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Supporting Information

Chemoenzymatic cascade reaction as a sustainable and scalable access to *para*-quinols

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Quinone chemical reduction:

Hydroquinones **1d-f** were synthesized according to the general literature method[1] – reduction with zinc in glacial acetic acid: Quinone (10 mmol) (**2d-f**) was dissolved in glacial acetic acid (15 mL) and zinc powder (40 mmol) was added. Then reaction was stirred under reflux for four hours and monitored using TLC plate (hexane:ethyl acetate ratio: 8:2). After reaction completion, reaction mixture was filtrated through thin layer of celite and the celite was washed with ethyl acetate. Filtrates were combined and solvents were removed on rotary evaporator to obtain crude product, purified by recrystallization from mixture of ethyl acetate and hexane. Reaction yields are provided with analytical data.

Hydroquinones **1a-c** were purchased from Sigma-Aldrich.

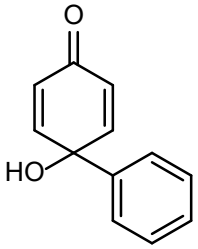
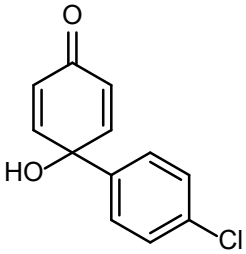
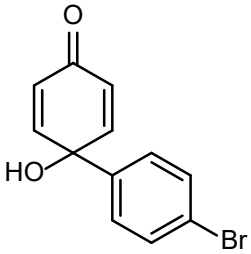
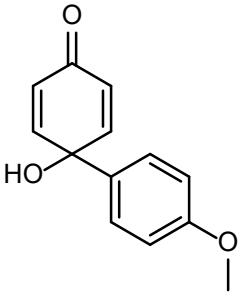
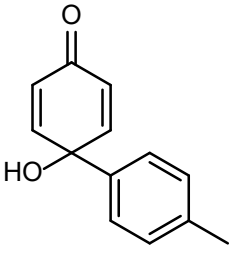
Synthesis of 2d - Decarboxylative coupling of quinones

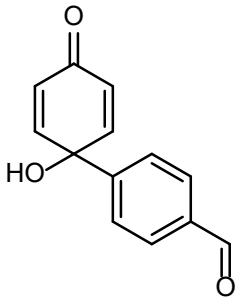
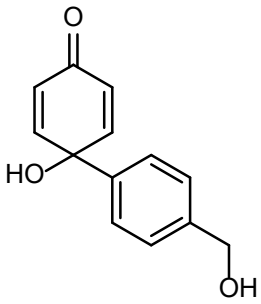
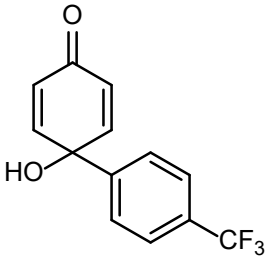
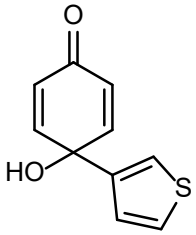
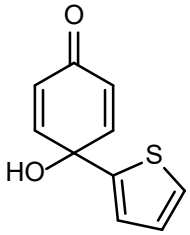
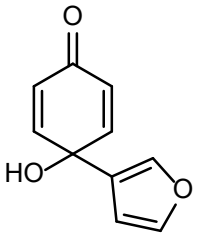
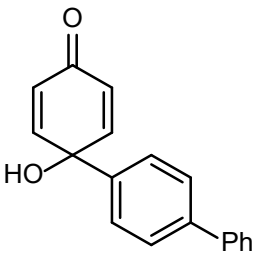
Compound **2d** was synthesised according to literature procedure for radical decarboxylative coupling[2]: 1,4-benzoquinone (5 mmol) and butenoic acid (7.5 mmol) were dissolved in acetonitrile:water 1:1 mixture (20 mL). Then $AgNO_3$ (0.2 mmol) and $(NH_4)_2S_2O_8$ were added at rt. After heating the mixture at 70 °C for 5 h the reaction was cooled to 25 °C. The solvent was evaporated and residue was diluted with ethyl acetate and washed with saturated aqueous solution of $NaHCO_3$. Organic phase was dried over anhydrous $MgSO_4$ and solvent was removed. The residue was purified using chromatography (hexane/ethyl acetate). Product **2d** was obtained with 44 % yield.

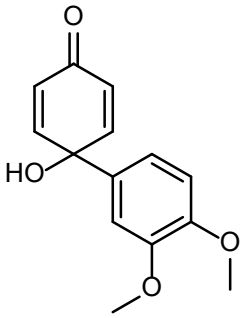
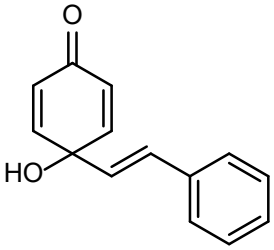
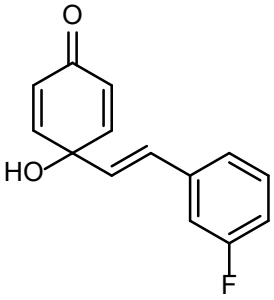
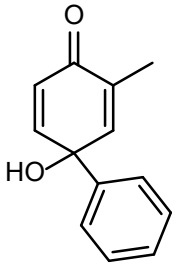
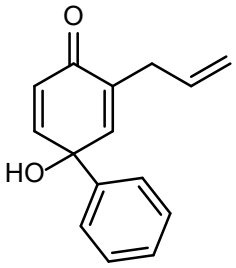
Synthesis of Standards *via* C-C coupling

Quinone **2a**, **b**, and **d** (1 mmol), phenylboronic acid **3a-o** (1 mmol, 1 equiv.) and CuI (0.1 mmol; 0.1 equiv.; 19 mg) were placed in 10 mL glass vial and 4 mL of distilled water was added. Reaction was protected from light with aluminum foil and stirred for 18 h at rt. Then, 6 mL of water was added and reaction mixture was extracted with ethyl acetate (3 x 10 mL). Organic phase was dried over anhydrous $MgSO_4$ and solvent was removed on rotary evaporator under reduced pressure. Residue was purified by column chromatography (hexanes/ethyl acetate) to obtain pure product (**Table S1**).[3]

Table S1. Dependence of model oxidation reaction conversion on solvent.

Compound No[a)]	Product	Yield after product isolation (%)
4a		53
4b		52
4c		35
4d		53
4e		21

4f		26
4g		38
4h		18
4i		62
4j		42
4k		48
4l		46

4m		12
4n		25
4o		36
4p		61
4r		43

[a)] According to description in Scheme 3 (Main article).

Reaction conditions optimization – hydroquinone oxidation

Enzyme screening

Procedure for the screening of laccases: In 10 mL glass vial hydroquinone (1 mmol) and laccase (20 mg) were placed, and 2 mL of distilled water were added. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, rt) for 24 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$. Then, organic phase was diluted for conversion measurements with GC (**Table S2**).

Table S2. Dependence of the model oxidation reaction conversion on an used laccase.

Laccase	Conversion (%)(t_r = 4h)[a)]	Conversion (%) (t_r = 24h)[a)]	Yield (%)(t_r = 24 h)
***Trametes* sp.**	**79**	**>99**	**>99**
Aspergillus niger	39	43	42
Trametes vesicolor	44	47	47

[a)] According to GC measurements,

Procedure for the optimization of laccase amount: In 10 mL glass vial hydroquinone (1 mmol) and laccase *Trametes* sp. were placed, and 2 mL of distilled water were added. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, rt) for 3 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for the conversion measurements with GC (**Figure S1**).

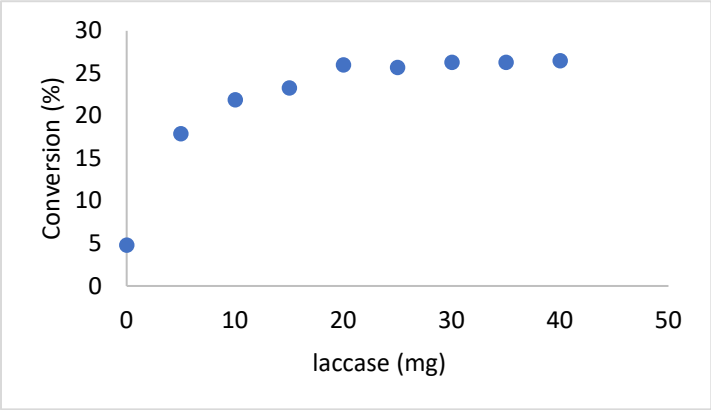


Figure S1. Dependence of the model oxidation reaction conversion on the laccase amount.

Addition of the radical mediator

In 10 mL glass vial hydroquinone (1 mmol), TEMPO (10 mg, 6.4 % mol) and laccase *Trametes* sp. (20 mg) were placed, and 4 mL of distilled water were added. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, rt) for 24 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for conversion measurements with GC (**Table S3**)

Table S3. Dependence of model oxidation reaction conversion on used laccase.

Mediator	Conversion (%)[a)]	Yield (%)[a)]
No mediator	>99	>99
TEMPO	29	19

[a)] According to GC measurements,

Temperature optimization:

In 10 mL glass vial hydroquinone (1 mmol) and laccase *Trametes* sp. (20 mg) were placed, and 2 mL of distilled water were added. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, set temperature) for 4 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for conversion measurements with GC (**Figure S2**).

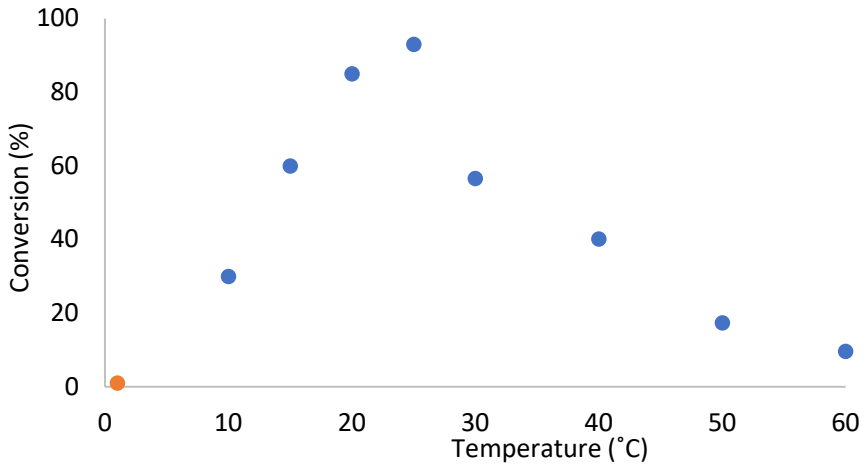


Figure S2. Dependence of model oxidation reaction on temperature.

Solvent optimization:

In 10 mL glass vial hydroquinone (1 mmol) and laccase *Trametes* sp.(20 mg) were placed, and 2 mL of solvent were added. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, rt) for 4 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for conversion measurements with GC (**Table S4**).

Table S4. Dependence of model oxidation reaction conversion on solvent.

Solvent	Conversion (%)[a)]	Yield (%)[a)]
H_2O (dist.)	**>99**	**>99**
citrate buffer pH 5.5	>99	>99

acetonitrile:H_2O 1:1	>99	>99
ethanol:H_2O 1:1	88	83
methanol:H_2O 1:1	83	79
THF:H_2O 1:1	61	59
Tert-butyl alcohol:H_2O 1:1	76	75
TBME:H_2O 1:1	49	48
DMSO:H_2O 1:1	21	23
DMF:H_2O 1:1	36	32
dioxane:H_2O 1:1	57	56

[a)] According to GC measurements,

Analysis of laccase-CuI interactions:

In 10 mL glass vial hydroquinone (1 mmol), CuI and laccase *Trametes* sp. (20 mg) were placed, and 4 mL of distilled water were added. Reaction was performed in open vial under air atmosphere on shaker (200 rpm, set temperature) for 2, 4 and 24 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for conversion measurements with GC (**Figure S3**) Points are overlaid and there is no significant difference in an enzyme activity.

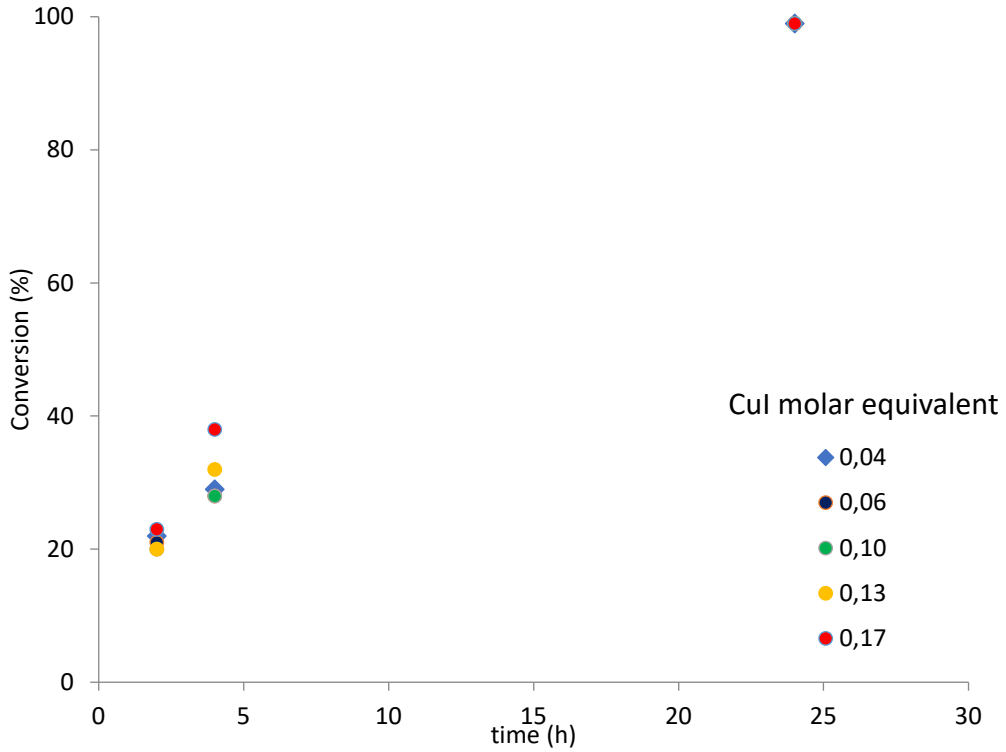


Figure S3 - Dependence of model oxidation reaction conversion on addition of CuI (molar equivalent per 1 mmol of hydroquinone).

Reaction time course curve:

In 10 mL glass vial: hydroquinone (1 mmol) and laccase *Trametes* sp. (20 mg) were placed, and 2 mL of solvent (ACN:water 1:1 or distilled water) were added. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, set temperature). Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for conversion measurements with GC (**Figure S4**). After 24 hours for both studied solvents the conversion was quantitative.

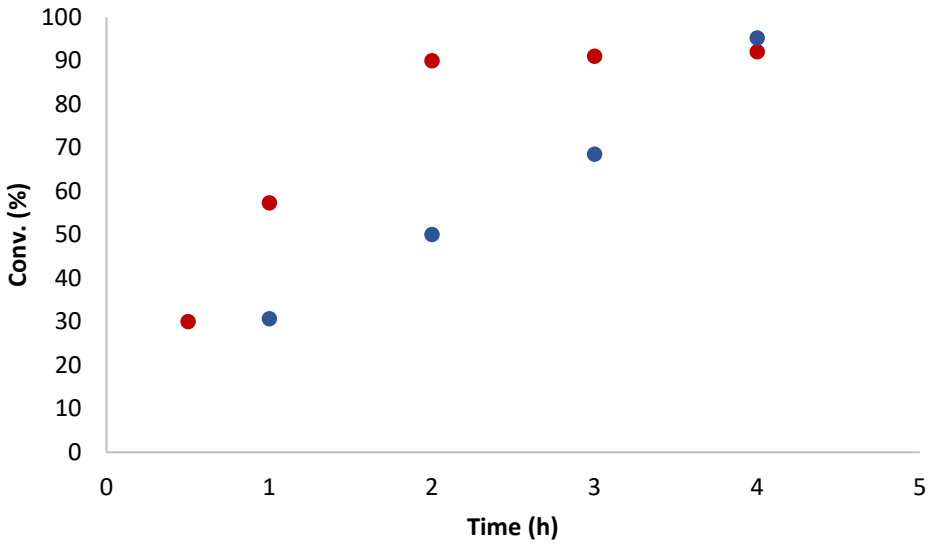


Figure S4. Model oxidation reaction time course ● MeCN:H_2O (dist.) 1:1; ● H_2O (dist)

Reaction conditions optimization - cascade

Enzyme optimization

In 10 mL glass vial hydroquinone (1 mmol), CuI (0.1 mmol), phenylboronic acid (1 mmol) and laccase (20 mg) were placed, and 4 mL of distilled water were added. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, rt.) for 24 h. Reaction was protected from light with aluminum foil. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$, and diluted for the conversion measurements with HPLC (**Table S5**).

Table S5. Dependence of model cascade reaction conversion on used laccase.

Laccase	Unreacted **1a** (%)[a]	Unreacted **2a** (%)[a]	Yield **4a** (%)[a]
***Trametes* sp.**	<1	39	59
Aspergillus niger	76	11	10
Trametes vesicolor	71	14	13

[a)] According to HPLC measurements,

Addition of radical mediator

In 10 mL glass vial hydroquinone (1 mmol), phenylboronic acid (1 mmol), TEMPO (10 mg, 6.4 % mol) and laccase *Trametes* sp. (20 mg) were placed, and 4 mL of distilled water was added. Reaction was protected from light with aluminum foil. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, rt) for 16 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$, and diluted for conversion measurements with HPLC. (**Table S6**)

Table S6. Dependence of model cascade reaction conversion on used laccase.

Mediator	Unreacted **1a** (%)[a]	Unreacted **2a** (%)[a]	Yield **4a** (%)[a]
No mediator	<1	39	59
TEMPO	58	20	7

[a)] According to HPLC measurements,

Temperature optimisation:

In 10 mL glass vial hydroquinone (1 mmol), CuI (0.1 mmol), phenylboronic acid (1 mmol) and laccase *Trametes* sp. (20 mg) were placed, and 4 mL of distilled water were added. Reaction was protected from light with aluminum foil. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, set temperature) for 24 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for conversion measurements with HPLC (**Table S7**).

Table S7. Dependence of model cascade reaction conversion on temperature.

Temperature (°C)	Unreacted **1a** (%)[a]	Unreacted **2a** (%)[a]	Yield **4a** (%)[a]
20	<1	49	49
22 (room temp.)	<1	39	59
30	<1	57	36
40	19	59	10

[a)] According to HPLC measurements,

Solvent optimisation:

In 10 mL glass vial hydroquinone (1 mmol), CuI (0.1 mmol), phenylboronic acid (1 mmol) and laccase *Trametes* sp.(20 mg) were placed, and 4 mL of corresponding solvent were added. Reaction was protected from light with aluminum foil. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, rt.) for 24 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for cascade yields measurements with HPLC (**Table S8**).

Table S8. Dependence of model cascade reaction conversion on solvent.

Solvent	Unreacted **1a** (%)[a]	Unreacted **2a** (%)[a]	Yield **4a** (%)[a]
H_2O (dist.)	<1	39	**59**
acetonitrile:H_2O 1:1	<1	51	47
ethanol:H_2O 1:1	14	60	23
methanol:H_2O 1:1	11	55	29
THF:H_2O 1:1	31	54	11
*tert*butyl alcohol:H_2O 1:1	26	62	10
MTBE:H_2O 1:1	48	36	13
DMSO:H_2O 1:1	77	12	9
DMF:H_2O 1:1	65	17	13
dioxane:H_2O 1:1	42	32	22

[a)] According to HPLC measurements,

Stirring optimisation:

During reaction condition optimization, the tendency to phenylboronic acid and CuI sedimentation was observed which may be the result for the low conversion of C-C coupling step, thus mixing optimization was performed: In 10 mL glass vial hydroquinone (1 mmol), CuI (0.1 mmol), phenylboronic acid (1 mmol) and laccase *Trametes* sp. (20 mg) were placed, and 4 mL of distilled water were added. Reaction was protected from light with aluminum foil. Reaction was performed in an open vial under air atmosphere and at room temperature (20 °C). Than mixing was performed with magnetic stirrer (400 rpm) or shaker (200 rpm, rt) for 24 h. Subsequently, reaction mixture was extracted with ethyl acetate (3 mL) and organic

phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for conversion measurements with HPLC. Conversions' dependence on type of mixing are gathered in **Table S9**.

