Synthesis of the Gymnodimine Tetrahydrofuran Core.

Sylvestre Toumieux,[c] Redouane Beniazza,[a] Valérie Desvergnes,[a] Romulo Araoz,[b] Jordi Molgo,[b] and Yannick Landais[a]*

[a], *University of Bordeaux, Institut des Sciences Moléculaires, UMR-CNRS-5255, 351 cours de la libération, 33405 Talence, Cedex, France*

[b],*Institut Fédératif de Neurobiologie Alfred Fessard*

Laboratoire de Neurobiologie et Développement, UPR 3294

1, Avenue de la Terrasse, Bâtiments 32-33,

91198-Gif sur Yvette cedex, France

[c], *Present address : Laboratoire des Glucides UMR-CNRS 6219, Université de Picardie Jules Verne, 33 Rue Saint Leu, 80 039 AMIENS, France*

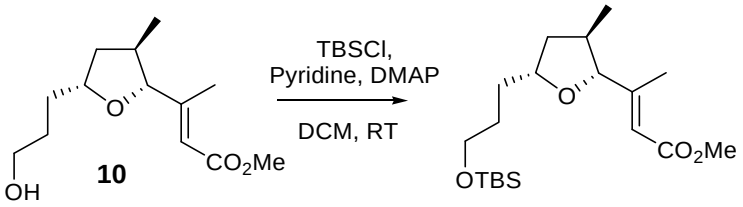
Supporting information

General Considerations:

^{1}H NMR and ^{13}C NMR were recorded on a Bruker AC-250 FT (^{1}H: 250 MHz, ^{13}C: 62.9 MHz), Bruker Avance-300 FT (^{1}H: 300 MHz, ^{13}C: 75.46 MHz), and Bruker DPX-400 FT (^{1}H: 400 MHz, ^{13}C: 100.6 MHz) using $CDCl_3$ as internal reference unless otherwise indicated. The chemical shifts (δ) and coupling constants (J) are expressed in ppm and hertz respectively. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, m = multiplet, br = broad. IR spectra were recorded on a Perkin-Elmer Paragon 1000 FT-IR spectrophotometer as neat films on NaCl windows or as KBr pellets or using a diamond ATR accessory (Golden gate). HRMS were recorded on a Micromass ZABSpec TOF apparatus, on a Q-Tof Applied Biosystems and on Waters Q-Tof 2 apparatus (for ESI). Melting points were determined by using a Stuart scientific digital 7SMP3 apparatus and are uncorrected.

Merck silica gel (0.043-0.063 mm) was used for flash chromatography. All reactions were carried out under nitrogen or Argon atmosphere unless specified. CH_2Cl_2 and acetonitrile were distilled over CaH_2. THF and Et_2O were distilled from sodium/benzophenone prior to use. All commercially available reagent-grade chemicals were used as received, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials.

(E)-methyl 3-((2R,3R,5R)-5-(3-(tert-butyldimethylsilyloxy)propyl)-3-methyltetrahydrofuran-2-yl)but-2-enoate



To a solution of (*E*)-methyl 3-((*2R,3R,5R*)-5-(3-hydroxypropyl)-3-methyl-tetrahydrofuran-2-yl)but-2-enoate **10** (47 mg, 0.186 mmol) in DCM (3.6 ml) was added at RT, pyridine (65 µL, 0.465 mmol, 2.5 eq.), TBSCl (56 mg, 0.372 mmol, 2 eq.) and finally DMAP (4.5 mg, 0.037 mmol, 0.2 eq.). The clear solution was then stirred for 16h at RT (~ 15°C). The mixture was quenched by water, extracted with DCM (3x15 mL). The organic layers were combined and dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification on silica gel (PE/EA: 98/2 to 95/5) provided the (*E*)-methyl 3-((*2R,3R,5R*)-5-allyl-3-methyl-tetrahydrofuran-2-yl)but-2-enoate as a colorless oil (47 mg, 71%).

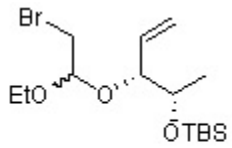
$[\alpha]^D$ = - 12.6 (C = 0.22 , $CHCl_3$)

IR (film, NaCl): ν (cm^{-1}) = 2957, 2861, 1722, 1655, 1159, 1096

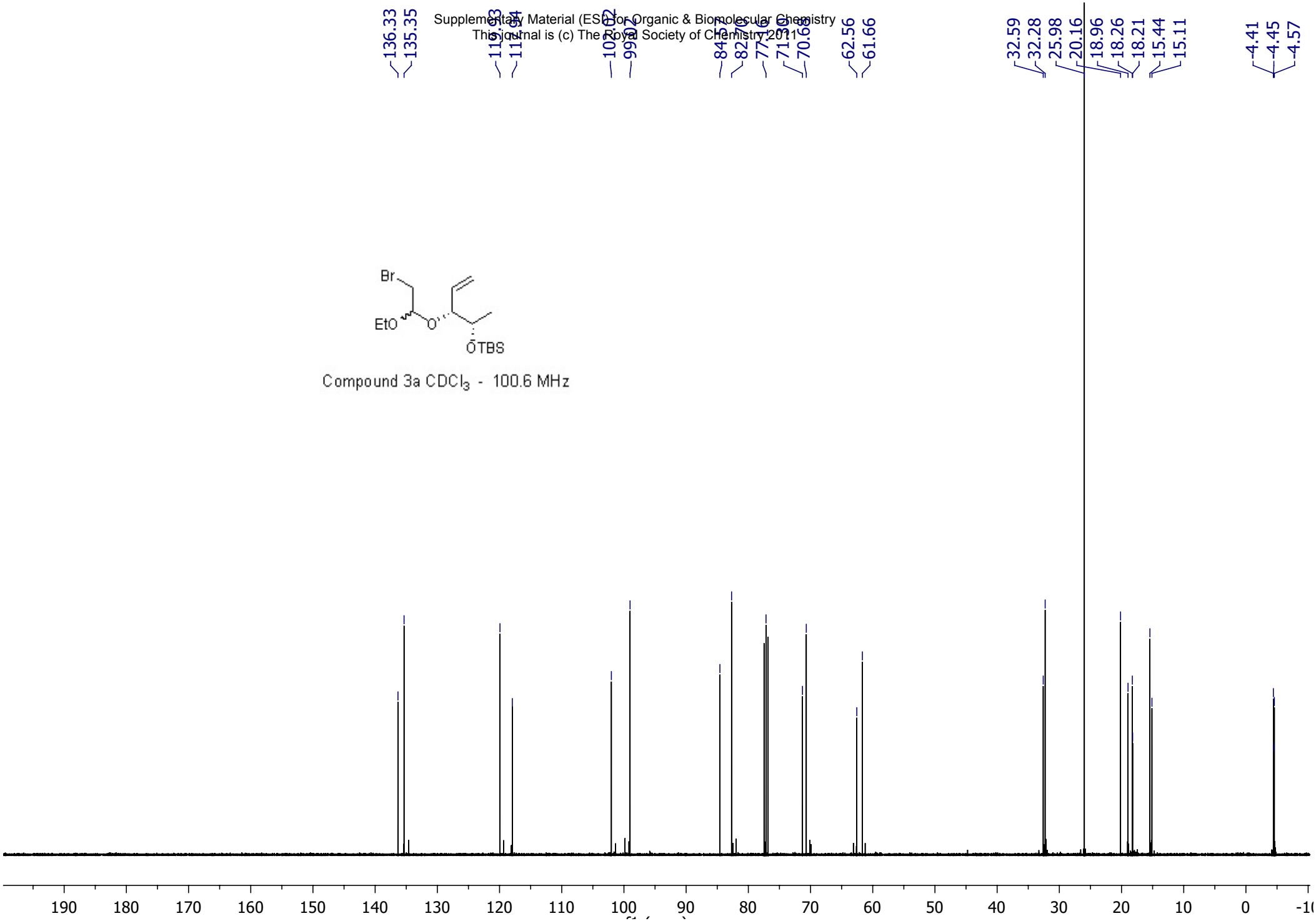
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 5.91-5.86 (m, 1 H), 4.09-3.97 (m, 1 H), 3.78 (d, J ~ 6.6 Hz, 1 H), 3.71-3.58 (m, 2 H), 3.68 (s, 3H), 2.17-1.97 (m, 1 H), 2.11 (d, J ~ 1.2 Hz, 3H), 1.78-1.48 (m, 6 H), 1.05 (d, J ~ 6.6 Hz, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H).

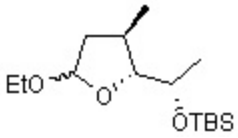
^{13}C NMR ($CDCl_3$, 75.5 MHz): δ (ppm) = 167.3, 158.7, 114.9, 90.5, 78.8, 63.2, 51.0, 39.7, 38.3, 32.5, 29.6, 26.1, 18.5, 14.8, -5.2.

