Electronic Supporting Information (ESI)

For

A Novel Rapanone Derivatives Via Organocatalytic Reductive C-Alkylation, their Biological Evaluation in Antioxidant and *In Vivo* Zebrafish Embryo Toxicity, its Docking Studies †

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(1) General Information

All reactions were performed using oven-dried glassware and standard Schlenk tubes. The compounds were characterised using ^{1}H-NMR (500.30 MHz) and ^{13}C-NMR (100.64 and 125.80 MHz) Bruker NMR spectrometers. The chemical shift (δ) values are given in parts per million (ppm), and the coupling constant (J) is given in hertz (Hz). The spectra were recorded using $CDCl_3$ and DMSO-d_6 solvents. ^{1}H-NMR chemical shifts are referenced to tetramethylsilane (TMS, 0 ppm), with the solvent resonance employed as the internal standard ($CDCl_3$ at 7.26 ppm, DMSO-d_6 at 2.50 ppm and H_2O at 3.35 ppm). The following abbreviations are used to designate signal multiplicities: singlet (s); doublet (d); doublets of doublet (dd); triplet (t); quartet (q); multiplets (m). The ^{13}C-NMR is referenced to $CDCl_3$ (77.2 ppm) and DMSO-d_6 (39.51 ppm). Additionally, all the unknown compounds (**5a–5ze**) were characterised by HRMS recorded with QTOF-ESI source M/S Bruker Daltonik GmbH, Germany. The melting point of compounds was determined using a digital melting point apparatus (Model 33/0112) from VEEGO-VMP-DS. Thin layer chromatography (TLC) was used to monitor all reactions and product mixtures using silica gel plates precoated with silica gel 60 F_{254} (Merck, Darmstadt, Germany). TLC sheets used 0.25 mm commercial silica gel plates with ethyl acetate and hexane as eluting solvents, and compound visualisation was performed using a UV lamp. The purification of products was accomplished through the use of column chromatography with silica gel (100–200 mesh, Merck, Darmstadt, Germany). All chemicals (**2a-2zf**) and solvents were purchased from Merck, Avra, Carbanio and SRL. The starting material compound (**1**) was isolated according to the previously reported literature method[1].

(2) Experimental set up for extraction, isolated of compound 1, synthesis of 5a-5ze, Antioxidant activity and Zebrafish embryo toxicity studies.

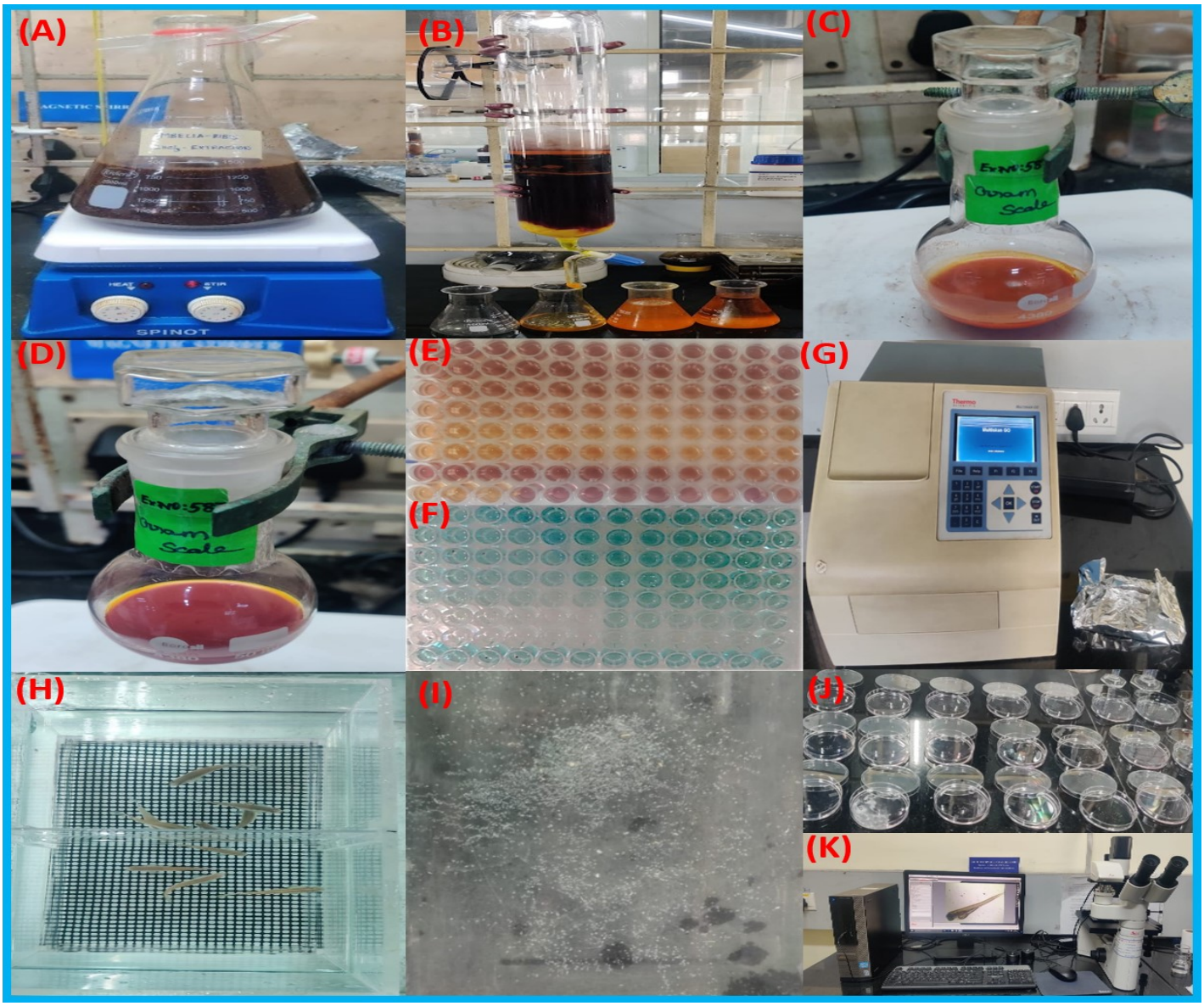
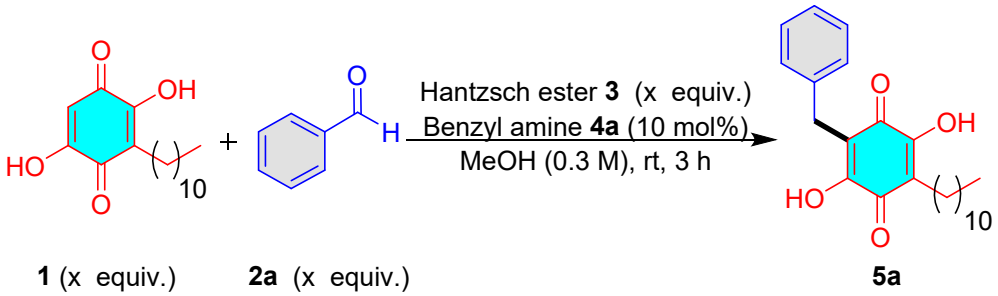


Fig. S1. Model experimental setup for (**A**) Extraction of *Embelia ribes* fruits using mechanical stirrer, (**B**) Isolation of rapanone from *Embelia ribes* extract by column chromatography, (**C**) Semi-synthesis of rapanone derivative before starting the reaction, (**D**) After completion of the reaction, (**E**) Antioxidant of DPPH Assay by 96-well plate (**F**) Antioxidant of ABTS assay by 96-well plate, (**G**) DPPH and ABTS assay with compounds after reduction reaction being measured absorptance using Elisa plate reader, (**H**) Egg culture, (**I**) After culture

separated embryos, (**J**) Zebrafish embryo toxicity study, (**K**) The lethality of each embryo was determined using an inverted microscope.

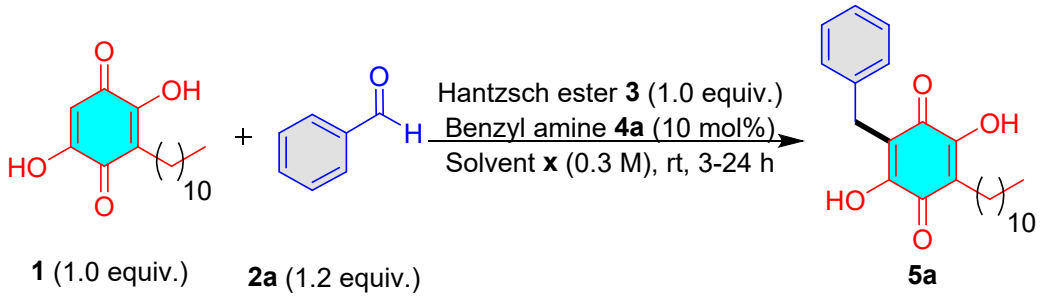
(2) Optimization of the reaction condition.

Table S1. Benzaldehyde and hantzsch este**r** equivalent variation studies.



Entry	Rapanone (1) (equiv.)	Aldehyde (2a) (equiv.)	Hantzsch (3) (equiv.)	Catalyst (4) (10 mol%)	Solvent (0.3 M)	Time (h)	Yield (%)
1	1.0	1.2	1.0	Benzylamine (4a)	MeOH	3	61
2	1.0	1.5	1.0	Benzylamine (4a)	MeOH	3	46
3	1.0	1.0	1.0	Benzylamine (4a)	MeOH	3	53
4	1.0	1.2	0.5	Benzylamine (4a)	MeOH	3	51
5	1.0	1.2	1.5	Benzylamine (4a)	MeOH	3	48

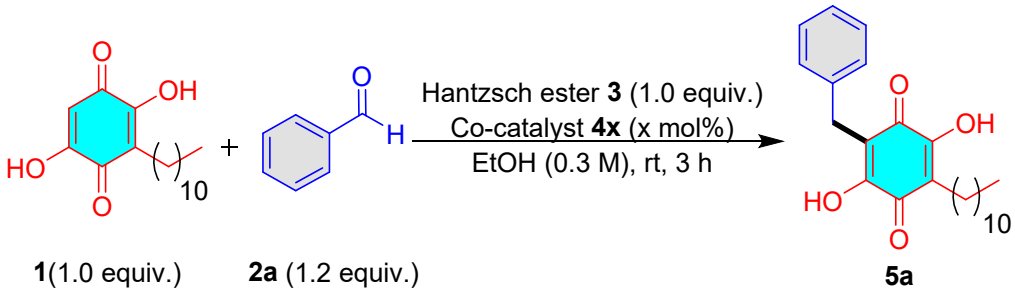
Table S2. Solvents and time screening studies.



Entry	Rapanone (1) (equiv.)	Aldehyde (2a) (equiv.)	Hantzsch (3) (equiv.)	Catalyst (4) (10 M %)	Solvent (0.3 M)	Time (h)	Yield (%)
1	1.0	1.2	1.0	Benzylamine (4a)	Dioxane	24	12

2	1.0	1.2	1.0	Benzylamine (4a)	DMF	12	20
3	1.0	1.2	1.0	Benzylamine (4a)	DMSO	12	36
4	1.0	1.2	1.0	Benzylamine (4a)	Acetone	12	Trace
5	1.0	1.2	1.0	Benzylamine (4a)	CH_3CN	12	00
6	1.0	1.2	1.0	**Benzylamine (4a)**	**EtOH**	**3**	**93**
8	1.0	1.2	1.0	Benzylamine (4a)	Neat	3	00
9	1.0	1.2	1.0	Benzylamine (4a)	$CHCl_3$	3	00
10	1.0	1.2	1.0	Benzylamine (4a)	DCM	3	00

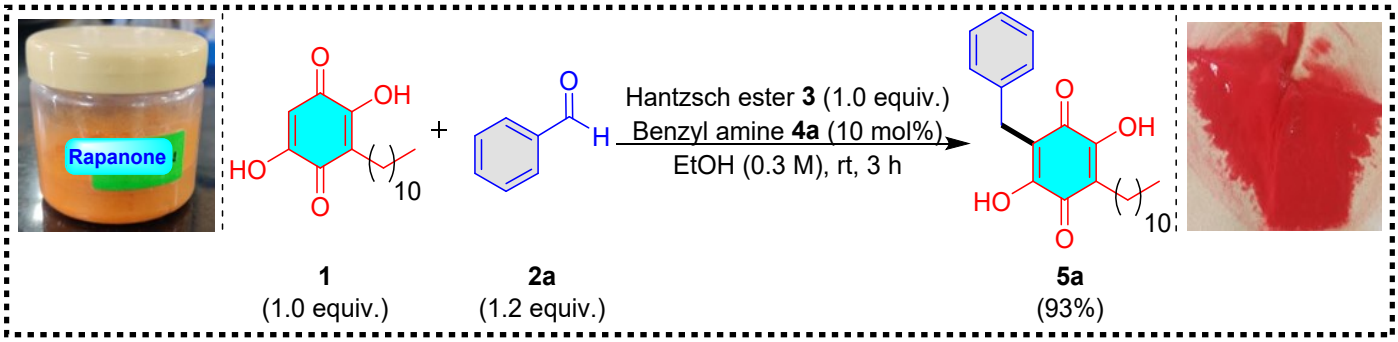
Table S3. Co-catalyst screening and equivalent variation studies



1(1.0 equiv.) **2a** (1.2 equiv.) **5a**

Entry	Rapanone (1) (equiv.)	Aldehyde (2a) (equiv.)	Hantzsch (3) (equiv.)	Co-catalyst (4) (10 mol%)	Solvent (0.3 M)	Time (h)	Yield (%)
1	1.0	1.2	1.0	(S)-Proline (4b)	EtOH	3	43
2	1.0	1.2	1.0	Piperidine (4c)	EtOH	3	08
3	1.0	1.2	1.0	Pyridine (4d)	EtOH	3	14
4	1.0	1.2	1.0	Aniline (4e)	EtOH	3	Trace
5	1.0	1.2	1.0	Without catalyst	EtOH	3	00
6	1.0	1.2	1.0	Benzylamine (5 mol%)	EtOH	3	77
7	1.0	1.2	1.0	Benzylamine (20 mol%)	EtOH	3	89

Optimised condition:



(3) Experimental procedure

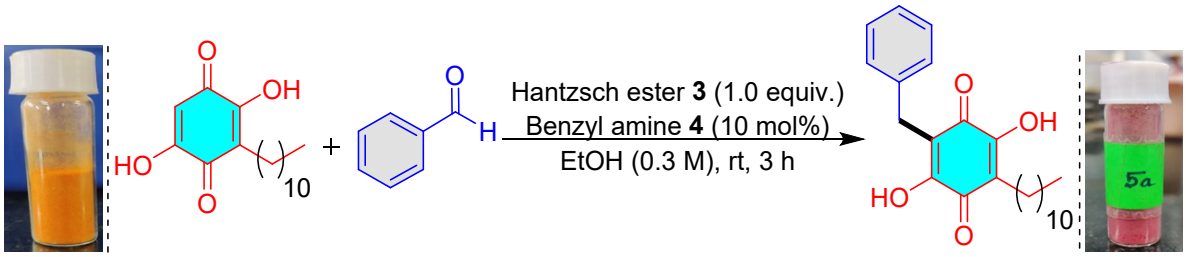
(i) General experimental procedure A for the extraction and isolation of rapanone (1) from *Embelia ribes.*

The raw (*Embelia ribes)* false black pepper (500 g) was purchased from the sasta-pooja store in the month of December 2022 at railway station road, Urapakkam west, Vandalur taluk, Chengalpattu district- 603 211, Tamil Nadu, India, and professor Dr. K. N. Sunil Kumar, Department of Pharmacognosy, Central Council for Research in Siddha, Arumbakkam, Chennai - 600 106, Tamil Nadu, India, identified the plant specimen. On May 9, 2023, the plant specimen was kept in the herbarium, Interdisciplinary Institute of Indian System of Medicine (IIISM), SRM Institute of Science and Technology, Kattankulathur-603 203, Chengalpattu district, Tamil Nadu, India, with voucher specimen accession number: E09052301R. The black pepper (500 g) was shade dried and grinded well into a coarse powder, which was extracted with chloroform ($CHCl_3$) in 1 L for 24 h (3 times) with mechanical stirring at room temperature. This extract was partitioned with ethyl acetate under ultrasonication (5–10 min), the oil and crude extract were separated and concentrated to obtain the final crude extract (44.60 g). The crude extract was purified by column chromatography (silica gel 100–200 mesh) using a mixture of solvents hexane with increasing polarity of ethyl acetate (8–10%) to get a pure product of rapanone (**1**). The fractions were 31–71 (R_f 0.42), matched with standard rapanone (R_f 0.42) in TLC, which was observed in white light, mobile phase (chloroform 50%, ethyl acetate 45% and formic acid 5%)[2,3]. This similar rapanone fraction was evaporated in the rotary evaporator until a constant weight of 20.11 g was obtained (44.60% yield). The finally isolated (**1**) confirmed by ^1H, ^{13}C NMR and (ESI) HRMS spectrums.

(ii) General experimental procedure B for the synthesis of 5a-5ze.

To an ordinary glass vial with an inner cap equipped with a magnetic stirring bar, a compound of 0.16 mmol (50 mg) of rapanone (**1**) in ethanol (1.13 mL 0.3 M), 0.19 mmol (1.2 equiv.) aldehyde **2a-2zf**, 0.16 mmol (41.73 mg 1.0 equiv.) of Hantzsch ester **3** (for aromatic or aliphatic aldehyde) and (10 mol%, 1.81mg) benzyl amine **4a** dissolved in ethanol (0.2 mL) was added dropwise. The reaction mixture was stirred for 3 h and the completion of the reaction was monitored by TLC. After the complete disappearance of the starting material, the formed precipitated solid was filtered and washed with water (2x3 mL) to afford the pure derivatives (**5a–5zf**) from light-maroon to dark maroon-coloured solids (yield = 51–93%).

(iii) General experimental procedure C for the gram scale synthesis of 5a.



1 1.0 g (1.0 equiv.) **2a** 0.42 mL (1.2 equiv.) **5a** 1.11 g (93%)

To an ordinary glass vial with a cap equipped with a magnetic stirring bar, a compound of 3.39 mmol (1g) of rapanone **1** in ethanol (11.3 mL 0.3 M), 4.07 mmol (1.2 equiv.) of aldehyde **2a**, 3.39 mmol (860.35mg 1.0 equiv.) of Hantzsch ester **3**, and (10 mol%, 35.35mg) of benzyl amine **4a** dissolved in ethanol (2 mL) was added dropwise. The reaction mixture was stirred for 3 h and the completion of the reaction was monitored by TLC. After the completion, the precipitated solid was filtered and washed with water (2x3 mL) to afford the pure compound 2-benzyl-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione **5a** as a light dark maroon colour solid (yield = 93%).

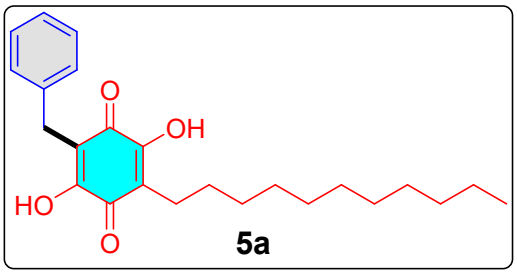
(5) Spectral characterizations of ^{1}H, ^{13}C NMR, and ESI HRMS data of the products (1) and (5a-5ze).

Rapanone (1). The title compound was extracted and purified according to the general procedure A, and the product was isolated by column chromatography (Hexane/Ethyl acetate = 10%) orange solid (20g, yield = 44%); mp: 144-146 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.69 (s, 1H), 3.28 (s, 2-OH),

1

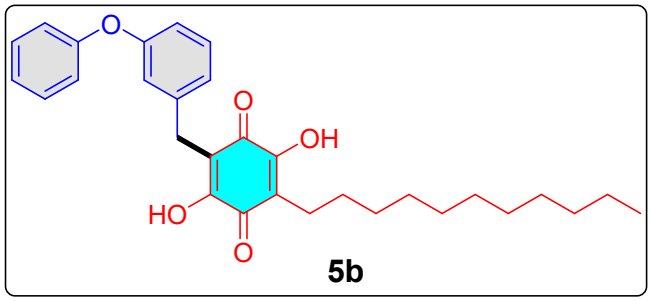
2.22 – 2.19 (m, 2H), 1.15 (s, 18H), 0.78 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.59, 183.47, 130.24, 130.02, 116.99, 102.18, 31.93, 29.92, 29.65, 29.62, 29.55, 29.54, 29.38, 29.34, 27.95, 22.70, 22.52, 14.13; HR-MS (ESI) Calculated for $C_{17}H_{26}O_4$ $[M+H]^+$; 293.1758 found 293.1740 these date matching with the previous literature report[1].

2-benzyl-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5a). The synthesis of the title compound followed by the general procedure B, and the product was isolated by filtration to obtain maroon colour solid (57mg, yield = 93%); mp:150-152 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.47 (d, J = 8.1 Hz, 1H), 7.36 (t, J = 6.2 Hz, 1H), 7.35 (t, J = 6.4 Hz, 1H), 7.33 (t, J = 8.4 Hz, 1H), 7.26 (d, J = 8.2 Hz, 1H), 3.97 (s, 2H), 2.11 (t, J = 7.1 Hz, 2H), 1.1 (s, 18H), 0.77 (t, J = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.69, 179.20, 158.95, 156.25, 140.25, 130.34, 129.28, 127.58, 126.09, 120.42, 33.61, 31.70, 29.92, 29.79, 28.84, 28.70, 28.46, 28.32, 26.05, 22.24, 14.42; HR-MS (ESI) Calculated for $C_{24}H_{32}O_4$ $[M+H]^+$; 385.2340 found 385.2345.



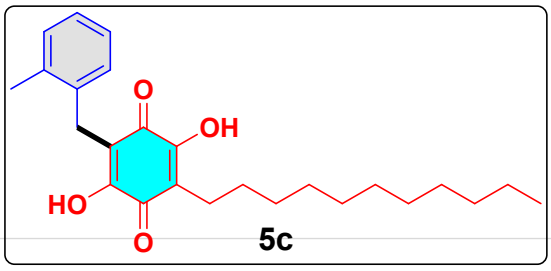
5a

2,5-dihydroxy-3-(3-phenoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5b). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (68mg, yield = 90%); mp:164-166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.34 (d, J = 2.6 Hz, 1H), 7.33 (d, J = 6.8 Hz, 1H), 7.20 (t, J = 7.5 Hz, 2H), 7.09 – 7.05 (m, 1H), 7.00 – 6.95 (m, 1H), 6.90 (d, J = 1.5 Hz, 1H), 6.89 (d, J = 1.4 Hz, 1H), 4.06 (s, 2H), 2.18 (t, J = 5.8 Hz, 2H), 1.56 – 1.49 (m, 2H), 1.37 (dd, J = 13.4, 6.8 Hz, 2H), 1.35 – 1.23 (m, 14H), 0.98 (t, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.54, 179.62, 157.29, 156.73, 156.50, 156.02, 139.81, 130.01, 129.66, 125.88, 123.34, 123.04, 121.36, 120.80, 119.76, 119.71, 118.44, 34.08, 31.01, 29.67, 29.10, 28.98, 28.95, 28.91, 28.90, 28.73, 25.84, 22.79, 14.17; HR-MS (ESI) Calculated for $C_{30}H_{36}O_5$ $[M+H]^+$; 477.2663 found 477.2668.



5b

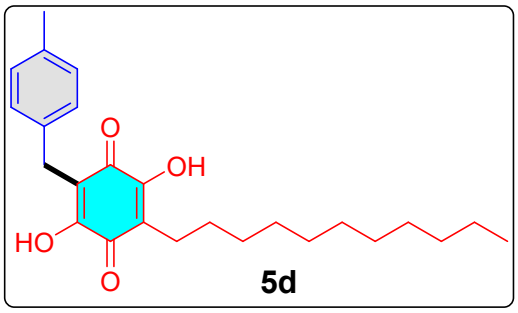
2,5-dihydroxy-3-(2-methylbenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5c). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (59mg, yield = 93%); mp:161-163 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.31 (d, J = 7.3 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H),



5c

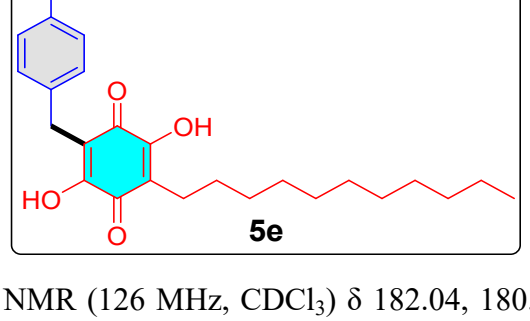
7.26 (t, J = 7.2 Hz, 1H), 7.20 (t, J = 7.2 Hz, 1H), 3.76 (s, 2H), 2.41 (s, 3H), 1.47 – 1.40 (m, 2H), 1.33 – 1.21 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H), ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.71, 178.73, 156.58, 155.29, 140.08, 134.42, 130.17, 129.81, 127.48, 126.54, 125.76, 122.39, 31.02, 29.65, 29.13, 28.92, 28.82, 28.67, 28.52, 28.41, 27.45, 26.04, 22.73, 19.62, 14.06; HR-MS (ESI) Calculated for $C_{25}H_{34}O_4$ $[M+H]^+$; 399.2587 found 399.2592.

2,5-dihydroxy-3-(4-methylbenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5d). The semi-synthesis of the title compound followed the by general experimental procedure B, and the product was isolated by filtration to obtain maroon color solid. (56mg, yield = 89%); mp:164-166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J = 7.6 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.26 (d, J = 3.5 Hz, 1H), 7.20 (d, J = 14.2 Hz, 1H), 3.76 (s, 2H), 2.29 (s, 3H), 1.50 – 1.39 (m, 2H), 1.28 – 1.24 (m, 18H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.25, 177.49, 156.87, 155.39, 140.45, 137.90, 129.70, 129.26, 128.28, 128.22, 125.99, 121.56, 33.88, 31.10, 29.38, 29.23, 28.72, 28.67, 28.47, 28.46, 28.06, 26.00, 22.21, 21.15, 14.77; HR-MS (ESI) Calculated for $C_{25}H_{34}O_4$ $[M+H]^+$; 399.2577 found 399.2574.



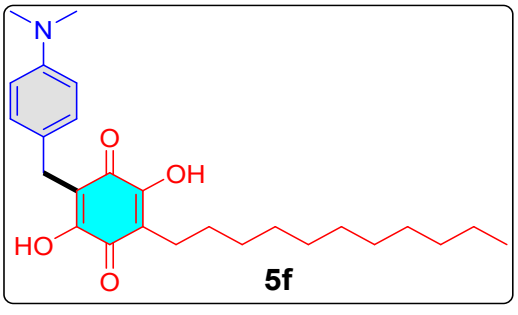
5d

2,5-dihydroxy-3-(4-isopropylbenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5e). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (60mg, yield = 88%); mp:159-161 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, J = 19.2, 7.4 Hz, 2H), 7.21 (dd, J = 21.8, 14.8 Hz, 2H), 4.25 – 4.07 (m, 1H), 3.76 (s, 2H), 2.48 (t, J = 6.4 Hz 2H), 1.53 – 1.34 (m, 6H), 1.32 – 1.22 (m, 18H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.04, 180.04, 156.75, 156.20, 148.06, 140.21, 130.21, 130.10, 127.14, 127.05, 126.21, 120.46, 33.92, 33.14, 31.08, 29.71, 29.10, 28.96, 28.83, 28.71, 28.36, 28.16, 26.55, 23.86, 23.31, 21.14, 14.15; HR-MS (ESI) Calculated for $C_{27}H_{38}O_4$ $[M+H]^+$; 427.1543 found 427.1549.



5e

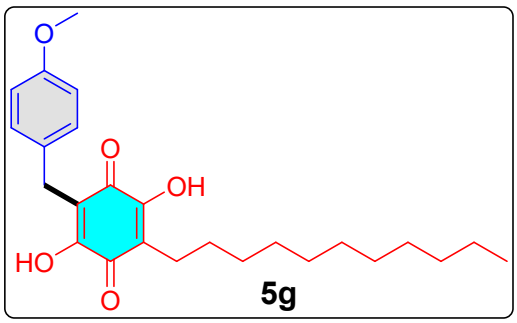
2-(4-(dimethylamino)benzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5f). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (57mg, yield = 84%); mp:163-165 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J = 7.6 Hz, 2H), 7.20 (d, J = 7.1 Hz, 2H), 3.76 (s, 2H), 2.51 (s, 6H), 2.40 (t, J = 7.6 Hz, 2H), 1.29 – 1.24 (m, 18H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ



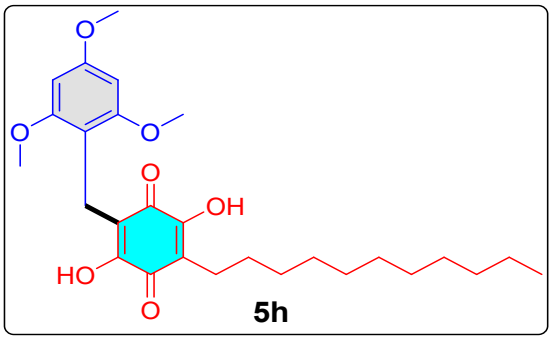
5f

182.80, 180.06, 157.11, 155.44, 150.09, 134.04, 130.76, 128.94, 126.30, 120.39, 114.10, 40.94, 33.02, 31.09, 29.81, 29.10, 29.00, 28.90, 28.87, 28.81, 28.73, 26.56, 23.25, 14.05; HR-MS (ESI) Calculated for $C_{26}H_{37}NO_4$ $[M+H]^+$; 428.1676 found 427.1672.

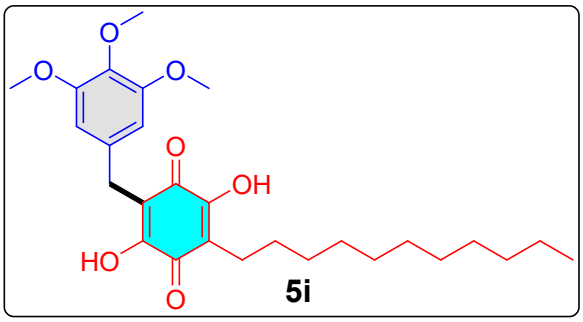
2,5-dihydroxy-3-(4-methoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5g). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (51mg, yield = 77%); mp:164-166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J = 7.6 Hz, 2H), 7.26 (d, J = 7.2 Hz, 2H), 3.76 (s, 3H), 3.51 (s, 2H), 1.49 – 1.38 (t, J = 4.6 Hz, 2H), 1.29 – 1.24 (m, 18H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.08, 180.09, 163.74, 158.16, 155.09, 132.65, 130.82, 130.14, 128.51, 122.54, 114.10, 111.77, 55.08, 37.06, 32.41, 30.81, 29.80, 29.12, 28.94, 28.61, 28.27, 27.41, 26.91, 24.92, 14.52; HR-MS (ESI) Calculated for $C_{25}H_{34}O_5$ $[M+H]^+$; 416.3453 found 427.3452.



2,5-dihydroxy-3-(2,4,6-trimethoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5h). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (58mg, yield = 76%); mp:162-164 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.35 (s, 1H), 3.97 (s, 2H), 3.28 (s, 9H), 2.11 (t, J = 7.1 Hz, 2H), 1.24 – 1.10 (m, 18H), 0.77 (t, J = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.40, 180.05, 161.51, 159.79, 159.59, 157.10, 154.97, 126.31, 120.43, 114.13, 90.69, 90.26, 57.84, 57.62, 56.31, 31.09, 29.80, 29.11, 28.85, 28.62, 28.53, 28.35, 28.10, 26.56, 23.29, 20.04, 14.42; HR-MS (ESI) Calculated for $C_{27}H_{38}O_7$ $[M+H]^+$; 475.1967 found 475.1965.

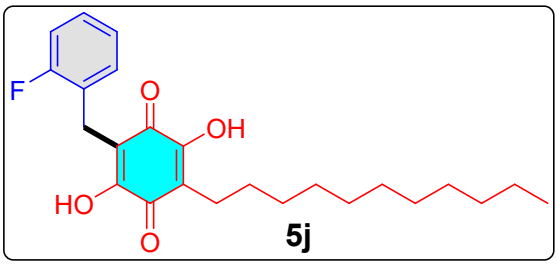


2,5-dihydroxy-3-(3,4,5-trimethoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5i). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (57mg, yield = 75%); mp:164-166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.46 (s, 1H), 5.14 (s, 2H), 3.97 (s, 3H), 3.28 (s, 6H), 2.11 (t, J = 7.1 Hz, 2H), 1.24 – 1.10 (m, 18H), 0.77 (t, J = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.36, 180.13, 157.00, 156.87, 153.83, 153.56, 138.39, 135.22, 126.01, 120.43, 107.18, 107.17,

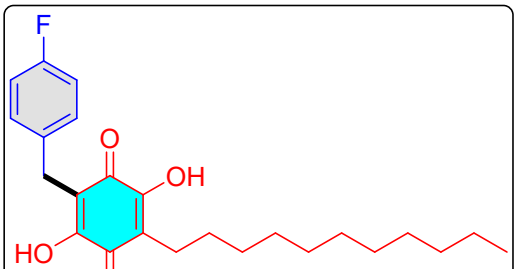


60.13, 60.02, 56.31, 33.87, 31.09, 29.80, 29.11, 28.85, 28.62, 28.53, 28.35, 28.10, 26.56, 23.29, 14.42; HR-MS (ESI) Calculated for $C_{27}H_{38}O_7$ $[M+H]^+$; 475.3542 found 475.3547.

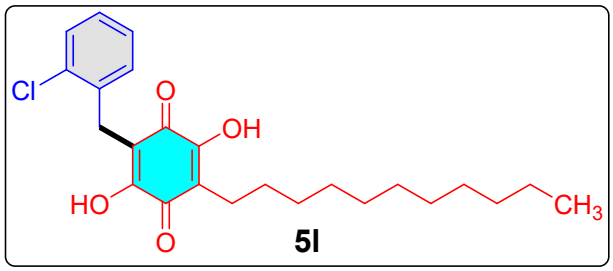
2-(2-fluorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5j). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (58mg, yield = 91%); mp:155-157 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, *J* = 11.8 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 6.2 Hz, 1H), 3.76 (s, 2H), 1.43 (t, *J* = 7.2 Hz, 2H), 1.29 – 1.24 (m, 8H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.39, 180.91, 162.57, 156.90, 156.05, 134.05, 127.79, 127.38, 126.53, 125.44, 120.43, 115.19, 31.40, 31.09, 29.95, 29.74, 28.95, 28.88, 28.76, 28.59, 28.39, 26.56, 23.29, 14.02; HR-MS (ESI) Calculated for $C_{24}H_{31}FO_4$ $[M+H]^+$; 403.2507 found 403.2517.



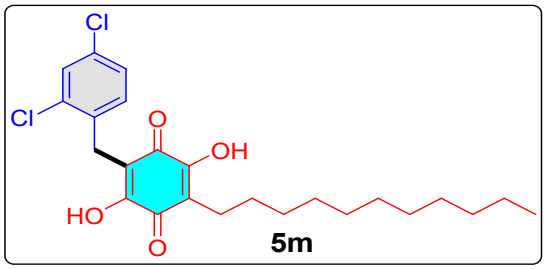
2-(4-fluorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5k). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (57mg, yield = 89%); mp:158-160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.3 Hz, 1H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.26 (d, *J* = 7.2 Hz, 1H), 7.20 (d, *J* = 7.1 Hz, 1H), 3.76 (s, 2H), 2.41 (t, *J* = 7.5 Hz, 2H), 1.33 – 1.21 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.22, 180.04, 162.04, 160.60, 157.55, 156.09, 135.02, 131.68, 130.09, 125.88, 119.76, 116.50, 114.71, 33.70, 31.96, 29.71, 29.10, 28.87, 28.73, 28.65, 28.54, 28.42, 28.34, 25.84, 22.65, 14.14; HR-MS (ESI) Calculated for $C_{24}H_{31}FO_4$ $[M+H]^+$; 403.3756 found 403.3755.



2-(2-chlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5l). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (60mg, yield = 90%); mp:158-160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.20 (t, *J* = 7.1 Hz, 1H), 3.76 (s, 2H), 2.41 (t, *J* = 7.5 Hz, 2H), 1.48 – 1.39 (m, 2H), 1.28 – 1.24 (m, 16H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.33, 180.18, 156.60, 154.22, 138.72, 134.84, 131.28, 130.20,

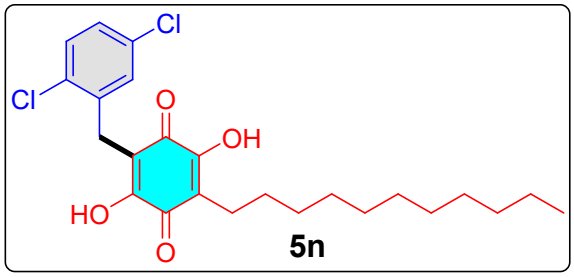


128.27, 127.63, 126.35, 122.35, 31.94, 30.86, 29.71, 29.37, 28.99, 28.76, 28.58, 28.28, 28.02, 26.04, 22.70, 14.12; HR-MS (ESI) Calculated for $C_{24}H_{31}ClO_4$ $[M+H]^+$; 419.1952 found 419.1952.

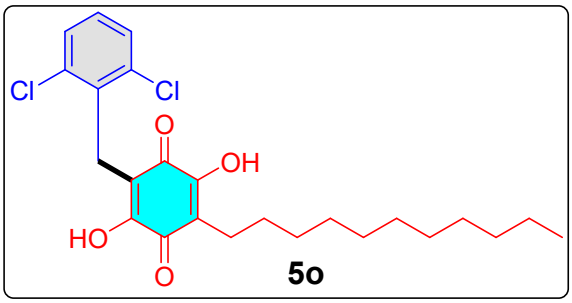


2-(2,4-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5m). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (58mg, yield = 81%); mp:159-161 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.10 (d, *J* = 8.2 Hz, 1H), 3.88 (s, 2H), 2.41 (t, *J* = 6.7 Hz, 2H), 1.45 (t, *J* = 6.2 Hz, 2H), 1.27– 24 (m, 16H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.39, 180.04, 157.74, 156.05, 135.09, 134.02, 132.91, 132.02, 131.33, 128.02, 126.35, 122.04, 31.08, 30.84, 30.42, 29.84, 29.66, 29.28, 28.92, 28.64, 28.11, 26.55, 21.14, 14.03. HR-MS (ESI) Calculated for $C_{24}H_{30}Cl_2O_4$ $[M+H]^+$; 453.1654 found 453.1654.

2-(2,5-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5n). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (59mg, yield = 82%); mp:159-161 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.1 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.31 (s, 1H), 3.97 (s, 2H), 2.11 (t, *J* = 7.1 Hz, 2H), 1.23 – 1.11 (m, 18H), 0.77 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.25, 180.01, 157.51, 155.17, 142.46, 135.06, 133.63, 131.53, 130.27, 127.70, 126.38, 122.00, 33.94, 31.92, 29.68, 29.58, 28.96, 28.84, 28.64, 28.43, 28.20, 27.20, 22.68, 14.10; HR-MS (ESI) Calculated for $C_{24}H_{30}Cl_2O_4$ $[M+H]^+$; 453.1864 found 453.1869.

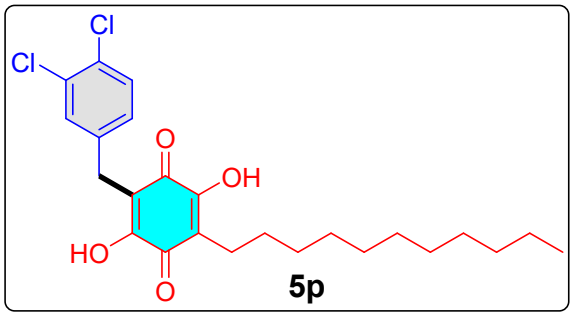


2-(2,6-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5o). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (61mg, yield = 85%); mp:167-169 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.1 Hz, 1H), 3.76 (s, 2H), 2.40 (t, *J* = 7.6 Hz, 2H), 1.46 (t, *J* = 7.4 Hz, 2H), 1.28 (m, 16H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.22, 180.04, 157.48, 156.40, 136.91, 135.28, 135.11, 130.62, 130.03,

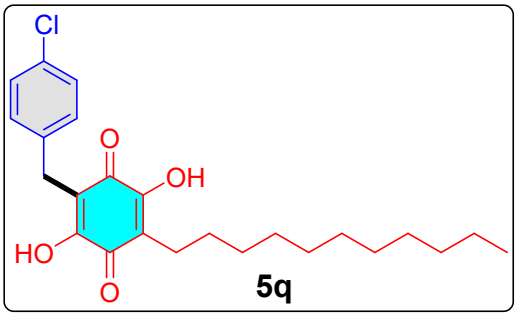


129.70, 125.14, 121.32, 31.94, 31.56, 29.71, 29.37, 28.87, 28.71, 28.48, 28.30, 28.01, 26.04, 22.70, 14.13; HR-MS (ESI) Calculated for $C_{24}H_{30}Cl_2O_4$ $[M+H]^+$; 453.1623 found 453.1622.

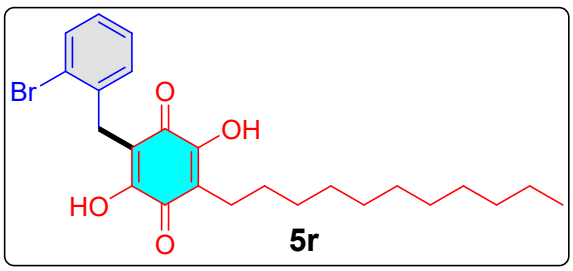
2-(3,4-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5p). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (60mg, yield = 83%); mp:168-170 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 8.1 Hz, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.31 (s, 1H), 3.97 (s, 2H), 2.11 (t, J = 7.1 Hz, 2H), 1.23 – 1.11 (m, 18H), 0.77 (t, J = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.31, 180.39, 158.89, 155.09, 143.98, 132.64, 130.10, 130.02, 129.02, 128.00, 126.03, 120.73, 36.36, 31.73, 29.55, 29.28, 28.97, 28.84, 28.53, 28.27, 28.03, 25.14, 22.60, 14.04; HR-MS (ESI) Calculated for $C_{24}H_{30}Cl_2O_4$ $[M+H]^+$; 453.1802 found 453.1802.



2-(4-chlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5q). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (61mg, yield = 91%); mp:165-167 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, J = 7.3 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H), 7.25 (d, J = 7.2 Hz, 1H), 7.20 (d, J = 7.2 Hz, 1H), 3.76 (s, 2H), 2.41 (t, J = 7.5 Hz, 3H), 1.33 – 1.21 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.78, 180.29, 158.90, 156.59, 138.39, 131.58, 130.32, 128.71, 126.08, 121.16, 33.85, 31.79, 29.77, 29.44, 28.97, 28.84, 28.54, 28.33, 28.04, 26.62, 22.15, 14.44; HR-MS (ESI) Calculated for $C_{24}H_{31}ClO_4$ $[M+H]^+$; 419.3657 found 419.3657.

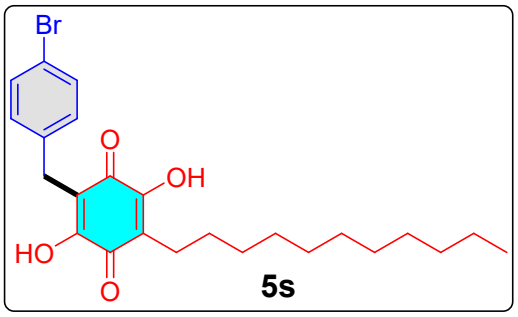


2-(2-bromobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5r). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (69mg, yield = 93%); mp:163-165 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, J = 7.3 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H), 7.25 (t, J = 7.6 Hz, 1H), 7.20 (t, J = 7.2 Hz, 1H), 3.76 (s, 2H), 1.44 (t, J = 6.2 Hz, 2H), 1.30 – 1.23 (m, 16H), 0.88 (t, J = 6.8 Hz, 7H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.96, 180.18, 157.45, 155.29, 139.36, 132.64, 131.03, 128.03, 126.00, 124.02, 120.73, 36.43, 31.73, 29.59,

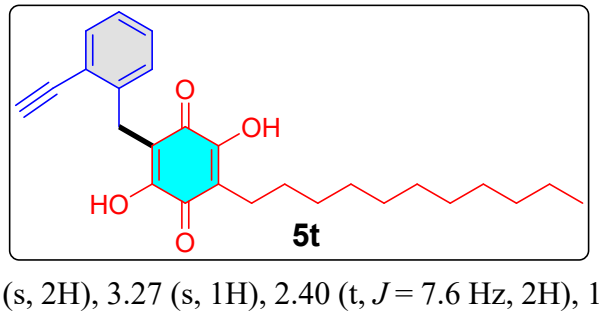


29.28, 28.97, 28.81, 28.56, 28.44, 28.27, 25.23, 22.60, 14.04; HR-MS (ESI) Calculated for $C_{24}H_{31}BrO_4$ $[M+H]^+$; 463.1401 found 463.1410.

