Electronic Supplementary Information (ESI) for

Facile access to 3,5-symmetrically disubstituted 1,2,4-thiadiazoles through phosphovanadomolybdic acids catalyzed aerobic oxidative dimerization of primary thioamides

Kazuhisa Yajima, Kazuya Yamaguchi, and Noritaka Mizuno*

Department of Applied Chemistry, School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan.

E-mail: tmizuno@mail.ecc.u-tokyo.ac.jp

Experimental details

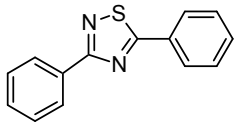
General: HPLC analyses were performed on Shimadzu Prominence system with a UV detector (Shimadzu SPD-20A, 254 nm) equipped with a Shiseido CAPCELL PAK UG80 column (4.6 mm ID × 250 mm length) using a mixture of acetonitrile/water as an eluent (9/1 v/v). GC analyses were performed on Shimadzu GC-2014 with a FID detector equipped with an InertCap 1 capillary column. GCMS spectra were recorded on Shimadzu GCMS-QP2010 at an ionization voltage of 70 eV equipped with an InertCap 5MS/Sil capillary column. Liquid state ^{1}H and ^{13}C NMR spectra were recorded on JEOL ECA-500. ^{1}H and ^{13}C NMR spectra were measured at 500 and 125 MHz, respectively, with TMS as an internal standard (δ = 0 ppm). $H_3PW_{12}O_{40}$, $H_4SiW_{12}O_{40}$, and $PMo_{12}O_{40}$ were obtained from Wako, and other heteropoly acids were obtained from Nippon Inorganic Colour & Chemical (the numbers of water of crystallization were 20–30 per polyanion). Solvents and substrates were obtained from Kanto Chemical, TCI, Wako, or Aldrich (reagent grade), and used as received.

Procedure for oxidative dimerization: 1 (0.5 mmol), $H_6PV_3Mo_9O_{40}$ (5 mol%), naphthalene (0.1 mmol, internal standard), and ethanol (4 mL) were placed in a Pyrex-glass tube reactor with a magnetic stir bar, and the reaction was carried out at 30 °C in 1 atm of O_2. The color of the reaction solution immediately after beginning was dark green for aromatic and heterocyclic thioamides (dark blue color of reduced $H_6PV_3Mo_9O_{40}$ + yellow color of thioamides) or dark blue (dark blue color of reduced $H_6PV_3Mo_9O_{40}$) and gradually changed to orange-yellow with the formation of elemental sulfur according to the consumption of **1** (Fig. S1). During the reaction, the conversion of **1** and the yield of **2** (based on **1**) were periodically monitored by HPLC analysis. The typical HPLC charts are shown in Fig. S3. With regard to aliphatic thioamides, the conversion of **1** and the yield of **2** were periodically monitored by GC analysis.

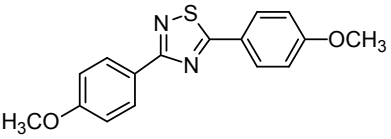
As for product isolation, naphthalene was not used. For the isolation of **2a**–**2d**, the reactions were carried out in acetonitrile. For other thiadiazoles, the reactions were carried out in ethanol. After complete conversion of **1**, *n*-hexane (25 mL) and water (25 mL) were added

to the reaction mixture (without removal of elemental sulfur), followed by extraction with *n*-hexane (25 mL × 3) to afford **2**. All products were confirmed by their MS and NMR data, and the data are summarized below.

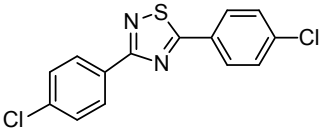
Compound data



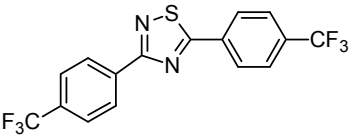
3,5-Diphenyl-1,2,4-thiadiazole (2a): As for isolation, the reaction was carried out in acetonitrile for 2 h. Melting point: 88.0−88.5 ºC. MS (EI) *m*/*z* (%): 238 (37) [M^+], 135 (100), 103 (18), 77 (19). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 8.39−8.41 (m, 2H), 8.05−8.07 (m, 2H), 7.50−7.55 (m, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$, TMS): δ 188.1, 173.8, 132.9, 131.9, 130.7, 130.3, 129.3, 128.7, 128.3, 127.5.



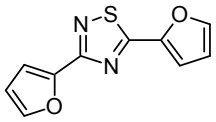
3,5-Bis(4-methoxyphenyl)-1,2,4-thiadiazole (2b): As for isolation, the reaction was carried out in acetonitrile for 2 h. Melting point: 138.5−139.0 ºC. MS (EI) *m*/*z* (%): 299 (11), 298 (53) [M^+], 166 (11), 165 (100), 150 (26), 133 (41), 103 (11), 90 (12). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 8.31−8.33 (m, 2H), 7.98−8.00 (m, 2H), 7.00−7.02 (m, 4H), 3.894 (s, 1H), 3.885 (s, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$, TMS): δ 187.4, 173.4, 162.5, 161.3, 129.9, 129.2, 126.0, 123.7, 114.5, 114.0, 55.5, 55.4.



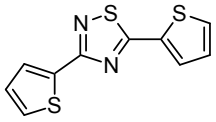
3,5-Bis(4-chlorophenyl)-1,2,4-thiadiazole (2c): As for isolation, the reaction was carried out in acetonitrile for 6 h. Melting point: 145.0−146.0 ºC. MS (EI) *m*/*z* (%): 308 (20), 306 (28), 171 (38), 169 (100), 102 (13), 75 (12). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 8.31−8.33 (m, 2H), 7.98−7.99 (m, 2H), 7.47−7.52 (m, 4H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$, TMS): δ 187.1, 172.8, 138.2, 136.6, 131.2, 129.7, 129.6, 129.0, 128.7.



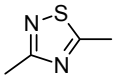
3,5-Bis(4-trifluoromethylphenyl)-1,2,4-thiadiazole (2d): As for isolation, the reaction was carried out in acetonitrile for 2 h. Melting point: 98.5−99.0 ºC. MS (EI) *m*/*z* (%): 374 (25) [M^+], 204 (10), 203 (100), 145 (12), 77 (19). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 8.51 (d, J = 8.0 Hz, 2H), 8.18 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$, TMS): δ 187.0, 172.8, 138.1, 136.5, 131.1, 129.6, 128.9, 128.6, 128.2.



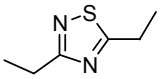
3,5-Bis(furan-2-yl)-1,2,4-thiadiazole (2e): As for isolation, the reaction was carried out in ethanol for 2 h. Melting point: 101.5−102.0 ºC. MS (EI) *m*/*z* (%) : 219 (10), 218 (76) [M^+], 125 (100), 97 (10), 93 (14), 70 (10). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.64 (dd, J = 2.0, 0.5 Hz, 1H), 7.61 (dd, J = 2.0, 0.5 Hz, 1H), 7.29 (dd, J = 3.5, 0.5 Hz, 1H), 7.23 (dd, J = 3.5, 0.5 Hz, 1H), 6.64 (dd, J = 3.5, 2.0 Hz, 1H), 6.57 (dd, J = 3.5, 2.0 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$, TMS): δ 177.0, 164.9, 148.1, 146.5, 145.6, 144.5, 112.71, 112.68, 112.6, 111.8.



3,5-Bis(thiophen-2-yl)-1,2,4-thiadiazole (2f): As for isolation, the reaction was carried out in ethanol for 2 h. Melting point: 90.0−91.0 ºC. MS (EI): *m*/*z* (%): 250 (51) [M^+], 141 (100), 109 (24). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.93 (dd, J = 3.5, 1.0 Hz, 1H), 7.70 (dd, J = 3.5, 1.0 Hz, 1H), 7.59 (dd, J = 5.0, 1.0 Hz, 1H), 7.46 (dd, J = 5.0, 1.0 Hz, 1H), 7.17 (dd, J = 5.0, 3.5 Hz, 1H), 7.15 (dd, J = 5.0, 3.5 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$, TMS): δ 180.7, 168.4, 136.2, 133.1, 130.6, 129.9, 129.2, 128.8, 128.4, 127.9.

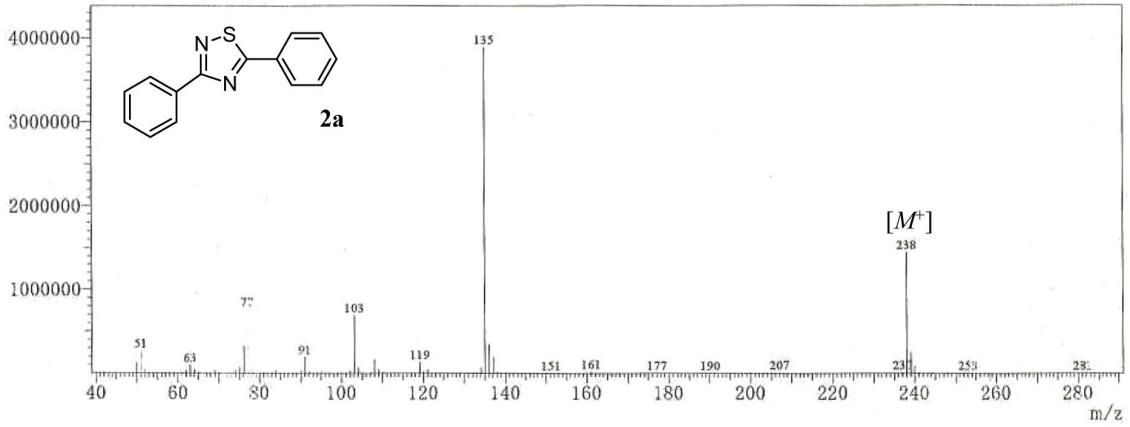


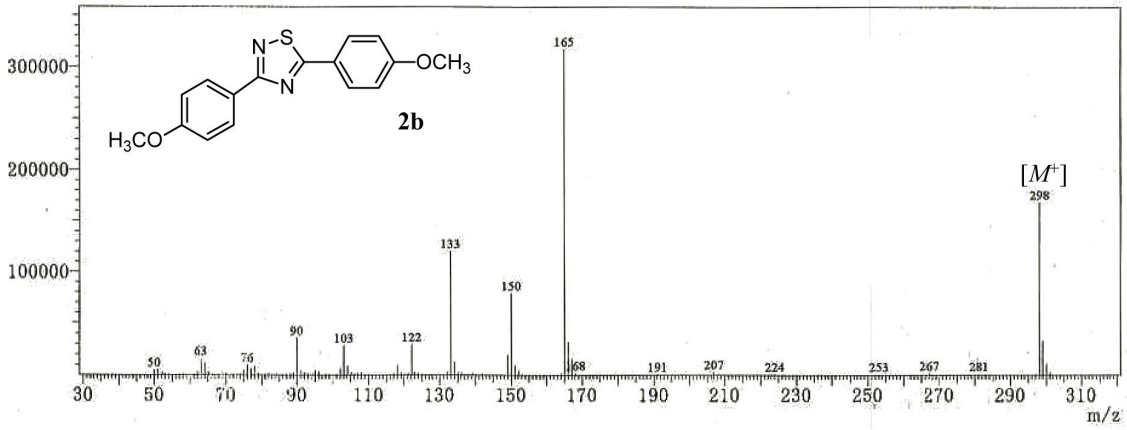
3,5-Dimethyl-1,2,4-thiadiazole (2g): MS (EI) *m*/*z* (%): 114 (38) [M^+], 73 (100). The reaction was carried out in CD_3OD, and the NMR spectra of the filtrate were measured after the reaction. ^{1}H NMR (500 MHz, CD_3OD, TMS): δ 2.79 (s, 3H), 2.58 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, CD_3OD, TMS): δ 189.1, 174.1, 18.3, 16.4.