HRMS (ESI): $[M+Na]^+$ $C_{19}H_{36}O_4Si$ Na: calcd. 379.22806, found 379.2283

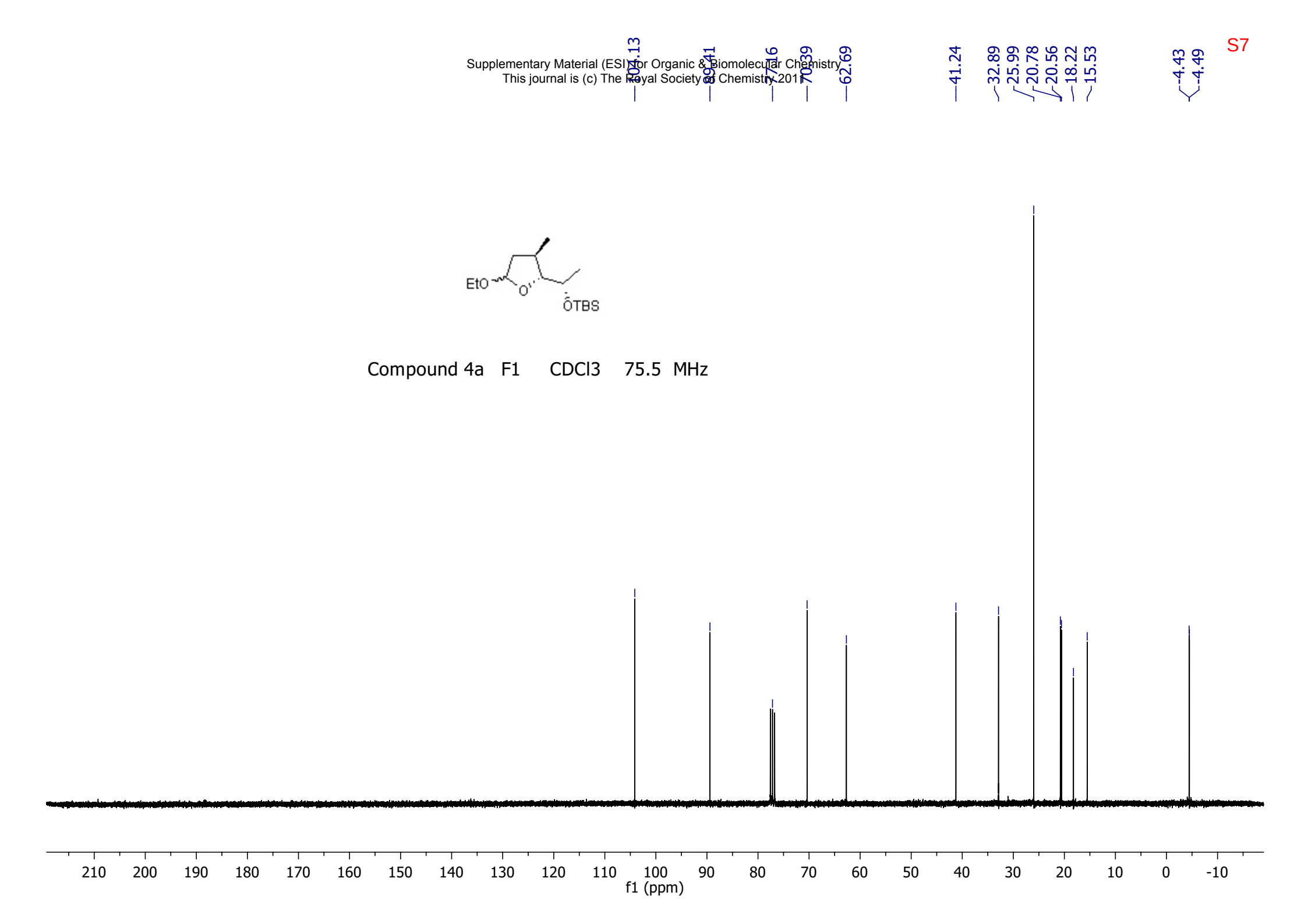


Compound 3a $CDCl_3$ - 400 MHz





Compound 4a F1 CDCl3 300 MHz


104.13
89.41
77.16
70.39
62.69
41.24
32.89
25.99
20.78
20.56
18.22
15.53
-4.43
-4.49
EtO
O
OTBS
Compound 4a F1 CDCl3 75.5 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

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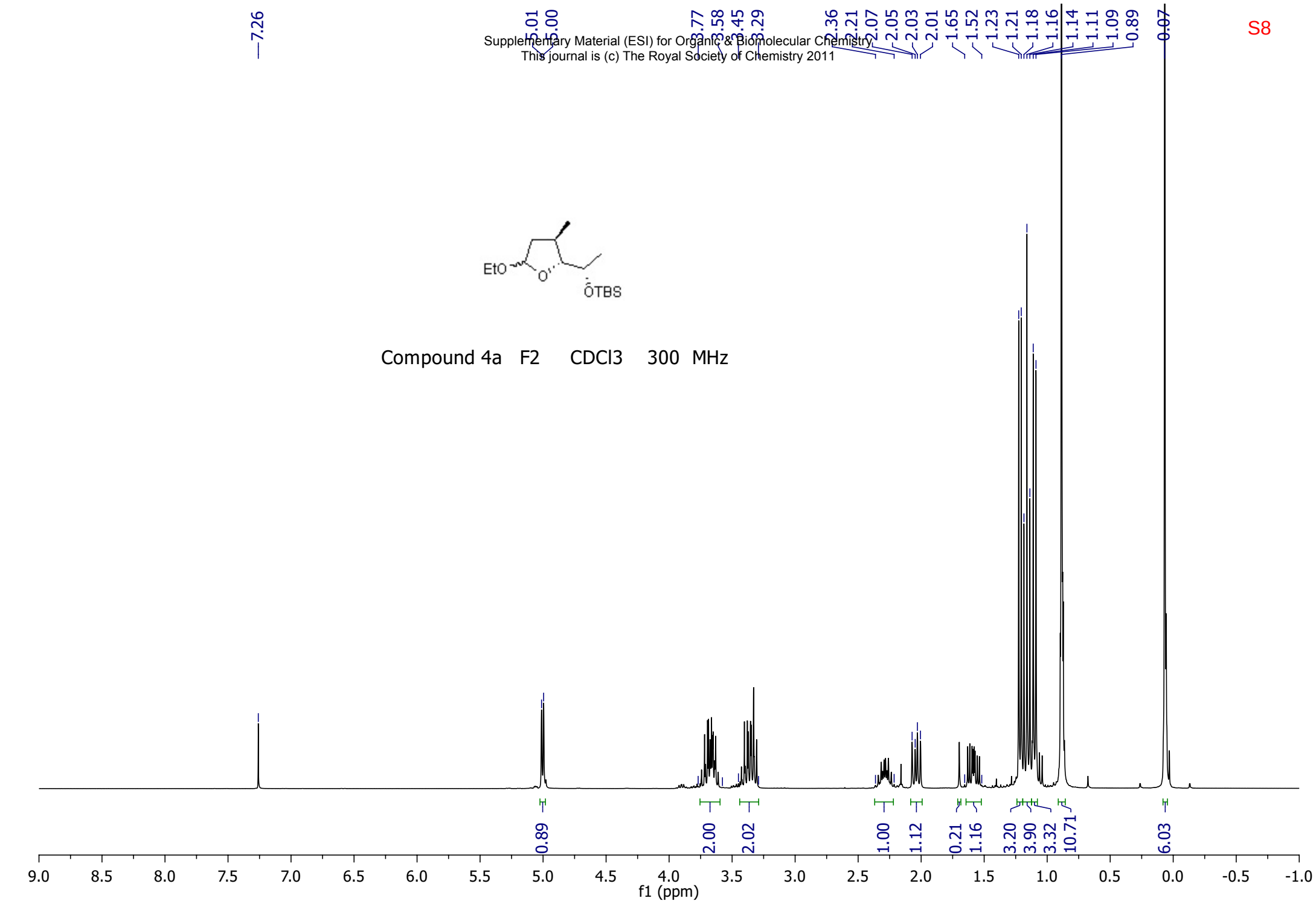

