A Tandem Organocatalytic α-Chlorination-Aldol Reaction that Proceeds with Dynamic Kinetic Resolution: a Powerful Tool for Carbohydrate Synthesis

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Supplementary information

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1. GENERAL EXPERIMENTAL

(*S*)- and (*R*)-Proline (99% purity) were purchased from Alfa Aesar. All reactions described were performed at ambient temperature and atmosphere unless otherwise specified. Column chromatography was carried out with 230-400 mesh silica gel (E. Merck, Silica Gel 60). Concentration and removal of trace solvents was done via a Buchi rotary evaporator using acetone-dry-ice condenser and a Welch vacuum pump.

Nuclear magnetic resonance (NMR) spectra were recorded using deuterochloroform ($CDCl_3$), deuteromethanol (CD_3OD) or deuteromethyl sulfoxide (DMSO-d_6) as the solvent. Signal positions (δ) are given in parts per million from tetramethylsilane (δ 0) and were measured relative to the signal of the solvent (**^{1}H NMR:** $CDCl_3$: δ 7.26; CD_3OD: δ 3.31; **^{13}C NMR:** $CDCl_3$: δ 77.0; CD_3OD: δ 49.0). Coupling constants (*J* values) are given in Hertz (Hz) and are reported to the nearest 0.1 Hz. ^{1}H NMR spectral data are tabulated in the order: multiplicity (*s*, singlet; *d*, doublet; *t*, triplet; *q*, quartet; s_{ept}, septet; *m*, multiplet; $_{br}$ broad), coupling constants, number of protons. NMR spectra were recorded on a Bruker Avance 600 equipped with a QNP or TCI cryoprobe (600 MHz), Bruker 400 (400 MHz) or Bruker 500 (500 MHz). Diastereomeric ratios (dr) are based on analysis of crude ^{1}H-NMR. Assignments of ^{1}H are based on analysis of ^{1}H-^{1}H-COSY, ^{1} TOCSY and nOe spectra. Assignments of ^{13}C are based on analysis of HSQC spectra.

High performance liquid chromatography (HPLC) analysis was performed on an Agilent 1100 HPLC, equipped with a variable wavelength UV-Vis detector and Chiralcel OD-H chiral column (0.46 cm x 25 cm). Enantiomeric excess (*ee*) has been determined using corresponding benzoylated esters of all *syn*-chlorohydrins except for **16i** that required no benzoyl derivatization.

Gas chromatography (GC) analysis was performed on a Hewlett Packard model 6890 gas chromatograph, equipped with a flame ionization detector (temperature = 250 °C) and a custom made fused silica column with a 1:1 mixture of heptakis-(2,6-di-*O*-methyl-3-*O*-pentyl)-*β*-cyclodextrin and OV-1701.

Infrared (IR) spectra were recorded neat on a Perkin Elmer Spectrum Two FTIR spectrometer. Only selected, characteristic absorption data are provided for each compound.

Optical rotation was measured on a Perkin-Elmer Polarimeter 341 at 589 nm.

UV-Visible spectrum of **24** was recorded on a Varian CARY 5000 spectrophotometer using a 0.200 cm cell.

Photoluminescence (PL) spectrum for **24** (12 nM), in DMSO, was recorded using a Photon Technology International PTI Felix32 system using a 1 cm cell.

Microwaves reactions were performed in a CEM Discover LabMate microwave reactor.

2. GENERAL PROCEDURES

2.1 General Procedure A (one-pot organocatalytic α-chlorination/aldol reaction)

A sample of aldehyde (1.00 equiv.) was added to a stirred suspension of NCS (1.05 equiv.) and (*S*)-Proline (0.80 equiv.) in CH_2Cl_2 (0.2 M) at 0°C. 2,2-Dimethyl-1,3-dioxan-5-one (**1**) (1.05 equiv.) was then added and the resulting mixture was allowed to warm gradually to room temperature. After a total of 24 hours, or when complete consumption of the intermediate α-chloroaldehyde was observed by ^{1}H-NMR spectroscopic analysis of small reaction aliquots, the mixture was diluted with Et_2O and the organic layer was removed and washed twice with water and once with brine. The organic layer was then dried over $MgSO_4$, concentrated under reduced pressure and the crude product was purified by flash chromatography as indicated.

2.2 General Procedure B (1,3-*syn*-selective reduction)[1]

A solution of the chlorohydrin (1.0 equiv.) in MeCN (0.9 M) was added to a stirred solution of $Me_4NBH(OAc)_3$ (5.0 equiv.) and AcOH (10.0 equiv.) in MeCN (0.2 M) at -24°C and the resulting mixture was stirred for 24 hours. The reaction mixture was then quenched by addition of a saturated aqueous solution of sodium tartrate. The aqueous layer was removed and extracted four times with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography as indicated.

2.3 General Procedure C (1,3-*anti*-selective reduction)

To a cold (0 °C), stirred solution of the chlorohydrin (1.0 equiv.) in dry THF (0.1 M) was added a solution of catechol borane in THF (1.0 M, 2.2 equiv.). The resulting mixture was allowed to warm gradually to room temperature and was then stirred for an additional 45 minutes or until complete consumption of starting chlorohydrin was observed by TLC analysis. The mixture was then diluted with MeOH (to 0.05 M) and a solution of saturated aqueous sodium tartrate was added. The biphasic mixture was stirred vigorously for 2 hours, after which time the aqueous layer was removed and extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure, and the crude product was purified by flash chromatography as indicated.

2.4 General Procedure D (thermal cyclization)

A stirred solution of the corresponding chlorodiol (1.0 equiv) in a mixture of MeOH-H_2O (1:6, 0.1 M) was heated to 60 °C and maintained at this temperature for 16 hours or until no starting material remained (as determined by TLC analysis). The reaction mixture was then concentrated under reduced pressure, and the crude product was purified by flash chromatography as indicated

2.5 General Procedure E (microwaves-assisted cyclization)

The chlorodiol (1.0 equiv) was added to a microwave vial and H_2O (0.2 M) was added. The vial was sealed in a CEM Discover LabMate microwave reactor and resulting mixture was heated in a microwave reactor at 110 °C (as monitored by a vertically focused IR temperature sensor) for 30 minutes, or until no starting material remained (as determined by TLC analysis). The reaction mixture was then concentrated under reduced pressure and the crude product was purified by flash chromatography as indicated.

2.6 General Procedure F (epoxide formation)[2]

A purified sample of the indicated aldol adduct was reduced by reaction with $NaBH_4$ (1.05 equiv) in MeOH (0.1 M). The resulting mixture was stirred at room temperature for 1 hour or until no starting material remained (as determined by TLC analysis). The reaction mixture was diluted with Et_2O and treated with H_2O. The organic layer was removed, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was dissolved in EtOH and NaOH (2.0M aqueous, 1.2 equiv) was added. The reaction mixture was stirred for 1 hour and concentrated under reduced pressure. The crude product was purified by flash chromatography (pentane-EtOAc).

2.7 General Procedure G (radical dechlorination)[3]

To a stirred solution of the purified aldol adduct (1.0 equiv) in toluene (0.1 M) was added tris(trimethylsilyl)silane (5.0 equiv) and the resultant mixture was sparged with N_2 for 20 minutes. A catalytic amount (1-2 mg) of AIBN was then added, and the reaction vessel was sealed and heated to 110 °C in an oil bath and maintained at this temperature for 16 hours. The reaction mixture was then cooled to room temperature and concentrated. The crude product was purified by flash chromatography (pentane-EtOAc).

2.8 General Procedure H (benzoylation)

To a stirred solution of racemic or optically enriched *syn*-chlorohydrin (1.0 equiv) in dry pyridine (0.1 M) was added benzoyl chloride (2.0 equiv) and dimethylaminopyridine (cat.), and the resulting mixture was stirred at room temperature for 24 hours or until no starting material remained (as determined by TLC analysis). The reaction mixture was then diluted with EtOAc and washed sequentially with aqueous HCl (3 x 1 mL, 1 M), saturated $NaHCO_3$ (1 mL), and brine (1 mL). The organic layer was dried over $MgSO_4$, concentrated under reduced pressure, and the crude product was purified by flash chromatography (pentane-CH_2Cl_2-EtOAc, 87:10:3).

2.9 General Procedure I (synthesis of Mosher's esters)[4]

To a stirred solution of *syn*-chlorohydrin (1.0 equiv) and either (*R*)-(+)-MTPA-OH or (*S*)-(-)-MTPA-OH (1.5 equiv) in dry CH_2Cl_2 (0.1 M) was added diisopropylcarbodiimide (1.5 equiv) and dimethylaminopyridine (cat.) and the resulting mixture was stirred at room temperature for 24 hours or until no starting material remained (as determined by TLC analysis). The reaction mixture was concentrated under reduced pressure, and the crude product was dissolved in EtOAc and filtered through a short plug silica gel (EtOAc eluent). The filtrate was then concentrated and the crude product was purified by flash chromatography (pentane-EtOAc).

3. EXPERIMENTAL DETAILS FOR SCHEME 2

*Determination of enantiomeric excess of α-chloroaldehyde (R)-**11** (proline-ca*talyzed *racemization).*

The enantiomeric excess of (*R*)-**11** was determined by chiral GC analysis of the primary alcohol derived from the reduction (*R*)-**11**. Thus, to a stirred solution of 100 mg of (*R*)-**11** (100 mg, 0.829 mmol, 78% ee), in CH_2Cl_2 (4 mL) was added either (*S*)- or (*R*)-proline (76 mg, 0.66 mmol). To monitor the excess of (*R*)-**11** (see Table 1), small aliquots (100 μL) of the reaction mixture were reduced by treatment with excess $NaBH_4$ (2 mg, excess) in MeOH (200 μL). The resulting mixture was stirred for 15 minutes at room temperature then quenched by the addition of water (200 μL), and diluted with pentane (500 μL), dried ($MgSO_4$) and filtered to afford a solution of 2-chloropentanol. Separation of the enantiomers of 2-chloropentanol was accomplished by chiral GC (see General Experimental). Temperature Injection = 250 °C; temperature program: 70 °C held for 20 minutes then increased by 5 °C per minute until 180 °C and run for 50 minutes ; retention time = 23.6 minutes ((*R*)-**11)**; retention time = 24.1 minutes ((*S*)-**11**).

*Determination of enantiomeric excess of α-chloroaldehyde (R)-**11** during chlorination reaction.*

To a mixture of (*S*)-proline (87 mg, 0.75 mmol) and NCS (150 mg, 1.13 mmol) in CH_2Cl_2 (4 mL) was added pentanal (100 μL, 0.94 mmol) and the reaction mixture was stirred for 24 hours. Enantiomeric excess of (*R*)-**11** was monitored as detailed above and summarized in Table 1.

Table 1: Determination of % ee for (*R*)-**11** by chiral GC analysis

time (h)	(*S*)-Proline + (*R*)-11 (% ee ; solid line)[a]	(*R*)-Proline + (*R*)-11 (% ee ; lond dash)[a]	(S)-Proline + (*R*)-11 (% ee ; short dash)[a]
0	78	78	20
0.5	n/a	n/a	12
1	69	67	8
3	62	64	n/a
6	n/a	n/a	2
23	42	42	0

[a] enantiomeric excess determined by chiral GC analysis, see General Experimental for details

*Determination of the ratio of **12**:**13** or ent-**12**:ent-**13** during the course of the proline-catalyzed aldol reactions of **1** and (r)-**11**.*

To a solution of (*R*)-**11** (27 mg, 0.16 mmol, 78% ee) and either (*S*)- or (*R*)-proline (4 mg, 0.04 mmol), in CD_2Cl_2 (1.5 mL), was added dioxanone **1** (20 μL, 0.17 mmol) and the mixture was stirred at room temperature. During the course of the reaction, small aliquots were removed and analyzed by ^{1}H-NMR spectroscopy to determine the ratio of diastereomers (see Table 2).

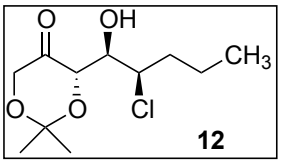
Table 2: Diastereomeric excess of **12** and *ent*-**12**

time (h)	% de of **12** (conversion)	% de of *ent*-**12** (conversion)
2	n.d. (0%)	n.d. (0%)
25	90 (40%)	23 (27%)
45	79 (63%)	24 (52%)
96	74 (87%)	33 (78%)
116	69 (90%)	39 (81%)
145	68 (95%)	47 (90%)

4. PREPARATION AND CHARACTERIZATION OF ALL COMPOUNDS

4.1. PREPARATION OF ALDOL ADDUCTS 12 and 13

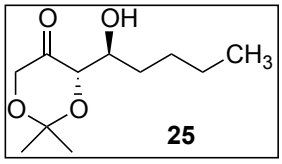
Following General Procedure **A**, a solution of pentanal (100 μL, 0.94 mmol), NCS (132 mg, 0.99 mmol), (*S*)-Proline (86 mg, 0.77 mmol) and dioxanone **1** (118 μL, 0.99 mmol) in CH_2Cl_2 (5 mL) was stirred for 24 hours. Purification of the crude chlorohydrins **12** and **13** (dr 6:1) by flash chromatography (pentane-EtOAc 9:1) afforded chlorohydrin **12** (146 mg, 62% yield) as a white solid and chlorohydrin **13** (24 mg, 10% yield) as a clear oil.



Data for *syn*-chlorohydrin **12**: mp = 46 - 48 °C; R_f (pentane-EtOAc 8:2) 0.30; $[\alpha]_D^{20}$ = -164 (*c* 0.528 in $CHCl_3$); **IR** (neat): υ = 3521, 2964, 1746, 1377, 1226, 1100, 864 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$): δ = 4.42 (*dd*, *J* = 1.4 Hz, *J* = 8.7 Hz, 1H), 4.29 (*dd*, *J* = 1.4 Hz, *J* = 17.6 Hz, 1H), 4.21 (*dddd*, *J* = 1.3 Hz, *J* = 1.7 Hz, *J* = 3.3 Hz, *J* = 9.3 Hz, 1H), 4.08 (*d*, *J* = 17.6 Hz, 1H), 3.93 (*ddd*, *J* = 1.8 Hz, *J* = 3.1 Hz, *J* = 8.7 Hz, 1H), 3.34 (*dd*, *J* = 1.3 Hz, *J* = 3.1 Hz, 1H), 1.99 (*m*, 1H), 1.77 (*m*, 1H), 1.63-1.57 (*m*, 1H), 1.52 (*s*, 3H), 1.49-1.41 (*m*, 1H), 1.43 (*s*, 3H), 0.96 ppm (*t*, *J* = 7.4 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 212.3, 101.6, 72.8, 71.7, 66.4, 62.0, 36.5, 23.8, 23.4, 20.0, 13.6 ppm; **HRMS** (ESI) *m/z* calcd for $C_{11}H_{20}ClO_4$ $[M + H]^+$ 251.1045, found 251.1046.

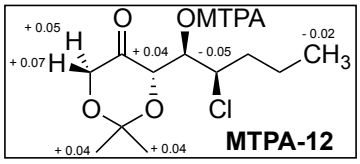
Determination of relative stereochemistry for chlorohydrin **12**

Following General Procedure **G**, the *syn*-chlorohydrin **12** (9 mg, 0.04 mmol) was converted into the known alcohol **25** (see inset).[3] Comparison of ^{1}H-NMR spectral data derived from **25** with that reported in the literature confirmed the *anti* stereochemistry of the two oxymethine stereocenters in **12**.



Determination of the absolute stereochemistry for chlorohydrin **12**

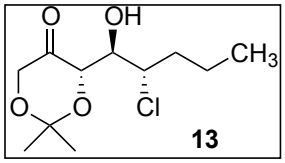
Following General Procedure **I**, the *syn*-chlorohydrin **12** (10 mg, 0.04 mmol) was converted into the corresponding (*R*)-(+)-MTPA-**12** and (*S*)-(+)-MTPA-**12** esters. The absolute stereochemistry of the hydroxymethine stereocenter in **12** was assigned using Mosher's method[4] (see $\delta_S - \delta_R$ (ppm) convention in inset).



Determination of enantiomeric excess of chlorohydrin **12**

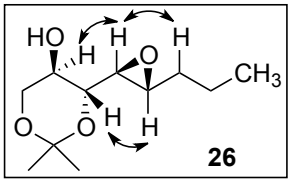
Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **12** was prepared. Following General Procedure **H**, optically enriched and racemic samples of **12** (50 mg, 0.20 mmol) were converted into the corresponding benzoyl esters. The enantiomeric benzoyl esters were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.5 mL/min; eluent: hexanes-*i*PrOH 94:6; detection at 230 nm; retention time = 3.03 min for (+)-**12-Bz**; 3.72 min for (-)-**12-Bz** (see chromatograms in section 6). The enantiomeric excess of the optically enriched benzoyl ester was determined using the same method (94% ee).

Data for *anti*-chlorohydrin **13**: (**13**:**12** ratio 10:1) R_f (pentane-EtOAc 8:2) 0.25; $[\alpha]_D^{20}$ = -91.2 (*c* 2.21 in $CHCl_3$); **IR** (neat): υ 3512, 2964, 1749, 1374, 1226, 1100, 864 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.46 (*dd*, *J* = 1.4 Hz, *J* = 6.7 Hz, 1H), 4.30 (*dd*, *J* = 1.4 Hz, *J* = 17.4 Hz, 1H), 4.24 (*m*, 1H), 4.10 (*m*, 1H), 4.06 (*d*, *J* = 17.4 Hz, 1H), 3.09 (*d*, *J* = 4.0 Hz, 1H), 1.84-1.77 (*m*, 2H), 1.71-1.59 (*m*, 1H), 1.49 (*s*, 3H), 1.45 (*s*, 3H), 1.47-1.36 (*m*, 1H), 0.95 ppm (*t*, *J* = 7.3 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 210.0, 101.2, 73.9, 73.8, 66.8, 62.6, 34.8, 23.8, 23.7, 19.6, 13.5 ppm; **HRMS** (ESI) *m/z* calcd for $C_{11}H_{19}ClNaO_4$ $[M + Na]^+$ 273.0864, found 273.0873.



Determination of relative stereochemistry for chlorohydrin **13**

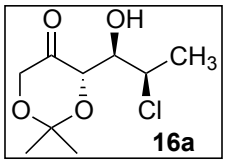
Following General Procedure **F**, the *anti*-chlorohydrin **13** (4 mg, 0.01 mmol) was converted into the corresponding epoxide **26**. Analysis of the ^{1}H-NMR spectrum recorded on the epoxide revealed that the two epoxide protons resonated at 2.94 and 2.90 ppm, and shared a coupling constant of 2.3 Hz, typical of a *trans* epoxide. Additionally, irradiation of either proton resonance did not result in an enhancement of the proton resonance in nOe experiments. These results confirm the *anti* stereochemistry of the chlorohydrin function in **13**. Following General Procedure **G**, the *anti*-chlorohydrin **13** (11 mg, 0.04 mmol) was converted into the known alcohol **25**.[3] Comparison of ^{1}H-NMR spectral data derived from **25** with that reported in the literature confirmed the *anti* stereochemistry of the two oxymethine stereocenters in **13**.



4.2. PREPARATION OF ALDOL ADDUCTS 16a AND 29

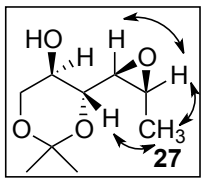
Following General Procedure **A**, a solution of propanal (450 μL, 6.18 mmol), NCS (866 mg, 6.49 mmol), (*S*)-Proline (568 mg, 4.94 mmol) and dioxanone **1** (775 μL, 6.49 mmol) in CH_2Cl_2 (30 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins **16a** and **29** (dr 2.5:1) by flash chromatography (pentane-EtOAc 9:1) afforded *syn*-chlorohydrin **16a** (606 mg, 44% yield) as a clear oil and *anti*-chlorohydrin **29** (242 mg, 18% yield) as a clear oil.

Data for *syn*-chlorohydrin **16a**: R_f (pentane-EtOAc 9:1) 0.20; $[\alpha]_D^{20}$ = -172 (*c* 0.998 in $CHCl_3$); **IR** (neat): υ = 3514, 2992, 1745, 1379, 1226, 1092, 865 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.39 (*qdd*, *J* = 1.3 Hz, *J* = 1.9 Hz, *J* = 6.9 Hz, 1H), 4.37 (*dd*, *J* = 1.5 Hz, *J* = 8.6 Hz, 1H), 4.29 (*dd*, *J* = 1.5 Hz, *J* = 17.6 Hz, 1H), 4.08 (*d*, *J* = 17.6 Hz, 1H), 3.85 (*ddd*, *J* = 2.0 Hz, *J* = 3.2 Hz, *J* = 8.6 Hz, 1H), 3.36 (*dd*, *J* = 1.3 Hz, *J* = 3.2 Hz, 1H), 1.61 (*d*, *J* = 6.9 Hz, 3H), 1.52 (*s*, 3H), 1.42 ppm (*s*, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 212.0, 101.6, 73.1, 72.8, 66.5, 57.1, 23.8, 23.4, 21.0 ppm; **HRMS** (ESI) *m/z* calcd for $C_9H_{15}ClNaO_4$ $[M + Na]^+$ 245.0551, found 245.0565.

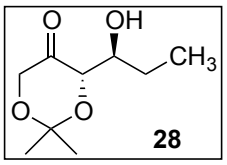


Determination of relative stereochemistry for chlorohydrin **16a**

Following General Procedure **F**, the *syn*-chlorohydrin **16a** (11 mg, 0.05 mmol) was converted into the corresponding epoxide **27**. Analysis of the ^{1}H-NMR spectrum recorded on the epoxide revealed that the two epoxide protons resonated at 3.14 and 3.06 ppm, and shared a coupling constant of 4.1 Hz, typical of a *cis* epoxide. Additionally, irradiation of either proton resonance did result in an enhancement of the proton resonance in nOe experiments. These results confirm the *syn* stereochemistry of the chlorohydrin function in **16a**.

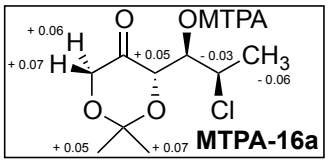


Following General Procedure **G**, the *syn*-chlorohydrin **16a** (10 mg, 0.04 mmol) was converted into the known alcohol **28**.[5] Comparison of ^{1}H-NMR spectral data derived from **28** with that reported in the literature confirmed the *anti* stereochemistry of the two oxymethine stereocenters in **16a**.



Determination of the absolute stereochemistry for chlorohydrin **16a**

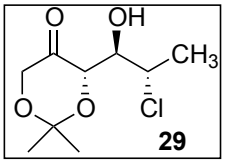
Following General Procedure **I**, the *syn*-chlorohydrin **16a** (5 mg, 0.02 mmol) was converted into the corresponding (*R*)-(+)-MTPA-**16a** and (*S*)-(+)-MTPA-**16a** esters. The absolute stereochemistry of the hydroxymethine stereocenter in **16a** was assigned using Mosher's method[4] (see $\delta_S - \delta_R$ (ppm) convention in inset).



Determination of enantiomeric excess of chlorohydrin **16a**

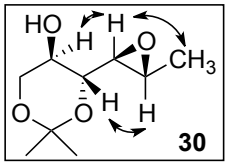
Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **16a** was prepared. Following General Procedure **H**, optically enriched and racemic samples of **16a** (50 mg, 0.22 mmol) were converted into the corresponding benzoyl esters. The enantiomeric benzoyl esters were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.5 mL/min; eluent: hexanes-*i*PrOH 88:12; detection at 230 nm; retention time = 3.01 min for (+)-**16a-Bz**; 4.41 min for (-)-**16a-Bz** (see chromatograms in section 6). The enantiomeric excess of the optically enriched benzoyl ester was determined using the same method (95% ee).

Data for *anti*-chlorohydrin **29**: (**29**:**16a** ratio 10:1) R_f (pentane-EtOAc 9:1) 0.15; $[\alpha]_D^{20}$ = -131 (*c* 0.604 in $CHCl_3$); **IR** (neat): υ 3489, 2988, 1746, 1376, 1226, 1092, 865 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$): δ = 4.39-4.34 (*m*, 1H), 4.36 (*dd*, *J* = 1.5 Hz, *J* = 7.1 Hz, 1H), 4.30 (*dd*, *J* = 1.4 Hz, *J* = 17.4 Hz, 1H), 4.06 (*d*, *J* = 17.5 Hz, 1H), 4.04 (*m*, 1H), 3.10 (*d*, *J* 3.8 Hz, 1H), 1.55 (*d*, *J* = 6.8 Hz, 3H), 1.49 (*s*, 3H), 1.45 ppm (*s*, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 209.9, 101.2, 74.1, 73.8, 66.7, 57.2, 23.7, 23.6, 19.3 ppm; **HRMS** (ESI) *m/z* calcd for $C_9H_{15}ClNaO_4$ $[M + Na]^+$ 245.0551, found 245.0569.



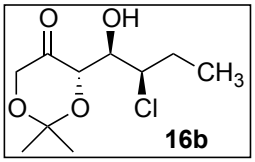
Determination of relative stereochemistry for chlorohydrin **29**

Following General Procedure **F**, the *anti*-chlorohydrin **29** (10 mg, 0.04 mmol) was converted into the corresponding epoxide **30**. Analysis of the ^{1}H-NMR spectrum recorded on the epoxide revealed that the two epoxide protons resonated at 3.02 and 2.87 ppm, and shared a coupling constant of 2.2 Hz, typical of a *trans* epoxide. Additionally, irradiation of either proton resonance did not result in an enhancement of the proton resonance in nOe experiments. These results confirm the *anti* stereochemistry of the chlorohydrin function in **29**. Following General Procedure **G**, the *anti*-chlorohydrin **29** (10 mg, 0.04 mmol) was converted into the known alcohol **28**.[5] Comparison of ^{1}H-NMR spectral data derived from **28** with that reported in the literature confirmed the *anti* stereochemistry of the two oxymethine stereocenters in **16a**.



4.3. PREPARATION OF ALDOL ADDUCTS 16b AND 32

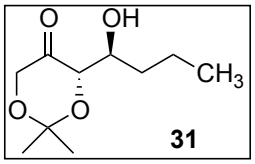
Following General Procedure **A**, a solution of butanal (100 μL, 1.11 mmol), NCS (156 mg, 1.16 mmol), (*S*)-Proline (102 mg, 0.89 mmol) and dioxanone **1** (138 μL, 1.16 mmol) in CH_2Cl_2 (5 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins **16b** and **32** (dr 3.8:1) by flash chromatography (pentane-EtOAc 85:15) afforded *syn*-chlorohydrin **16b** (154 mg, 59% yield) as a clear oil and *anti*-chlorohydrin **32** (41 mg, 15% yield) as a clear oil.



Data for *syn*-chlorohydrin **16b**: R_f (pentane-EtOAc 85:15) 0.33; $[\alpha]_D^{20}$ = -159 (*c* 0.497 in $CHCl_3$); **IR** (neat): υ = 3524, 2990, 1745, 1378, 1226, 1094, 865 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.42 (*dd*, *J* = 1.5 Hz, *J* = 8.7 Hz, 1H), 4.29 (*dd*, *J* = 1.5 Hz, *J* = 17.6 Hz, 1H), 4.12 (*dddd*, *J* = 1.7 Hz, *J* = 5.3 Hz, *J* = 9.2 Hz, 1H), 4.08 (*d*, *J* = 17.6 Hz, 1H), 3.95 (*ddd*, *J* = 1.8 Hz, *J* = 3.2 Hz, *J* = 8.7 Hz, 1H), 3.33 (*dd*, *J* = 1.4 Hz, *J* = 3.2 Hz, 1H), 2.00 (*ddq*, *J* = 7.3 Hz, *J* = 9.1 Hz, *J* = 14.7 Hz, 1H), 1.86 (*ddq*, *J* = 5.4 Hz, *J* = 7.3 Hz, *J* = 14.6 Hz, 1H), 1.52 (*s*, 3H), 1.43 (*s*, 3H), 1.08 ppm (*t*, *J* = 7.4 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 212.3, 101.6, 72.8, 71.4, 66.4, 63.9, 27.8, 23.8, 23.4, 11.5 ppm; **HRMS** (ESI) *m/z* calcd for $C_{10}H_{17}ClNaO_4$ $[M + Na]^+$ 259.0708, found 259.0706.

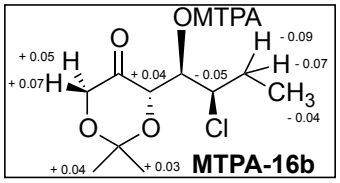
Determination of relative stereochemistry for chlorohydrin **16b**

Following General Procedure **G**, the *syn*-chlorohydrin **16b** (10 mg, 0.04 mmol) was converted into the known alcohol **31**.[6] Comparison of ^{1}H-NMR spectral data derived from **31** with that reported in the literature confirmed the *anti* stereochemistry of the two oxymethine stereocenters in **16b**.



Determination of the absolute stereochemistry for chlorohydrin **16b**

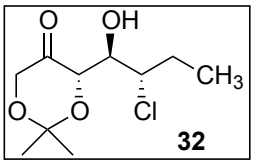
Following General Procedure **I**, the *syn*-chlorohydrin **16b** (5 mg, 0.02 mmol) was converted into the corresponding (*R*)-(+)-MTPA-**16b** and (*S*)-(+)-MTPA-**16b** esters. The absolute stereochemistry of the hydroxymethine stereocenter in **16b** was assigned using Mosher's method[4] (see $\delta_S - \delta_R$ (ppm) convention in inset).



Determination of enantiomeric excess of chlorohydrin **16b**

Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **16b** was prepared. Following General Procedure **H**, optically enriched and racemic samples of **16b** (40 mg, 0.17 mmol) were converted into the corresponding benzoyl esters. The enantiomeric benzoyl esters were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.5 mL/min; eluent: hexanes-*i*PrOH 88:12; detection at 230 nm; retention time = 2.88 min for (+)-**16b-Bz**; 3.58 min for (-)-**16b-Bz** (see chromatograms in section 6). The enantiomeric excess of the optically enriched benzoyl ester was determined using the same method (94% ee).

Data for *anti*-chlorohydrin **32**: (**32**:**16b** ratio 10:1) R_f (pentane-EtOAc 85:15) 0.22; $[\alpha]_D^{20}$ = -180 (*c* 0.303 in $CHCl_3$); **IR** (neat) υ = 3489, 2988, 1746, 1376, 1226, 1092, 865 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.50 (*dd*, *J* = 1.5 Hz, *J* = 6.2 Hz, 1H), 4.30 (*dd*, *J* = 1.5 Hz, *J* = 17.3 Hz, 1H), 4.17 (*ddd*, *J* = 3.3 Hz, *J* = 5.1 Hz, *J* = 9.8 Hz, 1H), 4.09-4.05 (*m*, 1H), 4.05 (*d*, *J* = 17.3 Hz, 1H), 3.04 (*d*, *J* = 4.2 Hz, 1H), 1.94 (*ddq*, *J* = 3.3 Hz, *J* = 7.3 Hz, *J* = 14.5 Hz, 1H), 1.80 (*ddq*, *J* = 7.3 Hz, *J* = 9.8 Hz, *J* = 14.5 Hz, 1H), 1.49 (*s*, 3H), 1.45 (*s*, 3H), 1.08 ppm (*t*, *J* = 7.3 Hz, 3H); **^{13}C-NMR**: (150 MHz, $CDCl_3$) δ 209.8, 101.2, 74.0, 73.8, 66.8, 64.7, 26.3, 23.8, 23.7, 11.1 ppm; **HRMS** (ESI) *m/z* calcd for $C_9H_{15}ClNaO_4$ $[M + Na]^+$ 259.0708, found 259.0705.



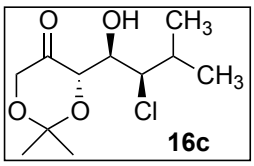
Determination of relative stereochemistry for chlorohydrin **32**

Following General Procedure **G**, the *anti*-chlorohydrin **32** (5 mg, 0.02 mmol) was converted into the known alcohol **31**.[6] Comparison of ^{1}H-NMR spectral data derived from **31** with that reported in the literature confirmed the *anti* stereochemistry of the two oxymethine stereocenters in **32**.

