

Supporting Information

Cobalt-Catalyzed Allylic C(sp³)–H Carboxylation with CO₂

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(A) Supplemental Data

(A-1) Optimization Details: Tables S1-S8

Several reaction parameters of allylic C–H carboxylation were investigated. In each table, the yields were determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

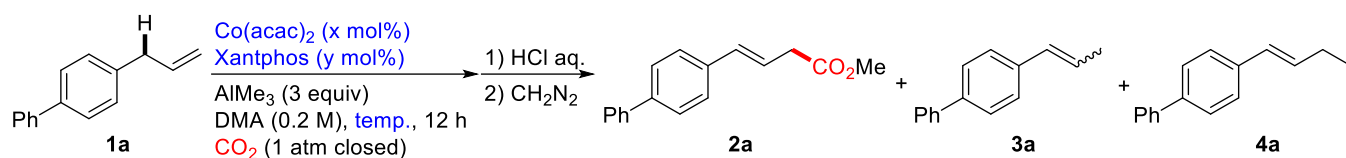
Table S1. Solvent Effect in Allylic C–H Carboxylation

<div><div></div><div><div>entry</div><div>solvent</div><div data-cs="5" data-kind="parent">yield (%)</div><div data-kind="ghost"></div><div data-kind="ghost"></div><div data-kind="ghost"></div><div data-kind="ghost"></div><div>2a</div><div><i>E</i>-3a</div><div><i>Z</i>-3a</div><div>4a</div><div>1a rec.</div></div></div>						
1 ^a	1,4-dioxane	-	-	-	-	99
2	1,4-dioxane	4	82	8	6	-
3	THF	-	82	11	-	-
4	toluene	-	86	11	-	-
5	MeCN	-	80	19	-	-
6	DMF	4	52	12	2	30
7	DMA	16	55	12	5	12
8	NMP	4	50	11	3	21
9	DMI	5	56	12	5	13

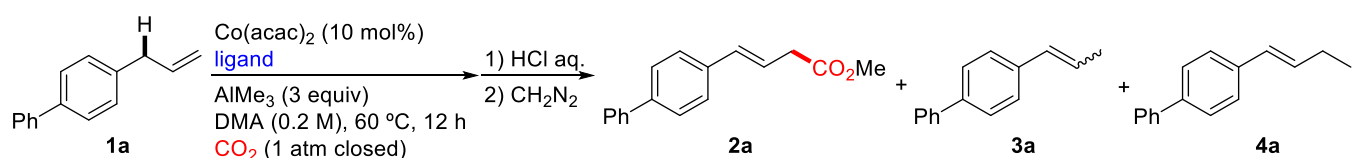
^aThe reaction was carried out in the absence of Co(acac)₂.

Table S2. Investigation of Alkylmetal Reagents

<div><div></div><div><div>entry</div><div>MR_n</div><div data-cs="5" data-kind="parent">yield (%)</div><div data-kind="ghost"></div><div data-kind="ghost"></div><div data-kind="ghost"></div><div data-kind="ghost"></div><div>2a</div><div><i>E</i>-3a</div><div><i>Z</i>-3a</div><div>4a</div><div>1a rec.</div></div></div>						
1	AlMe₃	16	55	12	5	12
2	AlEt ₃	-	90	2	-	-
3	ZnMe ₂	-	1	-	-	93
4	ZnEt ₂	-	11	2	-	87

Table S3. Screening of Reaction Temperature and the Amount of the Catalyst

entry	Co(acac) ₂ (x mol%)	Xantphos (y mol%)	temp. (°C)	yield (%)				
				2a	<i>E</i> -3a	<i>Z</i> -3a	4a	1a rec.
1	10	10	rt	16	55	12	5	12
2	10	10	0	-	33	5	-	59
3	10	10	60	24	60	6	10	-
4	10	10	100	10	71	3	7	-
5	10	20	60	32	34	7	13	-
6	10	30	60	25	36	7	14	-
7	20	40	60	24	48	6	21	-

Table S4. Ligand Screening

entry	ligand (mol%)	yield (%)				
		2a	<i>E</i> -3a	<i>Z</i> -3a	4a	1a rec.
1	<i>Xantphos</i> (20)	32	34	7	13	-
2	L1 (20)	-	8	1	-	86
3	L2 (20)	33	35	4	15	-
4	NiXantphos (20)	16	68	3	4	-
5	DBFphos (20)	-	80	3	-	14
6	DPEphos (20)	-	74	3	-	9
7	DPPF (20)	-	87	4	7	-
8	DPPP (20)	-	74	12	10	-
9	(<i>S</i>)-DTBM-SEGPHOS (20)	-	94	2	-	-
10	(<i>S,S</i>)-(R,R)-Ph-TRAP (20)	1	75	2	2	-
11	IPr·HCl (20), KO ^t Bu (20)	-	40	16	-	39
12	2,2'-bpy (20)	-	90	3	-	4
13	(<i>S,S</i>)-iPr-PyBox (10)	-	5	-	-	93

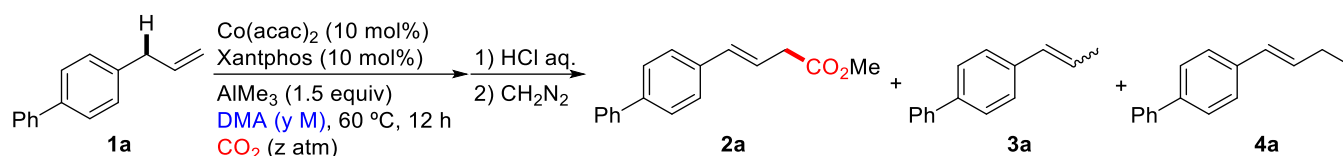
Table S5. Investigation of Transition-Metal Catalysts and the Amount of AlMe₃

Reaction scheme: **1a** (4-phenyl-1-butene) reacts with **catalyst, ligand**, **AlMe₃ (x equiv)**, **DMA (0.2 M), 60 °C, 12 h**, and **CO₂ (1 atm closed)** to form **2a** (methyl 4-phenyl-3-buten-1-yl carbonate), **3a** (E-4-phenyl-3-buten-1-yl carbonate), and **4a** (Z-4-phenyl-3-buten-1-yl carbonate).

Reaction conditions: 1) HCl aq., 2) CH₂N₂.

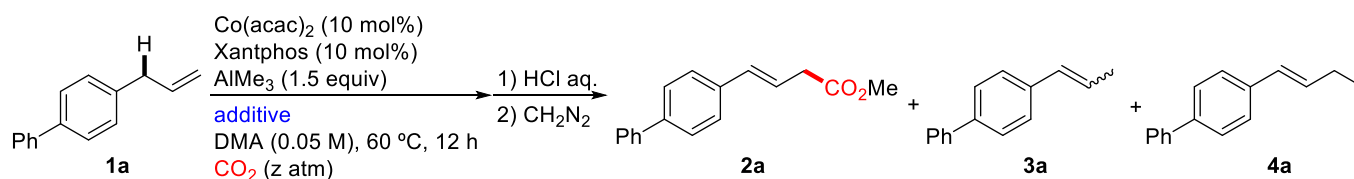
entry	catalyst (mol%)	ligand (mol%)	AlMe ₃ (x equiv)	yield (%)				
				2a	<i>E</i> - 3a	<i>Z</i> - 3a	4a	1a rec.
1	Co(acac) ₂ (10)	Xantphos (20)	3	32	34	7	14	0
2	CoCl(PPh ₃) ₃ (10)	Xantphos (20)	3	22	54	12	5	4
3	Co(acac) ₃ (10)	Xantphos (20)	3	21	58	9	-	-
4	[Cp*CoCl ₂] ₂ (5)	none	3	-	35	5	-	59
5	[Rh(cod)Cl] ₂ (5)	Xantphos (20)	3	-	25	6	-	67
6	Rh(acac) ₃ (10)	Xantphos (20)	3	-	-	-	-	97
7	[Ir(cod)Cl] ₂ (5)	Xantphos (20)	3	-	5	-	-	93
8	CrCl ₂ (10)	Xantphos (20)	3	-	-	-	-	99
9	MnCl ₂ (10)	Xantphos (20)	3	-	-	-	-	99
10	MnBr(CO) ₅ (10)	Xantphos (20)	3	-	-	-	-	98
11	Fe(acac) ₃ (10)	Xantphos (20)	3	-	9	2	-	86
12	[RuCl ₂ (PPh ₃) ₂] ₂ (5)	Xantphos (20)	3	-	11	2	-	67
13	Ni(acac) ₂ (10)	Xantphos (20)	3	-	27	3	-	69
14	CuI (10)	Xantphos (20)	3	-	6	2	-	89
15	Co(acac)₂ (10)	Xantphos (20)	1.5	45	26	5	15	-
16	CoBr ₂ (10)	Xantphos (20)	1.5	-	82	7	-	-
17	Co(hfacac) ₂ (10)	Xantphos (20)	1.5	19	37	7	13	9
18	Co(dbm) ₂ (10)	Xantphos (20)	1.5	27	33	5	20	3
19	Co(salen) (10)	Xantphos (20)	1.5	40	25	6	14	4

Chemical structures of catalysts: **Co(hfacac)₂**, **Co(dbm)₂**, and **Co(salen)**.

Table S6. Effect of Concentration and CO₂ Pressure

entry	DMA (y M)	CO ₂ (z atm)	yield (%)				
			2a	<i>E</i> -3a	<i>Z</i> -3a	4a	1a rec.
1	0.2	1 (closed)	45	26	5	15	-
2	0.1	1 (closed)	55	15	3	11	5
3	0.05	1 (closed)	58	11	3	9	3
4	0.2	10	56	18	5	5	15
5	0.1	10	40	13	4	3	29
6	0.05	10	33	13	4	2	39
7	0.2	5	56	17	5	9	6
8	0.1	5	51	12	4	4	23
9	0.05	5	46	11	4	9	27
10	0.2	3	61	13	3	12	2
11	0.1	3	62	11	3	7	7
12	0.05	3	66	15	5	4	9

When the reaction was conducted under 3 atm CO₂ pressure in the absence of CsF in DMA (0.05 M), the yield of **2a** was increased to 66% (entry 12, Table S6). This yield is nearly equal to that using CsF (entry 17, Table 1), indicating that solubility of CO₂ in DMA is a key factor for efficient carboxylation. However, much concentration of CO₂ somewhat inhibited the reaction (entries 4-9, Table S6).

Table S7. Examination of Additives and Re-Investigation of CO₂ Pressure

entry	additive (equiv)	CO ₂ (z atm)	yield (%)				
			2a	<i>E</i> -3a	<i>Z</i> -3a	4a	1a rec.
1	none	3	66	15	5	4	9
2	CsF (1)	3	47	20	5	-	20
3	CsF (1)	1 (closed)	71	17	3	1	2
4	CsF (3)	1 (closed)	32	7	2	-	50
5	CsF (1)	1 (balloon)	67	17	4	3	-
6	Cs ₂ CO ₃ (1)	1 (closed)	44	15	5	1	30
7	Cs ₂ CO ₃ (1)	1 (balloon)	57	16	5	2	15

Table S8. Screening of Xantphos Derivatives

Reaction scheme: **1a** (allylbenzene) reacts with $\text{Co}(\text{acac})_2$ (10 mol%), **ligand** (20 mol%), AlMe_3 (1.5 equiv), CsF (1 equiv), DMA (0.05 M), 60°C , 12 h, and CO_2 (1 atm closed) to yield **2a** (methyl 3-allylbenzoate), **3a** (*E*-3-allylbenzoate), and **4a** (*Z*-3-allylbenzoate).

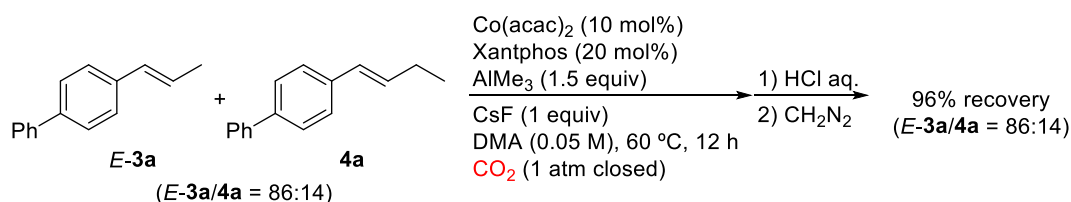
Reaction conditions: 1) HCl aq., 2) CH_2N_2 .

entry	ligand	yield (%)				
		2a	<i>E</i> - 3a	<i>Z</i> - 3a	4a	1a rec.
1	<i>Xantphos</i>	71	17	3	1	2
2	L2	58	28	8	3	9
3	L3	-	18	7	16	55
4	L4	40	45	6	2	10

Chemical structures of ligands **L2**, **L3**, and **L4** are shown. **L2** is a 1,1'-bis(diphenylphosphino)ferrocene derivative. **L3** and **L4** are ferrocene derivatives with *p*-tolyl and *p*-trifluoromethylphenyl groups, respectively. $\text{R} = \text{p-tolyl}$ (**L3**) or $\text{p-trifluoromethylphenyl}$ (**L4**).

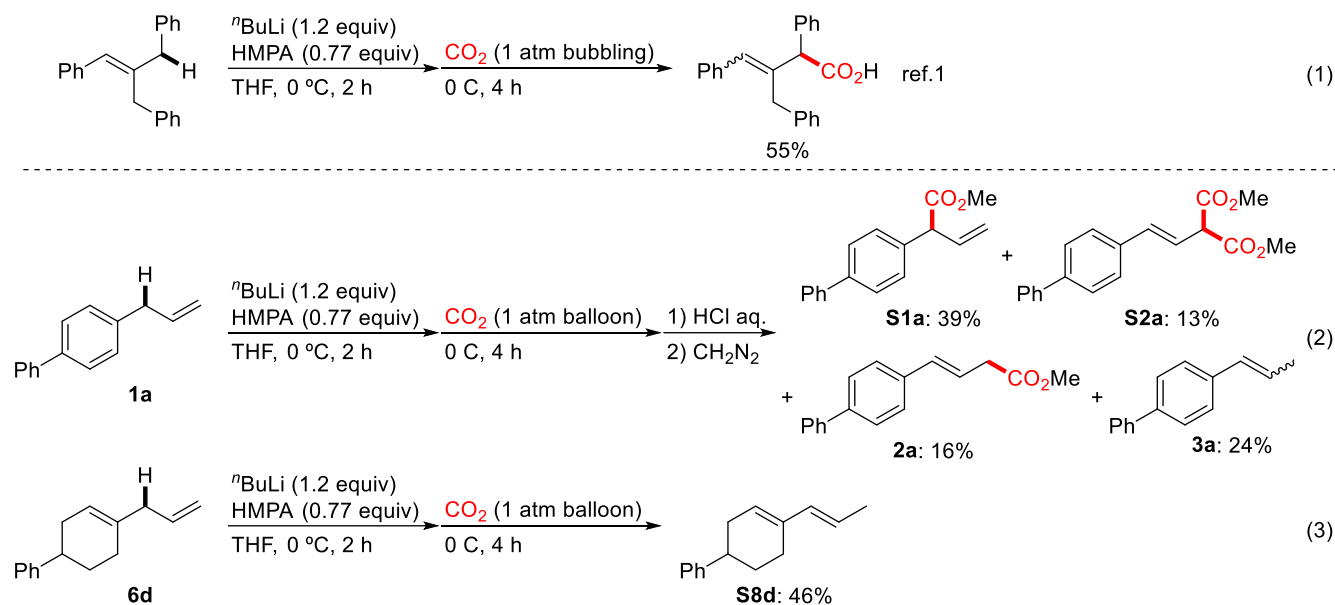
(A-2) Reaction of the Olefin Isomerization Product and the Methylated Product

When the mixture of byproducts **3a** and **4a** (*E*-**3a**/**4a** = 86:14) were subjected to the optimized conditions under CO_2 , any reactions did not occur and **3a** and **4a** were completely recovered with the same ratio.

Scheme S1. Attempt for Carboxylation of **3a** and **4a****(A-3) Carboxylation Using Alkylolithium**

Deprotonation/carboxylation of allylarene **1a** and 1,4-diene **6d** was conducted using $n\text{BuLi}$ and CO_2 according to the reported procedure (Scheme S2, eq 1).¹ The reaction of **1a** provided a regioisomeric mixture of carboxylated products including double carboxylated product **S2a** (Scheme S2, eq 2),² while the same reaction (without esterification) of **6d** afforded only the olefin isomerization product **S8d** in 46% yield (Scheme S2, eq 3).³ These results suggest that $\text{Co}(\text{acac})_2/\text{Xantphos}/\text{AlMe}_3$ catalytic system is advantageous in terms of both regioselectivity and reactivity.

Scheme S2. Carboxylation Using Alkyl lithium

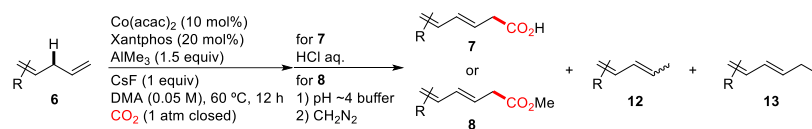


(A-4) Substrate Scope

The results of substrate scope of allylic C–H carboxylation are summarized in the following tables. In every substrate, isolated yields are described for carboxylated products, and the yields of olefin isomers, methylated products, and recovered starting materials were determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene.

substrate	products	substrate	products
 1	Co(acac) ₃ (10 mol%), Xantphos (20 mol%), AlMe ₃ (1.5 equiv), CsF (1 equiv), DMA (0.05 M), 60 °C, 12 h, CO ₂ (1 atm closed) for 5: HCl aq. for 2: 1) pH ~4 buffer, 2) CH ₂ N ₂	 5 or 2	 3 + 4
 1a	 5a: 71% 3a: 16% 4a: 1% 1a rec.: 0%	 1i	 5i: 69% (9%) 3i: 10% 4i: <1% 1i rec.: 0%
 1b	 5b: 68% (3%) 3b: N.D. ^a 4b: N.D. ^a 1b rec.: N.D. ^a	 1j	 5j: 72% 3j: 25% 4j: 4% 1j rec.: 0%
 1c	 5c: 63% (2%) 3c: 19% 4c: 1% 1c rec.: 15%	 1k	 5k: 54% (2%) 3k: 31% 4k: 2% 1k rec.: 0%
 1d	 5d: 41% 3d: 44% 4d: 1% 1d rec.: 0%	 1l	 5l: 63% 3l: 20% 4l: 5% 1l rec.: 0%
 1e	 5e: 65% (1%) 3e: N.D. ^a 4e: N.D. ^a 1e rec.: N.D. ^a	 1m	 5m: 77% (2%) 3m: 8% 4m: 2% 1m rec.: 0%
 1f	 5f: 55% 3f: 3% ^a 4f: N.D. ^a 1f rec.: N.D. ^a	 1n	 5n: 84% (8%) 3n: 8% 4n: <1% 1n rec.: 0%
 1g	 5g: 78% (4%) 3g: 9% 4g: <1% 1g rec.: 0%	 1o	 5o: 63% 3o: 16% 4o: 8% 1o rec.: 0%
 1h	 5h: 81% (11%) 3h: <7% 4h: 2% 1h rec.: 0%		

^aN.D. = Not determined. Yields were not determined because the materials were volatile under vacuum. The value in parentheses is the yield of the olefin isomer (α,β -unsaturated carboxylic acids)
^bThe reaction was carried out using 4 mmol of 1h in DMA (0.2 M) under CO₂ (1 atm, balloon).



substrate	products	substrate	products
 6a	 7a : 75% (<i>E/Z</i> = 90:10) 12a : N.D. ^a 13a : N.D. ^a 6a rec: 0%	 6d	 7d : 78% 12d : N.D. ^a 13d : 0% 6d rec: 6%
 6b (<i>E/Z</i> = 3:2)	 7b : 45% (<i>E/Z</i> = 65:35) 12b : 19% 13b : 6% 6b rec: 6%	 6e	 7e : 57% 12e : N.D. ^a 13e : 0% 6e rec: 31%
 6c (<i>E/Z</i> = 1:1)	 7c : 68% (<i>E/Z</i> = 55:45) 12c : N.D. ^a 13c : N.D. ^a 6c rec: 15%	 6f	 8f : 41% 12f : N.D. ^a 13f : 0% 6f rec: 46%

^aN.D. = Not determined. Yields were not correctly determined because the corresponding peaks were overlapped.

(B) General

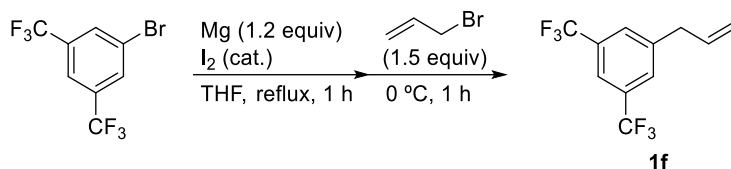
All manipulations were carried out under an atmosphere of argon or nitrogen unless otherwise noted. Carboxylation reactions under “1 atm, closed” CO₂ atmosphere were carried out in a pressure-proof mini vacuum tube (20 mL, ϕ 19 mm x 100 mm, ϕ 13 mm), which was purchased from OSAKA CHEMICAL Co., Ltd. The reactions under higher (≥ 3 atm) CO₂ pressure were carried out in an autoclave (10 mL, Portable reactor, TVS-1), which was purchased from TAIATSU TECHNO. Infrared (IR) spectra were recorded on a JASCO FT/IR 460 Plus Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL ECA-500 spectrometer, operating at 500 MHz (¹H) or 125 MHz (¹³C). Chemical shifts in CDCl₃ and acetone-*d*₆ were reported in the scale relative to CHCl₃ (7.26 ppm) and acetone (2.05 ppm) for ¹H NMR, and to CDCl₃ (77.0 ppm) and acetone-*d*₆ (29.84 ppm) for ¹³C NMR as internal references, respectively. NMR data are reported as follows: chemical shifts, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, quin: quintet, m: multiplet, br: broad signal, app: apparently), coupling constant (Hz), and integration. EI-HRMS and ESI-HRMS spectra were measured on a JEOL JMS-T100GCv and Thermo Scientific Exactive, respectively. Gel permeation chromatography was performed on HPLC LC-9201 (Japan Analytical Industry Co., Ltd). Optical rotations were measured on a Jasco P-1030 digital polarimeter at the sodium D line (589 nm). Chiral HPLC analyses were carried out using a Jasco PU-980 and using the indicated chiral column. Column chromatography was performed with Wakogel[®] FC-40 (20-40 μ m, spherical, neutral). Dry toluene, THF, MeCN, and DMF were purified under argon using the Ultimate Solvent System (Glass Counter Inc.). 1,4-Dioxane was distilled from Na/benzophenone. DMA, NMP, and DMI were distilled from CaH₂. CrCl₂ and DPEphos were purchased from Strem Chemicals Inc. MnCl₂, Co(hfacac)₂, Fe(acac)₃, DCPE, DPPF, **L1**, and AlMe₃ (2.0 M in toluene) were purchased from Sigma-Aldrich Co. LLC. CoCl₂, CoBr₂, 2,2'-bpy, AlEt₃ (1.0 M in hexane), ZnMe₂ (1.0 M in hexane), and ZnEt₂ (1.0 M in hexane) were purchased from Kanto Chemical Co., Inc. Co(acac)₂, Co(acac)₃, Ni(acac)₂, Xantphos, NiXantphos, DPPP, and (*S,S*)-*i*Pr-PyBox were purchased from Tokyo Kasei, Co., Ltd. CsF was purchased from Nacalai Tesque, Inc. Cs₂CO₃ was purchased from Kishida Chemical Co., Ltd. All materials purchased were used as received. MnBr(CO)₅,⁴ CoCl(PPh₃)₃,⁵ Co(dbm)₂,⁶ Co(salen),⁷ [Cp*CoCl₂]₂,⁸ [Rh(cod)Cl]₂,⁹ Rh(acac)₃,¹⁰ [Ir(cod)Cl]₂,¹¹ DBFphos,¹² (*S,S*)-(*R,R*)-Ph-TRAP,¹³ IPr-HCl,¹⁴ **L2**,¹⁵ **L3**,¹³ and **L4**¹⁶ were prepared according to the reported procedures. CH₂N₂ in Et₂O was prepared by the addition of 1-methyl-3-nitro-1-nitrosoguanidine into 40 w/w% KOH aq./Et₂O, 1:2 at 0 °C. DMDO (*ca.* 0.05 M in acetone) was prepared by the reaction of acetone with Oxone[®].¹⁷

(C) Materials and Methods

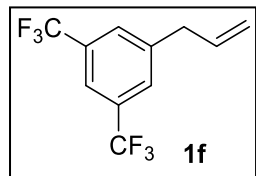
(C-1) Preparation of Substrates

Allylbenzene (**1b**), safrole (**1i**), and eugenol (**1j**) were purchased from Tokyo Kasei, Co. Ltd., which were used as received. 4-Allyl-1,1'-biphenyl (**1a**),¹⁸ 2-allyl-1,1'-biphenyl (**1c**),¹⁹ 2-allylnaphthalene (**1d**),²⁰ 1-allyl-4-(trifluoromethyl)benzene (**1e**),²¹ 3-allylanisole (**1g**),²¹ 2-allyl-1,4-dimethoxybenzene (**1h**),²² methyl 4-allylbenzoate (**1l**),²³ and 3-allylquinoline (**1o**)²⁴ were prepared by reported procedures.

(C-1-a) Grignard Reaction¹⁸



1-Allyl-3,5-bis(trifluoromethyl)benzene (1f): To an oven-dried two-necked round-bottom flask equipped

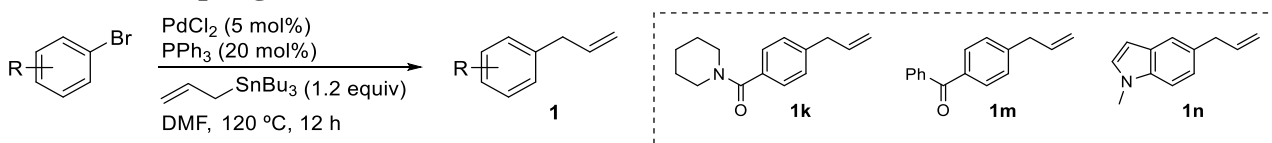


with reflux condenser and dropping funnel was placed Mg turnings (632.1 mg, 26 mmol, 1.2 equiv). A solution of 1-bromo-3,5-bis(trifluoromethyl)benzene (5.86 g, 20 mmol, 1 equiv) and a tiny crystal of I₂ in THF (12 mL, 1.6 M) was added to the dropping funnel, and a few milliliter of the solution was poured under vigorous stirring

to initiate the reaction. The remaining solution was further added dropwise over 4 h. After complete addition, the mixture was stirred under reflux for 1 h, then cooled to 0 °C. To the reaction mixture was added allyl bromide (3.63 g, 30 mmol, 1.5 equiv) dropwise followed by stirring at room temperature for 1 h before quenching by sat. NH_4Cl aq. The solids were filtered off and the filtrate was extracted with ethyl acetate (3 times). The combined organic layer was washed with brine and dried over Na_2SO_4 . After the solids were filtered off, the solvent was removed under reduced pressure, and the residue was roughly purified by silica-gel column chromatography (eluent: hexane). And the impurities were separated by GPC (eluent: CHCl_3) to afford **1f** as colorless liquid (1.19 g, 7.5 mmol, 38%).

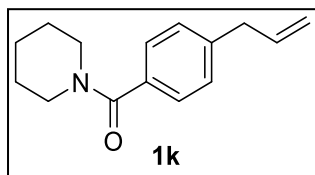
IR (neat) $\tilde{\nu}$: 3088, 2986, 2921, 1644, 1623, 1467, 1378, 1280, 1173, 1134, 993, 926, 902 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.73 (s, 2H), 7.64 (s, 1H), 5.99-5.91 (m, 1H), 5.20 (d, $J = 9.2$ Hz, 1H), 5.15 (d, $J = 16.6$ Hz, 1H), 3.52 (d, $J = 6.9$ Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 142.5, 135.2 (app d, $J_{\text{CF}} = 2.4$ Hz), 131.7 (q, $J_{\text{CF}} = 33.0$ Hz), 128.8 (app d, $J_{\text{CF}} = 2.4$ Hz), 124.5 (q, $J_{\text{CF}} = 270.3$ Hz), 120.2 (app quin, $J_{\text{CF}} = 3.6$ Hz), 117.8 (app t, $J_{\text{CF}} = 3.6$ Hz), 39.6 ppm; HRMS (EI) m/z calcd. for $\text{C}_{11}\text{H}_8\text{F}_6$, $[\text{M}]^+$: 254.0530, found: 254.0523.

(C-1-b) Stille Coupling^{25,26}



To an oven-dried 30 mL recovery flask were placed PdCl₂ (88.7 mg, 0.5 mmol, 5 mol%) and PPh₃ (524.6 mg, 2.0 mmol, 20 mol%), which were dissolved in DMF (10 mL) followed by the addition of aryl bromide (10 mmol, 1 equiv) and allyltributyltin (3.97 g, 12 mmol, 1.2 equiv). The resulting mixture was then stirred at 120 °C for 12 h. After cooling to room temperature, the mixture was diluted in 10 w/w% aq. KF. The resulting precipitate was filtered off through Celite®. After the cake was washed with ethyl acetate, the filtrate was extracted with ethyl acetate (2 times), and the combined organic layer was washed with brine and dried over Na₂SO₄. After the solids were filtered off, the solvent was removed under reduced pressure, and the residue was purified by silica-gel column chromatography to afford the corresponding allylarene.

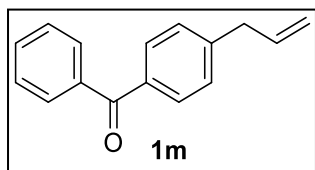
***N*-(4-Allylbenzoyl)piperidine (1k):** *N*-(4-Bromobenzoyl)piperidine²⁷ (2.68 g, 10 mmol, 1 equiv) was used



as a substrate. The crude product was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 3:1) to afford **1k** as pale yellow oil (1.99 g, 8.7 mmol, 87%)

IR (neat) $\tilde{\nu}$: 2936, 2854, 1631, 1431, 1275, 1108, 1001, 915, 852, 757 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.32 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 5.99-5.91 (m, 1H), 5.11-5.07 (m, 2H), 3.69 (app br s, 2H), 3.40 (d, J = 6.3 Hz, 2H), 3.35 (app br s, 2H), 1.66 (app br s, 4H), 1.51 (app br s, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 170.2, 141.4, 136.7, 134.2, 128.5, 126.9, 116.1, 48.7, 43.0, 39.9, 26.5, 25.5, 24.5 ppm; HRMS (EI) m/z calcd. for $\text{C}_{15}\text{H}_{18}\text{NO}$, $[\text{M}-\text{H}]^+$: 228.1388, found: 228.1390.

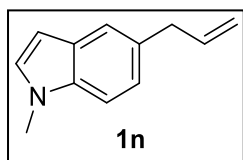
(4-Allylphenyl)(phenyl)methanone (1m): 4-Bromobenzophenone (2.61 g, 10 mmol, 1 equiv) was used as



a substrate. The crude product was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 40:1 to 20:1) and passing through 10 w/w% K_2CO_3 silica gel (eluent: hexane/ethyl acetate, 20:1) to afford **1m** as colorless oil (1.76 g, 7.9 mmol, 79%).

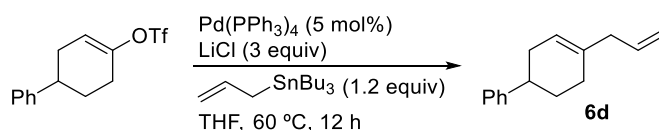
IR (neat) $\tilde{\nu}$: 3060, 1657, 1604, 1446, 1414, 1279, 1177, 999, 924, 702 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.79 (d, J = 7.7 Hz, 2H), 7.76 (d, J = 8.3 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (dd, J = 7.7, 7.4 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 6.03-5.95 (m, 1H), 5.15-5.11 (m, 2H), 3.48 (d, J = 6.9 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 196.4, 145.1, 137.8, 136.3, 135.5, 132.2, 130.4, 129.9, 128.5, 128.2, 116.6, 40.1 ppm; HRMS (EI) m/z calcd. for $\text{C}_{16}\text{H}_{14}\text{O}$, $[\text{M}]^+$: 222.1045, found: 222.1049.

5-Allyl-1-methyl-1*H*-indole (1n): 5-Bromo-1-methyl-1*H*-indole²⁸ (2.10 g, 10 mmol, 1 equiv) was used as

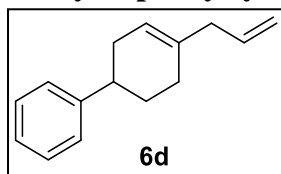


a substrate. After extraction, the combined organic layer was washed with 1% H_2O_2 aq. to oxidize PPh_3 to phosphine oxide. The crude material was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 100:1) followed by passing through 10 w/w% K_2CO_3 silica gel (eluent: hexane/ethyl acetate, 50:1), which afforded **1n** as colorless oil (1.36 g, 8.0 mmol, 80%).

IR (neat) $\tilde{\nu}$: 2975, 2900, 1637, 1492, 1422, 1338, 1244, 1079, 994, 911, 792, 720 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.45 (s, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.08 (dd, J = 7.6, 1.4 Hz, 1H), 7.03 (d, J = 2.9 Hz, 1H), 6.43 (d, J = 2.9 Hz, 1H), 6.09-6.01 (m, 1H), 5.11 (dd, J = 17.2, 1.6 Hz, 1H), 5.06 (dd, J = 10.0, 1.6 Hz, 1H), 3.78 (s, 3H), 3.51 (d, J = 6.9 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 138.7, 135.5, 130.8, 128.9, 128.7, 122.6, 120.3, 114.9, 109.0, 100.5, 40.4, 32.8 ppm; HRMS (EI) m/z calcd. for $\text{C}_{12}\text{H}_{12}\text{N}$, $[\text{M}-\text{H}]^+$: 170.1970, found: 170.0970.



1-Allyl-4-phenylcyclohex-1-ene (6d): In an argon-filled glove box, $\text{Pd}(\text{PPh}_3)_4$ (138.7 mg, 0.12 mmol, 5

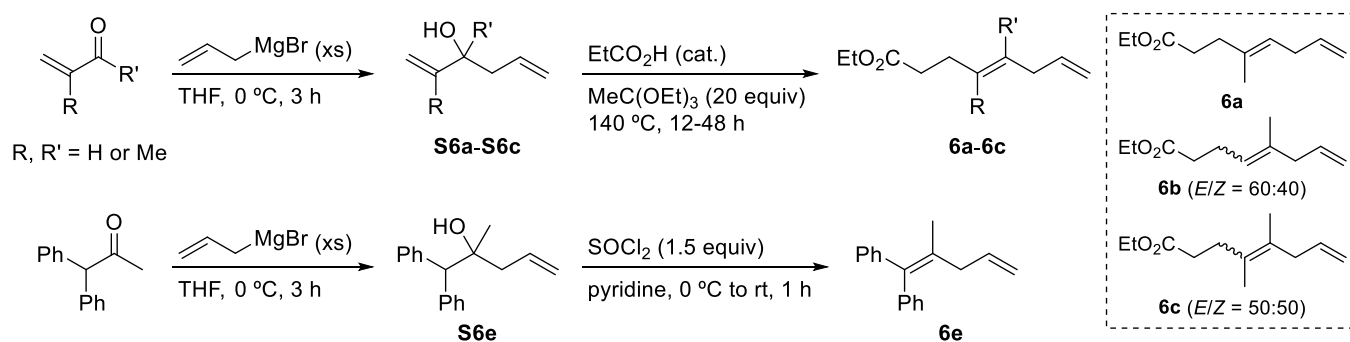


mol%) and LiCl (508.7 mg, 12 mmol, 3 equiv) were placed into the 50 mL recovery flask. The solids were then dissolved in THF (15 mL) followed by the addition of allyltributyltin (1.59 g, 4.8 mmol, 1.2 equiv) and 4-phenylcyclohex-1-en-1-yl

trifluoromethanesulfonate²⁹ (1.25 g, 4 mmol, 1 equiv) in THF (5 mL). The resulting mixture was stirred at 60 °C for 12 h before quenching by water, and the solution was extracted with ethyl acetate (3 times). The combined organic layer was washed with brine and dried over Na₂SO₄. After the solids were filtered off, the solvent was removed under reduced pressure, and the residue was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 100:0 to 20:1) followed by passing through 10 w/w% KF silica gel (eluent: hexane) to afford **6d** as colorless liquid (577.0 mg, 2.91 mmol, 73%).

IR (neat) $\tilde{\nu}$: 2915, 1637, 1603, 1494, 1453, 1434, 996, 913, 755, 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 7.31 (dd, *J* = 7.7, 7.4 Hz, 2H), 7.23 (d, *J* = 7.7 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 5.89-5.80 (m, 1H), 5.54 (d, *J* = 4.4 Hz, 1H), 5.09-5.03 (m, 2H), 2.79-2.74 (m, 3H), 2.31 (dd, *J* = 11.5, 4.4 Hz, 1H), 2.19-2.13 (m, 2H), 2.06 (dd, *J* = 17.8, 4.4 Hz, 1H), 1.98-1.95 (m, 1H), 1.81-1.73 (m, 1H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 147.2, 136.7, 136.2, 128.3, 126.9, 125.9, 121.5, 115.7, 42.1, 40.2, 33.6, 30.0, 29.0 ppm; HRMS (EI) *m/z* calcd. for C₁₅H₁₈, [M]⁺: 198.1409, found: 198.1406.

(C-1-c) Synthesis of 1,4-Dienes **6a-6c**, and **6e**

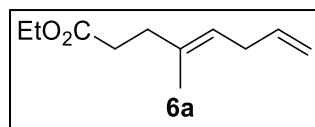


To an oven-dried three-necked round-bottom flask equipped with a condenser and a dropping funnel was placed Mg turnings (9.7 g, 0.4 mol, 1.2 equiv to allyl bromide). A solution of allyl bromide (36.3 g, 0.3 mol, 1 equiv) and a tiny crystal of I₂ in Et₂O (300 mL, 1 M) was added to the dropping funnel. The reaction was initiated by the addition of a few milliliter of the solution under vigorous stirring, and the remaining solution was dropped into the mixture under gentle reflux. After complete addition, the mixture was stirred for 30 minutes at the same temperature.

To an oven-dried 100 mL recovery flask were added α,β -unsaturated aldehyde or ketones (30 mmol, 1 equiv) and THF (30 mL, 1 M), which was then cooled to 0 °C. Allylmagnesium bromide in Et₂O (60 mL) was then added dropwise *via* syringe, and the resulting suspension was allowed to warm to room temperature and stirred overnight. The reaction was quenched by sat. NH₄Cl aq. and the solids were filtered off through Celite[®]. The filtrate was then extracted with ethyl acetate (3 times). The combined organic layer was washed with brine and dried over Na₂SO₄. The solids were filtered off, and the solvent was roughly evaporated, followed by Kugelrohr distillation of the residue under reduced pressure (*ca.* 150 mmHg), which afforded the corresponding alcohol **S6a-S6c** as a mixture with ethyl acetate, which was used to the next reaction without further purification.

The alcohol was diluted in MeC(OEt)₃ and a few drops of propionic acid were added. The resulting solution was heated at 140 °C for indicated time. After cooling to room temperature, MeC(OEt)₃ was roughly distilled off under ambient pressure (bath temp.: 170 °C) and the residue was purified by silica-gel column chromatography to afford the corresponding 1,4-diene **6a-6c**.

