Supporting Information

SYNTHESIS OF DIASTEREOMERICALLY AND ENANTIOMERICALLY PURE 2,3-DISUBSTITUTED TETRAHYDROFURANS USING A SULFOXONIUM YLIDE

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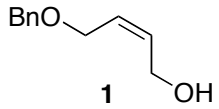
Experimental

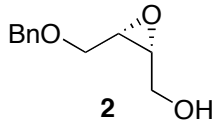
General: Tetrahydrofuran was freshly distilled from Na/benzophenone. Methylene chloride was dried over CaH_2 and freshly distilled prior to use. Dimethylsulfoxide was dried over CaH_2 and distilled under high vacuum at temperatures <60 ˚C and stored over molecular sieves. Trimethylsulfoxonium iodide was dried under high vacuum at 30 ˚C overnight prior to use. All other reagents were used as purchased from Aldrich or Fluka. NMR spectra were obtained using either a 300 MHz Inova or 500 MHz Varian NMR spectrometer and referenced using deuterated chloroform or DMSO. Gas chromatographic analyses were performed using a Hewlett Packard gas chromatograph (6890 series) equipped with a capillary AltechSE-54 column (30 m x 320 mm x 0.25 mm). IR spectra were recorded on Nicolet IR/42 spectrometer using NaCl cells. Column chromatography was performed using Silicycle (40-60 mm) silica gel. Pre-coated silica gel 60 F_{254} plates were used for analytical TLC. Preparation of MPA esters for determination of *ee* was done according to the Mosher's ester procedure.[1]

Preparation of 1.[2]



1

A solution of *cis*-2-buten-1,4-diol (8.8 g, 100 mmol, 1.0 eq) in 250 mL of THF was added dropwise to a suspension of NaH (4.4 g of a 60% dispersion in mineral oil, 110 mmol, 1.1 eq, washed 2x with dry pentane) in 500 mL of a 4:1 mixture of dry THF/DMSO. The mixture was stirred at rt for 30 min, then a solution of benzyl bromide (18.9 g, 110 mmol, 1.1 eq) in 250 mL of THF was added dropwise, followed immediately by tetrabutylammonium iodide (18.5 g, 50 mmol, 0.5 eq) in one portion. The mixture was heated to 60 ºC overnight. After cooling, an equal volume of water was added and the mixture extracted 3x with 200 mL portions of diethyl ether. The combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was column chromatographed using 3:1 hexanes/ethyl acetate to give the title compound as a clear to pale yellow oil (16.4 g, 92% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 5H), 5.8 (m, 2H), 4.5 (s, 2H), 4.15 (dd, 2H), 4.1 (d, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 132.3, 128.2, 127.6, 127.56, 127.5, 72.1, 65.4, 58.1.[1]

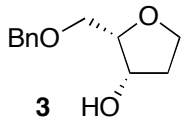


2

Molecular sieves (10 g, 4 Å) were dried overnight at 130 ºC under high vacuum. The sieves were cooled under nitrogen and 600 mL of dry dichloromethane added. The suspension was cooled to -23 ºC and (-)-diethyltartrate (2.0 mL, 11.8 mmol, 0.14 eq) was added dropwise, followed by $Ti(O^iPr)_4$ (2.5 mL, 8.4 mmol, 0.1 eq). The reaction was

stirred for 30 min at -23 ºC to age the catalyst, then ^{t}BuOOH (65.4 mL of a 3.68 M solution in toluene, 252.6 mmol, 3.0 eq) was added in one portion via syringe. The reaction was stirred for another 30 min and then the alcohol (15.0 g, 84.2 mmol, 1.0 eq) dissolved in 200 mL of dichloromethane was added dropwise via syringe pump over 1 h. The reaction was stirred at -23 ºC for 12 h, then warmed to -12 ºC for 1 h. Sodium hydroxide (30% in saturated NaCl) was added in one portion and the reaction stirred for 30 min while allowing the mixture to warm to rt. The molecular sieves were filtered off using a Celite pad and the filtrate phase-separated. The aqueous layer was washed 3x with small portions of dichloromethane and the combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified via column chromatography (hexanes/ethyl acetate) to yield the title epoxy alcohol in 89% yield and 92% *ee* as determined via NMR analysis of its corresponding MPA ester. ^{1}H NMR (300 MHz, $CDCl_3$) 7.35 (m, 5H), 4.6 (dd, 2H), 3.7 (d, 2H), 3.65 (d, 2H), 3.3 (dd, 1H), 3.2 (dd, 1H), 2.7 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 137.3, 128.4, 127.9, 127.8, 73.3, 67.9, 60.5, 55.7, 54.7.[3]

Preparation of 3. The following procedure for substrate **2** is representative for all ylide reactions run in DMSO as the solvent:



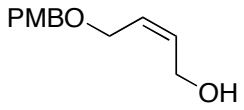
3

Dimethylsulfoxide was dried by stirring overnight over CaH_2 and distilled under high vacuum into a flame-dried flask containing molecular sieves. Trimethylsulfoxonium iodide was dried overnight at rt under high vacuum. Dimethylsulfoxonium methylide was prepared fresh for each reaction. Sodium hydride (4.0 g as a 60% dispersion in mineral oil, 100 mmol, 10.0 eq, washed twice with pentane dried over sodium metal) was placed in a flame-dried flask and dry dimethylsulfoxide (100 mL) was added via syringe. [Use of LiHMDS, NaHMDS, and KHMDS as bases entailed substitution of the aforementioned reagents (10 equiv, 1 M solution in either Toluene (KHMDS) or THF (LiHMDS and NaHMDS) in the reaction with 15 minutes of stirring prior to the addition of **2**. In cases were THF was introduced (LiHMDS and NaHMDS), it was removed quickly under vacuum.] Trimethylsulfoxonium iodide (22.0 g, 100 mmol, 10.0 eq) was added in small portions over 20-30 min. After addition of the trimethylsulfoxonium iodide was complete, the reaction was stirred for an additional 30 min until the bubbling of the milk-white suspension ceased. The epoxy alcohol (1.94 g, 10 mmol, 1.0 eq) dissolved in a small amount of DMSO was added dropwise and the reaction was covered with aluminum foil and heated to 80-85 ºC for 36 h. The dark brown mixture was cooled and diluted with 2x volume of water and saturated ammonium chloride (1 mL). The reaction was extracted several times with ethyl acetate, the combined organics were washed with brine and dried over sodium sulfate. After removal of solvent under reduced pressure, the residue was column chromatographed using a hexane/ethyl acetate gradient to give compound **3** in 96% yield as a thick oil. [Isolated yields for reactions employing LiHMDS, NaHMDS, and KHMDS were 59%, 92%, and 82%, respectively.] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.6 (s, 2H), 4.4 (br m, 1H), 4.0 (dd, 1H, J =

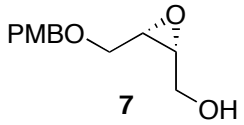
15.5, 8.2 Hz), 3.9 (dd, 1H, 5.3, 9.3 Hz), 3.7-3.8 (overlapping m, 3H), 3.0 (d, 1H, J = 4.9 Hz), 2.1 (m, 1H), 1.9 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 128.3, 127.7, 127.6, 80.3, 73.7, 72.7, 68.9, 66.3, 35.6. IR (neat, cm^{-1}) 3411, 3060, 3020, 2920, 2867, 1647, 1455, 1088. HRMS calculated: 208.1099; observed: 208.1107.[4]

General Procedure for Preperation of 3 via Microwave Irradiation. A 10 mL Teflon tube equipped with a screw-top cap was charged with dry DMSO (5.2 mL) and trimethylsulfoxonium iodide (1.14 g, 5.2 mmol, 10.0 eq). NaHMDS (5.2 mL as a 1 M solution in THF, 5.2 mmol, 10.0 equiv) was added in one aliquot and the suspension was stirred under nitrogen for 15 min. The THF was removed under vacuum and the epoxy alcohol **2** dissolved in DMSO (0.5 mL) was added in one portion. The tube was flushed well with nitrogen and capped tightly. The reaction was heated for a total of 450 seconds in a conventional cooking microwave in pulses of 15 seconds each. The tube was cooled for 2 min in-between pulses. The use of longer pulse times led to impurity formation from some loss of regioselectivity in the ylide attack on the epoxy alcohol. After completion of the reaction, standard work-up followed by column chromatography purification gave the desired **3** in 91% yield. The same procedure was attempted on substrate **25**, but no improvement in the regioselectivity or the yield was noted.

Preparation of 8.[5]

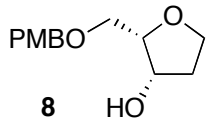


A solution of *cis*-2-buten-1,4-diol in 4:1 THF/DMSO was monoprotected using *p*-methoxybenzyl chloride as described above for benzylation of the same diol. The product was obtained in 83% yield as a thick oil.[3]



7

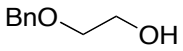
Following Sharpless asymmetric epoxidation, the epoxy alcohol was obtained in 81% yield and 89.5% *ee*.[4] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, 2H), 6.9 (d, 2H), 4.45-4.55 (dd, 2H), 3.8 (s, 3H), 3.6-3.8 (overlapping m, 5H), 3.25 (m, 1H), 3.2 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 129.5, 129.4, 113.9, 73.11, 67.7, 60.7, 55.6, 55.3, 54.7. The R(-)-MPA ester was prepared and analyzed by proton NMR (JSVI150A) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4 (m, 2H), 7.38 (overlapping signals, 3H), 7.2 (m, 2H), 6.83 (d, 2H), 4.8 (s, 1H), 4.5 (d, 1H), 4.4 (d, 1H), 4.3 (dd, 1H), 4.15 (dd, 1H), 3.8 (s, 3H), 3.6 (dd, 1H), 3.5 (dd, 1H), 3.4 (s, 3H), 3.2 (m, 1H), 3.1 (m, 1H).[5]



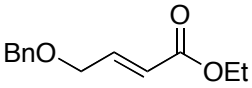
8

Formation of the tetrahydrofuran **8** on a 0.5 g scale proceeded in 86% yield to give the product as a thick oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.2 (d, 2H, *J* = 8.8 Hz), 6.85 (d, 2H, *J* = 8.8 Hz), 4.5 (s, 2H), 4.4 (m, 1H), 4.05 (dd, 1H, *J* = 15.7, 8.2 Hz), 3.85 (m, 1H), 3.8 (s, 3H), 3.7-3.8 (overlapping m, 3H), 2.6 (d, 1H, *J* = 9.3 Hz), 2.1 (m, 1H), 1.9 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 129.7, 129.4, 113.8, 80.3, 73.4, 72.9, 68.6, 66.5, 55.2, 35.6. IR (neat, cm^{-1}) 3418, 2936, 1613, 1514, 1073. HRMS calculated: 238.1205; observed: 238.1197. The R-(-)-MPA ester was made and shown to be 90% *ee*.

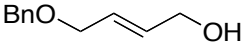
Preparation of 6.[6]



The monobenzylated alcohol of ethylene glycol was prepared as previously described for the benzylation of *cis*-2-buten-1,4-diol in 84% yield.

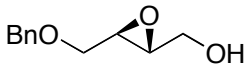


The alcohol (2.0 g, 13.2 mmol, 1.0 eq) was placed in dry dichloromethane (25 mL) and cooled to 0 ˚C. Pyridine (3.0 mL) and DMP (1.5 eq) were added and the reaction stirred at 15 ˚C for another 2 h. Triphenylphosphinocarboxyethyl ylide (1.6 eq) and additional dichloromethane (25 mL) were added and the reaction was warmed to rt and stirred for 36 h. The dichloromethane was removed by rotary evaporation and diethyl ether was added to the residue. The resulting solids were filtered through a pad of Celite and washed well with portions of diethyl ether. The filtrate was concentrated and the residue purified via column chromatography (9:1 hexanes/ethyl acetate) to give the ester in 66% yield over the two steps.[7]



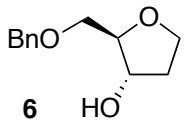
The ester (1.9 g, 8.1 mmol, 1.0 eq) was placed in dry THF (25 mL) and cooled to -20 ˚C. Diisobutylaluminum hydride (11.9 mL, 17.8 mmol as a 1.5 M solution in toluene, 2.2 eq) was added dropwise and the reaction was stirred at -20 ˚C for 3 h. The reaction was carefully quenched with saturated Rochelle's salt and then glycerol (0.2 mL/mmol DIBAL) was added and the reaction was stirred overnight to break up the aluminum complex. The phases were separated and the aqueous layer was washed several times with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified via column chromatography (hexanes/ethyl acetate gradient) to give the allylic alcohol in 97% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.2 (m, 5H), 5.7 (m, 2H), 4.4 (s, 2H), 4.0 (d,

2H), 3.85 (d, 2H), 1.9 (br s, 1H); ^{13}C NMR δ (75 MHz, $CDCl_3$) 138.0, 132.3, 128.3, 127.7, 127.6, 127.5, 72.2, 70.0, 62.7.[8]



5

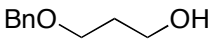
Sharpless asymmetric epoxidation gave the prerequisite epoxy alcohol **5** in 94% yield and 94% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.5 (dd, 2H), 3.8-3.9 (d of m, 1H), 3.7-3.75 (dd, 1H), 3.55 (m, 1H), 3.45 (dd, 1H), 3.2 (m, 1H), 3.9 (m, 1H), 2.9 (br t, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 128.4, 127.7, 127.69, 73.2, 69.5, 61.1, 55.7, 54.2.[9]



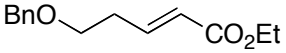
6

The tetrahydrofuran **6** was obtained in 78% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.6 (s, 2H), 4.2 (dd, 1H, J = 2.9, 6.0 Hz), 3.8-4.0 (overlapping m, 3H), 3.55 (dd, 1H, J = 4.9, 9.8 Hz), 3.45 (dd, 1H, J = 5.9, 9.8 Hz), 2.6 (br s, 1H), 2.1 (m, 1H), 1.8 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 128.3, 127.7, 84.6, 73.9, 73.4, 70.8, 67.0, 34.8, IR (neat, cm^{-1}) 3413, 3056, 3020, 2910, 2865, 1650, 1455, 1090.[4]

Preparation of 12.[10]



The 1,3-propanediol was monobenzylated to give the product in 92% yield after purification by column chromatography (8:2 hexanes/ethyl acetate).

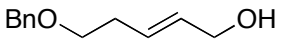


The monobenzylated alcohol (5.0 g, 30 mmol, 1.0 eq) was placed in dichloromethane (120 mL) and cooled to 0 ºC. Dess-Martin periodane (16.5 g, 39 mmol, 1.3 eq) was added and the reaction stirred for 3 h at 15 ºC. The dichloromethane was washed with water, saturated sodium bicarbonate, and brine. The organics were dried over sodium sulfate, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (9:1 hexanes/ethyl acetate) to give the aldehyde in 72% yield.

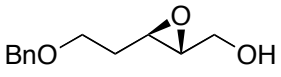
The aldehyde (3.5 g, 21.3 mmol, 1.0 eq) was placed in dichloromethane (300 mL), carboxyethyl phosphonium ylide (11.9 g, 34.1 mmol, 1.6 eq) was added, and the reaction was stirred at rt for 36 h. The dichloromethane was removed by evaporation and diethyl was added to the residue. The resulting solid was filtered and washed well with diethyl

ether. The filtrate was evaporated and the residue was purified by column chromatography (9:1 hexanes/ethyl acetate) to give the acrylate in 42% yield.[11]

Alternatively, the alcohol could be oxidized via a standard Swern protocol and the carboxyethylphosphonium ylide was added directly to the reaction. This provided the product in an overall yield of 78% over the two steps and was the preferred method for preparing these substrates.

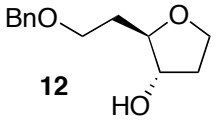


The ester (2.0 g, 8.5 mmol, 1.0 eq) was placed in dry tetrahydrofuran and cooled to -20 ˚C. Diisobutylaluminum hydride (12.5 mL, 18.7 mmol as a 1.5 M solution in toluene, 2.2 eq) was added dropwise and the reaction stirred at -20 ˚C for 3 h. The reaction was carefully quenched with saturated Rochelle's salt and then glycerol (0.2 mL/mmol DIBAL) was added and the reaction was stirred overnight to break up the aluminum complex. The phases were separated and the aqueous layer was washed several times with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified via column chromatography (hexanes/ethyl acetate gradient) to give the allylic alcohol in 92% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 5.7 (m, 2H), 4.5 (s, 2H), 4.0 (m, 2H), 3.5 (t, 2H), 2.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 131.0, 129.1, 128.3, 127.6, 127.5, 72.9, 69.6, 63.5, 32.6.[11]



11

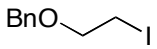
Sharpless asymmetric epoxidation gave the epoxy alcohol **11** in 78% yield and 92% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.5 (s, 2H), 3.9 (d of m, 1H), 3.6 (overlapping m, 3H), 3.1 (m, 1H), 2.95 (m, 1H), 2.2 (br s, 1H), 1.8-2.0 (overlapping m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 128.3, 127.6, 73.0, 66.8, 61.6, 58.4, 53.6, 32.0. The R-(-)-MPA ester was prepared and shown to be 92% *ee*.[12]



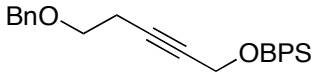
12

Formation of the tetrahydrofuran ring **12** occurred in 85% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.5 (s, 2H), 4.0 (dd, 1H, J = 12.6, 5.3 Hz), 3.9 (t, 2H, J = 7.7 Hz), 3.6 (overlapping signals, 3H), 3.0 (br s, 1H), 2.2 (m, 1H), 1.9 (overlapping m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 128.5, 127.9, 127.8, 84.4, 76.3, 73.4, 67.8, 66.1, 34.1, 33.7. IR (neat, cm^{-1}) 3413, 3040, 2930, 2870, 1454, 1092.[13]

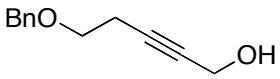
Preparation of 10.[14]



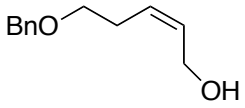
The monobenzylated ethylene glycol (5.0 g, 32.9 mmol, 1.0 eq) was placed in benzene and iodine (16.5 g, 66.0 mmol, 2.0 eq), triphenylphosphine (17.5 g, 72.5 mmol, 2.2 eq) and imidazole (5.5 g, 82.5 mmol, 2.5 eq) were added and the mixture was stirred vigorously for 4 h. The benzene was evaporated at rt and diethyl ether was added to the residue. The resulting slurry was filtered, the filtrate evaporated and the residue chromatographed (9:1 hexanes/ethyl acetate) to give the iodide in 90% yield.



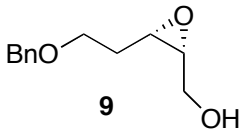
Dry tetrahydrofuran was combined with BPS-protected propargyl alcohol (11.2 g, 38.2 mmol, 2.0 eq) and cooled to -78 ºC. A solution of *n*BuLi (21.5 mL, 1.6 M solution in hexanes, 34.4 mmol, 1.8 eq) was added dropwise over 20 min. The reaction was allowed to stir for 1 h, then HMPA that had been distilled over calcium hydride was added and the reaction was stirred an additional 30 min. The iodide (5.0 g, 19.1 mmol, 1.0 eq) dissolved in THF was added dropwise over 15 min and the reaction was stirred at -78 ºC for 1 h, warmed to 0 ˚C for 1 h, then warmed to rt overnight. An equal volume of water was added and the mixture was extracted 3x with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure to give the product in 80% yield after column chromatography (9:1 hexanes/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.8 (m, 4H), 7.4 (m, 11H), 4.6 (s, 2H), 4.4 (m, 2H), 3.5 (m, 2H), 2.5 (m, 2H), 1.1 (s, 9H); ^{13}C NMR δ (75 MHz, $CDCl_3$) 135.6, 133.2, 129.8, 129.7, 129.4, 128.4, 127.6, 82.2, 79.5, 73.0, 72.9, 68.3, 52.9, 26.7, 20.2.



The protected propargyl alcohol (5.0 g, 11.7 mmol, 1.0 eq) was placed in tetrahydrofuran and a solution of tetrabutylammonium fluoride (35.1 mL, 1.0 M solution in tetrahydrofuran, 35.1 mmol, 3.0 eq) was added. The solution was stirred overnight and an equal volume of water added. The mixture was extracted 3x with ethyl acetate, the combined organics were washed with brine, dried over sodium sulfate and the solvent was removed under reduced pressure. The residue was purified by column chromatography (3:1 hexanes/ethyl acetate) to give the alcohol in 76% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.6 (s, 2H), 4.2 (m, 2H), 3.6 (t, 2H), 2.55 (m, 2H), 2.0 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 128.4, 127.7, 83.0, 79.5, 72.9, 68.2, 51.2, 20.1.[15]

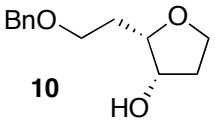


The propargylic alcohol (2.0 g, 10.5 mmol, 1.0 eq) was placed in ethyl acetate and Lindlar's catalyst (500 mg) was added. The reaction was stirred at rt for 6 h under an atmosphere of hydrogen and the mixture was filtered through a pad of Celite. The filtrate was evaporated and the residue was purified by column chromatography to give the allylic alcohol in 98% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 5.8 (m, 1H), 5.6 (m, 1H), 4.5 (s, 2H), 4.1 (m, 2H), 3.5 (t, 2H), 3.1 (br s, 1H), 2.4 (dd, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 130.7, 128.6, 128.2, 127.5, 127.46, 72.8, 68.9, 57.4, 27.7.[16]



9

Sharpless asymmetric epoxidation gave the desired epoxide **9** in 88% yield and 92% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.5 (s, 2H), 3.8 (m, 1H), 3.5-3.7 (overlapping m, 3H), 3.2 (br s and m, 2H), 3.05 (m, 1H), 2.05 (m, 1H), 1.8 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.0, 128.5, 128.1, 127.9, 73.5, 66.6, 59.9, 55.3, 54.8, 28.0.[16]

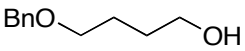


10

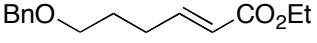
Preparation of the tetrahydrofuran **10** proceeded in 91% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.5 (s, 2H), 4.2 (m, 1H), 4.0 (dd, 1H, J = 15.6, 7.6 Hz), 3.7 (overlapping m, 3H), 3.5 (t of m, 1H, J = 10.6 Hz), 2.8 (br s, 1H), 2.1 (m, 2H), 1.9 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5, 128.5, 127.8, 127.7, 82.4, 73.5, 72.1, 67.2, 65.9, 34.8, 29.3. IR (neat, cm^{-1}) 3411, 3040, 2920, 2872, 1455, 1076. HRMS $[M+H]^+$ calculated: 223.1334; observed: 223.1333. The optical purity was shown to be 87-88% *ee* via preparation of the R-(-)-MPA ester.

Preparation of 16.

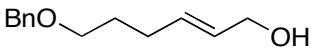
The same sequence of reactions was repeated as for **12** except that 1,4-butanediol was used as the starting material. Spectral data for selected intermediates is listed below.



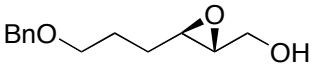
The monobenzylated alcohol was obtained in 78% yield.[17]



The tandem Swern oxidation/Wittig olefination was performed to give the product acrylate in 78% yield.[18]

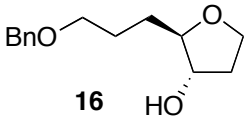


DIBAL reduction gave the allylic alcohol in 92% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 5.6 (m, 2H), 4.5 (s, 2H), 4.0 (d, 2H), 3.4 (t, 2H), 2.1 (dd, 2H), 1.7 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 132.2, 129.4, 128.3, 127.6, 127.5, 72.8, 69.5, 63.5, 29.0, 28.7.[19]



15

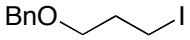
Sharpless asymmetric oxidation gave the epoxy alcohol **15** in 90% yield and 93% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.5 (s, 2H), 3.8 (m, 1H), 3.4-3.6 (overlapping m, 3H), 2.9 (2 m, 2H), 2.2 (br s, 1H), 1.6-1.8 (m, 4H); ^{13}C NMR δ (75 MHz, $CDCl_3$) 138.2, 128.3, 127.6, 127.5, 72.8, 69.5, 61.6, 58.4, 55.6, 28.3, 26.0.[20]



16

The tetrahydrofuran ring formation proceeded to give **16** in 68% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.5 (s, 2H), 4.0 (m, 1H), 3.9 (m, 1H), 3.7 (m, 1H), 3.5 (t of d, 2H, J = 6.4 Hz, 1.5 Hz), 2.1 (m, 1H), 2.0 (br s, 1H), 1.5-1.9 (overlapping m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 128.4, 127.7, 127.6, 86.0, 76.0, 72.9, 70.1, 66.2, 35.0, 30.4, 26.1.IR (neat, cm^{-1}) 3407, 3040, 2948, 2870, 1453, 1097. HRMS $[M+H]^+$ calculated: 237.1491; observed: 237.1483.

