Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Structure-enantioselectivity effects in 3,4-dihydropyrimido[2,1-*b*]benzothiazole-based enantioselective acylation catalysts

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I Experimental Procedures and Analytical Data

I.1. General Information

All reactions involving moisture sensitive reagents were performed under inert atmosphere *via* standard vacuum line techniques and with freshly dried solvents. All glassware was flame dried and allowed to cool under vacuum. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under an inert atmosphere or obtained dry from a solvent purification system (MBraun, SPS-800). Dichloromethane (CH_2Cl_2) was obtained dry from a solvent purification system (MBraun, SPS-800). Acetonitrile (MeCN) was distilled on calcium hydride under an inert atmosphere. Petrol is defined as petroleum ether 40-60 ˚C. All solvents and commercial reagents were used as supplied without further purification unless stated otherwise. Room temperature refers to 20-25 ˚C. Temperatures of 0 ˚C were obtained using an ice/water bath and reaction reflux conditions using an oil bath equipped with a contact thermometer. Lower temperatures were obtained using an immersion cooler. *In vacuo* refers to the use of a rotary evaporator.

Analytical thin layer chromatography was performed on aluminium sheets coated with 60 F_{254} silica. TLC visualisation was carried out with ultraviolet light (254 nm), followed by staining 1% aqueous $KMnO_4$ solution. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated.

^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were acquired at either δ_H (300 MHz or 400MHz) or δ_c (75 MHz or 100MHz) at ambient temperature and in the deuterated solvent stated. Coupling constants (*J*) are reported in Hz. Data are expressed in chemical shifts in parts per million (ppm) relative to residual solvent as internal standard. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintuplet) and m (multiplet). The abbreviation Ar is used to denote aromatic, br to denote broad and app. to denote apparent.

Infrared spectra (ν_{max}) were recorded using either thin films on NaCl plates or KBr discs as stated. Only the characteristic peaks are quoted. Melting points were recorded on an electrothermal apparatus and are uncorrected.

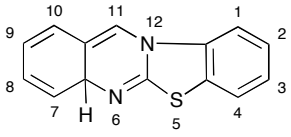
Mass spectrometric (*m/z*) data was acquired by electrospray ionisation (ESI), electron impact (EI), nano-electrospray ionisation (NSI) or chemical ionisation (CI), either at the University of St Andrews Mass Spectrometry Facility (quoted [M+H]) or from the EPSRC National Mass Spectrometry Service Centre, Swansea (quoted $[M+H]^+$).

Optical rotations were measured on a digital polarimeter operating at the sodium D line with a 100 mm path cell.

^1H NMR spectroscopic data for esters **47, 55, 58, 60, 61** and **56** were consistent with those previously reported in the literature (see scheme 2 for references).

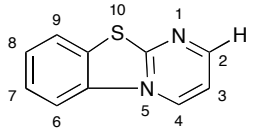
Nomenclature used in this paper:

Parent Heterocycle Skeleton



6a*H*-benzothiazolo[2,3-*b*]quinazoline

Parent Heterocycle Skeleton



2H-pyrimido[2,1-*b*]benzothiazole

I.1.a. Proof of Absolute stereochemistry

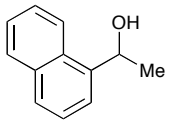
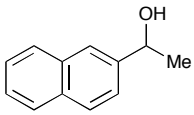
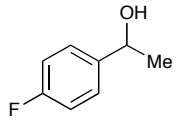
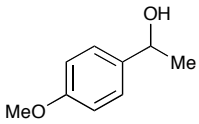
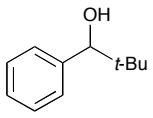
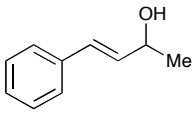
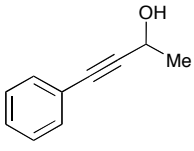
Substrate	HPLC condition % *i*PrOH/Hex (1 mL/min)	Retention time		Rotation sign	Absolute configu-ration	References
		Major (*S*)	Minor (*R*)			
 **46**	ODH- 10%	9.92	16.08	**(-)** $[\alpha]_D^{20}$ = - 64.0 (*c* 1.0 in $CHCl_3$) ee > 99 %	*S*	$[\alpha]_D^{20}$ = -54.8[1] (*S*) (*c* 3.3 in $CHCl_3$) ee = 86 %
 **48**	-	-	-	**(-)** $[\alpha]_D^{20}$ = - 53.0 (*c* 0.4 in $CHCl_3$) ee >99 %	*S*	$[\alpha]_D^{20}$ = + 46.0[2] (*R*) (*c* 1.0 in $CHCl_3$) ee = 92 %
 **50**	ASH-1.5% flow 0.5 mL/min	51.53	43.34	**(-)** $[\alpha]_D^{20}$ = - 37.0 (*c* 0.5 in $CHCl_3$) ee= 74.0 %	*S*	$[\alpha]_D^{20}$ = + 39.0[1] *(R)* (*c* 1.2 in $CHCl_3$) ee= 89.0 %
 **51**	ODH-3%	19.76	17.38	**(-)** $[\alpha]_D^{20}$ = - 33.0 (*c* 1.3 in $CHCl_3$) ee= 65.0 %	*S*	$[\alpha]_D^{20}$ = - 41.9[3] (*S)* (*c* 1.1 in $CHCl_3$) ee= 75.0 %
 **52**	ODH- 15%	4.70	5.96	**(-)** $[\alpha]_D^{20}$ = - 36.5 (*c* 0.3 in $CHCl_3$) ee > 99.0 %	*S*	$[\alpha]_D^{20}$ = - 22.9[4] (*S*) (*c* 2.3 in $CHCl_3$) ee= 86.0 %
 **53**	ODH- 10%	15.31	10.07	**(-)** $[\alpha]_D^{20}$ = - 31.0 (*c* 0.5 in $CHCl_3$) ee = 95 %	*S*	$[\alpha]_D^{20}$ = -30.0[5] (*S*) (*c* 0.8 in $CHCl_3$) ee= 92.0%
 **54**	ODH- 15%	11.33	5.89	**(-)** $[\alpha]_D^{20}$ = - 30.0 (*c* 0.7 in $CHCl_3$) ee > 99 %	*S*	$[\alpha]_D^{20}$ = + 34.8[6] (*R*) (*c* 0.4 in $CHCl_3$) ee= 94.0 %

Table 1: The absolute configuration of the unreacted alcohol obtained by kinetic resolution was assigned by comparison of the sign of optical rotation with the literature data.

[1] M. Locatelli and P. G. Cozzi., *Angew. Chem. Int. Ed*., **2003**, *42,* 4928-4930
[2] Y. Ma, H. Liu, L. Chen, X. Cui, J. Zhu and J. Deng, *Org. Lett*., **2003**, *5*, 2103-2106
[3] A. J. M. Janssen, A. J. H. Klunder and B. Zwanenburg, *Tetrahedron*, **1991** *47*, 7645-7662
[4] T. Sato, Y. Goto and T. Fujisawa, *Tetrahedron Lett.,* **1982**, *23*, 4111-4112
[5] E. Brenna, C. Fuganti, F. G. Gatti, M. Passoni, S. Serra, *Tetrahedron: Asymmetry*, **2003**, *14*, 2401-2406
[6] Y.Nakamura, H. Egami, K. Matsumoto, T. Uchida and T. Katsuki, *Tetrahedron. Lett.,* **2007**, *63*, 6383-6387

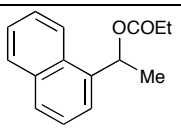
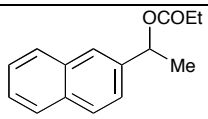
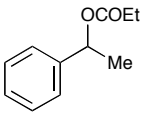
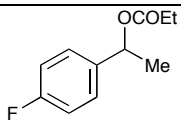
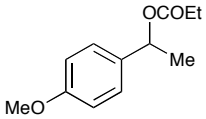
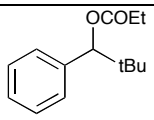
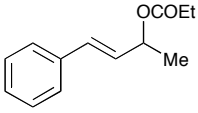
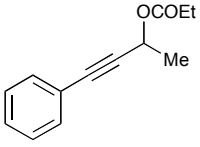
Substrate	Rotation Sign	ee (%)	Absolute configuration
 **47**[1]	$[\alpha]_D^{20} = +55.38$ (c 0.7 in $CHCl_3$)	74	*R*
 **55**[1]	$[\alpha]_D^{20} = +71.19$ (c 0.6 in $CHCl_3$)	67	*R*
 **58**[1]	$[\alpha]_D^{20} = +79.10$ (c 0.7 in $CHCl_3$) lit[2] $[\alpha]_D^{20} = +101.0$ (c 1.00 in Et_2O) ee > 95%}	73	*R*
 **59**	$[\alpha]_D^{20} = +76.36$ (c 0.3 in $CHCl_3$)	76	*R*
 **62**[3]	$[\alpha]_D^{20} = +69.06$ (c 0.6 in $CHCl_3$)	84	*R*
 **60**[1]	$[\alpha]_D^{20} = +57.97$ (c 0.6 in $CHCl_3$)	99	*R*
 **61**[1]	$[\alpha]_D^{20} = +70.00$ (c 0.6 in $CHCl_3$)	66	*R*
 **56**[4]	$[\alpha]_D^{20} = +70.00$ (c 0.6 in $CHCl_3$)	57	*R*

Table 2 : The absolute configuration of the propionate ester obtained by kinetic resolution was assigned by comparaison of the sign of the optical rotation with the literature data.

[1] V. B. Birman and |H. Jiang, *Org. Lett.,* **2005**, *16*, 3445-3447
[2] D. Bianchi, P. Cesti and E. Bettistel, *J. Org. Chem.,* **1988**, *53*, 5531-5534
[3] A. J. M. Janssen, A. J. H. Klunder and B. Zwanenburg, Tetrahedron, **1991** *47*, 7645-7662
[4] V. B. Birman; G. Lei, *Org. Lett.,* **2006**, *8*, 4859-4861

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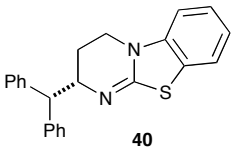

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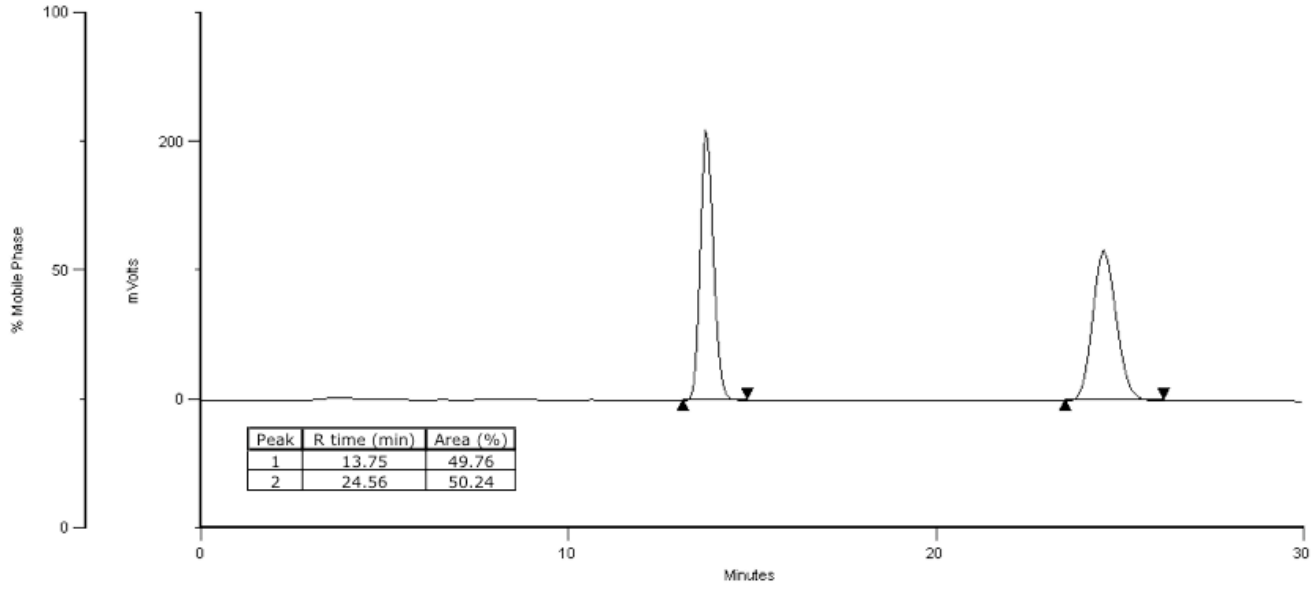
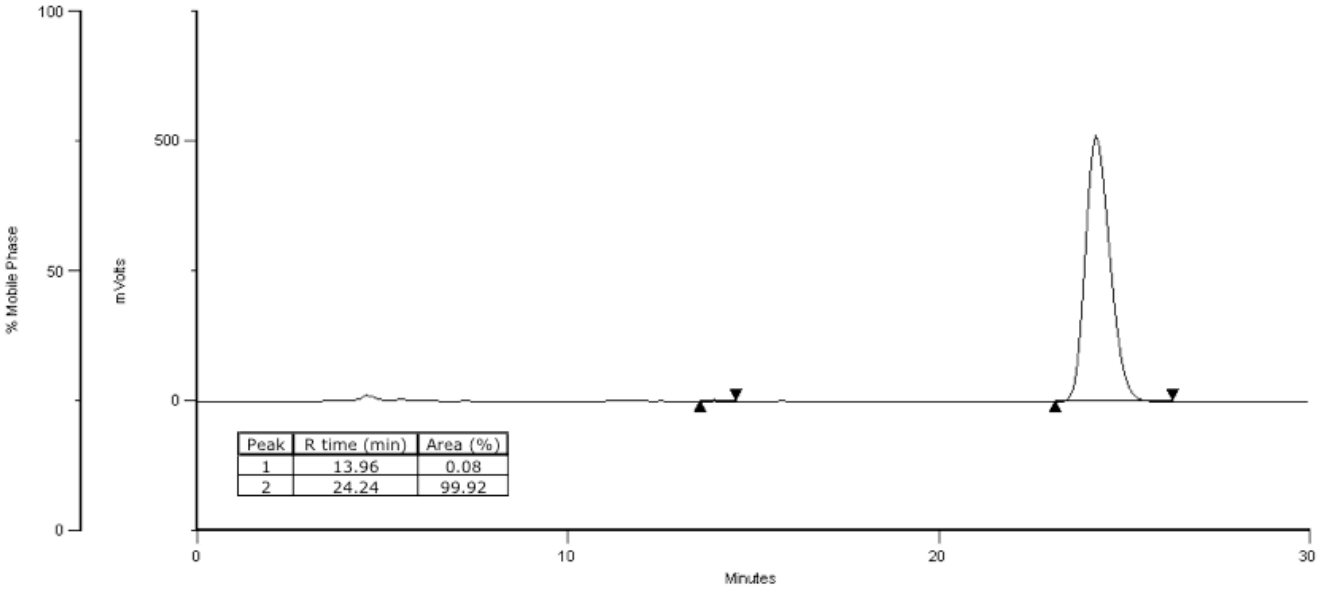
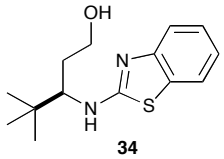


Peak	R time (min)	Area (%)
1	13.75	49.76
2	24.56	50.24



Peak	R time (min)	Area (%)
1	13.96	0.08
2	24.24	99.92



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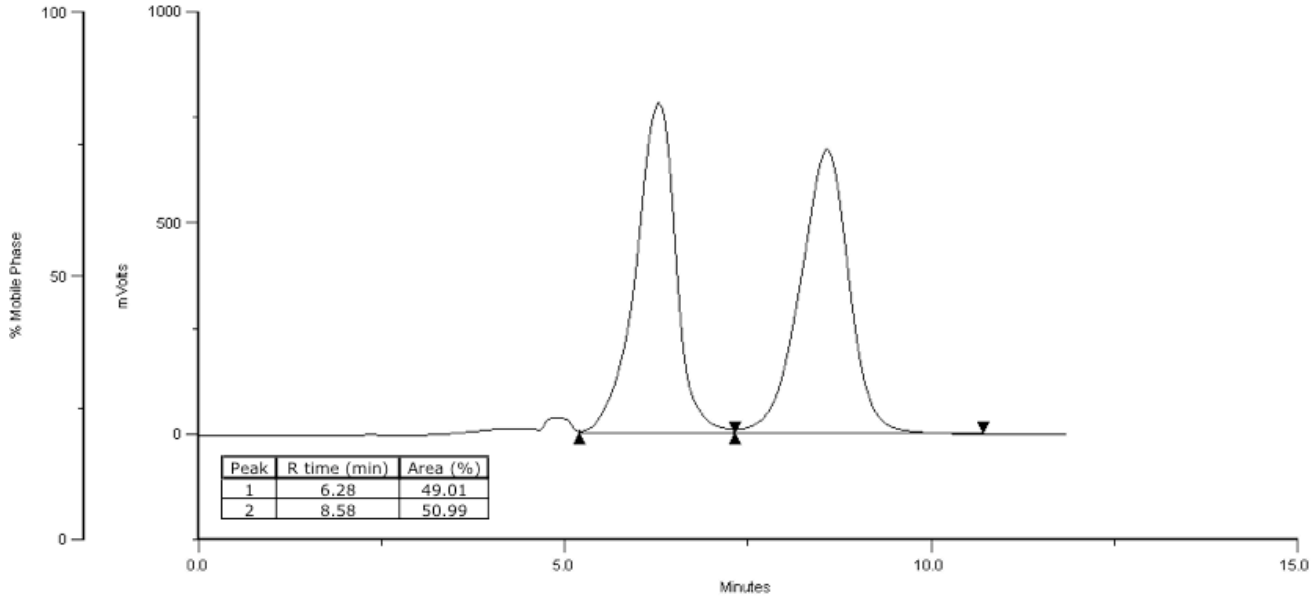
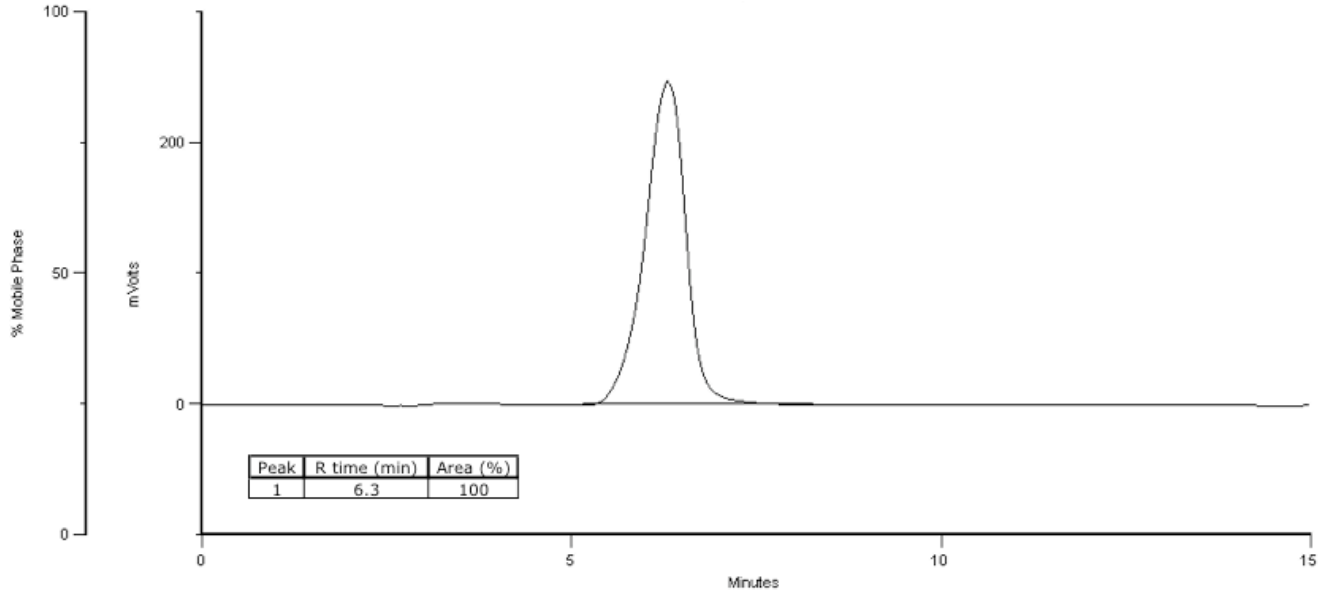
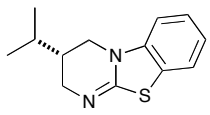


Peak	R time (min)	Area (%)
1	6.28	49.01
2	8.58	50.99



Peak	R time (min)	Area (%)
1	6.3	100



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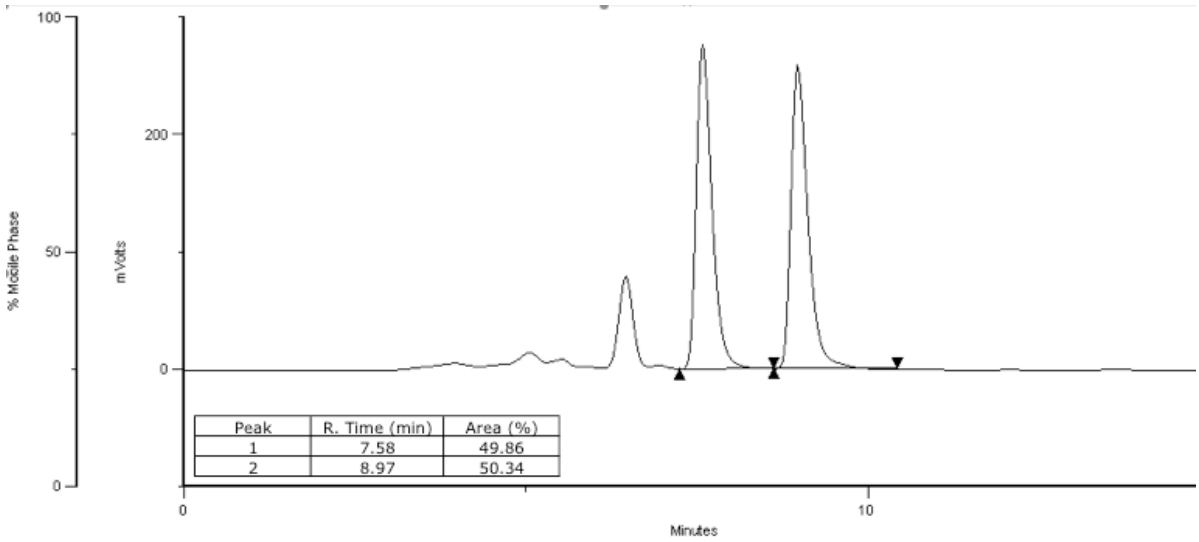
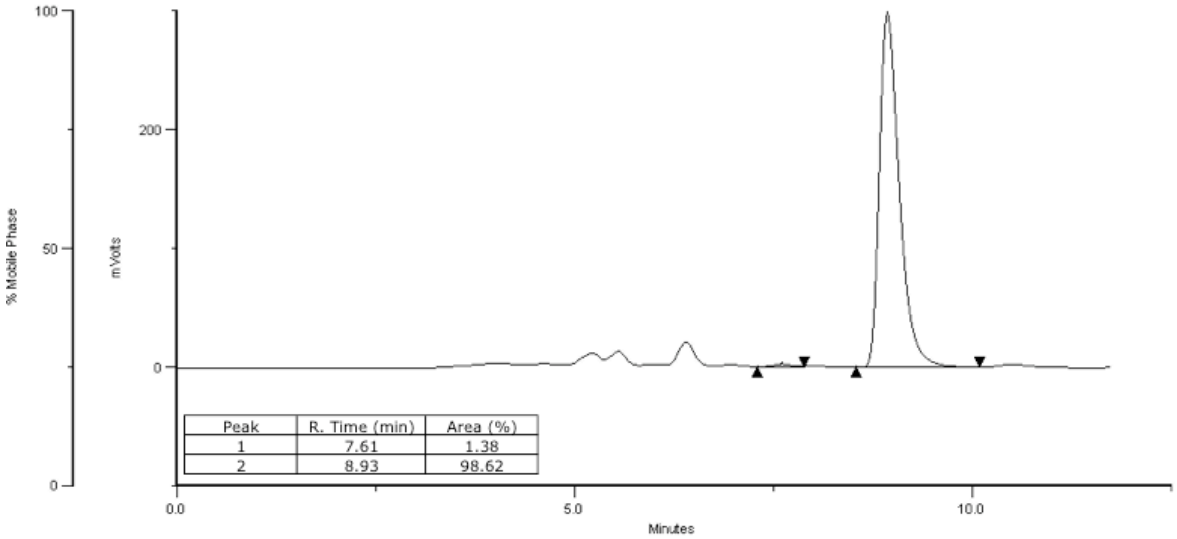
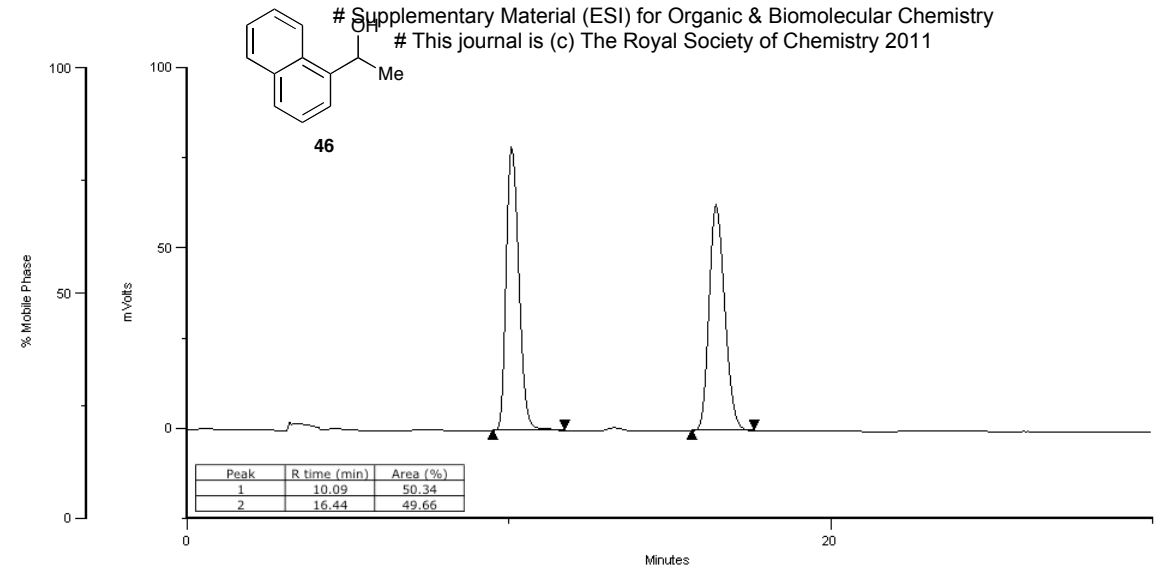
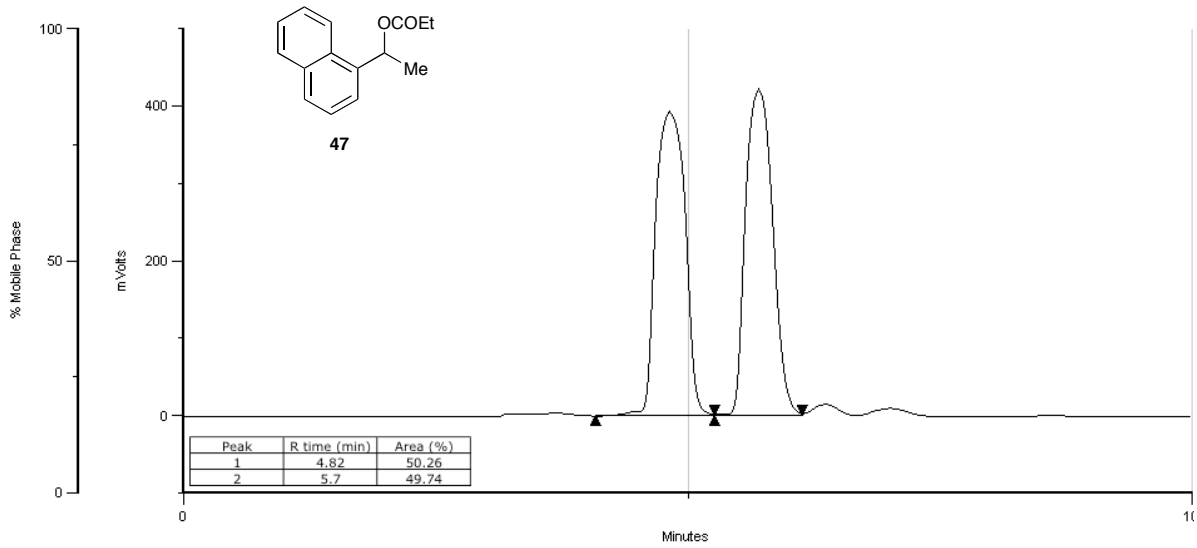


