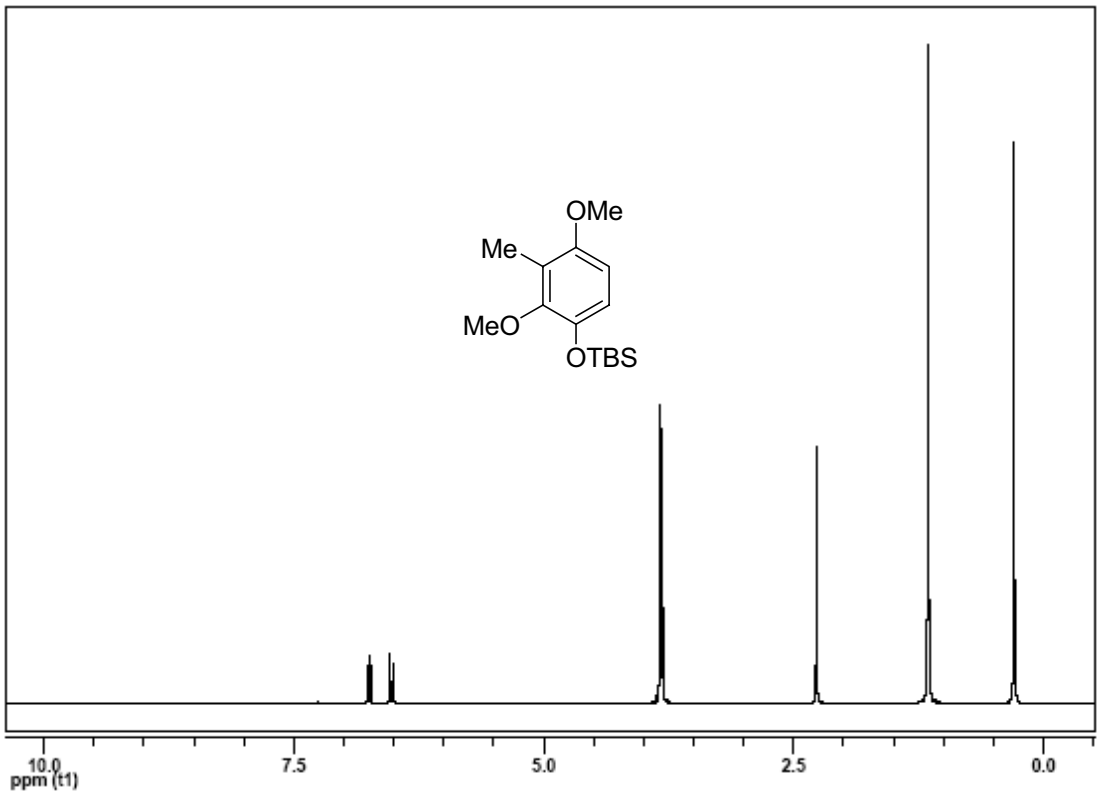


^{13}C NMR (75 MHz, $CDCl_3$)

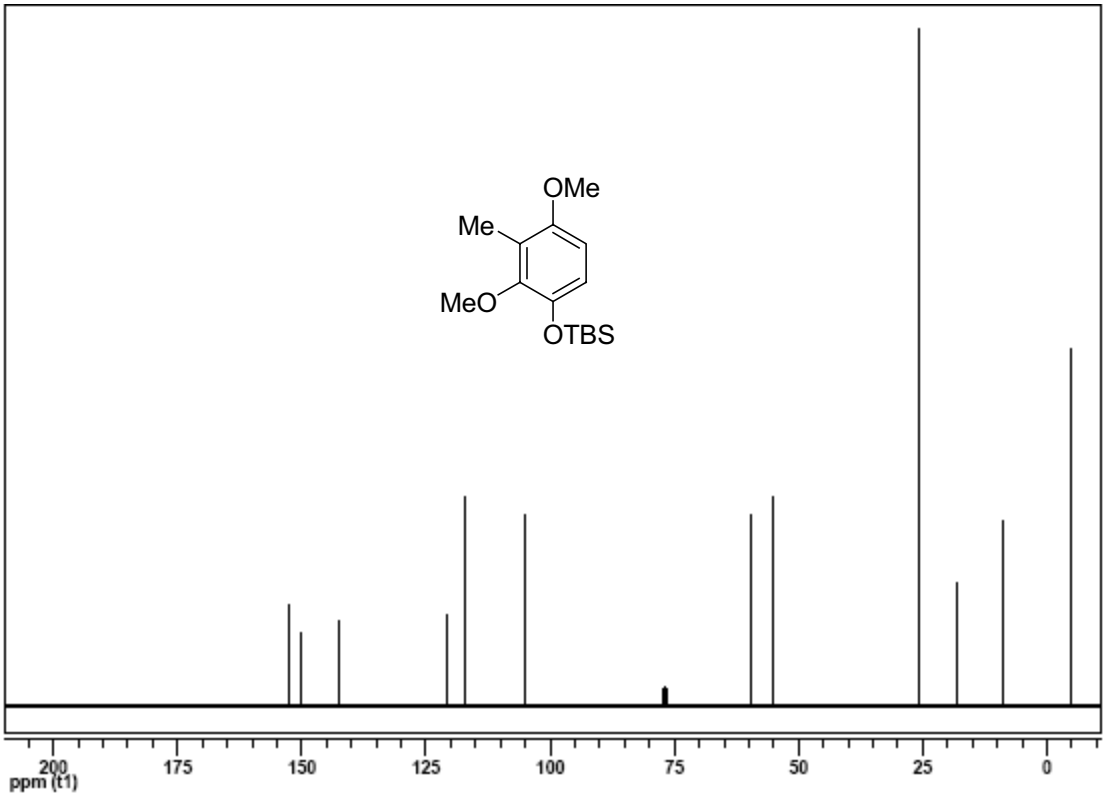


4ac. 1-*tert*-Butyldimethylsilyloxy-2,4-bimethoxy-3-methylbenzene (**34**)

^{1}H NMR (300 MHz, $CDCl_3$)

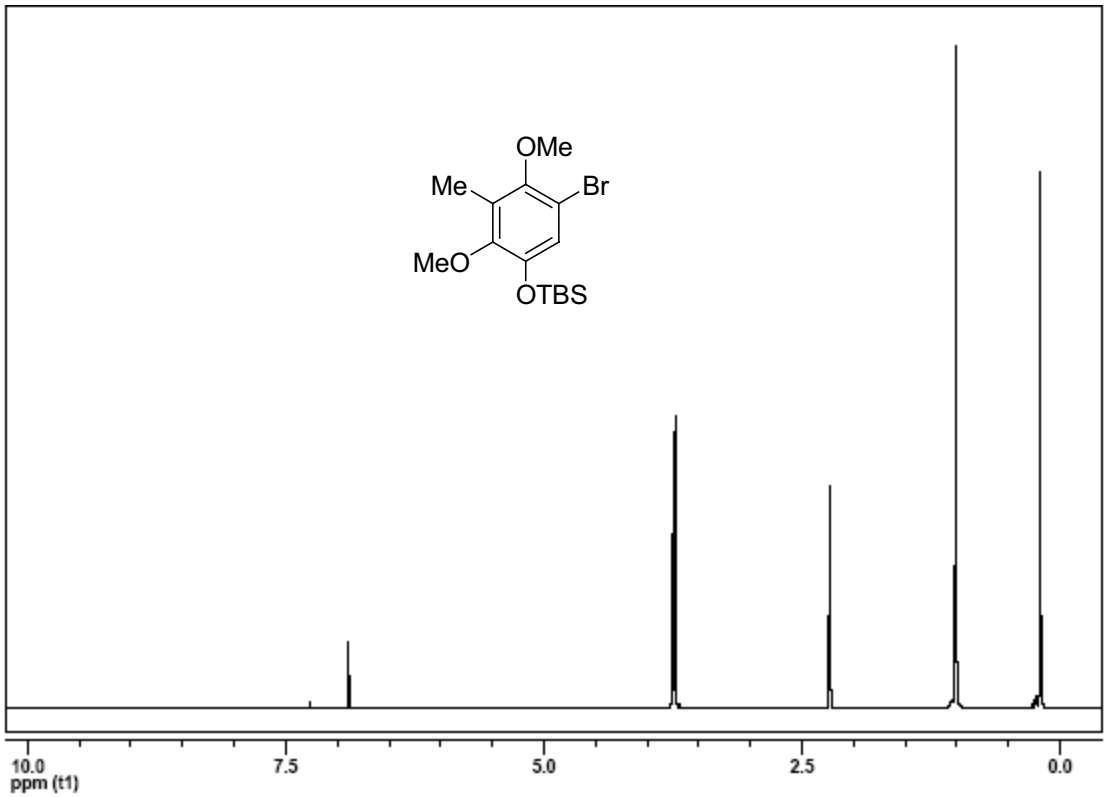


^{13}C NMR (75 MHz, $CDCl_3$)

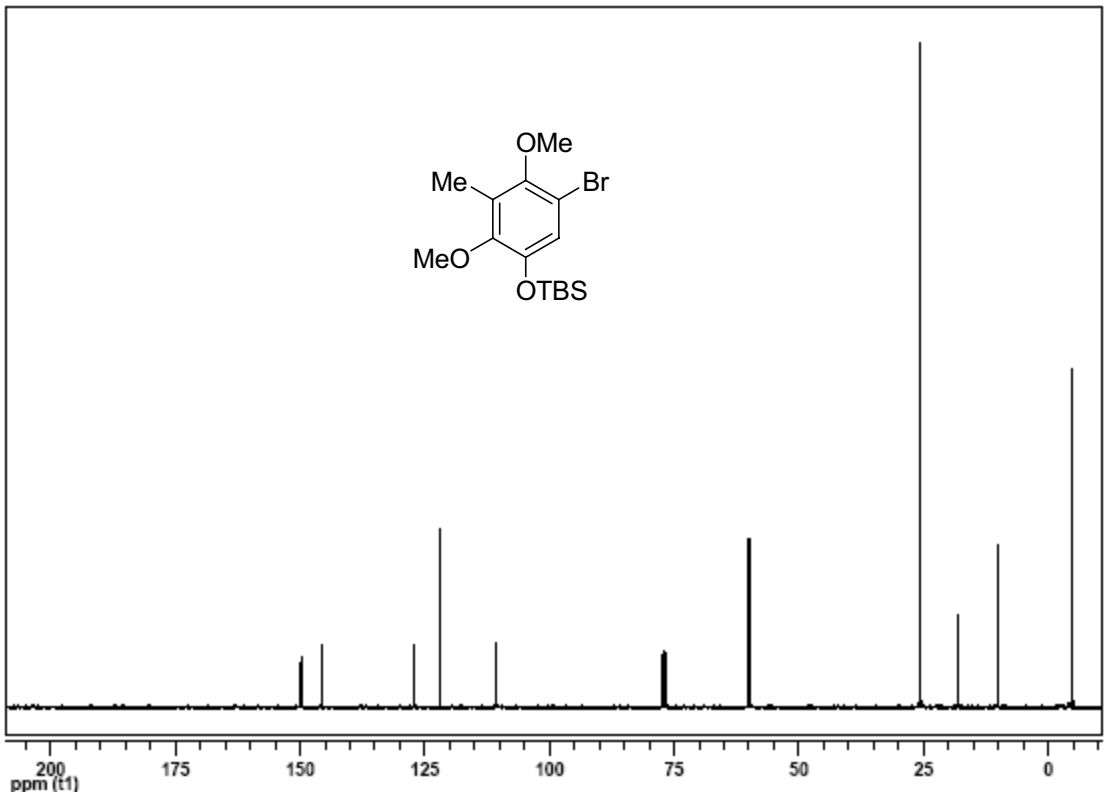


4ad. 5-Bromo-1-*tert*-butyldimethylsilyloxy-2,4-dimethoxy-3-methylbenzene (**35**)

^{1}H NMR (300 MHz, $CDCl_3$)

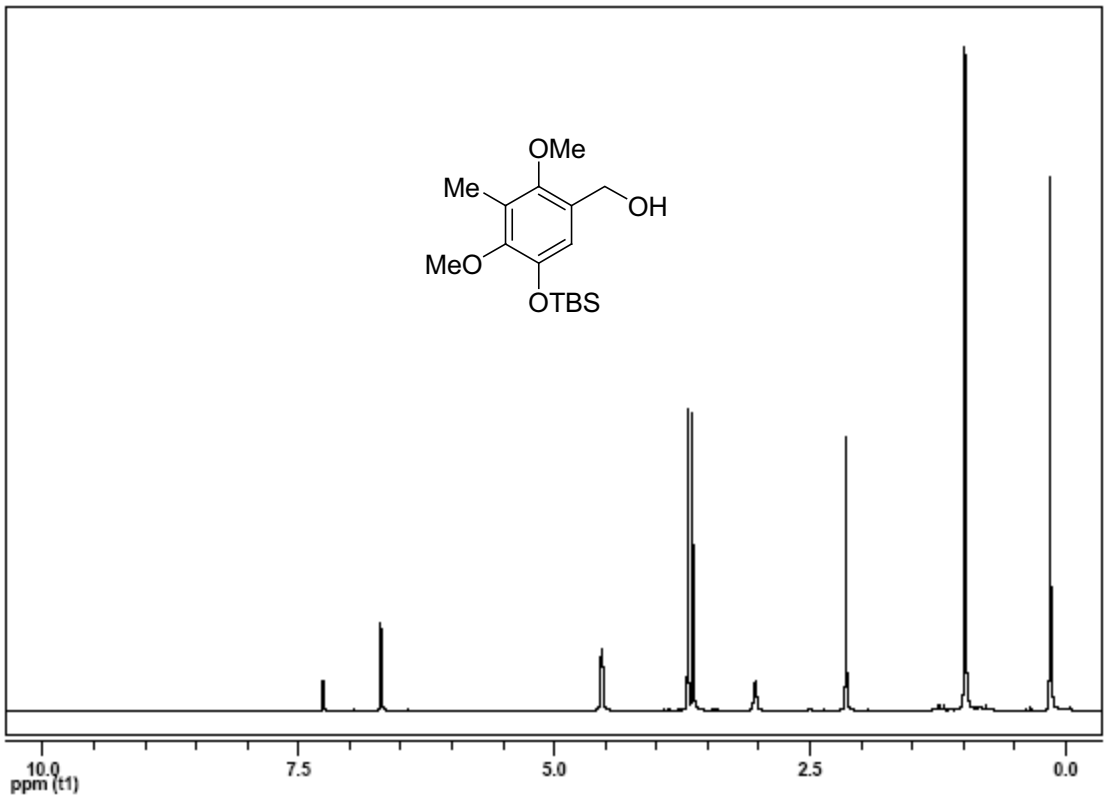


^{13}C NMR (75 MHz, $CDCl_3$)

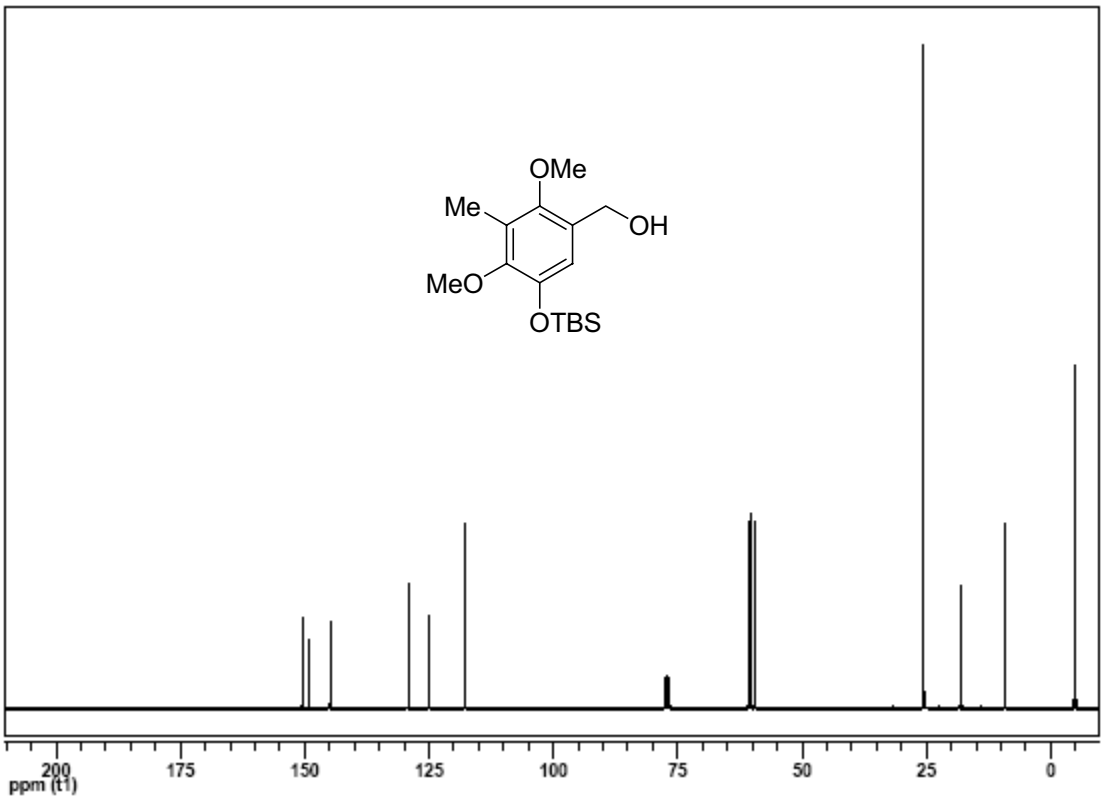


4ae. 5-*tert*-Butyldimethylsilyloxy-2,4-dimethoxy-3-methylbenzyl alcohol (**36**)

^{1}H NMR (300 MHz, $CDCl_3$)

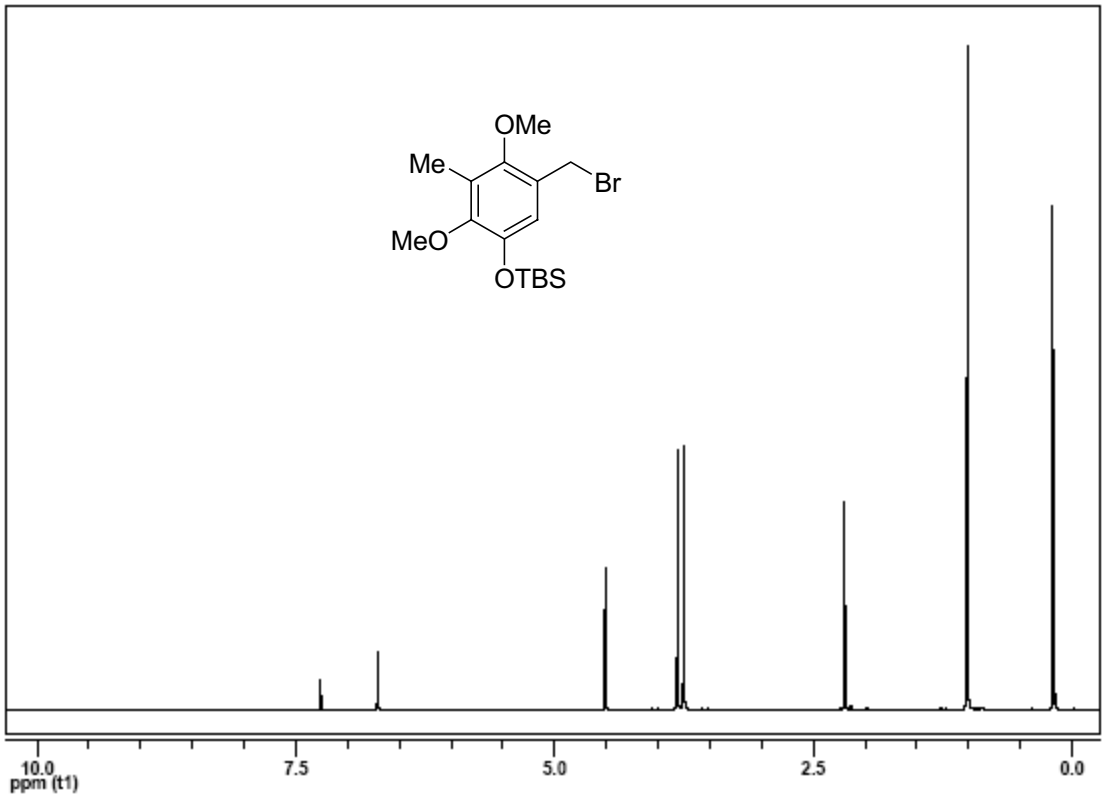


^{13}C NMR (75 MHz, $CDCl_3$)

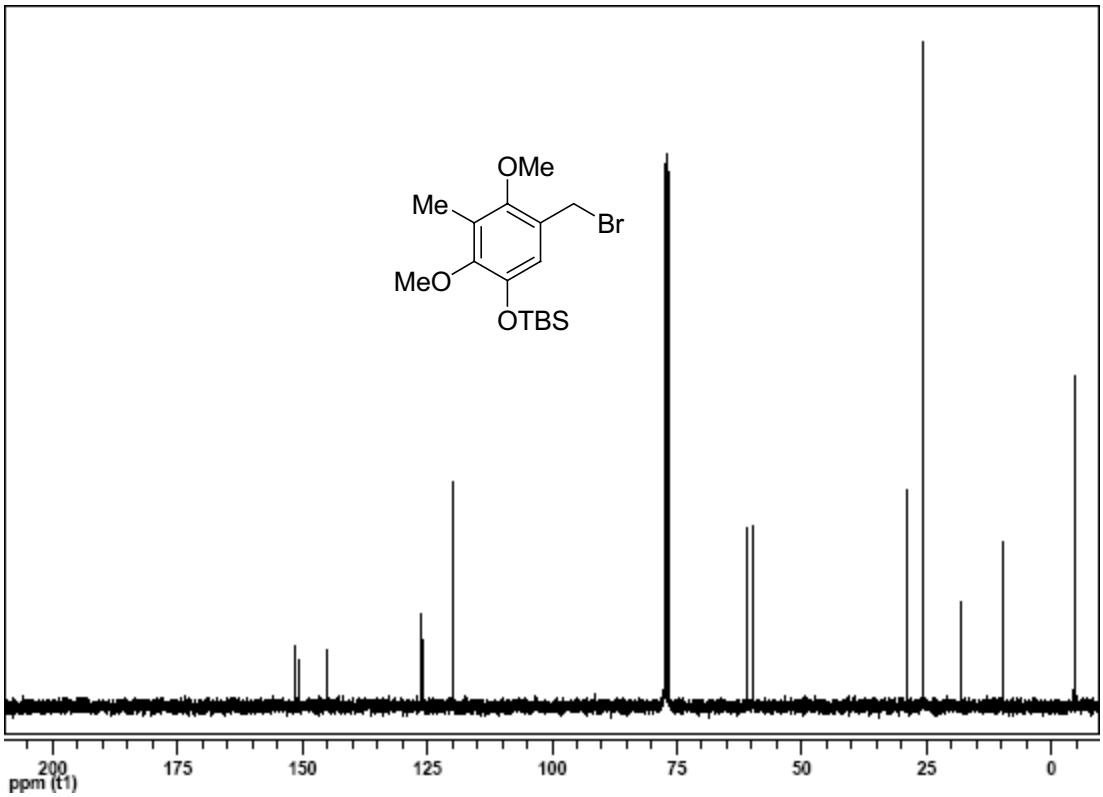


4af. 5-*tert*-Butyldimethylsilyloxy-2,4-dimethoxy-3-methylbenzyl bromide (**10**)

