

Ligand-Enabled Pd(II)-Catalyzed C(sp³)-H Lactonization using Molecular oxygen as oxidant

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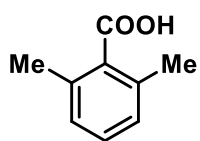
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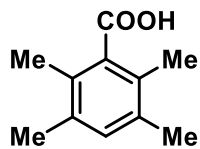
General information

Substrates were obtained from commercial sources or synthesized following literature procedures. Solvents were obtained from Sigma-Aldrich, Alfa-Aesar and Acros and used directly without further purification. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light. ^1H NMR was recorded on Bruker DRX-600 instrument (600 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to 0.0 ppm for tetramethylsilane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q =quartet, m = multiplet, br = broad. Coupling constants, J, were reported in Hertz (Hz). ^{13}C NMR spectra were recorded on Bruker DRX-600 instrument (150 MHz), and were fully decoupled by broadband proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.16 ppm of chloroform-d. High-resolution mass spectra (HRMS) were recorded on a Waters mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

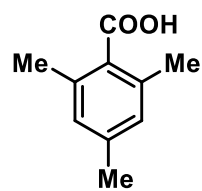
Substrate structure



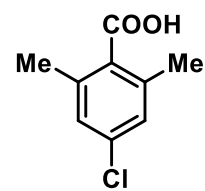
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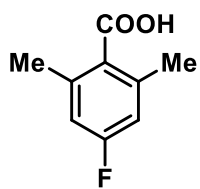
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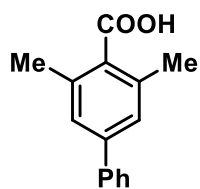
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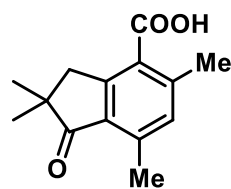
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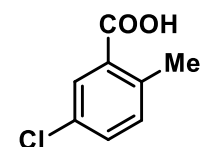
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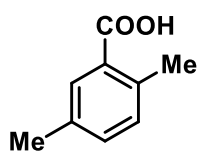
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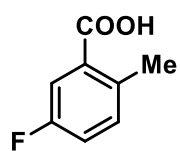
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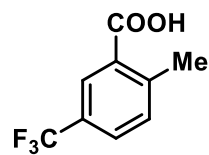
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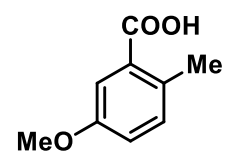
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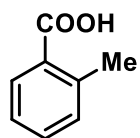
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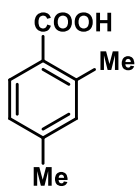
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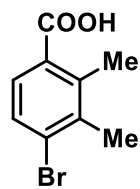
1l



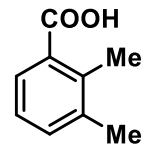
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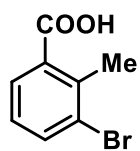
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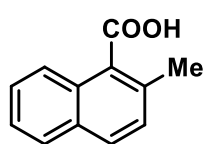
1o



1p



1q



1r

Experimental procedure

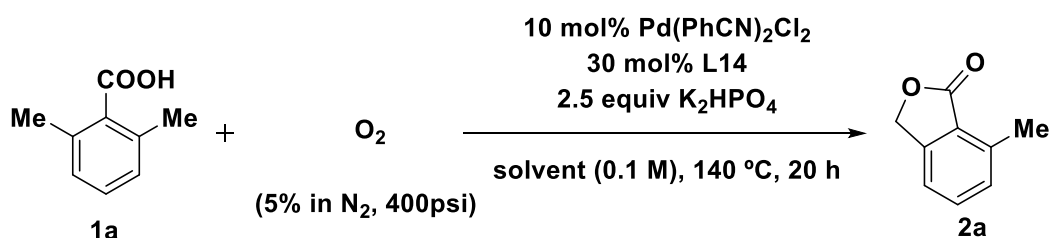
Substrate preparation

Substrate **1a-1e,1h-1r** are commercially available. Substrate **1g** is from the BMS compound collection. Substrate **1f** was prepared with the following procedure:

3,5-dimethyl-[1,1'-biphenyl]-4-carboxylic acid (**1f**): A mixture of 4-bromo-2,6-dimethylbenzoic acid (2.0 mmol), phenyl boronic acid (3.0 mmol) sodium bicarbonate (4 mL, 1 M), dioxane (20 mL) and palladium tetrakis(triphenylphosphine) (0.05 mmol) was heated at 100 °C for 12 hours. After cooled to room temperature, the mixture was filtered through celite and concentrated under reduced pressure. The crude product was then purified by chromatography to give the title compounds. Analytical data matched that reported in the literature¹.

Reaction condition optimization

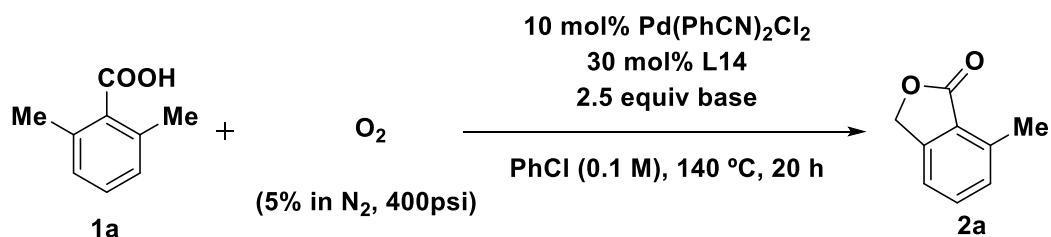
Table S1. Solvent investigation for Pd(II)-catalyzed C-H lactonization^{a,b}



Entry	solvent	Yield
1	toluene	45%
2	1,4-dioxane	18%
3	<i>t</i> -amyl OH	40%
4	PhCF_3	25%
5	PhCl	58%
6	NMP	trace
7	DMA	trace
8	HFIP	N.R.
9	DME	N.R.

^aReaction conditions: substrate **1a** (0.1 mmol), $\text{Pd}(\text{PhCN})_2\text{Cl}_2$ (10 mol%), ligand (30 mol%), K_2HPO_4 (2.5 equiv), solvent (1.0 mL), 140 °C, 20 h. ^bThe yields were determined by ¹H NMR analysis of the crude product using 1,3,5-trimethoxybenzene as the internal standard.

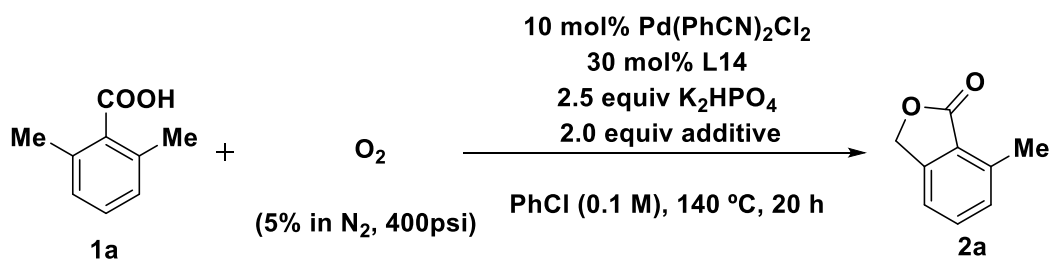
Table S2. Base investigation for Pd(II)-catalyzed C-H lactonization^{a,b}



Entry	base	Yield
1	Li_2CO_3	trace
2	LiF	trace
3	NaOAc	30%
4	Na_2CO_3	41%
5	KTFA	15%
6	K_3PO_4	42%
7	K_2HPO_4	58%
8	KHCO_3	33%
9	KF	44%

^aReaction conditions: substrate **1a** (0.1 mmol), $\text{Pd}(\text{PhCN})_2\text{Cl}_2$ (10 mol%), ligand (30 mol%), base (2.5 equiv), PhCl (1.0 mL), 140 °C, 20 h. ^bThe yields were determined by ^1H NMR analysis of the crude product using 1,3,5-trimethoxybenzene as the internal standard.

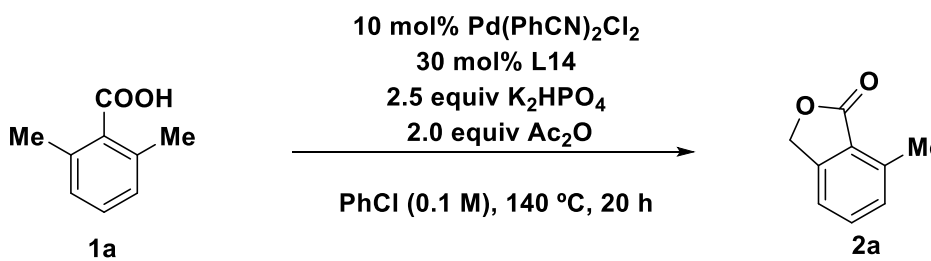
Table S3. Additive investigation for Pd(II)-catalyzed C-H lactonization^{a,b}



Entry	additive	Yield
1	AcOH	45%
2	Ac₂O	72%
3	TFA	30%
4	TFA ₂ O	41%
5	BQ	trace
6	Cu(OAc) ₂	10%
7	K ₂ S ₂ O ₈	20%
8	H ₂ O ₂ (30% in water)	22%
9	NHPI	35%

^aReaction conditions: substrate **1a** (0.1 mmol), Pd(PhCN)₂Cl₂ (10 mol%), ligand (30 mol%), K₂HPO₄ (2.5 equiv), additive (2.0 equiv), PhCl (1.0 mL), 140 °C, 20 h. ^bThe yields were determined by ¹H NMR analysis of the crude product using 1,3,5-trimethoxybenzene as the internal standard.

Table S4. Oxygen source investigation for Pd(II)-catalyzed C-H lactonization^{a,b}

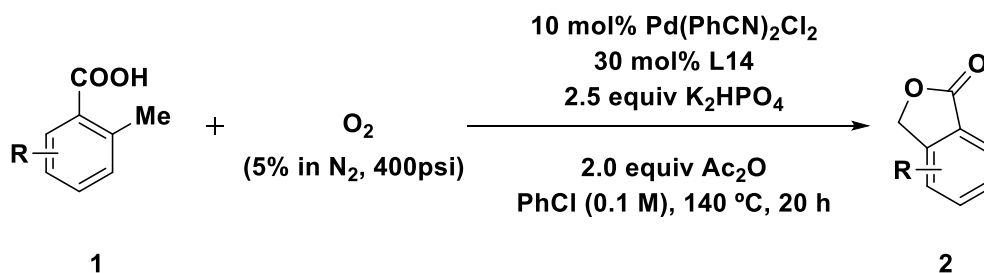


1a

Entry	oxygen source, pressure	Yield
1	pure O ₂ , 1 atm	71%
2	pure O ₂ , 2 atm	71%
3	25% O ₂ in N ₂ , 4 atm	70%
4	5% O ₂ in N ₂ , 10 atm	30%
5	5% O ₂ in N ₂ , 20 atm	62%
6	5% O ₂ in N ₂ , 400psi (27 atm)	72%

^aReaction conditions: substrate **1a** (0.1 mmol), Pd(PhCN)₂Cl₂ (10 mol%), ligand (30 mol%), K₂HPO₄ (2.5 equiv), Ac₂O (2.0 equiv), PhCl (1.0 mL), 140 °C, 20 h. ^bThe yields were determined by ¹H NMR analysis of the crude product using 1,3,5-trimethoxybenzene as the internal standard.

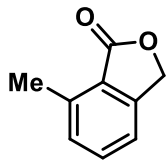
General procedure for Pd(II)-catalyzed C-H lactonization



General procedure: Substrate **1** (0.2 mmol), Pd(PhCN)₂Cl₂ (10 mol%, 7.6 mg), **L14** (30 mol%, 9.8 mg) and K₂HPO₄ (2.5 equiv, 87.0 mg) were weighed in open air and placed in a 12x75 mm borosilicate test tube (5 mL). Ac₂O (2.0 equiv, 18.9 μL) and PhCl (0.1 M, 2.0 mL) were added. The test tube and a stir paddle were placed in a Freeslate Junior with OSR module (Unchained Labs, Pleasanton, CA, USA) equipped with a small volume insert. The reaction was mechanically stirred at 250 rpm, pressurized to 100 psi using a 5% oxygen in nitrogen gas mix, and then heated to 140 °C with a heating mantle. After one hour at 140 °C, the reaction was further pressurized to 400 psi and stirred for 20 h. Afterwards, the reaction mixture was

cooled to room temperature and vented. The crude mixture was diluted with EtOAc and then filtered with Celite. The filtrate was concentrated *in vacuo*, and the resulting mixture purified by column chromatography or pTLC using hexane/EtOAc (2/1) as the eluent.