Peak	R. Time (min)	Area (%)
1	7.58	49.86
2	8.97	50.34

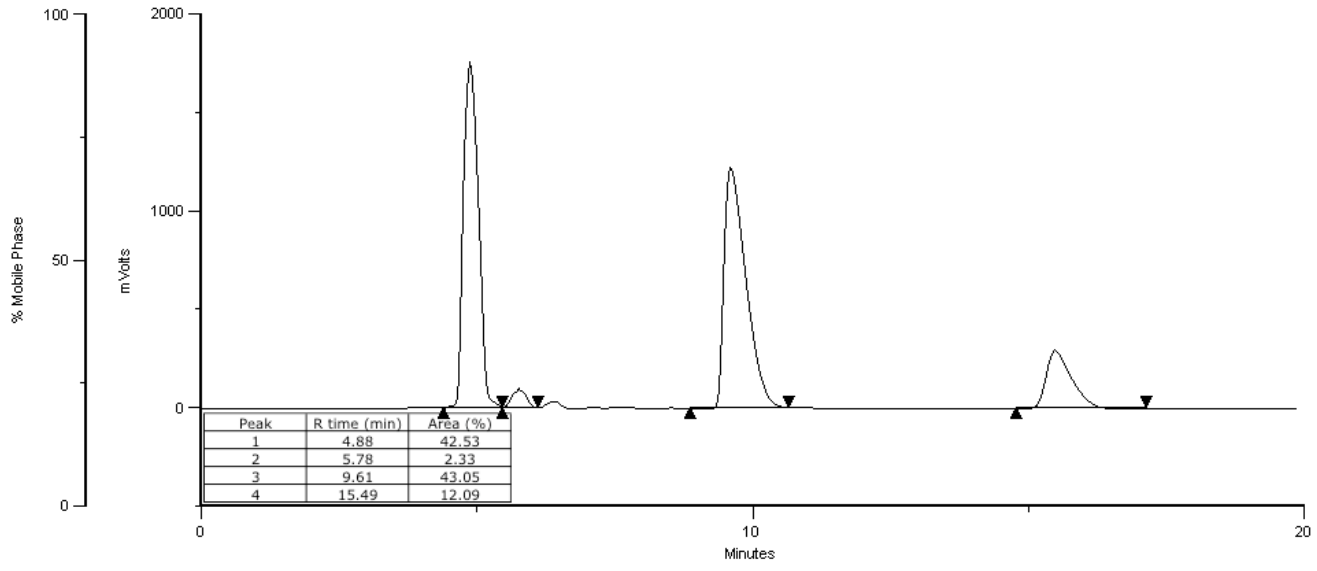


Peak	R. Time (min)	Area (%)
1	7.61	1.38
2	8.93	98.62

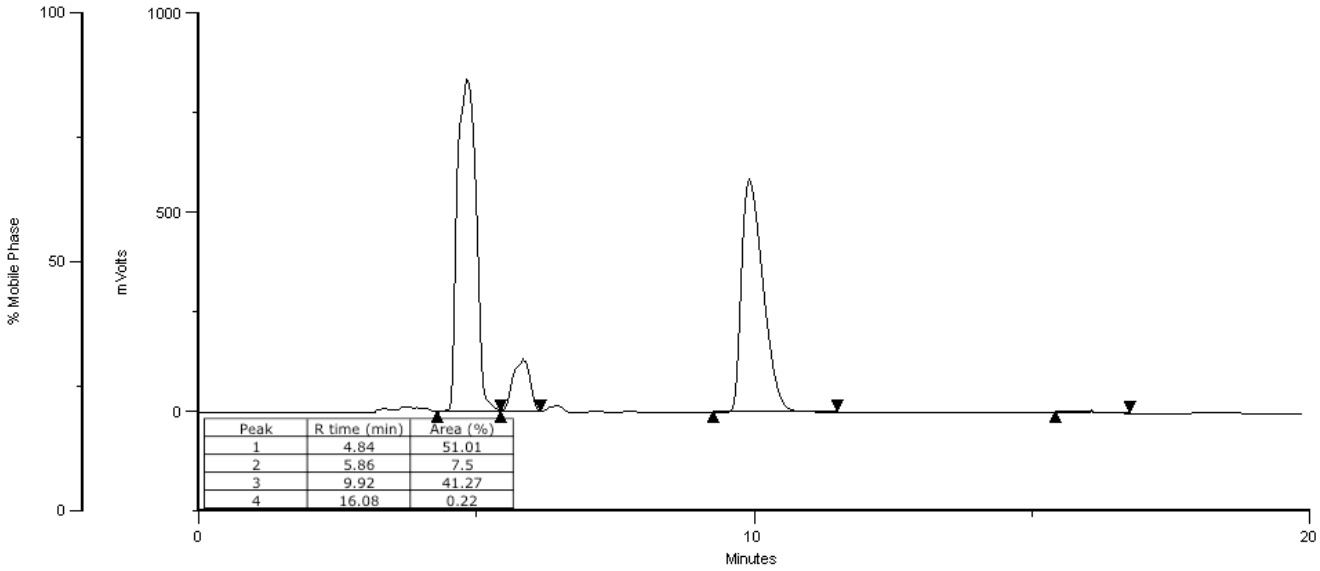




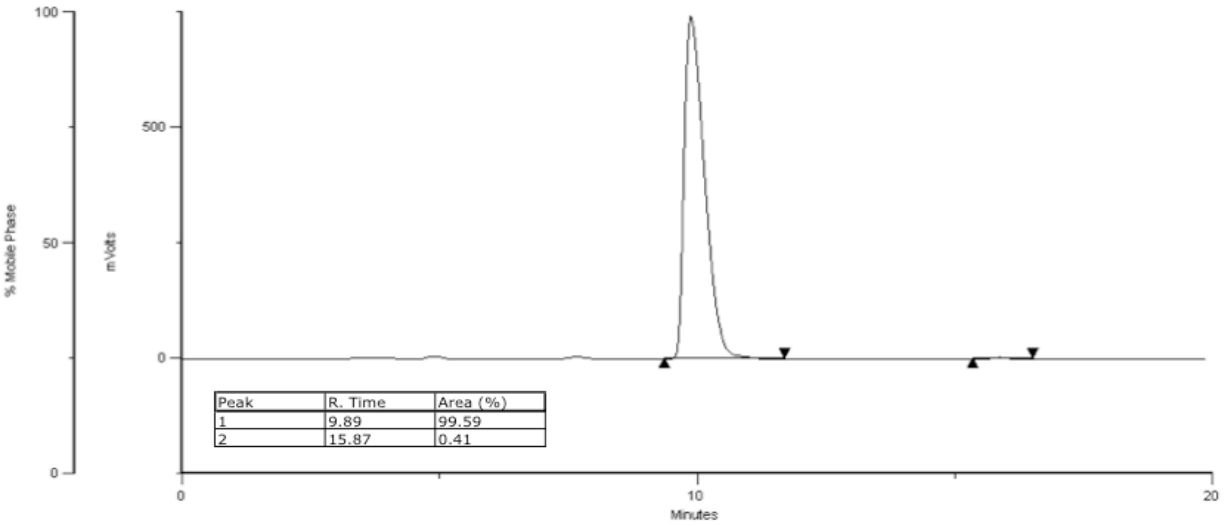
Entry 2 Table 4 : $ee_{alcohol}$ = 57 %; ee_{ester} = 91 %; c = 39; s = 38



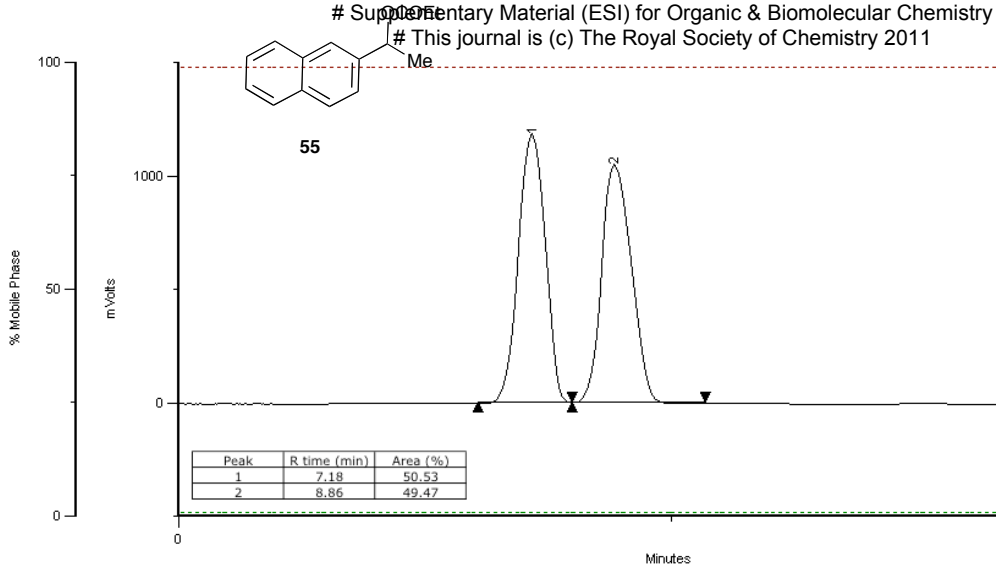
Entry 1 Table 7: $ee_{alcohol}$ > 99 %; ee_{ester} = 74 %; c = 57; s = 35



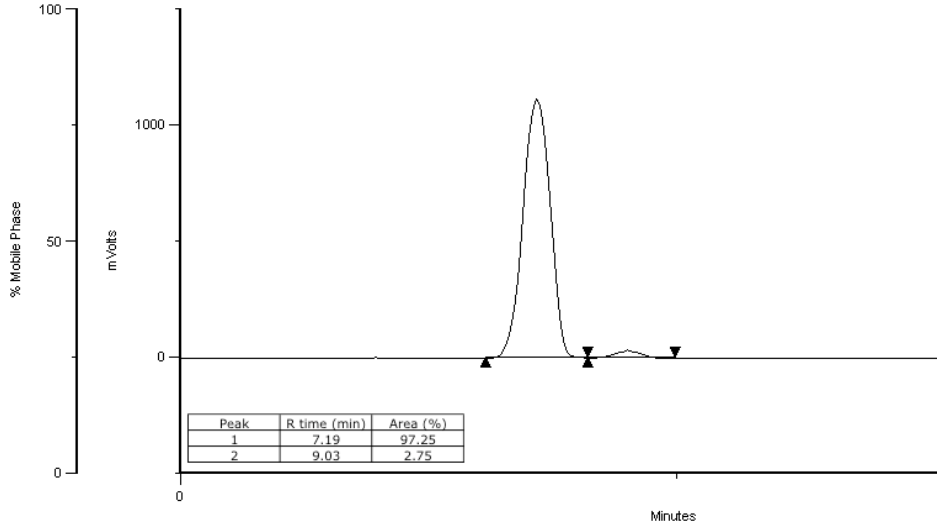
Peak	R time (min)	Area (%)
1	4.84	51.01
2	5.86	7.5
3	9.92	41.27
4	16.08	0.22

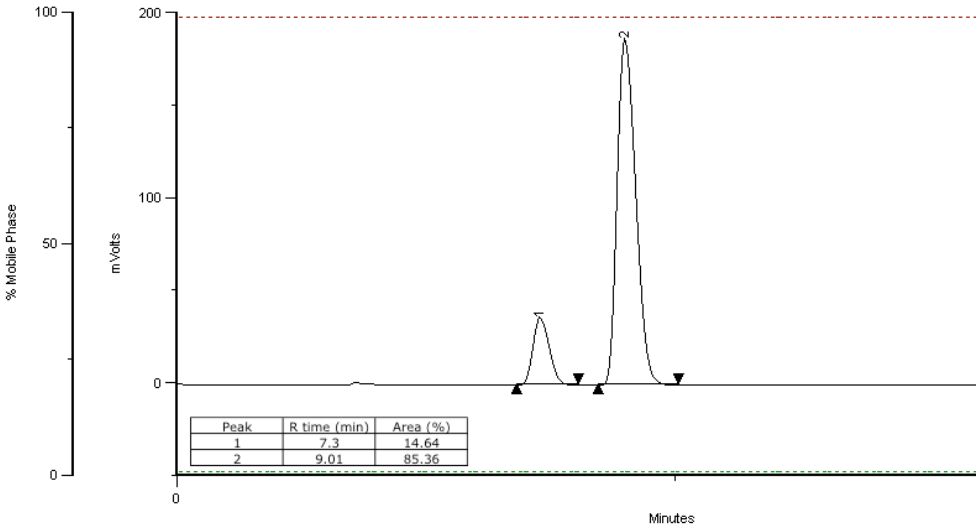


Peak	R. Time	Area (%)
1	9.89	99.59
2	15.87	0.41



Entry 4 Table 4: $ee_{alcohol} = 94\%$; $ee_{ester} = 71\%$; c = 43; s = 65





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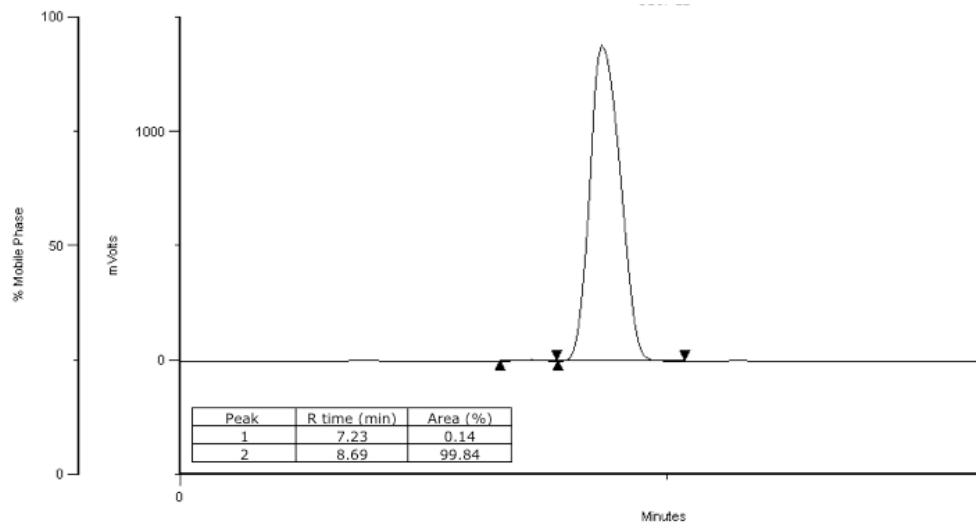
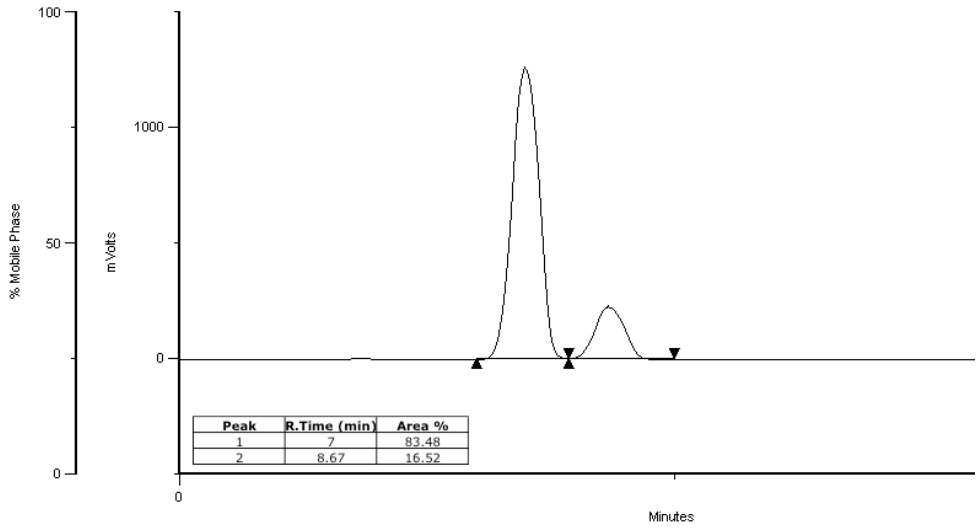
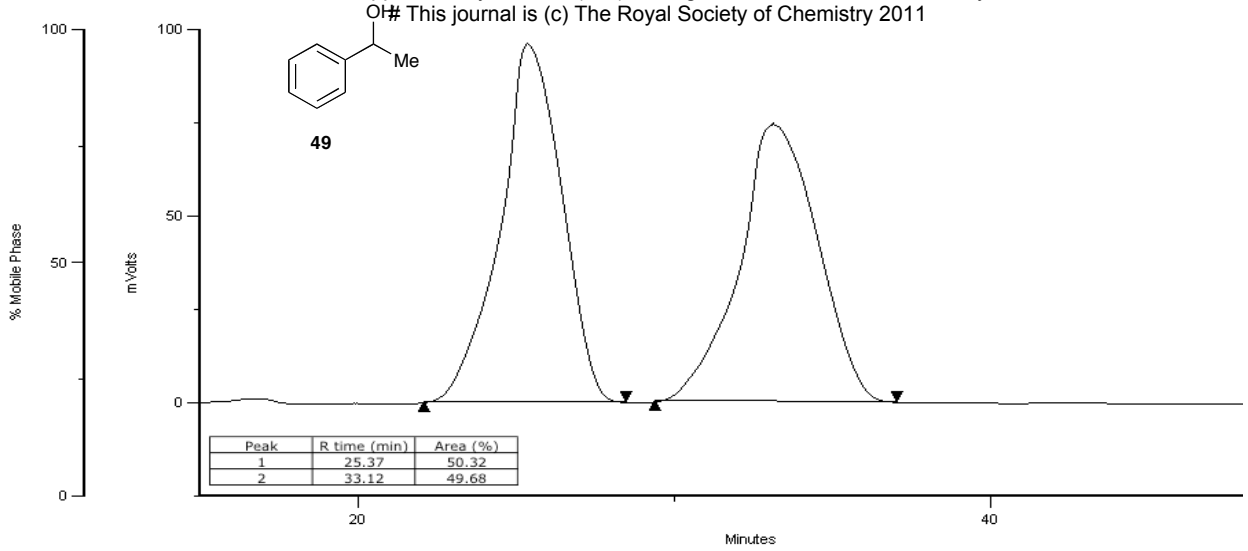
Entry 2 Table 7: $ee_{alcohol}$ > 99%; ee_{ester} = 67 %; c = 60; s = 30



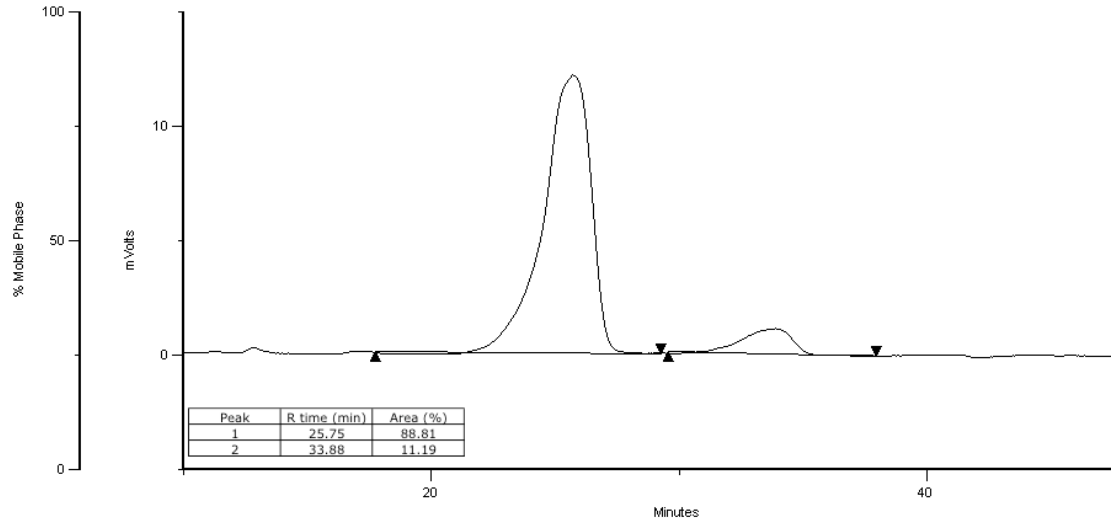
Peak	R time (min)	Area (%)
1	7.23	0.14
2	8.69	99.84

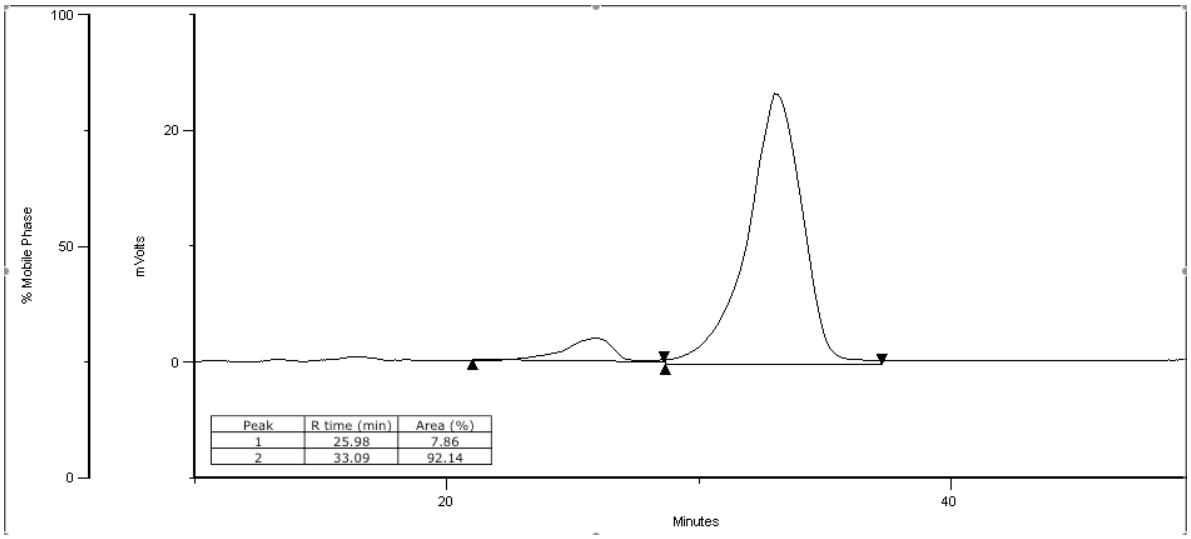


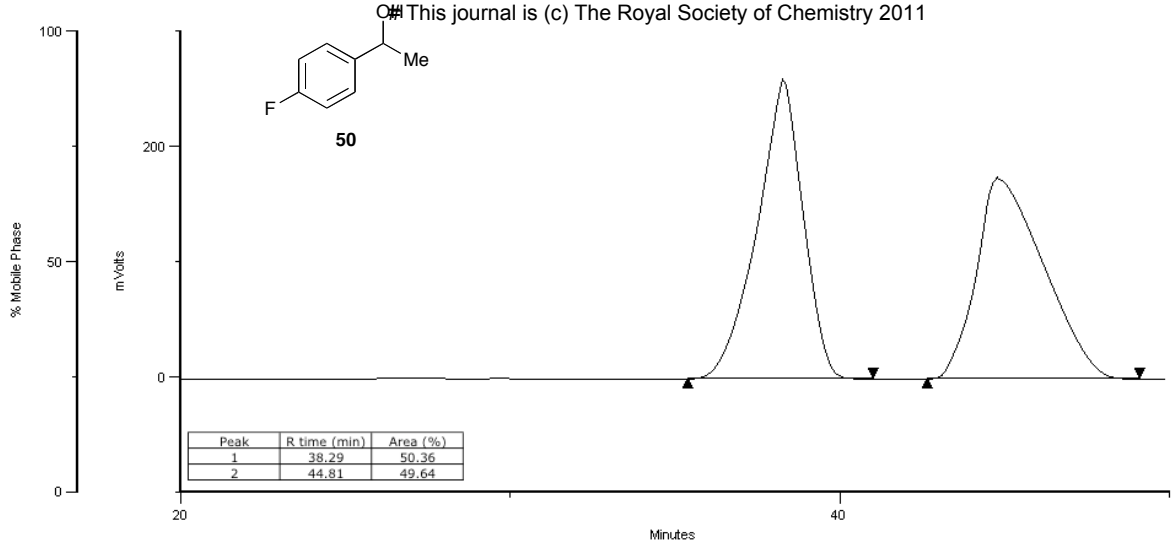
Peak	R.Time (min)	Area %
1	7	83.48
2	8.67	16.52



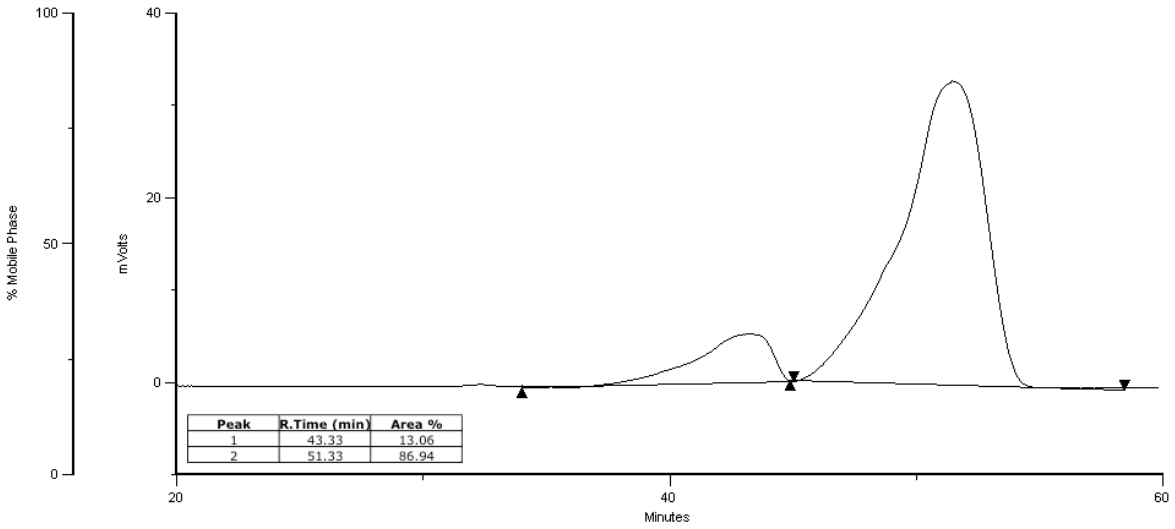
Entry 5 Table 4: $ee_{alcohol}$ = 77%; ee_{ester} = 84%; c = 52; s = 14

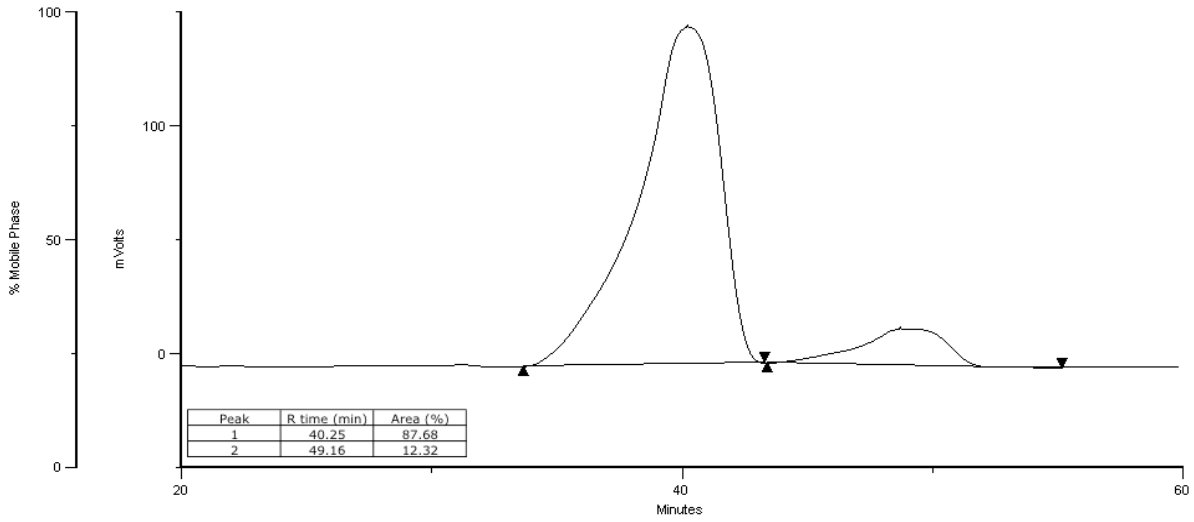


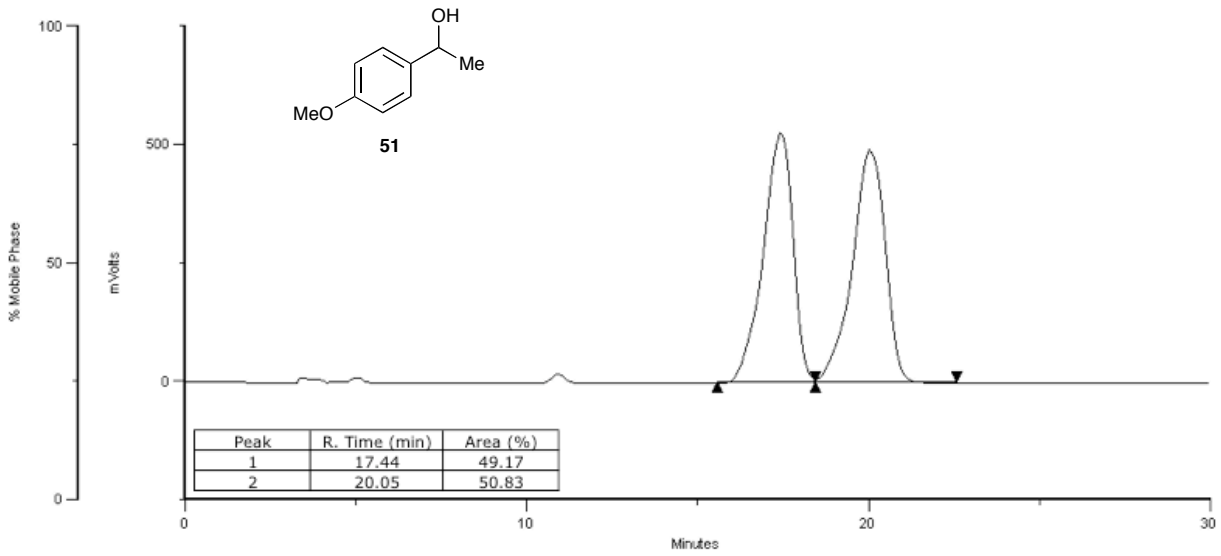




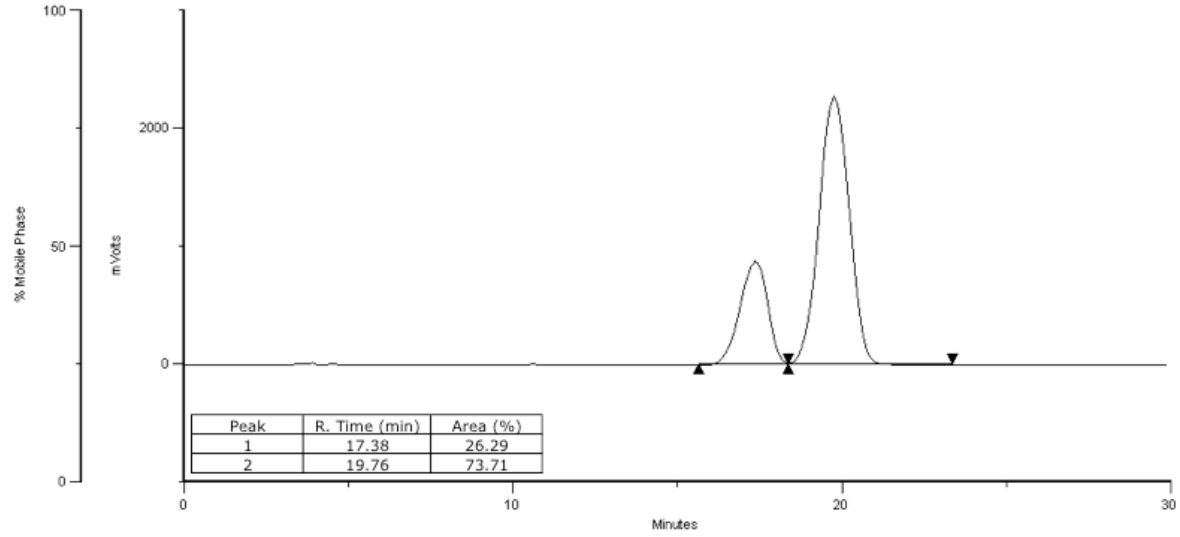
Entry 8 Table 4 : $ee_{alcohol}$= 74 %; ee_{ester} = 76 %; c = 49; s = 17

