Supporting Information

For

Pd-Catalyzed C–H Lactonization for Expedient Synthesis of Biaryl Lactones and Total Synthesis of Cannabinol

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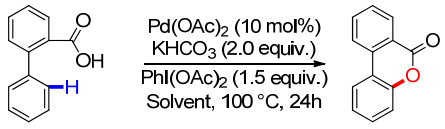
Tabel of Contents

General Information:

Solvents were obtained from Sinopharm and used directly without further purification. NMR spectra were recorded on Bruker-400 (400 MHz for ^{1}H; 100 MHz for ^{13}C) instruments internally referenced to $SiMe_4$ signal. High resolution mass spectra were recorded on P-SIMS-Gly of Bruker Daltonics Inc. using ESI-TOF (electrospray ionization-time of flight). Iodobenzene diacetate and *N*-acetyl amino acid were obtained from Darui Finechamical and used as received. Potassium acetate was purchased from Sinopharm and used as received. Palladium acetate was purchased from Strem.

Table 1. Solvent Screening without Ligand[a,b]

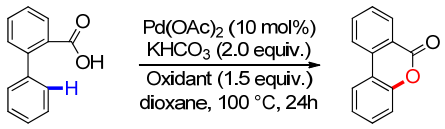


1a **2a**

entry	Solvent	yield (%)	entry	Solvent	yield (%)
1	THF	14	5	*t*-AmOH	7
2	MeCN	6	6	*n*-hexane	8
3	toluene	12	7	dioxane	23
4	DMF	10	8	DCE	10

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), $PhI(OAc)_2$ (0.3 mmol, 1.5 equiv.), $KHCO_3$ (0.4 mmol, 2.0 equiv.), solvent (2 mL), 100 °C, 24 h. [b] Isolated yield.

Table 2. Oxidant Screening without Ligand[a,b]

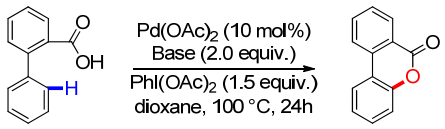


1a **2a**

entry	Oxidant	yield (%)	entry	Oxidant	yield (%)
1	$PhI(OAc)_2$	23	8	Oxone	0
2	NFSI	6	9	TEMPO	0
3	selectfluor	7	10	NBS	0
4	BPO	14	11	I_2	trace
5	DDQ	3	12	$Cu(OAc)_2$	0
6	$K_2S_2O_8$	0	13	AgOAc	0
7	$(NH_4)_2S_2O_8$	0	14	DMSO	0

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), oxidant (0.3 mmol, 1.5 equiv.), $KHCO_3$ (0.4 mmol, 2.0 equiv.), dioxane (2 mL), 100 °C, 24 h. [b] Isolated yield.

Table 3. Base Screening without Ligand[a,b]

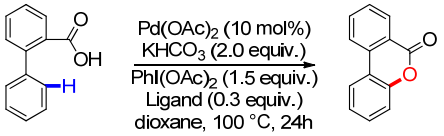


1a **2a**

entry	Base	yield (%)	entry	Base	yield (%)
1	$KHCO_3$	23	16	KOH	5
2	$NaHCO_3$	21	17	NaOH	7
3	K_2CO_3	8	18	*t*-BuOK	13
4	Na_2CO_3	15	19	*t*-BuONa	17
5	Li_2CO_3	12	20	*t*-BuOLi	18
6	Cs_2CO_3	7	21	*i*-Pr_2NH	3
7	Ag_2CO_3	10	22	Pipedine	4
8	KH_2PO_4	13	23	NMM	8
9	K_2HPO_4	14	24	Et_3N	14
10	$K_3PO_4•3H_2O$	7	25	DABCO	4
11	CsF	5	26	Pyridine	14
12	$KF•2H_2O$	8	27	DBU	6
13	AgOAc	11	28	DMAP	4
14	NaOAc	15	29	DMF	10
15	KOAc	8	30	HMTA	15

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), $PhI(OAc)_2$ (0.3 mmol, 1.5 equiv.), base (0.4 mmol, 2.0 equiv.), dioxane (2 mL), 100 °C, 24 h. [b] Isolated yield.

Table 4. Ligand Screening I[a,b]

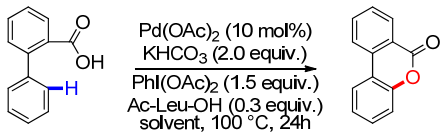


1a **2a**

entry	Ligand	yield (%)	entry	Ligand	yield (%)
1	-	23	8	Boc-Ala-OH	14
2	HOAc	9	9	Boc-Phe-OH	20
3	PivOH	9	10	Boc-Val-OH	15
4	1-$AdCO_2H$	22	11	Boc-Ser-OH	10
5	Ac-Gly-OH	8	12	Boc-Leu-OH	16
6	Ac-Phe-OH	20	13	Boc-Ile-OH	19
7	Ac-Leu-OH	20	14	Cbz-Phe-OH	15

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), $PhI(OAc)_2$ (0.3 mmol, 1.5 equiv.), $KHCO_3$ (0.4 mmol, 2.0 equiv.), Ligand (0.06 mmol, 0.3 equiv.), dioxane (2 mL), 100 °C, 24 h. [b] Isolated yield.

Table 5. Solvent Screening with Ligand[a,b]

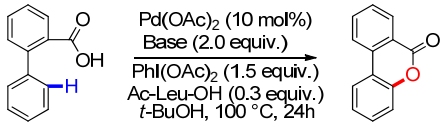


1a **2a**

entry	Solvent	yield (%)	entry	Solvent	yield (%)
1	dioxane	23	16	*n*-hexane	10
2	THF	13	17	*c*-hexane	10
3	toluene	14	18	$MeNO_2$	9
4	DME	4	19	MeCN	20
5	$PhNO_2$	9	20	acetone	16
6	xylene	8	21	EtOAc	21
7	PhCl	8	22	$CHCl_3$	17
8	DMA	14	23	DCE	8
9	DMF	15	24	CCl_4	9
10	DMSO	18	25	$Cl_2CHCHCl_2$	11
11	MeOH	21	26	$(HOCH_2)_2$	trace
12	EtOH	12	27	HOAc	14
13	*i*-PrOH	8	28	TFA	20
14	*t*-BuOH	32	29	NMP	12
15	*t*-AmOH	27			

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), $PhI(OAc)_2$ (0.3 mmol, 1.5 equiv.), $KHCO_3$ (0.4 mmol, 2.0 equiv.), Ac-Leu-OH (0.06 mmol, 0.3 equiv.), solvent (2 mL), 100 °C, 24 h. [b] Isolated yield.

Table 6. Base Screening with Ligand [a,b]

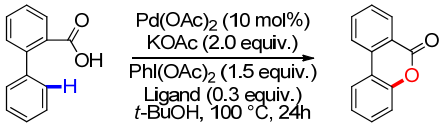


1a **2a**

entry	Base	yield (%)	entry	Base	yield (%)
1	$KHCO_3$	32	16	KOH	63
2	$NaHCO_3$	21	17	NaOH	30
3	K_2CO_3	26	18	*t*-BuOK	63
4	Na_2CO_3	53	19	*t*-BuONa	45
5	Li_2CO_3	11	20	*t*-BuOLi	16
6	Cs_2CO_3	21	21	$TBAF•3H_2O$	18
7	Ag_2CO_3	22	22	Pipedine	trace
8	KH_2PO_4	17	23	NMM	5
9	K_2HPO_4	53	24	Et_3N	trace
10	$K_3PO_4•3H_2O$	32	25	DABCO	8
11	CsF	64	26	Pyridine	7
12	$KF•2H_2O$	52	27	DBU	6
13	AgOAc	29	28	DMAP	trace
14	NaOAc	50	29	DMF	9
15	KOAc	67	30	HMTA	trace

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), $PhI(OAc)_2$ (0.3 mmol, 1.5 equiv.), base (0.4 mmol, 2.0 equiv.), Ac-Leu-OH (0.06 mmol, 0.3 equiv.), *t*-BuOH (2 mL), 100 °C, 24 h. [b] Isolated yield.

Table 7. Ligand Screening II[a,b]

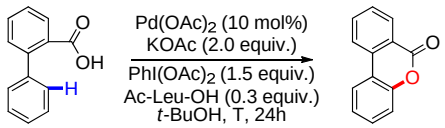


1a **2a**

entry	Ligand	yield (%)	entry	Ligand	yield (%)
1	-	18	27	Boc-Thr-OH	20
2	IMes	14	28	Boc-Trp-OH	trace
3	IPr	21	29	Boc-Val-OH	55
4	BQ	10	30	Boc-HPhe-OH	27
5	18-C-6	7	31	Boc-^{t}Leu-OH	27
6	HOAc	26	32	Boc-PhGly-OH	28
7	PivOH	28	33	Cbz-Ala-OH	34
8	1-AdCO$_2$H	25	34	Cbz-Arg-OH	32
9	5-Oxo-Pro-OH	8	35	Cbz-Phe-OH	26
10	Ac-Ala-OH	66	36	Cbz-Ser-OH	28
11	Ac-CyGly-OH	54	37	Fmoc-Ile-OH	33
12	Ac-Leu-OH	67	38	Fmoc-Leu-OH	29
13	Ac-Gly-OH	67	39	Fmoc-Phe-OH	28
14	Ac-Ile-OH	58	40	Fmoc-Pro-OH	26
15	Ac-^{n}Val-OH	65	41	Fmoc-Thr-OH	trace
16	Ac-^{t}Leu-OH	20	42	Fmoc-Trp-OH	trace
17	Ac-Phe-OH	60	43	Fmoc-Val-OH	31
18	Ac-Val-OH	49	44	Fmoc-Ala-OH	32
19	Ac-Cys-OH	7	45	Piv-Ala-OH	13
20	Ac-Tyr-OH	trace	46	Piv-CyGly-OH	11
21	Boc-Ala-OH	26	47	Piv-Ile-OH	8
22	Boc-Gly-OH	28	48	Piv-Leu-OH	11
23	Boc-Ile-OH	25	49	Piv-^{n}Val-OH	12
24	Boc-Leu-OH	18	50	Piv-^{t}Leu-OH	7
25	Boc-Phe-OH	48	51	Piv-Val-OH	11
26	Boc-Ser-OH	19			

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), Pd(OAc)$_2$ (0.02 mmol, 10 mol%), PhI(OAc)$_2$ (0.3 mmol, 1.5 equiv.), KOAc (0.4 mmol, 2.0 equiv.), Ligand (0.06 mmol, 0.3 equiv.), *t*-BuOH (2 mL), 100 °C, 24 h. [b] Isolated yield.

Table 8. Temperature Screening with Ligand [a,b]

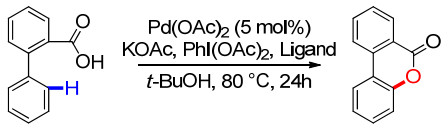


1a **2a**

entry	Temperature(°C)	yield (%)	entry	Temperature(°C)	yield (%)
1	40	19	7	100	67
2	50	41	8	110	67
3	60	74	9	120	70
4	70	77	10	130	69
5	80	80	11	140	65
6	90	78			

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), Pd(OAc)$_2$ (0.02 mmol, 10 mol%), PhI(OAc)$_2$ (0.3 mmol, 1.5 equiv.), KOAc (0.4 mmol, 2.0 equiv.), Ac-Leu-OH (0.06 mmol, 0.3 equiv.), *t*-BuOH (2 mL), Temperature, 24 h. [b] Isolated yield.

Table 9. Amount of Reagents Screening[a,b]

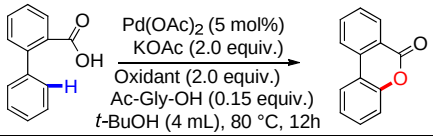


1a **2a**

entry	$PhI(OAc)_2$ (equiv.)	KOAc(equiv.)	Ac-Leu-OH(equiv.)	*t*-BuOH (mL)	yield (%)
1[c]	2.0	2.0	0.30	2	81
2[c]	1.5	3.0	0.30	2	76
3[c]	1.5	2.0	0.30	0.5	52
4[c]	1.5	2.0	0.30	1	63
5[c]	1.5	2.0	0.30	3	79
6[c]	1.5	2.0	0.30	4	90
7	1.5	2.0	0.15	4	84
8	1.2	2.0	0.15	4	75
9	2.0	2.0	0.15	4	88
10	0	2.0	0.15	4	trace
11	1.5	1.2	0.15	4	82
12	1.5	3.0	0.15	4	80
13	1.5	0	0.15	4	17
14	1.5	2.0	0.05	4	79
15	1.5	2.0	0.10	4	78
16[d]	1.5	2.0	0.15	4	trace
17	1.5	2.0	0.15	5	83
18	1.5	2.0	0.15	6	86
19[e]	2.0	2.0	0.15	4	91
20[e,f]	2.0	2.0	0.15	4	93
21[e,f,g]	2.0	2.0	0.09	4	91

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 5 mol%), $PhI(OAc)_2$, KOAc, Ac-Leu-OH, *t*-BuOH, 80 °C, 24 h. [b] Isolated yield. [c] 10 mol% $Pd(OAc)_2$ was used. [d] No $Pd(OAc)_2$. [e] 12 h. [f] Ac-Gly-OH was used as Ligand. [g] 3 mol% $Pd(OAc)_2$ was used.

Table 10. Oxidant Screening with Ligand [a,b]



entry	Oxidant	yield (%)	entry	Oxidant	yield (%)
1	BPO	40	13	NCS	0
2	$Cu(OAc)_2$	0	14	NBS	0
3	BQ	0	15	NIS	0
4	AgOAc	0	16	NFSI	trace
5	Ag_2CO_3	0	17	NFTPT	0
6	Ag_2O	0	18	DDQ	0
7	CAN	15	19	$CuCl_2$	0
8	$K_2S_2O_8$	3	20	V_2O_5	0
9	$(t\text{-BuO})_2$	0	21	$(NH_4)_2S_2O_8$	0
10	$BzOO^tBu$	trace	22	TEMPO	0
11	$PhI(TFA)_2$	9	23	$FeCl_3$	0
12	Oxone	trace	24	$Ce(SO_4)_2$	trace

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 5 mol%), $PhI(OAc)_2$ (0.4 mmol, 2.0 equiv.), KOAc (0.4 mmol, 2.0 equiv.), Ac-Leu-OH (0.06 mmol, 0.15 equiv.), *t*-BuOH (4 mL), 80 °C, 12 h.

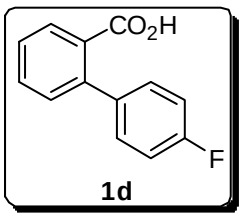
Preparation of Substrates

Substrate **1a** was purchased from Accela ChemBio Co. Ltd. and used as received. Substrates **1b**[1], **1c**[2], **1g**[1], **1h**[3], **1j**[2], **1p**[1], **1q**[1],**1s**[2], **1t**[2], **1v**[4], **1w**[4] were synthesized through the known methods. The other diarylcarboxylic acids were prepared via Suzuki cross coupling.

General procedure of synthesis of diarylcarboxylic acid (1d-1f, 1k-1n, 1r, 1u, 1ab)[2]

Methyl 2-iodobenzoate (2.5 mL, 17 mmol) was added to arylboronic acid (22 mmol) and Na_2CO_3 (3.6 g, 34 mmol) dissolved in THF (68 mL) and water (34 mL) mixed solvents. The reaction mixture was degassed three times and charged with Argon, after which $PdCl_2(PPh_3)_2$ (8 mol%, 1 g, 1.4 mmol) was added. The reaction mixture was heated to 60 °C overnight. The resulting reaction mixture was cooled to room temperature and added to water, the product was extracted with dichloromethane three times. The combined organic phases were dried with Na_2SO_4 and the solvent was evaporated via vacuo. The product was purified by column chromatography to give a colourless liquid. The methyl 2-arylbenzoate was dissolved in a solution of 3.4 g NaOH in 50 mL H_2O and 50 mL MeOH and stirred at 50 °C for 6 h. MeOH was removed under vacuum and the reation mixture was diluted with H_2O, and washed with Et_2O. The aqueous phase was acidified with 3N HCl, then extracted with Et_2O three times. The combined organic phase was washed with H_2O and brine, dried over Na_2SO_4, filtered and the filtration was evaporated under reduced pressure to give the desired product as a solid.

2-(4-fluoro)phenylbenzoic acid (**1d**):

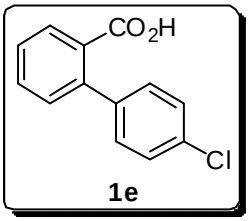


1d

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.92 (m, 1H), 7.56 (td, *J* = 7.6, 1.2 Hz, 1H), 7.43 (td, *J* = 7.7, 1.1 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.31 – 7.26 (m, 2H), 7.12 – 7.02 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 162.5 (d, *J* = 246.3 Hz), 142.7, 137.2 (d, *J* = 3.3 Hz), 132.4, 131.4, 131.0, 130.2 (d, *J* = 8.`

Hz), 129.3, 127.5, 115.1 (d, J = 21.5 Hz). HRMS (EI-TOF) calcd. for $C_{13}H_9O_2F$ (M^+): 216.0587, found: 216.0580.

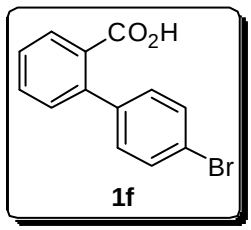
2-(4-chloro)phenylbenzoic acid (**1e**):



1e

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, J = 7.8, 1.2 Hz, 1H), 7.50 (td, J = 7.6, 1.4 Hz, 1H), 7.37 (td, J = 7.6, 1.3 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.25 (dd, J = 7.7, 1.0 Hz, 1H), 7.21 – 7.15 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 142.5, 139.7, 133.7, 132.5, 131.3, 131.1, 130.0, 129.1, 128.4, 127.7. HRMS (ESI) calcd. for $C_{13}H_8O_2Cl$ ($[M-H]^-$) 2132.0207, found 231.0213.

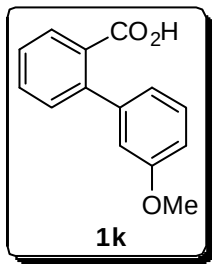
2-(4-bromo)phenylbenzoic acid (**1f**):



1f

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, J = 7.8, 1.1 Hz, 1H), 7.50 (td, J = 7.6, 1.4 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.38 (td, J = 7.6, 1.3 Hz, 1H), 7.26 (dd, J = 7.7, 0.9 Hz, 1H), 7.16 – 7.10 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 142.5, 140.2, 132.4, 131.3, 131.2, 1311, 130.3, 129.0, 127.8, 121.9. HRMS (ESI) calcd. for $C_{13}H_8O_2Br$ ($[M-H]^-$) 274.9702, found 274.9705.

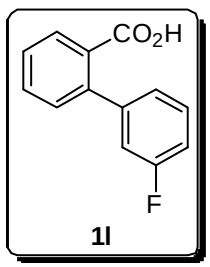
2-(3-methoxy)phenylbenzoic acid (**1k**):



1k

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, J = 7.8, 1.1 Hz, 1H), 7.47 (td, J = 7.6, 1.4 Hz, 1H), 7.34 (td, J = 7.6, 1.3 Hz, 1H), 7.30 (dd, J = 7.7, 0.9 Hz, 1H), 7.24 – 7.18 (m, 1H), 6.88 – 6.76 (m, 3H), 3.74 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 159.4, 143.2, 142.5, 132.1, 131.2, 130.7, 129.6, 129.2, 127.4, 121.2, 114.3, 113.2, 55.4. HRMS (ESI) calcd. for $C_{14}H_{11}O_3$ ($[M-H]^-$) 2227.0703, found 227.0707.

2-(3-fluoro)phenylbenzoic acid (**1l**):

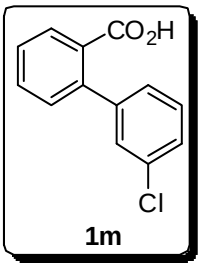


1l

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, J = 7.8, 1.3 Hz, 1H), 7.50 (td, J = 7.6, 1.3 Hz, 1H), 7.38 (td, J = 7.7, 1.2 Hz, 1H), 7.35 – 7.21 (m, 2H), 7.06 – 6.93 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 162.6 (d, J = 245.7 Hz), 143.4 (d, J = 8.0 Hz), 142.4 (d, J = 2.0 Hz), 132.4, 131.2, 131.0, 129.6 (d, J = 8.4 Hz), 129.3, 127.8, 124.5 (d, J

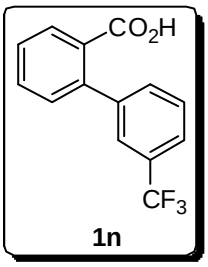
= 2.9 Hz), 115.7 (d, *J* = 22.1 Hz), 114.4 (d, *J* = 21.0 Hz). HRMS (ESI) calcd. for $C_{13}H_8O_2F$ ([M-H]$^-$) 215.0503, found 215.0509.

2-(3-chloro)phenylbenzoic acid (**1m**):



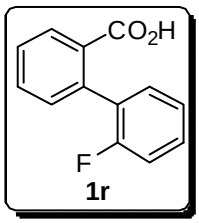
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.50 (td, *J* = 7.6, 1.4 Hz, 1H), 7.37 (td, *J* = 7.6, 1.3 Hz, 1H), 7.29 – 7.20 (m, 4H), 7.12 (dt, *J* = 6.8, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 143.1, 142.3, 134.0, 132.5, 131.3, 131.1, 129.3, 129.1, 128.6, 127.9, 127.6, 127.0. HRMS (ESI) calcd. for $C_{13}H_8O_2Cl$ ([M-H]$^-$) 231.0207, found 231.0213.

2-(3-trifluoromethyl)phenylbenzoic acid (**1n**):



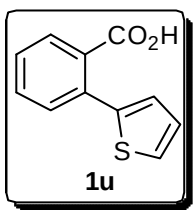
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.57 – 7.48 (m, 3H), 7.44 – 7.35 (m, 3H), 7.27 (dd, *J* = 7.6, 1.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 142.4, 142.0, 132.7, 132.0 (d, *J* = 1.1 Hz), 131.4, 131.3, 130.5 (q, *J* = 32.3 Hz), 129.0, 128.5, 128.1, 125.5 (q, *J* = 3.8 Hz), 124.3 (d, *J* = 272.4 Hz), 124.2 (q, *J* = 3.8 Hz). HRMS (ESI) calcd. for $C_{14}H_8O_2F_3$ ([M-H]$^-$) 265.0471, found 265.0472.

2-(2-fluoro)phenylbenzoic acid (**1r**):



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.53 (td, *J* = 7.6, 1.4 Hz, 1H), 7.39 (td, *J* = 7.7, 1.3 Hz, 1H), 7.31 – 7.19 (m, 3H), 7.11 (td, *J* = 7.5, 1.2 Hz, 1H), 6.99 (ddd, *J* = 9.2, 8.2, 1.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 159.6 (d, *J* = 245.8 Hz), 137.3, 132.7, 131.8, 131.0, 130.5 (d, *J* = 3.4 Hz), 129.8 (d, *J* = 0.6 Hz), 129.5 (d, *J* = 8.2 Hz), 129.0 (d, *J* = 15.9 Hz), 128.1, 124.1 (d, *J* = 3.6 Hz), 115.3 (d, *J* = 22.3 Hz). HRMS (ESI) calcd. for $C_{13}H_8O_2F$ ([M-H]$^-$) 215.0503, found 215.0509.

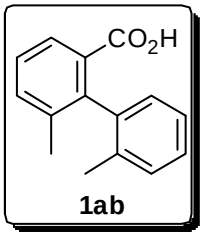
2-(thiophen-2-yl)benzoic acid (**1u**):



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.44 (dtd, *J* = 8.9, 7.7, 1.3 Hz, 2H), 7.35 (ddd, *J* = 7.4, 7.2, 1.6 Hz, 1H), 7.28 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.00 (ddd, *J* = 8.5, 4.3, 2.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 141.7, 135.3, 132.0, 131.9,

130.6, 130.3, 127.9, 127.4, 126.9, 126.2. HRMS (ESI) calcd. for $C_{11}H_7O_2S$ ($[M-H]^-$) 203.0161, found 203.0157.

2-(*o*-tolyl)-3-methylbenzoic acid (**1ab**):



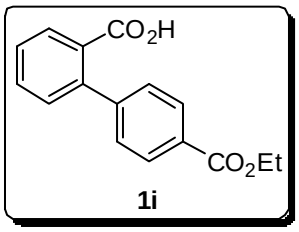
1ab

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.7 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.28 – 7.15 (m, 3H), 6.95 (d, *J* = 7.3 Hz, 1H), 1.97 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 142.5, 139.7, 137.7, 135.7, 134.3, 129.8, 129.5, 128.4, 128.2, 127.4, 127.2, 125.7, 20.4, 19.8. HRMS (EI-TOF) calcd. for $C_{15}H_{14}O_2$ (M^+): 226.0994, found: 224.0988.

General procedure of synthesis of diarylcarboxylic acid (1i, 1o)[5]

To a solution of 2-iodobenzoic acid (2.48 g, 10 mmol), K_2CO_3 (2.76 g, 20 mmol), TBAI (369 mg, 1 mmol) in THF (60 mL) was added PMBCl (1.63 mL, 12 mmol). The mixture was heated to reflux for 6 h. After cooling to room temperature, filtered off the insolubles, the filtrate was diluted with water, and extracted with dichloromethane for 3 times, the combined organic extracts was washed with $Na_2S_2O_3$ (sat.) and brine, dried over Na_2SO_4. The product was purified by column chromatography after removed the solvent. *p*-methoxybenzyl 2-iodobenzoate was added to arylboronic acid (12 mmol) and Na_2CO_3 (1.8 g, 17 mmol) dissolved in THF (34 mL) and water (17 mL) mixed solvents. The reaction mixture was degassed three times and charged with Argon, after which $PdCl_2(PPh_3)_2$ (8 mol%, 0.5 g, 0.7 mmol) was added. The reaction mixture was heated to 60 ^{o}C overnight. The resulting reaction mixture was cooled to room temperature and added to water, the product was extracted with dichloromethane three times. The combined organic phases were dried with Na_2SO_4 and the solvent was evaporated via vacuo. The product was purified by column chromatography to give a colourless liquid. The *p*-methoxybenzyl 2-arylbenzoate was dissolved in 35 mL dichloromethane, and trifluoroacetic acid (2.8 mL, 35 mmol) was added and the solution was stirred at room temperature for 1 h after which time the reaction mixture was evaporated to dryness. The residue was purified by column chromatography.

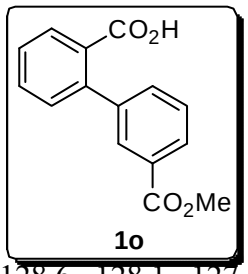
2-(4-ethoxycabonyl)phenylbenzoic acid (**1i**):



1i

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.02 (m, 2H), 7.99 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.57 (td, *J* = 7.6, 1.4 Hz, 1H), 7.45 (td, *J* = 7.7, 1.3 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.34 (dd, *J* = 7.7, 0.9 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 1H), 1.40 (t, *J* = 7.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 166.7, 146.0, 142.8, 132.4, 131.2, 131.1, 129.5, 129.4, 129.2 (2C), 128.7, 127.9, 61.1, 14.5. HRMS (EI-TOF) calcd. for $C_{16}H_4O_4$ (M^+): 270.0892, found: 270.0896.

2-(3-methoxycarbonyl)phenylbenzoic acid (**1o**):



1o

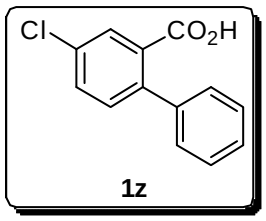
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.96 (m, 3H), 7.58 (td, *J* = 7.6, 1.3 Hz, 1H), 7.52 – 7.40 (m, 3H), 7.35 (dd, *J* = 7.6, 0.7 Hz, 1H), 3.90 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 167.2, 142.8, 141.6, 133.3, 132.5, 131.4, 131.2, 130.1, 129.6, 129.1, 128.6, 128.1, 127.8, 52.3. HRMS (EI-TOF) calcd. for $C_{15}H_{12}O_4$ (M^+): 256.0736, found: 256.0742.

General procedure of synthesis of diarylcarboxylic acid (1z, 1aa)[6]

To a solution of 2-hydroxyarylcarboxylic acid (11.5 mmol), Cs_2CO_3 (1.87 g, 5.7 mmol) in 100 mL DMF was added iodomethane (0.75 mL, 12 mmol) stirred at room temperature for 1.5 h, taken up in EtOAc, and washed with H_2O, $NaHCO_3$ (sat.), and brine, dried over Na_2SO_4, and concentrated in vacuo. The crude methyl ester was dissolved in dichloromethane (100 mL) under argon, cooled to -78 °C, and treatmented with Et_3N (3.2 mL, 23 mmol) was followed by the dropwise addition of Tf_2O (2.13 mL, 12.6 mmol). The mixture was stirred at -78 °C for 30 min and then warmed to room temperature overnight. The mixture was diluted with ether and washed with 1N HCl. The aqueous layer was back-extracted with additional ether, and the combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The product was purified by column chromatography. 2-methoxycarbonylaryl triflate was added to phenylboronic acid (1.2 g, 10 mmol) and K_3PO_4 (2.5 g, 12 mmol) dissolved in dioxane (25 mL). The reaction mixture was degassed three times and charged with

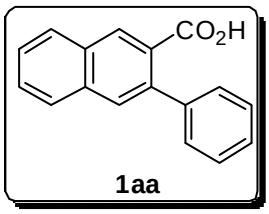
Argon, after which Pd (PPh_3)$_4$ (5 mol%, 290 mg, 0.25 mmol) was added. The reaction mixture was heated to 110 °C for 4 h. The resulting reaction mixture was cooled to room temperature and added to water, the product was extracted with dichloromethane three times. The combined organic phases were dried with Na_2SO_4 and the solvent was evaporated via vacuo. The product was purified by column chromatography to give a colourless liquid. The methyl 2-arylbenzoate was dissolved in a solution of 1 g NaOH in 15 mL H_2O and 15 mL MeOH and stirred at 50 °C for 6 h. MeOH was removed under vacuum and the reation mixture was diluted with H_2O, and washed with Et_2O. The aqueous phase was acidified with 3N HCl, then extracted with Et_2O three times. The combined organic phase was washed with H_2O and brine, dried over Na_2SO_4, filtered and the filtration was evaporated under reduced pressure to give the desired product as a solid.

2-phenyl-5-chlorobenzoic acid (**1z**):



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 2.3 Hz, 1H), 7.45 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.35 – 7.26 (m, 3H), 7.26 – 7.19 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 142.0, 140.0 133.5, 132.6, 132.2, 130.7 (2C), 128.5, 128.3, 127.9. HRMS (ESI) calcd. for $C_{13}H_8O_2Cl$ ([M-H]$^-$) 231.0207, found 231.0211.

3-phenyl-2-naphthioc acid (**1aa**):



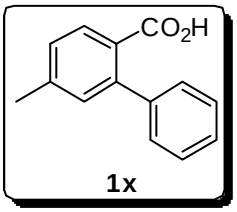
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.74 (s, 1H), 7.54 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.49 (ddd, *J* = 8.0, 7.0, 1.3 Hz, 1H), 7.39 – 7.28 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 141.3, 139.3, 134.9, 132.6, 131.6, 130.4, 128.9, 128.8, 128.2, 127.9, 127.7, 127.3, 127.0. HRMS (ESI) calcd. for $C_{17}H_{11}O_2$ ([M-H]$^-$) 247.0754, found 247.0758.

General procedure of synthesis of diarylcarboxylic acid (1x, 1y)[7]

2-Bromo-arylcarboxylic acid (4.3 g, 20 mmol), phenylboronic acid (2.9 g, 24 mmol), and $LiOH{\cdot}H_2O$ (1.85 g, 44 mmol). 60 mL NMP and 60 mL H_2O was added followed by $Pd_2(dba)_3$ (275 mg, 0.3 mmol) under a nitrogen blanket, and the reaction

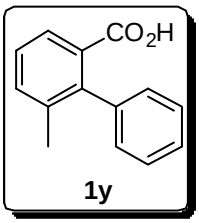
mixture was heated to 65 °C for 24 h. After cool to room temperature, the reaction mixture was acidified to pH=3 with 3N HCl, and extracted with diethyl ether three times. The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The product was purified by column chromatography.

2-phenyl-4-methylbenzoic acid (**1x**):



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 0H), 7.45 – 7.32 (m, 5H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.20 (s, 1H), 2.46 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 143.8, 142.9, 141.4, 132.2, 131.2, 128.6, 128.1, 128.0, 127.4, 126.4, 21.6. HRMS (ESI) calcd. for $C_{14}H_{11}O_2$ ([M-H]$^-$) 211.0754, found 211.0758.

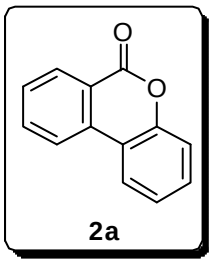
2-phenyl-3-methylbenzoic acid (**1y**):



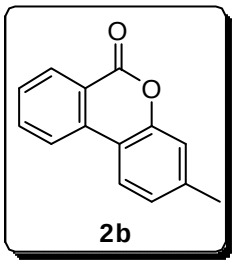
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.44 – 7.31 (m, 4H), 7.18 (dd, *J* = 5.1, 2.9 Hz, 2H), 2.11 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 142.7, 140.1, 137.7, 134.1, 130.2, 128.7, 128.1 (2C), 127.2, 127.1, 20.9. HRMS (ESI) calcd. for $C_{14}H_{11}O_2$ ([M-H]$^-$) 211.0754, found 211.0759.

General Procedure of $Pd(OAc)_2$-Catalyzed Carboxyl-Directed C-H Activation/C-O Cyclization:

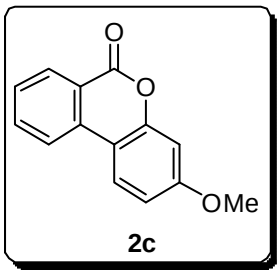
In a 35 mL sealed tube, 4.0 mL *t*-BuOH was added to a mixture of diaryl-carboxylic acid **1** (0.2 mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 5 mol%), N-acetylglycin (3.5 mg, 0.03 mmol, 0.15 equiv.), KOAc (39.2 mg, 0.4 mmol, 2.0 equiv.), $PhI(OAc)_2$ (128.8 mg, 2.0 equiv.) under air. The tube was sealed with a Teflon lined cap and the reaction mixture was stirred at 80 °C for 12 h. After cooling to room temperature, the mixture was concentrated under vacuum and the residue was purified by column chromatography on silica gel with a gradient eluent of petroleum ether, ethyl acetate and dichloromethane to give the corresponding products.



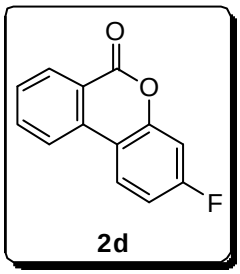
2a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (ddd, *J* = 8.0, 1.4, 0.5 Hz, 1H), 8.14 (d, *J* = 8.1 Hz 1H), 8.08 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.84 (ddd, *J* = 8.1, 7.3, 1.4 Hz, 1H), 7.60 (ddd, *J* = 8.3, 7.4, 1.1 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.41 – 7.32 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 151.4, 134.9, 134.8, 130.6, 130.5, 129.0, 124.6, 122.8, 121.8, 121.3, 118.1, 117.8. HRMS (APCI) calcd. for $C_{13}H_9O_2$ ($[M+H]^+$): 197.0597, found: 197.0592.



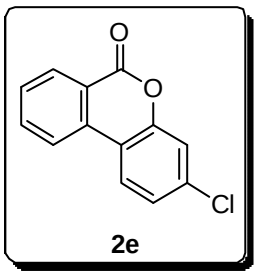
2b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.81 (ddd, *J* = 7.9, 7.7, 1.4 Hz, 1H), 7.55 (ddd, *J* = 7.6, 7.6, 1.1 Hz, 1H), 7.18 (s, 1H), 7.15 (d, *J* = 8.1 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 151.4, 141.4, 135.1, 134.9, 130.7, 128.5, 125.8, 122.6, 121.6, 121.0, 118.0, 115.6, 21.6. HRMS (APCI) calcd. for $C_{14}H_{11}O_2$ ($[M+H]^+$): 211.0754, found: 211.0747.



2c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (ddd, *J* = 8.0, 1.4, 0.5 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 7.78 (ddd, *J* = 8.1, 7.3, 1.4 Hz, 1H), 7.50 (ddd, *J* = 8.2, 7.3, 1.1 Hz, 1H), 6.92 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.87 (d, *J* = 2.5 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 161.5, 152.6, 135.2, 134.9, 130.5, 127.7, 123.8, 121.1, 120.0, 112.4, 111.2, 101.7, 55.7. HRMS (APCI) calcd. for $C_{14}H_{11}O_3$ ($[M+H]^+$): 227.0703, found: 227.0697.

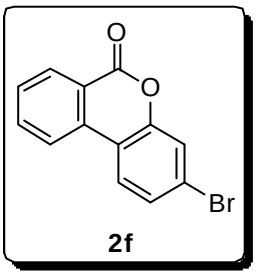


2d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.09 – 8.01 (m, 2H), 7.84 (ddd, *J* = 8.1, 7.4, 1.4 Hz, 1H), 7.59 (ddd, *J* = 7.6, 7.6, 1.0 Hz, 1H), 7.13 – 7.05 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6 (d, *J* = 251.3 Hz), 160.9, 152.3 (d, *J* = 12.3 Hz), 135.2, 134.4, 130.8, 128.9, 124.5 (d, *J* = 9.9 Hz), 121.6, 120.6 (d, *J* = 0.9 Hz), 114.7 (d, *J* = 3.2 Hz), 112.5 (d, *J* = 22.4 Hz), 105.2 (d, *J* = 25.3 Hz). HRMS (EI-TOF) calcd. for $C_{13}H_7O_2F$ (M^+): 214.0430, found: 214.0427.



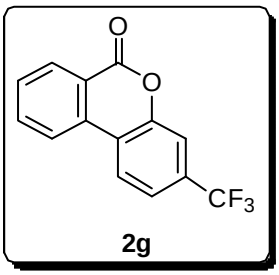
2e

2e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (ddd, *J* = 8.0, 1.4, 0.5 Hz, 1H), 8.11 – 8.05 (m, 1H), 7.99 (d, *J* = 8.6 Hz, 1H), 7.84 (ddd, *J* = 8.1, 7.3, 1.4 Hz, 1H), 7.61 (ddd, *J* = 8.3, 7.4, 1.1 Hz, 1H), 7.39 (d, *J* = 2.1 Hz, 1H), 7.32 (dd, *J* = 8.5, 2.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 151.6, 136.0, 135.2, 134.1, 130.8, 129.3, 125.1, 123.9, 121.8, 121.0, 118.0, 116.8. HRMS (EI-TOF) calcd. for $C_{13}H_7O_2Cl$ (M^+): 230.0135, found: 230.0130.



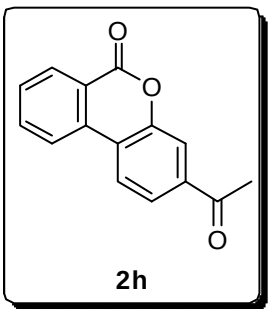
2f

2f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 7.9 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.84 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 1.8 Hz, 1H), 7.47 (dd, *J* = 8.5, 1.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 151.6, 135.2, 134.0, 130.8, 129.4, 127.9, 124.0, 123.8, 121.7, 121.1, 120.9, 117.2. HRMS (APCI) calcd. for $C_{13}H_8O_2Br$ ($[M+H]^+$): 274.9702, found: 274.9695.

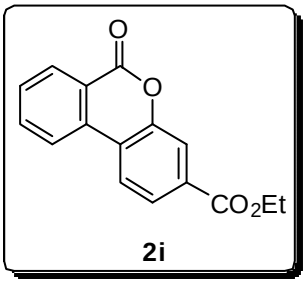


2g

2g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (dd, *J* = 7.9, 1.0 Hz, 1H), 8.19 (t, *J* = 8.1 Hz, 2H), 7.90 (ddd, *J* = 7.7, 7.4, 1.4 Hz, 1H), 7.69 (ddd, *J* = 7.7, 7.6, 1.0 Hz, 1H), 7.64 (s, 1H), 7.60 (dd, *J* = 8.3, 1.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 151.2, 135.3, 133.6, 132.4 (q, *J* = 33.5 Hz), 131.0, 130.3, 123.8, 123.4, (q, *J* = 272.6 Hz),122.3, 121.9, 121.2 (q, *J* = 3.8 Hz), 115.4 (q, *J* = 4.0 Hz). HRMS (EI-TOF) calcd. for $C_{14}H_7O_2F_3$ (M^+): 264.0398, found: 264.0349.

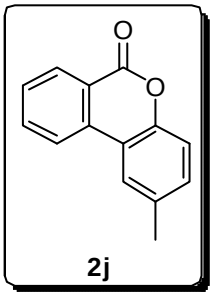


2h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.17 (t, *J* = 8.5 Hz, 2H), 7.95 – 7.85 (m, 3H), 7.67 (ddd, *J* = 7.6, 7.5, 1.1 Hz,1H), 2.67 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.6, 160.7, 151.2, 138.5, 135.2, 133.7, 130.9, 130.2, 124.0, 123.3, 122.5, 122.1, 121.9, 118.0, 26.8. HRMS (EI-TOF) calcd. for $C_{15}H_{10}O_3$ (M^+): 238.0630, found: 238.0636.

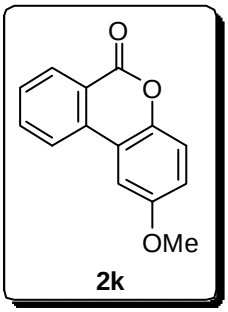


2i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (dd, *J* = 7.9, 1.0 Hz, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 8.07 (d, *J* = 8.7 Hz, 1H), 7.95

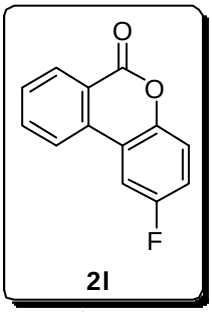
(td, J = 4.3, 1.6 Hz, 2H), 7.85 (td, J = 7.8, 1.4 Hz, 1H), 7.63 (ddd, J = 7.6, 7.6, 1.0 Hz, 1H), 4.42 (q, J = 7.1 Hz, 2H), 1.44 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 160.6, 151.0, 135.1, 133.8, 132.3, 130.8, 130.0, 125.3, 122.9, 122.4, 121.8, 119.0, 61.6, 14.4. HRMS (EI-TOF) calcd. for $C_{16}H_{12}O_4$ (M^+): 268.0736, found: 268.0736.



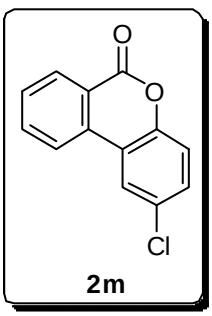
2j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 – 8.36 (m, 1H), 8.11 (dd, J = 11.2, 3.9 Hz, 1H), 7.87 – 7.78 (m, 2H), 7.62 – 7.53 (m, 1H), 7.31 – 7.22 (m, 2H), 2.46 (d, J = 3.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 149.4, 134.8, 134.7, 134.1, 131.4, 130.6, 128.7, 122.8, 121.6, 121.3, 117.6, 117.5, 21.2. HRMS (EI-TOF) calcd. for $C_{14}H_{10}O_2$ (M^+): 210.0681, found: 210.0684.



2k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (ddd, J = 7.9, 1.4, 0.5 Hz, 1H), 8.08 (d, J = 8.1 Hz, 1H), 7.83 (ddd, J = 8.1, 7.3, 1.4 Hz, 1H), 7.60 (ddd, J = 8.3, 7.4, 1.1 Hz, 1H), 7.51 (d, J = 2.9 Hz, 1H), 7.32 (d, J = 9.0 Hz, 1H), 7.06 (dd, J = 9.0, 2.9 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 156.4, 145.6, 134.7, 134.6, 130.6, 129.0, 121.7, 121.4, 118.7, 118.2, 117.2, 106.3, 55.9. HRMS (APCI) calcd. for $C_{14}H_{11}O_3$ ($[M+H]^+$): 227.0703, found: 227.0696.