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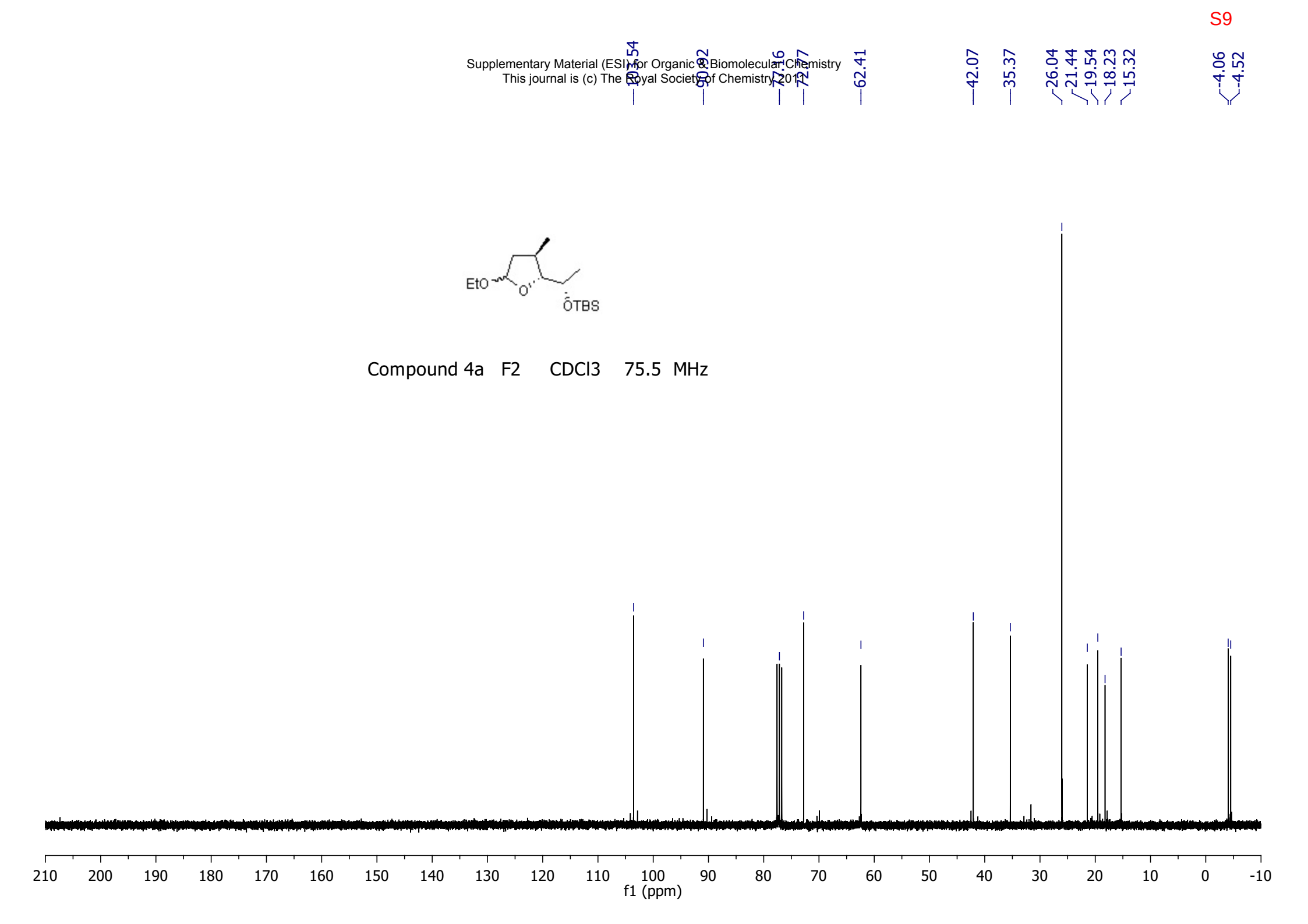
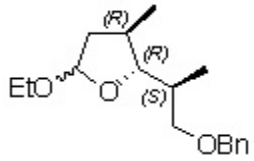
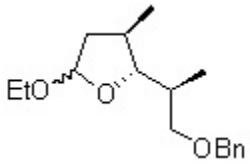
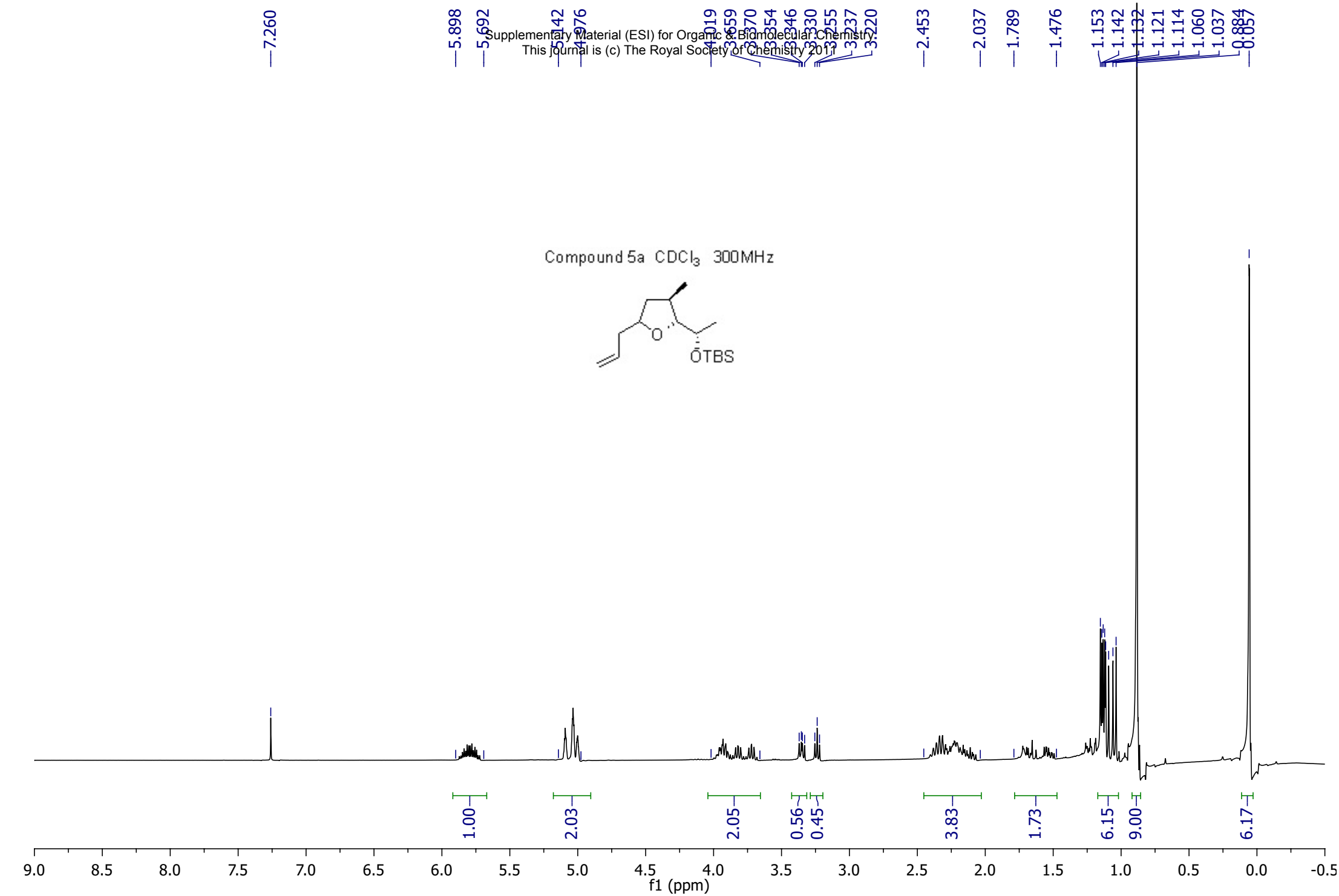