4.4. PREPARATION OF ALDOL ADDUCT 16c

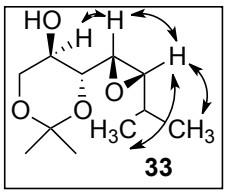
Following General Procedure **A**, a solution of isovaleraldehyde (100 μL, 0.93 mmol), NCS (131 mg, 0.98 mmol), (*S*)-Proline (85 mg, 0.74 mmol) and dioxanone **1** (117 μL, 0.98 mmol) in CH_2Cl_2 (5 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins (dr 22:1)[7]1 by flash chromatography (pentane-EtOAc 85:15) afforded *syn*-chlorohydrin **16c** (148 mg, 64% yield) as a white solid.

Data for *syn*-chlorohydrin **16c**: mp = 51-53 °C; R_f (pentane-EtOAc 85:15) 0.39; $[\alpha]_D^{20}$ = -173 (*c* 0.468 in $CHCl_3$); **IR** (neat): υ = 3524, 2989, 1740, 1377, 1226, 1098, 871 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.42 (*dd*, *J* = 1.5 Hz, *J* = 8.6 Hz, 1H), 4.29 (*dd*, *J* = 1.5 Hz, *J* = 17.6 Hz, 1H), 4.13 (*ddd*, *J* = 1.8 Hz, *J* = 3.2 Hz, *J* = 8.6 Hz, 1H), 4.07 (*d*, *J* = 17.6 Hz, 1H), 3.89 (*ddd*, *J* = 1.6 Hz, *J* = 8.7 Hz, 1H), 3.28 (*dd*, *J* = 1.3 Hz, *J* = 3.2 Hz, 1H), 2.20 (ds_{ept}, *J* = 6.7 Hz, *J* = 8.7 Hz, 1H), 1.52 (*s*, 3H), 1.43 (*s*, 3H), 1.15 (*d*, *J* = 6.7 Hz, 3H), 1.05 ppm (*d*, *J* = 6.7 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 212.6, 101.6, 73.0, 70.0, 68.7, 66.5, 32.1, 23.8, 23.5, 20.8, 20.0 ppm; **HRMS** (ESI) *m/z* calcd for $C_{11}H_{19}ClNaO_4$ $[M + Na]^+$ 273.0864, found 273.0881.

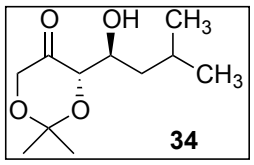


Determination of relative stereochemistry for chlorohydrin **16c**

Following General Procedure **F**, the *syn*-chlorohydrin **16c** (5 mg, 0.02 mmol) was converted into the corresponding epoxide **33** (see inset). Analysis of the ^{1}H-NMR spectrum recorded on the epoxide revealed that the two epoxide protons resonated at 3.09 and 2.68 ppm, and shared a coupling constant of 4.1 Hz, typical of a *cis* epoxide. Additionally, irradiation of either proton resonance did result in an enhancement of the proton resonance in nOe experiments. These results confirm the *syn* stereochemistry of the chlorohydrin function in **16c**.

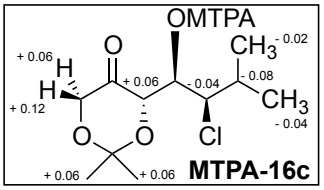


Following General Procedure **G**, the *syn*-chlorohydrin **16c** (10 mg, 0.04 mmol) was converted into the known alcohol **34** (see inset).[5,8] Comparison of ^{1}H-NMR spectral data derived from **34** with that reported in the literature confirmed the *anti* stereochemistry of the two oxymethine stereocenters in **16c**.



Determination of the absolute stereochemistry for chlorohydrin **16c**

Following General Procedure **I**, the *syn*-chlorohydrin **16c** (5 mg, 0.02 mmol) was converted into the corresponding (*R*)-(+)-MTPA-**16c** and (*S*)-(+)-MTPA-**16c** esters. The absolute stereochemistry of the hydroxymethine stereocenter in **16c** was assigned using Mosher's method[4] (see $\delta_S - \delta_R$ (ppm) convention in inset).

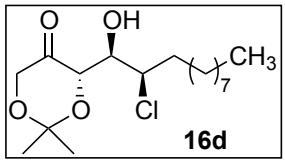


Determination of enantiomeric excess of chlorohydrin **16c**

Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **16c** was prepared. Following General Procedure **H**, optically enriched and racemic samples of **16c** (20 mg, 0.08 mmol) were converted into the corresponding benzoyl esters. The enantiomeric benzoyl esters were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.8 mL/min; eluent: hexanes-*i*PrOH 9:1; detection at 230 nm; retention time = 2.77 min for (+)-**16c-Bz**; 3.23 min for (-)-**16c-Bz** (see chromatograms in section 6). The enantiomeric excess of the optically enriched benzoyl ester was determined using the same method (92% ee).

4.5. PREPARATION OF ALDOL ADDUCT 16d

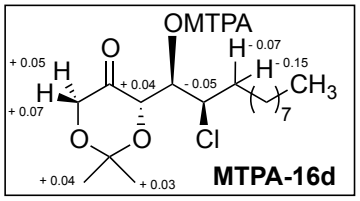
Following General Procedure **A**, a solution of undecanal (100 μL, 0.49 mmol), NCS (68 mg, 0.51 mmol), (*S*)-Proline (86 mg, 0.39 mmol) and dioxanone **1** (61 μL, 0.51 mmol) in CH_2Cl_2 (2.4 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins (dr 10:1)[7] by flash chromatography (pentane-EtOAc 85:15) afforded *syn*-chlorohydrin **16d** (105 mg, 64% yield) as a clear oil.



Data for *syn*-chlorohydrin **16d**: R_f (pentane-EtOAc 85:15) 0.42; $[\alpha]_D^{20}$ = -108 (*c* 0.538 in $CHCl_3$); **IR** (neat): υ = 3533, 2928, 2854, 1740, 1376, 1226, 1089, 865 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$): δ = 4.41 (*dd*, *J* = 1.4 Hz, *J* = 8.7 Hz, 1H), 4.28 (*dd*, *J* = 1.5 Hz, *J* = 17.6 Hz, 1H), 4.18 (*dddd*, *J* = 1.4 Hz, *J* = 1.8 Hz, *J* = 5.2 Hz, *J* = 9.3 Hz, 1H), 4.07 (*d*, *J* = 17.6 Hz, 1H), 3.93 (*ddd*, *J* = 1.8 Hz, *J* = 3.1 Hz, *J* = 8.7 Hz, 1H), 3.34 (*dd*, *J* = 1.3 Hz, *J* = 3.1 Hz, 1H), 2.01-1.93 (*m*, 1H), 1.83-1.76 (*m*, 1H), 1.56-1.50 (*m*, 1H), 1.51 (*s*, 3H), 1.45-1.38 (*m*, 1H), 1.42 (*s*, 3H), 1.33-1.24 (*m*, 12H), 0.88 ppm (*t*, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 212.3, 101.6, 72.8, 71.7, 66.4, 62.3, 34.5, 31.9, 29.5, 29.4, 29.3, 29.2, 26.9, 23.8, 23.4, 22.7, 14.1 ppm; **HRMS** (ESI) *m/z* calcd for $C_{17}H_{32}ClO_4$ $[M + H]^+$ 335.1984, found 335.1978.

Determination of the absolute stereochemistry for chlorohydrin **16d**

Following General Procedure **I**, the *syn*-chlorohydrin **16d** (5 mg, 0.01 mmol) was converted into the corresponding (*R*)-(+)-MTPA-**16d** and (*S*)-(+)-MTPA-**16d** esters. The absolute stereochemistry of the hydroxymethine stereocenter in **16d** was assigned using Mosher's method[4] (see $\delta_S - \delta_R$ (ppm) convention in inset).



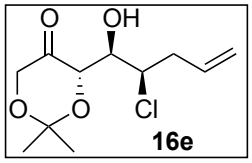
Determination of enantiomeric excess of chlorohydrin **16d**

Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **16d** was prepared. Following General Procedure **H**, optically enriched and racemic samples of **16d** (40 mg, 0.12 mmol) were converted into the corresponding benzoyl esters. The

enantiomeric benzoyl esters were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.5 mL/min; eluent: hexanes-*i*PrOH 95:5; detection at 230 nm; retention time = 3.30 min for (+)-*syn*-**16d-Bz**; 3.94 min for (-)-s*yn*-**16d-Bz** (see chromatograms in section 6). The enantiomeric excess of the optically enriched benzoyl ester was determined using the same method (96% ee).

4.6. PREPARATION OF ALDOL ADDUCTS 16e AND 35

Following General Procedure **A**, a solution of 4-pentenal (100 μL, 1.01 mmol), NCS (141 mg, 1.06 mmol), (*S*)-Proline (93 mg, 0.81 mmol) and dioxanone **1** (127 μL, 1.06 mmol) in CH_2Cl_2 (4 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins **16e** and **35** (dr 5:1) by flash chromatography (pentane-EtOAc 9:1) afforded *syn*-chlorohydrin **16e** (130 mg, 52% yield) as a glassy solid and *anti*-chlorohydrin **35** (43 mg, 17% yield) as a yellowish oil.



16e

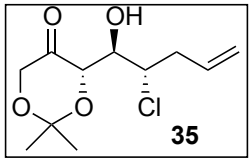
Data for *syn*-chlorohydrin **16e**: mp = 34-37 °C; R_f (pentane-EtOAc 85:15) 0.45; $[\alpha]_D^{20}$ = -118 (*c* 0.399 in $CHCl_3$); **IR** (neat): υ = 3458, 3083, 2991, 2886, 1737, 1376, 1254, 1220, 1082, 1031, 916, 860, 765 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$): δ = 5.84 (*ddt*, *J* = 7.0 Hz, *J* = 10.2 Hz, *J* = 17.1 Hz, 1H), 5.19 (*m*, 1H), 5.14 (*m*, 1H), 4.40 (*dd*, *J* = 1.5 Hz, *J* = 8.8 Hz, 1H), 4.28 (*dd*, *J* = 1.6 Hz, *J* = 17.6 Hz, 1H), 4.22 (*ddd*, *J* = 7.2 Hz, 1H), 4.07 (*d*, *J* = 17.6 Hz, 1H), 3.97 (*ddd*, *J* = 1.7 Hz, *J* = 2.6 Hz, *J* = 8.8 Hz, 1H), 3.35 (*dd*, *J* = 0.9 Hz, *J* = 2.7 Hz, 1H), 2.70 (*m*, 1H), 2.64 (*m*, 1H), 1.51 (*s*, 3H), 1.41 ppm (*s*, 3H); **^{13}C-NMR** (126 MHz, $CDCl_3$): δ = 212.2, 134.0, 118.4, 101.6, 72.7, 70.8, 66.4, 60.8, 38.7, 23.8, 23.4 ppm; **HRMS** (ESI) *m/z* calcd for $C_{11}H_{17}ClNaO_4$ $[M + Na]^+$ 271.0708, found 271.0714.

Determination of the absolute and relative stereochemistry for chlorohydrin **16e**

Absolute and relative stereochemistry has been confirmed by converting the *syn*-chlorohydrin **16e** (10 mg, 0.04 mmol) into **12** by catalytic hydrogenation with Pd/C (10 weight%) in MeOH (0.1 M); $[\alpha]_D^{20}$ = -163 (*c* 0.800 in $CHCl_3$).

Determination of enantiomeric excess of chlorohydrin **16e**

Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **16e** was prepared. Following General Procedure **H**, optically enriched and racemic samples of **16e** (20 mg, 0.08 mmol) were converted into the corresponding benzoyl esters. The enantiomeric benzoyl esters were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.5 mL/min; eluent: hexanes-*i*PrOH 95:5; detection at 230 nm; retention time = 3.88 min for (+)-**16e-Bz**; 5.20 min for (-)-**16e-Bz** (see chromatograms in section 6). The enantiomeric excess of the optically enriched benzoyl ester was determined using the same method (92% ee).

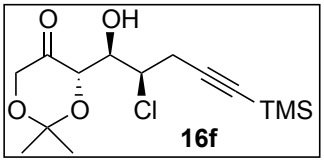


35

Data for *anti*-chlorohydrin **35**: (**35**:**16e** ratio 19:1) R_f (pentane-EtOAc 85:15) 0.33; $[\alpha]_D^{20}$ = -122 (*c* 2.68 in $CHCl_3$); **IR** (neat): υ = 3507, 3083, 2988, 2886, 1738, 1376, 1251, 1221, 1087, 1035, 916, 861, 732 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 5.89 (*ddt*, *J* = 6.9 Hz, *J* = 10.3 Hz, *J* = 17.0 Hz, 1H), 5.19-5.13 (*m*, 2H), 4.50 (*dd*, *J* = 1.5 Hz, *J* = 6.3 Hz, 1H), 4.30 (*dd*, *J* = 1.5 Hz, *J* = 17.4 Hz, 1H), 4.27 (*ddd*, *J* = 4.4 Hz, *J* = 5.1 Hz, *J* = 9.0 Hz, 1H), 4.09 (*dd*, *J* = 5.2 Hz, *J* = 6.2 Hz, 1H), 4.05 (*d*, *J* = 17.4 Hz, 1H), 3.10 (s_{br}, 1H), 2.67 (*m*, 1H), 2.57 (*m*, 1H), 1.50 (*s*, 3H), 1.45 ppm (*s*, 3H); **^{13}C-NMR** (126 MHz, $CDCl_3$): δ = 209.7, 134.0, 118.2, 101.2, 73.9, 73.4, 66.8, 61.5, 37.6, 23.8, 23.7 ppm; **HRMS** (ESI) *m/z* calcd for $C_{11}H_{17}ClNaO_4$ $[M + Na]^+$ 271.0708, found 271.0716.

4.7. PREPARATION OF ALDOL ADDUCTS 16f AND 36

Following General Procedure **A**, a solution of 5-(trimethylsilyl)pent-4-ynal[9] (47 mg, 0.30 mmol), NCS (43 mg, 0.32 mmol), (*S*)-proline (28 mg, 0.24 mmol) and dioxanone **1** (38 μL, 0.32 mmol) in CH_2Cl_2 (4 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins **16f** and **36** (dr 2:1) by flash chromatography (pentane-EtOAc 85:15) afforded *syn*-chlorohydrin **36** (50 mg, 52% yield) as a clear oil and *anti*-chlorohydrin **16f** (24 mg, 25% yield) as a clear oil.



16f

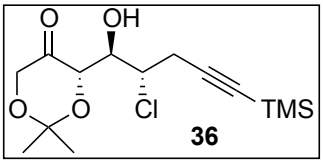
Data for *syn*-chlorohydrin **16f**: R_f (pentane-EtOAc 85:15) 0.20; $[\alpha]_D^{20}$ = -77.4 (*c* 1.97 in $CHCl_3$); **IR** (neat): υ = 3517, 2963, 2179, 1740, 1376, 1254, 1226, 1089, 846, 762 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.38 (*dd*, *J* = 1.4 Hz, *J* = 8.8 Hz, 1H), 4.31 (*dd*, *J* = 1.5 Hz, *J* = 17.6 Hz, 1H), 4.30 (*dddd*, *J* = 1.5 Hz, *J* = 1.8 Hz, *J* = 6.6 Hz, *J* = 8.4 Hz, 1H), 4.16 (*ddd*, *J* = 1.8 Hz, *J* = 3.2 Hz, *J* = 8.8 Hz, 1H), 4.09 (*d*, *J* = 17.6 Hz, 1H), 3.33 (*dd*, *J* = 1.3 Hz, *J* = 3.2 Hz, 1H), 2.91 (*dd*, *J* = 8.7 Hz, *J* = 17.0 Hz, 1H), 2.82 (*dd*, *J* = 6.6 Hz, *J* = 17.0 Hz, 1H), 1.52 (*s*, 3H), 1.44 (*s*, 3H), 0.16 ppm (*s*, 9H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 212.0, 102.1, 101.6, 87.5, 72.7, 69.8, 66.5, 58.9, 25.7, 23.8, 23.4, -0.0 ppm; **HRMS** (ESI) *m/z* calcd for $C_{14}H_{24}ClO_4Si$ $[M + H]^+$ 319.1127, found 319.1119.

Determination of the absolute and relative stereochemistry for chlorohydrin **16f**

Absolute and relative stereochemistry has been confirmed by converting the *syn*-chlorohydrin **16f** (10 mg, 0.04 mmol) into **12** by TBAF (1.1 equiv, 0.03 mmol) cleavage of TMS in THF (0.1 M) followed by catalytic hydrogenation with Pd/C (10 weight%) in MeOH (0.1 M); $[\alpha]_D^{20}$ = -166 (*c* 0.500 in $CHCl_3$).

Determination of enantiomeric excess of chlorohydrin **16f**

Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **16f** was prepared. Following General Procedure **H**, optically enriched and racemic samples of **16f** (48 mg, 0.15 mmol) were converted into the corresponding benzoyl esters. The enantiomeric benzoyl esters were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.8 mL/min; eluent: hexanes-*i*PrOH 97:3; detection at 230 nm; retention time = 2.96 min for (+)-**16f-Bz**; 4.16 min for (-)-**16f-Bz** (see chromatograms in section 6). The enantiomeric excess of the optically enriched benzoyl ester was determined using the same method (98% ee).

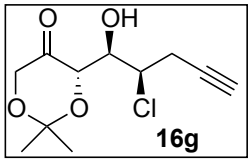


36

Data for *anti*-chlorohydrin **36**: (**36**:**16f** ratio 19:1) R_f (pentane-EtOAc 85:15) 0.15; $[\alpha]_D^{20}$ = -76.8 (*c* 2.79 in $CHCl_3$); **IR** (neat): υ = 3483, 2960, 2182, 1749, 1376, 1251, 1226, 1092, 846, 762 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.58 (*dd*, *J* = 1.4 Hz, *J* = 5.8 Hz, 1H), 4.36 (*ddd*, *J* = 5.6 Hz, *J* = 7.0 Hz, 1H), 4.31 (*dd*, *J* = 1.5 Hz, *J* = 17.3 Hz, 1H), 4.19 (*ddd*, *J* = 4.1 Hz, *J* = 5.6 Hz, 1H), 4.05 (*d*, *J* = 17.3 Hz, 1H), 3.15 (*d*, *J* = 4.1 Hz, 1H), 2.89 (*dd*, *J* = 5.8 Hz, *J* = 17.4 Hz, 1H), 2.82 (*dd*, *J* = 7.0 Hz, *J* = 17.4 Hz, 1H), 1.52 (*s*, 3H), 1.47 (*s*, 3H), 0.17 ppm (*s*, 9H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 209.5, 102.0, 101.2, 87.7, 74.1, 73.0, 66.9, 59.2, 25.8, 23.9, 23.7, -0.0 ppm; **HRMS** (ESI) *m/z* calcd for $C_{14}H_{23}ClNaO_4Si$ $[M + Na]^+$ 341.0946, found 341.0959.

4.8. PREPARATION OF ALDOL ADDUCTS 16g AND 37

Following General Procedure **A**, a solution of 4-pentynal (2.00 g, 24.4 mmol), NCS (3.42 g, 25.6 mmol), (*S*)-proline (2.24 g, 19.5 mmol) and dioxanone **1** (3.06 mL, 25.6 mmol) in CH_2Cl_2 (120 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins **16g** and **37** (dr 3:1) by flash chromatography (pentane-EtOAc 85:15) afforded *syn*-chlorohydrin **16g** (3.21 g, 54% yield) as a clear oil and *anti*-chlorohydrin **37** (1.04 g, 18% yield) as a clear oil.



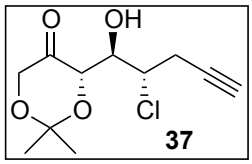
Data for *syn*-chlorohydrin **16g**: R_f (pentane-EtOAc 8:2) 0.50; $[\alpha]_D^{20}$ -142 (*c* 1.02 in $CHCl_3$); **IR** (neat): υ = 3518, 3293, 2988, 2892, 2126, 1738, 1376, 1221, 1083, 861, 633 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.39 (*dd*, *J* = 1.5 Hz, *J* = 8.9 Hz, 1H), 4.33 (*dddd*, *J* = 1.5 Hz, *J* = 6.8 Hz, *J* = 8.5 Hz, 1H), 4.30 (*dd*, *J* = 1.5 Hz, *J* = 17.6 Hz, 1H), 4.20 (*ddd*, *J* = 1.8 Hz, *J* = 2.9 Hz, *J* = 8.9 Hz, 1H), 4.09 (*d*, *J* = 17.7 Hz, 1H), 3.37 (*dd*, *J* = 1.4 Hz, *J* = 3.1 Hz, 1H), 2.90 (*ddd*, *J* = 2.6 Hz, *J* = 8.6 Hz, *J* = 16.8 Hz, 1H), 2.80 (*ddd*, *J* = 2.6 Hz, *J* = 6.7 Hz, *J* = 16.8 Hz, 1H), 2.09 (*t*, *J* = 2.6 Hz, 1H), 1.51 (*s*, 3H), 1.43 ppm (*s*, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 212.1, 101.7, 79.9, 72.6, 70.9, 69.7, 66.4, 58.7, 24.3, 23.8, 23.4 ppm; **HRMS** (ESI) *m/z* calcd for $C_{11}H_{16}ClO_4$ $[M + H]^+$ 247.0732, found 247.0730.

Determination of the absolute and relative stereochemistry for chlorohydrin **16g**

Absolute and relative stereochemistry has been confirmed by converting the *syn*-chlorohydrin **16g** (10 mg, 0.04 mmol) into **12** by catalytic hydrogenation with Pd/C (10 weight%) in MeOH (0.1 M); $[\alpha]_D^{20}$ = -163 (*c* 0.700 in $CHCl_3$).

Determination of enantiomeric excess of chlorohydrin **16g**

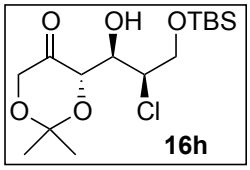
Following General Procedure **H**, optically enriched of **12** (7 mg, 0.03 mmol; prepared by hydrogenation of **16g**) were converted into the corresponding benzoyl esters. The enantiomeric excess of the optically enriched benzoyl ester was determined as described for **12** (93% ee).



Data for *anti*-chlorohydrin **37**: R_f (pentane-EtOAc 8:2) 0.31; $[\alpha]_D^{20}$ -84 (*c* 0.99 in $CHCl_3$); **IR** (neat): υ = 3456, 3292, 2987, 2898, 2122, 1743, 1376, 1222, 1088, 860, 647 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.58 (*dd*, *J* = 1.4 Hz, *J* = 5.7 Hz, 1H), 4.41 (*dt*, *J* = 5.7 Hz, *J* = 6.5 Hz, 1H), 4.31 (*dd*, *J* = 1.5 Hz, *J* = 17.3 Hz, 1H), 4.22 (*dt*, *J* = 4.2 Hz, *J* = 5.7 Hz, 1H), 4.06 (*d*, *J* = 17.3 Hz, 1H), 3.09 (*d*, *J* = 4.2 Hz, 1H), 2.85 (*dd*, *J* = 1.9 Hz, *J* = 2.7 Hz, 1H), 2.84 (*t*, *J* = 2.7 Hz, *J* = 6.7 Hz, *J* = 16.8 Hz, 1H), 2.11 (*t*, *J* = 2.7 Hz, 1H), 1.51 (*s*, 3H), 1.47 ppm (*s*, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 209.4, 101.3, 79.7, 74.1, 72.9, 71.0, 66.9, 58.8, 24.4, 23.9, 23.7 ppm; **HRMS** (ESI) *m/z* calcd for $C_{11}H_{16}ClO_4$ $[M + H]^+$ 247.0732, found 247.0721.

4.9. PREPARATION OF ALDOL ADDUCTS 16h AND 38

Following General Procedure **A**, a solution of 3-((*tert*-butyldimethylsilyl)oxy)propanal[10] (508 mg, 2.70 mmol), NCS (379 mg, 2.84 mmol), (*S*)-proline (248 mg, 2.16 mmol) and dioxanone **1** (339 μL, 2.84 mmol) in CH_2Cl_2 (13 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins **16h** and **38** (dr 2:1) by flash chromatography (pentane-EtOAc 9:1) afforded *syn*-chlorohydrin **16h** (464 mg, 49% yield) as a clear oil and *anti*-chlorohydrin **38** (223 mg, 23% yield) as a clear oil.



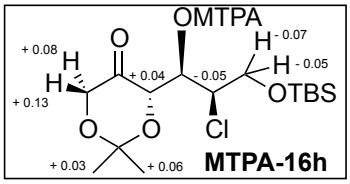
Data for *syn*-chlorohydrin **16h**: R_f (pentane-EtOAc 8:2) 0.65; $[\alpha]_D^{20}$ = -104 (*c* 1.02 in $CHCl_3$); **IR** (neat): υ = 3526, 2925, 1743, 1375, 1257, 1223, 1096, 839, 780 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.40 (*dd*, *J* = 1.4 Hz, *J* = 8.8 Hz, 1H), 4.30 (*dd*, *J* = 1.5 Hz, *J* = 17.6 Hz, 1H), 4.25-4.19 (*m*, 2H), 4.08 (*d*, *J* = 17.6 Hz, 1H), 3.98 (*dd*, *J* = 8.2 Hz, *J* = 10.1 Hz, 1H), 3.85 (*dd*, *J* = 5.6 Hz, *J* = 10.2 Hz, 1H), 3.32 (*dd*, *J* = 1.3 Hz, *J* = 2.9 Hz, 1H), 1.51 (*s*, 3H), 1.43 (*s*, 3H), 0.90 (*s*, 9H), 0.09 ppm (*s*, 6H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 212.0, 101.6, 72.4, 68.1, 66.5, 63.5, 60.4, 29.7, 25.8, 23.8, 23.4, -5.4, -5.5 ppm; **HRMS** (ESI) *m/z* calcd for $C_{15}H_{30}ClO_5Si$ $[M + H]^+$ 353.1546, found 353.1563.

Determination of relative stereochemistry for chlorohydrin **16h**

Relative stereochemistry of **16h** was determined from derived structures **19**-**21**.

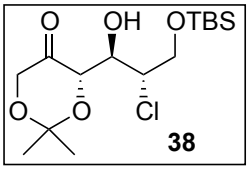
Determination of the absolute stereochemistry for chlorohydrin **16h**

Following General Procedure **I**, the *syn*-chlorohydrin **16h** (5 mg, 0.01 mmol) was converted into the corresponding (*R*)-(+)-MTPA-**16h** and (*S*)-(+)-MTPA-**16h** esters. The absolute stereochemistry of the hydroxymethine stereocenter in **16h** was assigned using Mosher's method[4] (see $\delta_S - \delta_R$ (ppm) convention in inset).



Determination of enantiomeric excess of chlorohydrin **16h**

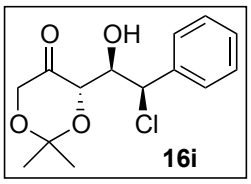
Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **16h** was prepared. Following General Procedure **H**, optically enriched and racemic samples of the *syn*-chlorohydrin **16h** (40 mg, 0.11 mmol) were converted into the corresponding benzoyl esters. The enantiomeric benzoyl esters were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.7 mL/min; eluent: hexanes-*i*PrOH 97:3; detection at 230 nm; retention time = 4.21 min for (+)-**16h-Bz**; 4.80 min for (-)-**16h-Bz** (see chromatograms in section 6). The enantiomeric excess of the optically enriched benzoyl ester was determined using the same method (98% ee).



Data for *anti*-chlorohydrin **38**: R_f (pentane-EtOAc 85:15) 0.55; $[\alpha]_D^{20}$ = -65 (*c* 0.61 in $CHCl_3$); **IR** (neat): υ = 3483, 2930, 1749, 1375, 1257, 1226, 1099, 837, 781 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 4.57 (*dd*, *J* = 1.4 Hz, *J* = 4.6 Hz, 1H), 4.32 (*dd*, *J* = 1.5 Hz, *J* = 17.0 Hz, 1H), 4.33-4.25 (*m*, 2H), 4.02 (*d*, *J* = 17.0 Hz, 1H), 3.99 (*dd*, *J* = 5.0 Hz, *J* = 10.6 Hz, 1H), 3.93 (*dd*, *J* = 6.4 Hz, *J* = 10.6 Hz, 1H), 3.60 (*d*, *J* = 3.2 Hz, 1H), 1.50 (*s*, 3H), 1.47 (*s*, 3H), 0.90 (*s*, 9H), 0.10 ppm (*s*, 6H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 209.0, 101.0, 75.0, 73.1, 66.9, 65.6, 59.9, 29.7, 25.8, 24.1, 23.5, -5.4, -5.5 ppm; **HRMS** (ESI) *m/z* calcd for $C_{15}H_{30}ClO_5Si$ $[M + H]^+$ 353.1546, found 353.1549.

4.10. PREPARATION OF ALDOL ADDUCTS 16i AND 39

Following General Procedure **A**, a solution of phenylacetaldehyde (664 μL, 5.94 mmol), NCS (832 mg, 6.23 mmol), (*S*)-proline (546 mg, 4.75 mmol) and dioxanone **1** (743 μL, 6.23 mmol) in CH_2Cl_2 (30 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins **16i** and **39** (dr 2:1) by flash chromatography (pentane-EtOAc 9:1 to 85:15) afforded *syn*-chlorohydrin **16i** (711 mg, 42% yield) as a yellowish oil and *anti*-chlorohydrin **39** (353 mg, 21% yield) as a yellowish oil.



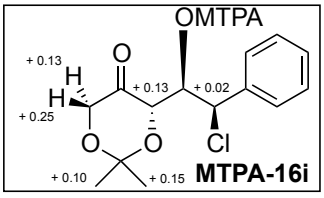
Data for *syn*-chlorohydrin **16i**: R_f (pentane-EtOAc 8:2) 0.25; $[\alpha]_D^{20}$ = -82 (*c* 1.1 in $CHCl_3$); **IR** (neat): υ = 3504, 3035, 2988, 1746, 1376, 1226, 1086, 865, 749, 707 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.53-7.49 (*m*, 2H), 7.38-7.32 (*m*, 3H), 5.28 (*dd*, *J* = 0.8 Hz, *J* = 3.8 Hz, 1H), 4.41 (*dd*, *J* = 1.5 Hz, *J* = 7.0 Hz, 1H), 4.22 (*ddd*, *J* = 3.3 Hz, *J* = 3.7 Hz, *J* = 7.0 Hz, 1H), 4.15 (*dd*, *J* = 1.5 Hz, *J* = 17.4 Hz, 1H), 4.00 (*d*, *J* = 17.4 Hz, 1H), 3.25 (*dd*, *J* = 0.8 Hz, *J* = 3.1 Hz, 1H), 1.51 (*s*, 3H), 1.48 ppm (*s*, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 210.2, 138.1, 128.6, 128.4, 128.3, 101.5, 73.9, 73.7, 66.5, 62.9, 23.7, 23.6 ppm; **HRMS** (ESI) *m/z* calcd for $C_{14}H_{17}ClNaO_4$ $[M + Na]^+$ 307.0708, found 307.0713.

Determination of relative stereochemistry for chlorohydrin **16i**

Relative stereochemistry of **16i** was determined from derived structures **17** and **18**.

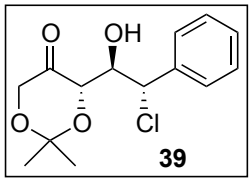
Determination of the absolute stereochemistry for chlorohydrin **16i**

Following General Procedure **I**, the *syn*-chlorohydrin **16i** (5 mg, 0.02 mmol) was converted into the corresponding (*R*)-(+)-MTPA-**16i** and (*S*)-(+)-MTPA-**16i** esters. The absolute stereochemistry of the hydroxymethine stereocenter in **16i** was assigned using Mosher's method[4] (see $\delta_S - \delta_R$ (ppm) convention in inset).



Determination of enantiomeric excess of chlorohydrin **16i**

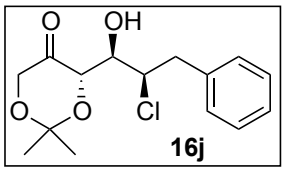
Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **16i** was prepared. The enantiomeric *syn*-chlorohydrins were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.3 mL/min; eluent: hexanes-*i*PrOH 9:1; detection at 230 nm; retention time = 4.15 min for (+)-**16i**; 5.47 min for (-)-**16i** (see chromatograms in section 6). The enantiomeric excess of the optically enriched *syn*-chlorohydrin **16i** was determined using the same method (96% ee).