^{1}H NMR (300 MHz, $CDCl_3$)

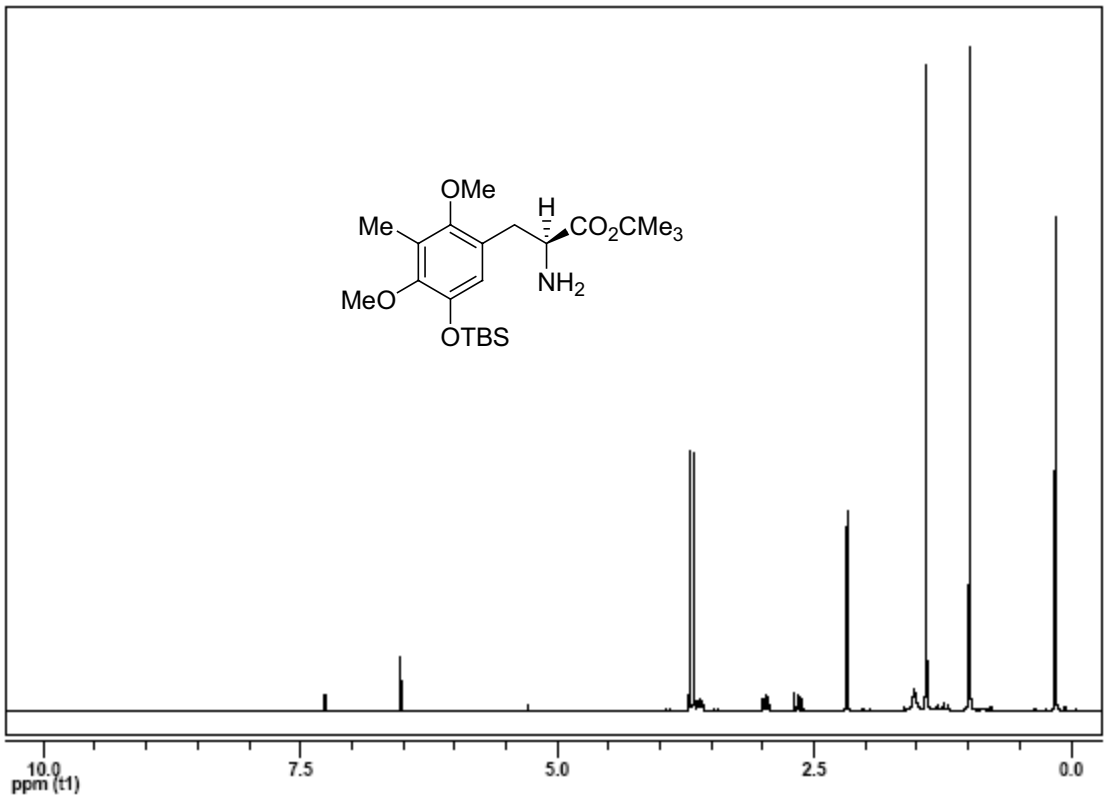


^{13}C NMR (75 MHz, $CDCl_3$)

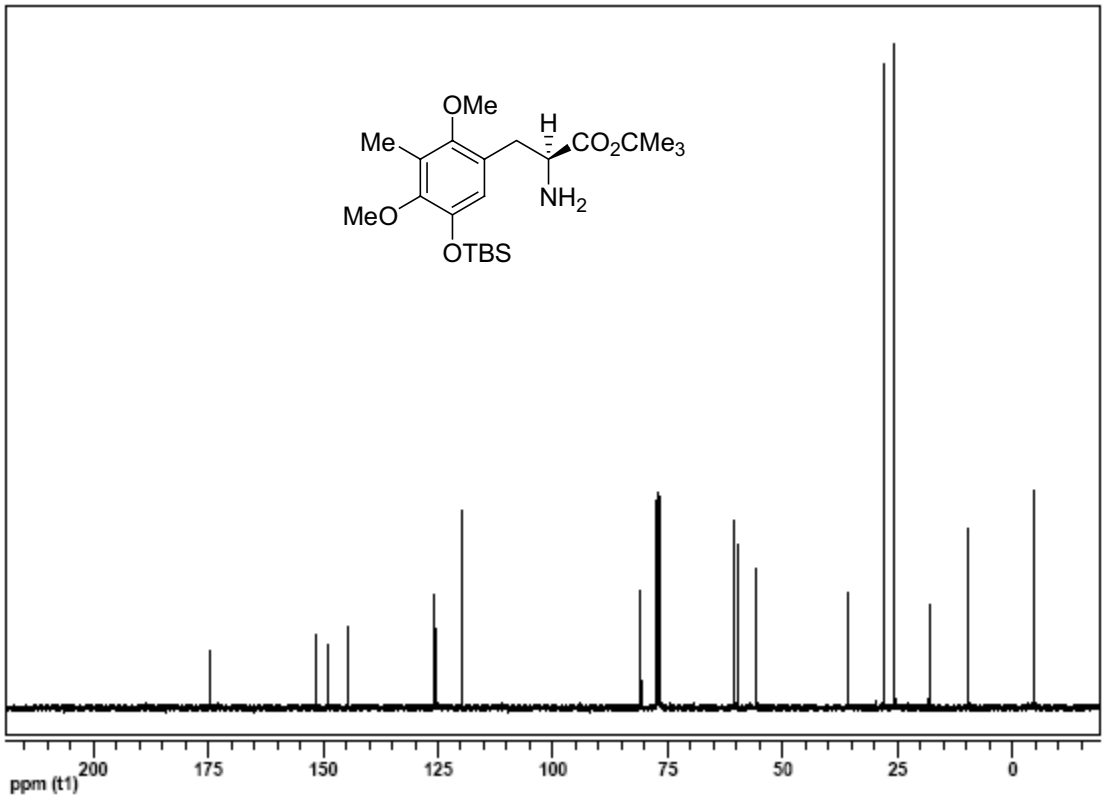


4ag. (*S*)-Amino ester **13**

^{1}H NMR (300 MHz, $CDCl_3$)

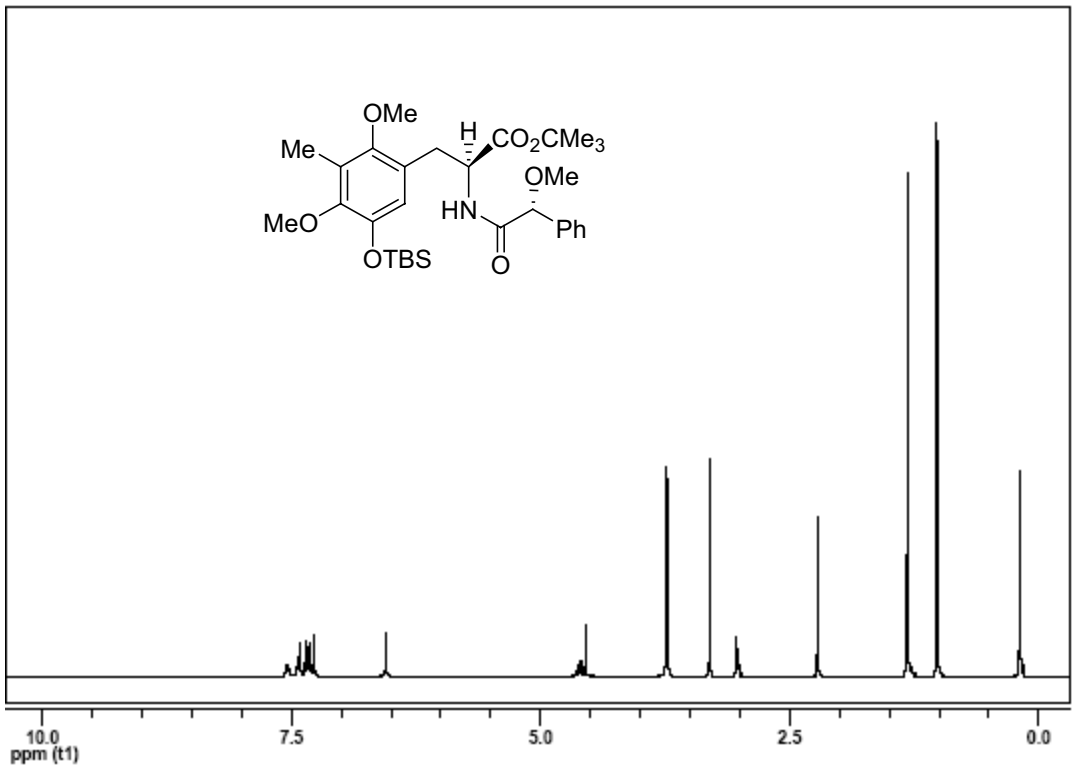


^{13}C NMR (75 MHz, $CDCl_3$)

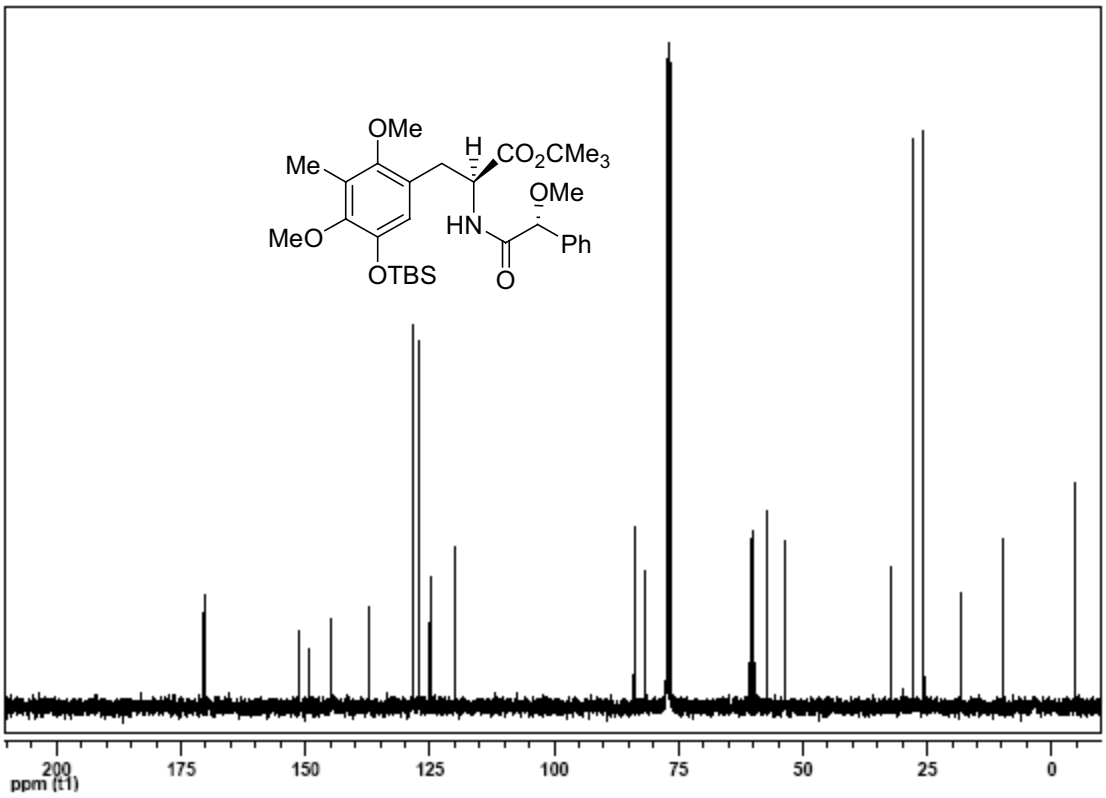


4ah. *R*-Amino ester **37**

^{1}H NMR (300 MHz, $CDCl_3$)

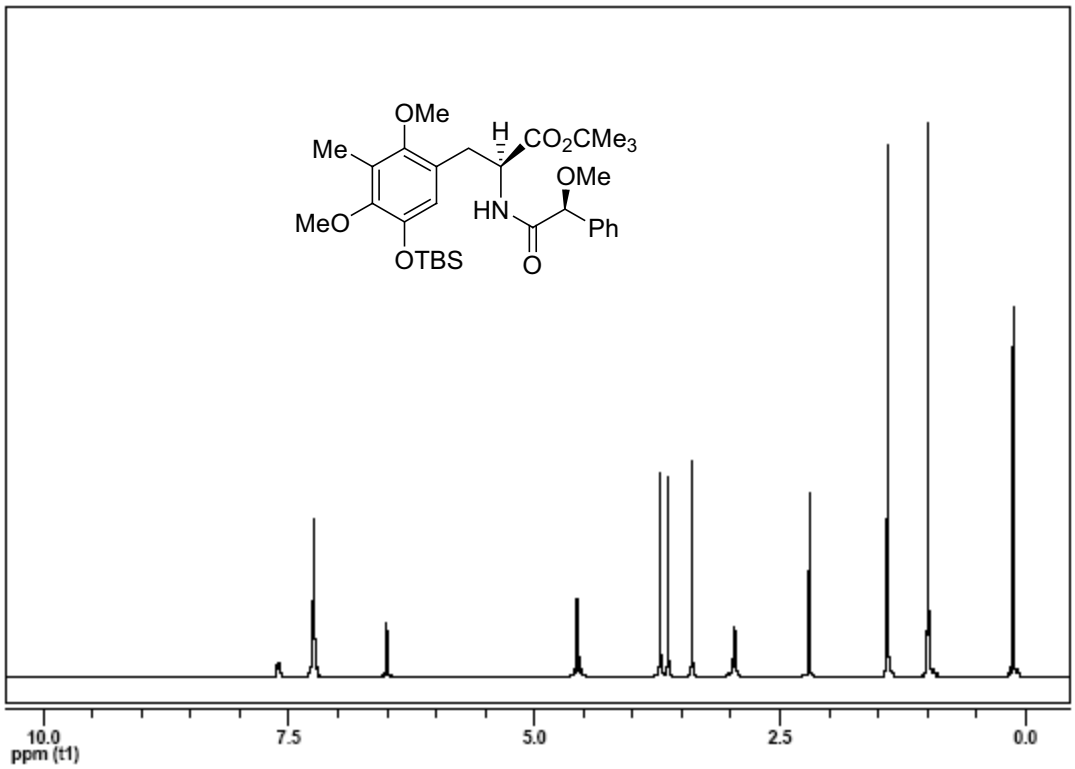


^{13}C NMR (75 MHz, $CDCl_3$)

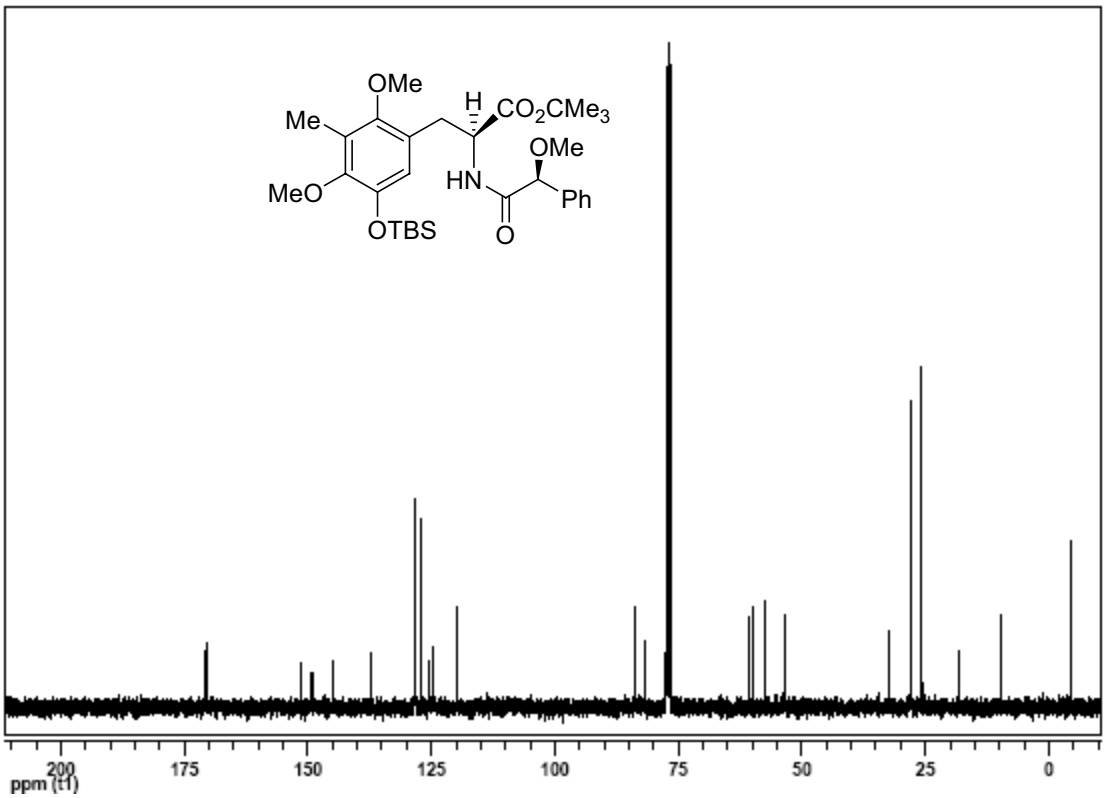


4ai. *S*-Amino ester **38**

^{1}H NMR (300 MHz, $CDCl_3$)

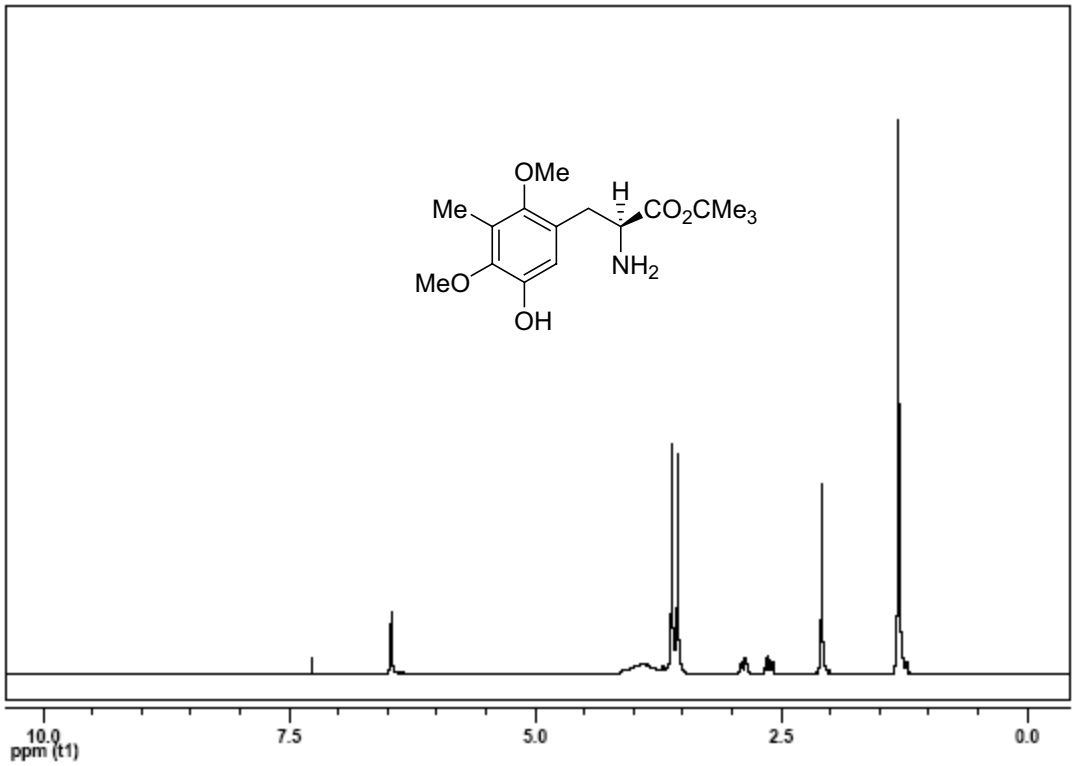


^{13}C NMR (75 MHz, $CDCl_3$)

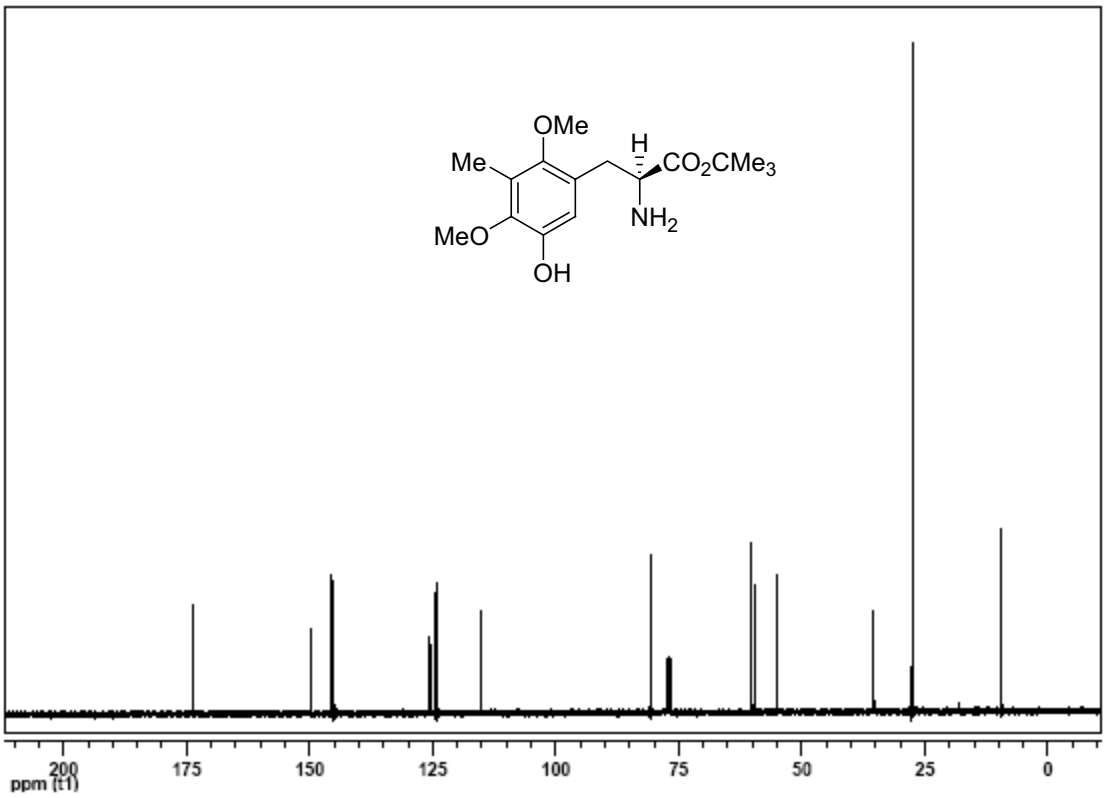


4aj. (*S*)-*tert*-Butyl 2-amino-3-(5-hydroxy-2,4-dimethoxy-3-methylphenyl)propanoate (**14**)

