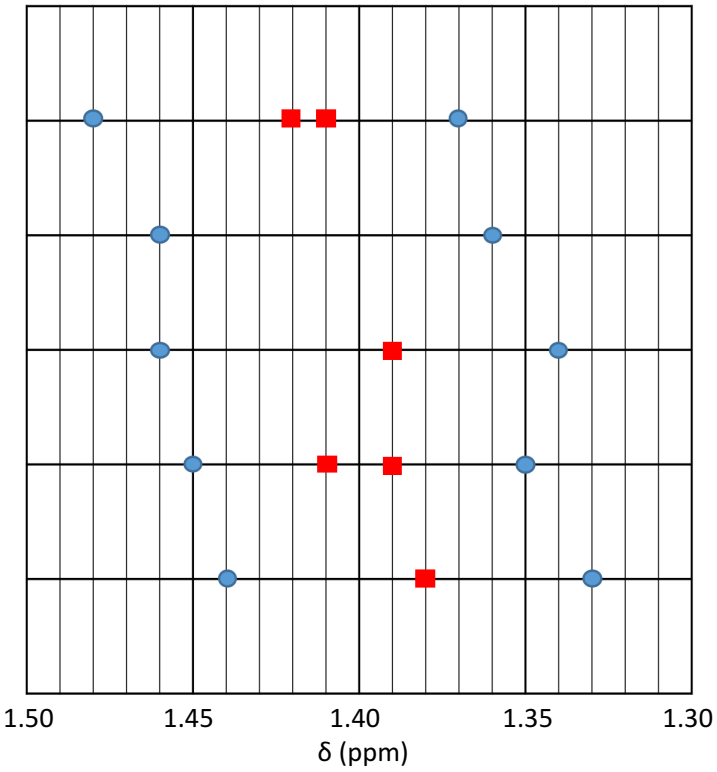
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Stereoselective synthesis of 17,18-epoxy derivative of EPA and stereoisomers of isoleukotoxin diol by ring opening of TMS-substituted epoxide with dimsyl sodium

Yutaro Nanba, Riku Shinohara, Masao Morita, and Yuichi Kobayashi*

Department of Biotechnology, Tokyo Institute of Technology,
B-52, Nagatsuta-cho 4259, Midori-ku, Yokohama 226-8501, Japan



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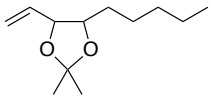
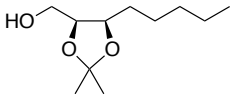
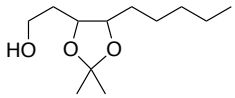
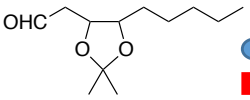
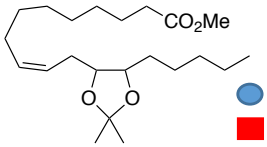
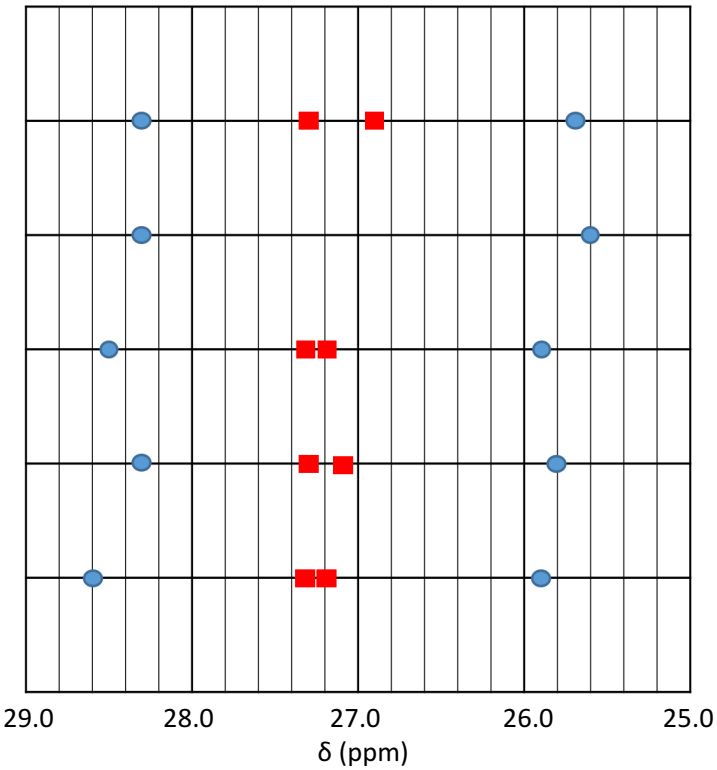
0.11	0.01		**33** *anti* **41** *syn*
0.10	—		**38** *anti*
0.12	0		**34** *anti* **42** *syn*
0.10	0.02		**35** *anti* **43** *syn*
0.11	0		**36** *anti* **44** *syn*

Fig. S1 Chemical shifts of the acetonide methyl groups in the ^{1}H NMR spectra.



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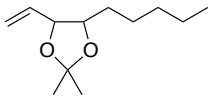
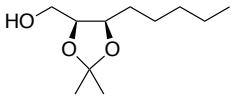
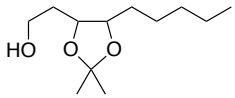
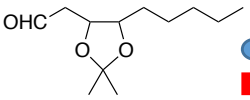
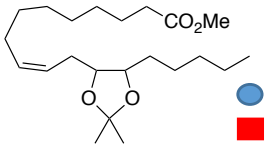
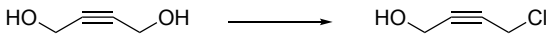
2.6	0.4		**33** *anti* **41** *syn*
2.7	—		**38** *anti*
2.6	0.1		**34** *anti* **42** *syn*
2.5	0.2		**35** *anti* **43** *syn*
2.7	0.1		**36** *anti* **44** *syn*

Fig. S2 Chemical shifts of the acetonide methyl groups in the ^{13}C NMR spectra.

Synthesis of phosphonium salt 7

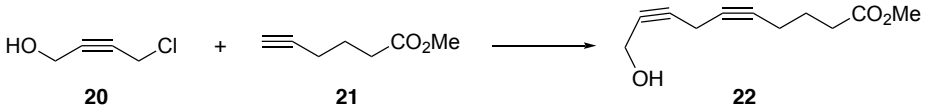
4-Chlorobut-2-yn-1-ol (20)



20

To a solution of but-2-yne-1,4-diol (2.09 g, 24.2 mmol) in benzene (2.4 mL) was added pyridine (2.14 mL, 26.7 mmol). The mixture was stirred for 10 min, and $SOCl_2$ (1.92 mL, 26.6 mmol) was added dropwise over a period of 30 min. The mixture was stirred overnight at rt, poured into ice-water. The benzene layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with saturated $NaHCO_3$ and then with brine, dried over $MgSO_4$, and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc 6:1) to afford chloride **20** (1.28 g, 51%): liquid; R_f = 0.23 (hexane/EtOAc 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.51 (br s, 1 H), 4.20 (t, J = 1.8 Hz, 2 H), 4.34 (t J = 1.8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.4, 50.9, 80.5, 84.7. The ^{1}H and ^{13}C NMR spectra were identical with those reported.[S1]

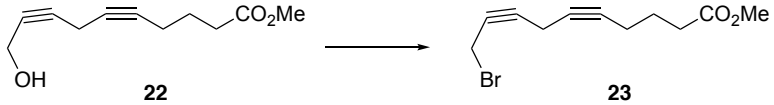
Methyl 10-hydroxydeca-5,8-diynoate (22)



20 **21** **22**

To a mixture of chloride **20** (1.50 g, 14.4 mmol), NaI (2.80 g, 18.7 mmol), CuI (3.56 g, 18.7 mmol), and Cs_2CO_3 (6.60 g, 18.7 mmol) in DMF (29 mL) were added methyl hex-5-ynote (**21**) (2.36 g, 18.7 mmol). After being stirred overnight at rt, the mixture was diluted with EtOAc, filtered through a pad of Celite. The filtrate was washed with saturated NH_4Cl. The aqueous layer was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc 2:1) to afford diyne **22** (1.69 g, 60%): liquid; R_f = 0.33 (hexane/EtOAc 3:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.82 (quint., J = 7.2 Hz, 2 H), 2.13 (br s, 1 H), 2.24 (tt, J = 7.2, 2.4 Hz, 2 H), 2.45 (t, J = 7.2 Hz, 2 H), 3.19 (quint., J = 2.4 Hz, 2 H), 3.69 (s, 3 H), 4.27 (t, J = 2.4 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.9, 18.2, 23.8, 32.9, 51.3, 51.7, 74.5, 78.6, 79.8, 80.5, 173.8. The ^{1}H and ^{13}C NMR spectra were identical with those reported.[S2]

Methyl 10-bromodeca-5,8-diynoate (23)

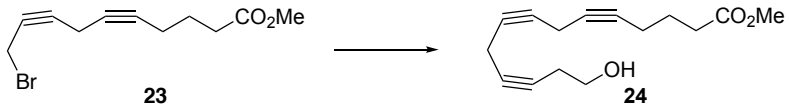


22 **23**

To an ice-cod solution of diyne **22** (1.68 g, 8.65 mmol) in CH_2Cl_2 (17 mL) were added PPh_3 (3.16 g, 9.51 mmol) and CBr_4 (2.49 g, 9.51 mmol). After being stirred at 0 °C for 3 h, the mixture was diluted with hexane/EtOAc (1:1), filtered through a plug of silica gel. The filtrate was concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc 5:1) to afford bromide **23** (1.89 g, 85%): liquid; R_f = 0.50 (hexane/EtOAc 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.82 (quint., J = 7.1 Hz, 2 H), 2.24 (tt, J =7.1, 2.4 Hz, 2 H), 2.44 (t, J = 7.1 Hz, 2 H), 3.22 (quint., J = 2.4 Hz, 2 H), 3.69 (s, 3 H), 3.92 (t, J = 2.4 Hz,

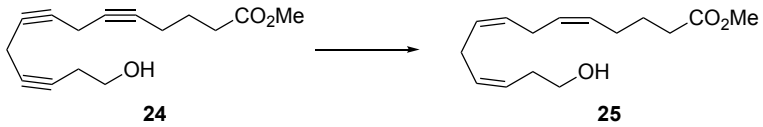
2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.1, 14.9, 18.2, 23.8, 32.9, 51.7, 73.9, 75.4, 80.0, 81.9, 173.7. The ^{1}H and ^{13}C NMR spectra were identical with those reported.[S2]

Methyl 14-hydroxytetradeca-5,8,11-triynoate (24)



To a mixture of 3-butyn-1-ol (0.20 mL, 5.4 mmol), NaI (811 mg, 5.41 mmol), CuI (1.02 g, 5.36 mmol), and Cs_2CO_3 (1.91 g, 5.36 mmol) in DMF (7.0 mL) was added bromide **23** (1.07 g, 4.16 mmol) in DMF (7.0 mL). After being stirred overnight at rt, the mixture was diluted with EtOAc, filtered through a pad of Celite. The filtrate was washed with saturated NH_4Cl. The aqueous layer was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc 2:1) to afford triyne **24** (789 mg, 77%): liquid; R_f = 0.27 (hexane/EtOAc 2:1); IR (neat) 3447, 1733, 1218 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.82 (quint., J = 7.3 Hz, 2 H), 2.24 (tt, J = 7.3, 2.1 Hz, 2 H), 2.39–2.52 (m, 4 H), 3.11–3.19 (m, 4 H), 3.68 (s, 3 H), 3.71 (t, J = 6.3 Hz, 2 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 9.78 (–), 9.86 (–), 18.2 (–), 23.1 (–), 23.8 (–), 32.9 (–), 51.7 (+), 61.1 (–), 74.6 (–), 74.8 (–), 75.0 (–), 76.1 (–), 77.3 (–), 79.6 (–), 173.8 (–); HRMS (FAB$^+$) calcd for $C_{15}H_{18}O_3Na$ [(M+Na)$^+$] 269.1154, found 269.1150. The ^{1}H spectrum was identical with that reported.[S3]

Methyl (5*Z*,8*Z*,11*Z*)-14-hydroxytetradeca-5,8,11-trienoate (25)



To a solution of $Ni(OAc)_2 \cdot 4H_2O$ (550 mg, 2.21 mmol) in MeOH (2.7 mL) was added $NaBH_4$ (89 mg, 2.35 mmol). The flask was purged with hydrogen and ethylenediamine (0.247 mL, 3.66 mmol) was added to the mixture. After 10 min, triyne **24** (451 mg, 1.83 mmol) in MeOH (1.0 mL) was added. The mixture was stirred at rt for 3.5 h, and diluted with hexane/EtOAc (1:1), filtered through a pad of silica gel. The filtrate was washed with saturated NH_4Cl. The aqueous layer was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc 5:2) to afford triene **25** (215 mg, 47%): liquid; R_f = 0.28 (hexane/EtOAc 3:1); IR (neat) 3413, 1737, 1438, 1049 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70 (quint., J = 7.3 Hz, 2 H), 2.06–2.18 (m, 2 H), 2.33 (t, J = 7.3 Hz, 2 H), 2.30–2.43 (m, 2 H), 2.77–2.89 (m, 4 H), 3.66 (t, J = 6.6 Hz, 2 H), 3.67 (s, 3 H), 5.28–5.59 (m, 6 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 24.7 (–), 25.6 (–), 25.7 (–), 26.5 (–), 30.8 (–), 33.4 (–), 51.5 (+), 62.1 (–), 125.6 (+), 127.9 (+), 128.3 (+), 128.8 (+), 128.9 (+), 130.8 (+), 174.3 (–); HRMS (FAB$^+$) calcd for $C_{15}H_{24}O_3Na$ [(M+Na)$^+$] 275.1623, found 275.1622. The ^{1}H spectrum was identical with that reported.[S3]

Methyl (5*Z*,8*Z*,11*Z*)-14-(triphenylphosphonio)tetradeca-5,8,11-trienoate (7)

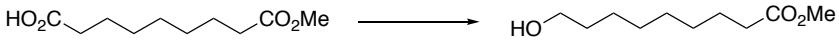
25 **7**

To an ice-cold solution of triene **25** (541 mg, 2.14 mmol) in CH_2Cl_2 (4.3 mL) were added imidazole (200 mg, 2.94 mmol), PPh_3 (740 mg, 2.82 mmol), and I_2 (624 mg, 2.46 mmol). After 3.5 h at 0 °C, the solution was diluted with petroleum ether/ether (4:1) and filtered through a pad of silica gel to afford iodide (637 mg, 82%): liquid; R_f = 0.70 (hexane/EtOAc 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.71 (quint., J = 7.5 Hz, 2 H), 2.04–2.18 (m, 2 H), 2.33 (t, J = 7.5 Hz, 2 H), 2.67 (q, J = 7.5 Hz, 2 H), 2.74–2.88 (m, 4 H), 3.16 (t, J = 7.2 Hz, 2 H), 3.67 (s, 3 H), 5.30–5.47 (m, 5 H), 5.53 (J = 10.5, 7.3, 1.2 Hz, 1 H). The ^{1}H spectrum was identical with that reported.[S3]

A solution of the above iodide (637 mg, 1.76 mmol) and PPh_3 (690 mg, 2.63 mmol) in MeCN (11 mL) was refluxed overnight. The solvent was removed under reduced pressure and the oily residue was washed with hexane/benzene (1:1, 1 mL) ten times. The solvent was removed and oily residue was dried by vacuum pump overnight to afford phosphonium salt **7** (1.07 g, 98%): gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.68 (quint., J = 7.5 Hz, 2 H), 2.05 (q, J = 7.0 Hz, 2 H), 2.30 (t, J = 7.5 Hz, 2 H), 2.40–2.56 (m, 2 H), 2.53–2.71 (m, 4 H), 3.65 (s, 3 H), 3.79–3.91 (m, 2 H), 5.14–5.46 (m, 1 H), 5.65 (dtm, J = 10.5, 7.0 Hz, 1 H), 7.66–7.92 (m, 15 H). The ^{1}H spectrum was identical with that reported.[S3]

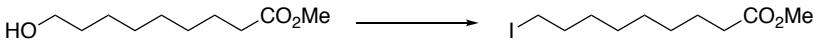
Synthesis of phosphonium salt 27

Methyl 9-hydroxynonanoate



To a solution of azelaic acid monomethyl ester (56 mg, 0.28 mmol) in THF (0.5 mL) was added BH_3·THF (1.0 M in THF, 0.28 mL, 0.28 mmol) at –10 °C (ice-salt bath). The solution was stirred at –10 °C to rt for 2 h and cooled to 0 °C. The reaction was quenched by adding H_2O (2 mL) and K_2CO_3 (73 mg, 0.53 mmol). After 15 min of stirring at 0 °C, the resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford methyl 9-hydroxynonanoate (43 mg, 82%): liquid; R_f 0.52 (hexane/EtOAc 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24–1.42 (m, 8 H), 1.50–1.72 (m, 4 H), 2.31 (t, J = 7.2 Hz, 2 H), 3.64 (t, J = 6.9 Hz, 2 H), 3.67 (s, 3 H). The ^{1}H NMR spectrum was consistent with that reported.[S4]

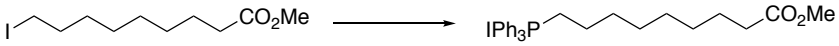
Methyl 9-iodononanoate



To an ice-cold solution of imidazole (27 mg, 0.40 mmol) and PPh_3 (79 mg, 0.30 mmol) in CH_2Cl_2 (1 mL) was added I_2 (73 mg, 0.29 mmol). After 30 min of stirring at 0 °C, a solution of methyl 9-hydroxynonanoate (39 mg, 0.21 mmol) in CH_2Cl_2 (1 mL) was added. The mixture was stirred at rt for 2 h and diluted with aqueous $Na_2S_2O_3$. The resulting

mixture was extracted with CH_2Cl_2 twice. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford methyl 9-iodononanoate (51 mg, 82%): liquid; R_f 0.77 (hexane/EtOAc 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23–1.46 (m, 8 H), 1.56–1.70 (m, 2 H), 1.82 (quint., J = 7.2 Hz, 2 H), 2.31 (t, J = 7.5 Hz, 2 H), 3.19 (t, J = 6.9 Hz, 2 H), 3.67 (s, 3 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 7.2 (–), 24.8 (–), 28.3 (–), 29.0 (–), 30.4 (–), 33.5 (–), 34.0 (–), 51.4 (+), 174.1 (–). The ^{1}H NMR and ^{13}C NMR spectra were consistent with those reported.[S5]

(9-Methoxy-9-oxononyl)triphenylphosphonium iodide (27)



27

A mixture of methyl 9-iodononanoate (51 mg, 0.17 mmol) and PPh_3 (78 mg, 0.30 mmol) in MeCN (5 mL) was heated under reflux overnight, cooled to rt, and concentrated. The residue was purified by chromatography on silica gel ($CHCl_3$/MeOH) to give phosphonium salt **27** (82 mg, 85%): yellow oil; R_f 0.40 ($CHCl_3$/MeOH 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14–1.40 (m, 6 H), 1.50–1.74 (m, 6 H), 2.26 (t, J = 7.5 Hz, 2 H), 3.58–3.78 (m, 2 H), 3.65 (s, 3 H), 7.66–8.00 (m, 15 H). The ^{1}H NMR spectrum was consistent with that reported.[S5]

References

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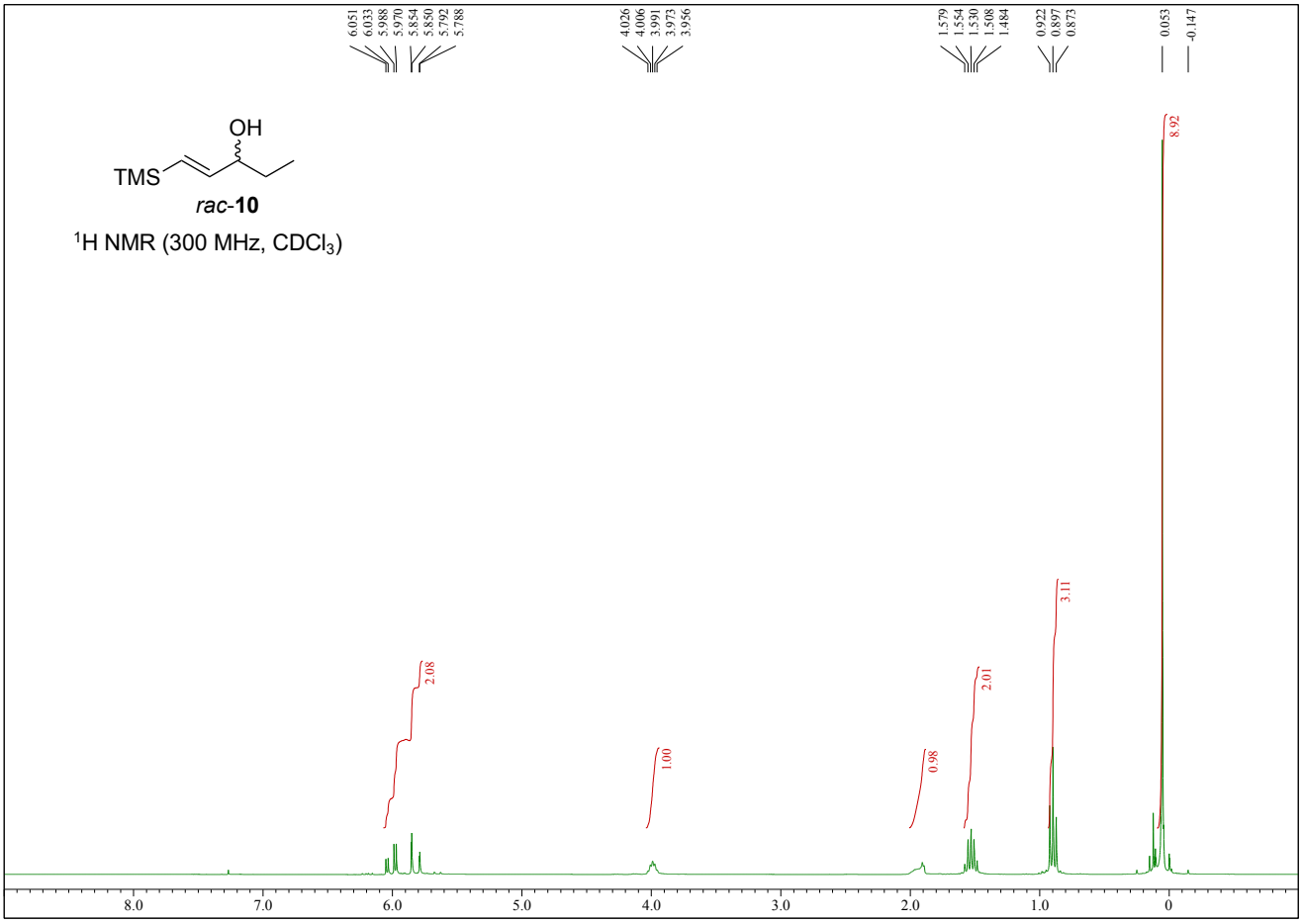
S5 B. P. Gunn, *Heterocycles*, 1985, **23**, 3061.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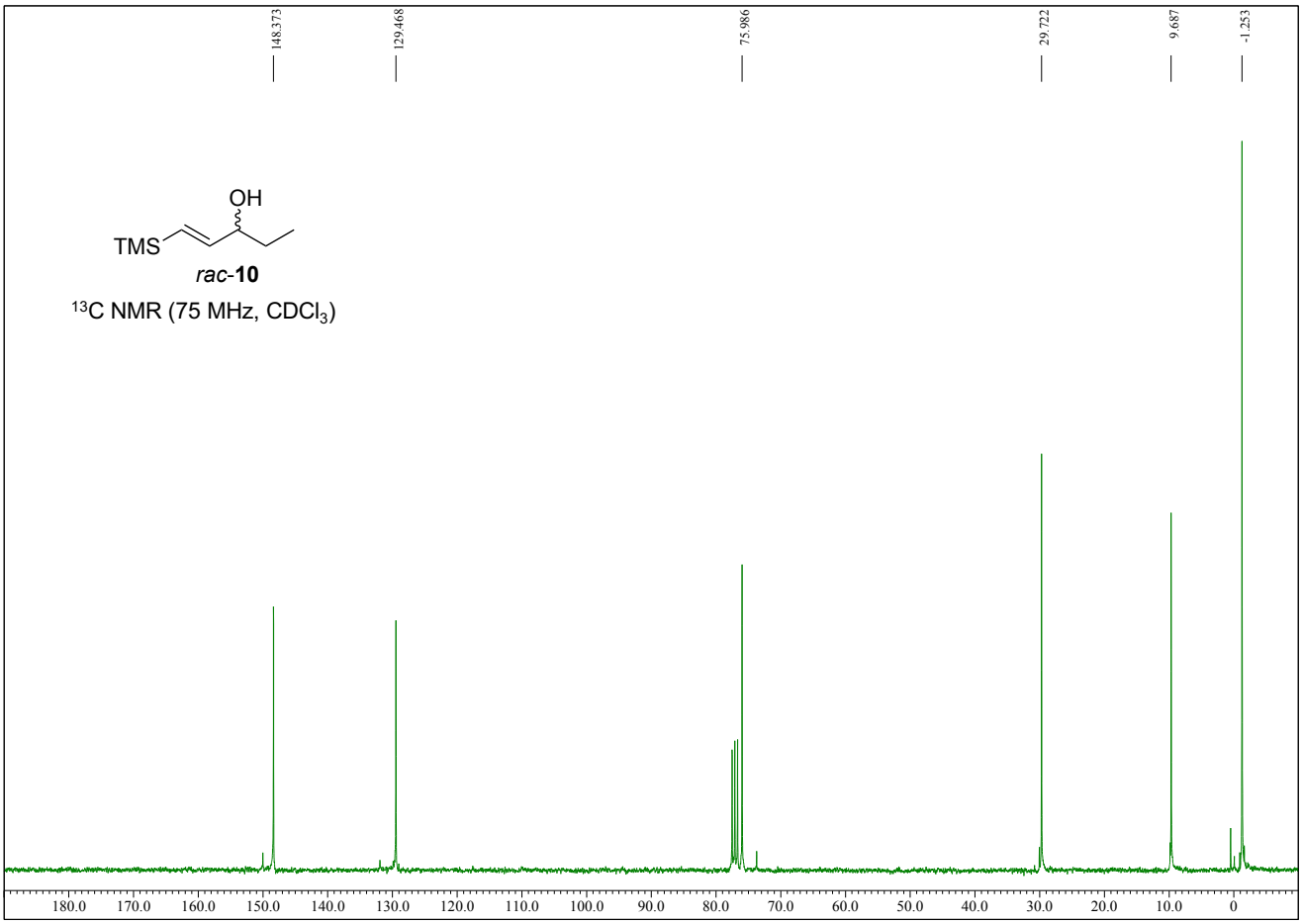
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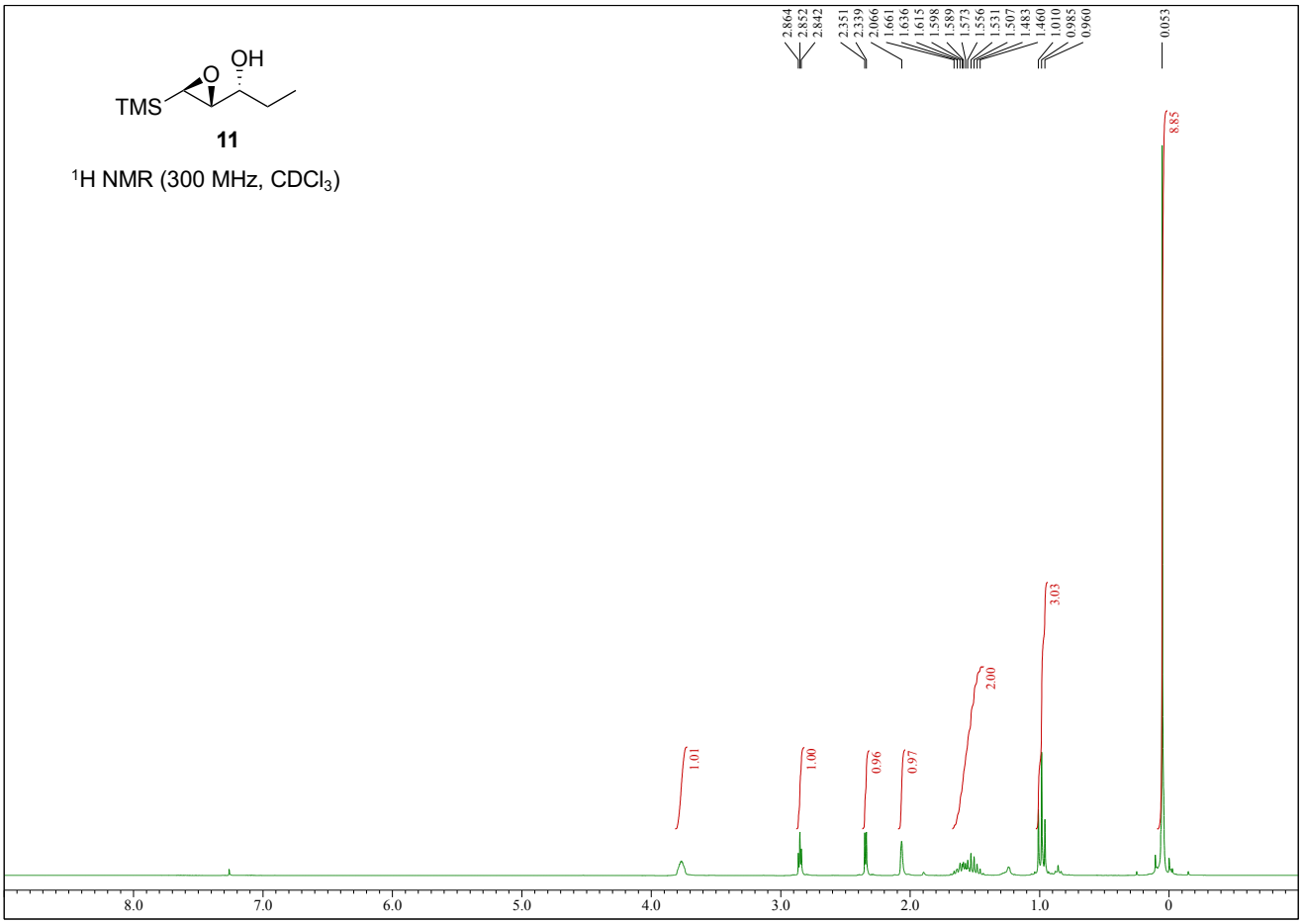
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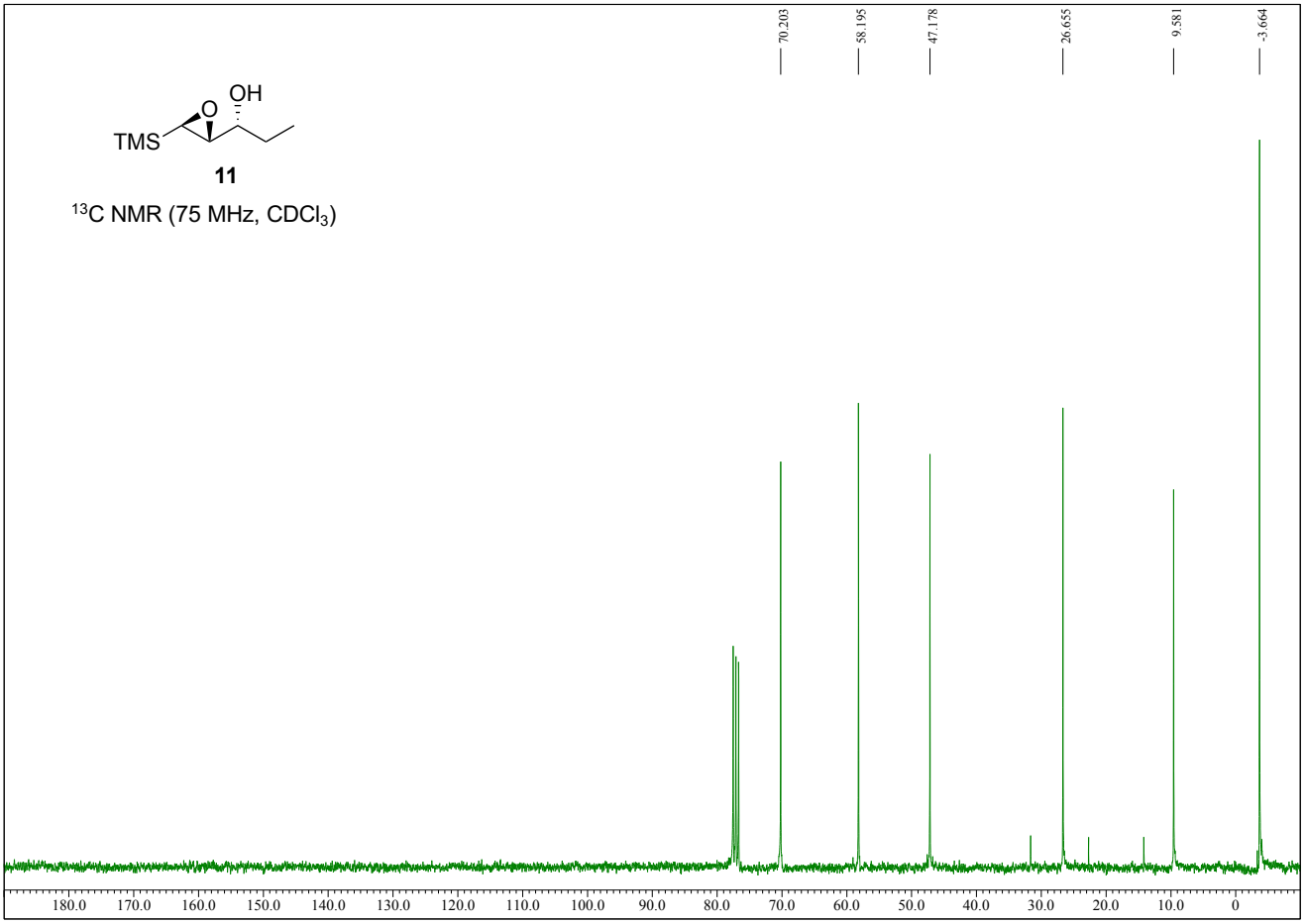
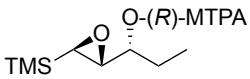
1.0
0

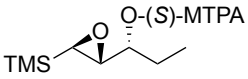

TMS
O
OH
11
13C NMR (75 MHz, CDCl3)
70.203
58.195
47.178
26.655
9.581
-3.664
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0



(*R*)-MTPA ester of **11**

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

See next page for expansion and % de calculation.

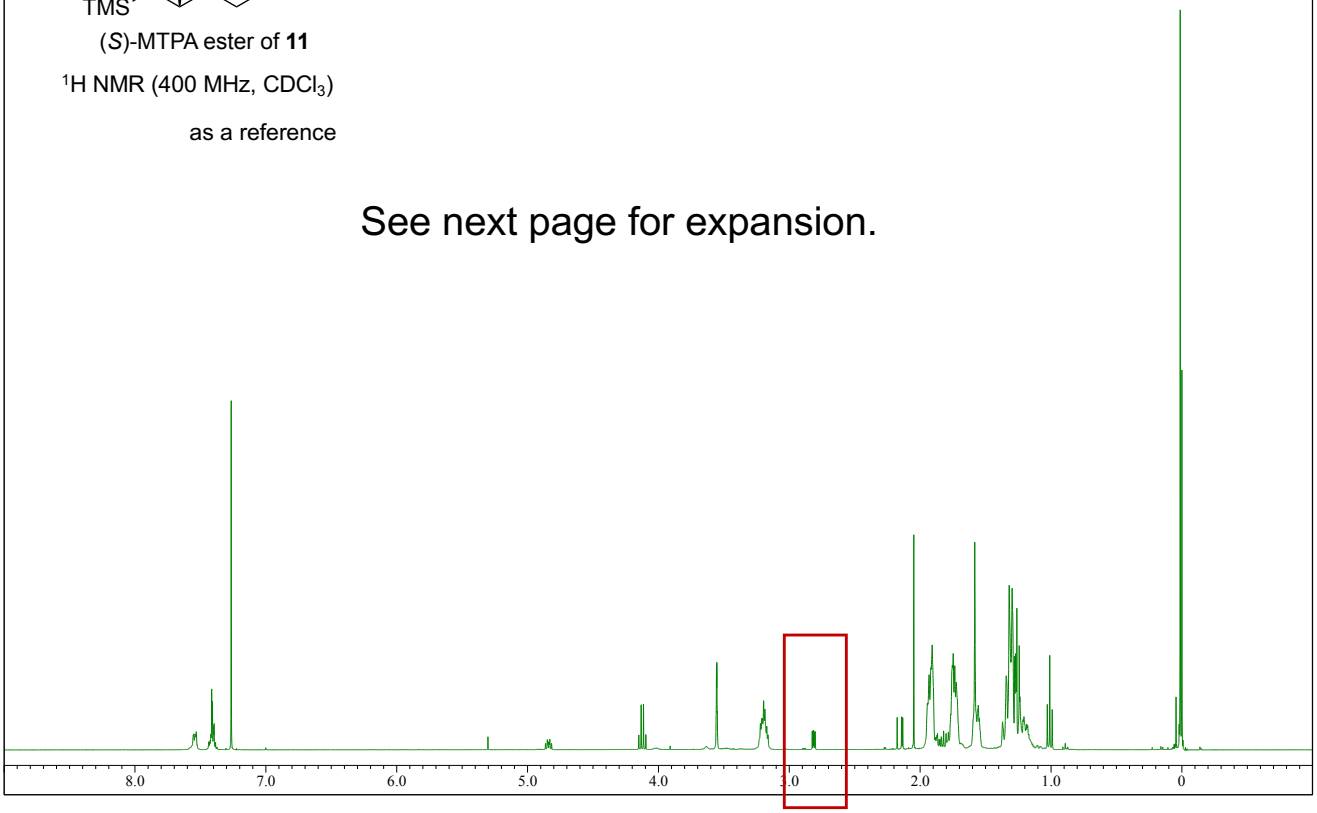


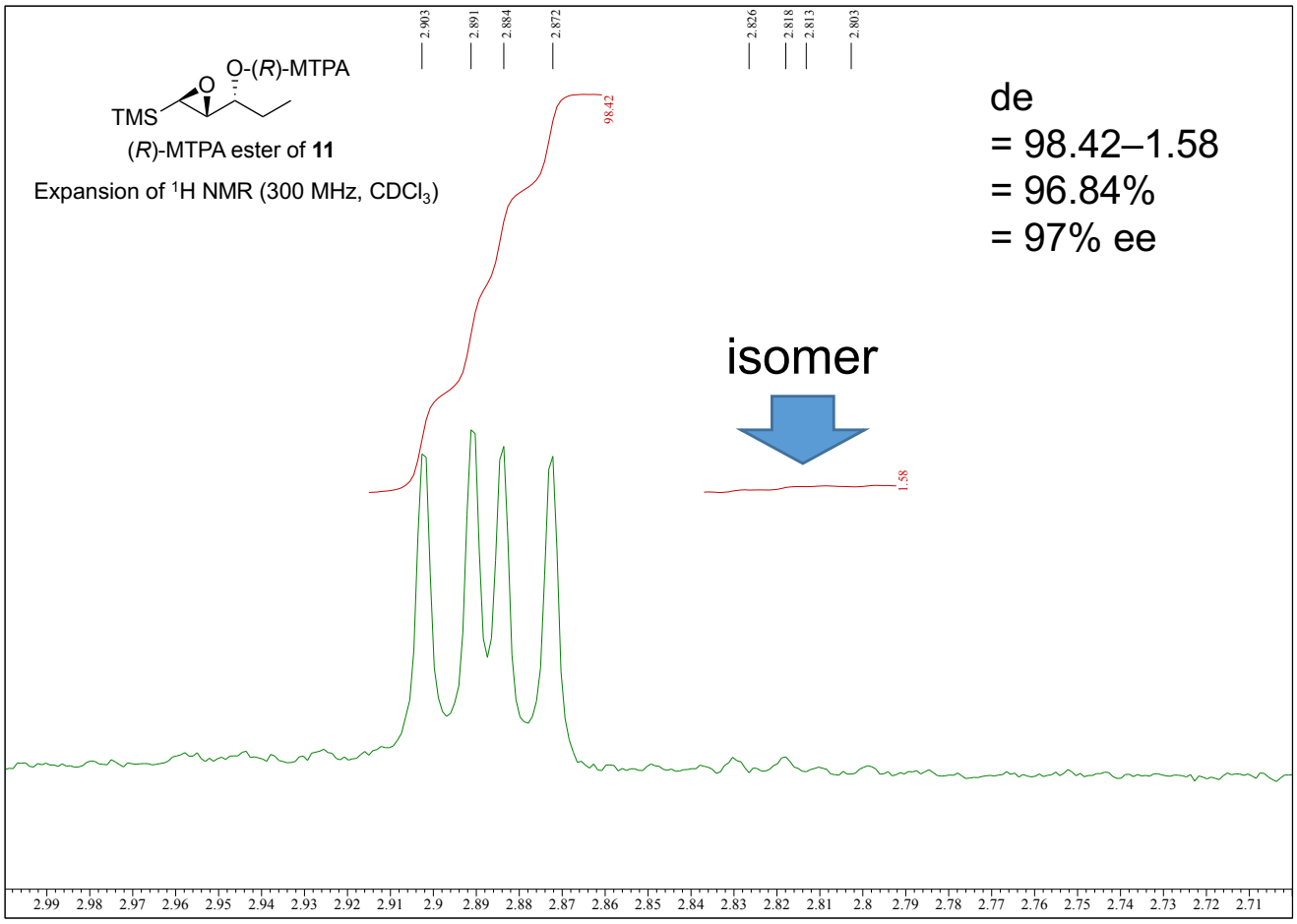
(*S*)-MTPA ester of **11**

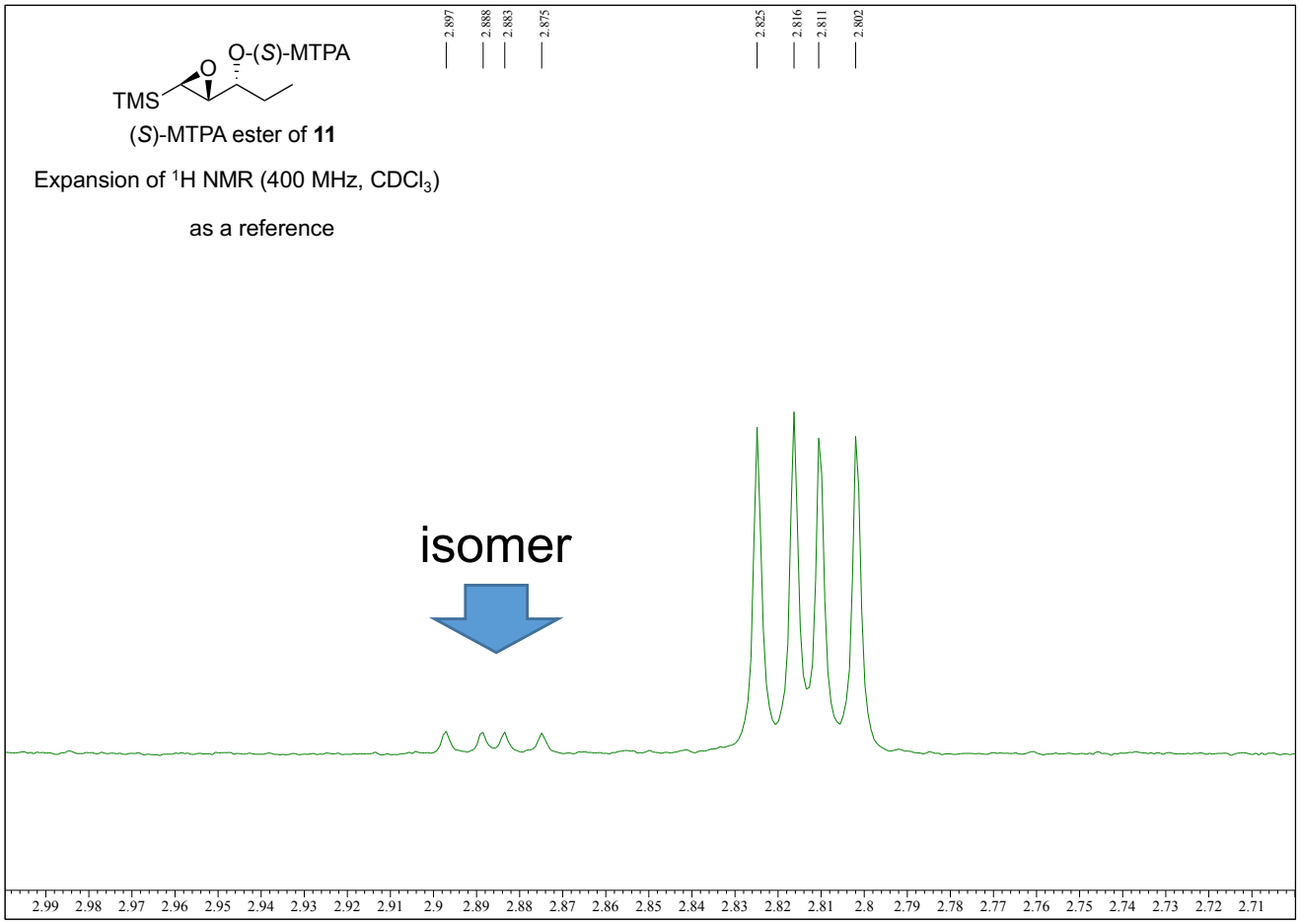
^{1}H NMR (400 MHz, $CDCl_3$)

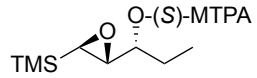
as a reference

See next page for expansion.




2.903
2.891
2.884
2.872
2.826
2.818
2.813
2.803
O-(R)-MTPA
TMS
(R)-MTPA ester of 11
Expansion of ¹H NMR (300 MHz, CDCl3)
98.42
1.58
de
= 98.42–1.58
= 96.84%
= 97% ee
isomer
2.99 2.98 2.97 2.96 2.95 2.94 2.93 2.92 2.91 2.9 2.89 2.88 2.87 2.86 2.85 2.84 2.83 2.82 2.81 2.8 2.79 2.78 2.77 2.76 2.75 2.74 2.73 2.72 2.71

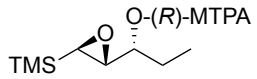

2.897
2.888
2.883
2.875
2.825
2.816
2.811
2.802
O-(S)-MTPA
TMS
(S)-MTPA ester of 11
Expansion of ¹H NMR (400 MHz, CDCl3)
as a reference
isomer
2.99 2.98 2.97 2.96 2.95 2.94 2.93 2.92 2.91 2.9 2.89 2.88 2.87 2.86 2.85 2.84 2.83 2.82 2.81 2.8 2.79 2.78 2.77 2.76 2.75 2.74 2.73 2.72 2.71



(*S*)-MTPA ester of **11** of (*R*)-**10**

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

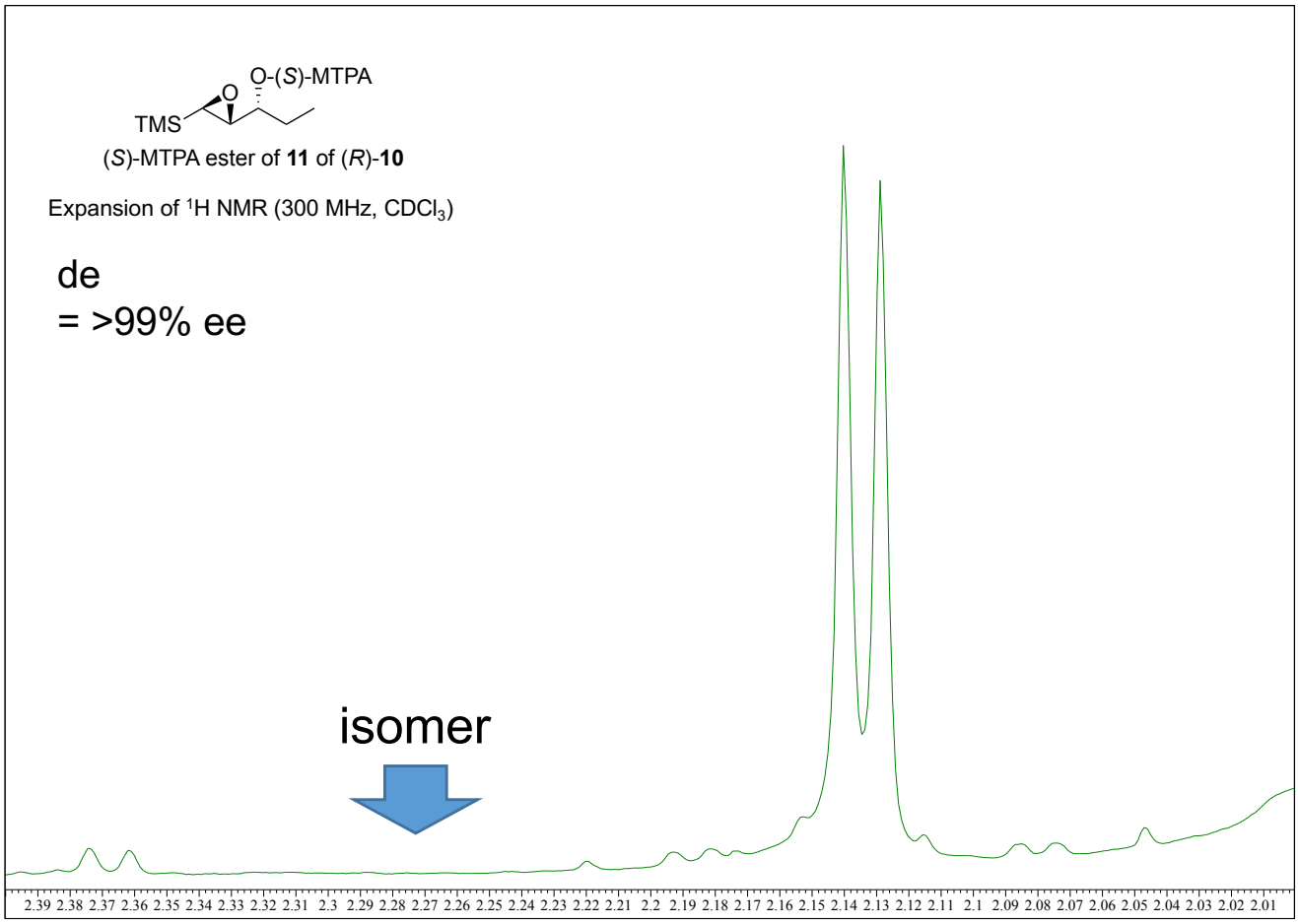
See next page for expansion and % de calculation.