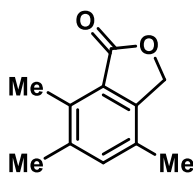
Scope of benzoic acid



2a

7-methylisobenzofuran-1(3H)-one (2a)

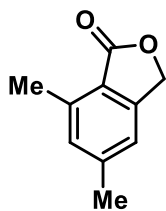
Following the general procedure, **2a** was obtained as a white solid, 70% yield (20.8mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.53 (t, J = 7.5 Hz, 1H), 7.30 – 7.27 (m, 2H), 5.25 (s, 2H), 2.70 (s, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 171.4, 147.2, 139.9, 133.9, 130.7, 123.4, 119.4, 69.0, 17.4. HRMS (ESI-TOF) Calcd for $\text{C}_9\text{H}_9\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 149.0603, found:149.0600



2b

4,6,7-trimethylisobenzofuran-1(3H)-one (2b)

Following the general procedure, **2b** was obtained as a white solid, 55% yield (19.4mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.21 (s, 1H), 5.12 (s, 2H), 2.59 (s, 3H), 2.32 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 172.2, 143.6, 138.3, 136.4, 135.5, 128.7, 122.9, 67.8, 19.2, 17.0, 12.9. HRMS (ESI-TOF) Calcd for $\text{C}_{11}\text{H}_{13}\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 177.0916, found:177.0914

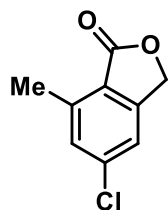


2c

5,7-dimethylisobenzofuran-1(3H)-one (2c)

Following the general procedure, **2c** was obtained as a white solid, 70% yield (22.7mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.07 (d, J = 10.8 Hz, 2H), 5.20 (s, 2H), 2.65 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (151 MHz,

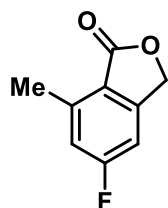
Chloroform-d) δ 171.4, 147.8, 145.0, 139.5, 131.9, 121.0, 119.9, 68.8, 22.0, 17.4. HRMS (ESI-TOF) Calcd for $C_{10}H_{11}O_2^+$ $[M+H]^+$: 163.0759, found:163.0756



2d

5-chloro-7-methylisobenzofuran-1(3H)-one (2d)

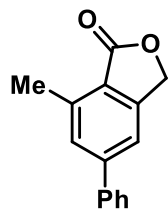
Following the general procedure, **2d** was obtained as a white solid, 42% yield (15.3mg). 1H NMR (600 MHz, Chloroform-d) δ 7.28 (m, 2H), 5.23 (s, 2H), 2.67 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 170.3, 148.7, 141.6, 140.3, 131.2, 122.1, 119.9, 68.4, 17.3. HRMS (ESI-TOF) Calcd for $C_9H_8ClO_2^+$ $[M+H]^+$: 183.0213, found:183.0213



2e

5-fluoro-7-methylisobenzofuran-1(3H)-one (2e)

Following the general procedure, **2e** was obtained as a white solid, 39% yield (12.9mg). 1H NMR (600 MHz, Chloroform-d) δ 7.02 – 6.94 (m, 2H), 5.23 (s, 2H), 2.69 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 170.2, 167.1, 165.4, 149.9, 149.8, 143.1, 143.0, 119.6, 118.6, 118.4, 106.9, 106.8, 68.5, 17.6. HRMS (ESI-TOF) Calcd for $C_9H_8FO_2^+$ $[M+H]^+$: 167.0508, found:167.0505

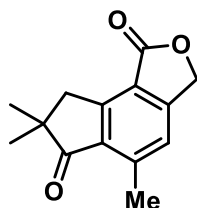


2f

7-methyl-5-phenylisobenzofuran-1(3H)-one (2f)

Following the general procedure, **2f** was obtained as a white solid, 39% yield (17.5mg). 1H NMR (600 MHz, Chloroform-d) δ 7.62 – 7.59 (m, 2H), 7.50 – 7.46 (m, 3H), 7.46 (m, 1H), 7.44 – 7.41 (m, 1H), 5.30 (s, 2H),

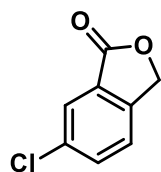
2.75 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 171.3, 148.0, 147.3, 140.1, 140.0, 130.1, 129.2, 128.6, 127.6, 122.3, 118.1, 69.0, 17.6. HRMS (ESI-TOF) Calcd for $\text{C}_{15}\text{H}_{13}\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 225.0916, found:225.0917



2g

5,7,7-trimethyl-7,8-dihydro-1H-indeno[4,5-c]furan-1,6(3H)-dione (2g)

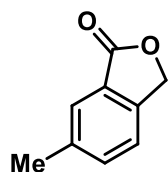
Following the general procedure, **2g** was obtained as a white solid, 56% yield (25.8mg). ^1H NMR (600 MHz, Chloroform-d) δ 7.25 – 7.23 (m, 1H), 5.35 (s, 2H), 3.31 (s, 2H), 2.77 (s, 3H), 1.25 (s, 6H). ^{13}C NMR (151 MHz, Chloroform-d) δ 210.9, 170.1, 153.2, 152.7, 146.7, 134.3, 123.1, 121.0, 69.9, 45.8, 40.3, 25.5, 19.4. HRMS (ESI-TOF) Calcd for $\text{C}_{13}\text{H}_{13}\text{O}_3^+$ $[\text{M}+\text{H}]^+$: 231.1021, found:231.1025



2h

6-chloroisobenzofuran-1(3H)-one (2h)

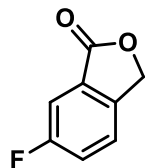
Following the general procedure, **2h** was obtained as a white solid, 45% yield (15.1mg). ^1H NMR (600 MHz, Chloroform-d) δ 7.90 (d, J = 1.5 Hz, 1H), 7.66 (dd, J = 8.1, 1.9 Hz, 1H), 7.47 – 7.44 (m, 1H), 5.31 (s, 2H). ^{13}C NMR (151 MHz, Chloroform-d) δ 169.7, 144.7, 135.6, 134.5, 127.8, 125.9, 123.5, 69.6. HRMS (ESI-TOF) Calcd for $\text{C}_8\text{H}_6\text{ClO}_2^+$ $[\text{M}+\text{H}]^+$: 169.0056, found:169.0053



2i

6-methylisobenzofuran-1(3H)-one (2i)

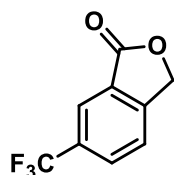
Following the general procedure, **2i** was obtained as a white solid, 47% yield (13.9mg). ^1H NMR (600 MHz, Chloroform-d) δ 7.76 – 7.70 (m, 1H), 7.49 (ddd, J = 7.8, 1.6, 0.8 Hz, 1H), 7.37 (dd, J = 7.8, 1.0 Hz, 1H), 5.28 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 171.4, 144.0, 139.4, 135.3, 126.1, 125.9, 121.9, 69.7, 21.4. HRMS (ESI-TOF) Calcd for $\text{C}_9\text{H}_9\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 149.0603, found:149.0599



2j

6-fluoroisobenzofuran-1(3H)-one (2j)

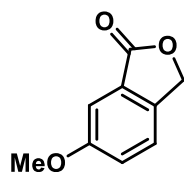
Following the general procedure, **2j** was obtained as a white solid, 36% yield (10.9mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.61 – 7.55 (m, 1H), 7.48 (ddq, J = 8.4, 4.3, 0.8 Hz, 1H), 7.41 (td, J = 8.5, 2.4 Hz, 1H), 5.31 (s, 2H). ^{13}C NMR (151 MHz, Chloroform- d) δ 170.0, 164.1, 162.4, 142.0, 142.0, 128.0, 128.0, 123.9, 123.9, 122.3, 122.1, 112.4, 112.3, 69.6. HRMS (ESI-TOF) Calcd for $\text{C}_8\text{H}_6\text{FO}_2^+$ $[\text{M}+\text{H}]^+$: 153.0352 , found:153.0346



2k

6-(trifluoromethyl)isobenzofuran-1(3H)-one (2k)

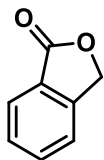
Following the general procedure, **2k** was obtained as a white solid, 59% yield (23.8mg). ^1H NMR (600 MHz, Chloroform- d) δ 8.24 – 8.19 (m, 1H), 7.96 (dd, J = 8.1, 1.6 Hz, 1H), 7.67 (m, 1H), 5.41 (s, 2H). ^{13}C NMR (151 MHz, Chloroform- d) δ 169.6, 149.8, 149.8, 149.8, 149.8, 132.7, 132.4, 132.2, 132.0, 131.0, 131.0, 131.0, 131.0, 126.9, 126.2, 124.4, 123.4, 123.4, 123.4, 123.3, 123.2, 122.6, 120.8, 69.7. HRMS (ESI-TOF) Calcd for $\text{C}_9\text{H}_6\text{F}_3\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 203.0320 , found:203.0321



2l

6-methoxyisobenzofuran-1(3H)-one (2l)

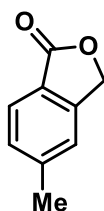
Following the general procedure, **2l** was obtained as a white solid, 49% yield (16.1mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.39 – 7.36 (m, 1H), 7.36 (d, J = 2.3 Hz, 1H), 7.25 (dd, J = 8.4, 2.4 Hz, 1H), 5.27 (s, 2H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 171.4, 160.7, 139.0, 127.2, 123.3, 123.0, 107.6, 69.7, 55.9. HRMS (ESI-TOF) Calcd for $\text{C}_9\text{H}_9\text{O}_3^+$ $[\text{M}+\text{H}]^+$: 165.0552 , found:165.0550



2m

isobenzofuran-1(3H)-one (2m)

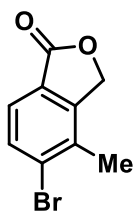
Following the general procedure, **2m** was obtained as a white solid, 41% yield (11.0mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.94 (d, J = 7.7 Hz, 1H), 7.70 (td, J = 7.6, 1.0 Hz, 1H), 7.55 (td, J = 7.6, 0.8 Hz, 1H), 7.51 (dt, J = 7.7, 0.9 Hz, 1H), 5.33 (s, 2H). ^{13}C NMR (151 MHz, Chloroform- d) δ 171.2, 146.7, 134.1, 129.2, 125.9, 125.9, 122.2, 69.8. HRMS (ESI-TOF) Calcd for $\text{C}_8\text{H}_7\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 135.0446 , found:135.0447



2n

5-methylisobenzofuran-1(3H)-one (2n)

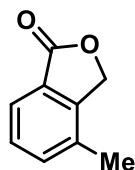
Following the general procedure, **2n** was obtained as a white solid, 39% yield (11.6mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.84 – 7.78 (m, 1H), 7.34 (ddq, J = 7.9, 1.3, 0.7 Hz, 1H), 7.28 (dp, J = 1.6, 0.8 Hz, 1H), 5.27 (s, 2H), 2.50 (s, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 171.3, 147.3, 145.4, 130.4, 125.7, 123.4, 122.5, 69.5, 22.2. HRMS (ESI-TOF) Calcd for $\text{C}_9\text{H}_9\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 149.0603 , found: 149.0598



2o

5-bromo-4-methylisobenzofuran-1(3H)-one (2o)

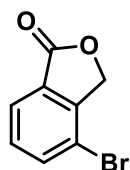
Following the general procedure, **2o** was obtained as a white solid, 43% yield (19.3mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.73 (d, J = 8.1 Hz, 1H), 7.61 (dd, J = 8.1, 0.7 Hz, 1H), 5.26 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 170.8, 147.0, 133.9, 132.8, 131.8, 124.9, 124.4, 69.1, 18.3. HRMS (ESI-TOF) Calcd for $\text{C}_9\text{H}_8\text{BrO}_2^+$ $[\text{M}+\text{H}]^+$: 226.9708 , found:226.9703



2p

4-methylisobenzofuran-1(3H)-one (2p)

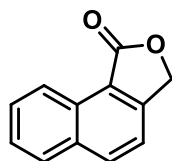
Following the general procedure, **2p** was obtained as a white solid, 40% yield (11.9mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.78 – 7.72 (m, 1H), 7.48 – 7.42 (m, 2H), 5.26 (s, 2H), 2.36 (s, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 171.7, 145.6, 134.8, 132.5, 129.4, 125.6, 123.3, 69.2, 17.6. HRMS (ESI-TOF) Calcd for $\text{C}_9\text{H}_9\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 149.0603 , found:149.0597



2q

4-bromoisobenzofuran-1(3H)-one (2q)

Following the general procedure, **2q** was obtained as a yellow solid, 34% yield (14.3mg). ^1H NMR (600 MHz, Chloroform- d) δ 7.89 (d, J = 8.3 Hz, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.46 (t, J = 7.7 Hz, 1H), 5.23 (s, 2H). ^{13}C NMR (151 MHz, Chloroform- d) δ 170.2, 146.9, 137.0, 131.1, 128.2, 124.8, 116.8, 70.1. HRMS (ESI-TOF) Calcd for $\text{C}_8\text{H}_6\text{BrO}_2^+$ $[\text{M}+\text{H}]^+$: 212.9551 , found:212.9552

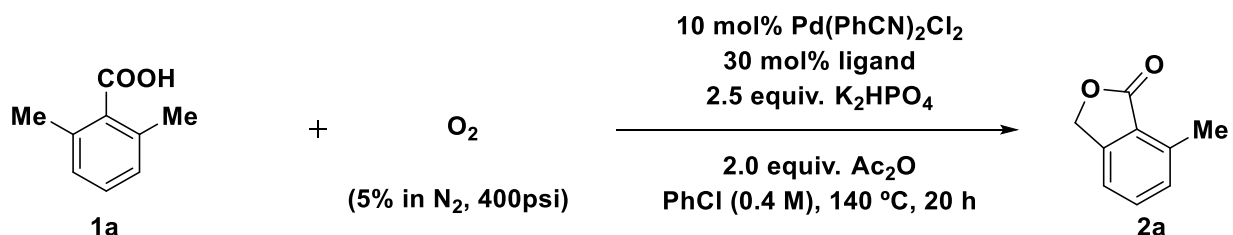


2r

naphtho[1,2-c]furan-1(3H)-one (2r)

Following the general procedure, **2r** was obtained as a white solid, 35% yield (12.9mg). ^1H NMR (600 MHz, Chloroform- d) δ 9.01 (dq, J = 8.4, 1.0 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 7.99 – 7.95 (m, 1H), 7.73 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.64 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 5.39 (s, 2H). ^{13}C NMR (151 MHz, Chloroform- d) δ 171.5, 148.5, 135.6, 133.5, 129.4, 129.2, 128.6, 127.5, 123.6, 120.2, 118.8, 69.3. HRMS (ESI-TOF) Calcd for $\text{C}_{12}\text{H}_9\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 185.0603 , found:185.0601

Gram scale experiment for Pd(II)-catalyzed C-H lactonization

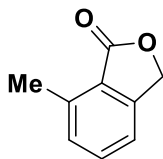


2,6-dimethylbenzoic acid **1** (6.0 mmol), $Pd(PhCN)_2Cl_2$ (10 mol%, 228.0 mg), **L14** (30 mol%, 294.0 mg), and K_2HPO_4 (2.5 equiv, 2.61 g) were weighed in open air and placed in a 30 mL borosilicate vial for the OSR module. Ac_2O (2.0 equiv, 1.05 mL) and PhCl (0.4 M, 15.0 mL) were added. The borosilicate vial and a stir paddle were placed in a Freeslate Junior with OSR module (Unchained Labs, Pleasanton, CA, USA). The reaction mixture was mechanically stirred at 250 rpm, pressurized to 100 psi using a 5% oxygen in nitrogen gas mix, and then heated to 140 °C. Upon reaching the target temperature, the reaction was further pressurized to 405 psi with an automatic refill once the pressure dropped to 395 psi. Approximately once every 30 minutes, the pressure was manually vented to ca. 100 psi before continuing with the automated pressure control. After 20 hours, the reaction mixture was cooled to room temperature and vented. The crude mixture was diluted by EtOAc and filtered with Celite. The filtrate was concentrated *in vacuo*, and the resulting mixture purified by column chromatography using hexane/EtOAc (2/1) as the eluent. 7-methylisobenzofuran-1(3H)-one (**2a**) was obtained as a white solid, 61% yield (0.54g).