^{1}H NMR (300 MHz, $CDCl_3$)

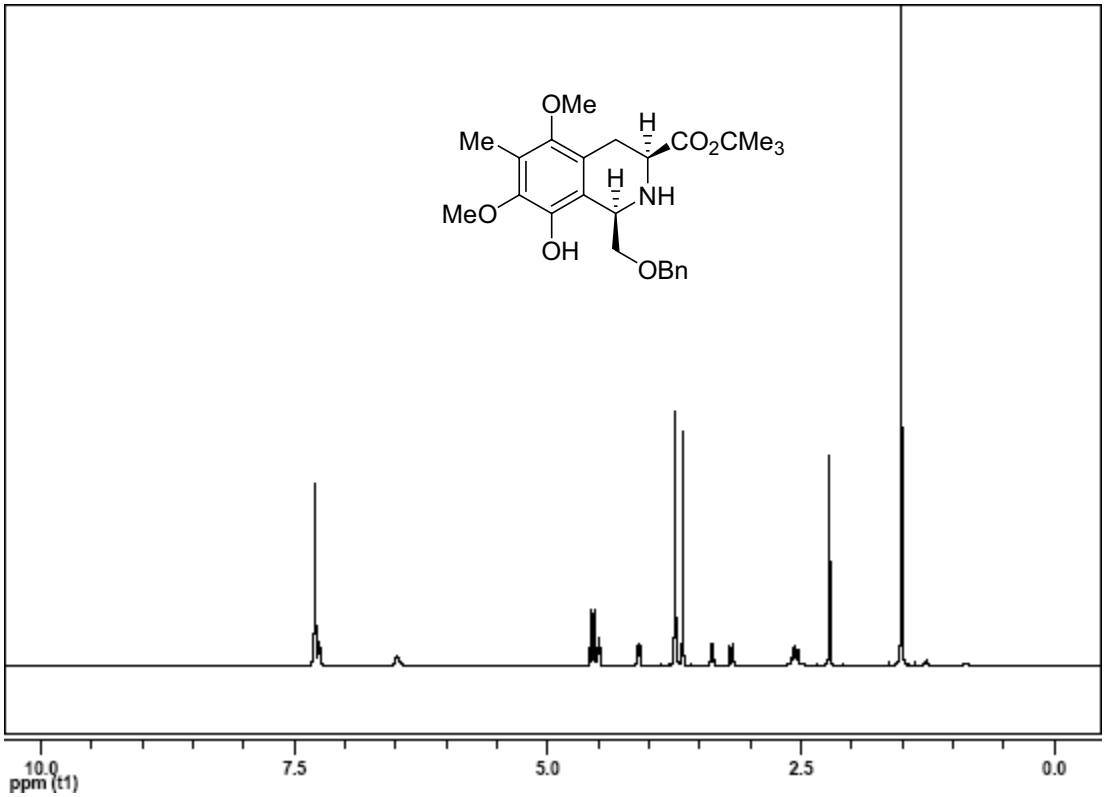


^{13}C NMR (75 MHz, $CDCl_3$)

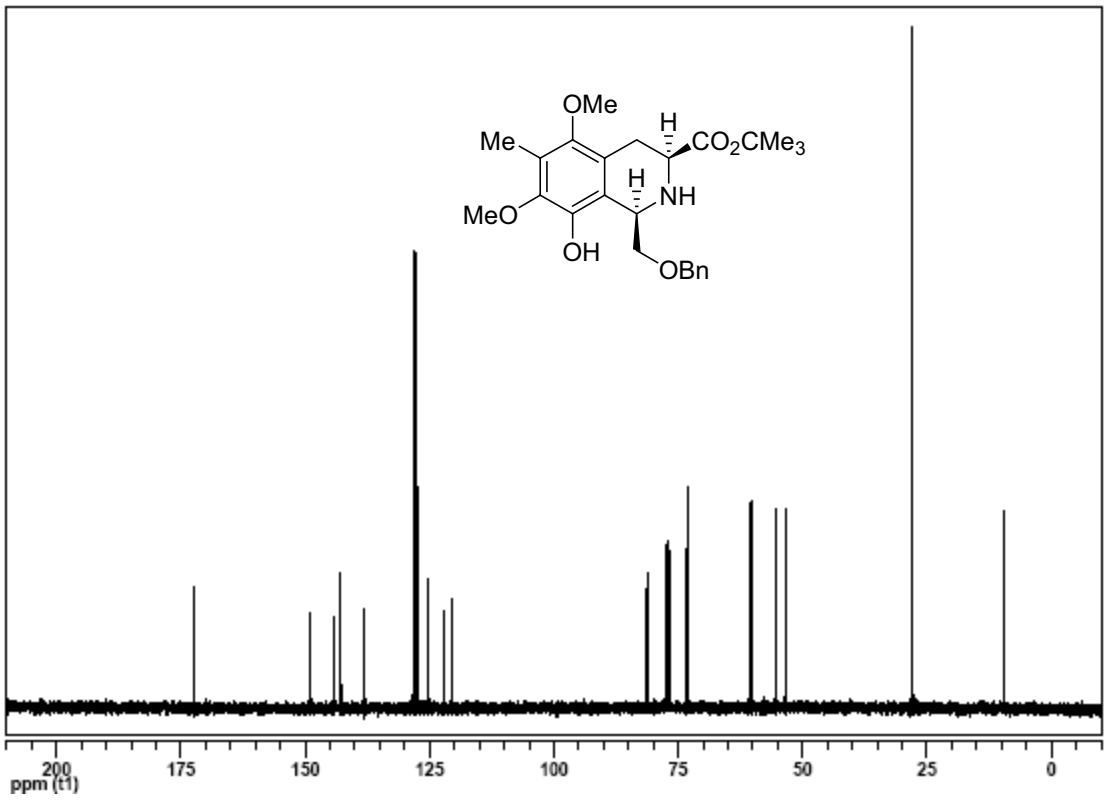


4ak. (1*R,*3*S*)-*tert*-Butyl 1-((benzyloxy)methyl)-1,2,3,4-tetrahydro-8-hydroxy-5,7-dimethoxy-6-methylisoquinoline-3-carboxylate (**16**)

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

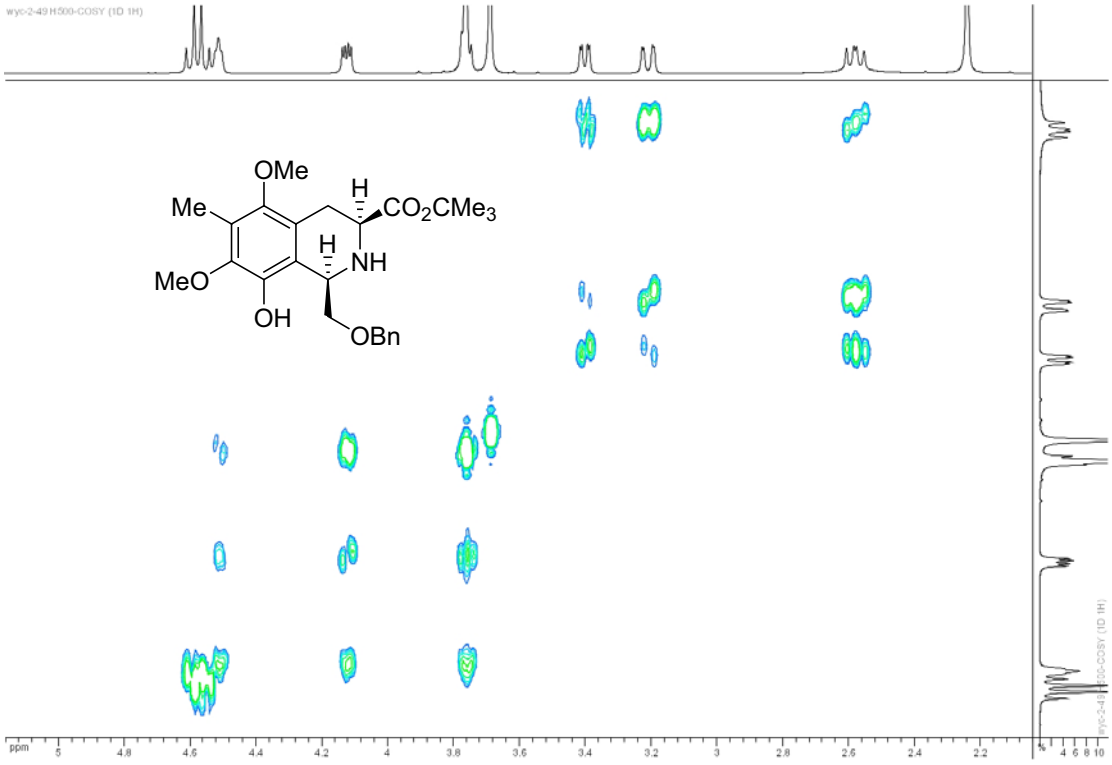


^{13}C NMR (75 MHz, $CDCl_3$)

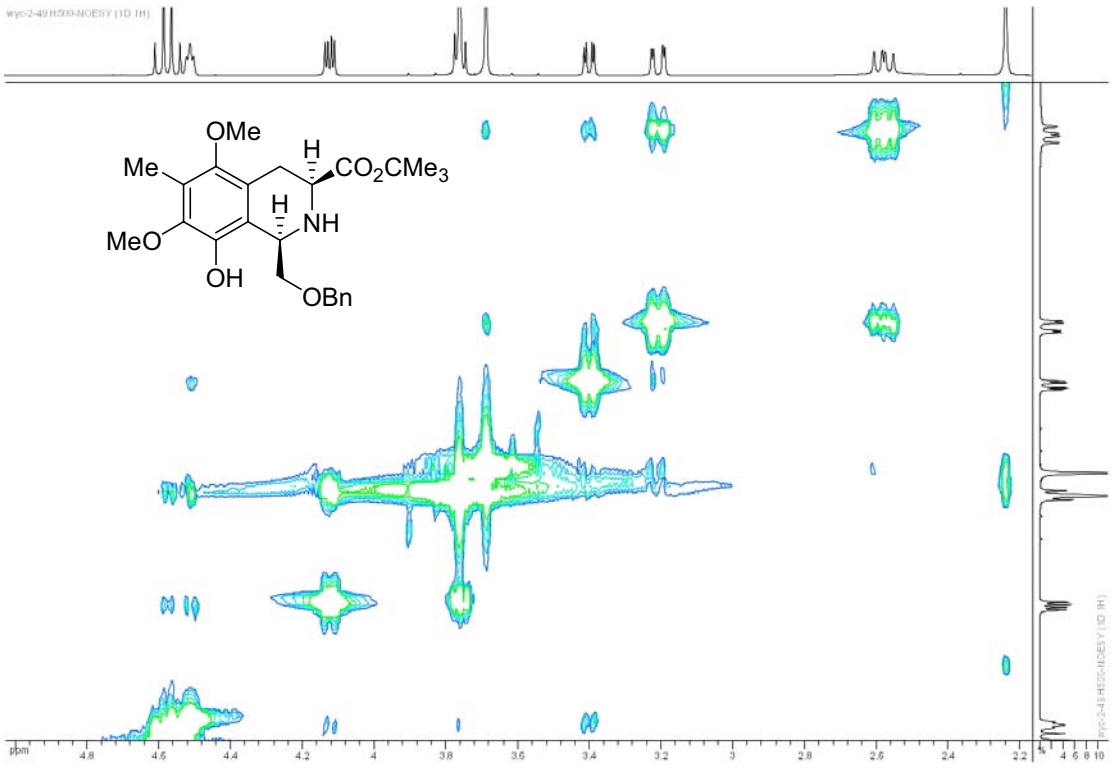


4ak. (1*R*,3*S*)-*tert*-Butyl 1-((benzyloxy)methyl)-1,2,3,4-tetrahydro-8-hydroxy-5,7-dimethoxy-6-methylisoquinoline-3-carboxylate (**16**)

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

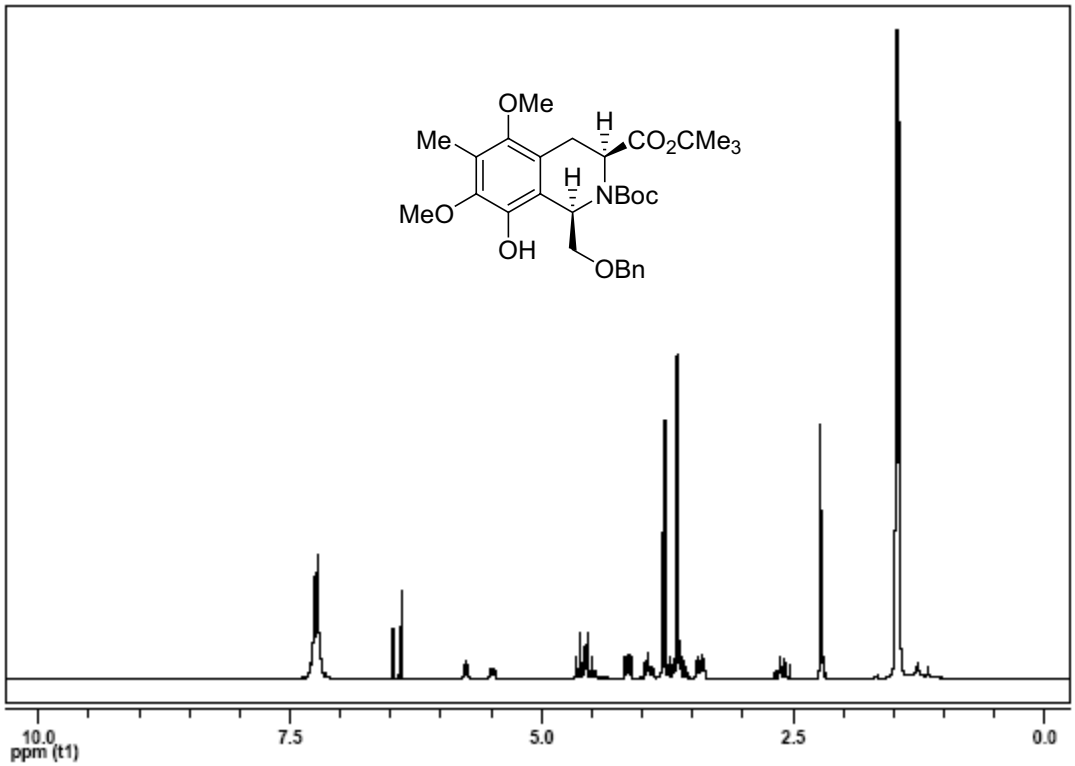


^{1}H-^{1}H NOESY (500 MHz, $CDCl_3$)

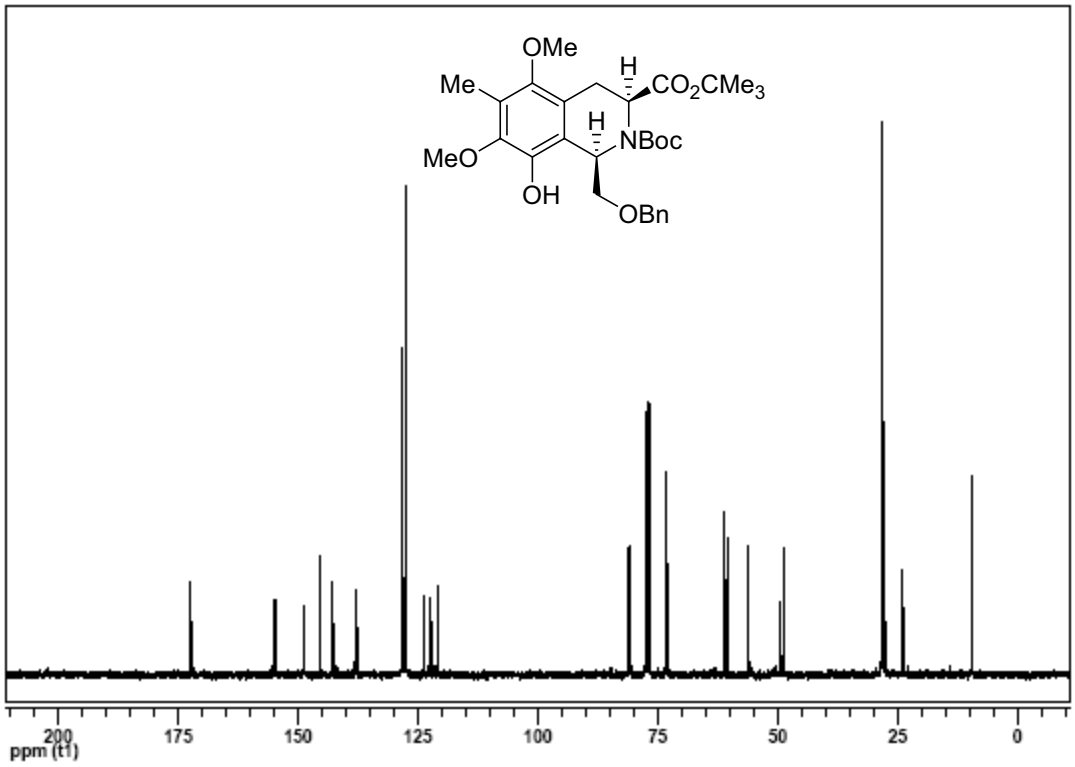


4al. (1*R*,3*S*)-di-tert-Butyl 1-((benzyloxy)methyl)-3,4-dihydro-8-hydroxy-5,7-dimethoxy-6-methylisoquinoline-2,3(1*H*)-dicarboxylate (**39**)

^{1}H NMR (300 MHz, $CDCl_3$)

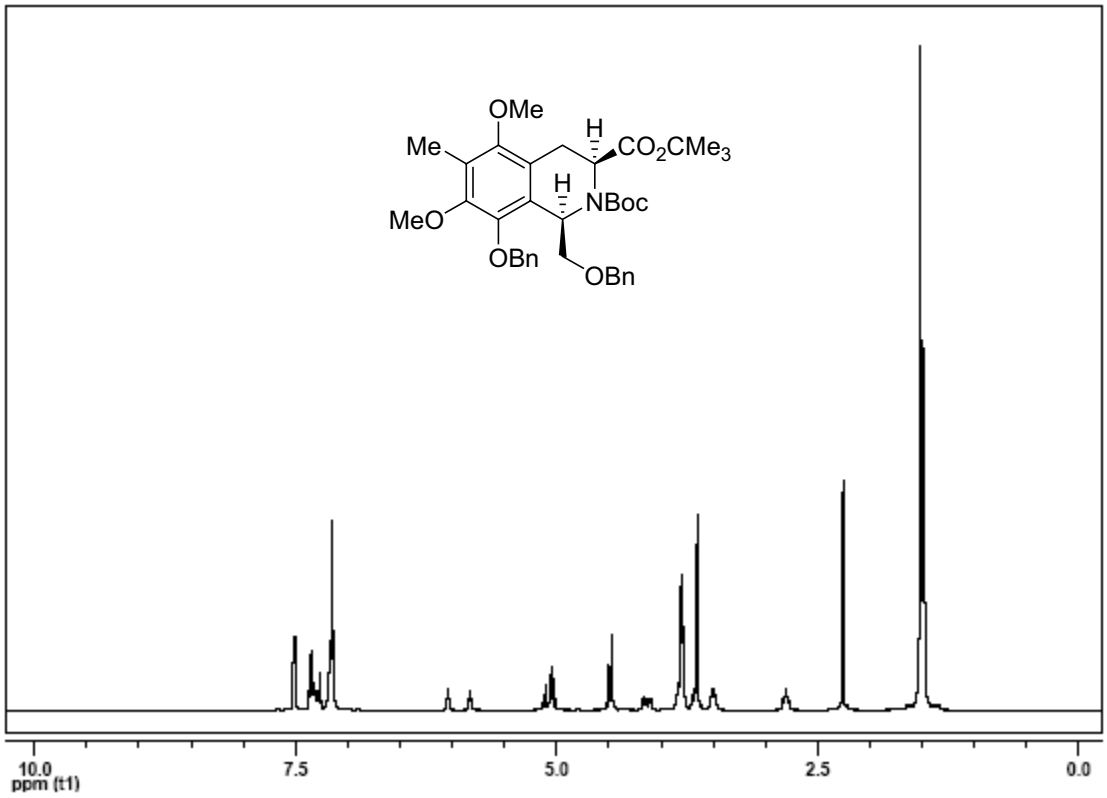


^{13}C NMR (75 MHz, $CDCl_3$)