Preparation of 14. Monobenzylated 1,3-propanediol was prepared and then converted to the iodide via a tosylation/iodination sequence similar to that described for **10**.

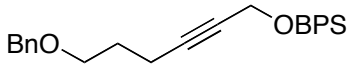


The monobenzylated alcohol (5.0 g, 30.1 mmol, 1.0 eq) as a 0.1 M solution in dry dichloromethane was treated with *p*-toluenesulfonyl chloride (6.3 g, 33.1 mmol, 1.1 eq) and triethylamine (3.7 g, 36.1 mmol, 1.2 eq). The solution was stirred at rt overnight, then washed with water, saturated sodium bicarbonate, and brine. The organics were dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. The residue was purified via column chromatography (8:2 hexanes/ethyl acetate) to give the tosylate in 88% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.8 (d, 2H), 7.3 (m, 7H), 4.4 (s, 2H), 4.2 (t, 2H), 3.5 (t, 2H), 2.4 (s, 3H), 2.0 (m, 2H).[21]

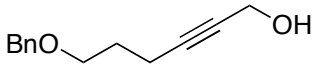
The tosylate (3.5 g, 10.9 mmol, 1.0 eq) was placed in dry acetone (150 mL) and treated with sodium iodide that had been dried at 120 ºC under vacuum overnight (8.2 g, 54.5 mmol, 5.0 eq). The reaction was stirred at rt for 6 h, then at reflux for 1 h. The mixture

was diluted with water and extracted 3x with ethyl acetate. The combined organics were washed with 10% sodium thiosulfate, water, then brine and dried over sodium sulfate. After removal of the solvents via rotary evaporation, the residue was purified via column chromatography (98:2 hexanes/ethyl acetate) to give the iodide in 95% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4 (m, 5H), 4.6 (s, 2H), 3.7 (t, 2H), 3.4 (t, 2H), 2.2 (m, 2H).[21]

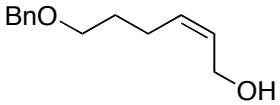
The iodide was then converted to the allylic alcohol via the same sequence of steps as described for the preparation of **Entry 5, Table 1**.



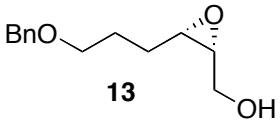
The BPS-protected alkyne was obtained in 91% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.6 (m, 4H), 7.3 (m, 11H), 4.4 (s, 2H), 4.2 (s, 2H), 3.4 (t, 2H), 2.2 (t, 2H), 1.7 (m, 2H), 1.0 (s, 9H).



The propargyl alcohol was obtained in 81% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.4 (s, 2H), 4.1 (d, 2H), 3.4 (m, 2H), 2.2 (t, 2H), 1.7 (m, 2H).[19]

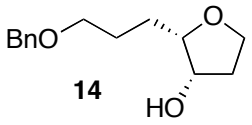


The allylic alcohol was obtained in quantitative yield via Lindlar reduction in ethyl acetate/chloroform: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 5.6 (m, 1H), 5.45 (m, 1H), 4.45 (s, 2H), 4.1 (d, 2H), 3.5 (t, 2H), 2.8 (br s, 1H), 2.15 (m, 2H), 1.65 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2, 131.5, 129.4, 128.4, 127.6, 127.5, 72.6, 69.1, 58.0, 29.1, 23.7.[16]



13

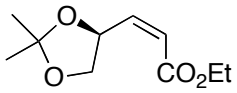
Epoxidation using Sharpless conditions in dichloromethane gave the epoxy alcohol **13** in 94% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.5 (s, 2H), 3.9 (br s, 1H), 3.4-3.8 (m, 5H), 3.1 (m, 1H), 3.0 (m, 1H), 1.6-1.9 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 128.3, 127.6, 72.7, 69.2, 60.4, 56.8, 56.77, 26.4, 24.3.[3]

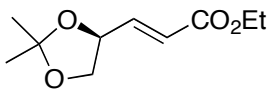


14

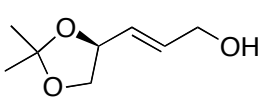
The tetrahydrofuran **14** was formed in 66% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.5 (s, 2H), 4.2 (br m, 1H), 4.0 (dd, 1H, *J* = 15.9, 7.9 Hz), 3.7 (m, 1H), 3.4-3.6 (overlapping m, 3H), 2.2 (m, 2H), 1.9 (m, 1H), 1.6-1.8 (overlapping m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2, 128.3, 127.6, 127.55, 82.9, 72.9, 72.1, 70.0, 65.6, 35.4, 26.2, 25.1. IR (neat, cm^{-1}) 3412, 3040, 2930, 2850, 1455, 1090. HRMS $[M+H]^+$ calculated: 237.1491; observed: 237.1489.

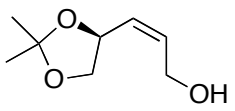
Preparation of 18 and 20.





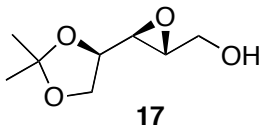
Commercial R-(-)-2,2-dimethyl-1,3-dioxolane-4-methanol (2.0 g, 15.2 mmol, 1.0 eq) was oxidized using a Swern protocol. Oxalyl chloride (1.33 mL, 15.2 mmol, 1.0 eq) in dichloromethane (150 mL, 0.1 M solution) was cooled to –78 ºC and then dry DMSO (3.02 mL, 42.6 mmol, 2.8 eq) was added dropwise via syringe over 5 min. The reaction was stirred for 5 min, then a solution of the alcohol in dichloromethane (5 mL) was added over 5 min. The reaction was stirred for an additional 15 min, then triethylamine (15.2 mL, 1.0 mL/mmol) was added via syringe in one portion. The reaction was warmed to rt and stirred for 2 h. Following this, carboxyethyl phosphonium ylide (6.9 g, 19.8 mmol, 1.3 eq) was added to the clear solution in one portion and the reaction stirred overnight at rt. The solvent was then removed via rotary evaporation and diethyl ether added to the residue. The ether was decanted and the solid washed 2x with more diethyl ether. The combined organics were evaporated and the residue purified via column chromatography to give the product as a mixture of *cis*/*trans* isomers in a ratio of 2:1 in 92% yield over the two steps. *Trans*: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (dd, 1H), 6.1 (dd, 1H), 4.65 (dd, 1H) 4.2 (overlapping signals, 3H), 3.7 (t, 1H), 1.45 (s, 3H), 1.35 (s, 3H), 1.3 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 144.6, 122.3, 110.1, 74.9, 68.7, 60.5, 26.4, 25.7, 14.1. *Cis*: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.3 (dd, 1H), 5.75 (d, 1H), 4.3 (t, 1H), 4.0-4.2 (m, 3H), 3.55 (m, 1H), 1.45 (s, 3H), 1.35 (s, 3H), 1.2 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 149.1, 120.6, 109.7, 73.4, 69.2, 60.3, 26.4, 25.2, 14.1.[22]





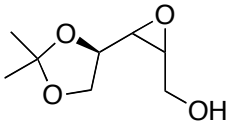
The mixture of *cis/trans* isomers was reduced using DIBAL in THF to give a mixture of allylic alcohols in 87% yield. *trans*: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.8 (m, 1H), 5.5 (t, 1H), 4.8 (m, 1H), 4.25 (m, 1H), 4.0-4.1 (m, 2H), 3.5 (m, 1H), 2.7 (br s, 1H), 1.4 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.2, 129.1, 109.3, 71.7, 69.3, 58.2, 26.6,

25.8. *cis*: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.9 (m, 1H), 5.65 (m, 1H), 4.5 (dd, 1H), 4.1 (dd, 2H), 4.05 (m, 1H), 3.5 (t, 1H), 2.5 (br s, 1H), 1.4 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.6, 128.1, 109.3, 76.4, 69.2, 62.3, 26.6, 25.8.[23]



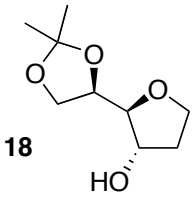
17

The mixture was subjected to Sharpless asymmetric epoxidation conditions. Only the *trans* isomer reacted to give the product **17** in 89% yield and >95% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.1 (m, 2H), 3.7-3.9 (m, 2H), 3.6 (dd, 1H), 3.05 (m, 2H), 2.5 (br s, 1H), 1.4 (s, 3H), 1.3 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.9, 75.1, 65.9, 60.8, 55.4, 55.0, 26.2, 25.4.[24]



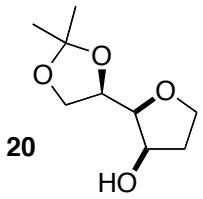
19

The *cis* isomer was recovered unchanged from the Sharpless asymmetric epoxidation and treated with *m*CPBA in dichloromethane at 0 ºC to give the epoxy alcohol as a mixture of diastereomers **19** in 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.65-4.1 (several overlapping m, 10H), 3.3-3.5 (br s, 2H), 3.15 (2 overlapping m, 2H), 3.0 (2 overlapping m, 2H), 1.40 (s, 3H), 1.38 (s, 3H), 1.30 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.2, 110.0, 75.1, 74.6, 66.3, 65.9, 60.7, 60.3, 57.5, 55.8, 55.4, 55.0, 26.5, 26.2, 25.4, 25.4.[25]



18

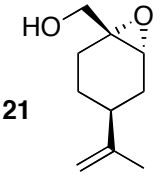
The tetrahydrofuran ring formation proceeded to give **18** in 55% yield for the *trans* epoxy alcohol. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.25 (m, 1H), 4.15 (m, 1H), 3.9-4.0 (m, 3H), 3.8 (t, 1H), 3.7 (t, 1H), 2.15 (m, 1H), 1.9 (m, 1H), 1.4 (s, 3H), 1.35 (s, 3H); ^{13}C NMR δ (75 MHz, $CDCl_3$) 109.5, 85.6, 76.3, 73.8, 67.4, 65.6, 35.6, 26.3, 25.4. IR (neat, cm^{-1}) 3424, 2986, 2920, 2880, 1456, 1372, 1215, 1063.[26]



20

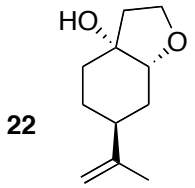
The same reaction for the mixture of *cis* diastereomers proceeded to give **20** in 61% yield. Less polar diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.5 (br m, 1H), 4.25 (m, 1H), 4.1 (dd, 1H, *J* = 8.6, 6.2 Hz), 4.0 (m, 1H), 3.9 (m, 1H), 3.8 (t of d, 1H, *J* = 8.2, 3.7 Hz), 3.6 (dd, 1H, *J* = 8.4, 3.7 Hz), 2.3 (br s, 1H), 2.1 (m, 1H), 1.95 (m, 1H), 1.4 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.2, 83.5, 74.0, 72.3, 67.9, 67.1, 35.1, 26.8, 25.2. More polar diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.4 (overlapping signals, 2H), 4.1 (m, 1H), 4.0 (dd, 1H, *J* = 8.4, 15.5 Hz), 3.9 (dd, 1H, *J* = 8.4, 7.1 Hz), 3.8 (m, 1H), 3.7 (t or overlapping dd, 1H, *J* = 4.9 Hz), 2.7 (br s, 1H), 2.1 (m, 1H), 1.9 (m, 1H), 1.45 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.8, 81.7, 75.5, 73.1, 66.6, 66.2, 36.3, 26.2, 25.5. IR (neat, cm^{-1}) 3430, 2980, 2920, 2875, 1456, 1370, 1215, 1060.[26]

Preparation of 22.



21

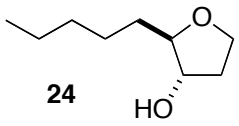
Molecular sieves (0.62 g, 4 Å) were dried overnight under vacuum at 130 ºC. The sieves were placed in a flask that had been flamed-dried under nitrogen and dry dichloromethane (50 mL) was added. The suspension was cooled to -23 °C and stirred for 30 min, then (-)-diethyltartrate (0.41 g, 2.0 mmol, 0.12 eq) and titanium isopropoxide (0.47 g, 1.6 mmol, 0.1 eq) were added dropwise. The catalyst mixture was allowed to cure for 30 min, then a solution of *t*BuOOH in toluene (6.2 mL of a 4.01 M solution, 1.5 eq) was added over 5 min and the was reaction stirred for 30 min. The alcohol (2.5 g, 16.4 mmol, 1.0 eq) was dissolved in dichloromethane (10 mL) and was added dropwise over 30 min. The reaction was stirred overnight at –23 °C. The reaction was quenched with water (10 mL) and the aqueous layer was extracted with dichloromethane (2 x 10 mL). The organics were combined, washed with brine and dried over sodium sulfate. The solvent was removed under reduced pressure to yield an oil that was purified via column chromatography (hexanes/ethyl acetate gradient) to give **22** in 85% yield and >95% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.7 (m, 1H), 4.65 (m, 1H), 3.65 (dd, 1H), 3.5 (m, 1H), 3.3 (s, 1H), 2.1-2.2 (m, 3H), 1.7-1.9 (m, 2H), 1.65 (s, 3H), 1.5-1.7 (m, 2H), 1.2 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.7, 109.2, 64.3, 60.0, 56.7, 36.8, 30.2, 25.8, 24.7, 20.9.[27]



22

The tetrahydrofuran **22** was formed in 90% yield as one diastereomer. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.7 (s, 2H), 3.95 (t of d, 1H, J = 8.8, 3.8 Hz), 3.85 (dd, 1H, J = 16.8, 8.6 Hz), 3.65 (br m, 1H), 2.1 (t of t, 1H), 1.9-2.0 (overlapping m, 3H), 1.6-1.7 (m, 5H), 1.5 (m, 2H), 1.45 (t of d, 1H, J = 11.7, 3.8 Hz) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.4, 108.7, 80.0, 74.7, 64.9, 40.0, 38.2, 34.1, 30.8, 26.3, 20.8. HRMS calculated: 182.1307; observed: 182.1310.

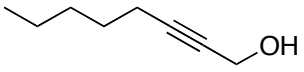
Preparation of 24.



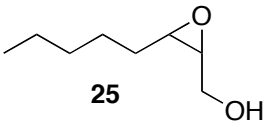
24

A solution of 2-octen-1-ol was epoxided with *m*CPBA in dichloromethane to yield the epoxy alcohol **23** in 74% yield after purification by column chromatography. Standard conditions gave three products in a 1.3:1.3:1 ratio in a combined yield of 48%. The desired product **24** was obtained in 17% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.0 (m, 1H), 3.8 (m, 2H), 3.55 (m, 1H), 2.6 (br s, 1H), 2.0 (m, 1H), 1.7 (m, 1H), 1.0-1.5 (overlapping signals, 8H), 0.75 (t, 3H, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.3, 76.0, 66.0, 34.9, 33.5, 31.7, 25.6, 22.5, 13.9.[28]

Preparation of 26.

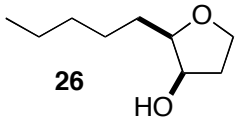


A solution of 2-octynaldehyde (2.0 g, 16.1 mmol, 1.0 eq) was placed in dry THF (100 mL) and cooled to -20 ˚C. DIBAL (11.8 mL of 1.5 M solution in toluene, 17.7 mmol, 1.1 eq) was added dropwise and the reaction was stirred for 3 h. A saturated solution of Rochelle's salt was carefully added, followed by 0.2 mL glycerol/mmol of DIBAL and the biphasic system was stirred at rt for 6 h. The reaction was extracted 3x with portions of ethyl acetate, the combined organics were washed with brine and dried over sodium sulfate. The crude product was purified via column chromatography (hexanes/ethyl acetate) to give the alcohol in 91% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.2 (d, 2H, J = 6.8 Hz), 2.2 (t, 2H, J = 7.1 Hz), 1.9 (br s, 1H), 1.5 (t, 2H, J = 7.1 Hz), 1.2-1.4 (br m, 4H), 0.9 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.1, 78.3, 51.0, 30.9, 28.2, 22.0, 18.5, 13.8.[29]



25

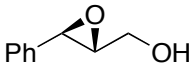
The alcohol from above (1.0 g, 7.9 mmol, 1.0 eq) was placed in ethyl acetate (20 mL) and 5 drops of chloroform. Lindlar's catalyst (500 mg) was added and the flask was evacuated and filled with a hydrogen atmosphere using a balloon. The suspension was stirred at rt for 5 h, the catalyst was removed via filtration through a pad of Celite and the filtrate evaporated under reduced pressure. The crude product was obtained in quantitative yield and was not further purified, but subjected to epoxidation using mCPBA in dichloromethane to give the desired allylic epoxide in 76% yield.[30,31]



26

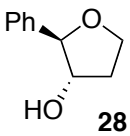
The *cis* epoxy alcohol **25** was subjected to the standard conditions to yield the tetrahydrofuran product in 48% yield as a 4:1 mixture of isomers. Major desired product: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.1 (br m, 1H), 4.0 (dd, 1H, *J* = 15.7, 7.7 Hz), 3.6 (t of d, 1H, *J* = 8.4, 4.9 Hz), 3.4 (m, 1H), 2.75 (br s, 1H), 2.1 (m, 1H), 1.8 (m, 1H), 1.5 (m, 2H), 1.1-1.4 (m, 6H), 0.8 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 83.0, 71.9, 65.3, 35.4, 31.8, 28.5, 25.9, 22.3, 13.8.[28]

Preparation of 28 and 30.



27

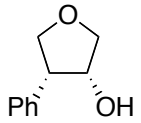
The requisite epoxy alcohol was prepared from cinnamyl alcohol according to the procedure of Sharpless *et. al*. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.1 (d of m, 1H), 3.9 (s, 1H), 3.8 (m, 1H), 3.2 (m, 1H), 2.6 (m, 1H); ^{13}C NMR δ (75 MHz, $CDCl_3$) 136.5, 128.4, 128.2, 125.6, 62.5, 61.2, 55.6.[3]



28

The tetrahydrofuran ring **28** was prepared in less than 20% yield using the standard procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.2-7.4 (m, 5H), 4.8 (m, 1H), 4.1-4.3 (m, 3H),

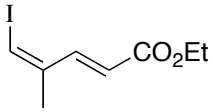
2.1 (m, 1H), 1.9 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 128.5, 127.0, 126.6, 87.4, 78.4, 67.1, 33.7.[32]



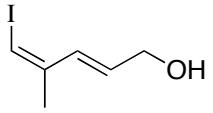
30

The product **30** was obtained in 51% yield using THF as the solvent and *n*BuLi as the base to generate the dimethylsulfoxonium methylide (see procedure described below). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.4 (m, 1H), 4.3 (dd, 1H, *J* = 9.7, 7.5 Hz), 4.05 (dd, 1H, *J* = 9.7, 5.3 Hz), 3.9 (dd, 1H, *J* = 9.1, 5.9 Hz), 3.8 (dd, 1H, *J* = 9.7, 3.3 Hz), 3.3 (m, 1H), 2.8 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 128.5, 127.0, 126.6, 79.0, 74.3, 73.0, 54.2. IR (neat, cm^{-1}) 3405, 3040, 2940, 2880, 1603, 1493, 1071. HRMS calculated: 164.0837; observed: 164.0841.

Preparation of 32.

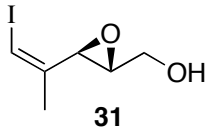


The allylic alcohol (6.4 g, 32.3 mmol, 1.0 eq) was dissolved in dry dichloromethane (100 mL). Manganese dioxide (30.0 eq) was added and the mixture was stirred at rt for 3 h. The black solids were removed by filtration through Celite and washed well with portions of dichloromethane. The filtrate was placed back into the reaction flask and triphenylphosphinocarboxyethyl ylide (1.5 eq) was added and the reaction was stirred overnight at rt. The dichloromethane was removed via rotary evaporation and diethyl ether was added to the residue. The resulting solids were filtered and washed well with portions of diethyl ether. The filtrate was concentrated via rotary evaporation and the semi-solid residue was purified via column chromatography (98:2 hexanes/ethyl acetate) to give the ester in 69% yield over the two steps. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.6 (d, 1H), 6.6 (s, 1H), 6.0 (d, 1H), 4.2 (q, 2H), 2.0 (s, 3H), 1.3 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 144.3, 140.4, 122.3, 87.9, 60.3, 20.6, 13.9. IR (neat, cm^{-1}) 3061, 2980, 1715, 1624, 1443, 1300, 1275, 1183, 1028. HRMS calculated: 265.9804; observed: 265.9810.



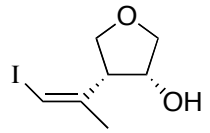
The ester (1.3 g, 4.9 mmol, 1.0 eq) was dissolved in dry tetrahydrofuran (25 mL) and treated with DIBAL as described previously. The product was obtained in 89% yield. ^{1}H

NMR (300 MHz, $CDCl_3$) δ 6.6 (d, 1H), 6.1 (s, 1H), 6.0 (t, 1H), 4.2 (dd, 2H), 1.95 (s, 3H), 1.9 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.2, 133.3, 132.3, 79.7, 63.3, 21.1.[33]



31

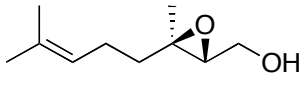
A suspension of 4 Å molecular sieves (1.0 g) in dry dichloromethane (30 mL) was cooled to -23 ˚C. $Ti(O^iPr)_4$ (52.7 μL, 0.18 mmol, 0.05 eq) was added, followed by (-)-DET (42.8 μL, 0.25 mmol, 0.07 eq). The reaction was stirred for 30 min, then a solution of *t*BuOOH in toluene (2.9 mL, 3.0 eq, 3.68 M) was added and the reaction was stirred for another 30 min. A solution of the allylic alcohol (0.8 g, 3.57 mmol, 1.0 eq) dissolved in dry dichloromethane (5 mL) was added dropwise via syringe pump over 30 min. The reaction was stirred overnight at -23 ˚C. Water was added to quench the reaction and the molecular sieves were removed by filtration through a pad of Celite. The phases were separated and the aqueous phase was extracted 3x with portions of dichloromethane. The combined organics were washed with brine, dried over sodium sulfate and concentrated. The residue was purified via column chromatography (hexanes/ethyl acetate gradient) to give the epoxy alcohol **31** in 82% yield as a white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 6.2 (m, 1H), 4.0 (d, 1H), 3.7-3.8 (m, 2H), 3.2 (m, 1H), 2.7 (br s, 1H), 1.7 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 77.4, 61.5, 59.4, 57.4, 19.2. HRMS calculated: 239.9647; observed: 239.9651.



32

The tetrahydrofuran ring **32** was prepared in 33% yield using THF as the solvent. ^1H NMR (300 MHz, $CDCl_3$) δ 6.1 (s, 1H), 4.35 (br m, 1H), 4.1 (dd, 1H, J = 7.9, 9.1 Hz), 3.95 (dd, 1H, J = 9.7, 5.7 Hz), 3.7 (dd, 1H, J = 9.7, 4.0 Hz), 3.6 (dd, 1H, J = 9.1, 5.7 Hz), 3.4 (m, 1H), 2.1 (br s, 1H), 1.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 77.7, 76.4, 74.9, 69.7, 56.9, 20.6. IR (neat, cm^{-1}) 3401, 3080, 2946, 2880, 1653, 1437, 1281, 1148, 1069. HRMS calculated: 253.9804; observed: 253.9813.

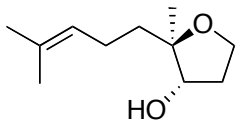
Preparation of 34.



