

## Electronic supplementary Information

### **Introducing the Use of a Recyclable Solid Electrolyte for Waste Minimization in Electrosynthesis: Preparation of 2-aryl-benzoxazoles in Flow**

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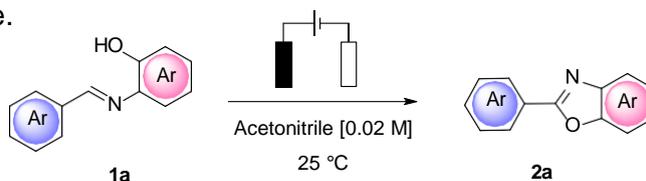
## 1. General remarks.

All chemicals were used as obtained from commercial sources without any further purification unless otherwise noted. GC analyses were performed by using Hewlett-Packard HP 5890 SERIES II equipped with a capillary column DB-5MS (30 m, 0.32 mm), a FID detector and nitrogen as gas carrier. GC-EIMS analyses were carried out by using a Hewlett-Packard HP 6890N Network GC system/5975 Mass Selective Detector equipped with an electron impact ionizer at 70 eV. NMR spectra in solution were recorded on a Bruker DRXADVANCE 400 MHz ( $^1\text{H}$  at 400 MHz and  $^{13}\text{C}$  at 100.6 MHz). The Amberlyst anion exchanges were carried out following reported procedure<sup>1</sup>. The Amberlyst functionalization measurements were carried out using Elementar UNICUBE® elemental analyzer in two different configurations, CHNS mode and Cl mode. Carbon Anode and Aluminium cathode were polished using alumina-water slurry and carefully dried before and after each experiment. Elemental analysis of aluminium content was carried out using an Agilent 4210 MP-AES instrument. Cyclic voltammetry was completed on an IKA ElectroSyn 2.0 operating in CV mode at a scan rate of  $100\text{ mVs}^{-1}$ . An IKA glassy carbon working electrode, an IKA platinum plated counter electrode, and an IKA  $\text{Ag}/\text{AgNO}_3$  reference electrode filled with 0.1 M solution of  $\text{AgNO}_3$  in acetonitrile were used together in a 10 mL ElectroSyn glass vial.

## 2. General Procedures for optimization using homogeneous $\text{NH}_4\text{Cl}$ as supporting electrolyte:

A beaker-type cell was equipped with the electrodes of choice, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added  $\text{NH}_4\text{Cl}$  (0.5 mmol, 26.7 mg), imine **1a** (0.1 mmol, 19.7 mg) and 100  $\mu\text{L}$  of water if indicated in tables. The mixture was electrolyzed using constant current conditions (as indicated in tables) at a temperature of  $25^\circ\text{C}$  while stirring. The electrolysis was continued until the indicated times in tables. Once the electrolysis was stopped, the solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. If needed the pure product **2a** was obtained by column chromatography on silica gel using petroleum ether and ethyl acetate as eluents (9:1)

**Table S1:** Screening of solvent, electrode and current for the electrosynthesis of **2a** using  $\text{NH}_4\text{Cl}$  as supporting electrolyte.



Entry	solvent	Cathode/Anode	CCE	<b>3</b> [%] <sup>b</sup>
1	$\text{CH}_3\text{CN}$	Al/Al	8mA	54
2	$\text{CH}_3\text{CN}$	Al/Al	6ma	44
3	$\text{CH}_3\text{CN}$	Al/Al	2ma	38
4	$\text{CH}_3\text{CN}^c$	Al/Al	8mA	50
5	$\text{CH}_3\text{CN}$	C/Al	8mA	89
6	<b><math>\text{CH}_3\text{CN}</math></b>	<b>C/Al</b>	<b>6mA</b>	<b>90</b>
7	$\text{CH}_3\text{CN}$	C/Al	2mA	80
8	$\text{CH}_3\text{CN}^c$	C/Al	8mA	84
9	$\text{CH}_3\text{CN}$	Al/C	8mA	14
10	$\text{CH}_3\text{CN}$	Al/C	6mA	10
11	$\text{CH}_3\text{CN}$	Al/C	2mA	-

12	CH <sub>3</sub> CN	C/C	8mA	68
13	CH <sub>3</sub> CN	C/C	6mA	65
14	CH <sub>3</sub> CN	C/C	2mA	60
15	CH <sub>3</sub> CN <sup>c</sup>	C/C	8mA	57
16	CH <sub>3</sub> CN	C/SS	8mA	37
17	CH <sub>3</sub> CN	GC/Pt	10mA	90
18	CH <sub>3</sub> CN	GC/Pt	6mA	74
19	CH <sub>3</sub> CN <sup>c</sup>	GC/Pt	8mA	78
20	CH <sub>3</sub> CN	Pt/Pt	8mA	86
21	CH <sub>3</sub> CN	C/Pt	8mA	88
22	CH <sub>3</sub> CN <sup>c</sup>	C/Pt	8mA	85
23	CH <sub>3</sub> CN	C/Cu	8mA	64
24	CH <sub>3</sub> CN <sup>d</sup>	C/Al	6mA	67
25	CH <sub>3</sub> CN <sup>e</sup>	C/Al	6mA	43
26	CH <sub>3</sub> CN	C/Al	4mA	86
27	CH <sub>3</sub> CN <sup>f</sup>	C/Al	-	6
28	CH <sub>3</sub> CN <sup>g</sup>	C/Al	2mA	-
29	CH <sub>3</sub> CN/water 1:1 v/v	C/Al	6mA	54
30	CH <sub>3</sub> CN/water (Azeotrope)	C/Al	6mA	62
31	CH <sub>3</sub> CN/MeOH 1:1 v/v	C/Al	6mA	68
32	CH <sub>3</sub> CN/MeOH (Azeotrope)	C/Al	6mA	44
33	MeOH	C/Al	6mA	25
34	EtOH	C/Al	6mA	56
35	water	C/Al	6mA	-
36	THF	C/Al	6mA	84
37	2MeTHF	C/Al	6mA	34
38	2MeTHF <sup>c</sup>	C/Al	6mA	-
39	2MeTHF/MeOH/water <sup>h</sup>	C/Al	6mA	78
40	2MeTHF/ CH <sub>3</sub> CN /water <sup>k</sup>	C/Al	6mA	62

[a] Reaction conditions: undivided cell, **1a** (0.1 mmol), solvent 5 mL, NH<sub>4</sub>Cl (0.5 mmol), 100  $\mu$ L of water, at constant current, 3 h at 25 °C. [b] Isolated yield. [c] Without water; [d] NH<sub>4</sub>Cl (0.2 mmol); [e] NH<sub>4</sub>Cl (0.1 mmol); [f] Reaction run without current at 24h. [g] Reaction run without NH<sub>4</sub>Cl is not conductive and led to partial decomposition of **1a**; [h] in the followed composition: 2MeTHF (5 mL), MeOH (0.8 mL), Water (0.2 mL); [k] in the followed composition: 2MeTHF (5 mL), CH<sub>3</sub>CN (0.8 mL), Water (0.2 mL);

### 3. General procedures for gAmb/mmol1a and gAmb/Vmed plot construction

#### 3.1 General Procedures for gAmb/mmol1a plot construction

A 12 mL volume beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added the Amberlyst of choice (0.2, 0.5, 1, 2, 5 grams) and imine **1a** (1 mmol, 197.2 mg, each experiment). The experiments were repeated using 10 mL (purple line), 5 mL (red line), and 2mL (blue line) adding a constant ratio (50:1) between acetonitrile and water. The mixtures were electrolyzed using constant current conditions (current set at 6 mA) at a temperature of 25°C while stirring. The voltage value of the DC regulated power supply was taken every 10 seconds during 60 seconds and mediated to give the values indicated in the plots.

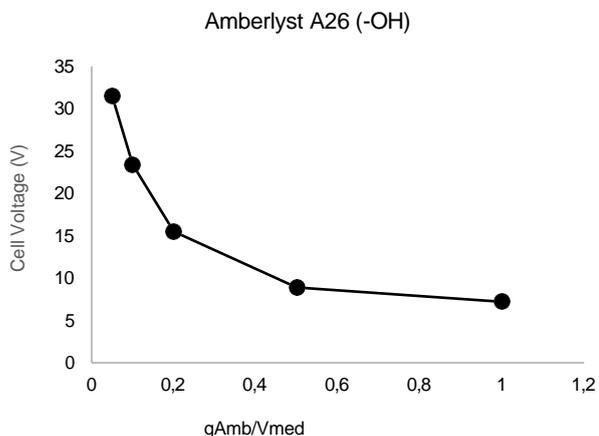
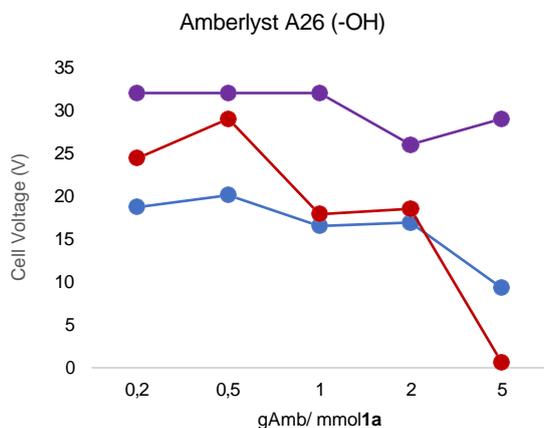
#### 3.2 General Procedures for gAmb/Vmed plot construction

A 12 mL volume beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added the Amberlyst of choice (1g), and acetonitrile (1, 2, 5, 10 mL), and for the last point 0.5 g of Amberlyst of choice in 10 mL of acetonitrile was used adding a constant ratio (50:1) between acetonitrile and water for each experiment. Finally, imine **1a** (1 mmol, 197.2 mg) was introduced in the reaction mixture. The mixtures were electrolyzed using constant current conditions (current set at 6 mA) at a

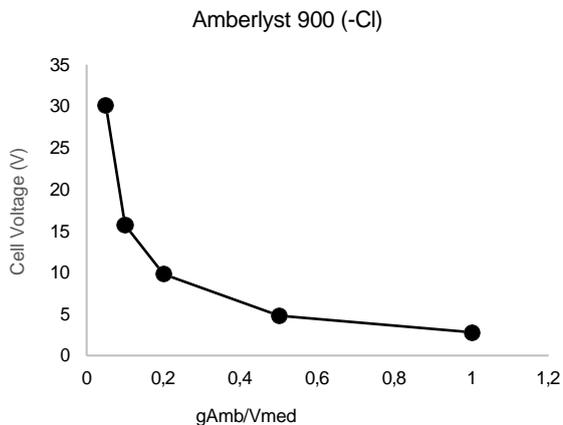
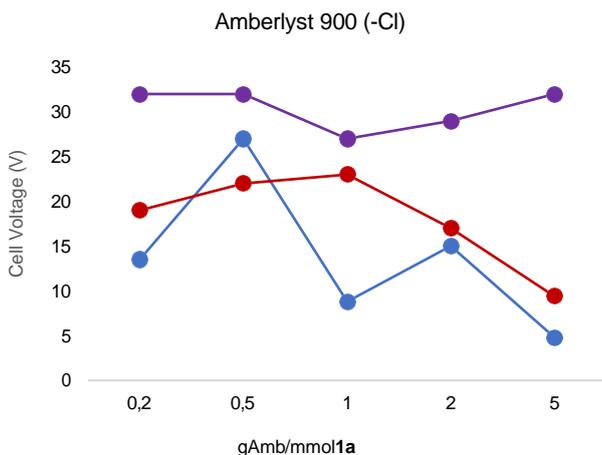
temperature of 25°C while stirring. The voltage value of the DC regulated power supply was taken every 10 seconds during 60 seconds and mediated to give the values indicated in the plots.

### 3.3 Plot gAmb/mmol 1a and gAmb/Vmed for different Amberlyst materials

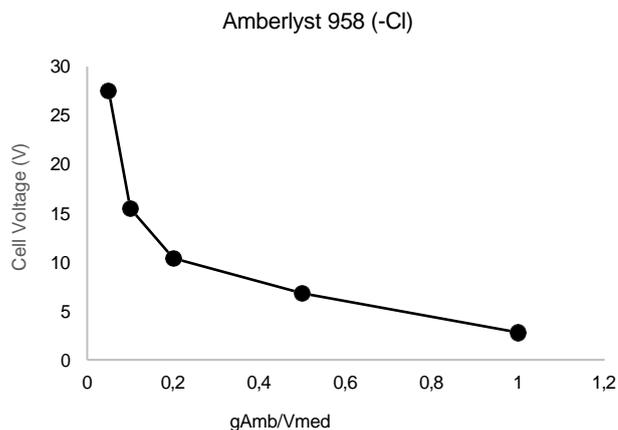
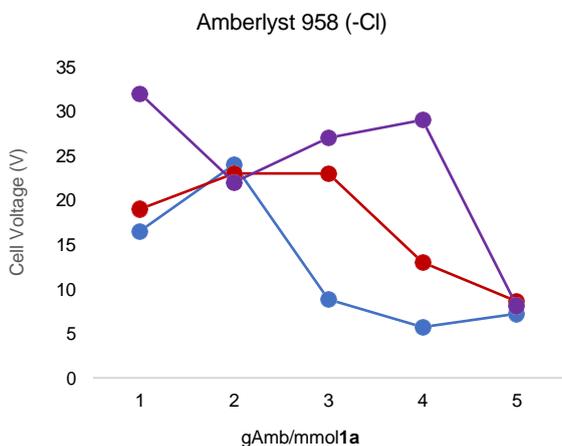
#### AMBERLYST A26 (-OH)



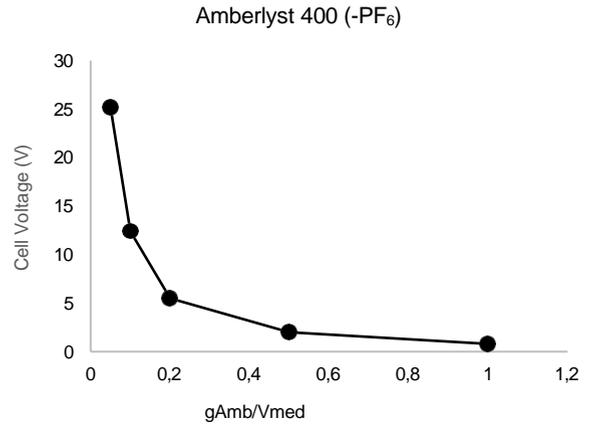
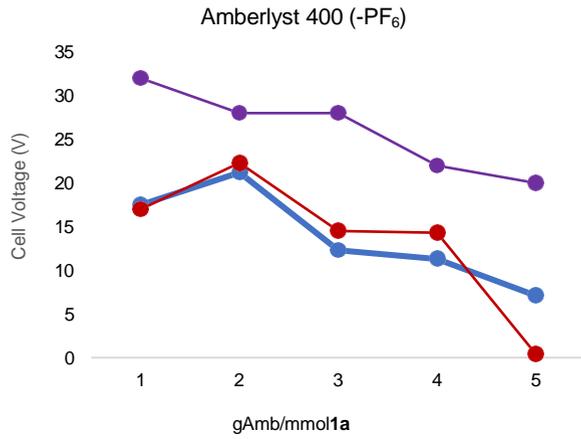
#### AMBERLYST 900 (-Cl)



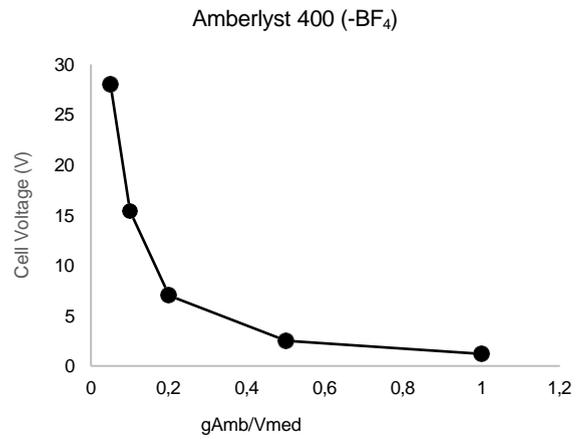
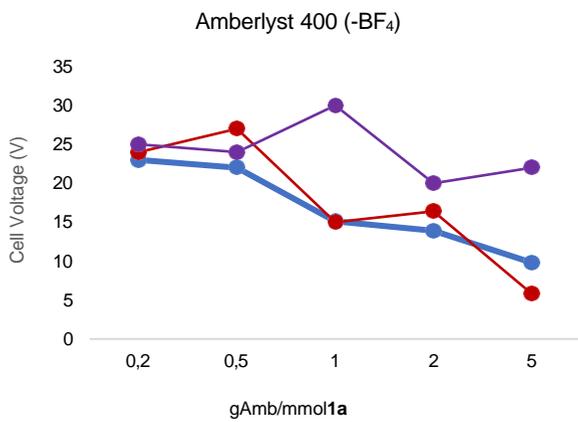
#### AMBERLYST 958 (-Cl)



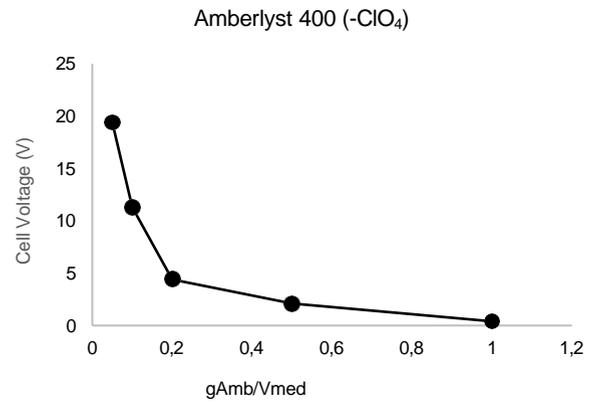
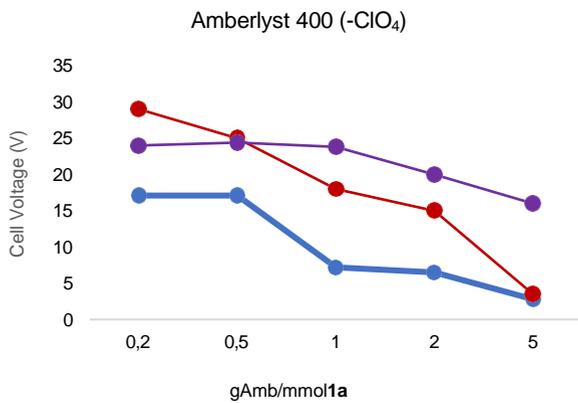
AMBERLYST 400 (-PF<sub>6</sub>)



AMBERLYST 400 (-BF<sub>4</sub>)



AMBERLYST 400 (-ClO<sub>4</sub>)



### 3.4 Resistance of the solution during gAmb/mmol 1a and gAmb/Vmed experiments for different Amberlyst materials.

Amberlyst 400-(Cl)	Current Intensity (A)	gAmb/mmol1a <sup>a</sup>	Cell Voltage (V)	Resistance (Ω)	gAmb/Vmed (g/mL)	Cell Voltage (V)	Resistance (Ω)
	0.006	0.2	32.0	5333	0.05	28.8	4800
	0.006	0.5	32.0	5333	0.1	14.3	2383
	0.006	1	31.0	5166	0.2	7.2	1200
	0.006	2	29.0	4833	0.5	3.8	633
	0.006	5	29.0	4833	1	1.7	283
	0.006	0.2	31.1	5183			
	0.006	0.5	29.0	4833			
	0.006	1	14.5	2416			
	0.006	2	7.3	1216			
	0.006	5	0.6	100			
	0.006	0.2	13.5	2250			
	0.006	0.5	25.0	4166			
	0.006	1	14.0	2333			
	0.006	2	15.0	2500			
	0.006	5	2.8	4667			

<sup>a</sup> Purple: in 10 mL of acetonitrile; Red: in 5 mL of acetonitrile; Blue: in 2 mL of acetonitrile.

Amberlyst A26 (-OH)	Current Intensity (A)	gAmb/mmol1a <sup>a</sup>	Cell Voltage (V)	Resistance (Ω)	gAmb/Vmed (g/mL)	Cell Voltage (V)	Resistance (Ω)
	0.006	0.2	32.0	5333	0.05	31.5	5250
	0.006	0.5	32.0	5333	0.1	23.4	3900
	0.006	1	32.0	5333	0.2	15.5	2583
	0.006	2	26.0	4333	0.5	8.9	1483
	0.006	5	29.0	4833	1	7.2	1200
	0.006	0.2	24.4	4067			
	0.006	0.5	29.0	4833			
	0.006	1	17.9	2983			
	0.006	2	18.5	3083			
	0.006	5	0.6	100			
	0.006	0.2	18.7	3117			
	0.006	0.5	20.1	3350			
	0.006	1	16.5	2750			
	0.006	2	16.9	2817			
	0.006	5	9.3	1550			

<sup>a</sup> Purple: in 10 mL of acetonitrile; Red: in 5 mL of acetonitrile; Blue: in 2 mL of acetonitrile.

Amberlyst 900-(Cl)	Current Intensity (A)	gAmb/mmol1a <sup>a</sup>	Cell Voltage (V)	Resistance (Ω)	gAmb/Vmed (g/mL)	Cell Voltage (V)	Resistance (Ω)
	0.006	0.2	32.0	5333	0.05	30.1	5017
	0.006	0.5	32.0	5333	0.1	15.7	2617
	0.006	1	27.0	4500	0.2	9.8	1633
	0.006	2	29.0	4833	0.5	4.8	800
	0.006	5	32.0	5333	1	2.8	467
	0.006	0.2	19.0	3167			
	0.006	0.5	22.0	3667			
	0.006	1	23.0	3833			
	0.006	2	17.0	2833			
	0.006	5	9.4	1567			
	0.006	0.2	13.5	2250			
	0.006	0.5	27.0	4166			
	0.006	1	8.8	2333			
	0.006	2	15.0	2500			
	0.006	5	4.8	800			

<sup>a</sup> Purple: in 10 mL of acetonitrile; Red: in 5 mL of acetonitrile; Blue: in 2 mL of acetonitrile.

Amberlyst 958-(Cl)	Current Intensity (A)	gAmb/mmol1a <sup>a</sup>	Cell Voltage (V)	Resistance (Ω)	gAmb/Vmed (g/mL)	Cell Voltage (V)	Resistance (Ω)
	0.006	0.2	32.0	5333	0.05	27.5	4583
	0.006	0.5	22.0	3667	0.1	15.5	2583
	0.006	1	27.0	4500	0.2	10.4	1733
	0.006	2	29.0	4833	0.5	6.8	1133
	0.006	5	8.1	1350	1	2.8	467
	0.006	0.2	19.0	3167			
	0.006	0.5	23.0	3833			
	0.006	1	23.0	3833			
	0.006	2	13.0	2167			
	0.006	5	8.6	1433			
	0.006	0.2	16.5	2750			
	0.006	0.5	24.0	4000			
	0.006	1	8.8	1467			
	0.006	2	5.7	950			
	0.006	5	7.2	1200			

<sup>a</sup> Purple: in 10 mL of acetonitrile; Red: in 5 mL of acetonitrile; Blue: in 2 mL of acetonitrile.

Amberlyst 400-(PF <sub>6</sub> )	Current Intensity (A)	gAmb/mmol1a <sup>a</sup>	Cell Voltage (V)	Resistance (Ω)	gAmb/Vmed (g/mL)	Cell Voltage (V)	Resistance (Ω)
	0.006	0.2	17.5	2917	0.05	25.2	4200
	0.006	0.5	21.2	3533	0.1	12.4	2067
	0.006	1	12.3	2050	0.2	5.5	917
	0.006	2	11.3	1883	0.5	2.0	333
	0.006	5	7.1	1183	1	0.8	133
	0.006	0.2	17.0	2833			
	0.006	0.5	22.3	3717			
	0.006	1	14.5	2417			
	0.006	2	14.3	2383			
	0.006	5	0.4	67			
	0.006	0.2	32.0	5333			
	0.006	0.5	28.0	4667			
	0.006	1	28.0	4667			
	0.006	2	22.0	3667			
	0.006	5	20.0	3333			

<sup>a</sup> Purple: in 10 mL of acetonitrile; Red: in 5 mL of acetonitrile; Blue: in 2 mL of acetonitrile.

Amberlyst 400-(BF <sub>4</sub> )	Current Intensity (A)	gAmb/mmol1a <sup>a</sup>	Cell Voltage (V)	Resistance (Ω)	gAmb/Vmed (g/mL)	Cell Voltage (V)	Resistance (Ω)
	0.006	0.2	23.0	3833	0.05	28.0	4667
	0.006	0.5	22.0	3667	0.1	15.4	2567
	0.006	1	15.1	2517	0.2	7.0	1167
	0.006	2	13.9	2317	0.5	2.5	417
	0.006	5	9.8	1633	1	1.2	200
	0.006	0.2	24.0	4000			
	0.006	0.5	27.0	4500			
	0.006	1	15.0	2500			
	0.006	2	16.4	2733			
	0.006	5	5.8	967			
	0.006	0.2	25.0	4167			
	0.006	0.5	24.0	4000			
	0.006	1	30.0	5000			
	0.006	2	20.0	3333			
	0.006	5	22.0	3667			

<sup>a</sup> Purple: in 10 mL of acetonitrile; Red: in 5 mL of acetonitrile; Blue: in 2 mL of acetonitrile.