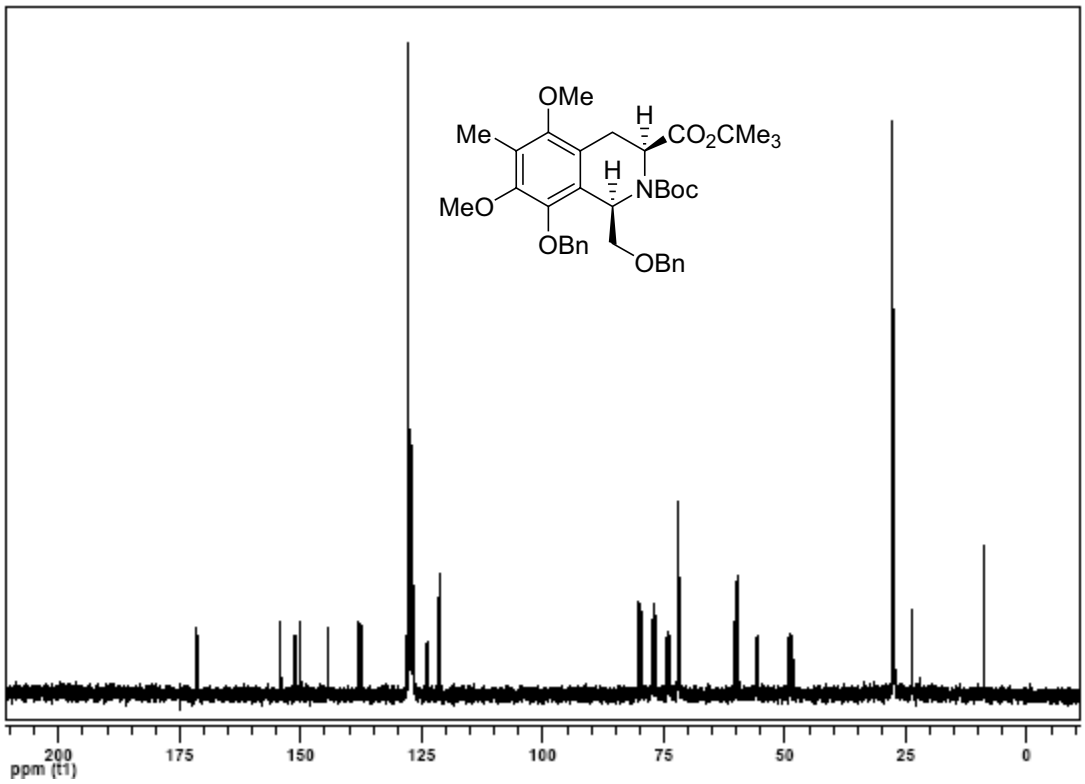


4am. (1*R*,3*S*)-di-tert-Butyl 8-(benzyloxy)-1-((benzyloxy)methyl)-3,4-dihydro-5,7-dimethoxy-6-methylisoquinoline-2,3(1*H*)-dicarboxylate (**17**)

^{1}H NMR (300 MHz, $CDCl_3$)

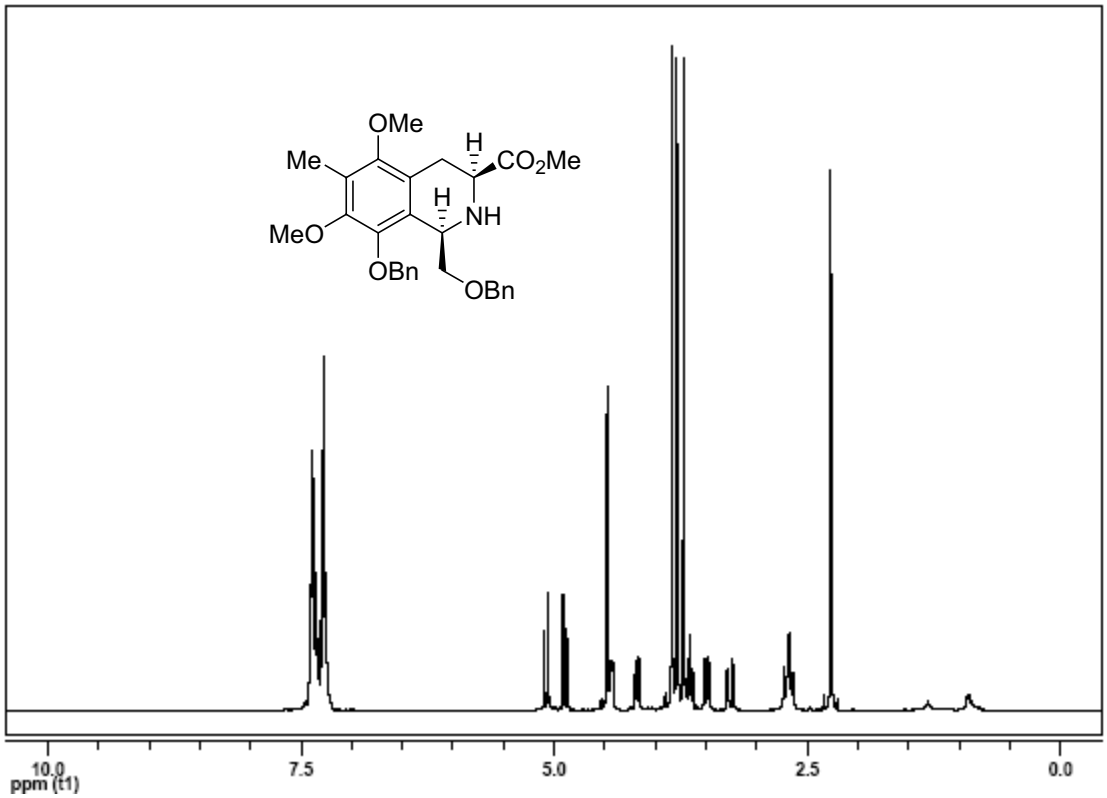


^{13}C NMR (75 MHz, $CDCl_3$)

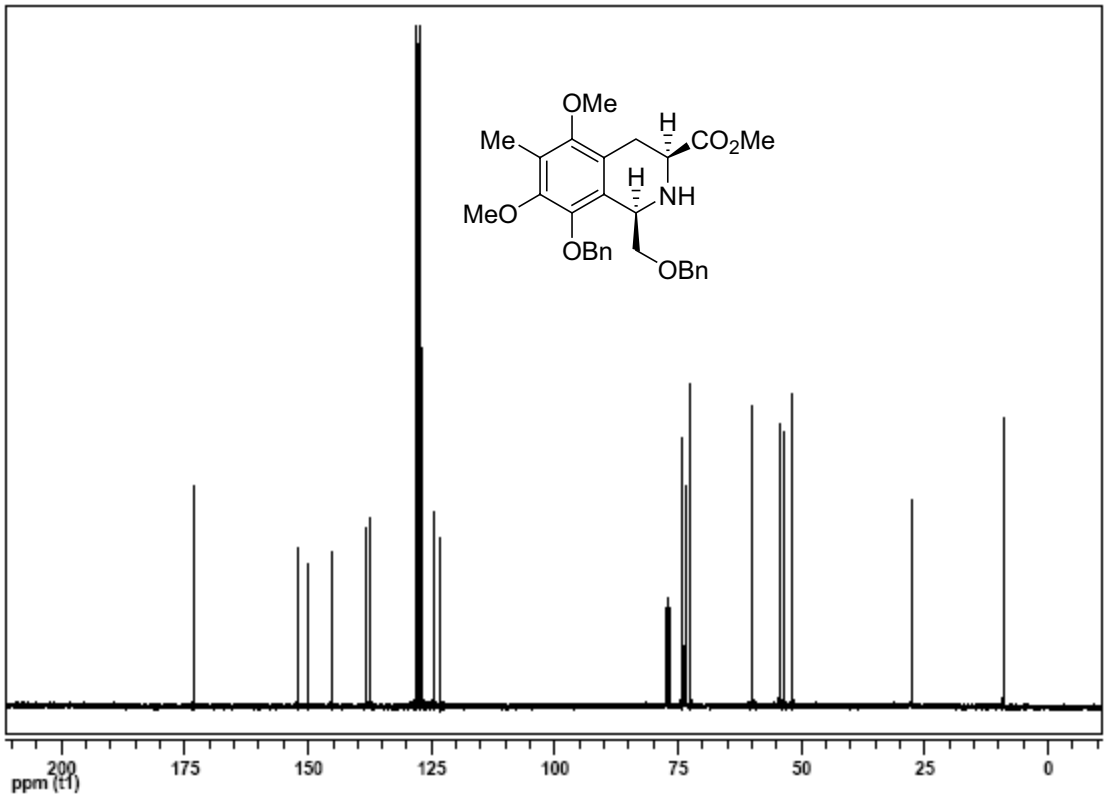


4an. (1*R*,3*S*)-Methyl 8-(benzyloxy)-1-((benzyloxy)methyl)-1,2,3,4-tetrahydro-5,7-dimethoxy-6-methylisoquinoline-3-carboxylate (**8**)

^{1}H NMR (300 MHz, $CDCl_3$)



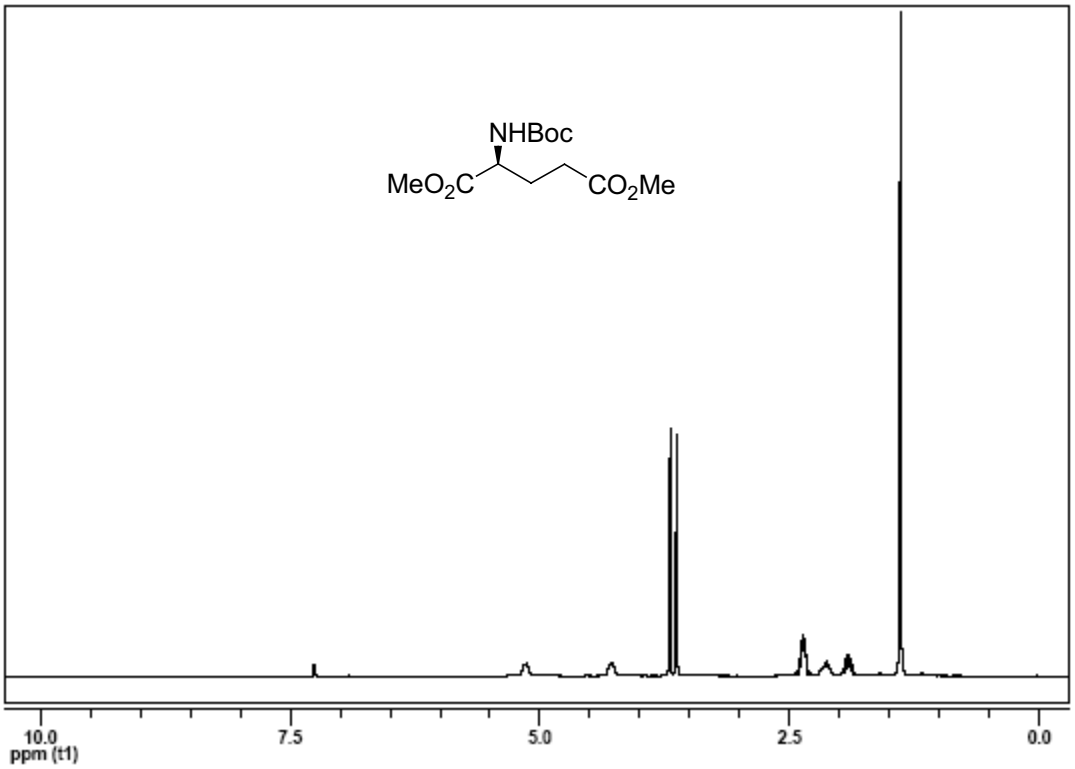
^{13}C NMR (75 MHz, $CDCl_3$)



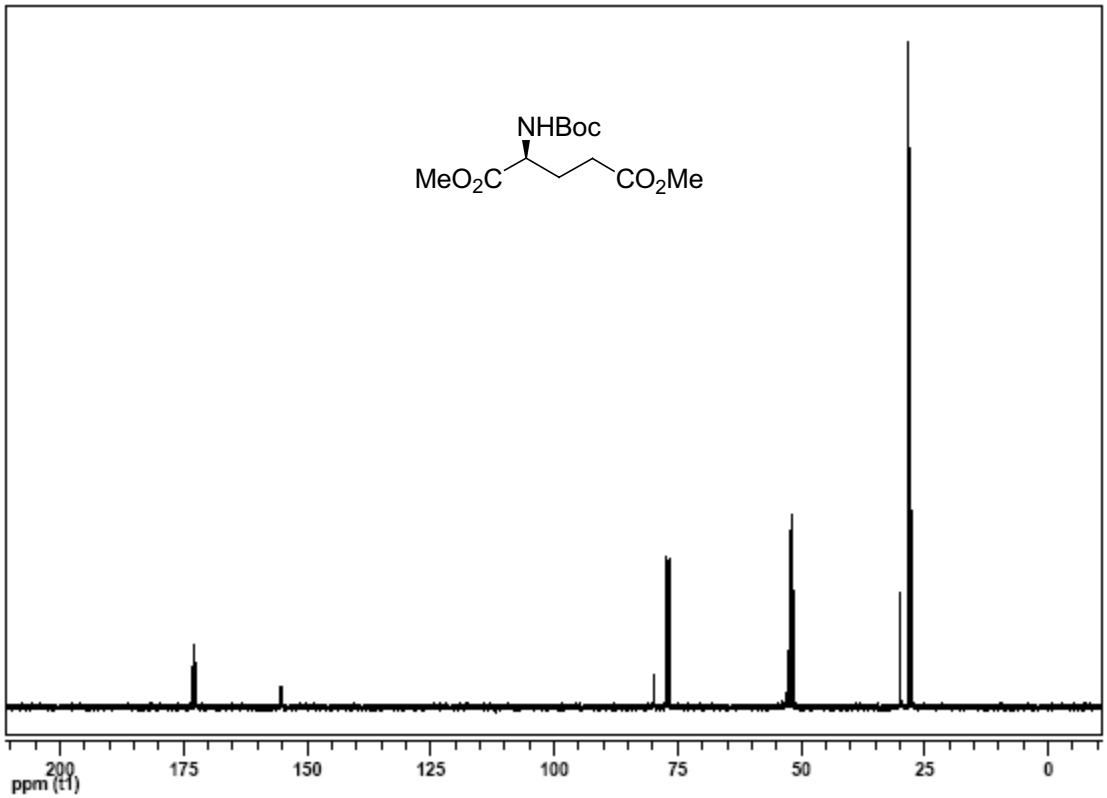
4b. *N*-Boc amino acid **9** and the Intermediates

4ba. *tert*-Butyl (*S*)-1,3-di(methoxycarbonyl)propylcarbamate (**19**)

^{1}H NMR (300 MHz, $CDCl_3$)

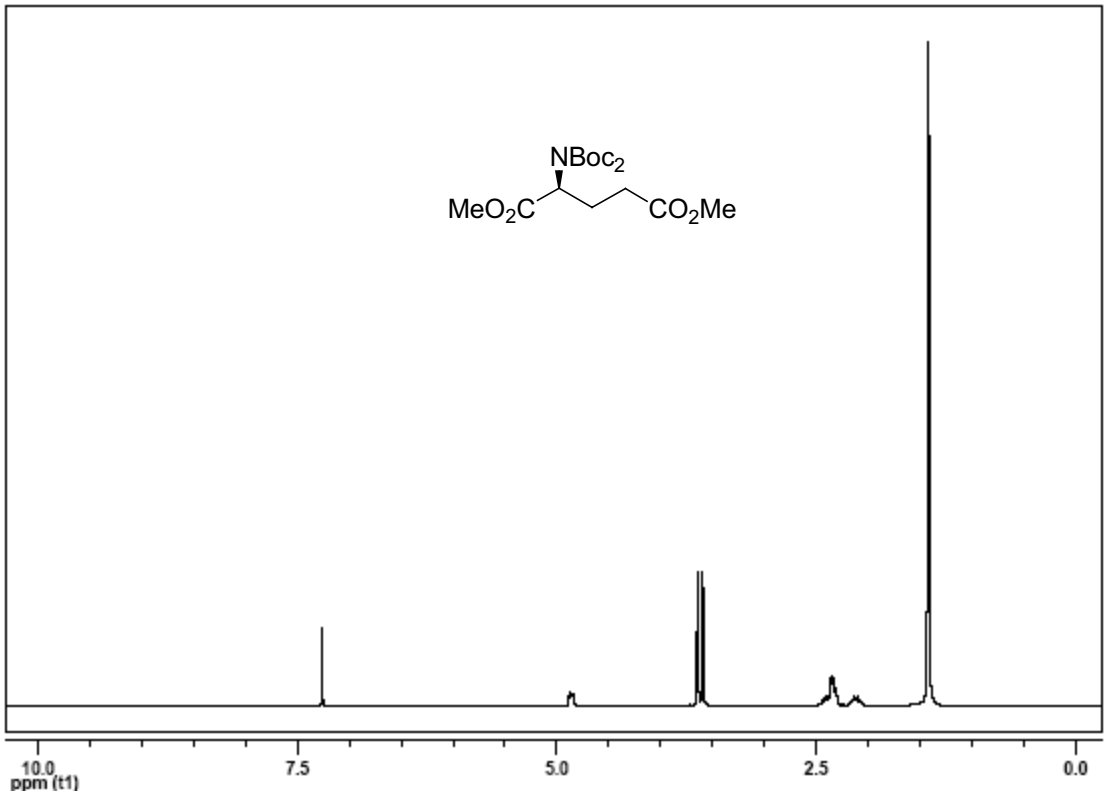


^{13}C NMR (75 MHz, $CDCl_3$)

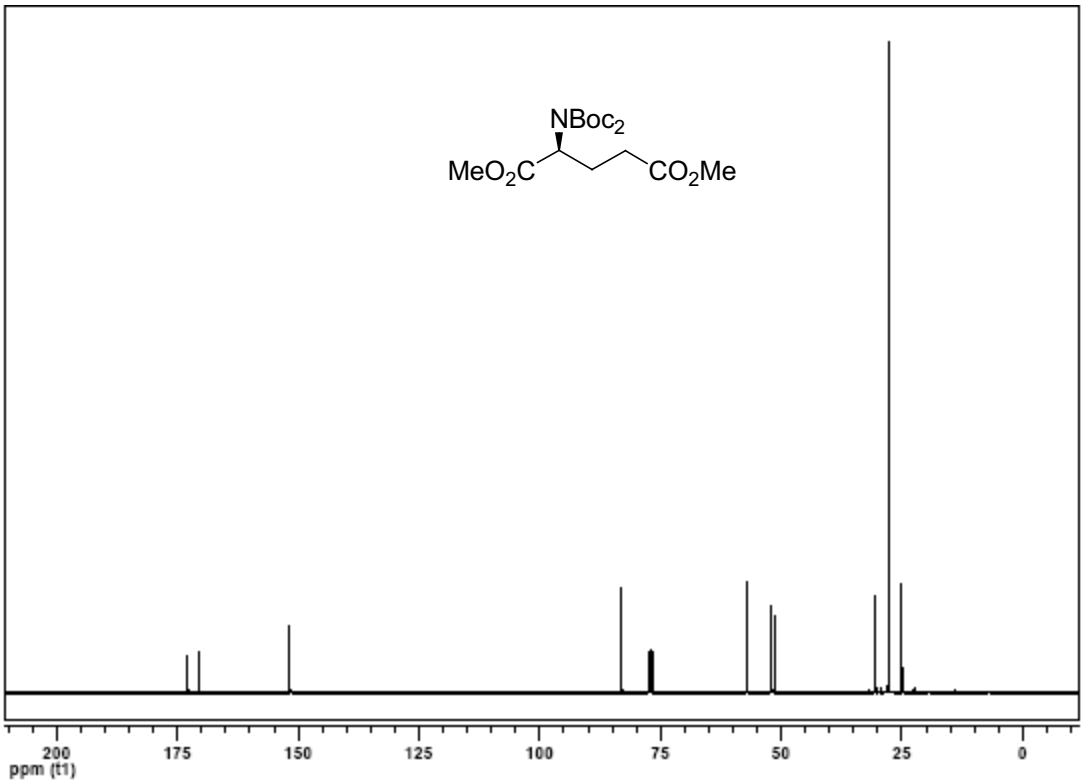


4bb. (*S*)-Dimethyl 2-(*N*,*N*-di-Boc-amino)pentanedioate (**40**)

^{1}H NMR (300 MHz, $CDCl_3$)

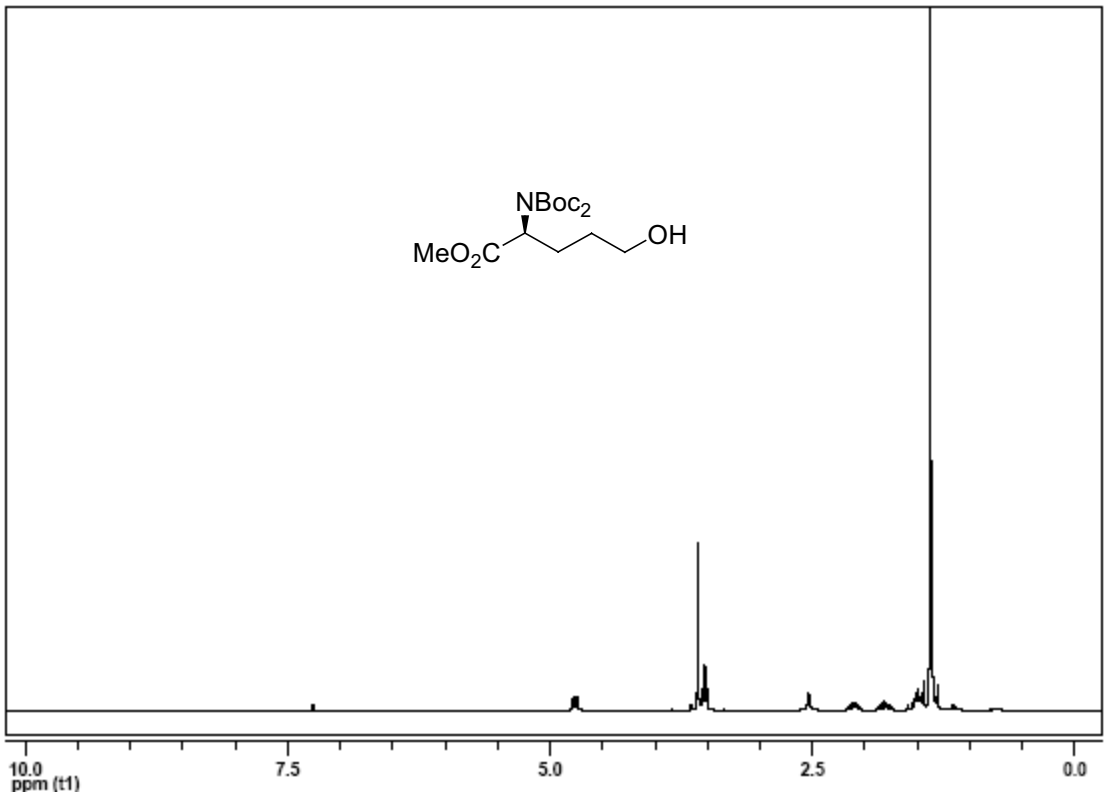


^{13}C NMR (75 MHz, $CDCl_3$)