Reference

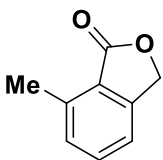
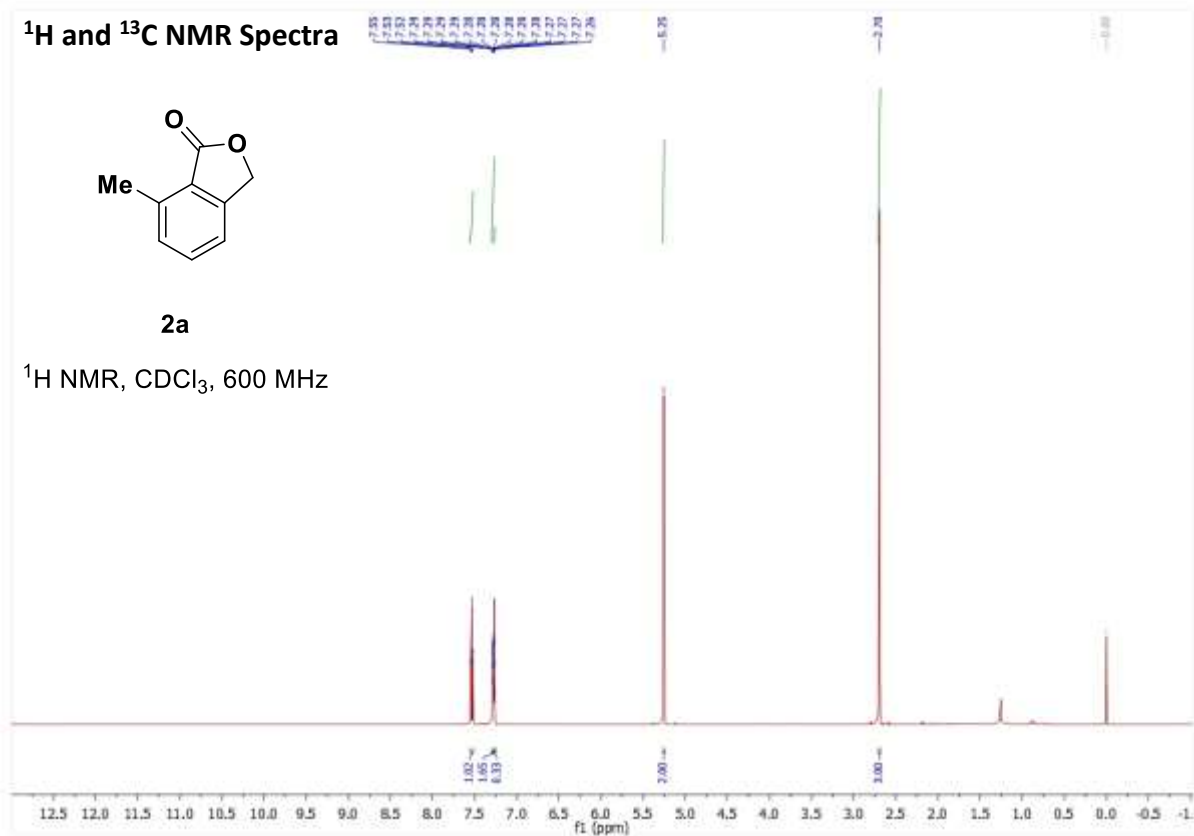
- (1) Novák, P.; Correa, A.; Gallardo-Donaire, J.; Martín, R. Synergistic Palladium-Catalyzed C(sp³)-H Activation/C(sp³)-O Bond Formation: A Direct, Step-Economical Route to Benzolactones. *Angew. Chem. Int. Ed.* **2011**, *50*, 12236–12239.

^1H and ^{13}C NMR Spectra



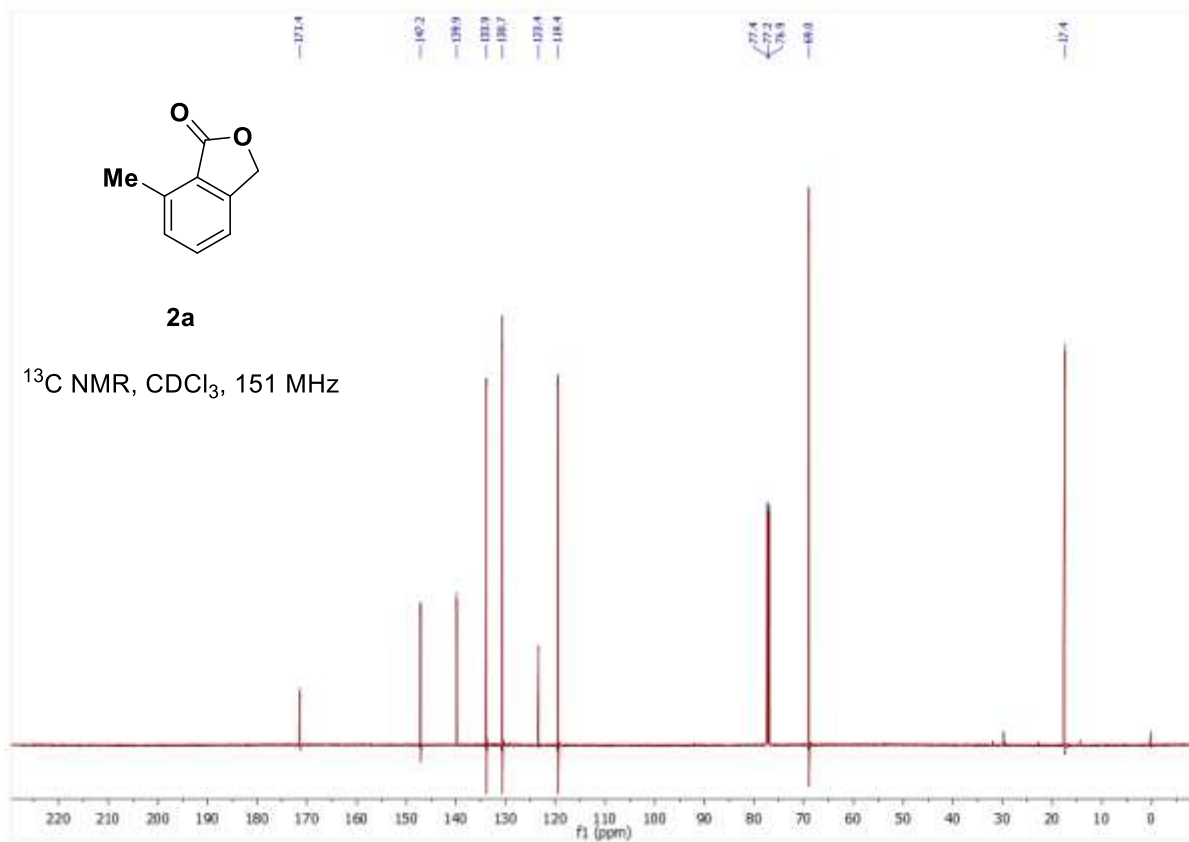
2a

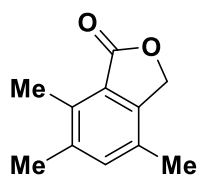
^1H NMR, CDCl_3 , 600 MHz



2a

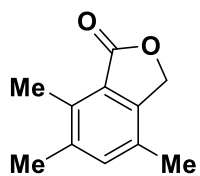
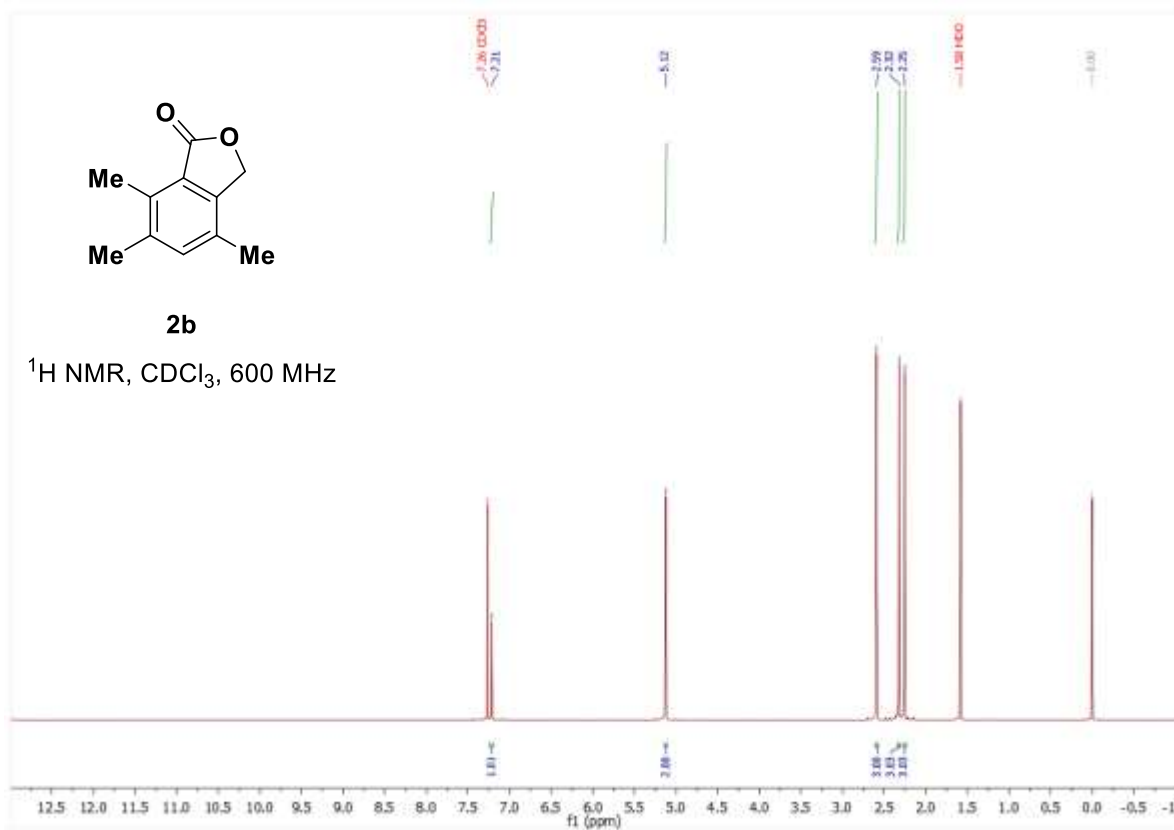
^{13}C NMR, CDCl_3 , 151 MHz





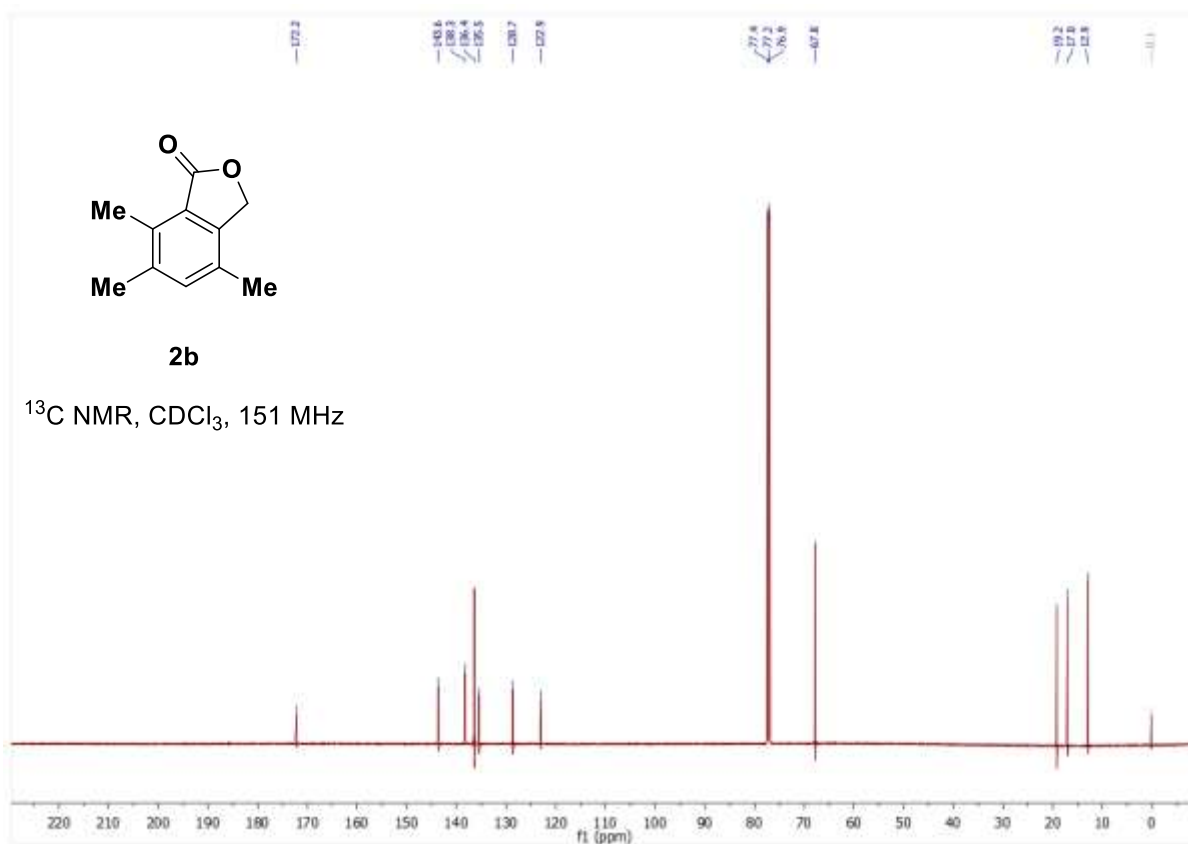
2b

^1H NMR, CDCl_3 , 600 MHz



2b

^{13}C NMR, CDCl_3 , 151 MHz





2c

¹H NMR, CDCl₃, 600 MHz

Chemical structure of **2c** is shown above the spectrum. The spectrum displays the following peaks and integrations:

