Supplementary Information (SI) for Organic & Biomolecular Chemistry.
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Supporting Information

Dual Palladium-Organophotoredox Catalysed C-H Olefination-Annulation of Aryl Carboxylic Acids

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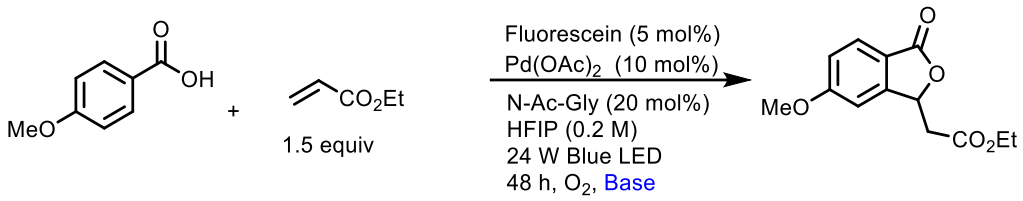
1. General information:

Unless and otherwise noted, all the vials (Borosil) used for carrying out the reactions were dried overnight in a hot air oven at 120 °C. All the chemicals were purchased from Sigma Aldrich, TCI, Spectrochem and were used without any further purification. All the anhydrous solvents required were purchased from Sigma Aldrich. Aldrich micro photochemical reactor, Kessil Blue LEDs (40 W, 456nm), Penn PhD Photoreactor (450 nm) and Smartchemsynths blue LED lights (24 W, 452 nm) were used for the reactions. Reactions were monitored using aluminium supported precoated silica gel 60 F254 TLC (thin layer chromatography) plates (Merck) and visualised by UV light at 254 nm. The final products were purified using column chromatography (230-400 mesh silica gel purchased from Merck). ^{1}H NMR (400 MHz), ^{19}F NMR (377 MHz), and ^{13}C NMR (101 MHz) spectra were recorded on the Bruker AVANCE NEO 400 MHz spectrometer. $CDCl_3$, DMSO-d_6, & ACN-d_3 were used as NMR solvents. Chemical shifts (δ) for ^{1}H and ^{13}C NMR spectra are given in ppm relative to tetramethylsilane (TMS) or the NMR solvents [δ7.27 for ^{1}H (chloroform-d), δ 77.0 for ^{13}C (chloroform-d); δ 2.50 for ^{1}H (DMSO-d6), δ 39.52 for ^{13}C (DMSO-d6). ^{19}F-NMR spectra are not externally calibrated and chemical shifts is given relative to CCl_3F as received from the automatic data processing. Abbreviations used in the ^{1}H NMR data: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; sep, septet; dd, doublet of doublet; m, multiplet. High resolution mass spectra (HRMS) was obtained from Orbitrap Elite HybridIon Trap-Orbitrap (Thermofischer scientific, Newington, NH, USA) Mass Spectrometer in electrospray ionization mode (ESI+) and Agilent Bio-QTOF-6545XT high resolution mass spectrometer in electrospray ionization mode (ESI+). Stern-Volmer studies were performed using an FP-8500 spectro-fluorometer (JASCO).

2. Experimental section

2.1 Optimisation of reaction conditions

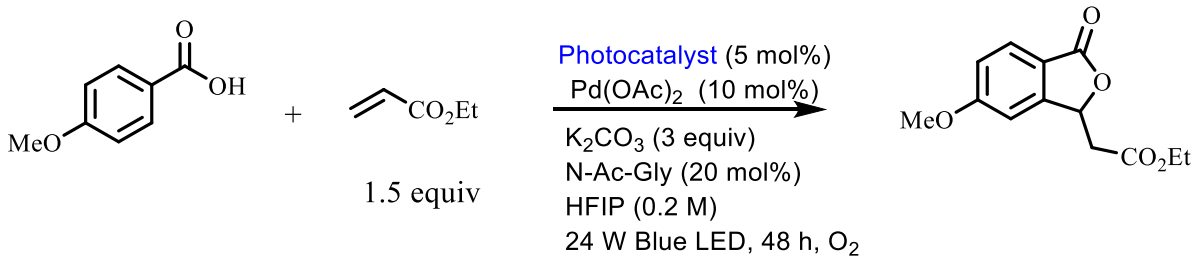
Table S1: Optimization of base



Entry	Base	Crude NMR yield (%)[a]
1	K_2CO_3 (1 equiv)	20
2	Na_2CO_3 (1 equiv)	19
3	Cs_2CO_3 (1 equiv)	12
4	$NaHCO_3$ 1 equiv)	15
5	K_2HPO_4 (2 equiv)	14
6	Na_2HPO_4 (2 equiv)	26
7	K_2CO_3 (2 equiv)	52
8	Na_2CO_3 (2 equiv)	30
9	Na_3PO_4 (2 equiv)	46
10	K_3PO_4 (2 equiv)	16
11	$NaHCO_3$ (2 equiv)	16
12	KH_2PO_4 (2 equiv)	26
13	NaH_2PO_4 (2 equiv)	13
14	LiOAc (2 equiv)	11
15	NaOAc (2 equiv)	23
16	KOAc (2 equiv)	20
17	Et_3N (2 equiv)	40
18	DBU (2 equiv)	25
19	DIPEA (2 equiv)	33
20	K_2CO_3 (3 equiv)	69
21	Na_3PO_4 (3 equiv)	60

[a]crude NMR yield was calculated using 1,1,2,2 tetrachloroethane as the internal standard

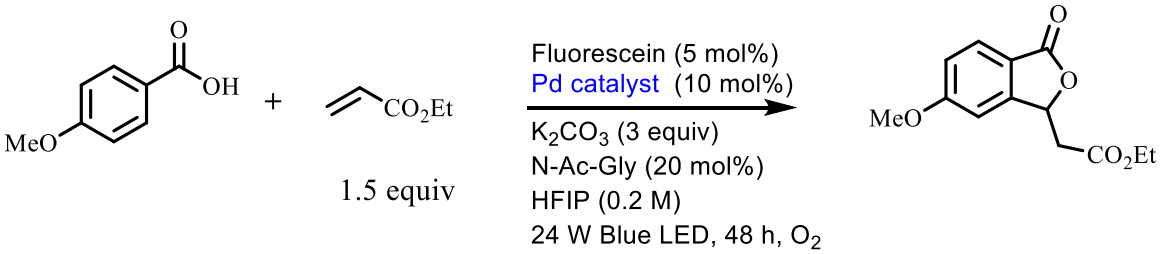
Table S2: Optimisation of photocatalysts



Entry	Photocatalyst (5 mol%)	Crude NMR yield (%)
1	Fluorescein	69
2	Eosin Y	50
3	$Ru(bpy)_3Cl_2$	32
4	Rose Bengal	Trace
5	4-CzIPN	39
6	$Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$	30
7	$Ru(bpm)_3Cl_2$	22
8	$Ru(bpz)_3PF_6$	25
9[a]	No PC	n.r
10[b]	No PC	n.r
11[c]	Fluorescein	n.r

[a]Reaction in the absence of light and O_2, [b]Reaction in the absence of light and in presence of O_2, [c]Reaction in the absence of O_2, and in presence of light.

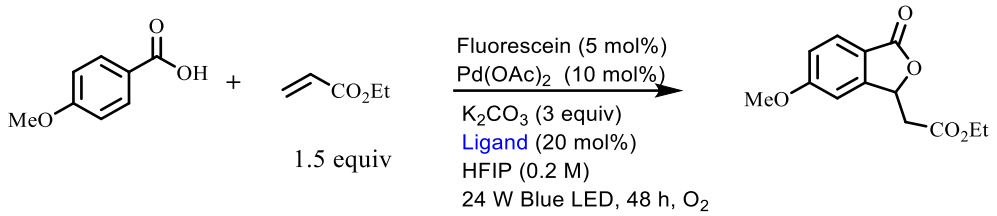
Table S3: Optimisation of Pd catalysts



Entry	Pd catalyst (10 mol%)	Crude NMR yield (%)
1	$Pd(OAc)_2$	69
2	$Pd(TFA)_2$	49
3	$PdCl_2$	32
4	$Pd(PPh_3)_2Cl_2$	Trace

5	$Pd(acac)_2$	30
6	$PdBr_2$	-
7	$Pd(MeCN)_2Cl_2$	35
8	$Pd(PCy_3)_2Cl_2$	-
9	$Pd(OPiv)_2$	32
10	$Pd(C_6H_5CN)_2Cl_2$	29
11	$Pd(PPh_3)_4$	-

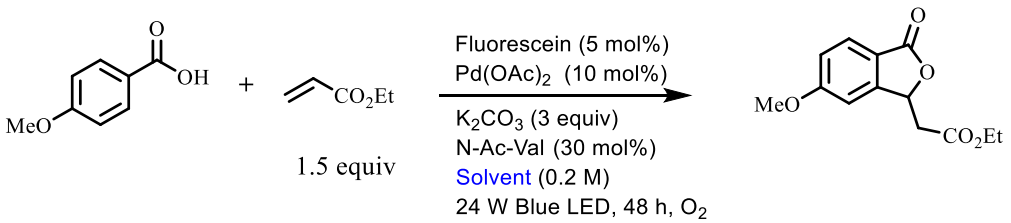
Table S4: Optimisation of ligands



Entry	Ligand (20 mol%)	Crude NMR yield (%)
1	N-Ac-Gly	69
2	N-Formyl-Gly	19
3	N-Ac-Phenyl-Ala	31
4	N-Ac-L-Leucine	43
5	N-Ac-L-Valine	72
6	N-Boc-Glycine	-
7	N-Boc-L-Alanine	-
8	N-Boc-Val	Trace
9	N-Fmoc-Gly	-
10	N-Fmoc-L-Leu	-
11	N-Ac-L-Valine (30 mol%)	82 (79)[a]
12	No ligand	trace

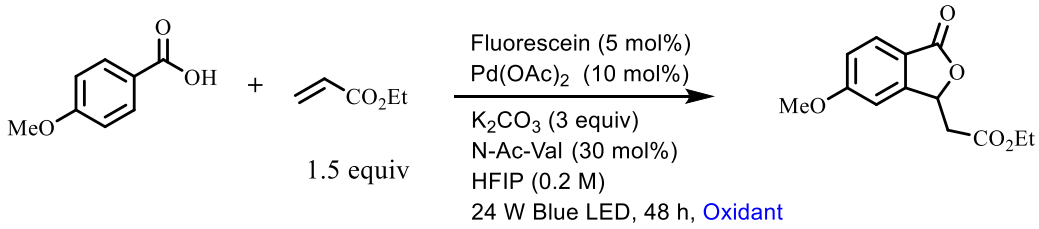
[a]Isolated yield

Table S5: Optimisation of solvents



Entry	Solvent	Crude nmr yield (%)
1	HFIP	82
2	TFE	-
3	$PhCF_3$	-
4	MeOH	-
5	DCE	-
6	HFIP + AcOH (9:1)	30
7	TFA	22
8	^{t}AmOH	-
9	MeCN	-
10	THF	-

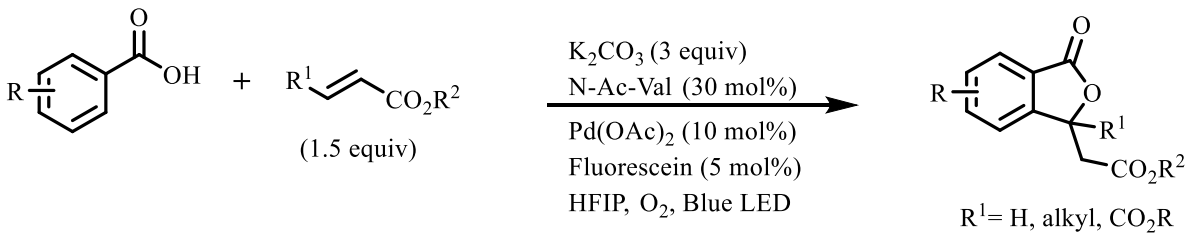
Table S6: Optimisation of oxidants



Entry	Oxidant (1 equiv)	Crude NMR yield (%)
1[a]	O_2	82
2	H_2O_2	47
3	$K_2S_2O_8$	55
4	$(NH_4)_2S_2O_8$	50

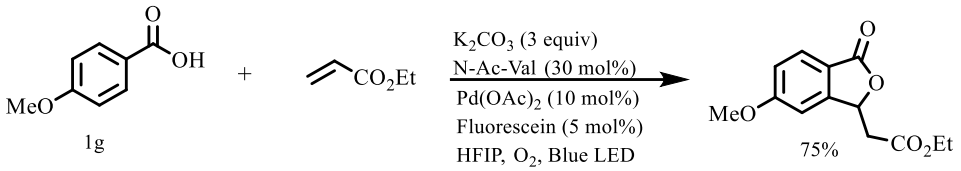
[a]Oxygen balloon was used

2.2 General procedure for the synthesis of products



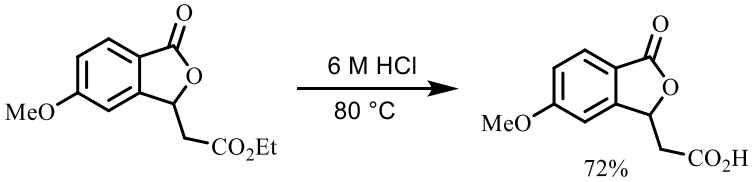
To an oven dried 4 mL vial containing a magnetic stir bar, was added aryl carboxylic acid (0.2 mmol), corresponding acrylate (0.3 mmol), K_2CO_3 (83 mg, 0.6 mmol), N-Ac-Val (9.5 mg, 0.06 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and Fluorescein (3.3 mg, 0.01 mmol) in 2 mL of HFIP. The reaction mixture was irradiated under 24 W blue LED (452 nm) at room temperature in presence of oxygen (balloon was used) and stirred until the disappearance of starting materials (based on TLC) for 16-48 h. After the completion of reaction, solvent was evaporated under reduced pressure and the remaining residue was diluted with ethyl acetate and washed with saturated $NaHCO_3$ solution. The aqueous layer was extracted with EtOAc (2X) and the combined organic layers were concentrated under reduced pressure. The crude residue was purified by column chromatography using EtOAc/hexane.

2.3 General procedure for gram scale synthesis



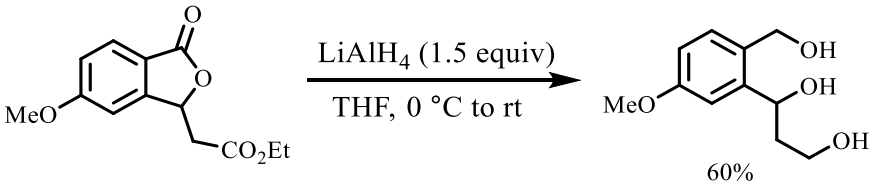
Same procedure as described in section 2.2 was followed for the gram scale synthesis of isobenzofuranone derivative. The corresponding lactone product was obtained in 75% yield.

2.4 Selective hydrolysis of the ester



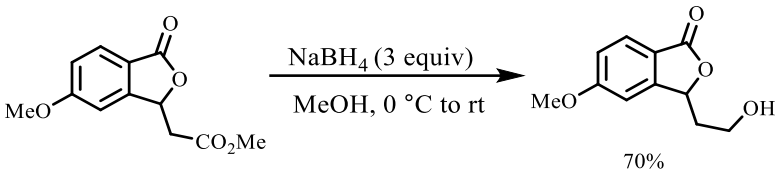
To a round bottom flask containing the ester (50 mg, 0.2 mmol), was added 2 ml of 6 M HCl and the reaction mixture was heated at 80 ºC for 12 h. [1] The reaction mixture was then cooled to room temperature, and extracted with DCM. The organic phase was dried with anhydrous Na_2SO_4, and the solvent was removed under vacuum. The residue was purified by column chromatography to afford the corresponding acid (31 mg, 72%).

2.5 Reduction with $LiAlH_4$



To a solution of lactone (50 mg, 0.2 mmol) in THF (2.0 mL) was added 0.3 mL of LAH solution (1.0 M in THF) at 0 ºC, and the reaction mixture was brought to room temperature and stirred for 1 h. The reaction mixture was then quenched with $Na_2SO_4.10H_2O$ (10 mg) followed by water (2 mL), and then extracted with DCM.[1] The organic phase was dried with anhydrous Na_2SO_4, and the solvent was removed under vacuum. The residue was purified by column chromatography to afford the ring opening product (25 mg, 60%).