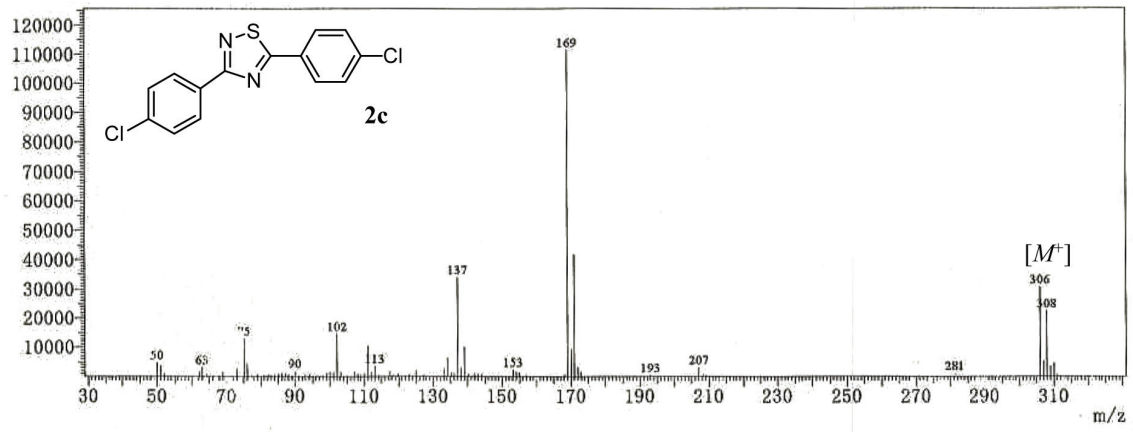


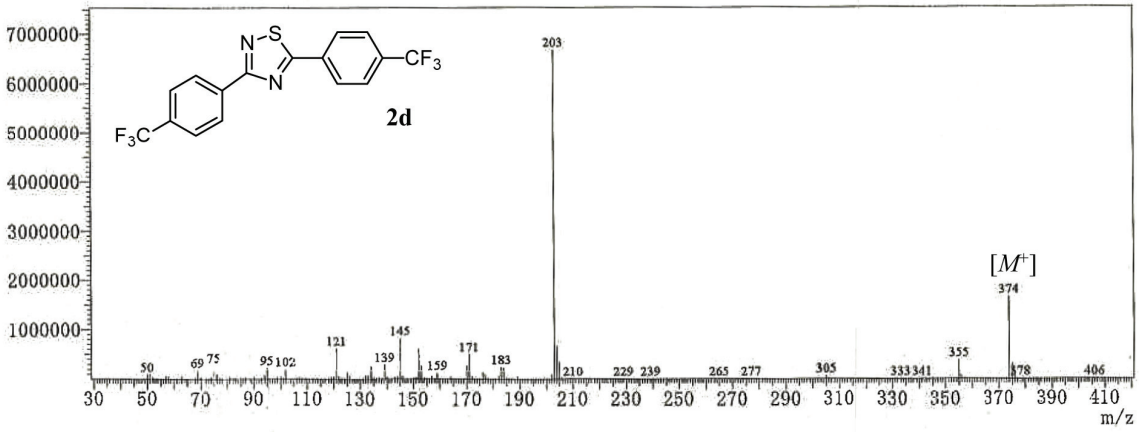
3,5-Diethyl-1,2,4-thiadiazole (2h): MS (EI) *m*/*z* (%): 142 (35) [M^+], 87 (100), 86 (24), 59 (10). The reaction was carried out in CD_3OD, and the NMR spectra of the filtrate were measured after the reaction. ^{1}H NMR (500 MHz, CD_3OD, TMS): δ 3.14 (q, J = 7.5 Hz, 2H), 2.94 (q, J = 7.5 Hz, 2H), 1.41 (t, J = 7.5 Hz, 3H), 1.34 (t, J = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, CD_3OD, TMS): δ 195.6, 179.3, 27.0, 25.5, 13.8, 12.6.

MS spectra

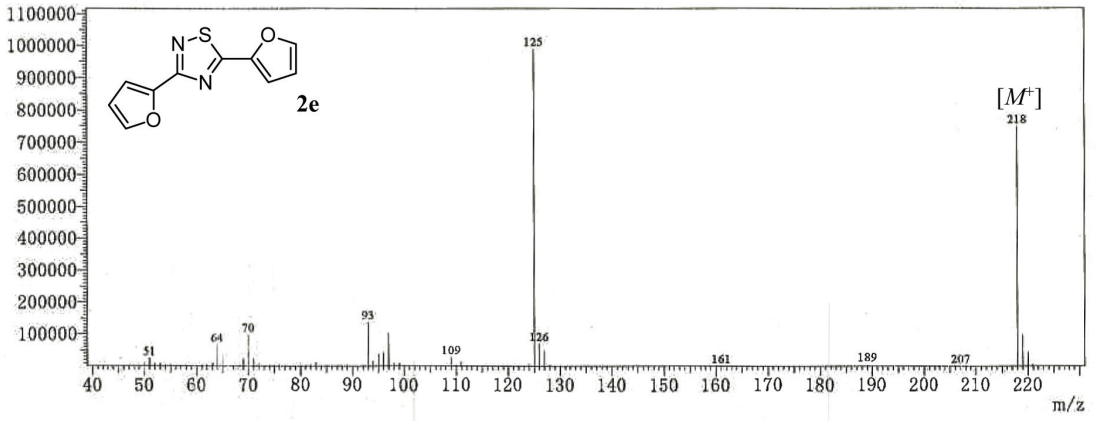

2a
[M+]
238
135
103
77
51
63
91
119
151
161
177
190
207
m/z

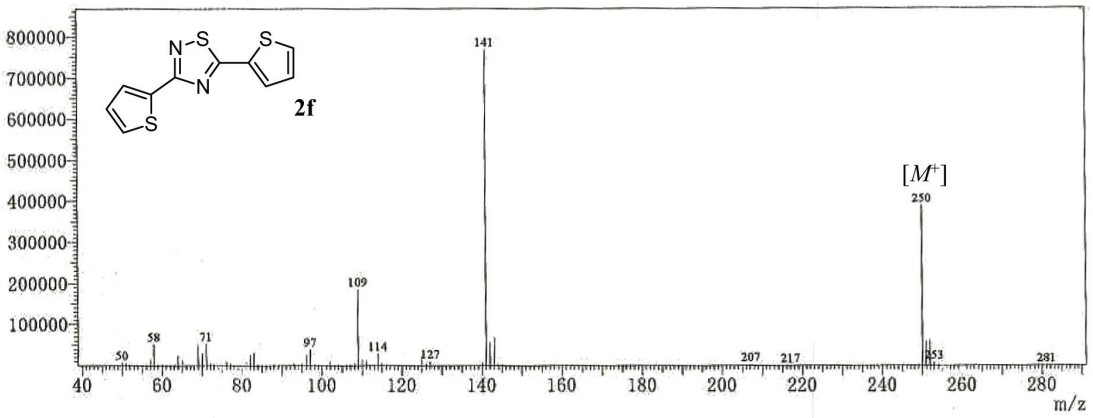

2b
OCH3
H3CO
[M+]
298
165
133
150
90
103
122
50
63
76
68
191
207
224
253
267
281
m/z

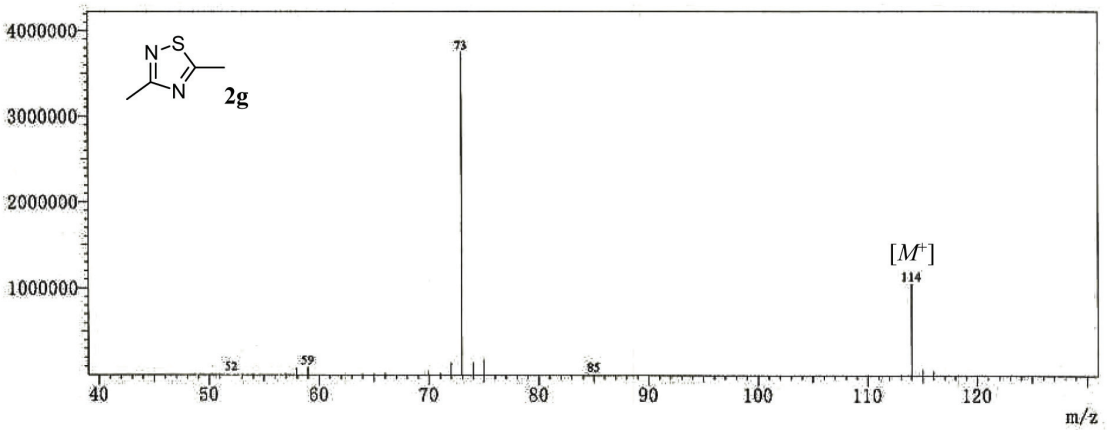

2c
Cl
Cl
[M+]
306
308
169
137
102
50
65
75
90
113
153
193
207
281
m/z

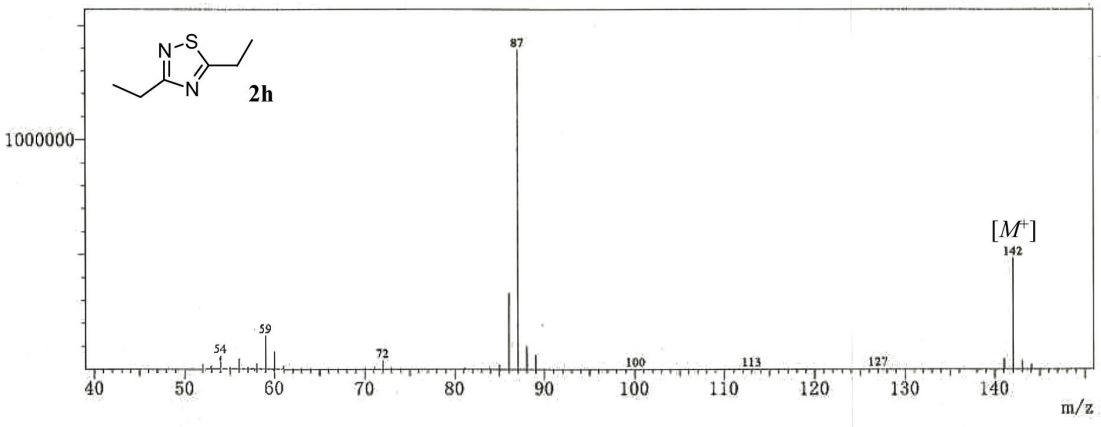

2d
CF3
F3C
[M+]
374
203
145
121
139
171
159
183
50
69
75
95
102
210
229
239
265
277
305
333
341
355
378
406
m/z