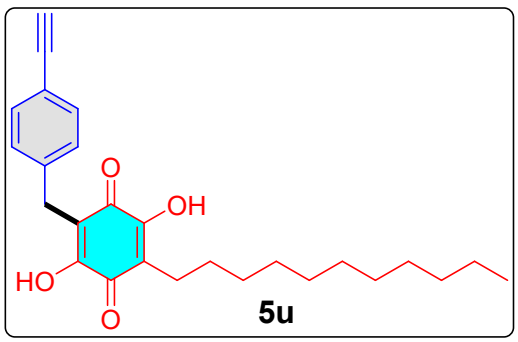
2-(4-bromobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5s). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (59mg, yield = 89%); mp:165-167 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J = 7.6 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.26 (d, J = 3.5 Hz, 1H), 7.20 (d, J = 14.2 Hz, 1H), 3.76 (s, 2H), 1.43 (t, J = 7.6 Hz, 2H), 1.28 (m, 19H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.75, 180.19, 156.37, 155.08, 138.01, 132.29, 131.58, 130.06, 129.43, 126.08, 122.46, 121.31, 33.57, 31.11, 29.84, 29.71, 28.91, 28.77, 28.51, 28.33, 28.16, 26.62, 22.18, 14.17; HR-MS (ESI) Calculated for $C_{24}H_{31}BrO_4$ $[M+H]^+$; 463.1843 found 463.1848.



2-(2-ethynylbenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5t). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (36mg, yield = 53%); mp:174-176 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J = 7.6 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.25 (t, J = 8.4 Hz 1H), 7.20 (t, J = 7.5 Hz, 1H), 3.76 (s, 2H), 3.27 (s, 1H), 2.40 (t, J = 7.6 Hz, 2H), 1.28 – 24 (m, 18H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.17, 180.01, 157.44, 155.02, 142.56, 132.74, 130.03, 127.55, 126.75, 122.56, 119.20, 85.30, 82.70, 31.93, 31.54, 29.63, 29.55, 28.79, 28.54, 28.35, 28.21, 27.95, 26.07, 22.70, 14.14; HR-MS (ESI) Calculated for $C_{26}H_{32}O_4$ $[M+H]^+$; 409.2901 found 409.2908.

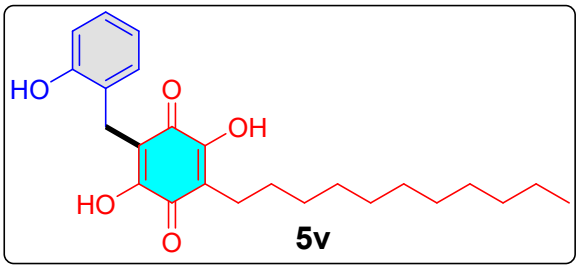


2-(4-ethynylbenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5u). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (35mg, yield = 52%); mp:170-172 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, J = 7.1 Hz, 1H), 7.28 (d, J = 7.7 Hz, 1H), 7.23 (d, J = 22.2 Hz, 1H), 7.20 (d, J = 7.2 Hz, 1H), 3.76 (s, 2H), 2.85 (s, 1H), 2.60 – 2.20 (m, 2H), 1.42 (t, J = 6.6 Hz, 2H), 1.41 – 1.10 (m, 16H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.38, 180.02, 157.76, 155.08, 147.90, 132.80, 131.58, 130.04, 129.06, 126.08, 121.50, 118.05, 84.36, 33.70, 31.76,

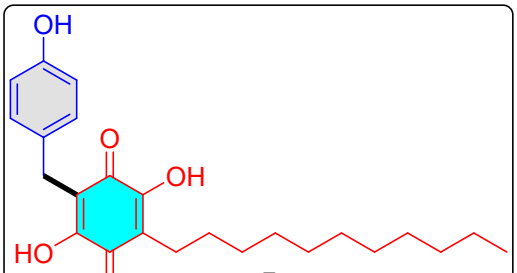


29.99, 29.72, 28.91, 28.72, 28.56, 28.38, 28.13, 26.62, 22.58, 14.20; HR-MS (ESI) Calculated for $C_{26}H_{32}O_4$ $[M+H]^+$; 409.2865 found 409.2872.

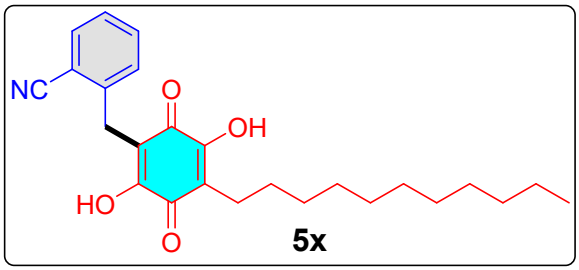
2,5-dihydroxy-3-(2-hydroxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5v). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (42mg, yield = 65%); mp:155-157 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, J = 7.3 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H), 7.26 (t, J = 7.5 Hz, 1H), 7.20 (t, J = 7.2 Hz, 1H), 3.76 (s, 2H), 1.45 (t, J = 6.2 Hz, 9H), 1.33 – 1.21 (m, 18H), 0.88 (t, J = 6.8 Hz, 14H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.38, 180.01, 157.44, 156.68, 155.62, 130.04, 128.04, 127.05, 126.04, 122.04, 121.08, 116.00, 31.81, 29.57, 29.15, 28.82, 28.60, 28.51, 28.27, 28.03, 26.82, 24.04, 21.24, 19.62, 14.05; HR-MS (ESI) Calculated for $C_{24}H_{32}O_5$ $[M+H]^+$; 401.2361 found 401.2365.



2,5-dihydroxy-3-(4-hydroxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5w). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (37mg, yield = 58%); mp:156-158 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 8.1 Hz, 1H), 7.37 (d, J = 7.0 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H), 3.97 (s, 2H), 2.11 (t, J = 7.1 Hz, 2H), 1.15 (s, 18H), 0.77 (t, J = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.23, 180.15, 160.85, 158.99, 156.99, 134.12, 132.55, 130.06, 126.69, 121.51, 117.00, 114.91, 33.56, 31.93, 29.66, 29.56, 28.99, 28.89, 28.75, 28.63, 28.54, 27.95, 26.05, 22.70, 14.14; HR-MS (ESI) Calculated for $C_{24}H_{32}O_5$ $[M+H]^+$; 401.2387 found 401.2387.

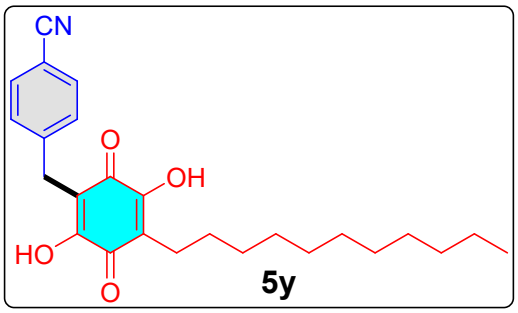


2-((2,5-dihydroxy-3,6-dioxo-4-undecylcyclohexa-1,4-dien-1-yl)methyl)benzonitrile (5x). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (47mg, yield = 72%); mp:146-148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, J = 7.3 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H), 7.25 (t, J = 7.2 Hz, 1H), 7.20 (t, J = 7.2 Hz, 1H), 3.76 (s, 2H), 2.48 – 2.37 (m, 2H), 1.43 (t, J = 12.5 Hz, 2H), 1.30 – 1.23 (m, 16H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.17, 180.02, 157.19, 155.04, 141.41, 132.64, 131.79, 130.50,

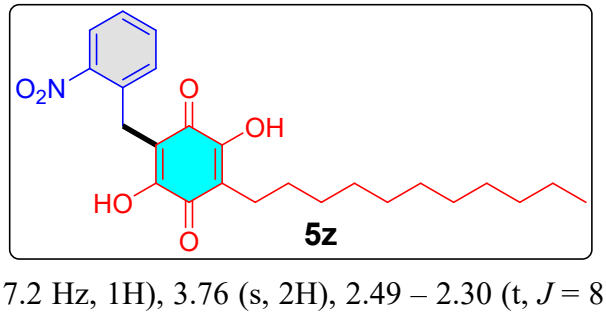


127.75, 126.36, 122.41, 120.73, 111.02, 31.93, 31.73, 29.59, 29.28, 28.87, 28.76, 28.62, 28.42, 28.31, 28.14, 25.14, 22.60, 14.04; HR-MS (ESI) Calculated for $C_{25}H_{31}NO_4$ $[M+H]^+$; 409.2394 found 410.2387.

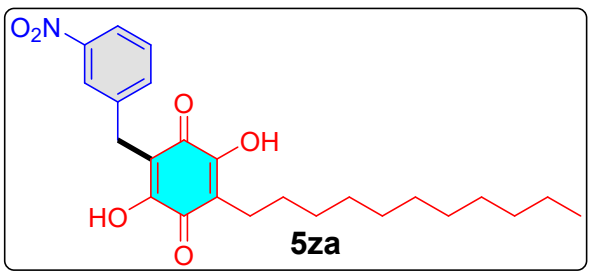
4-((2,5-dihydroxy-3,6-dioxo-4-undecylcyclohexa-1,4-dien-1-yl)methyl)benzonitrile (5y). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (44mg, yield = 67%); mp:146-148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.1 Hz, 1H), 7.37 (d, *J* = 7.0 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.27 (d, *J* = 7.5 Hz, 1H), 3.97 (s, 2H), 2.11 (t, *J* = 7.1 Hz, 2H), 1.15 (s, 18H), 0.77 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.03, 180.06, 156.74, 155.04, 148.45, 132.88, 131.41, 130.40, 129.21, 126.46, 121.10, 118.29, 84.20, 81.42, 33.02, 31.93, 29.66, 29.63, 29.56, 29.55, 29.39, 29.35, 28.99, 28.71, 27.95, 26.01, 22.70, 14.14; HR-MS (ESI) Calculated for $C_{25}H_{31}NO_4$ $[M+H]^+$; 409.1087 found 410.1094.



2,5-dihydroxy-3-(2-nitrobenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5z). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (64mg, yield = 93%); mp:136-138 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 7.4 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 3.76 (s, 2H), 2.49 – 2.30 (t, *J* = 8.2 Hz, 2H), 1.43 – 1.11 (m, 18H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.07, 180.04, 157.35, 155.01, 148.43, 134.01, 133.18, 131.22, 127.61, 126.58, 125.52, 122.11, 31.08, 29.74, 29.30, 29.00, 28.60, 28.46, 28.29, 28.13, 28.08, 26.55, 22.01, 14.42; HR-MS (ESI) Calculated for $C_{24}H_{31}NO_6$ $[M+H]^+$; 430.4175 found 430.4184.

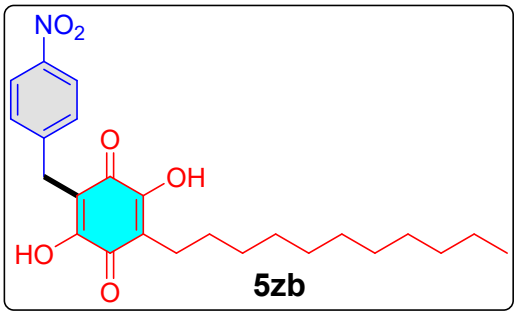


2,5-dihydroxy-3-(3-nitrobenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5za). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (61mg, yield = 89%); mp:132-134 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 3.76 (s, 2H), 2.40 (t, *J* = 7.6 Hz, 2H), 1.28 (m, 18H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.16, 180.12, 157.18, 155.13, 149.46, 140.05, 135.06, 128.30, 126.34, 125.45,



124.73, 121.82, 34.06, 31.02, 29.66, 29.18, 28.93, 28.76, 28.55, 28.30, 28.08, 25.66, 22.01, 14.05; HR-MS (ESI) Calculated for $C_{24}H_{31}NO_6$ $[M+H]^+$; 430.5867 found 430.5872.

2,5-dihydroxy-3-(4-nitrobenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (5zb). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (59mg, yield = 86%); mp:152-154 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.47 (d, J = 8.1 Hz, 1H), 7.37 (d, J = 7.0 Hz, 1H), 7.34 (d, J = 7.4 Hz, 1H), 7.24 (d, J = 7.2 Hz, 1H), 3.97 (s, 2H), 2.11 (t, J = 7.1 Hz, 2H), 1.23 – 1.11 (m, 18H), 0.77 (t, J = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.38, 180.04, 158.31, 155.40, 150.30, 147.39, 129.70, 128.42, 126.73, 124.39, 121.49, 33.71, 31.81, 29.57, 29.15, 28.91, 28.78, 28.60, 28.40, 28.23, 26.82, 21.24, 14.05; HR-MS (ESI) Calculated for $C_{24}H_{31}NO_6$ $[M+H]^+$; 430.6243 found 430.6247.



5zb

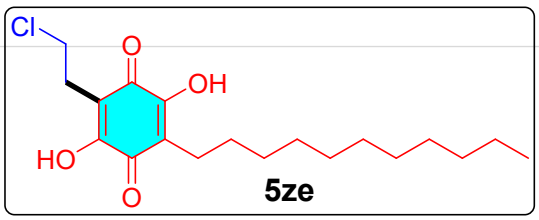
2-ethyl-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5zc). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (35mg, yield = 68%); mp:132-134 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.40 (t, J = 7.6 Hz, 2H), 1.43 (T, J = 7.9 Hz, 2H), 1.28 (dd, J = 16.1, 10.0 Hz, 16H), 1.09 (t, J = 7.5 Hz, 3H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.76, 180.39, 157.87, 155.30, 124.84, 122.56, 31.93, 29.66, 29.63, 29.56, 29.55, 29.39, 29.35, 27.95, 22.70, 22.53, 14.14; HR-MS (ESI) Calculated for $C_{19}H_{30}O_4$ $[M+H]^+$; 323.4532 found 323.4538.

5zc

2,5-dihydroxy-3-isobutyl-6-undecylcyclohexa-2,5-diene-1,4-dione (5zd). The semi-synthesis of the title compound followed by the general experimental procedure B, and the product was isolated by filtration to obtain maroon colour solid. (32mg, yield = 57%); mp:135-137 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.40 (m, 1H), 2.18 (d, J = 7.8 Hz, 2H), 1.43 (dd, J = 7.9 Hz, 2H), 1.28 (m, 16H), 1.20 (d, J = 5.9 Hz, 6H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.50, 180.17, 157.58, 155.21, 124.30, 123.01, 32.84, 32.20, 30.17, 29.71, 28.72, 28.71, 28.52, 28.44, 27.07, 26.43, 22.93, 22.24, 21.03, 14.10; HR-MS (ESI) Calculated for $C_{21}H_{34}O_4$ $[M+H]^+$; 351.2106 found 351.2112.

5zd

2-(2-chloroethyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (5ze). The semi-synthesis of the title compound followed by the general experimental procedure B,



5ze

and the product was isolated by filtration to obtain maroon colour solid. (30mg, yield = 53%); mp:130-132 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.17 (t, *J* = 10.6 Hz, 2H), 2.40 (t, *J* = 7.6 Hz, 2H), 2.23 (t, *J* = 7.4 Hz, 2H), 1.28 (m, 18H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.17, 180.05, 157.75, 155.19, 122.54, 122.23, 32.41, 29.70, 29.37, 28.76, 28.58, 28.25, 28.15, 28.06, 26.91, 24.92, 22.53, 14.35; HR-MS (ESI) Calculated for $C_{19}H_{29}ClO_4$ $[M+H]^+$; 357.1065 found 357.1073.

Biological evaluations

1. Antioxidant activity assays

Table S4. Antioxidant (DPPH and ABTS assay) activity of rapanone (**1**), C-alkylation of rapanone derivatives (**5a-5ze**) and standard drug IC_{50} and SEM values.

Entry	Compounds	[a]DPPH-Radical scavenging activity [c]IC_{50} ± [d]SEM (μM)	[b]ABTS-Radical scavenging activity IC_{50} ± SEM (μM)
1	**1**[e]	3.12 ±1	3.12 ± 0.66
2	**5a**[f]	3.18 ± 1.42	2.71 ± 0.86
3	**5b**	2.88 ± 1	2.36 ± 0.67
4	**5c**	2.51 ± 0.66	2.05 ± 0.94
5	**5d**	1.81 ± 2	1.81 ± 0.74
6	**5e**	1.91 ± 0.66	1.91 ± 1.20
7	**5f**	3.37 ± 1	2.91 ± 1
8	**5g**	3.16 ± 0.33	2.72 ± 0.44
9	**5h**	3.07 ± 1	2.60 ± 0.54
10	**5i**	2.95 ± 0.66	2.48 ± 0.68
11	**5j**	4.62 ± 1.33	5.44 ± 0.38
12	**5k**	4.65 ± 0.66	5.22 ± 0.98
13	**5l**	4.62 ± 1.33	5.54 ± 0.74
14	**5m**	4.74 ± 1.66	4.43 ± 0.34

15	**5n**	4.69 ± 0.66	5.32 ± 1.24
16	**5o**	4.87 ± 0.33	5.21 ± 1.25
17	**5p**	4.87 ± 0.68	5.09 ± 1.45
18	**5q**	4.93 ± 0.39	4.99 ± 1.30
19	**5r**	4.57 ± 0.76	5.54 ± 1.36
20	**5s**	4.59 ± 0.32	5.14 ± 1.12
21	**5t**	4.94 ± 0.34	4.96 ± 1.16
22	**5u**	4.90 ± 0.38	4.72 ± 0.66
23	**5v**	3.05 ± 1.66	2.87 ± 2.20
24	**5w**	2.83 ± 1	2.70 ± 0.43
25	**5x**	4.43 ± 0.67	5.01 ± 0.78
26	**5y**	4.58 ± 0.38	5.15 ± 0.67
27	**5z**	4.76 ± 0.30	5.34 ± 0.74
28	**5za**	4.80 ± 0.39	5.36 ± 0.30
29	**5zb**	4.90 ± 0.10	5.25 ± 0.45
30	**5zc**	2.61 ± 0.	2.44 ± 0.71
31	**5zd**	2.48 ± 0.37	2.30 ± 0.42
32	**5ze**	4.60 ± 0.65	4.41 ± 0.72
33	**L-Aa**[g]	1.87 ± 1	1.42 ± 0.68

[a] α-diphenyl-β-picrylhydrazyl (DPPH), [b] 2,2′-azino-bis-(3-ethylbenzothiazoline-6-sulfonic) acid (ABTS) for free radical scavenging, [c]Inhibitory concentration is estimated to inhibit 50% of specific assay activity, [d] standard error mean, [e] Isolated compound rapanone form *embelia ribes,* [f] synthesis of rapanone derivatives, [g] standard drug for DPPH and ABTS-radical scavenging activity of L-Ascosporic acid.

Antioxidant activity evaluation of derivatives through DPPH and ABTS assays

The synthesised rapanone derivatives (**5a–5ze**) were tested for antioxidant activity using two different methods: the 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay and the 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)

(ABTS) radical scavenging method[4]. The amount of 0.2 mM in 7.88 mg DPPH in 100 mL amber bottle was precisely measured and dissolved in methanol (AR grade) and the solution was covered with aluminium foil and kept in a dark place. It was also protected from light. After 30 mins in the dark at room temperature, absorbance was measured and found to be at 517nm. Using results obtained at 517nm, the percentage of DPPH radical scavenging activity was calculated. Briefly, an equal volume of a 7 mmol ABTS stock solution was mixed with a 2.45 mmol potassium persulfate solution to make it a 100 mL ABTS solution. The mixture was then stored at room temperature in the dark for 12–16 h. After diluting the ABTS solution with 10 mmol of phosphate-buffered saline (PBS, pH 7.4), the absorbance was measured and found to be at 734nm, which was 0.70 ± 0.02. And 800 mM of all compounds was dissolved in 1 mL of dimethyl sulfoxide (DMSO) using ultrasonic bath equipment and the results were compared to standard L-ascorbic acid.

DPPH and ABTS+ scavenging abilities of compounds (**1** and **5a-5ze**) at various concentrations studied for antioxidant activity against free radicals. The ability of a pure anti-oxidant compound (**1**) isolated from Embelia ribes to donate electrons or hydrogen have both been extensively studied using the stable radical DPPH[5]. It is a stable free radical that is commonly used as a substrate to assess anti-oxidant activity. The scavenging activity of compounds (**1**) and (**5a–5ze**) at 5–160 μM was determined by method[6] with some modifications. Another approach, ABTS, is based on the ability of antioxidants to quench the long-lived ABTS radical cation, a blue/green chromophore with a characteristic absorption at 734nm. The radical scavenging activity of the ABTS was determined using the method described[7] with some modifications. Various concentrations 5–160 μM of compounds were mixed with the ABTS+ solution, and a decrease in absorbance at 734nm was recorded. The percentages of radical inhibition absorbance (I%) in relation to the control values are expressed in the following equation[8]:

$$I\%\ RSA = \left[\left(\frac{Ac - As}{Ac}\right) \times 100\right]$$

Where, RSA represents the Radical Scavenging Activity, Ac represents the Absorbance of the Control compounds excluding the test compounds; while as represents the absorbance of the tested compounds and all assays were carried out in triplicate[9]. A methanolic solution of DPPH and ABTS was tested in a 96-well plate, followed by a sample or solvent for the blank. The reaction mixture was then incubated at room temperature for 30 mins before being measured for absorbance using a microplate spectrophotometer (Multiskan Go, Thermo Scientific, Waltham, MA USA 02451).

2. (i) Zebrafish maintenance and egg collection

A commercial dealer at (No. 3 Laxmi Avenue, Bhajan Kovil Street, Kolathur, Chennai-600 099, Tamil Nadu, India), provided the zebrafish (Danio rerio, wild type) in the month of January 2023. The Institute Animal Ethic Committee (IACE). In this study was performed in line with the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) for experimentation on zebrafish embryo and larvae (2022). approved this experiment at SRM College of Pharmacy, SRMIST, Kattankulathur, Chengalpattu-603203, Tamil Nadu, India[10]. Adult zebrafish were kept in a closed-circuit aquarium system with regulated physicochemical parameters such as temperature, pH, hardness, conductivity, and ammonia during a 14 h light / 10 h dark cycle[11]. Micro pellet feed was given three times per day. Prior to the intense spawning activity, males and females were separated. Eggs were harvested and cleaned with sterile, dechlorinated tap water immediately after spawning[10]. Any eggs that failed to hatch or were deformed were rejected after a visual inspection to confirm fecundity. The ten embryos were then transferred one at a time into petri dish plates for embryotoxicity testing.

Zebrafish Embryo Toxicity (ZET)

The compound (**1**) and each rapanone derivatives (**5a–5ze**) were diluted with milli-Q water in a 2 mL Eppendorf tube at a concentration of 160 μM/mL. The screening medium contained DMSO, which was used to dissolve the compounds at a concentration that was 0.25 v/v or less in the final solutions. To test the effect of the solvent, milli-Q water was used as a negative control and milli-Q water with 0.5% DMSO as a positive control. Embryos were kept in an incubator at 26.8 ± 1 °C. The number of coagulated embryos indicates developmental delay, deformity (which indicates general developmental retardation), tail detachment, and the absence of a heartbeat (visible after 48 hpf). All normal-developing embryos were tested for lethal endpoints at 96 hpf and the morphological changes were monitored as mentioned earlier[12]. The hatching time was also recorded in order to investigate the effects of a delay on embryo development. From the beginning of the experiment until 48 hpf, all of the significant effects on the embryos caused by (**1** and **5a-5ze**) were noted at every 24 hpf. The lethality of each embryo was determined and imaged using an inverted microscope (LEICA, Lab India). Zebrafish were cared for carefully and treated in accordance with protocols approved by appropriate authorities.

Molecular docking

In this study, Auto dock version 4.2 with Auto Dock tools and MGL tools were used to investigate the binding energy values[13]. The H_2O molecules were removed, and polar hydrogen atoms were introduced into the compounds' structures. The docking output LES were opened in Pymol version 1.7.4.5 Edu to investigate the binding interaction. It should be noted that no previous docking studies of those with the (**1, 5a-5i, 5v, 5w, 5zc, 5zd** and **L-Aa**) compounds target DPPH and ABTS assay antioxidant protein (PDB: 1ZB6) were conducted[14]. From there, we investigated their interaction behaviour using in silico analysis. The correlations of (**1, 5a-5i, 5v, 5w, 5zc, 5zd** and **L-Aa**) crystal structures were investigated. The insertion of (**1, 5a-5i, 5v, 5w, 5zc, 5zd** and **L-Aa**) as ligands within the crystal structure binding site of a protein (PDB: 1ZB6) was used to gain a better understanding of the molecule's potency and the structure-activity relationship (SAR).

Statistical Analysis

The experimental results were presented as means ± standard deviation (SD) to demonstrate the differences between groups. ANOVA was used for statistical analysis, followed by a Newman-Keuls multiple comparison test wherever necessary. At a probability of less than 5%, the differences were considered statistically significant ($p<0.05$)[15]. Every test was repeated at least three times in duplicate. The IC_{50} values (the sample concentration required to scavenge 50% of the free radicals) were calculated using a graph of the scavenging effect percentage versus compound concentration.

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Scanned copies of ^{1}H and ^{13}C NMR Spectra 1 and 5a-5ze.

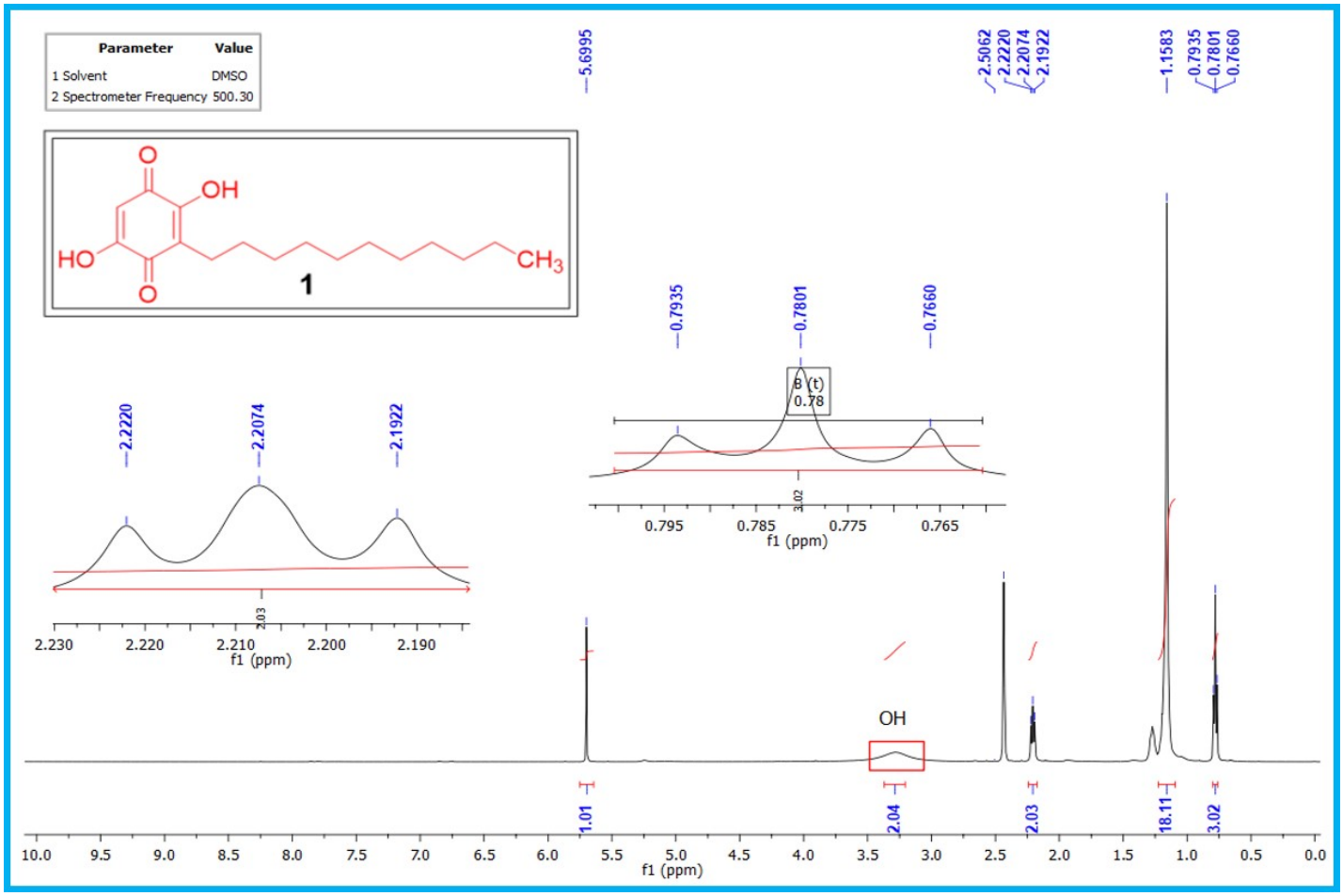


Fig. S2. ^{1}H NMR spectrum of rapanone (**1**).

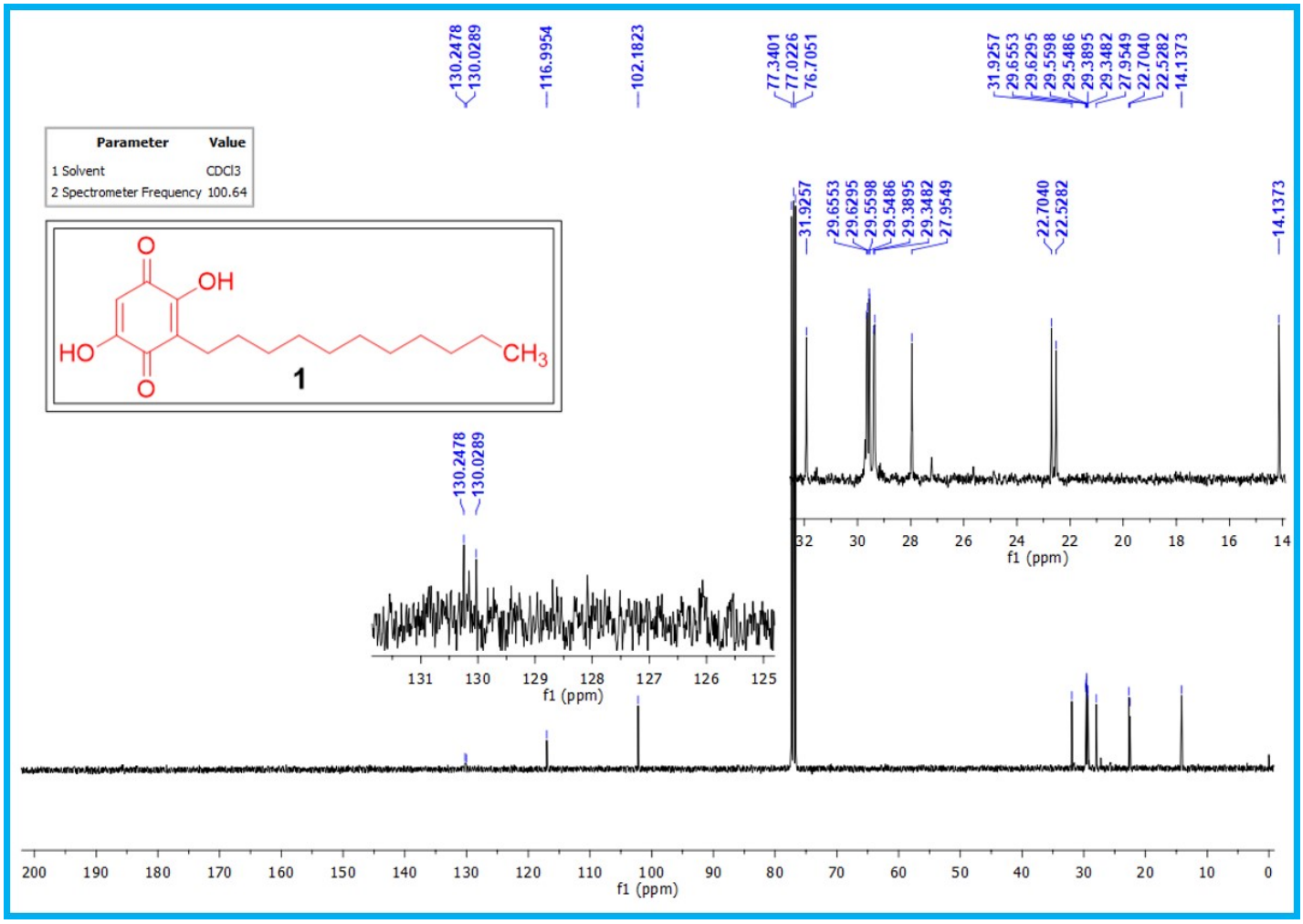


Fig. S3. ^{13}C NMR spectrum of rapanone (**1**).

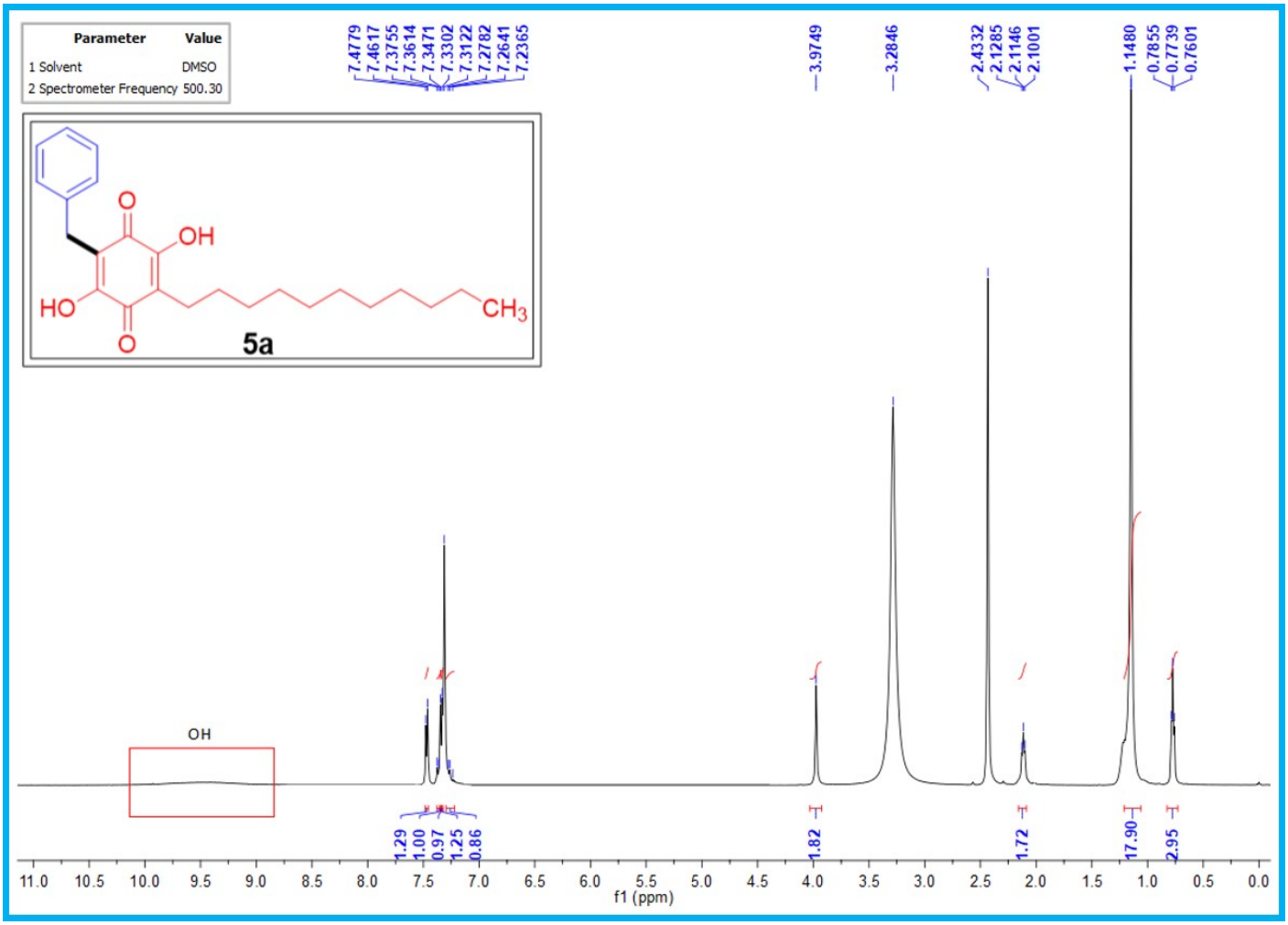


Fig. S4. ^{1}H NMR spectrum of 2-benzyl-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5a**).

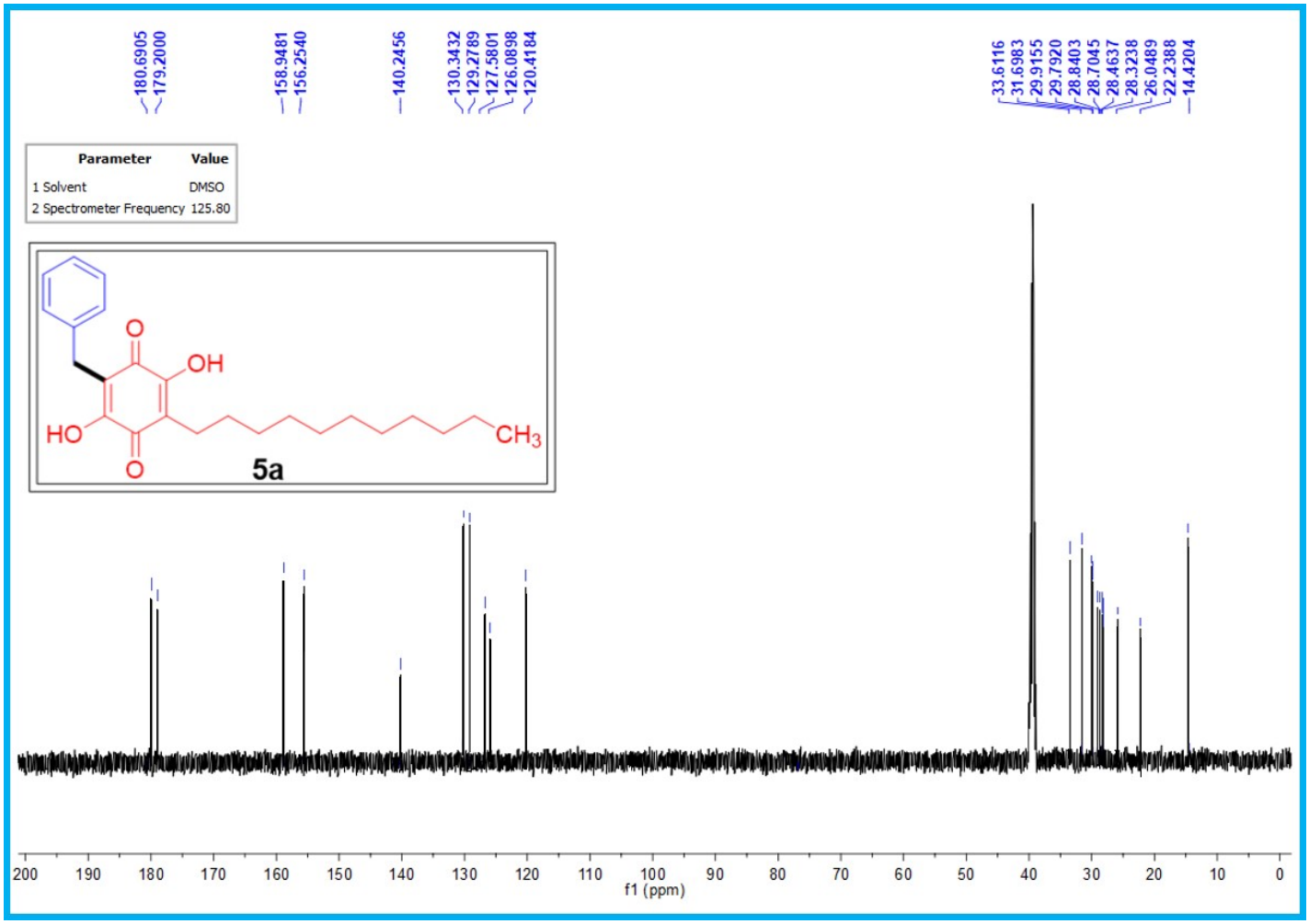


Fig. S5. ^{13}C NMR spectrum of 2-benzyl-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5a**).

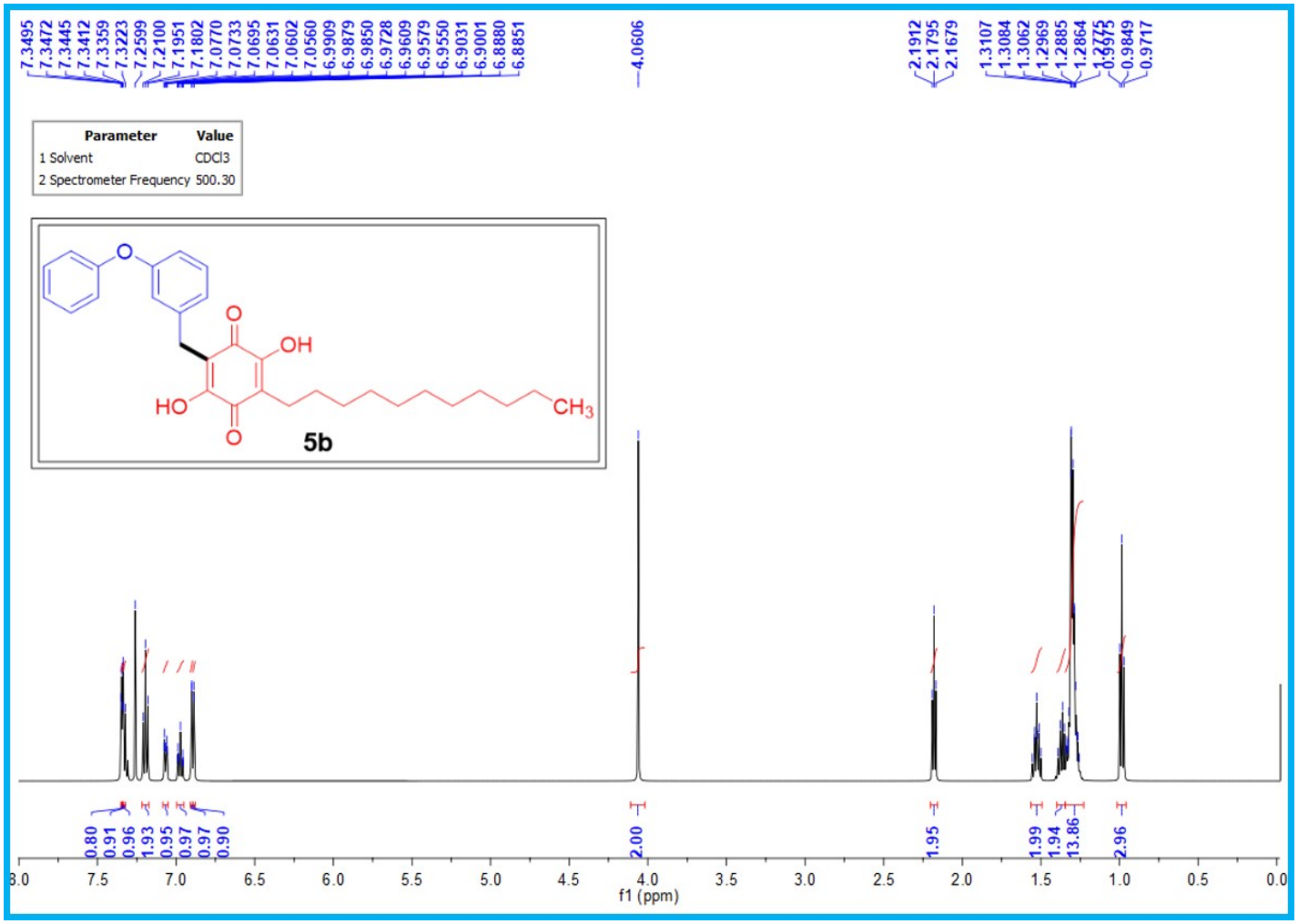


Fig. S6. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(3-phenoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5b**).