Table S9. Dependence of model cascade reaction conversion on stirring.

Entry	Shaker (time (h))	Magnetic stirring (time (h))	Unreacted **1a** (%)[a]	Unreacted **2a** (%)[a]	Yield **4a** (%)[a]
1	-	overnight	57	3	39
2	1	overnight	12	7	79
3	2	overnight	3	13	82
4	3	overnight	<1	8	91
5	**4**	**overnight**	<1	<1	**>99**
6	overnight	-	<1	39	59

[a)] According to HPLC measurements,

Reaction time course curve:

In 10 mL glass vial hydroquinone (1 mmol), CuI (0.1 mmol), phenylboronic acid (1 mmol) and laccase *Trametes* sp. (20 mg) were placed, and 4 mL of distilled water were added. Reaction was protected from light with aluminum foil. Reaction was performed in an open vial under air atmosphere on a shaker (200 rpm, rt) for 4 h and stirred for 21 h. Regularly, samples for the conversion measurement were prepared as follows: 0.5 mL of reaction mixture was extracted with ethyl acetate (1 mL) and organic phase was dried over anhydrous $MgSO_4$. Then obtained organic phase was diluted for conversion measurements with HPLC.

Regioselectivity induction in catalytic C-C bond formation:

Quinone **2a** (1 mmol), tiophen-2-ylboronic acid **3j** (1 mmol, 1 equiv.), *Trametes* sp. laccase and CuI (0.1 mmol; 19 mg) were placed in 10 mL glass vial and 4 mL of distilled water were added. Reaction was protected from light with aluminum foil and stirred for 18 h at room temperature. Then, 6 mL of water were added and reaction mixture was extracted with ethyl acetate (3 x 10 mL). Organic phase was dried over anhydrous $MgSO_4$ and diluted for conversion measurements (**Figure S5**).

The amount of laccase which stopped the reaction was 5 mg of enzyme per 19 mg of CuI. And 2 mg of laccase per 19 mg of CuI decreased the yield from 24% to 6%.

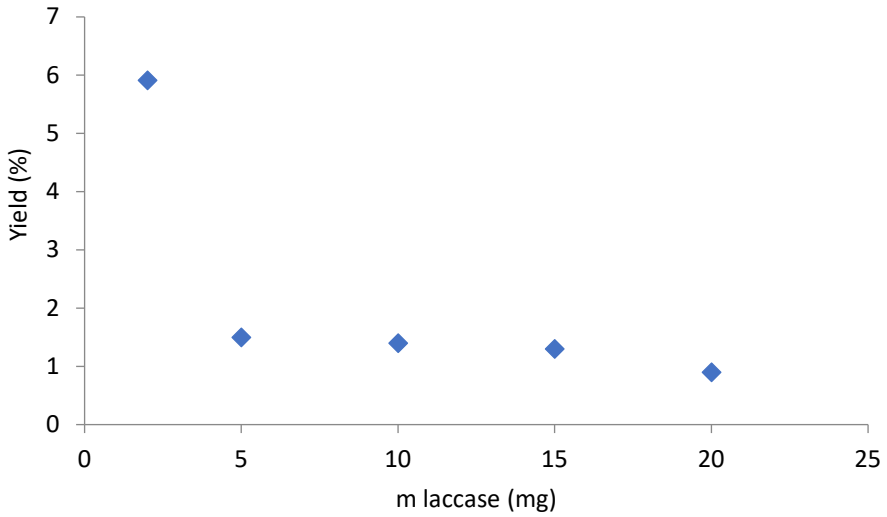


Figure S5. Selectivity induction by addition of *Trametes* sp. laccase – synthesis of compound **4j**.

Conversion studies – Scope and limitation

Hydroquinone **1a-e** (1 mmol), laccase *Trametes* sp. (20 mg), CuI (0.1 mmol) and phenylboronic acid **3a-o** (1 mmol) were placed in 10 mL glass vial and 4 mL of distilled water was added. Reaction was protected from light and performed with constant atmospheric air supply. For 4 h reaction was agitated on a shaker (200 rpm, r.t.), then reaction was stirred using magnetic stirrer (400 rpm, r.t., overnight). Reaction mixture was diluted with 6 mL of distilled water, and extracted with ethyl acetate (3x10 mL). Collected organic phases were dried over anhydrous $MgSO_4$ and solvent was removed under reduced pressure. Residue was purified by column chromatography (hexanes/EtOAc) to obtain target product **4a**-**s**.

Table S10. The reaction scope.

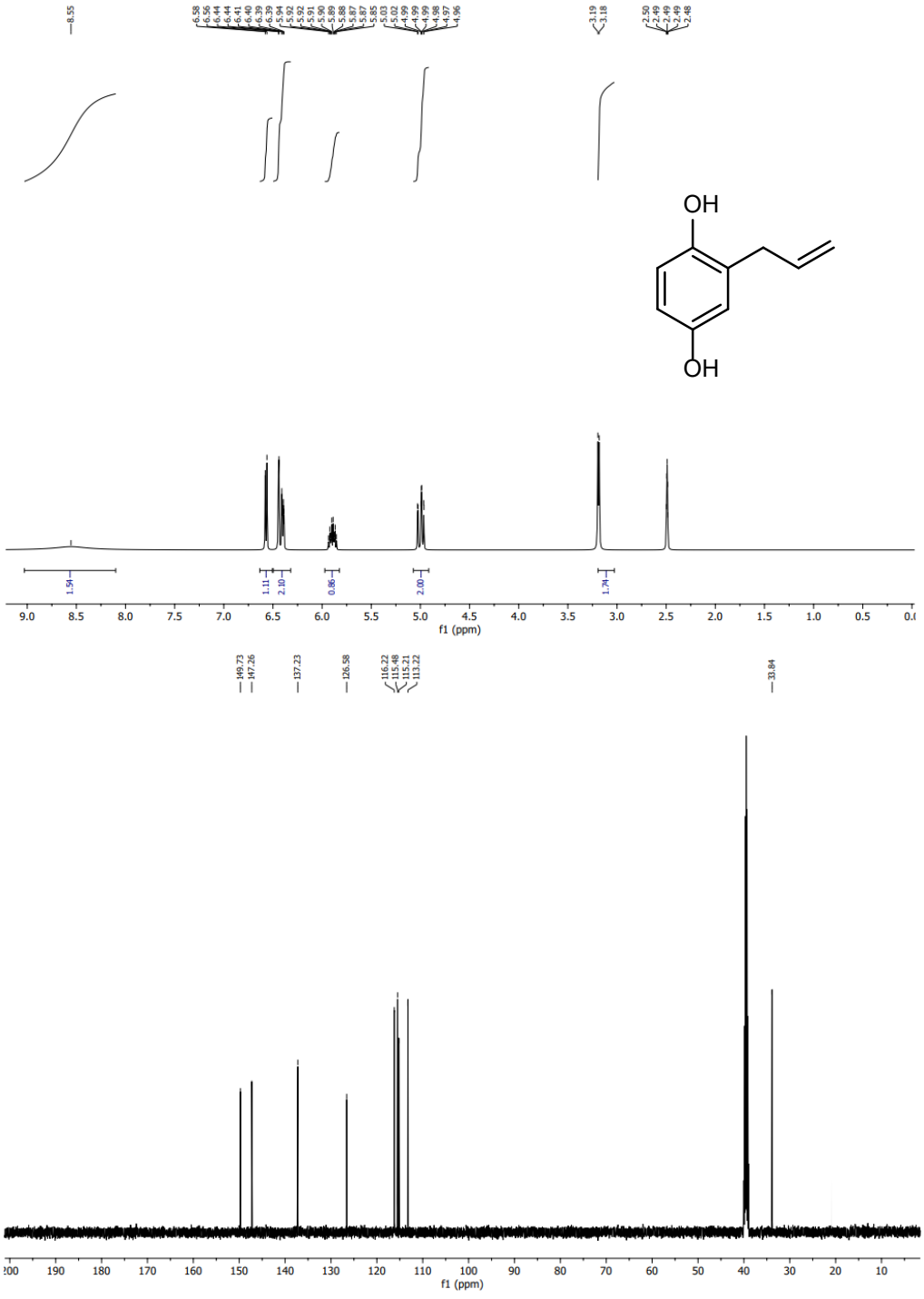
Compound	Unreacted **1a-e** (%)[a)]	Unreacted **2a-e** (%)[a)]	Yield **4a** (%)[a]	Yield of isolated product (%)
4a	<1	<1	>99	93
4b	<1	31	67	56
4c	<1	14	85	57
4d	<1	21	76	68
4e	<1	80	11	8
4f	<1	76	20	13
4g	<1	28	71	48
4h	<1	89	7	3
4i	<1	<1	>99	93
4j	<1	>99	<1	<1
4k	<1	<1	>99	92
4l	<1	37	61	41
4m	<1	81	16	10
4n	<1	64	35	26
4o	<1	33	63	57
4p	<1	6	92	88
4q	<1	76	24	19
4r	<1	2	97	90
4s	<1	61	36	29

[a)] According to HPLC measurements,

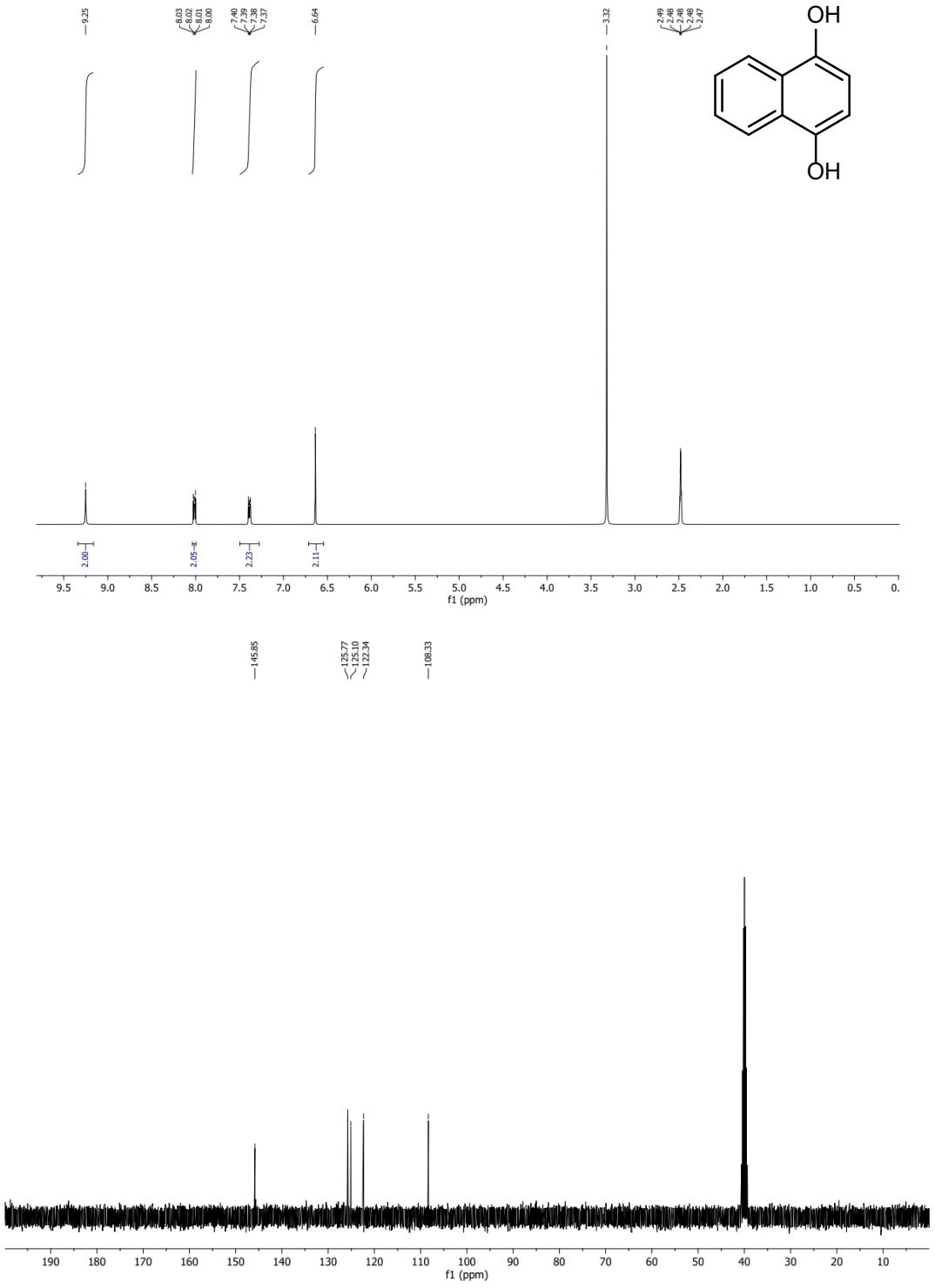
Analytical data

Hydroquinones:

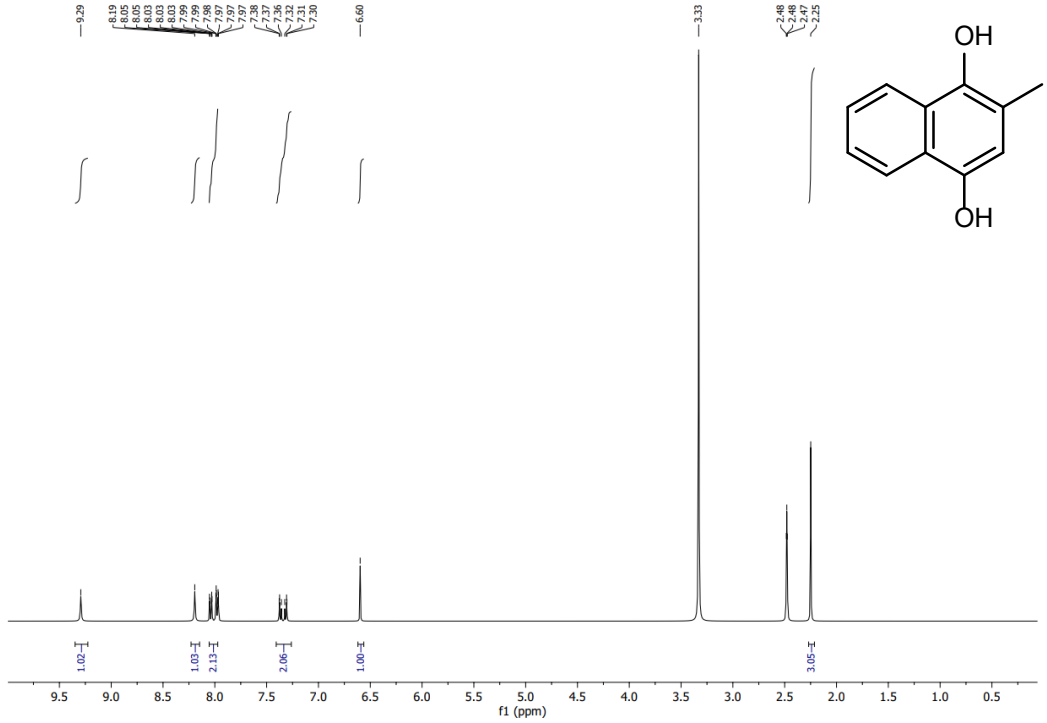
2-Allylhydroquinone **1d**; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 2H), 6.57 (d, J = 8.5 Hz, 1H), 6.50 – 6.32 (m, 2H), 5.89 (ddt, J = 16.9, 10.0, 6.7 Hz, 1H), 5.07 – 4.92 (m, 2H), 3.18 (s, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 149.73, 147.26, 137.23, 126.58, 116.22, 115.48, 115.21, 113.22, 33.84.; melting point: literature: 92-93 °C; measured: 91-92 °C; Spectroscopic data in agreement with literature.[4] Retention time (general GC method): t_r=17.32 min; Compound was obtained according to general method for quinone reduction with 95 % yield (1.43 g; 9.5 mmol).

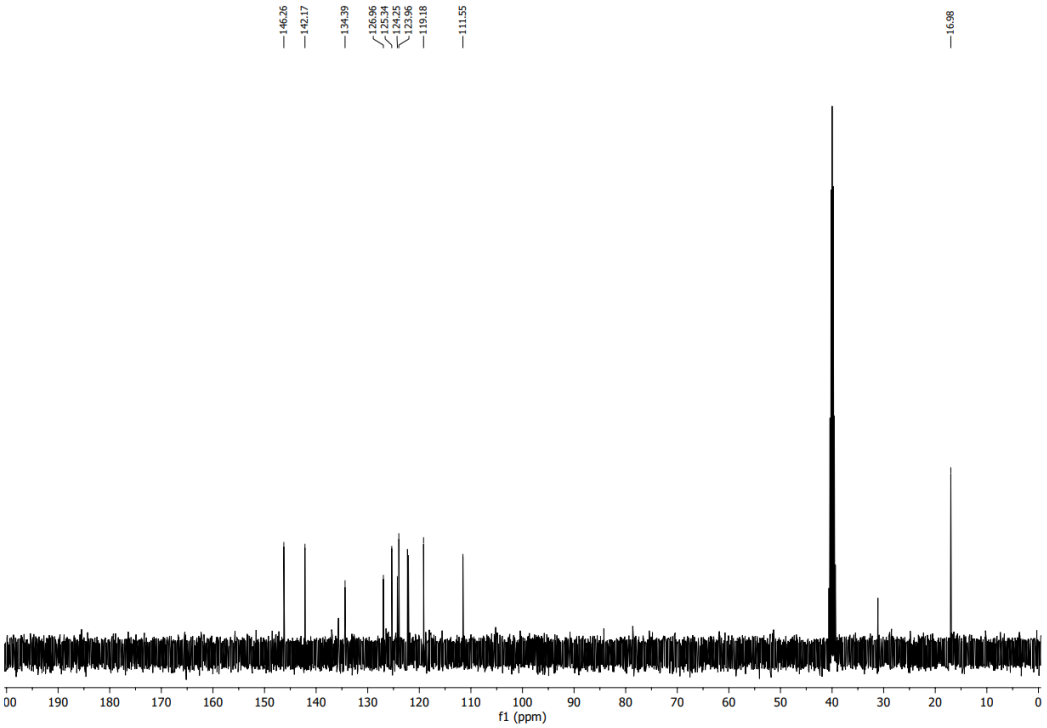


1,4-dihydroxynaphtalene **1e**; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.25 (s, 2H), 8.01 (dd, J = 6.4, 3.3 Hz, 2H), 7.39 (dd, J = 6.4, 3.3 Hz, 2H), 6.64 (s, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.8, 125.7, 125.1, 122.3, 108.3.; Spectroscopic data in agreement with literature.[5] Retention time (general GC method): t_r=14.06 min; Compound was obtained according to general method for quinone reduction with 93 % yield (1.49 g; 9.3 mmol).