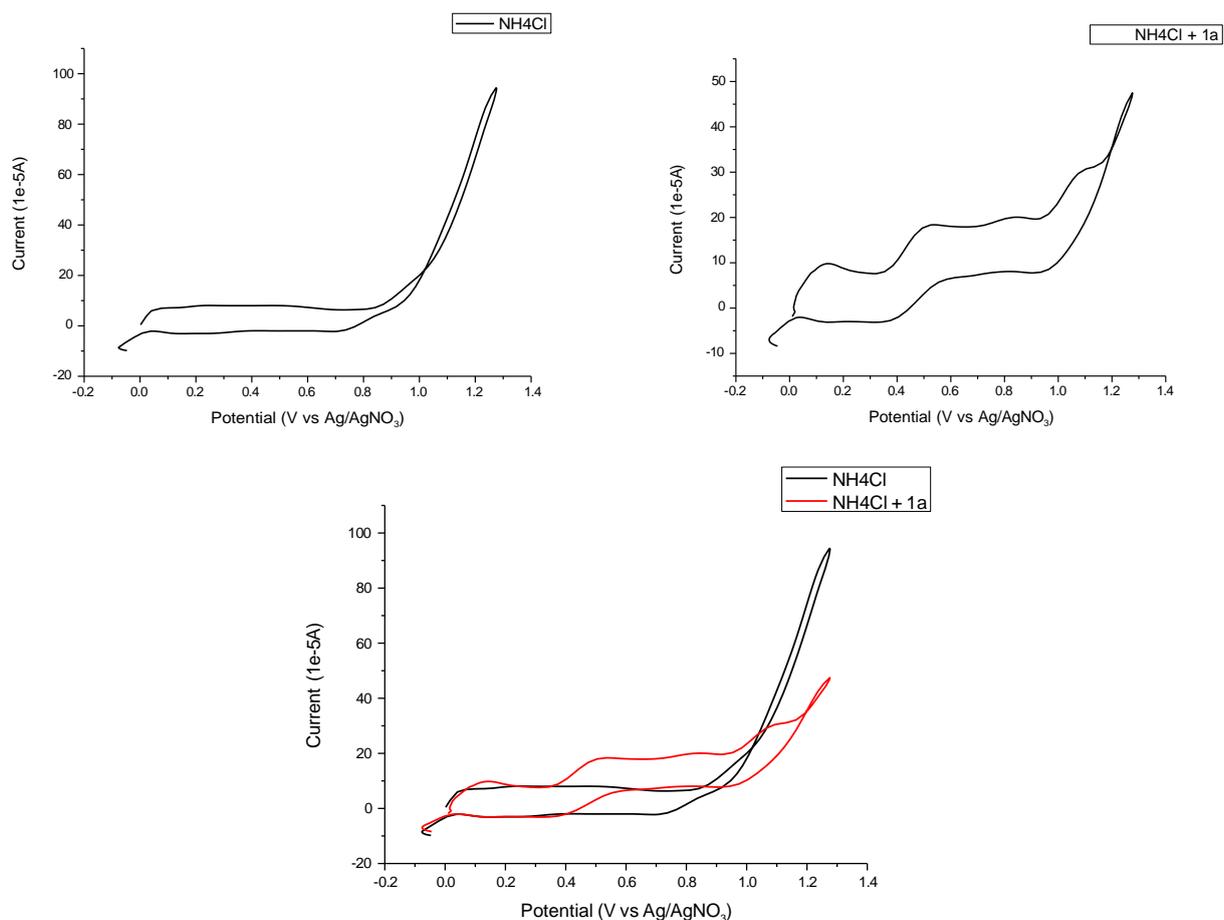
Amberlyst 400-(ClO <sub>4</sub> )	Current Intensity (A)	gAmb/mmol1a <sup>a</sup>	Cell Voltage (V)	Resistance (Ω)	gAmb/Vmed (g/mL)	Cell Voltage (V)	Resistance (Ω)
	0.006	0.2	17.1	2850	0.05	19.4	3233
	0.006	0.5	17.1	2850	0.1	11.3	1883
	0.006	1	7.2	1200	0.2	4.4	733
	0.006	2	6.5	1083	0.5	2.1	350
	0.006	5	2.8	467	1	0.4	67
	0.006	0.2	29.0	4833			
	0.006	0.5	25.0	4167			
	0.006	1	18.0	3000			
	0.006	2	15.0	2500			
	0.006	5	3.5	583			
	0.006	0.2	24.0	4000			
	0.006	0.5	24.4	4067			
	0.006	1	23.8	3967			
	0.006	2	20.0	3333			
	0.006	5	16.0	2667			

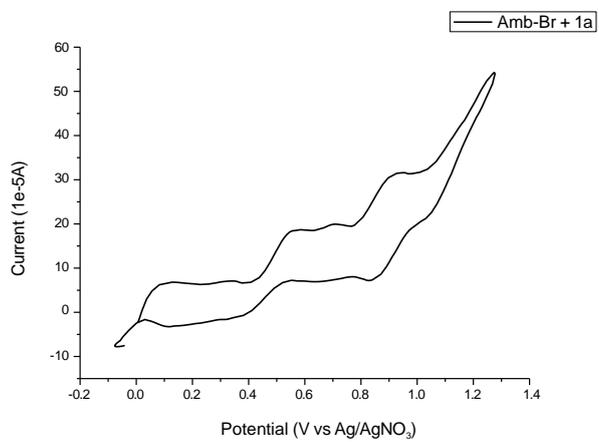
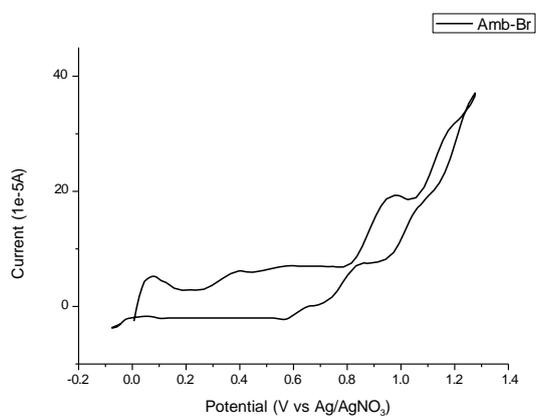
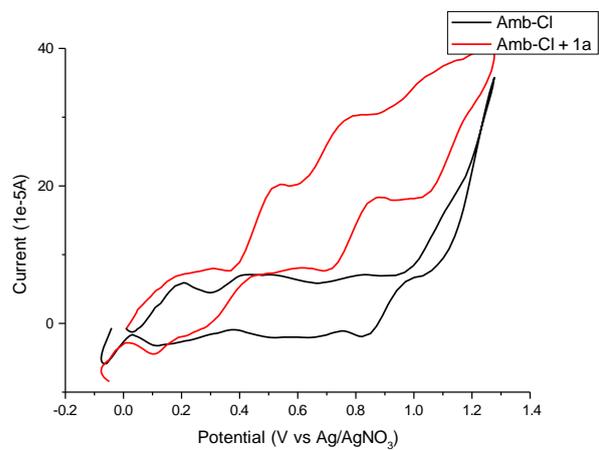
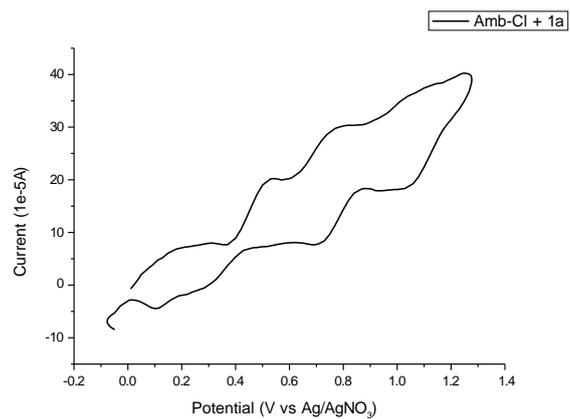
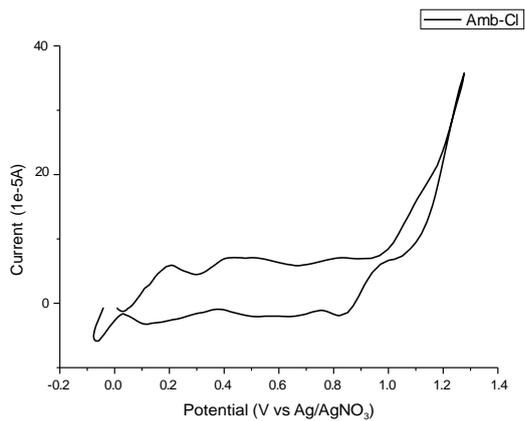
<sup>a</sup> Purple: in 10 mL of acetonitrile; Red: in 5 mL of acetonitrile; Blue: in 2 mL of acetonitrile.

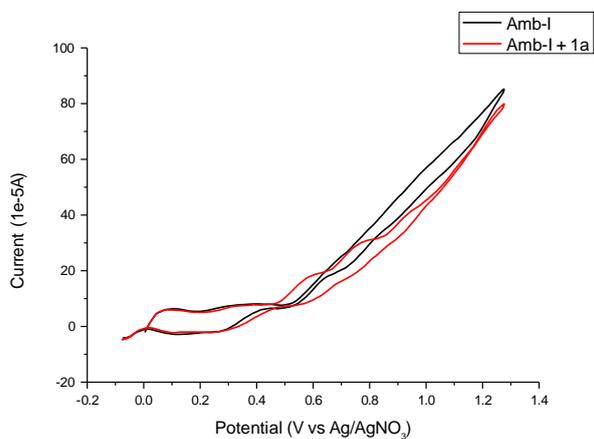
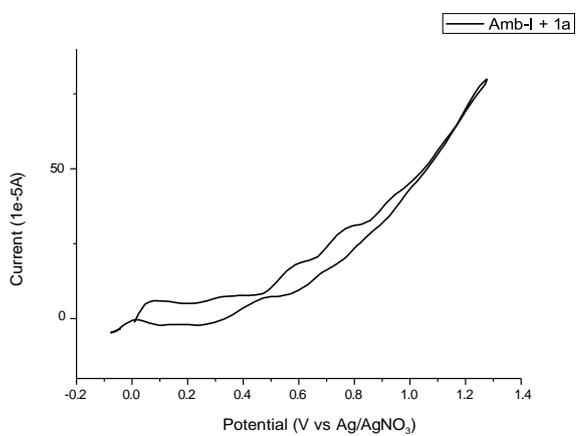
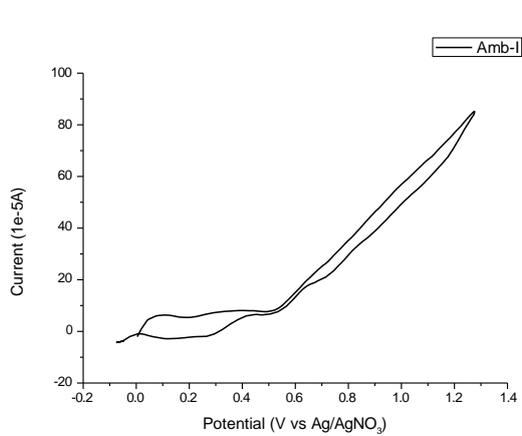
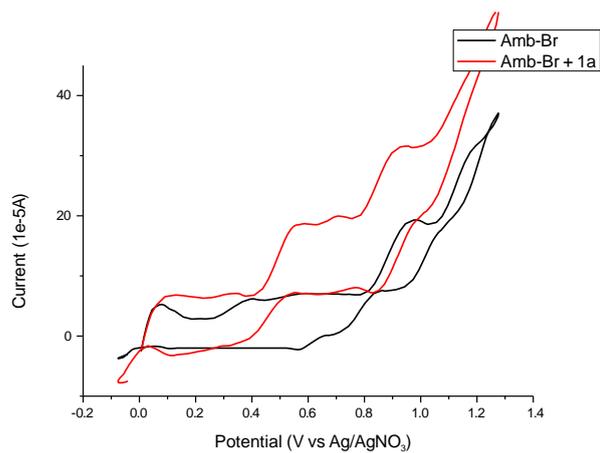
#### 4. General procedure for cyclic voltammetry (CV)

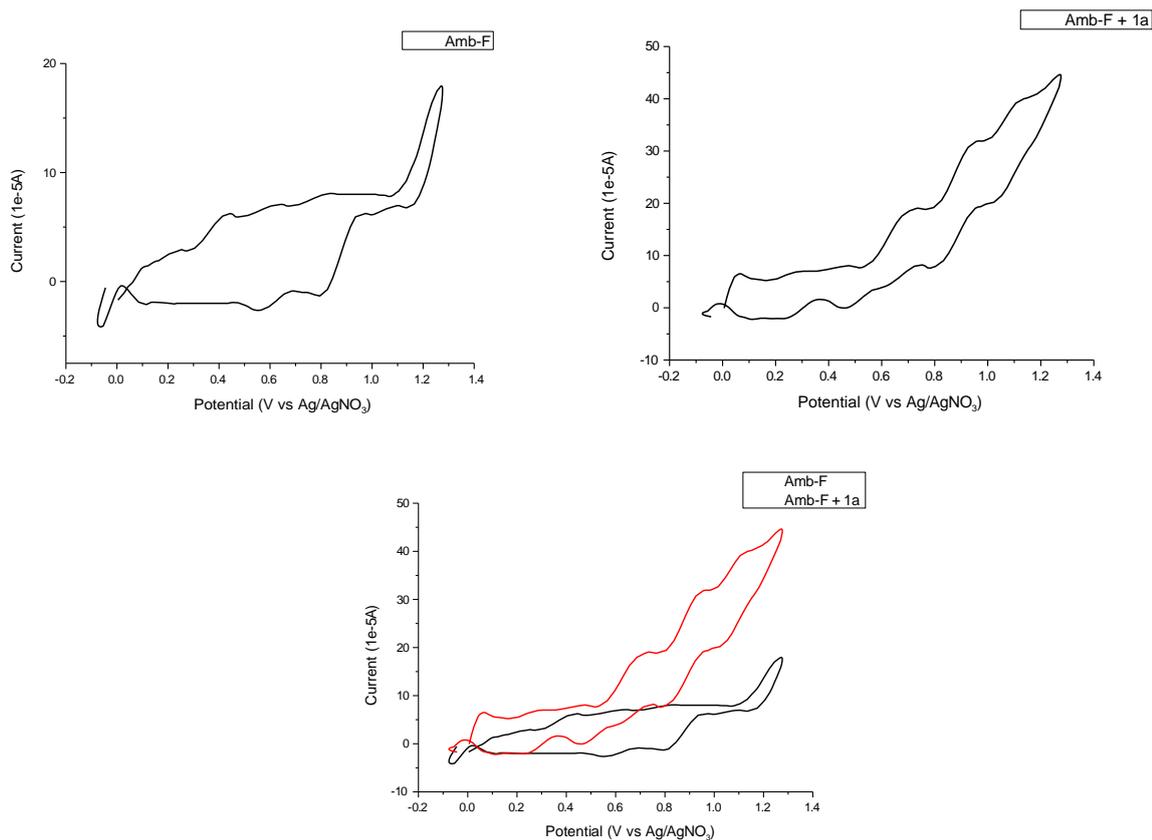
Cyclic voltammetry was completed on an IKA ElectraSyn 2.0 operating in CV mode at a scan rate of  $100 \text{ mVs}^{-1}$ . Initial potential was  $V=0$  with oxidative direction to the upper potential of  $V=1.3$  and lower potential of  $V=-0.1\text{V}$  and the final potential was  $V=0$ . All measurements were conducted at a room temperature of  $25 \text{ }^\circ\text{C}$ . An IKA glassy carbon working electrode, an IKA platinum plated counter electrode, and an IKA  $\text{Ag}/\text{AgNO}_3$  reference electrode filled with  $0.1 \text{ M}$  solution of  $\text{AgNO}_3$  in acetonitrile were used together in a  $10 \text{ mL}$  ElectraSyn glass vial. Acetonitrile was degassed prior to use with three freeze-pump-thaw cycle. The glassy carbon working electrode was rinsed with water, acetone, acetonitrile, allowed to air dry and polished with an alumina slurry before use and between measurements. The platinum counter electrode was rinsed with water, acetone and acetonitrile and allowed to air dry before use and between measurements. The  $\text{Ag}/\text{AgNO}_3$  reference electrode was stored in  $0.1 \text{ M}$  acetonitrile  $\text{AgNO}_3$  solution (keep in dark) between measurements. The Electrasyn 2.0 technical data sheet provides a specification for the current measuring accuracy being  $\pm 0.1 \text{ mA}$ , a voltage measuring accuracy of  $\pm 0.01 \text{ V}$ , a current measuring resolution of  $0.1 \text{ mA}$ , and a voltage measuring resolution of  $0.01 \text{ V}$ .

#### 4.1 Cyclic Voltammetry of $\text{NH}_4\text{Cl}$ and different Amberlyst 400 (Halogen) with and without 1a





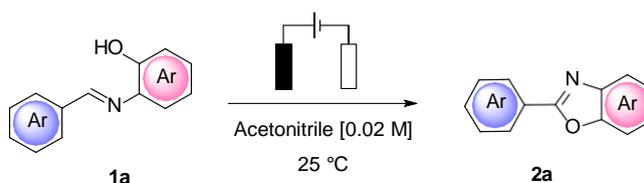




## 5. General Procedures for optimization of solvents, electrode and current using Amberlyst 400 (-Cl) as supporting electrolyte:

A beaker-type cell was equipped with the electrodes of choice, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1g of Amberlyst 400 (-Cl), imine **1a** (0.1 mmol, 19.7 mg), the solvent of choice (5mL) and 100  $\mu$ L of water if indicated in tables. The mixture was electrolyzed using constant current conditions (as indicated in tables) at a temperature of 25°C while stirring. The electrolysis was continued until the indicated times in tables. Once the electrolysis was stopped, the solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. If needed the pure product **2a** was obtained by column chromatography on silica gel using petroleum ether and ethyl acetate as eluents (9:1)

**Table S2: Screening of solvent, electrode and current for the electrosynthesis of 2a using Amberlyst400 (-Cl) as supporting electrolyte.**



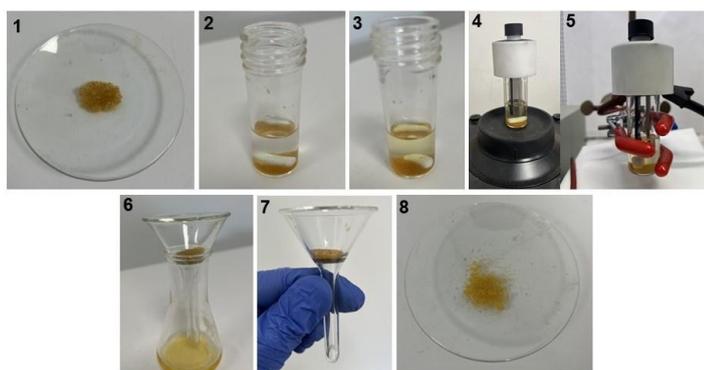
Entry	solvent	Cathode/Anode	CCE	<b>3</b> [%] <sup>p</sup>
1	CH <sub>3</sub> CN	C/AI	6mA	92
2	CH <sub>3</sub> CN	C/AI	8mA	92

3	CH <sub>3</sub> CN	C/Al	2mA	88
4	CH <sub>3</sub> CN	Al/Al	6mA	49
5	CH <sub>3</sub> CN	Al/Al	8mA	53
6	CH <sub>3</sub> CN	Al/Al	2mA	43
7	CH <sub>3</sub> CN	GC/Al	6mA	94
8	CH <sub>3</sub> CN	GC/Al	8mA	94
9	CH <sub>3</sub> CN	GC/Al	2mA	92
10	CH <sub>3</sub> CN	C/Pt	6mA	88
11	CH <sub>3</sub> CN	C/Pt	8mA	92
12	CH <sub>3</sub> CN	C/Pt	2mA	84
13	CH <sub>3</sub> CN	Pt/Pt	6mA	68
14	CH <sub>3</sub> CN	Pt/Pt	8mA	65
15	CH <sub>3</sub> CN	Pt/Pt	2mA	45
16	CH <sub>3</sub> CN	GC/Pt	6mA	95
17	CH <sub>3</sub> CN	GC/Pt	8mA	95
18	CH <sub>3</sub> CN	GC/Pt	2mA	92
19	CH <sub>3</sub> CN	C/C	6mA	83
20	CH <sub>3</sub> CN <sup>c</sup>	C/Al	6mA	90
21	CH <sub>3</sub> CN <sup>d</sup>	C/Al	6mA	-
22	CH <sub>3</sub> CN <sup>e</sup>	C/Al	6mA	-
23	CH <sub>3</sub> CN/water (Azeotrope)	C/Al	6mA	74
24	CH <sub>3</sub> CN/MeOH 1:1 v/v	C/Al	6mA	73
25	CH <sub>3</sub> CN/MeOH (Azeotrope)	C/Al	6mA	58
26	THF	C/Al	6mA	67
27	2MeTHF/MeOH/water <sup>f</sup>	C/Al	6mA	79
28	2MeTHF/ CH <sub>3</sub> CN /water <sup>g</sup>	C/Al	6mA	77
29	CH <sub>3</sub> CN	C/Al	6mA	7 <sup>[h]</sup>
30	CH <sub>3</sub> CN	C/Al	-	- <sup>[k]</sup>

[a] Reaction conditions: undivided cell, **1a** (0.1 mmol), solvent 5 mL, Amberlyst400 (-Cl) (1g), 100  $\mu$ L of water, at constant current, 3 h at 25 °C. [b] Isolated yield. [c] Without water; [d] Reaction run without current at 3h. [e] Reaction run without current at 24h; [f] in the followed composition: 2MeTHF (5 mL), MeOH (0.8 mL), Water (0.2 mL); [g] in the followed composition: 2MeTHF (5 mL), CH<sub>3</sub>CN (0.8 mL), Water (0.2 mL); [h] reaction without Amberlyst 400 (-Cl); [k] reaction without current.

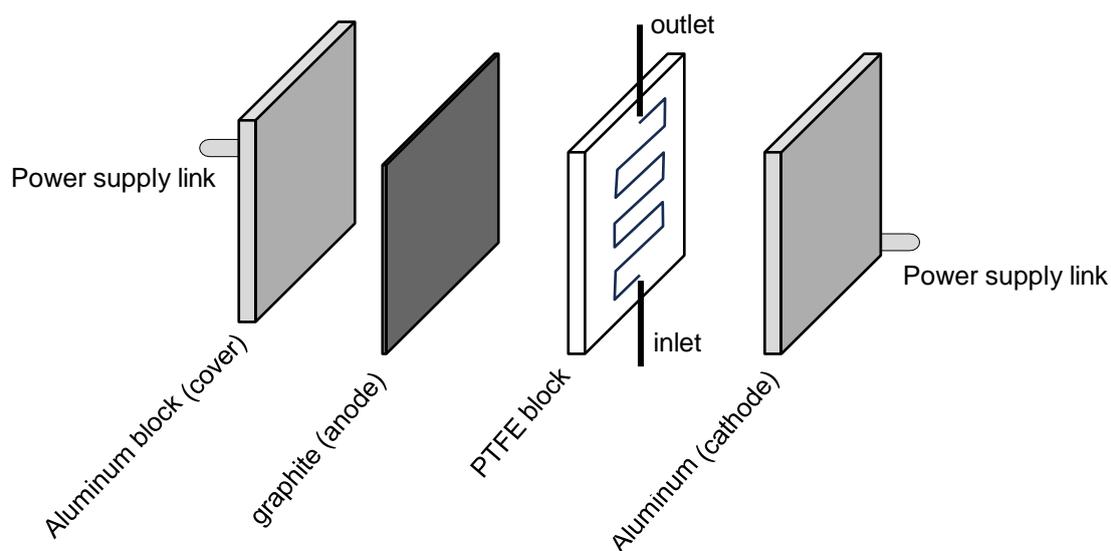
## 6. General Procedures for optimized protocol using Amberlyst 400 (-Cl) as supporting electrolyte:

A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1g of Amberlyst 400 (-Cl), imine **1a** (0.1 mmol, 19.7 mg), acetonitrile (5mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped, the solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2a** was obtained in 92% yield (18.0 mg) simply by evaporating ethyl acetate.



1. Amberlyst was weighed
2. Amberlyst was loaded in a vial
3. **1a** was loaded in the vial
4. Analytical electrochemical set-up
5. Preparative electrochemical set-up
6. Filtration over sintered funnel
7. Dry
8. Ready to use for second run

**Figure S1** Flow system exploded-view.



## 7. General procedures for flow experiments

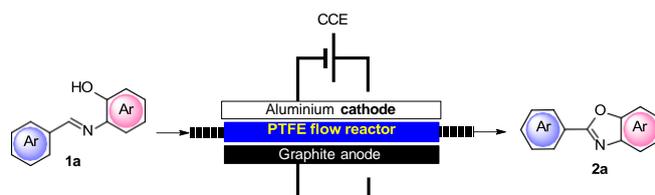
### 7.1 General Procedures for flow optimization using syringe pump.