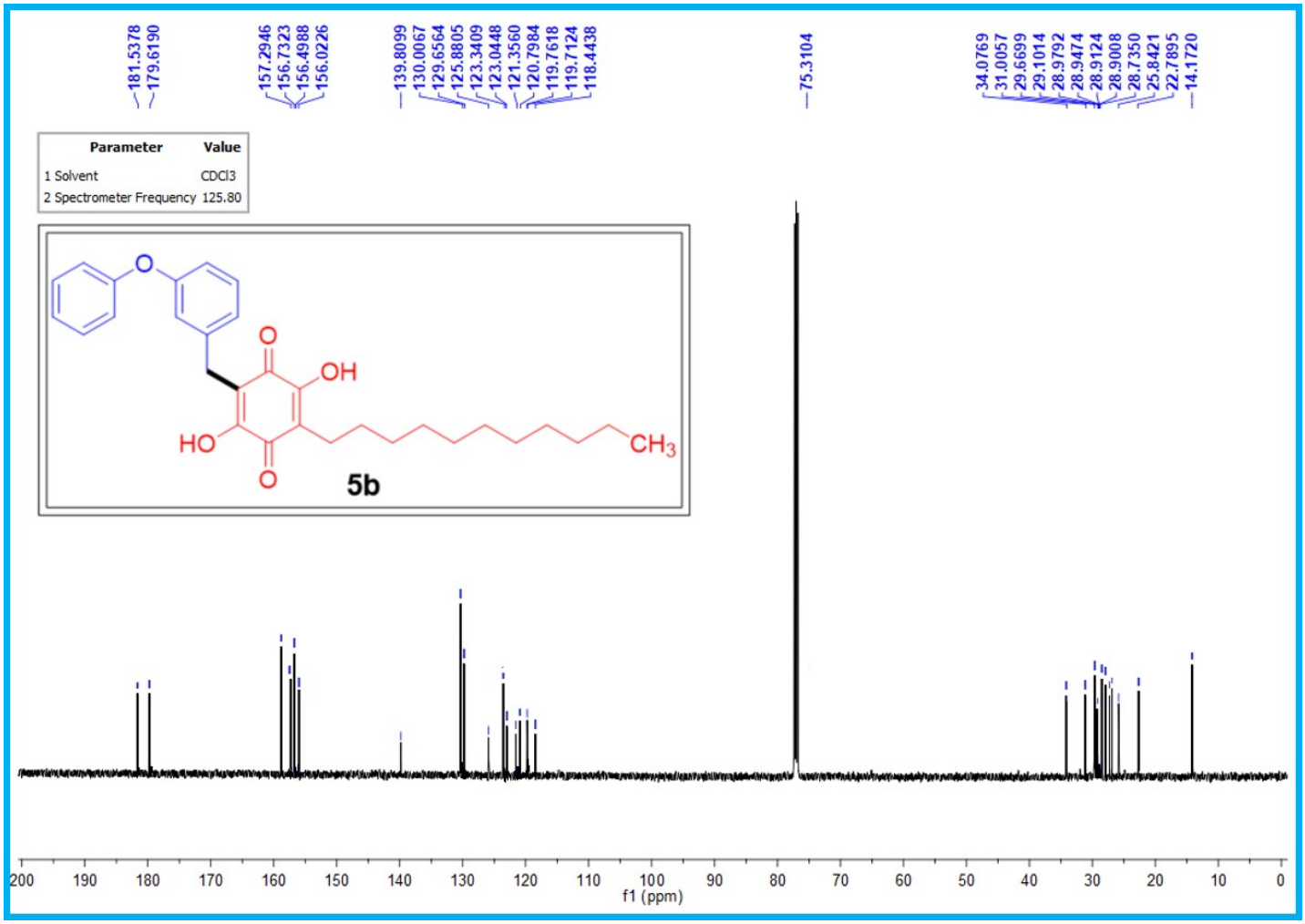


Fig. S7. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(3-phenoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5b**).

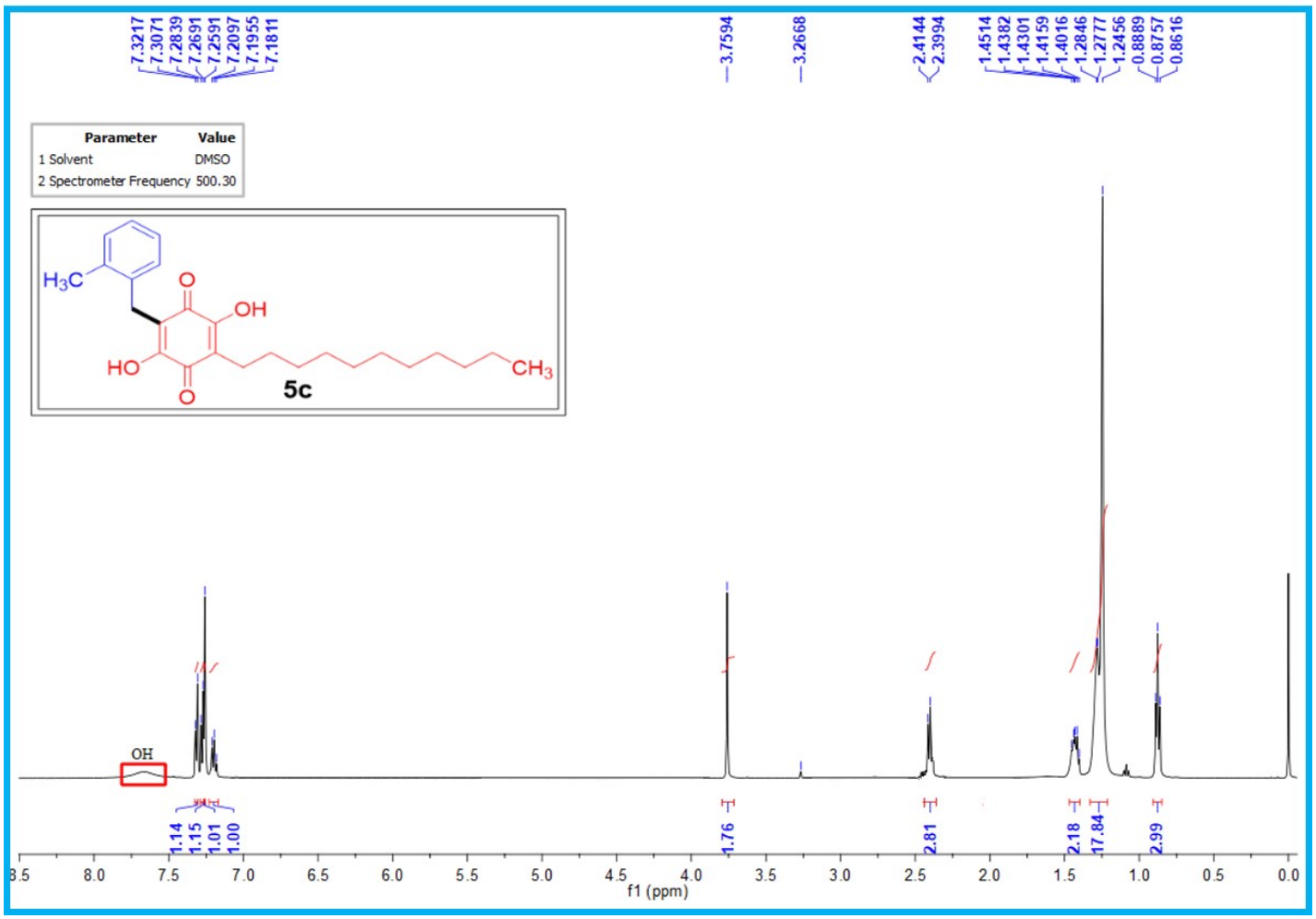


Fig. S8. [1]H NMR spectrum of 2,5-dihydroxy-3-(2-methylbenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5c**).

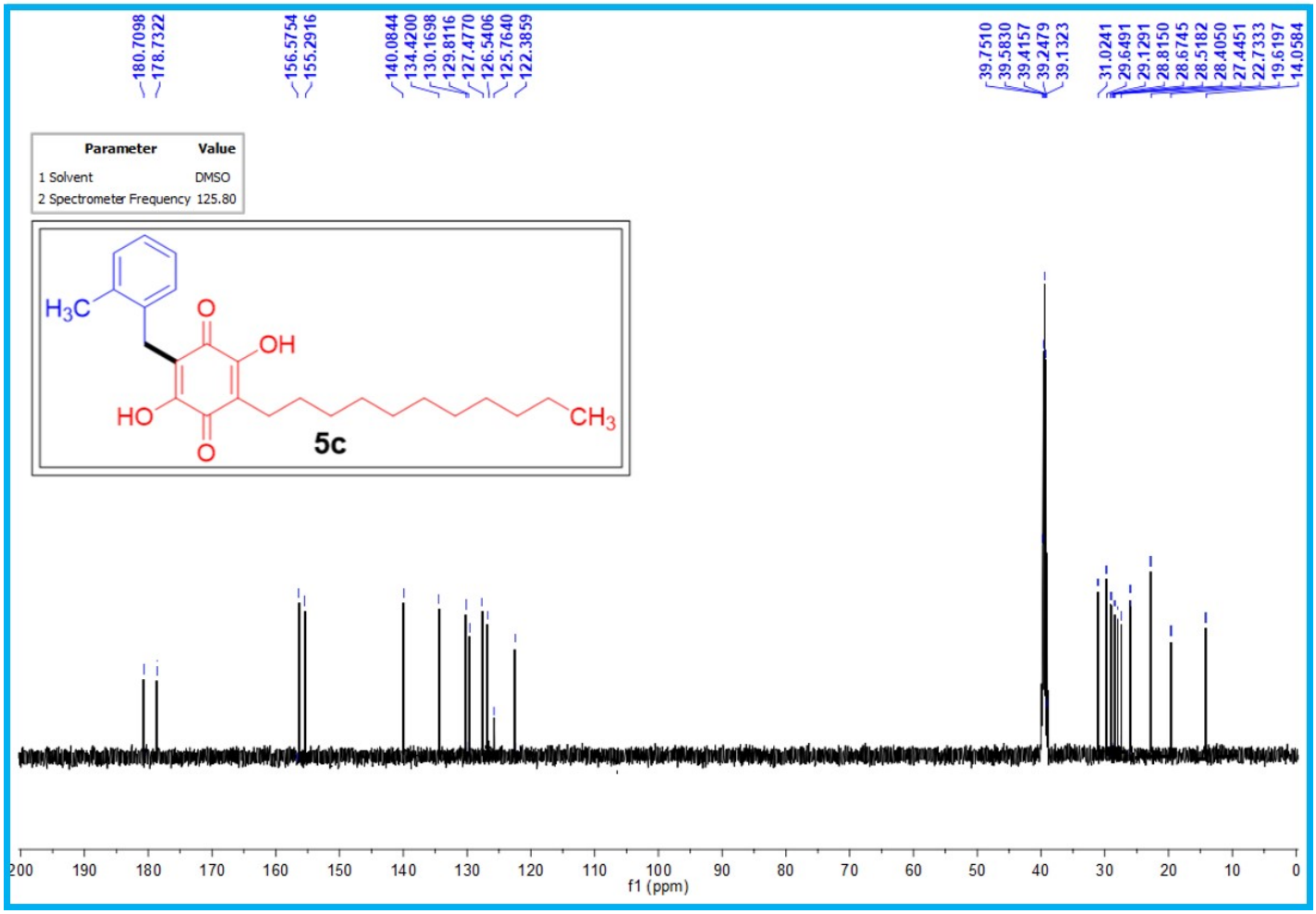


Fig. S9. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(2-methylbenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5c**).

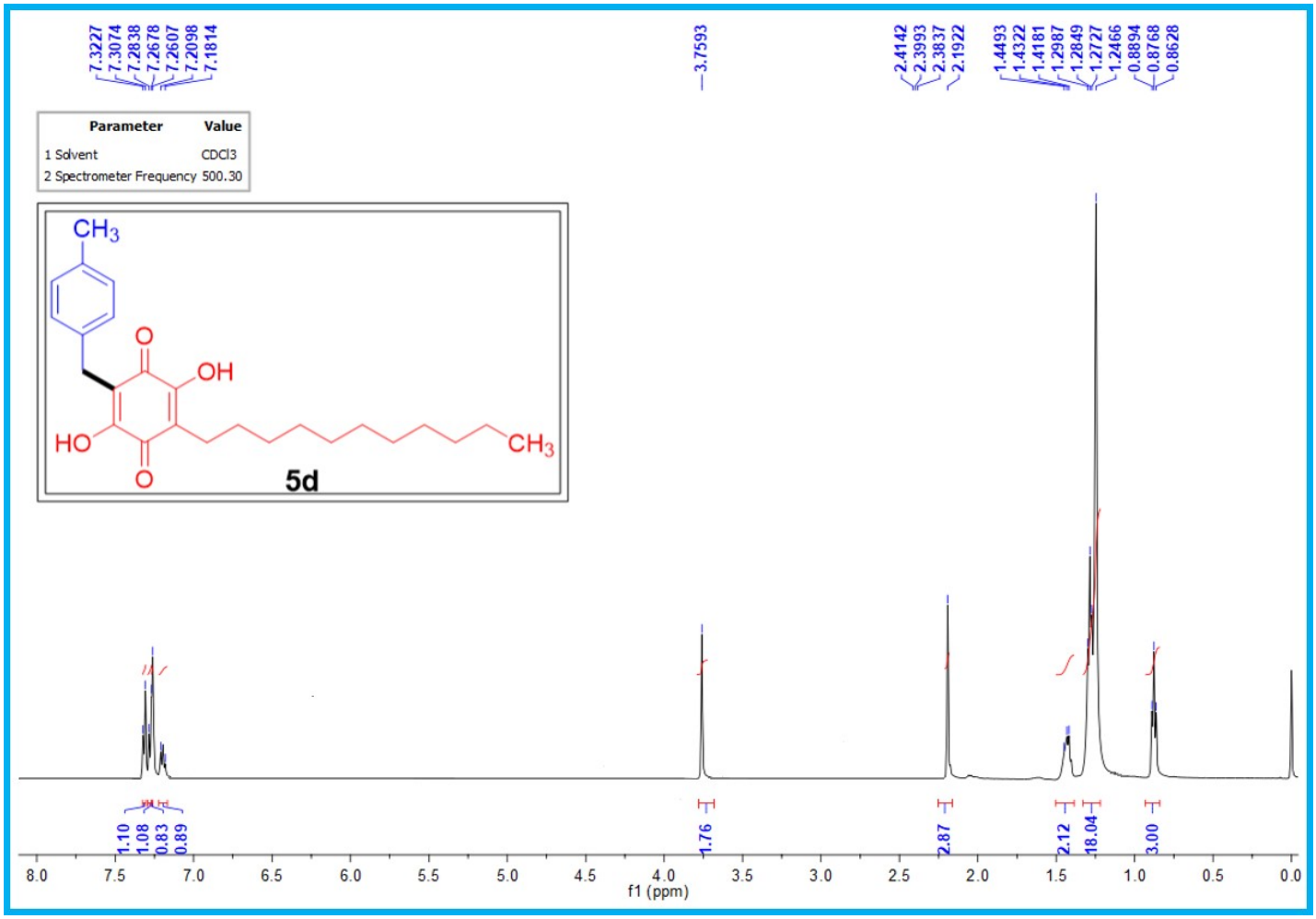


Fig. S10. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(4-methylbenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5d**).

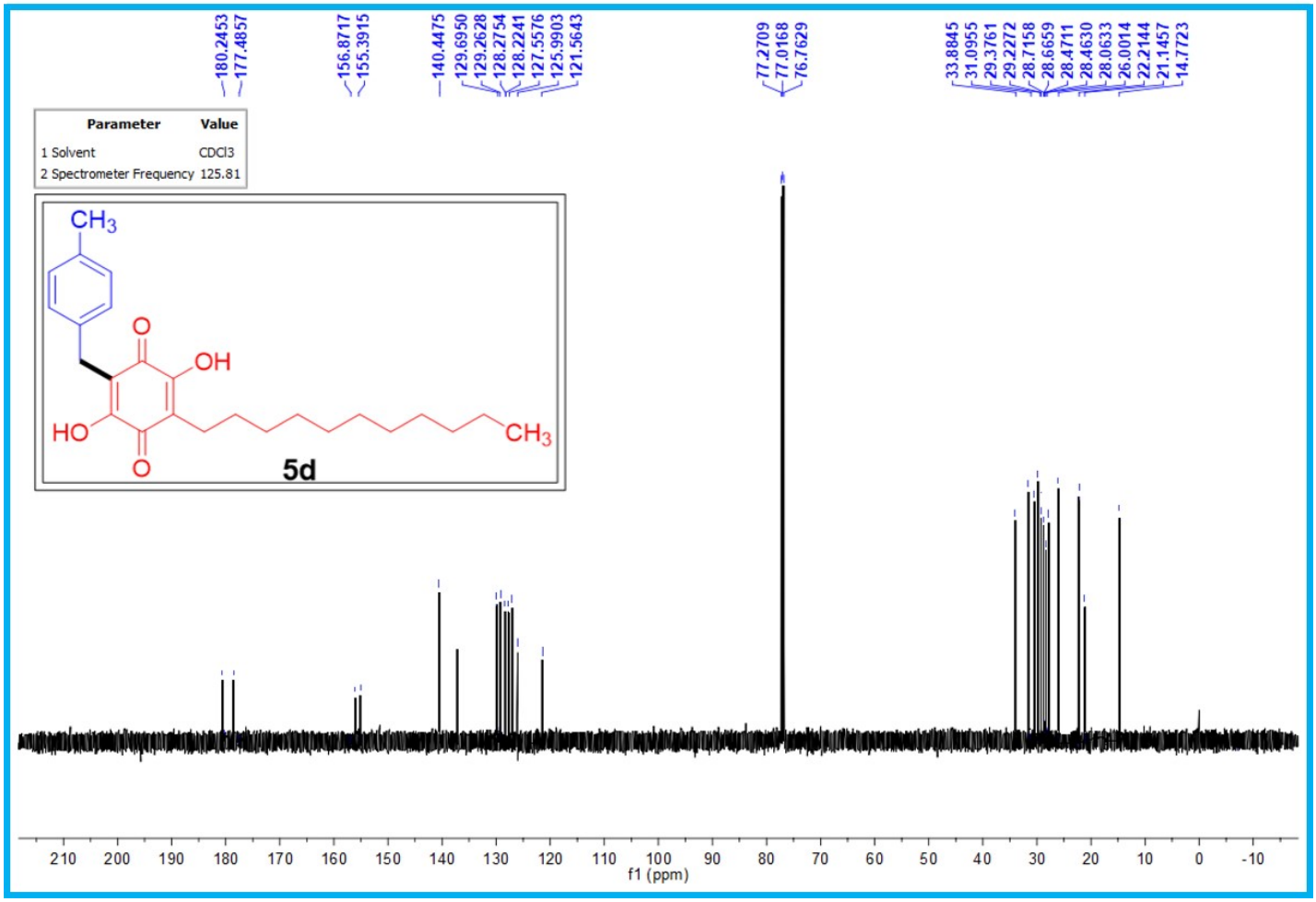


Fig. S11. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(4-methylbenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5d**).

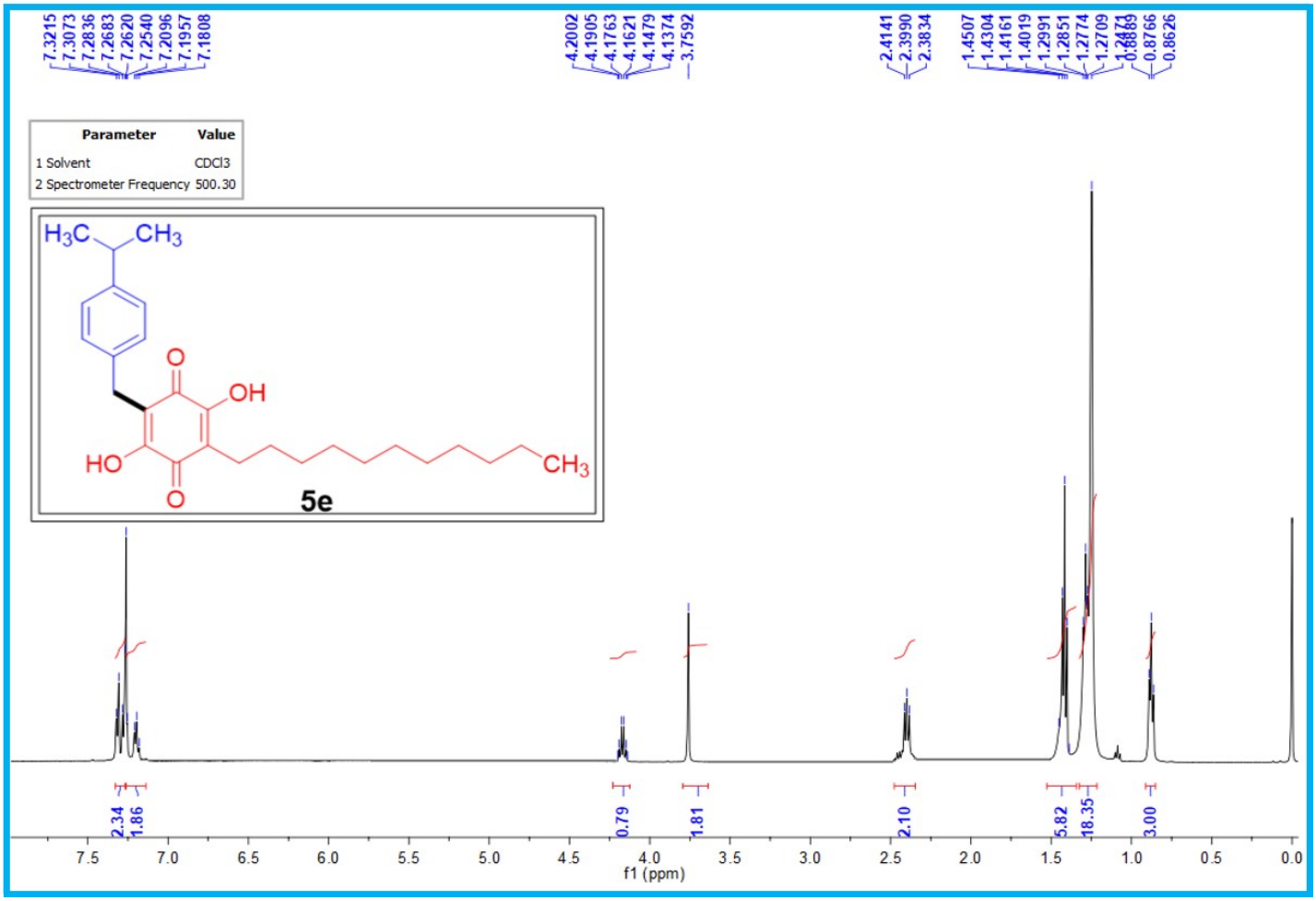


Fig. S12. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(4-isopropylbenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5e**).

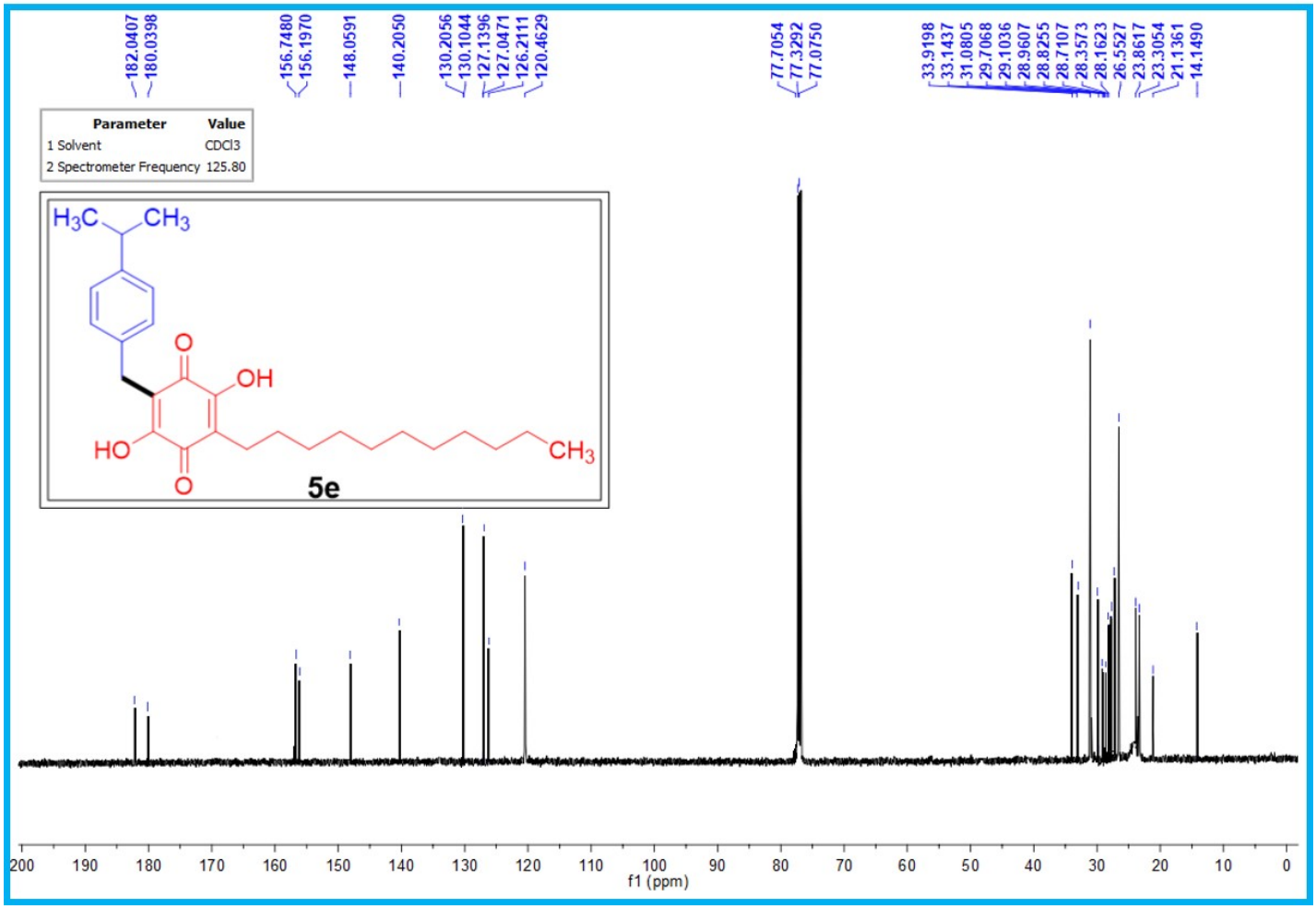


Fig. S13. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(4-isopropylbenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5e**).

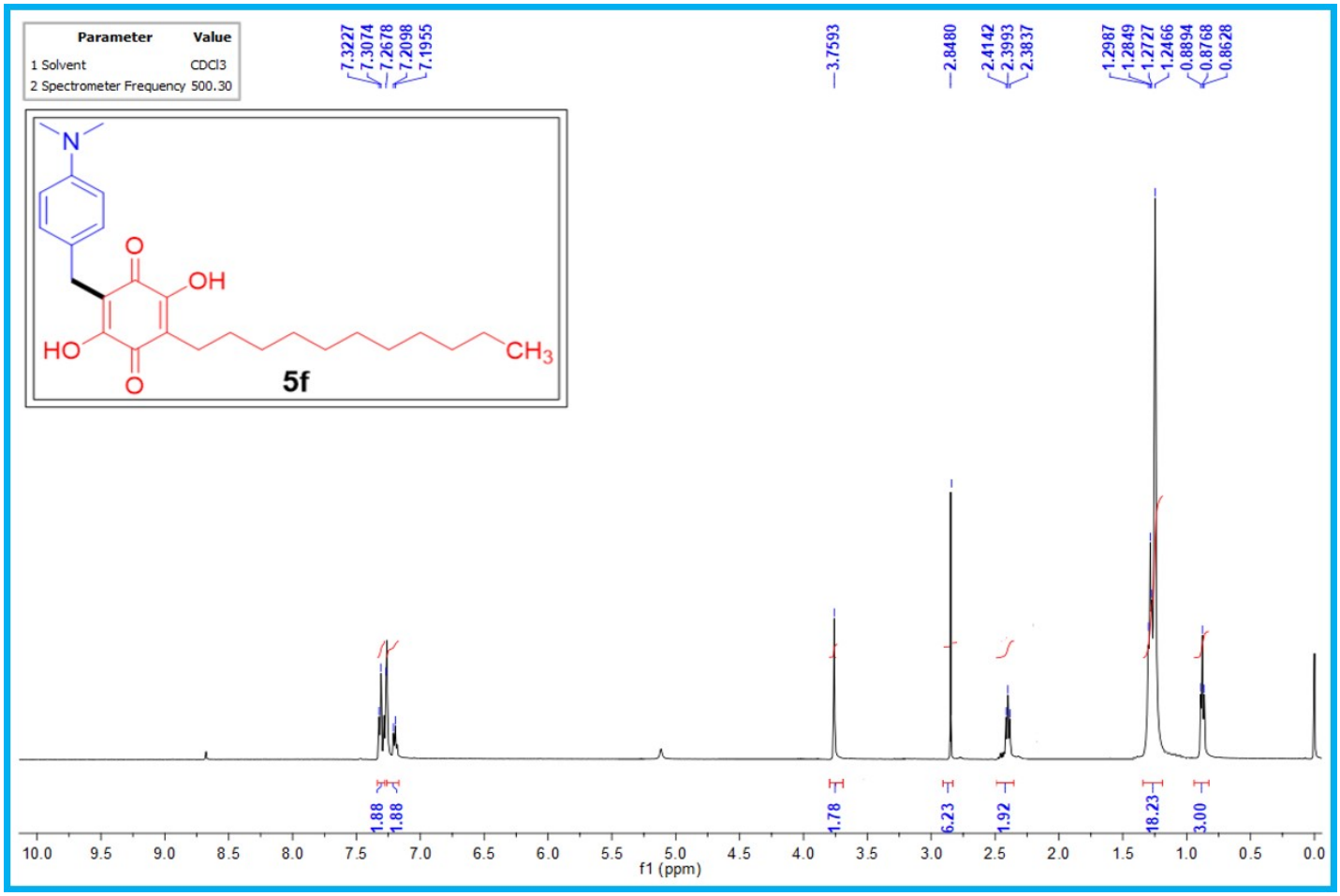


Fig. S14. ^{1}H NMR spectrum of 2-(4-(dimethylamino)benzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5f**).

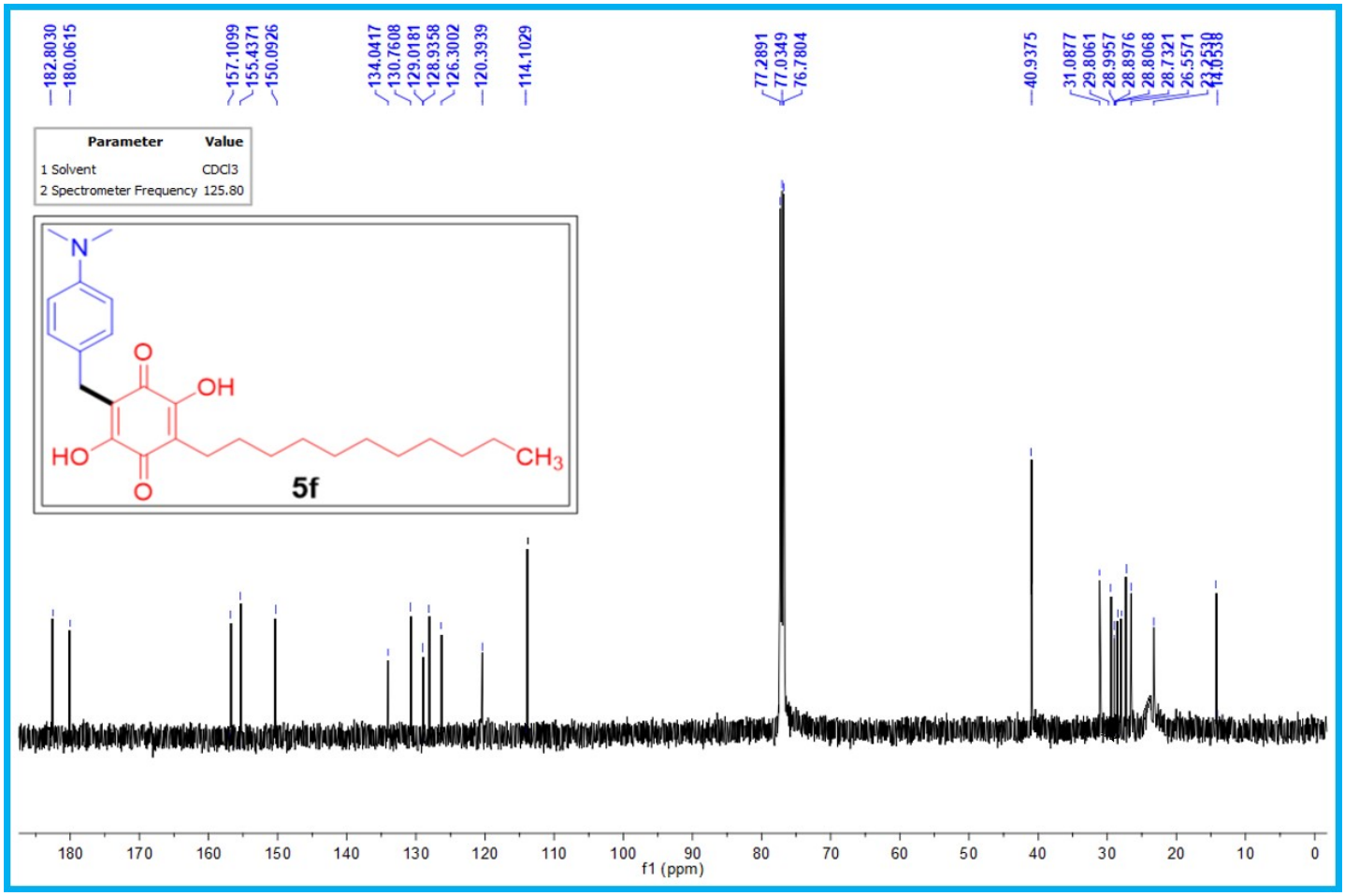


Fig. S15. ^{13}C NMR spectrum of 2-(4-(dimethylamino)benzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5f**).

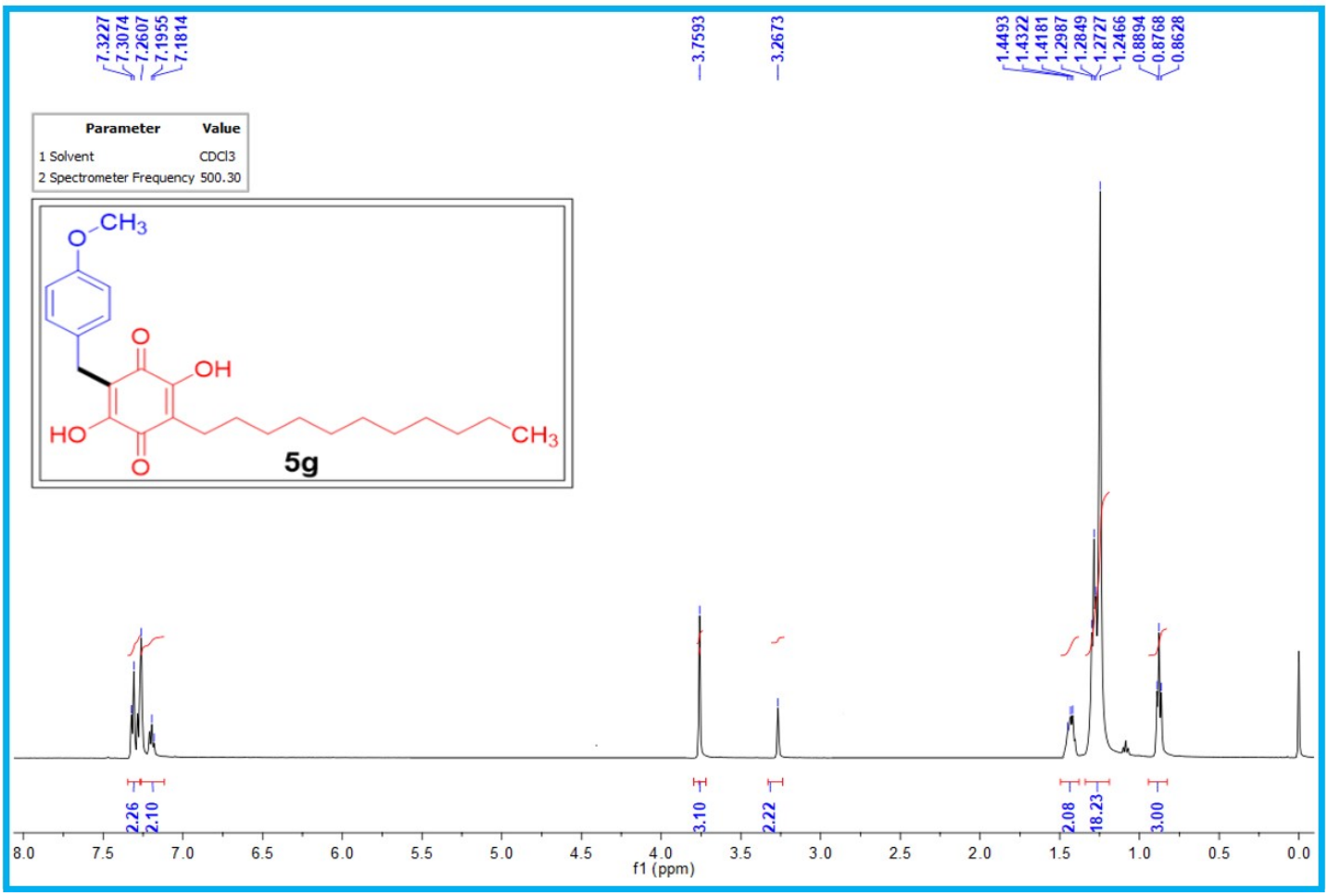


Fig. S16. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(4-methoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5g**).

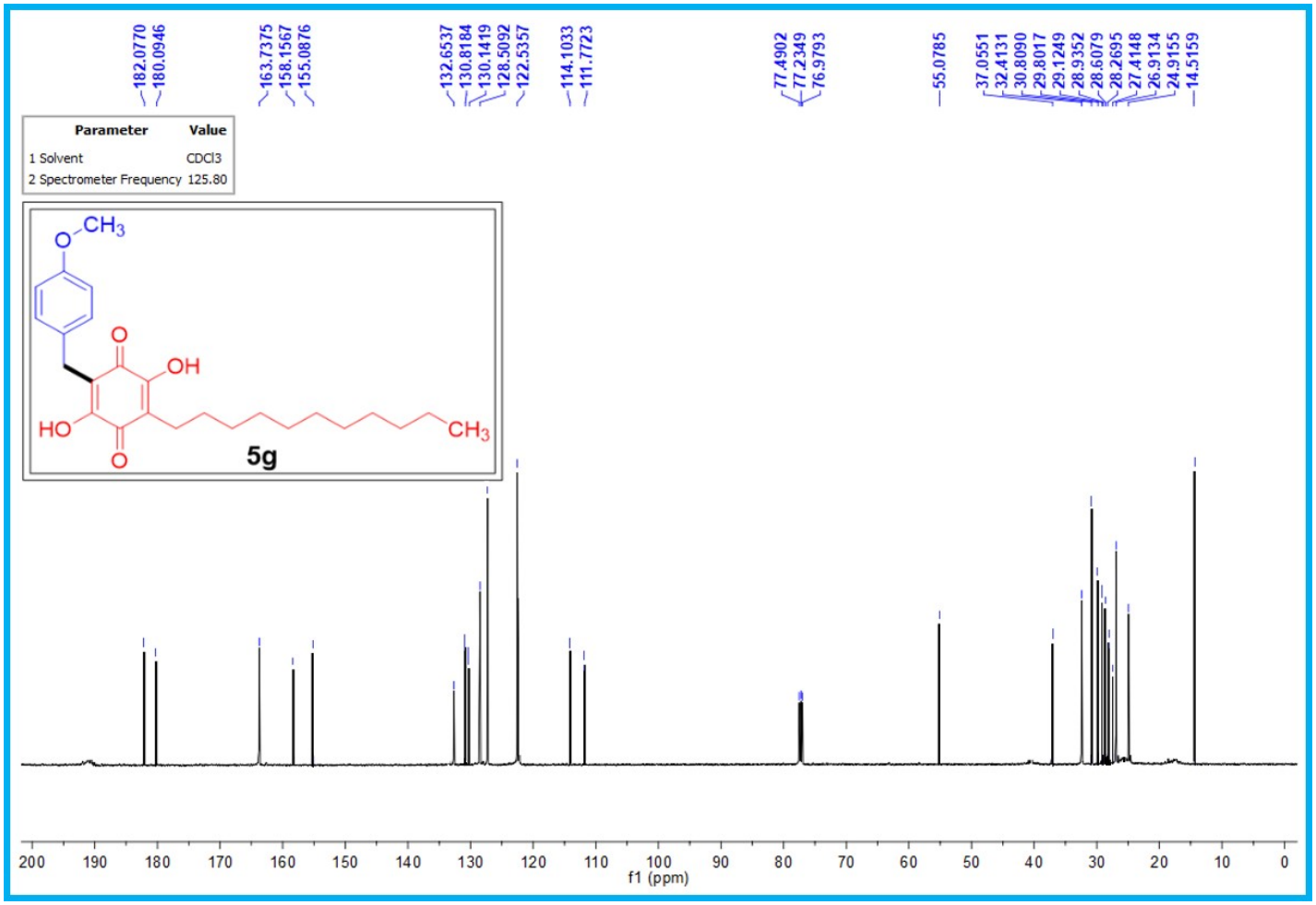


Fig. S17. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(4-methoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5g**).