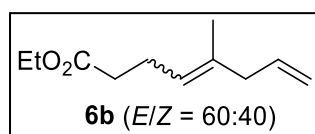
Ethyl (E)-4-methylocta-4,7-dienoate (6a): Metacrolein (2.10 g, 30 mmol, 1 equiv) was used as a substrate.



The obtained alcohol **S6a** (*ca.* 20 mmol) was heated in MeC(OEt)₃ (64.9 g, 0.4 mol, 20 equiv) with a few drops of propionic acid for 24 h, and after silica-gel column chromatography (eluent: hexane/ethyl acetate, 50:1), **6a** was obtained as colorless liquid (1.77 g, 9.7 mmol, 34%, 2 steps).

IR (neat) $\tilde{\nu}$: 2979, 1738, 1637, 1446, 1371, 1253, 1157, 1037, 910 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 5.82-5.74 (m, 1H), 5.20 (td, *J* = 7.0, 1.3 Hz, 1H), 5.00 (dd, *J* = 17.2, 1.7 Hz, 1H), 4.95 (dd, *J* = 10.3, 1.7 Hz, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 2.74 (t, *J* = 7.0 Hz, 2H), 2.41 (t, *J* = 7.6 Hz, 2H), 2.33 (t, *J* = 7.6 Hz, 2H), 1.62 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 173.4, 137.0, 134.7, 122.2, 114.3, 60.2, 34.6, 33.1, 32.1, 15.8, 14.2 ppm; HRMS (EI) *m/z* calcd. for C₁₁H₁₈O₂, [M]⁺: 182.1307, found: 182.1301.

Ethyl 5-methylocta-4,7-dienoate (6b, E/Z = 60:40): Methyl vinyl ketone (2.10 g, 30 mmol, 1 equiv) was

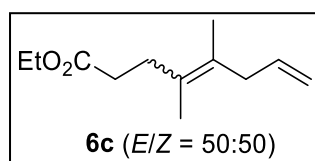


used as a substrate. The obtained alcohol **S6b** (*ca.* 8 mmol) was heated in MeC(OEt)₃ (26.0 g, 0.16 mol, 20 equiv) with a few drops of propionic acid for 36 h, and after silica-gel column chromatography (eluent: hexane/ethyl acetate,

50:1), a regioisomeric mixture of **6b** was obtained as colorless liquid (217.0 mg, 1.2 mmol, 4%, 2 steps).

IR (neat) $\tilde{\nu}$: 2979, 1738, 1637, 1445, 1372, 1252, 1180, 1042, 913 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 5.80-5.70 (m, 1H), 5.19 (t, *J* = 6.8 Hz, 0.4H, *Z* isomer), 5.15 (t, *J* = 6.9 Hz, 0.6H, *E* isomer), 5.05-4.98 (m, 2H), 4.12 (q, *J* = 7.0 Hz, 2H), 2.78 (d, *J* = 6.8 Hz, 0.8H, *Z* isomer), 2.70 (d, *J* = 6.9 Hz, 1.2H, *E* isomer), 2.33-2.32 (m, 4H), 1.67 (s, 1.2H, *Z* isomer), 1.61 (s, 1.8H, *E* isomer), 1.25 (t, *J* = 7.0 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 173.33, 173.28, 136.7, 135.8, 135.0, 134.5, 123.9, 123.3, 115.7, 115.2, 60.2, 44.0, 36.6, 34.5, 34.4, 23.6, 23.4, 23.3, 16.0, 14.2 ppm; HRMS (EI) *m/z* calcd. for C₁₁H₁₈O₂, [M]⁺: 182.1307, found: 182.1310.

Ethyl 4,5-dimethylocta-4,7-dienoate (6c, E/Z = 50:50): 2-Methylbut-1-ene-3-one (2.52 g, 30 mmol, 1

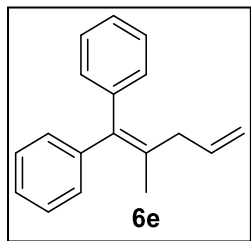


equiv) was used as a substrate. The obtained alcohol **S6c** (*ca.* 9 mmol) was heated in MeC(OEt)₃ (29.2 g, 0.18 mol, 20 equiv) with a few drops of propionic acid for 48 h, and after silica-gel column chromatography (eluent: hexane/ethyl acetate, 50:1), a regioisomeric mixture of **6c** was obtained as colorless liquid (403.0 mg,

2.1 mmol, 7%, 2 steps).

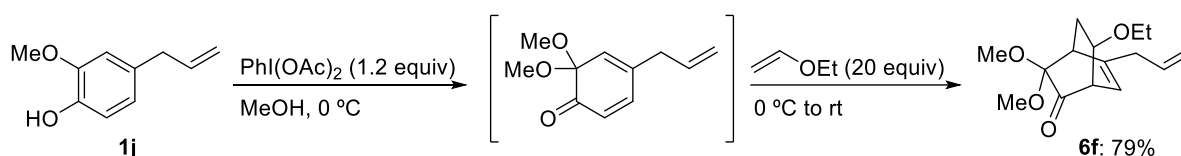
IR (neat) $\tilde{\nu}$: 2979, 1737, 1636, 1446, 1371, 1254, 1166, 1039, 911 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 5.78-5.69 (m, 1H), 5.02-4.95 (m, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 2.79 (d, *J* = 7.0 Hz, 1H, *Z* isomer), 2.75 (d, *J* = 6.5 Hz, 1H, *E* isomer), 2.40-2.31 (m, 4H), 1.66-1.62 (m, 6H), 1.25 (t, *J* = 7.2 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 173.5, 136.5, 135.8, 127.6, 127.5, 127.3, 114.8, 114.5, 60.2, 38.9, 38.5, 33.3, 33.0, 30.0, 29.5, 18.04, 18.01, 17.6, 14.2 ppm; HRMS (EI) *m/z* calcd. for C₁₂H₂₀O₂, [M]⁺: 196.1463, found: 196.1466.

1,1-Diphenyl-2-methylpenta-1,4-diene (6e): To an oven-dried 50 mL recovery flask was added 1,1-diphenylacetone (2.10 g, 10 mmol, 1 equiv), which was dissolved in THF (10 mL) and cooled to 0 °C. Allylmagnesium bromide in Et₂O (15 mL) was added dropwise *via* syringe, and the resulting mixture was allowed to warm to ambient temperature and stirred overnight. The reaction was quenched by 1 M HCl aq. (20 mL), and extracted with ethyl acetate (2 times). The combined organic layer was washed with brine and dried over Na₂SO₄. After the solids were filtered off, the solvent was removed under reduced pressure, the residue was passed through a plug of silica gel (eluent: hexane/ethyl acetate, 30:1) to afford the alcohol **S6e** as a mixture with starting material (1.32 g, *ca.* 5.2 mmol), which was used to the next reaction without further purification. The obtained mixture (1.0 g, *ca.* 4 mmol, 1 equiv) was diluted in pyridine (16 mL) and cooled to -40 °C. To this solution was added SOCl₂ (713.8 mg, 6.0 mmol, *ca.* 15 equiv) dropwise. The resulting mixture was stirred at the same temperature for 10 min, then warmed to 0 °C and further stirred for 30 min. The reaction was quenched with 1 M HCl aq. (20 mL) and extracted with hexane (3 times). The combined organic layer was washed with 1 M HCl aq. (3 times) followed by brine. After the organic layer was dried over Na₂SO₄, the solids were filtered off and the solvent was removed under reduced pressure. The residue was then purified by silica-gel column chromatography (eluent: hexane) to afford **6e** as colorless oil (823.0 mg, 3.51 mmol, 35%, 2 steps).

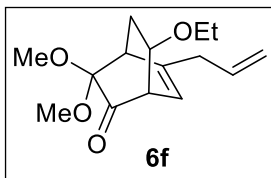


IR (neat) $\tilde{\nu}$: 2911, 1636, 1598, 1492, 1442, 1073, 992, 913, 766, 701 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 7.32-7.28 (m, 4H), 7.23-7.18 (m, 6H), 5.93-5.85 (m, 1H), 5.11-5.08 (m, 2H), 2.89 (d, *J* = 6.3 Hz, 2H), 1.81 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 143.1, 142.9, 138.6, 136.8, 132.4, 129.6, 129.3, 127.92, 127.89, 126.3, 126.2, 115.8, 40.1, 19.6 ppm; HRMS (EI) *m/z* calcd. for C₁₈H₁₈ [M]⁺: 234.1409, found: 234.1413.

(C-1-d) Synthesis of 1,4-Diene **6f**³⁰



5-Allyl-7-ethoxy-3,3-dimethoxybicyclo[2.2.2]oct-5-en-2-one (6f): To a 500 mL recovery flask was placed PhI(OAc)₂ (7.73 g, 24 mmol, 1.2 equiv), which was dissolved in MeOH (200 mL) at 0 °C. Eugenol (3.28 g, 20 mmol, 1 equiv) was added dropwise to the solution, and the resulting yellowish mixture was stirred for 20 min at 0 °C. Afterwards, ethyl vinyl ether (28.8 g, 400 mmol, 20 equiv) was added in one portion and the mixture was stirred at rt for 22 h. The solvent and volatile materials were then evaporated, and the residue was dissolved in ethyl acetate, which was washed with sat. NaHCO₃ aq. followed by brine, and the organic layer was dried over Na₂SO₄. After the solids were filtered off, the solvent was removed under reduced pressure. The crude mixture was purified by Kugelrohr bulb-to-bulb distillation (*ca.* 1 mmHg, *ca.* 150 °C) to afford **6f** as yellow oil (4.22 g, 15.9 mmol, 79%).

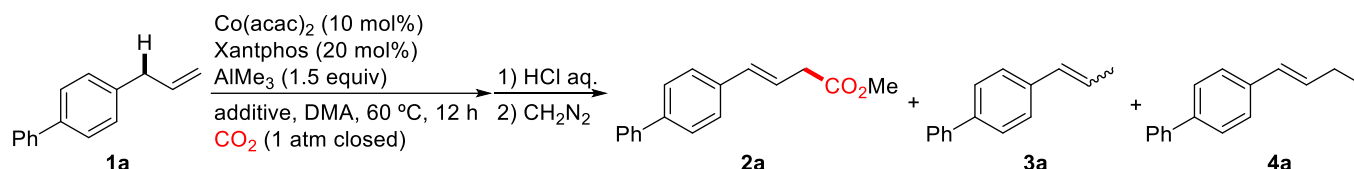


IR (neat) $\tilde{\nu}$: 2975, 1738, 1636, 1440, 1373, 1350 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 5.88-5.79 (m, 1H), 5.67 (d, *J* = 6.3 Hz, 1H), 5.15 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.11 (dd, *J* = 10.9, 1.1 Hz, 1H), 3.96-3.93 (m, 1H), 3.50 (dq, *J* = 15.2, 7.0 Hz, 1H), 3.45 (dd, *J* = 6.3, 2.9 Hz, 1H), 3.39 (dq, *J* = 15.2, 7.0 Hz, 1H), 3.32 (s, 3H),

3.27 (s, 3H), 3.03-2.94 (m, 2H), 2.89 (dd, $J = 4.5, 2.8$ Hz, 1H), 2.38 (ddd, $J = 13.5, 8.3, 2.8$ Hz, 1H), 1.23 (dt, $J = 13.5, 4.5, 3.5$ Hz, 1H), 1.16 (t, $J = 7.0$ Hz) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 146.7, 134.5, 117.3, 116.8, 94.0, 74.3, 64.2, 53.4, 50.5, 49.6, 41.4, 39.6, 30.4, 15.3 ppm; HRMS (ESI) m/z calcd. for $\text{C}_{15}\text{H}_{22}\text{NaO}_4$ $[\text{M}+\text{Na}]^+$: 289.1410, found: 289.1411.

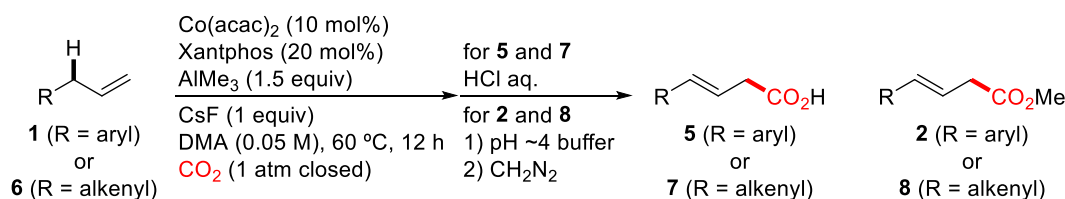
(C-2) General Procedure for Allylic C–H Carboxylation

(C-2-a) Representative Procedure ~ Condition Screening



To an oven-dried 20 mL sealed tube were placed $\text{Co}(\text{acac})_2$ (5.1 mg, 20 μmol , 10 mol%) and Xantphos (23.1 mg, 40 μmol , 20 mol%). (The additive was added inside an argon-filled glove box). The tube was evacuated and backfilled with CO_2 (3 times) followed by the addition of DMA. The resulting mixture was stirred at room temperature until the materials dissolved completely. The solution was then cooled to 0 °C and stirred for 5 minutes before AlMe_3 (2 M in toluene, 0.15 mL, 0.3 mmol, 1.5 equiv) was added. The resulting solution was stirred for another 1 minute, then the substrate **1a** (38.9 mg, 0.2 mmol, 1.0 equiv) was added. The tube was closed tightly and the mixture was stirred at 60 °C for 12 h. After cooling the mixture to 0 °C, the sealed tube was carefully opened and the reaction was quenched by 20 mL of 1 M HCl aq. and extracted with ethyl acetate (5 mL, 3 times). The combined organic layer was washed with brine (20 mL) and dried over Na_2SO_4 . After the solids were filtered off, the solvent was removed under reduced pressure and the residue was then dried under vacuum. The crude mixture was dissolved in Et_2O , and the mixture was treated with excess CH_2N_2 in Et_2O . After the mixture was stirred for at room temperature for 10 minutes, the solvent was evaporated and the residue was dried under vacuum. The yields of the corresponding ester **2a** and other products were determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

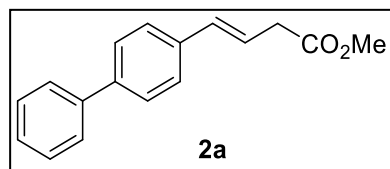
(C-2-b) General Procedure ~ Substrate Scope



To an oven-dried 20 mL a vacuum tube sealed tube were placed $\text{Co}(\text{acac})_2$ (10.3 mg, 40 μmol , 10 mol%) and Xantphos (46.3 mg, 80 μmol , 20 mol%). The tube was taken into an argon-filled glove box, and CsF (60.8 mg, 0.4 mmol, 1 equiv) was added. Outside the glove box, the tube was then evacuated and backfilled with CO_2 (3 times) followed by the addition of DMA (8 mL). The resulting mixture was stirred at room temperature until the materials dissolved completely. The solution was cooled to 0 °C and stirred for 5 minutes before AlMe_3 (2 M in toluene, 0.3 mL, 0.6 mmol, 1.5 equiv) was added. The dark green solution was stirred for another 1 minute, then a substrate **1** or **6** (0.4 mmol, 1.0 equiv) was added. The tube was closed tightly and the mixture was stirred at 60 °C for 12 h. After cooling the mixture to 0 °C, the sealed

tube was carefully opened and the reaction was quenched by 30 mL of 1 M HCl aq. and extracted with ethyl acetate (5 mL, 3 times). The combined organic layer was washed with brine (20 mL) and dried over Na₂SO₄. After the solids were filtered off, the solvent was removed under reduced pressure and the residue was dried under vacuum to afford the crude mixture, which was basically purified by silica-gel column chromatography (detail methods are described for each compounds).

Methyl (*E*)-4-((1,1'-biphenyl)-4-yl)but-3-enoate (2a**):** **1a** (38.9 mg, 0.2 mmol, 1 equiv) was subjected to

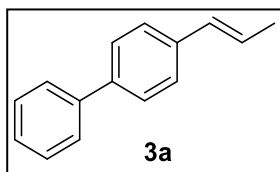


the reaction according to the procedure **C-2-a**. 1,3,5-trimethoxybenzene, which was used as an internal standard for determination of the yields by ¹H NMR analysis, was hard to remove in chromatographic purification. If it is not used, the crude mixture can be purified by silica-gel column

chromatography (eluent: hexane/ethyl acetate, 30:1) to afford **2a** as white solids.

mp. 97.0-98.0 °C; IR (neat) $\tilde{\nu}$: 2955, 1731, 1487, 1436, 1400, 1300, 1195, 1164, 971, 755, 683 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 7.60 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.46 (m, 4H), 7.34 (t, *J* = 7.4 Hz, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.35 (dt, *J* = 15.8, 7.3 Hz, 1H), 3.73 (s, 3H), 3.29 (d, *J* = 7.3 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 172.0, 140.6, 140.3, 135.8, 133.0, 128.7, 127.3, 127.2, 126.9, 126.7, 121.7, 51.9, 38.3 ppm; HRMS (EI) *m/z* calcd. for C₁₇H₁₆O₂ [M]⁺: 252.1150, found: 252.1151.

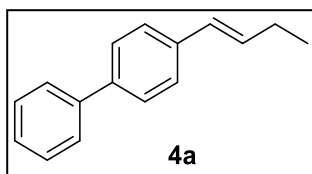
(*E*)-4-(-Prop-1-ene-1-yl)-1,1'-biphenyl (3a**)**³¹: A mixture of **3a** and **4a**, which was obtained during the



purification of **2a**, was separated by GPC (eluent: CHCl₃) to afford *E*-**3a** as white solids.

¹H NMR (500 MHz, CDCl₃) δ : 7.59 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.43 (dd, *J* = 8.3, 7.4 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 6.44 (d, *J* = 16.0 Hz, 1H), 6.33-6.25 (m, 1H), 1.91 (dd, *J* = 6.6, 1.4 Hz, 3H) ppm.

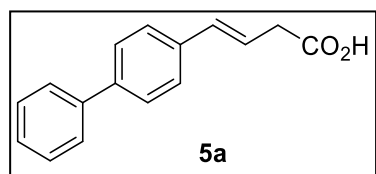
(*E*)-4-(But-1-ene-1-yl)-1,1'-biphenyl (4a**):** Purification of the above mixture was purified by GPC (eluent:



CHCl₃), which provided **4a** as white solids.

mp. 109.0-110.0 °C; IR (neat) $\tilde{\nu}$: 3026, 2966, 1599, 1486, 967, 856, 697, 667 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 7.60 (d, *J* = 7.4 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.45-7.41 (m, 4H), 7.33 (t, *J* = 7.4 Hz, 1H), 6.42 (d, *J* = 15.9 Hz, 1H), 6.32 (dt, *J* = 15.9, 7.0 Hz, 1H), 2.23 (dq, *J* = 7.3, 7.0 Hz, 2H), 1.11 (t, *J* = 7.3 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 140.9, 139.5, 137.0, 132.9, 128.7, 128.3, 127.2, 127.1, 126.9, 126.3, 26.1, 13.7 ppm; HRMS (EI) *m/z* calcd. for C₁₆H₁₆ [M]⁺: 208.1252, found: 208.1256.

(*E*)-4-((1,1'-Biphenyl)-4-yl)but-3-enoic acid (5a**)**³²: **1a** (77.8 mg, 0.4 mmol, 1 equiv) was subjected to the



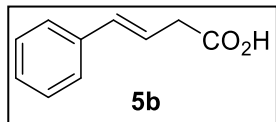
reaction according to the procedure **C-2-b**. The obtained crude material was dissolved in Et₂O (10 mL) and extracted with 1 M NaOH aq. (2 mL, 3 times). The combined water layer was washed with Et₂O (5 mL, 2 times), then acidified by conc. HCl. The resulting precipitates were collected by filtration,

and the solids were washed with water to afford **5a** as off-white solids (67.4 mg, 282.9 μ mol, 71%).

mp. 182.5-184.0 °C; IR (neat) $\tilde{\nu}$: 3033, 1708, 1406, 1243, 1092, 969, 849, 756 cm⁻¹; ¹H NMR (500 MHz,

acetone-*d*₆) δ : 7.67 (d, J = 7.7 Hz, 2H), 7.64 (d, J = 7.7 Hz, 2H), 7.53 (d, J = 8.0 Hz, 2H), 7.45 (dd, J = 8.0, 7.4 Hz, 2H), 7.35 t, J = 7.4 Hz, 1H), 6.60 (d, J = 15.5 Hz, 1H), 6.44 (dt, J = 15.5, 7.2 Hz, 1H), 3.28 (d, J = 7.2 Hz, 2H) ppm; ¹³C NMR (125 MHz, acetone-*d*₆) δ : 172.7, 141.4, 140.8, 137.3, 133.1, 129.7, 128.2, 127.9, 127.6, 127.5, 123.9, 38.4 ppm; HRMS (EI) m/z calcd. for C₁₆H₁₄O₂ [M]⁺: 238.0994, found: 238.0998.

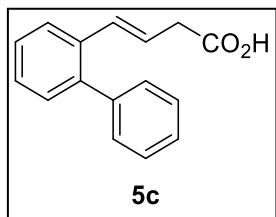
(*E*)-4-Phenylbut-3-enoic acid (5b)³³: **1b** (47.3 mg, 0.4 mmol, 1 equiv) was subjected to the reaction



according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 3:1 with 1% AcOH) afforded **5b** as white solids containing a small amount of α,β -unsaturated carboxylic acid (44.4 mg, 273.8 μ mol, 68% (the olefin isomer: 3%)).

mp. 82.5-84.0 °C; IR (neat) $\tilde{\nu}$: 2925, 1703, 1403, 1298, 1223, 1066, 975, 915, 744, 692 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 7.38 (d, J = 7.4 Hz, 2H), 7.32 (dd, J = 7.4, 7.1 Hz, 2H), 7.25 (t, J = 7.1 Hz, 1H), 6.53 (d, J = 15.8 Hz, 1H), 6.30 (dt, J = 15.8, 7.4 Hz, 1H), 3.31 (dd, J = 7.4, 1.1 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 178.0, 136.6, 134.0, 128.5, 127.7, 126.3, 120.8, 38.0 ppm; HRMS (EI) m/z calcd. for C₁₀H₁₀O₂ [M]⁺: 162.0681, found: 162.0678.

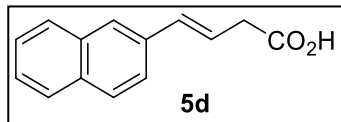
(*E*)-4-((1,1'-Biphenyl)-2-yl)but-3-enoic acid (5c): **1c** (77.8 mg, 0.4 mmol, 1 equiv) was subjected to the



reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 2:1 with 1% AcOH) afforded **5c** as white solids containing a small amount of α,β -unsaturated carboxylic acid (60.0 mg, 251.8 μ mol, 63% (the olefin isomer: 2%)).

mp. 103.5-104.5 °C; IR (neat) $\tilde{\nu}$: 3024, 1696, 1475, 1410, 1300, 1218, 964, 749, 705 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 7.63-7.62 (m, 1H), 7.42 (dd, J = 7.5, 6.5 Hz, 2H), 7.37-7.31 (m, 5H), 7.29 (dddd, J = 7.8, 7.3, 3.0, 2.0 Hz, 1H), 6.51 (d, J = 15.9 Hz, 1H), 6.23 (dt, J = 15.9, 7.1 Hz, 1H), 3.21 (dd, J = 7.1, 1.1 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 178.2, 140.74, 140.69, 134.7, 132.9, 130.1, 129.8, 128.0, 127.6, 127.5, 127.0, 126.0, 121.5, 38.1 ppm; HRMS (EI) m/z calcd. for C₁₆H₁₄O₂ [M]⁺: 238.0994, found: 238.0992.

(*E*)-4-(Naphthalene-2-yl)but-3-enoic acid (5d)³⁴: **1d** (67.3 mg, 0.4 mmol, 1 equiv) was subjected to the

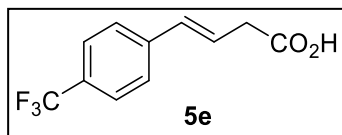


reaction according to the procedure **C-2-b**. The obtained crude material was dissolved in Et₂O (10 mL) and extracted with 1 M NaOH aq. (2 mL, 3 times).

The combined water layer was washed with Et₂O (5 mL, 2 times), then acidified by conc. HCl. The resulting precipitates were collected by filtration, and the solids were washed with water to afford **5d** as white solids (34.4 mg, 162.1 μ mol, 41%).

mp. 158.0-159.0 °C; IR (neat) $\tilde{\nu}$: 3048, 1720, 1418, 1401, 1295, 1222, 966, 862, 802, 740 cm⁻¹; ¹H NMR (500 MHz, acetone-*d*₆) δ : 7.88-7.82 (m, 4H), 7.70 (dd, J = 8.6, 1.7 Hz, 1H), 7.50-7.44 (m, 2H), 6.73 (d, J = 15.9 Hz, 1H), 6.53 (dt, J = 15.9, 7.1 Hz, 1H), 3.32 (dd, J = 7.1, 1.4 Hz, 2H) ppm; ¹³C NMR (125 MHz, acetone-*d*₆) δ : 172.7, 135.6, 134.7, 133.9, 133.6, 129.1, 128.8, 128.5, 127.2, 126.7, 124.3, 124.2, 124.1, 38.4 ppm; HRMS (EI) m/z calcd. for C₁₄H₁₂O₂ [M]⁺: 212.0837, found: 212.0831.

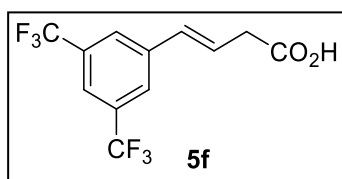
(E)-4-(4-(Trifluoromethyl)phenyl)but-3-enoic acid (5e)³⁵: **1e** (74.5 mg, 0.4 mmol, 1 equiv) was subjected



to the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 3:1 with 1% AcOH) afforded **5e** as white amorphous solids containing a small amount of α,β -unsaturated carboxylic acid (60.4 mg, 262.4 μ mol, 65% (the olefin isomer: 1%)).

mp. 48.0-49.5 °C; IR (neat) $\tilde{\nu}$: 2925, 1713, 1614, 1416, 1324, 1172, 1121, 1065, 856, 809 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.57 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H), 6.56 (d, J = 16.0 Hz, 1H), 6.39 (dt, J = 16.0, 7.3 Hz, 1H), 3.34 (d, J = 7.3 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 177.5, 140.0, 132.7, 129.5 (q, J_{CF} = 32.2 Hz), 126.5, 125.5 (q, J_{CF} = 3.6 Hz), 124.1 (q, J_{CF} = 270.3 Hz), 123.6, 37.9 ppm; HRMS (EI) m/z calcd. for $\text{C}_{11}\text{H}_9\text{F}_3\text{O}_2$ $[\text{M}]^+$: 230.0555, found: 230.0562.

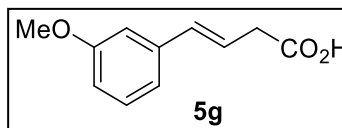
(E)-4-(3,5-Bis(trifluoromethyl)phenyl)but-3-enoic acid (5f): **1f** (101.7 mg, 0.4 mmol, 1 equiv) was



subjected to the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 10:1 to 4:1 with 1% AcOH) afforded **5f** as white solids (65.2 mg, 218.6 μ mol, 55%).

mp. 115.0-116.0 °C; IR (neat) $\tilde{\nu}$: 2919, 1711, 1422, 1410, 1380, 1342, 1288, 1232, 1176, 1124, 967, 897 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.79 (s, 2H), 7.74 (s, 1H), 6.60 (d, J = 16.0 Hz, 1H), 6.47 (dt, J = 16.0, 7.2 Hz, 1H), 3.378 (d, J = 7.2 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 177.1, 138.6, 132.2 (q, J_{CF} = 33.1 Hz), 131.4, 126.2 (app t, J_{CF} = 3.6 Hz), 125.2, 123.2 (q, J_{CF} = 275.1 Hz), 121.2 (app quin, J_{CF} = 3.5 Hz), 37.7 ppm; HRMS (EI) m/z calcd. for $\text{C}_{12}\text{H}_8\text{F}_6\text{O}_2$ $[\text{M}]^+$: 298.0429, found: 298.0427.

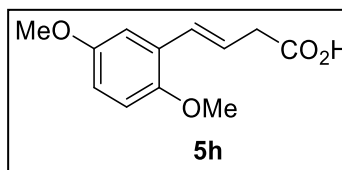
(E)-4-(3-Methoxyphenyl)but-3-enoic acid (5g): **1g** (59.3 mg, 0.4 mmol, 1 equiv) was subjected to the



reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 1:1 with 1% AcOH) afforded **5g** as white solids containing a small amount of α,β -unsaturated carboxylic acid (60.1 mg, 312.7 μ mol, 78% (the olefin isomer: 4%)).

mp. 91.0-92.0 °C; IR (neat) $\tilde{\nu}$: 2898, 1696, 1604, 1578, 1492, 1429, 1389, 1344, 1264, 1220, 1150, 1038, 778 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.23 (dd, J = 8.0, 7.8 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.91 (dd, J = 2.4, 1.5 Hz, 1H), 6.80 (dd, J = 7.8, 2.4 Hz, 1H), 6.50 (d, J = 15.9 Hz, 1H), 6.28 (dt, J = 15.9, 7.2 Hz, 1H), 3.82 (s, 3H), 3.30 (dd, J = 7.2, 1.4 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 177.9, 159.8, 138.0, 133.9, 129.5, 121.1, 119.0, 113.4, 111.5, 55.2, 38.0 ppm; HRMS (EI) m/z calcd. for $\text{C}_{11}\text{H}_{12}\text{O}_3$ $[\text{M}]^+$: 192.0786, found: 192.0791.

(E)-4-(2,5-Dimethoxyphenyl)but-3-enoic acid (5h)³⁶: **1h** (71.3 mg, 0.4 mmol, 1 equiv) was subjected to



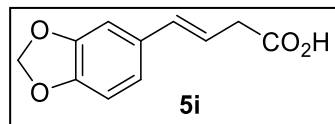
the reaction according to the procedure **C-2-b**. The crude material was dissolved in 1 M NaOH aq. (2 mL) and washed with Et_2O (5 mL, 2 times), then acidified by conc. HCl followed by extraction with ethyl acetate (3 mL, 3 times). The combined organic layer was washed with brine and dried over

Na_2SO_4 , which the solvent was removed under reduced pressure. The residue was passed through a pad of silica gel (eluent: hexane/ethyl acetate, 1:1) to afford **5h** as white solids containing a small amount of α,β -

unsaturated carboxylic acid (72.1 mg, 324.3 μ mol, 81% (the olefin isomer: 11%)).

mp. 110.0-111.0 $^{\circ}$ C; IR (neat) $\tilde{\nu}$: 2912, 1713, 1496, 1416, 1386, 1317, 1287, 1219, 1043, 978, 912 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.00 (d, J = 2.9 Hz, 1H), 6.83-6.76 (m, 3H), 6.29 (dt, J = 16.0, 7.2 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.32 (d, J = 7.2 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 178.0, 153.6, 151.0, 128.7, 126.5, 121.7, 113.9, 112.2, 112.1, 56.2, 55.7, 38.4 ppm; HRMS (EI) m/z calcd. for $\text{C}_{12}\text{H}_{14}\text{O}_4$ $[\text{M}]^+$: 222.0892, found: 222.0888.

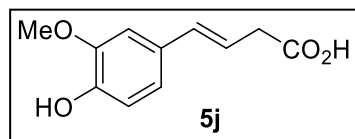
(*E*)-4-(Benzo[d][1,3]dioxol-5-yl)but-3-enoic acid (5i)³⁶: **1i** (64.9 mg, 0.4 mmol, 1 equiv) was subjected to



the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 2:1 with 1% AcOH) afforded **5i** as white solids containing a small amount of α,β -unsaturated carboxylic acid (57.0 mg, 276.4 μ mol, 69% (the olefin isomer: 9%)).

mp. 113.5-114.5 $^{\circ}$ C; IR (neat) $\tilde{\nu}$: 2898, 1693, 1505, 1428, 1259, 1233, 1102, 1040, 970, 932, 788 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 6.92 (d, J = 1.7 Hz, 1H), 6.80 (dd, J = 8.0, 1.7 Hz, 1H), 6.75 (d, J = 8.0 Hz, 1H), 6.42 (d, J = 15.9 Hz, 1H), 6.11 (dt, J = 15.9, 7.2 Hz, 1H), 5.95 (s, 2H), 3.27 (dd, J = 7.2, 1.4 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 177.9, 148.0, 147.3, 133.5, 131.1, 121.0, 119.0, 108.2, 105.7, 101.1, 37.9 ppm; HRMS (EI) m/z calcd. for $\text{C}_{11}\text{H}_{10}\text{O}_4$ $[\text{M}]^+$: 206.0579, found: 206.0585.

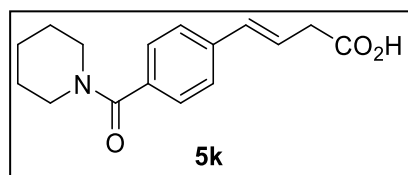
(*E*)-4-(4-Hydroxy-3-methoxyphenyl)but-3-enoic acid (5j): **1j** (65.7 mg, 0.4 mmol, 1 equiv) was



subjected to the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 1:1 with 1% AcOH) afforded **5j** as off-white solids (59.7 mg, 286.7 μ mol, 72%).

mp. 87.0-88.0 $^{\circ}$ C; IR (neat) $\tilde{\nu}$: 3507, 2943, 1695, 1600, 1514, 1401, 1275, 1233, 1151, 1028, 955, 798 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 6.91 (s, 1H), 6.86 (m, 2H), 6.44 (d, J = 15.8 Hz, 1H), 6.12 (dt, J = 15.8, 7.5 Hz, 1H), 5.65 (br s, 1H), 3.91 (s, 3H), 3.28 (d, J = 7.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 178.0, 146.6, 145.5, 133.8, 129.3, 120.2, 118.4, 114.4, 108.1, 55.9, 37.9 ppm; HRMS (EI) m/z calcd. for $\text{C}_{11}\text{H}_{12}\text{O}_4$ $[\text{M}]^+$: 208.0736, found: 208.0742.

(*E*)-4-(4-(Piperidine-1-carbonyl)phenyl)but-3-enoic acid (5k): **1k** (91.7 mg, 0.4 mmol, 1 equiv) was

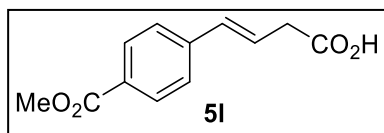


subjected to the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 1:1) afforded **5k** as white solids containing a small amount of α,β -unsaturated carboxylic acid (58.8 mg, 215.1 μ mol,

54% (the olefin isomer: 2%)).

mp. 169.0-170.0 $^{\circ}$ C; IR (neat) $\tilde{\nu}$: 3159, 2940, 1715, 1599, 1451, 1394, 1287, 1175, 981, 853 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 9.17 (br s, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 6.46 (d, J = 16.0 Hz, 1H), 6.30 (dt, J = 16.0, 7.5 Hz, 1H), 3.70 (app br s, 2H), 3.34 (app br s, 2H), 3.24 (d, J = 7.5 Hz, 2H), 1.67 (app br s, 4H), 1.51 (app br s, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 175.5, 170.5, 138.1, 134.8, 132.6, 127.2, 126.2, 123.0, 48.9, 43.3, 38.1, 26.4, 25.5, 24.5 ppm; HRMS (EI) m/z calcd. for $\text{C}_{16}\text{H}_{18}\text{NO}_3$ $[\text{M}-\text{H}]^+$: 272.1287, found: 272.1288.

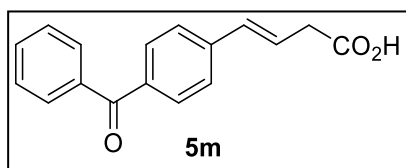
(*E*)-4-(4-(Methoxycarbonyl)phenyl)but-3-enoic acid (5l): **1l** (70.5 mg, 0.4 mmol, 1 equiv) was subjected



to the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 1:1 with 1% AcOH) to afford **5l** as white solids (55.5 mg, 252.0 μ mol, 63%).

mp. 125.0-126.0 °C; IR (neat) $\tilde{\nu}$: 2958, 1722, 1683, 1607, 1432, 1280, 1234, 1105, 974, 900, 759 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.98 (ddd, J = 8.6, 2.0, 1.5 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 6.56 (d, J = 15.9 Hz, 1H), 6.41 (dt, J = 15.9, 7.1 Hz, 1H), 3.91 (s, 3H), 3.34 (dd, J = 7.1, 1.4 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 177.1, 166.9, 141.0, 133.1, 129.9, 129.1, 126.2, 123.6, 52.1, 37.9 ppm; HRMS (EI) m/z calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_4$ $[\text{M}]^+$: 220.0736, found: 220.0738.

(*E*)-4-(4-Benzoylphenyl)but-3-enoic acid (5m): **1m** (88.9 mg, 0.4 mmol, 1 equiv) was subjected to the

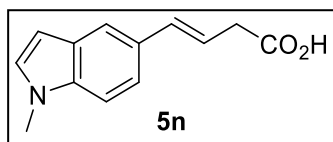


reaction according to the procedure **C-2-b**. The crude material was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 1:1 with 1% AcOH) to afford **5m** as pale yellow solids containing a small amount of α,β -unsaturated carboxylic acid (81.8 mg,

307.2 μ mol, 77% (the olefin isomer: 2%)).

mp. 99.0-100.0 °C; IR (neat) $\tilde{\nu}$: 2925, 1731, 1643, 1443, 1415, 1391, 1285, 1245, 1146, 962, 865, 693 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.79 (m, 4H), 7.59 (t, J = 7.4 Hz, 1H), 7.50-7.47 (m, 4H), 6.59 (d, J = 15.8 Hz, 1H), 6.45 (dt, J = 15.8, 7.1 Hz, 1H), 3.36 (dd, J = 7.1, 1.4 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 196.2, 177.1, 140.7, 137.7, 136.5, 133.1, 132.4, 130.6, 129.9, 128.3, 126.1, 123.8, 38.0 ppm; HRMS (EI) m/z calcd. for $\text{C}_{17}\text{H}_{14}\text{O}_3$ $[\text{M}]^+$: 266.0943, found: 266.0951.

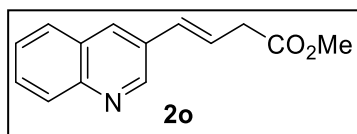
(*E*)-4-(1-Methyl-1*H*-indol-5-yl)but-3-enoic acid (5n): **1n** (68.5 mg, 0.4 mmol, 1 equiv) was used as a



substrate for the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 2:1 with 1% AcOH) afforded **5n** as beige solids containing a small amount of α,β -unsaturated carboxylic acid (72.5 mg, 336.7 μ mol, 84% (the olefin isomer: 8%)).

mp. 140.0-141.0 °C; IR (neat) $\tilde{\nu}$: 2926, 1719, 1613, 1510, 1420, 1301, 1214, 972, 897, 792, 712 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.60 (s, 1H), 7.33 (dd, J = 8.8, 1.6 Hz, 1H), 7.26 (d, J = 8.8 Hz, 1H), 7.03 (d, J = 2.9 Hz, 1H), 6.64 (d, J = 15.9 Hz, 1H), 6.46 (d, J = 2.9 Hz, 1H), 6.23 (dt, J = 15.9, 7.2 Hz, 1H), 3.78 (s, 3H), 3.32 (dd, J = 7.2, 1.4 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 178.1, 136.5, 135.1, 129.3, 128.6, 128.3, 119.9, 119.4, 117.6, 109.3, 101.3, 38.2, 32.9 ppm; HRMS (EI) m/z calcd. for $\text{C}_{13}\text{H}_{13}\text{NO}_2$ $[\text{M}]^+$: 215.0946, found: 215.0950.