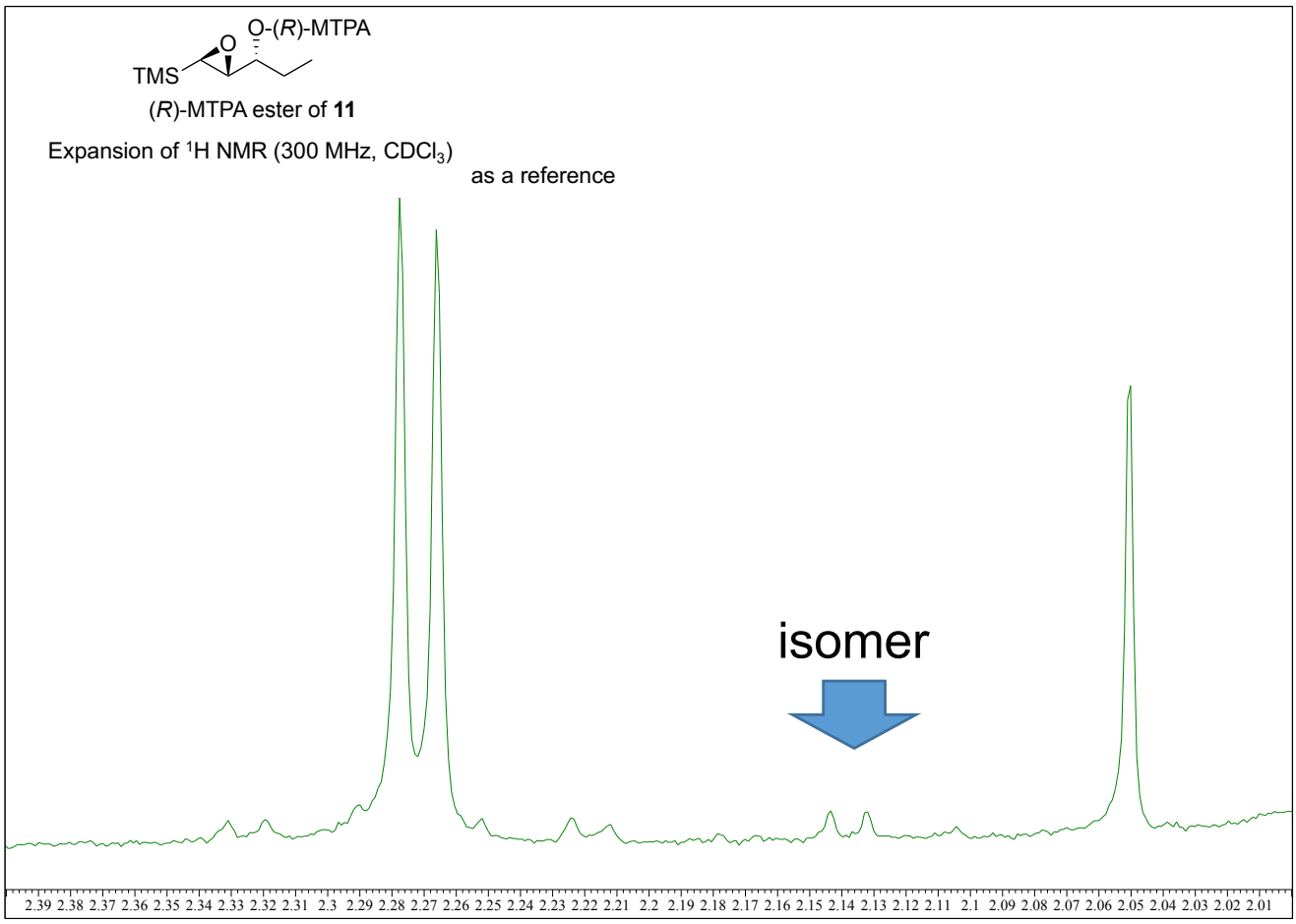


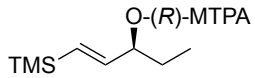
(*R*)-MTPA ester of **11**

Expansion of ^{1}H NMR (300 MHz, $CDCl_3$) as a reference

See next page for expansion.


O-(S)-MTPA
TMS
(S)-MTPA ester of 11 of (R)-10
Expansion of 1H NMR (300 MHz, CDCl3)
de
= >99% ee
isomer
2.39 2.38 2.37 2.36 2.35 2.34 2.33 2.32 2.31 2.3 2.29 2.28 2.27 2.26 2.25 2.24 2.23 2.22 2.21 2.2 2.19 2.18 2.17 2.16 2.15 2.14 2.13 2.12 2.11 2.1 2.09 2.08 2.07 2.06 2.05 2.04 2.03 2.02 2.01

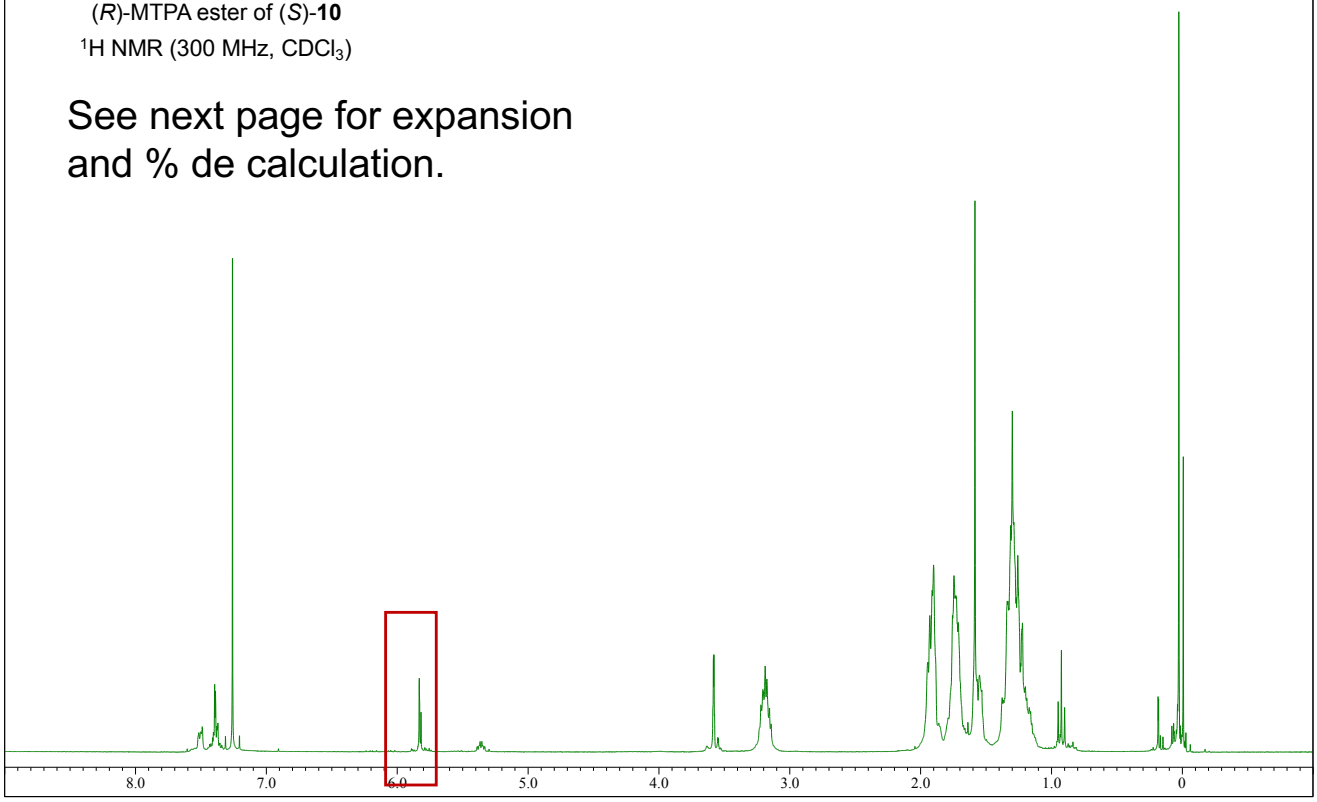

O-(R)-MTPA
TMS
(R)-MTPA ester of 11
Expansion of 1H NMR (300 MHz, CDCl3)
as a reference
isomer
2.39 2.38 2.37 2.36 2.35 2.34 2.33 2.32 2.31 2.3 2.29 2.28 2.27 2.26 2.25 2.24 2.23 2.22 2.21 2.2 2.19 2.18 2.17 2.16 2.15 2.14 2.13 2.12 2.11 2.1 2.09 2.08 2.07 2.06 2.05 2.04 2.03 2.02 2.01

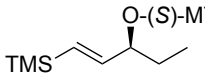


(*R*)-MTPA ester of (*S*)-**10**

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

See next page for expansion and % de calculation.

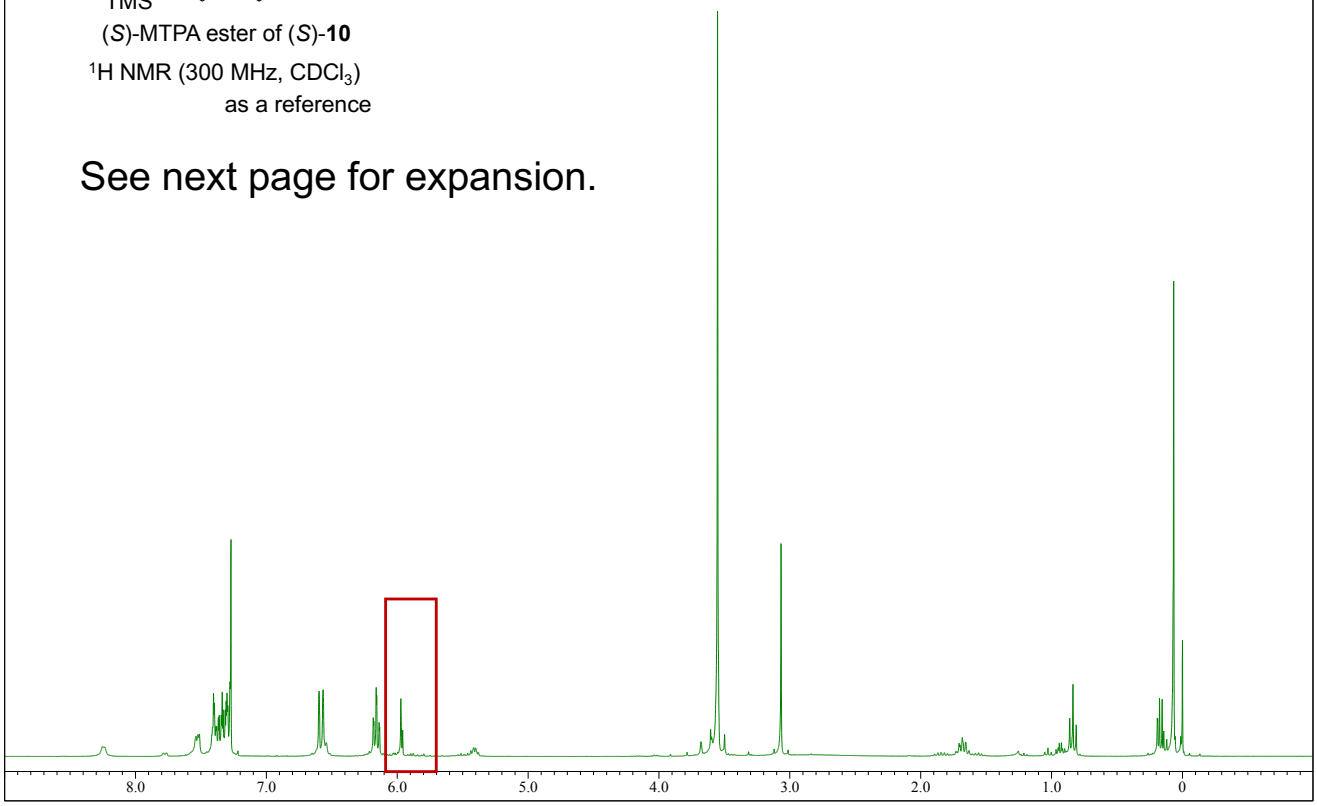


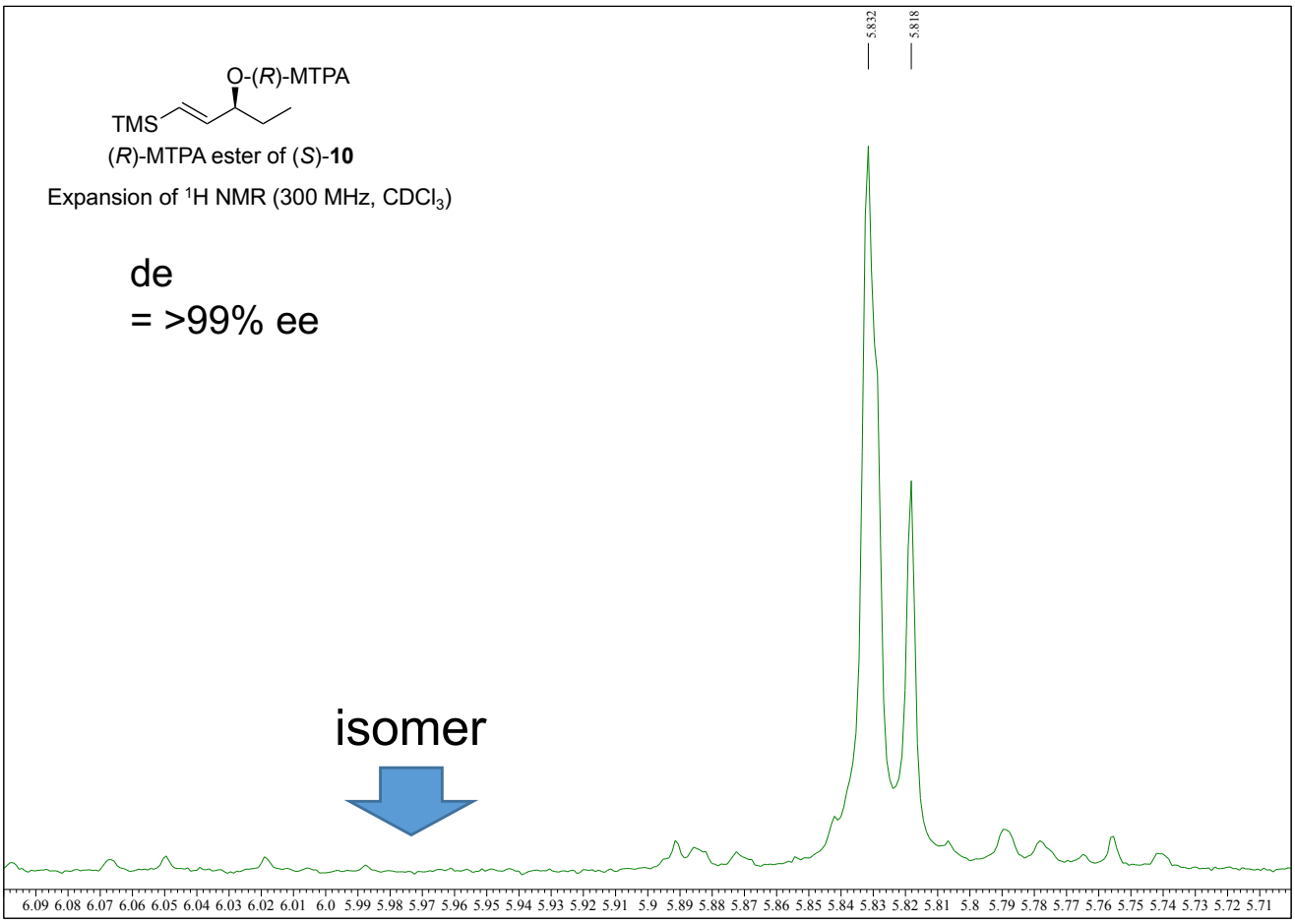


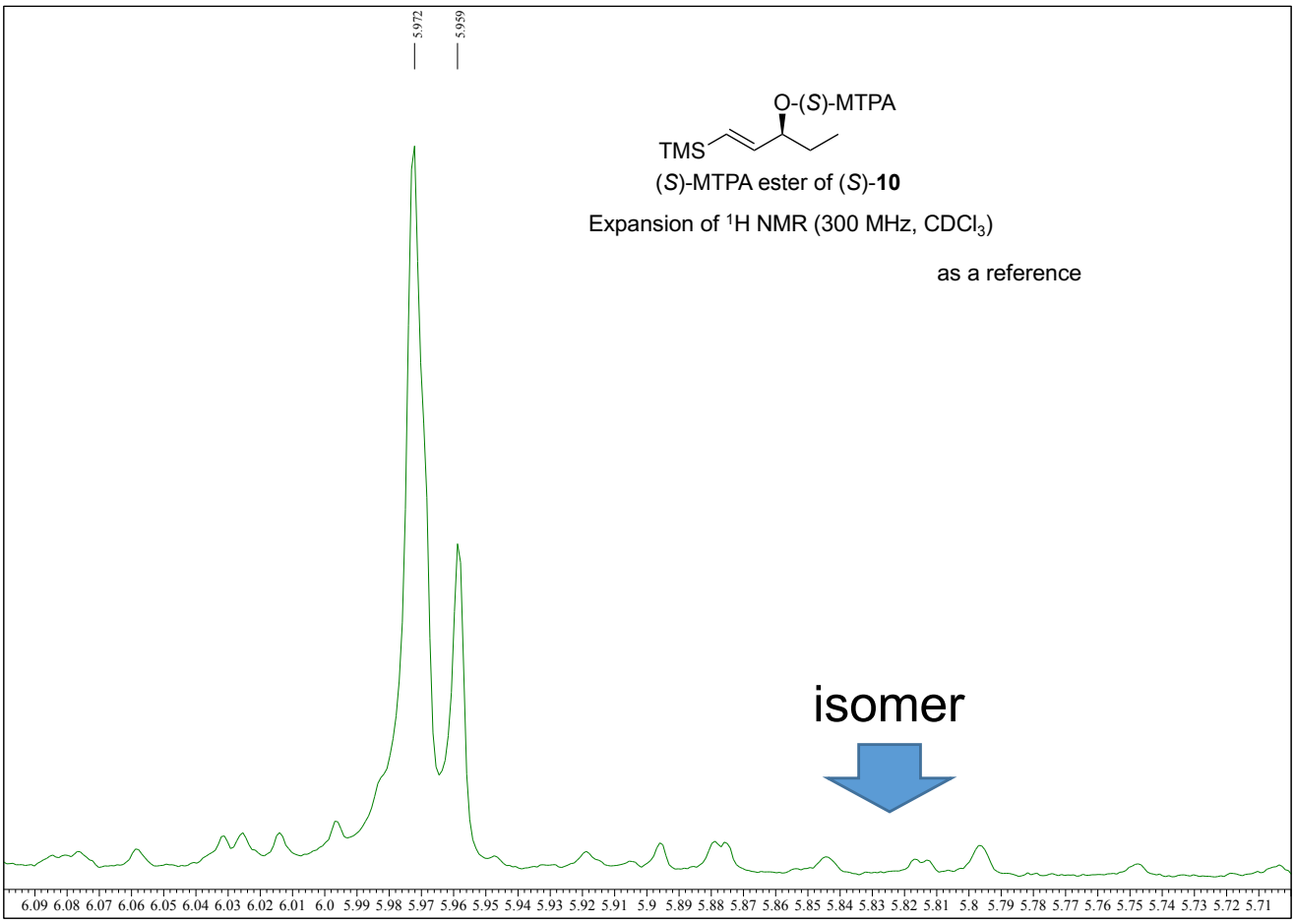
(*S*)-MTPA ester of (*S*)-**10**

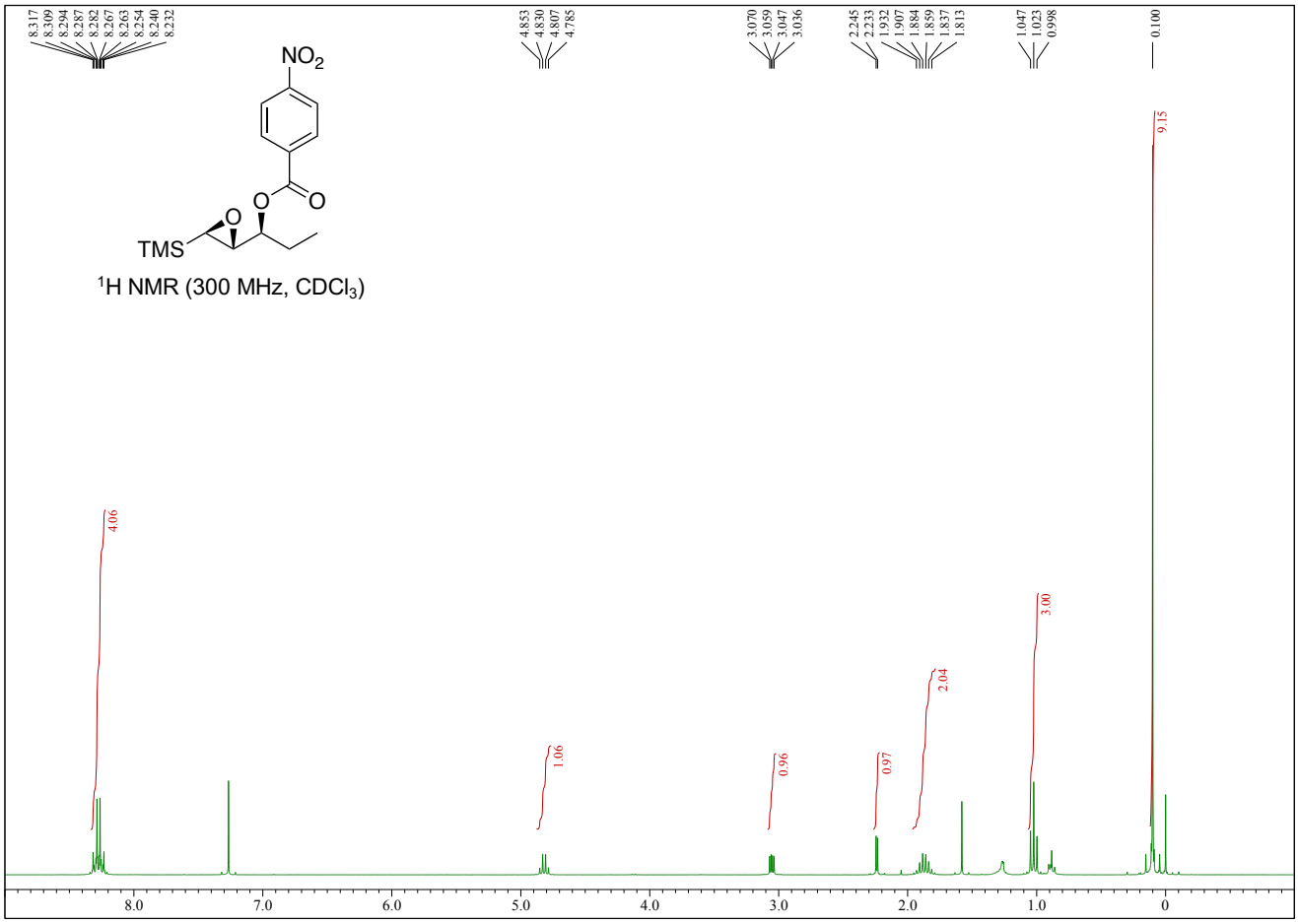
^{1}H NMR (300 MHz, $CDCl_3$)
as a reference

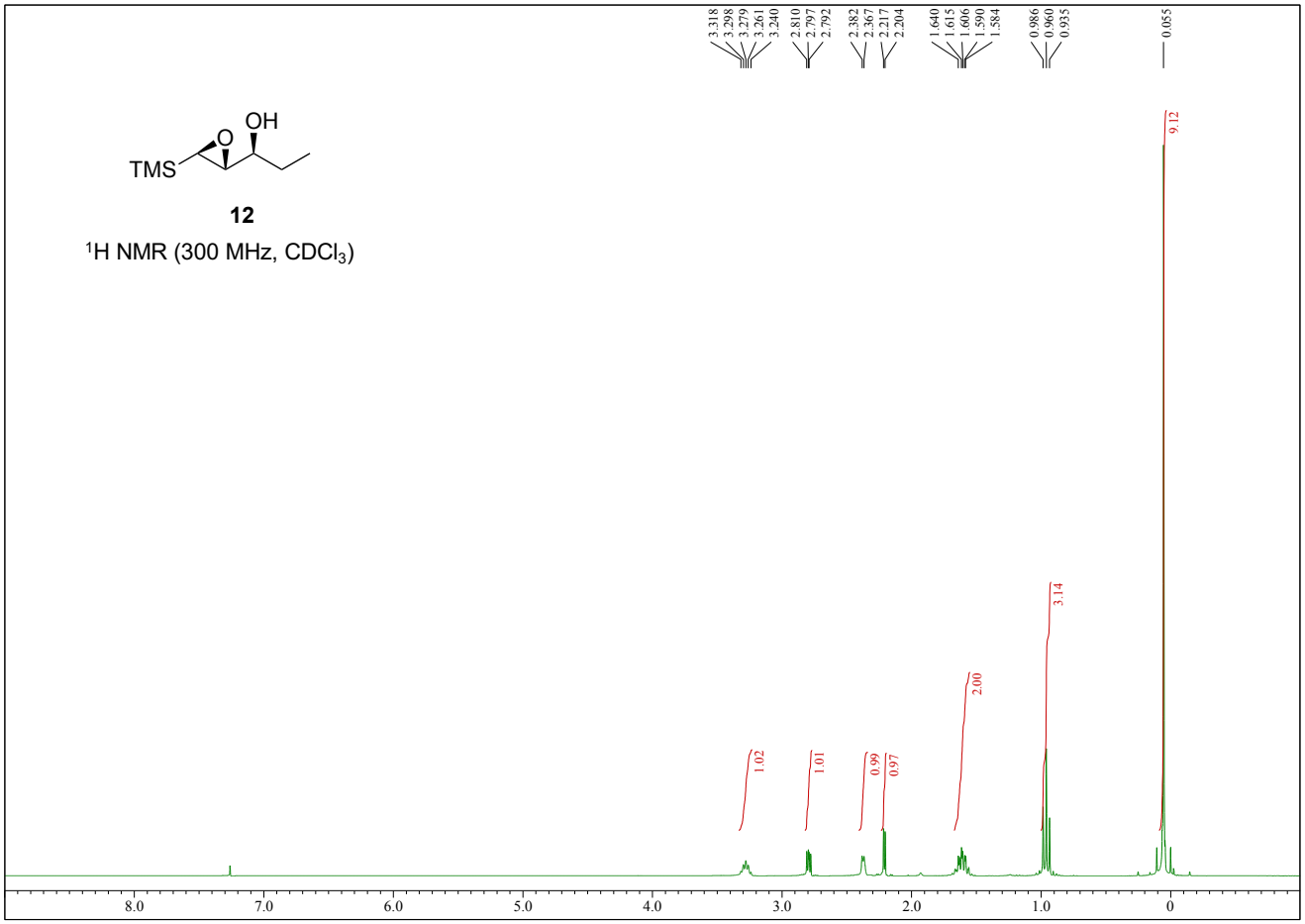
See next page for expansion.




O-(R)-MTPA
TMS
(R)-MTPA ester of (S)-10
Expansion of 1H NMR (300 MHz, CDCl3)
de
= >99% ee
5.832
5.818
isomer
6.09 6.08 6.07 6.06 6.05 6.04 6.03 6.02 6.01 6.0 5.99 5.98 5.97 5.96 5.95 5.94 5.93 5.92 5.91 5.9 5.89 5.88 5.87 5.86 5.85 5.84 5.83 5.82 5.81 5.8 5.79 5.78 5.77 5.76 5.75 5.74 5.73 5.72 5.71

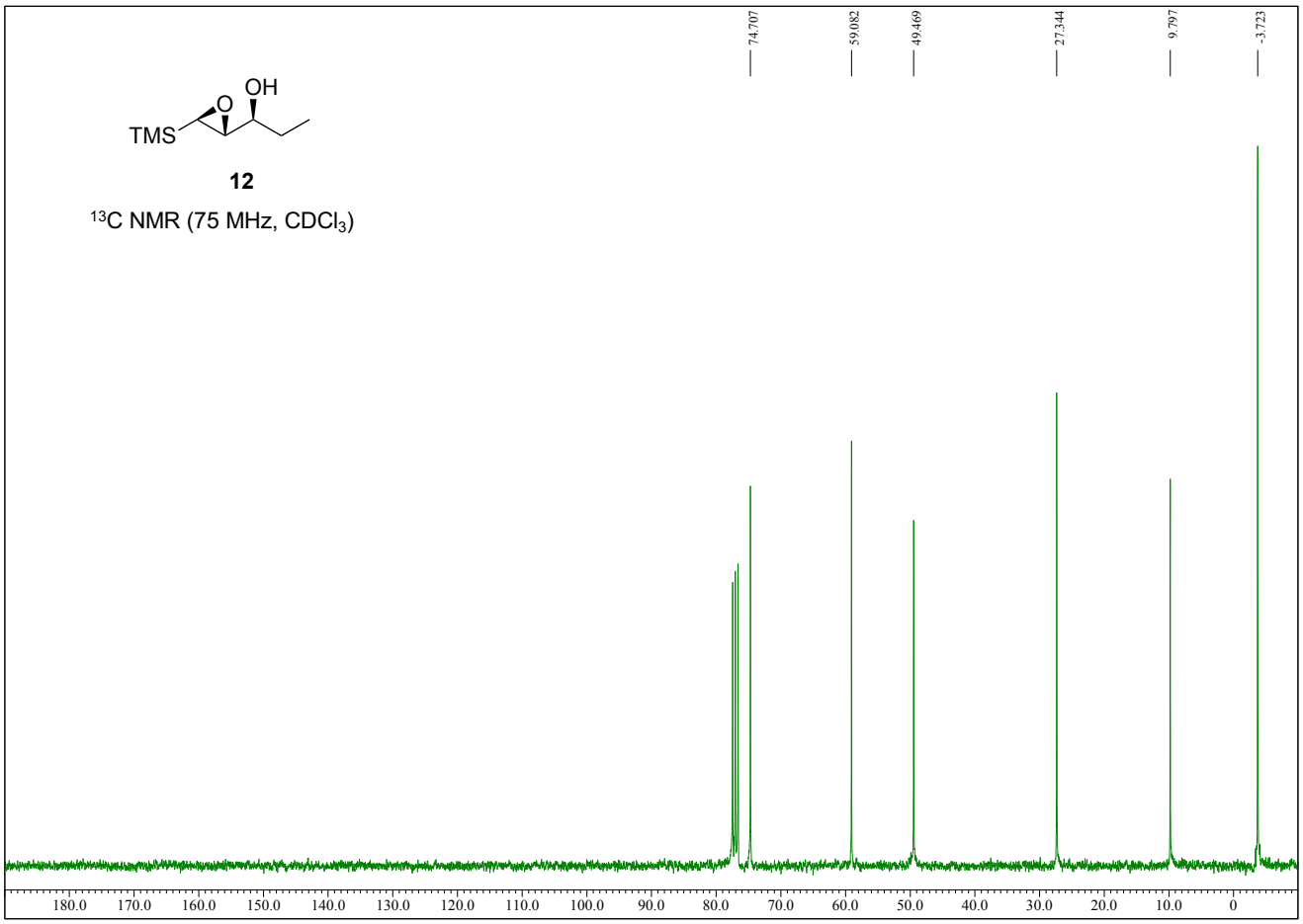

5.972
5.959
O-(S)-MTPA
TMS
(S)-MTPA ester of (S)-10
Expansion of 1H NMR (300 MHz, CDCl3)
as a reference
isomer
6.09 6.08 6.07 6.06 6.05 6.04 6.03 6.02 6.01 6.0 5.99 5.98 5.97 5.96 5.95 5.94 5.93 5.92 5.91 5.9 5.89 5.88 5.87 5.86 5.85 5.84 5.83 5.82 5.81 5.8 5.79 5.78 5.77 5.76 5.75 5.74 5.73 5.72 5.71


8.317
8.309
8.294
8.287
8.282
8.267
8.263
8.254
8.240
8.232
4.853
4.830
4.807
4.785
3.070
3.059
3.047
3.036
2.245
2.233
1.932
1.907
1.884
1.859
1.837
1.813
1.047
1.023
0.998
0.100
NO2
O
O
O
TMS
1H NMR (300 MHz, CDCl3)
4.06
1.06
0.96
0.97
2.04
3.00
9.15
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0



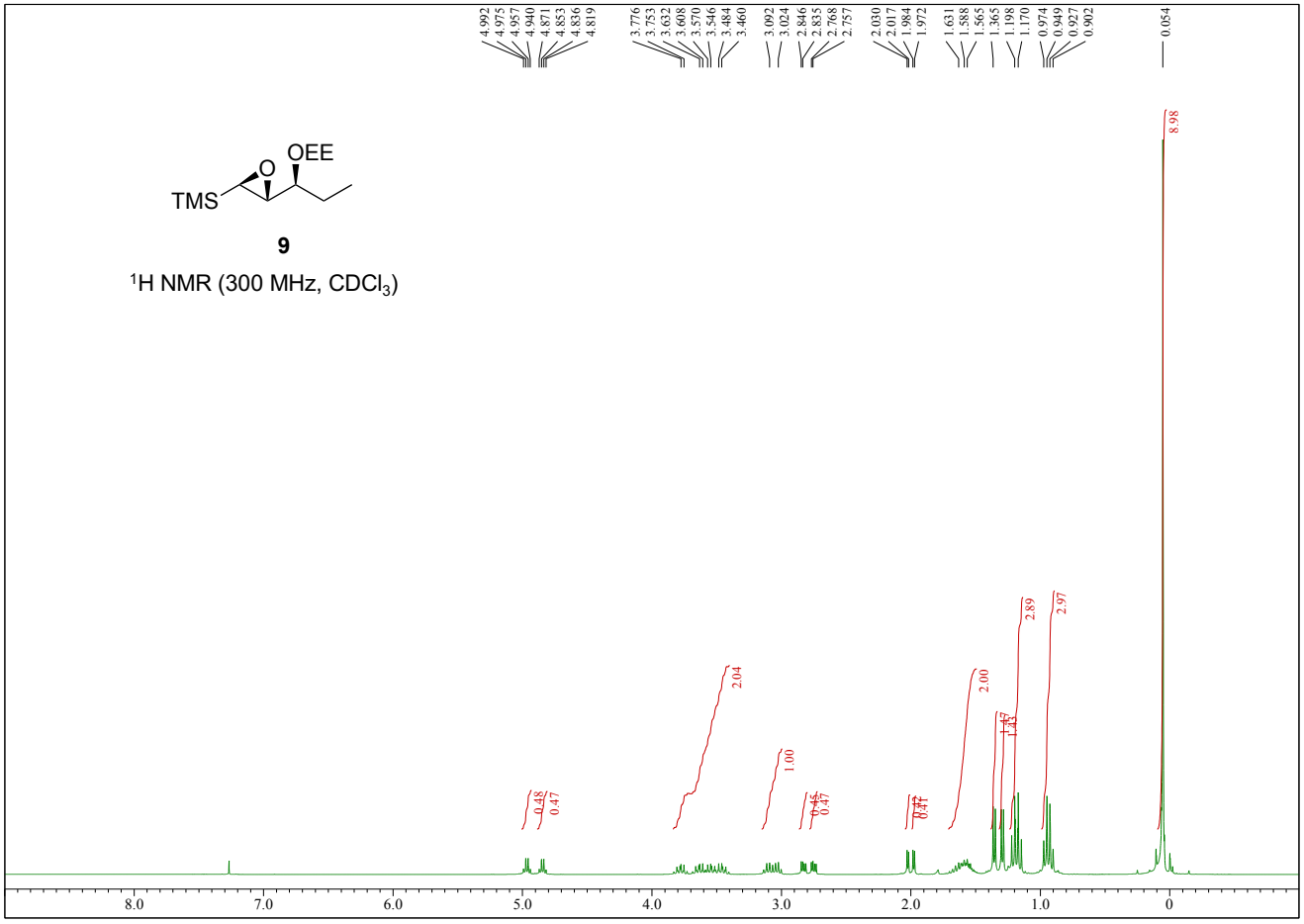
12

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



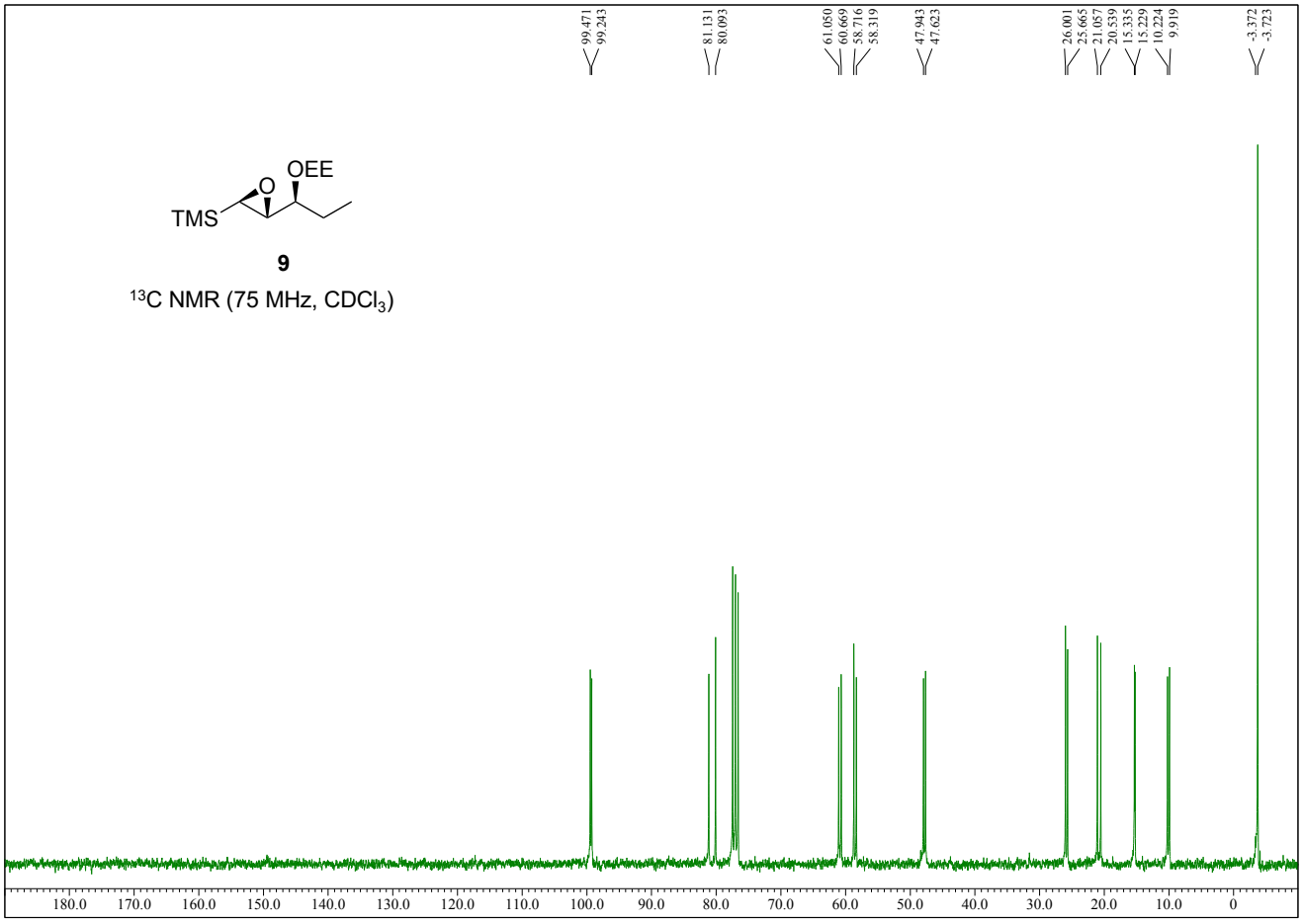
12

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



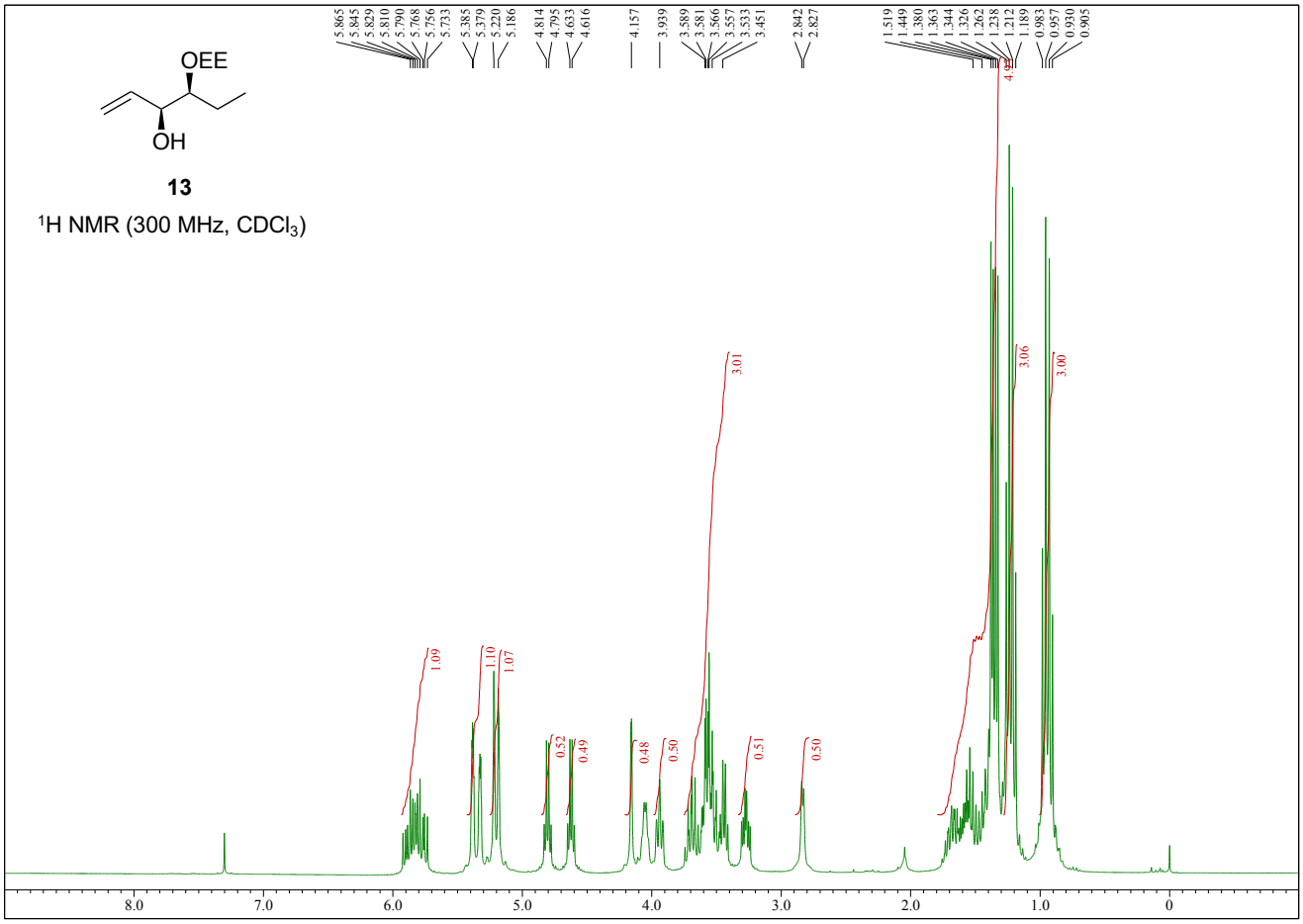
9

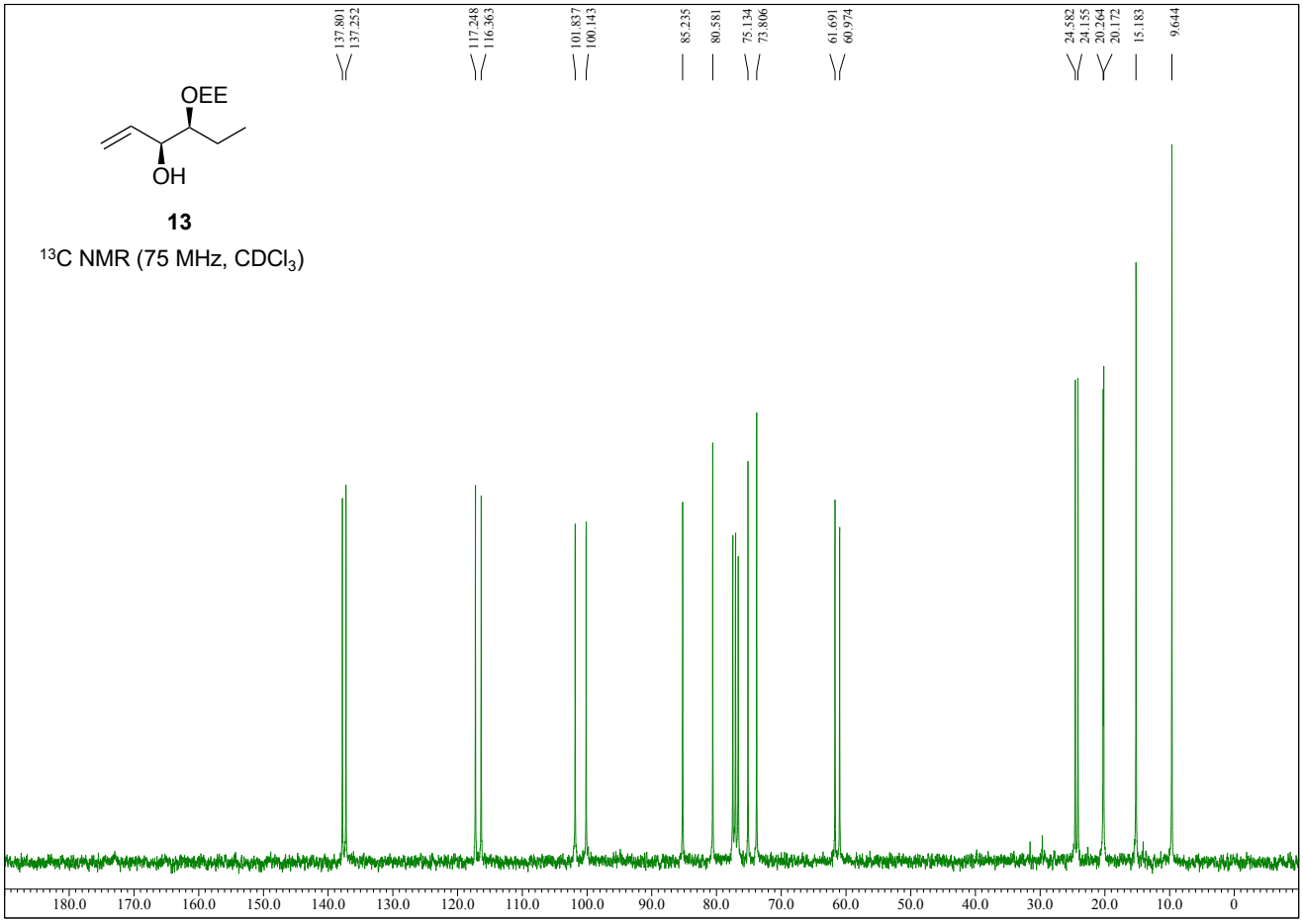
^{1}H NMR (300 MHz, $CDCl_3$)

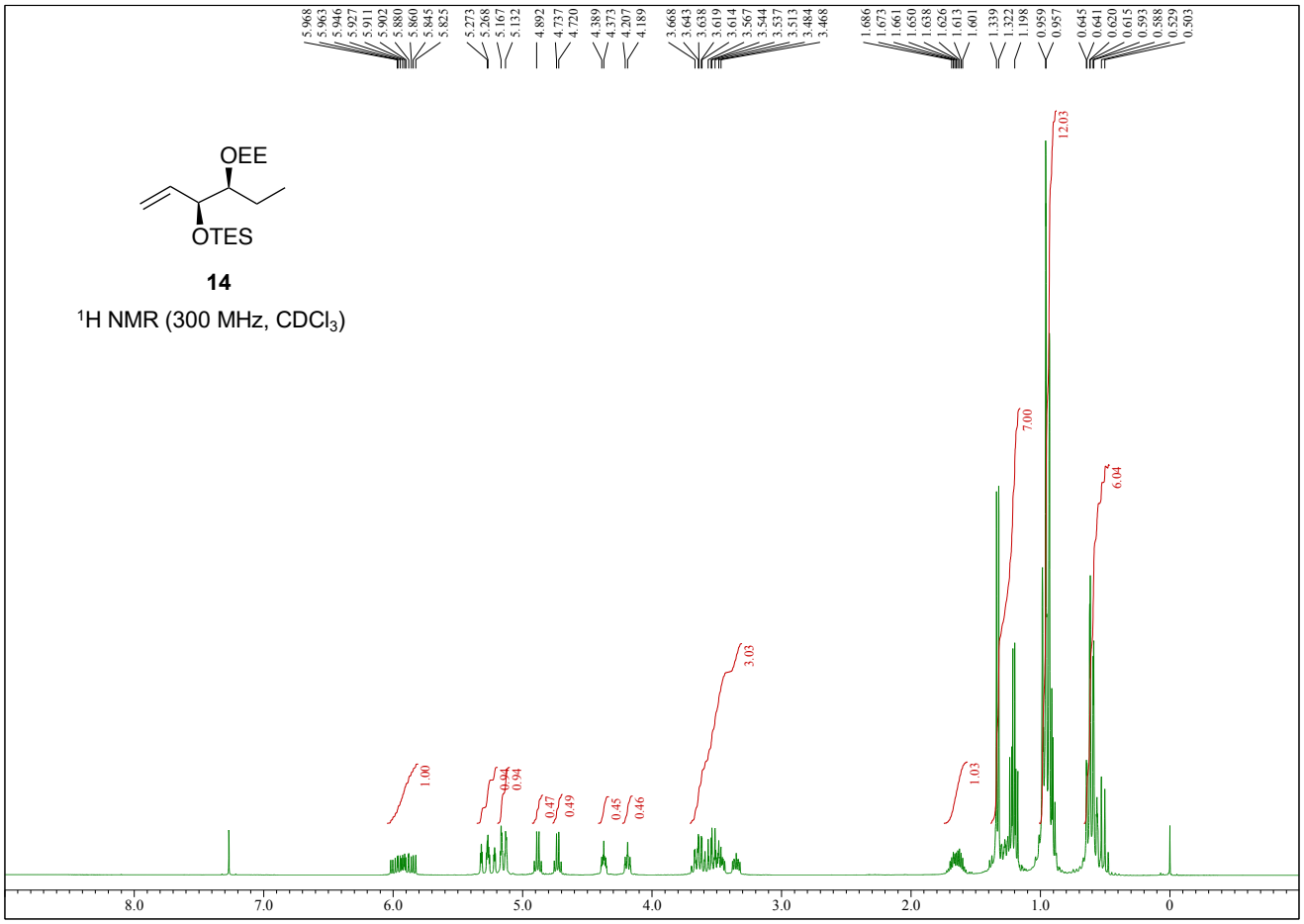


9

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

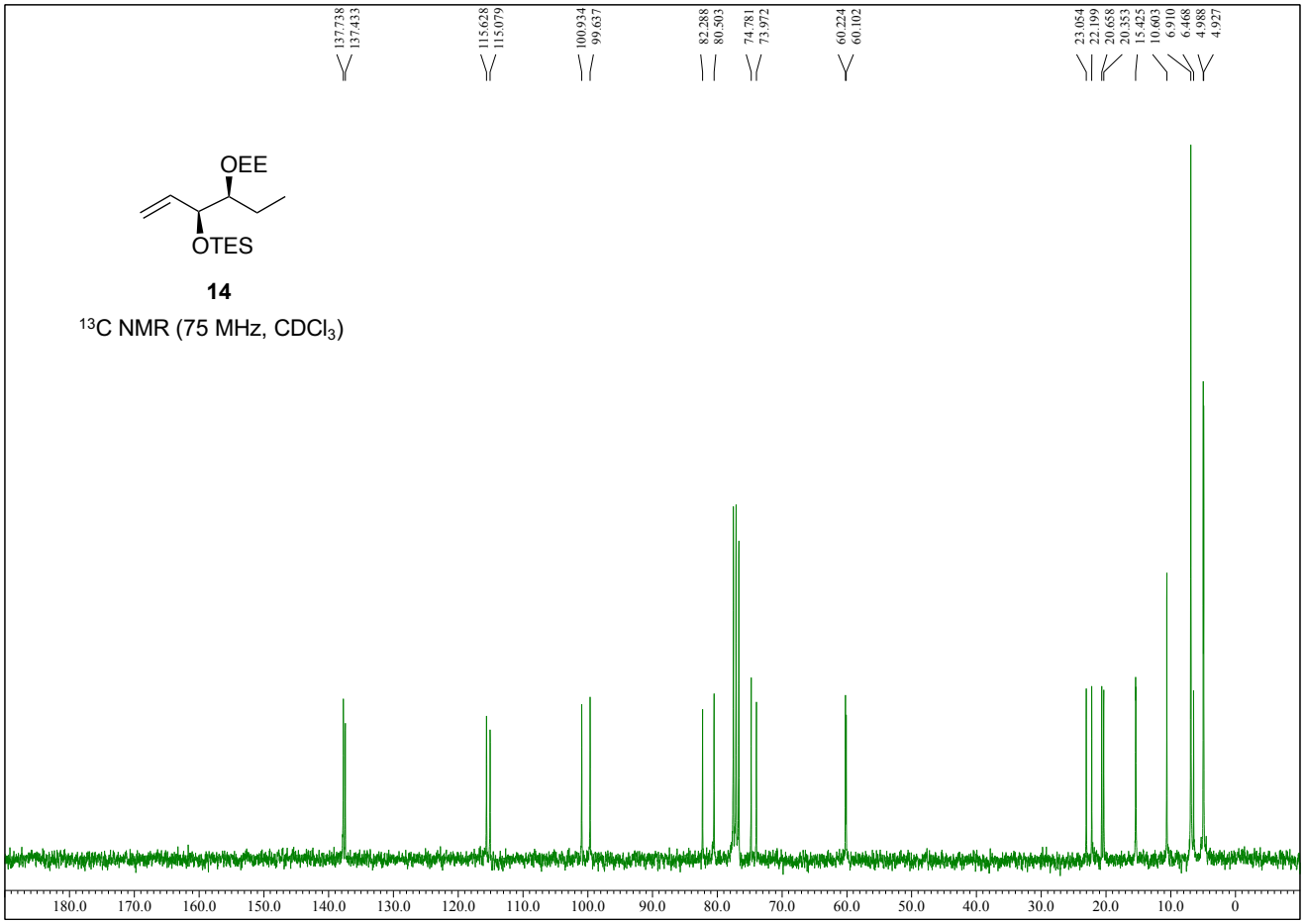

OEE
OH
13
1H NMR (300 MHz, CDCl3)
5.865 5.845 5.829 5.810 5.790 5.768 5.756 5.733
5.385 5.379 5.220 5.186
4.814 4.795 4.633 4.616
4.157
3.939
3.589 3.581 3.566 3.557 3.533 3.451
2.842 2.827
1.519 1.449 1.380 1.363 1.344 1.326 1.262 1.238 1.212 1.189
0.983 0.957 0.930 0.905
4.99
3.06
3.00
3.01
1.09
1.10
1.07
0.52
0.49
0.48
0.50
0.51
0.50
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0