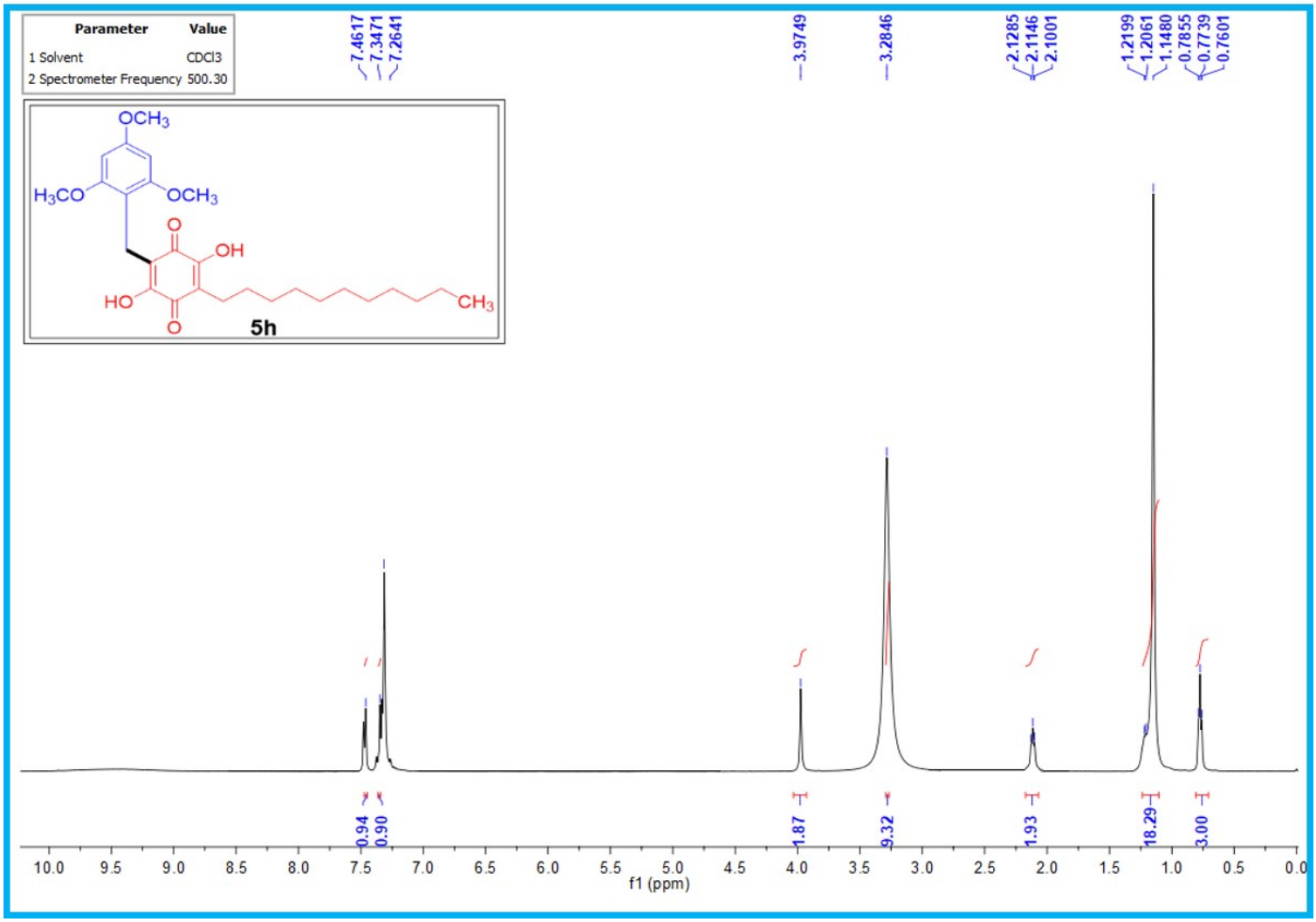


Fig. S18. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(2,4,6-trimethoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5h**).

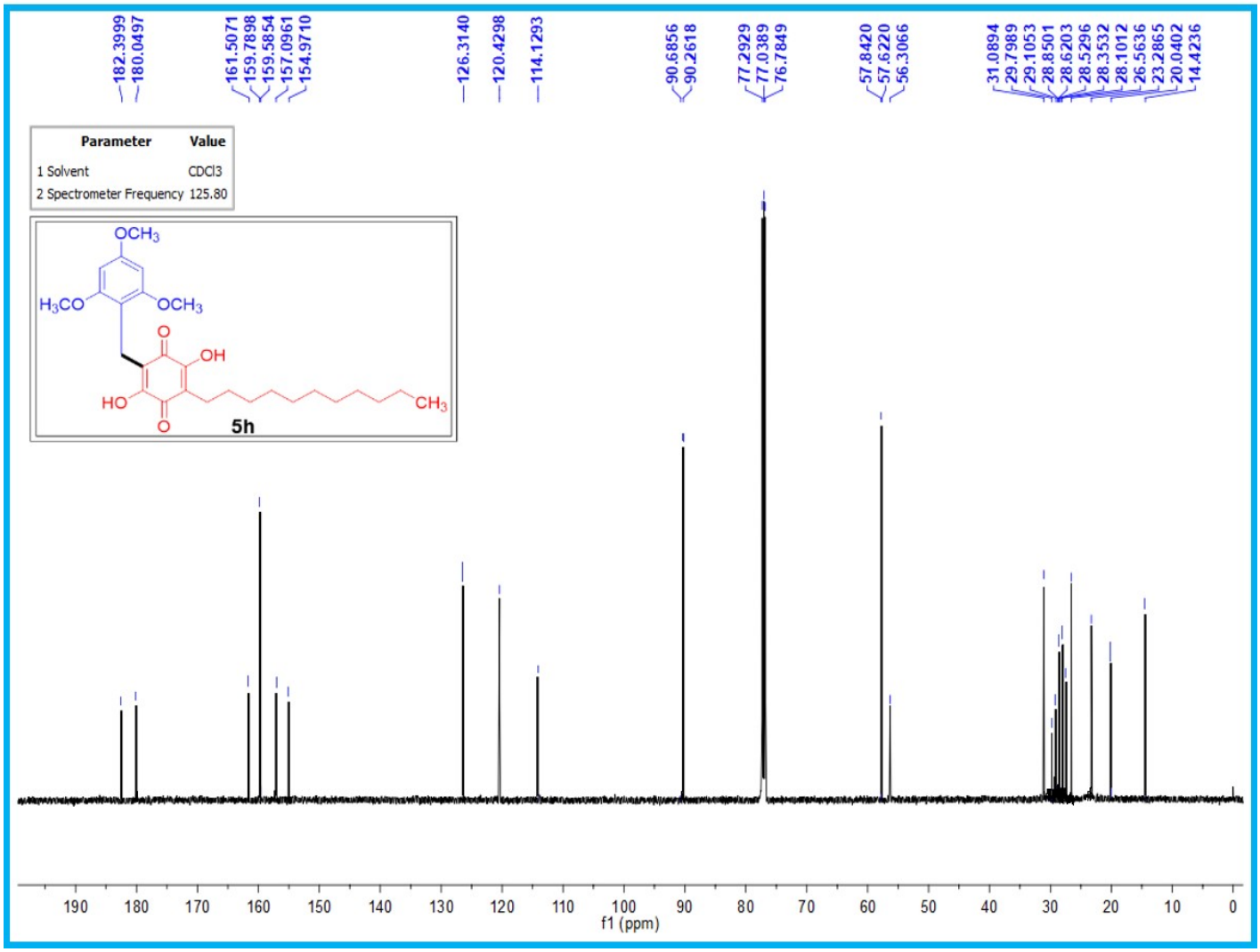


Fig. S19. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(2,4,6-trimethoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5h**).

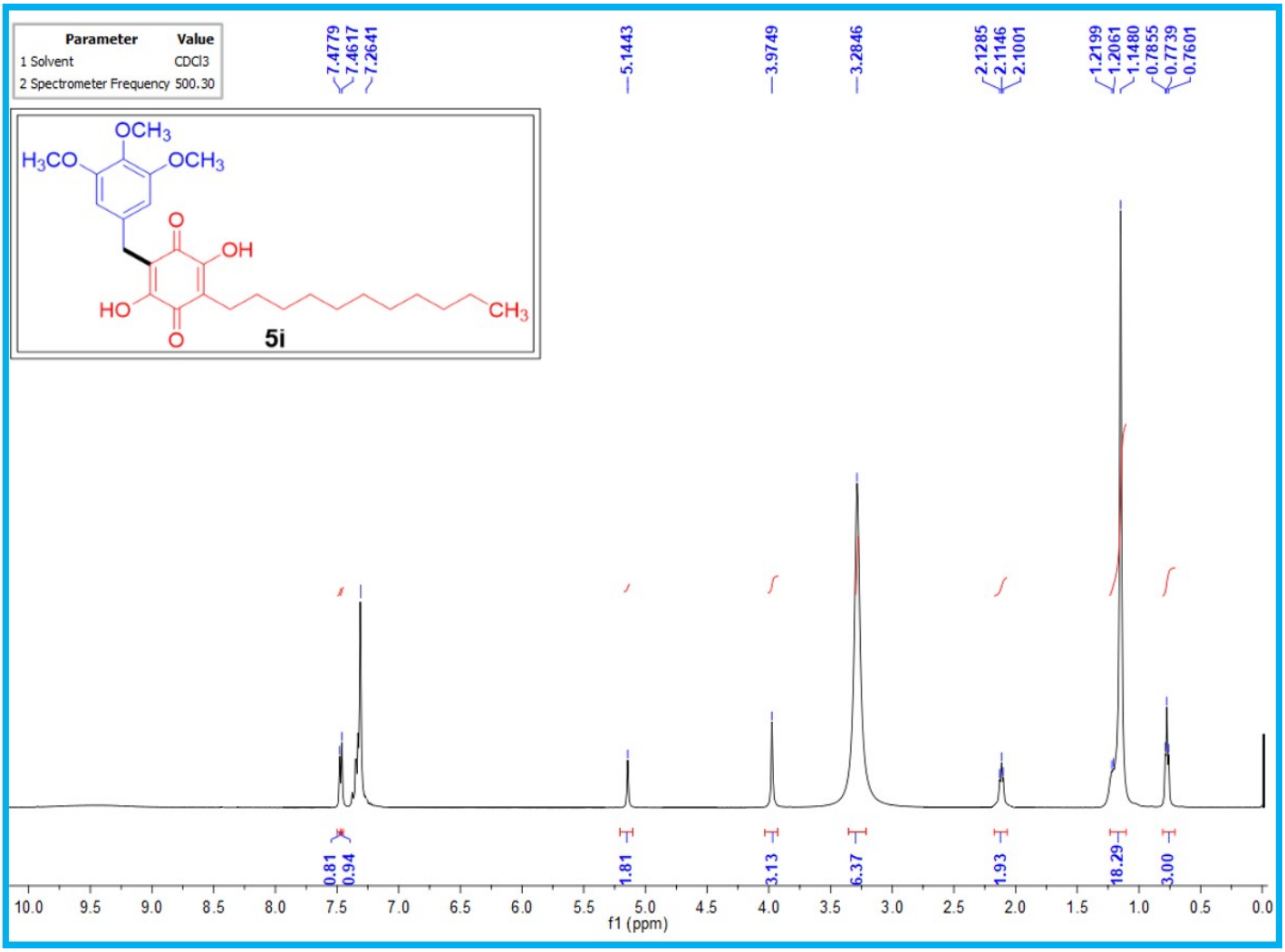


Fig. S20. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(3,4,5-trimethoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5i**).

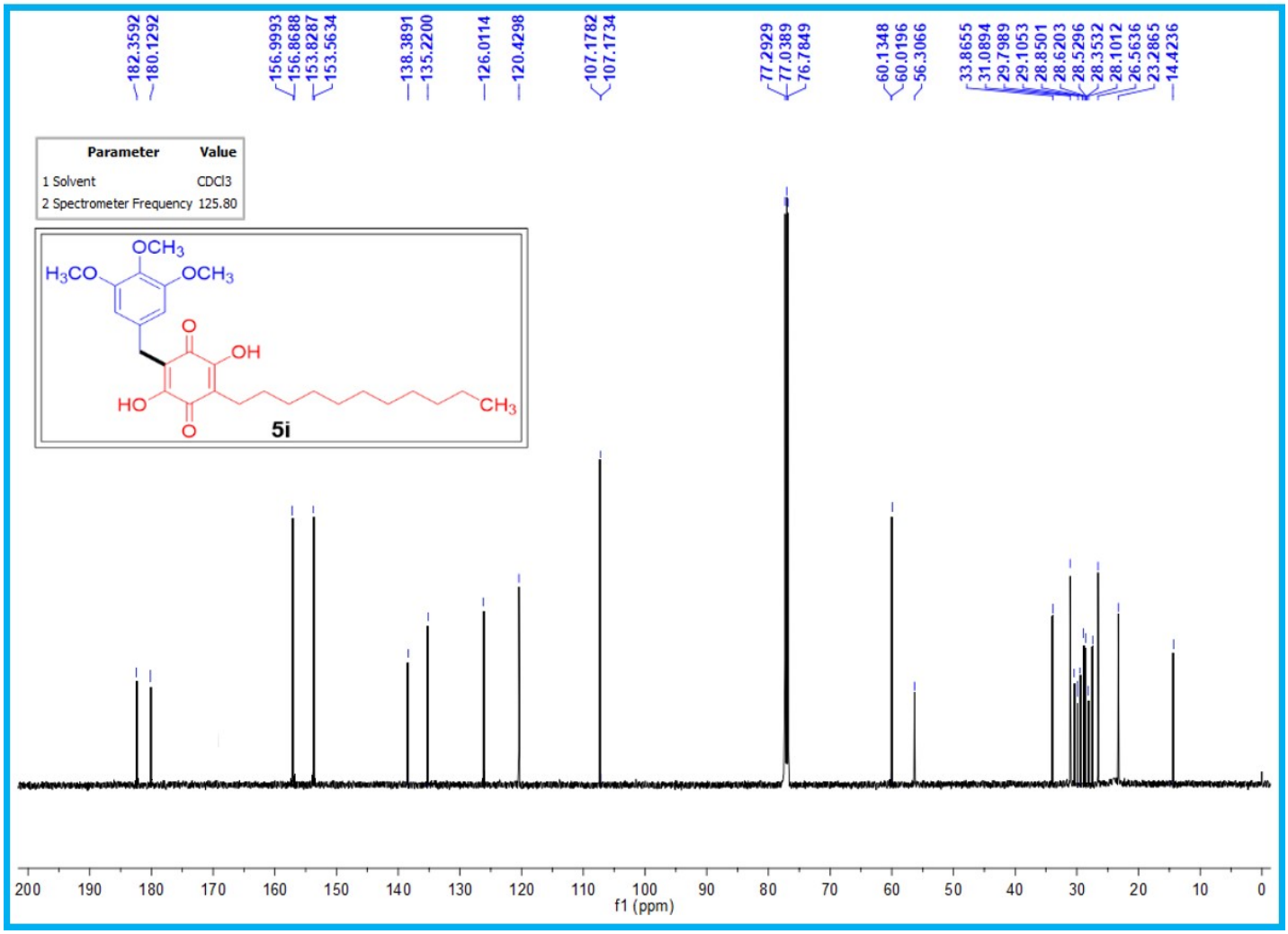


Fig. S21. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(3,4,5-trimethoxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5i**).

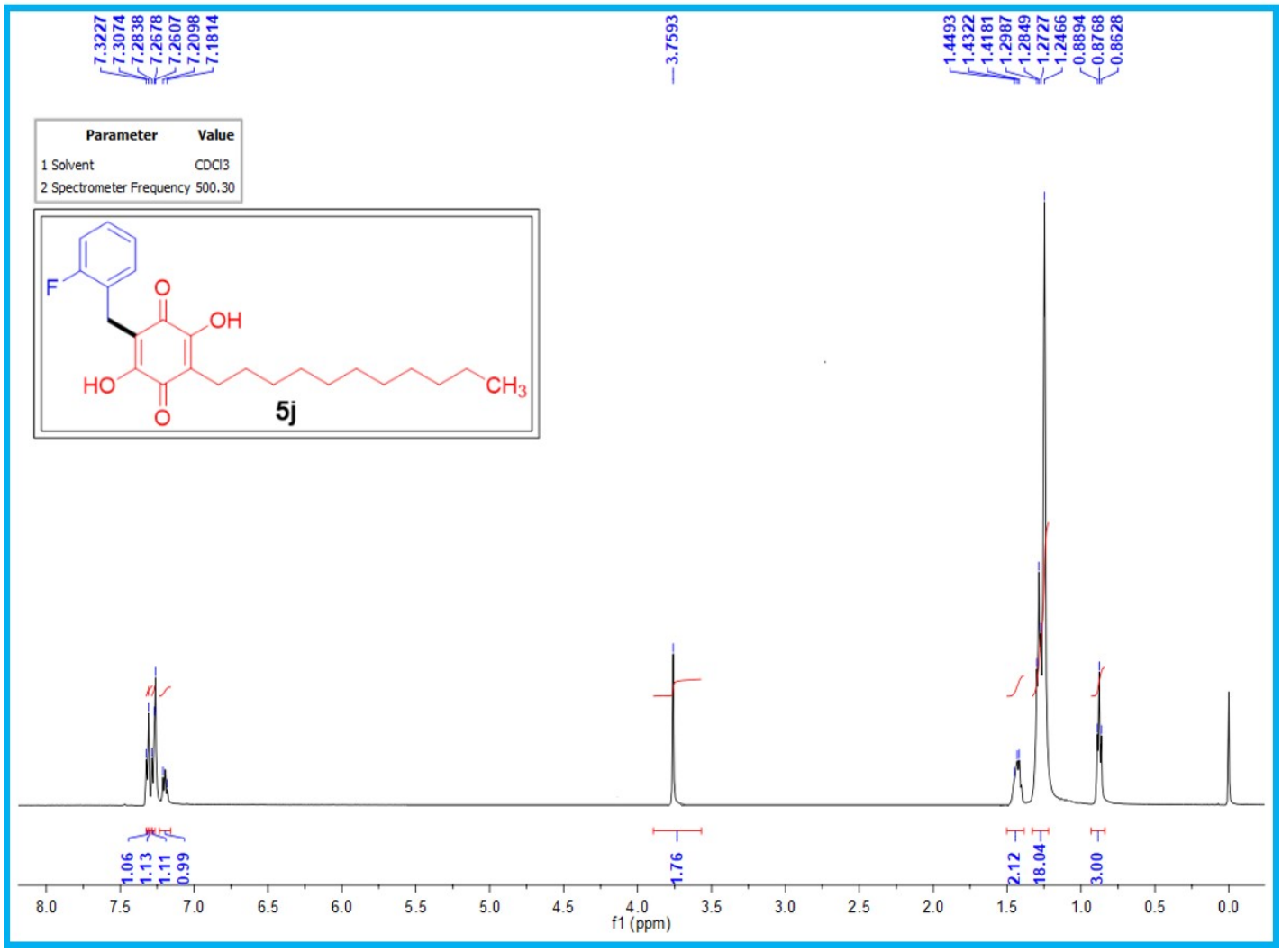


Fig. S22. ^{1}H NMR spectrum of 2-(2-fluorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5j**).

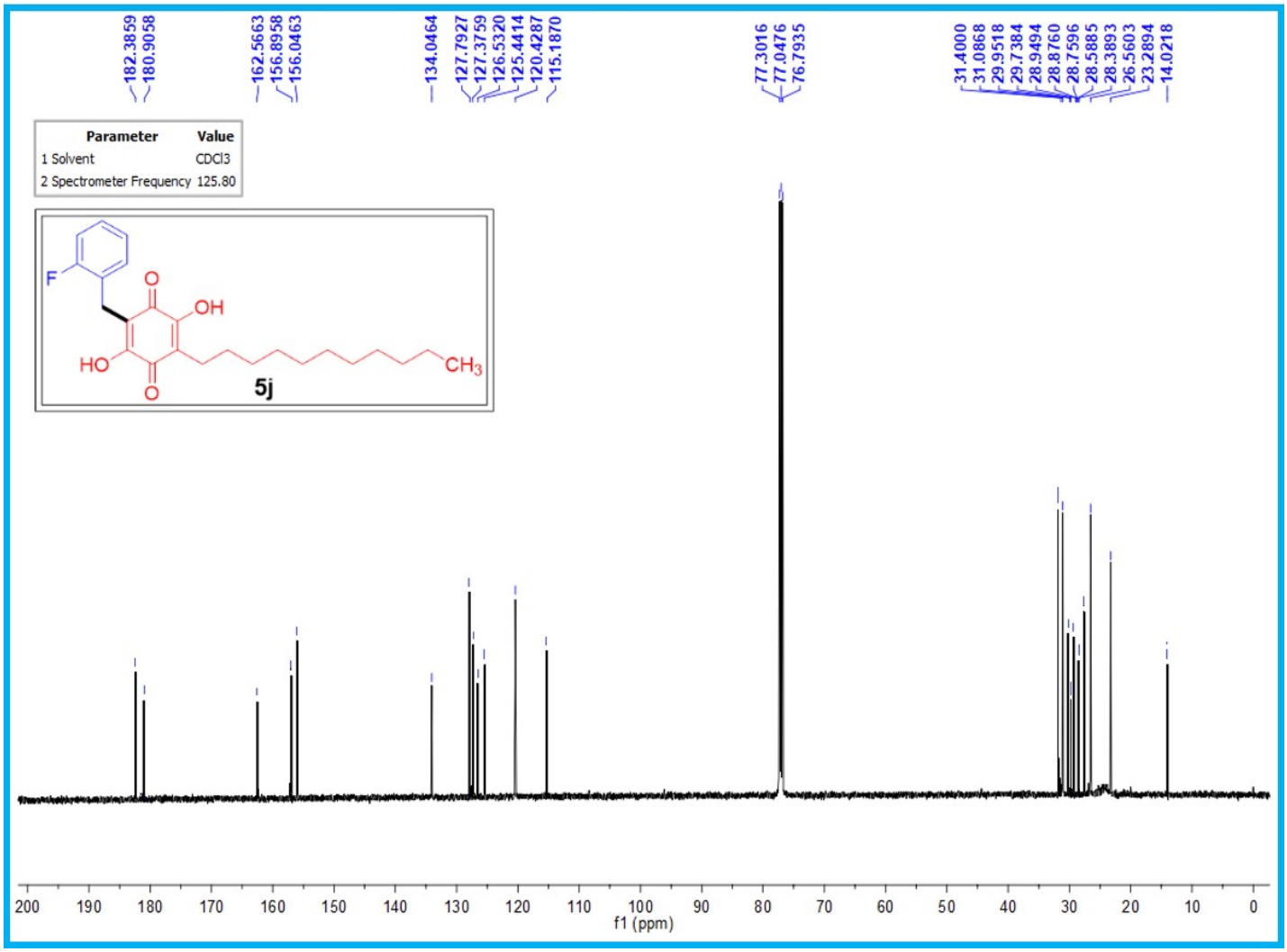


Fig. S23. ^{13}C NMR spectrum of 2-(2-fluorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5j**).

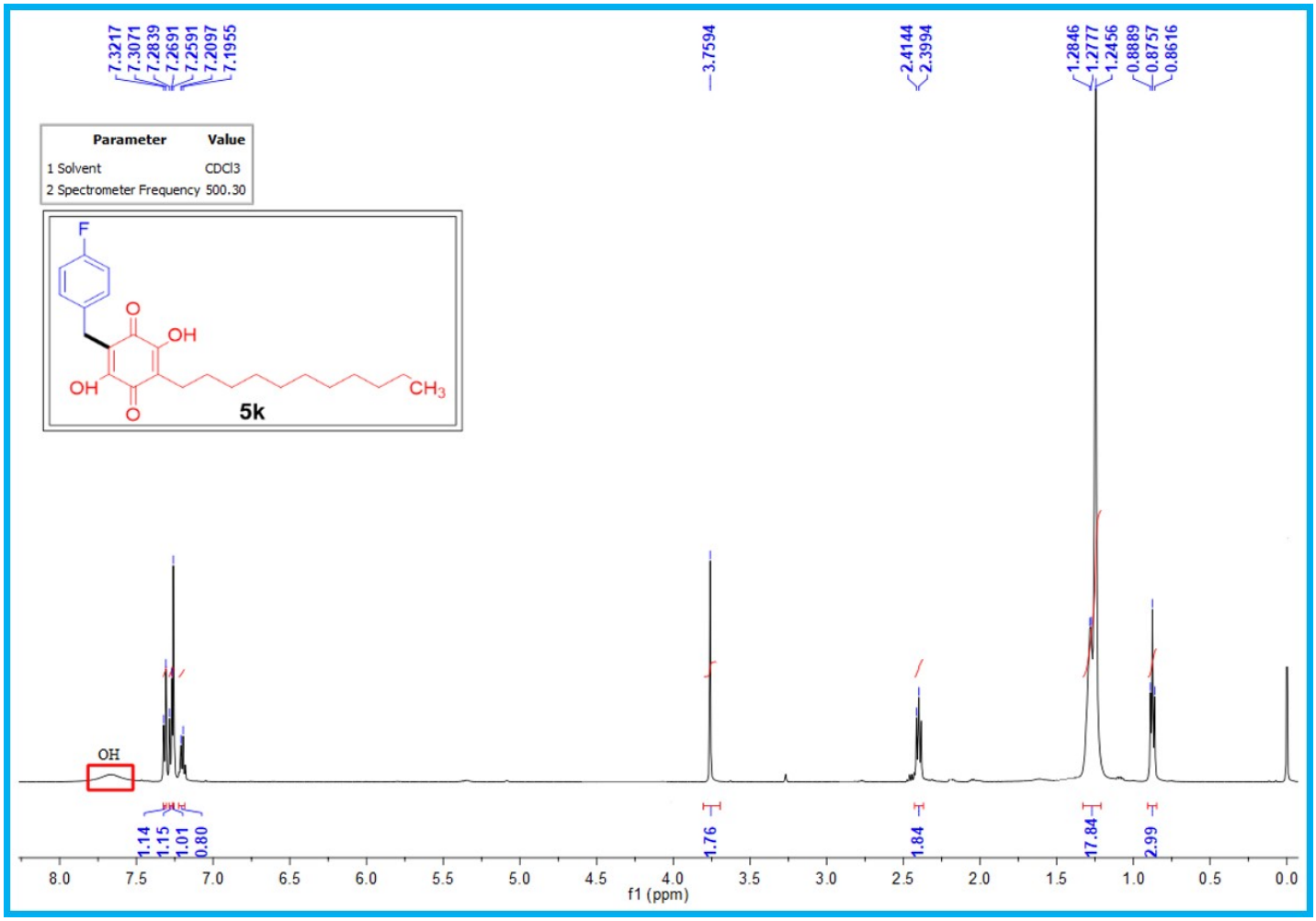


Fig. S24. ^{1}H NMR spectrum of 2-(4-fluorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5k**).

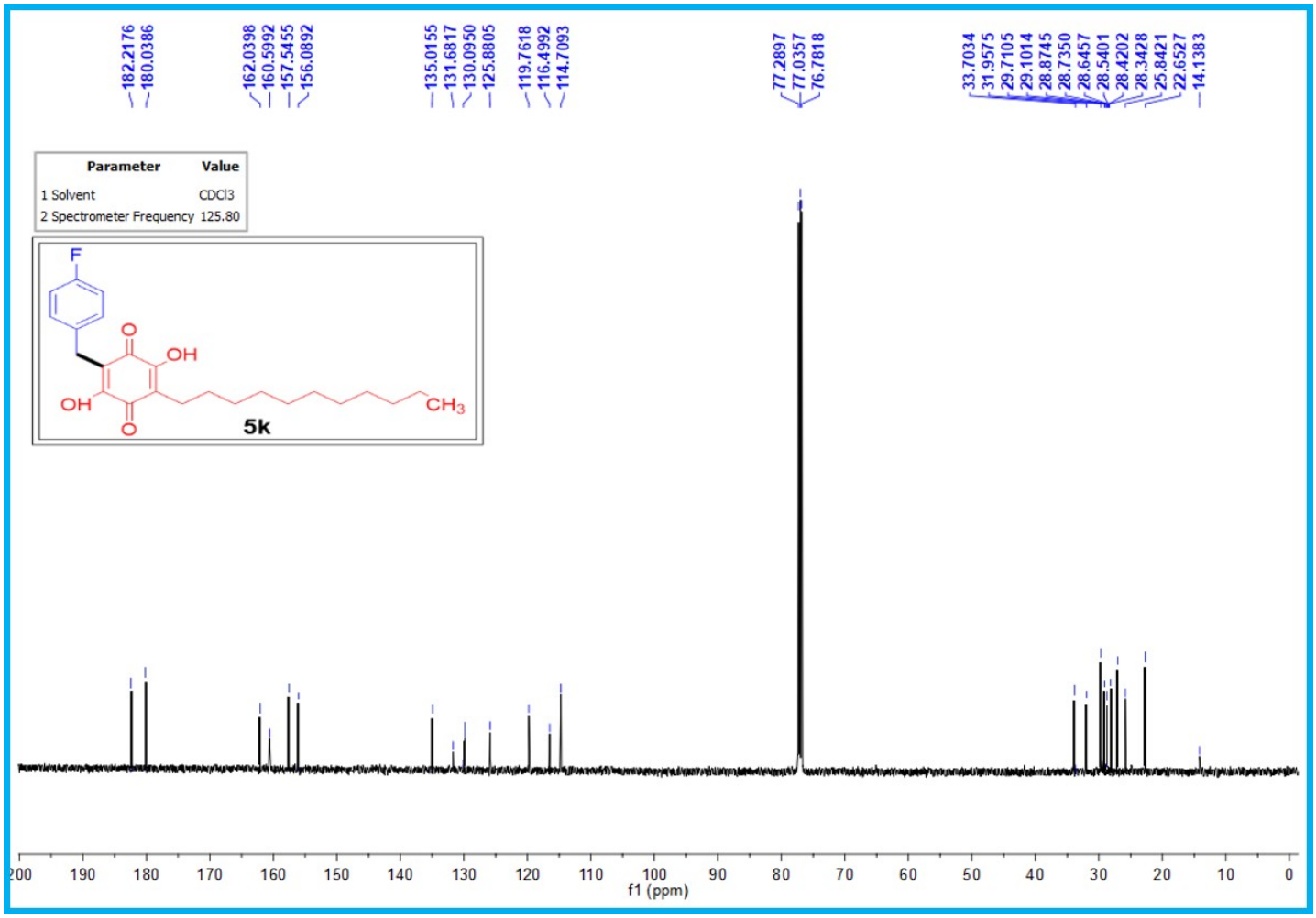


Fig. S25. ^{13}C NMR spectrum of 2-(4-fluorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5k**).

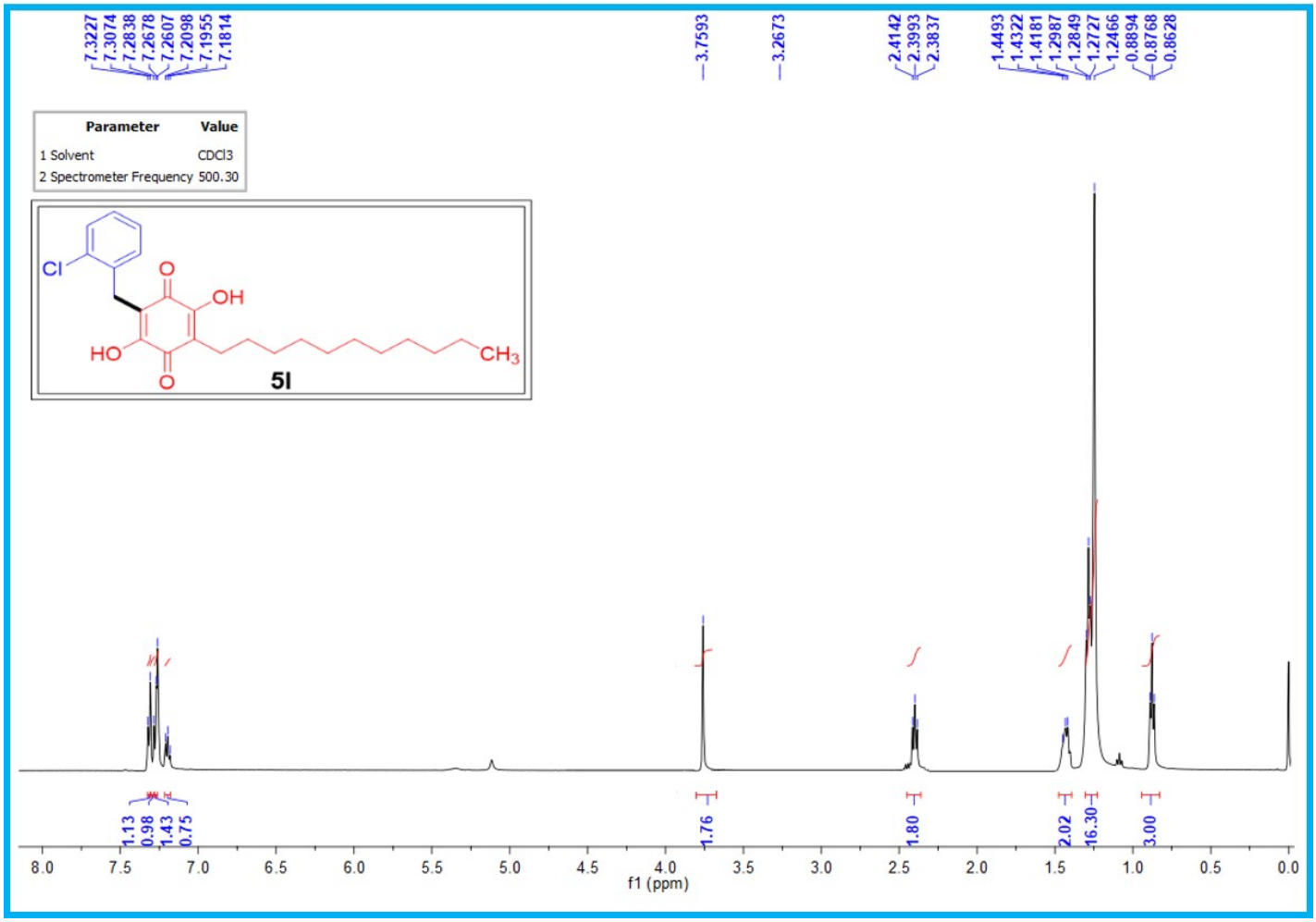


Fig. S26. ^{1}H NMR spectrum of 2-(2-chlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5l**).

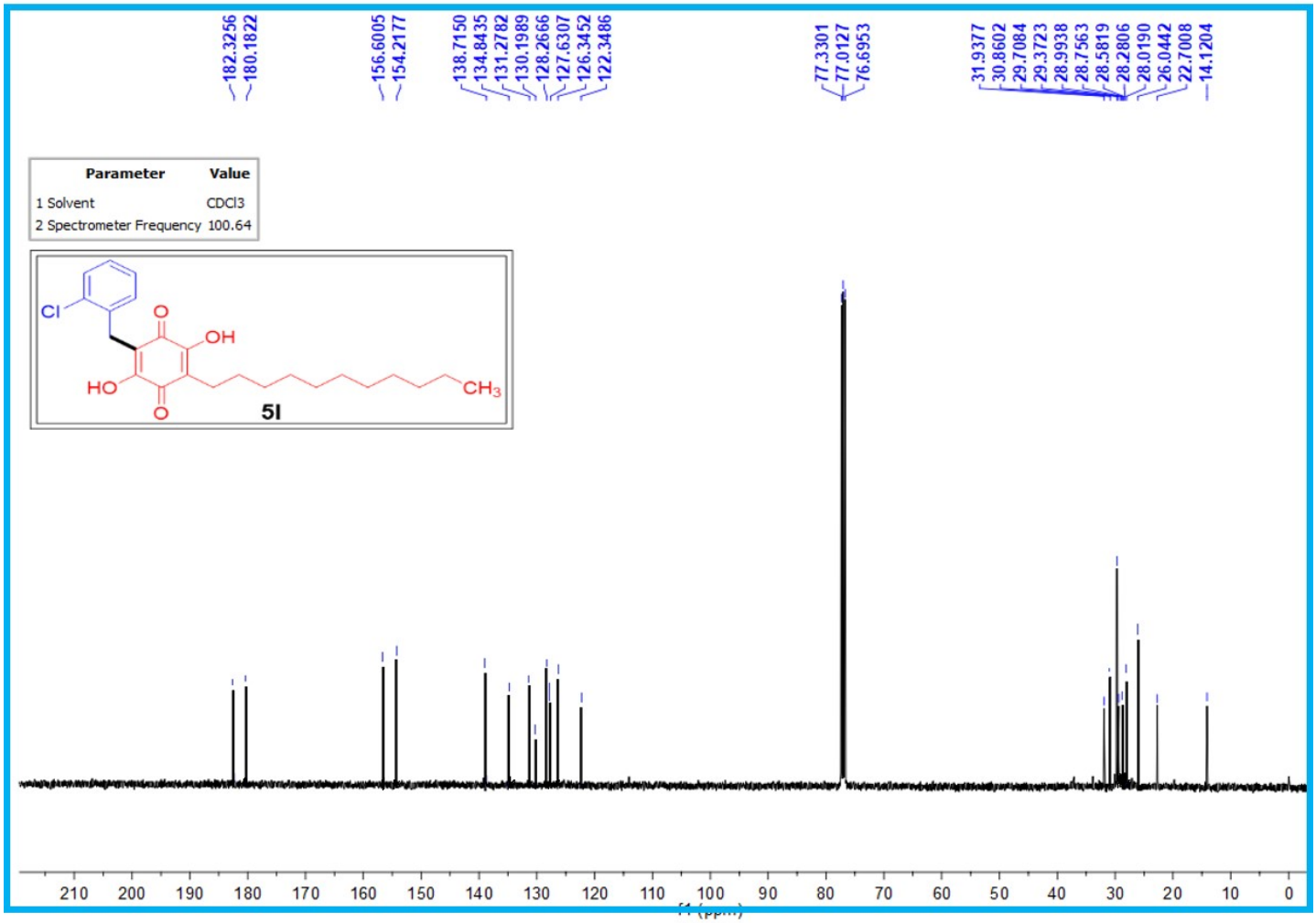


Fig. S27. ^{13}C NMR spectrum of 2-(2-chlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5l**).

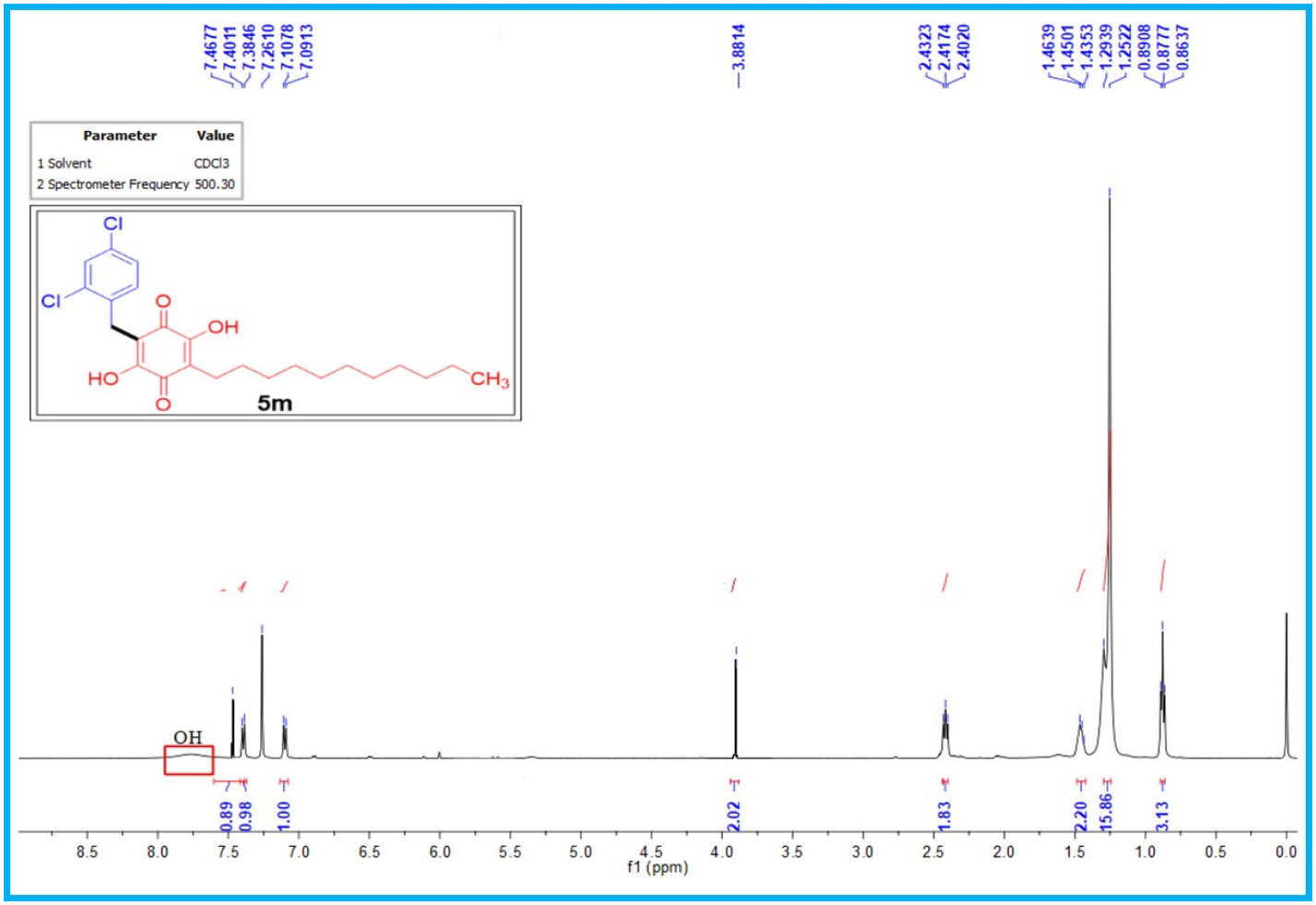


Fig. S28. ^{1}H NMR spectrum of 2-(2,4-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5m**).

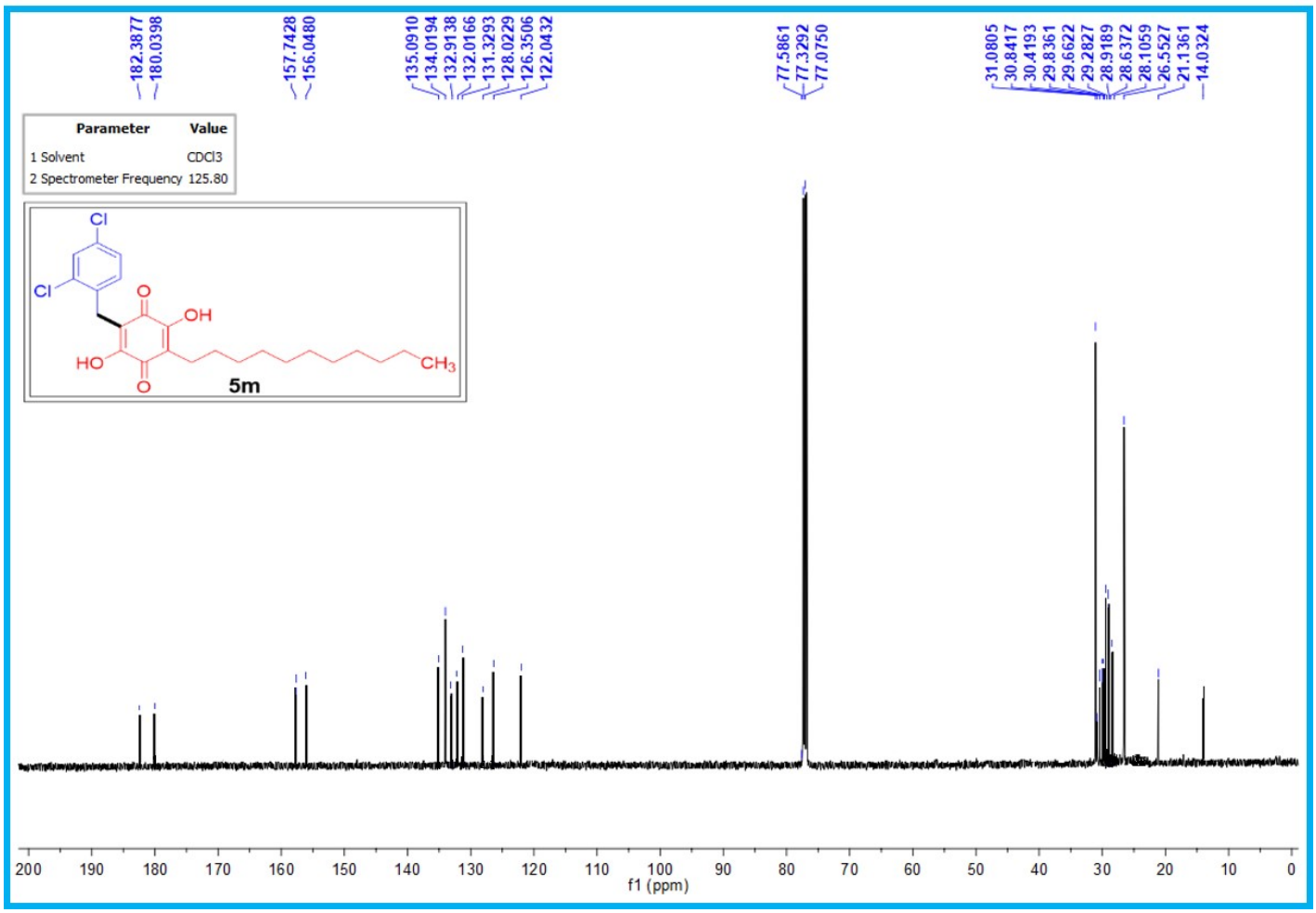


Fig. S29. ^{13}C NMR spectrum of 2-(2,4-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5m**).