A 8 mL glass vial was charged with 0.1 mmol of **1a** (19.7 mg) and 5mL of acetonitrile. The electrochemical flow cell equipped with a graphite foil as anode and an aluminum block as cathode was connected to a DC regulated power supply and to a syringe pump through proper PTFE connections and wires. The reaction mixture was transferred from the glass vial to the syringe pump and flowed inside the cell at the desired flow rate while electrolyzed using constant current conditions (as indicated in tables). The electrolysis was continued until the indicated times in tables. Once the electrolysis was stopped and the whole reaction mixture flowed through the flow cell for the desired residence time, the solvent was evaporated, and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography.

### 7.2 General Procedures for flow optimization using peristaltic pump.

A 8 mL glass vial was charged with 0.1 mmol of **1a** (19.7 mg) and 5mL of acetonitrile. The electrochemical flow cell equipped with a graphite foil as anode and an aluminum block as cathode was connected to a DC regulated power supply and to a peristaltic pump through proper PTFE connections and wires. The reaction mixture was directly pumped from the 12mL glass vial inside the electrochemical cell at the desired flow rate while electrolyzed using constant current conditions (as indicated in tables). The electrolysis was continued until the indicated times in tables. Once the electrolysis was stopped and the whole reaction mixture flowed through the flow cell for the desired residence time, the solvent was evaporated, and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography.

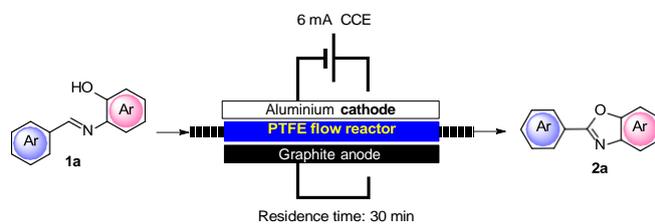
**Table S3:** Flow parameters optimization for the synthesis of **2a**



Entry	Residence time (min)	CCE	2a [%] <sup>b</sup>
1	10	8 mA	38
2	20	8 mA	65
3	30	8 mA	60
4	40	8 mA	56
5	90	8 mA	44
6	10	6 mA	32
7	20	6 mA	77
8	30	6 mA	95
9	40	6 mA	95
10	90	6 mA	92
11	10	4 mA	15
12	20	4 mA	45
13	30	4 mA	79
14	40	4 mA	87
15	90	4 mA	93
16	10	2 mA	11
17	20	2 mA	44
18	30	2 mA	75
19	40	2 mA	81
20	90	2 mA	94
21 <sup>c</sup>	90	-	-

[a] Reaction conditions: **1a** (0.1 mmol), solvent 5 mL, Amberlyst400 (-Cl) (1g), at constant current and 25 °C. [b] Isolated yield; [c] without current

**Table S4:** Screening of different concentration for the flow electro-synthesis of **2a**



Entry	Concentration of <b>1a</b> [M]	2a [%] <sup>b</sup>
1	0.01	95
2	0.02	95
3	0.03	95
4	0.05	95

5	0.1	90
6	0.2	90
7	0.5	86

---

[a] Reaction conditions: **1a** (0.1 mmol), Amberlyst400 (-Cl) (1g), at constant current of 6 mA, 30 min at 25 °C. [b] Isolated yield.

### 7.3 Optimized Procedures for 12 h continuous electrochemical flow using peristaltic pump

A 100 mL round bottom flask was charged with 5 mmol of **1a** (986 mg) and 100 mL of acetonitrile. The electrochemical flow cell equipped with a graphite foil as anode and an aluminum block as cathode was connected to a DC regulated power supply and to a peristaltic pump through proper PTFE connections and wires. The reaction mixture was directly pumped from the flask inside the electrochemical cell at a flow rate of 130  $\mu\text{L min}^{-1}$  using constant current conditions (6 mA). The electrolysis was continued during 12 h. The electrolysis was stopped, the solvent was evaporated to give **2a** in 90 % yield (878 mg).

#### 7.4 Yields comparison from batch to flow experiments.

Yields in flow were obtained following the optimized Procedures for flow optimization using peristaltic pump as follows:

A 4 mL glass vial was charged with 0.1 mmol of substrate and 2mL of acetonitrile. The electrochemical flow cell equipped with a graphite foil as anode and an aluminum block as cathode was connected to a DC regulated power supply and to a peristaltic pump through proper PTFE connections and wires. The reaction mixture was directly pumped from the 4 mL glass vial inside the electrochemical cell at the desired flow rate while electrolyzed using constant current conditions (6mA). Once the electrolysis was stopped and the whole reaction mixture flowed through the flow cell for the desired residence time (30 minutes), the solvent was evaporated to yield products **2a-p**. To obtain product **2q** the same procedures was followed by using 3mL of 2MeTHF:MeOH (5:1) as reaction medium.

Product	 Batch	 Flow
<b>2a</b>	92 %	95%
<b>2b</b>	95%	96%
<b>2c</b>	87%	90%
<b>2d</b>	85%	85%
<b>2e</b>	82%	84%
<b>2f</b>	82%	83%
<b>2g</b>	96%	96%
<b>2h</b>	90%	93%
<b>2i</b>	92%	96%
<b>2j</b>	87%	90%
<b>2k</b>	90%	92%
<b>2l</b>	97%	97%
<b>2m</b>	95%	97%
<b>2n</b>	92%	94%
<b>2o</b>	77%	79%
<b>2p</b>	78%	79%
<b>2q (Tafamidis)</b>	72%	74%

## 8. Metrics Calculations<sup>2</sup>

Colors have been used to differentiate the contribution to the E-factor as follows: E-kernel, E-reaction solvent, E-catalyst, E-work-up, Product. Supporting Electrolyte Mass is differentiated inside the kernel parenthesis. RME and MRP were calculated as follows from the E-factor values: RME:  $1/(1 - \text{E-factor}) * 100$ ; MRP:  $[(\text{RME}/100)*\text{SF}]/(0.01*\text{AE}*0.01*\text{Yield})$ . eE-factor were calculated using Supporting Electrolyte Mass/Product Mass.

a) *Adv. Synth. Catal.* 2013, **355**, 2884-2890

E-factor:  $[(0.1972 + 0.0299 + 0.1059 + 0.0840) + 6.6500 + 10.0000 + 58.5000 - 0.1542] / 0.1542 = 489.06$

b) *RSC Adv.* 2013, **3**, 7330-7336

E-factor:  $[(0.1000 + 0.5376 + 0.2127) + 7.9200 + 13.3000 - 0.0858] / 0.0858 = 255.96$

c) *Chem. – Eur. J.*, 2016, **22**, 5425–5429

E-factor:  $[(0.0540 + 0.0818 + 0.0531) + 3.8500 + 0.1000 + 0.1102 + 0.0281 + 40.6000 - 0.0390] / 0.0390 = 1148.52$

d) *J. Electroanal. Chem.*, 2016, **767**, 13–17

E-factor:  $[(0.0986 + 0.1071 + 0.1224) + 7.9200 + 0.0229 + 58.5000 - 0.0585] / 0.0585 = 1139.21$

e) *J. Org. Chem.*, 2017, **82**, 11669–11681

E-factor:  $[(0.0591 + 0.1288) + 7.1520 + 0.8000 + 35.6500 - 0.0509 - 0.1210_{(\text{recovered SE})}] / 0.0509 = 856.09$

f) *Angew. Chem., Int. Ed.*, 2019, **58**, 9811–9815

E-factor:  $[(0.1045 + 0.1081 + 0.0085) + 5.5020 + 7.3670 + 10.0000 + 31.5700 + 30.0000 - 0.1040] / 0.1040 = 813.04$

g) *ChemElectroChem* 2020, **7**, 3969–3974

E-factor:  $[(0.0106 + 0.0109 + 0.0270) + 3.9300 + 40.5900 - 0.01698] / 0.01698 = 2623.76$

h) *Org. Lett.*, 2020, **22**, 4000-4005

E-factor:  $[(0.0500 + 0.0700 + 0.0380) + 7.9200 + 8.0000 - 0.0312] / 0.0312 = 514.32$

i) *ChemistrySelect* 2021, **6**, 8080–8084

E-factor:  $[(0.0970 + 0.0993 + 0.3150) + 3.9300 - 0.0900] / 0.0900 = 48.34$

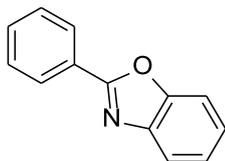
j) *ChemElectroChem*, 2022, **9**, e202200787

E-factor:  $[(0.0327 + 0.1099 + 0.1063) + 7.8600 + 0.0083 + 10.0000 + 80.000 + 18.0400 - 0.0135] / 0.0135 = 8603.24$

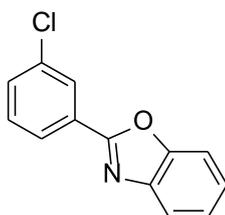
*This work*

E-factor:  $[(0.9860) + 78.6000 - 0.8780 - 71.2000_{(\text{recovered acetonitrile})}] / 0.8780 = 8.55$

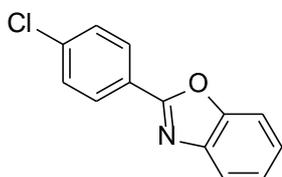
## 9. Characterization Data of synthesized products 1a-q



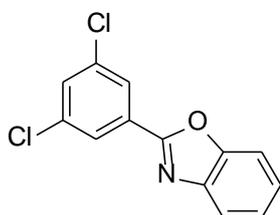
**2-phenylbenzo[d]oxazole (2a):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1a** (0.2 mmol, 39.4 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2a** was obtained in 92% yield (36.0 mg) simply by evaporating ethyl acetate. Pale brown powder. **m.p.** 103-104 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.28 – 8.26 (m, 2H), 7.80 – 7.77 (m, 1H), 7.60 – 7.58 (m, 1H), 7.54 – 7.53 (m, 3H), 7.37 – 7.35 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  163.2, 150.9, 142.2, 131.7, 129.1, 127.8, 127.3, 125.2, 124.7, 120.2, 110.7. **GC-EIMS** (m/z, %): 195 (M<sup>+</sup>, 100), 169 (42), 143 (25), 117 (15), 93 (15). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>9</sub>NO: C: 79.98, H: 4.65, N: 7.17; Found: C: 79.99, H: 4.64, N: 7.21



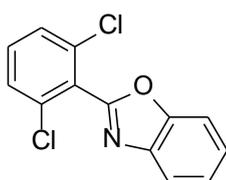
**2-(3-chlorophenyl)benzo[d]oxazole (2b):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1b** (0.2 mmol, 46.3 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2b** was obtained in 95% yield (43.6 mg) simply by evaporating ethyl acetate. Yellowish powder. **m.p.** 123-125 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.26 (t, *J* = 1.9 Hz, 1H), 8.14 (d, *J* = 7.5 Hz, 1H), 7.79 – 7.77 (m, 1H), 7.60 – 7.58 (m, 1H), 7.51 – 7.44 (m, 2H), 7.39 – 7.36 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  161.8, 150.9, 142.0, 135.2, 131.6, 130.4, 129.0, 127.8, 125.8, 125.7, 125.0, 120.4, 110.8. **GC-EIMS** (m/z, %): 231 (M<sup>+</sup>+2, 33), 229 (M<sup>+</sup>, 100), 209 (21), 207 (64), 194 (15), 167 (25). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>8</sub>NO: C: 67.99, H: 3.51, N: 6.10; Found: C: 68.01, H: 3.54, N: 6.15



**2-(4-chlorophenyl)benzo[d]oxazole (2c):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1c** (0.2 mmol, 46.3 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2c** was obtained in 87% yield (40.0 mg) simply by evaporating ethyl acetate. Pale brown powder. **m.p.** 150-153 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.18 (d,  $J$  = 8.6 Hz, 2H), 7.78 – 7.75 (m, 1H), 7.59 – 7.57 (m, 1H), 7.50 (d,  $J$  = 8.6 Hz, 2H), 7.38 – 7.35 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  162.2, 150.9, 142.1, 137.9, 129.4, 129.0, 125.7, 125.5, 124.9, 120.2, 110.8. **GC-EIMS** (m/z, %): 231 (M<sup>+</sup>+2, 33), 229 (M<sup>+</sup>, 100), 193 (57), 165 (15), 118 (17). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>8</sub>NO: C: 67.99, H: 3.51, N: 6.10; Found: C: 67.95, H: 3.55, N: 6.12

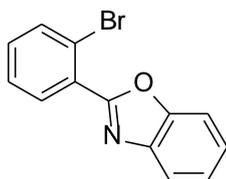


**2-(3,5-dichlorophenyl)benzo[d]oxazole (2d):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1d** (0.2 mmol, 53.2 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2d** was obtained in 85% yield (44.9 mg) simply by evaporating ethyl acetate. **m.p.** 139-140 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.14 (d,  $J$  = 2.0 Hz, 2H), 7.80 – 7.77 (m, 1H), 7.61 – 7.58 (m, 1H), 7.51 (t,  $J$  = 1.9 Hz, 1H), 7.41 – 7.39 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  160.5, 151.0, 141.9, 135.9, 131.4, 130.0, 126.1, 126.0, 125.2, 120.6, 111.0. **GC-EIMS** (m/z, %): 265 (M<sup>+</sup>+2, 100), 263 (M<sup>+</sup>, 65), 231 (47), 229 (15), 132 (20), 118 (15). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>7</sub>Cl<sub>2</sub>NO: C: 59.12, H: 2.67, N: 5.30; Found: C: 59.15, H: 2.70, N: 5.32

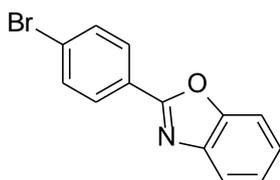


**2-(2,6-dichlorophenyl)benzo[d]oxazole (2e):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1e** (0.2 mmol, 53.2 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove

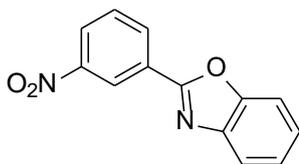
the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2e** was obtained in 82% yield (43.3 mg) simply by evaporating ethyl acetate. **m.p.** 174-175 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.89 – 7.87 (m, 1H), 7.65 – 7.63 (m, 1H), 7.47 – 7.41 (m, 5H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 158.2, 150.9, 141.2, 136.3, 132.3, 128.3, 128.0, 125.9, 124.8, 120.9, 111.1. **GC-EIMS** (m/z, %): 265 (M<sup>+</sup>+2, 100), 263 (M<sup>+</sup>, 63), 231 (42), 229 (15), 133 (15), 117 (22). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>7</sub>Cl<sub>2</sub>NO: C: 59.12, H: 2.67, N: 5.30; Found: C: 59.17, H: 2.64, N: 5.35



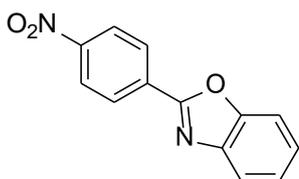
**2-(2-bromophenyl)benzo[d]oxazole (2f):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1f** (0.2 mmol, 55.2 mg), acetonitrile (7mL) and 100 μL of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2f** was obtained in 82% yield (44.9 mg) simply by evaporating ethyl acetate. **m.p.** 138-140 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.09 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.87 – 7.85 (m, 1H), 7.78 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.64 – 7.62 (m, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.42 – 7.37 (m, 3H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 161.7, 150.8, 141.8, 134.8, 132.3, 132.2, 128.6, 127.6, 125.7, 124.8, 122.1, 120.7, 110.9. **GC-EIMS** (m/z, %): 275 (M<sup>+</sup>+2, 98), 273 (M<sup>+</sup>, 100), 223 (57), 221 (55), 167 (45), 142 (15). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>8</sub>BrNO: C: 56.96, H: 2.94, N: 5.11; Found: C: 56.92, H: 2.93, N: 5.14



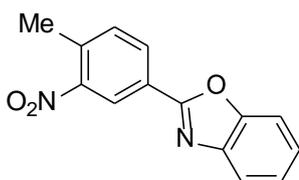
**2-(4-bromophenyl)benzo[d]oxazole (2g):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1g** (0.2 mmol, 55.2 mg), acetonitrile (7mL) and 100 μL of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2g** was obtained in 96% yield (52.6 mg) simply by evaporating ethyl acetate. **m.p.** 158-161 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.13 (d, *J* = 8.6 Hz, 2H), 7.79 – 7.76 (m, 1H), 7.67 (d, *J* = 8.6 Hz, 2H), 7.60 – 7.57 (m, 1H), 7.38 – 7.36 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 162.3, 150.9, 142.2, 132.4, 129.2, 126.4, 126.3, 125.5, 124.9, 120.3, 110.8. **GC-EIMS** (m/z, %): 275 (M<sup>+</sup>+2, 98), 273 (M<sup>+</sup>, 100), 223 (15), 221 (17), 167 (15), 142 (23). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>8</sub>BrNO: C: 56.96, H: 2.94, N: 5.11; Found: C: 56.98, H: 2.95, N: 5.18



**2-(3-nitrophenyl)benzo[d]oxazole (2h):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1h** (0.2 mmol, 48.4 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2h** was obtained in 90% yield (43.2 mg) simply by evaporating ethyl acetate. **m.p.** 210-213 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  9.09 (t,  $J$  = 2.0 Hz, 2H), 8.58 (d,  $J$  = 7.8 Hz, 1H), 8.40 – 8.37 (m, 1H), 7.83 – 7.81 (m, 2H), 7.73 (t,  $J$  = 8.0 Hz, 2H), 7.65 – 7.63 (m, 2H), 7.43 – 7.40 (m, 4H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  160.7, 151.0, 148.9, 141.9, 133.2, 130.3, 129.1, 126.2, 125.9, 125.3, 122.6, 120.7, 111.0. **GC-EIMS** (m/z, %): 240 (M<sup>+</sup>, 100), 214 (45), 194 (15), 188 (24), 92 (15). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>8</sub>N<sub>2</sub>O<sub>3</sub>: C: 65.00, H: 3.36, N: 11.66; Found: C: 65.04, H: 3.40, N: 11.69



**2-(4-nitrophenyl)benzo[d]oxazole (2i):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1i** (0.2 mmol, 48.4 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2i** was obtained in 92% yield (44.2 mg) simply by evaporating ethyl acetate. **m.p.** 258-262 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.46 – 8.38 (m, 4H), 7.83 (dd,  $J$  = 7.4, 1.9 Hz, 1H), 7.64 (dd,  $J$  = 7.6, 1.7 Hz, 1H), 7.45 – 7.42 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  160.8, 151.2, 149.5, 142.1, 133.0, 128.5, 126.5, 125.4, 124.4, 120.8, 111.1. **GC-EIMS** (m/z, %): 240 (M<sup>+</sup>, 100), 218 (15), 193 (15), 92 (15), 78 (15). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>8</sub>N<sub>2</sub>O<sub>3</sub>: C: 65.00, H: 3.36, N: 11.66; Found: C: 65.02, H: 3.38, N: 11.64

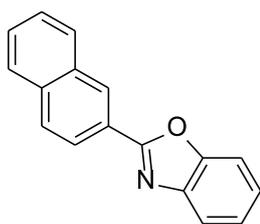


**2-(4-methyl-3-nitrophenyl)benzo[d]oxazole (2j):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1j** (0.2 mmol, 51.2 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current

conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2j** was obtained in 87% yield (44.2 mg) simply by evaporating ethyl acetate. **m.p.** 238-239 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.83 (d, *J* = 1.8 Hz, 1H), 8.36 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.80 – 7.78 (m, 1H), 7.62 – 7.60 (m, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.41 – 7.38 (m, 2H), 2.69 (s, 3H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 160.9, 150.9, 149.8, 142.0, 136.9, 133.7, 131.4, 126.7, 126.0, 125.1, 123.8, 120.5, 110.9, 20.8. **GC-EIMS** (*m/z*, %): 254 (*M*<sup>+</sup>, 100), 240 (56), 206 (15), 192 (48), 176 (15). **Elemental Analysis:** Calc. for C<sub>14</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub>: C: 66.14, H: 3.96, N: 11.02; Found: C: 66.18, H: 3.99, N: 11.05

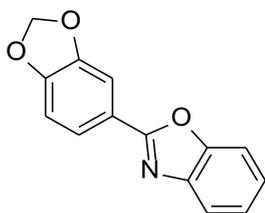


**2-(benzo[d]oxazol-2-yl)phenol (2k):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1j** (0.2 mmol, 42.6 mg), acetonitrile (7mL) and 100 μL of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2j** was obtained in 90% yield (38.0 mg) simply by evaporating ethyl acetate. **m.p.** 121-123 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 11.48 (s, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.74 – 7.72 (m, 1H), 7.62 – 7.60 (m, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.40 – 7.37 (m, 2H), 7.13 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 163.0, 158.9, 149.2, 140.1, 133.7, 127.2, 125.5, 125.1, 119.7, 119.4, 117.6, 110.8, 110.7. **GC-EIMS** (*m/z*, %): 211 (*M*<sup>+</sup>, 100), 183 (48), 157 (42), 118 (15), 76 (20). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>9</sub>NO<sub>2</sub>: C: 73.92, H: 4.30, N: 6.63; Found: C: 73.97, H: 4.35, N: 6.65

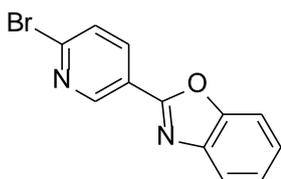


**2-(naphthalen-2-yl)benzo[d]oxazole (2l):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1l** (0.2 mmol, 48.2 mg), acetonitrile (7mL) and 100 μL of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2l** was obtained in 97% yield (47.6 mg) simply by evaporating ethyl acetate. **m.p.** 116-117 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.78 – 8.77 (m, 1H), 8.32 (dd, *J* = 8.6, 1.7 Hz, 1H), 8.00 – 7.96 (m, 2H), 7.90 – 7.88 (m, 1H), 7.83 – 7.81 (m, 1H), 7.64 – 7.56 (m, 3H), 7.39 – 7.37 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 163.3, 151.0, 142.3, 134.9, 133.1, 129.1,

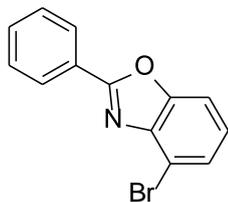
128.9, 128.3, 128.0, 127.9, 127.0, 125.3, 124.8, 124.5, 124.1, 120.2, 110.7. **GC-EIMS** (m/z, %): 245 ( $M^+$ , 100), 219 (15), 205 (22), 143 (17), 112 (16). **Elemental Analysis**: Calc. for  $C_{17}H_{11}NO$ : C: 83.25, H: 4.52, N: 5.71; Found: C: 83.29, H: 4.55, N: 5.74



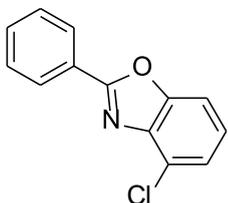
**2-(benzo[d][1,3]dioxol-5-yl)benzo[d]oxazole (2m)**: A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1m** (0.2 mmol, 48.3 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2m** was obtained in 95% yield (45.4 mg) simply by evaporating ethyl acetate. **m.p.** 148-150 °C.  **$^1H$  NMR** (400 MHz,  $CDCl_3$ )  $\delta$  7.83 (dd,  $J = 8.2, 1.7$  Hz, 1H), 7.74 – 7.72 (m, 1H), 7.70 (d,  $J = 1.7$  Hz, 1H), 7.56 – 7.53 (m, 1H), 7.34 – 7.32 (m, 2H), 6.94 (d,  $J = 8.2$  Hz, 1H), 6.07 (s, 2H).  **$^{13}C$  NMR** (101 MHz,  $CDCl_3$ )  $\delta$  163.0, 150.8, 150.7, 148.4, 142.3, 124.9, 124.6, 122.9, 121.3, 119.8, 110.6, 108.9, 107.8, 101.9. **GC-EIMS** (m/z, %): 239 ( $M^+$ , 67), 227 (100), 195 (58), 167 (22), 142 (15). **Elemental Analysis**: Calc. for  $C_{14}H_9NO_3$ : C: 70.29, H: 3.79, N: 5.86; Found: C: 70.32, H: 3.81, N: 5.88



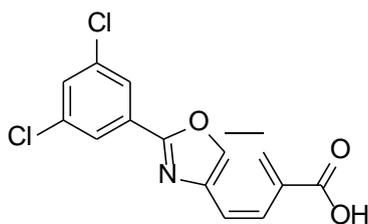
**2-(6-bromopyridin-3-yl)benzo[d]oxazole (2n)**: A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1n** (0.2 mmol, 55.4 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2n** was obtained in 92% yield (51.0 mg) simply by evaporating ethyl acetate. **m.p.** 282-284 °C.  **$^1H$  NMR** (400 MHz,  $CDCl_3$ )  $\delta$  9.21 (d,  $J = 2.5$  Hz, 1H), 8.35 (dd,  $J = 8.3, 2.4$  Hz, 1H), 7.80 – 7.78 (m, 1H), 7.67 (d,  $J = 8.3$  Hz, 1H), 7.62 – 7.60 (m, 1H), 7.42 – 7.39 (m, 2H).  **$^{13}C$  NMR** (101 MHz,  $CDCl_3$ )  $\delta$  160.0, 150.9, 149.1, 145.1, 141.8, 136.9, 128.6, 126.2, 125.3, 123.0, 120.5, 111.0. **GC-EIMS** (m/z, %): 277 ( $M^+ + 2$ , 100), 275 ( $M^+$ , 98), 196 (75), 195 (44), 156 (27), 143 (15). **Elemental Analysis**: Calc. for  $C_{12}H_7BrN_2O$ : C: 52.39, H: 2.56, N: 10.18; Found: C: 52.42, H: 2.58, N: 10.22