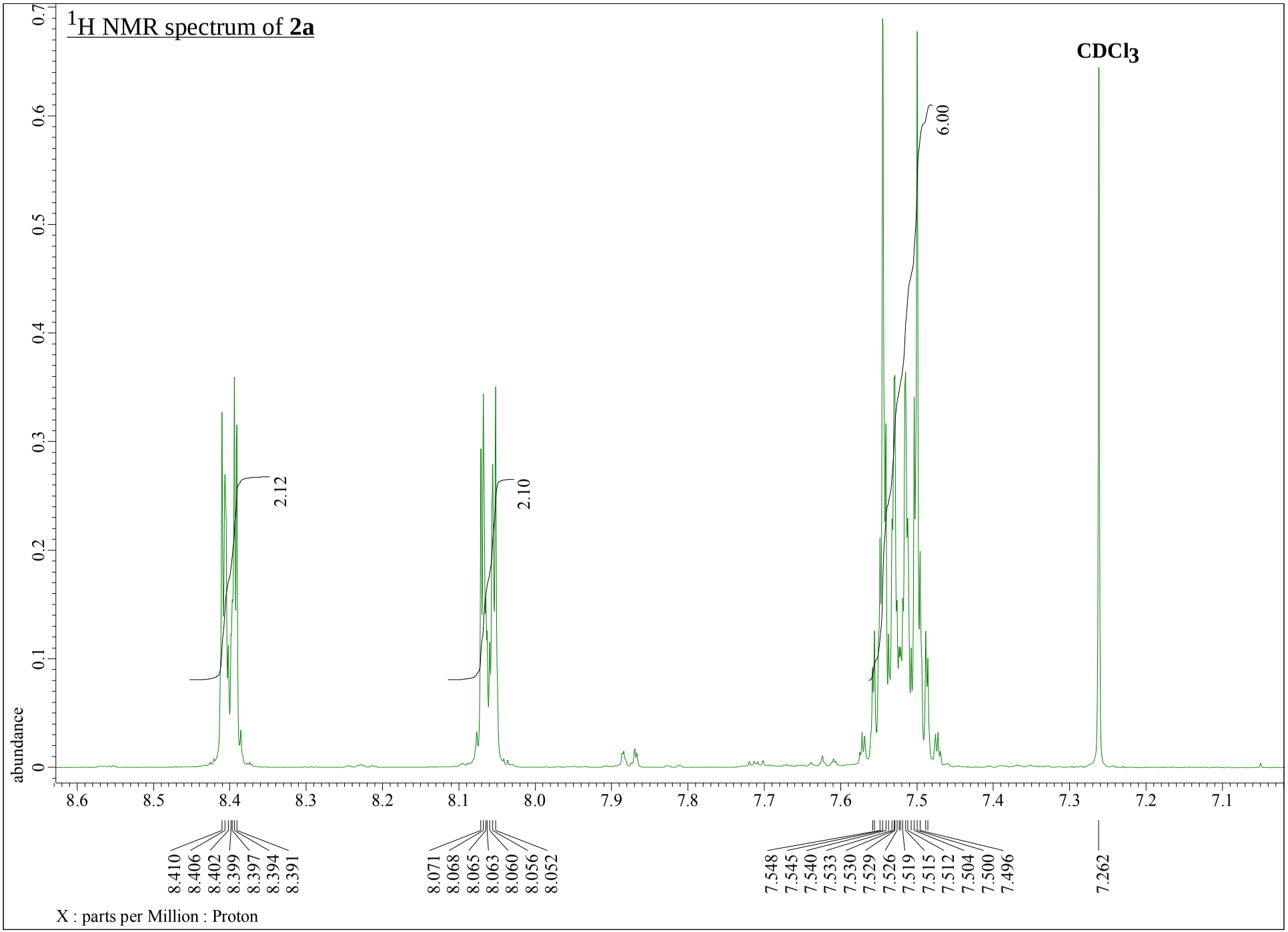
MS spectra

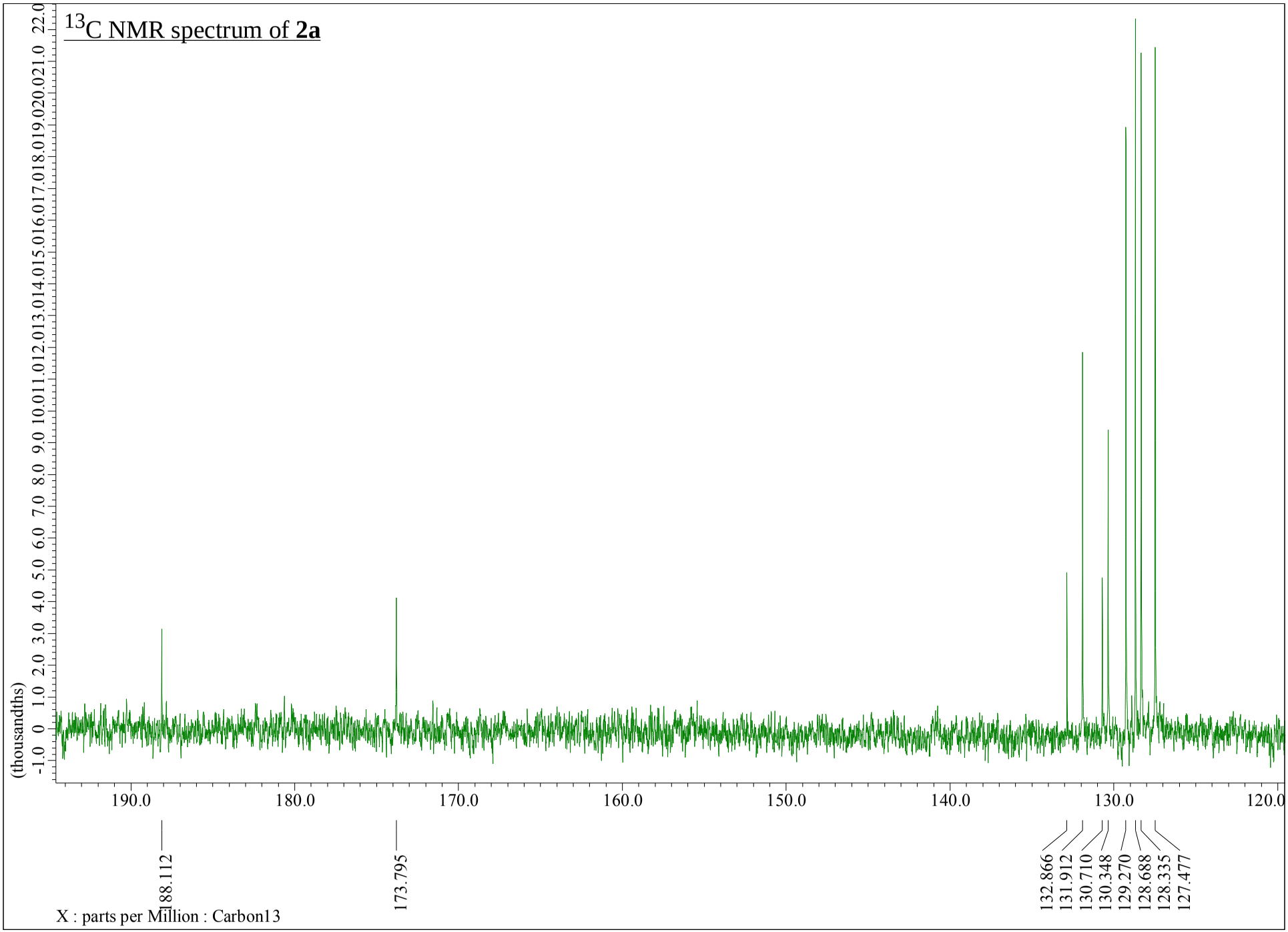

2e
125
[M+]
218
93
70
64
51
109
126
161
189
207
m/z

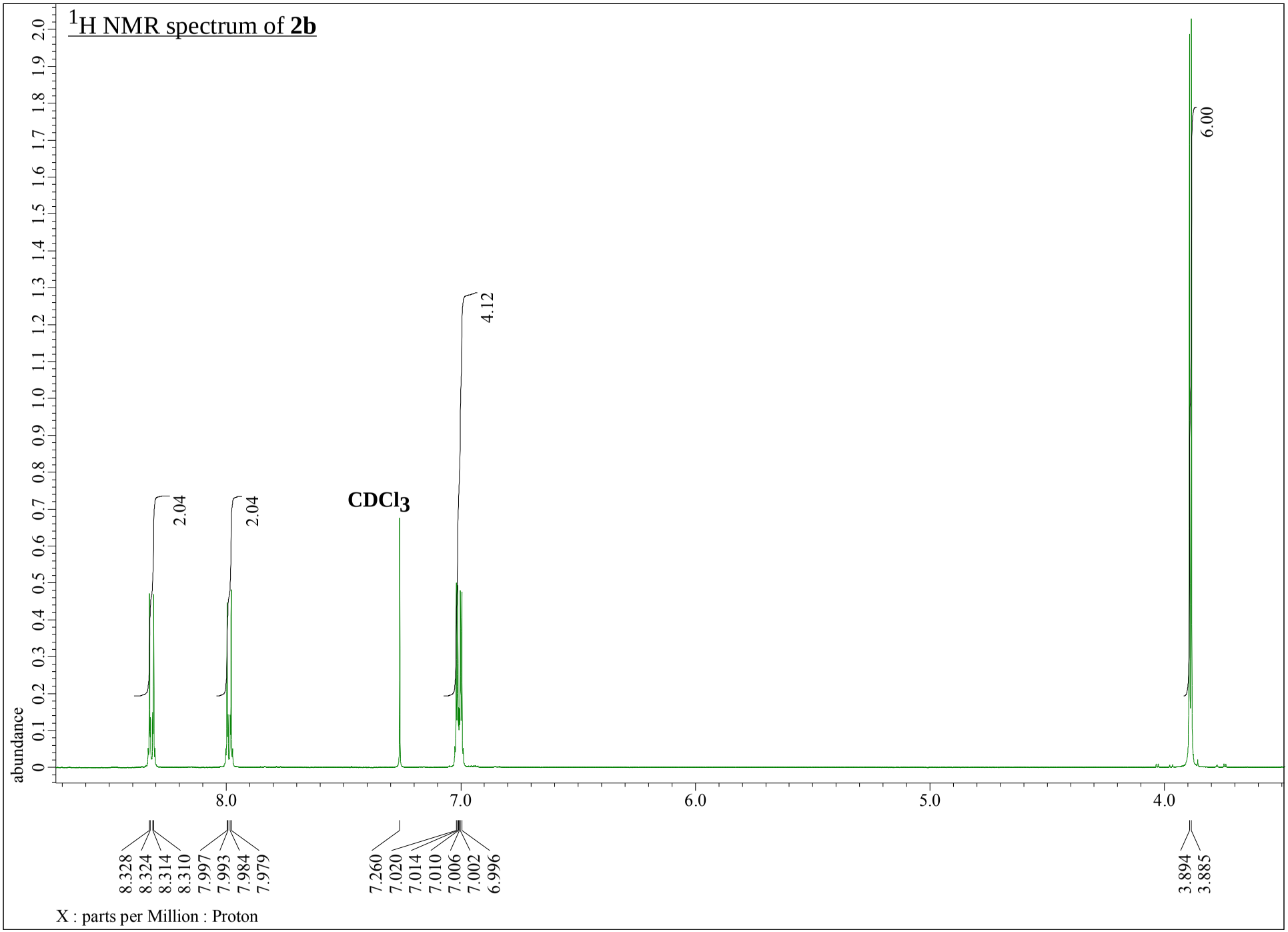

2f
141
[M+]
250
109
58
71
97
114
127
207
217
253
281
m/z

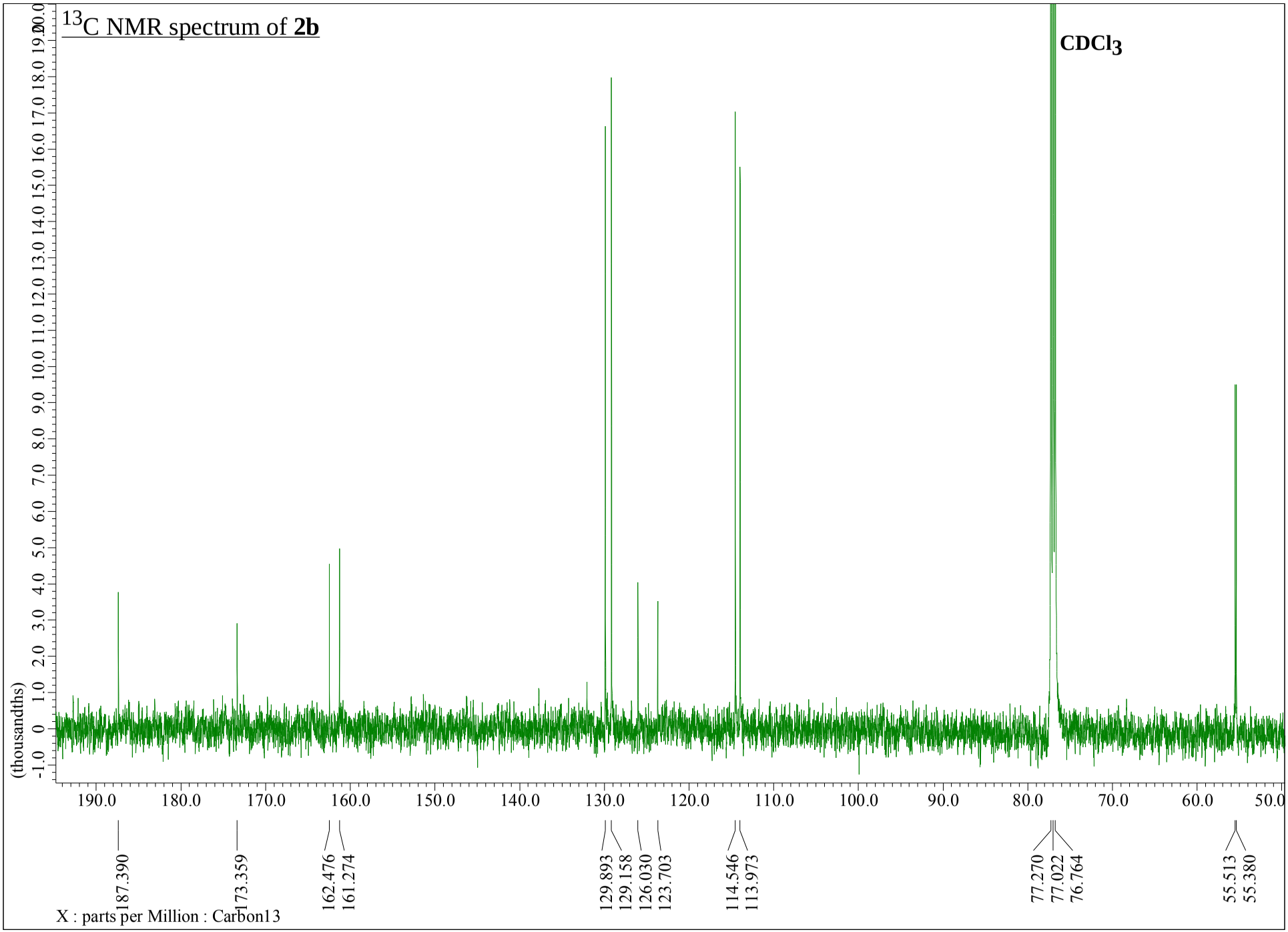

2g
73
[M+]
114
52
59
85
m/z

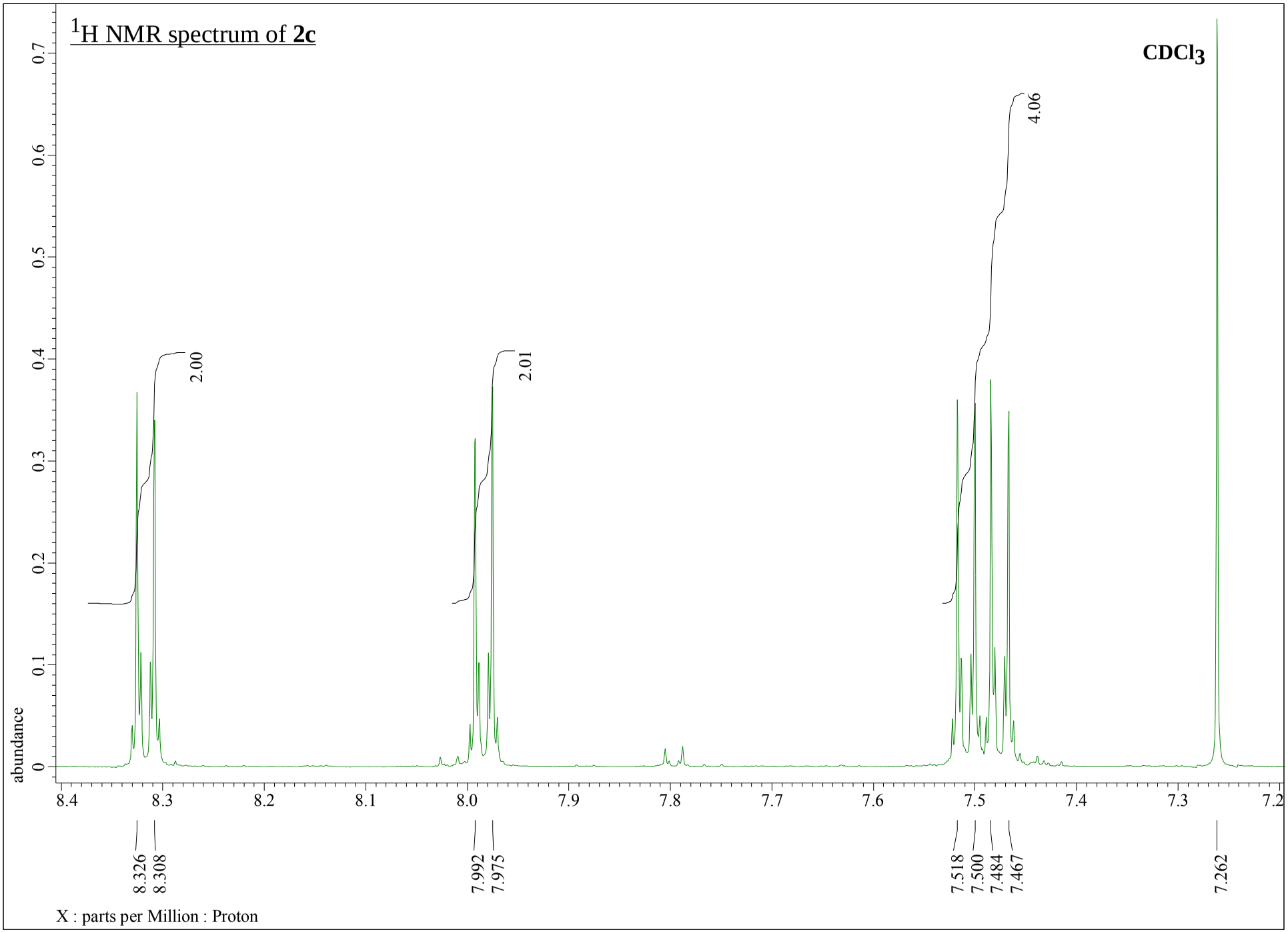

2h
87
[M+]
142
59
54
72
100
113
127
m/z

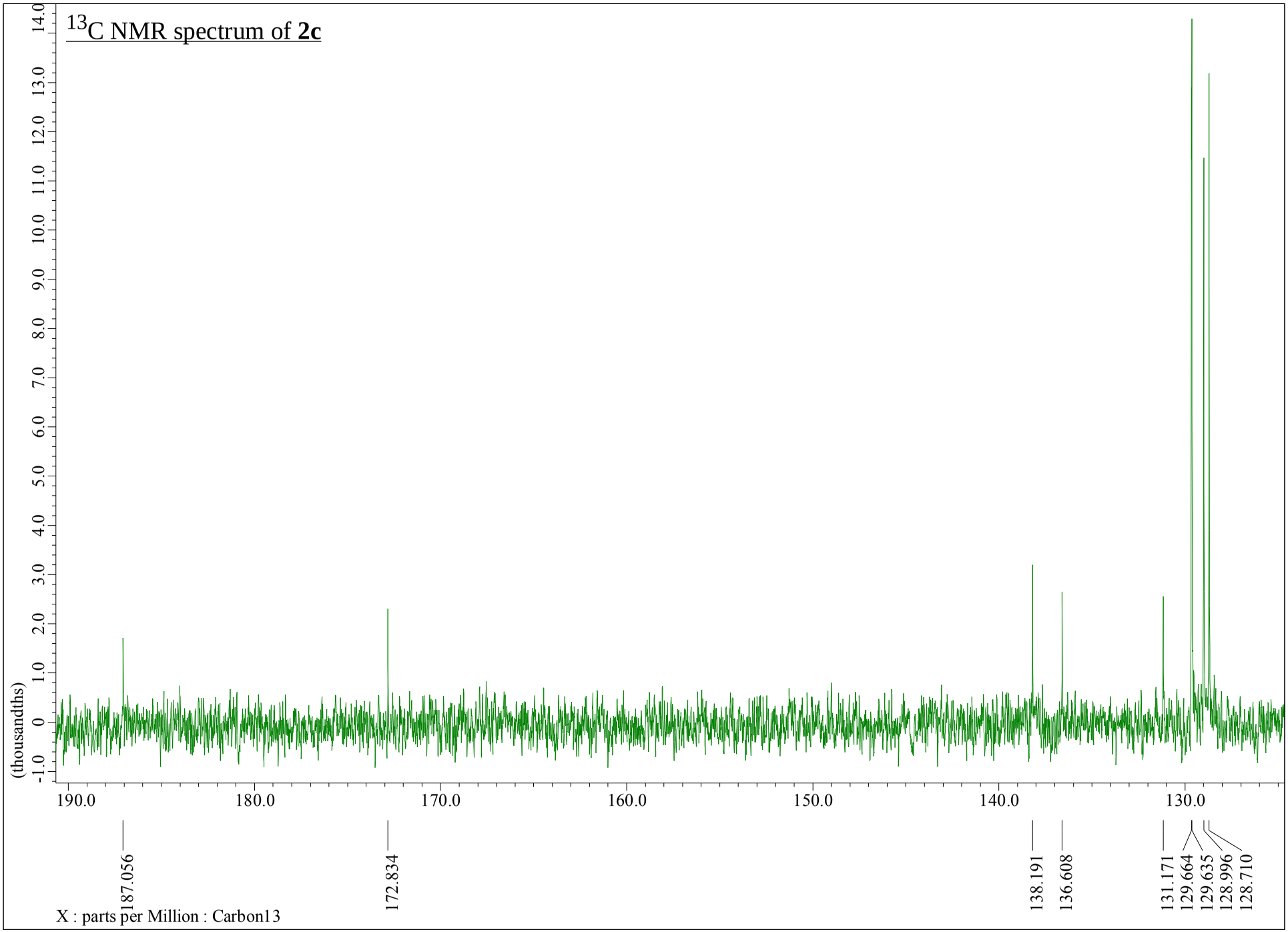

^{1}H NMR spectrum of **2a**
$CDCl_3$
6.00
2.12
2.10
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