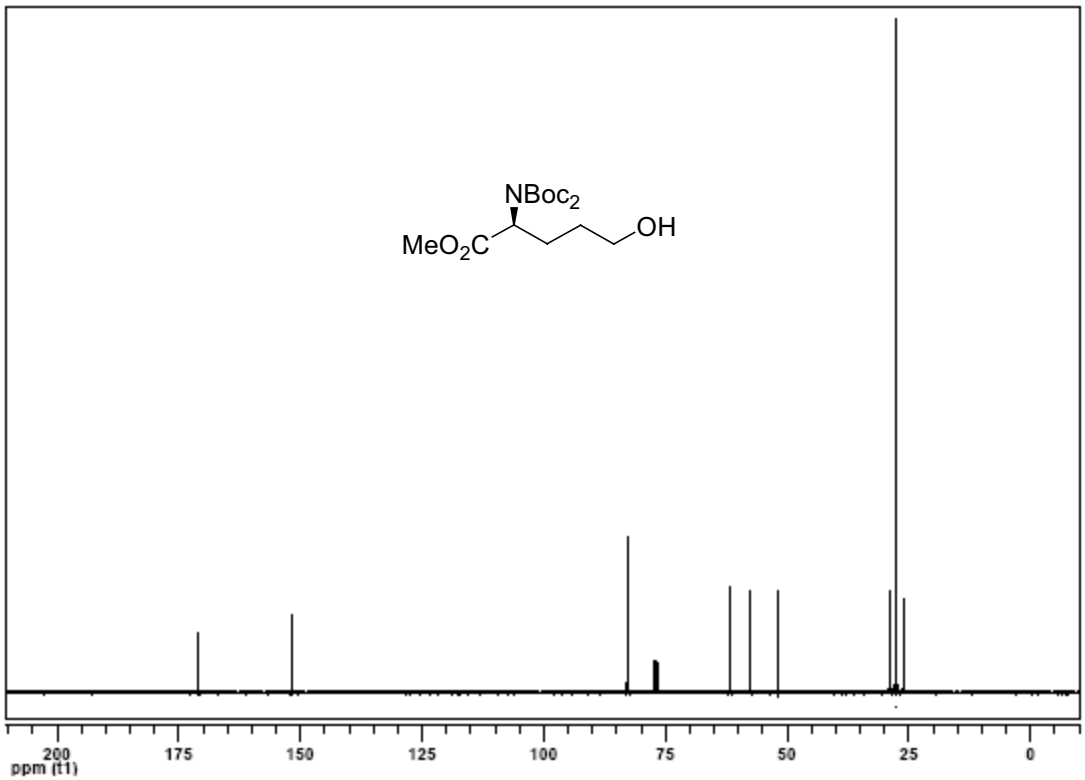


4bc. (*S*)-Methyl 2-(*N*,*N*-di-Boc-amino)-5-hydroxypentanoate (**20**)

^{1}H NMR (300 MHz, $CDCl_3$)

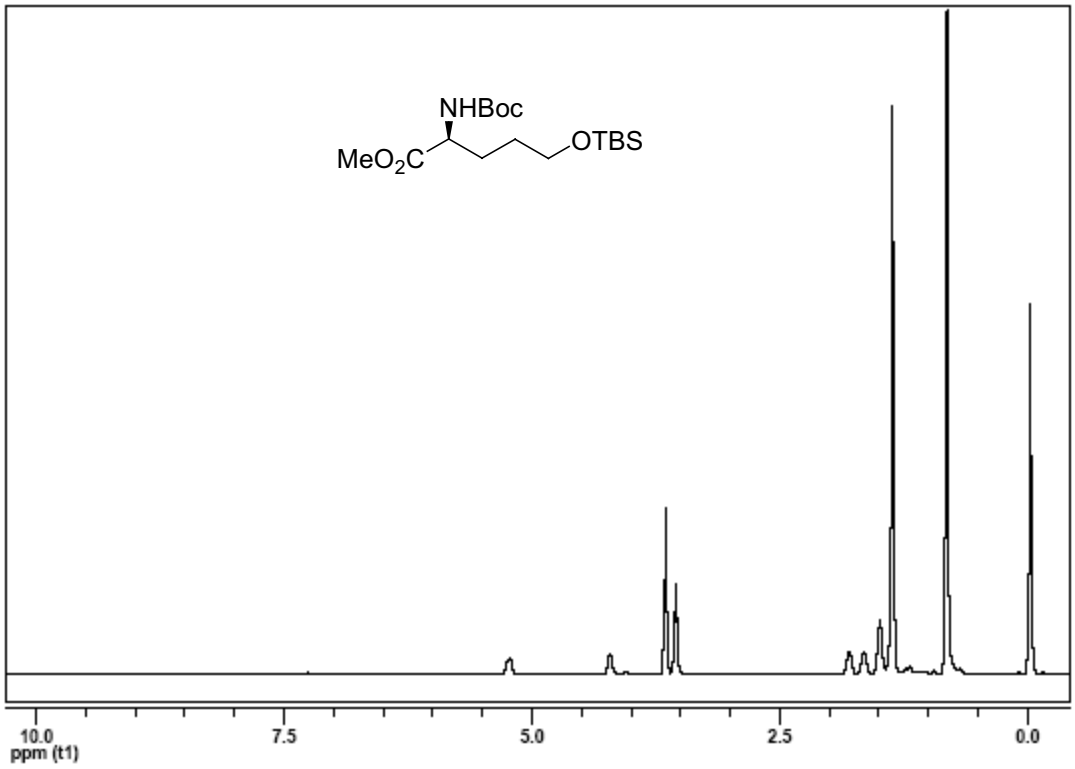


^{13}C NMR (75 MHz, $CDCl_3$)

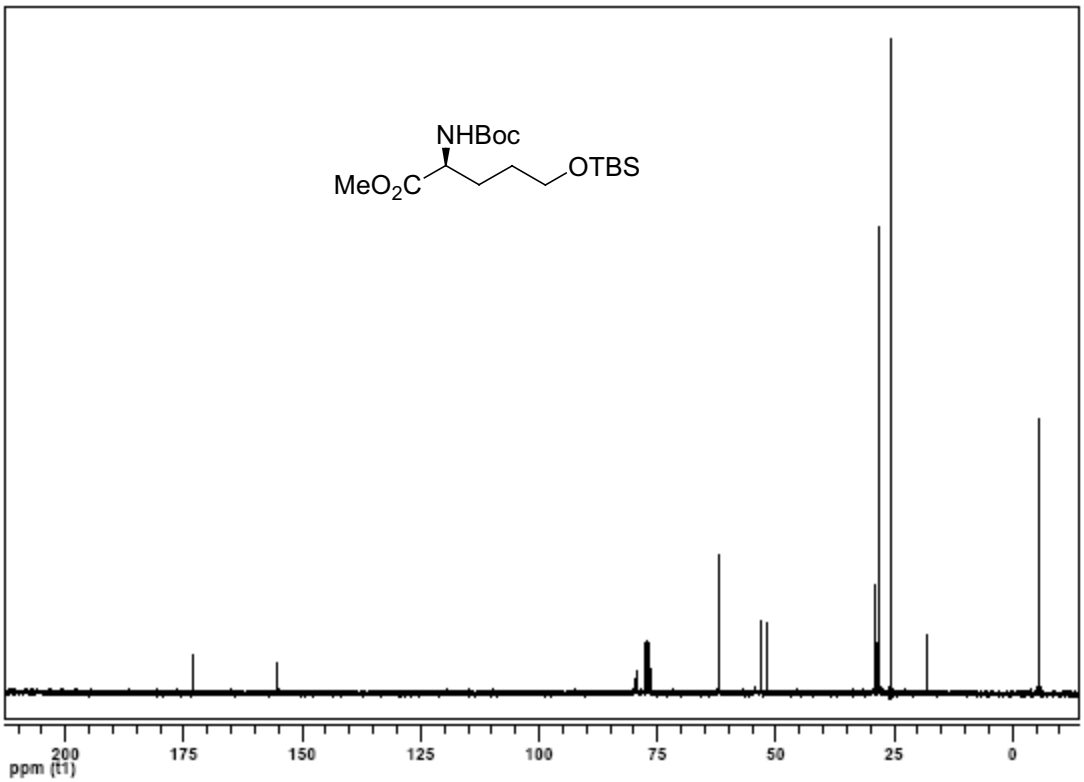


4bd. (*S*)-Methyl 5-*tert*-butyldimethylsilyloxy-2-(*N*-Boc-amino)pentanoate (**21**)

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

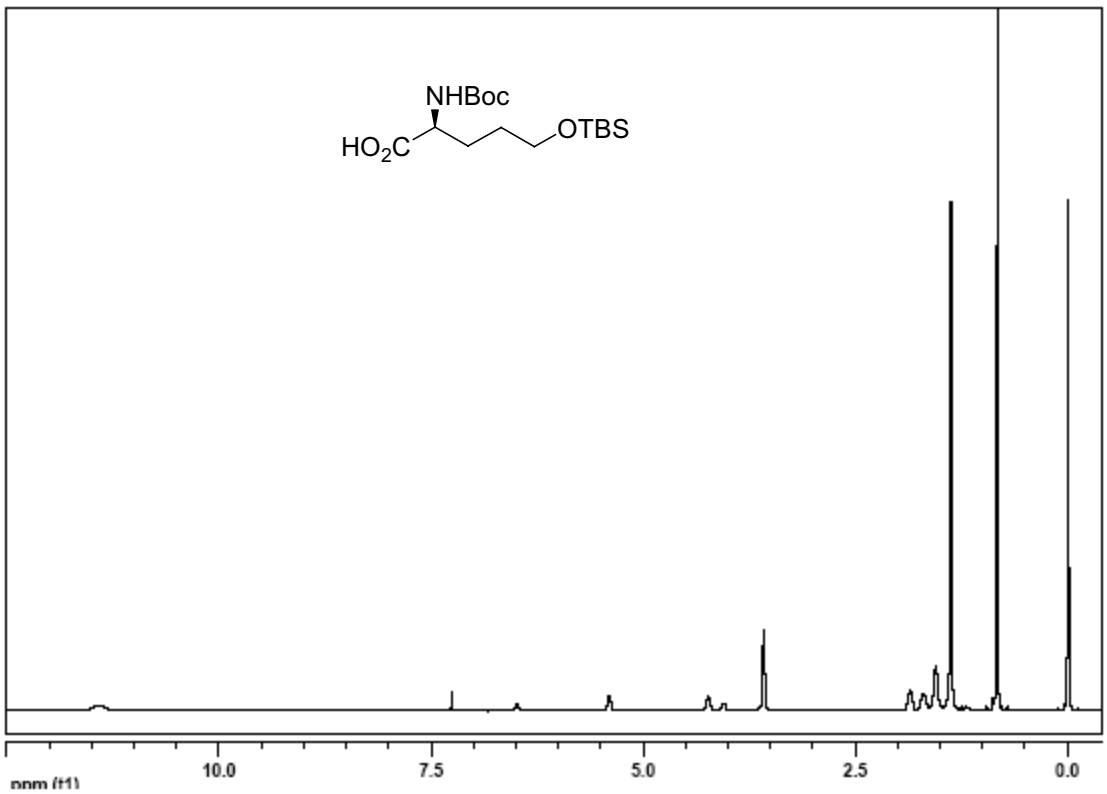


^{13}C NMR (75 MHz, $CDCl_3$)

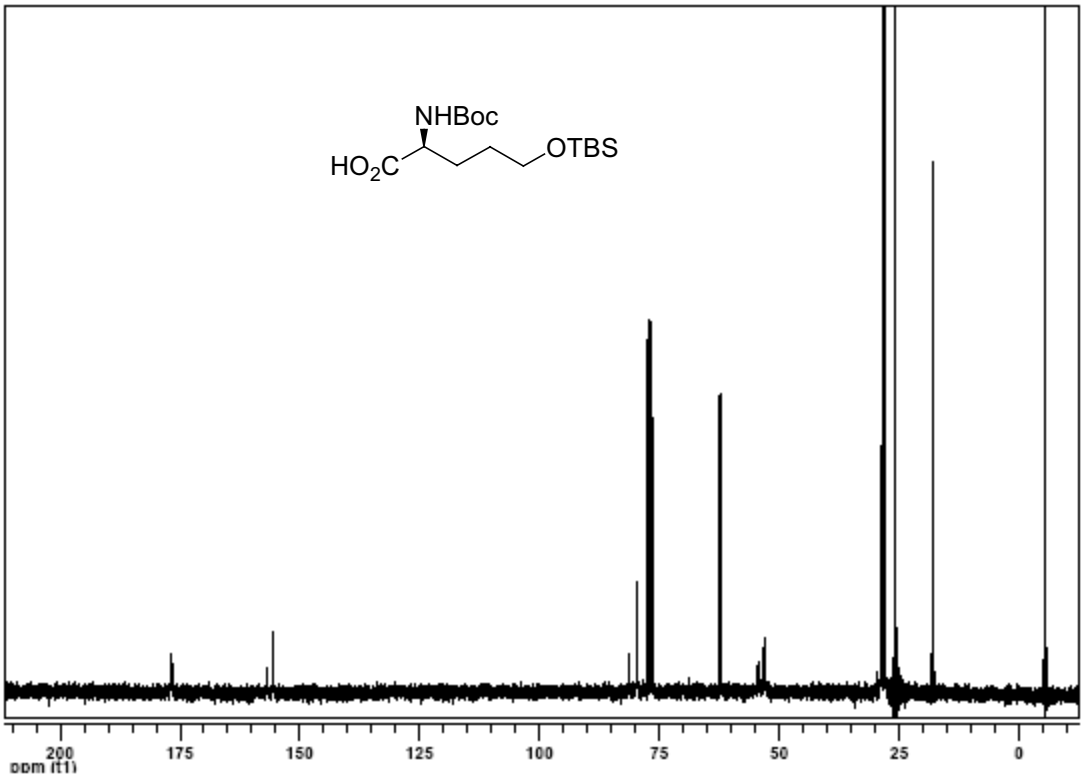


4be. (*S*)-5-*tert*-Butyldimethylsilyloxy-2-(*N*-Boc-amino)pentanoic acid (**9**)

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



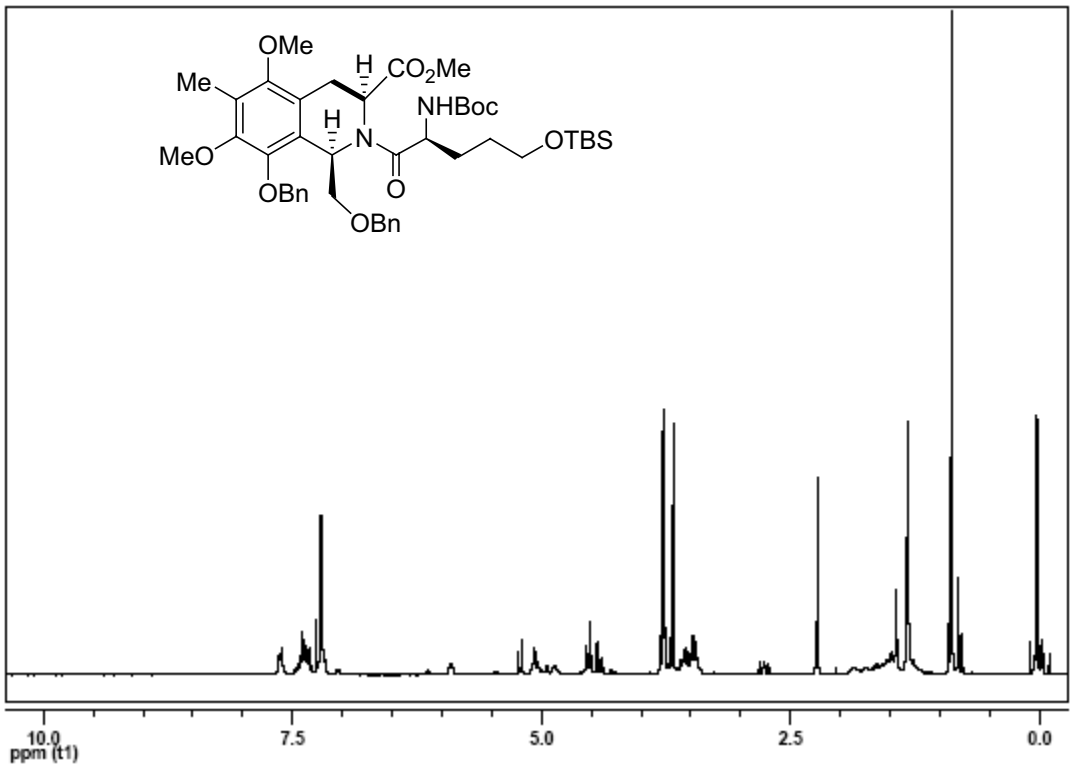
^{13}C NMR (75 MHz, $CDCl_3$)



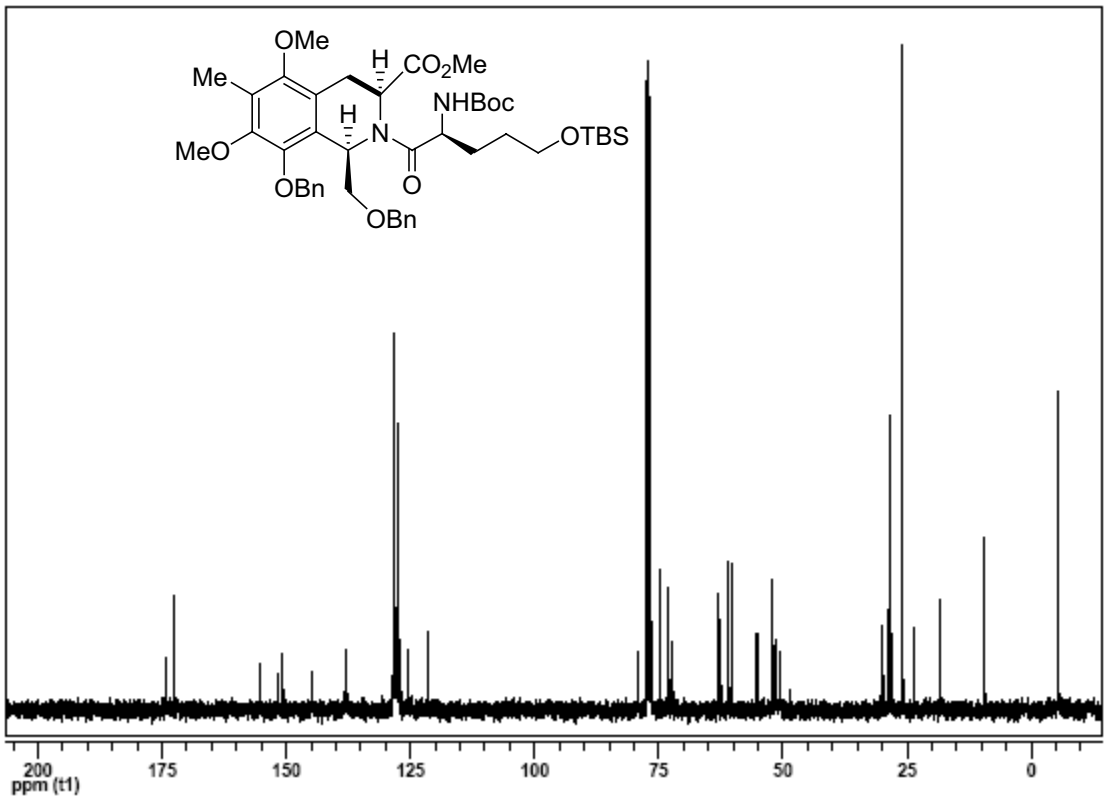
4c. (–)-Lemonomycinone amide (**2**) and the Intermediates

4ca. Amide ester **22**

^{1}H NMR (300 MHz, $CDCl_3$)

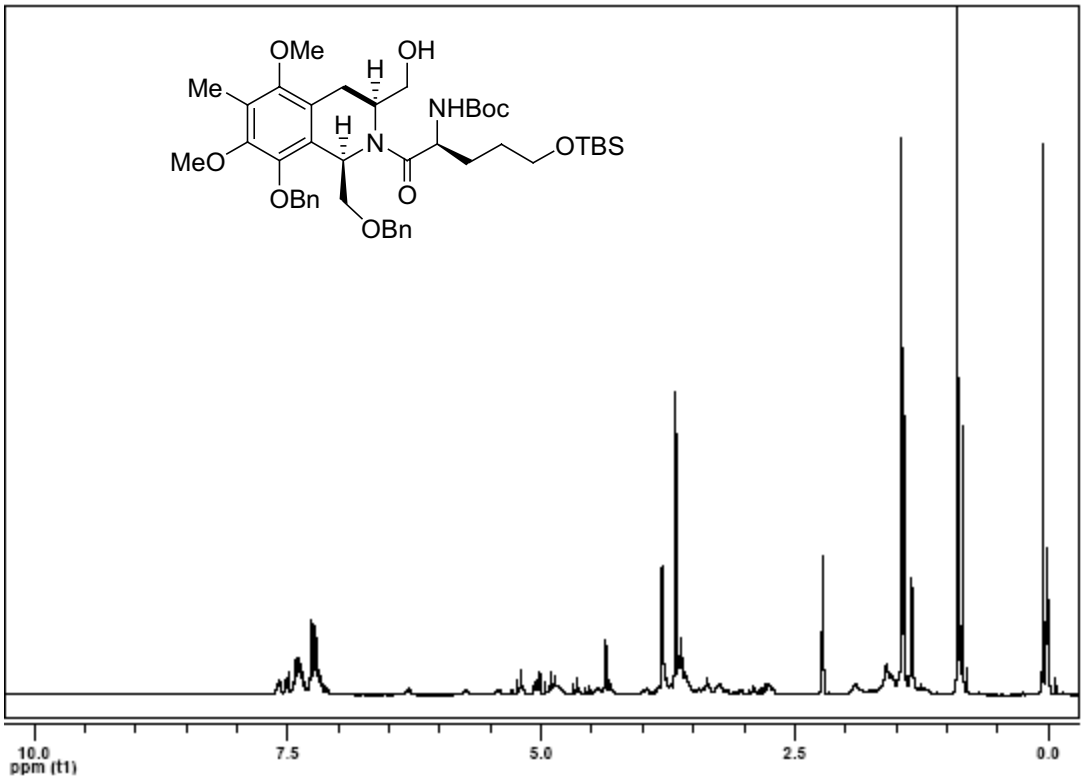


^{13}C NMR (75 MHz, $CDCl_3$)