**4-bromo-2-phenylbenzo[d]oxazole (2o):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1o** (0.2 mmol, 55.2 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2o** was obtained in 77% yield (42.2 mg) simply by evaporating ethyl acetate. **m.p.** 115-117 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.29 (dd,  $J$  = 7.7, 2.0 Hz, 2H), 7.70 (d,  $J$  = 7.9 Hz, 1H), 7.56 – 7.54 (m, 3H), 7.51 – 7.48 (m, 1H), 7.23 (d,  $J$  = 7.9 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  163.4, 149.1, 143.0, 132.1, 129.1, 128.4, 128.0, 126.7, 125.9, 119.2, 102.7. **GC-EIMS** ( $m/z$ , %): 275 ( $M^+$ +2, 98), 273 ( $M^+$ , 100), 223 (57), 221 (55), 142 (15), 114 (15). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>8</sub>BrNO: C: 56.96, H: 2.94, N: 5.11; Found: C: 56.99, H: 2.98, N: 5.15



**4-chloro-2-phenylbenzo[d]oxazole (2p):** A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 1.2g of Amberlyst 400 (-Cl), imine **1p** (0.2 mmol, 46.3 mg), acetonitrile (7mL) and 100  $\mu$ L of water. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 3 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in ethyl acetate (1.5 mL) and subjected to gas chromatography. Pure product **2p** was obtained in 78% yield (35.8 mg) simply by evaporating ethyl acetate. **m.p.** 109-110 °C. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.30 (dd,  $J$  = 7.8, 2.0 Hz, 2H), 7.67 (dd,  $J$  = 7.7, 1.2 Hz, 1H), 7.57 – 7.53 (m, 3H), 7.35 (dd,  $J$  = 8.0, 1.2 Hz, 1H), 7.30 (t,  $J$  = 7.9 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  163.6, 147.5, 143.5, 132.1, 129.1, 128.0, 126.7, 125.6, 125.5, 118.6, 116.1. **GC-EIMS** ( $m/z$ , %): 231 ( $M^+$ +2, 33), 229 ( $M^+$ , 100), 209 (21), 207 (64), 109 (20), 94 (15). **Elemental Analysis:** Calc. for C<sub>13</sub>H<sub>8</sub>NO: C: 67.99, H: 3.51, N: 6.10; Found: C: 67.94, H: 3.57, N: 6.12



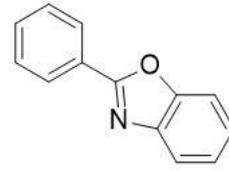
**2-(3,5-dichlorophenyl)benzo[d]oxazole-6-carboxylic acid (2q)** (Tafamidis): A beaker-type cell was equipped with a graphite anode and an aluminum cathode, a magnetic stir bar and connected to a DC regulated power supply. To the beaker-type cell was added 3g of Amberlyst 400 (-Cl), imine **1q** (0.2 mmol, 62.0 mg), 2MeTHF (16mL), MeOH (4mL) and 250  $\mu$ L of a 0.02 M water solution of NaOH. The mixture was electrolyzed using constant current conditions (6 mA) at a temperature of 25°C while stirring. The electrolysis was continued for 6 h. The electrolysis was stopped and the reaction mixture was filtrated on a sintered glass funnel to remove the Amberlyst 400 (-Cl). The solvent was evaporated and the residue was redissolved in 2MeTHF (1.5 mL) and subjected to gas chromatography. Pure product **2q** was obtained in 72% yield (44.4 mg) simply by evaporating 2MeTHF. **m.p.** 202-204 °C. **<sup>1</sup>H NMR** (400 MHz, DMSO)  $\delta$  13.23 (s, 1H), 8.29 (d,  $J = 1.5$  Hz, 1H), 8.17 (d,  $J = 1.9$  Hz, 2H), 8.04 (dd,  $J = 8.4, 1.5$  Hz, 1H), 7.97 (t,  $J = 1.9$  Hz, 1H), 7.96 – 7.92 (m, 1H). **<sup>13</sup>C NMR** (101 MHz, DMSO)  $\delta$  166.7, 162.1, 150.1, 144.8, 135.2, 131.8, 129.2, 128.7, 126.5, 126.0, 120.0, 112.3. **LC-MS** (m/z, %): 328.9 (M<sup>+</sup>+Na, 68), 307.9 (MH<sup>+</sup>, 100), 306.9 (68). **Elemental Analysis:** Calc. for C<sub>14</sub>H<sub>7</sub>Cl<sub>2</sub>NO<sub>3</sub>: C: 54.58, H: 2.29, N: 4.55; Found: C: 54.61, H: 2.32, N: 4.58

## 10. References

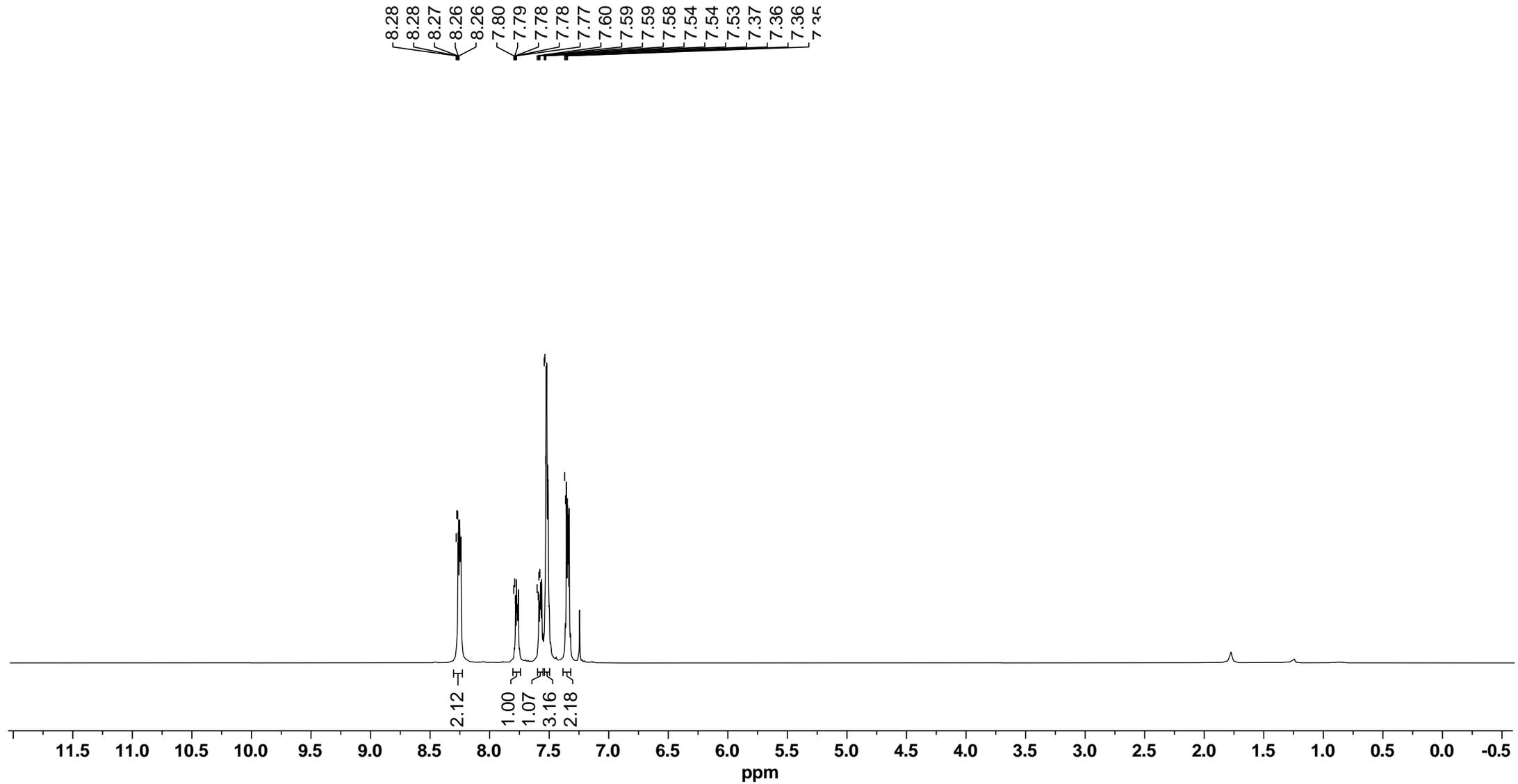
- 1) (a) S. Martin, R. Porcar, E. Peris, M. I. Burguete, E. Garcia-Verdugo, S. V. Luis, *Green Chem.* 2014, **16**, 1639-1647; (b) I. Dinares, C. Garcia de Miguel, A. Ibanez, N. Mesquida, E. Alcalde, *Green Chem.* 2009, **11**, 1507-1510; (c) M. I. Burguete, H. Erytropel, E. Garcia-Verdugo, S. V. Luis, V. Sans, *Green Chem.* 2008, **10**, 401-407.
- 2) (a) R. A. Sheldon, *Chem. Commun.*, 2008, 3352–3365; (b) J. Andraos, A. Hent J. *Chem. Educ.* 2015, **92**, 11, 1820–1830.

## 11. NMR spectra

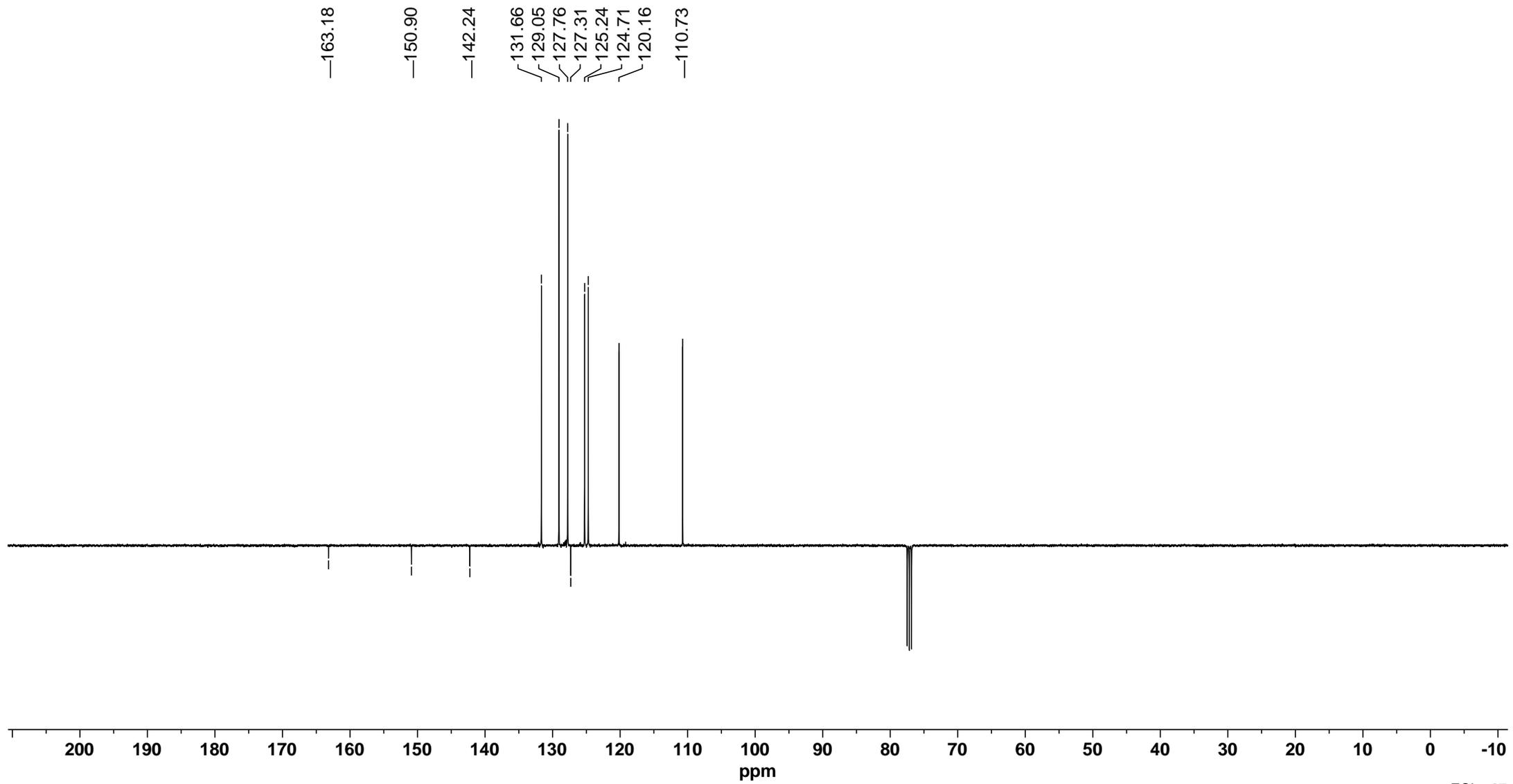
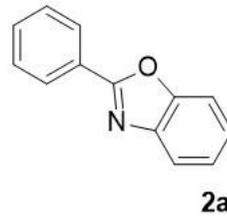
2-phenylbenzo[d]oxazole (2a)



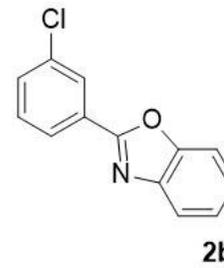
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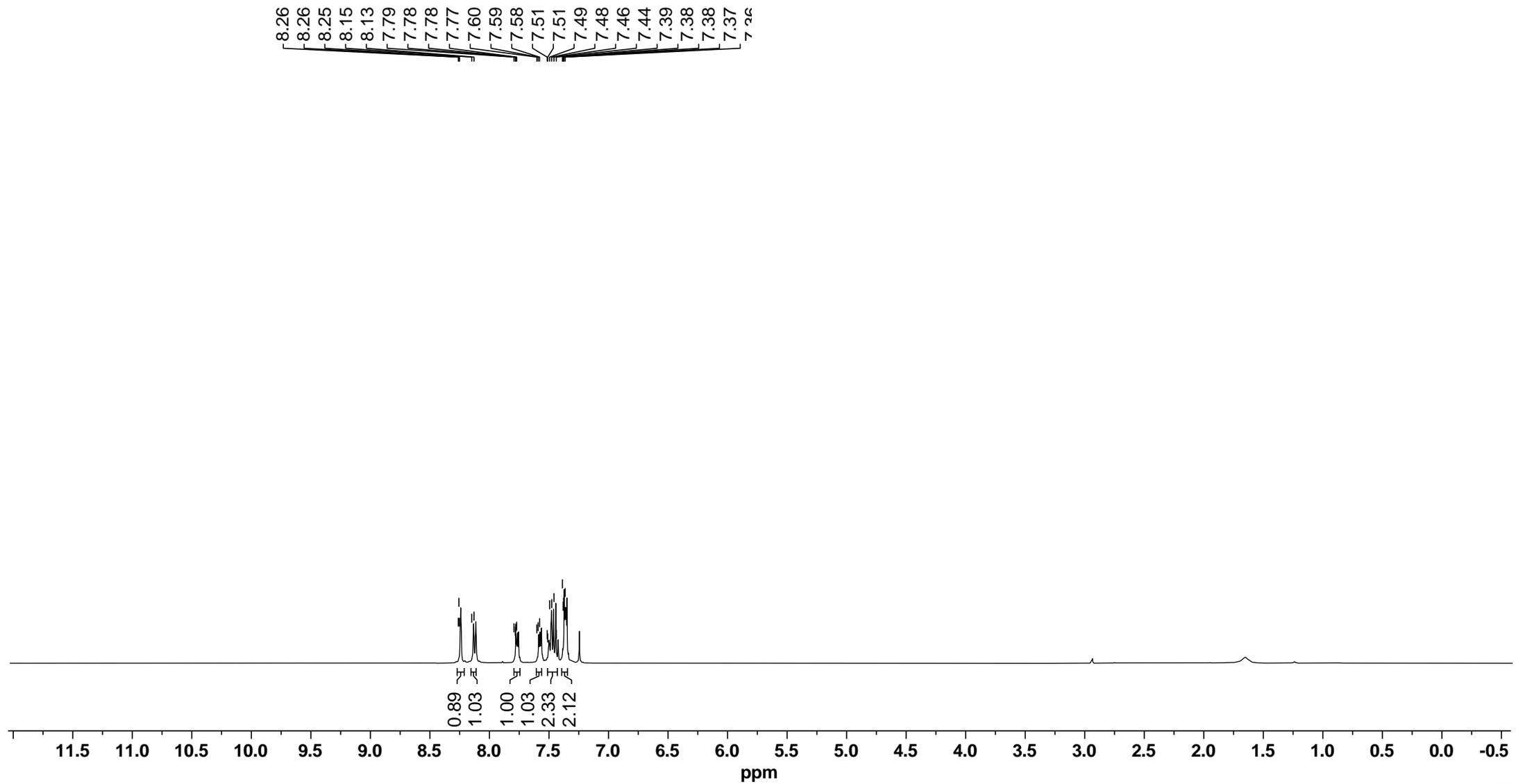
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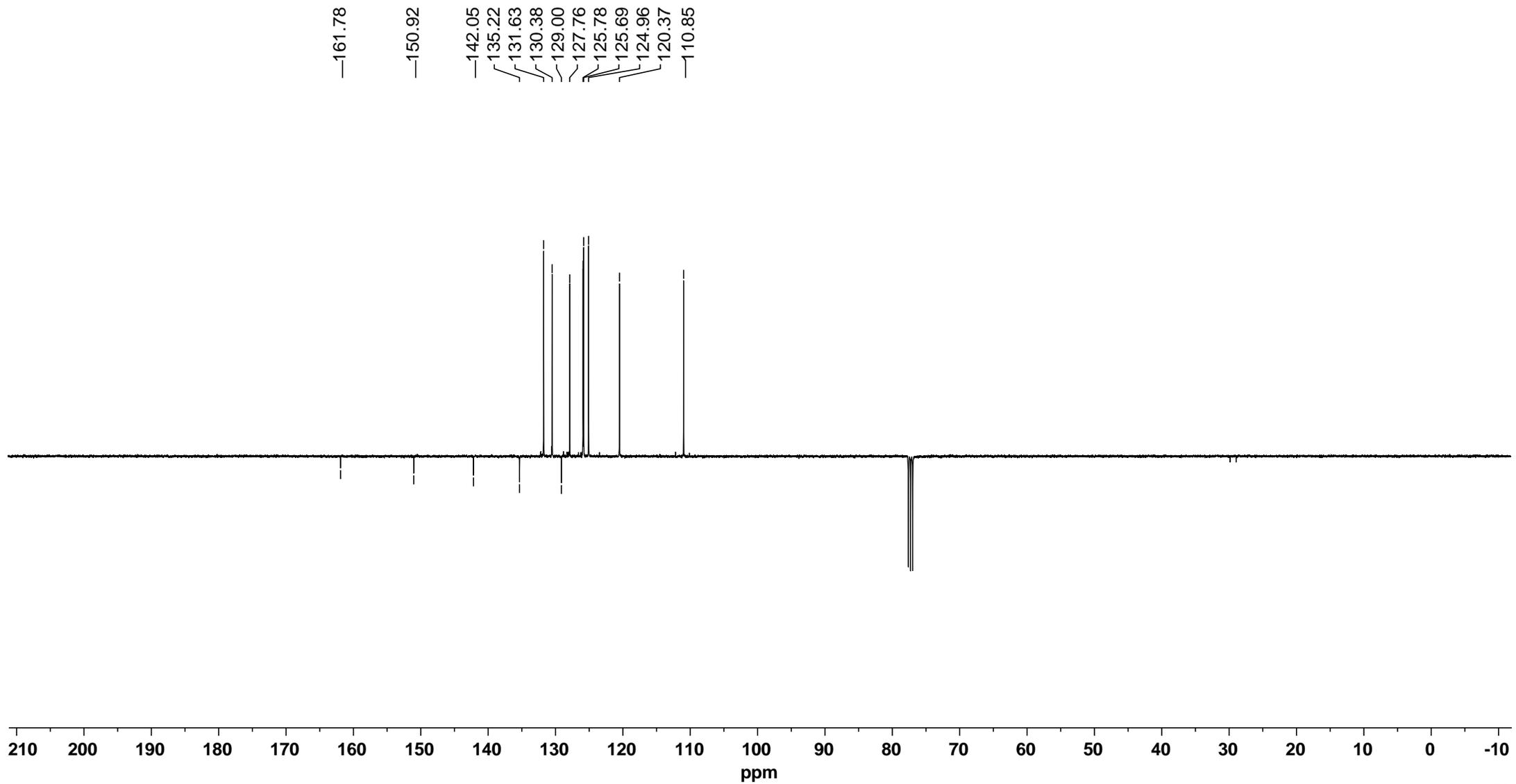
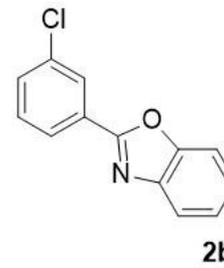
2-(3-chlorophenyl)benzo[d]oxazole (**2b**)