8.6
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
8.410
8.406
8.402
8.399
8.397
8.394
8.391
8.071
8.068
8.065
8.063
8.060
8.056
8.052
7.548
7.545
7.540
7.533
7.530
7.529
7.526
7.519
7.515
7.512
7.504
7.500
7.496
7.262
X : parts per Million : Proton

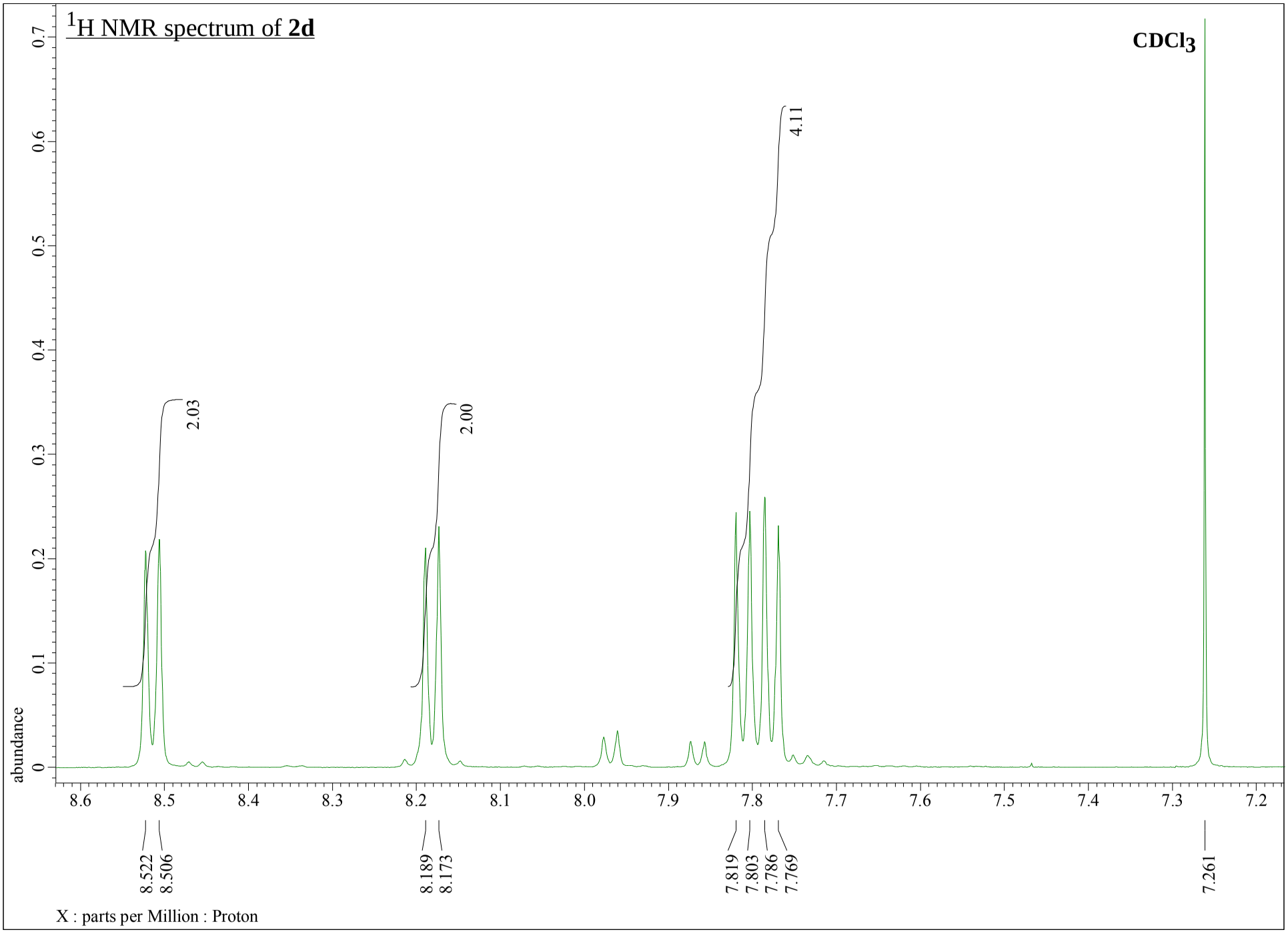

13C NMR spectrum of 2a
(thousandths)
-1.0 0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0 15.0 16.0 17.0 18.0 19.0 20.0 21.0 22.0
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0
188.112
173.795
