

A flexible enantioselective total synthesis of Diospongins A, B and their stereoisomers using catalytic hetero-Diels-Alder/Rh-catalyzed 1,4-addition and asymmetric transfer hydrogenation reactions as key steps

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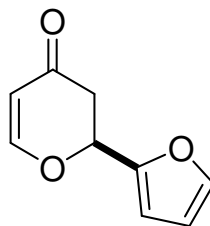
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GENERAL EXPERIMENTAL PROCEDURES: All reactions were conducted under inert atmosphere, if argon mentioned. Apparatus used for reactions are perfectly oven dried. THF was distilled from sodium benzophenone ketyl, and CH_2Cl_2 , DMSO, from CaH_2 . 4A° Molecular sieves were powdered, flame dried before use. ^1H NMR spectra were recorded at 200, 300, 400, 500 and ^{13}C NMR 50, 75, 100, 125 MHz in CDCl_3 solutions unless otherwise mentioned, δ in ppm, J in Hz. IR (FT-IR) spectrometer measured as KBr pellet or as film. Mass spectral data were obtained using MS (EI) ESI, HRMS mass spectrometers. Optical rotations are measured on Horiba rectangular 20 polarimeter. HPLC was carried on a Shimadzu LC-10AT vp dual pump system. Column chromatography was carried out on silica gel, grade 60-120, and 100-200 mesh. The TBAF used in reactions was supplied by Spectrochem. Pvt.Ltd., (India) and Aldrich, USA.

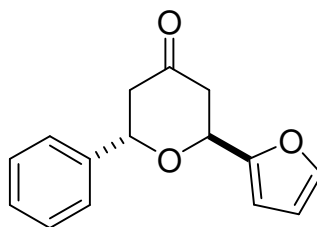
(S)-2-(Furan-2-yl)-2, 3-dihydropyran-4-one (7):



A mixture of (*S*)-(+)-BINOL (0.276 g, 0.96 mmol), 1M $\text{Ti}(\text{O}^i\text{Pr})_4$ in CH_2Cl_2 (0.48 mL, 0.48 mmol), $\text{CF}_3\text{CO}_2\text{H}$ (0.028 mL, 0.5 M in CH_2Cl_2), and flame dried powdered 4A° molecular sieves (1.86 g) in ether (20 mL) was heated at reflux for 1 h. The red-brown mixture was cooled to room temperature, and furfuraldehyde (0.460 g (0.39 mL, 4.83 mmol) was added. The mixture was stirred for 5 min and cooled to -78°C , Danishefsky's diene (1.0 g, 5.80 mmol) was added, and the reaction mixture was stirred for 10 min and then placed in a -20°C bath. After 40 h, saturated NaHCO_3 (0.5 mL) was added, and the reaction mixture was stirred for 1 h and then filtered through a plug of celite. The organic layer was separated, and the aqueous layer was extracted with ether (3 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under

reduced pressure. The crude product was dissolved in CH_2Cl_2 (60 mL) and cooled to 0°C . To this solution was added $\text{CF}_3\text{CO}_2\text{H}$ (0.25 mL) and stirred for 1 h, saturated NaHCO_3 (30 mL) was added, the reaction mixture was stirred for 10 min, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL), and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (10% acetone in hexane), to afford 1.25 g of product **7** as a crystalline solid. M. P = $73\text{--}75^\circ\text{C}$; $[\alpha]_{\text{D}}^{23} = +355$ ($c = 1.3$, CH_2Cl_2) [a single recrystallization from 1:2 Et_2O :hexanes gave white needle like crystals in 60% yield (1.05 g), $[\alpha]_{\text{D}}^{23} = +359$ ($c = 1.2$, CH_2Cl_2)]; IR ν (cm^{-1}): 2923, 2852, 1724, 1595, 1268, 1114, 1039, 747; ^1H NMR (400 MHz, CDCl_3): δ 7.48 (d, $J = 1.4$ Hz, 1H), 7.38 (d, $J = 6.6$ Hz, 1H), 6.46 (d, $J = 3.6$ Hz, 1H), 6.42 (t, $J = 1.4$ Hz, 1H), 5.51 (t, $J = 5.8$ Hz, 1H), 5.47 (d, $J = 3.6$ Hz, 1H), 3.10 (dd, $J = 13.1, 16.8$ Hz, 1H), 2.74 (dd, $J = 3.6, 16.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.3, 162.4, 149.9, 143.5, 110.5, 109.6, 107.3, 73.5, 39.4; MS (ESI) m/z 165 ($\text{M}+\text{H}$) $^+$.

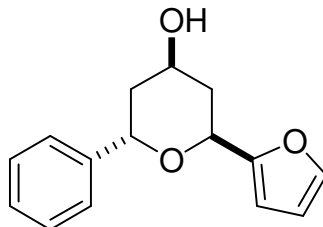
(2*S*, 6*S*)-2-(Furan-2-yl)-6-phenyl-tetrahydropyran-4-one (8):



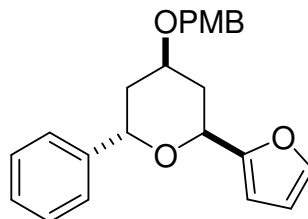
A mixture of **7** (1.05 g, 6.40 mmol), phenyl boronic acid (1.56 g, 12.8 mmol), $\text{Rh(I)(cod)}_2\text{BF}_4$ (0.052 g, 0.16 mmol), 1.0 mL of H_2O , KOH (0.018 g, 0.32 mmol) and 20 mL of dioxane was heated at reflux for 4 h. The reaction mixture was cooled to room temperature and diluted with ethyl acetate (40 mL) and filtered through a pad of silica gel. The filtrate was concentrated in *vacuo* and the residue was subjected to silica gel flash column chromatography (5% EtOAc in hexane) to afford 1.51 g (98%) of product **8** as a crystalline solid. M. P = $84\text{--}86^\circ\text{C}$; $[\alpha]_{\text{D}}^{23} = -10$ ($c = 0.5$, CHCl_3); IR ν (cm^{-1}): 2923, 2853, 1721, 1458, 1255, 1064, 1016, 752, 700; ^1H NMR (400 MHz, CDCl_3): δ 7.44 (d, $J = 1.5$ Hz, 1H), 7.40–7.25 (m, 5H), 6.36 (t, $J = 5.3$ Hz, 2H), 5.44 (dd, $J = 3.0, 6.8$ Hz, 1H), 4.74 (t, $J = 7.5$ Hz, 1H), 2.96 (dd, $J = 6.8, 15.1$ Hz, 1H), 2.87 (dd, $J = 3.02, 15.1$ Hz, 1H), 2.72 (d, $J =$

7.5 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 151.1, 143.2, 140.2, 128.6, 128.1, 126.1, 110.2, 73.2, 69.0, 48.5, 43.4; MS (ESI) m/z 243 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) m/z 243.1026 (calcd for $\text{C}_{15}\text{H}_{15}\text{O}_3$: 243.1016).

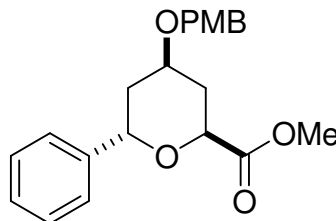
(2*S*, 4*R*, 6*S*)-2-(Furan-2-yl)-6-phenyl-tetrahydro-2*H*-pyran-4-ol (9):



To a solution of **8** (1.51 g, 6.24 mmol) in anhydrous EtOAc (12 mL) under argon was added Et_3N : HCOOH (5:2) mixture (0.90 mL) followed by the addition of Ru-catalyst A (0.019 g, 0.031 mmol, 0.5 mol %) which was pre-dissolved in CH_2Cl_2 (2 x 1 mL). The resulting reaction mixture was heated to 50°C for 3h. After cooling the reaction mixture to room temperature diluted with ethyl acetate (20 mL) and filtered through a pad of silica gel. The filtrate was concentrated in *vacuo* and the residue was subjected to silica gel flash column chromatography (25% EtOAc in Hexane) to afford 1.46 g (96%) of compound **9** as a crystalline solid. M. P = 65-68 °C; $[\alpha]_{\text{D}}^{23} = -17$ ($c = 0.5$, CHCl_3); IR ν (cm^{-1}): 3404, 2925, 2856, 1451, 1366, 1060, 1011, 738; ^1H NMR (400 MHz, CDCl_3): δ 7.44 (d, $J = 8.3$ Hz, 1H), 7.37-7.21 (m, 5H), 6.32 (t, $J = 3.0$ Hz, 1H), 6.29 (d, $J = 3.7$ Hz, 1H), 5.21 (t, $J = 4.5$ Hz, 1H), 4.66 (dd, $J = 3.7, 9.0$ Hz, 1H), 4.03 (m, 1H), 2.48 (dt, $J = 4.5, 13.5$ Hz, 1H), 2.13 (dt, $J = 3.7, 12.8$ Hz, 1H), 2.02-1.95 (m, 2H); ^{13}C (100 MHz, CDCl_3): δ 154.3, 142.2, 140.1, 128.6, 127.2, 126.3, 110.2, 106.9, 72.3, 65.8, 64.1, 37.4, 36.8; MS (ESI) m/z 267 ($\text{M}+\text{Na}$) $^+$; HRMS (ESI) m/z 267.1000 (calcd for $\text{C}_{15}\text{H}_{16}\text{O}_3\text{Na}$: 267.0997).

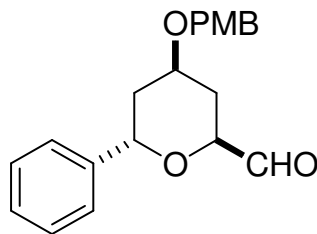
(2*S*, 4*R*, 6*S*)-2-(Furan-2-yl)-4-(4-methoxybenzyloxy)-6-phenyl-tetrahydro-2*H*-pyran (10):

To a solution of **9** (1.46 g, 5.98mmol) in DMF (30 mL) was added 60 % dispersion sodium hydride (0.718 g, 29.9 mmol) at 0°C. After the solution was stirred for 30 min at the same temperature, 4-Methoxybenzyl chloride (3.74 g, 23.9 mmol) was added. The resulting reaction mixture was stirred for 12 h at room temperature under argon. The reaction mixture was quenched with water and extracted with EtOAc (3 X 30 mL). The organic layers were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by flash chromatography (10% EtOAc in hexane) to afford 2.13 g (98%) of product **10** as a colourless oil. $[\alpha]_D^{23} = -36.5$ ($c = 0.7$, CHCl₃); IR ν (cm⁻¹): 3448, 2929, 2860, 1612, 1513, 1248, 1089, 1035, 816, 737; ¹H NMR (400 MHz, CDCl₃): δ 7.46-7.34 (m, 6H), 7.28 (d, $J = 8.0$ Hz, 2H), 6.90 (d, $J = 8.8$ Hz, 2H), 6.36 (t, $J = 3.6$ Hz, 1H), 6.34 (d, $J = 3.6$ Hz, 1H), 5.29 (t, $J = 4.4$ Hz, 1H), 4.65 (dd, $J = 3.6, 10.2$ Hz, 1H), 4.59 (d, $J = 11.7$ Hz, 1H), 4.51 (d, $J = 11.7$ Hz, 1H), 3.82 (s, 3H), 3.78 (m, 1H), 2.59 (m, 1H), 2.23 (m, 1H), 2.07 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 159.2, 154.2, 142.1, 140.2, 130.5, 129.2, 128.6, 127.1, 126.4, 113.8, 110.1, 106.6, 72.8, 70.4, 69.6, 65.9, 55.2, 34.9, 33.8; MS (ESI) m/z 387 (M+Na)⁺; HRMS (ESI) m/z 387.1588 (calcd for C₂₃H₂₄O₄Na: 387.1572).

(2*S*, 4*R*, 6*S*)-Methyl 4-(4-methoxybenzyloxy)-6-phenyl-tetrahydro-2*H*-pyran-2-carboxylate:

Ozone was passed for 10 min through a cooled (-78°C) solution of **10** (2.13 g, 5.85 mmol) in 150 mL MeOH:CH₂Cl₂ (1:1), Me₂S (0.725 g, 11.7 mmol) was added to the reaction mixture and further stirring was continued for 30 min at -78 °C and 1 h at room temperature. The solvent was removed under reduced pressure. The crude residue was dissolved in diethyl ether (10 mL) and cooled to 0°C in an ice bath. To this, ethereal solution of diazomethane (10 equiv) (**Caution:** Liquid diazomethane, is an explosive compound and explosions may occur in the gaseous state if the substance is dry and undiluted) was added and resulting reaction mixture stirred for 1 h (the reaction progress was monitored by TLC). Then, the reaction mixture was allowed to stand overnight to escape the left over diazomethane in a well ventilated fuming cupboard. The residual solvent was removed under reduced pressure and the crude residue was purified by column chromatography (15% EtOAc in hexane) to yield methyl ester 1.79 g (86%) as a colourless oil. $[\alpha]_D^{23} = -32.1$ ($c = 0.7$, CHCl₃); IR ν (cm⁻¹): 2923, 2853, 1746, 1512, 1246, 1173, 1034, 819, 755; ¹H NMR (400 MHz, CDCl₃): δ 7.41-7.32 (m, 5H), 7.27 (d, $J = 8.8$ Hz, 2H), 6.89 (d, $J = 8.8$, 2H), 5.38 (dd, $J = 2.2$, 10.2 Hz, 1H), 4.54 (d, $J = 11.7$ Hz, 1H), 4.50 (dd, $J = 0.7$, 2.2 Hz, 1H), 4.40 (d, $J = 11.7$ Hz, 1H), 3.88 (m, 1H), 3.81 (s, 3H), 3.67 (s, 3H), 2.52 (m, 2H), 2.06 (m, 2H), 1.89 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 172.9, 158.9, 141.8, 128.8, 128.3, 127.4, 126.2, 113.7, 113.6, 70.4, 70.0, 69.8, 69.6, 55.2, 51.9, 36.8, 30.4; MS (ESI) m/z 379 (M+Na)⁺; HRMS (ESI) m/z 379.1542 (calcd for C₂₁H₂₄O₅Na: 379.1521).

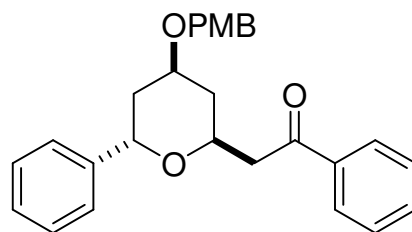
(2*S*,4*R*,6*S*)-4-(4-Methoxybenzyloxy)-6-phenyl-tetrahydro-2*H*-pyran-2-carbaldehyde (11):



To a solution of methyl ester (1.79 g, 5.02 mmol) in CH₂Cl₂ (20 mL) was added DIBAL-H (1.07 g, 7.54 mmol, 1M solution in toluene) at -78°C. The reaction mixture was stirred for 1 h at the same temperature and then quenched with saturated sodium potassium tartarate solution. The aqueous layer extracted with CH₂Cl₂ (3x25 mL). The combined organic layers were washed

with brine solution, dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10% EtOAc in hexane) to yield 1.47 g (90%) of product **11** as a colourless oil. $[\alpha]_{\text{D}}^{23} = -86.5$ ($c = 1.0$, CHCl_3); IR ν (cm^{-1}): 3444, 2929, 1729, 1610, 1512, 1248, 1089, 1034, 822, 757, 700; ^1H NMR (400 MHz, CDCl_3): δ 10.01 (s, 1H), 7.41- 7.24 (m, 7H), 6.89 (d, $J = 8.2$ Hz, 1H), 5.23 (dd, $J = 3.0, 11.2$ Hz, 1H), 4.48 (d, $J = 11.2$ Hz, 1H), 4.33 (d, $J = 11.2$ Hz, 1H), 4.28 (dd, $J = 2.2, 6.7$ Hz, 1H), 3.89 (m, 1H), 3.81 (s, 3H), 2.42 (m, 1H), 2.01 (m, 2H), 1.83 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 203.3, 159.1, 141.7, 130.1, 129.2, 128.4, 127.7, 126.0, 113.8, 76.8, 70.4, 69.6, 69.4, 55.2, 36.9, 29.5; HRMS (ESI) m/z 349.1421 (calcd for $\text{C}_{20}\text{H}_{22}\text{O}_4\text{Na}$: 349.1415).

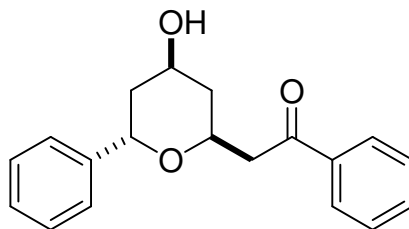
(2-((2S, 4S, 6S)-4-(4-Methoxybenzyloxy)-6-phenyl-tetrahydro-2H-pyran-2-yl)-1-phenylethanone) (13):



To a -78°C stirred solution of **12** (1.14 g, 4.96 mmol) in THF (40 mL) was slowly added $n\text{-BuLi}$ (0.316 g, 4.96 mmol, 3.0 mL, 1.6 M solution in hexane). After stirring the solution for 15 min, a solution of **11** (1.47 g, 4.50 mmol) in THF (25 mL) was added, then stirred for 1 h. The reaction mixture was warmed to room temperature, and resulting solution was carefully concentrated to 1/3 of original volume under reduced pressure. To the resulting reaction mixture, a acetone solution (0.8 M) of Cl_3COOH (25 mL) was added and resulting reaction mixture stirred at room temperature for 6 h. The reaction mixture was neutralized by addition of saturated aq NaHCO_3 until gas evolution subsides and extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine solution and dried over anhydrous Na_2SO_4 , then concentrated under reduced pressure. The crude residue was purified by flash column chromatography over silica gel (10% EtOAc in hexane) to afforded product **13** (1.40 g, 75%) as colourless oil. $[\alpha]_{\text{D}}^{23} = -45.5$ ($c = 1.0$, CHCl_3); IR ν (cm^{-1}): 3061, 2926, 2854, 1683, 1598, 1513,

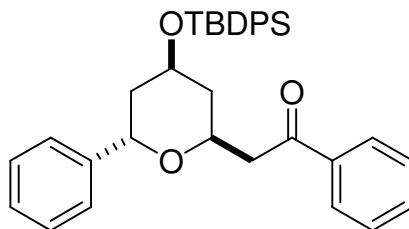
1448, 1250, 1068, 755, 698; ^1H NMR (400 MHz, CDCl_3): δ 7.96 (d, $J = 7.3$ Hz, 2H), 7.57 (t, $J = 7.3$ Hz, 1H), 7.45 (t, $J = 7.3$ Hz, 2H), 7.31-7.21 (m, 7H), 6.86 (d, $J = 8.8$ Hz, 2H), 5.14 (t, $J = 5.1$ Hz, 1H), 4.50 (m, 2H), 4.28 (m, 1H), 3.80 (s, 3H), 3.72 (m, 1H), 3.43 (dd, $J = 6.6, 16.1$ Hz, 1H), 3.27 (dd, $J = 5.8, 16.1$ Hz, 1H), 2.39 (ddd, $J = 3.6, 8.0, 13.2$ Hz, 1H), 2.05 (ddd, $J = 3.6, 8.0, 13.2$ Hz, 1H), 1.95 (m, 1H), 1.58 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 198.4, 140.6, 137.2, 133.1, 130.6, 129.2, 128.5, 128.4, 128.2, 127.1, 126.3, 126.1, 113.8, 71.9, 70.7, 69.8, 67.3, 55.3, 44.4, 36.4, 34.4; MS (ESI) m/z 439 ($\text{M}+\text{Na}$) $^+$; HRMS (ESI) m/z 439.1888 (calcd for $\text{C}_{27}\text{H}_{28}\text{O}_4\text{Na}$: 439.1885).

Diospongins B (1):

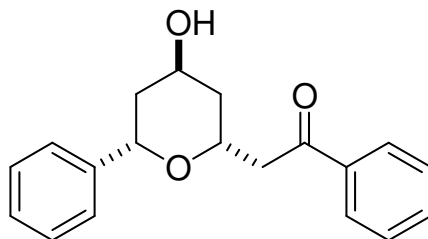


To a stirred solution of **13** (1.40 g, 3.37 mmol) in $\text{CH}_2\text{Cl}_2:\text{H}_2\text{O}$ (9:1) (70 mL) was added DDQ (0.919 g, 4.05 mmol) at 0°C and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was quenched with saturated NaHCO_3 solution and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with H_2O followed by brine solution and dried over anhydrous Na_2SO_4 , then concentrated under reduced pressure. The crude residue was purified by flash column chromatography (30% EtOAc in hexane) to afford the product 0.91 g (92%) as an amorphous solid. $[\alpha]_D^{25} = -22.5$ ($c = 0.2$, CHCl_3); IR ν (cm^{-1}): 3624, 2925, 2857, 2312, 1740, 1682, 1515, 1452, 1174, 753; ^1H NMR (400 MHz, CDCl_3): δ 7.98 (d, $J = 8.9$ Hz, 2H), 7.57 (t, $J = 7.6$ Hz, 1H), 7.47 (t, $J = 8.2$ Hz, 2H), 7.34 (m, 5H), 5.19 (t, $J = 4.4$ Hz, 1H), 4.23 (m, 1H), 4.02 (m, 1H), 3.45 (dd, $J = 7.0, 15.7$ Hz, 1H), 3.17 (dd, $J = 5.9, 15.7$ Hz, 1H), 2.51 (ddd, $J = 3.8, 5.1, 13.4$ Hz, 1H), 2.05 (ddd, $J = 4.4, 8.9, 14.6$ Hz, 1H), 1.92 (ddd, $J = 5.0, 9.7, 13.5$ Hz, 1H), 1.50 (dt, $J = 9.3, 12.3$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 198.3, 140.2, 137.2, 133.2, 128.6, 128.5, 128.3, 127.1, 126.3, 72.3, 66.9, 64.2, 44.6, 40.1, 36.7; MS (ES) m/z 319 ($\text{M}+\text{Na}$) $^+$; HRMS (ESI) m/z 319.1301 (calcd for $\text{C}_{19}\text{H}_{20}\text{O}_3\text{Na}$: 319.1310).

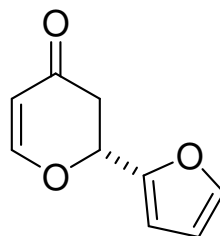
[2-((2*S*, 4*S*, 6*S*)-4-(*tert*-Butyldiphenylsilyloxy)-6-phenyl-tetrahydro-2*H*-pyran-2-yl)-1-phenylethanone] (14**):**



To a stirred solution of **1** (0.5 g, 1.68 mmol) in CH₂Cl₂ (15 mL) was added Et₃N (0.341 g, 3.37 mmol) at 0°C. After stirring the solution for 15 min, *tert*-Butyldiphenylsilyl chloride (0.927 g, 3.37 mmol) and DMAP (0.020 g, 0.16 mmol) was sequentially at the same temperature. The resulting reaction mixture was stirred at room temperature for 6 h, quenched with saturated NH₄Cl solution and extracted with CH₂Cl₂ (3 x 20 mL). The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (10% EtOAc in hexane) to afford the product **14** 0.853 g (95%) as colourless oil. $[\alpha]_D^{23} = -31.0$ ($c = 0.25$, CHCl₃); IR ν (cm⁻¹): 3068, 2927, 2855, 1681, 1466, 1215, 1110, 760, 701; ¹H NMR (400 MHz, CDCl₃): δ 7.94 (d, $J = 7.3$ Hz, 2H), 7.71 (d, $J = 6.7$ Hz, 2H), 7.62 (m, 3H), 7.47-7.36 (m, 8H), 7.05 (d, $J = 4.8$ Hz, 3H), 6.71 (t, $J = 4.8$ Hz, 2H), 4.97 (t, $J = 3.7$ Hz, 1H), 4.03 (m, 1H), 3.94 (m, 1H), 3.37 (dd, $J = 7.0, 15.7$ Hz, 1H), 3.01 (dd, $J = 5.9, 15.7$ Hz, 1H), 2.11 (m, 1H), 2.00 (m, 1H), 1.86 (m, 1H), 1.65 (m, 1H), 1.05 (s, 9H); ¹³C (100 MHz, CDCl₃): δ 198.3, 139.8, 137.0, 135.9, 135.7, 134.0, 133.7, 133.0, 129.7, 129.6, 128.5, 128.2, 128.1, 127.7, 127.6, 126.6, 126.1, 72.2, 66.8, 65.4, 44.7, 40.2, 36.5, 26.9, 19.0; MS (ESI) m/z 557 (M+Na)⁺; HRMS (ESI) m/z 535.2692 (calcd for C₃₅H₃₉O₃ Si: 535.2668).

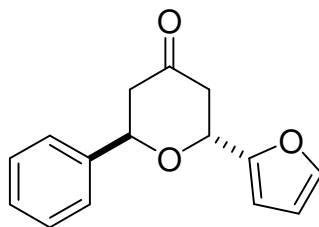
Diospongin A (2):

To a stirred solution of **14** (0.853 g, 1.59 mmol) in THF (15 mL) was added TBAF (Specrochem Pvt.Ltd., India) (15.7 mL 15.9 mmol, 1M solution in THF) at 0°C and the reaction mixture was stirred at room temperature over night. The reaction mixture was quenched with H₂O and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine solution and dried over anhydrous Na₂SO₄, then concentrated under reduced pressure. The crude residue was purified by column chromatography over silica gel (26% EtOAc in hexane) to afford product **2** (0.238 g, 86%) as an amorphous solid. $[\alpha]_D^{23} = -19.2$ ($c = 1.2$, CHCl₃); IR ν (cm⁻¹): 3624, 2925, 2857, 2312, 1740, 1682, 1515, 1452, 1174, 753; ¹H NMR (400 MHz, CDCl₃): δ 7.97 (d, $J = 6.8$ Hz, 2H), 7.53 (t, $J = 6.8$ Hz, 1H), 7.43 (t, $J = 7.5$ Hz, 2H), 7.22 (m, 2H), 4.90 (dd, $J = 1.5, 11.3$ Hz, 1H), 4.60 (m, 1H), 4.34 (t, $J = 2.3$ Hz, 1H), 3.39 (dd, $J = 5.3, 15.9$ Hz, 1H), 3.04 (dd, $J = 7.5, 16.6$ Hz, 1H), 1.95 (m, 2H), 1.67 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 198.3, 142.8, 137.5, 133.0, 128.5, 128.3, 128.2, 127.2, 125.8, 73.8, 69.1, 64.7, 45.2, 40.4, 38.8; MS (ESI) m/z 319 (m+Na)⁺; HRMS (ESI) m/z 319.1319 (calcd for C₁₉H₂₀O₃Na: 319.1310).

(R)-2-(Furan-2-yl)-2,3-dihydropyran-4-one (ent-7):

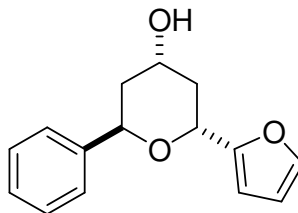
Same procedure was used for preparation of compound **ent-7** as used for **7** by using (*R*)-(+)-BINOL catalyst. $[\alpha]_D^{23} = -352$ ($c = 1.0$, CH_2Cl_2) [a single recrystallization from 1:2 Et₂O:hexanes gave white needle like crystals, M. P = 70-72 °C; $[\alpha]_D^{23} = -358$ ($c = 1.4$, CH_2Cl_2)]; IR ν (cm^{-1}): 2923, 2852, 1724, 1595, 1268, 1114, 1039, 747; ^1H NMR (400 MHz, CDCl_3): δ 7.48 (d, $J = 1.46$ Hz, 1H), 7.38 (d, $J = 5.8$ Hz, 1H), 6.46 (d, $J = 2.9$ Hz, 1H), 6.42 (dd, $J = 2.2, 3.6$ Hz, 1H), 5.50 (dd, $J = 5.8, 7.3$ Hz, 1H), 5.47 (d, $J = 4.39$ Hz, 1H), 3.10 (dd, $J = 12.4, 16.8$ Hz, 1H), 2.74 (dd, $J = 3.6, 16.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.4, 162.4, 149.4, 143.5, 110.5, 109.6, 107.3, 73.5, 39.4; MS (ES) m/z 165 ($\text{M}+\text{H}$)⁺.

(2*R*, 6*R*)-2-(Furan-2-yl)-6-phenyl-tetrahydropyran-4-one (ent-8):



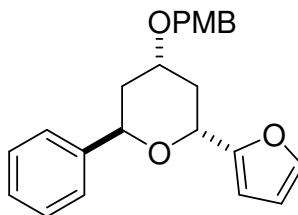
Same procedure was used for preparation of compound **ent-8** as used for **8**.

