Catalytic Enantioselective Synthesis of Chiral Spirocyclic 1,3-Diketones via Organo-Cation Catalysis

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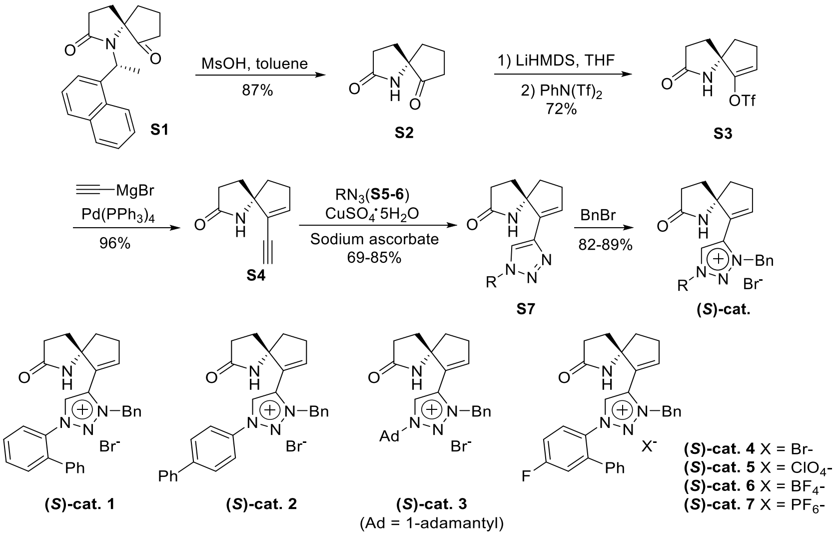
Table of Contents

1. General information

In addition to commercially available extra dry solvents, all solvents were purified by standard operating method. Toluene, tetrahydrofuran (THF), diethyl ether (Et_2O) and methyl tert-butyl ether (MTBE) were distilled from sodium; Dichloromethane (DCM) and 1,2-dichloroethane (DCE) were distilled from calcium hydride; Acetonitrile was distilled from phosphorus pentoxide; *N*,*N*-dimethylformamide (DMF) was distilled from K_2CO_3 under reduced pressure. All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on gel F254 plates. Silica gel (200-300 mesh), petroleum ether (b.p. 60-90 °C), ethyl acetate were used for product purification by flash column chromatography. **^{1}H NMR** spectra were acquired on a Bruker 400 or 600 MHz; **^{13}C NMR** spectra were acquired at 101 or 151 MHz and **^{19}F NMR** spectra were acquired at 376 MHz. Chemical shifts (δ) were reported in ppm relative to residual solvent signals (**$CDCl_3$**: 7.26 ppm for **^{1}H NMR**; 77.0 ppm for **^{13}C NMR**.) The following abbreviations are used to indicate the multiplicity in **NMR** spectra: s, singlet; d, doublet; t, triplet; q, quartet; dd, double of doublets; td, triplet of doublets; m, multiplet. High-resolution mass spectral analysis (**HRMS**) data were determined on an APEXII 47e FT-ICR spectrometer by means of the ESI technique. **IR** spectra were recorded on a fourier transform infrared spectrometer. Enantioselectivities were recorded on Waters UPC^2. Optical rotations were detected on RUDOLPH A21202-J APTV/GW. Melting points were recorded on a melting point apparatus and uncorrected. **X-ray diffraction** data were collected on Agilent SuperNova Eos diffractometer.

2. Synthesis of chiral SPA-triazolium bromide catalysts

General procedure for the preparation of catalysts

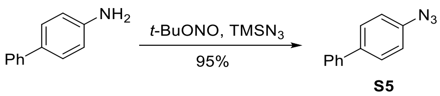


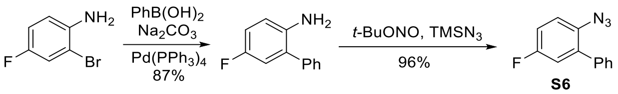
(*S*)-cat. 1 and **(*S*)-3** were prepared according to our previous work.[1]

Preparation of chiral alkyne

Compound **S1**- **S4** were prepared according to our previous work.[1]

Preparation of azides

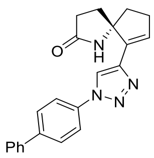




Azides **S5** and **S6** were prepared following the procedure of literature.[2]

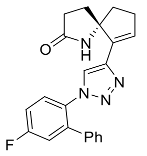
Synthesis of triazoles

(*S*)-6-(1-([1,1'-biphenyl]-4-yl)-1H-1,2,3-triazol-4-yl)-1-azaspiro[4.4]non-6-en-2-one



To a stired solution of alkyne (3.0 mmol, 1.0 equiv) and 4-azido-1,1-biphenyl (3.6 mmol, 1.2 equiv) in a mixed solvent of water (14 mL) and EtOH (14 mL) was added $CuSO_4{\cdot}5H_2O$ (0.3 mmol, 0.1 equiv) and sodium ascorbate (0.9 mmol, 0.3 equiv) under argon atmosphere. The resulting mixture was refluxed at 90 °C until consumption of substrate. The reaction mixture was cooled to room temperature, filtered through celite and concentrated under vacuum. The crude residue was purified by flash silica gel chromatography.[1]

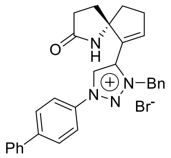
(*S*)-6-(1-(5-fluoro-[1,1'-biphenyl]-2-yl)-1H-1,2,3-triazol-4-yl)-1-azaspiro[4.4]non-6-en-2-one



To a stired solution of alkyne (3.0 mmol, 1.0 equiv) and 4-azido-5-fluoro-1,1-biphenyl (3.6 mmol, 1.2 equiv) in a mixed solvent of water (14 mL) and EtOH (14 mL) was added $CuSO_4 \cdot 5H_2O$ (0.3 mmol, 0.1 equiv) and sodium ascorbate (0.9 mmol, 0.3 equiv) under argon atmosphere. The resulting mixture was refluxed at 90 °C until consumption of substrate. The reaction mixture was cooled to room temperature, filtered through celite and concentrated under vacuum. The crude residue was purified by flash silica gel chromatography.[1]

Synthesis of triazoliums catalyst[1]

(*S*)-6-(1-([1,1'-biphenyl]-4-yl)-3-benzyl-1H-1,2,3l4-triazol-4-yl)-1-azaspiro[4.4]non-6-en-2-one



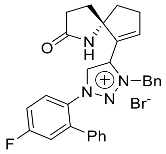
Brown solid (433 mg, 82% yield, m.p. = 139-141 ºC).

To CH_3CN (8 mL) and BnBr (4 mL) in a 100 mL sealed tube was added corresponding triazoles (1.0 mmol) and then the sealed tube was filled with argon. The reaction mixture was stirred at 90 °C for about 3 days. The mixture was cooled to room temperature and concentrated under vacuum and the crude residue was purified by column chromatography to give **(*S*)-cat. 2**.

$[\alpha]_D^{21}$ = 108 (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.25 (s, 1H), 8.17 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 7.0 Hz, 2H), 7.46-7.31 (m, 8H), 6.61-6.59 (m, 1H), 6.21 (d, *J* = 15.3 Hz, 1H), 5.99 (d, *J* = 15.4 Hz, 1H), 2.65-2.58 (m, 1H), 2.51-2.42 (m, 1H), 2.17-2.10 (m, 4H), 1.89-1.80 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.1, 144.2, 138.4, 138.1, 133.5, 132.0, 129.2, 129.1, 128.9, 128.5, 128.3, 128.1, 127.3, 126.9, 121.7, 72.6, 56.0, 38.4, 31.4, 30.4, 30.0. **HRMS** (ESI) m/z calculated for $C_{29}H_{27}N_4O$ $[M-Br]^+$ 447.2179, found 447.2183.

(*S*)-6-(3-benzyl-1-(5-fluoro-[1,1'-biphenyl]-2-yl)-1H-1,2,3l4-triazol-4-yl)-1-azaspiro[4.4]non-6-en-2-one



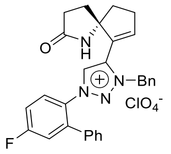
Brown solid (396 mg, 85% yield, m.p. = 193-194 ºC).

To CH_3CN (8 mL) and BnBr (4 mL) in a 100 mL sealed tube was added corresponding triazoles (1.0 mmol) and then the sealed tube was filled with argon. The reaction mixture was stirred at 90 °C for about 3 days. The mixture was cooled to room temperature and concentrated under vacuum and the crude residue was purified by column chromatography to give **(*S*)-cat. 4**.

$[\alpha]_D^{22}$ = 71 (c = 1.0, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.23 (s, 1H), 8.10-8.08 (m, 1H), 7.85 (s, 1H), 7.39-7.15 (m, 10H), 6.89 (d, *J* = 7.5 Hz, 2H), 6.62 (s, 1H), 6.04 (d, *J* = 15.3 Hz, 1H), 5.78 (d, *J* = 15.3 Hz, 1H), 2.64-2.59 (m, 1H), 2.47-2.41 (m, 1H), 2.13-2.07 (m, 3H), 1.92-1.88 (m, 1H), 1.71-1.67 (m, 1H), 1.39-1.33 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.5, 164.6, 162.9, 144.3, 140.9 (d, *J* = 9.06 Hz), 137.1, 134.9, 131.8, 131.4, 129.8 (d, *J* = 10.75 Hz), 129.1, 129.1, 129.0, 128.8 (d, *J* = 3.02 Hz), 128.7, 128.1, 128.0, 127.7, 118.0 (d, J = 24.16 Hz), 116.1 (d, J = 22.65 Hz), 72.3, 55.9, 38.4, 31.3, 30.2 (d, J = 78.52 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -106.1. **HRMS** (ESI) m/z calculated for $C_{29}H_{26}FN_4O$ $[M-Br]^+$ 465.2085, found 465.2090.

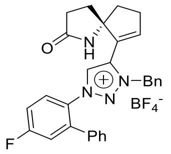
(*S*)-6-(3-benzyl-1-(5-fluoro-[1,1'-biphenyl]-2-yl)-1H-1,2,3l4-triazol-4-yl)-1-azaspiro[4.4]non-6-en-2-one



Yellow solid (2684 mg, 95% yield, m.p. = 111-113 ºC).

(*S*)-cat. 4 (5 mmol, 1.0 equiv) was dissolved in DCM (10 mL) and $AgClO_4$ (7.5 mmol, 1.5 equiv) was added. The mixture was stirred at room temperature until yellow precipitate was observed. Then filtration would give yellow solid **(*S*)-cat. 5**.

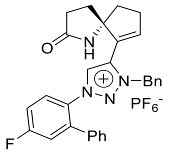
(*S*)-6-(3-benzyl-1-(5-fluoro-[1,1'-biphenyl]-2-yl)-1H-1,2,3l4-triazol-4-yl)-1-azaspiro[4.4]non-6-en-2-one



White solid (2486 mg, 90% yield, m.p. = 189-191 ºC).

(*S*)-cat. 6 was synthesized from **(*S*)-cat. 4** and $AgBF_4$ following the similar procedure of **(*S*)-cat. 5**.

(*S*)-6-(3-benzyl-1-(5-fluoro-[1,1'-biphenyl]-2-yl)-1H-1,2,3l4-triazol-4-yl)-1-azaspiro[4.4]non-6-en-2-one

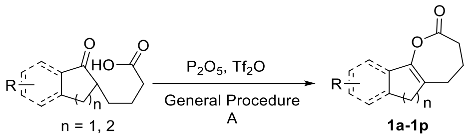


Brown solid (2839 mg, 93% yield, m.p. = 125-126 ºC).

(*S*)-cat. 7 was synthesized from **(*S*)-cat. 4** and $AgPF_6$ following the similar procedure of **(*S*)-cat. 5**.

3. General procedure for the preparation of enol lactones

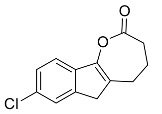
Preparation of substrates **1a-1p**.



The requisite carboxylic acid dericatices were prepared following the procedure of literature.[2b, 3]

General Procedures A: To a solution of carboxylic acid dericatices (2 mmol, 1.0 equiv) in DCM (20 mL) was added P_2O_5 (36 mmol, 18.0 equiv) and Tf_2O (2 mmol, 1.0 equiv) at 0 °C. When the product was observed, the reaction was quenched immediately with saturated $NaHCO_3$ (20 mL) and extracted with DCM (20 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The resulting crude product was purified by flash silica gel chromatography.

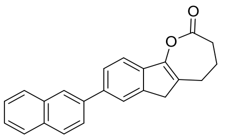
8-chloro-3,4,5,6-tetrahydro-2H-indeno[1,2-b]oxepin-2-one (1a)



white solid (239 mg, 51% yield, m.p. = 136-137 ºC).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 -7.30 (m, 2H), 7.28-7.26 (m, 1H), 3.33 (s, 2H), 2.82-2.79 (m, 2H), 2.66 (t, *J* = 7.0 Hz, 2H), 2.16-2.10 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.5, 144.8, 141.6, 138.8, 131.7, 127.1, 124.1, 122.9, 119.0, 39.4, 34.9, 28.8, 20.6. **HRMS** (ESI) m/z calculated for $C_{13}H_{11}ClO_2H$ $[M+H]^+$ 235.0520, found 235.0522.

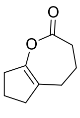
8-(naphthalen-2-yl)-3,4,5,6-tetrahydro-2H-indeno[1,2-b]oxepin-2-one (1i)



white solid (293 mg, 45% yield, m.p. = 71-73 ºC).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.92-7.85 (m, 3H), 7.77-7.68 (m, 3H), 7.54-7.45 (m, 3H), 3.46 (s, 2H), 2.86-2.83 (m, 2H), 2.73-2.70 (m, 2H), 2.20-2.14 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.6, 145.1, 140.4, 139.2, 138.7, 138.5, 133.7, 132.5, 128.3, 128.1, 127.6, 126.2, 126.0, 125.8, 125.6, 122.8, 122.5, 118.2, 39.5, 34.6, 28.5, 20.6. **HRMS** (ESI) m/z calculated for $C_{23}H_{18}O_2H$ $[M+H]^+$ 327.1380, found 327.1379.

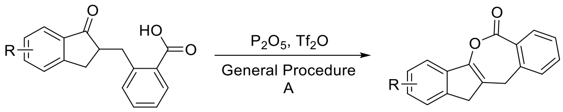
3,4,5,6,7,8-hexahydro-2H-cyclopenta[b]oxepin-2-one (1p)



colourless oil (113 mg, 37% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66-2.63 (m, 2H), 2.50-2.45 (m, 2H), 2.35-2.32 (m, 2H), 2.16-2.11 (m, 2H), 1.96-1.90 (m, 2H), 1.86-1.79 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.2, 144.9, 117.0, 35.3, 34.5, 33.6, 28.3, 20.4, 19.0. **HRMS** (ESI) m/z calculated for $C_9H_{12}O_2H$ $[M+H]^+$ 153.0910, found 153.0911.

Preparation of substrates **1q-1t**.

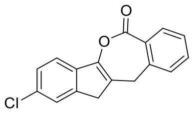


1q-1t

The requisite carboxylic acid dericatices were prepared following the procedure of literature.[4]

General Procedures A: To a solution of carboxylic acid dericatices (2 mmol, 1.0 equiv) in DCM (20 mL) was added P_2O_5 (36 mmol, 18.0 equiv) and Tf_2O (2 mmol, 1.0 equiv) at 0 °C. When the product was observed, the reaction was quenched immediately with saturated $NaHCO_3$ (20 mL) and extracted with DCM (20 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The resulting crude product was purified by flash silica gel chromatography.

2-chloro-11,12-dihydro-6H-benzo[e]indeno[1,2-b]oxepin-6-one (1q)

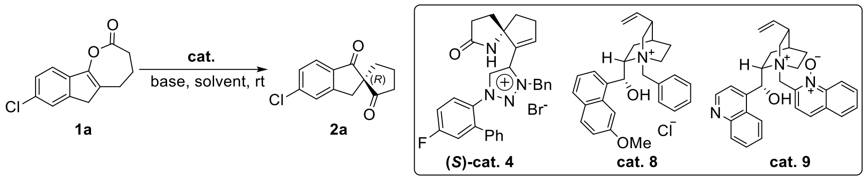


white solid (237 mg, 42% yield, m.p. = 118-119 ºC).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.6 Hz, 1H), 7.48-7.45 (m, 1H), 7.36-7.32 (m, 3H), 7.28-7.26 (m, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 3.75 (s, 2H), 3.43 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.3, 146.7, 142.0, 141.5, 137.1, 133.7, 133.2, 131.5, 129.7, 127.4, 127.2, 127.0, 125.2, 124.4, 118.5, 37.2, 32.1. **HRMS** (ESI) m/z calculated for $C_{17}H_{11}ClO_2H$ $[M+H]^+$ 283.0520, found 283.0521.

4.Optimization of reaction conditions

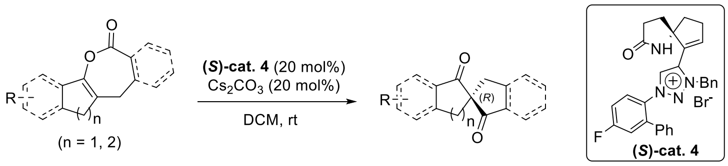
Table S1. Screening of conditions[a]



entry	catalyst	base (equiv.)	solvent	yield (%)[b]	ee (%)[c]
1	**cat. 8**	Cs_2CO_3 (0.2)	DCM	61	60
2	**cat. 9**	Cs_2CO_3 (0.2)	DCM	58	54
3	**(*S*)-cat. 4**	**Cs_2CO_3 (0.2)**	**DCM**	**80**	**87**
4	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	$CHCl_3$	51	71
5	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	chlorobenzene	45	68
6	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	xylene	50	52
7	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	mesitylene	trace	2
8	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	THF	trace	4
9	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	MTBE	trace	11
10	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	1,4-dioxand	49	16
11	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	EtOAc	trace	49
12	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	CH_3CN	trace	1
13	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	DMF	trace	1
14	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	DMSO	48	0
15	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	DCM+H_2O (5 μL)	43	65
16	**(*S*)-cat. 4**	Cs_2CO_3 (0.2)	DCM+DMSO (5 μL)	58	31
17	**(*S*)-cat. 4**	Li_2CO_3 (0.2)	DCM	trace	0
18	**(*S*)-cat. 4**	Na_2CO_3 (0.2)	DCM	trace	2
19	**(*S*)-cat. 4**	NaOEt (0.2)	DCM	57	73
20	**(*S*)-cat. 4**	K_2HPO_4 (0.2)	DCM	53	7
21	**(*S*)-cat. 4**	*t*-BuOK (0.2)	DCM	NR[d]	-
22	**(*S*)-cat. 4**	CsOH•H_2O (0.2)	DCM	NR	-
23	**(*S*)-cat. 4**	Et_3N (0.2)	DCM	trace	18
24	**(*S*)-cat. 4**	DBU (0.2)	DCM	54	26
25	**(*S*)-cat. 4**	Cs_2CO_3 (0.1)	DCM	trace	65
26	**(*S*)-cat. 4**	Cs_2CO_3 (0.4)	DCM	51	67
27	**(*S*)-cat. 4**	Cs_2CO_3 (0.6)	DCM	58	61
28	**(*S*)-cat. 4**	Cs_2CO_3 (0.8)	DCM	78	52
29	**(*S*)-cat. 4**	Cs_2CO_3 (1.0)	DCM	77	27
30	**(*S*)-cat. 4**	Cs_2CO_3 (1.5)	DCM	81	26
31	**(*S*)-cat. 4**	Cs_2CO_3 (2.0)	DCM	80	15
32[e]	**(*S*)-cat. 4**	Cs_2CO_3 (2.0)	DCM	30	69
33[f]	**(*S*)-cat. 4**	Cs_2CO_3 (2.0)	DCM	42	63
34[g]	**(*S*)-cat. 4**	Cs_2CO_3 (2.0)	DCM	75	66

[a]Reactions were conducted with **1a** (0.05 mmol, 1.0 equiv.), catalyst (20 mol%), and base in solvent (0.5 mL). [b]Isolated yield. [c]Ee determined by UPC^2. [d]Not detected. [e]The reaction was carried out at 0 ºC. [f]The reaction was carried out at -10 ºC. [g]The reaction was carried out at 30 ºC.

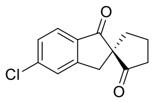
5. General Procedure



Enol lactones (0.05 mmol, 1.0 equiv), **(*S*)-cat. 4** (0.01 mmol, 0.2 equiv), and Cs_2CO_3 (0.01 mmol, 0.2 equiv) were dissolved in DCM (0.5 mL) at room temperature and the reaction mixture was stirred at the same temperature until consumption of enol lactones detected by TLC. The solution was then quenched with saturated $NaHCO_3$ (2 mL) and extracted by DCM (3 mL×3). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford spirocyclic 1,3-diketones.

6. Characterization Data

(*R*)-5'-chlorospiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2a)

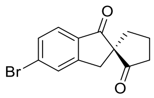


Following the above general procedure, **2a** was obtained in 80% yield (9.36 mg) with 87% ee as an white solid (m.p. = 86-88 ºC). $[\alpha]_D^{24}$ = 19 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 1.0 Hz, 1H), 7.38-7.35 (m, 1H), 3.47 (d, *J* = 17.2 Hz, 1H), 2.91 (d, *J* = 17.2 Hz, 1H), 2.63-2.55 (m, 2H), 2.49-2.33 (m, 2H), 2.09-2.01 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.3, 202.2, 154.8, 141.8, 133.7, 128.6, 126.5, 125.5, 65.0, 37.8, 37.4, 34.5, 19.5. **HRMS** (ESI) m/z calculated for $C_{13}H_{11}ClO_2Na$ $[M+Na]^+$ 257.0340, found 257.0334. **FT-IR** (cm^{-1}): 2960, 2921, 2851, 1740, 1700, 1598, 1578, 1261, 1204, 1070, 1019, 904, 799.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 254.5 nm, t_{major} = 0.699 min, t_{minor} = 0.789 min).

(*R*)-5'-bromospiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2b)

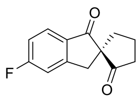


Following the above general procedure, **2b** was obtained in 70% yield (9.73 mg) with 86% ee as an white solid (m.p. = 94-95 ºC). $[\alpha]_D^{26}$ = 18 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 1.6 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.52 (dd, *J* = 8.3, 1.5 Hz, 1H), 3.47 (d, *J* = 17.2 Hz, 1H), 2.90 (d, *J* = 17.2 Hz, 1H), 2.62-2.53 (m, 2H), 2.48-2.32 (m, 2H), 2.11-1.99 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.1, 202.4, 154.9, 134.0, 131.4, 130.6, 129.5, 125.5, 64.9, 37.7, 37.3, 34.5, 19.4. **HRMS** (ESI) m/z calculated for $C_{13}H_{11}BrO_2Na$ $[M+Na]^+$ 300.9835, found 300.9833. **FT-IR** (cm^{-1}): 2960, 2920, 2851, 1741, 1699, 1594, 1461, 1413, 1261, 1096, 1019, 900, 800.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 258.1 nm, t_{major} = 0.786 min, t_{minor} = 0.910 min).

(*R*)-5'-fluorospiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2c)



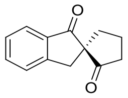
Following the above general procedure, **2c** was obtained in 73% yield (7.96 mg) with 66% ee as an white solid (m.p. = 47-49 ºC). $[\alpha]_D^{25}$ = 16 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.4, 5.3 Hz, 1H), 7.14 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.13-7.06 (m, 1H), 3.48 (d, *J* = 17.2 Hz, 1H), 2.91 (d, *J* = 17.3 Hz, 1H), 2.63-2.53 (m, 2H), 2.49-2.32 (m, 2H), 2.11-1.98 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.4, 201.8, 167.3 (d, *J* = 257.2 Hz), 156.3 (d, *J* = 10.3 Hz), 131.5 (d, *J* = 1.7 Hz), 126.7 (d, *J* = 10.6 Hz), 116.1 (d, *J* = 24.0 Hz), 112.9 (d, *J* = 22.5 Hz), 65.1, 37.8, 37.6 (d, *J* = 2.3 Hz), 34.5, 19.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -102.0. **HRMS** (ESI) m/z calculated for $C_{13}H_{11}FO_2Na$ $[M+Na]^+$ 241.0635, found 241.0635. **FT-IR** (cm^{-1}): 2963, 2919, 2850, 1708, 1260, 1088, 1019, 864, 799.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 246.2

nm, t_{major} = 0.566 min, t_{minor} = 0.613 min).

(*R*)-spiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2d)

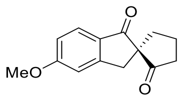


Following the above general procedure, **2d** was obtained in 65% yield (6.50 mg) with 75% ee as an white solid (m.p. = 53-54 ºC). $[\alpha]_D^{23}$ = 34 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 3.49 (d, *J* = 17.0 Hz, 1H), 2.92 (d, *J* = 17.0 Hz, 1H), 2.62-2.53 (m, 2H), 2.47-2.32 (m, 2H), 2.11-1.98 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.7, 203.7, 153.4, 135.2, 135.0, 127.7, 126.1, 124.4, 64.7, 37.9, 37.8, 34.6, 19.5. **HRMS** (ESI) m/z calculated for $C_{13}H_{12}O_2Na$ $[M+Na]^+$ 223.0730, found 223.0728. **FT-IR** (cm^{-1}): 2958, 2918, 1739, 1698, 1606, 1463, 1427, 1276, 1151, 992, 902, 767.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 95/5, v = 2.0 mL/min, λ= 241.5 nm, t_{major} = 1.528 min, t_{minor} = 1.654 min).

(*R*)-5'-methoxyspiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2e)

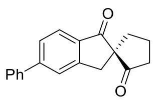


Following the above general procedure, **2e** was obtained in 58% yield (7.96 mg) with 40% ee as an white solid (m.p. = 77-79 ºC). $[\alpha]_D^{25}$ = 15 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 9.2 Hz, 1H), 6.91-6.89 (m, 2H), 3.87 (s, 3H), 3.43 (d, *J* = 17.0 Hz, 1H), 2.86 (d, *J* = 17.0 Hz, 1H), 2.61-2.50 (m, 2H), 2.47-2.30 (m, 2H), 2.09-1.96 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 216.1, 201.7, 165.6, 156.4, 128.3, 126.0, 115.8, 109.3, 64.9, 55.6, 37.8, 37.7, 34.6, 19.4. **HRMS** (ESI) m/z calculated for $C_{14}H_{14}O_3Na$ $[M+Na]^+$ 253.0835, found 253.0834. **FT-IR** (cm^{-1}): 2944, 2882, 2838, 1731, 1682, 1606, 1490, 1338, 1300, 926, 846, 750.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 267.6 nm, t_{major} = 0.864 min, t_{minor} = 1.013 min).

(*R*)-5'-phenylspiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2f)

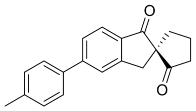


Following the above general procedure, **2f** was obtained in 55% yield (7.59 mg) with 78% ee as an white solid (m.p. = 115-117 ºC). $[\alpha]_D^{25}$ = 14 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 1.5 Hz, 1H), 7.63-7.59 (m, 3H), 7.50-7.43 (m, 2H), 7.42-7.39 (m, 1H), 3.55 (d, *J* = 17.0 Hz, 1H), 2.97 (d, *J* = 17.0 Hz, 1H), 2.66-2.55 (m, 2H), 2.52-2.34 (m, 2H), 2.14-1.99 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 215.8, 203.3, 154.1, 148.2, 140.0, 134.1, 128.9, 128.4, 127.5, 127.2, 124.8, 124.7, 65.1, 37.9, 37.9, 34.7, 19.5. **HRMS** (ESI) m/z calculated for $C_{19}H_{16}O_2Na$ $[M+Na]^+$ 299.1043, found 299.1042. **FT-IR** (cm^{-1}): 3359, 2920, 2850, 1739, 1694, 1632, 1603, 1466, 1418, 1120, 1074, 1040, 766, 696.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 280.6 nm, t_{major} = 1.227 min, t_{minor} = 1.624 min).

(*R*)-5'-(*p*-tolyl)spiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2g)

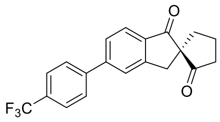


Following the above general procedure, **2g** was obtained in 56% yield (8.12 mg) with 62% ee as an white solid (m.p. = 150-152 ºC). $[\alpha]_D^{22}$ = 19 (c = 1.0, CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 1H), 7.63 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 7.9 Hz, 2H), 3.53 (d, *J* = 16.9 Hz, 1H), 2.95 (d, *J* = 16.9 Hz, 1H), 2.64-2.56 (m, 2H), 2.49-2.44 (m, 1H), 2.43-2.35 (m, 4H), 2.11-2.01 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 215.9, 203.2, 154.1, 148.1, 138.4, 137.1, 133.8, 129.6, 127.3, 127.0, 124.8, 124.3, 65.1, 37.9, 37.9, 34.7, 21.1, 19.5. **HRMS** (ESI) m/z calculated for $C_{20}H_{18}O_2Na$ $[M+Na]^+$ 313.1199, found 313.1198. **FT-IR** (cm^{-1}): 2964, 1739, 1694, 1605, 1420, 1401, 1279, 1154, 907, 812.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 290.1 nm, t_{major} = 1.272 min, t_{minor} = 1.668 min).

(*R*)-5'-(4-(trifluoromethyl)phenyl)spiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2h)

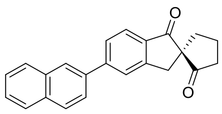


Following the above general procedure, **2h** was obtained in 55% yield (9.46 mg) with 81% ee as an white solid (m.p. = 103-105 ºC). $[\alpha]_D^{24}$ = 18 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.0 Hz, 1H), 7.74 -7.70 (m, 4H), 7.66 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 3.56 (d, *J* = 17.0 Hz, 1H), 2.99 (d, *J* = 17.0 Hz, 1H), 2.67-2.56 (m, 2H), 2.51-2.36 (m, 2H), 2.15 -2.02 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.6, 203.1, 154.1, 146.5, 143.5, 134.8, 130.3 (q, *J* = 32.0 Hz), 124.0 (q, *J* = 270 Hz), 127.8, 127.3, 125.8 (q, *J* = 4.0 Hz), 125.0, 65.2, 37.9, 37.8, 34.6, 19.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.5. **HRMS** (ESI) m/z calculated for $C_{20}H_{15}F_3O_2Na$ $[M+Na]^+$ 367.0916, found 367.0919. **FT-IR** (cm^{-1}): 2920, 1742, 1700, 1609, 1427, 1400, 1326, 1286, 1214, 1167, 1124, 1070, 1014, 907, 834.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 274.7 nm, t_{major} = 0.777 min, t_{minor} = 0.969 min).

(*R*)-5'-(naphthalen-2-yl)spiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2i)

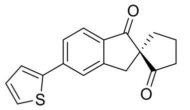


Following the above general procedure, **2i** was obtained in 61% yield (9.95 mg) with 75% ee as an yellow solid (m.p. = 134-136 ºC). $[\alpha]_D^{23}$ = 35 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.94-7.86 (m, 3H), 7.81-7.71 (m, 4H), 7.53-7.51 (m, 2H), 3.57 (d, *J* = 17.0 Hz, 1H), 2.98 (d, *J* = 17.0 Hz, 1H), 2.67-2.57 (m, 2H), 2.51-2.36 (m, 2H), 2.14-2.02 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.9, 203.3, 154.2, 148.1, 137.3, 134.1, 133.5, 133.1, 128.7, 128.4, 127.7, 127.5, 126.7, 126.6, 125.3, 124.9, 124.9, 65.2, 37.9, 37.9, 34.7, 19.6. **HRMS** (ESI) m/z calculated for $C_{23}H_{18}O_2Na$ $[M+Na]^+$ 349.1199, found 349.1198. **FT-IR** (cm^{-1}): 3055, 2920, 1738, 1694, 1606, 1423, 1271, 1213, 1152, 911, 847, 737.

The ee value was determined by the chiral UPC^2 analysis (CHIRALPAK® AD-3, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 272.3 nm, t_{major} = 6.249 min, t_{minor} = 7.736 min).

(*R*)-5'-(thiophen-2-yl)spiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2j)

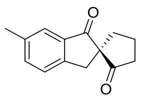


Following the above general procedure, **2j** was obtained in 51% yield (7.19 mg) with 63% ee as an yellow solid (m.p. = 130-132 ºC). $[\alpha]_D^{23}$ = 38 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.47 (m, 2H), 7.43 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.24 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.19 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.92 (dd, *J* = 5.1, 3.6 Hz, 1H), 3.31 (d, *J* = 17.0 Hz, 1H), 2.73 (d, *J* = 17.0 Hz, 1H), 2.44-2.35 (m, 2H), 2.29-2.15 (m, 2H), 1.92 -1.79 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.7, 202.8, 154.3, 142.9, 140.9, 134.0, 128.4, 126.9, 125.7, 125.1, 125.0, 122.8, 65.1, 37.9, 37.7, 34.7, 19.5. **HRMS** (ESI) m/z calculated for $C_{17}H_{14}O_2SNa$ $[M+Na]^+$ 305.0607, found 305.0608. **FT-IR** (cm^{-1}): 2957, 2920, 2849, 1738, 1693, 1604, 1422, 1321, 1210, 990, 827, 716.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 323.5 nm, t_{major} = 1.595 min, t_{minor} = 2.131 min).

(*R*)-6'-methylspiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2k)

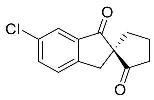


Following the above general procedure, **2k** was obtained in 75% yield (8.03 mg) with 83% ee as an white solid (m.p. = 80-82 ºC). $[\alpha]_D^{24}$ = 42 (c = 1.0, CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 3.44 (d, *J* = 16.8 Hz, 1H), 2.87 (d, *J* = 16.8 Hz, 1H), 2.61-2.53 (m, 2H), 2.47-2.33 (m, 5H), 2.09-2.04 (m, 1H), 2.03-1.99 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.9, 203.9, 150.9, 137.8, 136.4, 135.5, 125.9, 124.4, 65.2, 38.0, 37.6, 34.7, 21.1, 19.6. **HRMS** (ESI) m/z calculated for $C_{14}H_{14}O_2Na$ $[M+Na]^+$ 237.0886, found 237.0878. **FT-IR** (cm^{-1}): 2962, 2919, 2850, 1738, 1695, 1616, 1492, 1261, 1155, 1095, 1019, 800, 761.

The ee value was determined by the chiral UPC^2 analysis (CHIRALPAK® AD-3, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 245.0 nm, t_{major} = 0.871 min, t_{minor} = 1.068 min).

(*R*)-6'-chlorospiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2l)

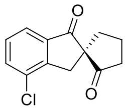


Following the above general procedure, **2l** was obtained in 64% yield (8.03 mg) with 67% ee as an white solid (m.p. = 103-105 ºC). $[\alpha]_D^{24}$ = 20 (c = 1.0, CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (d, *J* = 2.0 Hz, 1H), 7.55 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 1H), 3.44 (d, *J* = 17.0 Hz, 1H), 2.88 (d, *J* = 17.0 Hz, 1H), 2.61-2.54 (m, 2H), 2.45-2.33 (m, 2H), 2.10-1.99 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 215.1, 202.4, 151.5, 136.7, 135.0, 134.1, 127.4, 124.1, 65.4, 37.8, 37.3, 34.5, 19.5. **HRMS** (ESI) m/z calculated for $C_{13}H_{11}ClO_2Na$ $[M+Na]^+$ 257.0340, found 257.0339. **FT-IR** (cm^{-1}): 2945, 2883, 2827, 1734, 1702, 1466, 1429, 1252, 1147, 886, 847, 831, 746.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 95/05, v = 2.0 mL/min, λ= 240.3 nm, t_{major} = 1.553 min, t_{minor} = 1.682 min).

(*R*)-4'-chlorospiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2m)

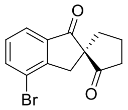


Following the above general procedure, **2m** was obtained in 75% yield (8.78 mg) with 70% ee as an white solid (m.p. = 70-73 ºC). $[\alpha]_D^{24}$ = 30 (c = 1.0, CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62-7.59 (m, 2H), 7.36 (t, *J* = 7.7 Hz, 1H), 3.49 (d, *J* = 17.5 Hz, 1H), 2.90 (d, *J* = 17.5 Hz, 1H), 2.63-2.56 (m, 2H), 2.49-2.37 (m, 2H), 2.14-2.08 (m, 1H), 2.07-2.02 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 215.2, 203.0, 151.1, 137.1, 134.8, 132.5, 129.4, 122.7, 64.8, 37.9, 36.9, 34.7, 19.6. **HRMS** (ESI) m/z calculated for $C_{13}H_{11}ClO_2Na$ $[M+Na]^+$ 257.0340, found 257.0339. **FT-IR** (cm^{-1}): 3358, 2920, 2850, 1743, 1706, 1659, 1633, 1461, 1421, 1331, 1263, 1134, 996, 913, 738.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 246.2 nm, t_{major} = 0.672 min, t_{minor} = 0.736 min).

(*R*)-4'-bromospiro[cyclopentane-1,2'-indene]-1',2(3'H)-dione (2n)

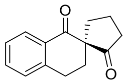


Following the above general procedure, **2n** was obtained in 70% yield (9.73 mg) with 63% ee as an white solid (m.p. = 69-70 ºC). $[\alpha]_D^{26}$ = 5 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.67 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.32-7.26 (m, 1H), 3.45 (d, *J* = 17.5 Hz, 1H), 2.86 (d, *J* = 17.6 Hz, 1H), 2.64-2.55 (m, 2H), 2.52-2.35 (m, 2H), 2.15-2.02 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.0, 203.1, 153.1, 137.8, 137.1, 129.5, 123.3, 121.7, 64.8, 38.9, 37.9, 34.7, 19.5. **HRMS** (ESI) m/z calculated for $C_{13}H_{11}BrO_2$ $[M+Na]^+$ 300.9835, found 300.9834. **FT-IR** (cm^{-1}): 2945, 2883, 2821, 1741, 1703, 1457, 1329, 1123, 909, 786, 752.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 252.1 nm, t_{major} = 0.764 min, t_{minor} = 0.853 min).