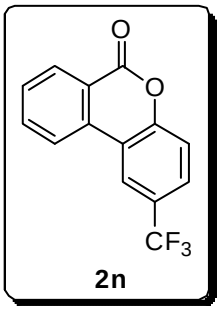


2l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, J = 8.0, 0.9 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.84 (td, J = 7.7, 1.4 Hz, 1H), 7.69 (dd, J = 9.1, 2.9 Hz, 1H), 7.62 (ddd, J = 7.6, 7.5, 1.0 Hz, 1H), 7.33 (dd, J = 9.0, 4.7 Hz, 1H), 7.18 (ddd, J = 9.0, 7.7, 2.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 159.4 (d, J = 243.4 Hz), 147.5 (d, J = 2.1 Hz), 135.1, 134.0 (d, J = 2.7 Hz), 130.8, 129.7, 122.0, 121.3, 119.4 (d, J = 8.6 Hz), 119.3 (d, J = 8.3 Hz), 117. (d, J = 24.2 Hz), 108.9 (d, J = 24.9 Hz). HRMS (EI-TOF) calcd. for $C_{13}H_7O_2F$ (M^+): 214.0430, found: 214.0428.



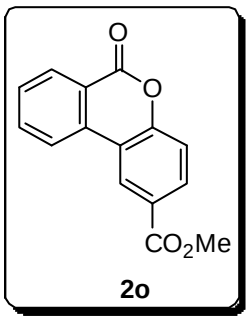
2m: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (dd, J = 7.9, 0.9 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.95 (d, J = 2.4 Hz, 1H), 7.83 (ddd, J = 7.9, 7.7, 1.3 Hz, 1H), 7.61 (ddd, J = 7.6, 7.6, 0.9 Hz, 1H), 7.40 (dd, J =

8.8, 2.4 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 149.7, 135.1, 133.6, 130.8, 130.4, 130.1, 129.7, 122.7, 121.8, 121.3, 119.4, 119.2. HRMS (EI-TOF) calcd. for $C_{13}H_7O_2Cl$ (M^+): 230.0135, found: 230.0130.



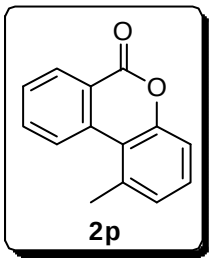
2n

2n: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (dd, J = 7.9, 0.9 Hz, 1H), 8.33 (d, J = 1.3 Hz, 1H), 8.17 (d, J = 8.1 Hz, 1H), 7.90 (ddd, J = 8.1, 7.4, 1.4 Hz, 1H), 7.73 (dd, J = 8.6, 1.6 Hz, 1H), 7.67 (ddd, J = 7.6, 7.5, 1.0 Hz, 1H), 7.48 (d, J = 8.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 153.3 (d, J = 1.1 Hz), 153.3, 135.4, 133.7, 131.0, 130.0, 127.3 (q, J = 3.5 Hz), 127.2 (q, J = 33.1 Hz), 123.9, (q, J = 272.1 Hz), 122.0, 121.5, 120.6 (q, J = 4.0 Hz), 118.7, 118.6. HRMS (EI-TOF) calcd. for $C_{14}H_7O_2F_3$ (M^+): 264.0398, found: 264.0367.



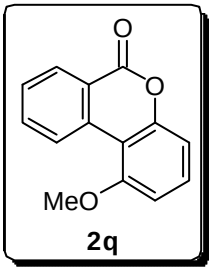
2o

2o: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, J = 2.0 Hz, 1H), 8.41 (dd, J = 8.0, 1.0 Hz, 1H), 8.22 (d, J = 8.1 Hz, 1H), 8.13 (dd, J = 8.6, 2.0 Hz, 1H), 7.87 (ddd, J = 8.1, 7.4, 1.4 Hz, 1H), 7.64 (ddd, J = 8.1, 8.0, 1.0 Hz, 1H), 7.40 (d, J = 8.6 Hz, 1H), 3.98 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 160.6, 154.3, 135.3, 134.2, 131.5, 130.8, 129.6, 126.7, 125.2, 122.3, 121.3, 118.2, 118.1, 52.6. HRMS (EI-TOF) calcd. for $C_{15}H_{10}O_4$ (M^+): 254.0579, found: 254.0575.



2p

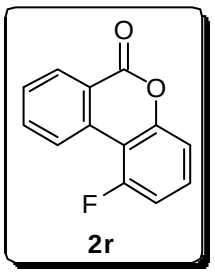
2p: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (dd, J = 7.9, 1.3 Hz, 1H), 8.40 (d, J = 8.4 Hz, 1H), 7.84 (ddd, J = 7.8, 7.3, 1.6 Hz, 1H), 7.60 (ddd, J = 7.6, 7.5, 1.0 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.28 (dd, J = 8.2, 1.0 Hz, 1H), 7.18 (d, J = 7.4 Hz, 1H), 2.91 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 152.3, 136.3, 136.1, 134.4, 130.9, 129.4, 128.9, 128.2, 126.3, 122.2, 117. 6, 116.3, 25.6. HRMS (APCI) calcd. for $C_{14}H_{11}O_2$ ($[M+H]^+$): 211.0754, found: 211.0748.



2q

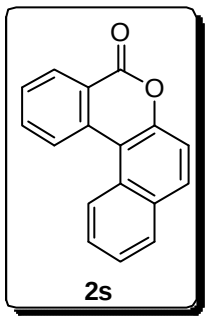
2q: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (dd, J = 8.4, 0.5 Hz, 1H), 8.42 (ddd, J = 7.9, 1.5, 0.4 Hz, 1H), 7.77 (ddd, J = 8.5, 7.3, 1.6 Hz, 1H), 7.53 (ddd, J = 7.9, 7.4, 1.1 Hz, 1H), 7.38 (t, J = 8.3 Hz, 1H), 7.00 (dd, J = 8.3, 1.1 Hz, 1H), 6.86 (dd, J = 8.3, 0.8 Hz, 1H), 4.04

(s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 158.5, 152.7, 134.8, 134.7, 130.2, 130.0, 128.1, 127.6, 121.1, 110.5, 108.4, 107.0, 56.1. HRMS (EI-TOF) calcd. for $C_{14}H_{10}O_3$ (M^+): 226.0630, found: 226.0625.



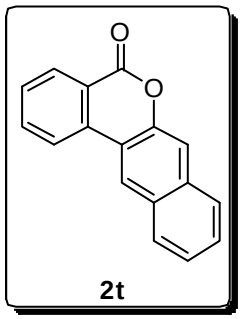
2r

2r: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.3 Hz, 1H), 8.47 (dd, *J* = 7.9, 1.5 Hz,1H), 7.86 (ddt, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.64 (ddd, 1H), 7.43 (td, *J* = 8.3, 5.8 Hz, 1H), 7.22 (dt, *J* = 8.3, 1.1 Hz, 1H), 7.09 (ddd, *J* = 12.3, 8.3, 1.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 160.6 (d, *J* = 254.0 Hz), 152.3 (d, *J* = 6.5 Hz), 135.4 (d, *J* = 1.9 Hz), 132.5 (d, *J* = 4.6 Hz), 130.7, 130.1 (d, *J* = 11.3 Hz), 129.3 (d, *J* = 1.7 Hz), 126.8 (d, *J* = 21.8 Hz), 121.3, 113.8 (d, *J* = 3.5 Hz), 112.2 (d, *J* = 23.6 Hz), 108.5 (d, *J* = 13.2 Hz). HRMS (APCI) calcd. for $C_{13}H_8O_2F$ ($[M+H]^+$): 215.0503, found: 215.0498.



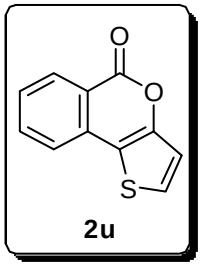
2s

2s: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 8.6 Hz, 1H), 8.64 (d, *J* = 8.3 Hz, 1H), 8.53 – 8.46 (m, 1H), 7.98 – 7.84 (m, 3H), 7.70 – 7.59 (m, 2H), 7.55 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 150.2, 135.3, 134.3, 131.6, 131.5, 130.6, 129.4, 129.3, 128.1, 127.8, 126.3, 125.4, 124.9, 122.3, 117.5, 112.4. HRMS (APCI) calcd. for $C_{17}H_{11}O_2$ ($[M+H]^+$): 247.0754, found: 247.0747.



2t

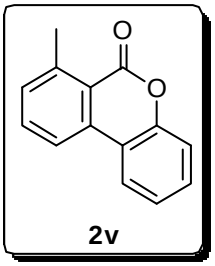
2t: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.44 (dd, *J* = 7.9, 1.0 Hz, 1H), 8.31 (d, *J* = 8.1 Hz, 1H), 7.96 (dd, *J* = 8.1, 0.6 Hz, 1H), 7.91 – 7.83 (m, 2H), 7.77 (s, 1H), 7.61 (ddd, *J* = 7.6, 7.5, 1.1 Hz, 1H), 7.54 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.51 (dd, *J* = 8.1, 1.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 148.8, 134.9, 134.7, 134.1, 130.8, 130.3, 129.1, 128.3, 127.7, 127.3, 125.8, 122.6, 122.1, 121.5, 118.2, 113.6. HRMS (APCI) calcd. for $C_{17}H_{11}O_2$ ($[M+H]^+$): 247.0754, found: 247.0750.



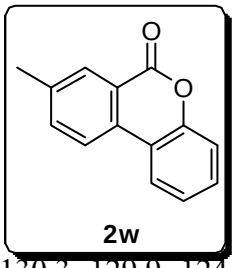
2u

2u: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.75 (td, *J* = 7.9, 1.3 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.49 (ddd, *J*

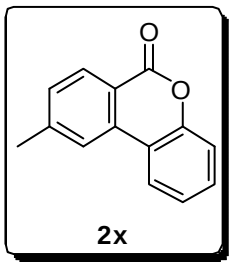
= 7.7, 7.7, 1.1 Hz, 1H), 7.40 (d, *J* = 5.4 Hz, 1H), 7.06 (d, *J* = 5.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 150.0, 134.3, 132.8, 130.1, 126.8, 124.5, 121.0, 117.7, 117.5, 115.1. HRMS (EI-TOF) calcd. for $C_{11}H_6O_2S$ (M^+): 202.0089, found: 202.0081.



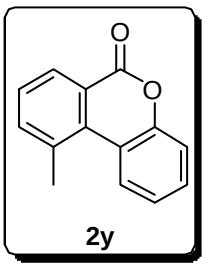
2v: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.43 (ddd, *J* = 8.5, 7.2, 1.5 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.33 – 7.24 (m, 2H), 2.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 151.4, 144.5, 136.2, 134.0, 132.3, 130.3, 124.3, 123.1, 119.8 (2C), 118.4, 117.4, 24.0. HRMS (EI-TOF) calcd. for $C_{14}H_{10}O_2$ (M^+): 210.0681, found: 210.0674.



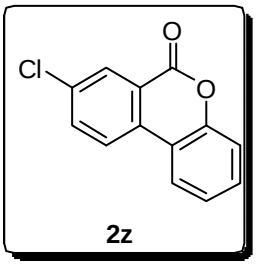
2w: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.01 (dd, *J* = 11.5, 4.9 Hz, 2H), 7.62 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.44 (ddd, *J* = 8.5, 7.2, 1.5 Hz, 1H), 7.32 (ddd, *J* = 8.4, 7.9, 1.2 Hz, 2H), 2.49 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 151.0, 139.2, 136.1, 132.2, 130.3, 129.9, 124.5, 122.6, 121.7, 121.1, 118.2, 117.7, 21.3. HRMS (EI-TOF) calcd. for $C_{14}H_{10}O_2$ (M^+): 210.0681, found: 210.0669.



2x: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.1 Hz, 1H), 8.02 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.87 (s, 1H), 7.45 (ddd, *J* = 8.5, 7.2, 1.5 Hz, 1H), 7.37 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.35 – 7.28 (m, 2H), 2.54 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 151.6, 146.0, 134.8, 130.6, 130.4, 130.3, 124.5, 122.8, 121.9, 118.9, 118.2, 117.8, 22.4. HRMS (EI-TOF) calcd. for $C_{14}H_{10}O_2$ (M^+): 210.0681, found: 210.0675.

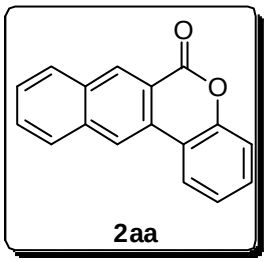


2y: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 7.9, 1.4, 0.4 Hz, 1H), 8.26 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.59 (ddd, *J* = 7.5, 1.5, 0.7 Hz, 1H), 7.46 – 7.38 (m, 2H), 7.35 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.27 (ddd, *J* = 7.7, 7.1, 1.6 Hz, 1H), 2.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 151.4, 139.2, 135.2, 133.8, 129.8, 129.4, 128.4, 127.3, 124.1, 123.0, 119.9, 118.1, 25.5. HRMS (EI-TOF) calcd. for $C_{14}H_{10}O_2$ (M^+): 210.0681, found: 210.0689.

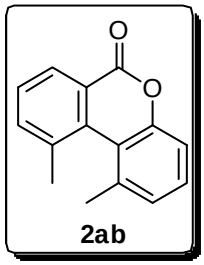


2z: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 2.3 Hz, 1H), 8.04

(d, *J* = 8.6 Hz, 1H), 7.99 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.75 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.52 – 7.45 (m, 1H), 7.39 – 7.31 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 151.2, 135.2, 135.1, 133.3, 130.9, 130.1, 124.9, 123.5, 122.9, 122.6, 118.0, 117.4. HRMS (EI-TOF) calcd. for $C_{13}H_7O_2Cl$ (M^+): 230.0135, found: 230.0127.

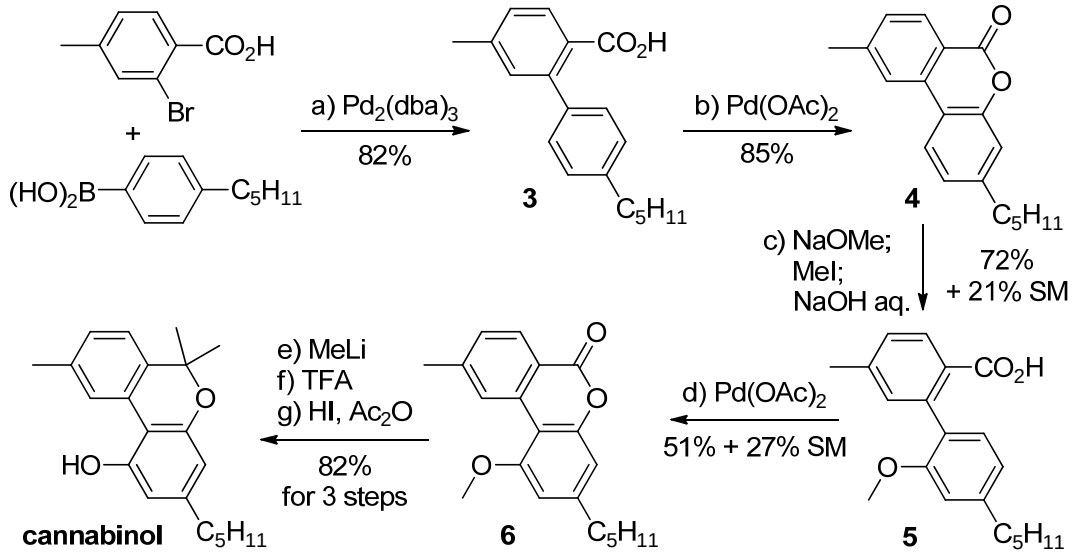


2aa: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.55 (s, 1H), 8.23 (dd, *J* = 7.5, 2.2 Hz, 1H), 8.03 (dd, *J* = 13.3, 8.4 Hz, 2H), 7.69 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.60 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.51 – 7.44 (m, 1H), 7.41 – 7.33 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 150.9, 136.2, 132.8, 132.5, 130.2, 129.7, 129.6 (2C), 128.2, 127.2, 124.7, 122.9, 120.7, 119.2, 118.4, 118.0. HRMS (EI-TOF) calcd. for $C_{17}H_{10}O_2$ (M^+): 246.0681, found: 246.0675.



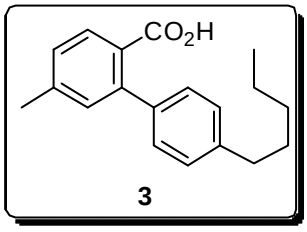
2ab: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.20 (t, *J* = 8.6 Hz, 2H), 2.46 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 151.3, 137.0, 136.5, 135.6, 134.8, 129.0, 128.0, 127.7, 127.2, 124.9, 119.3, 114.1, 22.1, 22.0. HRMS (EI-TOF) calcd. for $C_{15}H_{12}O_2$ (M^+): 224.0837, found: 224.0844.

Total Synthesis of cannabinol:



2-(4-pentylphenyl)-4-methylbenzoic acid (**3**):

A nitrogen-filled schlenk tube was charged in sequence with 2-bromo-4-methylbenzoic acid (4.3 g, 20 mmol), 4-pentylphenylboronic acid (4.6 g, 24 mmol), and $LiOH·H_2O$ (1.85 g, 44 mmol). 60 mL NMP and 60 mL H_2O was added followed by $Pd_2(dba)_3$ (275 mg, 0.3 mmol) under a nitrogen blanket, and the reaction mixture was heated to 65 °C for 24 h. After cool to room temperature, the reaction mixture was acidified to pH=3 with 3N HCl, and extracted with diethyl ether three times. The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The product was purified by column chromatography (silica gel, petroleum ether/diethyl ether = 5:1 to 3:1) to give a white solid in 82% yield (4.64 g).

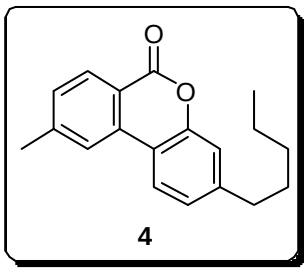


3

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.9 Hz, 1H), 7.18 – 7.14 (m, 2H), 7.14 – 7.06 (m, 4H), 2.56 (t, *J* = 7.8 Hz, 2H), 2.34 (s, 3H), 1.65 – 1.52 (m, 2H), 1.34 – 1.22 (m, 4H), 0.88 – 0.78 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 143.9, 142.8, 142.1, 138.6, 132.3, 131.2, 128.5, 128.3, 127.9, 126.5, 35.8, 31.8, 31.1, 22.7, 21.6, 14.2. HRMS (EI-TOF) calcd. for $C_{19}H_{22}O_2$ (M^+): 282.1620, found: 282.1581.

3-pentyl-9-methyl-6*H*-benzo[*c*]chromen-6-one (**4**)

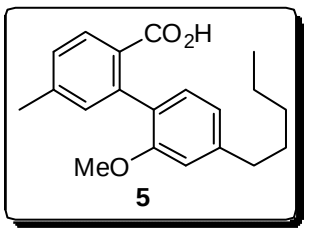
In a 500 mL sealed tube, 276 mL *t*-BuOH was added to a mixture of xx (3.9 g, 13.8 mmol), $Pd(OAc)_2$ (155 mg, 0.69 mmol, 5 mol%), N-acetylglycin (243 mg, 2.07 mmol), KOAc (2.71 g, 27.6 mmol), $PhI(OAc)_2$ (8.9 g, 27.6 mmol) under air. The tube was sealed with a Teflon lined cap and the reaction mixture was stirred at 80 °C for 12 h. After cooling to room temperature, the mixture was concentrated under vacuum and the palladium and salt were filtered, the filter cake was washed with ethyl acetate, and the filtrate was concentrated in vacuo, and the residue was purified by column chromatography on silica gel with a gradient eluent of petroleum ether/ethyl acetate/dichloromethane (100:1:10) to give **4** (3.3 g, 85%) as a white solid.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.74 (s, 1H), 7.24 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.08 – 7.00 (m, 2H), 2.59 (t, *J* = 7.7 Hz, 2H), 2.44 (s, 3H), 1.63 – 1.52 (m, 2H), 1.31 – 1.21 (m, 4H), 0.82 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 151.6, 146.2, 145.9, 135.1, 130.6, 129.7, 124.9, 122.6, 121.7, 118.5, 117.3, 115.7, 35.8, 31.5, 30.8, 22.6, 22.4, 14.1. HRMS (EI-TOF) calcd. for $C_{19}H_{20}O_2$ (M^+): 280.1463, found: 280.1451.

2-(2-methoxy-4-pentyl)-4-methylbenzoic acid (**5**):

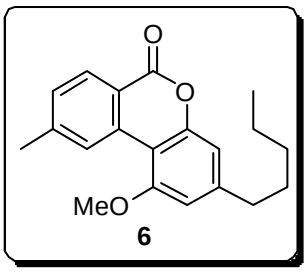
To a solution of xx (2.5 g, 8.9 mmol) in anhydrous THF (54 mL) was added MeONa (1.2 g, 22.3 mmol) in an ice bath. The mixture was stirred at 35 °C for 1 h, then MeI (8.3 mL, 133.7 mmol) was added. The temperature was risen to 45 °C, the resulting mixture was stirred overnight. After cooling to 0 °C, 27 mL MeOH and 27 mL NaOH (6.6 M) was added to the mixture, then heat to 55 °C for 6 h. The reaction was acidified to pH = 3 with 4N HCl at 0 °C, and extracted with diethyl ether three times. The combined organic phase was dried over Na_2SO_4, filtered and the filtration was evaporated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 15:1 to 8:1, and then petroleum ether/diethyl ether = 8:1) to provide **5** (2.02 g, 72%) as a pale yellow solide, and recover 0.53 g **4** (21%).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.17 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.13 (s, 1H), 6.84 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.67 (d, *J* = 1.1 Hz, 1H), 3.68 (s, 3H), 2.63 (t, *J* = 7.8 Hz, 2H), 2.40 (s, 3H), 1.73 – 1.61 (m, 2H), 1.43 – 1.31 (m, 4H), 0.92 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 156.2, 144.3, 142.9, 139.4, 132.5, 130.2, 129.6, 128.0, 127.8, 127.7, 120.9, 110.9, 55.2, 36.3, 31.8, 31.2, 22.7, 21.6, 14.2. HRMS (EI-TOF) calcd. for $C_{20}H_{24}O_3$ (M^+): 312.1725, found: 312.1724.

1-methoxy-3-pentyl-9-methyl-6*H*-benzo[*c*]chromen-6-one (**6**):

In a 150 mL sealed tube, 37 mL *t*-BuOH was added to a mixture of xx (3.9 g, 1.86 mmol), $Pd(OAc)_2$ (20.8 mg, 0.09 mmol, 5 mol%), N-acetylglycin (32.6 mg, 0.28 mmol), KOAc (364 mg, 3.71 mmol), $PhI(OAc)_2$ (1.2 g, 3.71 mmol) under air. The tube was sealed with a Teflon lined cap and the reaction mixture was stirred at 100 °C for 12 h. After cooling to room temperature, the mixture was concentrated under vacuum and the palladium and salt were filtered, the filter cake was washed with ethyl acetate, and the filtrate was concentrated in vacuo, and the residue was purified by column chromatography on silica gel with an eluent of petroleum ether/ethyl acetate/dichloromethane (100:1:16) to furnish **6** (294 mg, 51%) as a white solid, and petroleum ether/diethyl ether (4:1) to recover **5** (159 mg, 27%).

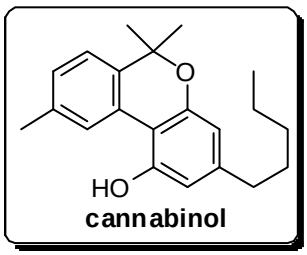


6

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.29 (d, *J* = 8.1 Hz, 1H), 7.31 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.83 (d, *J* = 1.6 Hz, 1H), 6.67 (d, *J* = 1.4 Hz, 1H), 4.04 (s, 3H), 2.66 (t, *J* = 7.7 Hz, 2H), 2.52 (s, 3H), 1.72 – 1.62 (m, 2H), 1.42 – 1.29 (m, 4H), 0.91 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 158.3, 152.8, 145.8, 145.6, 134.9, 130.2, 128.8, 127.4, 118.3, 110.1, 107.4, 106.1, 56.0, 36.2, 31.6, 30.7, 22.7, 22.6, 14.1. HRMS (EI-TOF) calcd. for $C_{20}H_{22}O_3$ (M^+): 310.1569, found: 310.1572.

Cannabinol[8]

Cannabinol (356.6 mg, 72% for three steps) was obtained through three steps following the reported methods[8] as a white solid.

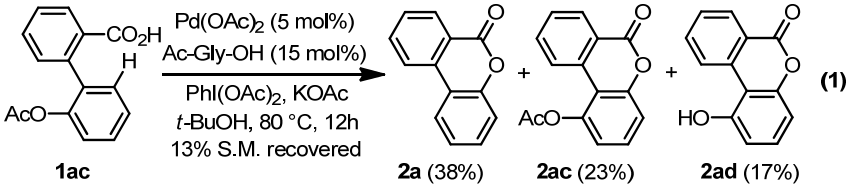


cannabinol

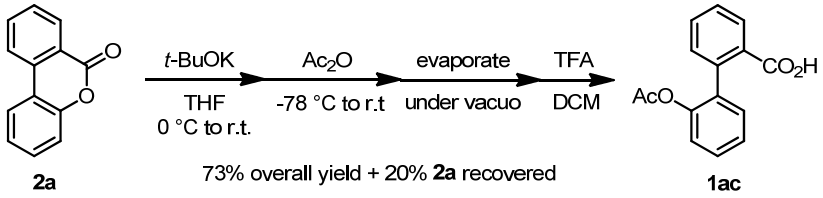
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 1.1, 0.5 Hz, 1H), 7.14 (d, *J* = 7.9 Hz, 1H), 7.06 (ddd, *J* = 7.9, 1.7, 0.6 Hz, 1H), 6.43 (d, *J* = 1.6 Hz, 1H), 6.27 (d, *J* = 1.6 Hz, 1H), 5.31 (s, 1H), 2.48 (t, *J* = 7.9 Hz, 2H), 2.38 (s, 3H), 1.64 – 1.55 (m, 8H), 1.36 – 1.27 (m, 4H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ

154.8, 153.2, 144.7, 137.0 (2C), 127.7 (2C), 126.6, 122.7, 110.9, 110.0, 108.8, 77.5, 35.7, 31.6, 30.6, 27.2, 22.7, 21.7, 14.2. HRMS (EI-TOF) calcd. for $C_{21}H_{26}O_2$ (M^+): 310.1933, found: 310.1940.

Discussion of Mechanism:



With **1a** under standard reaction conditions for 1 h, trace possible acetoxylation product **1ac** observed by TLC and none checked by GC-MS (decomposed at high temperature), compared with standard compound **1ac**. We also subjected the suggested intermediate **1ac** to the catalytic system. It was found that C–H activation/C–O cyclization products **2ac** (23%) and **2ad** (17%) were obtained along with lactone **2a** (38%) (Eq. 1), whereas neither of them was observed with **1a** used directly (entry 20, Table 1). Because **1ac** may be generated in low concentration and phenol was then afforded by following rapid hydrolysis, the real catalytic system is possible to be different from Eq. 1. In this context, the stepwise route involve acetoxylation followed by condensation can't be excluded at this stage.

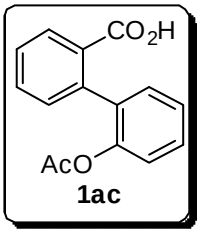


Procedure of synthesis of 2-(2-acetoxy)phenylbenzoic acid (1ac)

To a solution of **2a** (528 mg, 2.69 mmol) in anhydrous THF (12 mL) was added ^{t}BuOK (604 mg, 5.38 mmol) in an ice bath. The mixture was stirred at room temperature for 1 h, then Ac_2O (8.3 mL, 133.7 mmol) was added under -78 ^{o}C, warmed to room temperature and stirred over night. After evaporation of the solvent under reduced pressure, the residue was dissolved in 27 mL DCM, 9 mL TFA was added to the reaction mixture, and stirred for 6 hours. The solvent was removed and the product was purified by flash column chromatography (petroleum ether/ethyl

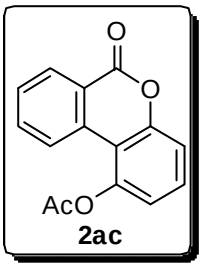
acetate = 8:1 to 4:1) to provide **1ac** (502.6 mg, 73%) as a pale yellow solid, and recover 39.4 mg **2a** (20%).

2-phenyl-3-acetoxybenzoic acid (**1ac**):



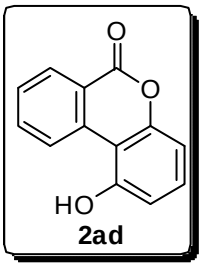
1ac

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.47 – 7.28 (m, 5H), 7.11 (d, *J* = 8.0 Hz, 1H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 169.6, 147.6, 137.9, 134.1, 132.4, 131.5, 130.6, 130.4, 130.4, 129.1, 128.0, 126.5, 122.1, 20.6. HRMS (ESI) calcd. for $C_{15}H_{13}O_4$ ($[M+H]^+$) 257.0808, found 257.0796.



2ac

2ac: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 8.3 Hz, 1H), 8.47 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.82 (td, *J* = 7.9, 1.6 Hz, 1H), 7.61 (td, *J* = 7.5, 1.0 Hz, 1H), 7.47 (t, *J* = 8.2 Hz, 1H), 7.31 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.07 (dd, *J* = 8.1, 1.2 Hz, 1H), 2.50 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 160.8, 152.4, 148.2, 135.1, 133.3, 131.0, 129.8, 129.2, 125.5, 121.9, 120.2, 115.9, 112.1, 21.7.HRMS (EI-TOF) calcd. for $C_{15}H_{10}O_4$ (M^+): 254.0579, found: 254.0577.



2ad

2ad: ^{1}H NMR (400 MHz, DMSO) δ 11.07 (s, 1H), 9.15 (dd, *J* = 8.3, 0.5 Hz, 1H), 8.29 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.93 (ddd, *J* = 8.5, 7.3, 1.6 Hz, 1H), 7.64 (ddd, *J* = 7.6, 7.2, 1.1 Hz, 1H), 7.36 (t, *J* = 8.2 Hz, 1H), 6.93 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.89 (dd, *J* = 8.2, 1.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 160.4, 156.6, 152.2, 135.1, 134.6, 130.2, 129.4, 128.0, 127.1, 120.1, 112.0, 107.7, 106.1. HRMS (EI-TOF) calcd. for $C_{13}H_8O_3$ (M^+): 246.0473, found: 246.0472.

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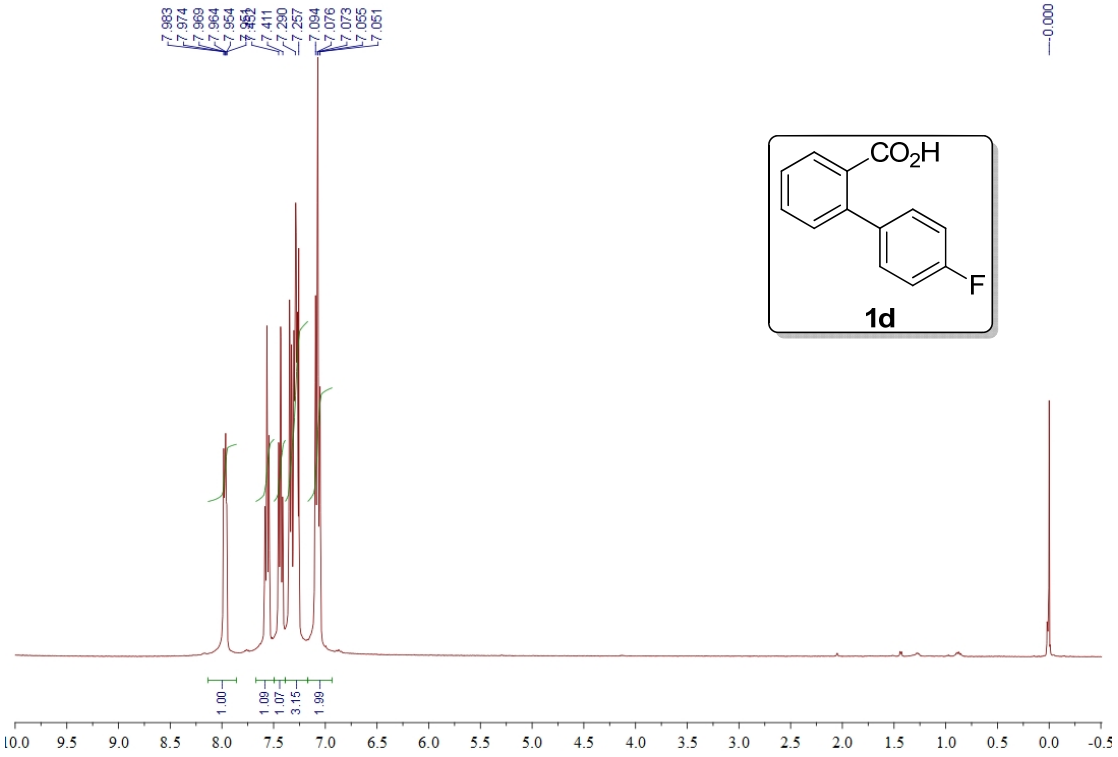
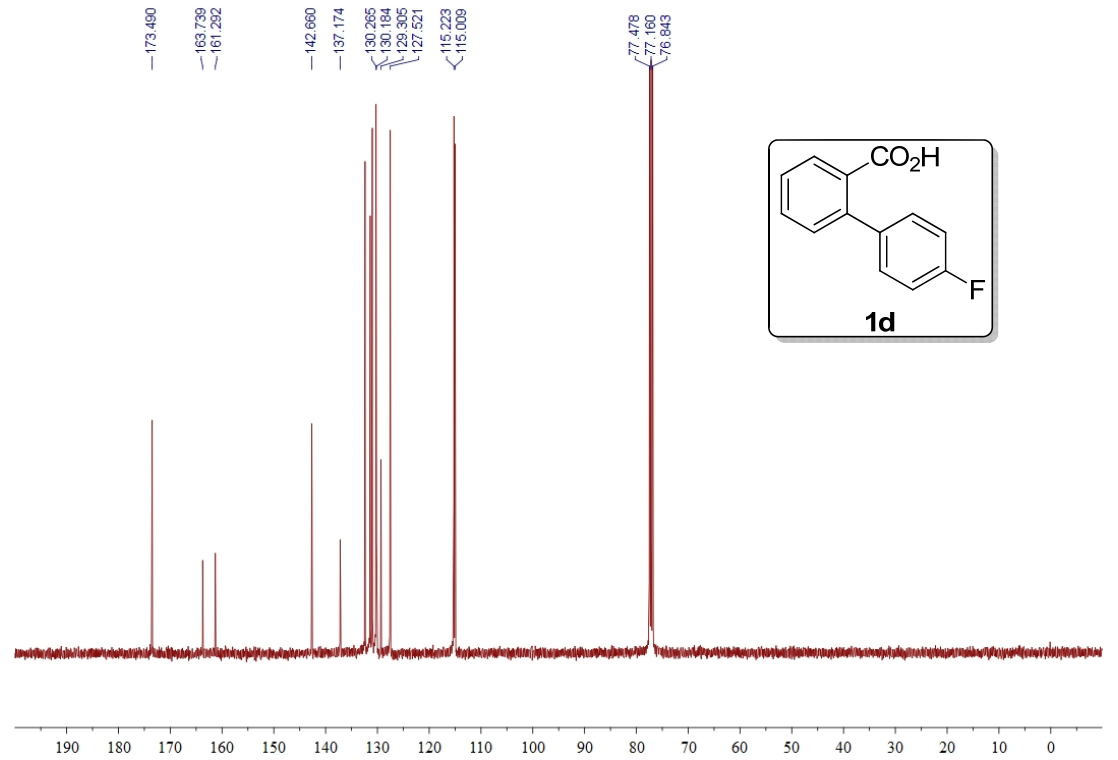
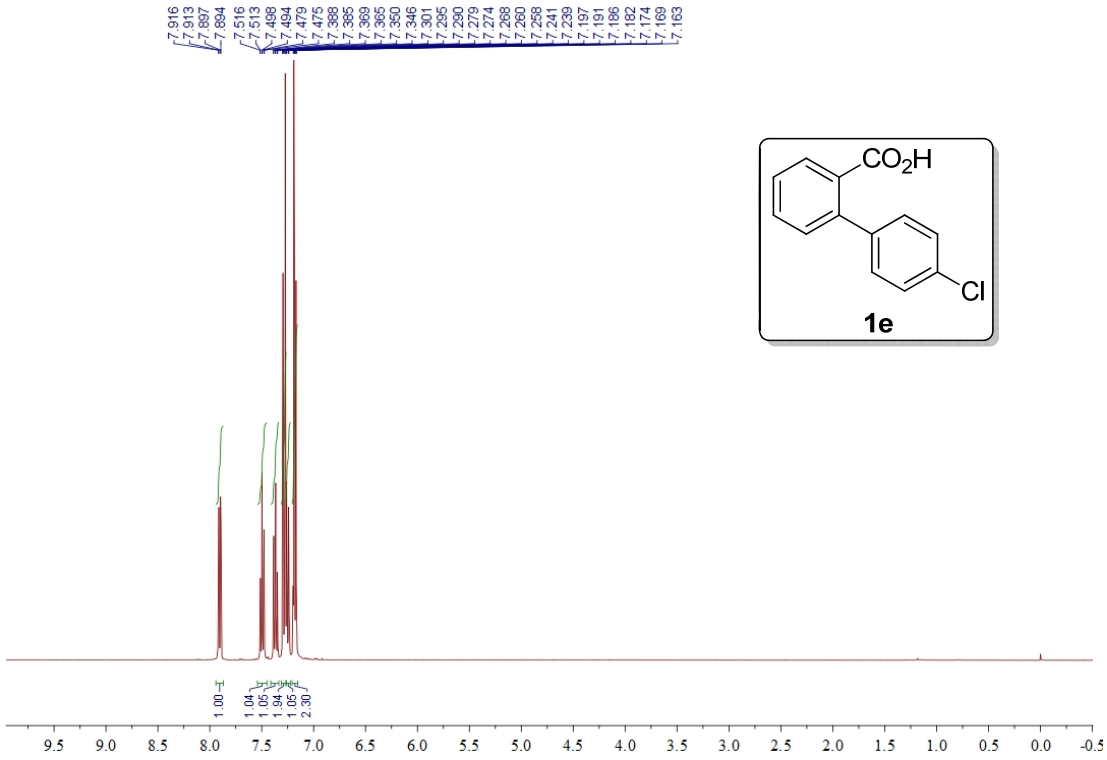
Copies of ^{1}H and ^{13}C NMR Spectra



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Cl
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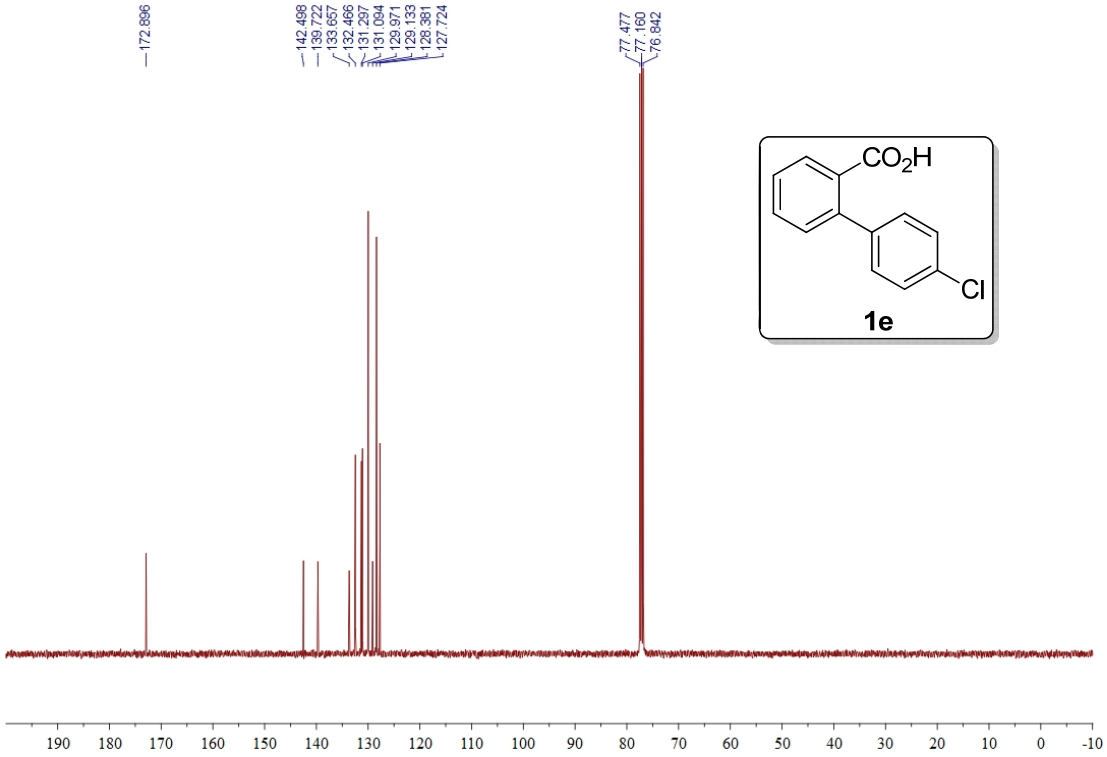
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CO2H
Cl
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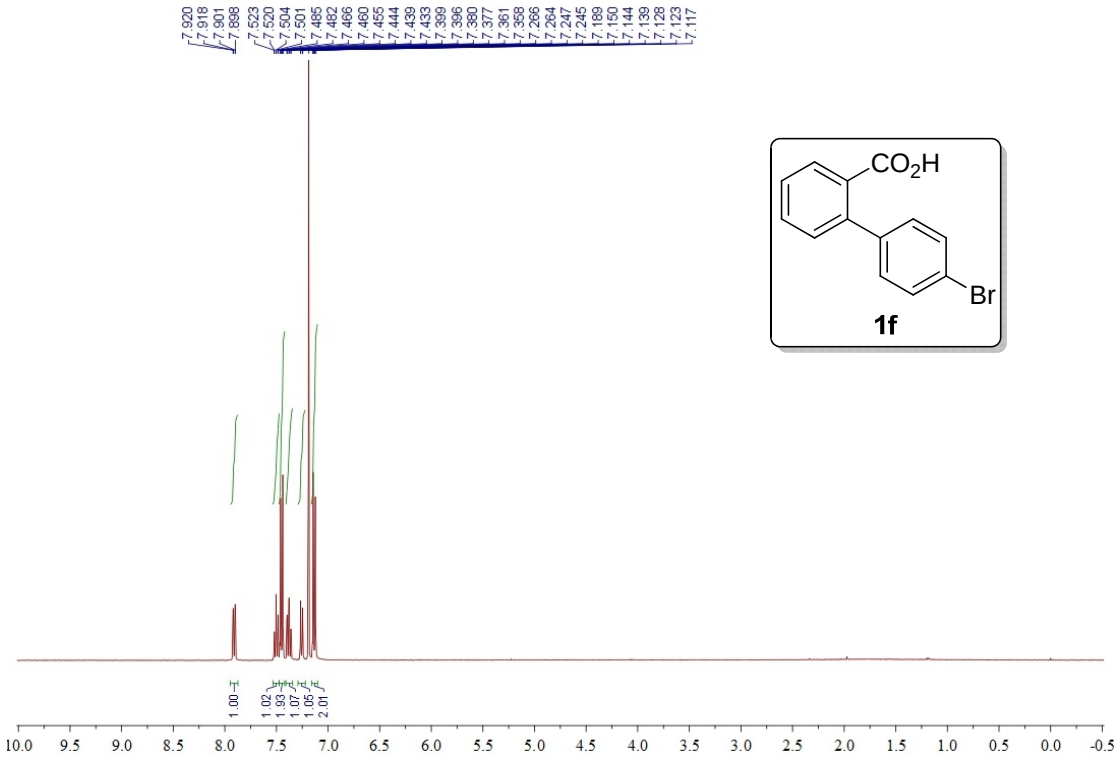
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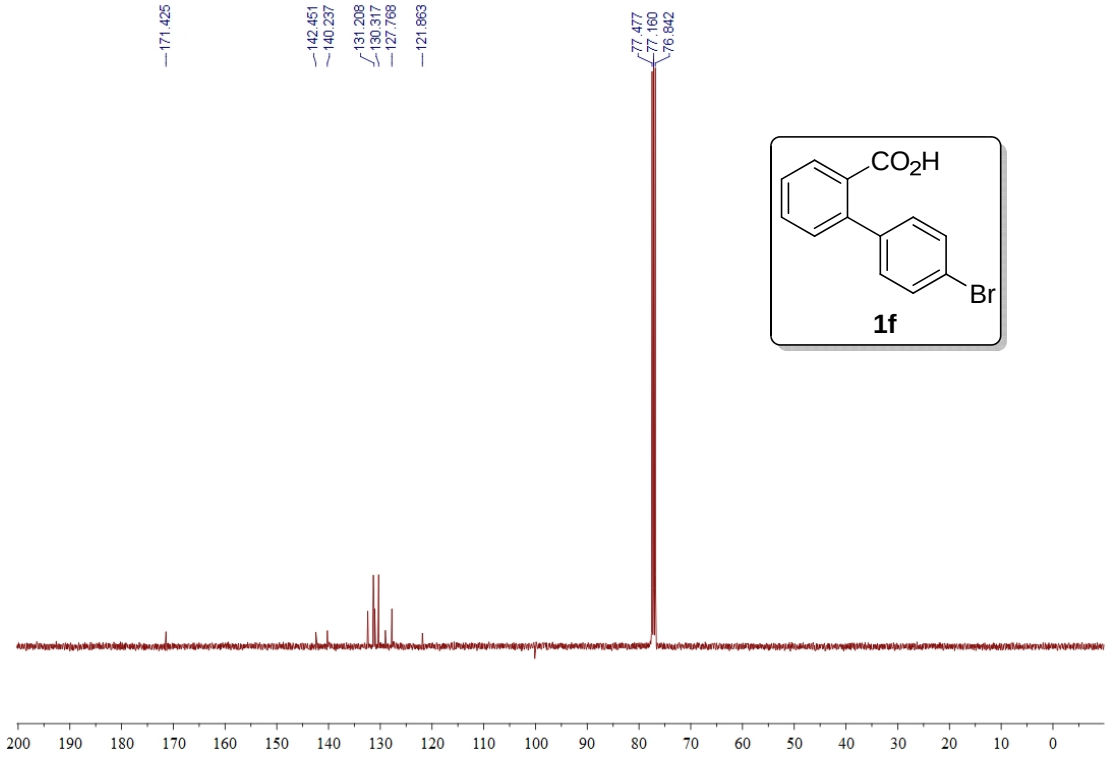
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