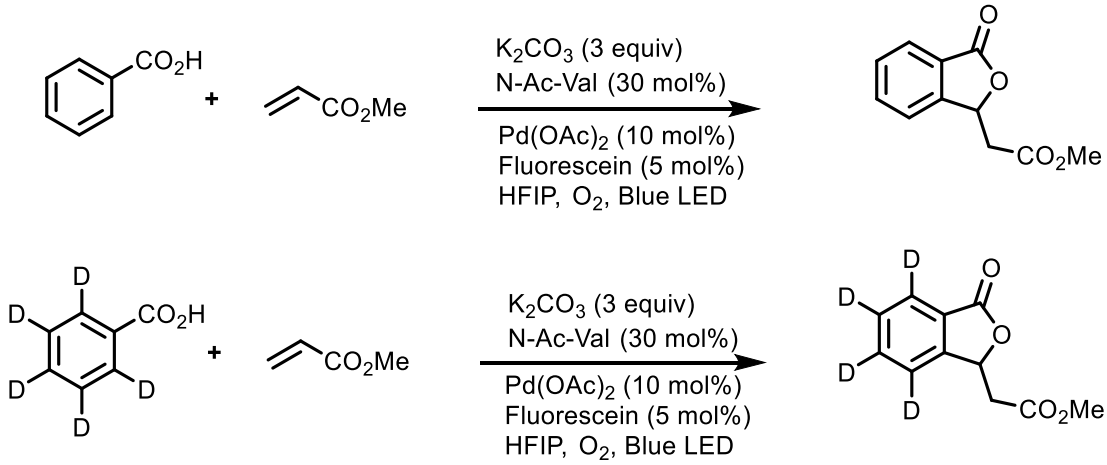
2.6 Reduction with $NaBH_4$



To a solution of lactone (50 mg, 0.2 mmol) in MeOH (2.0 mL) was added $NaBH_4$ (23 mg, 0.6 mmol) at 0 ºC and the reaction mixture was brought to room temperature and stirred for 6 h. The reaction mixture was quenched with 1N HCl, and then extracted with DCM. The organic phase was dried with anhydrous Na_2SO_4, and the solvent was removed under vacuum. The residue was purified by column chromatography to afford the corresponding alcohol (31 mg, 70%).

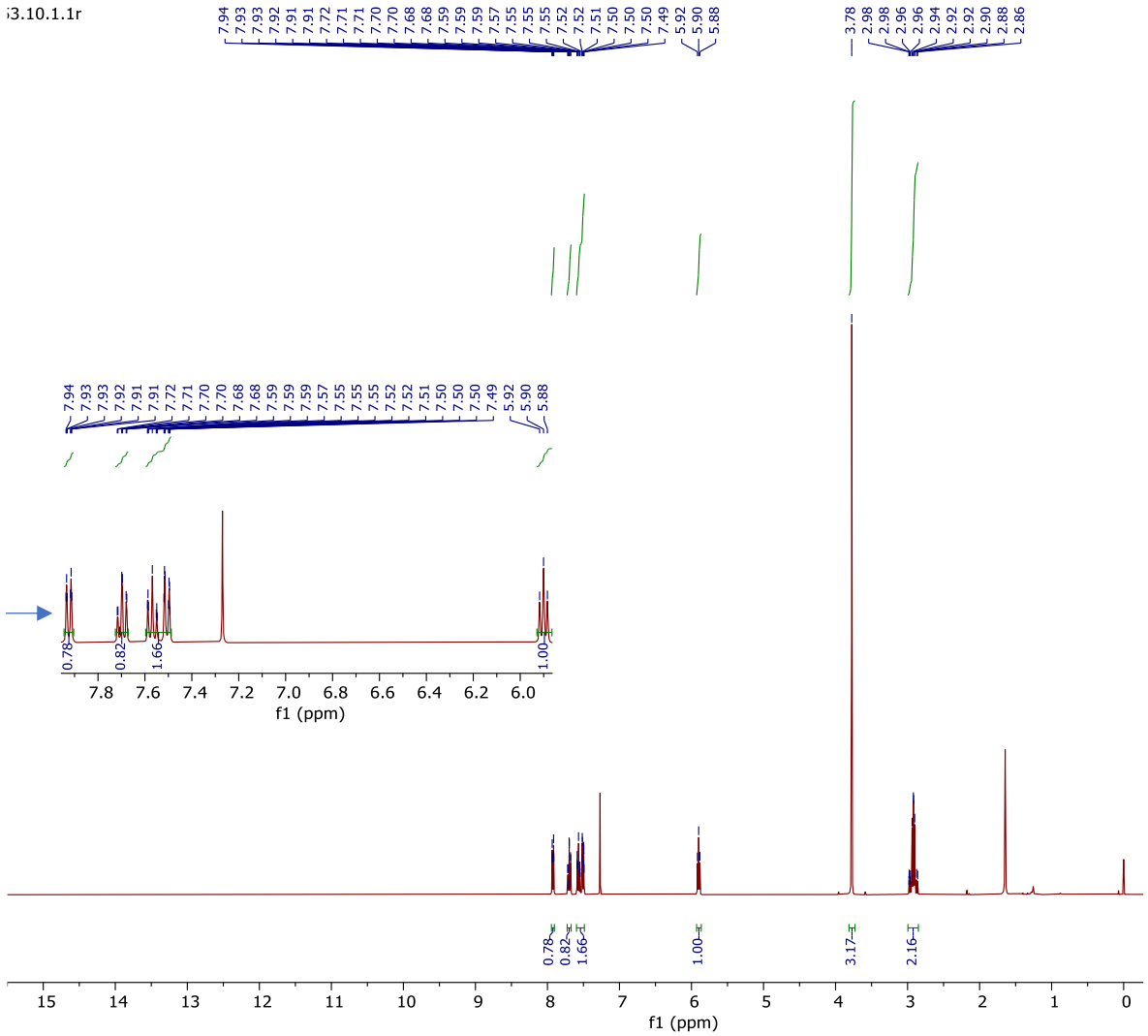
2.7 Kinetic Isotope Effect experiments

a) Parallel KIE experiment between benzoic acid and benzoic acid d5

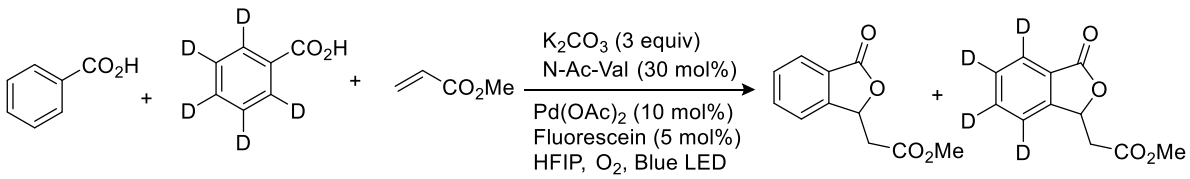


Two separate oven dried 4 mL vial containing a magnetic stir bar was taken and to this was added benzoic acid (12 mg, 0.1 mmol) in one vial and in another vial benzoic acid d-5 (13 mg, 0.1 mmol) was added. To both the vials methyl acrylate (13 µl, 0.15 mmol), K_2CO_3 (40 mg, 0.3 mmol), N-Ac-Val (4.6 mg, 0.03 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and Fluorescein (1.6

mg, 0.005 mmol) in 1 mL of HFIP was added. The reaction mixture was irradiated under 24 W blue LED (452 nm) at room temperature in presence of oxygen (balloon was used) for 12 h. Then both the reaction mixtures were quenched at the same time, and the two mixtures combined, filtered, concentrated in vacuum, and purified by column chromatography to give the corresponding products.[2] The products were analyzed by 1H NMR and KIE value for parallel competition experiment was found to be 3.5 (K_H/K_D = 3.5).

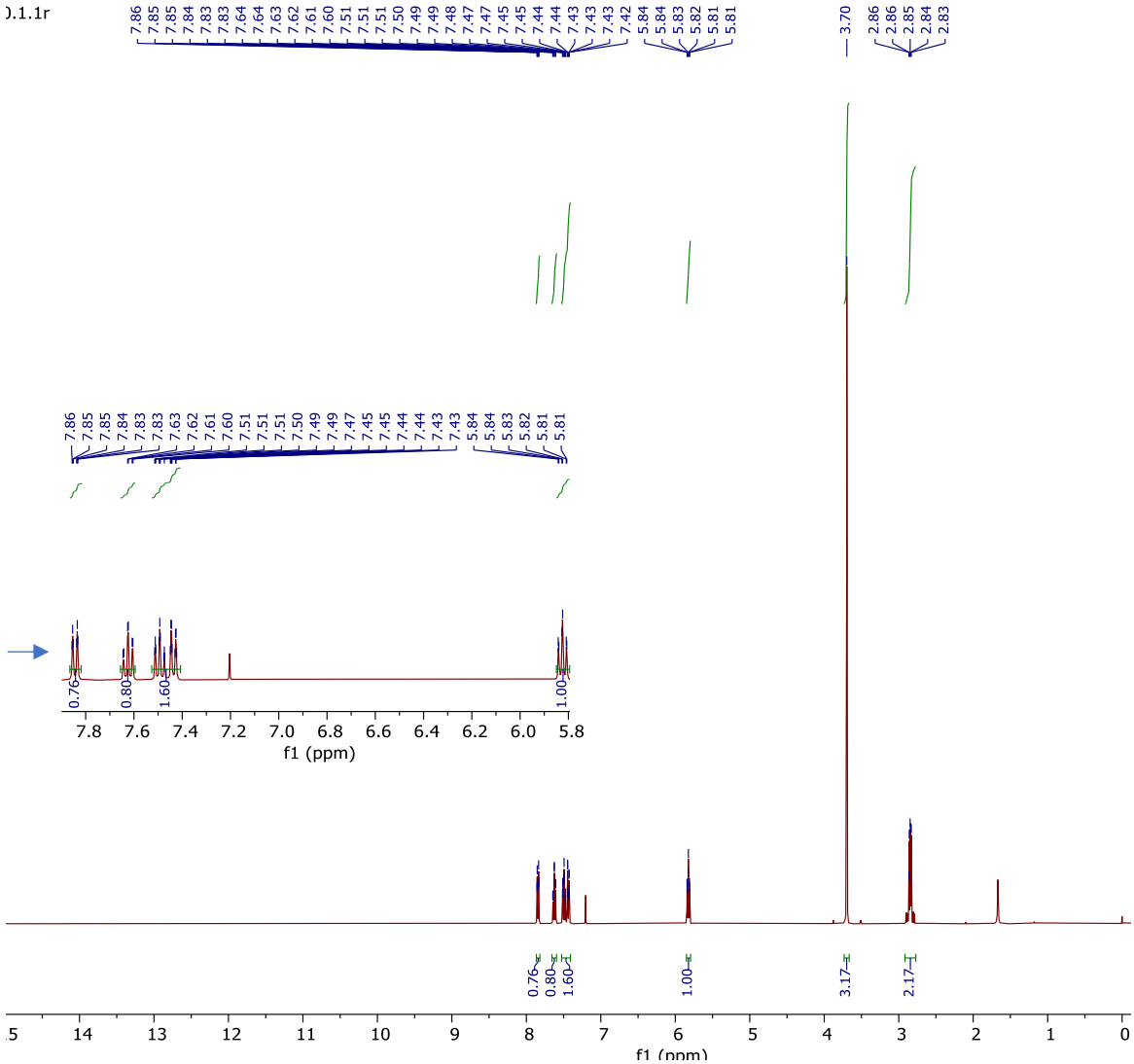


b) Intermolecular KIE experiment between benzoic acid and benzoic acid d5



To an oven dried 4 mL vial containing a magnetic stir bar, was added benzoic acid (6 mg, 0.05 mmol), benzoic acid d-5 (7 mg, 0.05 mmol), methyl acrylate (13 µl, 0.15 mmol), K_2CO_3 (40

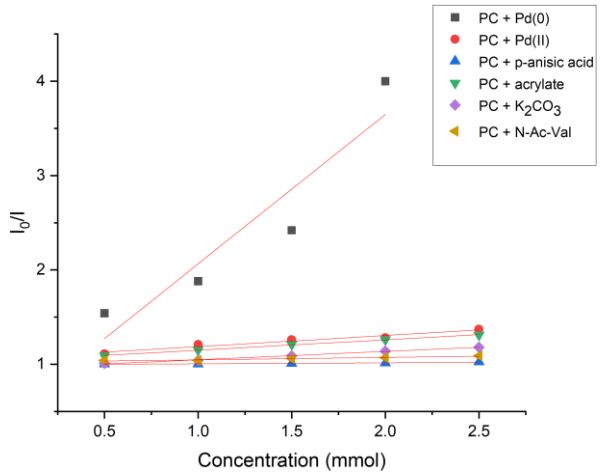
mg, 0.3 mmol), N-Ac-Val (4.6 mg, 0.03 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and Fluorescein (1.6 mg, 0.005 mmol) as photocatalyst in 2 mL of HFIP. The reaction mixture was irradiated under 24 W blue LED (452 nm) at room temperature in presence of oxygen (balloon) for 12 h. After the solvent evaporation, the residue was purified by column chromatography with petroleum ether/ethyl acetate as the eluent giving the desired products. The product was analyzed by ^{1}H NMR and KIE value for intermolecular competition experiment was found to be 3.2 ($K_H/K_D = 3.2$).



2.8 Stern-Volmer Quenching studies

Stern-Volmer studies has been performed by adding various concentrations of Pd(0), Pd(II), p-anisic acid, ethyl acrylate, K_2CO_3 and N-Ac-Val separately to a freshly prepared 0.25 mM solution of fluorescein in HFIP. The solution was excited at 450 nm and the luminescence was measured over the range of 470-800 nm. We repeated this experiment two times and the

average was taken to plot a graph with I_0/I on the Y-axis and the quencher concentration on the X-axis. Note: $Pd(PPh_3)_4$ was used as Pd(0) source for the quenching study



3. Crystallographic data

General data collection and structure solution details:

X-ray data for the compound was collected at room temperature on a Bruker D8 VENTURE diffractometer instrument with an IμS 3.0 Mo source (λ = 0.7107 Å) and a PHOTON-III C28 detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 4 software suite programs. The structure was refined with the SHELXL2 program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. CCDC contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/.

3.1 Crystallographic data 3e

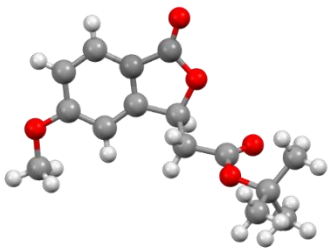


Figure S1. Crystal structure of 3e

Table S6: Crystal data and structure refinement of 3e

CCDC number	2376512
Crystal data	

Chemical formula	$C_{15}H_{18}O_5$
M_r	278.29
Crystal system, space group	Orthorhombic, Fdd2
Temperature (K)	100.00
a, b, c (Å)	15.9986(7), 28.8588(12), 12.5342(5)
β (°)	90
V (Å^3)	5787.0(4)
Z	16
Radiation type	MoKα
μ (mm^{-1})	0.096
Crystal size (mm^3)	0.9 × 0.12 × 0.08
Data collection	
Diffractometer	Bruker D8 Venture
Absorption correction	-
No. of measured, independent and observed [I > 2σ(I)] reflections	57843, 3594, 2581
R_{int}	0.0394
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	-0.772
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.0266, 0.0641, 1.098
No. of reflections	2604
No. of parameters	186
H-atom treatment	H atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.28/-0.17

3.2 Crystallographic data 5u

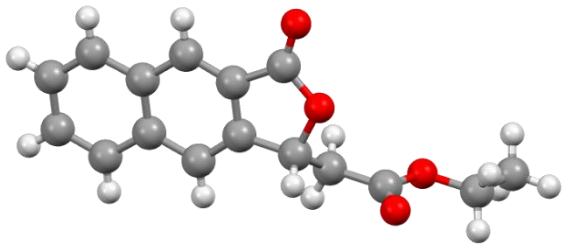


Figure S1. Crystal structure of 5u

Table S7: Crystal data and structure refinement of 5u

CCDC number	2376513
Crystal data	
Chemical formula	$C_{16}H_{14}O_4$
M_r	270.27
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	100.00
a, b, c (Å)	4.7983(2), 12.3215(6), 22.0080(11)
β (°)	90
V (Å^3)	1301.16(11)
Z	4

Radiation type	MoKα
μ (mm^{-1})	0.099
Crystal size (mm^3)	0.1 × 0.08 × 0.05
Data collection	
Diffractometer	Bruker D8 Venture
Absorption correction	-
No. of measured, independent and observed [I > 2σ(I)] reflections	31758, 3232, 3241
R_{int}	0.0365
$(\sin \theta/\lambda)_{max}$ ($Å^{-1}$)	0.821
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.0348, 0.0932, 1.034
No. of reflections	3232
No. of parameters	183
H-atom treatment	H atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	0.43/-0.17

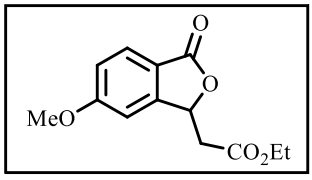
4. References

1. Z. Zhuang, C. Bin Yu, G. Chen, Q. F. Wu, Y. Hsiao, C. L. Joe, J. X. Qiao, M. A. Poss, J. Q. Yu, *J. Am. Chem. Soc.* **2018**, *140*, 10363–10367.