(*R*)-3',4'-dihydro-1'H-spiro[cyclopentane-1,2'-naphthalene]-1',2-dione (2o)

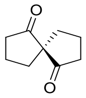


Following the above general procedure, **2o** was obtained in 80% yield (8.56 mg) with 58% ee as an amorphous solid. $[\alpha]_D^{25}$ = 26 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.47 (td, *J* = 7.5, 1.5 Hz, 1H), 7.29 (t, *J* = 7.0 Hz, 1H), 7.23 (d, *J* = 7.7 Hz, 1H), 3.14-3.07 (m, 1H), 3.00-2.92 (m, 1H), 2.58-2.43 (m, 3H), 2.39-2.30 (m, 1H), 2.17-2.06 (m, 1H), 2.04-1.90 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 217.3, 197.5, 143.6, 133.6, 131.0, 128.6, 127.6, 126.7, 60.4, 38.7, 33.6, 30.3, 25.4, 19.0. **HRMS** (ESI) m/z calculated for $C_{14}H_{14}O_2Na$ $[M+Na]^+$ 237.0886, found 237.0885. **FT-IR** (cm^{-1}): 3066, 2936, 1712, 1673, 1601, 1455, 1295, 1226, 947, 847, 740.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 95/5, v = 2.0 mL/min, λ= 246.2 nm, t_{major} = 2.199 min, t_{minor} = 2.516 min).

(R)-spiro[4.4]nonane-1,6-dione (2p)

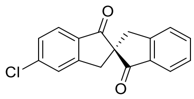


Following the above general procedure, **2p** was obtained in 73% yield (5.55 mg) with 39% ee as an white solid (m.p. = 32-34 ºC). $[\alpha]_D^{23}$ = 2 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43-2.25 (m, 6H), 2.23-2.13 (m, 2H), 1.96-1.87 (m, 2H), 1.86-1.79 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 216.7, 64.3, 38.4, 34.2, 19.7. **FT-IR** (cm^{-1}): 2959, 2919, 2850, 1746, 1716, 1658, 1632, 1406, 1313, 1157, 1065, 916.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 95/5, v = 2.0 mL/min, λ= 202.6 nm, t_{major} = 0.641 min, t_{minor} = 0.684 min).

(R)-5-chloro-2,2'-spirobi[indene]-1,1'(3H,3'H)-dione (2q)

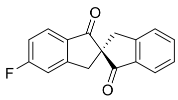


Following the above general procedure, **2q** was obtained in 84% yield (11.85 mg) with 87% ee as an white solid (m.p. = 181-183 ºC). $[\alpha]_D^{25}$ = 28 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.7 Hz, 1H), 7.69-7.64 (m, 2H), 7.56 (dt, J = 4.7, 2.1 Hz, 2H), 7.43-7.38 (m, 2H), 3.70 (dd, J = 17.0, 14.8 Hz, 2H), 3.17 (dd, J = 17.0, 8.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.1, 201.0, 155.1, 153.6, 141.8, 135.3, 135.1, 133.8, 128.5, 127.8, 126.5, 126.3, 125.7, 124.8, 65.4, 37.7, 37.5. **FT-IR** (cm^{-1}): 1715, 1693, 1599, 1464, 1421, 1318, 1206, 1136, 1068, 1034.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 251.0 nm, tmajor = 1.309 min, tminor = 1.559 min)

(R)-5-fluoro-2,2'-spirobi[indene]-1,1'(3H,3'H)-dione (2r)

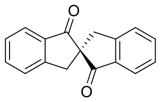


Following the above general procedure, **2r** was obtained in 65% yield (8.65 mg) with 63% ee as an white solid (m.p. = 175-176 ºC). $[\alpha]_D^{25}$ = 14 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dt, J = 8.7, 3.0 Hz, 2H), 7.66 (td, J = 7.5, 1.2 Hz, 1H), 7.56 (dt, J = 7.7, 1.0 Hz, 1H), 7.43-7.39 (m, 1H), 7.22 (dd, J = 8.4, 2.2 Hz, 1H), 7.11 (td, J = 8.6, 2.3 Hz, 1H), 3.71 (dd, J = 17.1, 11.6 Hz, 2H), 3.18 (dd, J = 17.1, 5.5 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 202.3, 200.7, 167.5 (d, J = 257.5 Hz), 156.7 (d, J = 10.5 Hz), 153.7, 135.4, 135.2, 131.8 (d, J = 1.8 Hz), 127.8, 127.1 (d, J = 10.7 Hz), 126.3, 124.9, 116.2 (d, J = 24.0 Hz), 113.1 (d, J = 22.4 Hz), 65.6, 37.8, 37.7 (d, J = 2.3 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -101.7. **FT-IR** (cm^{-1}): 1723, 1693, 1614, 1591, 1482, 1425, 1252, 1086.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 247.4 nm, t_{major} = 0.963 min, t_{minor} = 1.097 min).

(*R*)-2,2'-spirobi[indene]-1,1'(3H,3'H)-dione (2s)

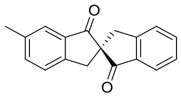


Following the above general procedure, **2s** was obtained in 90% yield (11.16 mg) with 47% ee as an white solid (m.p. = 172-173 ºC). $[\alpha]_D^{25}$ = 9 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.7 Hz, 1H), 7.65 (td, *J* = 7.5, 1.2 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 1H), 3.72 (d, *J* = 17.0 Hz, 1H), 3.19 (d, *J* = 16.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.6, 153.8, 135.4, 135.2, 127.8, 126.3, 124.9, 65.3, 38.1.

The ee value was determined by the chiral UPC^2 analysis (Trefoil™ CEL2, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 246.2 nm, t_{major} = 1.253 min, t_{minor} = 1.328 min).

(*R*)-6-methyl-2,2'-spirobi[indene]-1,1'(3H,3'H)-dione (2t)



Following the above general procedure, **2t** was obtained in 95% yield (12.45 mg) with 76% ee as an white solid (m.p. = 176-178 ºC). $[\alpha]_D^{25}$ = 6 (c = 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 1.2 Hz, 1H), 7.56-7.54 (m, 2H), 7.48-7.38 (m, 3H), 3.69 (dd, *J* = 21.3, 16.9 Hz, 2H), 3.16 (t, *J* = 17.2 Hz, 2H), 2.41 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.8, 202.7, 153.8, 151.2, 137.8, 136.5, 135.6, 135.5, 135.2, 127.7, 126.3, 126.0, 124.8, 124.8, 65.7, 38.0, 37.8, 21.0.

The ee value was determined by the chiral UPC^2 analysis (CHIRALPAK® AD-3, CO_2/MeOH = 80/20, v = 2.0 mL/min, λ= 247.4 nm, t_{major} = 1.587 min, t_{minor} = 1.774 min).

7. X-ray crystallographic information

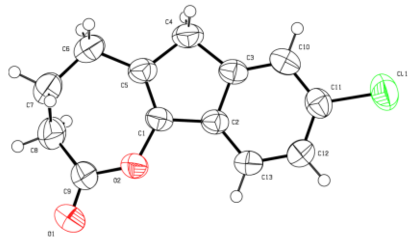


Table S2. Crystal data and structure refinement for compound 1a. (CCDC : 2099870)

Empirical formula	$C_{13}H_{11}ClO_2$
Temperature/K	292.69(10)
Crystal system	monoclinic
Space group	P21/n
a/Å	13.6872(8)
b/Å	6.0620(3)
c/Å	14.0247(9)
α/°	90
β/°	105.577(7)
γ/°	90
Volume/Å^3	1120.91(12)
Z	4
ρcalcg/cm^3	1.391
μ/mm^{-1}	2.863
F(000)	488.0
Crystal size/mm^3	0.1 × 0.05 × 0.04
Radiation	Cu K_α (λ = 1.54184)
2Θ range for data collection/°	8.014 to 133.2
Index ranges	$-12 \le h \le 16, -7 \le k \le 5, -15 \le l \le 16$
Reflections collected	3650
Independent reflections	1975 [R_{int} = 0.0217, R_{sigma} = 0.0316]
Data/restraints/parameters	1975/0/145
Goodness-of-fit on F^2	1.026
Final R indexes [I>=2σ (I)]	R_1 = 0.0460, wR_2 = 0.1158
Final R indexes [all data]	R_1 = 0.0624, wR_2 = 0.1323
Largest diff. peak/hole / e Å^{-3}	0.16/-0.24

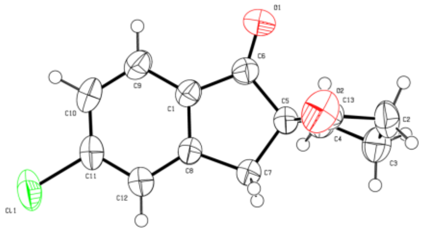
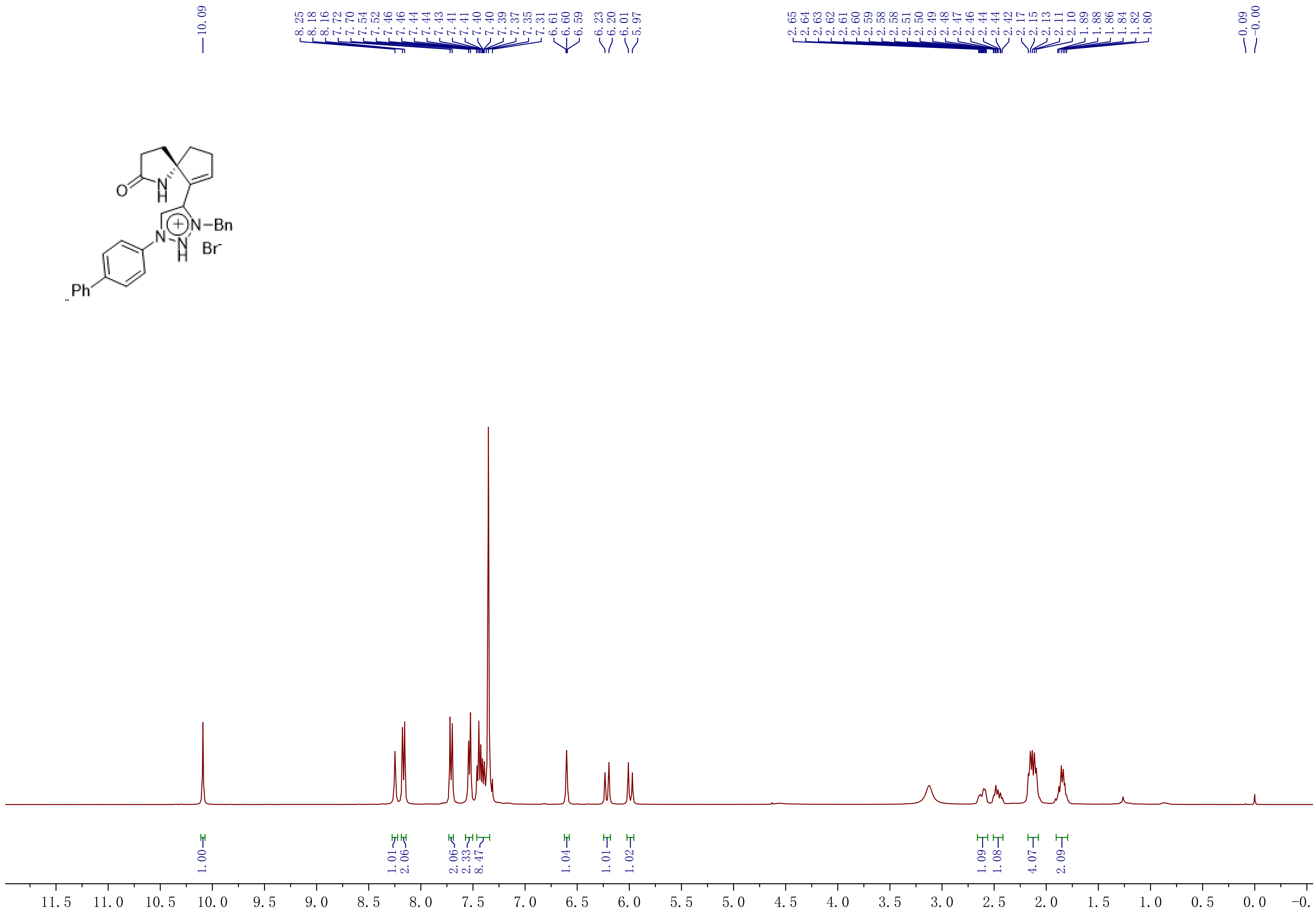


Table S3. Crystal data and structure refinement for compound 2a. (CCDC : 2092879)

Empirical formula	$C_{13}H_{11}ClO_2$
Formula weight	234.67
Temperature/K	293.0(7)
Crystal system	orthorhombic
Space group	P212121
a/Å	6.90260(14)
b/Å	6.93126(15)
c/Å	23.3243(4)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1115.92(4)
Z	4
ρcalcg/cm^3	1.397
μ/mm^{-1}	2.876
F(000)	488.0
Crystal size/mm^3	0.11 × 0.08 × 0.05
Radiation	Cu K_α (λ = 1.54184)
2Θ range for data collection/°	7.58 to 152.36
Index ranges	$-8 \leq h \leq 8$, $-5 \leq k \leq 8$, $-28 \leq l \leq 29$
Reflections collected	8732
Independent reflections	2262 [R_{int} = 0.0237, R_{sigma} = 0.0182]
Data/restraints/parameters	2262/0/145
Goodness-of-fit on F^2	1.075
Final R indexes [I>=2σ (I)]	R_1 = 0.0335, wR_2 = 0.0862
Final R indexes [all data]	R_1 = 0.0363, wR_2 = 0.0884
Largest diff. peak/hole / e Å^{-3}	0.15/-0.25
Flack parameter	0.000(8)

8. NMR spectroscopic data and UPC^2 data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6.61 6.60 6.59
6.23 6.20 6.01 5.97
2.65 2.64 2.63 2.62 2.61 2.60 2.59 2.58 2.58 2.51 2.50 2.49 2.48 2.47 2.46 2.44 2.44 2.42 2.17 2.15 2.13 2.11 2.10 1.89 1.88 1.86 1.84 1.82 1.80
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H
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N
N
H
Br⁻
Ph
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2.06 2.33 8.47
1.04
1.01 1.02
1.09 1.08
4.07 2.09
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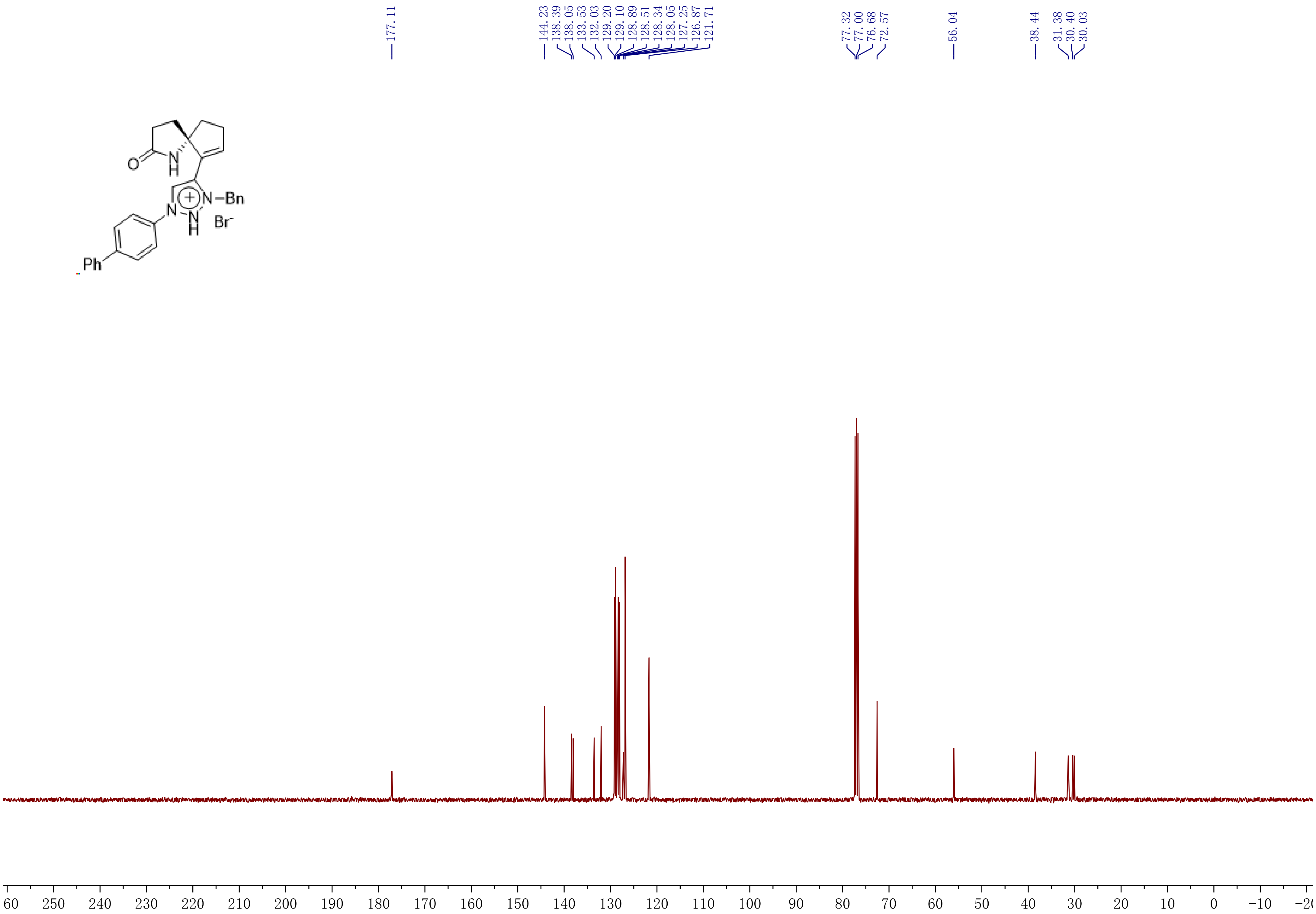
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56.04
38.44
31.38
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30.03
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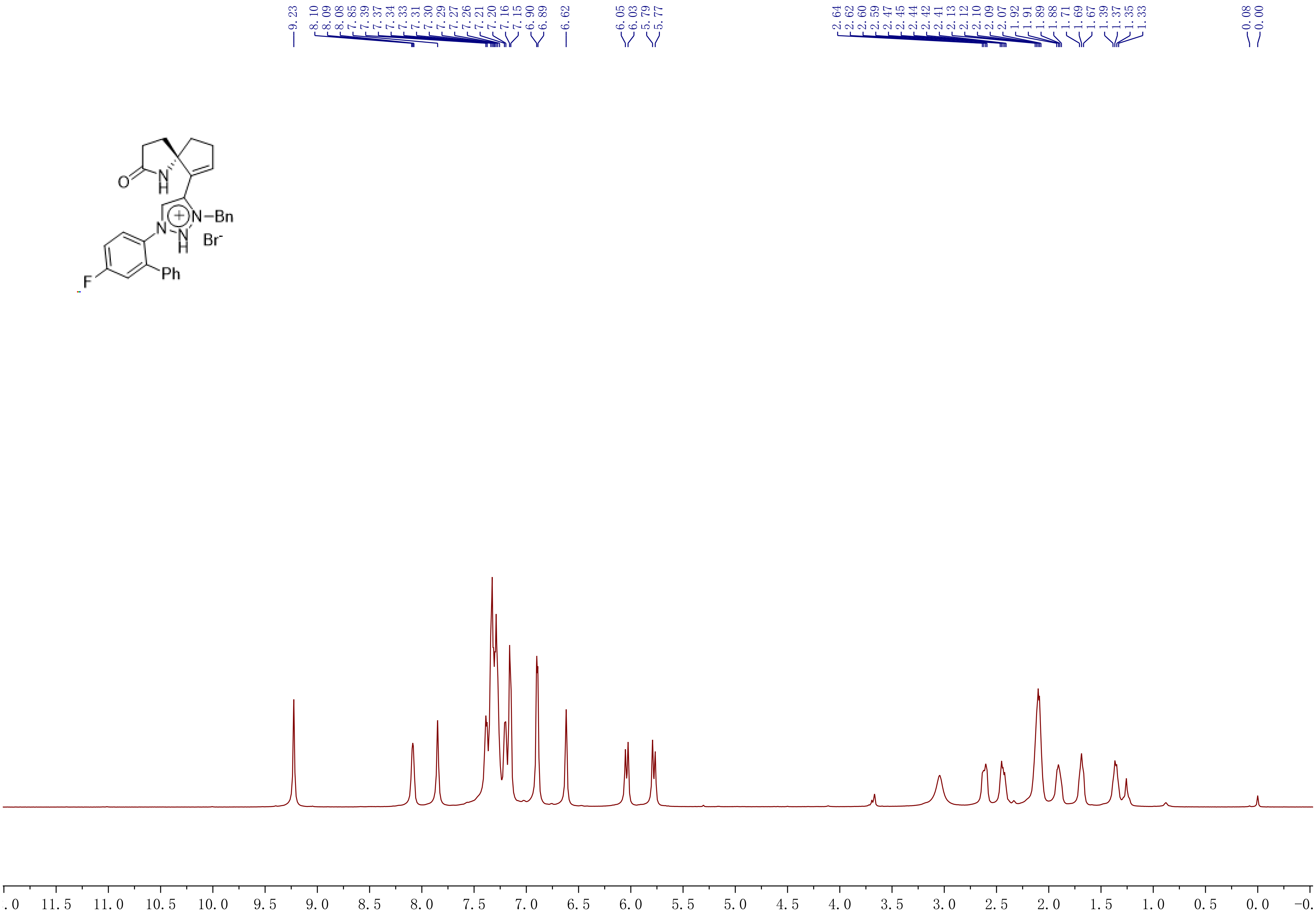
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6.62
6.05 6.03 5.79 5.77
2.64 2.62 2.60 2.59 2.47 2.45 2.44 2.42 2.41 2.13 2.12 2.10 2.09 2.07 1.92 1.91 1.89 1.88 1.71 1.69 1.67 1.39 1.37 1.35 1.33
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H
N
N
N
H
N−Bn
Br⁻
F
Ph
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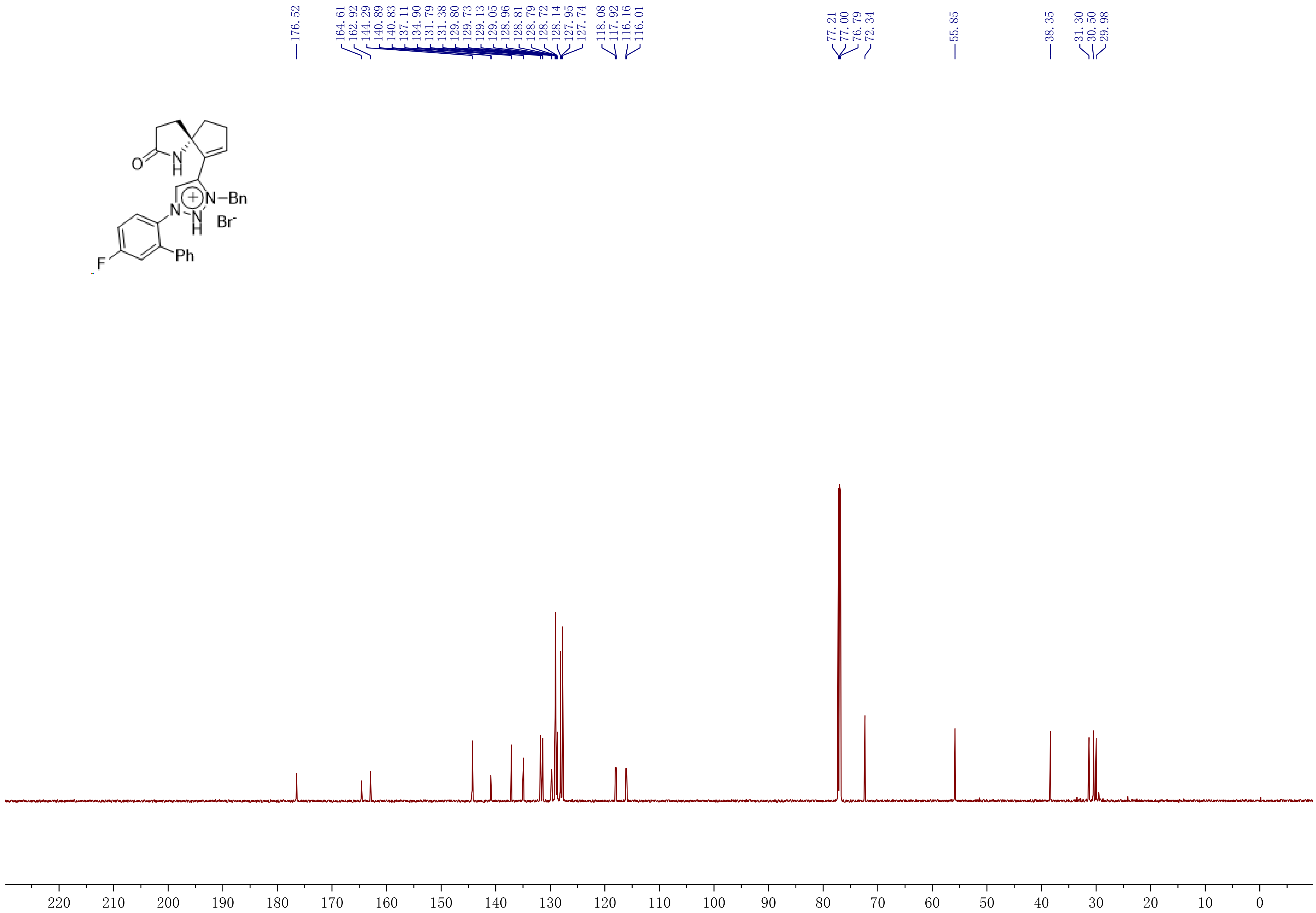
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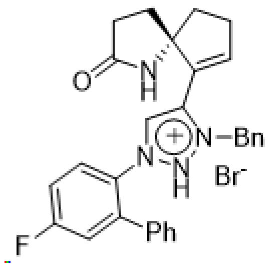
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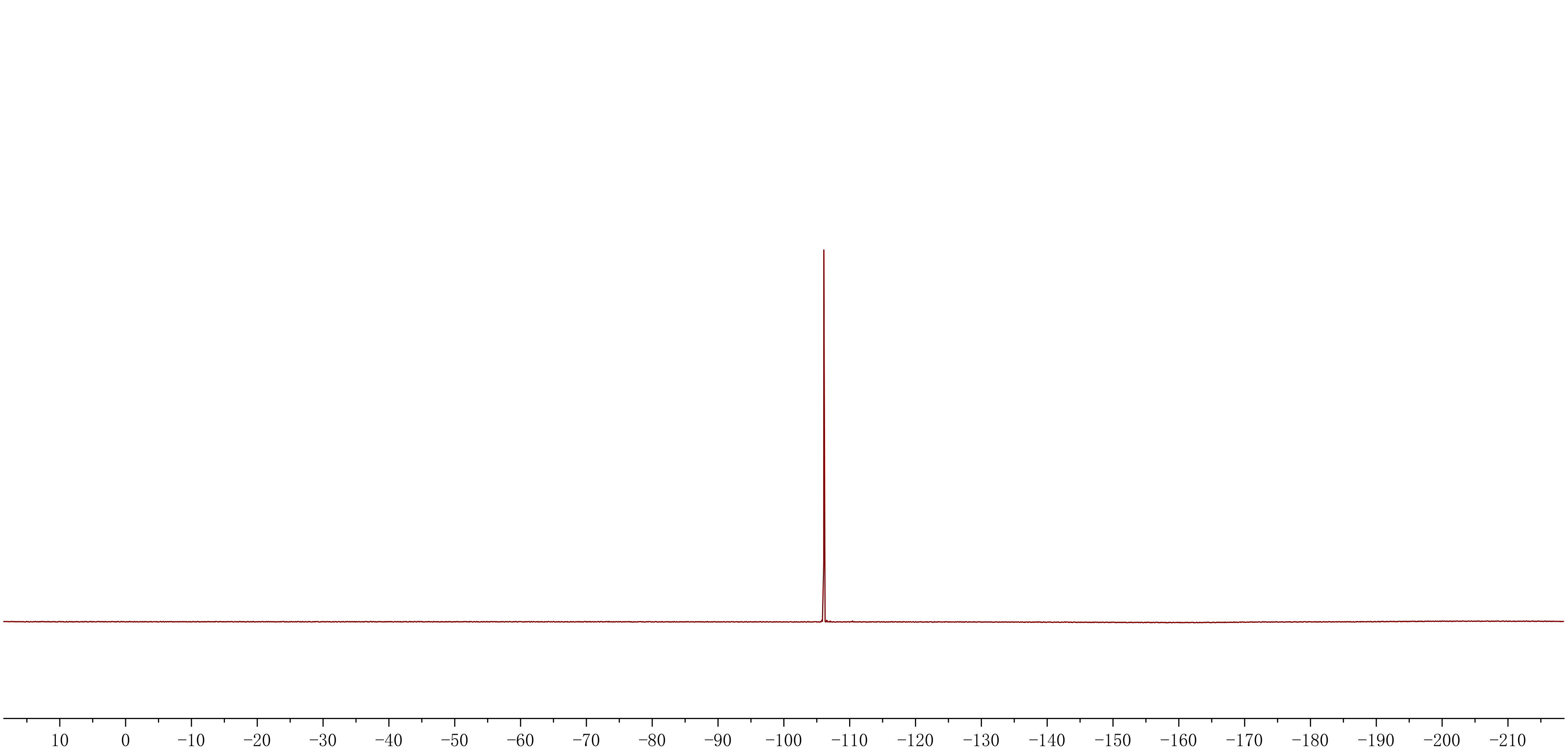
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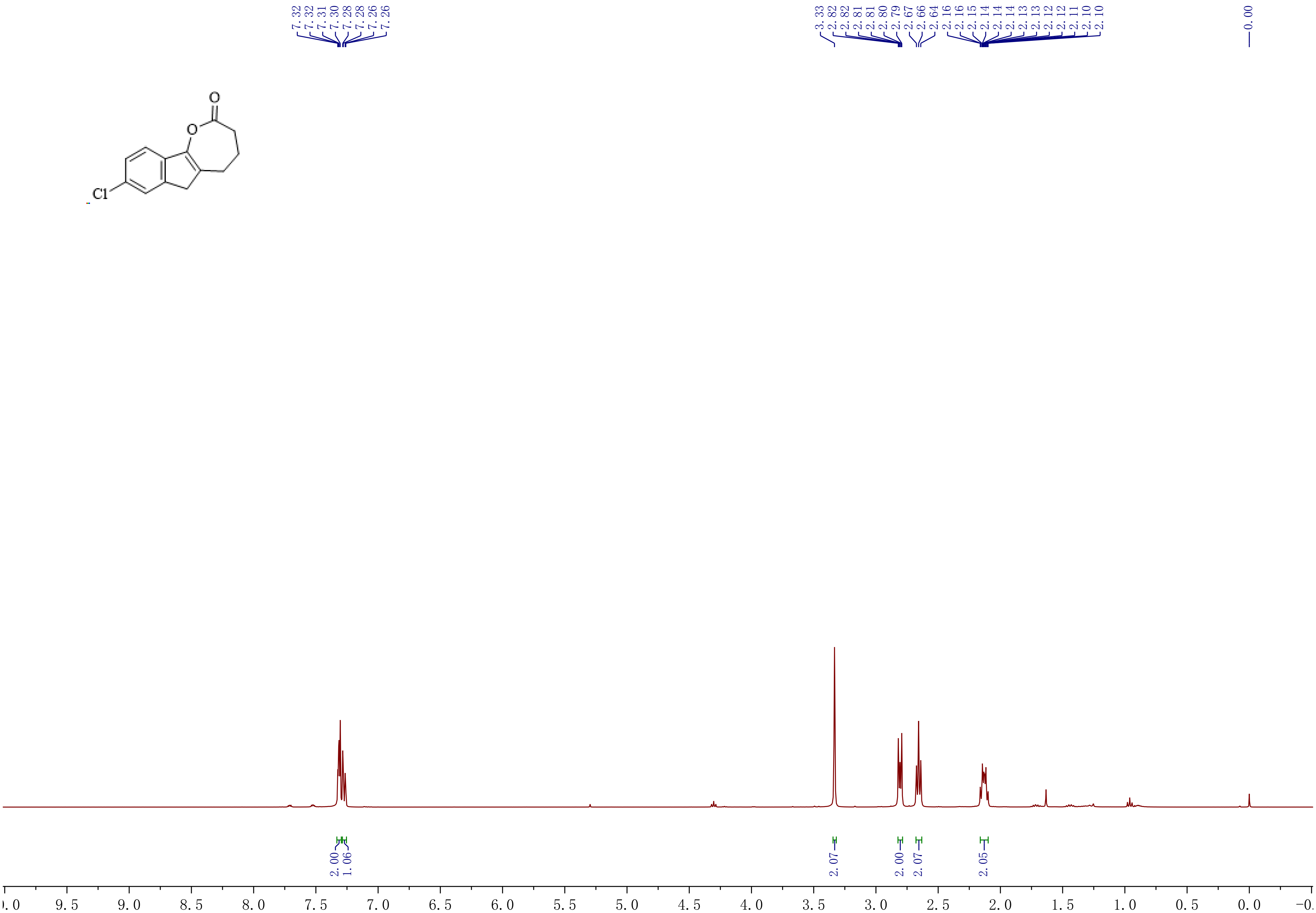