OEE
OH
13
13C NMR (75 MHz, CDCl3)
137.801 137.252
117.248 116.363
101.837 100.143
85.235
80.581
75.134 73.806
61.691 60.974
24.582 24.155 20.264 20.172
15.183
9.644
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0



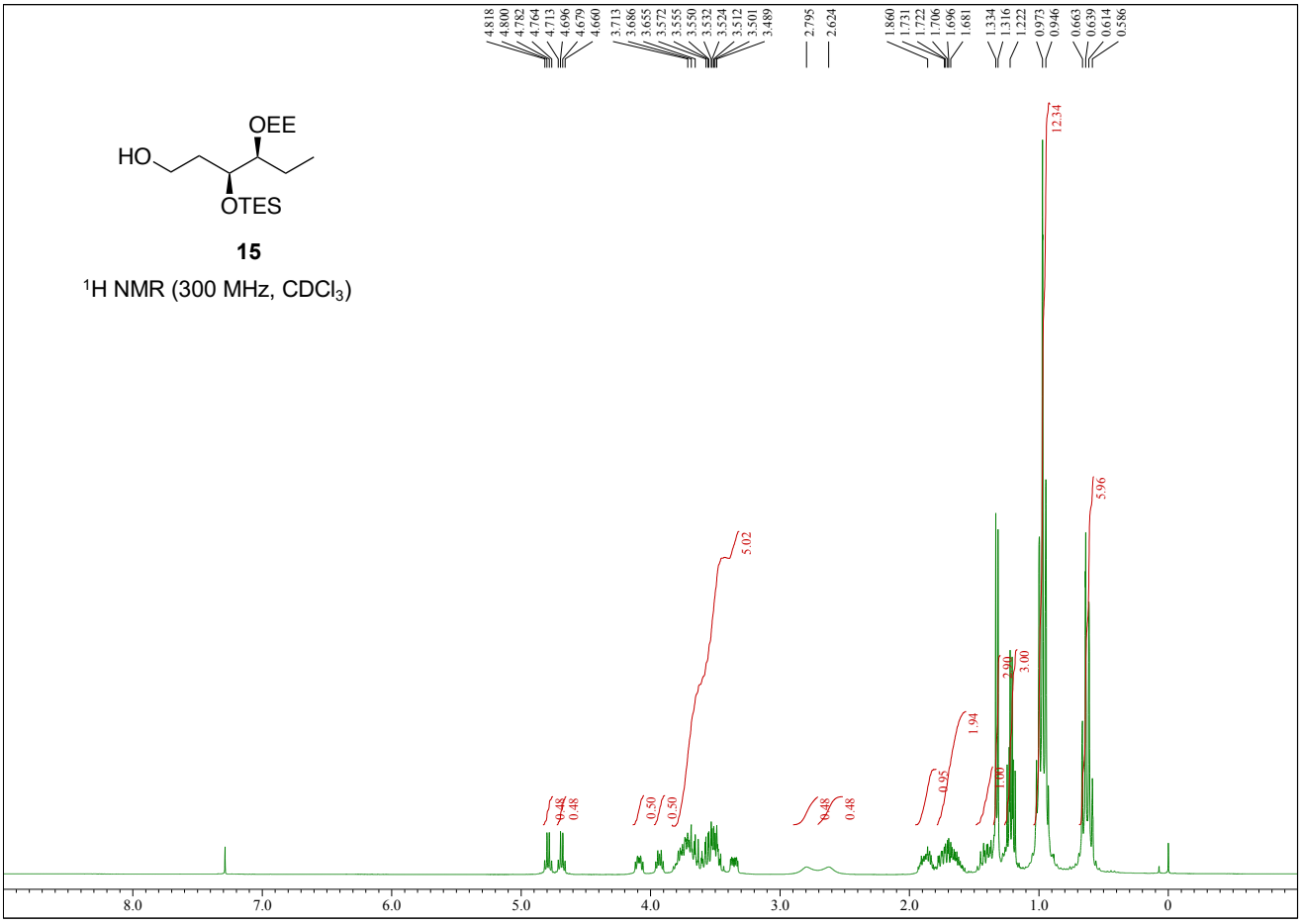
14

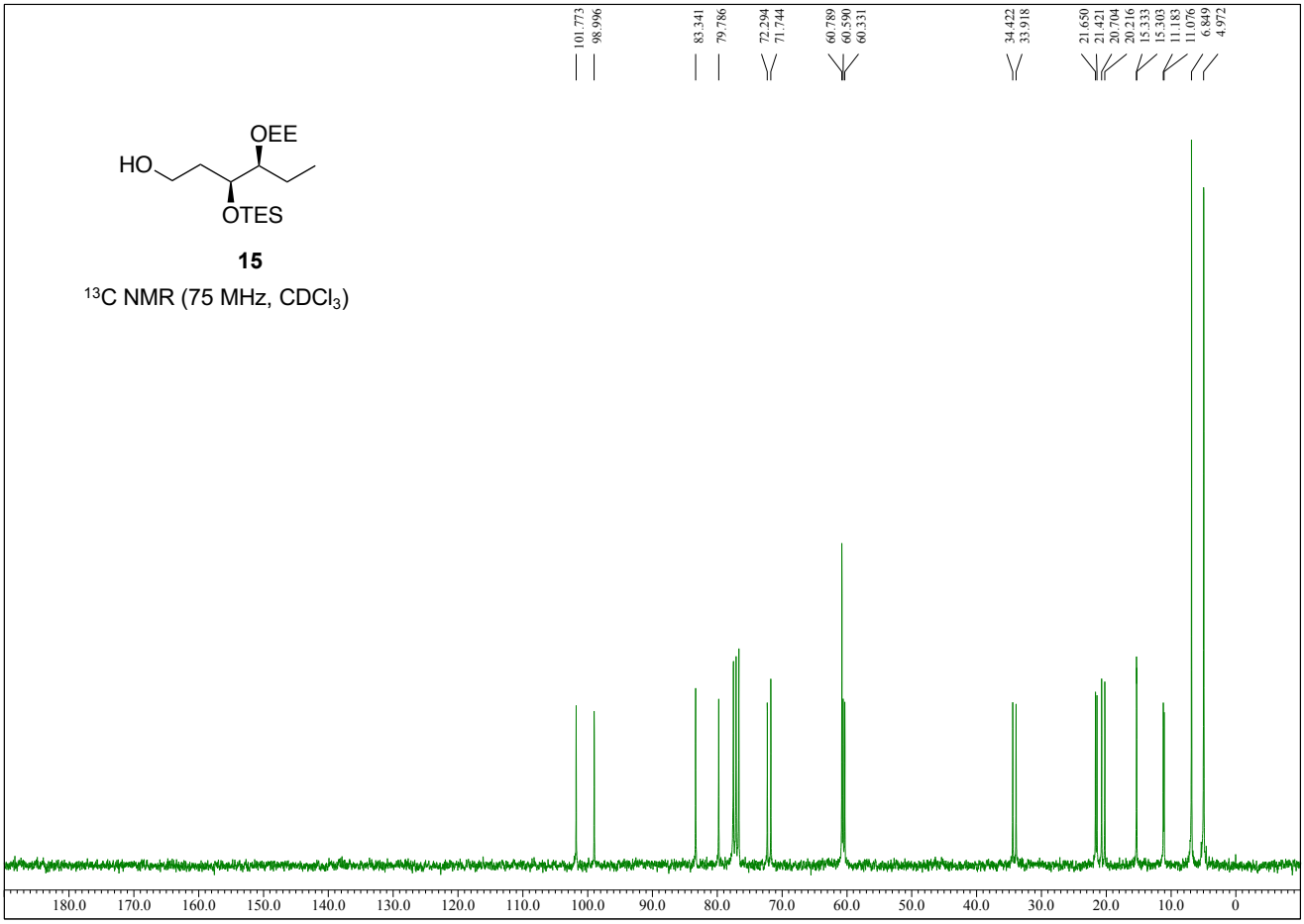
^{1}H NMR (300 MHz, $CDCl_3$)

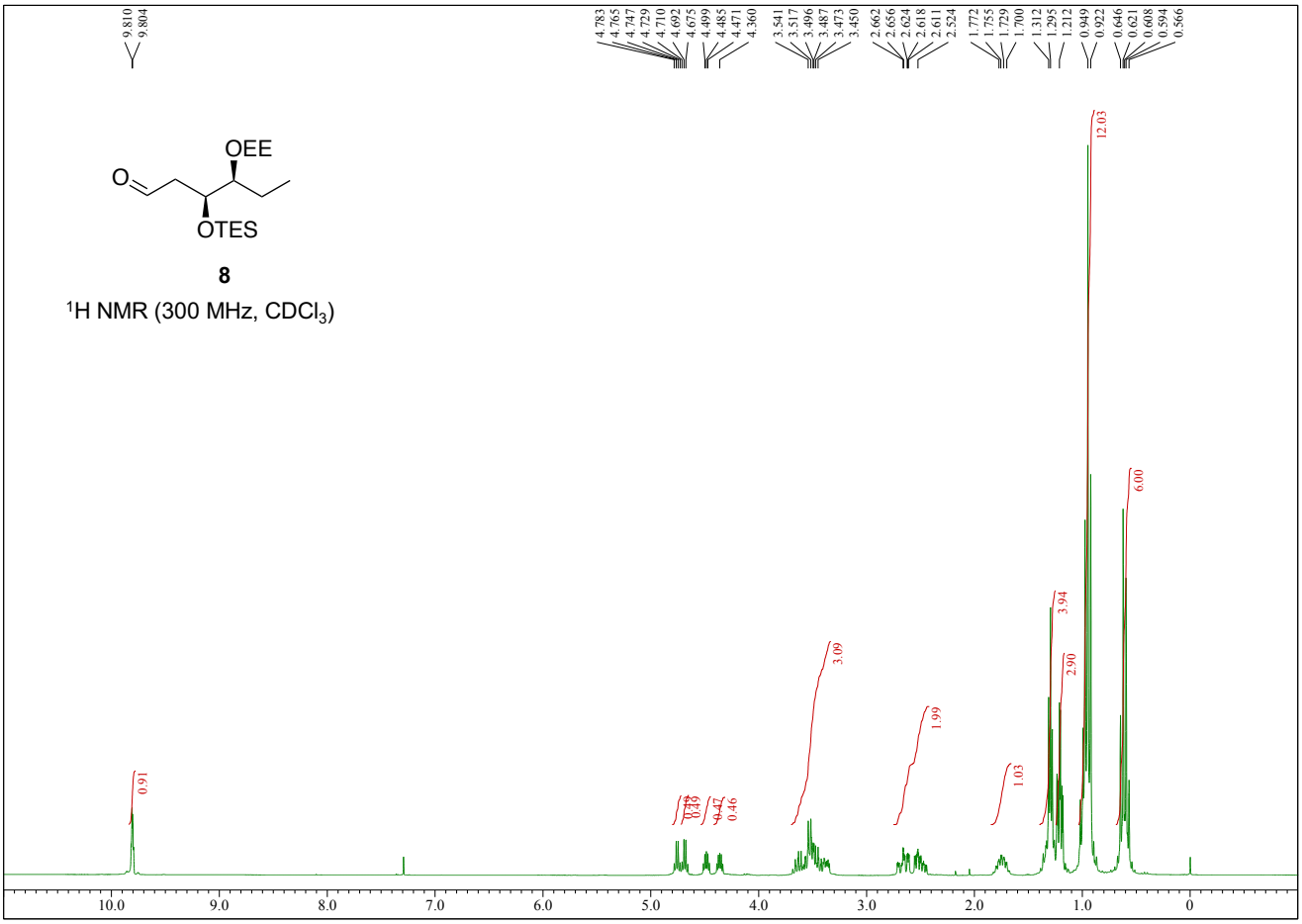


14

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

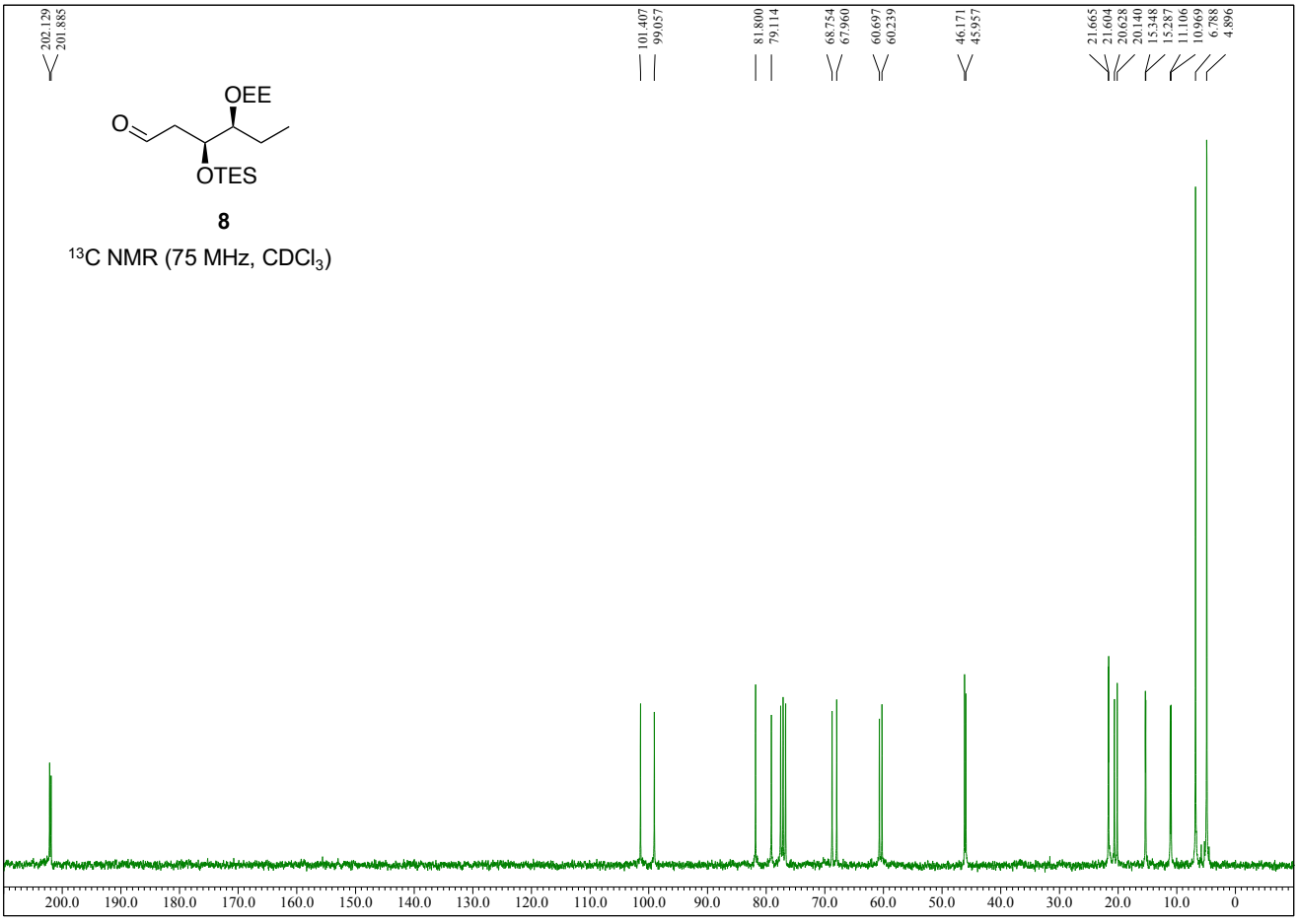

OEE
HO
OTES
15
1H NMR (300 MHz, CDCl3)
4.818
4.800
4.782
4.764
4.713
4.696
4.679
4.660
3.713
3.686
3.655
3.572
3.555
3.550
3.532
3.524
3.512
3.501
3.489
2.795
2.624
1.860
1.731
1.722
1.706
1.696
1.681
1.334
1.316
1.222
0.973
0.946
0.663
0.639
0.614
0.586
12.34
5.96
5.02
3.00
2.00
1.94
1.00
0.95
0.50
0.50
0.48
0.48
0.48
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


OEE
HO
OTES
15
13C NMR (75 MHz, CDCl3)
101.773
98.996
83.341
79.786
72.294
71.744
60.789
60.590
60.331
34.422
33.918
21.650
21.421
20.704
20.216
15.333
15.303
11.183
11.076
6.849
4.972
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0



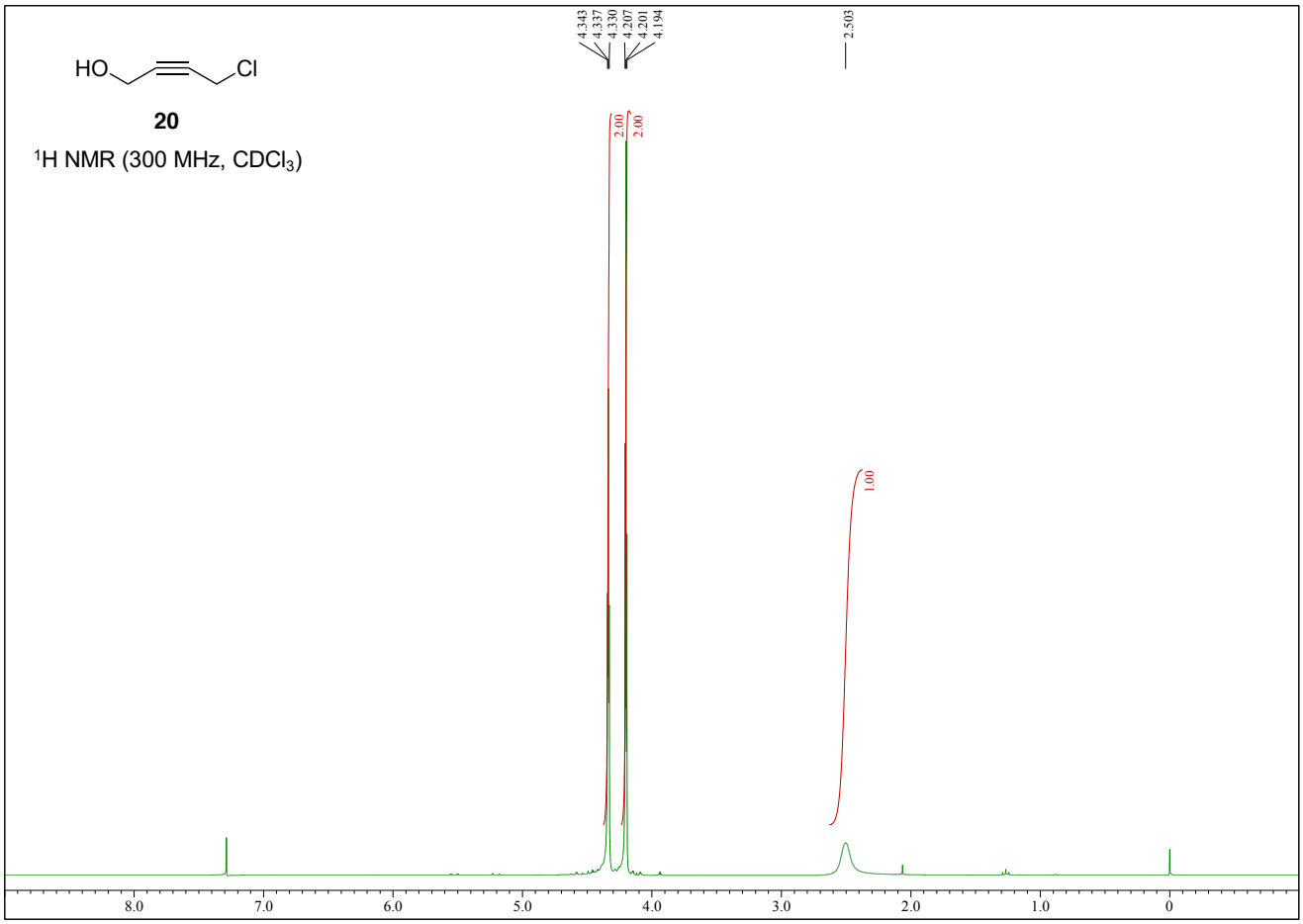
8

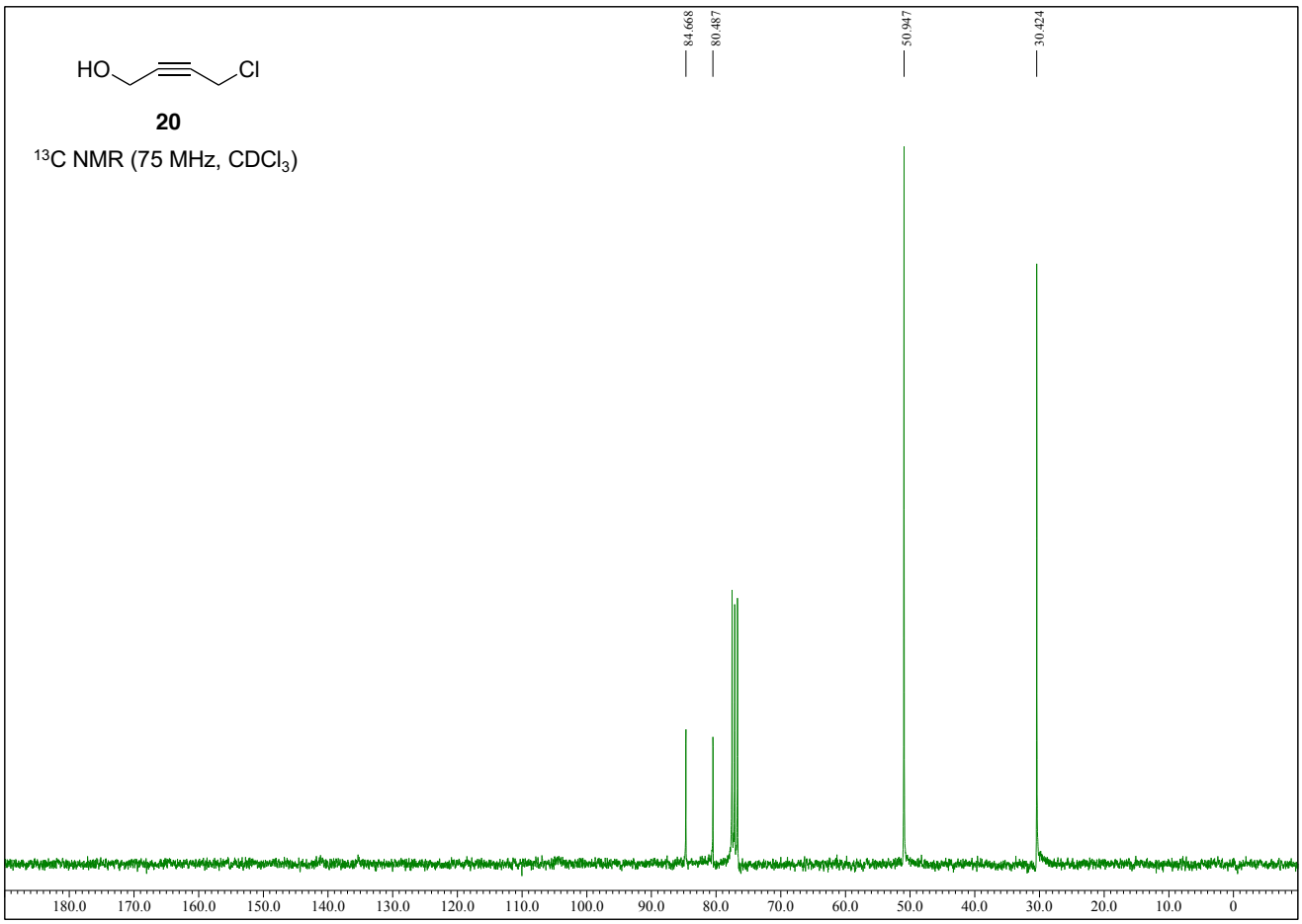
^{1}H NMR (300 MHz, $CDCl_3$)

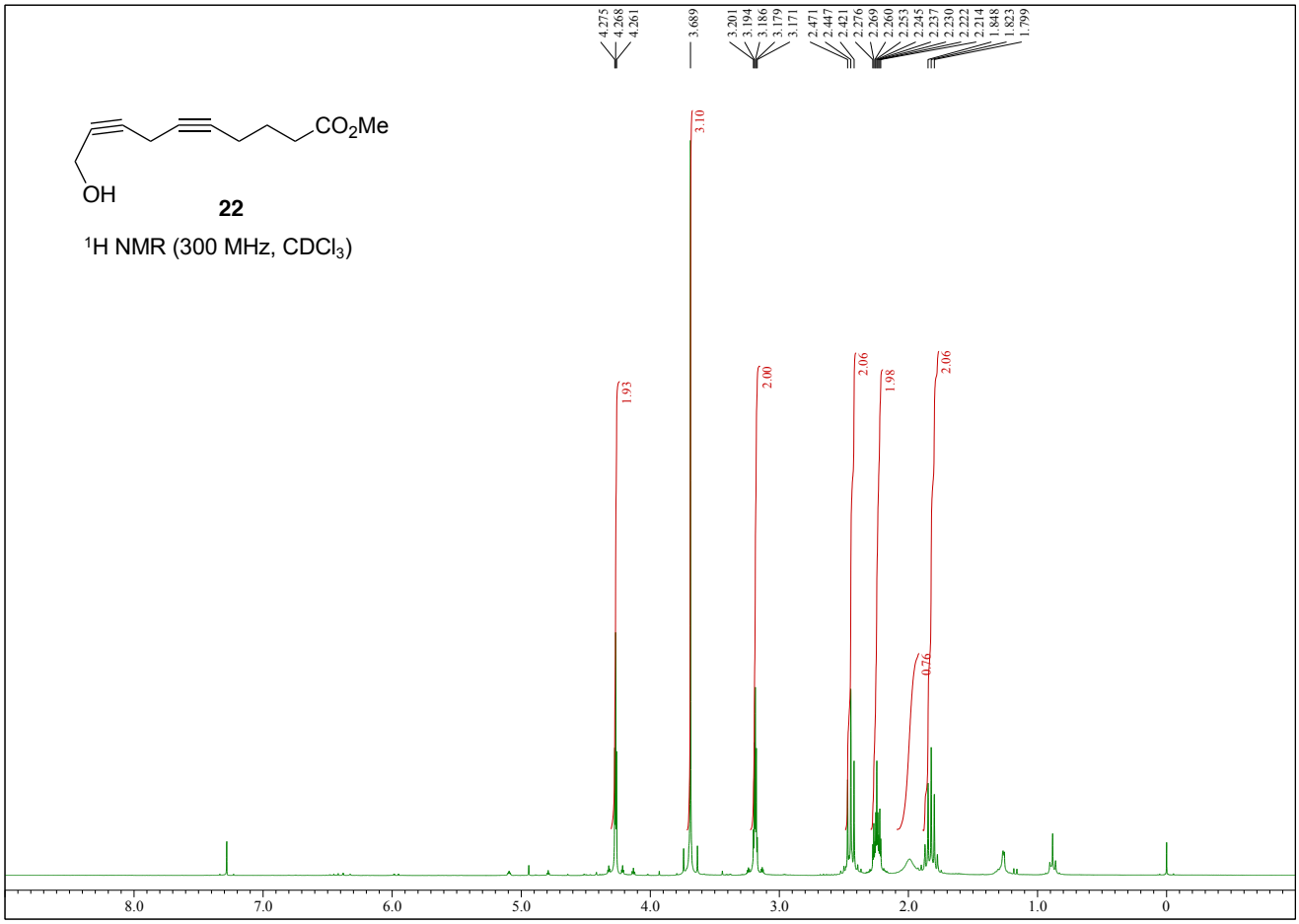


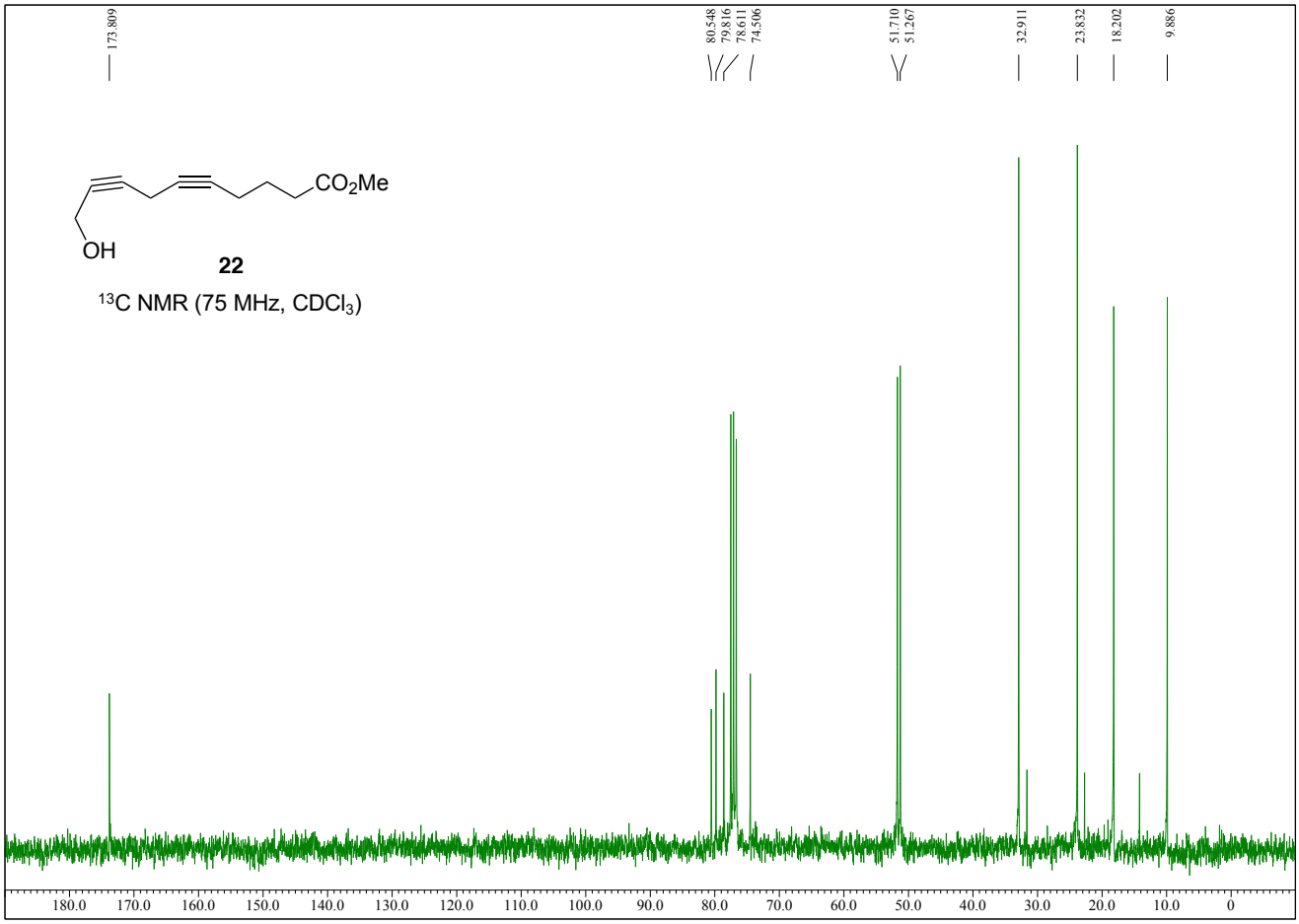
8

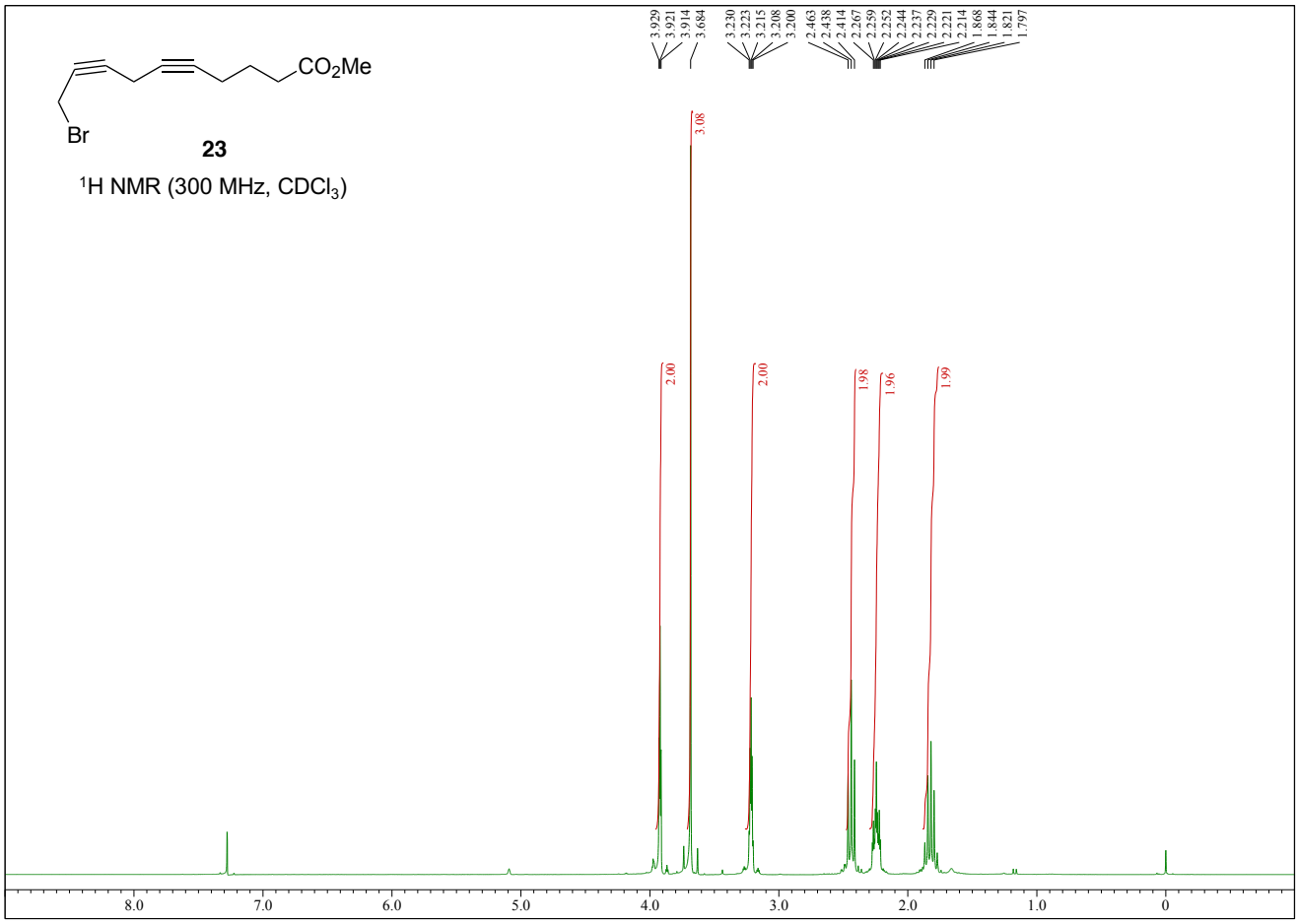
^{13}C NMR (75 MHz, $CDCl_3$)

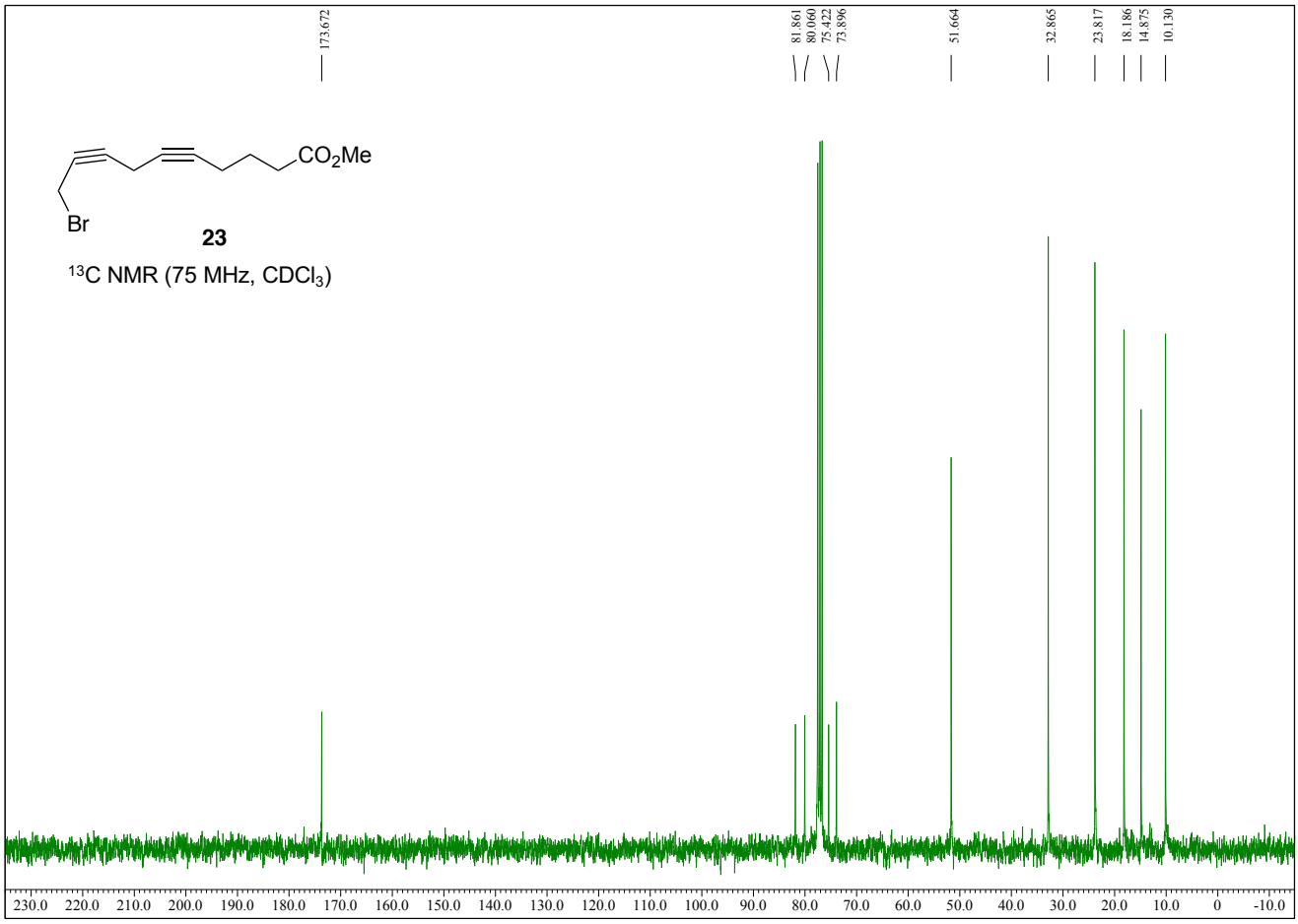

HO
Cl
20
1H NMR (300 MHz, CDCl3)
4.343
4.337
4.330
4.207
4.201
4.194
2.503
2.00
2.00
1.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

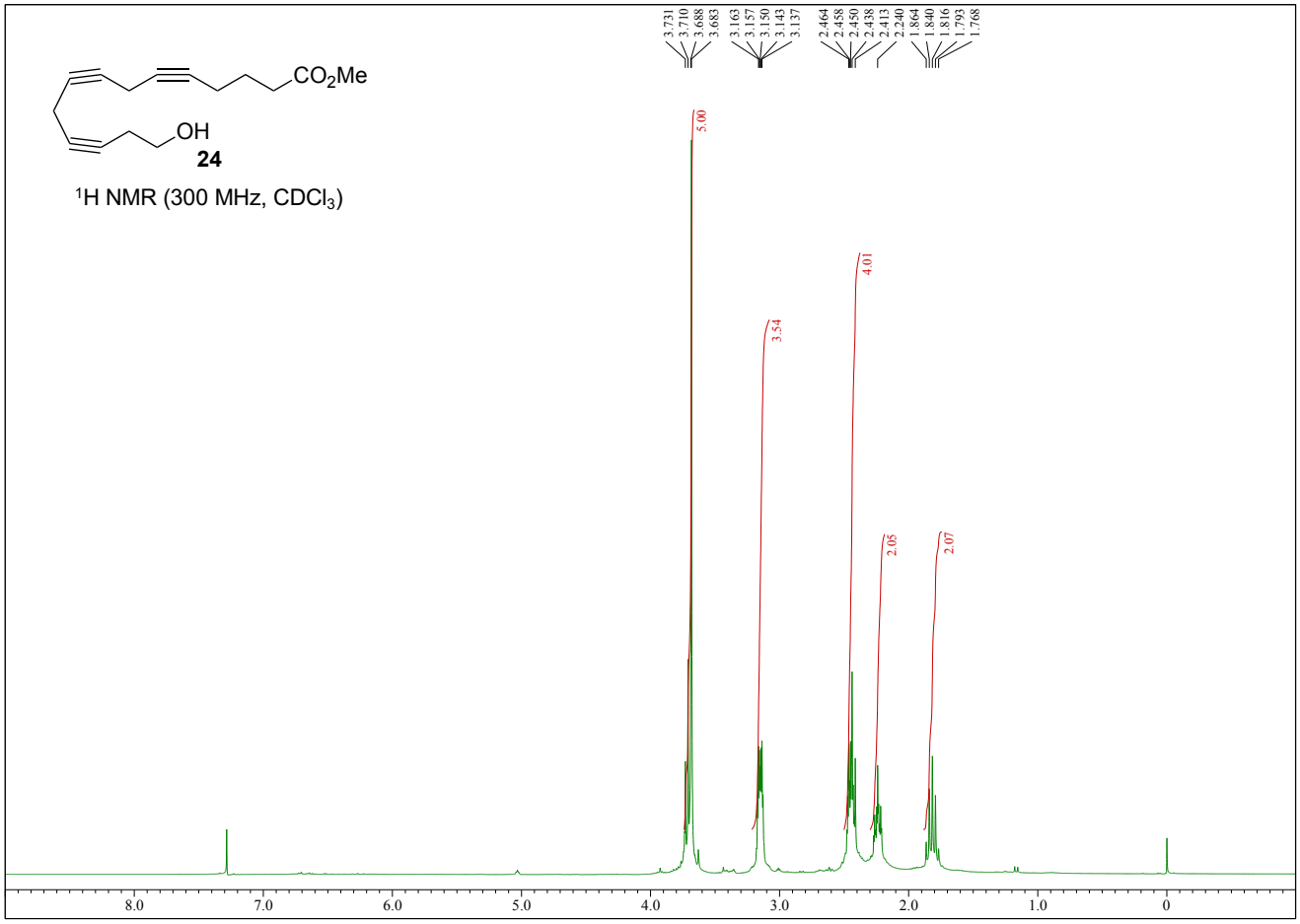

HO
Cl
20
13C NMR (75 MHz, CDCl3)
84.668
80.487
50.947
30.424
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0

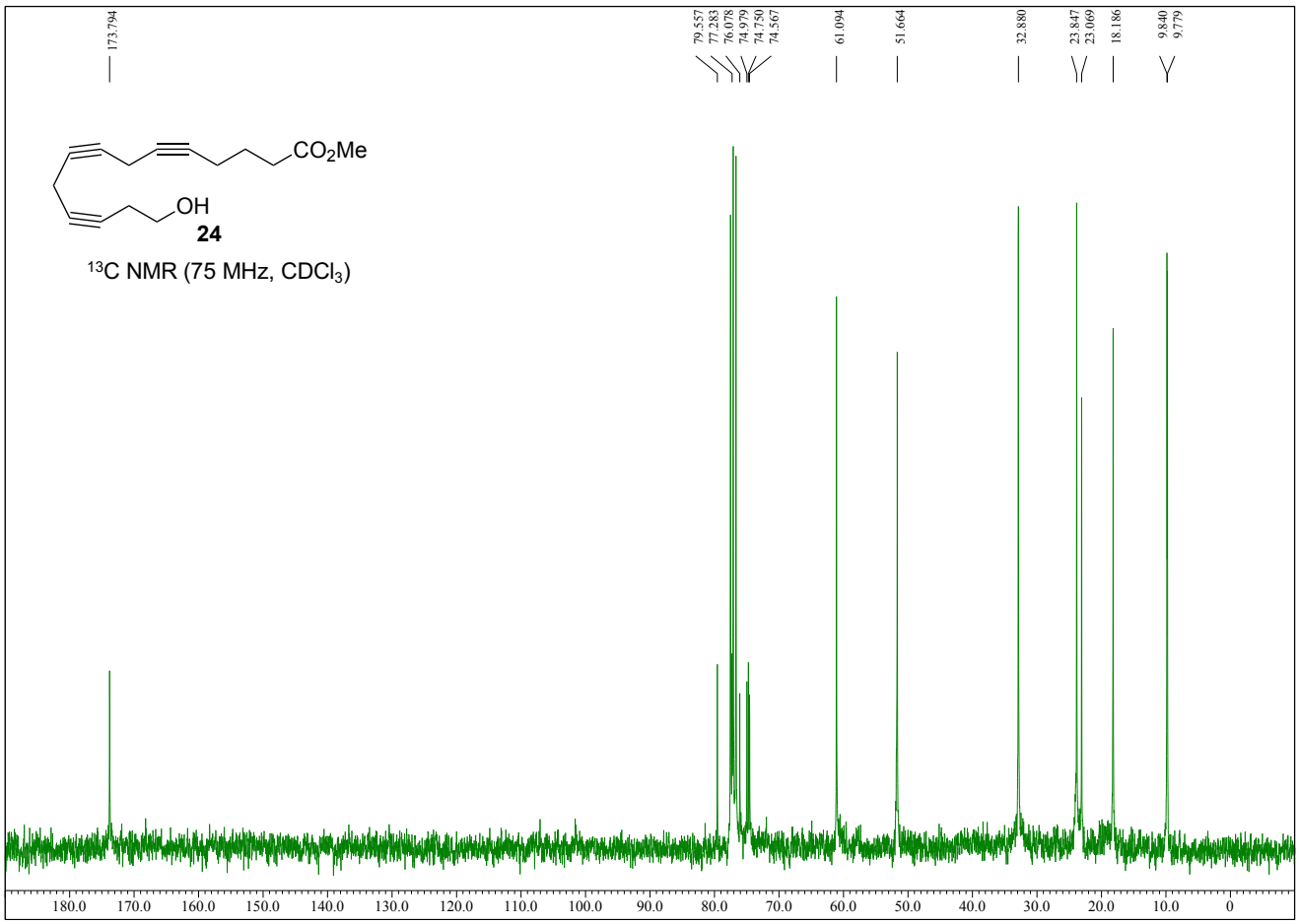

4.275
4.268
4.261
3.689
3.201
3.194
3.186
3.179
3.171
2.471
2.447
2.421
2.276
2.269
2.260
2.253
2.245
2.237
2.230
2.222
2.214
1.848
1.823
1.799
CO2Me
OH
22
1H NMR (300 MHz, CDCl3)
3.10
1.93
2.00
2.06
1.98
2.06
0.76
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

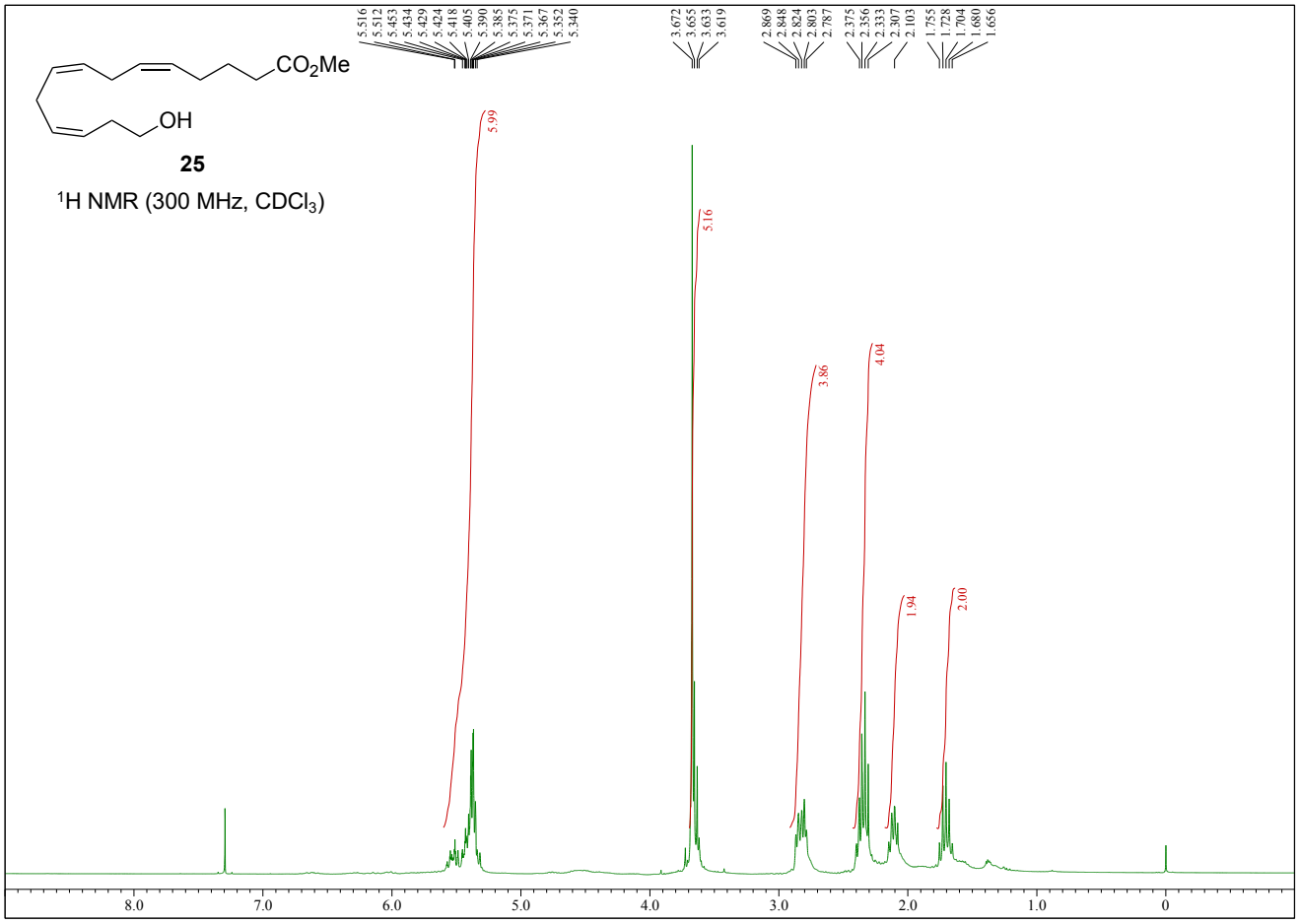

173.809
80.548
79.816
78.611
74.506
51.710
51.267
32.911
23.832
18.202
9.886
CO2Me
OH
22
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0