2. P. Muthuraja, R. Usman, R. Sajeev, P. Gopinath, *Org Lett* **2021**, *23*, 6014–6018.

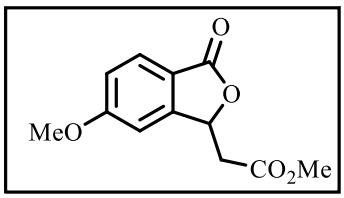
5. Analytical data of compounds

Ethyl 2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3a):



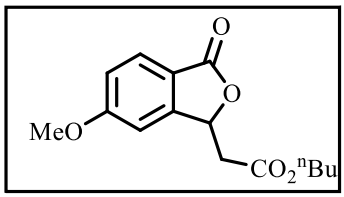
Yield (0.2 mmol scale, 39 mg, 79%), yellowish oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.5 Hz, 1H), 6.98 (dd, J = 8.5, 2.2 Hz, 1H), 6.87 (d, J = 2.1 Hz, 1H), 5.73 (t, J = 6.6 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 2.82 (qd, J = 16.5, 6.6 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.66, 169.41, 164.86, 151.63, 127.36, 118.16, 116.76, 106.28, 76.31, 61.29, 55.89, 39.66, 14.15. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{13}H_{14}O_5^+$ 251.0919; found 251.0917.

Methyl 2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3b):



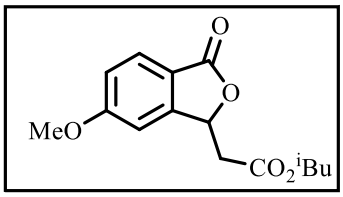
Yield (0.2 mmol scale, 33 mg, 70%), white solid. m.p: 106.5-109 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.5 Hz, 1H), 6.98 (dd, J = 8.5, 2.2 Hz, 1H), 6.86 (d, J = 2.1 Hz, 1H), 5.73 (t, J = 6.7 Hz, 1H), 3.83 (s, 3H), 3.70 (s, 3H), 2.82 (qd, J = 16.5, 6.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.88, 169.58, 164.88, 151.53, 127.43, 118.14, 116.74, 106.32, 76.23, 55.89, 52.24, 39.48. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{12}H_{12}O_5^+$ 237.0757; found 237.0760.

n-Butyl-2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3c):



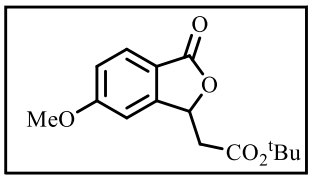
Yield (0.2 mmol scale, 41 mg, 74%), yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.5, 2.2 Hz, 1H), 6.94 (d, J = 2.2 Hz, 1H), 5.80 (t, J = 6.6 Hz, 1H), 4.17 (t, J = 6.7 Hz, 2H), 3.90 (s, 3H), 3.04 – 2.78 (m, 2H), 1.64 (td, J = 15.7, 8.3 Hz, 2H), 1.42 - 1.33 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.64, 169.49, 164.86, 151.65, 127.36, 118.18, 116.76, 106.26, 76.31, 65.18, 55.87, 39.64, 30.55, 19.08, 13.67. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{15}H_{19}O_5^+$ 279.1227; found 279.1224.

Isobutyl 2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3d):



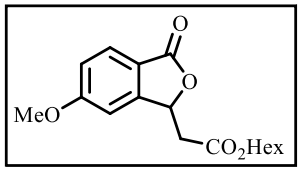
Yield (0.2 mmol scale, 39 mg, 70%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.5 Hz, 1H), 6.97 (dd, J = 8.6, 2.1 Hz, 1H), 6.87 (d, J = 2.2 Hz, 1H), 5.73 (t, J = 6.6 Hz, 1H), 3.88 (dd, J = 6.7, 1.7 Hz, 2H), 3.82 (s, 3H), 2.92 – 2.75 (m, 2H), 1.87 (dt, J = 13.4, 6.7 Hz, 1H), 0.86 (dd, J = 6.7, 2.1 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.66, 169.47, 164.87, 151.64, 127.33, 118.13, 116.81, 106.22, 76.33, 71.34, 55.89, 39.60, 27.65, 19.05. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{15}H_{19}O_5^+$ 279.1227; found 279.1223.

tert-Butyl-2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3e):



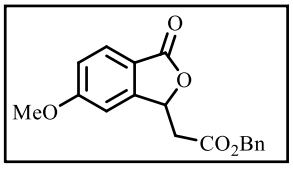
Yield (0.2 mmol scale, 43 mg, 78%), white crystalline solid. m.p: 115.8-118.2 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.5, 2.2 Hz, 1H), 6.94 (s, 1H), 5.77 (t, J = 6.6 Hz, 1H), 3.89 (s, 3H), 2.93 – 2.69 (m, 2H), 1.47 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.83, 168.60, 164.81, 151.90, 127.24, 118.23, 116.86, 106.11, 81.96, 76.60, 55.85, 40.68, 28.01. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{15}H_{19}O_5^+$ 279.1227; found 279.1219.

Hexyl-2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3f):



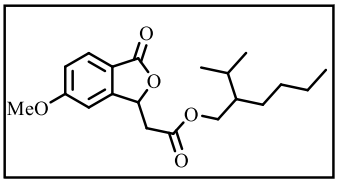
Yield (0.2 mmol scale, 44 mg, 72%), white sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.5, 2.2 Hz, 1H), 6.95 (d, J = 2.1 Hz, 1H), 5.80 (t, J = 6.6 Hz, 1H), 4.16 (t, J = 6.8 Hz, 2H), 3.90 (s, 3H), 2.90 (qd, J = 16.5, 6.6 Hz, 2H), 1.72 – 1.55 (m, 2H), 1.31 (d, J = 2.6 Hz, 6H), 0.95 – 0.84 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.66, 169.50, 164.85, 151.64, 127.33, 118.14, 116.76, 106.27, 76.32, 65.48, 55.88, 39.61, 31.38, 28.47, 25.52, 22.50, 14.00. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{17}H_{23}O_5^+$ 307.1545; found 307.1550.

Benzyl-2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3g):



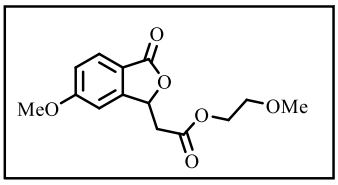
Yield (0.2 mmol scale, 47 mg, 75%), yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.5 Hz, 1H), 7.28 (d, J = 3.6 Hz, 5H), 6.95 (dd, J = 8.5, 2.2 Hz, 1H), 6.80 (d, J = 2.2 Hz, 1H), 5.73 (t, J = 6.6 Hz, 1H), 5.20 – 5.07 (m, 2H), 3.75 (s, 3H), 2.98 – 2.74 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.59, 169.22, 164.88, 151.53, 135.27, 128.68, 128.55, 128.48, 127.37, 118.11, 116.92, 106.15, 76.19, 67.07, 55.84, 39.64. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{18}H_{17}O_5^+$ 313.1076; found 313.1072.

2-Isopropylhexyl-2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3h):



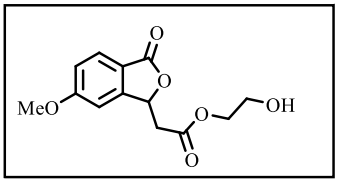
Yield (0.2 mmol scale, 47 mg, 71%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) 7.80 (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.5, 2.2 Hz, 1H), 6.95 (d, J = 2.2 Hz, 1H), 5.80 (t, J = 6.6 Hz, 1H), 4.09 (q, J = 5.4 Hz, 2H), 3.90 (s, 3H), 2.91 (qd, J = 16.5, 6.6 Hz, 2H), 1.58 (d, J = 5.9 Hz, 1H), 1.42 – 1.21 (m, 7H), 0.89 (t, J = 7.3 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.63, 169.58, 164.86, 151.65, 127.33, 118.15, 116.76, 106.25, 76.31, 67.70, 55.87, 39.62, 38.66, 30.32, 30.26, 28.88, 23.67, 22.92, 14.04, 10.94. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{20}H_{29}O_5^+$ 335.1853; found 335.1859.

2-Methoxyethyl-2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3i):



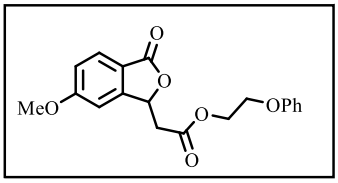
Yield (0.2 mmol scale, 38 mg, 68%), colourless sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ .74 (d, J = 8.5 Hz, 1H), 6.98 (dd, J = 8.5, 2.2 Hz, 1H), 6.88 (d, J = 2.1 Hz, 1H), 5.74 (t, J = 6.7 Hz, 1H), 4.29 – 4.22 (m, 2H), 3.83 (s, 3H), 3.58 – 3.51 (m, 2H), 3.32 (s, 3H), 2.98 – 2.77 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.64, 169.40, 164.89, 151.55, 127.38, 118.10, 116.78, 106.35, 76.20, 70.21, 64.21, 59.01, 55.89, 39.53. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{14}H_{17}O_6^+$ 281.1020; found 281.1033.

2-Hydroxyethyl-2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3j):



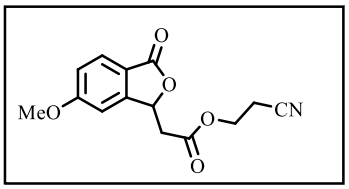
Yield (0.2 mmol scale, 33 mg, 65%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) 7.79 (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.5, 2.2 Hz, 1H), 6.96 (d, J = 2.1 Hz, 1H), 5.81 (t, J = 6.5 Hz, 1H), 4.29 (td, J = 4.2, 1.4 Hz, 2H), 3.90 (s, 3H), 3.88 – 3.79 (m, 2H), 3.02 – 2.87 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.92, 169.61, 164.99, 151.49, 127.33, 117.89, 116.93, 106.24, 76.37, 66.75, 60.69, 55.95, 39.48. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{13}H_{15}O_6^+$ 267.0869; found 267.0878.

2-Phenoxyethyl-2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3k):



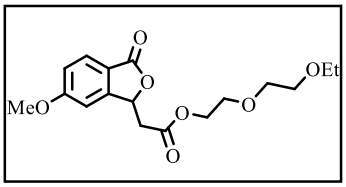
Yield (0.2 mmol scale, 42 mg, 62%), yellowish sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.5 Hz, 1H), 7.33 – 7.24 (m, 2H), 7.10 – 6.84 (m, 5H), 5.80 (t, J = 6.6 Hz, 1H), 4.57 – 4.46 (m, 2H), 4.23 – 4.13 (m, 2H), 3.87 (s, 3H), 3.04 – 2.86 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.63, 169.32, 164.89, 158.32, 151.45, 129.57, 127.37, 121.32, 118.09, 116.74, 114.61, 106.35, 76.14, 65.58, 63.61, 55.90, 39.46. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{19}H_{19}O_6^+$ 343.1176; found 343.1189.

2-cyanoethyl-2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (3l):



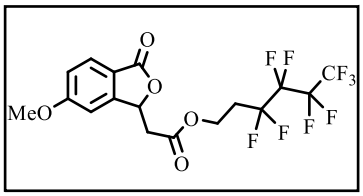
Yield (0.2 mmol scale, 33 mg, 60%), white sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.5 Hz, 1H), 7.00 (dd, J = 8.5, 2.2 Hz, 1H), 6.86 (d, J = 2.1 Hz, 1H), 5.77 – 5.70 (m, 1H), 4.40 – 4.23 (m, 2H), 3.84 (s, 3H), 2.99 – 2.80 (m, 2H), 2.76 – 2.59 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.49, 168.81, 164.99, 151.12, 127.50, 118.05, 116.93, 116.58, 106.17, 75.89, 59.34, 55.97, 39.29, 17.98. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{14}H_{14}NO_5^+$ 276.0866; found 276.0875.

2-(2-ethoxyethoxy)ethyl-2-(6-methoxy-oxo-1,3dihydroisobenzofuran-1-yl)acetate (3m):



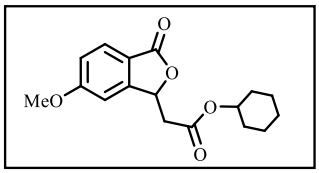
Yield (0.2 mmol scale, 43 mg, 64%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.5, 2.2 Hz, 1H), 6.96 (d, J = 2.1 Hz, 1H), 5.81 (t, J = 6.7 Hz, 1H), 4.34 (dd, J = 6.0, 3.6 Hz, 2H), 3.90 (s, 3H), 3.77 – 3.70 (m, 2H), 3.69 – 3.64 (m, 2H), 3.61 – 3.58 (m, 2H), 3.52 (q, J = 7.0 Hz, 2H), 2.94 (qd, J = 16.6, 6.7 Hz, 2H), 1.20 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.63, 169.38, 164.87, 151.56, 127.31, 118.04, 116.78, 106.34, 76.22, 70.64, 69.74, 68.87, 66.67, 64.30, 55.90, 39.54, 15.13. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{17}H_{23}O_7^+$ 339.1448; found 339.1468.

3,3,4,4,5,5,6,6,6-Nonaflourohexyl-2-(6-methoxy-oxo-1,3dihydroisobenzofuran-1-yl)acetate (3n):



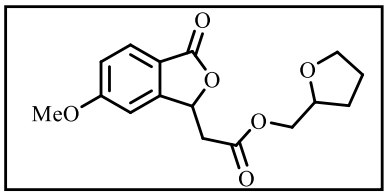
Yield (0.2 mmol scale, 55 mg, 59%), yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.5 Hz, 1H), 6.98 (dd, J = 8.5, 2.2 Hz, 1H), 6.85 (d, J = 2.1 Hz, 1H), 5.72 (t, J = 6.5 Hz, 1H), 4.40 (q, J = 6.5 Hz, 2H), 3.82 (s, 3H), 2.92 – 2.77 (m, 2H), 2.51 – 2.33 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.53, 168.97, 164.95, 151.25, 127.43, 118.06, 116.82, 106.19, 75.96, 56.99, 55.86, 39.36, 30.27 (t, $J_{C\text{-}F}$ = 21.8 Hz). **^{19}F NMR** (377 MHz, $CDCl_3$) δ -81.05, -113.90, -113.93, -124.53, -124.55, -124.57, -126.03, -126.06, -126.09. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{17}H_{14}F_9O_5^+$ 469.0692; found 469.0706.

Cyclohexyl-2-(6-methoxy-oxo-1,3dihydroisobenzofuran-1-yl)acetate (3o):



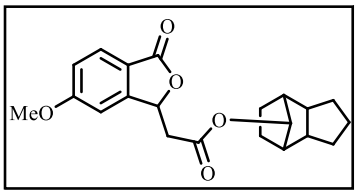
Yield (0.2 mmol scale, 41 mg, 69%), white solid. m.p: 102.2-105 ºC. **H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.5, 2.2 Hz, 1H), 6.94 (d, J = 2.2 Hz, 1H), 5.80 (t, J = 6.6 Hz, 1H), 4.84 (dt, J = 9.0, 4.7 Hz, 1H), 3.89 (s, 3H), 3.02 – 2.76 (m, 2H), 1.94 – 1.78 (m, 2H), 1.72 (s, 2H), 1.61 – 1.19 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.70, 168.79, 164.84, 151.74, 127.30, 118.23, 116.79, 106.21, 76.42, 73.88, 55.87, 39.90, 31.53, 25.25, 23.69.. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{17}H_{21}O_5^+$ 305.1384; found 305.1385.

Tetrahydrofuran-2-yl 2-(6-methoxy-oxo-1,3dihydroisobenzofuran-1-yl)acetate (3p):



Yield (0.2 mmol scale, 39 mg, 65%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.5, 2.2 Hz, 1H), 6.96 (s, 1H), 5.82 (t, J = 6.7 Hz, 1H), 4.25 (d, J = 7.7 Hz, 1H), 4.18 – 4.06 (m, 2H), 3.90 (s, 3H), 3.89 – 3.84 (m, 1H), 3.83 – 3.77 (m, 1H), 3.04 – 2.85 (m, 2H), 2.11 – 1.97 (m, 1H), 1.89 (d, J = 35.4 Hz, 2H), 1.62 (dd, J = 13.7, 6.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.63, 169.36, 169.32, 164.90, 151.57, 127.32, 118.04, 116.90, 116.87, 106.28, 106.24, 76.30, 76.26, 76.21, 68.46, 67.15, 55.90, 39.55, 27.93, 25.66. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{16}H_{19}O_6^+$ 307.1173; found 307.1186.