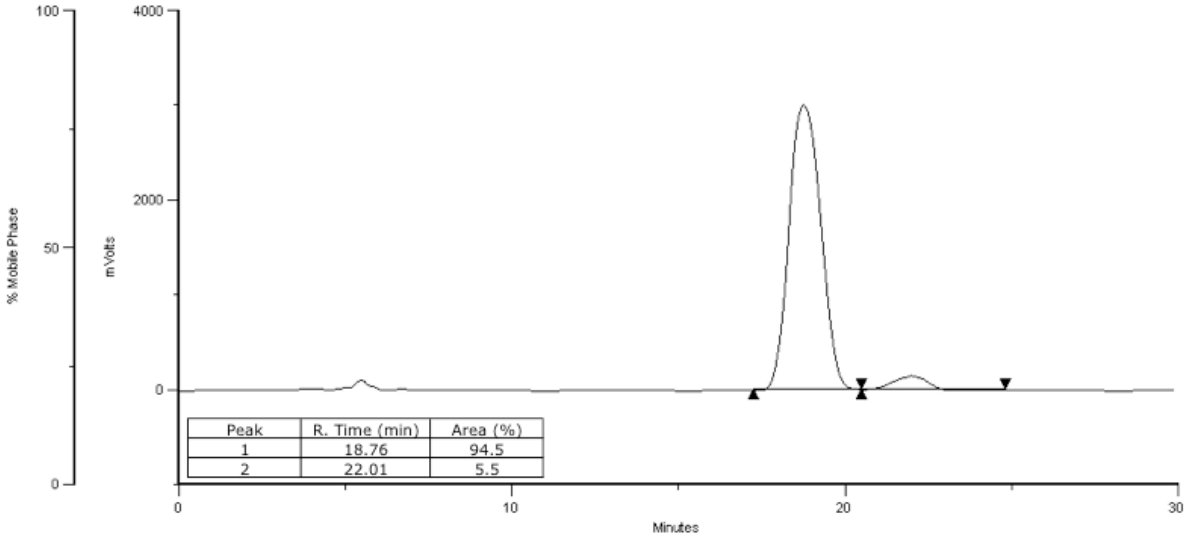


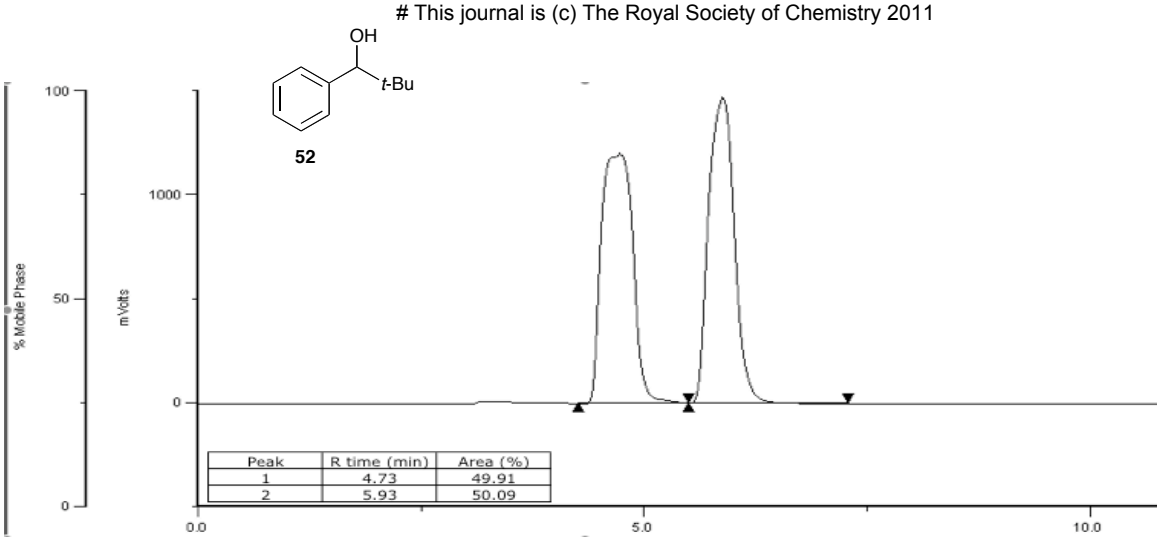




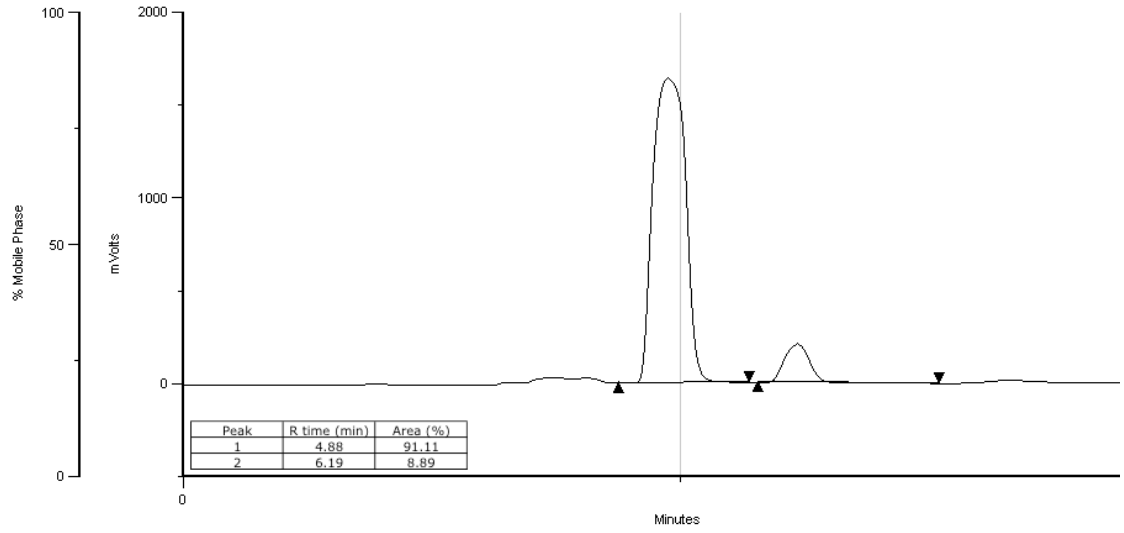
Entry 10 Table 4 : $ee_{alcohol}$= 47 %; ee $_{ester}$ = 89 %; c = 34; s = 35

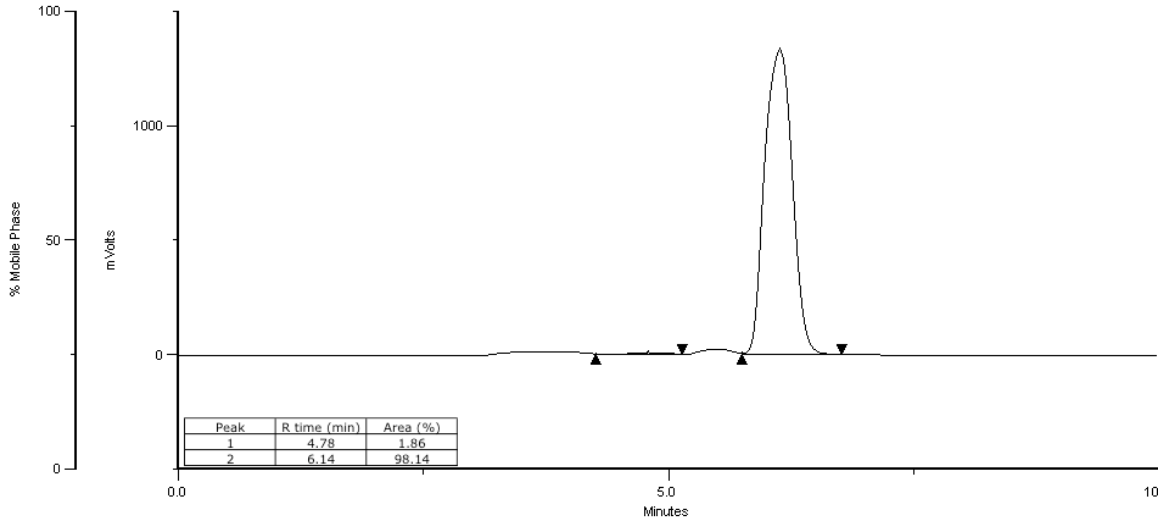




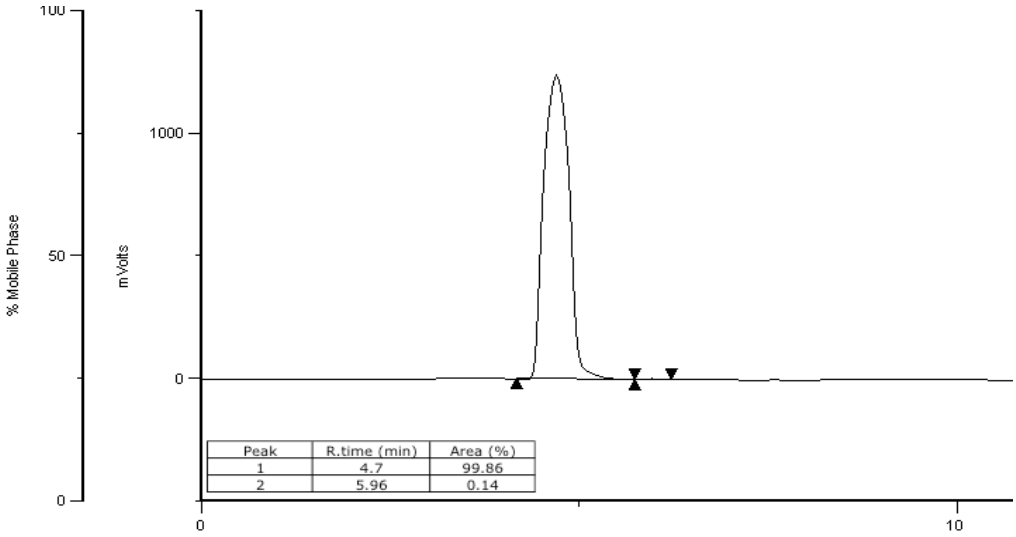


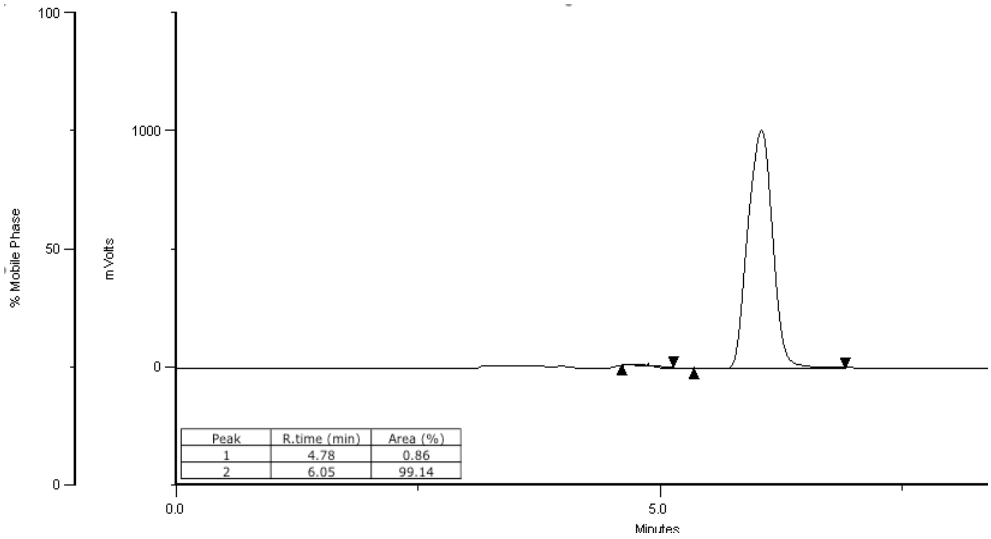
Entry 11 Table 4: $ee_{alcohol}$ = 82%; ee_{ester} = 96 %; c = 46; s > 100

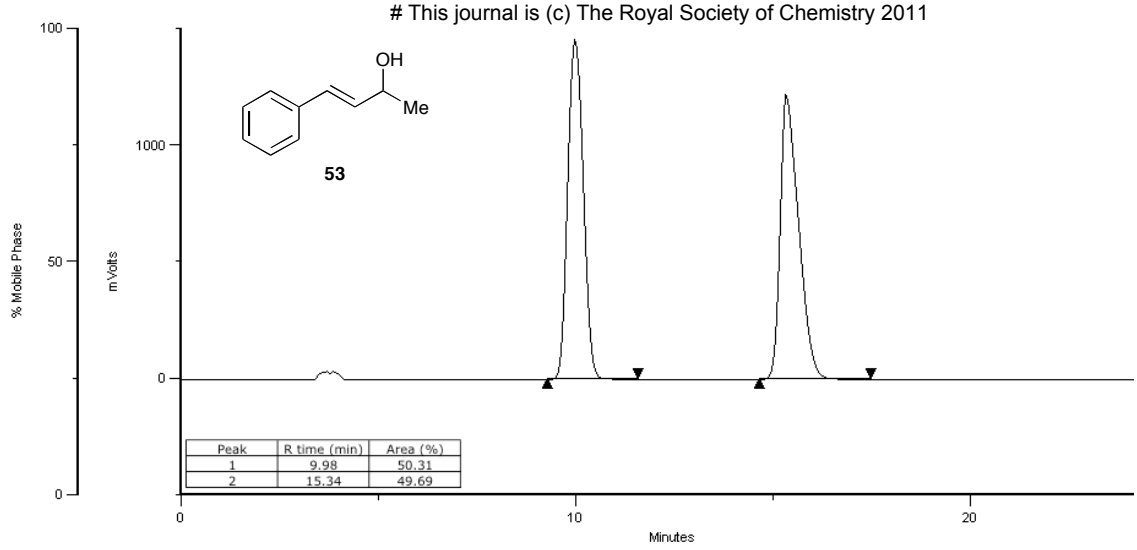




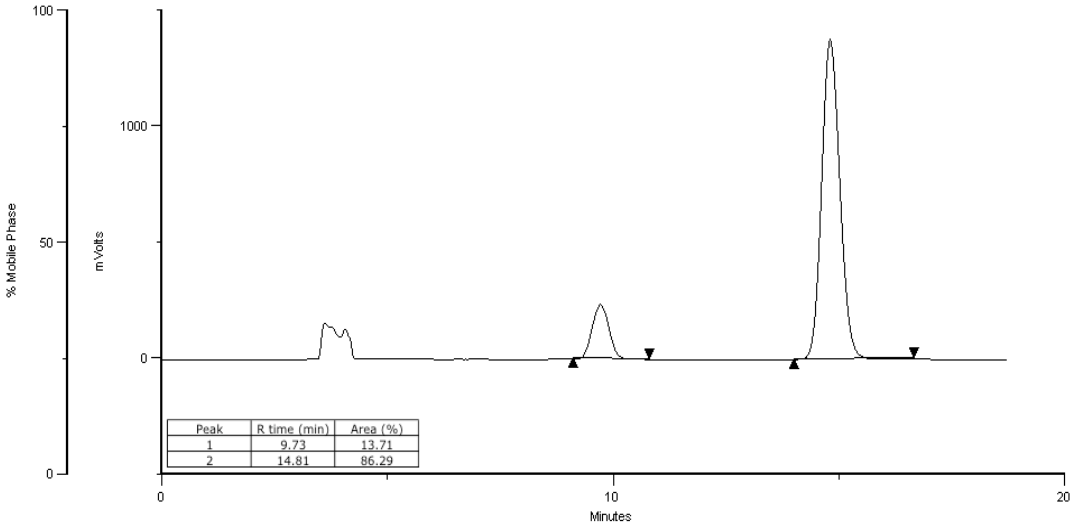
Entry 3 Table 7: $ee_{alcohol}$ > 99 %; ee_{ester} > 99 %; c = 50; s >100

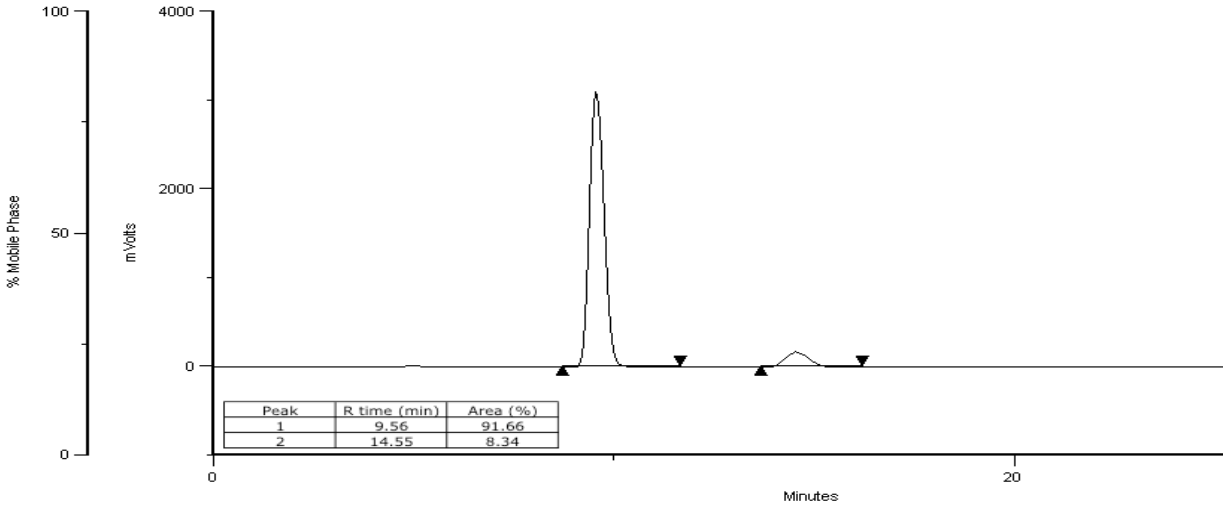






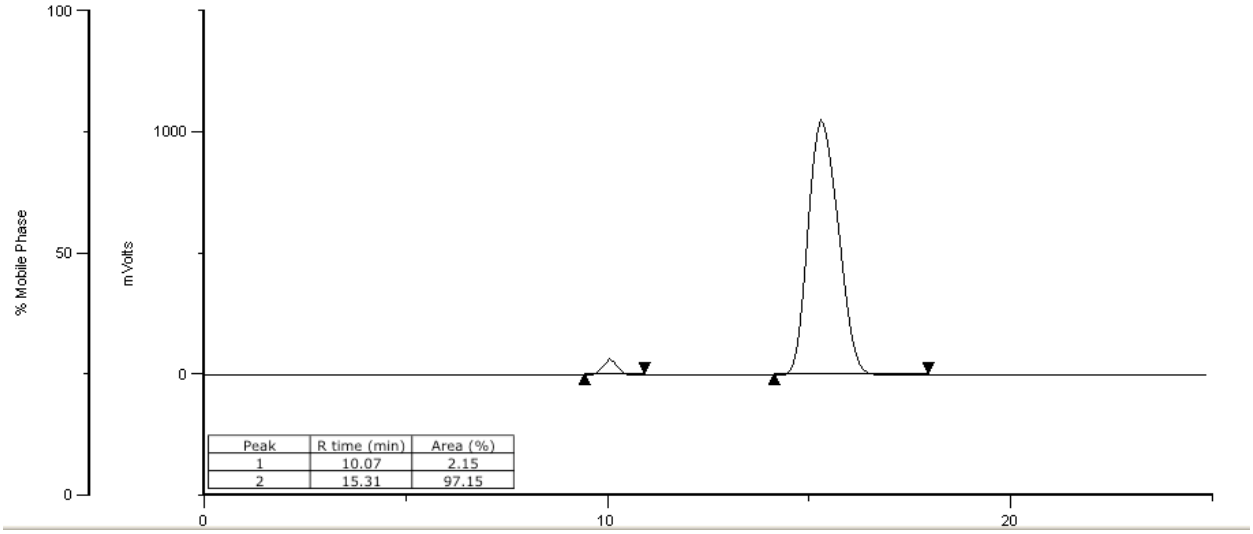
Entry 14 Table 4: $ee_{alcohol}$ = 73%; ee_{ester} = 83 %; c = 47; s = 22

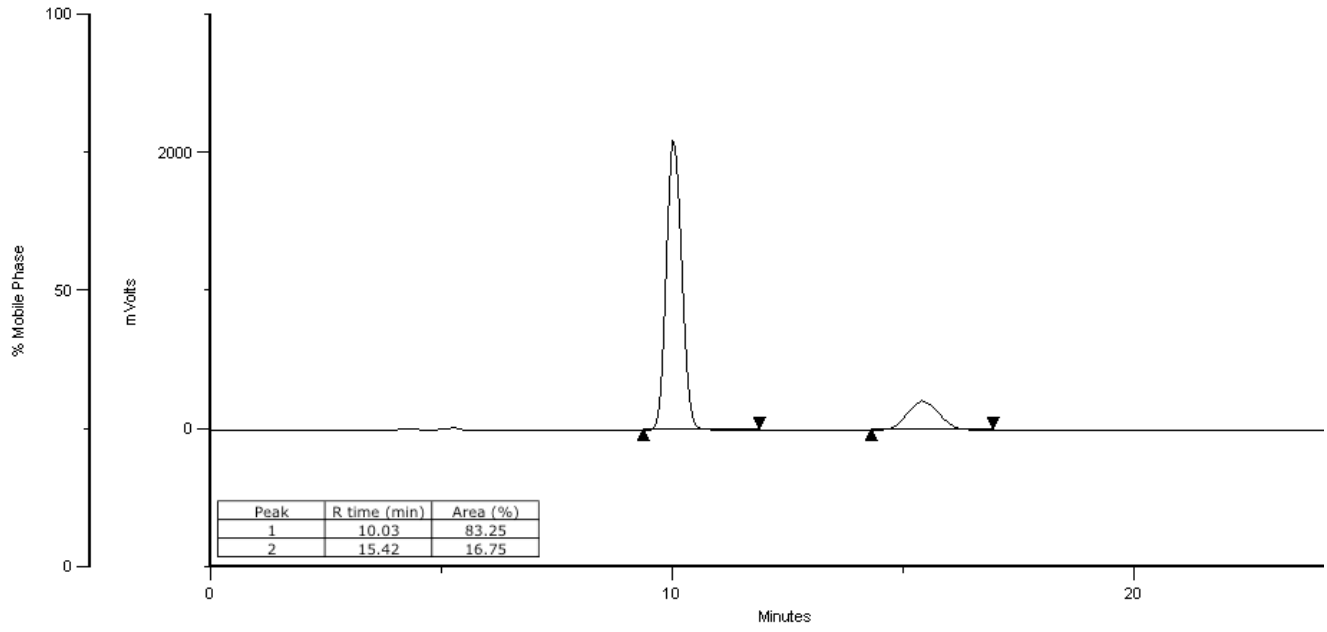


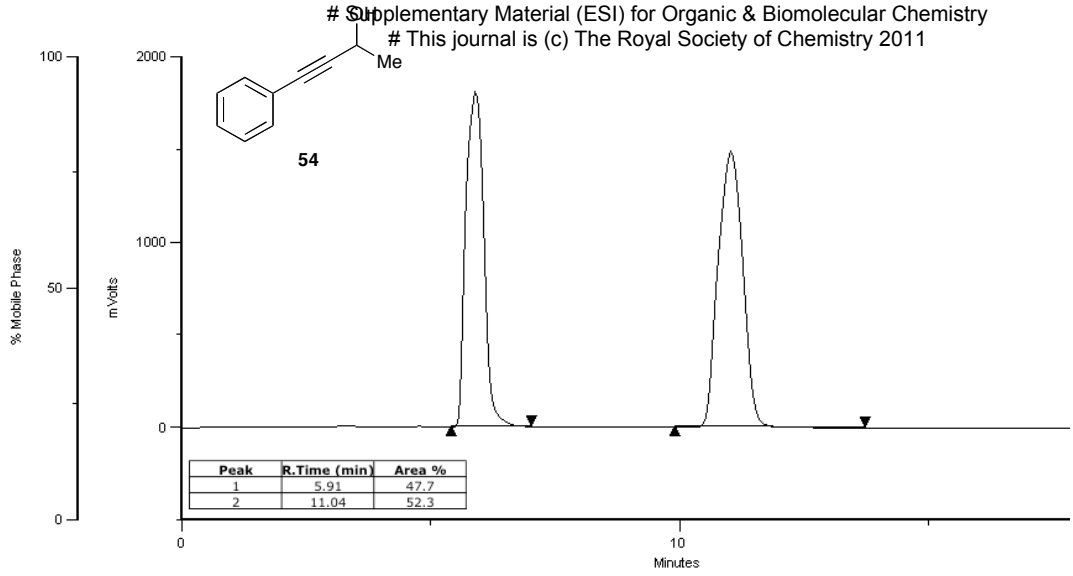


Supplementary Material (ESI) for Organic & Biomolecular Chemistry

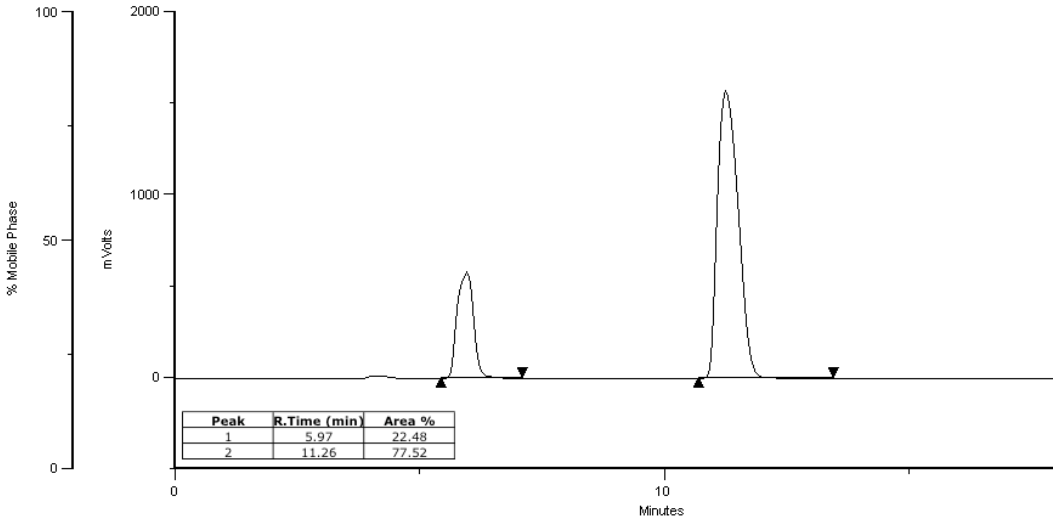
Entry 4 Table 7: $ee_{alcohol}$ = 95%; ee_{ester} = 66 %; c = 59; s =17

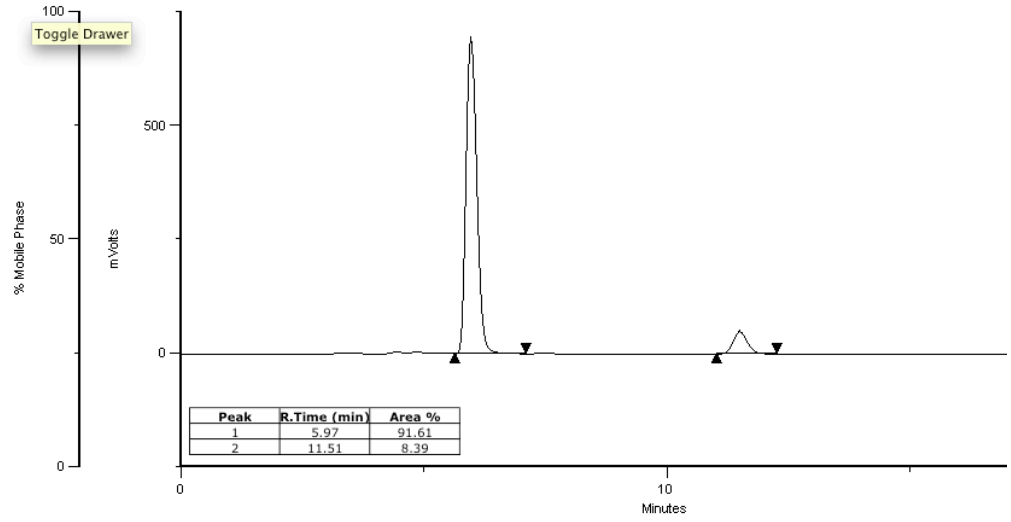




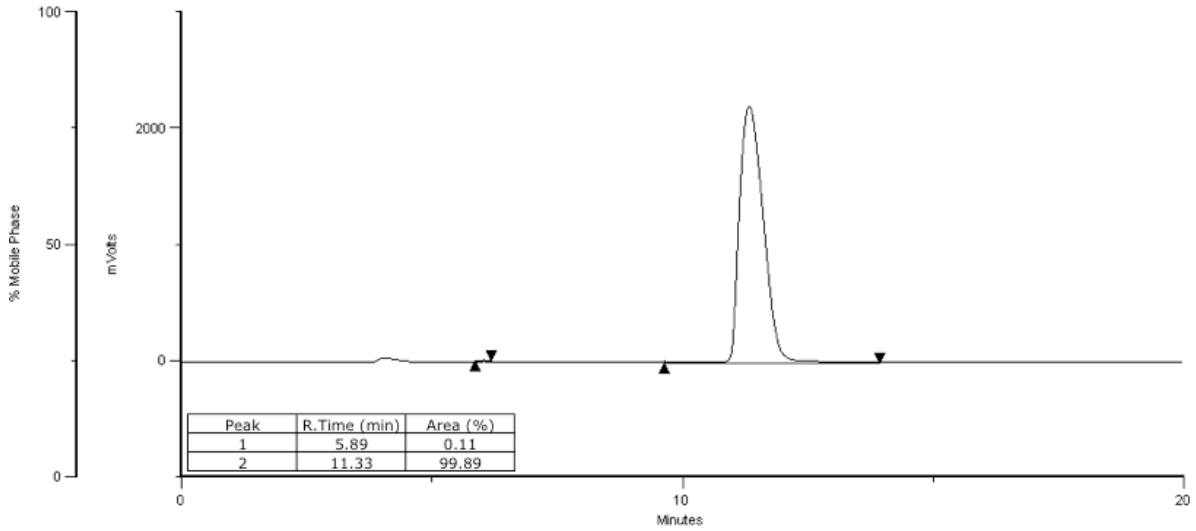


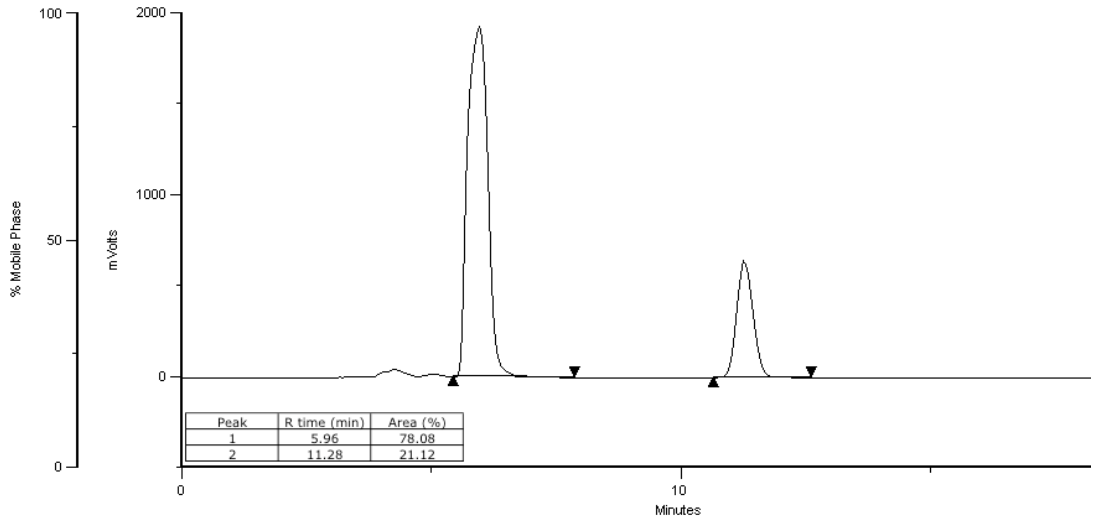
Entry 16 scheme 4: $ee_{alcohol}$ = 55%; ee_{ester} = 83 %; c = 40; s = 18