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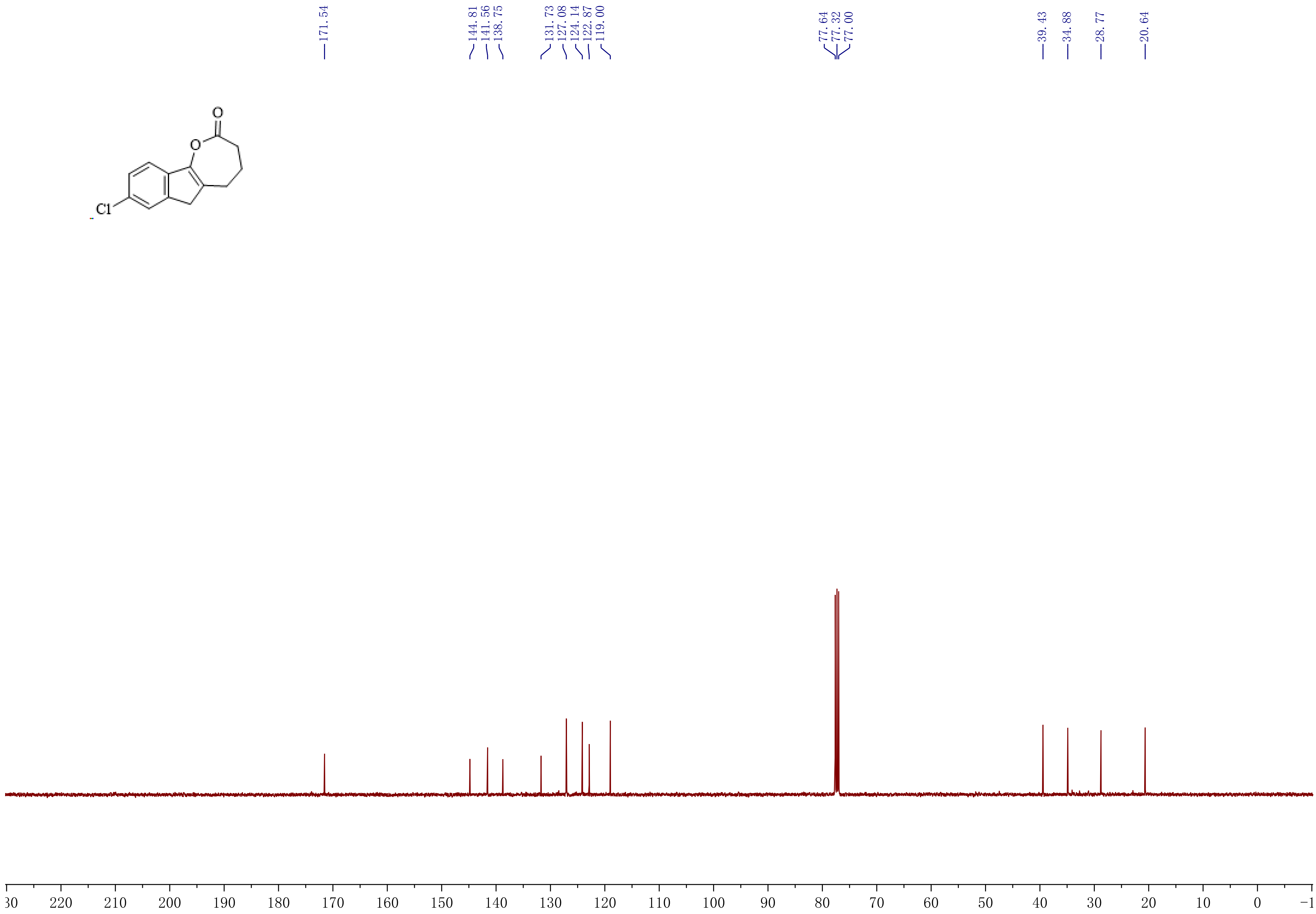
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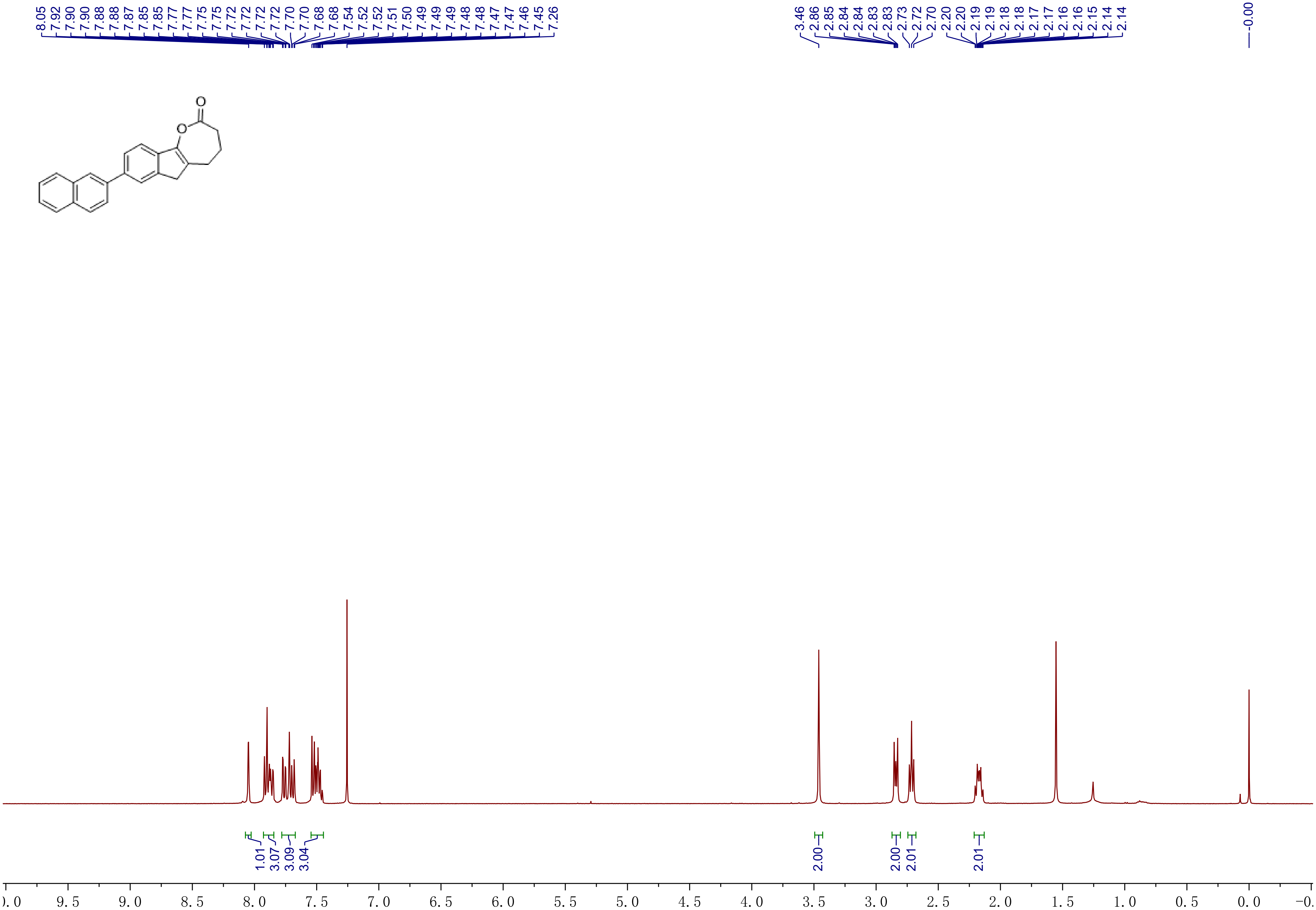

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2.00
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2.01
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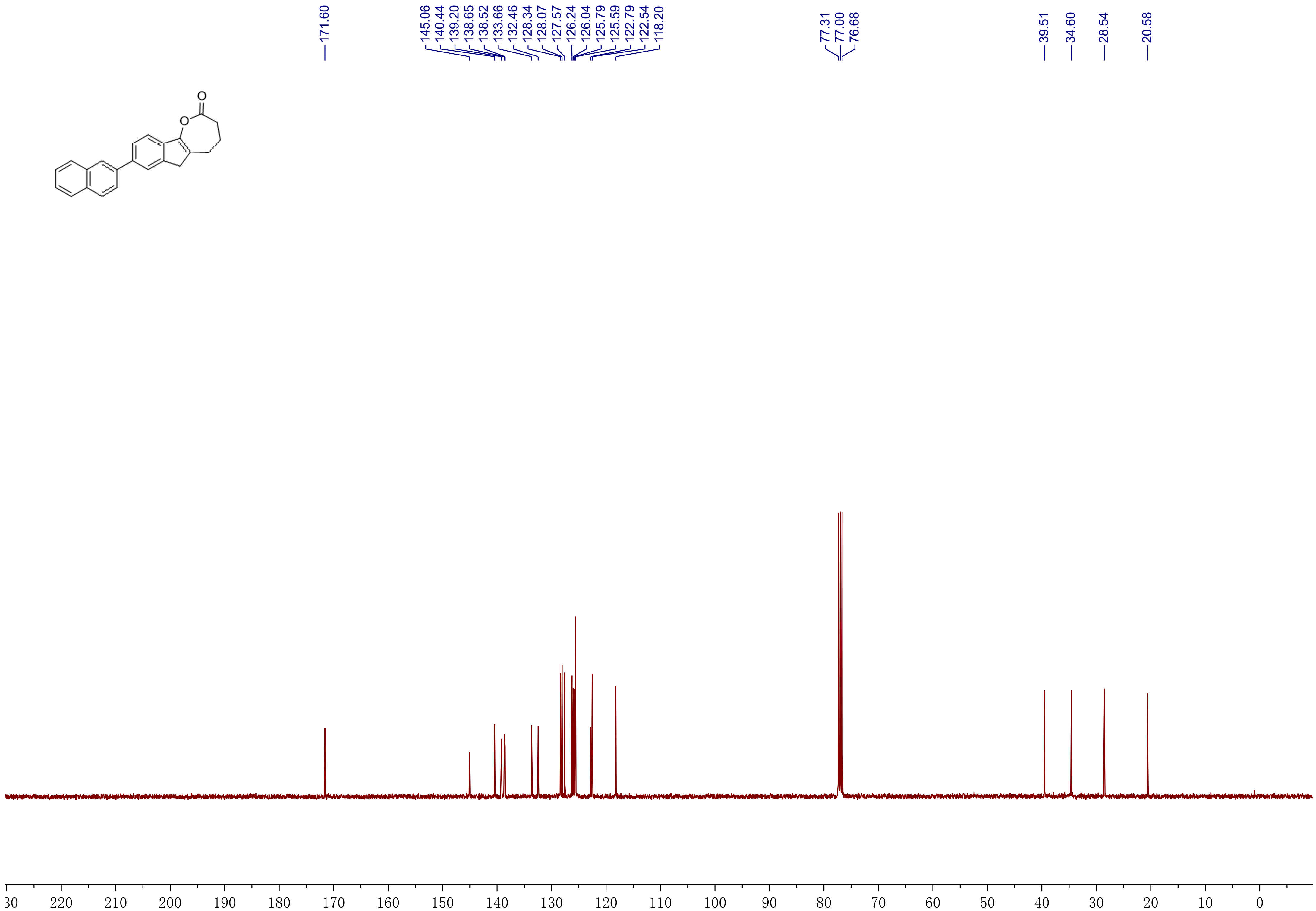
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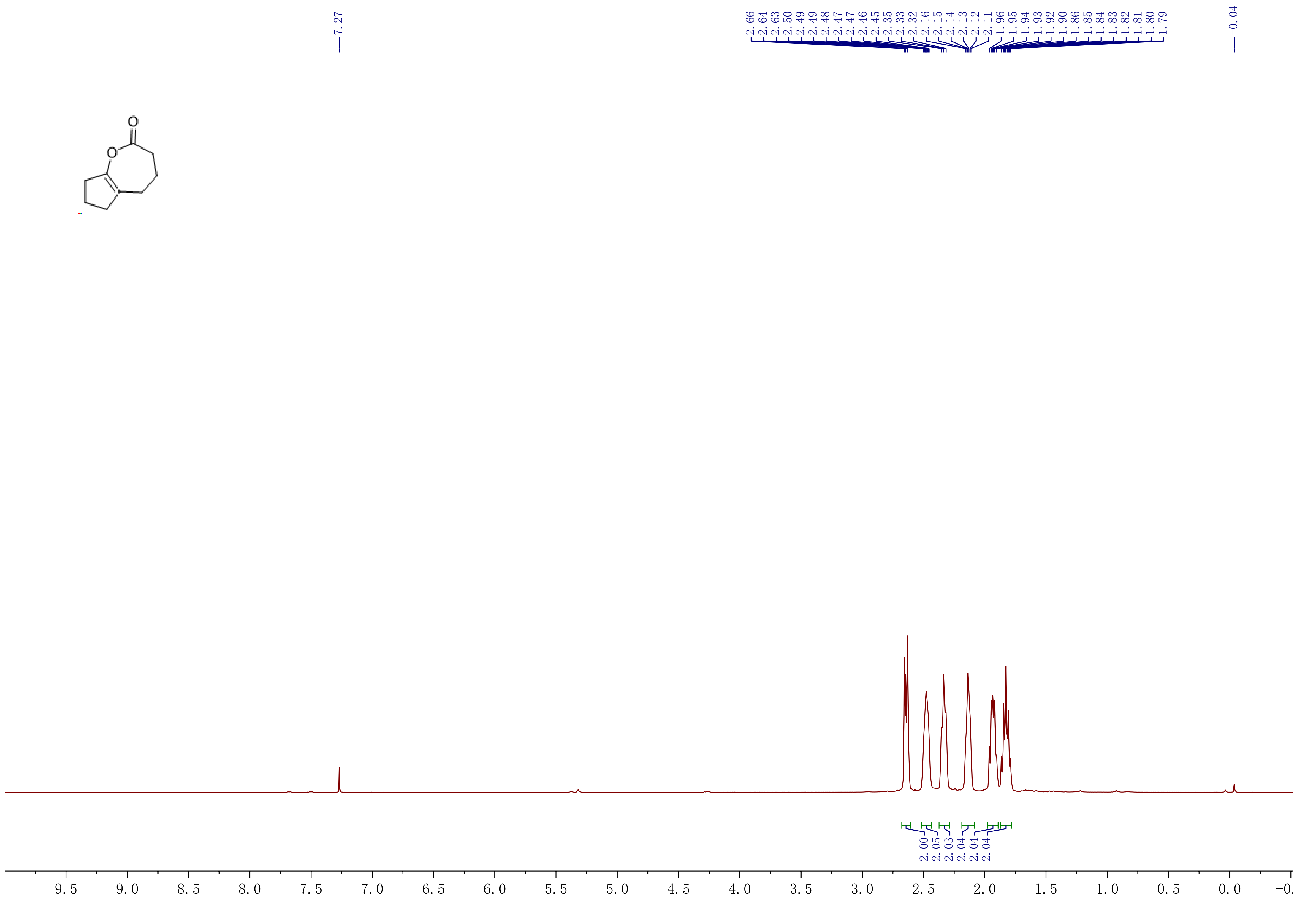
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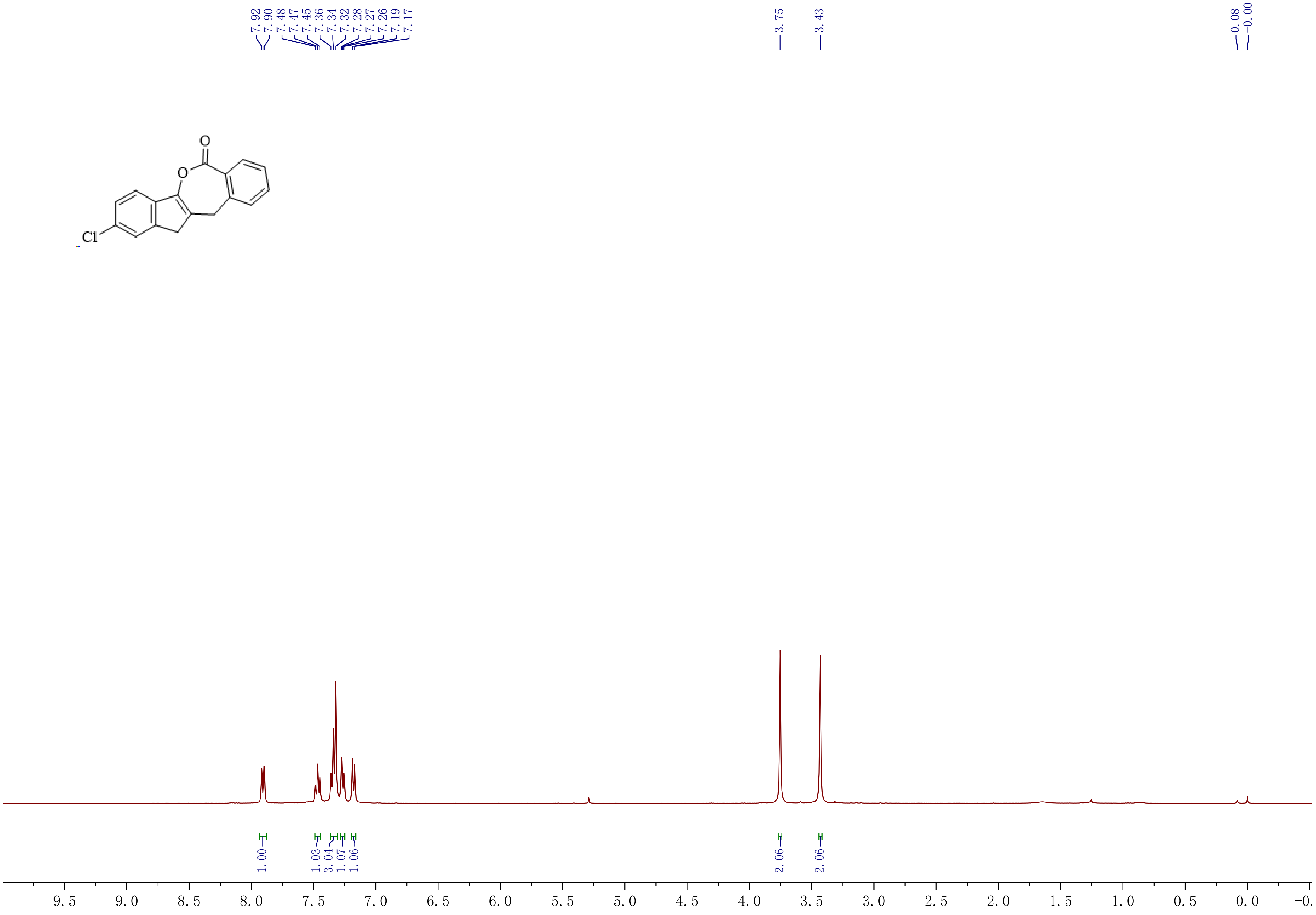

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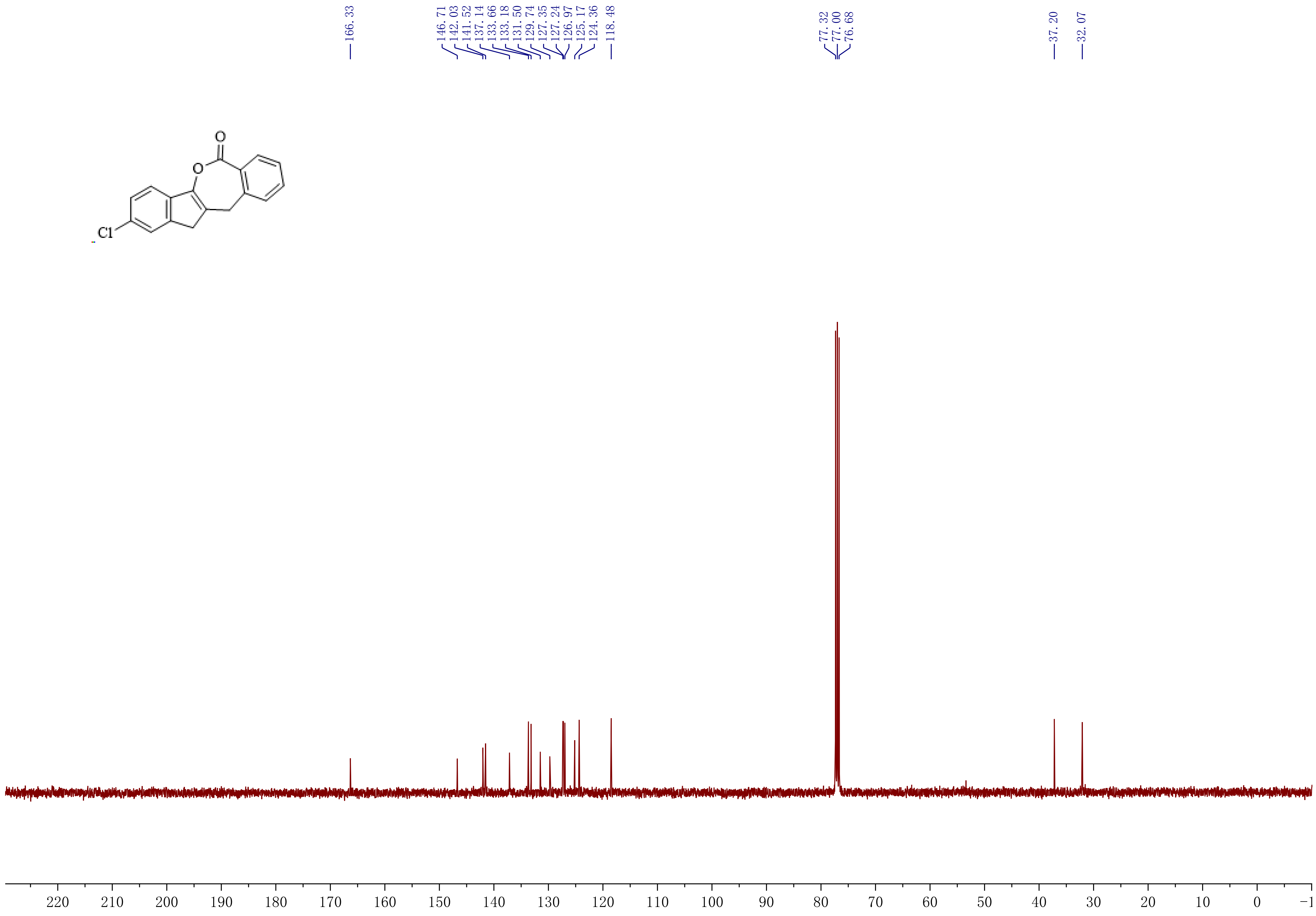

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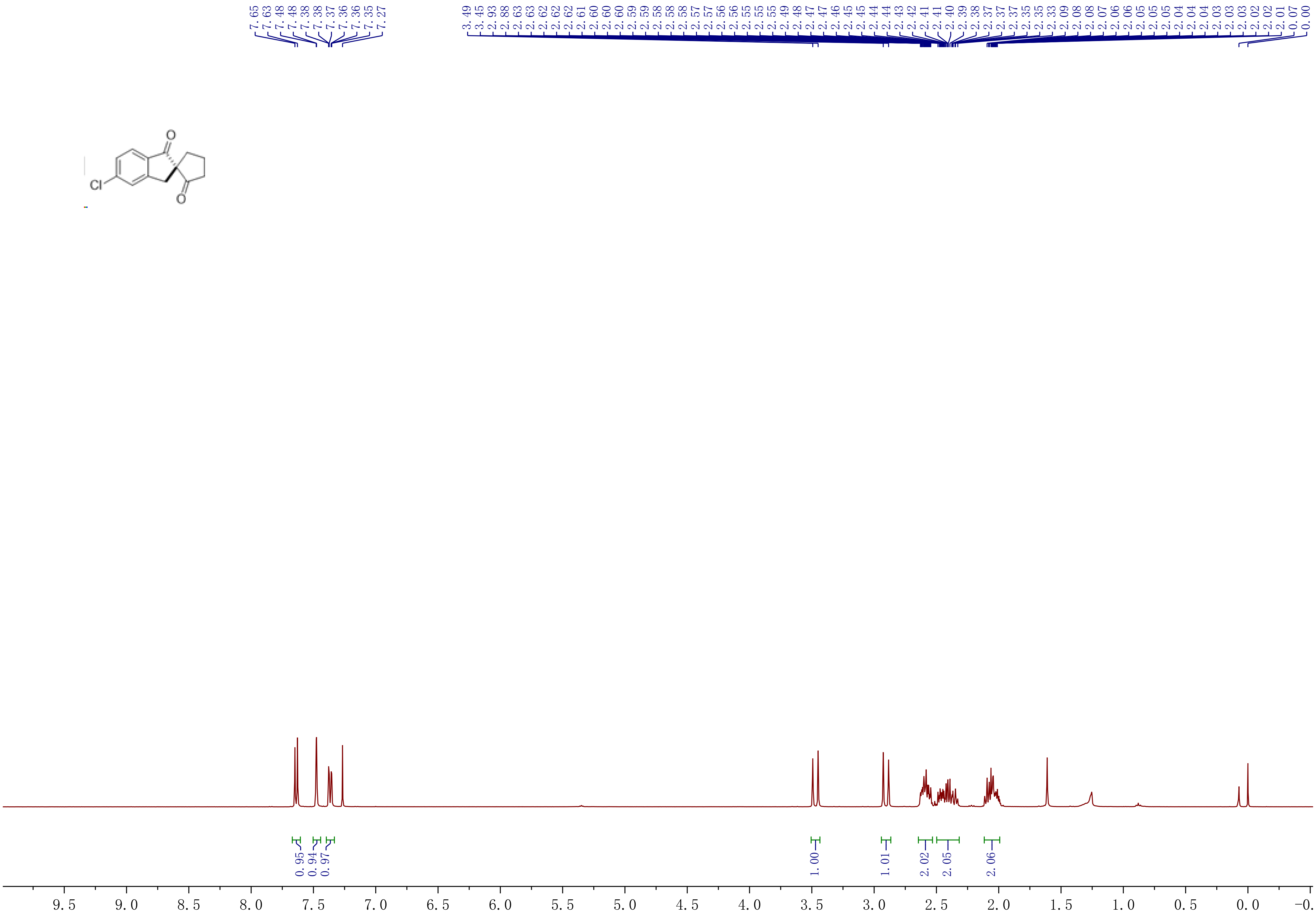