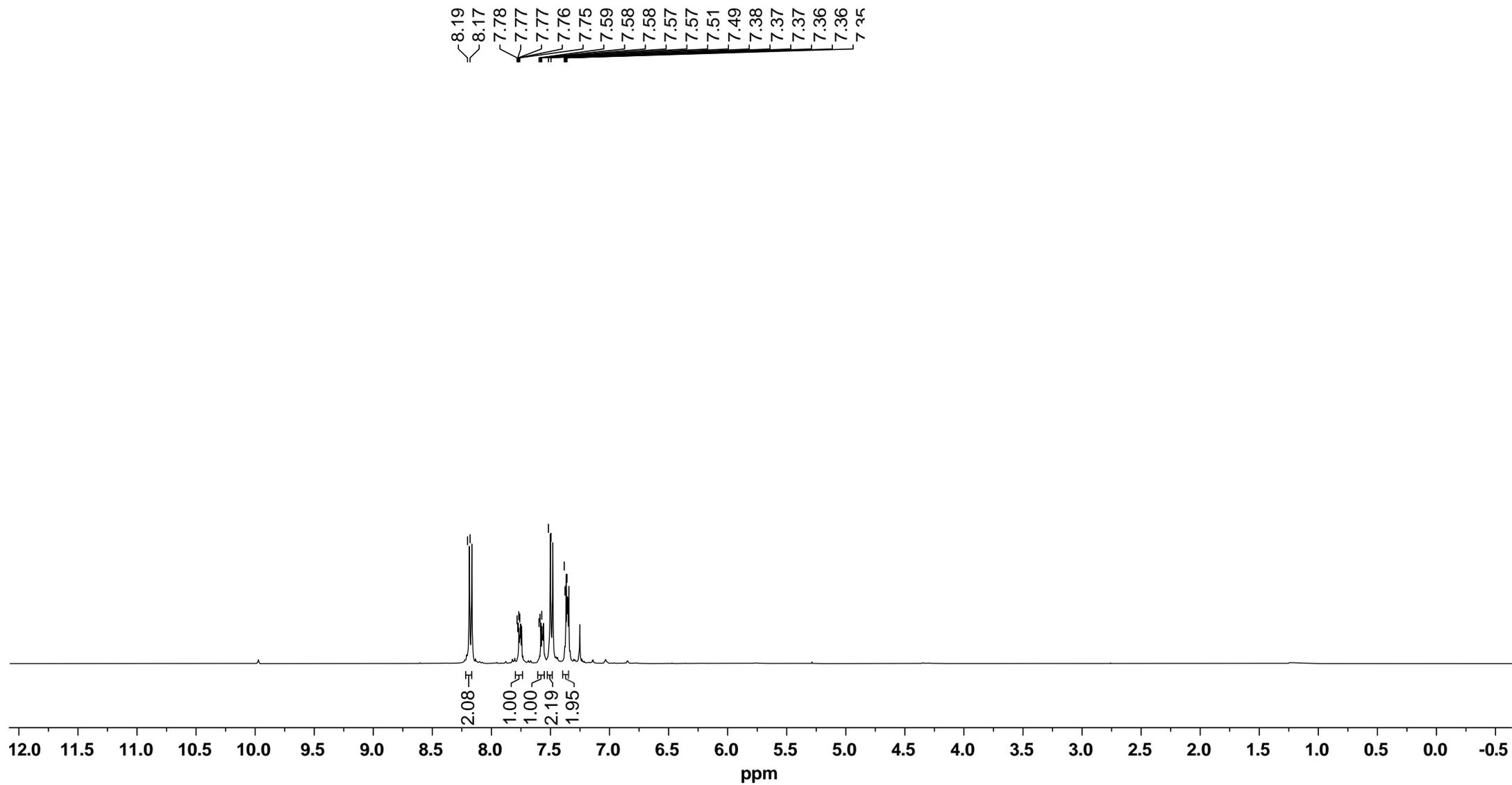
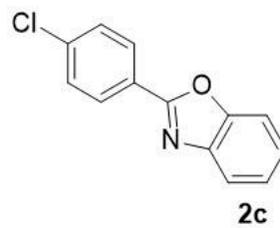
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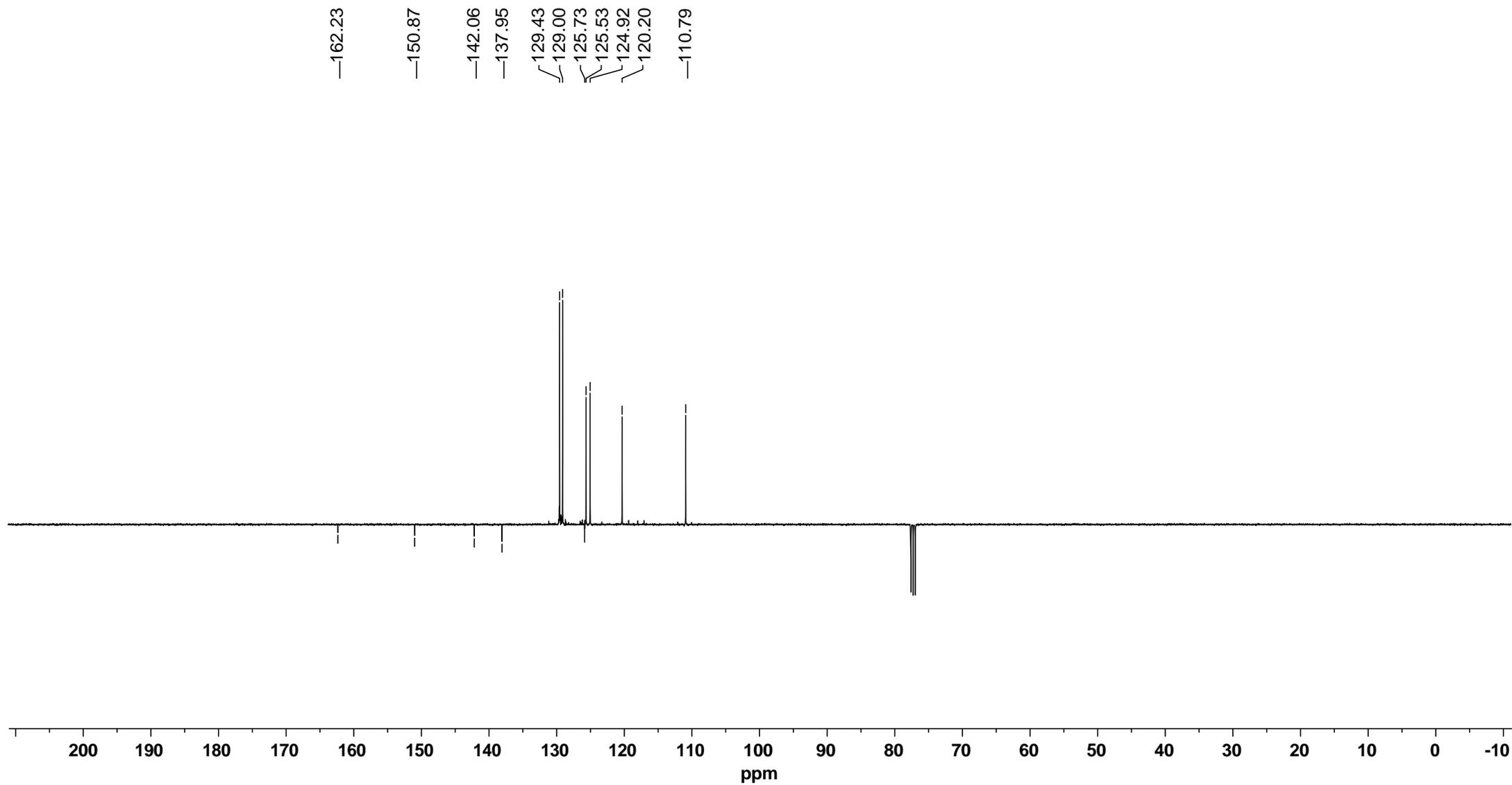
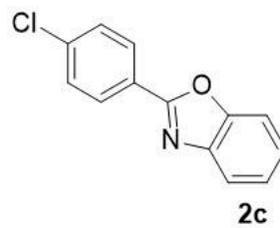
2-(3-chlorophenyl)benzo[d]oxazole (**2b**)



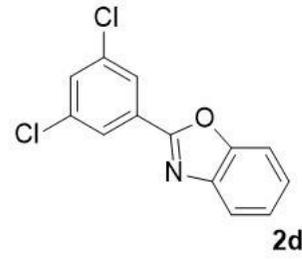
2-(4-chlorophenyl)benzo[d]oxazole (**2c**)



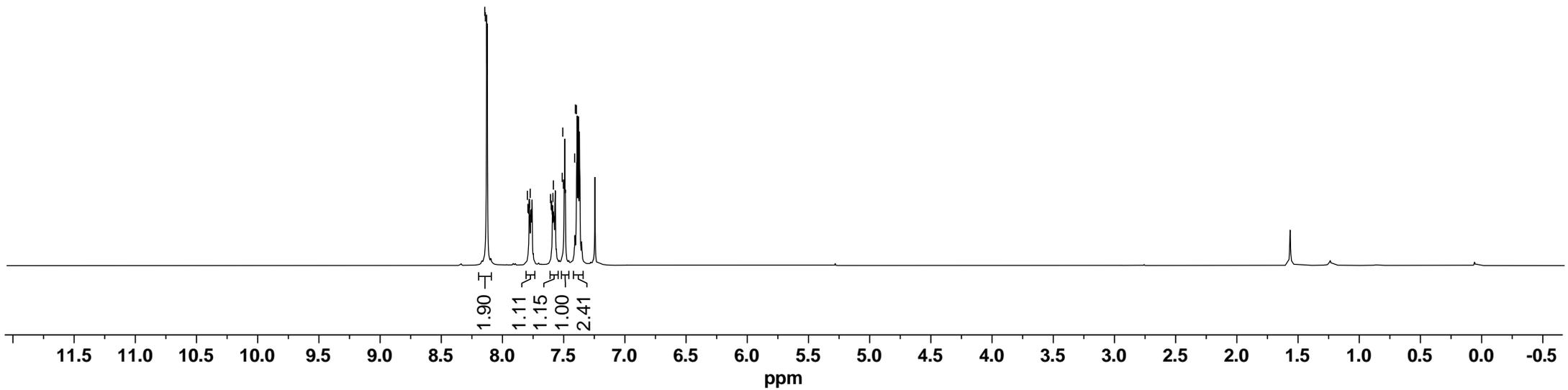
2-(4-chlorophenyl)benzo[d]oxazole (**2c**)



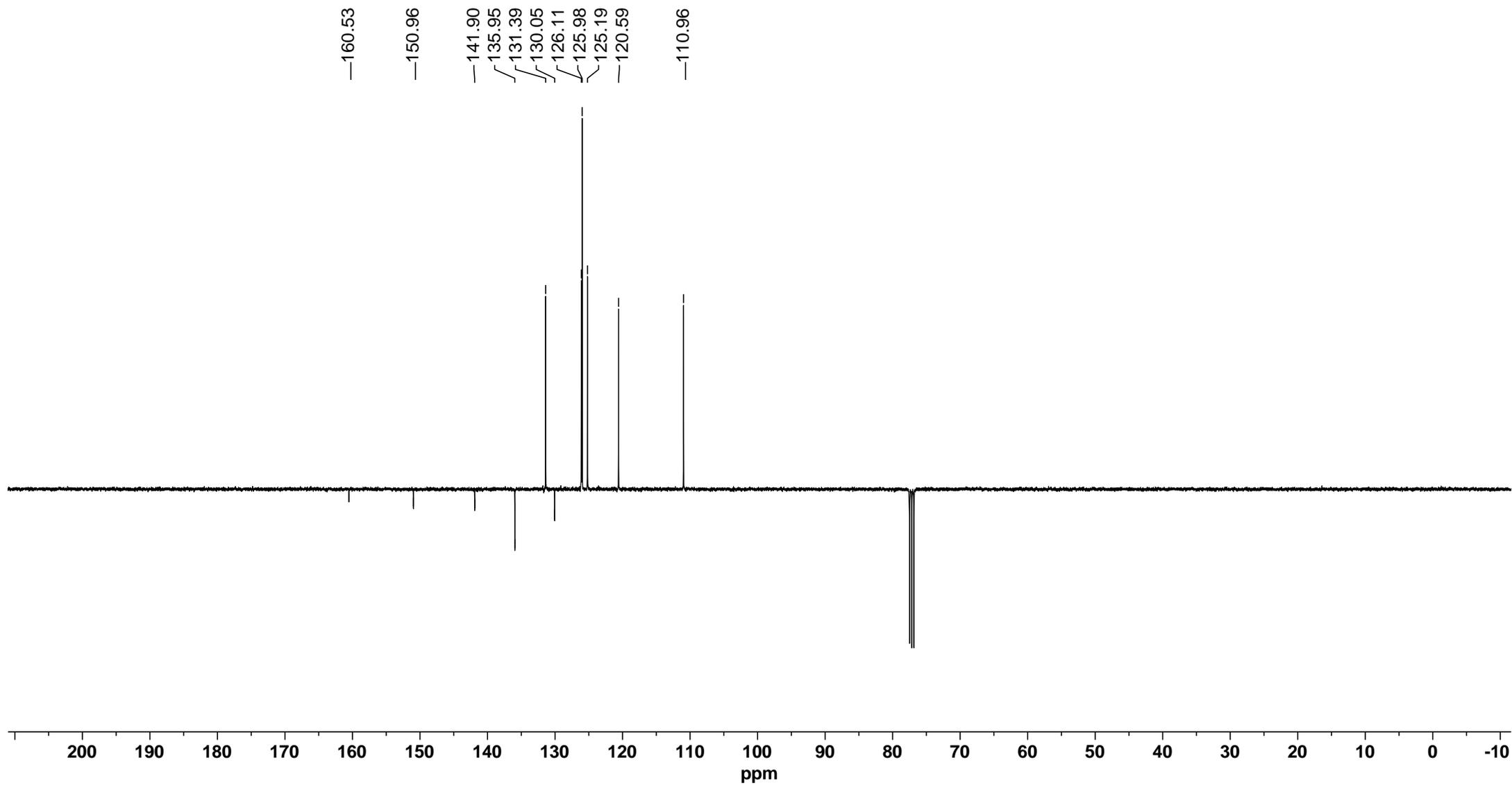
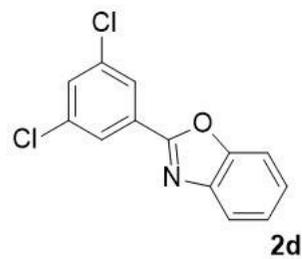
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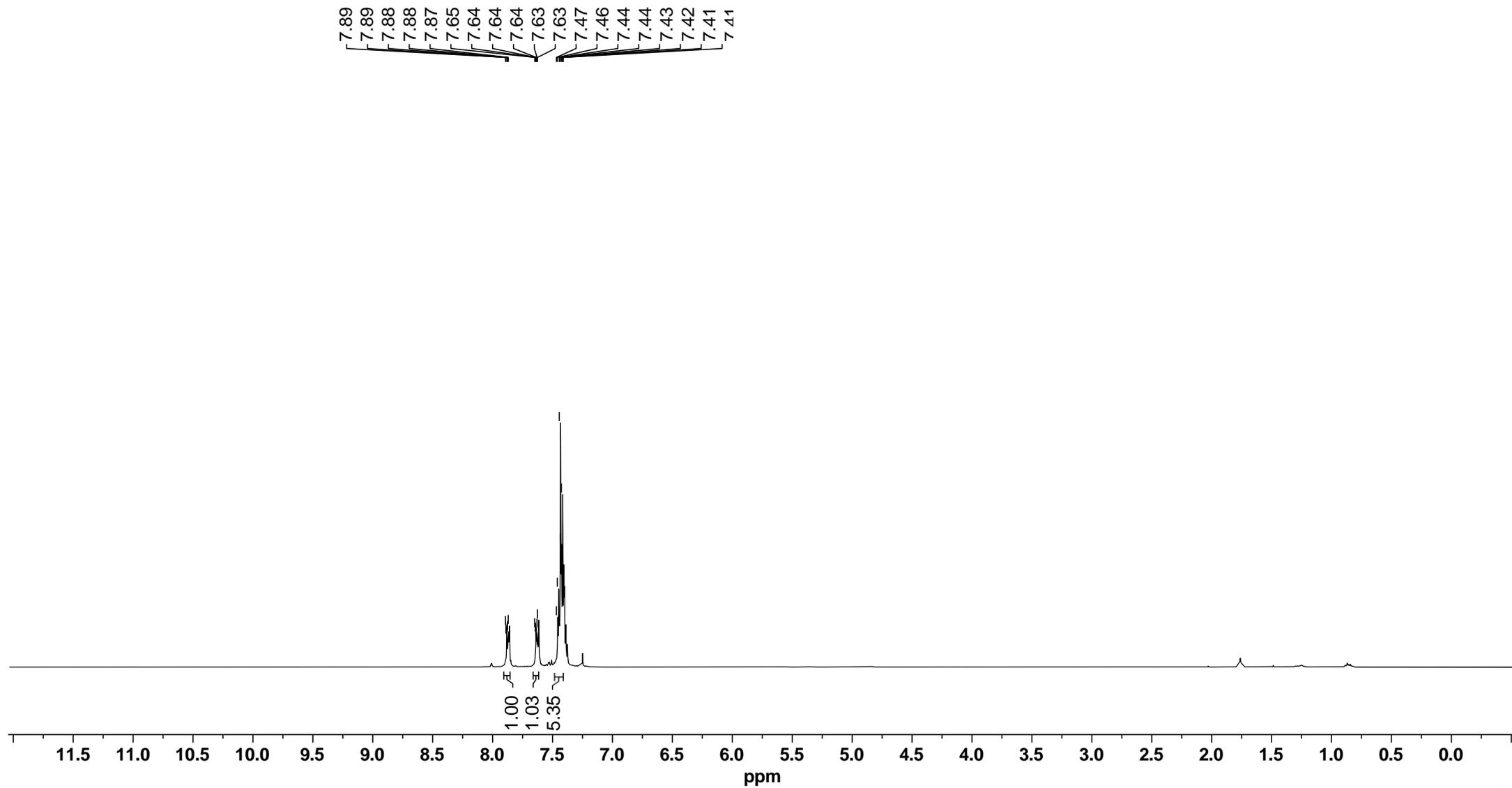
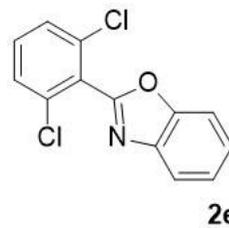
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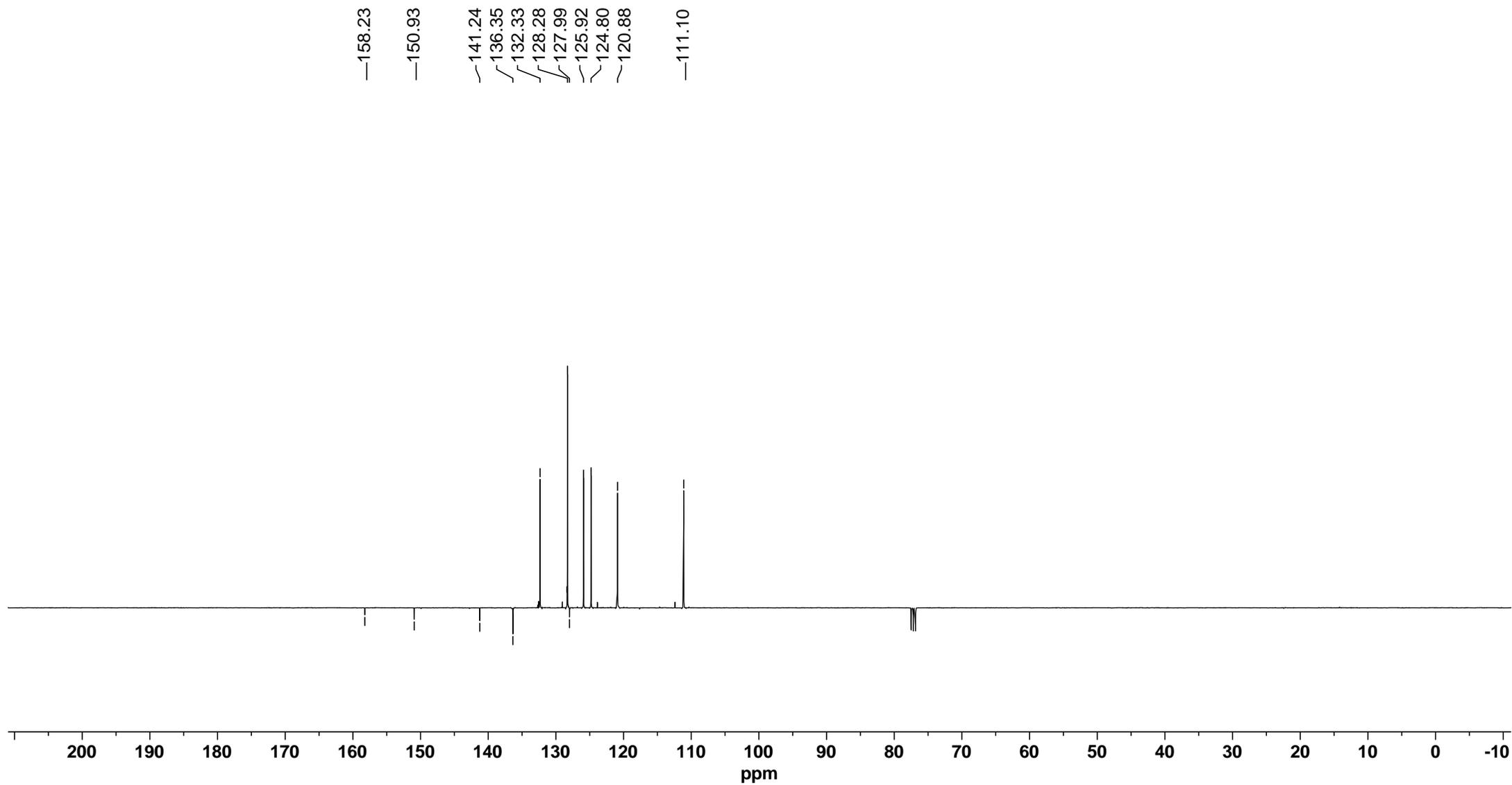
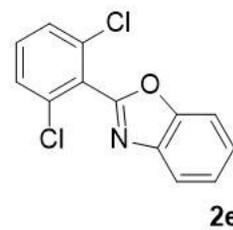
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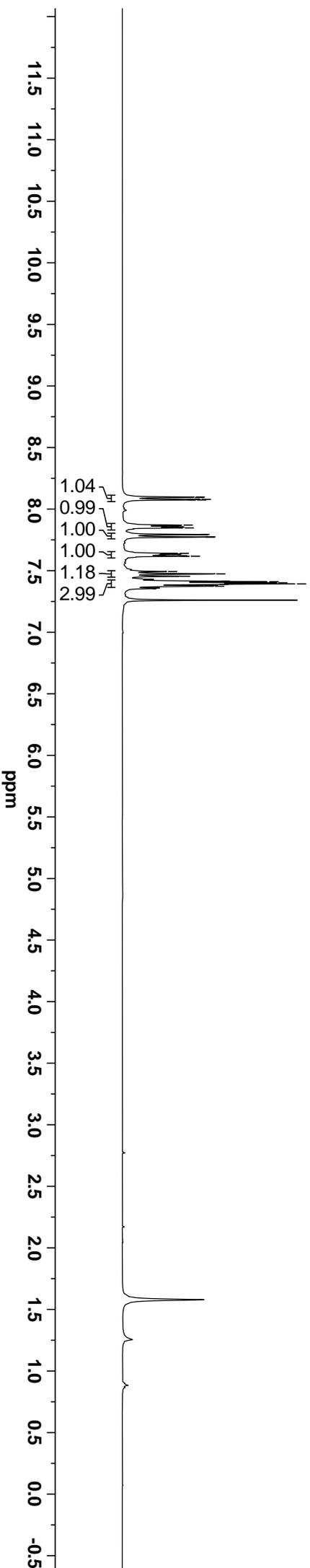
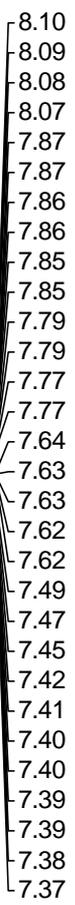
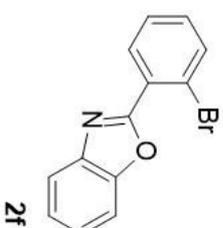
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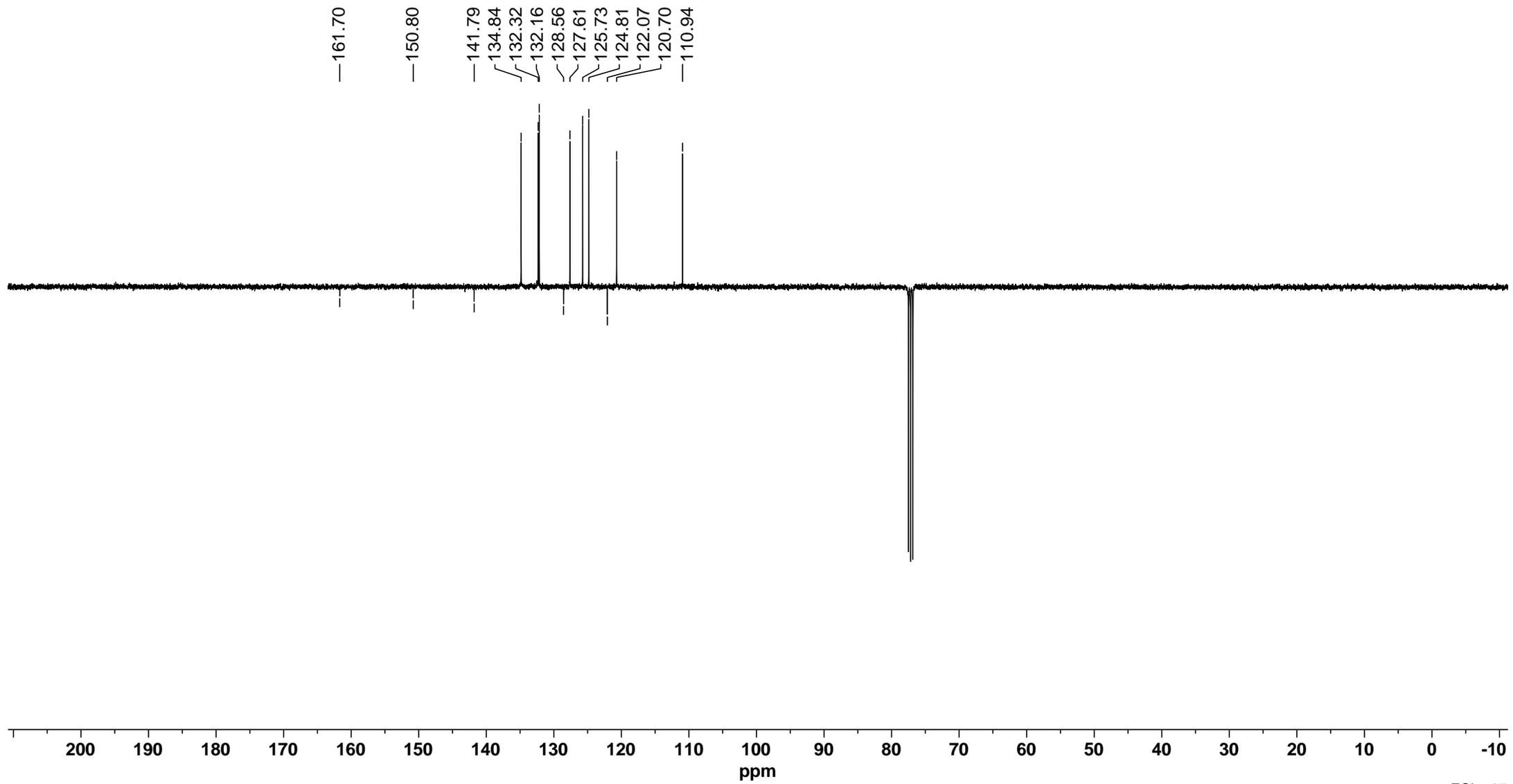
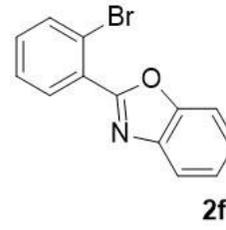
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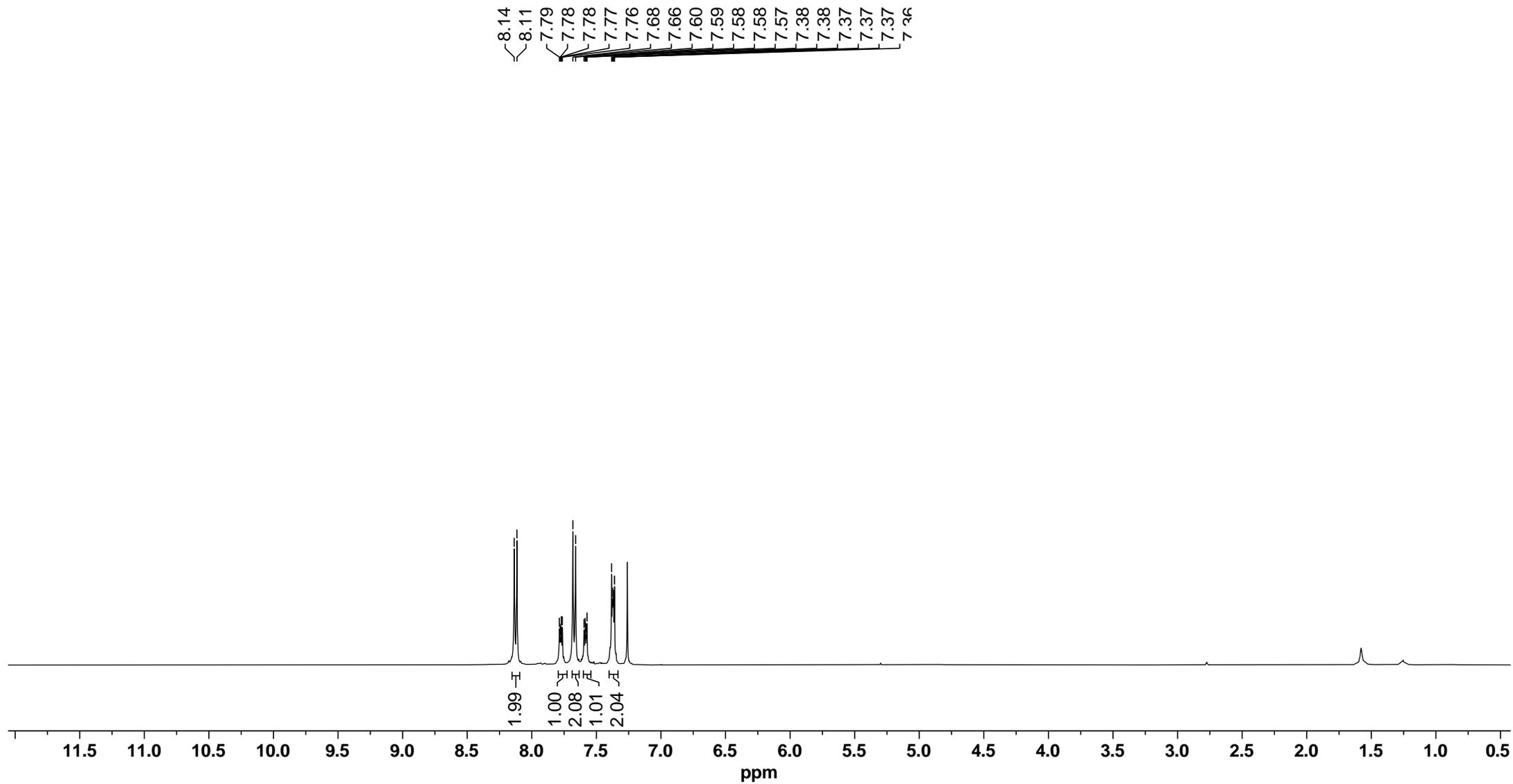
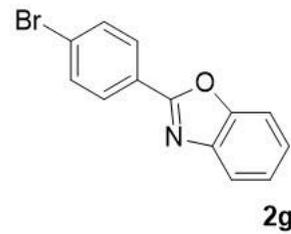
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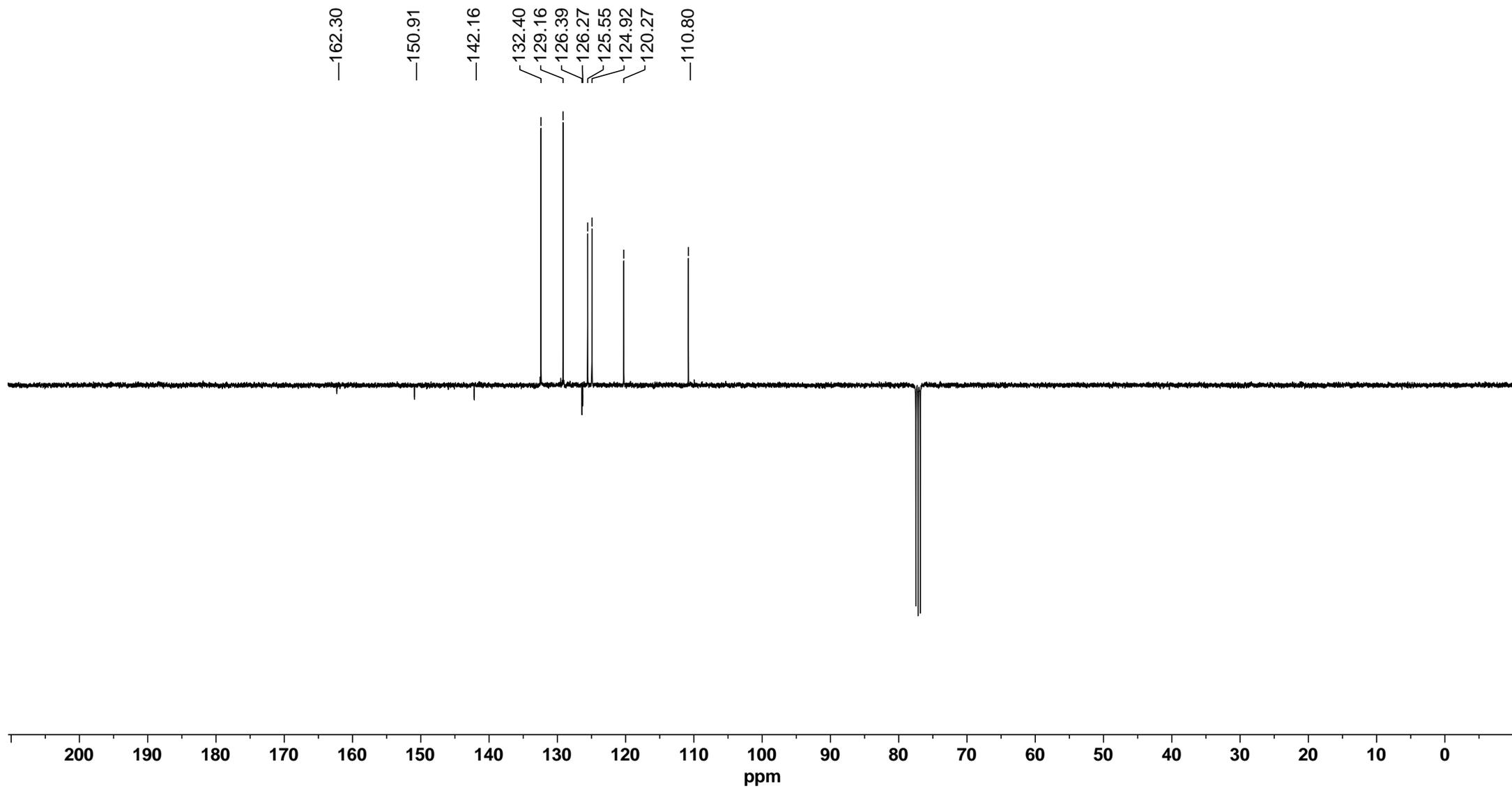
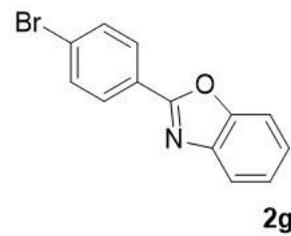
2-(2-bromophenyl)benzo[d]oxazole (2f)