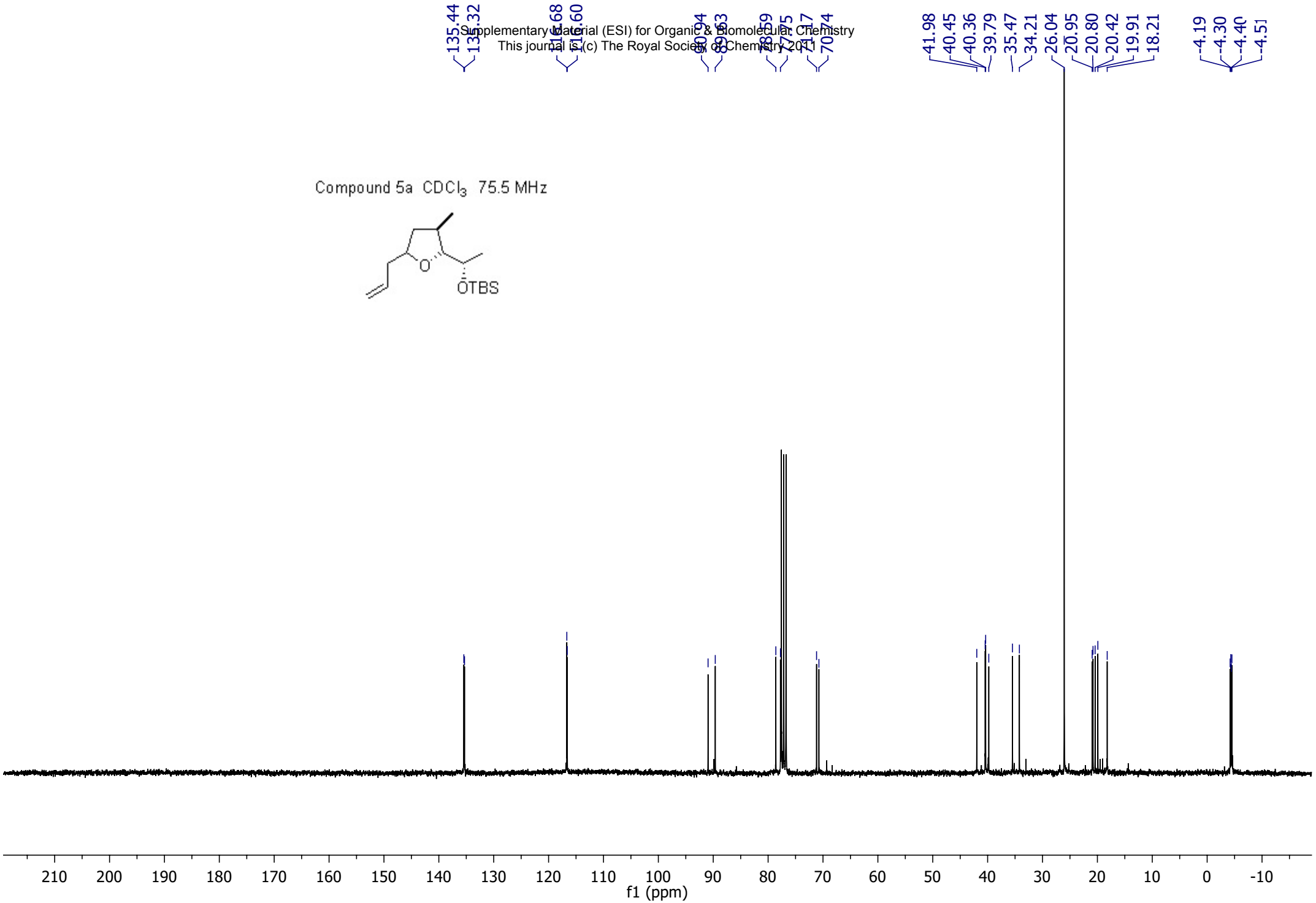


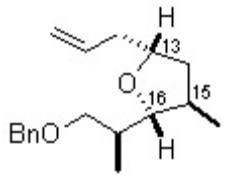
compound 4b CDCl3 200MHz



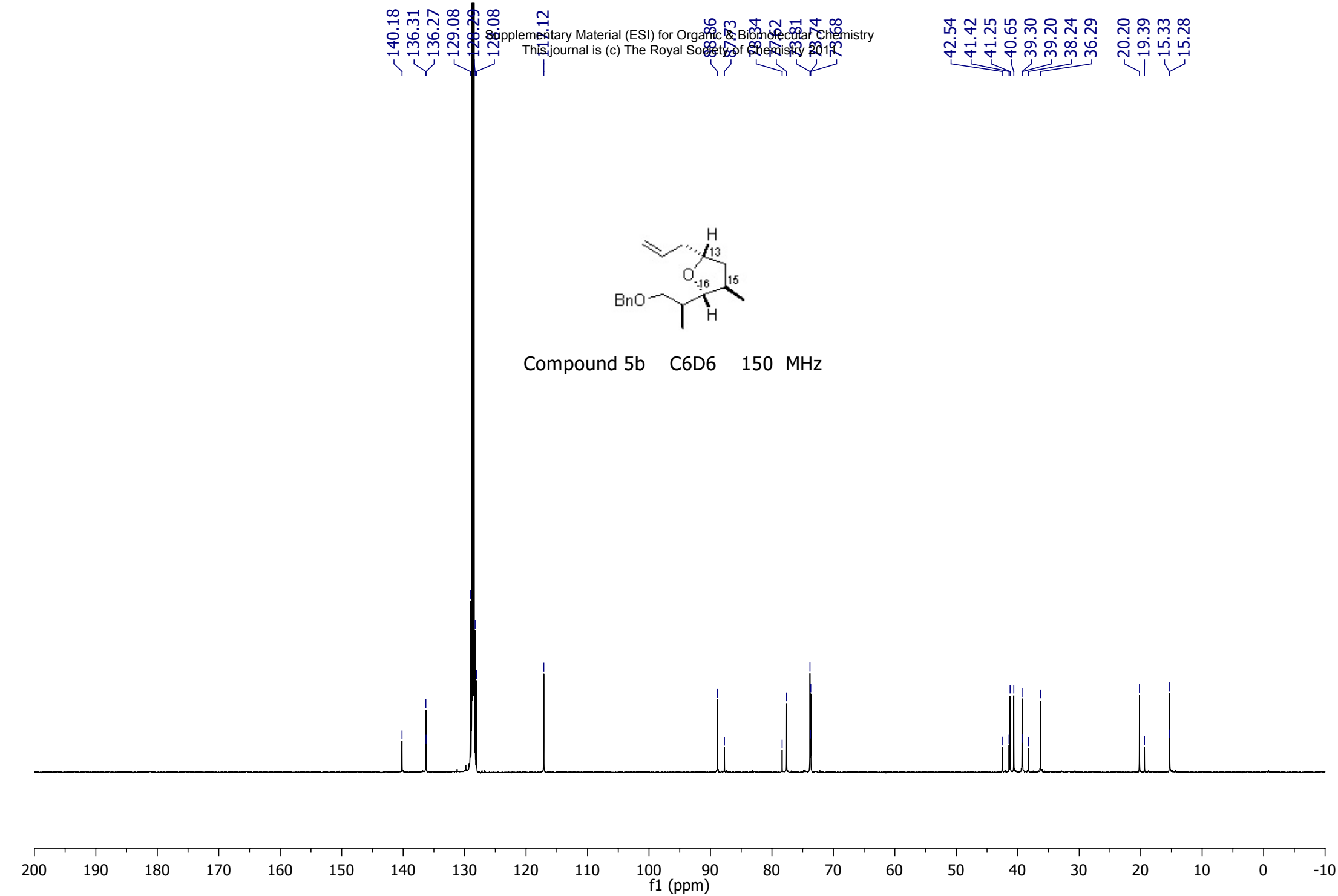
compound 4b CDCl3 52.5 MHz

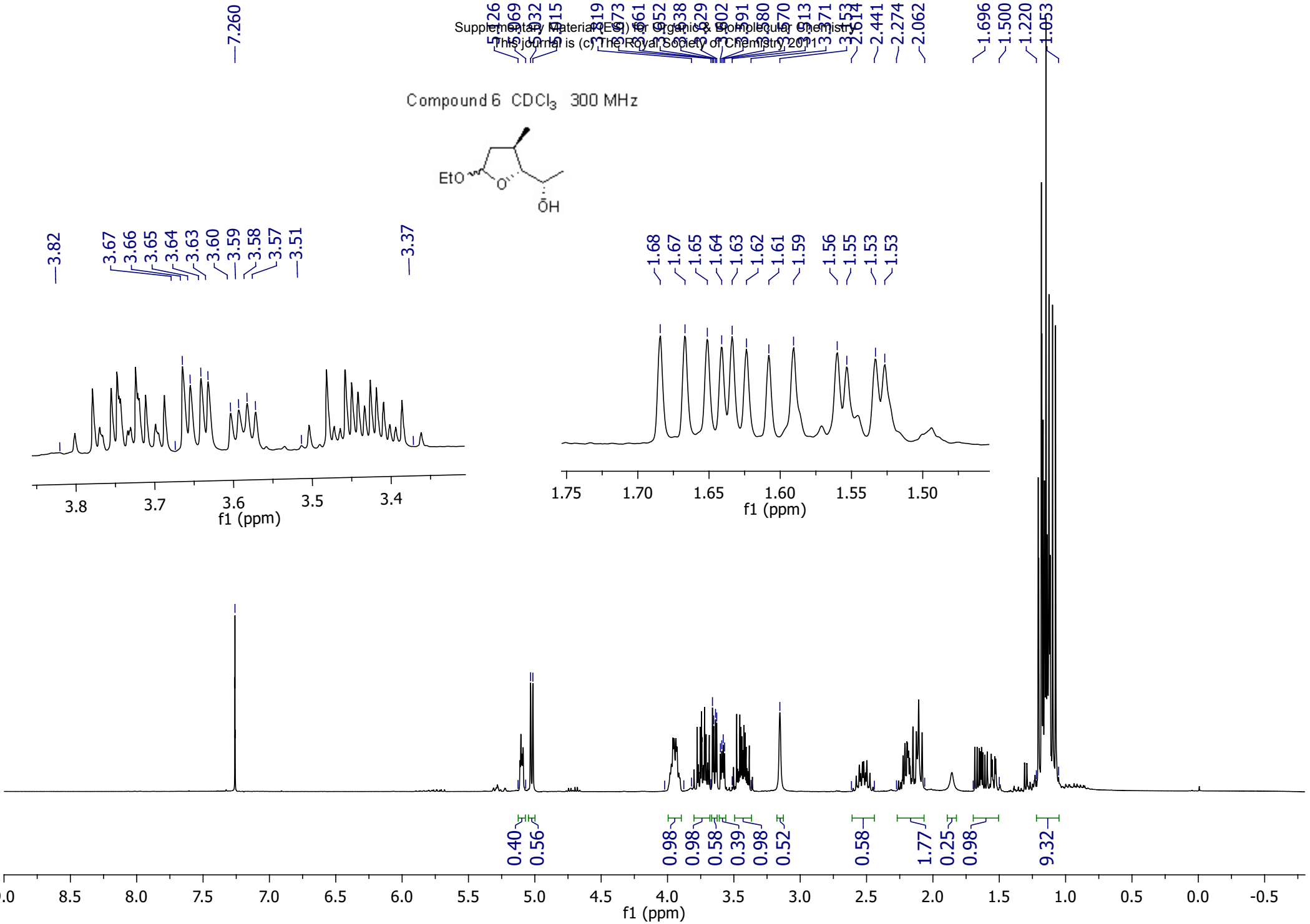