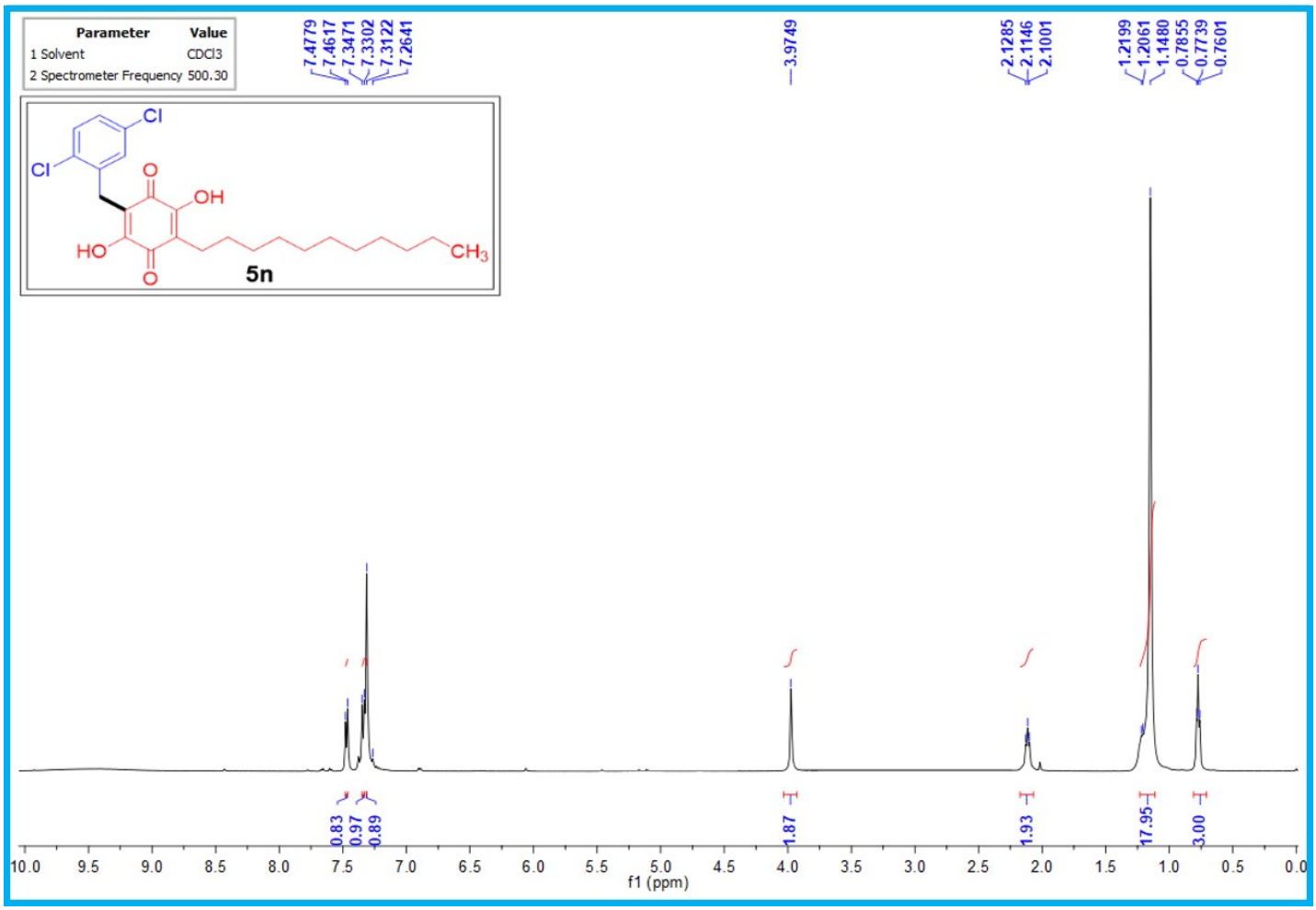


Fig. S30. ^{1}H NMR spectrum of 2-(2,5-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione **(5n).**

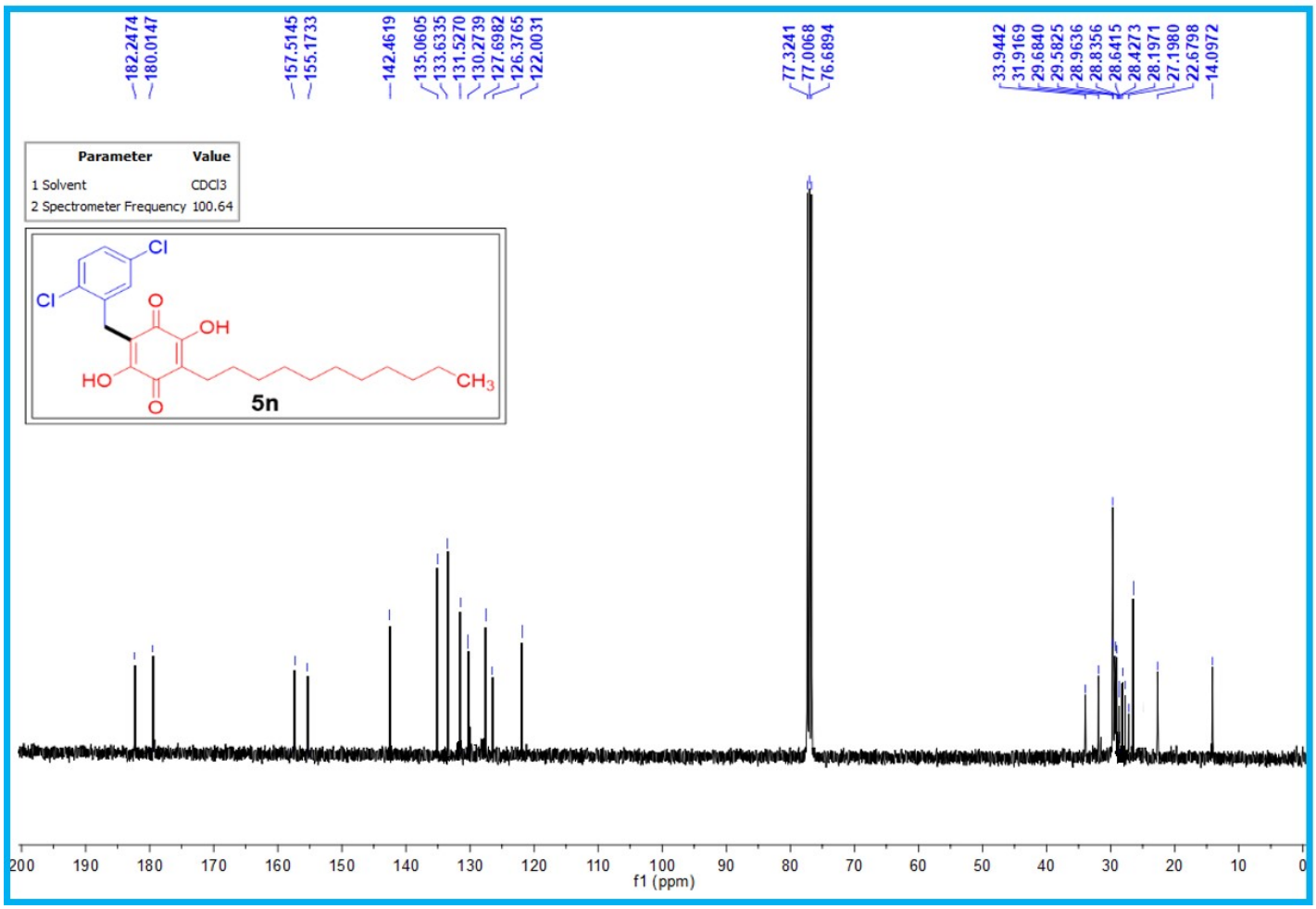


Fig. S31. ^{13}C NMR spectrum of 2-(2,5-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione **(5n).**

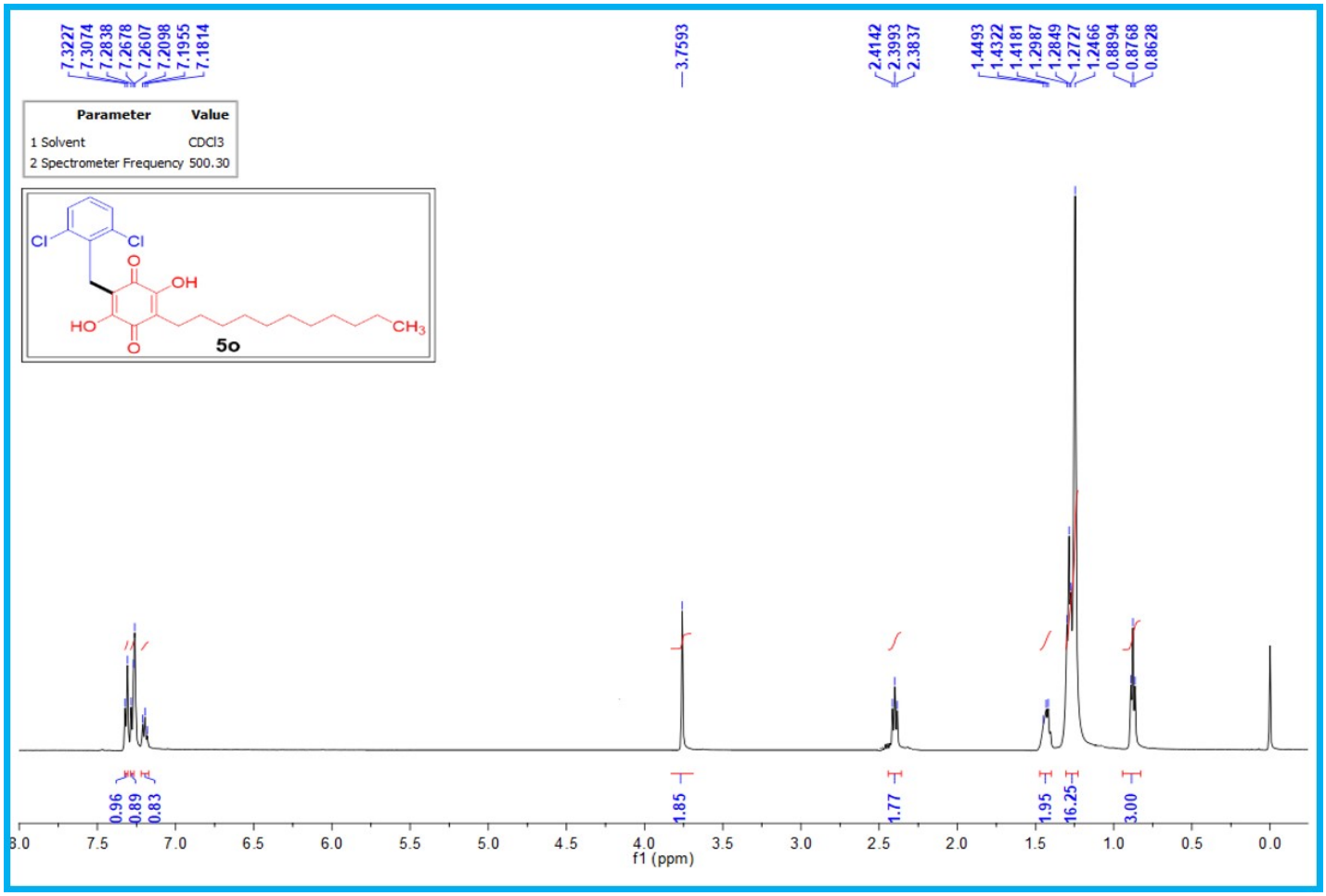


Fig. S32. ^{1}H NMR spectrum of 2-(2,6-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5o**).

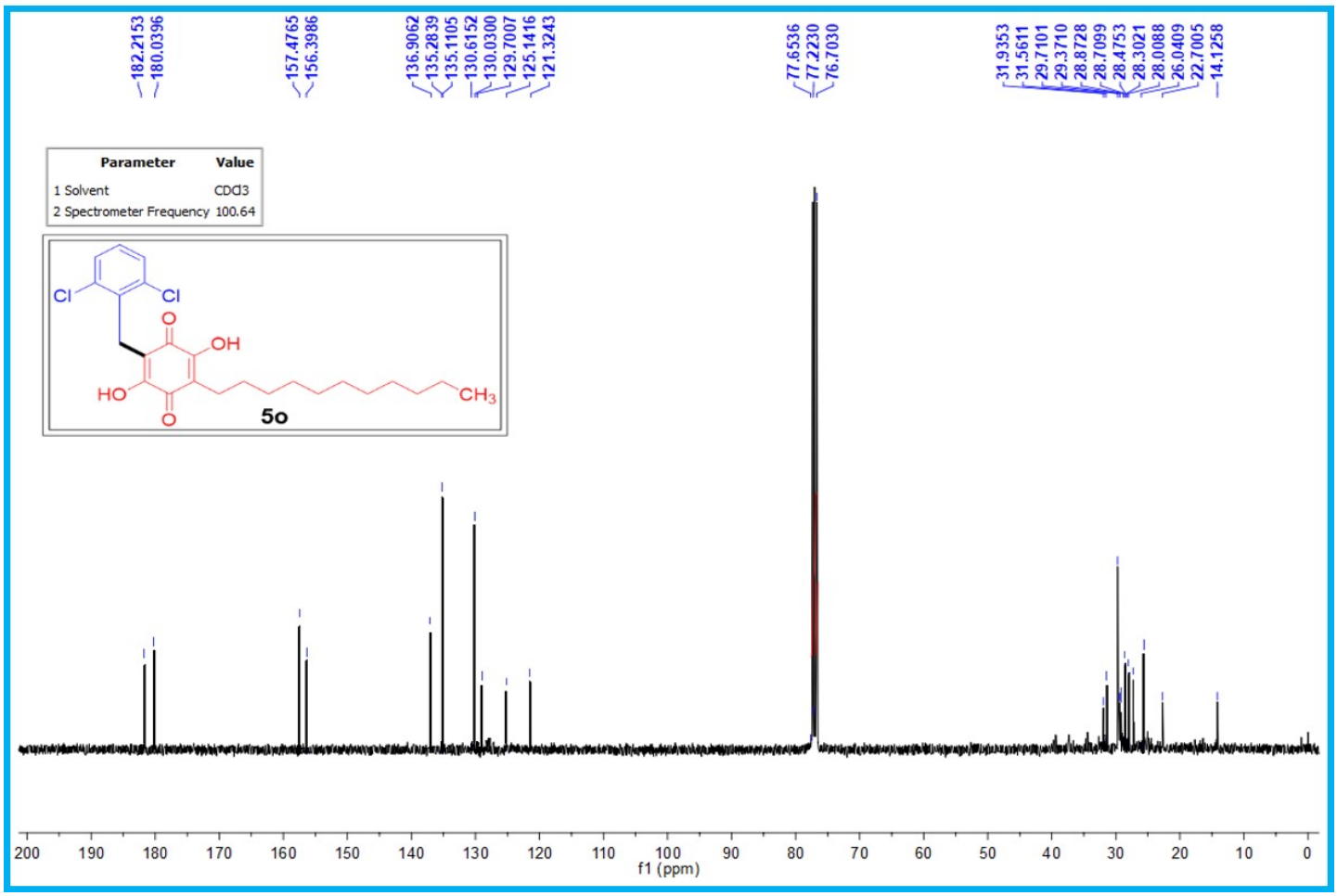


Fig. S33. ^{13}C NMR spectrum of 2-(2,6-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5o**).

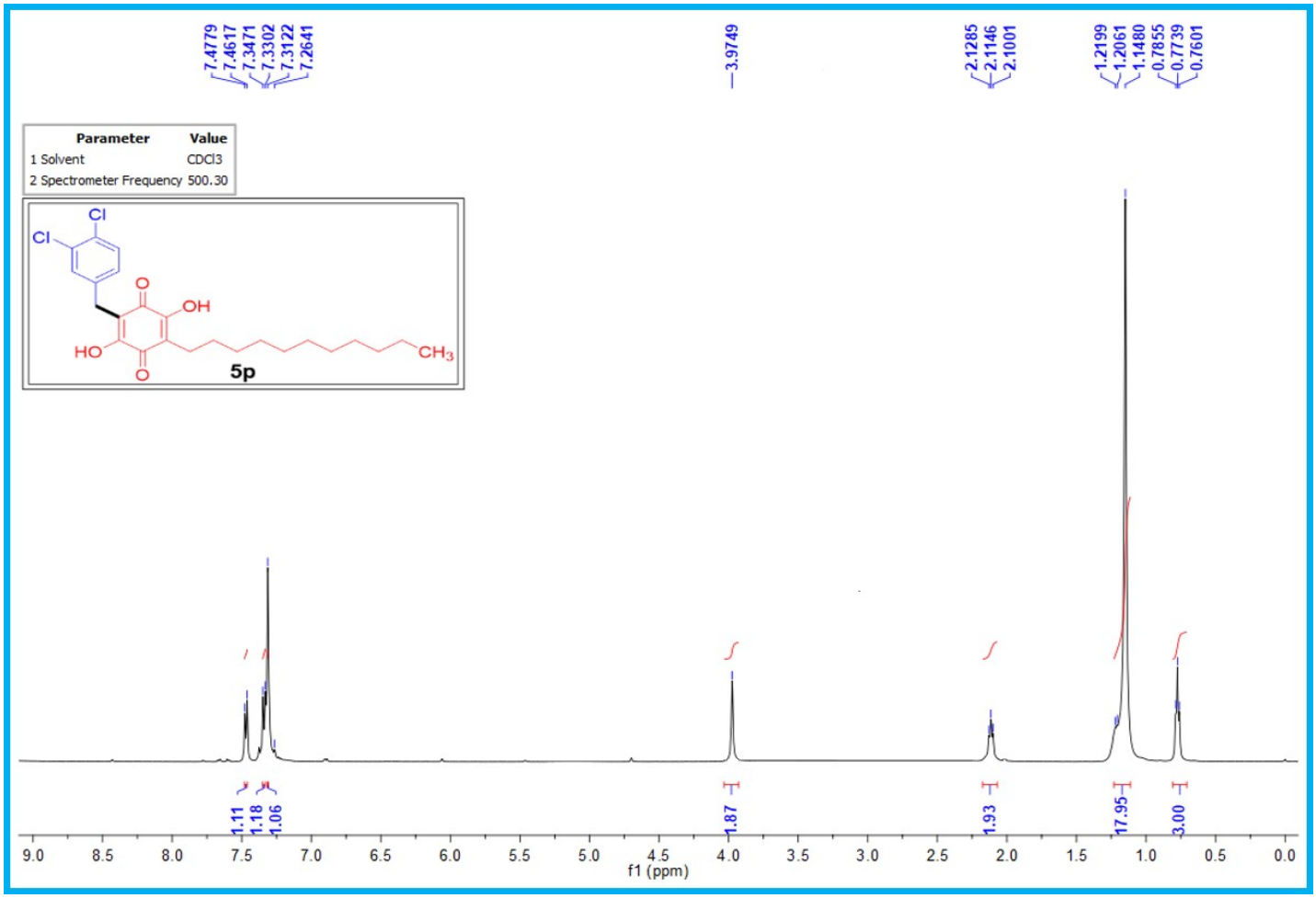


Fig. S34. [1]H NMR spectrum of 2-(3,4-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5p**).

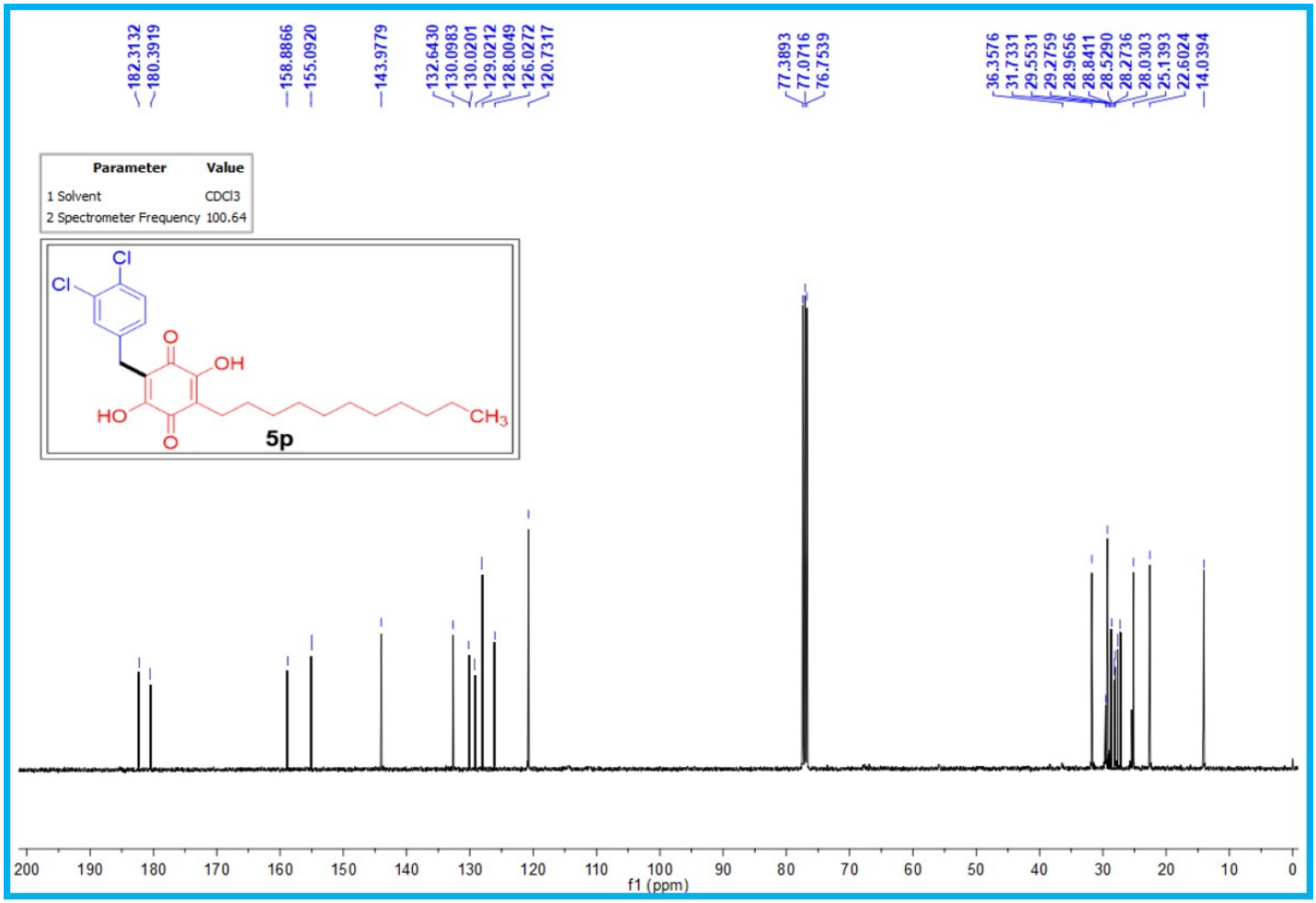


Fig. S35. ^{13}C NMR spectrum of 2-(3,4-dichlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5p**).

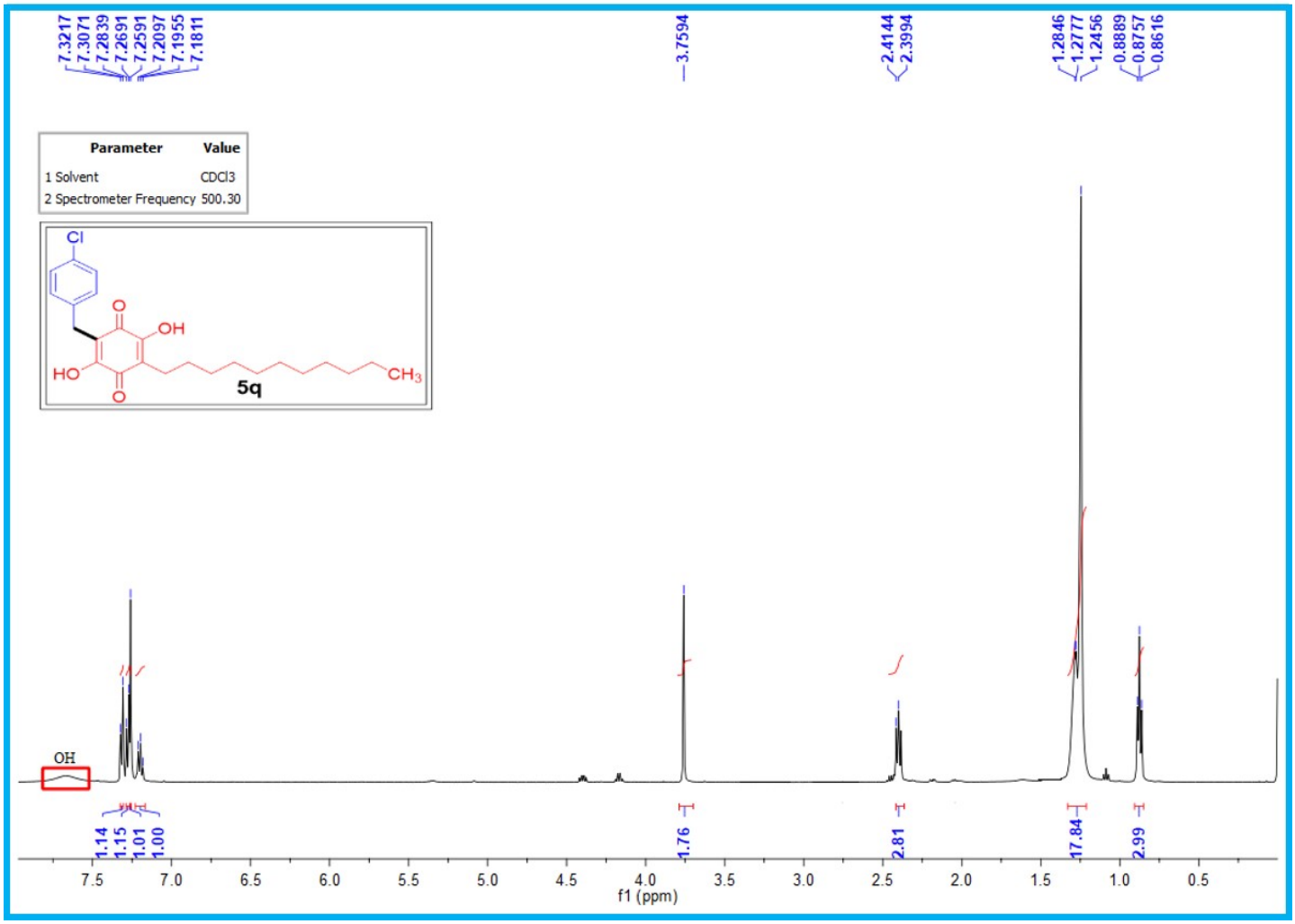


Fig. S36. ^{1}H NMR spectrum of 2-(4-chlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5q**).

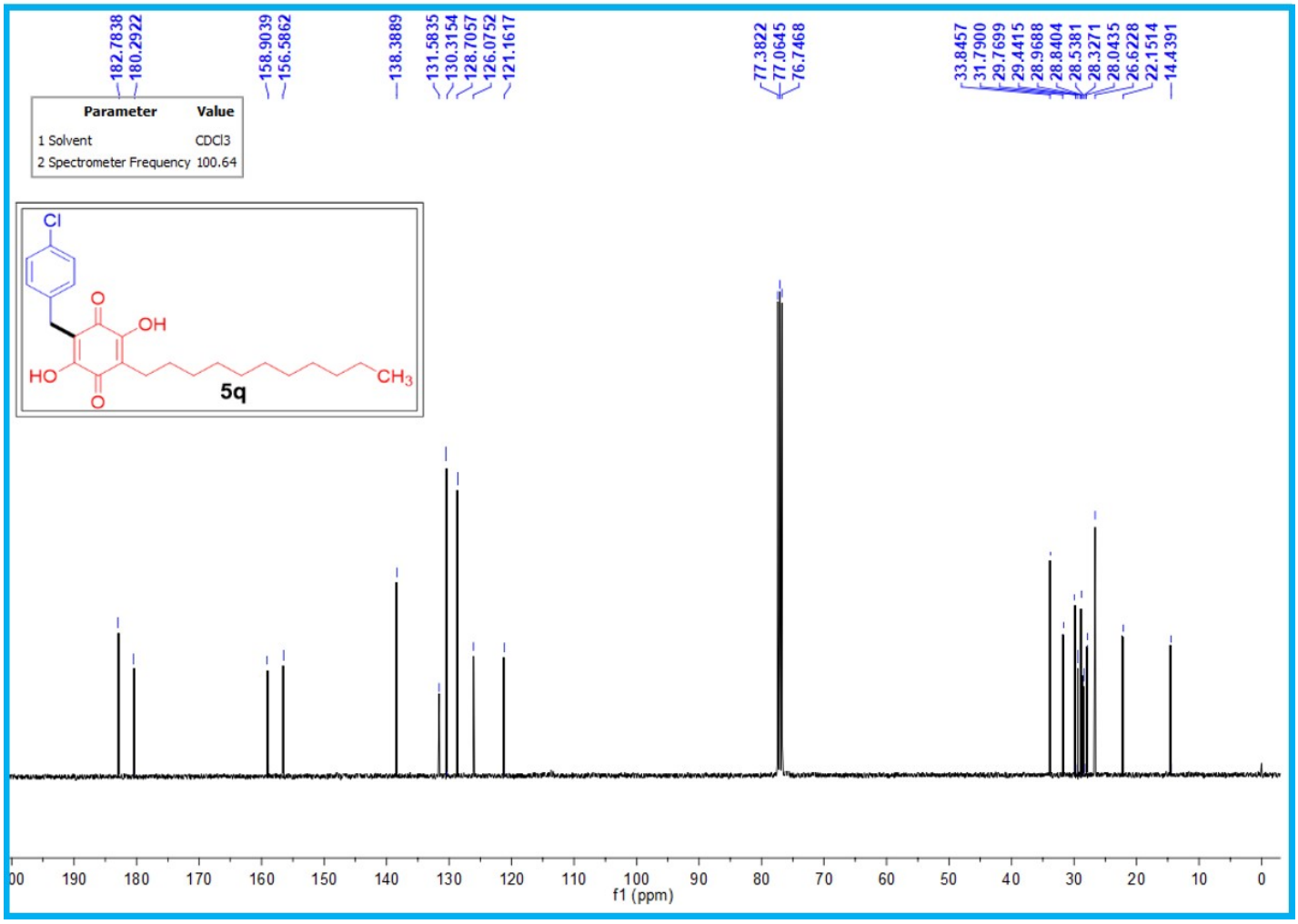


Fig. S37. ^{13}C NMR spectrum of 2-(4-chlorobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5q**).

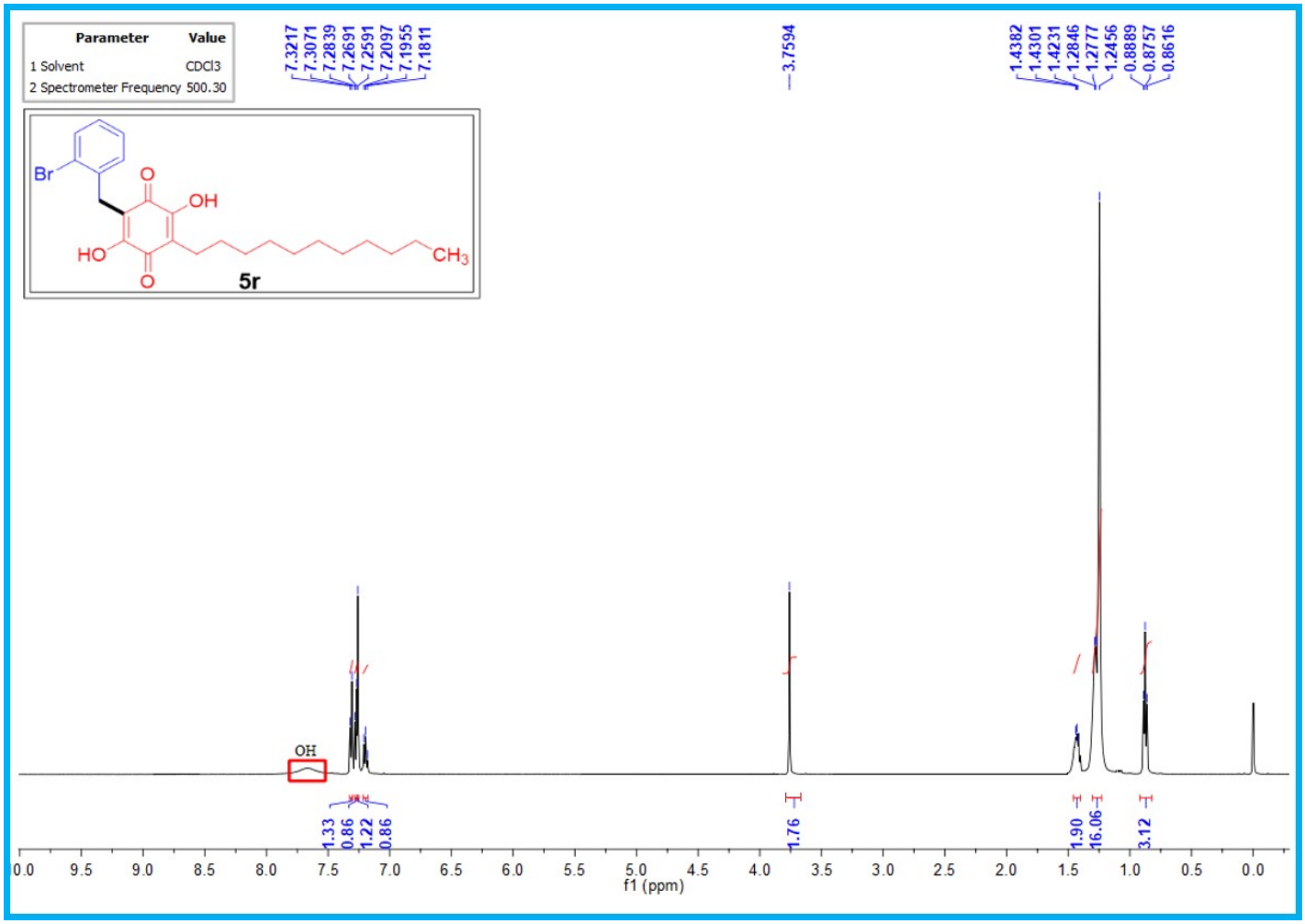


Fig. S38. ^{1}H NMR spectrum of 2-(2-bromobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5r**).

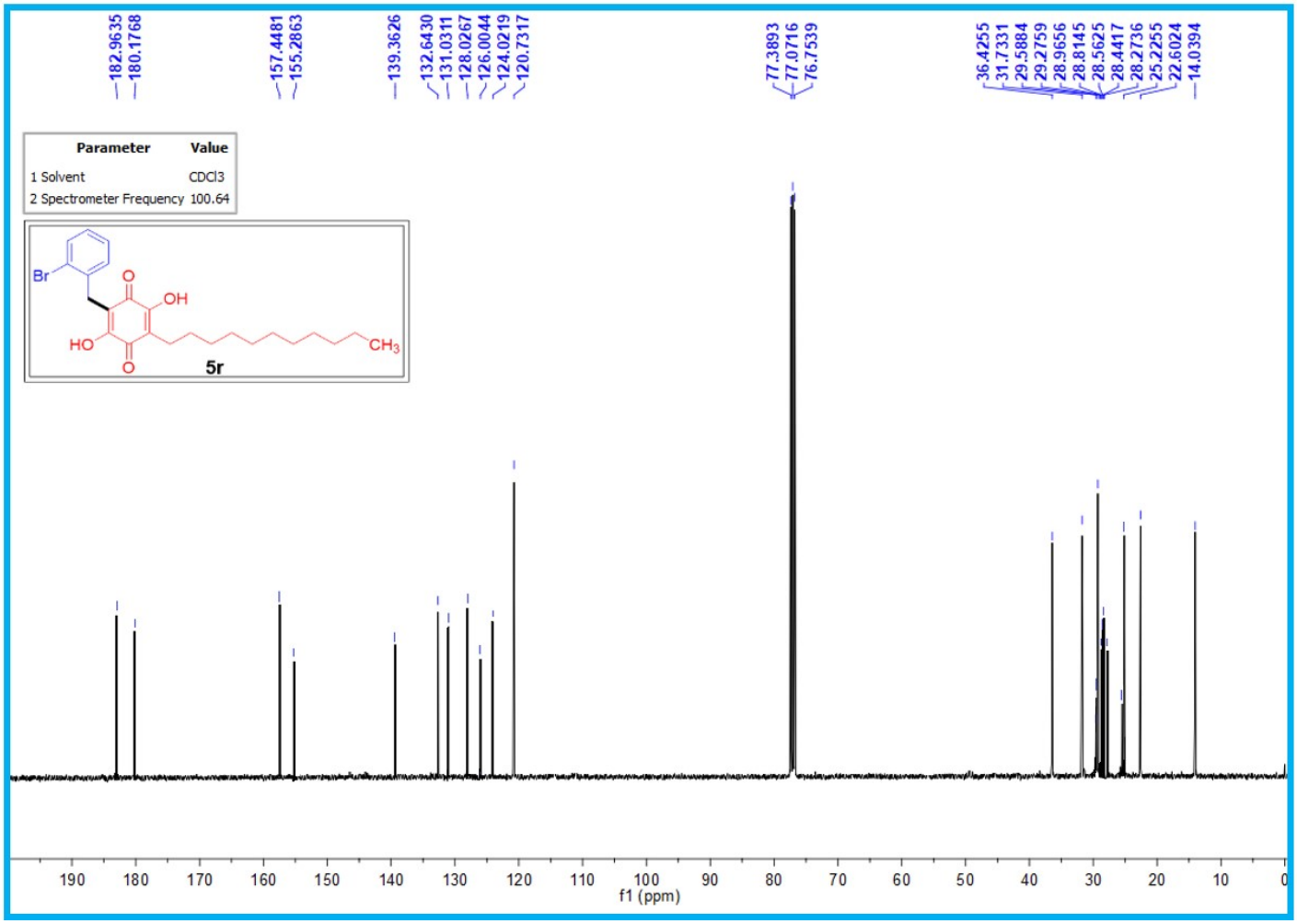


Fig. S39. ^{13}C NMR spectrum of 2-(2-bromobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5r**).

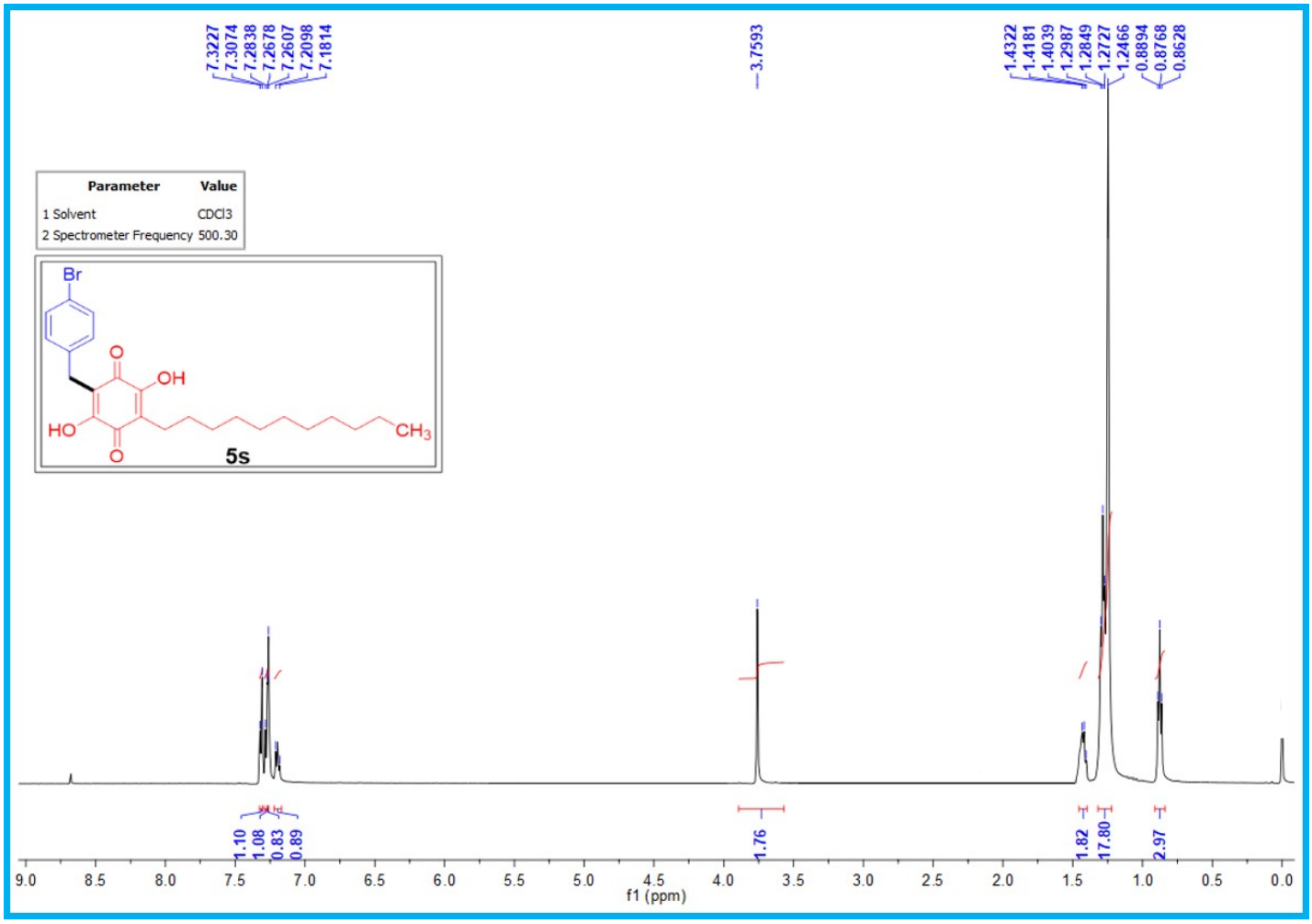


Fig. S40. ^{1}H NMR spectrum of 2-(4-bromobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5s**).