33

The requisite epoxy alcohol **33** was prepared from geraniol according to the procedure of Sharpless *et. al.* in 97 % yield and 96% *ee*. ^1H NMR (300 MHz, $CDCl_3$) δ 5.3 (m, 1H),

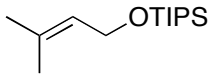
5.1 (m, 1H), 3.8 (m, 1H), 3.65 (m, 1H), 3.0 (m, 1H), 2.5 (br s, 1H), 2.05 (m, 2H), 1.65 (s, 3H), 1.6 (m, 3H), 1.45 (m, 1H), 1.3 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.1, 123.3, 63.0, 61.4, 61.2, 38.4, 25.6, 23.6, 17.6, 16.7.[34]



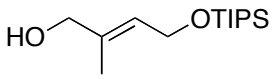
34

The tetrahydrofuran ring **34** was obtained in 14% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.1 (t, 1H, *J* = 7.1 Hz), 4.0 (br t, 1H, *J* = 4.6 Hz), 3.9 (dd, 1H, *J* = 15.2, 7.1 Hz), 3.75 (m, 1H), 2.3 (m, 1H), 2.0 (m, 2H), 1.9 (m, 1H), 1.65 (s, 3H), 1.6 (s, 3H), 1.4 (m, 2H), 1.3 (m, 1H), 1.2 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7, 124.3, 84.2, 76.7, 63.9, 48.7, 38.9, 34.8, 25.6, 22.8, 18.6. IR (neat, cm^{-1}) 3403, 3075, 2975, 2910, 1640, 1456, 1107. HRMS calculated: 184.1463; observed: 184.1465.

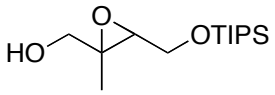
Preparation of 36.



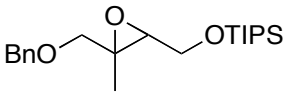
A solution of 3-methyl-2-butenol (3.0 g, 34.9 mmol, 1.0 eq) in DMF (25 mL) was treated with triisopropylsilyl chloride (7.4 g, 38.4 mmol, 1.1 eq) and imidazole (5.9 g, 87.3 mmol, 2.5 eq). The reaction was stirred at rt overnight, then diluted with 2x volume of water. The reaction was extracted 3x with diethyl ether, the combined organics were washed with brine and dried over sodium sulfate. The organics were removed via rotary evaporation and the residue was purified via column chromatography (9:1 hexanes/ethyl acetate) to give the product in 82% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.3 (m, 1H), 4.2 (m, 2H), 1.7 (s, 3H), 1.6 (s, 3H), 1.0 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.0, 125.0, 60.4, 25.7, 18.0, 12.1.[35]



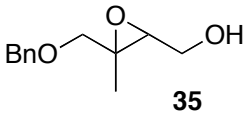
Selenium dioxide (0.23 g, 2.1 mmol, 0.5 eq) and *t*BuOOH (2.1 mL of a 4 M solution in toluene, 8.3 mmol, 2.0 eq) were combined in dichloromethane, cooled to -15 ºC and stirred for 30 min. The alkene (1.0 g, 4.1 mmol, 1.0 eq) dissolved in dichloromethane was added dropwise to the solution over 10 min. The reaction was stirred for 48 h and following standard workup and purification by column chromatography gave a 35% yield of the desired allylic alcohol. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.6 (t, 1H), 4.3 (d, 2H), 3.9 (s, 2H), 3.0 (br s, 1H), 1.6 (s, 3), 1.0 (m, 21H).[36]



The allylic alcohol prepared above (0.29 g, 1.1 mmol, 1.0 eq) was epoxidized using *m*CPBA (0.27 g using 77% by weight active reagent, 1.2 mmol, 1.1 eq) in dichloromethane at 0 ºC for 3 h to give, after purification by column chromatography, the epoxide in 75% yield.

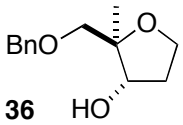


The epoxy alcohol was benzylated according to standard procedures described previously in this experimental to give the protected alcohol in 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.55 (s, 2H), 3.9 (d, 2H), 3.5 (dd, 2H), 3.1 (t, 1H), 1.4 (s, 3H), 1.1 (21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 128.3, 127.6, 127.5, 74.3, 72.9, 62.0, 60.8, 59.3, 17.9, 14.5, 11.9.



35

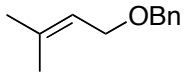
The TIPS group was removed using 3.0 eq of a TBAF solution in a 0.1 M solution of THF to give the desired epoxy alcohol **35** in 88% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (s, 5H), 4.6 (dd, 2H), 3.8 (dd, 1H), 3.7 (dd, 1H), 3.45 (dd, 2H), 3.1 (dd, 1H), 2.9 (br s, 1H), 1.3 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 128.3, 127.6, 74.0, 73.1, 60.8, 60.4, 59.9, 14.4.[37]



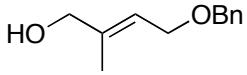
36

The tetrahydrofuran ring-forming reaction proceeded to give two major products of which one was the desired **36** in 20% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.55 (s, 2H), 4.0 (dd, 1H, J = 11.4, 5.6 Hz), 3.95 (t, 1H, 6.9 Hz), 3.6 (overlapping signals, 3H), 3.0 (br s, 1H), 2.2 (m, 1H), 1.9 (s, 3H), 1.2 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 128.5, 127.9, 127.8, 84.5, 76.3, 73.4, 67.9, 66.1, 34.1, 33.7.

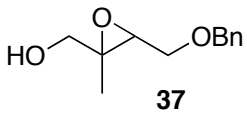
Preparation of 38.



This substrate was prepared by benzylation of 3-methyl-2-butenol according to standard procedure to give the desired product in 94% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4 (m, 5H), 5.5 (m, 1H), 4.6 (s, 2H), 4.1 (d, 2H), 1.8 (s, 3H), 1.7 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 137.0, 128.2, 127.6, 127.4, 121.0, 72.0, 66.5, 25.7, 18.0.[38]

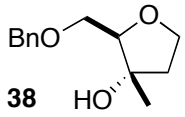


The protected allylic alcohol was subjected to allylic oxidation using SeO_2/peroxide as described for the preparation of compound **36** to give the alcohol in 51% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4 (m, 5H), 5.7 (t, 1H), 4.6 (s, 2H), 4.1 (d, 2H), 4.0 (s, 2H), 3.1 (br s, 1H), 1.6 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3, 138.0, 128.2, 127.7, 127.5, 120.8, 72.1, 67.4, 66.0, 13.7.[39]



37

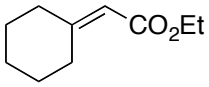
The allylic alcohol was epoxidized using 1.1 eq of *m*CPBA in dichloromethane to give the epoxy alcohol **37** in 81% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4 (m, 5H), 4.5-4.7 (dd, 2H), 3.5-3.8 (m, 4H), 3.3 (m, 1H), 2.2 (br s, 1H), 1.3 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 128.4, 127.8, 73.2, 68.3, 65.0, 60.2, 58.1, 14.2.[40]



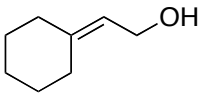
38

The tetrahydrofuran formation gave a 33% yield of product **38**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5H), 4.6 (s, 2H), 4.0 (m, 2H), 3.8 (t, 1H, J = 5.5 Hz), 3.5 (overlapping signals, 3H), 2.0 (m, 2H), 1.3 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 128.4, 127.7, 84.9, 78.8, 73.6, 70.1, 66.4, 40.8, 22.3. IR (neat, cm^{-1}) 3420, 3060, 3020, 2920, 2867, 1653, 1455, 1098. HRMS calculated: 222.1256; observed: 222.1257.

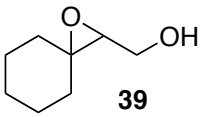
Preparation of 40.



The desired ester was prepared according to the method of Rathke and coworkers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.6 (s, 1H), 4.1 (q, 2H), 2.8 (m, 2H), 2.2 (m, 2H), 1.6 (m, 6H), 1.2 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 163.4, 112.9, 59.4, 37.9, 29.7, 28.6, 27.7, 26.2, 14.3.[41]

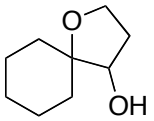


Allylic alcohol. The ester (2.0 g, 11.8 mmol, 1.0 eq) was reduced using DIBAL according to the procedure previously described to give the desired product in 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.4 (t, 1H), 4.1 (d, 2H), 2.0-2.2 (m, 4H), 1.4-1.8 (m, 7H).[42]



39

Epoxy Alcohol. The allylic alcohol (1.0 g, 7.9 mmol, 1.0 eq) was placed in dichloromethane (70 mL) and *m*CPBA (1.05 eq, 1.9 g as a 77 weight % reagent) was added. The reaction was stirred at rt for 3 h and quenched with water and sodium carbonate. The organic layer was separated and the aqueous layer was extracted 3x with portions of dichloromethane. The combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified via column chromatography (hexanes/ethyl acetate) to give the product **39** in 83% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (m, 1H), 3.7 (m, 1H), 3.0 (m, 1H), 2.7 (br s, 1H)1.4-1.8 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 64.3, 63.5, 60.9, 35.3, 29.4, 25.5, 24.8.[43]

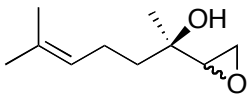


40

The tetrahydrofuran formation proceeded to give **40** in 21% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.9 (overlapping m, 2H), 3.8 (t of d, 1H, J = 8.8, 4.7 Hz), 2.3 (m, 1H), 1.6-2.0 (overlapping m, 2H), 1.2-1.7 (overlapping signals, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 84.1, 76.3, 63.8, 34.6, 34.5, 30.3, 25.7, 23.1, 23.0. HRMS calculated: 156.1150; observed: 156.1154. The major elimination product was obtained in 30% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.8 (s, 1H), 4.1 (m, 1H), 3.4-3.7 (m, 2H), 2.9-3.15 (2 br s, 2H), 1.8-2.1 (m, 4H), 1.5-1.7 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.6, 123.8, 76.2, 65.4,

24.8, 24.78, 22.5, 22.4. IR (neat, cm^{-1}) 3413, 2932, 2880, 1449, 1061. HRMS calculated: 142.0994; observed: 142.0997.

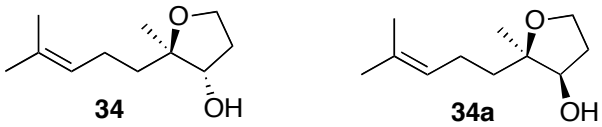
Preparation of 34.



41

The epoxy alcohol **41** was prepared via $VO(acac)_2$ oxidation of linalool as described by Sharpless *et. al.* The product was obtained as a 2:1 mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.1 (m, 1H), 2.6-3.0 (m, 3H), 1.9-2.2 (m, 3H), 1.4-1.7 (m, 6H), 1.1-1.3 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7, 124.1, 124.0, 69.2, 69.0, 57.8, 57.6, 44.2, 43.2, 41.1, 38.6, 25.9, 25.6, 22.6, 22.1, 21.9, 17.5.[44]

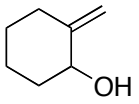
Representative procedure for tetrahydrofuran formation using dimethylsulfoxonium methylide ylide in tetrahydrofuran as the solvent:



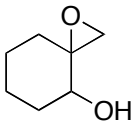
34 **34a**

Trimethylsulfoxonium iodide (1.9 g, 8.8 mmol, 3.0 eq) was combined with dry tetrahydrofuran (80 mL) and cooled to -78 ºC. A solution of *n*BuLi in hexanes (5.5 mL, 8.8 mmol, 3.0 eq as a 1.6 M solution in hexanes) was added dropwise and the reaction slowly warmed to 0 ˚C over 30 min. The cloudy solution was then recooled to -78 ˚C and a solution of the epoxy alcohol (0.5 g, 2.9 mmol, 1.0 eq) in THF was added dropwise over 5 min. The reaction was warmed slowly to rt, then refluxed for 2 h. The reaction was cooled, diluted with 2x volume of water and extracted several times with ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. Purification of the residue via column chromatography (hexanes/ethyl acetate) gave the desired product **34** and **34a** in 51% yield (2:1 mixture of diastereomers). ^{1}H NMR (300 MHz, $CDCl_3$) both diastereomers, δ 5.0-5.2 (2 t with further fine coupling, 1H, J = 7.2 Hz), 3.7-4.0 (overlapping m, 3H), 1.8-2.4 (m, 4H), 1.5-1.7 (2 s, 6 H), 1.4-1.5 (m, 1H), 1.1-1.3 (2 s and 1 m, 4H) ; ^{13}C NMR (75 MHz, $CDCl_3$) (minor diastereomer, **34**) δ 131.9, 124.4, 84.6, 76.6, 64.0, 38.8, 34.6, 34.3, 22.9, 22.6, 17.5. (major diastereomer, **34a**) δ 131.6, 124.2, 84.3, 76.6, 63.8, 38.8, 34.6, 34.5, 25.6, 22.7, 18.6. IR (neat, cm^{-1}) 3403, 3075, 2975, 2910, 1640, 1456, 1107. HRMS calculated: 184.1463; observed: 184.1465.

Preparation of 43.

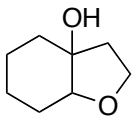


Cyclohexene oxide was converted to the desired allylic alcohol using a literature procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.9 (s, 1H), 4.7 (s, 1H), 4.1 (m, 1H), 1.2-2.5 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5, 104.9, 72.4, 36.5, 33.4, 27.6, 23.7.[45]



42

The allylic alcohol (0.65 g, 5.8 mmol, 1.0 eq) was dissolved in dichloromethane (7 mL) and *m*CPBA (1.43 g as 77% by weight, 6.38 mmol, 1.1 eq) was added in one portion. The reaction was stirred at rt for 3 h, then worked up by washing with cold 1 N NaOH. The aqueous layer was further extracted with 3x portions of dichloromethane, the combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified via column chromatography (hexanes/ethyl acetate gradient) to give the epoxy alcohol **42** as a mixture of diastereomers in 78% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.5-3.7 (m, 1H), 2.9-3.0 (1H), 2.35 and 2.75 (1H), 2.5 (1H), 1.3-1.9 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 69.3, 68.8, 62.0, 60.9, 51.1, 49.7, 33.3, 32.8, 31.7, 31.0, 24.9, 23.6, 23.2, 22.7. The diastereomers were further separated by an additional column chromatographic purification.[46] One of the diastereomers was used in the THF ring formation to simplify the NMR spectra.

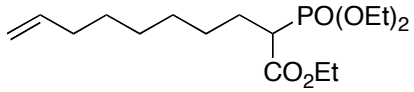


43

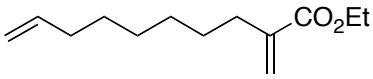
THF ring formation in DMSO occurred to give product **43** in 55% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.0 (ddd, 1H, J = 16.8, 8.4, 1.8 Hz), 3.8 (m, 1H), 3.1 (dd, 1H, J = 11.9, 4.2 Hz), 2.05 (m, 1H), 1.95 (m, 1H), 1.7-1.9 (overlapping signals, 3H), 1.6 (m, 2H), 1.5 (m, 1H), 1.1-1.3 (overlapping signals, 3H); ^{13}C NMR δ (75 MHz, $CDCl_3$) 83.0, 75.7, 64.8, 38.5, 33.2, 24.9, 23.6, 20.6. IR (neat, cm^{-1}) 3426, 2934, 2810, 1450, 1098. HRMS calculated: 142.0994; observed: 142.0990.

THF ring formation in THF as the solvent gave the same product in 55% yield.

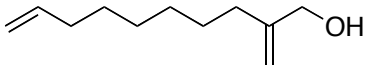
Preparation of 46.



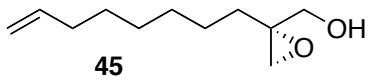
Sodium hydride (0.84 g as a 60% suspension in mineral oil, 10.48 mmol, 2.0 eq) was washed twice with dry pentane and then dry tetrahydrofuran (100 mL) was added. A solution of triethylphosphonoacetate (2.35 g, 10.48 mmol, 2.0 eq) dissolved in THF was added dropwise to the NaH and the resulting suspension was stirred at rt for 30 min. The 1-bromo-7-octene (1.0 g, 5.24 mmol, 1.0 eq) dissolved in THF (5 mL) was added dropwise and the reaction was heated to 60 ˚C overnight. The reaction was quenched with water and extracted 3x with portions of ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was used crude in the next step.



The crude phosphonate was placed in water (20 mL). Potassium carbonate (1.4 g, 10.48 mmol, 2.0 eq) and aqueous formaldehyde (1.7 g as a 37% solution in water, 20.96 mmol, 4.0 eq) were added and the biphasic reaction was heated to 80 ˚C for 4 h. The reaction was cooled and then extracted 3x with portions of ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified via column chromatography (95:5 hexanes/ethyl acetate) to give the ester in 58% yield over the two steps.

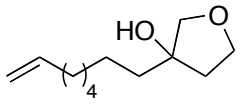


The ester was reduced to the allylic alcohol using the standard DIBAL reduction in 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.8 (m, 1H), 4.8-5.0 (m, 4H), 4.1 (t, 1H), 4.0 (d, 2H), 1.0-2.2 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2, 139.0, 114.1, 108.9, 65.8, 33.7, 32.9, 29.2, 28.9, 28.8, 27.7.



45

The epoxide was prepared using (-)-DET in the Sharpless asymmetric epoxidation as previously described to give the epoxy alcohol **45** in 67% yield and 88% *ee*.[3]



46

Preparation of the THF ring **46** proceeded in 56% yield using 3.0 eq of the dimethylsulfoxonium methylide generated from trimethylsulfoxonium iodide and *n*BuLi in THF at -78 ˚C, addition of **45**, followed by heating to reflux for 1 h. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.8 (m, 1H), 4.95 (d with further fine splitting, 1H, *J* = 17.2 Hz), 4.9 (d of m, 1H, *J* = 10.4 Hz), 4.0 (dd, 2H, *J* = 8.4, 16.8 Hz), 3.9 (t of d, 1H, *J* = 4.9, 8.4 Hz), 3.7 (d, 1H, *J* = 9.3 Hz), 3.5 (dd, 1H, *J* = 9.3, 0.9 Hz), 2.0 (m, 2H), 1.9 (m, 2H), 1.7 (br s, 1H), 1.6 (m, 2H), 1.2-1.5 (overlapping signals, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 114.2, 81.2, 78.9, 67.4, 39.8, 37.9, 33.7, 29.9, 29.0, 28.8, 24.6. IR (neat, cm^{-1}) 3411, 3060, 3020, 2920, 2867, 1647, 1455, 1088. HRMS calculated: 198.1620; observed: 198.1618. Conversion of the terminal alkene to a primary alcohol was accomplished via a $OsO_4/NaIO_4$ cleavage followed by a $NaBH_4$ reduction. The primary alcohol was then converted to the S-(+)-MPA ester and the presence of two diastereomers in approximately equal amounts indicated that racemization of the epoxy alcohol had occurred under the reaction conditions.