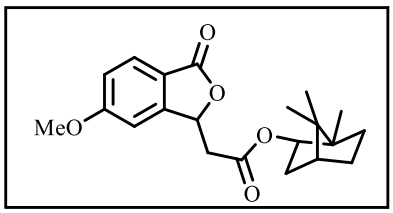
Dicyclopentanyl-2-(6-methoxy-oxo-1,3dihydroisobenzofuran-1-yl)acetate (3q):



Yield (0.2 mmol scale, 44 mg, 62%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.5 Hz, 1H), 6.97 (dd, J = 8.5, 2.2 Hz, 1H), 6.87 (s, 1H), 5.70 (t, J = 6.5 Hz, 1H), 4.57 (d, J = 6.9 Hz, 1H), 3.82 (d, J = 1.9 Hz, 3H), 2.90 – 2.70 (m, 2H), 1.99 (d, J = 18.9 Hz, 2H), 1.87 – 1.52 (m, 6H), 1.36 (d, J = 10.8 Hz, 2H), 1.19 – 1.10 (m,

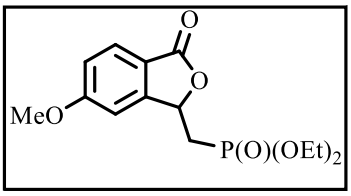
2H), 0.96 – 0.75 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.72, 169.16, 164.84, 151.71, 127.31, 118.20, 116.84, 106.17, 78.22, 76.44, 76.41, 55.89, 47.20, 46.11, 46.05, 42.90, 39.84, 39.51, 38.99, 38.92, 31.97, 31.63, 29.39, 29.35, 27.70. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{21}H_{25}O_5^+$ 357.1697; found 357.1702.

Isobornyl-2-(6-methoxy-oxo-1,3dihydroisobenzofuran-1-yl)acetate (3r):



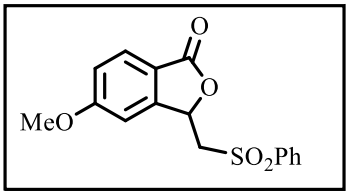
Yield (0.2 mmol scale, 42 mg, 60%), white sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.5 Hz, 1H), 6.97 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.87 (dd, *J* = 4.2, 2.2 Hz, 1H), 5.72 (td, *J* = 6.7, 3.9 Hz, 1H), 4.71 (ddd, *J* = 17.3, 7.5, 4.1 Hz, 1H), 3.82 (d, *J* = 1.6 Hz, 3H), 2.88 – 2.71 (m, 2H), 1.85 – 1.56 (m, 4H), 1.56 – 1.44 (m, 1H), 1.16 – 0.95 (m, 2H), 0.87 (d, *J* = 1.9 Hz, 3H), 0.80 – 0.75 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.69, 168.96, 168.91, 164.85, 127.32, 106.10, 76.42, 55.89, 46.95, 44.96, 26.98. 151.70 (d, J = 7.8 Hz), 118.12 (d, J = 3.5 Hz), 116.94 (d, J = 8.8 Hz), 82.10 (d, J = 16.0 Hz), 48.81 (d, J = 13.7 Hz), 39.99 (d, J = 3.6 Hz), 38.66 (d, J = 20.3 Hz), 33.65 (d, J = 6.6 Hz), 19.96 (d, J = 19.1 Hz), 11.55 (d, J = 3.7 Hz). **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{21}H_{27}O_5^+$ 359.1853; found 359.1861.

Diethyl((6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl)phosphonate (3s):



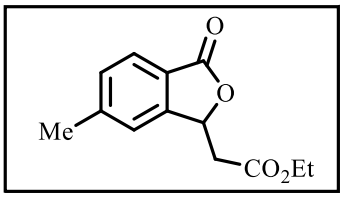
Yield (0.2 mmol scale, 28 mg, 45%), yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.5 Hz, 1H), 7.12 (d, *J* = 2.1 Hz, 1H), 7.05 (dd, *J* = 8.5, 2.2 Hz, 1H), 5.73 – 5.67 (m, 1H), 4.34 – 4.07 (m, 4H), 3.91 (s, 3H), 2.47 – 2.27 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.47, 164.91, 127.20, 117.84, 117.10, 106.43, 55.92, 152.07 (d, J = 9.9 Hz), 75.19 (d, $J_{C\text{-}P}$ = 2.9 Hz), 62.64 (d, $J_{C\text{-}P}$ = 6.4 Hz), 62.16 (d, $J_{C\text{-}P}$ = 6.5 Hz), 32.76, 31.35, 16.41 (dd, $J_{C\text{-}P}$ = 9.7, 6.2 Hz). **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{14}H_{20}O_6P^+$ 315.0992; found 315.1006.

5-methoxy-3-((phenylsulfonyl)methyl)isobenzofuran-1(3H)-one (3t):



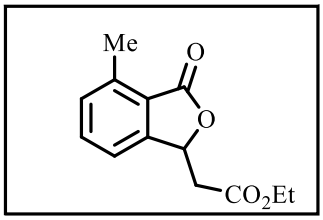
Yield (0.2 mmol scale, 31 mg, 49%), white solid. m.p: 167.6-170 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 – 7.88 (m, 2H), 7.72 – 7.60 (m, 2H), 7.60 – 7.50 (m, 2H), 7.05 – 6.95 (m, 2H), 5.81 (dd, *J* = 7.1, 4.5 Hz, 1H), 3.84 (s, 3H), 3.66 – 3.49 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.69, 165.21, 149.94, 139.02, 134.47, 129.53, 128.35, 127.47, 117.71, 117.59, 106.33, 74.03, 60.62, 56.05. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{16}H_{15}O_6S^+$ 319.0635; found 319.0643.

Ethyl 2-(6-methyl-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5a):



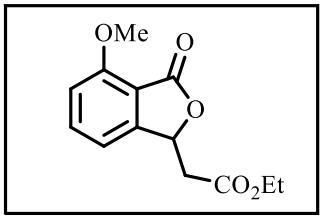
Yield (0.2 mmol scale, 35 mg, 75%), white solid. m.p: 98-100.2 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.8 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.21 (dt, *J* = 2.6, 1.3 Hz, 1H), 5.76 (t, *J* = 6.6 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.88 – 2.73 (m, 2H), 2.42 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.92, 168.34, 148.35, 144.58, 129.68, 124.56, 122.39, 121.37, 75.73, 60.23, 38.62, 21.09, 13.11. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{13}H_{15}O_4^+$ 235.0965; found 235.0972.

Ethyl 2-(4-methyl-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5b):



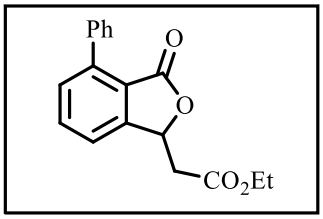
Yield (0.2 mmol scale, 32 mg, 70%), colourless oil .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (t, *J* = 7.6 Hz, 1H), 7.33 – 7.25 (m, 2H), 5.82 (t, *J* = 6.5 Hz, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 2.87 (d, *J* = 6.5 Hz, 2H), 2.69 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.11, 169.39, 149.29, 139.93, 133.98, 131.14, 123.41, 119.28, 76.09, 61.24, 39.80, 17.36, 14.13. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{13}H_{15}O_4^+$ 235.0965; found 235.0969.

Ethyl 2-(4-methoxy-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5c):



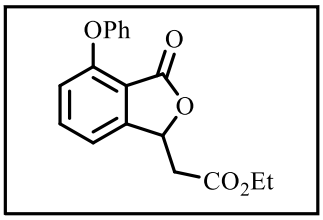
Yield (0.2 mmol scale, 36 mg, 72%), yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (t, *J* = 7.9 Hz, 1H), 6.92 (dd, *J* = 20.9, 7.9 Hz, 2H), 5.73 (t, *J* = 6.5 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 2.79 (d, *J* = 6.6 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H) **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.31, 167.94, 158.68, 151.58, 136.56, 113.58, 113.34, 111.15, 75.95, 61.27, 56.06, 39.74, 14.13. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{13}H_{15}O_5^+$ 251.0914; found 251.0923.

Ethyl 2-(3-oxo-4-phenyl-1,3dihydroisobenzofuran-1-yl)acetate (5d):



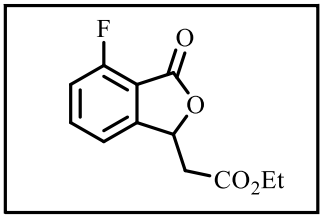
Yield (0.2 mmol scale, 38 mg, 65%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (t, *J* = 7.6 Hz, 1H), 7.54 (dd, J = 8.0, 1.7 Hz, 2H), 7.51 – 7.41 (m, 5H), 5.88 (t, *J* = 6.5 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.94 (dd, *J* = 6.6, 1.9 Hz, 2H), 1.33 – 1.21 (t, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.41, 168.66, 150.15, 142.99, 136.27, 134.06, 131.33, 129.53, 128.47, 128.04, 121.98, 120.74, 75.59, 61.31, 39.87, 14.15. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{18}H_{17}O_4^+$ 297.1121; found 297.1147.

Ethyl 2-(3-oxo-4-phenoxy-1,3dihydroisobenzofuran-1-yl)acetate (5e):



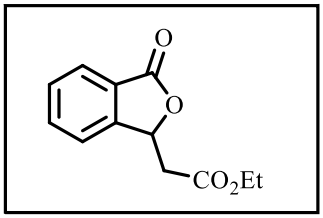
Yield (0.2 mmol scale, 42 mg, 68%), yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (t, *J* = 7.9 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.22 – 7.11 (m, 1H), 7.10 – 7.00 (m, 3H), 6.69 (d, *J* = 8.3 Hz, 1H), 5.79 (t, *J* = 6.5 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 2.92 – 2.76 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.28, 167.27, 157.19, 154.83, 151.49, 136.17, 130.07, 125.19, 120.75, 116.28, 115.41, 114.74, 76.07, 61.32, 39.74, 14.16. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{18}H_{17}O_5^+$ 313.1071; found 313.1076.

Ethyl 2-(4-flouro-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5f):



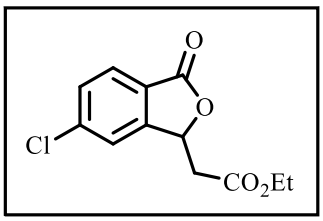
Yield (0.2 mmol scale, 39 mg, 58%), white solid. m.p: 50.2-52.3 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (td, *J* = 8.0, 4.6 Hz, 1H), 7.33 – 7.25 (m, 1H), 7.19 (t, *J* = 8.5 Hz, 1H), 5.92 – 5.84 (m, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.01 – 2.83 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.02, 165.91, 159.68 (d, $J_{C\text{-}F}$ = 265.0 Hz), 151.38, 136.90 (d, $J_{C\text{-}F}$ = 7.6 Hz), 118.06 (d, $J_{C\text{-}F}$ = 4.4 Hz), 116.63 (d, $J_{C\text{-}F}$ = 18.8 Hz), 113.89 (d, $J_{C\text{-}F}$ = 14.3 Hz), 76.64, 61.43, 39.41, 14.12. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -108.21. **HRMS** (ESI$^+$) m/z: [M + Na] $^+$ calcd for $C_{12}H_{11}NaFO_4$ $^+$ 261.0534; found 261.0536).

Ethyl 2-(3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5g):



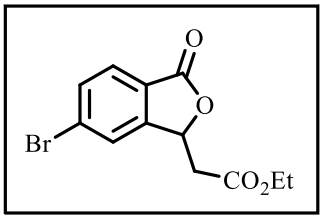
Yield (0.2 mmol scale, 30 mg, 69%), colourless sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.70 (td, *J* = 7.5, 1.1 Hz, 1H), 7.61 – 7.48 (m, 2H), 5.94 – 5.86 (m, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.99 – 2.83 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.94, 169.28, 148.80, 134.31, 129.58, 125.96, 125.86, 122.11, 76.74, 61.31, 39.57, 14.13. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{12}H_{13}O_4^+$ 221.0808; found 221.0797.

Ethyl 2-(6-chloro-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5h):



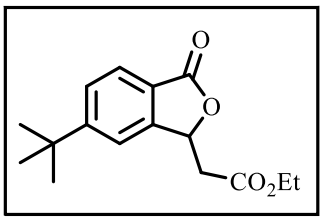
Yield (0.2 mmol scale, 30 mg, 60%), white sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.6 Hz, 1H), 7.50 – 7.43 (m, 2H), 5.77 (t, *J* = 6.6 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.91 (dd, *J* = 16.7, 6.6 Hz, 1H), 2.78 (dd, *J* = 16.7, 6.6 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.02, 167.73, 149.40, 140.02, 129.34, 125.99, 123.48, 121.79, 75.36, 60.44, 38.18, 13.09. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{12}H_{12}ClO_4^+$ 255.0419; found 255.0420.

Ethyl 2-(6-bromo-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5i):



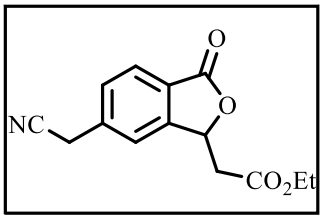
Yield (0.2 mmol scale, 34 mg, 58%), white solid. m.p: 90.2-93.5 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 – 7.66 (m, 1H), 7.66 – 7.58 (m, 2H), 5.78 (t, *J* = 6.6 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 2.98 – 2.69 (m, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.06, 168.92, 150.55, 133.24, 129.59, 127.13, 125.82, 124.98, 76.36, 61.48, 39.23, 14.14. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{12}H_{12}BrO_4^+$ 298.9913; found 298.9909.

Ethyl 2-(6-(tert-butyl)-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5j):



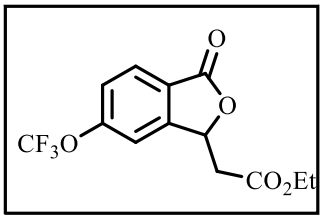
Yield (0.2 mmol scale, 38 mg, 70%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.1 Hz, 1H), 7.53 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.40 (dd, *J* = 1.6, 0.8 Hz, 1H), 5.80 (t, *J* = 6.6 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.91 – 2.75 (m, 2H), 1.30 (s, 9H), 1.22 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.02, 169.45, 158.82, 149.16, 127.30, 125.43, 123.29, 118.55, 76.73, 61.29, 39.85, 35.68, 31.26, 14.19. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{16}H_{21}O_4^+$ 277.1434; found 277.1438.

Ethyl 2-(6-(cyanomethyl)-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5k):



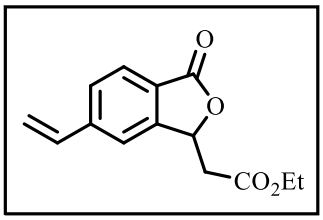
Yield (0.2 mmol scale, 31 mg, 60%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.8 Hz, 1H), 7.58 – 7.50 (m, 2H), 5.89 (t, *J* = 6.5 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.92 (s, 2H), 3.14 – 2.81 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.11, 169.03, 149.95, 136.81, 129.58, 126.66, 126.12, 121.88, 116.70, 76.80, 61.49, 39.27, 24.06, 14.14. **HRMS** (ESI^+) m/z: $[M + H]^+$ calcd for $C_{14}H_{14}NO_4^+$ 260.0917; found 260.0926.

Ethyl 2-(3-oxo-6-(triflouoromethoxy)-1,3dihydroisobenzofuran-1-yl)acetate (5l):



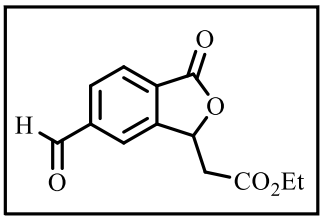
Yield (0.2 mmol scale, 37 mg, 62%), yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 – 7.85 (m, 1H), 7.33 (d, *J* = 12.0 Hz, 2H), 5.81 (t, *J* = 6.6 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 2.95 (dd, *J* = 16.6, 6.5 Hz, 1H), 2.79 (dd, *J* = 16.7, 6.8 Hz, 1H), 1.21 (t, *J* = 7.2 Hz, 3H) **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.00, 168.41, 153.66, 151.01, 127.79, 124.22, 122.25, 121.50, 120.21 (q, J_{C-F} = 259.7 Hz). 114.49, 76.46, 61.48, 39.19, 14.07. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -57.59. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{13}H_{12}F_3O_5$ $^+$ 305.0631; found 305.0654.

Ethyl 2-(3-oxo-6-vinyl-1,3dihydroisobenzofuran-1-yl)acetate (5m):



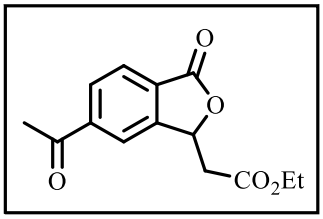
Yield (0.2 mmol scale, 33 mg, 68%), white sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.49 (s, 1H), 6.81 (dd, *J* = 17.5, 10.9 Hz, 1H), 6.03 – 5.78 (m, 2H), 5.48 (d, *J* = 10.9 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.00 – 2.83 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.67, 169.33, 149.49, 143.79, 135.68, 127.74, 126.01, 125.09, 119.53, 118.09, 76.85, 61.33, 39.59, 14.15. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{14}H_{15}O_4^+$ 247.0965; found 247.0966.