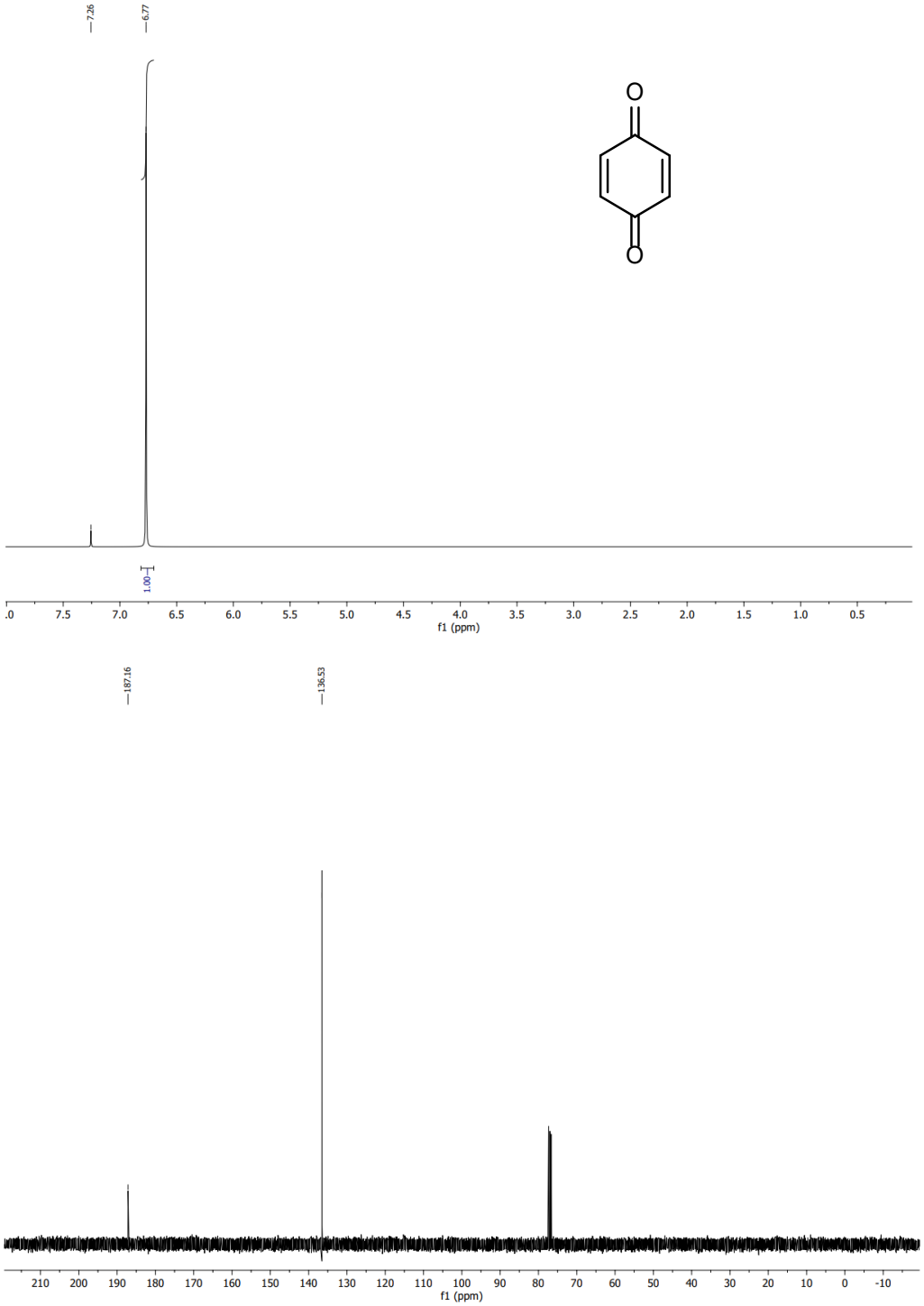
2-Methyl-1,4-naphthohydroquinone **1f**; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.29 (s, 1H), 8.19 (s, 1H), 8.05 – 7.97 (m, 2H), 7.41 – 7.26 (m, 2H), 6.60 (s, 1H), 2.25 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 146.2, 142.1, 134.3, 126.9, 125.3, 124.2, 123.9, 119.1, 111.5, 16.9.; Spectroscopic data in agreement with literature.[5] Retention time (general GC method): t_r=16.40 min; Compound was obtained according to general method for quinone reduction with 94 % yield (1.64 g; 9.4 mmol).



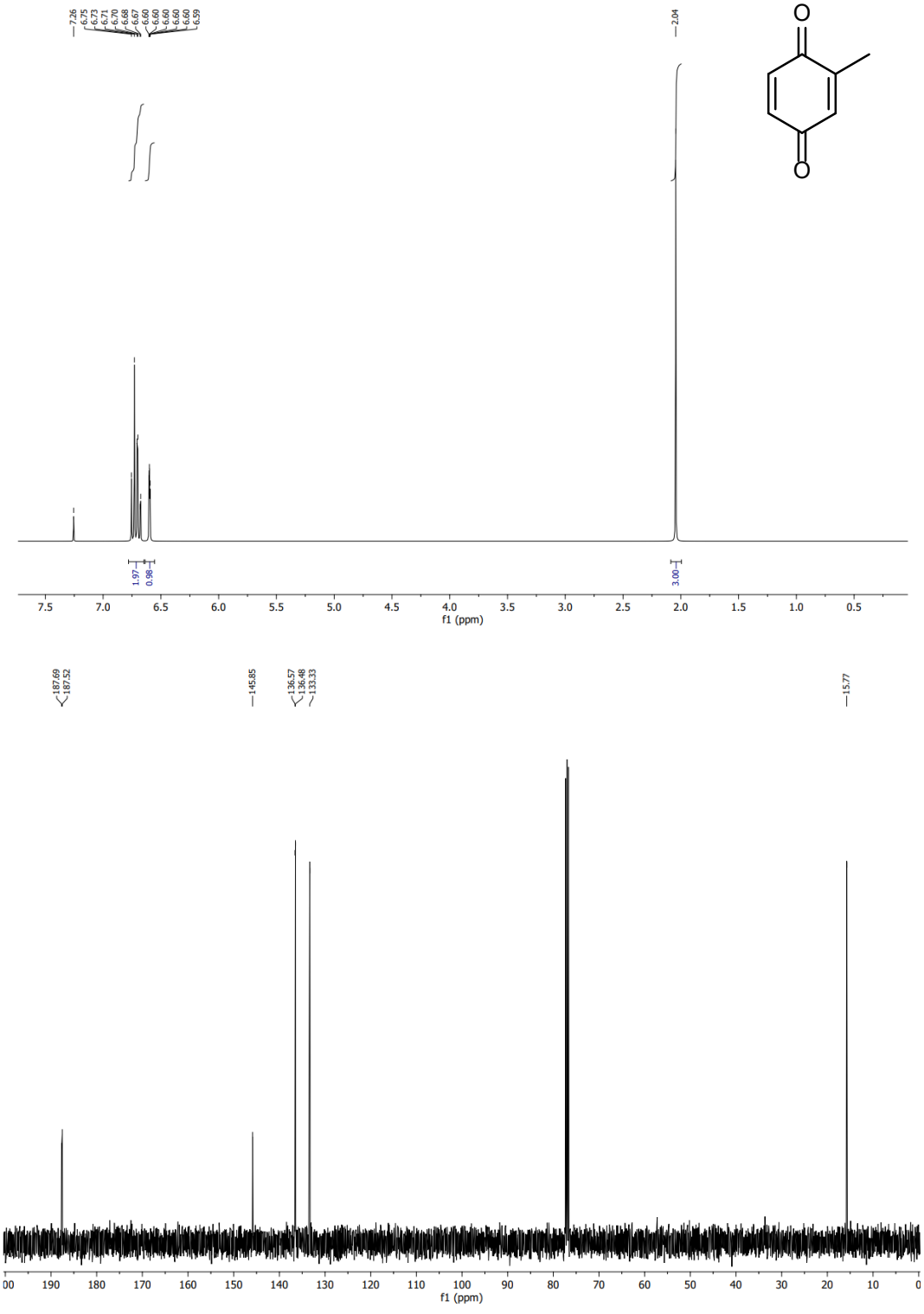


Quinones

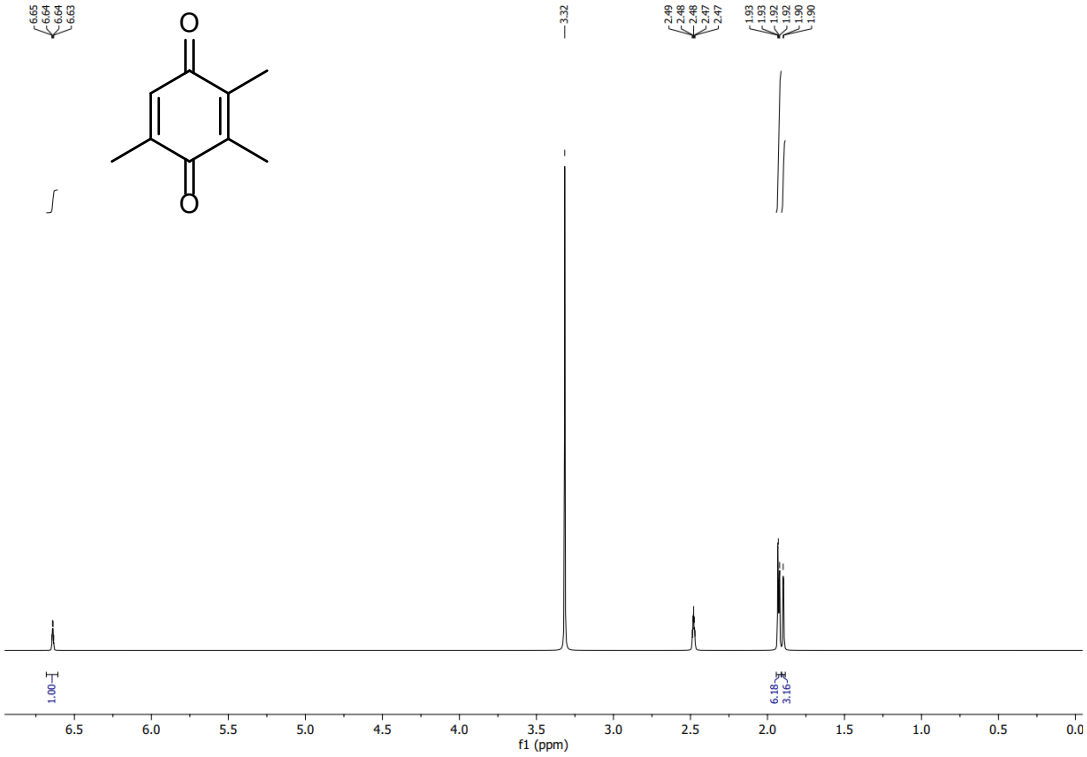
p-Benzoquinone **2a**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.1, 136.5. Spectroscopic data in agreement with literature.[6] Retention time (general HPLC method): t_r=5.04 min; Retention time (general GC method): t_r=5.62 min;

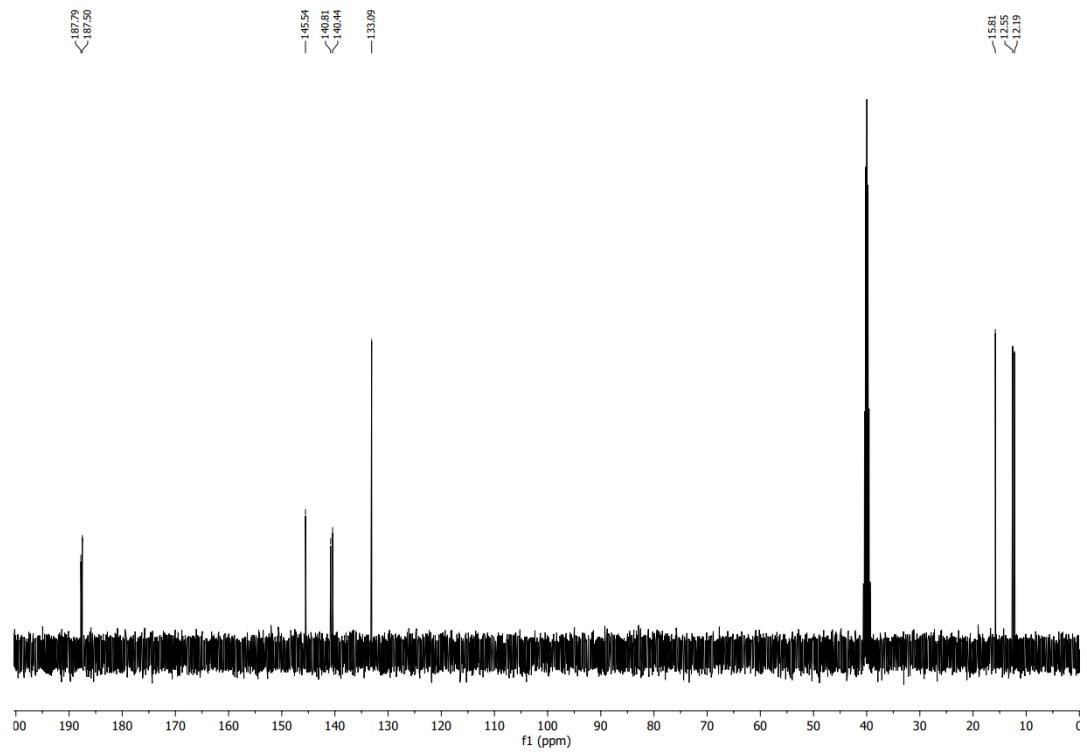


2-Methyl-p-benzoquinone **2b**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 – 6.65 (m, 2H), 6.64 – 6.55 (m, 1H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.6, 187.5, 145.8, 136.5, 136.4, 133.3, 15.7. Spectroscopic data in agreement with literature.[7] Retention time (general HPLC method): t_r=4.51 min; Retention time (general GC method): t_r=6.72 min;

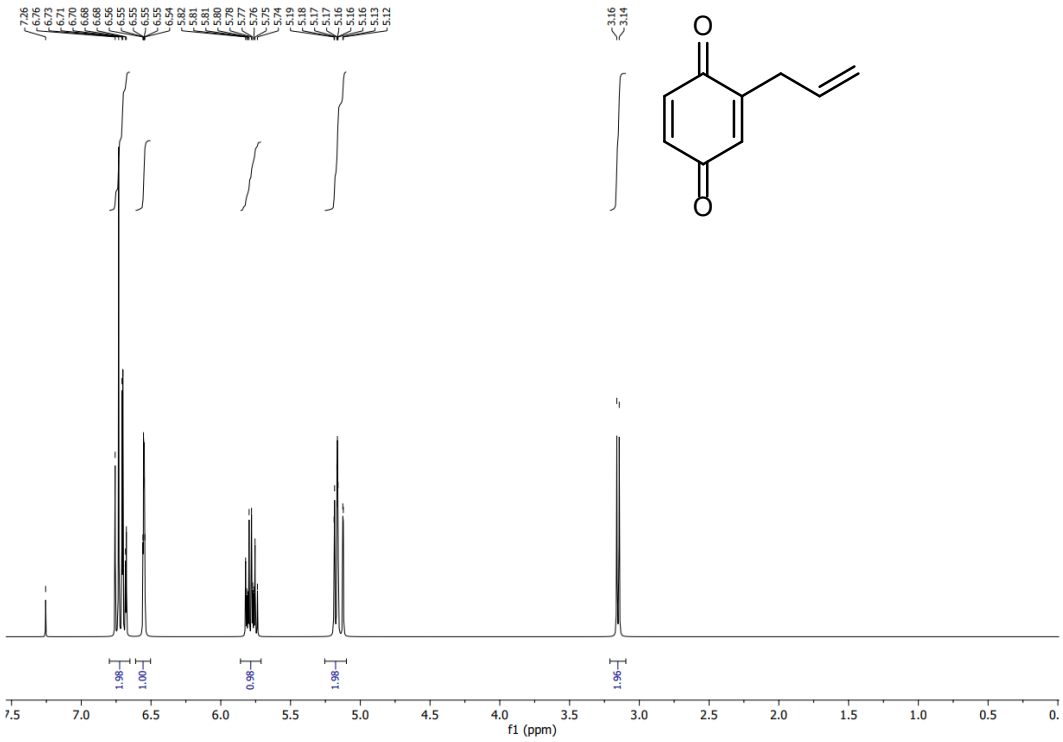


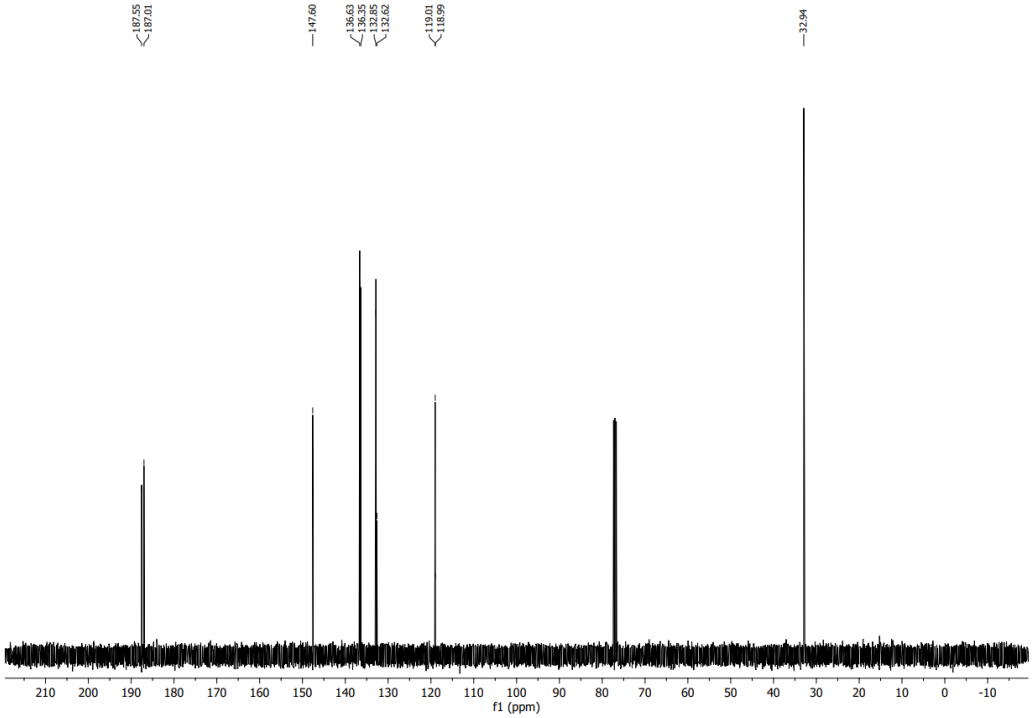
2,3,5-Trimethylcyclohexa-2,5-diene-1,4-dione **2c**; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.64 (q, J = 1.6 Hz, 1H), 1.93 (dd, J = 3.6, 1.4 Hz, 6H), 1.90 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.79, 187.50, 145.54, 140.81, 140.44, 133.09, 15.81, 12.55, 12.19. Spectroscopic data in agreement with literature.[8] Retention time (general HPLC method): t_r= 3.96 min; Retention time (general GC method): t_r=9.97 min;