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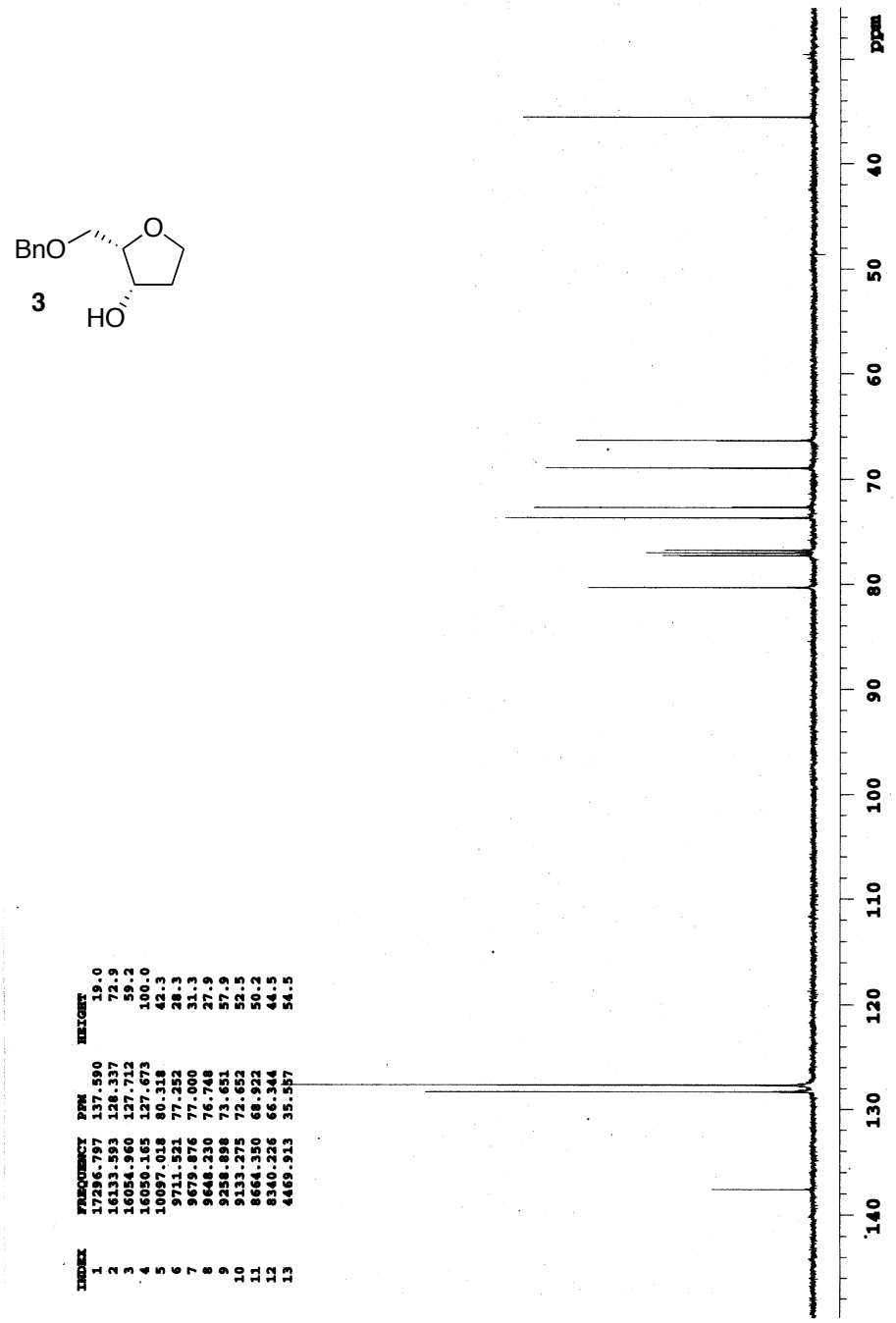
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O
HO
3
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4 16050.165 127.673 100.0
5 10097.018 80.318 42.3
6 9711.521 77.252 28.3
7 9679.876 77.000 31.3
8 9648.230 76.748 27.9
9 9238.898 73.651 57.9
10 9133.275 72.652 52.5
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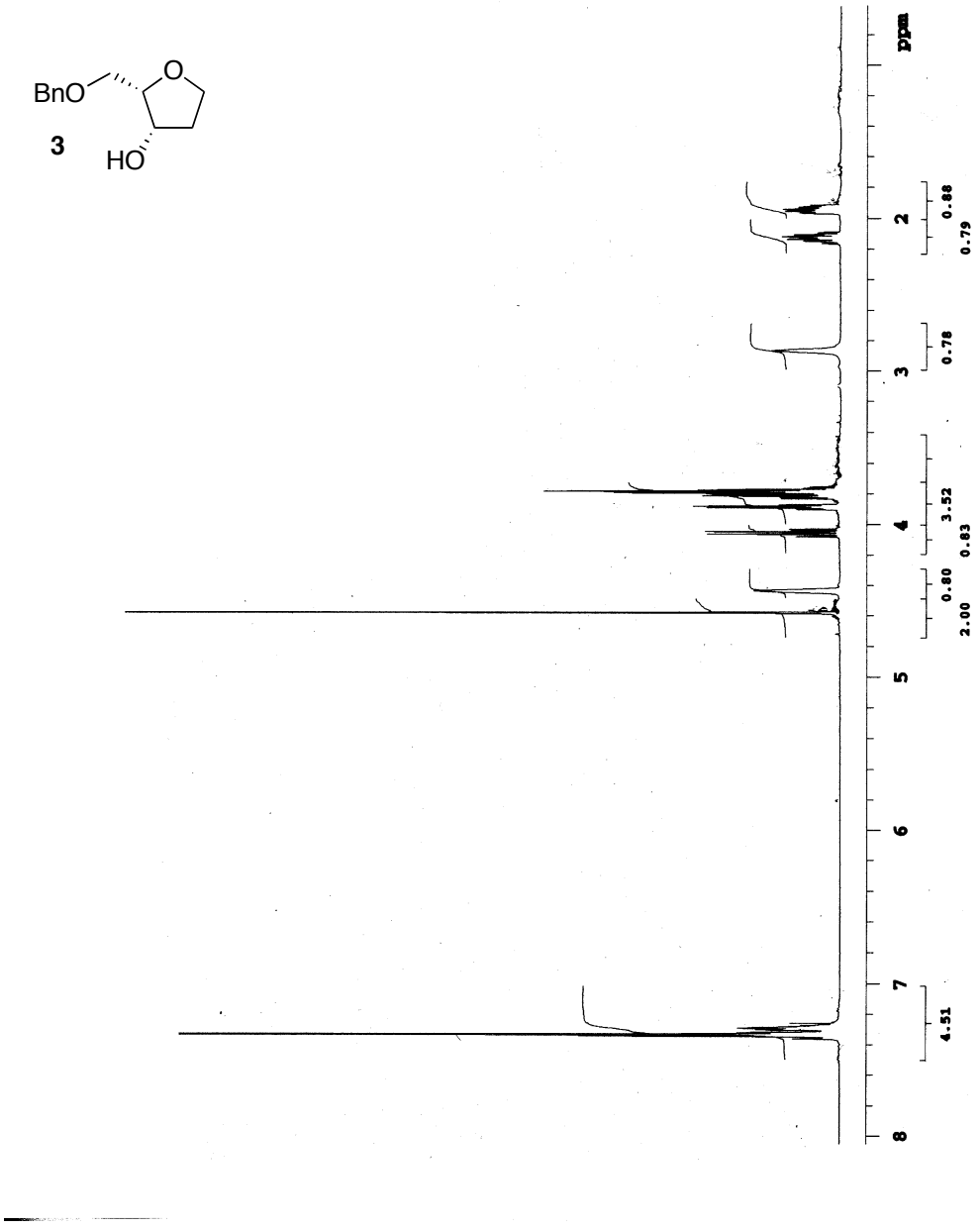
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O
HO
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ppm
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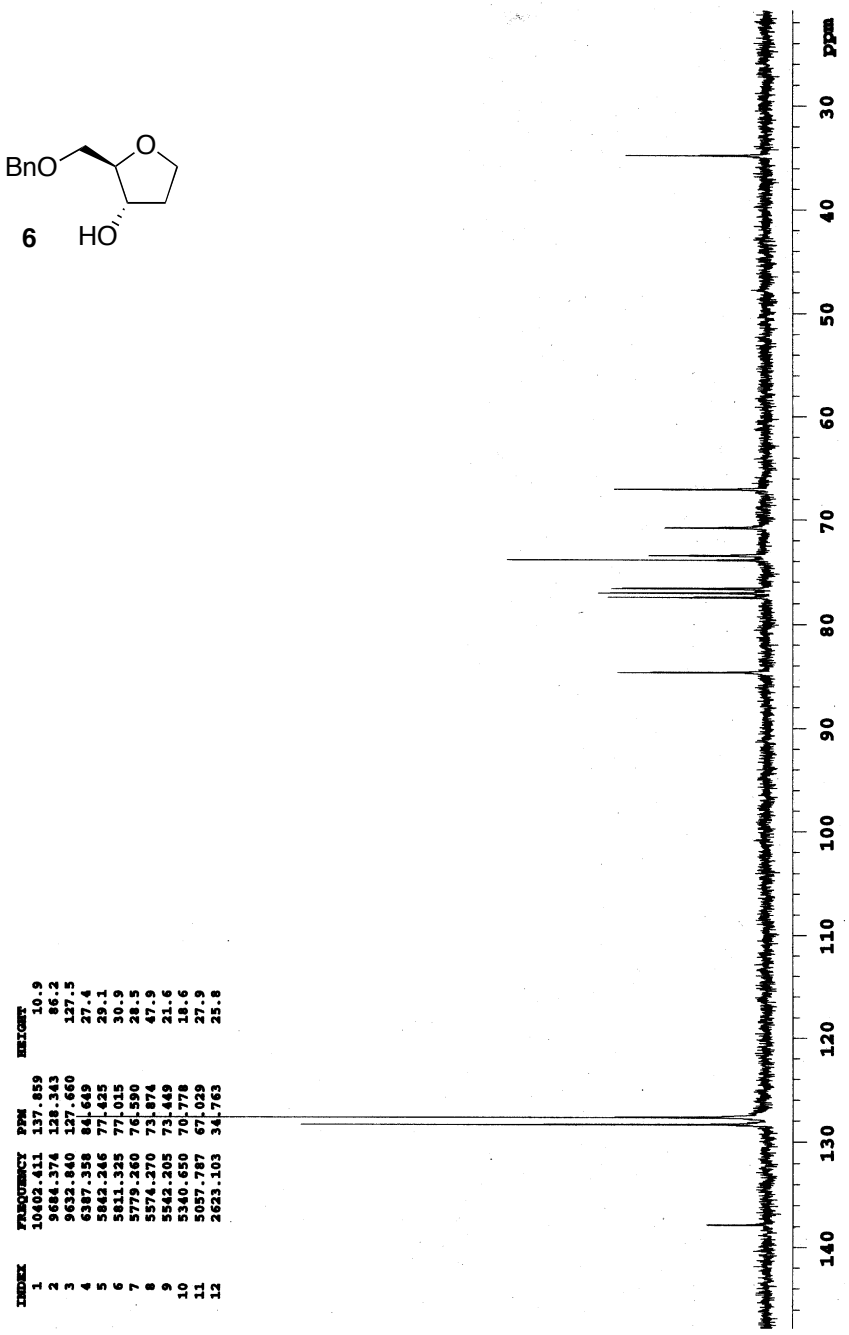
2.00
4.51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O
HO
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2 9684.374 128.343 86.2
3 9632.840 127.660 127.5
4 6387.358 84.649 27.4
5 5842.246 77.425 29.1
6 5811.325 77.015 30.9
7 5779.260 76.590 28.5
8 5574.270 73.874 47.9
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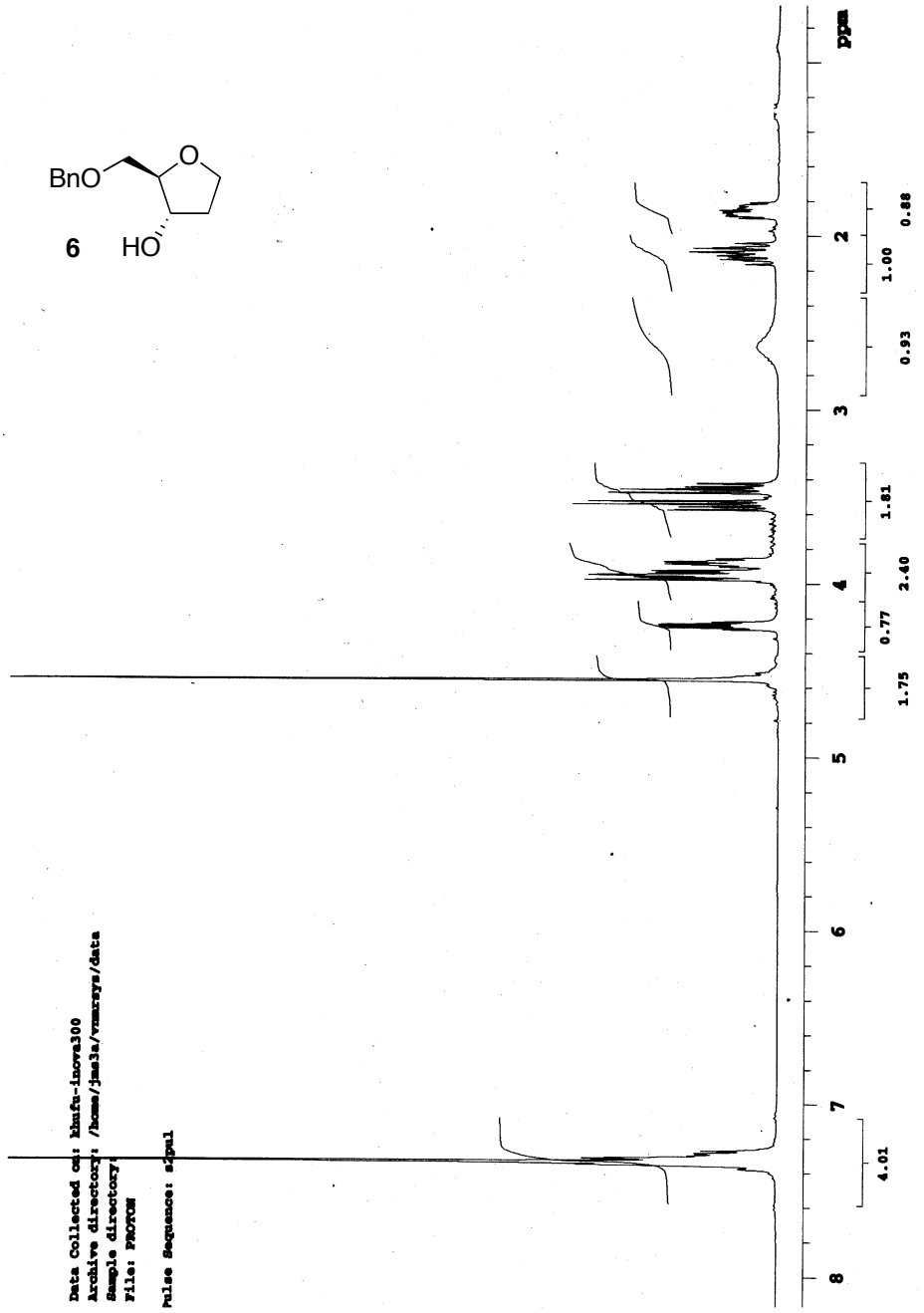
11 5057.787 67.029 27.9
12 2623.103 34.763 25.8
ppm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O
6
HO
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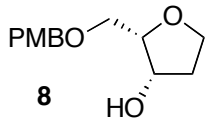

8

INDEX	FREQUENCY	PPM	HEIGHT
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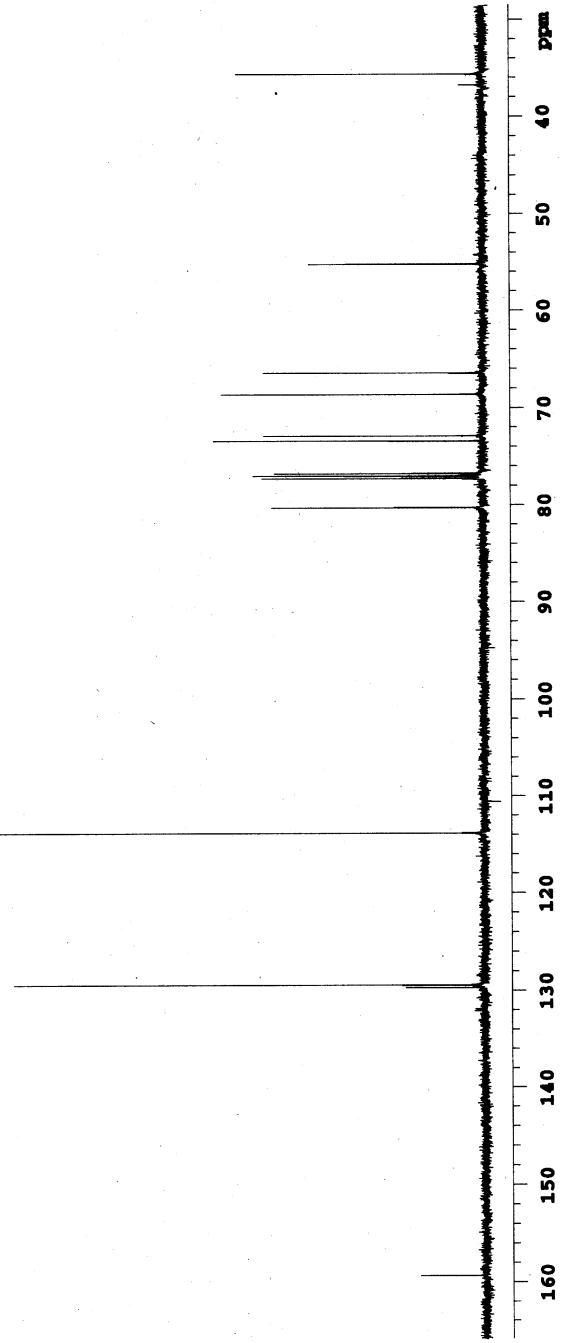
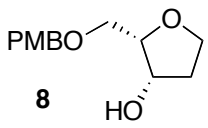
2	16304.285	129.695	14.6
3	16270.722	129.428	87.0
4	14312.551	113.851	100.0
5	10091.263	80.272	39.0
6	9711.520	77.252	40.7
7	9679.875	77.000	42.4
8	9647.271	76.741	38.5
9	9229.169	73.415	49.7
10	9161.084	72.873	40.4
11	8627.909	68.632	48.2
12	8354.609	66.458	40.4
13	6939.202	55.199	31.9
14	4481.419	35.648	45.3





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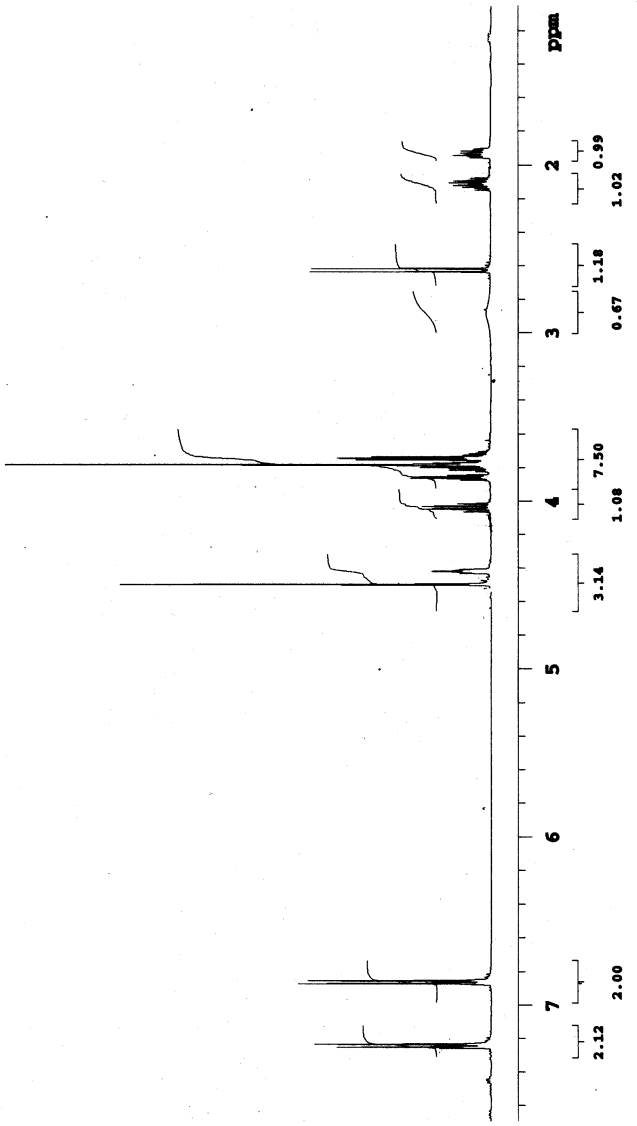