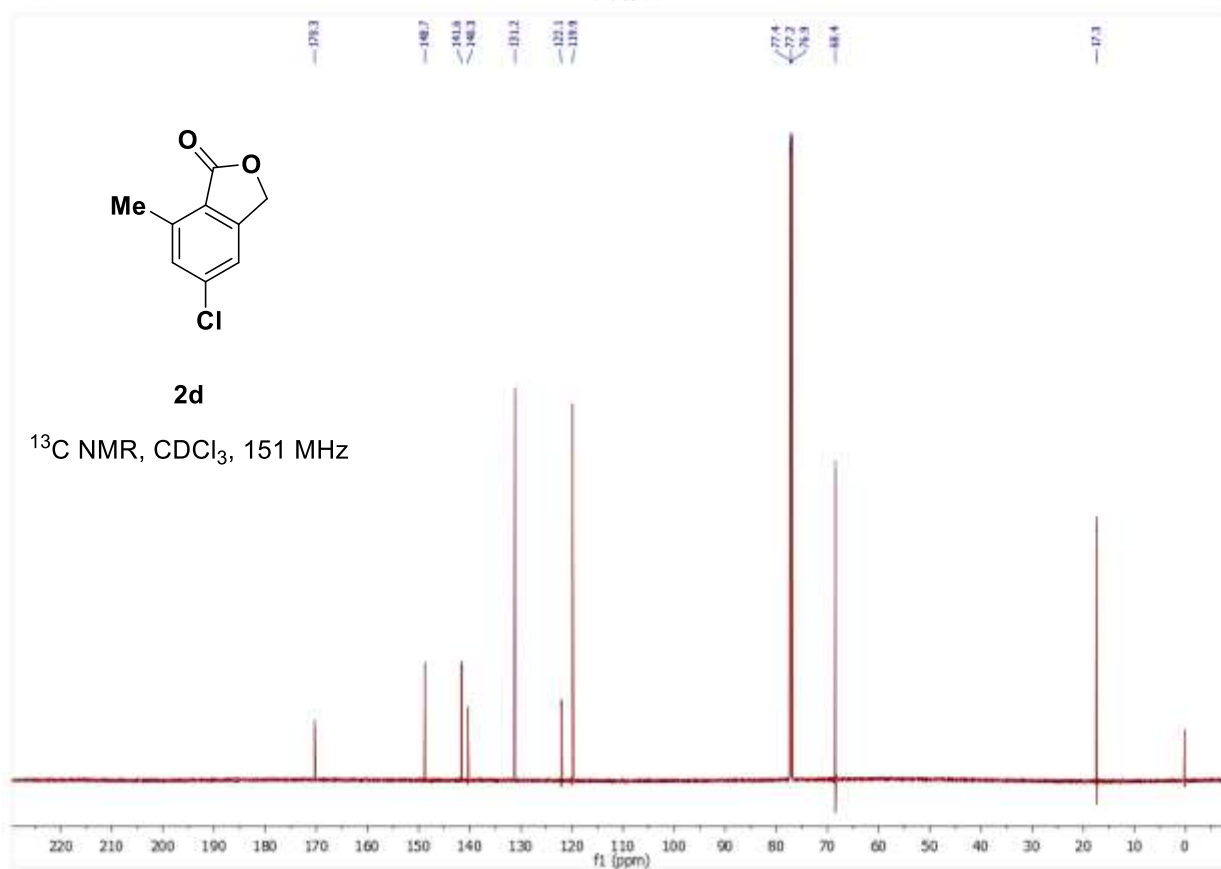
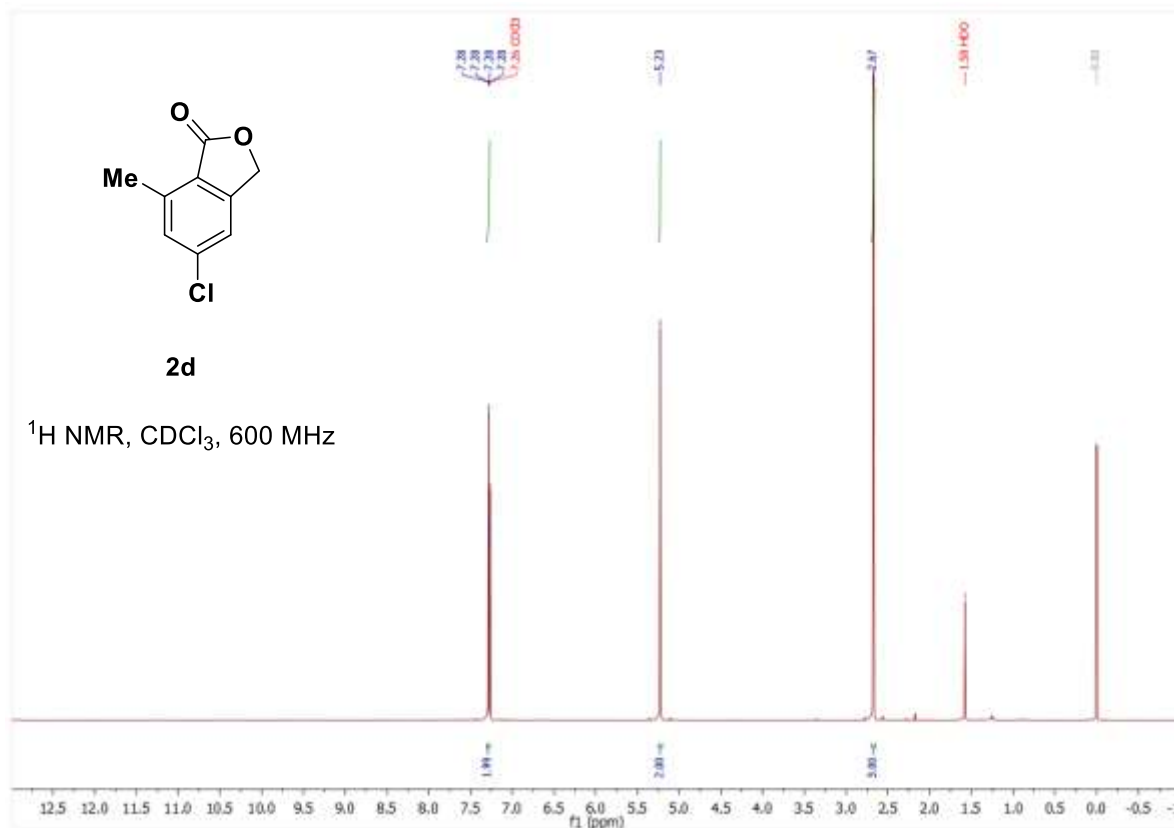
Chemical Shift (ppm)	Integration
7.10	1.00
7.08	2.00
5.20	3.01
2.55	2.96
2.42	
1.58	
0.00	



2c

¹³C NMR, CDCl₃, 151 MHz

Chemical structure of **2c** is shown as an inset: Cc1cc2c(c1)oc(=O)o2. The spectrum displays peaks at 171.8, 147.8, 146.2, 139.5, 131.9, 121.8, 119.6, 77.4, 77.2, 76.8, 68.8, 22.8, 17.4, and 0 ppm.





2e

¹H NMR, CDCl₃, 600 MHz

Chemical structure of **2e** is shown above the spectrum. The structure is a benzofuran derivative with a methyl group (Me) and a fluorine atom (F) on the benzene ring.

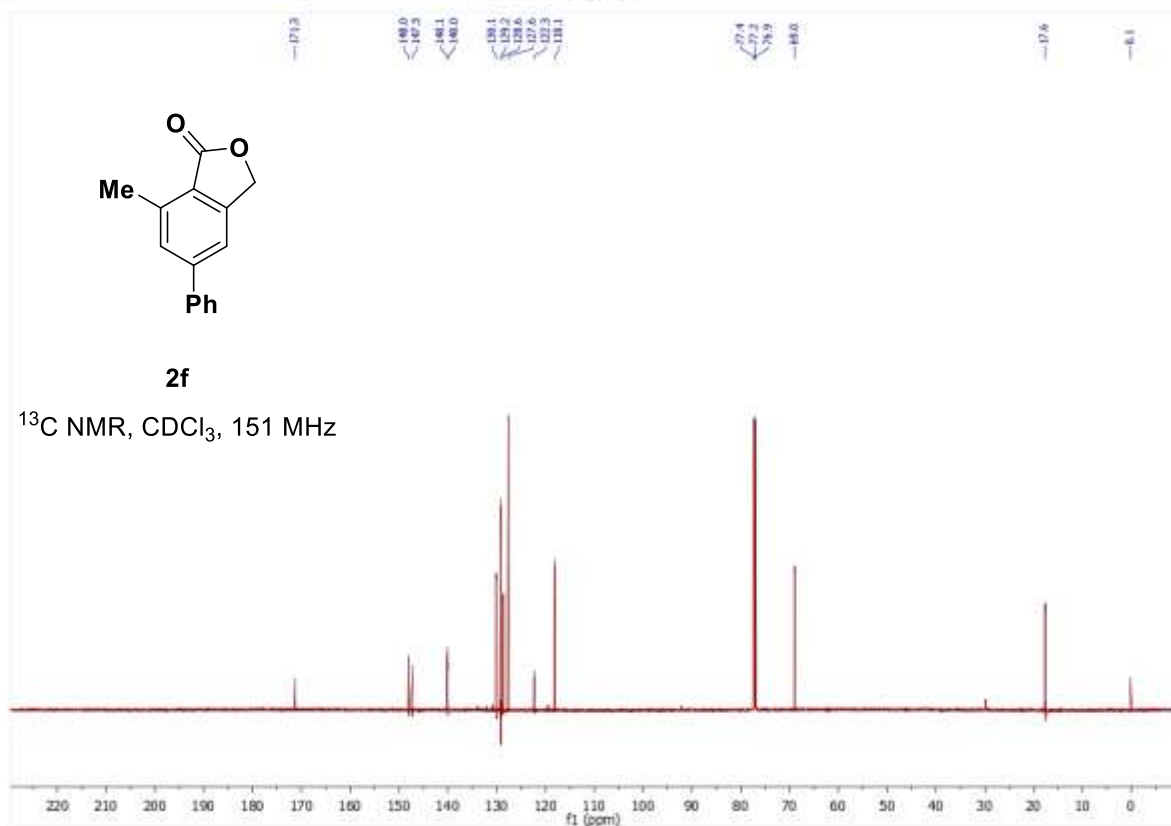
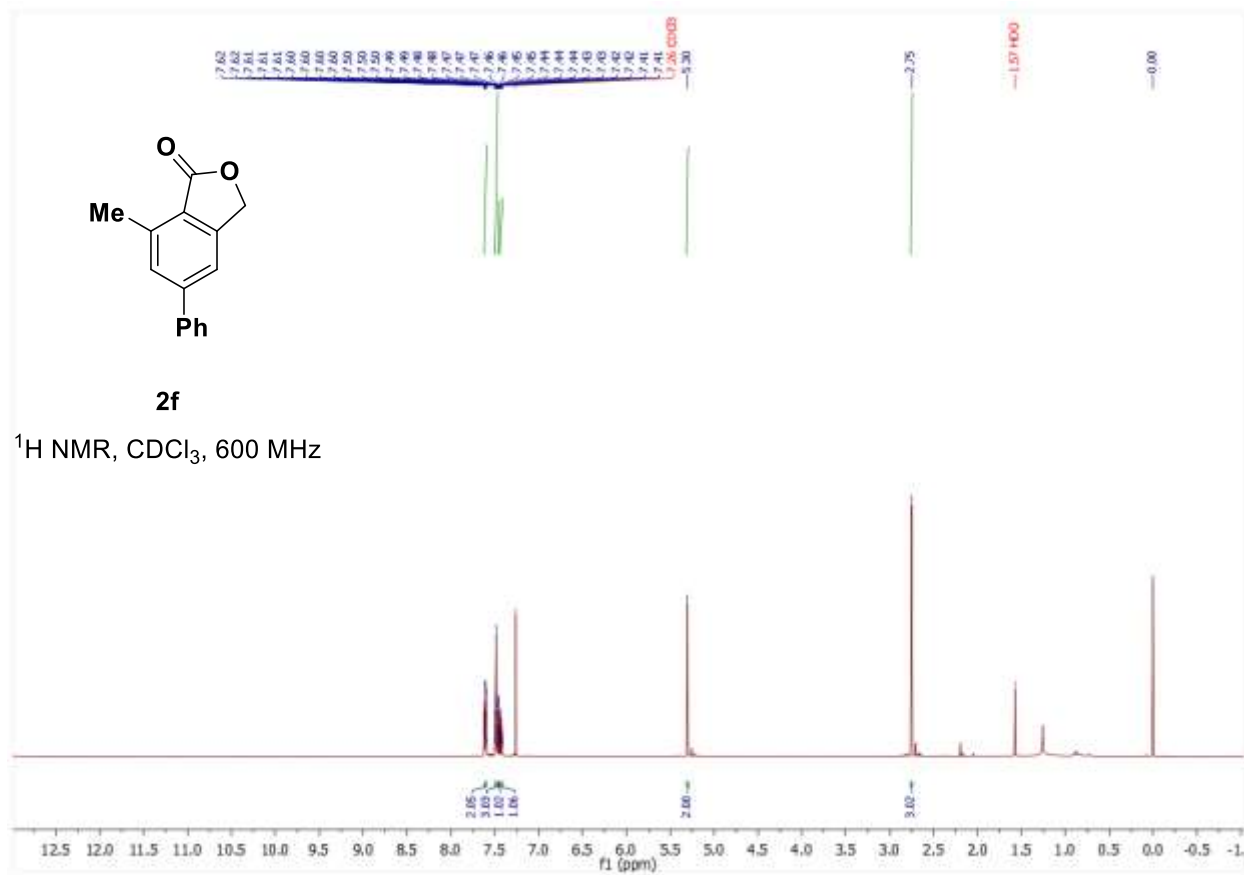