Methyl (*E*)-4-(quinolin-3-yl)but-3-enoate (2o): **1o** (67.7 mg, 0.4 mmol, 1 equiv) was subjected to the

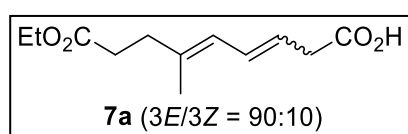


reaction according to the procedure **C-2-b**. The reaction was quenched by a buffer solution of citric acid/ NaHCO_3 (pH ~4, 10 mL), which was poured into a separatory funnel containing the same buffer (10 mL), and extracted with ethyl acetate (5 mL, 12 times). The combined organic layer was dried over Na_2SO_4 , and the solids were filtered off. The solvent was then removed under reduced pressure, and the residue was diluted in Et_2O ,

which was treated with excess CH_2N_2 in Et_2O . After stirring the mixture at room temperature for 10 minutes, the mixture was diluted in ethyl acetate (10 mL) and washed with brine (20 mL, 2 times). The organic layer was dried over Na_2SO_4 , and the solids were filtered off. After the solvent was removed under reduced pressure, the residue was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 5:1 to 3:2) to afford **2o** as pale yellow solids (53.5 mg, 250.9 μmol , 63%).

mp. 85.0-86.0 $^\circ\text{C}$; IR (neat) $\tilde{\nu}$: 2953, 1728, 1572, 1493, 1438, 1290, 1202, 979, 810, 751 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 8.98 (d, $J = 1.7$ Hz, 1H), 8.07-8.05 (m, 2H), 7.79 ($J = 8.0$ Hz, 1H), 7.67 (ddd, $J = 7.5$, 7.0, 1.1 Hz, 1H), 7.53 (ddd, $J = 8.0$, 7.0, 1.1 Hz, 1H), 6.65 (d, $J = 16.0$ Hz, 1H), 6.54 (dt, $J = 16.0$, 6.9 Hz, 1H), 3.75 (s, 3H), 3.35 (dd, $J = 6.9$, 1.1 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 171.8, 149.4, 147.7, 132.5, 130.5, 129.8, 129.39, 129.37, 128.1, 128.0, 127.1, 124.4, 52.2, 38.5 ppm; HRMS (EI) m/z calcd. for $\text{C}_{14}\text{H}_{13}\text{NO}_2$ $[\text{M}]^+$: 227.0946, found: 227.0941.

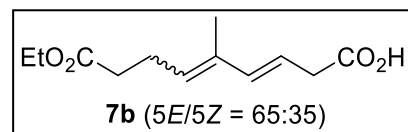
(5E)-9-Ethoxy-6-methyl-9-oxonona-3,5-dienoic acid (7a, 3E/3Z = 90:10): **6a** (72.9 mg, 0.4 mmol, 1



equiv) was subjected to the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 2:1) afforded a regioisomeric mixture of **7a** as colorless oil (68.1 mg, 301.0 μmol , 75%).

IR (neat) $\tilde{\nu}$: 3185, 2982, 1732, 1713, 1374, 1161, 1043, 966, 757 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 6.34 (dd, $J = 15.3$, 10.9 Hz, 1H), 6.01 (d, $J = 11.3$ Hz, 0.1H, Z isomer), 5.84 (d, $J = 10.9$ Hz, 0.9H, E isomer), 5.64 (dt, $J = 15.3$, 7.2 Hz, 0.9H, E isomer), 5.51 (dt, $J = 11.3$, 7.3 Hz, 0.1H, Z isomer), 4.12 (q, $J = 7.2$ Hz, 2H), 3.25 (dd, $J = 7.3$, 1.1, 0.2 Hz, Z isomer), 3.16 (d, $J = 7.2$ Hz, 1.8H, E isomer), 2.44-2.40 (m, 2H), 2.38-2.35 (m, 2H), 1.76 (s, 0.3H, Z isomer), 1.74 (s, 2.7H, E isomer), 1.24 (t, $J = 7.2$ Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 177.9, 177.8, 173.2, 173.1, 139.3, 137.1, 130.5, 127.6, 124.4, 122.3, 119.7, 119.6, 60.44, 60.39, 37.9, 35.1, 34.7, 32.9, 32.8, 16.52, 16.48, 14.2 ppm; HRMS (EI) m/z calcd. for $\text{C}_{12}\text{H}_{18}\text{O}_4$ $[\text{M}]^+$: 226.1205, found: 226.1208.

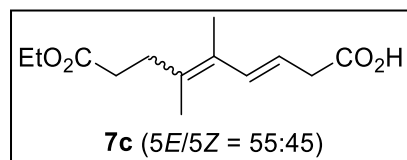
(3E)-9-Ethoxy-5-methyl-9-oxonona-3,5-dienoic acid (7b, 5E/5Z = 65:35): **6b** ($E/Z = 60:40$, 72.9 mg, 0.4



mmol, 1 equiv) was subjected to the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 2:1) afforded a regioisomeric mixture of **7b** as colorless oil (40.0 mg, 176.8 μmol , 45%).

IR (neat) $\tilde{\nu}$: 3202, 2982, 1731, 1714, 1375, 1270, 1181, 1038, 967 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 6.55 (d, $J = 15.5$ Hz, 0.4H, Z isomer), 6.14 (d, $J = 15.8$ Hz, 0.6H, E isomer), 5.75 (dt, $J = 15.5$, 7.2 Hz, 0.4H, Z isomer), 5.63 (dt, $J = 15.8$, 7.2 Hz, 0.6H, E isomer), 5.40 (t, $J = 7.2$ Hz, 0.6H, E isomer), 5.30 (t, $J = 7.4$ Hz, 0.4H, Z isomer), 4.12 (q, $J = 7.2$ Hz, 2H), 3.21 (d, $J = 7.2$ Hz, 0.8H, Z isomer), 3.15 (d, $J = 7.2$ Hz, 1.2H, E isomer), 2.49-2.42 (m, 2H), 2.37-2.33 (m, 2H), 1.81 (s, 1H, Z isomer), 1.76 (s, 2H, E isomer), 1.24 (t, $J = 7.2$ Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 178.1, 177.9, 173.15, 173.13, 138.5, 134.2, 132.5, 130.8, 130.3, 128.3, 121.1, 118.1, 60.4, 38.2, 37.8, 34.4, 34.0, 23.7, 22.9, 20.4, 14.2, 12.3 ppm; HRMS (EI) m/z calcd. for $\text{C}_{12}\text{H}_{18}\text{O}_4$ $[\text{M}]^+$: 226.1205, found: 226.1209.

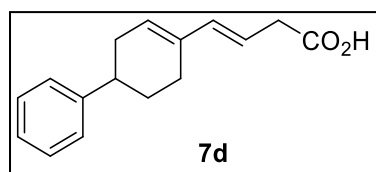
(3E)-9-Ethoxy-5,6-dimethyl-9-oxonona-3,5-dienoic acid (7c, 5E/5Z = 55:45): **6c** (*E/Z* = 50:50, 78.5 mg,



0.4 mmol, 1 equiv) was subjected to the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (hexane/ethyl acetate, 4:1 to 2:1) afforded a regioisomeric mixture of **7c** as colorless oil (65.0 mg, 270.5 μ mol, 68%).

IR (neat) $\tilde{\nu}$: 3198, 2983, 1732, 1714, 1375, 1286, 1179, 1099, 1035, 962, 757 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 6.59 (app dd, J = 15.5, 10.3 Hz, 1H), 5.67 (dt, J = 15.5, 7.5 Hz, 1H), 4.12 (app qd, J = 7.3, 2.4 Hz, 2H), 3.20 (d, J = 7.5 Hz, 2H), 2.51 (t, J = 8.0 Hz, 0.9H, *Z* isomer) 2.46 (t, J = 7.7 Hz, 1.1H, *E* isomer), 2.38-2.33 (m, 2H), 1.80 (s, 1.6H, *E* isomer), 1.79 (s, 1.6H, *E* isomer), 1.77 (s, 1.4H, *Z* isomer), 1.76 (s, 1.4H, *Z* isomer), 1.25 (td, J = 7.3, 2.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 178.1, 173.3, 133.3, 132.9, 132.5, 127.3, 127.0, 119.1, 118.9, 60.4, 38.38, 38.35, 33.4, 32.8, 30.8, 29.4, 19.4, 18.0, 14.5, 14.2, 14.0 ppm; HRMS (EI) m/z calcd. for $\text{C}_{13}\text{H}_{20}\text{O}_4$ $[\text{M}]^+$: 240.1362, found: 240.1364.

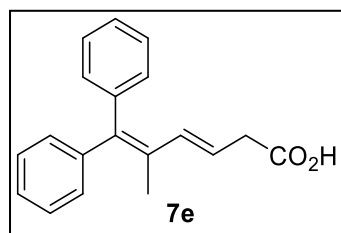
(E)-4-(1,2,3,6-Tetrahydro-(1,1'-biphenyl)-4-yl)but-3-enoic acid: 6d (79.3 mg, 0.4 mmol, 1 equiv) was



subjected to the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 2:1) afforded **7d** as white solids (76.0 mg, 313.6 μ mol, 78%).

mp. 104.0-105.0 $^{\circ}\text{C}$; IR (neat) $\tilde{\nu}$: 3084, 2920, 1715, 1651, 1493, 1433, 1391, 1276, 1032, 971, 702 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.31 (dd, J = 8.0, 7.5 Hz, 2H), 7.24-7.19 (m, 3H), 6.21 (d, J = 15.5 Hz, 1H), 5.82 (d, J = 5.2 Hz, 1H), 5.67-5.61 (m, 1H), 3.19 (d, J = 6.9 Hz, 2H), 2.83-2.77 (m, 1H), 2.44-2.35 (m, 2H), 2.31-2.25 (m, 2H), 2.06-2.03 (m, 1H), 1.84-1.75 (m, 1H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 178.3, 146.7, 137.0, 134.9, 129.0, 128.4, 126.8, 126.1, 117.1, 40.1, 37.9, 33.9, 29.5, 25.0 ppm; HRMS (EI) m/z calcd. for $\text{C}_{16}\text{H}_{18}\text{O}_2$ $[\text{M}]^+$: 242.1307, found: 242.1312.

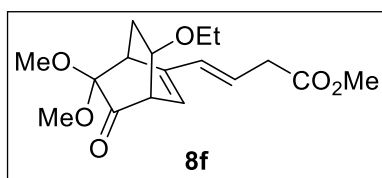
(E)-5-Methyl-6,6-diphenylhexa-3,5-dienoic acid (7e): 6e (93.7 mg, 0.4 mmol, 1 equiv) was subjected to



the reaction according to the procedure **C-2-b**. Purification of the crude product by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1 to 2:1) afforded **7e** as pale yellow solids (63.5 mg, 228.1 μ mol, 57%).

mp. 135.5-136.0 $^{\circ}\text{C}$; IR (neat) $\tilde{\nu}$: 3053, 2918, 1709, 1597, 1491, 1442, 1285, 1074, 1019, 969, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 7.31-7.28 (m, 4H), 7.26-7.20 (m, 2H), 7.14-7.12 (m, 4H), 6.43 (d, J = 15.6 Hz, 1H), 5.87 (dt, J = 15.6, 7.3 Hz, 1H), 3.15 (dd, J = 7.3, 1.1 Hz, 2H), 1.95 (s, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 177.3, 142.9, 142.1, 135.2, 130.6, 130.5, 129.9, 127.92, 127.90, 126.8, 126.7, 121.0, 38.1, 16.8 ppm; HRMS (EI) m/z calcd. for $\text{C}_{19}\text{H}_{18}\text{O}_2$ $[\text{M}]^+$: 278.1307, found: 278.1229.

Methyl (E)-4-(8-ethoxy-6,6-dimethoxy-5-oxobicyclo[2.2.2]oct-2-en-2-yl)but-3-enoate (8f): 6f (106.5



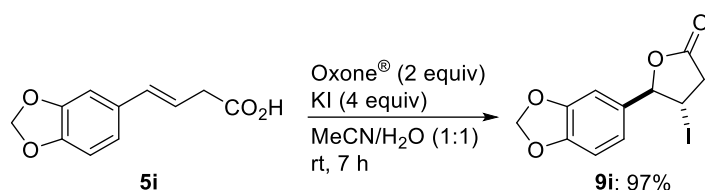
mg, 0.4 mmol, 1 equiv) was subjected to the reaction according to the procedure **C-2-b**. The reaction was quenched with pH ~4 buffer (citric acid/ NaHCO_3) and extracted with ethyl acetate (3 mL, 10 times). The crude mixture was once dried under vacuum (5 min), then treated with CH_2N_2 in

Et₂O. After concentration, the residue was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 10:1 to 4:1) to afford **8f** as pale yellow oil (53.0 mg, 163.4 μmol, 41%).

IR (neat) $\tilde{\nu}$: 2976, 1739, 1437, 1352, 1250, 1201, 1165, 1102, 1050 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 6.23 (d, J = 16.0 Hz, 1H), 5.97 (dt, J = 16.0, 7.4 Hz, 1H), 5.88 (d, J = 6.3 Hz, 1H), 3.99 (ddd, J = 8.1, 3.5, 2.7 Hz, 1H), 3.69 (s, 3H), 3.54 (dq, J = 6.3, 2.7 Hz, 1H), 3.49 (dq, J = 9.0, 6.9 Hz, 1H), 3.42-3.35 (m, 2H), 3.31 (s, 3H), 3.30 (s, 3H), 3.24-3.15 (m, 2H), 2.46 (ddd, J = 13.7, 8.1, 3.2 Hz, 1H), 1.27 (ddd, J = 13.7, 3.5, 3.2 Hz, 1H), 1.14 (t, J = 6.9 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 171.8, 143.8, 131.2, 121.6, 121.3, 93.4, 74.9, 64.3, 54.0, 51.9, 50.7, 49.8, 37.8, 37.6, 30.3, 15.3 ppm; HRMS (ESI) m/z calcd. for C₁₇H₂₄NaO₆ [M+Na]⁺: 347.1465, found: 347.1461.

(C-3) Derivatization of the Carboxylated Products

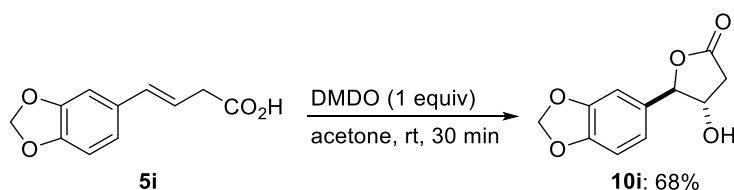
(C-3-a) Iodolactonization of **5i**



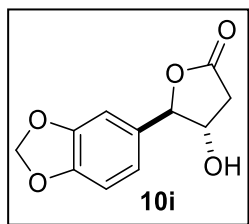
anti-5-(Benzo[*d*][1,3]dioxol-5-yl)-4-iododihydrofuran-2(3*H*)-one (9i): To a 10 mL recovery flask was added Oxone[®] (245.8 mg, 0.4 mmol, 2.0 equiv) and KI (132.8 mg, 0.8 mmol, 4.0 equiv) under air, which was dissolved in MeCN/H₂O (1:1, 2 mL) resulted in a brown suspension. To this mixture was added **5i** (41.2 mg, 0.2 mmol, 1.0 equiv) and stirred at ambient temperature for 7 h. Water (10 mL) was added and the reaction was quenched by the addition of Na₂S₂O₃ until the color of iodine disappeared. The mixture was extracted with ethyl acetate (3 mL, 2 times) and the combined organic layer was washed with brine, then dried over Na₂SO₄. After the solids were filtered off, the solvent was evaporated and the residue was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 4:1) to afford *anti*-β-iodobutyrolactone **9i** as pale yellow waxy oil (64.6 mg, 194.5 μmol, 97%).

IR (neat) $\tilde{\nu}$: 2902, 1790, 1610, 1505, 1448, 1342, 1253, 1199, 1139, 1104, 1038, 979, 933, 813 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 6.90-9.86 (m, 2H), 6.82 (d, J = 8.0 Hz, 1H), 6.00 (s, 2H), 5.57 (d, J = 8.8 Hz, 1H), 4.20 (ddd, J = 9.6, 8.8, 7.9 Hz, 1H), 3.26 (dd, J = 17.9, 7.9 Hz, 1H), 3.02 (dd, 17.9, 9.6 Hz, 1H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 173.5, 148.6, 148.3, 129.0, 120.4, 108.5, 106.2, 101.5, 89.5, 41.0, 17.9 ppm; HRMS (EI) m/z calcd. for C₁₁H₉IO₄ [M]⁺: 331.9546, found: 331.9537.

(C-3-b) Tandem Olefin Epoxidation/Ring-Opening Lactonization

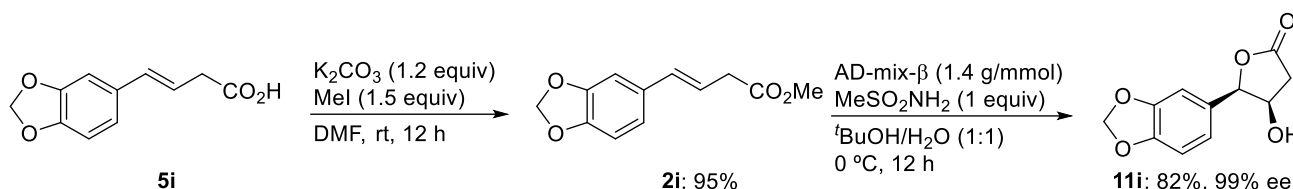


***anti*-5-(Benzo[*d*][1,3]dioxol-5-yl)-4-hydroxydihydrofuran-2(3*H*)-one (10i):** To a 10 mL recovery flask was added **5i** (20.6 mg, 0.1 mmol, 1 equiv) under air, which was dissolved in acetone (1 mL). To the solution was then added dimethyl dioxirane (DMDO) (*ca.* 0.05 M in acetone, 2 mL, *ca.* 0.1 mmol, *ca.* 1 equiv) by a pipette at ambient temperature. The resulting mixture was stirred for 30 min. and the solvent was removed under reduced pressure. The residue was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 1:1) to afford *anti*-β-hydroxybutyrolactone **10i** as white solids (15.0 mg, 67.5 μmol, 68%).

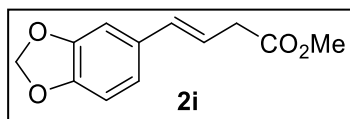


mp. 98.5-99.5 °C; IR (neat) $\tilde{\nu}$: 3512, 2945, 1772, 1503, 1257, 1173, 1038, 984, 868, 793 cm^{-1} ; ^1H NMR (500 MHz, acetone- d_6) δ : 6.89-6.86 (m, 3H), 6.02 (s, 2H), 5.23 (d, J = 4.0 Hz, 1H), 5.01 (d, J = 2.9 Hz, 1H), 4.47 (ddd, J = 8.4, 4.6, 4.0 Hz, 1H), 2.89 (dd, J = 17.5, 8.4 Hz, 1H), 2.49 (dd, J = 17.5, 4.6 Hz, 1H) ppm; ^{13}C NMR (125 MHz, acetone- d_6) δ : 175.2, 149.0, 148.6, 132.8, 120.2, 109.0, 106.8, 102.3, 74.6, 37.5 ppm; HRMS (EI) m/z calcd. for $\text{C}_{11}\text{H}_{10}\text{O}_5$ $[\text{M}]^+$: 222.0528, found: 222.0526.

(C-3-c) Sharpless Asymmetric Dihydroxylation of **5i** and *in situ* Lactonization

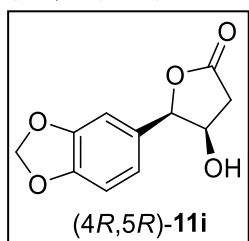


Methyl (*E*)-4-(benzo[*d*][1,3]dioxol-5-yl)but-3-enoate (2i): To a 10 mL recovery flask was added **5i** (433.0 mg, 2.1 mmol, 1.0 equiv) under air, which was diluted in DMF (2 mL). To this solution were added K_2CO_3 (348.3 mg, 2.5 mmol, 1.2 equiv) and MeI (0.2 mL, 3.2 mmol, 1.5 equiv), and the resulting suspension was vigorously stirred at room temperature overnight. Water (20 mL) was added and extracted with ethyl acetate (3 mL, 3 times). The combined organic layer was washed with sat. NaHCO_3 aq. and brine, then dried over Na_2SO_4 . After the solids were filtered off, the solvent was removed under reduced pressure, and the crude mixture was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 10:1 to 4:1) to afford the methyl ester **2i** as colorless oil (439.3 mg, 1.99 mmol, 95%).



IR (neat) $\tilde{\nu}$: 2952, 2898, 1737, 1504, 1491, 1446, 1251, 1199, 1166, 1039, 934 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ : 6.92 (d, J = 1.4 Hz, 1H), 6.78 (dd, J = 8.0, 1.4 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.39 (d, J = 15.7 Hz, 1H), 6.11 (dt, J = 15.7, 7.3 Hz, 1H), 5.94 (s, 2H), 3.71 (s, 3H), 3.21 (dd, J = 7.3, 1.1 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ : 172.1, 148.0, 147.2, 133.0, 131.3, 120.9, 119.8, 108.2, 105.6, 101.0, 51.9, 38.1 ppm; HRMS (EI) m/z calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_4$ $[\text{M}]^+$: 220.0736, found: 220.0734.

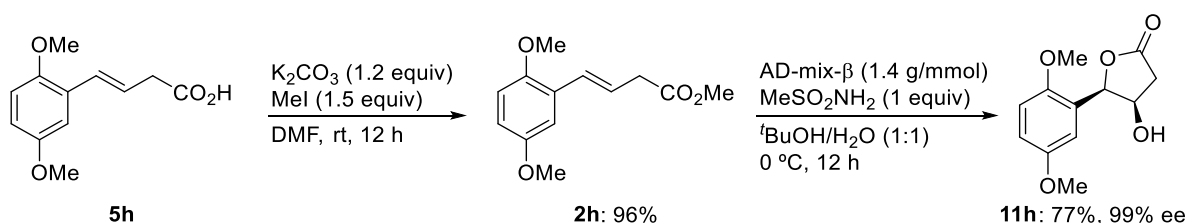
(4*R*,5*R*)-5-(Benzo[*d*][1,3]dioxol-5-yl)-4-iododihydrofuran-2(3*H*)-one (11i): To a 10 mL recovery flask was added MeSO_2NH_2 (19.2 mg, 0.2 mmol, 1.0 equiv) under air, which was dissolved in $t\text{BuOH}/\text{H}_2\text{O}$ (1:1, 2 mL). To the mixture were added **2i** (44.0 mg, 0.2 mmol, 1.0 equiv) and AD-mix-β (240 mg, *ca.* 4 mol% $\text{K}_2\text{OsO}_4 \cdot 2\text{H}_2\text{O}$, *ca.* 10 mol% $(\text{DHQD})_2\text{PHAL}$, 3.0 equiv $\text{K}_3\text{Fe}(\text{CN})_6$, and 3.0 equiv K_2CO_3) at 0 °C. The resulting orange suspension was stirred at 0 °C for 20 h. The reaction was quenched by $\text{Na}_2\text{S}_2\text{O}_3$



(316.2 mg, 2 mmol, 10 equiv) and stirred at ambient temperature for 1 h. Water (10 mL) was added and the mixture was extracted with ethyl acetate (3 mL, 2 times) and the combined organic layer was washed with brine, then dried over Na₂SO₄. After the solids were filtered off, the solvent was evaporated and the crude mixture was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 1:1) to afford *syn*-β-hydroxybutyrolactone **11i** as white solids (35.7 mg, 160.1 μmol, 80%, 99% ee).

mp. 88.0-89.0 °C; $[\alpha]_D^{24}$ -13.3 (c 0.17, MeOH); IR (neat) $\tilde{\nu}$: 3453, 2921, 1769, 1505, 1447, 1325, 1257, 1159, 1077, 1037, 931, 787 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ : 6.89-6.84 (m, 3H), 6.01 (s, 2H), 5.43 (d, *J* = 3.7 Hz, 1H), 5.43 (dd, *J* = 4.6, 3.7 Hz, 1H), 2.87 (dd, *J* = 17.8, 4.6 Hz, 1H), 2.74 (d, *J* = 17.8 Hz, 1H), 1.42 (s, 1H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ : 175.4, 148.2, 148.1, 126.6, 119.8, 108.6, 107.0, 101.4, 84.9, 70.2, 38.4 ppm; HRMS (EI) *m/z* calcd. for C₁₁H₁₀O₅ [M]⁺: 222.0528, found: 222.0530. The enantiomeric excess was determined by HPLC analysis (DAICEL CHIRALPAK IA-3, eluent: hexane/2-propanol = 90/10, flow rate: 1.0 mL/min. detector: UV at 290 nm), *t*_R = 21.9 min (minor), 34.4 min (major). The absolute configuration was elucidated to be 4*R*,5*R* according to the Sharpless's original report (Scheme S3).³⁷

(C-3-d) Sharpless Asymmetric Dihydroxylation of **5h** and *in situ* Lactonization

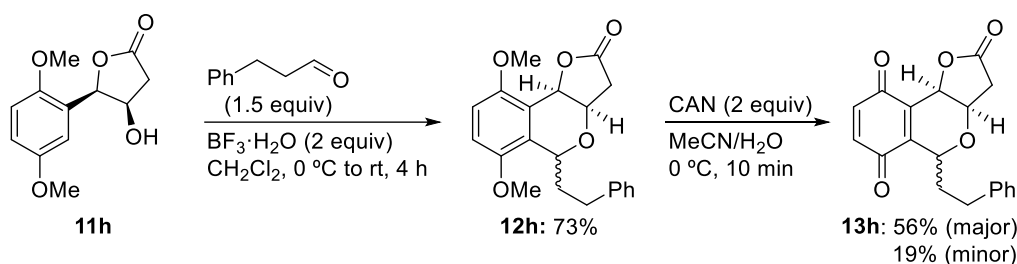


Methyl (E)-4-(2,5-dimethoxyphenyl)but-3-enoate (2h): To a 500 mL flask was added **5h** (19.6 g, 88.3 mmol, 1.0 equiv) under air, which was diluted in DMF (200 mL). To this solution were added K₂CO₃ (12.2 g, 88.3 mmol, 1.0 equiv) and MeI (6.6 mL, 106.0 mmol, 1.2 equiv), and the resulting suspension was vigorously stirred at room temperature overnight. Water (100 mL) was added and extracted with ethyl acetate (100 mL, 3 times). The combined organic layer was washed with brine, then dried over Na₂SO₄. After the solids were filtered off, and the crude mixture was distilled under reduced pressure (bp. 230 °C/10 mmHg) to afford the product, which was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 2:1) to afford the methyl ester **2h** as yellow oil (19.9 mg, 84.4 mmol, 96%). The spectrum data was consistent with the reported one.^{38,39}

(4*R*,5*R*)-5-(2,5-Dimethoxyphenyl)-4-hydroxydihydrofuran-2(3*H*)-one (11h): To a 5 mL recovery flask was added **2h** (47.3 mg, 0.2 mmol, 1.0 equiv) under air, which was dissolved in *t*BuOH/H₂O (1:1, 2 mL). To the mixture were added MeSO₂NH₂ (19.2 mg, 0.2 mmol, 1.0 equiv) and AD-mix-β (240 mg, *ca.* 4 mol% K₂OsO₄·2H₂O, *ca.* 10 mol% (DHQD)₂PHAL, 3.0 equiv K₃Fe(CN)₆, and 3.0 equiv K₂CO₃) at 0 °C. The resulting orange suspension was stirred at 0 °C for 12 h. The reaction was quenched by Na₂S₂O₃·5H₂O (496.3 mg, 2 mmol, 10 equiv) and stirred at ambient temperature for 1 h. Water (10 mL) was added and the mixture was extracted with ethyl acetate (3 mL, 2 times) and the combined organic layer was washed with brine, then dried over Na₂SO₄. After the solids were filtered off, the solvent was evaporated and the crude

mixture was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate, 1:1) to afford *syn*- β -hydroxybutyrolactone **11h** as pale yellow oil (36.7 mg, 154.0 μ mol, 77%, 99% ee). The enantiomeric excess was determined by HPLC analysis (DAICEL CHIRALPAK IA-3, eluent: hexane/2-propanol = 90/10, flow rate: 1.0 mL/min. detector: UV at 290 nm), t_R = 15.9 min (minor), 19.5 min (major). The spectrum data was consistent with the reported one.^{38,39} The absolute configuration was determined to be 4*R*,5*R* based on the comparison of the optical rotation with the reported one. $[\alpha]_D^{20}$ -46.5 (c 1.00, CHCl₃). [lit. $[\alpha]_D^{20}$ -40 (c 1.05, CHCl₃ for 4*R*,5*R* enantiomer),³⁹ lit. $[\alpha]_D^{18}$ +47.3 (c 1.05, CHCl₃) for 4*S*,5*S* enantiomer³⁸].

Lactone **11h** was converted into tricyclic lactone **12h** by Oxa-Pictet-Spengler cyclization using 3-phenylpropanal and BF₃·OEt₂. The following oxidation afforded tricyclic quinone **13h**.³⁹

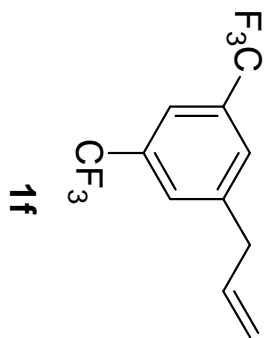


(D) References

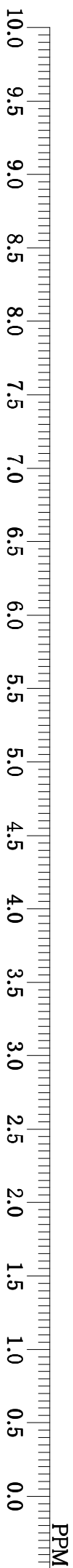
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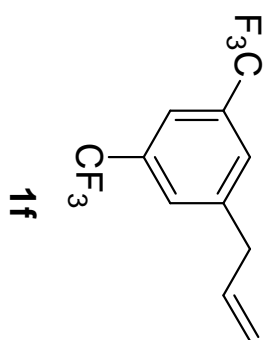
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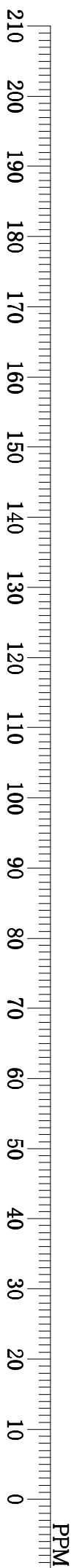
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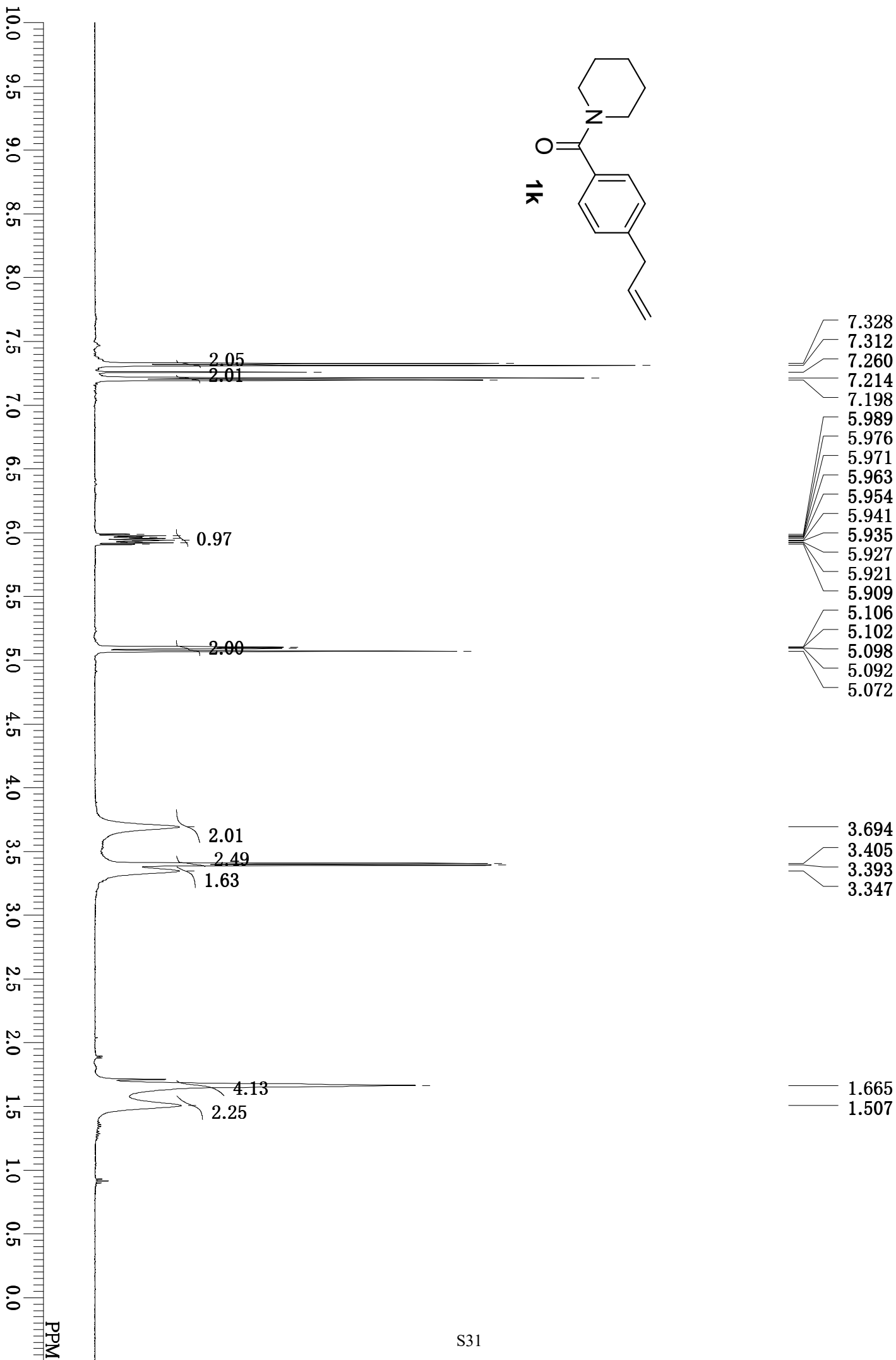
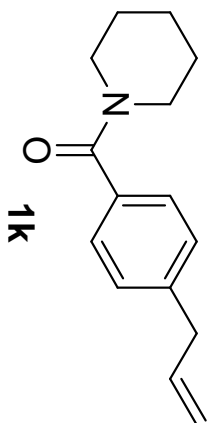
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77.000