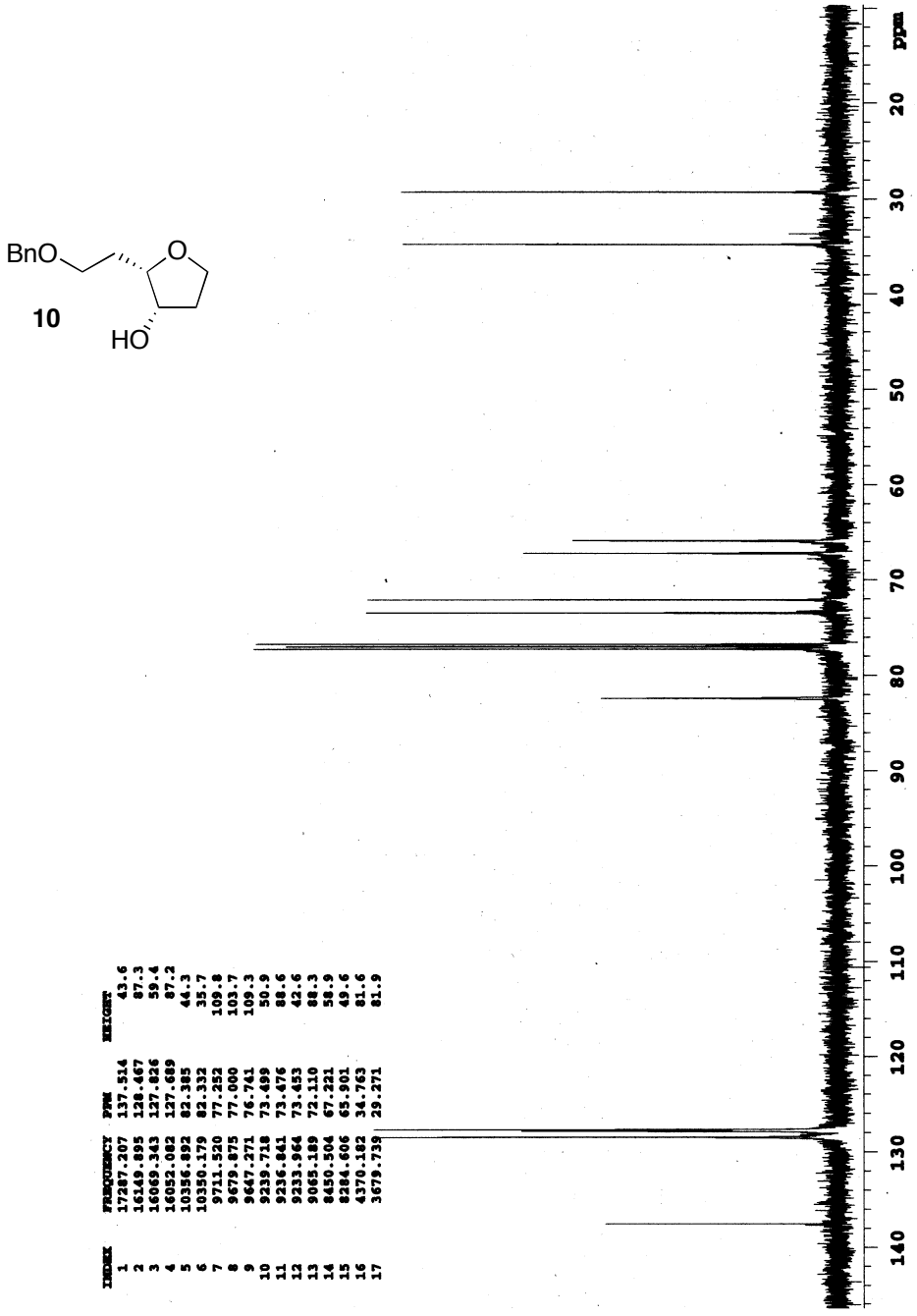
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HO
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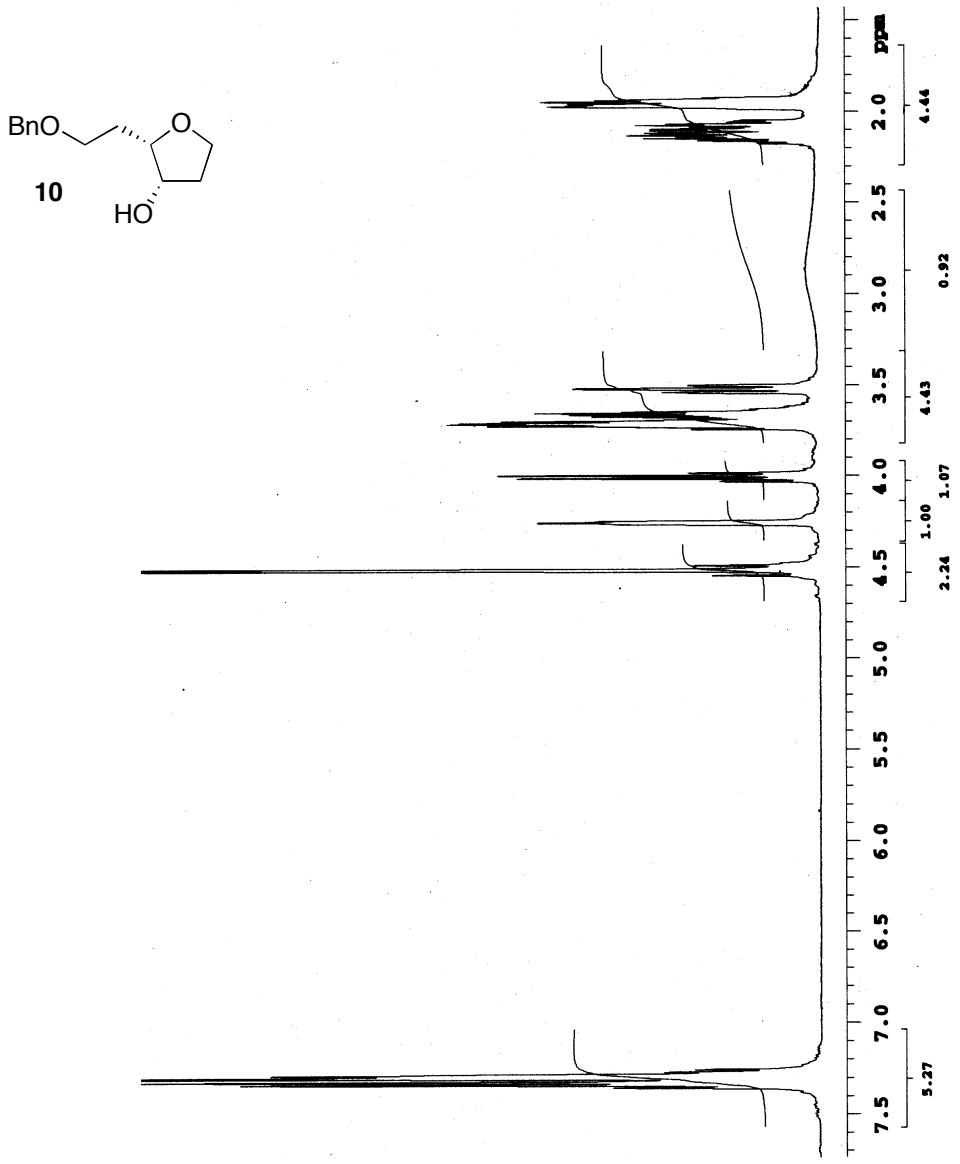
3 16069.343 127.826 59.4
4 16052.082 127.689 87.2
5 10356.892 82.385 44.3
6 10350.179 82.332 35.7
7 9711.520 77.252 109.8
8 9679.675 77.000 103.7
9 9647.271 76.741 109.3
10 9239.718 73.489 50.9
11 9236.841 73.476 88.6
12 9233.964 73.453 42.6
13 9065.189 72.110 88.3
14 8450.504 67.221 58.9
15 8284.606 65.901 49.6
16 4370.182 34.763 81.6
17 3679.739 29.271 81.9
ppm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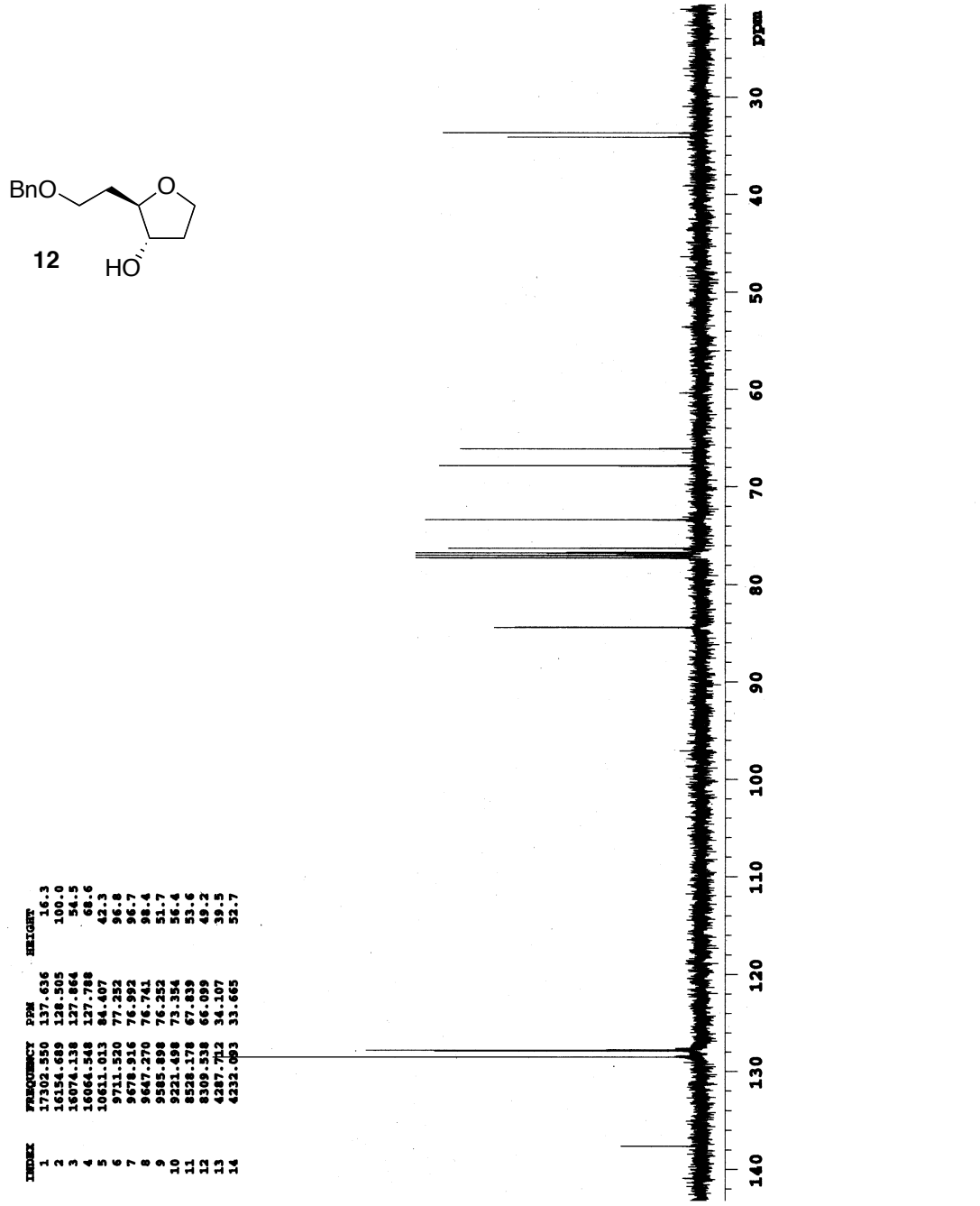
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4 16064.548 127.788 68.6
5 10611.013 84.407 42.3
6 9711.520 77.252 96.8
7 9678.916 76.992 96.7
8 9647.270 76.741 98.4
9 9585.898 76.252 51.7
10 9221.498 73.354 56.4
11 8528.178 67.839 53.6
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14 4232.083 33.665 52.7
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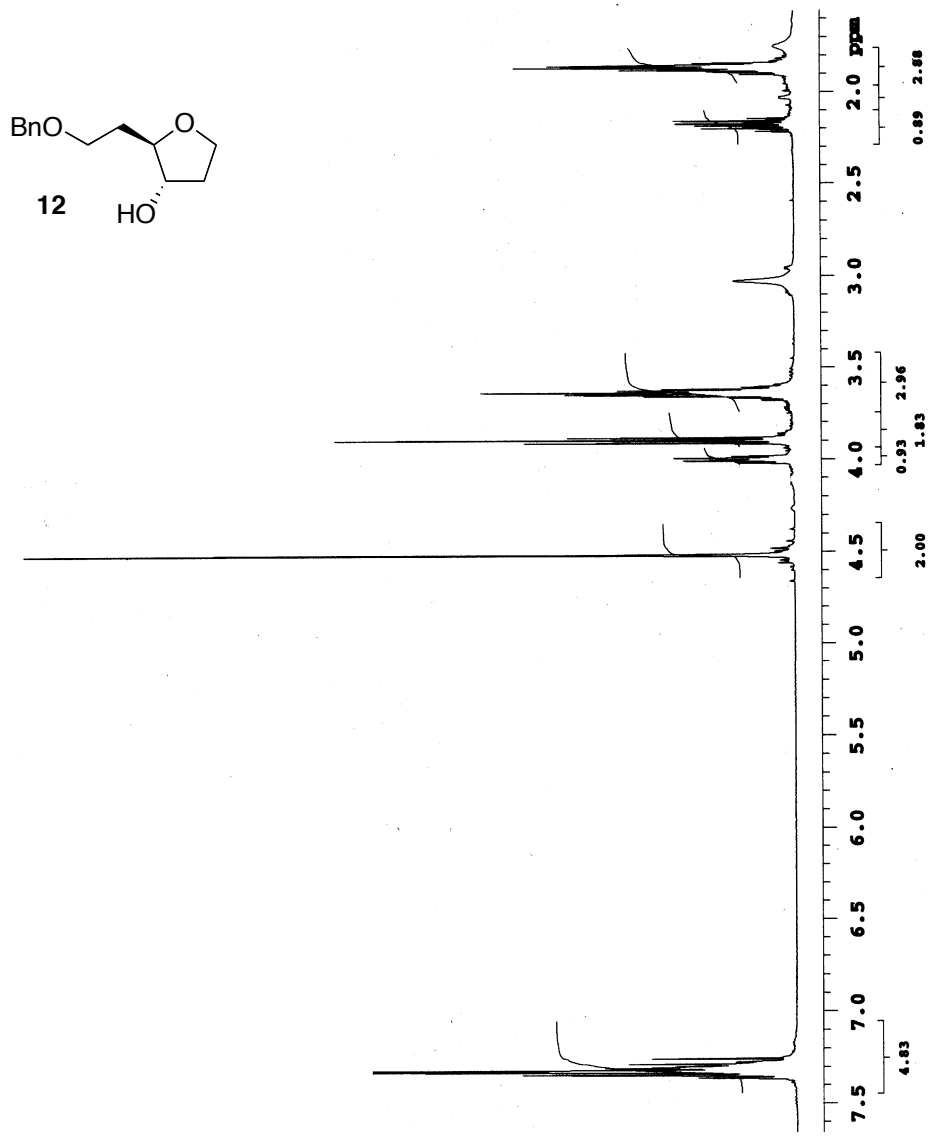
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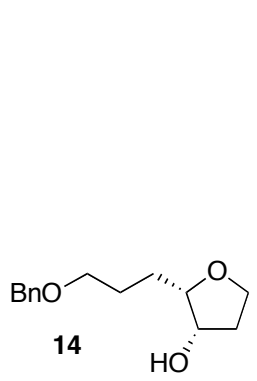
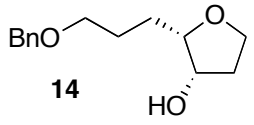
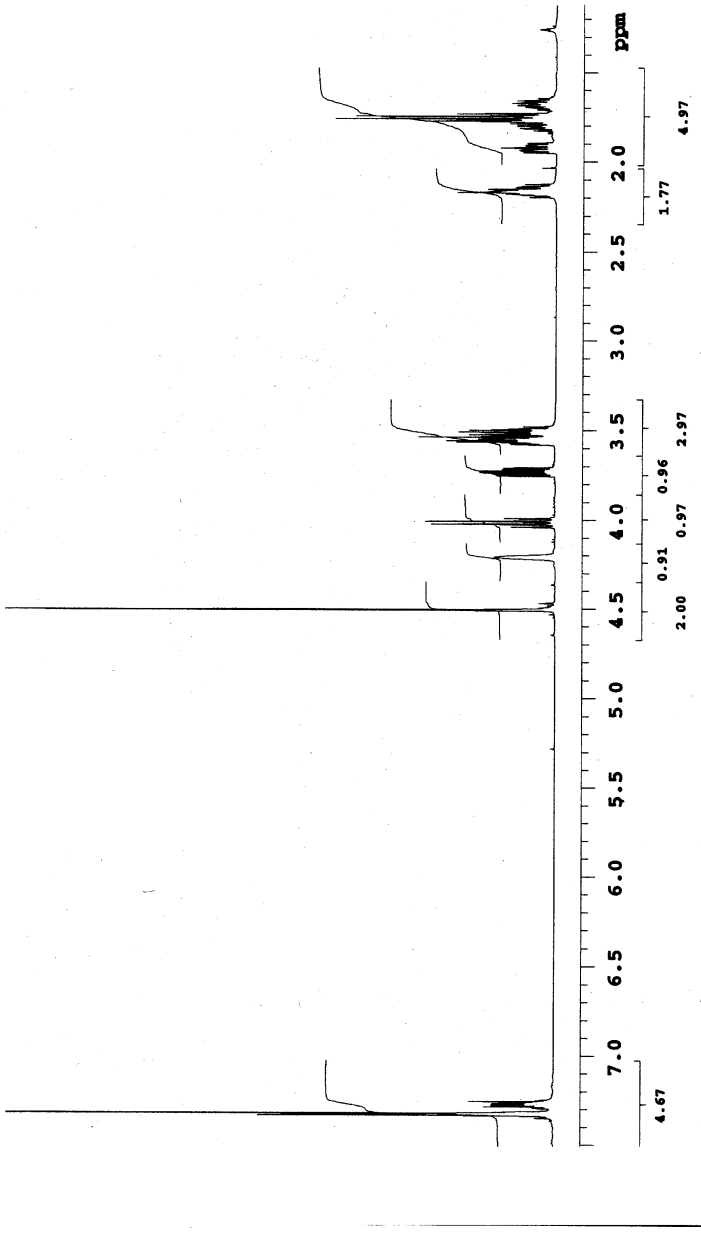


14

INDEX	FREQUENCY	PPM	HEIGHT
1	10433.306	138.163	16.7
2	9883.220	128.328	130.7
3	9631.686	127.645	135.2
4	9624.815	127.554	76.3
5	6257.943	82.934	63.4
6	5841.092	77.410	59.8
7	5810.171	77.000	59.4
8	5776.106	76.575	62.7
9	5498.678	72.872	48.9
10	5436.838	72.052	57.3
11	5283.382	70.019	51.7
12	4948.985	65.587	44.5
13	2667.757	35.355	54.9
14	1976.059	26.188	75.2
15	1897.041	25.141	65.1


BnO
O
HO

14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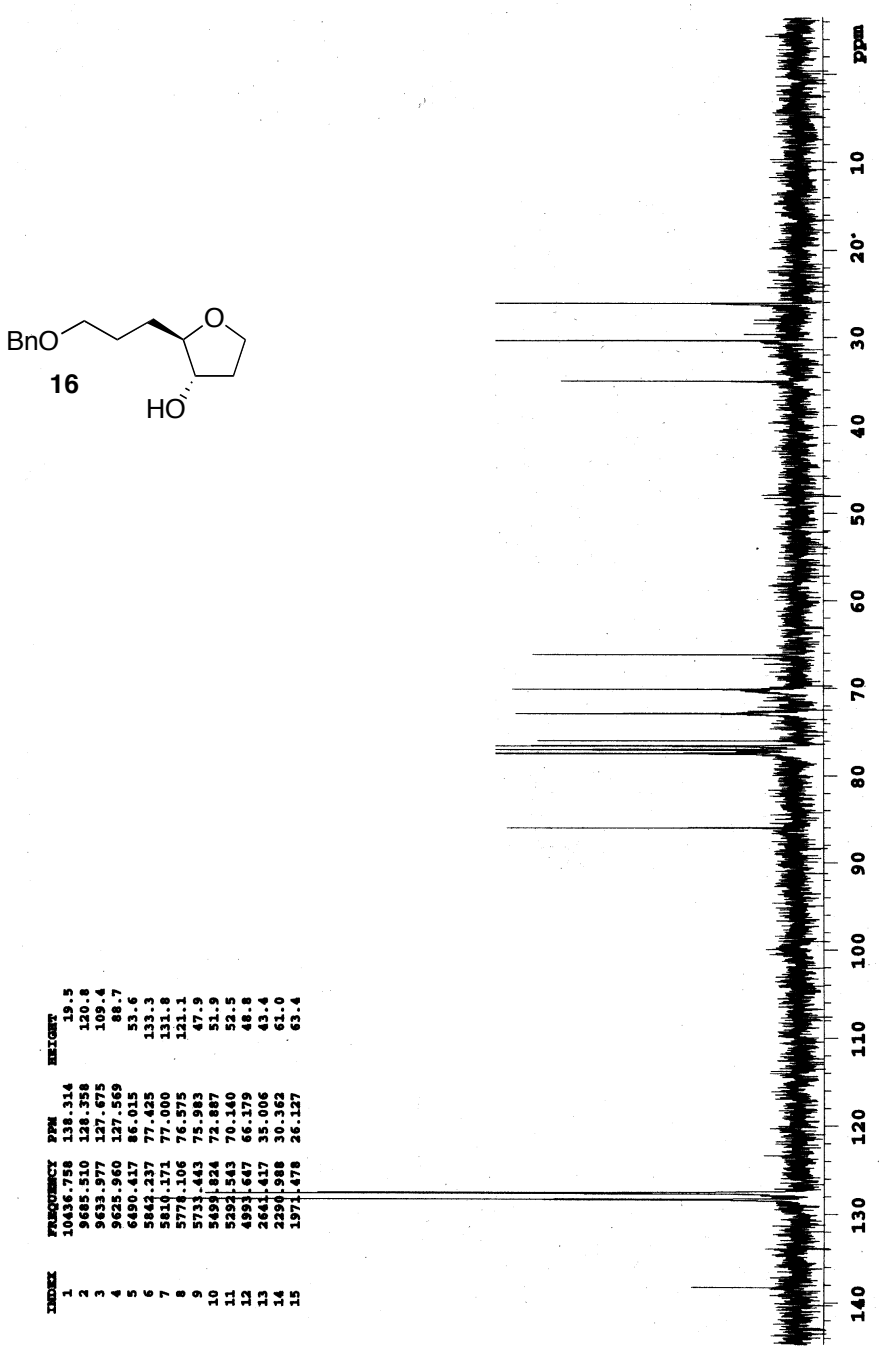
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4 9625.960 127.569 88.7
5 6490.417 86.015 53.6
6 5842.237 77.425 133.3
7 5810.171 77.000 131.8
8 5774.106 76.575 121.1
9 5733.443 75.983 47.9
10 5499.824 72.887 51.9
11 5292.543 70.140 52.5
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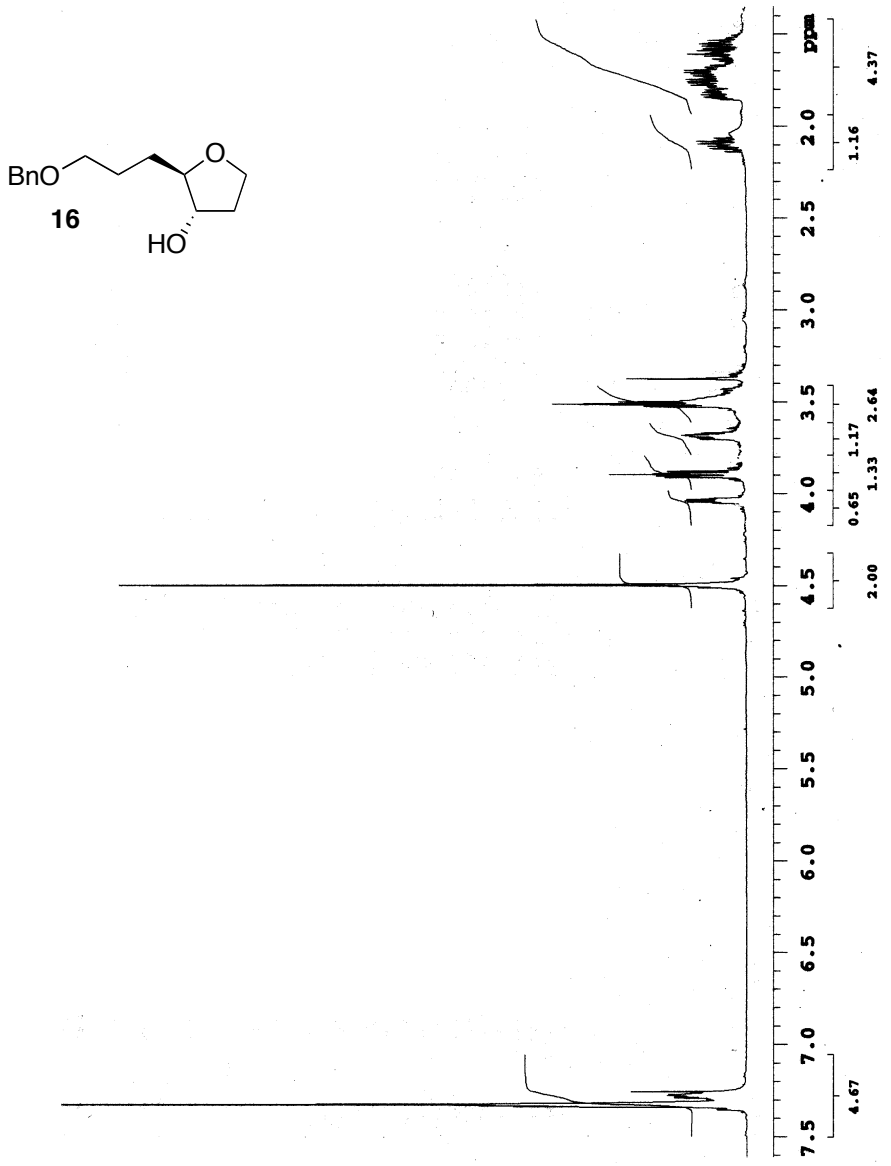
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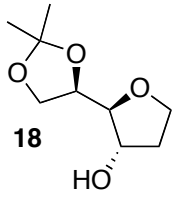

18

INDEX	FREQUENCY	PPM	HEIGHT
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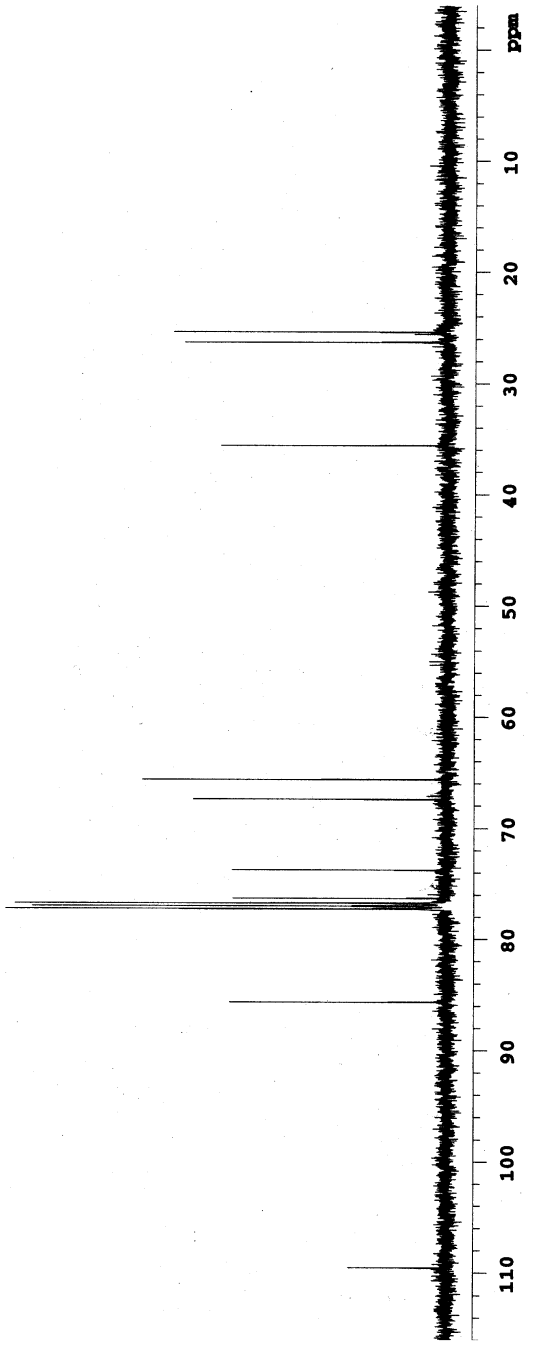
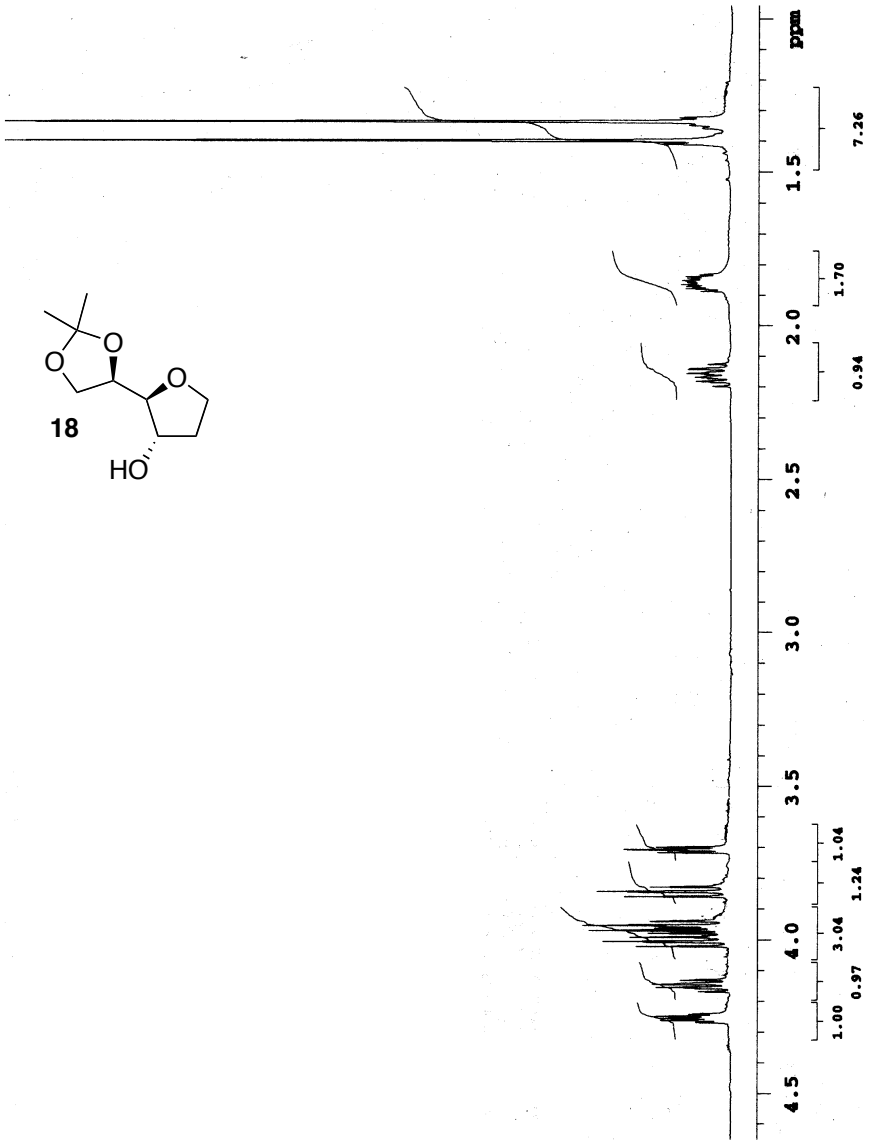
2	10766.362	85.643	39.9
3	9711.520	77.252	81.3
4	9678.915	76.992	76.4
5	9647.270	76.741	79.6
6	9590.692	76.291	39.3
7	9271.363	73.750	39.5
8	8473.518	67.404	46.7
9	8249.124	65.619	56.1
10	4472.788	35.579	41.7
11	3301.913	26.266	48.6
12	3187.799	25.358	50.5