CO2H
Br
1f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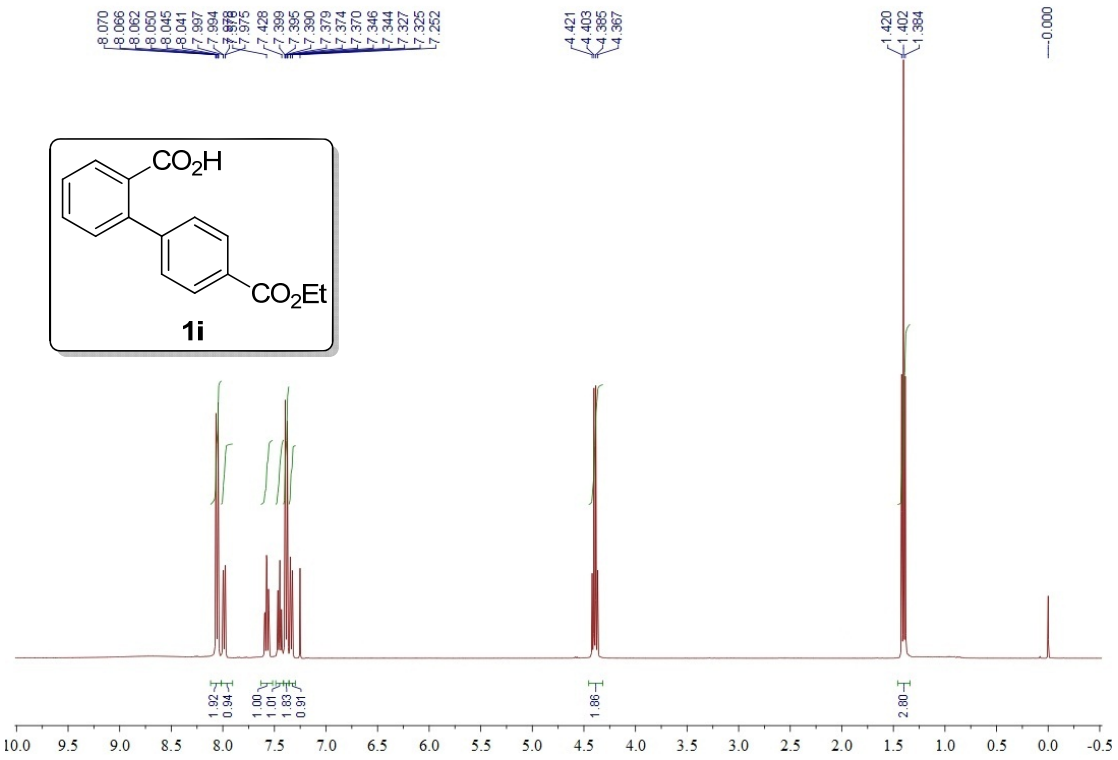
CO2H
Br
1f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CO2H
CO2Et
1i
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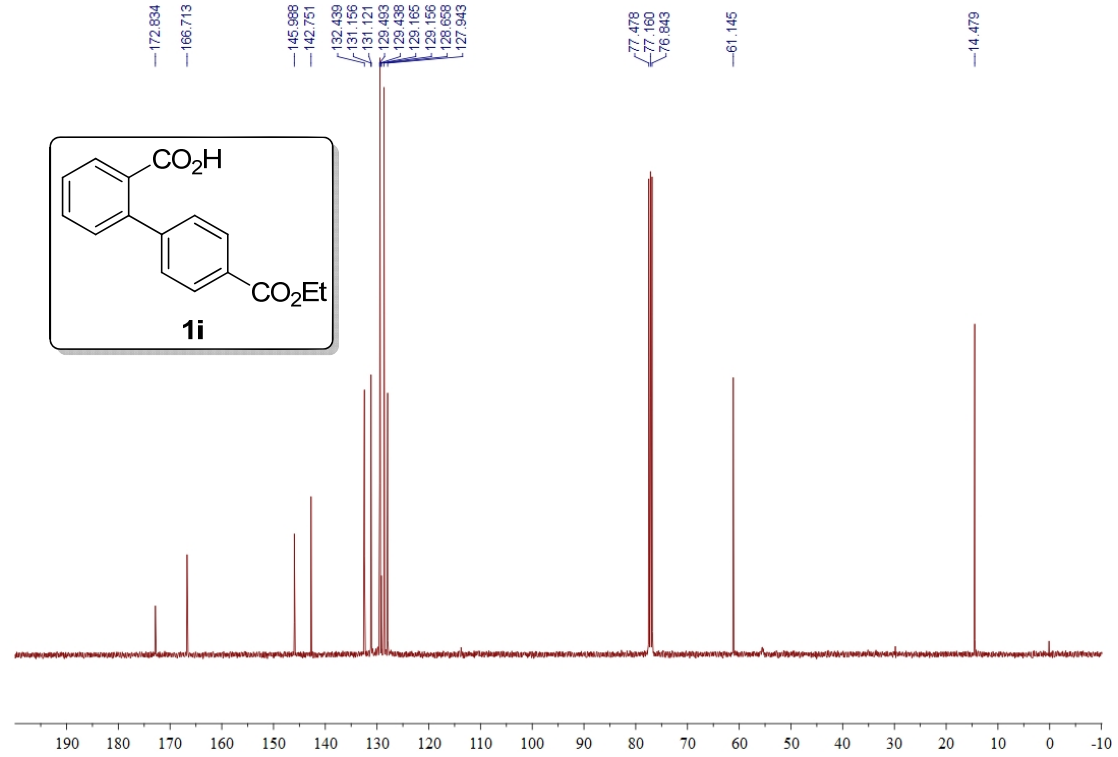
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CO2Et
1i
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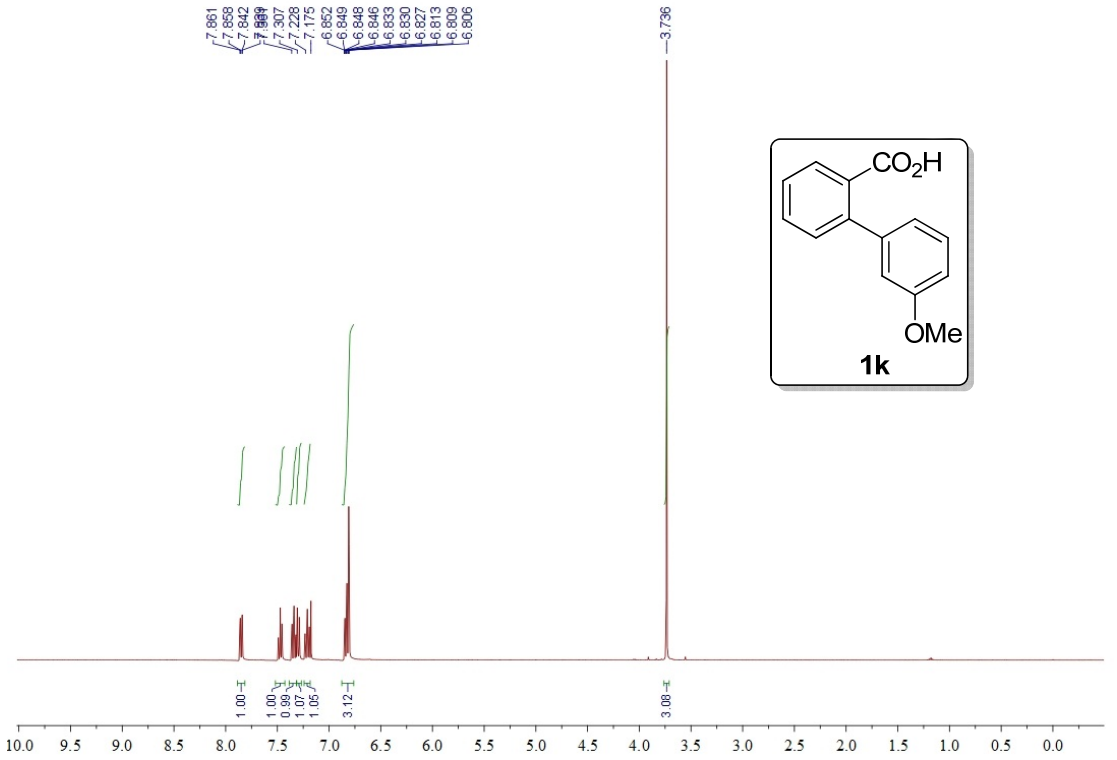
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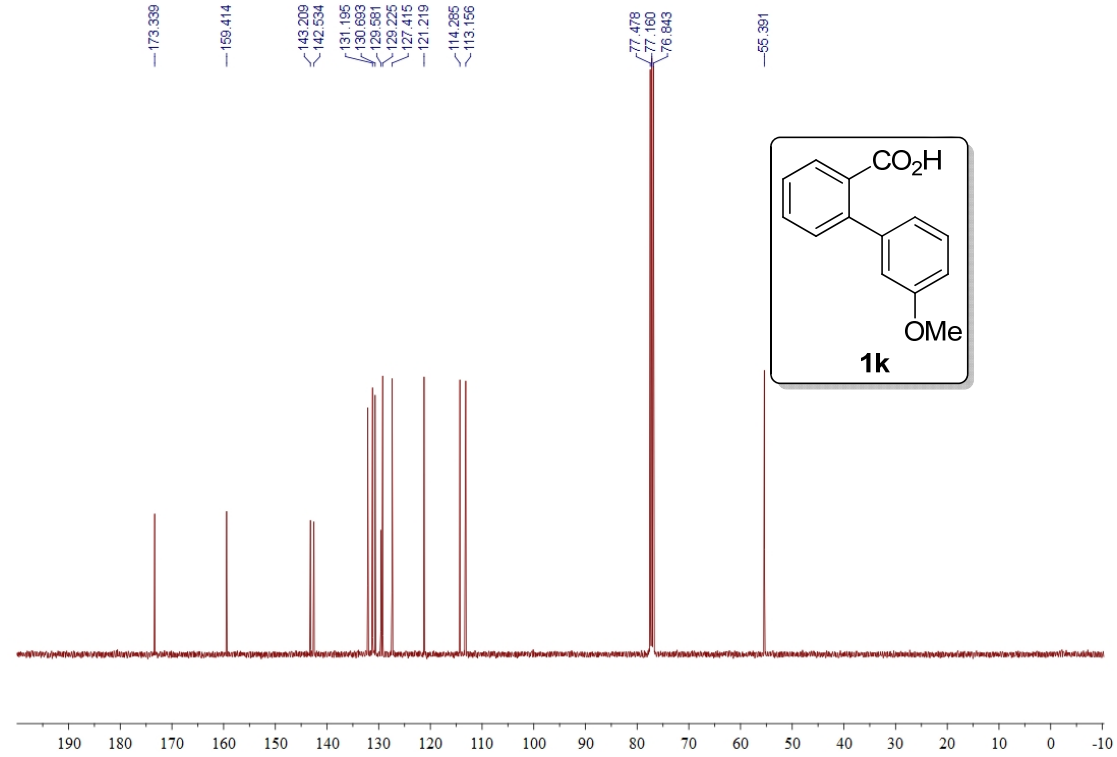
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OMe
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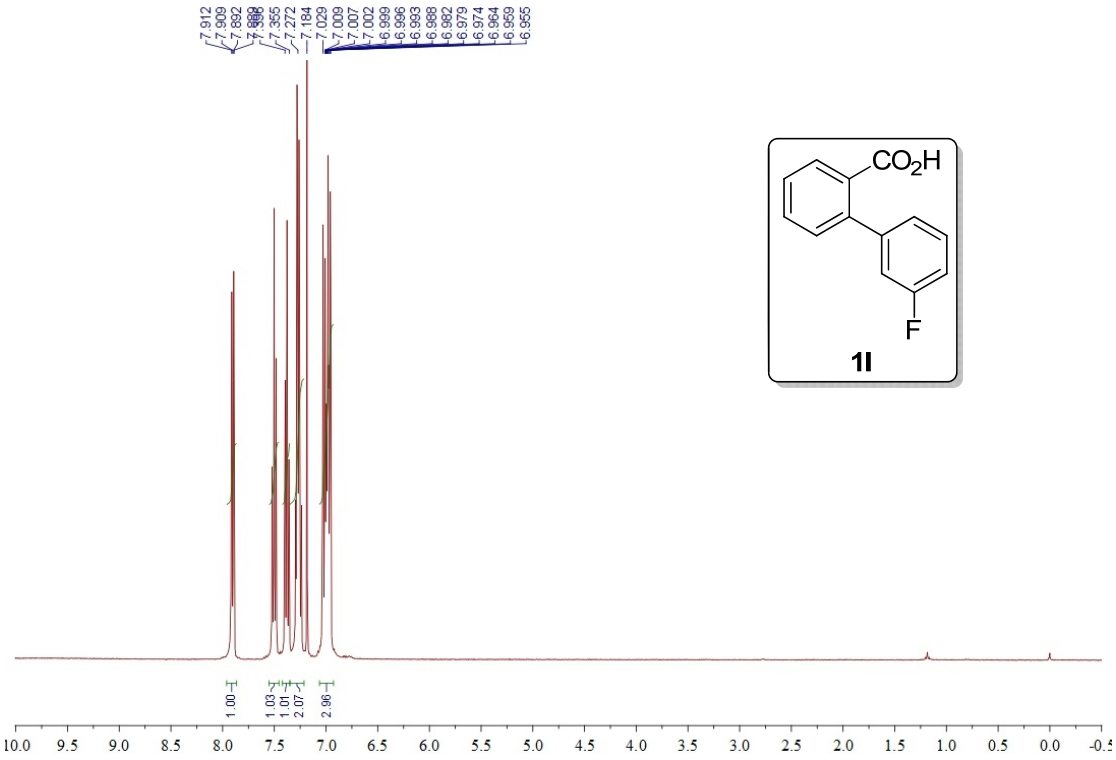
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1.01
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F
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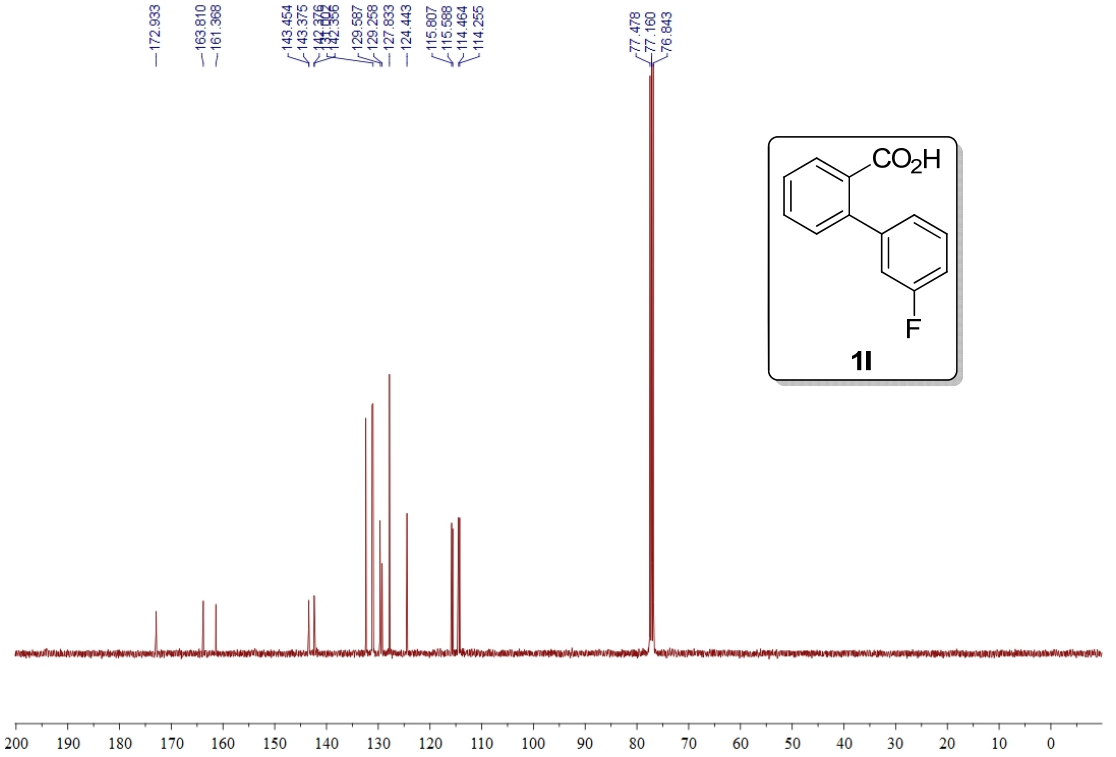
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CO2H
F
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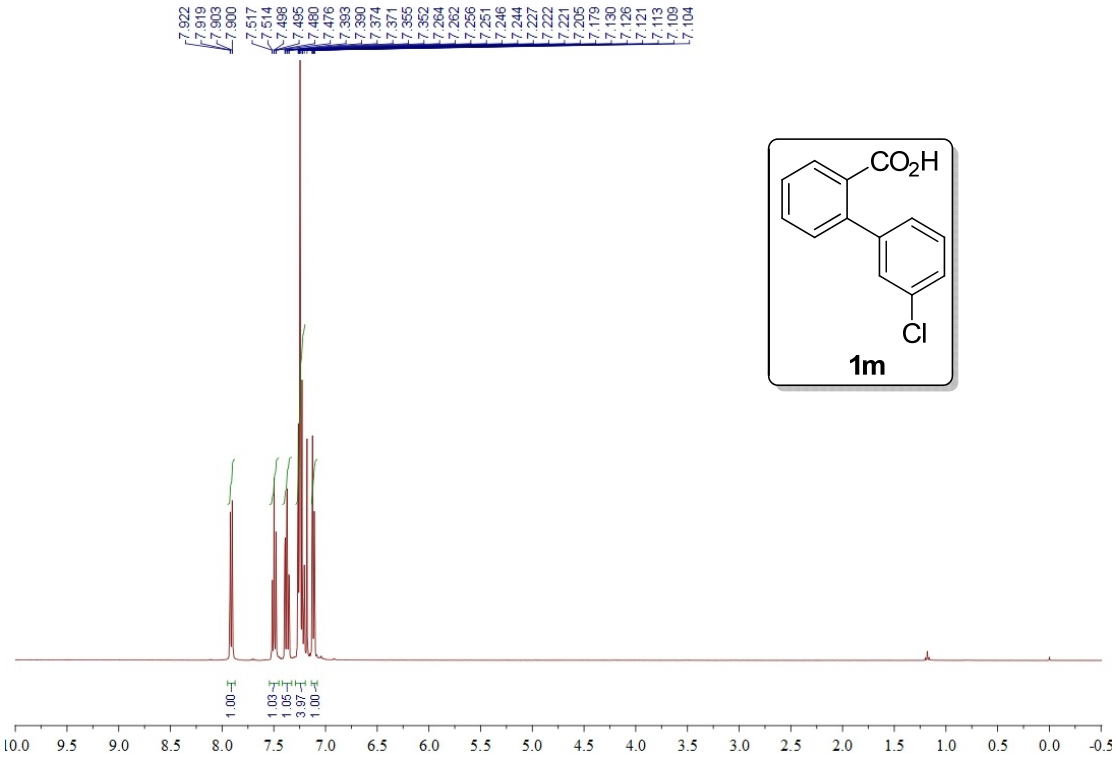
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Cl
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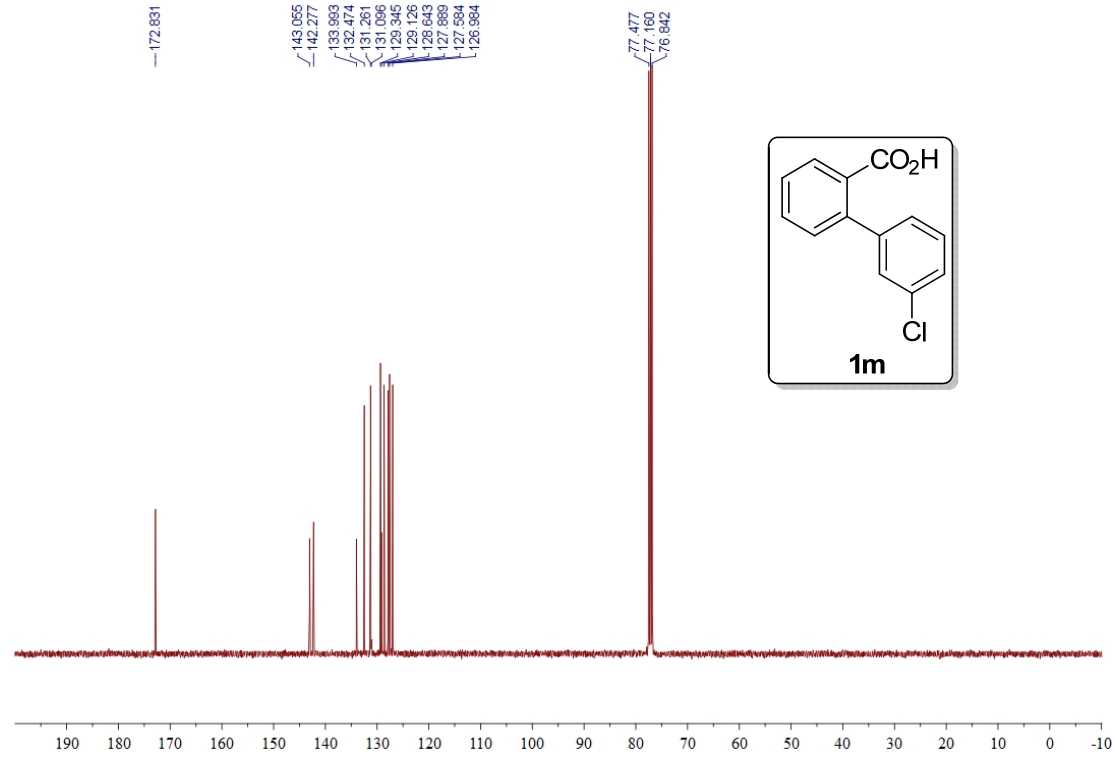
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Cl
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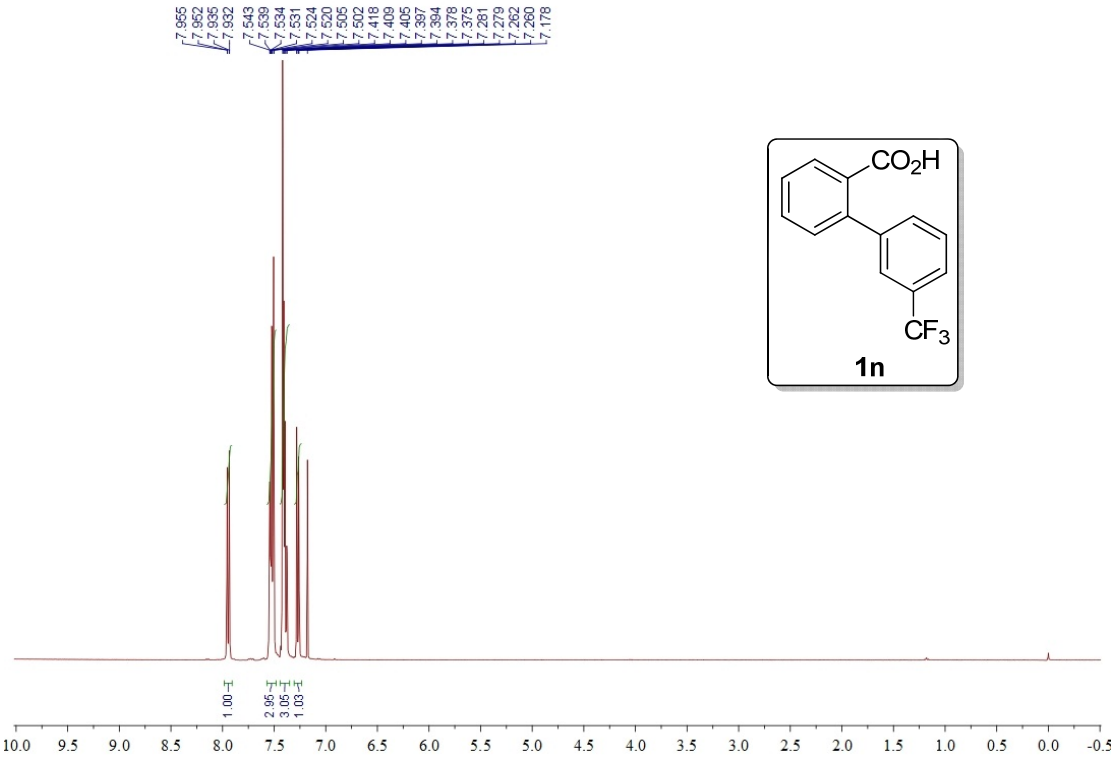
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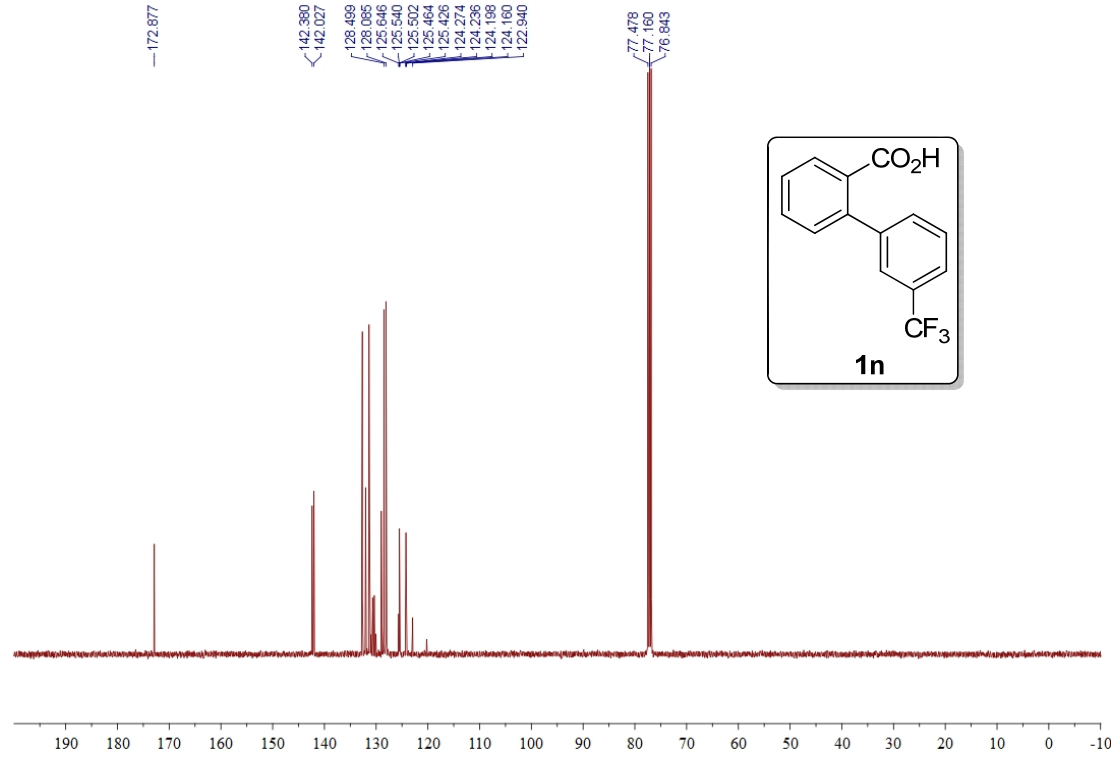
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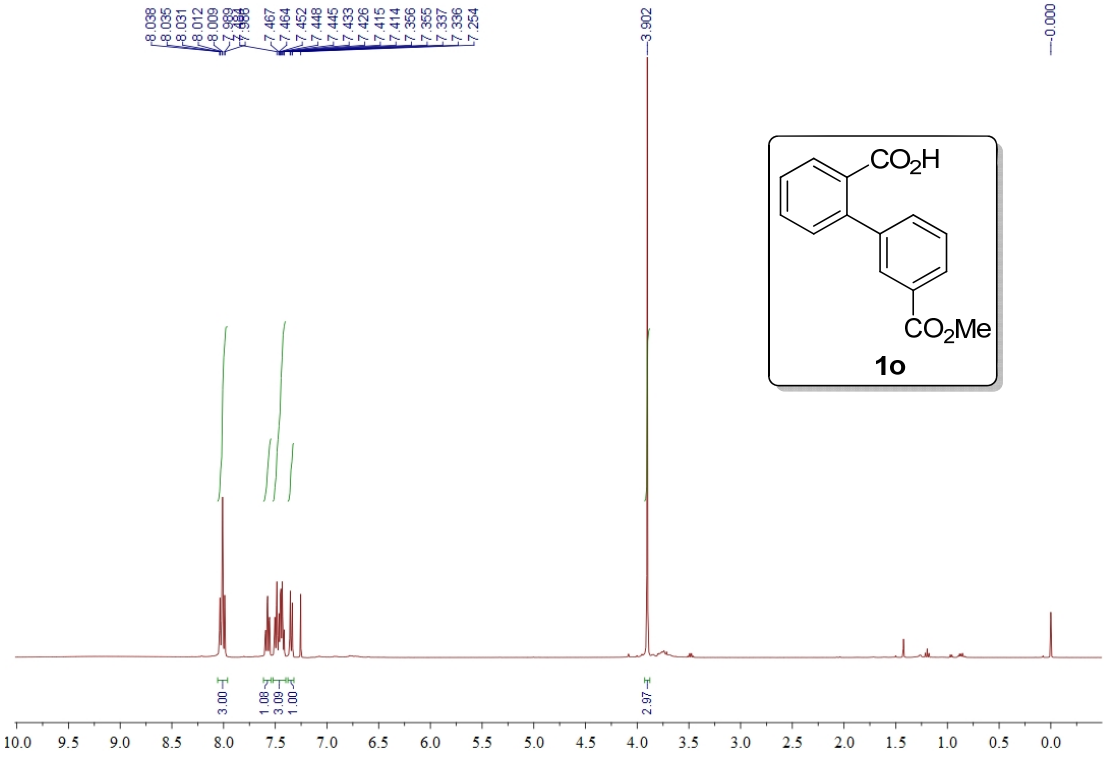
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CO2Me
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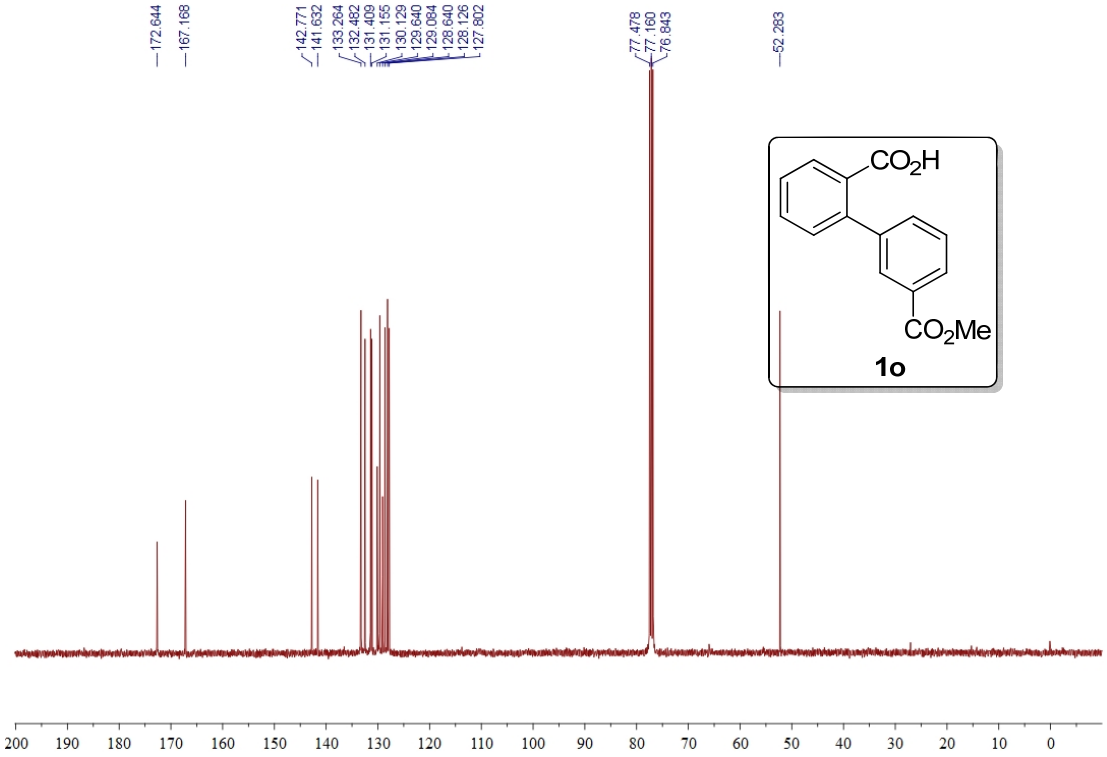
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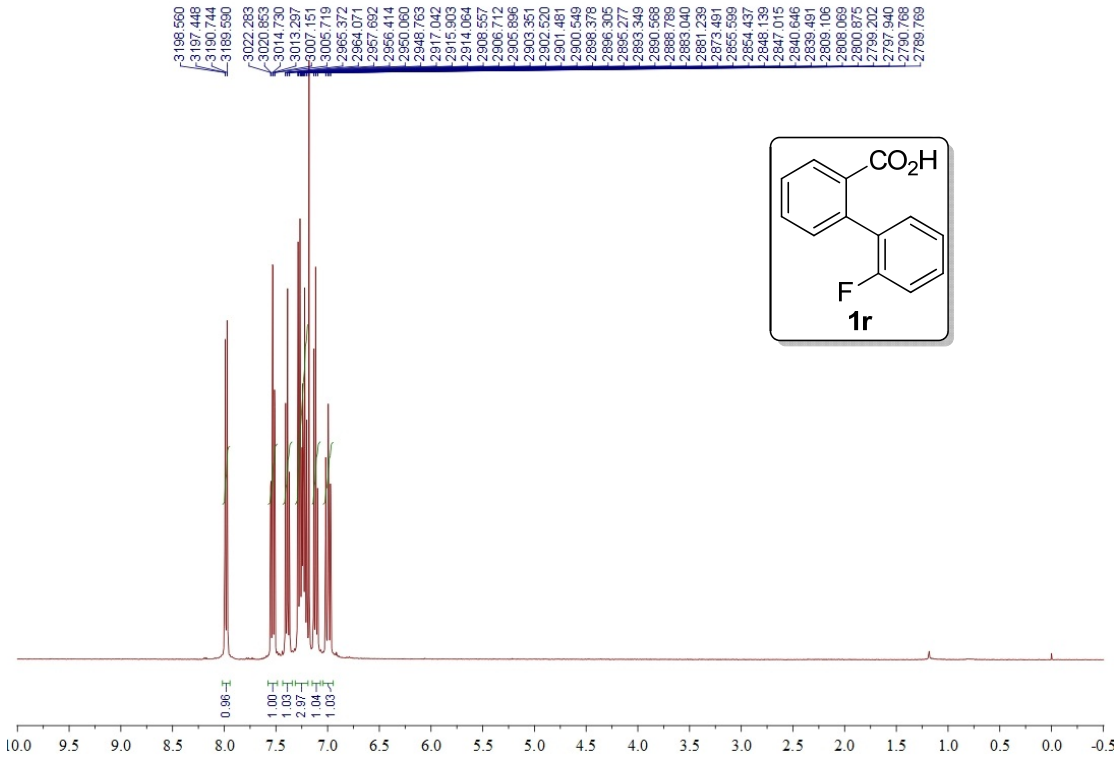
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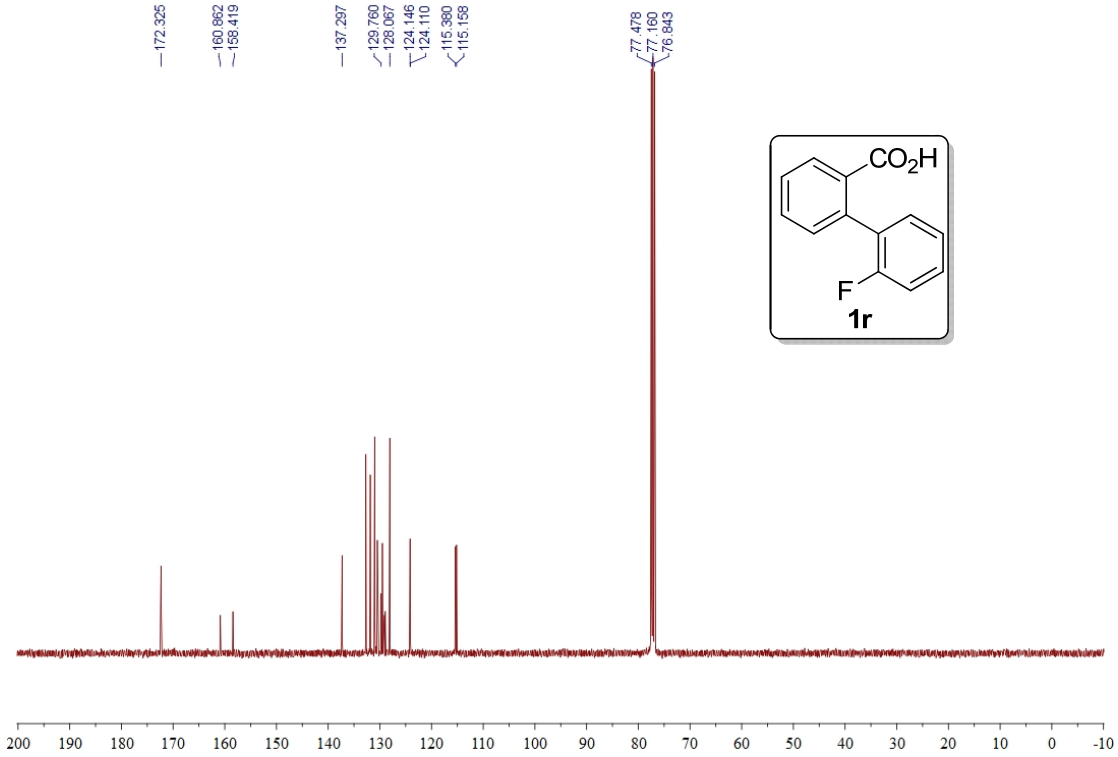
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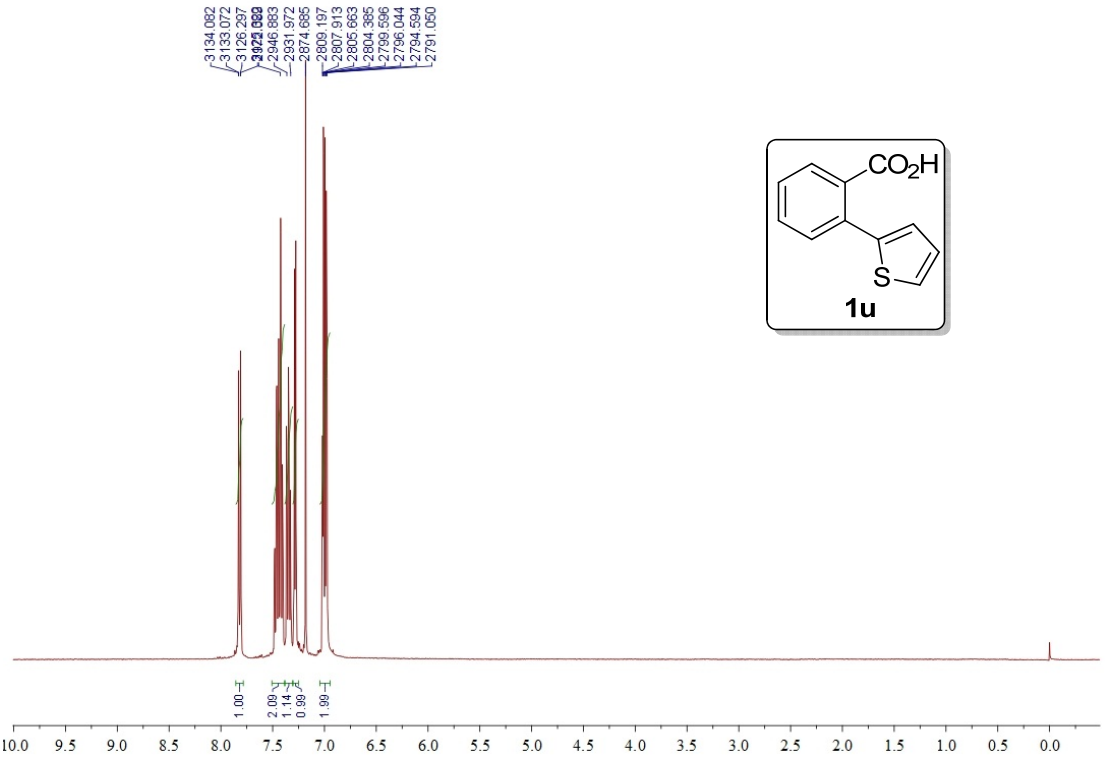
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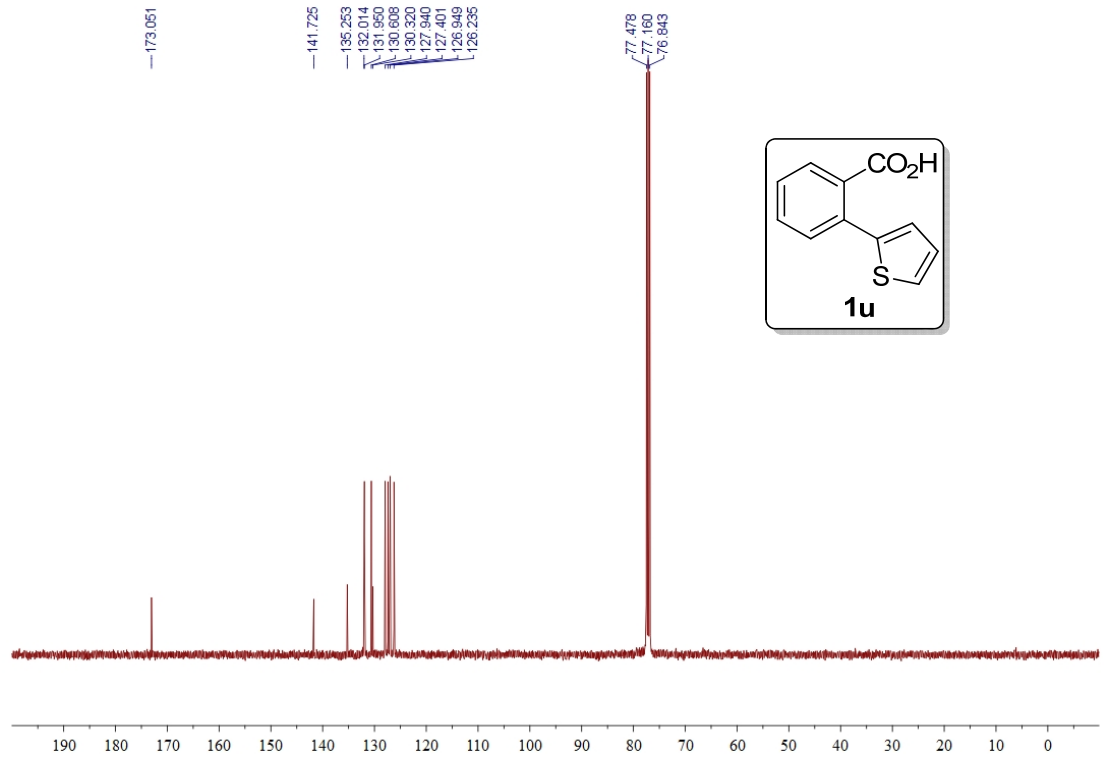
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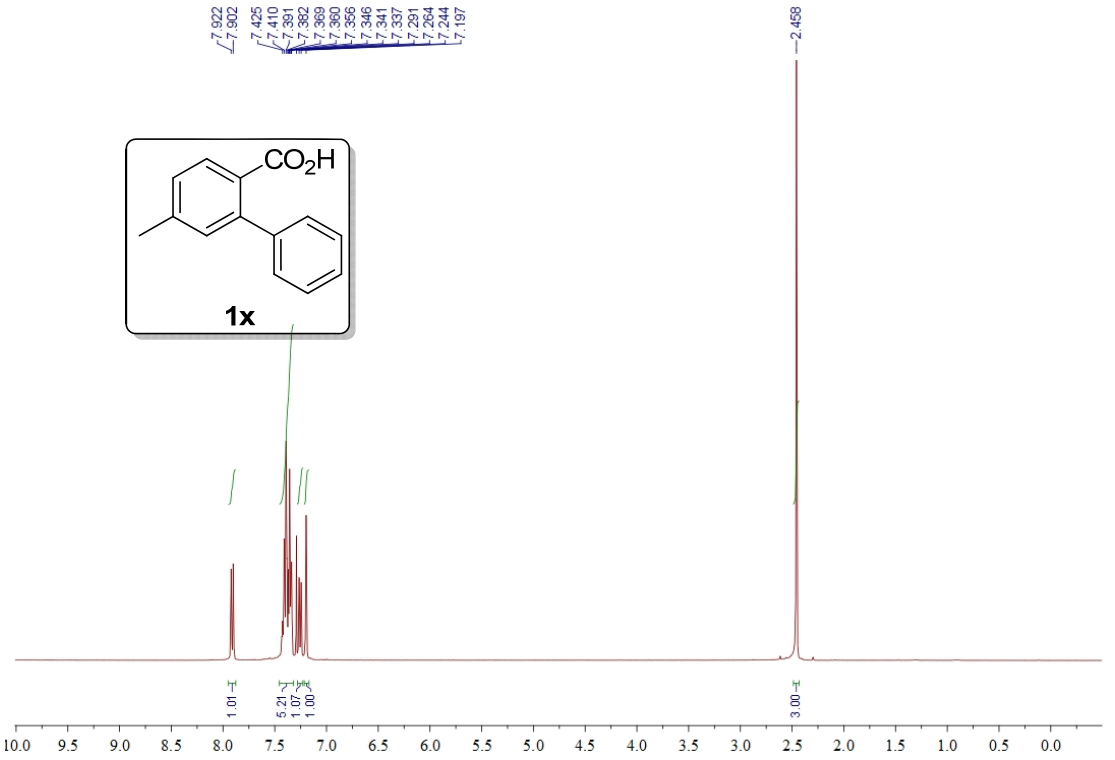
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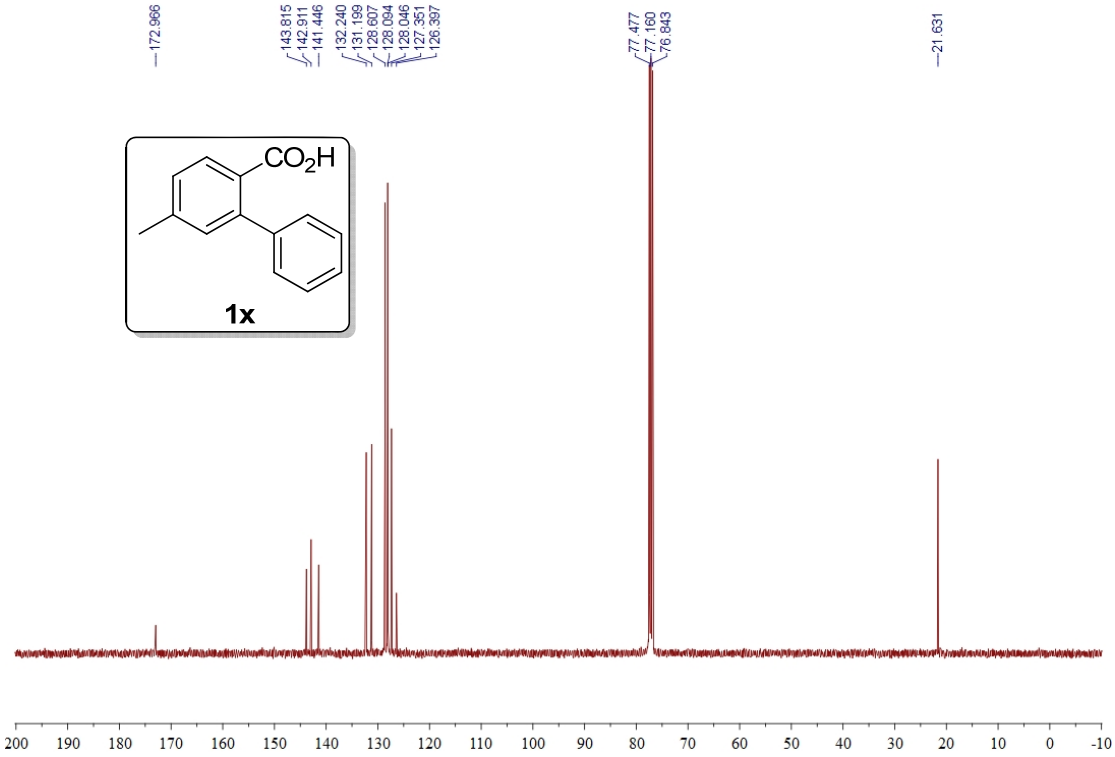