132.866
131.912
130.710
130.348
129.270
128.688
128.335
127.477
X : parts per Million : Carbon13


1H NMR spectrum of 2b
abundance
2.04
2.04
CDCl3
4.12
6.00
8.328
8.324
8.314
8.310
7.997
7.993
7.984
7.979
7.260
7.020
7.014
7.010
7.006
7.002
6.996
3.894
3.885
X : parts per Million : Proton

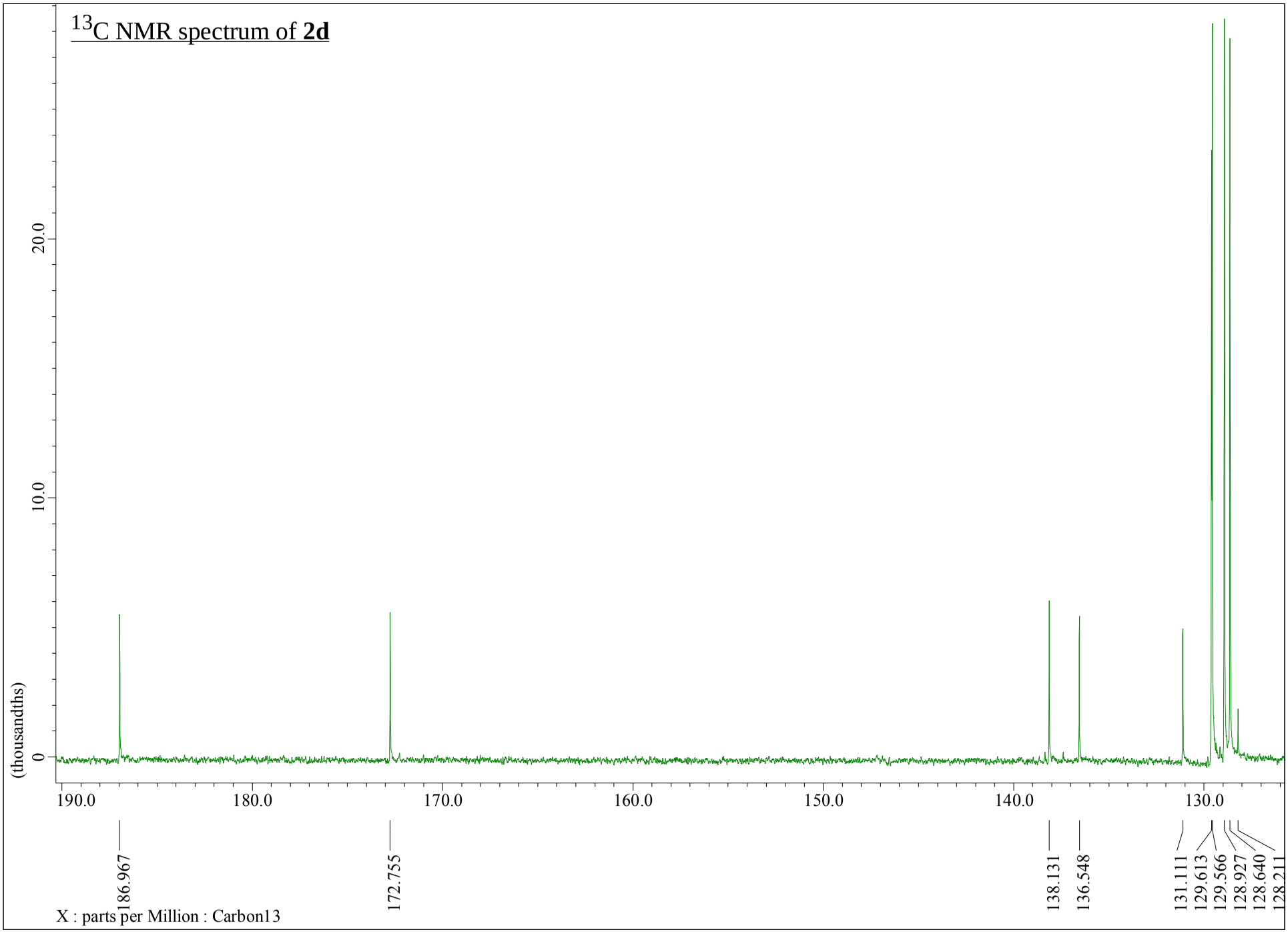

^{13}C NMR spectrum of **2b**
$CDCl_3$
(thousandths)
X : parts per Million : Carbon13
187.390
173.359
162.476
161.274
129.893
129.158
126.030
123.703
114.546
113.973
77.270
77.022
76.764
55.513
55.380