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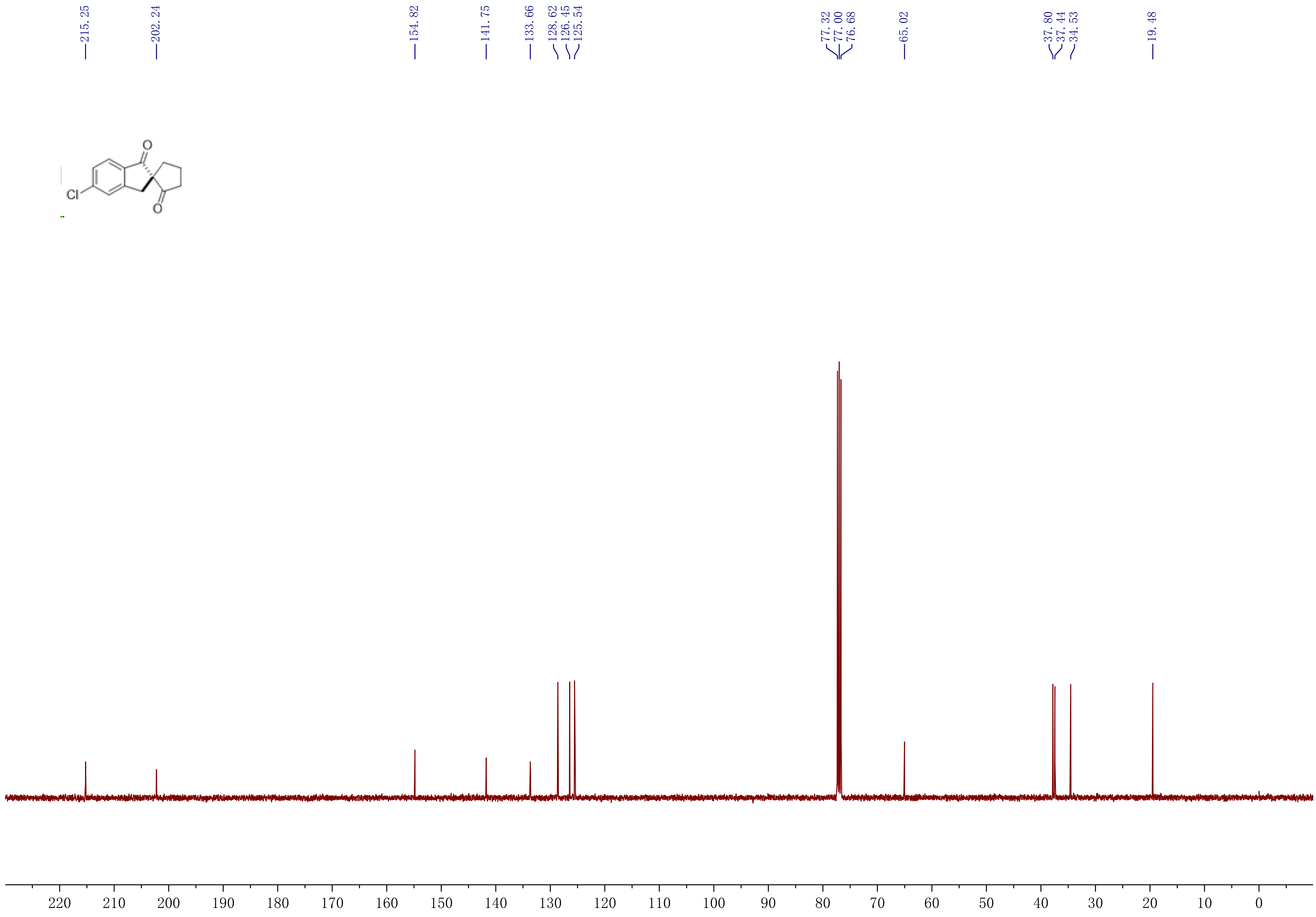
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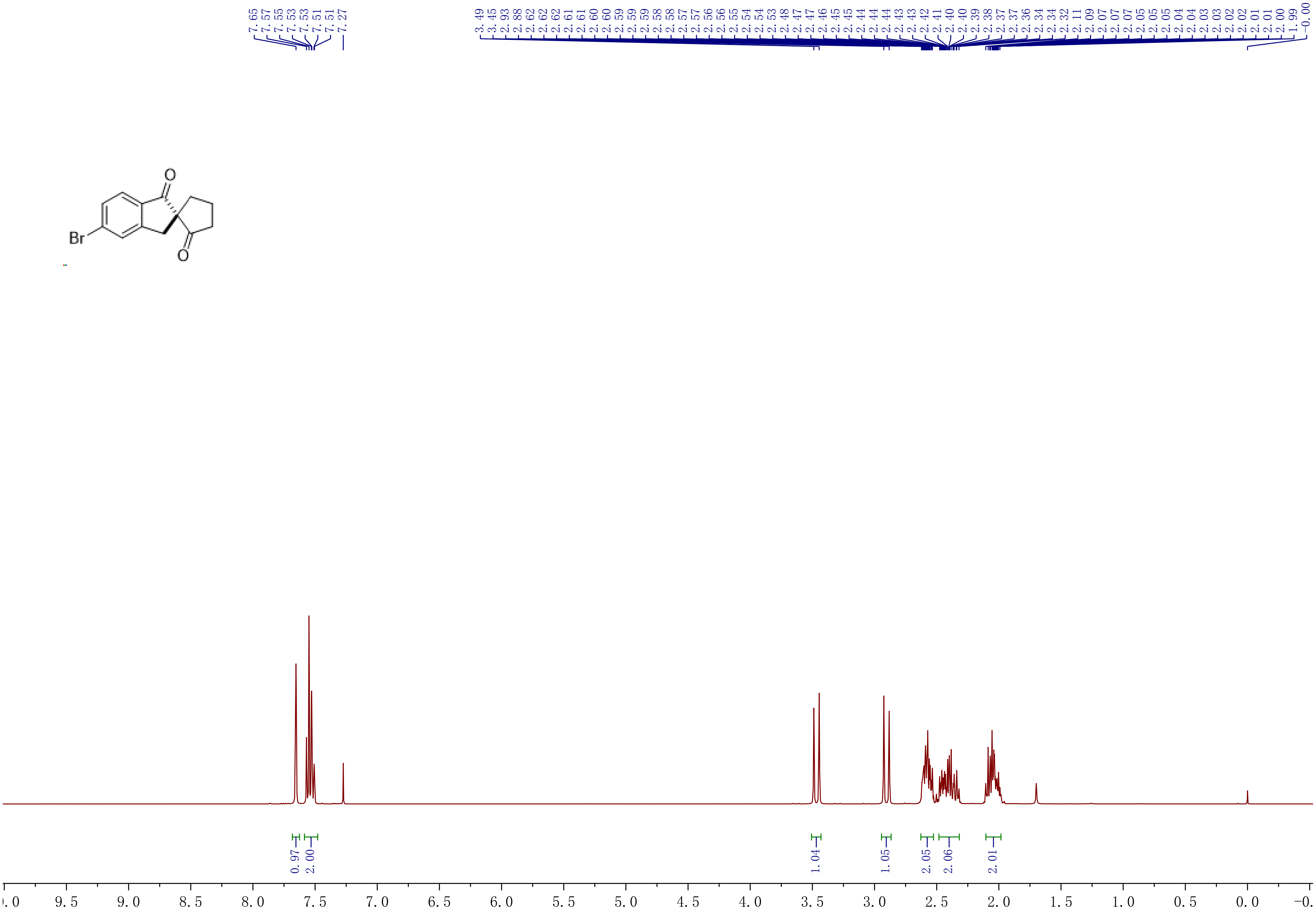
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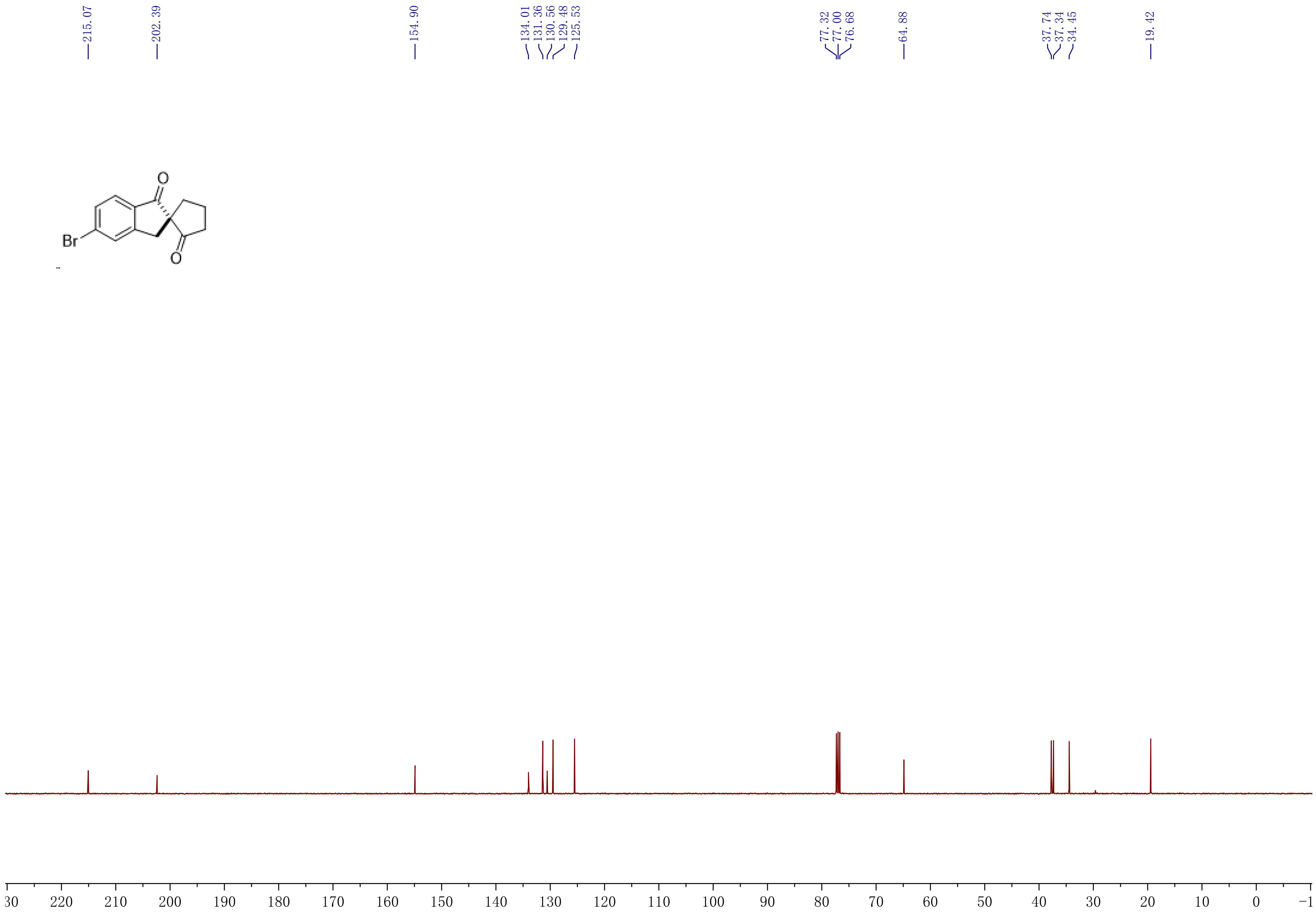
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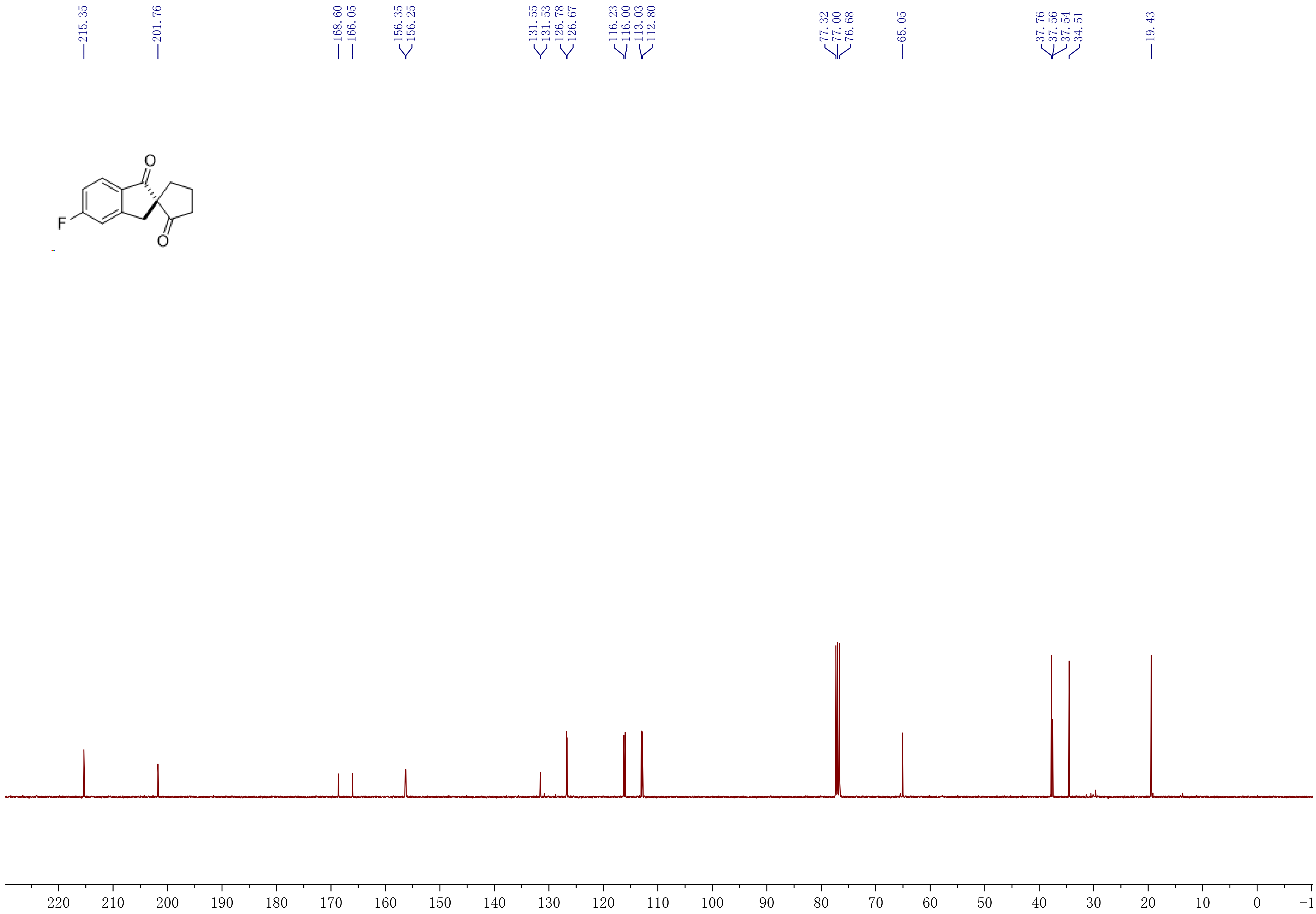
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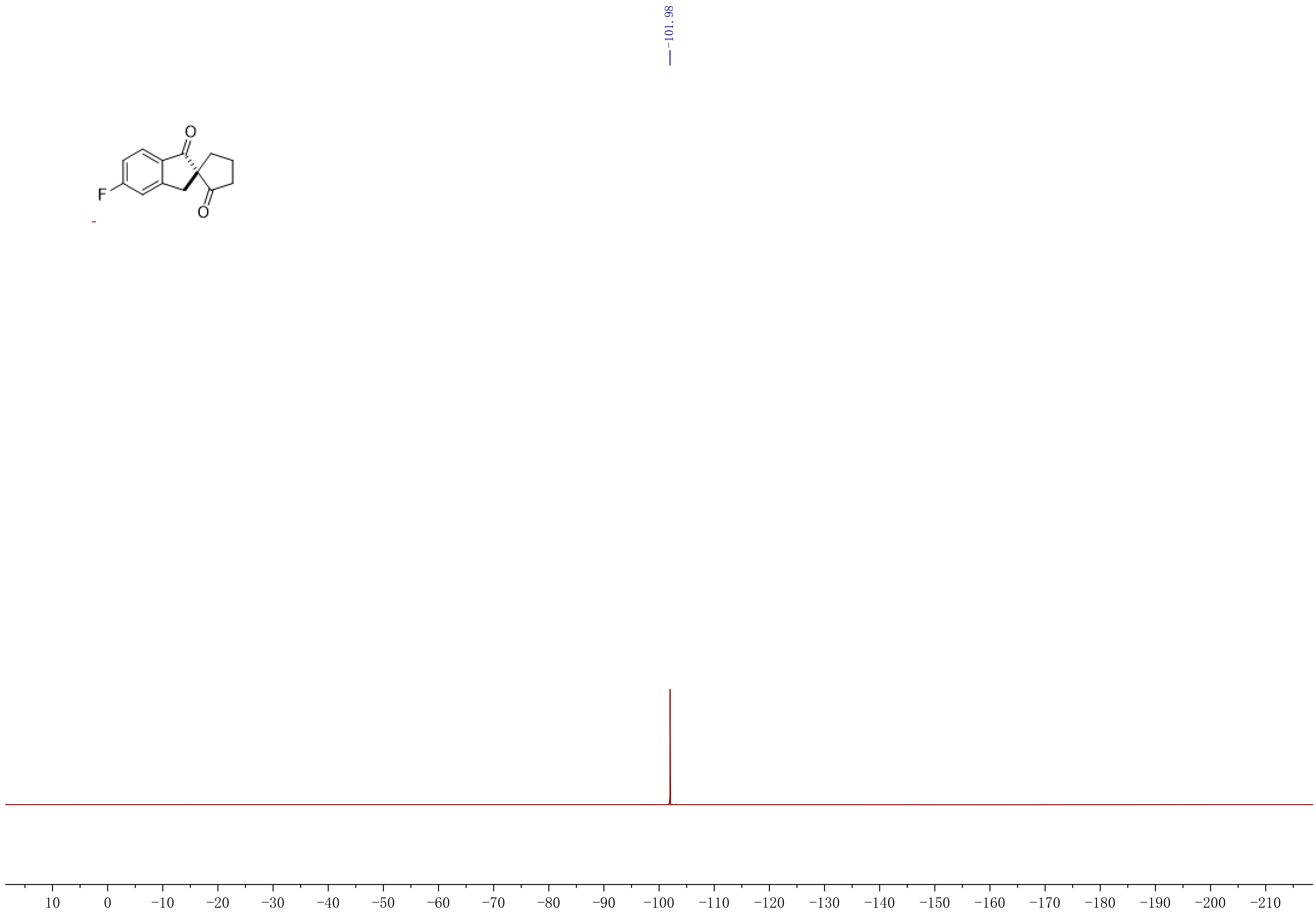
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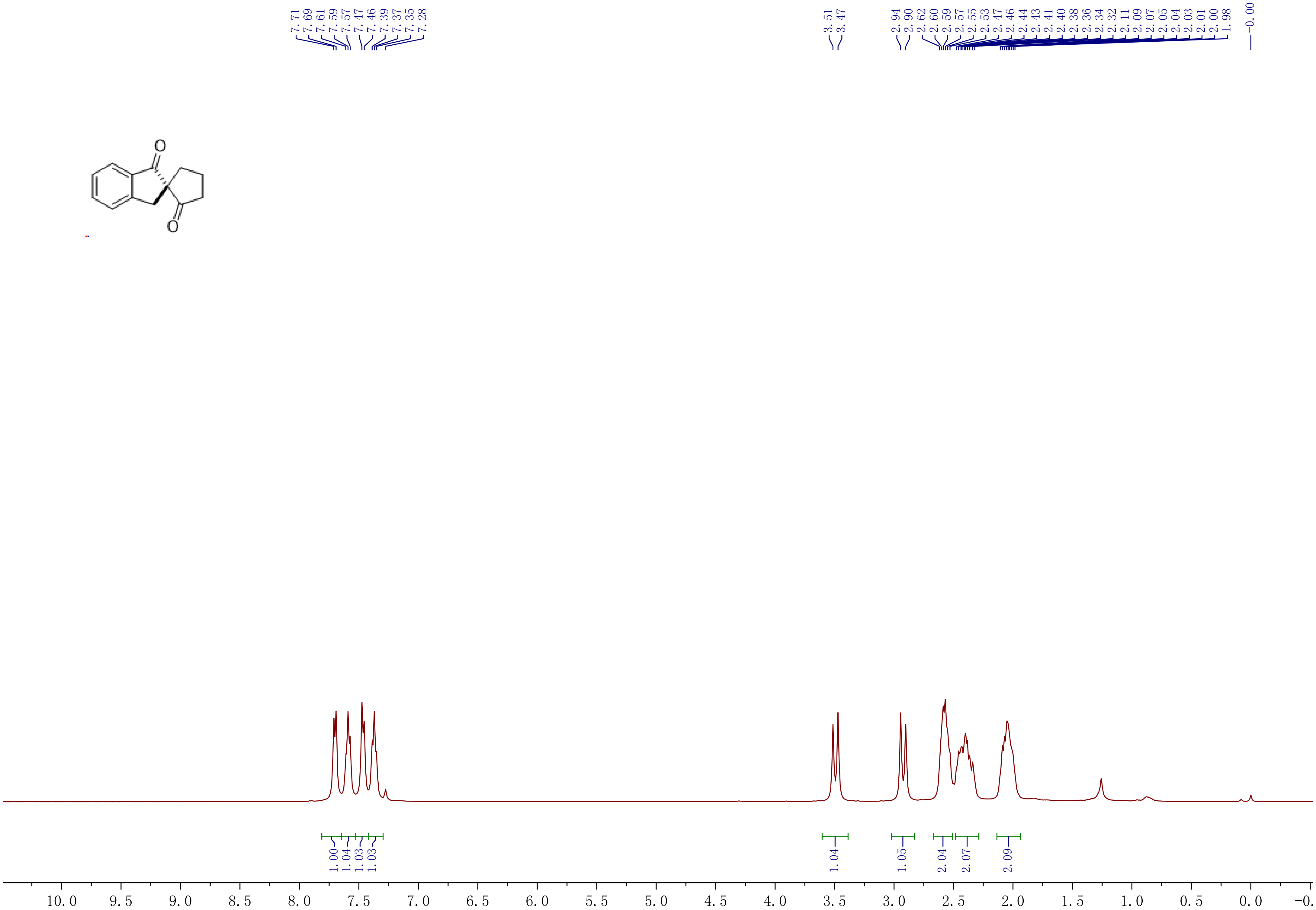
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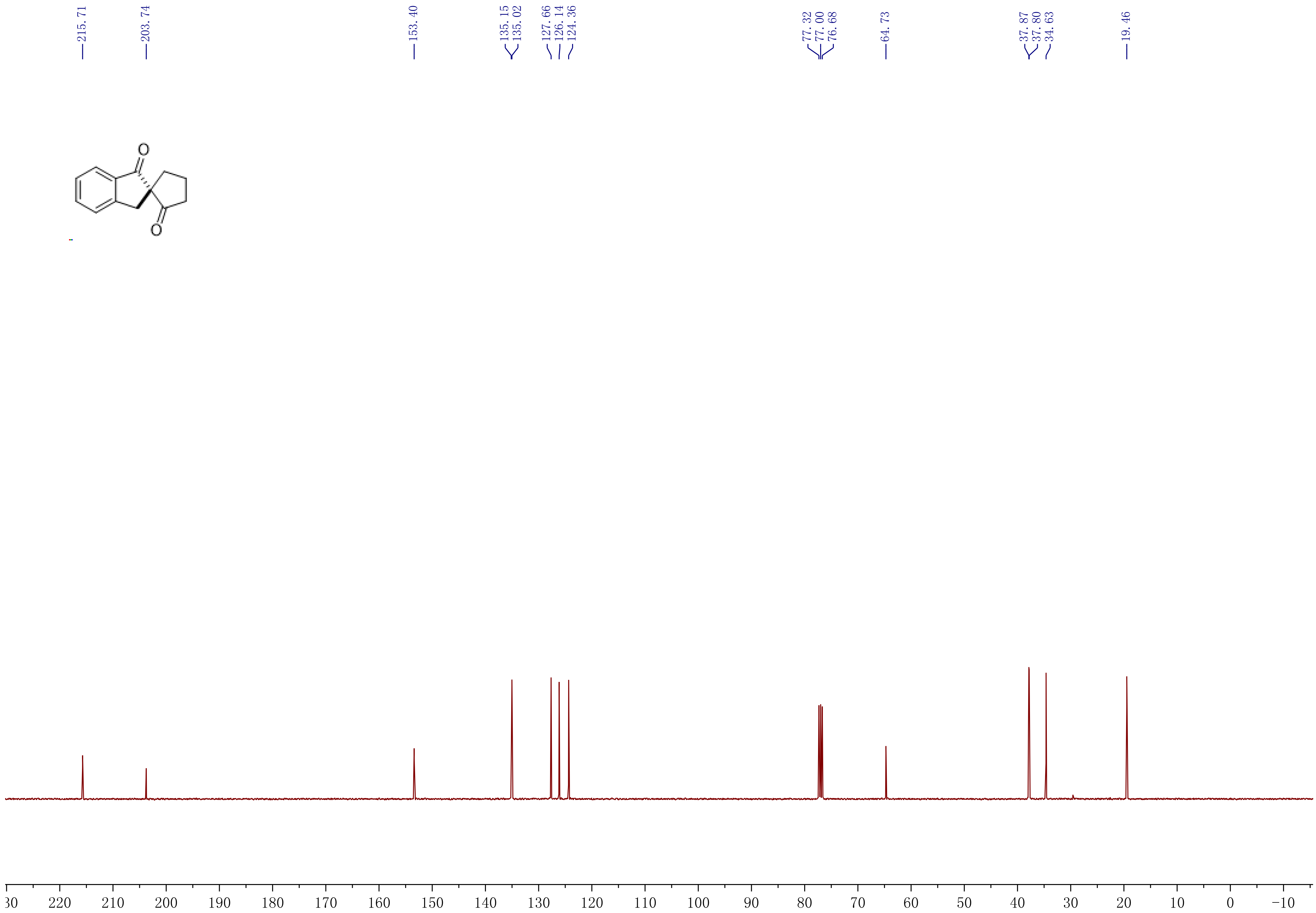
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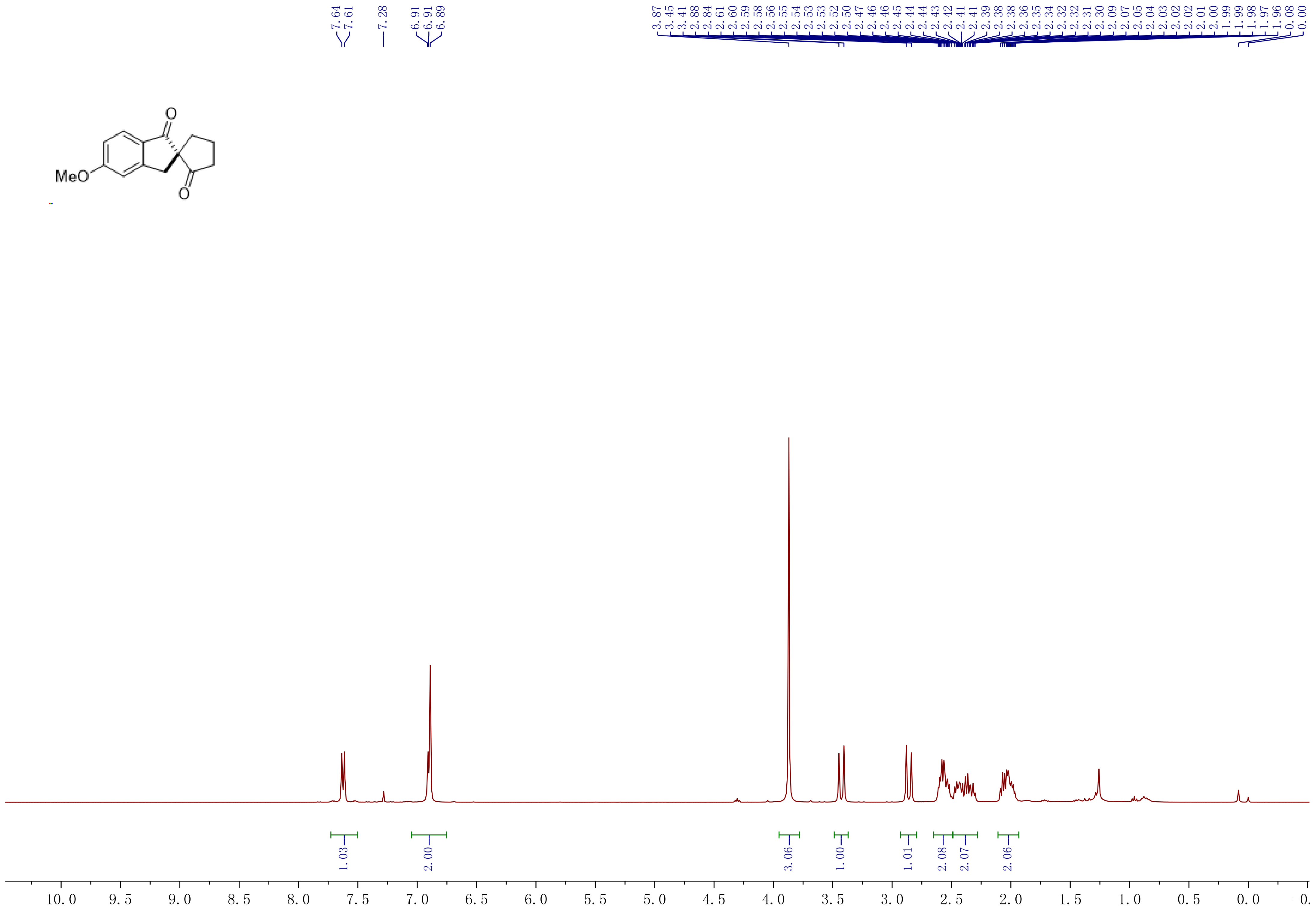
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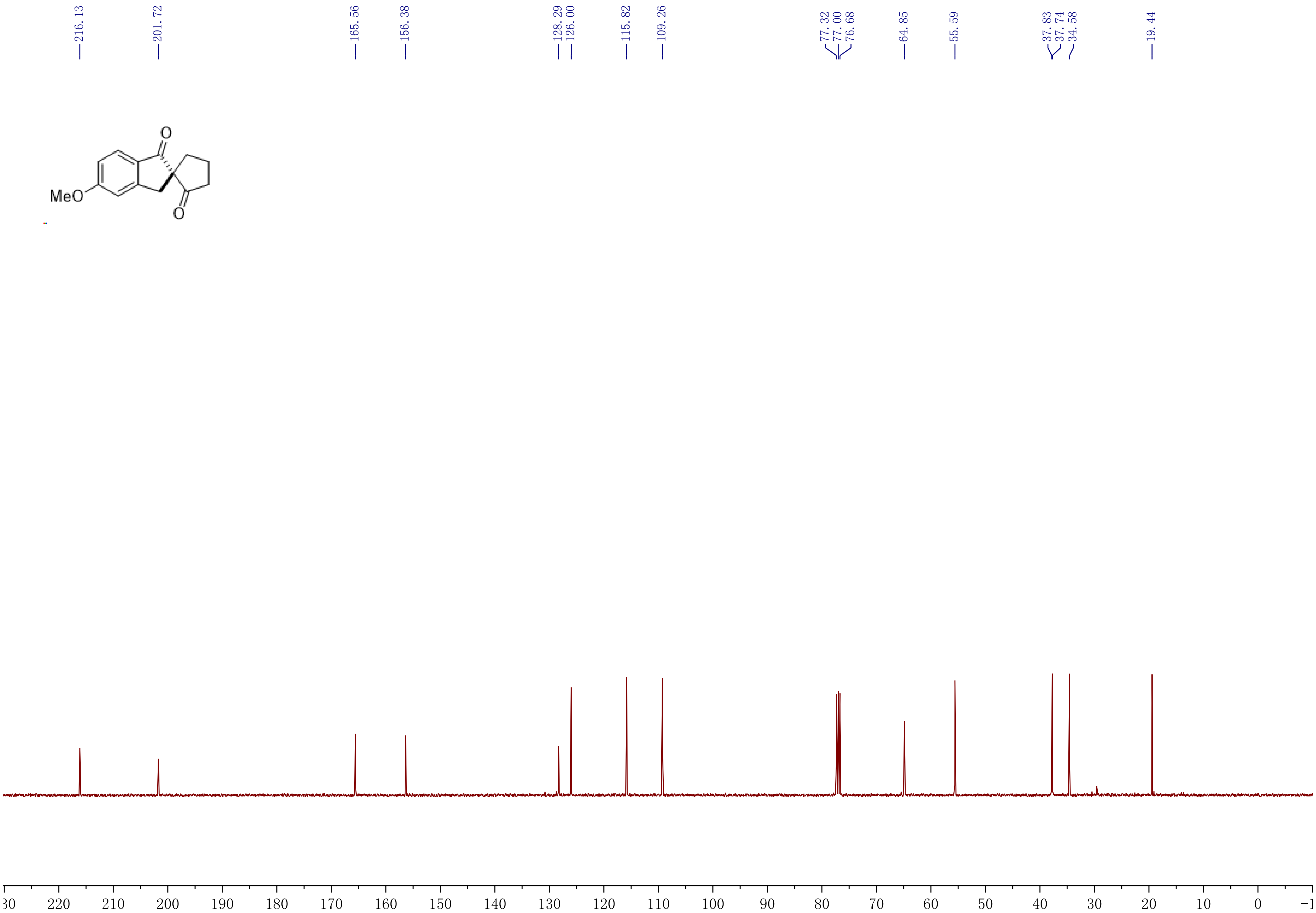
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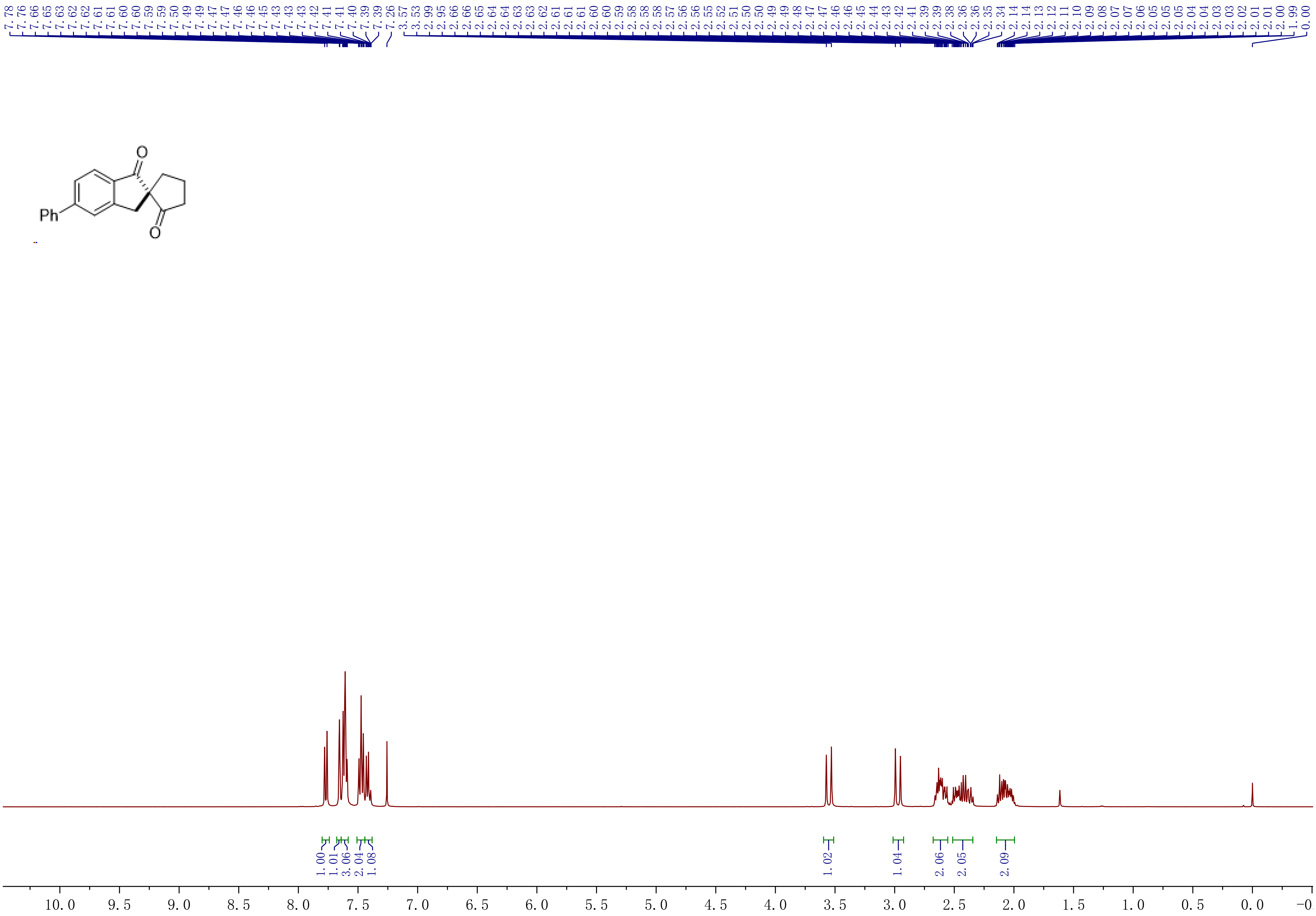
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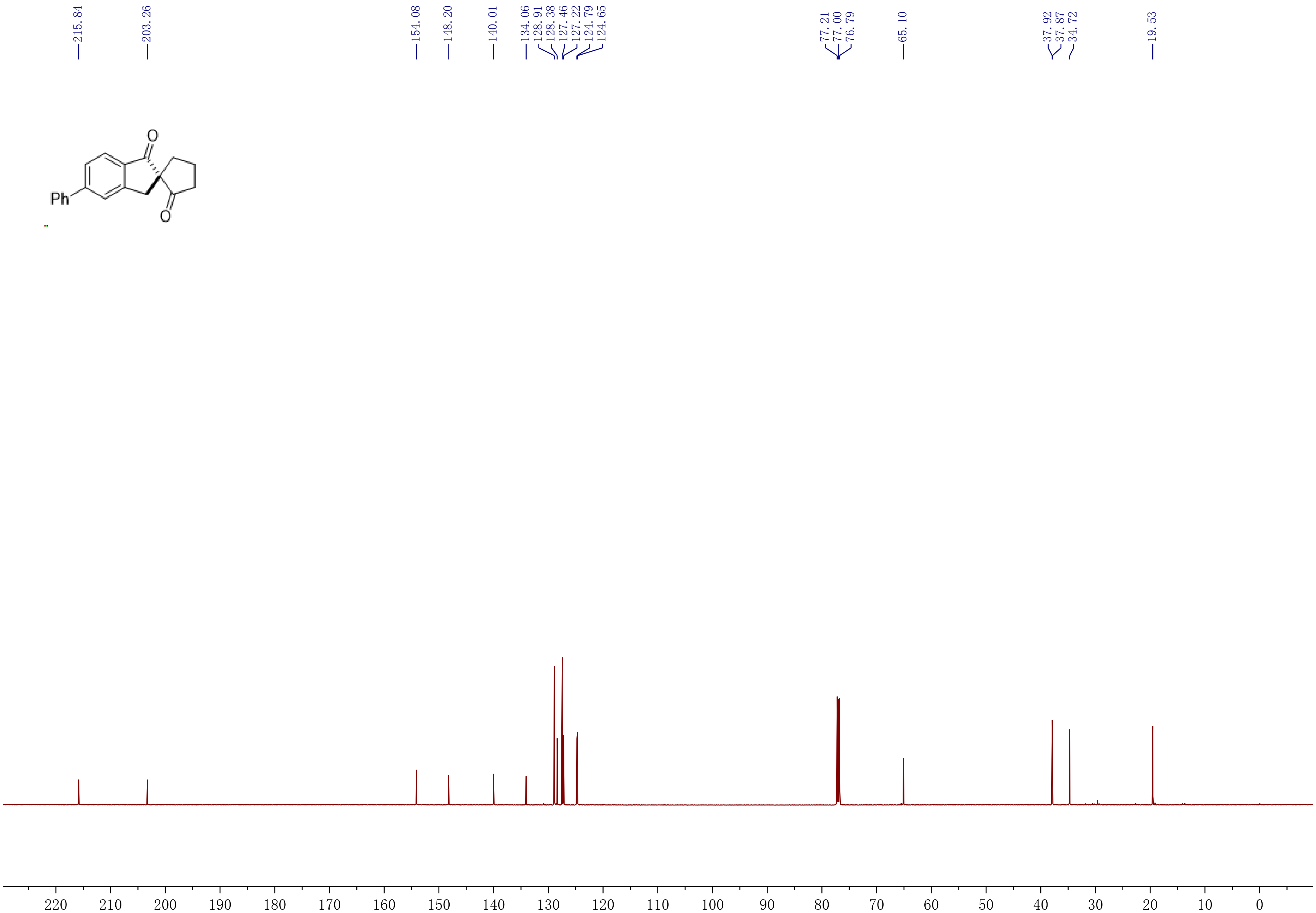
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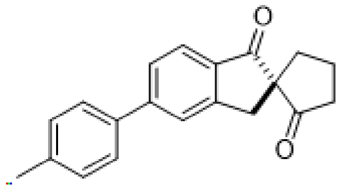