Ethyl 2-(6-formyl-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5n):



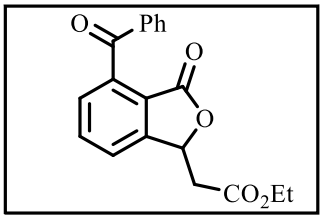
Yield (0.2 mmol scale, 31 mg, 64%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.09 (d, *J* = 0.8 Hz, 1H), 8.05 – 7.91 (m, 3H), 5.89 (t, *J* = 6.4 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.01 – 2.82 (m, 2H), 1.21 (t, *J* = 8.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.91, 168.95, 168.65, 149.31, 140.56, 131.21, 130.82, 126.70, 123.12, 77.24, 61.53, 39.10, 14.13. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{13}H_{13}O_5^+$ 249.0757; found 249.0760.

Ethyl 2-(6-acetyl-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5o):



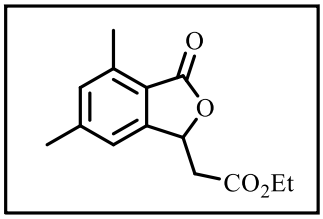
Yield (0.2 mmol scale, 35 mg, 68%), colourless sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 8.00 (m, 2H), 7.94 (d, J = 7.9 Hz, 1H), 5.87 (t, J = 6.4 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 2.97 – 2.81 (m, 2H), 2.62 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.89, 169.00, 168.90, 149.05, 141.77, 129.71, 129.61, 126.24, 121.95, 77.16, 61.49, 39.22, 27.16, 14.14. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{14}H_{15}O_5^+$ 263.0914; found 263.0919.

Ethyl 2-(4-benzoyl-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5p):



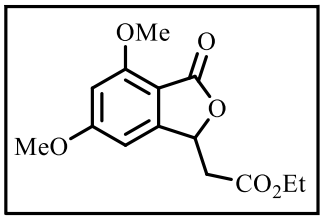
Yield (0.2 mmol scale, 43 mg, 67%), white sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 – 7.68 (m, 3H), 7.62 – 7.45 (m, 3H), 7.39 (t, *J* = 7.7 Hz, 2H), 5.88 (t, *J* = 6.6 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.89 (qd, *J* = 16.6, 6.5 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.54, 169.19, 167.56, 149.44, 139.22, 136.46, 134.19, 133.96, 129.91, 128.64, 128.51, 123.75, 123.56, 76.92, 61.45, 39.44, 14.16. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{19}H_{17}O_5^+$ 325.1071; found 325.1074.

Ethyl 2-(4,6-dimethyl-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5q):



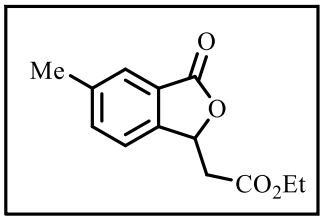
Yield (0.2 mmol scale, 34 mg, 69%), yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.02 (s, 1H), 6.99 (s, 1H), 5.68 (t, *J* = 6.5 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.77 (d, *J* = 6.6 Hz, 2H), 2.56 (s, 3H), 2.35 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.10, 168.46, 148.85, 144.16, 138.49, 131.20, 119.91, 118.68, 74.84, 60.18, 38.85, 20.89, 16.22, 13.11. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{14}H_{17}O_4^+$ 249.1121 ; found 249.1127.

Ethyl 2-(4,6-dimethoxy-3-oxo-1,3dihydroisobenzofuran-1-yl)acetate (5r):



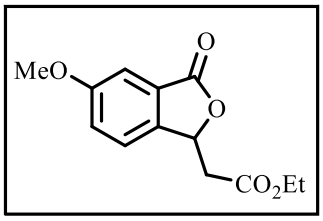
Yield (0.2 mmol scale, 40 mg, 73%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.42 (d, *J* = 16.0 Hz, 1H), 6.37 (d, *J* = 1.8 Hz, 1H), 5.65 (t, *J* = 6.6 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.88 (s, 3H), 3.81 (s, 3H), 2.86 – 2.69 (m, 2H), 1.21 (t, *J* = 8.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.46, 167.76, 166.93, 159.72, 153.85, 106.55, 99.10, 97.81, 75.66, 61.26, 56.06, 55.97, 39.83, 14.16. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{14}H_{17}O_6^+$ 281.1020; found 281.1024.

Ethyl 2-(5-methyl-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (5s):



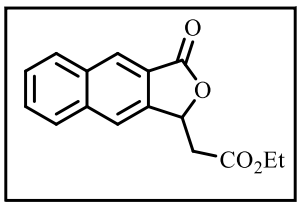
Yield (0.2 mmol scale, 32 mg, 70%), white solid. m.p: 101.2-104 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.53 – 7.46 (m, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 5.85 (t, *J* = 6.6 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.96 – 2.80 (m, 2H), 2.47 (d, *J* = 0.9 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) 170.09, 169.35, 146.19, 139.90, 135.43, 126.11, 125.79, 121.79, 76.94, 61.25, 39.69, 21.27, 14.14. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{13}H_{15}O_4^+$ 235.0965; found 235.0965.

Ethyl 2-(5-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (5t):



Yield (0.2 mmol scale, 36 mg, 72%), sticky white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 1H), 7.35 – 7.32 (m, 1H), 7.31 – 7.20 (m, 1H), 5.84 (t, *J* = 8.0 Hz, 1H), 4.22 (q, *J* = 8. 0 Hz, 2H), 3.88 (d, *J* = 1.2 Hz, 3H), 2.96 – 2.79 (m, 2H), 1.28 (td, *J* = 7.2, 1.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.01, 169.37, 160.94, 141.17, 127.33, 123.10, 123.04, 107.63, 76.92, 61.24, 55.80, 39.70, 14.13. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{13}H_{15}O_5^+$ 251.0914; found 251.0901.

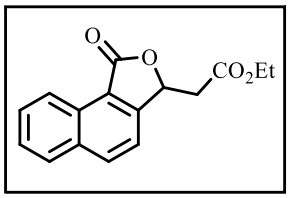
Ethyl-2-(3-oxo-1,3-dihydronaphtho[2,3-c]furan-1-yl)acetate (5u):



Yield (0.2 mmol scale, 37 mg, 68%), white crystalline solid. m.p: 99.2-103 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.98 – 7.90 (m, 2H), 7.69 – 7.59 (m, 2H), 6.09 – 6.01 (m, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.09 – 2.92 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.85, 168.37, 141.42, 135.23, 132.28, 128.89, 128.11,

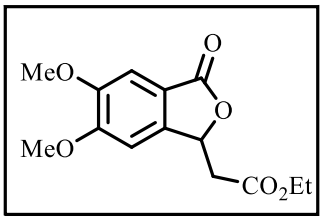
127.34, 126.19, 126.15, 122.54, 120.12, 75.99, 60.26, 39.10, 13.11. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{16}H_{15}O_4^+$ 271.0965; found 271.0970.

Ethyl-2-(1-oxo-1,3-dihydronaphtho[1,2-c]furan-3-yl)acetate (5v):



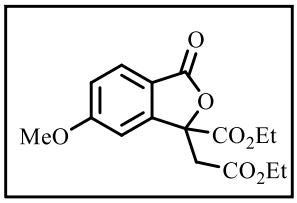
Yield (0.2 mmol scale, 33 mg, 62%), white sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.94 (dt, *J* = 8.3, 1.1 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.69 -7.65 (m, 1H), 7.60 -7.56 (m, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 5.89 (t, *J* = 6.6 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.88 (d, *J* = 6.6 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.20, 169.38, 150.43, 135.77, 133.53, 129.20, 128.49, 127.53, 123.56, 120.24, 118.48, 76.40, 61.35, 39.45, 14.14. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{16}H_{15}O_4^+$ 271.0965; found 271.0976.

Ethyl-2-(5,6-dimethoxy-3-oxo-1,3-dihydroisobenzofuarn-1-yl)acetate (5w):



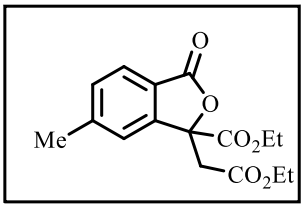
Yield (0.2 mmol scale, 35 mg, 64%), colourless oil .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (s, 1H), 6.87 (s, 1H), 5.71 (t, *J* = 8.0 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 3.87 (s, 3H), 2.99 – 2.62 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.17, 168.56, 153.91, 149.77, 142.43, 116.86, 105.15, 102.64, 75.37, 60.24, 55.39, 55.31, 38.72, 13.16. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{14}H_{17}O_6^+$ 281.1020; found 281.1016.

Ethyl 1-(2-ethoxy-2-oxoethyl)-6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-carboxylate (7a):



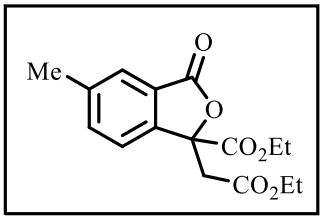
Yield (0.2 mmol scale, 41 mg, 64%), white sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.5 Hz, 1H), 7.09 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.03 (d, *J* = 2.2 Hz, 1H), 4.36 – 4.10 (m, 4H), 3.91 (s, 3H), 3.55 (d, *J* = 16.7 Hz, 1H), 2.92 (d, *J* = 16.7 Hz, 1H), 1.25 (dt, *J* = 16.6, 7.2 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.58, 168.50, 167.97, 165.10, 149.75, 127.55, 117.77, 117.54, 106.26, 83.53, 62.88, 61.37, 56.04, 41.98, 14.02, 13.98. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{16}H_{19}O_7^+$ 323.1125; found 323.1130.

Ethyl 1-(2-ethoxy-2-oxoethyl)-6-methyl-3-oxo-1,3-dihydroisobenzofuran-1-carboxylate (7b):



Yield (0.2 mmol scale, 37 mg, 62%), White solid. m.p: 101.6-104.2 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 1H), 7.36 – 7.30 (m, 2H), 4.27 – 4.02 (m, 4H), 3.50 (d, *J* = 16.7 Hz, 1H), 2.83 (d, *J* = 16.7 Hz, 1H), 2.43 (s, 3H), 1.17 (dt, *J* = 17.2, 7.1 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.92, 168.51, 168.00, 147.45, 146.20, 131.66, 125.80, 122.80, 122.44, 83.93, 62.85, 61.34, 41.85, 22.16, 14.01, 13.93. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{16}H_{19}O_6^+$ 307.1176; found 307.1181.

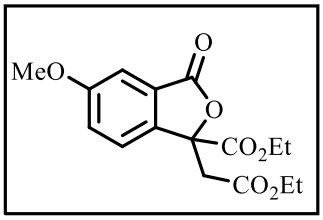
Ethyl 1-(2-ethoxy-2-oxoethyl)-5-methyl-3-oxo-1,3-dihydroisobenzofuran-1-carboxylate (7c):



Yield (0.2 mmol scale, 35 mg, 58%), White solid. m.p: 102.5-105 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.48 – 7.39 (m, 2H), 4.26 – 4.01 (m, 4H), 3.48 (d, *J* = 16.7 Hz, 1H), 2.85 (d, *J* = 16.7 Hz, 1H), 2.40 (s, 3H), 1.16 (dt, *J* = 13.4, 7.1 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.00, 168.41, 167.99, 144.38, 141.06, 135.80, 126.05, 125.58, 121.87, 84.07,

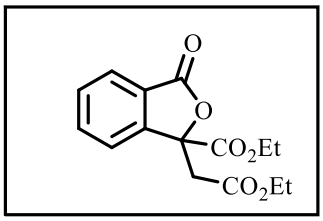
62.79, 61.32, 41.76, 21.32, 14.01, 13.97. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{16}H_{19}O_6^+$ 307.1176; found 307.1181.

Ethyl 1-(2-ethoxy-2-oxoethyl)-5-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-carboxylate (7d):



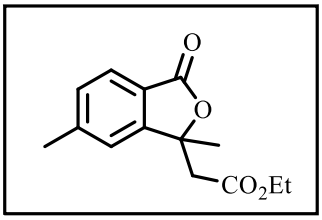
Yield (0.2 mmol scale, 38 mg, 60%), White sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.5 Hz, 1H), 7.26 (d, *J* = 2.4 Hz, 1H), 7.22 – 7.14 (m, 1H), 4.29 – 3.98 (m, 4H), 3.81 (s, 3H), 3.47 (d, *J* = 16.7 Hz, 1H), 2.85 (d, *J* = 16.7 Hz, 1H), 1.17 (dt, *J* = 12.8, 7.1 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.89, 168.41, 167.99, 161.71, 139.21, 126.95, 123.35, 123.11, 107.99, 84.00, 62.78, 61.32, 55.90, 41.76, 14.02, 13.94. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{16}H_{19}O_7^+$ 323.1125; found 323.1134.

Ethyl 1-(2-ethoxy-2-oxoethyl)-3-oxo-1,3-dihydroisobenzofuran-1-carboxylate (7e):



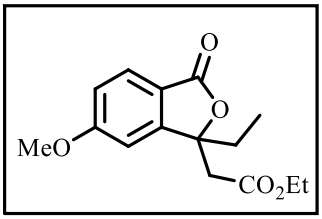
Yield (0.2 mmol scale, 32 mg, 55%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 8.0 Hz, 1H), 7.66 – 7.57 (m, 2H), 4.35 – 4.09 (m, 4H), 3.58 (d, *J* = 16.7 Hz, 1H), 2.95 (d, *J* = 16.8 Hz, 1H), 1.24 (dt, *J* = 17.5, 7.1 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.88, 168.27, 167.92, 146.95, 134.71, 130.53, 126.10, 125.42, 122.19, 84.22, 62.93, 61.40, 41.76, 14.01, 13.93. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{15}H_{17}O_6^+$ 293.1020; found 293.1023.

Ethyl 2-(1,6-dimethyl-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (7f):



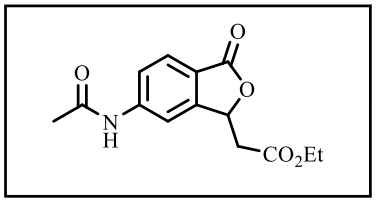
Yield (0.2 mmol scale, 49 mg, 68%), White solid. m.p: 111.2-114.6 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 8 Hz, 1H), 7.29 – 7.26 (m, 1H), 4.03 (q, *J* = 7.1 Hz, 2H), 2.97 (d, *J* = 1.4 Hz, 2H), 2.49 (s, 3H), 1.74 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.52, 168.57, 153.06, 145.41, 130.46, 125.42, 123.42, 121.78, 83.88, 60.81, 44.11, 26.32, 22.15, 13.94. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{14}H_{17}O_4^+$ 249.1121; found 249.1133.

Ethyl 2-(1-ethyl-6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (7g):



Yield (0.2 mmol scale, 33 mg, 60%), White sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.5 Hz, 1H), 6.95 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 3.94 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 2.91 (s, 2H), 2.15 – 2.08 (m, 1H), 1.98 – 1.91 (m, 1H), 1.04 (t, *J* = 7.2 Hz, 3H), 0.69 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.46, 168.63, 164.70, 153.71, 127.06, 119.32, 116.20, 106.09, 86.03, 60.78, 55.85, 42.91, 31.71, 13.94, 7.38. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{15}H_{19}O_5^+$ 279.1227; found 279.1228.

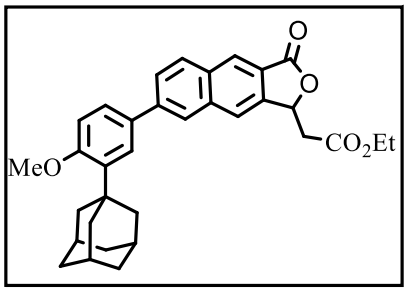
Ethyl 2-(6-acetamido-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (11a):



Yield (0.2 mmol scale, 38 mg, 69%), yellow sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.16 – 8.09 (m, 1H), 7.80 (d, *J* = 8.3 Hz, 1H), 7.43 (dd, *J* = 8.3, 1.8 Hz, 1H), 5.84 (dd, *J* = 7.4, 5.5 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.91 (qd, *J* = 16.5, 6.5 Hz, 2H), 2.24 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.90,

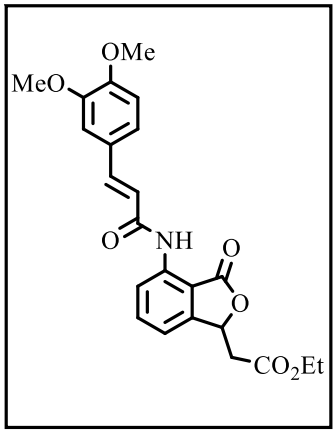
169.24, 169.17, 150.69, 144.03, 126.57, 120.70, 120.43, 111.99, 77.00, 61.40, 39.44, 24.78, 14.11. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{14}H_{16}NO_5^+$ 278.1023; found 278.1031.