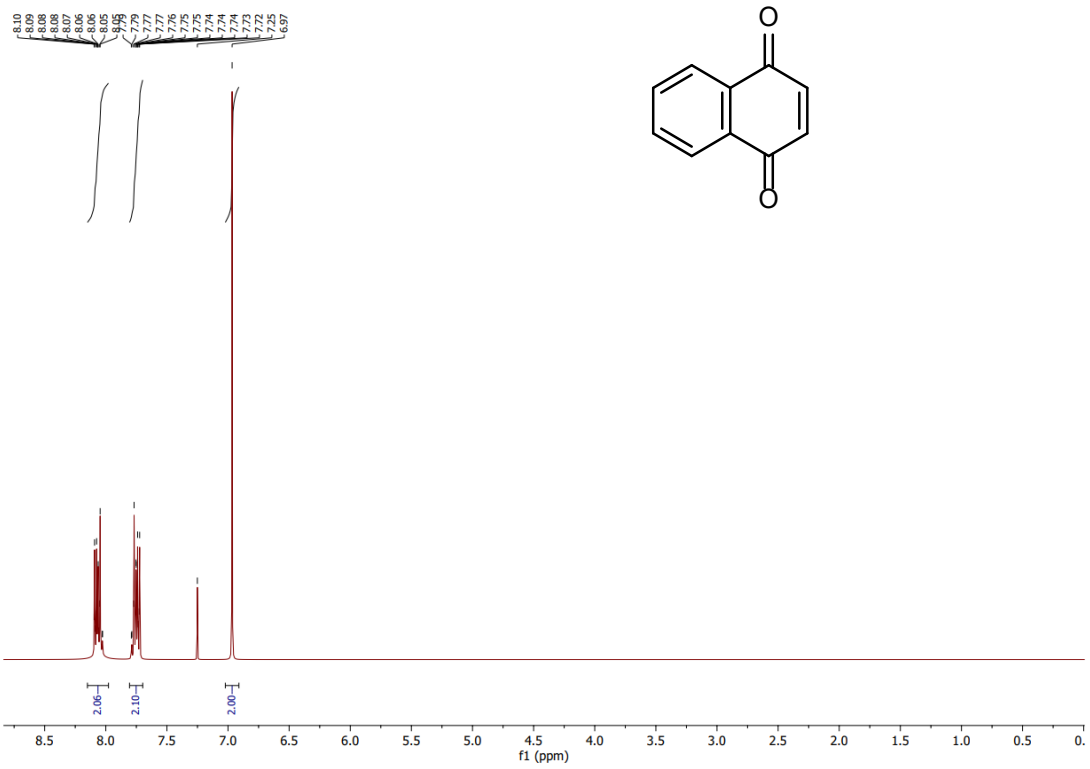


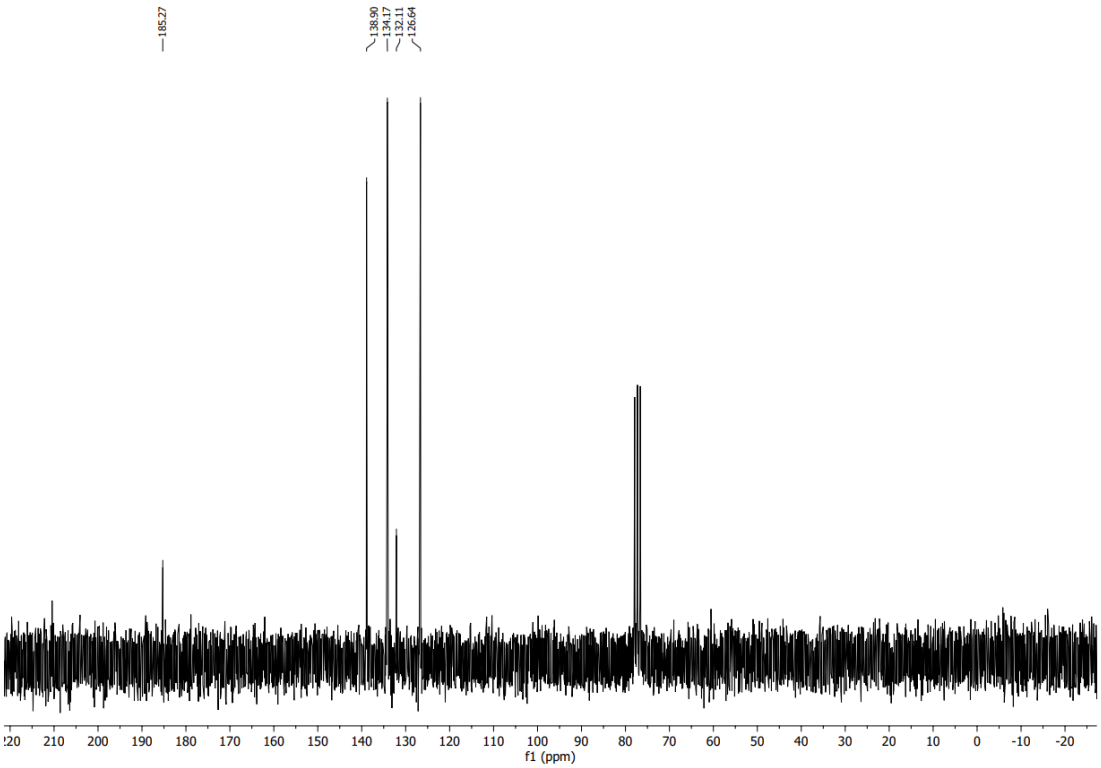
2-Allylbenzoquinone **2d**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 – 6.65 (m, 2H), 6.55 (dt, *J* = 2.4, 1.6 Hz, 1H), 5.86 – 5.71 (m, 1H), 5.25 – 5.10 (m, 2H), 3.15 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.55, 187.01, 147.60, 136.63, 136.35, 132.85, 132.62, 119.01, 118.99, 32.94.; Spectroscopic data in agreement with literature.[9] Retention time (general HPLC method): t_r=4.072 min; Retention time (general GC method): t_r=9.58 min;



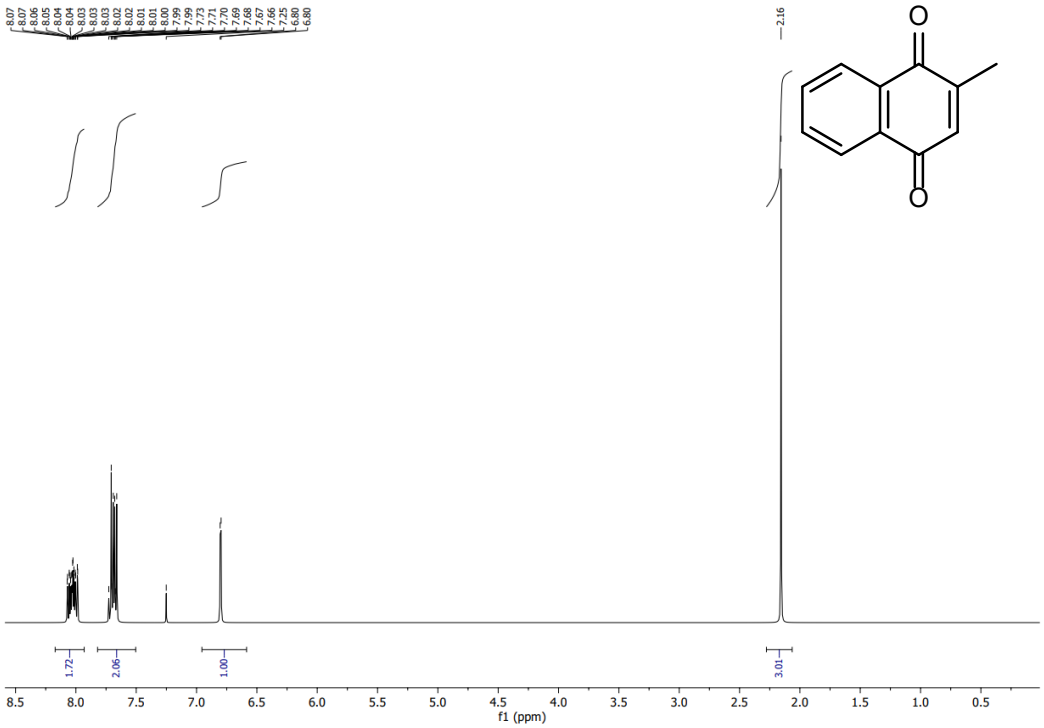


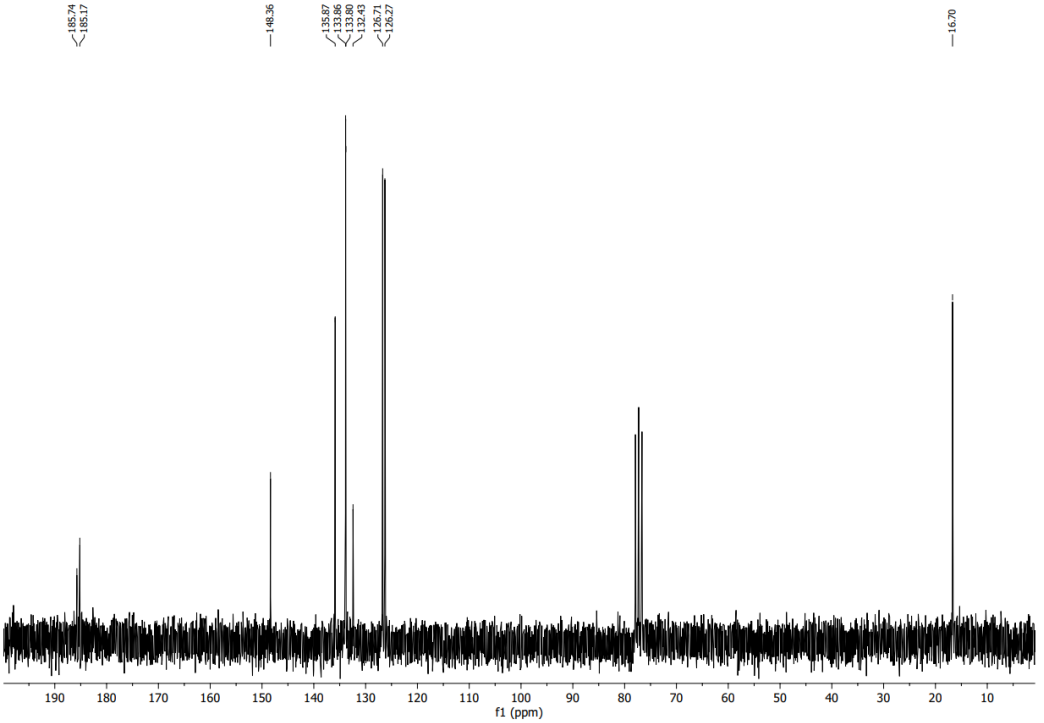
Naphthalene-1,4-dione **2e**; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.15 – 7.98 (m, 2H), 7.81 – 7.70 (m, 2H), 6.97 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 185.2, 138.9, 134.1, 132.1, 126.6. Spectroscopic data in agreement with literature.[10] Retention time (general HPLC method): t_r=4.36 min; Retention time (general GC method): t_r=16.60 min;





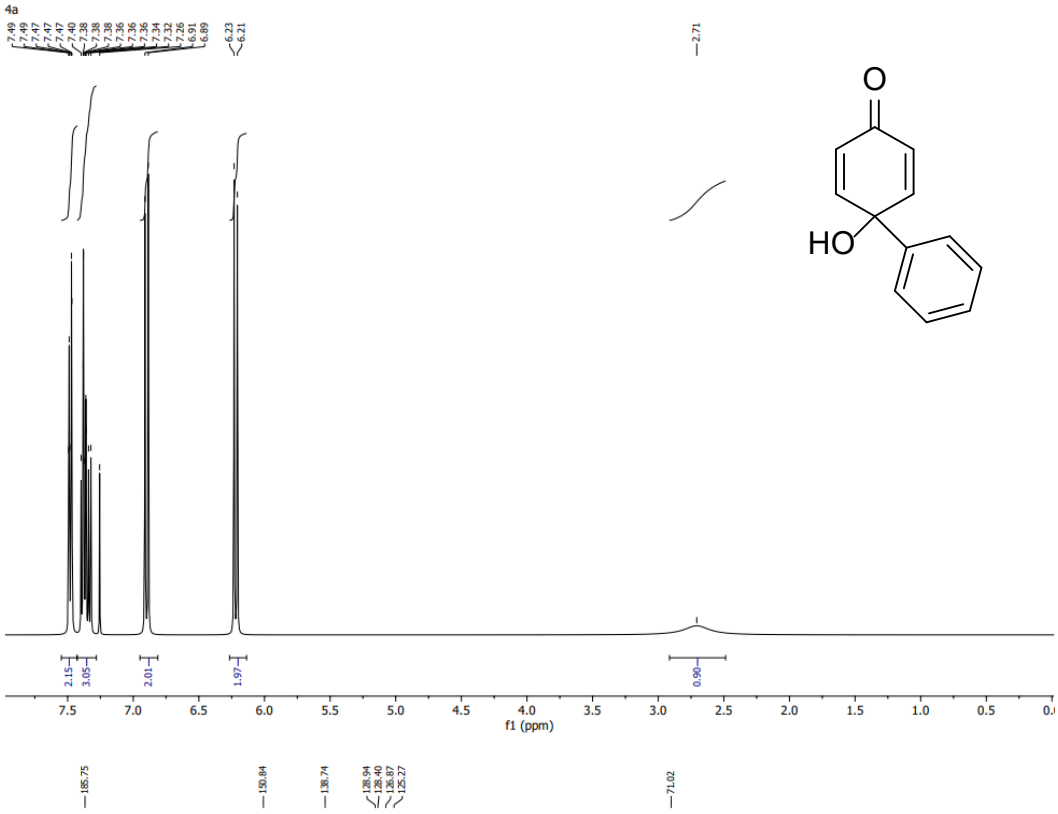
2-Methyl-1,4-naphthoquinone **2f**; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.03 (dddd, *J* = 7.8, 5.8, 3.3, 0.5 Hz, 2H), 7.82 – 7.50 (m, 2H), 6.80 (d, *J* = 1.6 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 185.7, 185.1, 148.3, 135.8, 133.8, 133.8, 132.4, 126.7, 126.2, 16.7. Spectroscopic data in agreement with literature.[8] Retention time (general HPLC method): t_r=4.08 min; Retention time (general GC method): t_r=16.03 min;

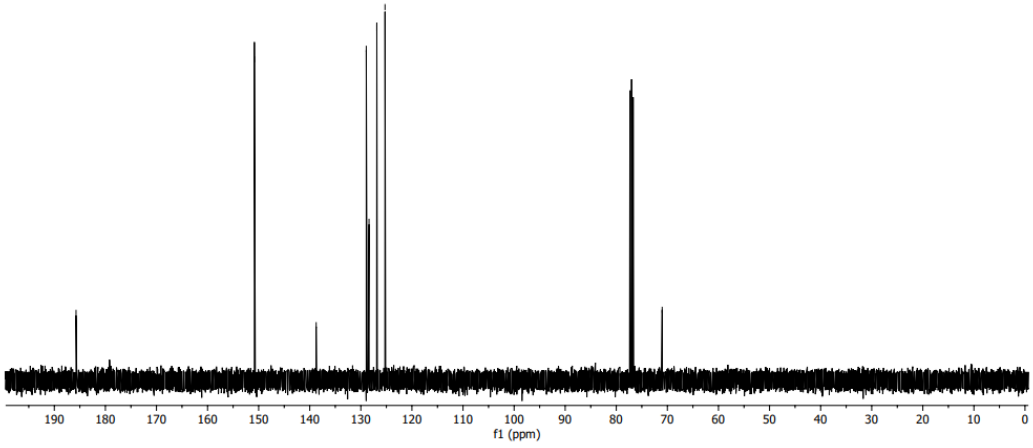




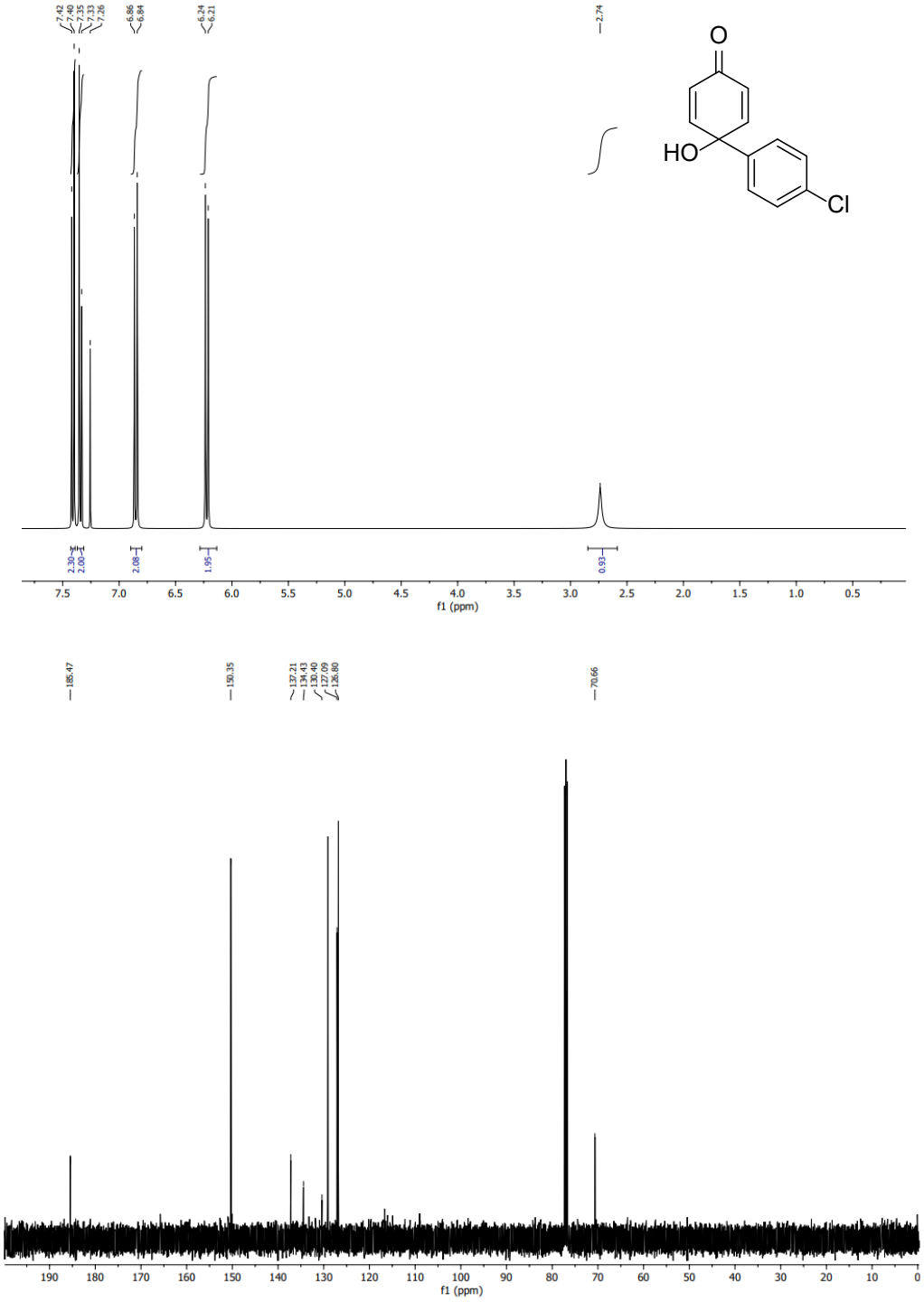
Cascade products:

Compound **4a**; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.40-7.49 (2H, m), 7.32-7.38 (3H, m), 6.89-6.91 (2H, m), 6.21-6.23 (2H, m), 2,71 (1H, s br, O*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 158.8, 150.8, 138.9, 128.9, 128.4, 126.9, 125.3, 71.0; Retention time (general HPLC method): t_r=6.34 min; NMR data were in accordance with those reported in the literature.[11]