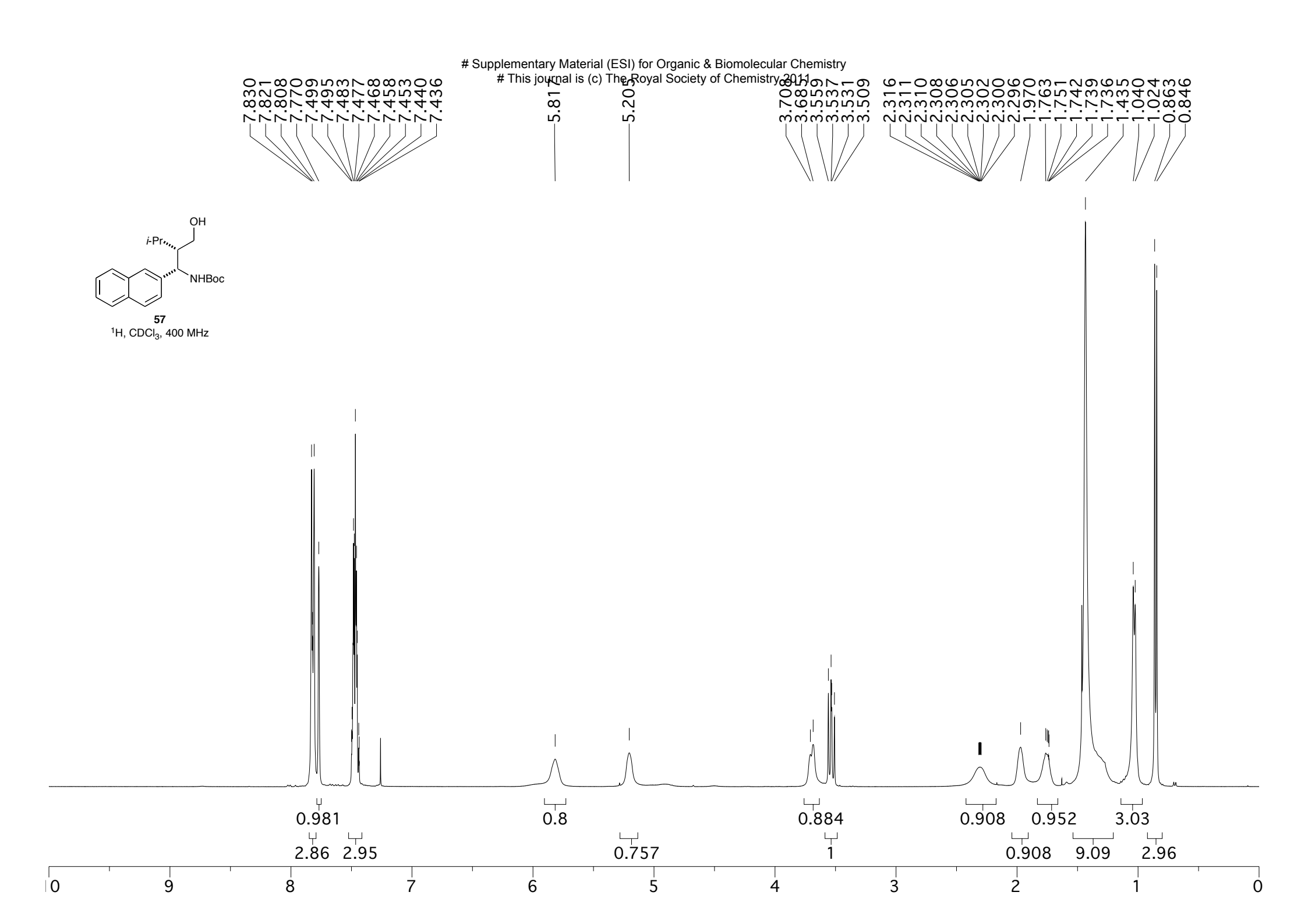




Entry 5 Table 7: $ee_{alcohol} > 99\%$; $ee_{ester} = 57\ \%$; c = 63; s = 18

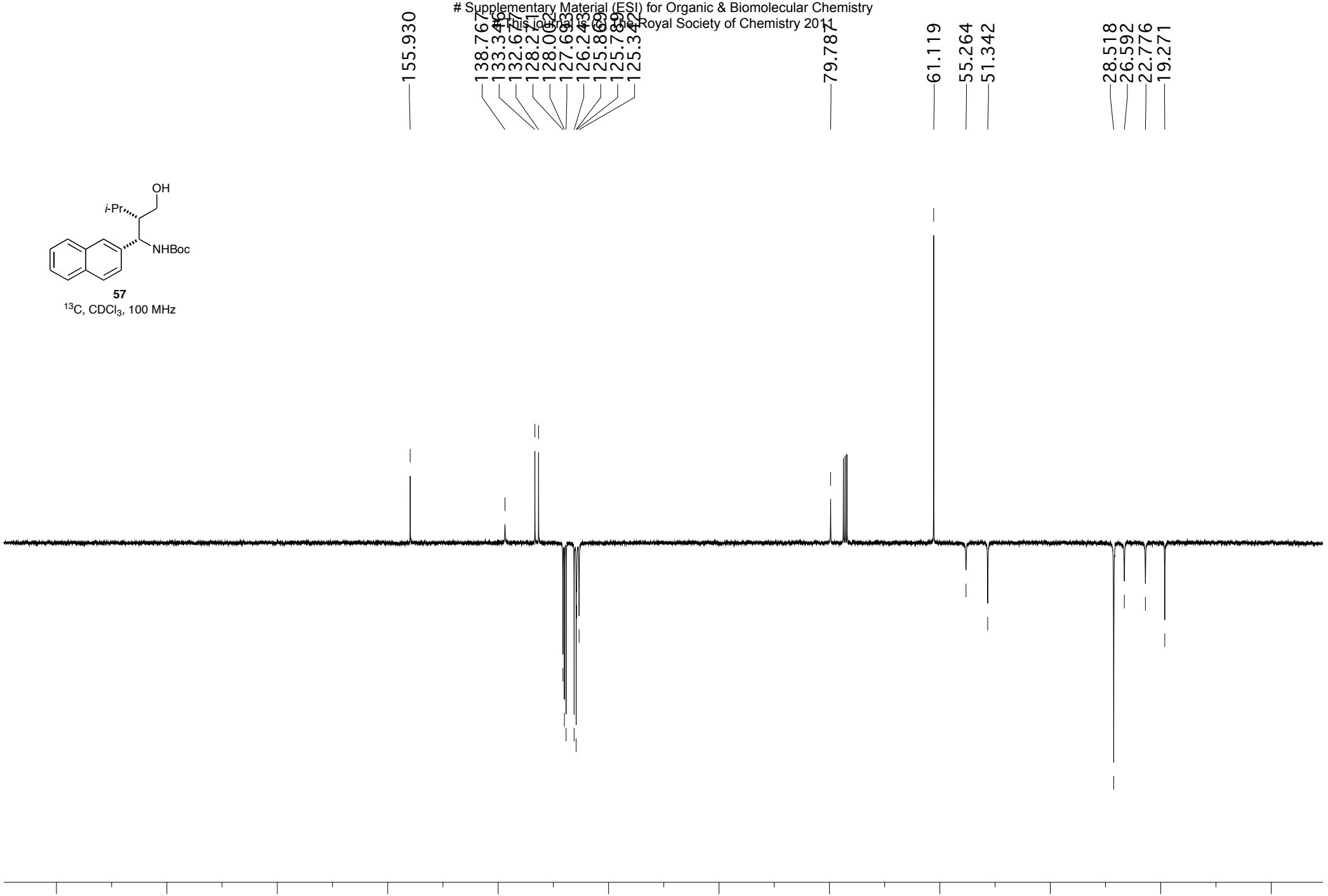






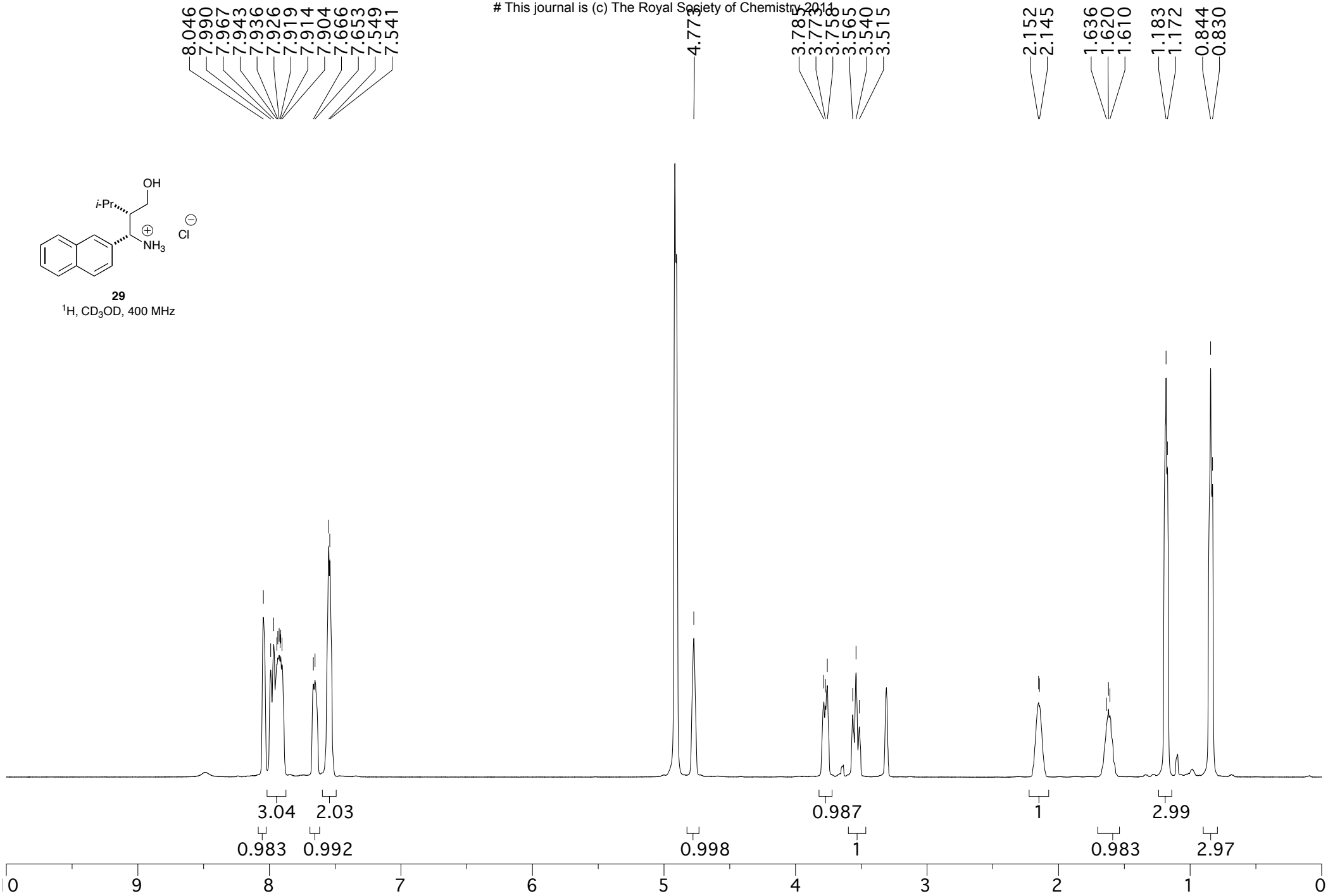
57

^{13}C, $CDCl_3$, 100 MHz



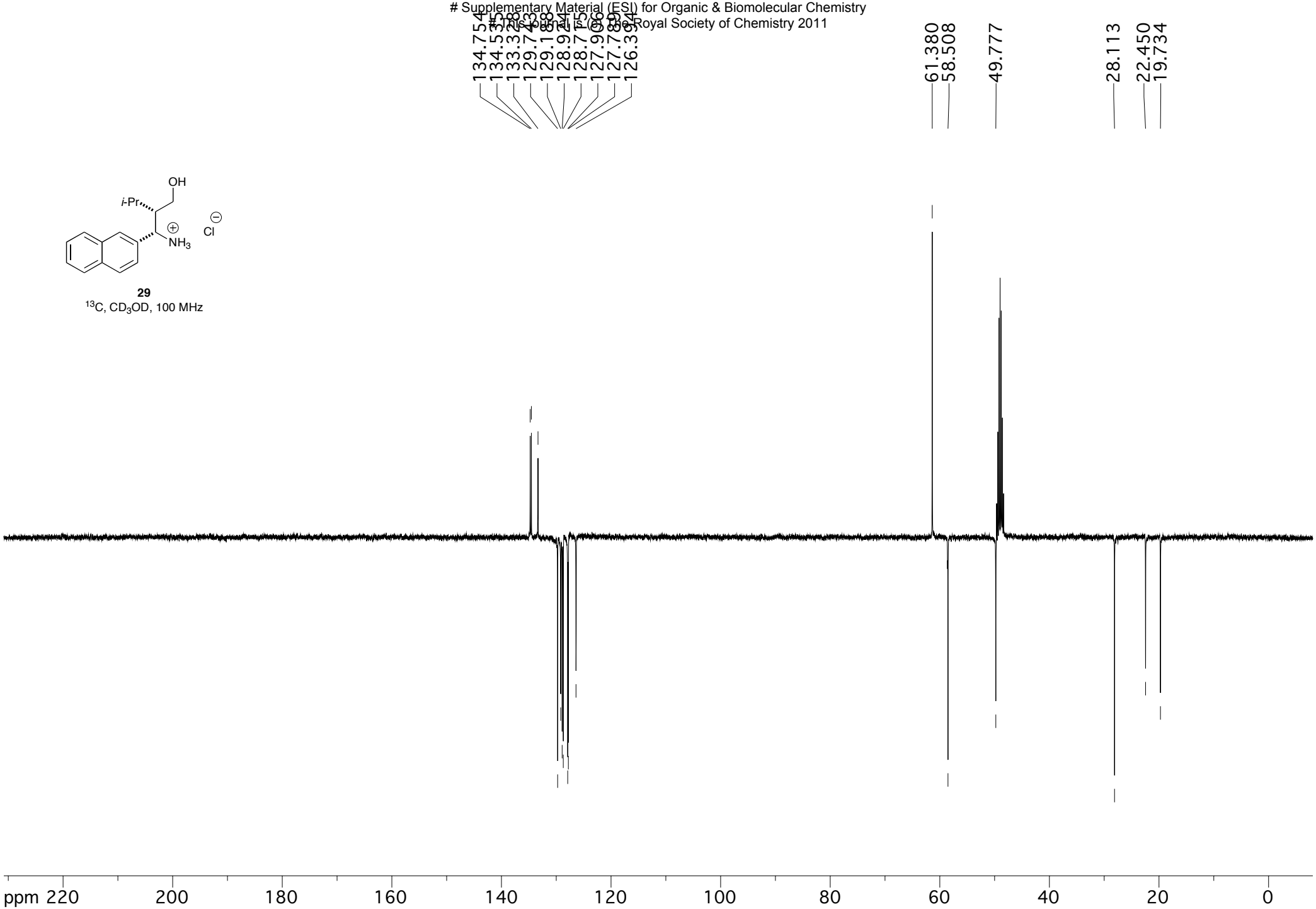
29

^{1}H, CD_3OD, 400 MHz



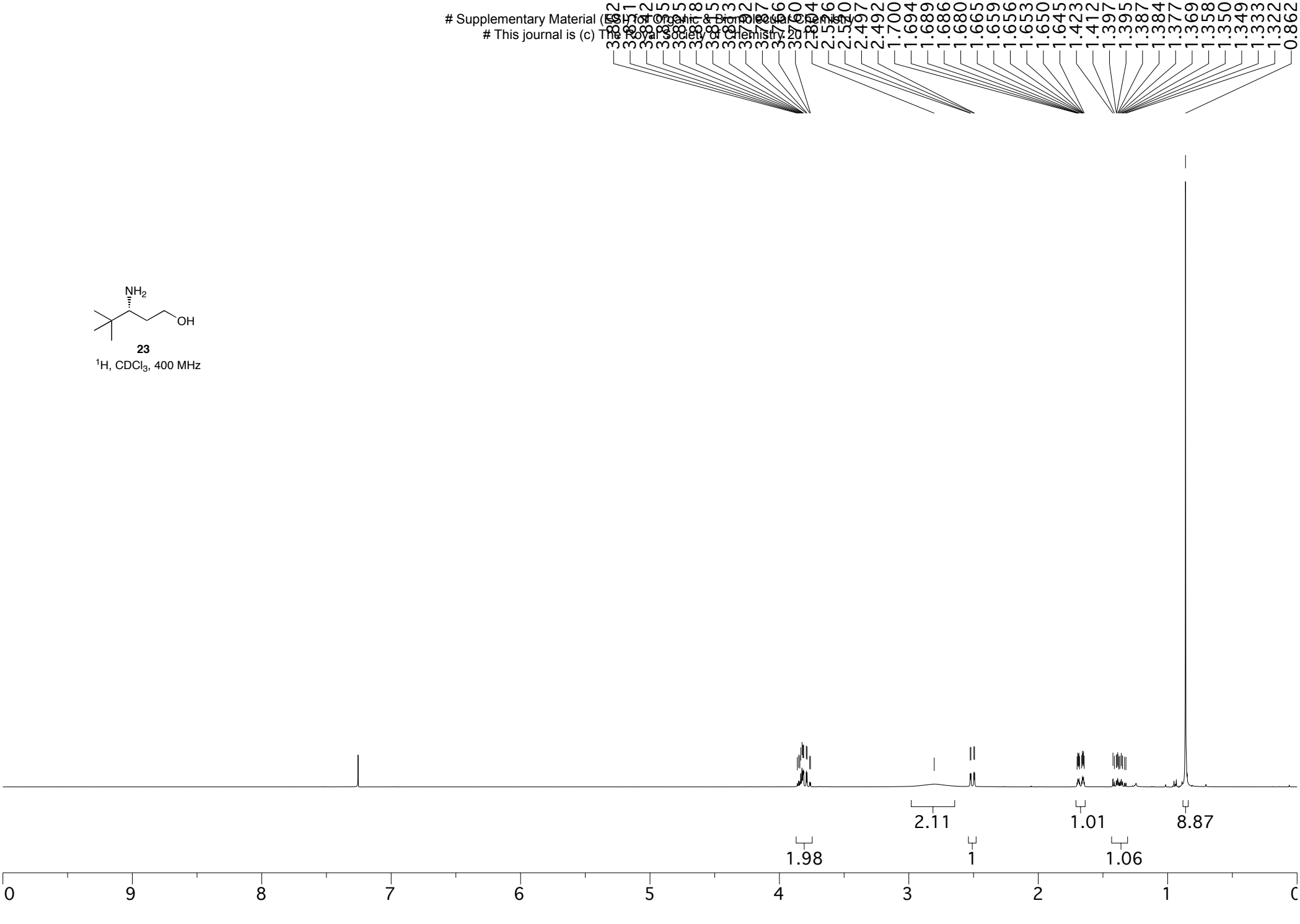
29

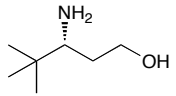
^{13}C, CD_3OD, 100 MHz



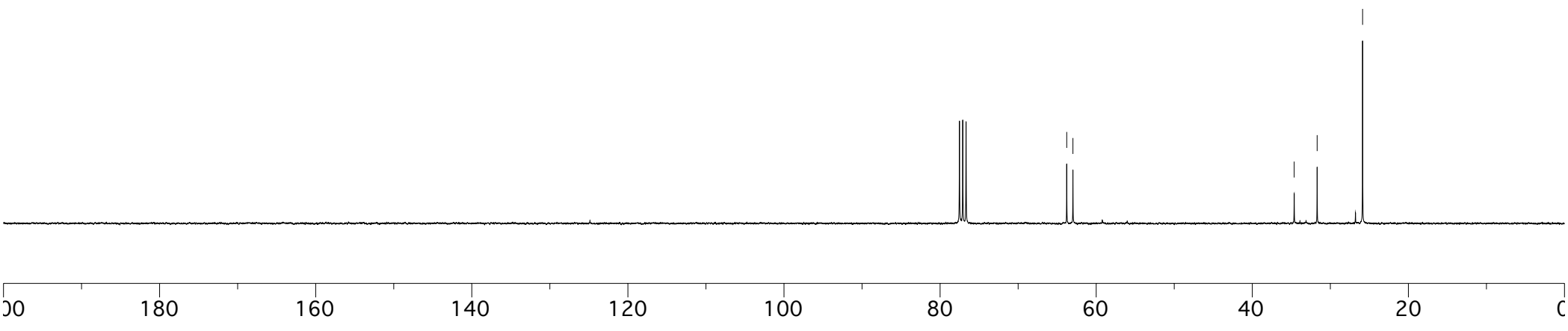
23

^{1}H, $CDCl_3$, 400 MHz

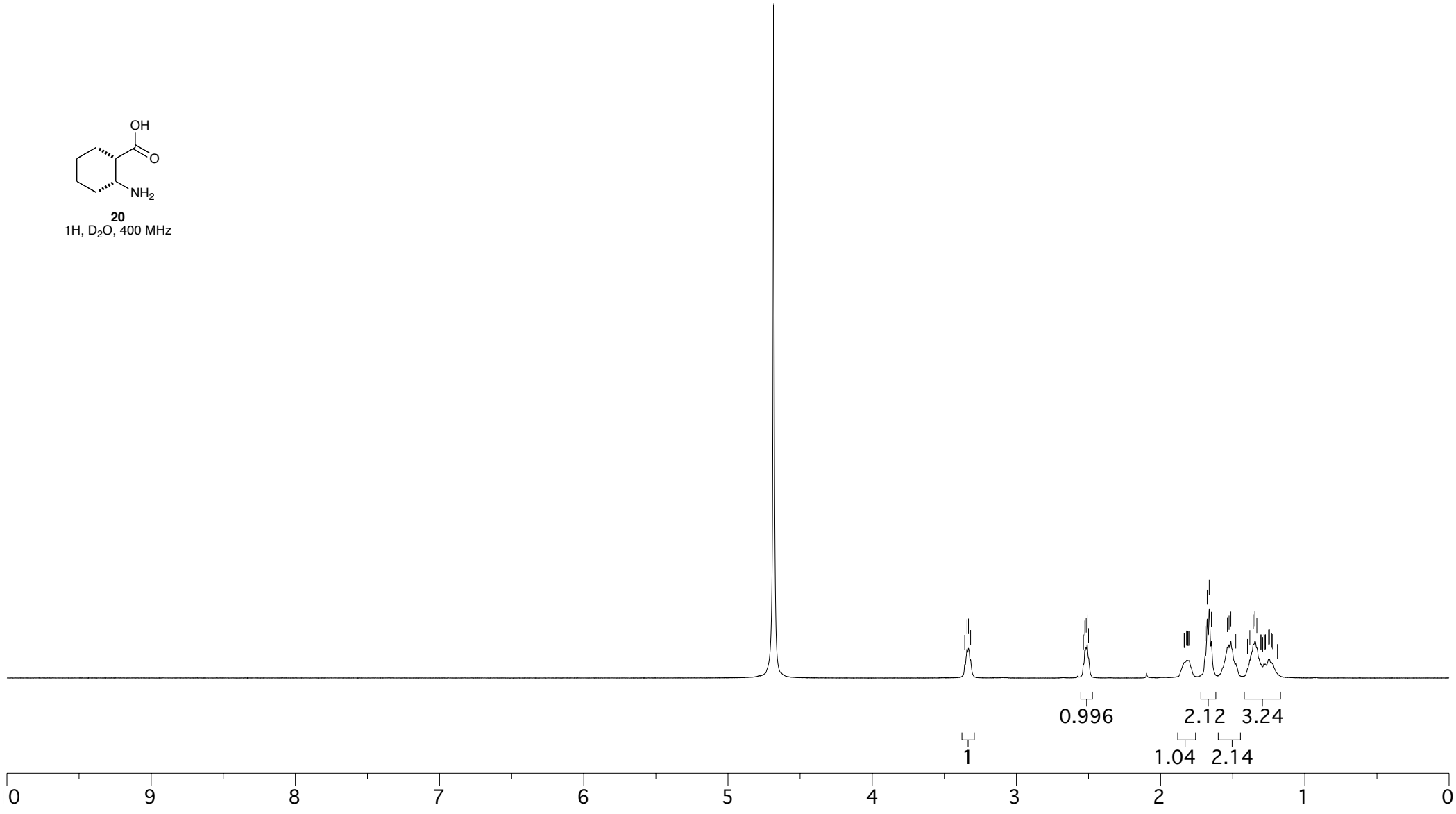


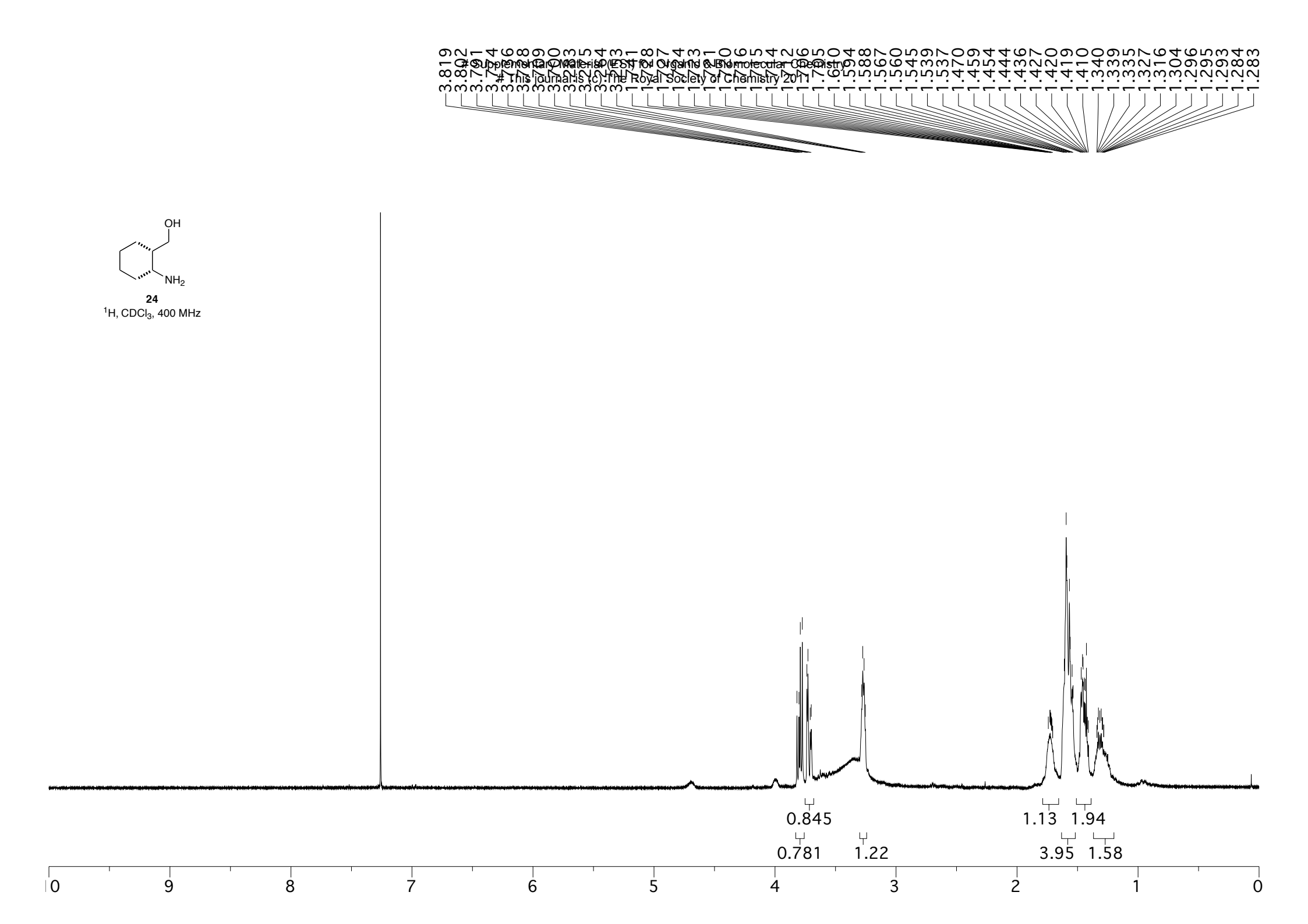


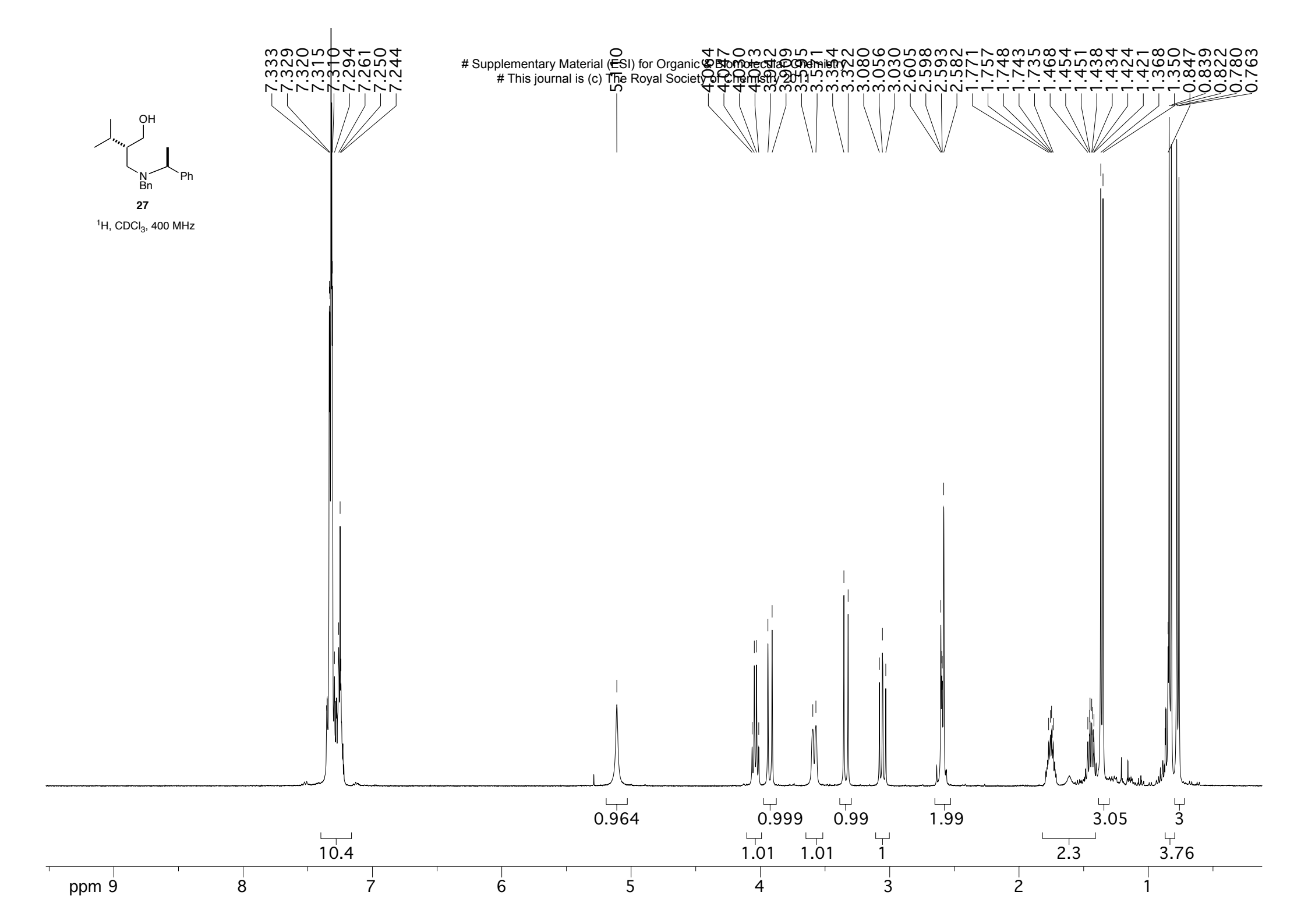
23
^{1}H, $CDCl_3$, 75 MHz



20
1H, D_2O, 400 MHz






OH
N
Bn
Ph
27
^{1}H, $CDCl_3$, 400 MHz
Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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7.333
7.329
7.320
7.315
7.310
7.294
7.261
7.250
7.244
5.510
4.004
4.000
3.997
3.993
3.989
3.355
3.351
3.344
3.322
3.080
3.056
3.030
2.605
2.598
2.593
2.582
1.771
1.757
1.748
1.743
1.735
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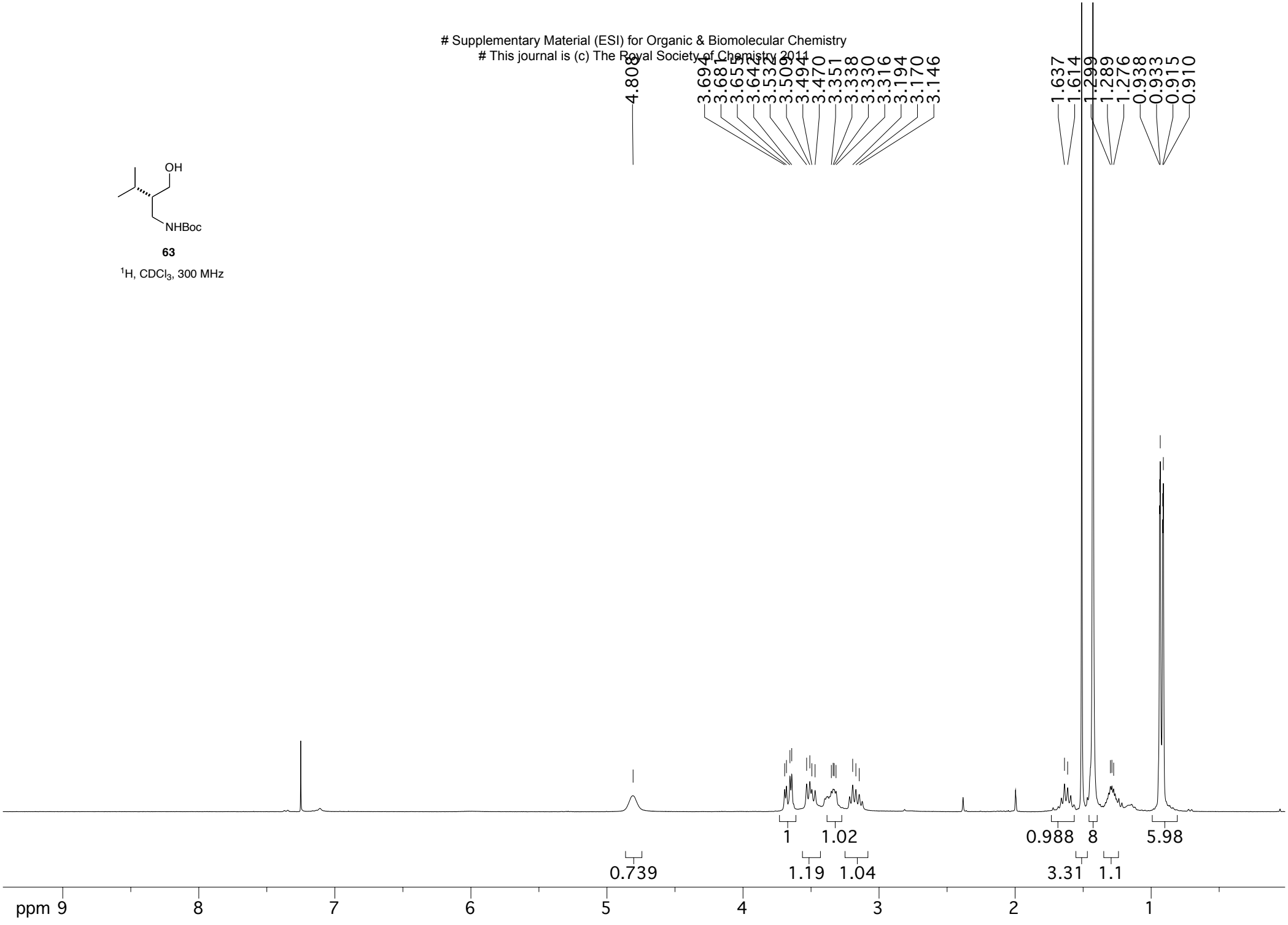
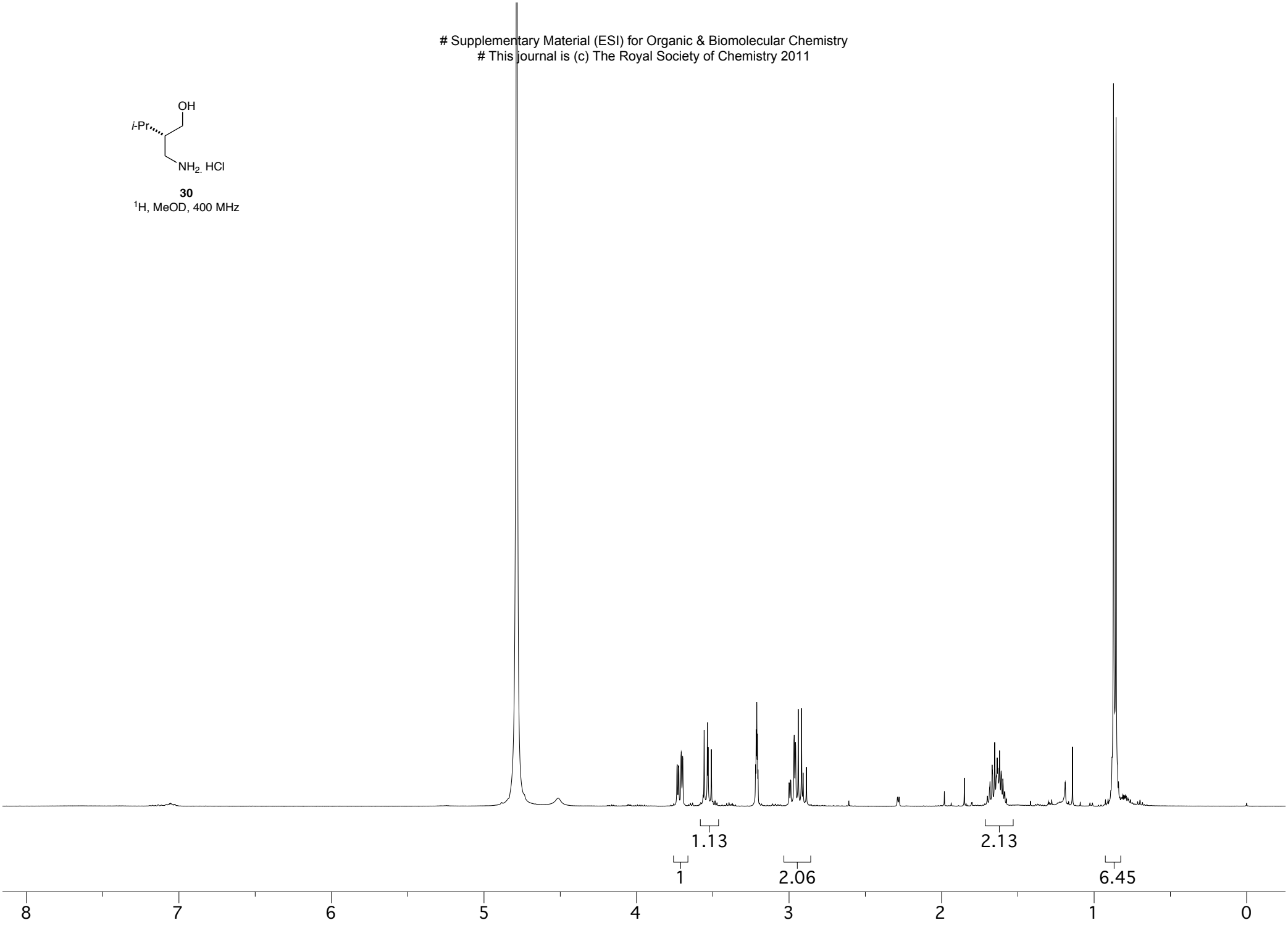
1.438
1.434
1.424
1.421
1.368
1.350
0.847
0.839
0.822
0.780
0.763
0.964
0.999
0.99
1.99
3.05
3
10.4
1.01
1.01
1
2.3
3.76
ppm 9
8
7
6
5
4
3
2
1