Data for *anti*-chlorohydrin **39**: (**39**:**16i** ratio 3:1) R_f (pentane-EtOAc 8:2) 0.20; **IR** (neat): υ = 3503, 3032, 2991, 1749, 1376, 1226, 1083, 864, 747, 703 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.53-7.50 (*m*, 2H), 7. 38-7.33 (*m*, 3H), 5.20 (*d*, *J* = 5.5 Hz, 1H), 4.42 (*m*, 1H), 4.31 (*dd*, *J* = 1.5 Hz, *J* = 17.2 Hz, 1H), 4.14 (*dd*, *J* = 1.5 Hz, *J* = 6.5 Hz, 1H), 4.01 (*d*, *J* = 17.2 Hz, 1H), 3.03 (*dd*, *J* = 0.5 Hz, *J* = 3.4 Hz, 1H), 1.46 (*s*, 3H), 1.34 ppm (*s*, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 209.5, 137.0, 129.1, 128.9, 128.4, 101.2, 74.6, 74.2, 66.6, 61.0, 23.9, 23.7 ppm; **HRMS** (ESI) *m/z* calcd for $C_{14}H_{17}ClNaO_4$ $[M + Na]^+$ 307.0708, found 307.0714.

4.11. PREPARATION OF ALDOL ADDUCTS 16j AND 41

Following General Procedure **A**, a solution of hydrocinnamaldehyde (100 μL, 0.76 mmol), NCS (106 mg, 0.80 mmol), (*S*)-proline (70 mg, 0.61 mmol) and dioxanone **1** (96 μL, 0.80 mmol) in CH_2Cl_2 (3.5 mL) was stirred for 24 hours. Purification of the crude *syn*- and *anti*-chlorohydrins **16j** and **41** (dr 3.2:1) by flash chromatography (pentane-EtOAc 85:15) afforded *syn*-chlorohydrin **16i** (144 mg, 64% yield) as a white solid and *anti*-chlorohydrin **41** (45 mg, 20% yield) as a clear oil.

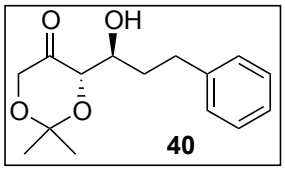


16j

Data for *syn*-chlorohydrin **16j**: mp = 51-53 °C; R_f (pentane-EtOAc 85:15) 0.33; $[\alpha]_D^{20}$ = -107 (*c* 1.89 in $CHCl_3$); **IR** (neat): υ = 3521, 3030, 2989, 1739, 1377, 1220, 1088, 867, 760, 707 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.36-7.17 (*m*, 5H), 4.42 (*dd*, *J* = 1.5 Hz, *J* = 8.9 Hz, 1H), 4.38 (*tdd*, *J* = 1.5 Hz, *J* = 7.8 Hz, 1H), 4.23 (*dd*, *J* = 1.5 Hz, *J* = 17.6 Hz, 1H), 4.05 (*d*, *J* = 17.6 Hz, 1H), 3.88 (*ddd*, *J* = 1.7 Hz, *J* = 3.0 Hz, *J* = 8.9 Hz, 1H), 3.42 (*dd*, *J* = 1.4 Hz, *J* = 3.0 Hz, 1H), 3.27 (*dd*, *J* = 7.9 Hz, *J* = 13.8 Hz, 1H), 3.21 (*dd*, *J* = 7.7 Hz, *J* = 13.8 Hz, 1H), 1.49 (*s*, 3H), 1.38 ppm (*s*, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 212.4, 137.5, 129.5, 128.6, 126.9, 101.6, 72.8, 70.0, 66.4, 62.2, 40.5, 23.8, 23.4 ppm; **HRMS** (ESI) *m/z* calcd for $C_{15}H_{20}ClO_4$ $[M + H]^+$ 299.1045, found 299.1036.

Determination of relative stereochemistry for chlorohydrin **16j**

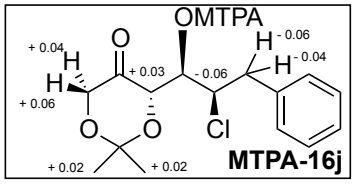
Following General Procedure **G**, the *syn*-chlorohydrin **16j** (10 mg, 0.03 mmol) was converted into the known alcohol **40**.[5] Comparison of ^{1}H-NMR spectral data derived from **40** with that reported in the literature confirmed the *anti* stereochemistry of the two oxymethine stereocenters in **16j**.



40

Determination of the absolute stereochemistry for chlorohydrin **16j**

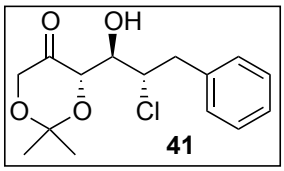
Following General Procedure **I**, the *syn*-chlorohydrin **16j** (5 mg, 0.02 mmol) was converted into the corresponding (*R*)-(+)-MTPA-**16j** and (*S*)-(+)-MTPA-**16j** esters. The absolute stereochemistry of the hydroxymethine stereocenter in **16j** was assigned using Mosher's method[4] (see $\delta_S - \delta_R$ (ppm) convention in inset).



Determination of enantiomeric excess of chlorohydrin **16j**

Following General Procedure **A**, using a 1:1 mixture of (*S*):(*R*) proline, a racemic sample of the chlorohydrin **16j** was prepared. Following General Procedure **H**, optically enriched and racemic samples of the *syn*-chlorohydrin **16j** (40 mg, 0.13 mmol) were converted into the corresponding benzoyl esters. The enantiomeric benzoyl esters were separated by chiral HPLC using a DIACEL CHIRALCEL-OD column; flow rate 1.5 mL/min; eluent: hexanes-*i*PrOH 95:5; detection at 230 nm; retention time = 4.07 min for (+)-**16j-Bz**; 5.24 min for (-)-**16j-Bz** (see chromatograms in section 6). The enantiomeric excess of the optically enriched benzoyl ester was determined using the same method (98% ee).

Data for *anti*-chlorohydrin **41**: R_f (pentane-EtOAc 85:15) 0.19; $[\alpha]_D^{20}$ = -83 (*c* 2.4 in $CHCl_3$); **IR** (neat): υ = 3496, 3030, 2992, 1752, 1374, 1226, 1100, 867, 757, 701 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.35-7.20 (*m*, 5H), 4.53 (*dd*, *J* = 1.4 Hz, *J* = 6.8 Hz, 1H), 4.46 (*ddd*, *J* = 4.5 Hz, *J* = 9.5 Hz, 1H), 4.32 (*dd*, *J* = 1.4 Hz, *J* = 17.4 Hz, 1H), 4.12 (*ddd*, *J* = 4.1 Hz, *J* = 6.9 Hz, 1H), 4.07 (*d*, *J* = 17.4 Hz, 1H), 3.28 (*dd*, *J* = 4.5 Hz, *J* = 14.3 Hz, 1H), 3.21 (*d*, *J* = 3.8 Hz, 1H), 3.05 (*dd*, *J* = 9.3 Hz, *J* = 14.4 Hz, 1H), 1.52 (*s*, 3H), 1.49 ppm (*s*, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 210.0, 137.6, 129.6, 128.4, 126.8, 101.3, 73.8, 73.1, 66.8, 63.3, 39.4, 23.8, 23.7 ppm; **HRMS** (ESI) *m/z* calcd for $C_{15}H_{20}ClO_4$ $[M + H]^+$ 299.1045, found 299.1065.

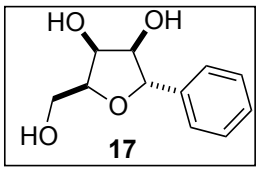


Determination of relative stereochemistry for chlorohydrin **41**
Following General Procedure **G**, the *anti*-chlorohydrin **41** (10 mg, 0.04 mmol) was converted into the known alcohol **40**.[5] Comparison of ^{1}H-NMR spectral data derived from **40** with that reported in the literature confirmed the *anti* stereochemistry of the two oxymethine stereocenters in **41**.

4.12. PREPARATION OF 17

Following General Procedure **C**, a solution of **16i** (50 mg, 0.18 mmol) and catechol borane (386 µL, 0.39 mmol) in THF (1.7 mL) was stirred for 45 minutes at 0°C. Purification of the crude product by flash chromatography (pentane-EtOAc 1:1 to 4:6) afforded the corresponding 1,3-*anti*-chlorodiol (37 mg, 74% yield) as a clear oil. Following General Procedure **D**, a solution of the corresponding 1,3-*anti*-chlorodiol (17 mg, 0.06 mmol), in a mixture of MeOH-H_2O (1:6, 600 µL), was heated to 60 °C and maintained at this temperature for 16 hours. Purification of the crude product **17** by flash chromatography (CH_2Cl_2-MeOH 95:5 to 9:1) afforded triol **17**[11] (10 mg, 83% yield) as a clear oil.

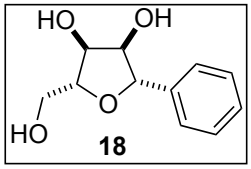
Data for α-L-lyxofuranosylbenzene (**17**): R_f (CH_2Cl_2-MeOH 9:1) 0.45; $[\alpha]_D^{20}$ = -29 (*c* 0.48 in MeOH); **IR** (neat): υ = 3357, 2922, 2856, 1454, 1023, 752, 698 cm^{-1}; **^{1}H-NMR** (400 MHz, CD_3OD): δ = 7.42-7.39 (*m*, 2H), 7.36-7.31 (m, 2H), 7.29-7.24 (*m*, 1H), 4.77 (*d*, *J* = 7.9 Hz, 1H), 4.31 (*ddd*, *J* = 4.1 Hz, *J* = 4.9 Hz, *J* = 6.1 Hz, 1H), 4.25 (*t*, *J* = 4.2 Hz, 1H), 3.99 (*d*, *J* = 4.4 Hz, *J* = 7.9 Hz, 1H), 3.87 (*dd*, *J* = 4.9 Hz, *J* = 11.6 Hz, 1H), 3.81 ppm (*dd*, *J* = 6.2 Hz, *J* = 11.6 Hz, 1H); **^{13}C-NMR** (150 MHz, CD_3OD): δ = 142.9, 129.4, 128.7, 127.1, 84.1, 82.8, 80.9, 73.6, 62.4 ppm; **HRMS** (ESI) *m/z* calcd for $C_{11}H_{14}NaO_4$ $[M + Na]^+$ 233.0784, found 233.0777.



4.13. PREPARATION OF TRIOL 18

Following General Procedure **B**, a solution of **16i** (50 mg, 0.18 mmol), AcOH (100 µL, 1.76 mmol) and $Me_4NBH(OAc)_3$ (277 mg, 1.05 mmol) in MeCN (1 mL) was stirred for 24 hours at -25 °C. Purification of the crude product by flash chromatography (pentane-EtOAc 7:3) afforded the corresponding 1,3-*syn*-chlorodiol (49 mg, 98% yield) as a clear oil. Following General Procedure **D**, a solution of the corresponding 1,3-*syn*-chlorodiol (27 mg, 0.09 mmol), in a mixture of MeOH-H_2O (1:6, 900 µL), was heated to 60 °C and maintained at this temperature for 16 hours to afford the known triol **18**[12] (17 mg, 85% yield) as a clear oil.

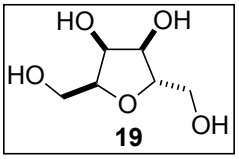
Data for β-D-ribofuranosylbenzene (**18**): R_f (EtOAc) 0.45; $[\alpha]_D^{20}$ = -29 (*c* 0.40 in MeOH), lit = -24.8 (*c* 0.44 in MeOH); **^{1}H-NMR** (400 MHz, CD_3OD): δ = 7.46-7.43 (*m*, 2H), 7.36-7.31 (m, 2H), 7.29-7.24 (*m*, 1H), 4.71 (*d*, *J* = 6.7 Hz, 1H), 4.04 (*dd*, *J* = 4.2 Hz, *J* = 5.5 Hz, 1H), 3.97 (*ddd*, *J* = 4.0 Hz, *J* = 4.8 Hz, 1H), 3.86 (*dd*, *J* = 5.6 Hz, *J* = 6.7 Hz, 1H), 3.79 (*dd*, *J* = 3.9 Hz, *J* = 11.9 Hz, 1H), 3.73 ppm (*dd*, *J* = 5.0 Hz, *J* = 11.9 Hz, 1H); consistent with the literature data.[12]



4.14. PREPARATION OF TETRAOL 19

Following General Procedure **C**, a solution of **16h** (50 mg, 0.14 mmol) and catechol borane (312 µL, 0.39 mmol) in THF (1.5 mL) was stirred for 45 minutes at 0°C. Purification of the crude product by flash chromatography (pentane-EtOAc 8:2 to 7:3) afforded the corresponding 1,3-*anti*-chlorodiol (29 mg, 58% yield) as a clear oil. Following General Procedure **E**, a stirred solution of the corresponding 1,3-*anti*-chlorodiol (25 mg, 0.07 mmol), in H_2O (1 mL), was heated to 110 °C and maintained at this temperature for 30 minutes. Purification of the crude product **19** by flash chromatography (CH_2Cl_2-MeOH 78:22) afforded the tetraol **19** (9 mg, 75% yield) as a clear oil.

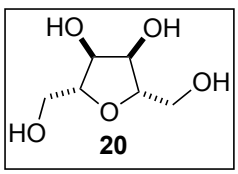
Data for 2,5-anhydro-L-altritol (**19**): R_f (CH_2Cl_2-MeOH 8:2) 0.20; $[\alpha]_D^{20}$ -40 (*c* 0.10 in MeOH); **IR** (neat)**:** υ = 3339, 2931, 2882, 1413, 1095, 1045 cm^{-1}; **^{1}H-NMR** (500 MHz, CD_3OD): δ = 4.15 (*dd*, *J* = 4.0 Hz, *J* = 4.6 Hz, 1H), 4.07 (*dd*, *J* = 4.6 Hz, *J* = 7.6 Hz, 1H), 4.03 (*ddd*, *J* = 4.0 Hz, *J* = 4.8 Hz, *J* = 6.4 Hz, 1H), 3.84 (*ddd*, *J* = 2.9 Hz, *J* = 4.6 Hz, *J* = 7.5 Hz, 1H), 3.78 (*dd*, *J* = 4.8 Hz, *J* = 11.5 Hz, 1H), 3.75 (*dd*, *J* = 2.7 Hz, *J* = 12.0 Hz, 1H), 3.72 (*dd*, *J* = 6.4 Hz, *J* = 11.5 Hz, 1H), 3.57 ppm (*dd*, *J* = 4.6 Hz, *J* = 12.0 Hz, 1H); **^{13}C-NMR** (150 MHz, CD_3OD): δ = 83.6, 82.4, 73.6, 73.3, 63.3, 62.2 ppm; **HRMS** (ESI) *m/z* calcd for $C_6H_{12}NaO_5$ $[M + Na]^+$ 187.0577, found 187.0585.



4.15. PREPARATION OF TETRAOL 20

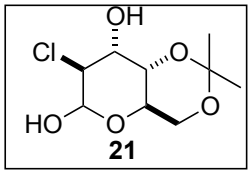
Following General Procedure **B**, a solution of **16h** (320 mg, 0.91 mmol), AcOH (512 µL, 9.07 mmol) and $Me_4NBH(OAc)_3$ (1.191 g, 4.53 mmol) in MeCN (5 mL) was stirred for 24 hours. Purification of the crude product by flash chromatography (pentane-EtOAc 7:3) afforded the corresponding 1,3-*syn*-chlorodiol (274 mg, 85% yield) as a clear oil. Following General Procedure **E**, a mixture of the corresponding 1,3-*syn*-chlorodiol (25 mg, 0.07 mmol), in H_2O (1 mL), was heated to 110 °C and maintained at this temperature for 20 minutes. Purification of the crude **20** by flash chromatography (CH_2Cl_2-MeOH 8:2) afforded known tetraol **20**[13] (11 mg, 92% yield) as a clear oil.

Data for 2,5-anhydro-allitol (**20**): R_f (CH_2Cl_2-MeOH 8:2) 0.33; **^{1}H-NMR** (500 MHz, CD_3OD): δ = 3.96 (*m*, 2H), 3.83 (*m*, 2H), 3.73 (*dd*, *J* = 3.3 Hz, *J* = 12.0 Hz, 2H), 3.58 ppm (*dd*, *J* = 4.5 Hz, *J* = 12.0 Hz, 2H); **^{13}C-NMR** (125 MHz, CD_3OD): δ = 85.4, 72.8, 63.3 ppm; consistent with the literature data.[13]



4.16. PREPARATION OF CHLOROHYDRIN 21

To a cold solution (0 °C) of the previously described 1,3-*syn*-chlorodiol (from **16h**) (100 mg, 0.2817 mmol) in THF (2.8 mL) was added a solution of tetrabutylammonium fluoride in THF (1M, 295 μL, 0.30 mmol), and the reaction mixture was stirred for 10 minutes. The reaction mixture was then diluted with Et_2O (2 mL) and was washed with a solution of saturated aqueous ammonium chloride (500 μL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude product by flash chromatography (pentane-EtOAc 3:7) afforded the deprotected 1,3-*syn*-chlorotriol (66 mg, 97% yield). To a cold (0°C) solution of bis-(acetoxy)iodobenzene (44 mg, 0,14 mmol) and the 1,3-*syn*-chlorotriol (30 mg, 0.12 mmol), in CH_2Cl_2 (1.3 mL), was added 2,2,6,6-tetramethylpiperidinyloxy (1 mg, cat.) and the reaction mixture was allowed to gradually warm to room temperature and stirred for 8 hours and the reaction mixture was concentrated under reduced pressure. Purification of the crude chlorohydrin **21** (dr 1:0.9)[14] by flash chromatography (pentane-EtOAc 6:4) afforded **21** (23 mg, 77% yield) as a clear oil.

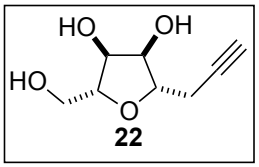


21

Data for 2-chloro-2-deoxy-4,6-*O*-isopropylidene-D-altrose (**21**): R_f (pentane/EtOAc 1:1) 0.60, 0.48; **IR** (neat)**:** υ = 3416, 2994, 2919, 1376, 1267, 1197, 1081, 877, 730 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ = (**21**) 5.25 (*s*, 1H), 4.27-4.25 (*m*, 2H), 4.09 (*dd*, *J* = 2.3 Hz, *J* = 9.6 Hz, 1H), 3.94 (*dd*, *J* = 4.8 Hz, *J* = 10.0 Hz, 1H), 3.90-3.85 (*m*, 1H), 3.82 (*dd*, *J* = 10.0 Hz, 1H), 1.53 (*s*, 3H), 1.42 ppm (*s*, 3H); (**21'**) 5.21 (*s*, 1H), 4.24-4.16 (*m*, 4H), 3.94 (*dd*, *J* = 4.8 Hz, *J* = 10.0 Hz, 1H), 3.88 (*dd*, *J* = 10.0 Hz, 1H), 1.56 (*s*, 3H), 1.44 ppm (*s*, 3H); δ = (OH) 3.38 (s_{br}, 1H), 2.52 (s_{br}, 1H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 100.4, 100.2, 95.1, 90.7, 70.7, 70.5, 67.7, 67.6, 65.4, 62.5, 62.1, 61.9, 59.6, 55.5, 29.0, 28.9, 19.4, 19.3 ppm; **HRMS** (ESI) *m/z* calcd for $C_{14}H_{24}ClO_4Si$ $[M + Na]^+$ 261.0500, found 261.0511.

4.17. PREPARATION OF TRIOL 22

Following General Procedure **B**, a solution of **16g** (200 mg, 0.81 mmol), AcOH (464 μL, 8.11 mmol) and $Me_4NBH(OAc)_3$ (1.3 g, 4.86 mmol) in MeCN (4 mL) was stirred for 24 hours. Purification of the crude product by flash chromatography (pentane-EtOAc 7:3) afforded the corresponding 1,3-*syn*-chlorodiol (195 mg, 97% yield) as a clear oil. Following General Procedure **E**, a mixture of the corresponding 1,3-*syn*-chlorodiol (190 mg, 0.77 mmol), in H_2O (3 mL), was heated to 100 °C and maintained at this temperature for 30 minutes. Purification of the crude triol **22** by flash chromatography (EtOAc-MeOH 99:1) afforded **22** (113 mg, 86% yield) as a clear oil.

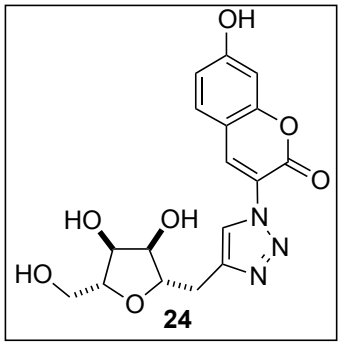


22

Data for 3-*C*-(β-D-ribofuranosyl)propyne (**22**): R_f (EtOAc-MeOH 99:1) 0.32; $[\alpha]_D^{20}$ -5.7 (*c* 0.33 in MeOH); **IR** (neat)**:** υ = 3364, 3284, 2922, 2122, 1417, 1098, 1029, 633 cm^{-1}; **^{1}H-NMR** (400 MHz, CD_3OD): δ = 3.96 (*t*, *J* = 5.3 Hz, 1H), 3.90 (*t*, *J* = 5.3 Hz, 1H), 3.87 (*q*, *J* = 5.3 Hz, 1H), 3.82 (*dt*, *J* = 3.9 Hz, *J* = 5.2 Hz, 1H), 3.68 (*dd*, *J* = 3.8 Hz, *J* = 11.9 Hz, 1H), 3.57 (*dd*, *J* = 5.1 Hz, *J* = 11.9 Hz, 1H), 2.51 (*ddd*, *J* = 2.6 Hz, *J* = 5.3 Hz, *J* = 17.0 Hz, 1H), 2.44 (*ddd*, *J* = 2.7 Hz, *J* = 5.3 Hz, *J* = 17.0 Hz, 1H), 2.31 ppm (*t*, *J* = 2.7 Hz, 1H); **^{13}C-NMR** (100 MHz, CD_3OD): δ = 85.7, 82.5, 81.4, 75.2, 72.8, 71.2, 63.6, 23.7 ppm; **HRMS** (ESI) *m/z* calcd for $C_8H_{12}NaO_4$ $[M + H]^+$ 173.0808, found 173.0802.

4.18. PREPARATION OF TRIAZOLE 24

A solution of **22** (19 mg, 0.12 mmol) and **23** (25 mg, 0.1219 mmol) in MeOH (1.2 mL) was added to a stirred solution of copper sulfate pentahydrate (1.5 mg, 5 mol%) and L-ascorbic acid (11 mg, 0.06 mmol) in H_2O (600 μL) and the resulting mixture was stirred for 48 hours at room temperature. The reaction mixture was concentrated and the crude product was purified by flash chromatography (CH_2Cl_2-MeOH 9:1) to afford the triazole **24** (26 mg, 58% yield) as a yellowish solid.



24

Data for **24**: mp = 240-242 °C (decomp); R_f (CH_2Cl_2-MeOH 9:1) 0.24; λ_{max} (DMSO) = 346 nm (ε 12127 L mol^{-1} cm^{-1}); **IR** (neat): υ = 3394, 3194, 3058, 2961, 2878, 1731, 1613, 1572, 1307, 1229, 1095, 1057, 989, 937, 850, 809, 756 cm^{-1}; **^{1}H-NMR** (400 MHz, DMSO-d_6): δ = 10.90 (*s*$_{br}$, 1H), 8.56 (*s*, 1H), 8.33 (*s*, 1H), 7.73 (*d*, *J* = 8.6 Hz, 1H), 6.89 (*m*, 1H), 6.83 (*m*, 1H), 4.83 (*d*, *J* = 5.9 Hz, 1H), 4.74 (*d*, *J* = 5.4 Hz, 1H), 4.63 (*t*, *J* = 5.7 Hz, 1H), 3.90 (*m*, 1H), 3.76 (*q*, *J* = 5.4 Hz, 1H), 3.68-3.63 (*m*, 2H), 3.44-3.36 (*m*, 1H), 3.00 (*dd*, *J* = 4.6 Hz, *J* = 14.9 Hz, 1H), 2.84 ppm (*dd*, *J* = 7.71 Hz, *J* = 14.9 Hz, 1H); **^{13}C-NMR** (100 MHz, DMSO-d_6): δ = 164.3, 158.2, 156.6, 137.2, 131.9, 125.7, 121.0, 115.5, 112.0, 103.4, 85.9, 83.1, 75.6, 72.7, 63.5, 30.4 ppm; **HRMS** (ESI) *m/z* calcd for $C_{17}H_{18}N_3O_7$ $[M + H]^+$ 376.1139, found 376.1126.

5. REFERENCES

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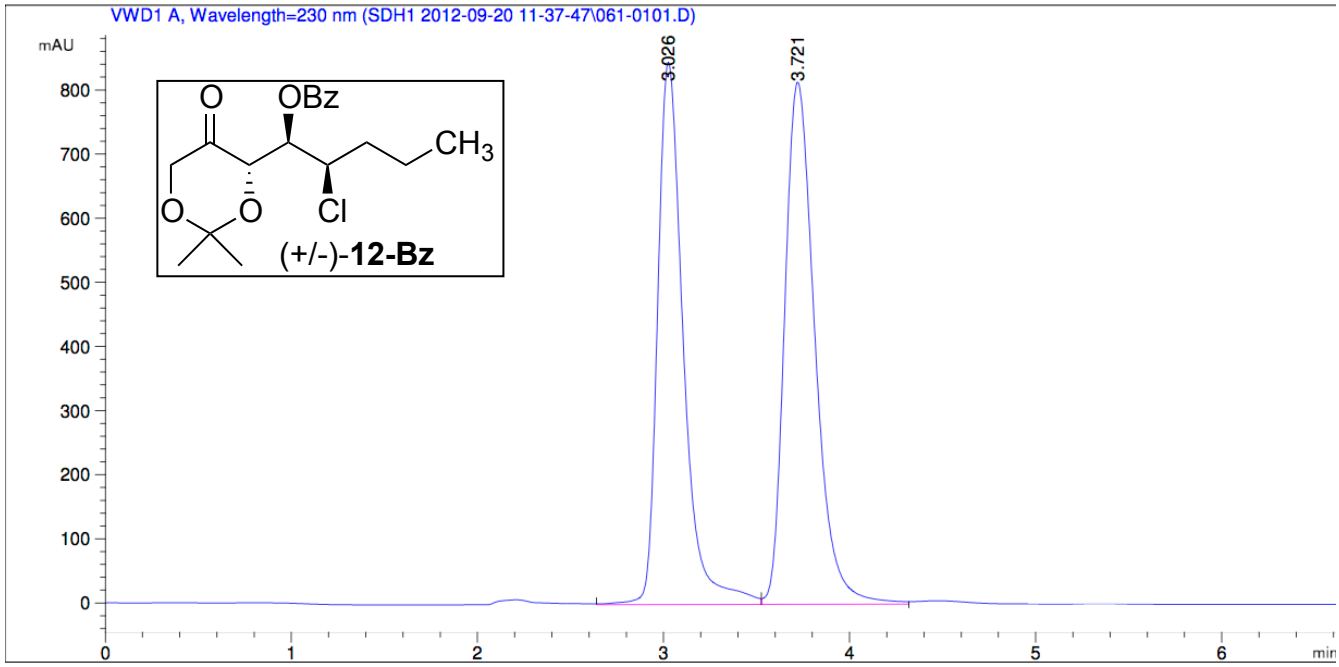
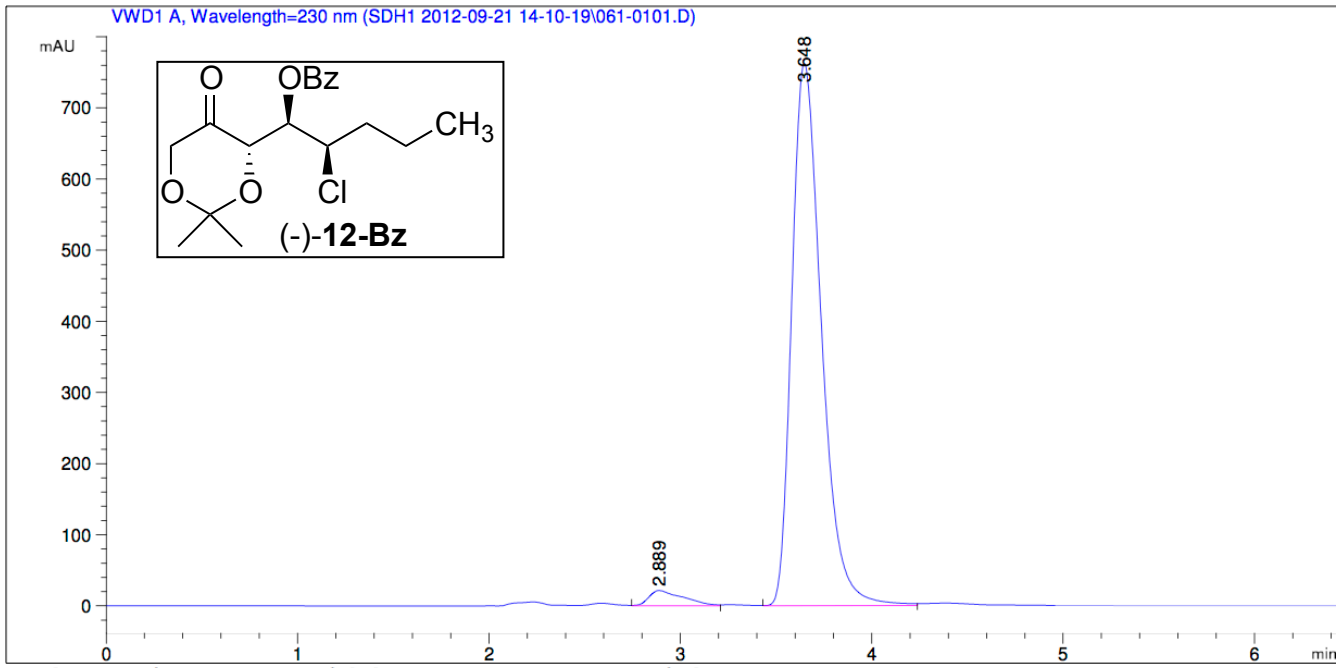
14. **24** was isolated as a mixture of *α*,*β* anomers.