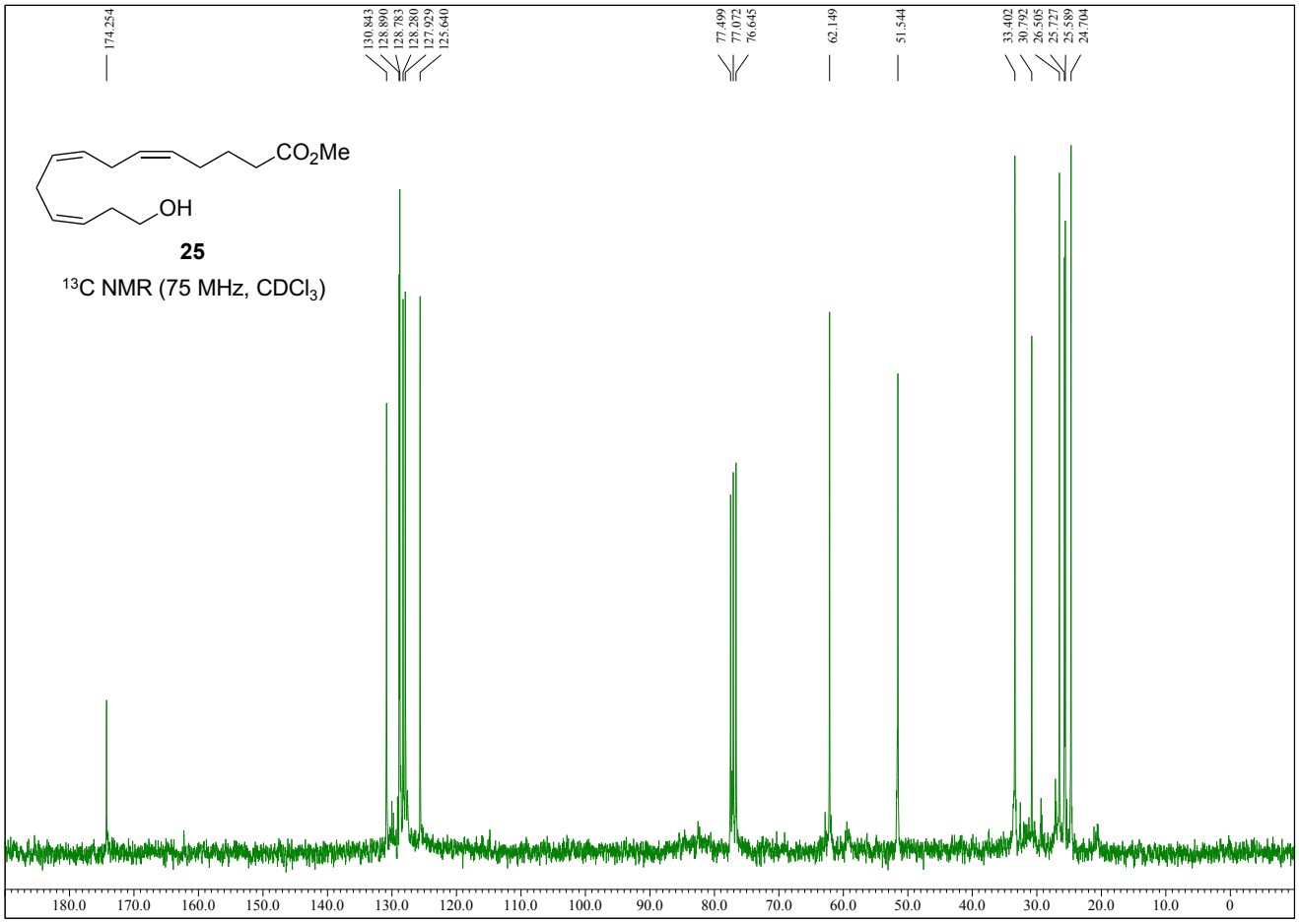

CO2Me
Br
23
1H NMR (300 MHz, CDCl3)
3.929
3.921
3.914
3.684
3.230
3.223
3.215
3.208
3.200
2.463
2.438
2.414
2.267
2.259
2.252
2.244
2.237
2.229
2.221
2.214
1.868
1.844
1.821
1.797
3.08
2.00
2.00
1.98
1.96
1.99
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

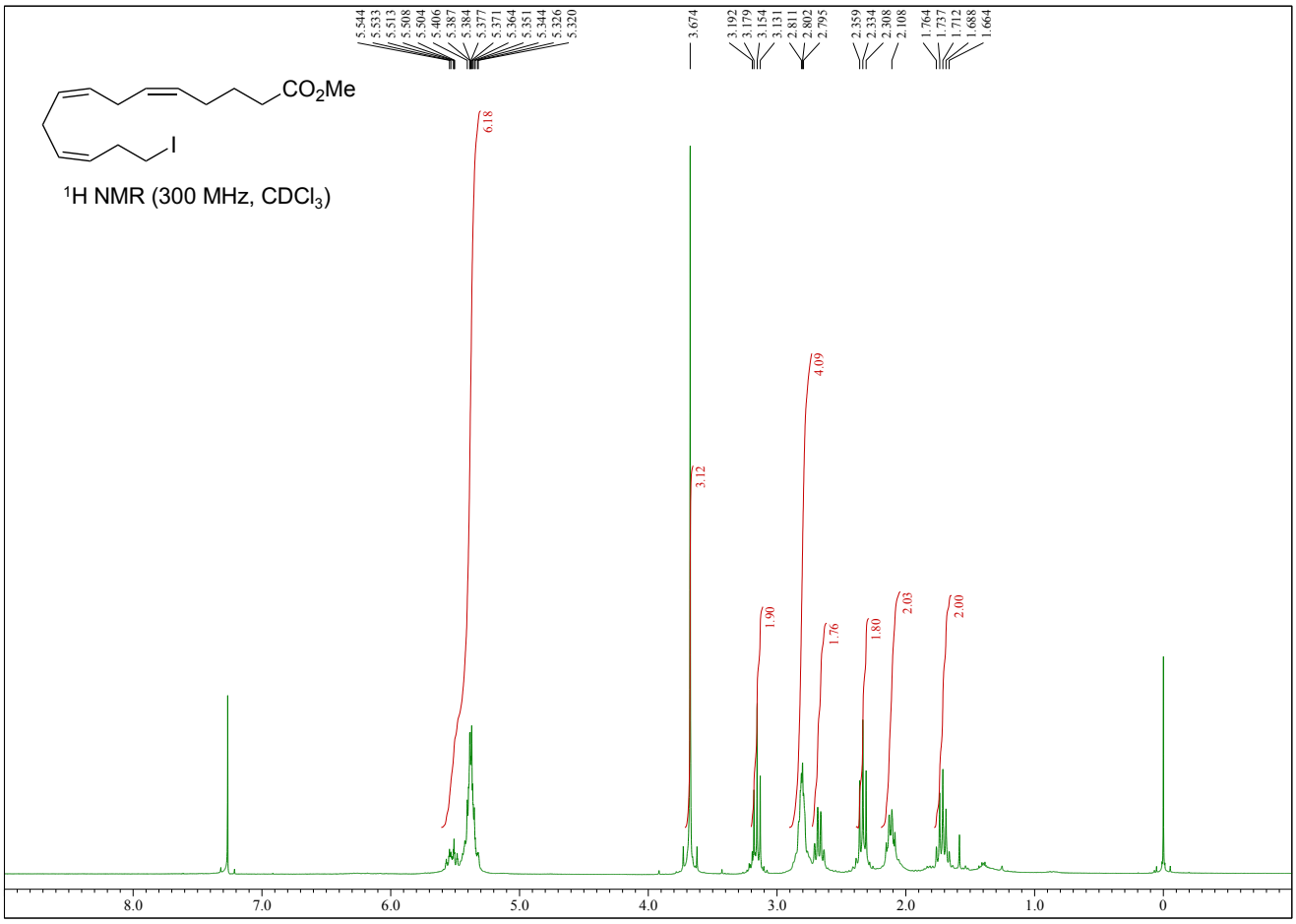

CO2Me
Br
23
13C NMR (75 MHz, CDCl3)
173.672
81.861
80.060
75.422
73.896
51.664
32.865
23.817
18.186
14.875
10.130
230.0
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0

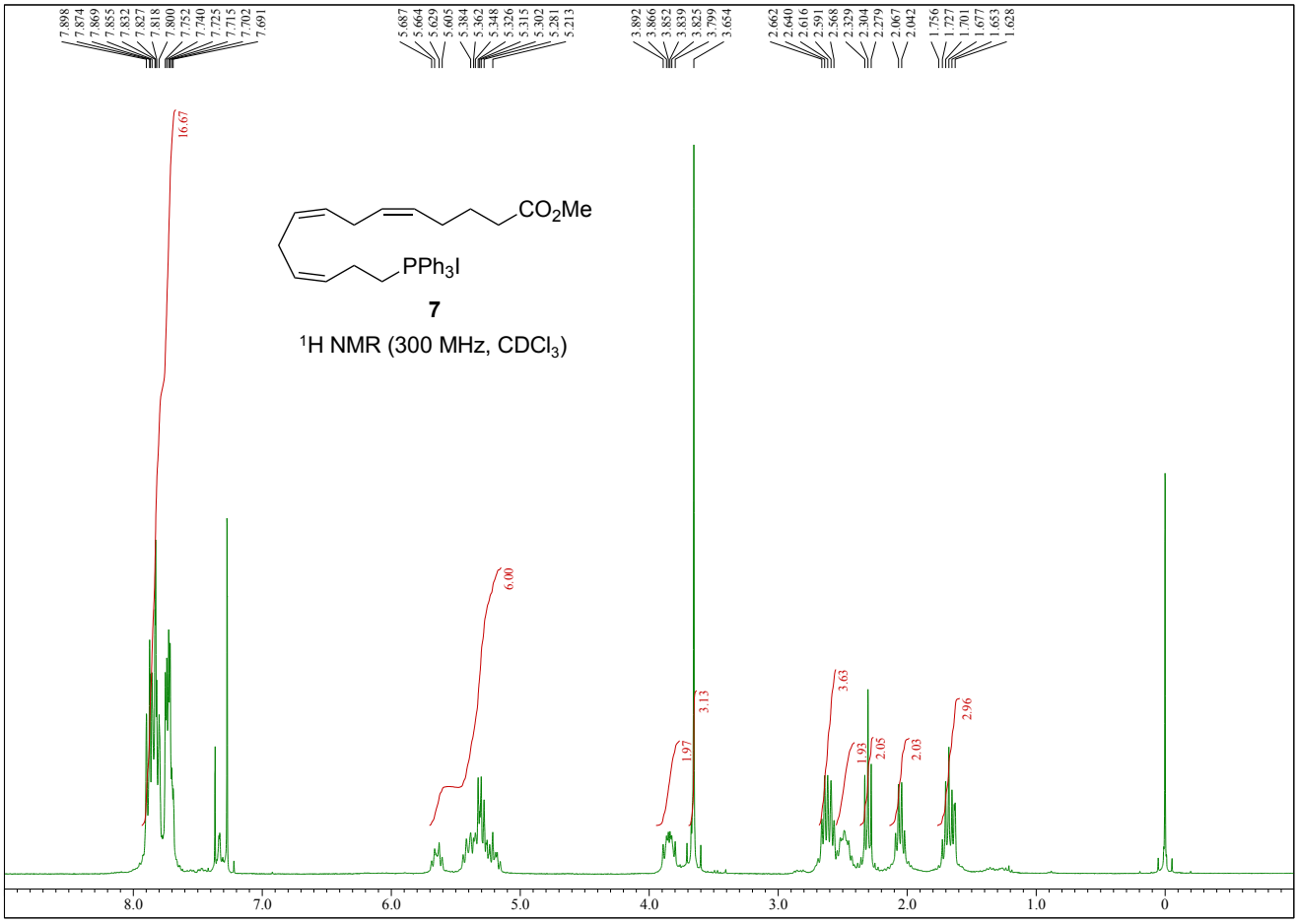

CO2Me
OH
24
1H NMR (300 MHz, CDCl3)
3.731
3.710
3.688
3.683
3.163
3.157
3.150
3.143
3.137
2.464
2.458
2.450
2.438
2.413
2.240
1.864
1.840
1.816
1.793
1.768
5.00
3.54
4.01
2.05
2.07
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

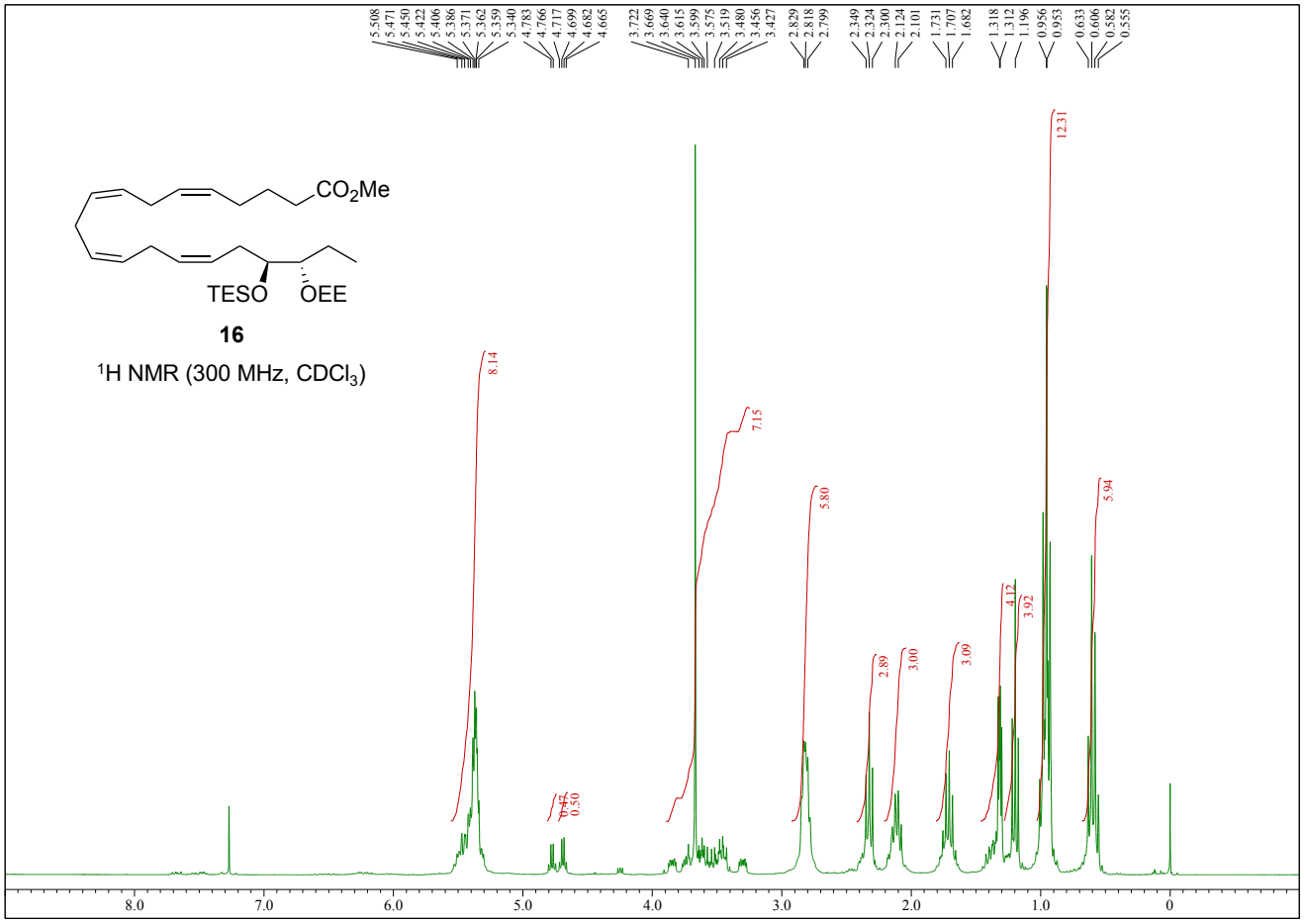

CO2Me
OH
24
13C NMR (75 MHz, CDCl3)
173.794
79.557
77.283
76.078
74.979
74.750
74.567
61.094
51.664
32.880
23.847
23.069
18.186
9.840
9.779
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0

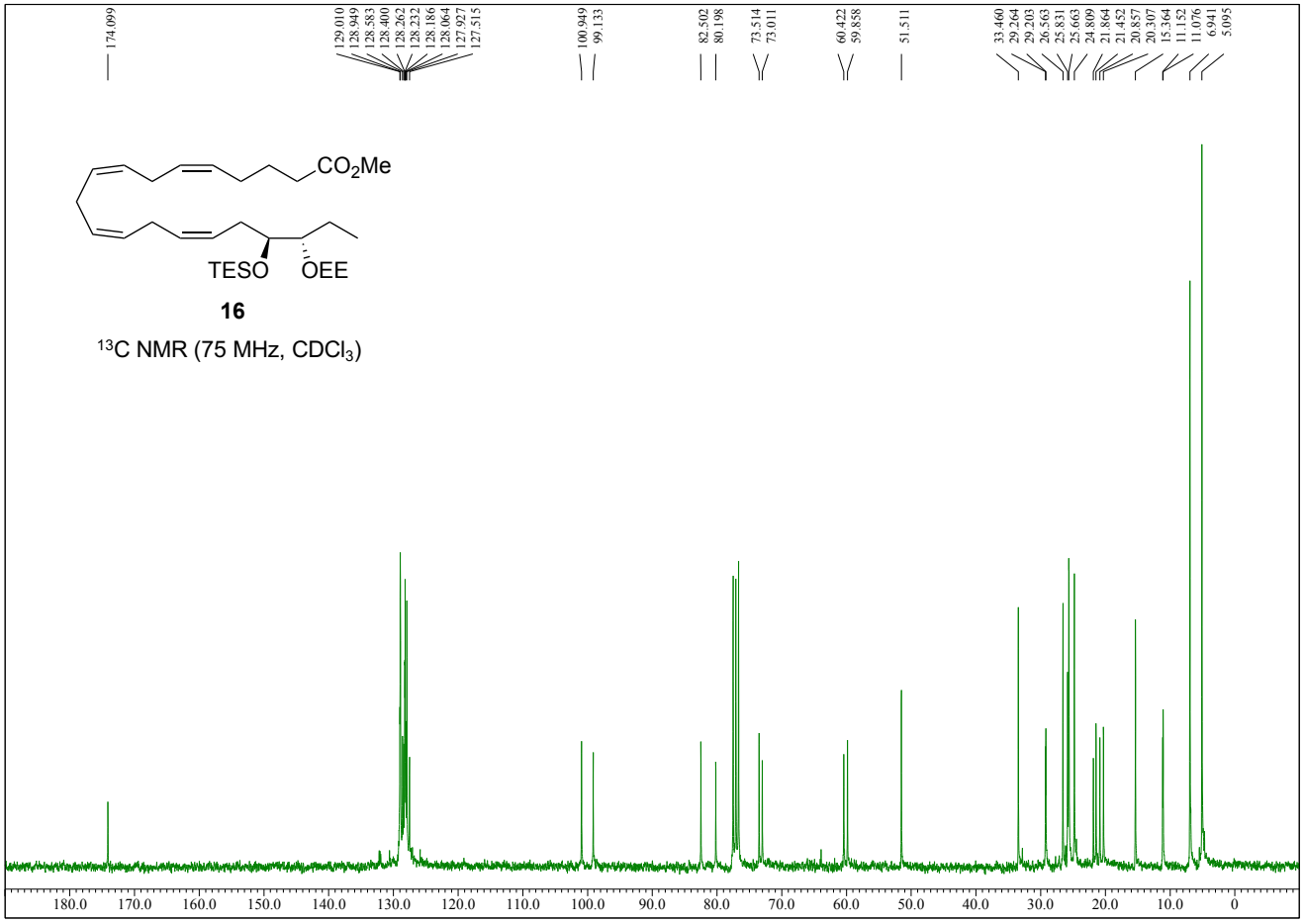

CO2Me
OH
25
1H NMR (300 MHz, CDCl3)
5.99
5.16
3.86
4.04
1.94
2.00

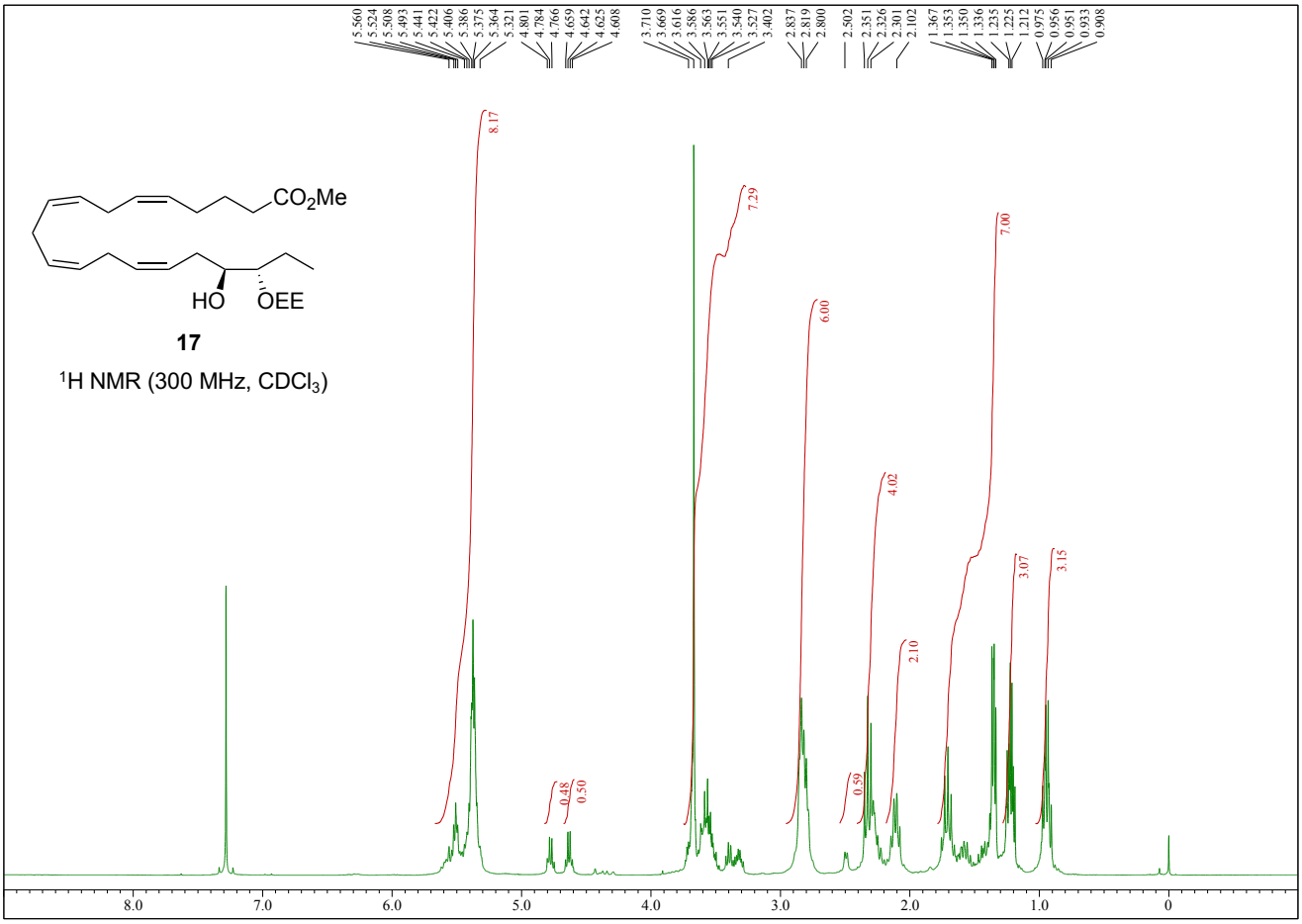

CO2Me
OH
25
13C NMR (75 MHz, CDCl3)

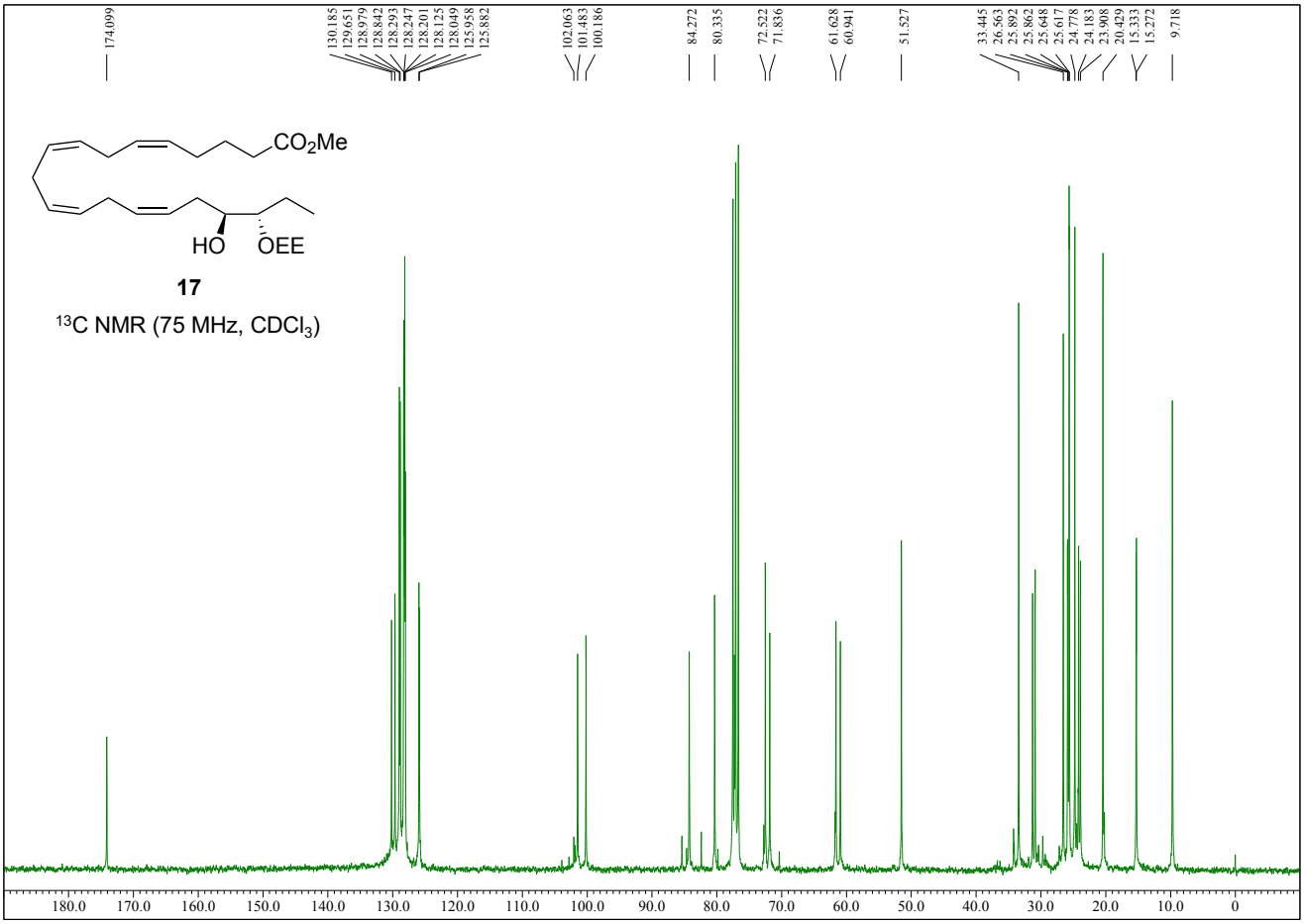

CO2Me
I
1H NMR (300 MHz, CDCl3)

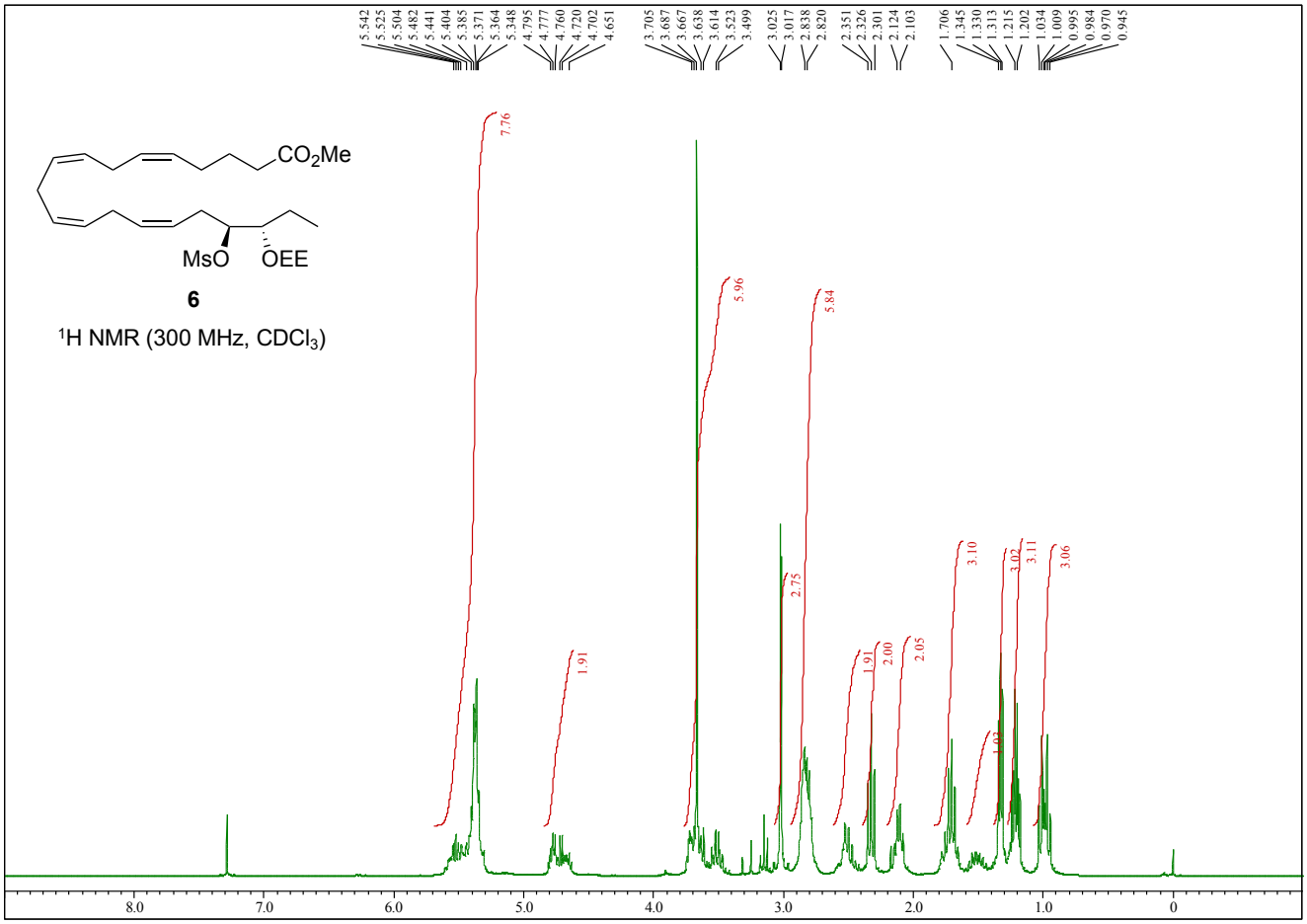

CO2Me
PPh3I
7
1H NMR (300 MHz, CDCl3)

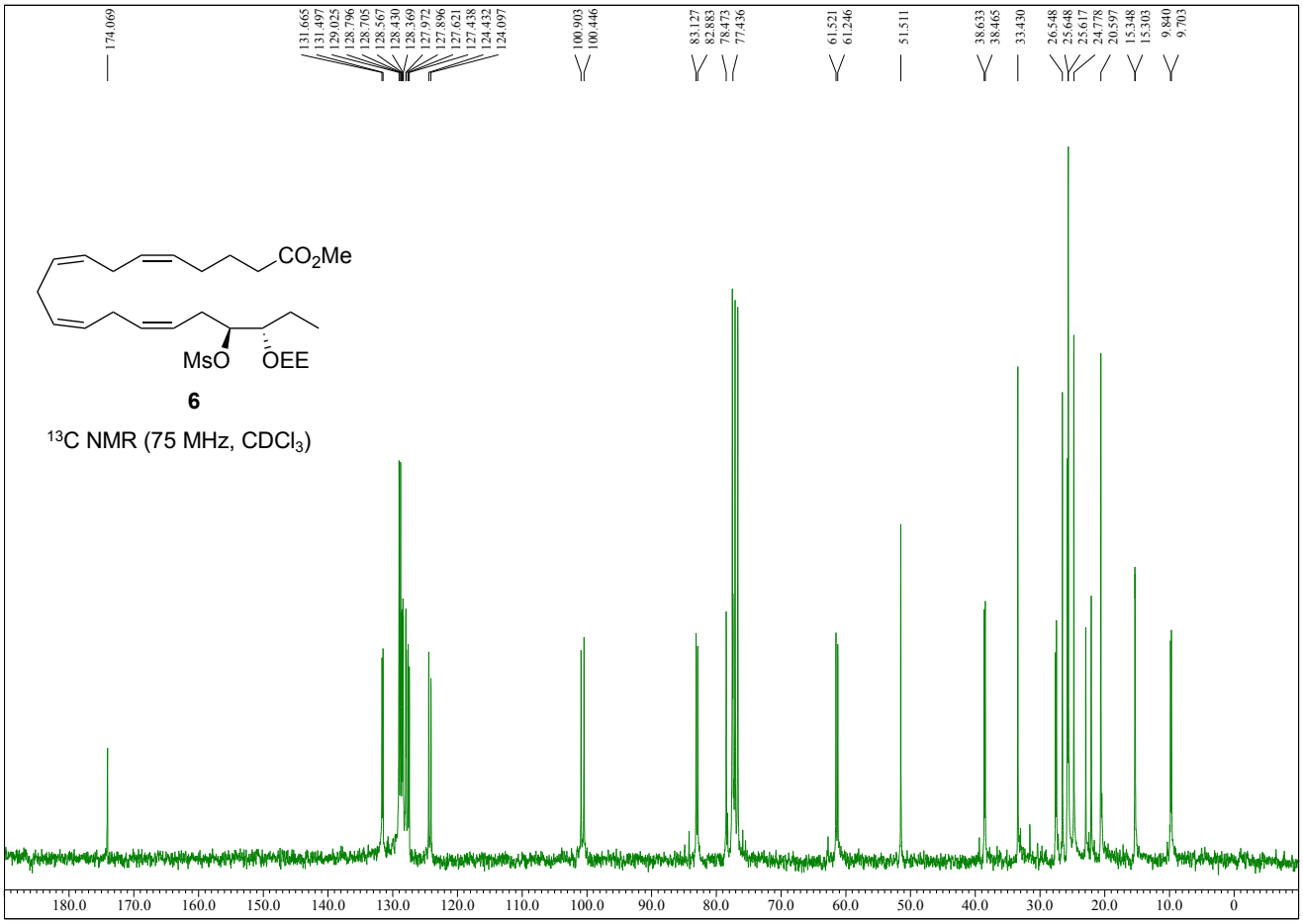

CO2Me
TESO
OEE
16
1H NMR (300 MHz, CDCl3)

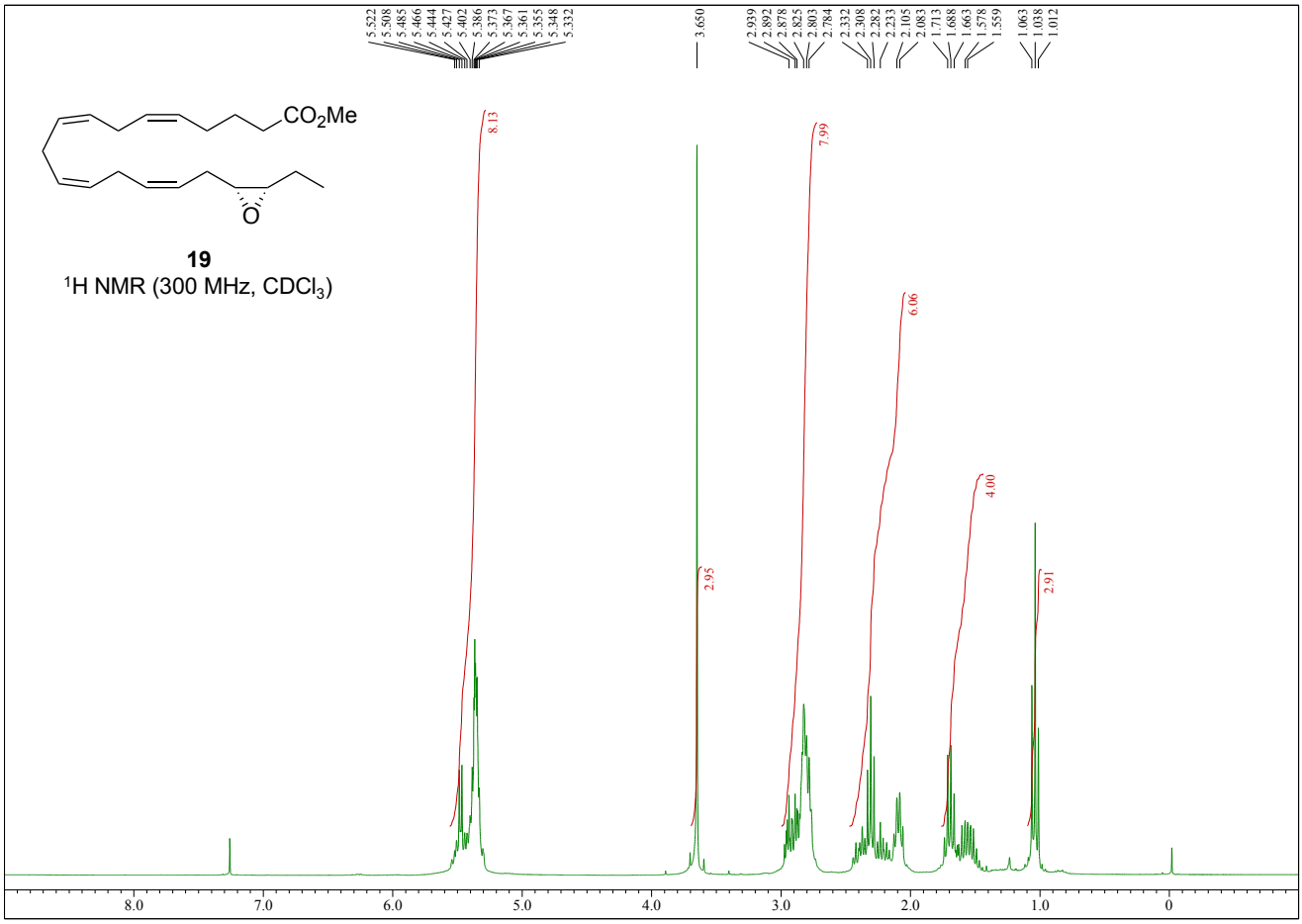

CO2Me
TESO
OEE
16
13C NMR (75 MHz, CDCl3)

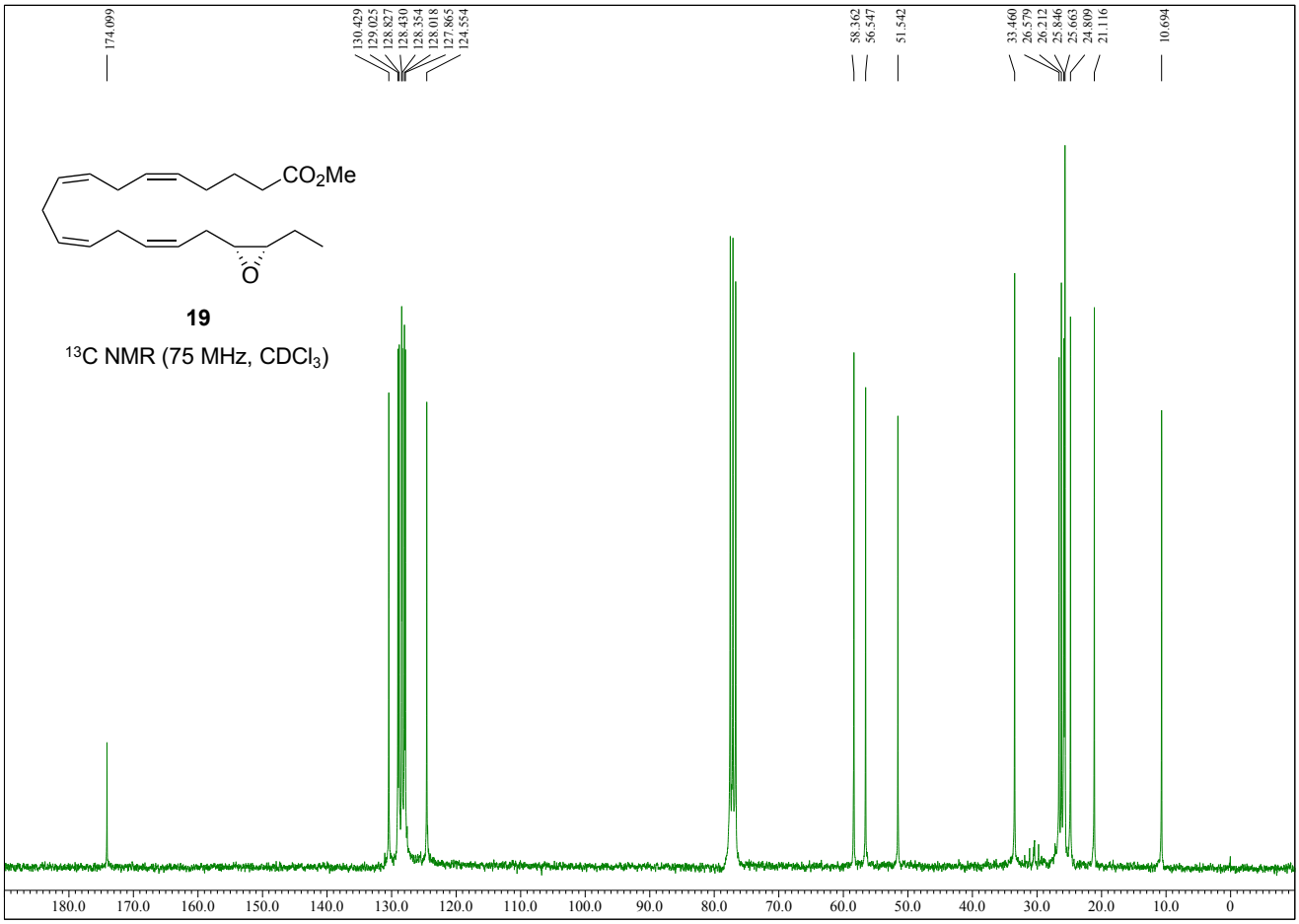

CO2Me
HO
OEE
17
1H NMR (300 MHz, CDCl3)


CO2Me
HO
OEE
17
13C NMR (75 MHz, CDCl3)


CO2Me
MsO
OEE
6
1H NMR (300 MHz, CDCl3)

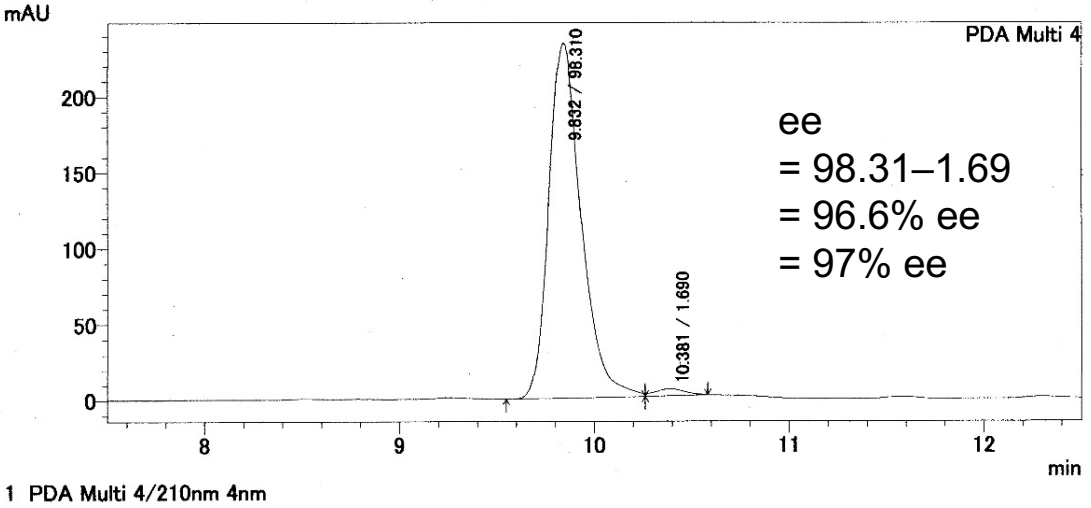

CO2Me
MsO
OEE
6
13C NMR (75 MHz, CDCl3)

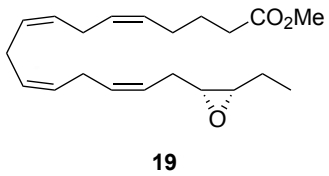

CO2Me
O
19
1H NMR (300 MHz, CDCl3)
5.522 5.508 5.485 5.466 5.444 5.427 5.402 5.386 5.373 5.367 5.361 5.355 5.348 5.332
3.650
2.939 2.892 2.878 2.825 2.803 2.784 2.332 2.308 2.282 2.233 2.105 2.083 1.713 1.688 1.663 1.578 1.559
1.063 1.038 1.012
8.13
7.99
6.06
4.00
2.95
2.91
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0


CO2Me
O
19
13C NMR (75 MHz, CDCl3)
174.099
130.429 129.025 128.827 128.430 128.354 128.018 127.865 124.554
58.362 56.547 51.542
33.460 26.579 26.212 25.846 25.663 24.809 21.116
10.694
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0

Determination of the enantiomeric purity of **19**

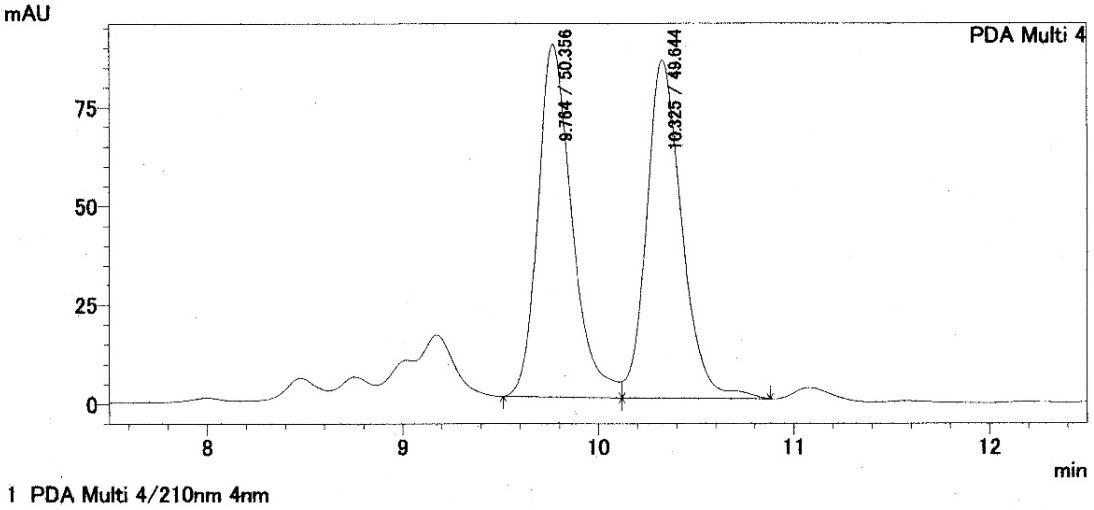
Condition : Chiralcel AD-H, hexane/*i*-PrOH = 99/1, 1.0 mL/min, 35 ºC