M. P = 86-89 °C; $[\alpha]_D^{23} = +10.9$ ($c = 0.5$, CHCl_3); IR ν (cm^{-1}): 2923, 2853, 1721, 1458, 1255, 1064, 1016, 752, 700; ^1H NMR (400 MHz, CDCl_3): δ 7.44 (d, $J = 1.5$ Hz, 1H), 7.39-7.29 (m, 5H), 6.37 (d, $J = 3.5$ Hz, 1H), 6.36 (t, $J = 1.4$ Hz, 1H), 5.44 (dd, $J = 3.5, 7.1$ Hz, 1H), 4.74 (dd, $J = 5.6, 7.8$ Hz, 1H), 2.96 (dd, $J = 6.3, 14.8$ Hz, 1H), 2.87 (dd, $J = 2.8, 15.5$ Hz, 1H), 2.72 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 205.5, 151.9, 143.2, 140.2, 128.6, 128.1, 126.1, 110.2, 73.2, 68.9, 48.4, 43.4; MS (ESI) m/z 243 ($\text{M}+\text{H}$)⁺; HRMS (ESI) m/z 243.1009 (calcd for $\text{C}_{15}\text{H}_{15}\text{O}_3$: 243.1016).

(2*R*, 4*S*, 6*R*)-2-(Furan-2-yl)-6-phenyl-tetrahydro-2*H*-pyran-4-ol (ent-9):

Same procedure was used for preparation of compound **ent-9** as used for **9**.

M. P = 64-66 °C; $[\alpha]_D^{23} = +18.5$ ($c = 1.0$, CHCl_3); IR ν (cm^{-1}): 3404, 2925, 2856, 1451, 1366, 1060, 1011, 738, 700; ^1H NMR (400 MHz, CDCl_3): δ 7.49 (d, $J = 8.0$ Hz, 1H), 7.42-7.27 (m, 5H), 6.37 (t, $J = 1.5$ Hz, 1H), 6.34 (d, $J = 2.9$ Hz, 1H), 5.26 (t, $J = 4.4$ Hz, 1H), 4.72 (dd, $J = 3.6, 8.7$ Hz, 1H), 4.10 (m, 1H), 2.53 (dt, $J = 4.4, 13.1$ Hz, 1H), 2.19 (dt, $J = 4.4, 13.2$ Hz, 1H), 2.02 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 154.3, 142.2, 140.2, 128.7, 127.3, 126.4, 110.4, 107.0, 72.2, 65.8, 64.2, 37.4, 36.9; MS (ESI) m/z 267 ($\text{M}+\text{Na}^+$); HRMS (ESI) m/z 267.1011 (calcd for $\text{C}_{15}\text{H}_{16}\text{O}_3\text{Na}$: 267.0997).

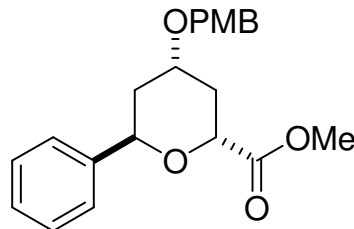
(2*R*,4*S*,6*R*)-2-(Furan-2-yl)-4-(4-methoxybenzyloxy)-6-phenyl-tetrahydro-2*H*-pyran (ent-10):

Same procedure was used for preparation of compound **ent-10** as used for **10**.

$[\alpha]_D^{23} = +37.0$ ($c = 0.9$, CHCl_3); IR ν (cm^{-1}): 3447, 2927, 2865, 1611, 1514, 1248, 1035, 816; ^1H NMR (400 MHz, CDCl_3): δ 7.44-7.33 (m, 6H), 7.27 (d, $J = 8.4$ Hz, 2H), 6.89 (d, $J = 8.8$ Hz, 2H), 6.35 (t, $J = 2.9$ Hz, 1H), 6.32 (d, $J = 2.9$ Hz, 1H), 5.28 (t, $J = 3.6$ Hz, 1H), 4.63 (dd, $J = 2.9, 10.2$ Hz, 1H), 4.57 (d, $J = 11.7$ Hz, 1H), 4.50 (d, $J = 11.0$ Hz, 1H), 3.81 (s, 3H), 3.78 (m, 1H), 2.58 (m, 1H), 2.24 (m, 1H), 2.05 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 159.1, 154.5, 142.1, 142.0, 130.5, 129.1, 128.6, 127.2, 126.4, 113.8, 110.2, 108.2, 72.6, 71.4, 69.5, 65.9, 55.3, 34.9, 33.8; MS (ESI) m/z 387 ($\text{M}+\text{Na}^+$); HRMS (ESI) m/z

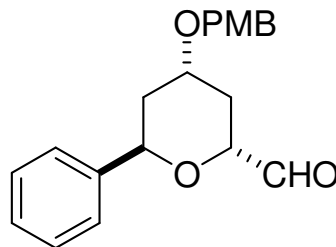
387.1582 (calcd for C₂₃H₂₄O₄Na: 387.1572).

(2*R*,4*S*,6*R*)-Methyl-4-(4-methoxybenzyloxy)-6-phenyl-tetrahydro-2*H*-pyran-2-carboxylate:



$[\alpha]_D^{23} = +32.4$ ($c = 0.3$, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.41-7.32 (m, 5H), 7.27 (d, $J = 8.8$ Hz, 2H), 6.89 (d, $J = 8.8$ Hz, 2H), 5.38 (dd, $J = 2.9, 11.0$ Hz, 1H), 4.54 (d, $J = 11.7$ Hz, 1H), 4.50 (dd, $J = 0.7, 2.2$ Hz, 1H), 4.40 (d, $J = 11.0$ Hz, 1H), 3.88 (m, 1H), 3.81 (s, 3H), 3.67 (s, 3H), 2.52 (m, 1H), 2.06 (m, 2H), 1.91 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 173.1, 159.0, 141.8, 128.8, 128.4, 127.5, 126.2, 113.8, 113.7, 70.5, 70.0, 69.8, 69.7, 55.2, 51.9, 36.8, 30.4; MS (ESI) m/z 379 (M+Na)⁺; HRMS (ESI) m/z 379.1535 (calcd for C₂₁H₂₄O₅Na: 379.1521).

(2*R*,4*S*,6*R*)-4-(4-Methoxybenzyloxy)-6-phenyl-tetrahydro-2*H*-pyran-2-carbaldehyde (ent-11):

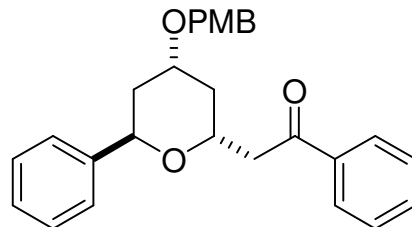


Same procedure was used for preparation of compound **ent-11** as used for **11**.

$[\alpha]_D^{23} = +74.3$ ($c = 1.5$, CHCl₃); IR ν (cm⁻¹): 3443, 2928, 1728, 1611, 1512, 1245, 1034, 822, 756; ¹H NMR (400 MHz, CDCl₃): δ 9.98 (s, 1H), 7.37-7.25 (m, 5H), 7.19 (d, $J = 8.3$ Hz, 2H), 6.83 (d, $J = 9.1$ Hz, 2H), 5.18 (dd, $J = 2.3, 10.6$ Hz, 1H), 4.45 (d, $J = 11.3$ Hz, 1H), 4.26 (d, $J = 11.3$ Hz, 1H), 4.20 (dd, $J = 2.3, 6.8$ Hz, 1H), 3.84 (m, 1H), 3.79 (s, 3H), 2.40 (m, 1H), 1.96 (m, 2H), 1.76 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 203.4, 159.2, 141.7, 130.2, 129.2, 128.4, 127.6, 126.0, 113.9, 77.5, 70.5, 69.7,

69.5, 55.3, 37.0, 29.6; HRMS (ESI) m/z 349.1420 (calcd for $C_{20}H_{22}O_4Na$: 349.1415).

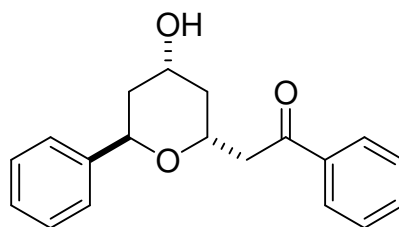
2-((2*R*,4*R*,6*R*)-4-(4-Methoxybenzyloxy)-6-phenyl-tetrahydro-2*H*-pyran-2-yl)-1-phenylethanone (ent-13):



Same procedure was used for preparation of compound **ent-13** as used for **13**.

$[\alpha]_D^{23} = +47.2$ ($c = 0.8$, $CHCl_3$); IR ν (cm^{-1}): 3061, 2926, 2854, 1683, 1598, 1513, 1448, 1250, 1068, 755, 698; 1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, $J = 7.3$ Hz, 2H), 7.55 (t, $J = 7.3$ Hz, 1H), 7.45 (t, $J = 6.6$ Hz, 2H), 7.31-7.22 (m, 7H), 6.86 (d, $J = 8.8$ Hz, 2H), 5.14 (t, $J = 5.1$ Hz, 1H), 4.50 (m, 2H), 4.28 (m, 1H), 3.80 (s, 3H), 3.73 (m, 1H), 3.43 (dd, $J = 6.6, 16.1$ Hz, 1H), 3.27 (dd, $J = 5.8, 16.1$ Hz, 1H), 2.43 (ddd, $J = 3.6, 8.0, 13.2$ Hz, 1H), 2.10 (ddd, $J = 6.3, 8.0, 13.2$ Hz, 1H), 1.97 (m, 1H), 1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.4, 140.6, 137.2, 133.0, 130.5, 129.2, 128.5, 128.4, 128.2, 127.0, 126.3, 126.1, 113.8, 71.9, 70.7, 69.8, 67.3, 55.2, 44.4, 36.4, 34.4; MS (ESI) m/z 439 ($M+Na$) $^+$ HRMS (ESI) m/z 439.1907 (calcd for $C_{27}H_{28}O_4Na$: 439.1885).

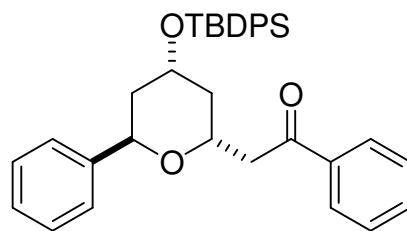
2-((2*R*,4*R*,6*R*)-4-hydroxy-6-phenyl-tetrahydro-2*H*-pyran-2-yl)-1-phenylethanone (ent-1):



Same procedure was used for preparation of compound **ent-1** as used for **1**.

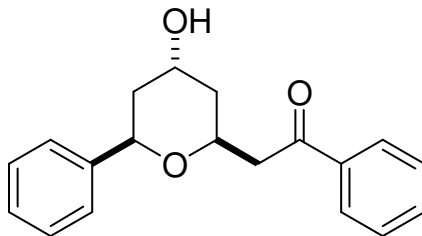
$[\alpha]_D^{23} = +23.3$ ($c = 0.2$, CHCl_3); IR ν (cm^{-1}): 3624, 2925, 2857, 2312, 1740, 1682, 1515, 1452, 1174, 753; ^1H NMR (400 MHz, CDCl_3): δ 7.98 (d, $J = 7.3$ Hz, 2H), 7.57 (t, $J = 7.3$ Hz, 1H), 7.49 (t, $J = 8.8$ Hz, 2H), 7.38-7.23 (m, 5H), 5.18 (t, $J = 4.4$ Hz, 1H), 4.22 (m, 1H), 4.00 (m, 1H), 3.45 (dd, $J = 6.6, 15.4$ Hz, 1H), 3.16 (dd, $J = 5.9, 16.1$ Hz, 1H), 2.15 (ddd, $J = 3.7, 7.3, 13.2$ Hz, 1H), 2.04 (m, 1H), 1.91 (ddd, $J = 3.7, 5.1, 8.8$ Hz, 1H), 1.50 (dt, $J = 9.5, 12.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 198.4, 140.2, 137.1, 133.1, 128.5, 128.4, 128.2, 127.0, 126.3, 72.3, 66.9, 64.0, 44.6, 40.0, 36.6; MS (ESI) m/z 319 ($\text{M}+\text{Na}$) $^+$; HRMS (ESI) m/z 319.1297 (calcd for $\text{C}_{19}\text{H}_{20}\text{O}_3\text{Na}$: 319.1310).

2-((2R, 4R, 6R)-4-(tert-Butyldiphenylsilyloxy)-6-phenyl-tetrahydro-2H-pyran-2-yl)-1-phenylethanone (ent-14):



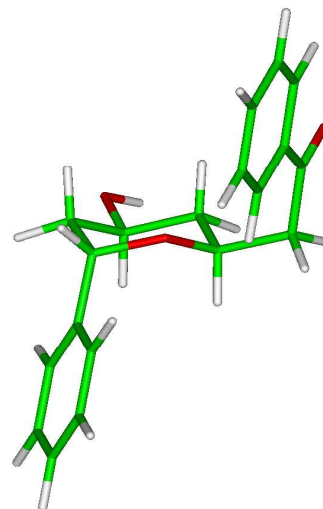
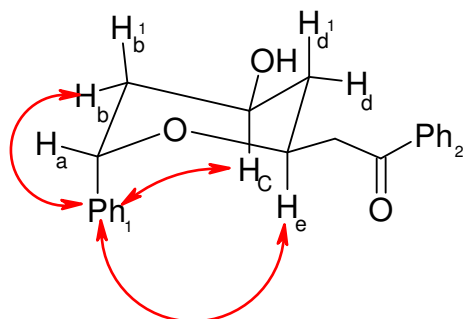
Same procedure was used for preparation of compound **ent-14** as used for **14**.

$[\alpha]_D^{23} = +36.0$ ($c = 0.25$, CHCl_3); IR ν (cm^{-1}): 3068, 2927, 2855, 1681, 1466, 1215, 1110, 760, 701; ^1H NMR (400 MHz, CDCl_3): δ 7.94 (d, $J = 6.6$ Hz, 2H), 7.72 (t, $J = 6.7$ Hz, 4H), 7.65 (d, $J = 6.7$ Hz, 2H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.44-7.36 (m, 7H), 7.05 (t, $J = 2.9$ Hz, 2H), 6.71 (t, $J = 2.9$ Hz, 2H), 4.97 (t, $J = 3.7$ Hz, 1H), 3.98 (m, 2H), 3.39 (dd, $J = 7.4, 15.5$ Hz, 1H), 3.05 (dd, $J = 5.9, 16.2$ Hz, 1H), 2.15 (m, 2H), 1.74 (m, 2H), 1.07 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 198.3, 142.9, 135.8, 135.7, 134.1, 132.9, 130.3, 129.8, 129.7, 128.5, 128.4, 128.3, 128.1, 127.6, 127.0, 126.4, 125.7, 73.9, 69.6, 66.1, 45.3, 40.6, 38.4, 27.0, 19.3; MS (ESI) m/z 557 ($\text{M}+\text{Na}$) $^+$; HRMS (ESI) m/z 535.2685 (calcd for $\text{C}_{35}\text{H}_{39}\text{O}_3\text{Si}$: 535.2668).

2-((2*R*,4*R*,6*S*)-4-Hydroxy-6-phenyl-tetrahydro-2*H*-pyran-2-yl)-1-phenylethanone (ent-2):

Same procedure was used for preparation of compound **ent-2** as used for **2**.

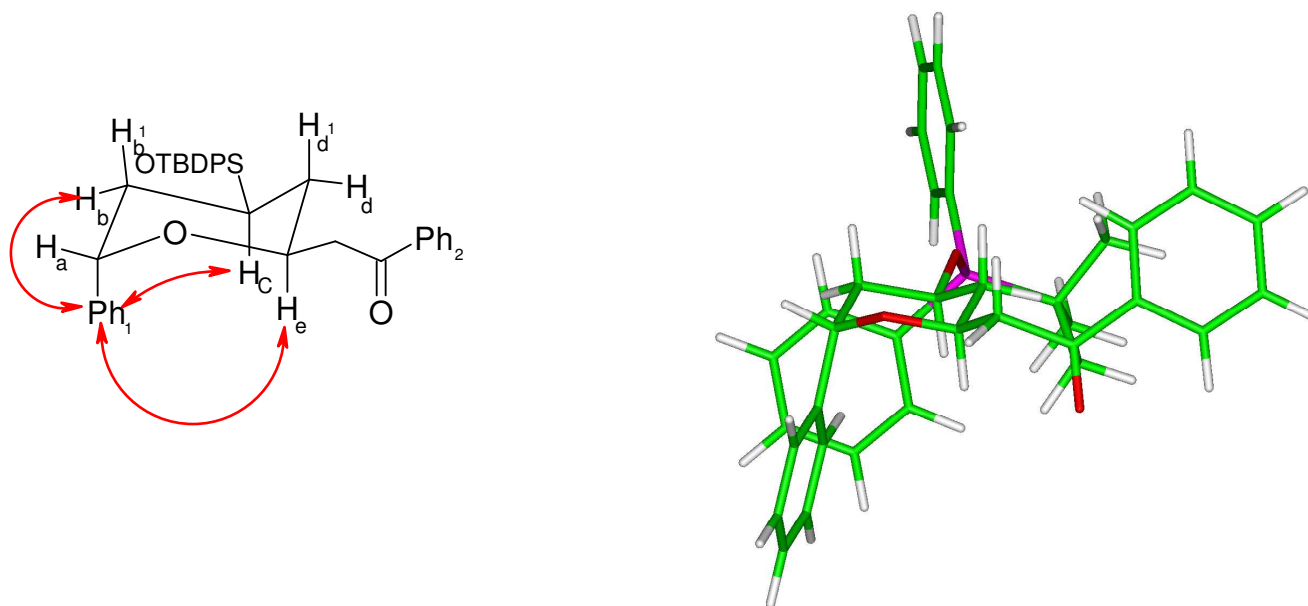
$[\alpha]_D^{23} = +18.9$ ($c = 1.8$, CHCl_3); IR ν (cm^{-1}): 3062, 2922, 2854, 1681, 1598, 1452, 1058, 751, 694; ^1H NMR (400 MHz, CDCl_3): δ 7.97 (d, $J = 6.9$ Hz, 2H), 7.53 (t, $J = 7.3$ Hz, 1H), 7.43 (t, $J = 7.7$ Hz, 2H), 7.26-7.22 (m, 5H), 4.90 (dd, $J = 1.9, 12.0$ Hz, 1H), 4.60 (m, 1H), 4.34 (t, $J = 3.0$, 1H), 3.39 (dd, $J = 5.7, 16.0$ Hz, 1H), 3.04 (dd, $J = 6.8, 16.0$ Hz, 1H), 1.94 (m, 2H), 1.75-1.60 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 198.3, 142.5, 137.0, 133.1, 128.5, 128.2, 127.2, 125.8, 73.7, 68.9, 64.6, 45.0, 39.8, 38.3; MS (ESI) m/z 319 ($\text{M}+\text{Na}^+$); HRMS (ESI) m/z 319.1325 (calcd for $\text{C}_{19}\text{H}_{20}\text{O}_3\text{Na}$: 319.1310).

NOE data for compound 1:**Chemical Shift assignment:**

- 1.50 (dt, 1H, J (H,H) = 9.3 Hz, 12.3 Hz, Hd¹)
- 1.92 (ddd, 1H, J (H,H) = 5.0 Hz, 9.7 Hz, 13.5 Hz, Hb¹)
- 2.05 (m, 1H, Hd)
- 2.51 (m, 1H, Hb)
- 3.17 (dd, 1H, J (H,H) = 5.9 Hz, 15.7 Hz, benzyl protons)
- 3.45 (dd, 1H, J (H,H) = 7.0 Hz, 15.7 Hz, benzyl protons)
- 4.02 (m, 1H, Hc)
- 4.23 (m, 1H, He)
- 5.19 (t, 1H, J (H,H) = 4.4 Hz, Ha)
- 7.24-7.34 (m, Phenyl (1) protons), 7.46-7.98 (m, Phenyl (2) protons)

Information on the coupling constants was obtained from selective homonuclear decoupling, where $^3J_{(\text{Hc-Hd})^1} = 9.3 \text{ Hz}$, $^3J_{(\text{Hd}^1\text{-Hc})} = 9.3 \text{ Hz}$, $^3J_{(\text{Hc-Hb})^1} = 9.7 \text{ Hz}$ and $^3J_{(\text{Ha-Hb})^1} = 5 \text{ Hz}$, $^3J_{(\text{Ha-Hb})} = 2.5 \text{ Hz}$, clearly fixes the stereochemistry of the corresponding protons (as shown in the figure), which is further supported by the NOEs between Phenyl (1) protons to He, Hb, Hc, indicating the syn or cis conformation of these protons. Whereas absence of NOE between Ha-Hc, Ha-He clearly indicates that He and Hc are cis to each other whereas both these protons are trans to Ha.

NOE data for compound 14:



Chemical Shift assignment:

1.65 (ddd, 1H, J (H,H) = 8.2 Hz, 9.4 Hz, 12.3 Hz, Hd¹)

1.87 (ddd, 1H, J (H,H) = 5.1 Hz, 9.7 Hz, 13.5 Hz, Hb¹)

1.98 (m, 1H, Hd)

2.11 (m, 1H, Hb)

3.01 (dd, 1H, J (H,H) = 5.9 Hz, 15.7 Hz, benzyl protons)

3.37 (dd, 1H, J (H,H) = 7.0 Hz, 15.7 Hz, benzyl protons)

3.91 (m, 1H, Hc)

3.99 (m, 1H, He)

4.94 (t, 1H, J (H,H) = 3.7 Hz, Ha)

6.67 (m, 2H, Phenyl (1) protons)

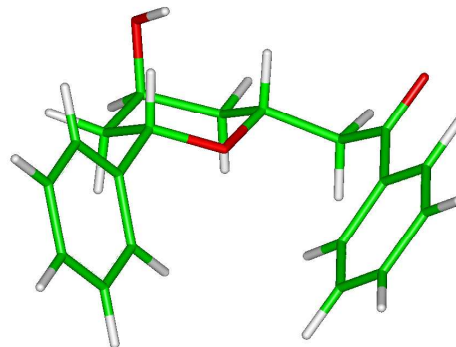
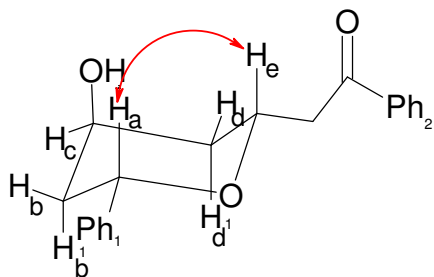
7.05 (m, 3H, Phenyl (1) protons)

7.35-7.71 (m, 10H, TBDPS phenyl protons)

7.43 (m, 3H, Phenyl (2) protons)

7.94 (m, 2H, Phenyl (2) protons)

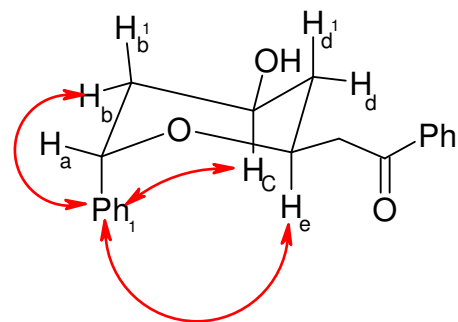
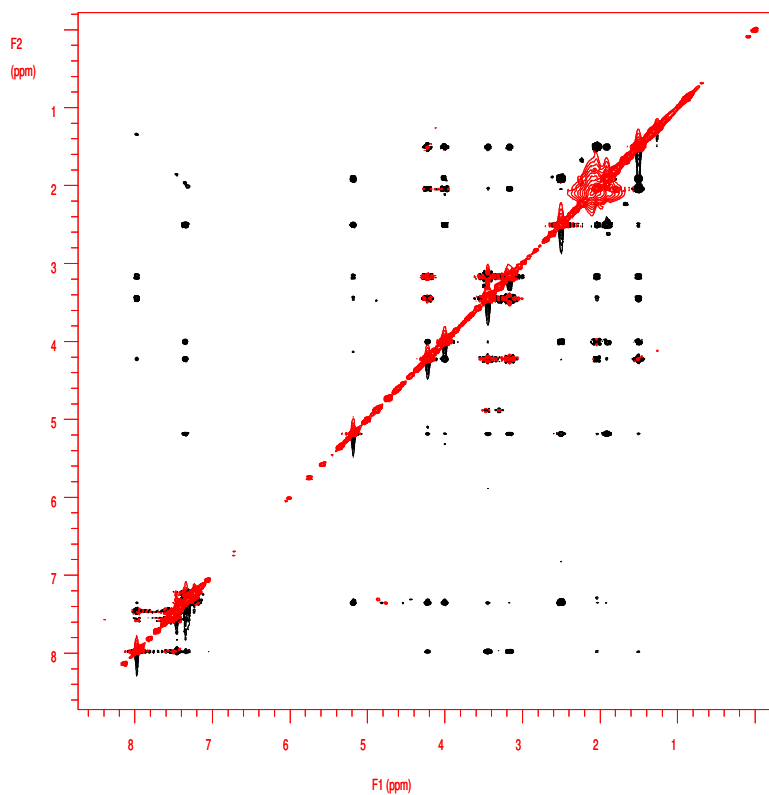
Information on the coupling constants was obtained from selective homonuclear decoupling, where $^3J_{(\text{He-Hd}^1)} = 8.2 \text{ Hz}$, $^3J_{(\text{Hd}^1\text{-Hc})} = 9.4 \text{ Hz}$, $^3J_{(\text{Hc-Hb}^1)} = 9.7 \text{ Hz}$ and $^3J_{(\text{Ha-Hb}^1)} = 4.8 \text{ Hz}$, $^3J_{(\text{Ha-Hb})} = 2.7 \text{ Hz}$, clearly fixes the stereochemistry of the corresponding protons (as shown in the figure), which is further supported by the NOEs between Phenyl (1) protons to He, Hb, Hc, indicating the syn or cis conformation of these protons. Whereas absence of NOE between Ha-Hc, Ha-He clearly indicates that He and Hc are cis to each other whereas both these protons are trans to Ha.