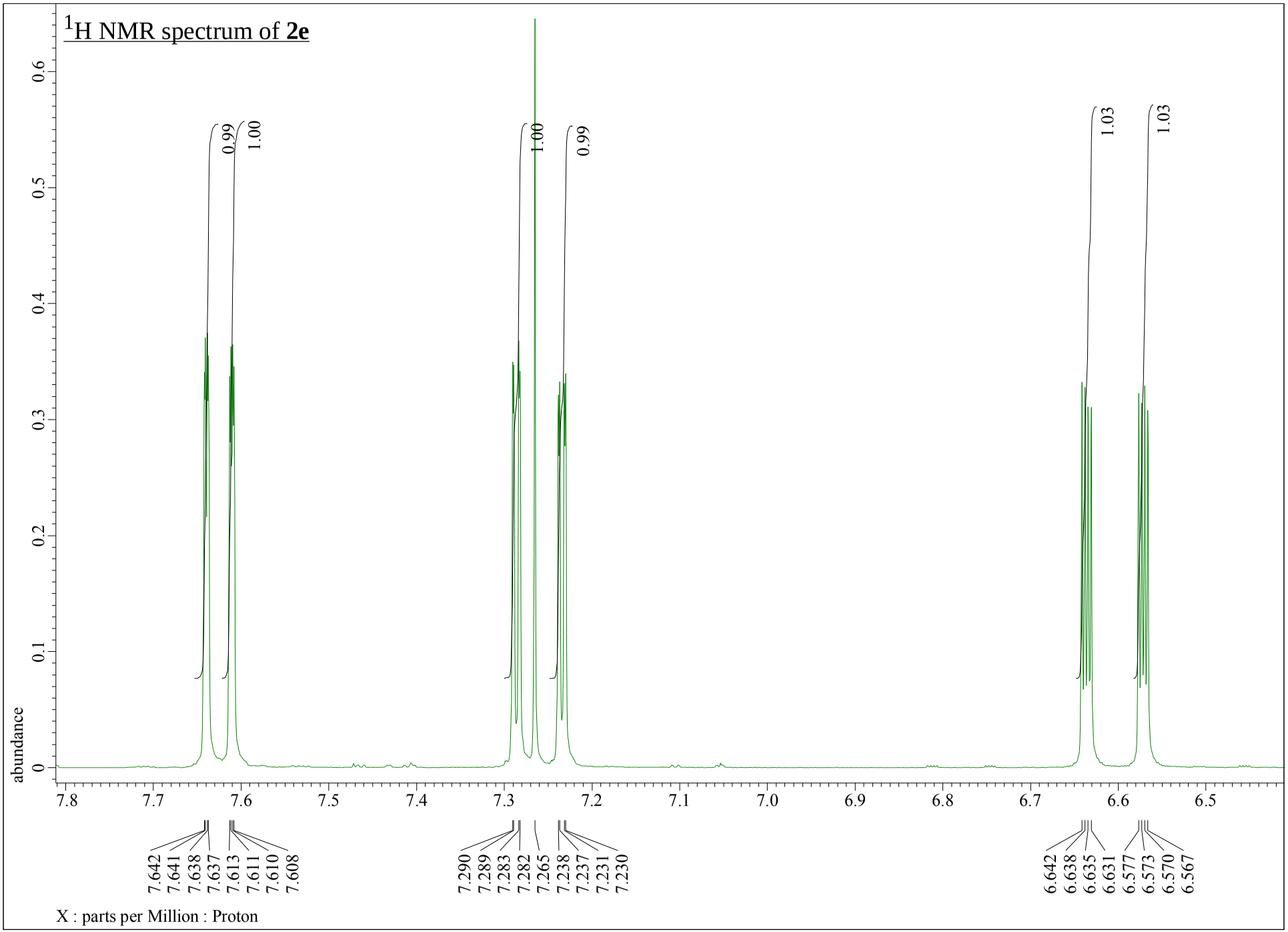

^{1}H NMR spectrum of **2c**
$CDCl_3$
4.06
2.00
2.01
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
8.326
8.308
7.992
7.975
7.518
7.500
7.484
7.467
7.262
X : parts per Million : Proton

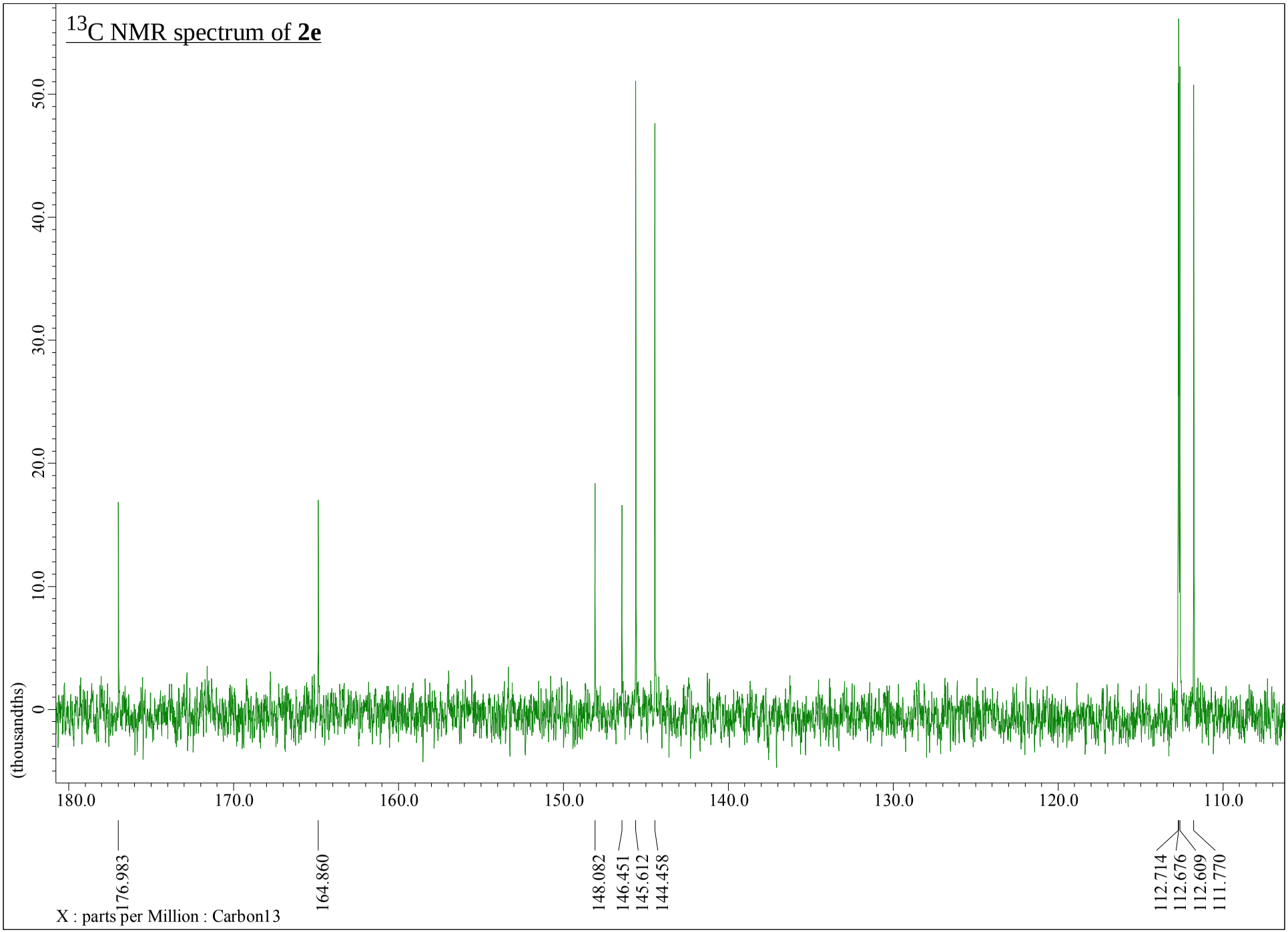

^{13}C NMR spectrum of **2c**
(thousandths)
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
-1.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
187.056
172.834
138.191
136.608
131.171
129.664
129.635
128.996
128.710
X : parts per Million : Carbon13


^{1}H NMR spectrum of **2d**
$CDCl_3$
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
2.03
2.00
4.11
8.6
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
8.522
8.506
8.189
8.173
7.819
7.803
7.786
7.769
7.261
X : parts per Million : Proton

^{13}C NMR spectrum of **2d**




1H NMR spectrum of 2e
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.99
1.00
1.00
0.99
1.03
1.03
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
7.642
7.641
7.638
7.637
7.613
7.611
7.610
7.608
7.290
7.289
7.283
7.282
7.265
7.238
7.237
7.231
7.230
6.642
6.638
6.635
6.631
6.577
6.573
6.570
6.567
X : parts per Million : Proton


^{13}C NMR spectrum of **2e**
(thousandths)
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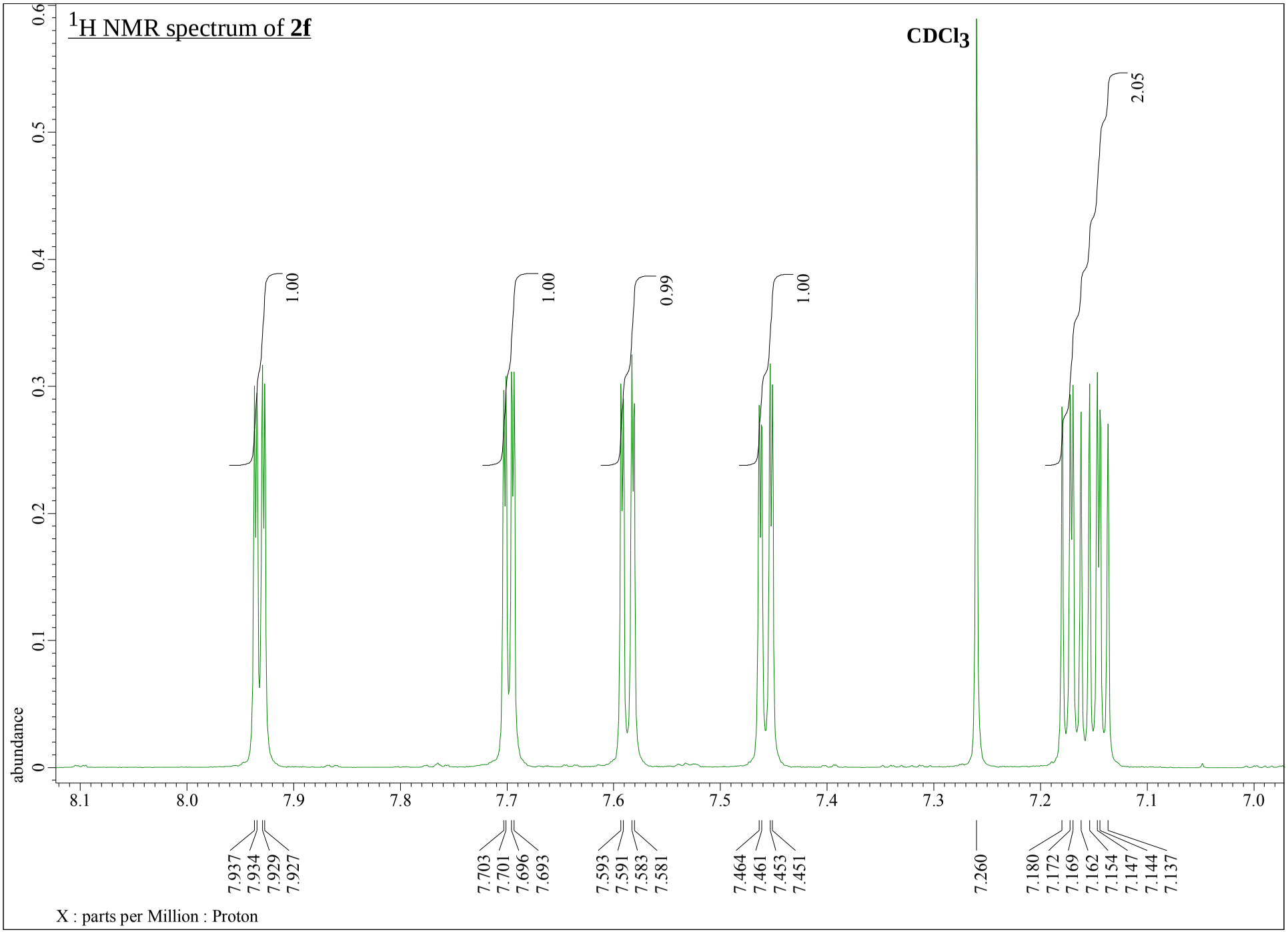
40.0
30.0
20.0
10.0
0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
176.983
164.860
148.082
146.451
145.612
144.458
112.714
112.676
112.609
111.770
X : parts per Million : Carbon13