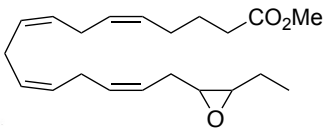




19

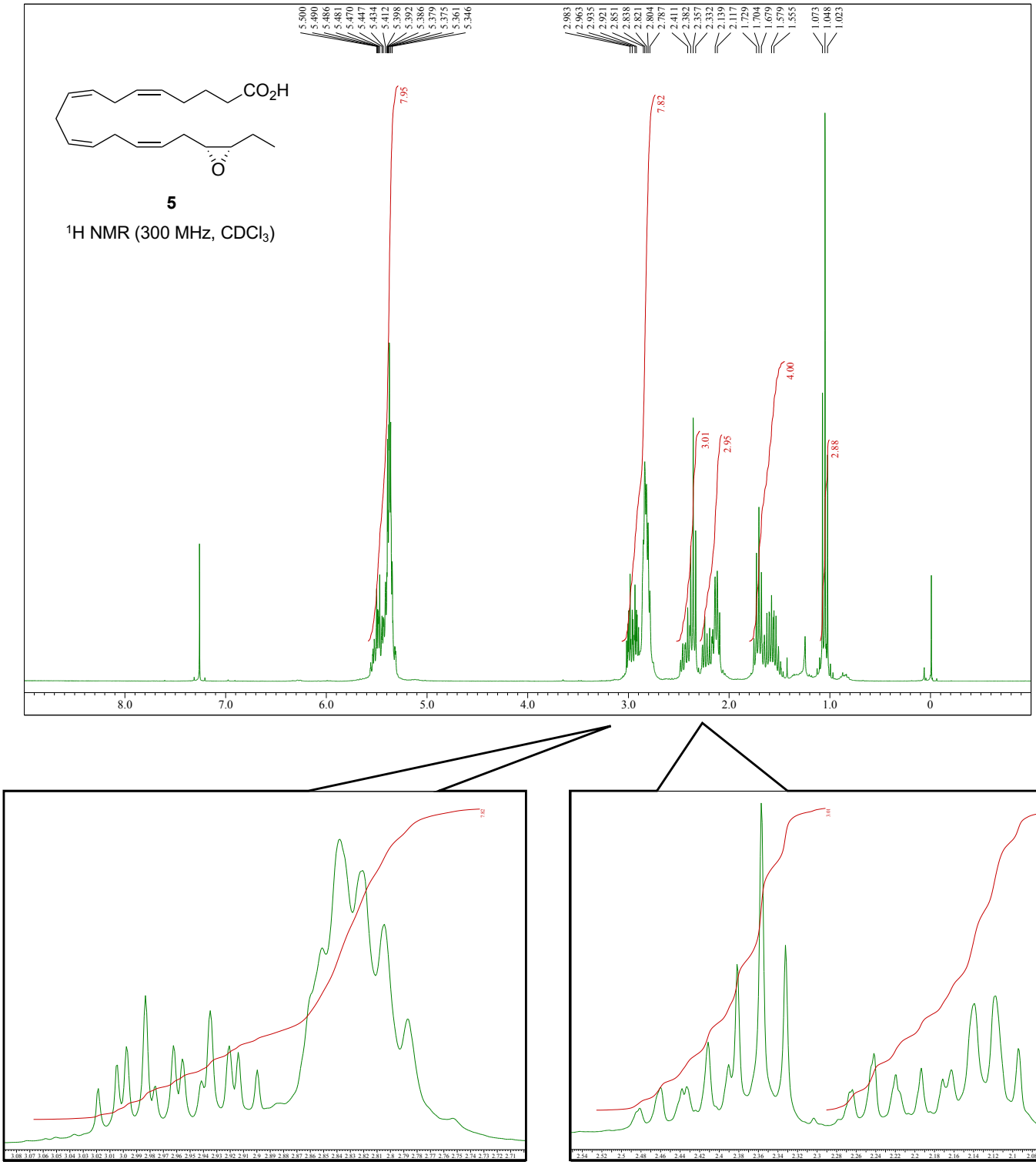
Figure S1. enantioenriched compound **19**

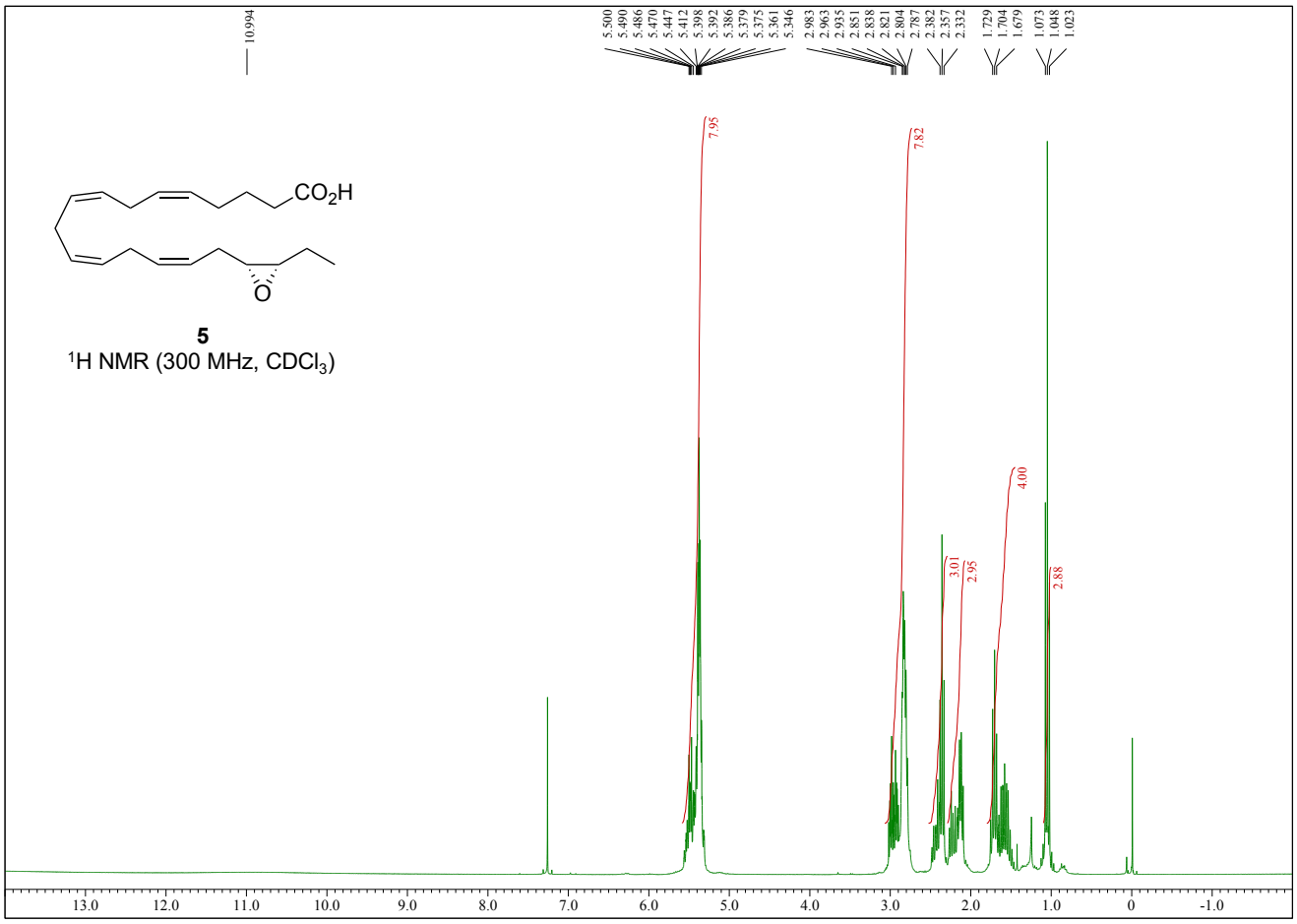




rac-**19**

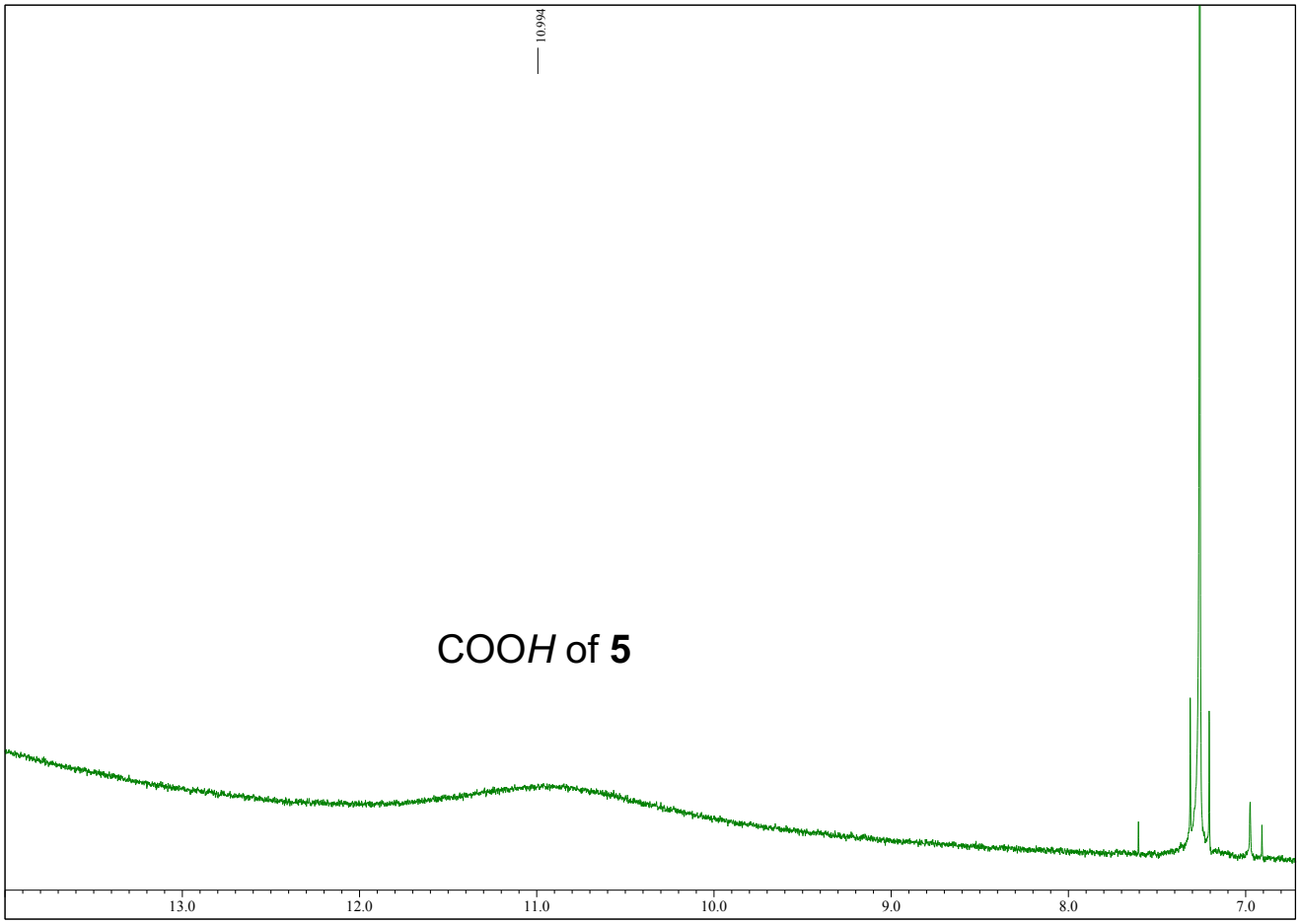
Figure S2. racemic compound **19**

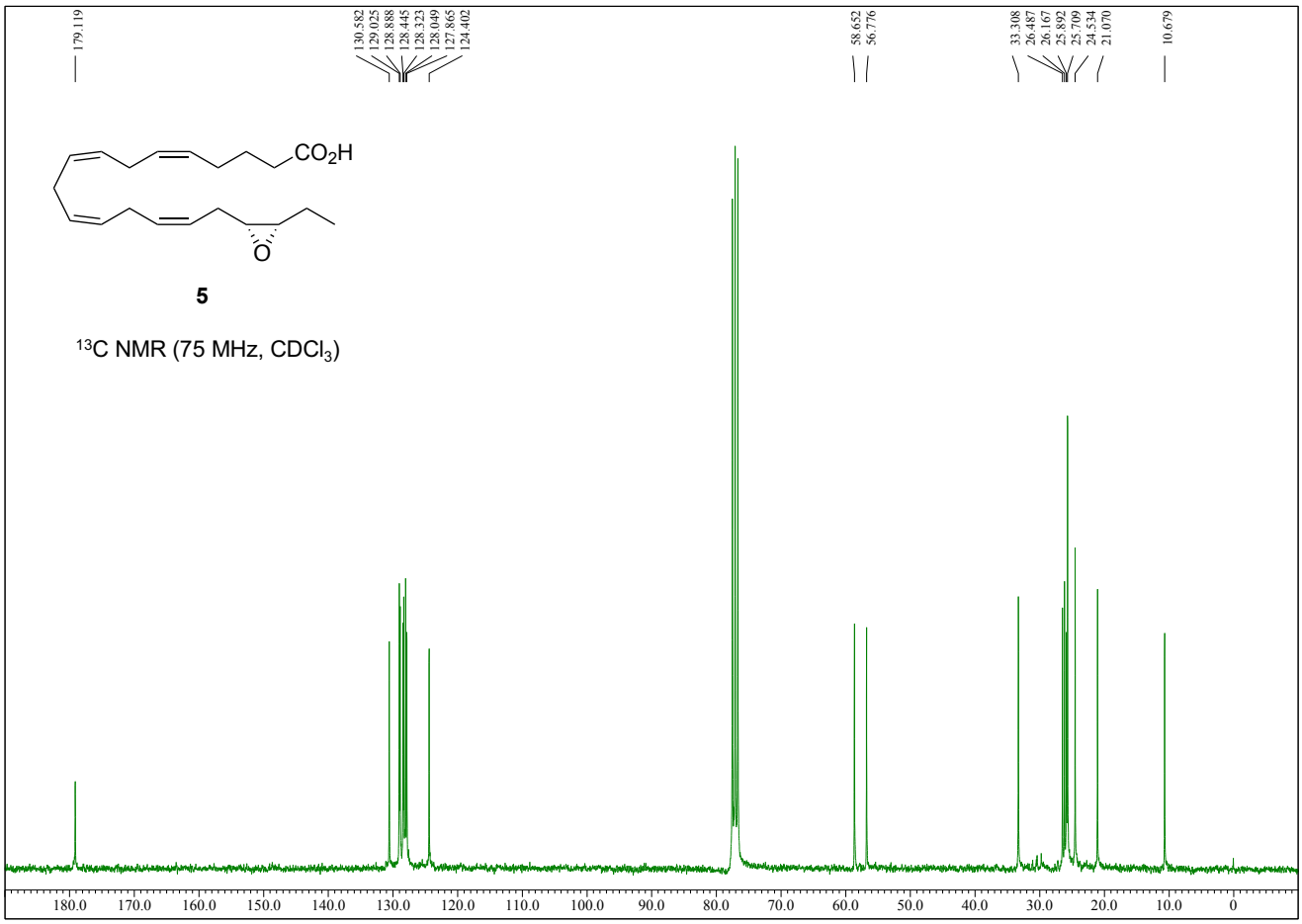

5.500
5.490
5.486
5.481
5.470
5.447
5.434
5.412
5.398
5.392
5.386
5.379
5.375
5.361
5.346
2.983
2.963
2.935
2.921
2.851
2.838
2.821
2.804
2.787
2.411
2.382
2.357
2.332
2.139
2.117
1.729
1.704
1.679
1.579
1.555
1.073
1.048
1.023
CO2H
O
5
1H NMR (300 MHz, CDCl3)
7.95
7.82
4.00
3.01
2.95
2.88
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

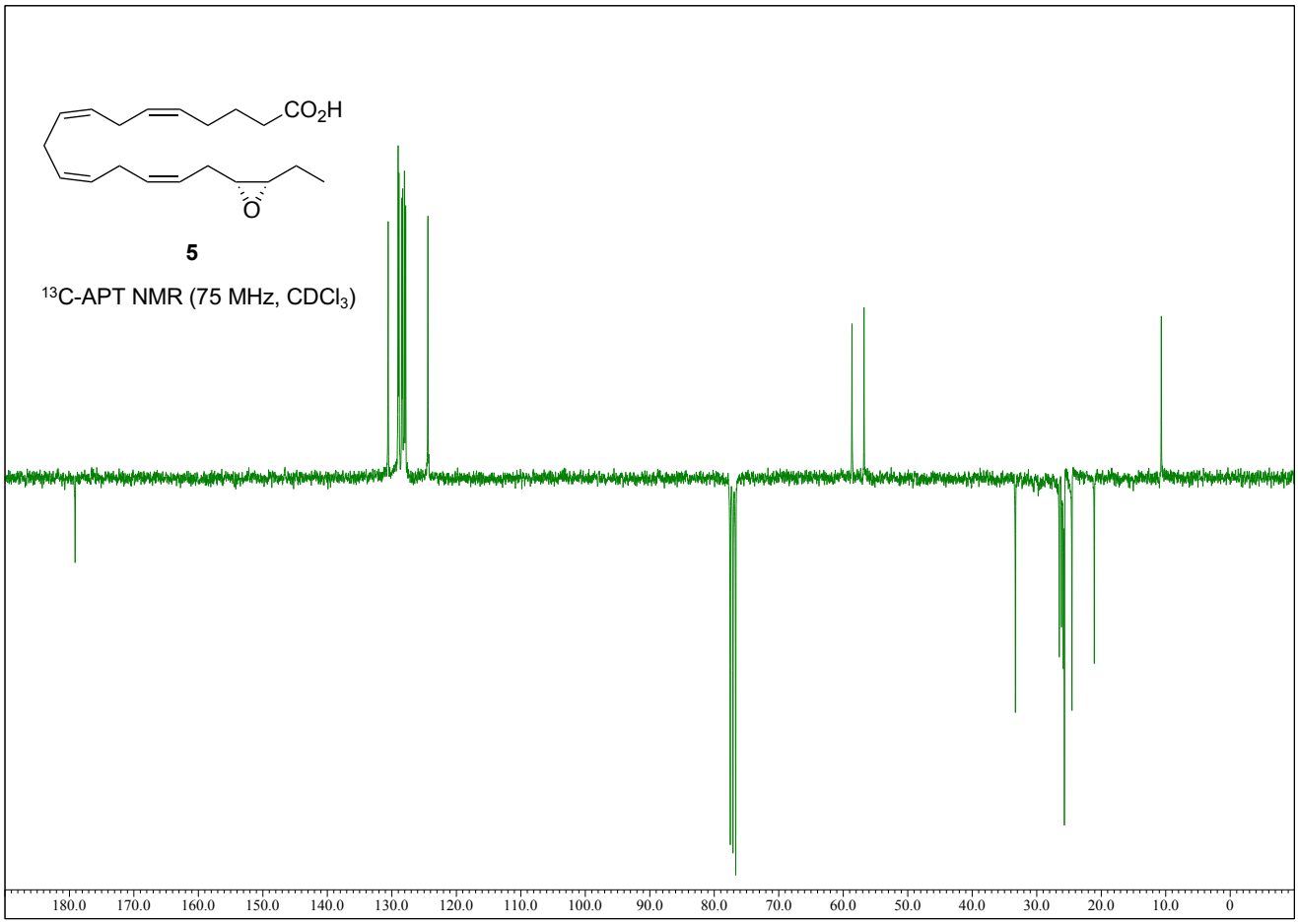


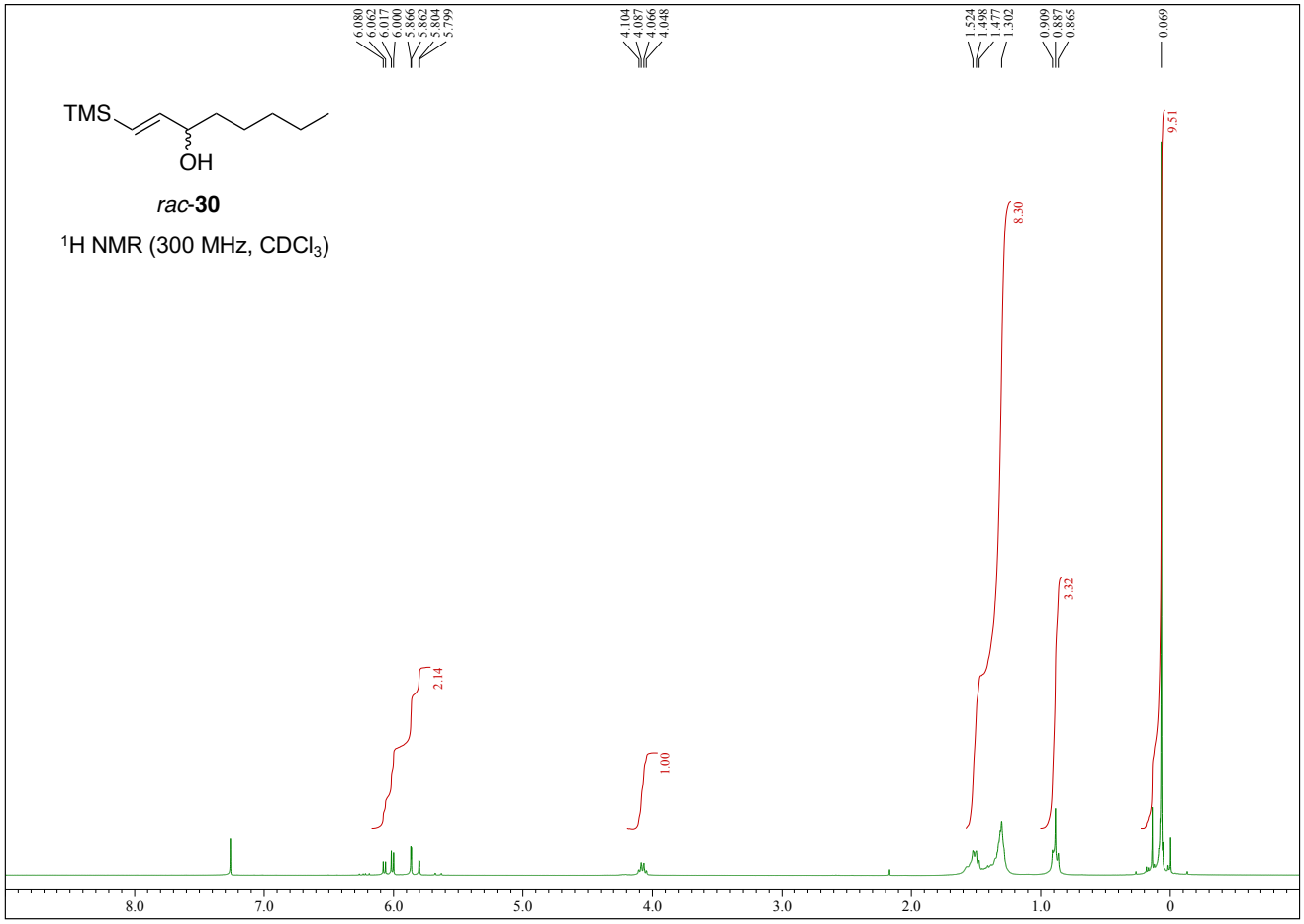
5

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



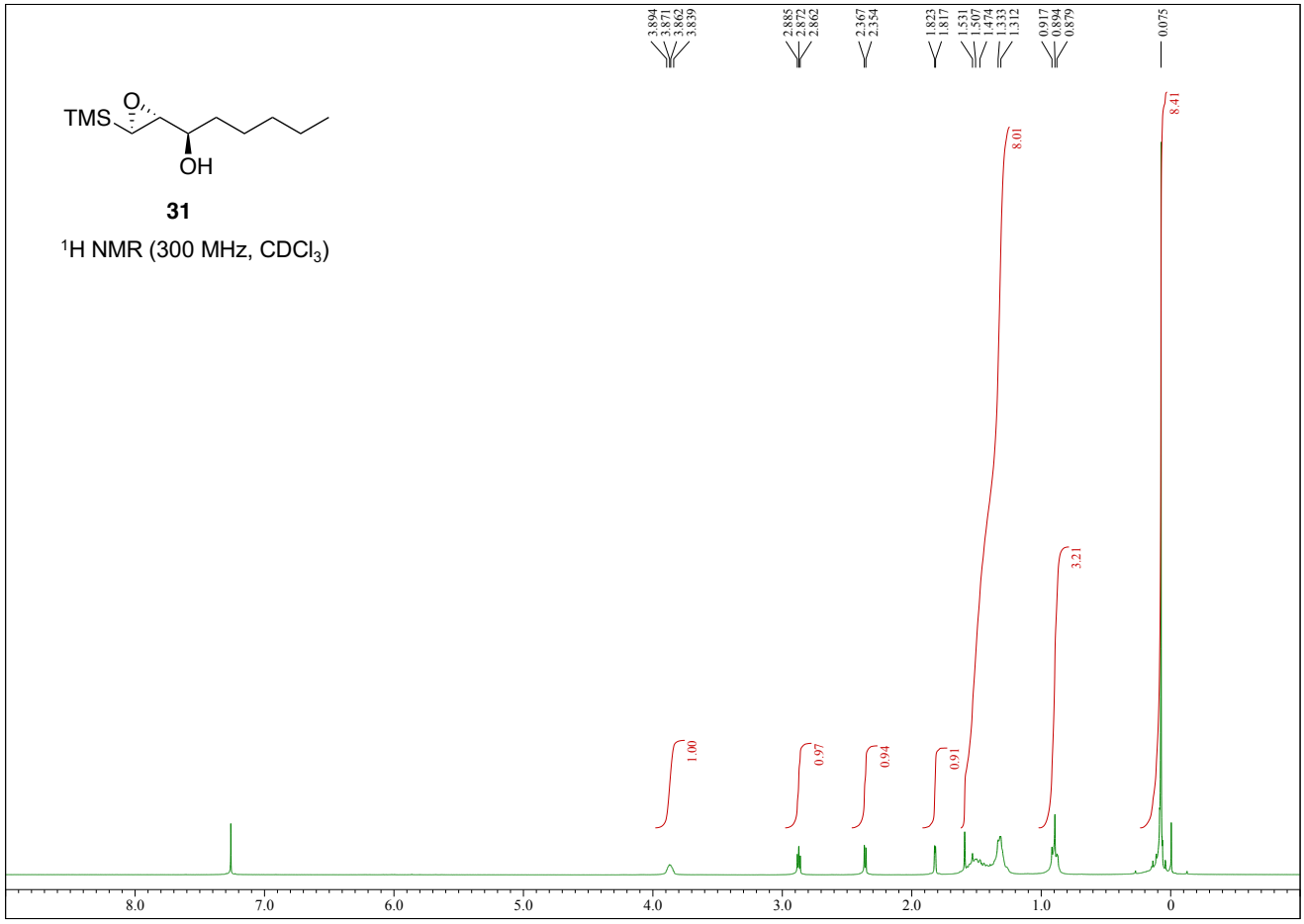

179.119
130.582
129.025
128.888
128.445
128.323
128.049
127.865
124.402
58.652
56.776
33.308
26.487
26.167
25.892
25.709
24.534
21.070
10.679
CO2H
O
5
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0


CO2H
O
5
13C-APT NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0



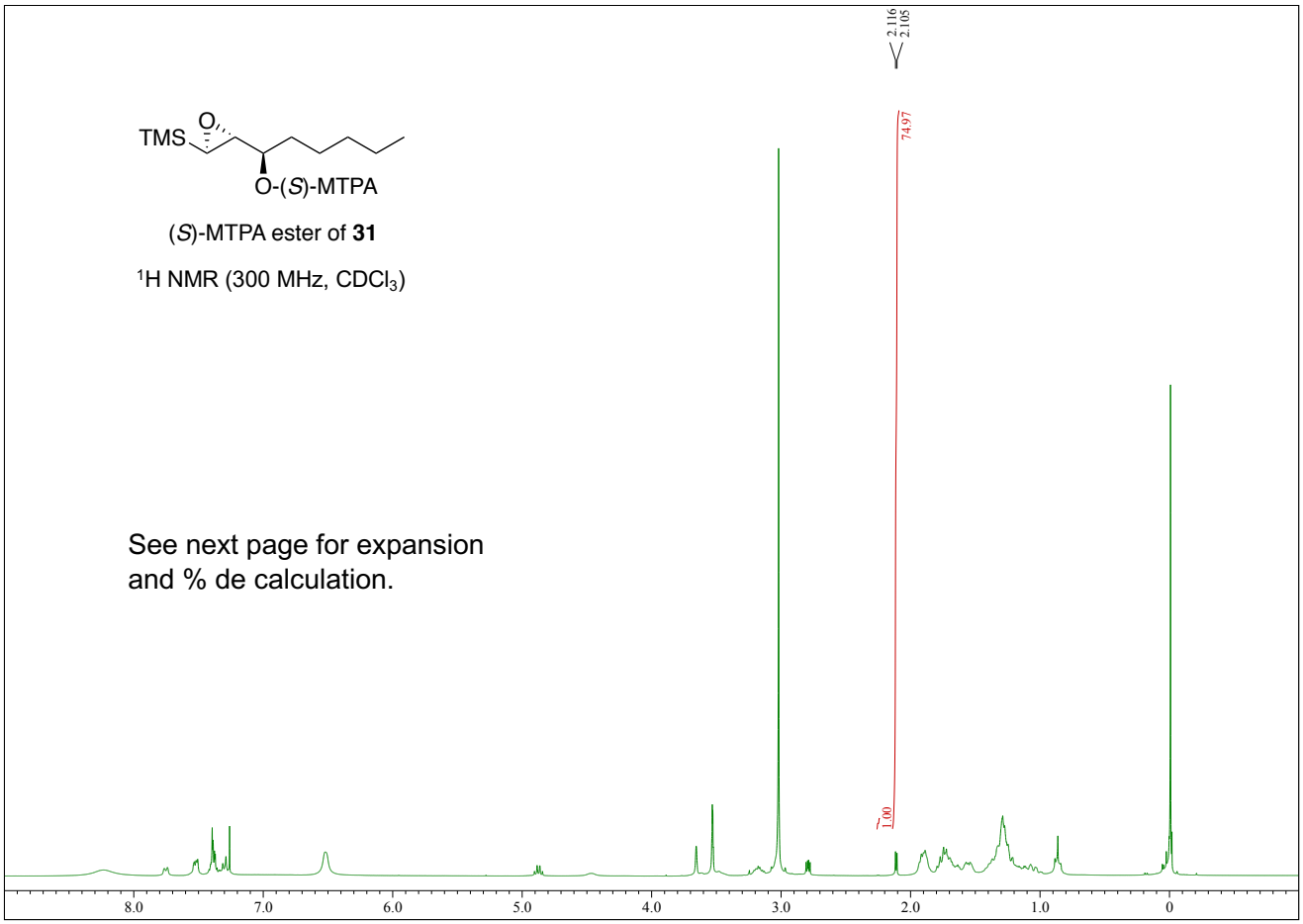
rac-**30**

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



31

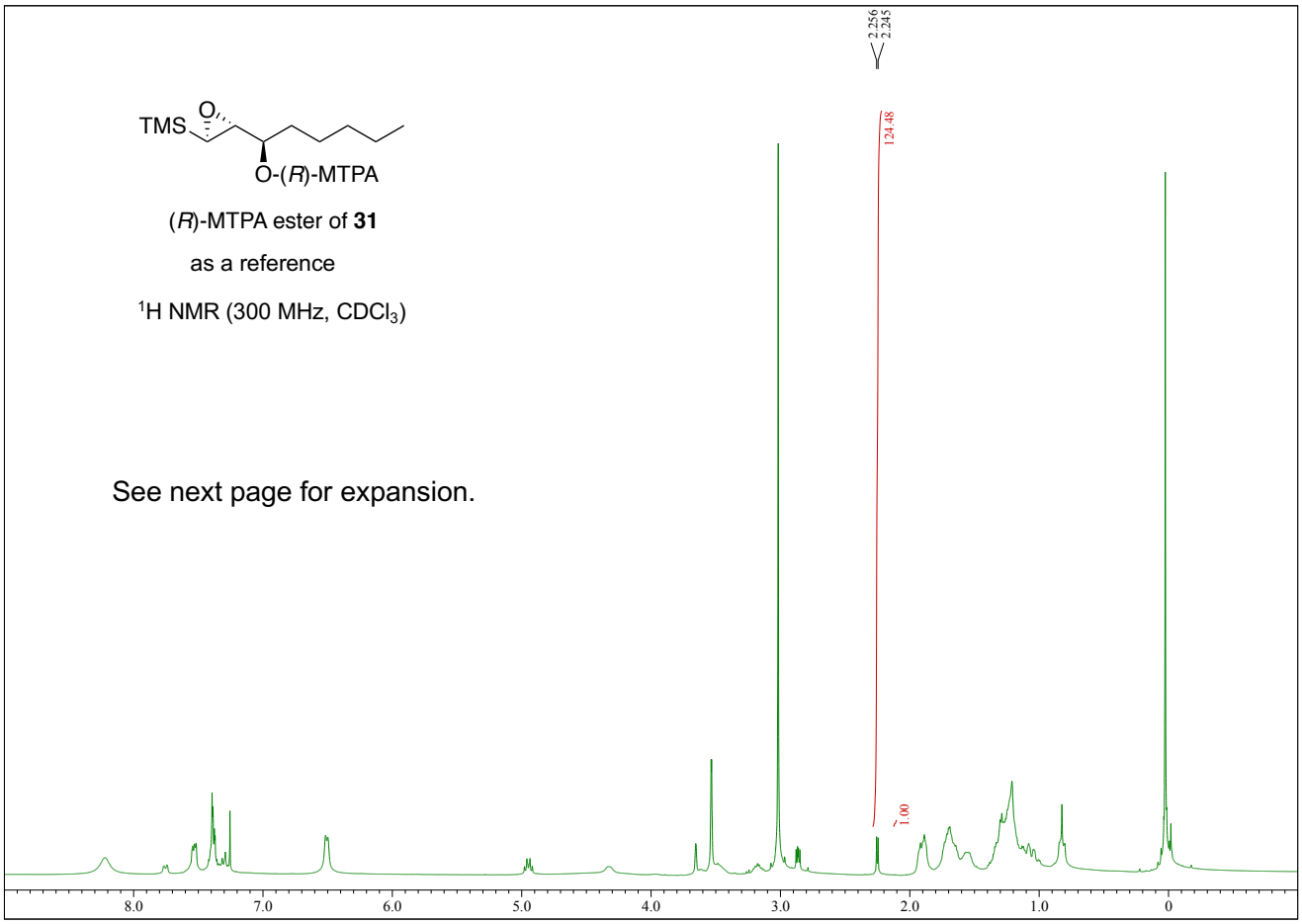
^{1}H NMR (300 MHz, $CDCl_3$)



(*S*)-MTPA ester of **31**

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

See next page for expansion and % de calculation.



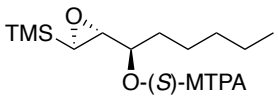
(*R*)-MTPA ester of **31**

as a reference

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

See next page for expansion.

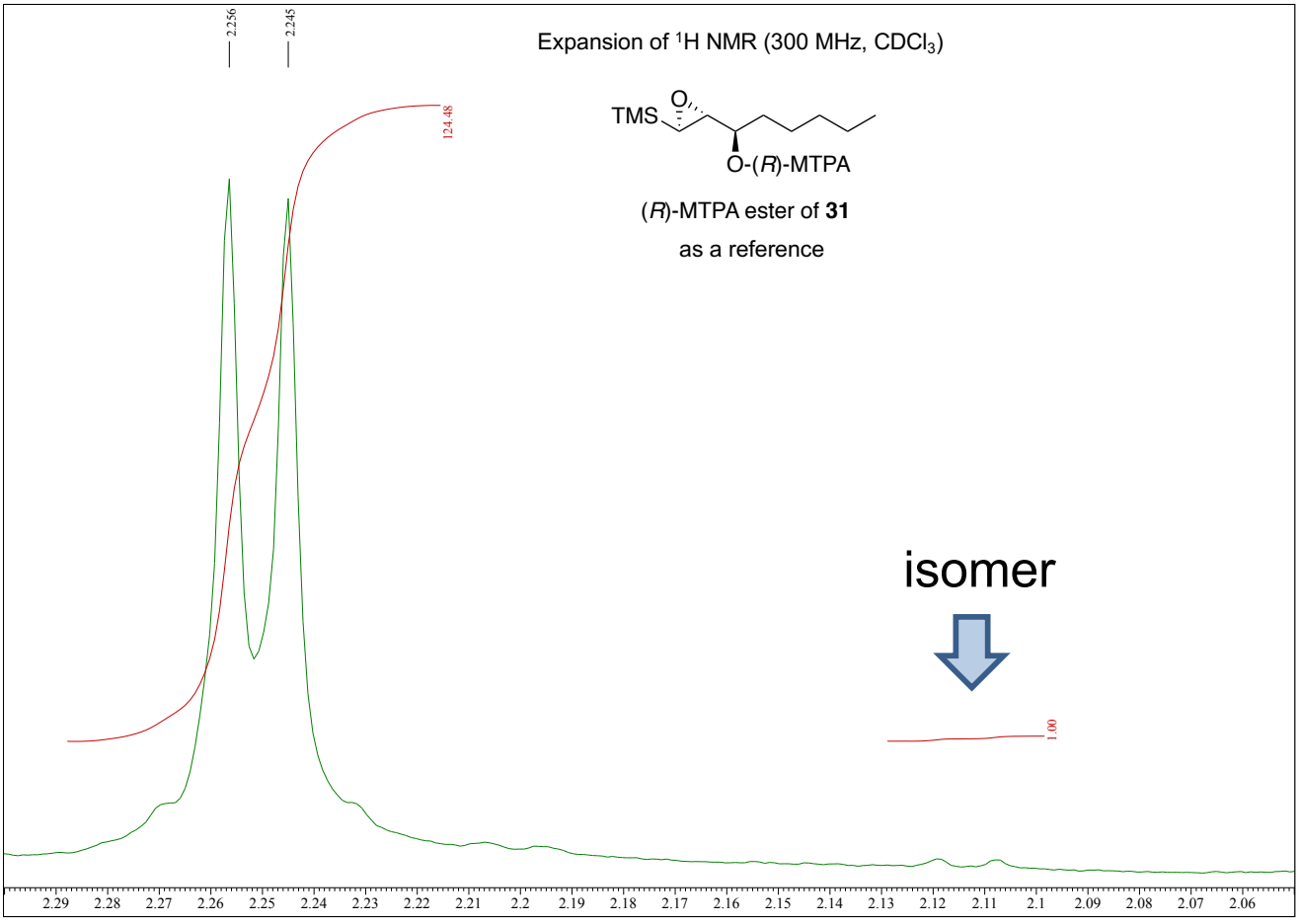
Expansion of ^{1}H NMR (300 MHz, $CDCl_3$)



(*S*)-MTPA ester of **31**

de
= (74.97–1.00)x100/(74.97+1.00)
= 97.4%
= >97% de

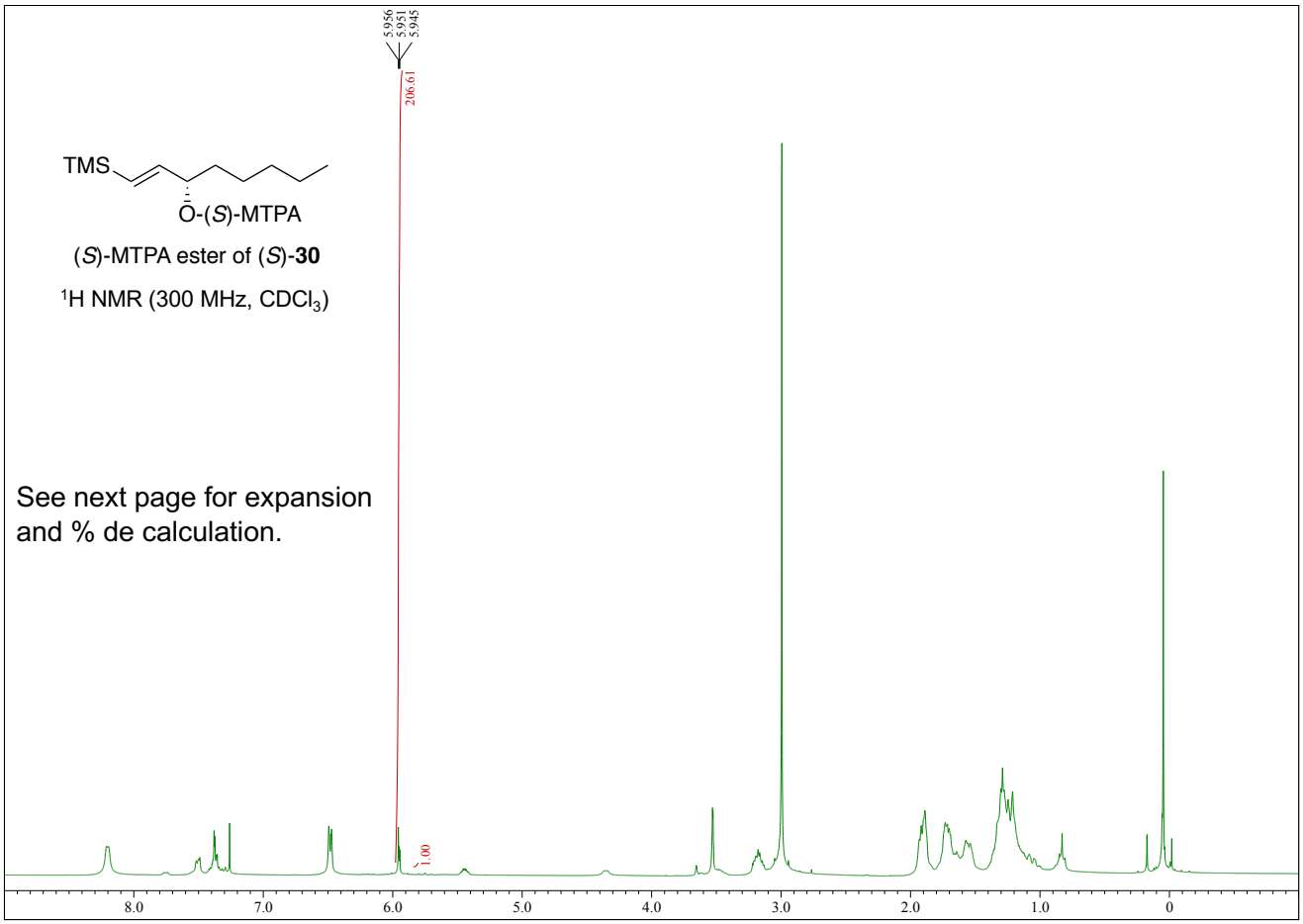
isomer



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

(*R*)-MTPA ester of **31**
as a reference

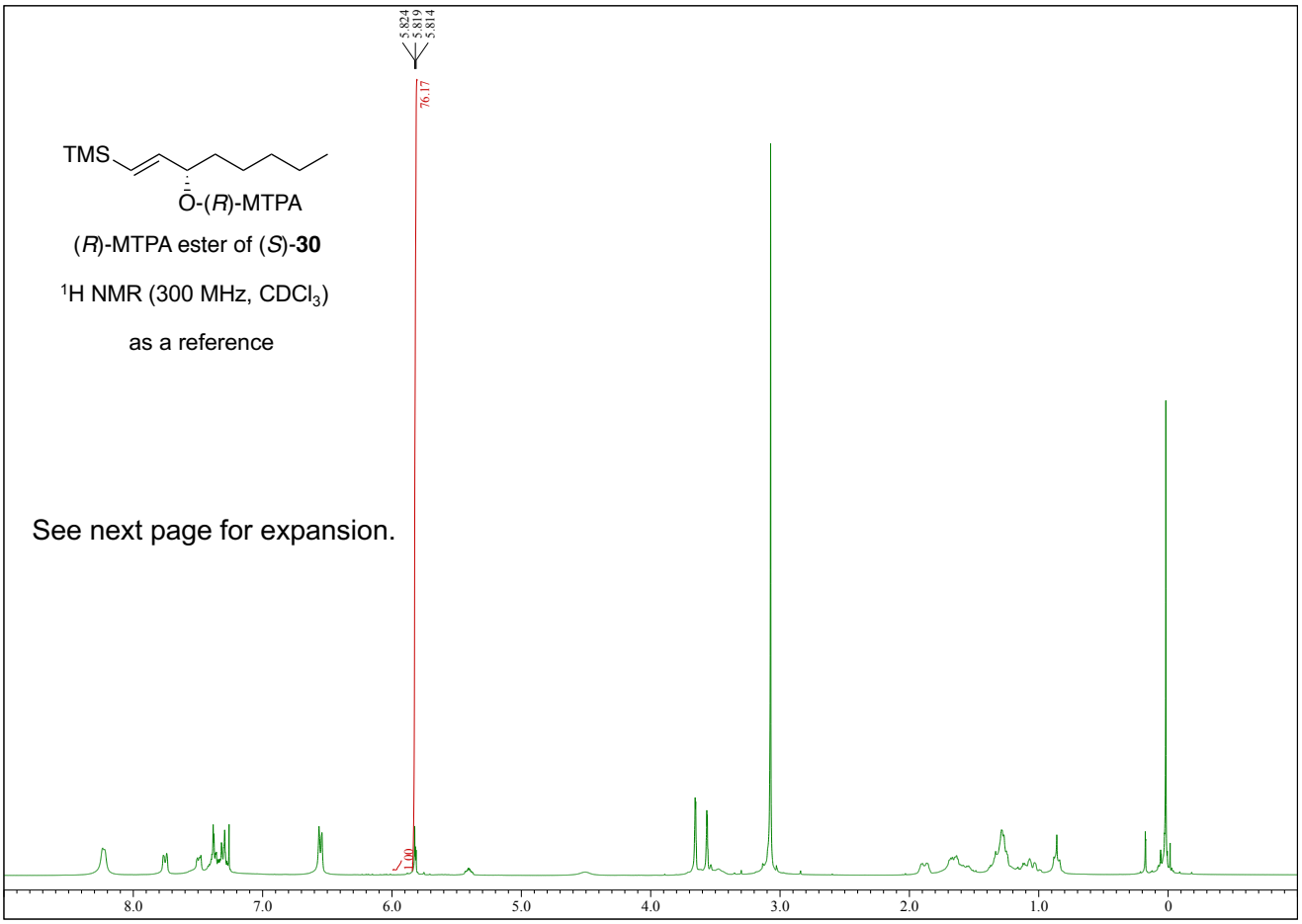
isomer



(*S*)-MTPA ester of (*S*)-**30**

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

See next page for expansion and % de calculation.