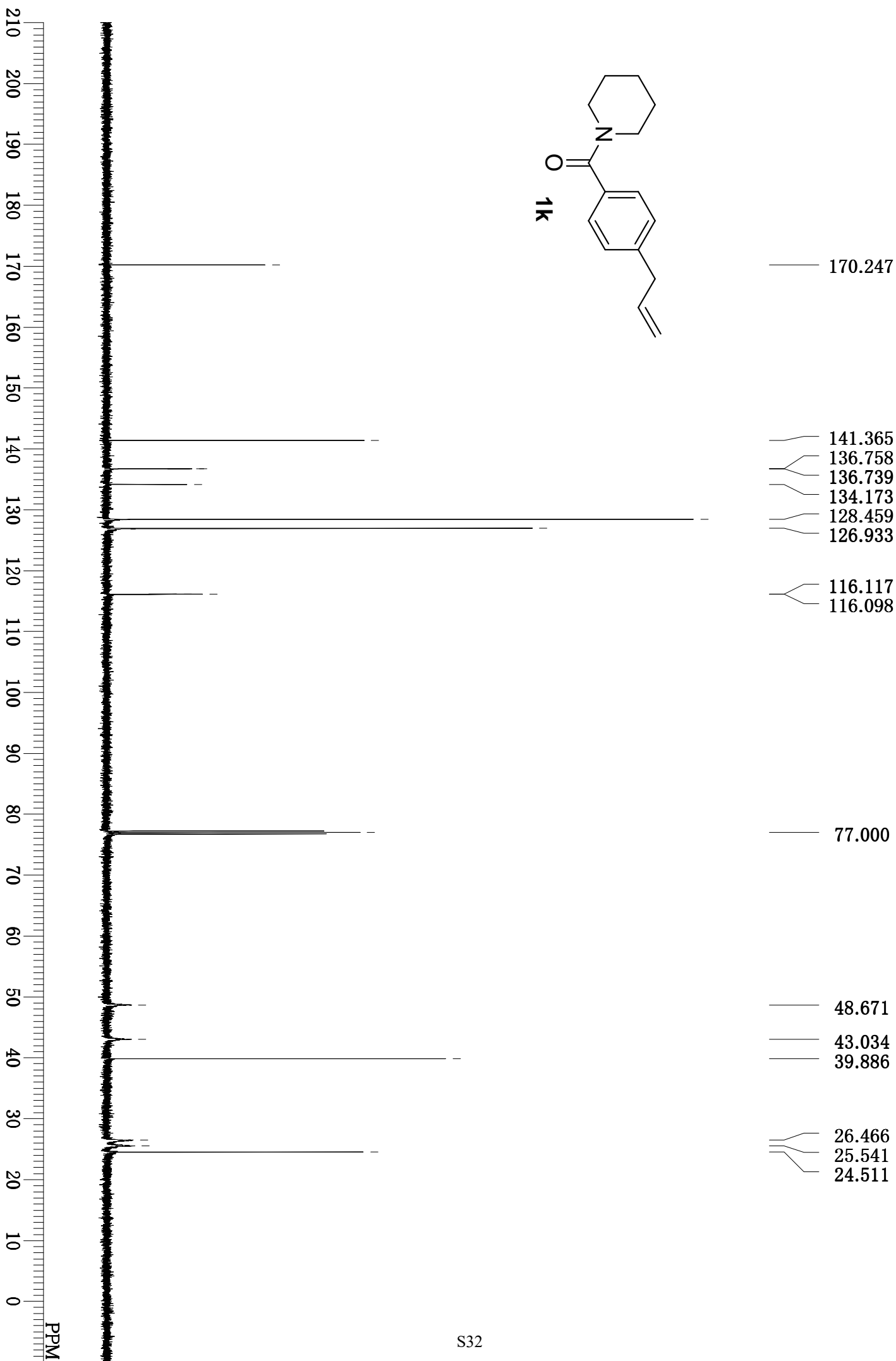
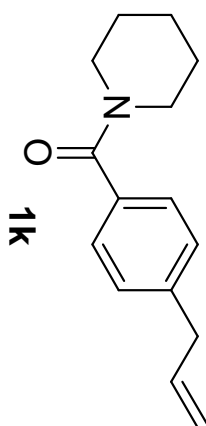
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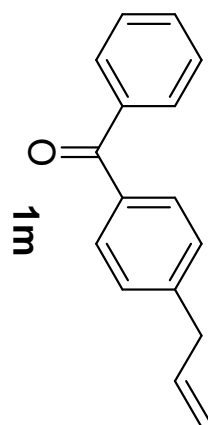
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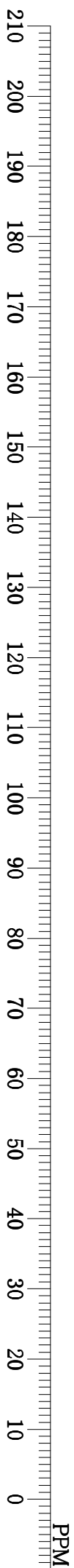
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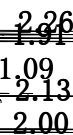
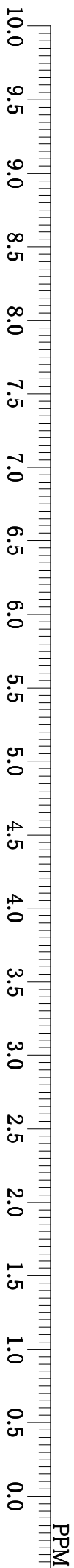
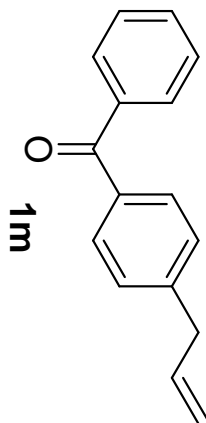
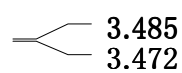
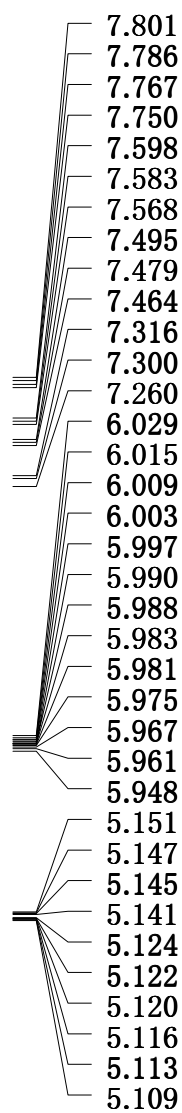
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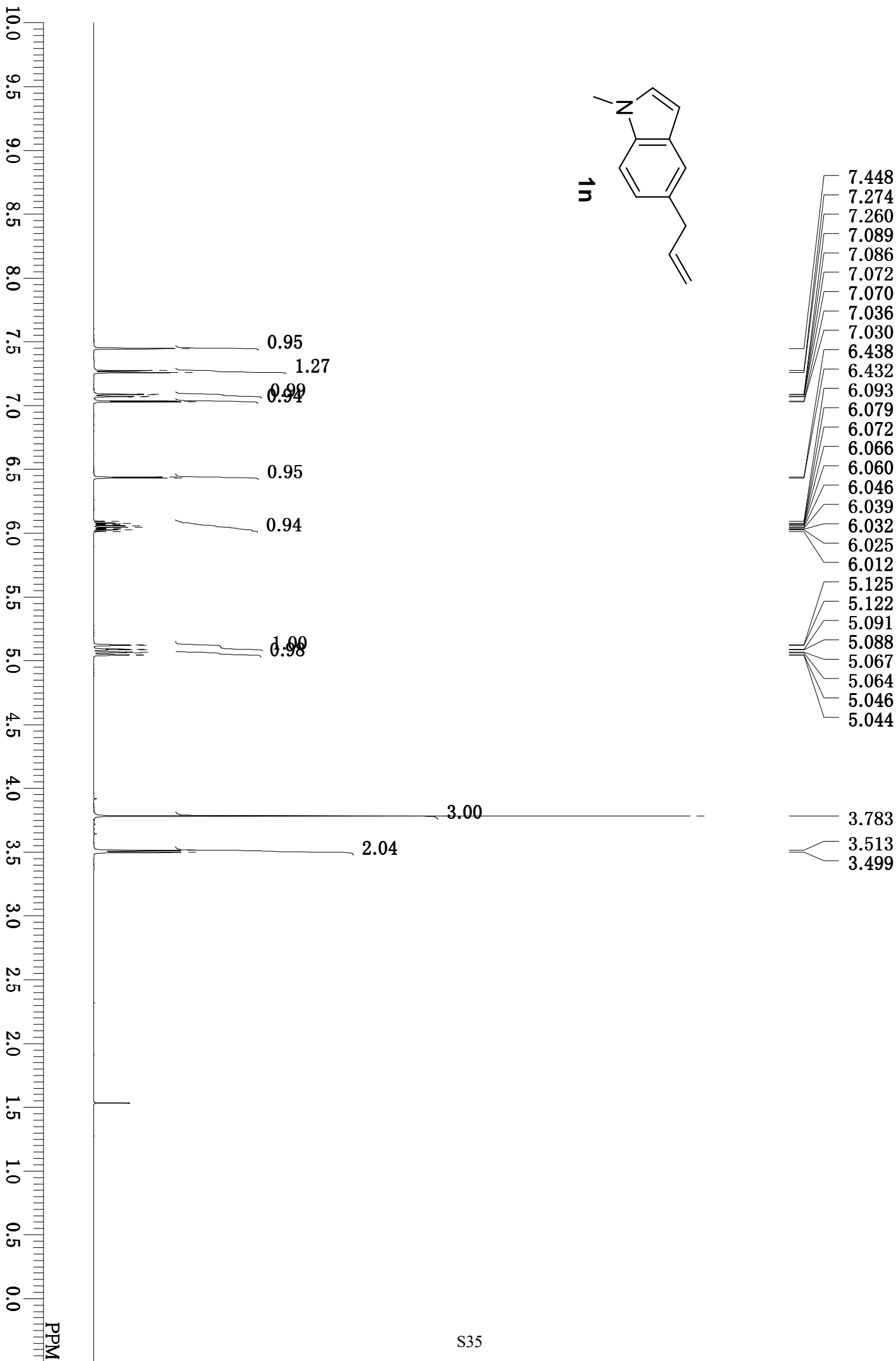
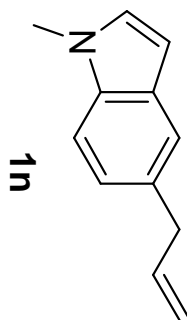
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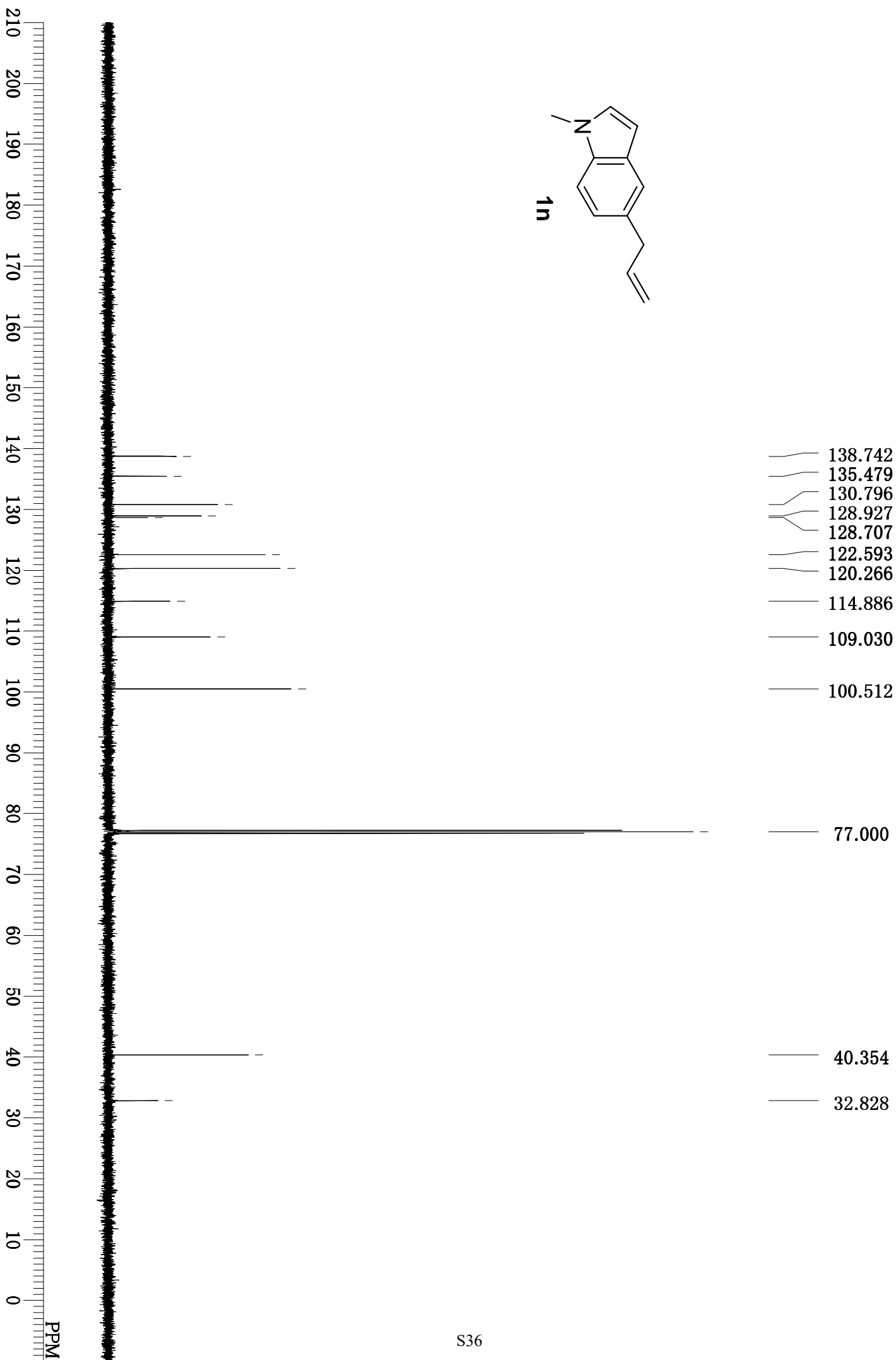
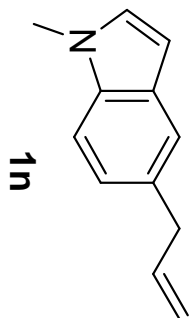
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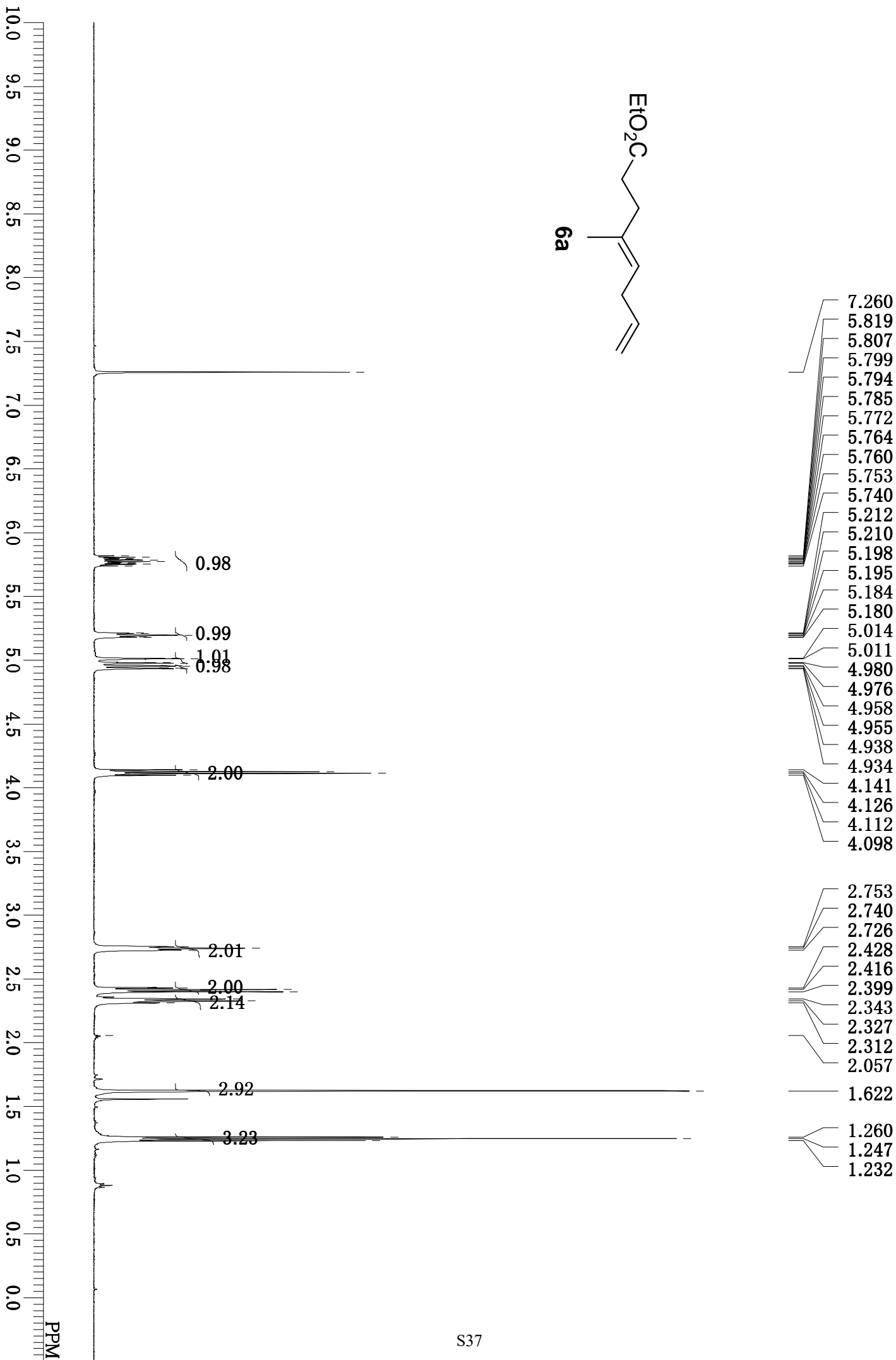
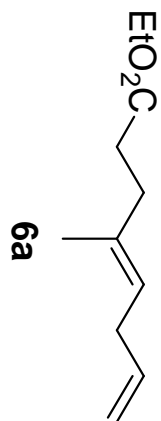
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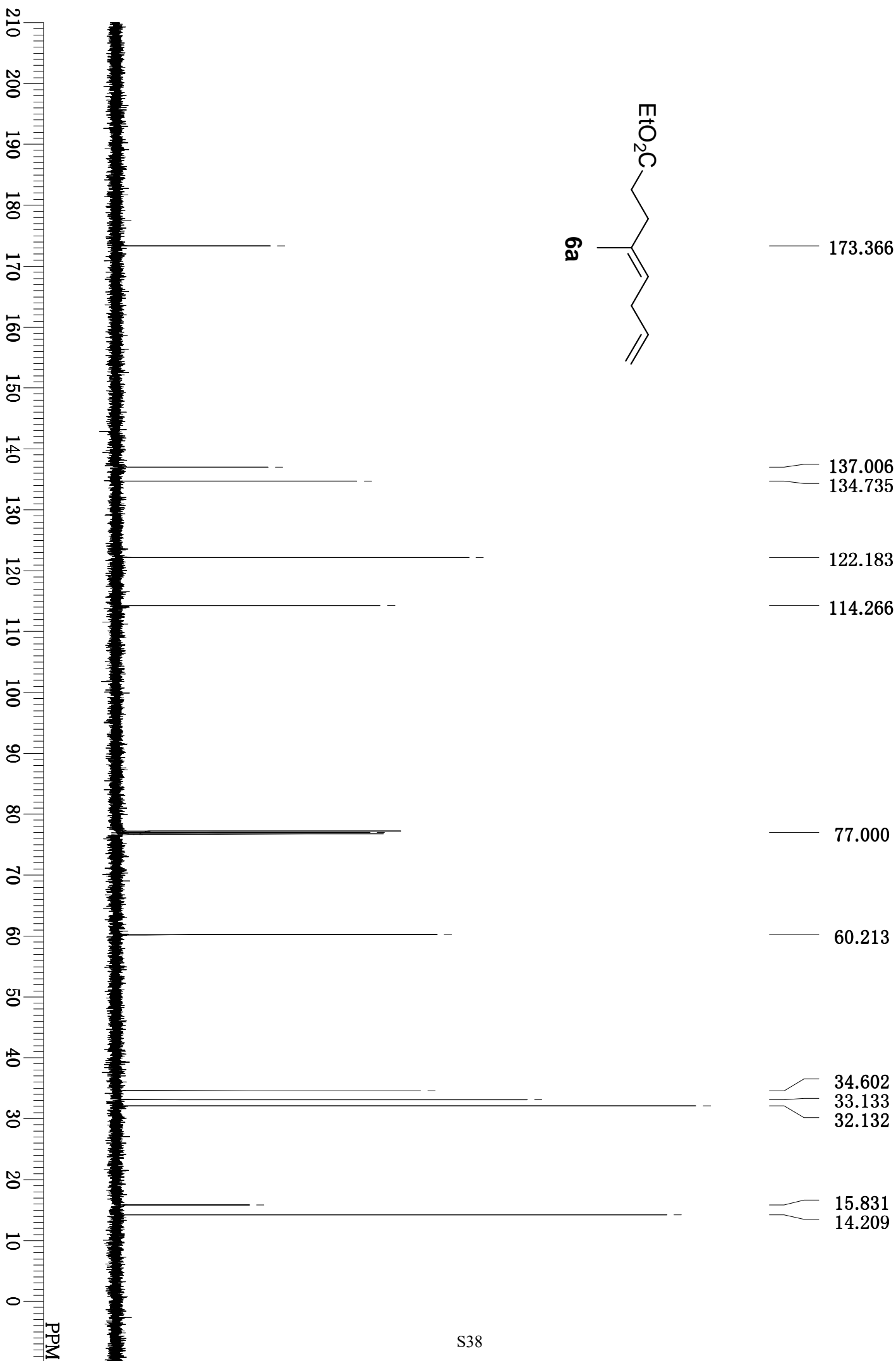
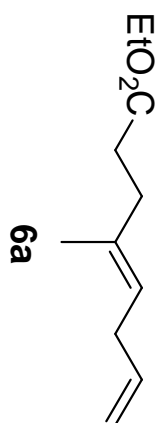
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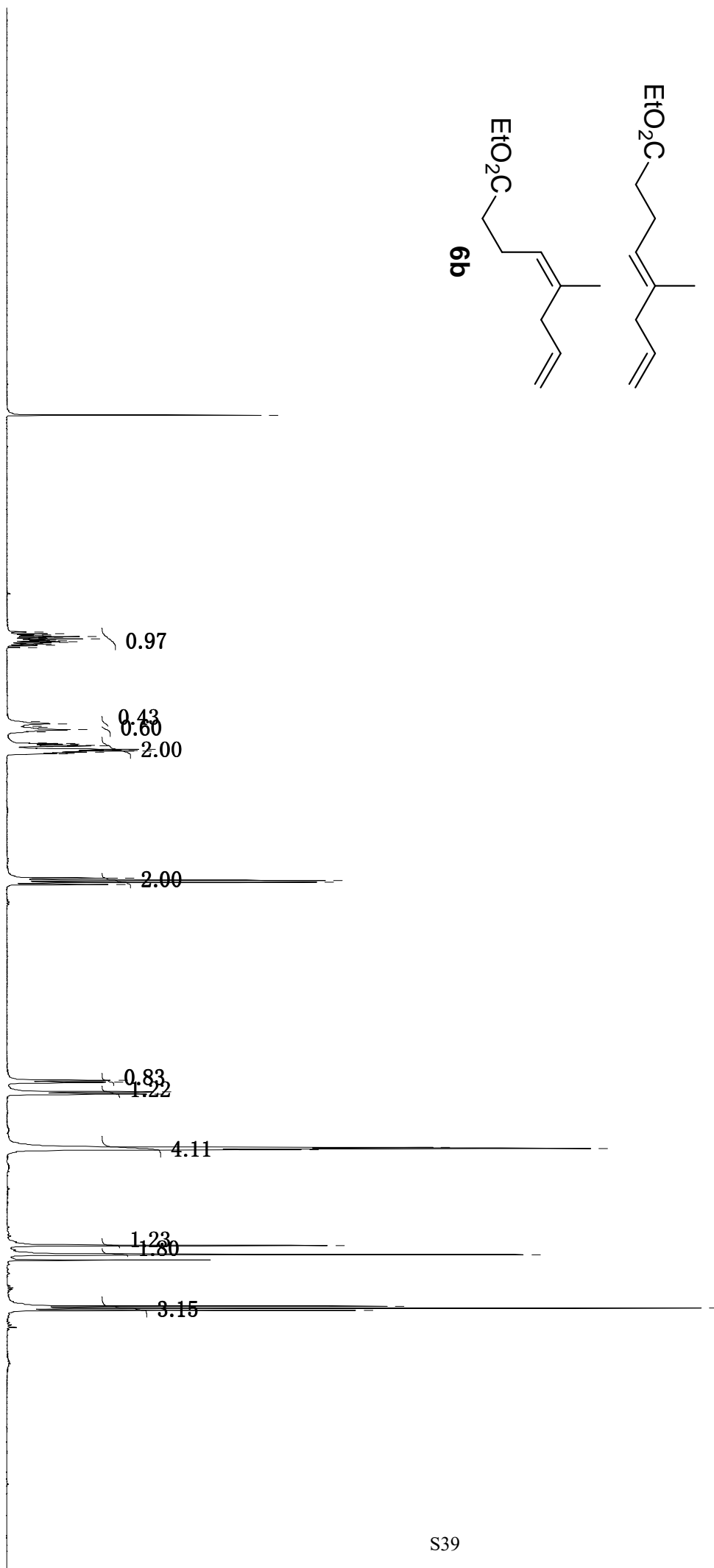
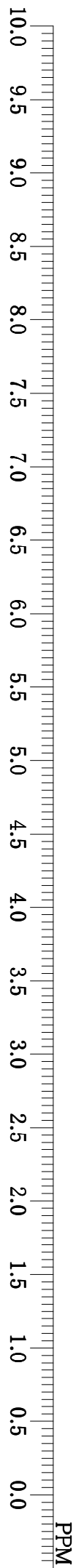
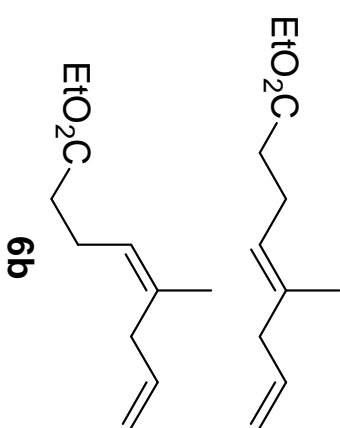
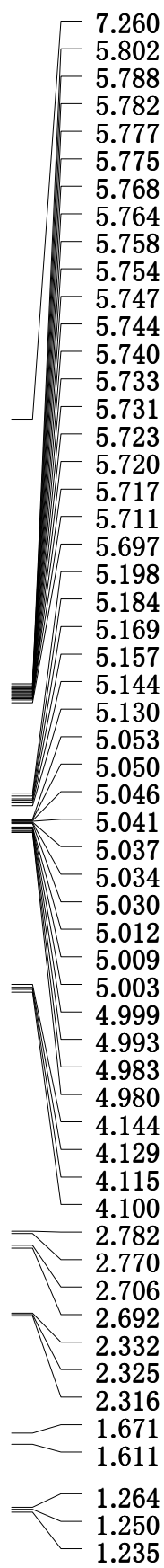
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500 MHz, CDCl₃



125 MHz, CDCl₃

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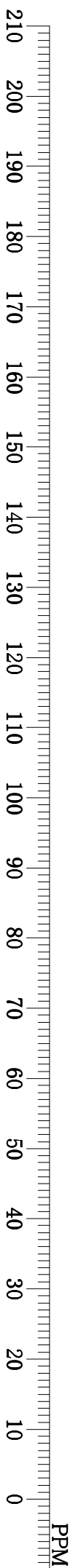
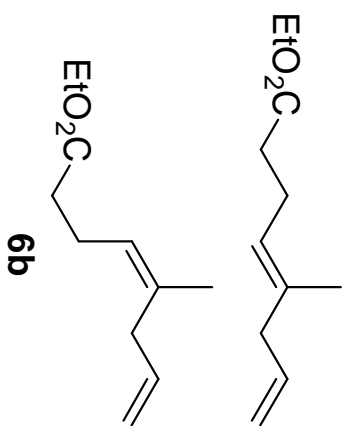
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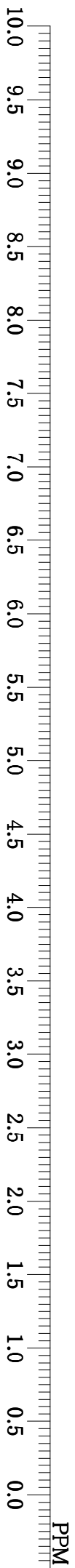
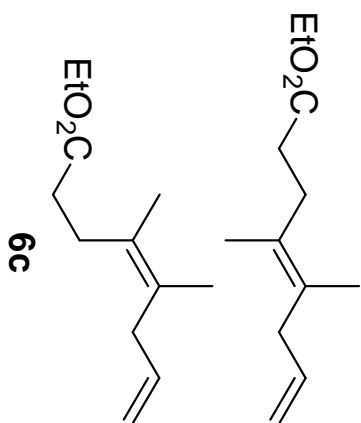
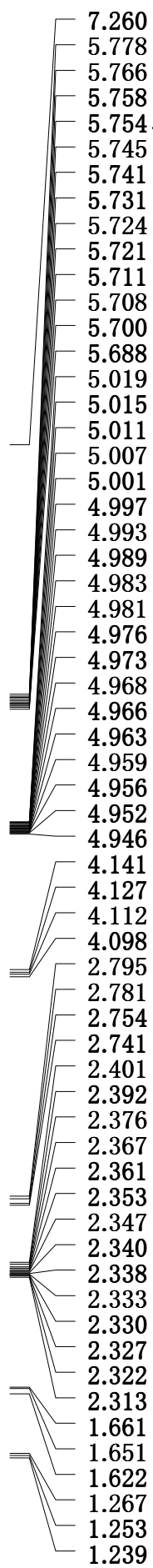
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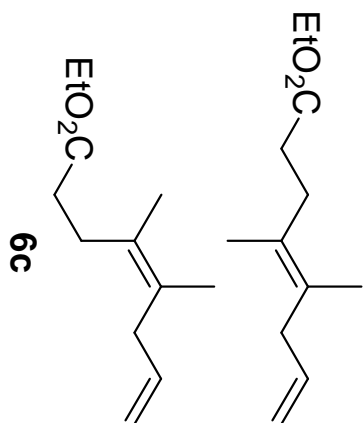
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500 MHz, CDCl₃



125 MHz, CDCl₃



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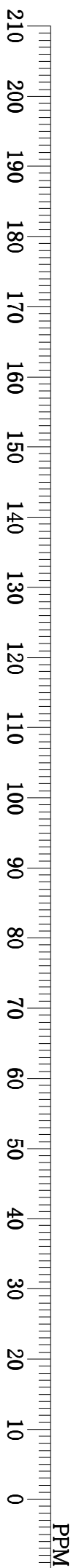
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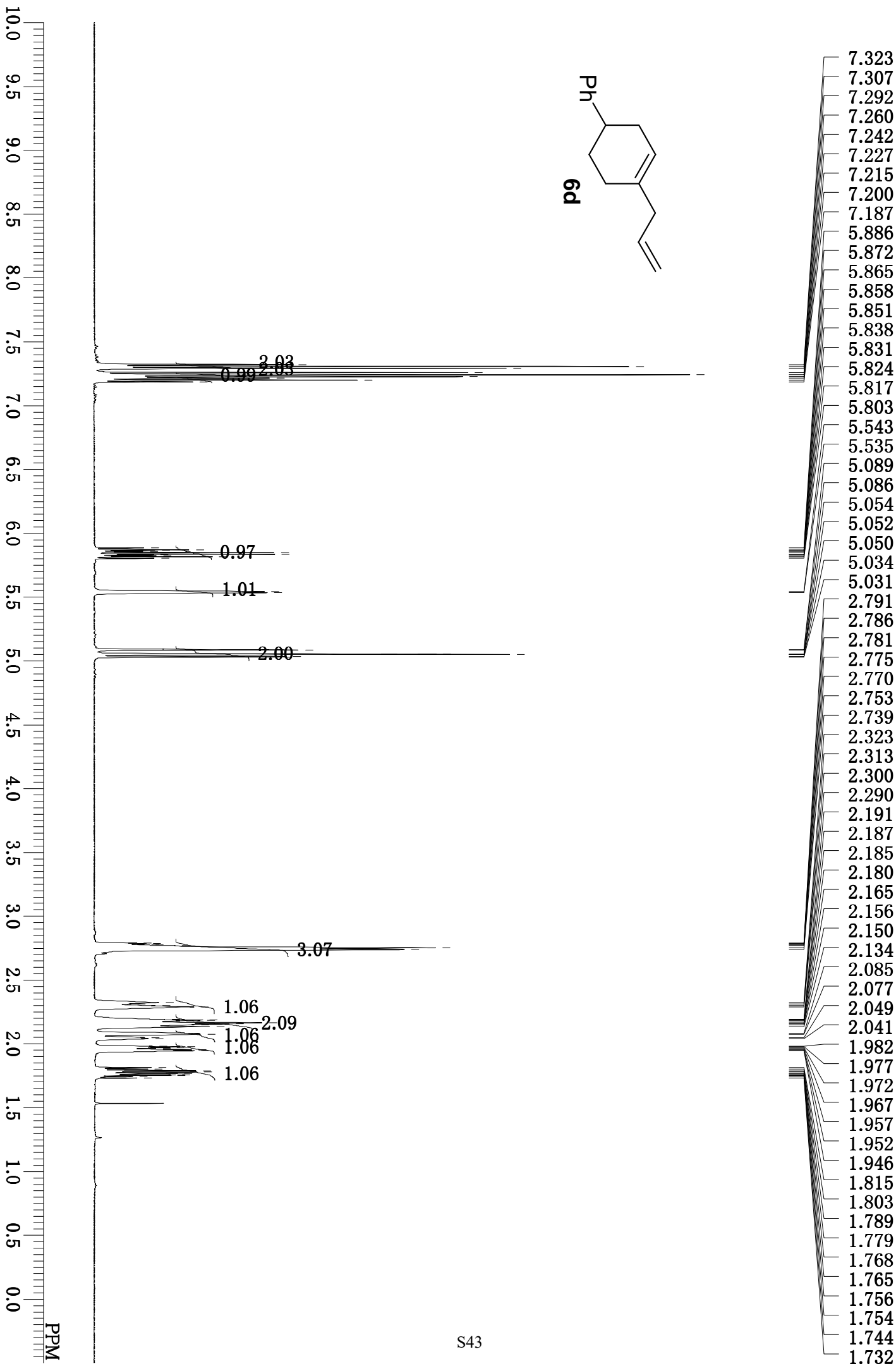
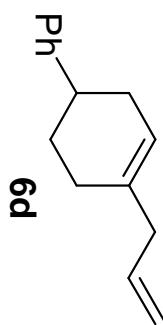
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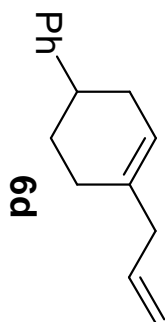
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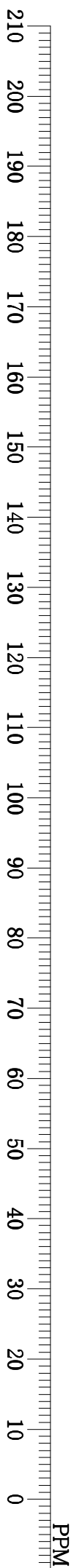
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125 MHz, CDCl₃



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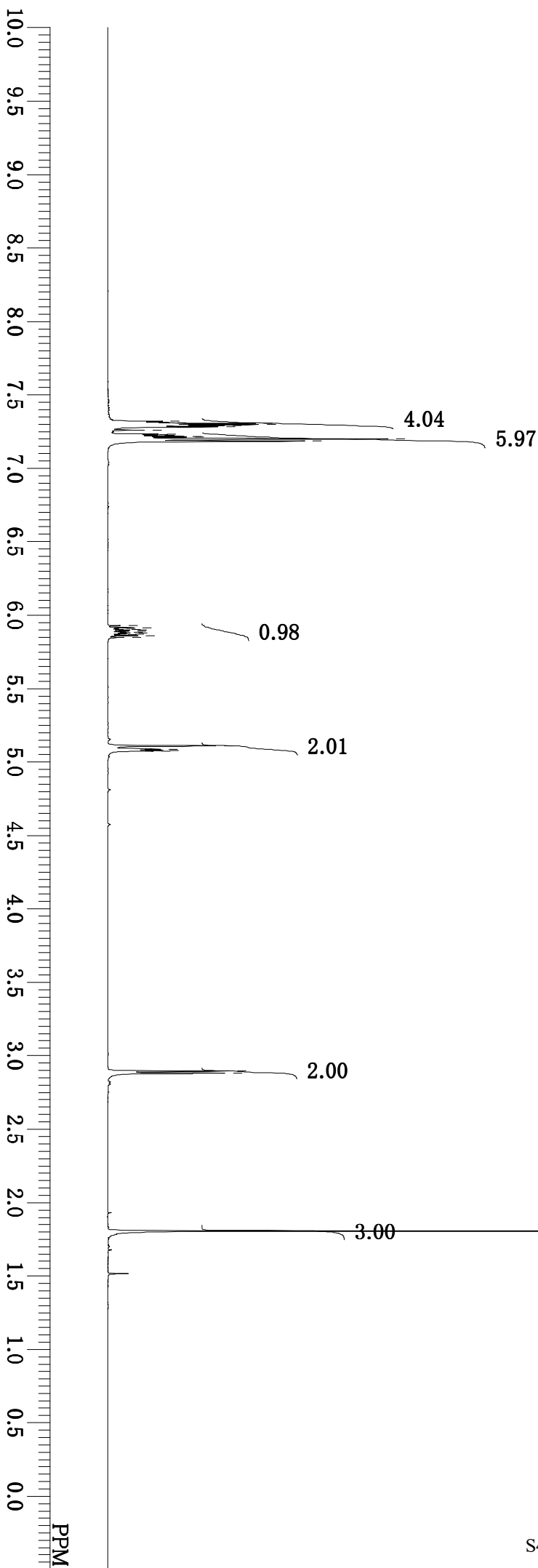
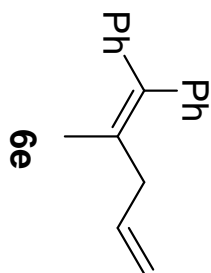


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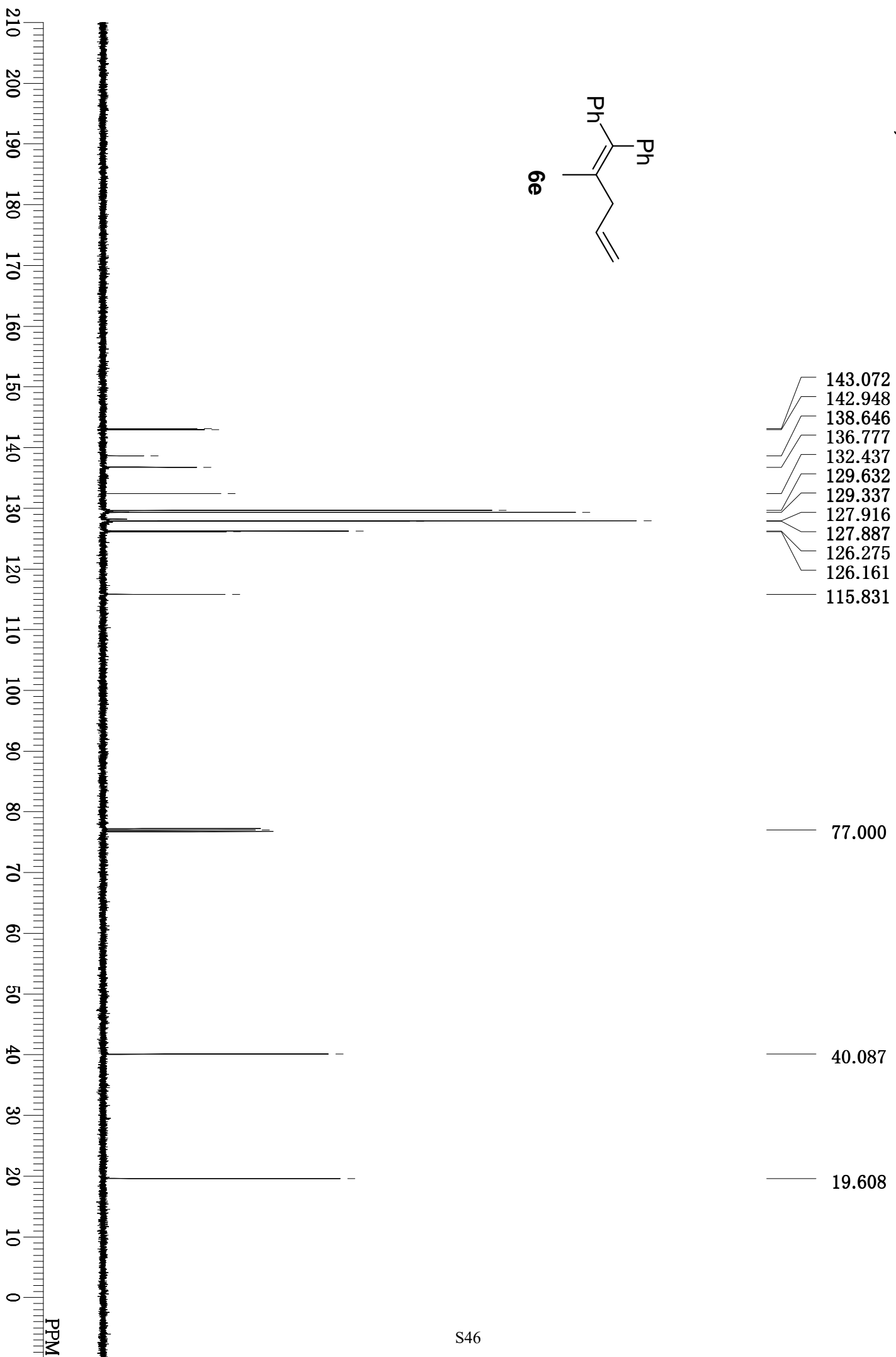
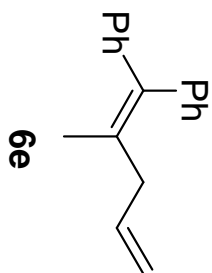
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5.076