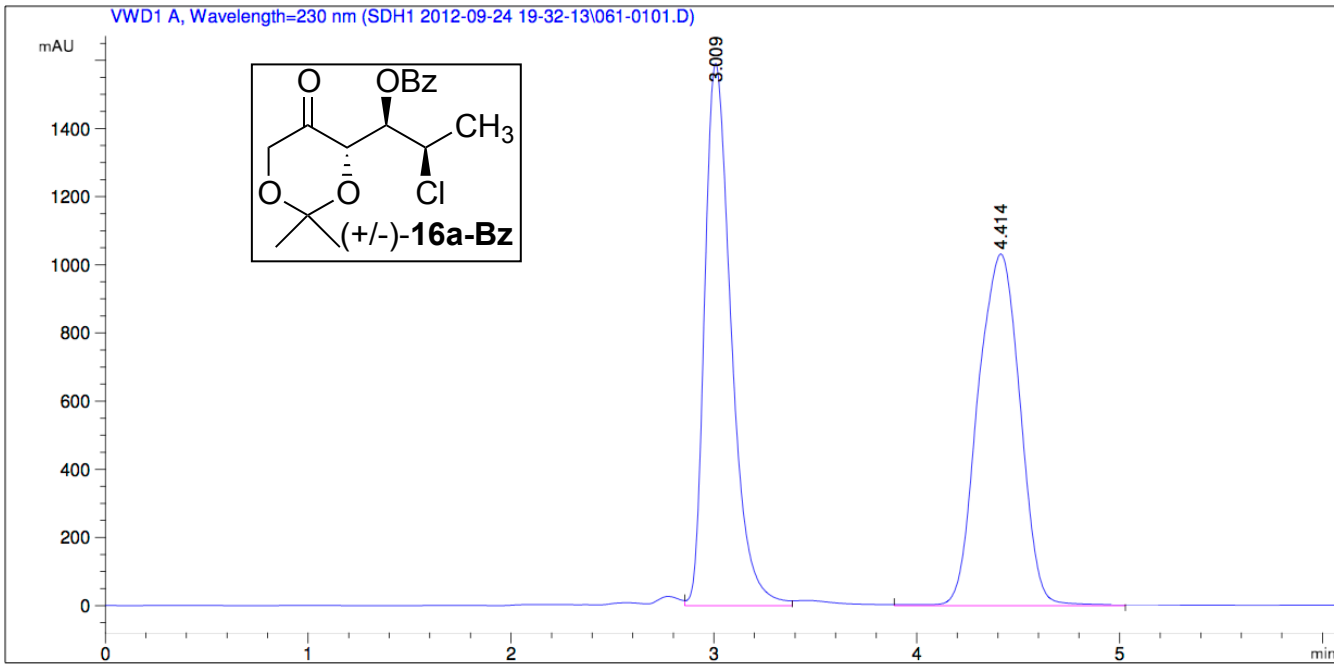
6. HPLC CHROMATOGRAMS OF BENZOYLATED **12**, **16a-h**, **16j** AND ALCOHOL **16i**



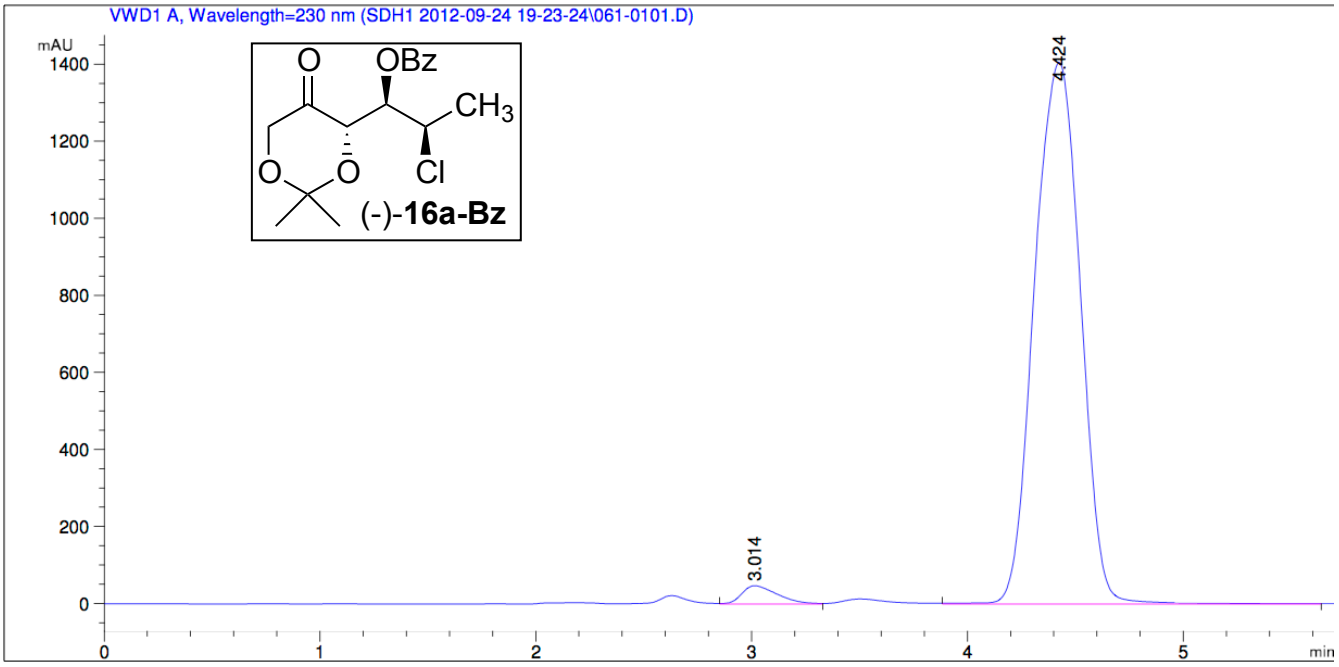
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	3.026	VV	0.1473	8148.48193	846.11102	46.9479
2	3.721	VV	0.1741	9207.96289	814.58142	53.0521



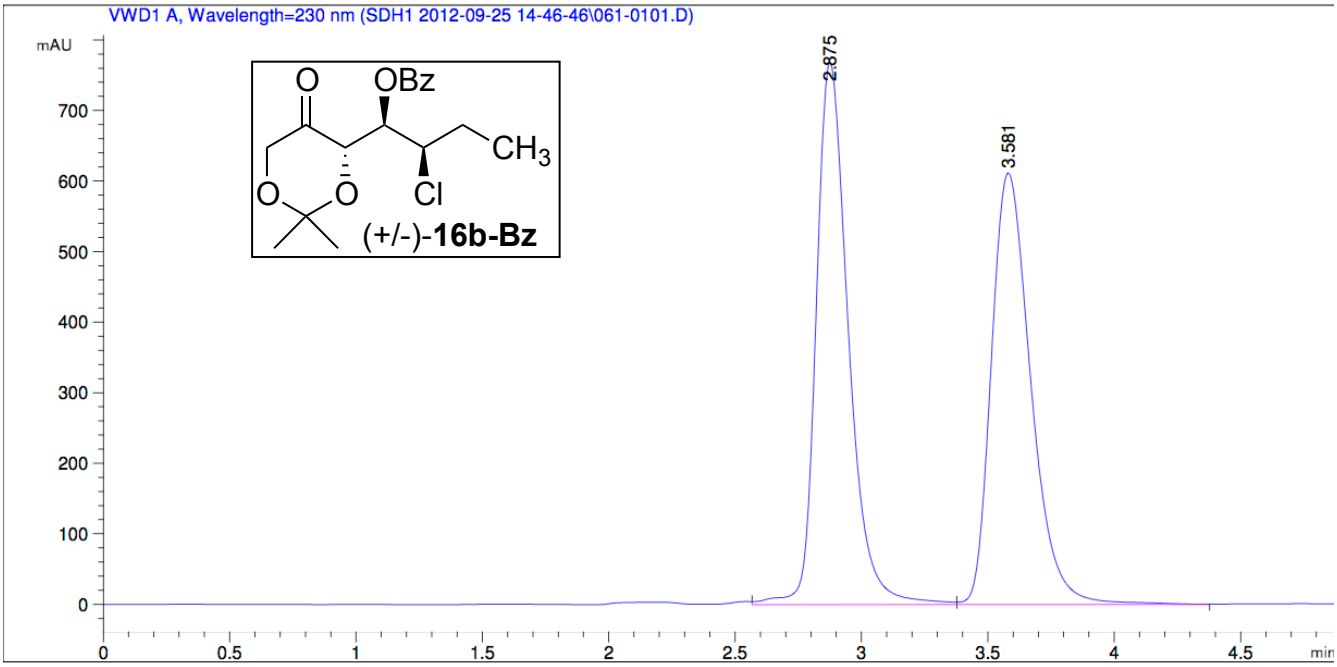
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	2.889	VV	0.1722	264.94098	21.38893	3.1302
2	3.648	VV	0.1662	8199.14453	762.41315	96.8698



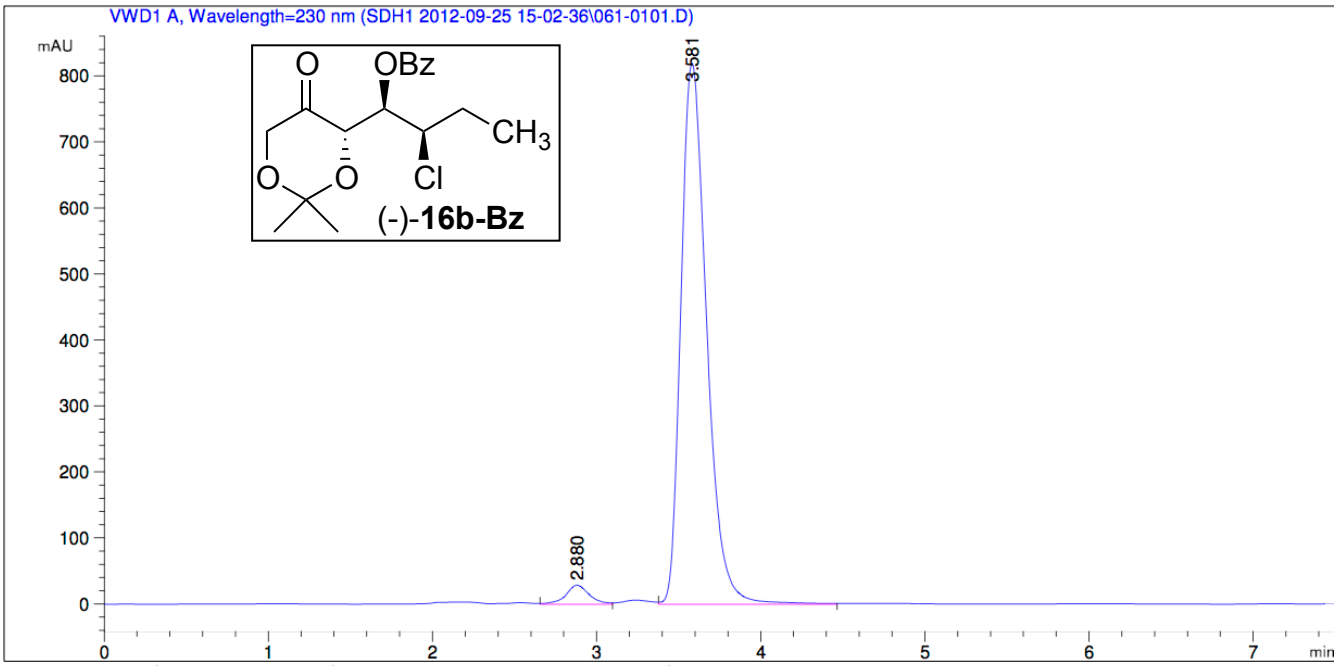
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	3.009	VV	0.1397	1.44826e4	1591.25464	49.3405
2	4.414	VB	0.2395	1.48697e4	1031.82458	50.6595



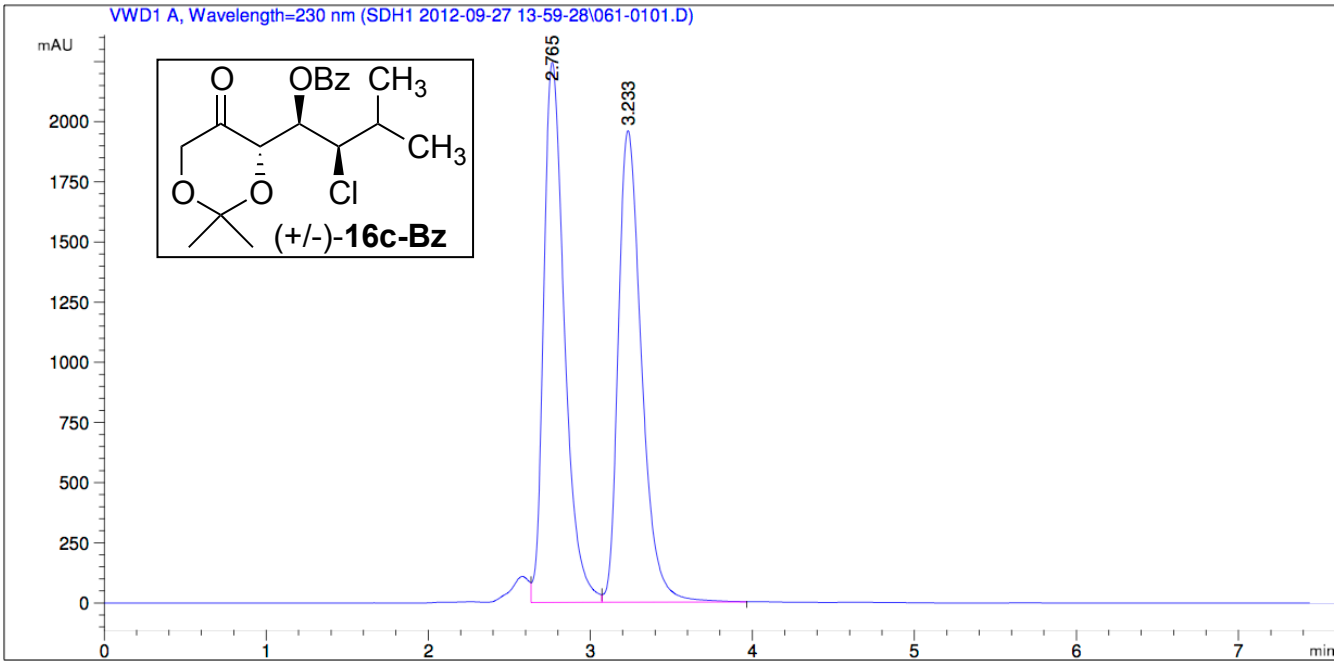
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	3.014	VV	0.1783	540.87207	47.37277	2.5379
2	4.424	VB	0.2437	2.07709e4	1406.11475	97.4621



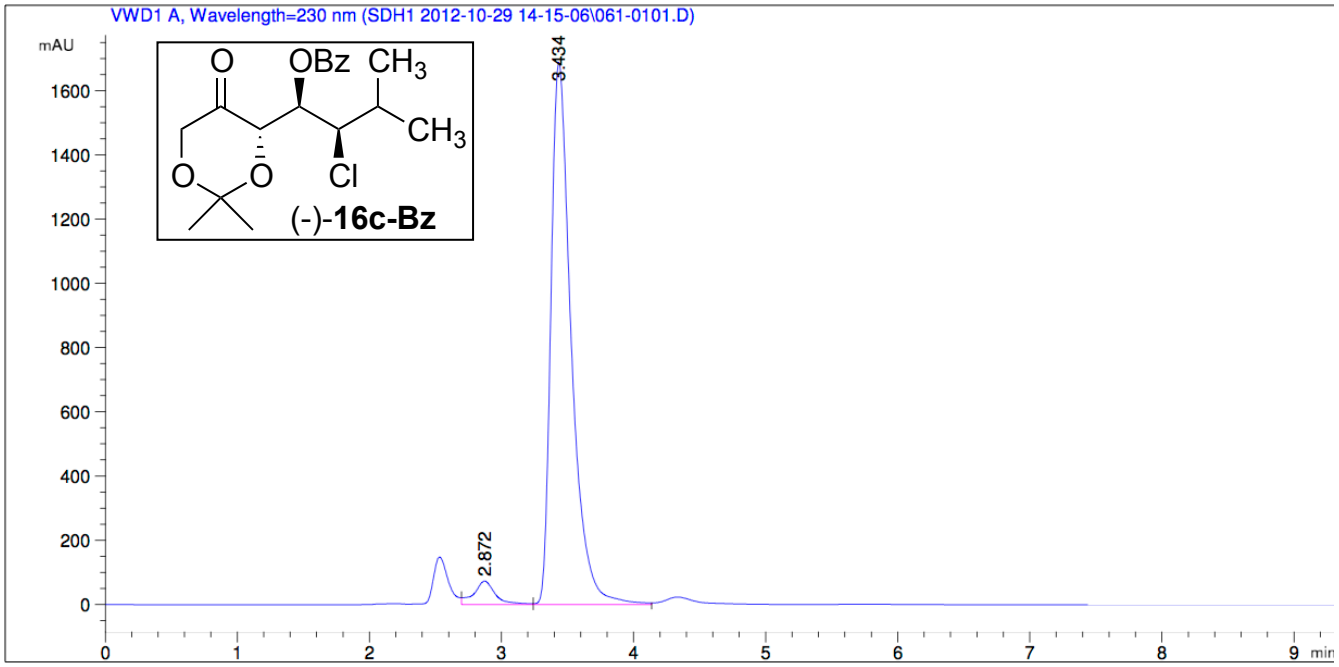
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	2.875	VV	0.1355	6821.04004	768.95245	50.6504
2	3.581	VB	0.1690	6645.85840	611.64502	49.3496



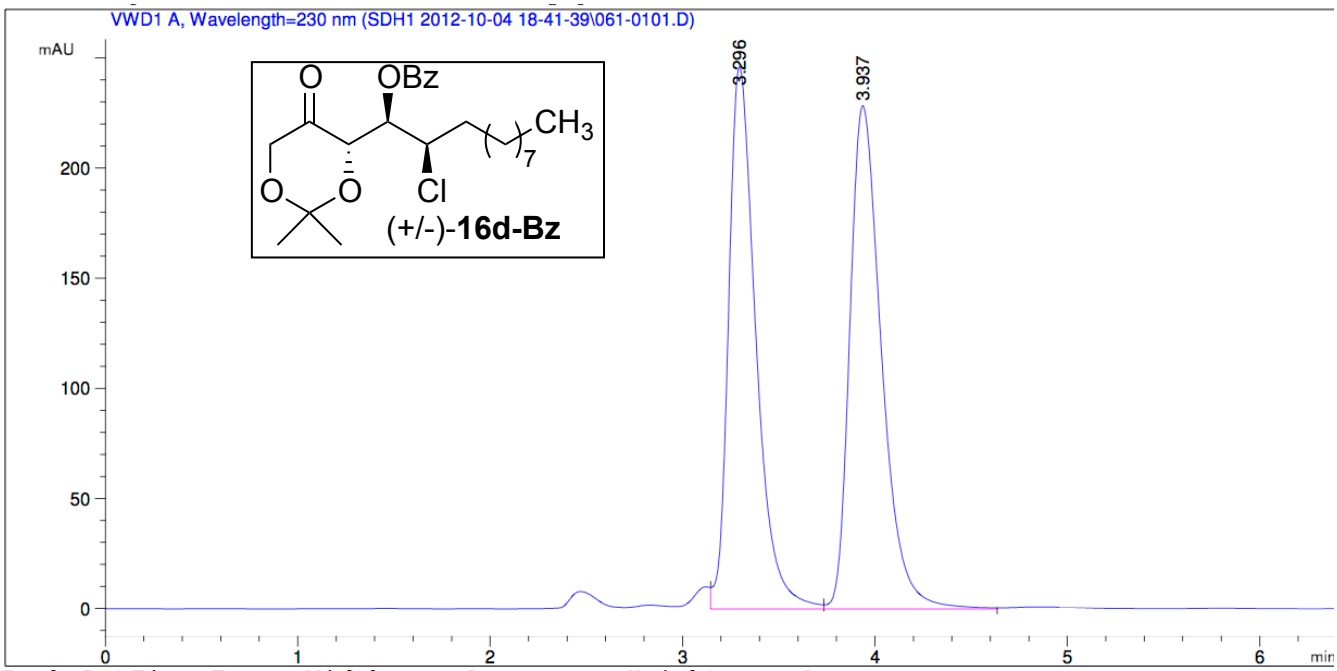
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	2.880	VV	0.1484	287.66812	28.82862	3.1302
2	3.581	VB	0.1689	8902.31543	819.83087	96.8698



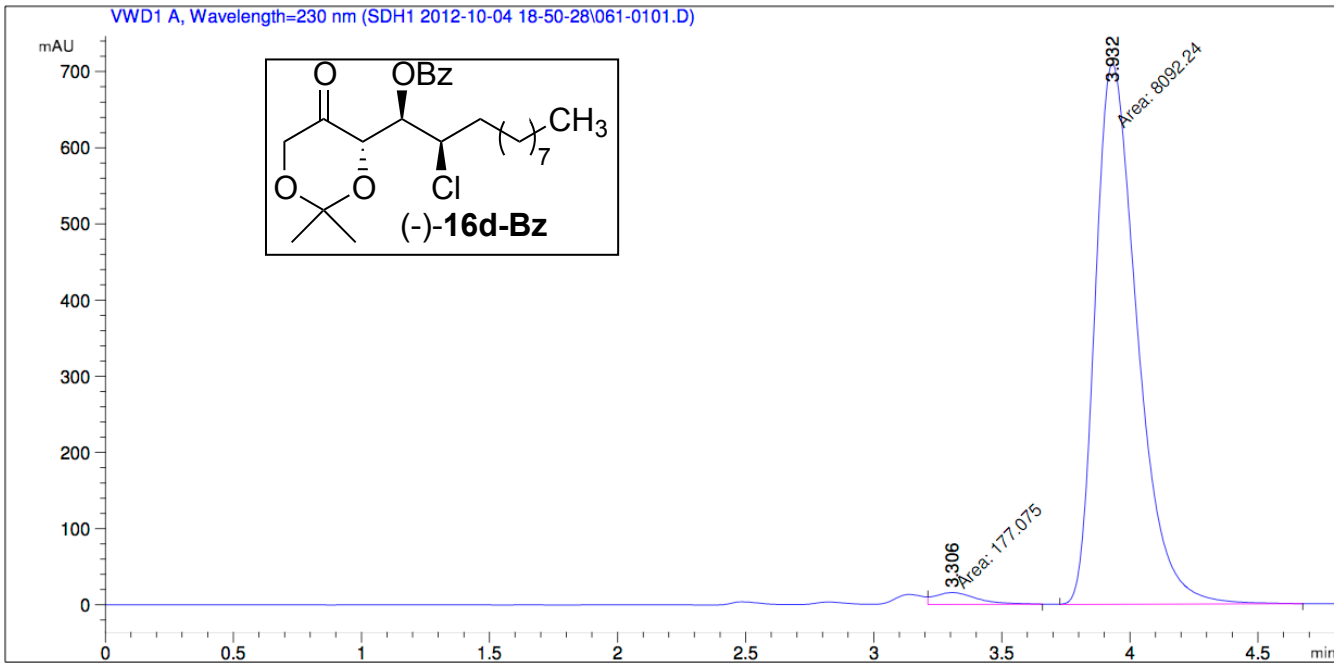
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	2.765	VV	0.1374	2.00082e4	2245.57251	50.5883
2	3.233	VB	0.1541	1.95428e4	1960.61511	49.4117



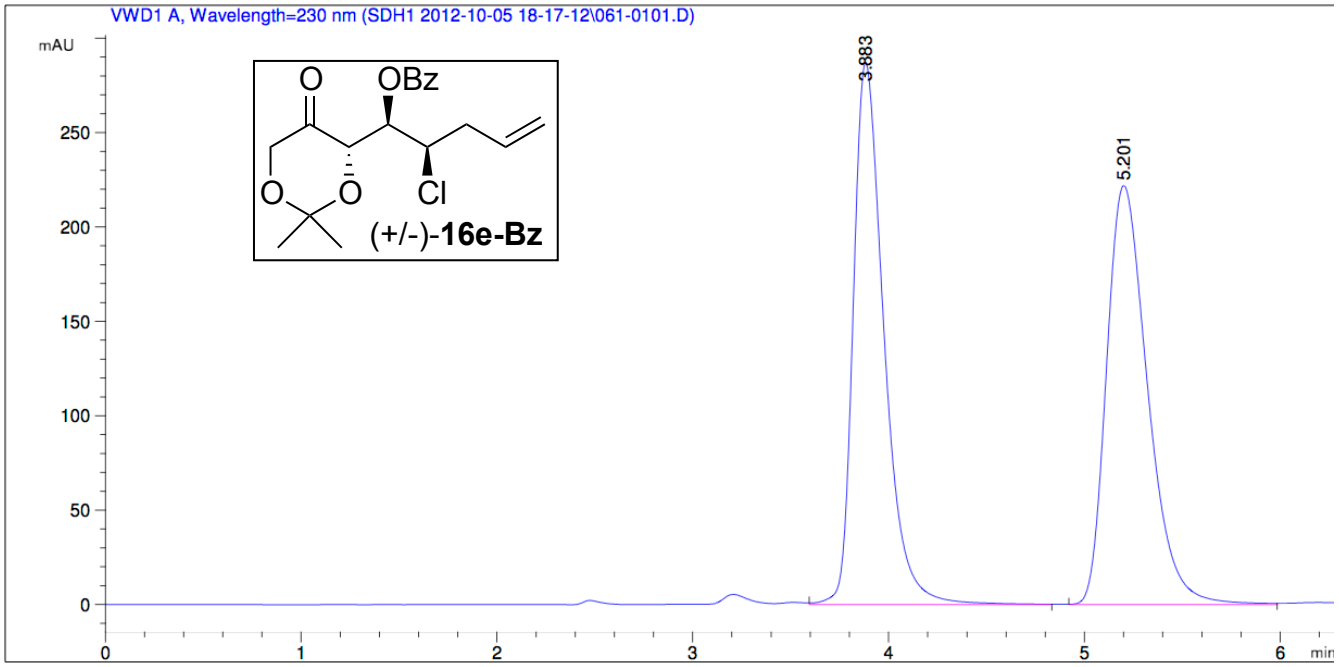
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	2.872	VV	0.1637	836.67883	73.33357	4.4302
2	3.434	VV	0.1626	1.80492e4	1688.70825	95.5698



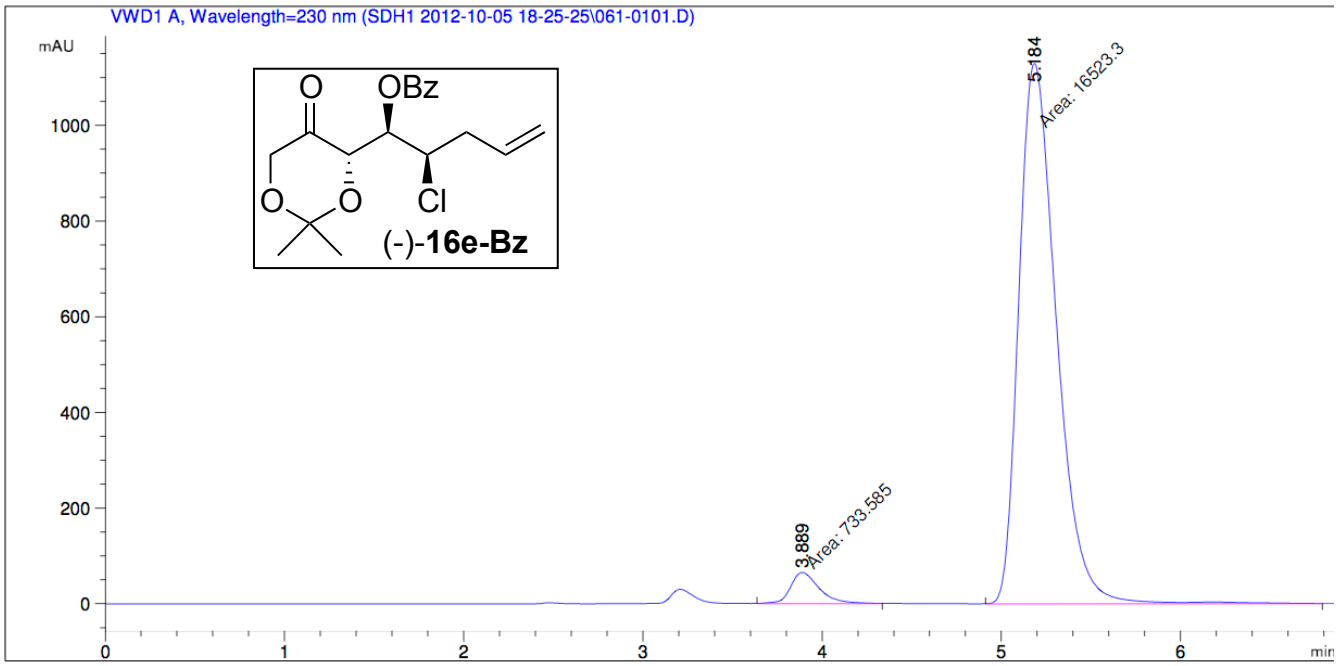
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	3.296	VV	0.1501	2430.11646	246.19205	48.1652
2	3.937	VB	0.1758	2615.26025	228.50117	51.8348



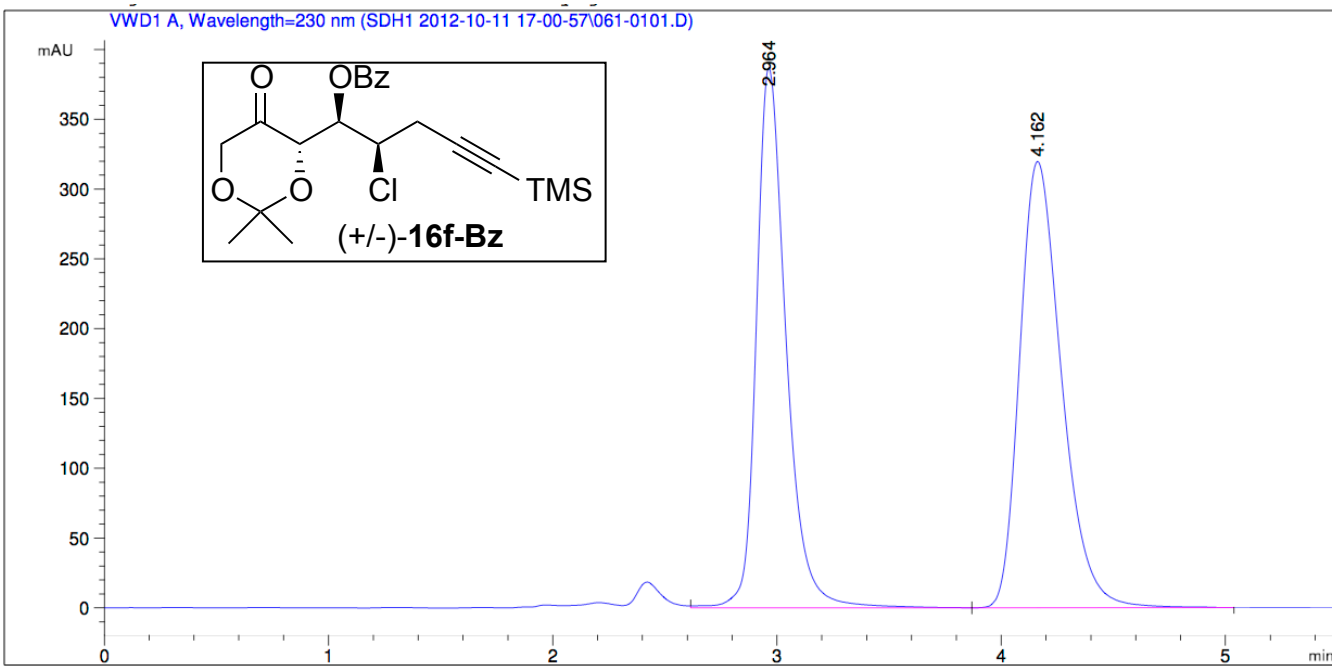
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	3.306	FM T	0.1908	177.07462	15.47062	2.1413
2	3.932	MM T	0.1899	8092.24316	710.22437	97.8587



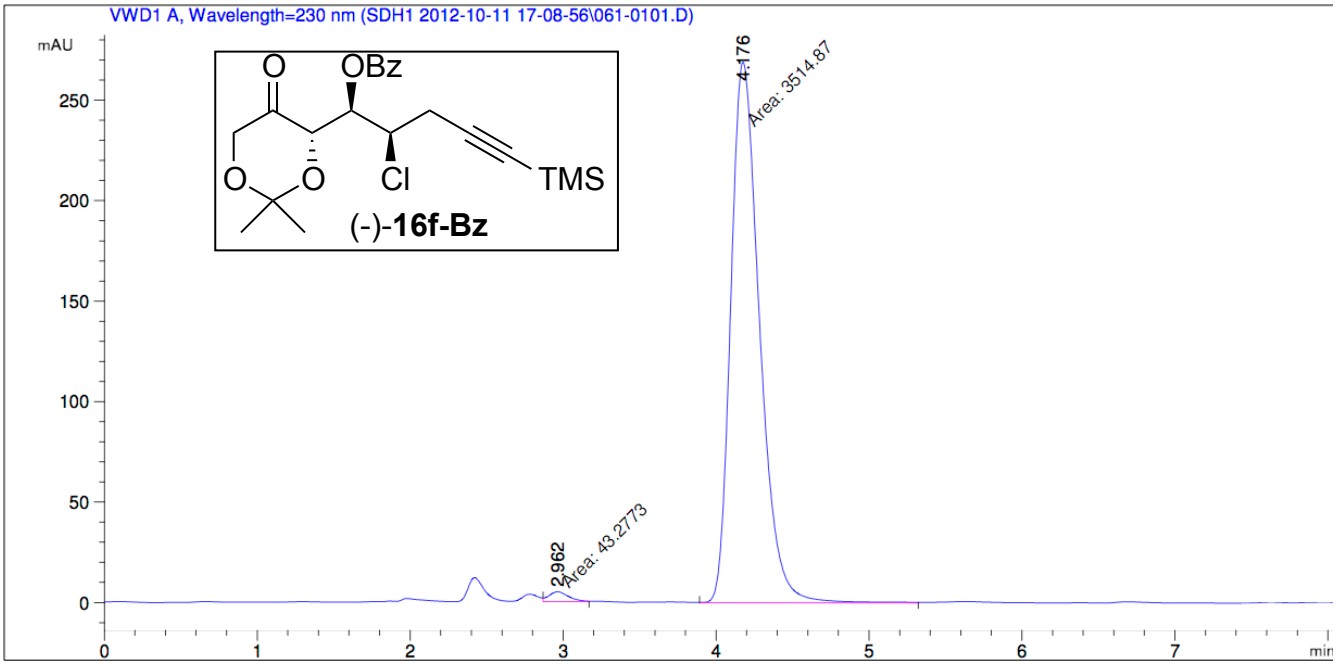
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	3.883	VB	0.1666	3133.98218	287.20499	49.2521
2	5.201	BB	0.2235	3229.15649	222.05569	50.7479