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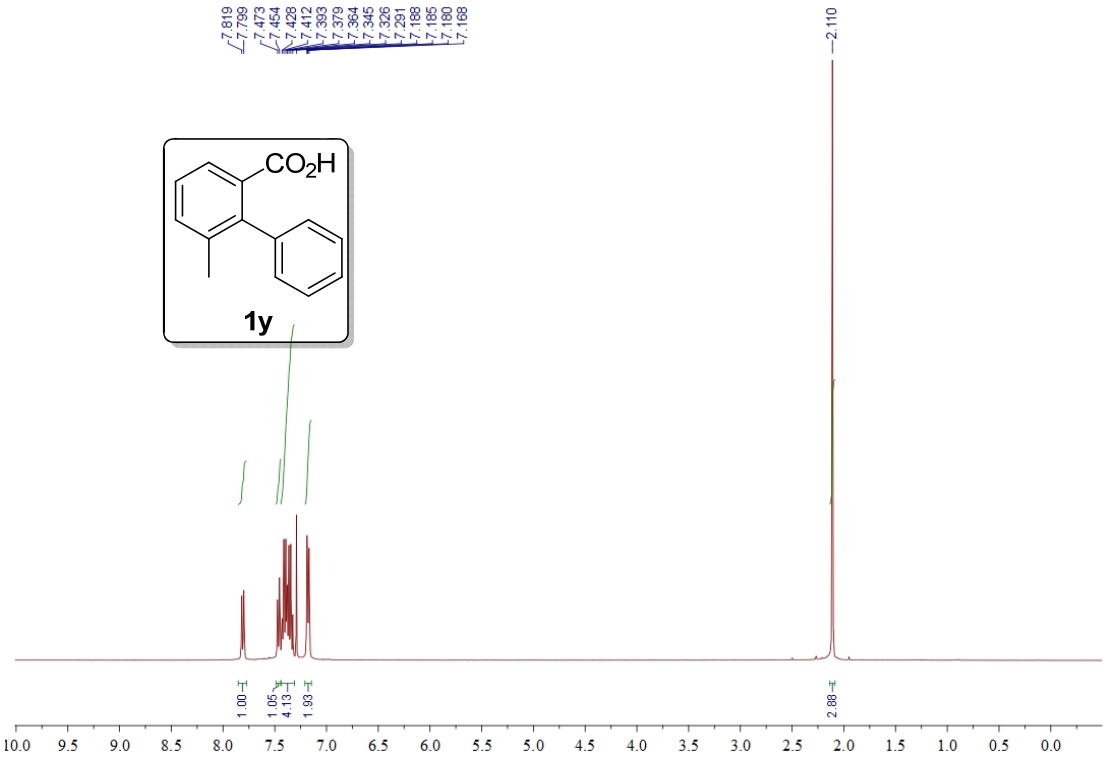
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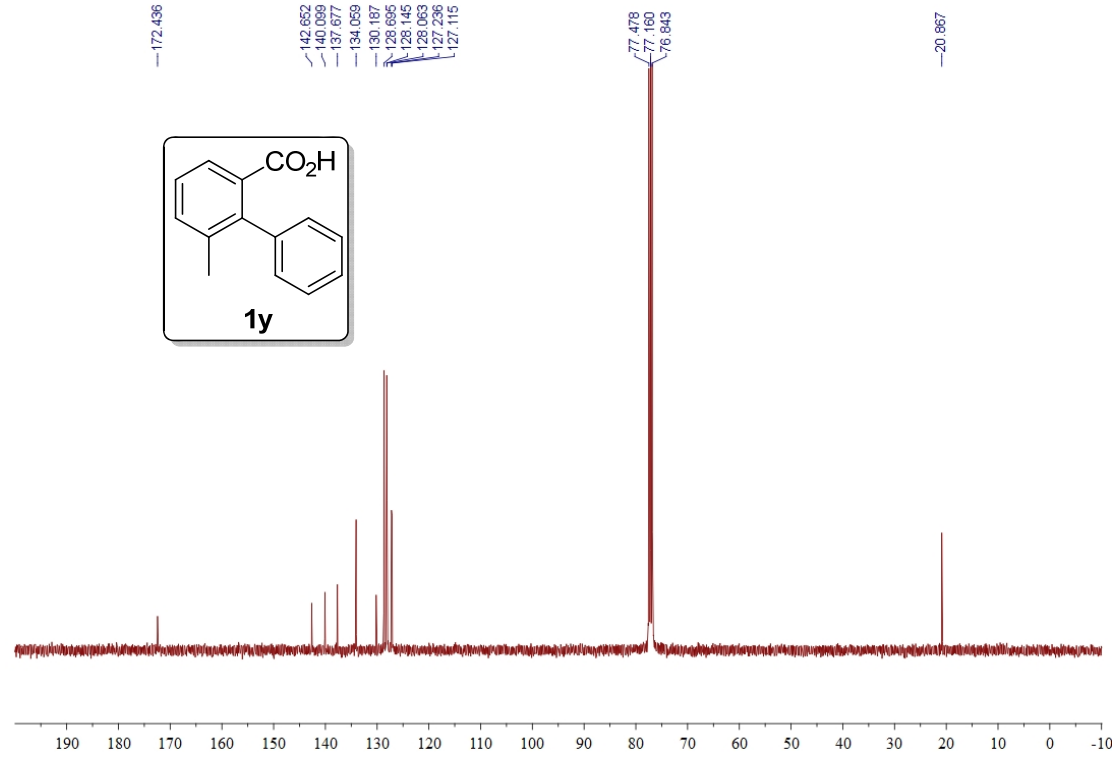
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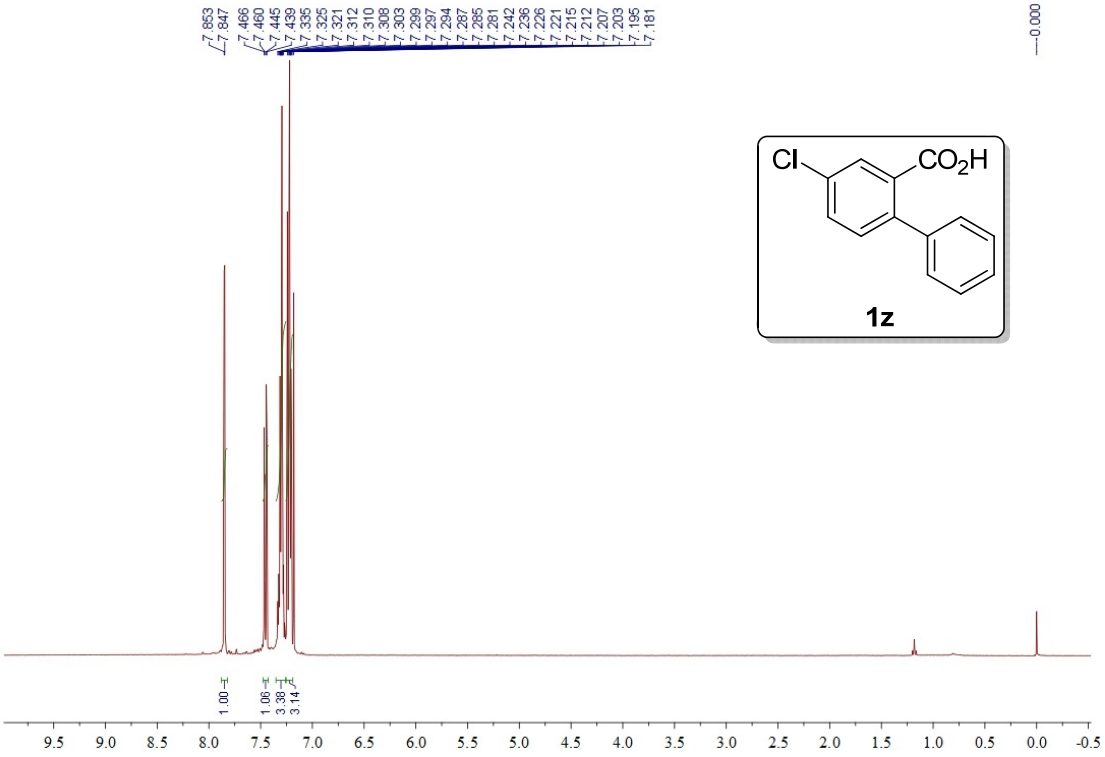
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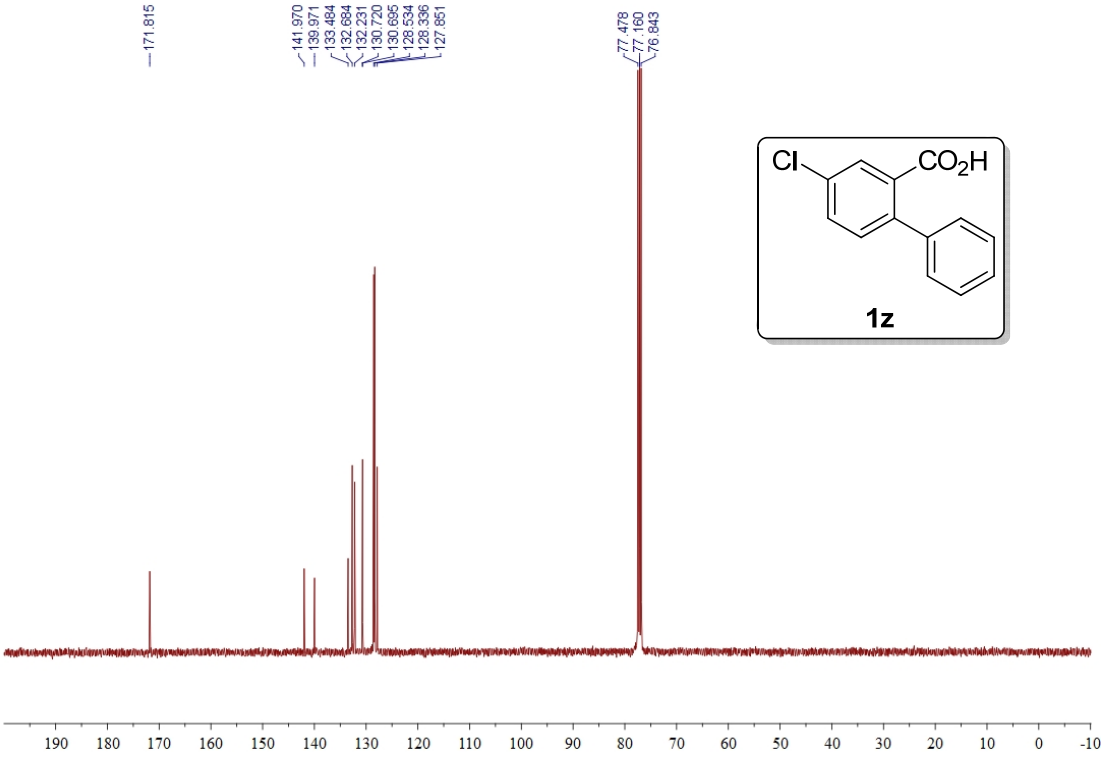
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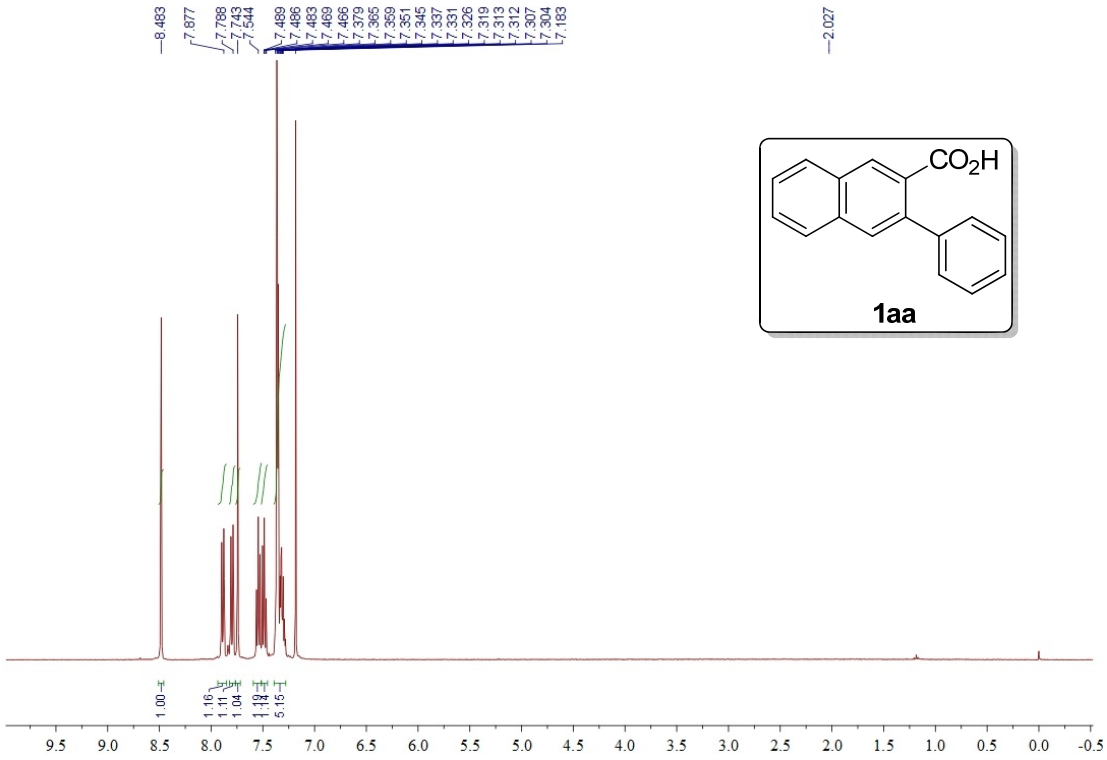
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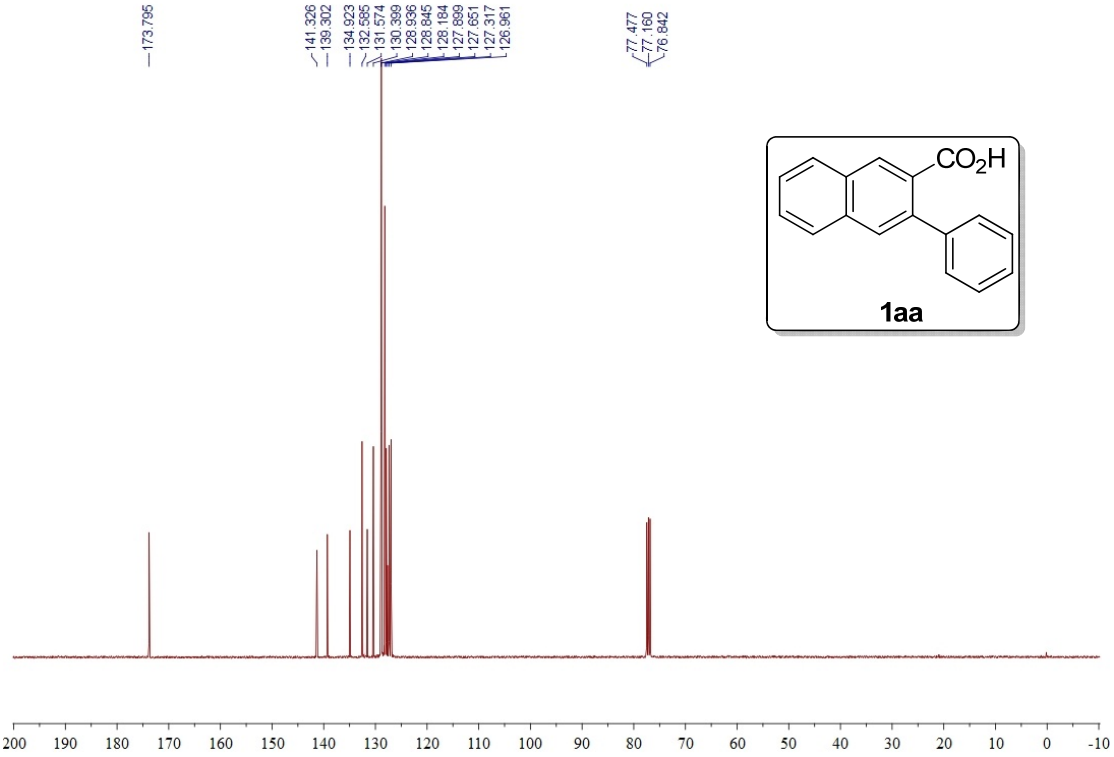
7.304
7.183
2.027
CO2H
1aa
1.00
1.16
1.11
1.04
1.19
5.15
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5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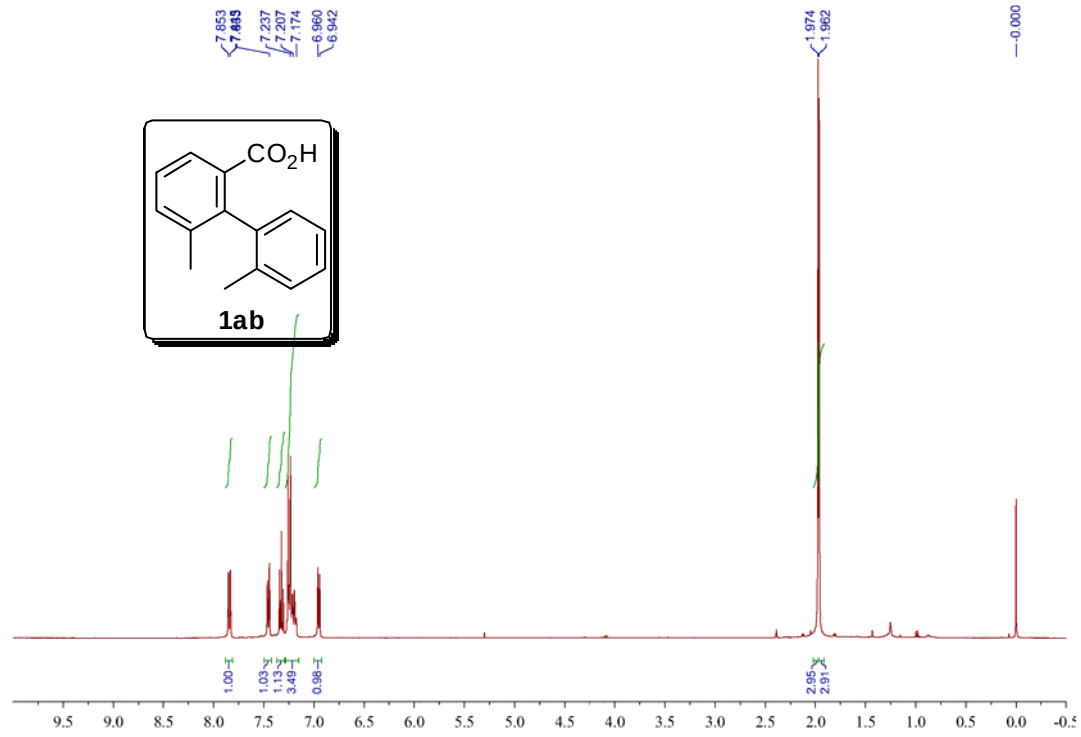
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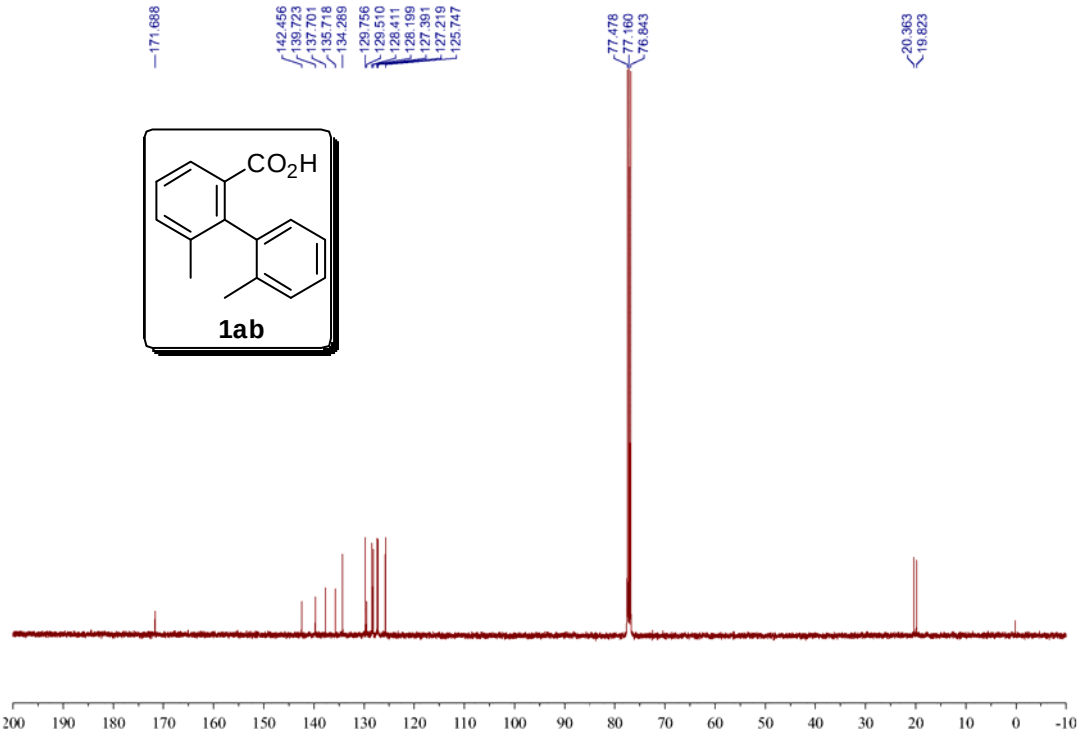
1.03
1.13
3.49
0.98
2.95
2.91
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5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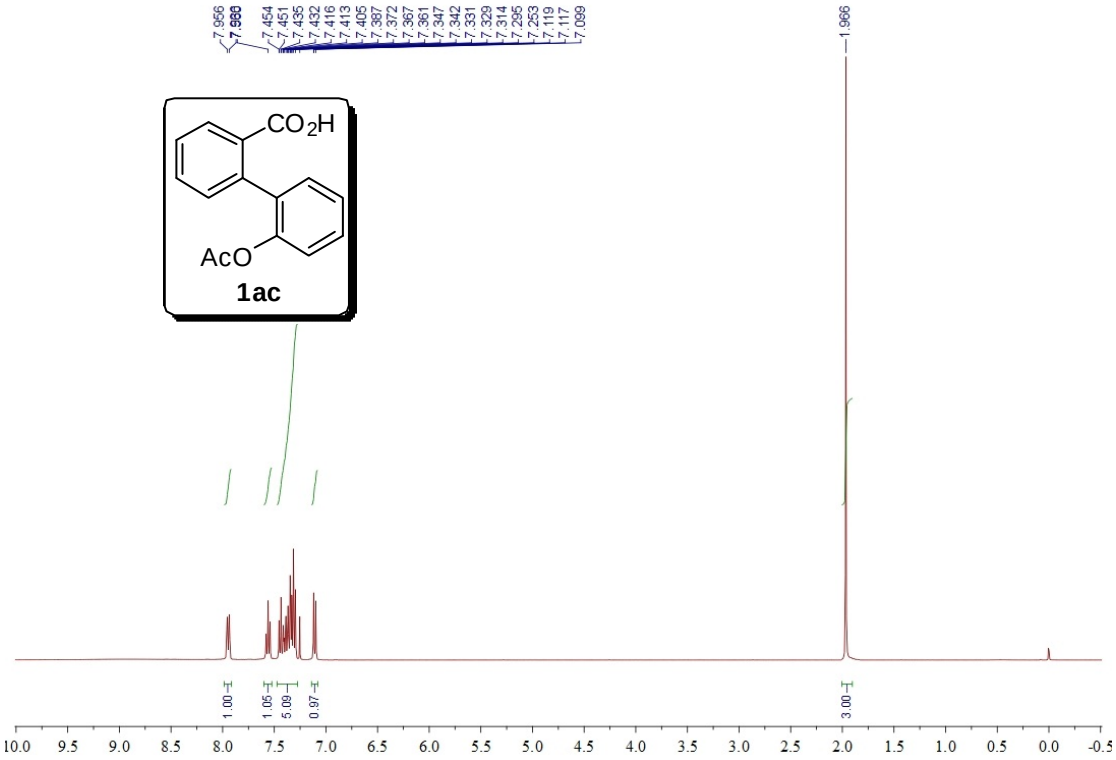
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AcO
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1.05
5.09
0.97
3.00
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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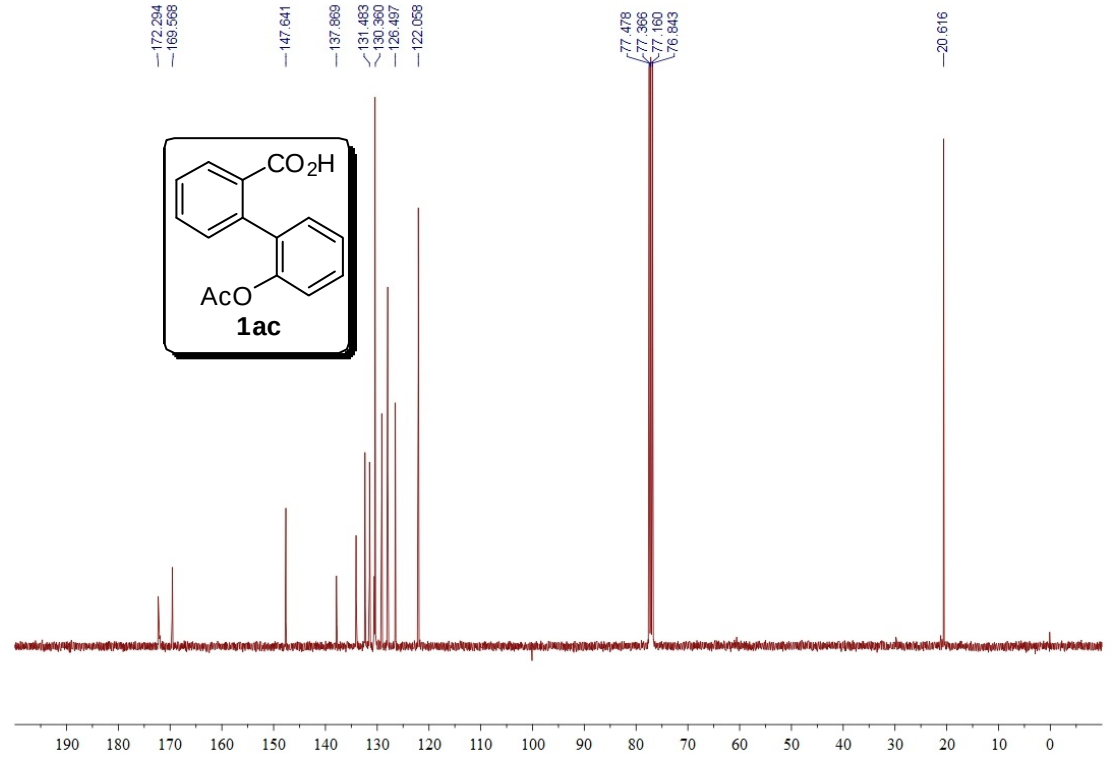
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AcO
1ac
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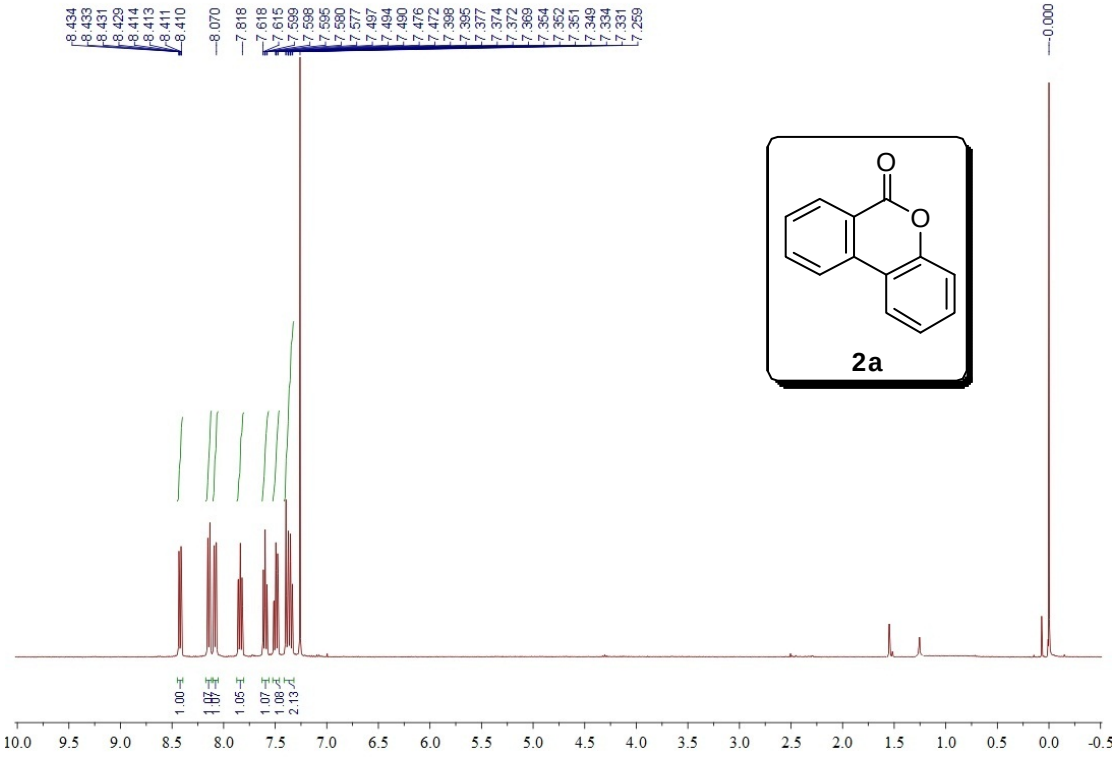
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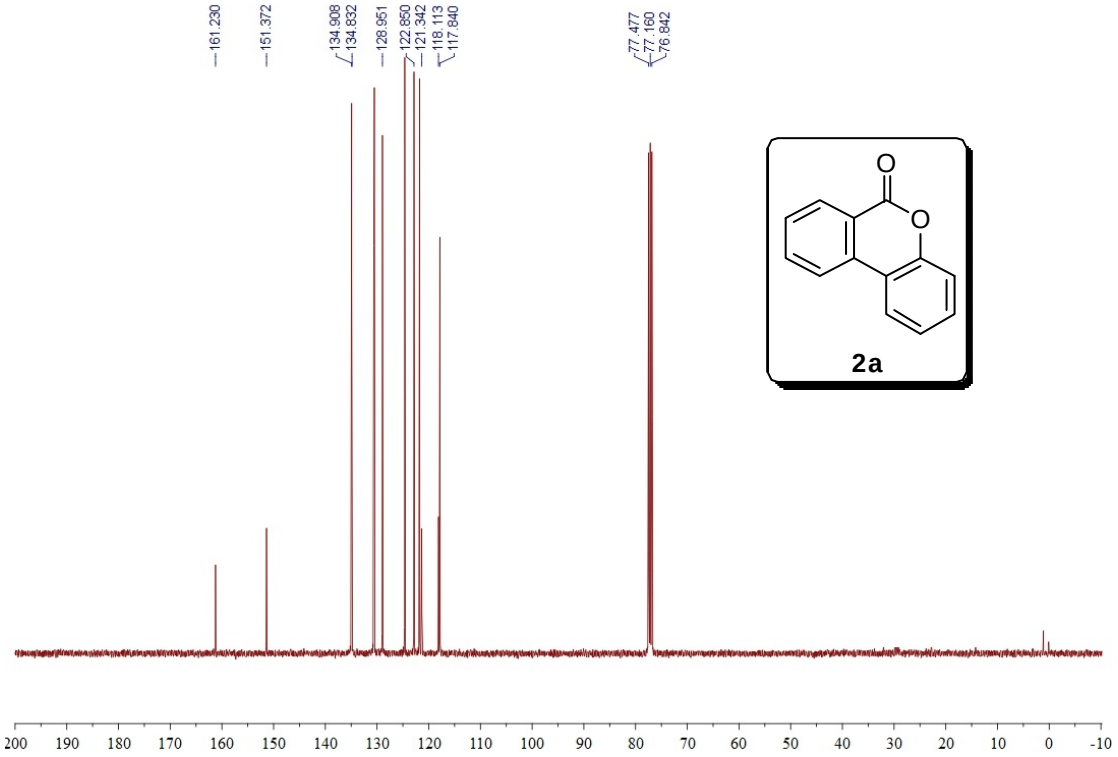
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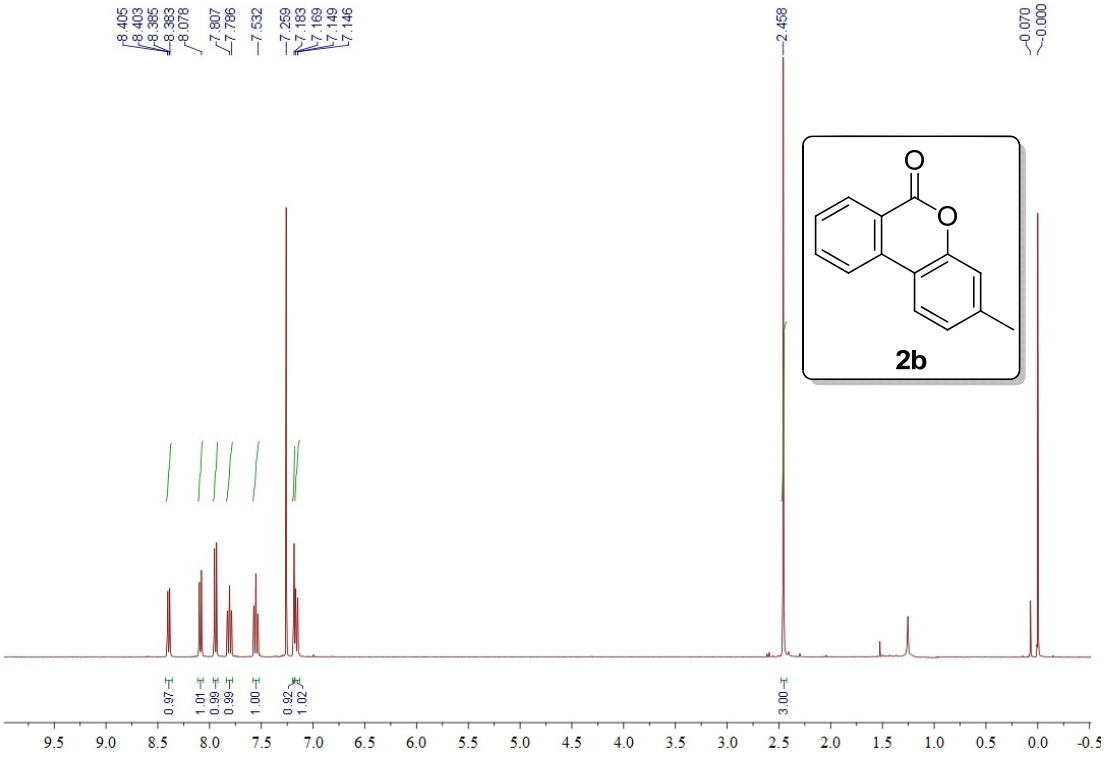
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0.99
0.99
1.00
0.92
1.02
3.00
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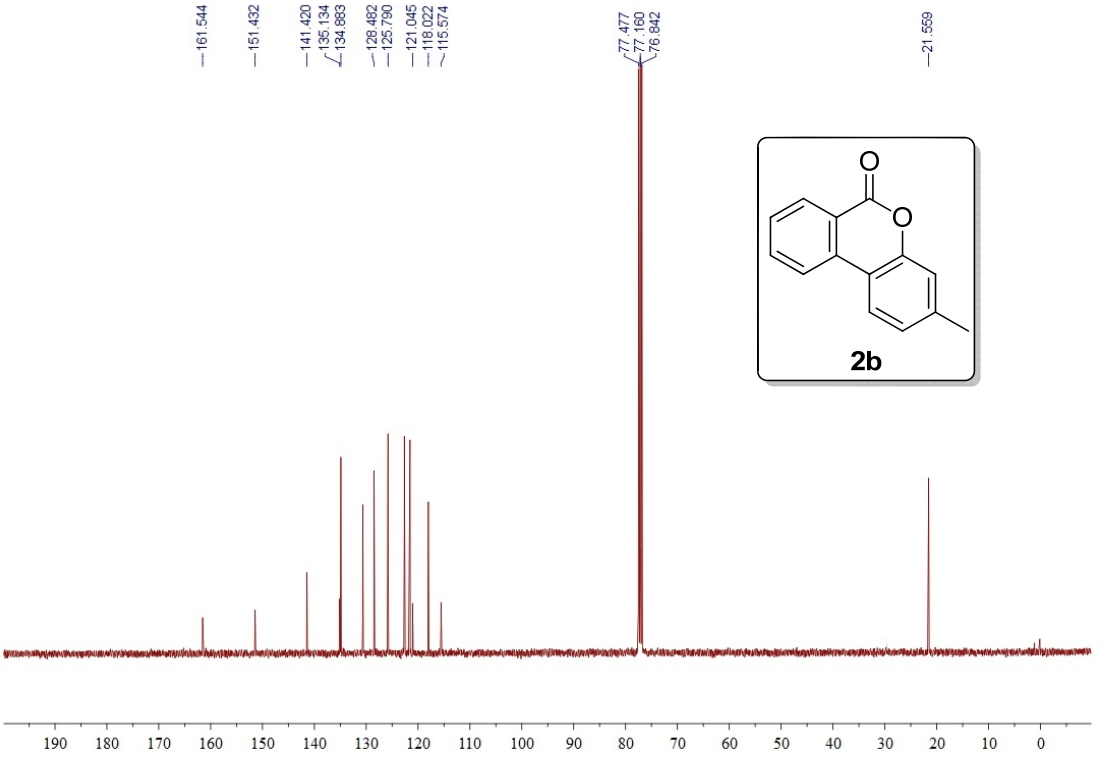
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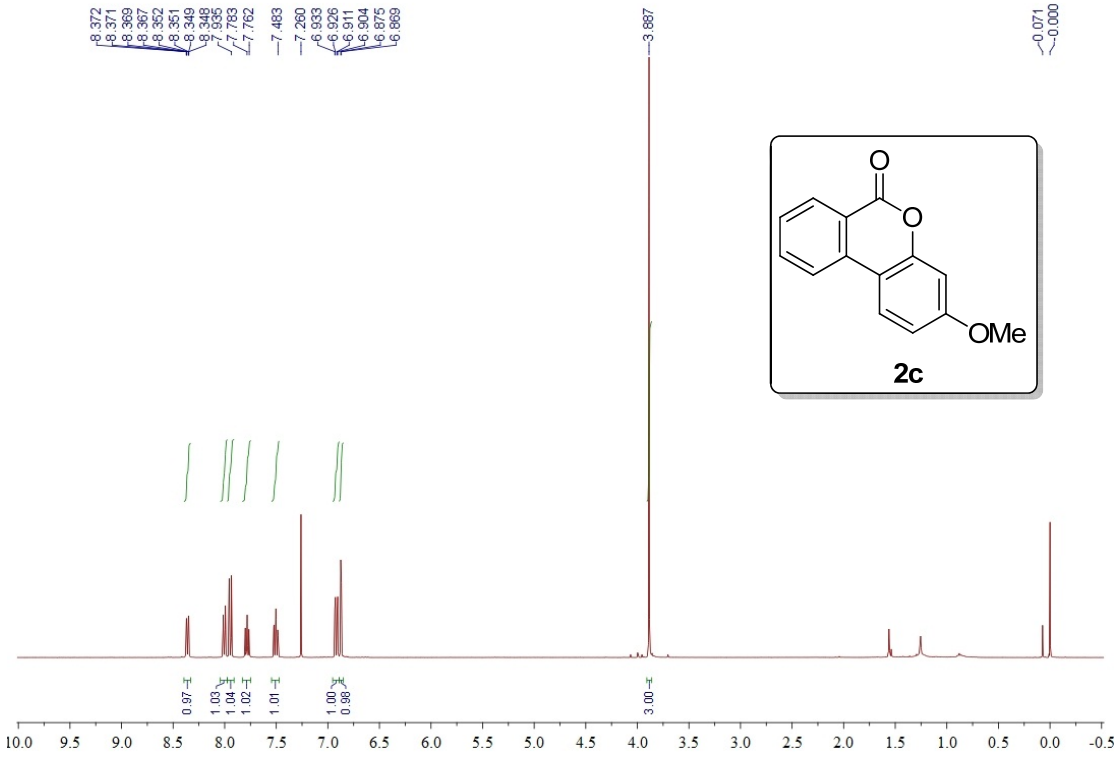
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6.926
6.911
6.904
6.875
6.869
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0.071
0.000
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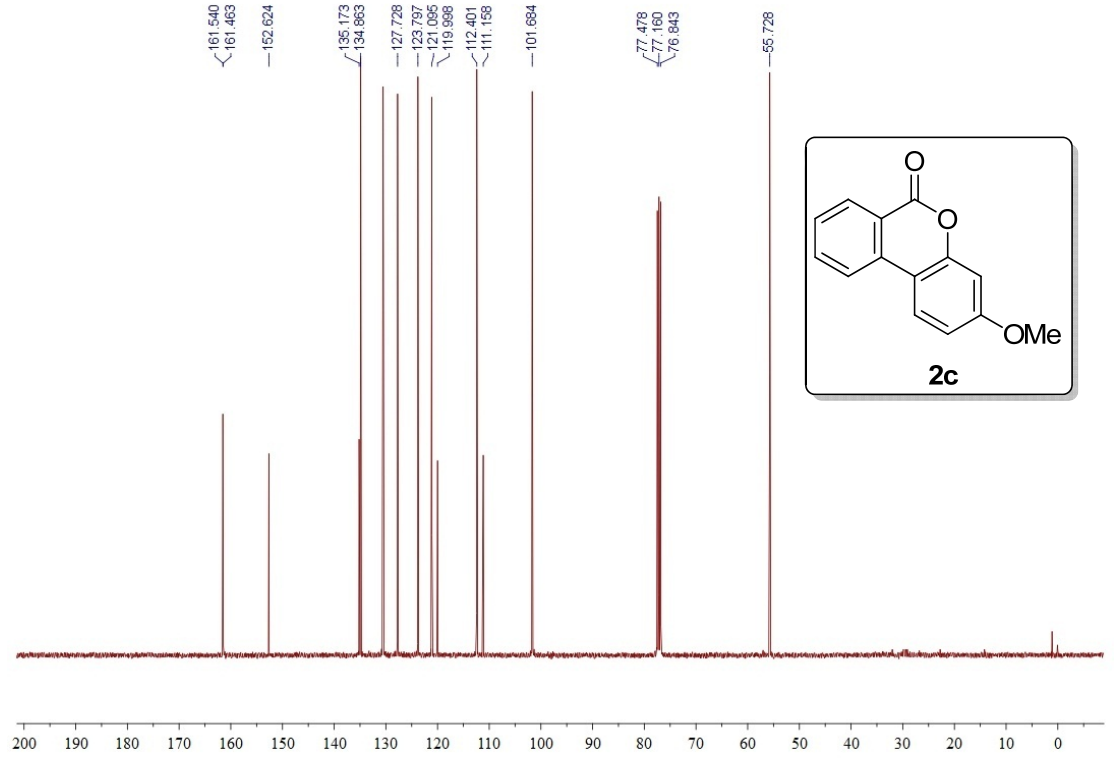
O
OMe
2c
0.97
1.03
1.04
1.02
1.01
1.00