Compound 5b C6D6 600 MHz





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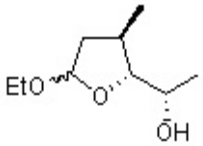
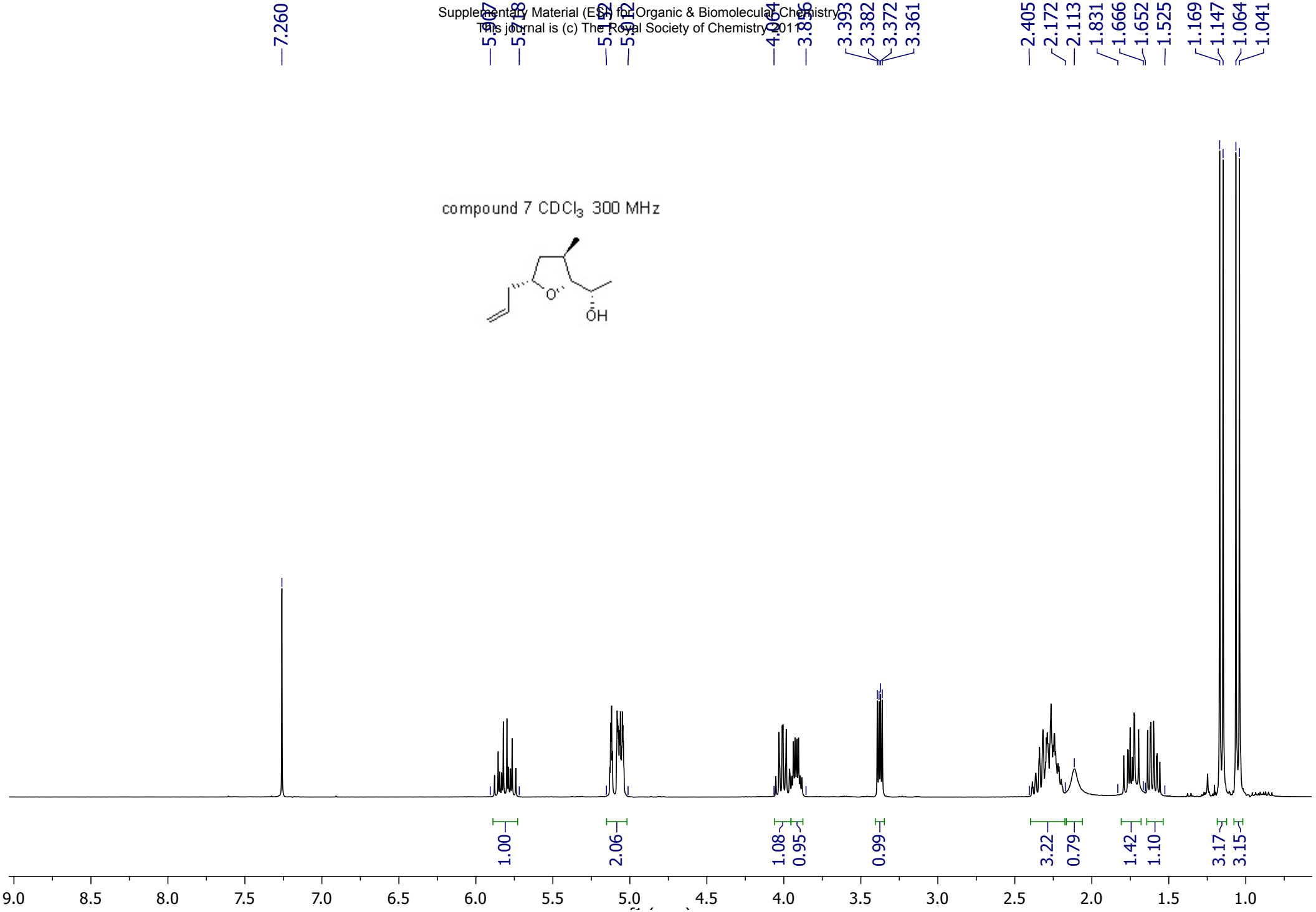
Compound 6 $CDCl_3$ 75.5 MHz