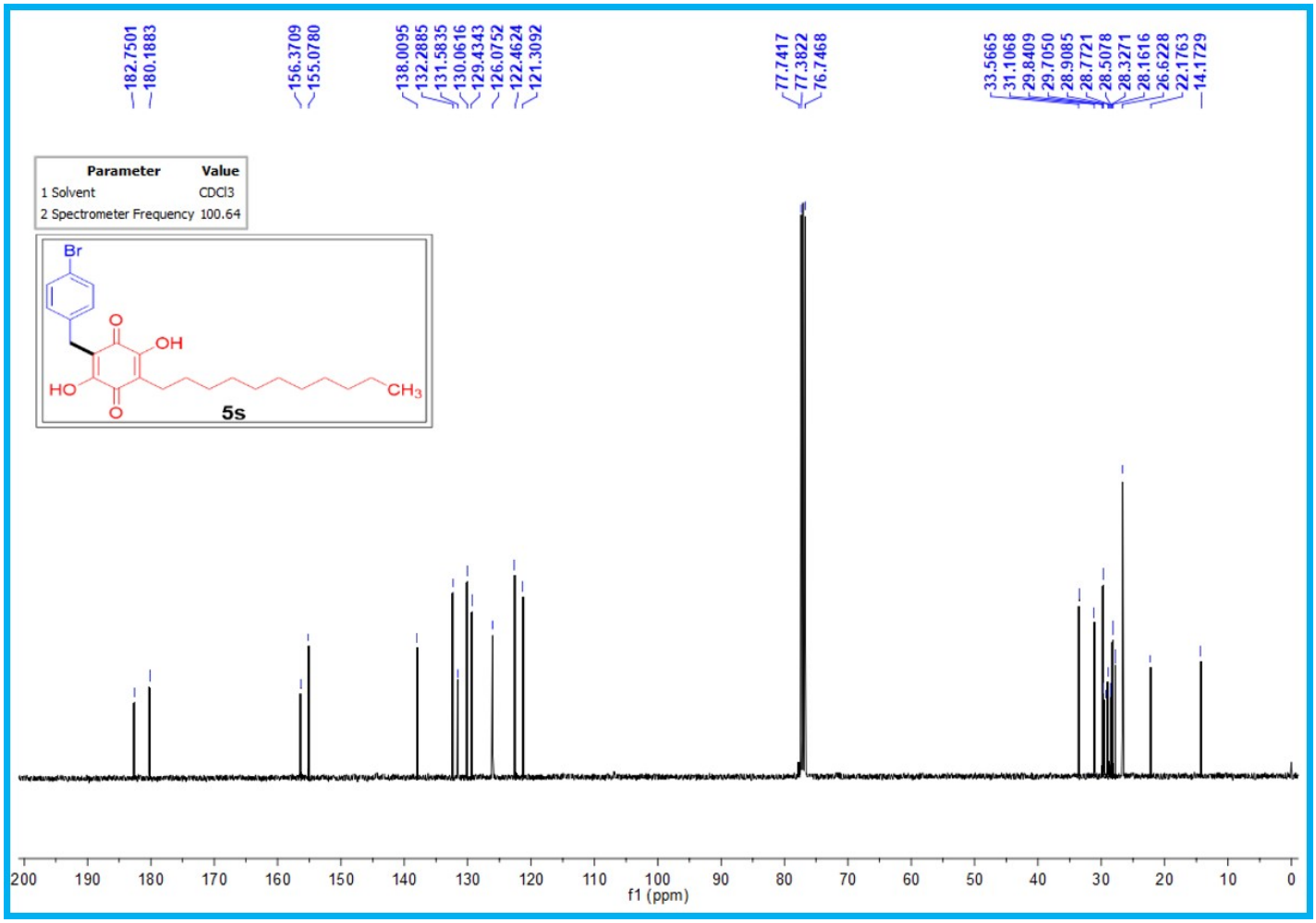


Fig. S41. ^{13}C NMR spectrum of 2-(4-bromobenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5s**).

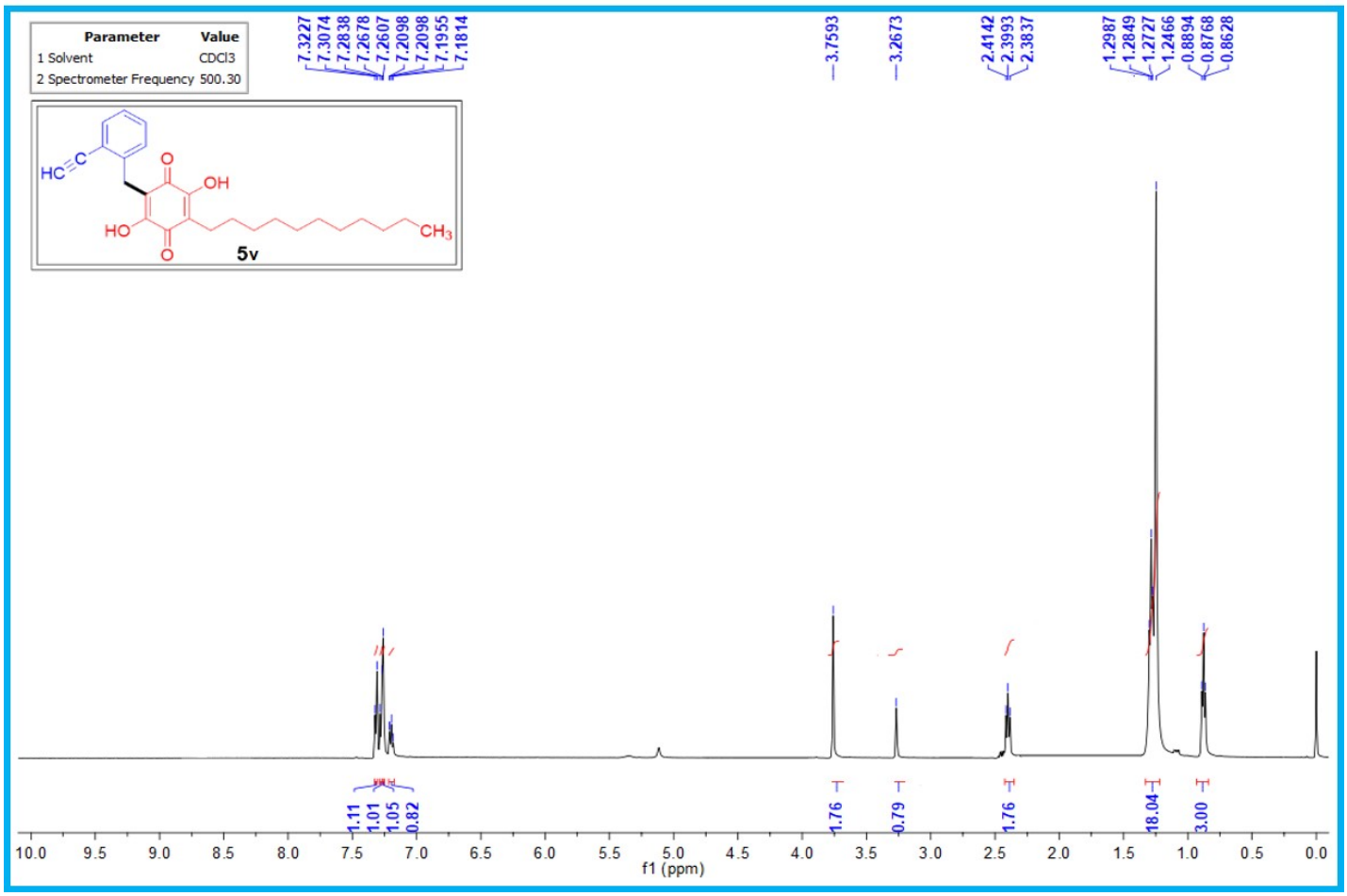


Fig. S42. ^{1}H NMR spectrum of 2-(2-ethynylbenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5t**).

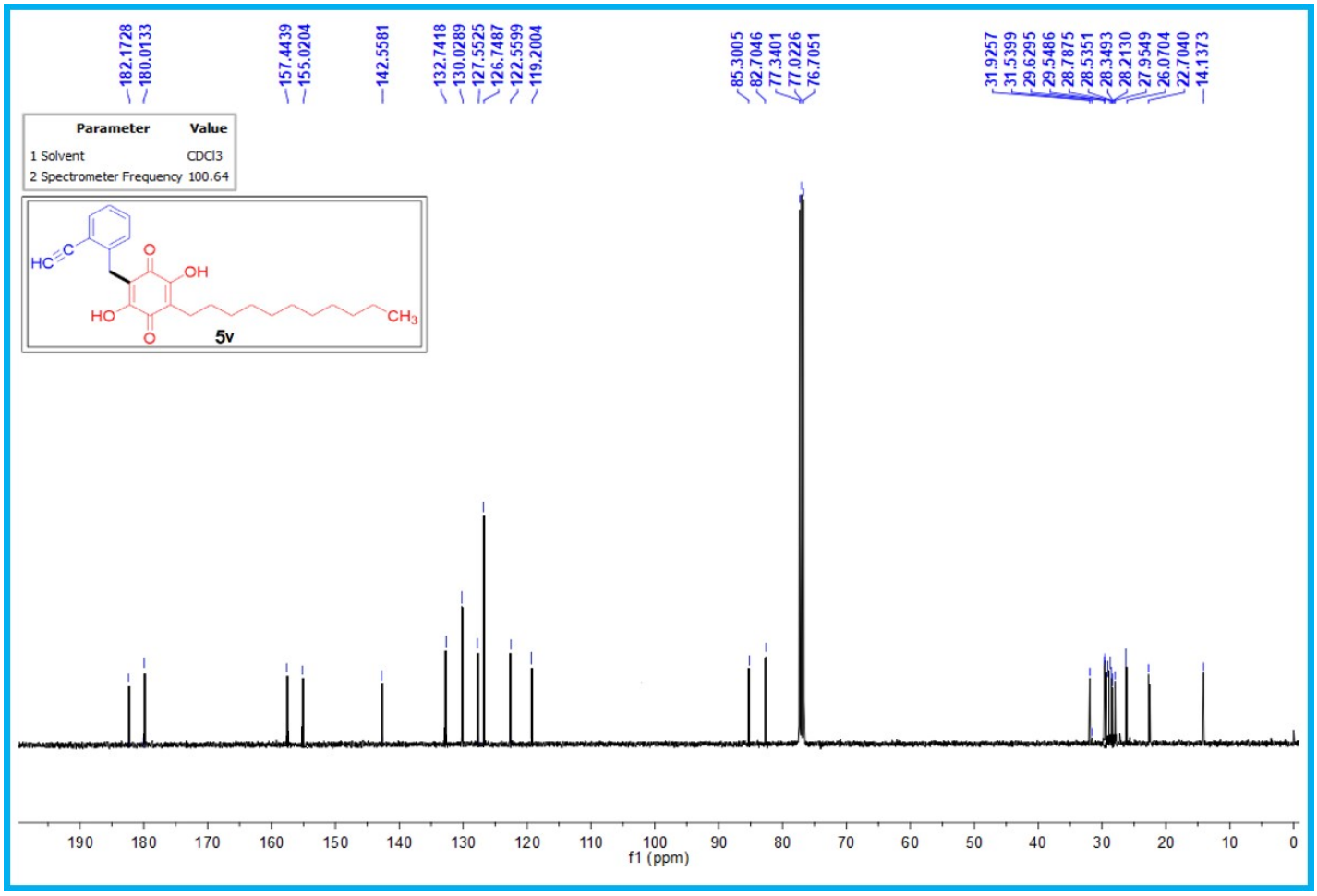


Fig. S43. ^{13}C NMR spectrum of 2-(2-ethynylbenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5t**).

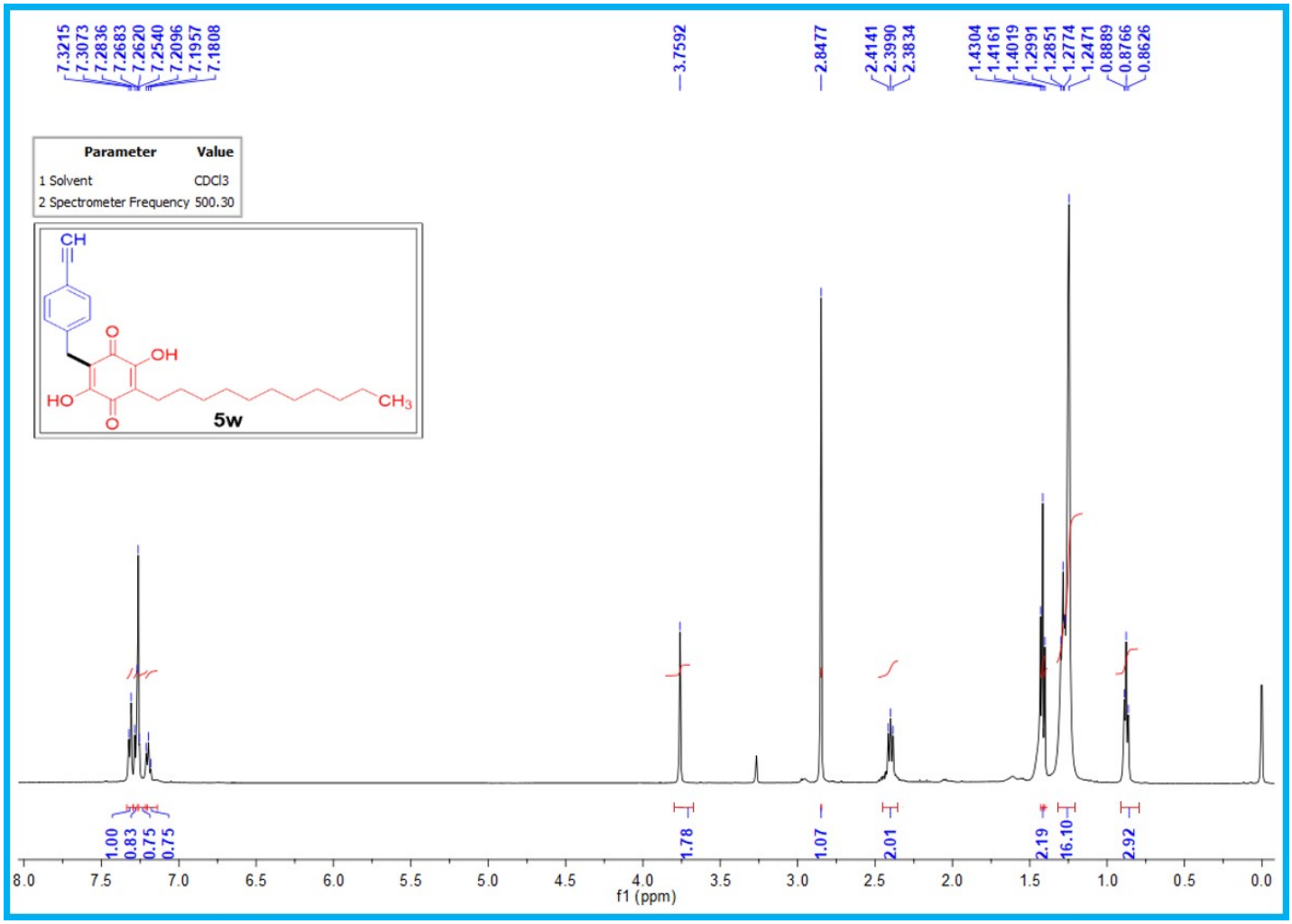


Fig. S44. ^{1}H NMR spectrum of 2-(4-ethynylbenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5u**).

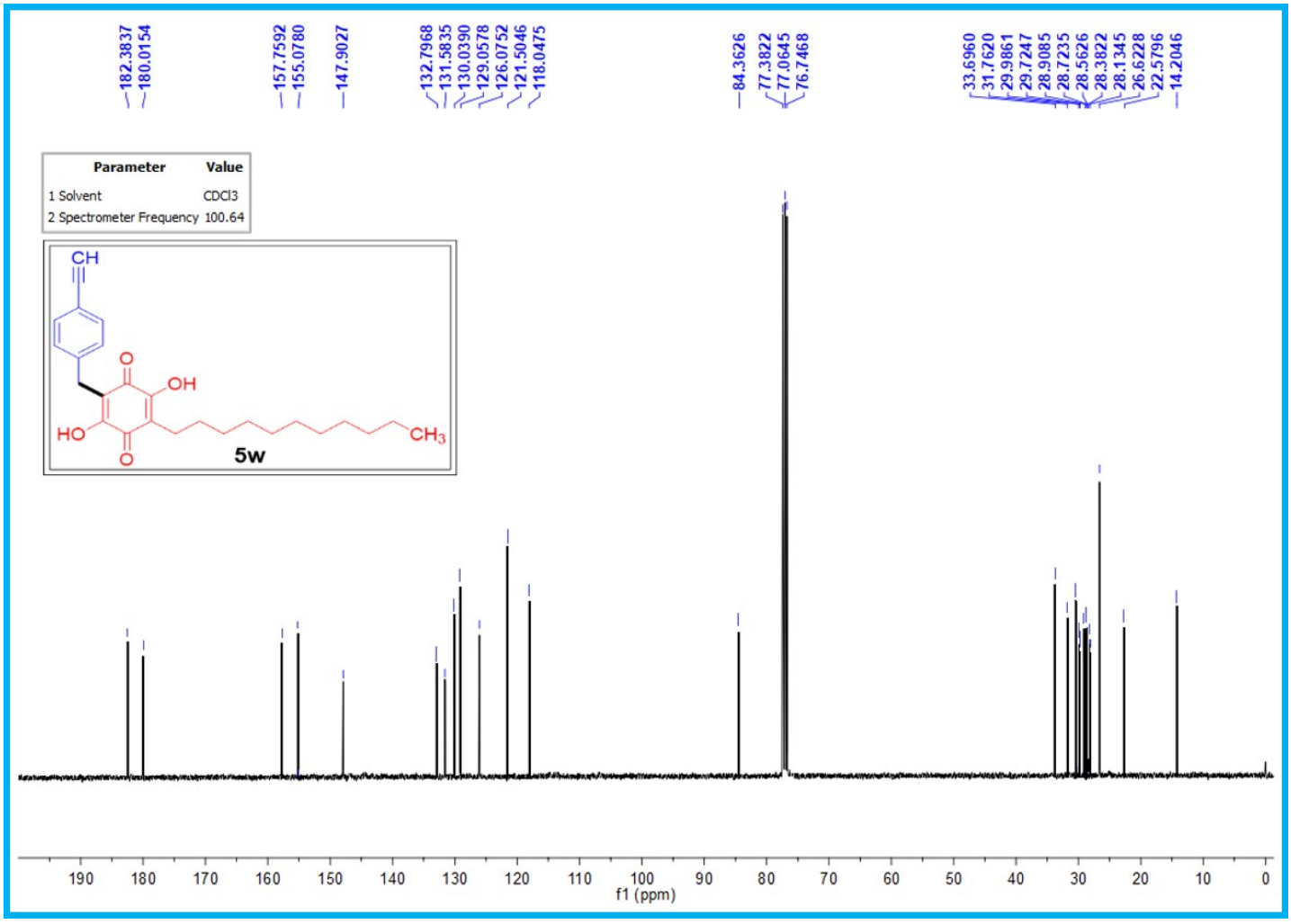


Fig. S45. ^{13}C NMR spectrum of 2-(4-ethynylbenzyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5u**).

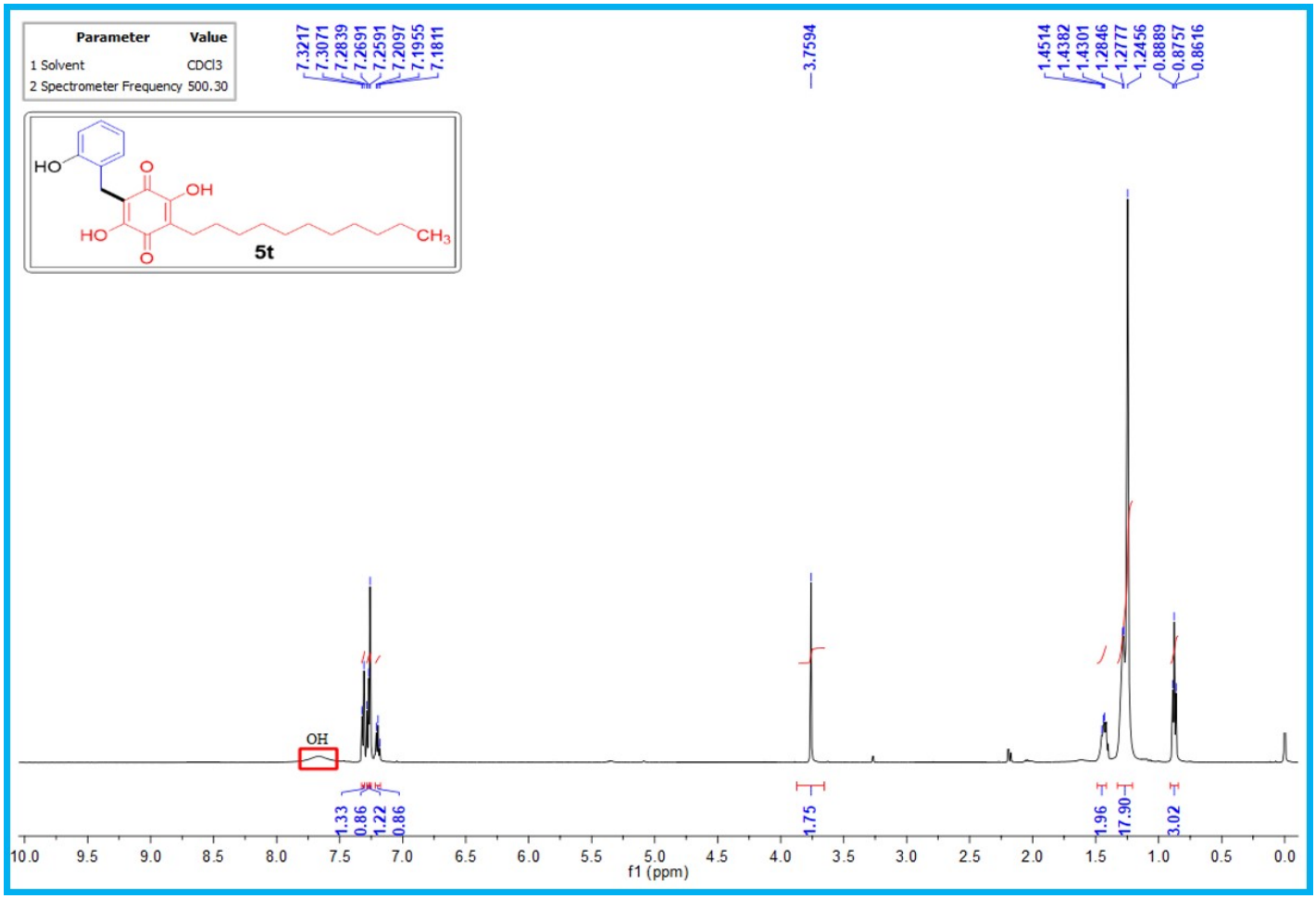


Fig. S46. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(2-hydroxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5v**).

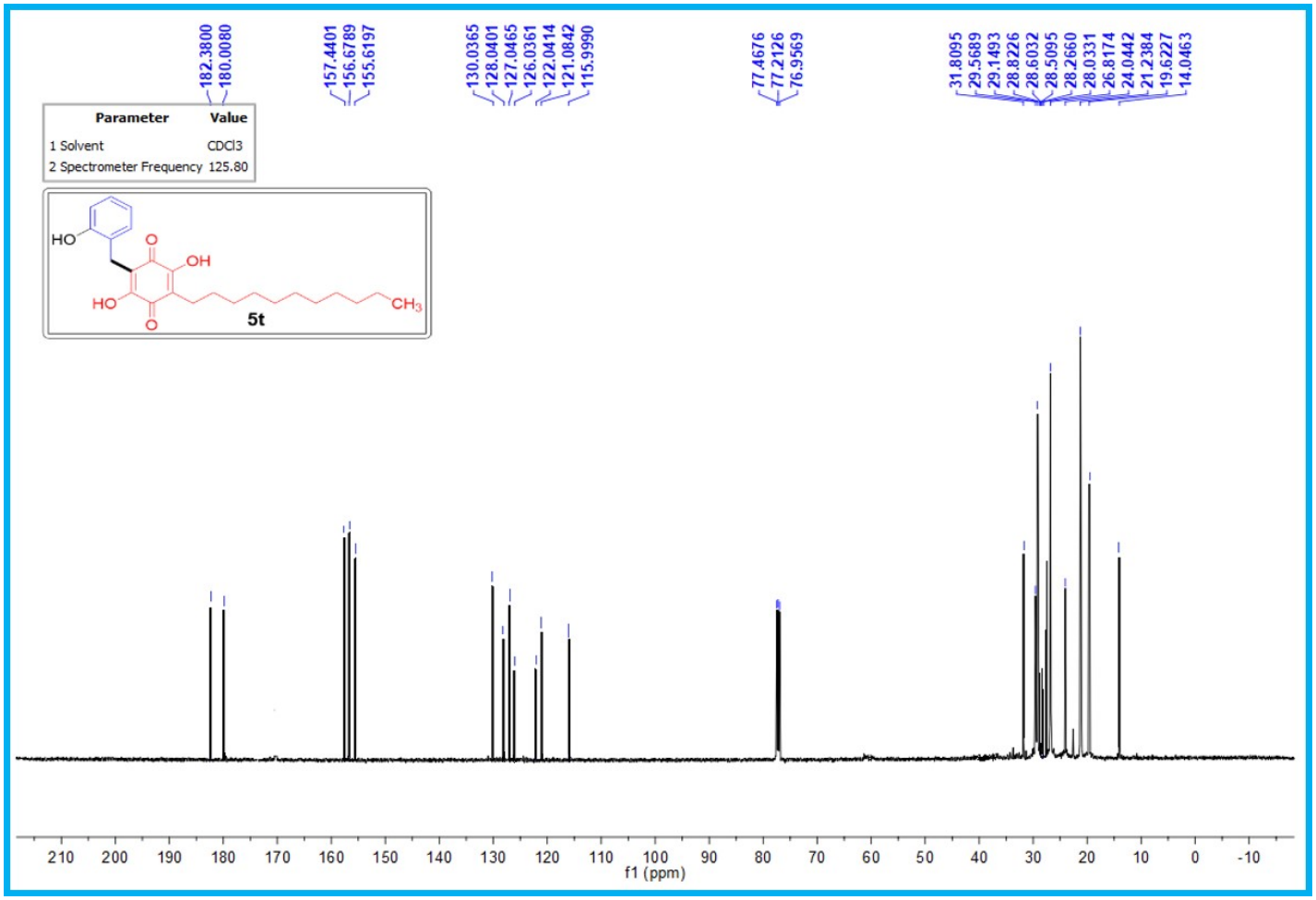


Fig. S47. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(2-hydroxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5v**).

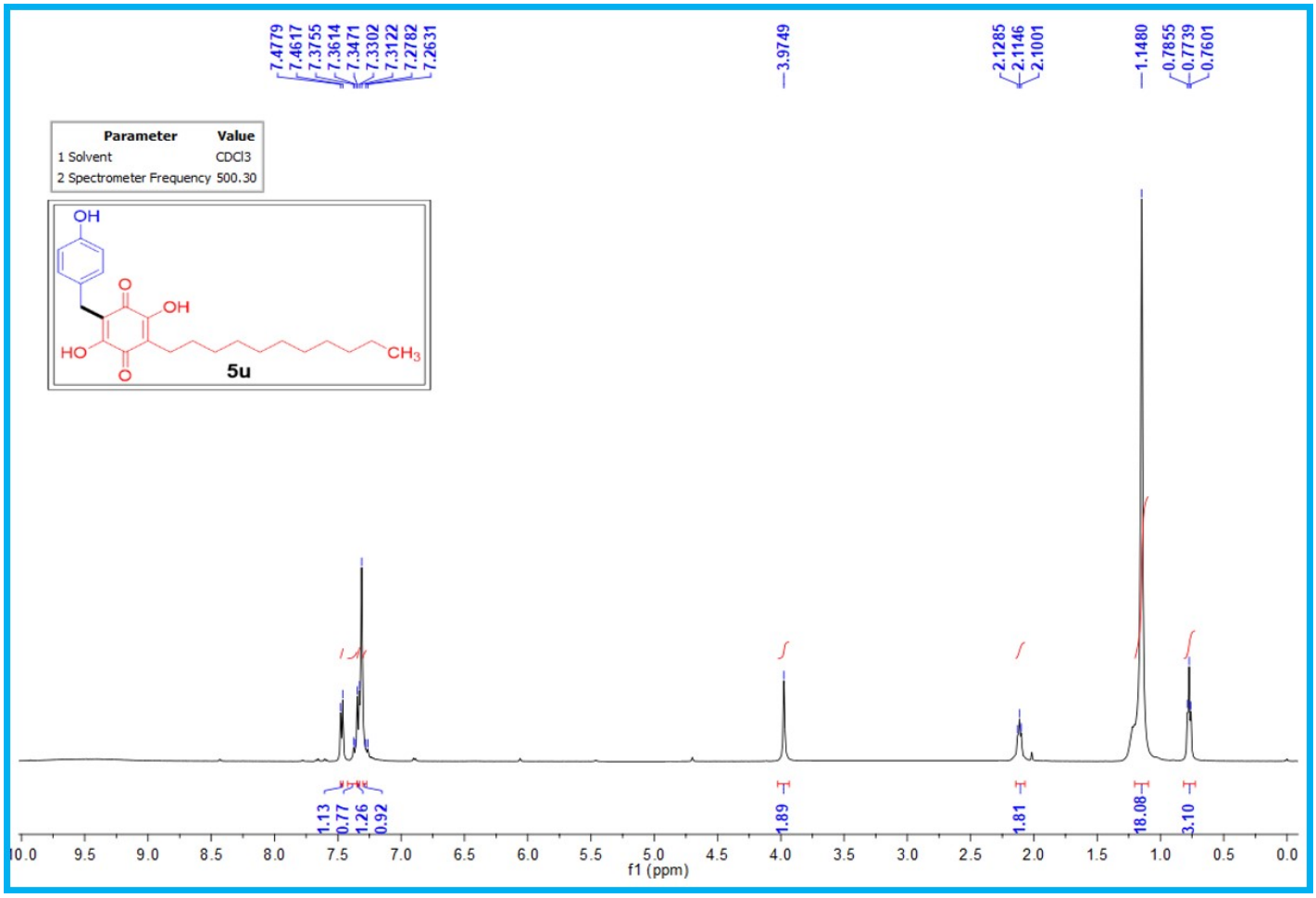


Fig. S48. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(4-hydroxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5w**).

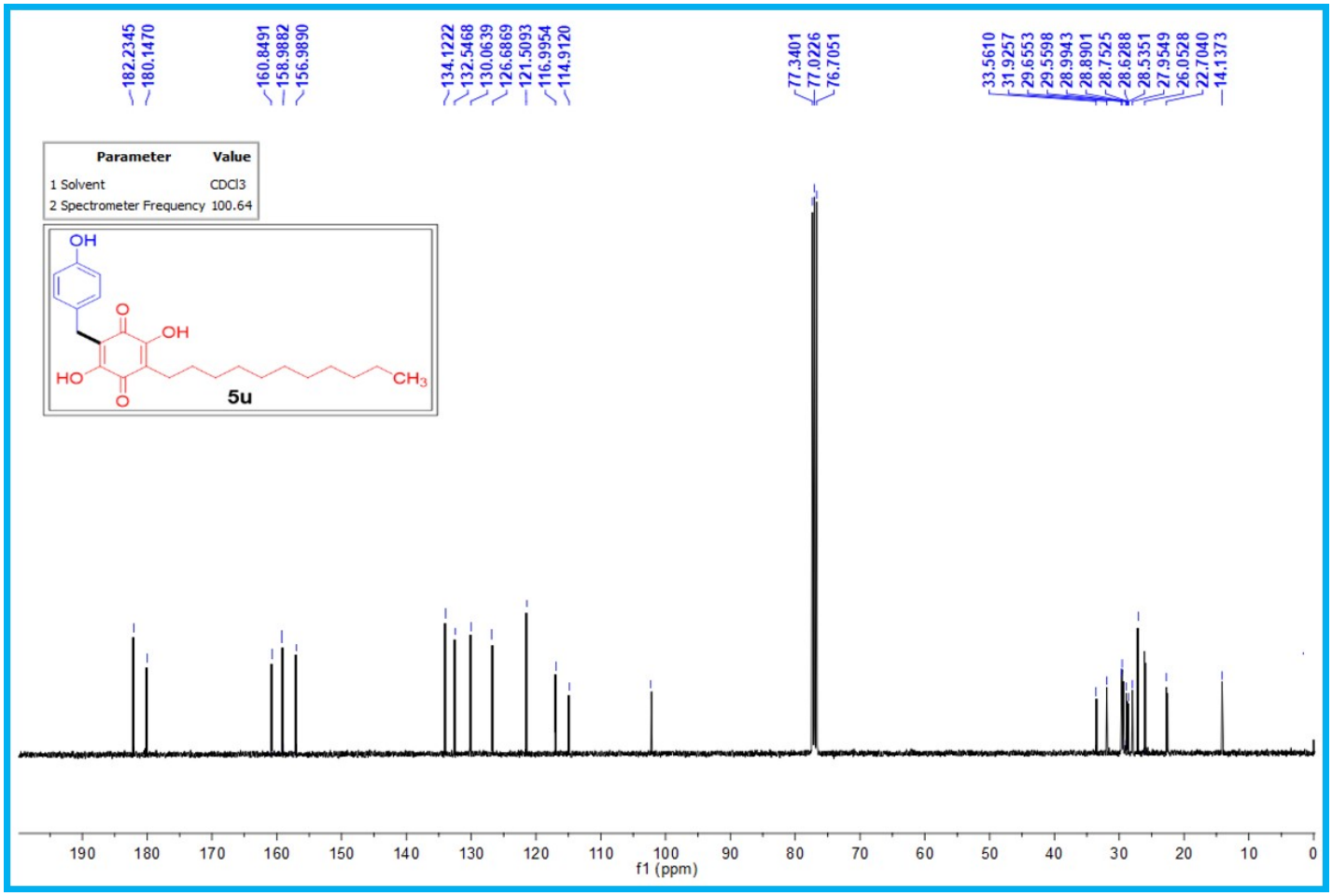


Fig. S49. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(4-hydroxybenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5w**).

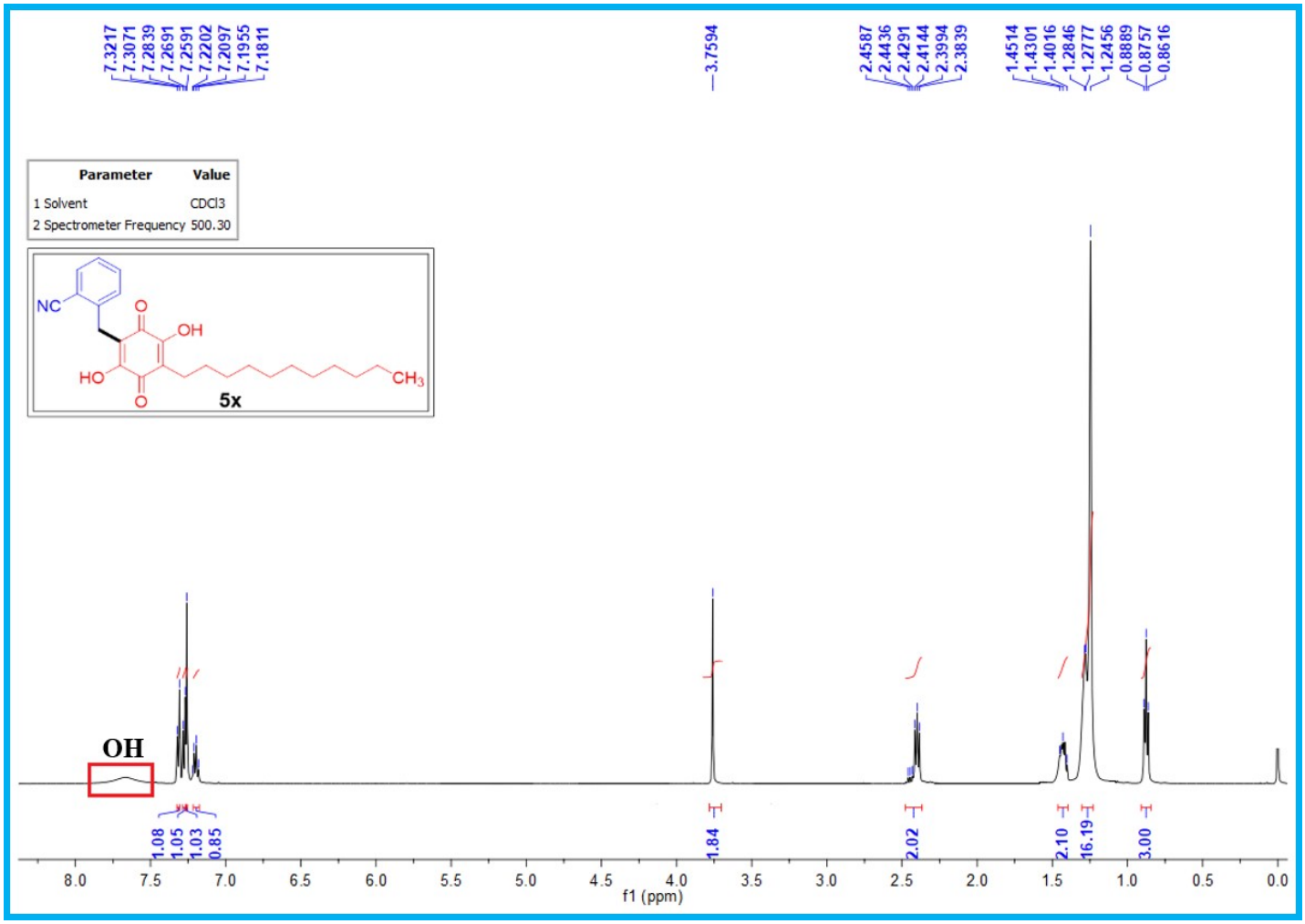


Fig. S50. ^{1}H NMR spectrum of 2-((2,5-dihydroxy-3,6-dioxo-4-undecylcyclohexa-1,4-dien-1-yl)methyl)benzonitrile (**5x**).

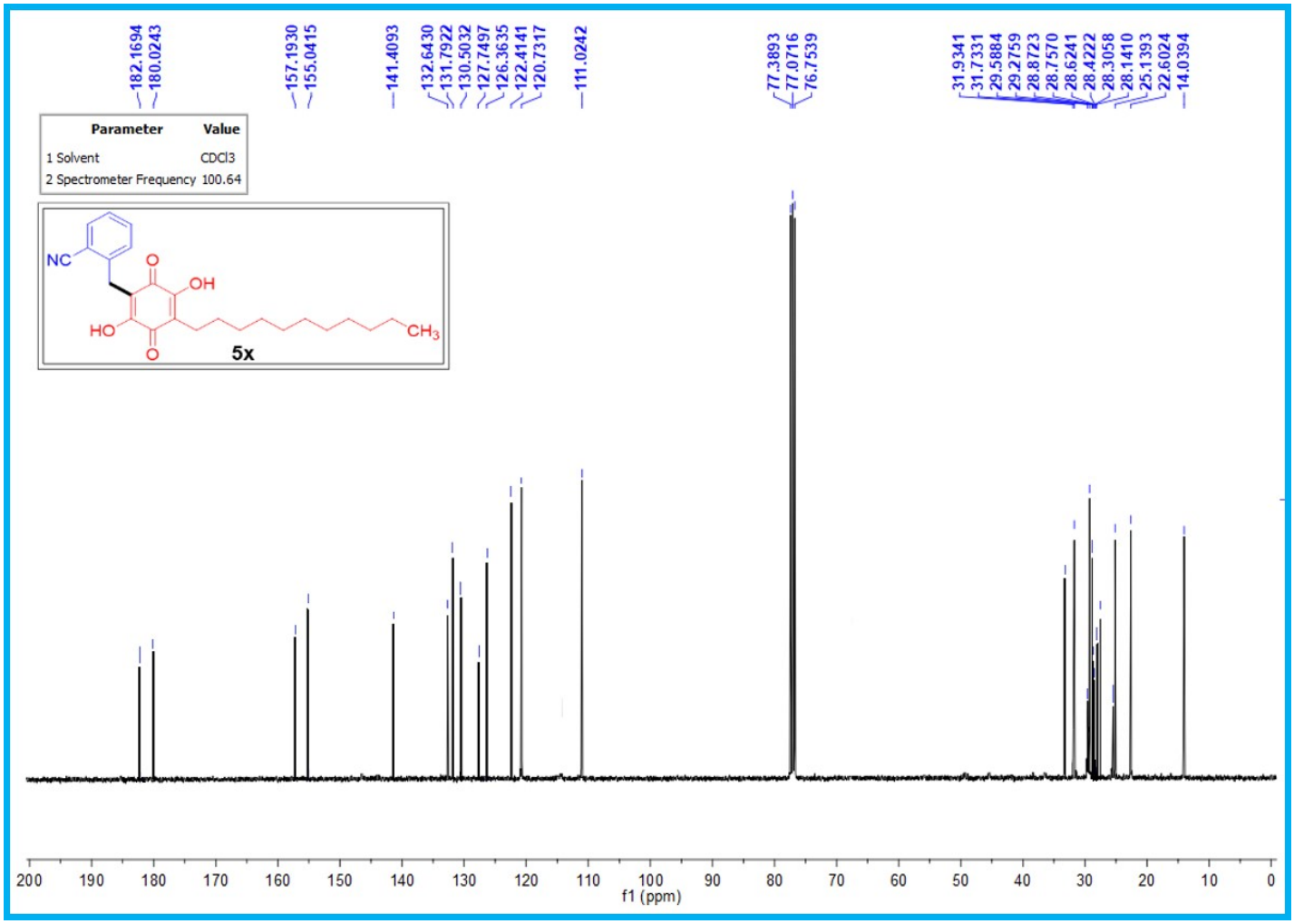


Fig. S51. ^{13}C NMR spectrum of 2-((2,5-dihydroxy-3,6-dioxo-4-undecylcyclohexa-1,4-dien-1-yl)methyl)benzonitrile (**5x**).

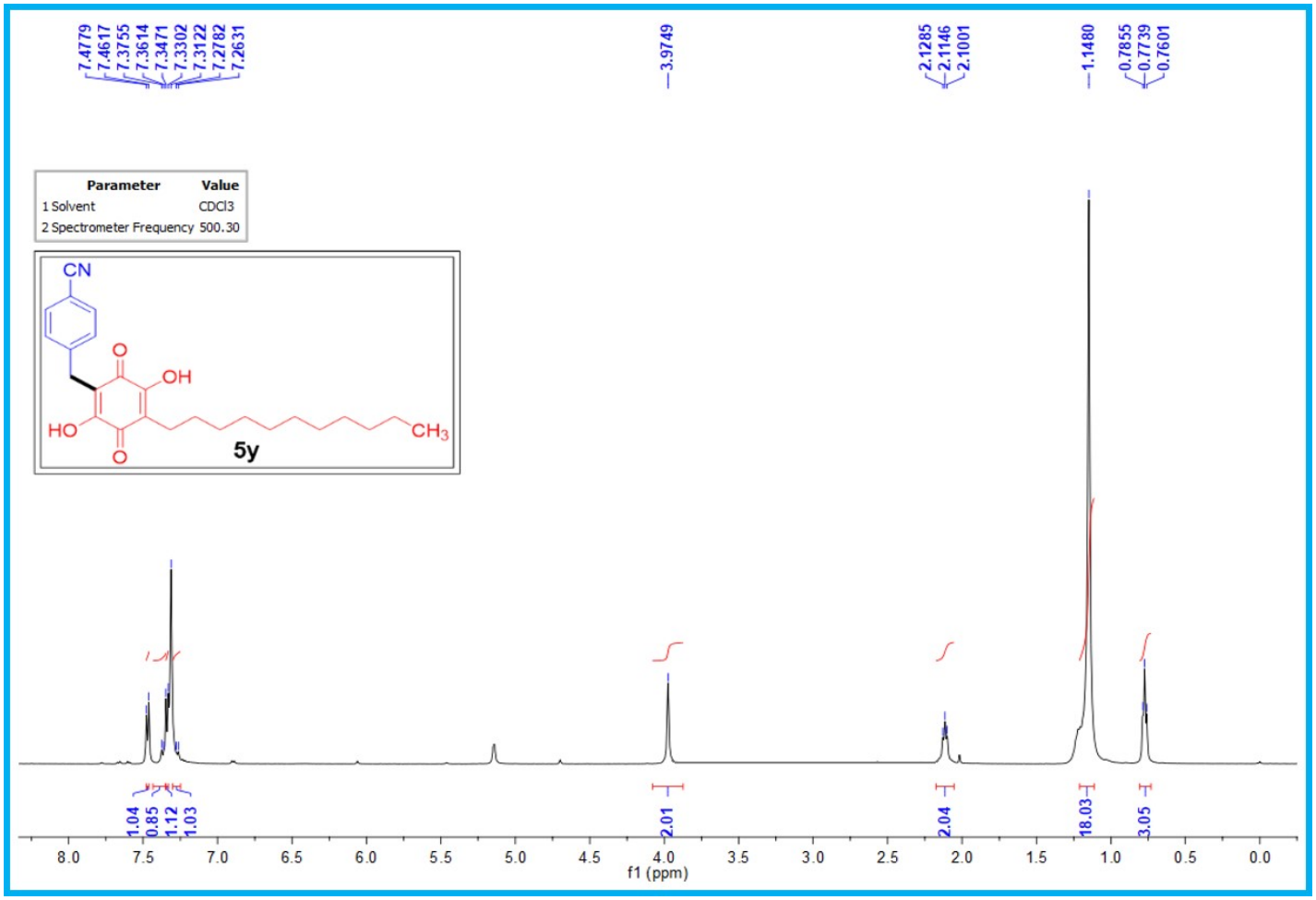


Fig. S52. ^{1}H NMR spectrum of 4-((2,5-dihydroxy-3,6-dioxo-4-undecylcyclohexa-1,4-dien-1-yl)methyl)benzonitrile (**5y**).