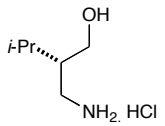
63

^{1}H, $CDCl_3$, 300 MHz



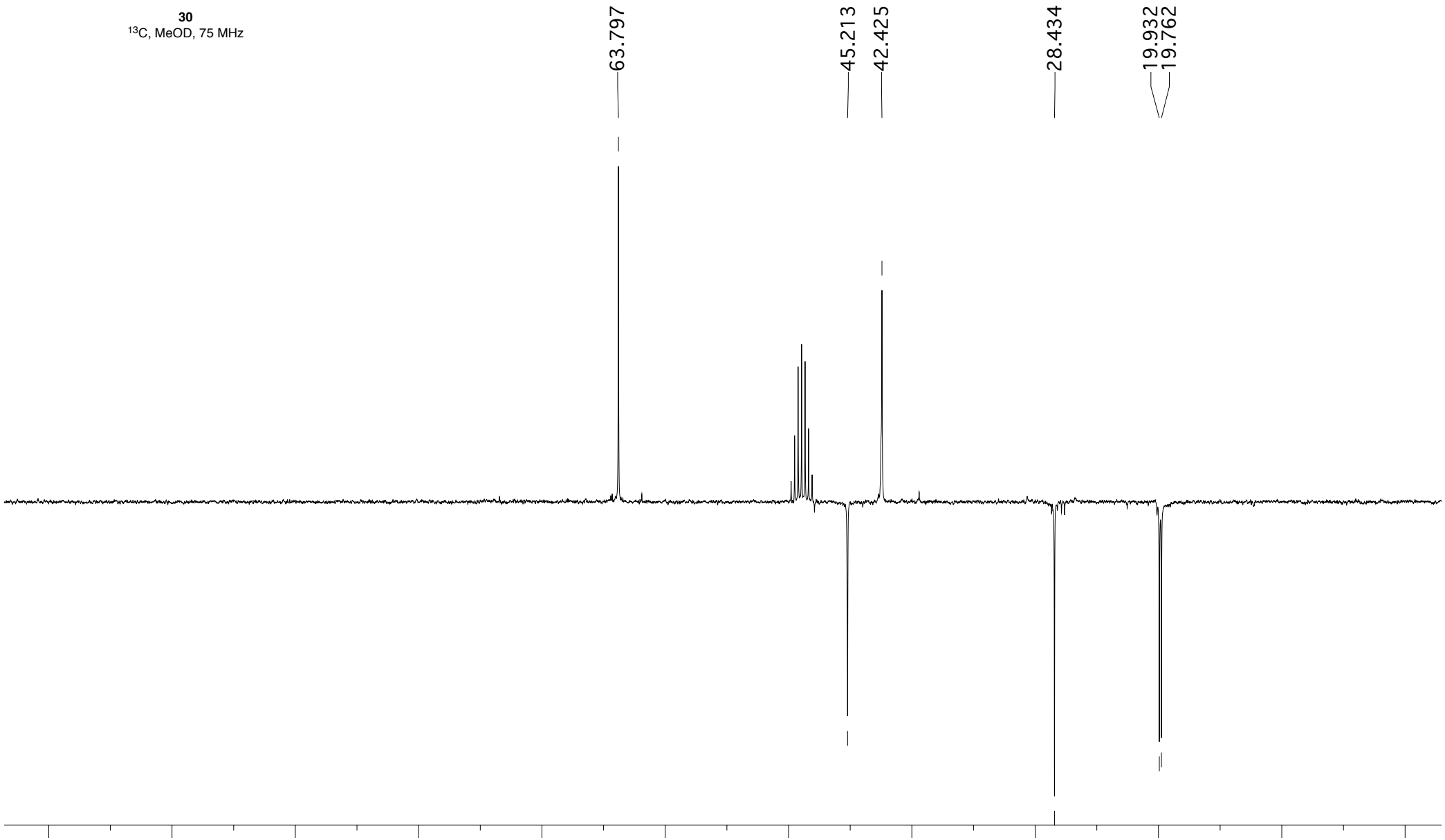
30
^{1}H, MeOD, 400 MHz

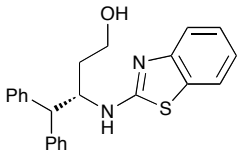




30

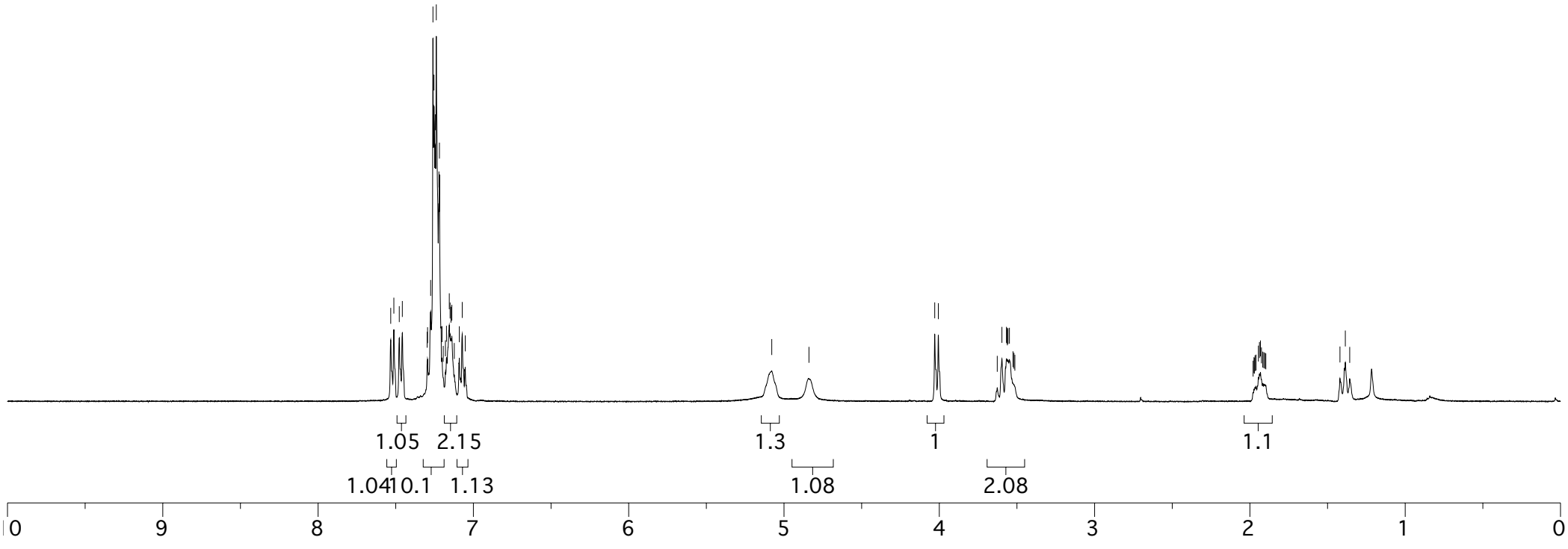
^{13}C, MeOD, 75 MHz

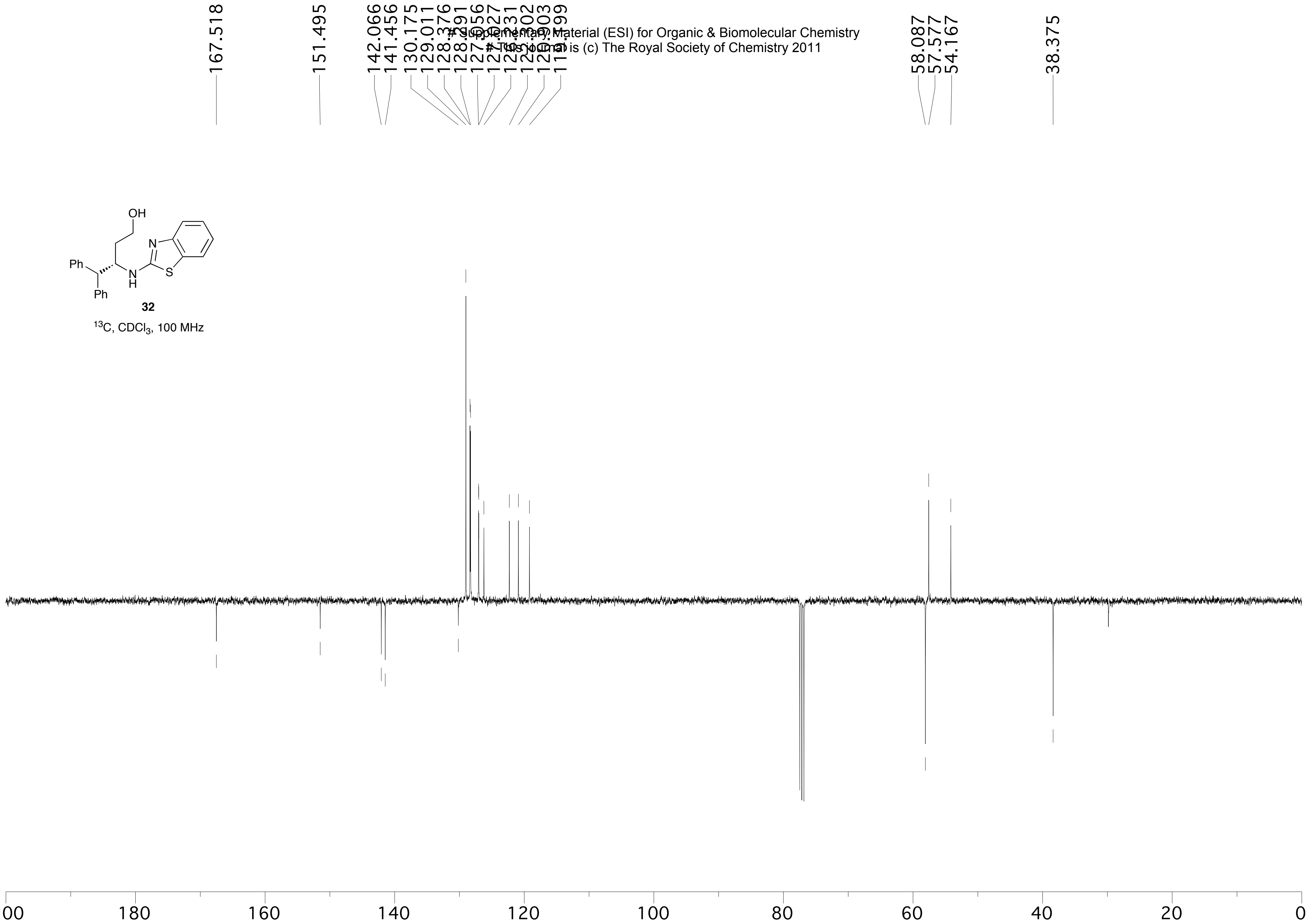


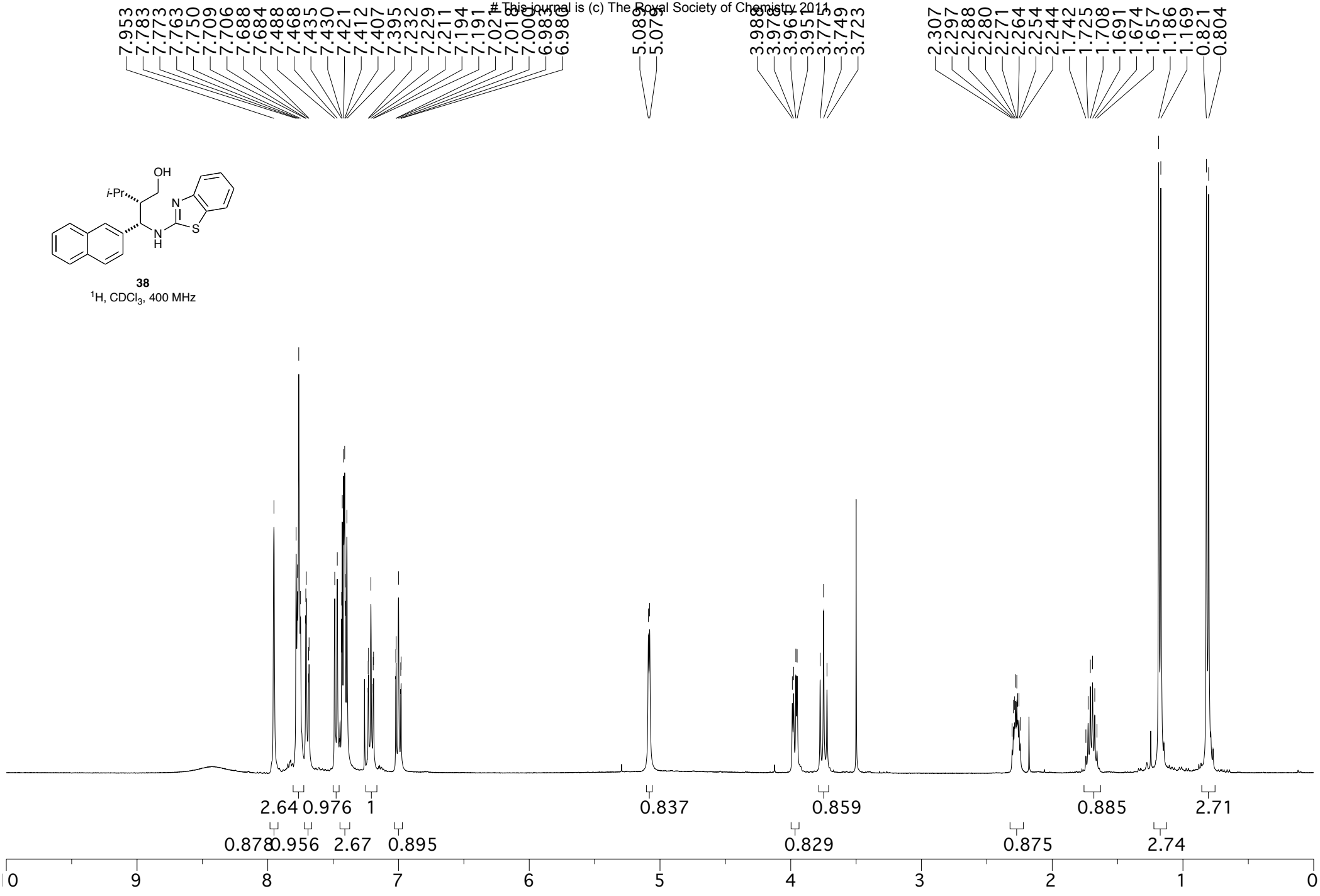


32

^{1}H, $CDCl_3$, 400 MHz

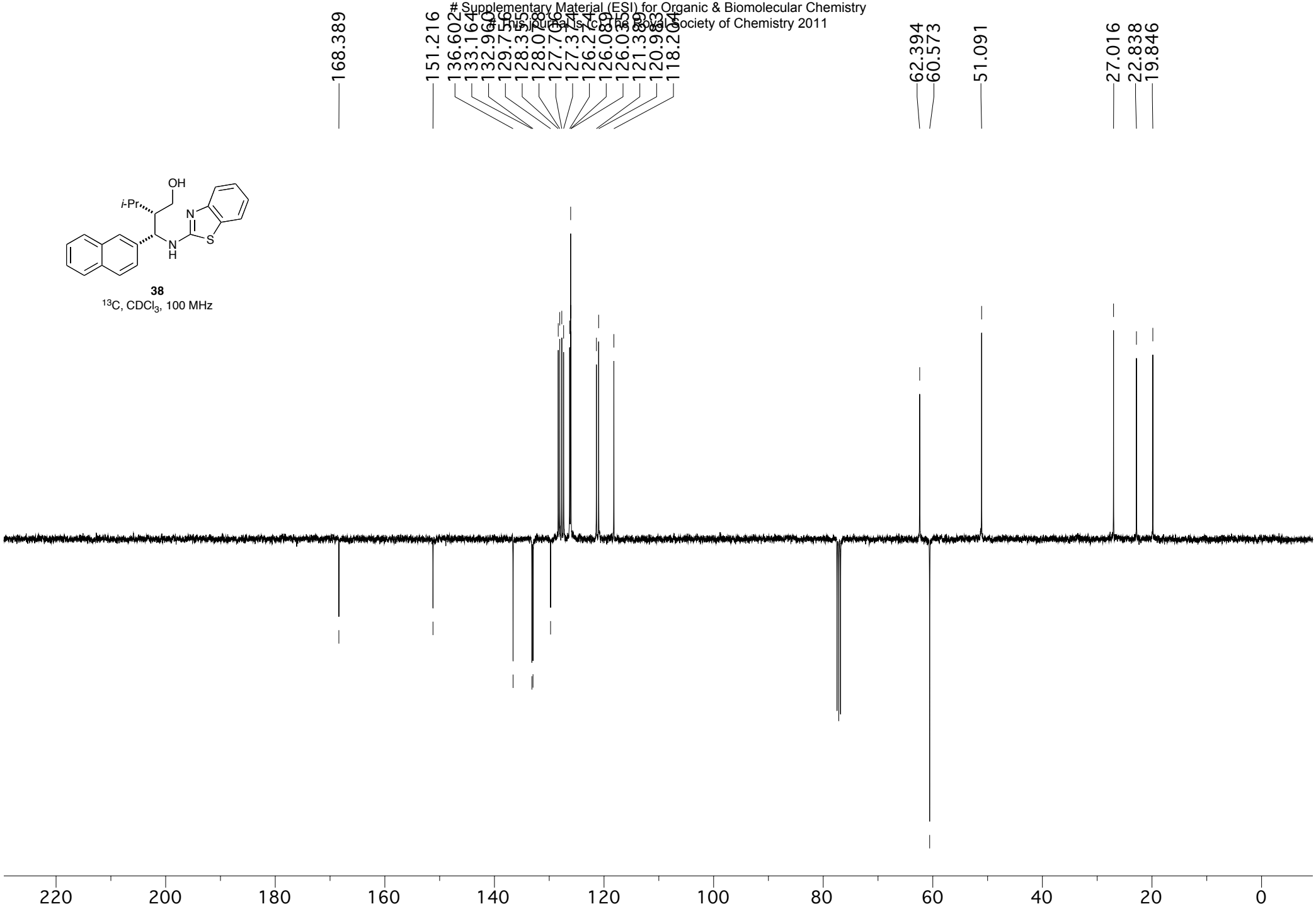






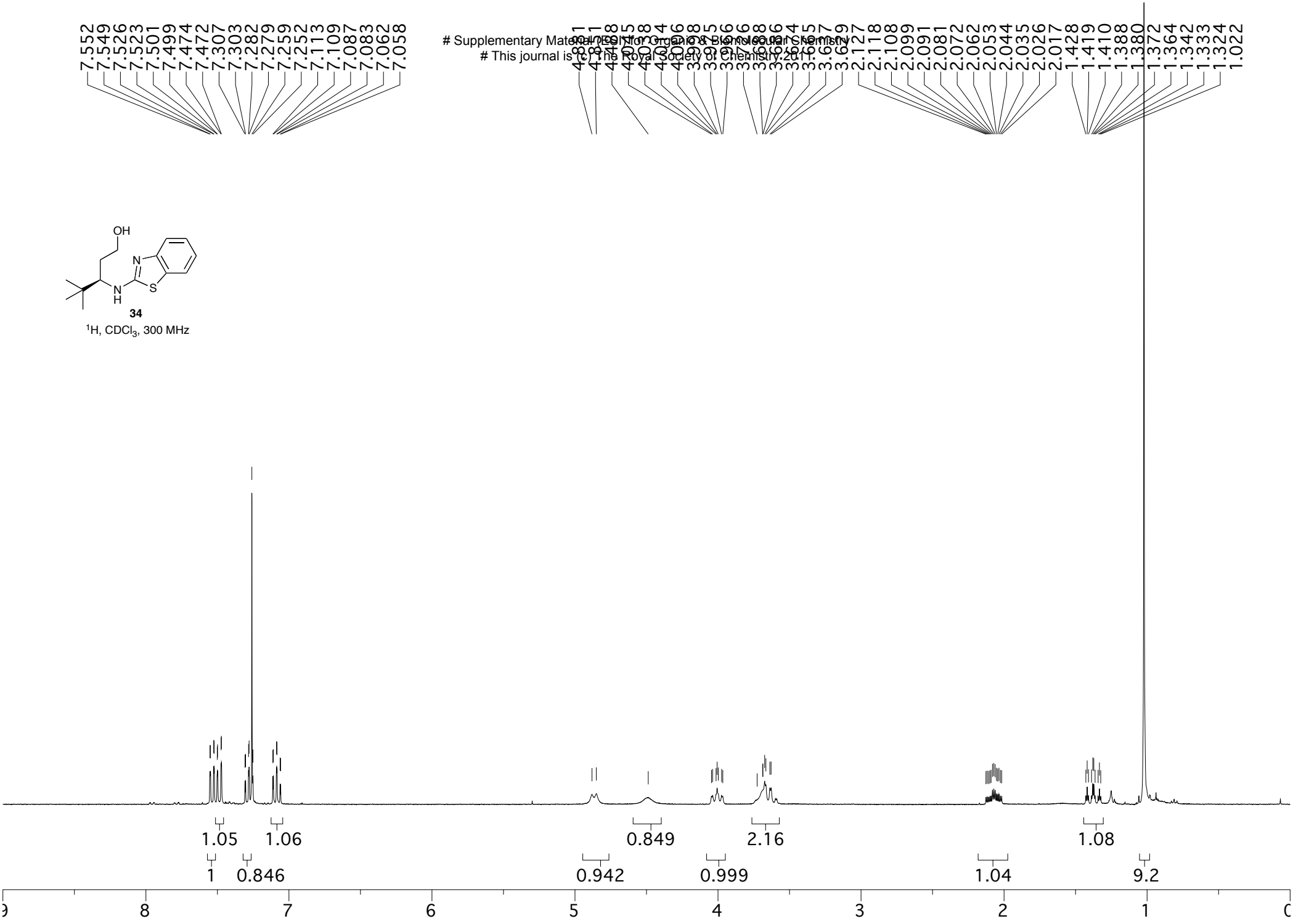
38

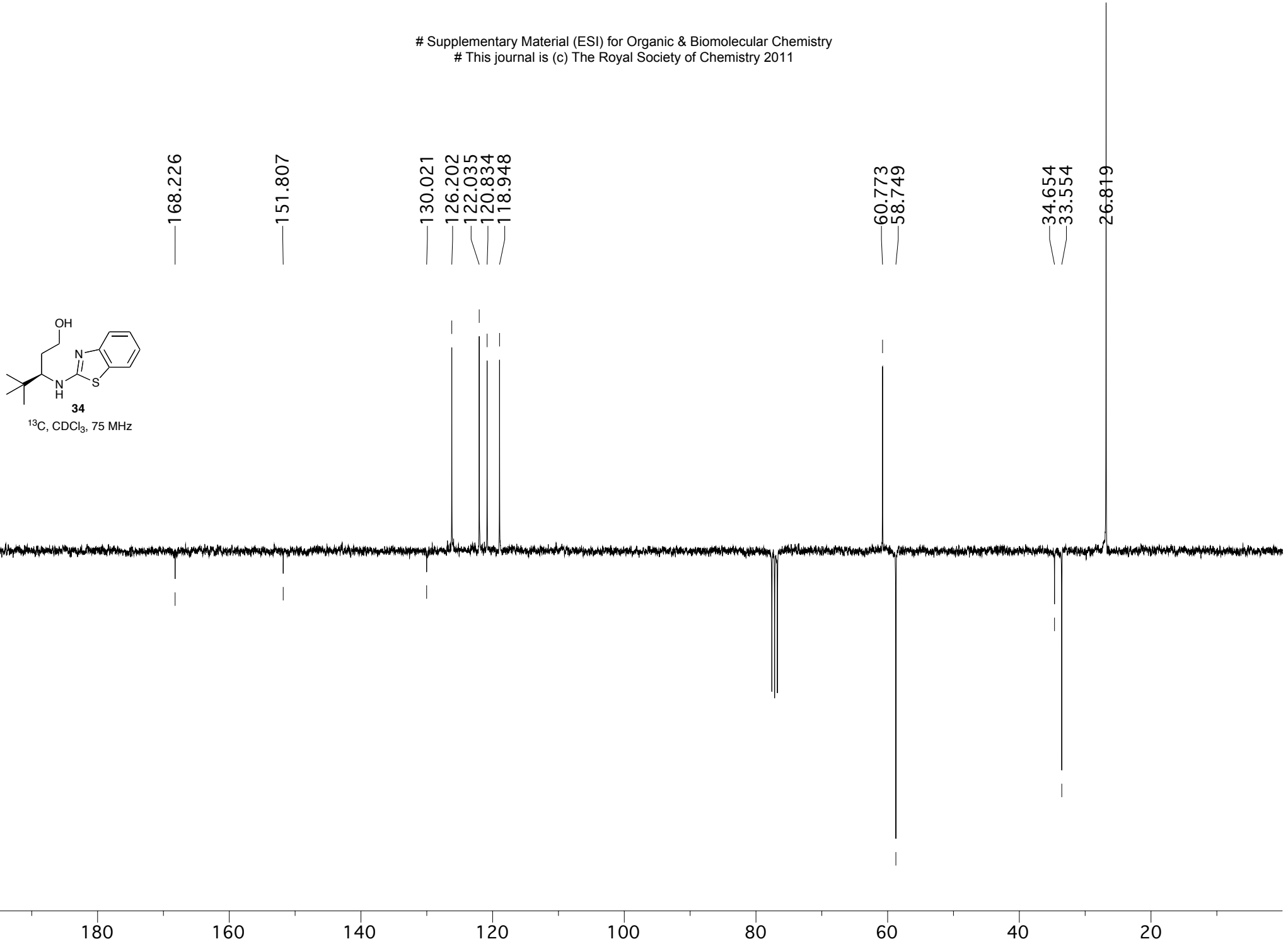
^{13}C, $CDCl_3$, 100 MHz

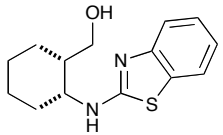


34

^{1}H, $CDCl_3$, 300 MHz

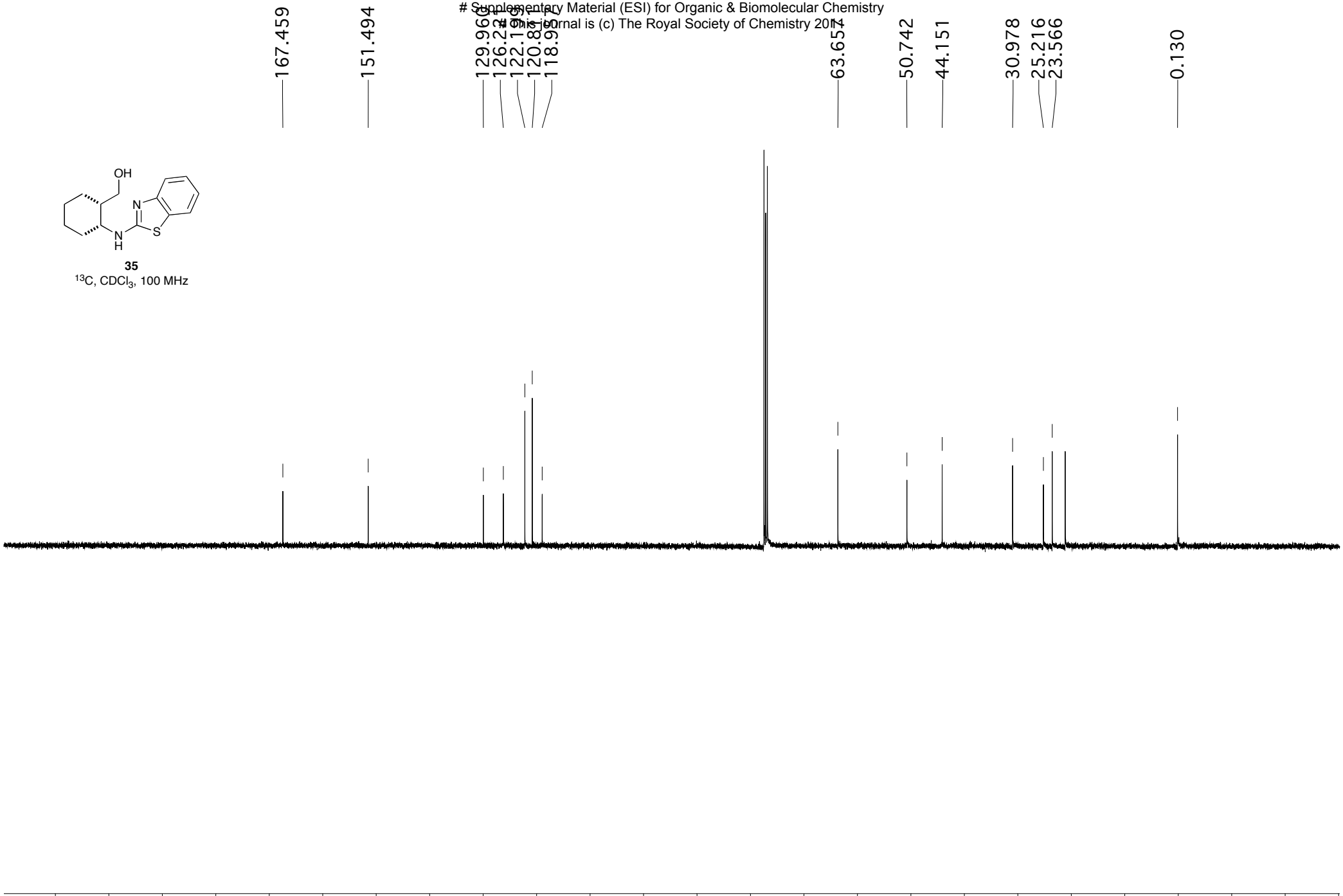






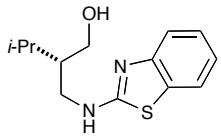
35

^{1}H, $CDCl_3$, 400 MHz



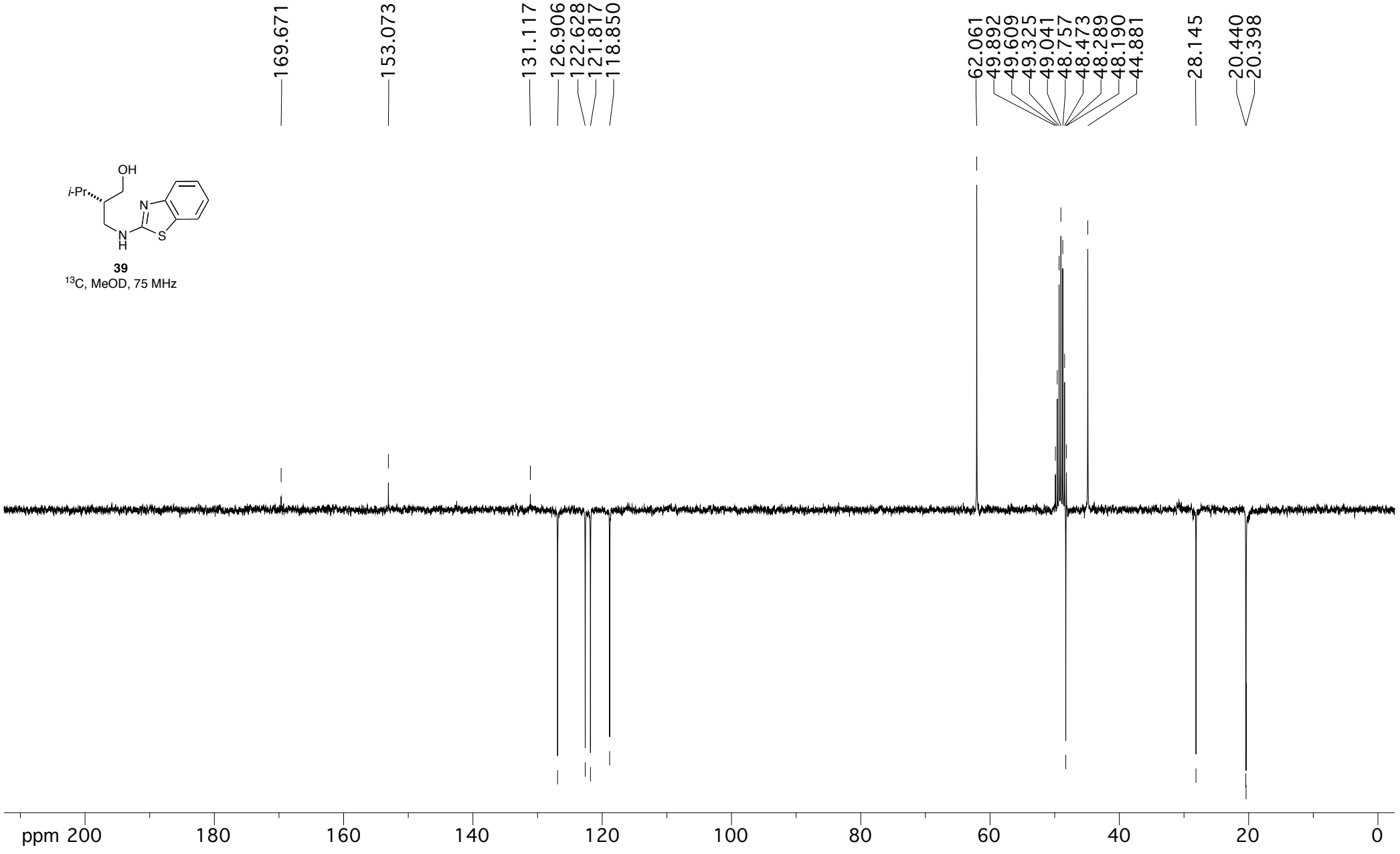
35

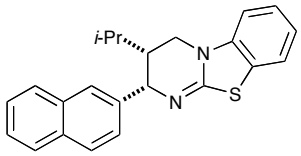