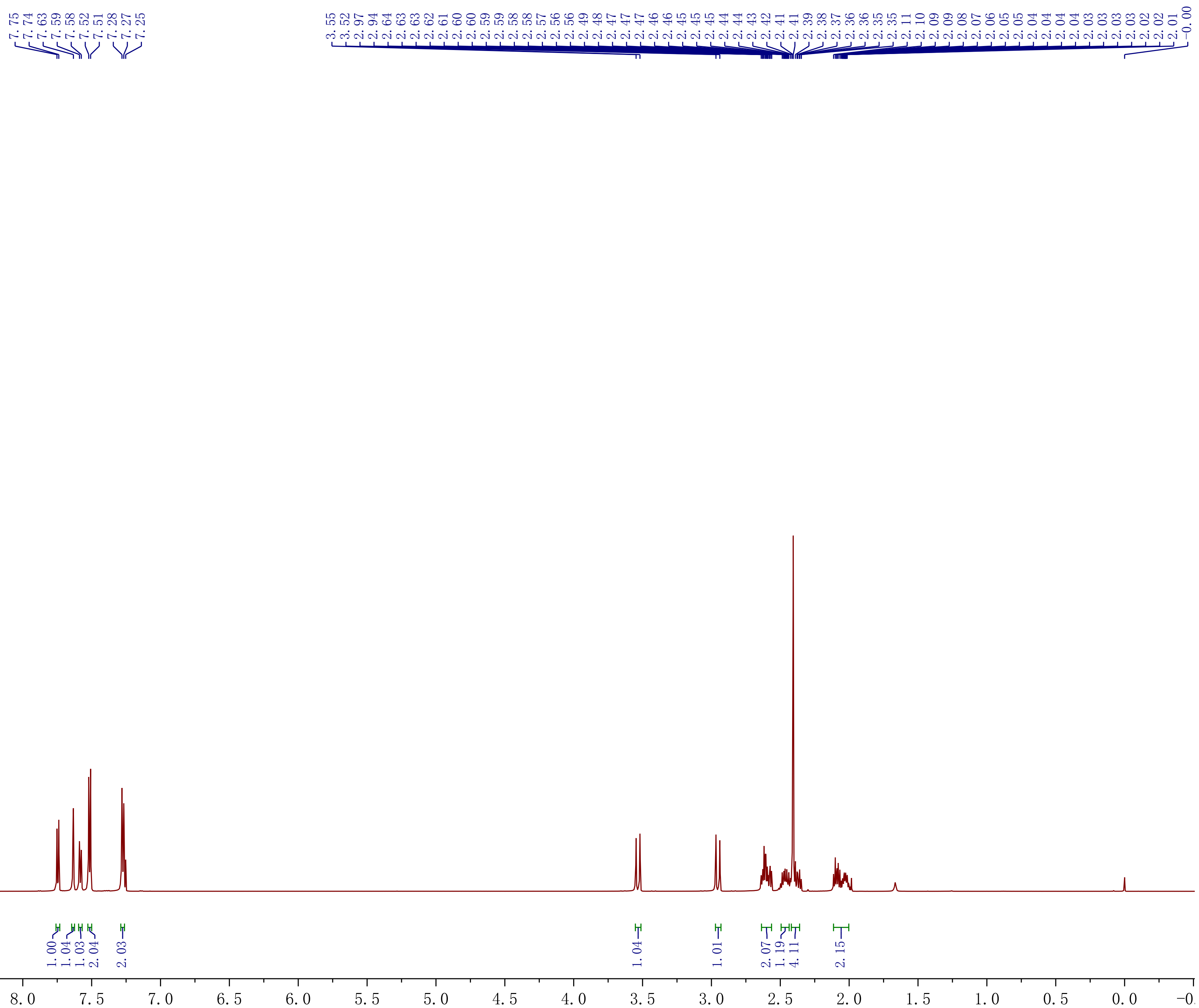

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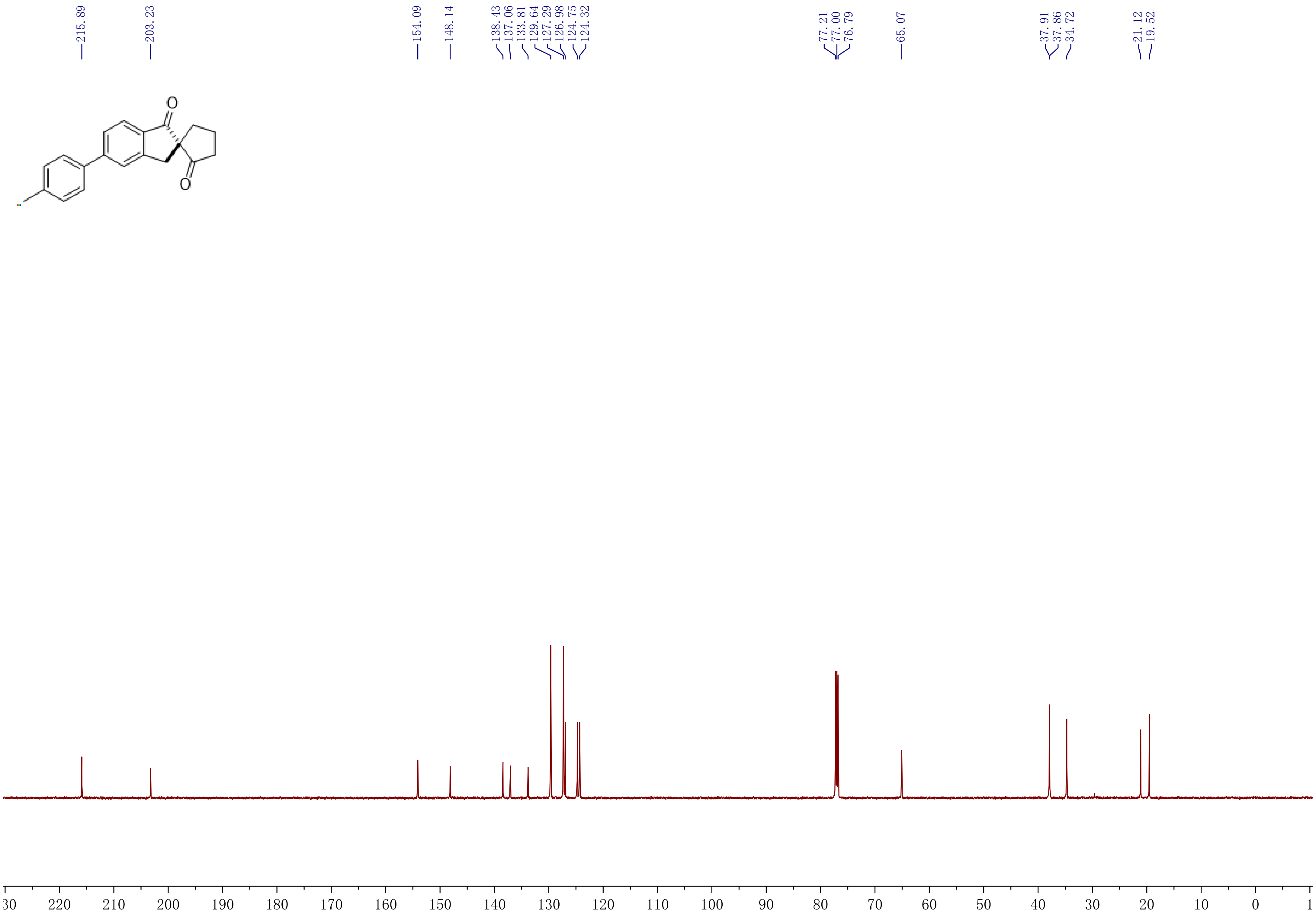
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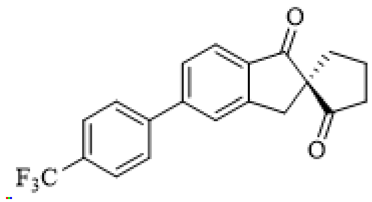
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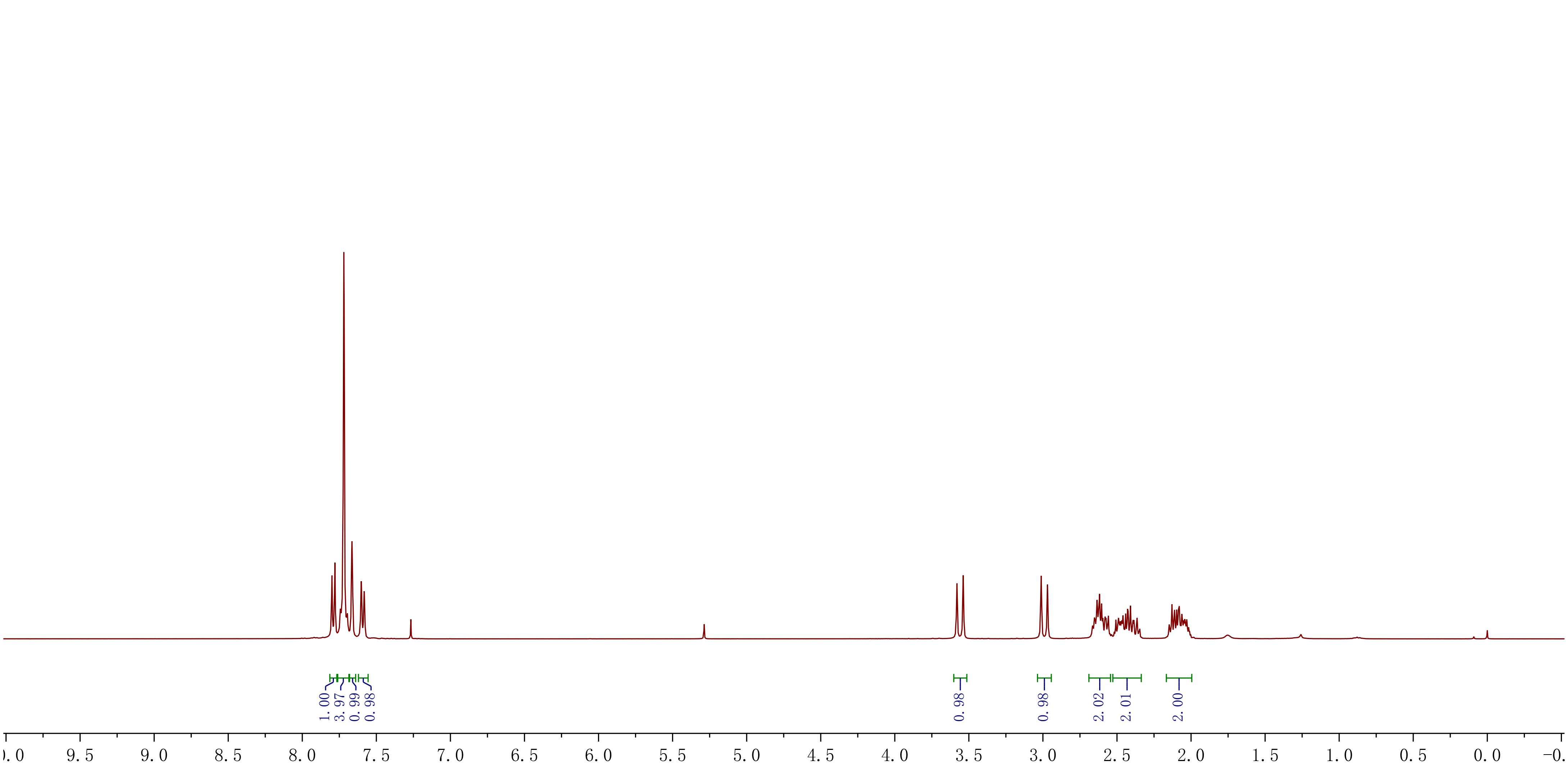
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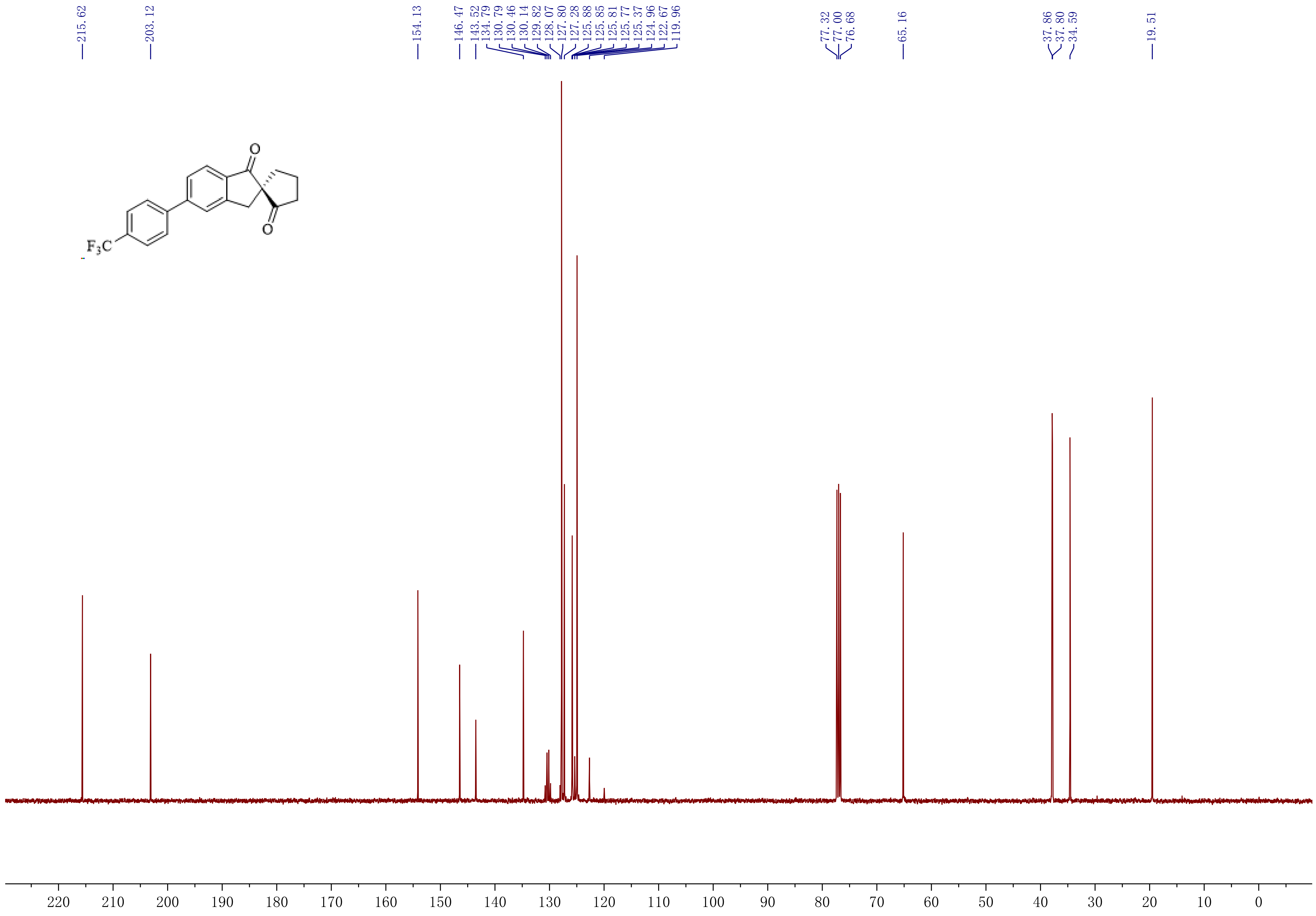
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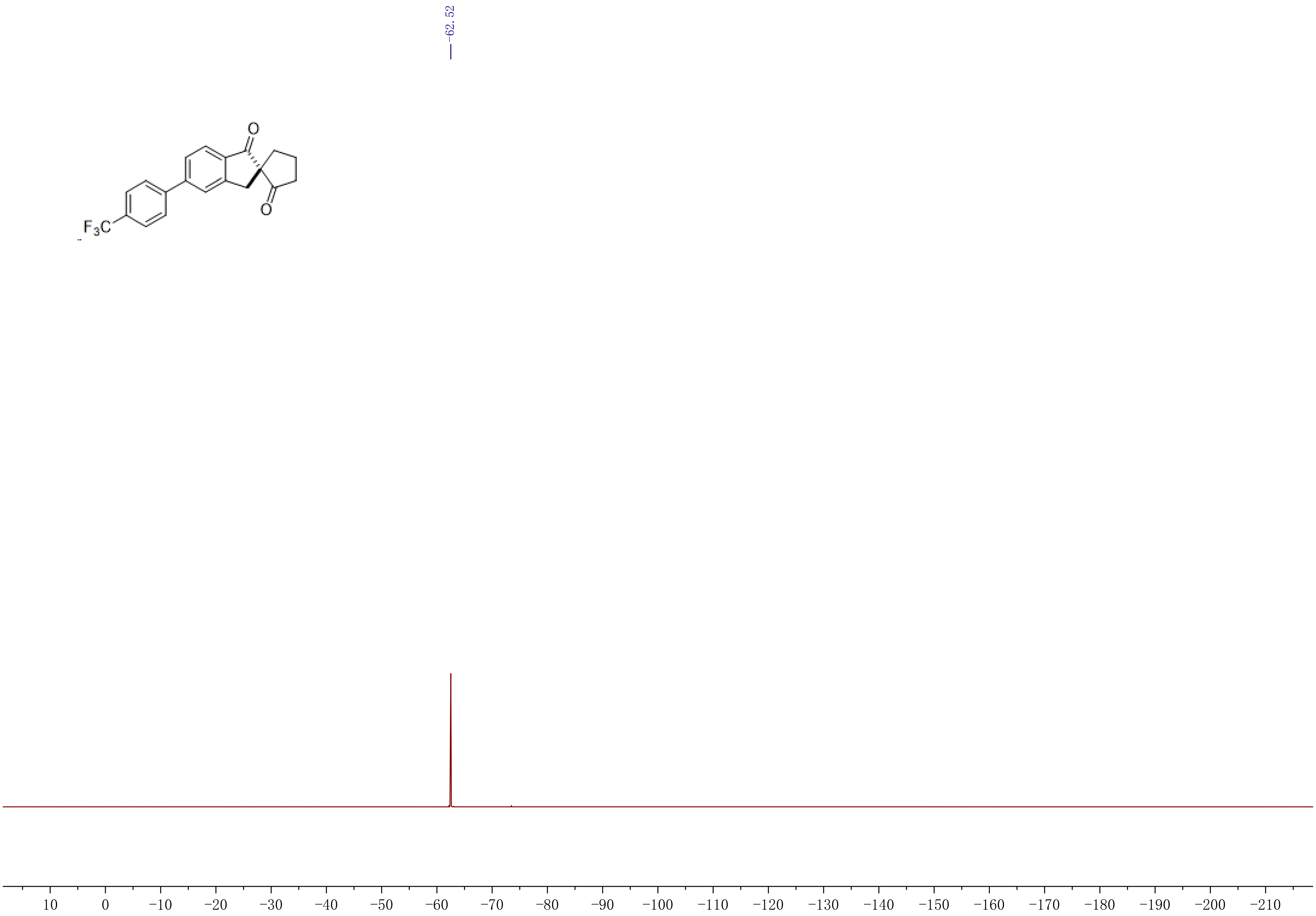
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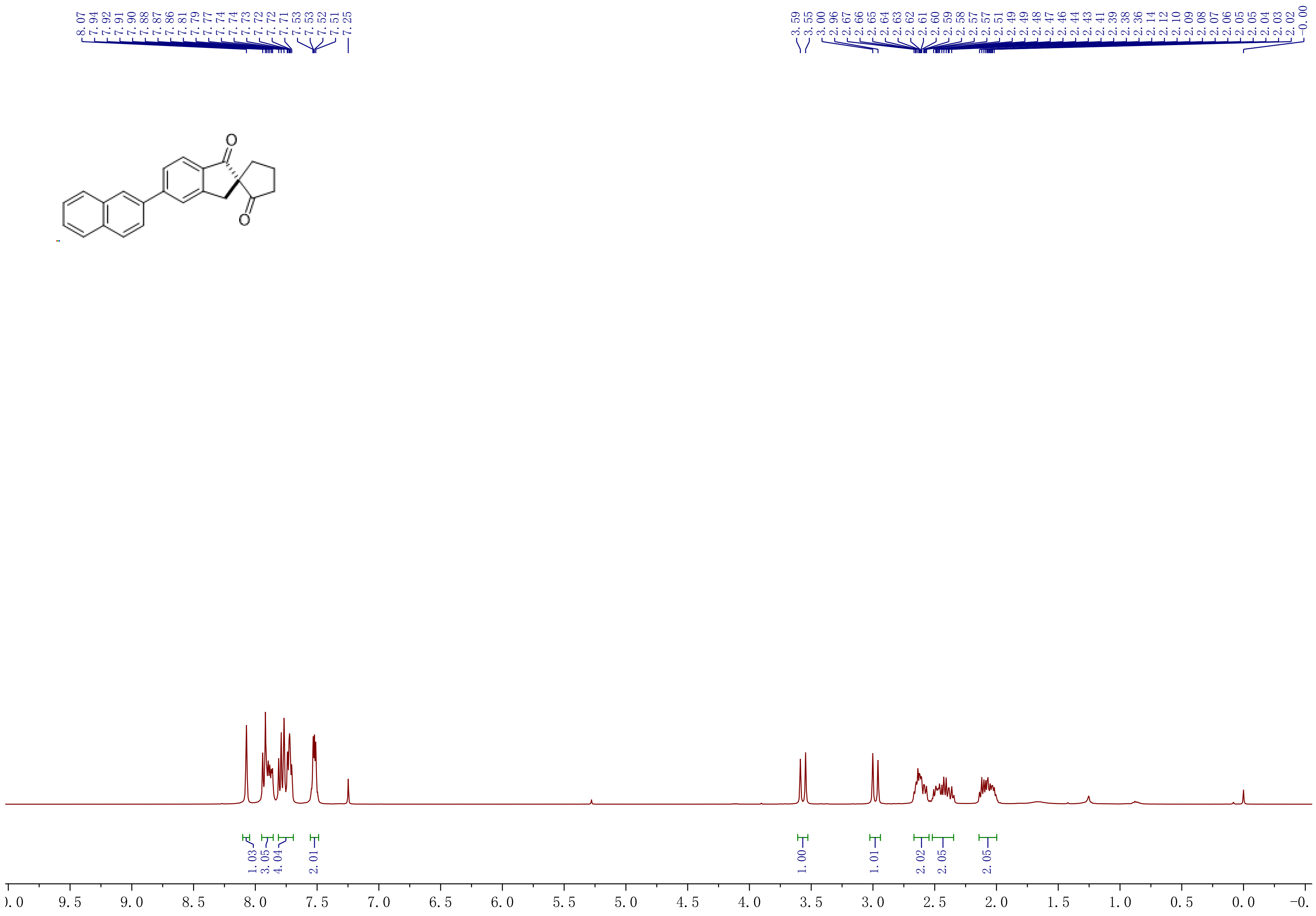
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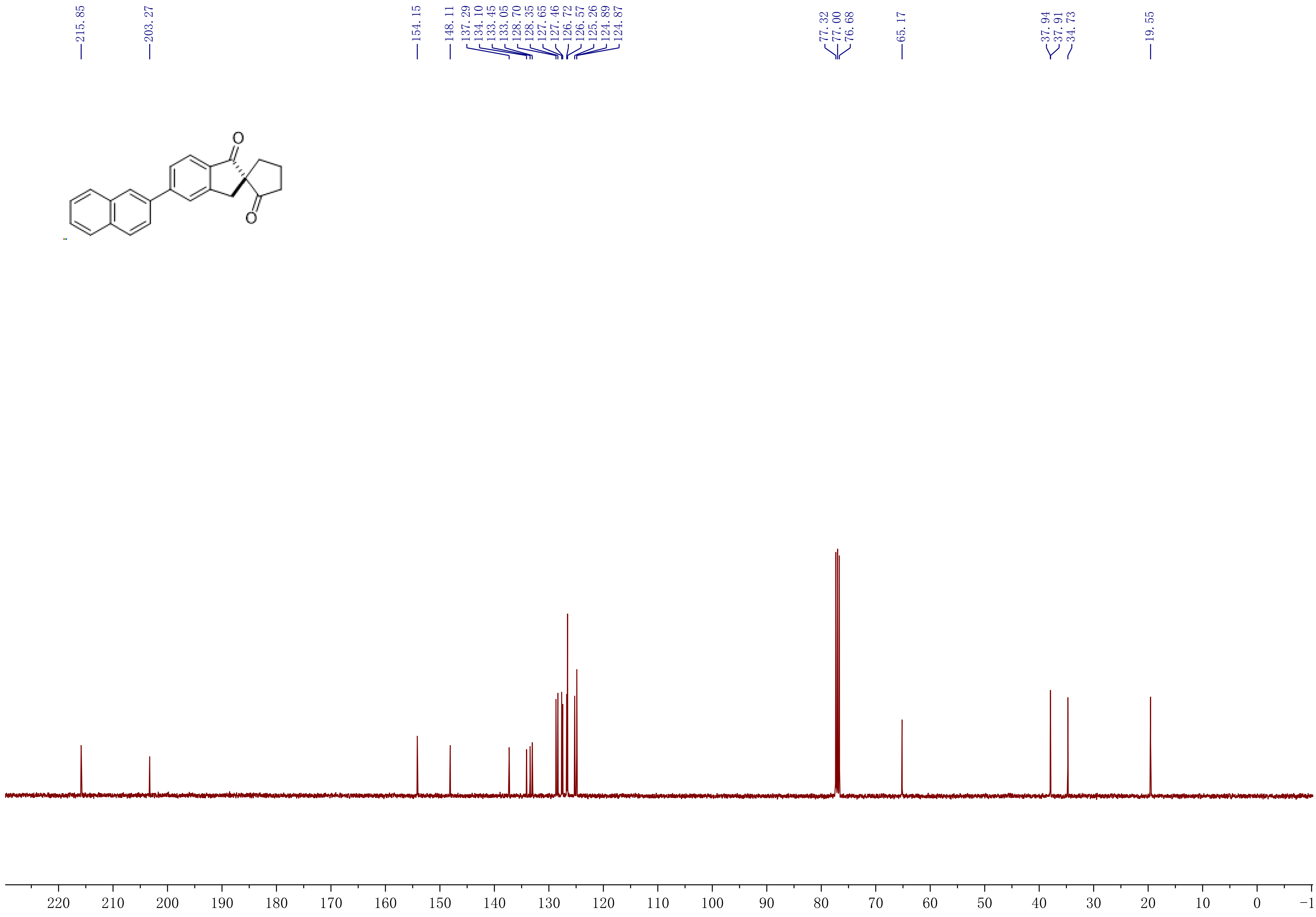

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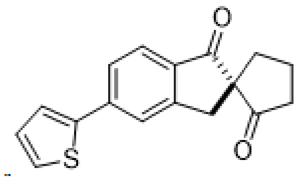

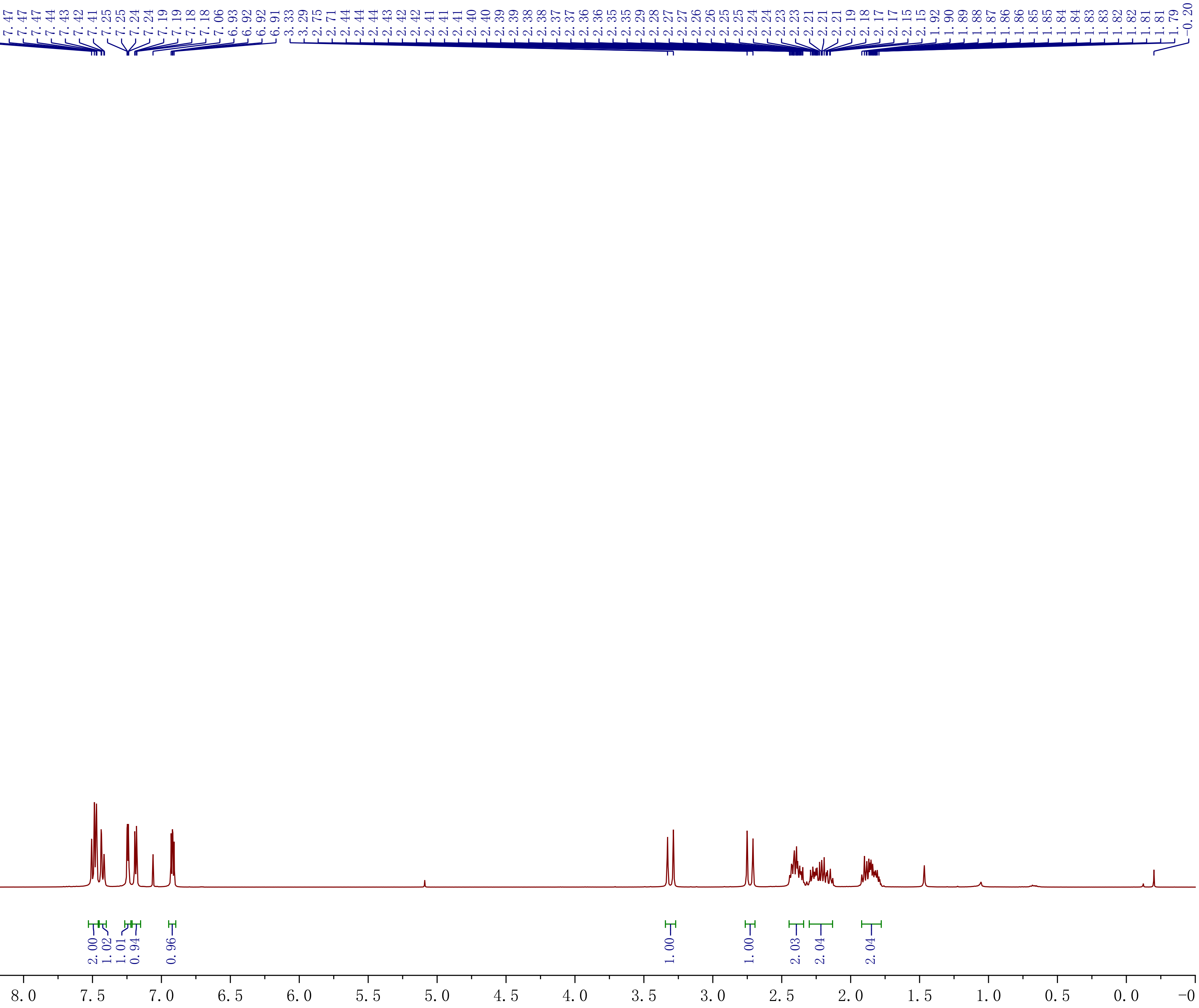

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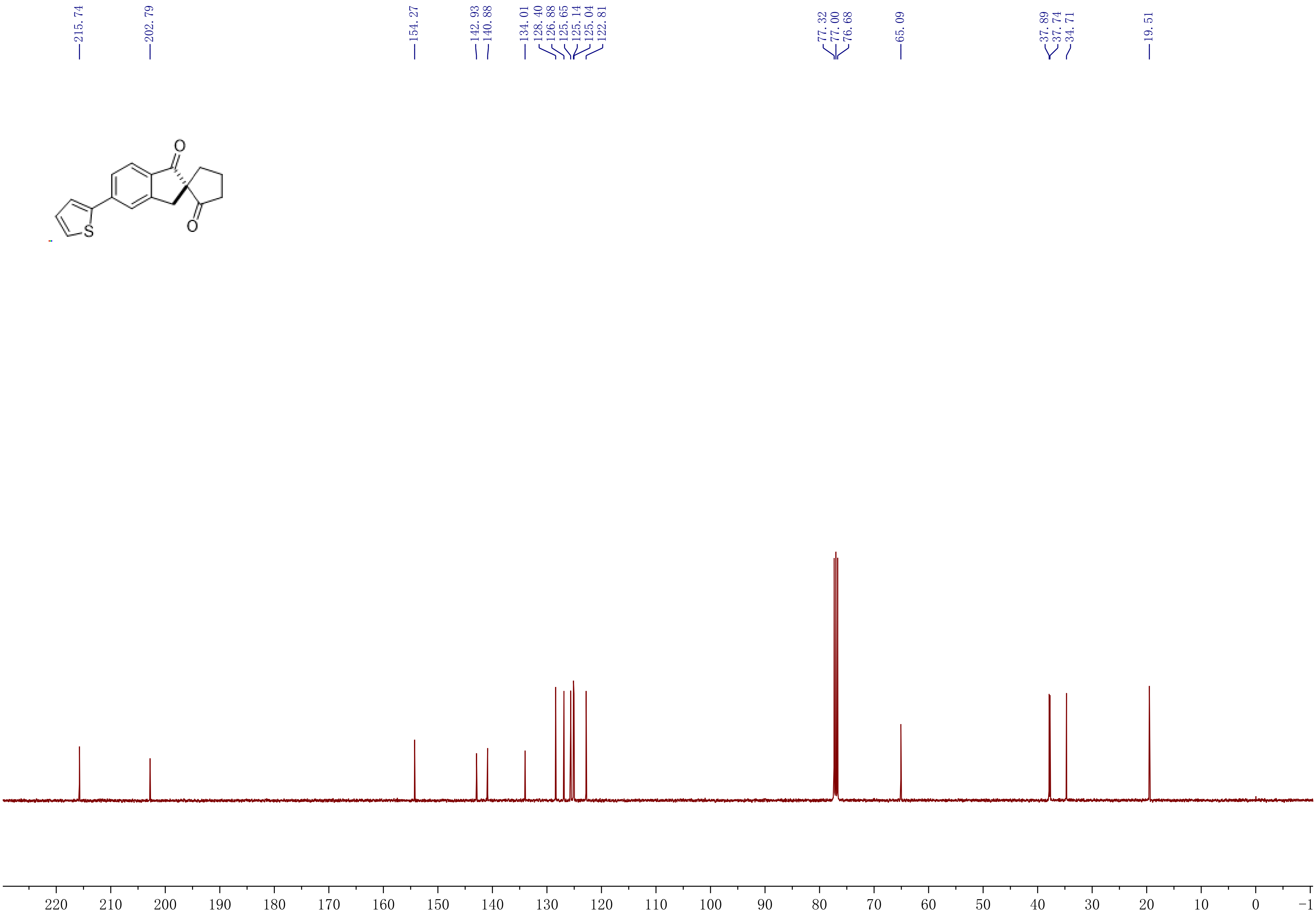

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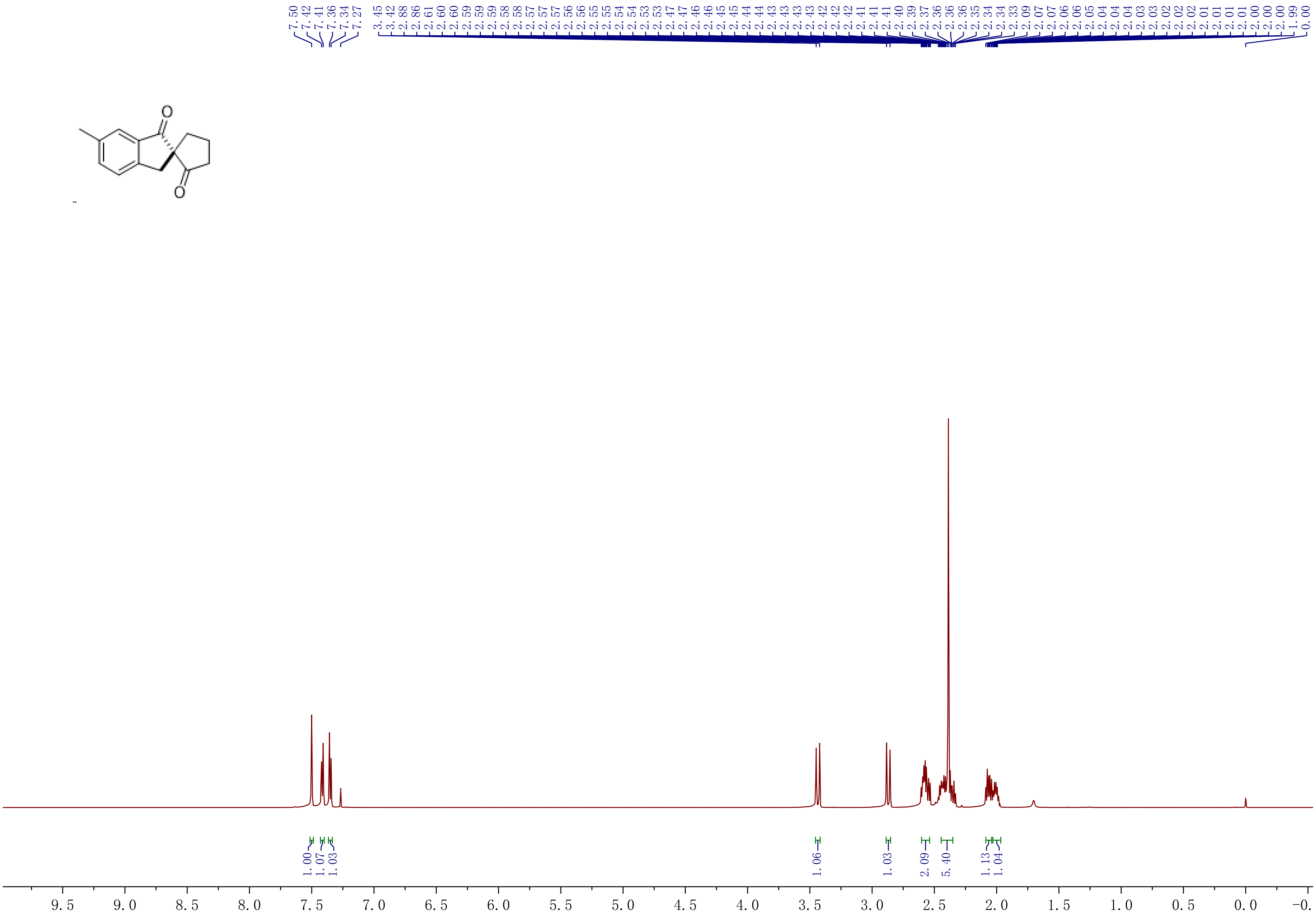
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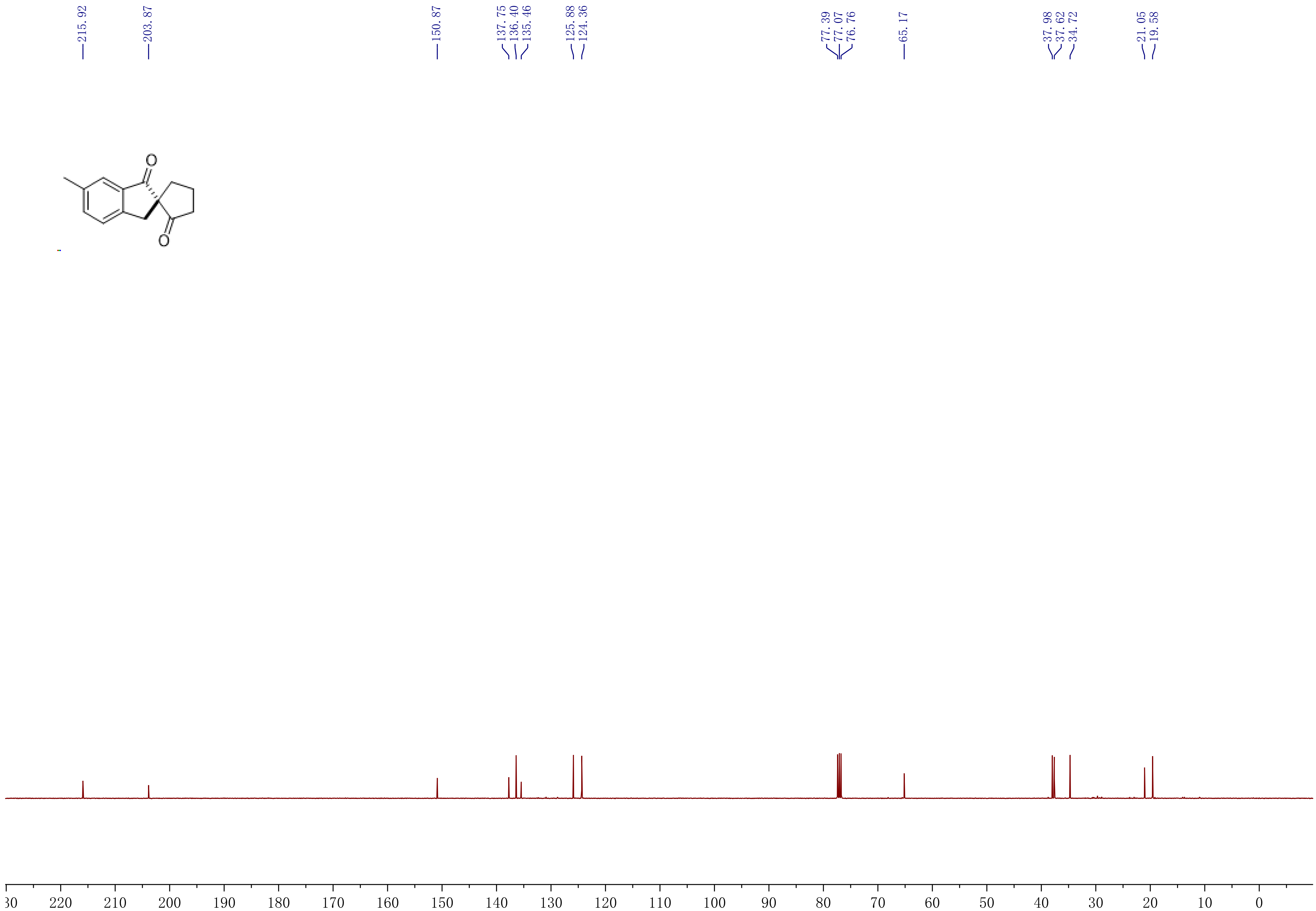