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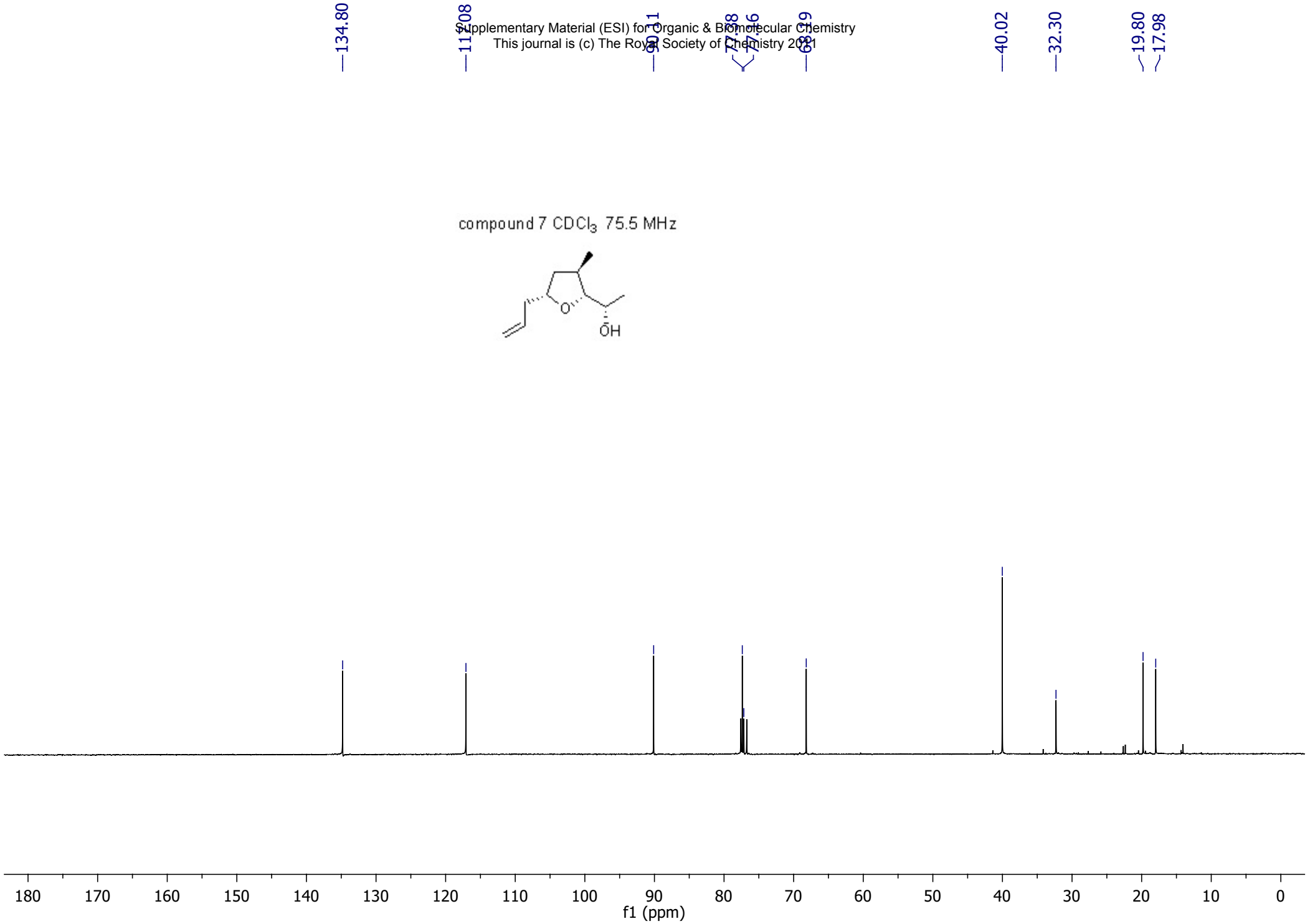
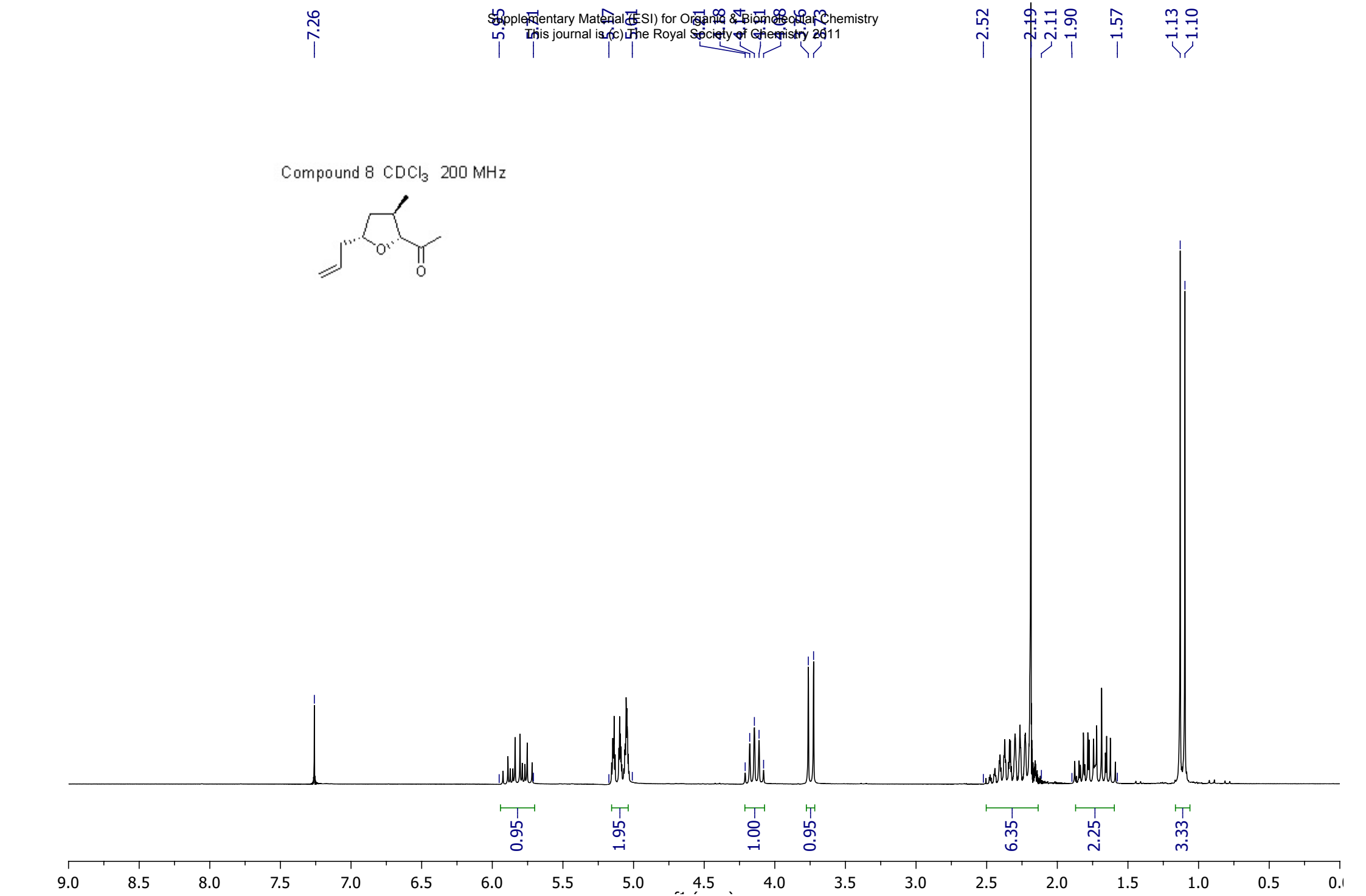
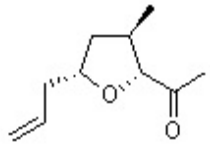
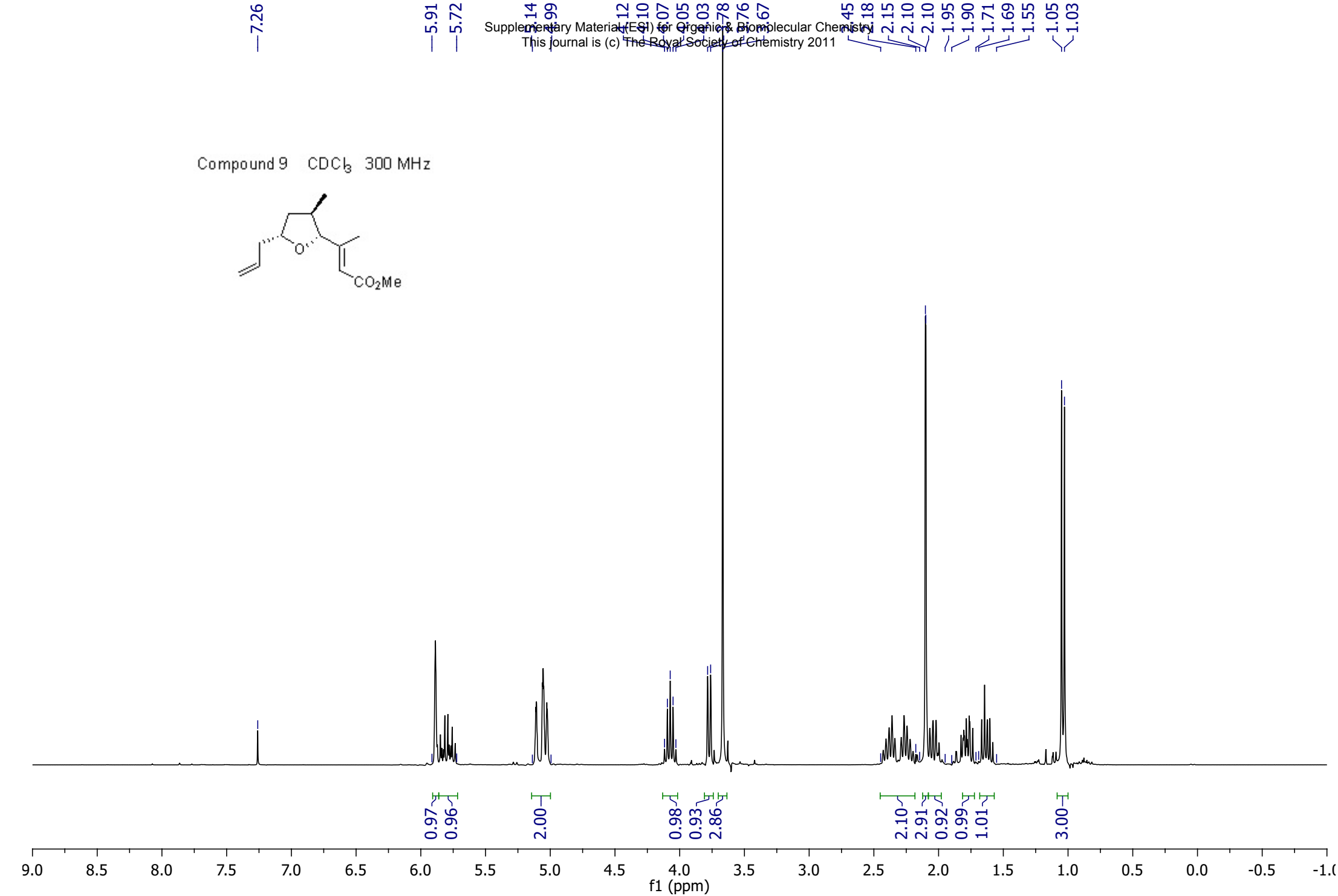