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O
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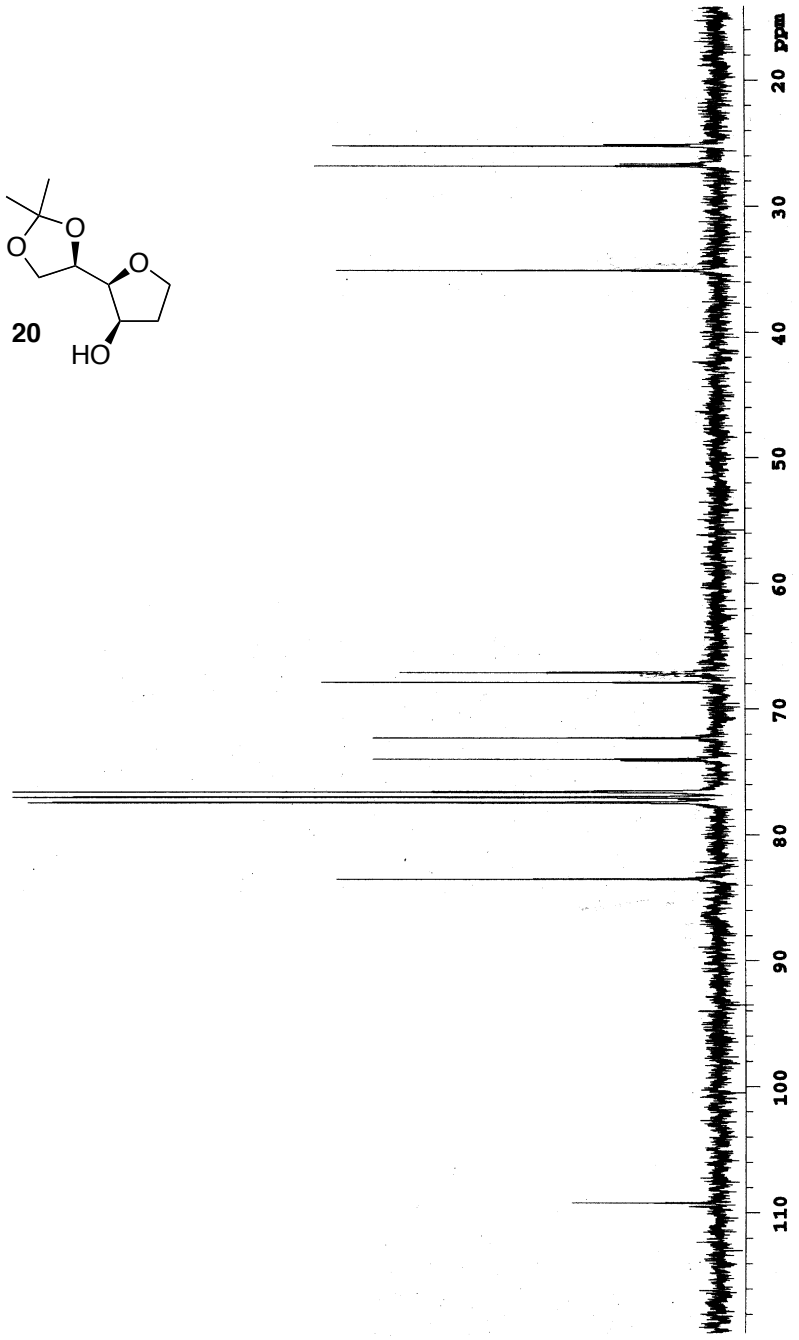
7.26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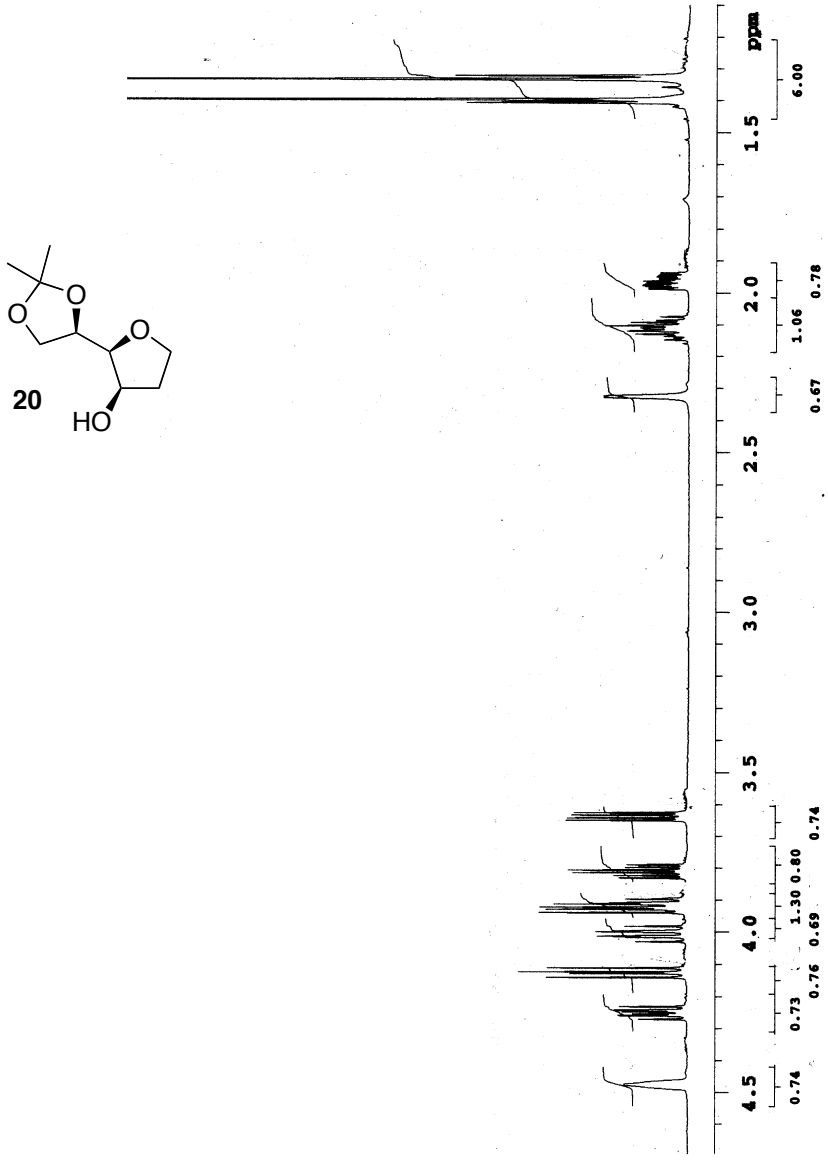
ppm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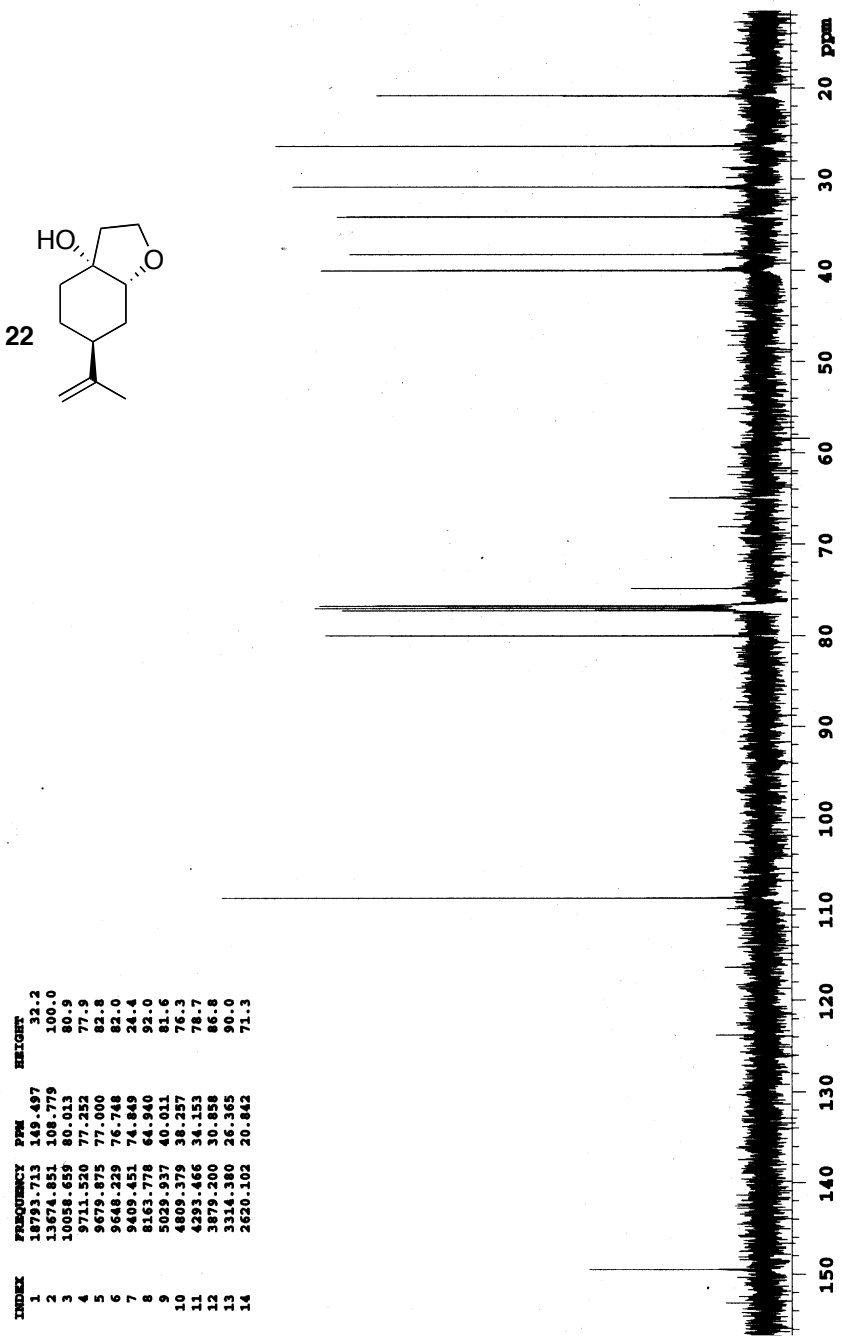
HO
O
22
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3 10058.659 80.013 80.9
4 9711.520 77.252 77.9
5 9679.875 77.000 82.8
6 9648.229 76.748 82.0
7 9409.451 74.849 24.4
8 8163.778 64.940 92.0
9 5029.937 40.011 81.6
10 4809.379 38.257 76.3
11 4293.466 34.153 78.7
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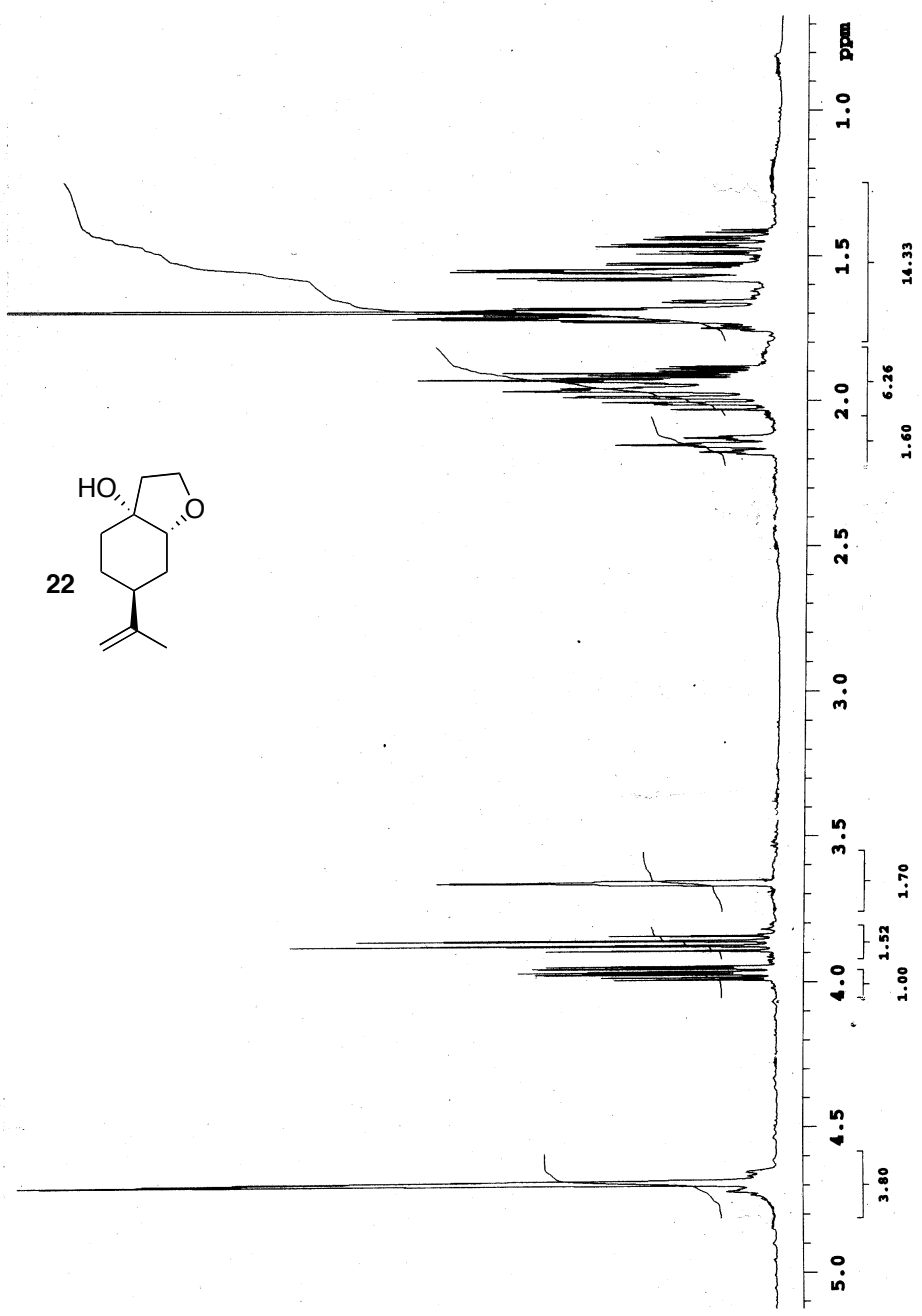
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4.0
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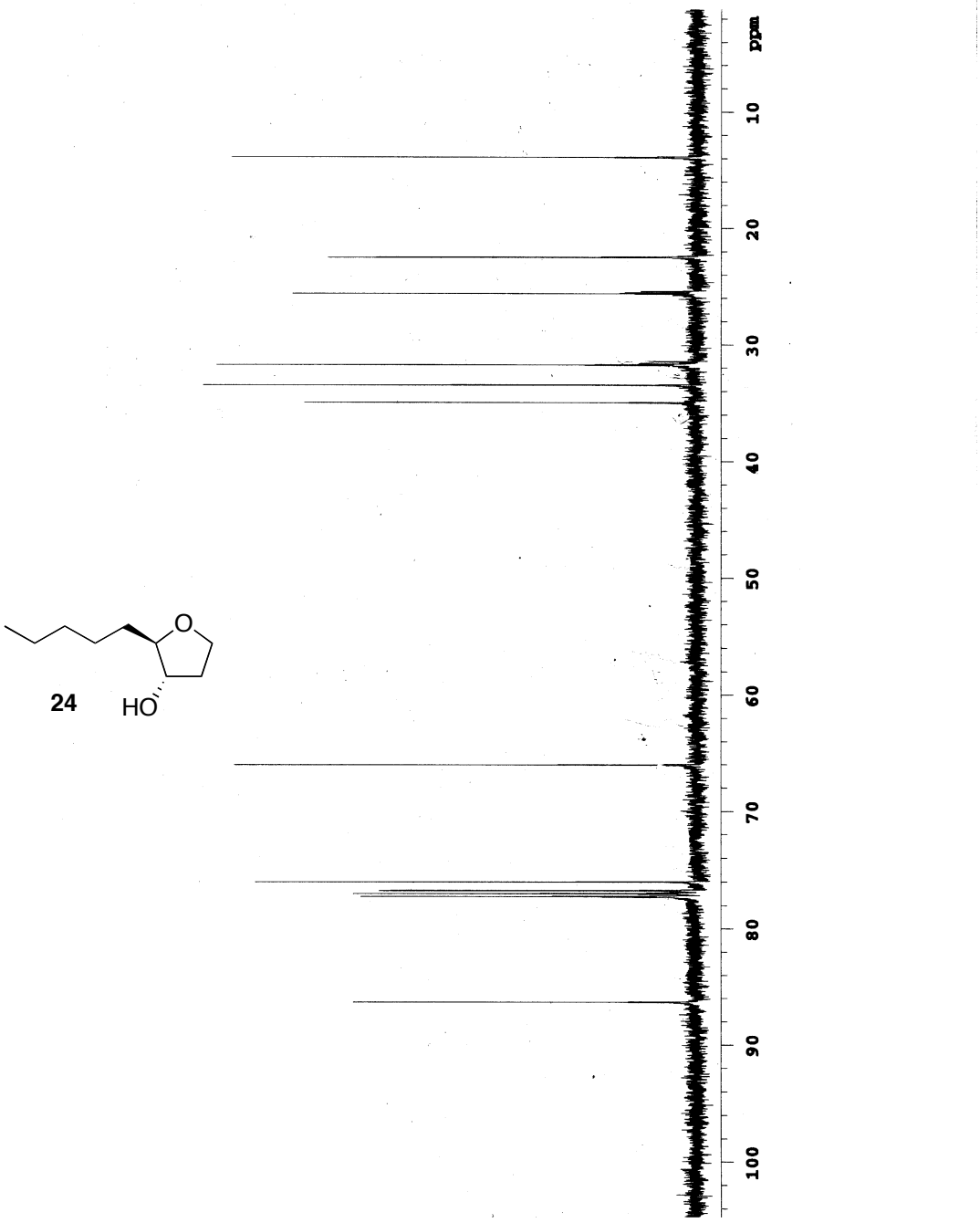
14.33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HO
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ppm
10
20
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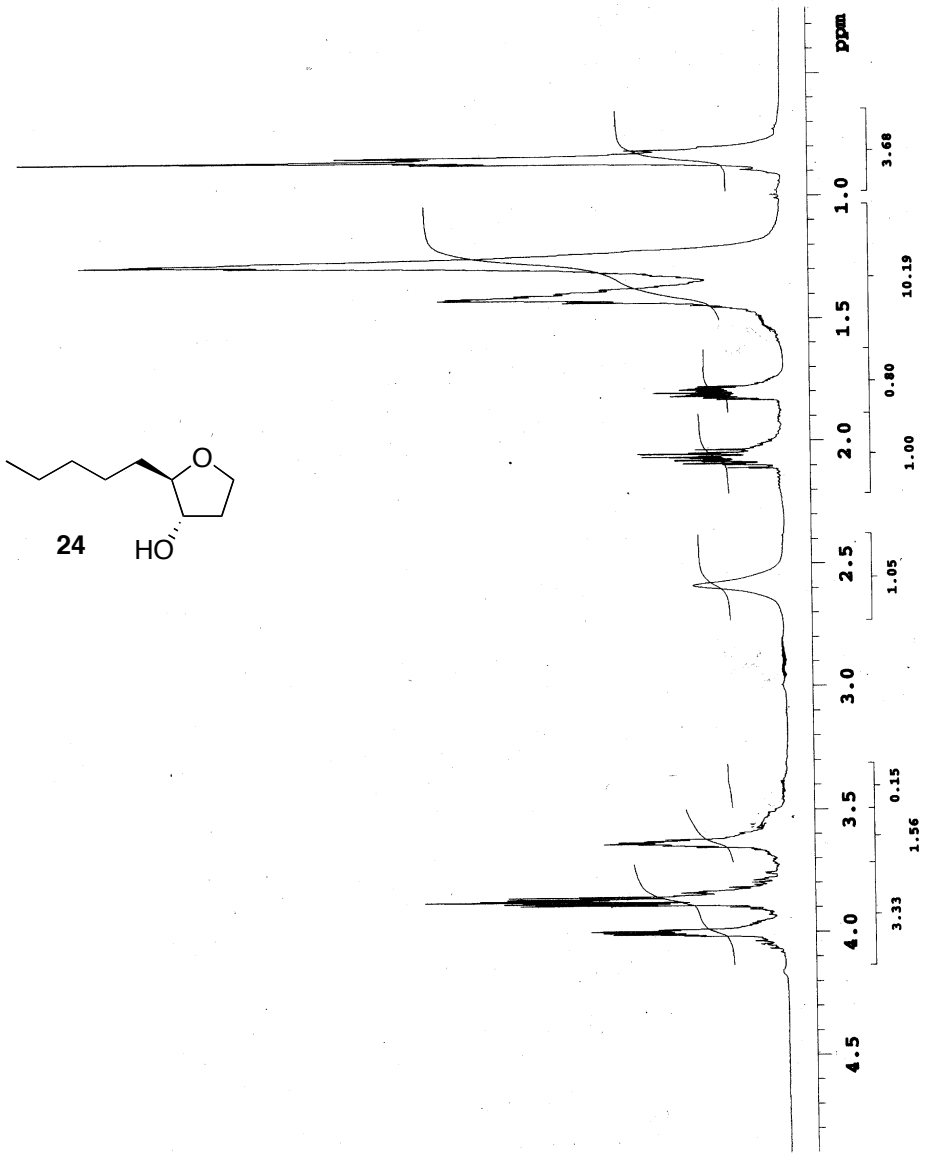
40
50
60
70
80
90
100


24
HO
O
ppm
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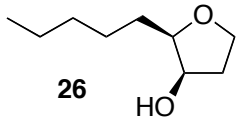
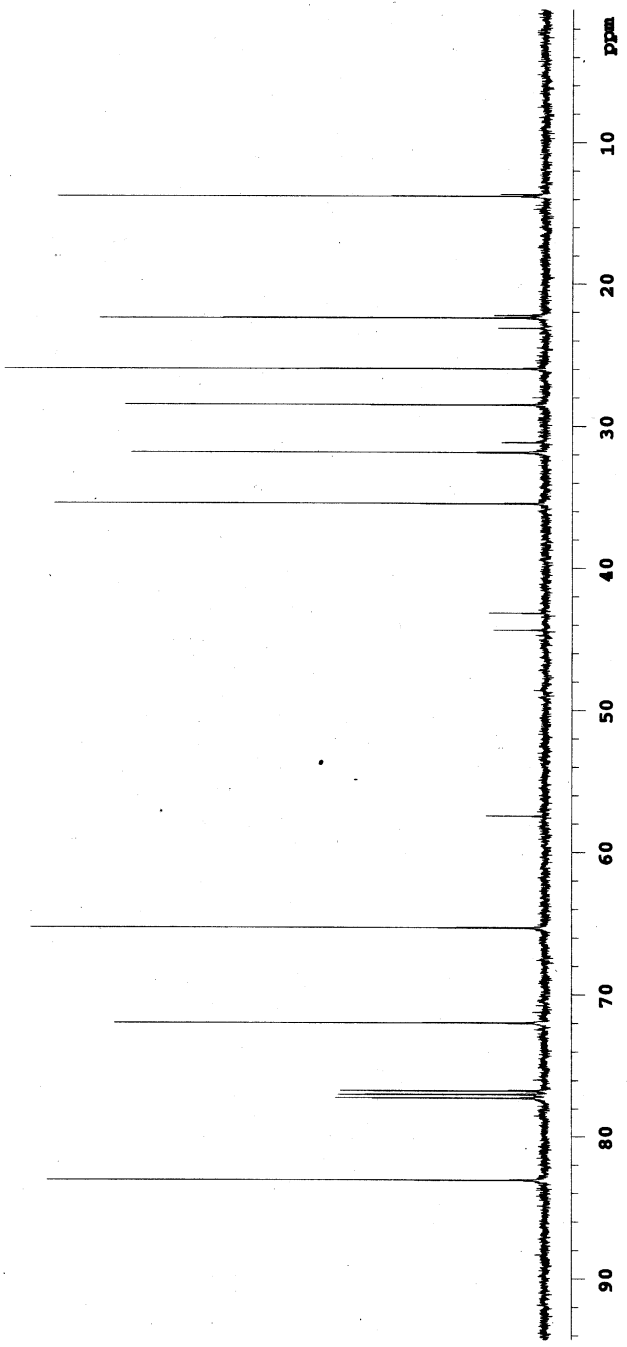
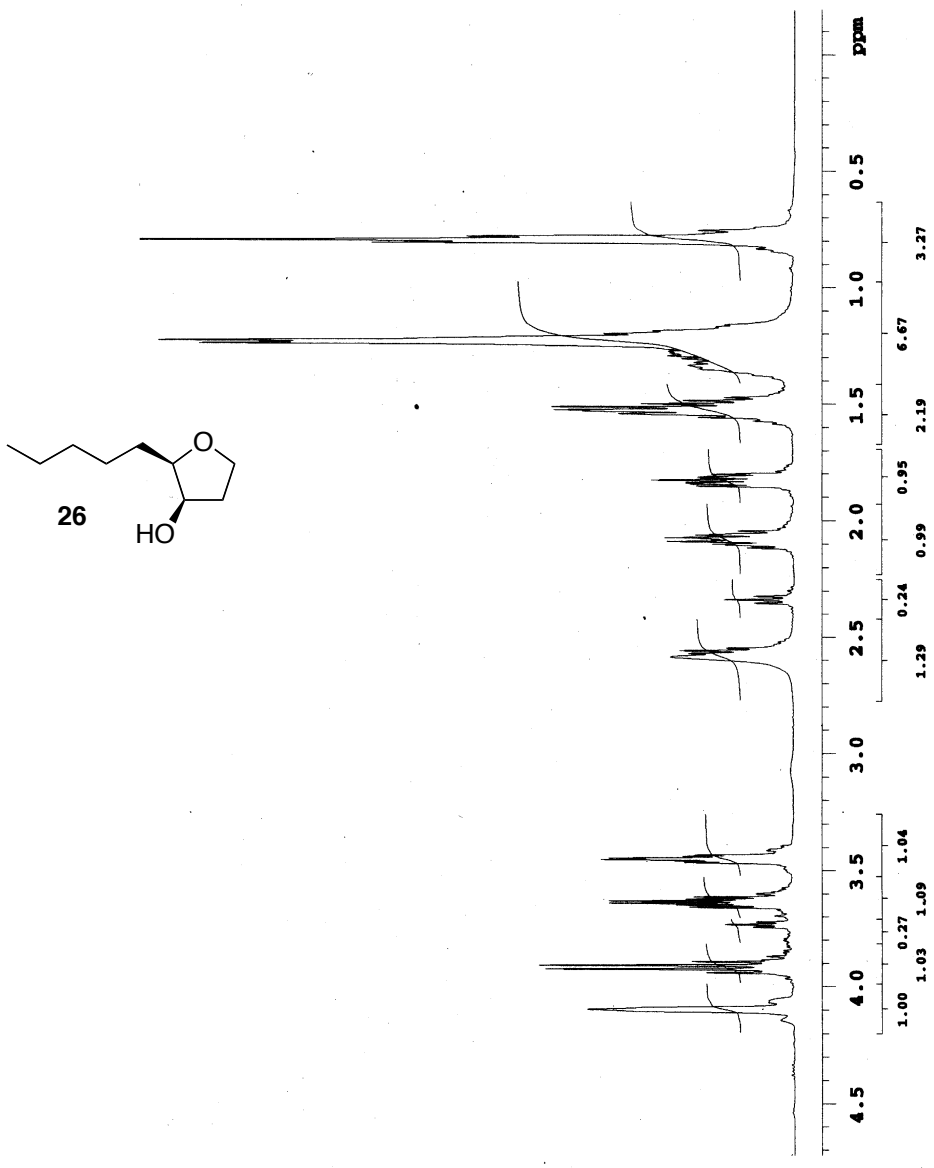
3.5
3.0
2.5
2.0
1.5
1.0
3.33
0.15
1.56
1.05
0.80
1.00
10.19
3.68