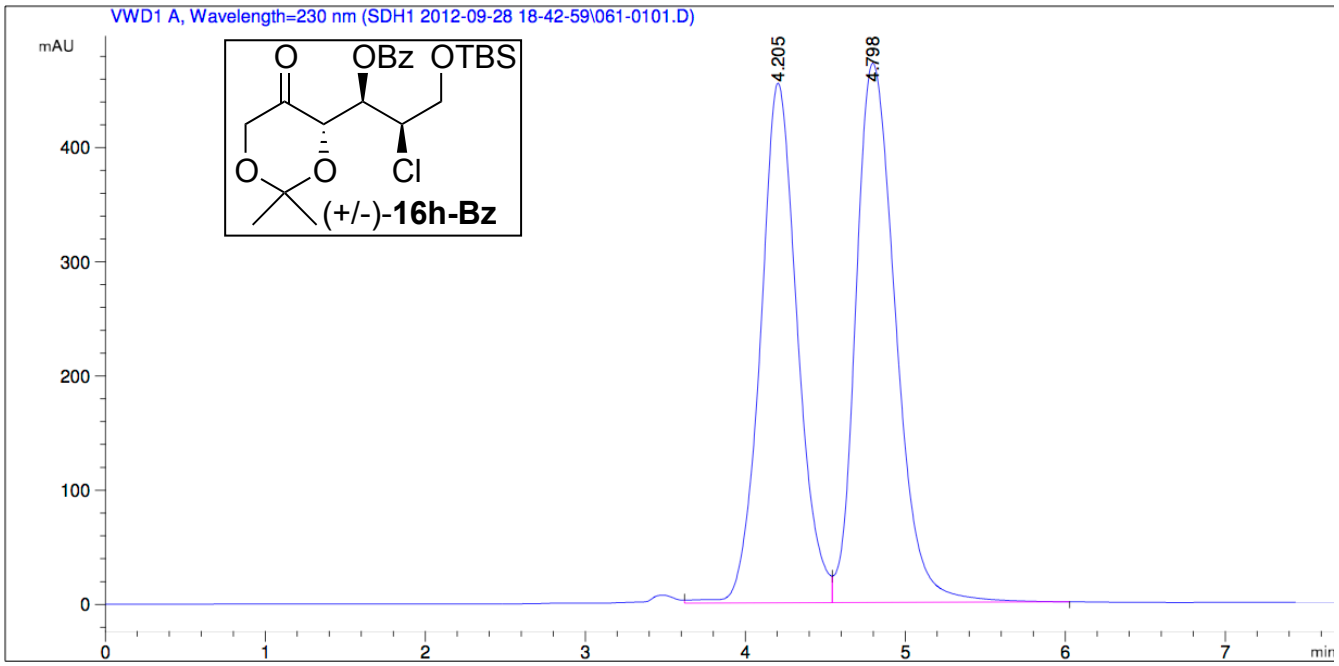
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	3.889	MM T	0.1876	733.58539	65.18202	4.2510
2	5.184	MM T	0.2437	1.65233e4	1130.08679	95.7490



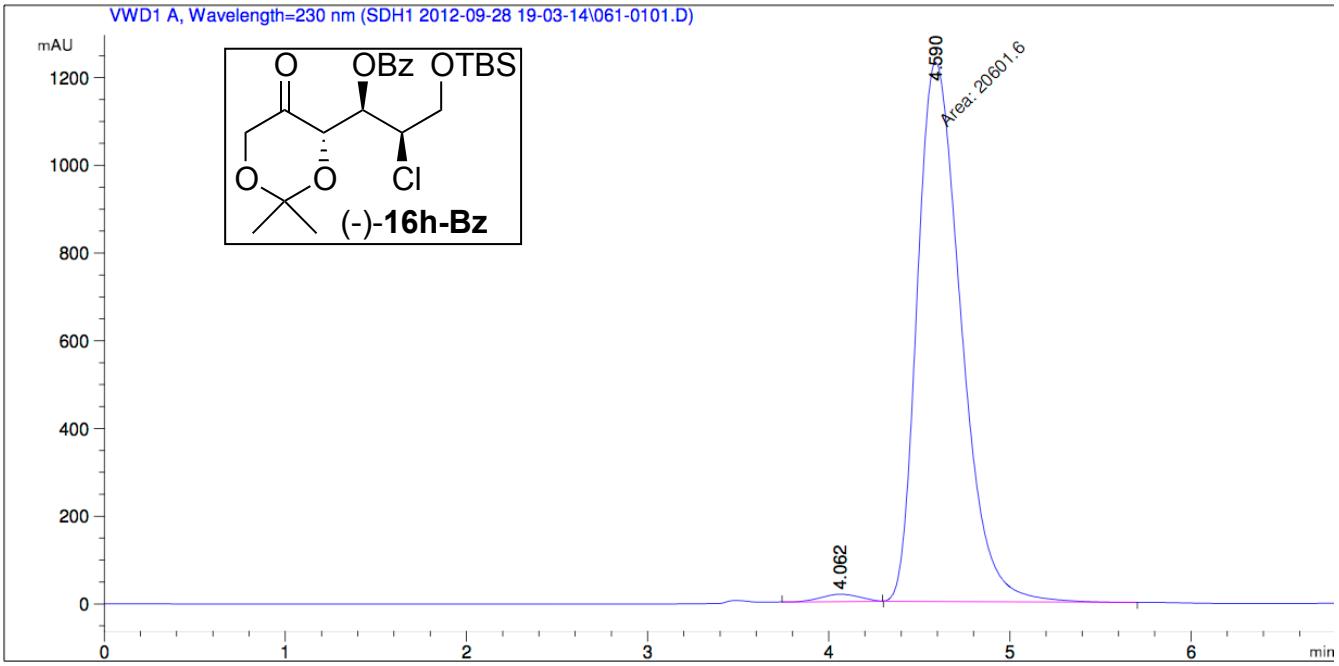
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	2.964	VV	0.1376	3550.66772	387.12531	46.1407
2	4.162	VB	0.1993	4144.63525	319.66577	53.8593



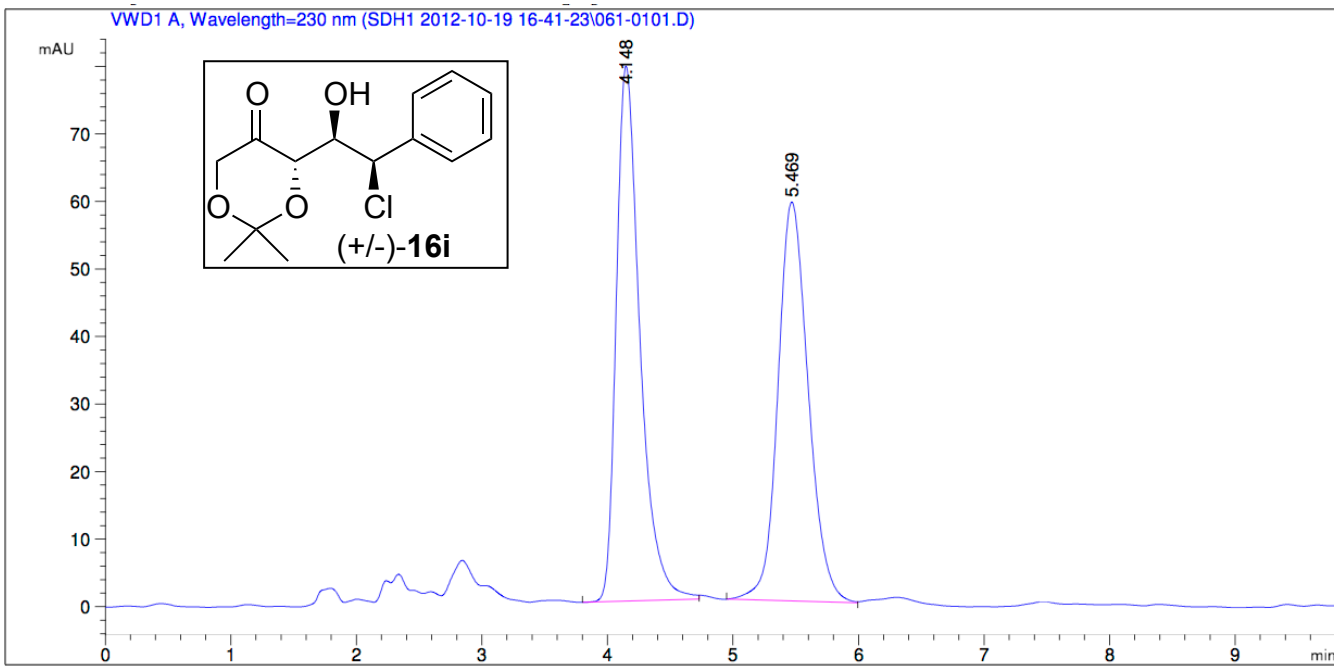
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	2.962	FM T	0.1480	43.27731	4.87370	1.2163
2	4.176	MM T	0.2177	3514.86597	269.12973	98.7837



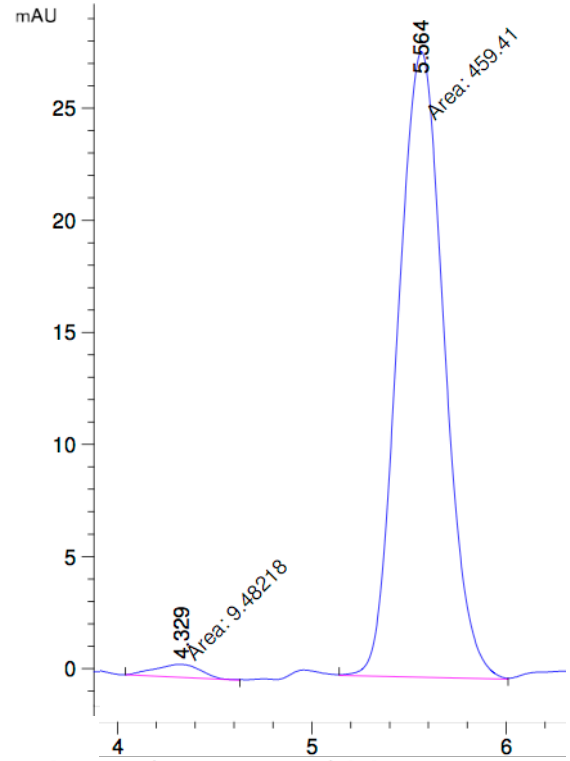
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.205	VV	0.2407	7290.59180	455.17679	47.2216
2	4.798	VB	0.2711	8148.49805	472.37381	52.7784

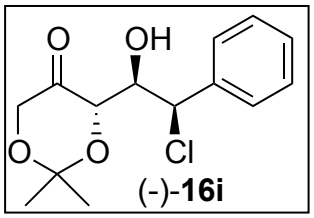


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.062	MM R	0.2491	254.72047	17.04164	1.2213
2	4.590	MM T	0.2793	2.06016e4	1229.34216	98.7787

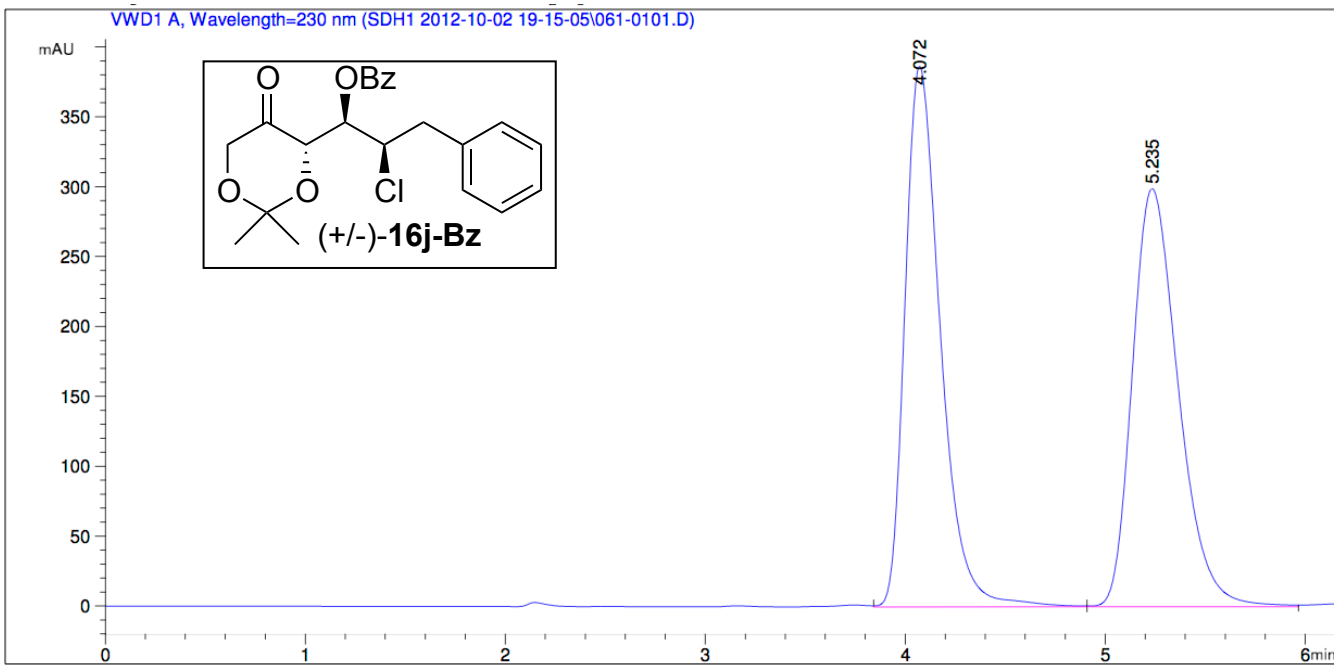


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.148	VB	0.1994	1037.75964	79.21947	51.0968
2	5.469	BV	0.2587	993.20837	59.09311	48.9032

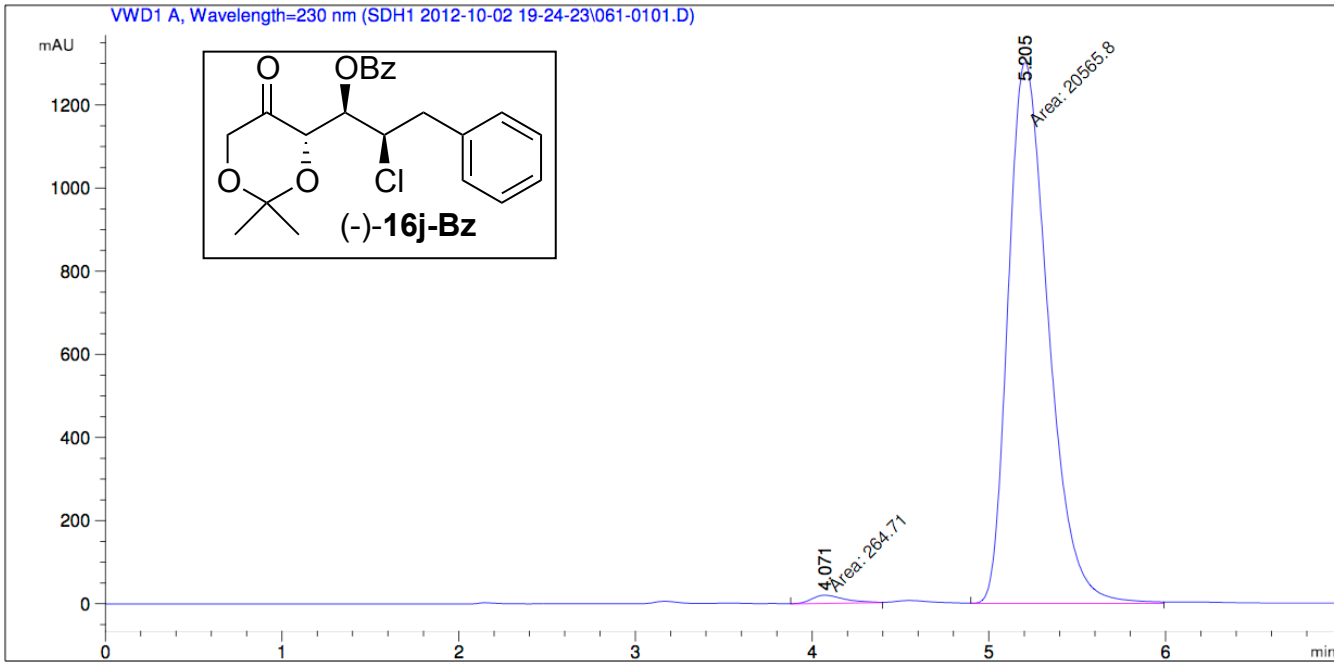




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.329	MM T	0.2712	9.48218	5.82671e-1	2.0223
2	5.564	MM T	0.2746	459.41019	27.88000	97.9777

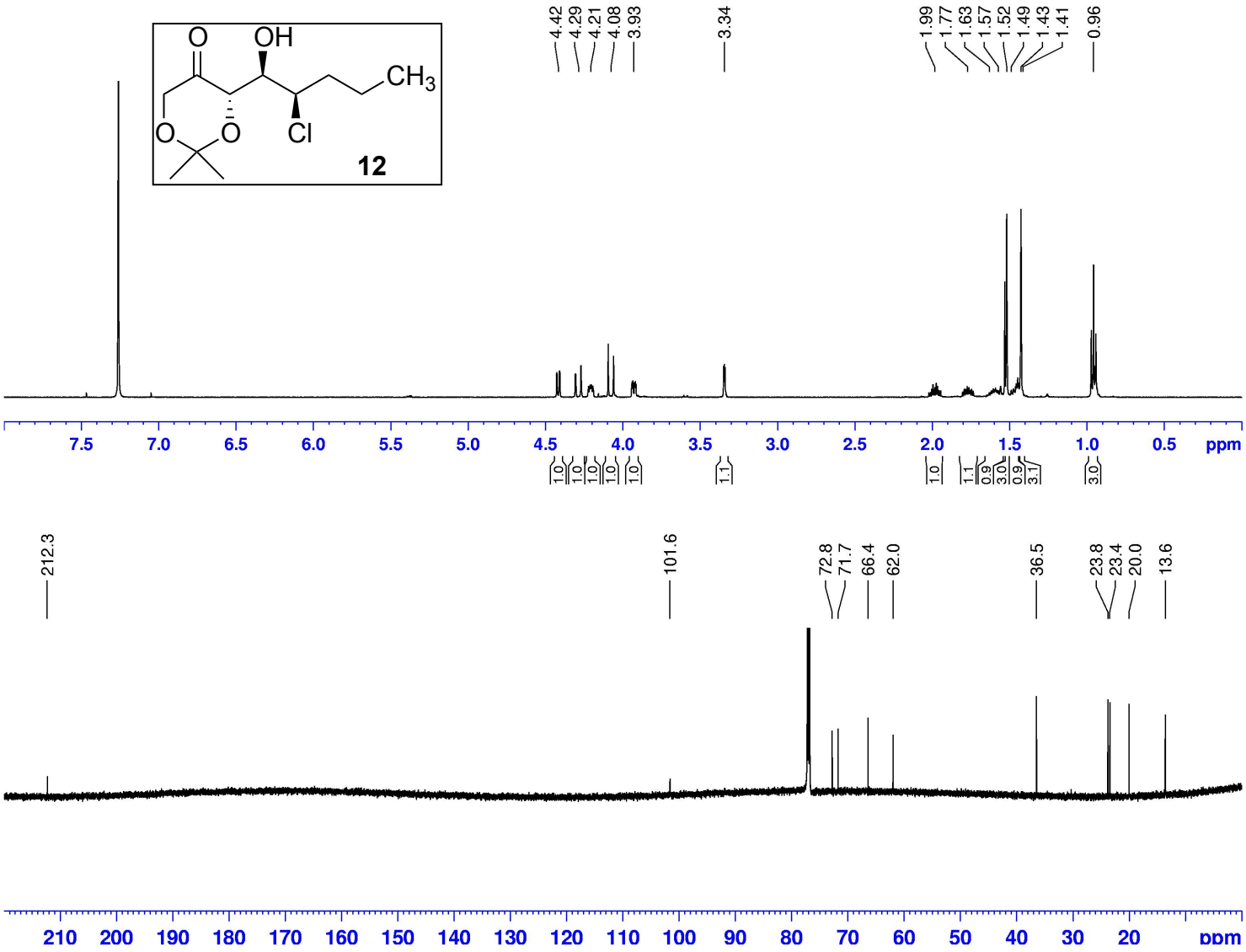


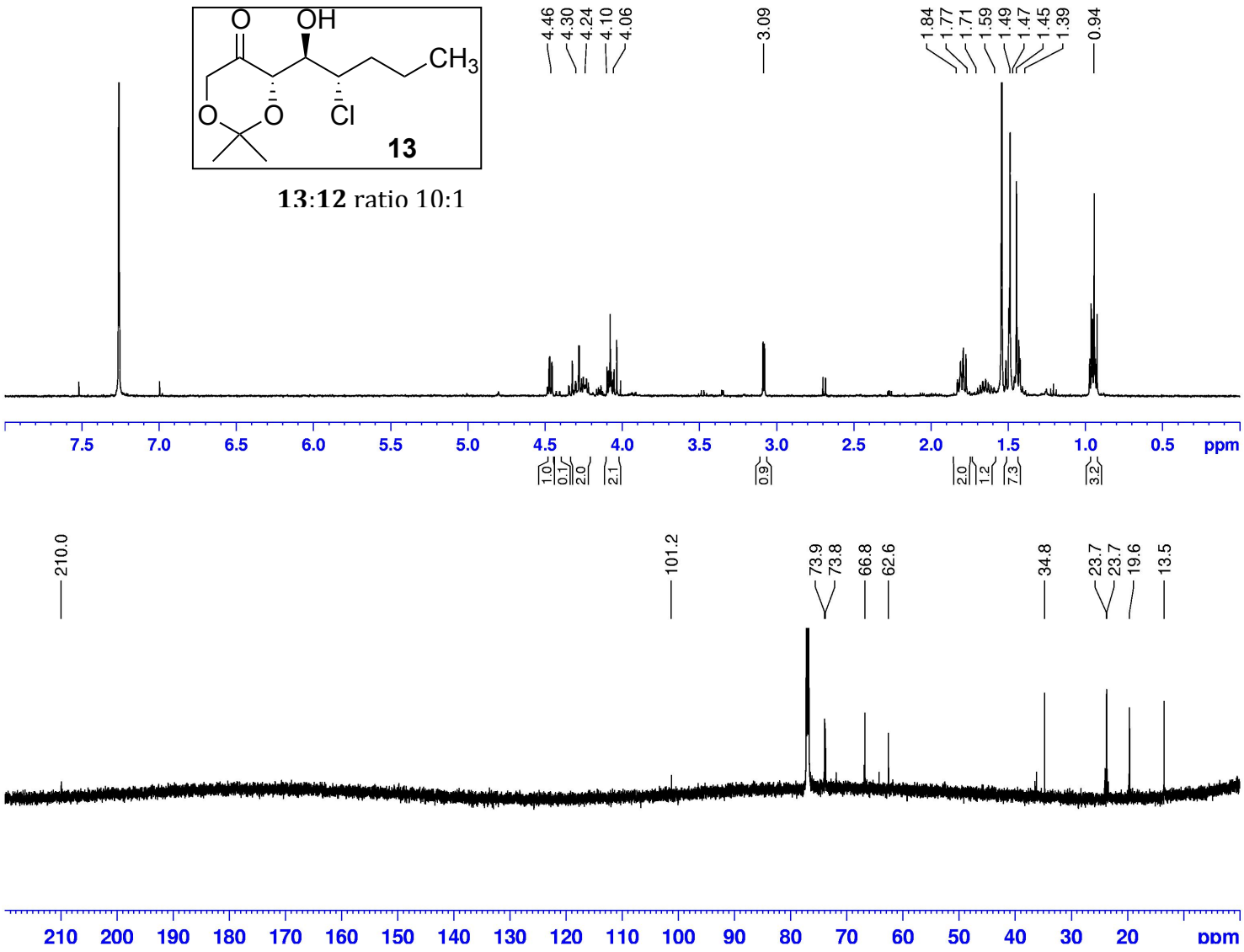
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.072	VV	0.1889	4764.59863	386.65536	49.9118
2	5.235	VV	0.2476	4781.43115	299.21729	50.0882



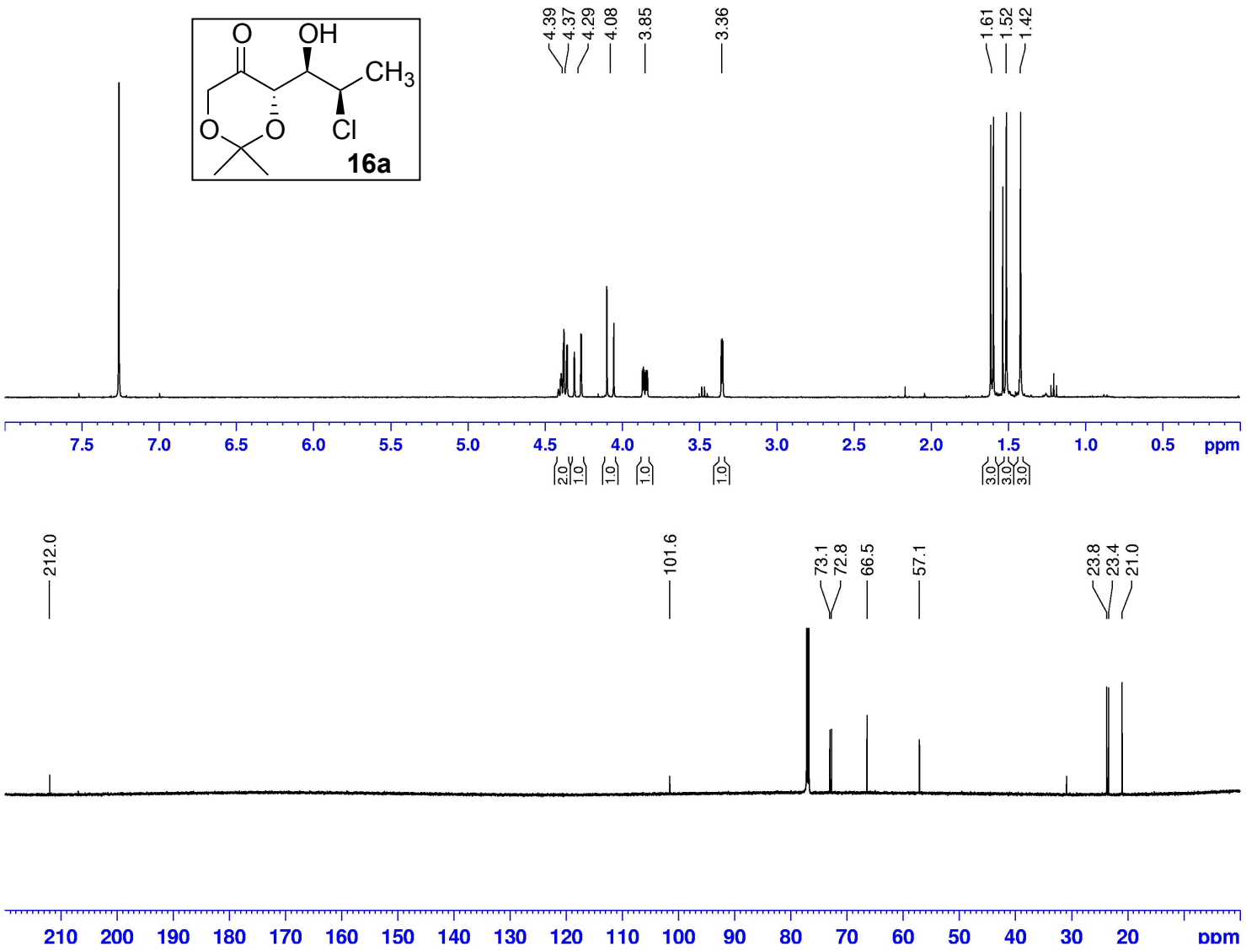
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.071	MM T	0.2195	264.70990	20.09658	1.2708
2	5.205	MF T	0.2633	2.05658e4	1301.97021	98.7292