^{13}C, $CDCl_3$, 100 MHz



39

^{1}H, $CDCl_3$, 300 MHz



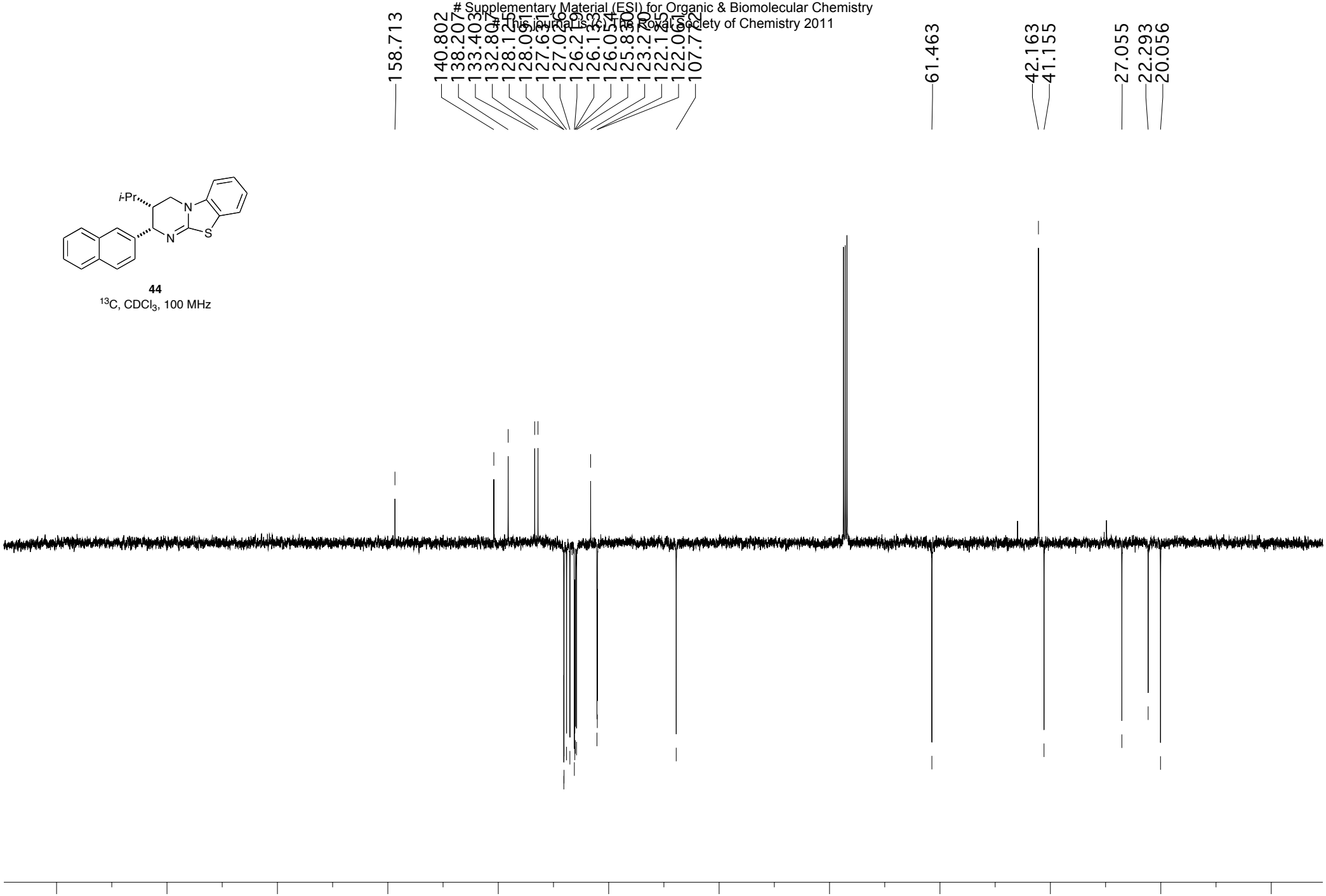


44

^{1}H, $CDCl_3$, 400 MHz

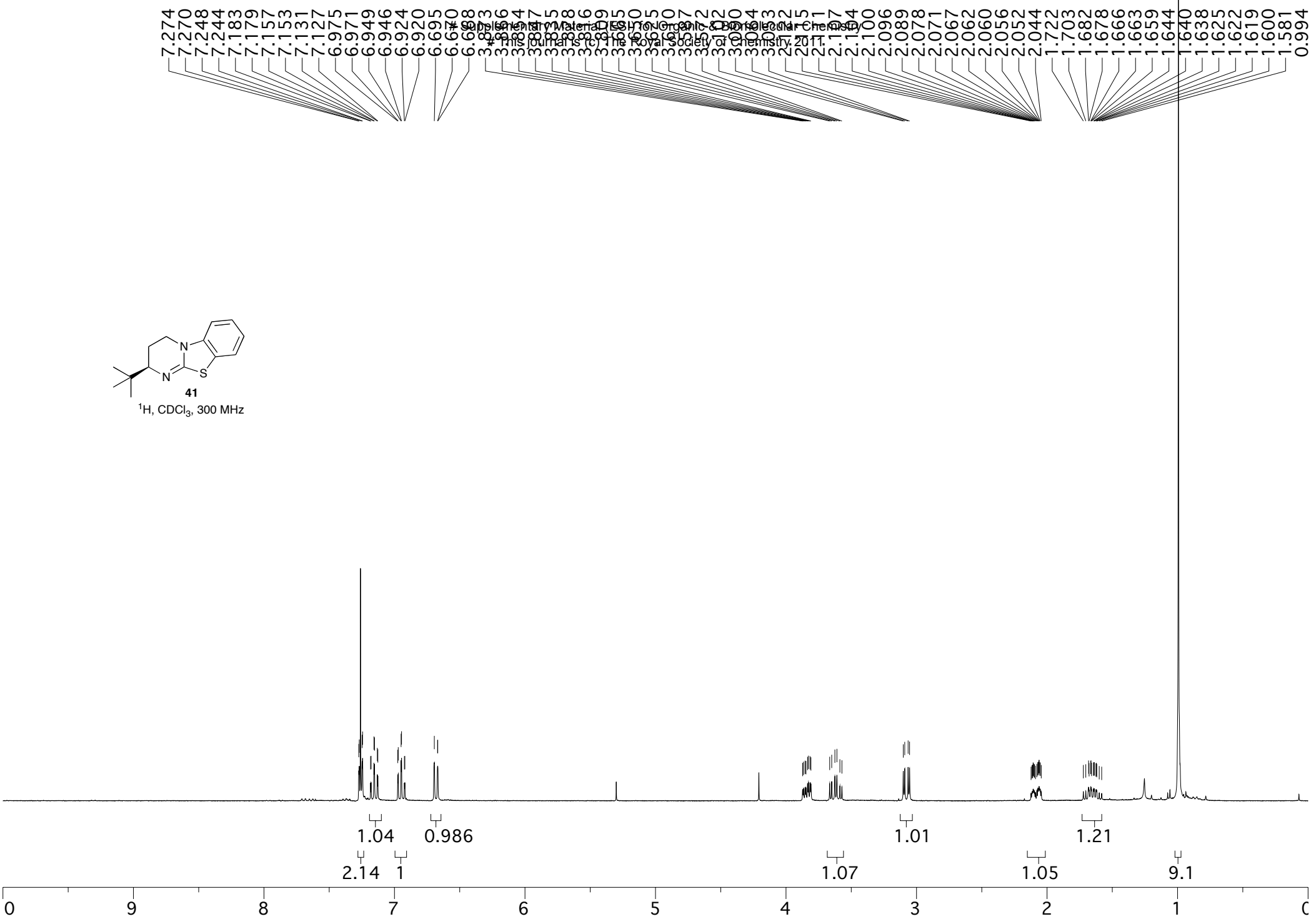
44

^{13}C, $CDCl_3$, 100 MHz

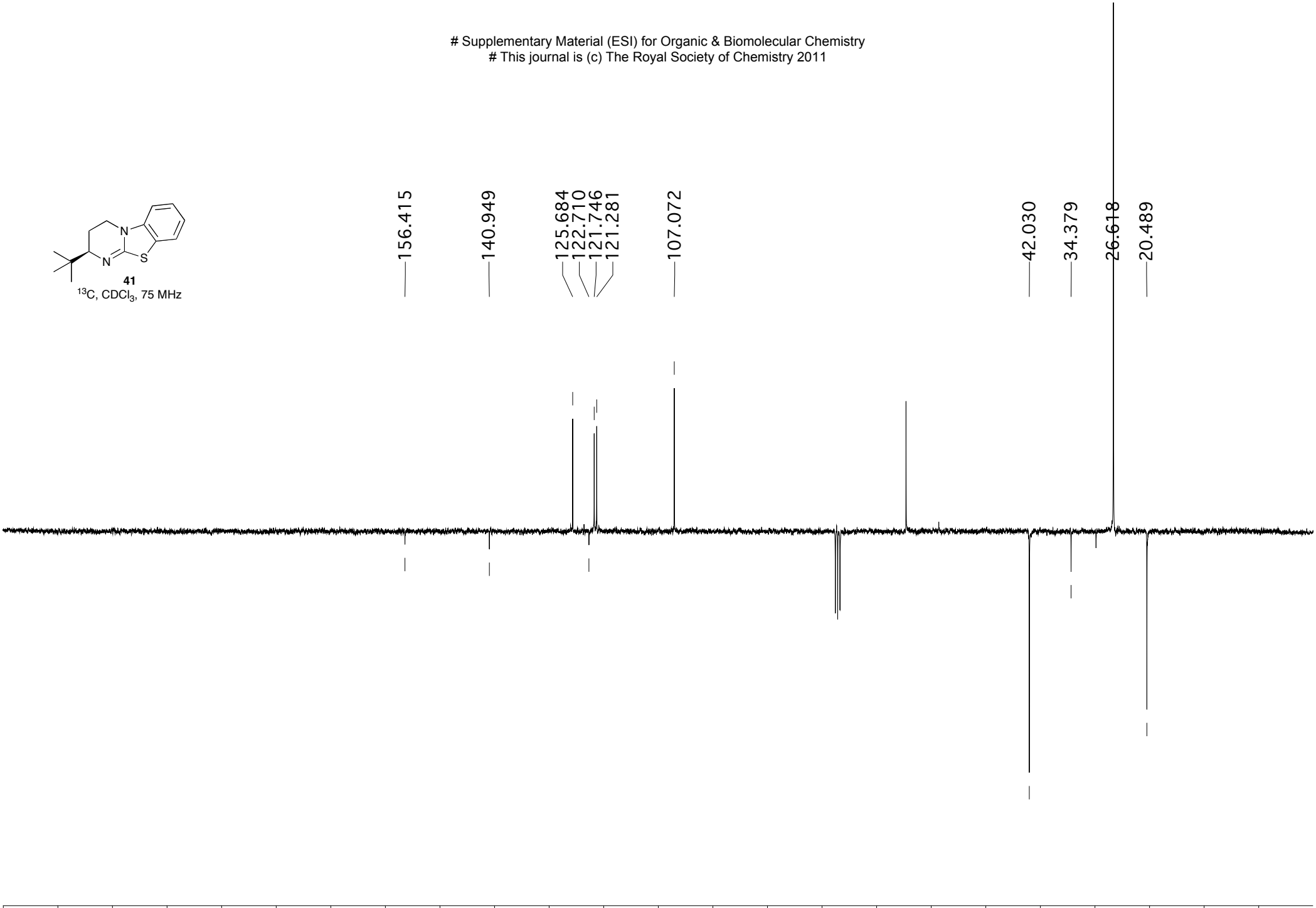


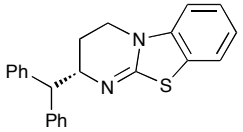
41

^{1}H, $CDCl_3$, 300 MHz



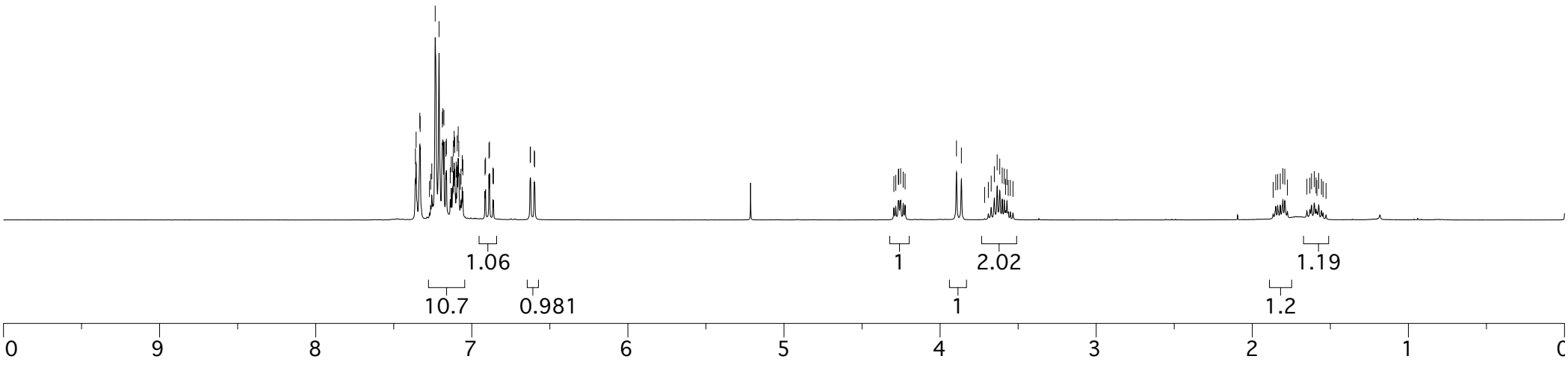
41
^{13}C, $CDCl_3$, 75 MHz





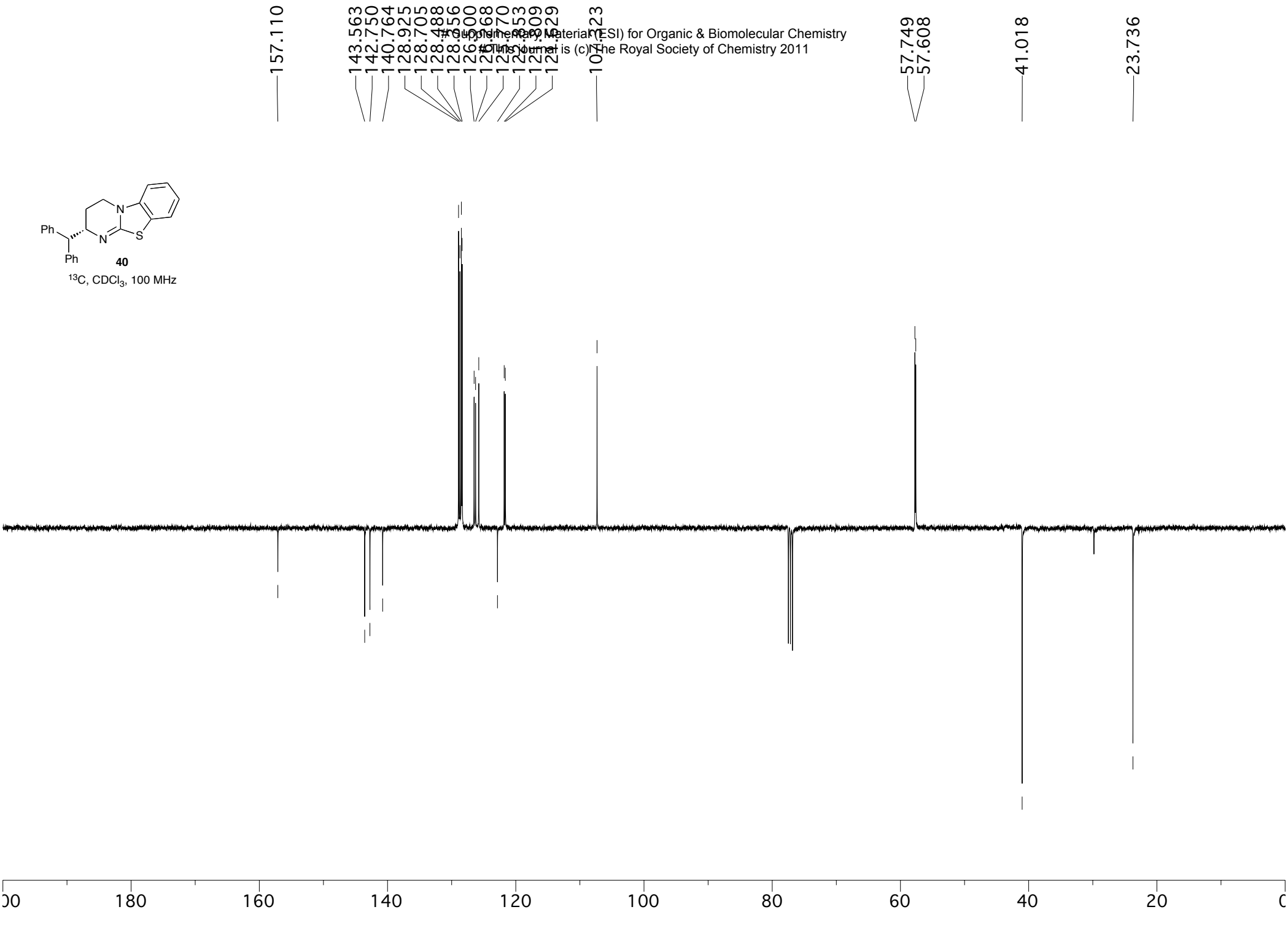
40

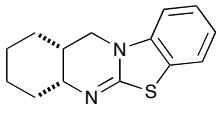
^{1}H, $CDCl_3$, 300 MHz



40

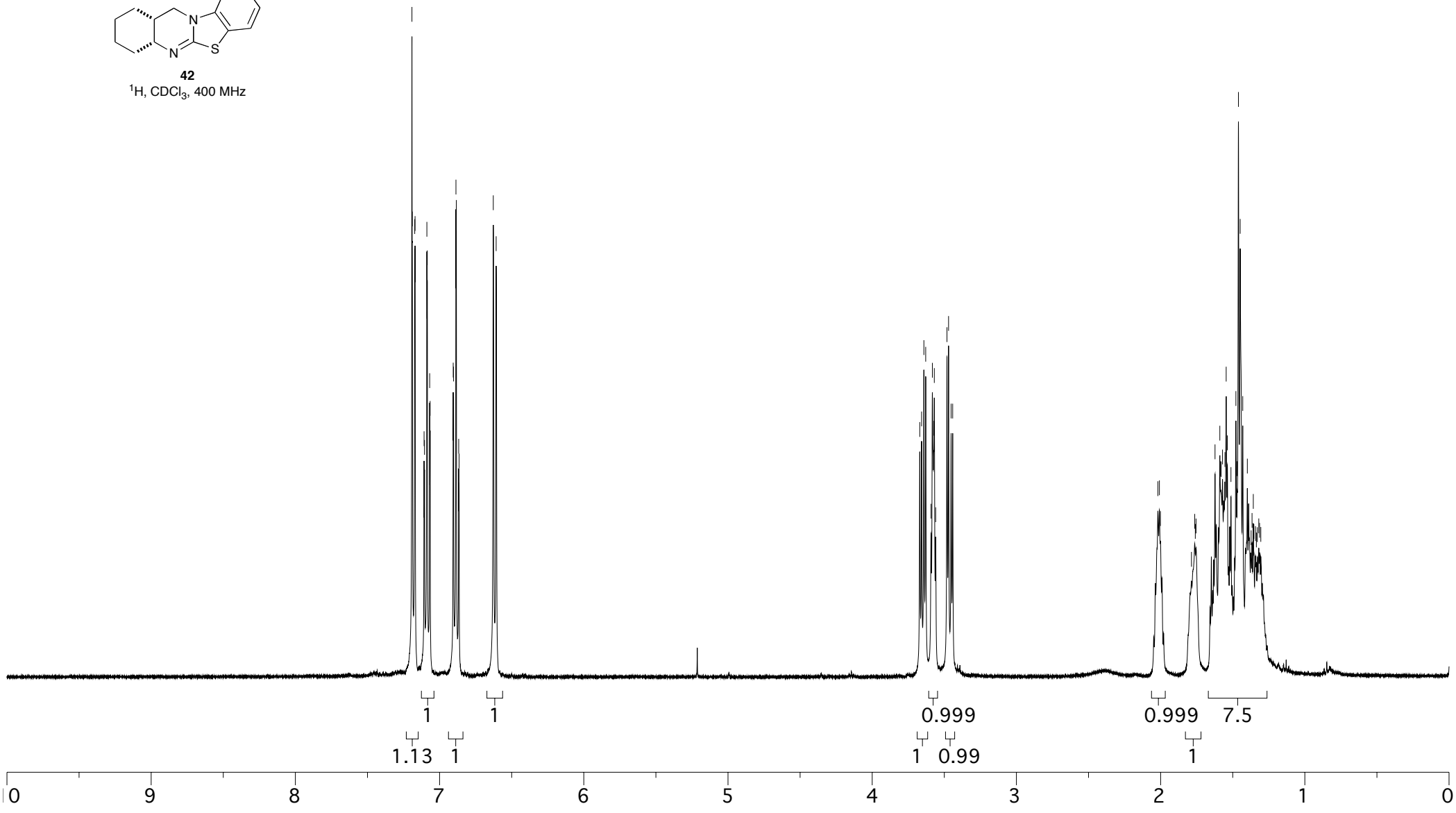
^{13}C, $CDCl_3$, 100 MHz





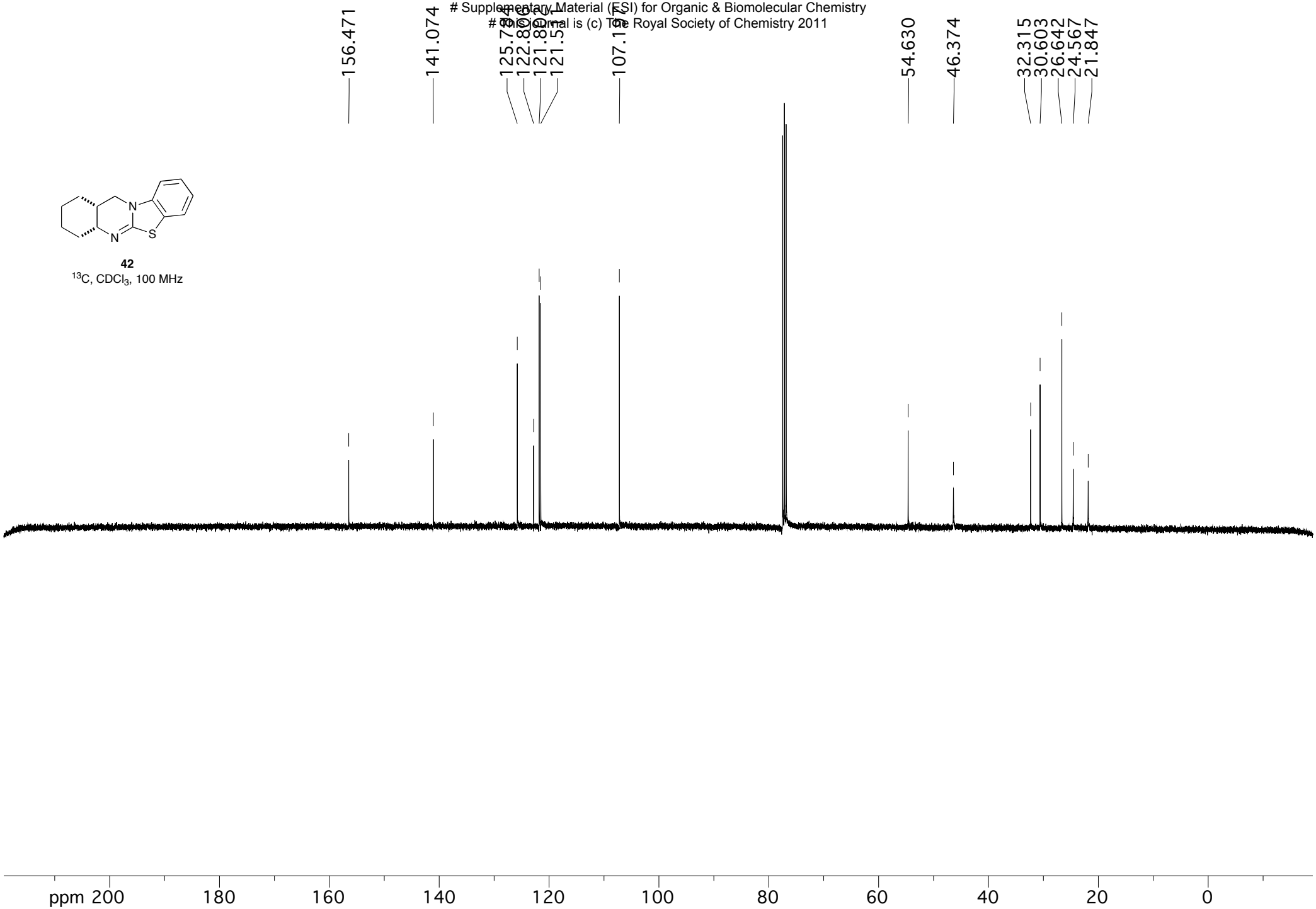
42

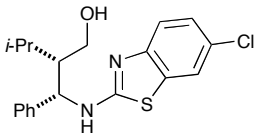
^{1}H, $CDCl_3$, 400 MHz



42

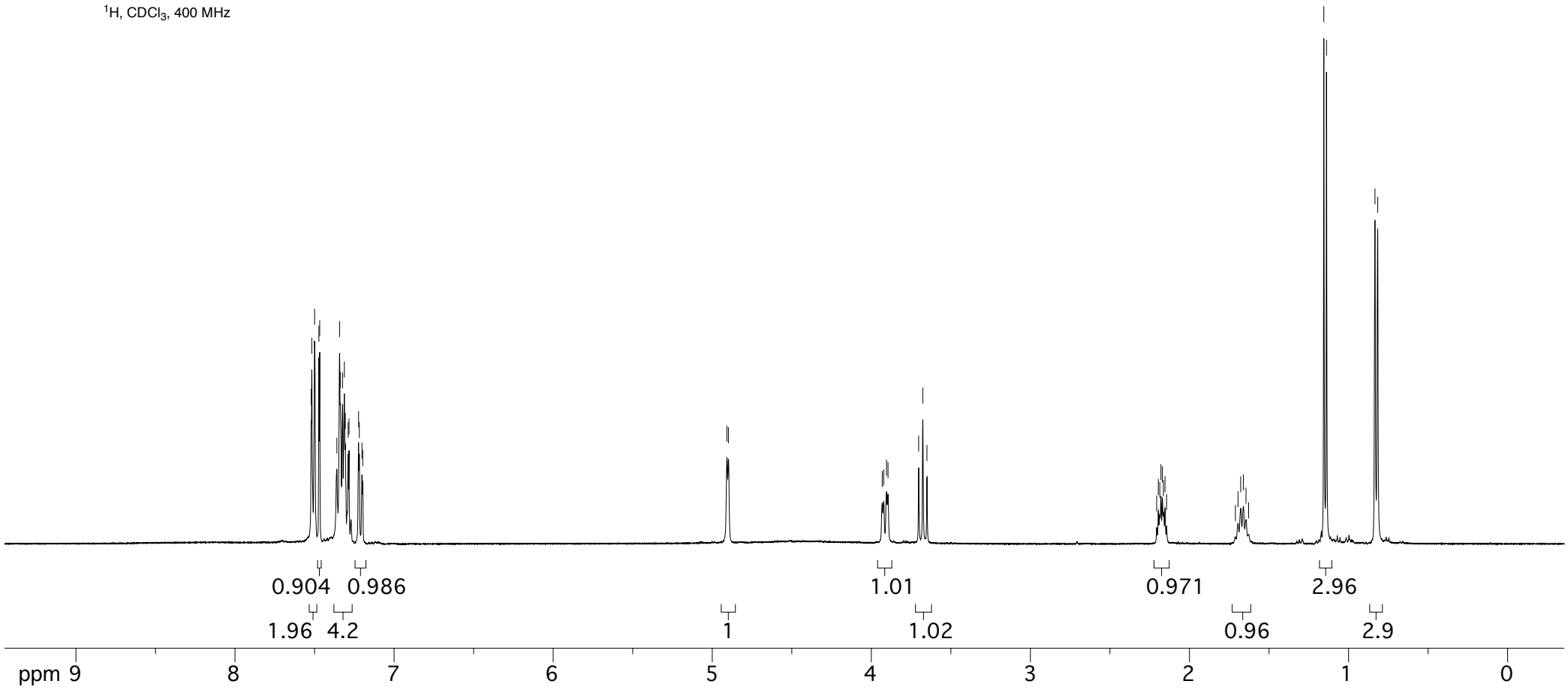
^{13}C, $CDCl_3$, 100 MHz