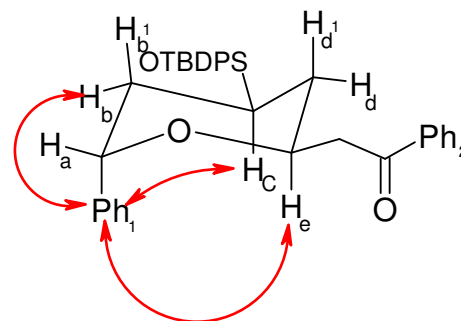
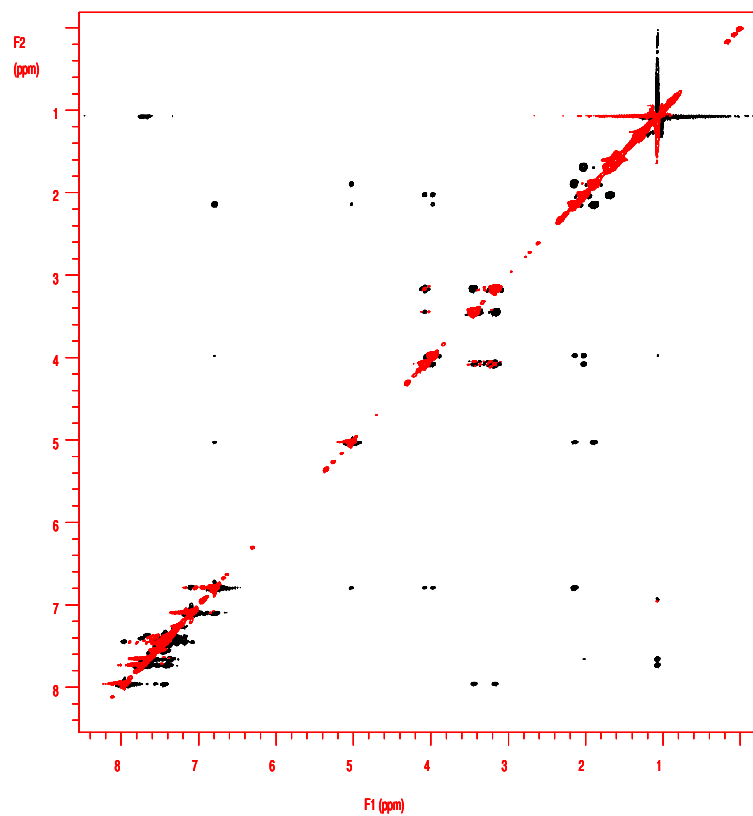
NOE data for compound 2:**Chemical Shift Assignment:**

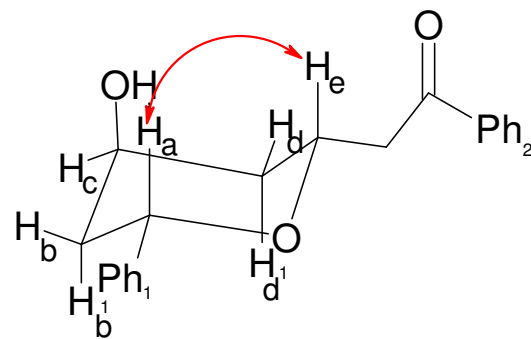
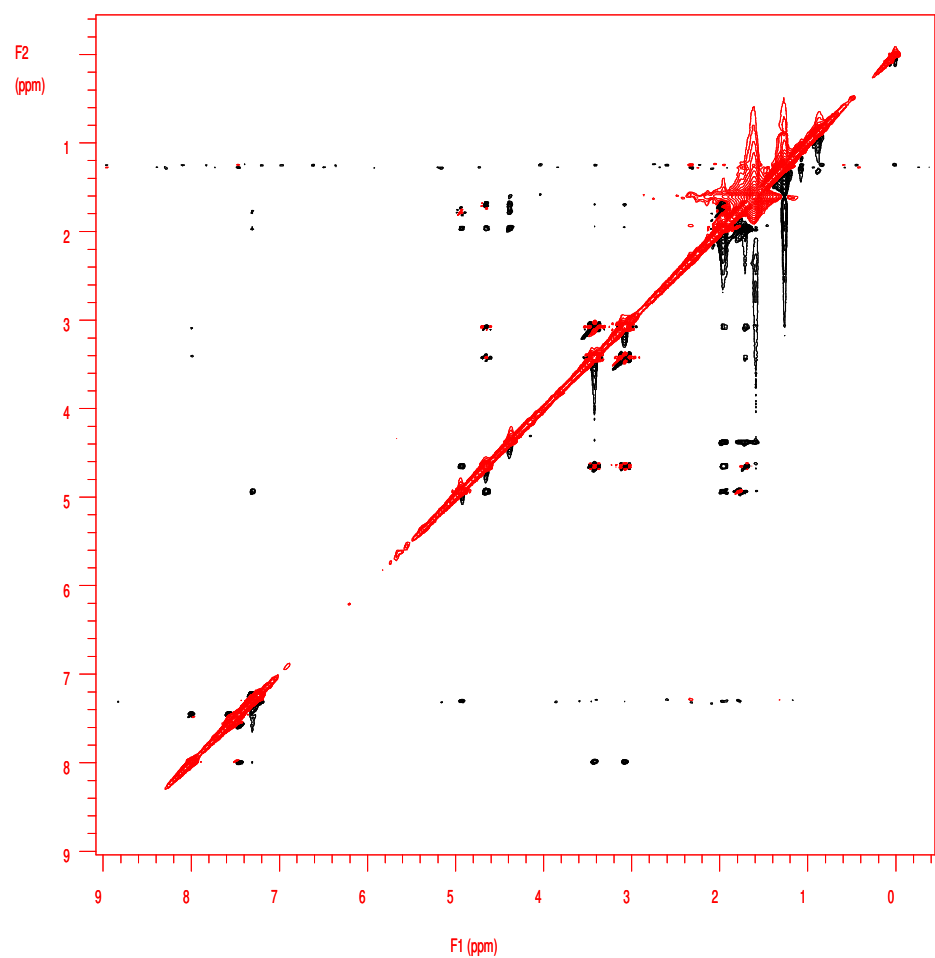
- 1.69 (ddd, 1H, J (H,H) = 2.7 Hz, 11.5 Hz, 13.7 Hz, H_d¹)
- 1.78 (ddd, 1H, J (H,H) = 2.9 Hz, 14.3 Hz, 12.0 Hz, H_b¹)
- 1.94 (m, 2H, H_b, H_d)
- 3.04 (dd, 1H, J (H,H)=6.82 Hz, 16.0 Hz, benzyl protons)
- 3.39 (dd, 1H, J (H,H)=5.76 Hz, 16.0 Hz, benzyl protons)
- 4.34 (t, J (H,H) = 3.0 Hz, H_c)
- 4.60 (m, 1H, H_e)
- 4.90 (dd, 1H, J (H,H)=1.9 Hz, 12.0 Hz, H_a)
- 7.24-7.30 (m, Phenyl (1) protons)
- 7.46-7.98 (m, Phenyl (2) protons)

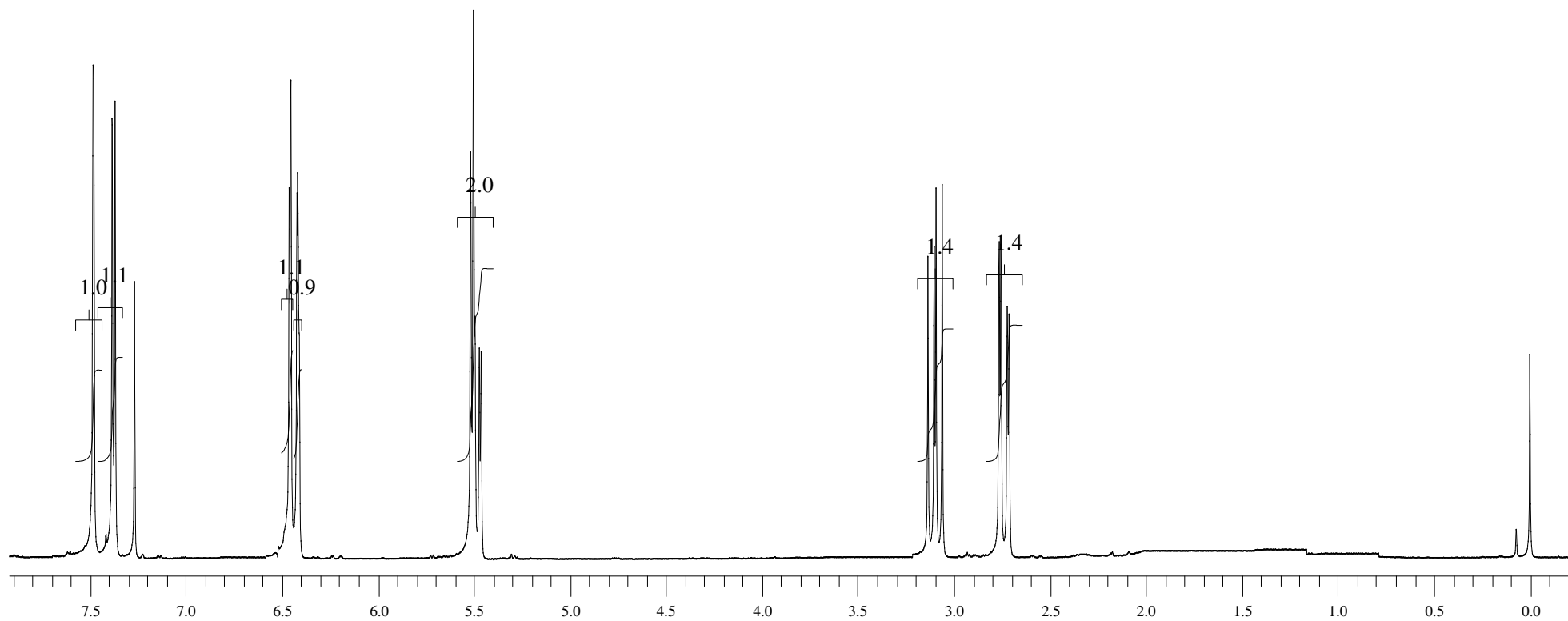
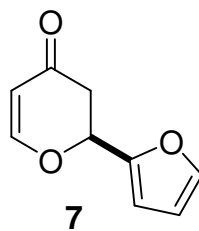
Information on the coupling constants was obtained from selective homonuclear decoupling, where $^3J_{(\text{Ha-Hb})^1} = 12.0 \text{ Hz}$, $^3J_{(\text{He-Hd})^1} = 11.5 \text{ Hz}$ and $^3J_{(\text{Hc-Hb}^1, \text{Hb}, \text{Hd}, \text{Hd}^1)} \approx 3.0 \text{ Hz}$ clearly fixes the stereochemistry of the corresponding protons (as shown in the figure), which is further supported by the NOE between Ha-He indicating the syn or cis conformation of these protons. Whereas no NOE was observed between Hc-He, Hc-Ha thus Hc is trans to He and Ha.

NOESY spectrum of compound 1 - [500MHz, 300K, CDCl₃]

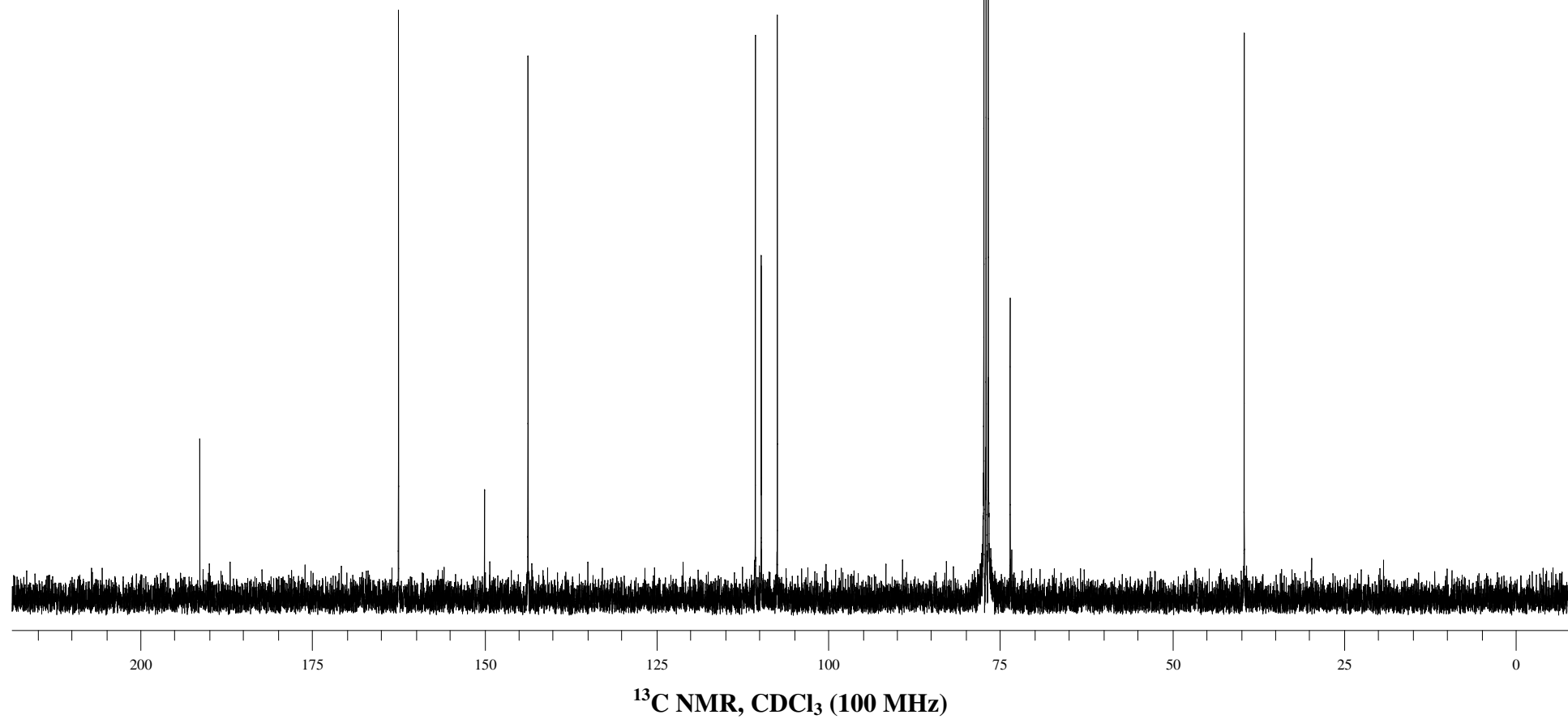
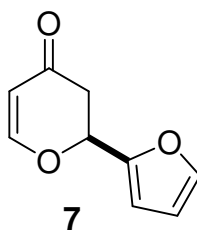


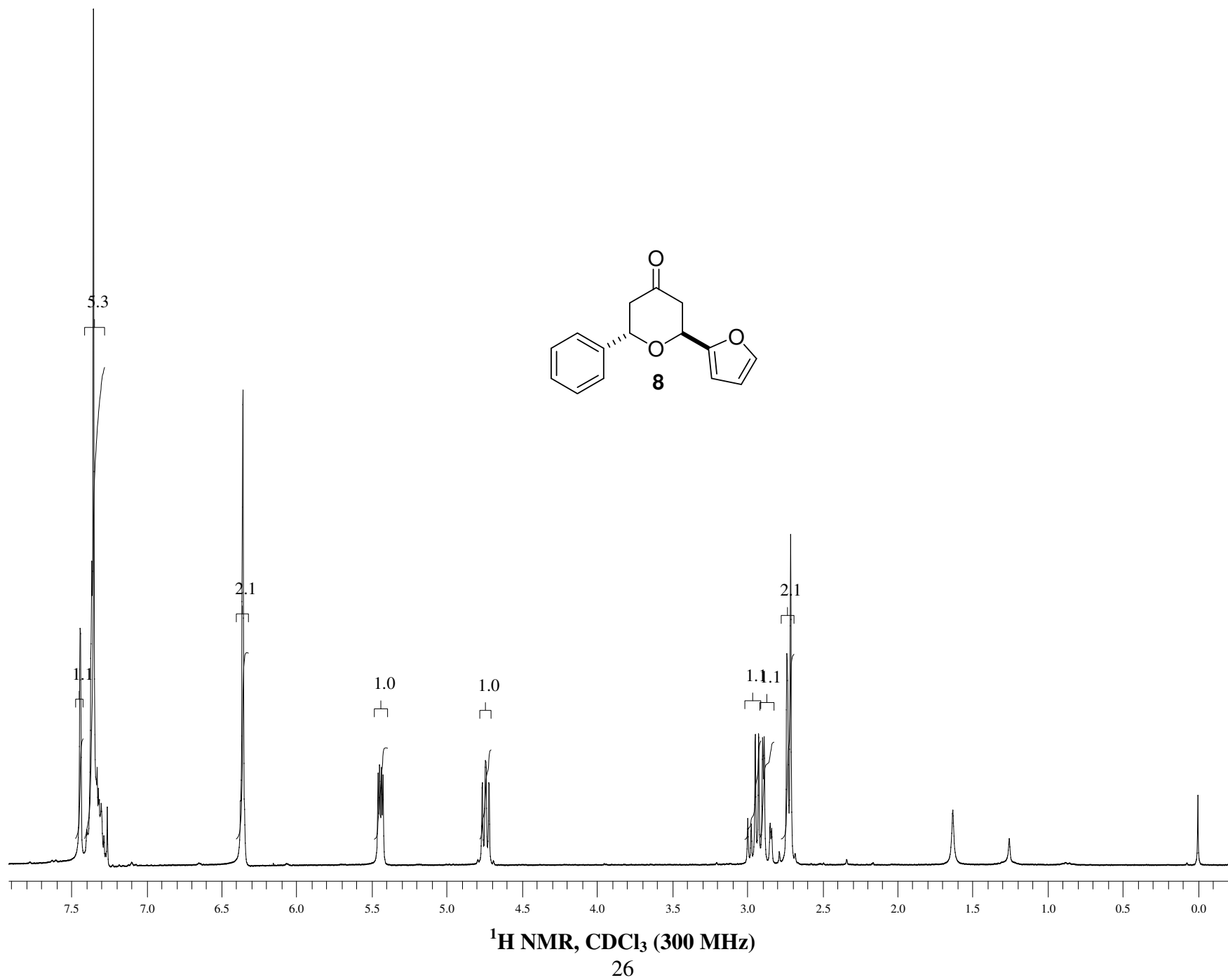
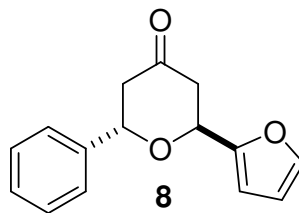
NOESY spectrum of compound 14 - [500MHz, 300K, CDCl₃]

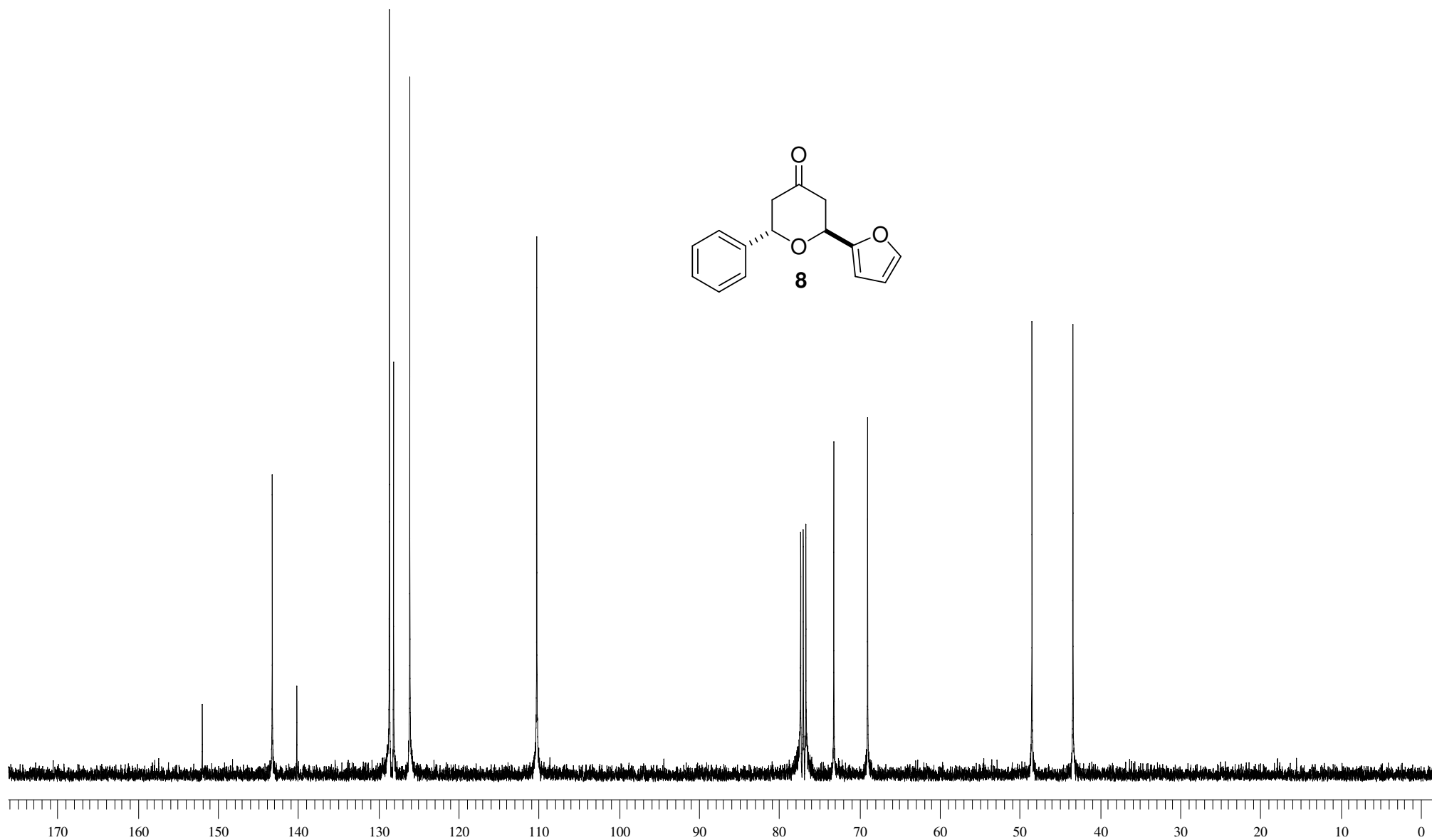
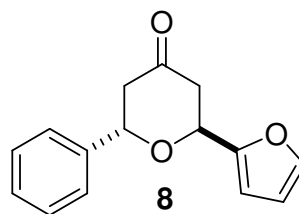
NOESY spectrum of compound 2 - [500MHz, 300K, CDCl₃]



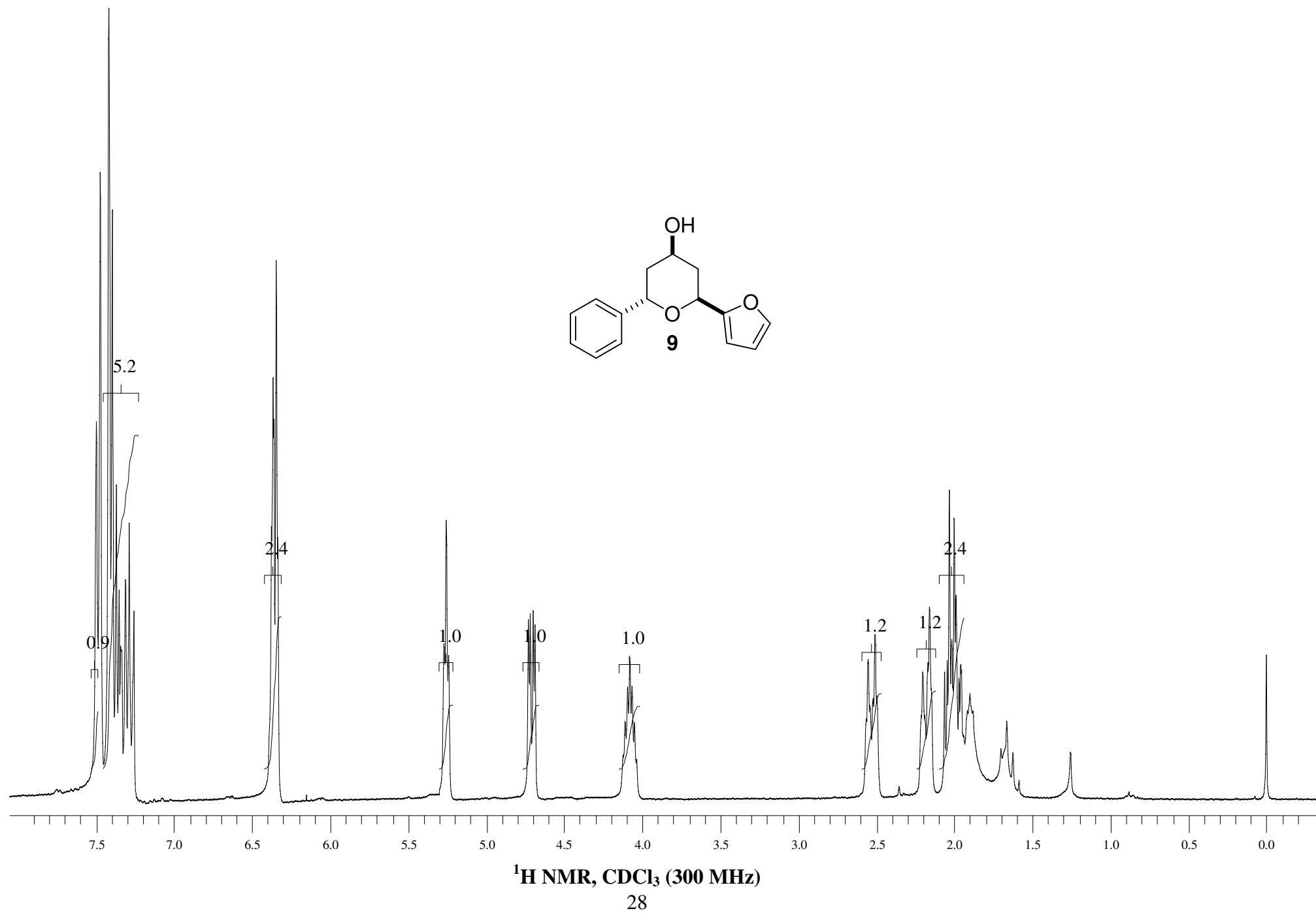
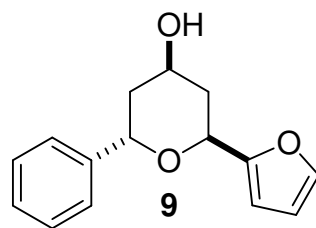
^1H NMR, CDCl_3 (400 MHz)

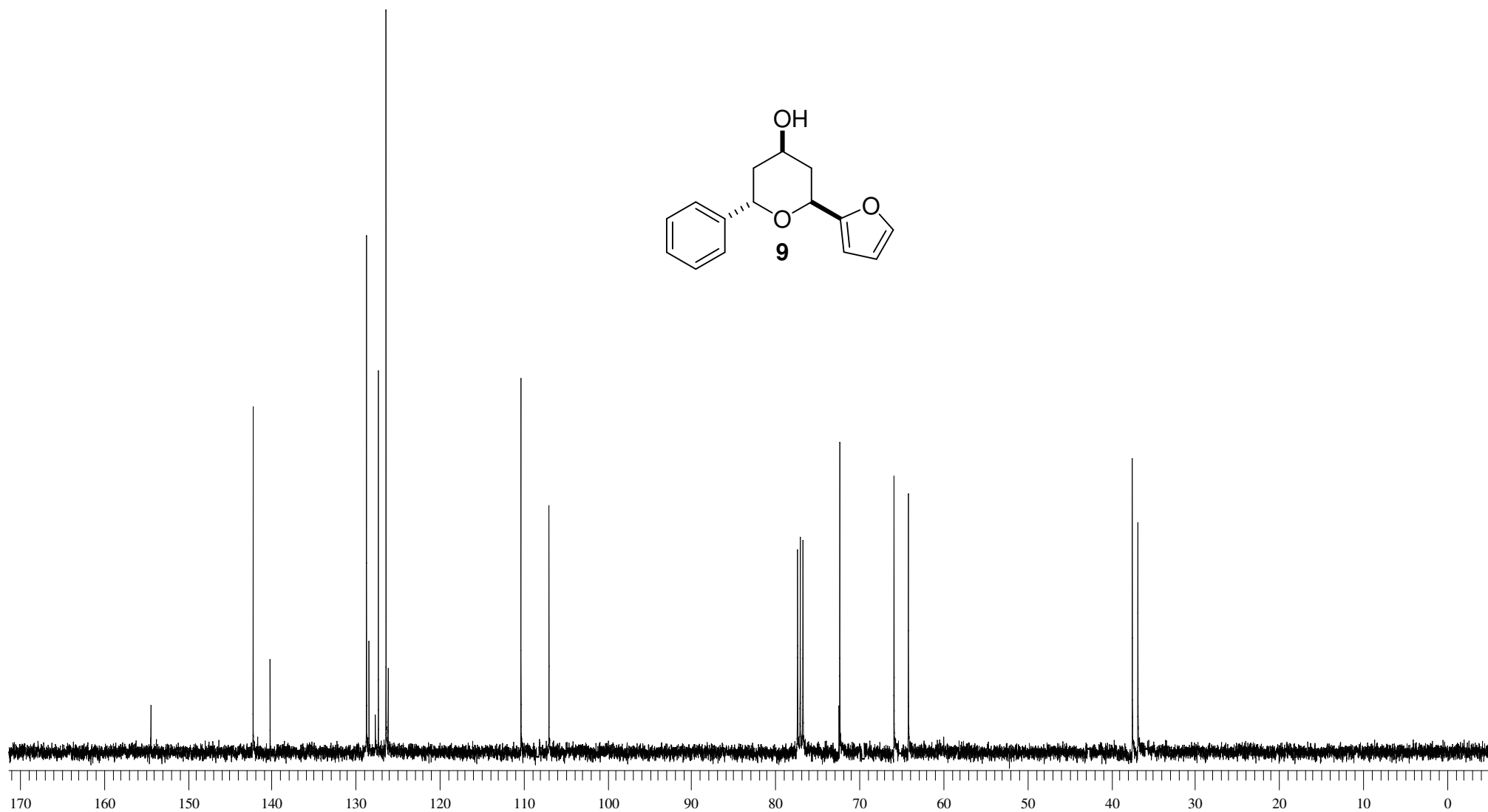
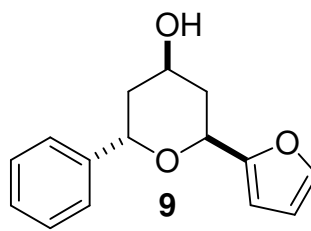




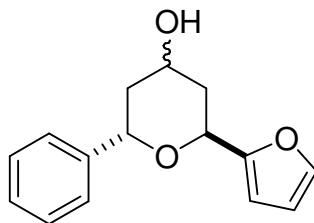


^{13}C NMR, CDCl_3 (100 MHz)