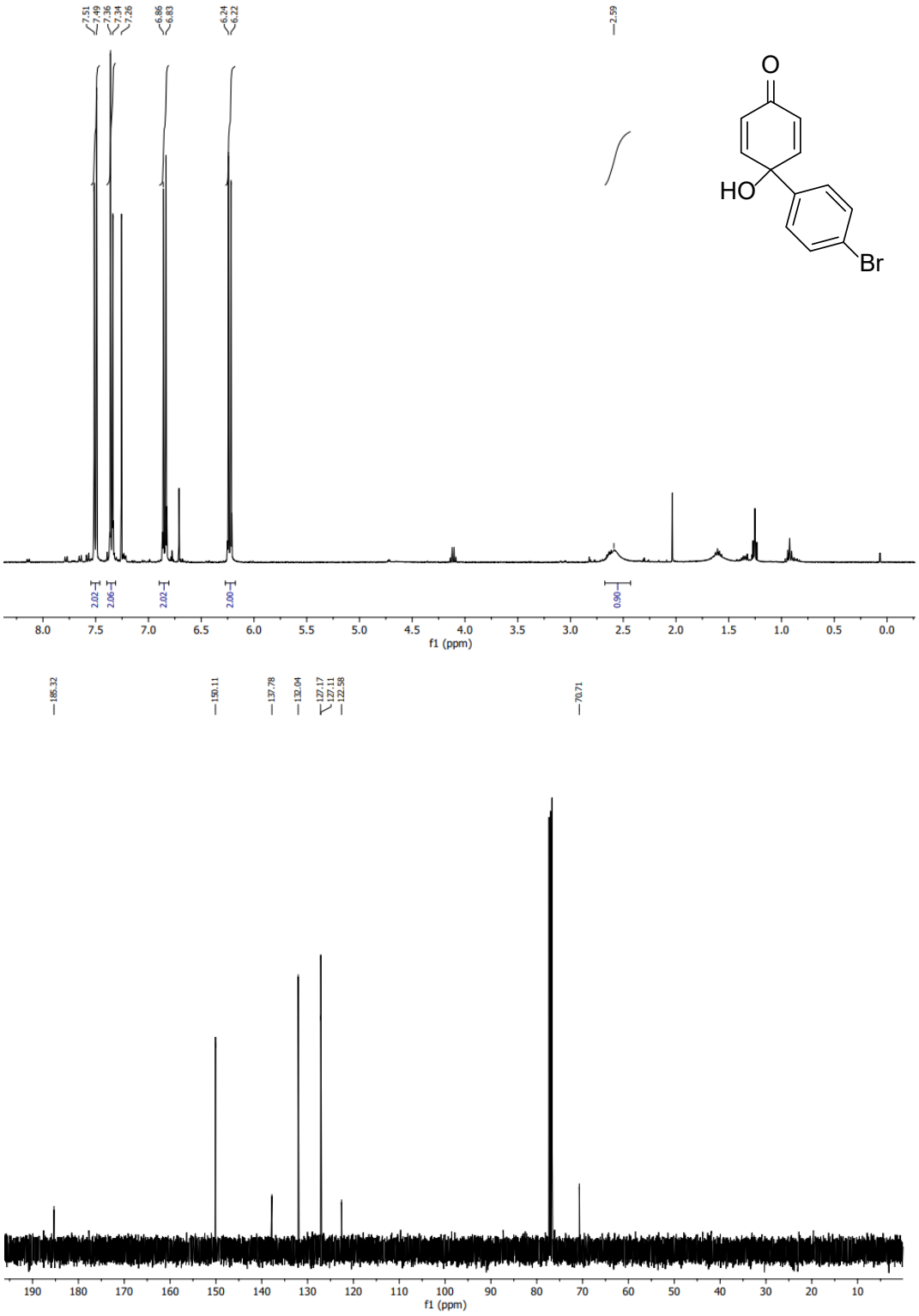




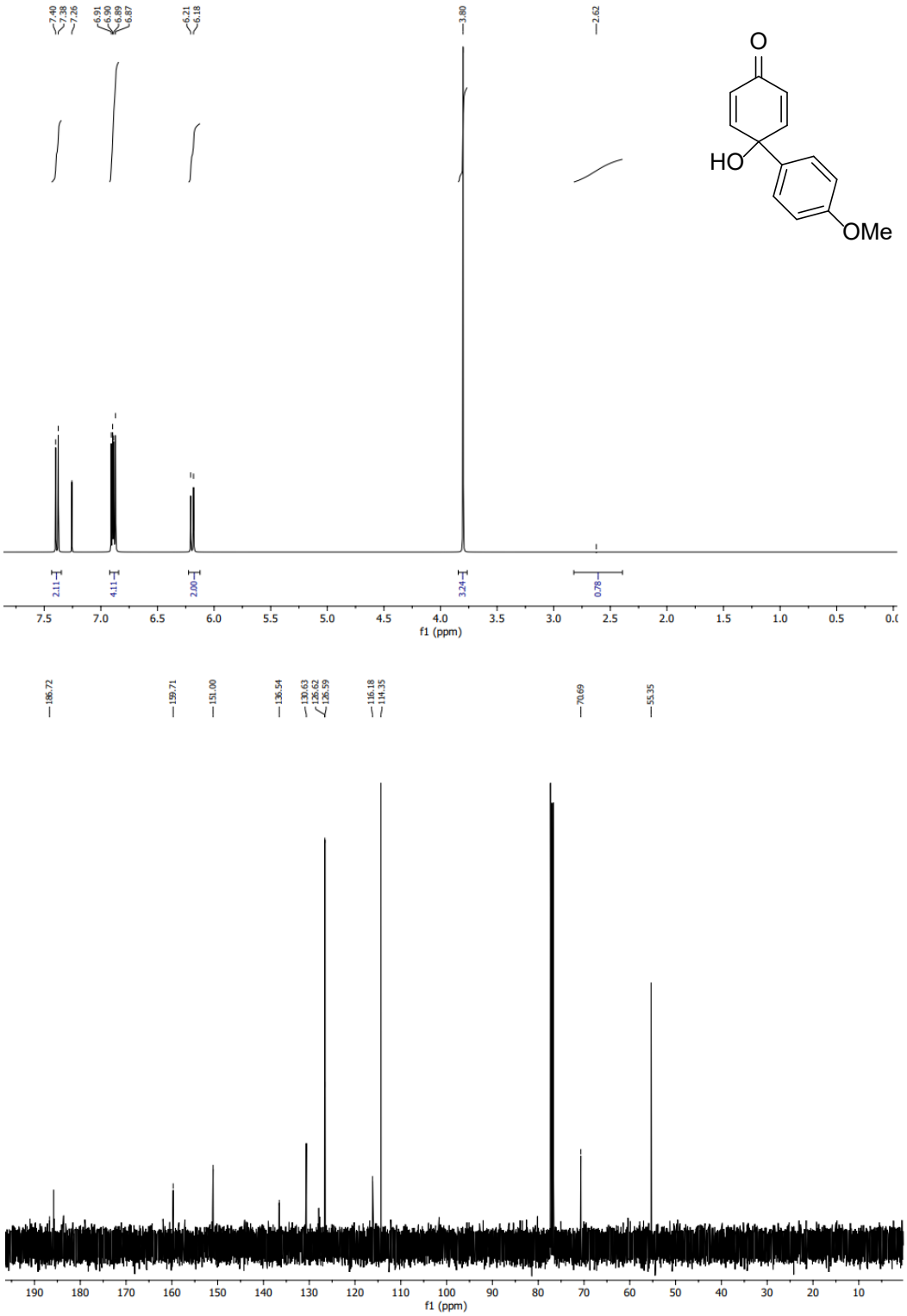
Compound **4b**; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.30-7.45 (4H, m), 6.85 (2H, d, *J = 10,1 Hz*), 6.22 (2H, d, *J = 10,1 Hz*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 185.5, 150.4, 137.2, 134.4, 130.4, 129.1, 127.1, 127.1, 126.8, 70.7; HRMS calcd. for $C_{12}H_8ClO_2$ $[M-H]^-$: 219.0213, found: 219.0210. Retention time (general HPLC method): t_r=6.50 min; NMR data were in accordance with those reported in the literature.[12]



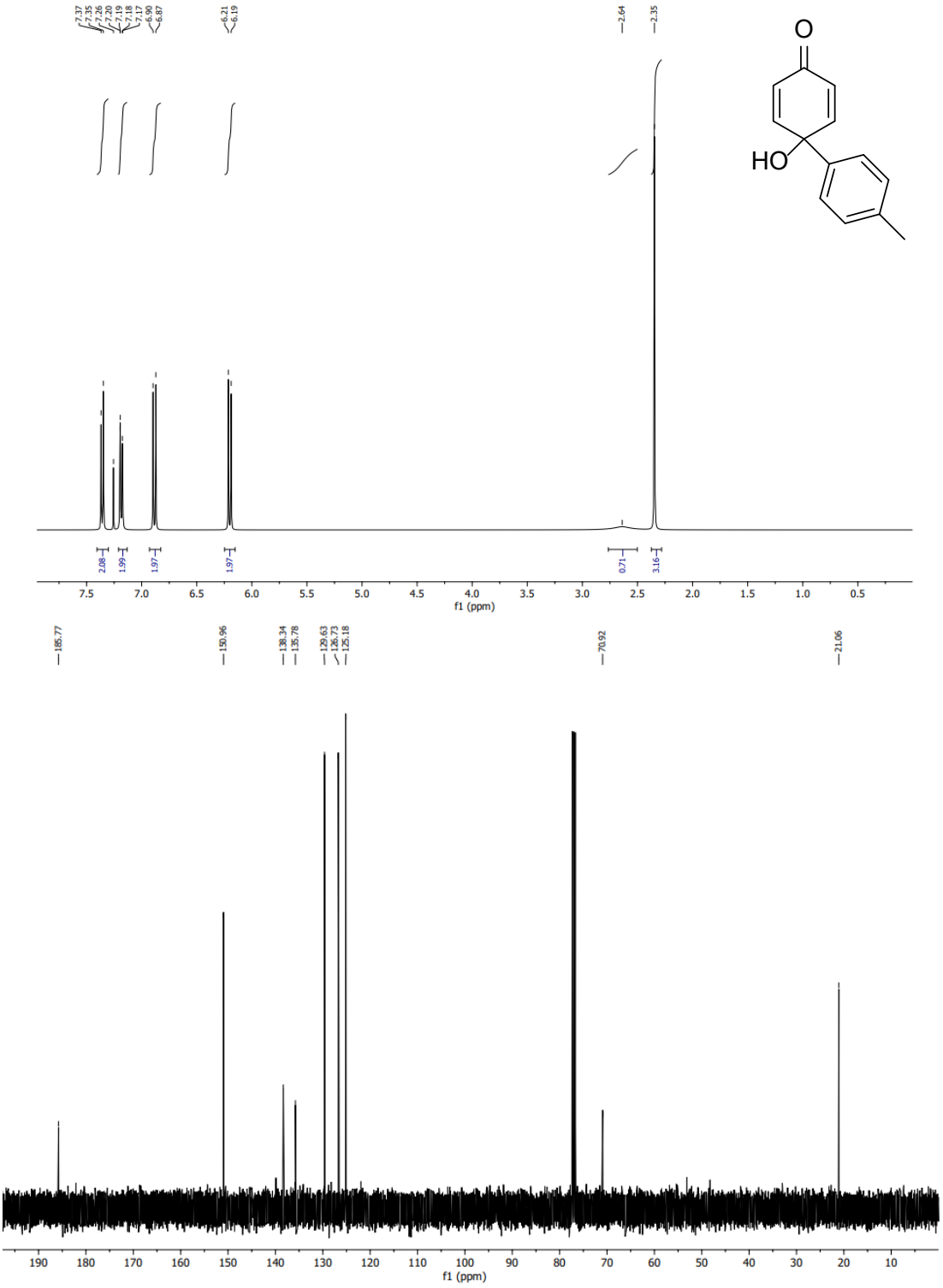
Compound **4c**; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7,49-7,51 (2H, m), 7,34-7,36 (2H, m), 6.83-6.86 (2H, m), 6.22-6.34 (2H, m), 2,60 (1H, s br, O*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 185.3, 150.1, 137.8, 132.0, 127.2, 127.1, 122.6, 70.7; Retention time (general HPLC method): t_r=6.33 min; NMR data were in accordance with those reported in the literature.[13]



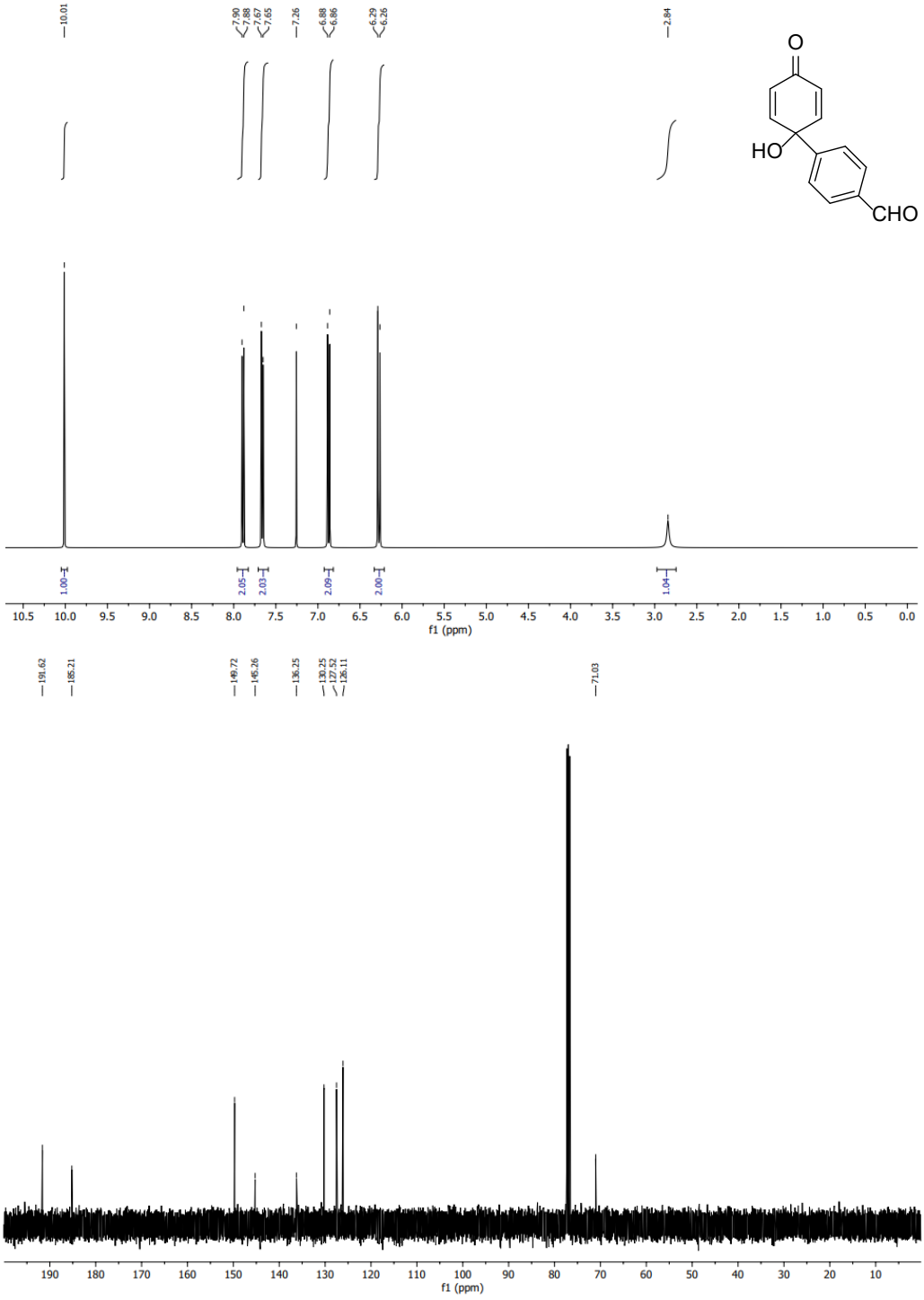
Compound **4d**; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.36-7,41 (2H, m), 6.85-6.93 (4H, m), 6.18-6.21 (2H, m), 3.80 (3H, s), 2.62 (1H, s br, O*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 159.7, 151.0, 136.5, 130.6, 126.6, 116.2, 114.4, 70.7, 55.4; Retention time (general HPLC method): t_r=7.86 min; NMR data were in accordance with those reported in the literature.[14]



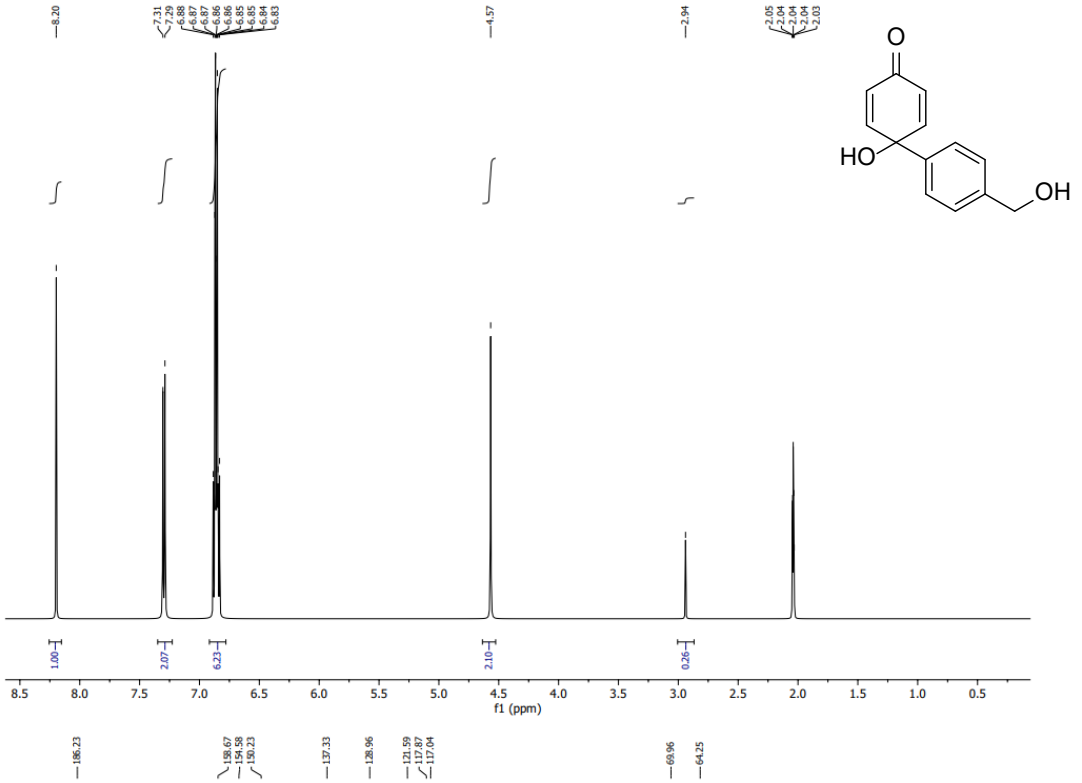
Compound **4e**; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7,34-7,38 (2H, m), 7.16-7.20 (2H, m), 6.86-6.91 (2H, m), 6.18-6.22 (2H, m), 2.64 (1H, s br, O*H*), 2.35 (3H, s, PhCH_3); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 185.8, 160.0, 138.3, 135.8, 129.6, 126.7, 125.2, 70.9, 21.0; Retention time (general HPLC method): t_r=6.46 min; NMR data were in accordance with those reported in the literature.[14]



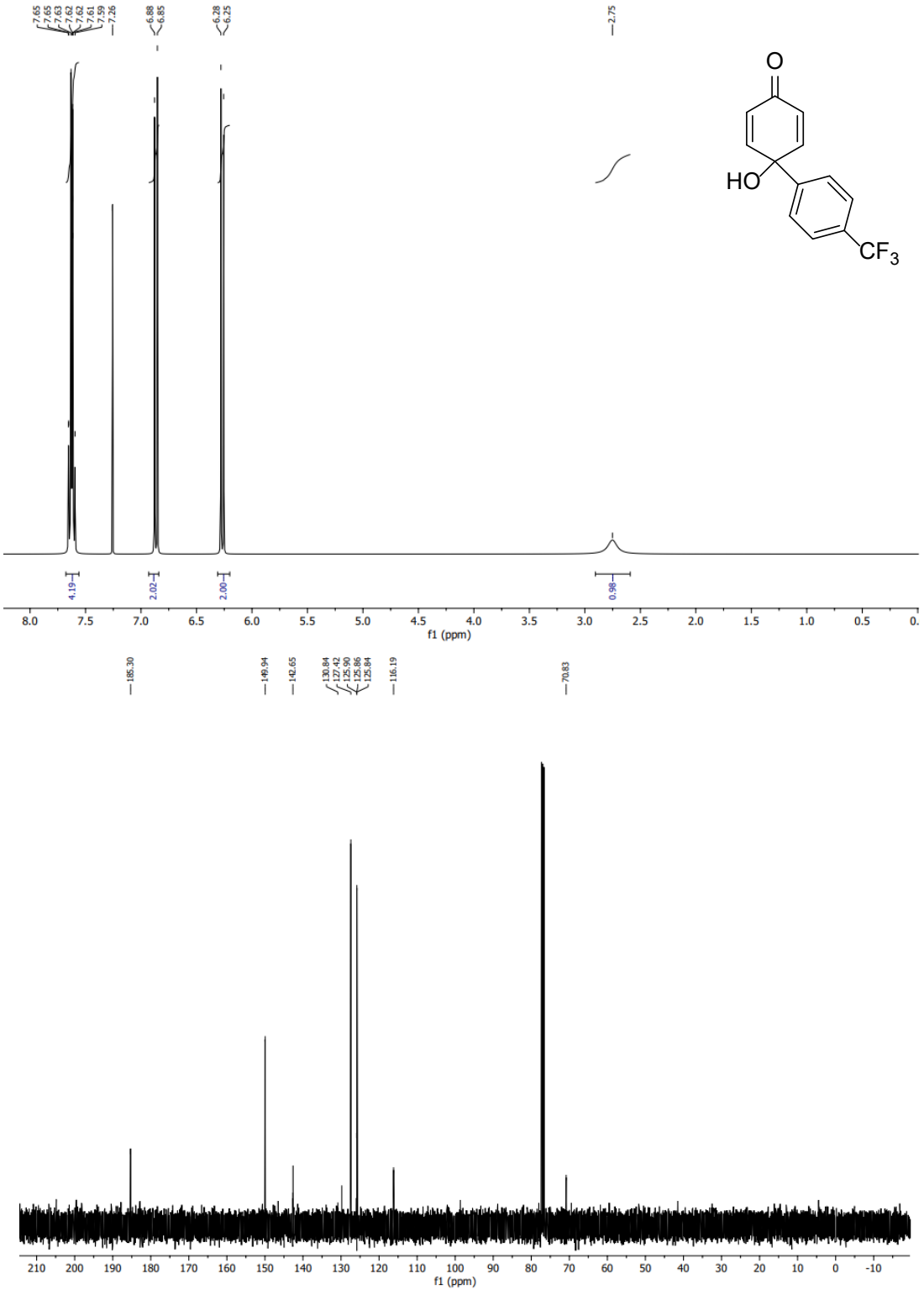
Compound **4f**; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 10.03 (1H, s), 7.89-7.91 (2H, m), 7.65-7.67 (2H, m), 6.86-6.98 (2H, m), 6.28-6.30 (2H, m), 2.46 (1H, s br, O*H*); ^{13}C NMR (100 MHz; CDCl3) δ_C (126 MHz; Acetone-d_6) δ_C 192.5, 192.0, 186.6, 152.0, 147.85, 137.2, 130.6, 127.5, 127.2, 71.5; HRMS calcd. for $C_{13}H_9O_3$ $[M-H]^-$: 213.0552, found: 213.0549. Retention time (general HPLC method): t_r=10.82 min;