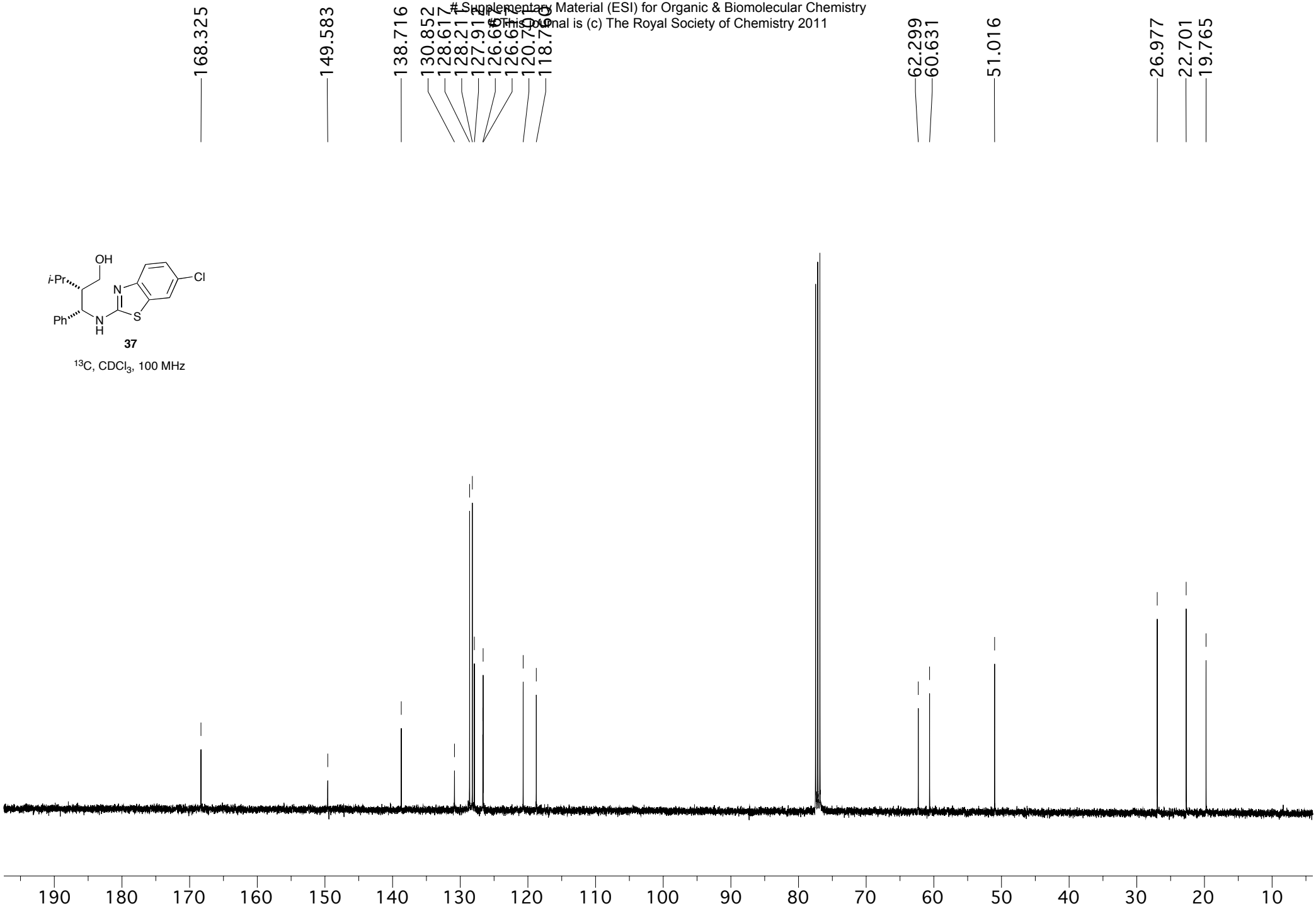
37

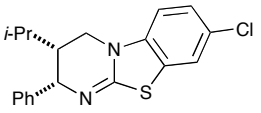
^{1}H, $CDCl_3$, 400 MHz



37

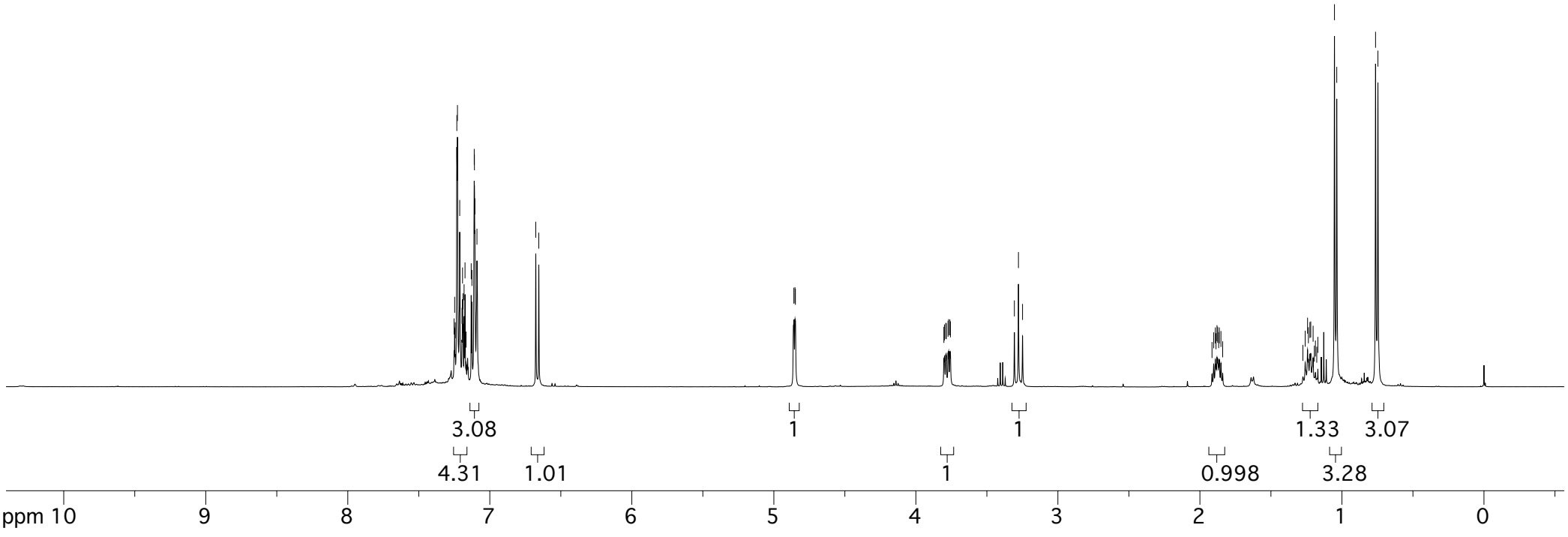
^{13}C, $CDCl_3$, 100 MHz

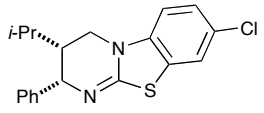




43

^{1}H, $CDCl_3$, 400 MHz





43

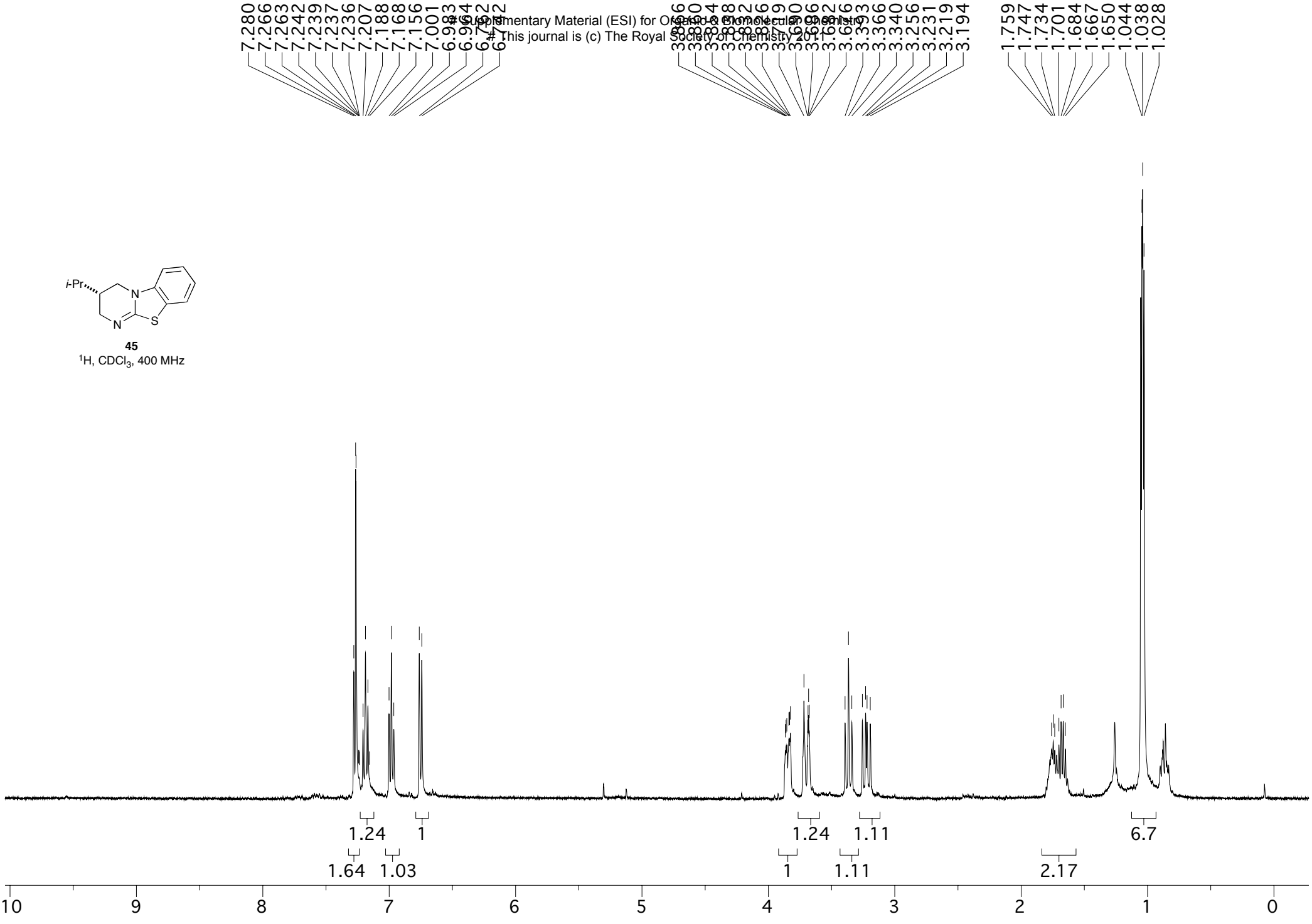
^{13}C, $CDCl_3$, 100 MHz

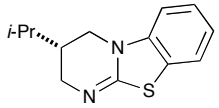
158.235
139.931
139.136
128.466
127.942
127.455
127.316
126.086
124.737
121.889
108.472
60.827
42.140
40.760
26.850
22.014
19.957

220 200 180 160 140 120 100 80 60 40 20 0

45

^{1}H, $CDCl_3$, 400 MHz

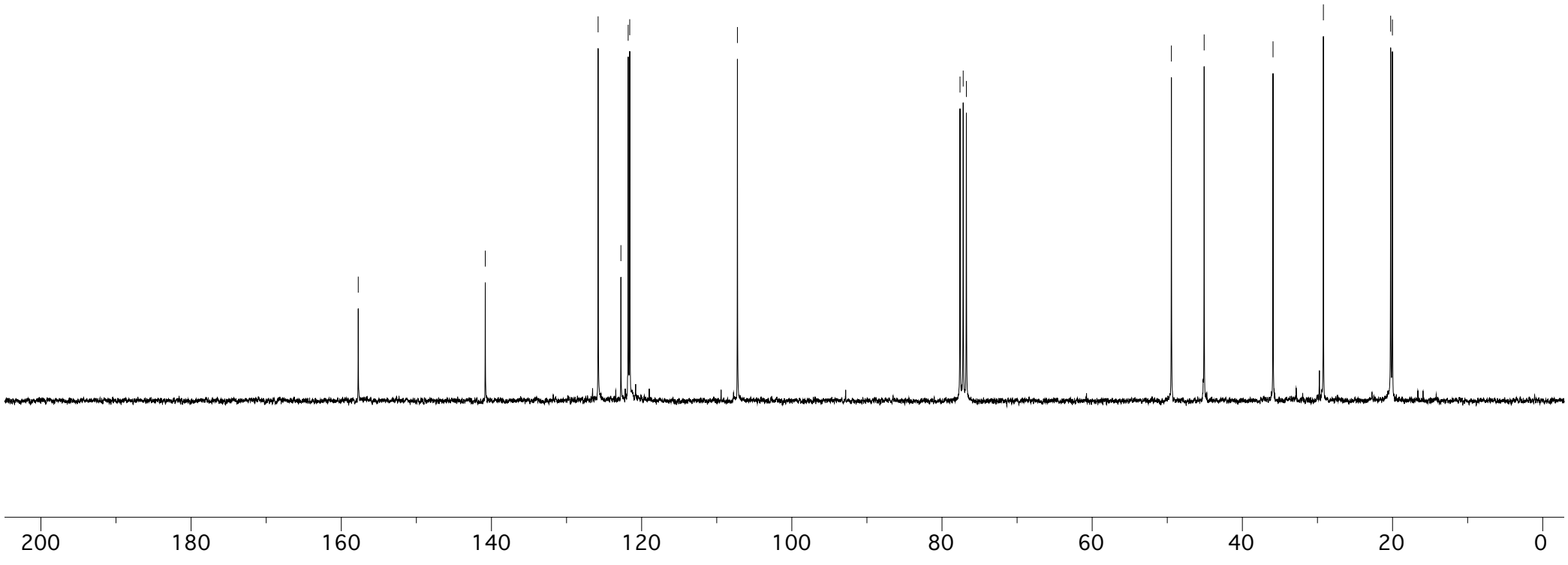




45

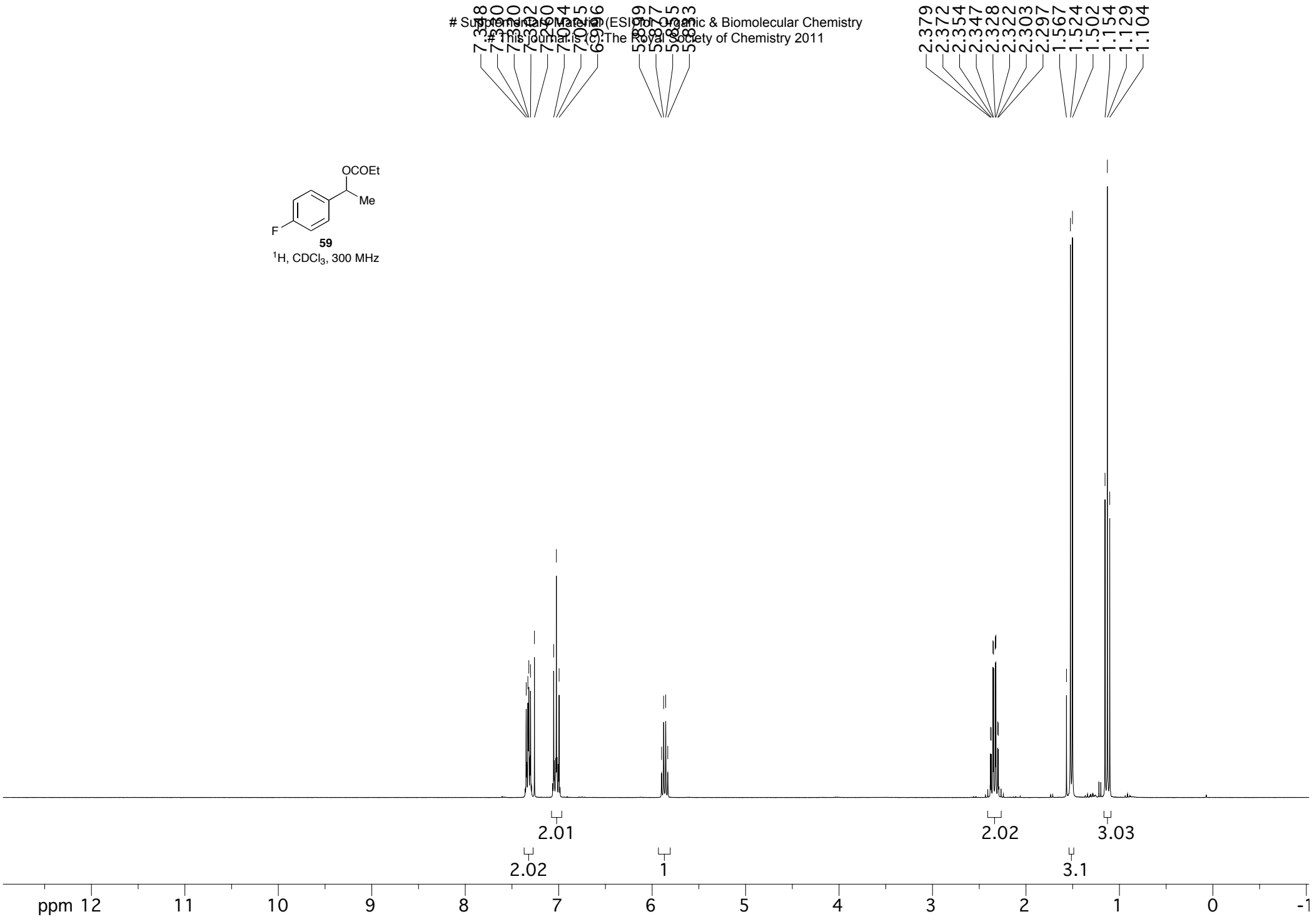
^{13}C, $CDCl_3$, 75 MHz

157.740
140.824
125.796
122.760
121.795
121.586
107.245
77.602
77.178
76.754
49.451
45.089
35.918
29.211
20.253
20.017