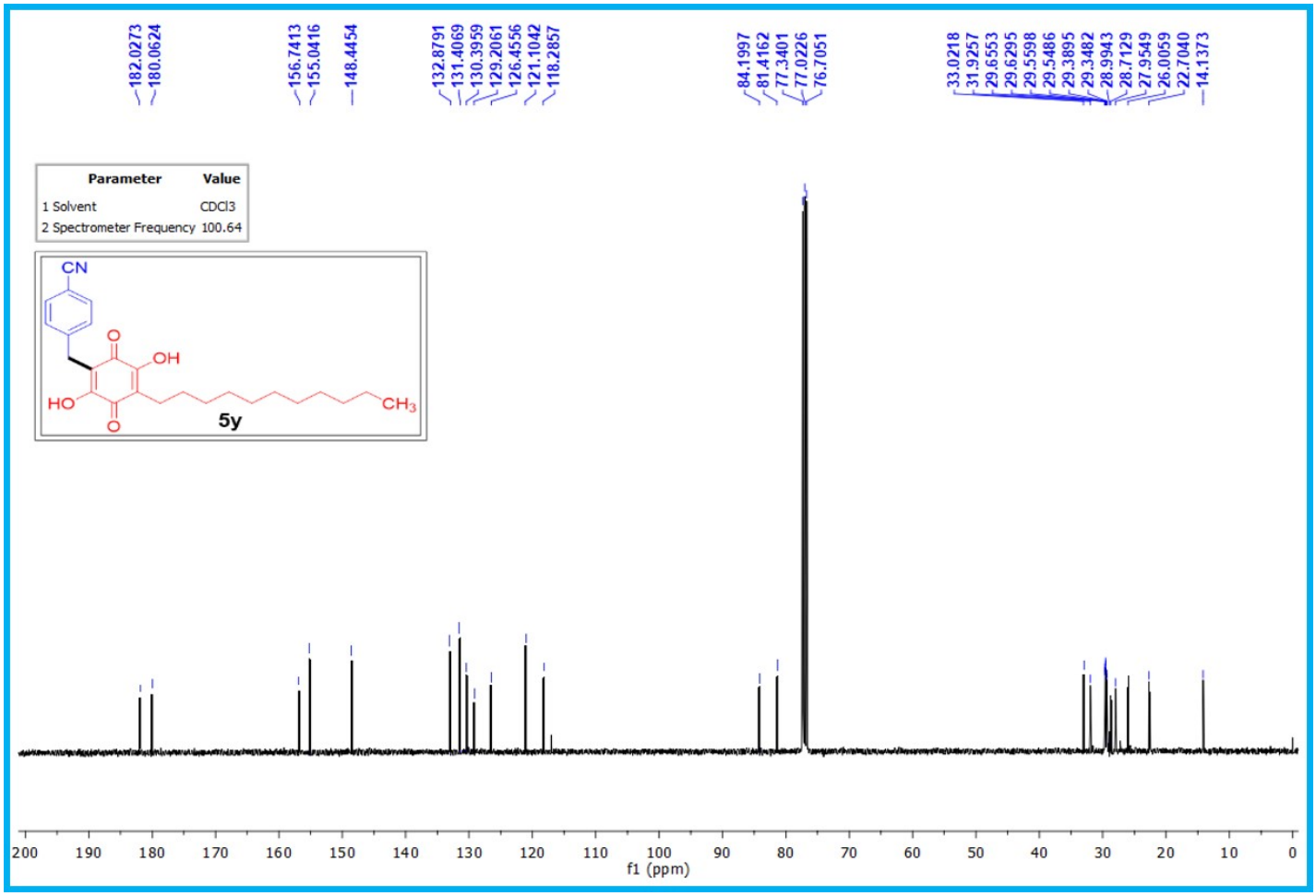


Fig. S53. ^{13}C NMR spectrum of 4-((2,5-dihydroxy-3,6-dioxo-4-undecylcyclohexa-1,4-dien-1-yl)methyl)benzonitrile (**5y**).

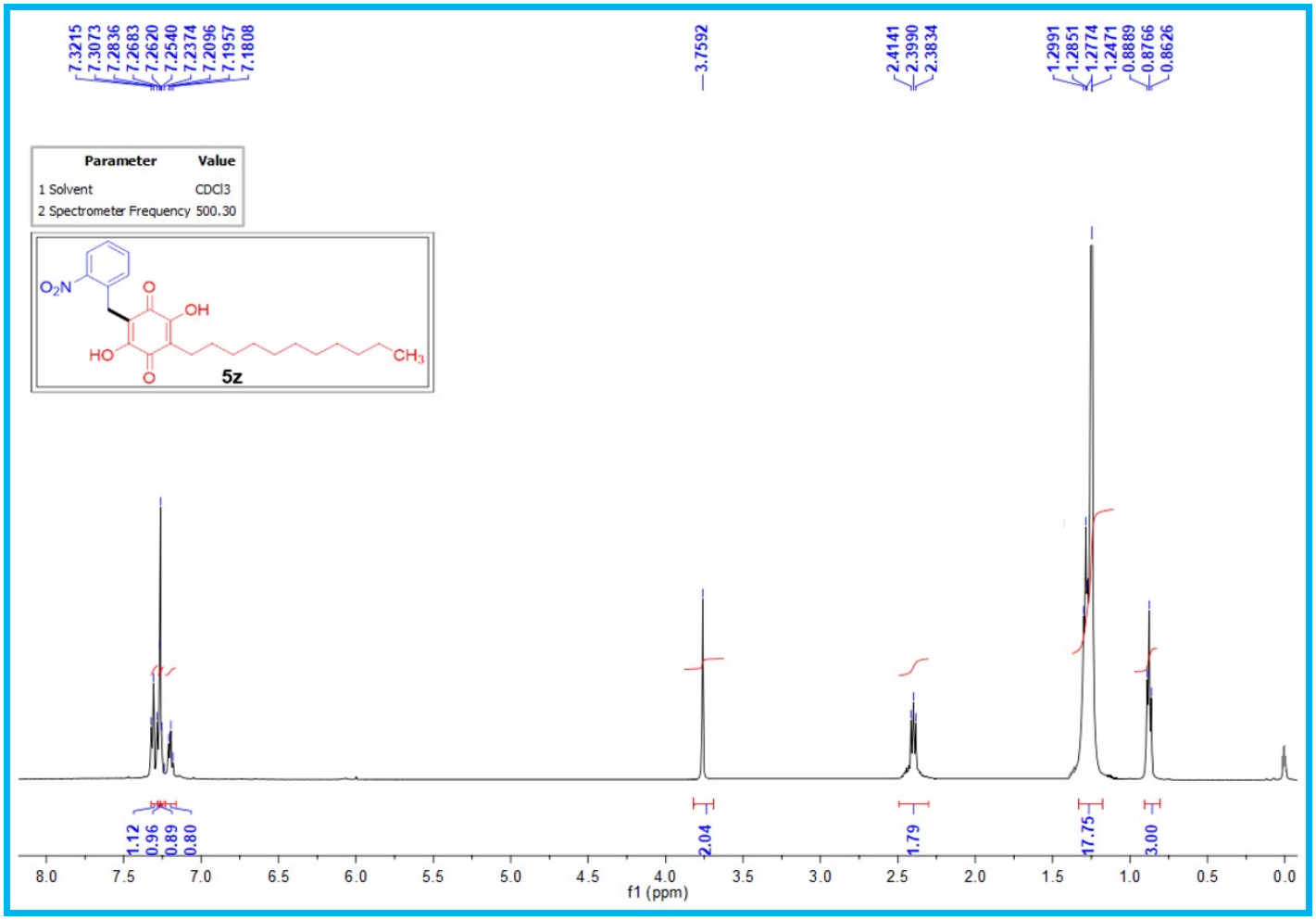


Fig. S54. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(2-nitrobenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5z**).

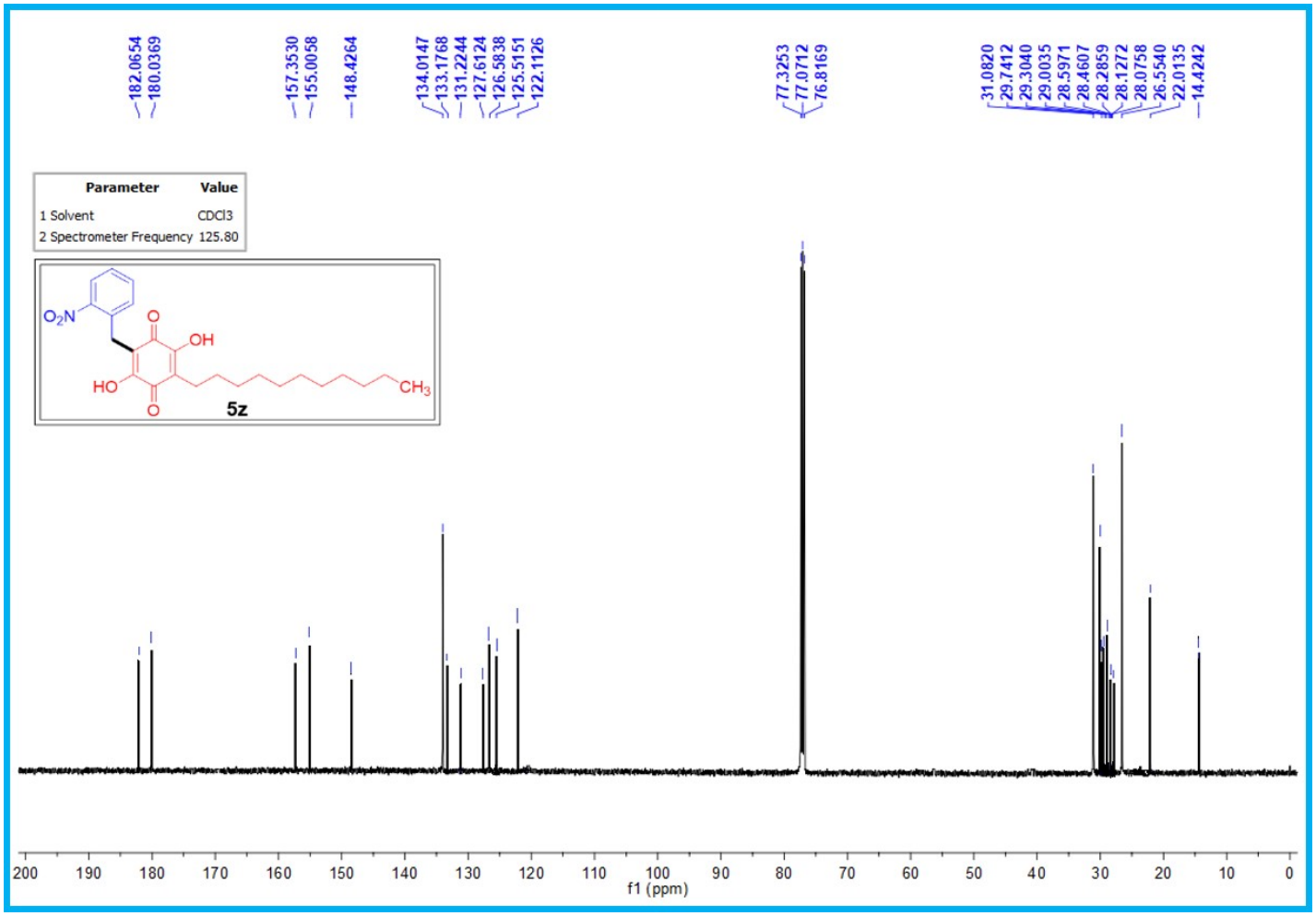


Fig. S55. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(2-nitrobenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5z**).

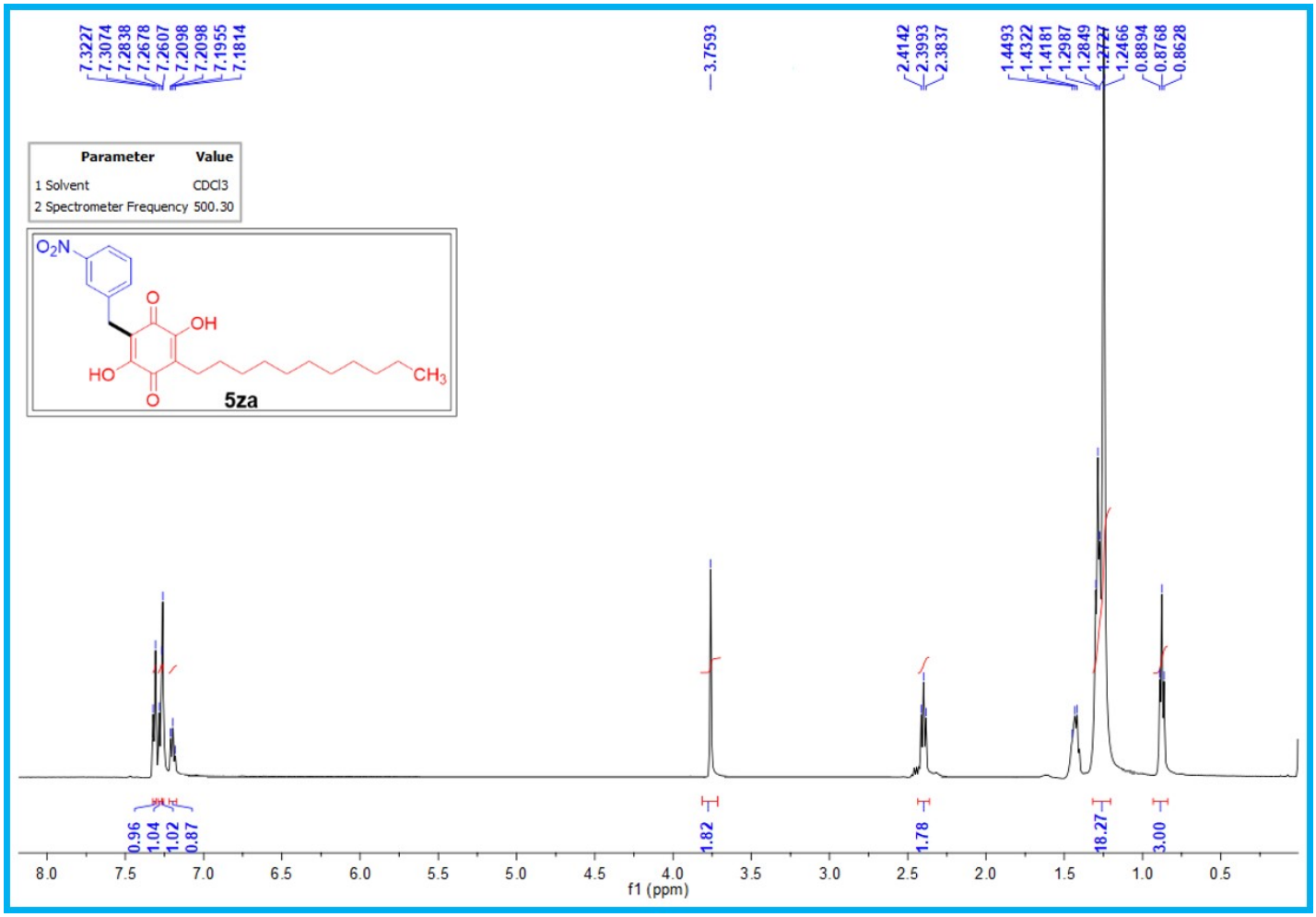


Fig. S56. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(3-nitrobenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5za**).

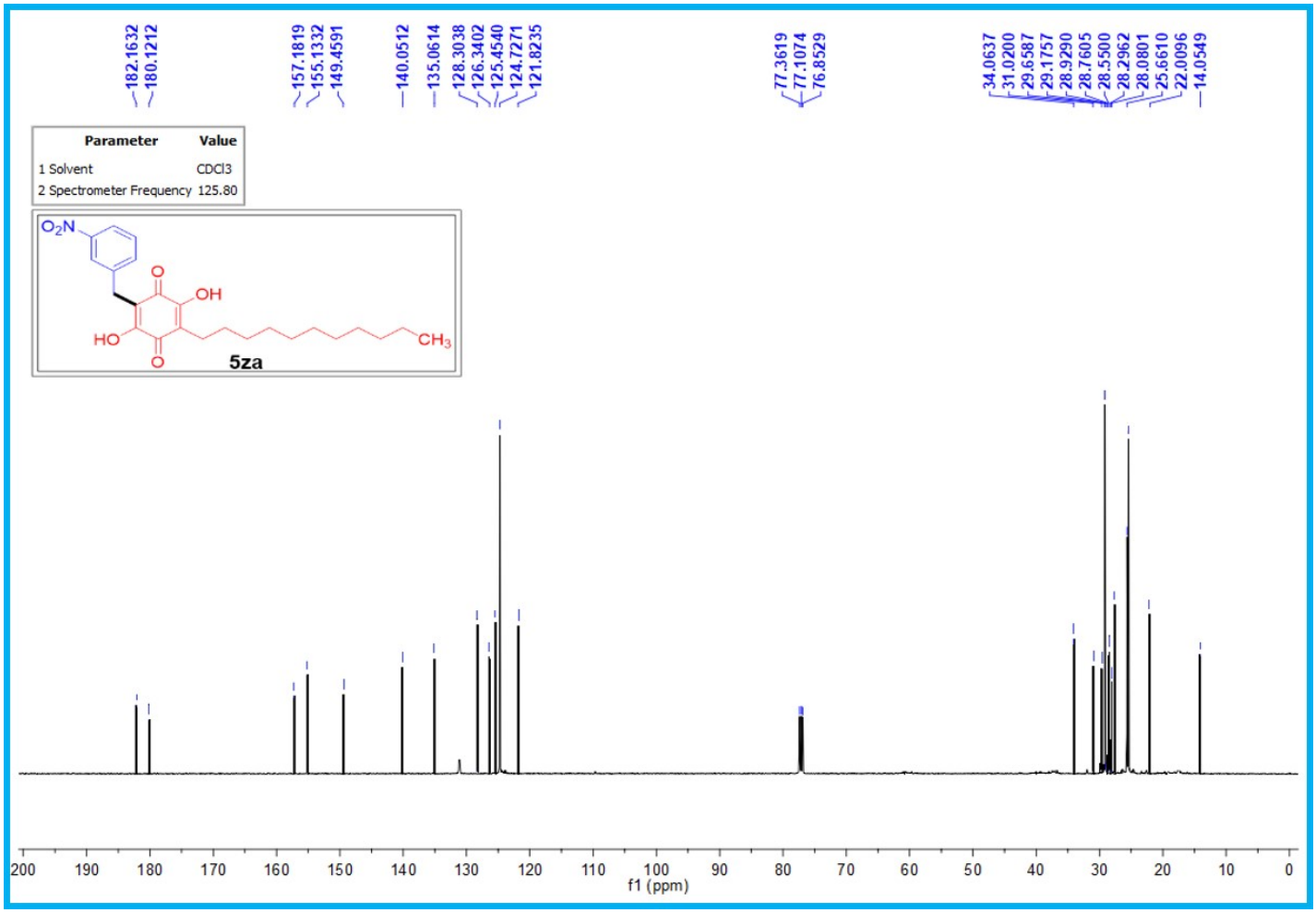


Fig. S57. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(3-nitrobenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5za**).

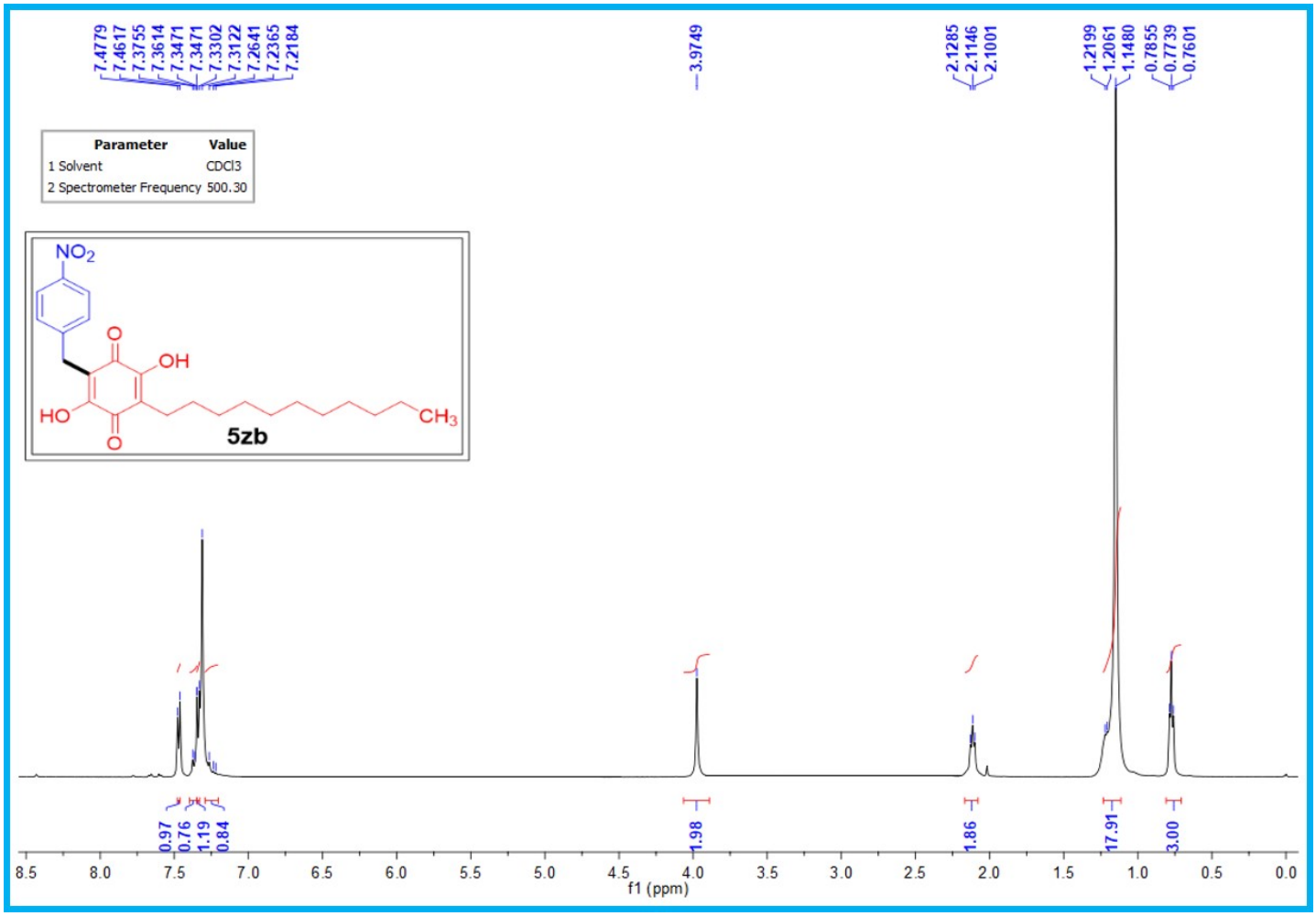


Fig. S58. ^{1}H NMR spectrum of 2,5-dihydroxy-3-(4-nitrobenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5zb**).

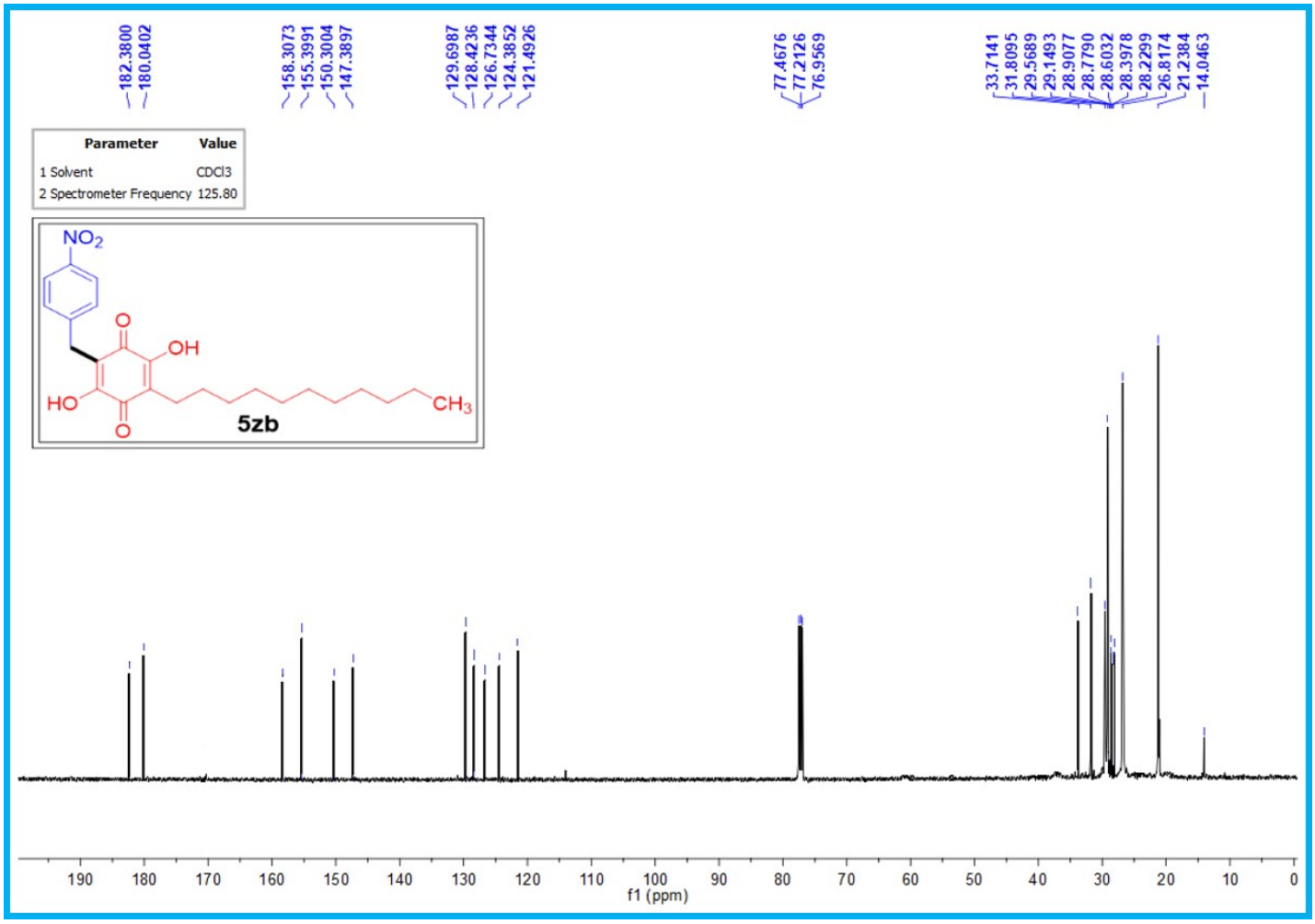


Fig. S59. ^{13}C NMR spectrum of 2,5-dihydroxy-3-(4-nitrobenzyl)-6-undecylcyclohexa-2,5-diene-1,4-dione (**5zb**).

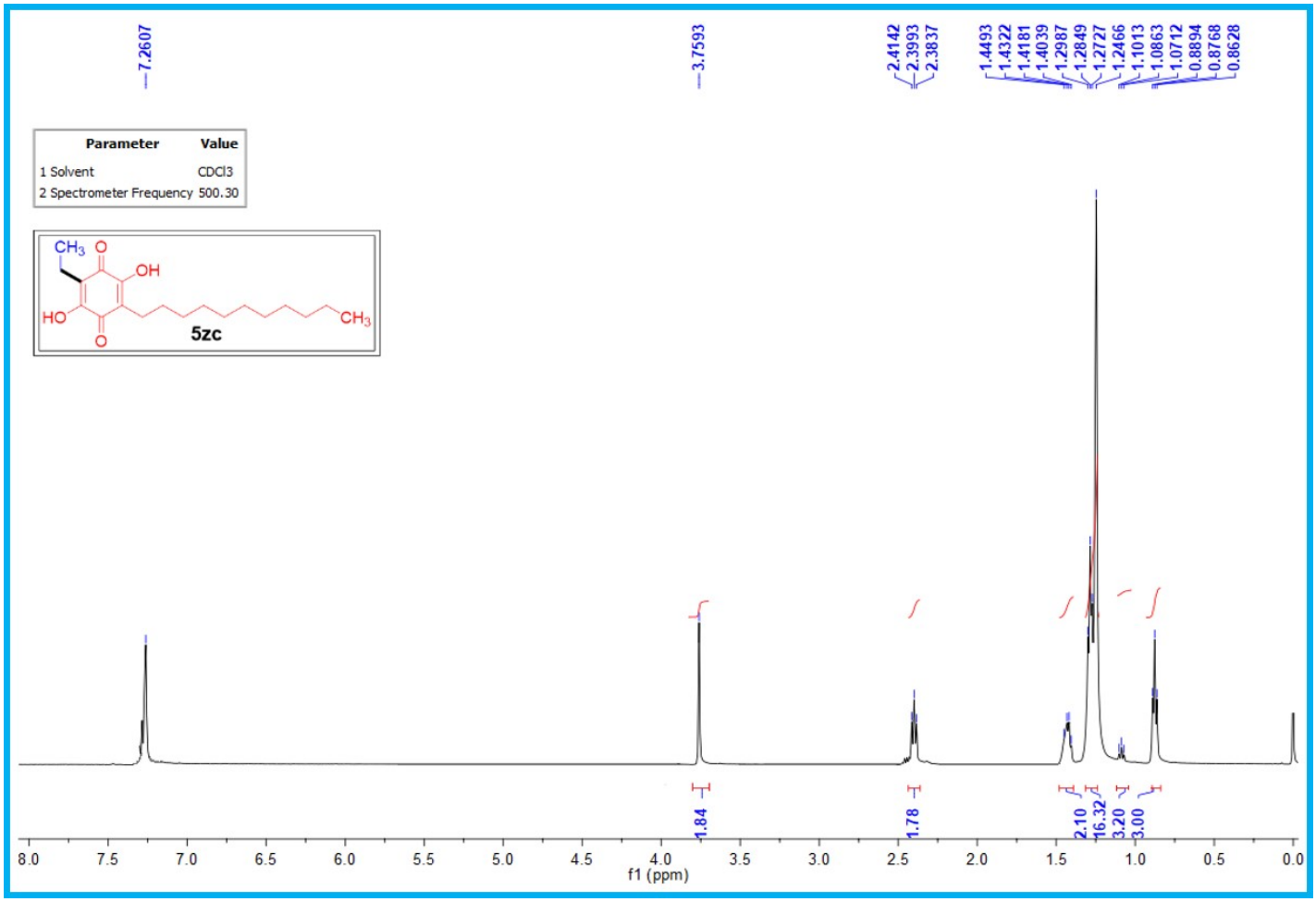


Fig. S60. ^{1}H NMR spectrum of 2-ethyl-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5zc**).

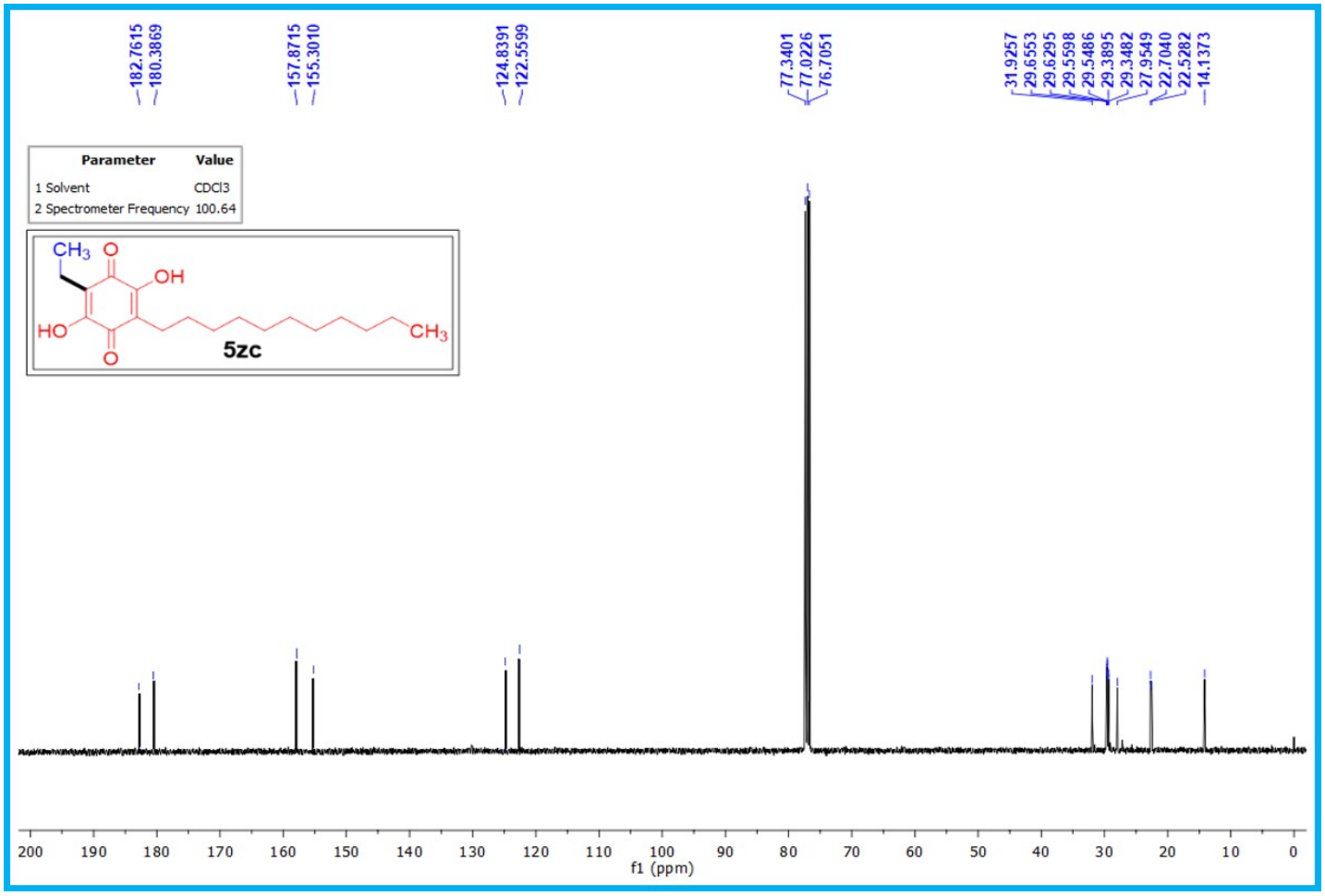


Fig. S61. ^{13}C NMR spectrum of 2-ethyl-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5zc**).

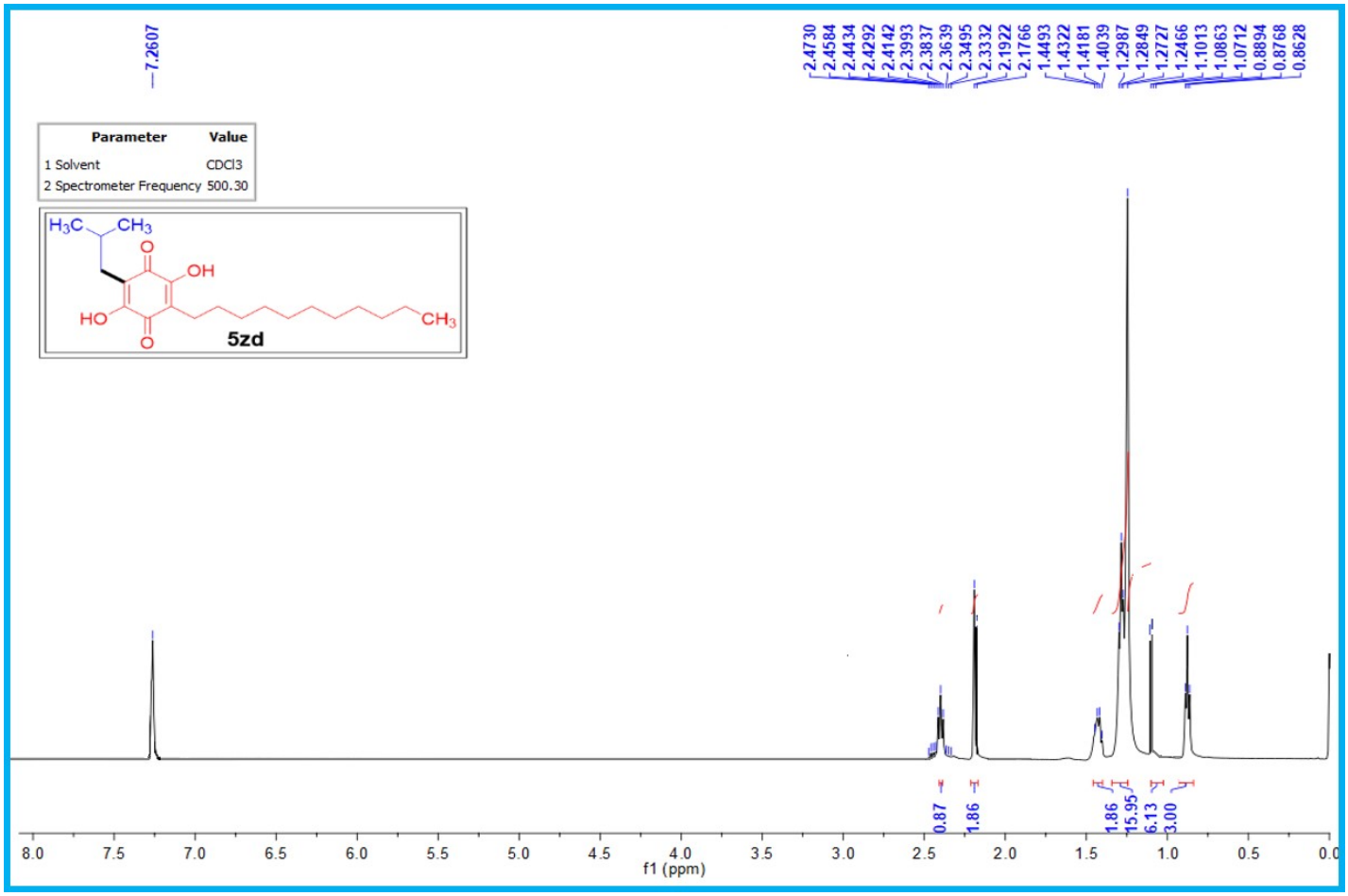


Fig. S62. [1]H NMR spectrum of 2,5-dihydroxy-3-isobutyl-6-undecylcyclohexa-2,5-diene-1,4-dione (**5zd**).

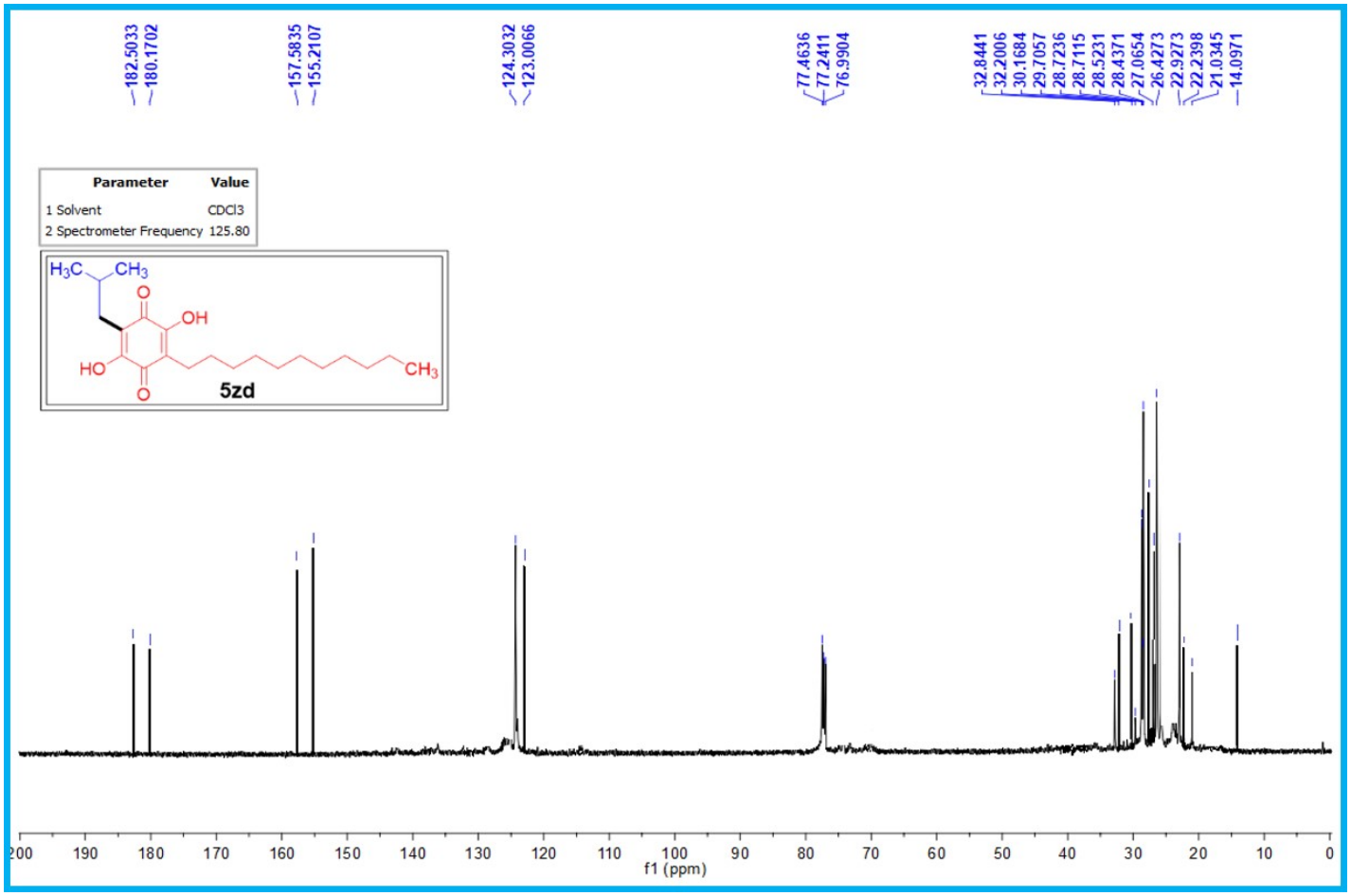


Fig. S63. ^{13}C NMR spectrum of 2,5-dihydroxy-3-isobutyl-6-undecylcyclohexa-2,5-diene-1,4-dione (**5zd**).