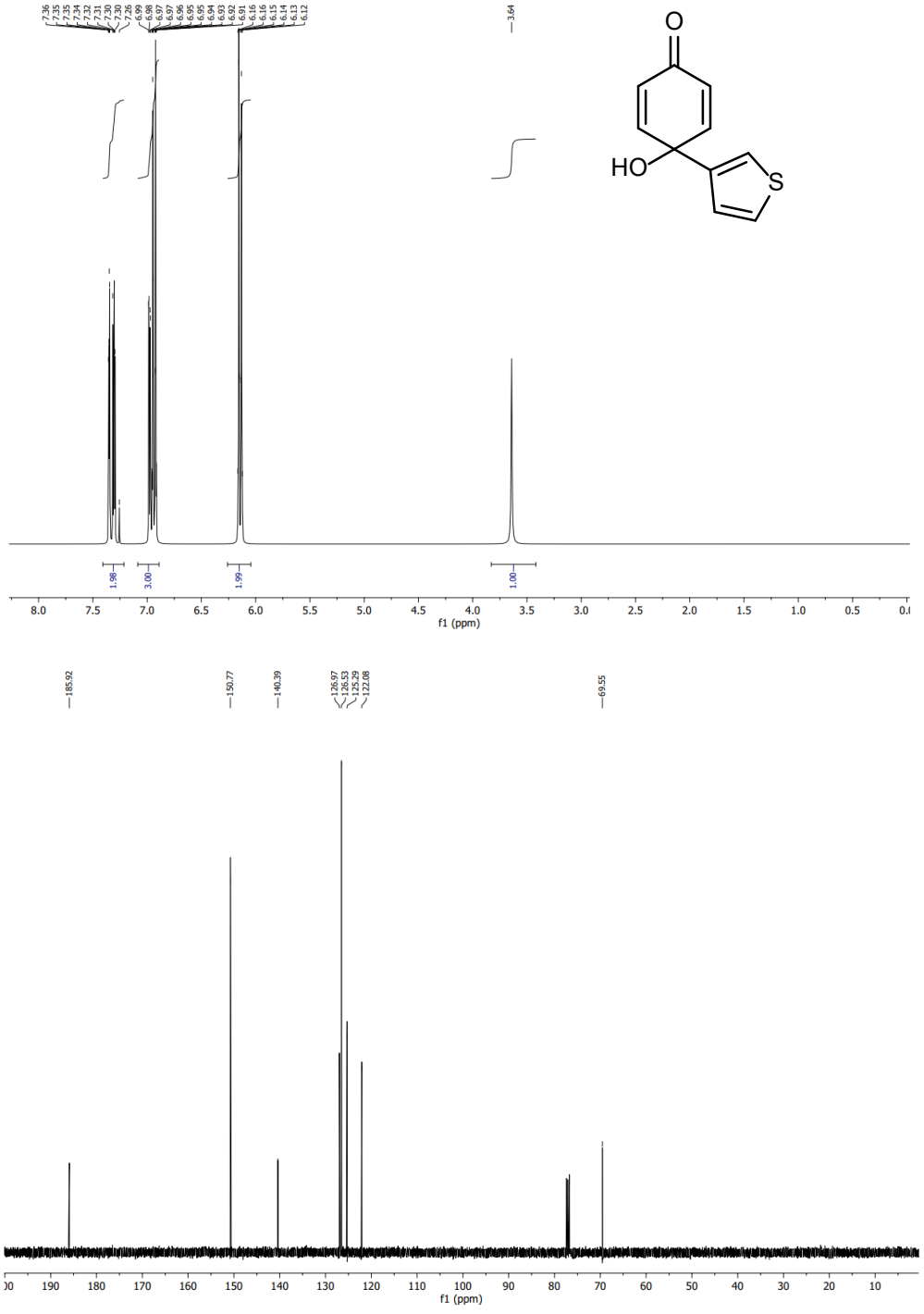
Compound **4g**; ^{1}H NMR (400 MHz; Acetone) δ_H 8.20 (1H, s), 7.29 (2H, t, *J* = 5,7 *Hz*), 6.73-6.92 (6H, m), 4.57 (2H, d, *J* = 5.7 *Hz*), 4.10 (1H, t, *J=5,8 Hz*, *OH*); ^{13}C NMR (100 MHz; Acetone) δ_C 158.7, 154.6, 150.2, 137.3, 129.0, 121.6, 117.9, 64.3; HRMS calcd. for $C_{13}H_{11}O_3$ $[M-H]^-$: 215.0708, found: 215.0704. Retention time (general HPLC method): t_r=11.18 min;



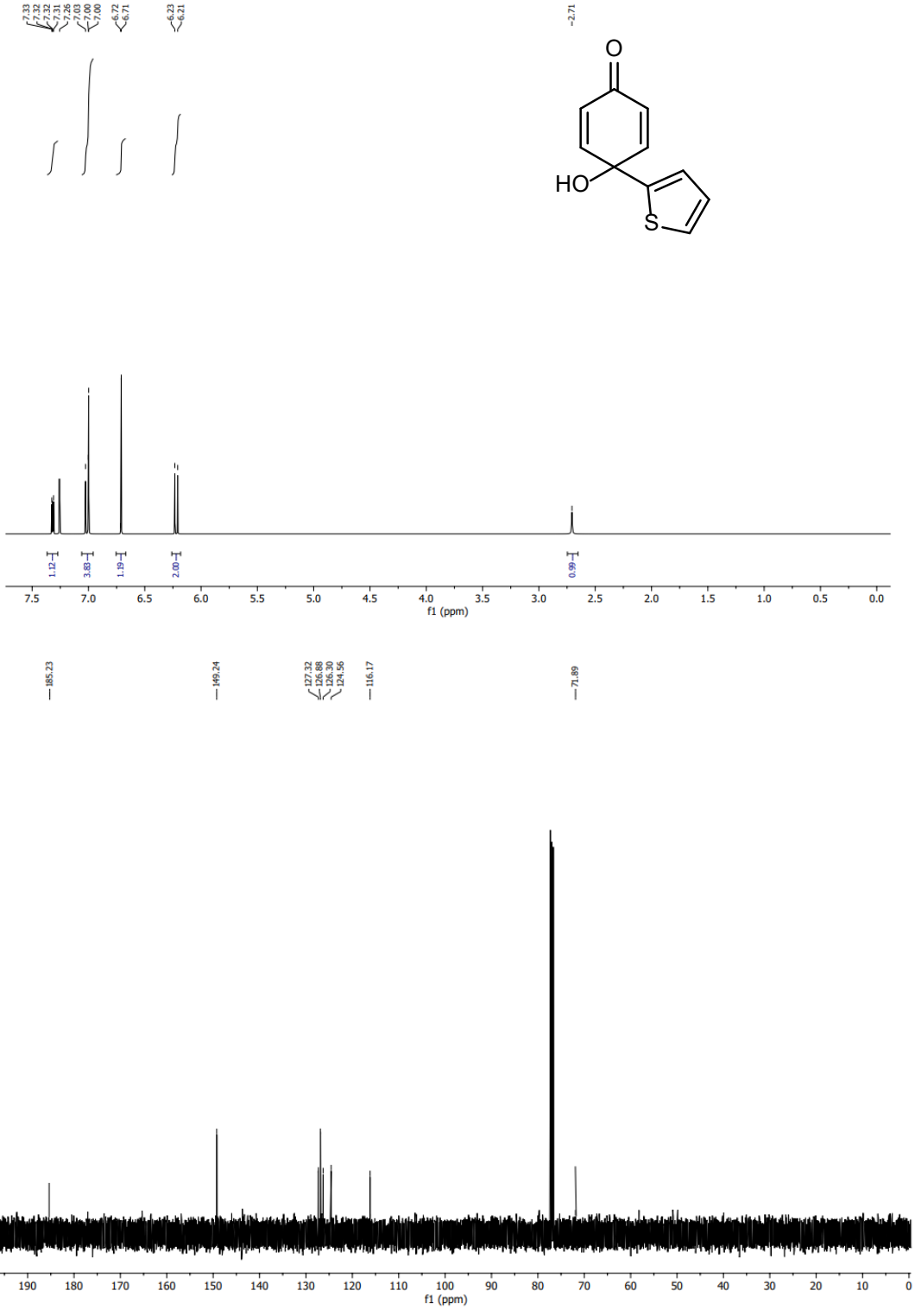
Compound **4h**;^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.68 – 7.56 (m, 4H), 6.86 (d, *J* = 10.1 Hz, 2H), 6.27 (d, *J* = 10.1 Hz, 2H), 2.75 (brs, 1H).; ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 185.3, 149.9, 142.6, 130.8, 127.4, 125.9, 125.9, 125.8, 125.8, 116.2, 70.8; HRMS calcd. for $C_{13}H_8F_3O_2$ $[M-H]^-$: 253.0476, found: 253.0473 Retention time (general HPLC method): t_r=6.68 min; NMR data were in accordance with those reported in the literature.[14]



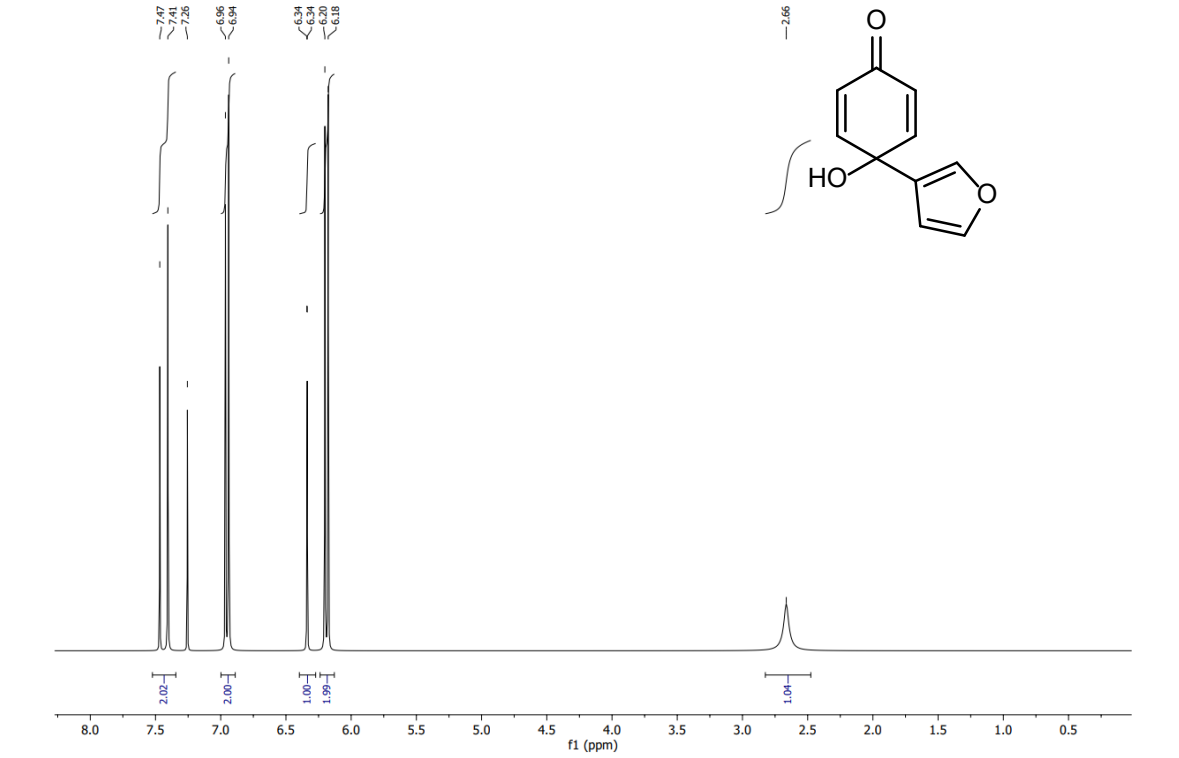
Compound **4i**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.21 (m, 2H), 7.09 – 6.89 (m, 3H), 6.26 – 6.04 (m, 2H), 3.64 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.92, 150.77, 140.39, 126.97, 126.53, 125.29, 122.08, 69.55.; HRMS calcd. for $C_{10}H_8O_2S$ $[M+H]^+$: 193.0323, found: 193.0320. Retention time (general HPLC method): t_r=7.23 min;

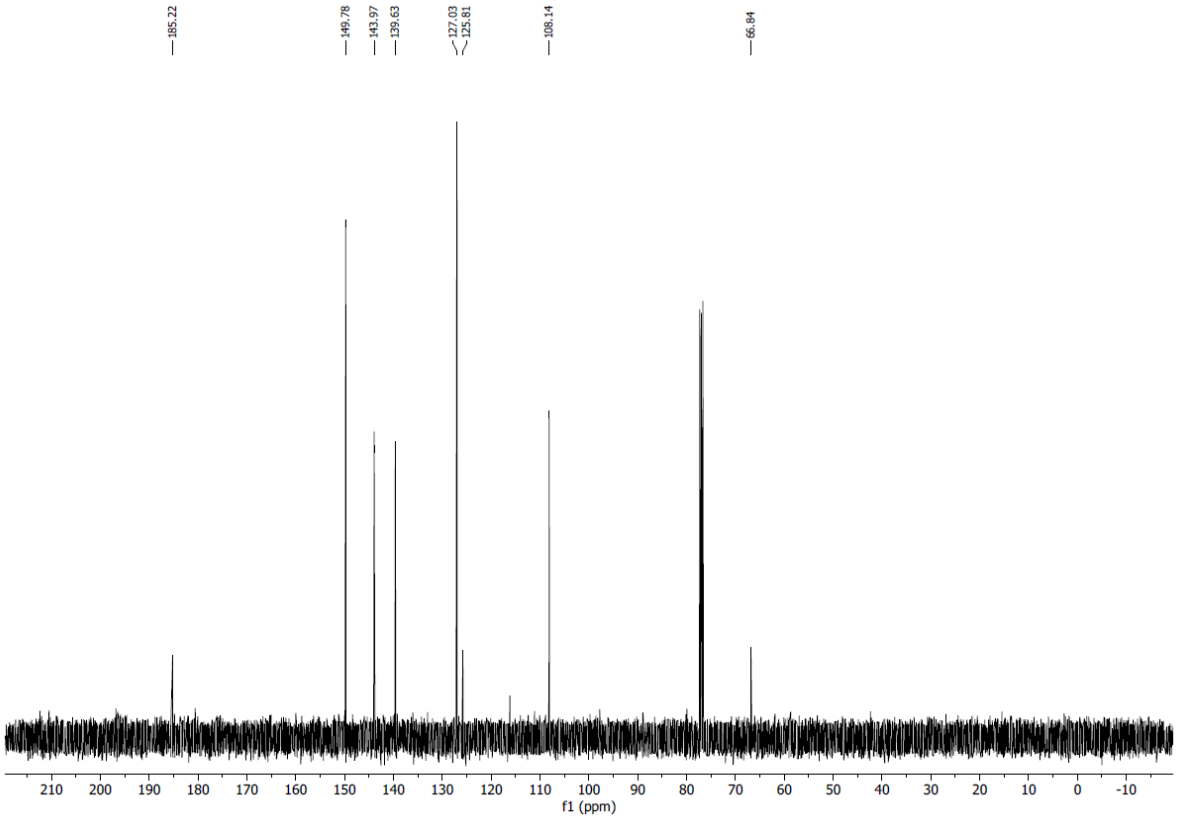


Compound **4j**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 4.0, 2.3 Hz, 1H), 7.05 – 6.97 (m, 4H), 6.71 (s, 1H), 6.22 (d, *J* = 10.1 Hz, 2H), 2.71 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.23, 149.24, 127.32, 126.88, 126.30, 124.56, 116.17, 71.89.; Melting point: literature: 103 °C, measured: 102-103 °C.[11] Retention time (general HPLC method): t_r=6.63 min;

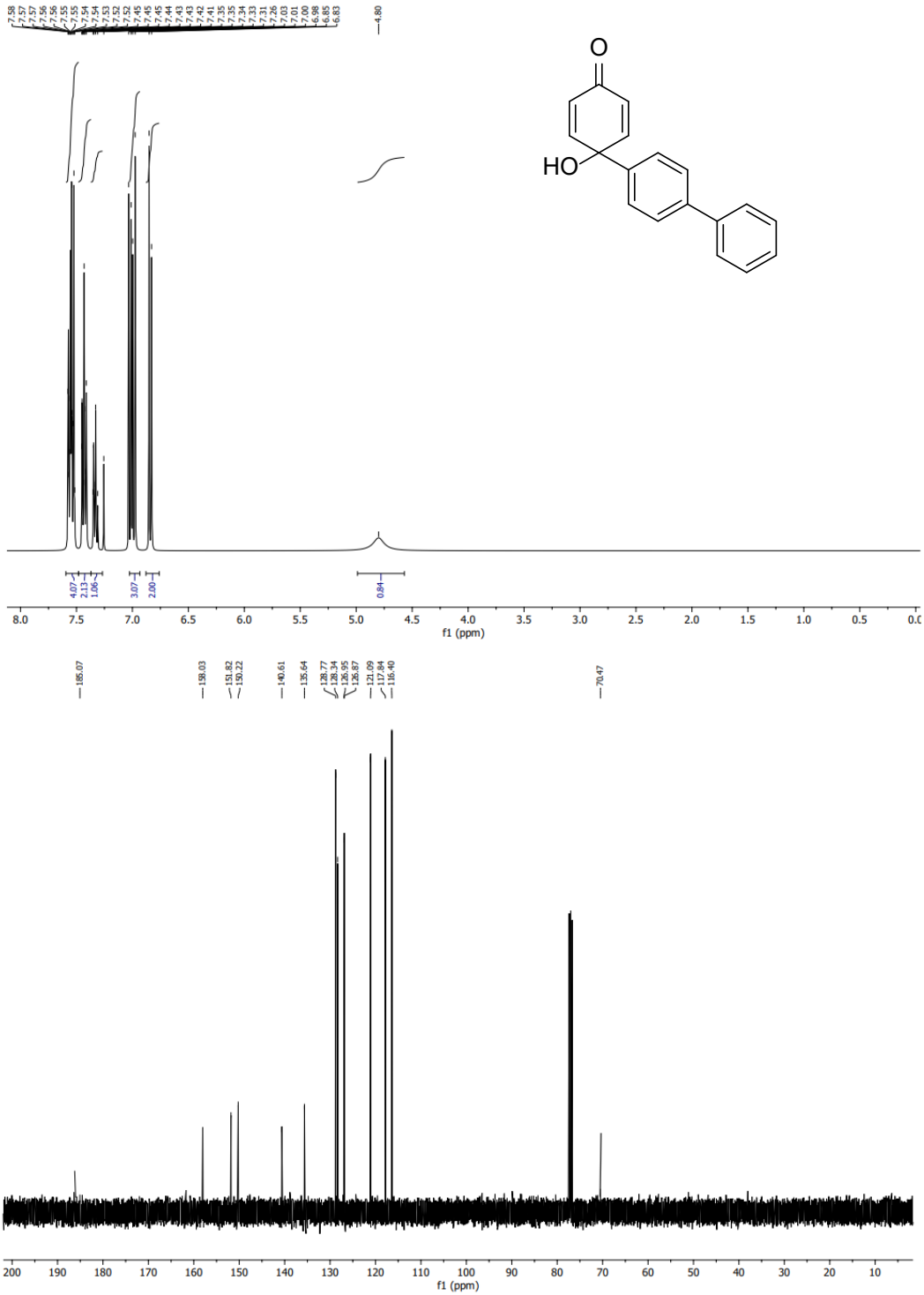


Compound **4k**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 24.8 Hz, 2H), 6.95 (d, *J* = 10.1 Hz, 2H), 6.34 (d, *J* = 1.0 Hz, 1H), 6.19 (d, *J* = 10.2 Hz, 2H), 2.66 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185,2, 149.7, 143.9, 139.6, 127.0, 125.8, 108.1, 66.8.; HRMS calcd. for $C_{10}H_8O_3$ $[M+H]^+$: 177.0552, found: 177.0555. Retention time (general HPLC method): t_r=8.28 min;