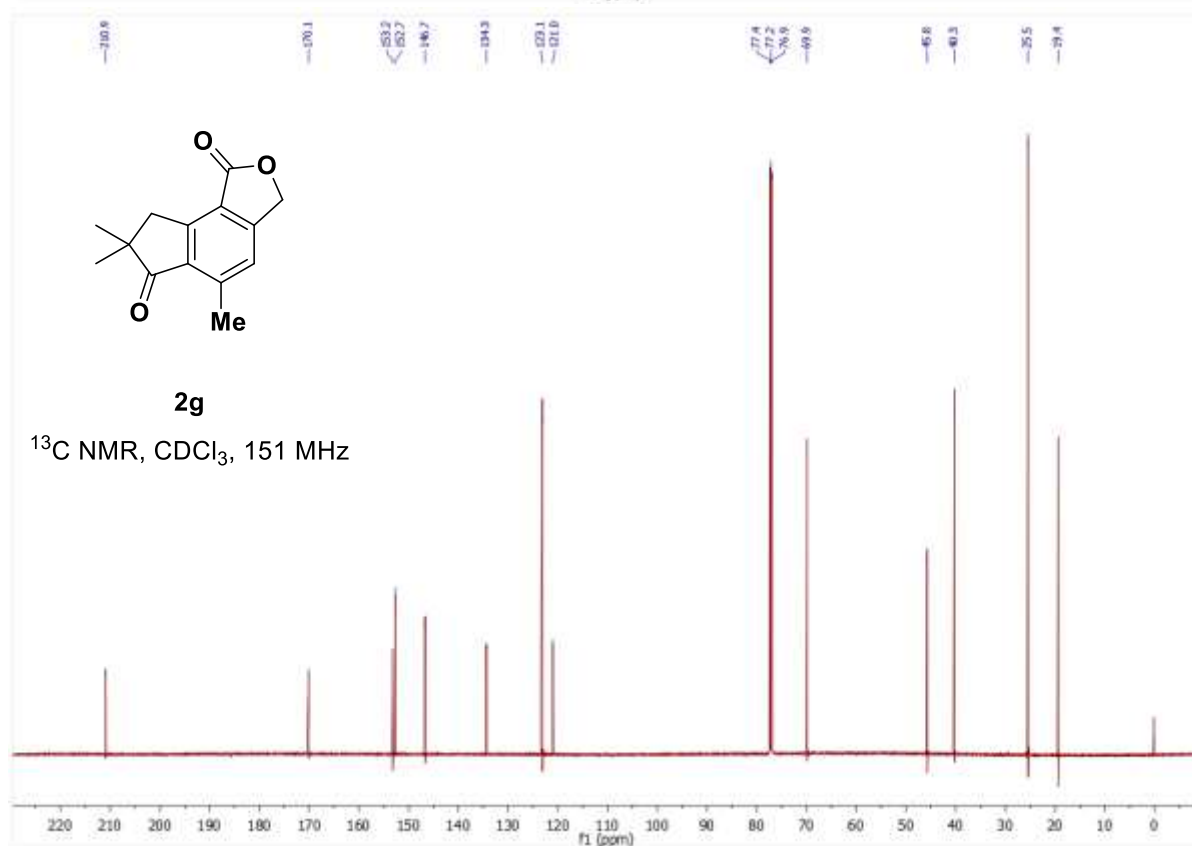
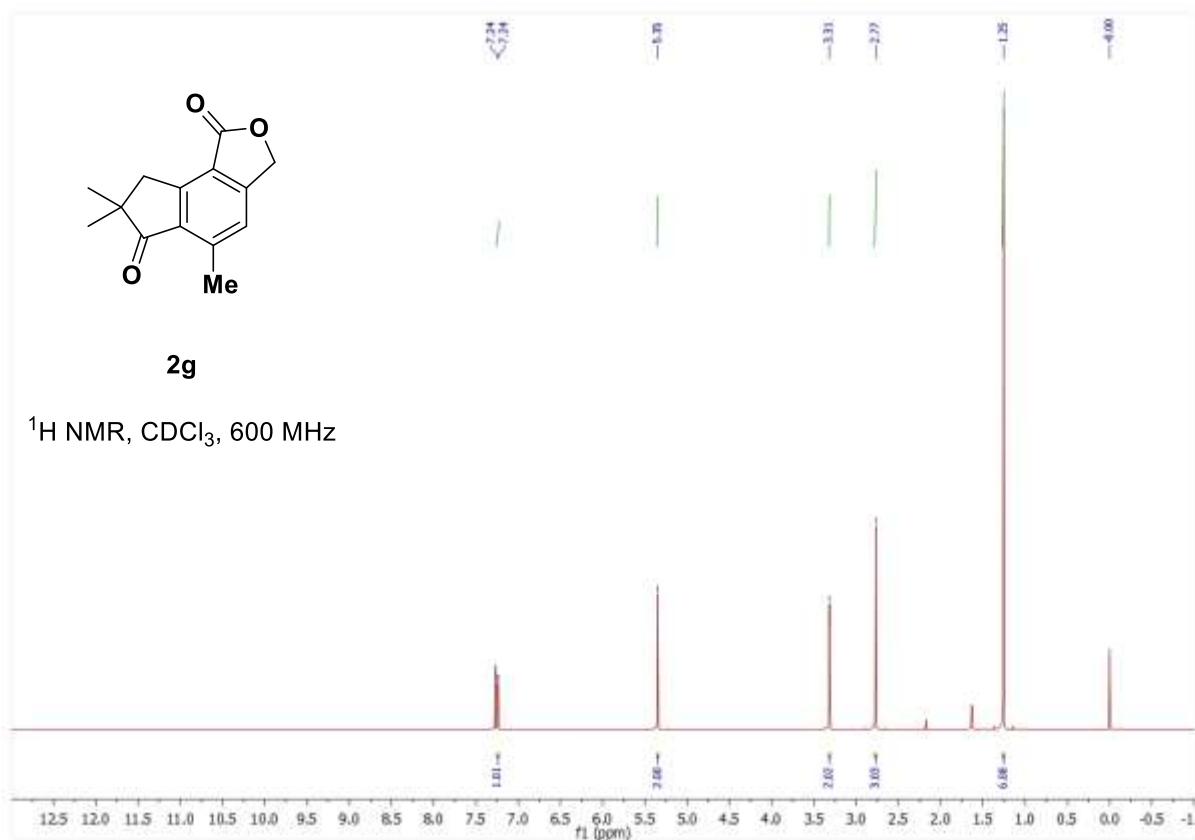
2e

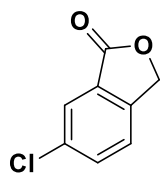
¹³C NMR, CDCl₃, 151 MHz

Chemical structure of **2e** is shown as an inset: Cc1cc(F)ccc2c1OCC2=O

Peak list (ppm): 170.2, 167.1, 165.4, 149.0, 148.8, 143.1, 143.0, 139.6, 138.6, 138.4, 136.9, 136.8, 77.4, 77.2, 76.9, 68.5, -17.6.

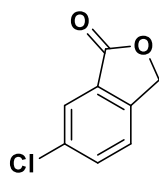
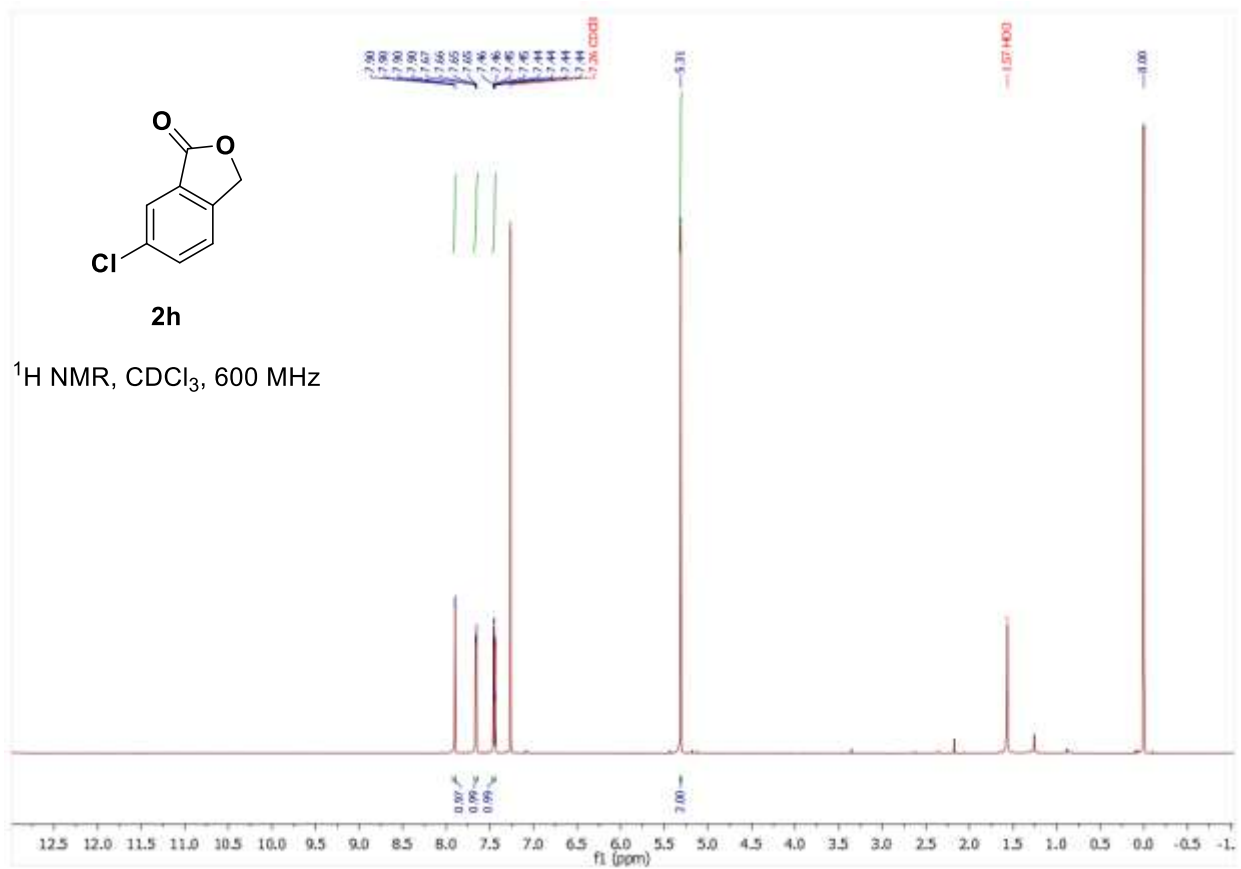






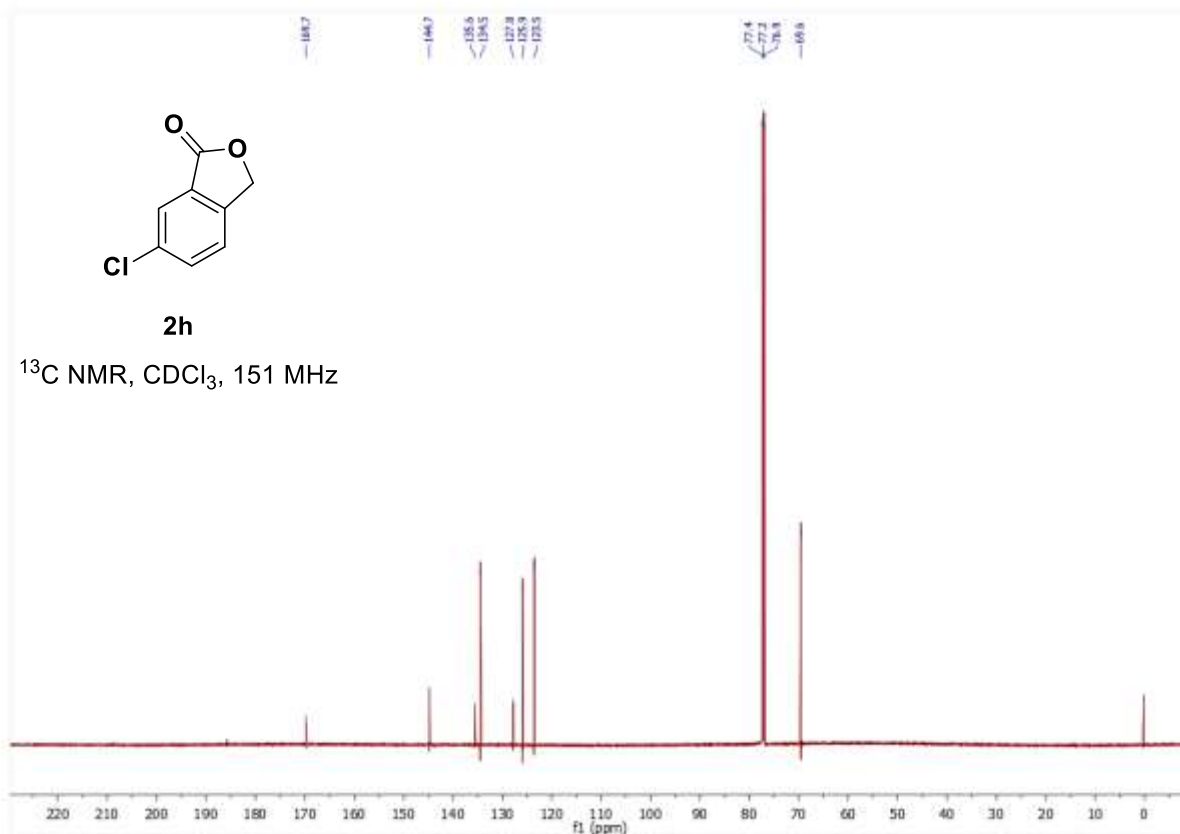
2h

^1H NMR, CDCl_3 , 600 MHz



2h

^{13}C NMR, CDCl_3 , 151 MHz





Cc1ccc2c(c1)oc(=O)o2

2i

^1H NMR, CDCl_3 , 600 MHz

1.00
0.98
1.00
0.96
2.00
3.00
1.00

7.73
7.72
7.72
7.72
7.72
7.50
7.50
7.49
7.49
7.49
7.38
7.37
7.37
5.30
2.47
1.51
0.00