2.895
2.882

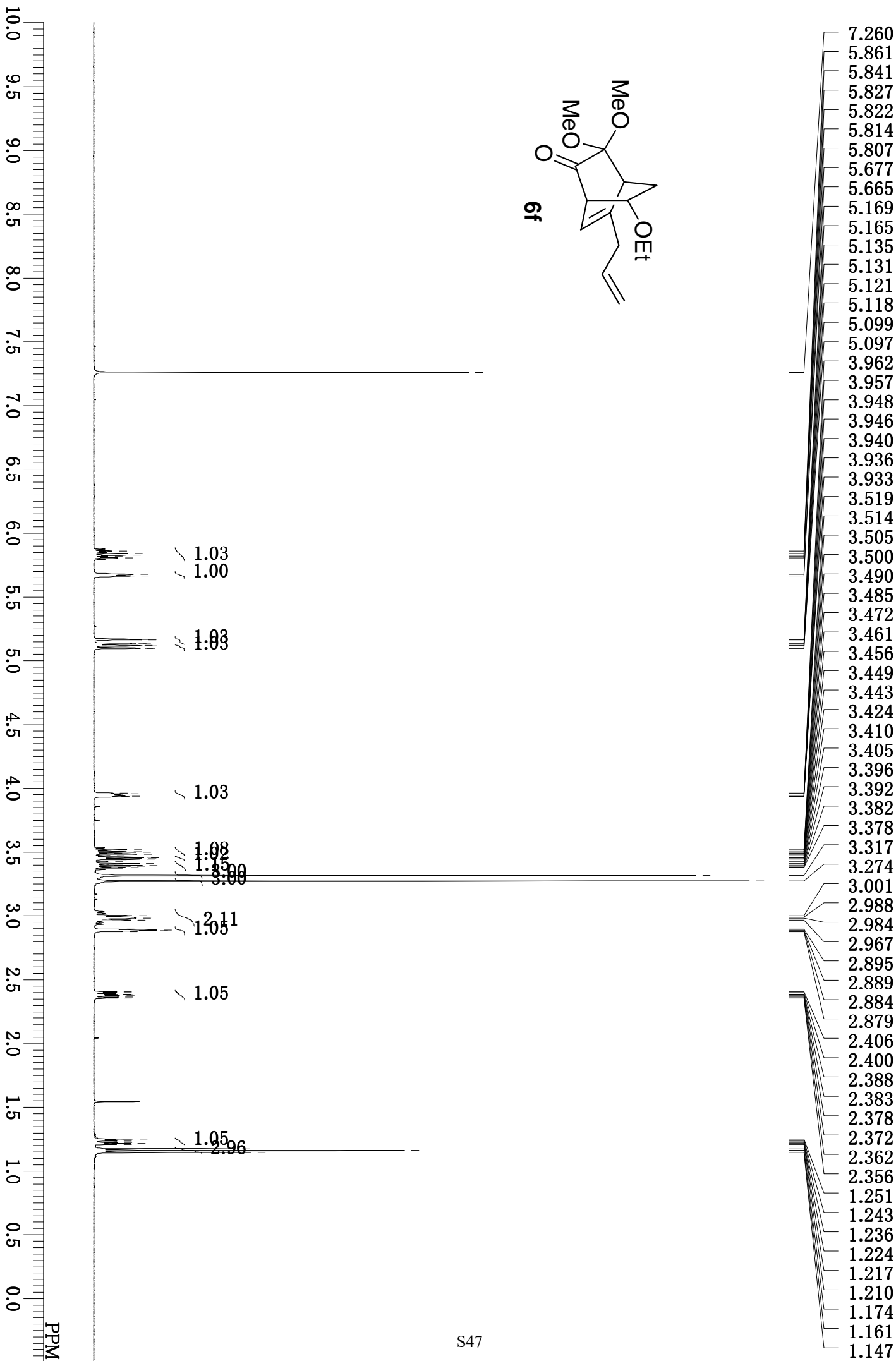
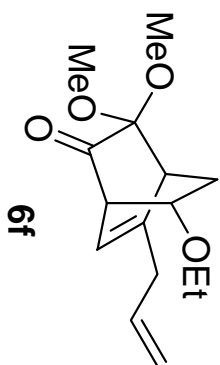
1.807



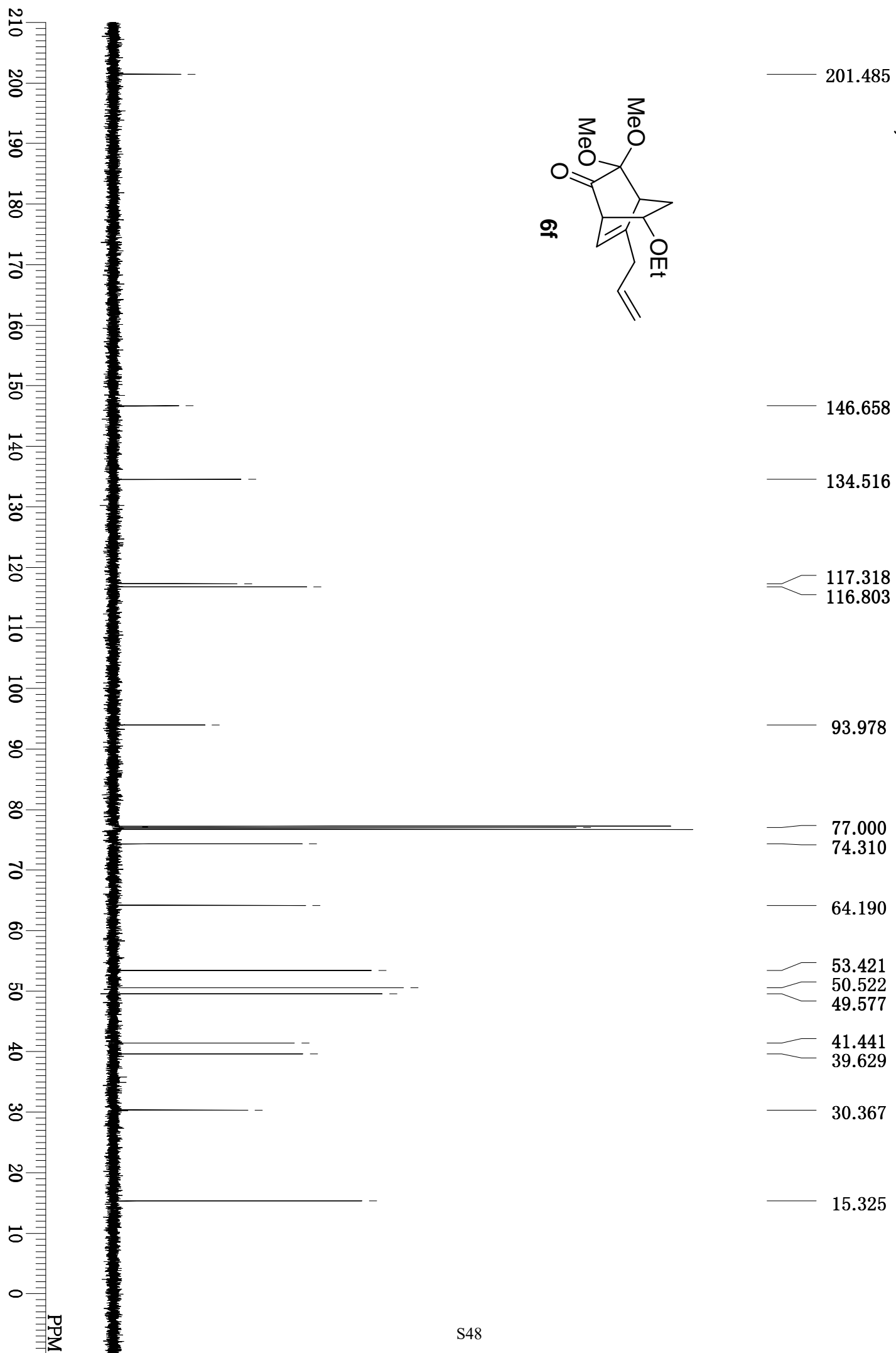
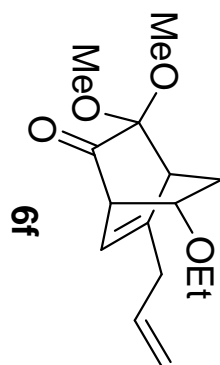
125 MHz, CDCl₃



500 MHz, CDCl₃

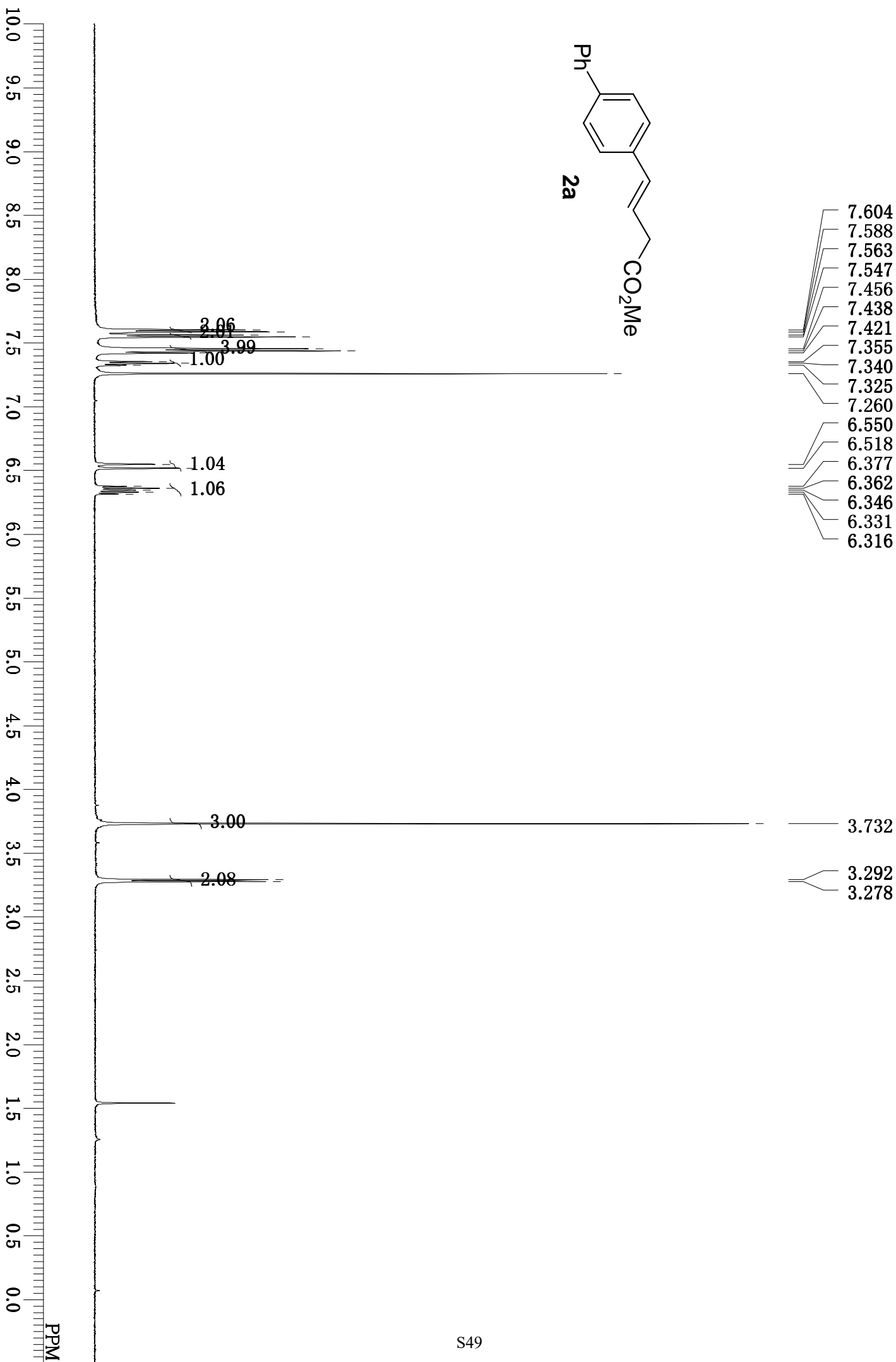
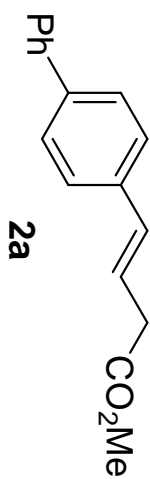


125 MHz, CDCl₃

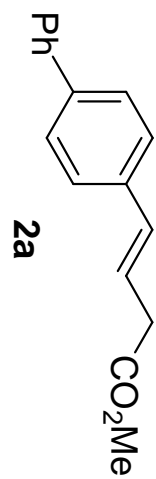


500 MHz, CDCl₃

7.604
7.588
7.563
7.547
7.456
7.438
7.421
7.355
7.340
7.325
7.260
6.550
6.518
6.377
6.362
6.346
6.331
6.316



125 MHz, CDCl₃



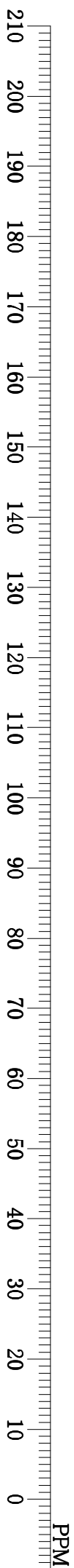
171.954

140.640
140.287
135.813
133.000
128.745
127.267
127.200
126.885
126.685
121.735

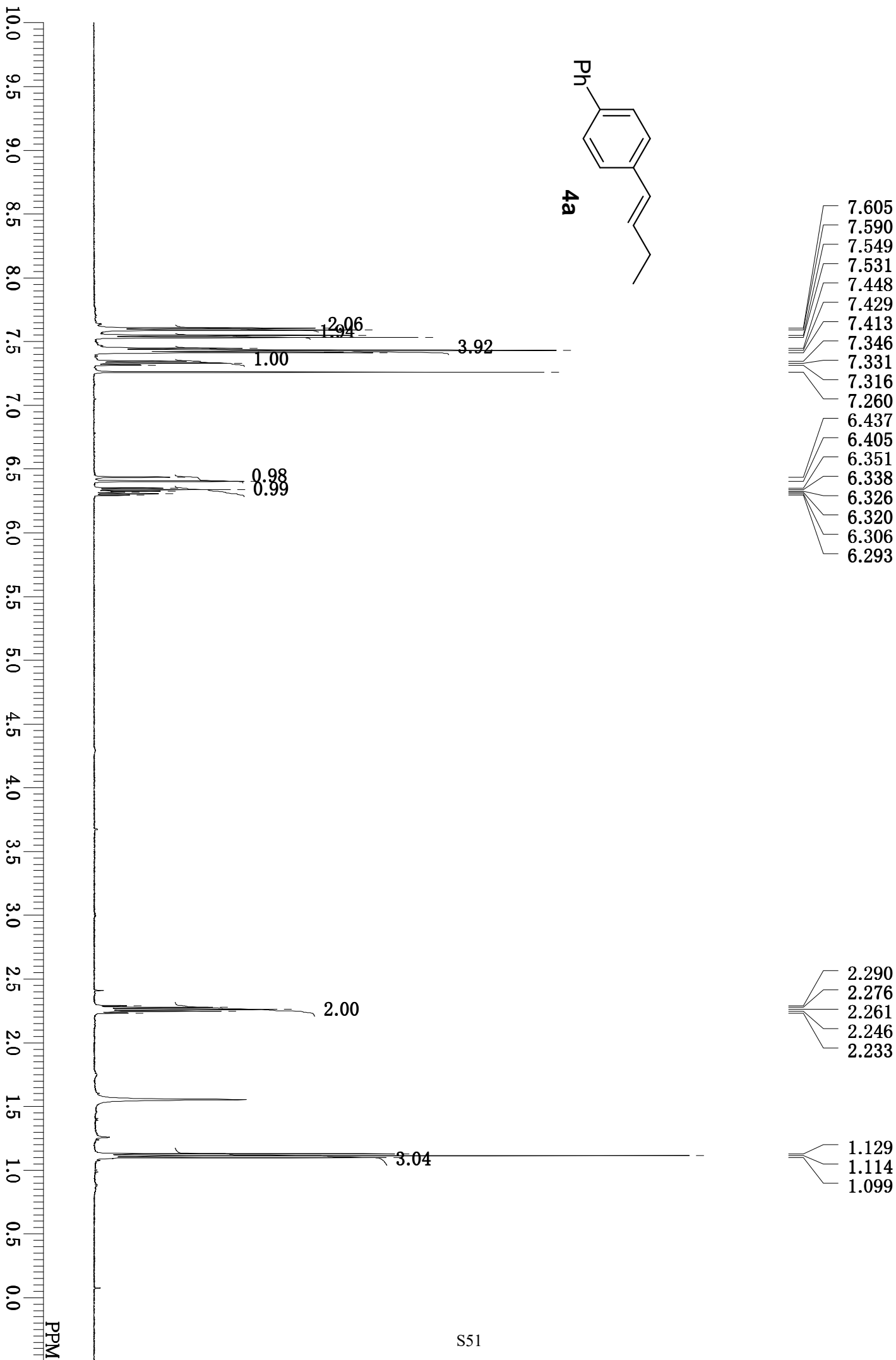
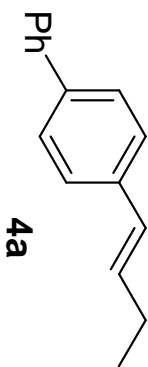
77.000

51.924

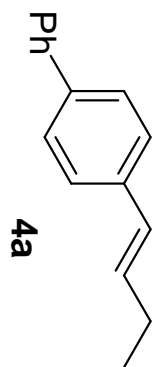
38.255



500 MHz, CDCl₃



125 MHz, CDCl₃

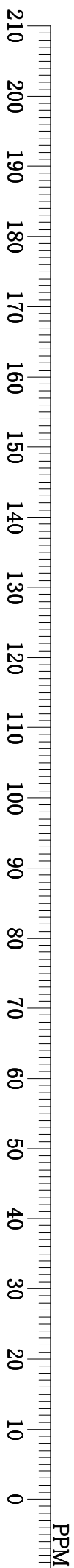


140.869
139.486
137.006
132.856
128.726
128.326
127.162
127.114
126.876
126.294

77.000

26.132

13.656

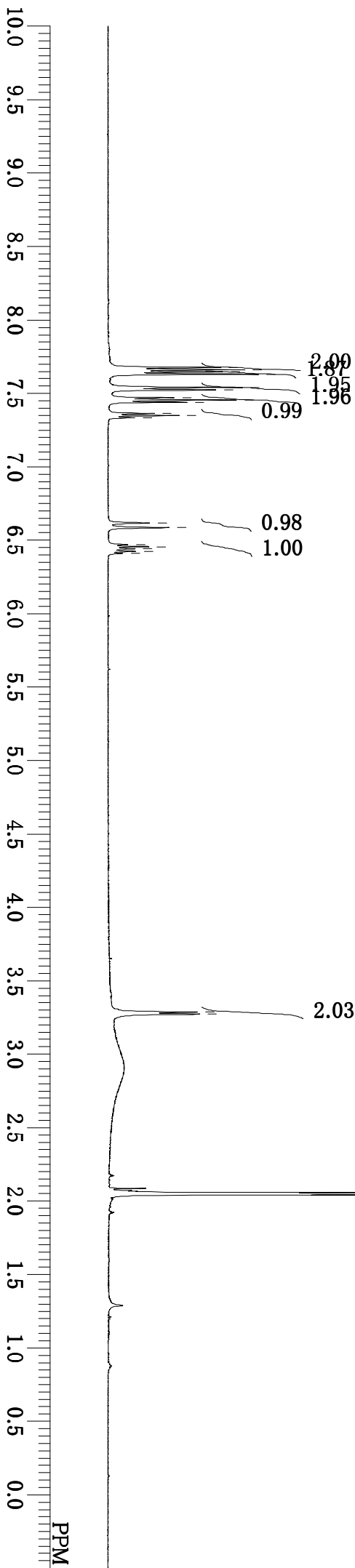
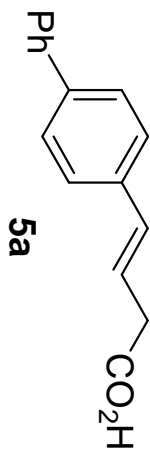


500 MHz, acetone-d₆

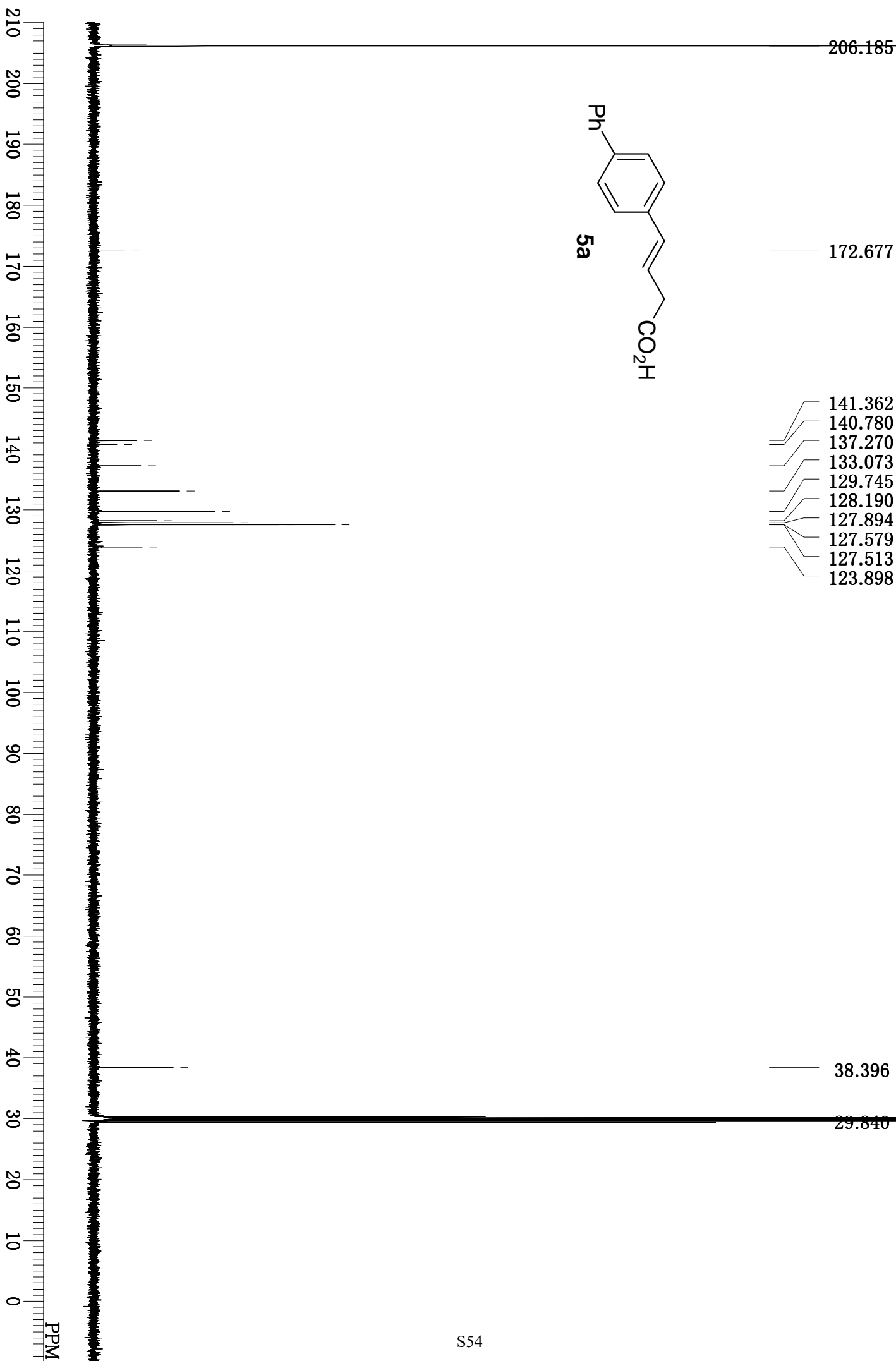
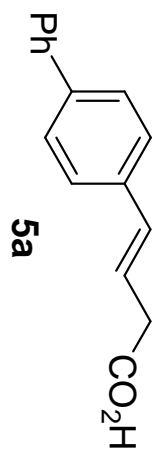
7.675
7.660
7.647
7.631
7.540
7.524
7.470
7.454
7.439
7.364
7.349
7.334
6.617
6.586
6.470
6.456
6.442
6.425
6.410

3.287
3.273

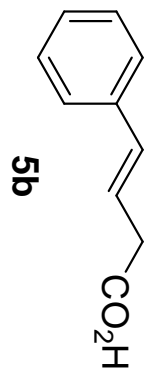
2.050



125 MHz, acetone-d₆



500 MHz, CDCl₃

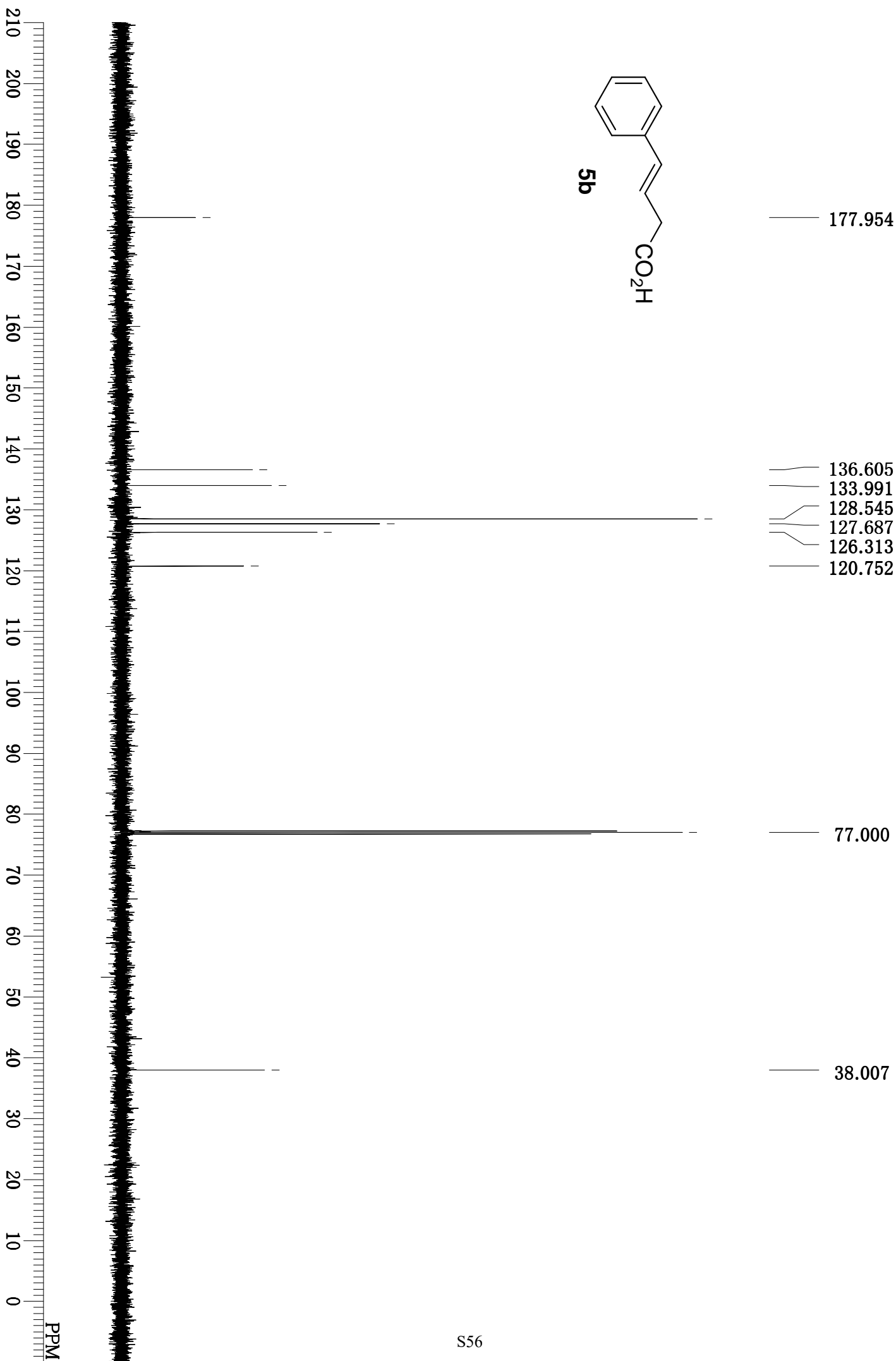
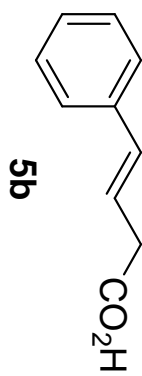


7.392
7.377
7.334
7.320
7.305
7.260
7.246
7.231
6.544
6.513
6.323
6.309
6.295
6.277
6.264

3.321
3.318
3.306
3.303

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
PPM

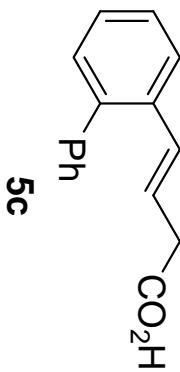
125 MHz, CDCl₃



500 MHz, CDCl₃

7.633
7.629
7.615
7.429
7.416
7.401
7.369
7.367
7.354
7.349
7.345
7.341
7.336
7.331
7.326
7.321
7.316
7.313
7.302
7.298
7.290
7.286
7.283
7.276
7.271
7.260
6.521
6.489
6.258
6.243
6.229
6.226
6.212
6.197

3.222
3.220
3.208
3.206



10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
PPM

1.01

2.01

1.21

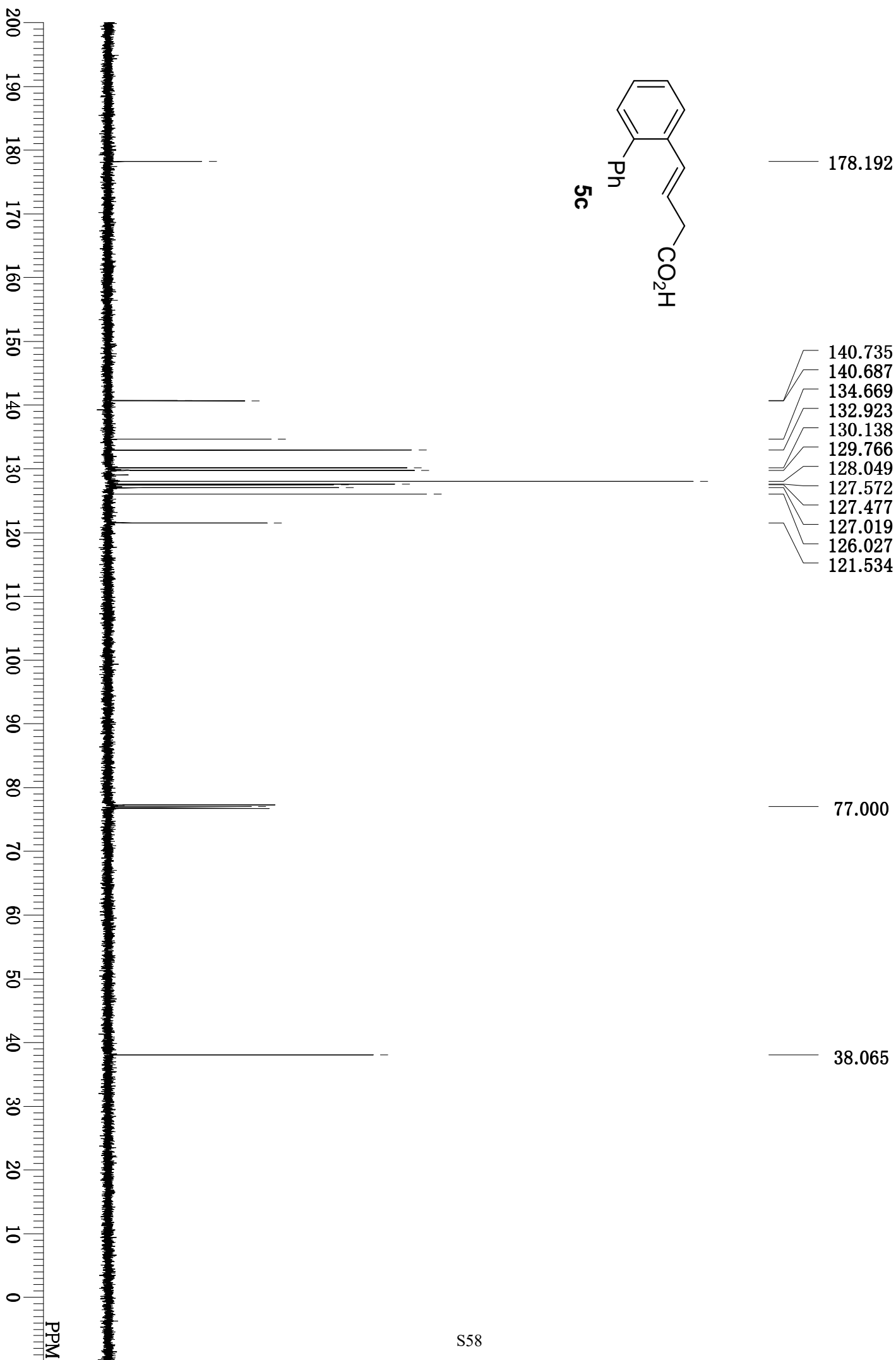
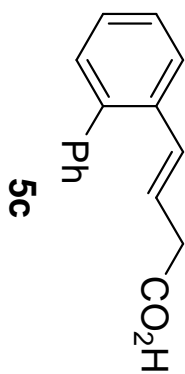
4.69

1.00

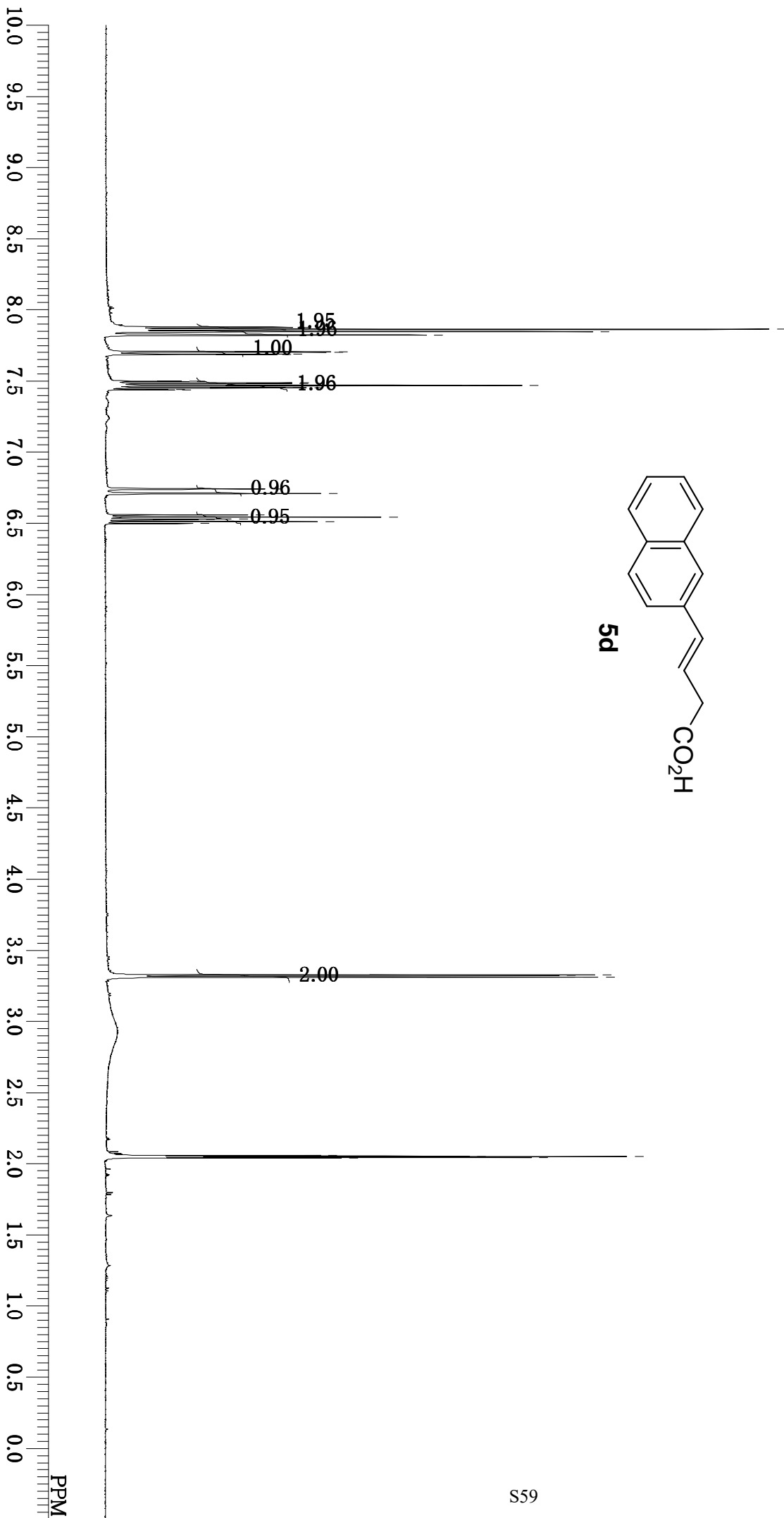
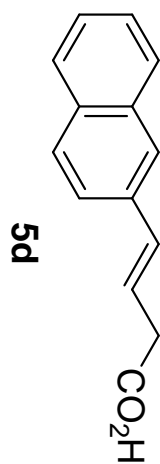
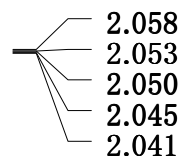
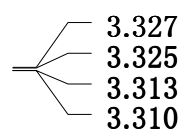
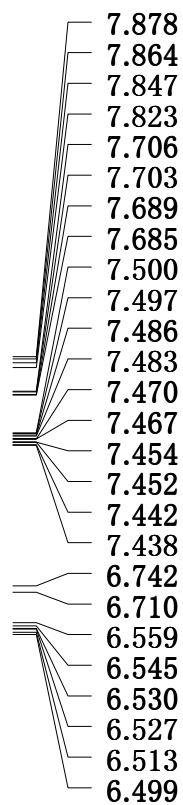
1.03