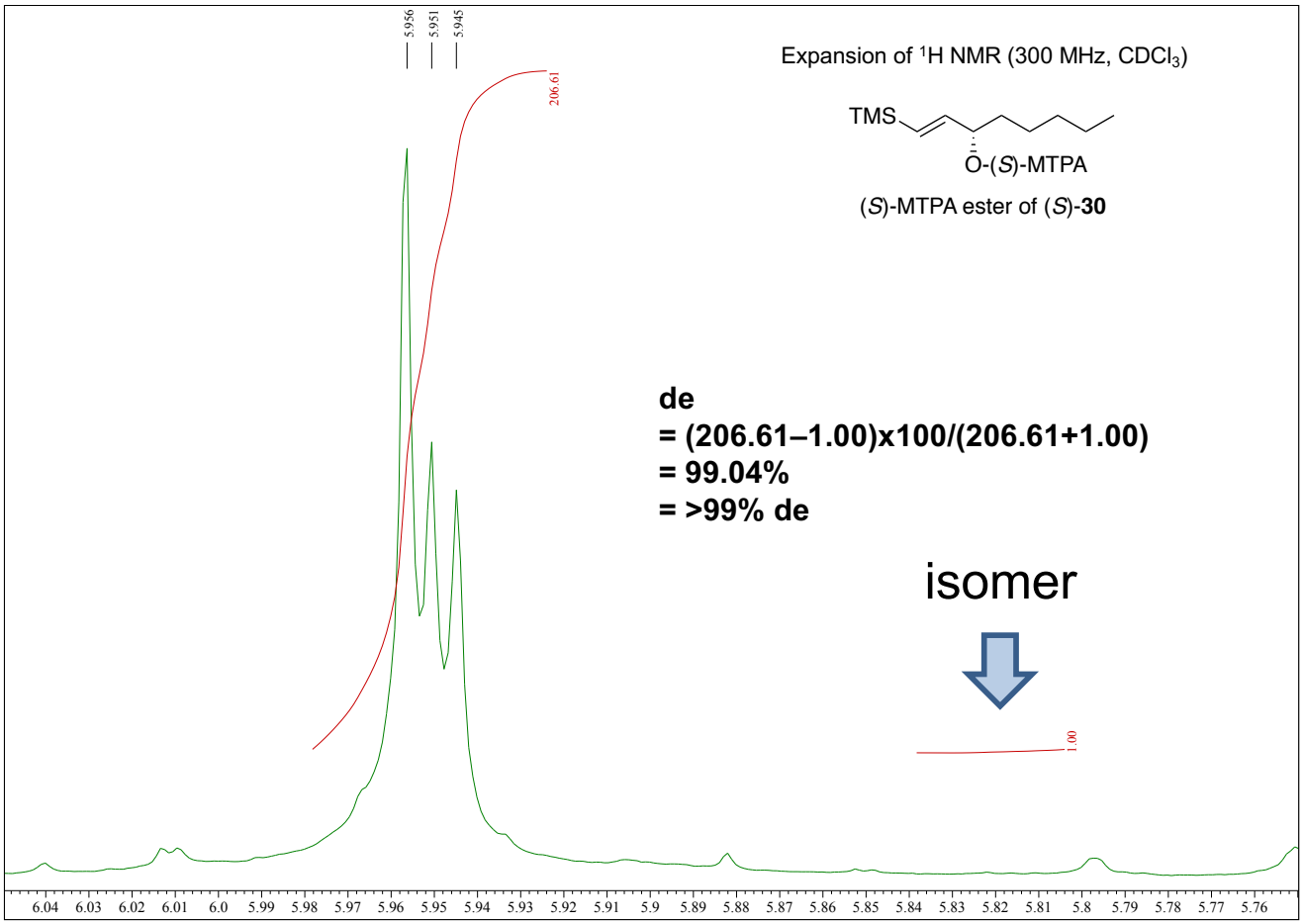


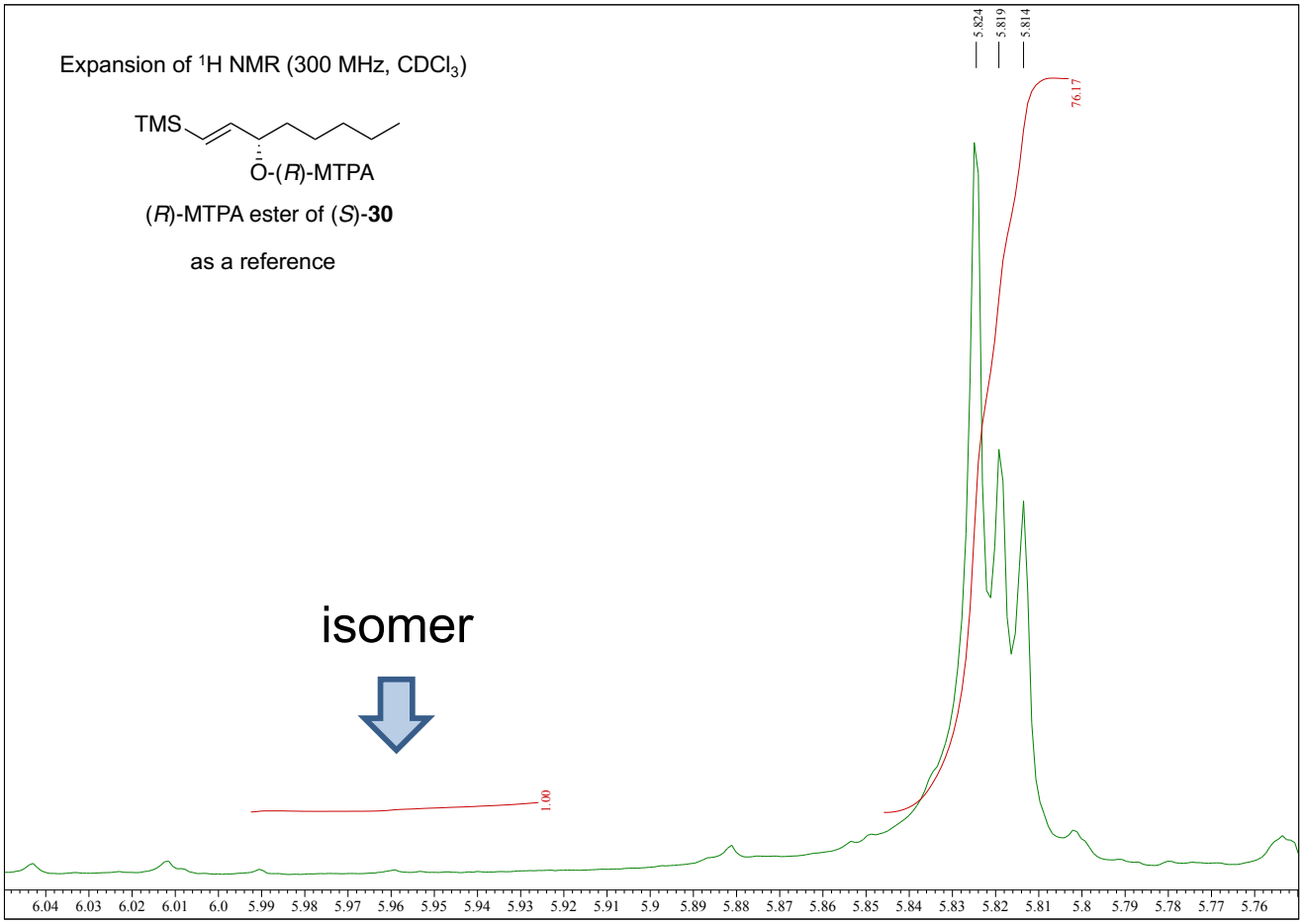
(*R*)-MTPA ester of (*S*)-**30**

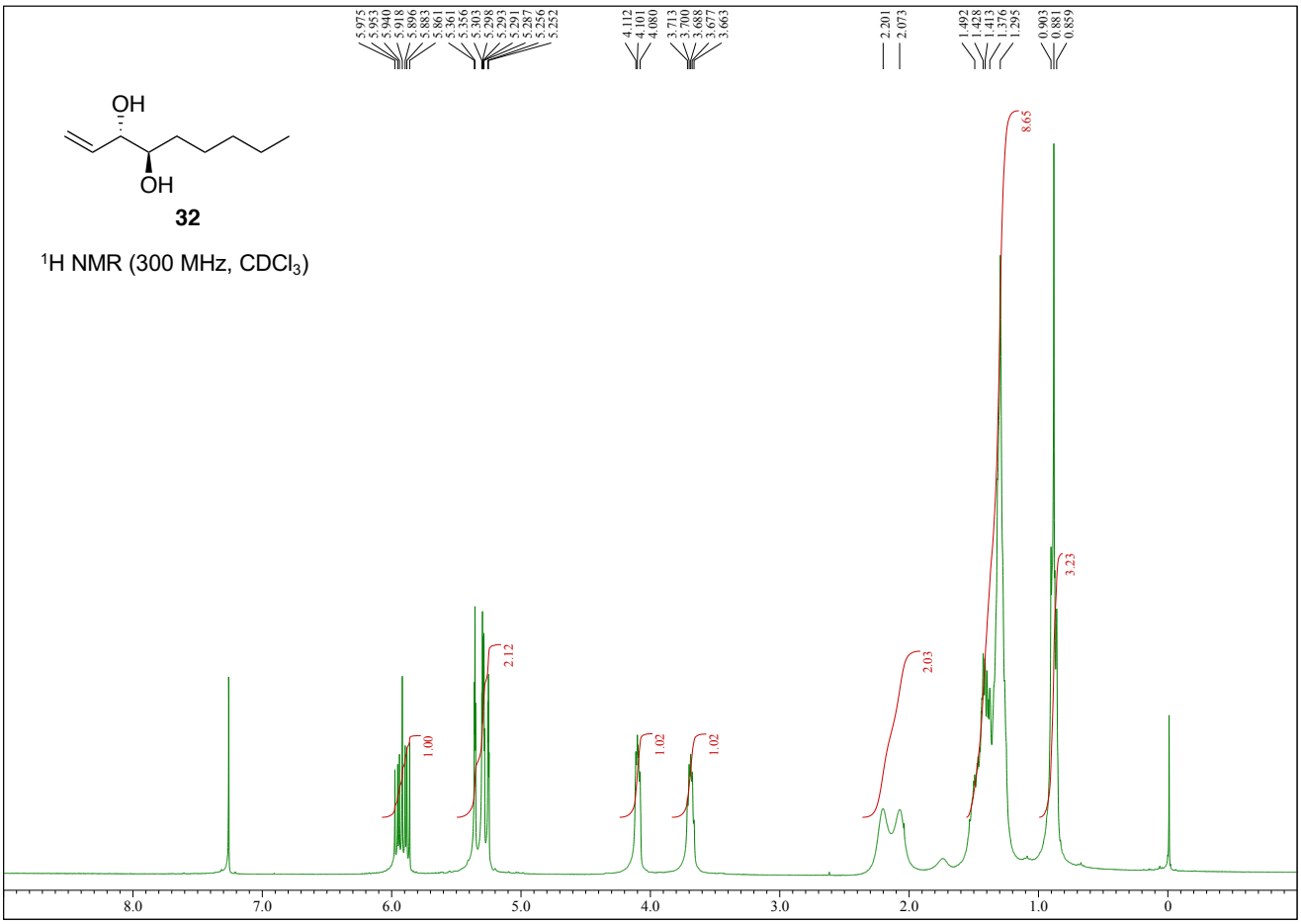
^{1}H NMR (300 MHz, $CDCl_3$)

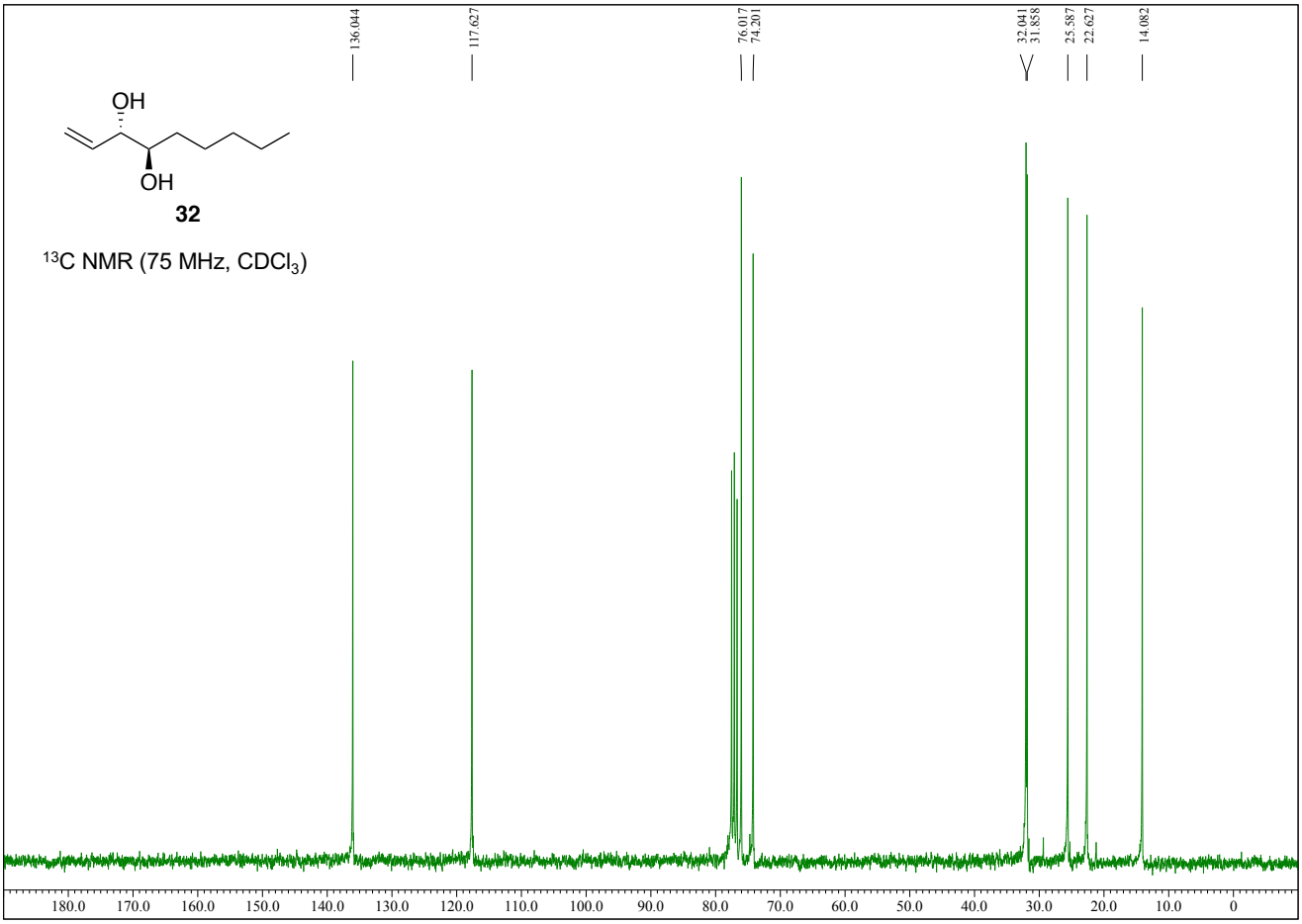
as a reference

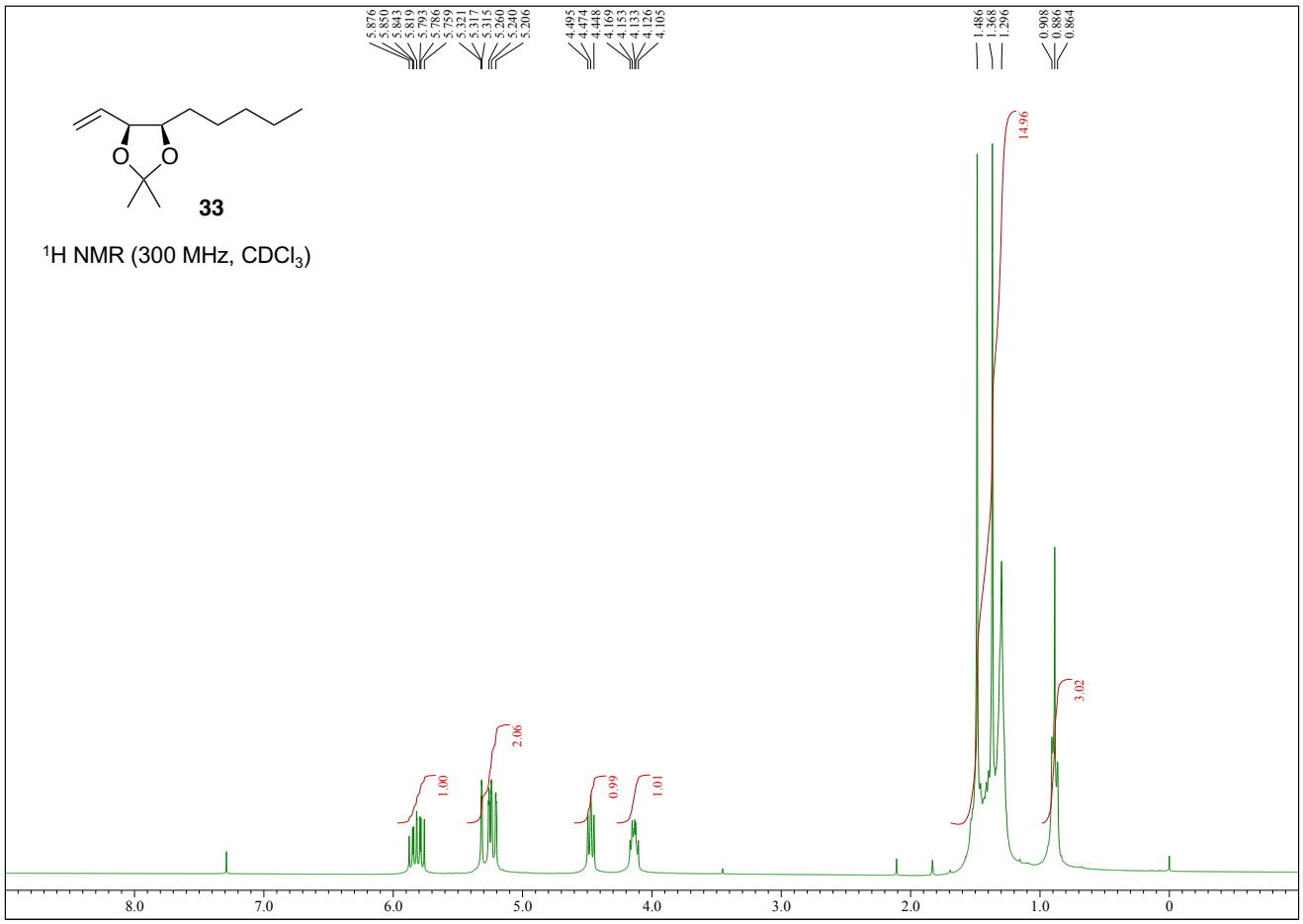
See next page for expansion.


5.956
5.951
5.945
206.61
Expansion of ^{1}H NMR (300 MHz, $CDCl_3$)
TMS
O-(S)-MTPA
(S)-MTPA ester of (S)-30
de
= (206.61–1.00)x100/(206.61+1.00)
= 99.04%
= >99% de
isomer
1.00
6.04 6.03 6.02 6.01 6.0 5.99 5.98 5.97 5.96 5.95 5.94 5.93 5.92 5.91 5.9 5.89 5.88 5.87 5.86 5.85 5.84 5.83 5.82 5.81 5.8 5.79 5.78 5.77 5.76


Expansion of ^{1}H NMR (300 MHz, $CDCl_3$)
TMS
O-(R)-MTPA
(R)-MTPA ester of (S)-30
as a reference
5.824
5.819
5.814
76.17
isomer
1.00
6.04 6.03 6.02 6.01 6.0 5.99 5.98 5.97 5.96 5.95 5.94 5.93 5.92 5.91 5.9 5.89 5.88 5.87 5.86 5.85 5.84 5.83 5.82 5.81 5.8 5.79 5.78 5.77 5.76

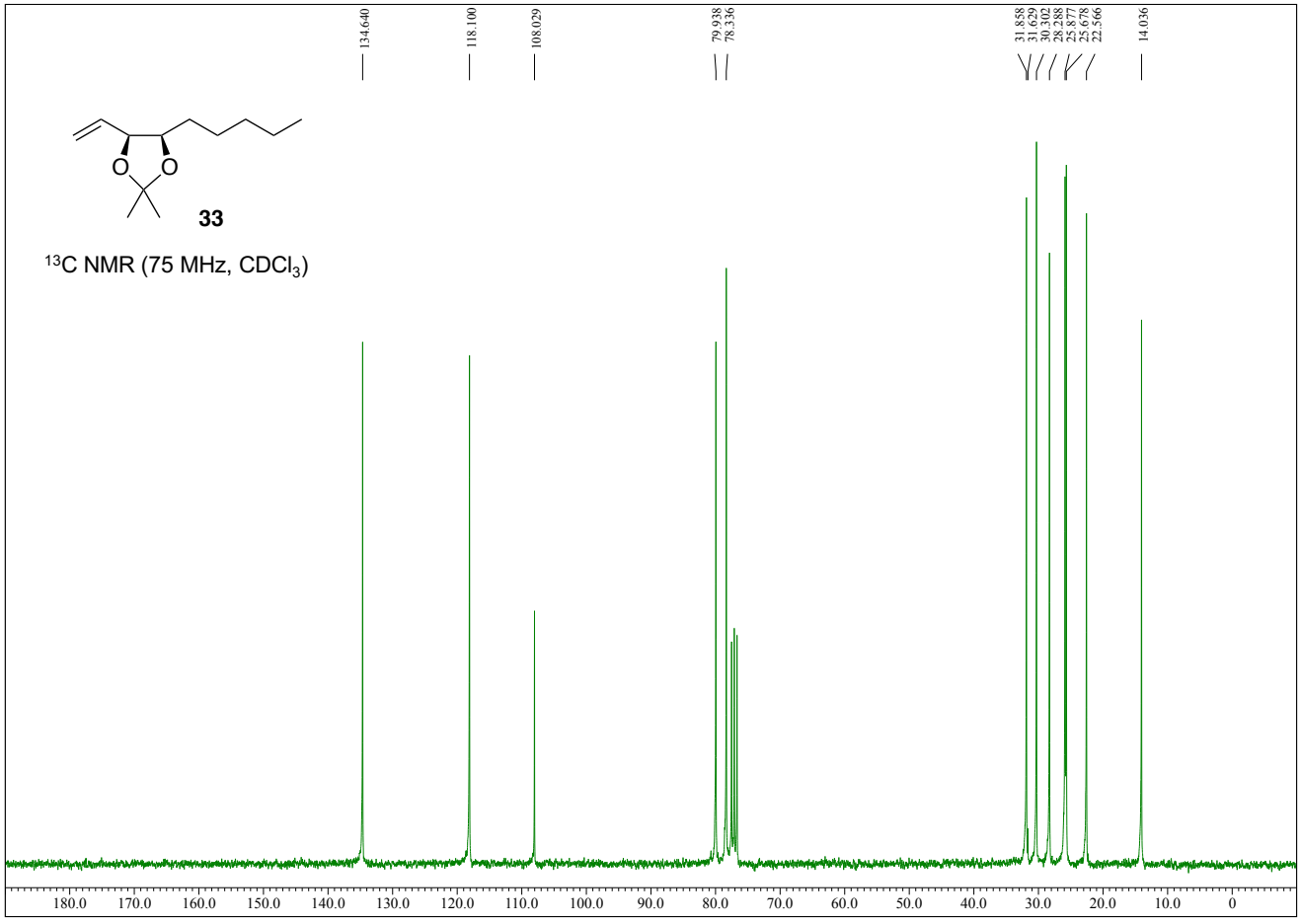

OH
OH
32
1H NMR (300 MHz, CDCl3)
5.975
5.953
5.940
5.918
5.896
5.883
5.861
5.361
5.356
5.303
5.298
5.293
5.291
5.287
5.256
5.252
4.112
4.101
4.080
3.713
3.700
3.688
3.677
3.663
2.201
2.073
1.492
1.428
1.413
1.376
1.295
0.903
0.881
0.859
8.65
3.23
2.12
2.03
1.00
1.02
1.02
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


OH
OH
32
13C NMR (75 MHz, CDCl3)
136.044
117.627
76.017
74.201
32.041
31.858
25.587
22.627
14.082
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0



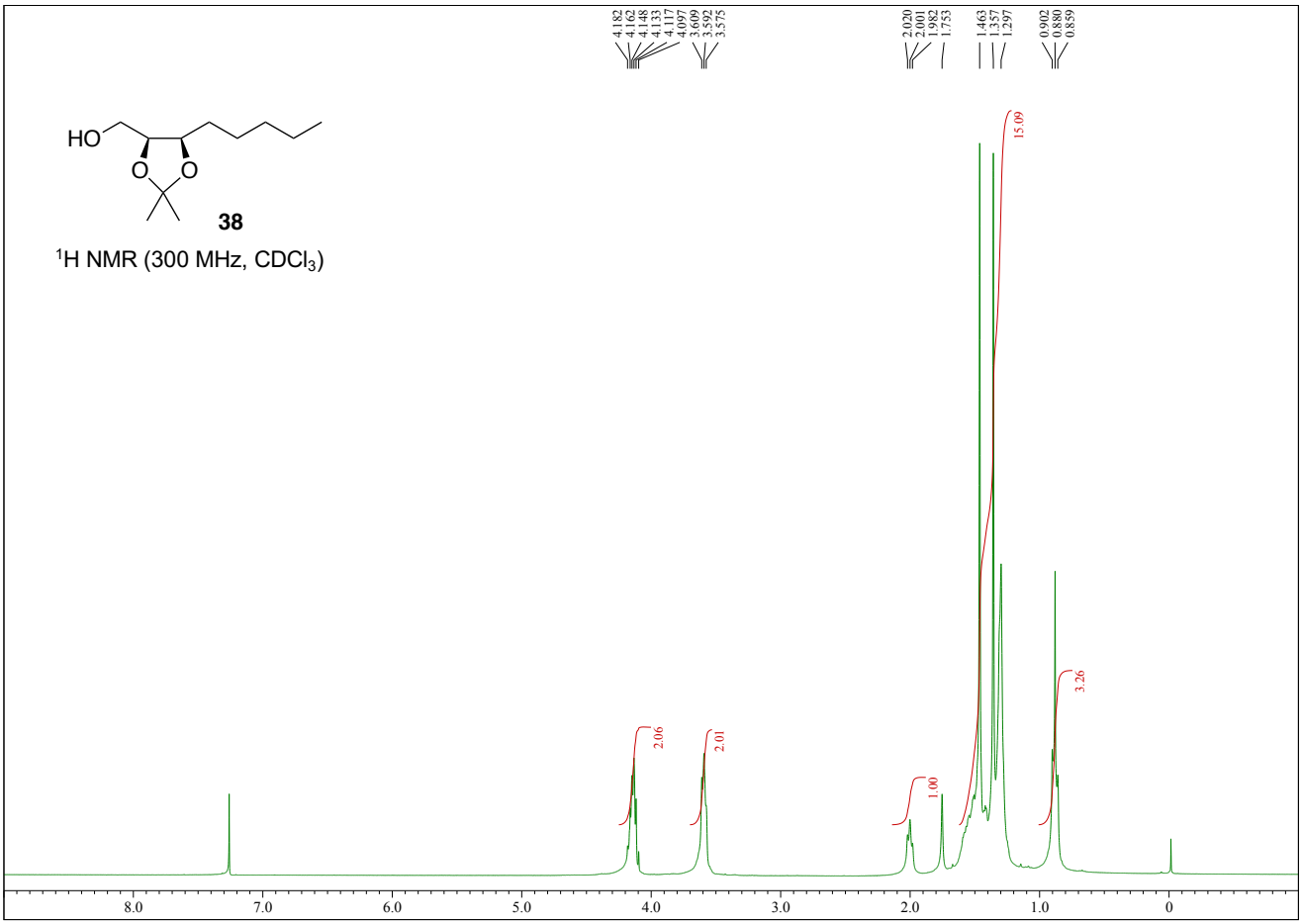
33

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



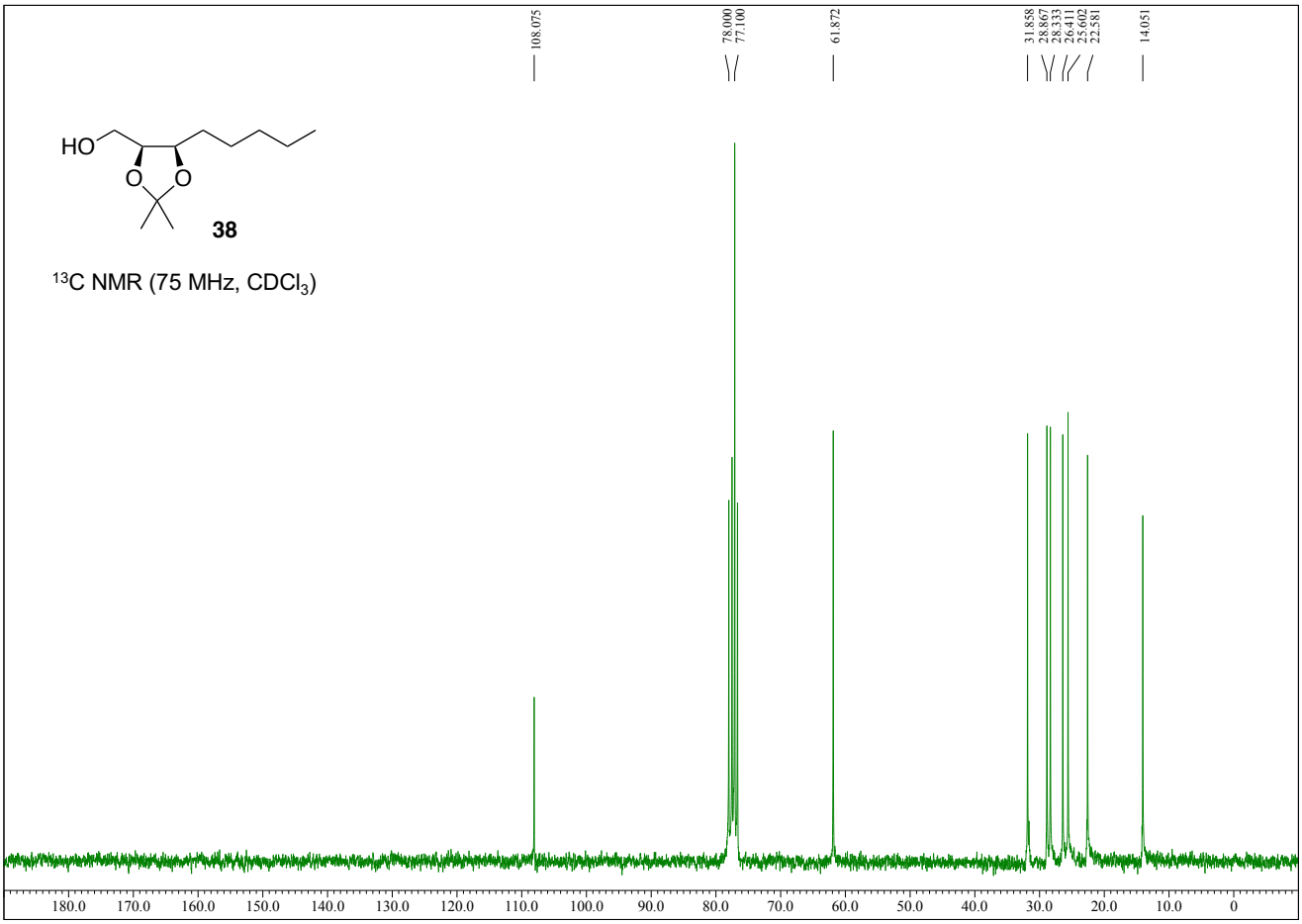
33

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



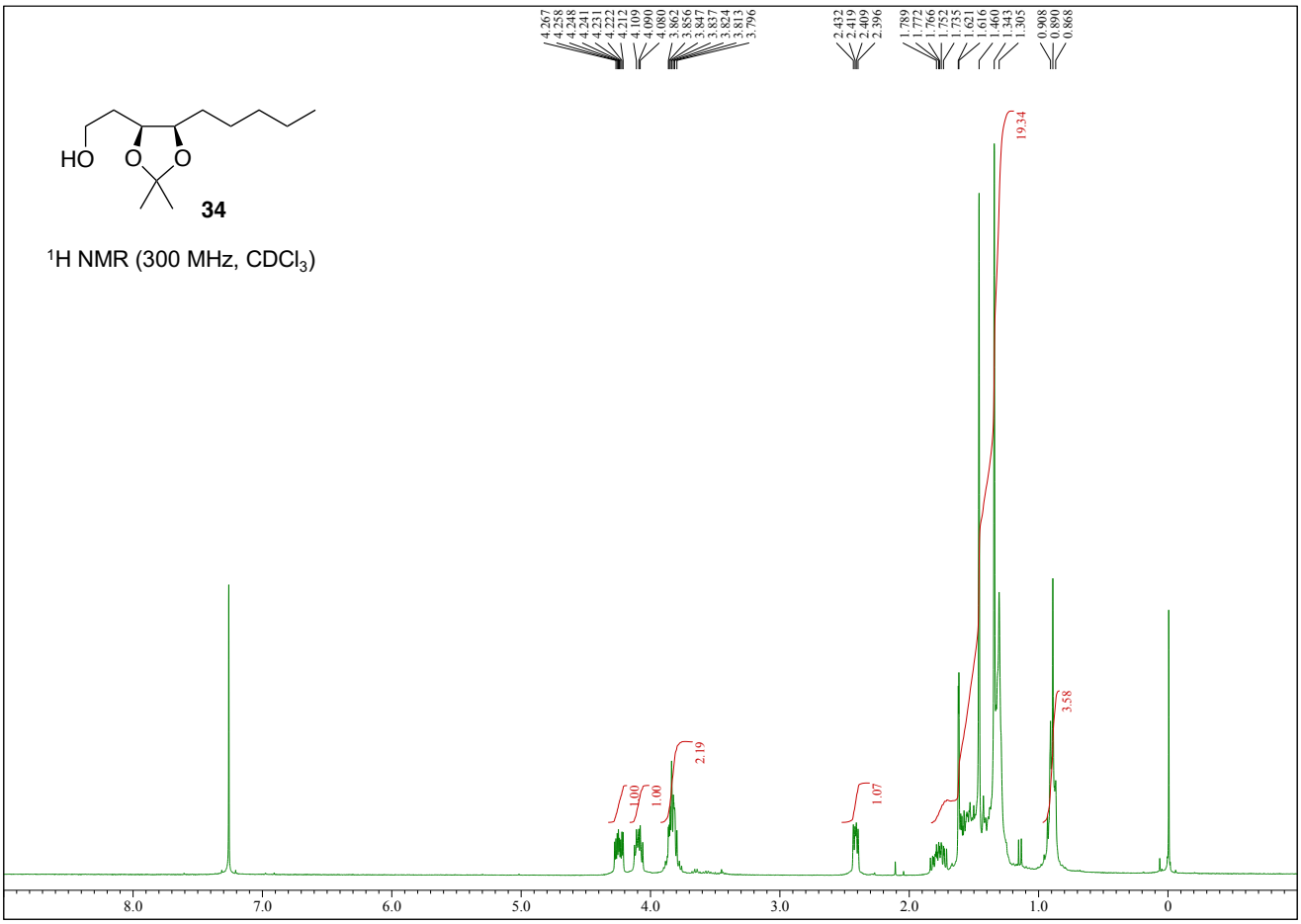
38

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

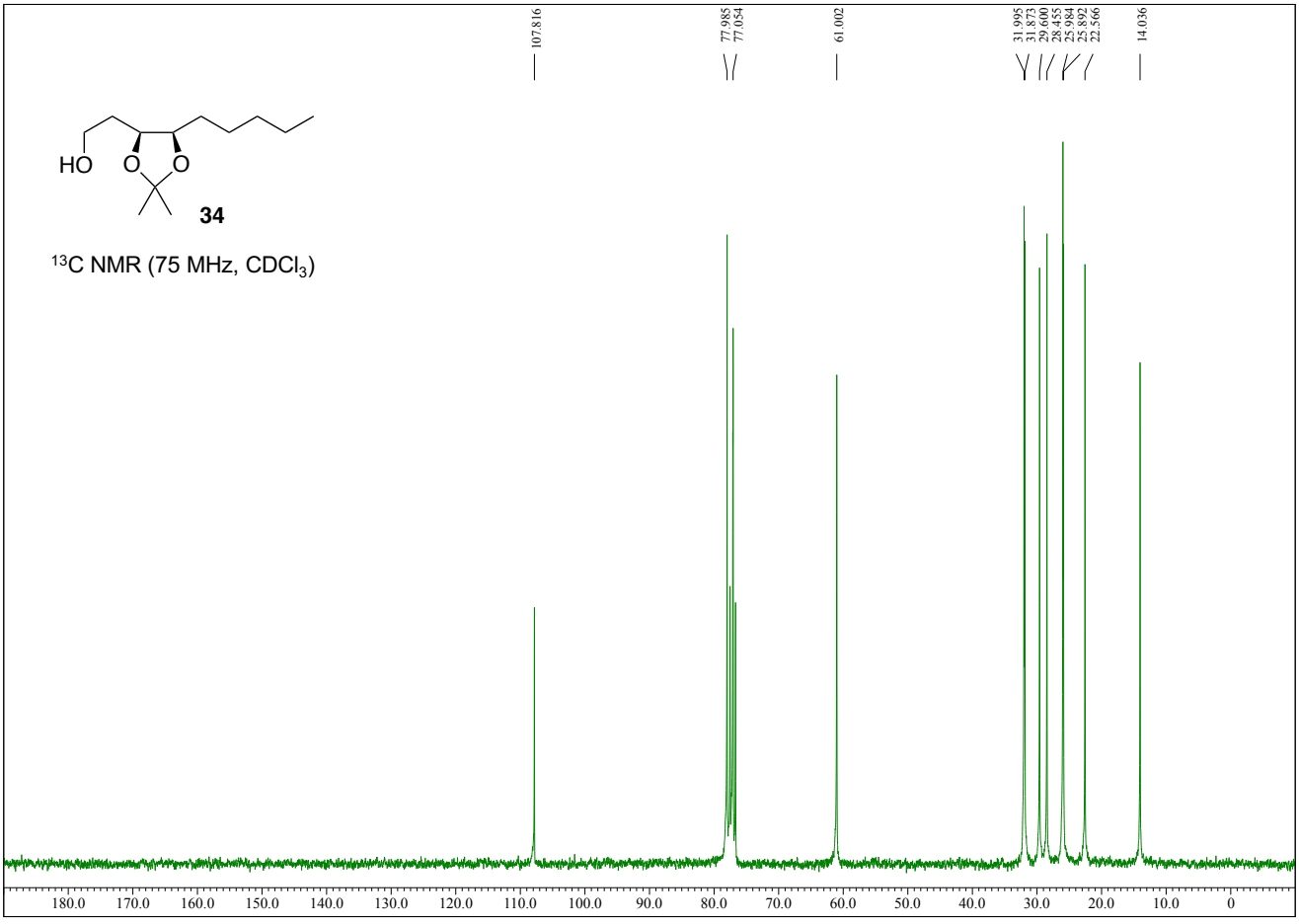


38

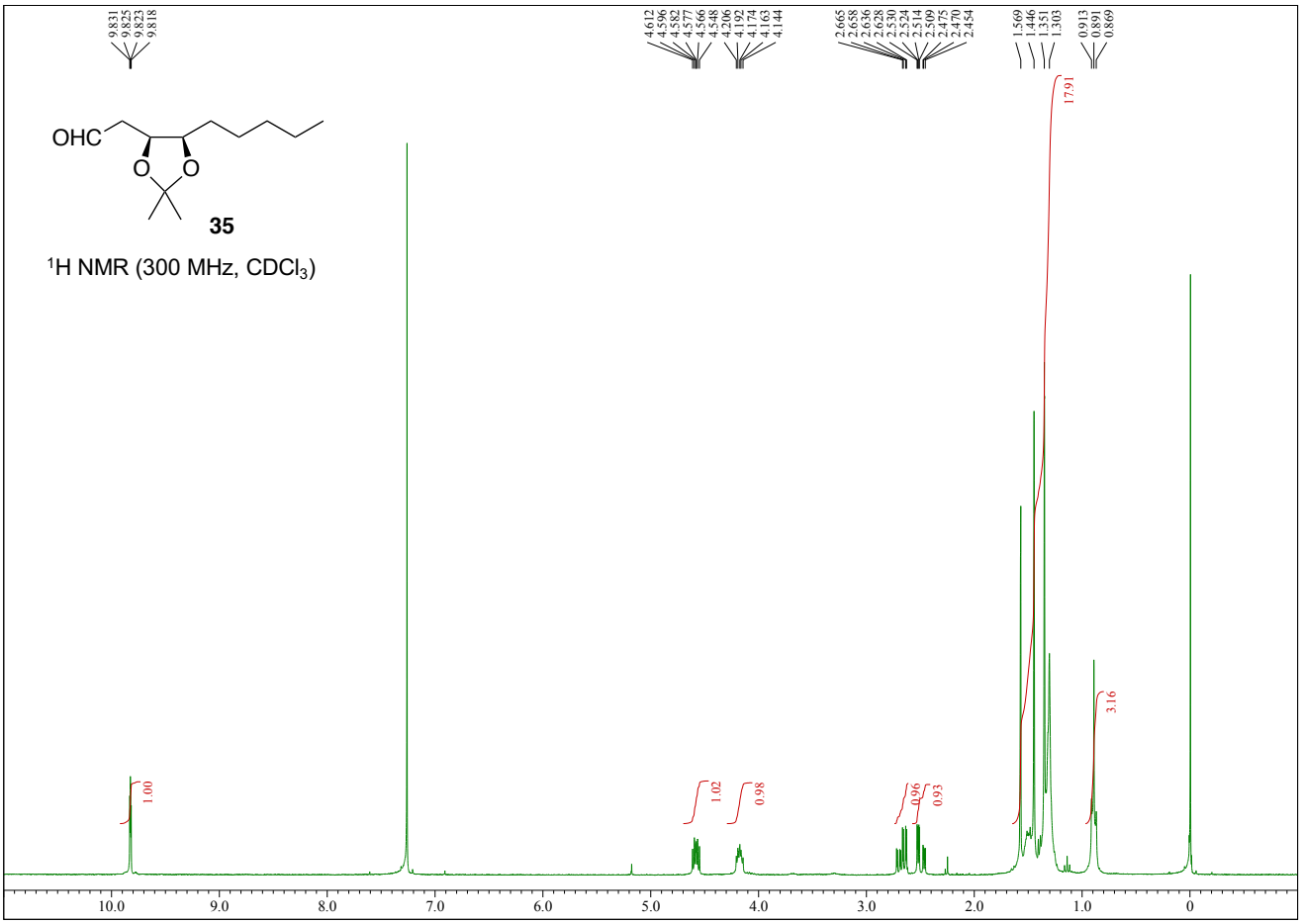
^{13}C NMR (75 MHz, $CDCl_3$)

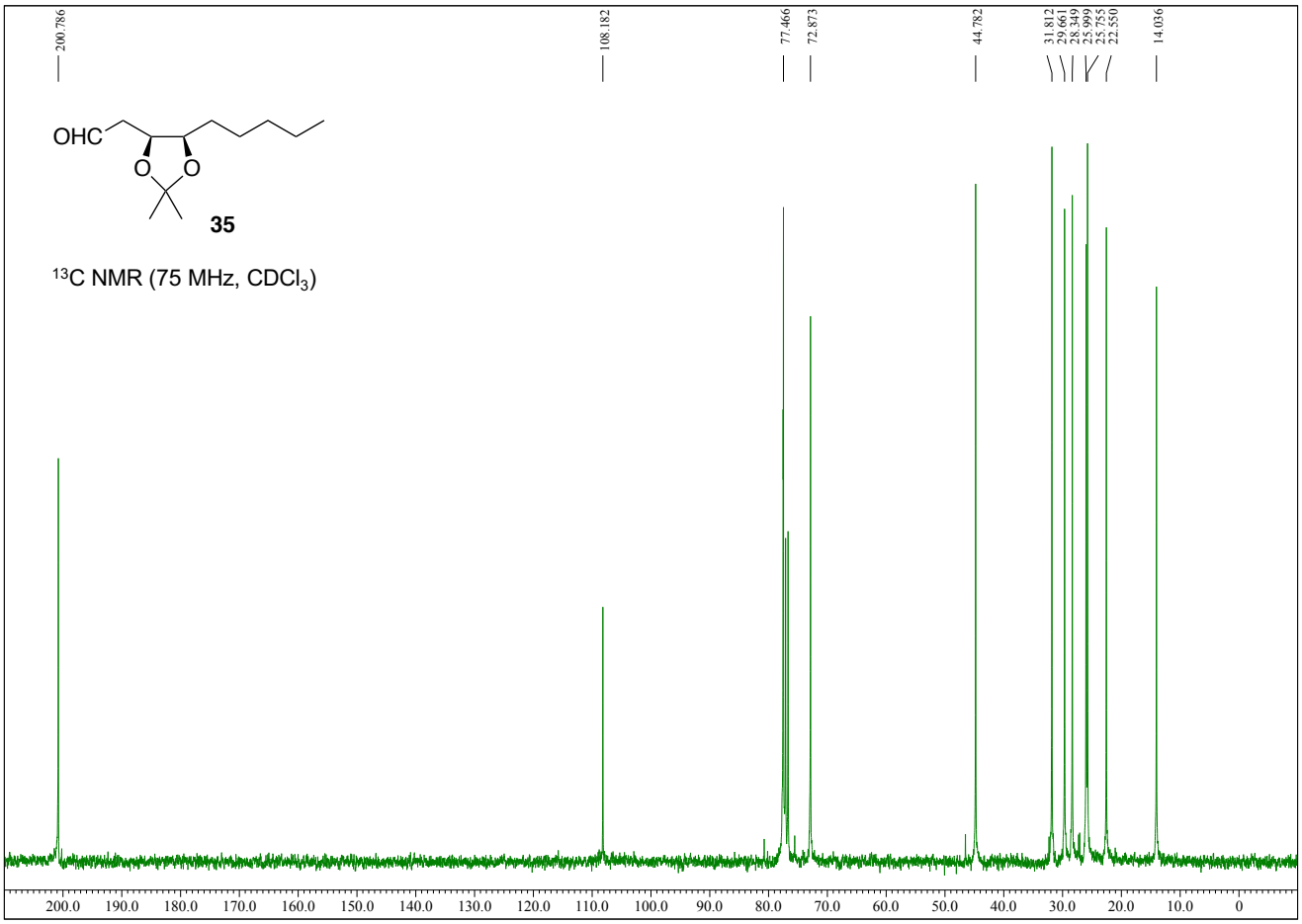


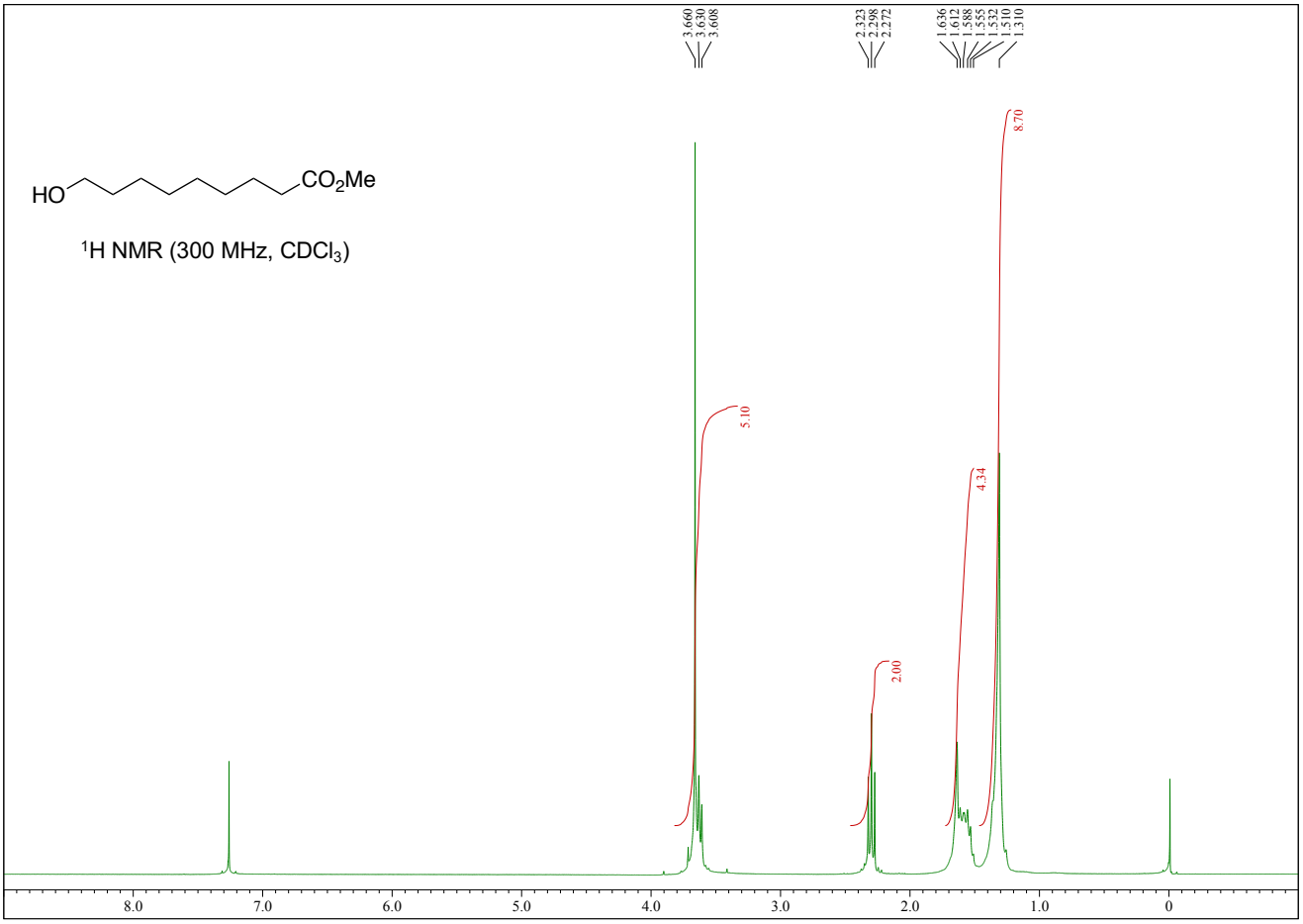
^{1}H NMR (300 MHz, $CDCl_3$)

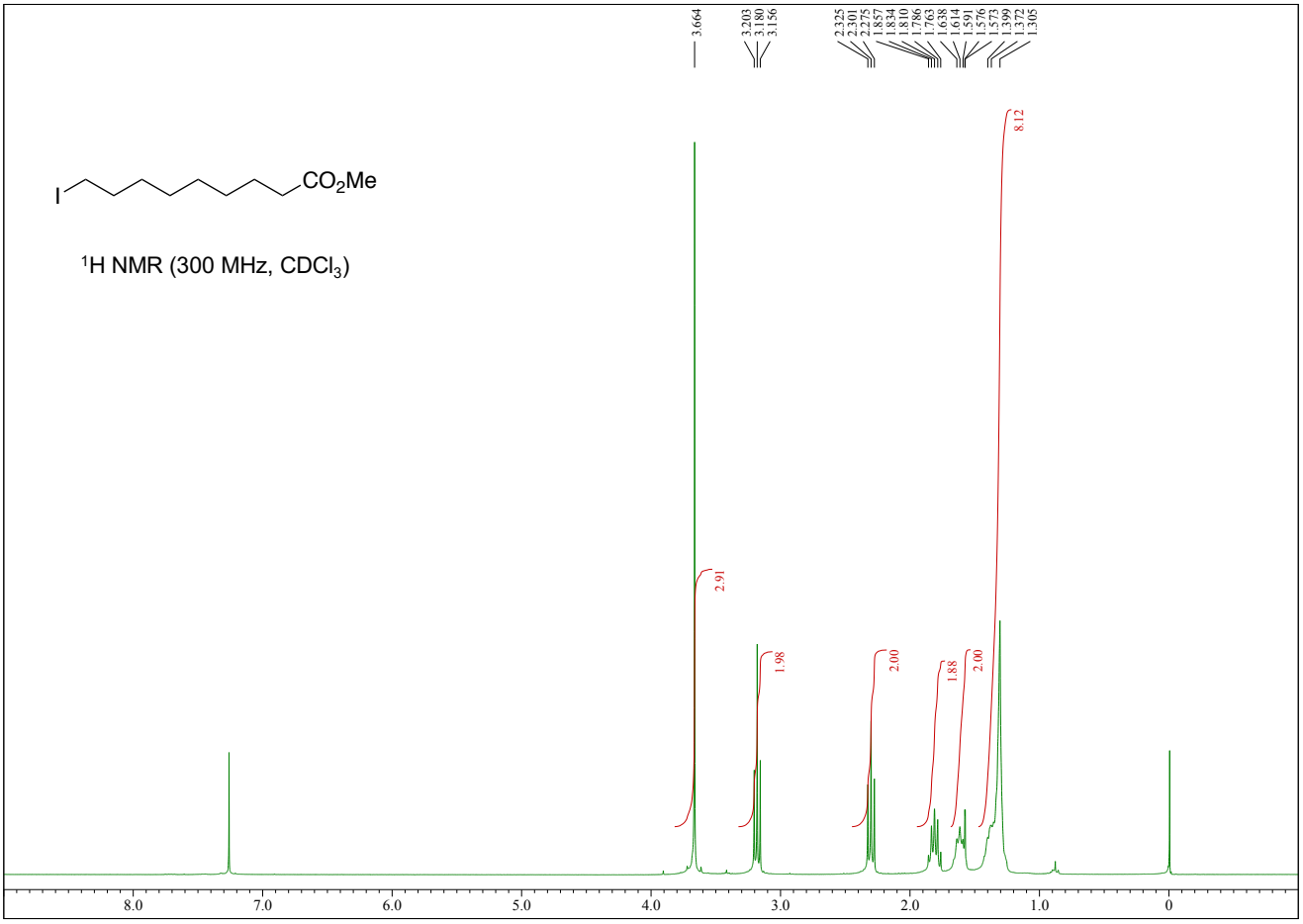


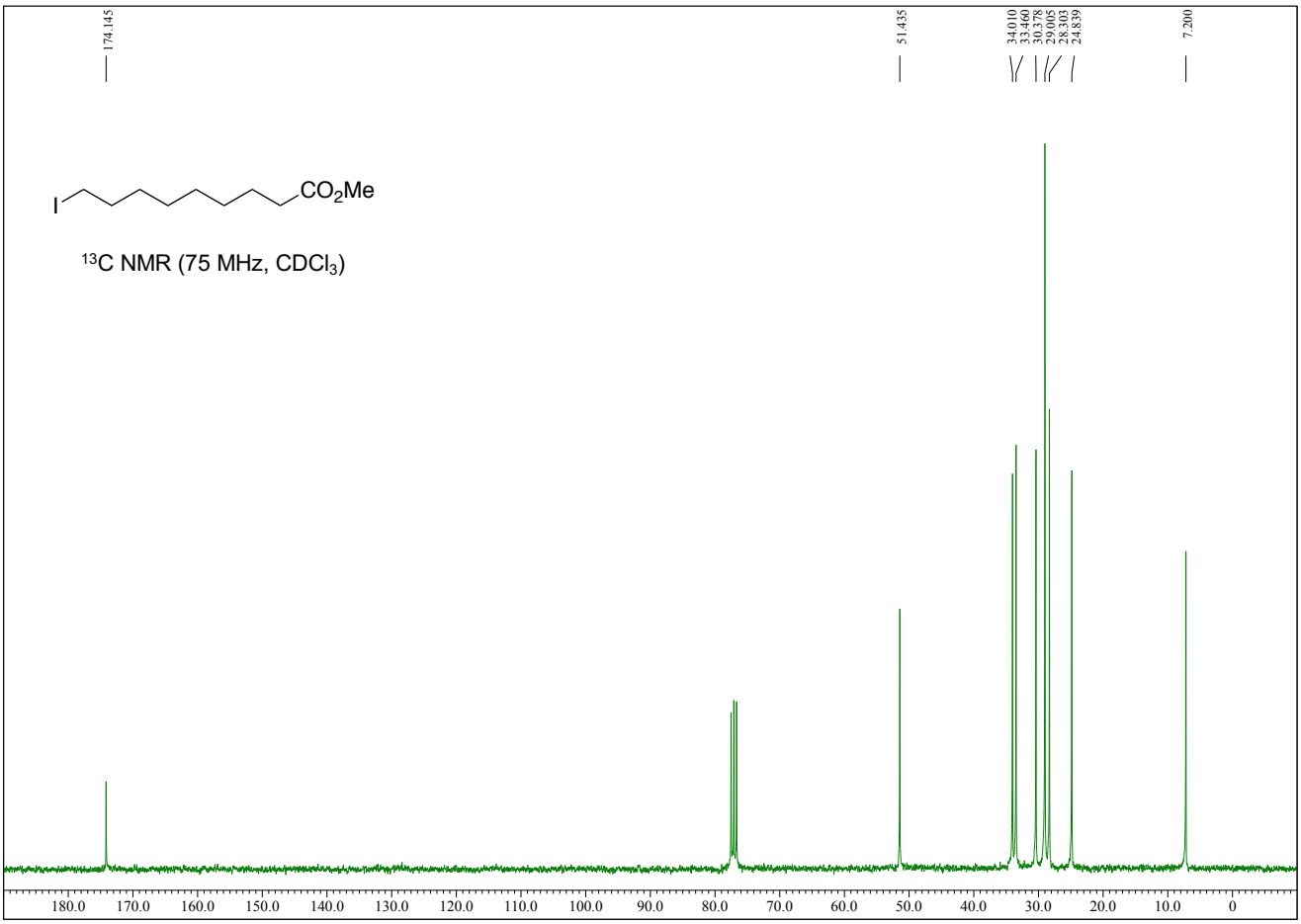
^{13}C NMR (75 MHz, $CDCl_3$)