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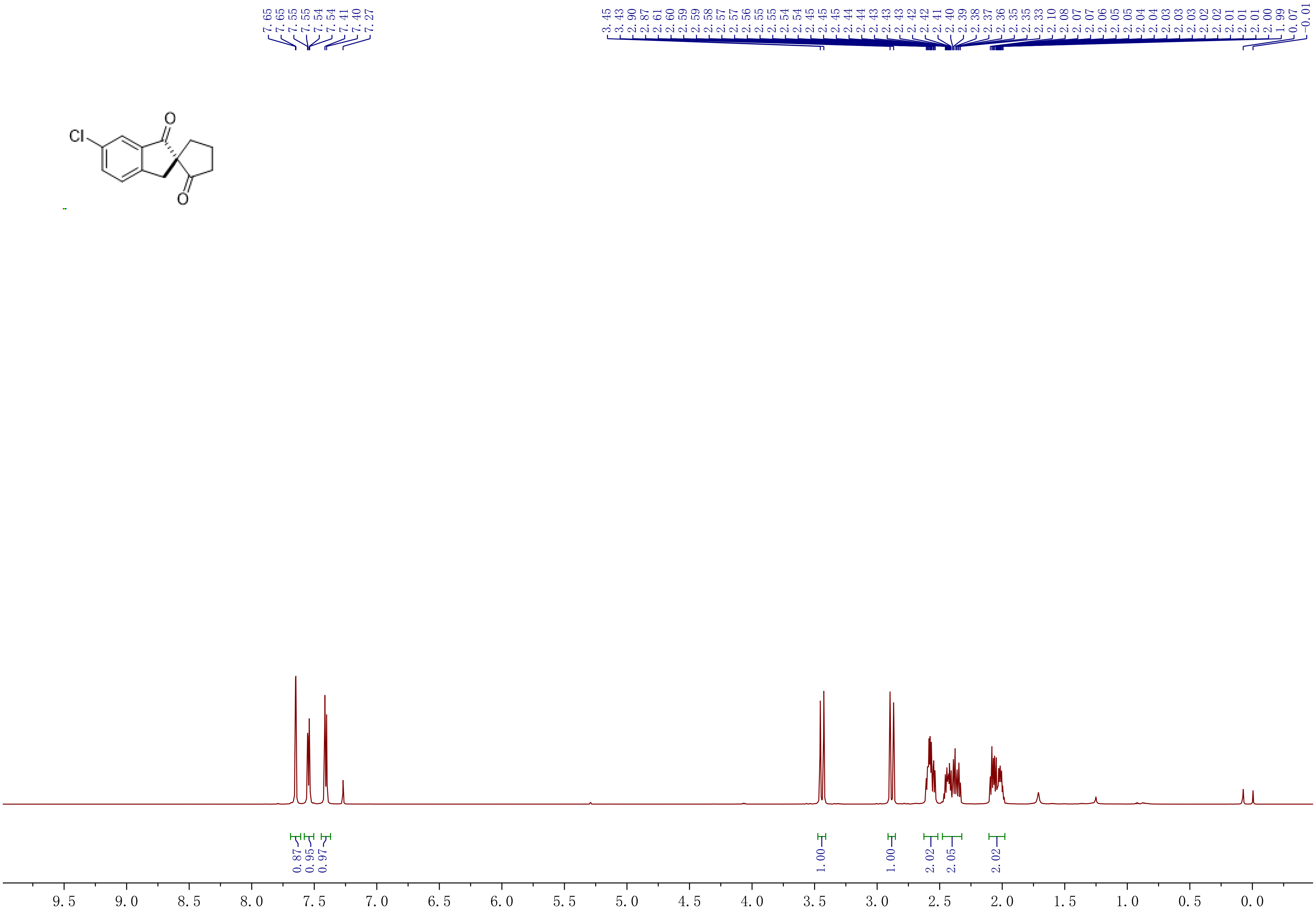
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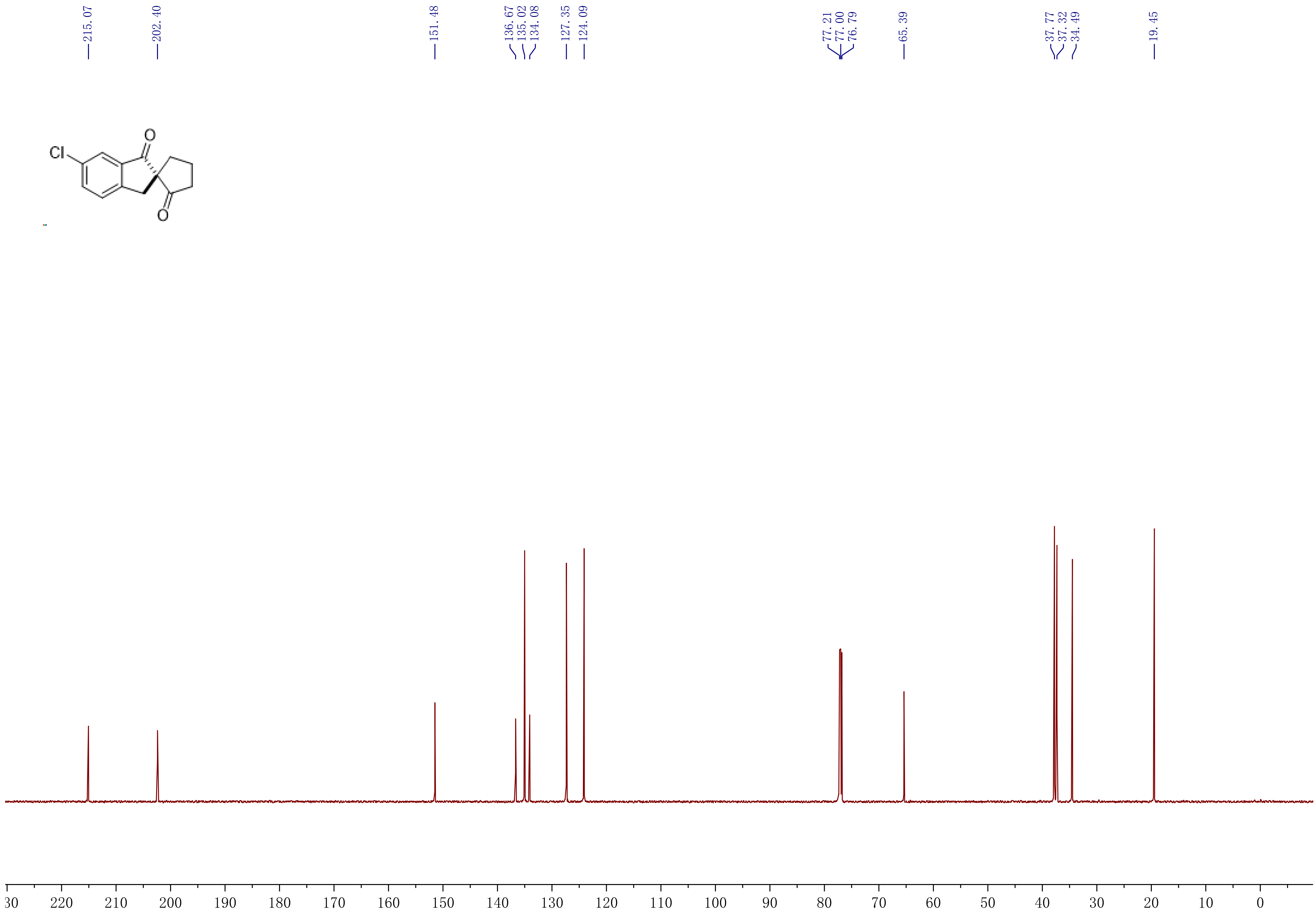
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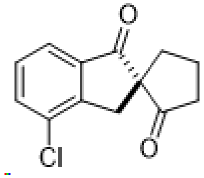
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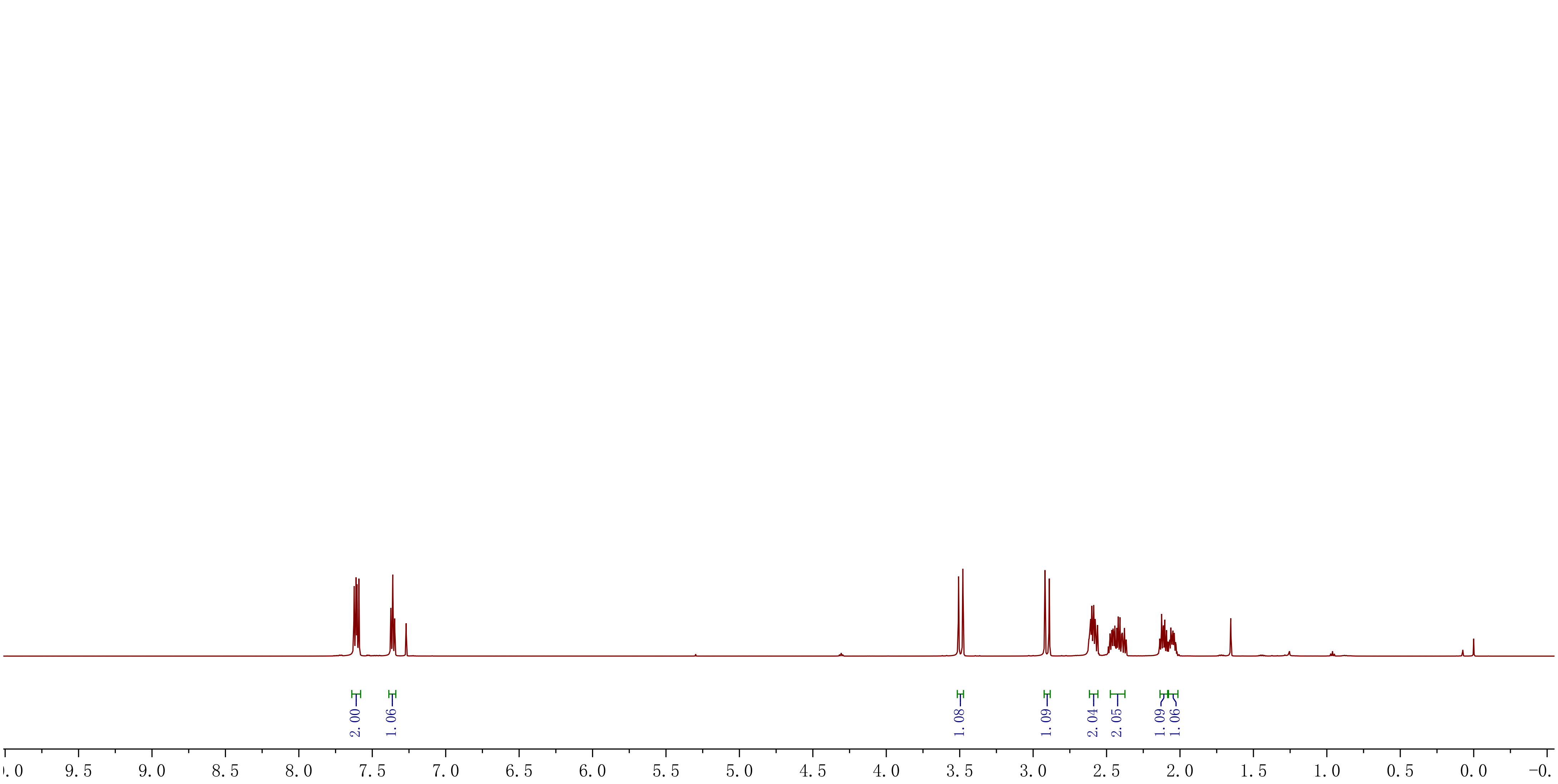
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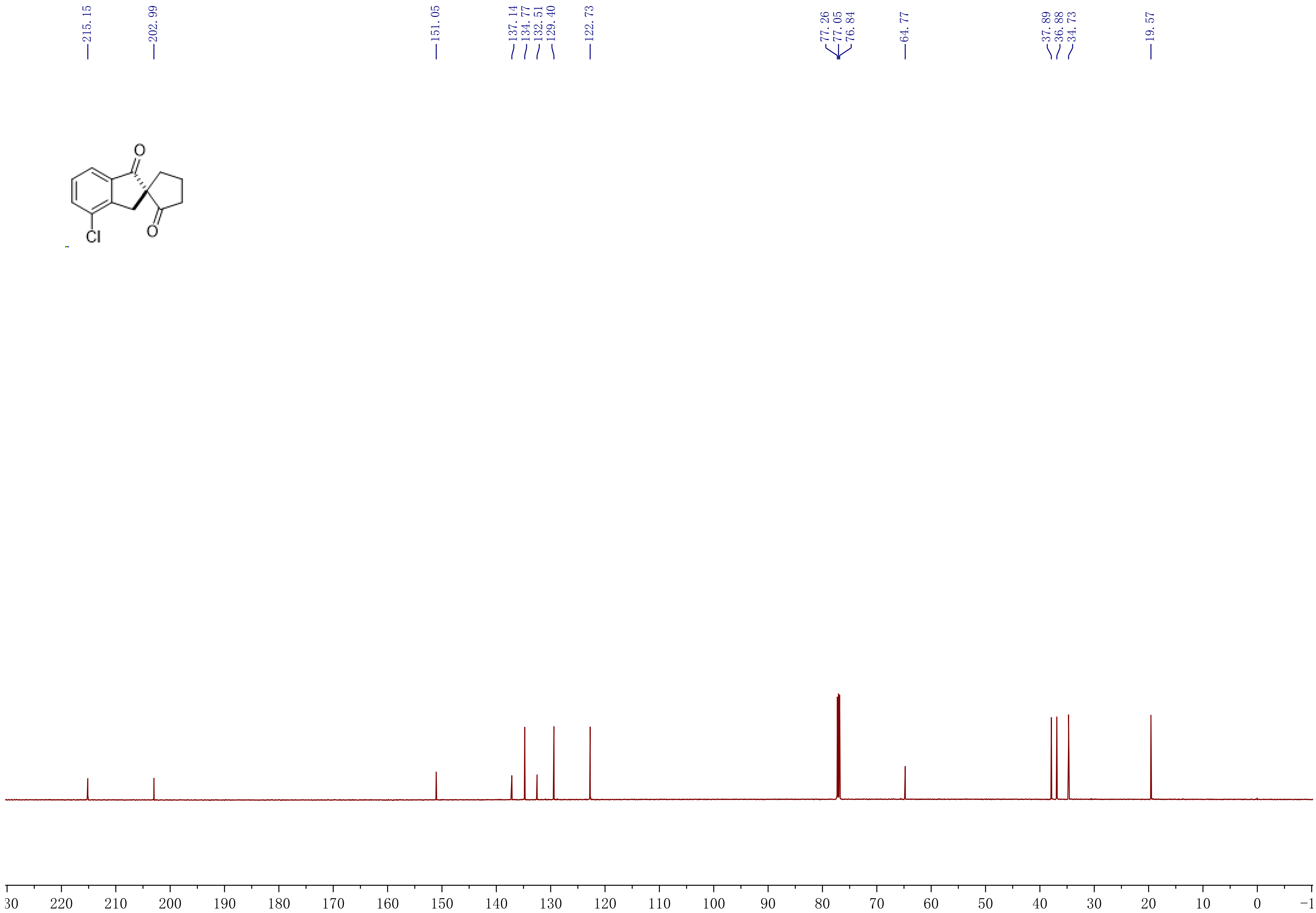
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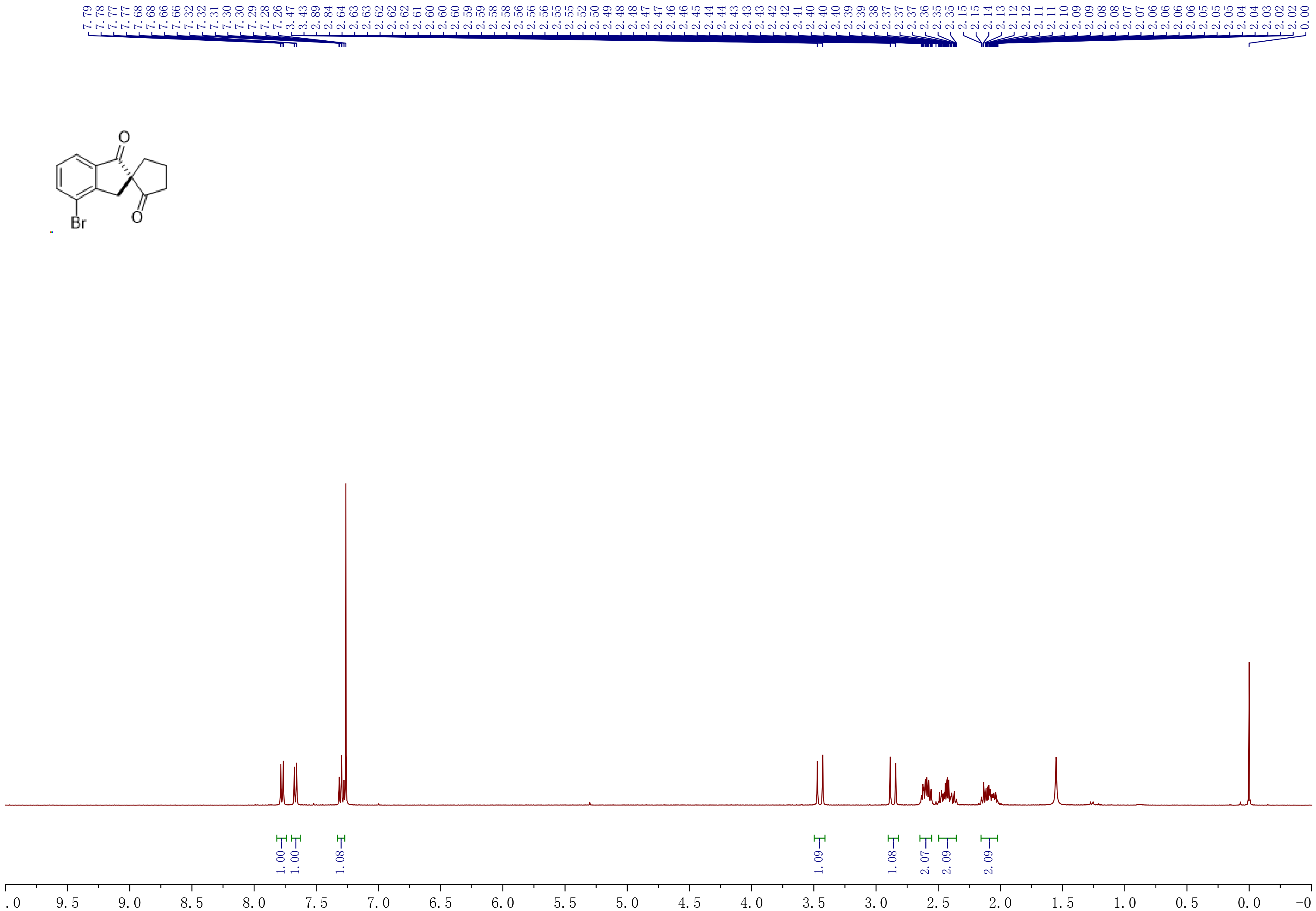

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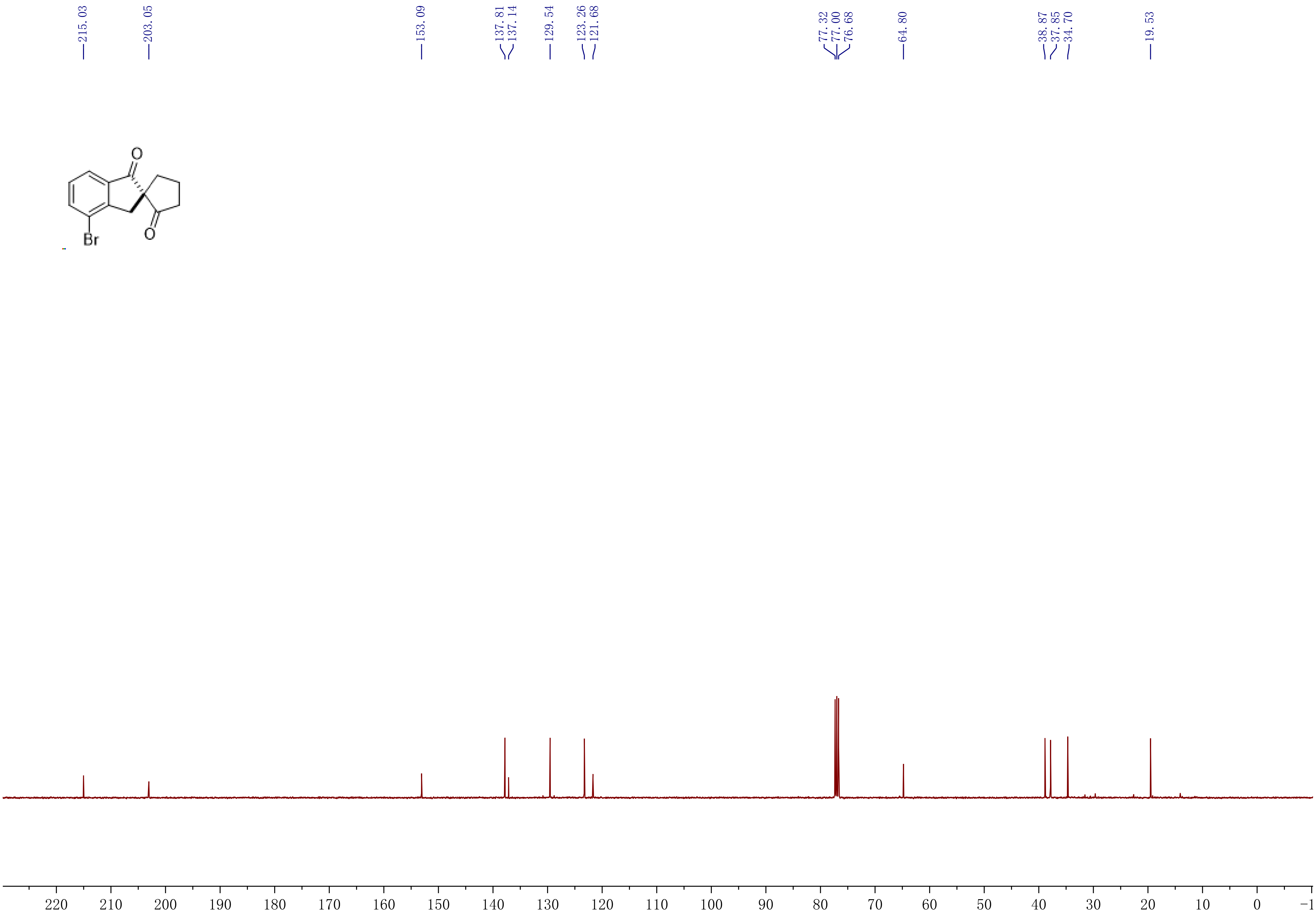
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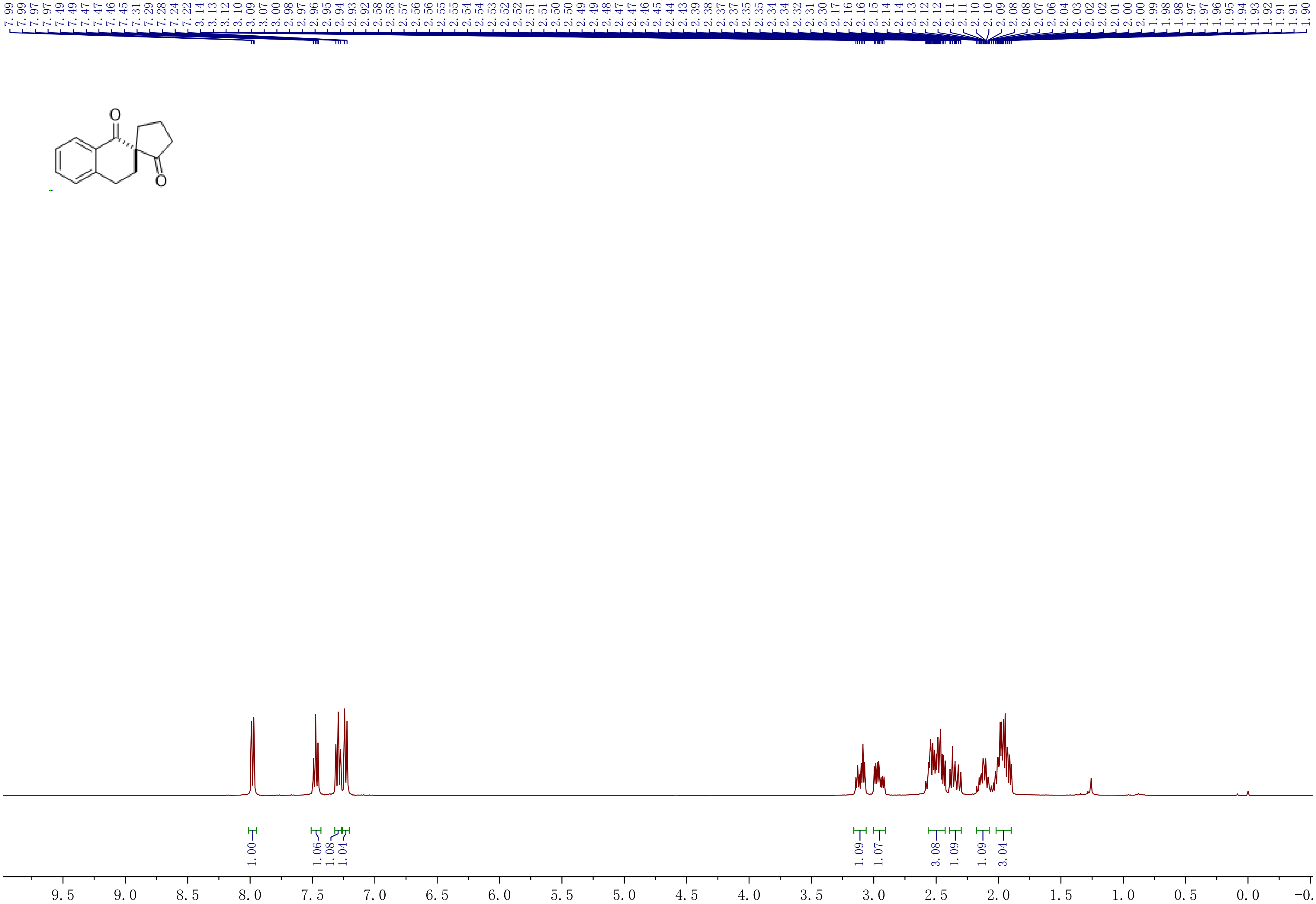

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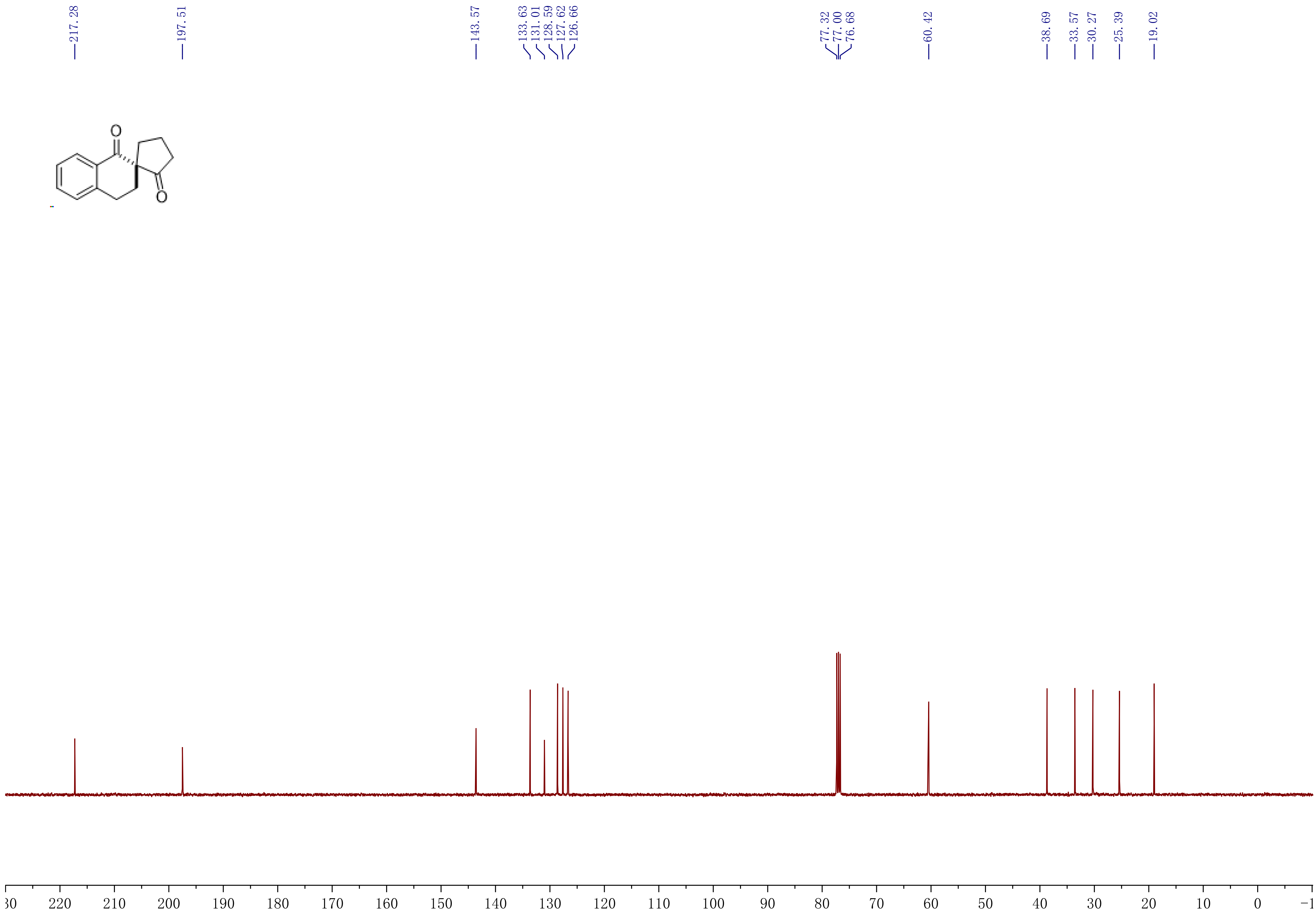

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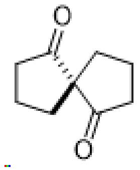

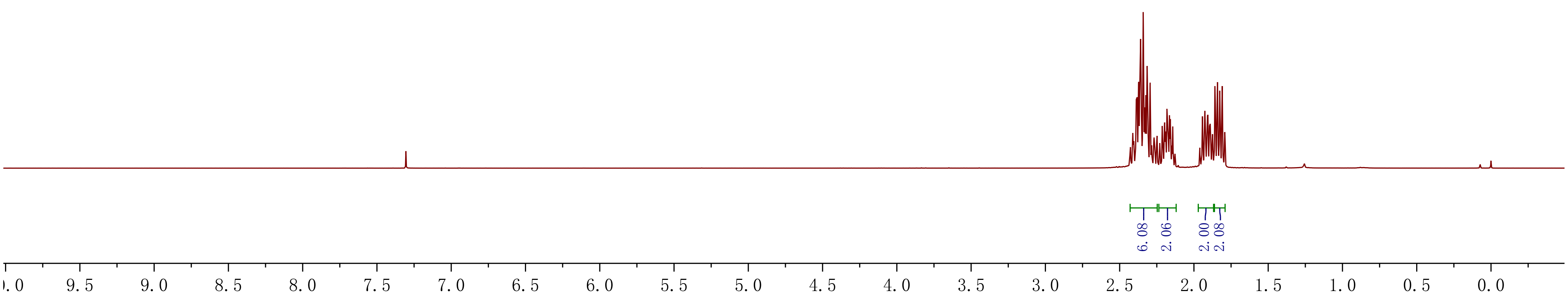
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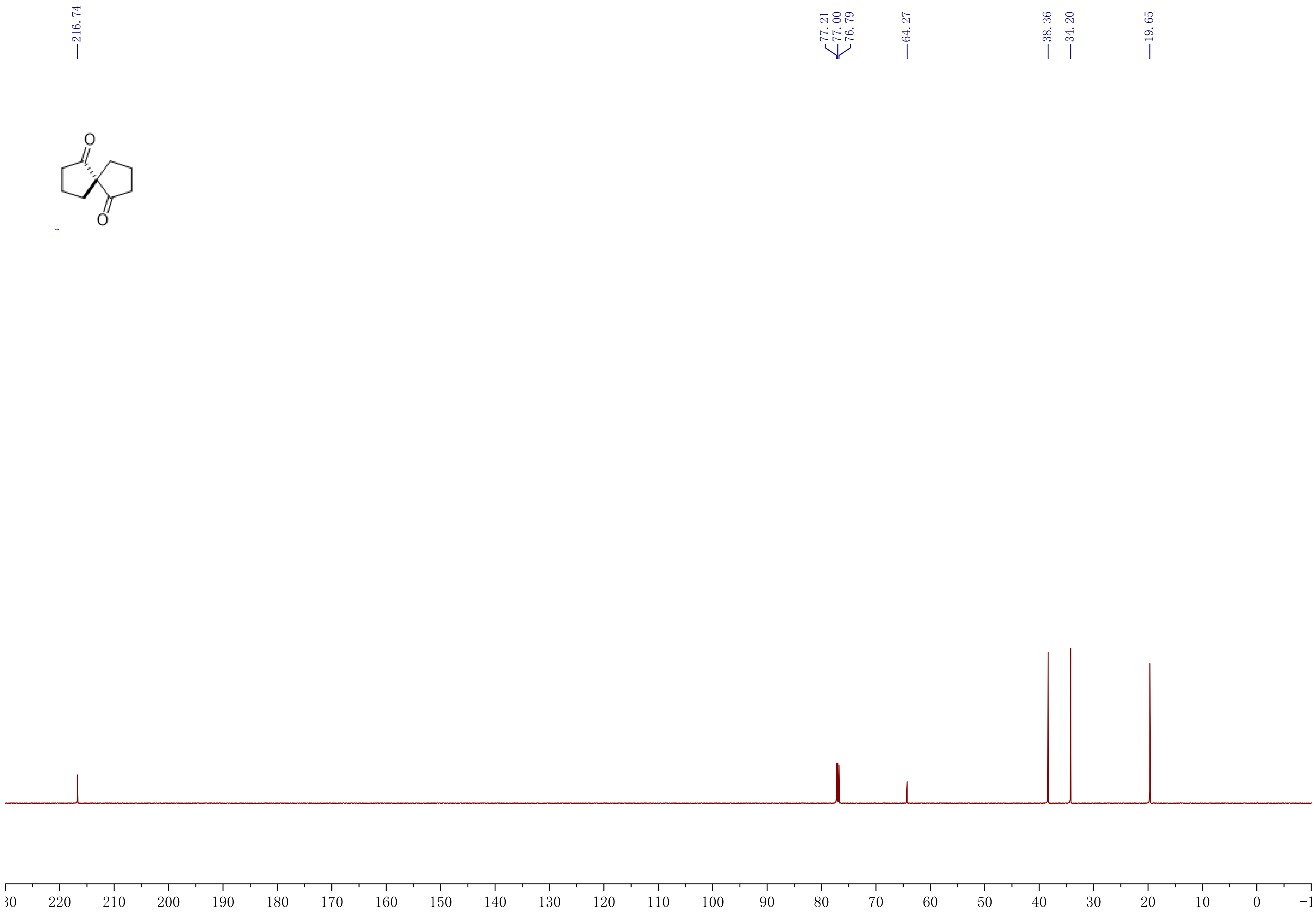
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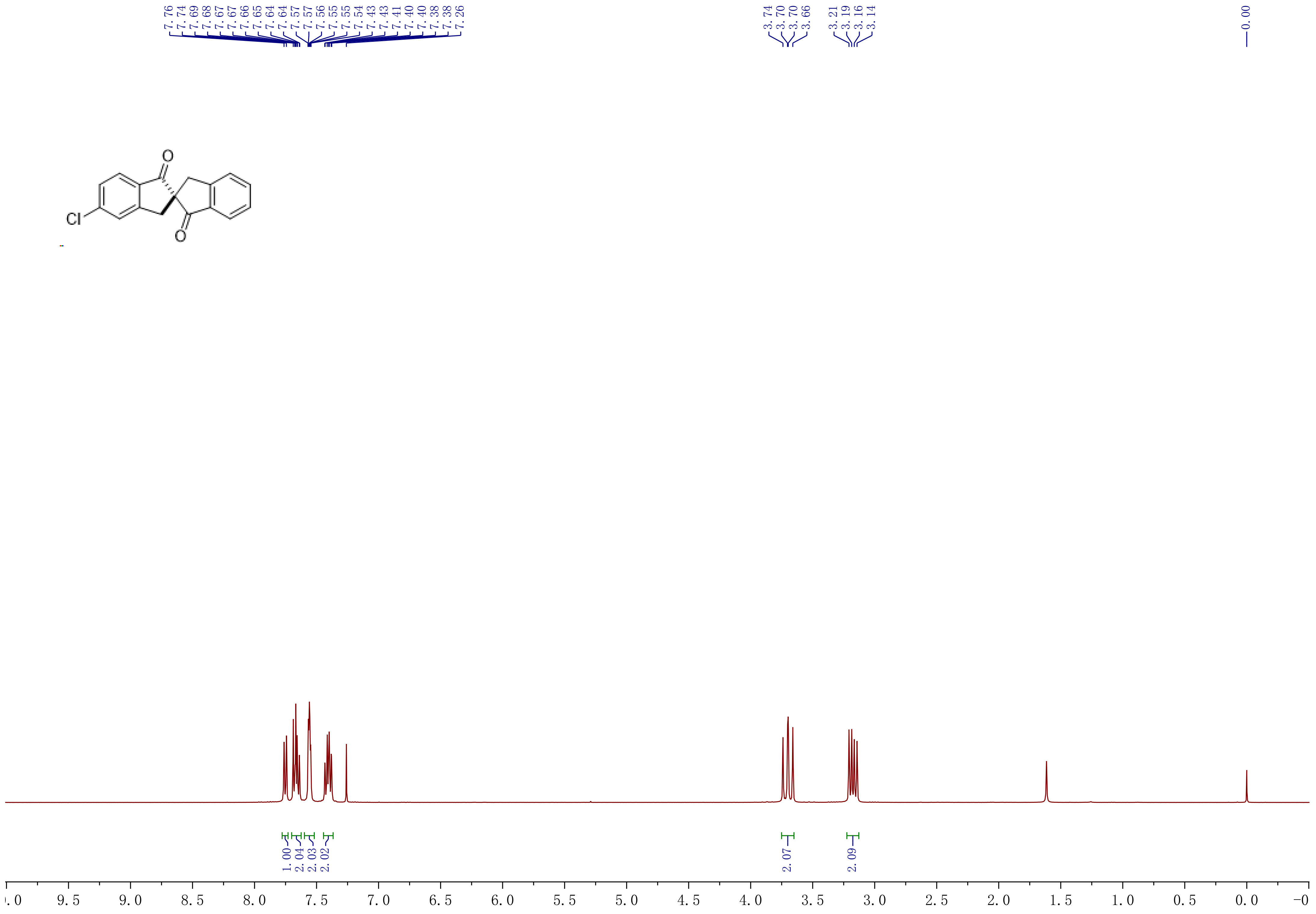
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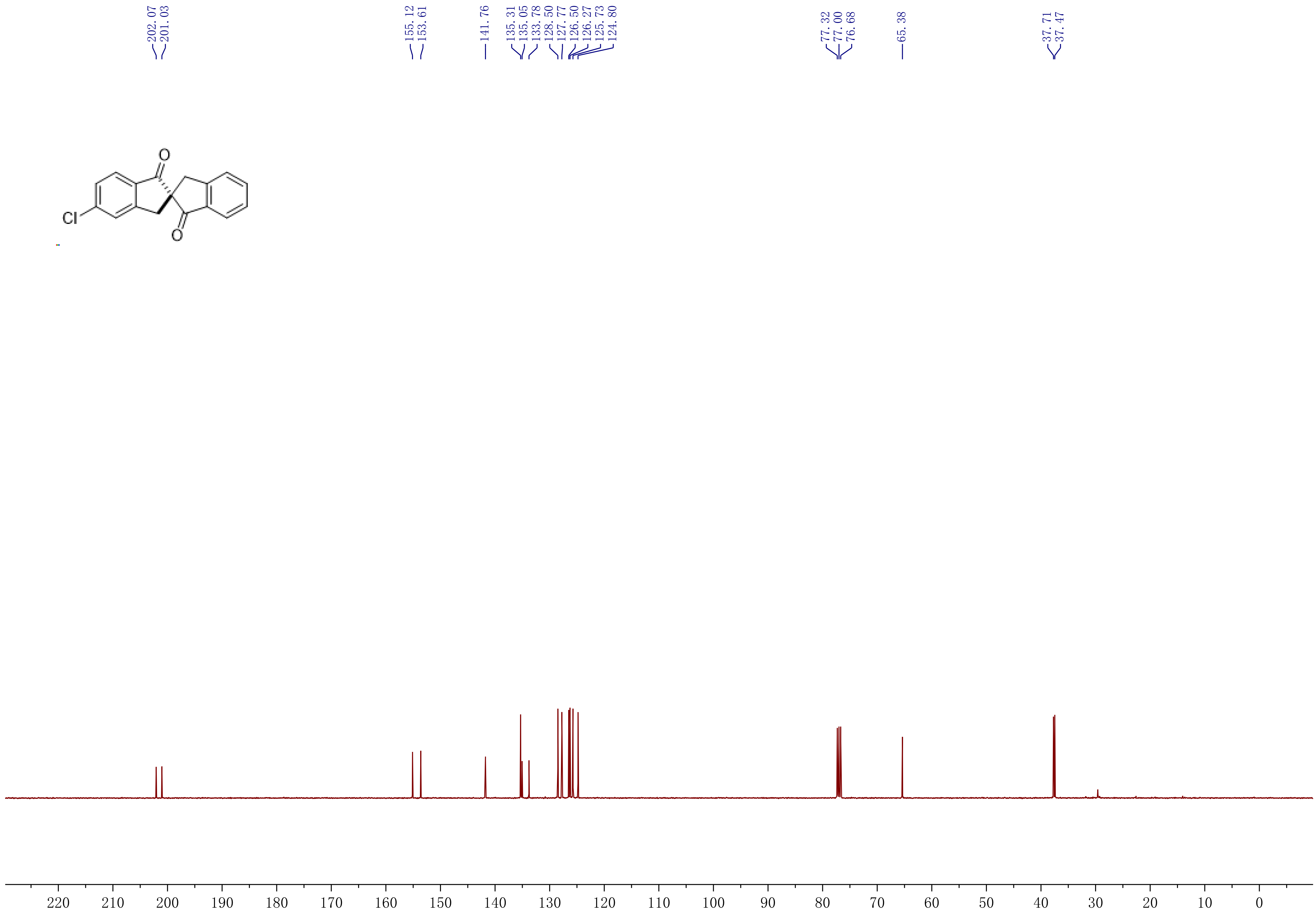
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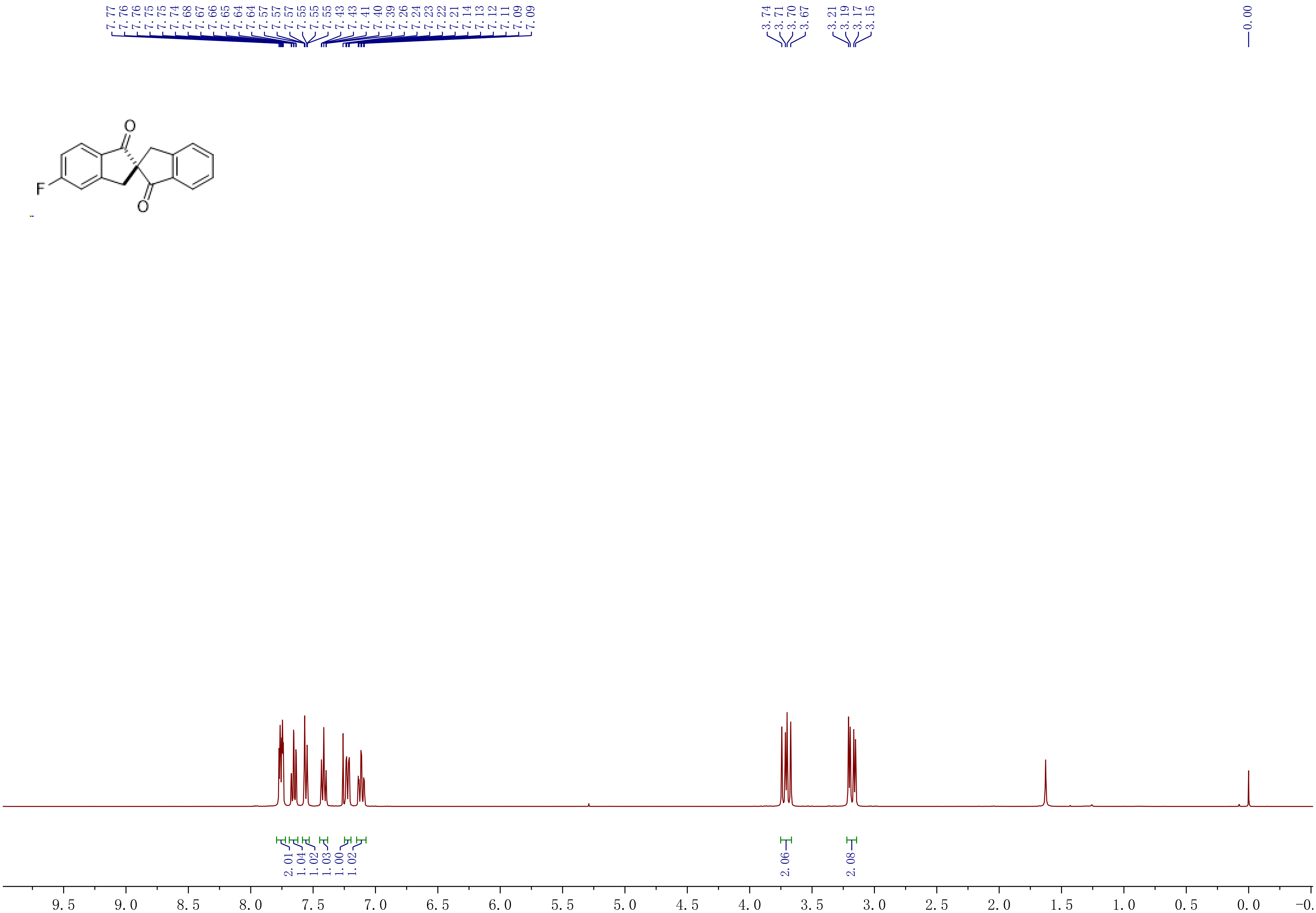
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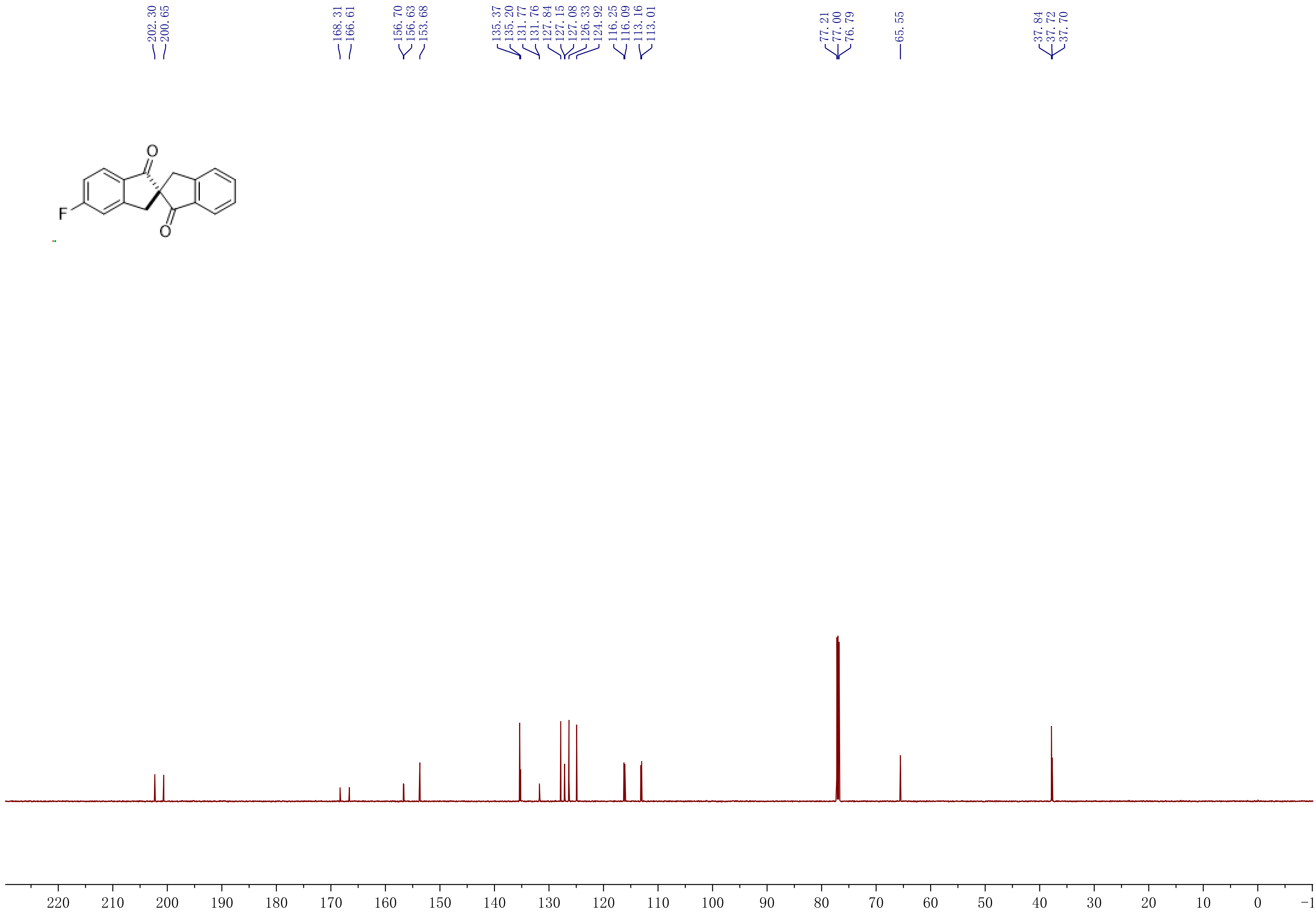