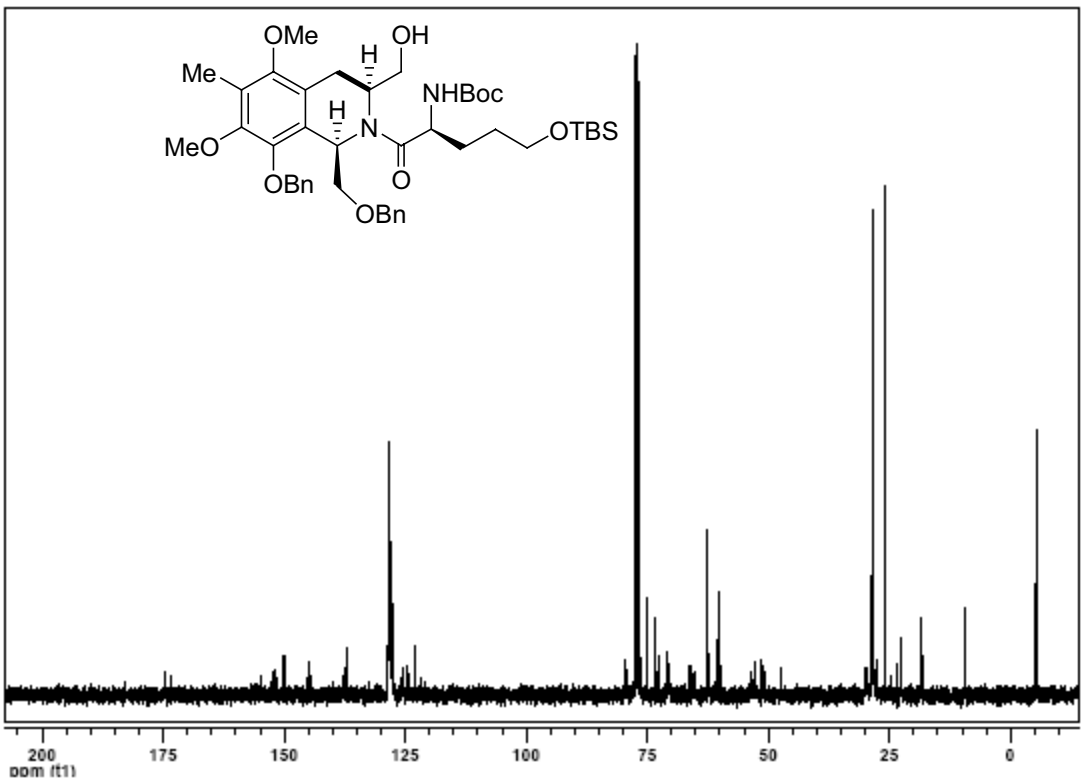


4cb. Amide alcohol **23**

^{1}H NMR (300 MHz, $CDCl_3$)

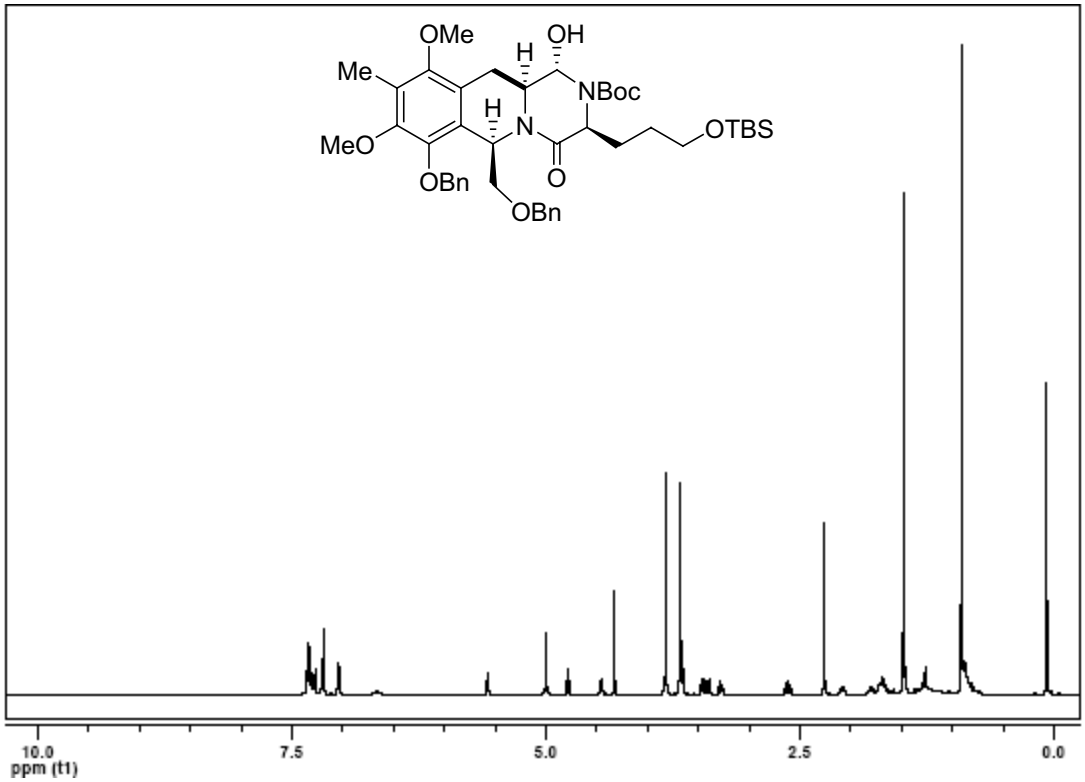


^{13}C NMR (75 MHz, $CDCl_3$)

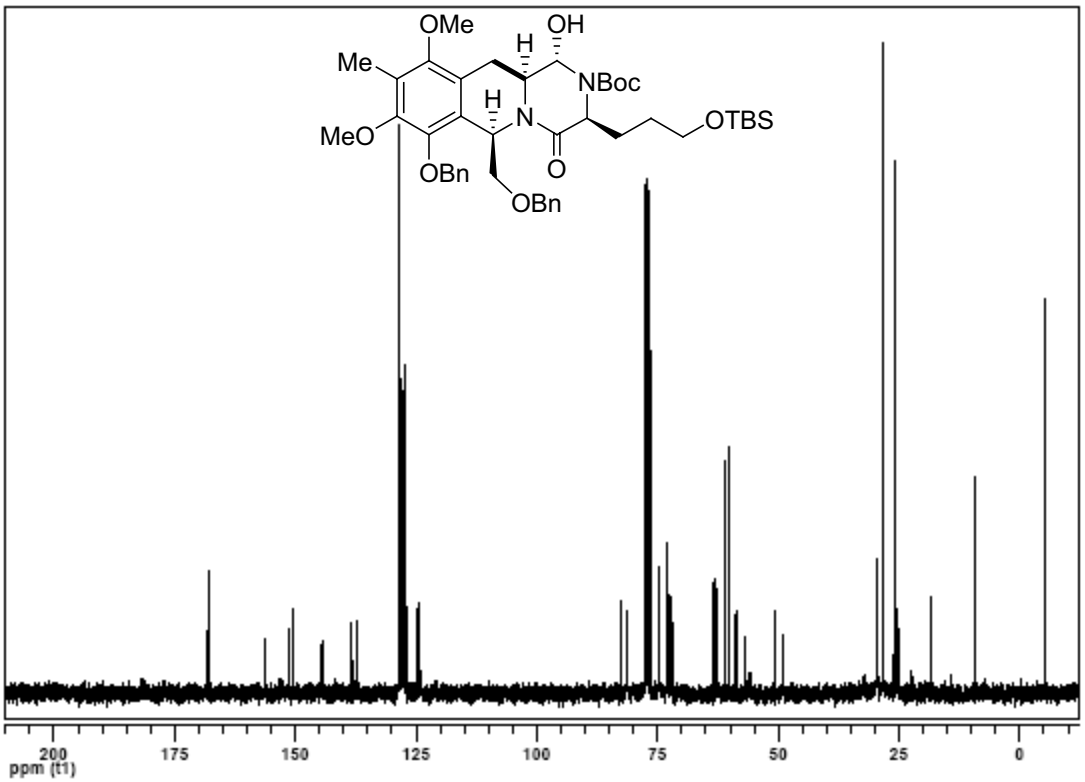


4cc. Hemi-aminal **24**: Trans-isomer **24a**

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

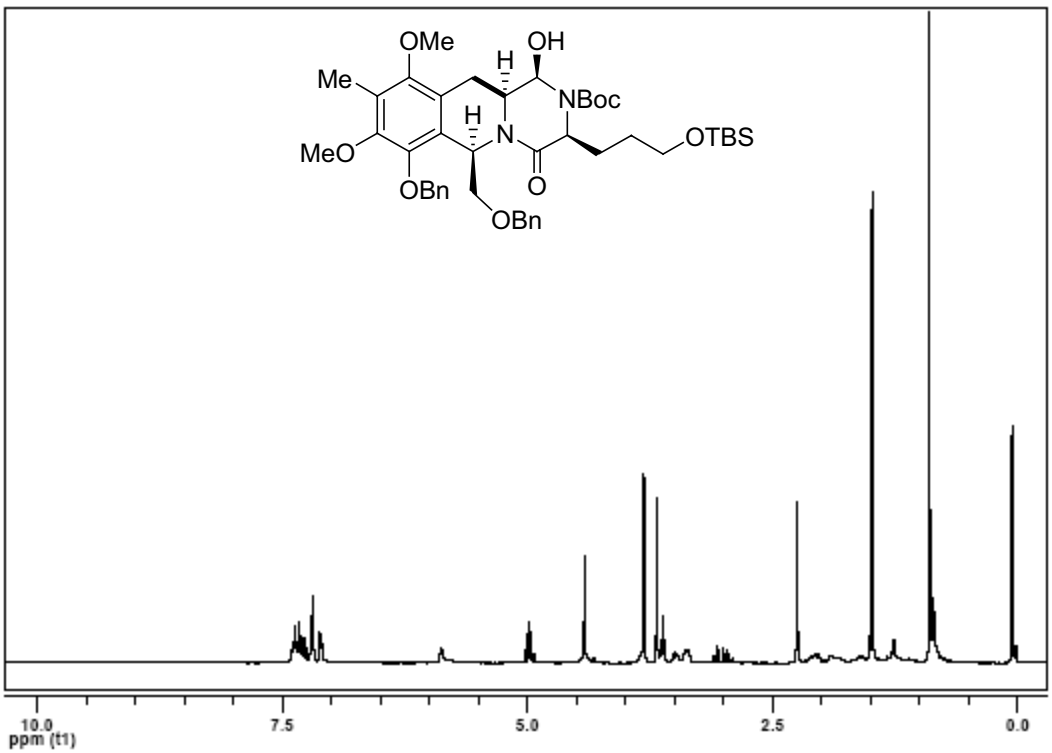


^{13}C NMR (75 MHz, $CDCl_3$)

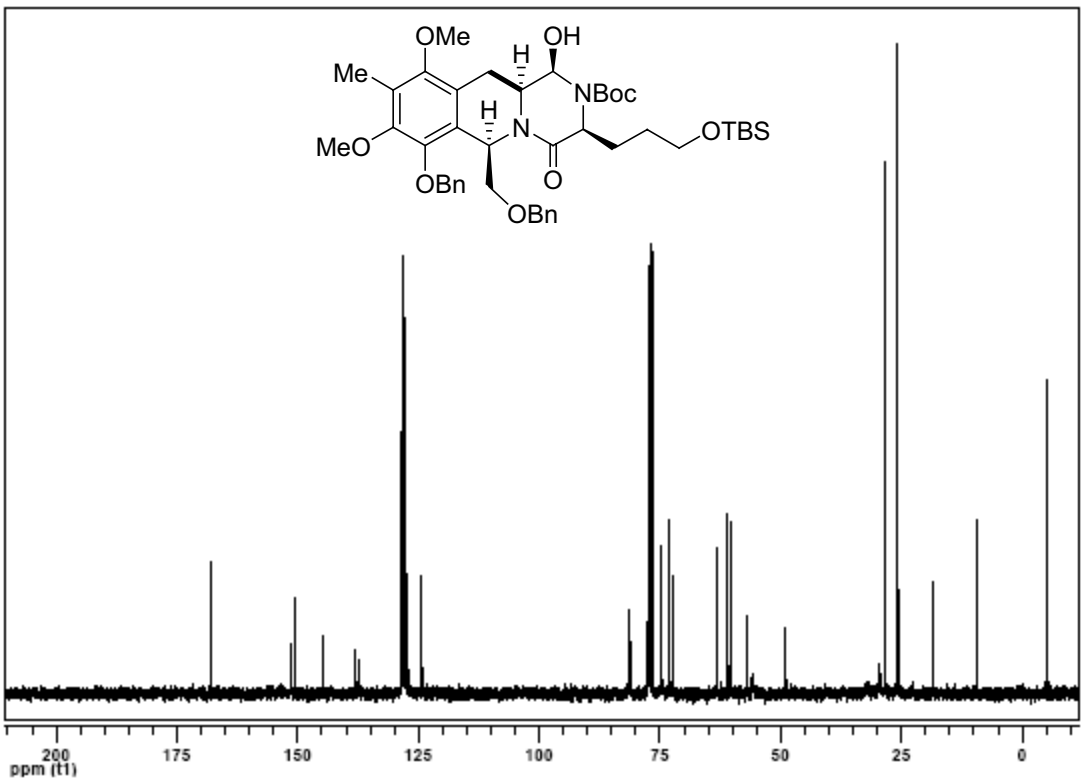


4cc. Cis-isomer **24b**

^{1}H NMR (300 MHz, $CDCl_3$)

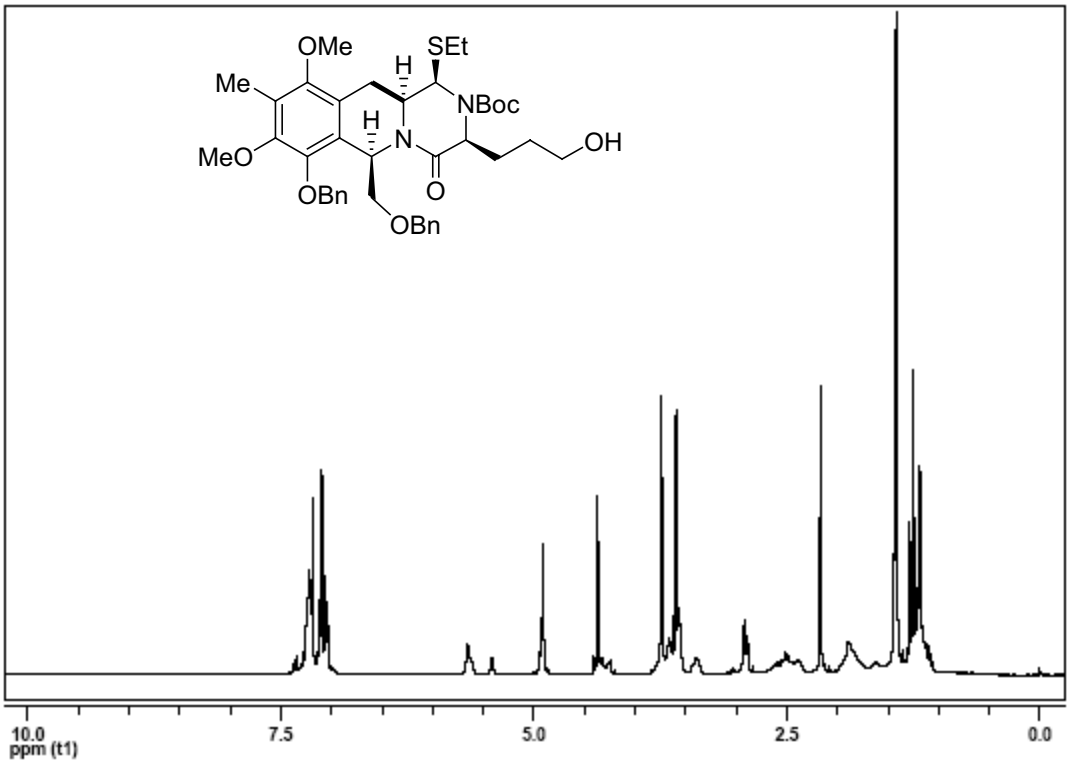


^{13}C NMR (75 MHz, $CDCl_3$)

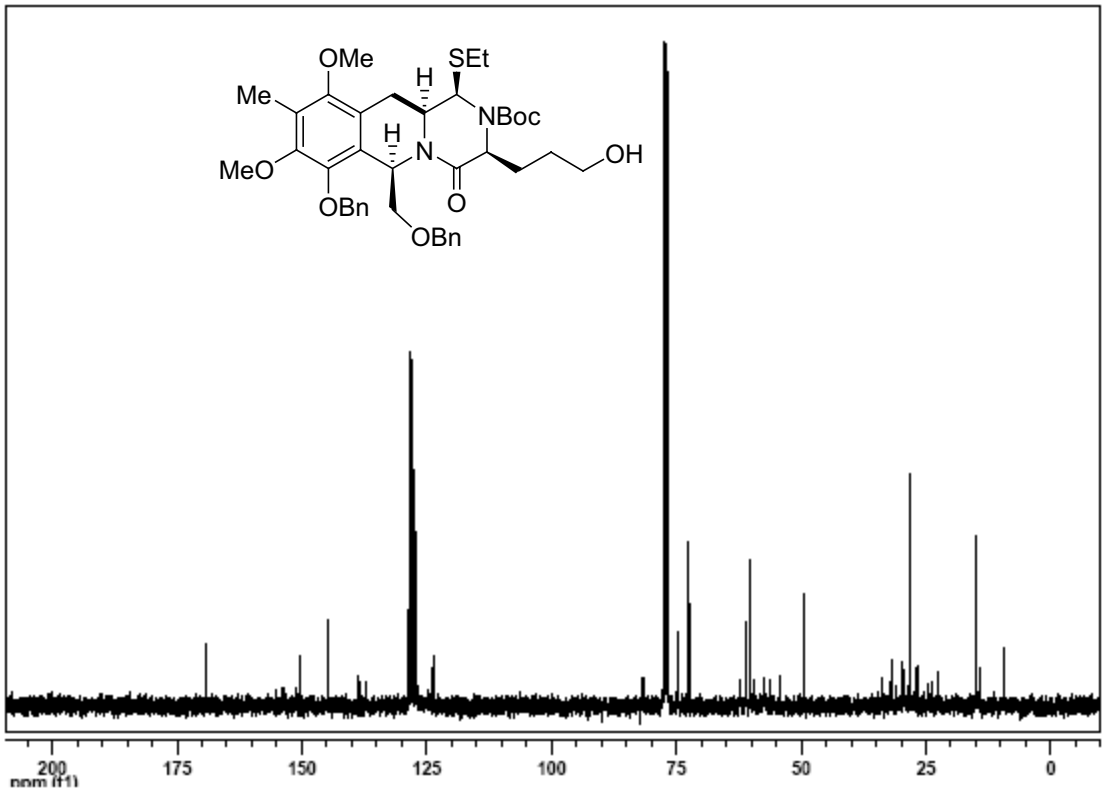


4cd. Thioaminal **25**

^{1}H NMR (300 MHz, $CDCl_3$)

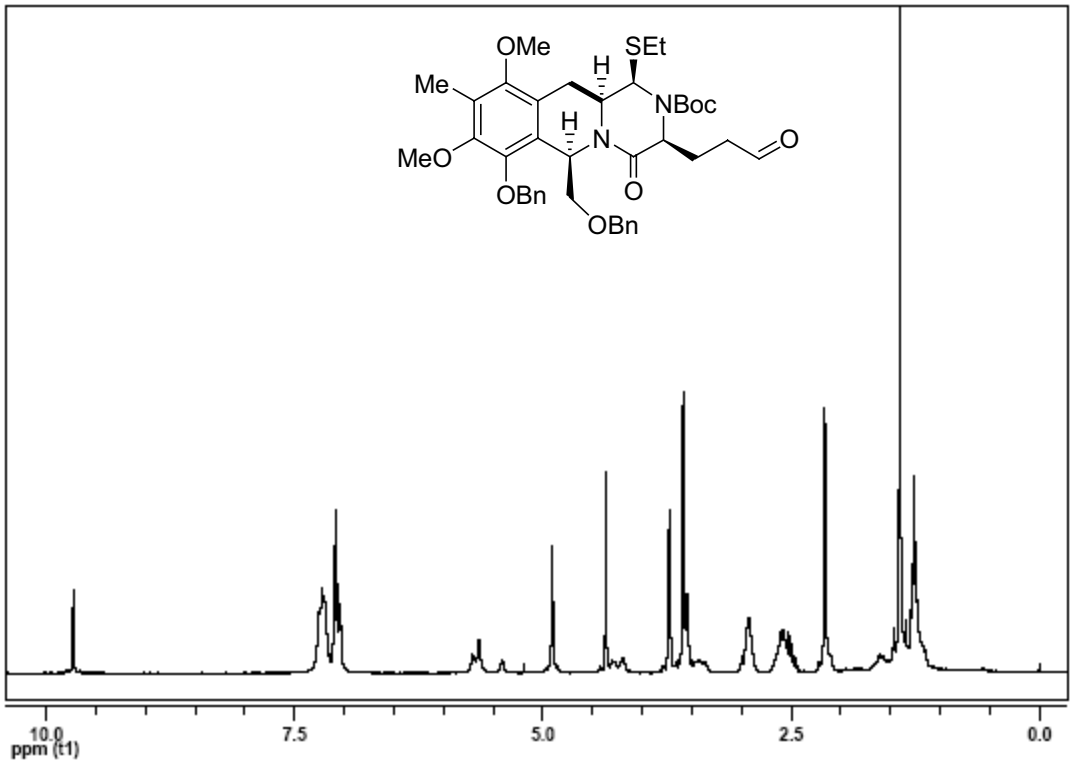


^{13}C NMR (75 MHz, $CDCl_3$)