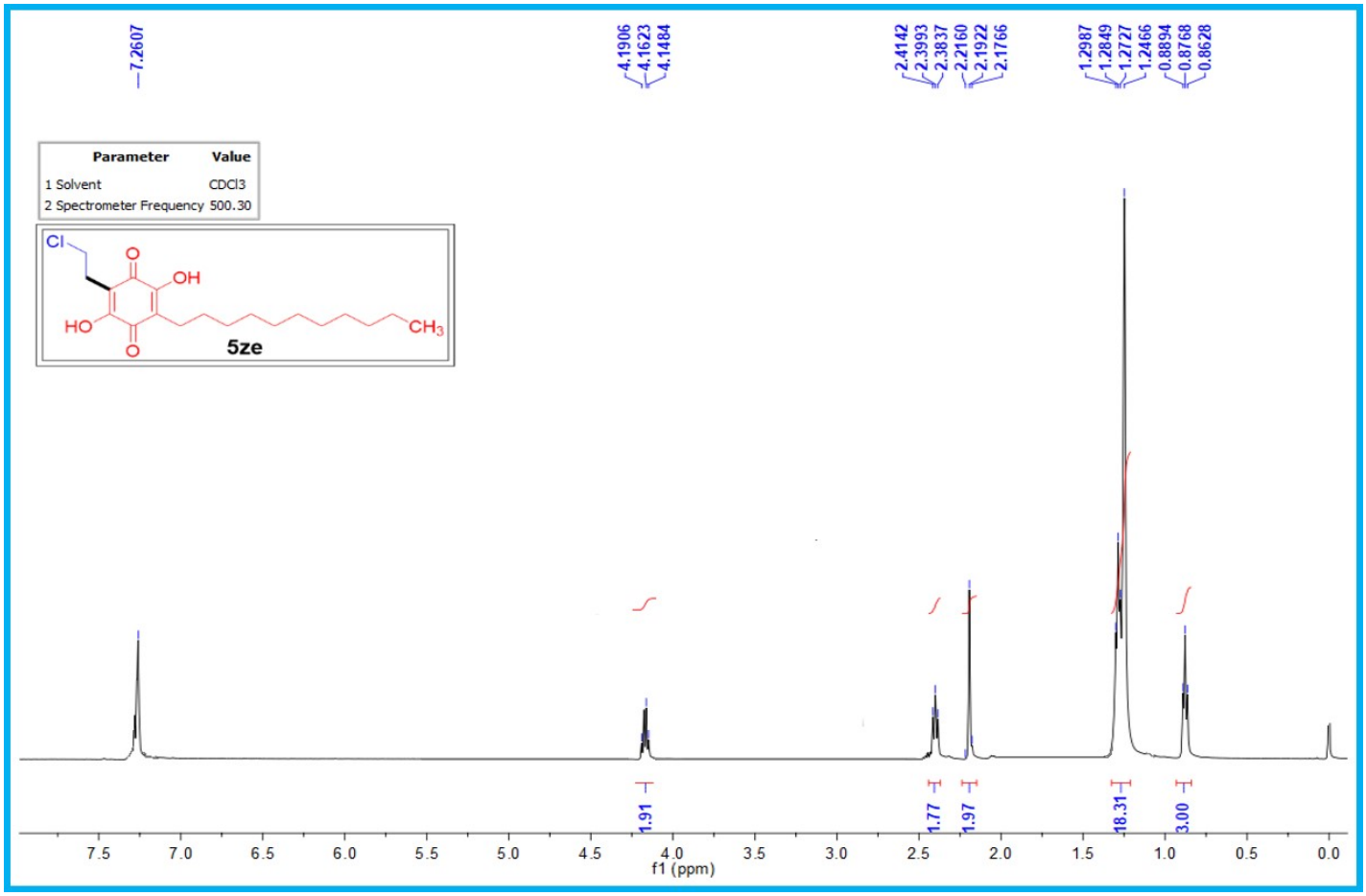


Fig. S64. ^{1}H NMR spectrum of 2-(2-chloroethyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5ze**).

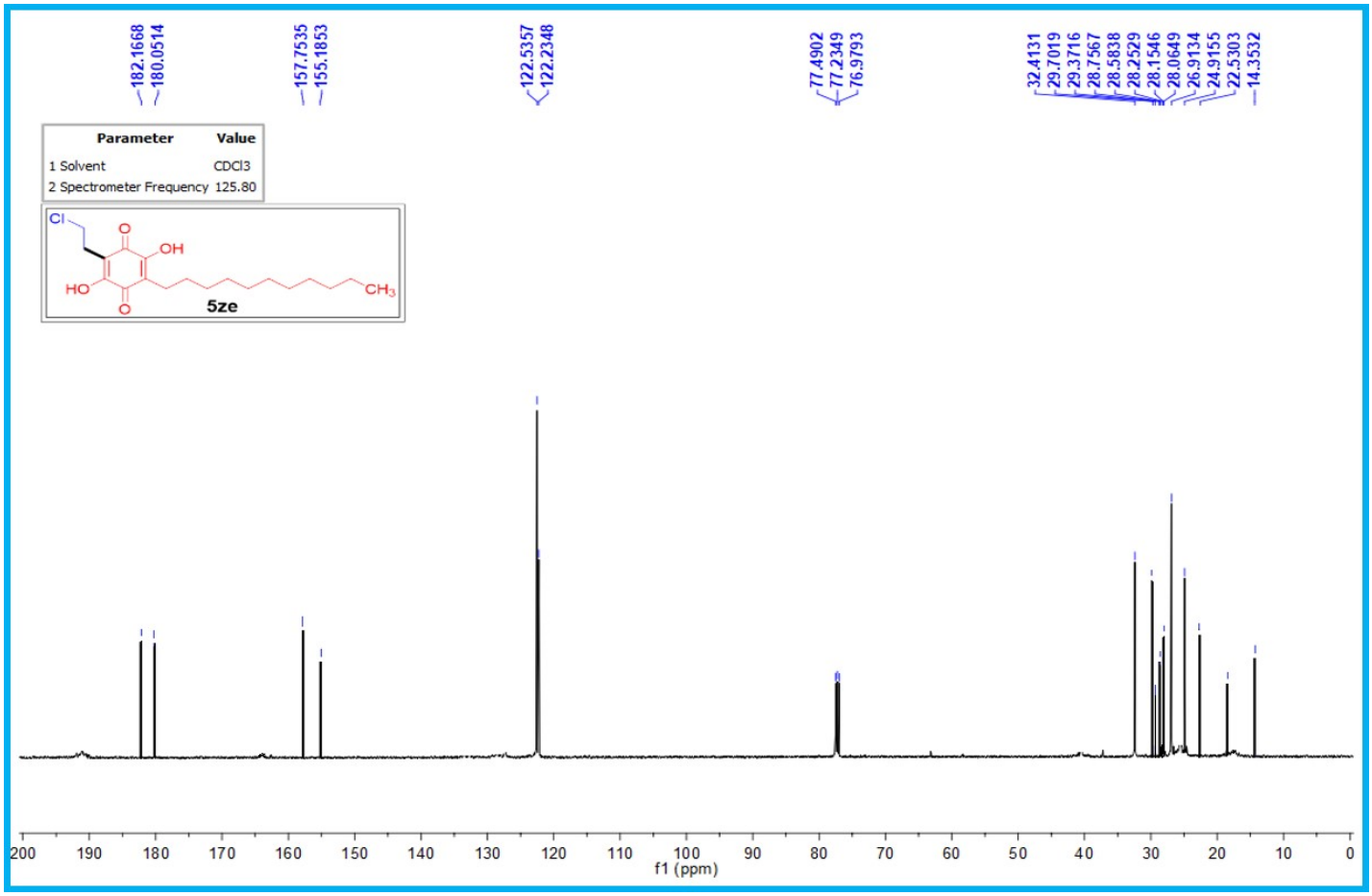


Fig. S65. ^{13}C NMR spectrum of 2-(2-chloroethyl)-3,6-dihydroxy-5-undecylcyclohexa-2,5-diene-1,4-dione (**5ze**).

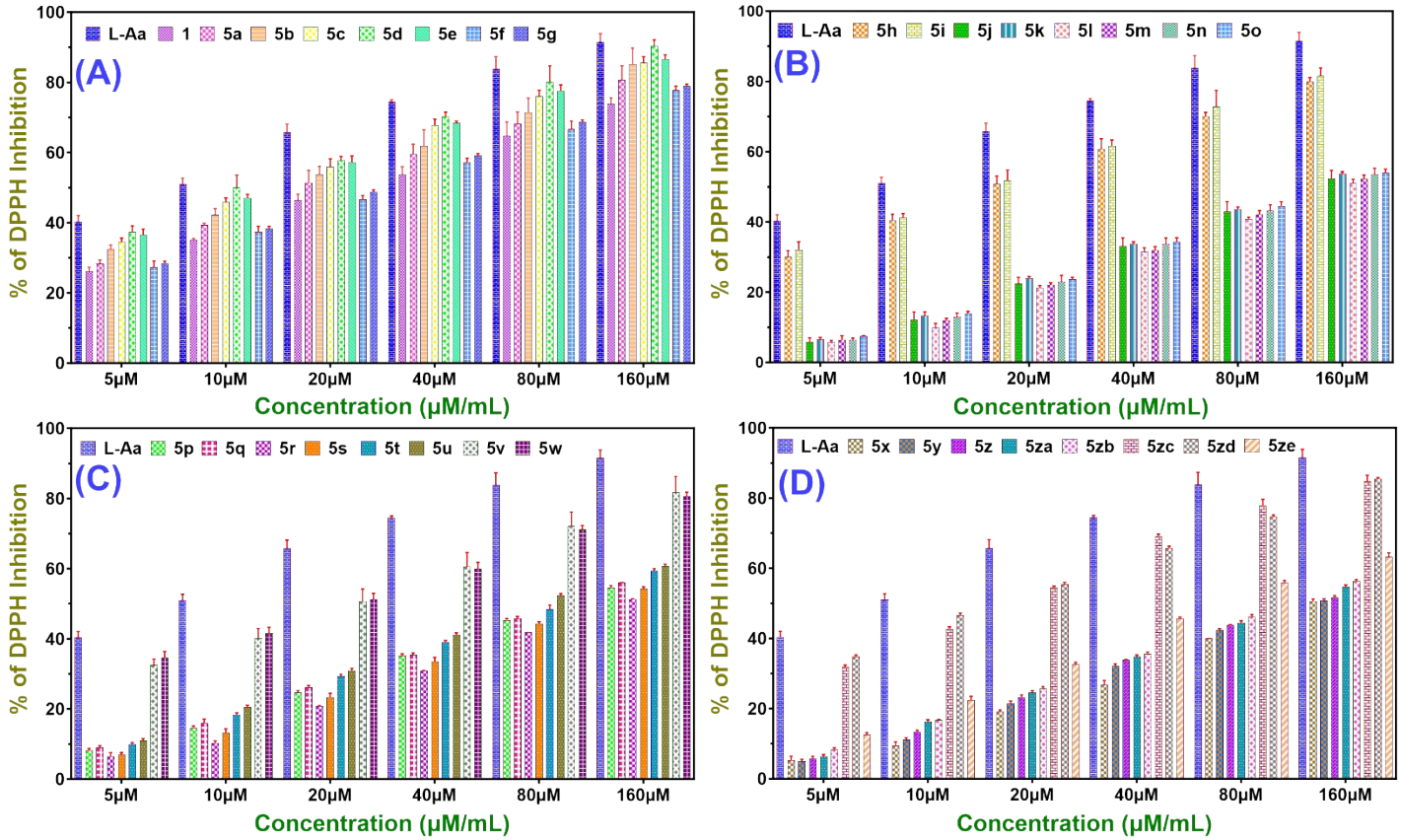


Fig. S66A-D. DPPH Free radical scavenging activity of compounds (**1** and **5a-5ze**) as compared with control L-Ascorbic acid (**L-Aa**). The signal asterisk denotes the significant difference between the control and treatment group 5, 10, 20, 40, 80 and 160 μM at $p < 0.05$ level by one-way ANOVA followed by Duncan's multiple range test. The experimental were performed in triplicates and the value were provides in mean ± SD.

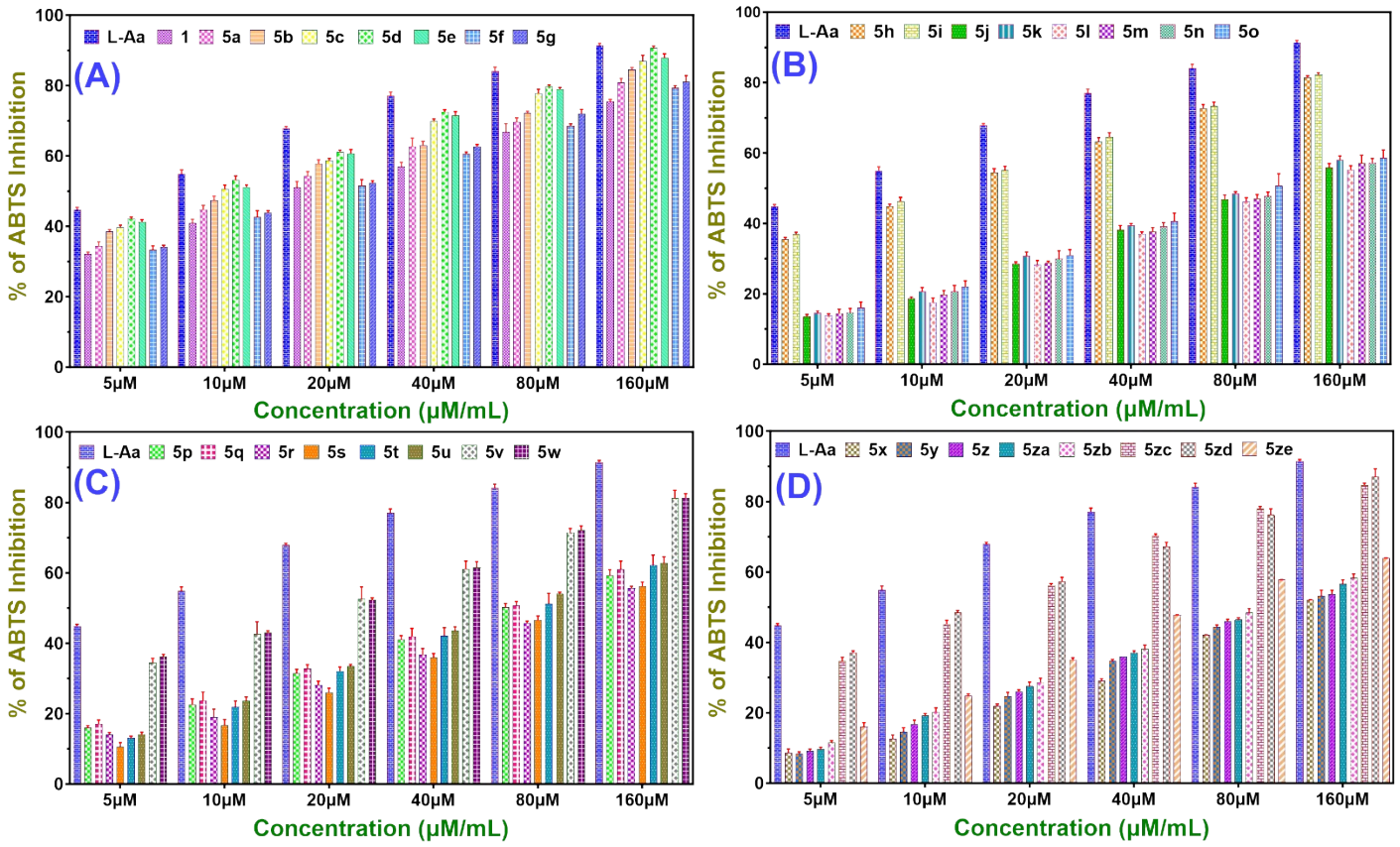
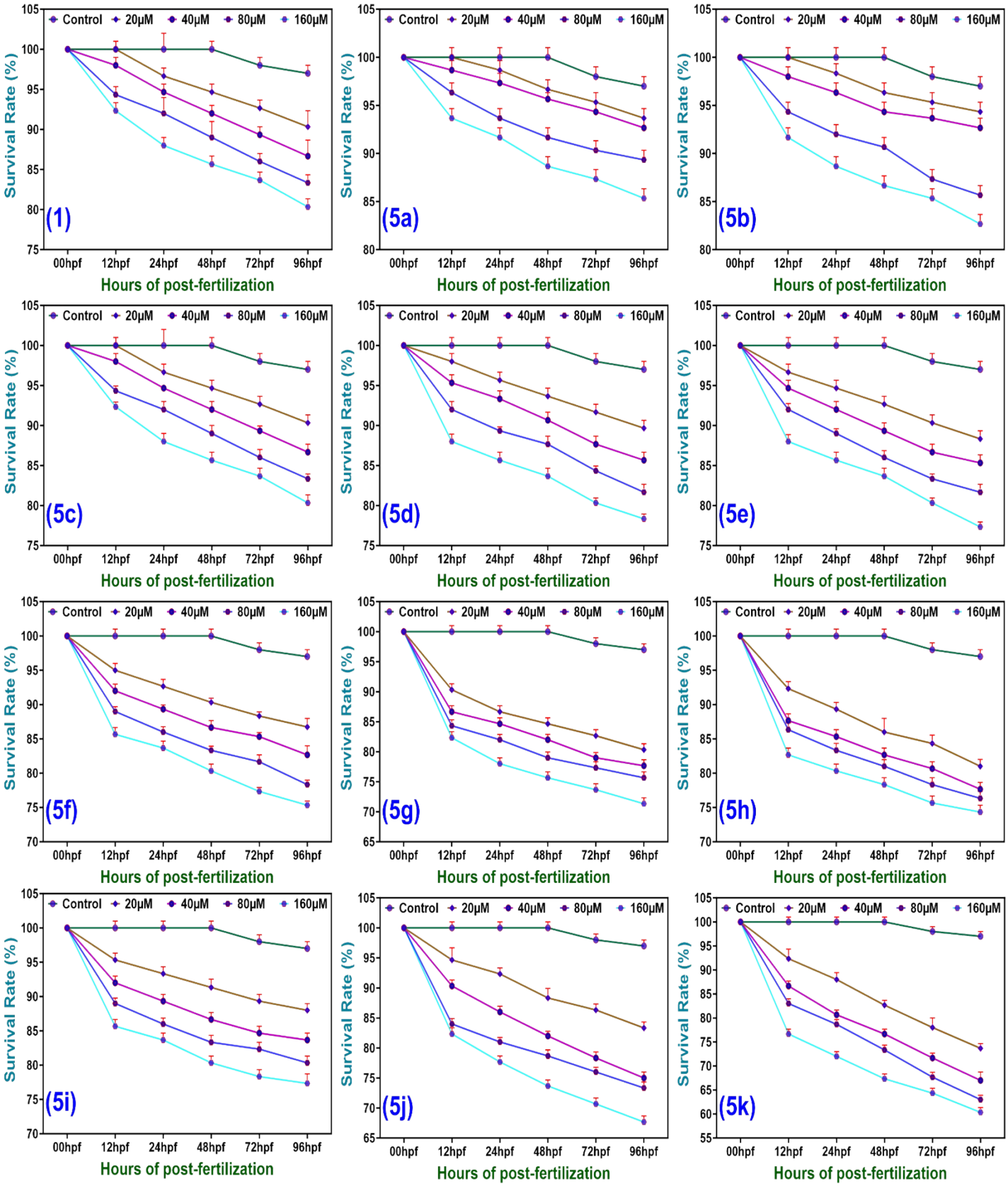
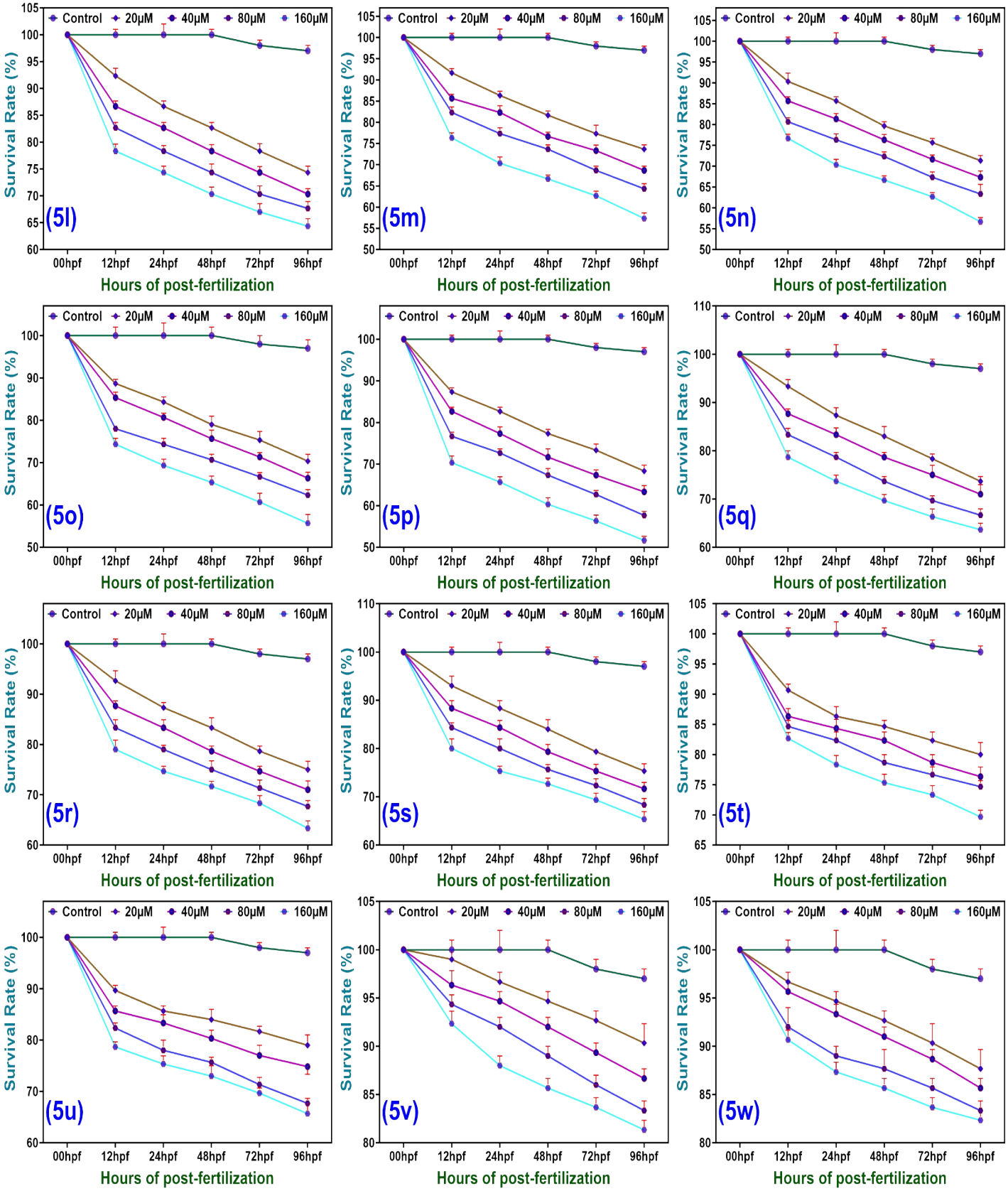


Fig. S67A-D. ABTS Free radical scavenging activity of compounds (**1**) and synthesised derivatives (**5a-5ze**) as compared with control L-Ascorbic acid (**L-Aa**). The signal asterisk denotes the significant difference between the control and treatment group 5, 10, 20, 40, 80 and 160 μM at $p < 0.05$ level by one-way ANOVA followed by Duncan's multiple range test. The experimental were performed in triplicates and the value were provides in mean ± SD.


Control
20μM
40μM
80μM
160μM
Survival Rate (%)
Hours of post-fertilization
00hpf
12hpf
24hpf
48hpf
72hpf
96hpf
(1)
(5a)
(5b)
(5c)
(5d)
(5e)
(5f)
(5g)
(5h)
(5i)
(5j)
(5k)


Control
20μM
40μM
80μM
160μM
Survival Rate (%)
Hours of post-fertilization
00hpf
12hpf
24hpf
48hpf
72hpf
96hpf
(5l)
(5m)
(5n)
(5o)
(5p)
(5q)
(5r)
(5s)
(5t)
(5u)
(5v)
(5w)

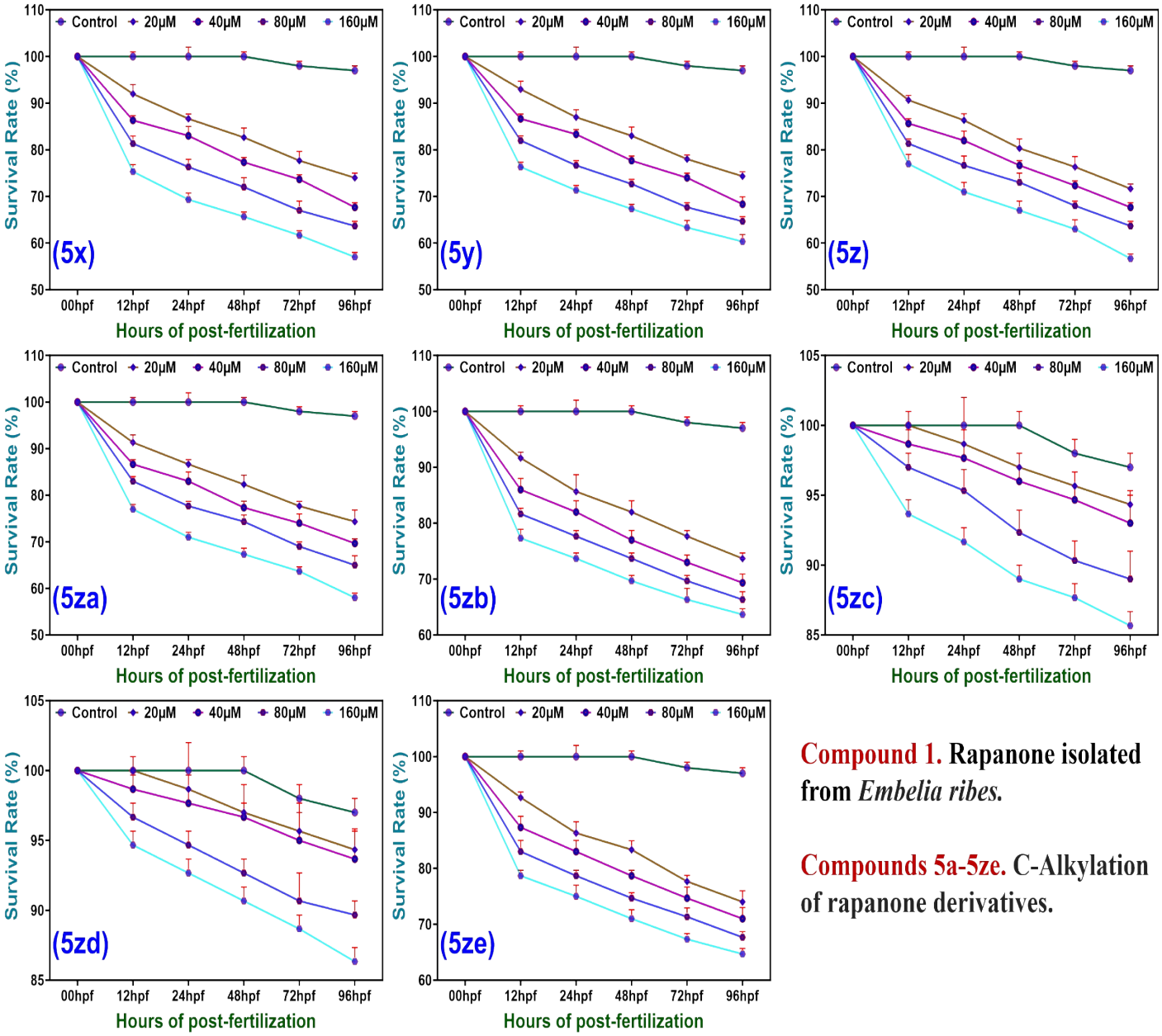
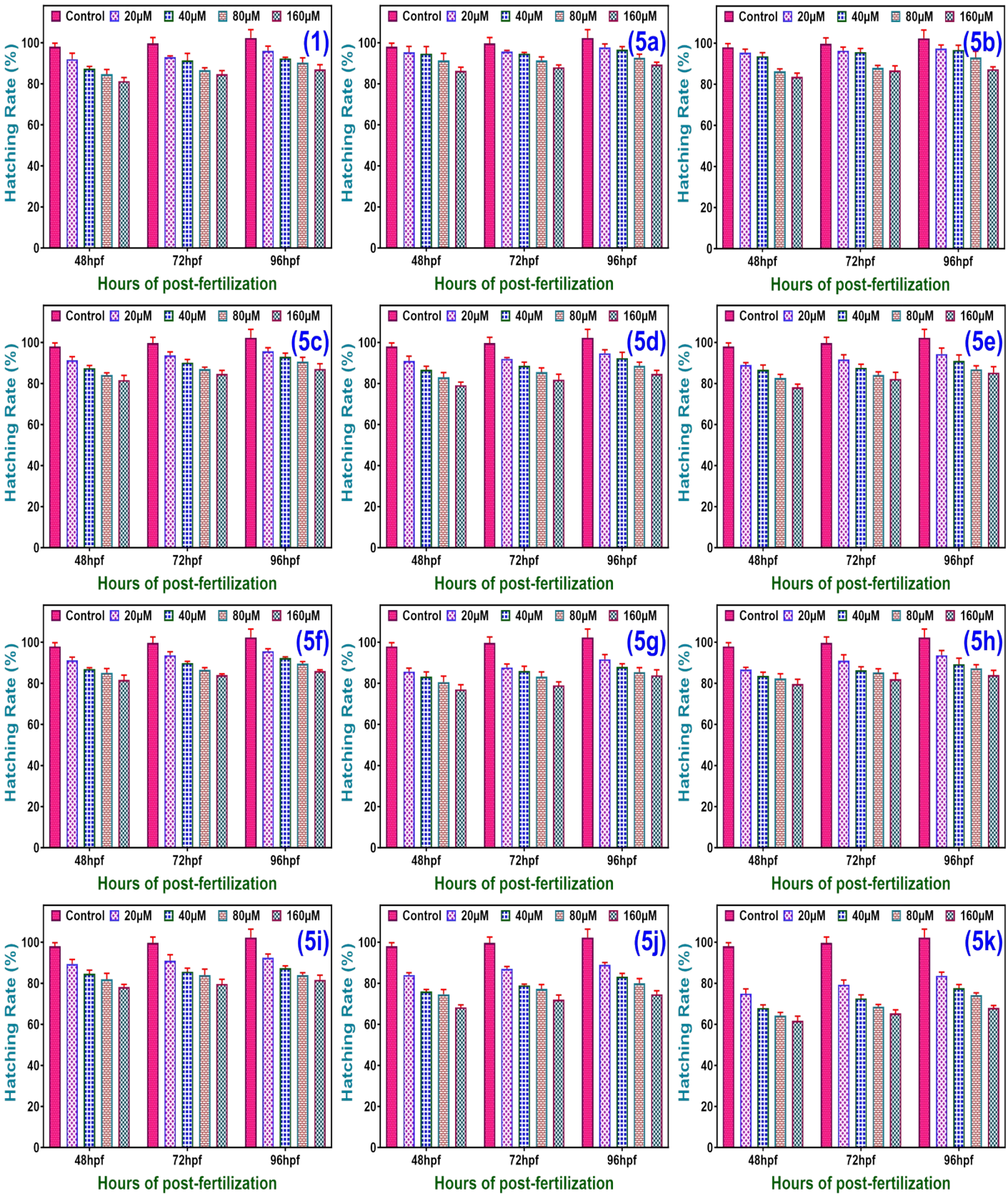
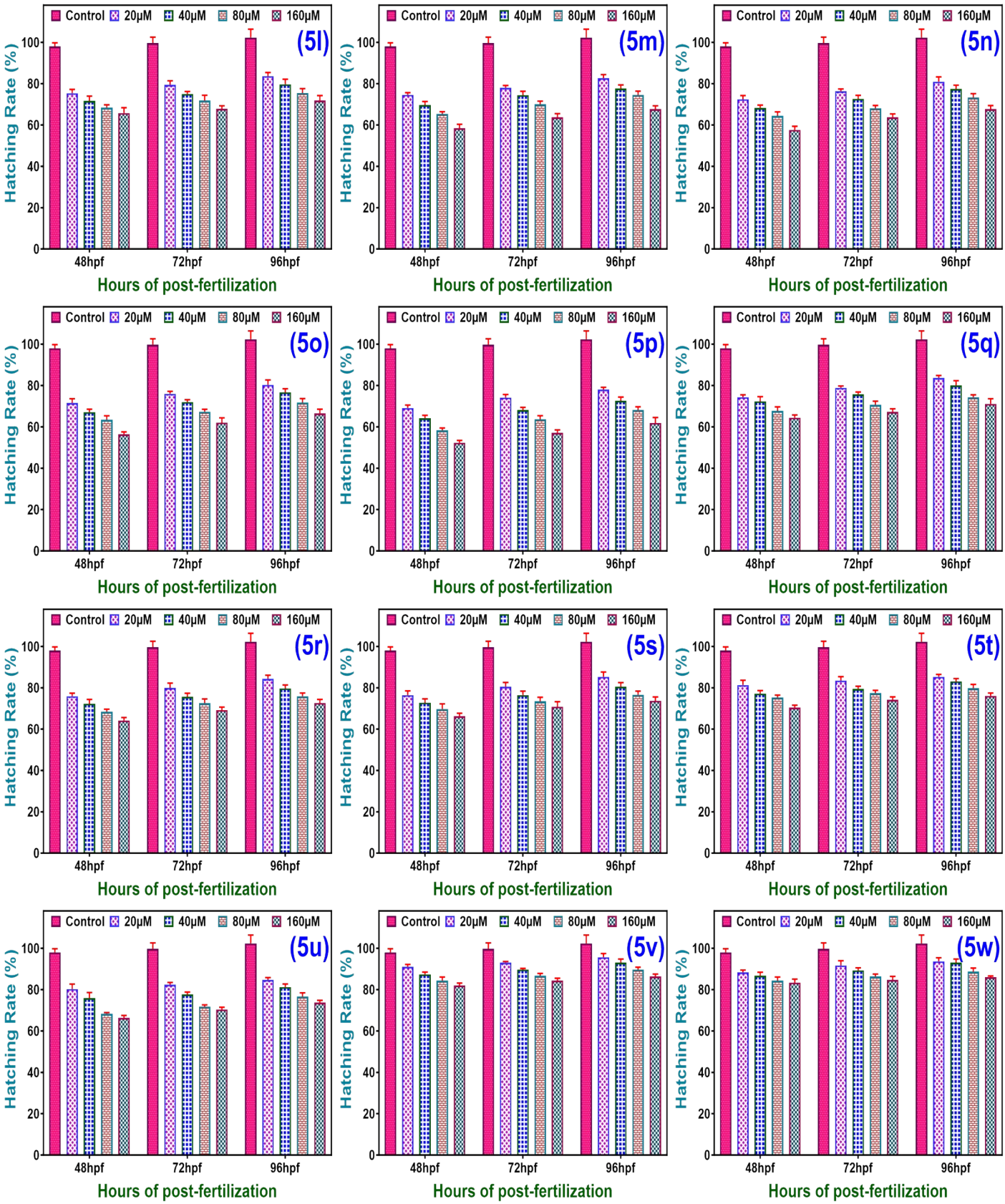


Fig. S68. Survival rates of zebrafish embryos treated with compound (**1**) and synthesised derivatives (**5a–5ze**) in 20, 40, 80 and 160 μM at 0–96 hpf. Data collected from 20 embryos per well condition. All the measurements were taken in triplicate (n=3) and the values are presented as mean ± SD of three independent experiments. $p < 0.05$ denotes significant change from untreated embryos respectively as obtained from ANOVA analysis.


Control 20μM 40μM 80μM 160μM
(1)
(5a)
(5b)
(5c)
(5d)
(5e)
(5f)
(5g)
(5h)
(5i)
(5j)
(5k)
Hatching Rate (%)
0
20
40
60
80
100
48hpf
72hpf
96hpf
Hours of post-fertilization


Control 20μM 40μM 80μM 160μM
(5l)
(5m)
(5n)
(5o)
(5p)
(5q)
(5r)
(5s)
(5t)
(5u)
(5v)
(5w)
Hatching Rate (%)
0
20
40
60
80
100
48hpf
72hpf
96hpf
Hours of post-fertilization

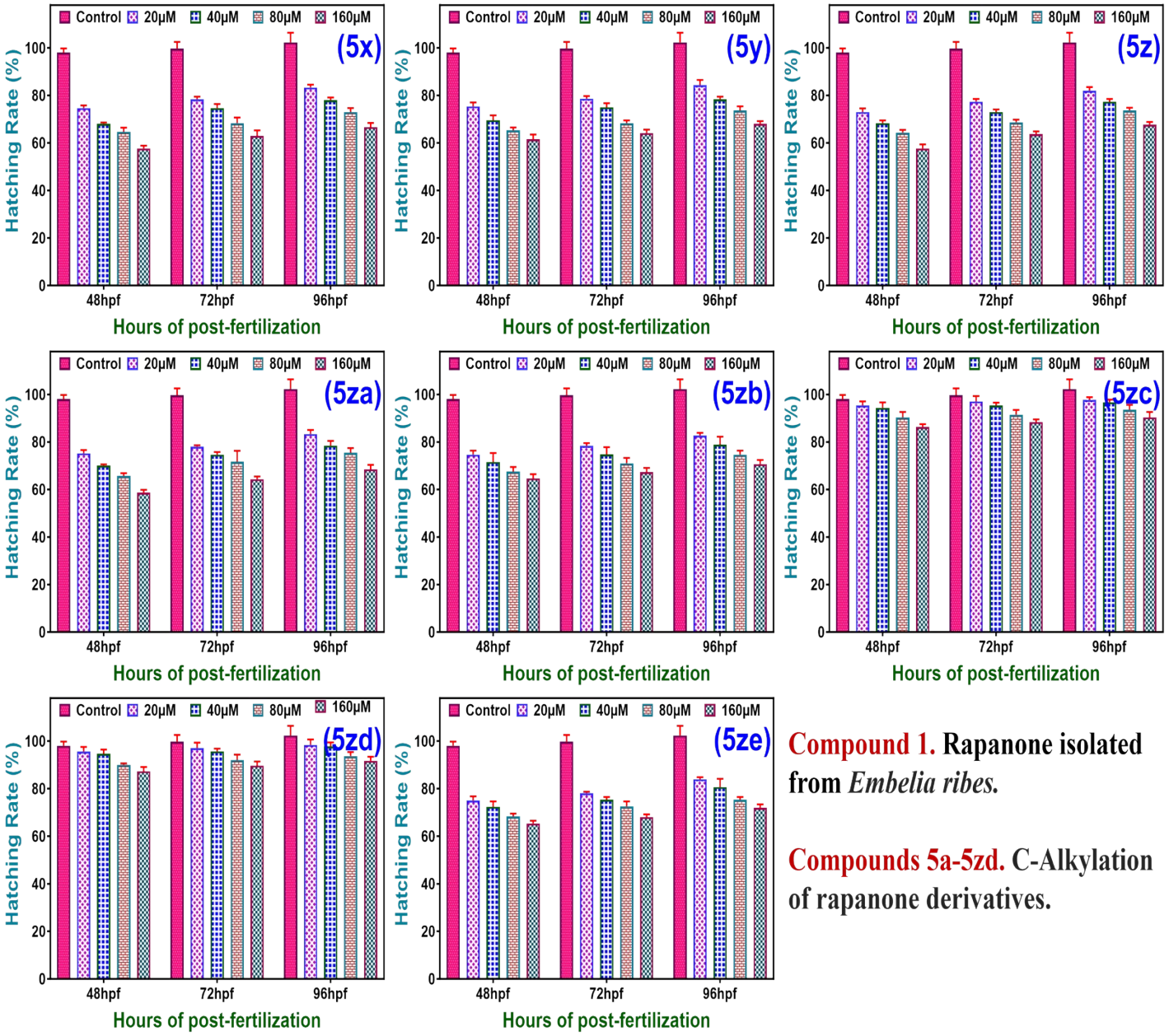


Fig. S69. Hatching rates of zebrafish embryos treated with compound (**1**) and synthesised derivatives (**5a–5ze**) in 20, 40, 80 and 160 μM at 0–96 hpf. Data collected from 20 embryos per well condition. All the measurements were taken in triplicate (n=3) and the values are presented as mean ± SD of three independent experiments. $p < 0.05$ denotes significant change from untreated embryos respectively as obtained from ANOVA analysis.

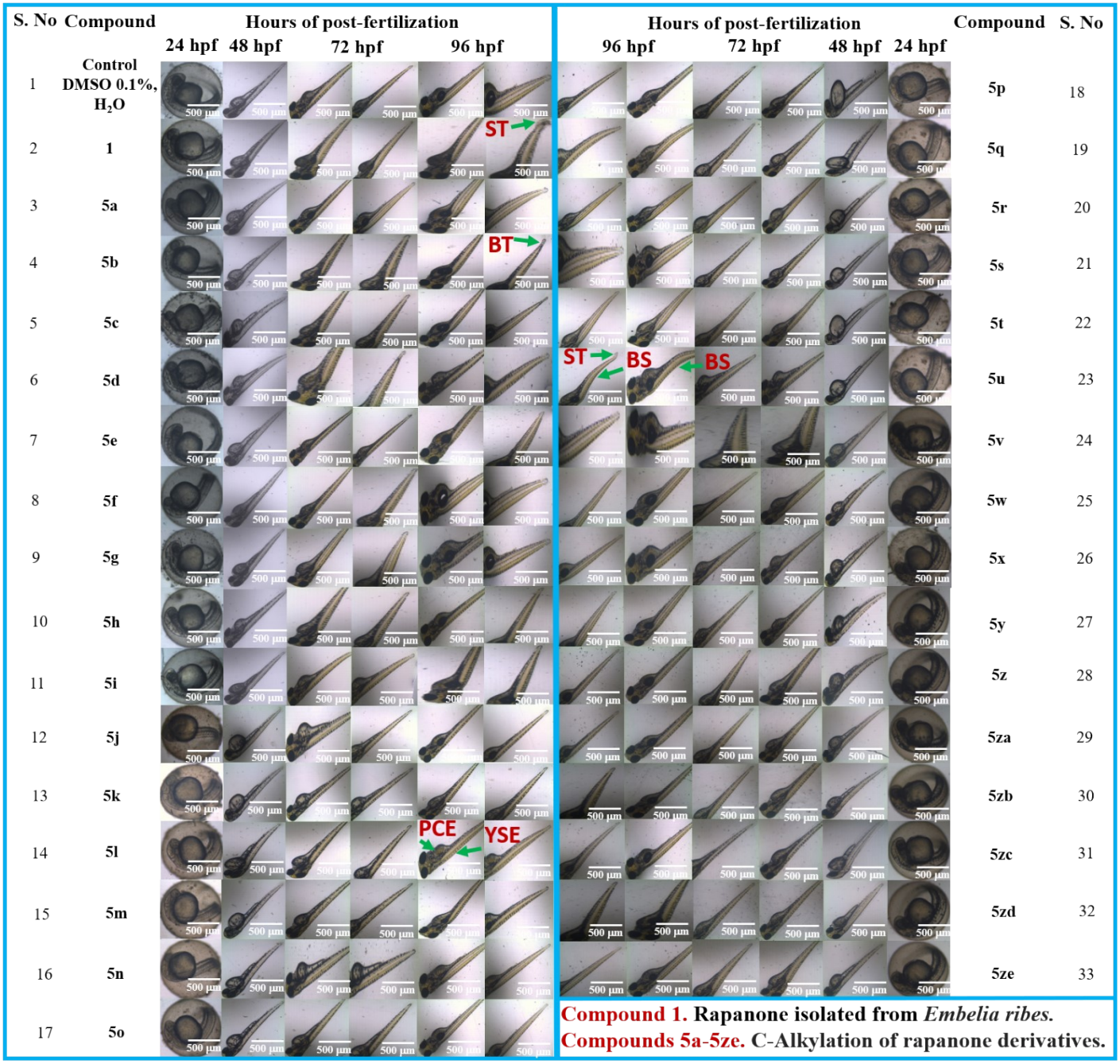


Fig. S70. During the exposure period, representative photomicrographs of morphological showed no malformations and Malformations such as bent spine (BS), yolk sac edema (YSE), pericardial edoema (PCE), short tail (ST), and bent tail (BT) were observed at 24–96 hpf in 160 µM concentration of compound (**1**) and (**5a–5ze**) synthesized derivatives were used as control DMSO 0.1% and H_2O. Similarly, after 72-96 hpf of compound (**1, 5b, 5l** and **5u**) treatment, larvae with malformations such as short tail (ST), bent tail (BT), pericardial edema (PCE), yolk sac edema (YSE) and bent spine (BS) were observed.