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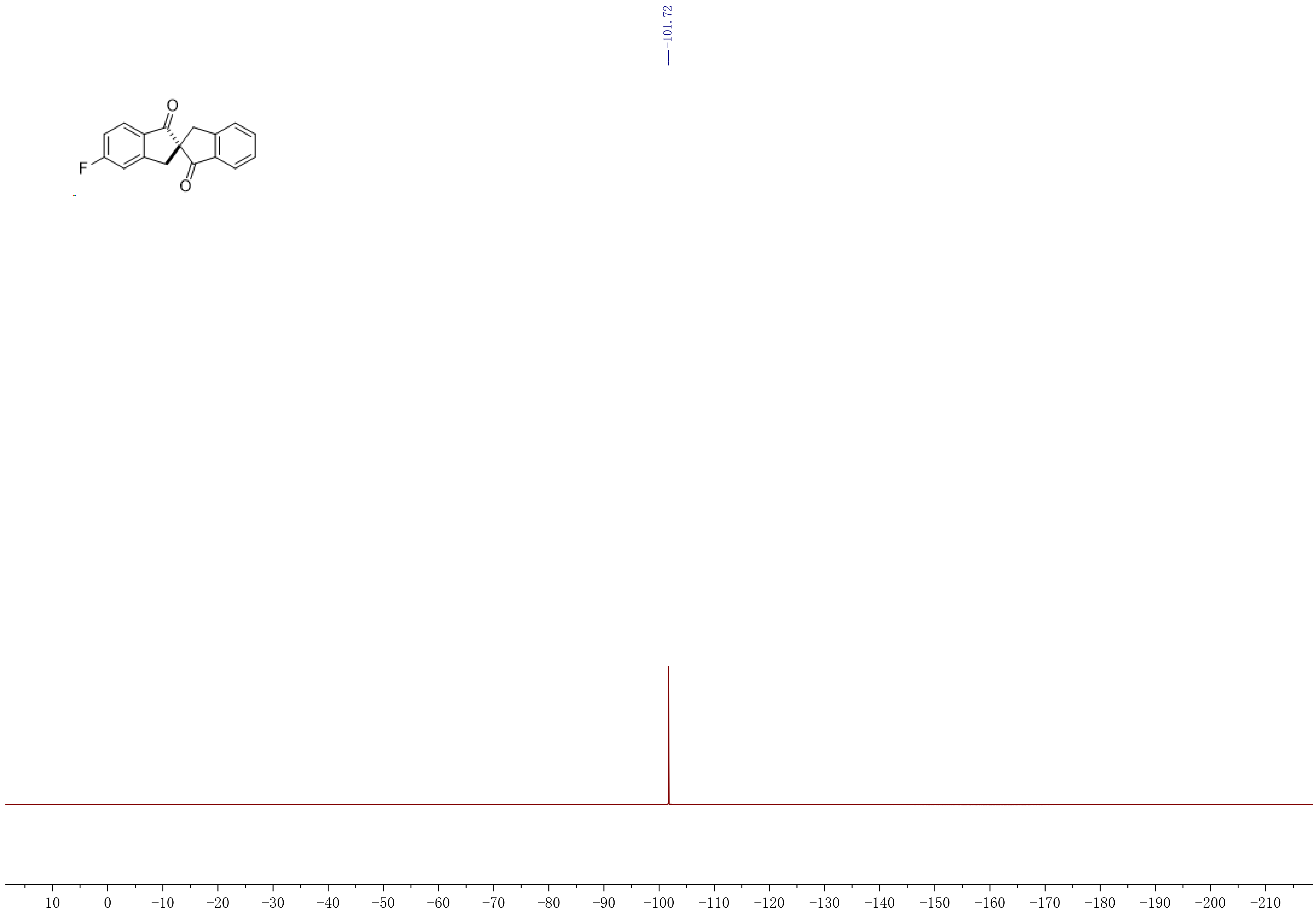

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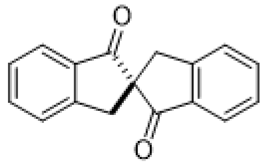
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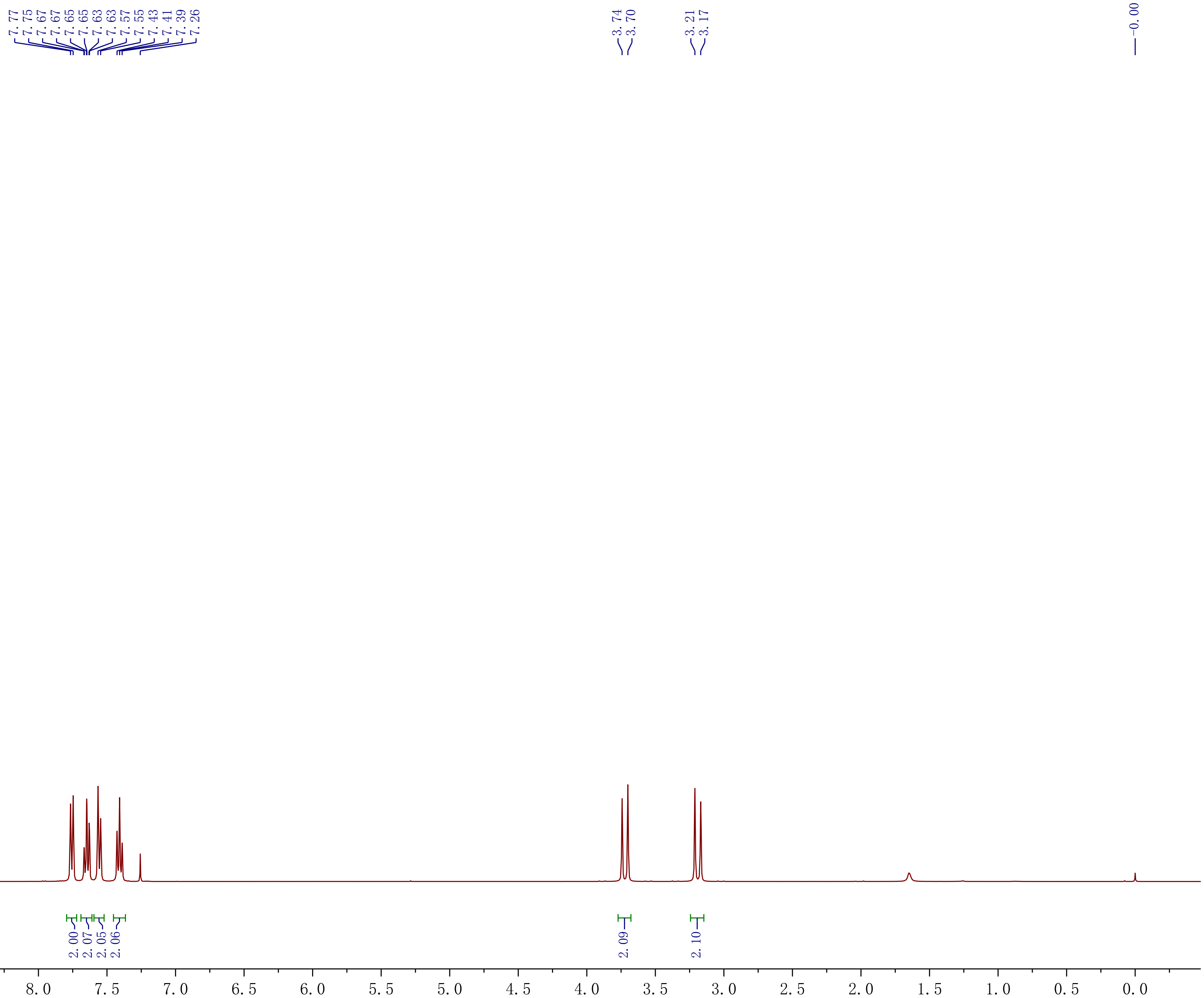
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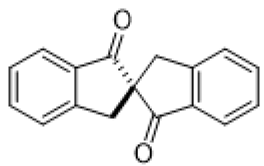
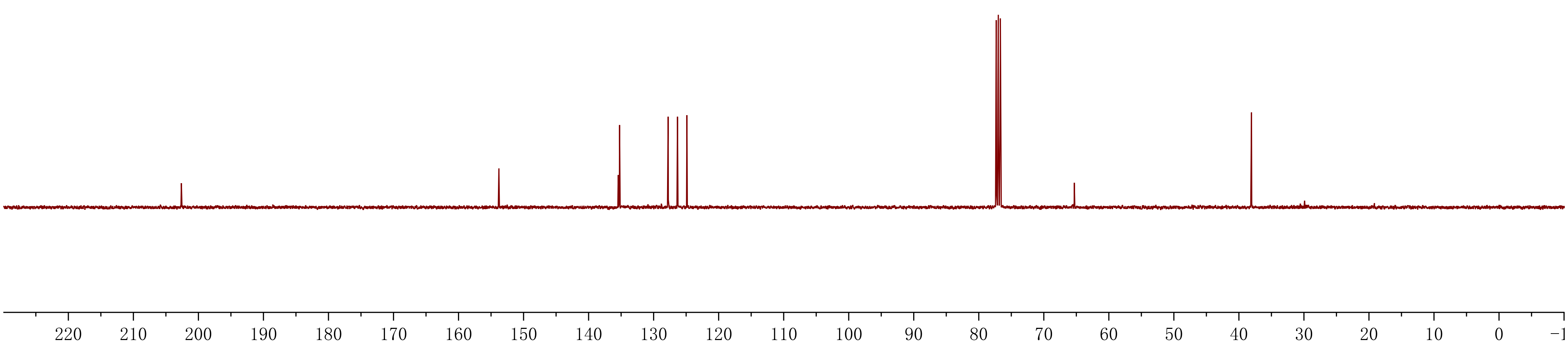
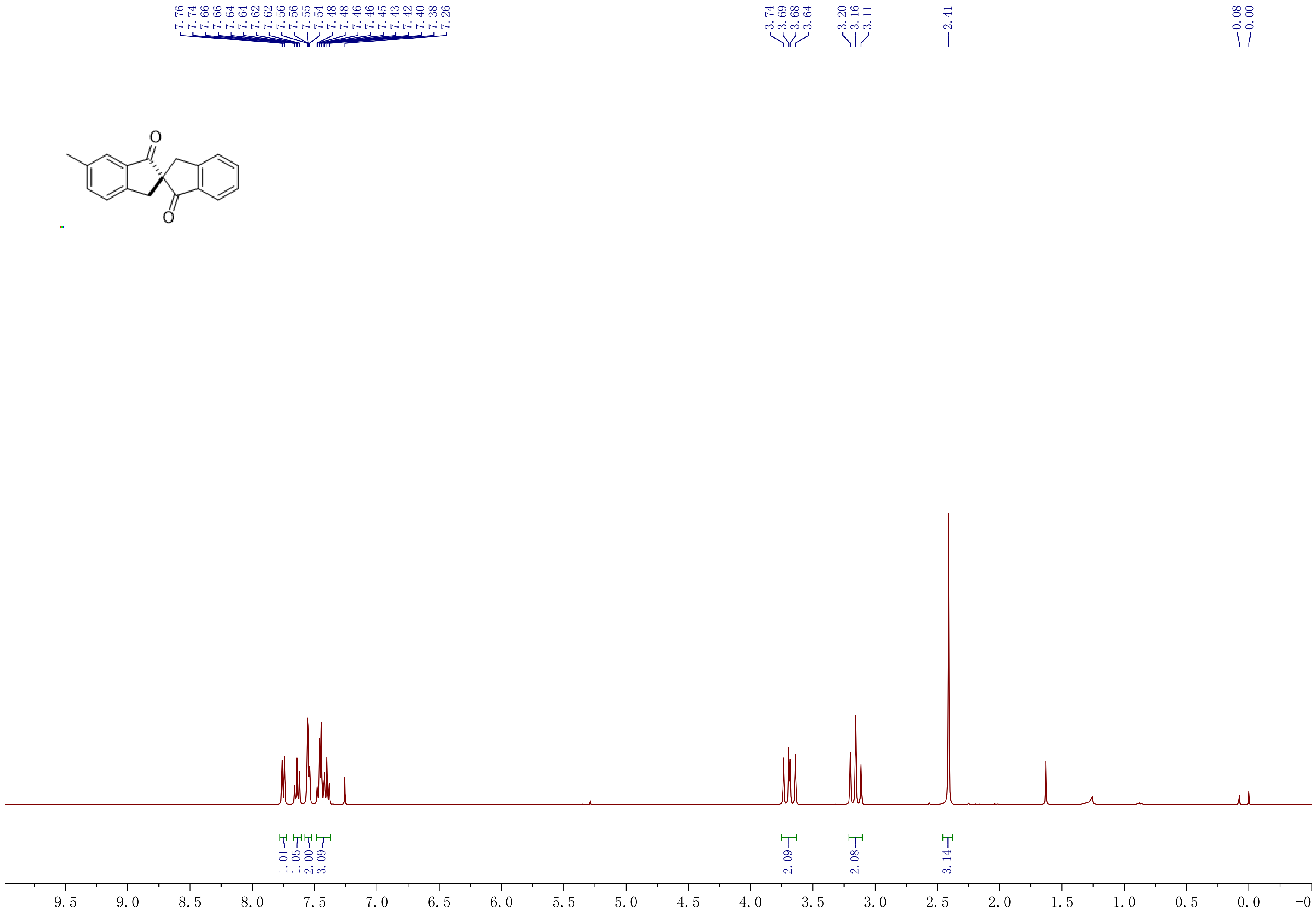
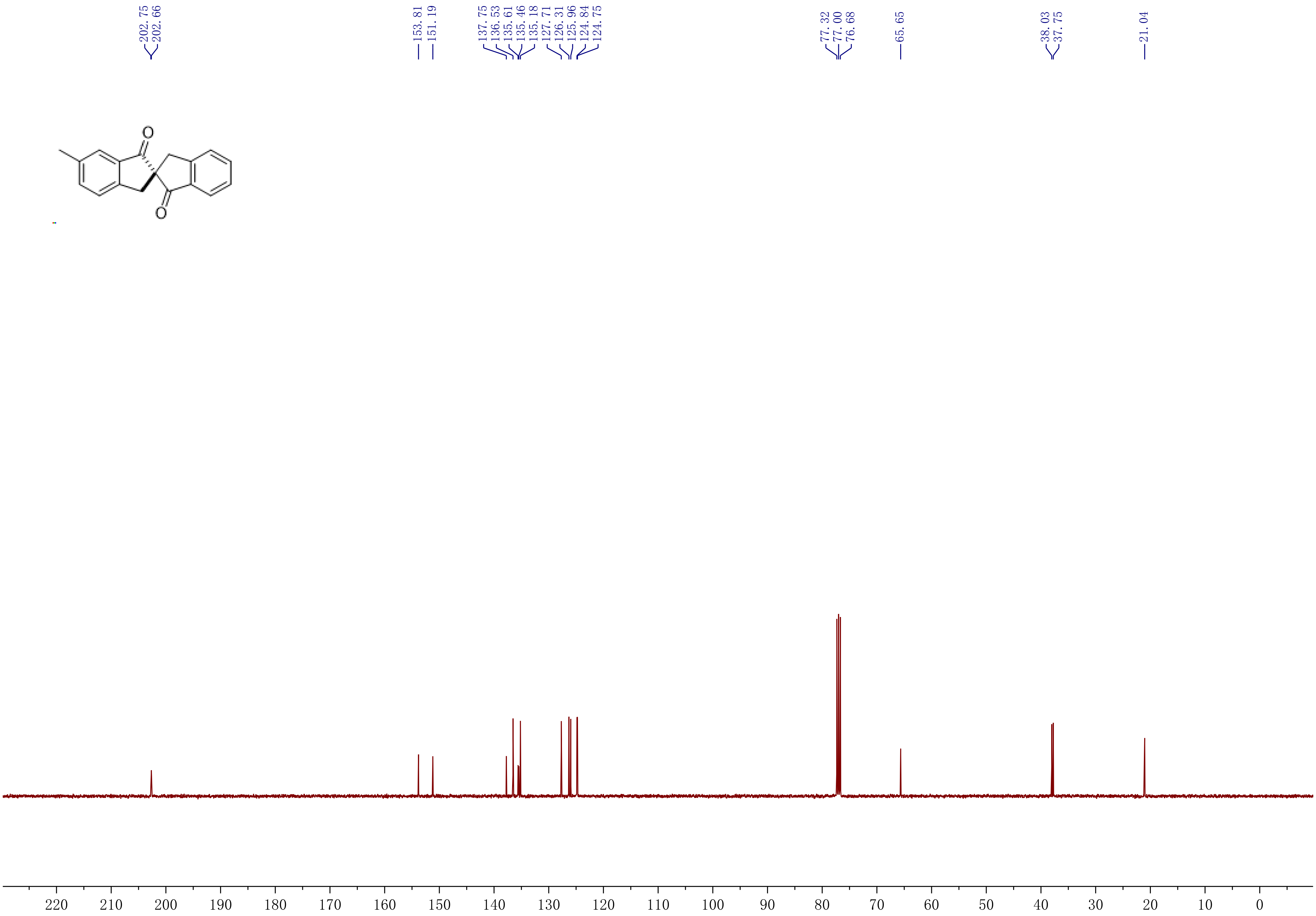




202.62
153.79
135.44
135.24
127.77
126.33
124.88
77.32
77.00
76.68
65.32
38.06
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1



7.76 7.74 7.66 7.66 7.64 7.64 7.62 7.62 7.56 7.56 7.55 7.54 7.48 7.48 7.46 7.46 7.45 7.43 7.42 7.40 7.38 7.26
3.74 3.69 3.68 3.64
3.20 3.16 3.11
2.41
0.08 0.00
O
O
1.01 1.05 2.00 3.09
2.09
2.08
3.14
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

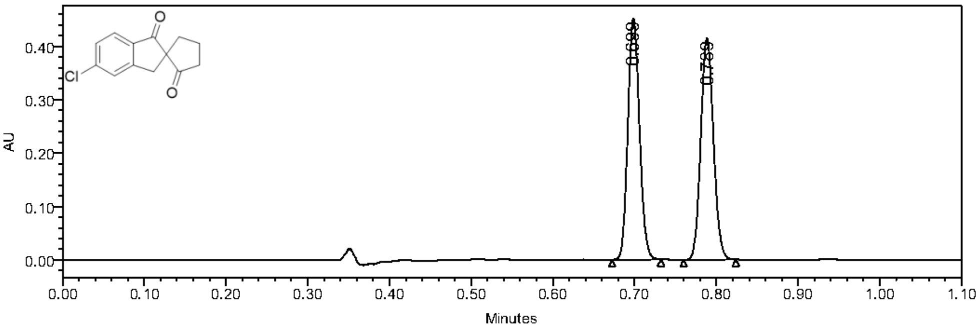


202.75
202.66
153.81
151.19
137.75
136.53
135.61
135.46
135.18
127.71
126.31
125.96
124.84
124.75
77.32
77.00
76.68
65.65
38.03
37.75
21.04
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

Sample Information

Sample Name: 2a-rac Wave Length: 254.5nm

Column: Trefoil™CEL2 80:20



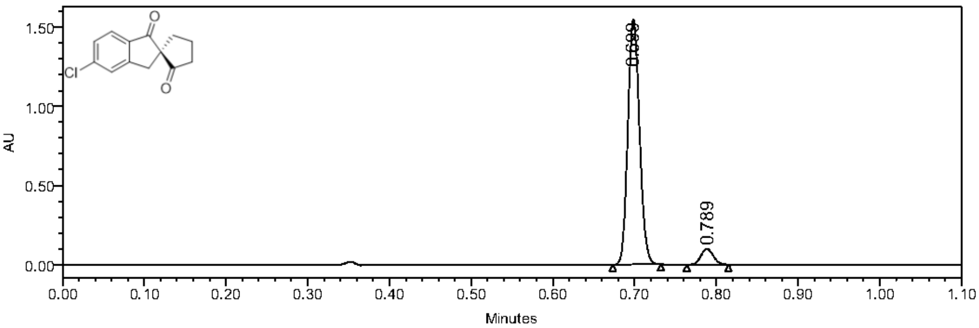
peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.699	446514	50.01	451526
2	0.789	446394	49.99	414730

Sample Information

Sample Name: 2a-sym Wave Length: 254.5nm

Column: Trefoil™ CEL2 80:20



peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.699	1536335	93.61	1549795
2	0.789	104894	6.39	99355

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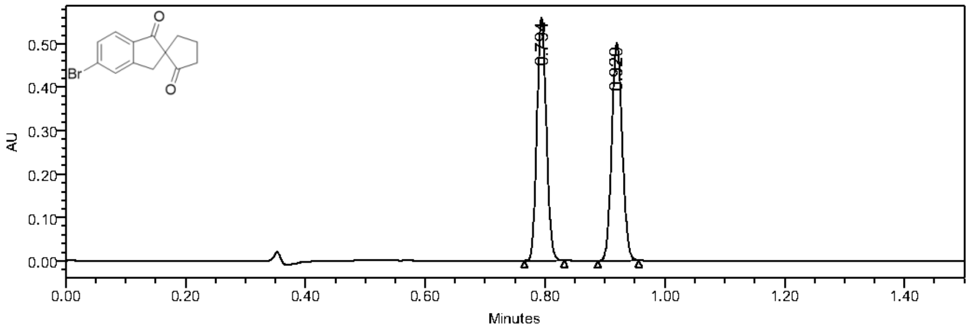
Sample Information

Sample Name: 2b-rac

Wave Length: 258.1nm

Column: Trefoil™ CEL2 80:20



peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.794	610049	50.00	557759
2	0.920	610100	50.00	500454

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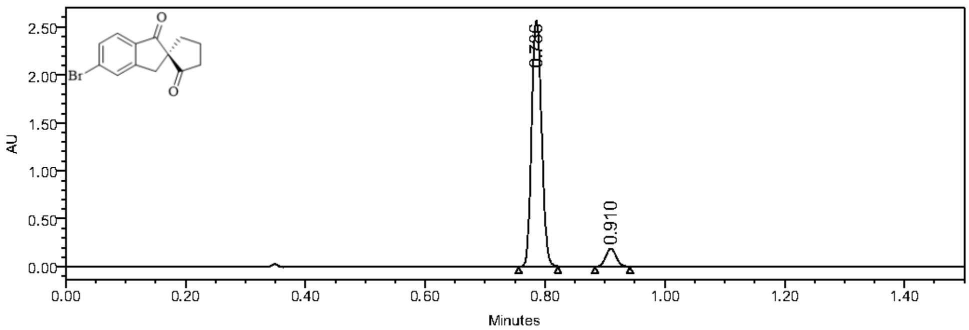
Sample Information

Sample Name: 2b-sym

Wave Length: 258.1nm

Column: Trefoil™CEL2 80:20

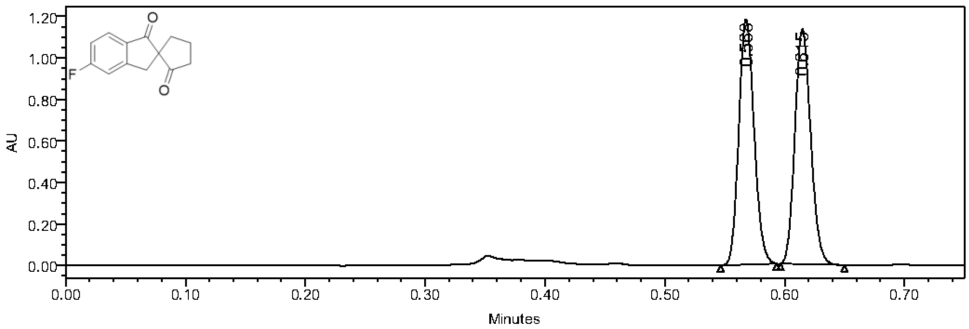


peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.786	2966543	92.89	2566707
2	0.910	226985	7.11	187705

Sample Information

Sample Name:	2c-rac	Wave Length:	246.2nm
Column:	Trefoil™CEL2 80:20		

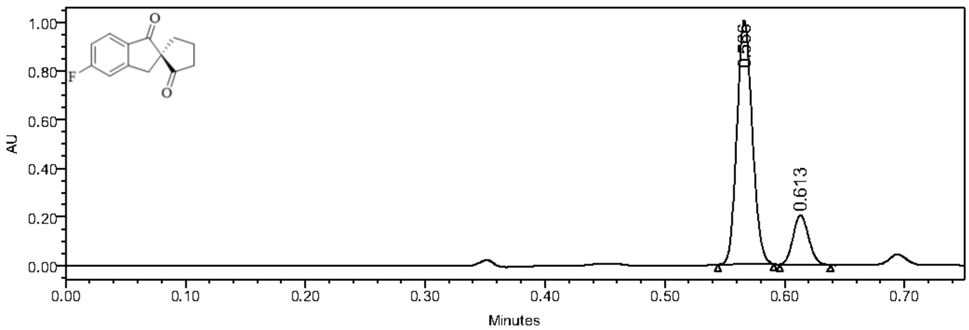


peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.568	1048758	50.10	1184397
2	0.615	1044398	49.90	1134787

Sample Information

Sample Name:	2c-sym	Wave Length:	246.2nm
Column:	Trefoil™CEL2 80:20		



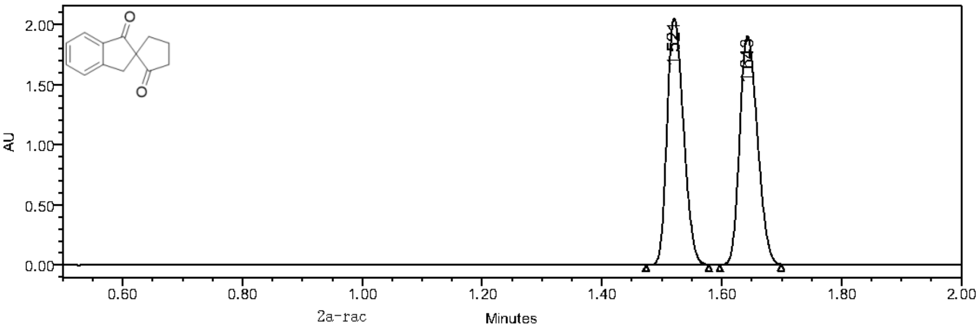
peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.566	892251	82.75	1003299
2	0.613	185961	17.25	204528

Sample Information

Sample Name: 2d-rac | Wave Length: 241.5nm

Column: Trefoil™CEL2 95:05



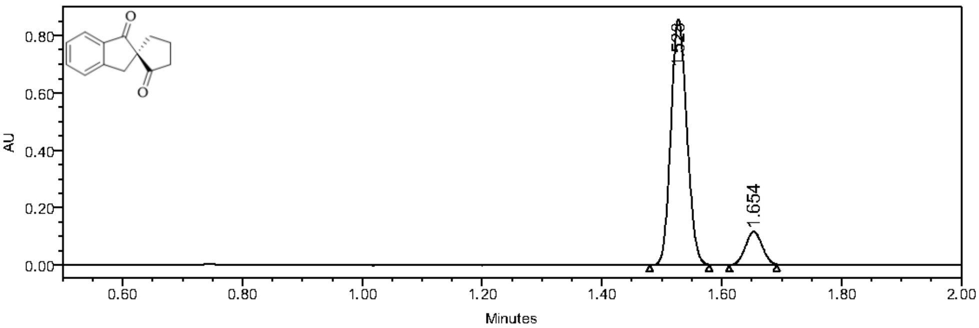
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	1.521	3917196	49.95	2047074
2	1.643	3925126	50.05	1901501

Sample Information

Sample Name: 2d-sym | Wave Length: 241.5nm

Column: Trefoil™CEL2 95:05



peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	1.528	1589210	87.70	854993
2	1.654	222822	12.30	115227

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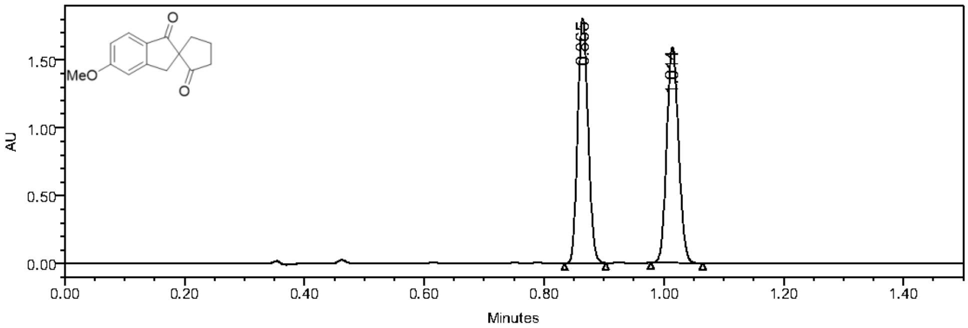
Sample Information

Sample Name: 2e-rac   Wave Length: 267.6nm

Column: Trefoil™CEL2 80:20



peak information:

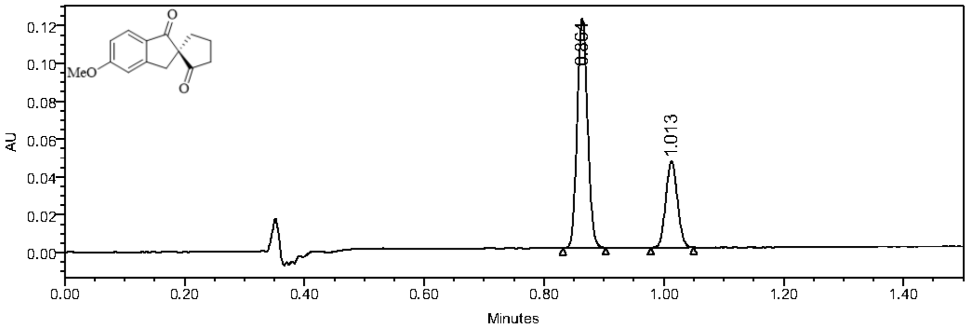
	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.865	2182807	49.92	1805174
2	1.014	2190237	50.08	1591270

Empower™ 3 SOFTWARE

Sample Information

Sample Name: 2e-sym   Wave Length: 267.6nm

Column: Trefoil™CEL2 80:20



peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.864	145956	70.19	121388
2	1.013	61997	29.81	45630

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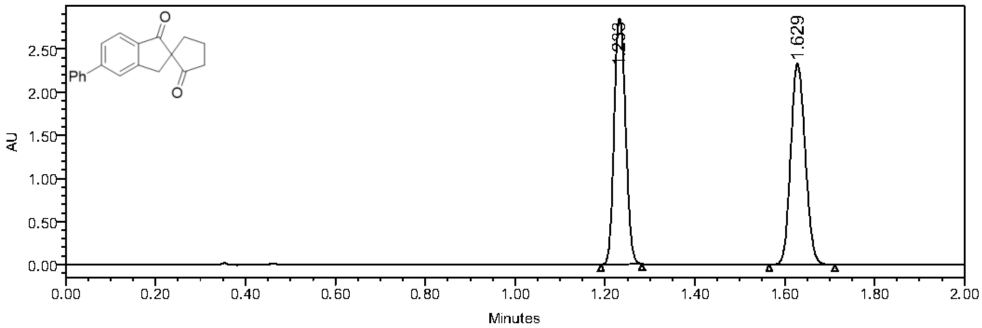
Sample Information