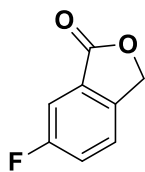
CDCl_3



2i

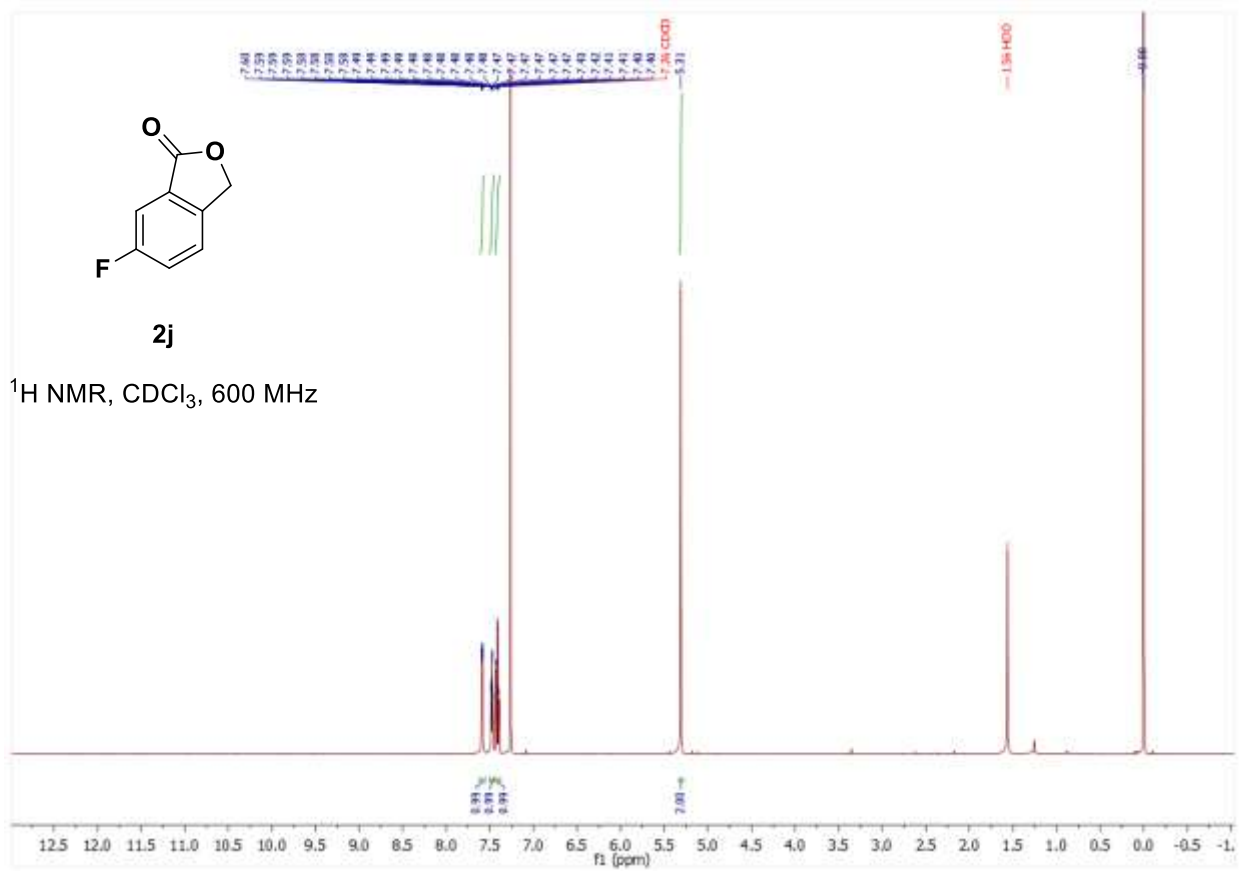
^{13}C NMR, CDCl_3 , 151 MHz

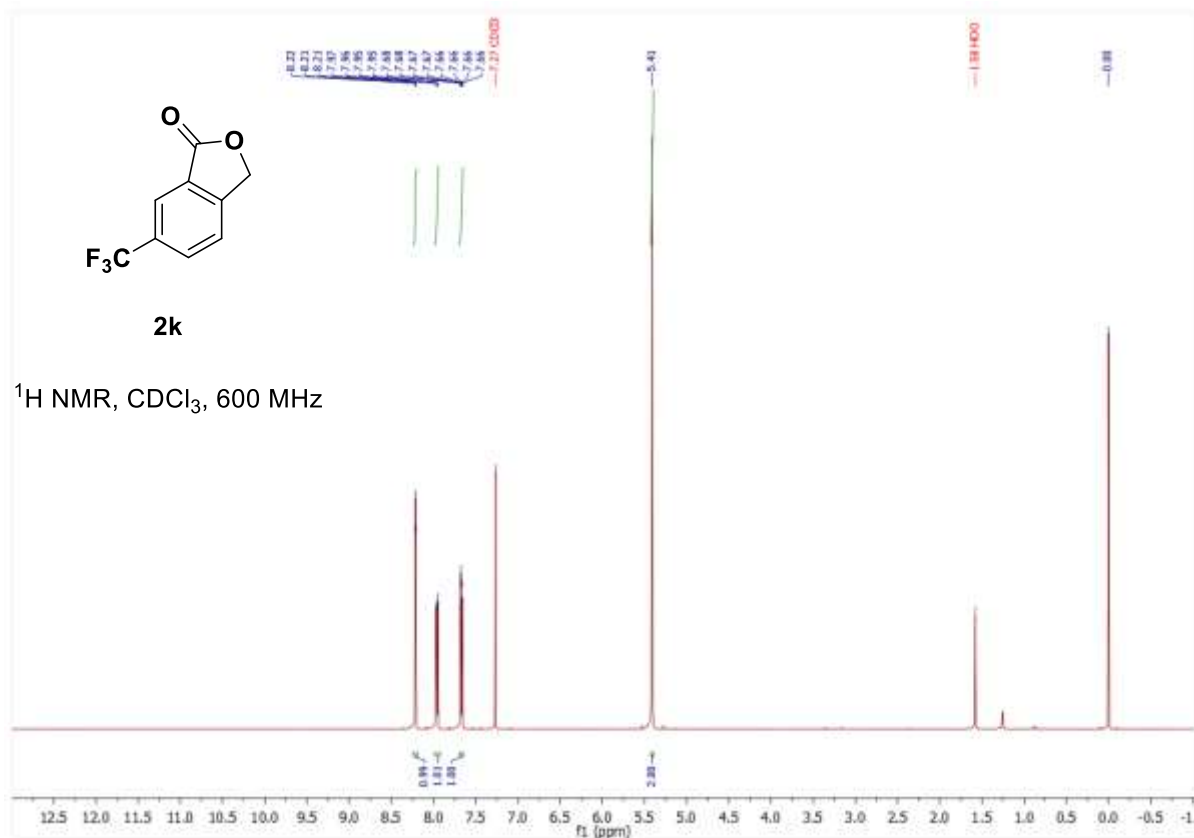
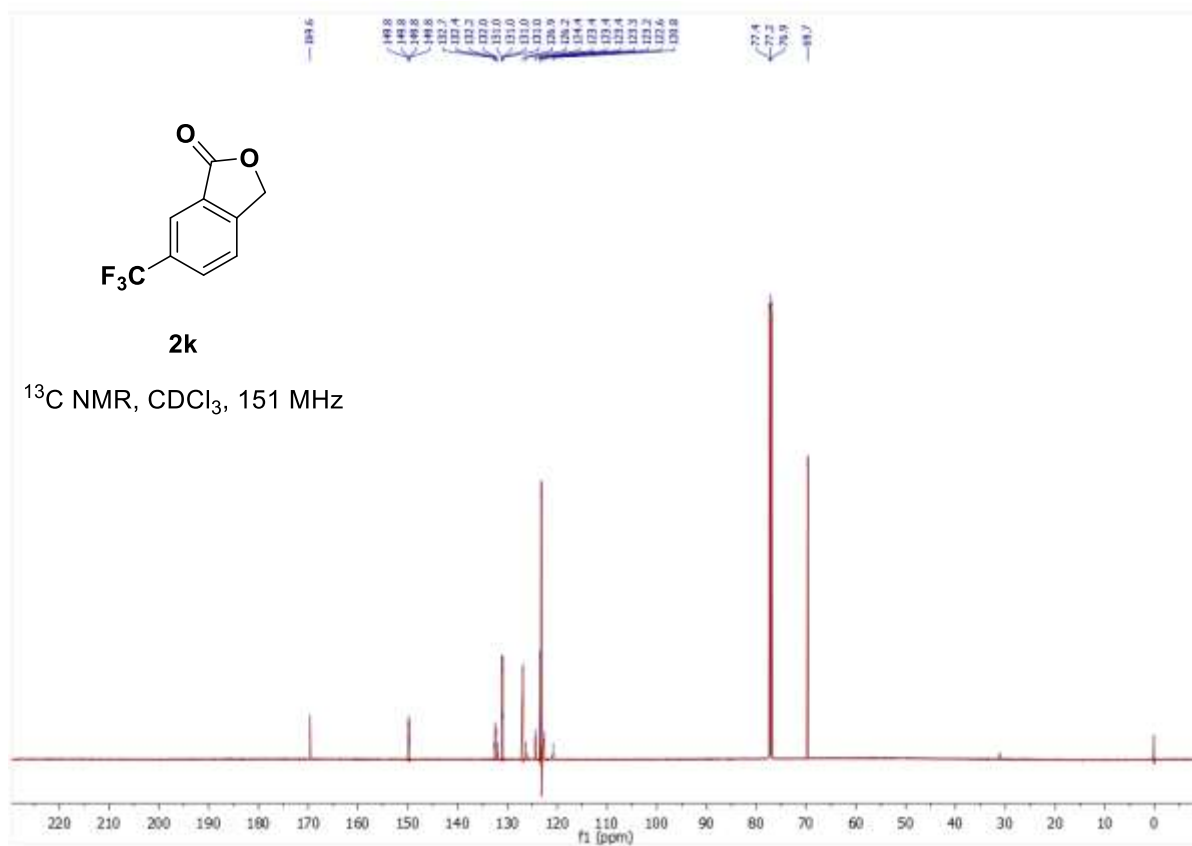
Chemical structure of **2i** is shown. The spectrum displays peaks at 171.4, 139.4, 135.3, 126.1, 125.5, 121.9, 77.4, 77.2, 76.5, 69.7, 21.8, and 0 ppm.

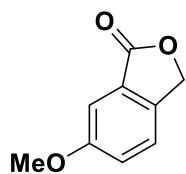


2j

^1H NMR, CDCl_3 , 600 MHz

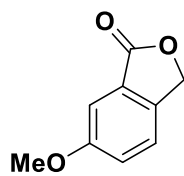
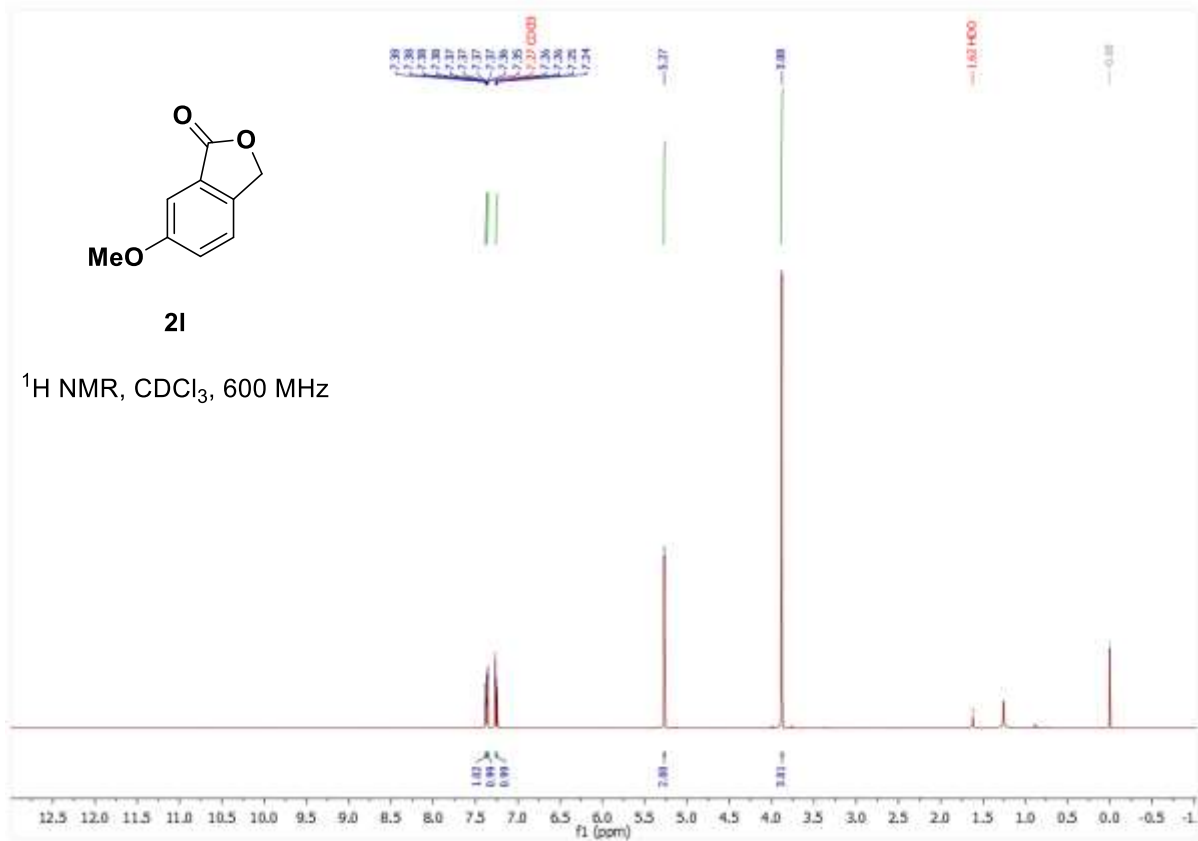