^{1}H NMR spectrum of **2f**
$CDCl_3$
abundance
X : parts per Million : Proton
1.00
1.00
0.99
1.00
2.05
7.937
7.934
7.929
7.927
7.703
7.701
7.696
7.693
7.593
7.591
7.583
7.581
7.464
7.461
7.453
7.451
7.260
7.180
7.172
7.169
7.162
7.154
7.147
7.144
7.137

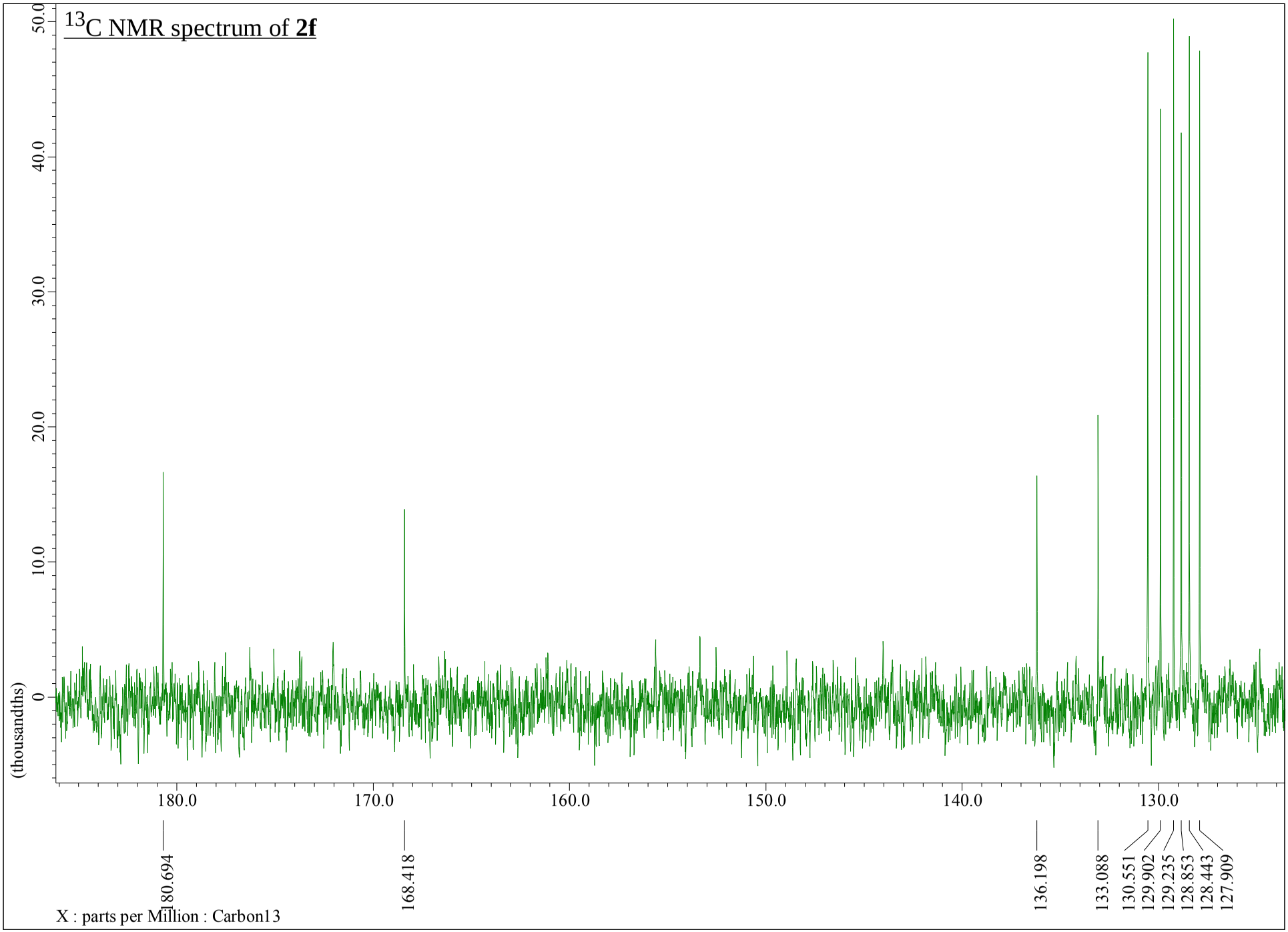

^{13}C NMR spectrum of **2f**
50.0
40.0
30.0
20.0
10.0
0
(thousandths)
180.0
170.0
160.0
150.0
140.0
130.0
180.694
168.418
136.198
133.088
130.551
129.902
129.235
128.853
128.443
127.909
X : parts per Million : Carbon13

Table S1 Comparison of the present phosphovanadomolybdic acids catalyzed system with previously reported ones (for dimerization of **1a** to **2a**)

Catalyst	**Oxidant**	**Additive**	**Solvent**	**Temp.(ºC)**	**Time**	**Yield (%)**	**TON**	**Ref.**
$H_6PV_3Mo_9O_{40}$ (0.4 mol%)	O_2 (1 atm)	—	EtOH	30	5 h	93	233 (Fig. 1, entry 2)	This work
—	Ar_2SeO (1.2 equiv.)	—	AcOH	75	24 h	84	Stoichiometric	6
—	Ar_2TeO (1.2 equiv.)	—	AcOH	RT	12 h	53	Stoichiometric	6
—	$PhTeOSO_2CF_3$ (1 equiv.)	—	CH_2Cl_2	RT	0.5 h	71	Stoichiometric	7
—	Iodobenzene diacetate (1 equiv.)	—	CH_2Cl_2	RT	3 min	95	Stoichiometric	8a
—	Iodobenzene diacetate (1 equiv.)	—	1-*n*-butylpyridinium tetrafluoroborate	75	15 min	91	Stoichiometric	8b
—	λ^3-Iodane (1 equiv.)	—	CH_3CN	Reflux	1 h	82	Stoichiometric	8c
—	*o*-iodoxybenzoic acid (1.1 equiv.)	Et_4NBr (1.1 eq.)	CH_3CN	RT	5 min	95	Stoichiometric	8d
—	Pentylpyridinium tribromide (1 equiv., prepared from pentylpyridinium bromide and Br_2)	—	—	RT	4 min	97	Stoichiometric	9
—	2,3-Dicyano-5,6-dichloro-1,4-benzoquinone (1 equiv.)	—	$ClCH_2CH_2Cl$	RT	<5 min	95	Stoichiometric	10
—	*N*-bromosuccinimide (1.05 equiv.)	Al_2O_3 (500 mg)	—	RT	5 min	92	Stoichiometric	11
—	DMSO (large excess)	1-Methyl-2-chloro pyridinium iodide (0.03 equiv.)	DMSO	60	2.5 h	>99	Stoichiometric	12a

(Continued)

Catalyst	**Oxidant**	**Additive**	**Solvent**	**Temp.(ºC)**	**Time**	**Yield (%)**	**TON**	**Ref.**
—	DMSO (1 equiv.)	2-chloro-1,3-dimethylimidazolinium chloride (1 equiv.)	CH_2Cl_2	RT	26 h	93	Stoichiometric	12b
—	DMSO (1 equiv.)	2,4,6-trichloro-1,3,5-triazine (0.3 equiv.)	[bmim]BF_4	RT	10 min	96	Stoichiometric	12c
—	DMSO (large excess)	HCl (0.6 equiv.)	DMSO	35	3 h	>99	Stoichiometric	12d
CuBr (10 mol%)	TBHP (1.4 equiv.)	—	$ClCH_2CH_2Cl$	RT	0.5 h	79	7.9	13
Eosin Y (2 mol%)	Air (1 atm)	Photoirradiation (18 W fluorescent lamp)	DMF	RT	4 h	91	45.5	14