Compound 8 $CDCl_3$ 52.5 MHz





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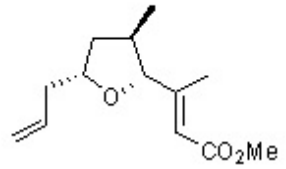
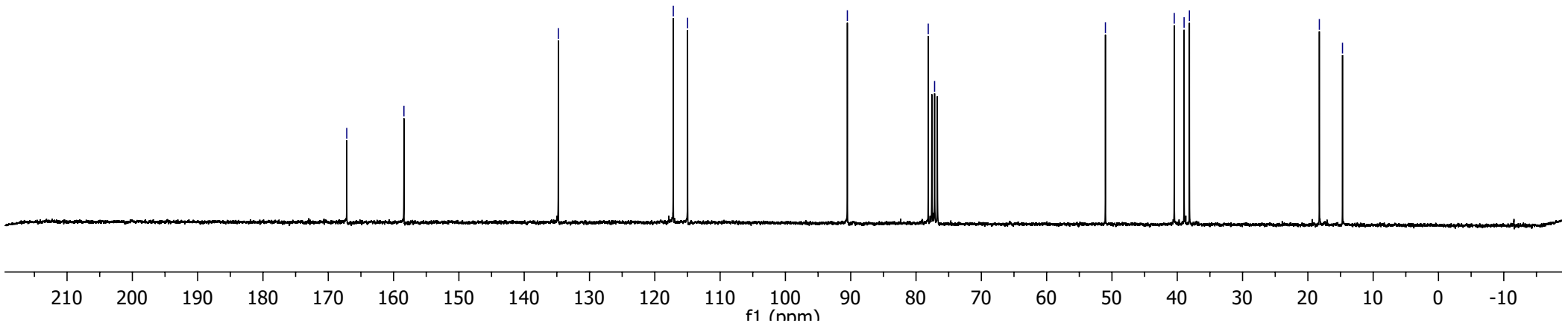
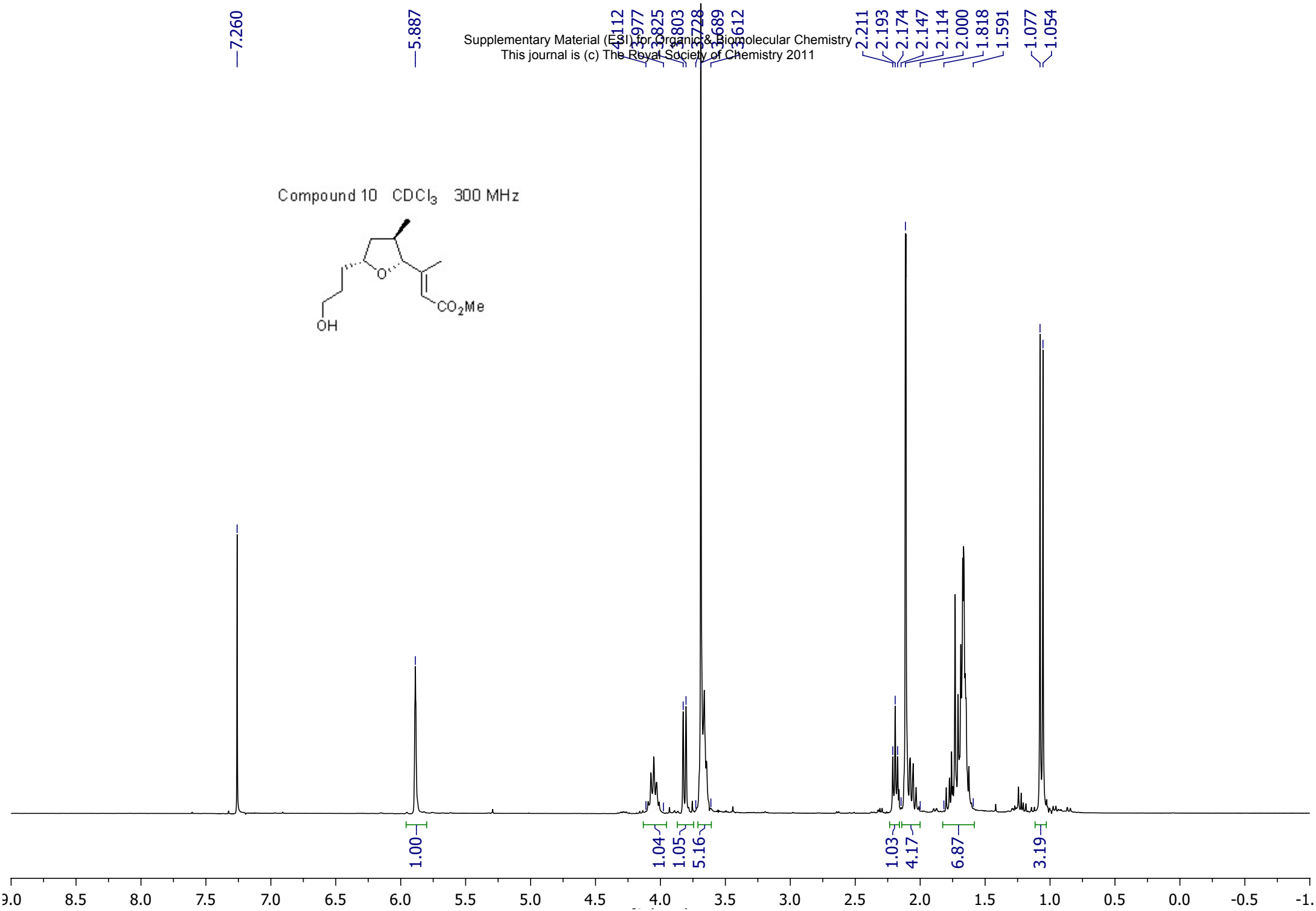
167.17
158.42
134.77
117.77
114.88
90.52
78.13
77.15
51.00
40.46
38.95
38.14
18.24
14.70

Compound 9 $CDCl_3$ 75.5 MHz







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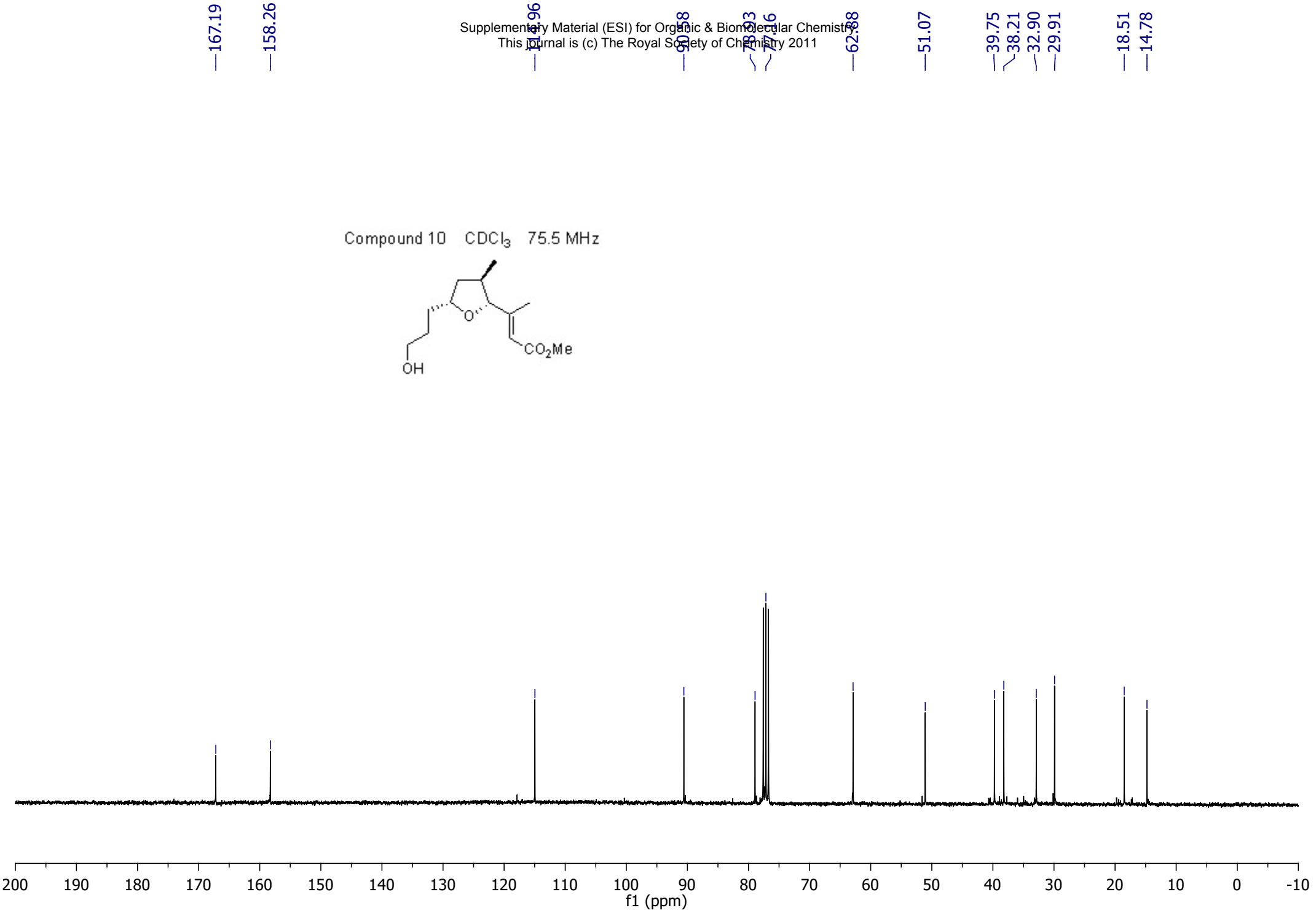