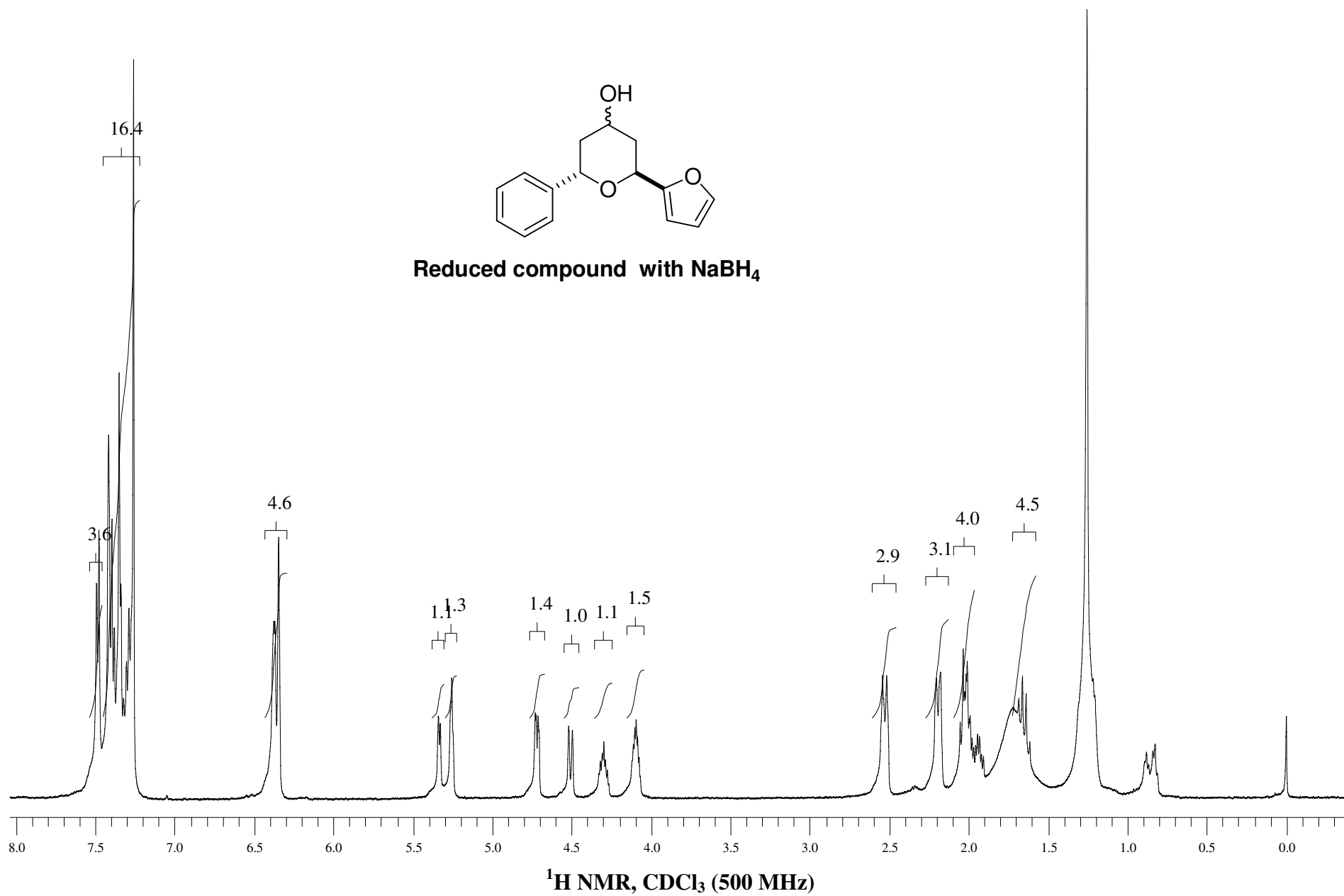




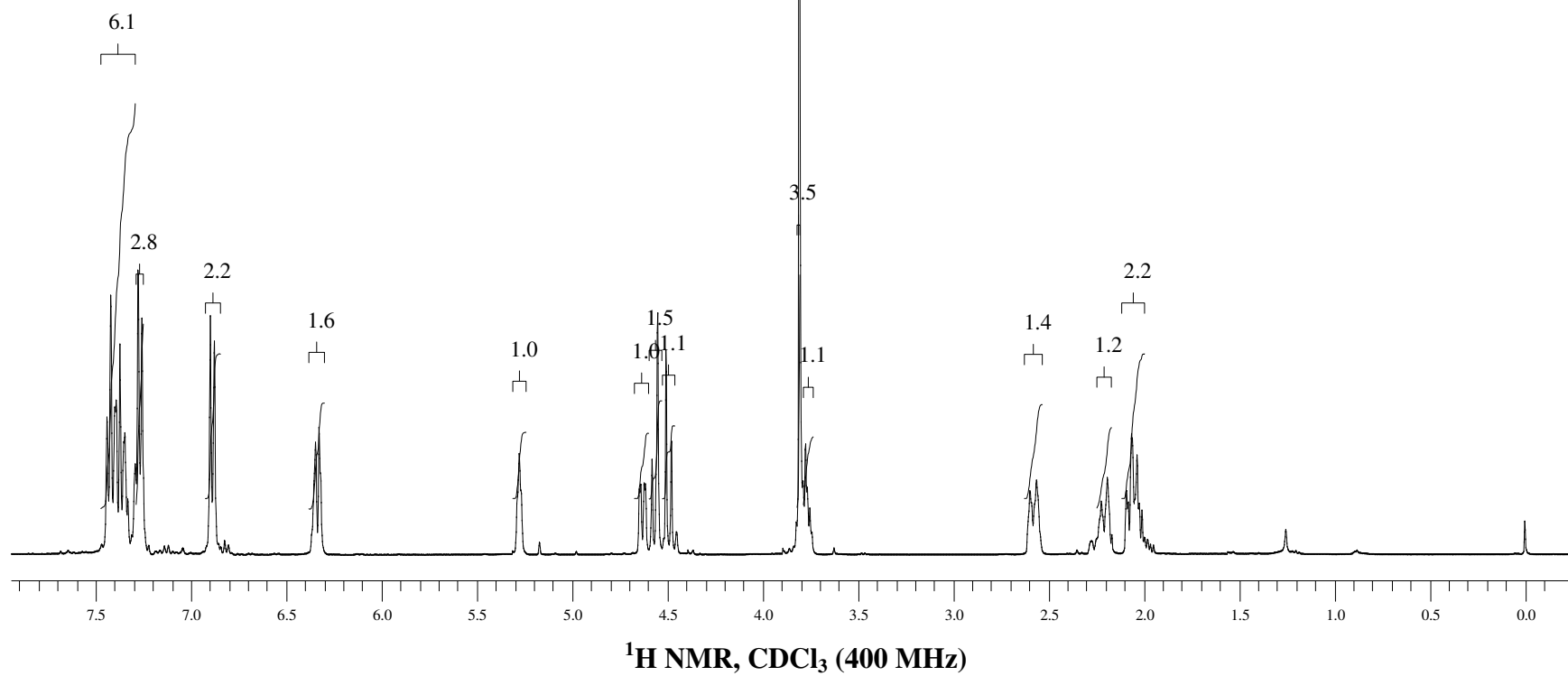
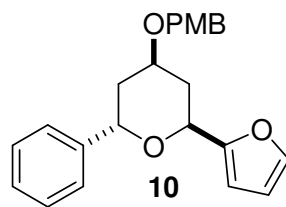
^{13}C NMR, CDCl_3 (100 MHz)



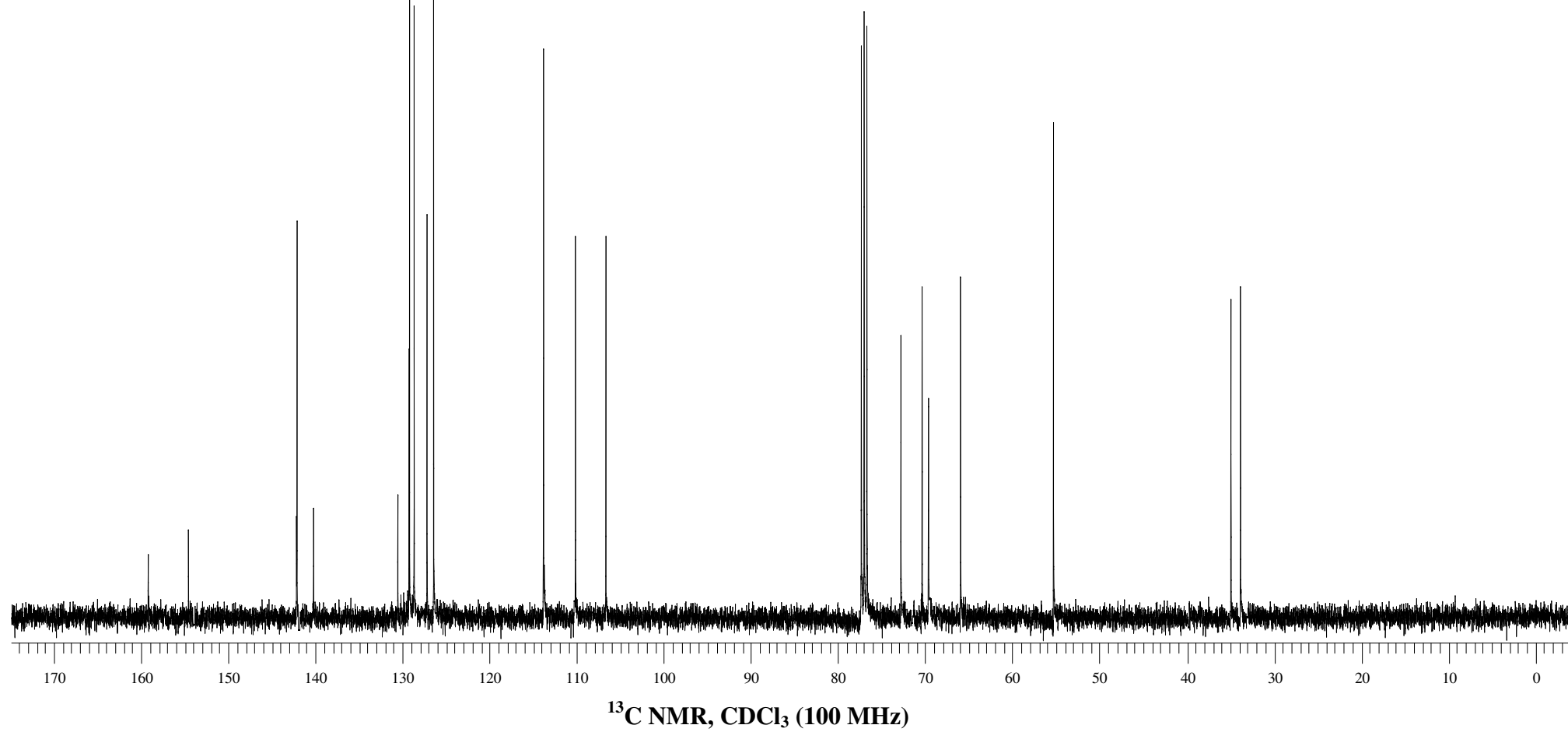
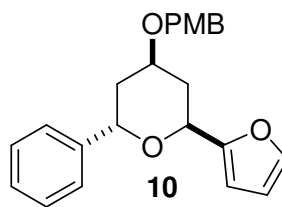
Reduced compound with NaBH₄



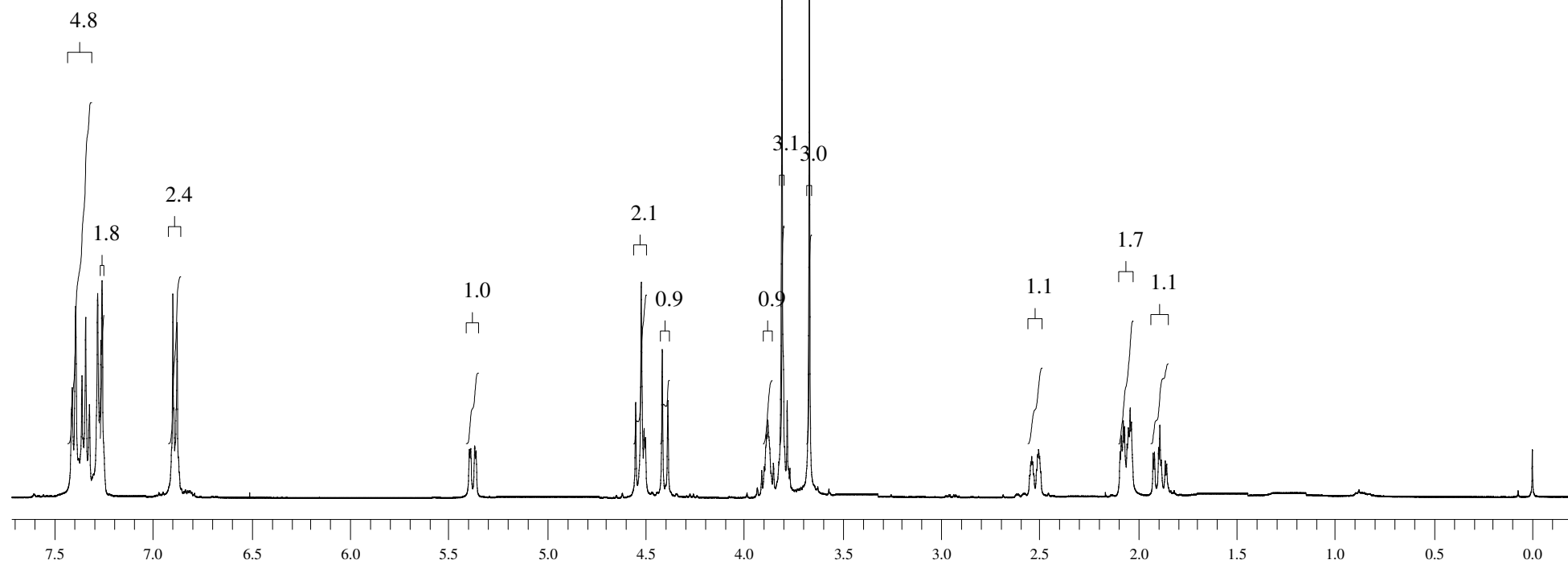
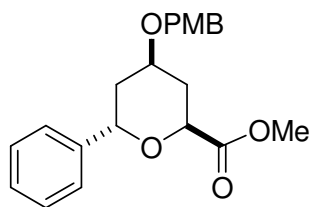
S 31



S 32

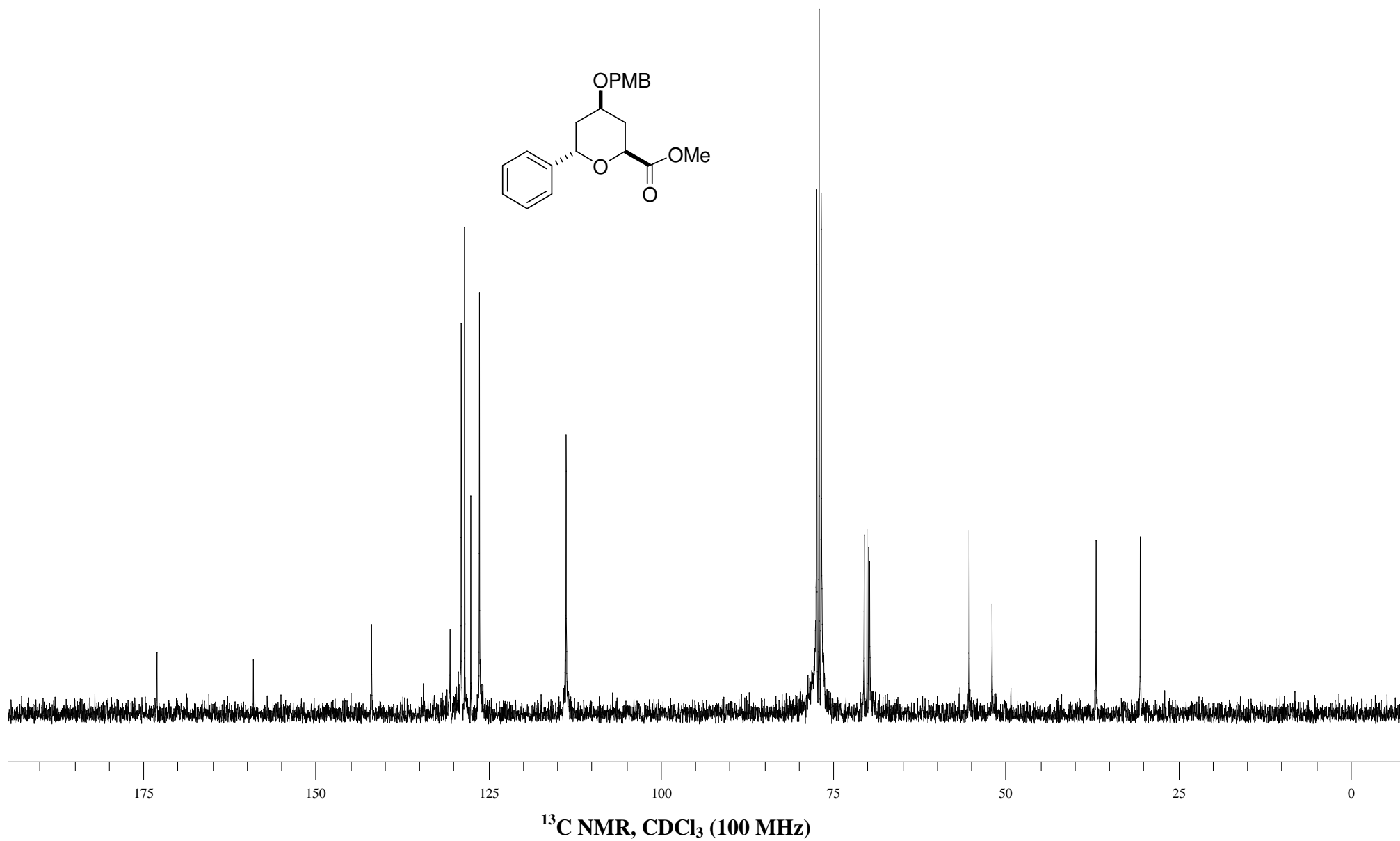
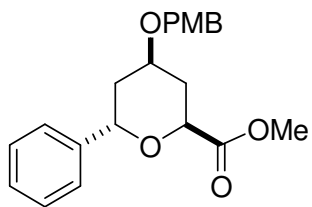


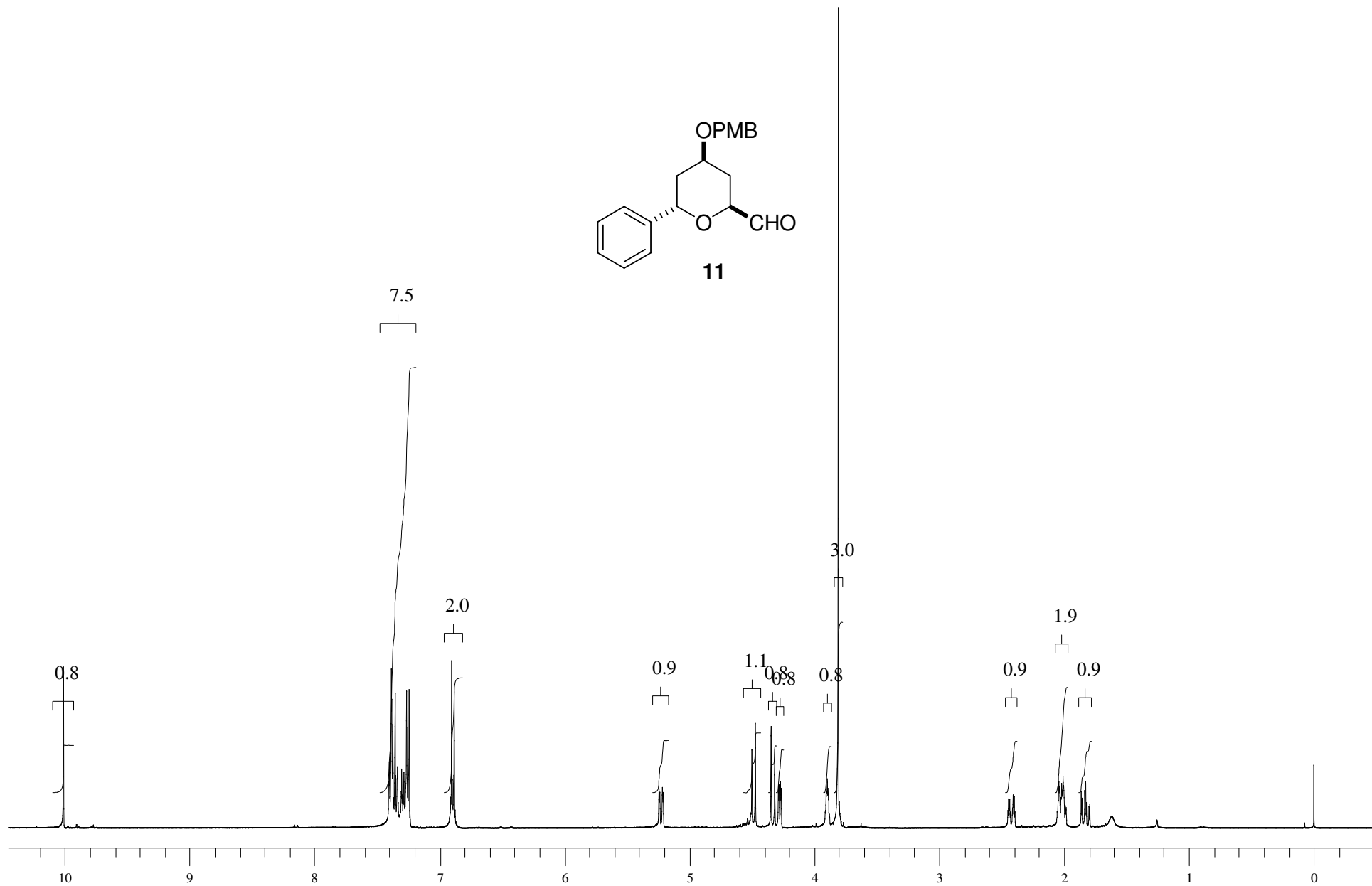
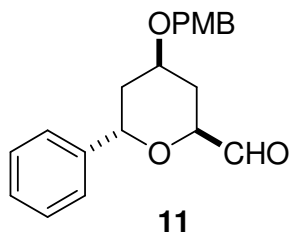
S 33



¹H NMR, CDCl₃ (400 MHz)

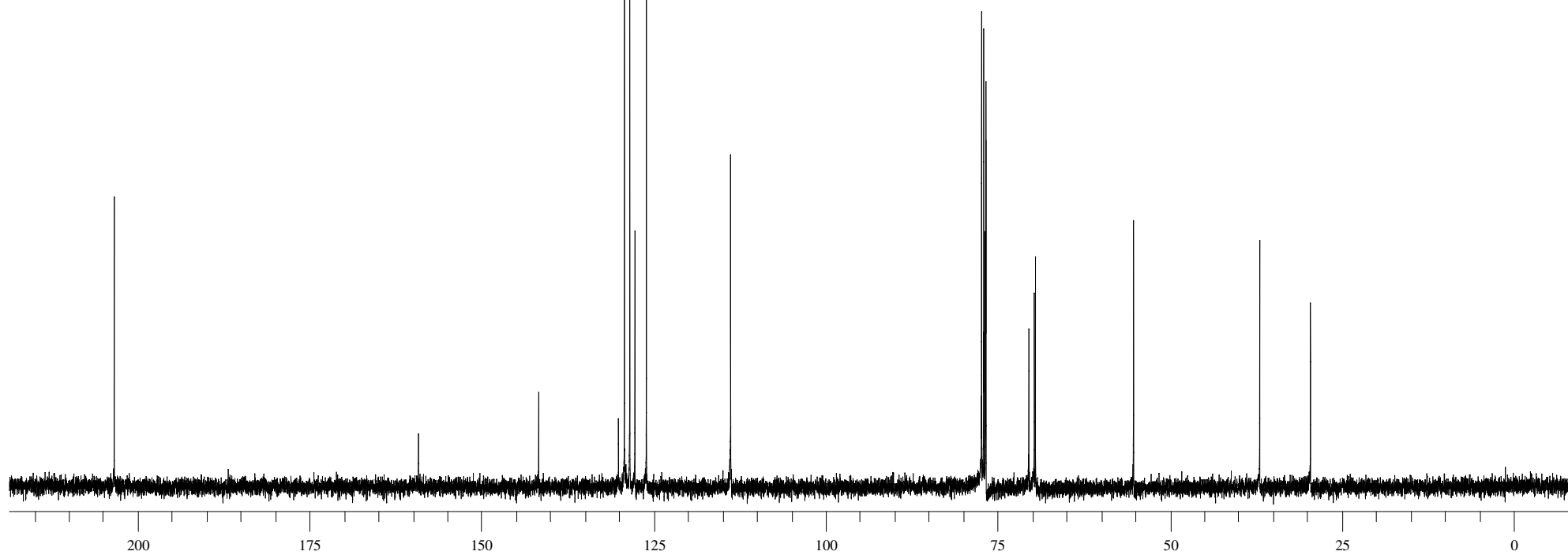
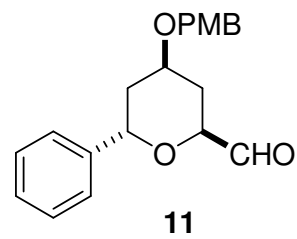
S 34





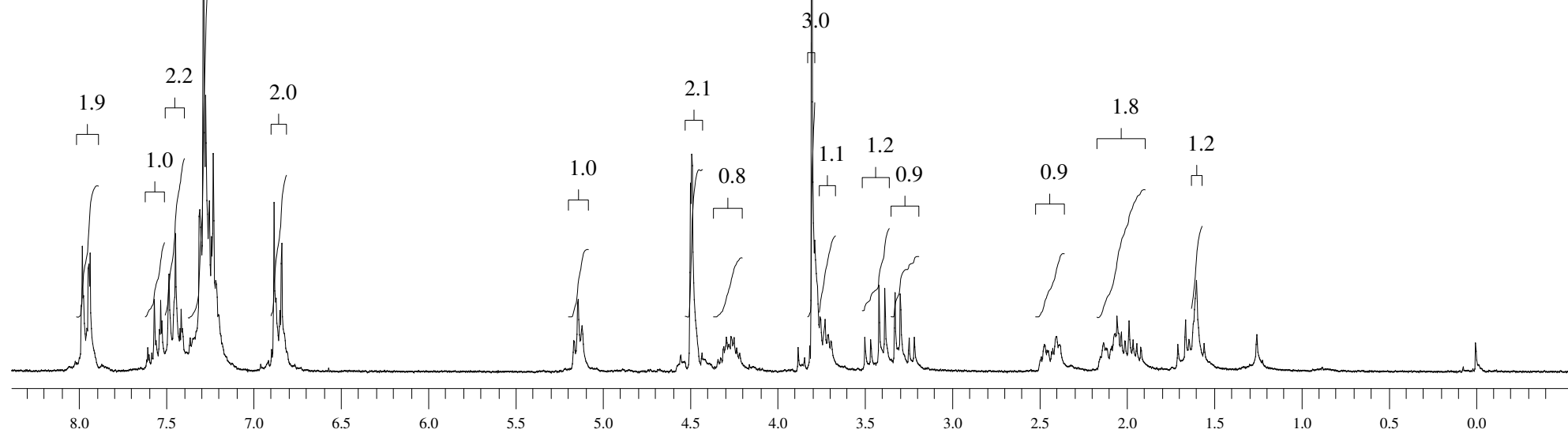
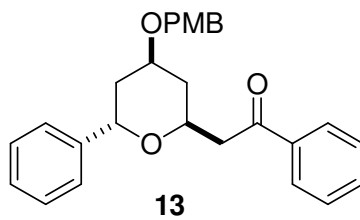
¹H NMR, CDCl₃ (400 MHz)