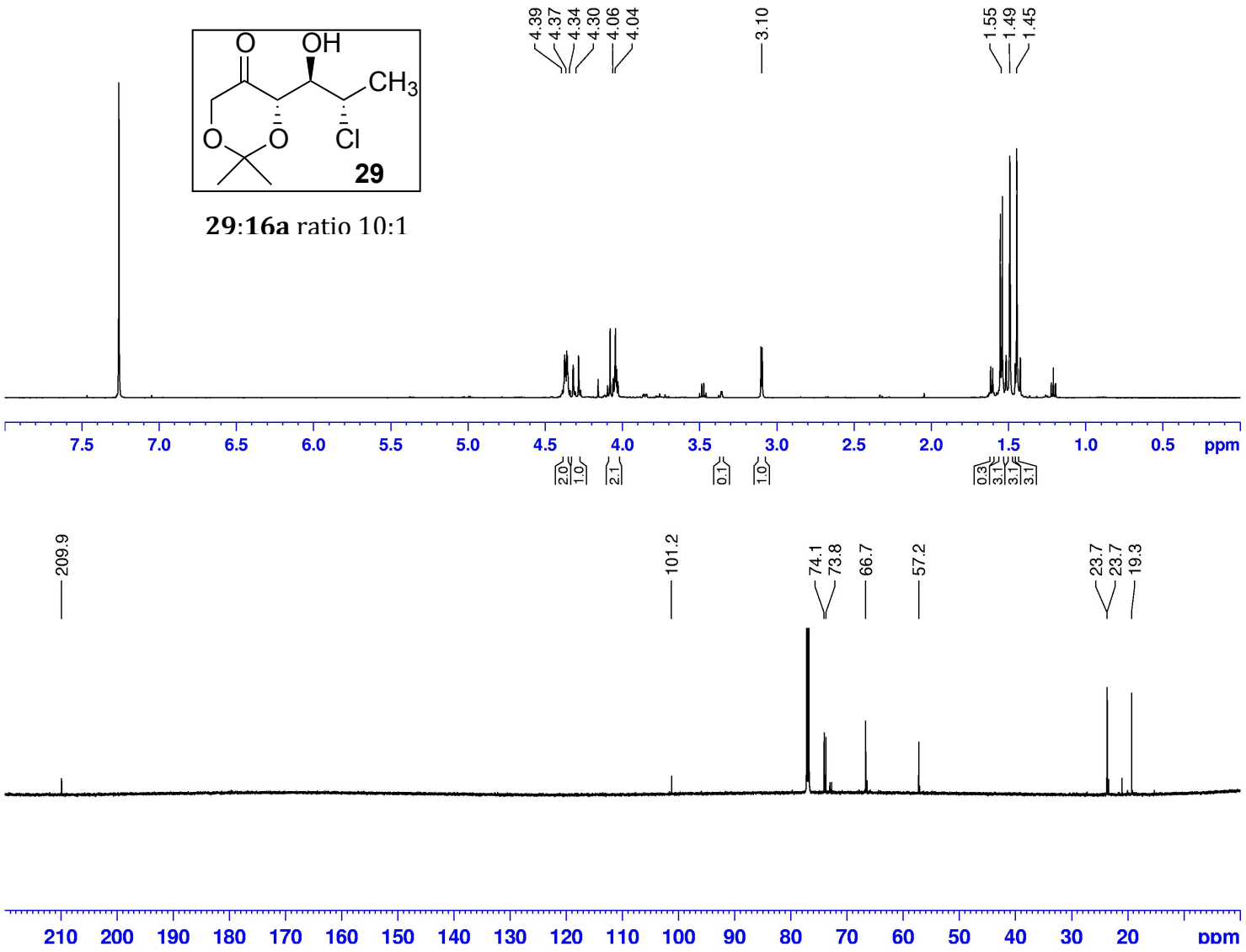
6. NMR SPECTRA

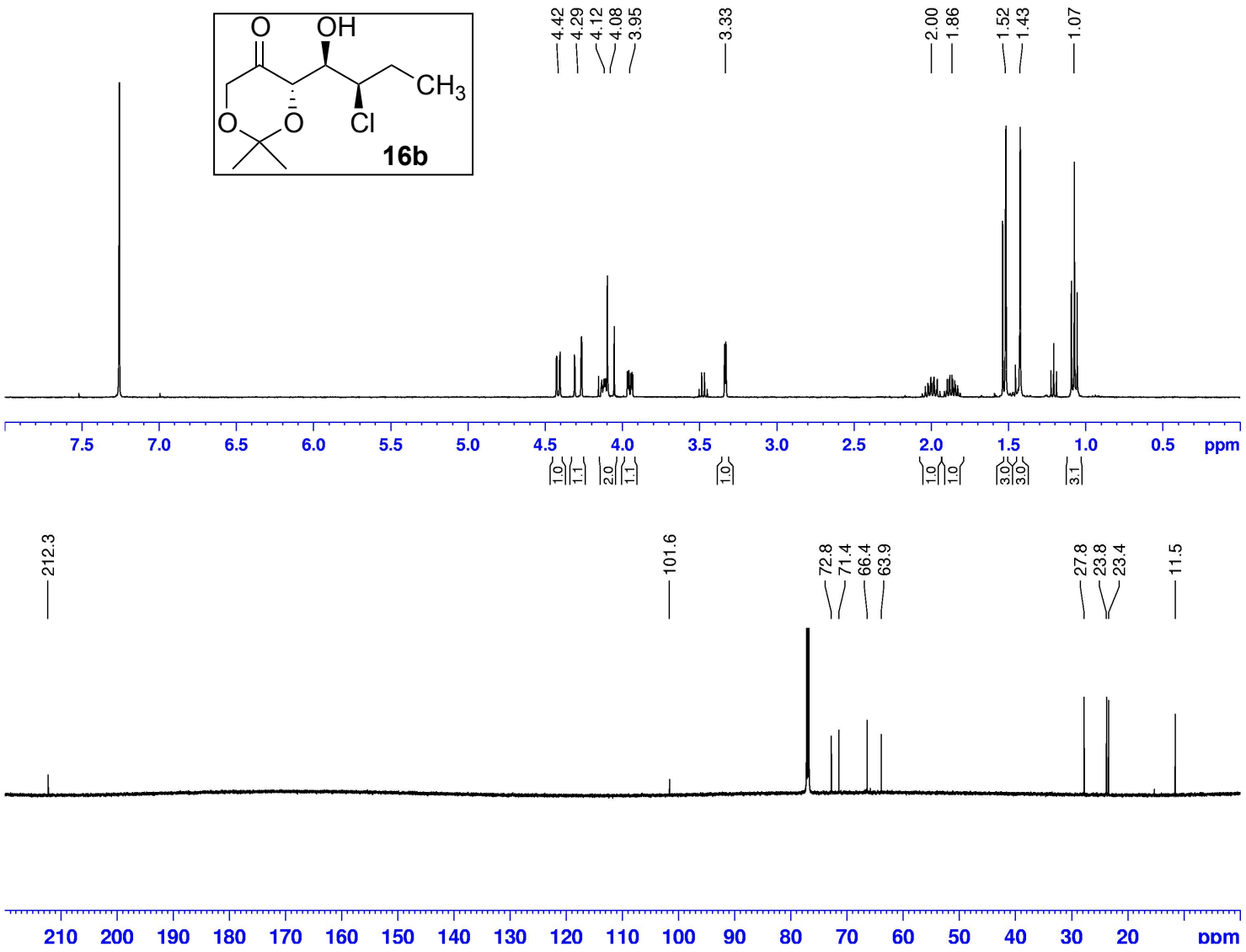


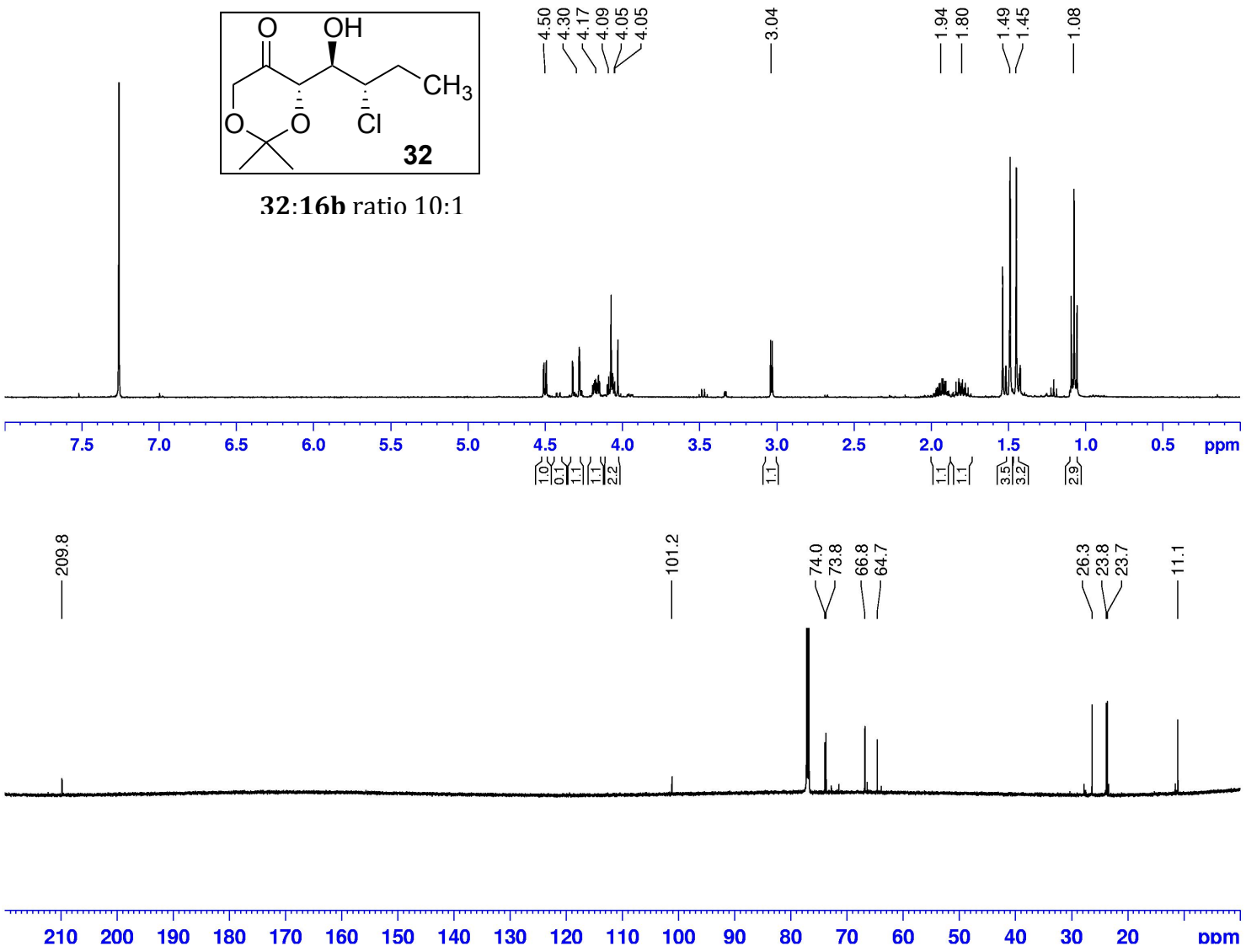


13:**12** ratio 10:1

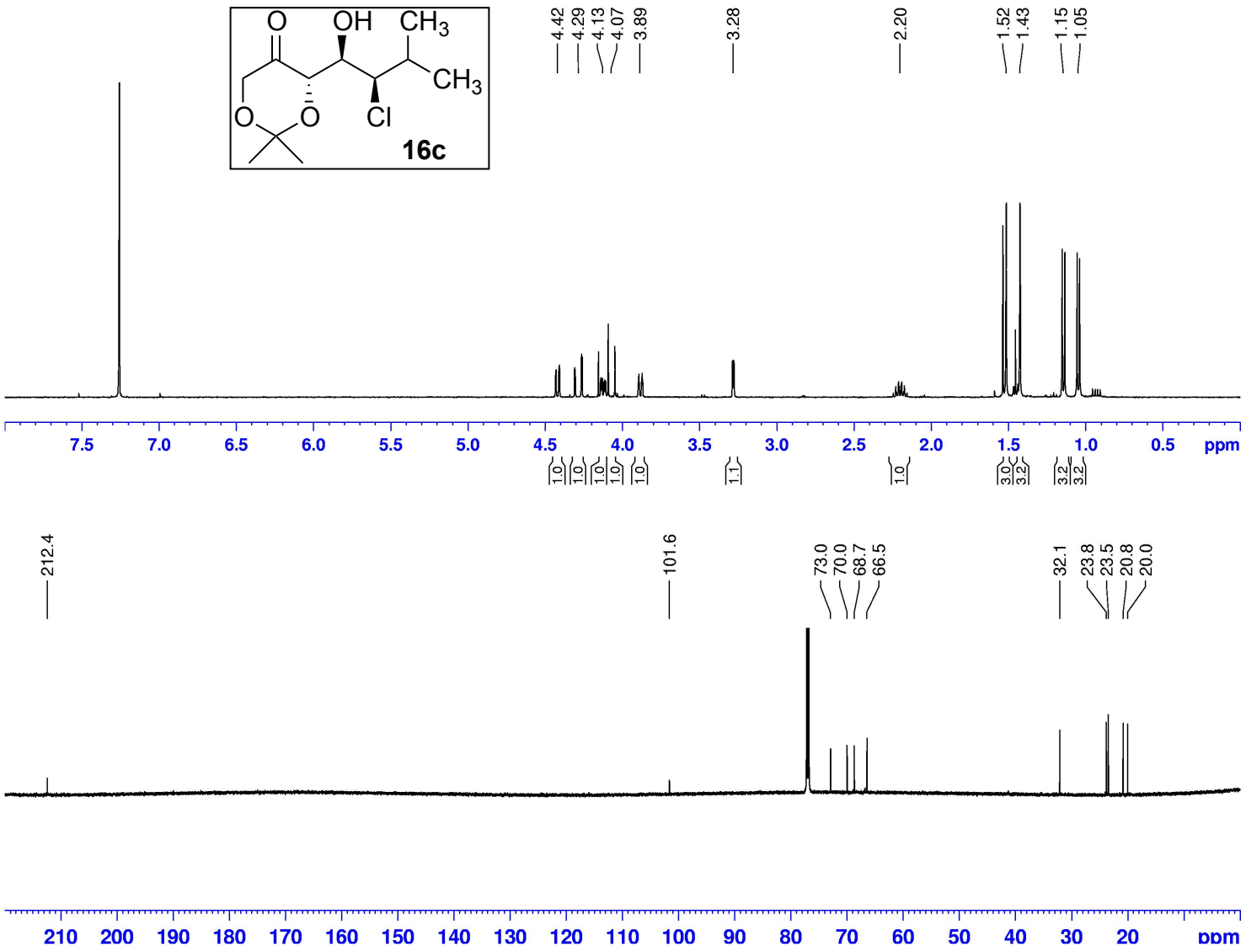

O
OH
CH3
O
O
Cl
16a
4.39
4.37
4.29
4.08
3.85
3.36
1.61
1.52
1.42
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.0
1.0
1.0
1.0
1.0
3.0
3.0
3.0
212.0
101.6
73.1
72.8
66.5
57.1
23.8
23.4
21.0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

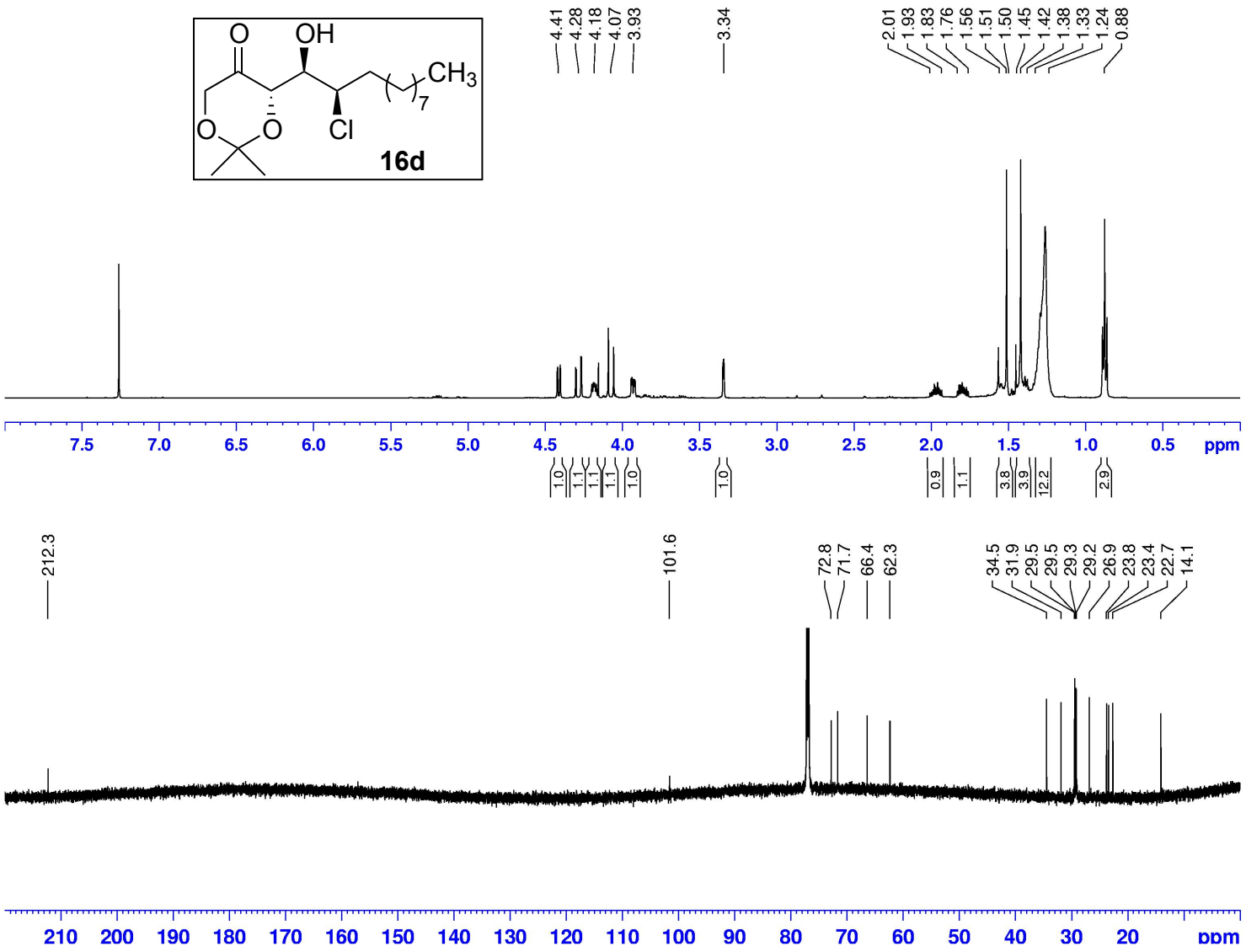

O
OH
CH3
O
O
Cl
29
29:16a ratio 10:1
4.39
4.37
4.34
4.30
4.06
4.04
3.10
1.55
1.49
1.45
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
209.9
101.2
74.1
73.8
66.7
57.2
23.7
23.7
19.3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

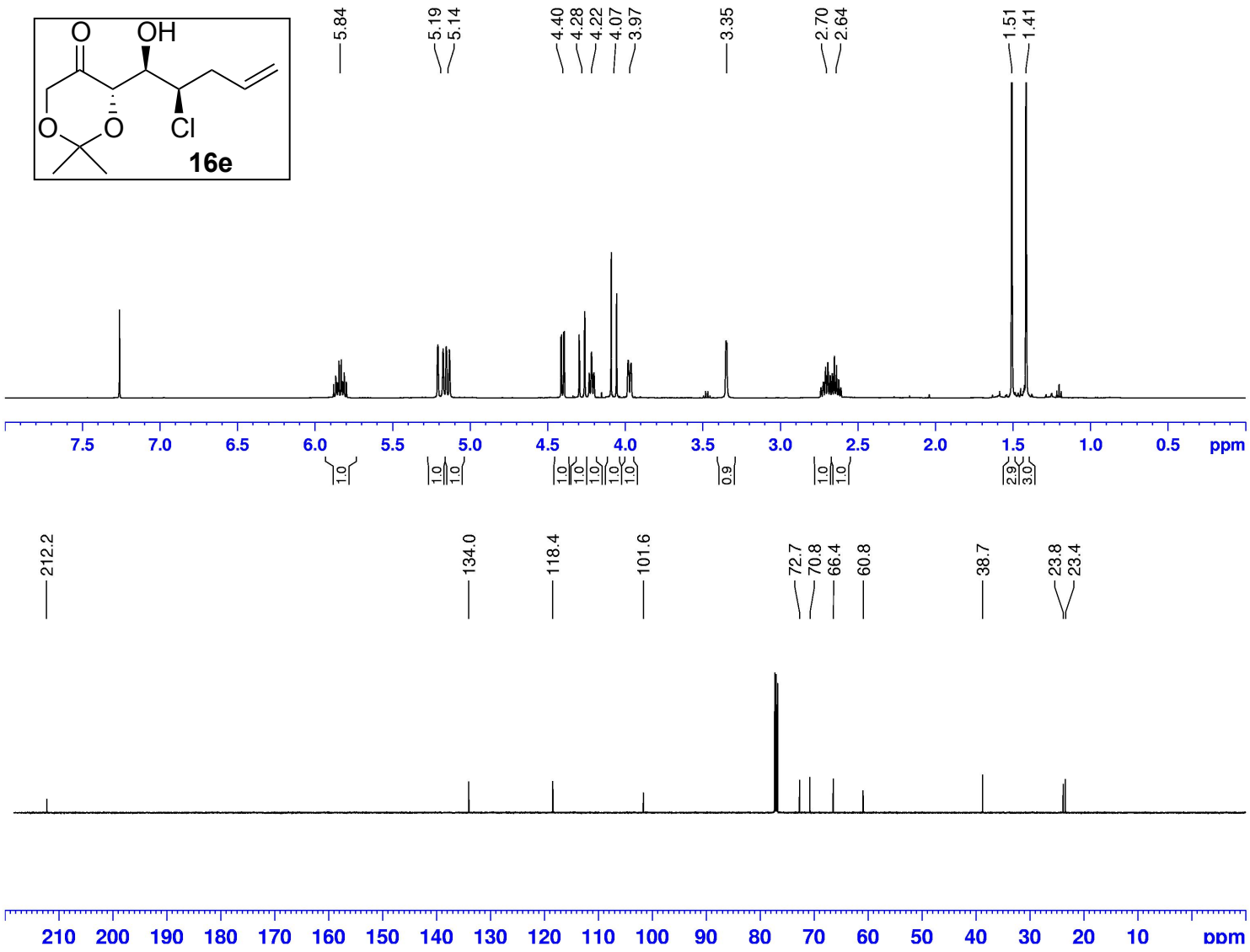

O
OH
CH3
O
O
Cl
16b
4.42
4.29
4.12
4.08
3.95
3.33
2.00
1.86
1.52
1.43
1.07
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.0
1.1
2.0
1.1
1.0
1.0
1.0
3.0
3.0
3.1
212.3
101.6
72.8
71.4
66.4
63.9
27.8
23.8
23.4
11.5
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

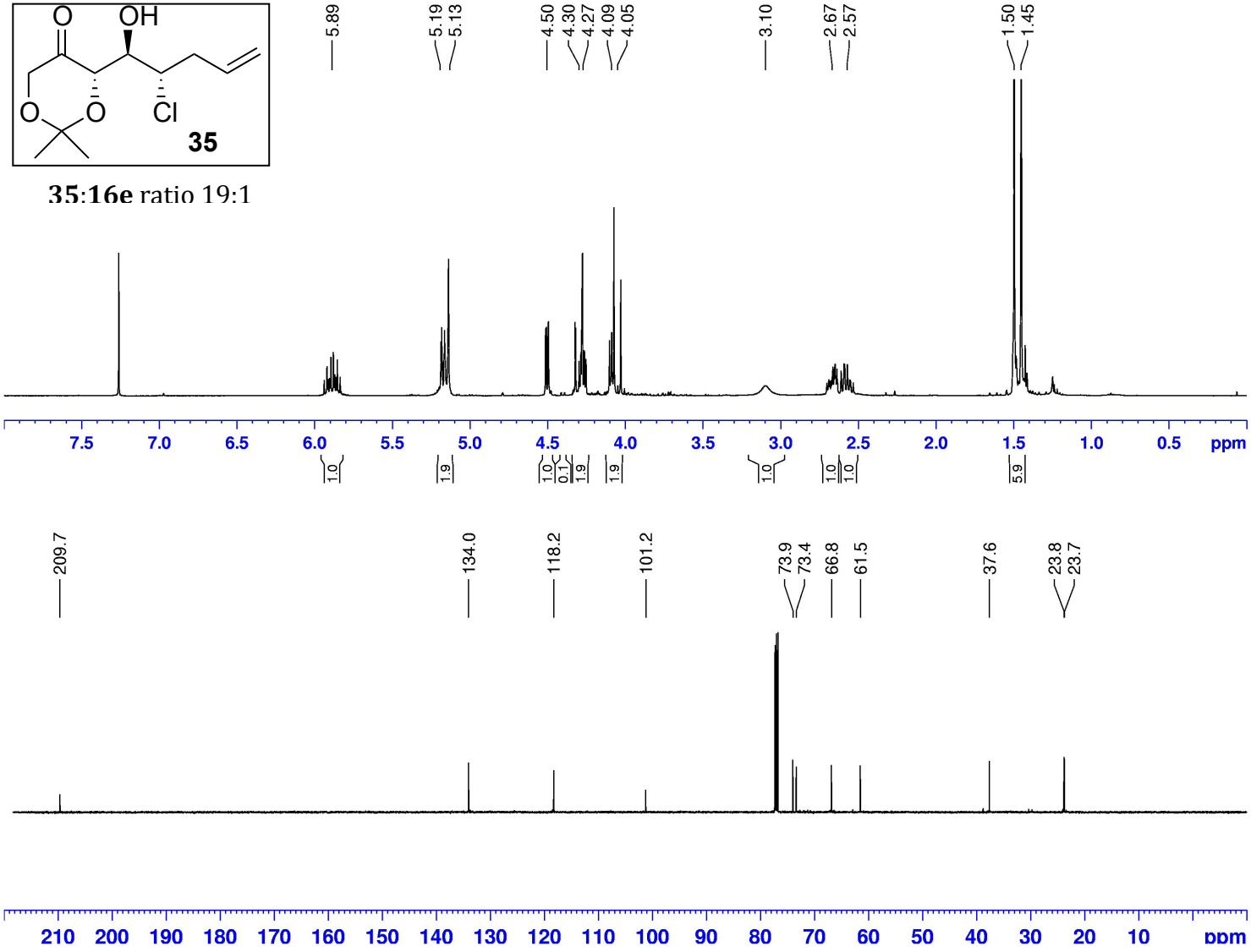


32:**16b** ratio 10:1

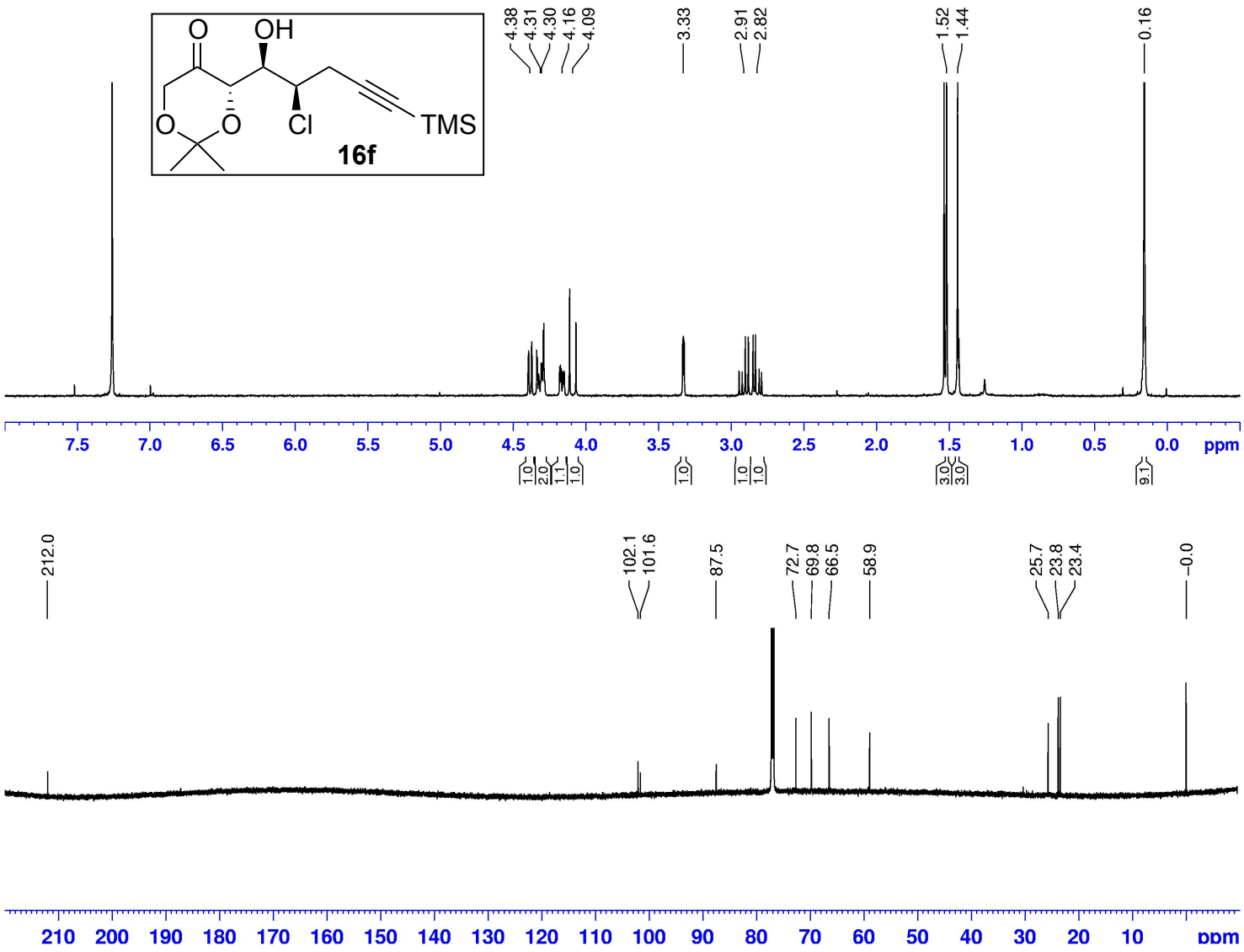

O
OH
CH3
CH3
O
O
Cl
16c
4.42
4.29
4.13
4.07
3.89
3.28
2.20
1.52
1.43
1.15
1.05
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
212.4
101.6
73.0
70.0
68.7
66.5
32.1
23.8
23.5
20.8
20.0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

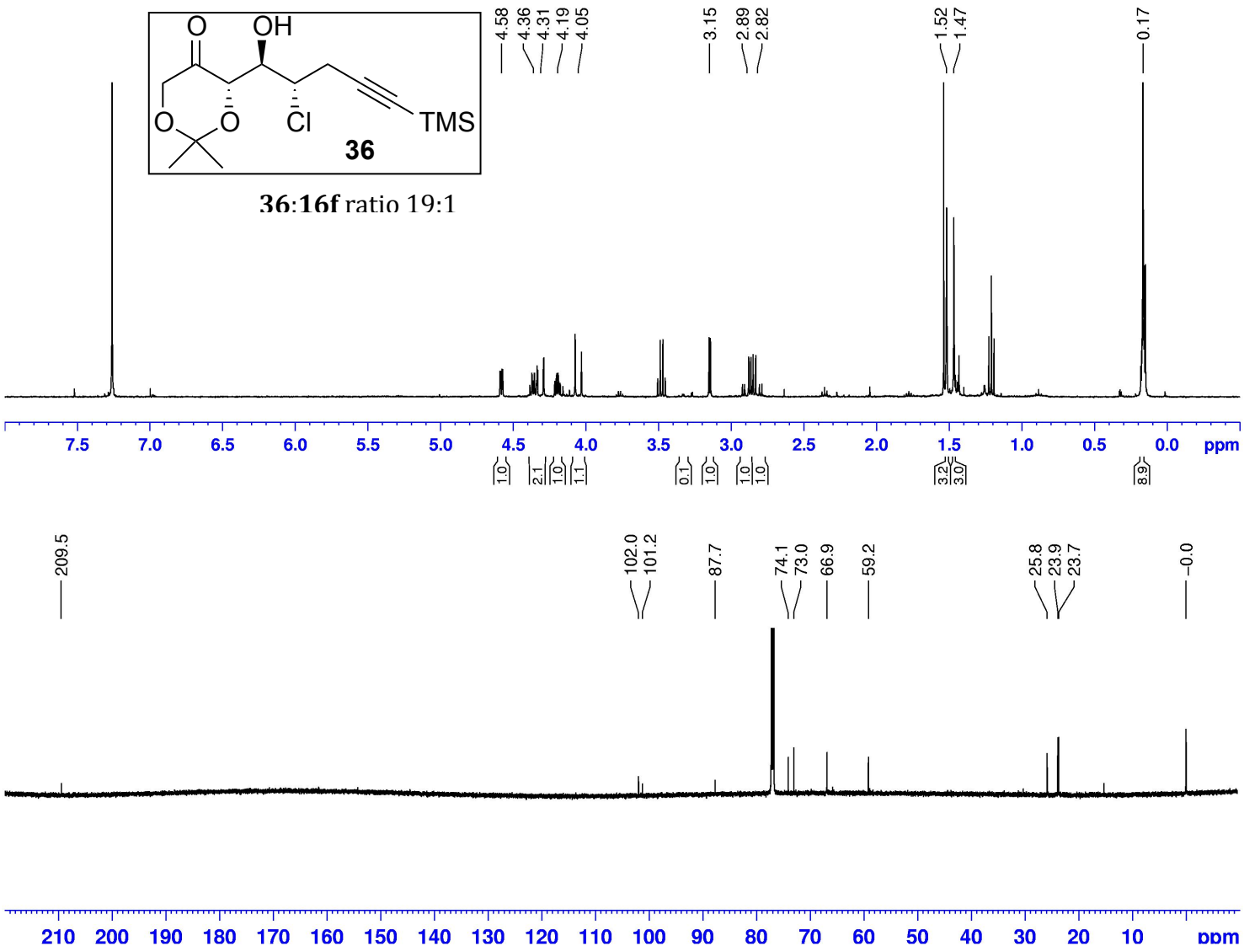

O
OH
CH3
7
O
O
Cl
16d
4.41
4.28
4.18
4.07
3.93
3.34
2.01
1.93
1.83
1.76
1.56
1.51
1.50
1.45
1.42
1.38
1.33
1.24
0.88
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.0
1.1
1.1
1.1
1.0
1.0
0.9
1.1
3.8
3.9
12.2
2.9
212.3
101.6
72.8
71.7
66.4
62.3
34.5
31.9
29.5
29.5
29.3
29.2
26.9
23.8
23.4
22.7
14.1
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


O
OH
O
O
Cl
16e
5.84
5.19
5.14
4.40
4.28
4.22
4.07
3.97
3.35
2.70
2.64
1.51
1.41
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
212.2
134.0
118.4
101.6
72.7
70.8
66.4
60.8
38.7
23.8
23.4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