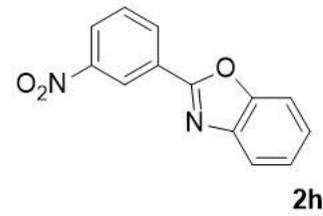
2-(4-bromophenyl)benzo[d]oxazole (2g)



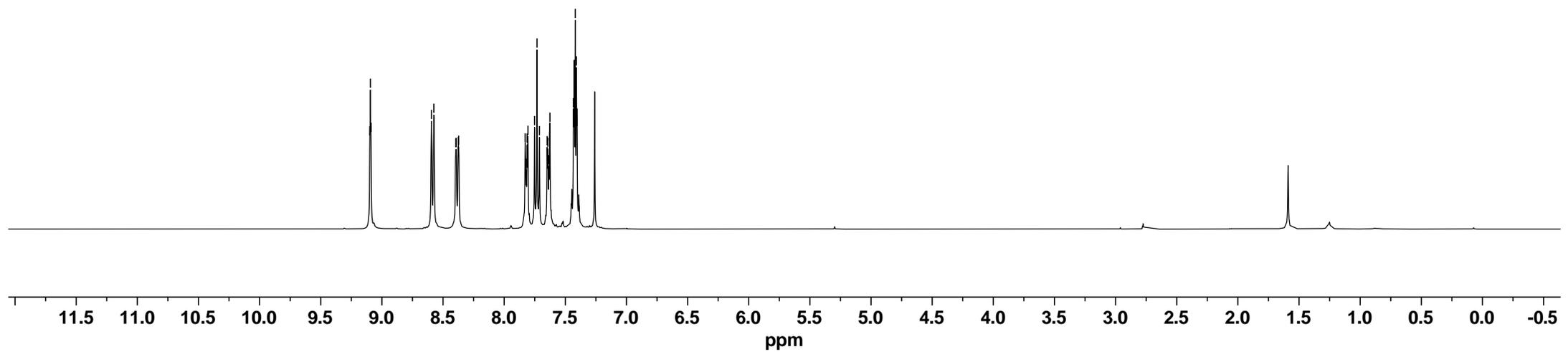
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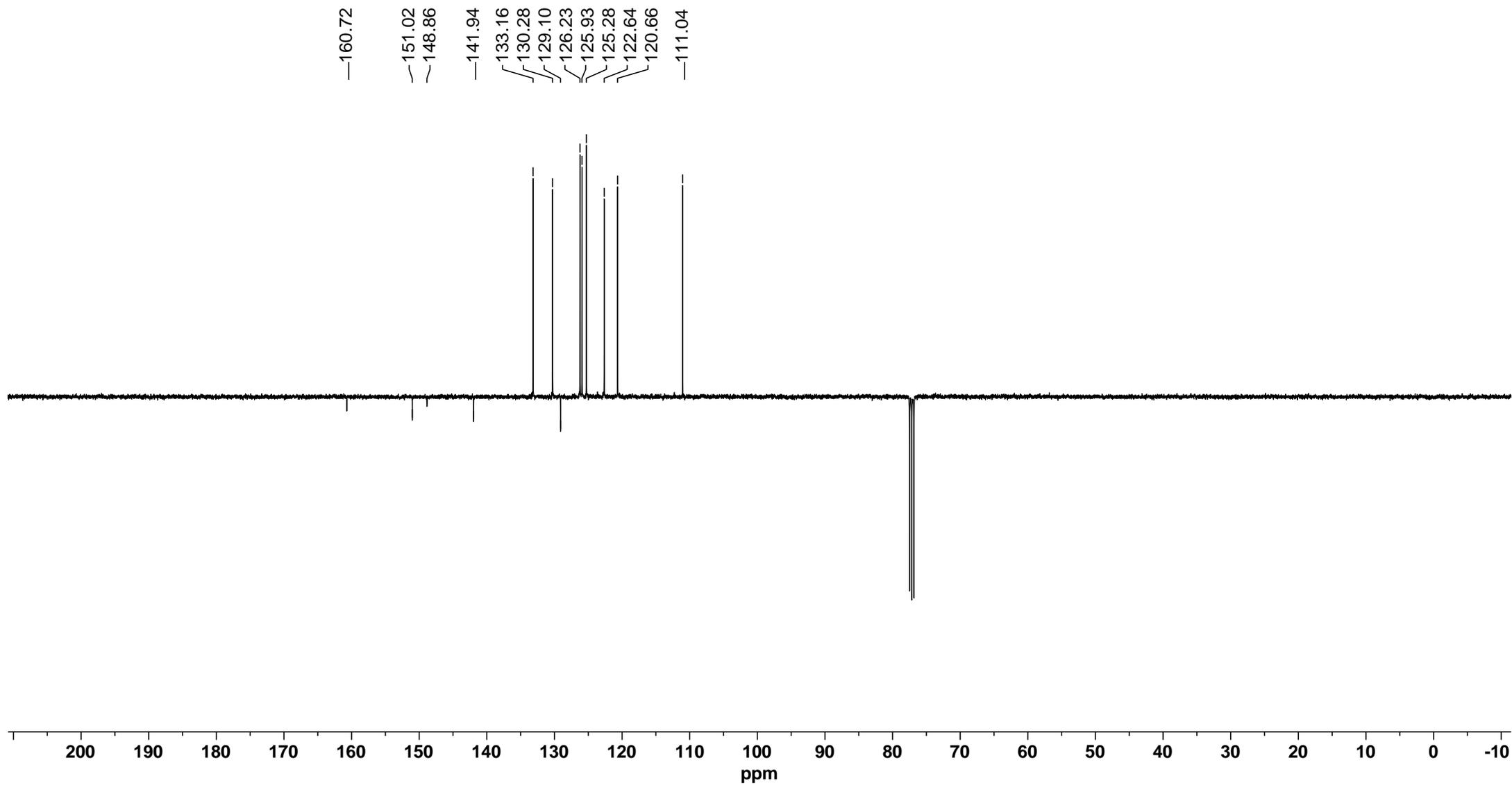
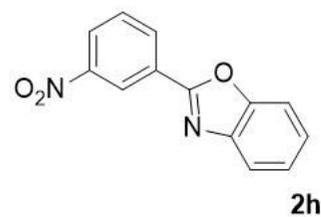
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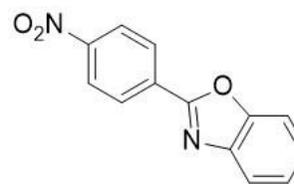
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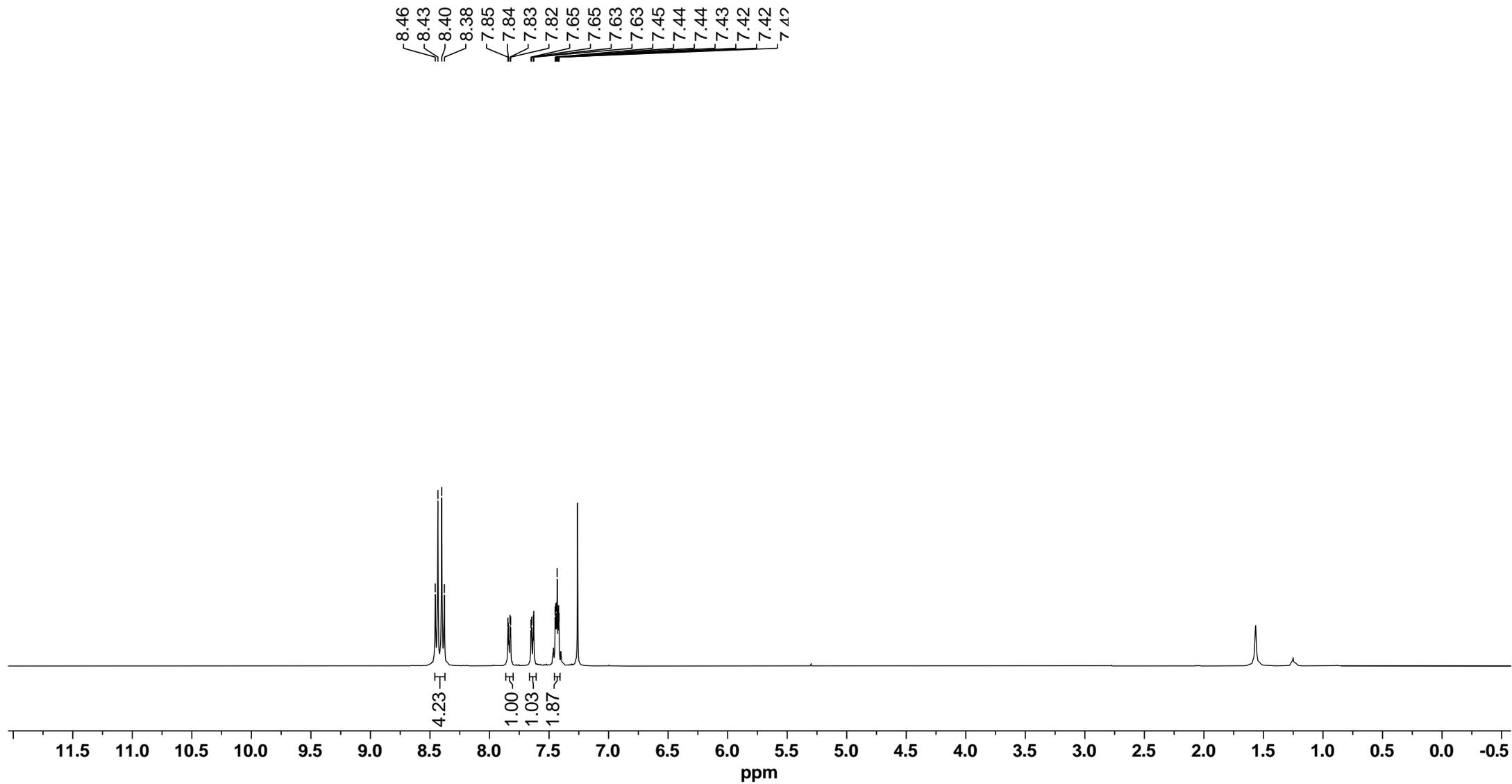


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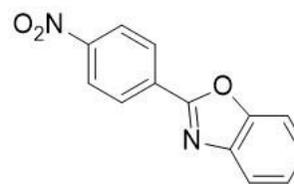


2i

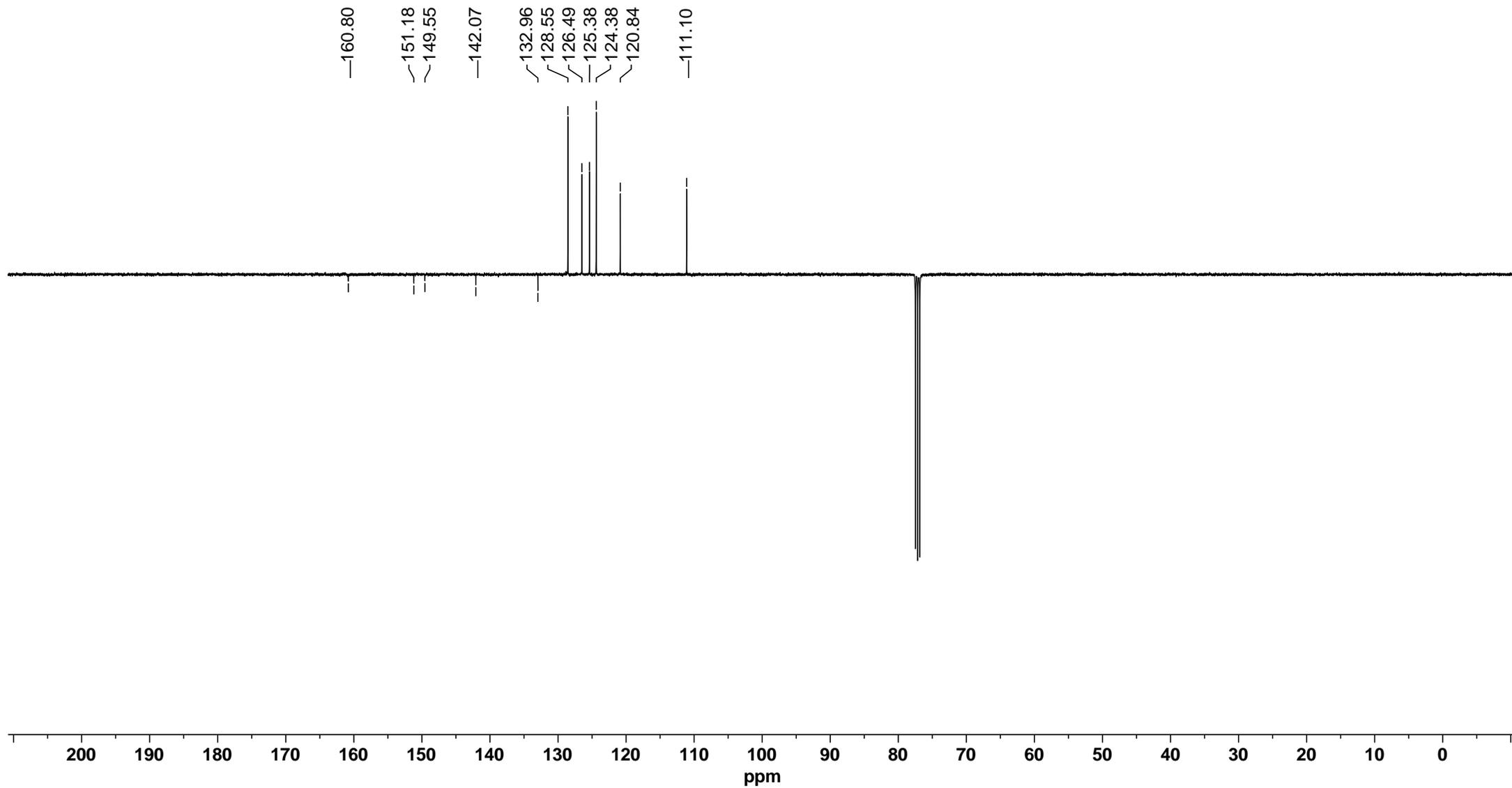
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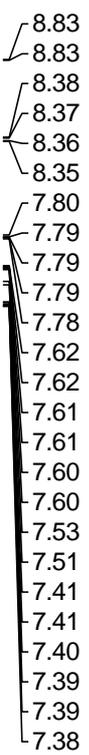
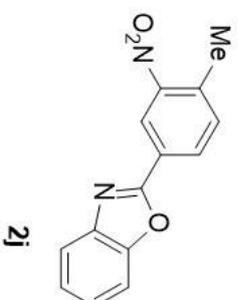
2-(4-nitrophenyl)benzo[d]oxazole (2i)



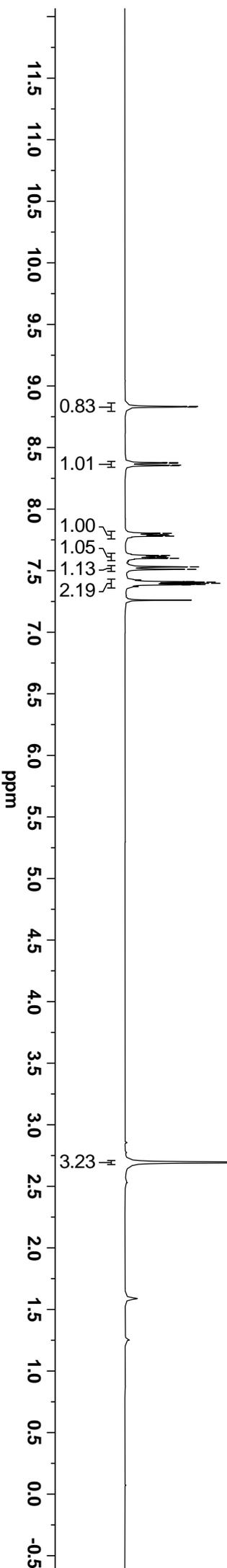
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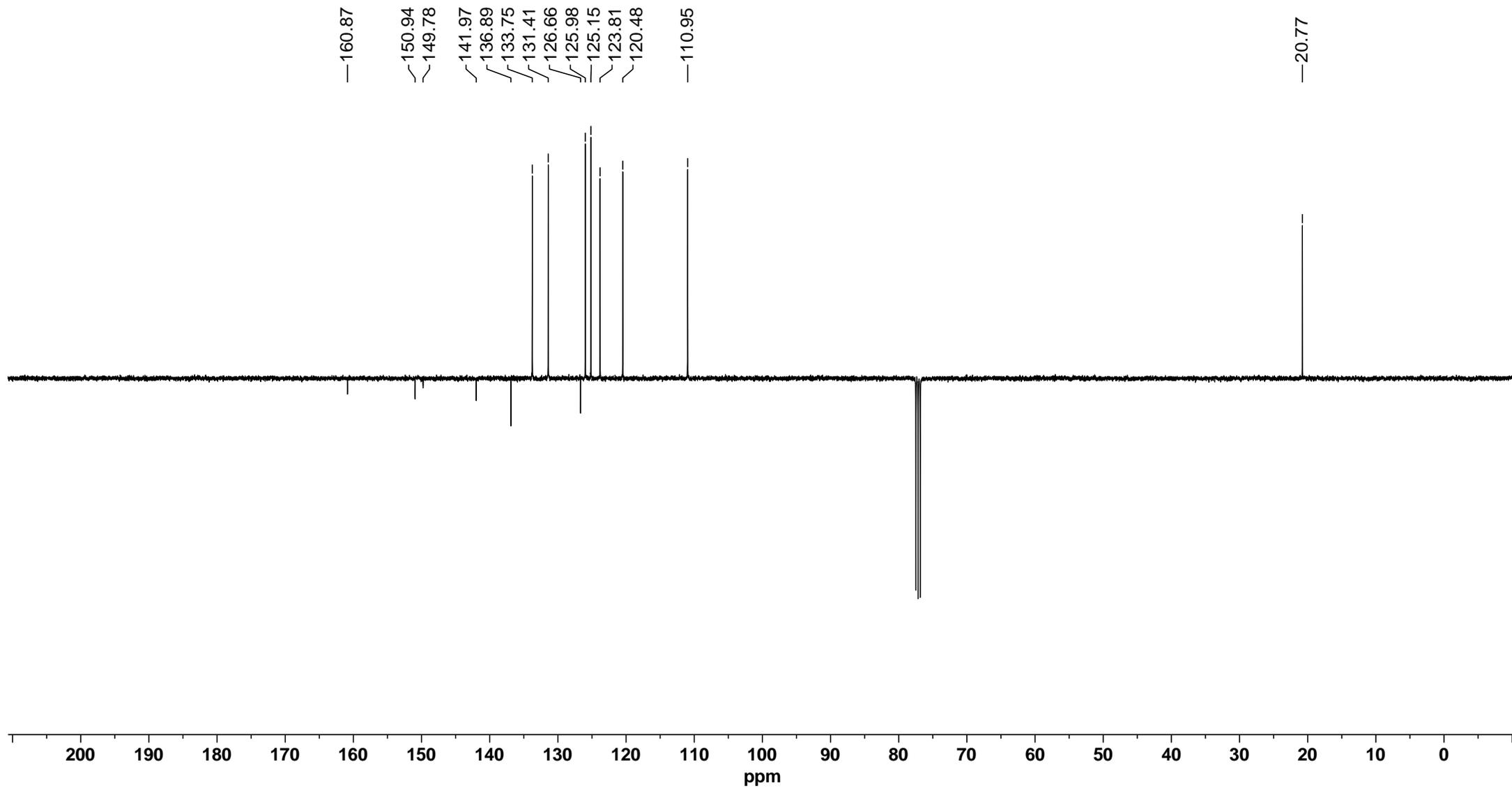
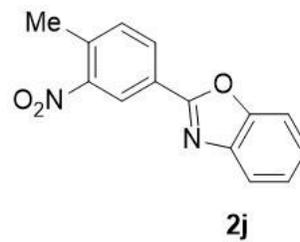
2-(4-methyl-3-nitrophenyl)benzo[d]oxazole (**2j**)