Ethyl 2-(7-(3-((3r,5r,7r)-adamantan-1-yl)-4-methoxyphenyl)-3-oxo-1,3-dihydronaphtho[2,3-c]furan-1-yl)acetate (11b):



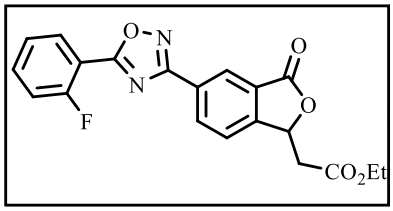
Yield (0.1 mmol scale, 29 mg, 60%), white sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.11 – 8.04 (m, 2H), 7.95 (s, 1H), 7.86 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.56 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.05 (t, *J* = 12 Hz, 1H), 4.25 (q, *J* = 16 Hz, 2H), 3.92 (s, 3H), 3.10 – 2.93 (m, 2H), 2.19 (d, *J* = 3.0 Hz, 6H), 2.11 (t, *J* = 3.1 Hz, 4H), 1.81 (t, *J* = 3.1 Hz, 6H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.99, 169.52, 159.19, 142.91, 142.29, 139.17, 136.82, 132.09, 132.02, 130.22, 127.14, 126.95, 126.03, 125.82, 125.12, 123.05, 121.11, 112.16, 77.24, 61.32, 55.20, 40.61, 40.19, 37.25, 37.12, 29.10, 14.17. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{33}H_{35}O_5^+$ 511.2479; found 511.2496.

Ethyl (E)-2-(4-(3-(3,4-dimethoxyphenyl)acrylamido)-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (11c):



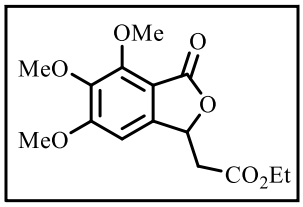
Yield (0.1 mmol scale, 20 mg, 48%), yellow sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.72 (d, *J* = 8.3 Hz, 1H), 7.77 – 7.57 (m, 2H), 7.18 – 7.07 (m, 3H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.52 (d, *J* = 15.4 Hz, 1H), 5.91 (t, *J* = 6.5 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.98 (s, 3H), 3.93 (s, 3H), 2.93 (d, *J* = 6.6 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.31, 169.07, 164.86, 151.22, 149.28, 148.93, 143.62, 139.24, 136.71, 127.30, 123.16, 119.14, 118.02, 115.74, 111.61, 111.00, 109.40, 77.56, 77.25, 61.44, 56.07, 56.02, 39.35, 14.13 (d, J = 6.0 Hz). **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{23}H_{24}NO_7^+$ 426.1547; found 426.1532.

Ethyl-2-(5-(5-(2-fluorophenyl)-1,2,4-oxadiazol-3-yl)-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (11d):



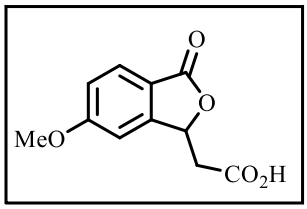
Yield (0.1 mmol scale, 20 mg, 52%), yellow sticky solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 1.5 Hz, 1H), 8.45 (dd, *J* = 8.0, 1.5 Hz, 1H), 8.17 (td, *J* = 7.4, 1.8 Hz, 1H), 7.64 – 7.52 (m, 2H), 7.35 – 7.17 (m, 2H), 5.90 (t, *J* = 6.6 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 2.91 (qd, *J* = 16.6, 6.6 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.05 (d, $J_{C\text{-}F}$ = 8.0 Hz), 167.55, 162.16, 159.57, 151.19, 134.96 (d, $J_{C\text{-}F}$ = 8.6 Hz), 124.84 (d, $J_{C\text{-}F}$ = 3.7 Hz), 117.27 (d, J = 20.8 Hz), 133.22, 130.97, 128.84, 127.03, 125.30, 122.91, 112.49, 77.08, 61.45, 39.34, 29.72, 14.14.**^{19}F NMR** (377 MHz, $CDCl_3$) δ -108.00. **HRMS** (ESI$^+$) m/z: $[M + H]^+$ calcd for $C_{20}H_{16}FN_2O_5^+$ 383.1038; found 383.1000.

Ethyl 2-(4,5,6-trimethoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetate (11e):



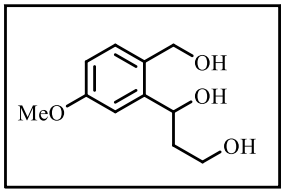
Yield (0.1 mmol scale, 21 mg, 68%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.63 (s, 1H), 5.64 (t, *J* = 6.6 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.08 – 4.05 (m, 3H), 3.87 (s, 3H), 3.80 (s, 3H), 2.89 – 2.69 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.55, 167.49, 159.76, 152.42, 146.70, 142.09, 110.42, 99.64, 77.26, 75.66, 62.39, 61.38 (d, J = 15.4 Hz), 56.49, 39.90, 14.19. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{15}H_{19}O_7^+$ 311.1125; found 311.1124.

2-(6-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)acetic acid (12a):



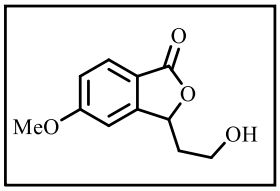
Yield (0.2 mmol scale, 30 mg, 72%), colourless sticky solid. **^{1}H NMR** (400 MHz, DMSO) δ 7.73 (d, *J* = 8.5 Hz, 1H), 7.30 (d, *J* = 2.2 Hz, 1H), 7.12 (dd, *J* = 8.5, 2.2 Hz, 1H), 5.78 (dd, *J* = 8.5, 3.8 Hz, 1H), 3.87 (s, 3H), 3.20 (dd, *J* = 16.8, 3.8 Hz, 1H), 2.67 (dd, *J* = 16.8, 8.6 Hz, 1H). **^{13}C NMR** (101 MHz, DMSO) δ 171.33, 169.76, 164.82, 152.63, 126.95, 118.00, 117.20, 107.28, 77.29, 56.46, 39.31. **HRMS** (ESI$^+$) m/z: [M + Na] $^+$ calcd for $C_{11}H_{10}O_5Na^+$ 240.0420; found 240.0427.

1-(2-(hydroxymethyl)-5-methoxyphenyl)propane-1,3-diol (12b):



Yield (0.2 mmol scale, 25 mg, 60%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 – 7.04 (m, 1H), 6.94 (d, *J* = 2.7 Hz, 1H), 6.72 – 6.60 (m, 1H), 5.08 (dd, *J* = 8.9, 4.2 Hz, 1H), 4.50 (s, 2H), 3.80 – 3.60 (m, 4H), 3.61 – 3.53 (m, 1H), 2.04 – 1.95 (m, 1H), 1.79 – 1.76 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.81, 144.38, 131.46, 129.69, 112.61, 112.28, 69.50, 62.78, 60.67, 55.30, 39.50. **HRMS** (ESI$^+$) m/z: [M + Na] $^+$ calcd for $C_{11}H_{16}O_4Na^+$ 235.0941; found 235.0947.

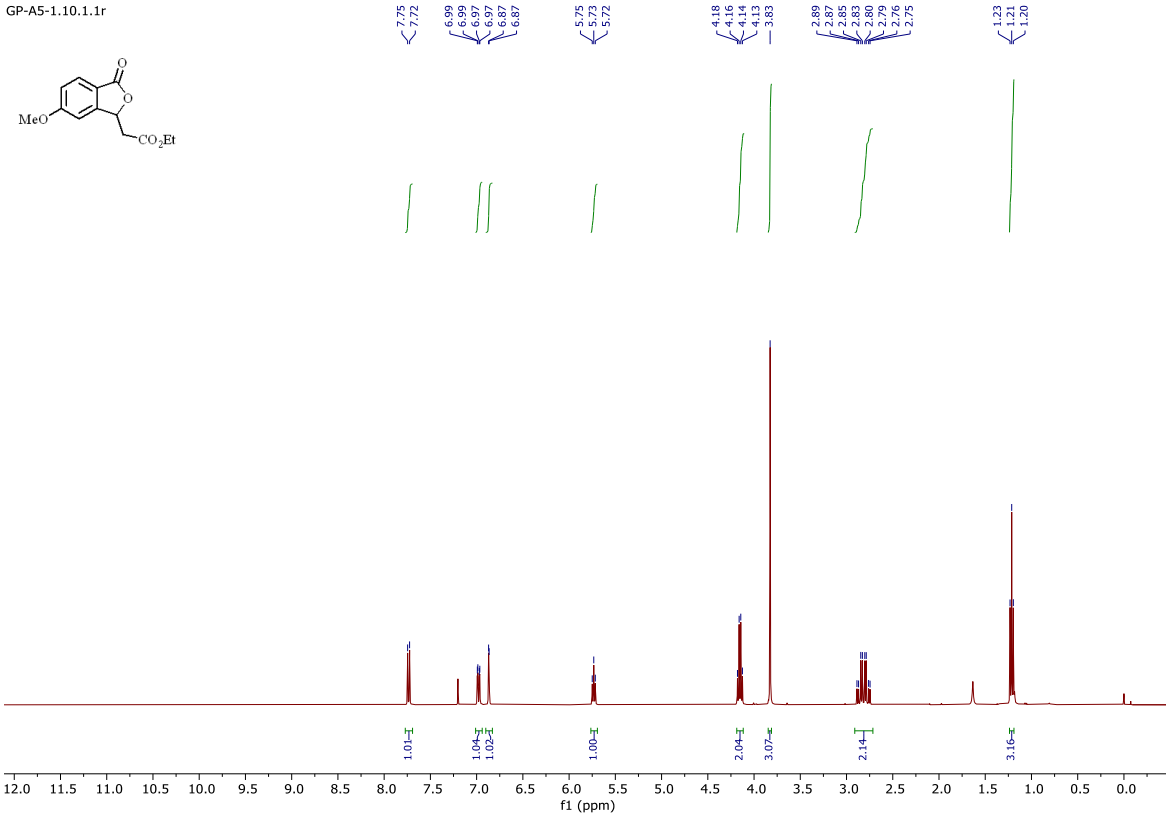
3-(2-hydroxyethyl)-5-methoxyisobenzofuran-1(3H)-one (12c):



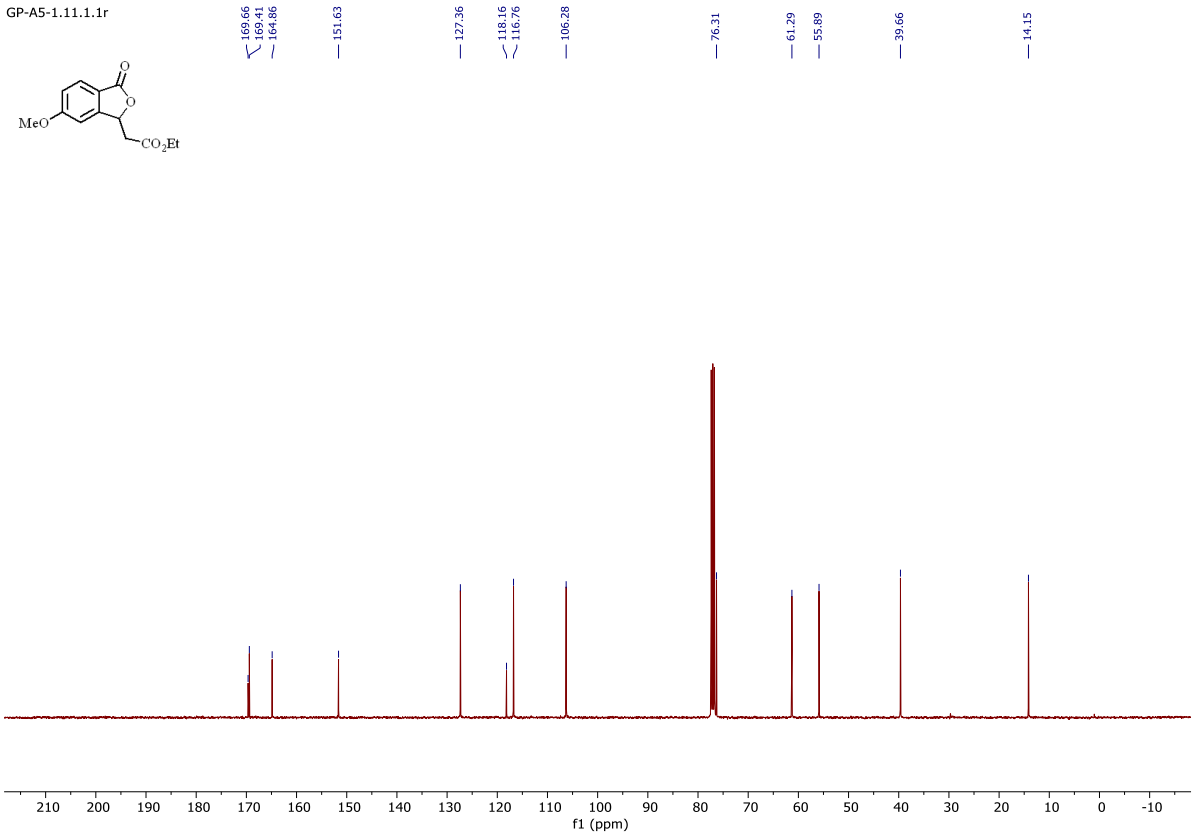
Yield (0.2 mmol scale, 29 mg, 70%), colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.5 Hz, 1H), 6.96 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 5.55 (dd, *J* = 9.7, 3.3 Hz, 1H), 3.95 – 3.84 (m, 2H), 3.84 (s, 3H), 2.27-2.19 (m, 1H), 1.83 (ddt, *J* = 14.5, 9.7, 4.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.35, 164.84, 152.91, 127.35, 117.98, 116.56, 105.87, 78.17, 58.94, 55.90, 37.74. **HRMS** (ESI$^+$) m/z: [M + H] $^+$ calcd for $C_{11}H_{13}O_4^+$ 209.0808; found 209.0805.

6. ^{1}H and ^{13}C Spectra

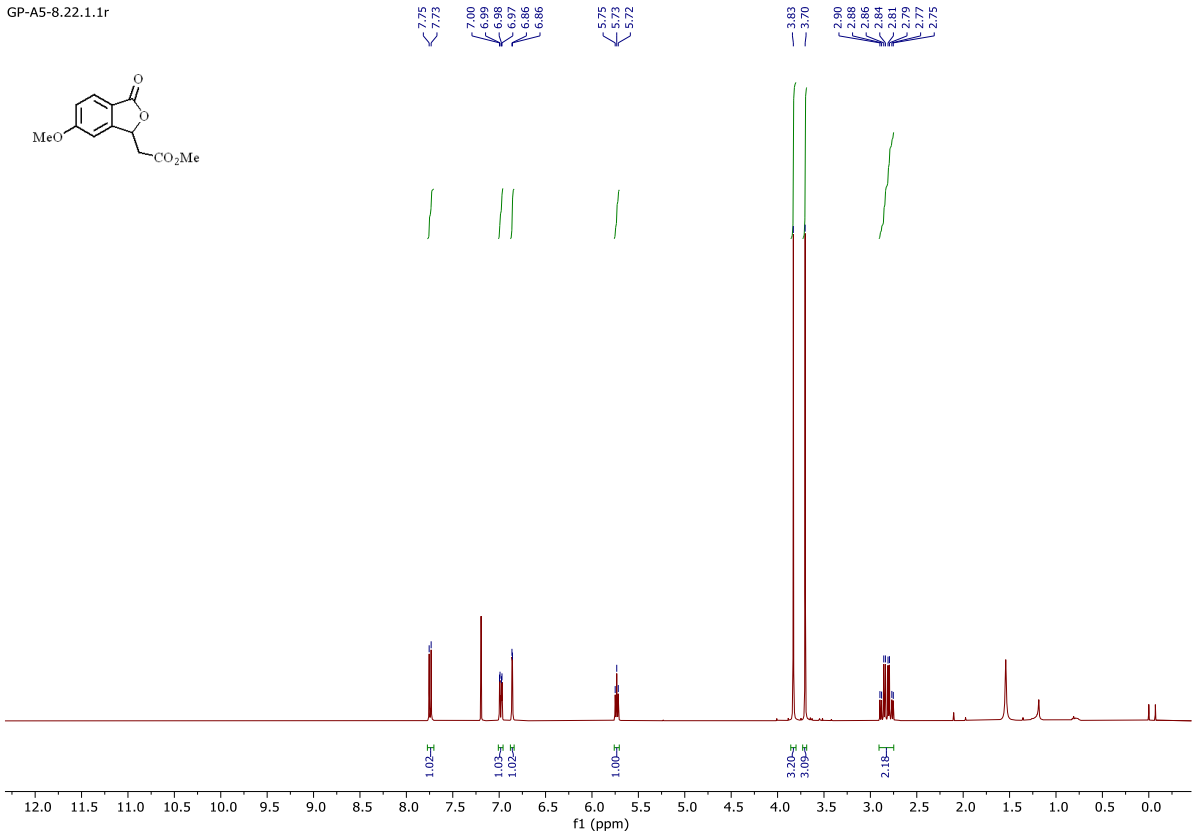
(3a) (^{1}H NMR 400 MHz, $CDCl_3$)