26

INDEX	FREQUENCY	PPM	HEIGHT
1	10441.280	83.057	92.0
2	9711.521	77.252	38.5
3	9679.875	77.000	38.0
4	9647.271	76.741	37.6
5	9048.888	71.981	79.6
6	8208.850	65.299	95.0
7	4455.528	35.442	90.8
8	4002.905	31.842	76.6
9	3581.927	28.493	77.8
10	3262.598	25.953	100.0
11	2815.728	22.398	82.5
12	1734.035	13.794	90.3




O
HO
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ppm
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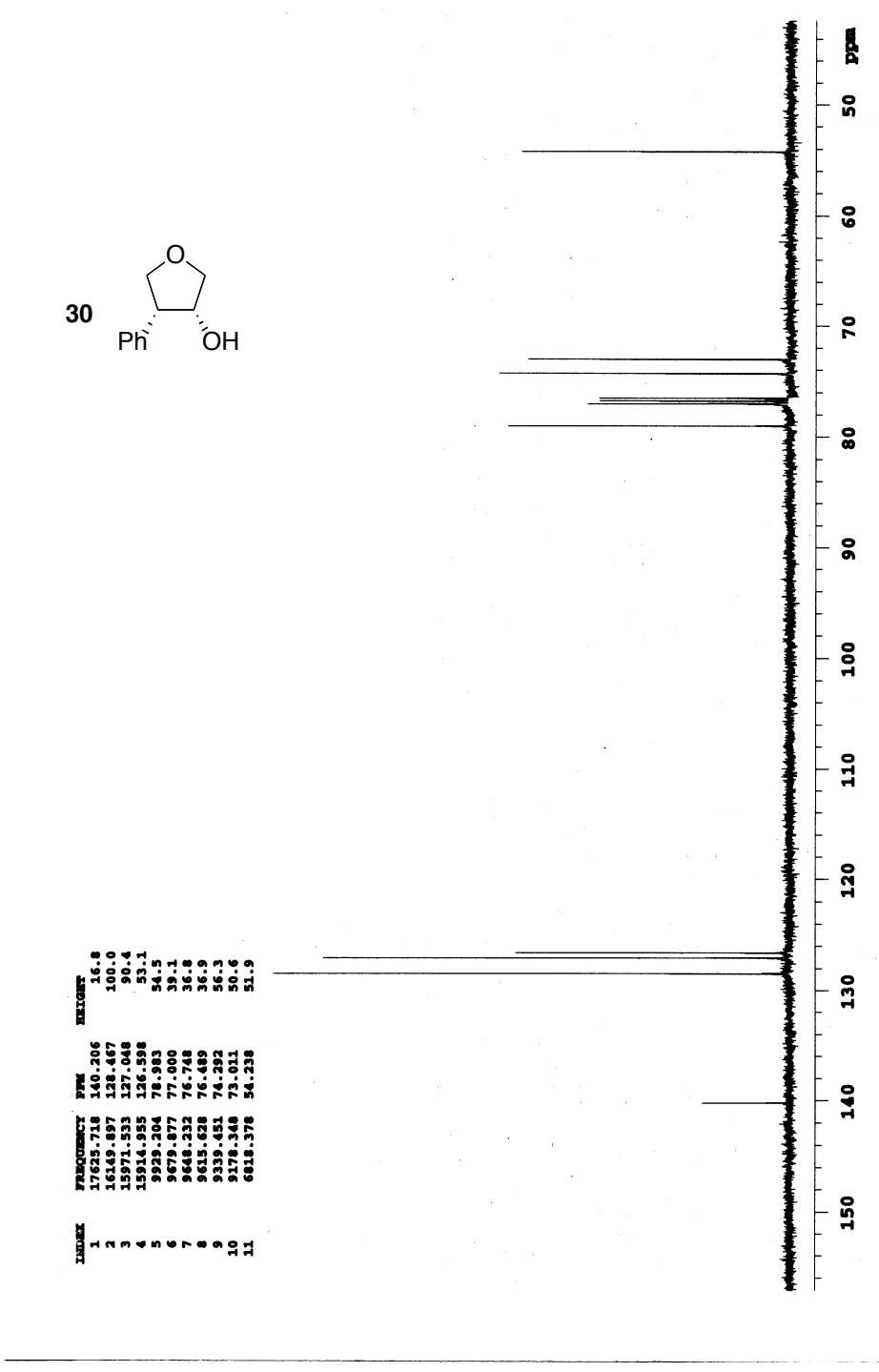
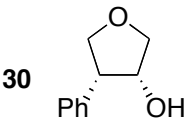
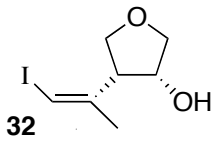
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.00
1.03
0.27
1.09
1.04
1.29
0.24
0.99
0.95
2.19
6.67
3.27


30
O
Ph
OH
INDEX FREQUENCY PPM HEIGHT
1 17625.716 140.206 16.8
2 16149.897 128.467 100.0
3 15971.533 127.048 90.4
4 15914.955 126.598 53.1
5 9929.204 78.983 54.5
6 9679.877 77.000 39.1
7 9648.232 76.748 36.8
8 9615.628 76.489 36.9
9 9339.451 74.292 56.3
10 9178.348 73.011 50.6
11 6818.378 54.238 51.9
150 140 130 120 110 100 90 80 70 60 50 ppm

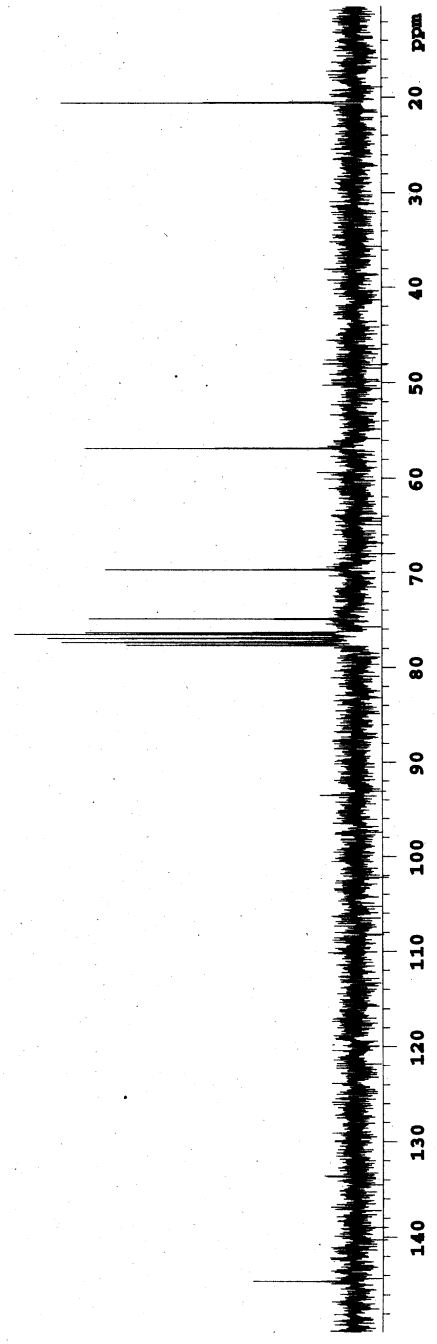
30

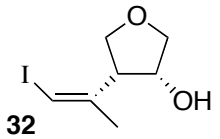




32

INDEX	FREQUENCY	PPM	HEIGHT
1	10913.139	144.628	19.0
2	5862.850	77.698	42.2
3	5842.237	77.425	54.2
4	5810.171	77.000	56.8
5	5778.106	76.575	63.0
6	5764.364	76.393	49.8
7	5654.425	74.936	49.1
8	5260.478	69.715	46.0
9	4292.788	56.891	49.9
10	1552.337	20.573	54.2





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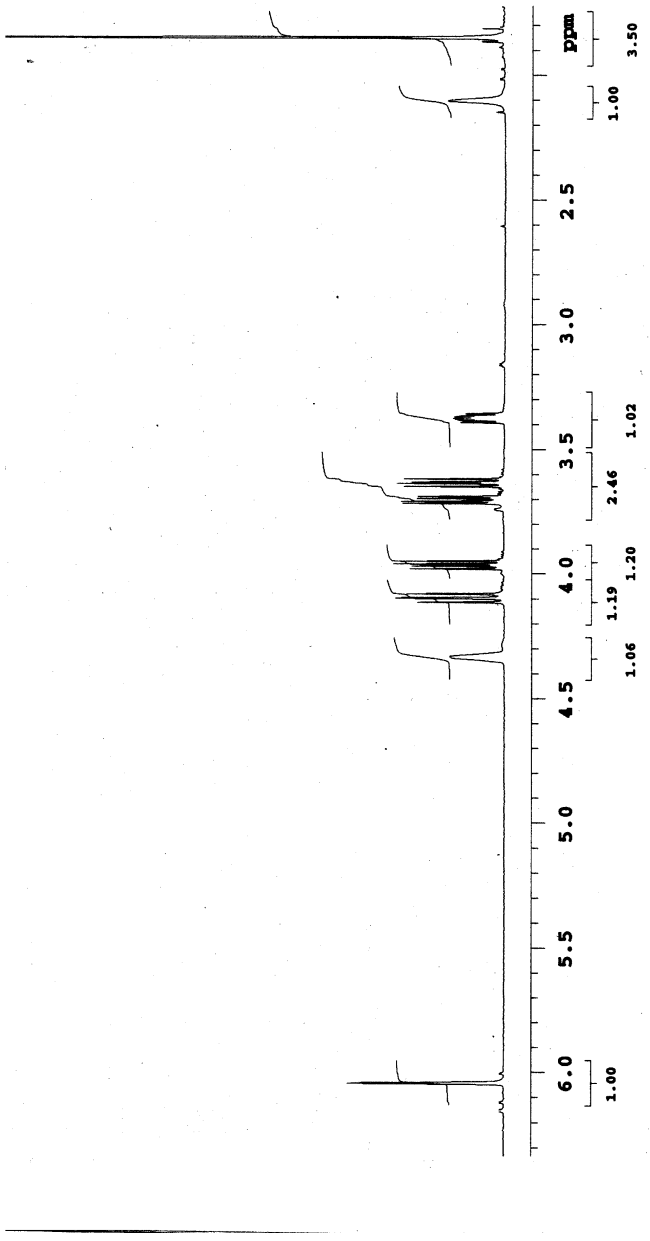
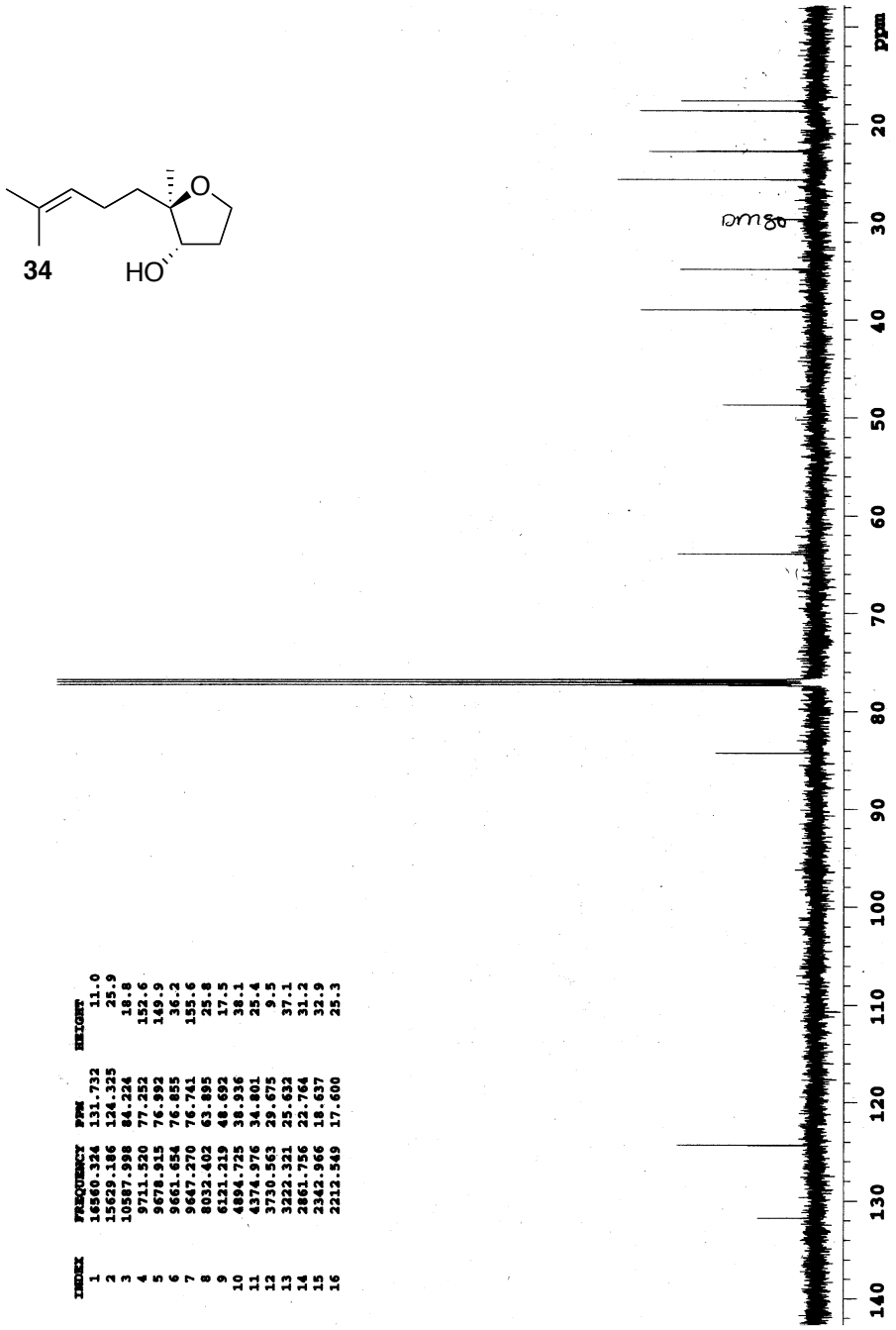
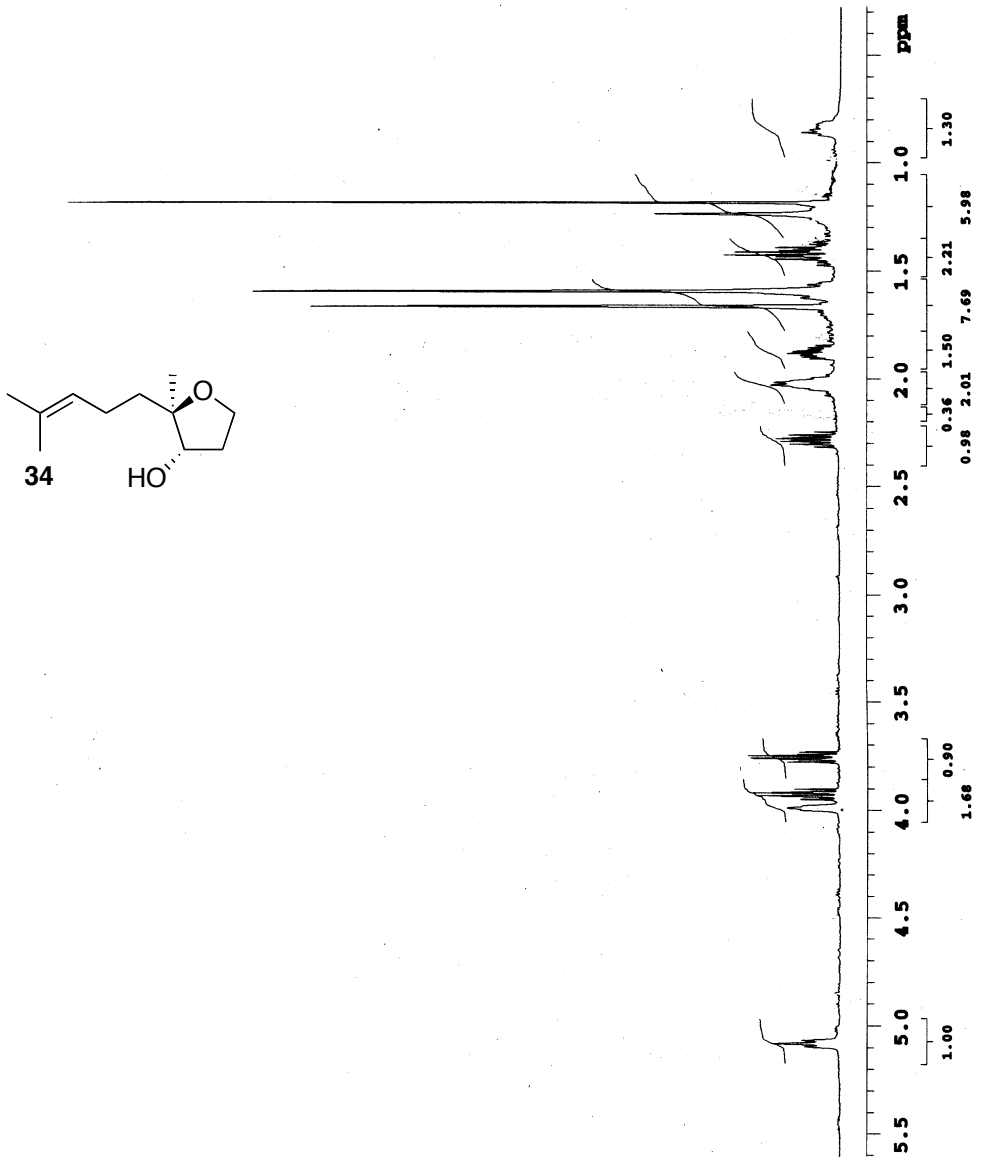