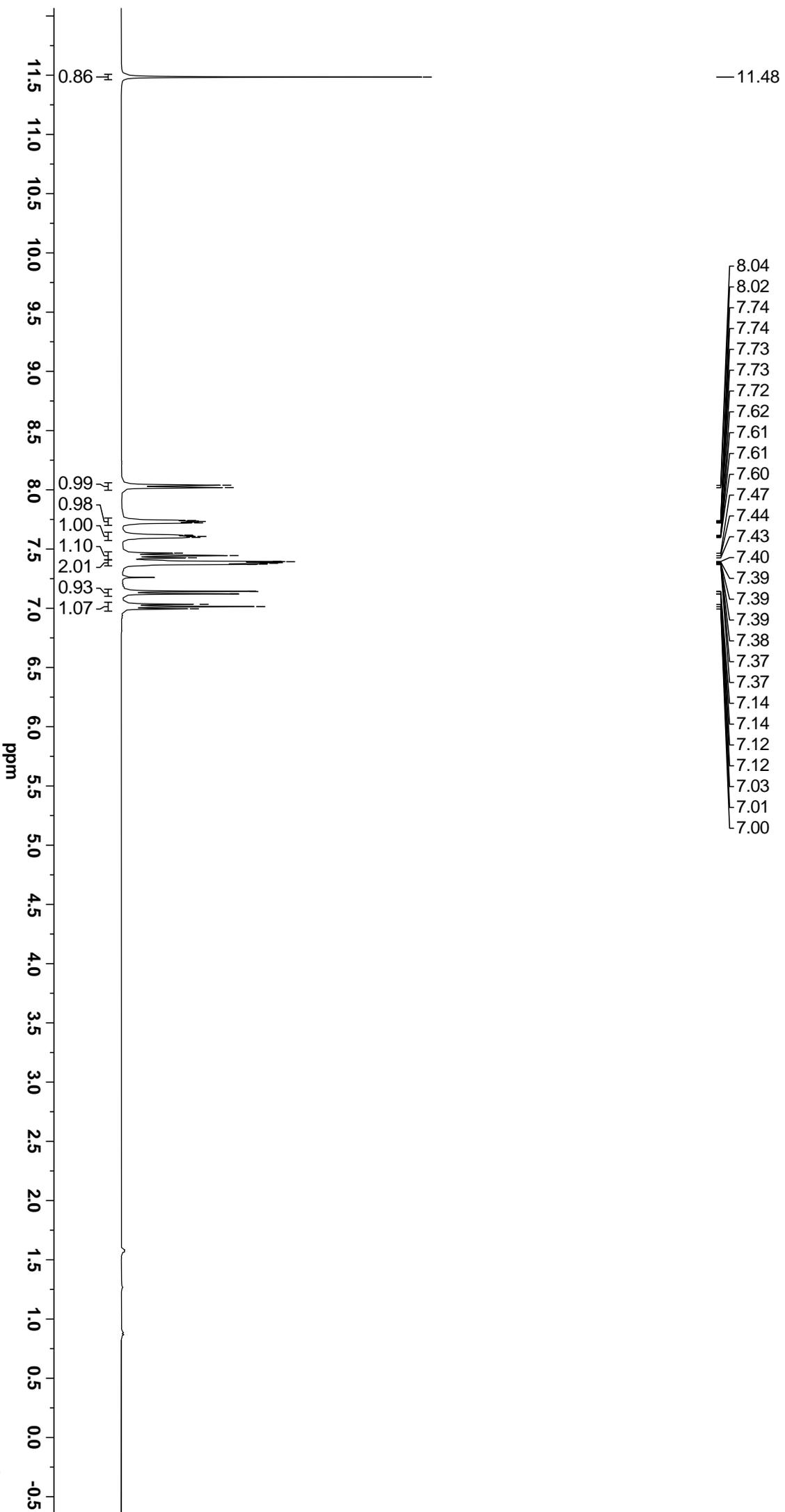
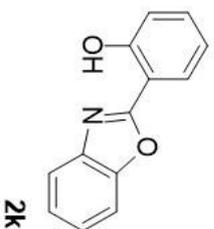
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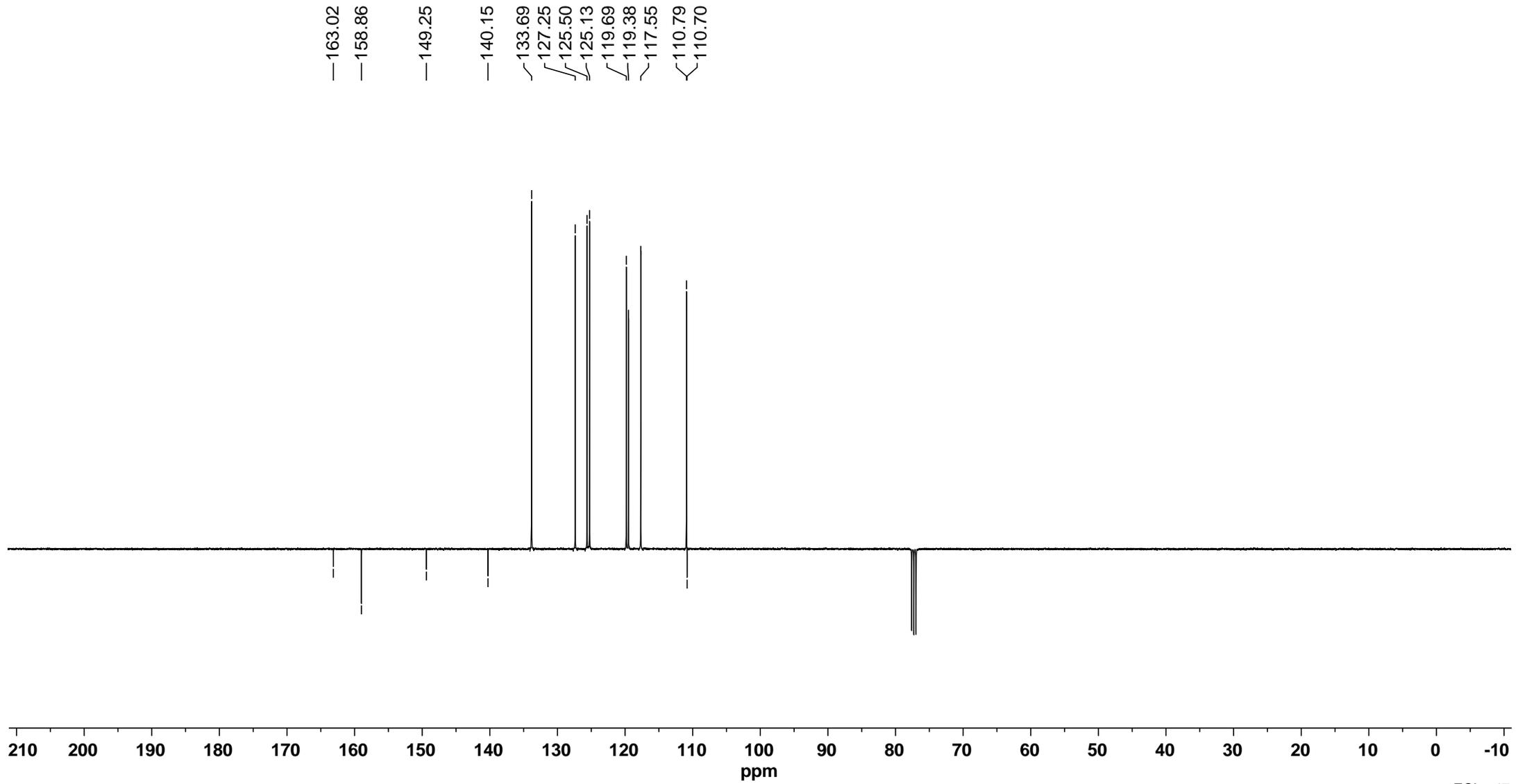
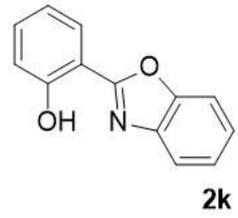
2-(4-methyl-3-nitrophenyl)benzo[d]oxazole (2j)



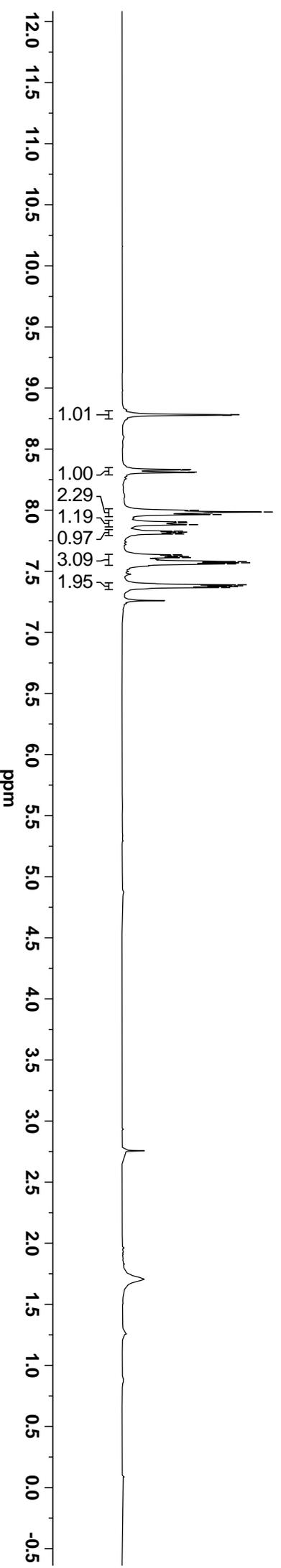
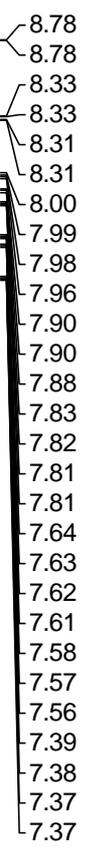
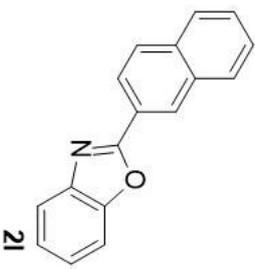
2-(benzo[d]oxazol-2-yl)phenol (**2k**)



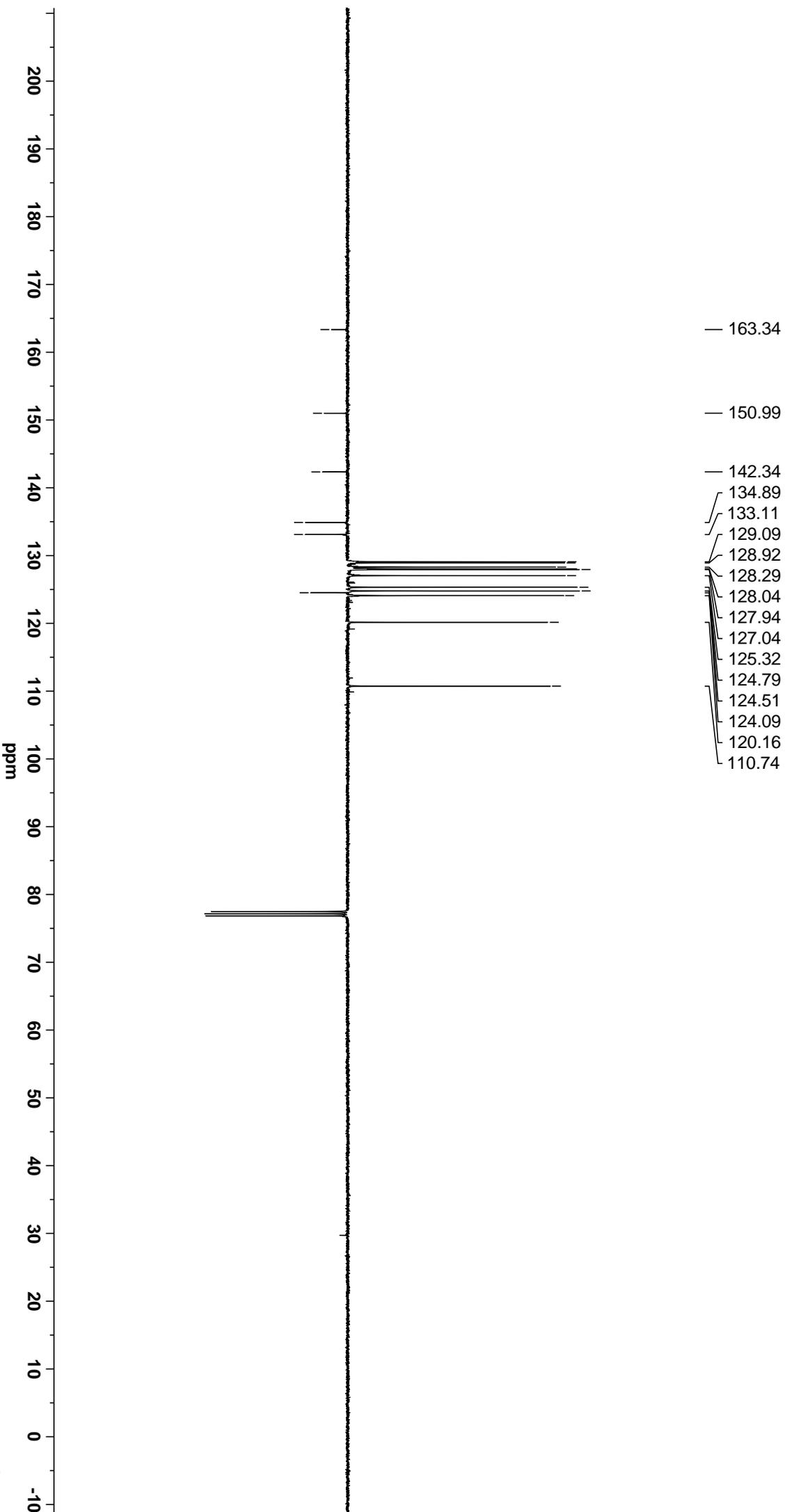
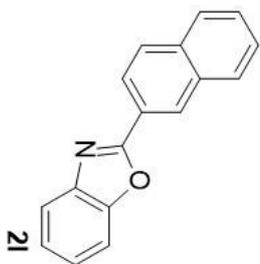
2-(benzo[d]oxazol-2-yl)phenol (**2k**)



2-(naphthalen-2-yl)benzof[d]oxazole (21)



2-(naphthalen-2-yl)benzof[d]oxazole (21)

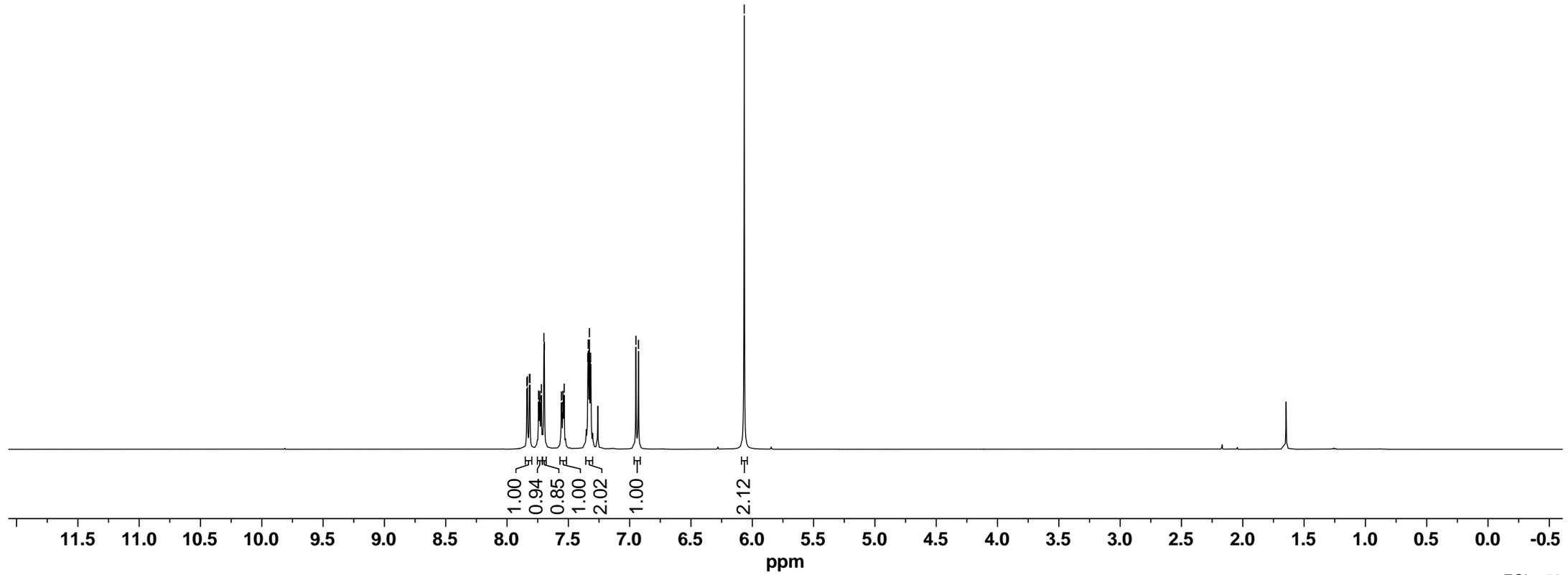


2-(benzo[d][1,3]dioxol-5-yl)benzo[d]oxazole (2m)

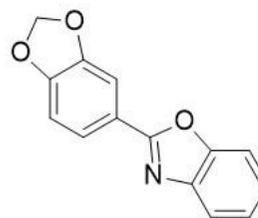


2m

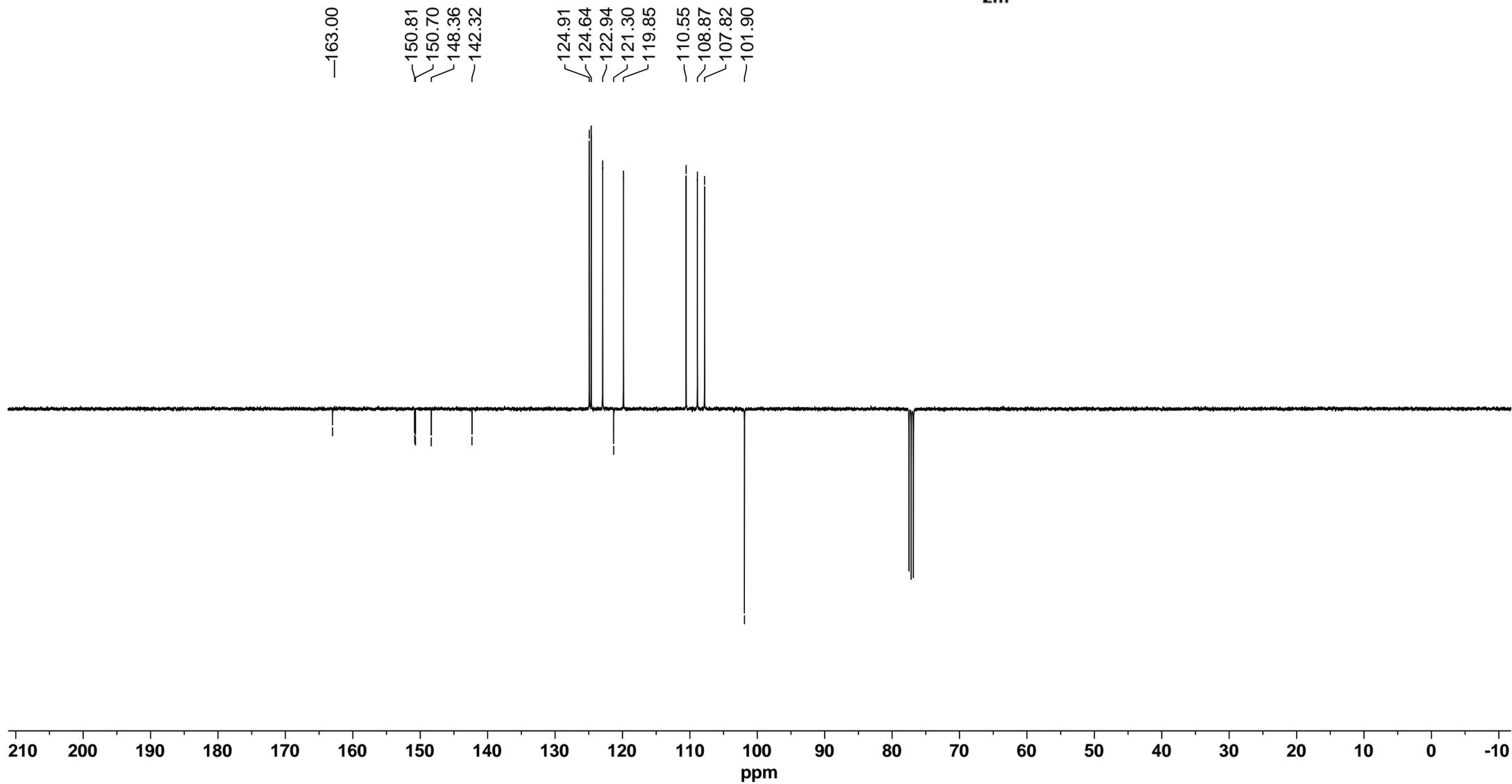
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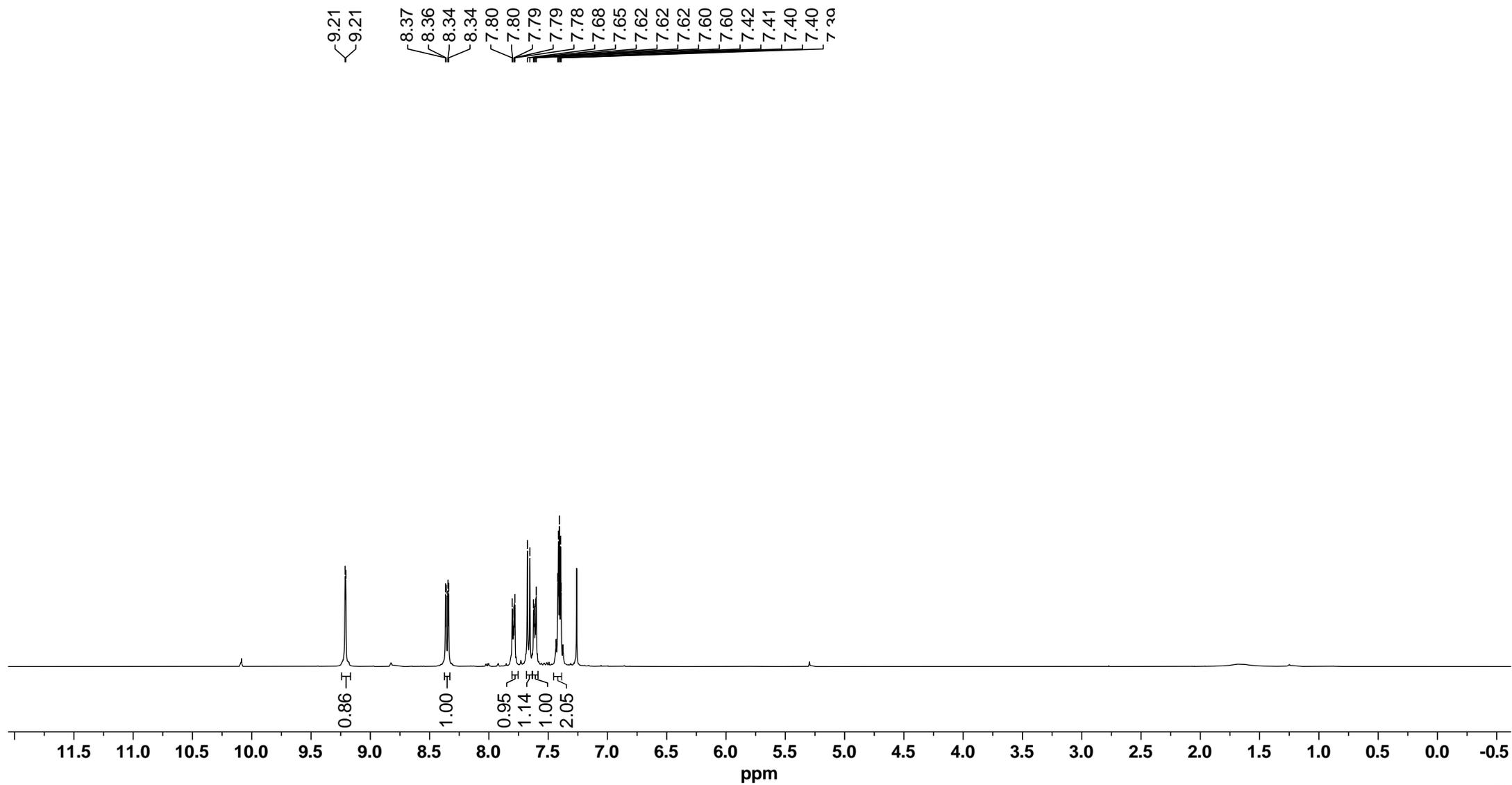
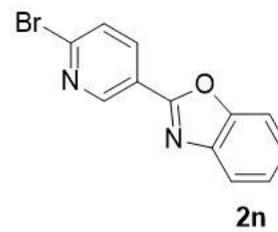
2-(benzo[d][1,3]dioxol-5-yl)benzo[d]oxazole (2m)