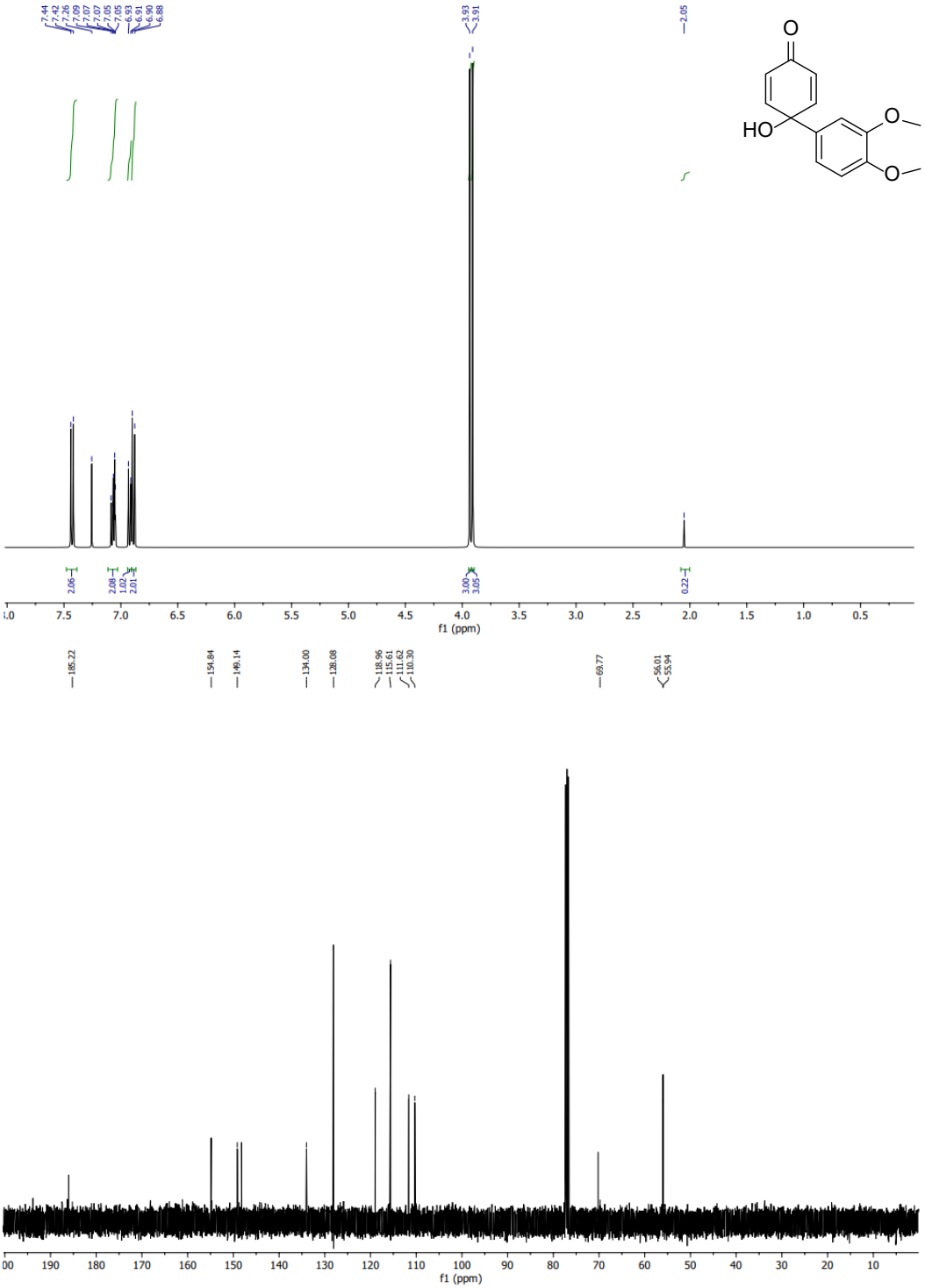




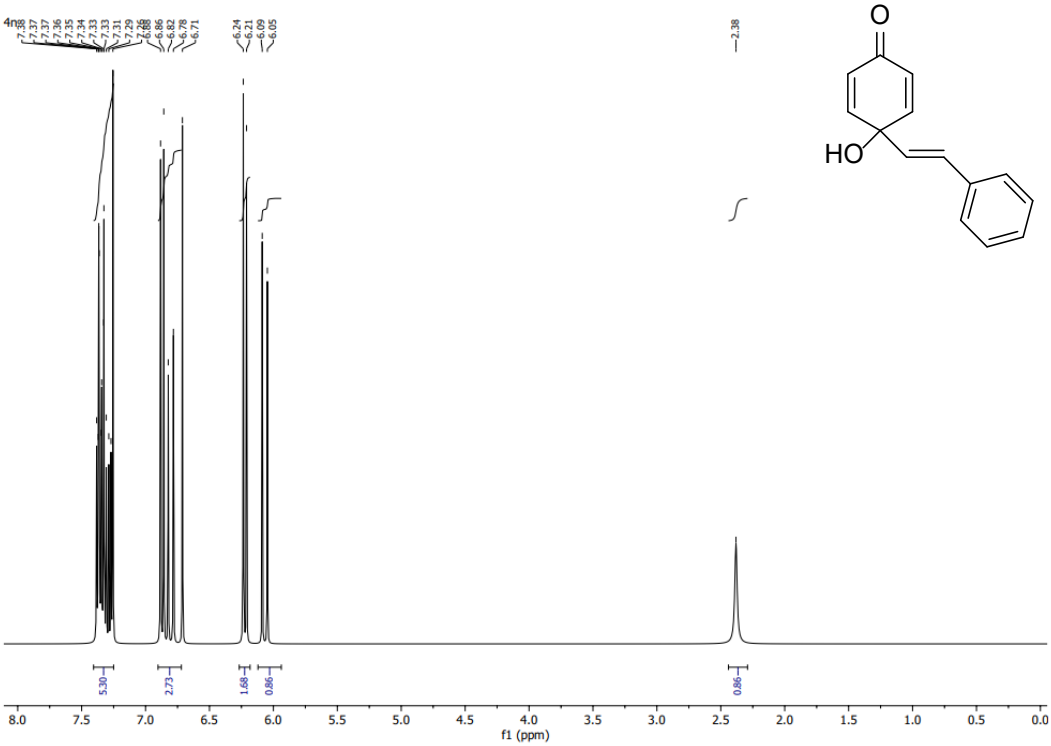
Compound **4l**; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.52-7.62 (4H, m), 7.41-7.49 (2H, m), 7.33-7.39 (1H, m), 6.97-7.09 (4H, m), 6.82-6.91 (2H, m), 4.83 (1H, s, *OH*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 158.0, 151.8, 150.2, 140.6, 135.6, 128.8, 128.3, 128.3, 126.9, 126.9, 121.1, 117.8, 116.4; HRMS calcd. for $C_{18}H_{13}O_2$ $[M-H]^-$: 261.0916, found: 261.0912. Retention time (general HPLC method): t_r=6.67 min;

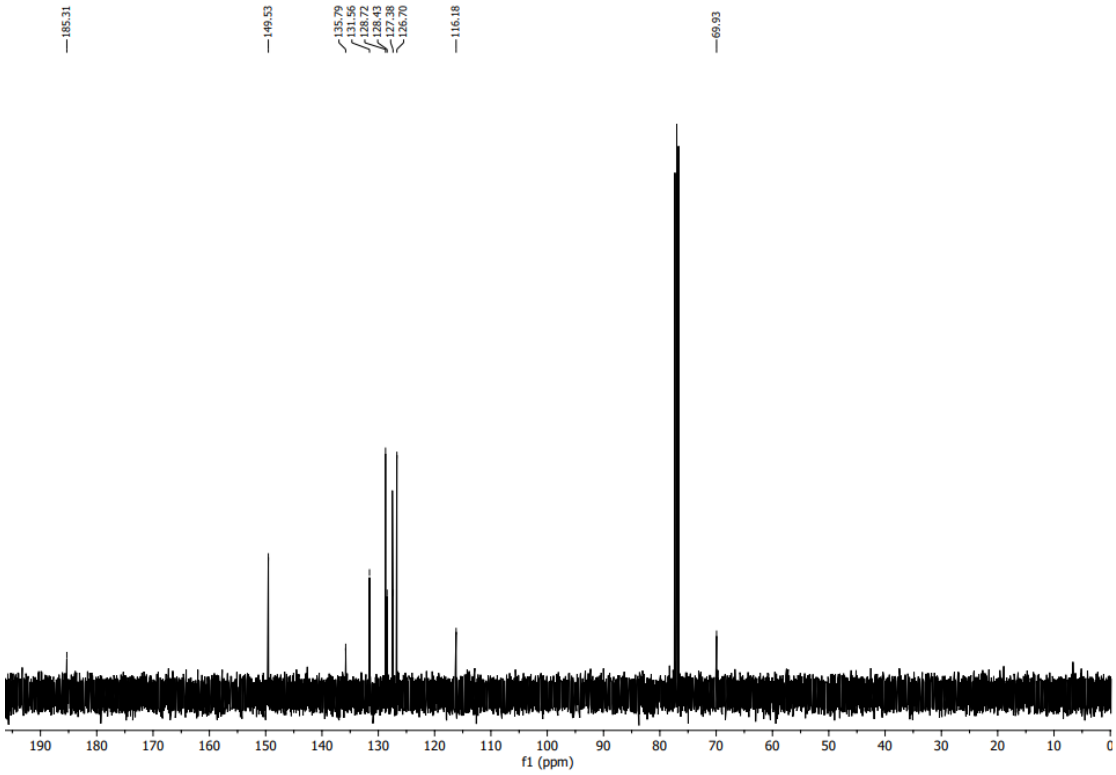


Compound **4m**; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.46 (2H, d, *J = 8,7 Hz*), 7.05-7.14 (2H, m), 6.89-6.98 (3H, m), 3.95 (6H, d, *J = 10,4 Hz*), 2.05(1H, s); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 154.8, 149.1, 148.2, 133.9, 134.0, 128.1, 119.0, 115.6, 111.6, 110.3, 56.0, 55.9; HRMS calcd. for $C_{14}H_{13}O_4$ $[M-H]^-$: 245.0814, found: 245.0805. Retention time (general HPLC method): t_r=7.04 min;

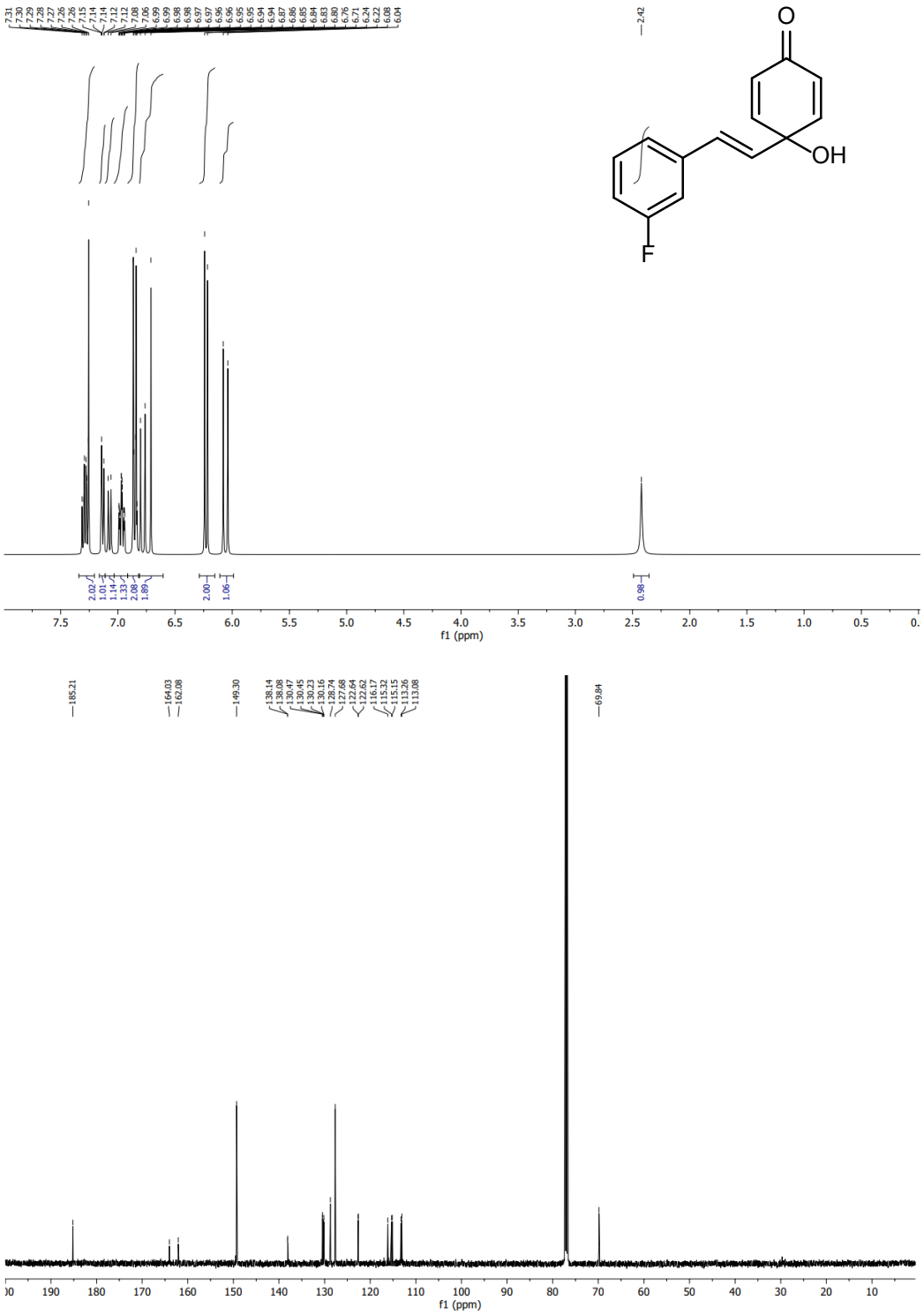


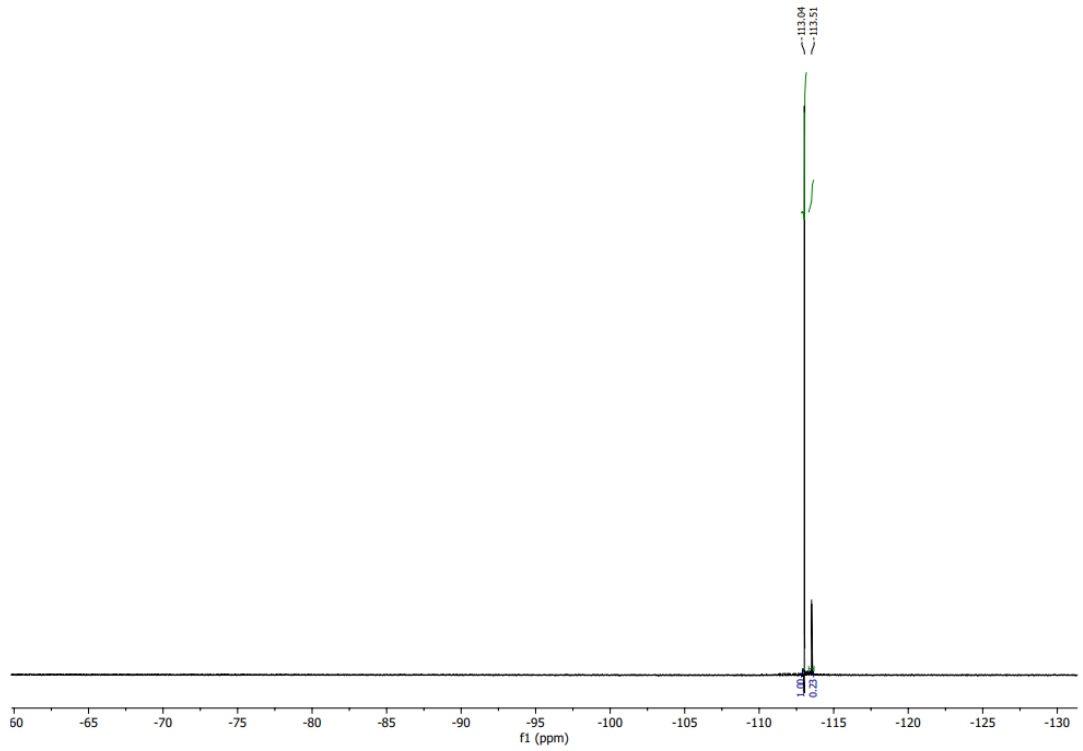
Compound **4n**;^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.27-7.38 (5H, m), 6.71-6.88 (3H, m), 6.21-6.24 (2H, m), 6.05-6.09 (1H, m,), 2.38 (1H, s br, O*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 185.3, 149.5, 135.8, 131.6, 128.7, 128.4, 127.5, 127.4, 126.7, 116.2, 69.9; HRMS calcd. for $C_{14}H_{11}O_2$ $[M-H]^-$: 211.0759, found: 211.0758 Retention time (general HPLC method): t_r=7.09 min;

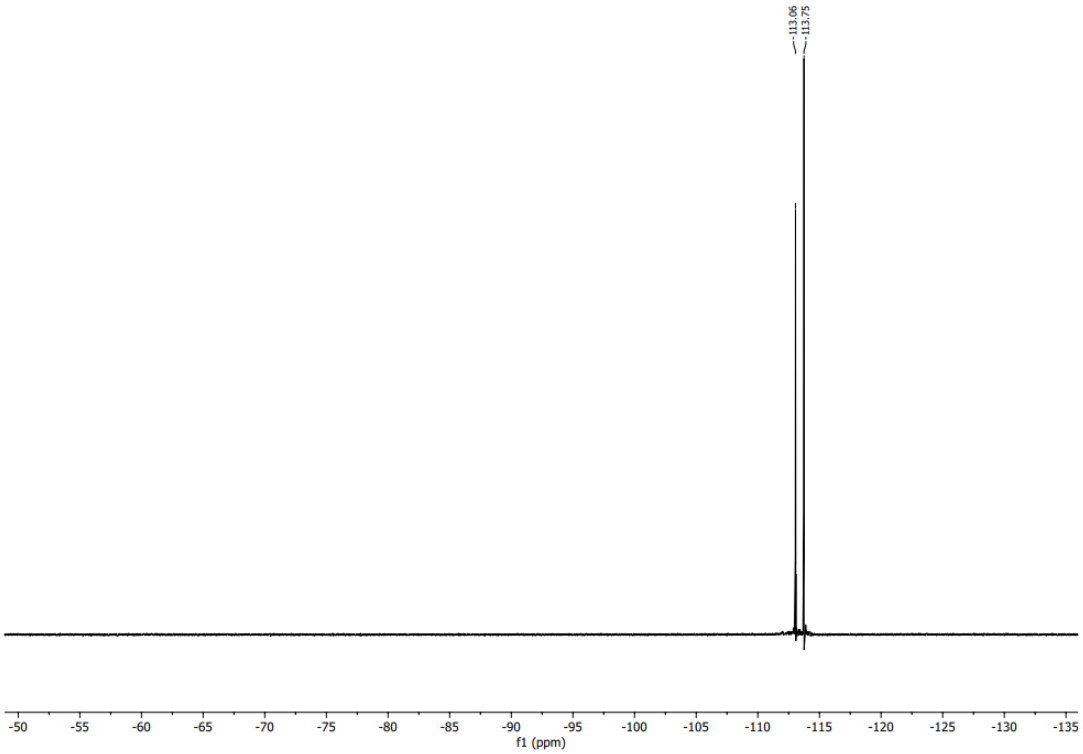




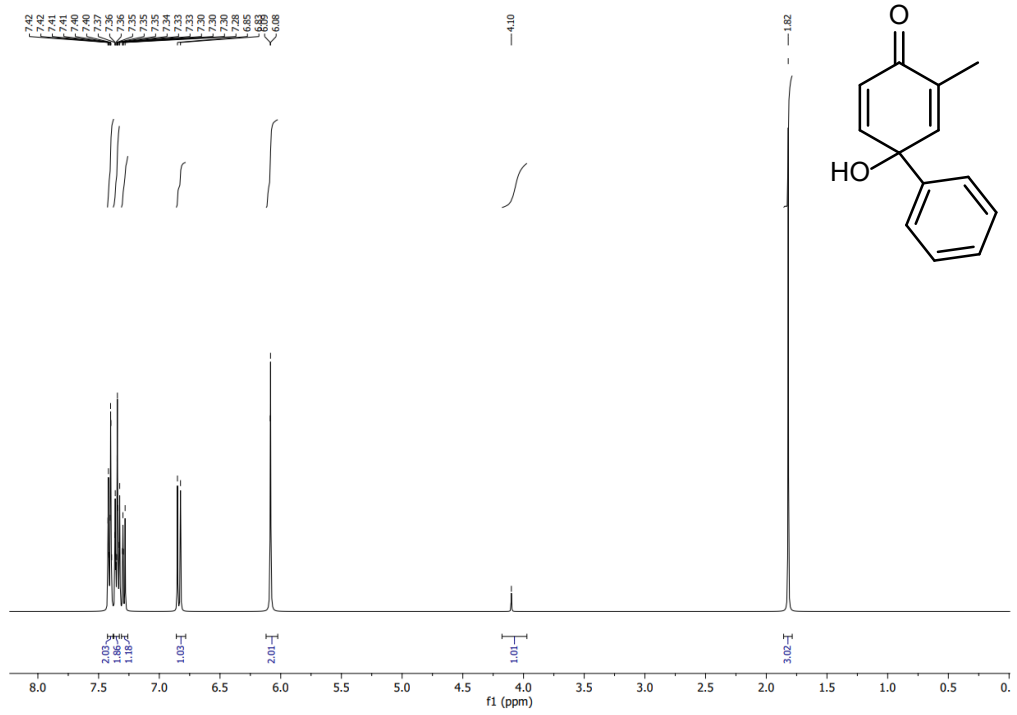
Compound **4o**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.21 (m, 2H), 7.16 – 7.11 (m, 1H), 7.07 (d, *J* = 9.9 Hz, 1H), 6.97 (tdd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 6.91 – 6.82 (m, 2H), 6.81 – 6.60 (m, 2H), 6.23 (d, *J* = 10.1 Hz, 2H), 6.06 (d, *J* = 16.0 Hz, 1H), 2.42 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.2, 164.0, 162.0, 149.3, 138.1, 138.0, 130.5, 130.4, 130.2, 130.1, 128.7, 127.6, 122.6, 122.6, 116.1, 115.3, 115.1, 113.2, 113.0, 69.8.; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.04, -113.51.(isolated from cascade reaction) ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.06, -113.75 (isolated from classical C-C coupling); HRMS calcd. for $C_{14}H_{10}O_2F$ $[M-H]^-$: 229.0665, found: 229.0666. Retention time (general HPLC method): t_r=7.341 min,