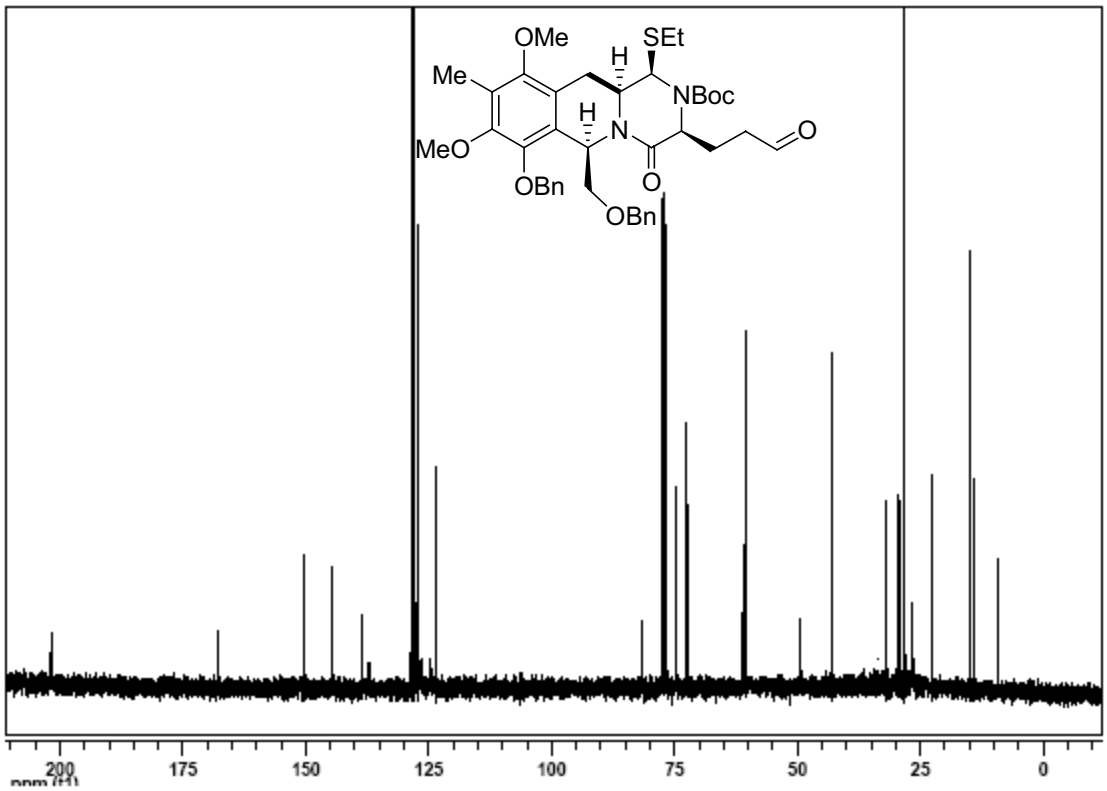


4ce. Aldehyde **41**

^{1}H NMR (300 MHz, $CDCl_3$)

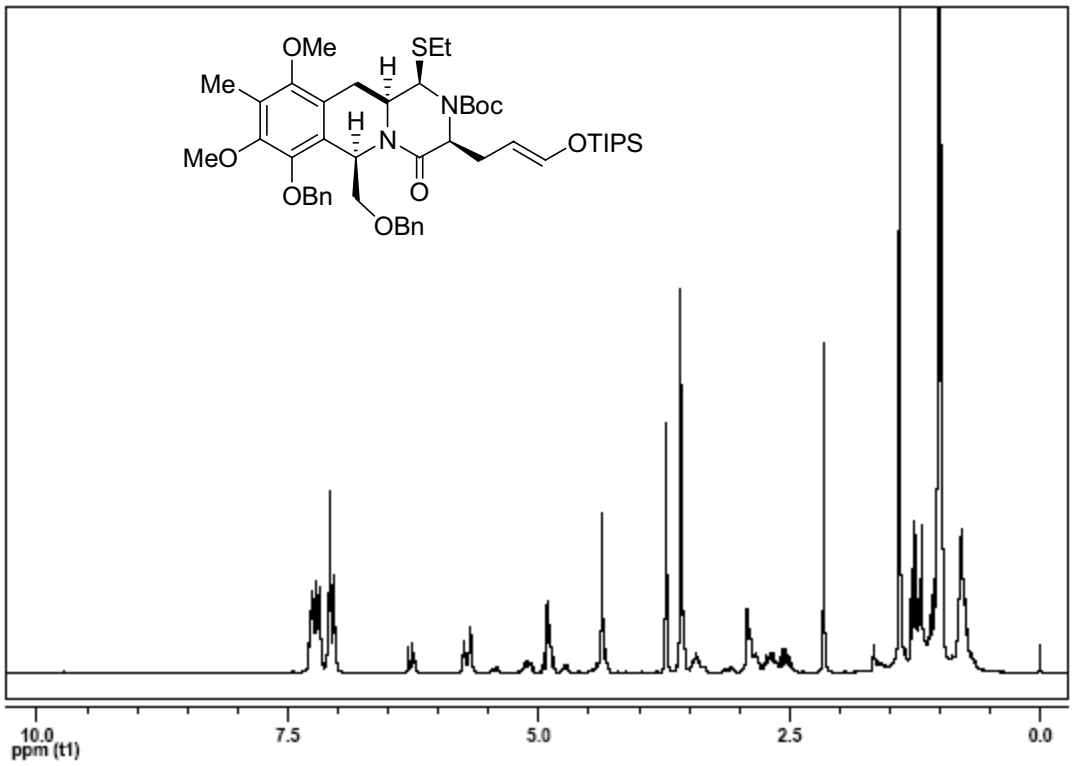


^{13}C NMR (75 MHz, $CDCl_3$)

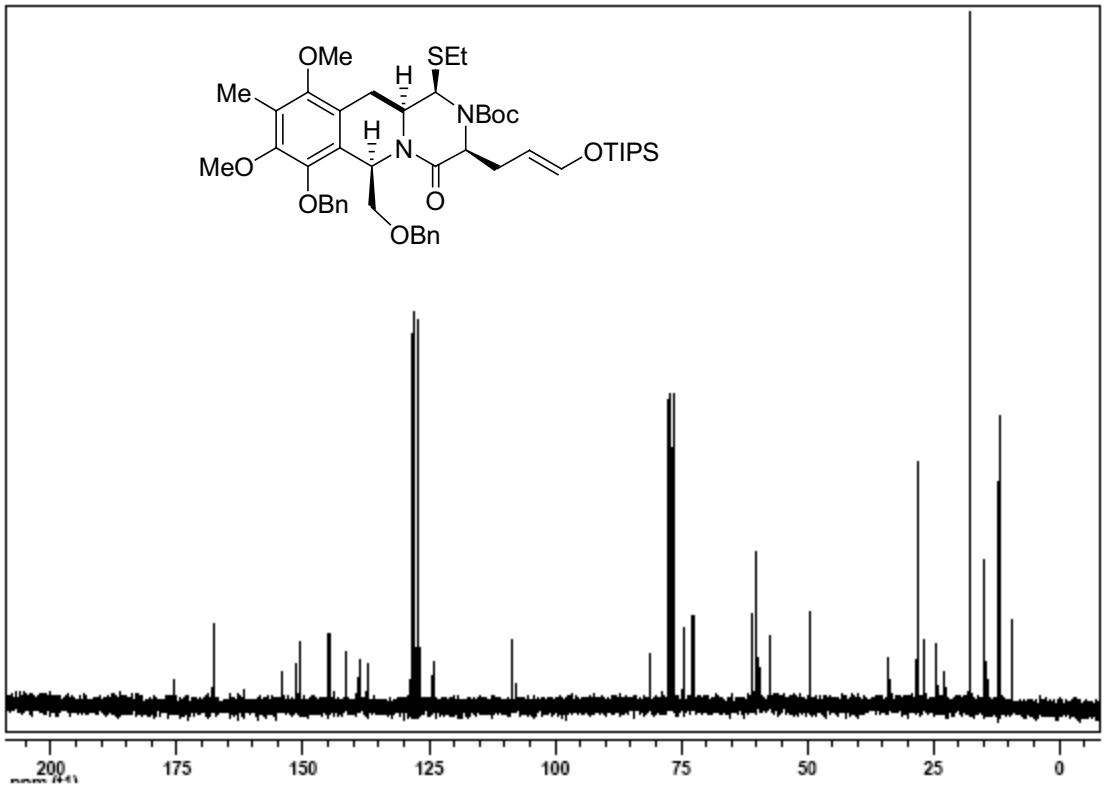


4cf. Silyl enol ether **26**

^{1}H NMR (300 MHz, $CDCl_3$)

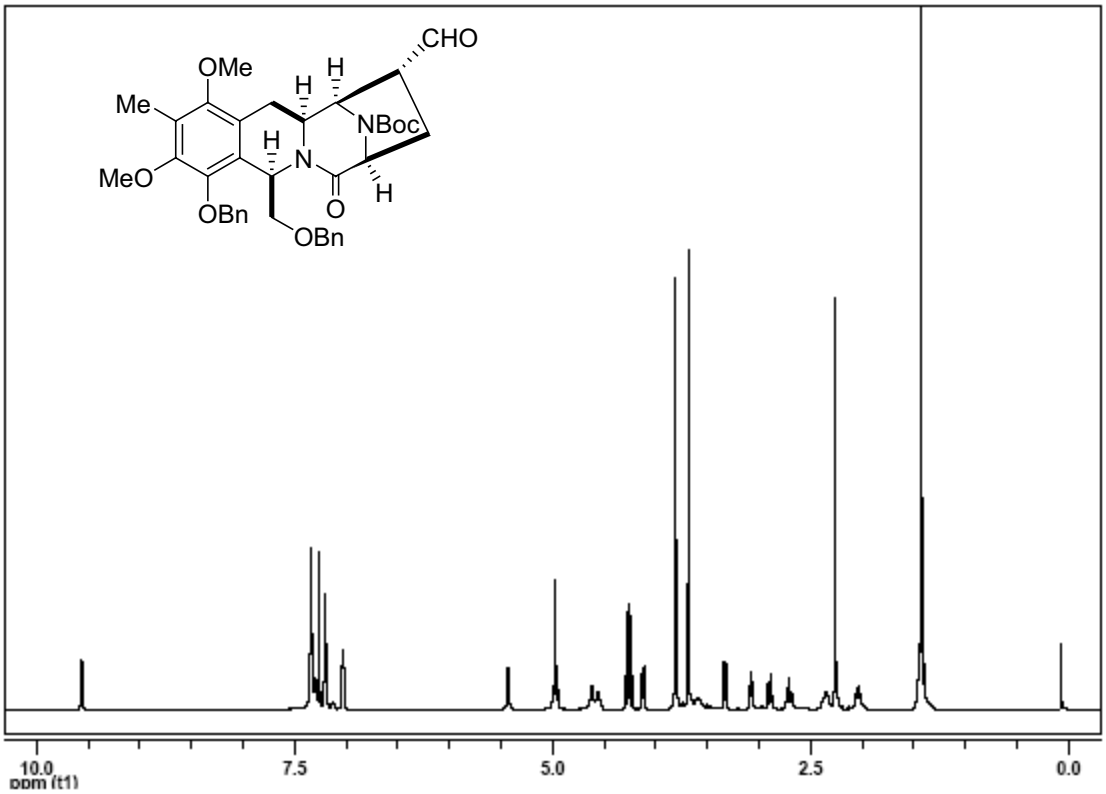


^{13}C NMR (75 MHz, $CDCl_3$)

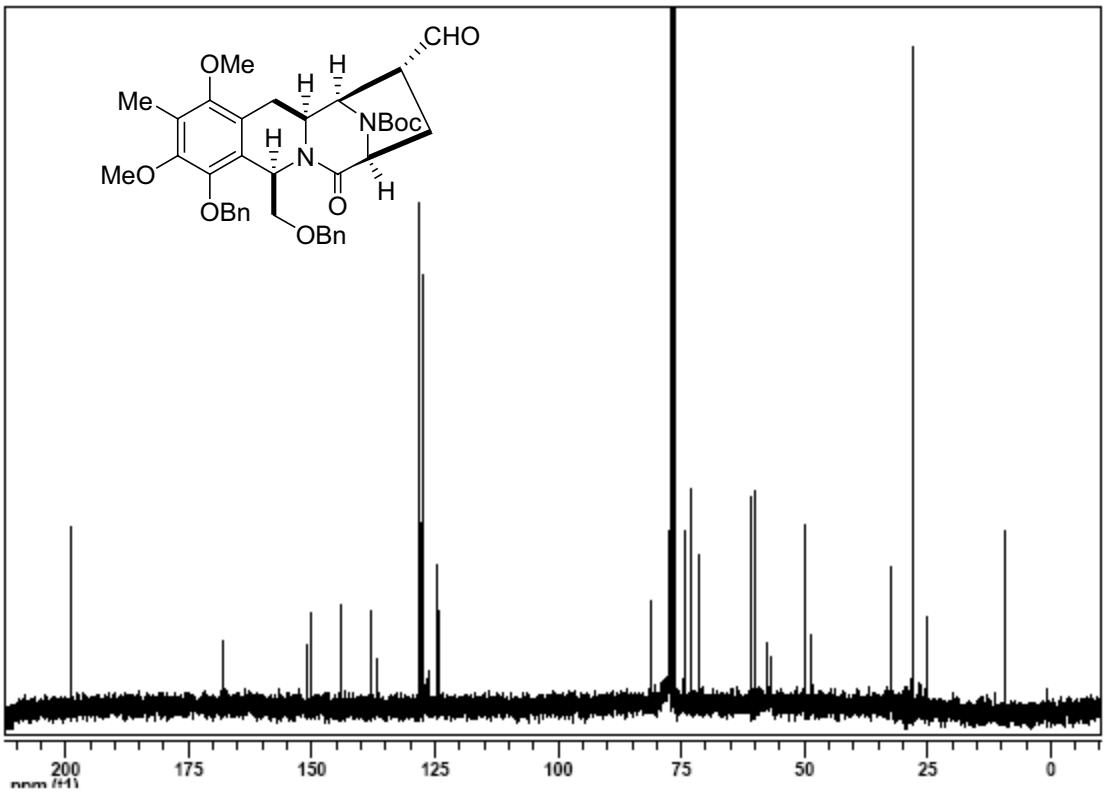


4cg. Tetracyclic aldehyde **27**

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

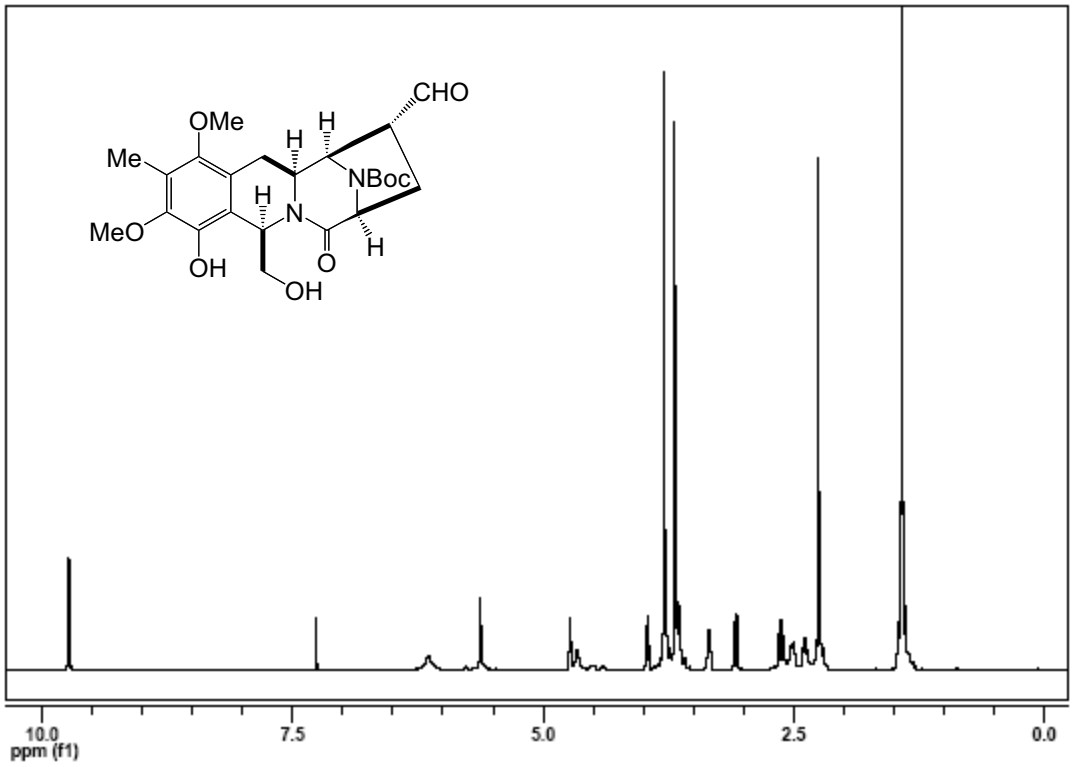


^{13}C NMR (75 MHz, $CDCl_3$)

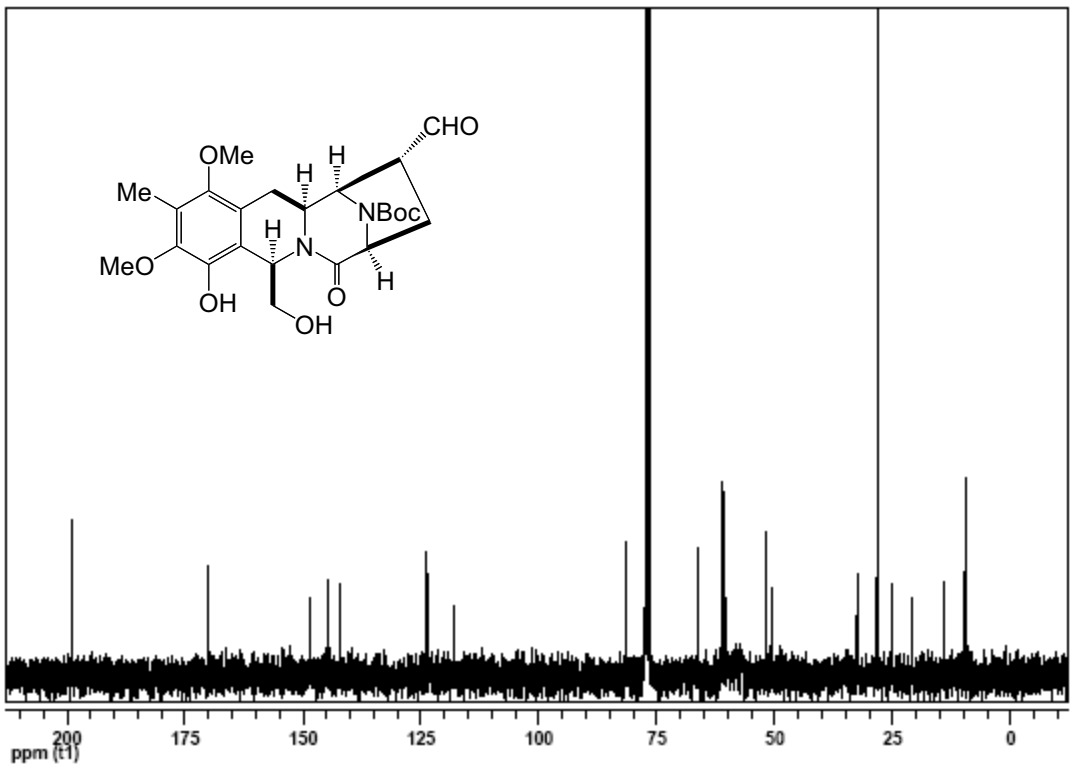


4ch. Tetracyclic alcohol **3**

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

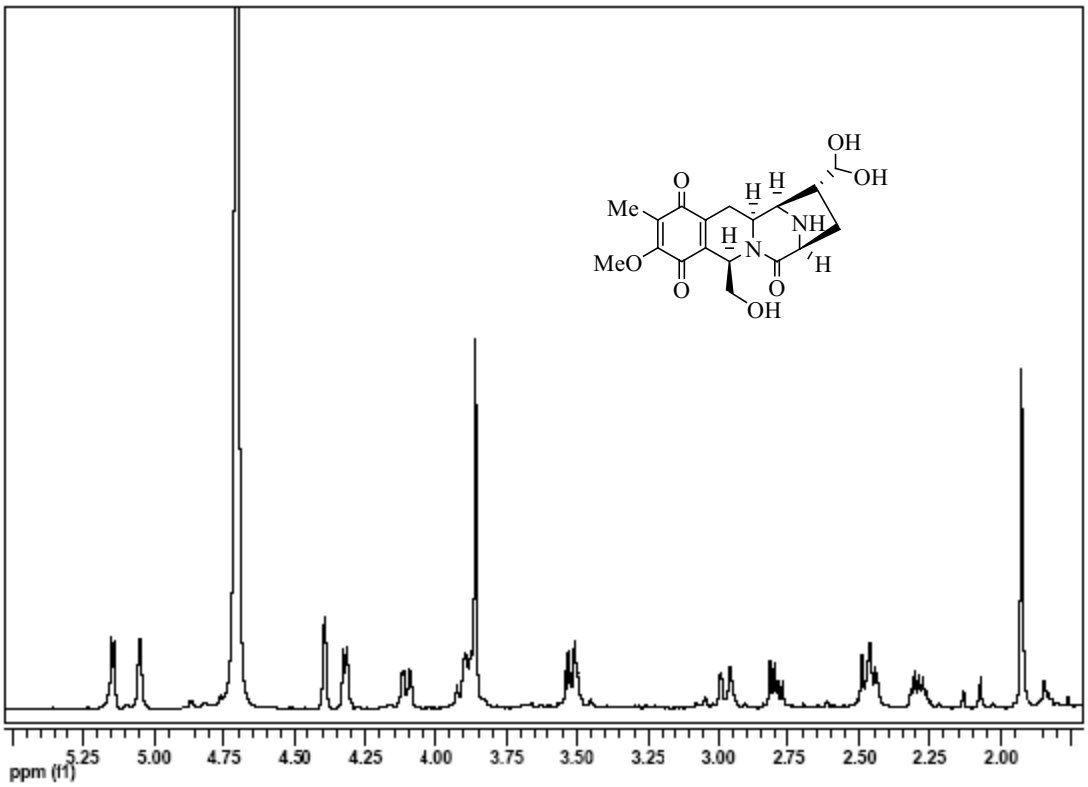


^{13}C NMR (75 MHz, $CDCl_3$)