S 36



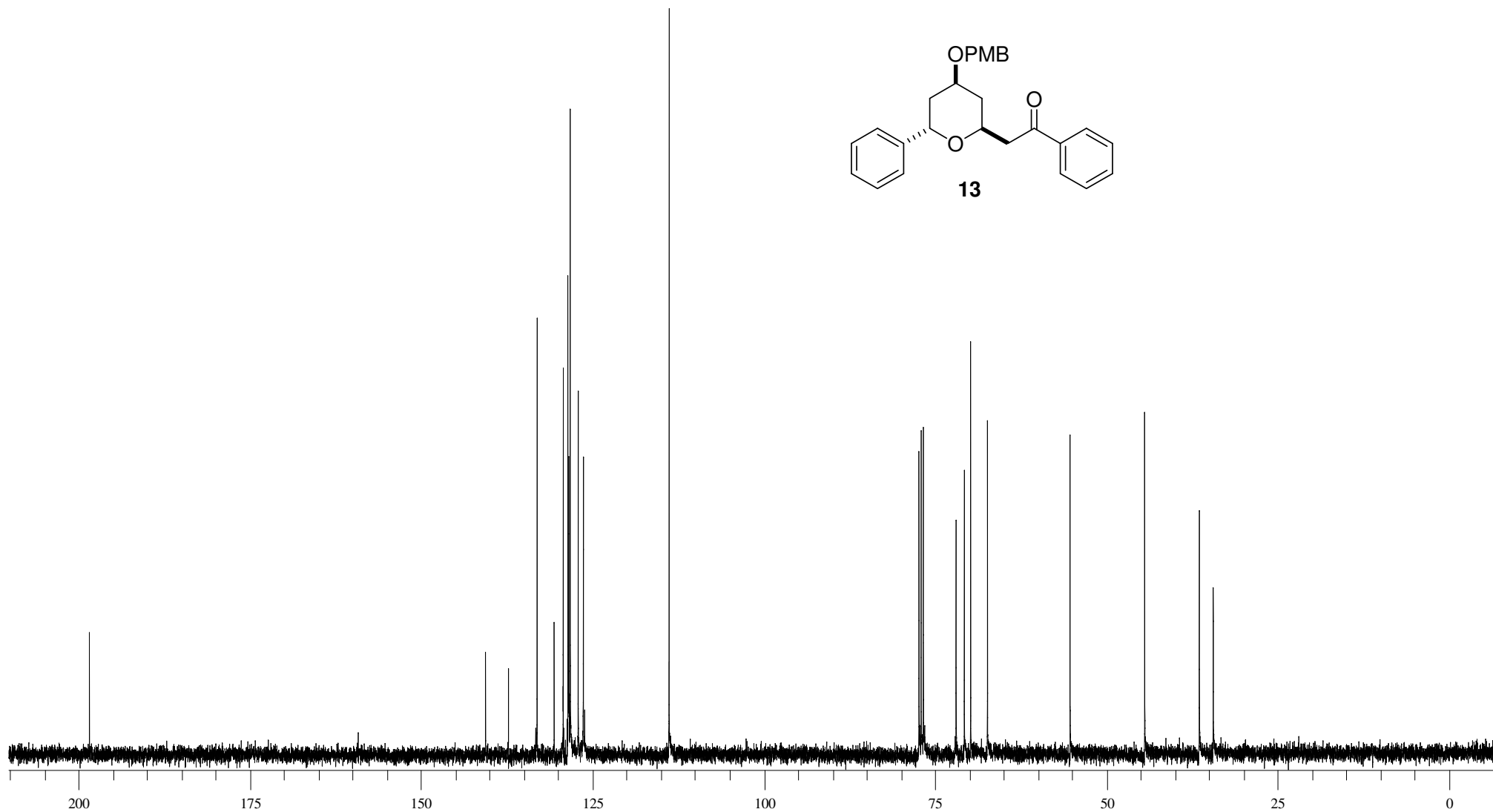
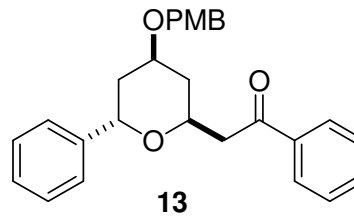
^{13}C NMR, CDCl_3 (100 MHz)

S 37

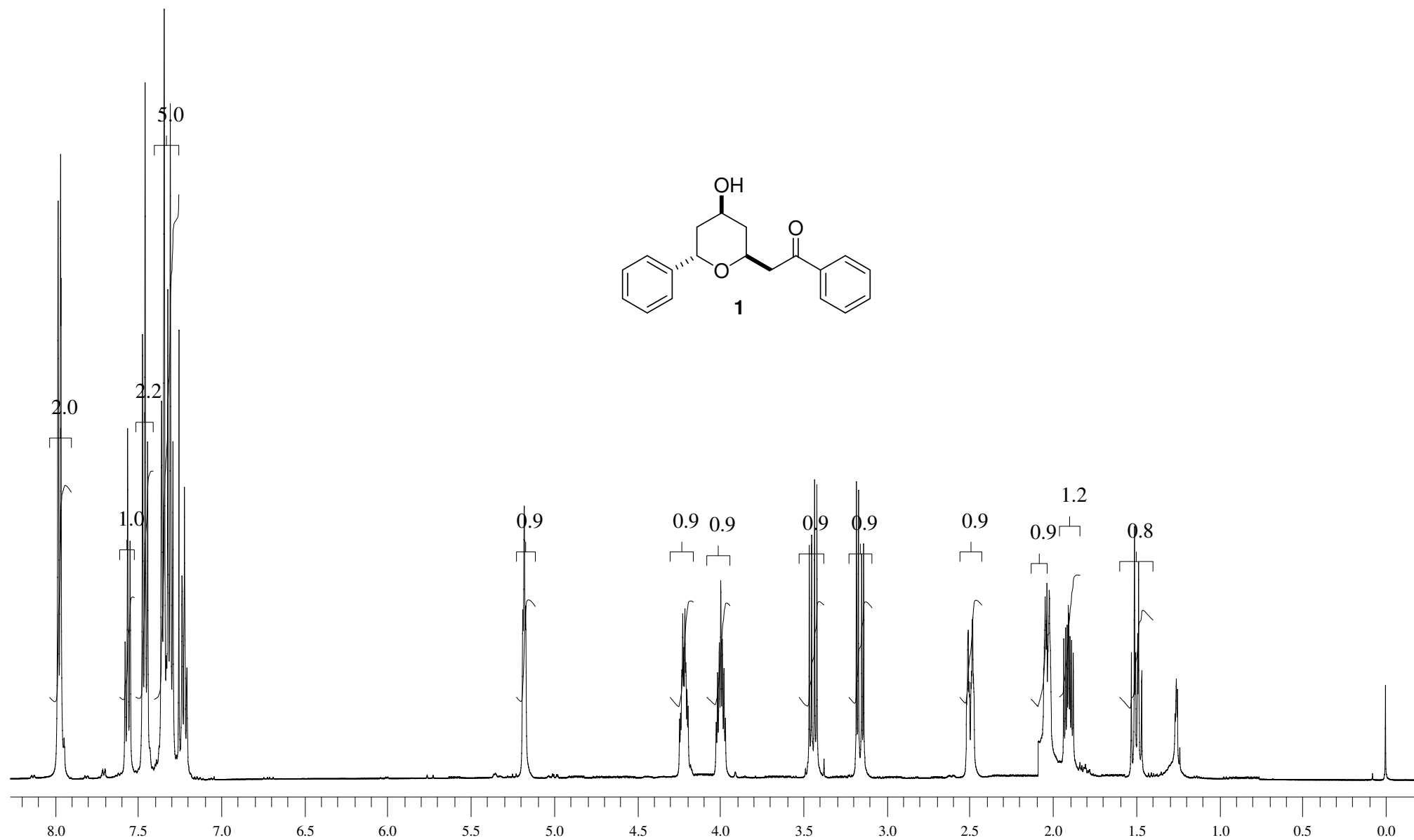
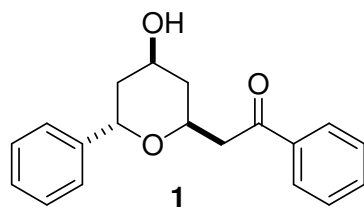


^1H NMR, CDCl_3 (400 MHz)

S 38

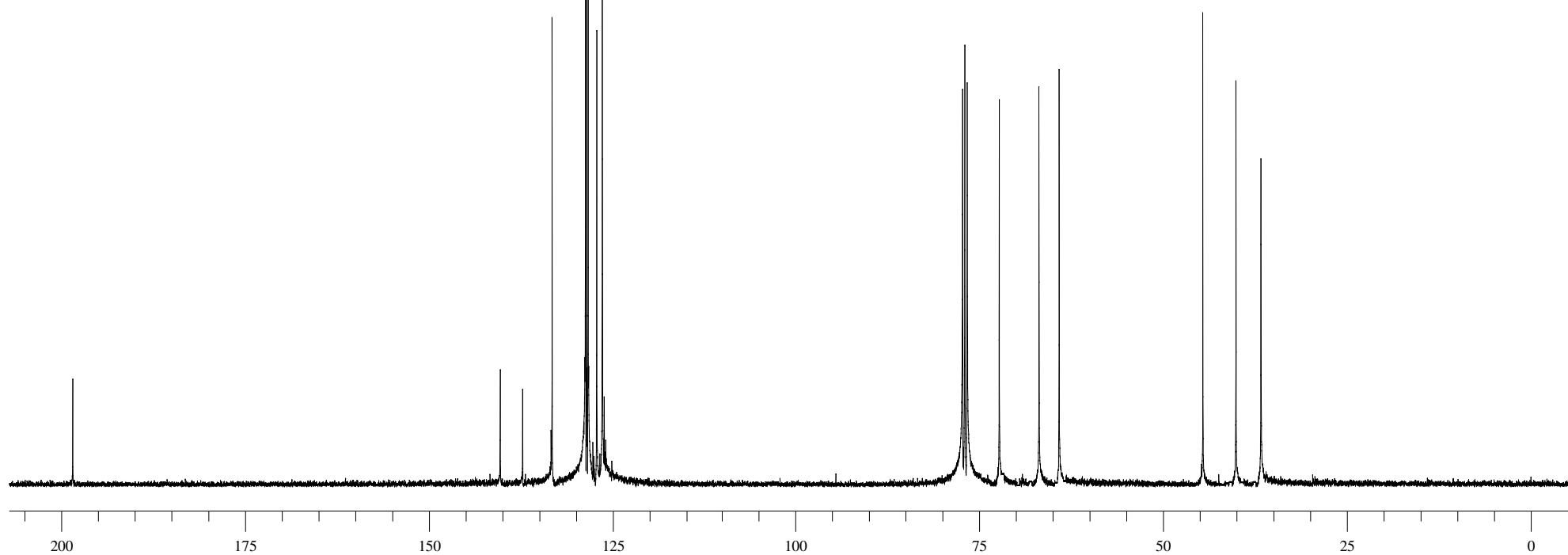
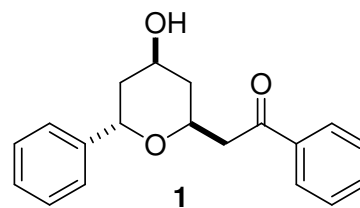


^{13}C NMR, CDCl_3 (100 MHz)

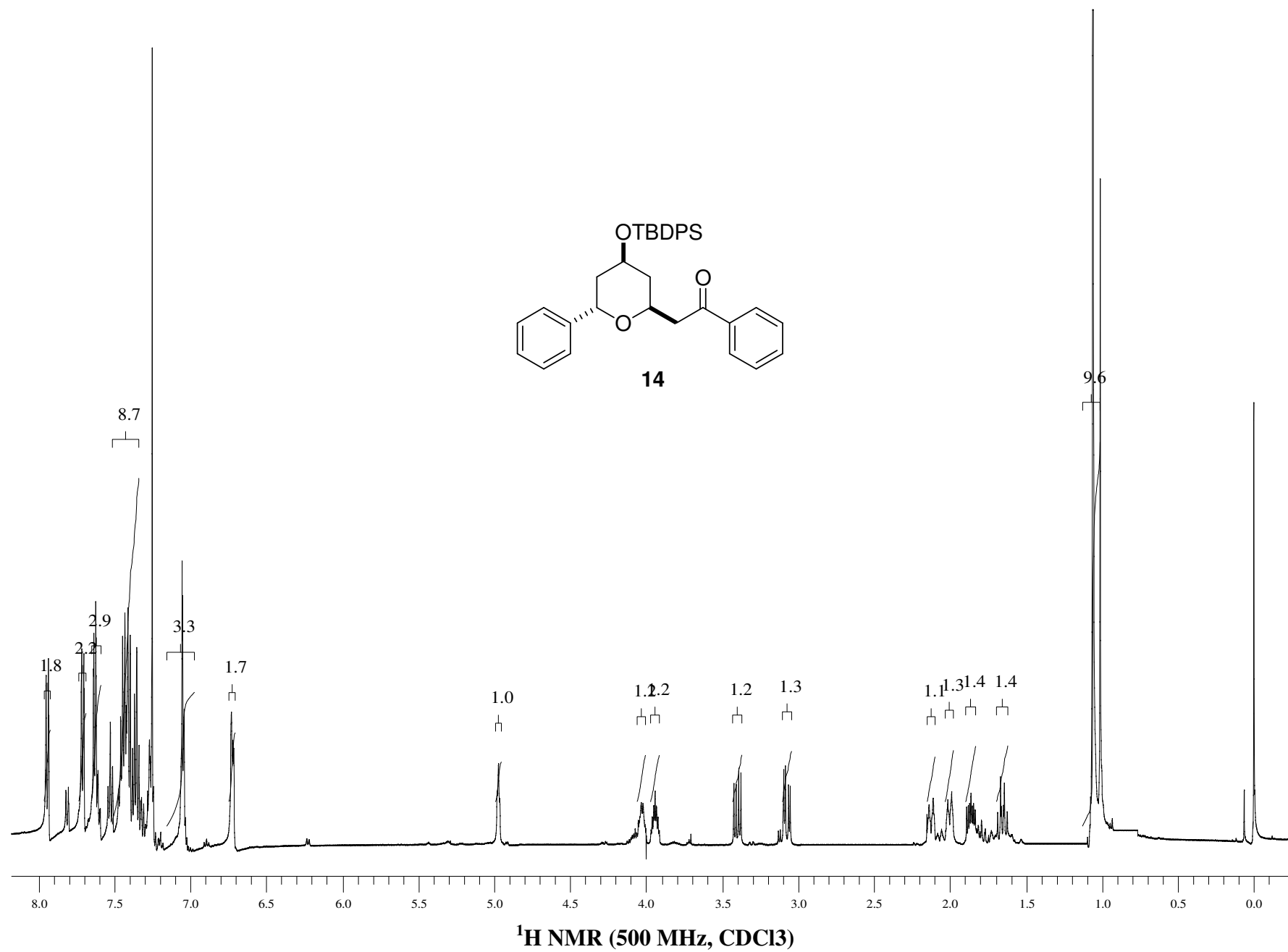


¹H NMR (500 MHz, CDCl₃)

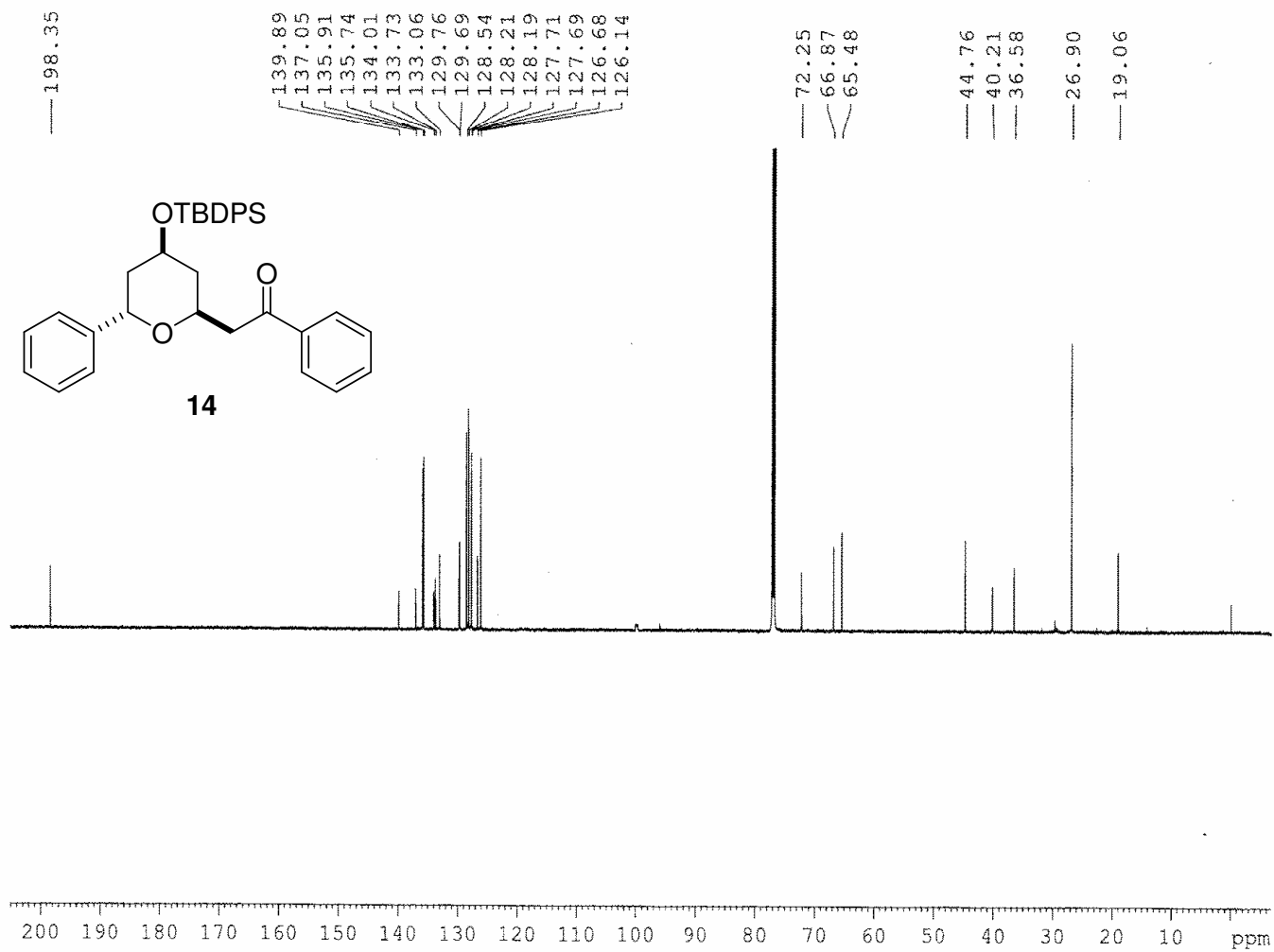
S 40



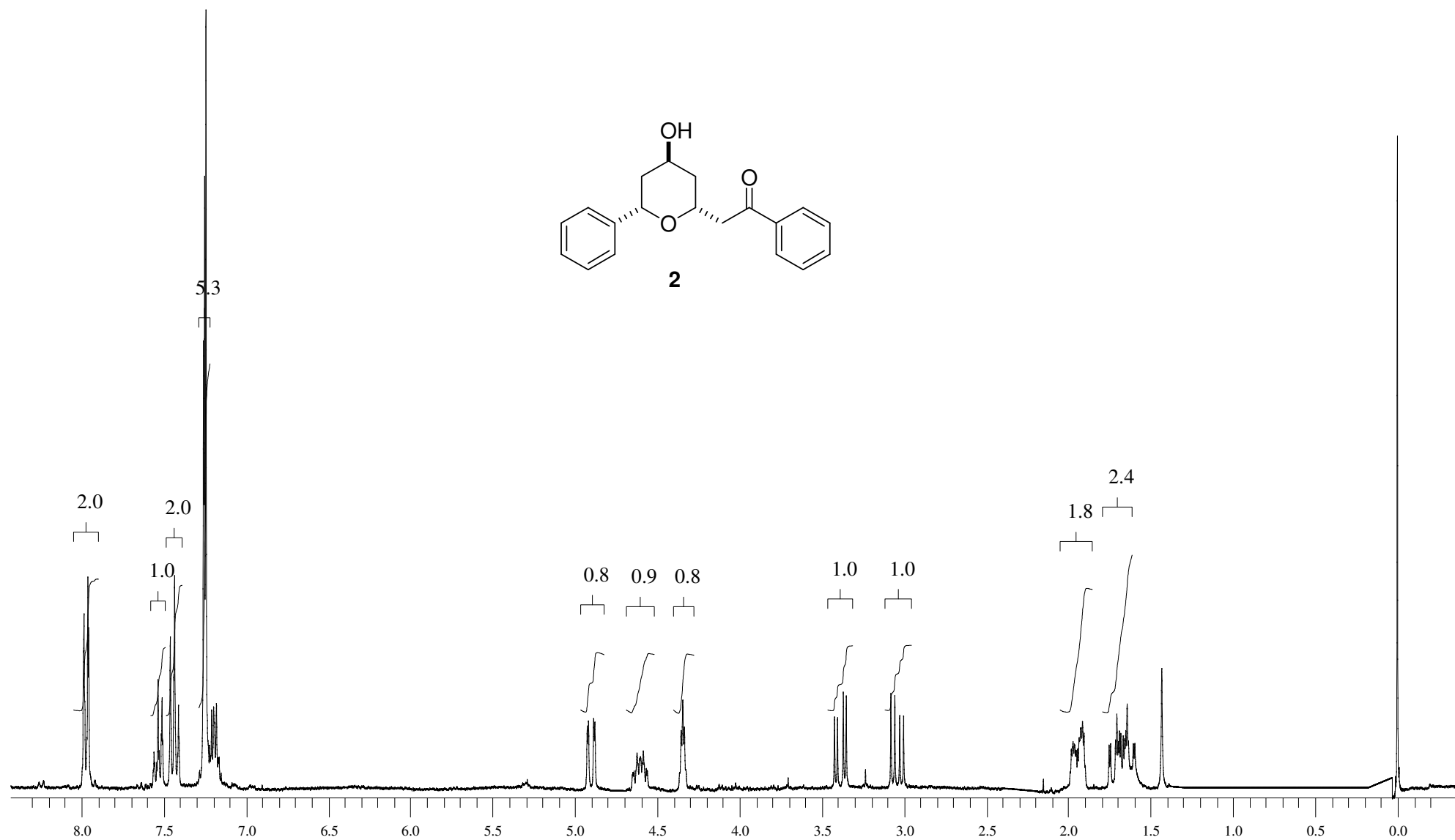
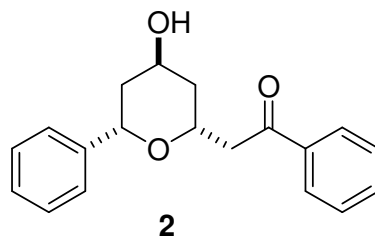
¹³C NMR, CDCl₃ (100 MHz)



RAMAKRISHNA-GKS-RGN-OXY-C13-12C

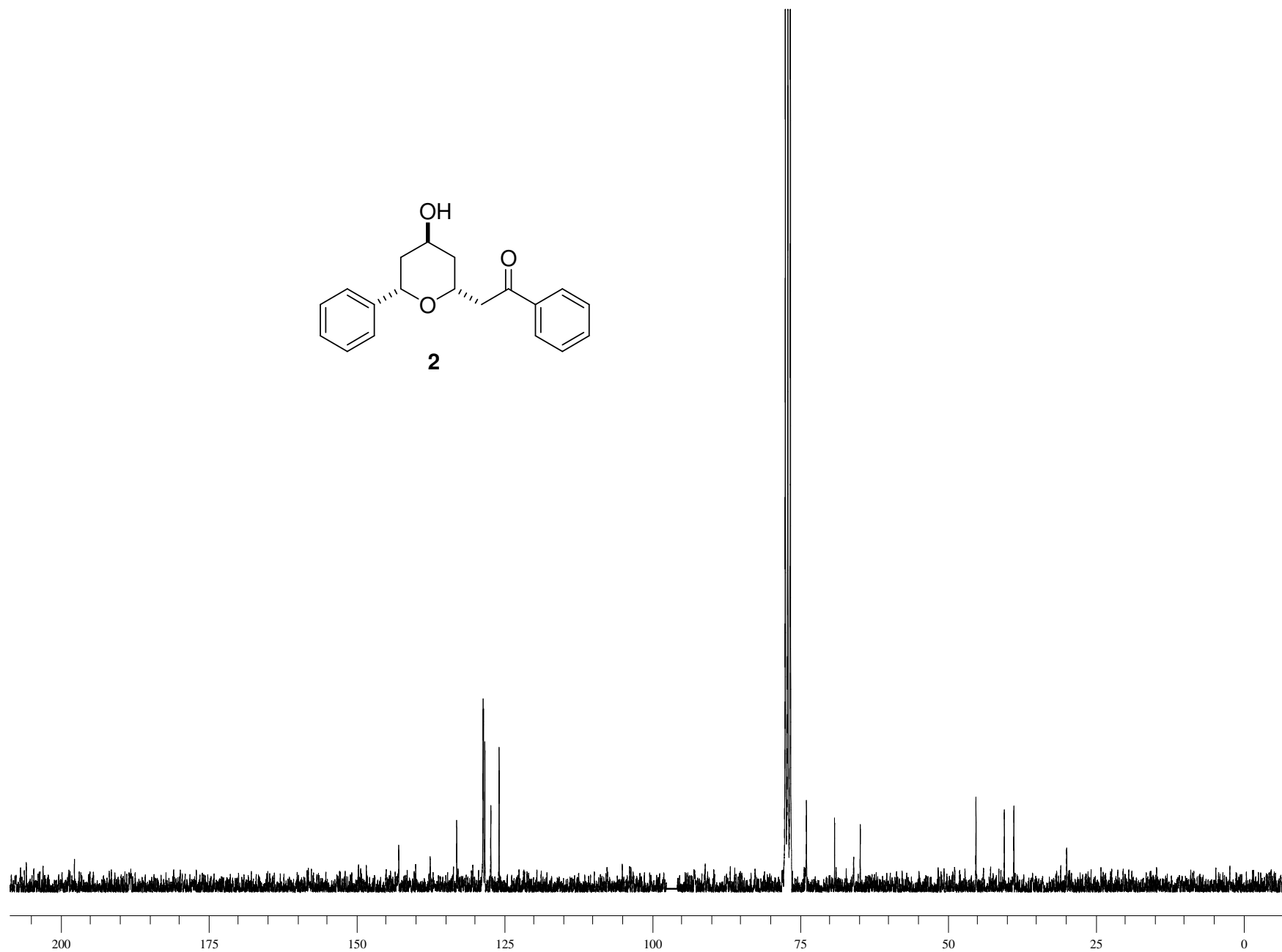
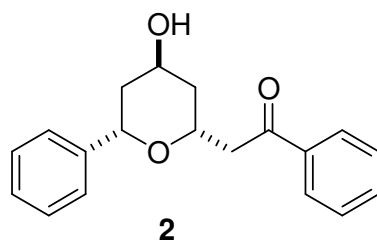
¹³CNMR, CDCl₃ 100 MHz)

S 43



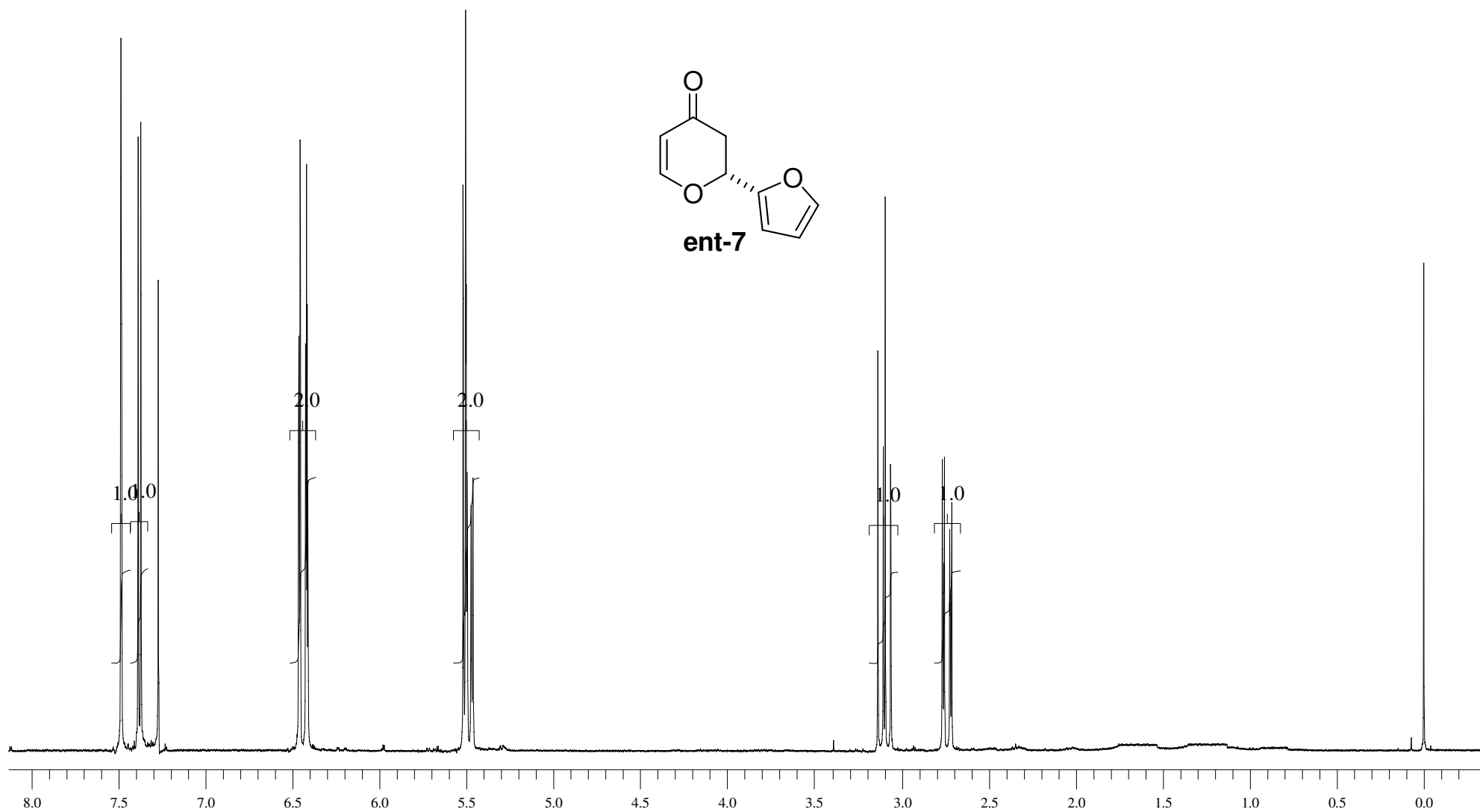
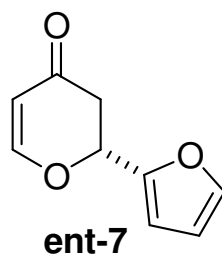
^1H NMR (400 MHz, CDCl_3)