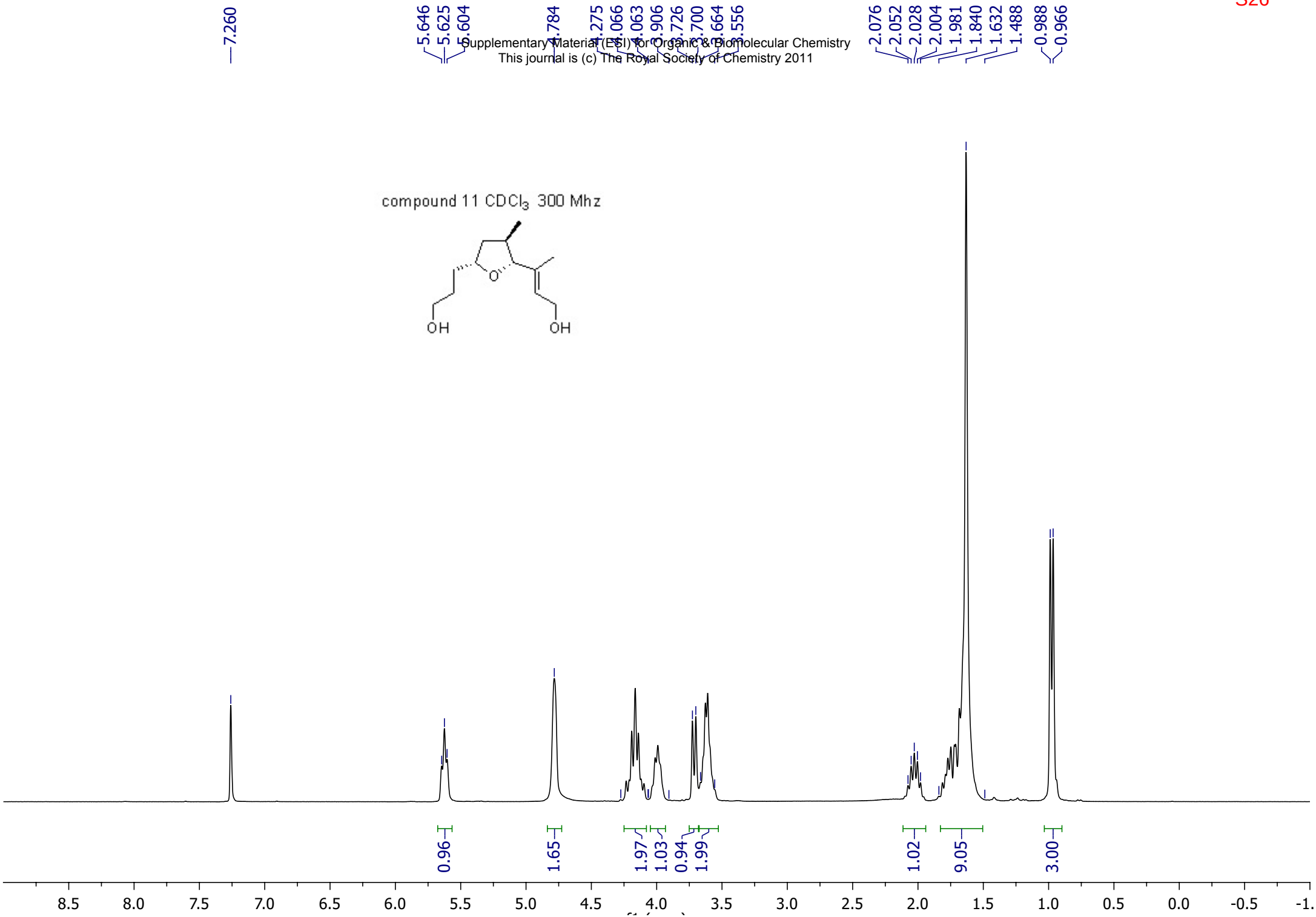

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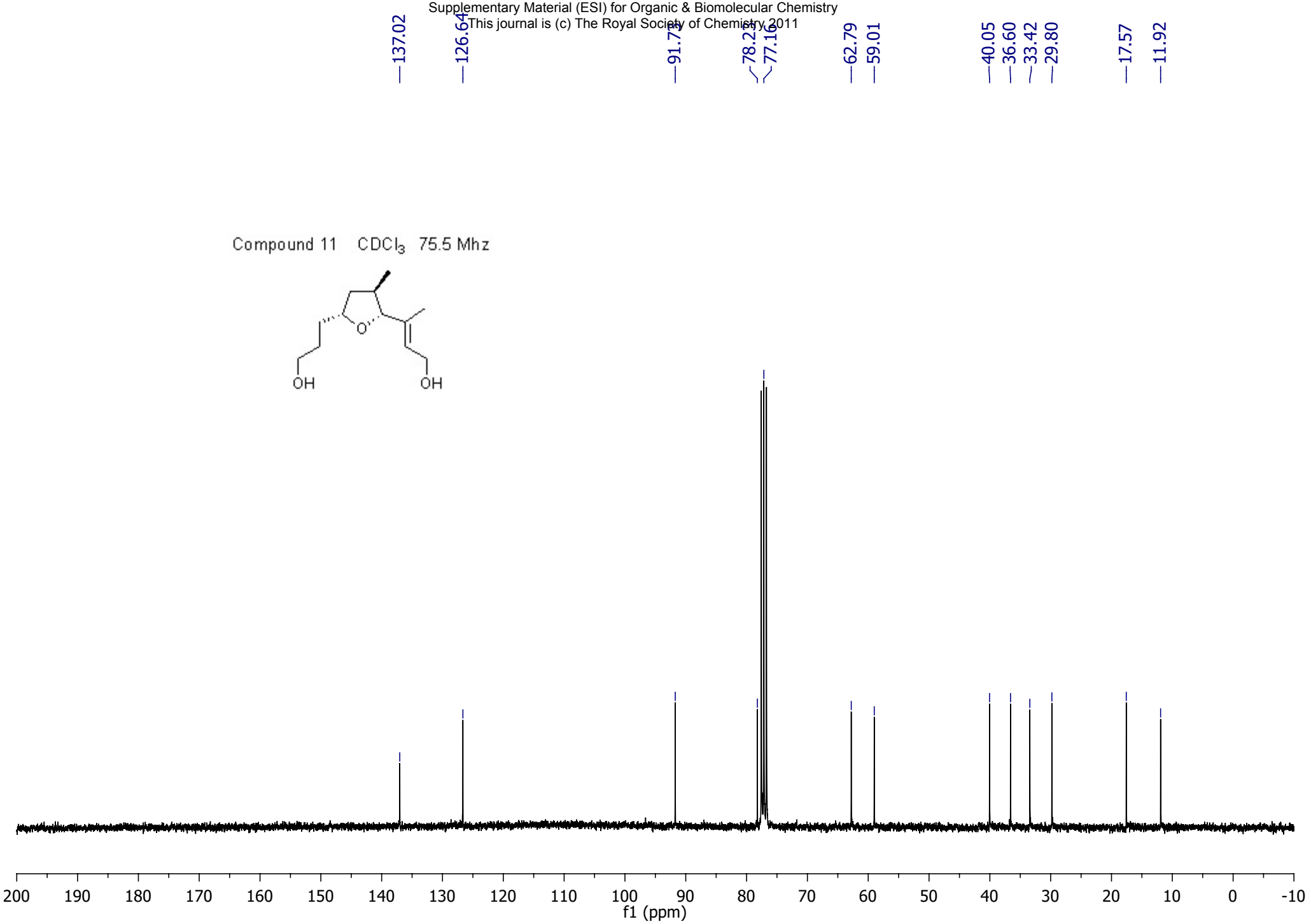

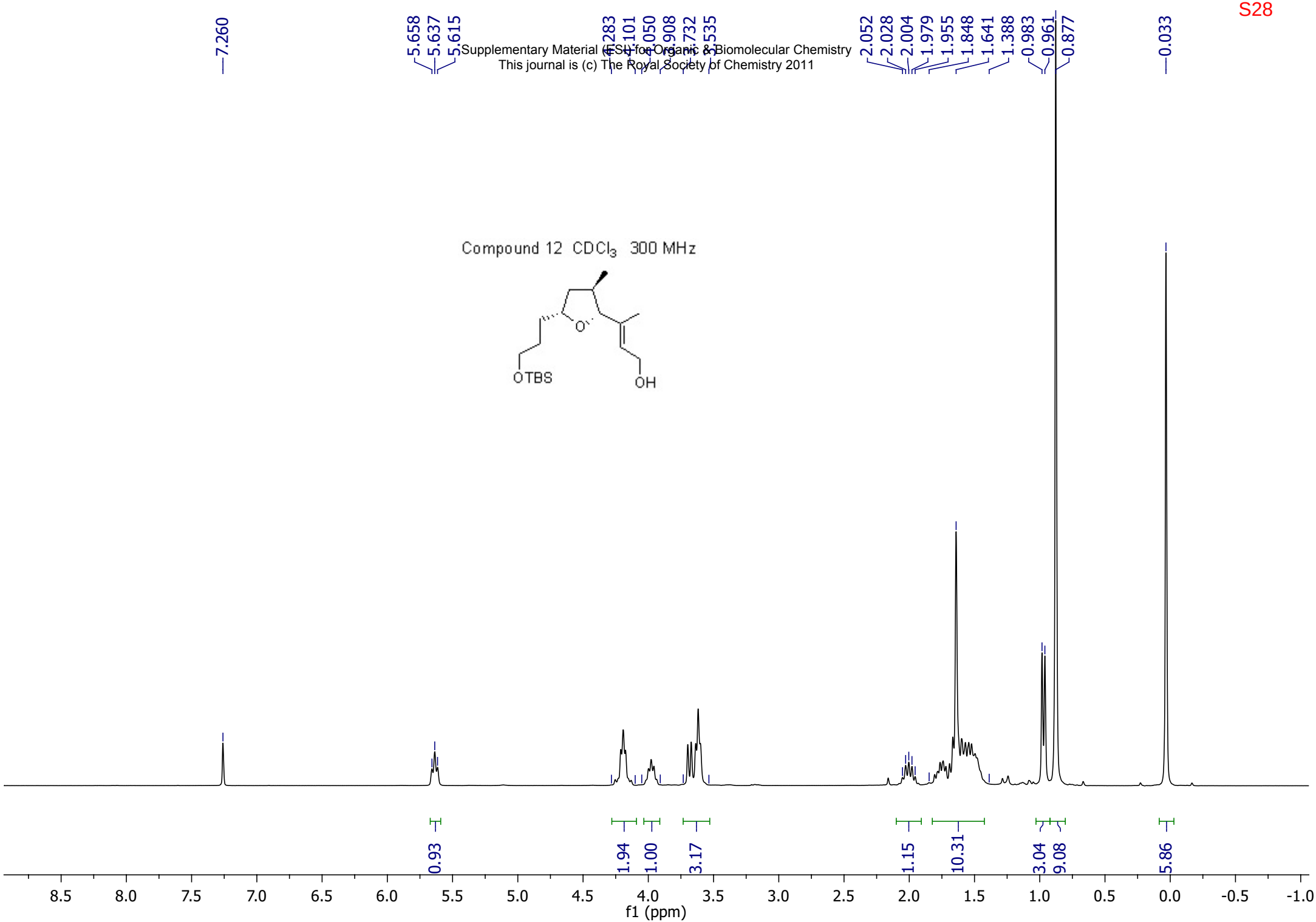

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