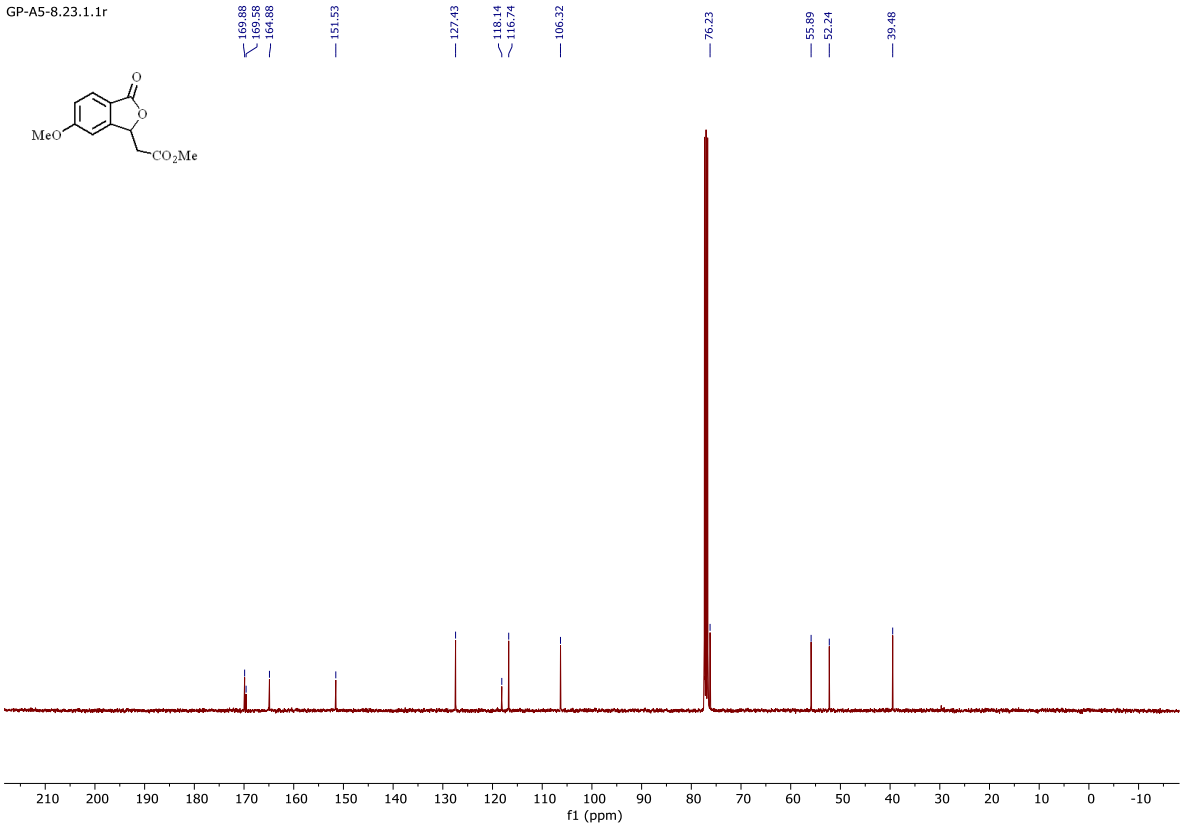
(3a) (^{13}C NMR 101 MHz, $CDCl_3$)



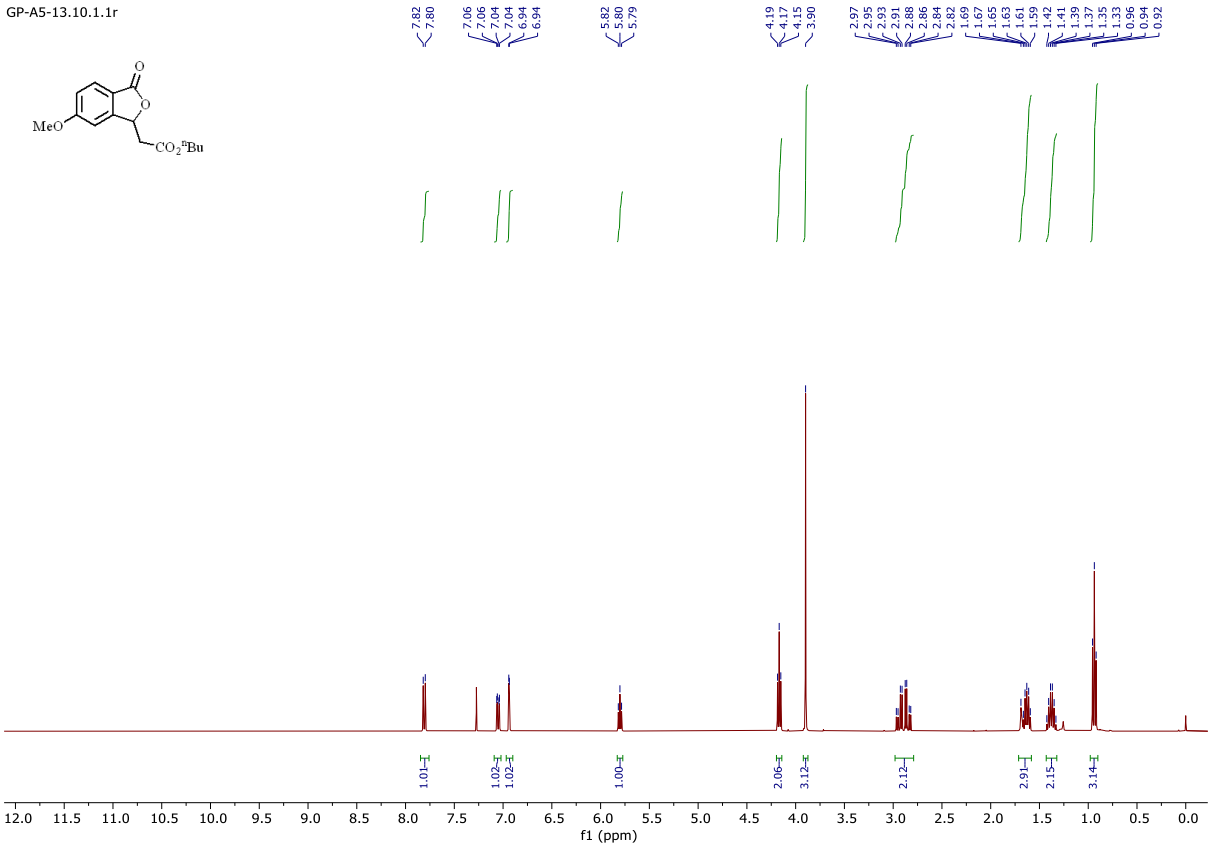
(3b) (^{1}H NMR 400 MHz, $CDCl_3$)



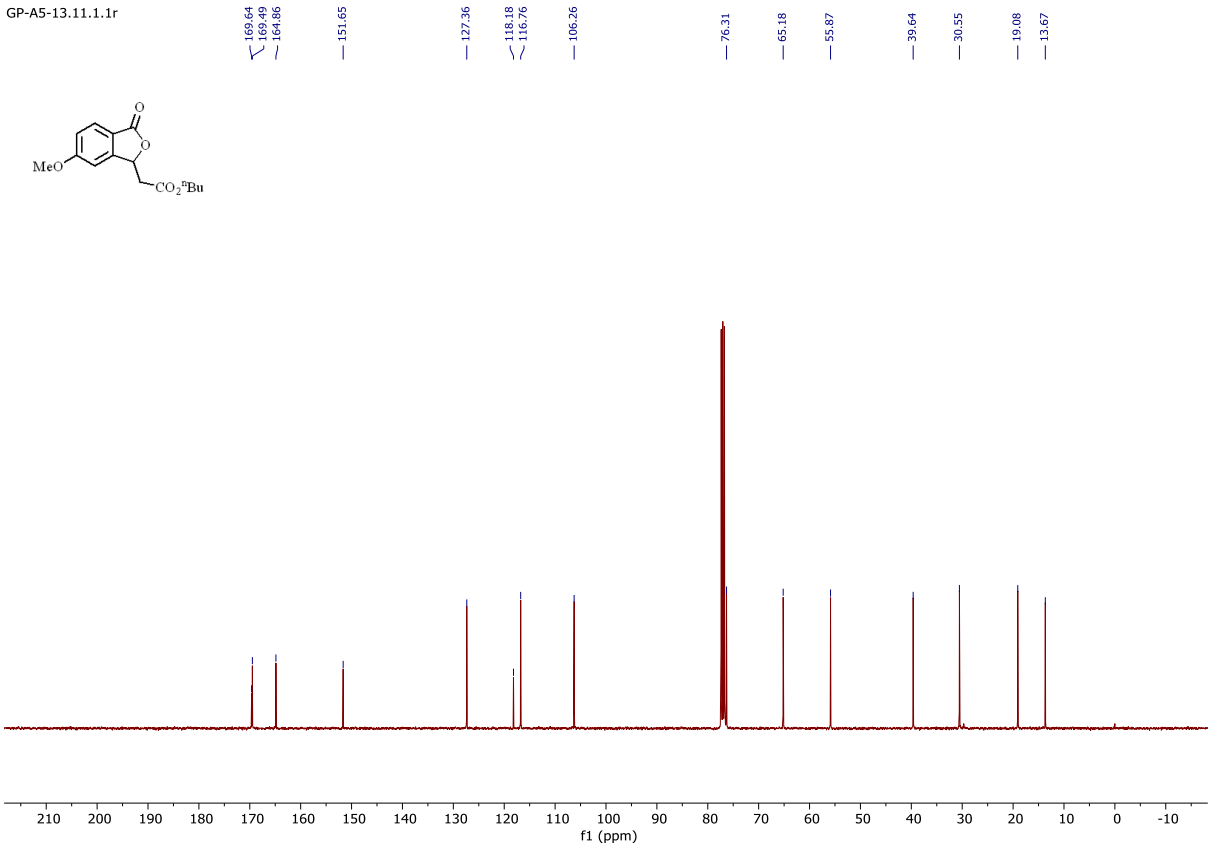
(3b) (^{13}C NMR 101 MHz, $CDCl_3$)



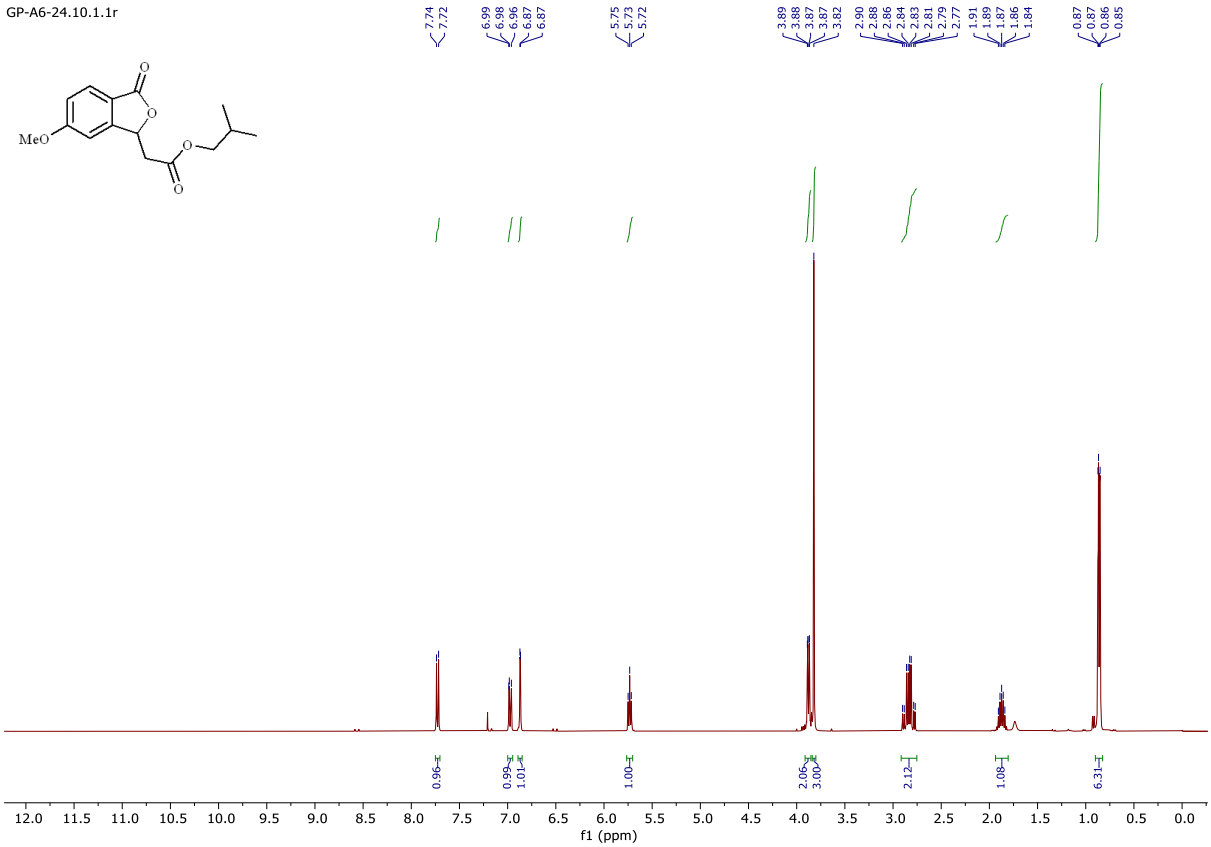
(3c) (^{1}H NMR 400 MHz, $CDCl_3$)



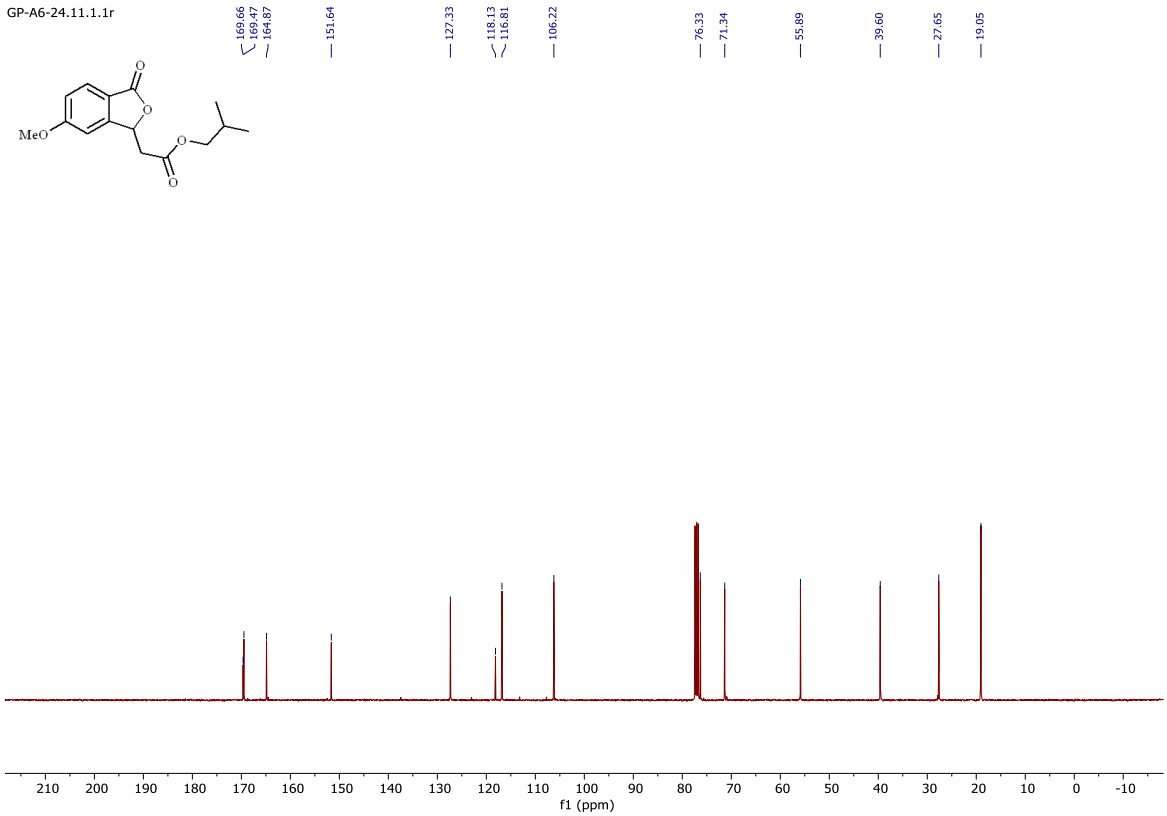
(3c) (^{13}C NMR 101 MHz, $CDCl_3$)