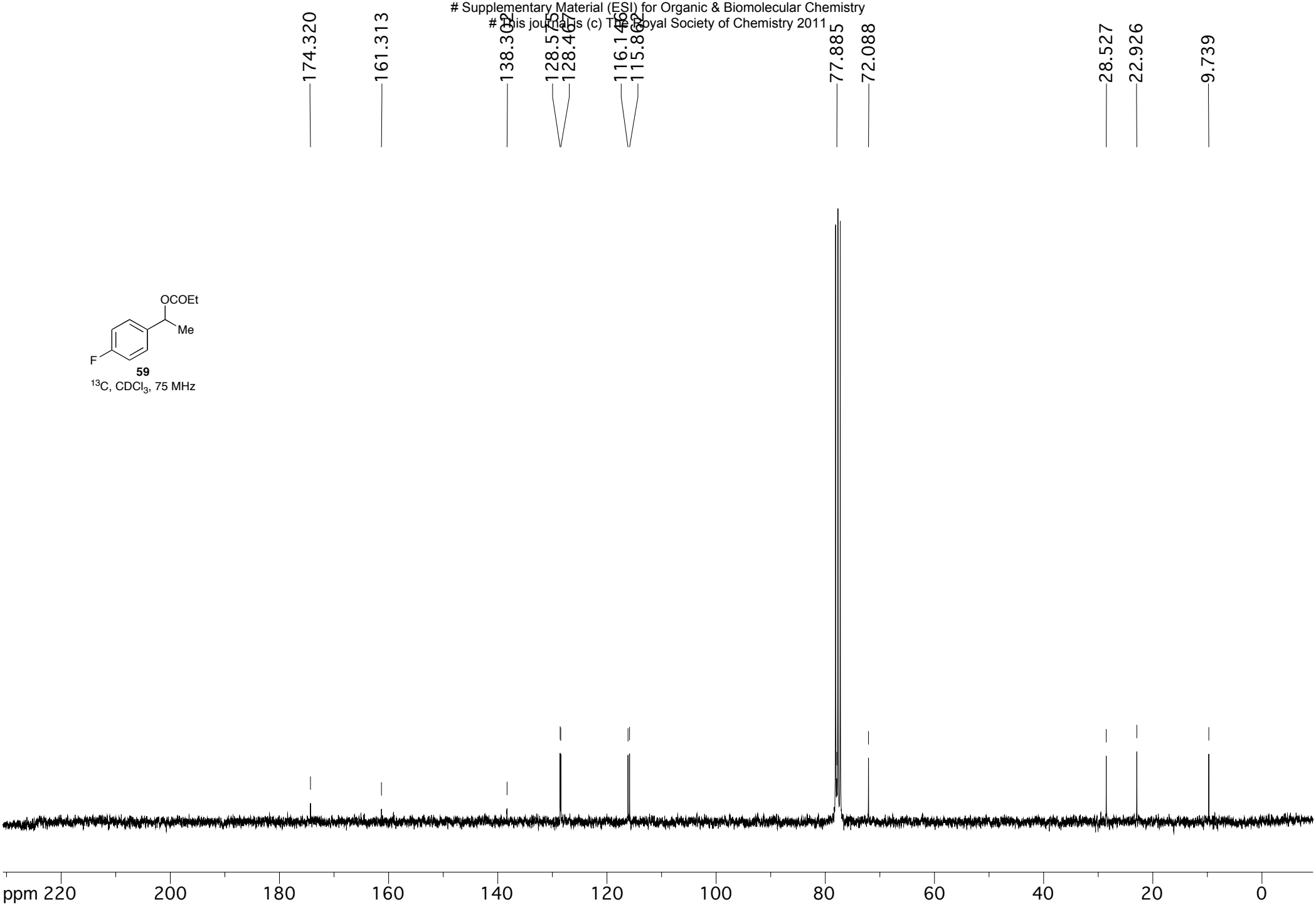
59

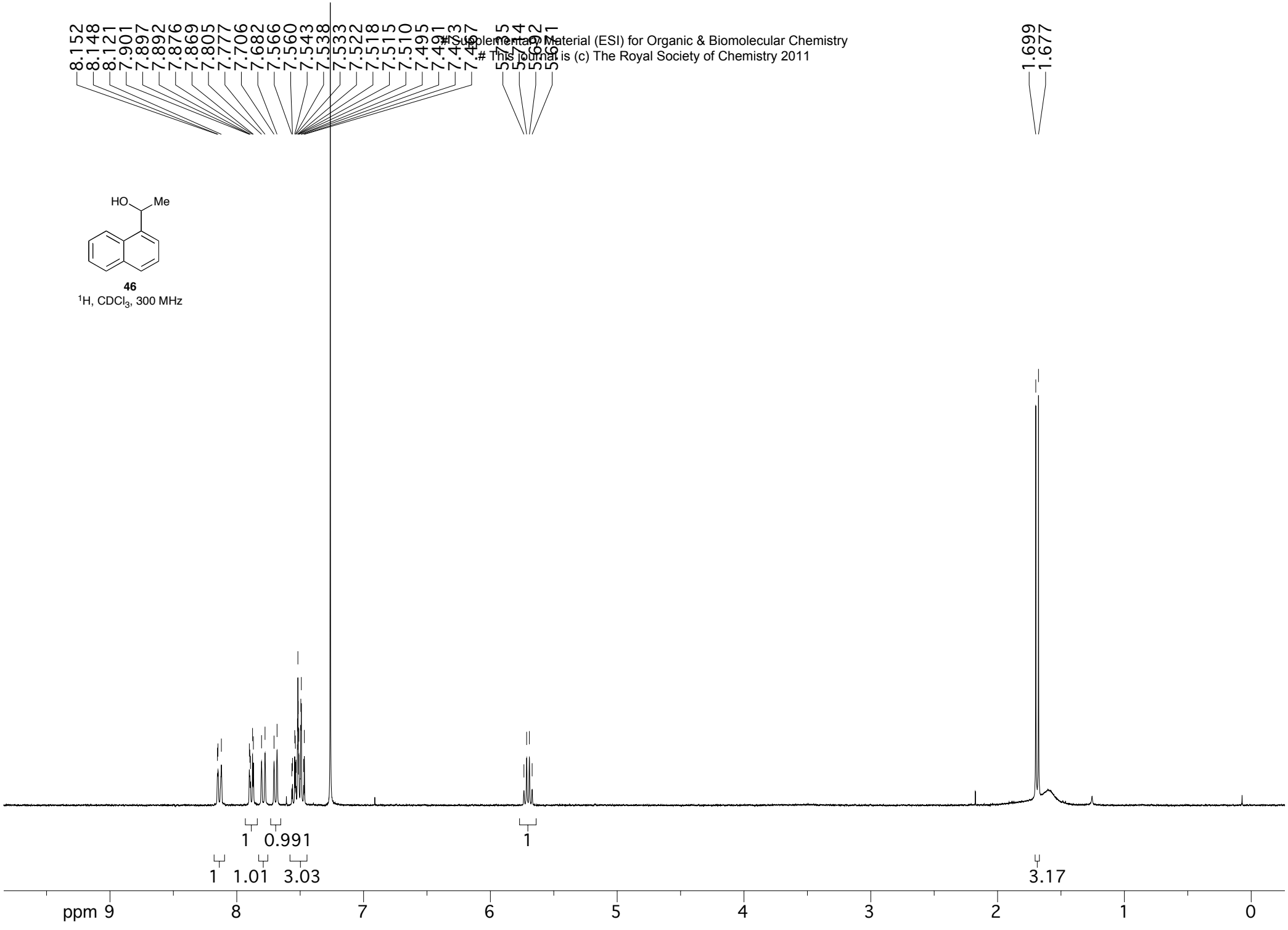
^{1}H, $CDCl_3$, 300 MHz



59

^{13}C, $CDCl_3$, 75 MHz



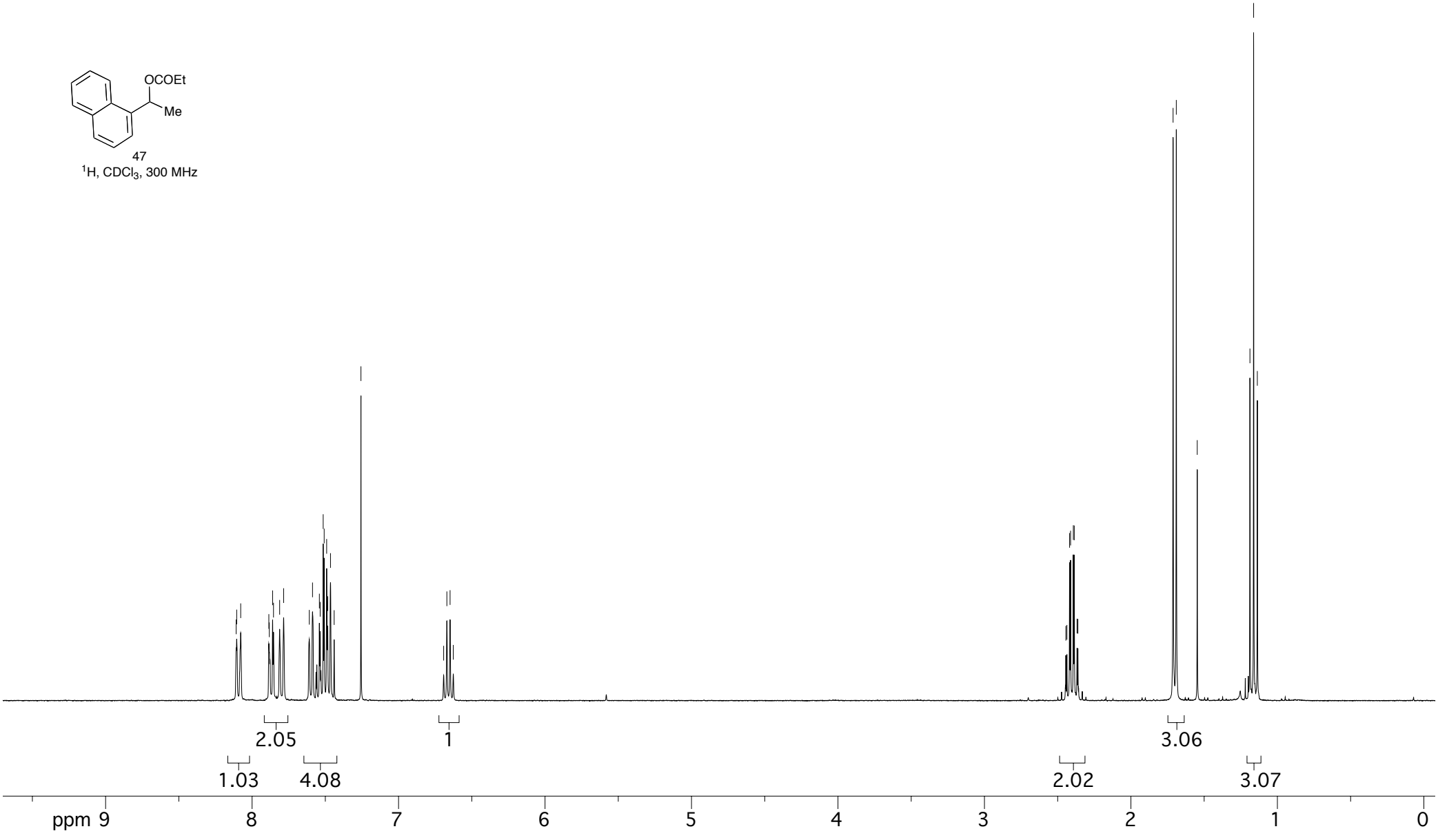


46

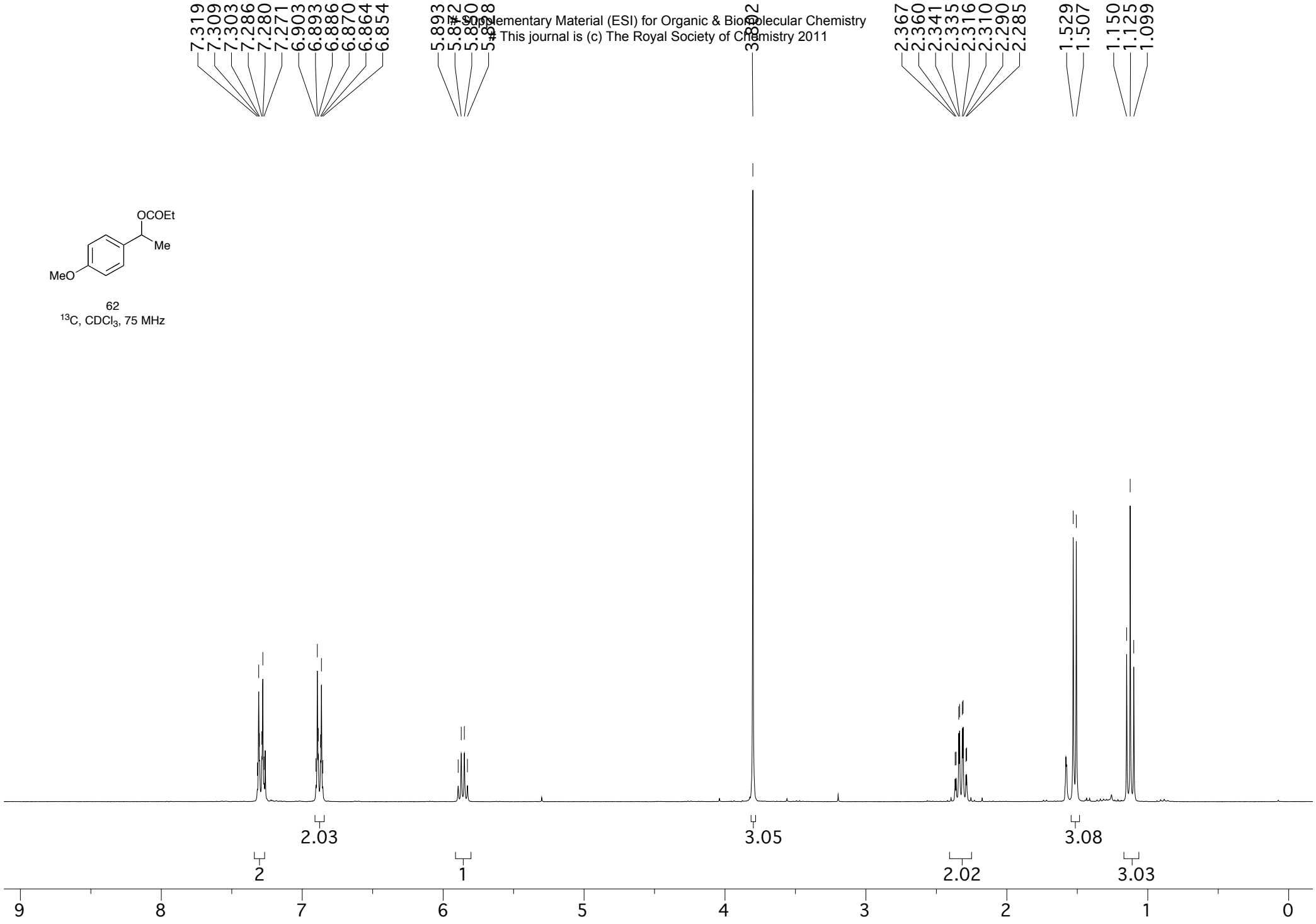
^{1}H, $CDCl_3$, 300 MHz

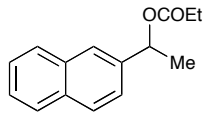
47

^{1}H, $CDCl_3$, 300 MHz



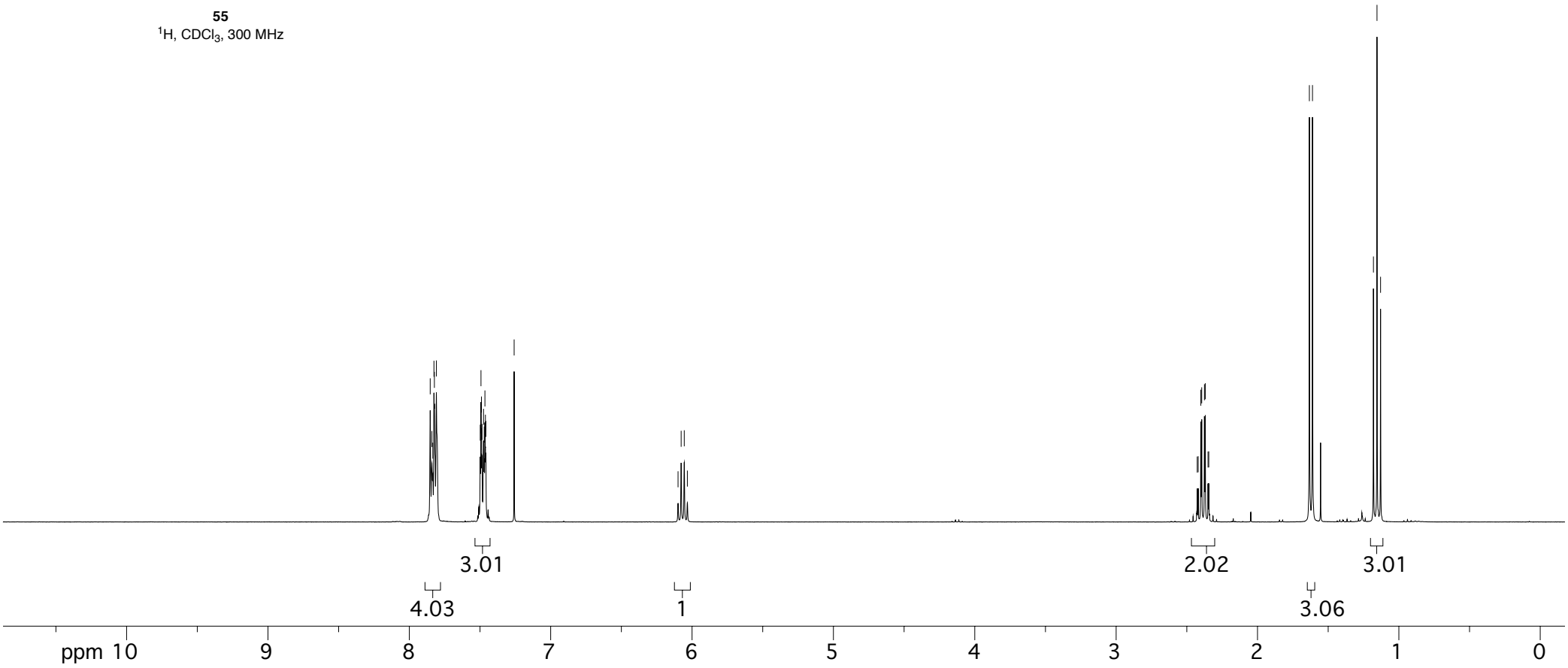
62
^{13}C, $CDCl_3$, 75 MHz

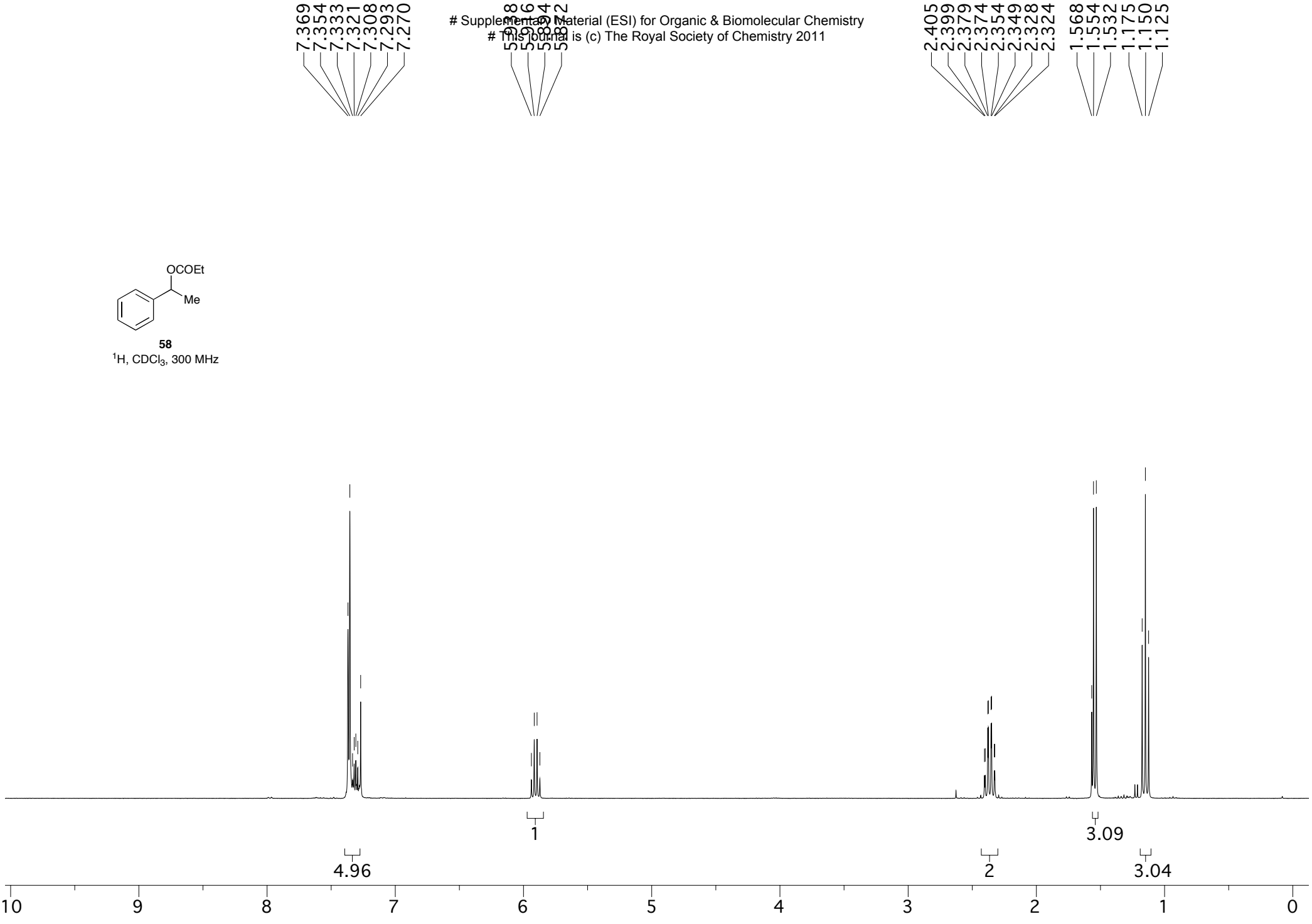




55

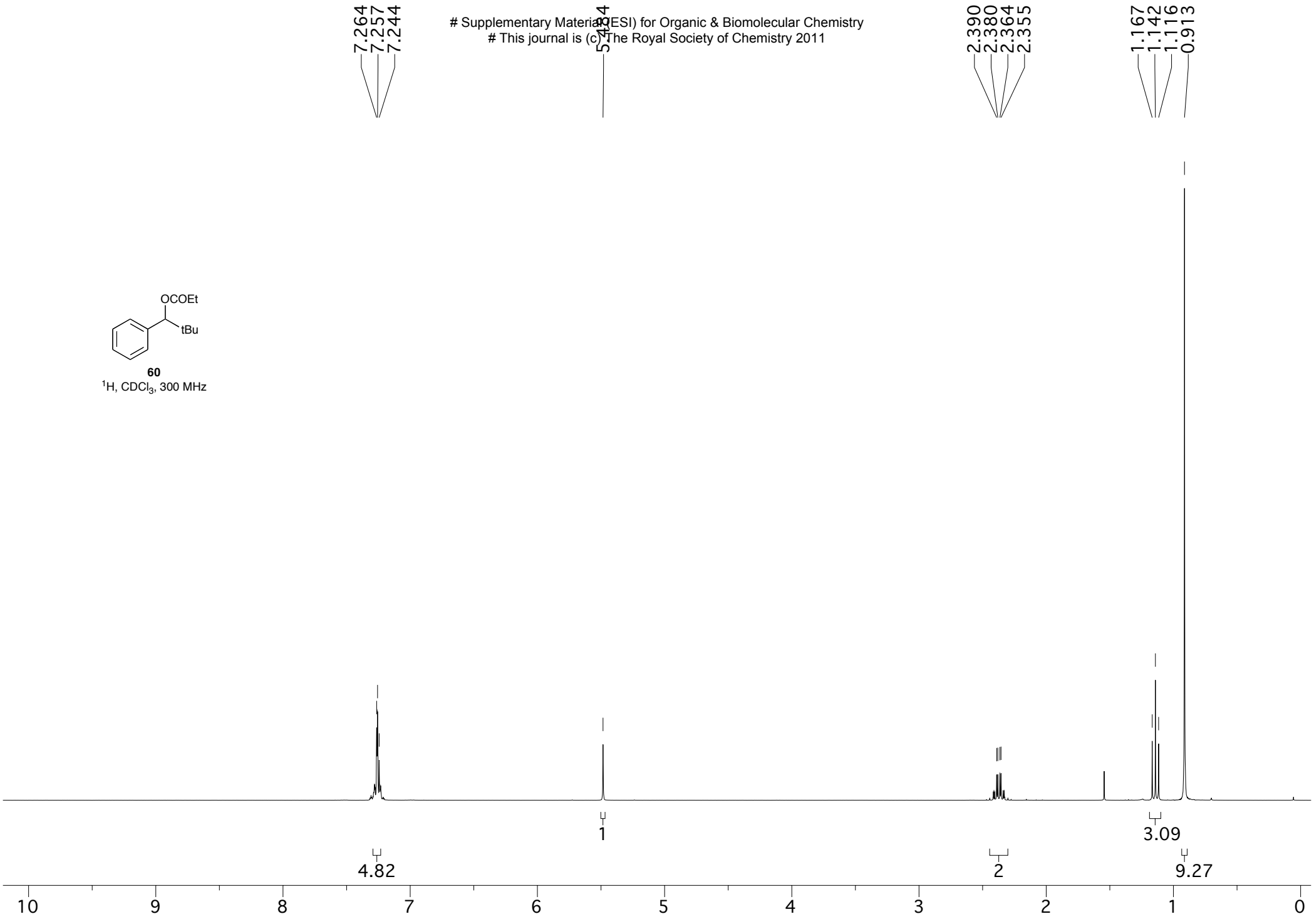
^{1}H, $CDCl_3$, 300 MHz

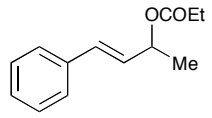




60

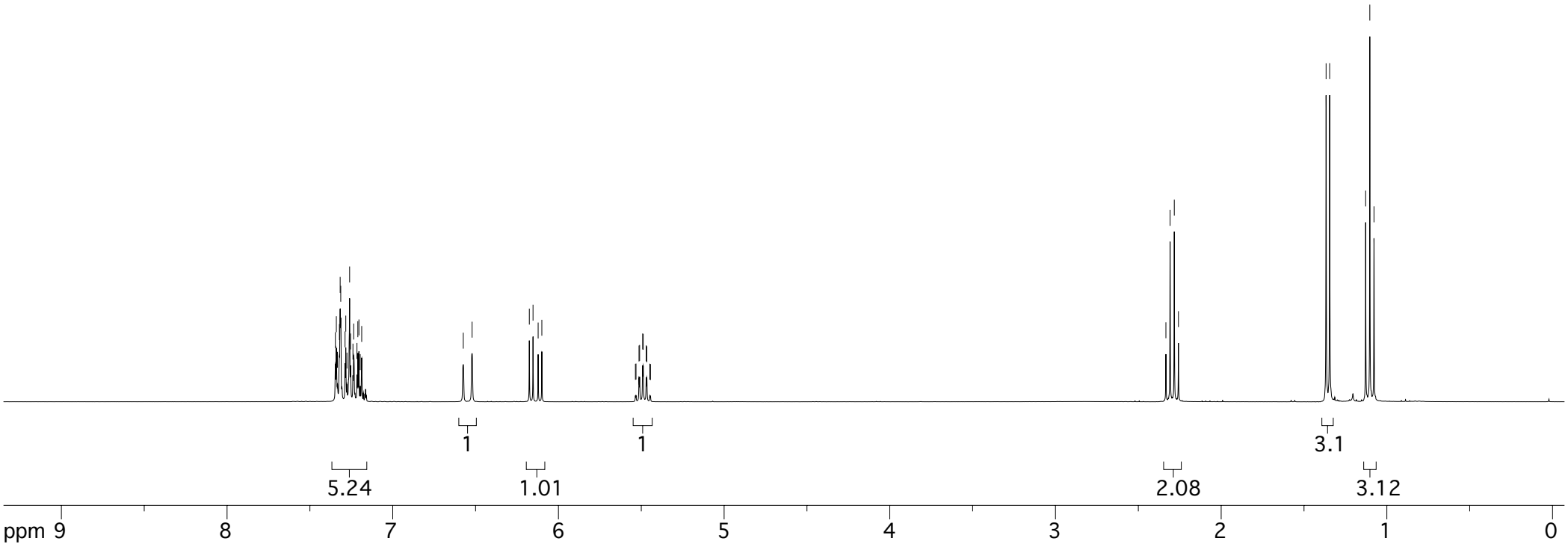
^{1}H, $CDCl_3$, 300 MHz

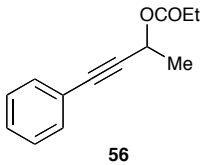




61

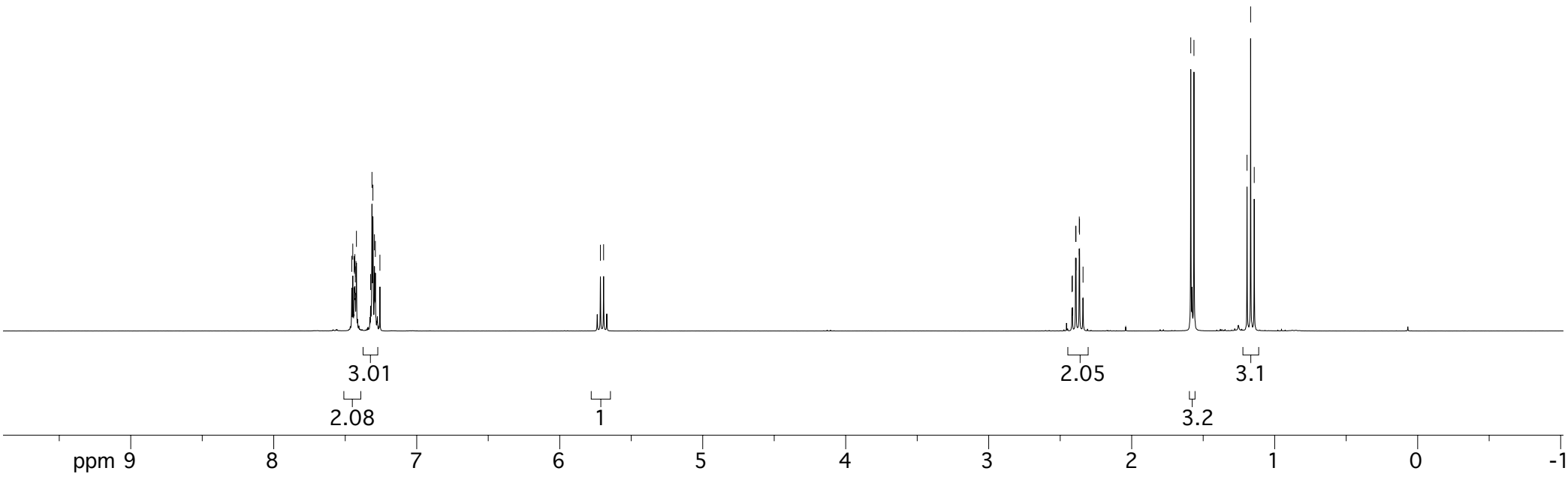
^{1}H, $CDCl_3$, 300 MHz





56

^{1}H, $CDCl_3$, 300 MHz



53

^{1}H, $CDCl_3$, 300 MHz