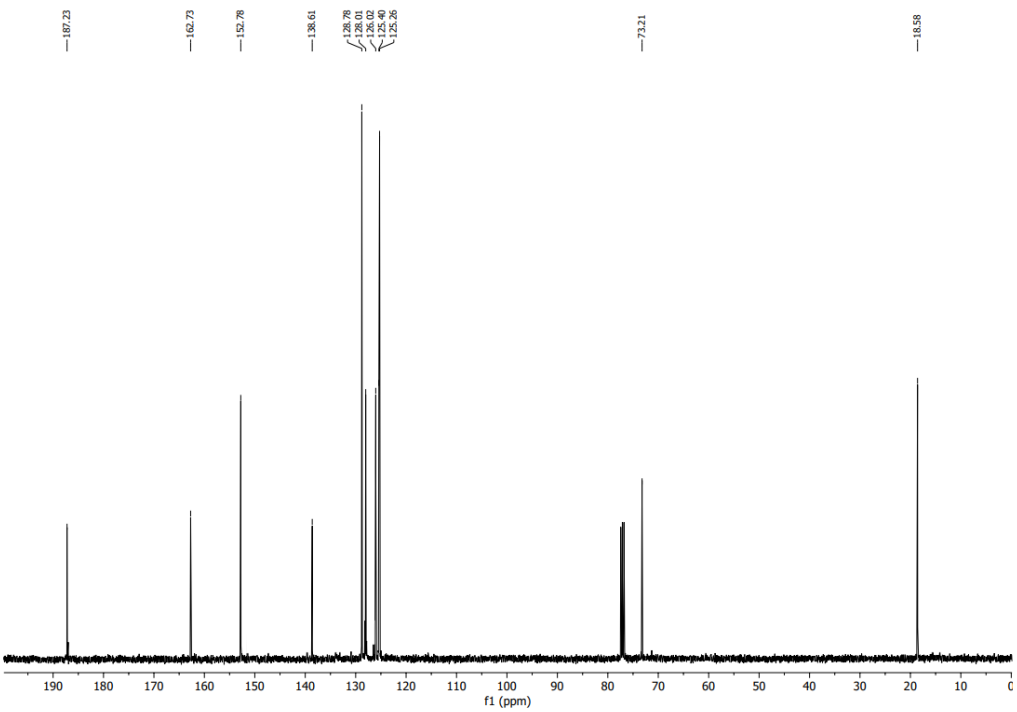



-113.04
-113.51
1.00
0.23
60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
f1 (ppm)

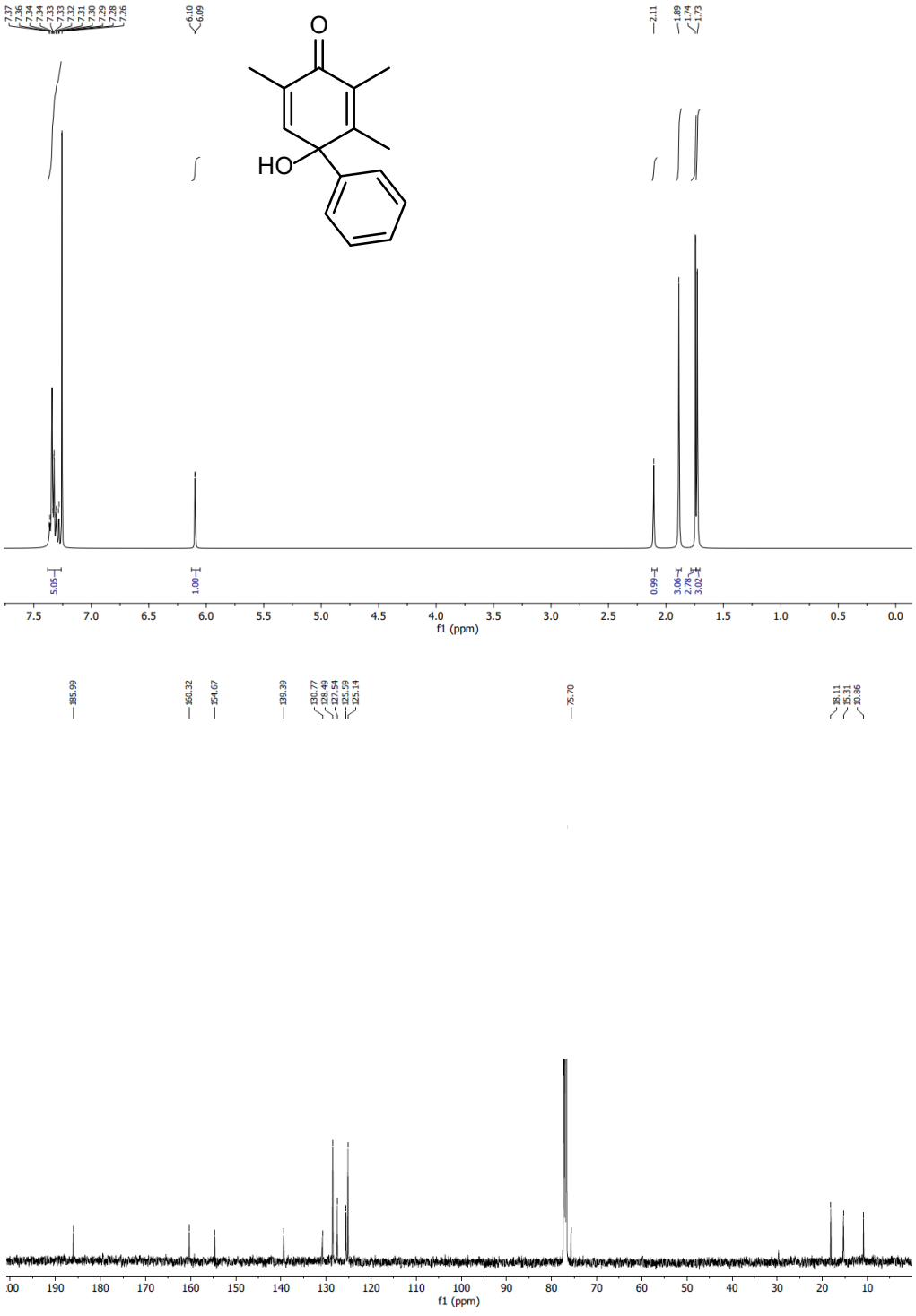

-113.06
-113.75
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
f1 (ppm)

4-Hydroxy-2-methyl-4-phenyl-2,5-cyclohexadienone Compound **4p**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 2H), 7.38 – 7.33 (m, 2H), 7.31 – 7.26 (m, 1H), 6.84 (d, *J* = 10.0 Hz, 1H), 6.08 (d, *J* = 0.9 Hz, 2H), 4.10 (s, 1H), 1.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.23, 162.73, 152.78, 138.61, 128.78, 128.01, 126.02, 125.40, 125.26, 73.21, 18.58. HRMS calcd. for $C_{13}H_{11}O_2$ $[M-H]^+$: 199.0759, found: 199.0760. Retention time (general HPLC method): t_r=6.06 min; NMR data were in accordance with those reported in the literature.[15]

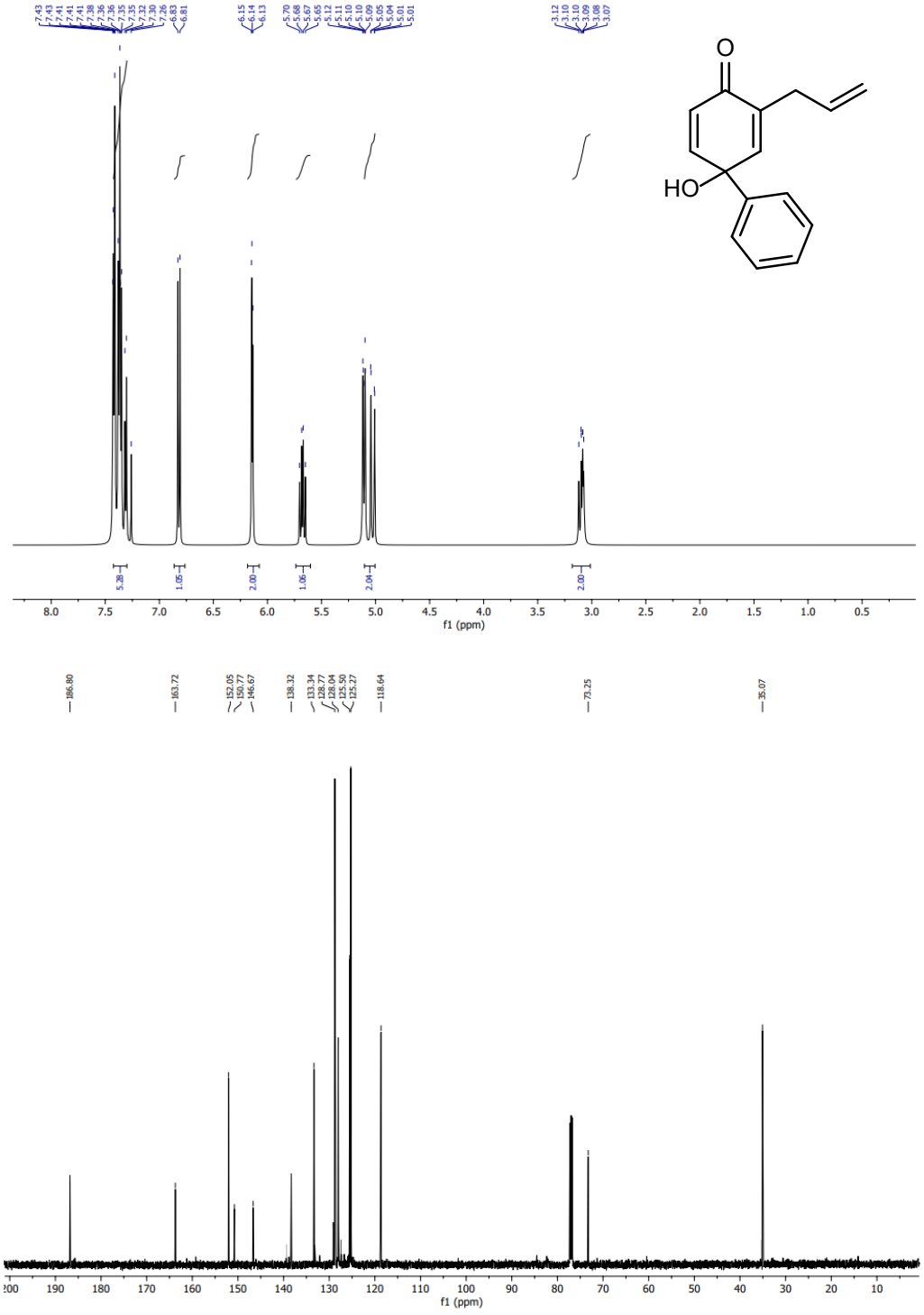




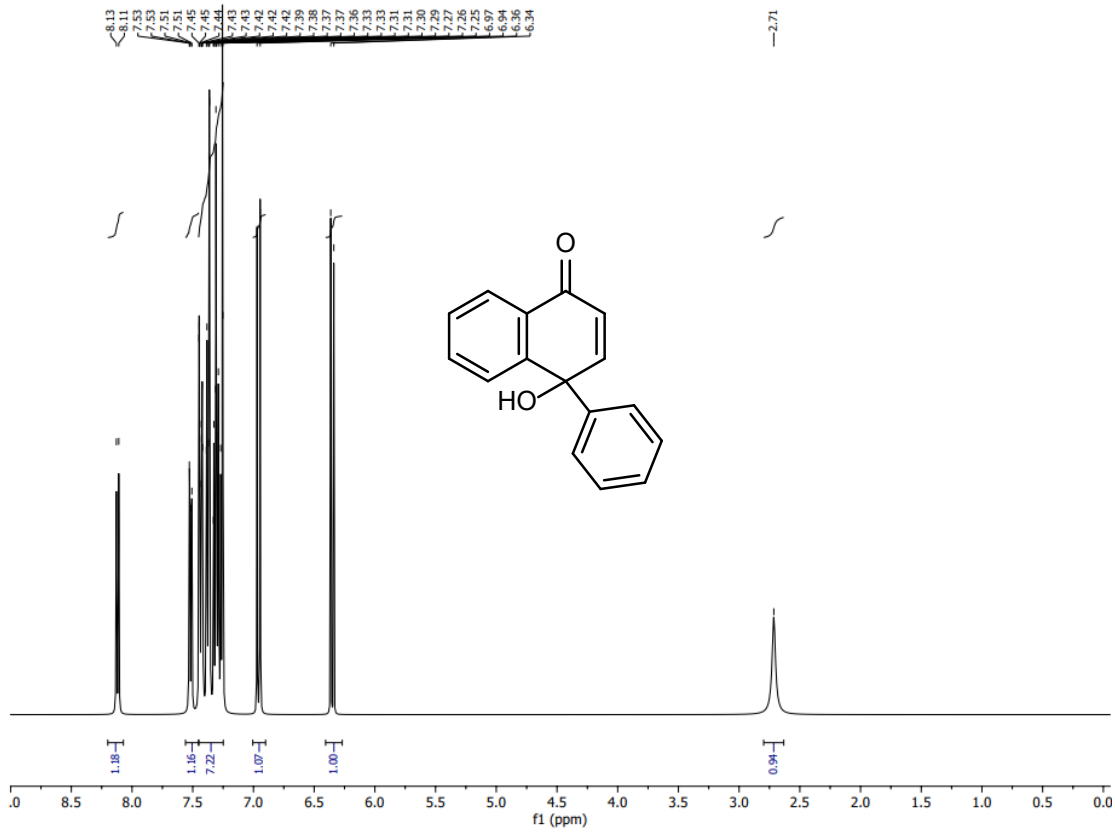
Compound **4q**; ^{1}H NMR ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 5H), 6.10 (d, *J* = 1.5 Hz, 1H), 2.11 (s, 1H), 1.89 (s, 3H), 1.74 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (126 MHz, $cdcl_3$) δ 185.99, 160.32, 154.67, 139.39, 130.77, 128.49, 127.54, 125.59, 125.14, 75.70, 18.11, 15.31, 10.86; HRMS calcd. for $C_{15}H_{17}O_2$ $[M-H]^-$: 229.1229, found: 229.1234. Retention time (general HPLC method): t_r=5.13 min;

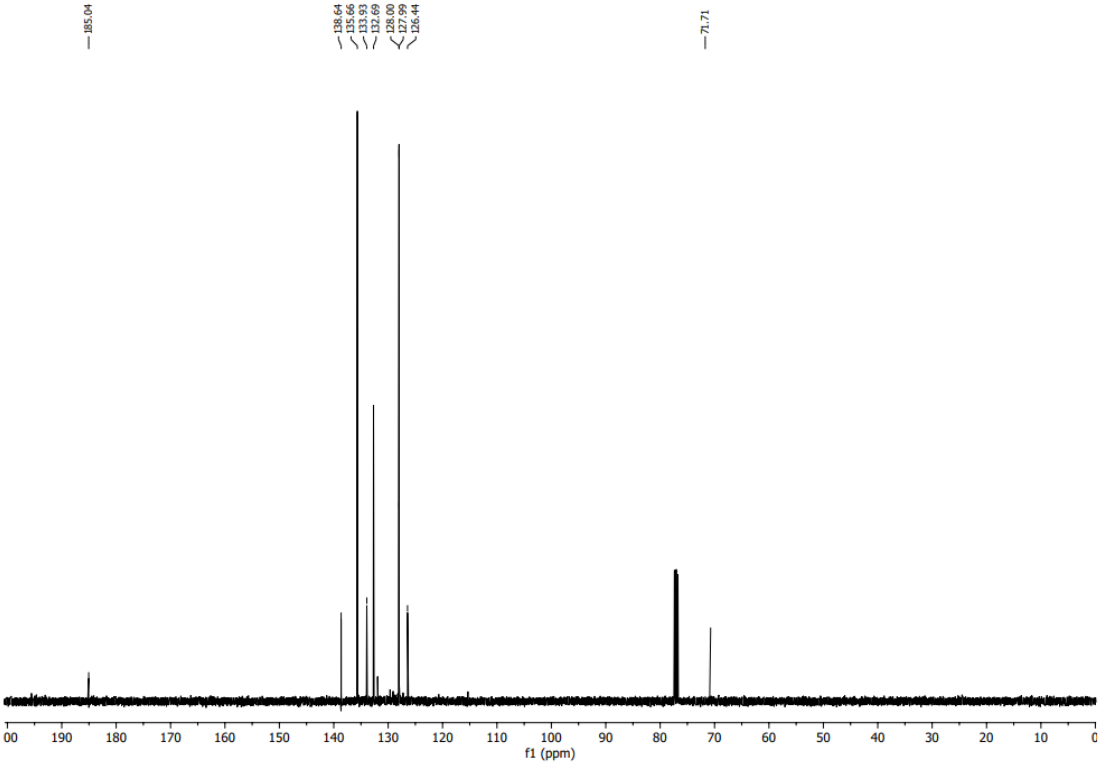


Compound **4r**; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 5H), 6.82 (d, *J* = 9.8 Hz, 1H), 6.18 – 6.08 (m, 2H), 5.74 – 5.60 (m, 1H), 5.10 – 5.01 (m, 2H), 3.18 – 3.01 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.80, 163.72, 152.05, 150.77, 146.67, 138.32, 133.34, 128.77, 128.04, 125.50, 125.27, 118.64, 73.25, 35.07; HRMS calcd. for $C_{15}H_{15}O_2$ $[M+H]^+$: 227.1072, found: 227.1074. Retention time (general HPLC method): t_r=5.328 min;



Compound **4s**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.8 Hz, 1H), 7.52 (dd, *J* = 6.9, 1.2 Hz, 1H), 7.45 – 7.25 (m, 7H), 6.96 (d, *J* = 10.2 Hz, 1H), 6.35 (d, *J* = 10.0 Hz, 1H), 2.71 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.04, 138.64, 135.66, 133.93, 132.69, 128.00, 127.99, 126.44, 71.71. HRMS calcd. for $C_{16}H_{11}O_2$ [M-H]$^-$: 235.0759, found: 235.0760. Retention time (general HPLC method): t_r=5.26 min;





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