2.00

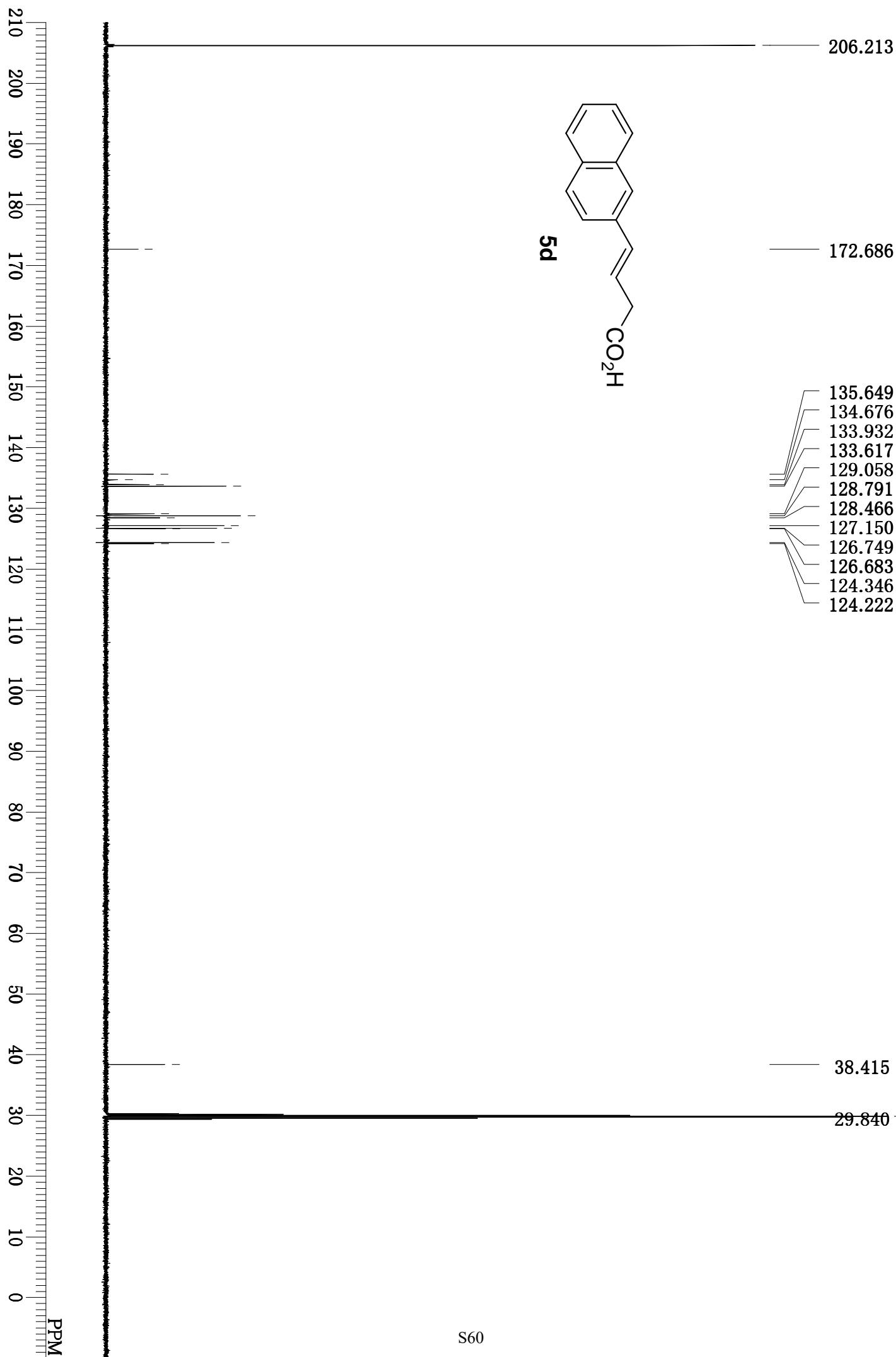
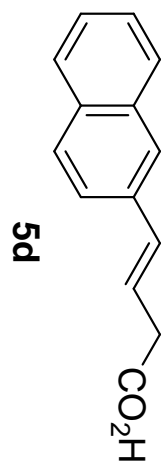
125 MHz, CDCl₃



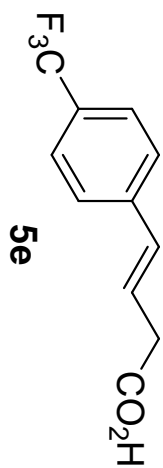
500 MHz, acetone-d₆



125 MHz, acetone-d₆

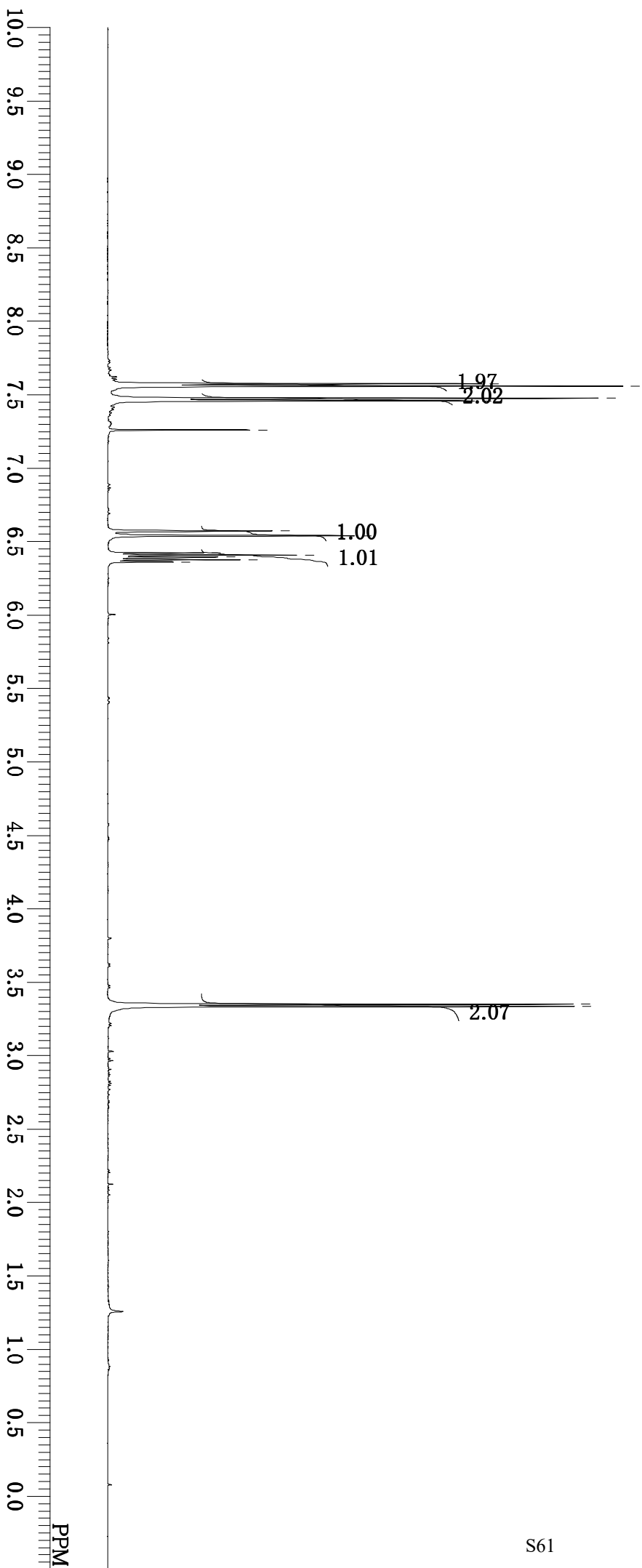


500 MHz, CDCl₃

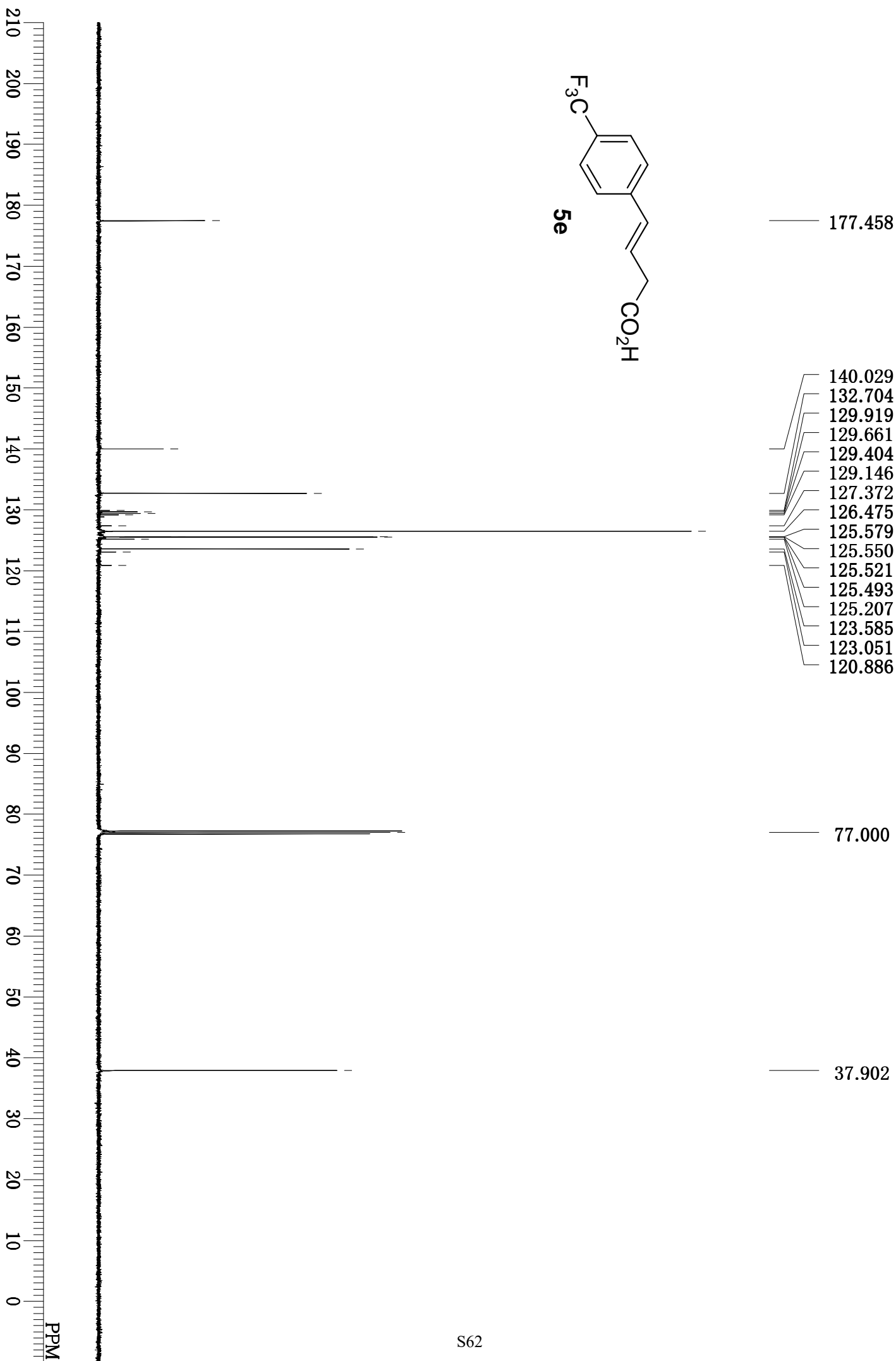
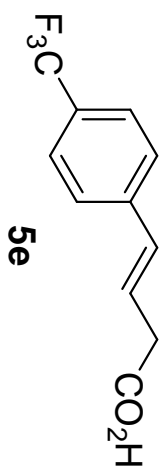


7.575
7.559
7.475
7.459
7.260
6.573
6.541
6.423
6.409
6.394
6.377
6.362

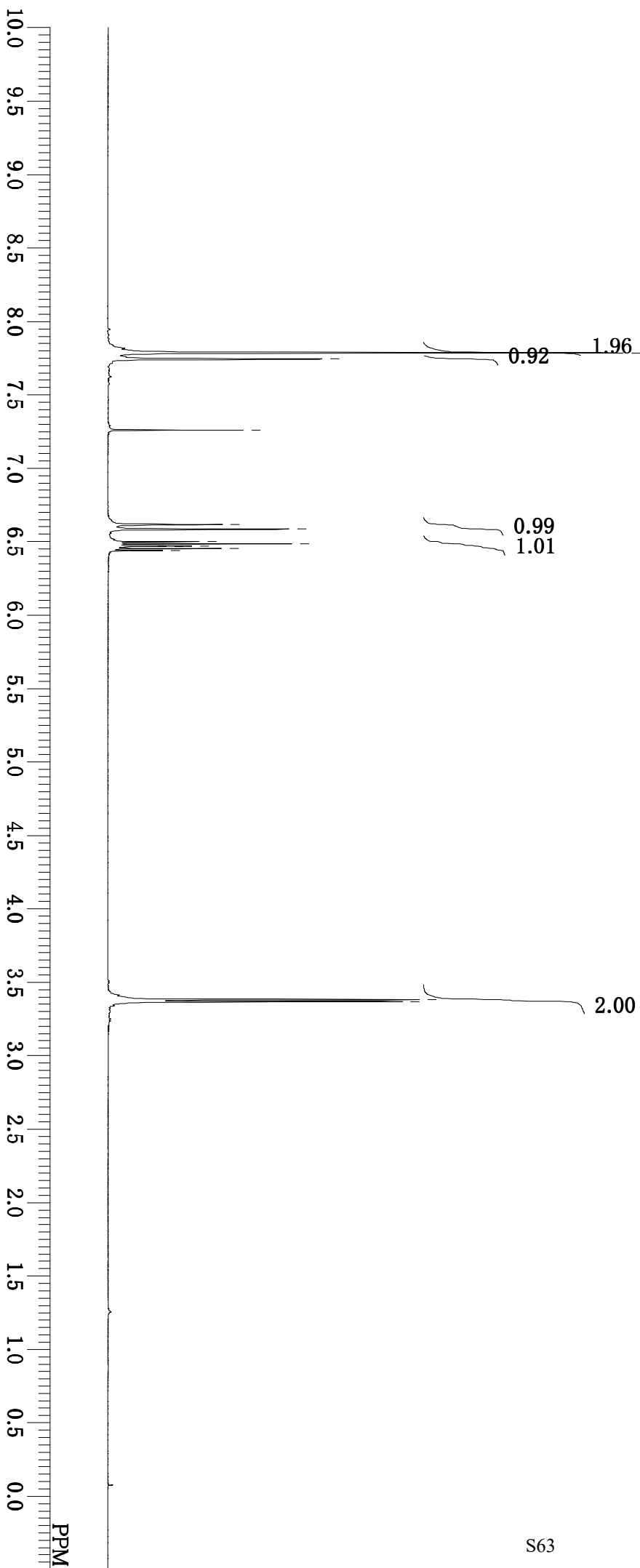
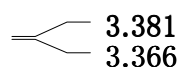
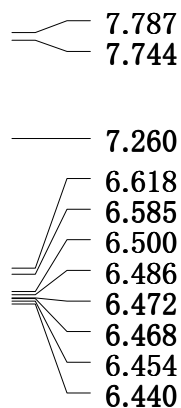
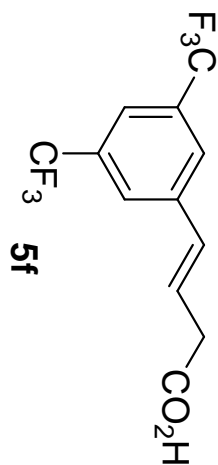
3.349
3.335



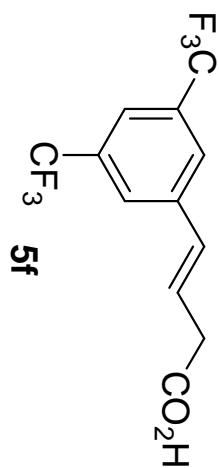
125 MHz, CDCl₃



500 MHz, CDCl₃



125 MHz, CDCl₃

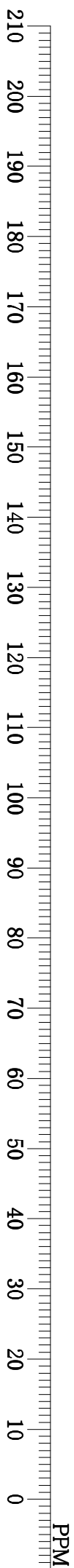


177.105

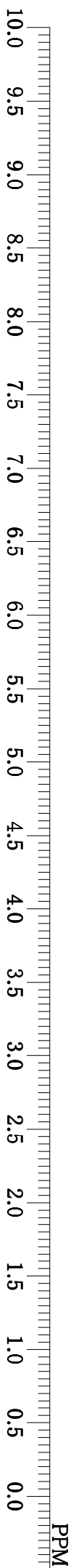
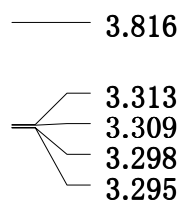
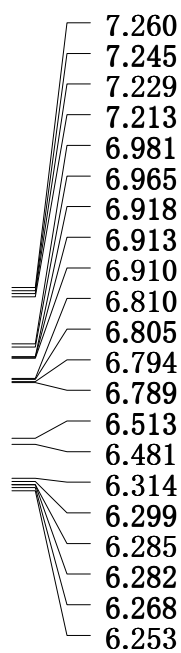
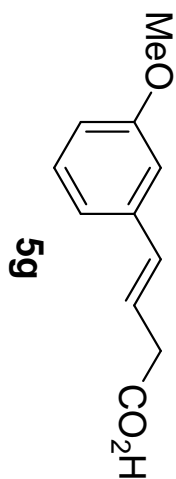
138.589
132.380
132.112
131.845
131.588
131.378
126.494
126.208
126.180
126.151
125.159
124.320
122.154
121.220
121.191
121.153
121.124
121.096
119.980

77.000

37.693



500 MHz, CDCl₃



1.03

1.01

1.01

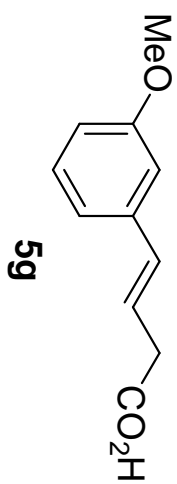
1.01

1.03

3.09

2.00

125 MHz, CDCl₃



177.858

159.755

138.045

133.887

129.528

121.105

119.007

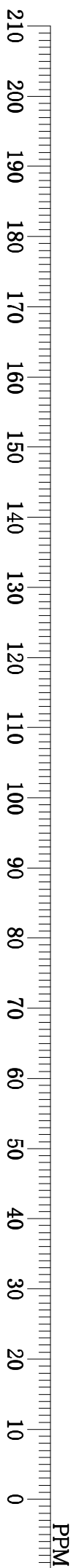
113.408

111.548

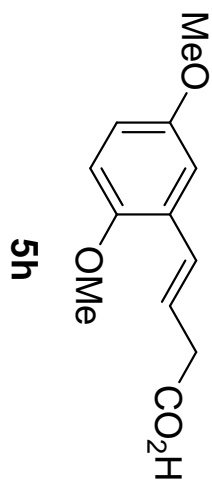
77.000

55.205

37.950



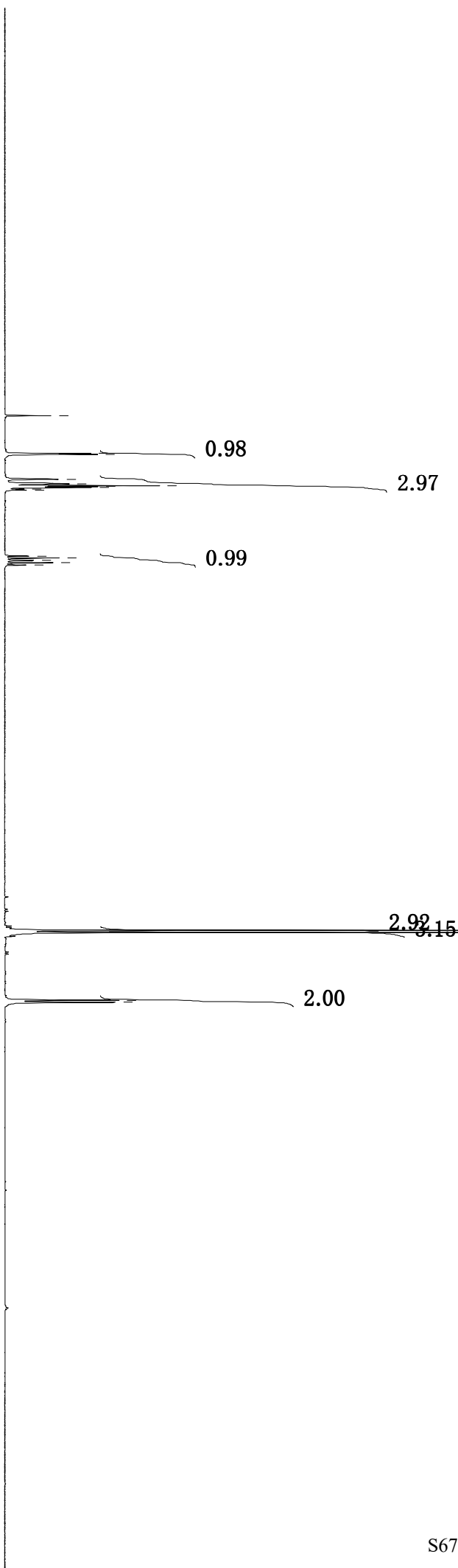
500 MHz, CDCl₃



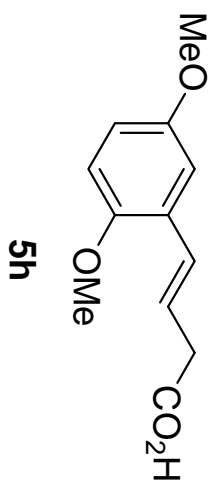
7.260
7.006
7.000
6.834
6.802
6.789
6.784
6.778
6.765
6.760
6.316
6.303
6.288
6.271
6.256

3.799
3.785
3.329
3.315

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
PPM



125 MHz, CDCl₃



177.963

153.631
151.036

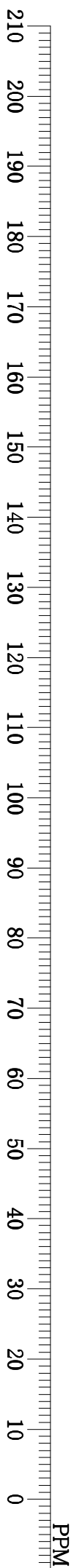
128.660
126.466
121.697

113.866
112.177
112.072

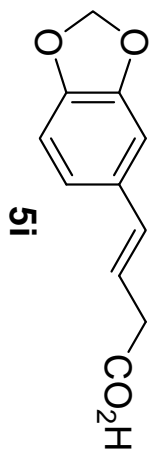
77.000

56.159
55.749

38.379



500 MHz, CDCl₃

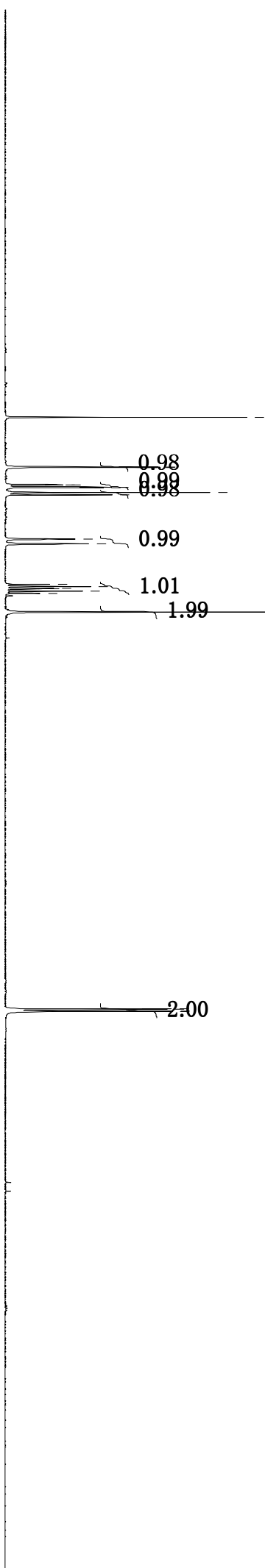


7.260
6.926
6.922
6.807
6.803
6.790
6.787
6.754
6.738
6.440
6.408
6.135
6.121
6.107
6.103
6.090
6.075
5.949

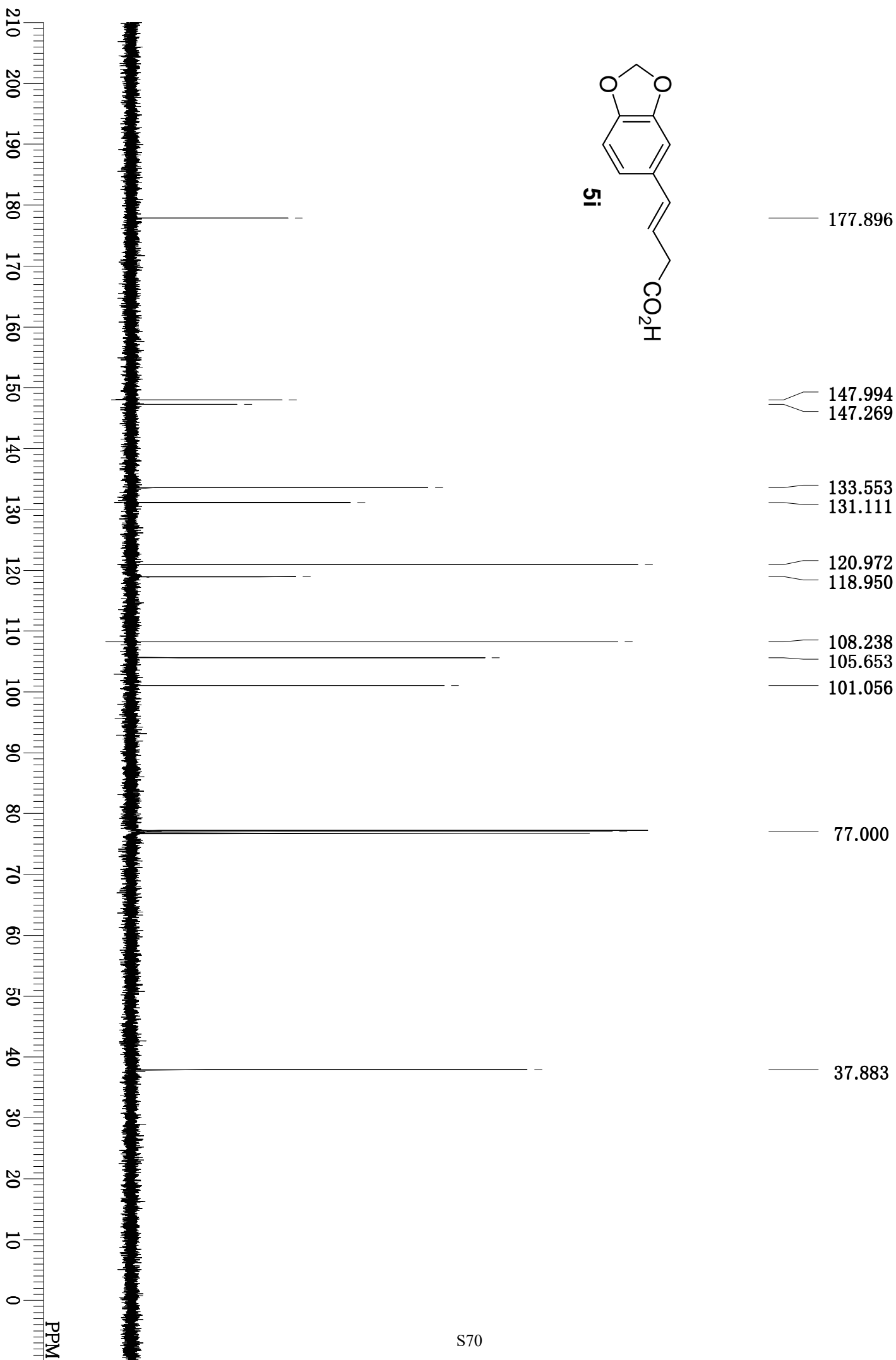
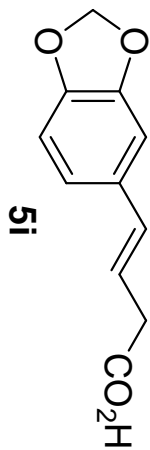
3.276
3.272
3.261
3.259

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

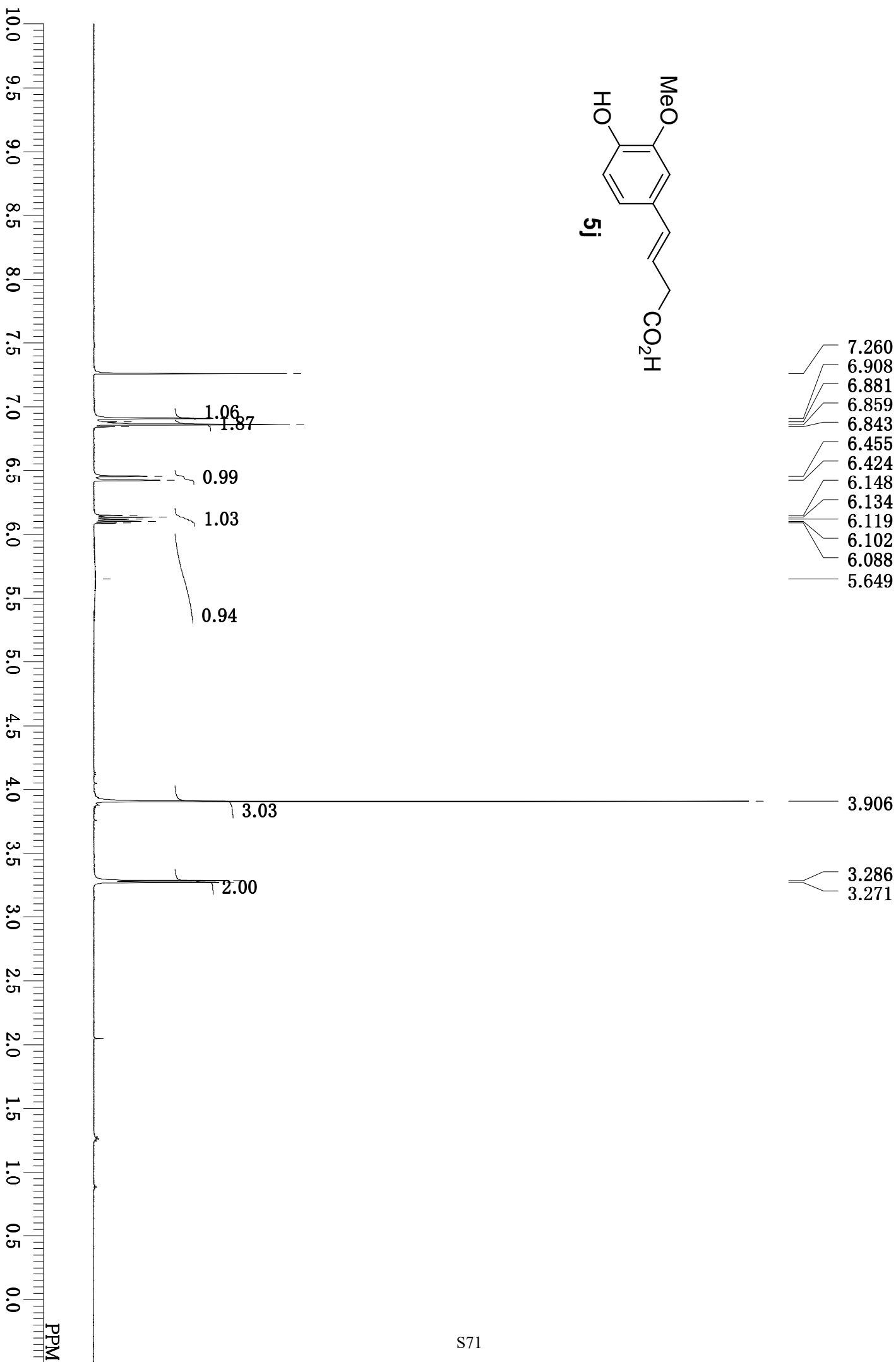
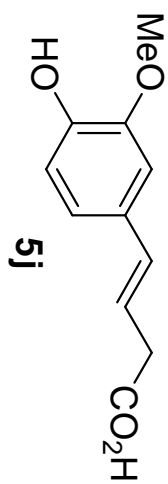
PPM



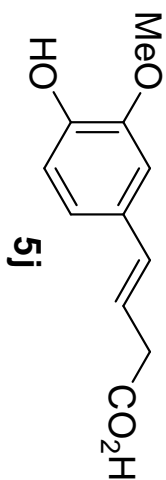
125 MHz, CDCl₃



500 MHz, CDCl₃



125 MHz, CDCl₃



177.954

146.582
145.485

133.782
129.251

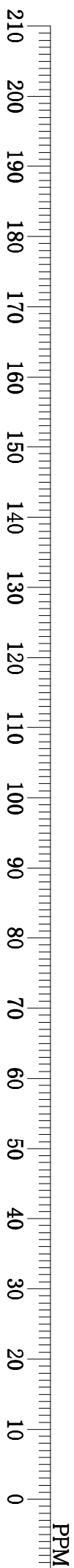
120.199
118.368
114.381

108.076

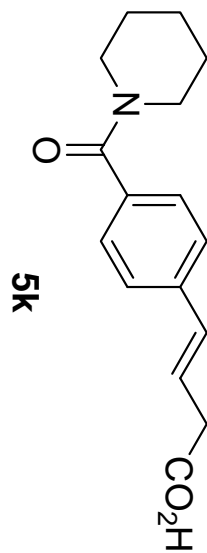
77.000

55.873

37.931



500 MHz, CDCl₃



9.170

7.370
7.354
7.338
7.321
7.260
6.473
6.441
6.328
6.314
6.300
6.282
6.268

3.703
3.341
3.246
3.231

1.665
1.509

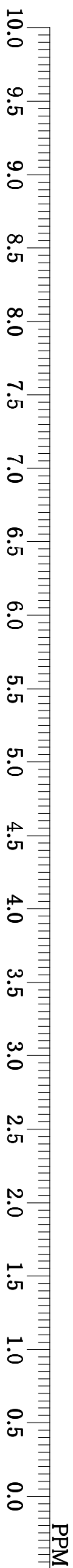
1.03

1.96
1.91

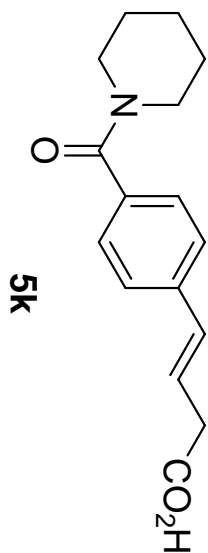
0.96
0.96

2.06
1.94
2.00

4.07
2.08



125 MHz, CDCl₃



175.550

170.466

138.093

134.783

132.628

127.229

126.170

122.994

77.000

48.852

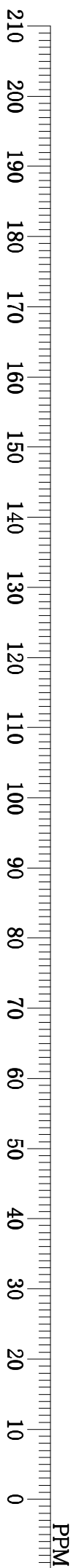
43.339

38.141

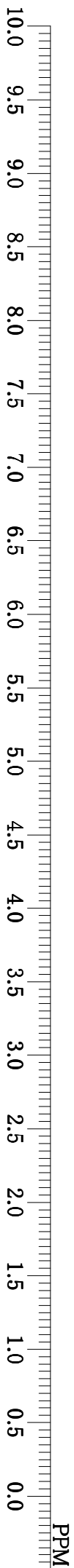
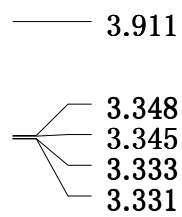
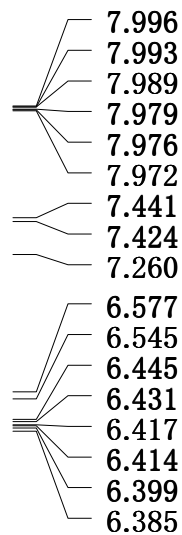
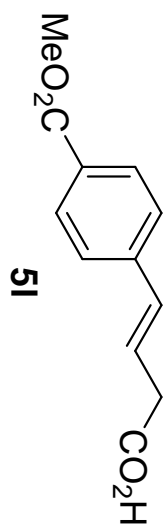
26.447

25.522

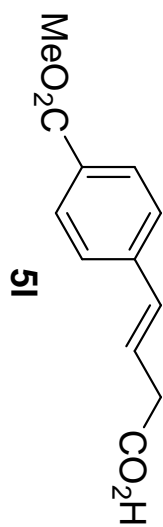
24.463



500 MHz, CDCl₃



125 MHz, CDCl₃



177.095

166.870

141.021

133.114

129.928

129.127

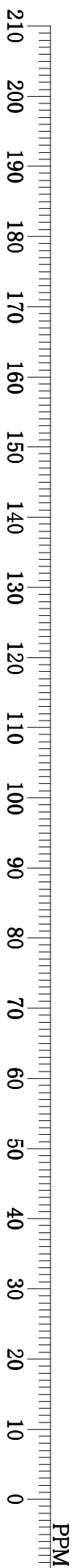
126.199

123.614

77.000

52.095

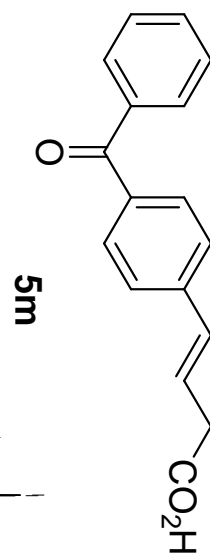
37.931



500 MHz, CDCl₃

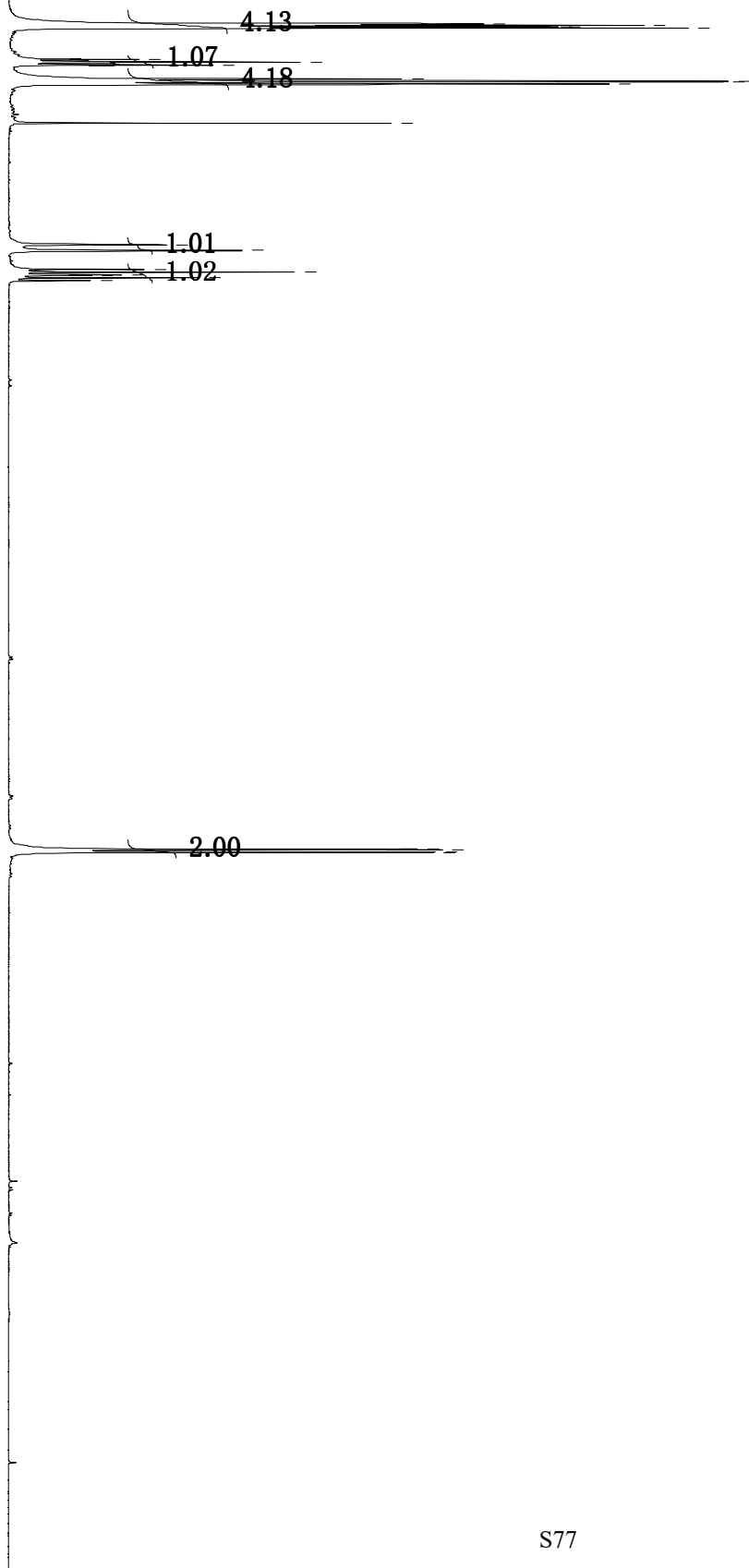
7.793
7.787
7.782
7.778
7.775
7.770
7.602
7.588
7.573
7.498
7.487
7.482
7.470
7.260
6.608
6.577
6.476
6.462
6.448
6.443
6.430
6.416