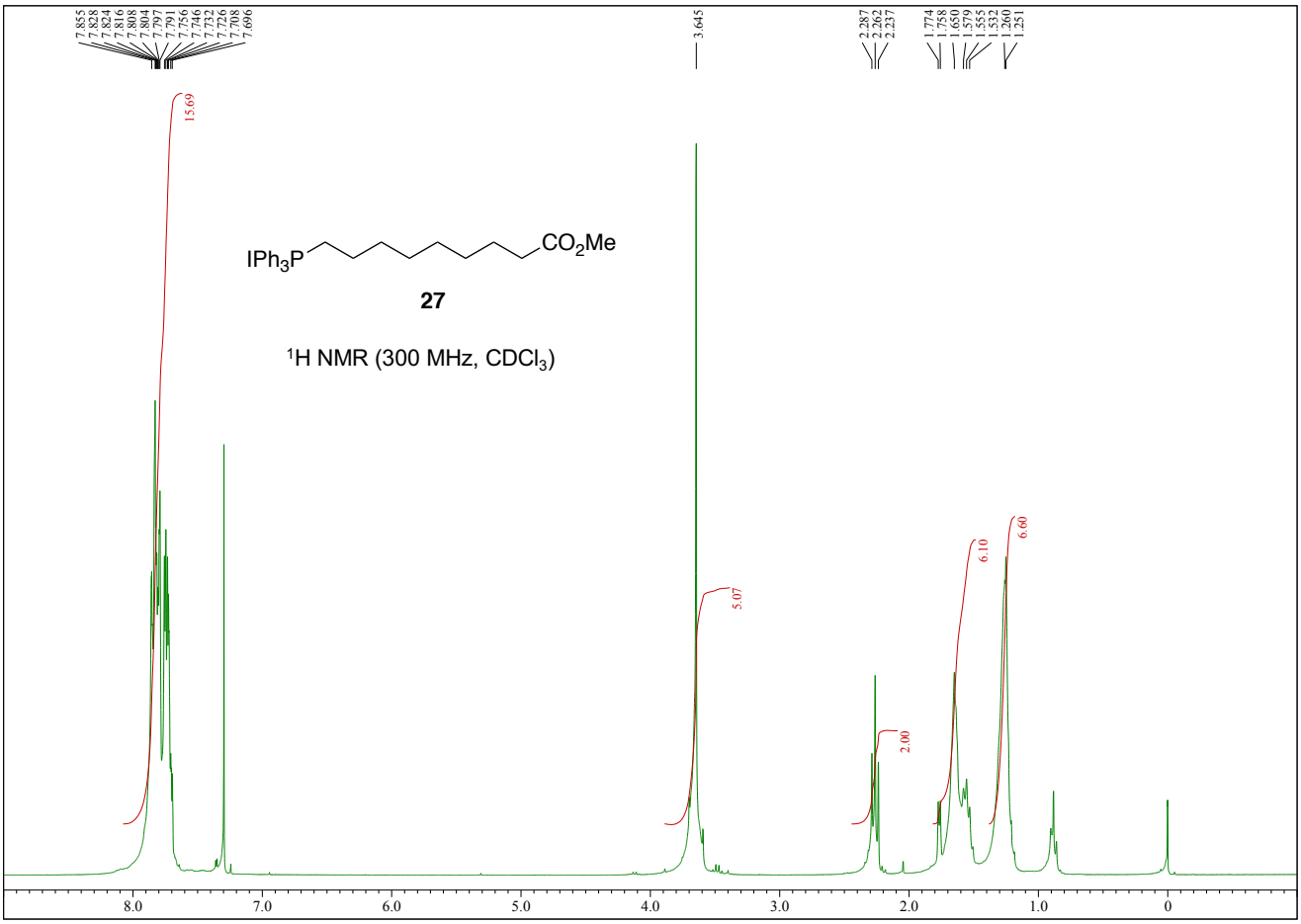

9.831
9.825
9.823
9.818
4.612
4.596
4.582
4.577
4.566
4.548
4.206
4.192
4.174
4.163
4.144
2.665
2.658
2.636
2.628
2.530
2.524
2.514
2.509
2.475
2.470
2.454
1.569
1.446
1.351
1.303
0.913
0.891
0.869
17.91
3.16
1.00
1.02
0.98
0.96
0.93
OHC
O
O
35
^{1}H NMR (300 MHz, $CDCl_3$)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

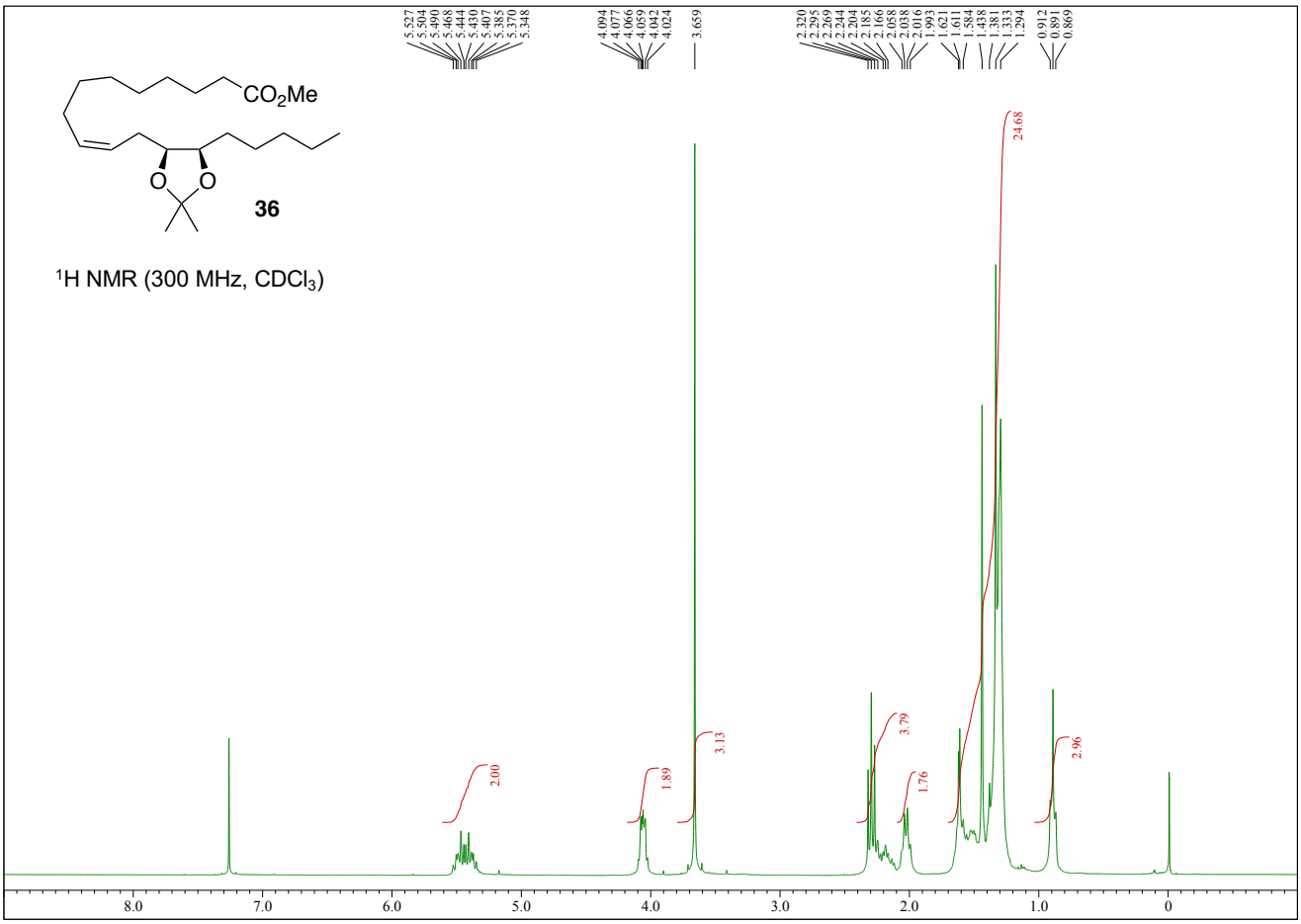

200.786
108.182
77.466
72.873
44.782
31.812
29.661
28.349
25.999
25.755
22.550
14.036
OHC
O
O
35
^{13}C NMR (75 MHz, $CDCl_3$)
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0

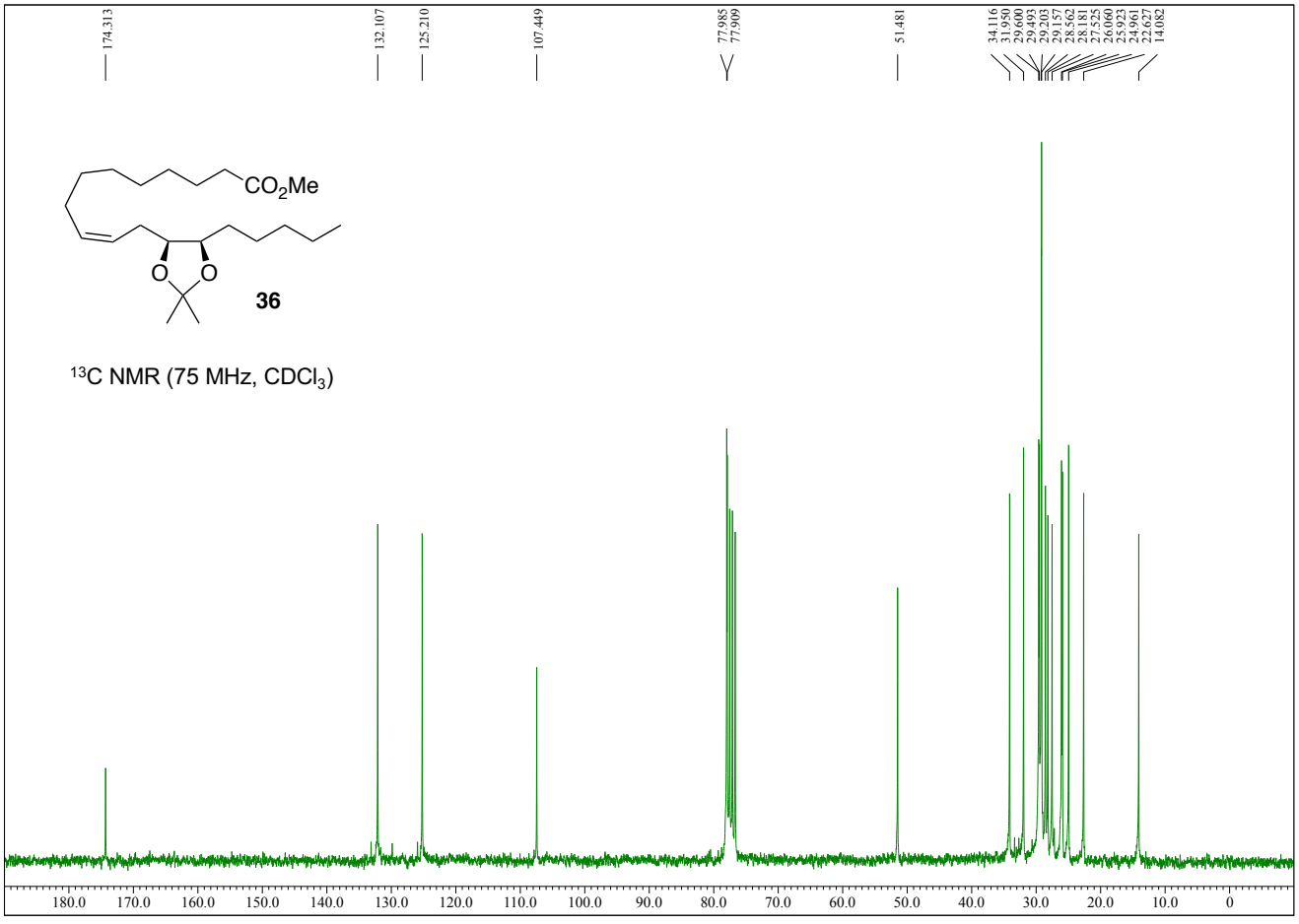

HO
CO2Me
1H NMR (300 MHz, CDCl3)
3.660
3.630
3.608
2.323
2.298
2.272
1.636
1.612
1.588
1.555
1.532
1.510
1.310
8.70
5.10
4.34
2.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

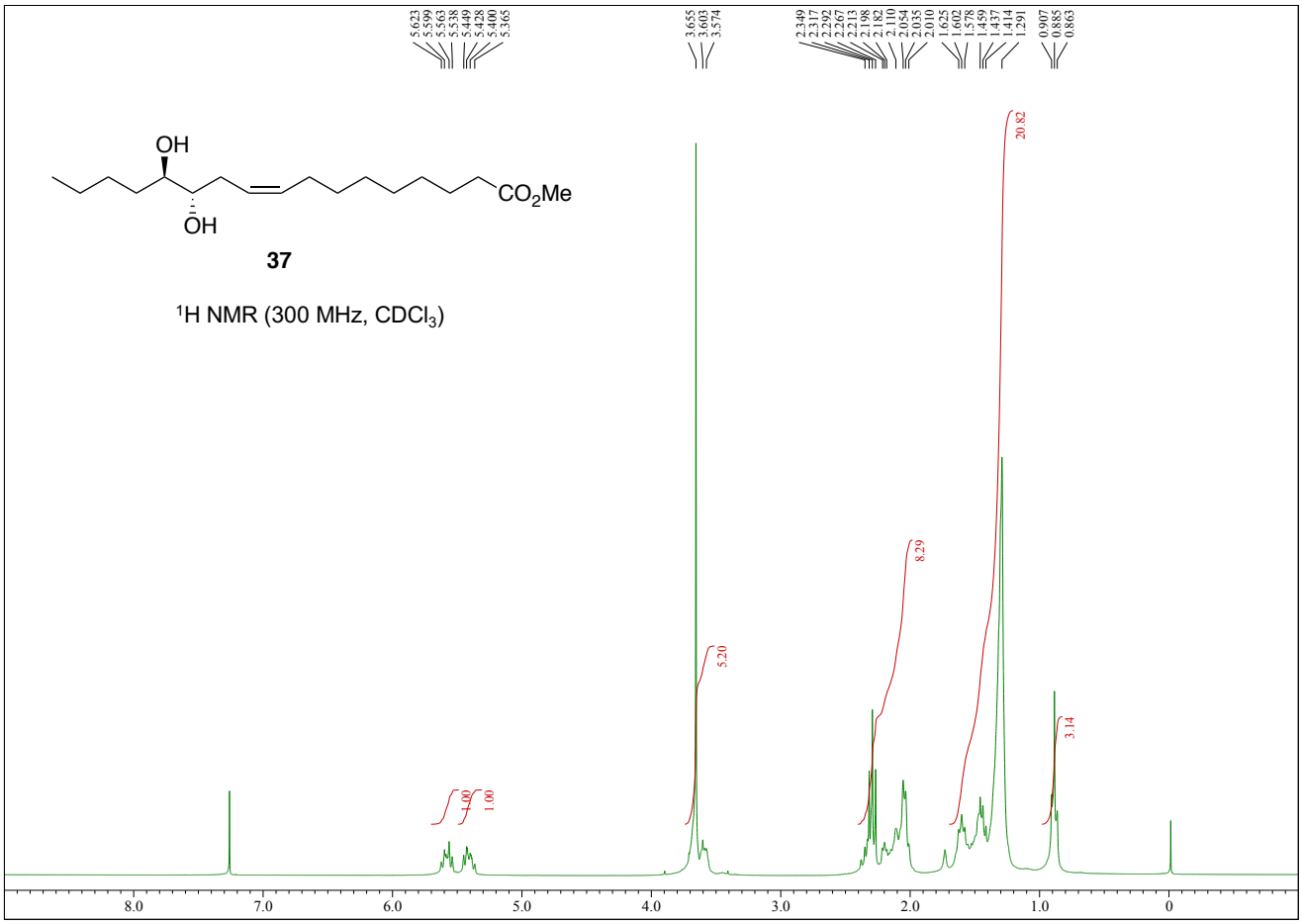

I
CO2Me
1H NMR (300 MHz, CDCl3)
3.664
3.203
3.180
3.156
2.325
2.301
2.275
1.857
1.834
1.810
1.786
1.763
1.638
1.614
1.591
1.576
1.573
1.399
1.372
1.305
8.12
2.91
1.98
2.00
1.88
2.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

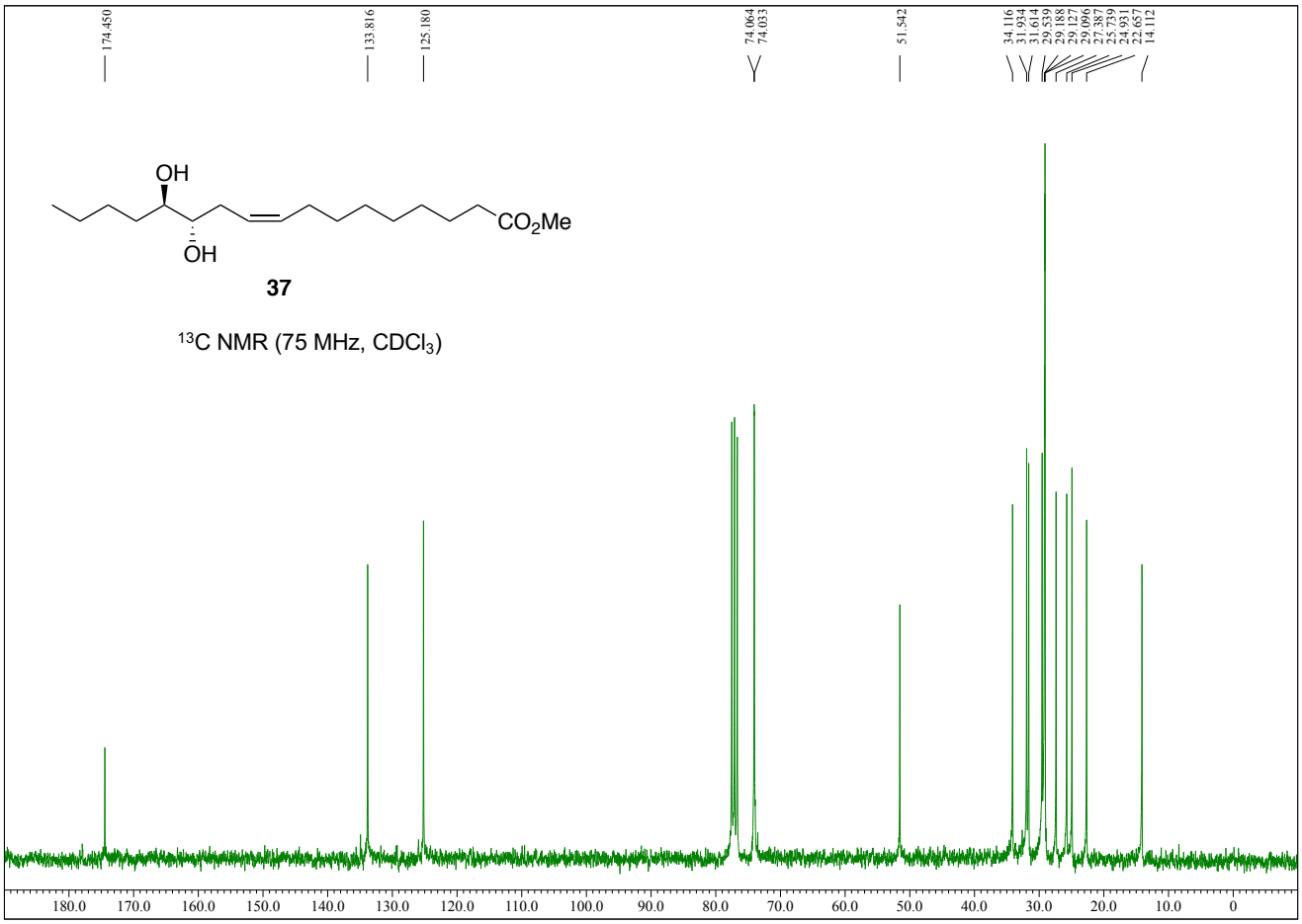

174.145
51.435
34.010
33.460
30.378
29.005
28.303
24.839
7.200
I
CO2Me
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0

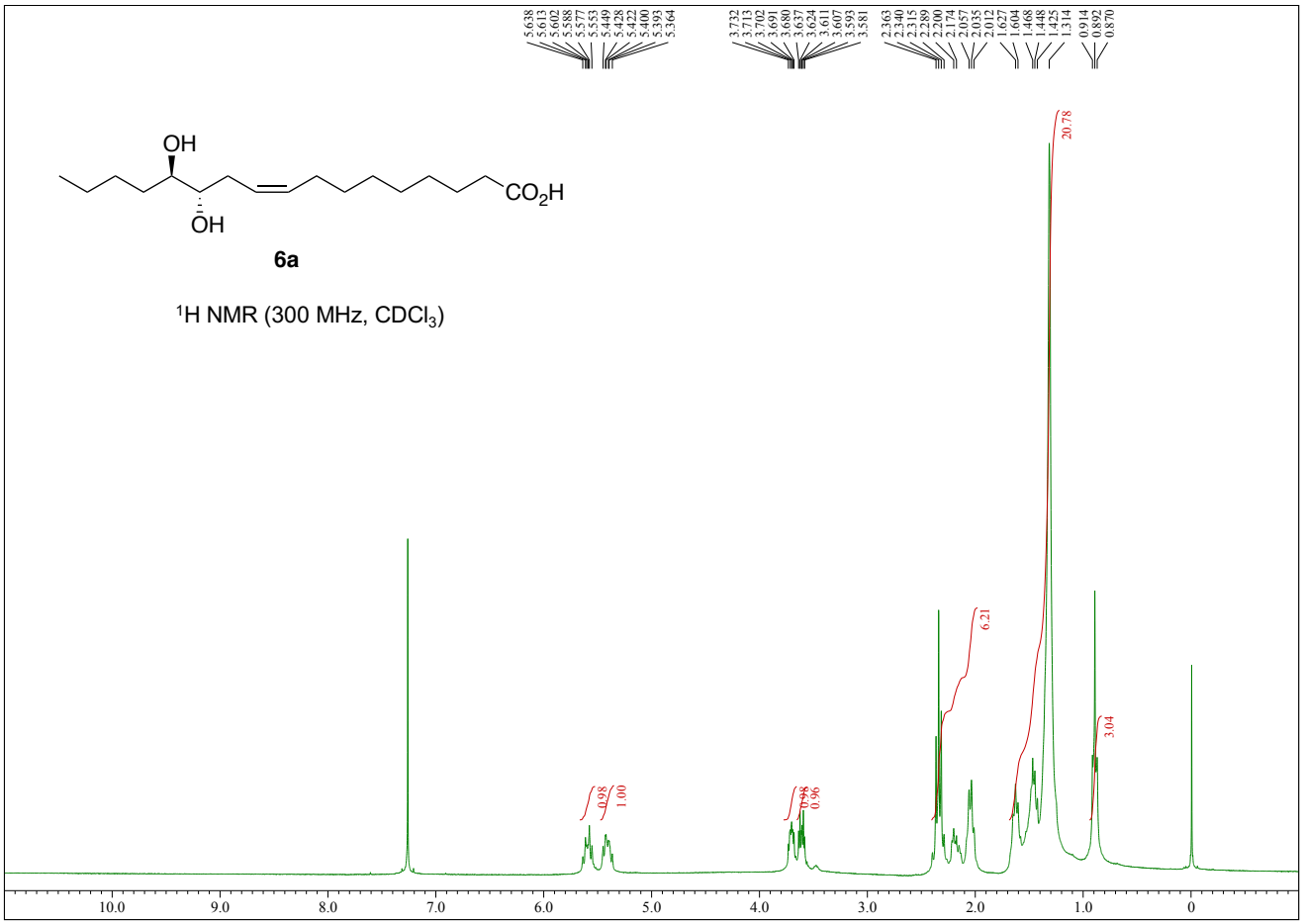

7.855
7.828
7.824
7.816
7.808
7.804
7.797
7.791
7.756
7.746
7.732
7.726
7.708
7.696
3.645
2.287
2.262
2.237
1.774
1.758
1.650
1.579
1.555
1.532
1.260
1.251
15.69
5.07
2.00
6.10
6.60
IPh3P
CO2Me
27
1H NMR (300 MHz, CDCl3)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

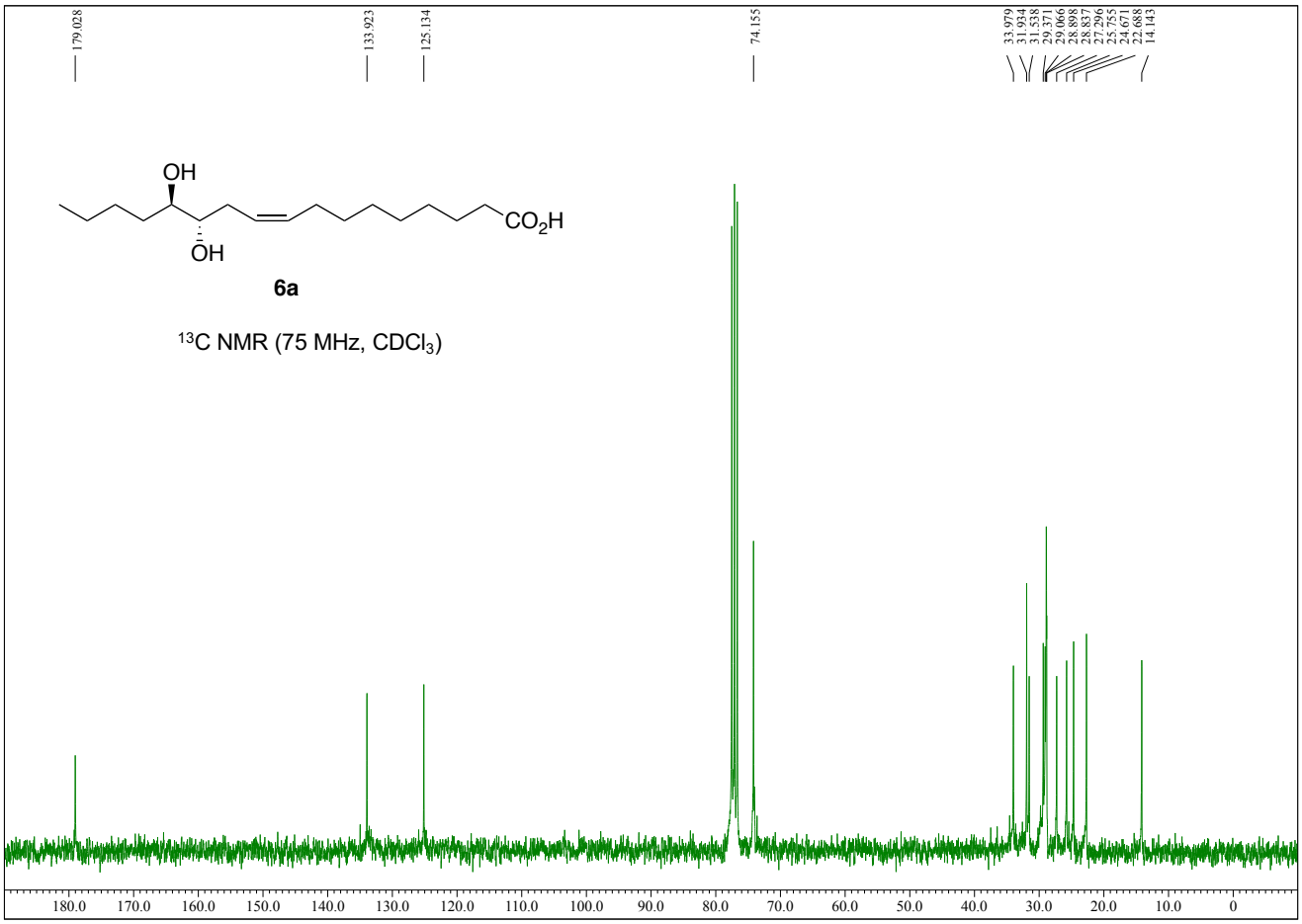

5.527
5.504
5.490
5.468
5.444
5.430
5.407
5.385
5.370
5.348
4.094
4.077
4.066
4.059
4.042
4.024
3.659
2.320
2.295
2.269
2.244
2.204
2.185
2.166
2.058
2.038
2.016
1.993
1.621
1.611
1.584
1.438
1.381
1.333
1.294
0.912
0.891
0.869
CO2Me
O
O
36
1H NMR (300 MHz, CDCl3)
24.68
3.79
3.13
2.96
2.00
1.89
1.76
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

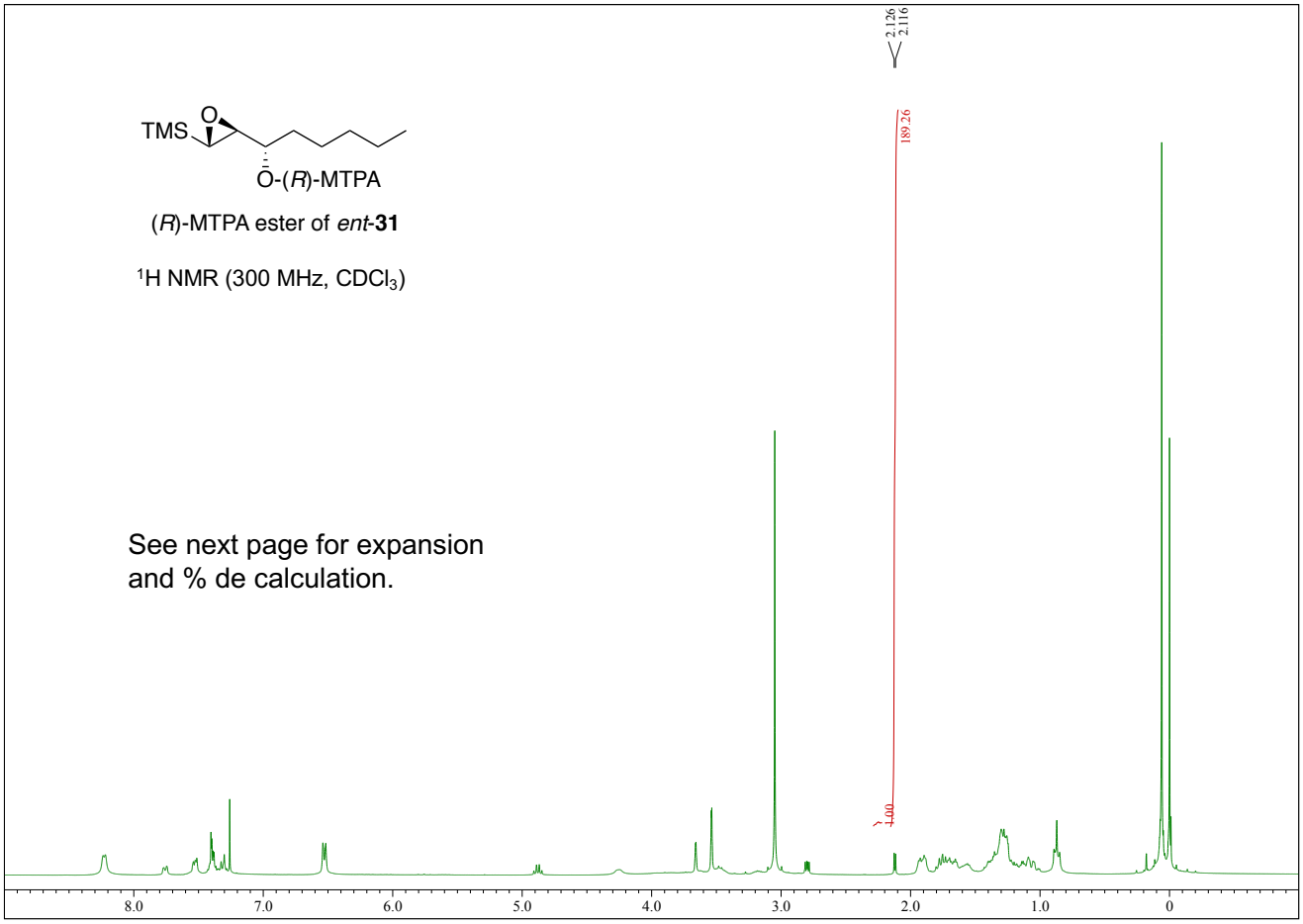

174.313
132.107
125.210
107.449
77.985
77.909
51.481
34.116
31.950
29.600
29.493
29.203
29.157
28.181
27.525
26.060
25.923
24.961
22.627
14.082
CO2Me
O
O
36
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0


OH
OH
CO2Me
37
1H NMR (300 MHz, CDCl3)


OH
OH
CO2Me
37
13C NMR (75 MHz, CDCl3)


OH
OH
CO2H
6a
1H NMR (300 MHz, CDCl3)
20.78
6.21
3.04
1.00
0.98
0.96
0.88

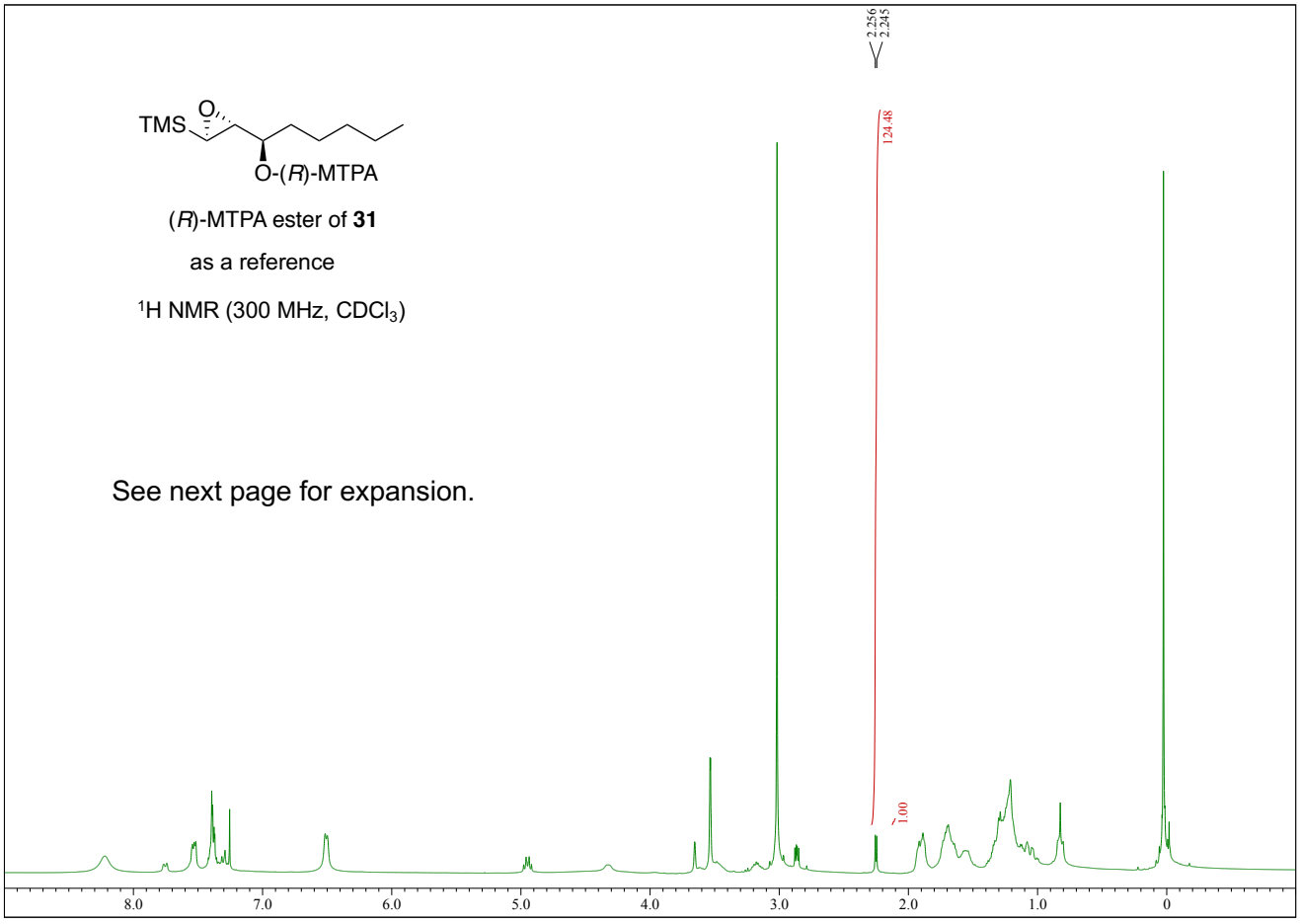

OH
OH
CO2H
6a
13C NMR (75 MHz, CDCl3)
179.028
133.923
125.134
74.155



(*R*)-MTPA ester of *ent*-**31**

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

See next page for expansion and % de calculation.



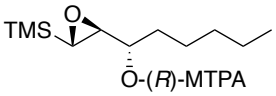
(*R*)-MTPA ester of **31**

as a reference

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

See next page for expansion.

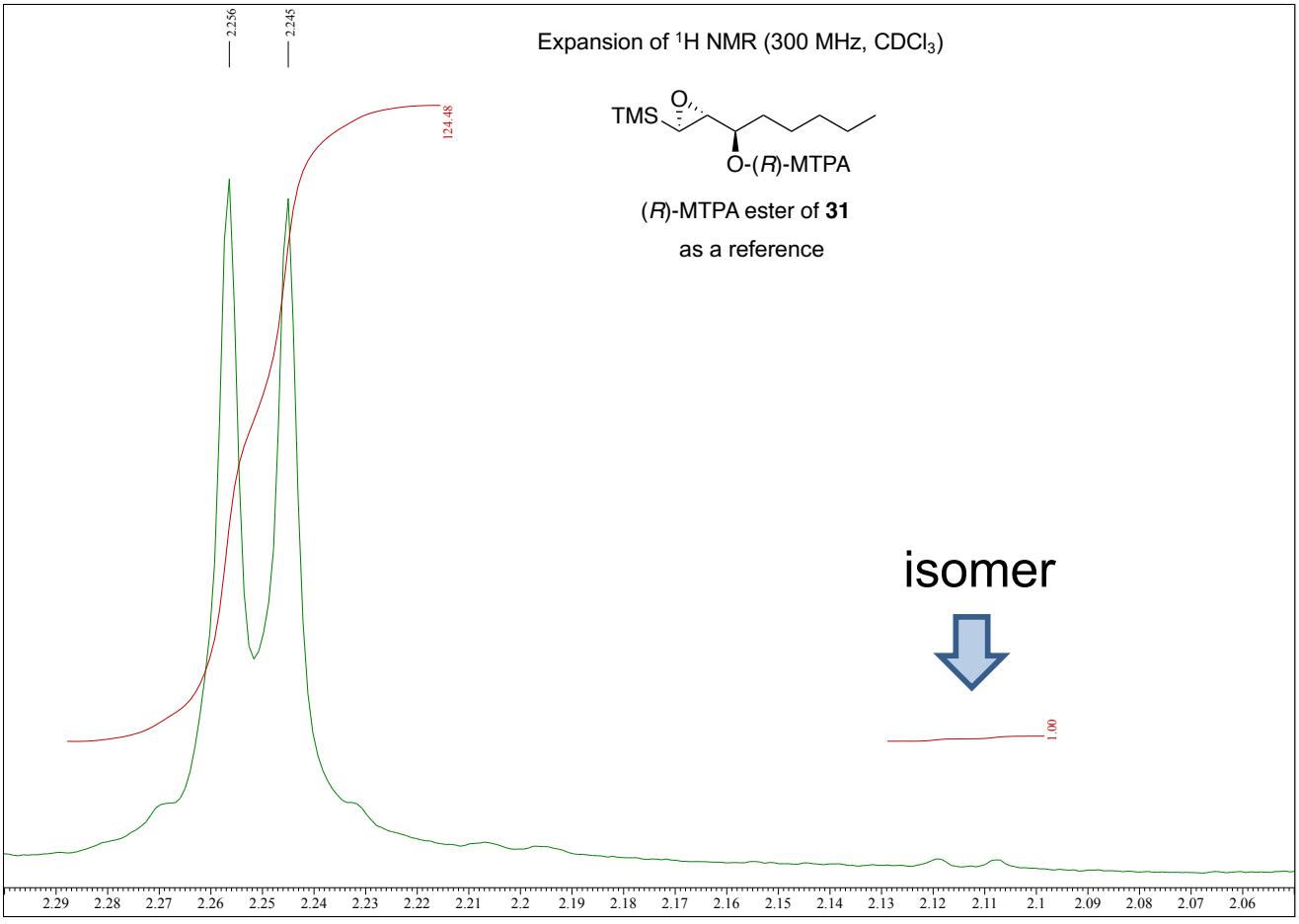
Expansion of ^{1}H NMR (300 MHz, $CDCl_3$)



(*R*)-MTPA ester of *ent*-**31**

de
= (189.26–1.00)x100/(189.26+1.00)
= 98.9%
= 99% de

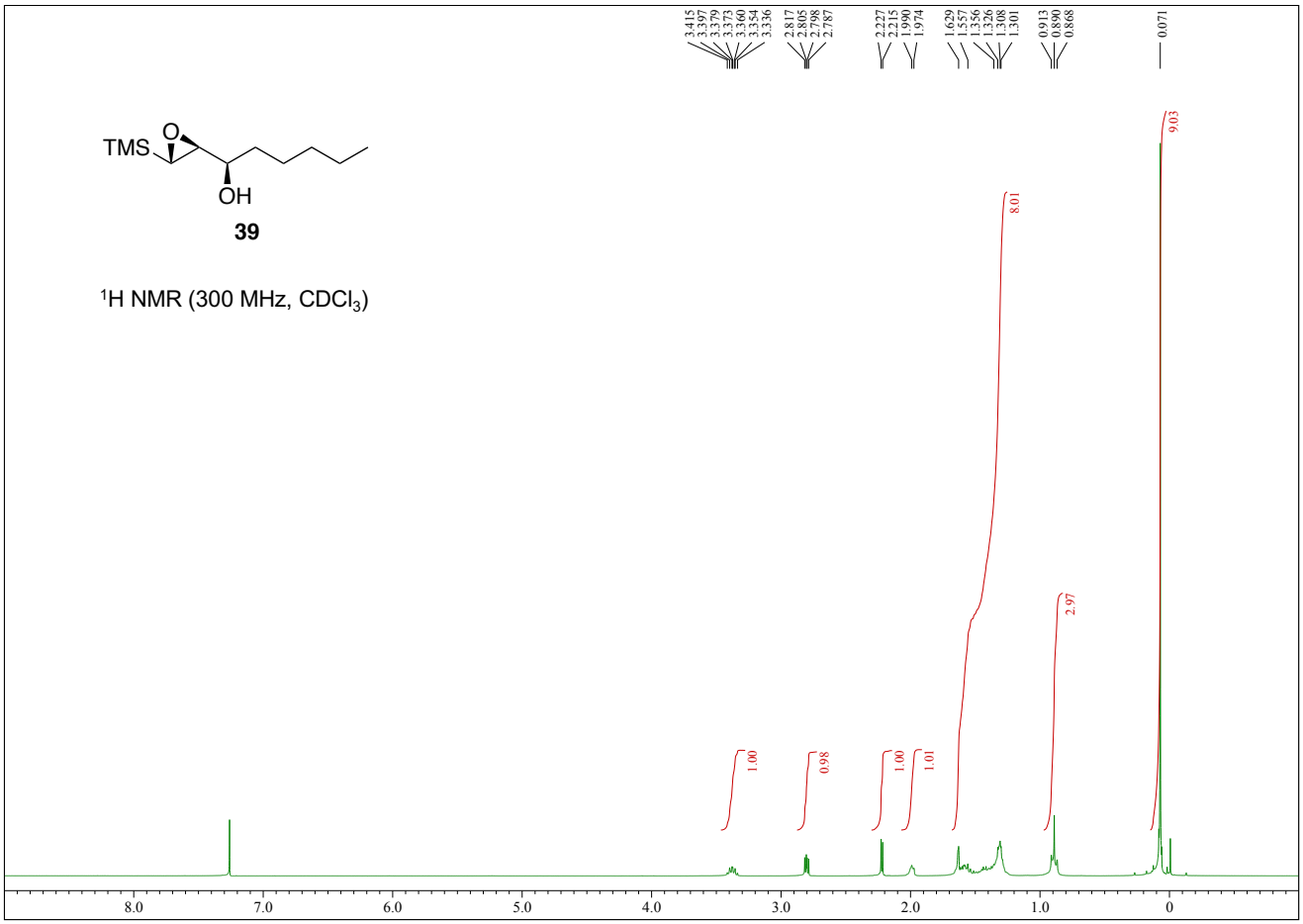
isomer

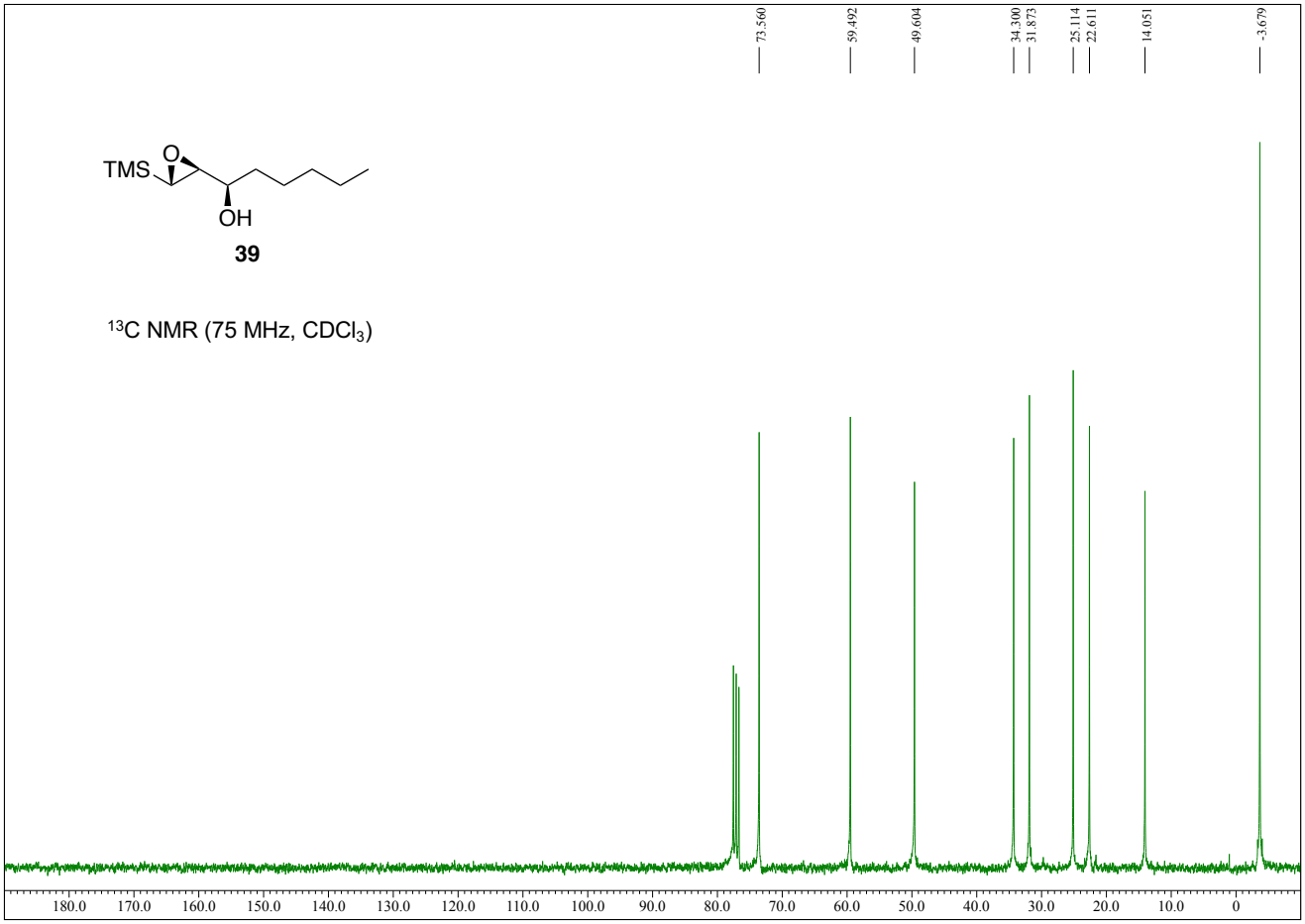


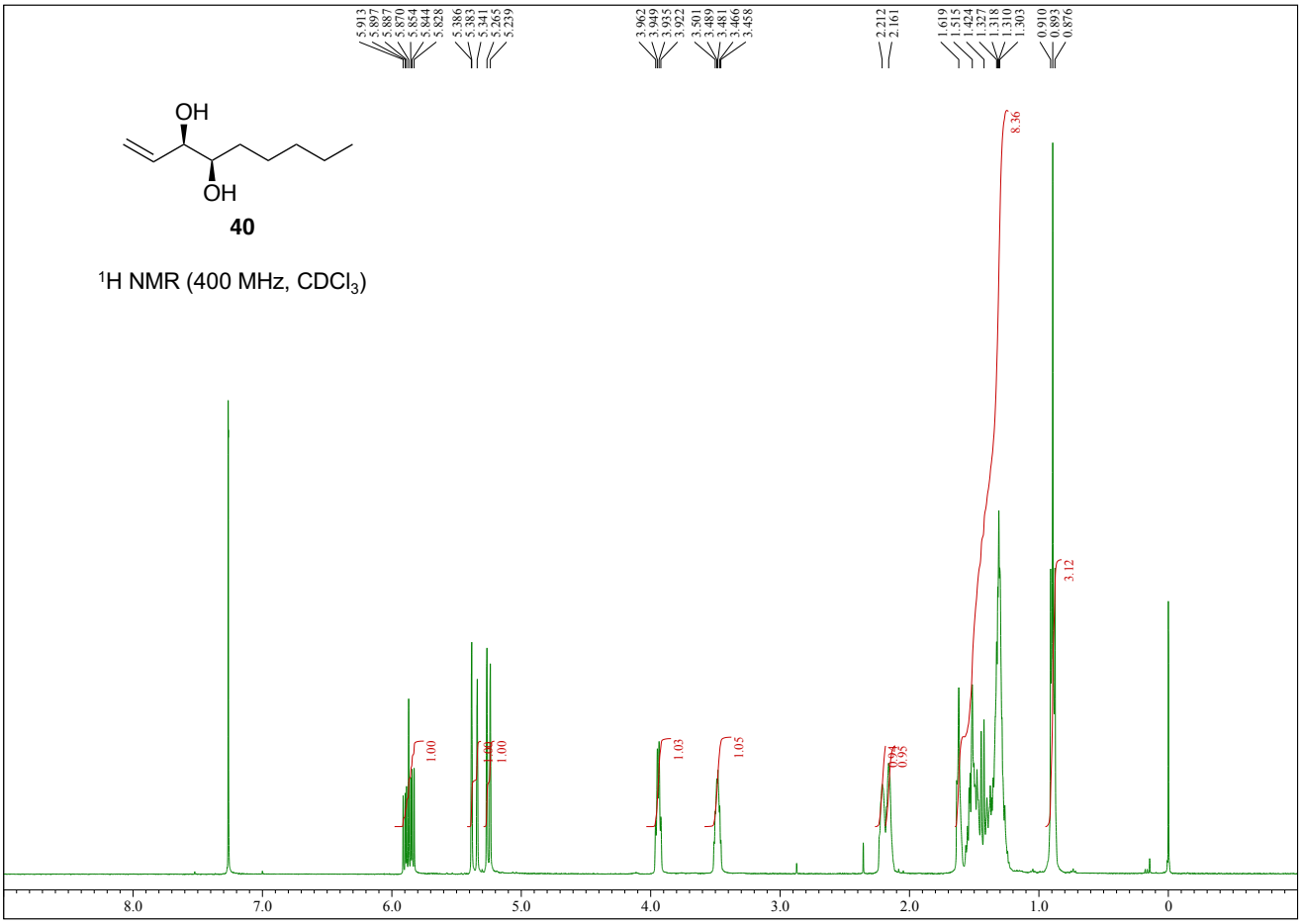
Expansion of ^{1}H NMR (300 MHz, $CDCl_3$)