0.98
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5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OMe
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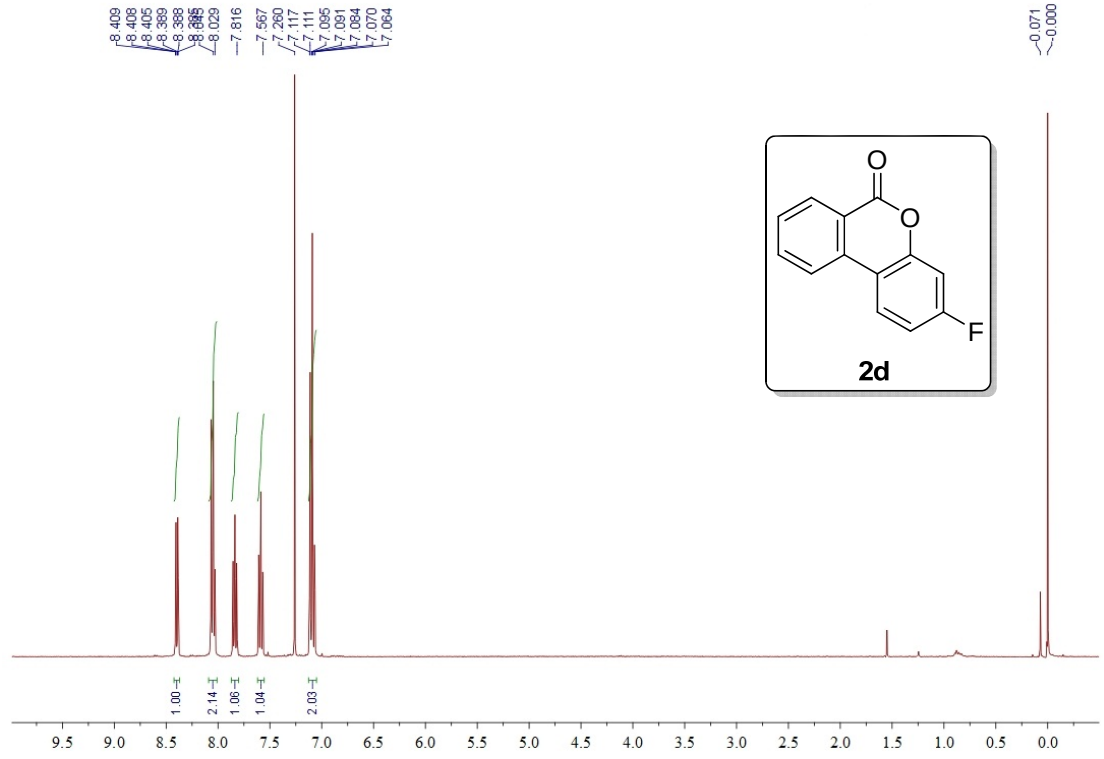
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7.064
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2.14
1.06
1.04
2.03
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
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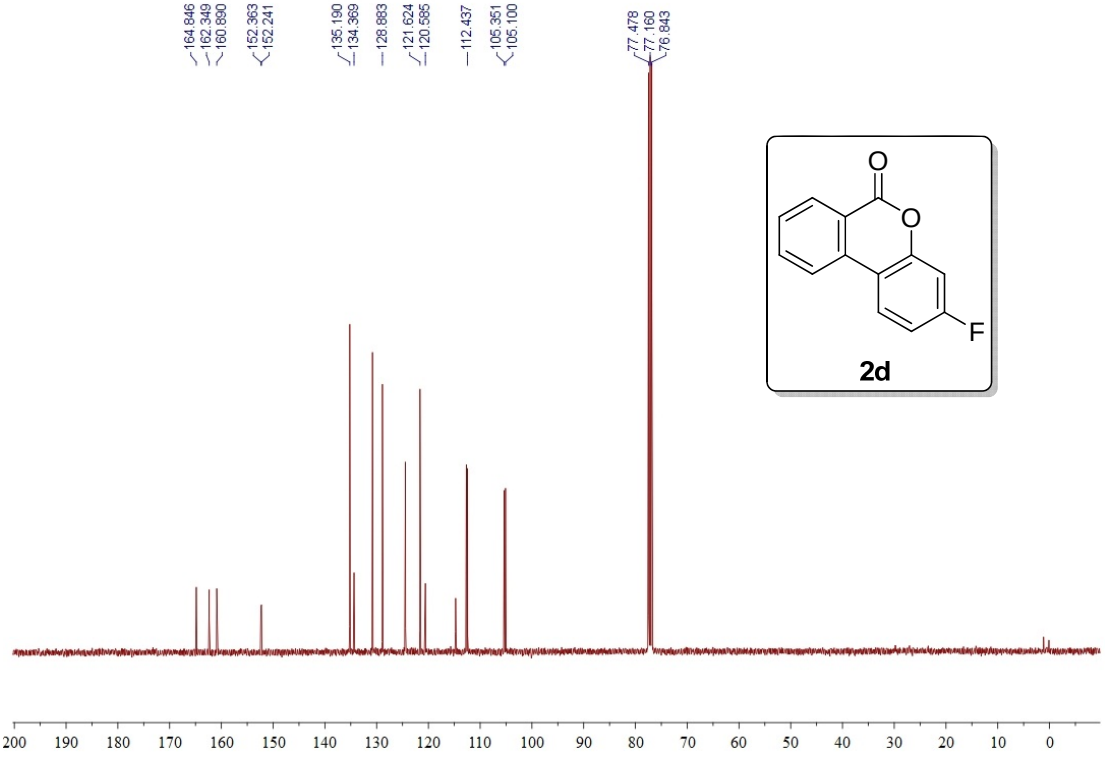
O
F
2d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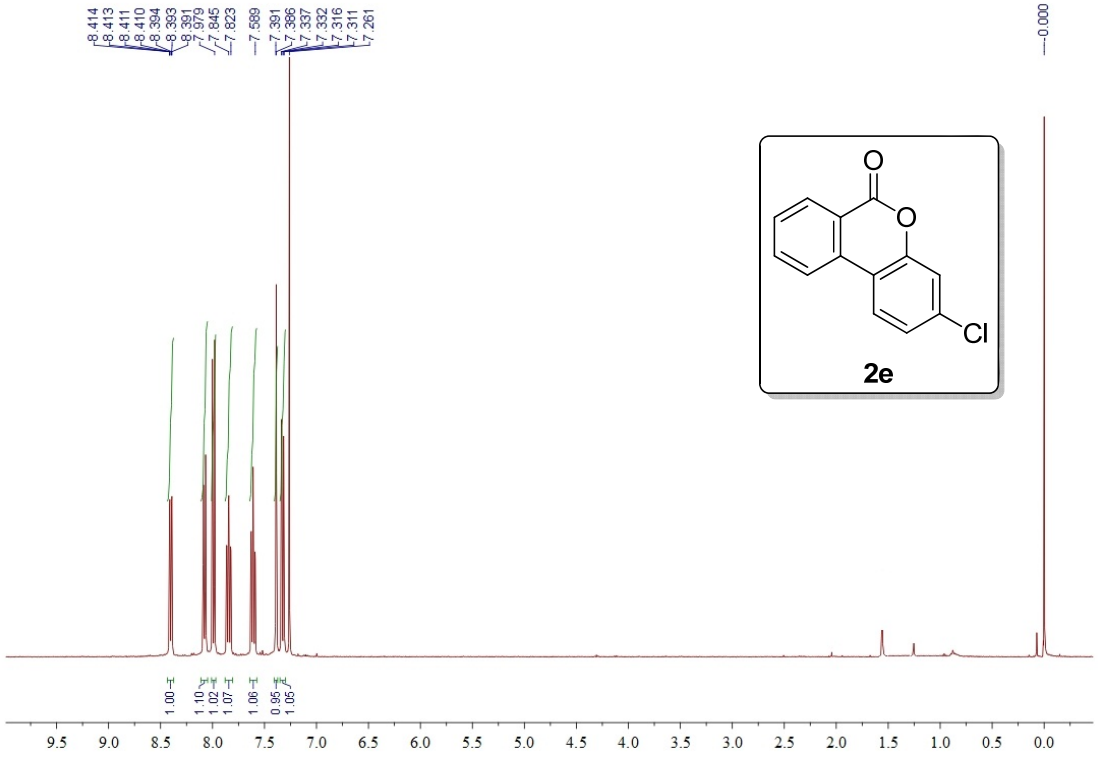
2d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Cl
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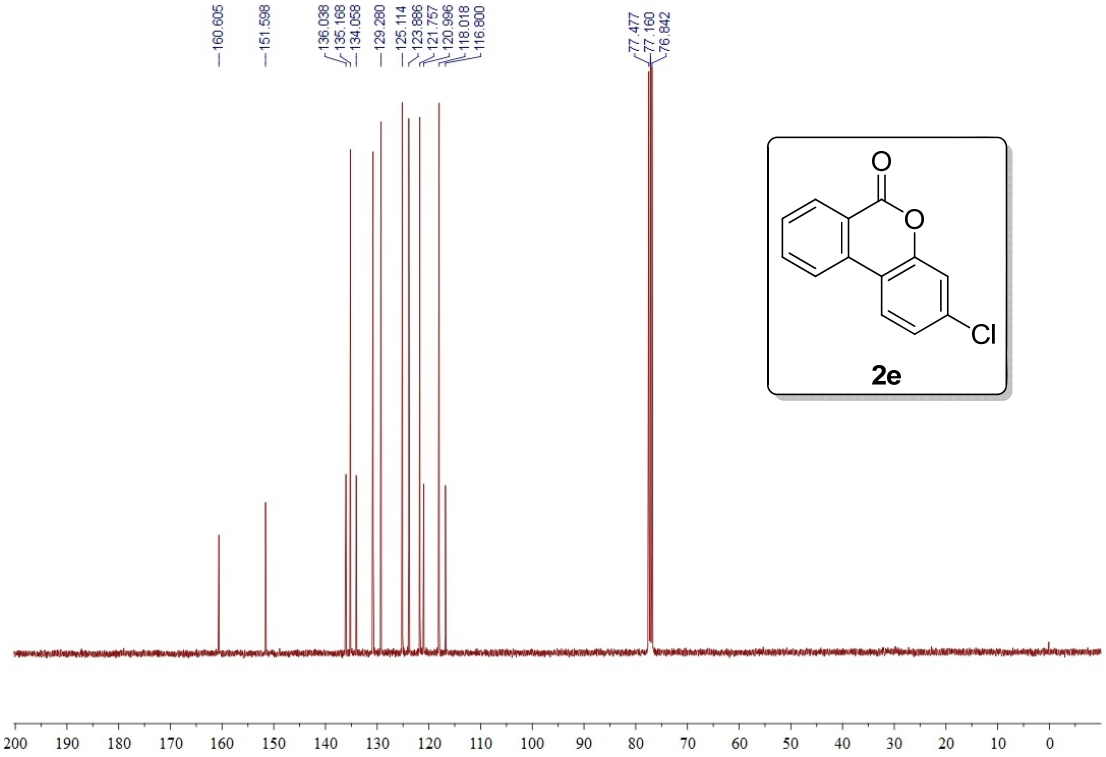
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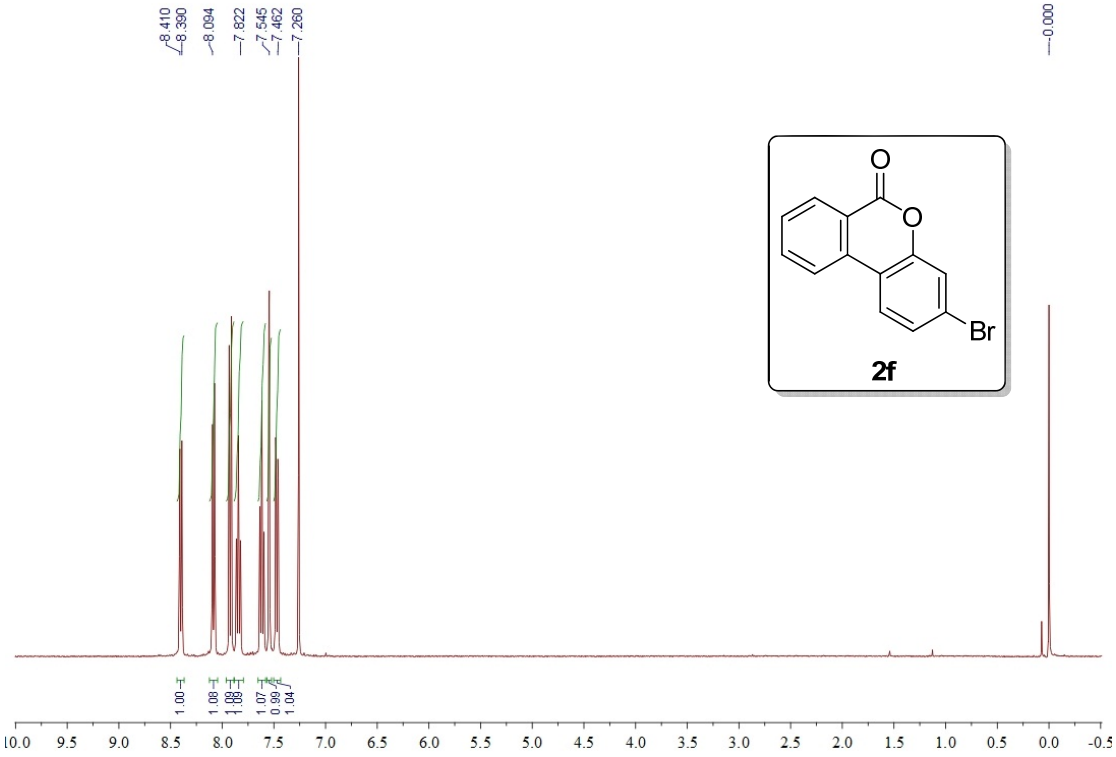
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O
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2f
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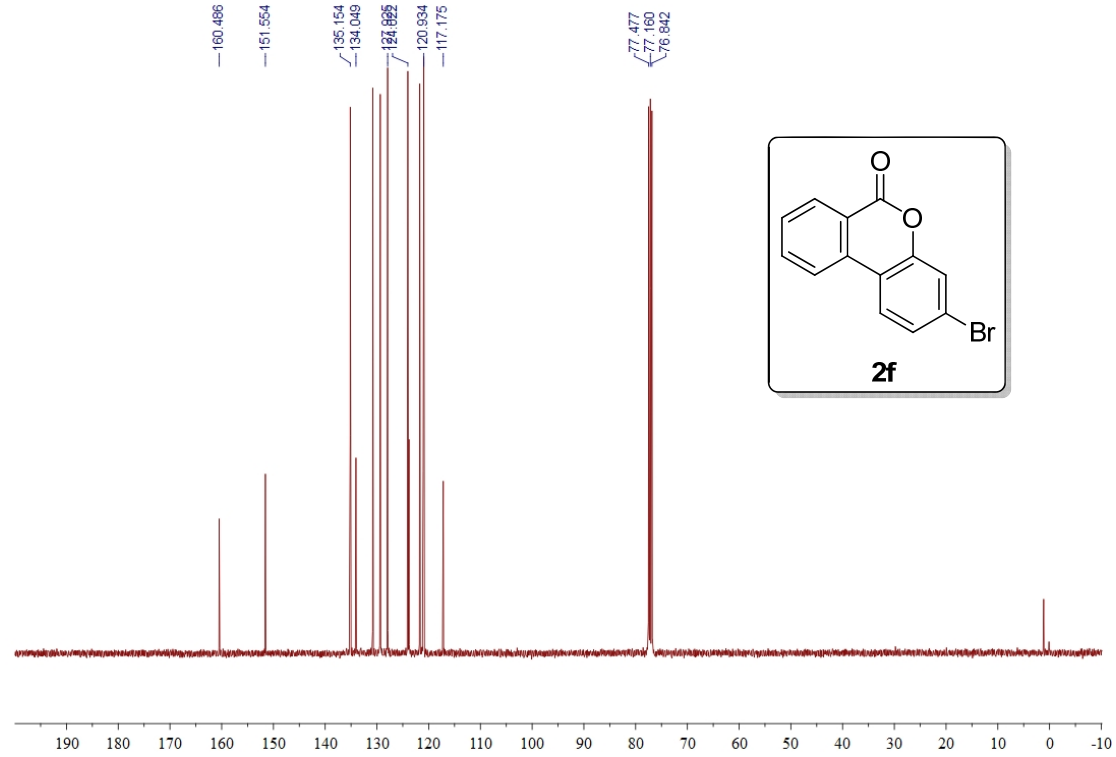
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O
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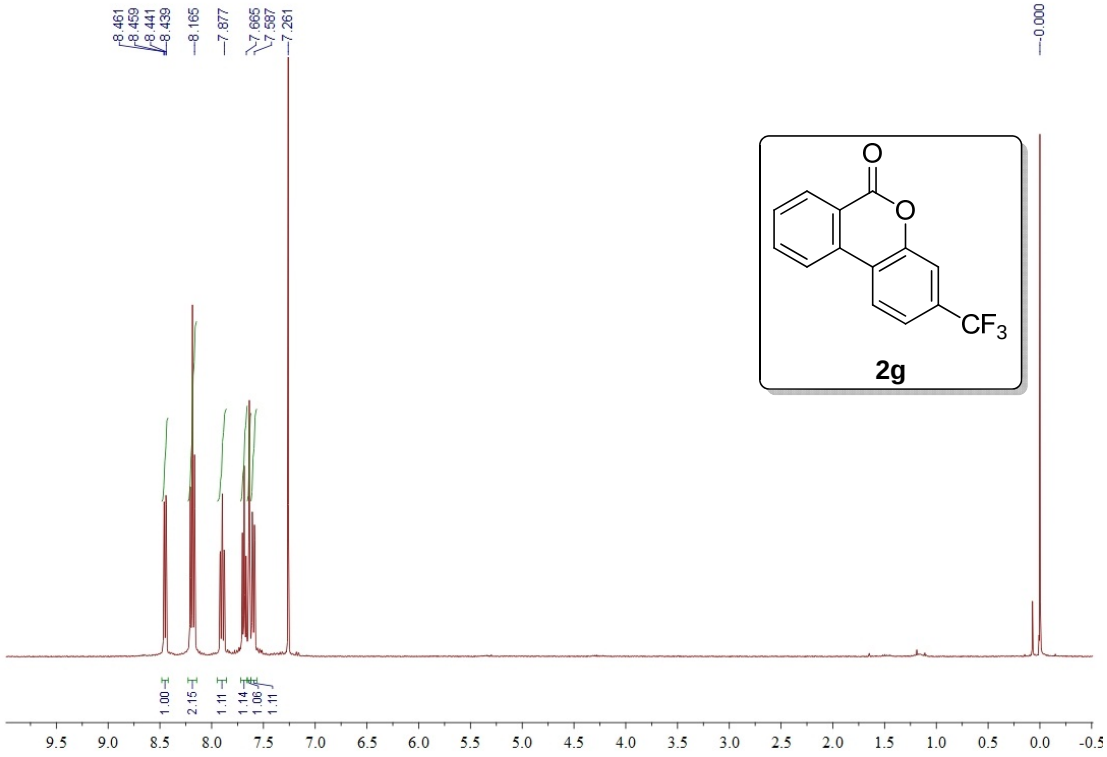
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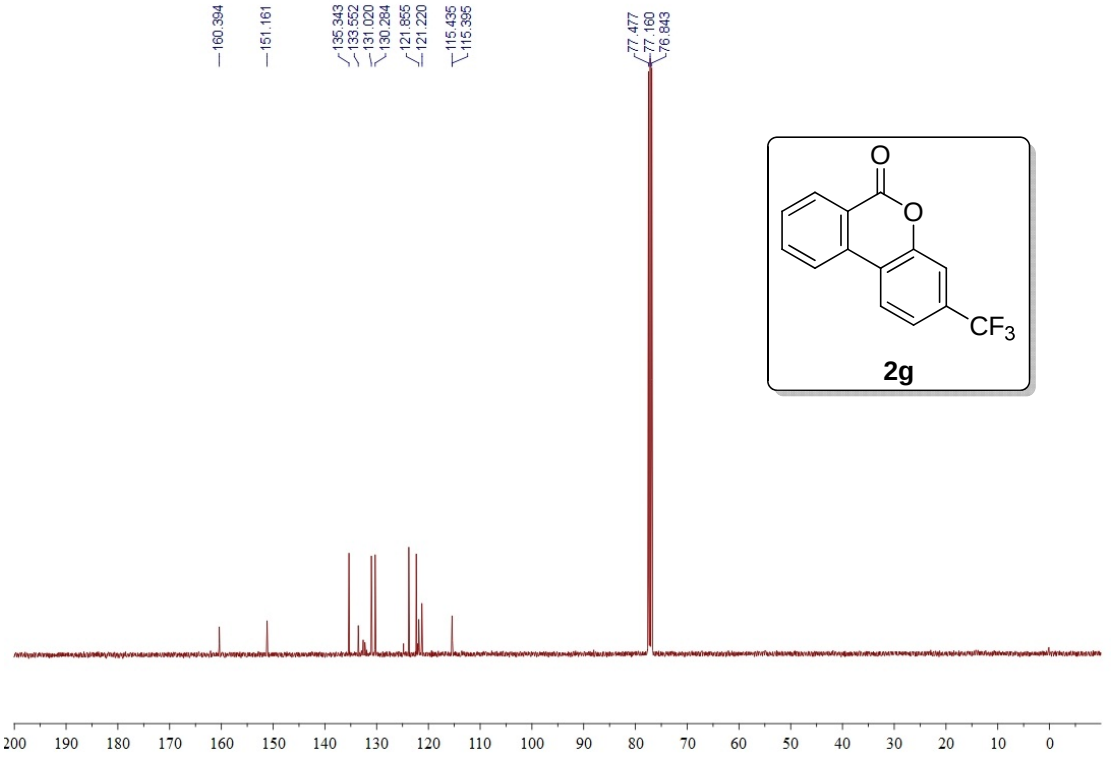
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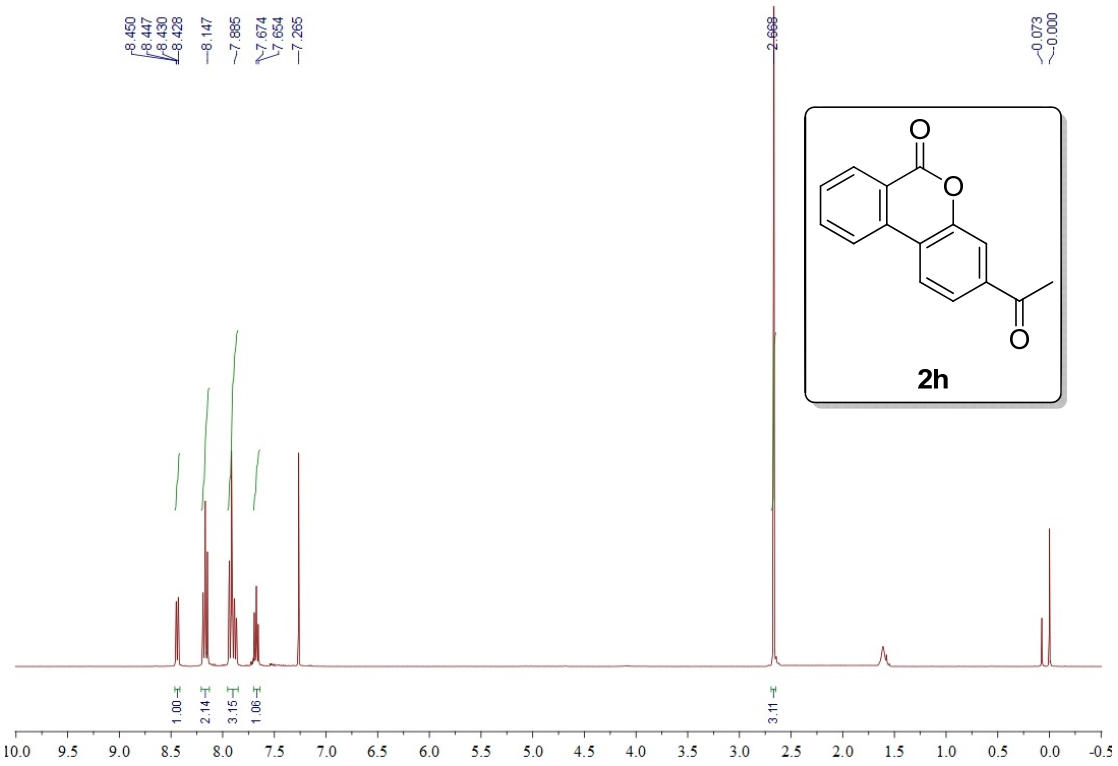
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3.15
1.06
3.11
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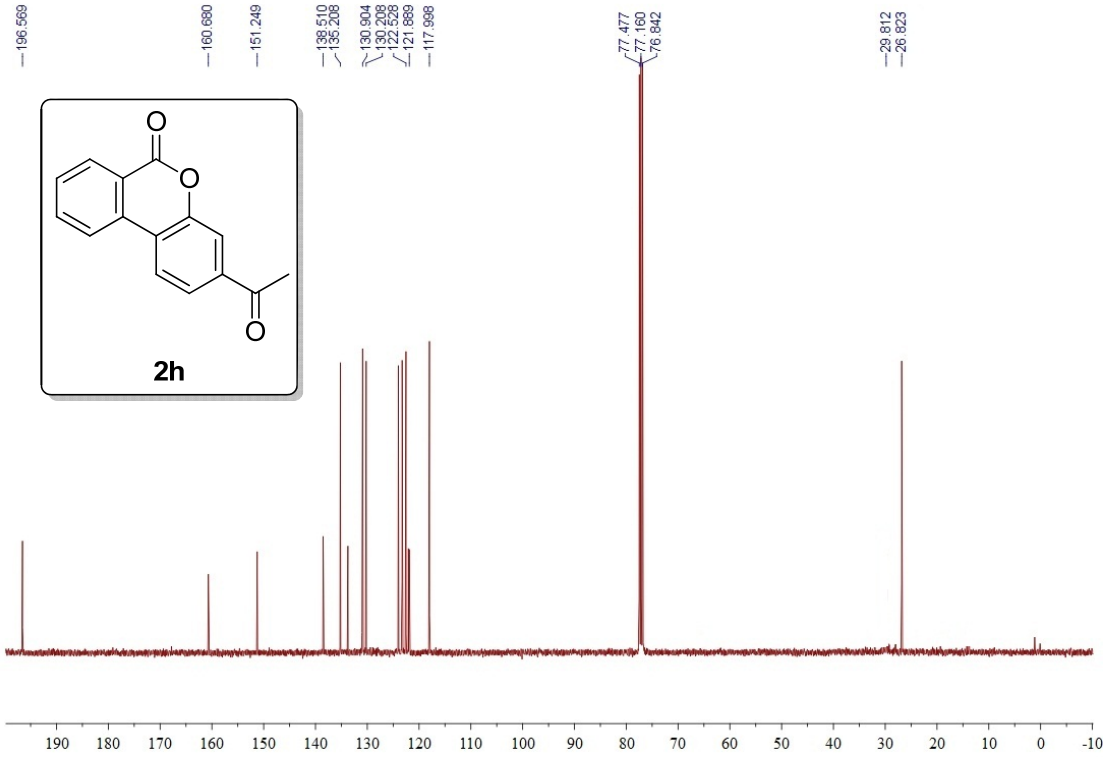
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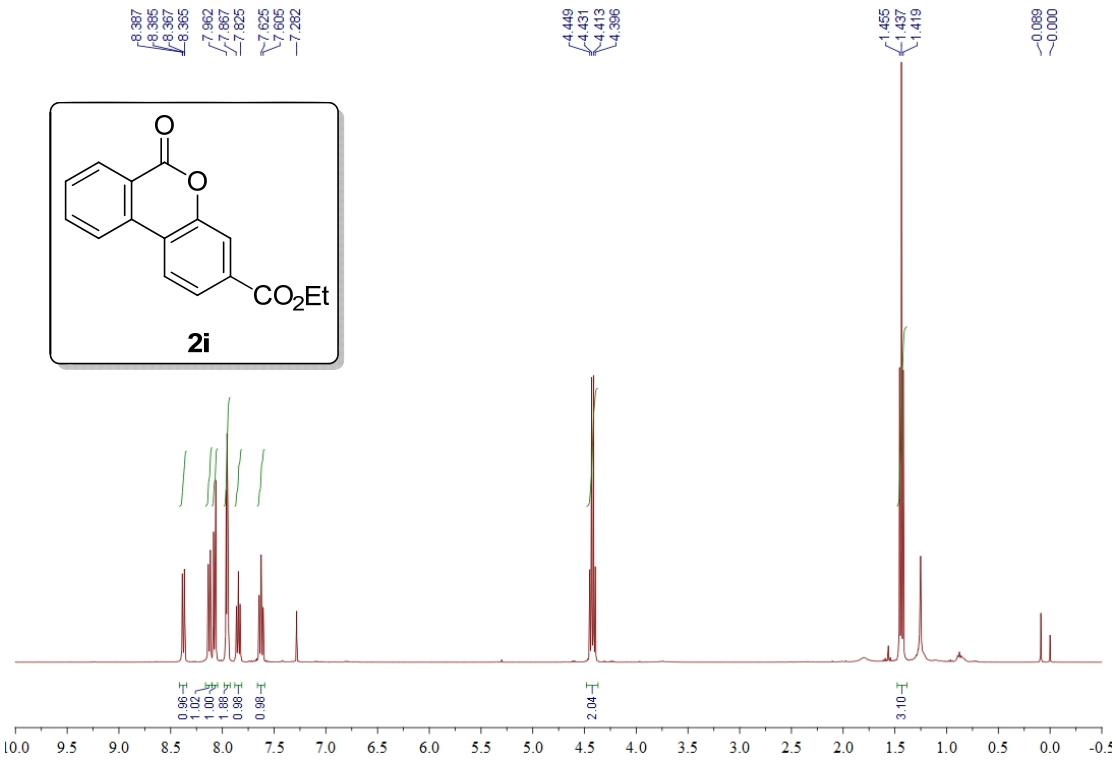
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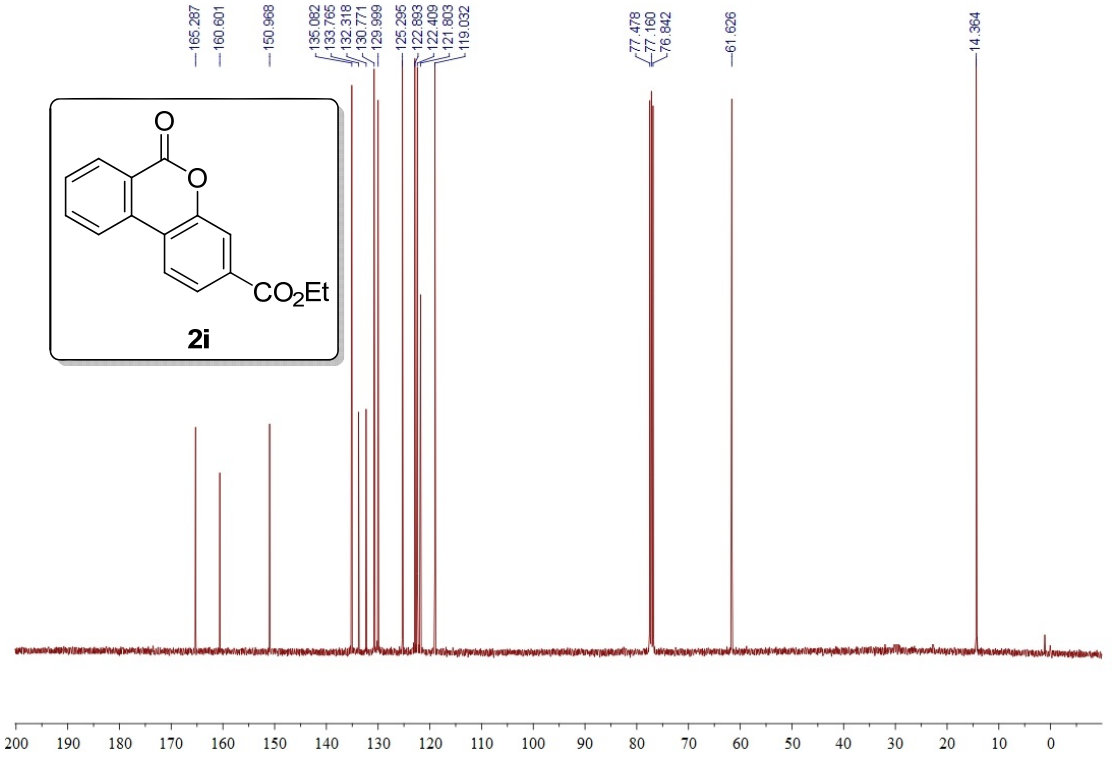
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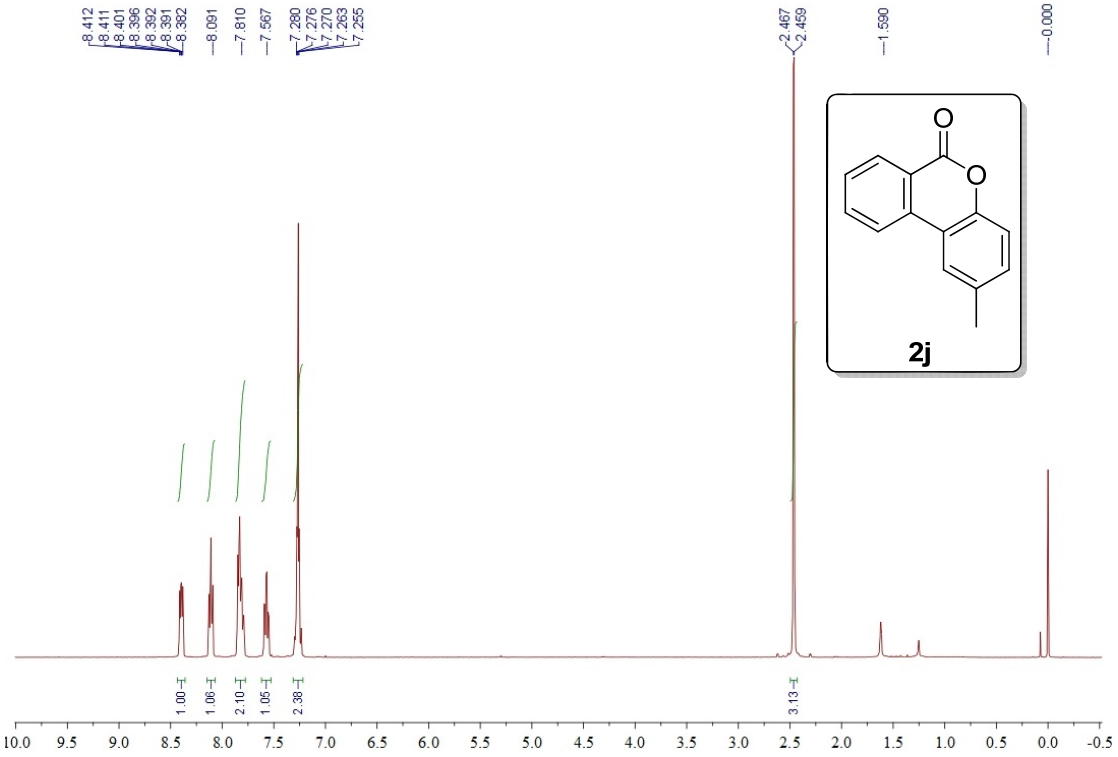
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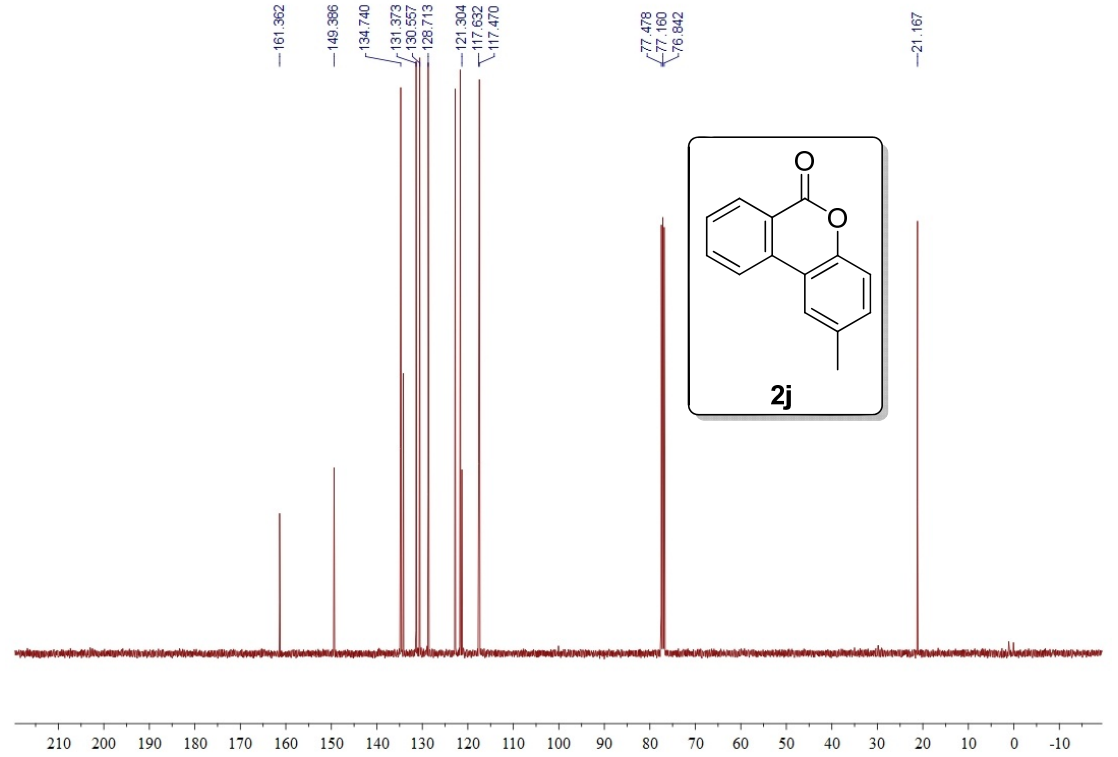
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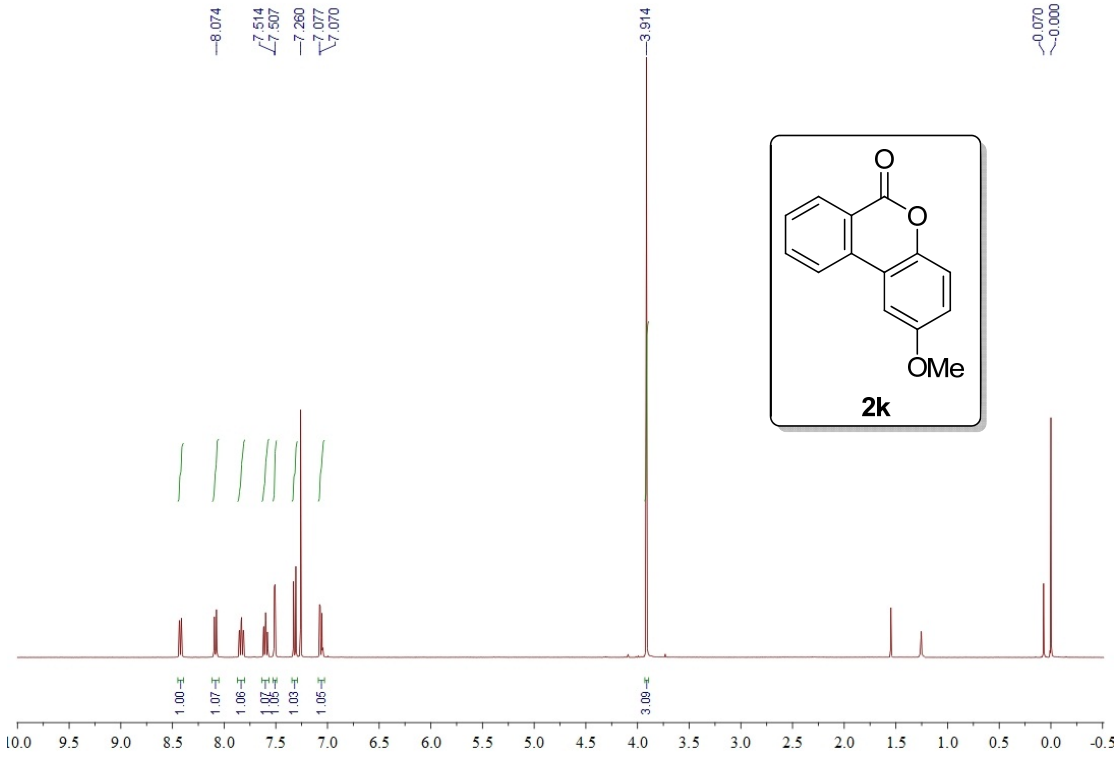
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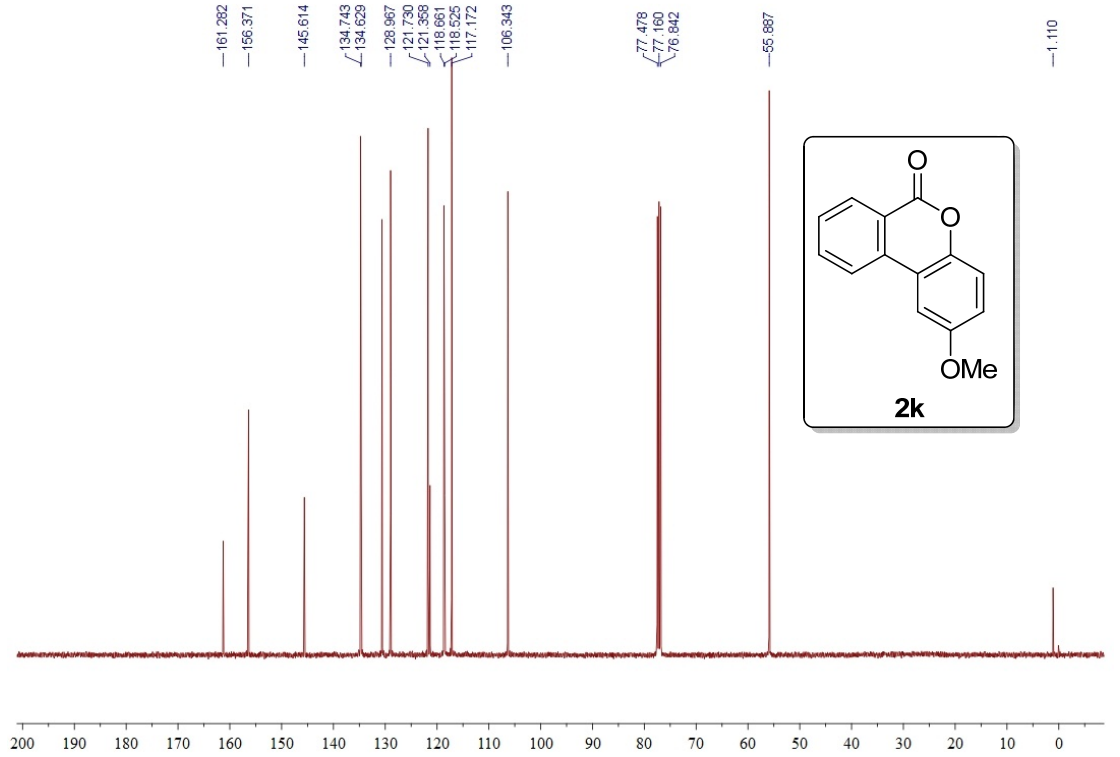
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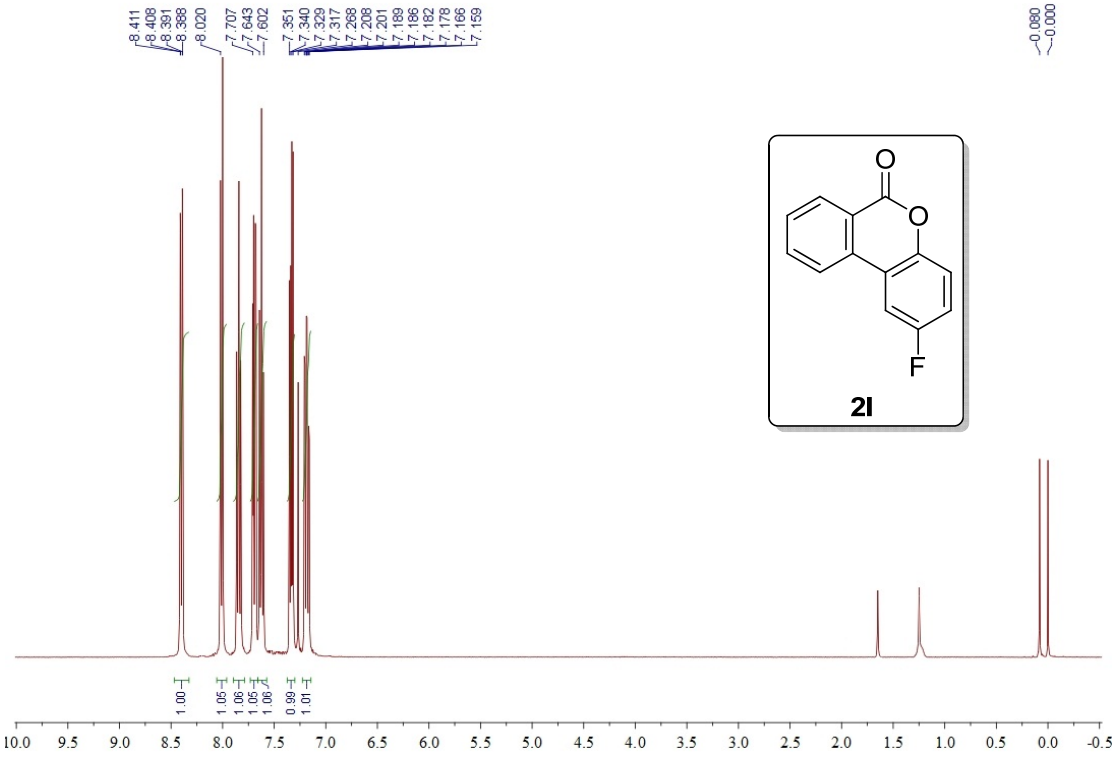