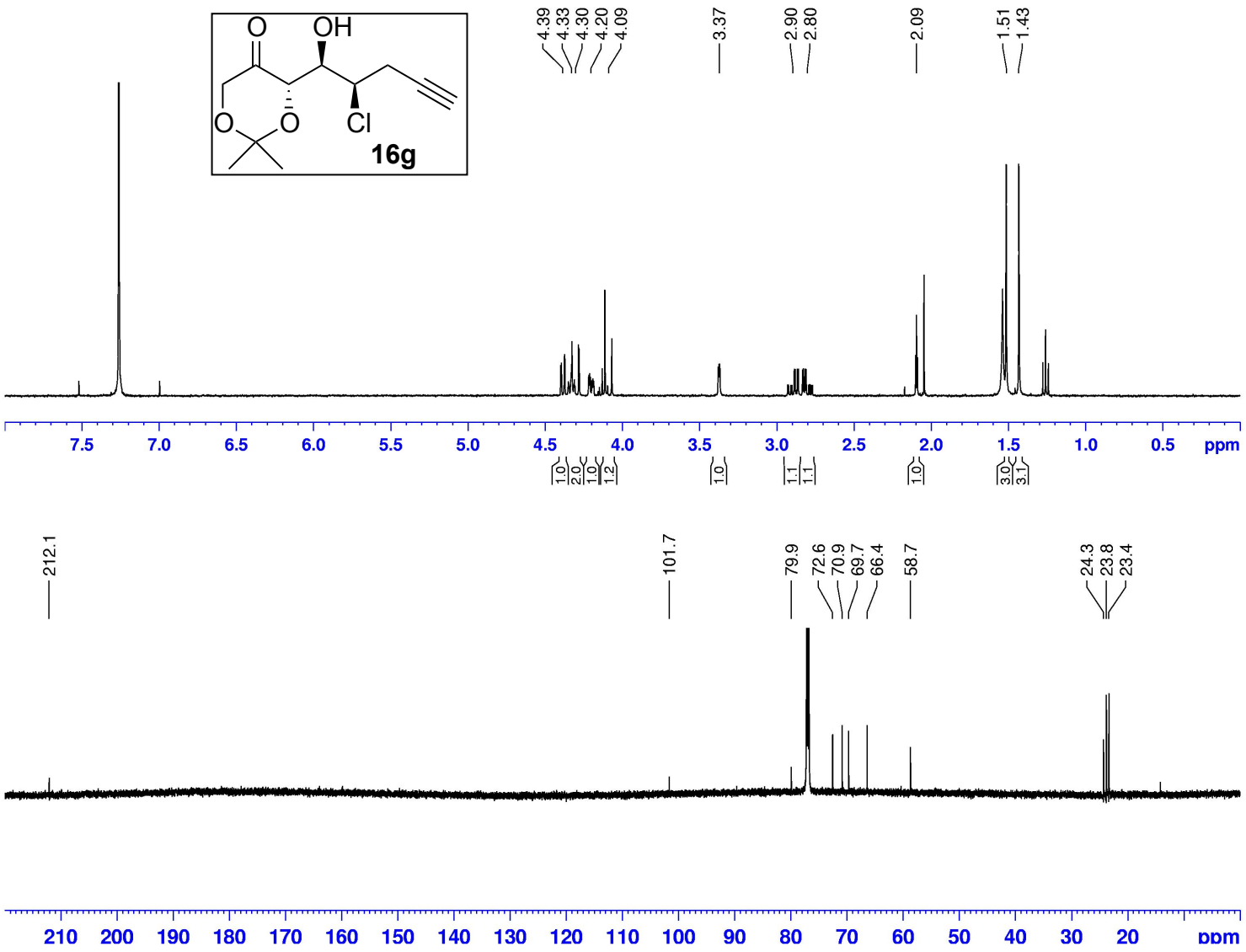


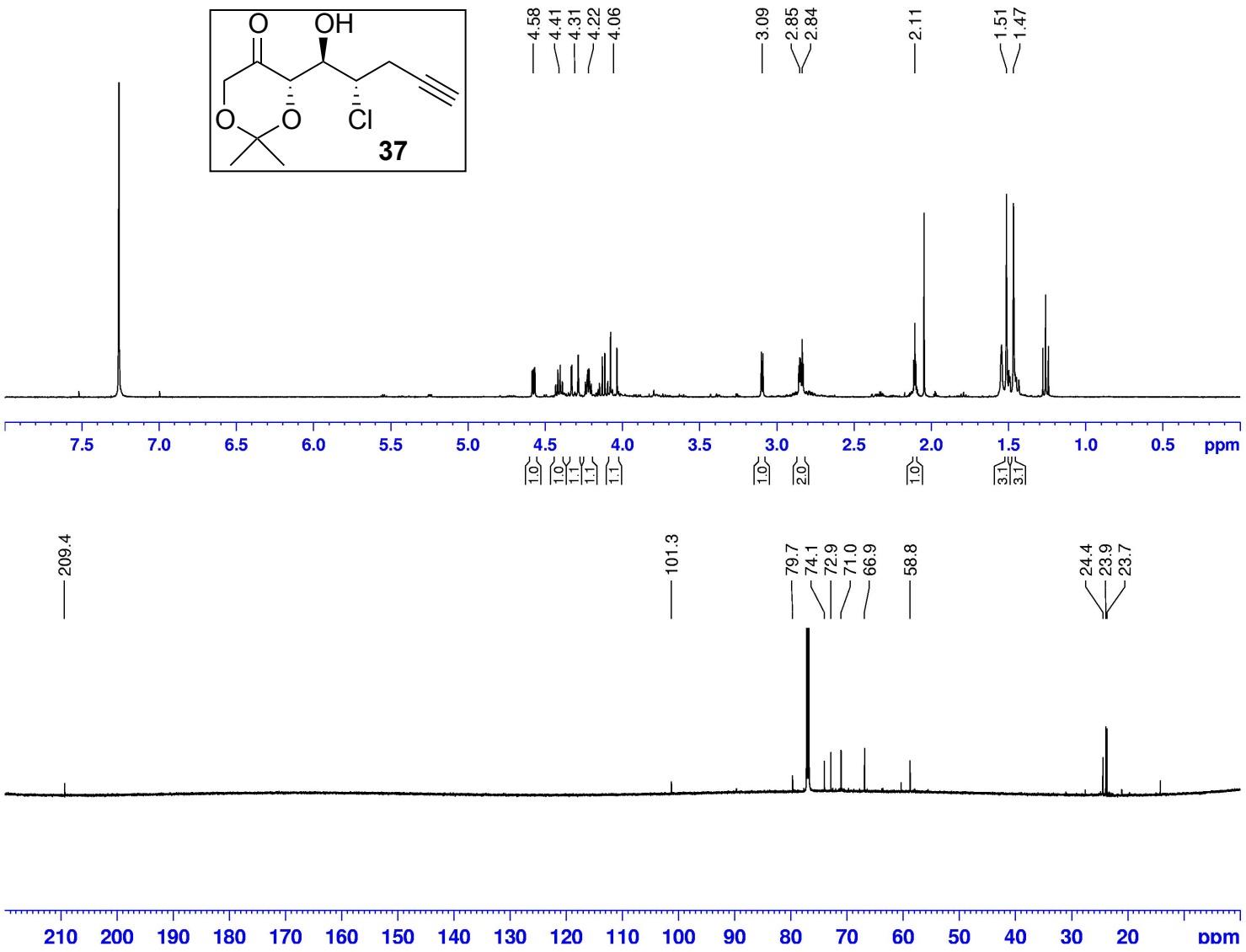
35:**16e** ratio 19:1

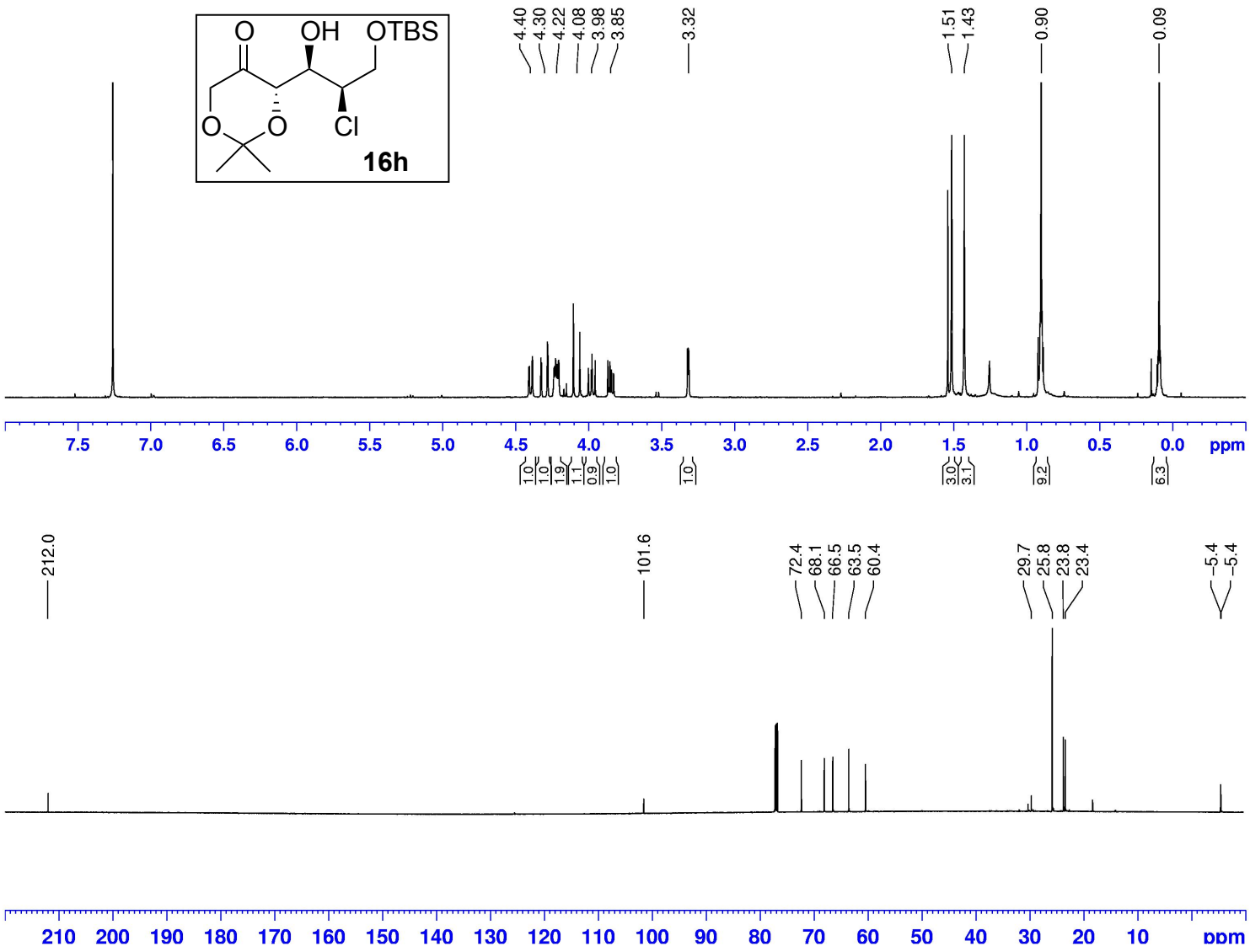

O
OH
O
O
Cl
TMS
16f
4.38
4.31
4.30
4.16
4.09
3.33
2.91
2.82
1.52
1.44
0.16
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
212.0
102.1
101.6
87.5
72.7
69.8
66.5
58.9
25.7
23.8
23.4
-0.0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

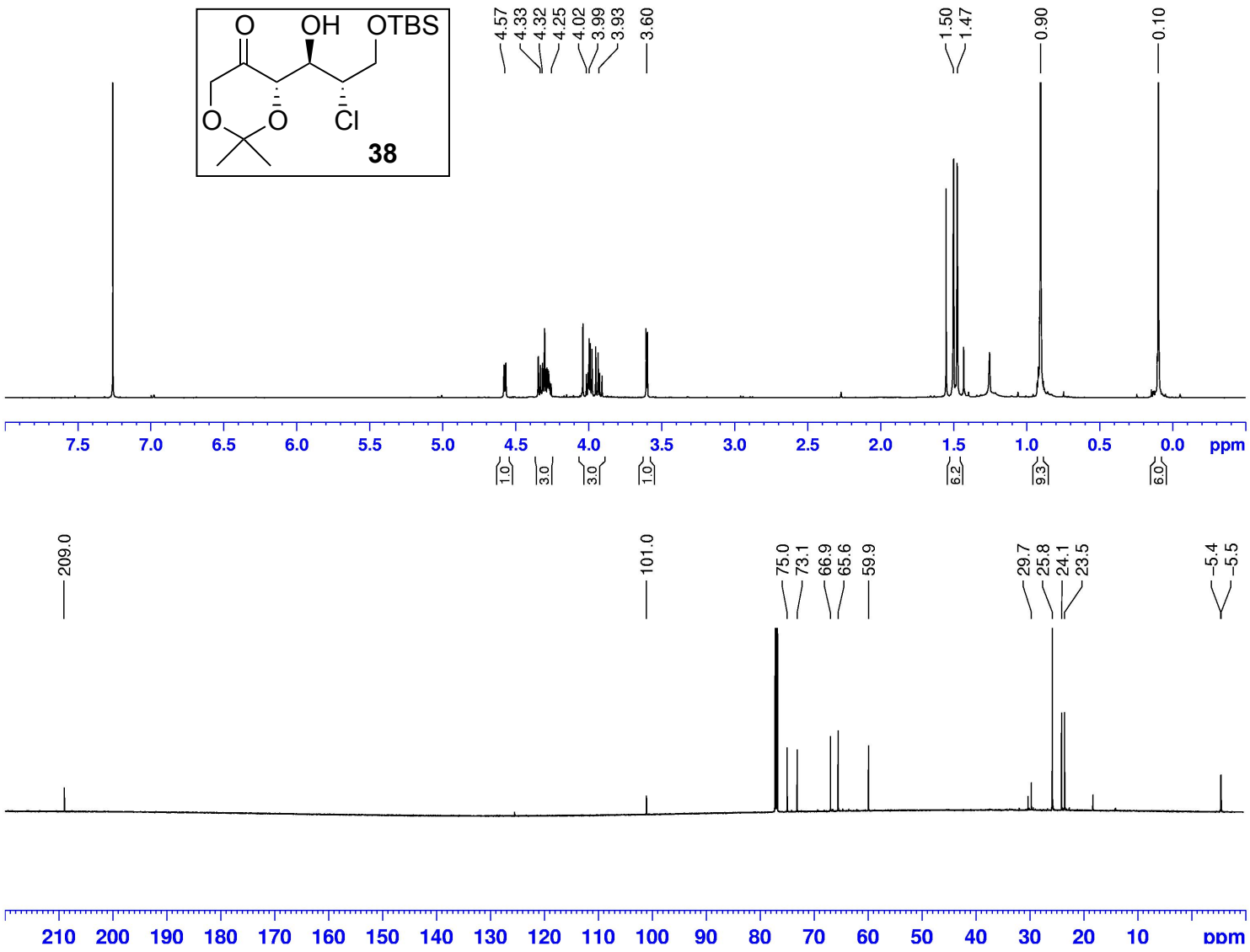


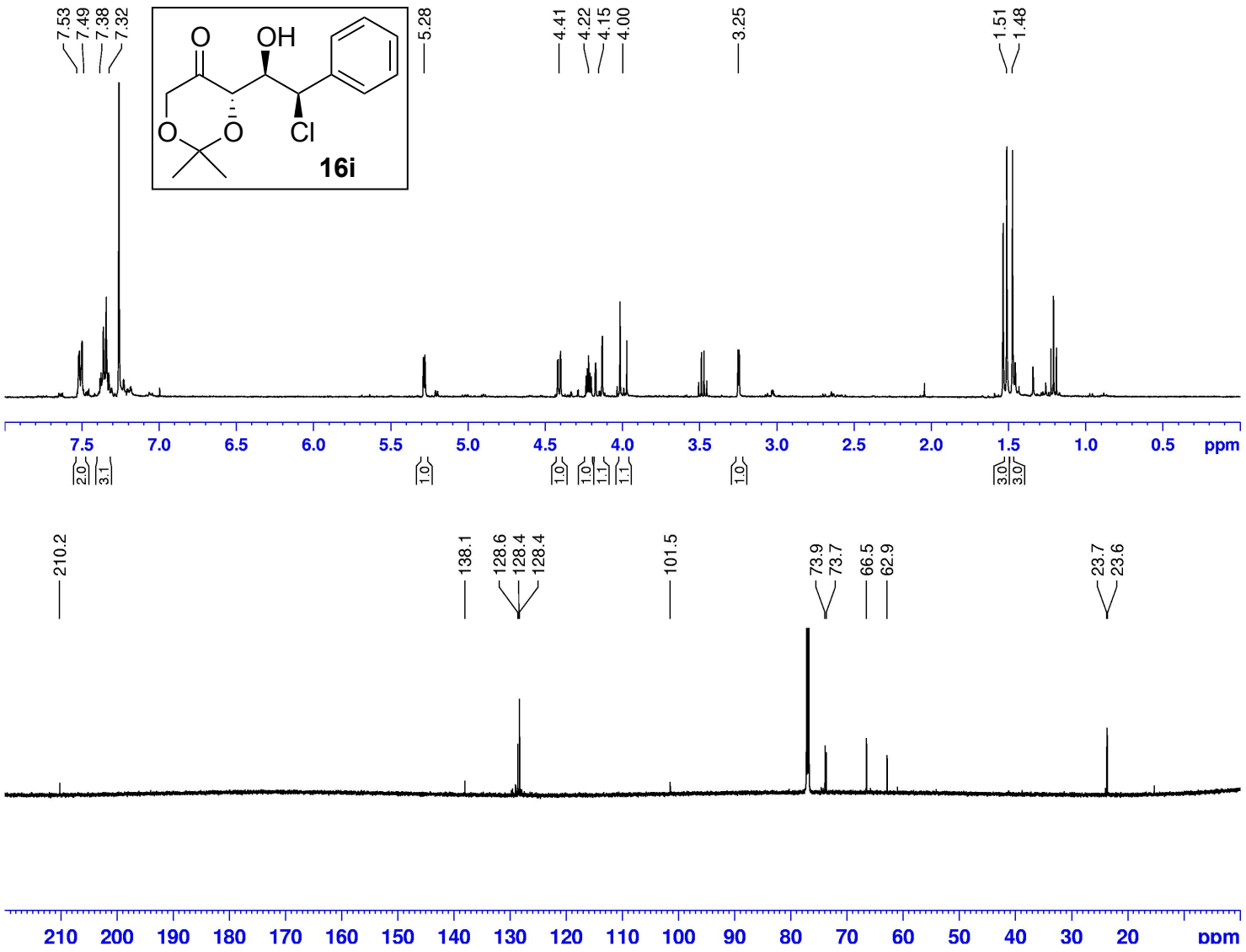
36:**16f** ratio 19:1

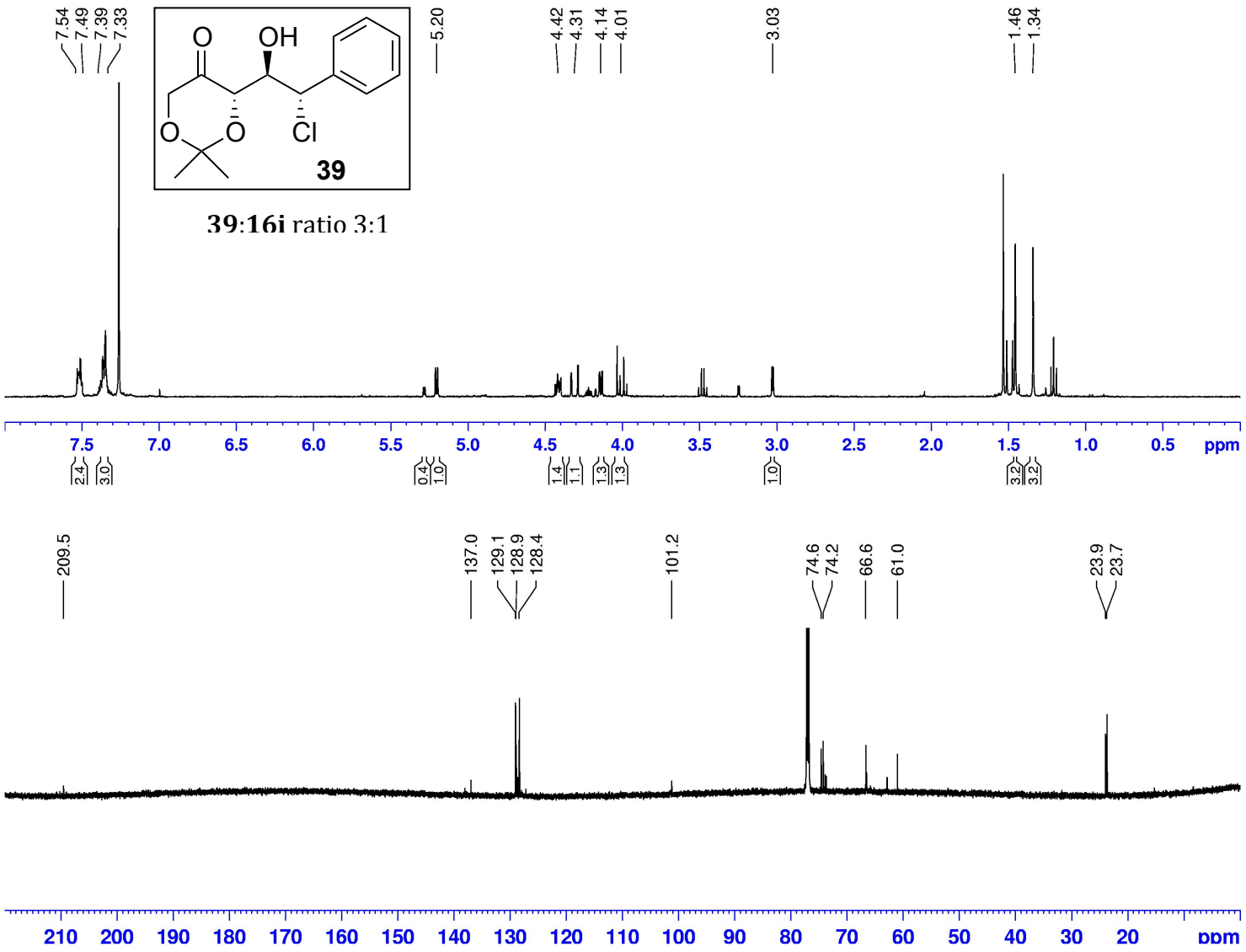

O
OH
O
O
Cl
16g
4.39
4.33
4.30
4.20
4.09
3.37
2.90
2.80
2.09
1.51
1.43
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.0
2.0
1.0
1.2
1.0
1.1
1.1
1.0
3.0
3.1
212.1
101.7
79.9
72.6
70.9
69.7
66.4
58.7
24.3
23.8
23.4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


O
OH
O
O
Cl
37
4.58
4.41
4.31
4.22
4.06
3.09
2.85
2.84
2.11
1.51
1.47
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
209.4
101.3
79.7
74.1
72.9
71.0
66.9
58.8
24.4
23.9
23.7
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

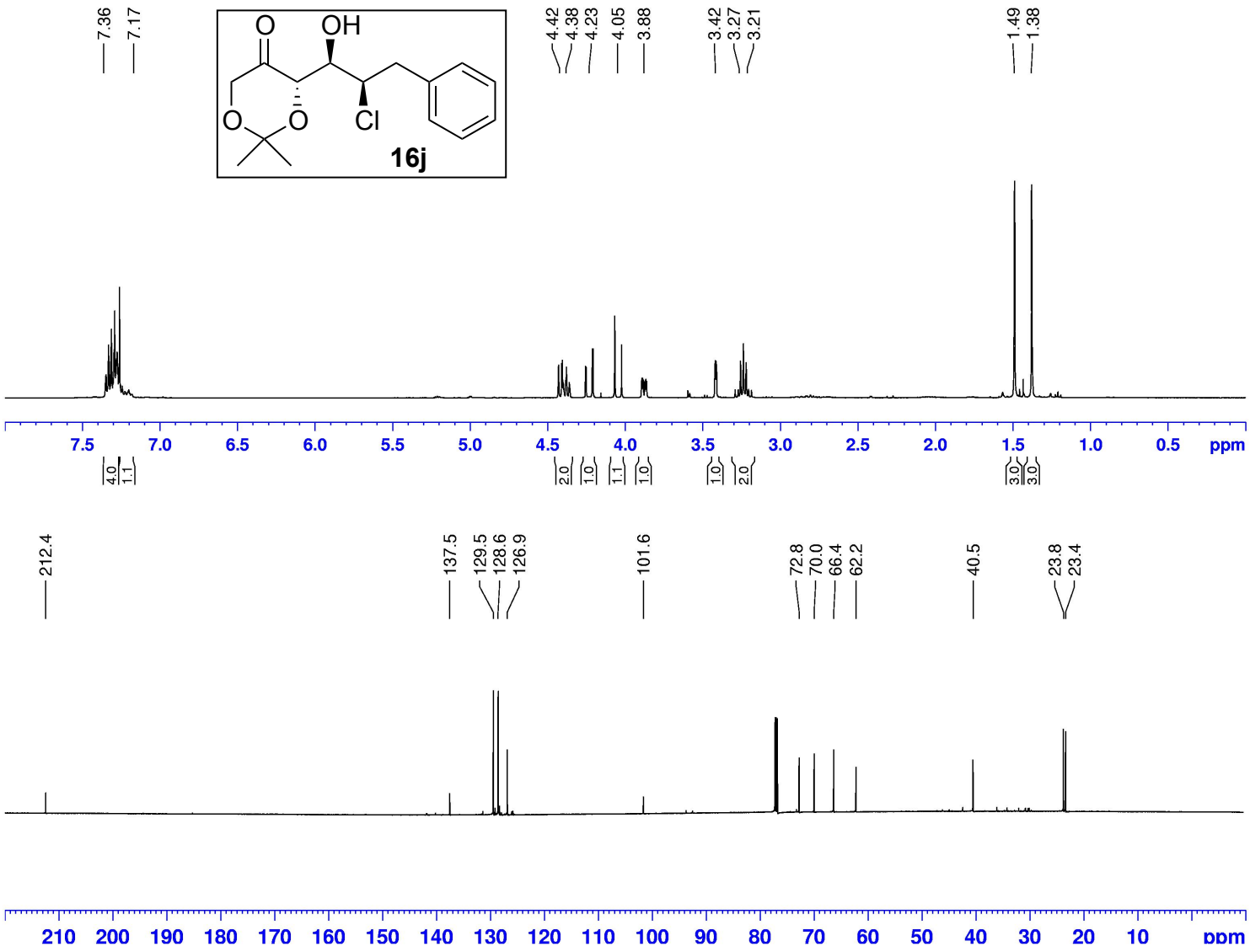

O
OH
OTBS
O
O
Cl
16h
4.40
4.30
4.22
4.08
3.98
3.85
3.32
1.51
1.43
0.90
0.09
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.0 1.0 1.9 1.1 0.9 1.0 1.0 3.0 3.1 9.2 6.3
212.0
101.6
72.4
68.1
66.5
63.5
60.4
29.7
25.8
23.8
23.4
-5.4
-5.4
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

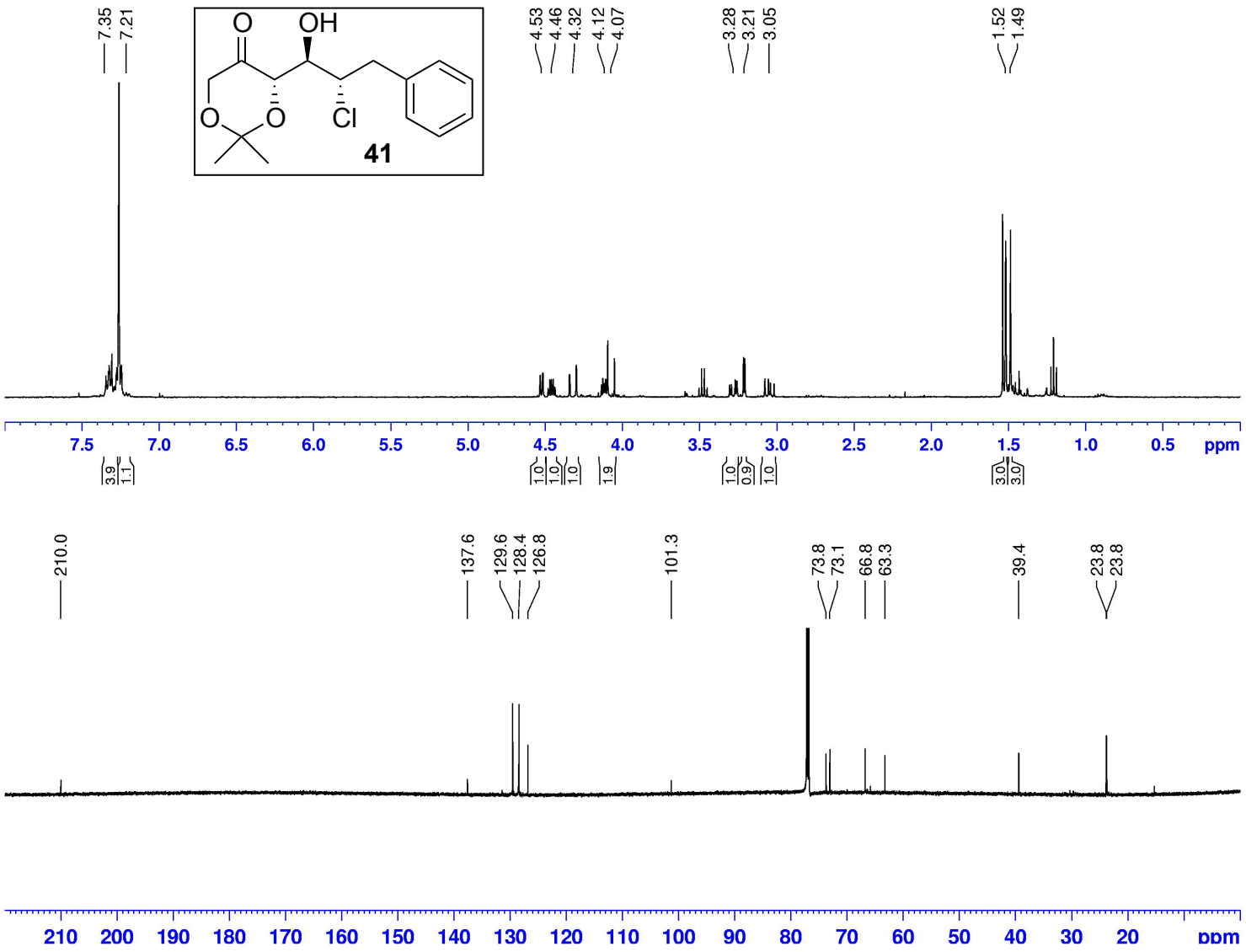

O
OH
OTBS
O
O
Cl
38
4.57
4.33
4.32
4.25
4.02
3.99
3.93
3.60
1.50
1.47
0.90
0.10
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.0
3.0
3.0
1.0
6.2
9.3
6.0
209.0
101.0
75.0
73.1
66.9
65.6
59.9
29.7
25.8
24.1
23.5
-5.4
-5.5
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