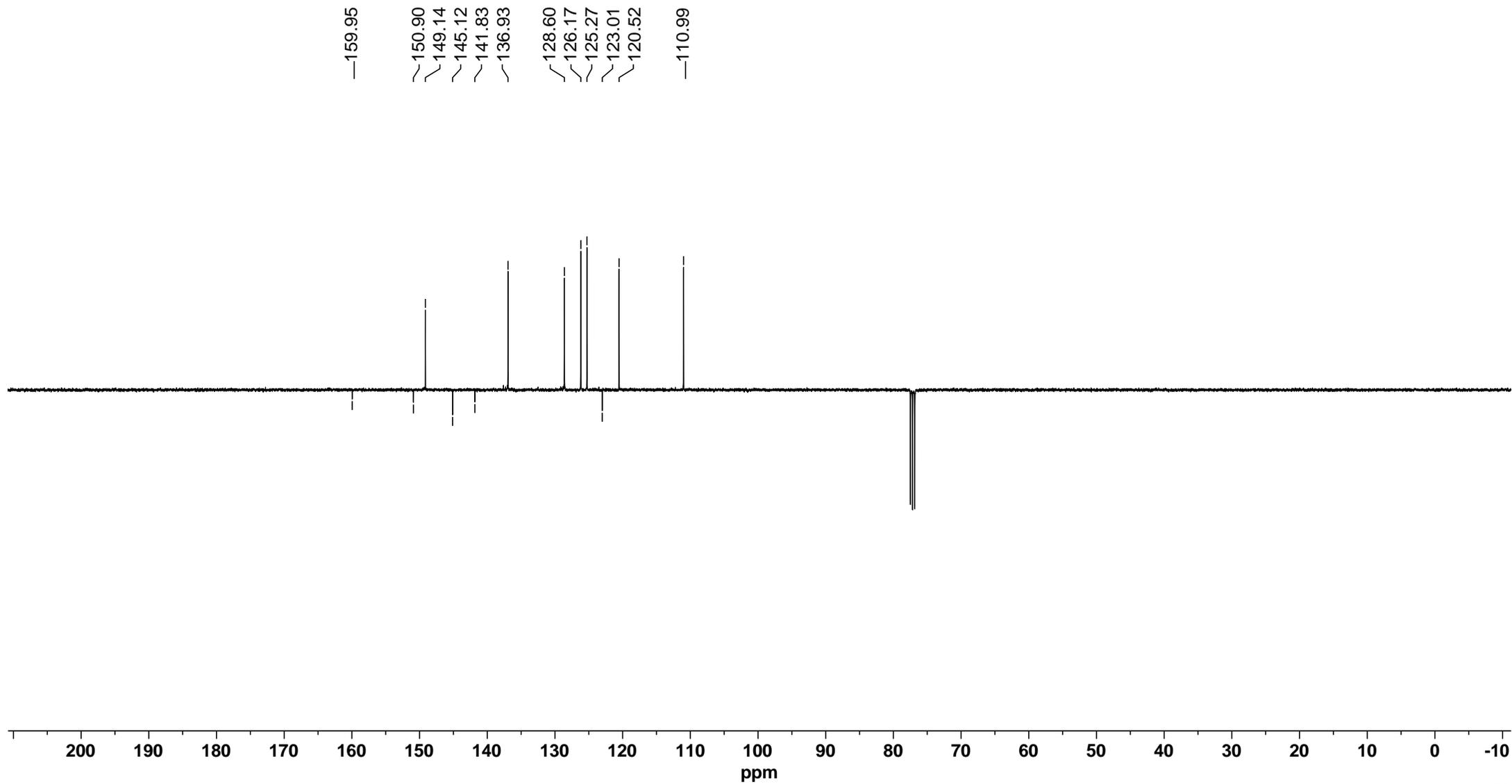
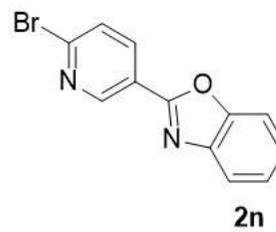
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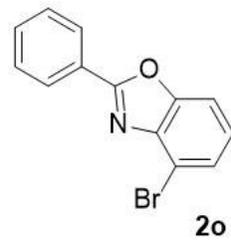
2-(6-bromopyridin-3-yl)benzo[d]oxazole (**2n**)



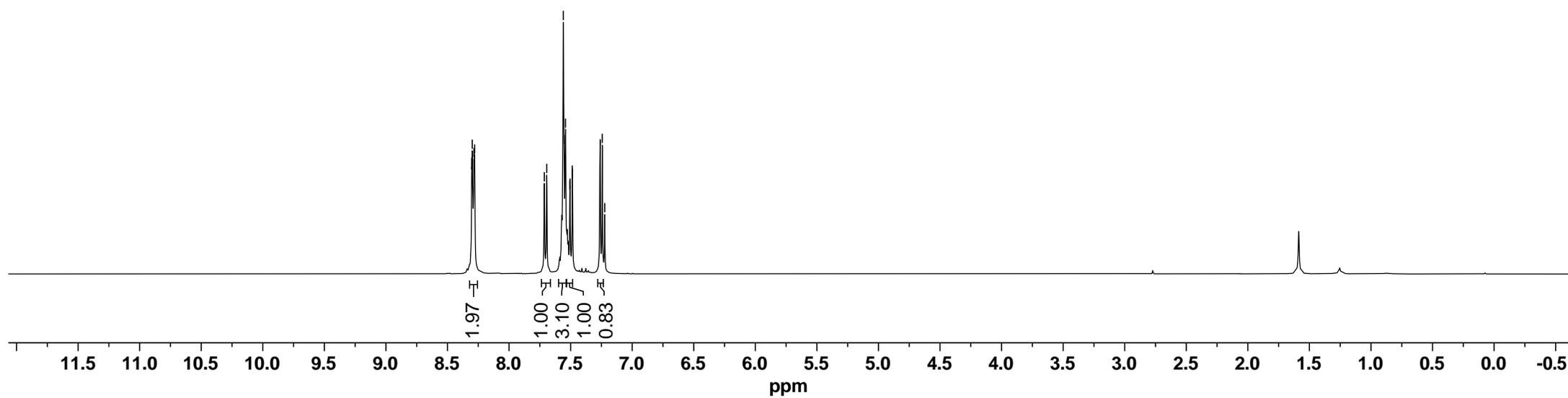
2-(6-bromopyridin-3-yl)benzo[d]oxazole (**2n**)



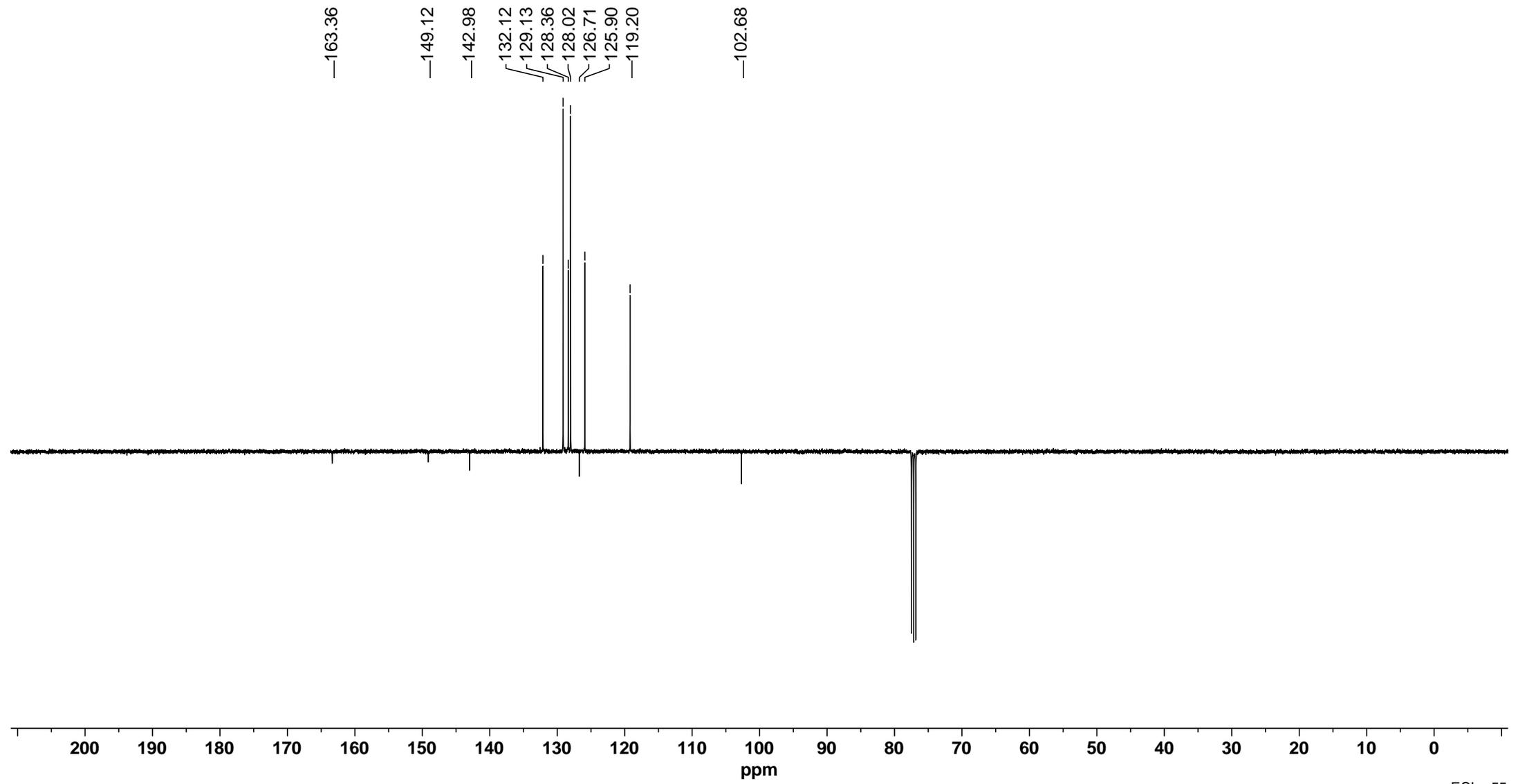
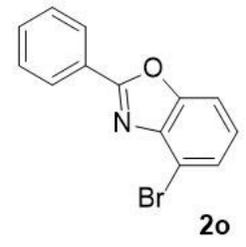
4-bromo-2-phenylbenzo[d]oxazole (**2o**)



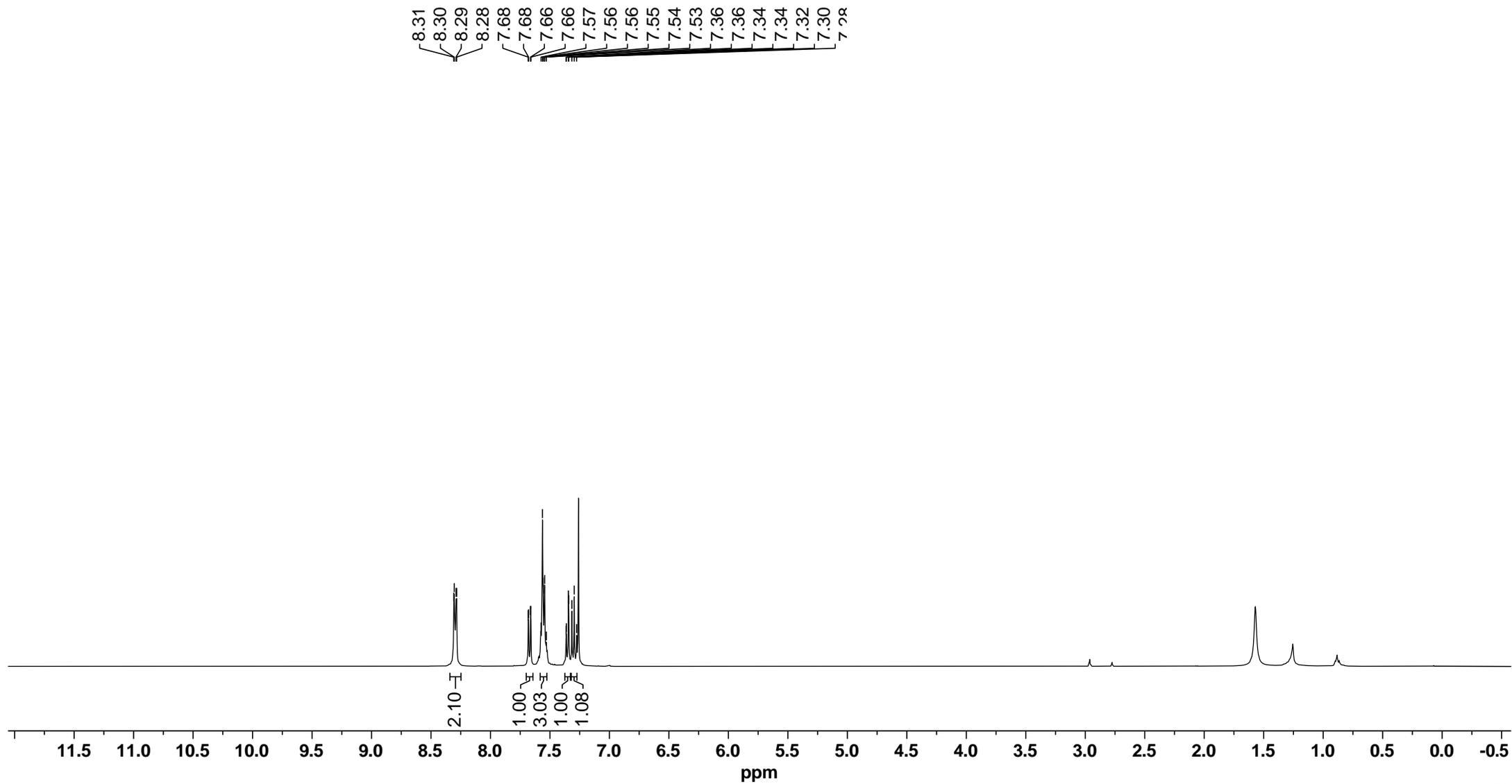
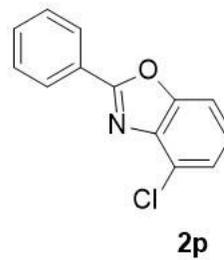
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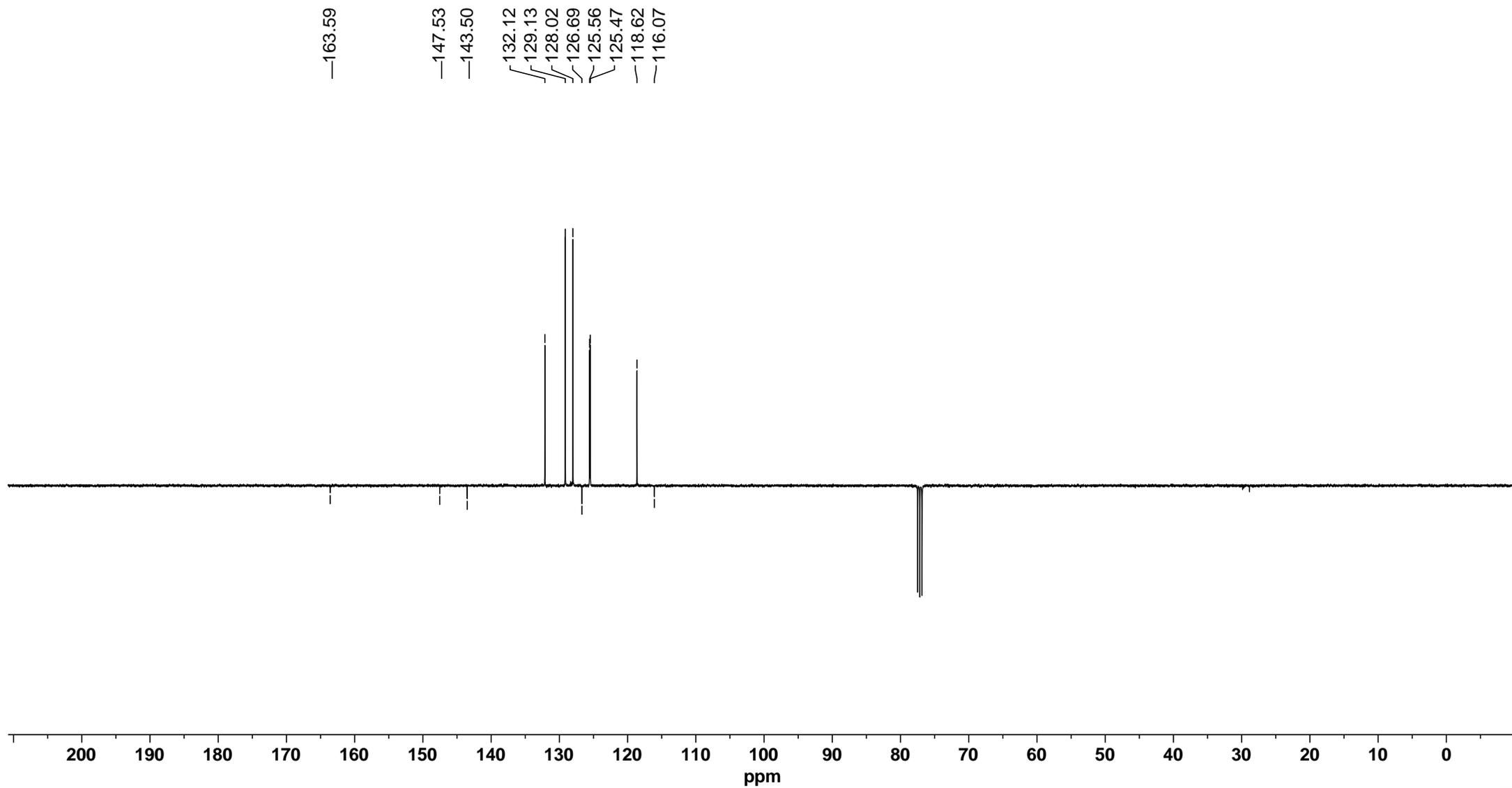
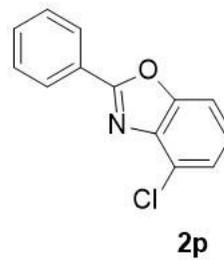
4-bromo-2-phenylbenzo[d]oxazole (2o)



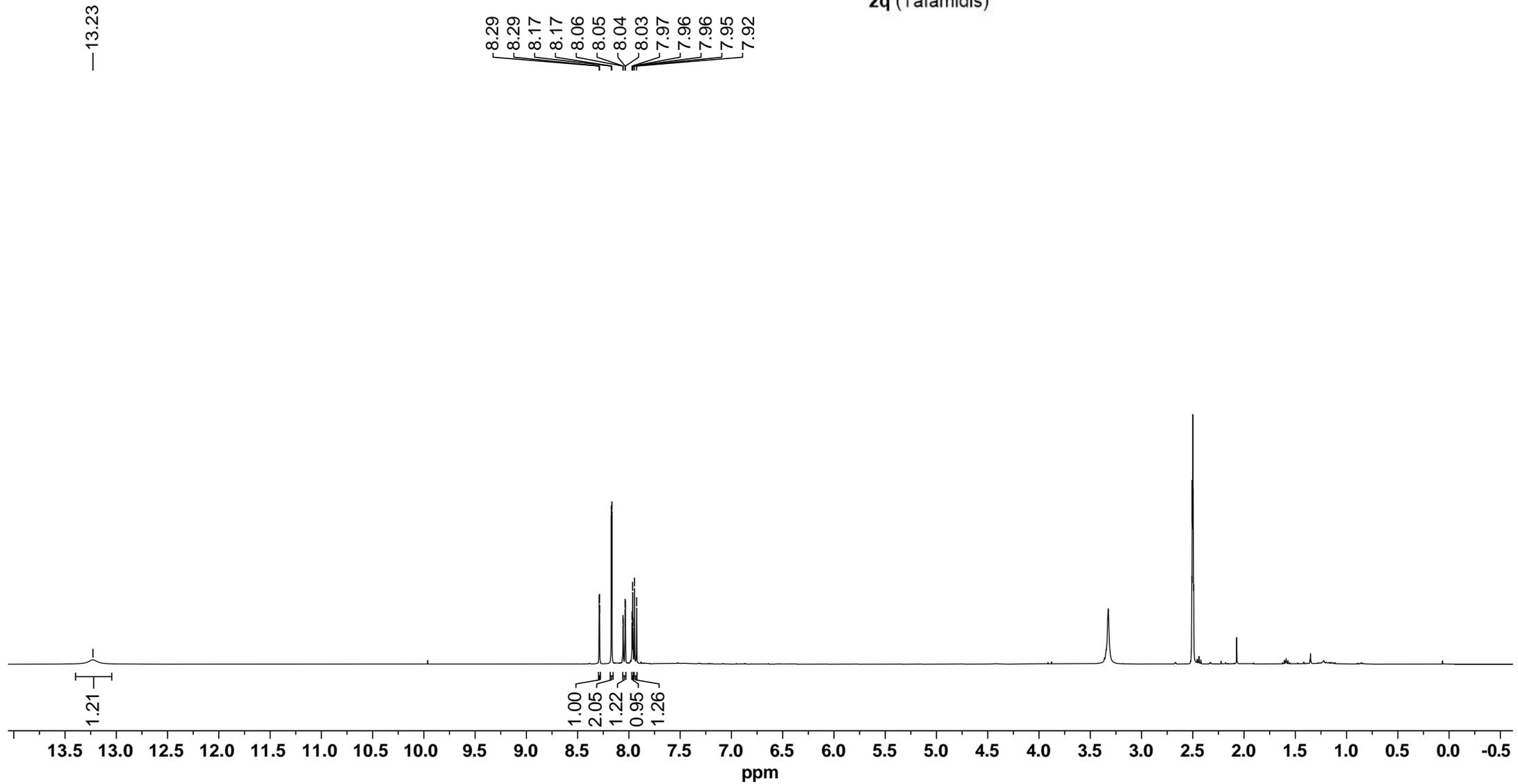
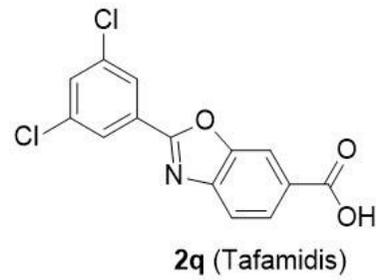
4-chloro-2-phenylbenzo[d]oxazole (2p)



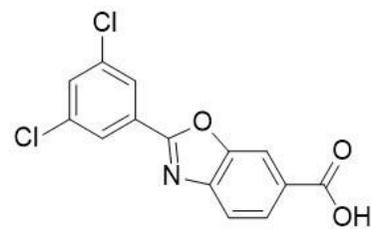
4-chloro-2-phenylbenzo[d]oxazole (2p)



2-(3,5-dichlorophenyl)benzo[d]oxazole-6-carboxylic acid (**2q**)



2-(3,5-dichlorophenyl)benzo[d]oxazole-6-carboxylic acid (**2q**)



**2q** (Tafamidis)