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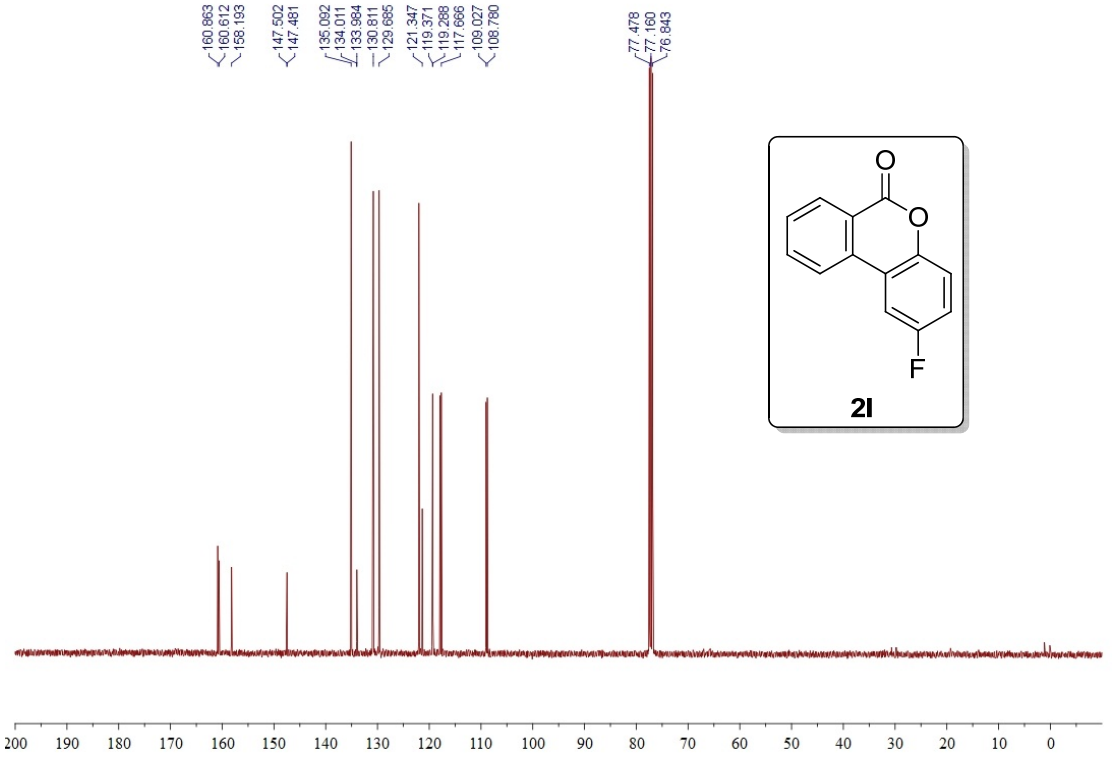
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O
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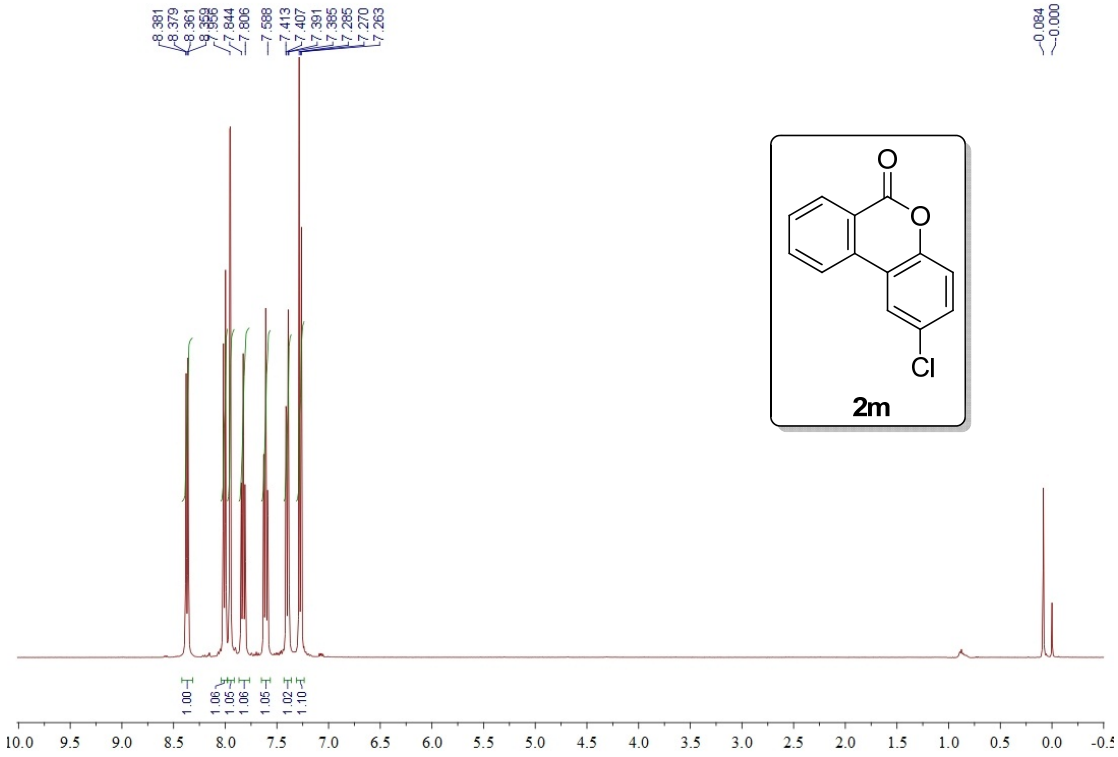
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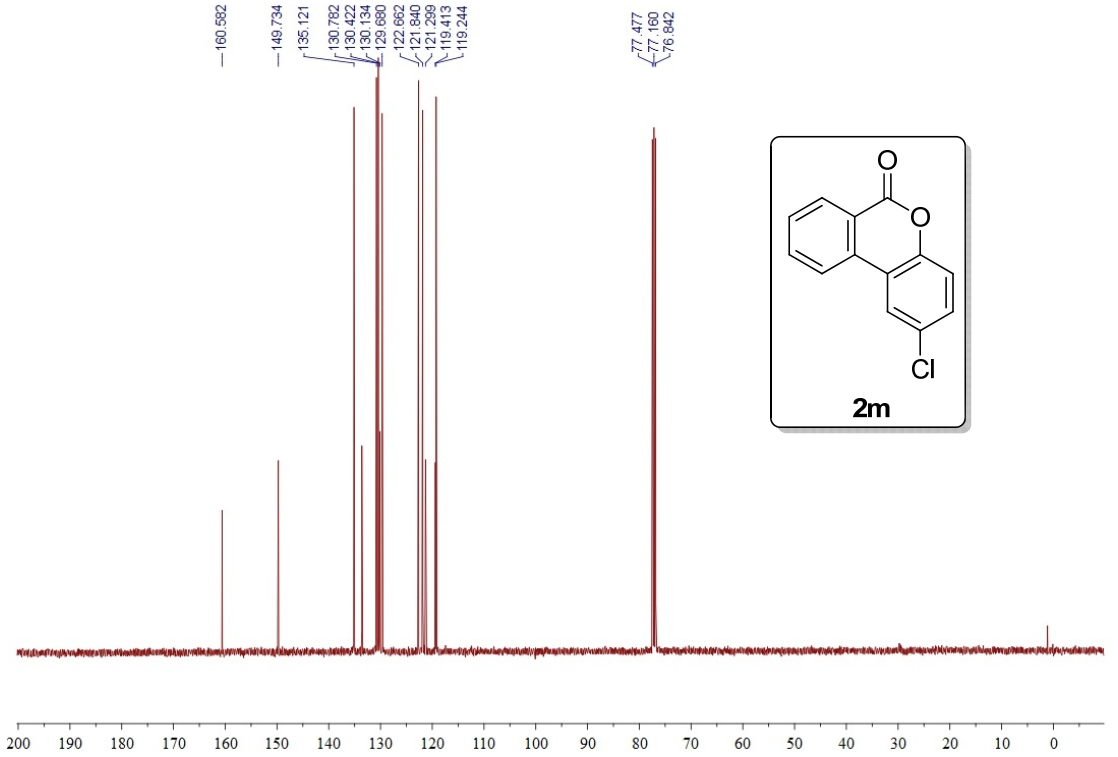
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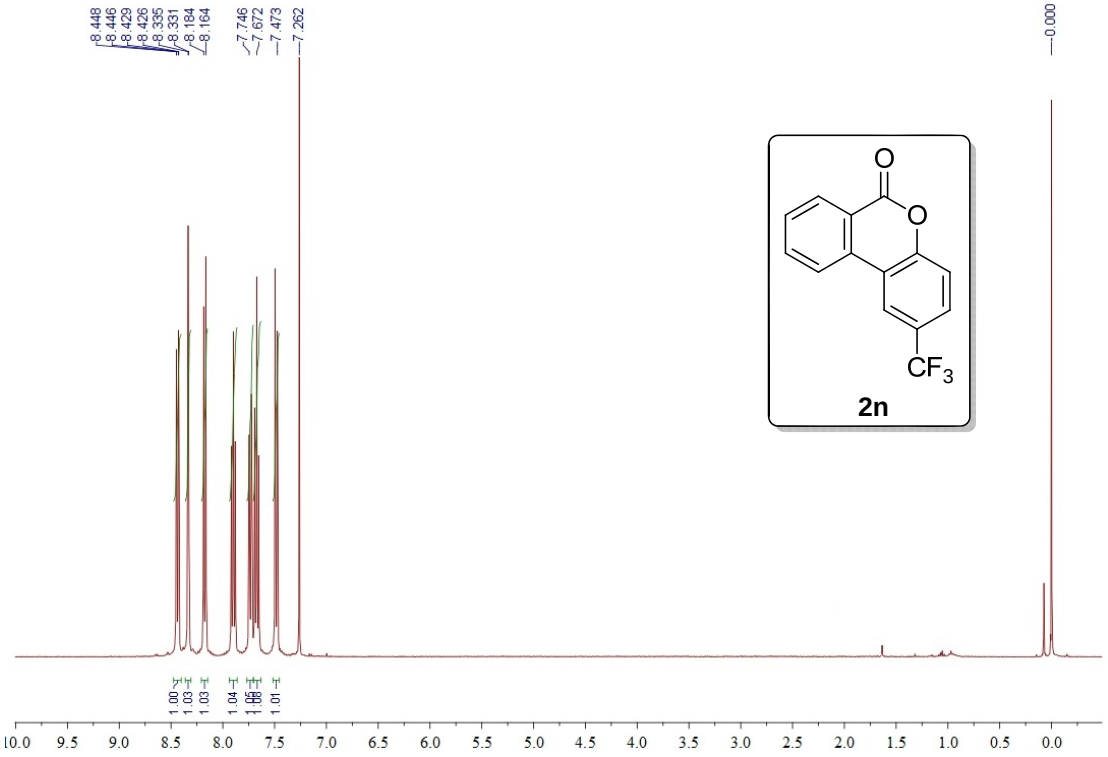
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1.04
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1.06
1.01
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O
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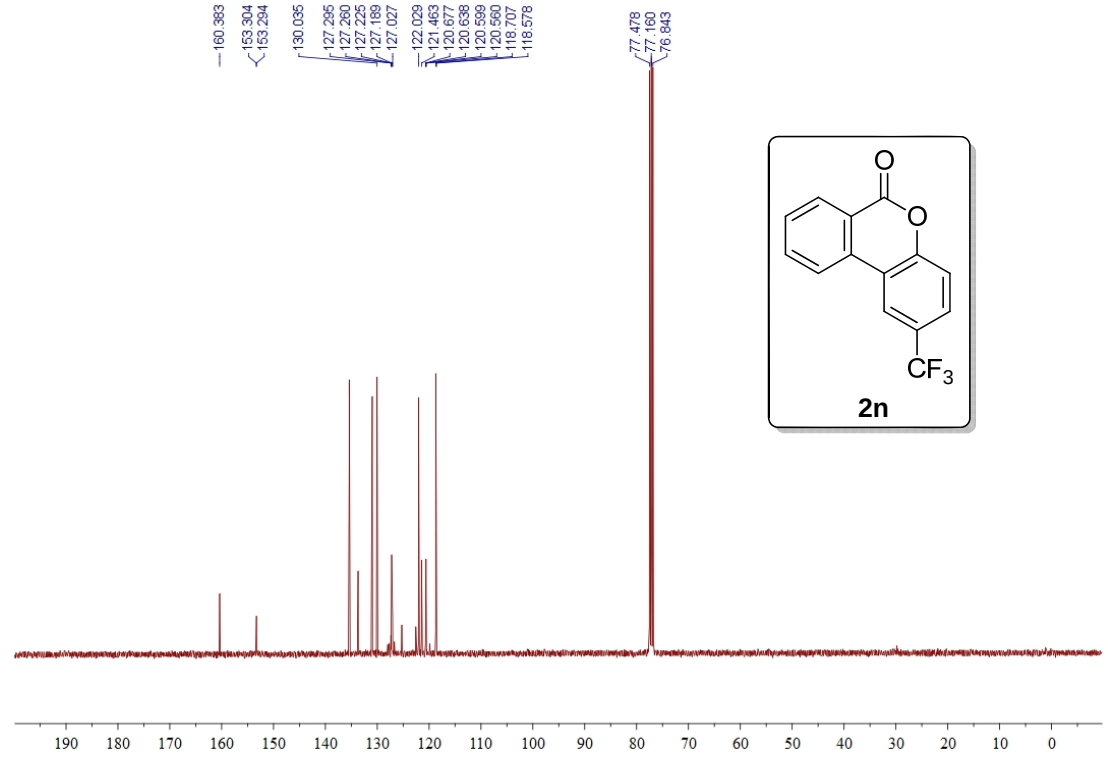
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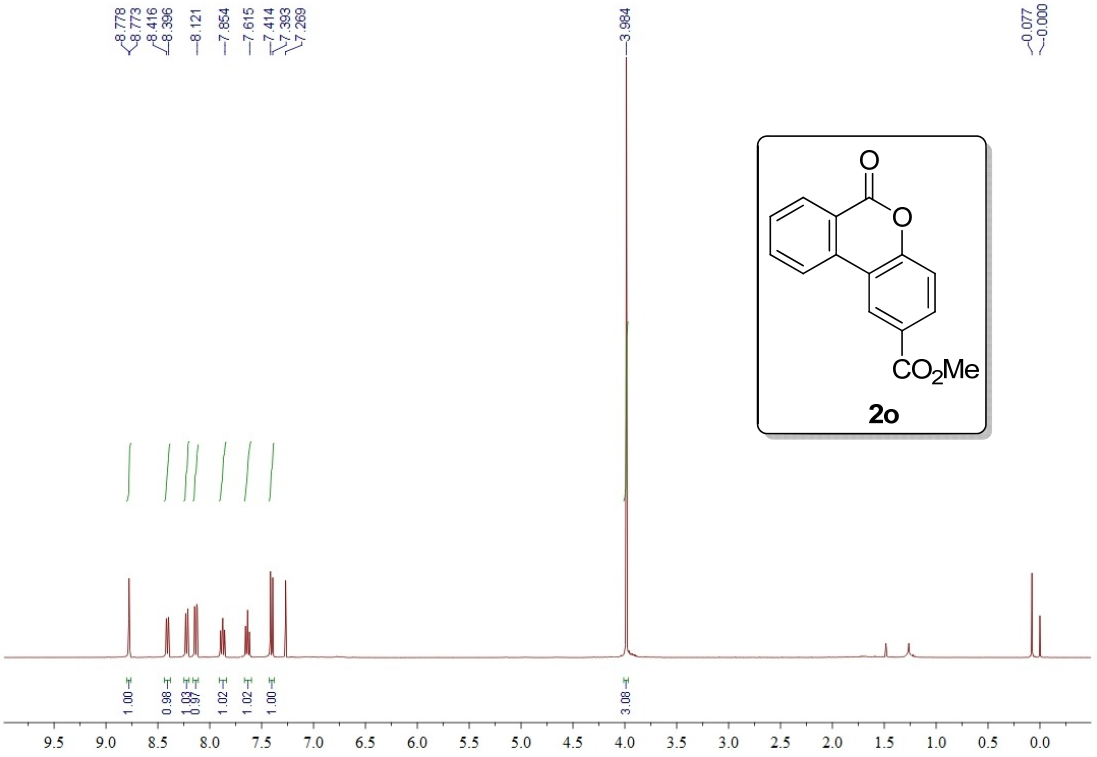
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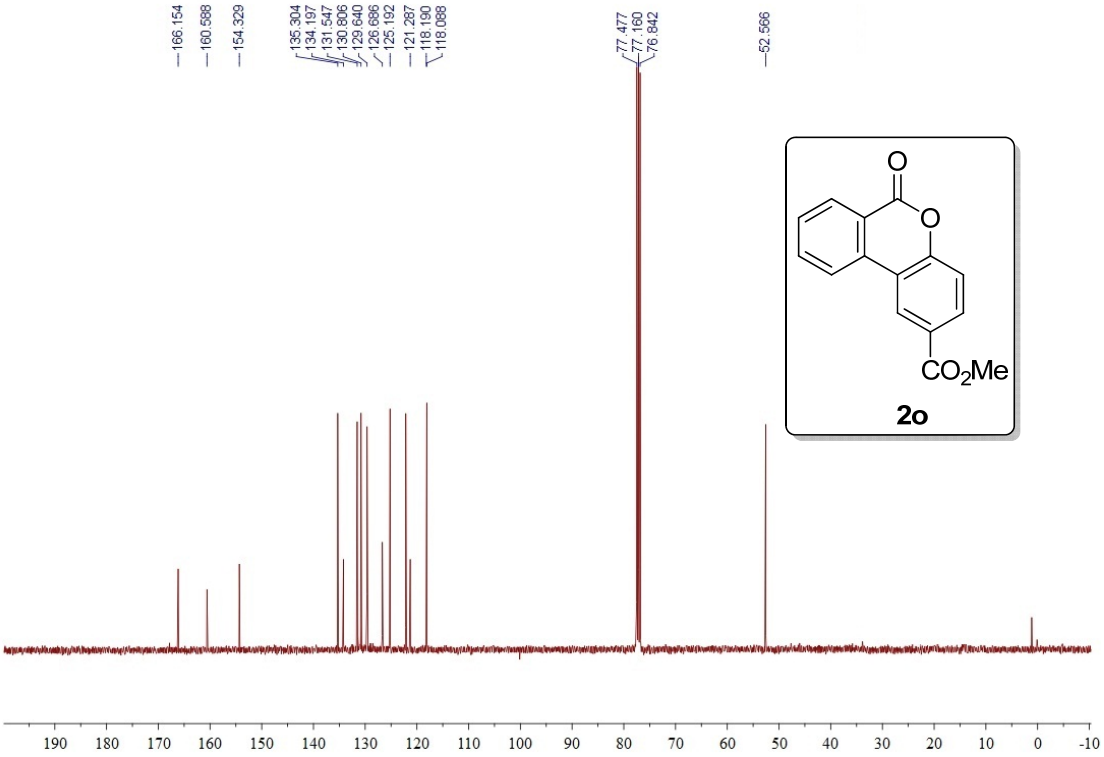
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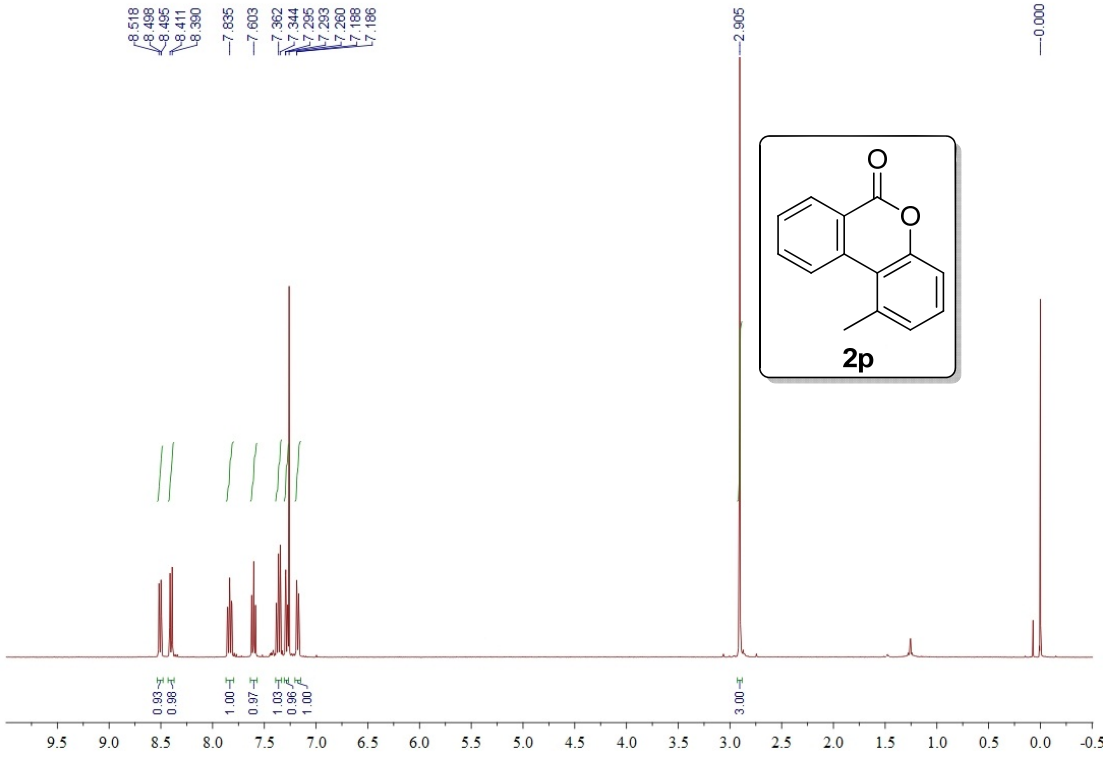
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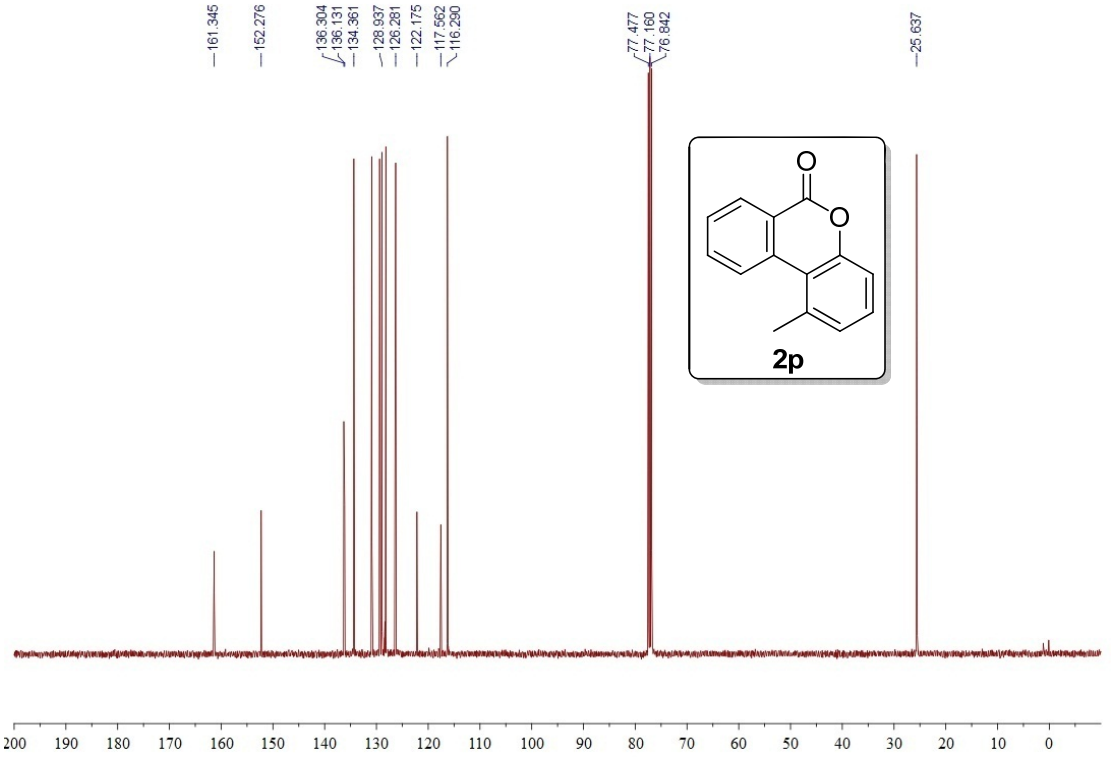
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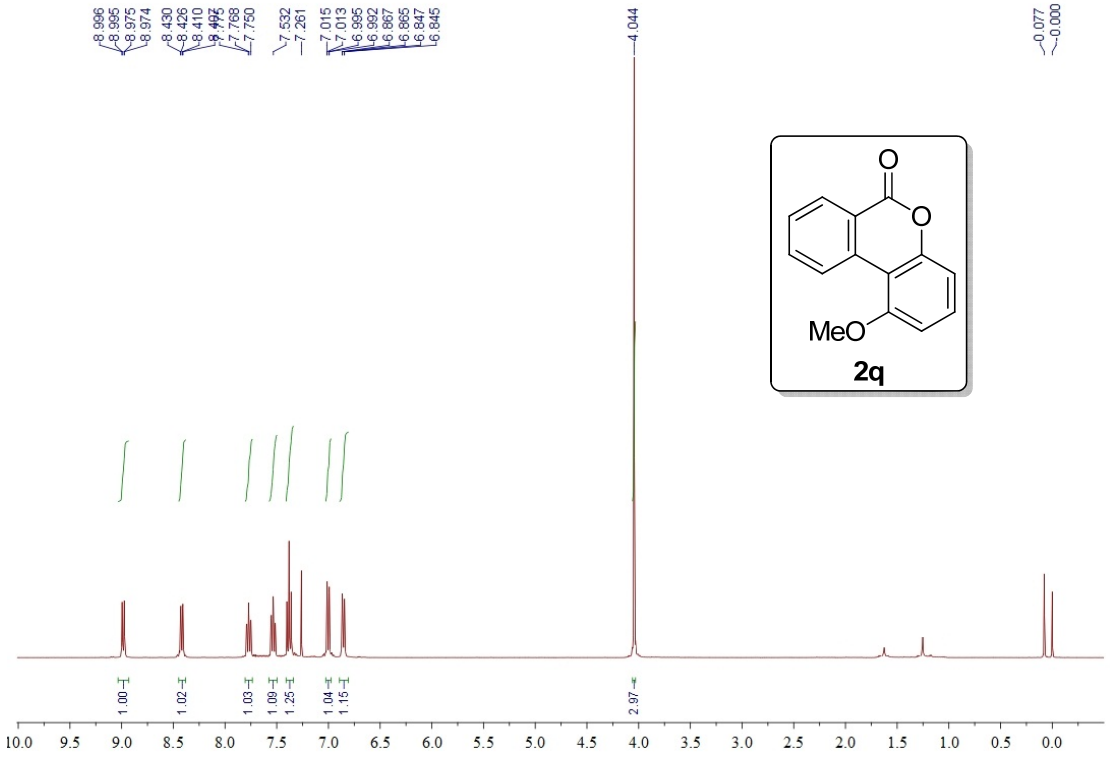
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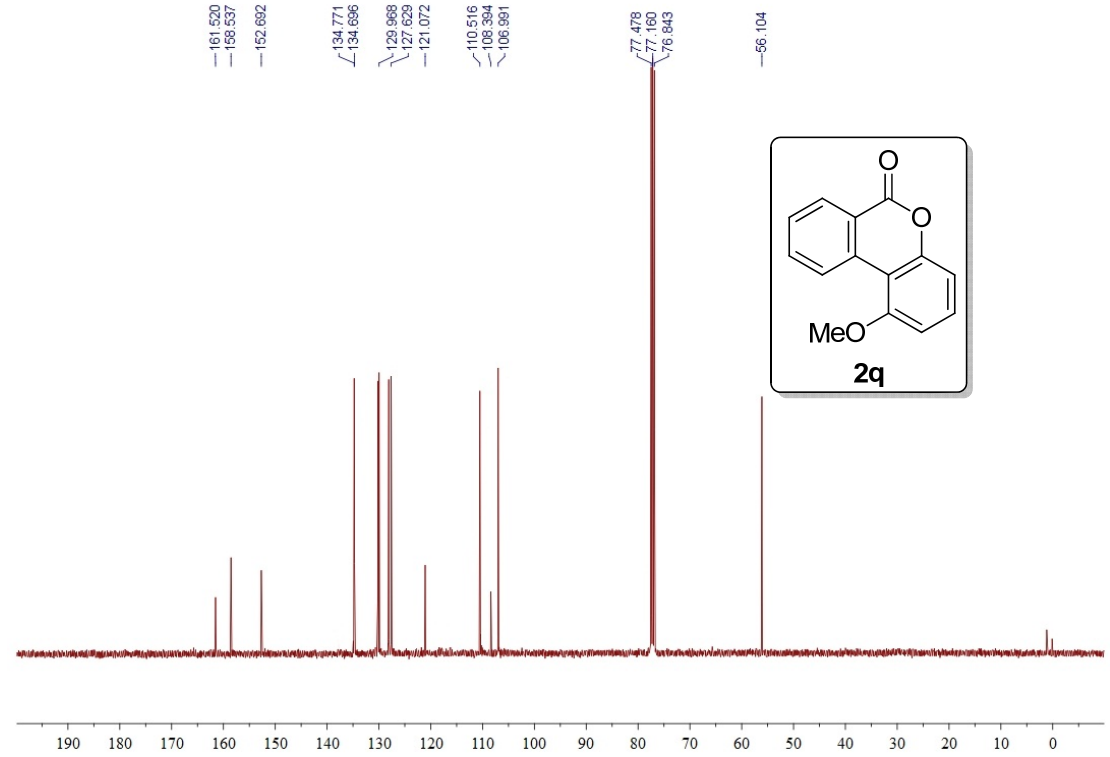
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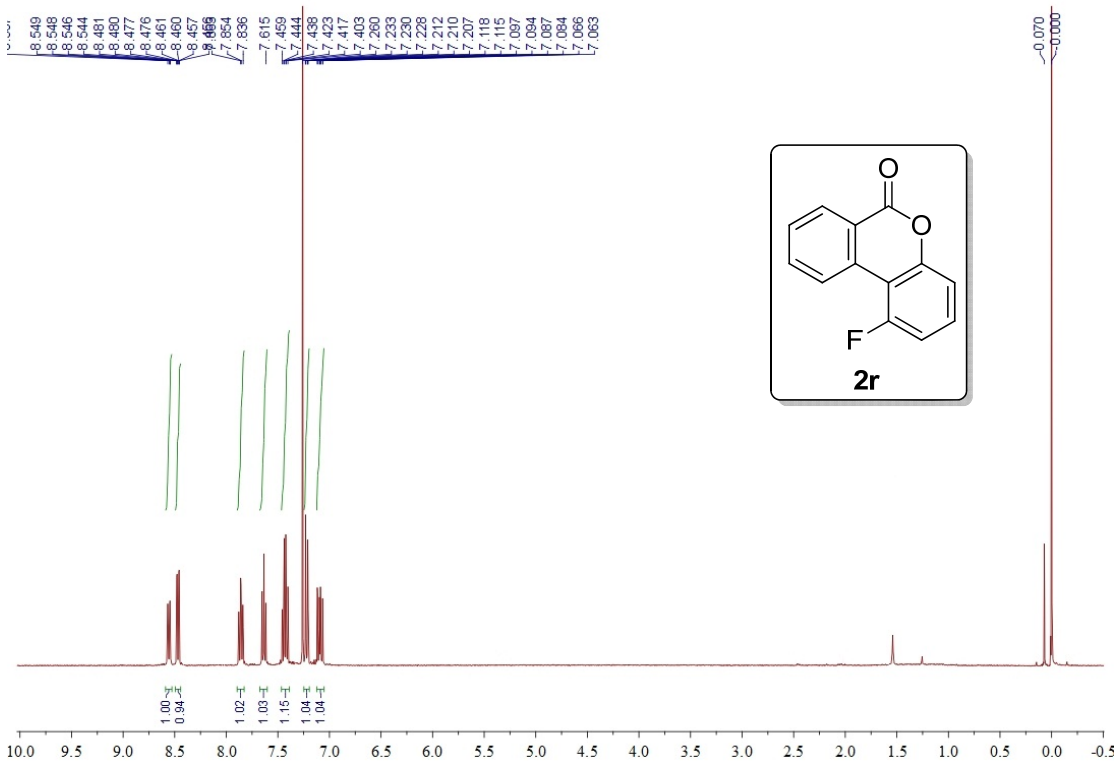
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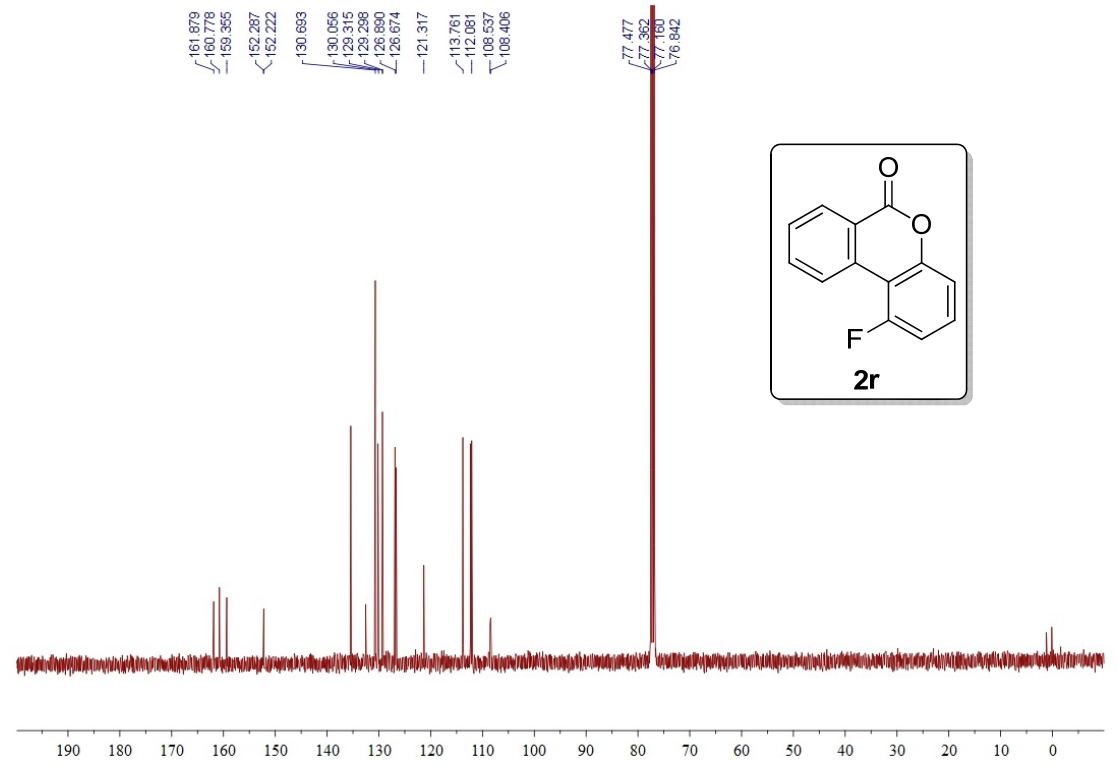
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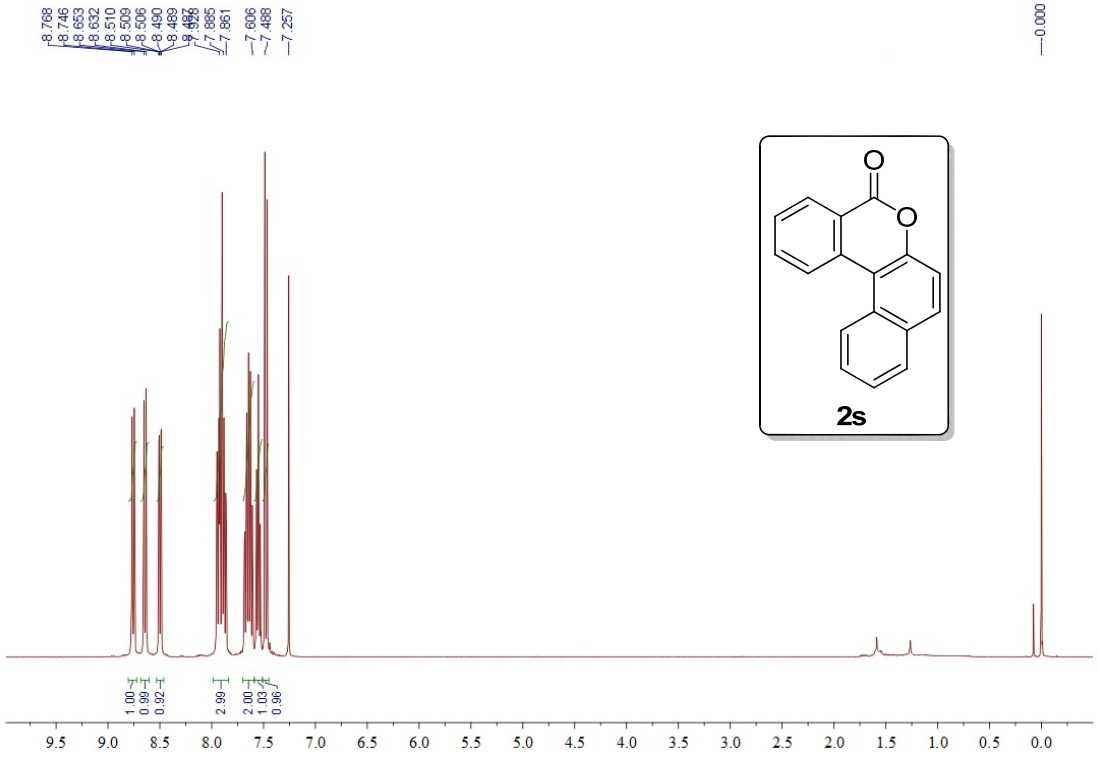
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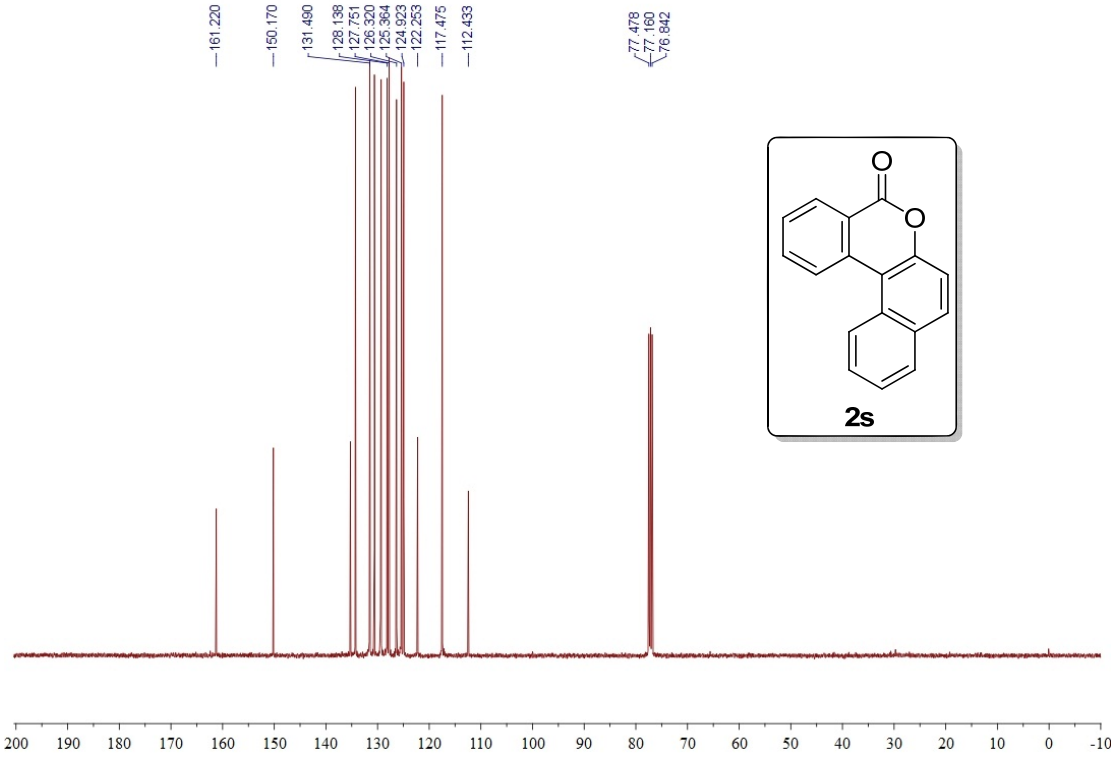
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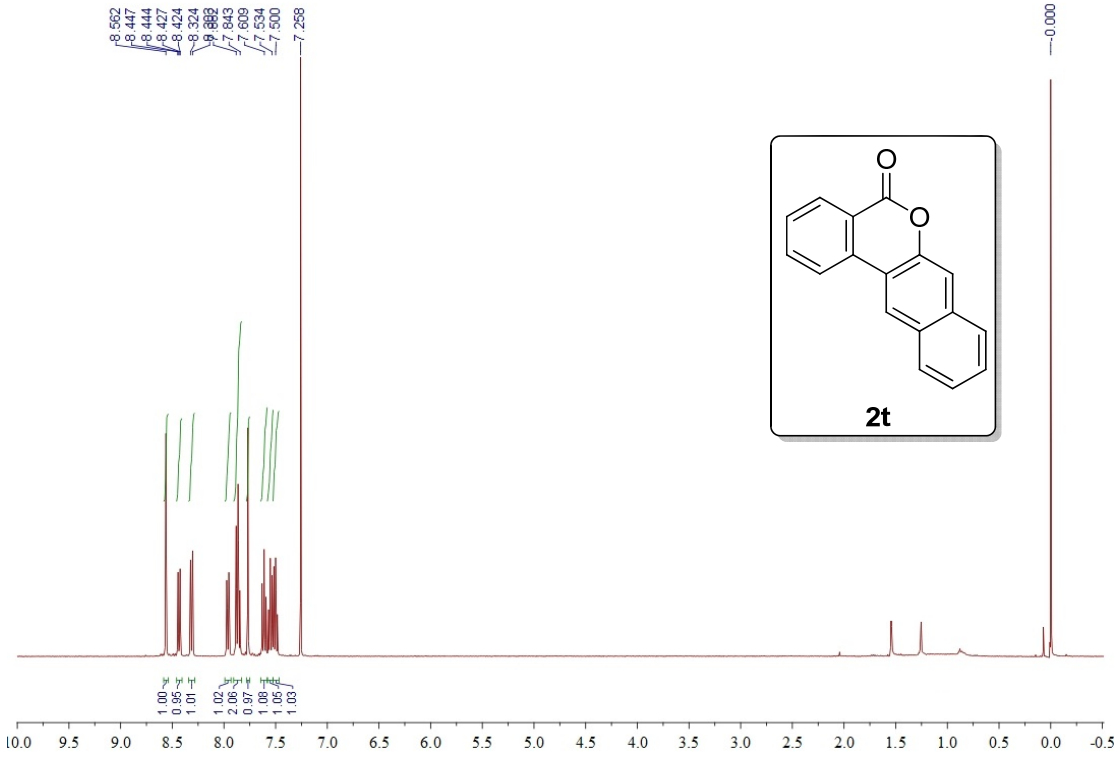
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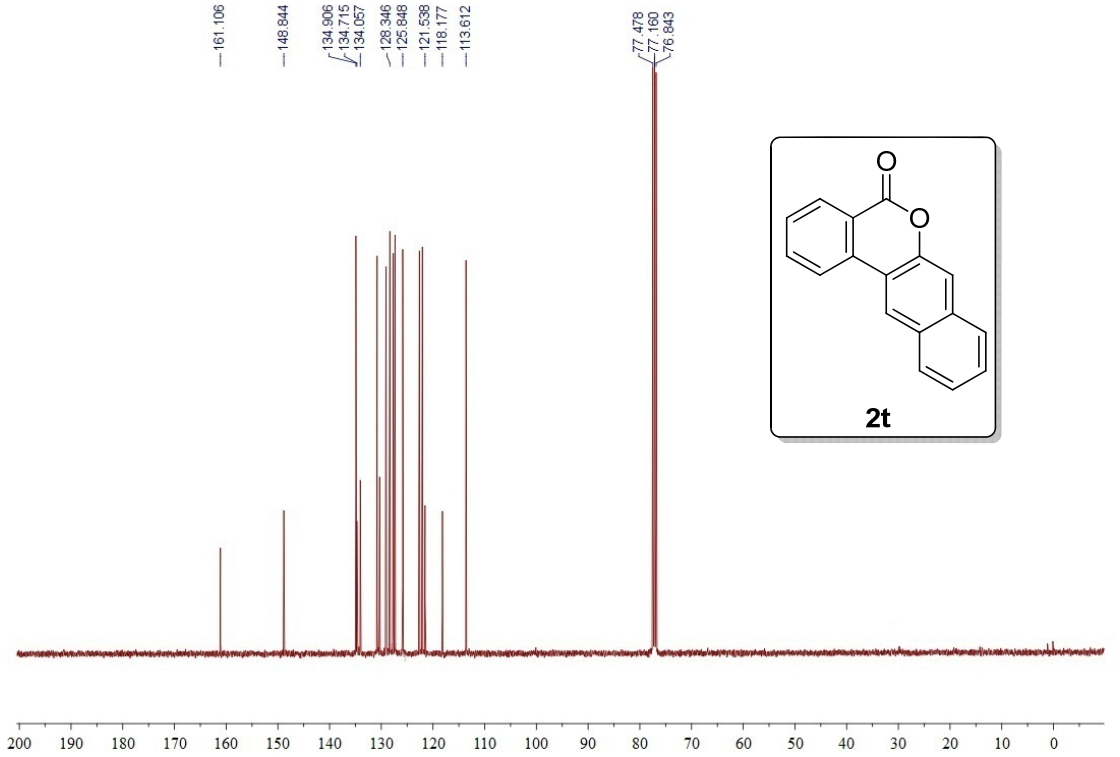
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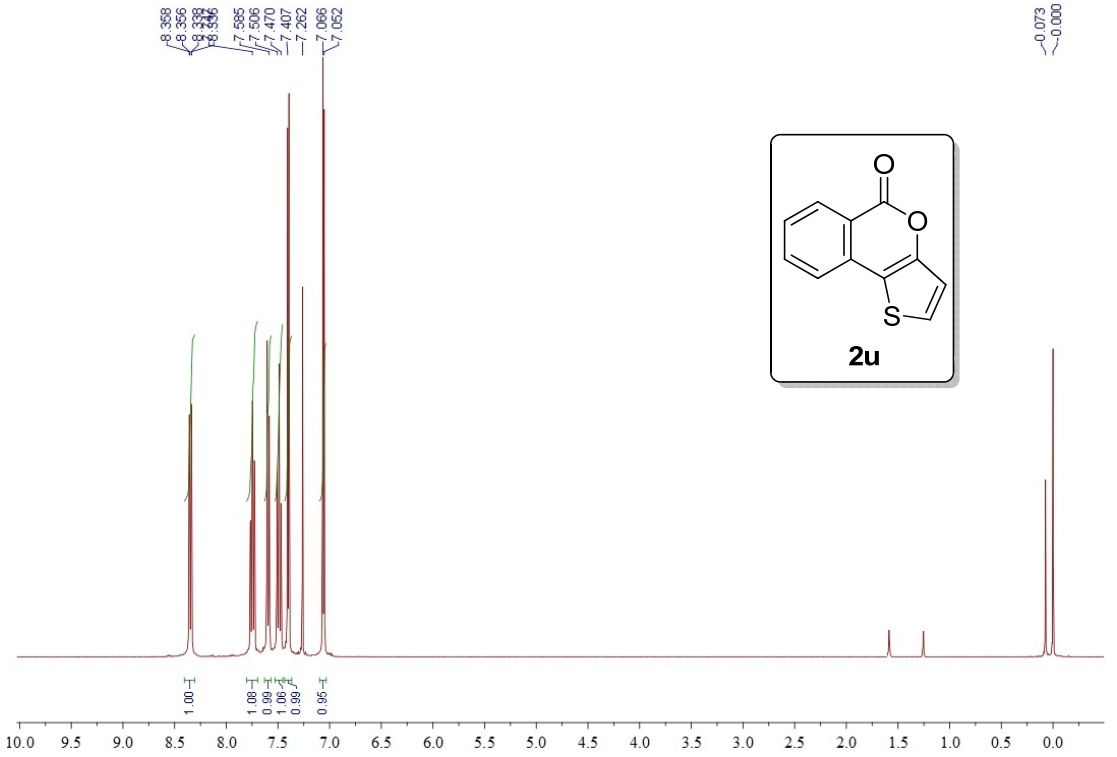
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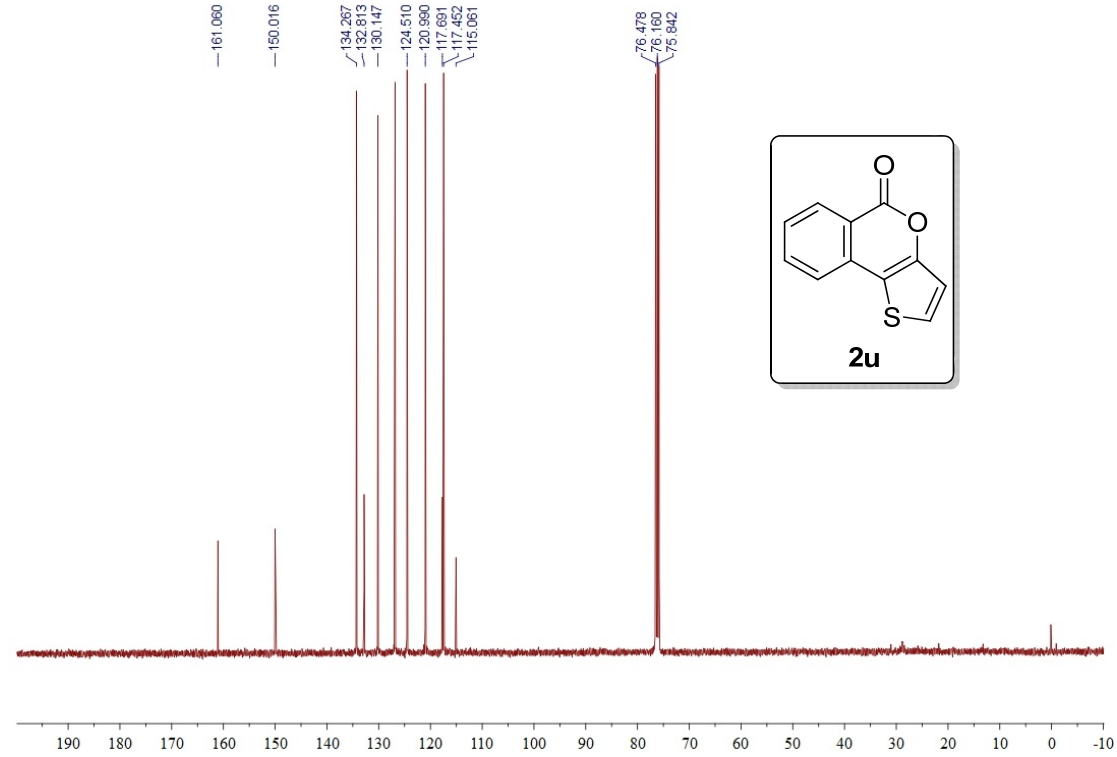
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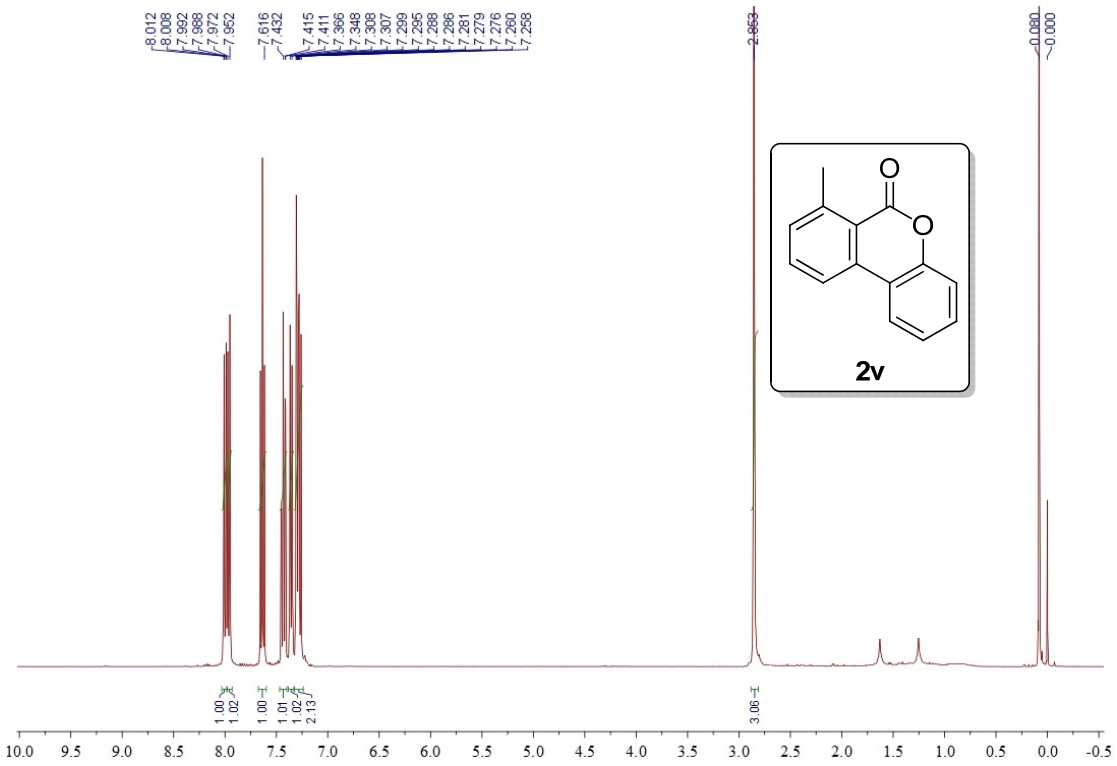
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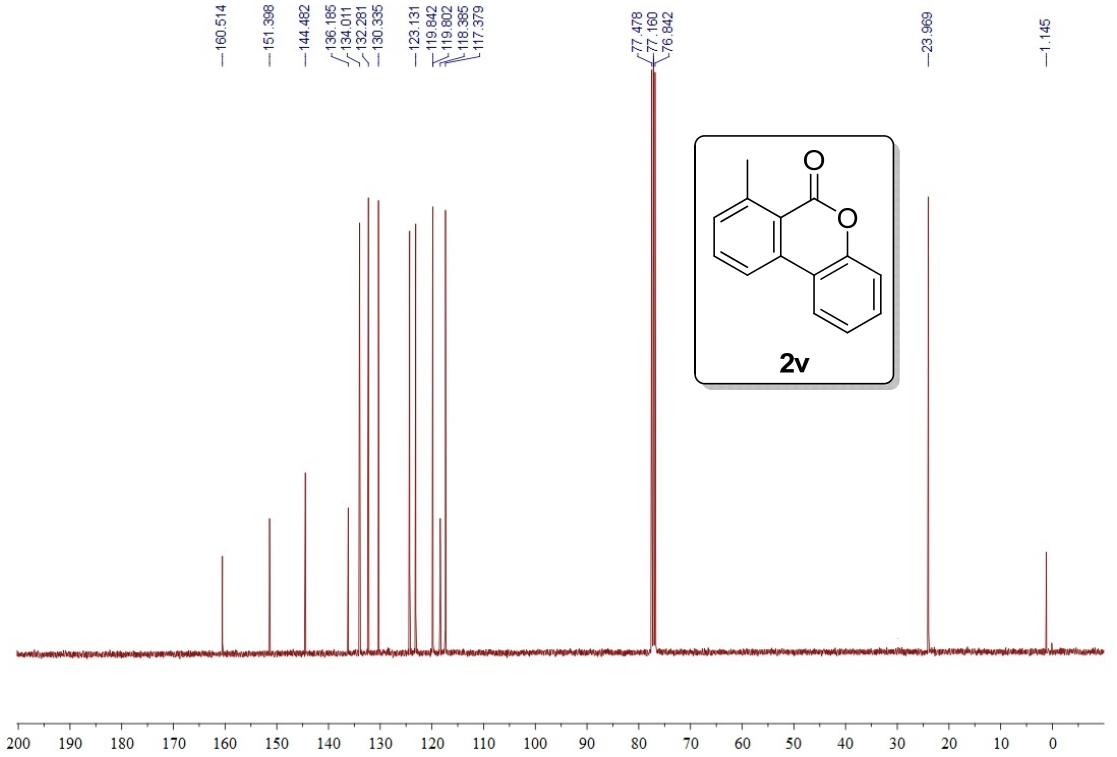
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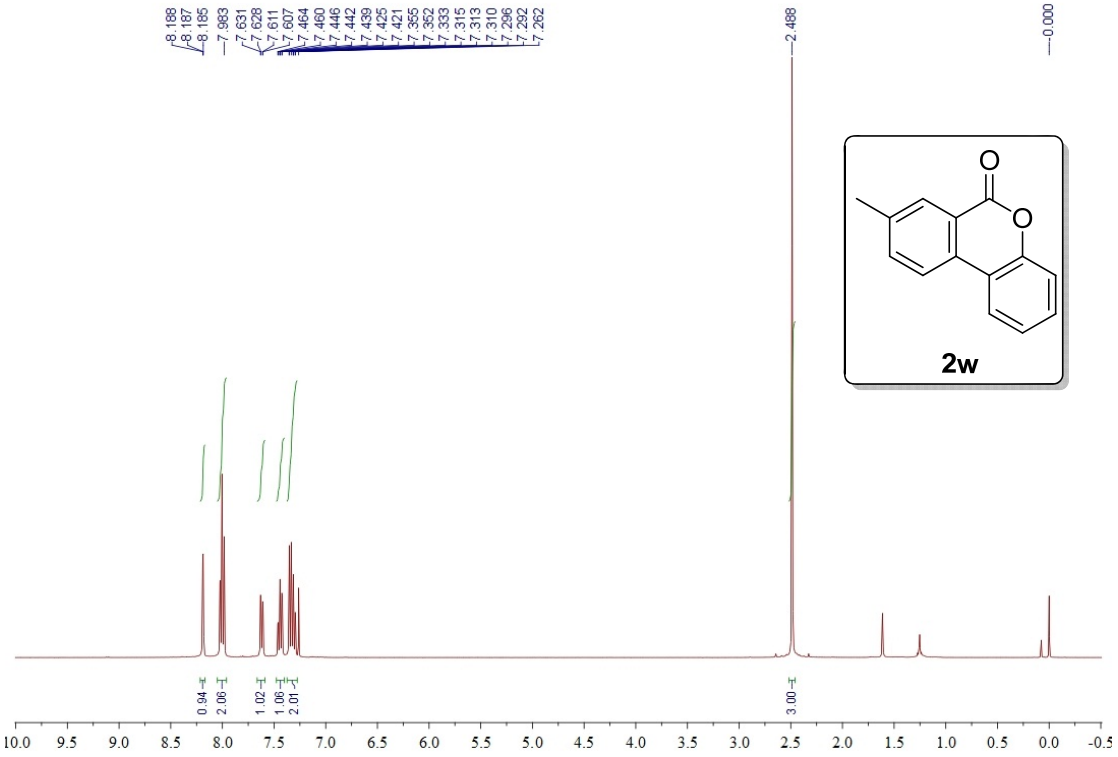