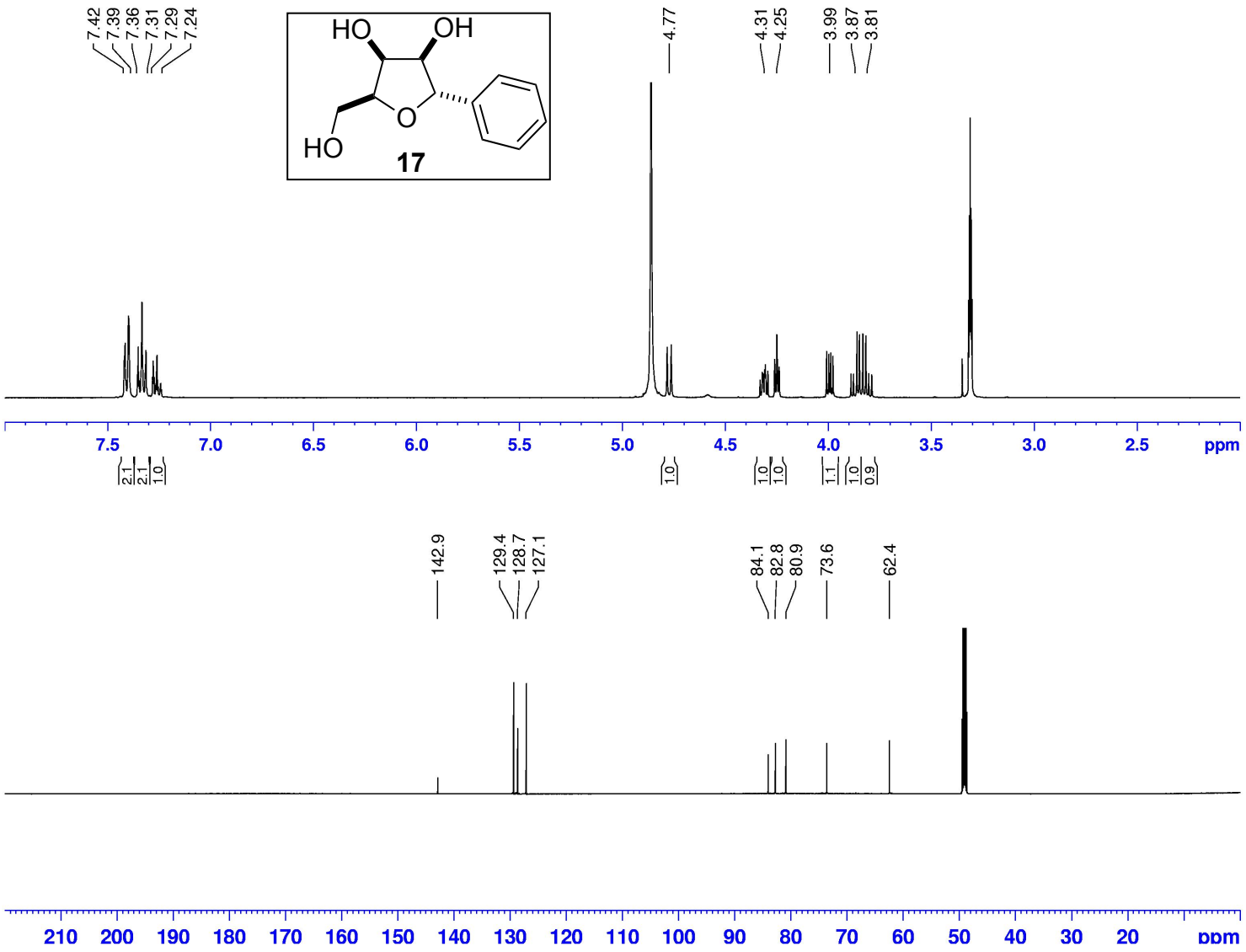

7.53
7.49
7.38
7.32
5.28
4.41
4.22
4.15
4.00
3.25
1.51
1.48
O
OH
O
O
Cl
16i
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
210.2
138.1
128.6
128.4
128.4
101.5
73.9
73.7
66.5
62.9
23.7
23.6
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

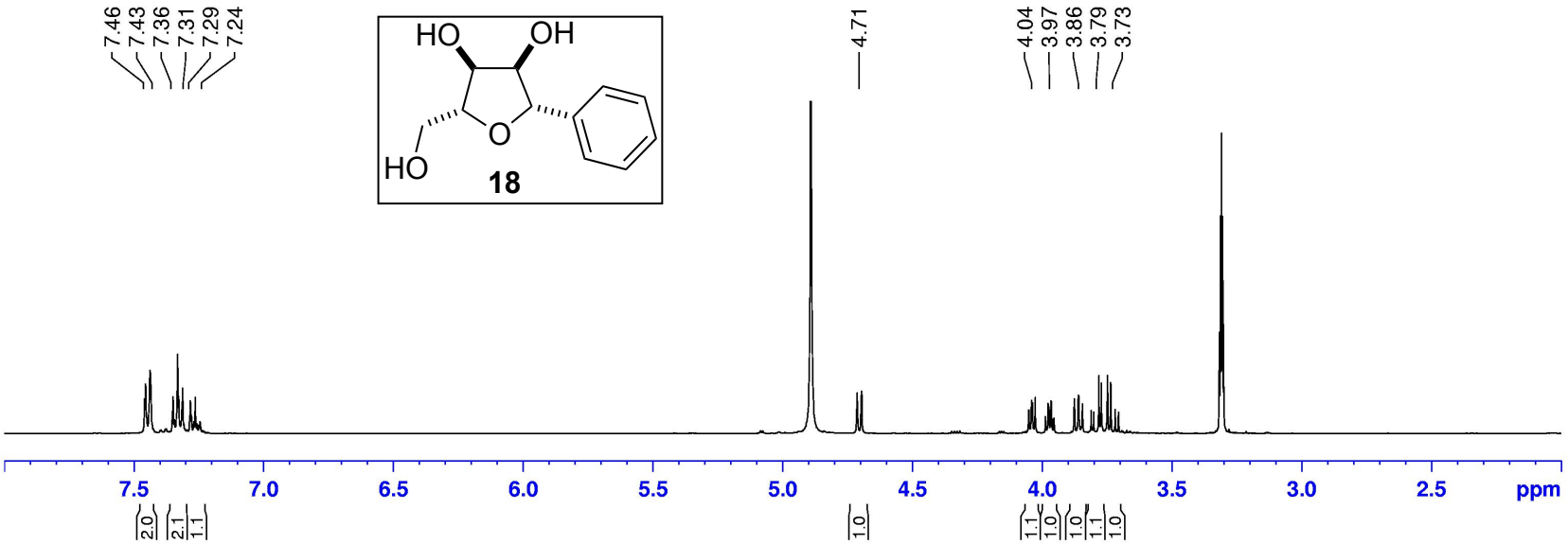


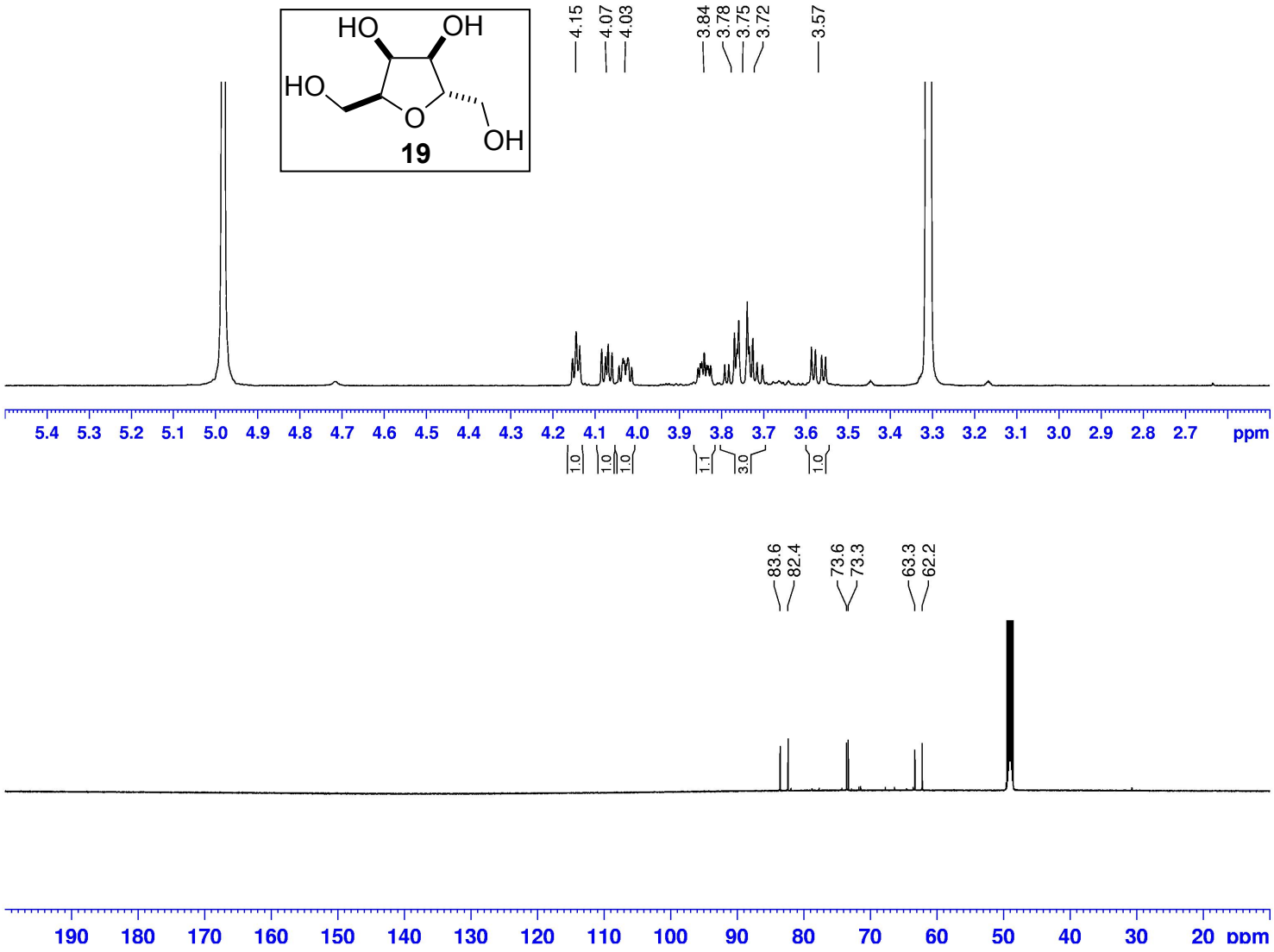
39:**16i** ratio 3:1

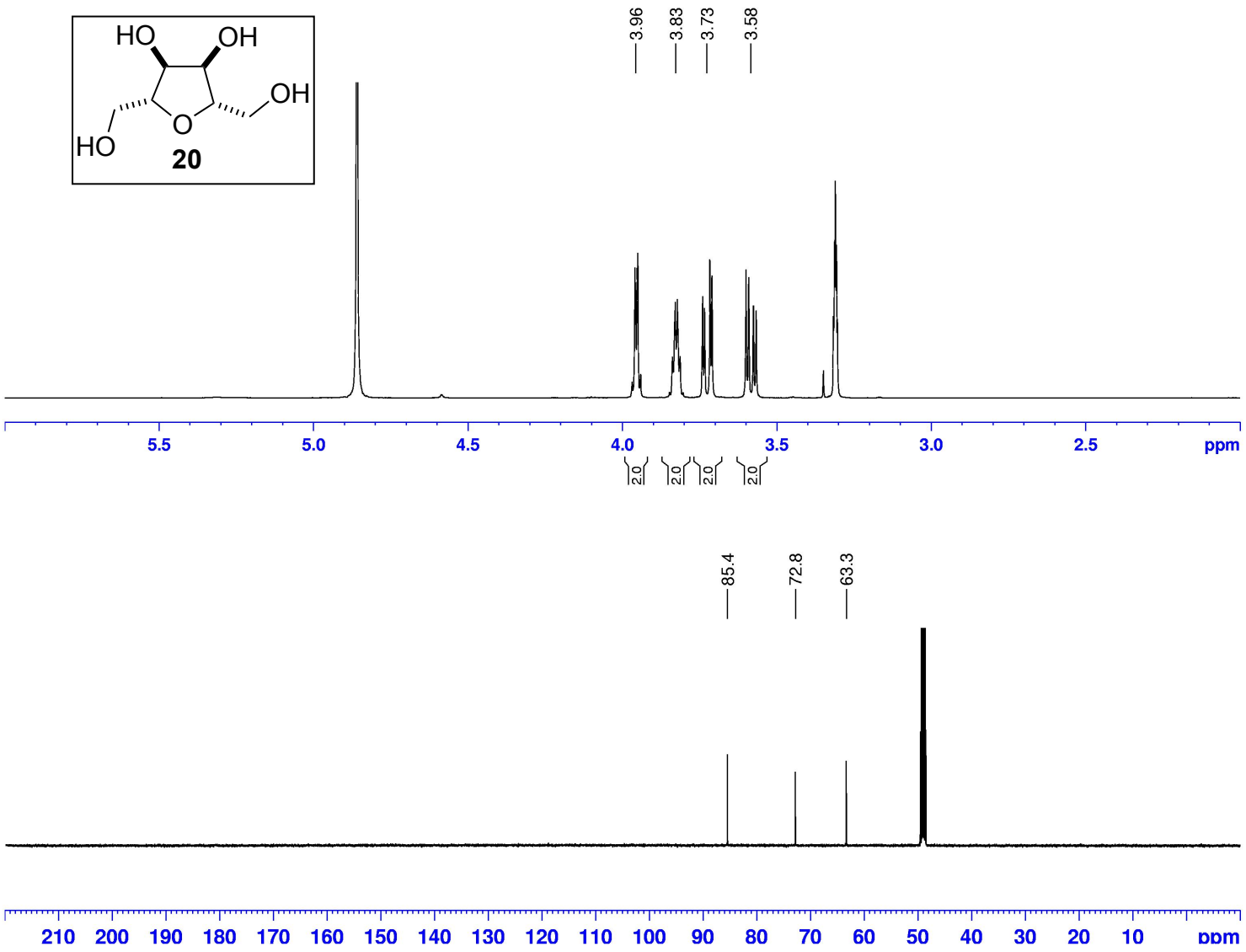

7.36
7.17
O
OH
O
O
Cl
16j
4.42
4.38
4.23
4.05
3.88
3.42
3.27
3.21
1.49
1.38
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.0
1.1
2.0
1.0
1.1
1.0
1.0
2.0
3.0
3.0
212.4
137.5
129.5
128.6
126.9
101.6
72.8
70.0
66.4
62.2
40.5
23.8
23.4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

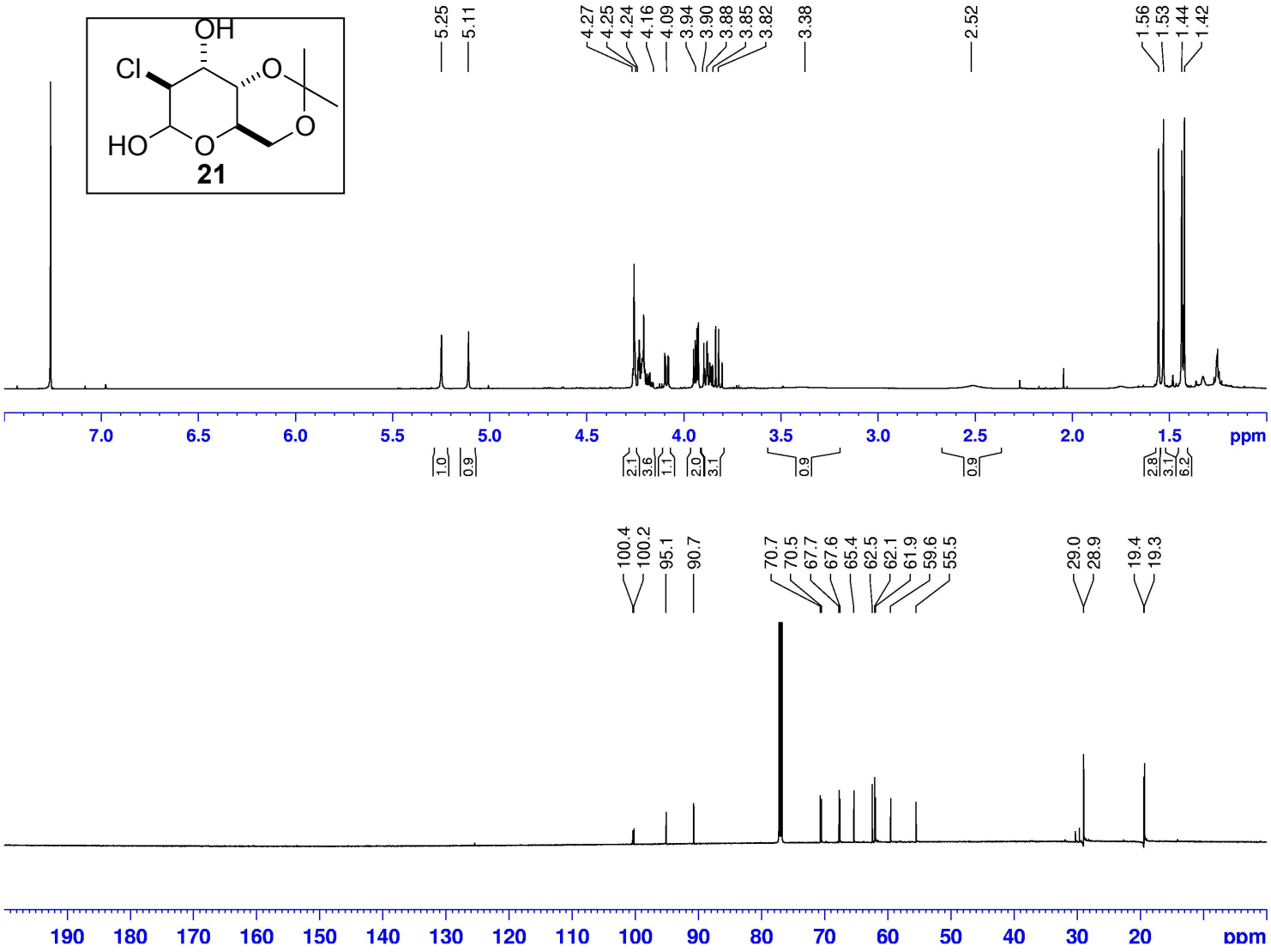

7.35
7.21
O
OH
O
O
Cl
41
4.53
4.46
4.32
4.12
4.07
3.28
3.21
3.05
1.52
1.49
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
3.9
1.1
1.0
1.0
1.0
1.9
1.0
0.9
1.0
3.0
3.0
210.0
137.6
129.6
128.4
126.8
101.3
73.8
73.1
66.8
63.3
39.4
23.8
23.8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

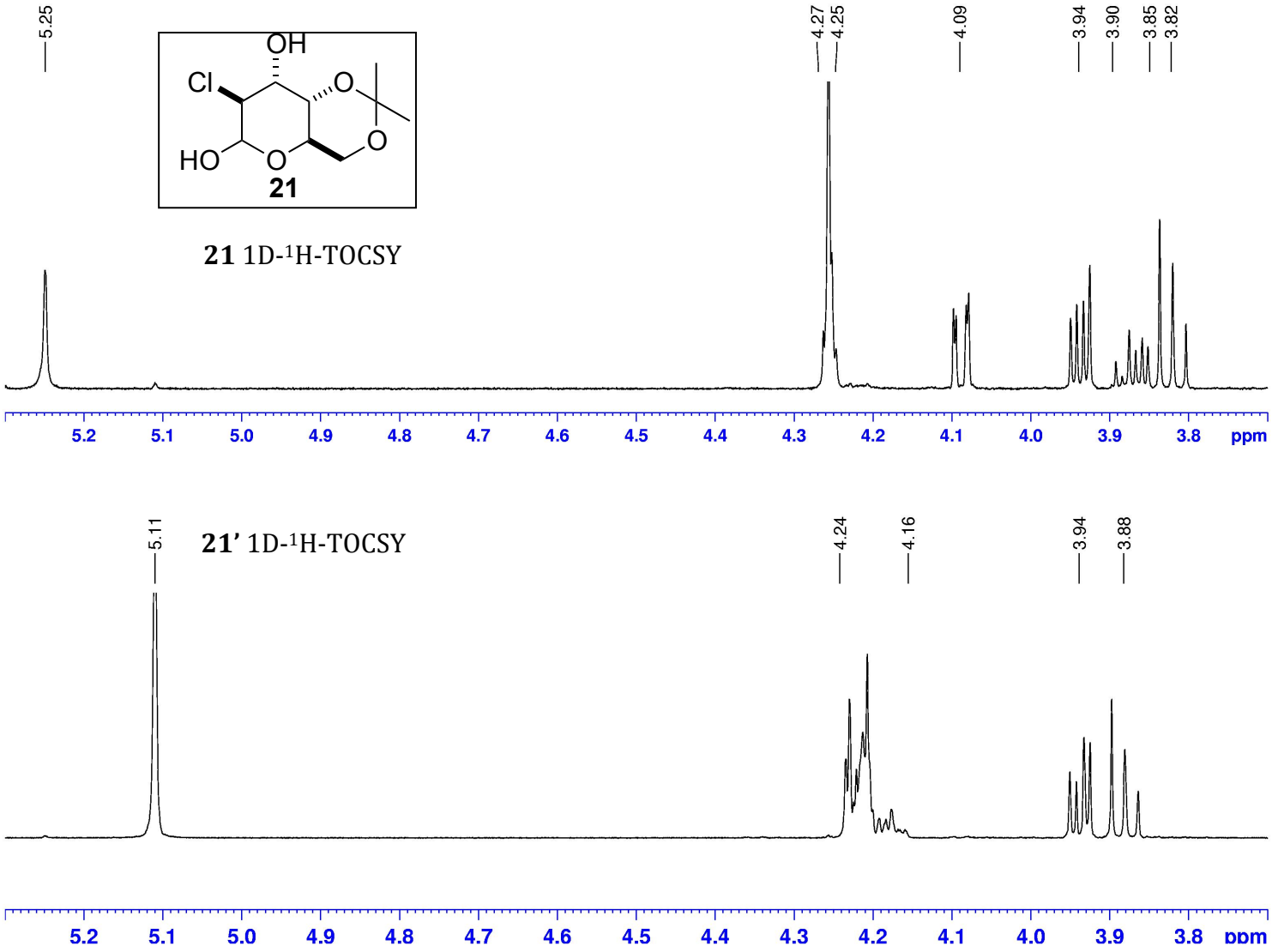

7.42
7.39
7.36
7.31
7.29
7.24
HO
OH
O
HO
17
4.77
4.31
4.25
3.99
3.87
3.81
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm
2.1
2.1
1.0
1.0
1.0
1.0
1.0
1.1
1.0
0.9
142.9
129.4
128.7
127.1
84.1
82.8
80.9
73.6
62.4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


7.46
7.43
7.36
7.31
7.29
7.24
HO
OH
O
HO
18
4.71
4.04
3.97
3.86
3.79
3.73
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm
2.0
2.1
1.1
1.0
1.1
1.0
1.0
1.1
1.0


HO
OH
HO
O
OH
19
4.15
4.07
4.03
3.84
3.78
3.75
3.72
3.57
5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 ppm
1.0
1.0
1.0
1.1
3.0
1.0
83.6
82.4
73.6
73.3
63.3
62.2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

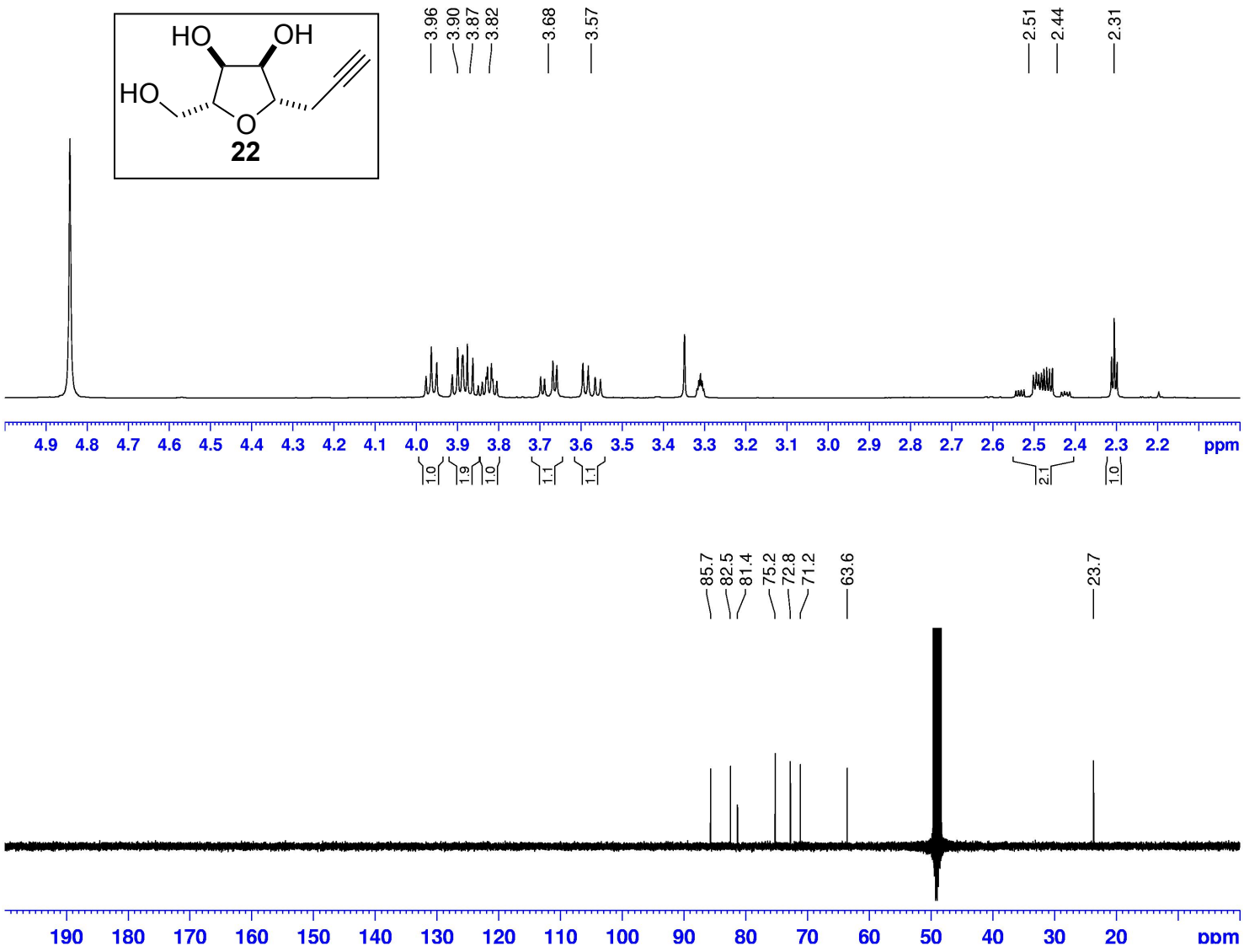

HO
OH
OH
HO
O
20
3.96
3.83
3.73
3.58
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm
2.0
2.0
2.0
2.0
85.4
72.8
63.3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

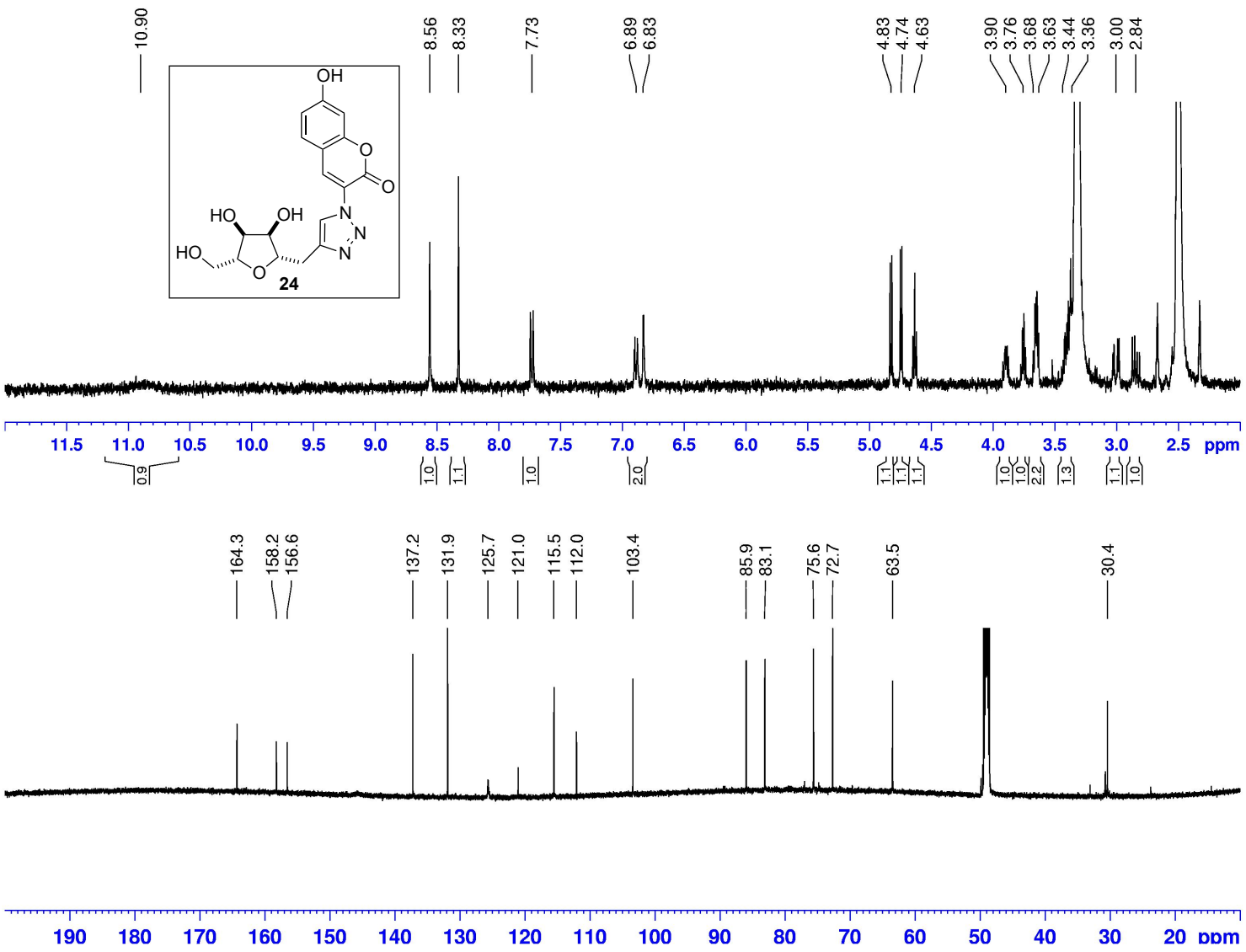

OH
Cl
O
HO
O
O
21
5.25
5.11
4.27
4.25
4.24
4.16
4.09
3.94
3.90
3.88
3.85
3.82
3.38
2.52
1.56
1.53
1.44
1.42
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
1.0
0.9
2.1
3.6
1.1
2.0
3.1
0.9
0.9
2.8
3.1
6.2
100.4
100.2
95.1
90.7
70.7
70.5
67.7
67.6
65.4
62.5
62.1
61.9
59.6
55.5
29.0
28.9
19.4
19.3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



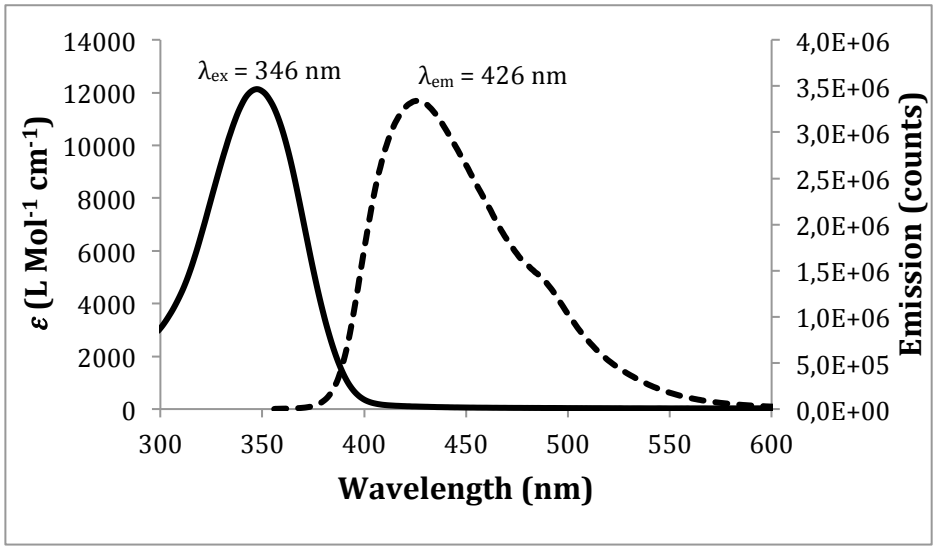
21 1D-^{1}H-TOCSY

21' 1D-^{1}H-TOCSY


HO
OH
HO
O
22
3.96
3.90
3.87
3.82
3.68
3.57
2.51
2.44
2.31
4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 ppm
1.0
1.9
1.0
1.1
1.1
2.1
1.0
85.7
82.5
81.4
75.2
72.8
71.2
63.6
23.7
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


10.90
8.56
8.33
7.73
6.89
6.83
4.83
4.74
4.63
3.90
3.76
3.68
3.63
3.44
3.36
3.00
2.84
OH
O
O
HO
OH
N
N
N
HO
O
24
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm
0.9
1.0
1.1
1.0
2.0
1.1
1.1
1.1
1.0
1.0
2.2
1.3
1.1
1.0
164.3
158.2
156.6
137.2
131.9
125.7
121.0
115.5
112.0
103.4
85.9
83.1
75.6
72.7
63.5
30.4
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

8. UV-VISIBLE AND PHOTOLUMINESCENCE SPECTRA FOR **24**



The emission (solid line) and excitation (dashed line) spectra of **24** measured in DMSO λ_{ex} = 346 nm; λ_{em} = 426 nm (c = 12 nM)