S 44



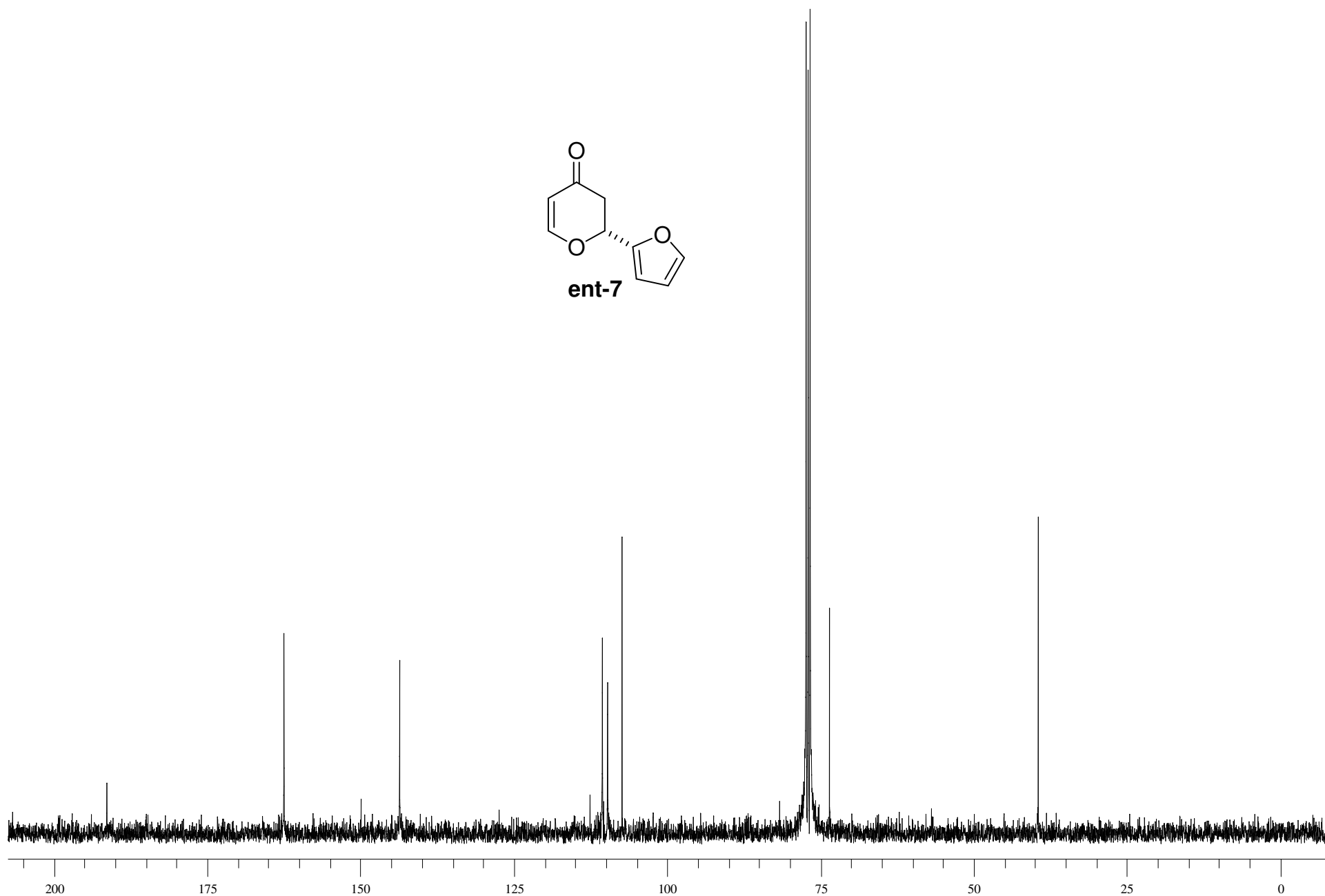
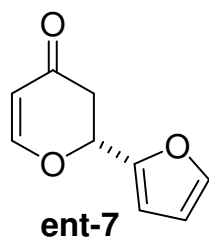
^{13}C NMR, CDCl_3 100 MHz)

S 45

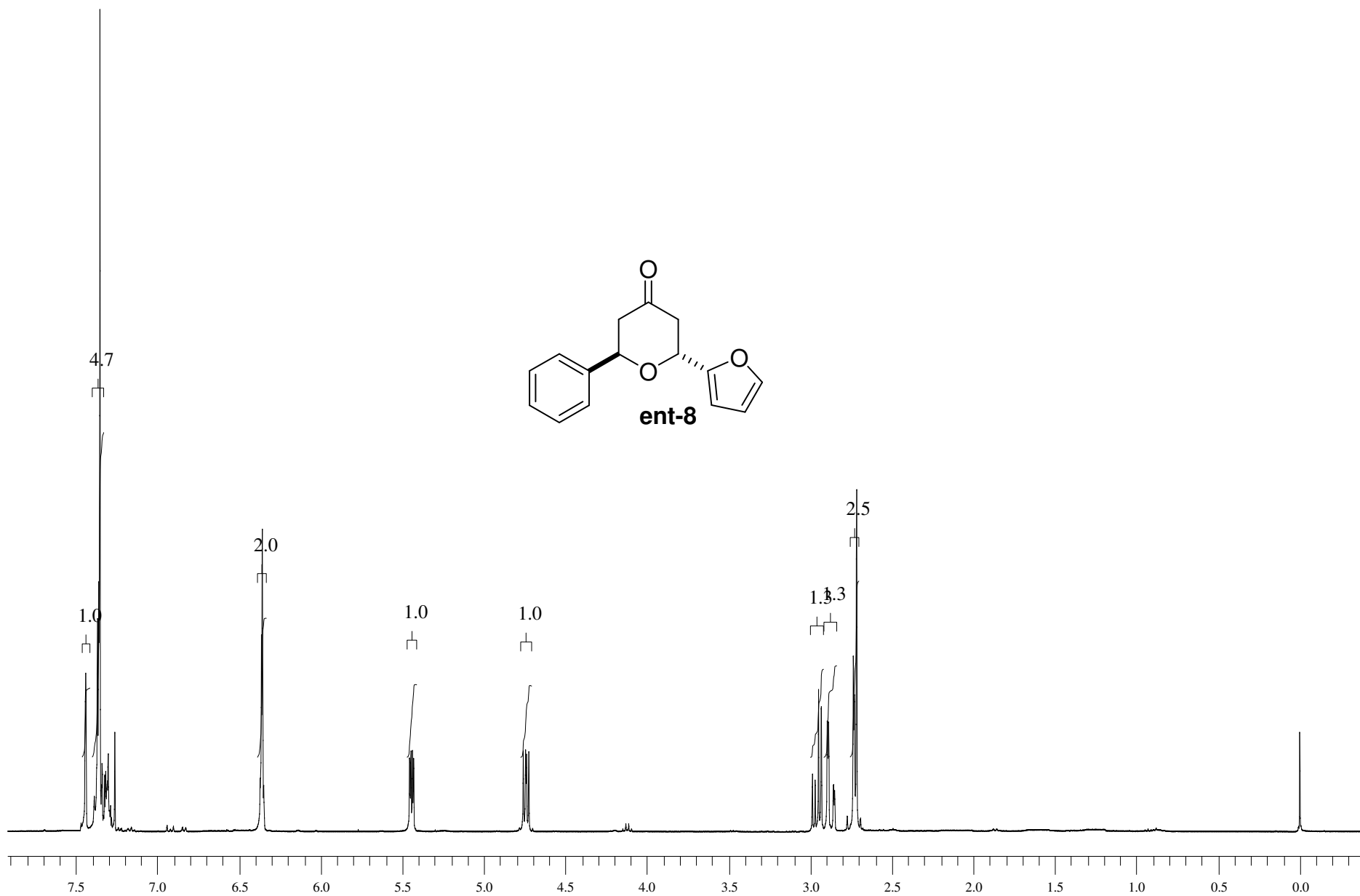
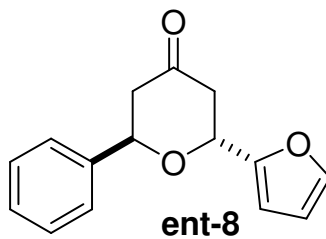


^1H NMR (400 MHz, CDCl_3)

S 46

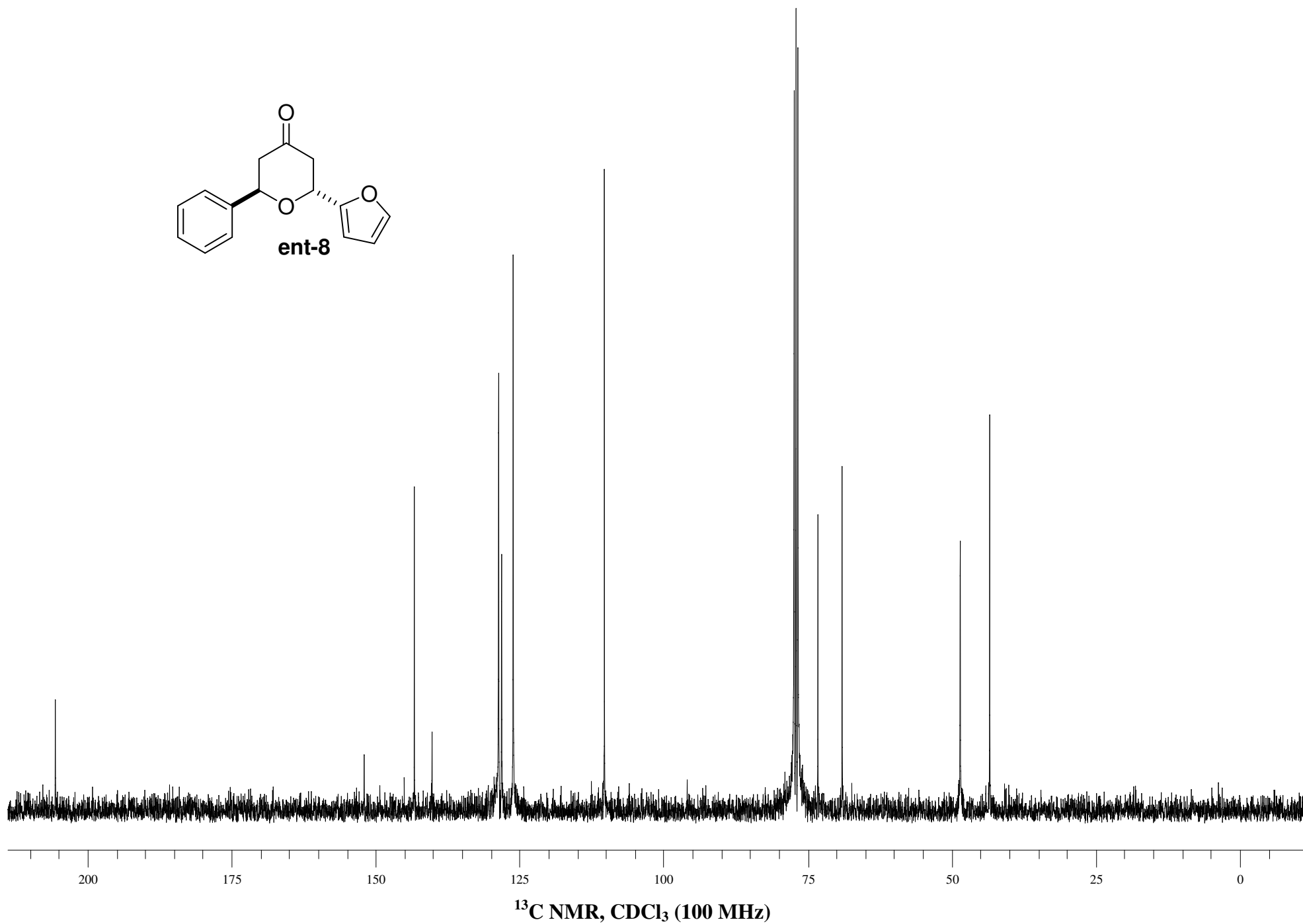
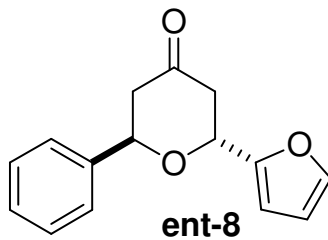


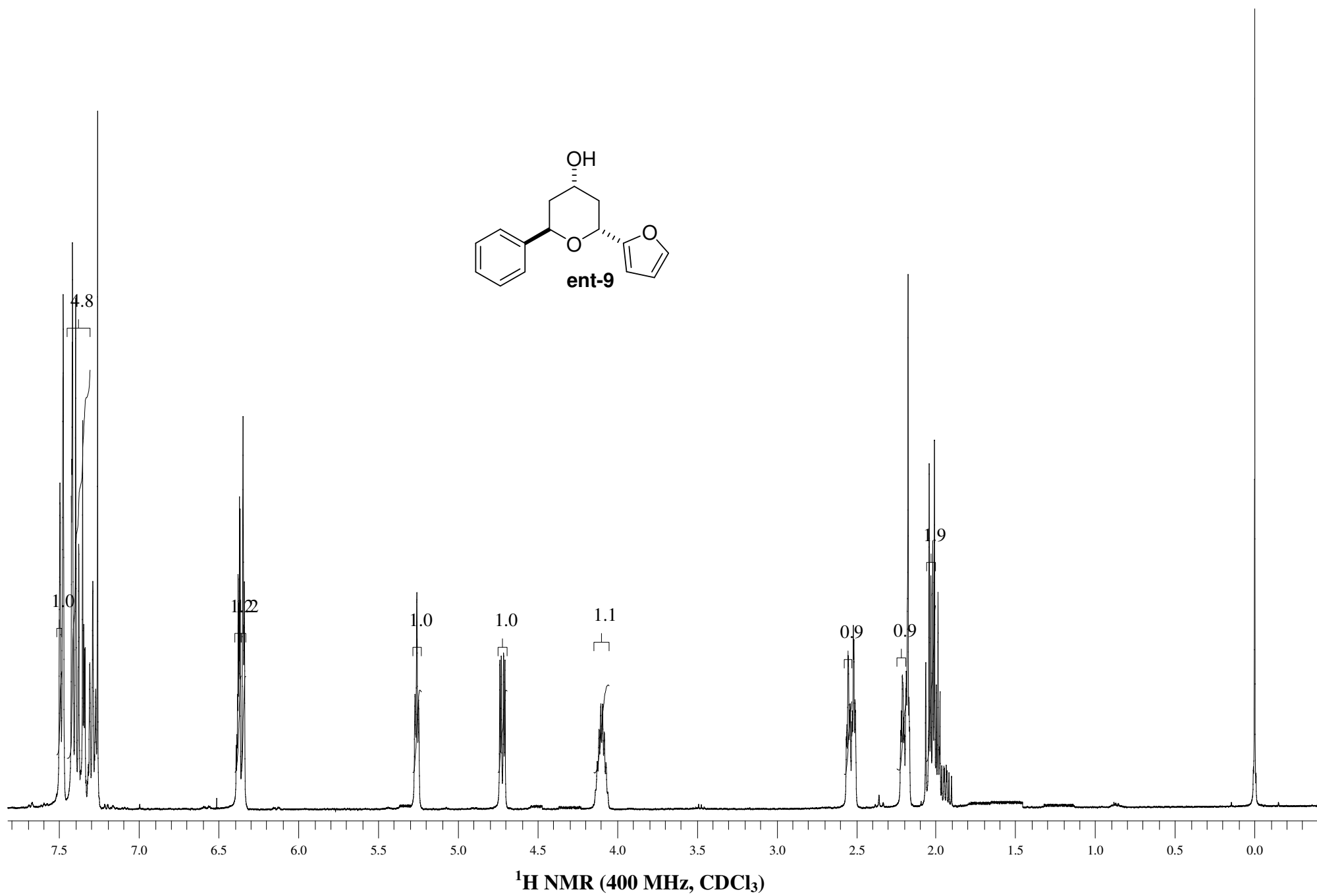
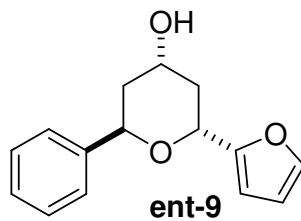
¹³C NMR, CDCl₃ (100 MHz)



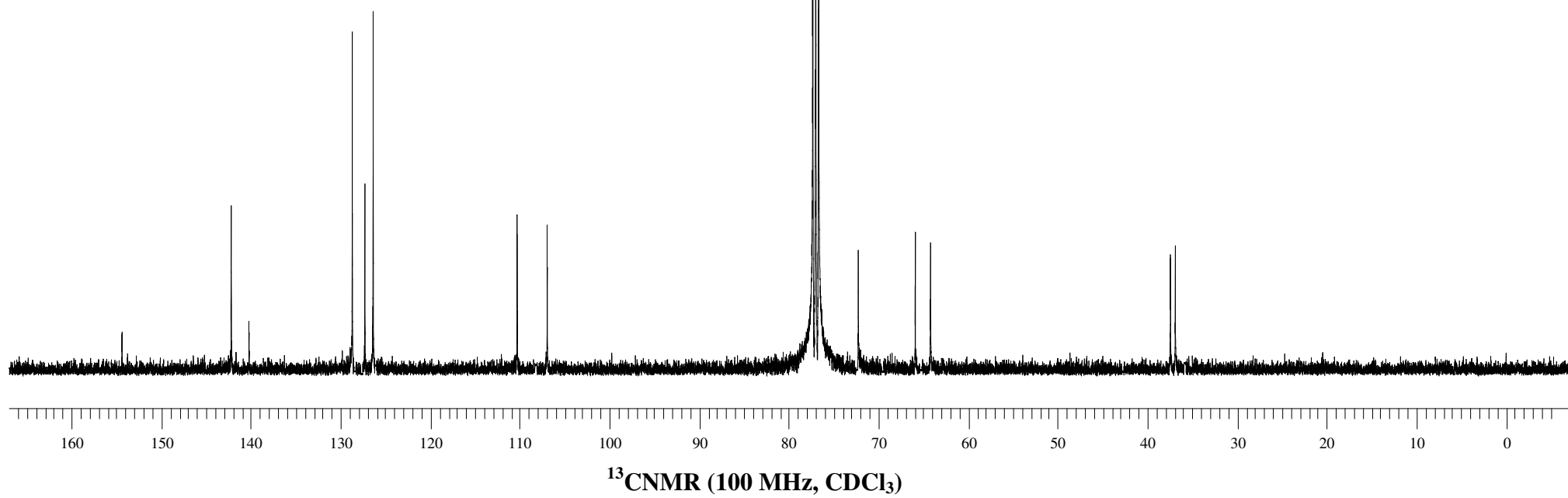
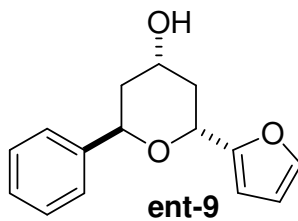
^1H NMR (400 MHz, CDCl_3)

S 48

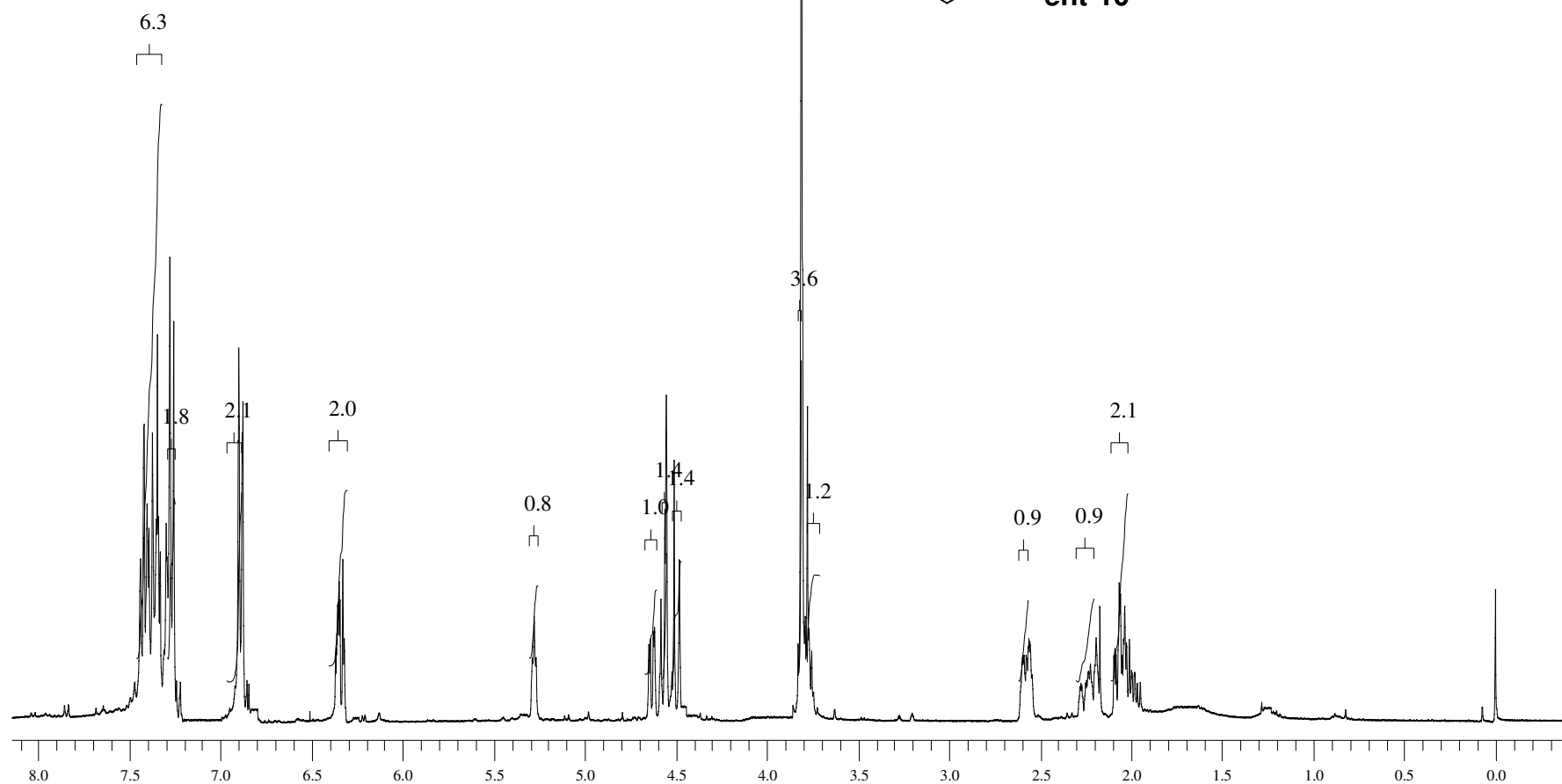
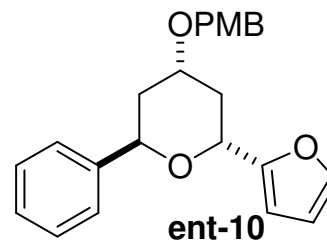




S 50

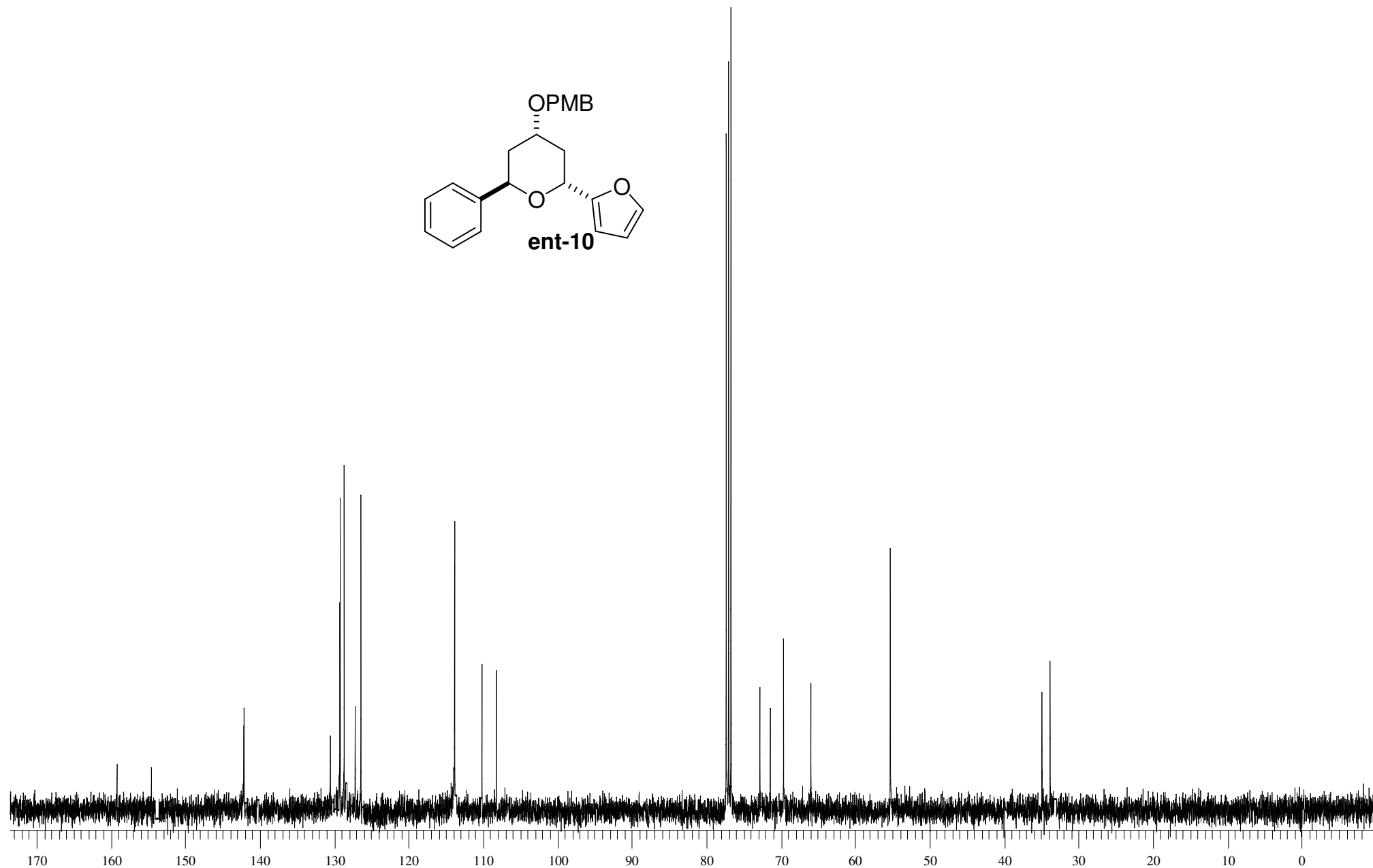
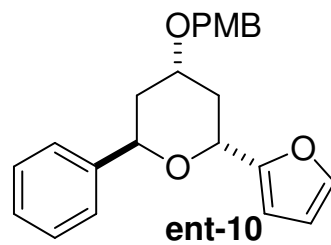