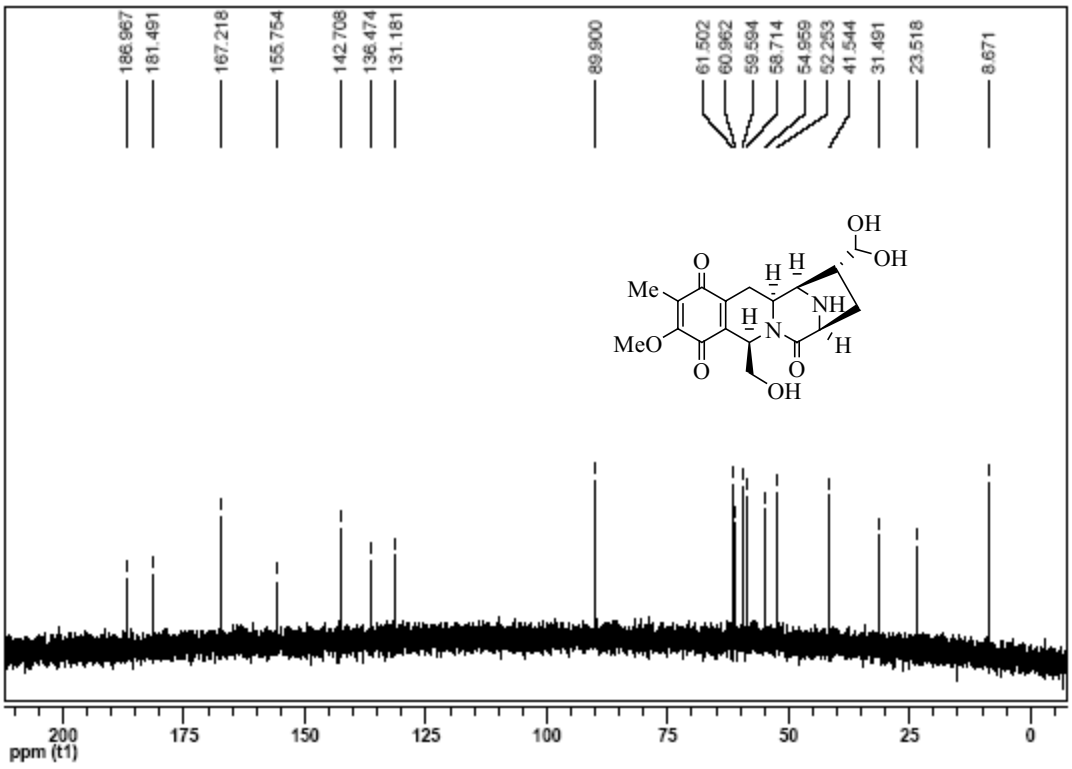


4ci. Lemonomycinone amide (**2**)

^{1}H NMR (500 MHz, D_2O)

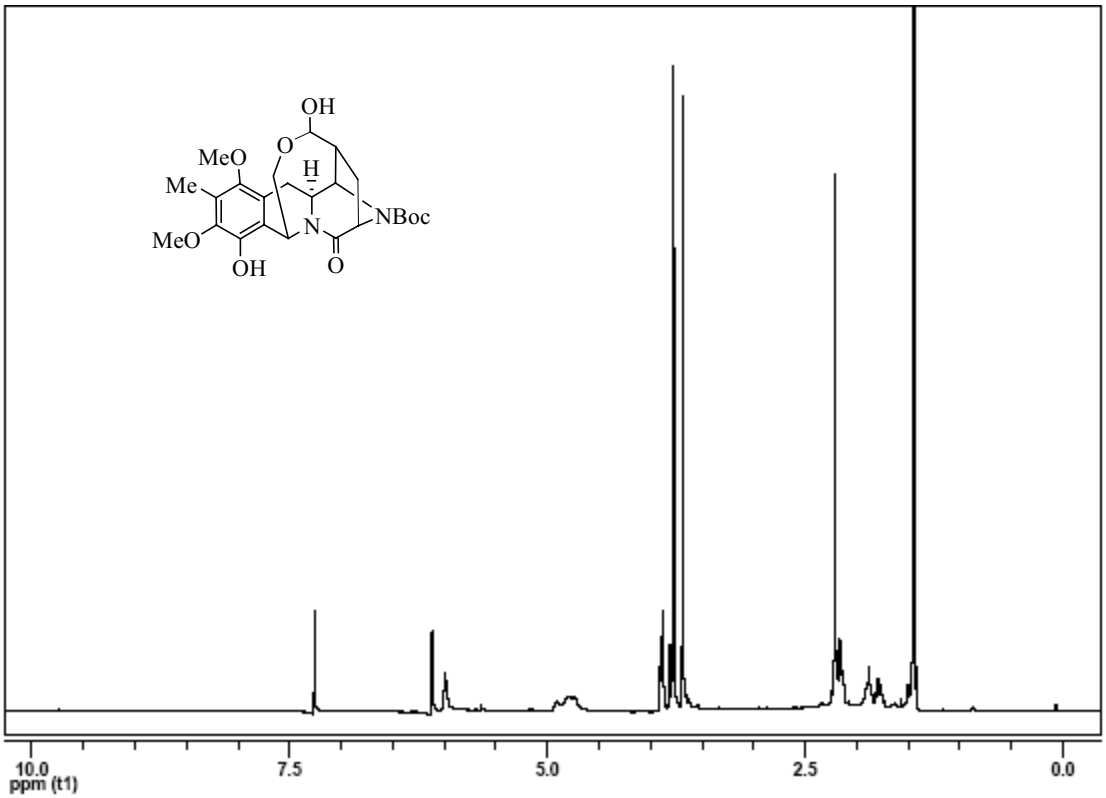


^{13}C NMR (75 MHz, D_2O)

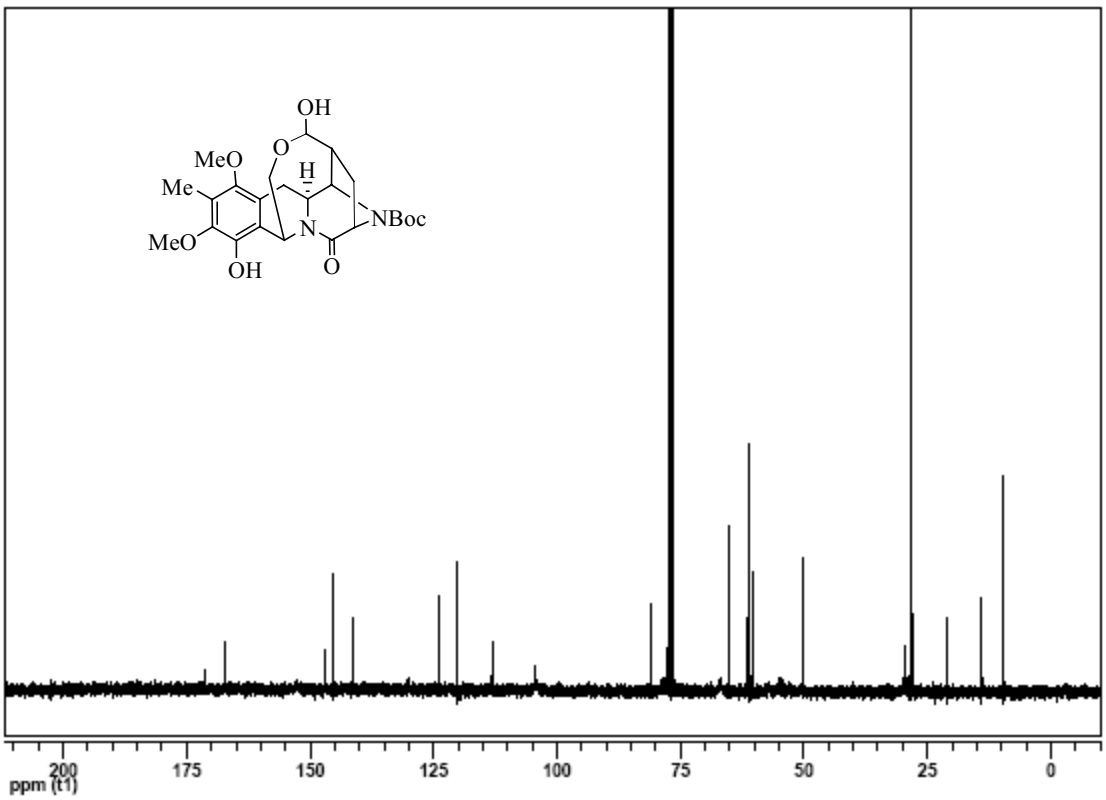


4cj Hemi-acetal **28**

^{1}H NMR (300 MHz, D_2O)

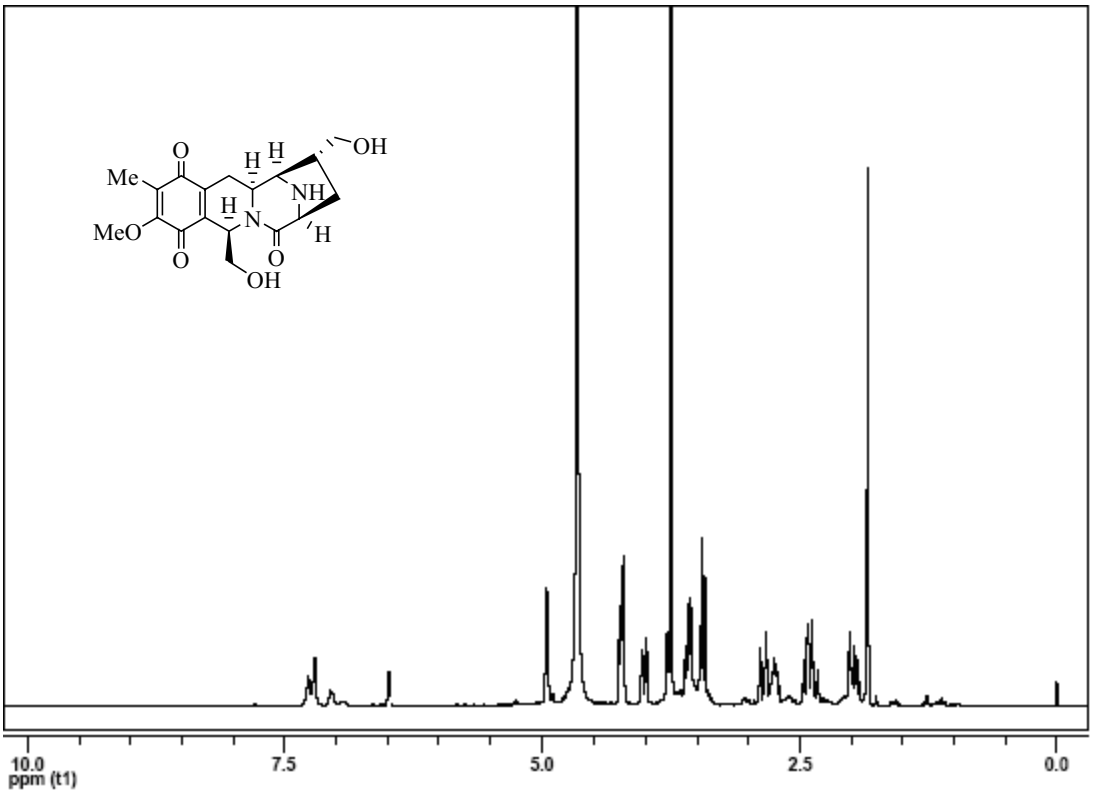


^{13}C NMR (75 MHz, D_2O)

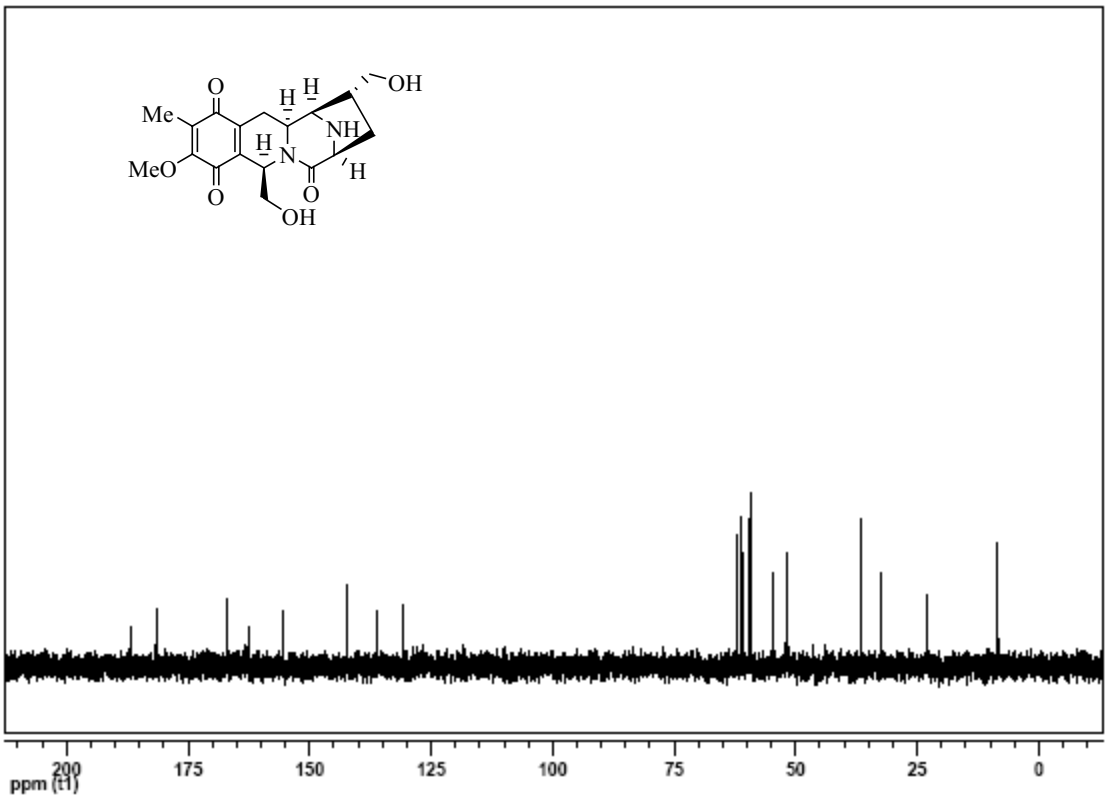


4cj Lemonomycinone alcohol **30**

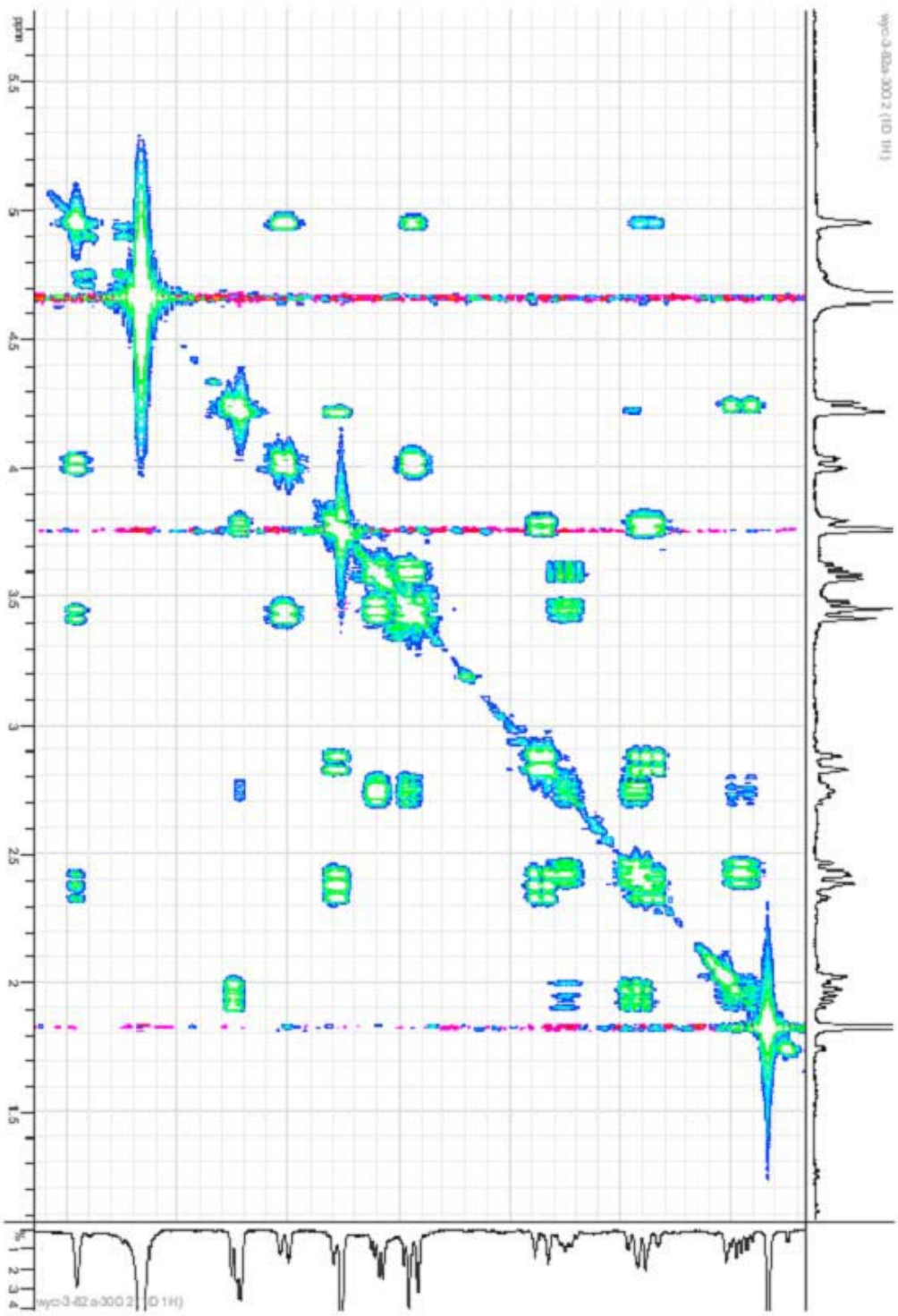
^{1}H NMR (300 MHz, D_2O)



^{13}C NMR (75 MHz, D_2O)

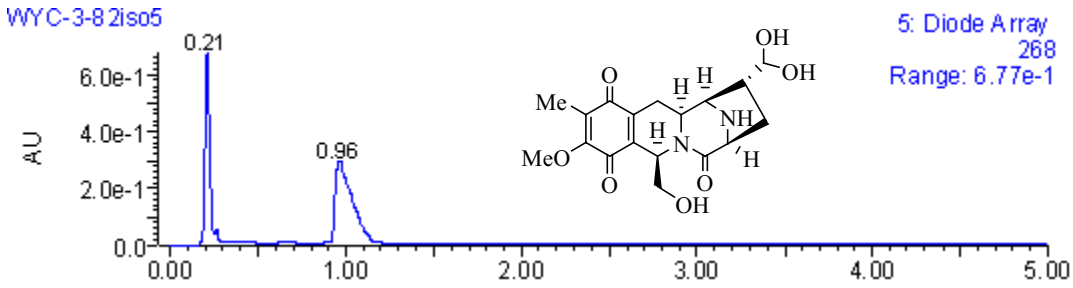


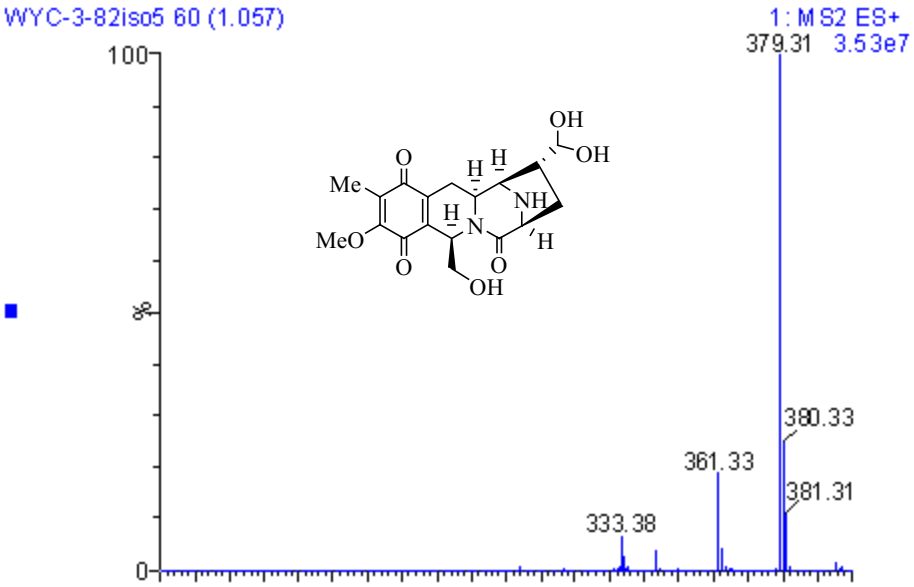
4cj Lemonomycinone alcohol **30**
COSY 1H/1H (300 MHz, D_2O)

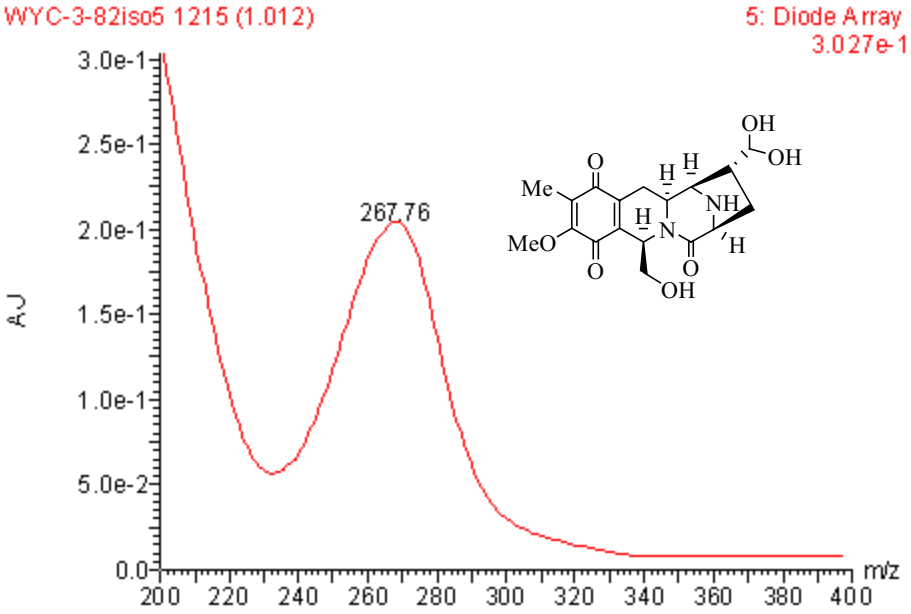


5. HPLC/ESI-MS Diagram

5a. Crude Lemonomycinone amide (**2**)







5b. Lemonomycinone alcohol **30**