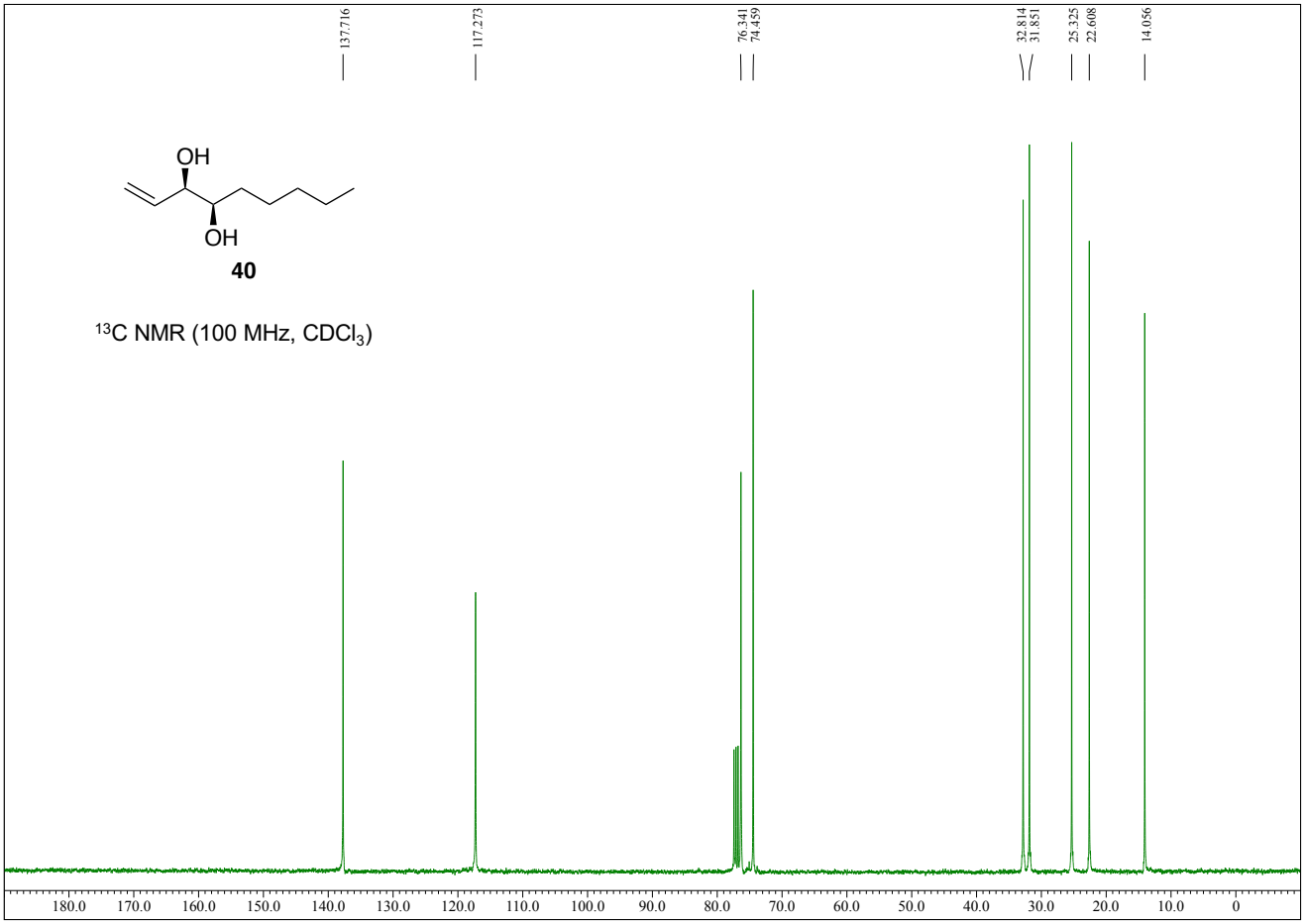
(*R*)-MTPA ester of **31**
as a reference

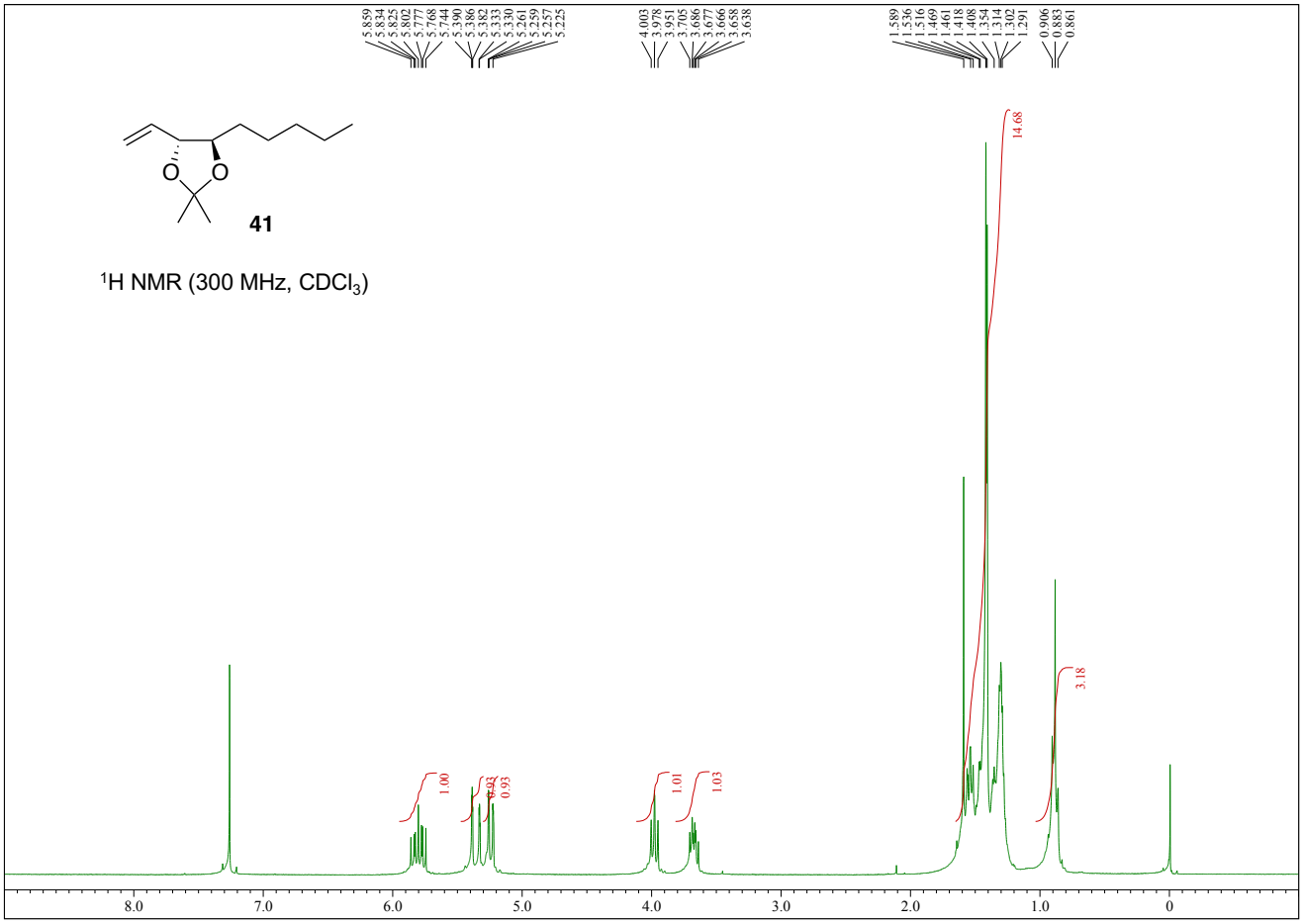
isomer


TMS
O
OH
39
^{1}H NMR (300 MHz, CDCl$_3$)
3.415
3.397
3.379
3.373
3.360
3.354
3.336
2.817
2.805
2.798
2.787
2.227
2.215
1.990
1.974
1.629
1.557
1.356
1.326
1.308
1.301
0.913
0.890
0.868
0.071
9.03
8.01
2.97
1.00
0.98
1.00
1.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


TMS
O
OH
39
^{13}C NMR (75 MHz, CDCl$_3$)
73.560
59.492
49.604
34.300
31.873
25.114
22.611
14.051
-3.679
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0

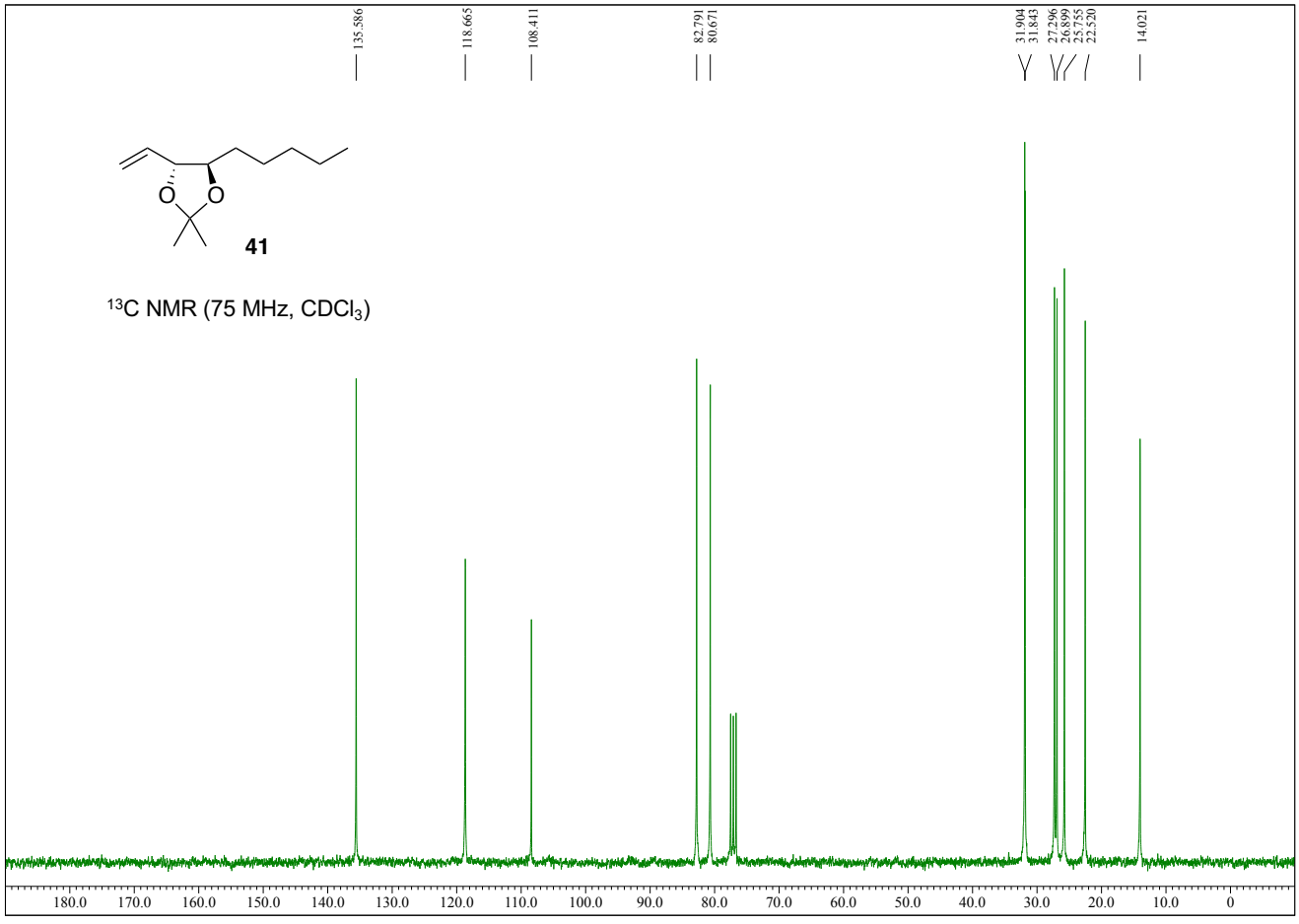

OH
OH
40
^{1}H NMR (400 MHz, $CDCl_3$)
5.913
5.897
5.887
5.870
5.854
5.844
5.828
5.386
5.383
5.341
5.265
5.239
3.962
3.949
3.935
3.922
3.501
3.489
3.481
3.466
3.458
2.212
2.161
1.619
1.515
1.424
1.327
1.318
1.310
1.303
0.910
0.893
0.876
8.36
3.12
1.00
1.03
1.05
0.95
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


OH
OH
40
^{13}C NMR (100 MHz, $CDCl_3$)
137.716
117.273
76.341
74.459
32.814
31.851
25.325
22.608
14.056
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0



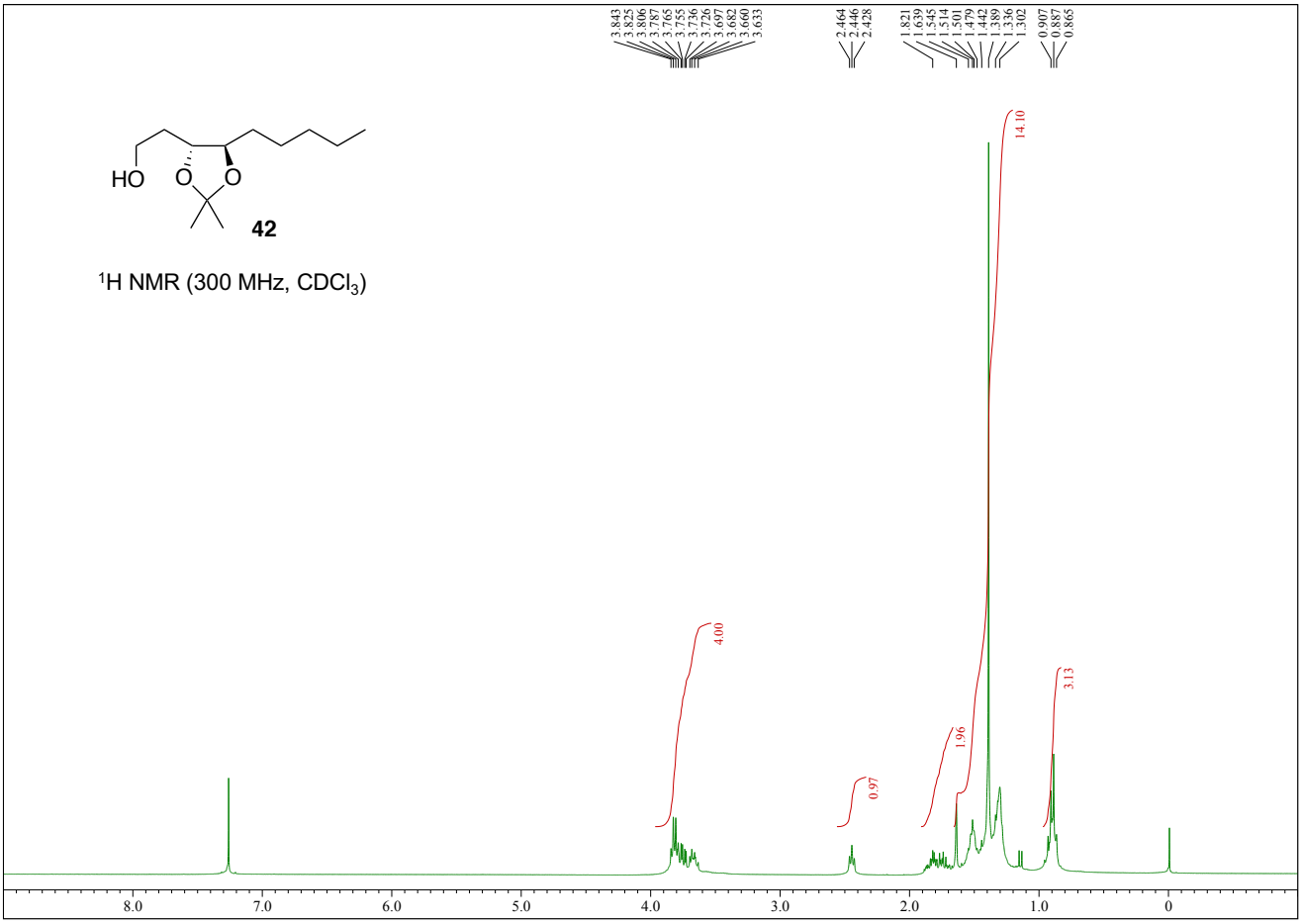
41

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

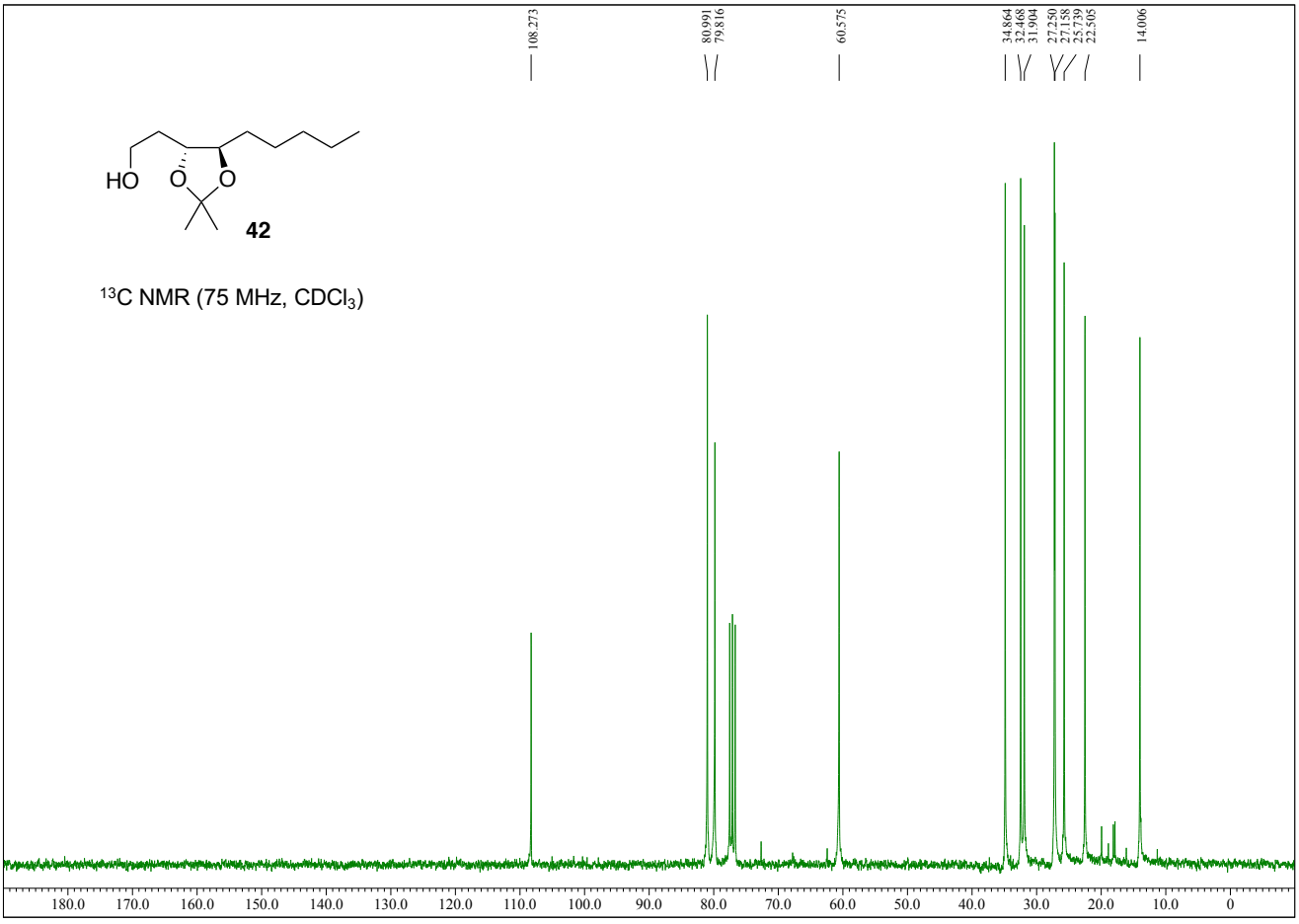


41

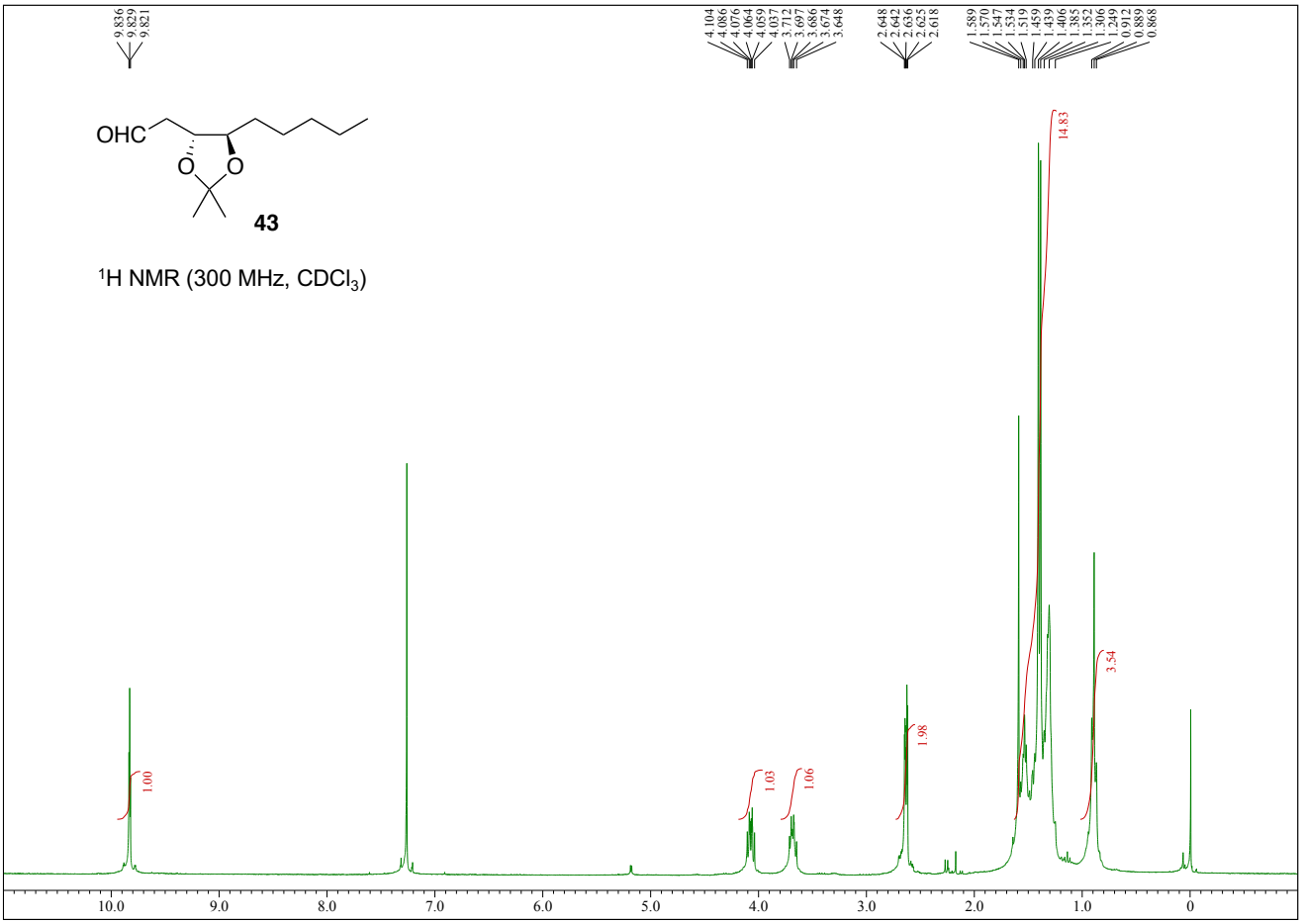
^{13}C NMR (75 MHz, $CDCl_3$)



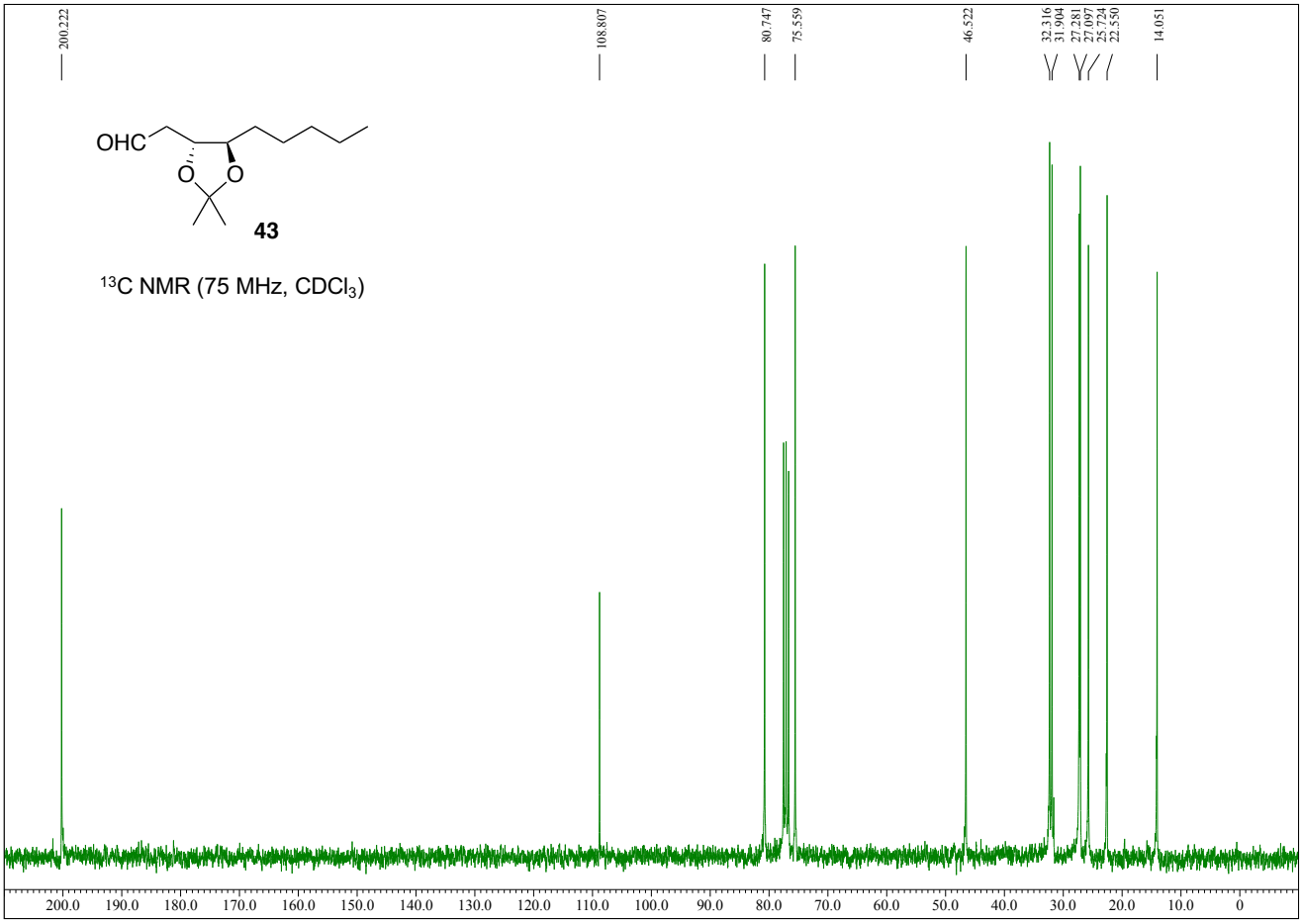
^{1}H NMR (300 MHz, $CDCl_3$)



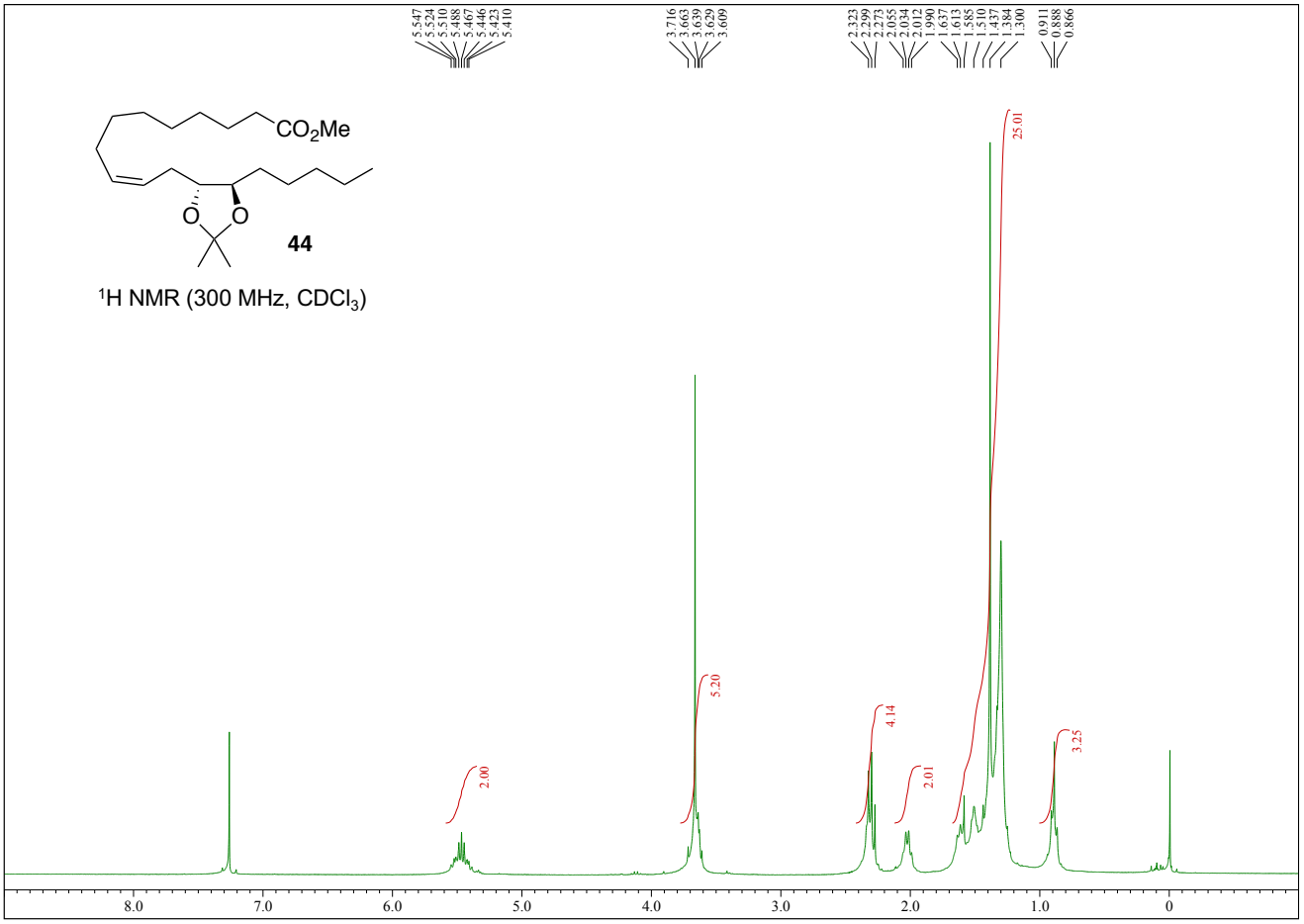
^{13}C NMR (75 MHz, $CDCl_3$)



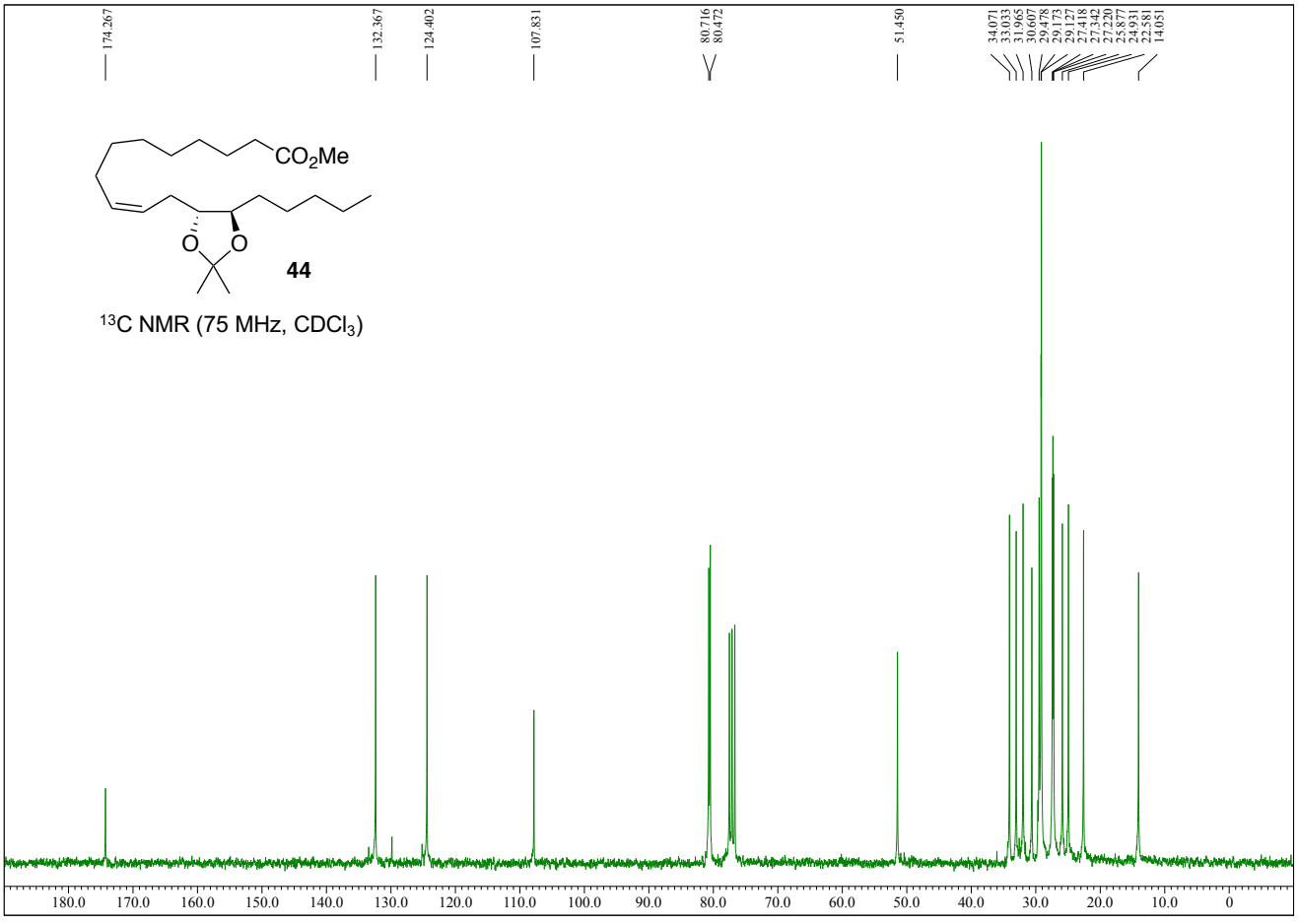
^{1}H NMR (300 MHz, $CDCl_3$)



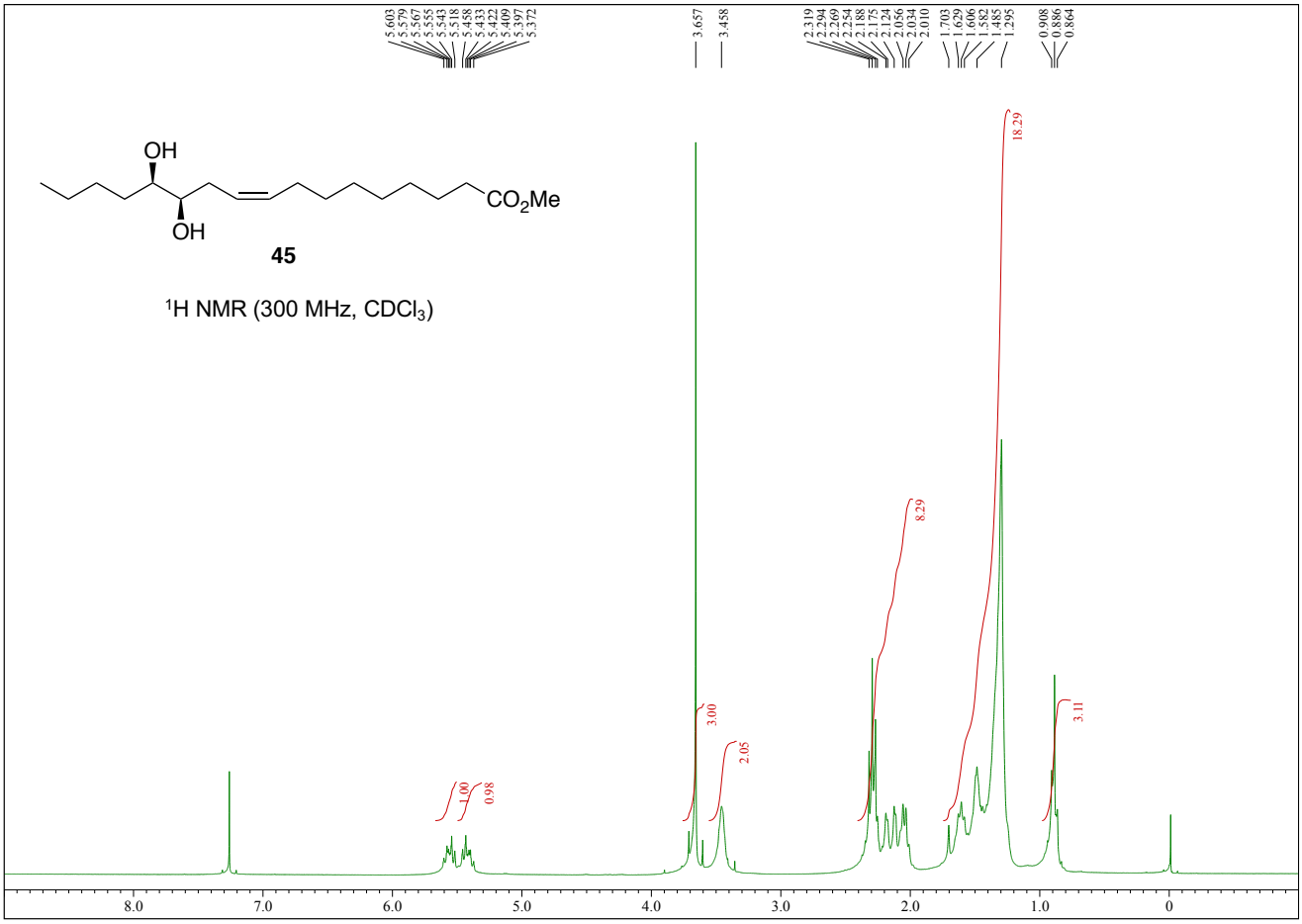
^{13}C NMR (75 MHz, $CDCl_3$)

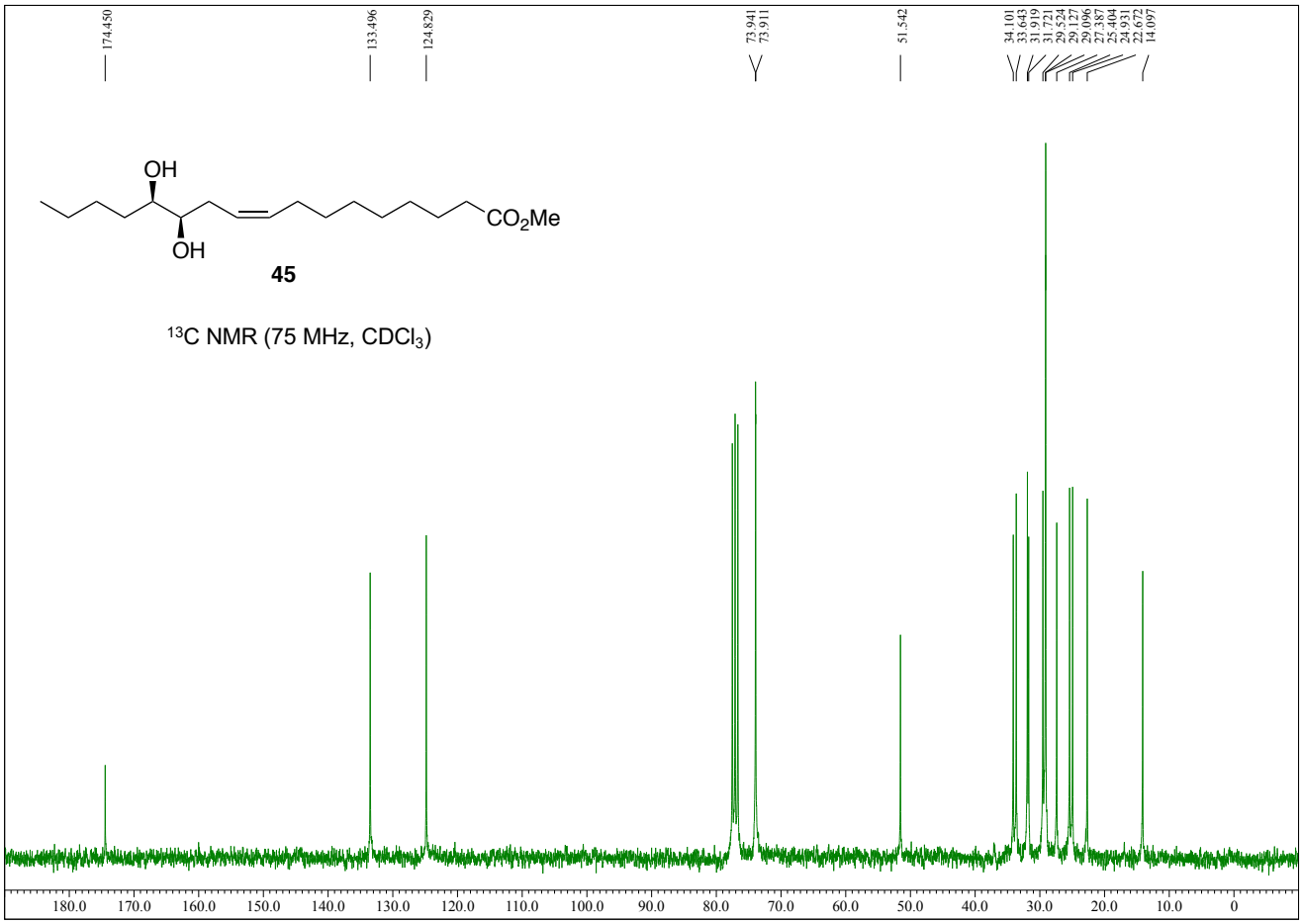


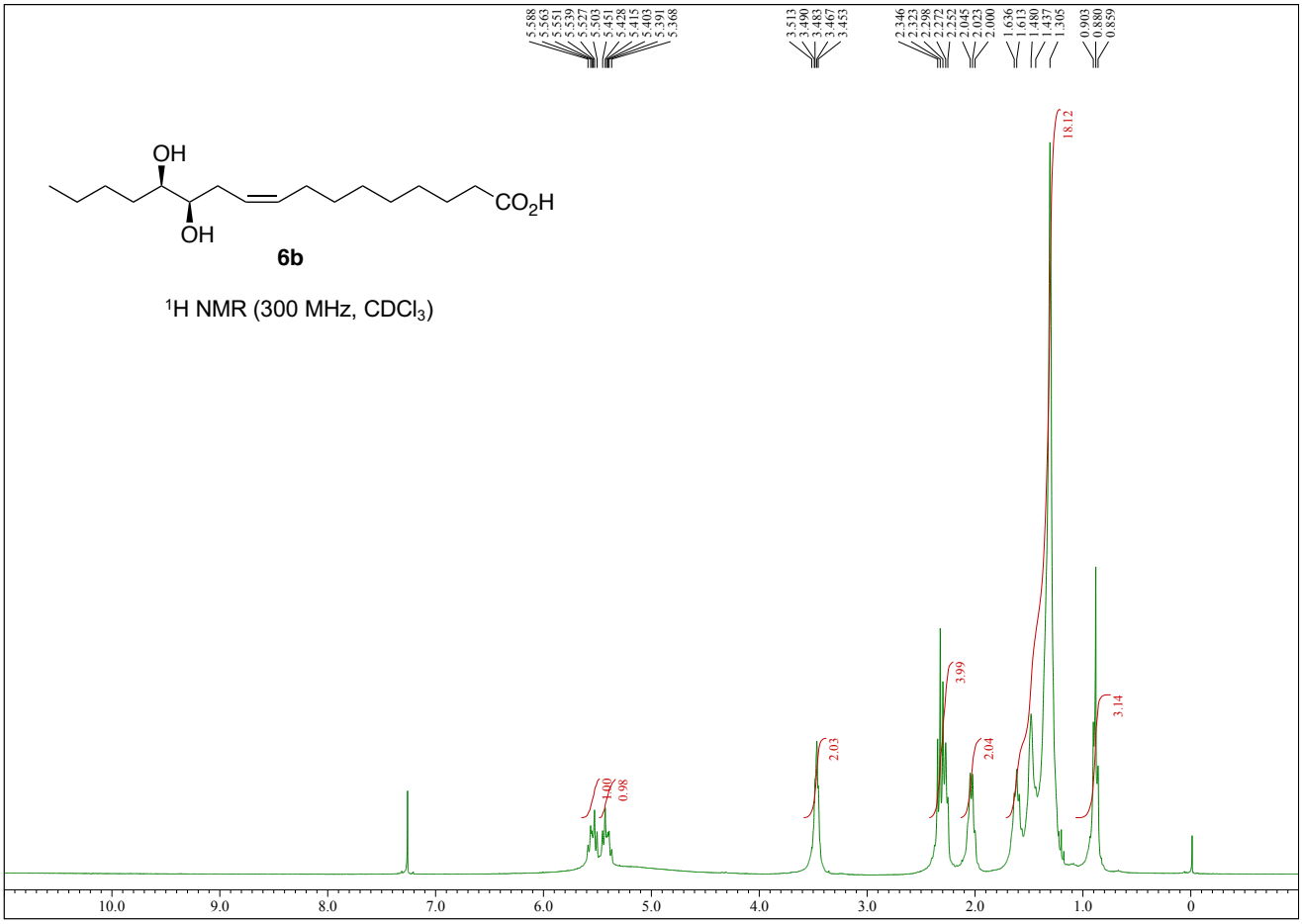
^{1}H NMR (300 MHz, $CDCl_3$)

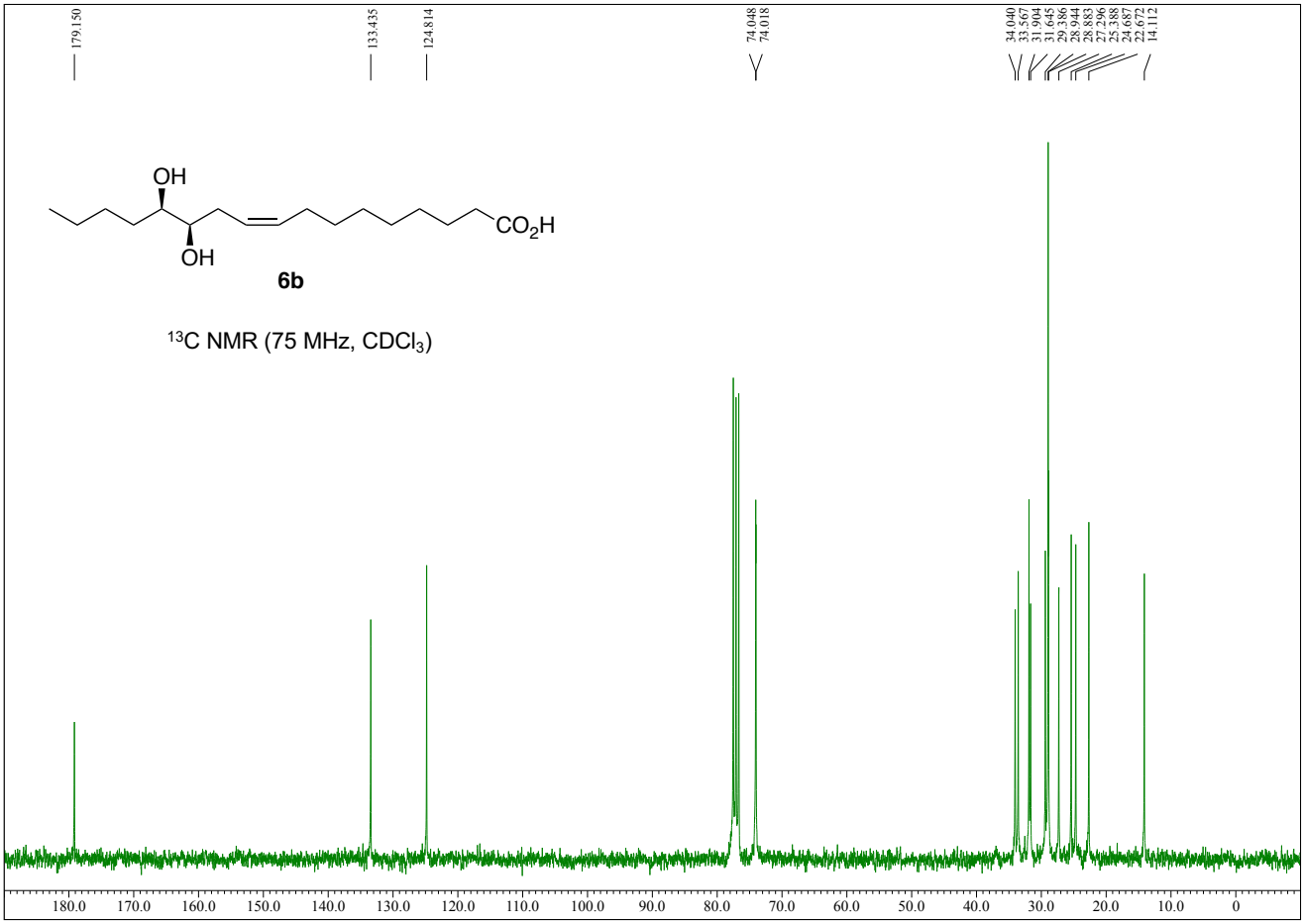


^{13}C NMR (75 MHz, $CDCl_3$)


OH
OH
CO2Me
45
1H NMR (300 MHz, CDCl3)
5.603
5.579
5.567
5.555
5.543
5.518
5.458
5.433
5.422
5.409
5.397
5.372
3.657
3.458
2.319
2.294
2.269
2.254
2.188
2.175
2.124
2.056
2.034
2.010
1.703
1.629
1.606
1.582
1.485
1.295
0.908
0.886
0.864
18.29
8.29
3.00
2.05
3.11
1.00
0.98
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


OH
OH
CO2Me
45
13C NMR (75 MHz, CDCl3)
174.450
133.496
124.829
73.941
73.911
51.542
34.101
33.643
31.919
31.721
29.524
29.127
29.096
27.387
25.404
24.931
22.672
14.097
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0


OH
OH
CO2H
6b
1H NMR (300 MHz, CDCl3)
5.588
5.563
5.551
5.539
5.527
5.503
5.451
5.428
5.415
5.403
5.391
5.368
3.513
3.490
3.483
3.467
3.453
2.346
2.323
2.298
2.272
2.252
2.045
2.023
2.000
1.636
1.613
1.480
1.437
1.305
0.903
0.880
0.859
18.12
3.99
3.14
2.04
2.03
1.00
0.98
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


179.150
133.435
124.814
74.048
74.018
34.040
33.567
31.904
31.645
29.396
28.944
28.883
27.206
25.388
24.687
22.672
14.112
OH
OH
CO2H
6b
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0