S 51



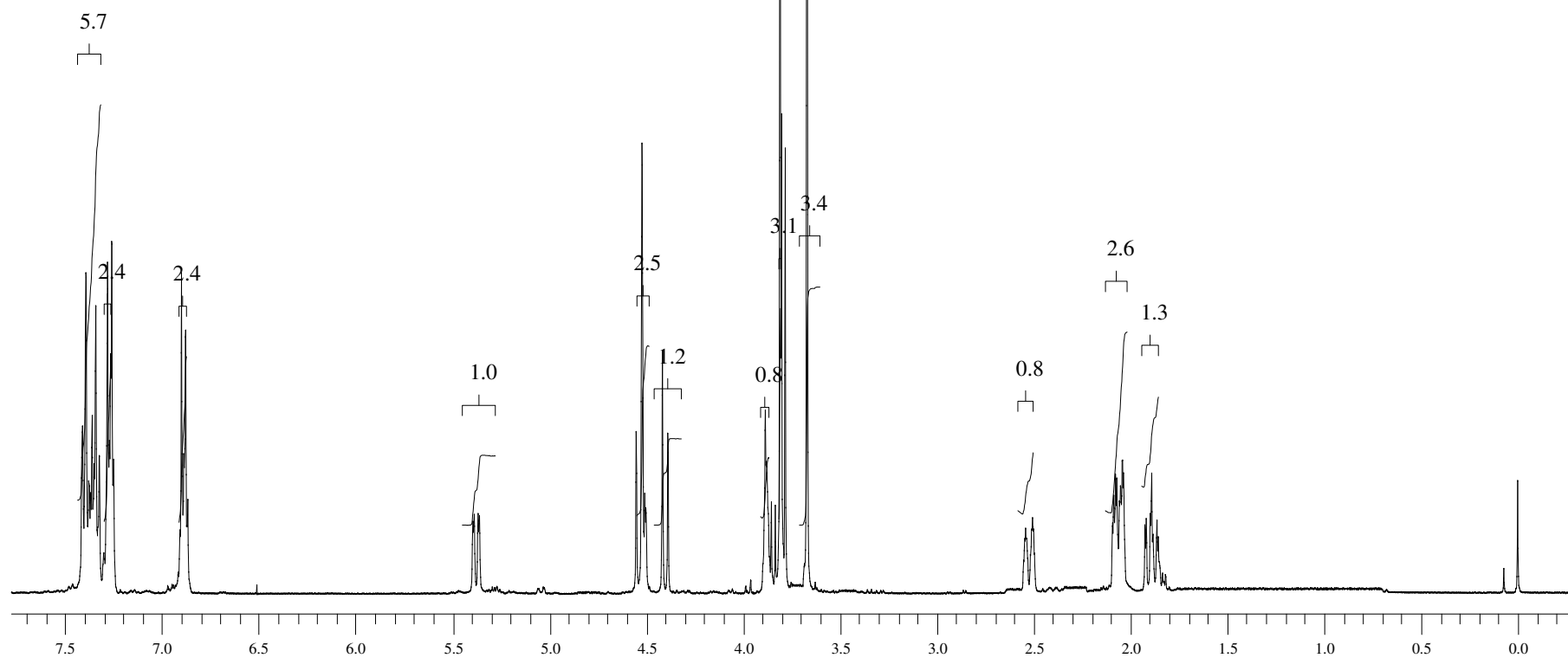
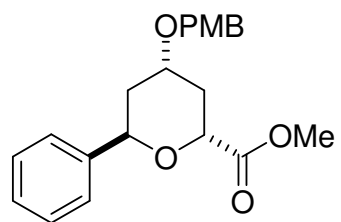
^1H NMR (400 MHz, CDCl_3)

S 52



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

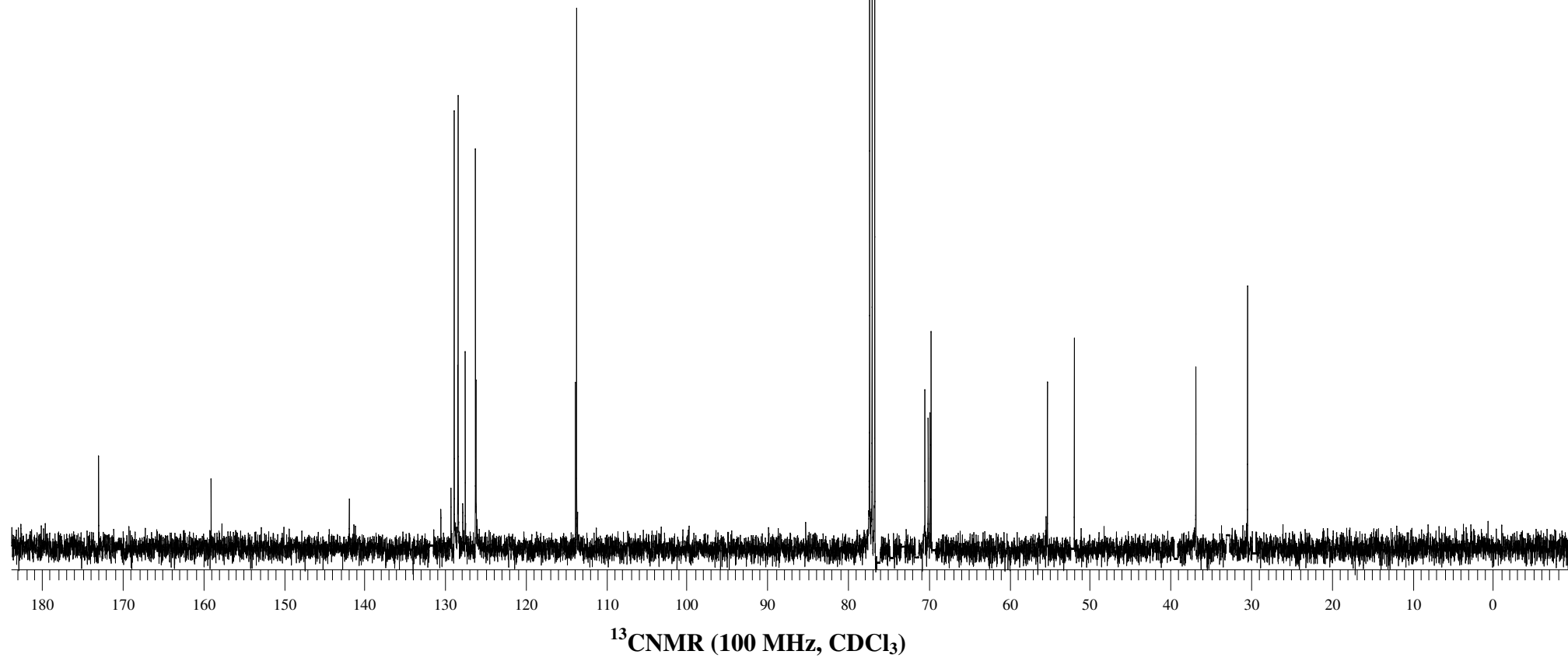
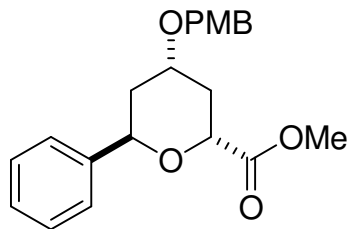
S 53



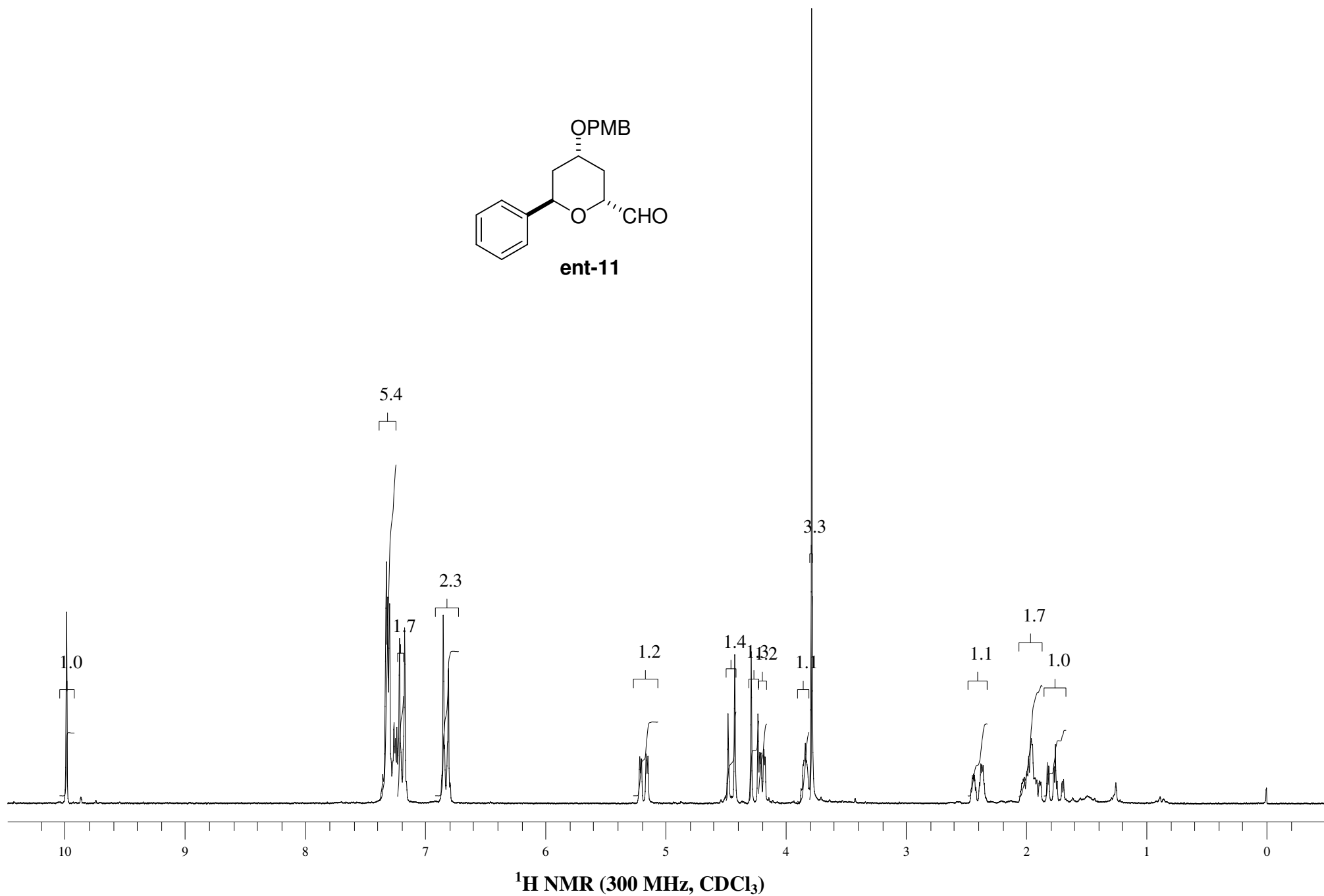
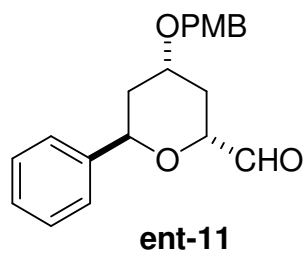
^1H NMR (400 MHz, CDCl_3)

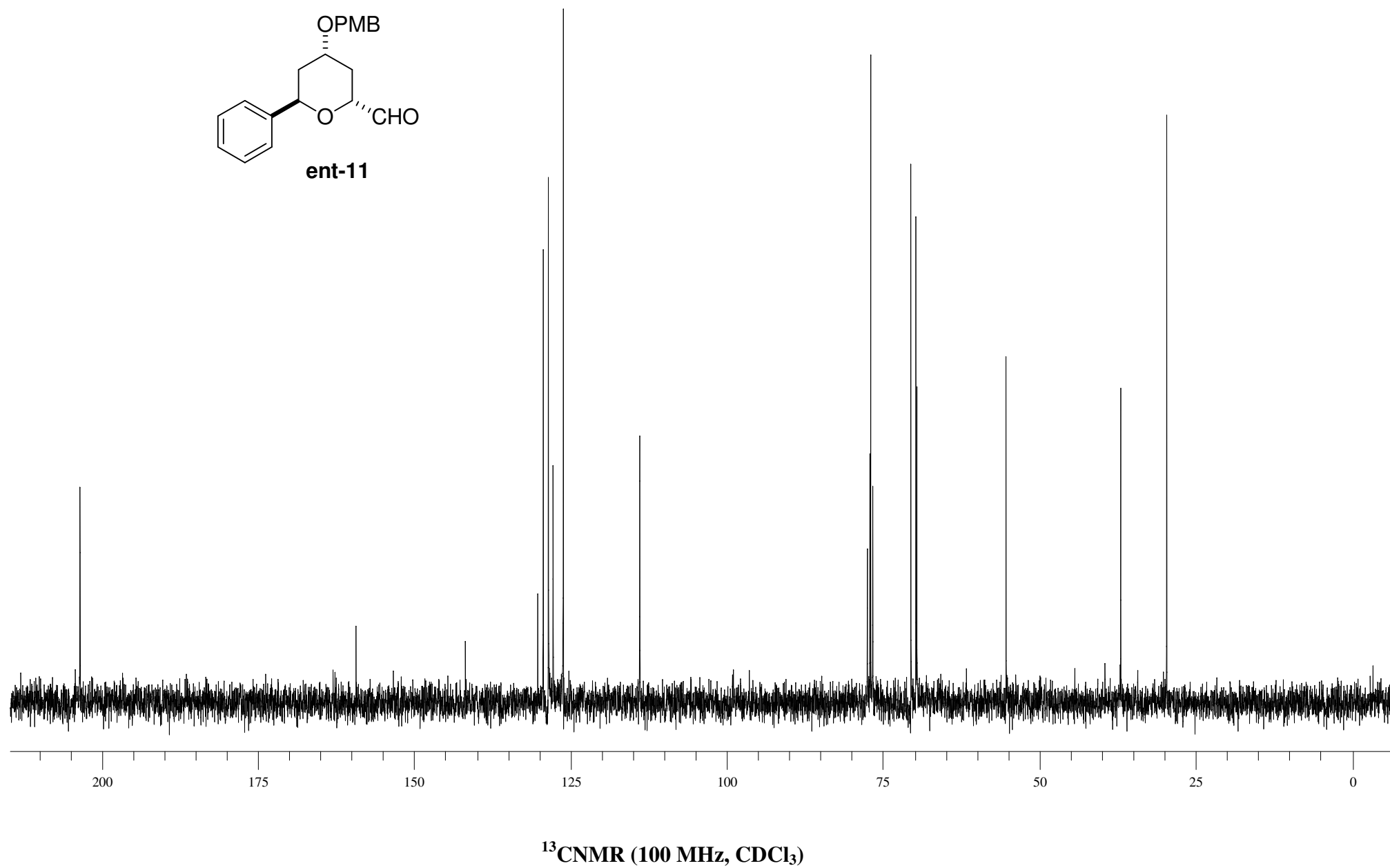
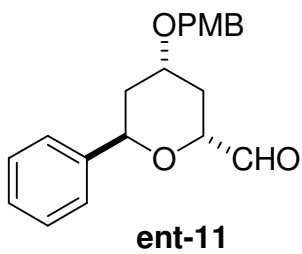
53

S 54

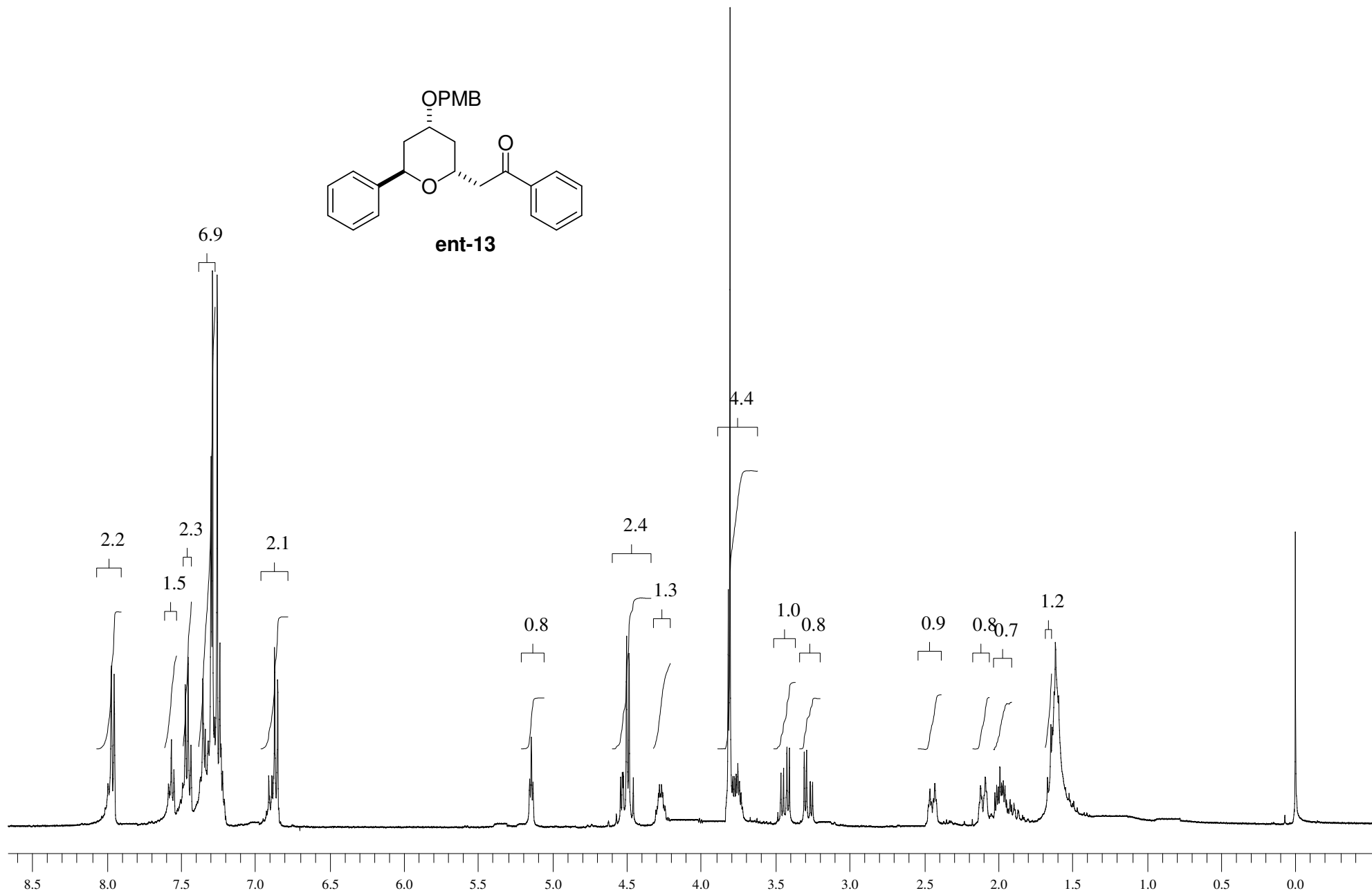
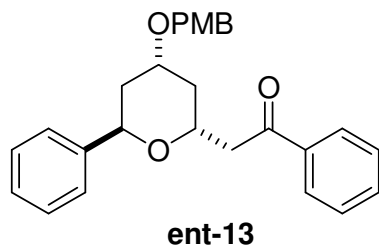


S 55



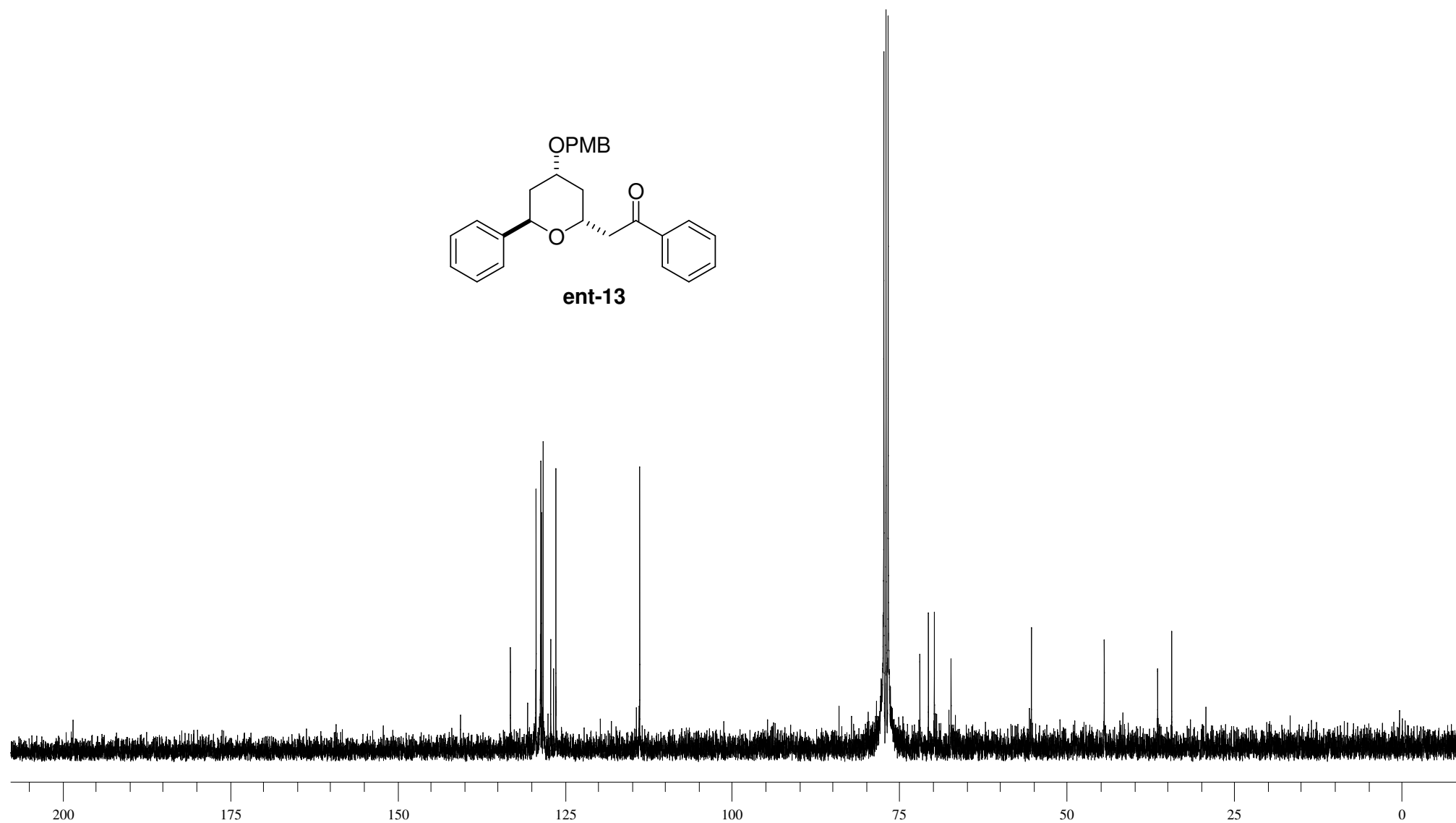
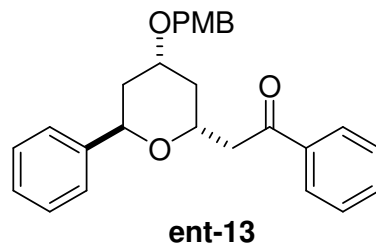


S 57



¹H NMR (400 MHz, CDCl₃)

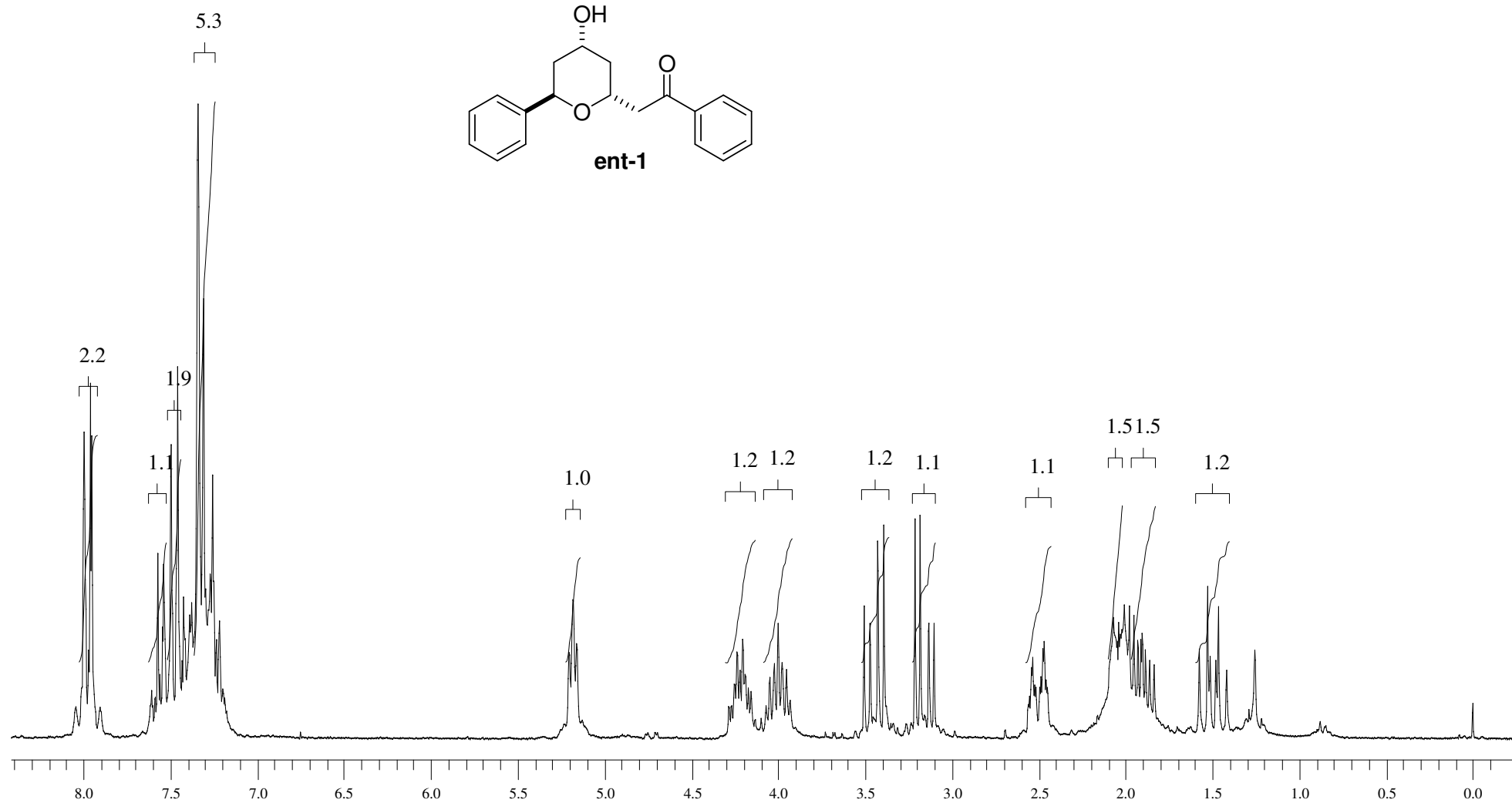
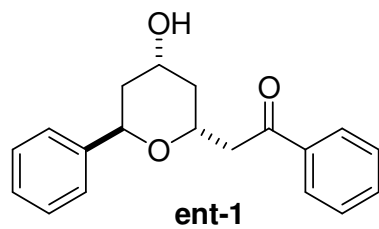
S 58



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

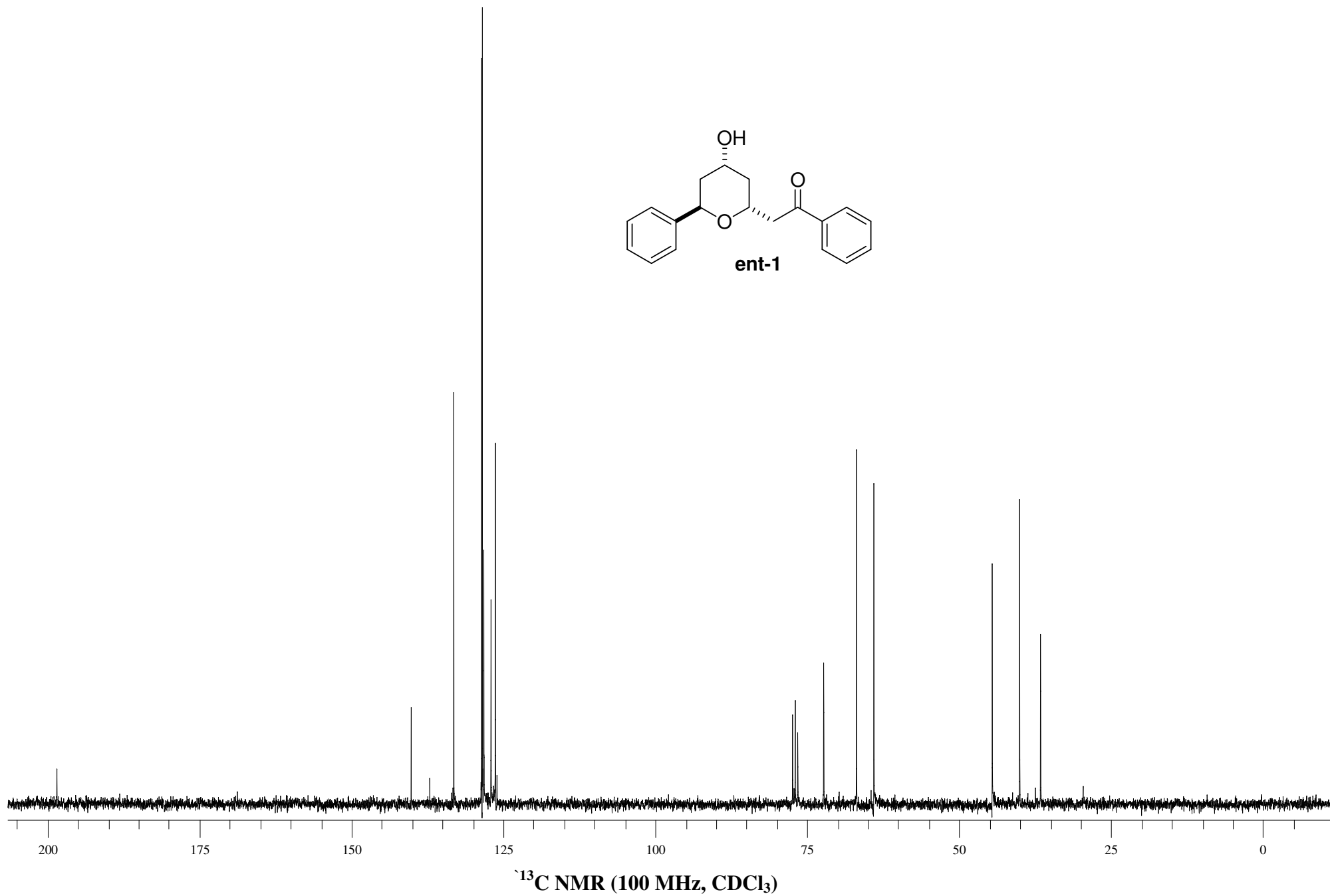
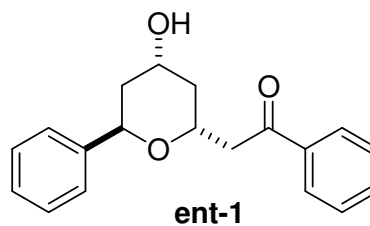
58