3.366
3.363
3.351
3.349

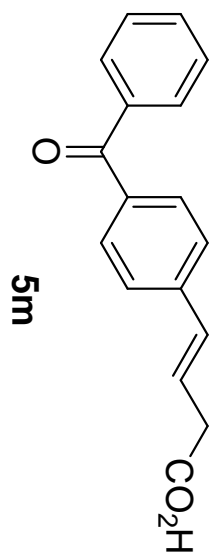


10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

PPM



125 MHz, CDCl₃



196.220

177.124

140.668

137.664

136.491

133.076

132.351

130.605

129.938

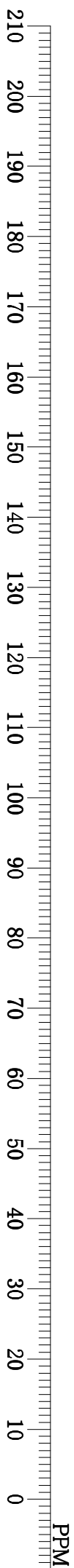
128.259

126.113

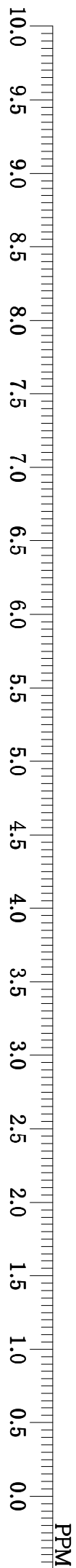
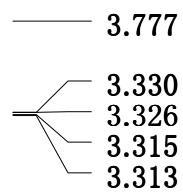
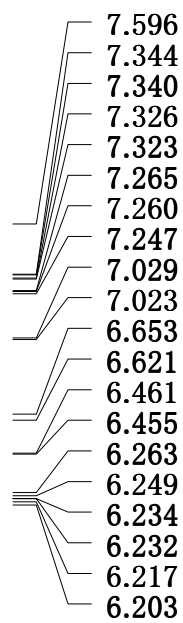
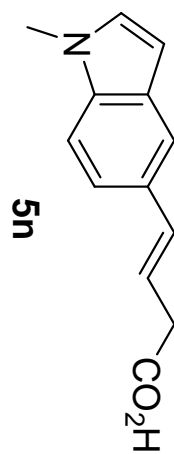
123.766

77.000

37.969



500 MHz, CDCl₃

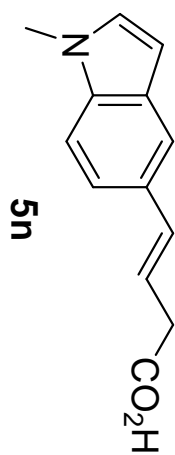


0.99
1.02
1.32
0.96
1.00
0.96
1.00

3.00

2.00

125 MHz, CDCl₃



178.068

136.462

135.098

128.583

128.297

119.942

119.360

117.614

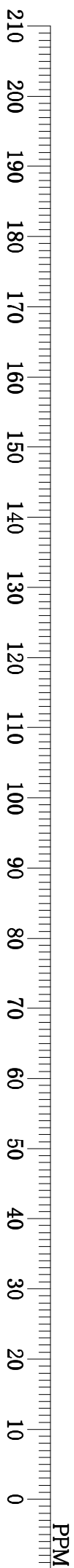
109.287

101.246

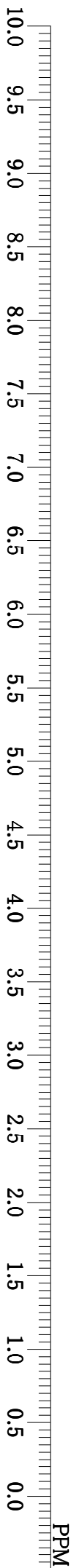
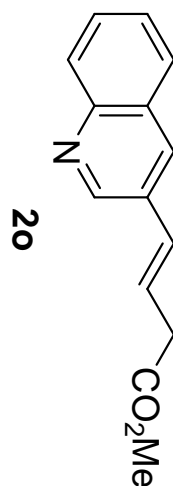
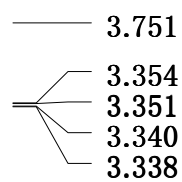
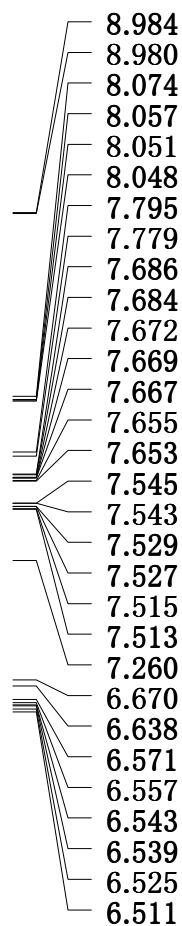
77.000

38.160

32.876



500 MHz, CDCl₃



1.00

2.02

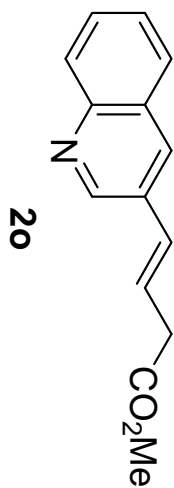
1.06
1.03
1.05

1.03
1.03

3.00

2.07

125 MHz, CDCl₃



171.630

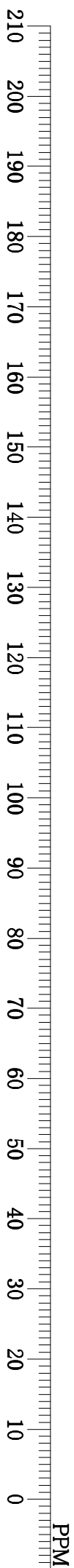
149.224
147.498

132.294
130.329
129.671
129.232
129.213
127.944
127.801
126.943
124.262

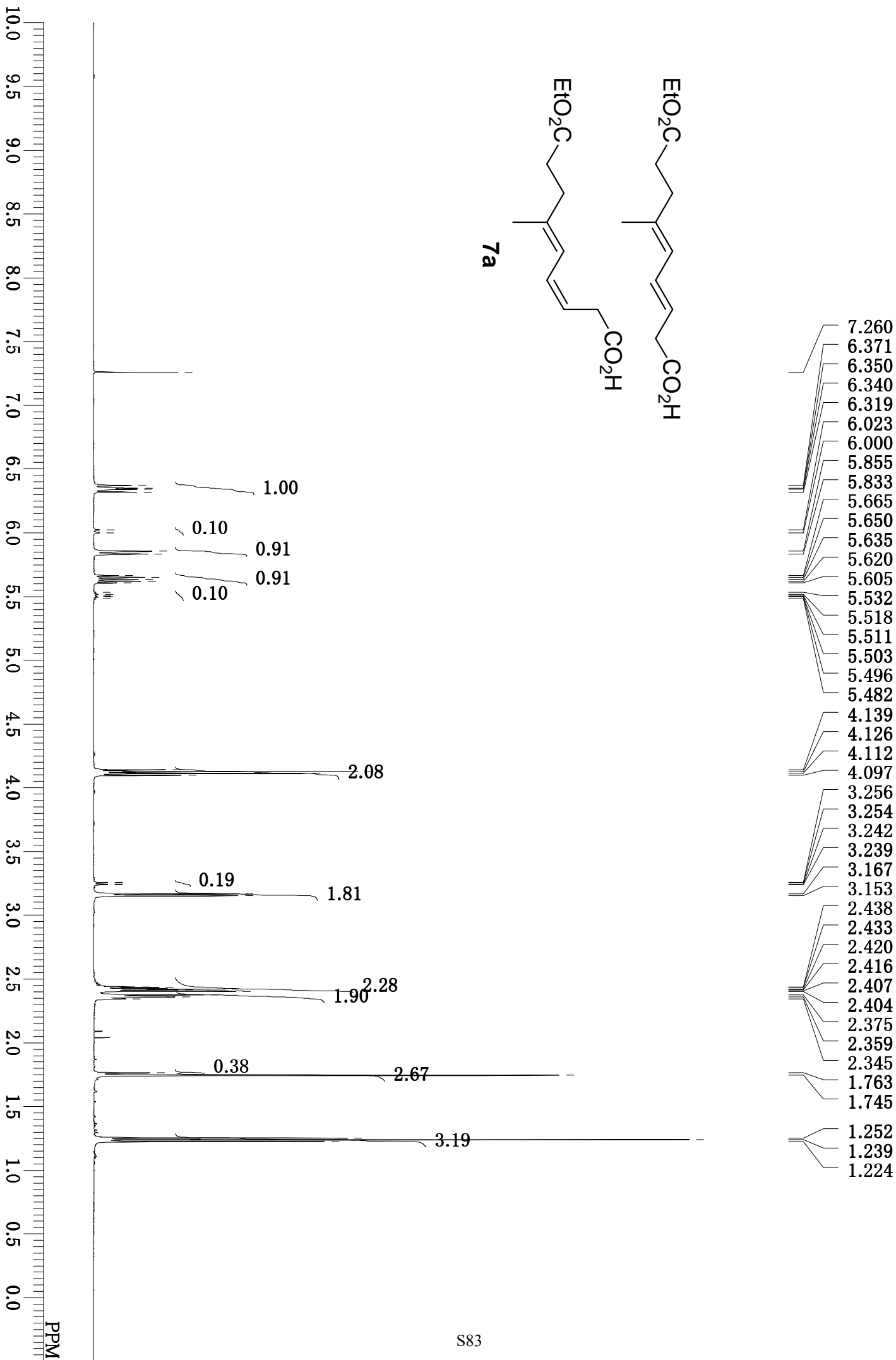
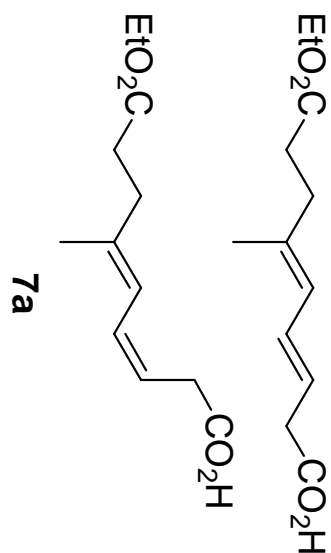
77.000

52.067

38.303



500 MHz, CDCl₃



125 MHz, CDCl₃

177.915
177.782
173.213
173.146

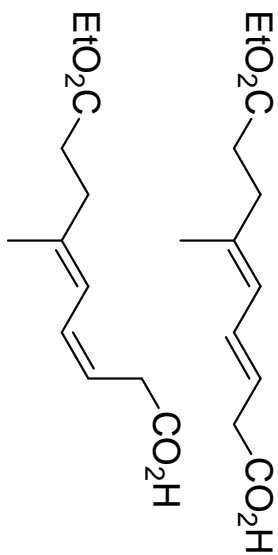
139.314
137.053
130.472
127.620
124.444
122.326
119.665
119.608

77.000

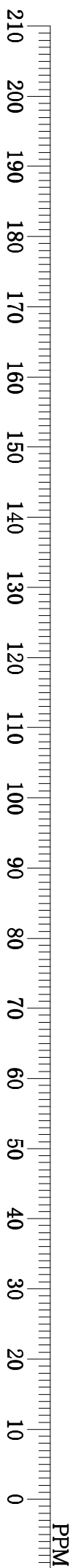
60.441
60.394

37.893
35.098
34.669
32.866
32.809

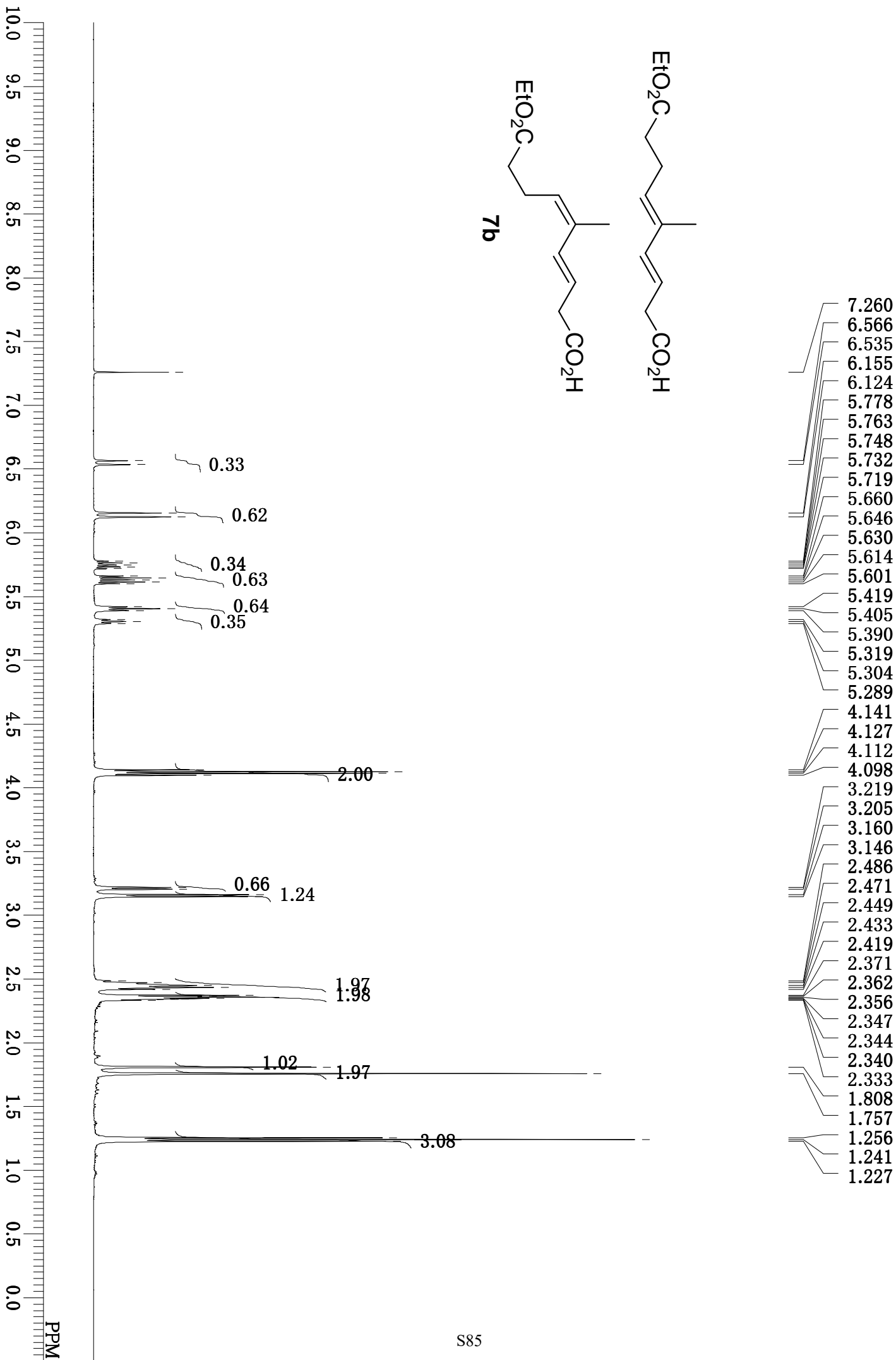
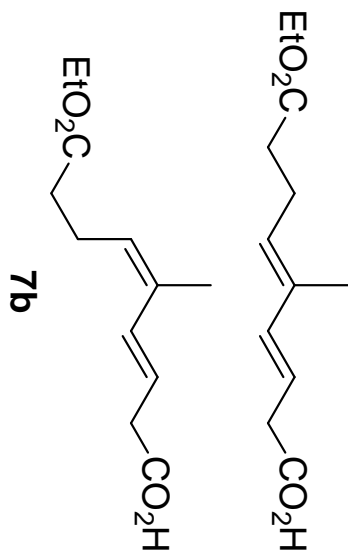
16.517
16.479
14.200



7a



500 MHz, CDCl₃



125 MHz, CDCl₃

178.068
177.858
173.146
173.127

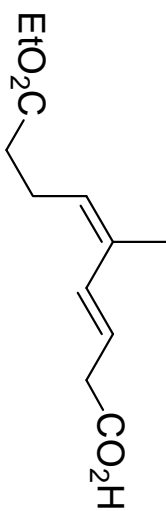
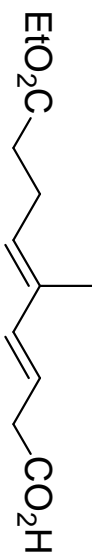
138.541
134.173
132.523
130.787
130.281
128.288
121.096
118.129

77.000

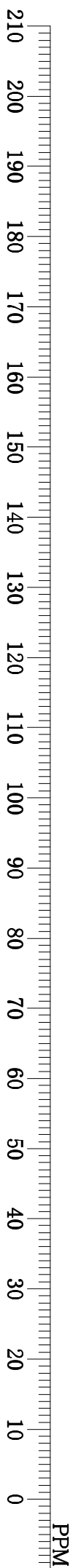
60.394

38.217
37.845
34.354
34.039

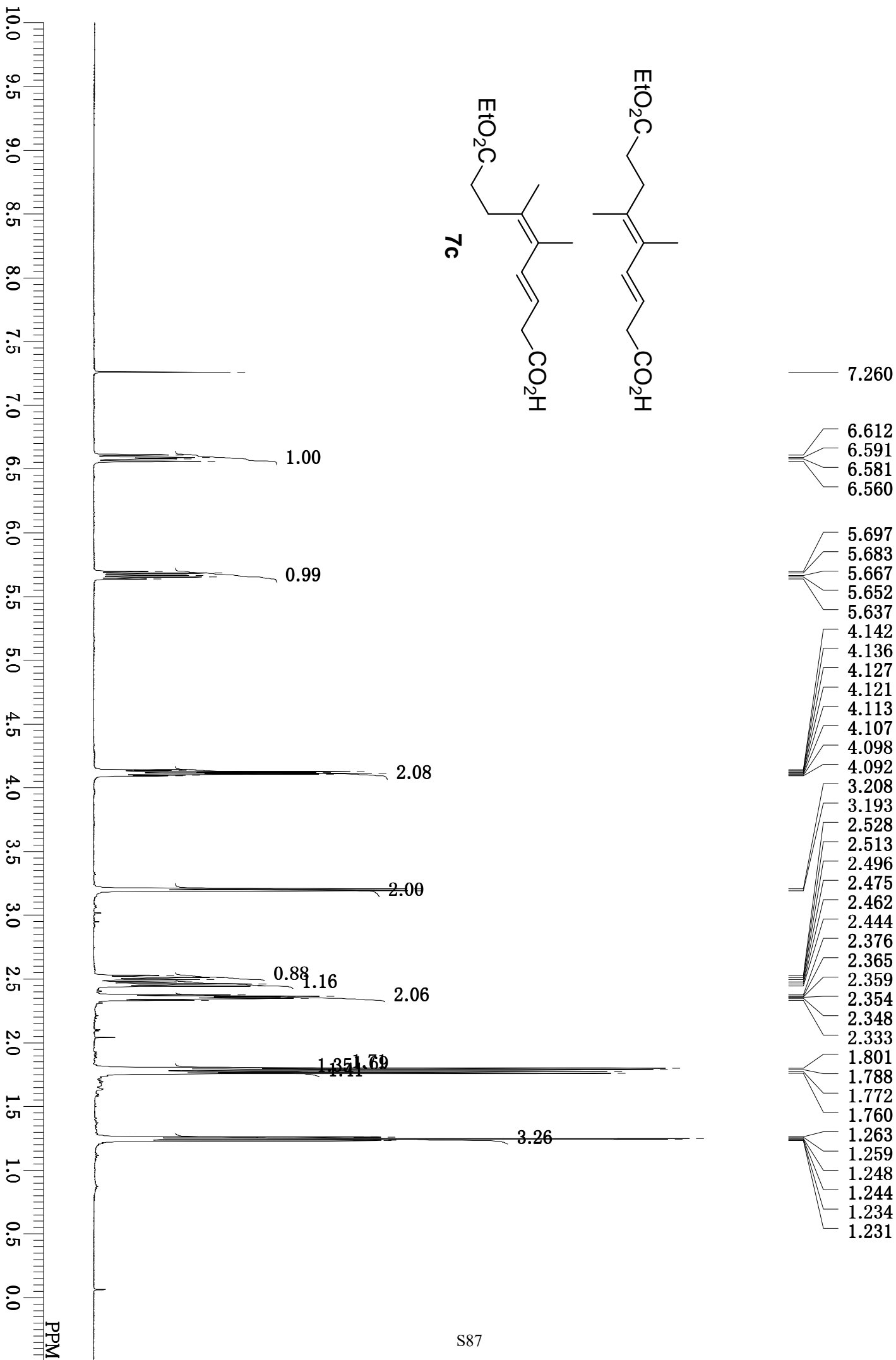
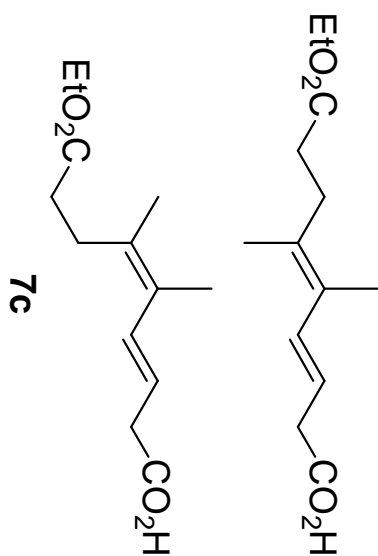
23.662
22.889
20.361
14.181
12.282



7b



500 MHz, CDCl₃



125 MHz, CDCl₃

178.135

173.337

133.305

132.856

132.504

127.257

127.029

119.064

118.921

77.000

60.432

38.379

38.351

33.353

32.761

30.844

29.356

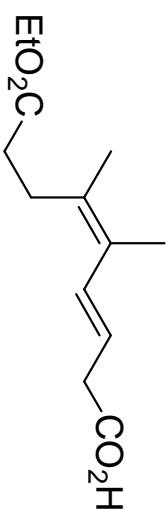
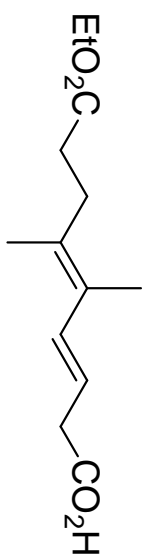
19.446

18.025

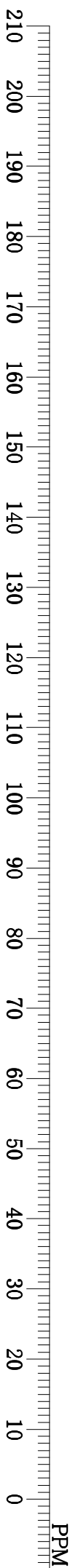
14.524

14.162

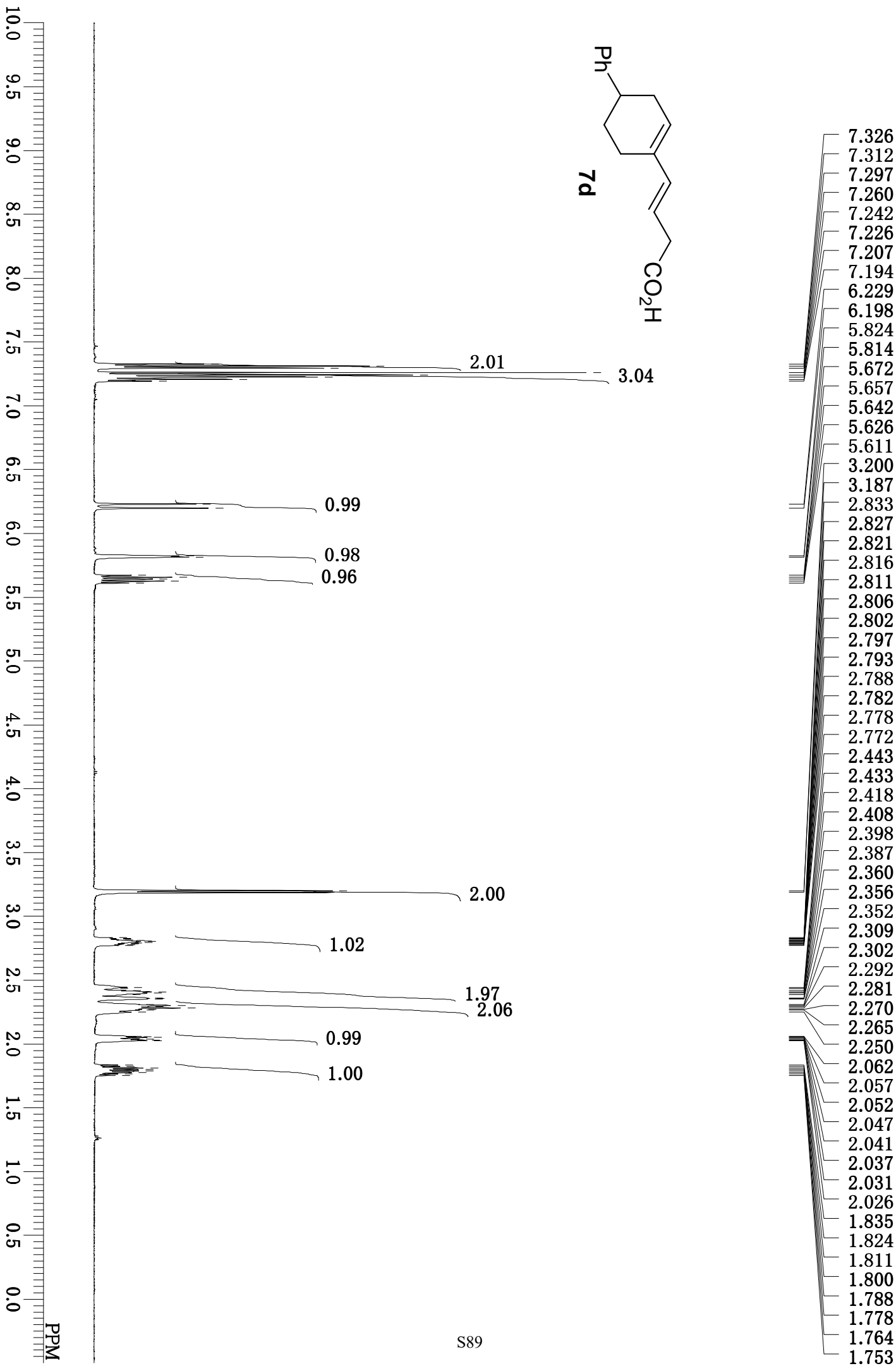
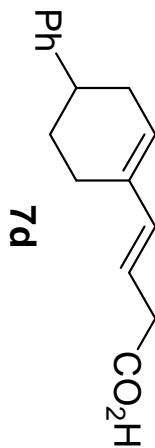
13.990



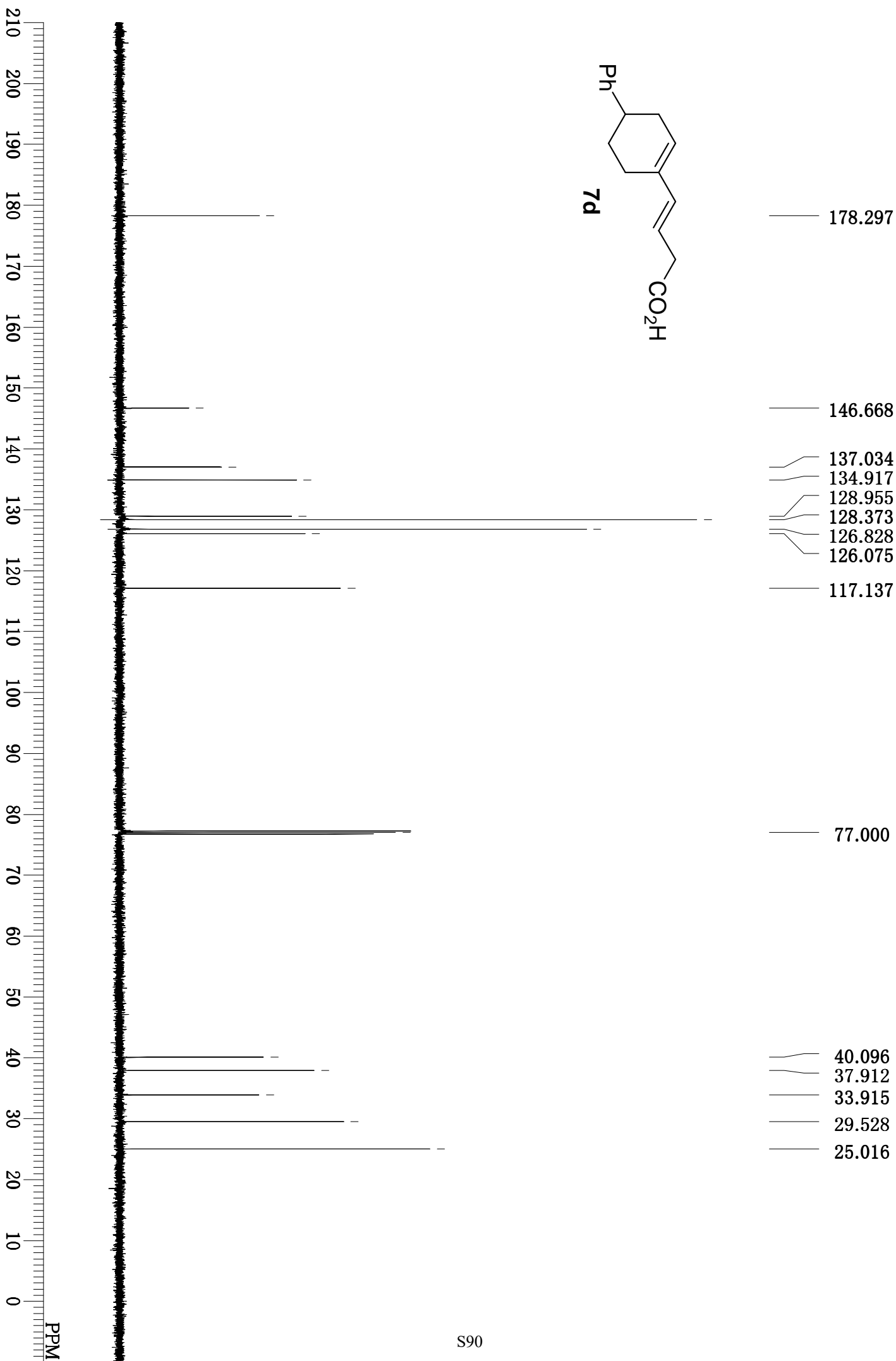
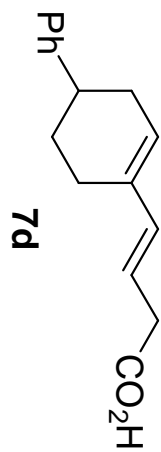
7c



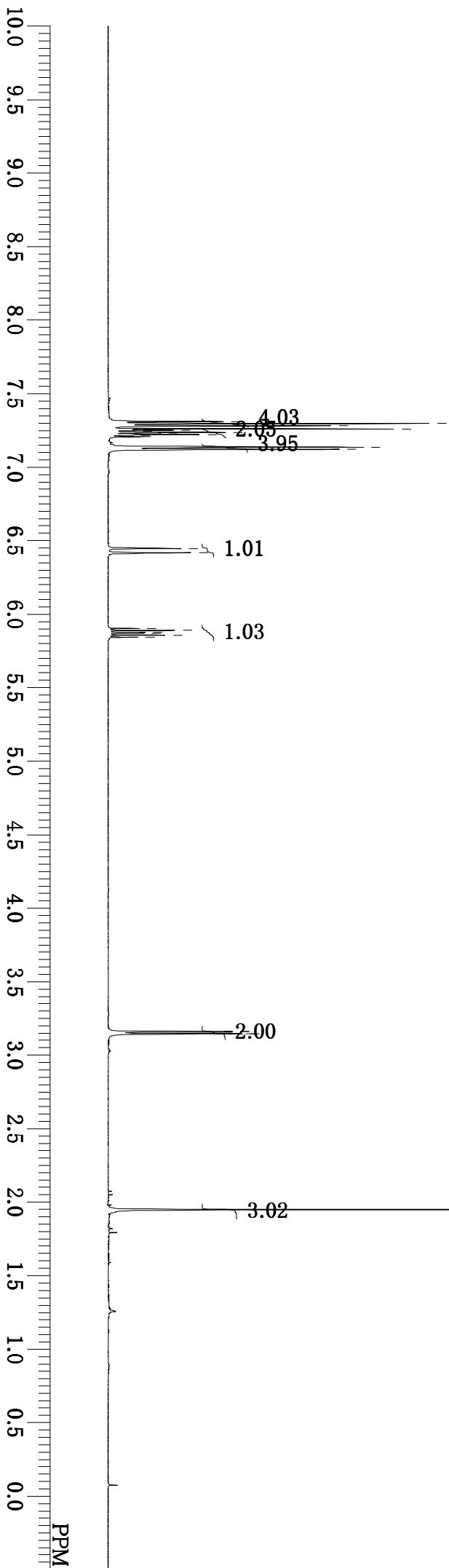
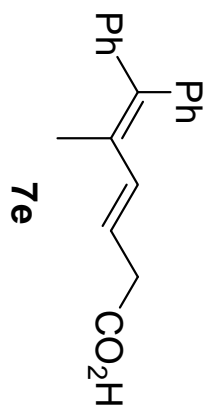
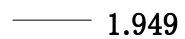
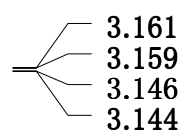
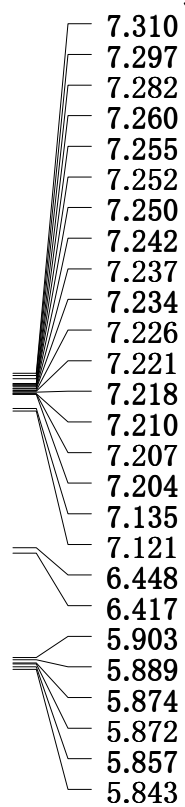
500 MHz, CDCl₃



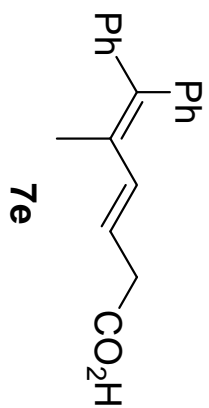
125 MHz, CDCl₃



500 MHz, CDCl₃



125 MHz, CDCl₃



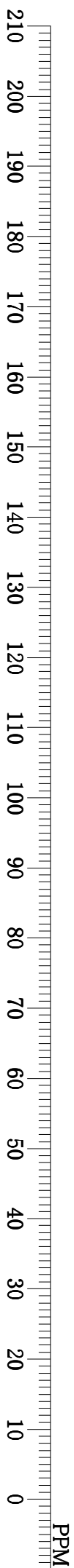
177.343

142.900
142.118
135.203
130.634
130.472
129.900
127.916
127.897
126.761
126.657
120.981

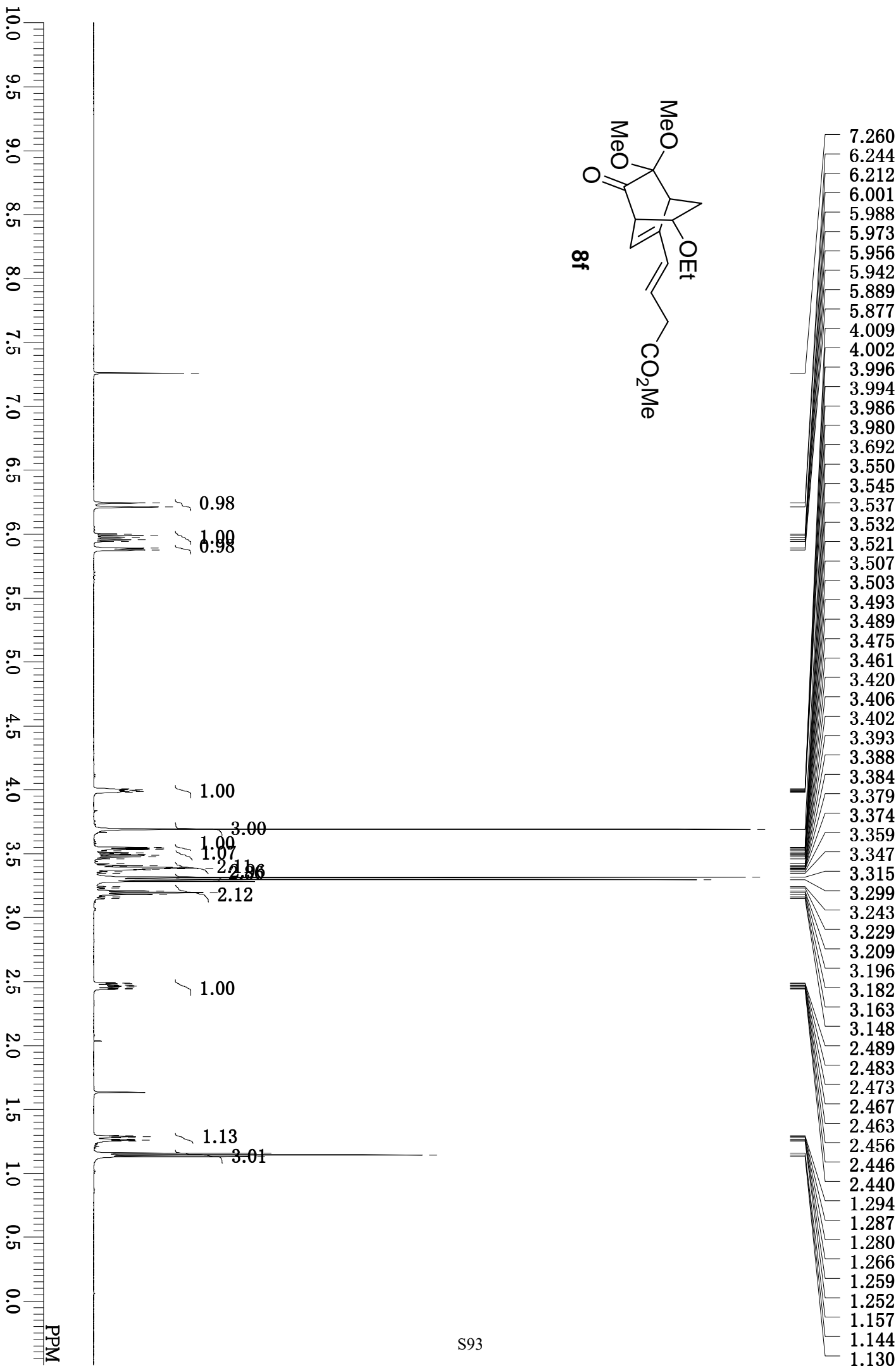
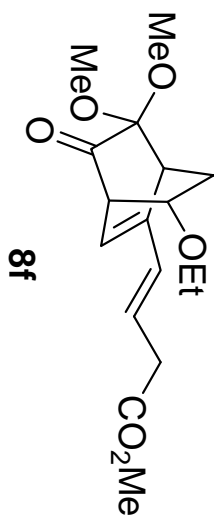
77.000