¹H NMR, CDCl₃, 600 MHz ^{13}C NMR, CDCl_3 , 151 MHz



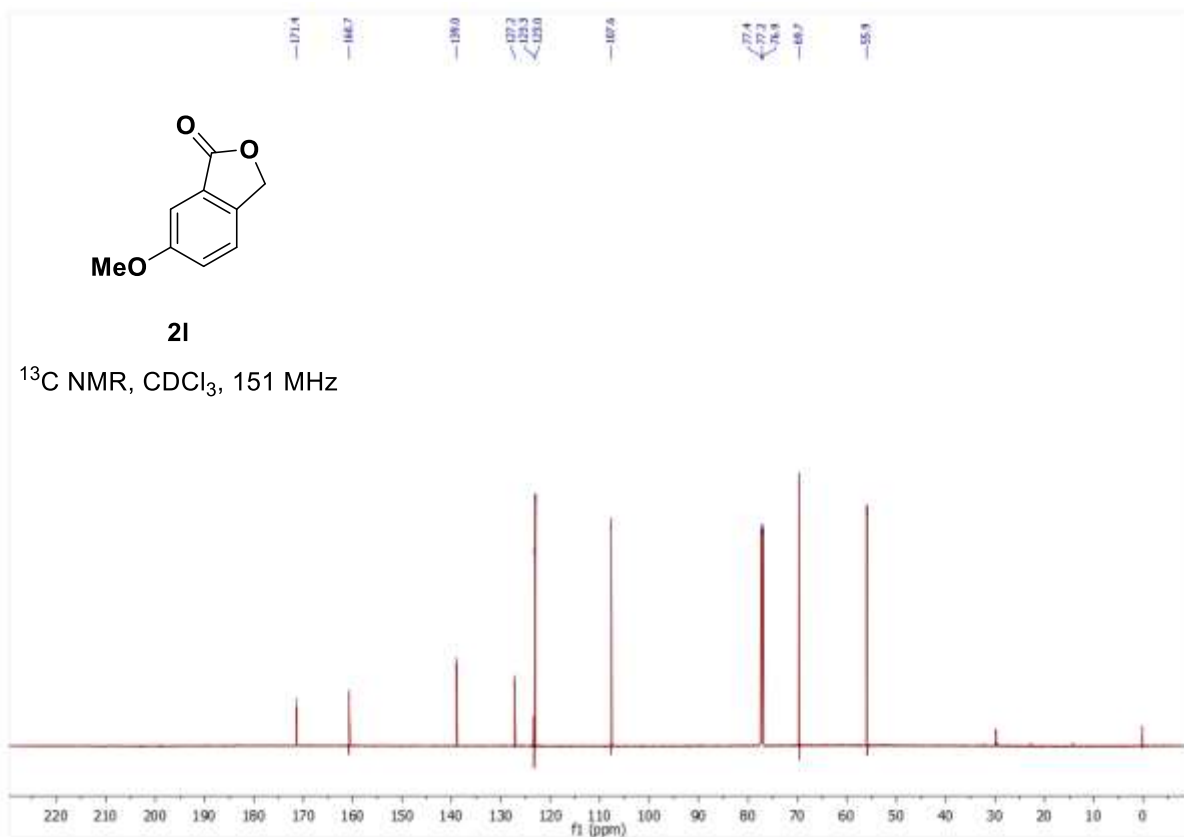
2I

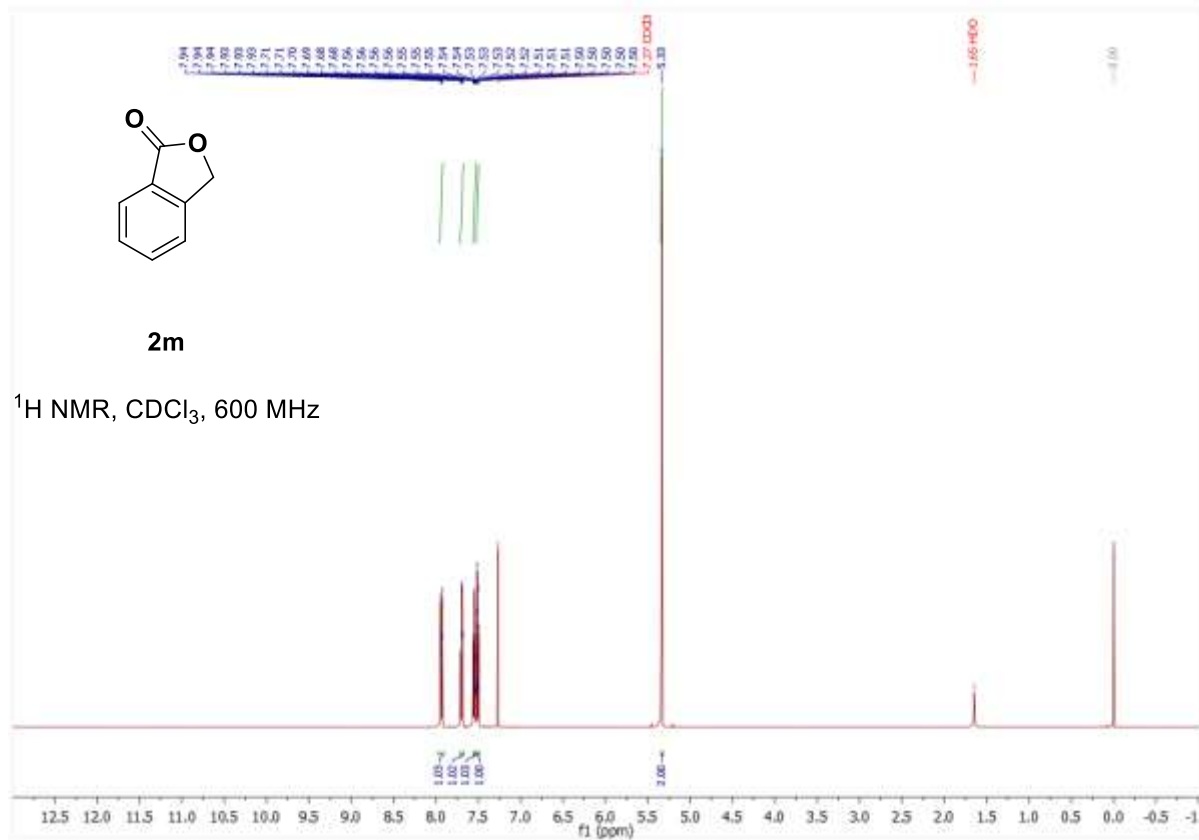
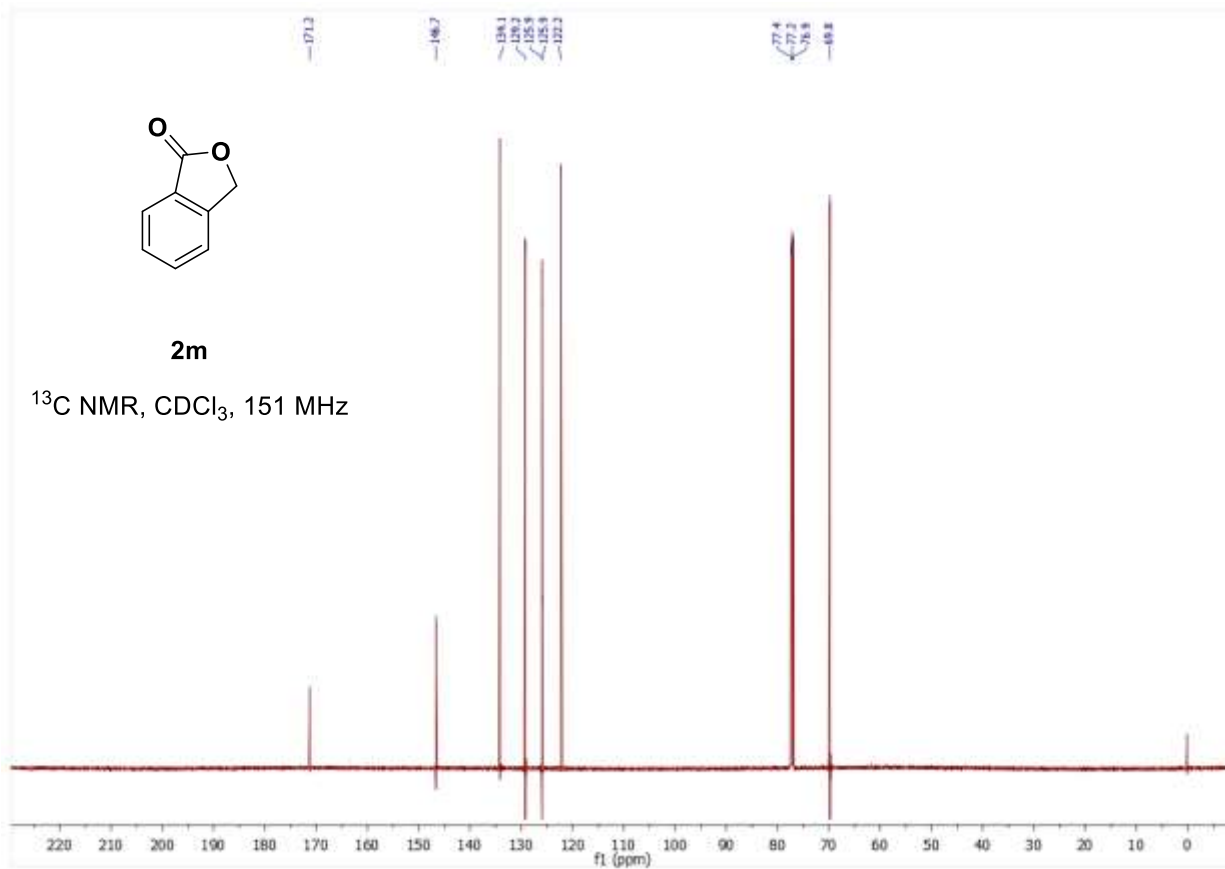
^1H NMR, CDCl_3 , 600 MHz



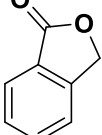
2I

^{13}C NMR, CDCl_3 , 151 MHz



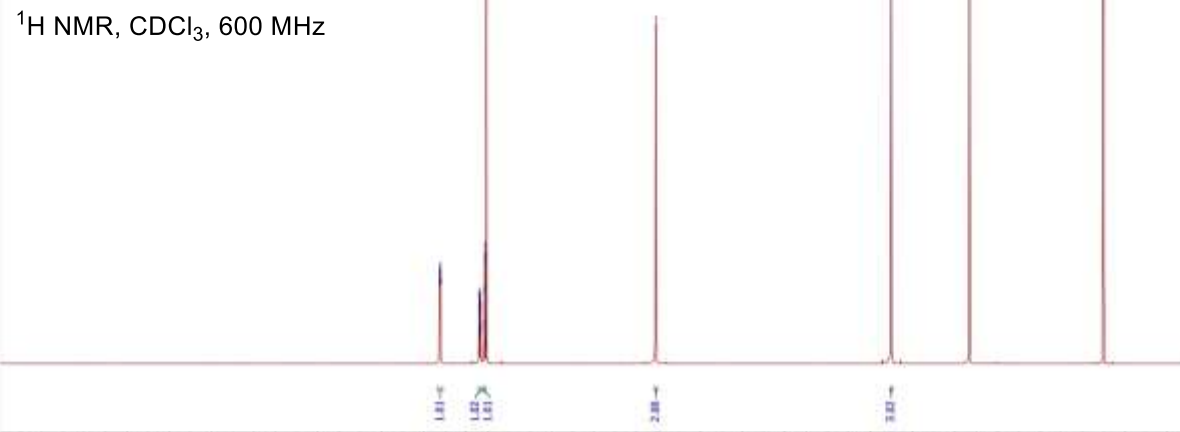
¹H NMR, CDCl₃, 600 MHz ^{13}C NMR, CDCl_3 , 151 MHz





2n

^1H NMR, CDCl_3 , 600 MHz



Chemical Shift (ppm)	Integration
~11.8	1.01
7.2-7.8	1.02
~5.4	1.01
~2.5	2.08
~1.5	3.02
0	3.01
0	1.00

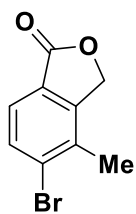


2n

¹³C NMR, CDCl₃, 151 MHz

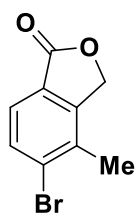
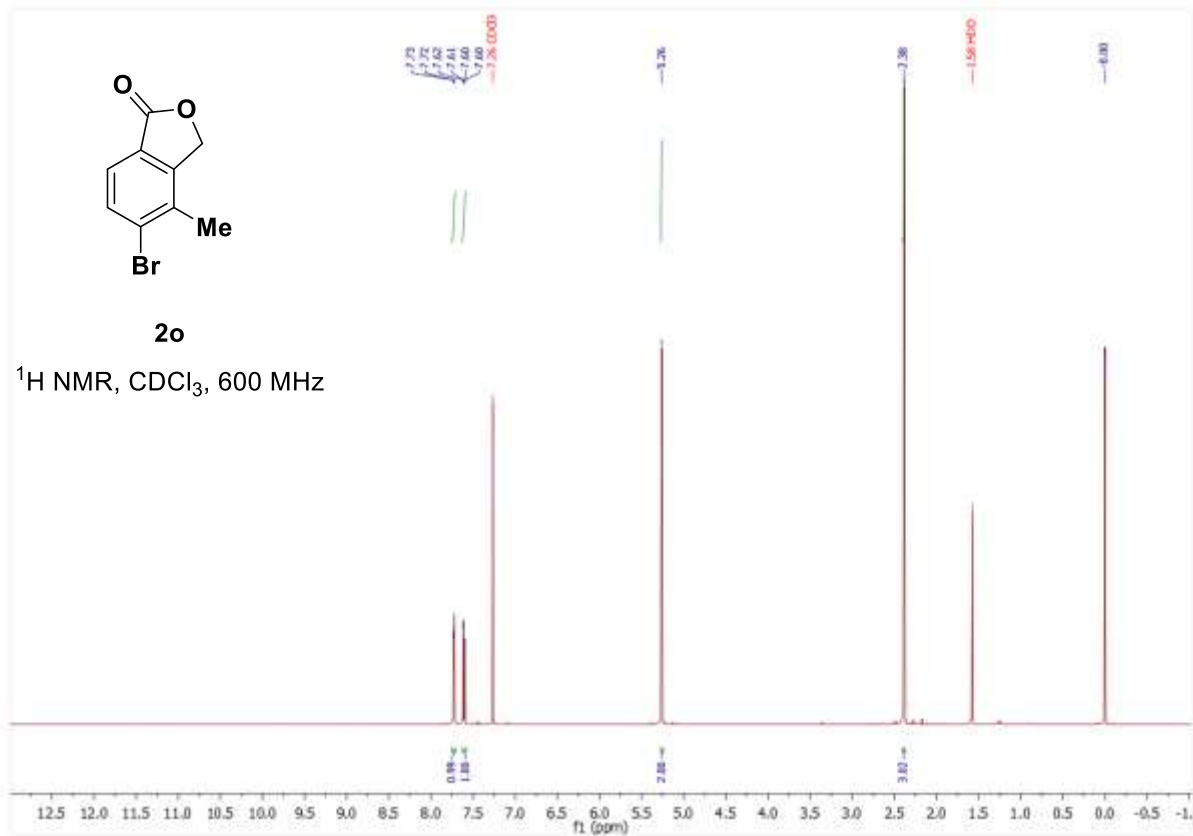
Chemical structure of **2n** is shown as an inset: Cc1ccc2c(c1)oc(=O)c2.

Peak list (ppm): 171.3, 147.3, 146.4, 130.4, 128.5, 125.4, 122.5, 77.4, 77.2, 76.8, 69.5, 22.2, 0.1.