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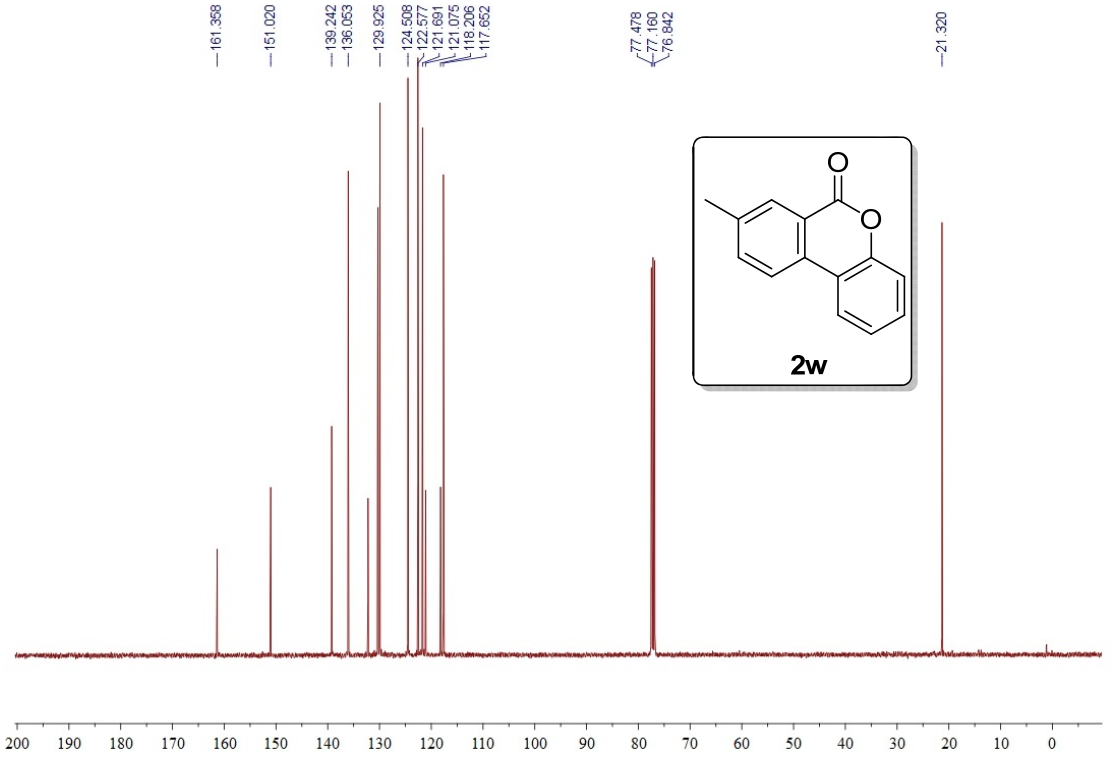
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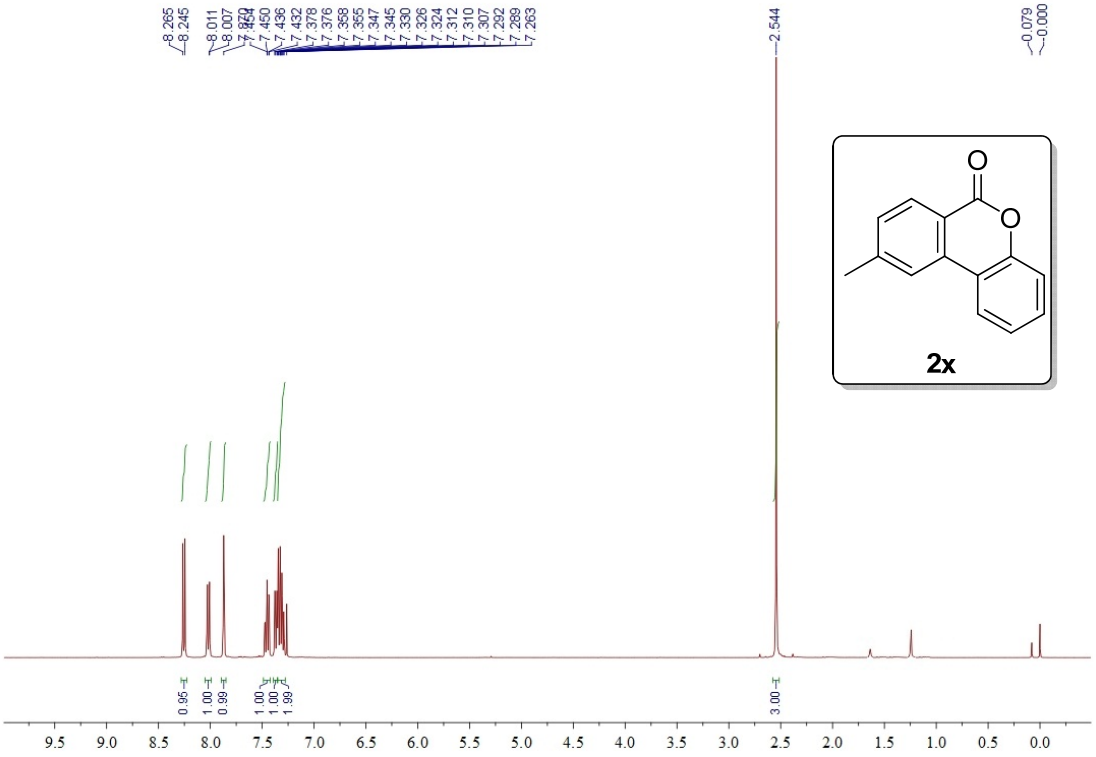
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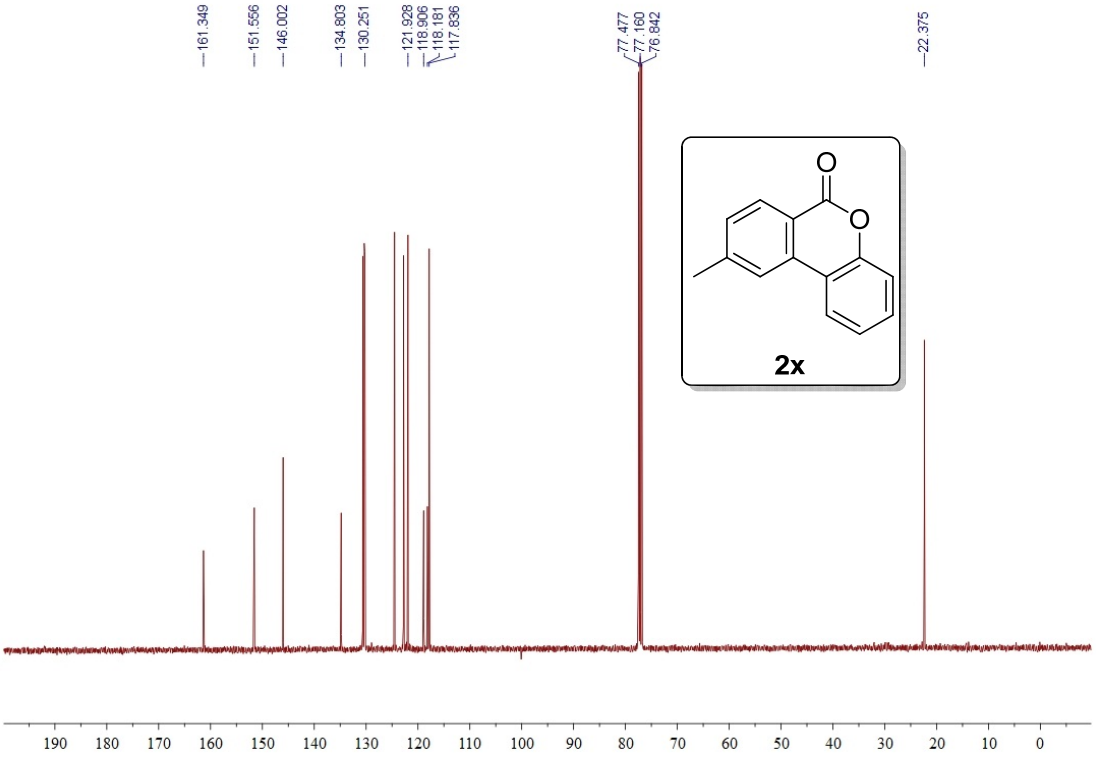
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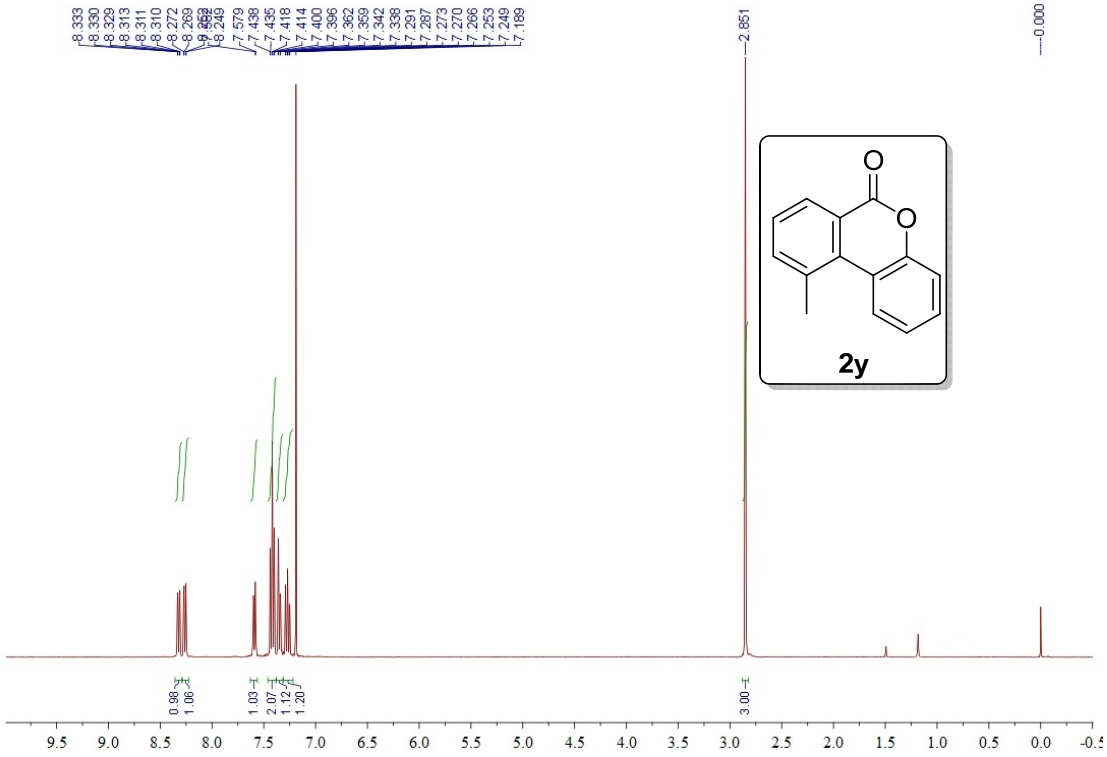
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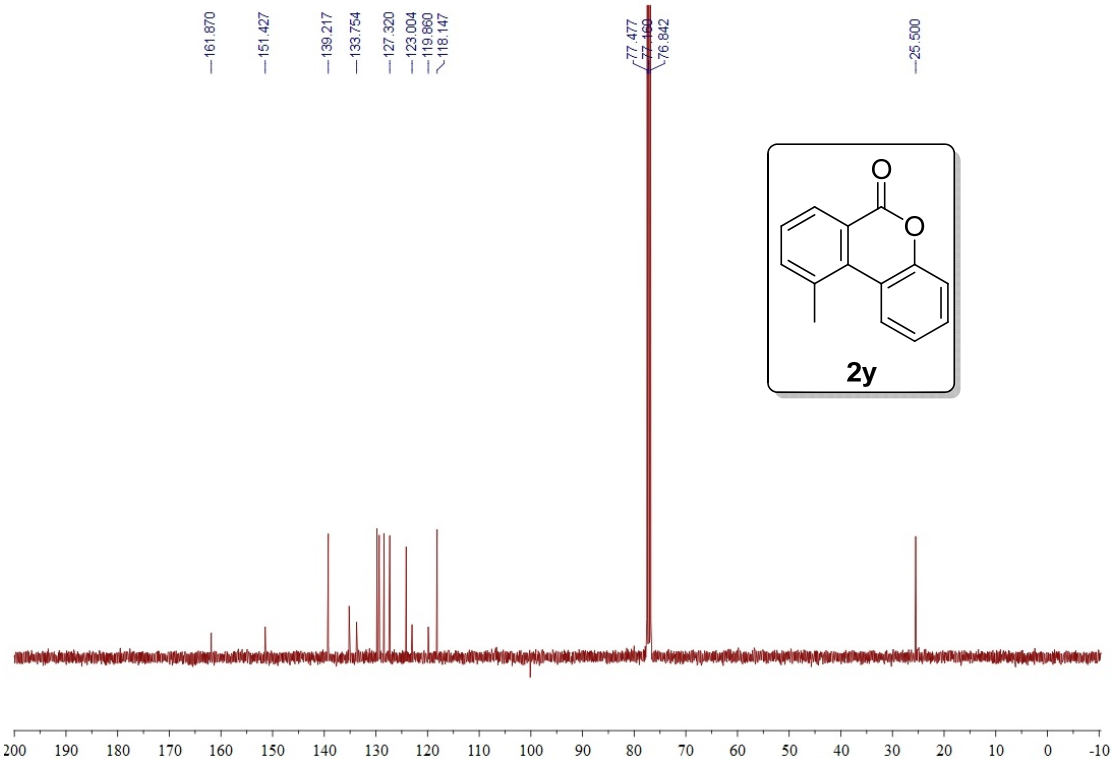
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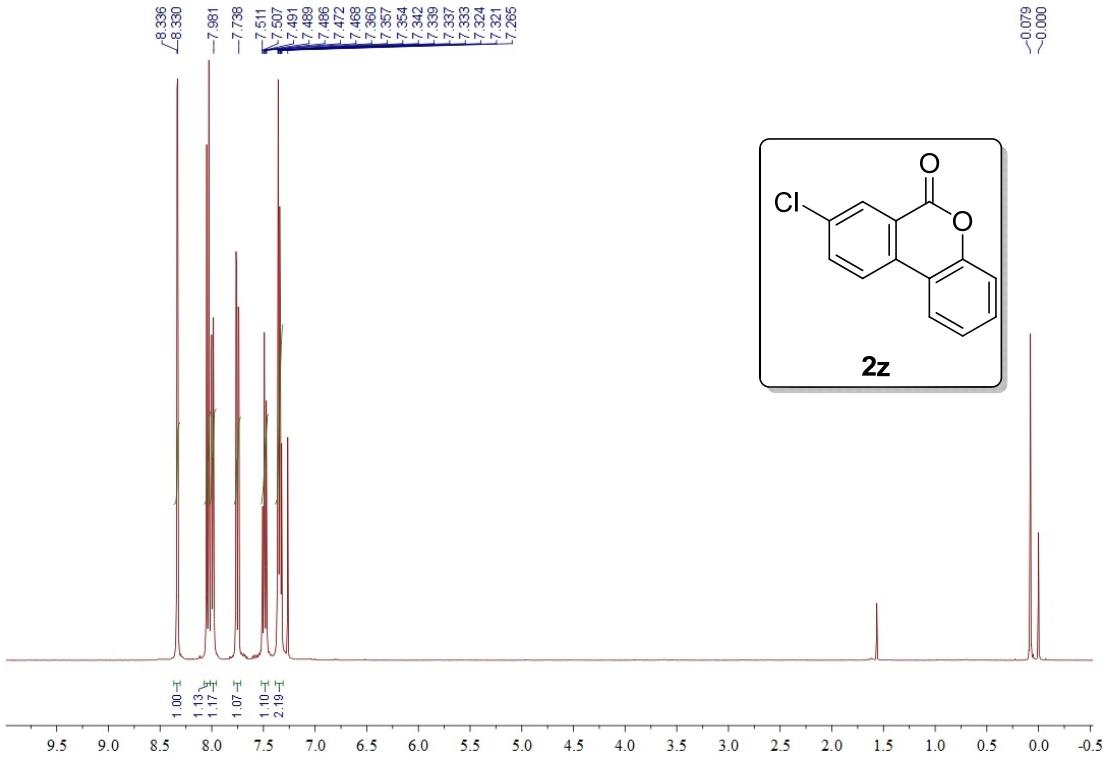
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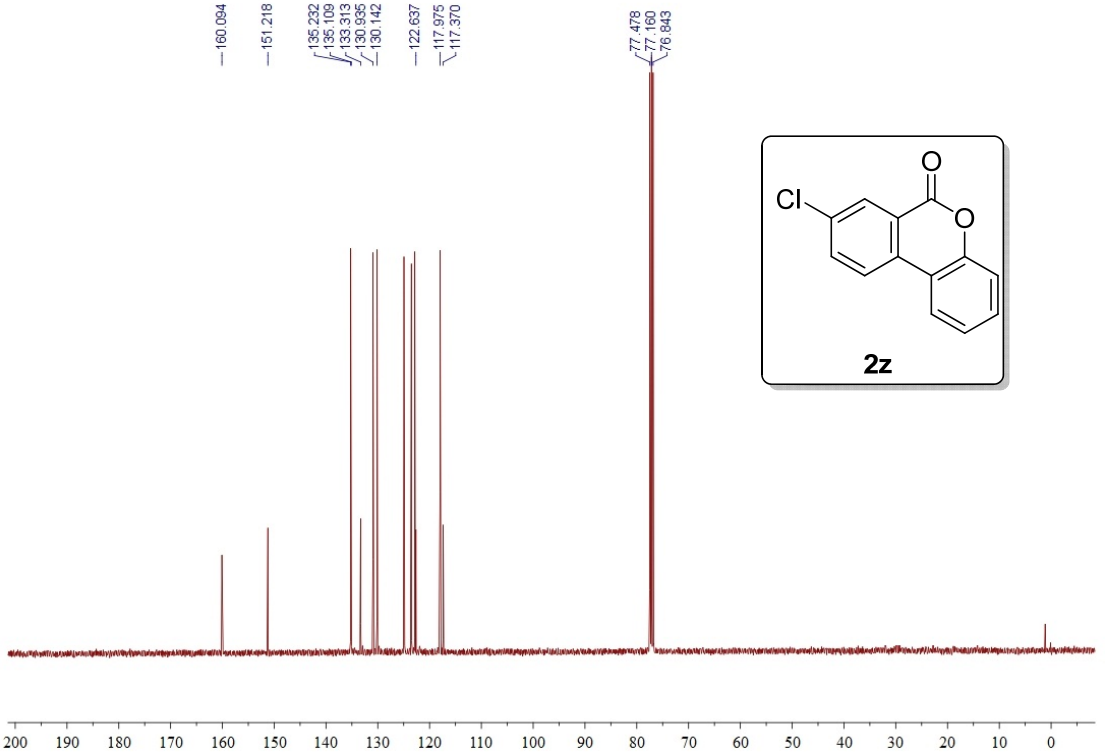
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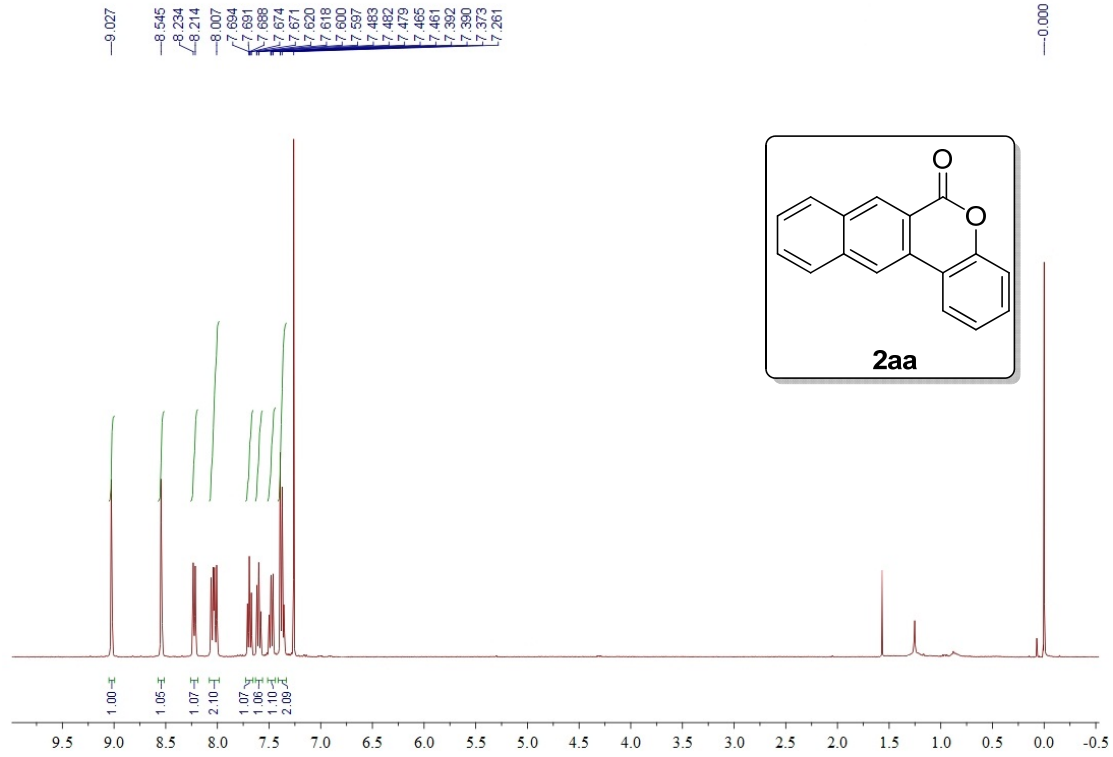
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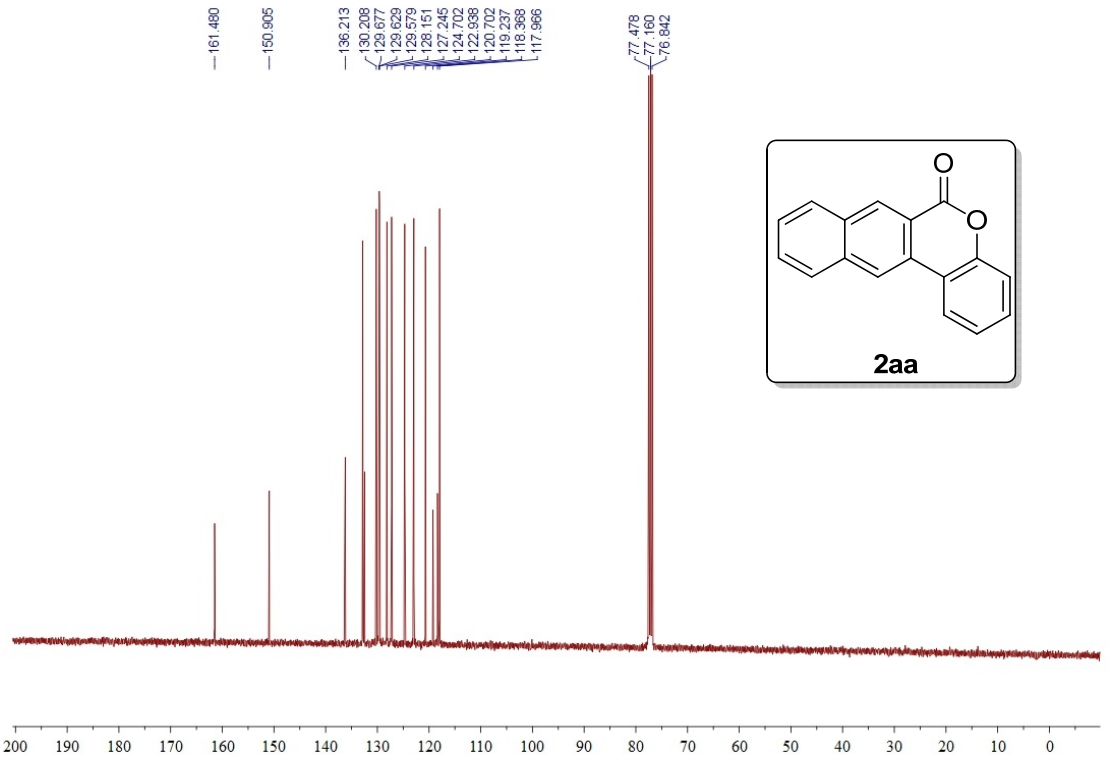
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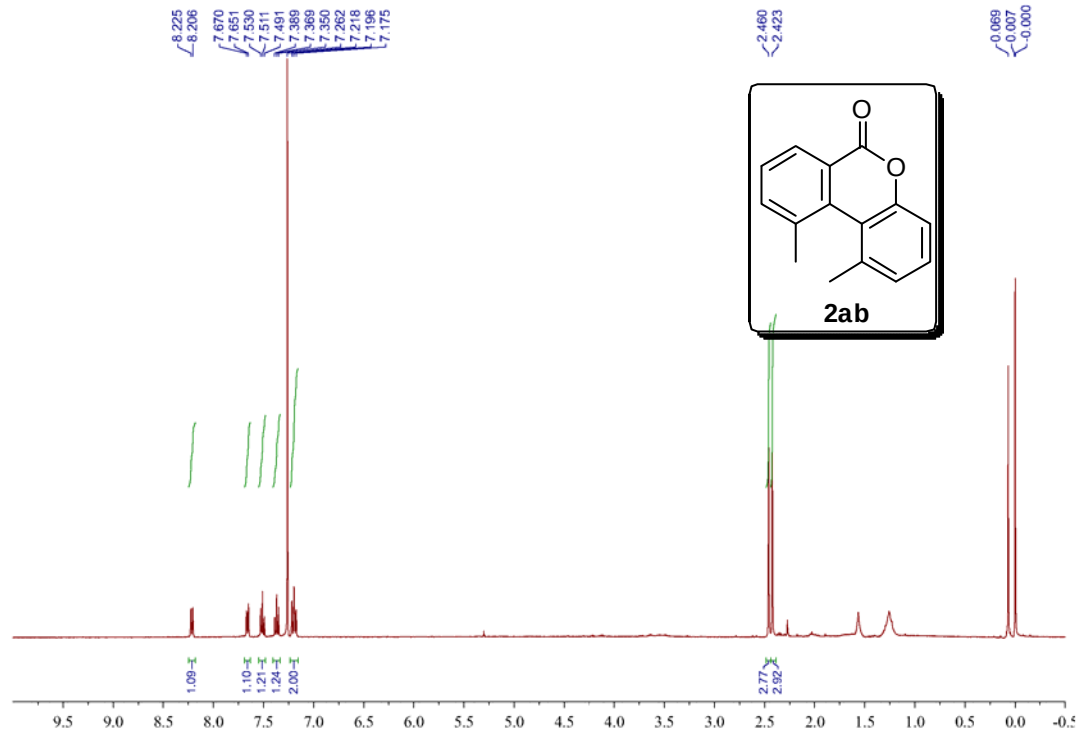
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1.24
2.00
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2.92
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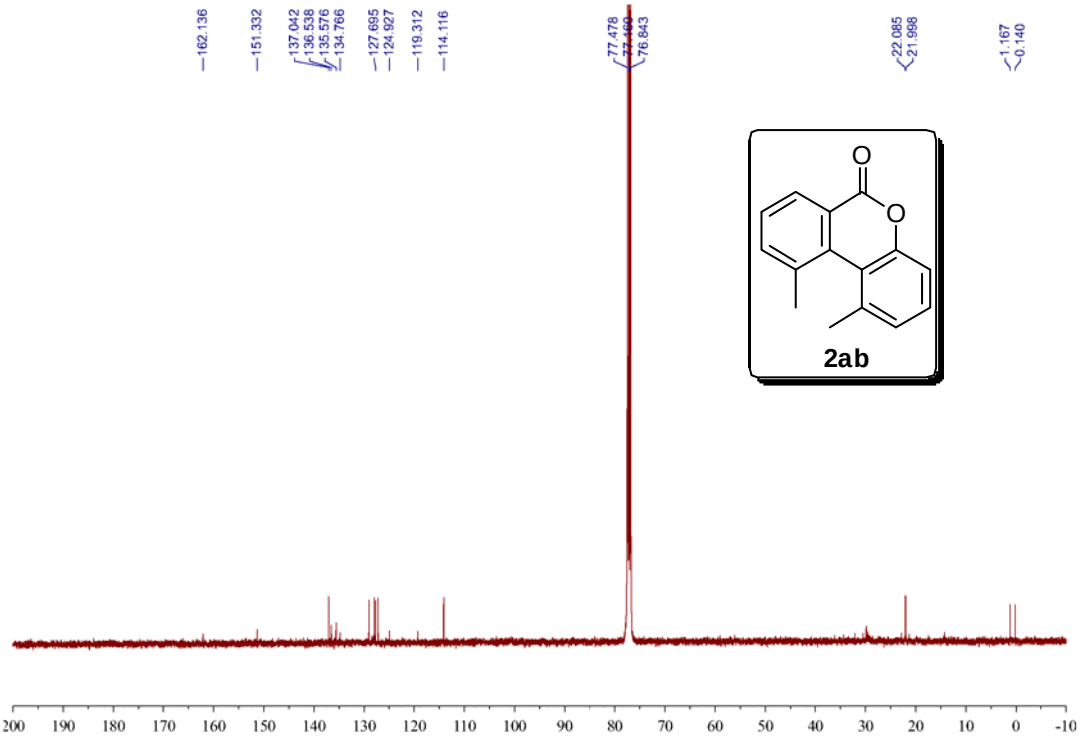
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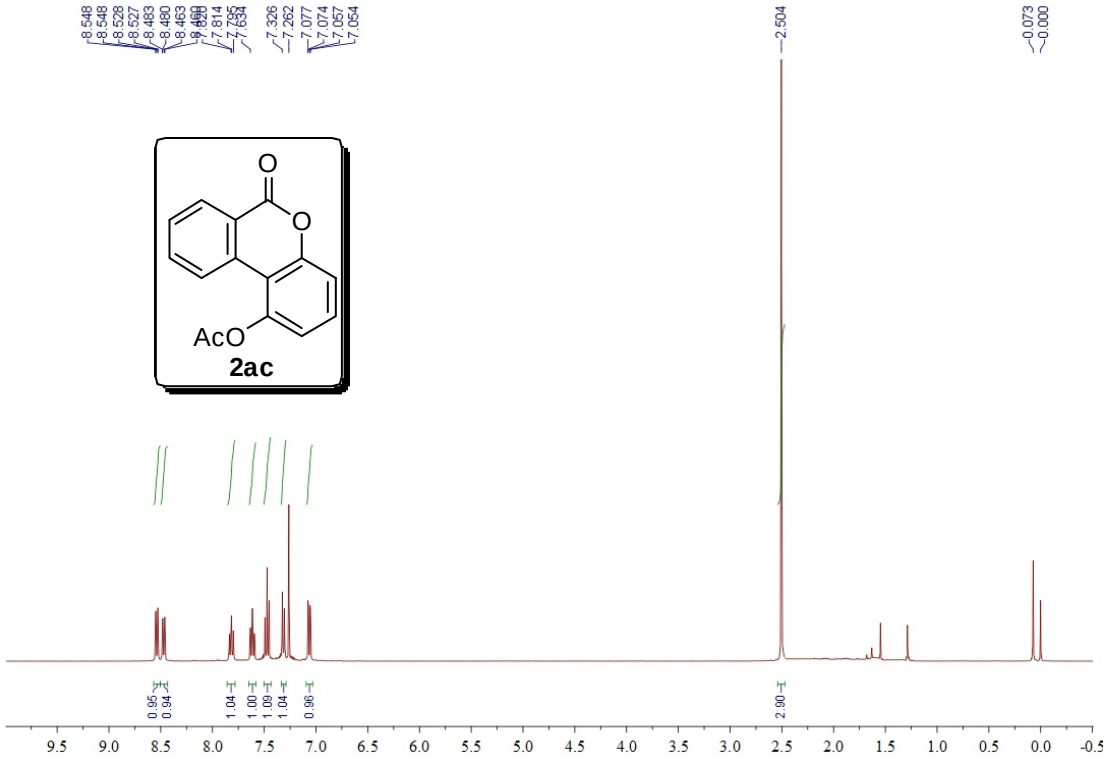
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O
AcO
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1.00
1.09
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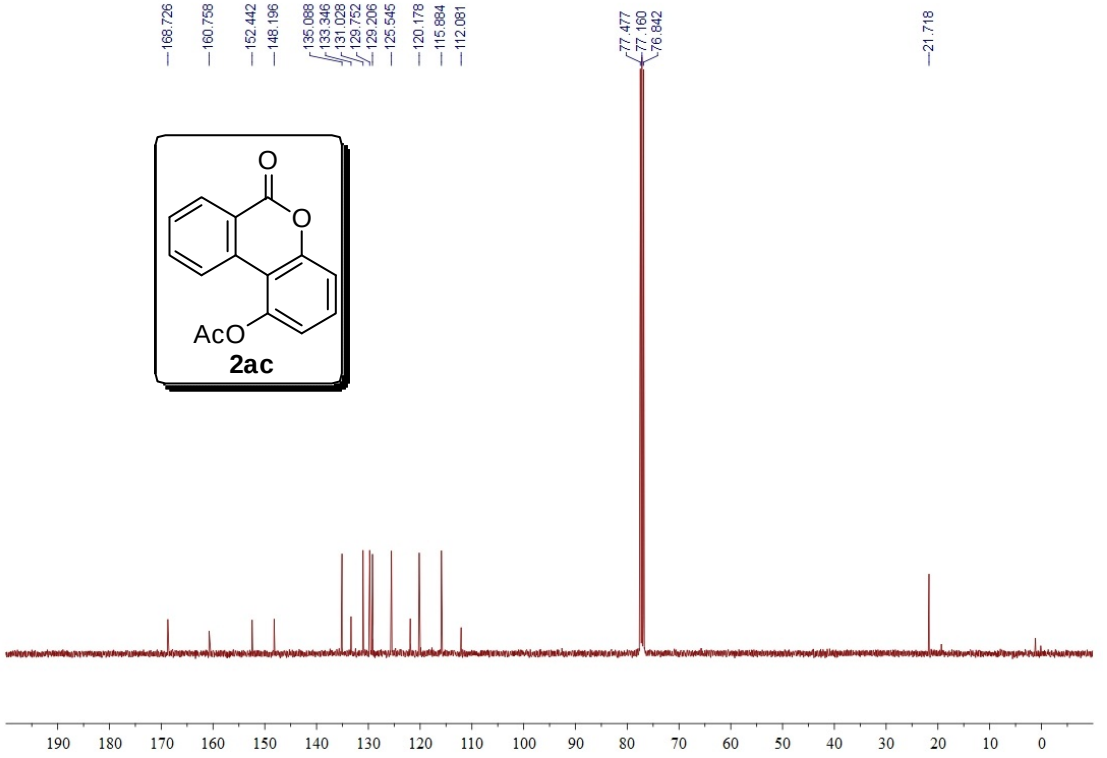
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AcO
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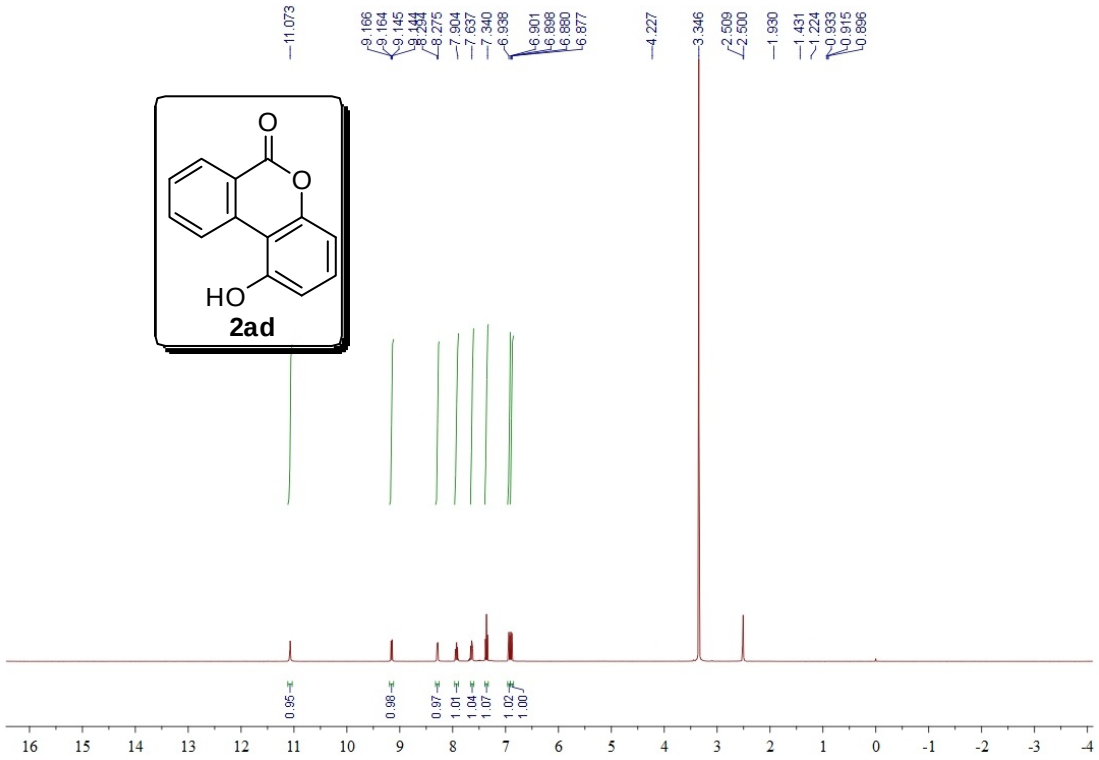
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4.227
3.346
2.509
2.500
1.990
1.431
1.224
0.933
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HO
2ad
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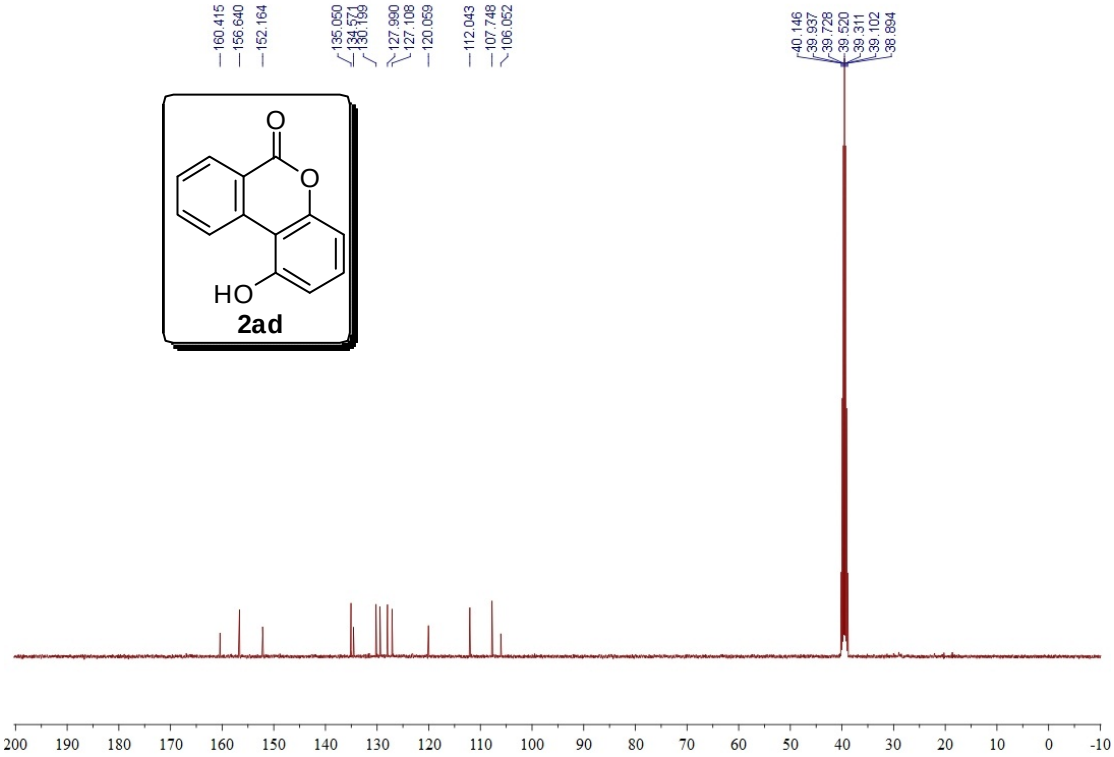
1.02
1.00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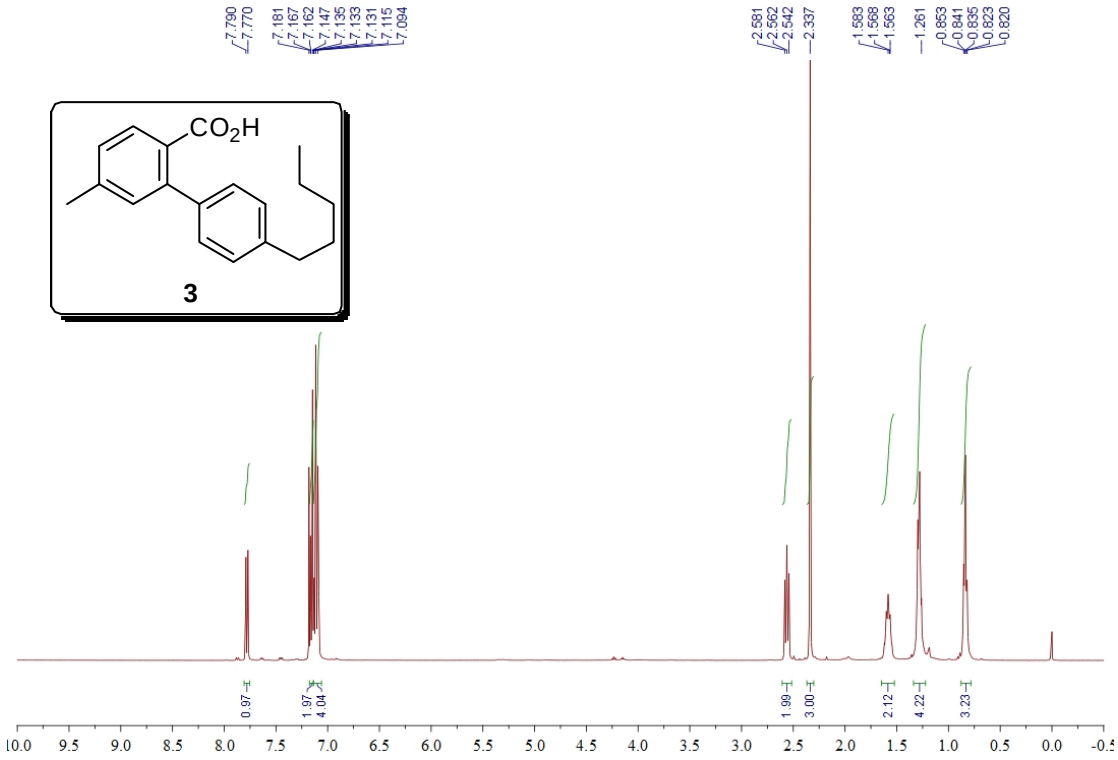
O
HO
2ad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2.337
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1.568
1.563
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0.841
0.835