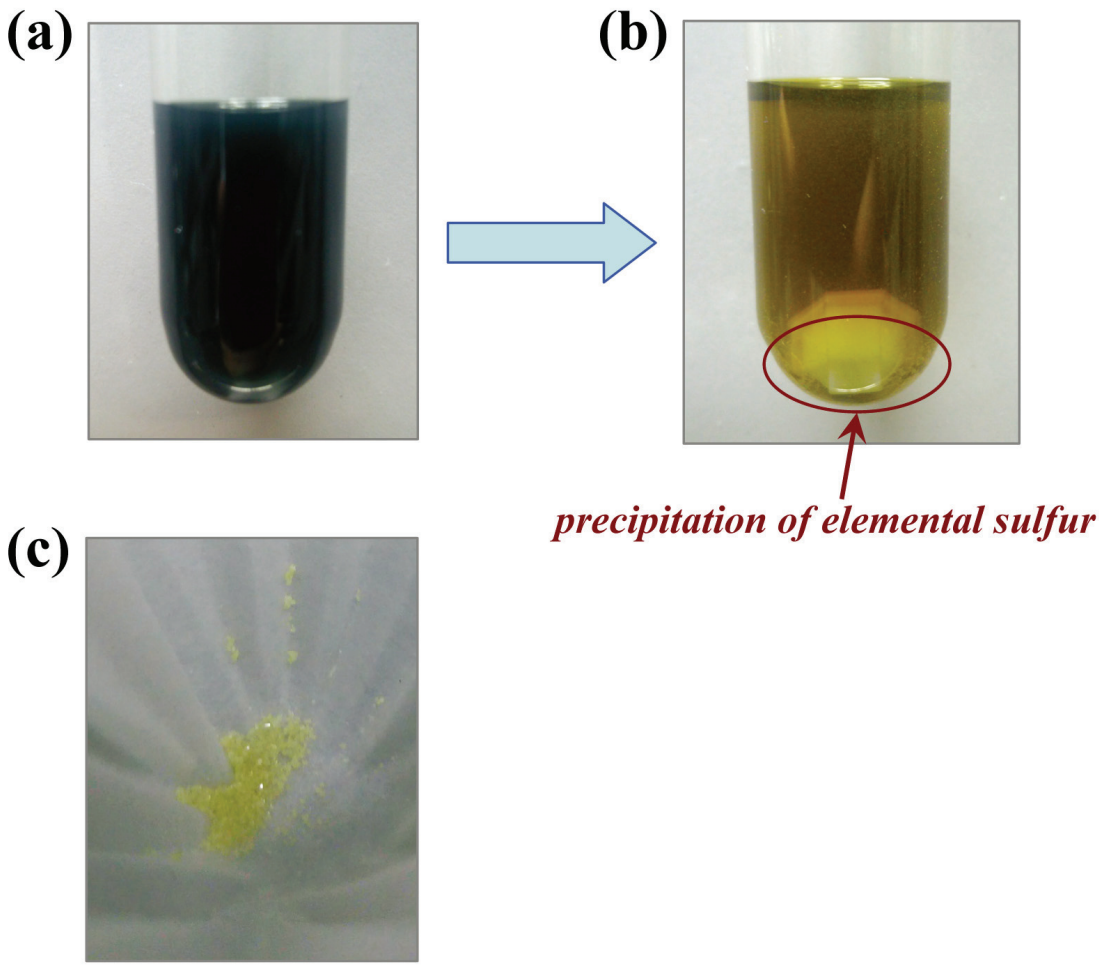


Fig. S1 Pictures of the reaction solution (a) immediately after beginning of the reaction and (b) at the end of the reaction (for the oxidative dimerization of **2g**, see entry 8 in Fig. 1) and (c) elemental sulfur retrieved after the reaction. Elemental sulfur was retrieved by filtration and washed with ethanol and water (69 % yield with respect to **2g**, 98.3 % purity by elemental analysis).

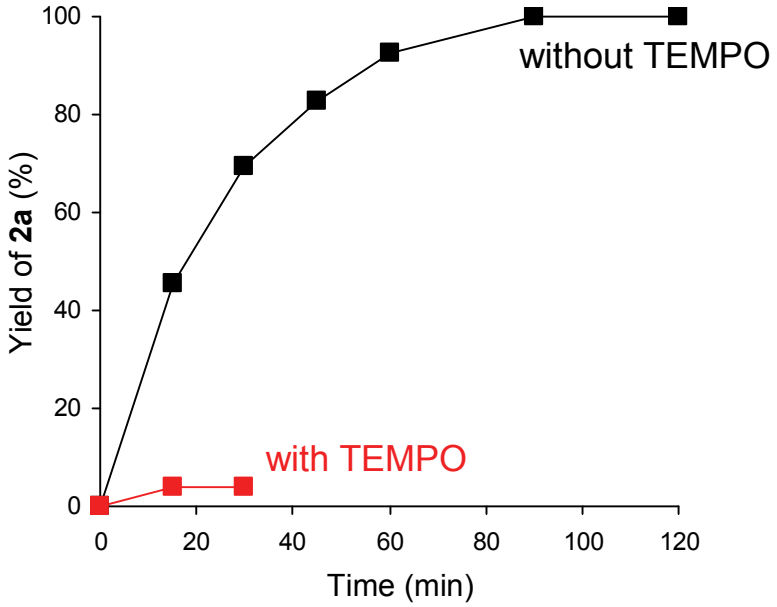


Fig. S2 Reaction profiles for the $H_6PV_3Mo_9O_{40}$-catalyzed oxidative dimerization of **1a** to **2a** with or without a radical scavenger of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO). Reaction conditions: **1** (0.5 mmol), $H_6PV_3Mo_9O_{40}$ (1 mol%), TEMPO (0 or 0.5 mmol), ethanol (4 mL), O_2 (1 atm), 30 °C.

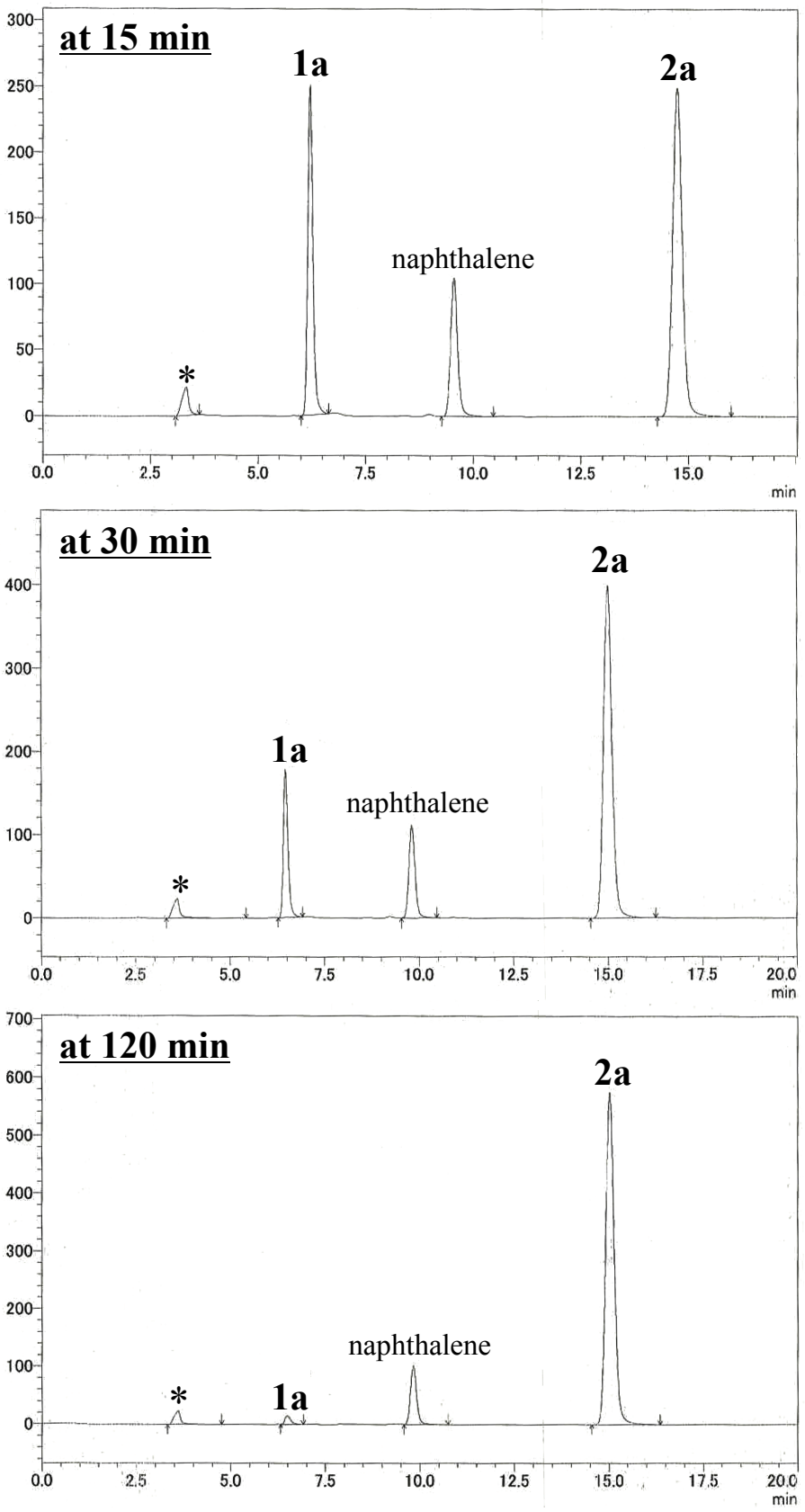
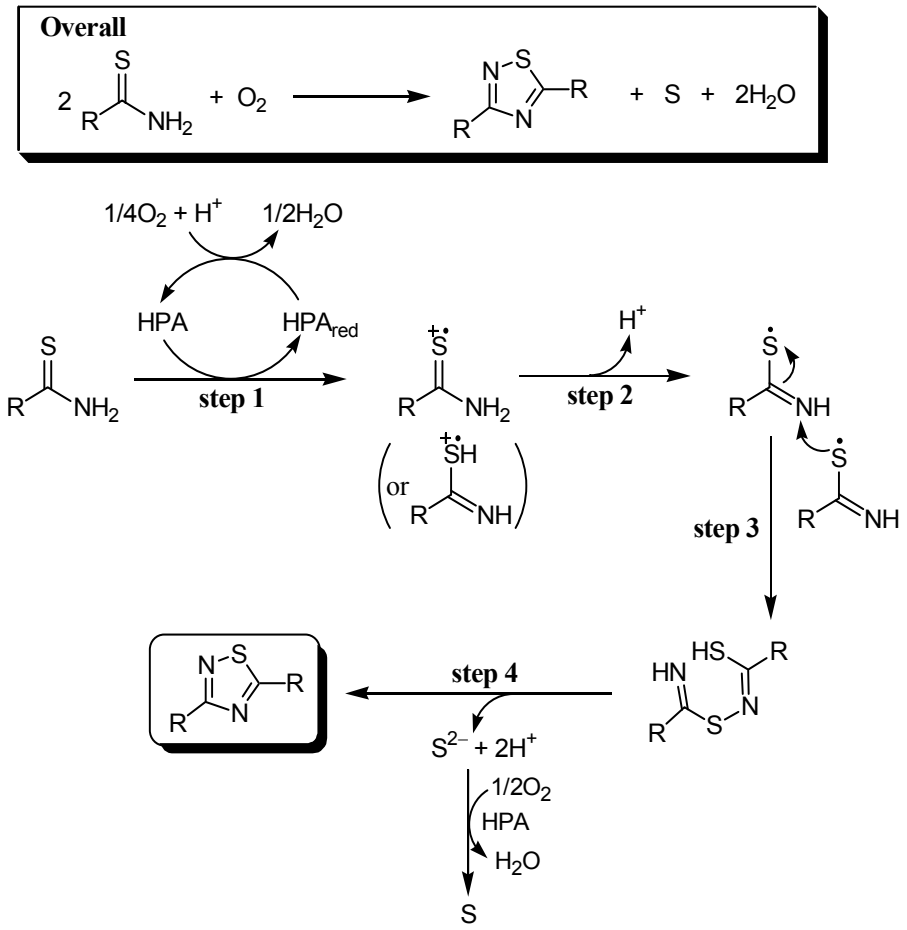


Fig. S3 HPLC charts for the $H_6PV_3Mo_9O_{40}$-catalyzed oxidative dimerization of **1a** to **2a** under the conditions described in Fig. S2. The asterisks indicate the signals due to $H_6PV_3Mo_9O_{40}$. Reaction conditions: **1** (0.5 mmol), $H_6PV_3Mo_9O_{40}$ (1 mol%), TEMPO (0 or 0.5 mmol), ethanol (4 mL), O_2 (1 atm), 30 °C.



Scheme S1 Possible reaction mechanism (HPA = heteropoly acid, HPA_{red} = reduced heteropoly acid).