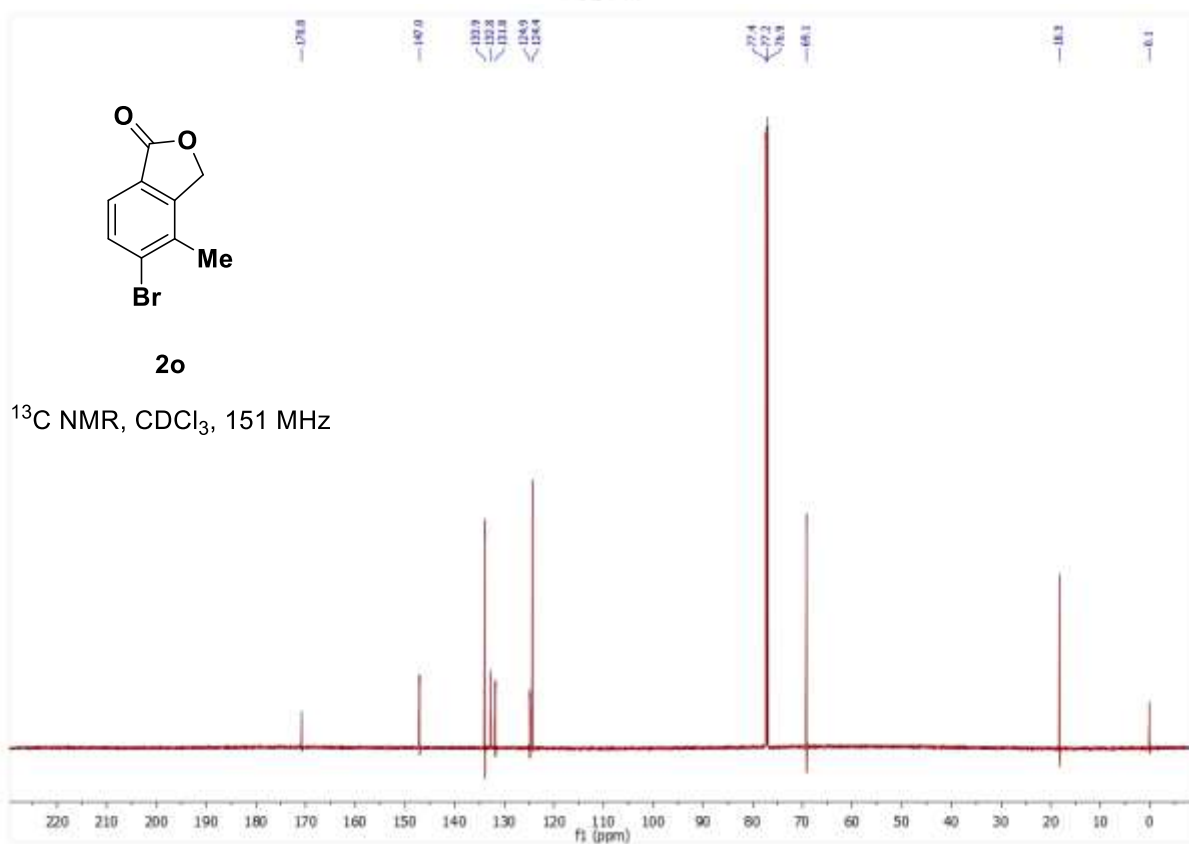
2o

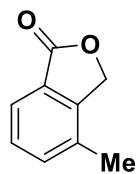
^1H NMR, CDCl_3 , 600 MHz



2o

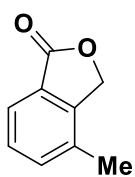
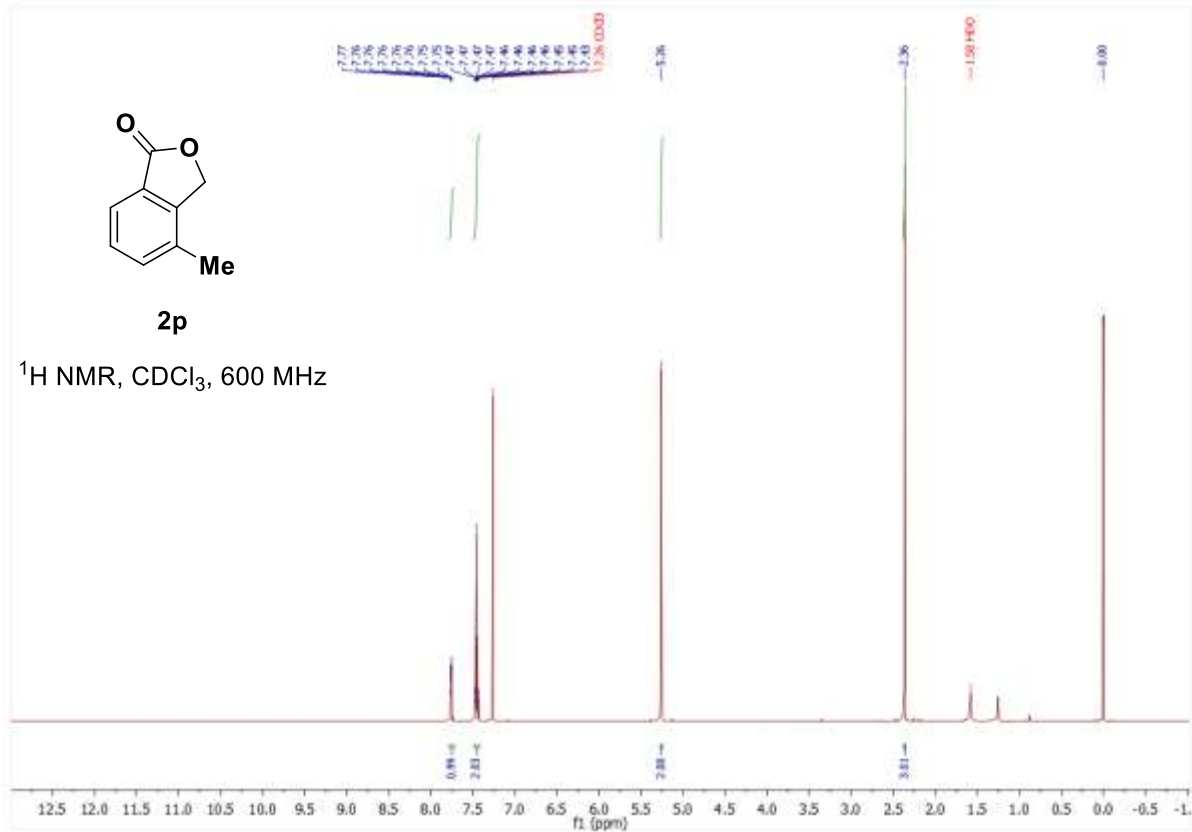
^{13}C NMR, CDCl_3 , 151 MHz





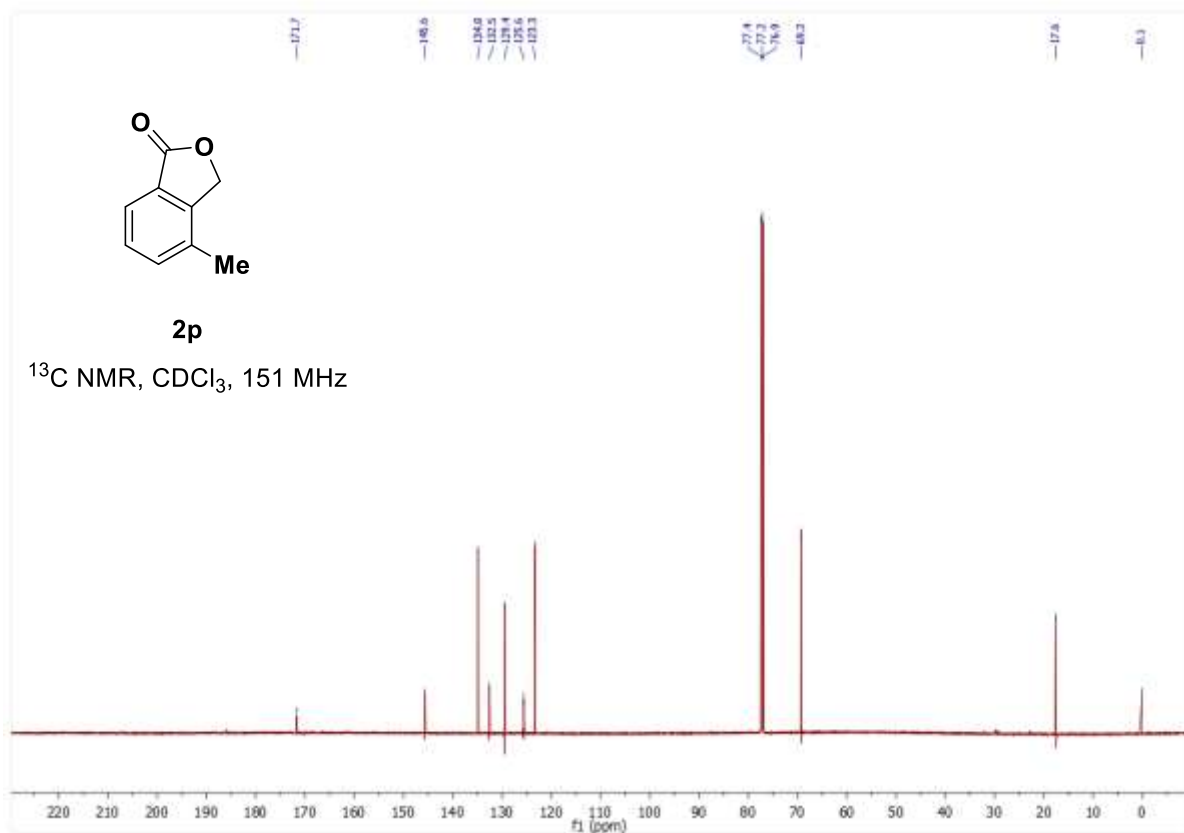
2p

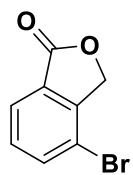
^1H NMR, CDCl_3 , 600 MHz



2p

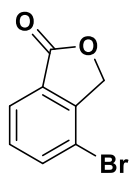
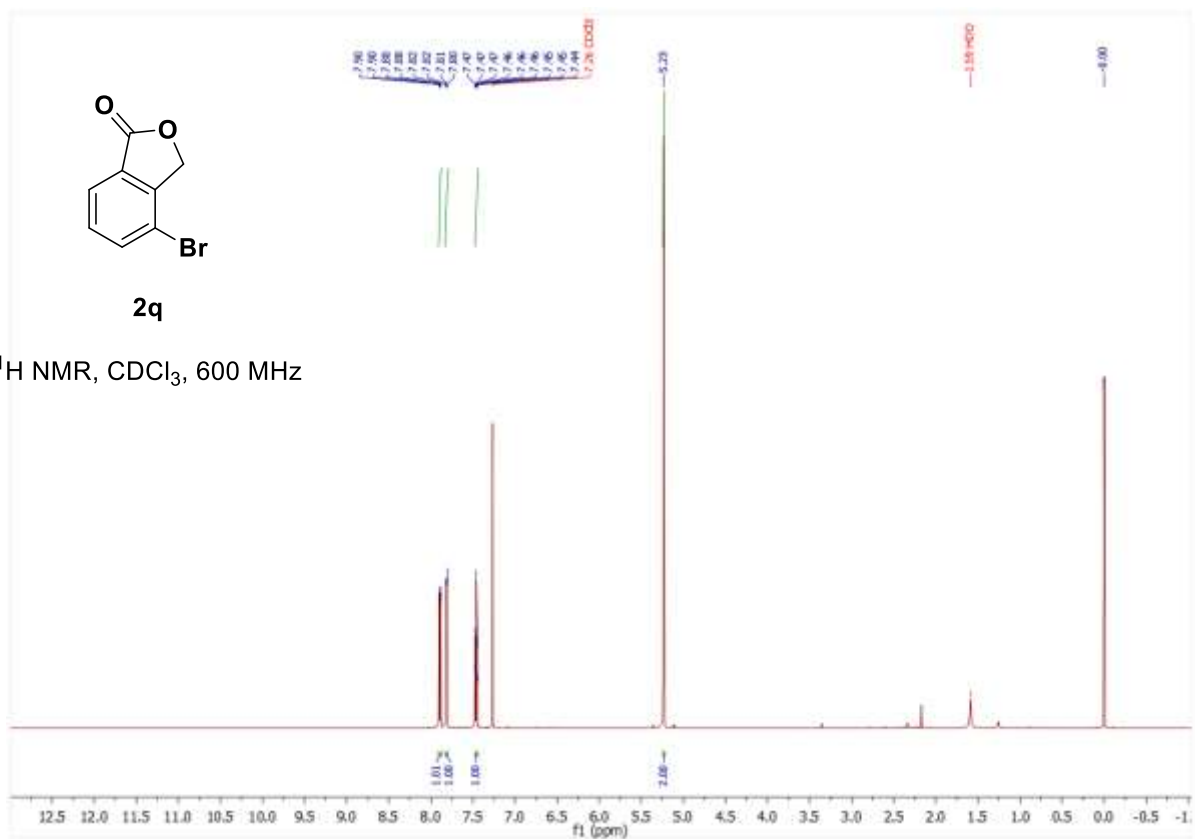
^{13}C NMR, CDCl_3 , 151 MHz





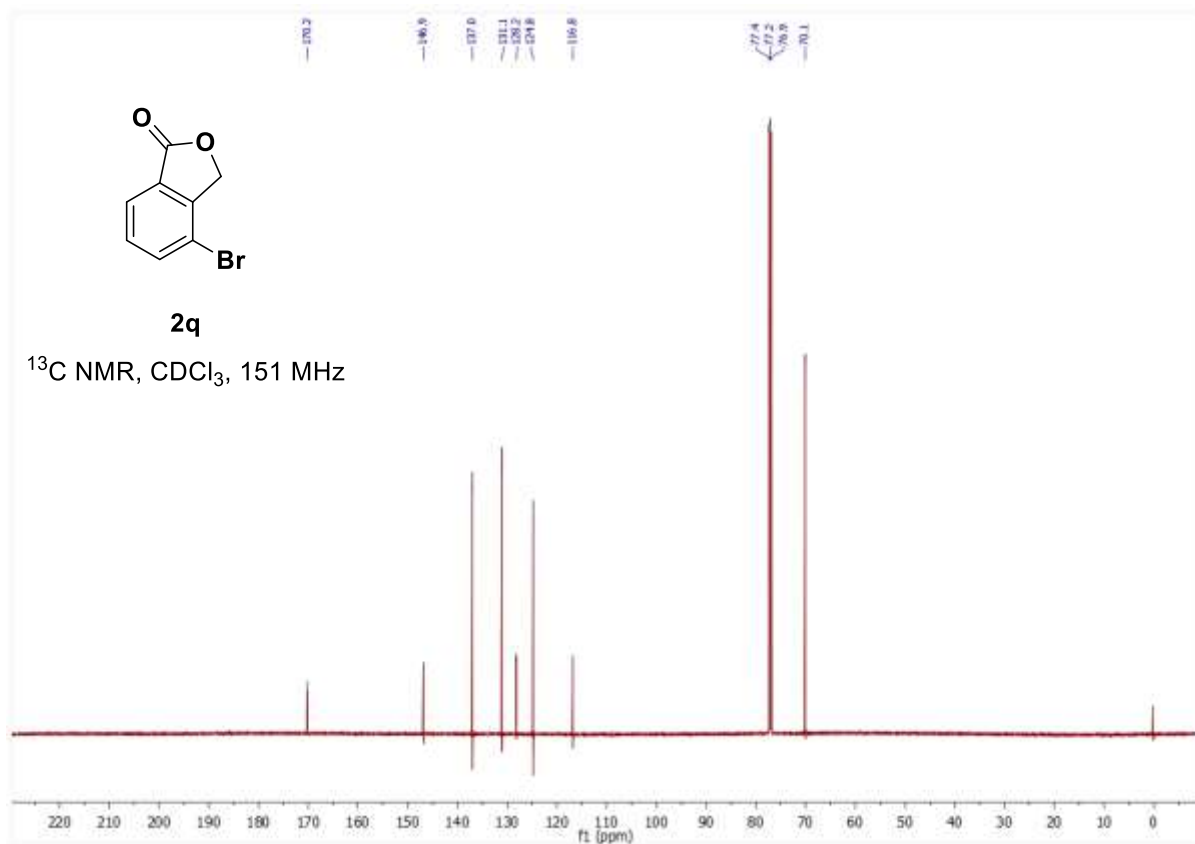
2q

^1H NMR, CDCl_3 , 600 MHz



2q

^{13}C NMR, CDCl_3 , 151 MHz





2r

¹H NMR, CDCl₃, 600 MHz

Chemical structure of **2r** is shown above the spectrum. The spectrum displays the following peaks and integration values:

Chemical Shift (ppm)	Integration
~8.9	0.06
~8.1	1.00
~8.0	0.98
~7.8	1.00
~7.7	1.00
~7.6	0.99
~7.3	2.00
7.26 (solvent)	-
~5.7	2.00
~1.5	-
~1.2	-
~0.8	-
0.0 (TMS)	-



2r

¹³C NMR, CDCl₃, 151 MHz

Chemical structure of **2r** is shown as an inset. The spectrum displays peaks at 171.5, 148.5, 135.4, 133.5, 129.4, 129.2, 127.5, 127.3, 123.4, 120.2, 118.9, 77.4, 77.2, 76.9, and 48.3 ppm.