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CO2H
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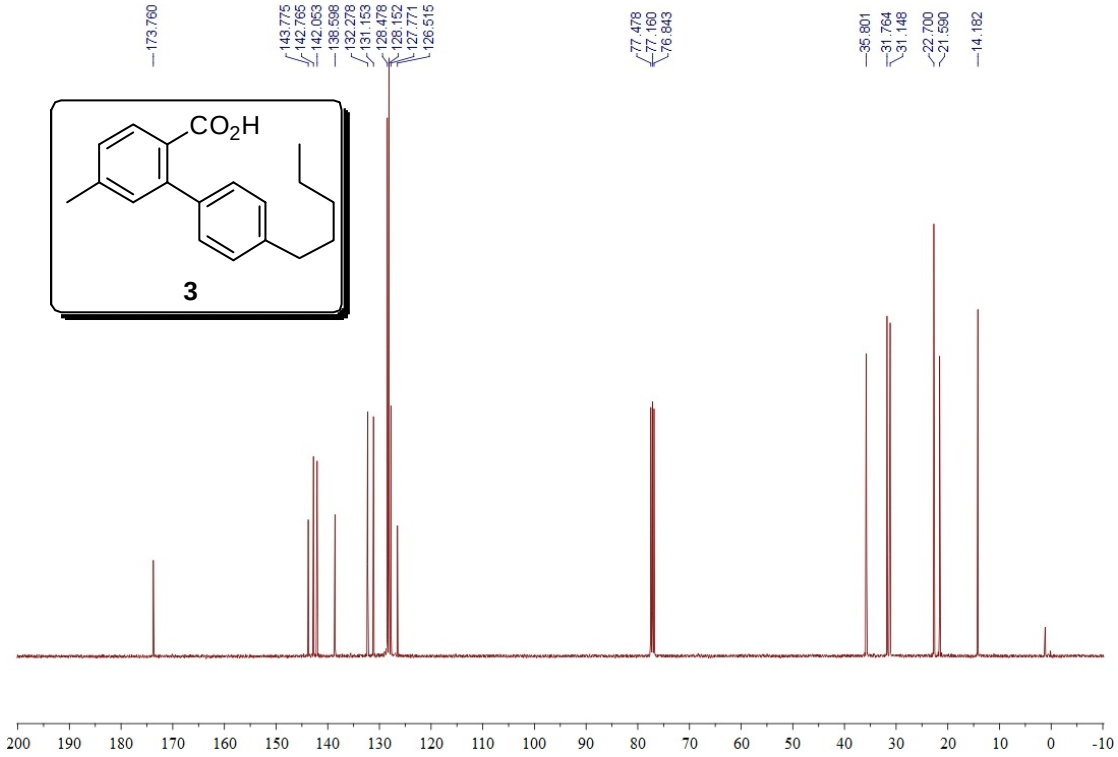
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22.700
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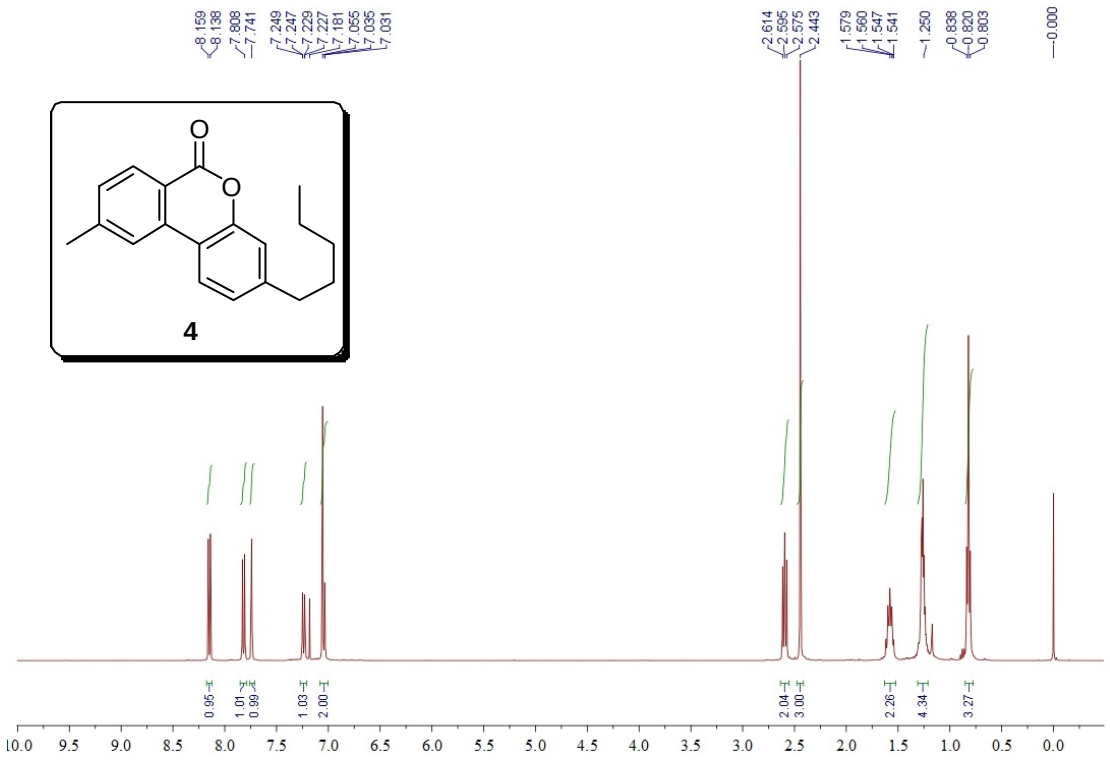
CO2H
3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O
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1.01
0.99
1.03
2.00
2.04
3.00
2.26
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3.27
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8.5
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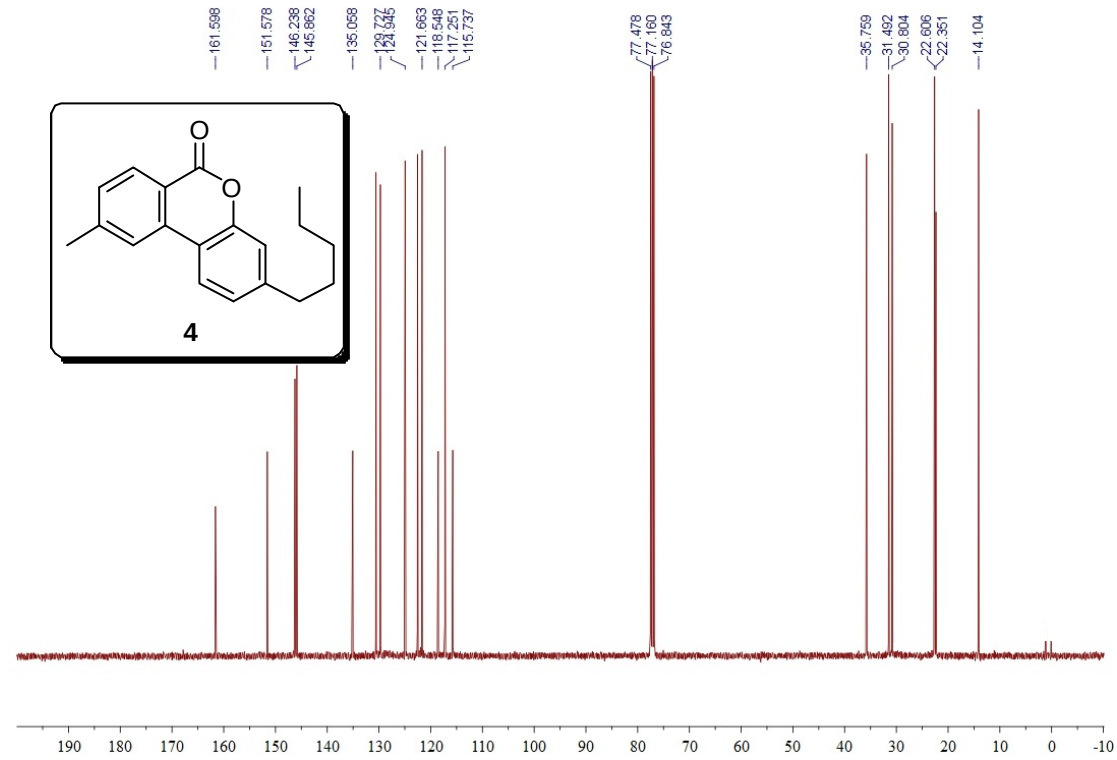
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77.160
76.843
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22.351
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O
O
4
190
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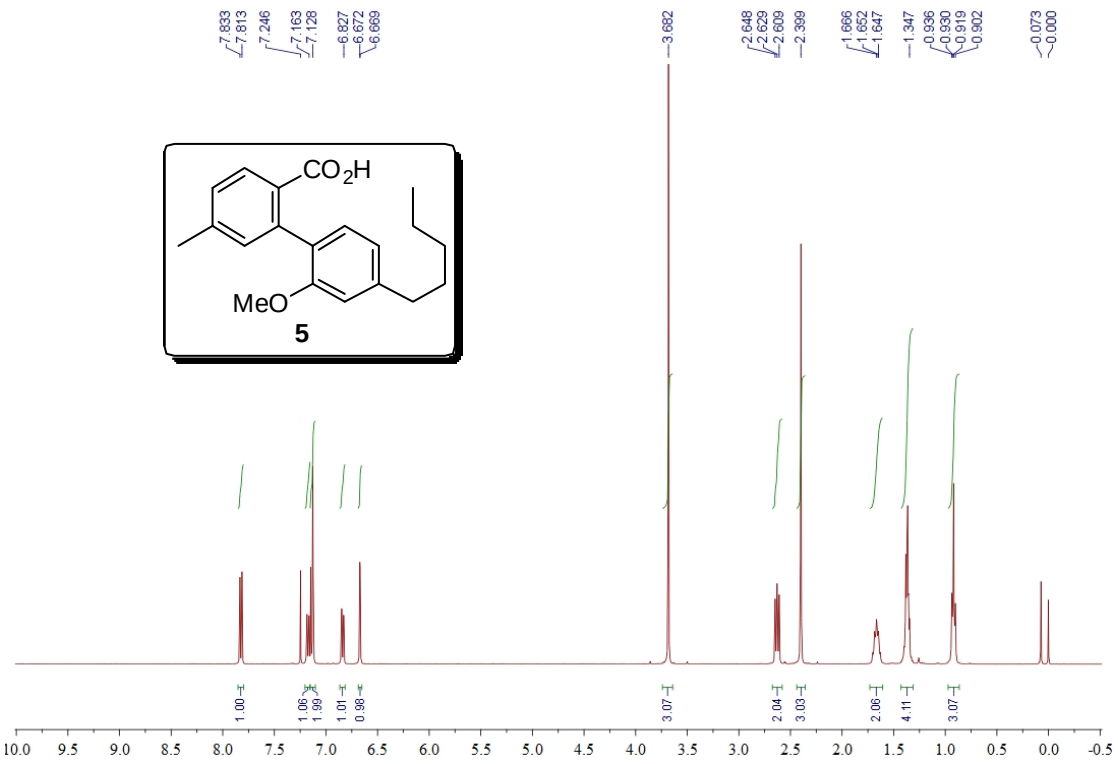
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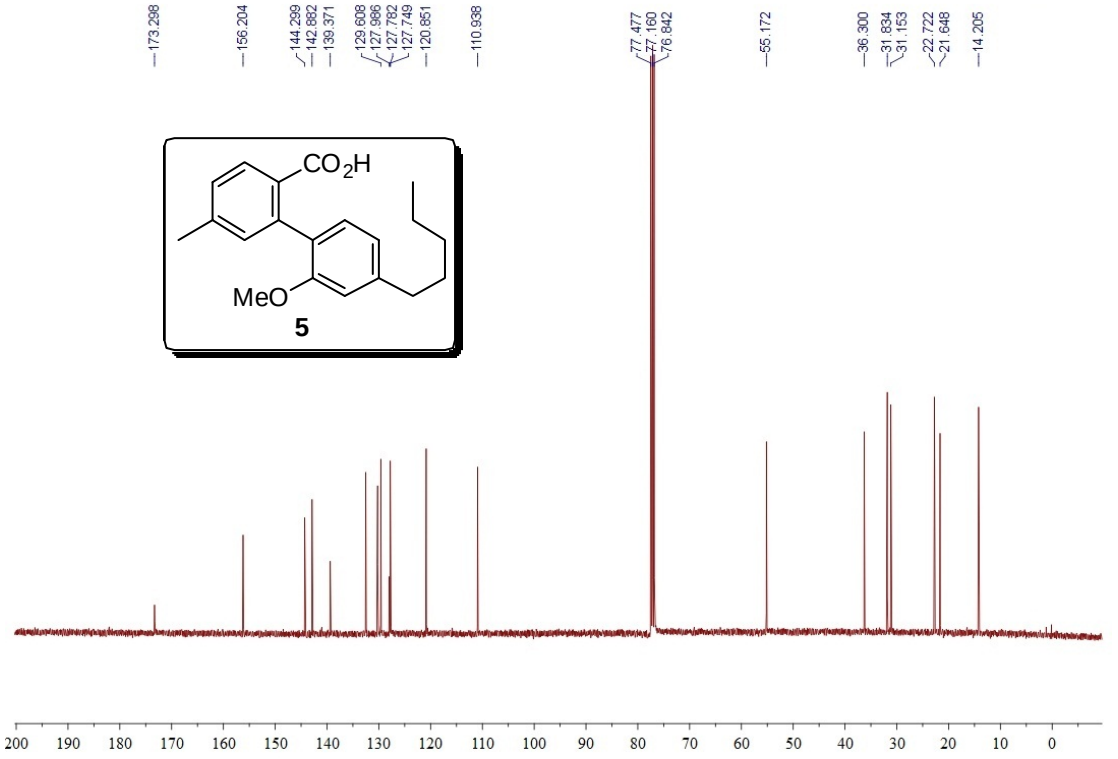
0.919
0.902
0.073
0.000
CO2H
MeO
5
1.00
1.06
1.99
1.01
0.98
3.07
2.04
3.03
2.06
4.11
3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5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55.172
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CO2H
MeO
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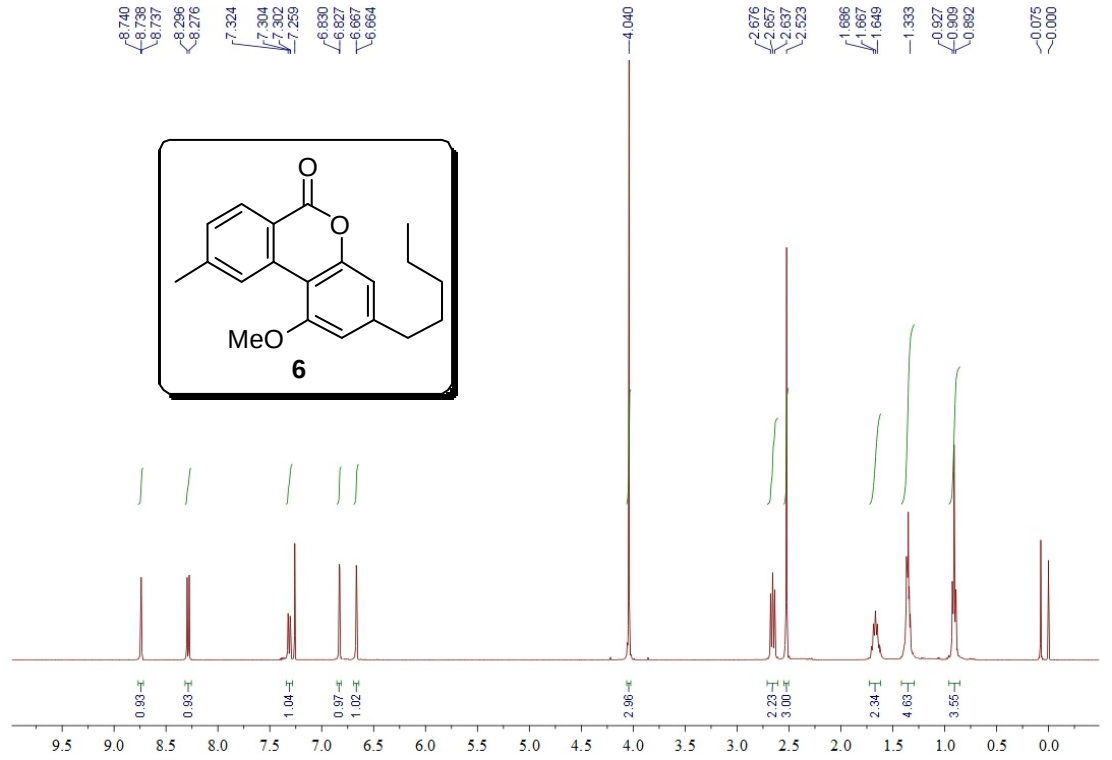
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O
O
MeO
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0.93
1.04
0.97
1.02
2.96
2.23
3.00
2.34
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3.55
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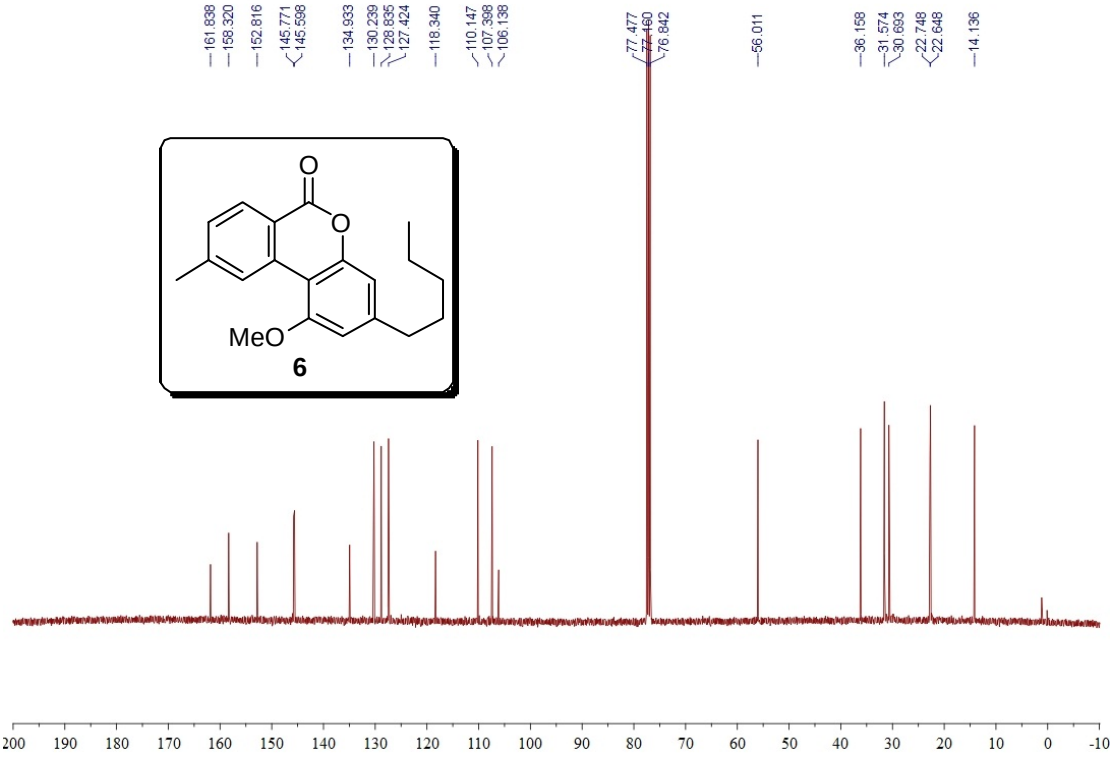
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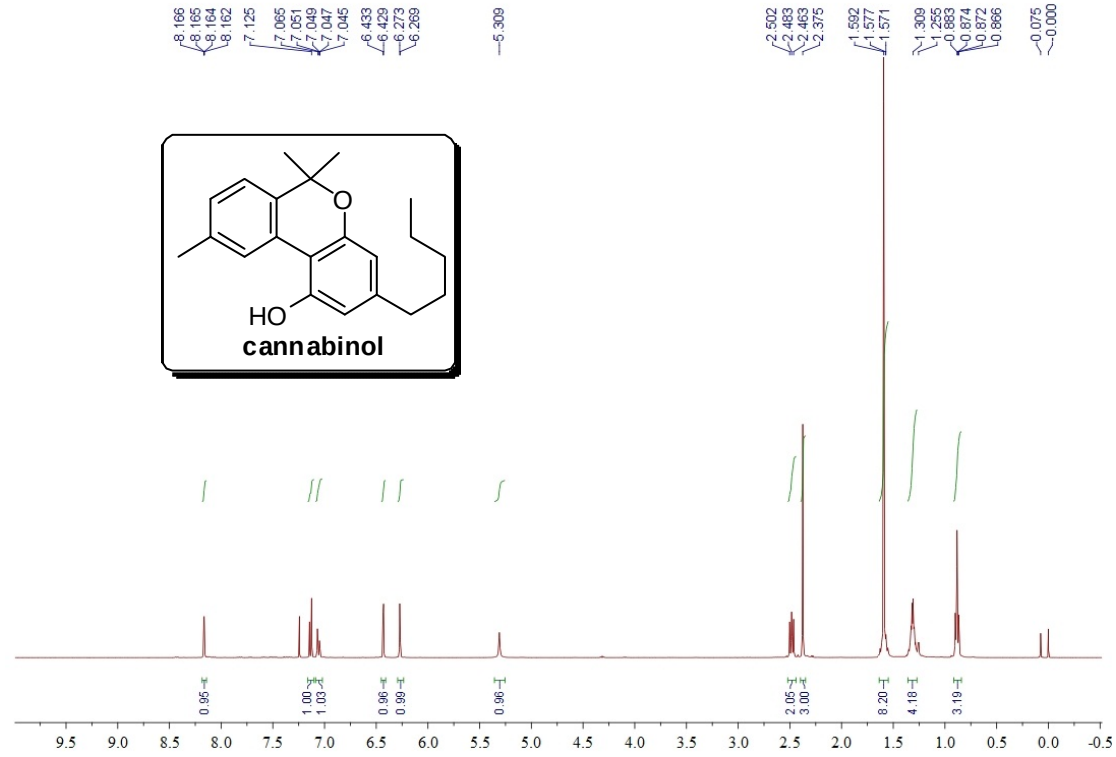
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HO
cannabinol
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1.00
1.03
0.96
0.99
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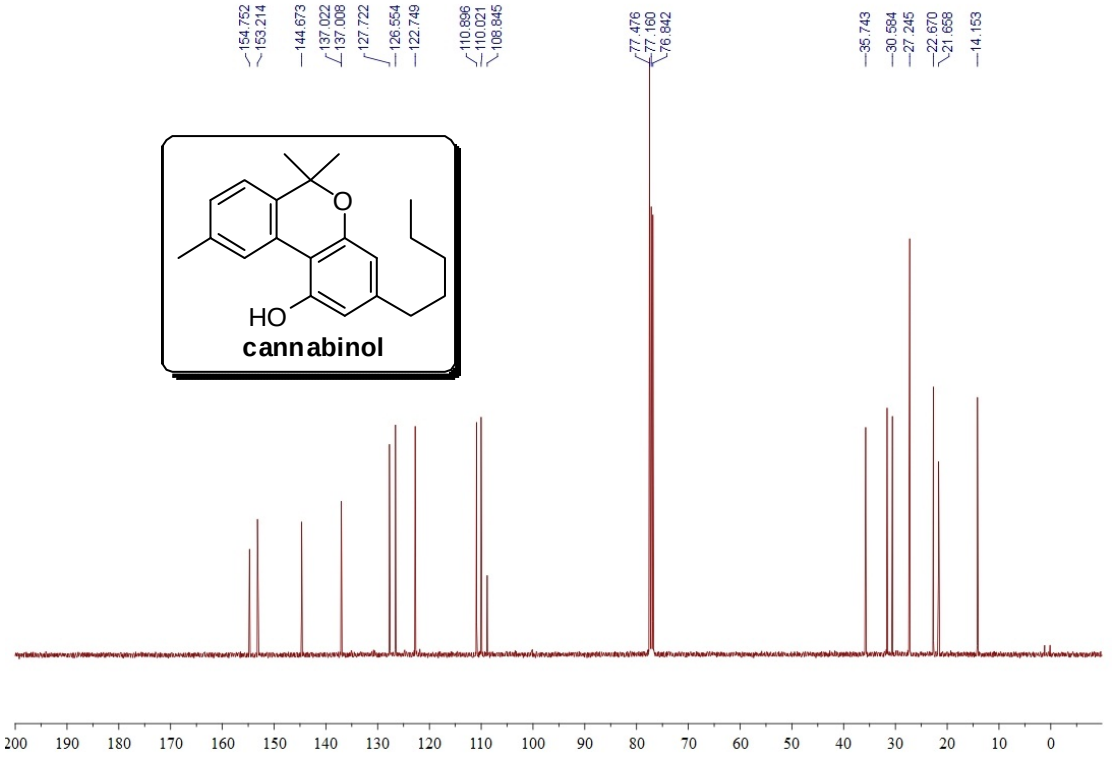
2.05
3.00
8.20
4.18
3.19
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5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14.153
HO
cannabinol
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0