INDEX	FREQUENCY	PPM	HEIGHT
1	16560.324	131.732	11.0
2	15629.186	124.335	25.9
3	10587.998	84.224	18.8
4	9711.520	77.252	152.6
5	9678.915	76.992	149.9
6	9661.654	76.855	36.2
7	9647.270	76.741	155.6
8	8032.402	63.895	25.8
9	6121.219	48.692	17.5
10	4894.725	38.936	38.1
11	4374.976	34.801	25.4
12	3730.563	29.675	9.5
13	3222.321	25.632	37.1
14	2861.756	22.764	31.2
15	2342.966	18.637	32.9
16	2212.549	17.600	25.3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HO
O
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4.0
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3.0
2.5
2.0
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1.00
0.90
1.68
0.36
1.50
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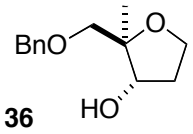
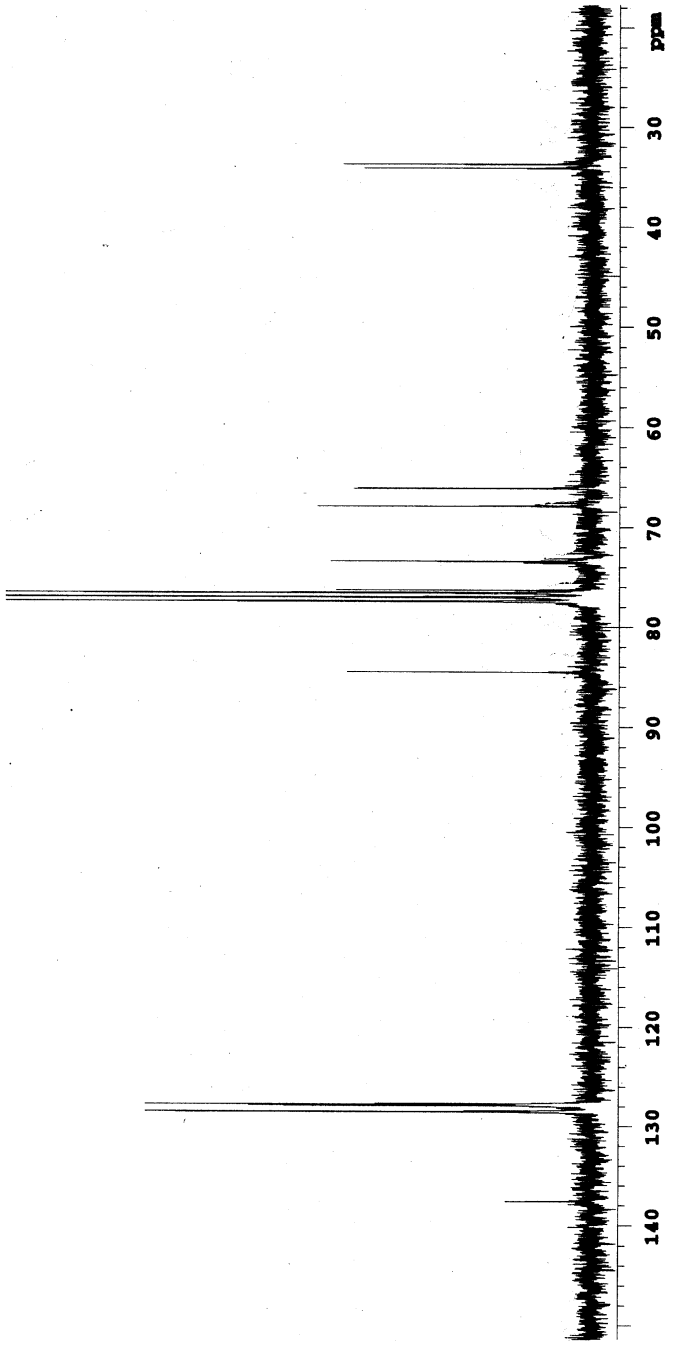
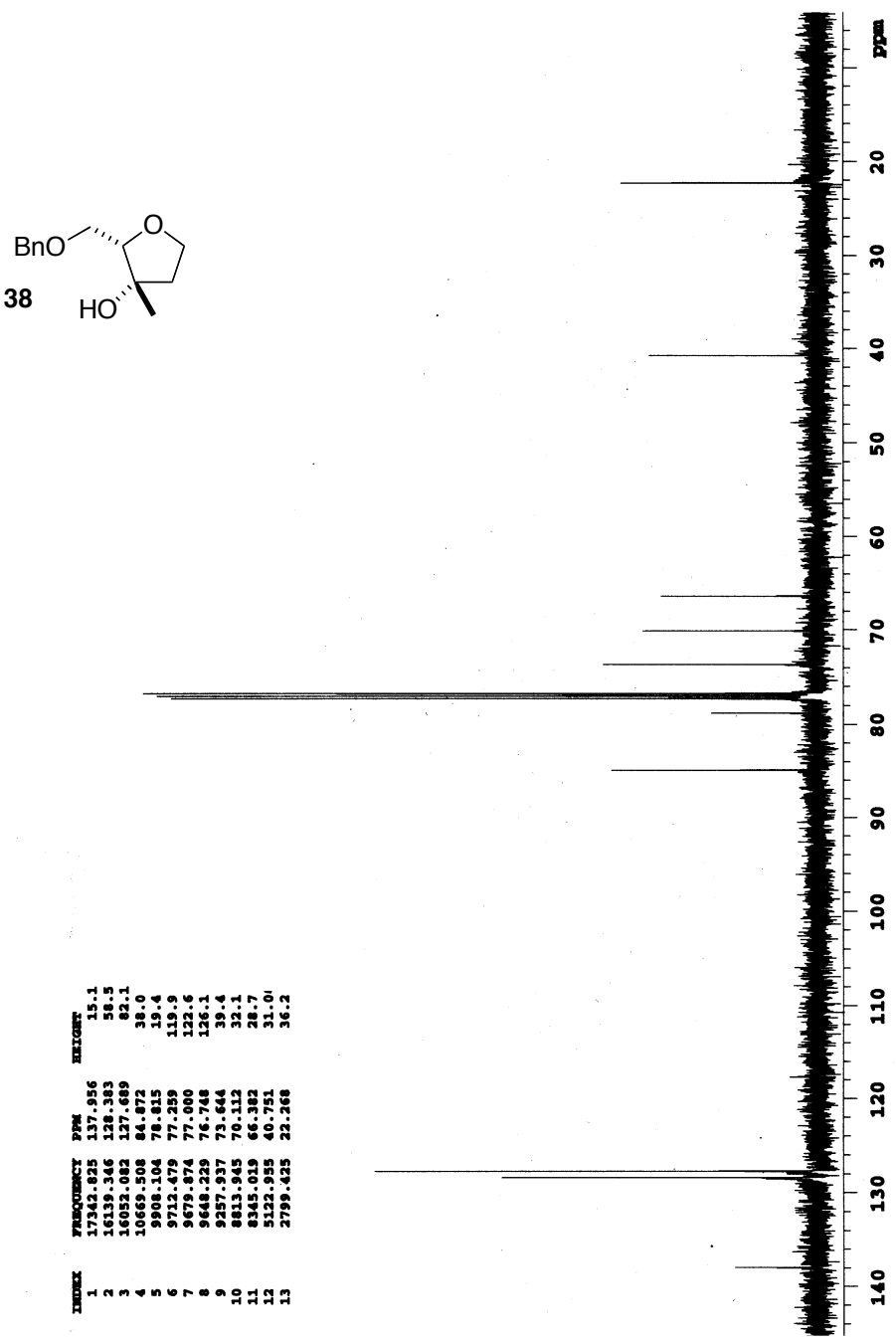
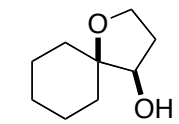
0.98
2.01
7.69
5.98
1.30



36

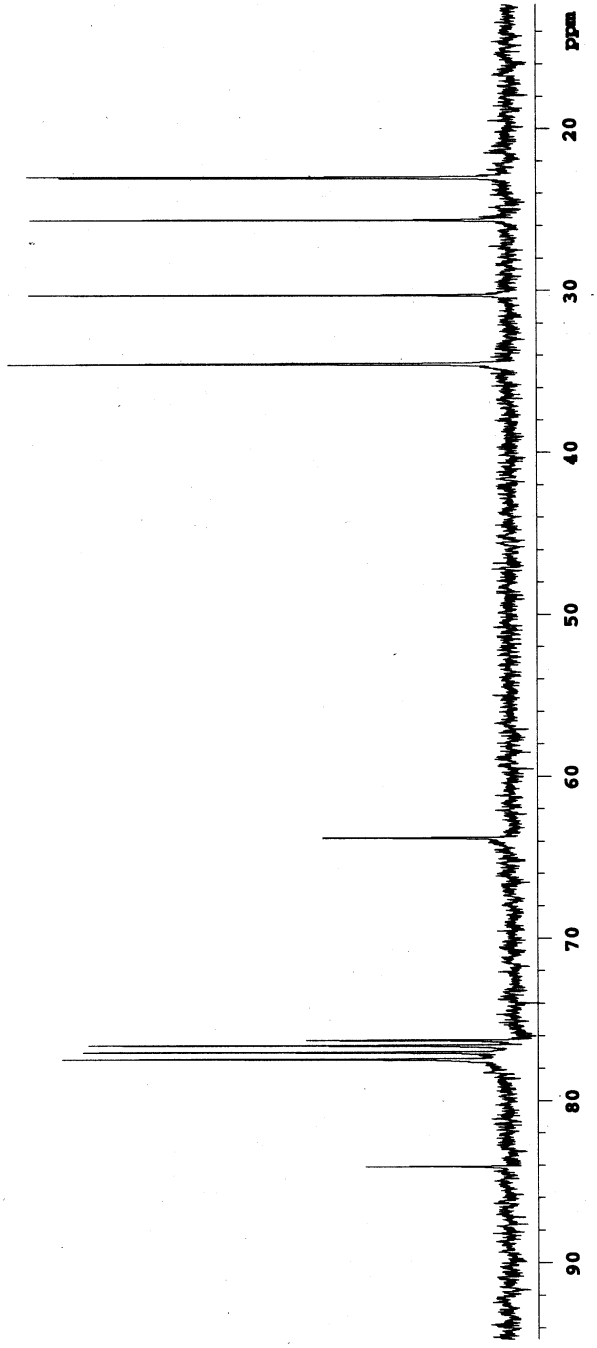


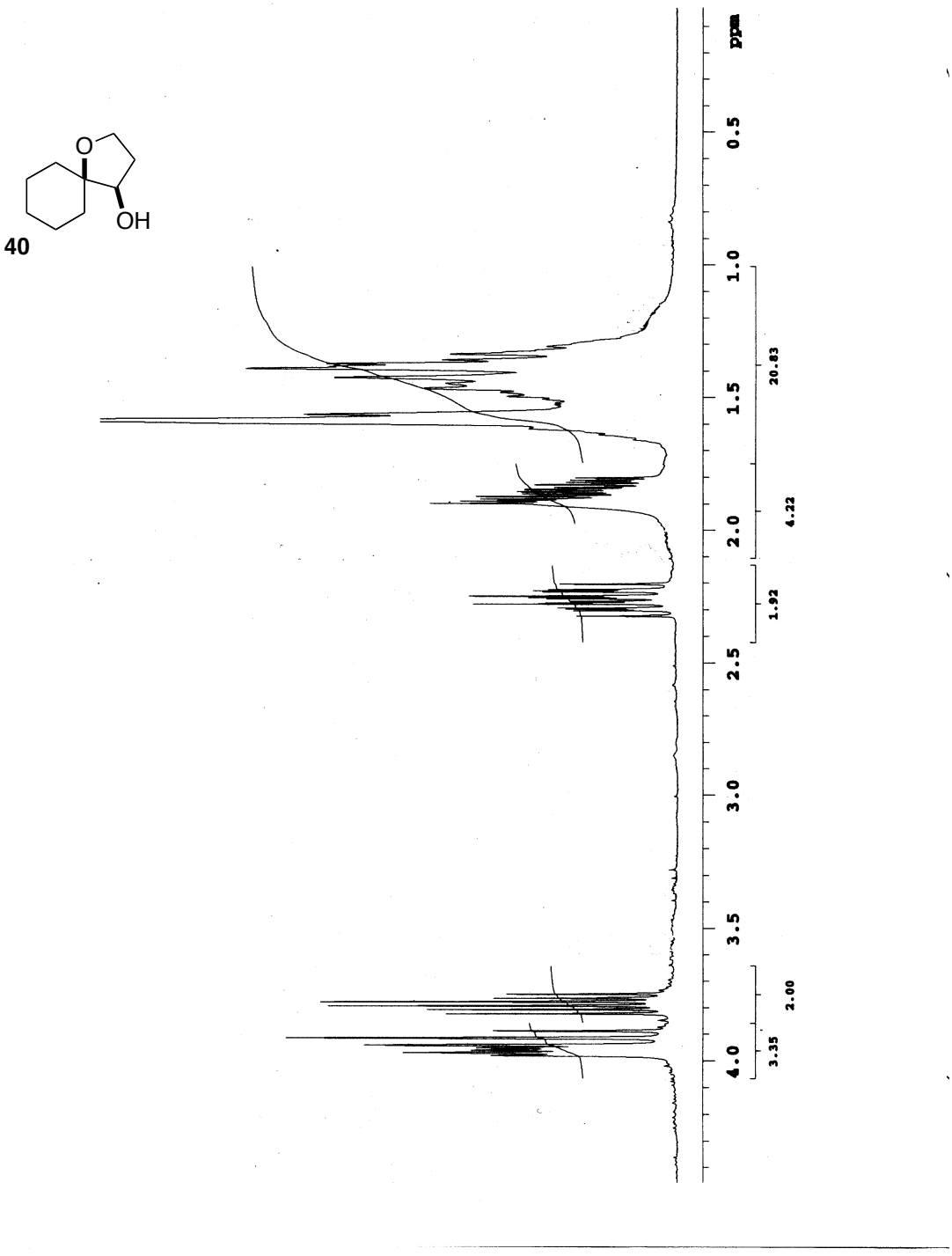

BnO
O
HO
38
INDEX FREQUENCY PPM HEIGHT
1 17342.825 137.956 15.1
2 16139.346 128.383 58.5
3 16032.082 127.689 82.1
4 10669.508 84.872 38.0
5 9908.104 78.815 19.4
6 9712.479 77.259 119.9
7 9679.874 77.000 122.6
8 9648.229 76.748 126.1
9 9257.937 73.644 39.4
10 8813.945 70.112 32.1
11 8345.019 66.382 28.7
12 5122.955 40.751 31.0
13 2799.425 22.268 36.2
ppm



40

INDEX	FREQUENCY	PPM	HEIGHT
1	6343.843	84.066	26.7
2	5842.318	77.420	82.8
3	5810.649	77.000	78.9
4	5778.404	76.573	77.9
5	5754.796	76.260	37.6
6	4812.782	63.777	60.0
7	2607.455	34.553	99.3
8	2603.425	34.499	67.1
9	2286.157	30.295	88.6
10	1936.644	25.664	88.3
11	1740.295	23.062	82.9
12	1735.689	23.001	89.0

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3.5
4.0
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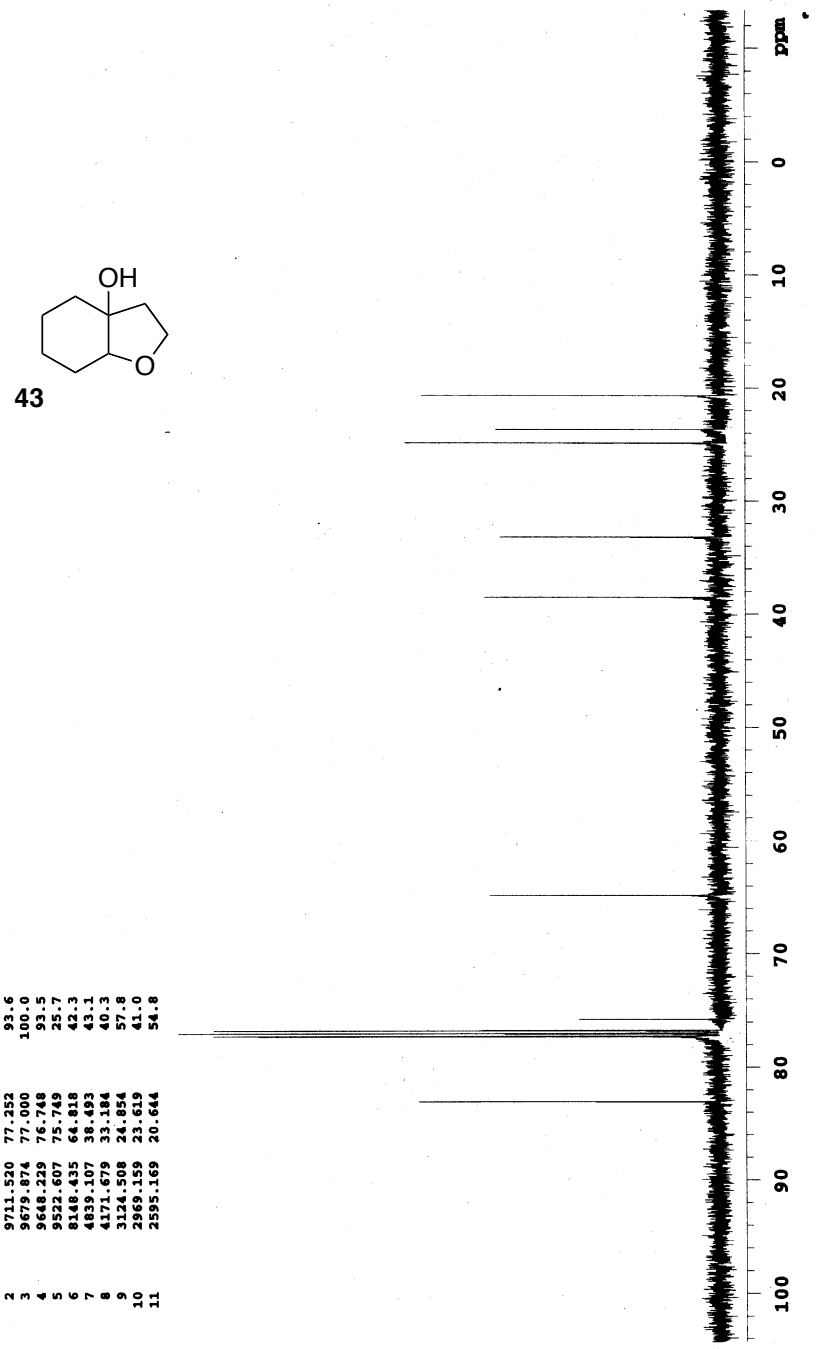
2.00
3.35


OH
O
43
INDEX FREQUENCY PPM HEIGHT
1 10438.402 83.034 55.5
2 9711.520 77.252 93.6
3 9679.874 77.000 100.0
4 9648.229 76.748 93.5
5 9522.607 75.749 25.7
6 8148.435 64.818 42.3
7 4839.107 38.493 43.1
8 4171.679 33.184 40.3
9 3124.508 24.854 57.8
10 2969.159 23.619 41.0
11 2595.169 20.644 54.8
ppm
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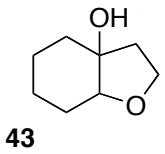
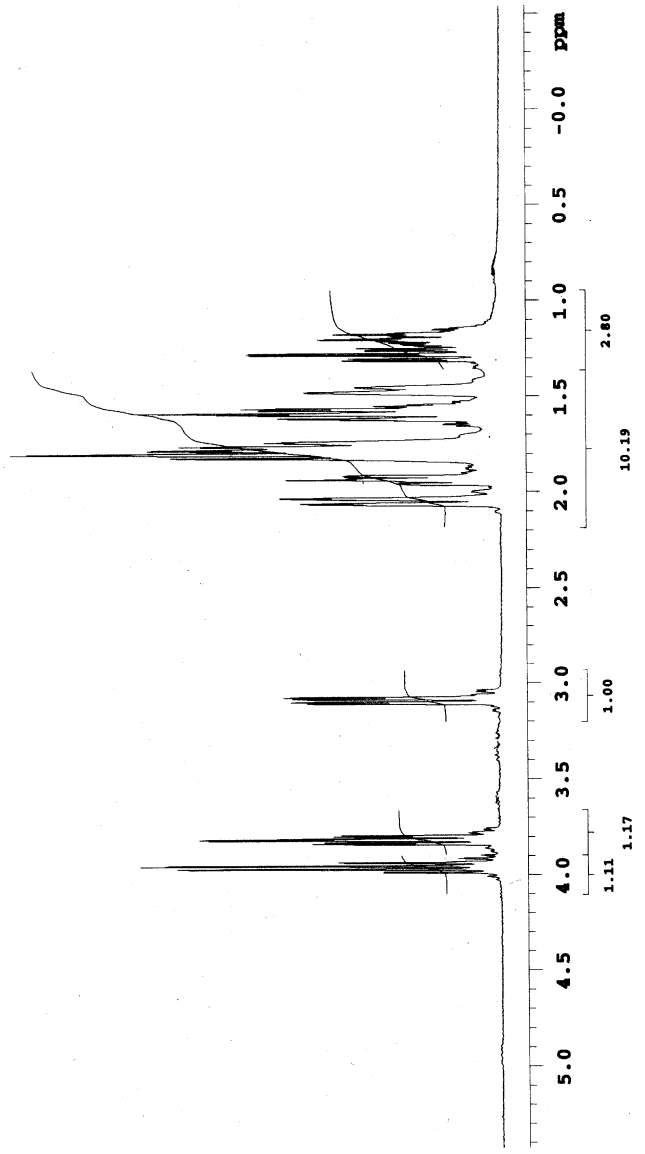
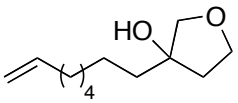


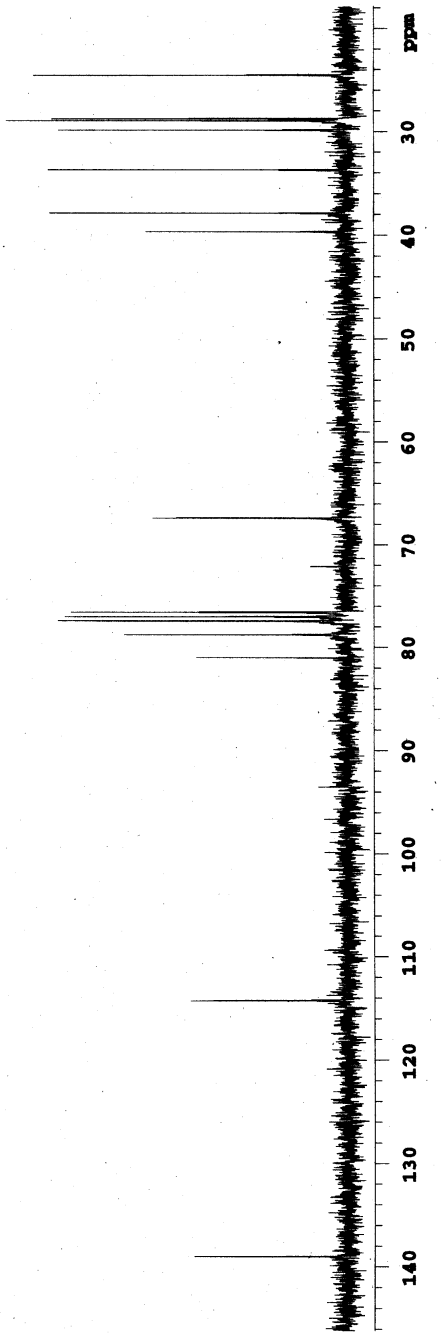
43

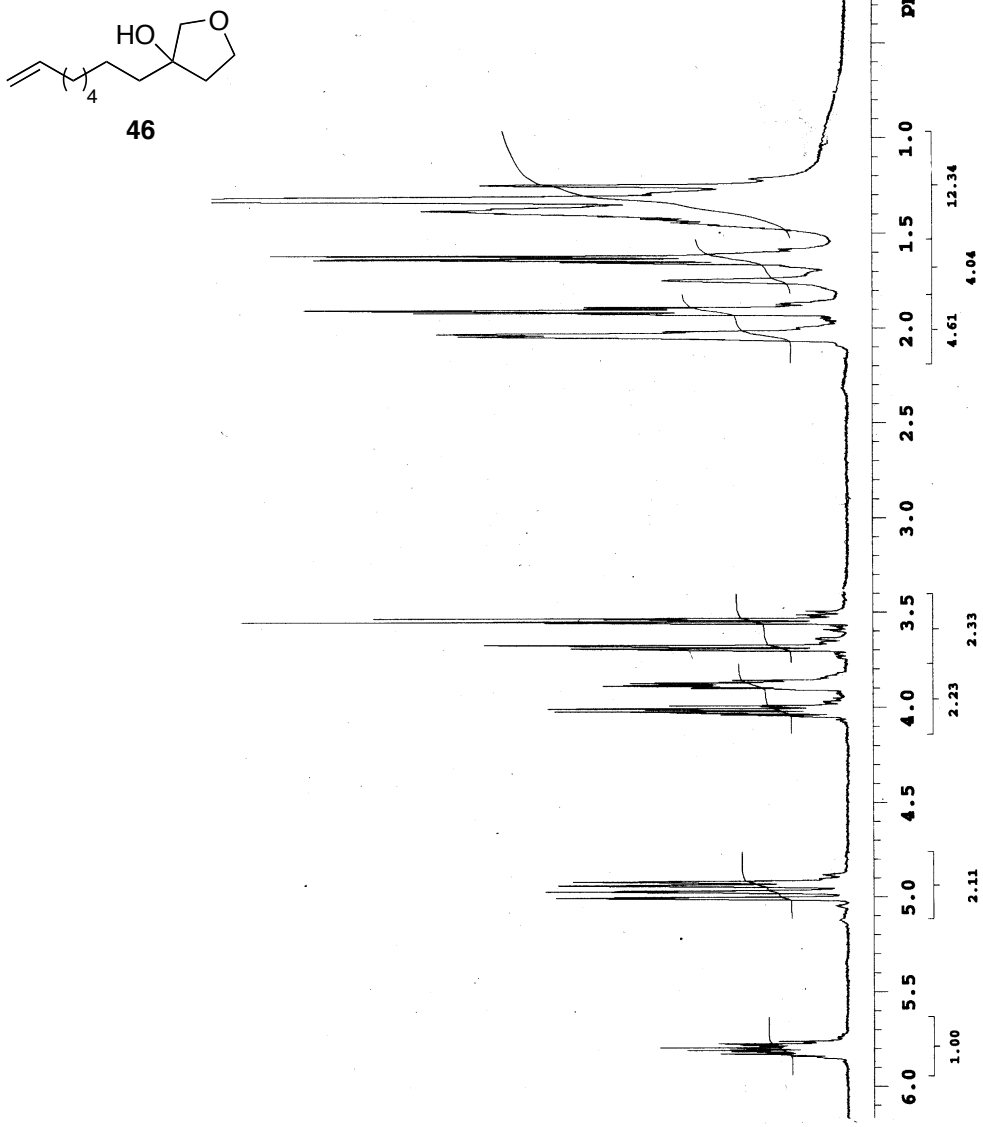




46

INDEX	FREQUENCY	PPM	HEIGHT
1	10488.292	138.997	28.3
2	8617.044	114.198	29.0
3	6111.358	80.992	27.7
4	5943.014	78.761	41.1
5	5842.237	77.425	53.5
6	5810.171	77.000	52.2
7	5779.251	76.590	51.0
8	5085.263	67.393	35.9
9	2991.847	39.650	37.1
10	2855.569	37.844	55.0
11	2541.705	33.685	55.3
12	2253.196	29.861	53.3
13	2184.485	28.950	63.0
14	2169.597	28.753	54.5
15	1851.233	24.534	57.9




HO
O
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46
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3.5
3.0
2.5
2.0
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1.0
1.00
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2.23
2.33
4.61
4.04
12.34