38.074

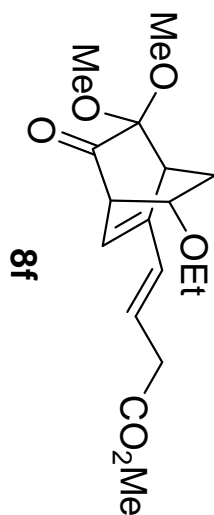
16.794



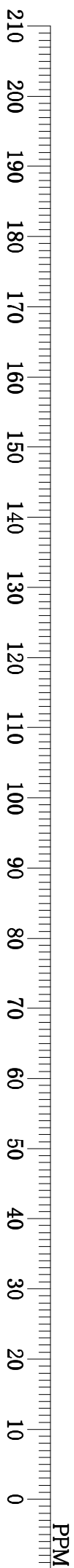
500 MHz, CDCl₃



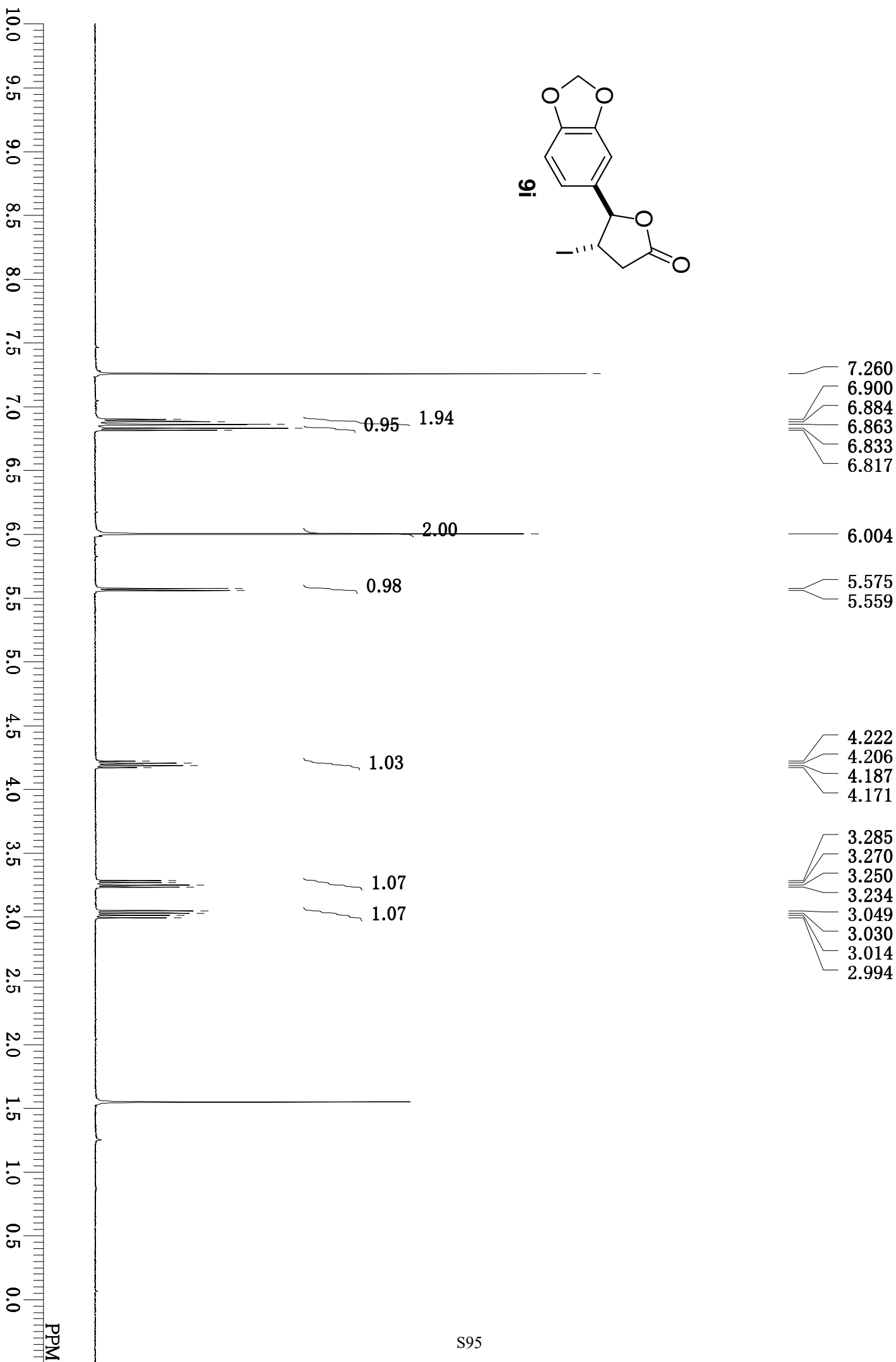
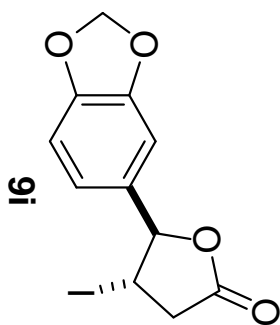
125 MHz, CDCl₃



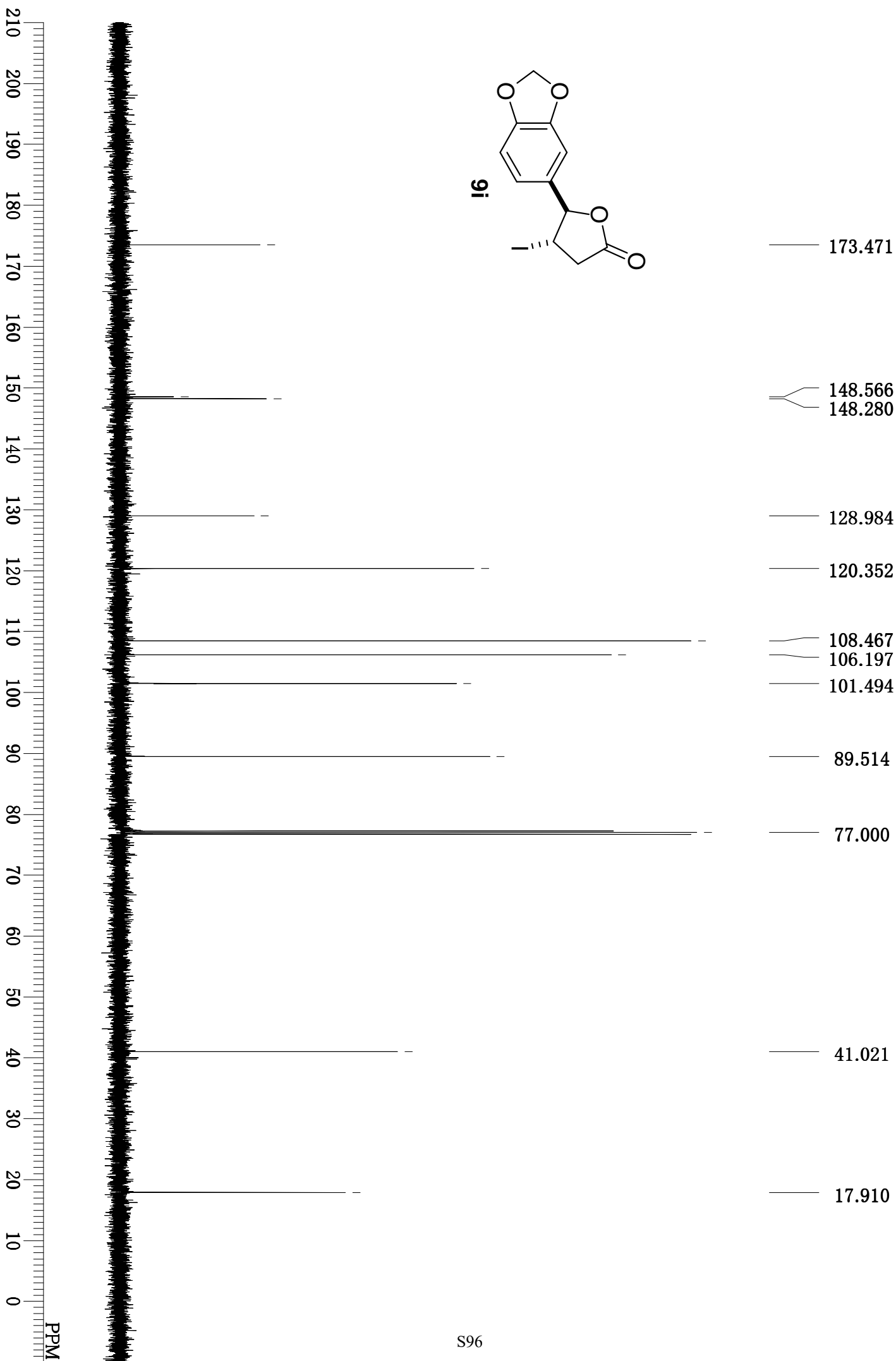
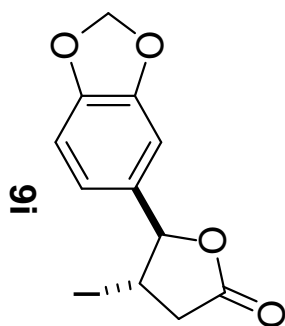
200.435	
171.801	
143.845	
131.178	
121.573	
121.267	
93.749	
77.000	
74.882	
64.285	
54.013	
51.905	
50.684	
49.844	
37.788	
37.607	
30.339	
15.287	



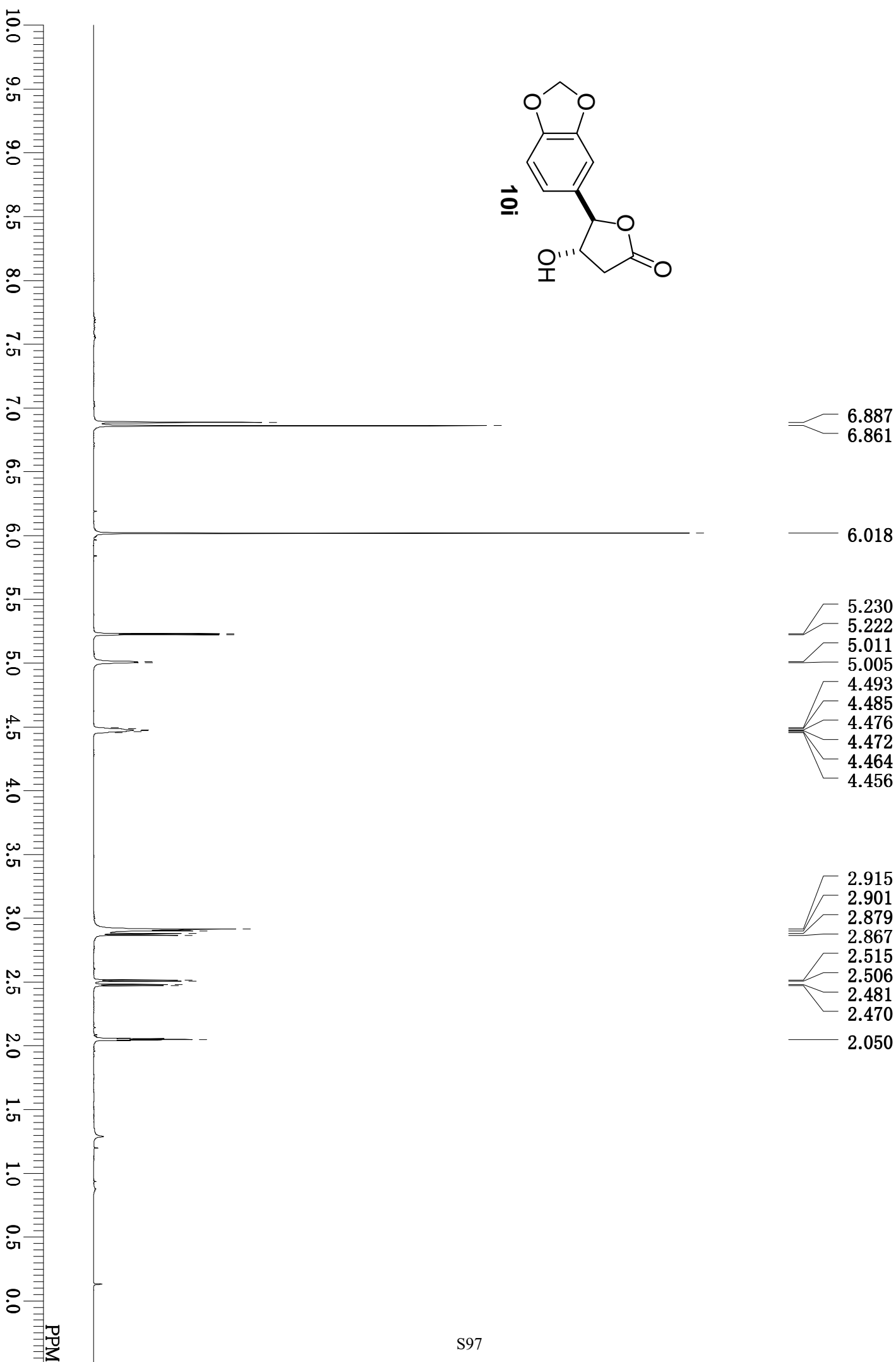
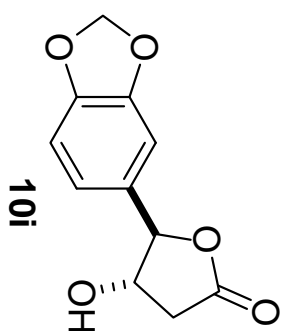
500 MHz, CDCl₃



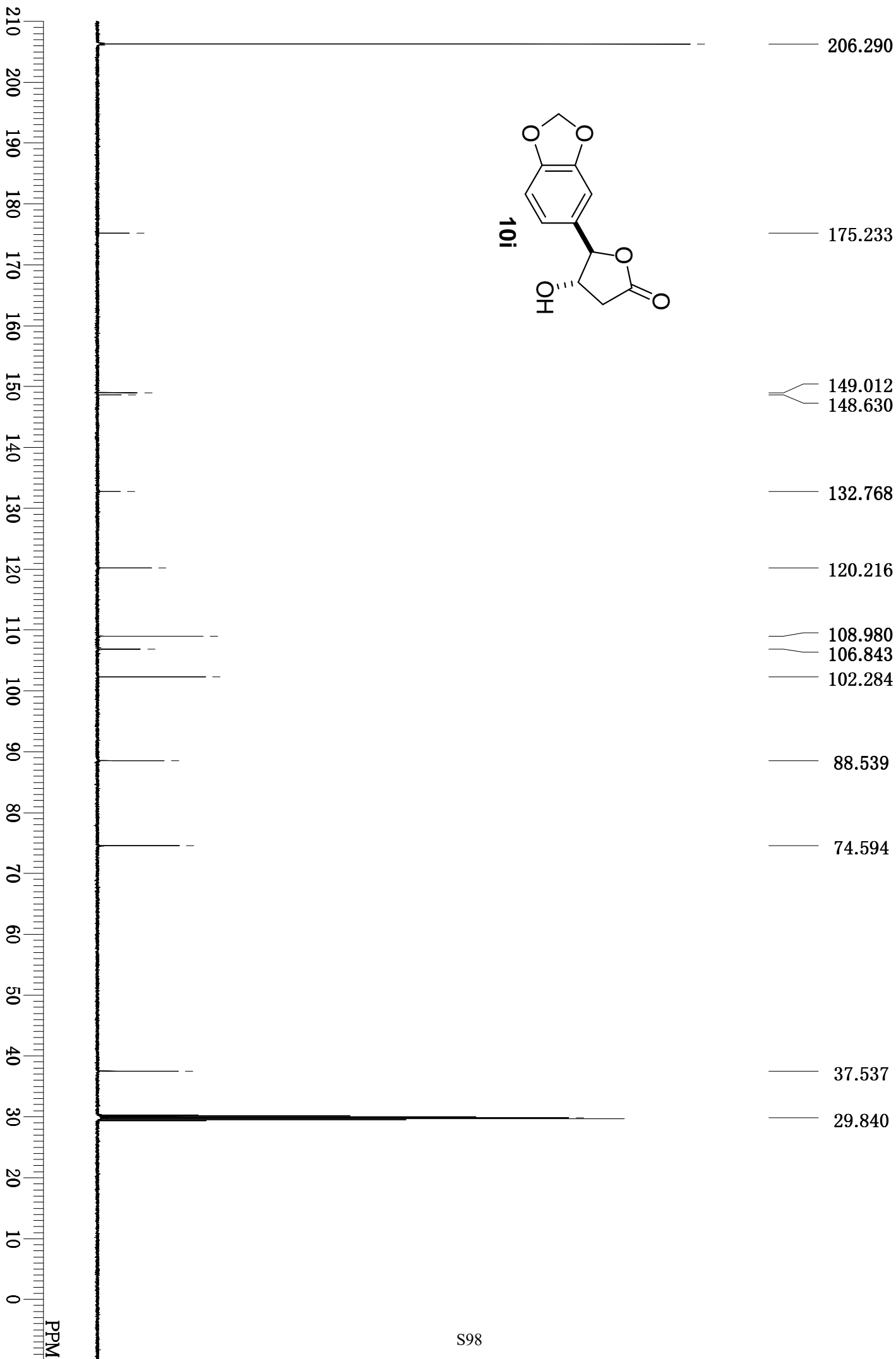
125 MHz, CDCl₃



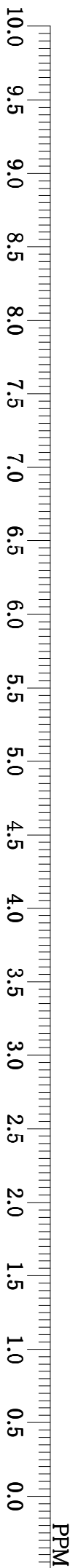
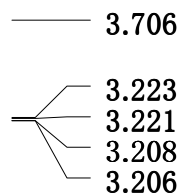
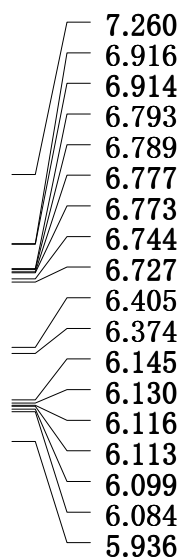
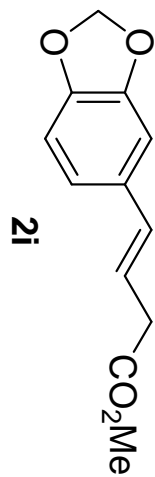
500 MHz, acetone-d₆



125 MHz, acetone-d₆



500 MHz, CDCl₃



0.99

0.99

1.00

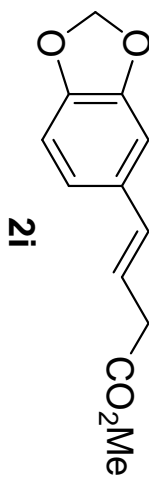
1.03

2.03

3.00

2.05

125 MHz, CDCl₃



172.078

147.975
147.164

133.019
131.283

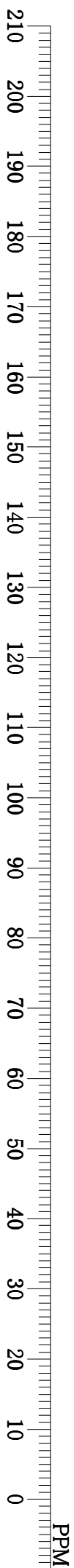
120.876
119.818

108.209
105.625
101.027

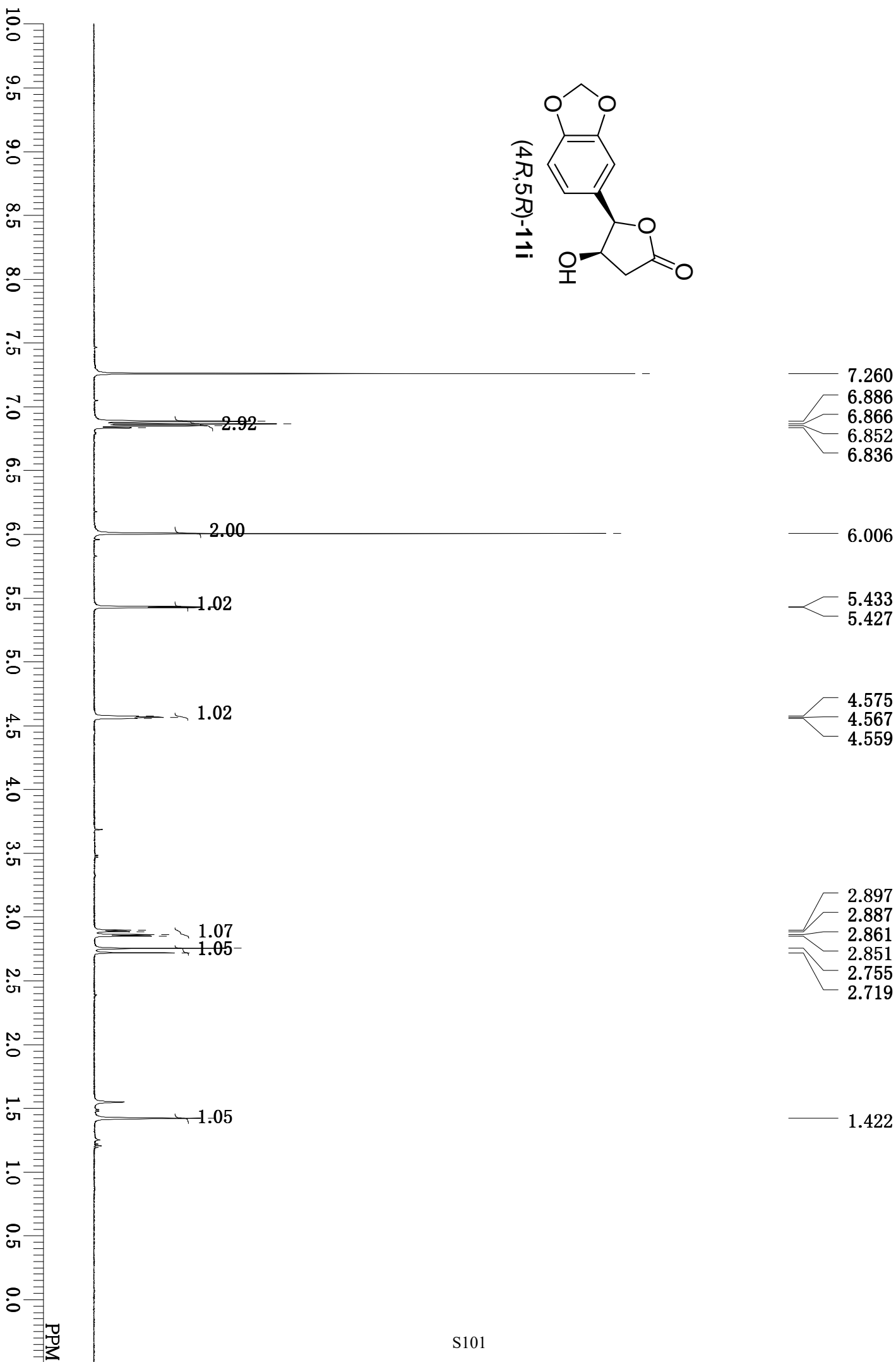
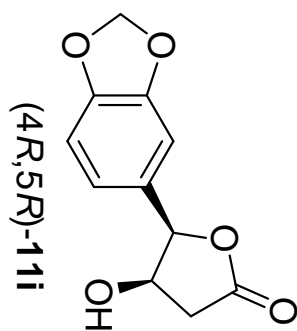
77.000

51.895

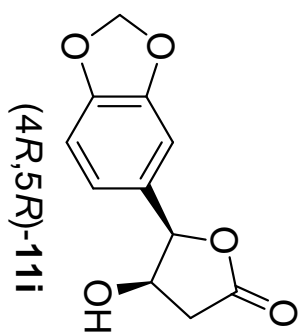
38.103



500 MHz, CDCl₃



125 MHz, CDCl₃



175.350

148.242
148.146

126.552

119.837

108.600
106.988

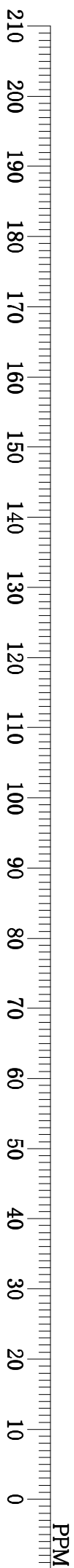
101.389

84.926

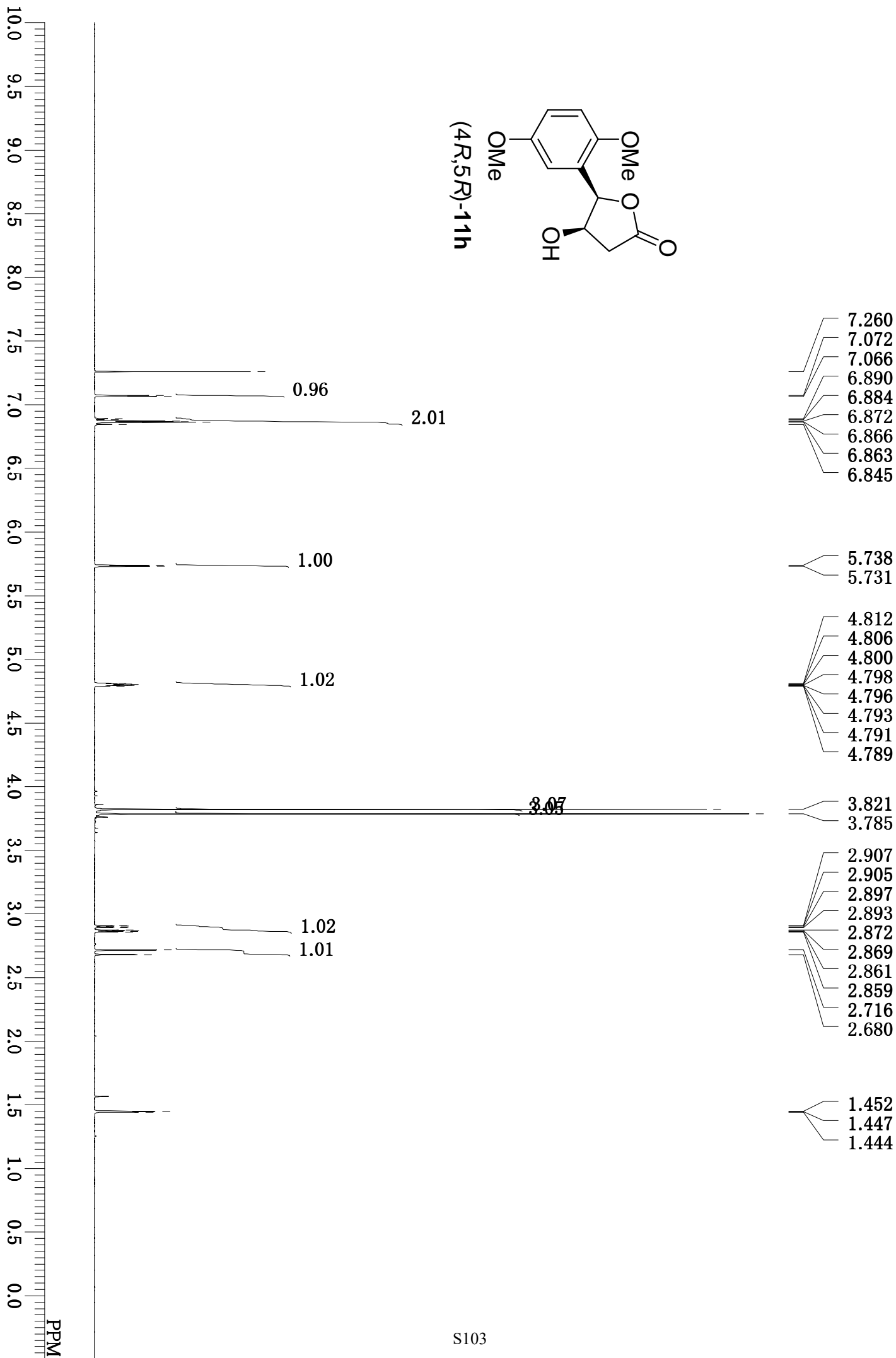
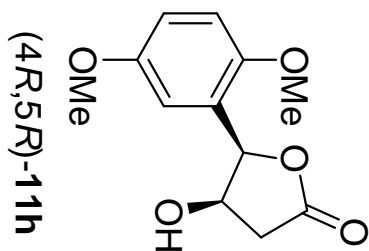
77.000

70.180

38.446

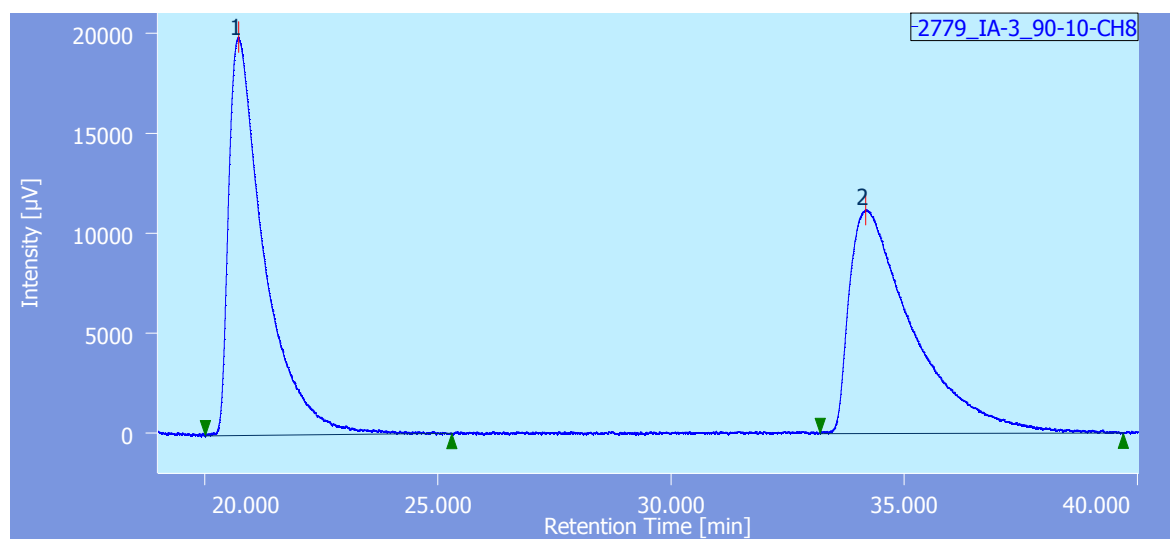


500 MHz, CDCl₃

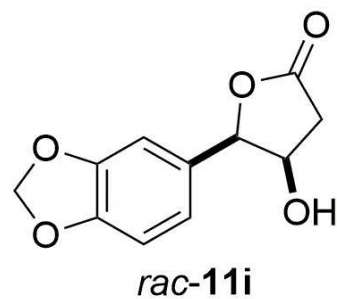


Chromatogram

HPLC (DAICEL CHIRALPAK IA-3, hexane/2-propanol = 90/10, 1.0 mL/min, 290 nm)

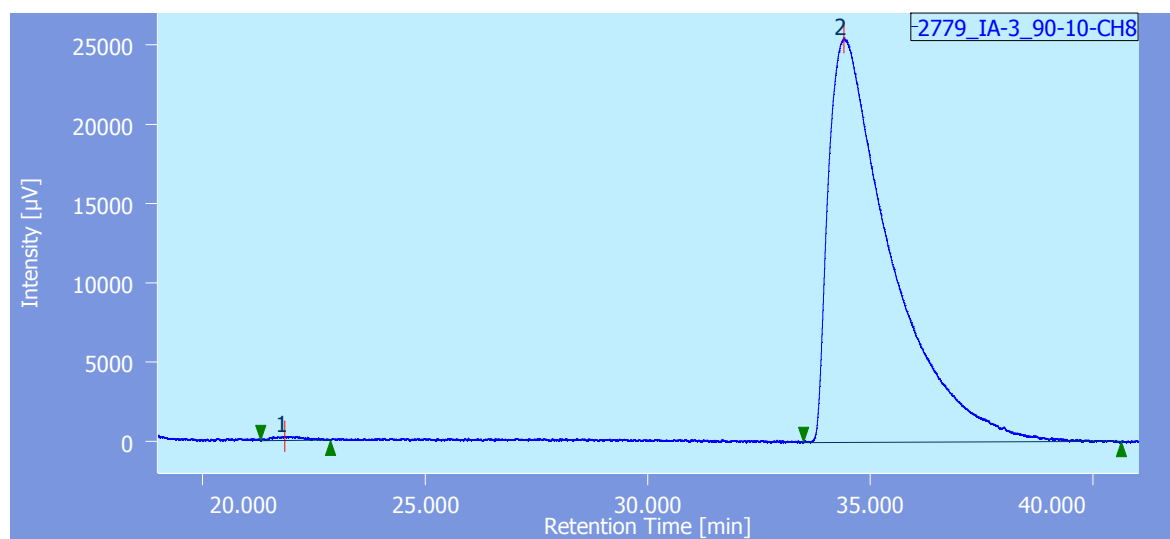


Peak #	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	8	20.732	1049739	19917	49.756	64.032
2	8	34.165	1060050	11188	50.244	35.968

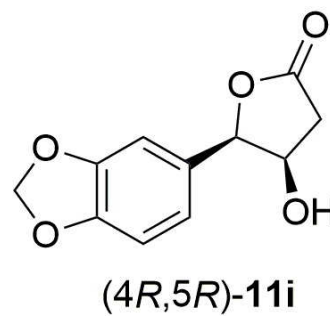


Chromatogram

HPLC (DAICEL CHIRALPAK IA-3, hexane/2-propanol = 90/10, 1.0 mL/min, 290 nm)

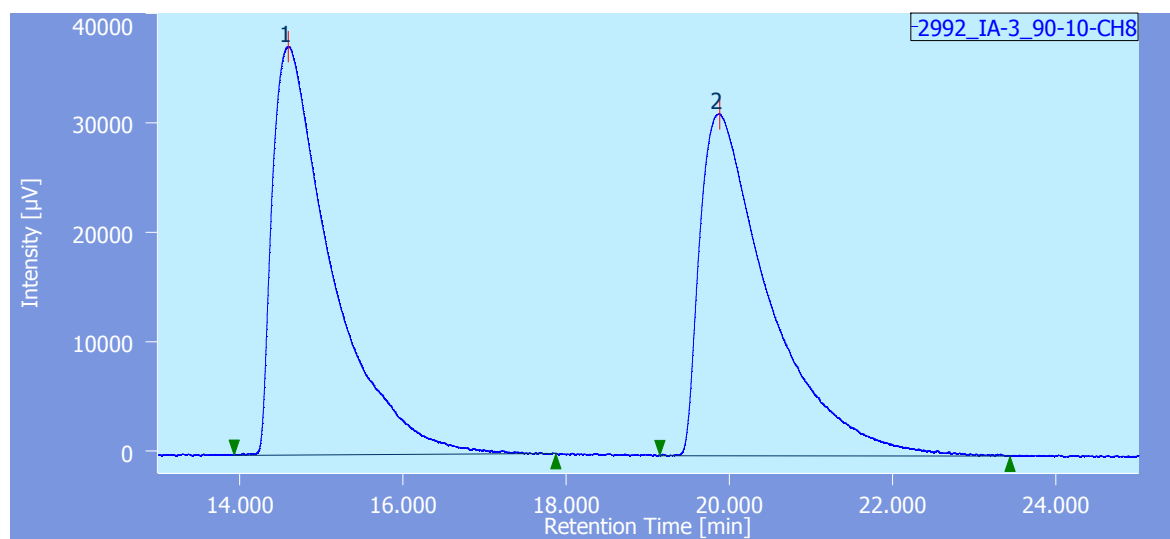


Peak #	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	8	21.853	12244	264	0.493	1.025
2	8	34.402	2471937	25491	99.507	98.975

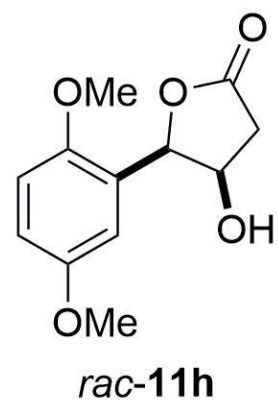


Chromatogram

HPLC (DAICEL CHIRALPAK IA-3, hexane/2-propanol = 90/10, 1.0 mL/min, 290 nm)

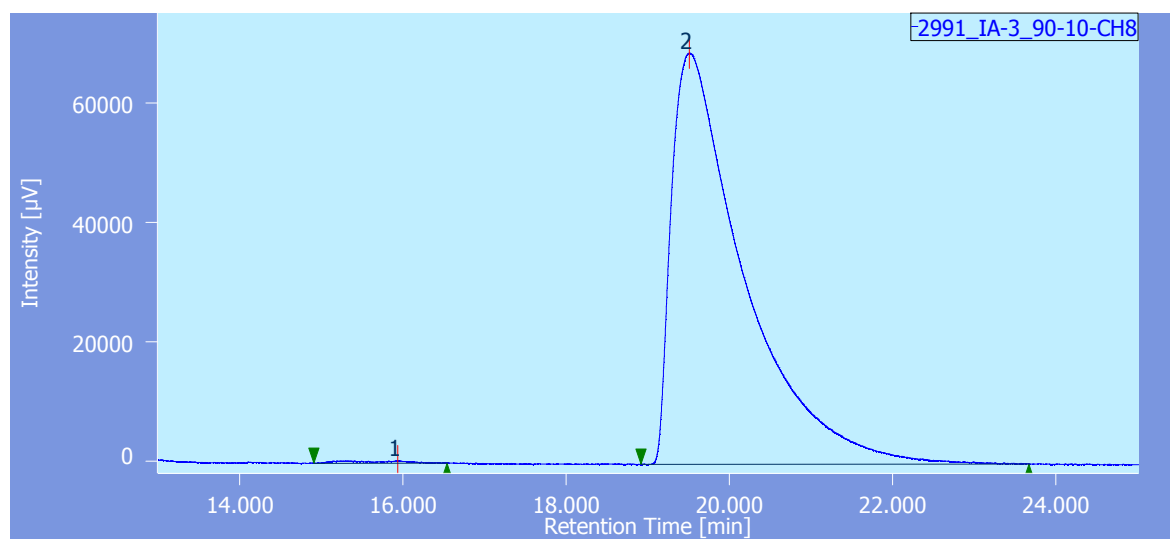


Peak #	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	8	14.597	1871857	37270	50.280	54.411
2	8	19.878	1851015	31227	49.720	45.589



Chromatogram

HPLC (DAICEL CHIRALPAK IA-3, hexane/2-propanol = 90/10, 1.0 mL/min, 290 nm)



Peak #	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	8	15.940	20307	389	0.477	0.562
2	8	19.507	4240940	68816	99.523	99.438