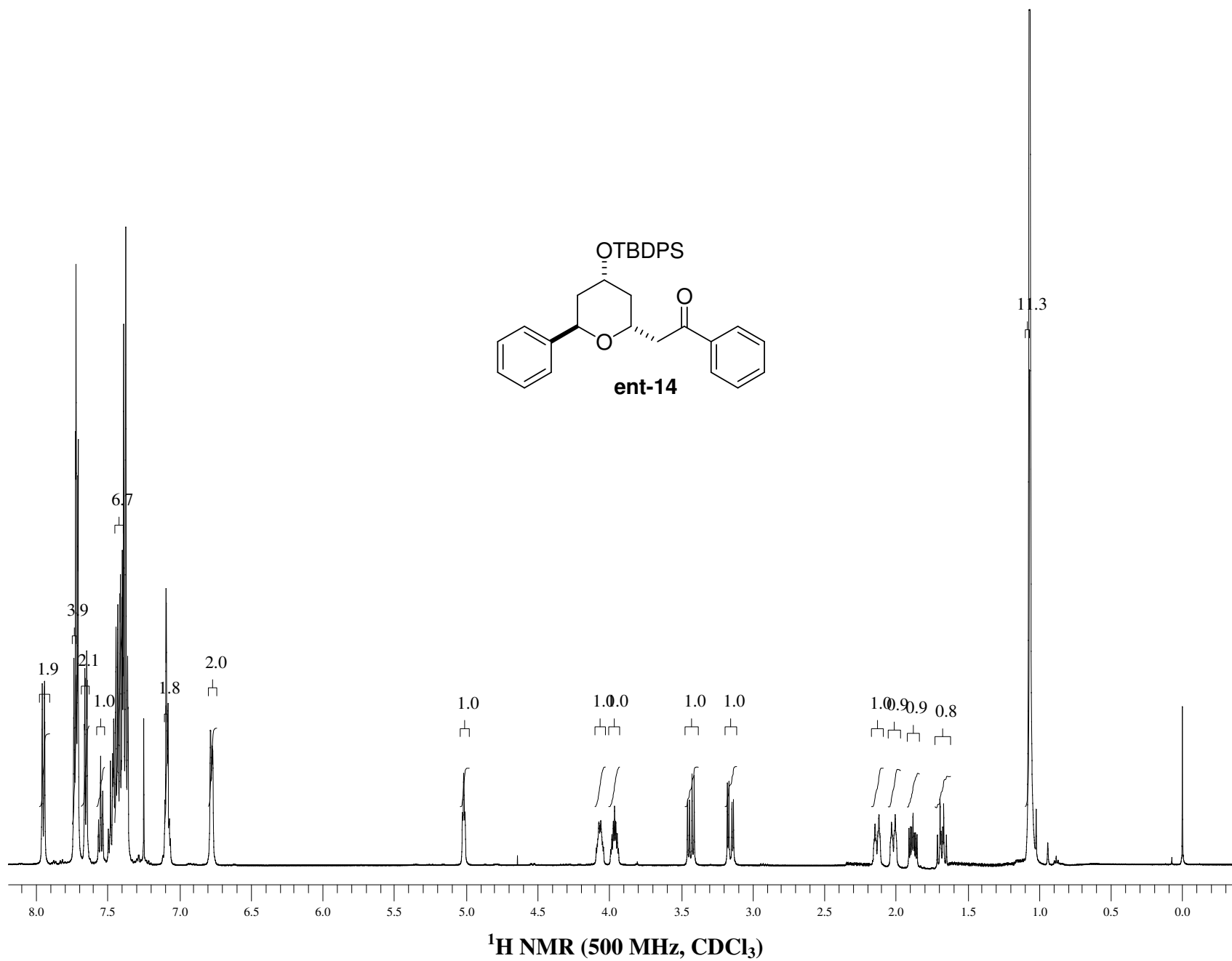
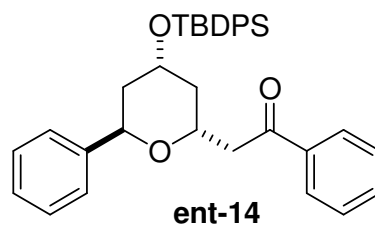
S 59



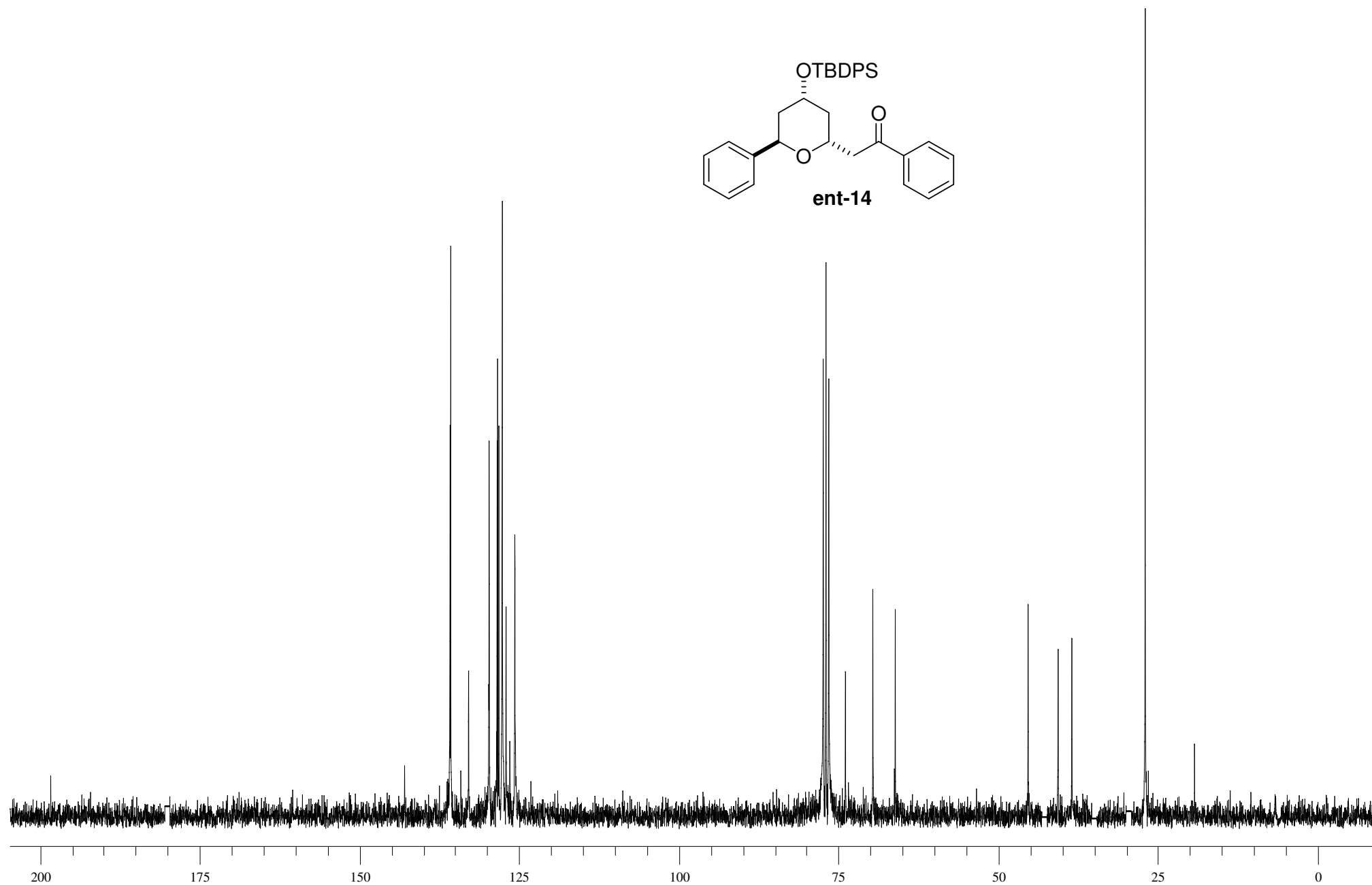
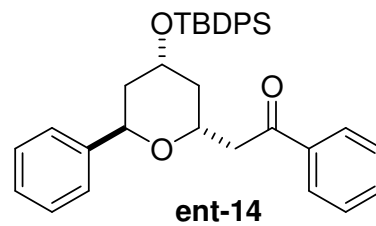
¹H NMR (400 MHz, CDCl₃)

S 60



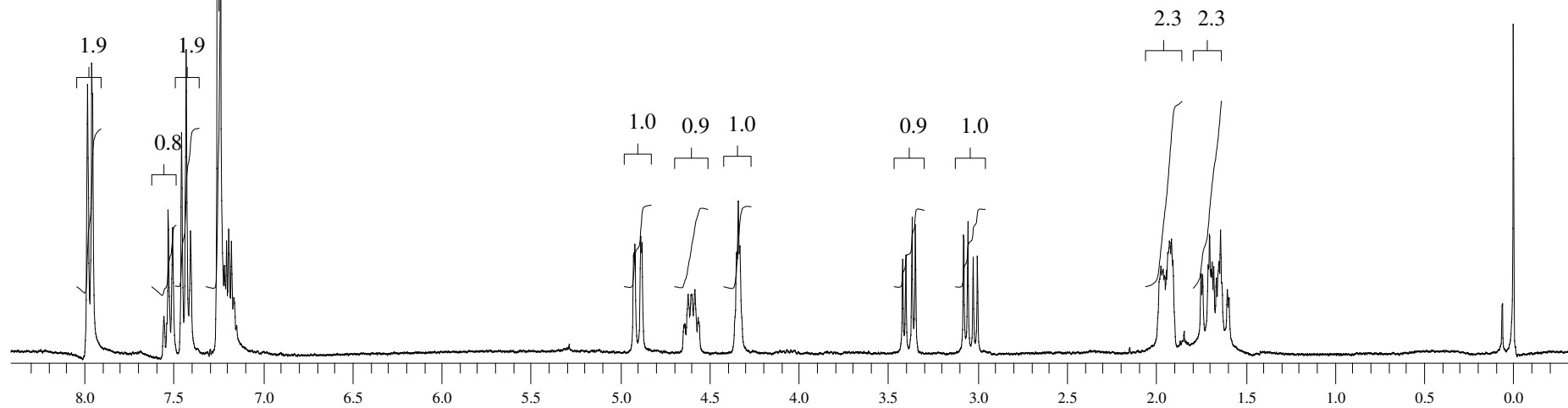
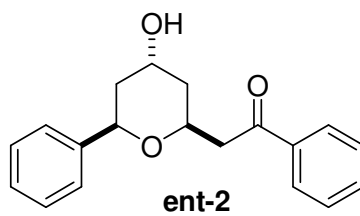


S 62



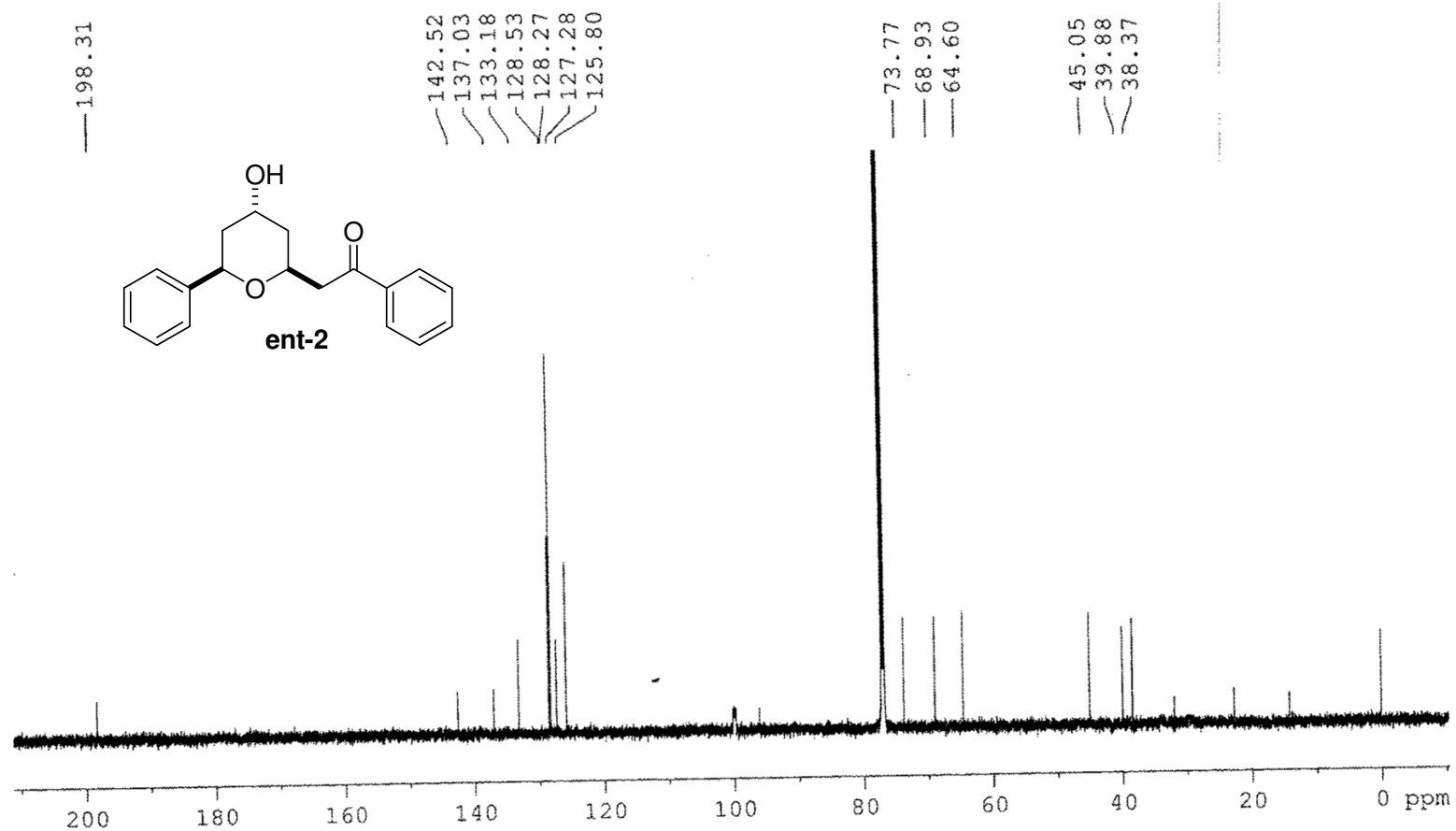
¹³CNMR (100 MHz, CDCl₃)

62



^1H NMR (400 MHz, CDCl_3)

RAMAKRISHNA-GKS-RGN-FINAL-1-C13-12C

¹³CNMR (75 MHz, CDCl₃)

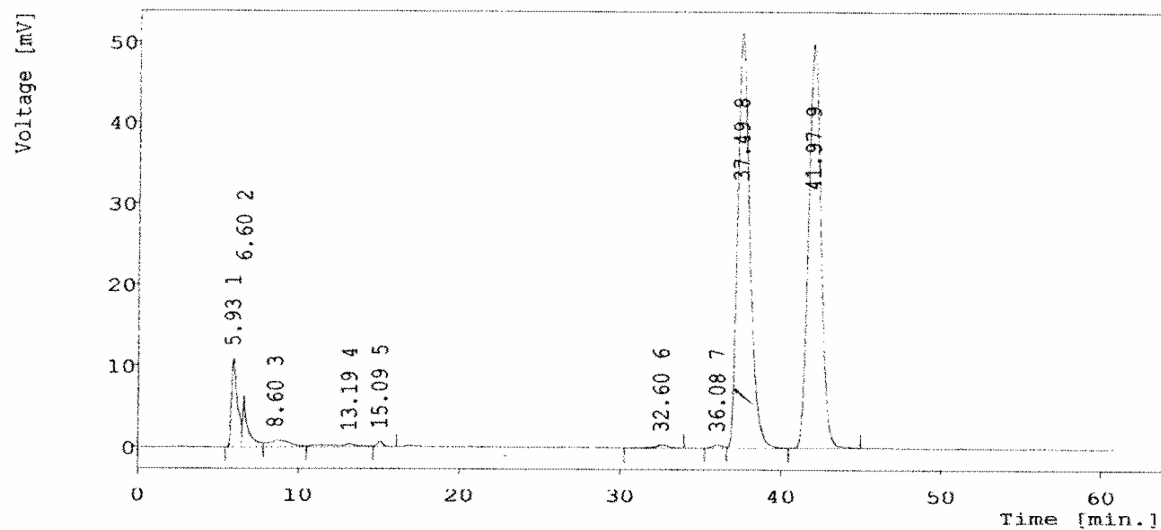
Tue, 27th Jan, 2009 19:38:54

ALREC

Page

Sample ID : **cbno2**
 Sample : **cbno2**
 Amount : **20**
 ISTD Amount: **0**
 Raw Data : **alrec**
 Primary : **alrec**
 Project : **work1**

Analyst :
 Dilution : **1**
 Inj. Volume: **20**
 From : **Tue, 27th Jan, 2009 18:37:27**
 Calibration : **(none)**
 Style : **report**



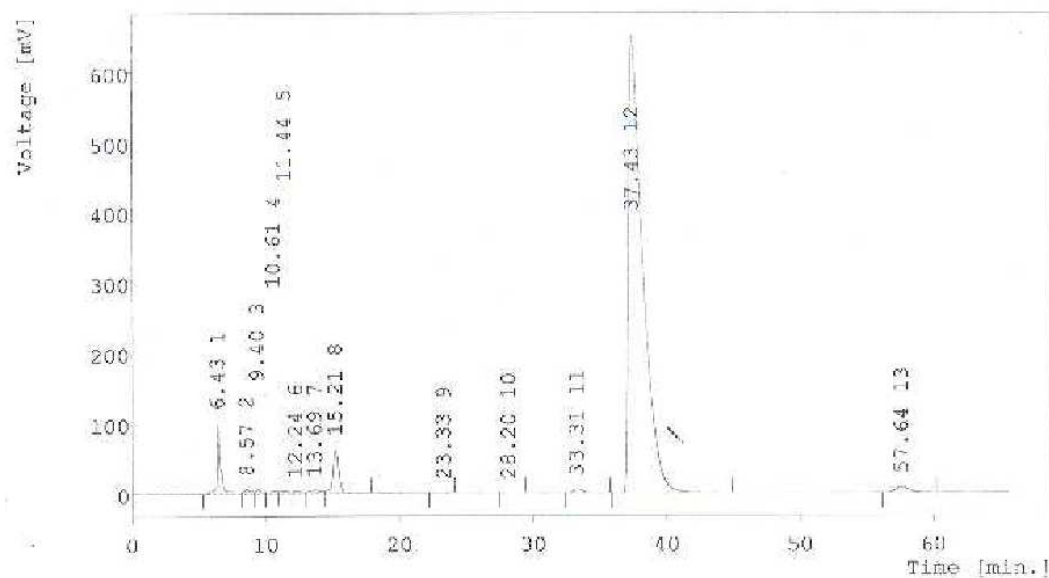
Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	5.933	279.4919	10.8524	0.3867	4.6480	8.9685
2	6.600	146.3637	6.2490	0.2667	2.4340	5.1642
3	8.600	78.6469	0.8302	1.7733	1.3079	0.6861
4	13.187	42.4147	0.3725	0.6267	0.7054	0.3078
5	15.093	16.8358	0.6903	0.3733	0.2800	0.5705
6	32.600	19.7809	0.3738	0.7867	0.3290	0.3089
7	36.080	18.0047	0.3985	0.7867	0.2994	0.3293
8	37.493	2705.5948	51.2829	0.8000	44.9940	42.3803
9	41.973	2706.0961	49.9567	0.8400	45.0023	41.2844
-	Total	6013.2294	121.0064			

HPLC data for compound **8** (Diastereomeric mixture)

Amount : 20
 ISTD Amount: 0
 Raw Data : chi-ii
 Primary : chi-ii
 Project : work1

Dilution : 1
 Inj. Volume: 20
 From : Tue, 27th Jan, 2009 19:47:36
 Calibration : (none)
 Style : report



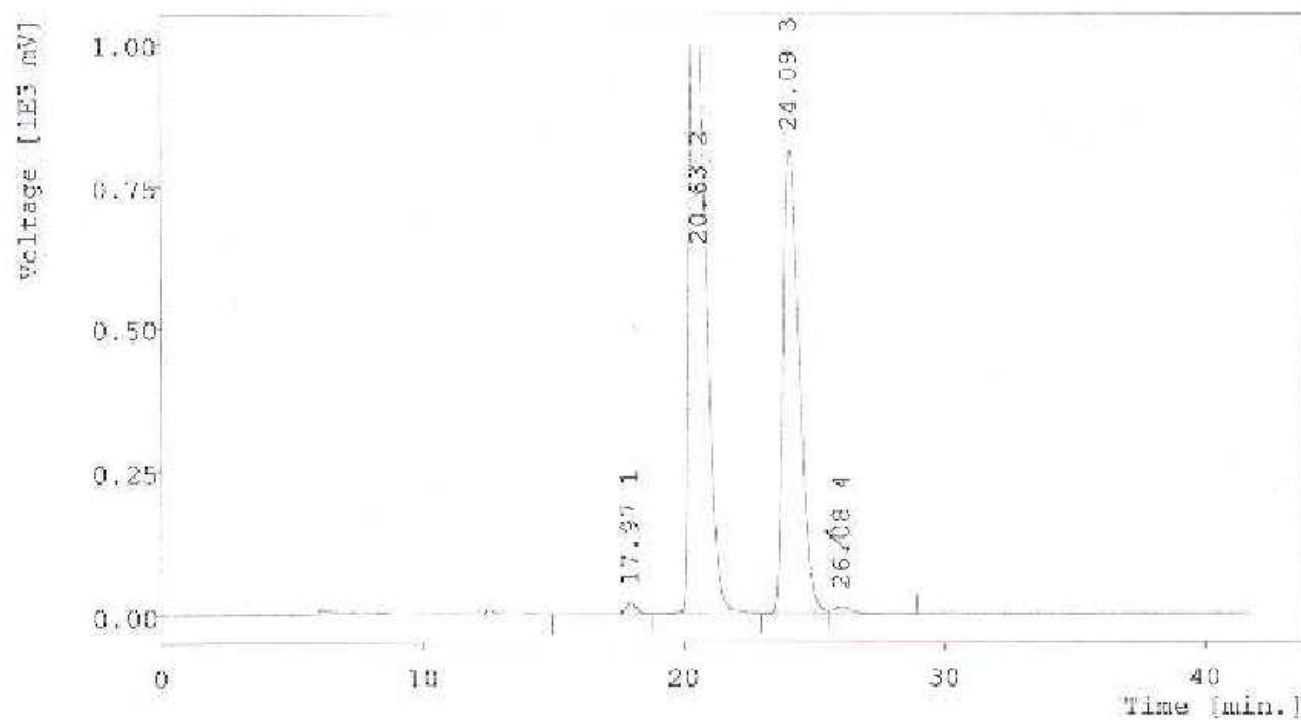
Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	6.427	1694.2729	99.5066	0.1333	3.1065	11.5928
2	8.573	233.3822	6.6844	0.7067	0.4279	0.7787
3	9.400	185.4219	6.3406	0.5200	0.3400	0.7387
4	10.613	187.2289	3.7174	1.0000	0.3433	0.4331
5	11.440	207.9350	4.2820	1.0000	0.3813	0.4989
6	12.240	187.2551	4.1065	0.9867	0.3433	0.4784
7	13.693	319.1805	4.6742	1.3733	0.5852	0.5446
8	15.213	1983.5427	62.5979	0.4667	3.6369	7.2928
9	23.333	25.9695	0.5653	0.6267	0.0476	0.0659
10	28.200	12.7592	0.2835	0.6933	0.0234	0.0330
11	33.307	265.9382	5.2583	0.7600	0.4876	0.6126
12	37.427	48673.8379	652.3043	1.1200	89.2446	75.9950
13	57.640	563.0887	8.0309	1.0933	1.0324	0.9355
-	Total	54539.8127	858.3521			

HPLC data for compound 8 (chiral)

Primary : ar-rec
Project : work1

Calculation : none
Style : report



Result Table Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	17.973	537.3855	18.9409	0.4267	0.6435	1.0276
2	20.627	47448.2149	1000.9677	0.7467	56.8190	54.3067
3	24.093	35045.7513	812.9918	0.6803	41.9671	44.1082
4	26.080	476.3582	10.2750	0.7333	0.5704	0.5575
-	Total	83507.7099	1843.1755			

HPLC data for compound **9** (Diastereomeric mixture)

Wed, 28th Jan, 2009 13:05:08

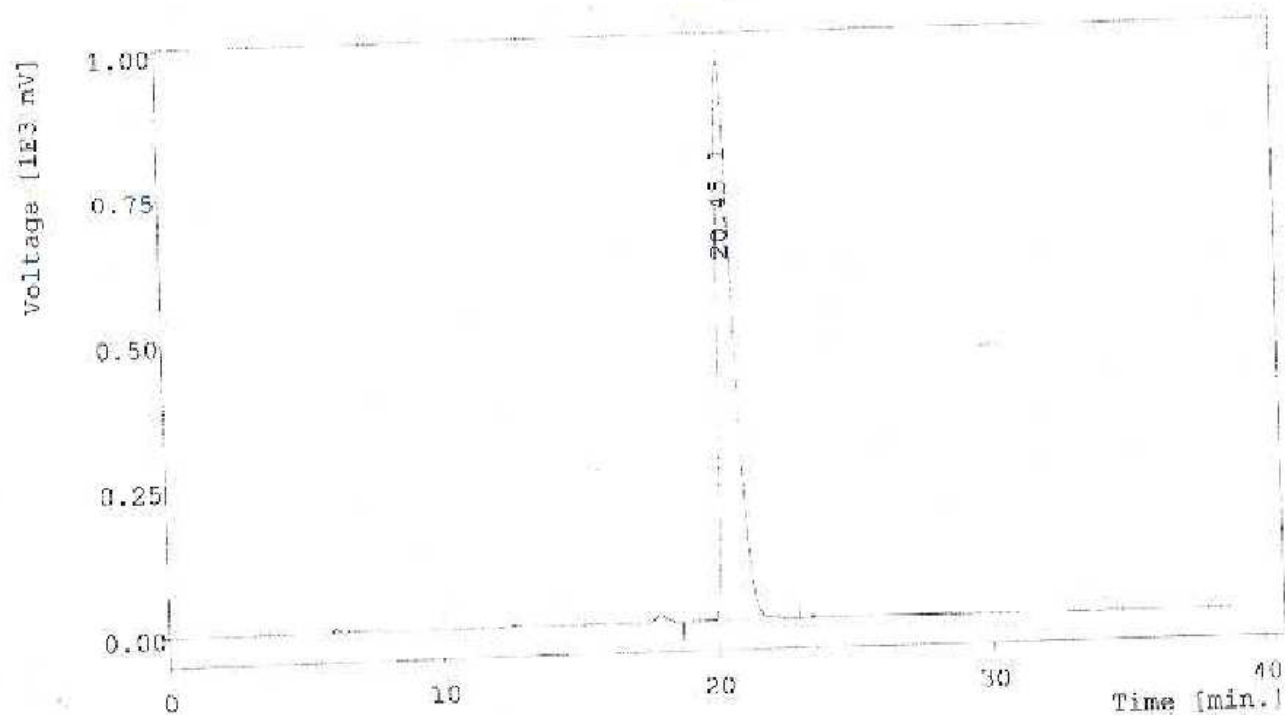
AL-CHIRA

Page 1

Sample ID : AL-rec
 Sample : AL-rec
 Amount : 20
 Raw Data : al-chira
 Primary : al-chira
 Project : work1

Analyst : GRK

Dilution : 1
 From : Wed, 28th Jan, 2009 12:21:59
 Calibration : (none)
 Style : report



Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	20.453	38281.1272	962.3213	0.6267	100.0000	100.0000
-	Total	38281.1272	962.3213			

HPLC data for compound 9 (Chiral)

ORTEP representation of 7 with 50% probability.