Sample Name: 2f-rac

Wave Length: 280.6nm

Column: Trefoil™CEL2 80:20



peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.233	5052605	49.05	2850984
2	1.629	5247521	50.95	2330634

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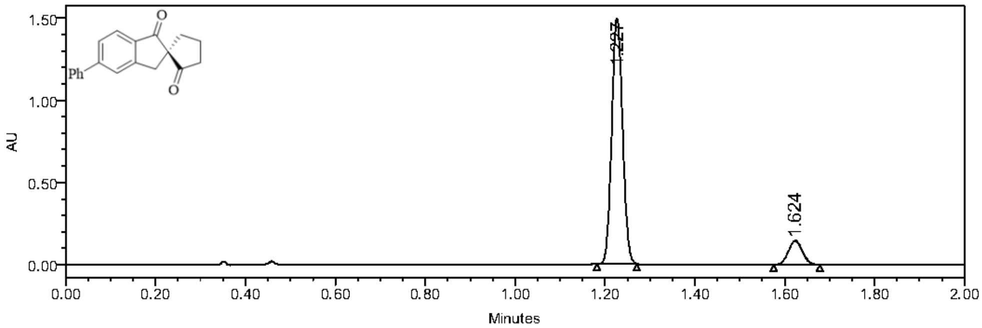
Sample Information

Sample Name: 2f-sym

Wave Length: 280.6nm

Column: Trefoil™CEL2 80:20



peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.227	2497841	88.79	1492129
2	1.624	315280	11.21	145555

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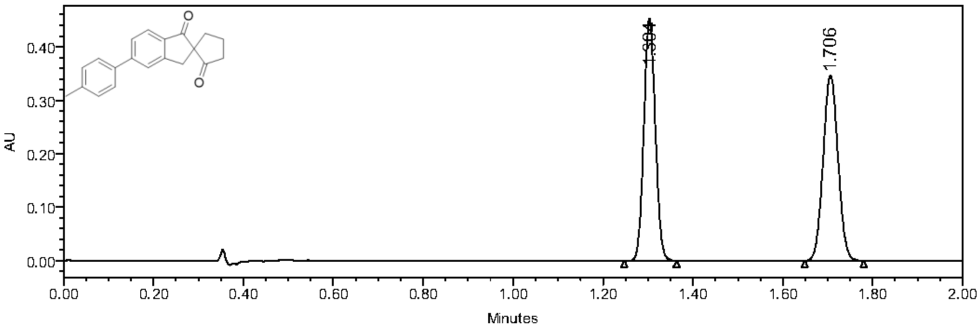
Sample Information

Sample Name: 2g-rac

Wave Length: 290.1nm

Column: Trefoil™CEL2 80:20



peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.304	798556	49.99	452278
2	1.706	799005	50.01	346227

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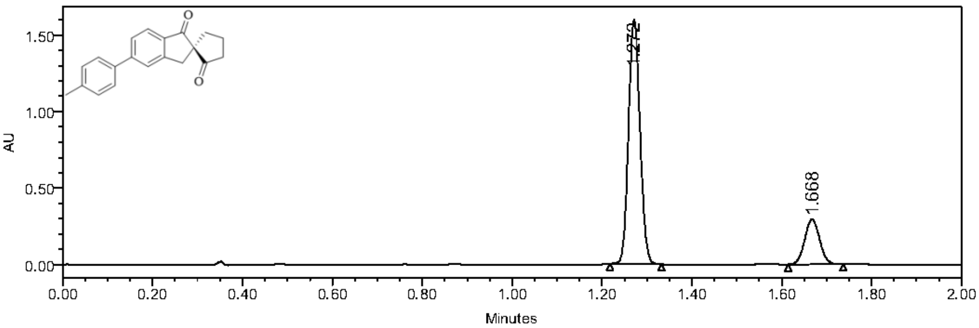
Sample Information

Sample Name: 2g-sym

Wave Length: 290.1nm

Column: Trefoil™CEL2 80:20



peak information:

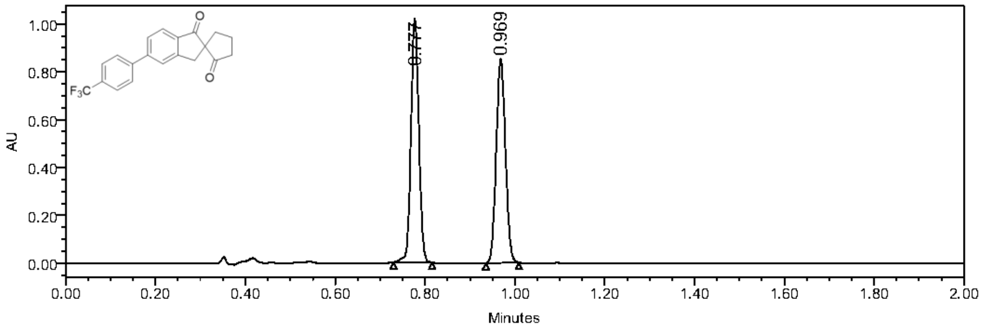
	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.272	2830467	80.84	1600220
2	1.668	670640	19.16	294031

Sample Information

Sample Name: 2h-rac

Wave Length: 274.7nm

Column: Trefoil™CEL2 80:20



peak information:

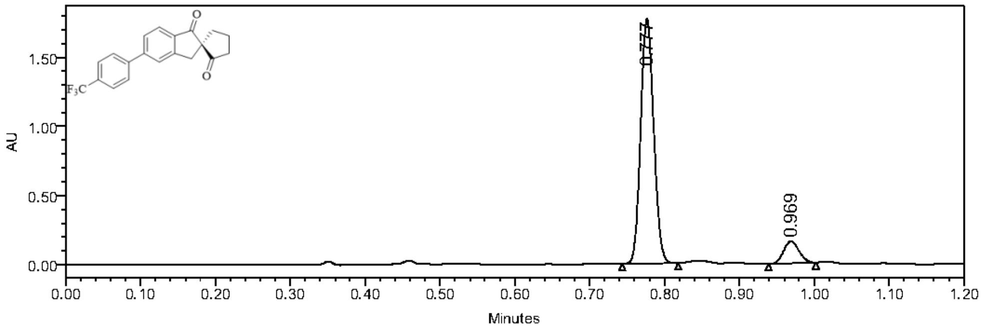
	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.777	1239691	50.52	1019726
2	0.969	1214076	49.48	851741

Sample Information

Sample Name: 2h-sym

Wave Length: 274.7nm

Column: Trefoil™CEL2 80:20



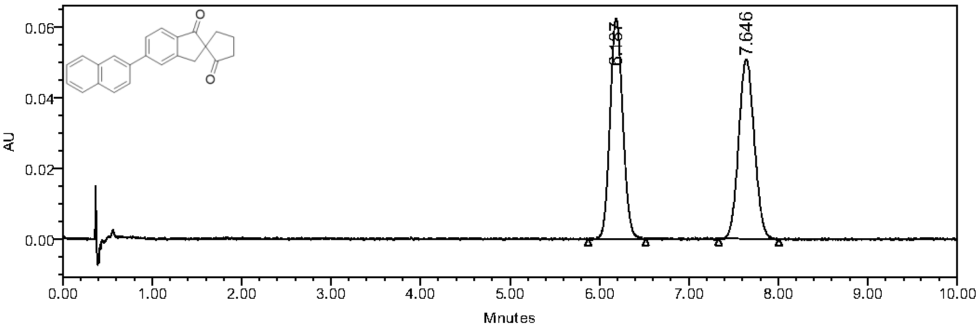
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.777	2145987	90.28	1777314
2	0.969	230917	9.72	159984

Sample Information

Sample Name: 2i-rac | Wave Length: 272.3nm

Column: CHIRALPAK®AD-3 80:20



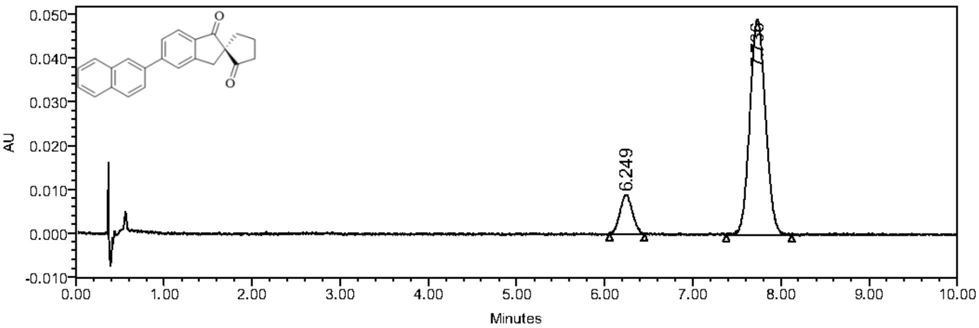
peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	6.187	618704	50.21	62315
2	7.646	613590	49.79	50612

Sample Information

Sample Name: 2i-sym | Wave Length: 272.3nm

Column: CHIRALPAK® AD-3 80:20



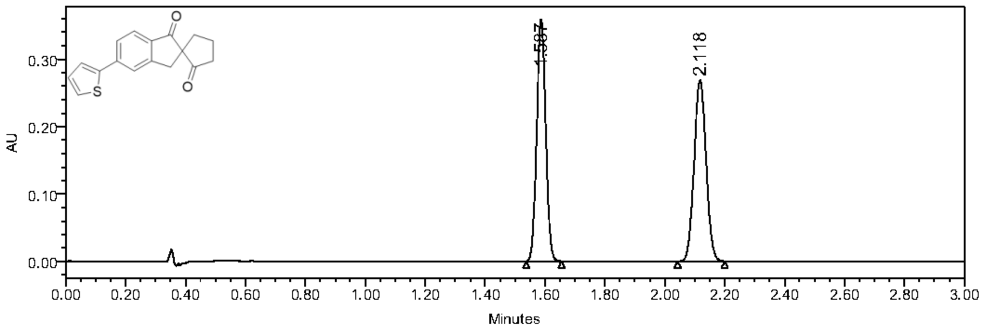
peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	6.249	86428	12.41	8829
2	7.736	610051	87.59	49246

Sample Information

Sample Name: 2j-rac Wave Length: 323.5nm

Column: Trefoil™CEL2 80:20



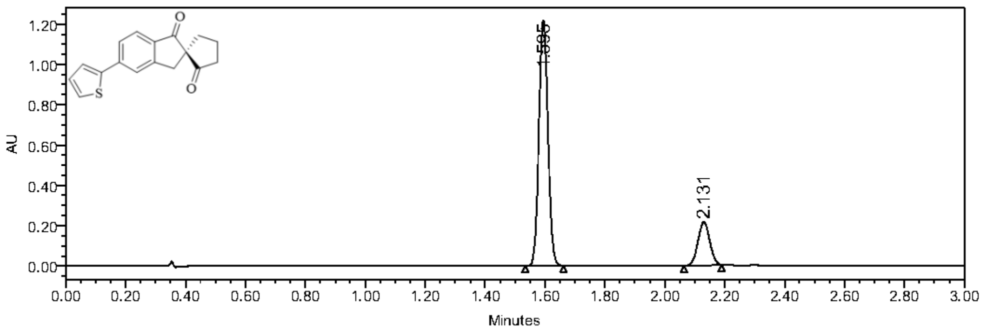
peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.587	749548	49.99	358588
2	2.118	749868	50.01	268700

Sample Information

Sample Name: 2j-sym Wave Length: 323.5nm

Column: Trefoil™CEL2 80:20



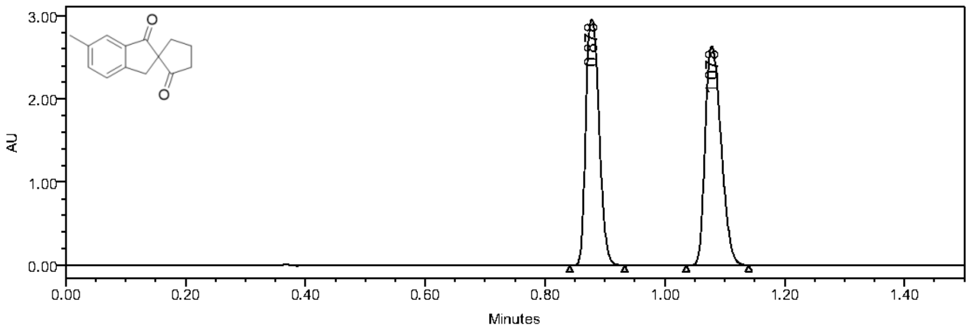
peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.595	2563520	81.32	1218437
2	2.131	588992	18.68	214436

Sample Information

Sample Name: 2k-rac Wave Length: 245.0nm

Column: CHIRALPAK® AD-3 80:20



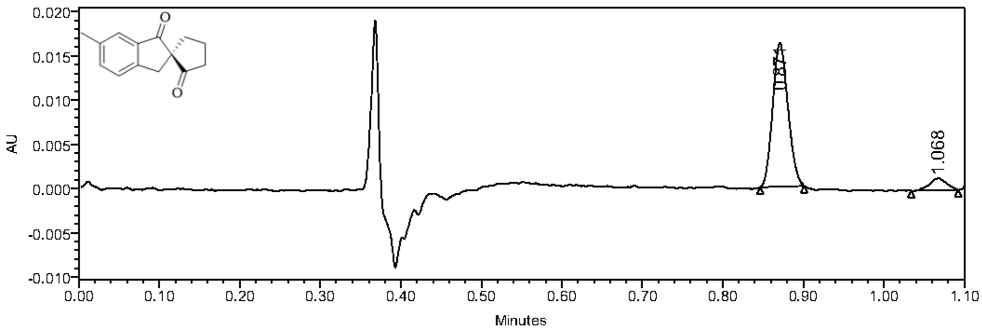
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.878	4566127	48.40	2957228
2	1.078	4868298	51.60	2628759

Sample Information

Sample Name: 2k-sym Wave Length: 245.0nm

Column: CHIRALPAK® AD-3 80:20



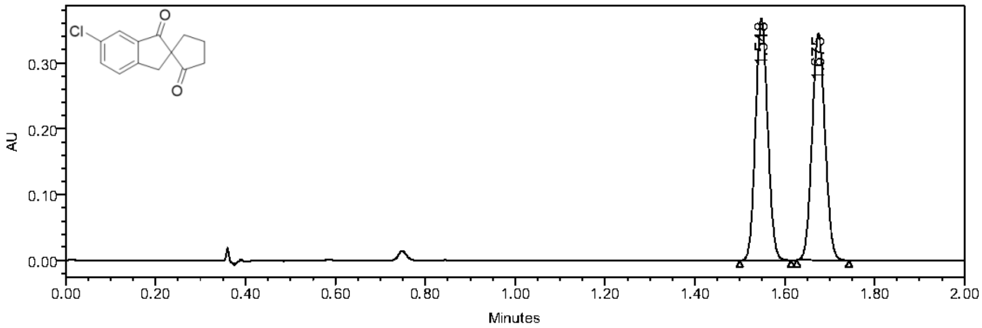
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.871	21191	91.58	16241
2	1.068	1949	8.42	1332

Sample Information

Sample Name: 2l-rac   Wave Length: 240.3nm

Column: Trefoil™CEL2 95:05



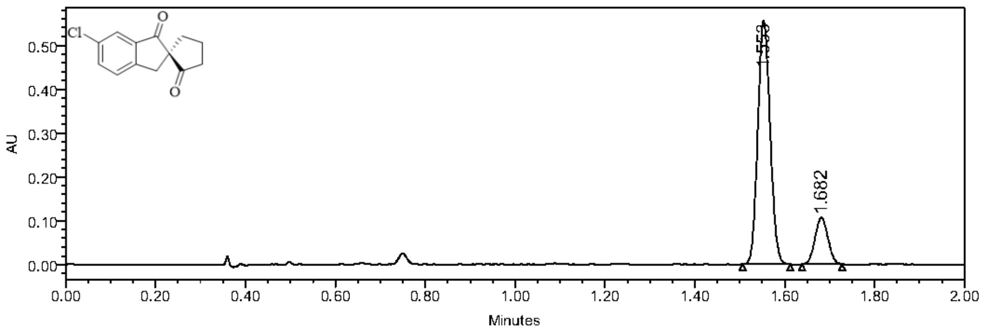
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	1.548	692325	50.00	367733
2	1.675	692408	50.00	344020

Sample Information

Sample Name: 2l-sym   Wave Length: 240.3nm

Column: Trefoil™CEL2 95:05



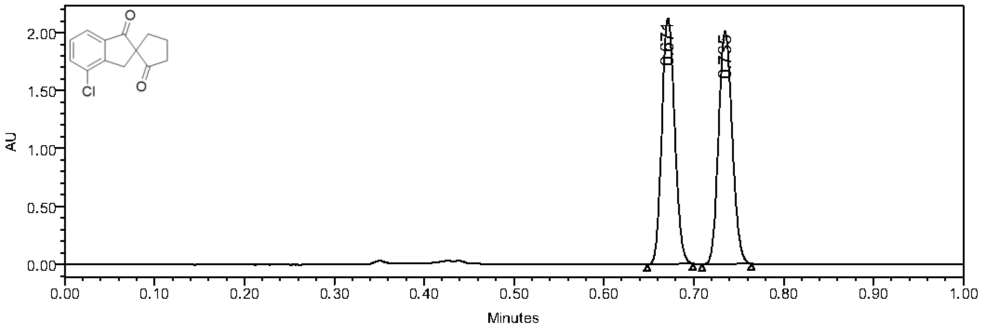
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	1.553	1056761	83.25	556228
2	1.682	212656	16.75	106254

Sample Information

Sample Name: 2m-rac   Wave Length: 246.2nm

Column: Trefoil™CEL2 80:20



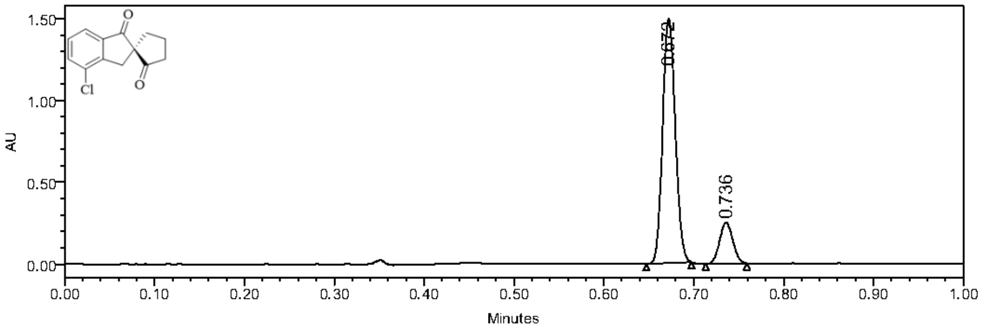
peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.671	2107154	49.88	2123168
2	0.735	2117069	50.12	2010733

Sample Information

Sample Name: 2m-sym   Wave Length: 246.2nm

Column: Trefoil™CEL2 80:20



peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	0.672	1457299	85.11	1495857
2	0.736	254955	14.89	250473

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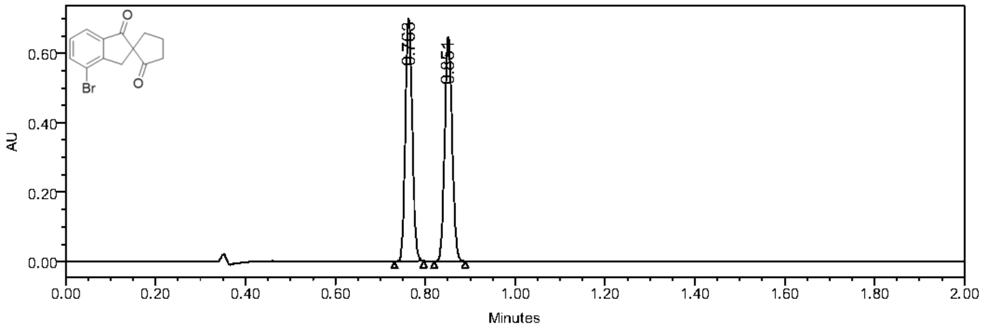
Sample Information

Sample Name: 2n-rac   Wave Length: 252.1nm

Column: Trefoil™CEL2 80:20



peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.763	747054	50.03	698773
2	0.851	746042	49.97	645821

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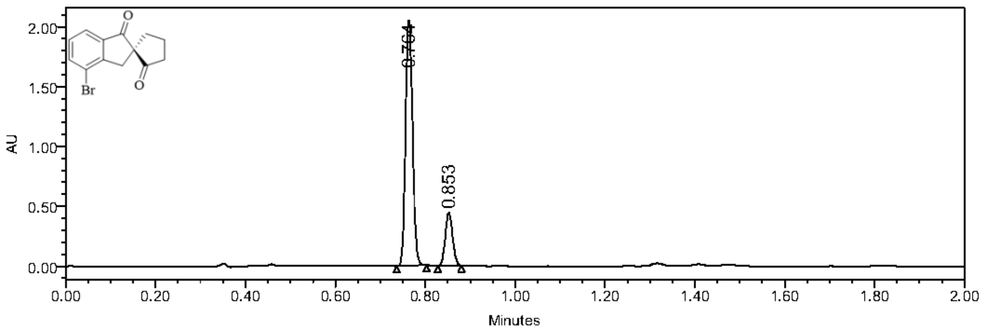
Sample Information

Sample Name: 2n-sym   Wave Length: 252.1nm

Column: Trefoil™CEL2 80:20



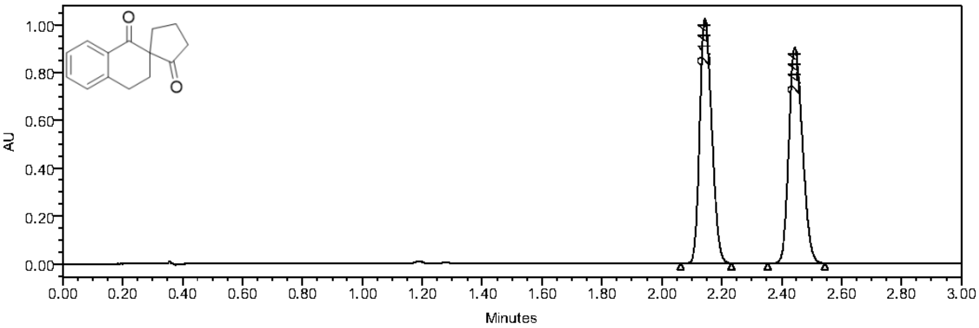
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.764	2209034	81.41	2048216
2	0.853	504269	18.59	444067

Sample Information

Sample Name: 2o-rac   Wave Length: 246.2nm

Column: Trefoil™CEL2 95:05



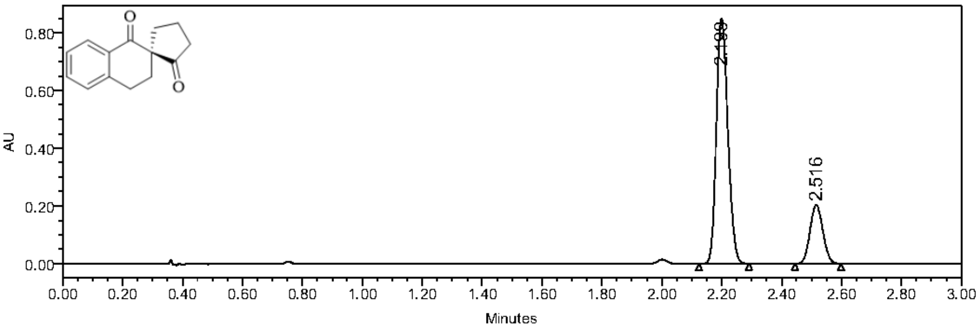
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	2.144	2844792	49.99	1022661
2	2.444	2845491	50.01	901586

Sample Information

Sample Name: 2o-sym   Wave Length: 246.2nm

Column: Trefoil™CEL2 95:05



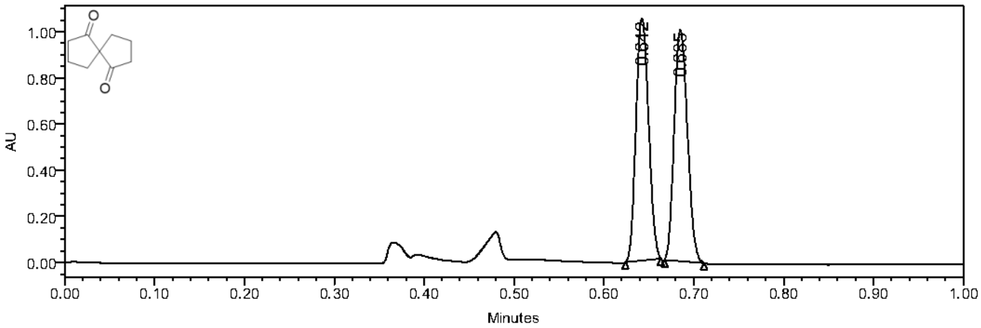
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	2.199	2272536	78.82	849710
2	2.516	610826	21.18	204409

Sample Information

Sample Name: 2p-rac Wave Length: 202.6nm

Column: Trefoil™CEL2 95:05



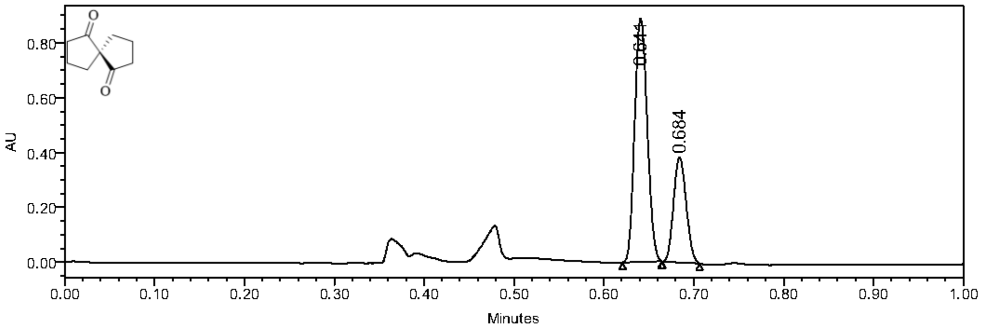
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.642	1019249	49.78	1048568
2	0.685	1028296	50.22	1002483

Sample Information

Sample Name: 2p-sym Wave Length: 202.6nm

Column: Trefoil™CEL2 95:05



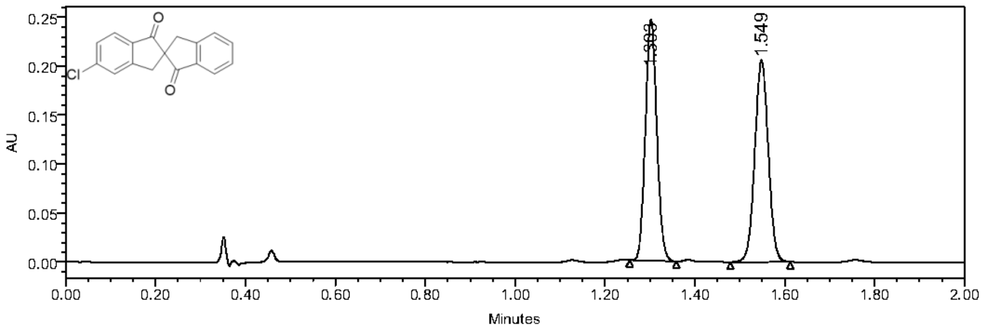
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.641	861219	69.69	887100
2	0.684	374572	30.31	382697

Sample Information

Sample Name: 2q-rac	Wave Length: 251.0nm

Column: Trefoil™CEL2 80:20



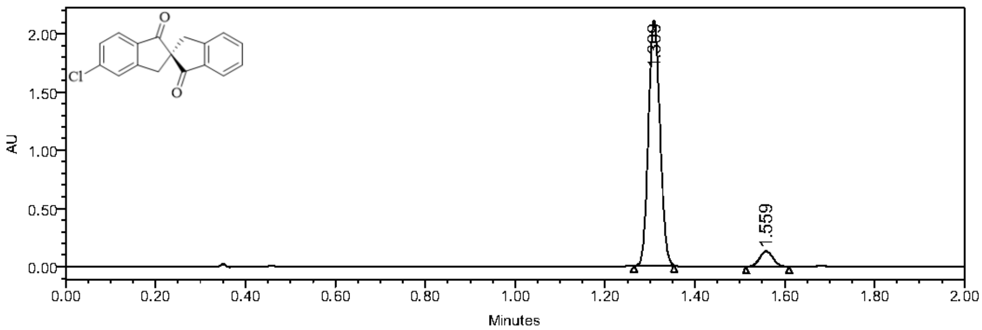
peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.303	434377	50.26	246584
2	1.549	429862	49.74	205972

Sample Information

Sample Name: 2q-sym	Wave Length: 251.0nm

Column: Trefoil™CEL2 80:20



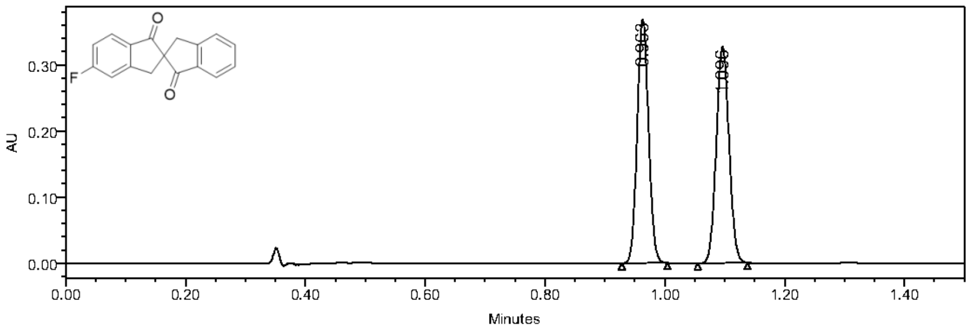
peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.309	3746966	93.29	2106421
2	1.559	269576	6.71	130916

Sample Information

Sample Name: 2r-rac Wave Length: 247.4nm

Column: Trefoil™CEL2 80:20



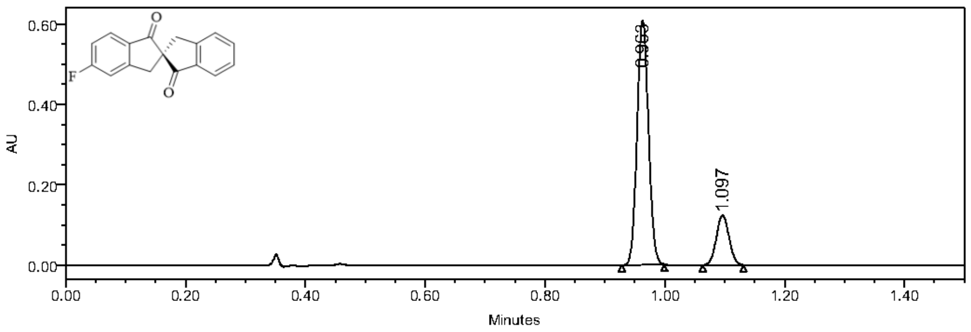
peak information:

	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.963	484892	50.02	368449
2	1.096	484499	49.98	327009

Sample Information

Sample Name: 2r-sym Wave Length: 247.4nm

Column: Trefoil™CEL2 80:20



peak information:

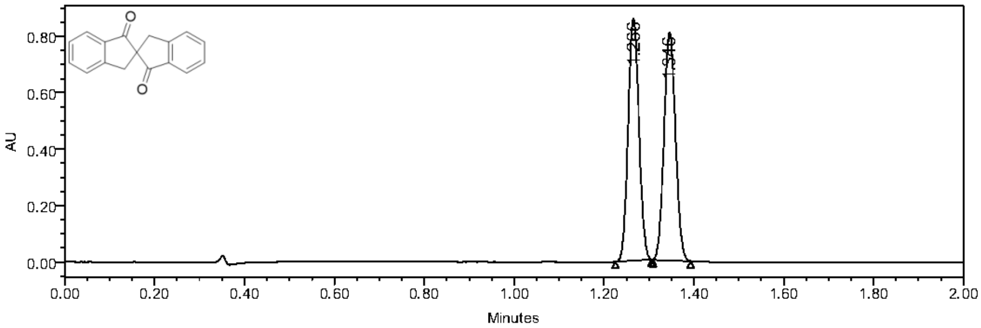
	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	0.963	801901	81.50	608448
2	1.097	182014	18.50	123871

Sample Information

Sample Name: 2s-rac

Wave Length: 246.2nm

Column: Trefoil™CEL2 80:20



peak information:

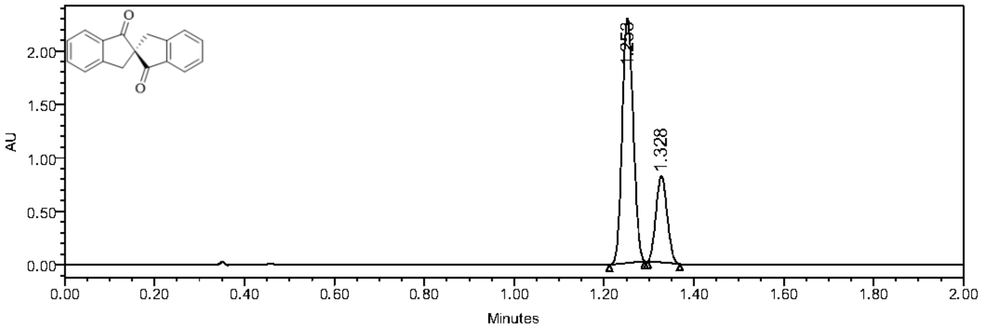
	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	1.266	1438063	50.09	858559
2	1.346	1432992	49.91	806892

Sample Information

Sample Name: 2s-sym

Wave Length: 246.2nm

Column: Trefoil™CEL2 80:20



peak information:

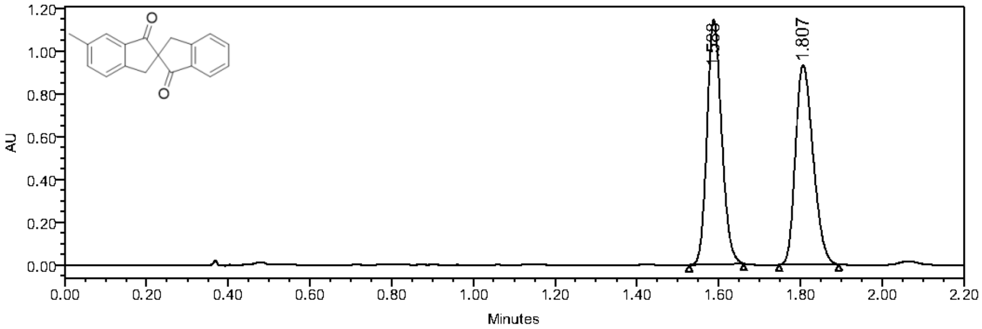
	RetTime (min)	Area (µV*s)	Area (%)	Height (µV)
1	1.253	3929783	73.72	2287995
2	1.328	1400636	26.28	810671

Sample Information

Sample Name: 2t-rac

Wave Length: 247.4nm

Column: CHIRALPAK® AD-3 80:20



peak information:

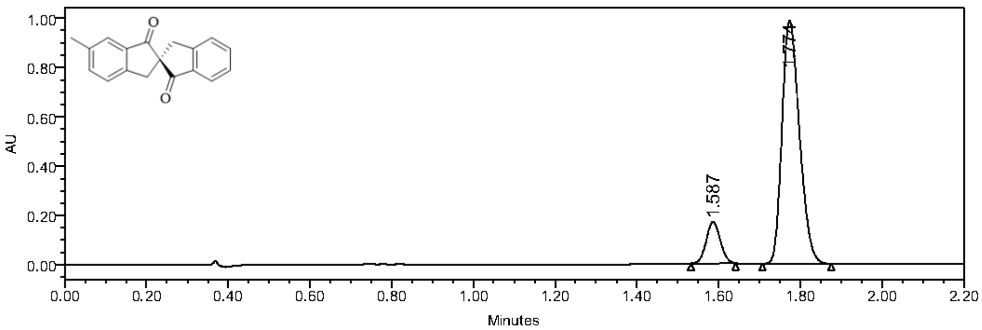
	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.588	2844228	50.37	1145368
2	1.807	2802083	49.63	931809

Sample Information

Sample Name: 2t-sym

Wave Length: 247.4nm

Column: CHIRALPAK® AD-3 80:20



peak information:

	RetTime (min)	Area (μV*s)	Area (%)	Height (μV)
1	1.587	404373	12.14	168840
2	1.774	2926961	87.86	986975

9. References

(1) S.-K. Chen, W.-Q. Ma, Z.-B. Yan, F.-M. Zhang, S.-H. Wang, Y.-Q. Tu, X.-M. Zhang, J.-M. Tian, *J. Am. Chem. Soc.* 2018**, 140**, 10099.

(2) (a) K. Barral, A. D. Moorhouse, J. E. Moses, *Org. Lett.* 2007, **9**, 1809; (b) M. A. E. Pinto-Bazurco Mendieta, M. Negri, C. Jagusch, U. Müller-Vieira, T. Lauterbach, R. W. Hartmann, *J. Med. Chem.* 2008, **51**, 5009.

(3) (a) J. A. Nieman, B. A. Keay, *Synth. Commun.* 1999, **29**, 3829; (b) X. Gu, Y. Zhang, Z.-J. Xu, C.-M. Che, *Chem. Commun*. 2014, **50**, 7870.

(4) B. F. Rahemtulla, H. F. Clark, M. D. Smith, *Angew. Chem., Int. Ed.* 2016, **55**, 13180.