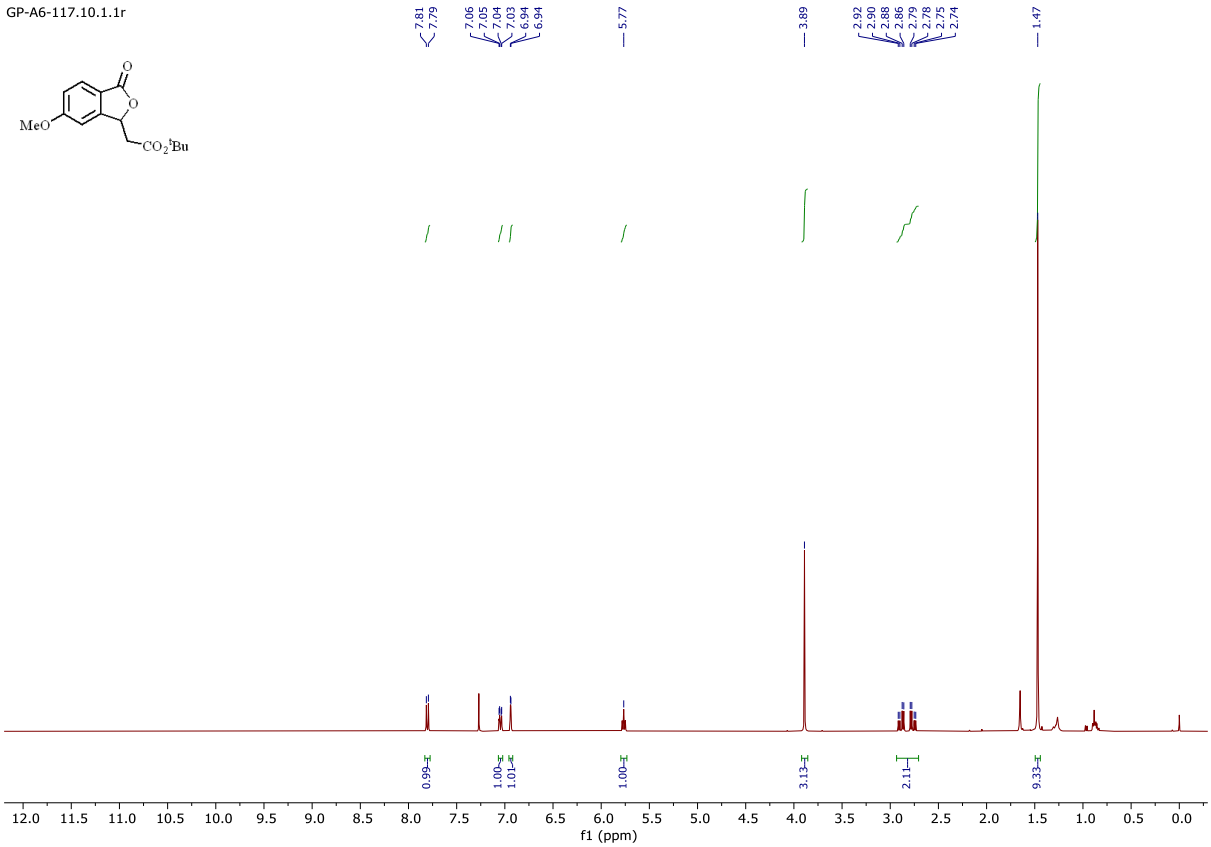
(3d) (^{1}H NMR 400 MHz, $CDCl_3$)



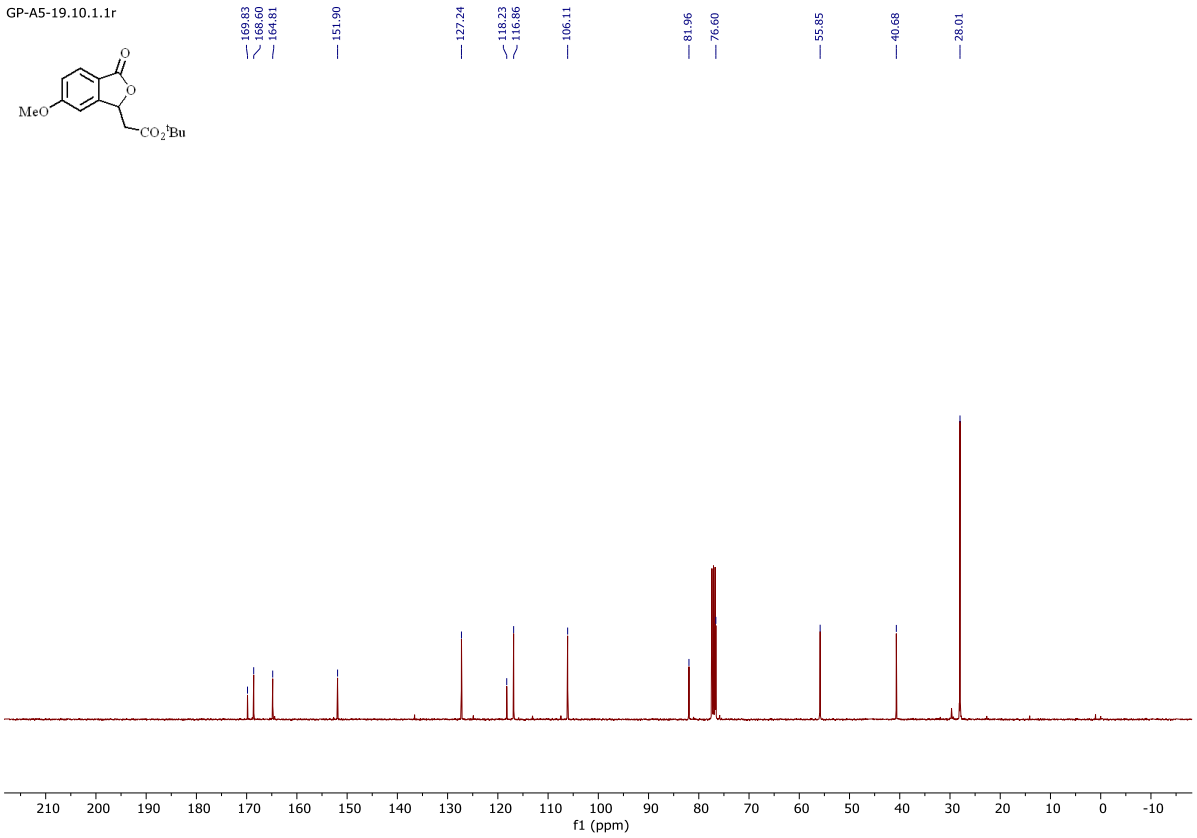
(3d) (^{13}C NMR 101 MHz, $CDCl_3$)



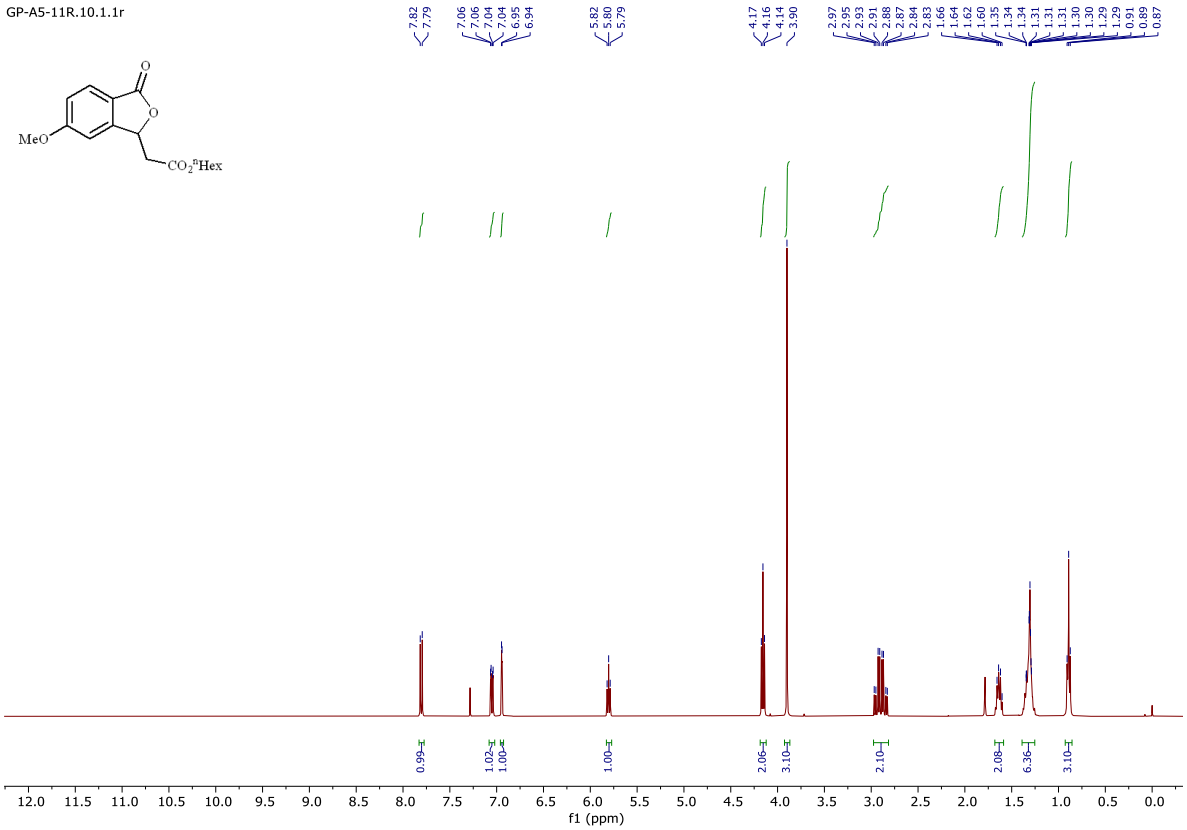
(3e) (^{1}H NMR 400 MHz, $CDCl_3$)



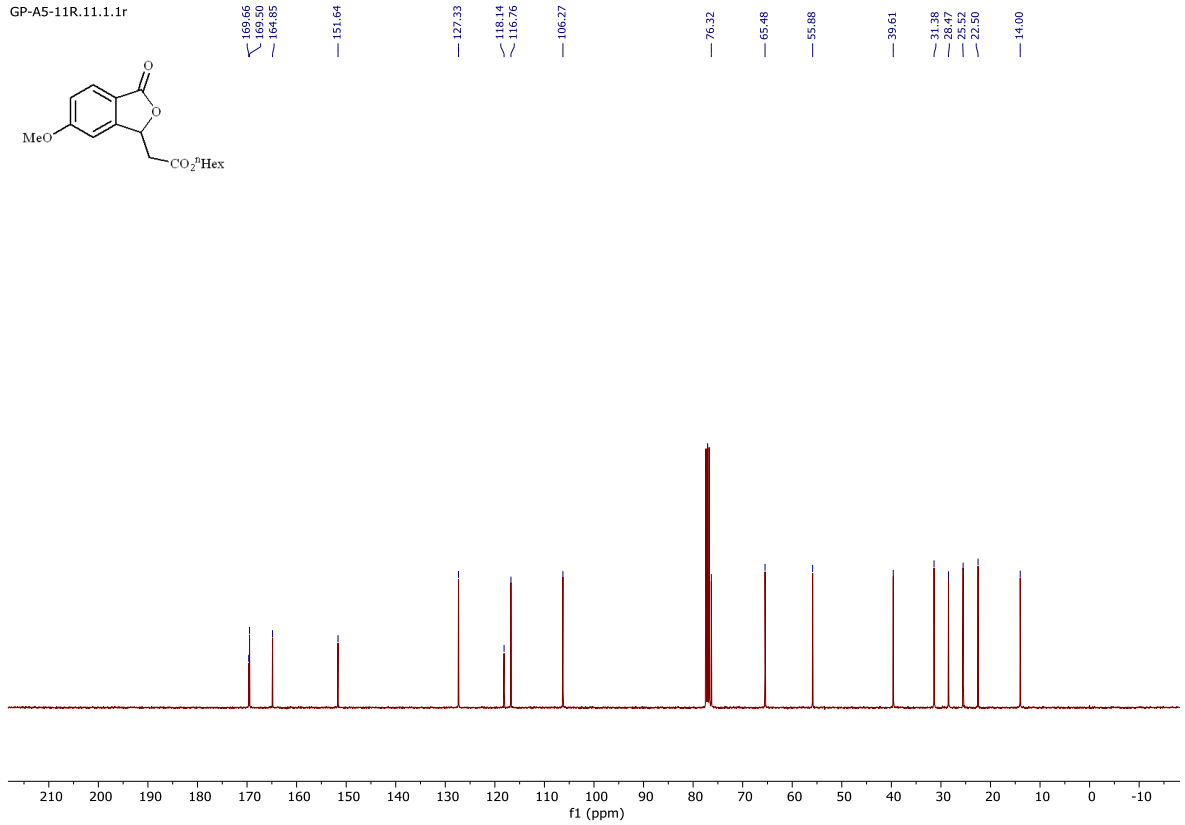
(3e) (^{13}C NMR 101 MHz, $CDCl_3$)



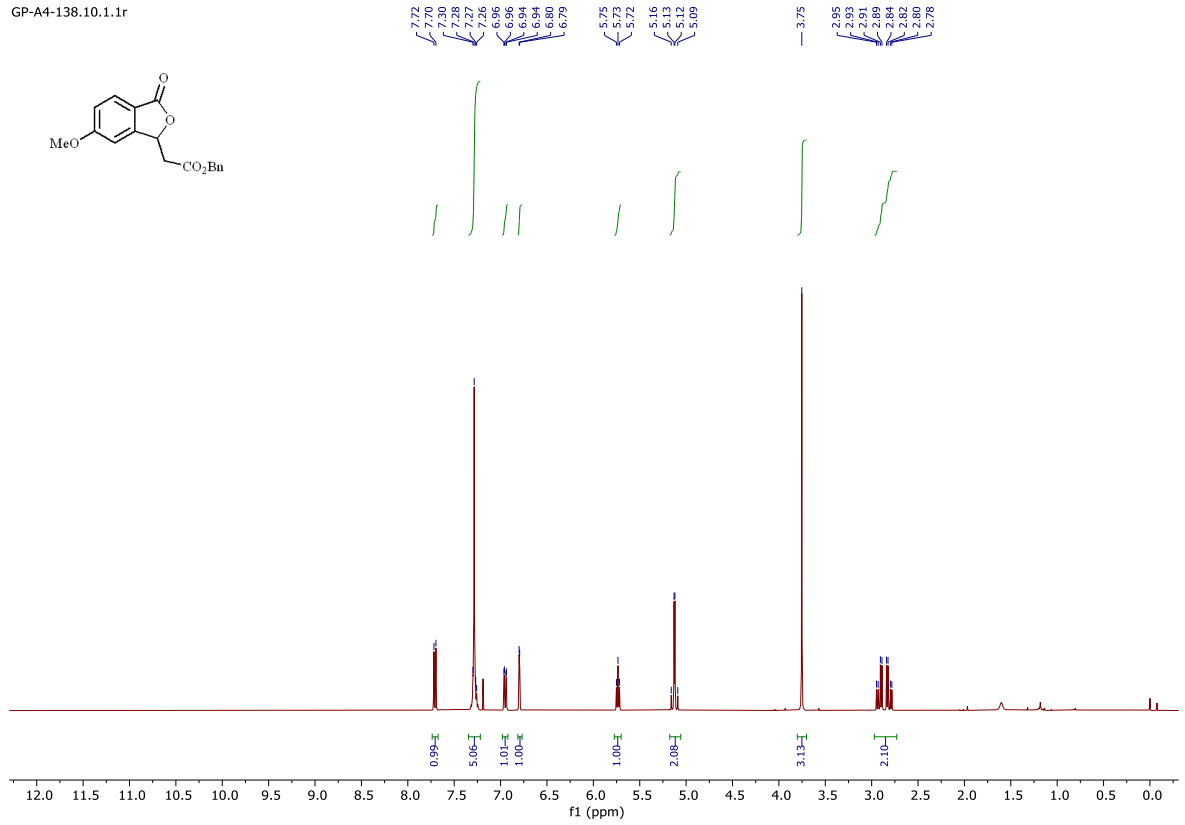
(3f) (^{1}H NMR 400 MHz, $CDCl_3$)



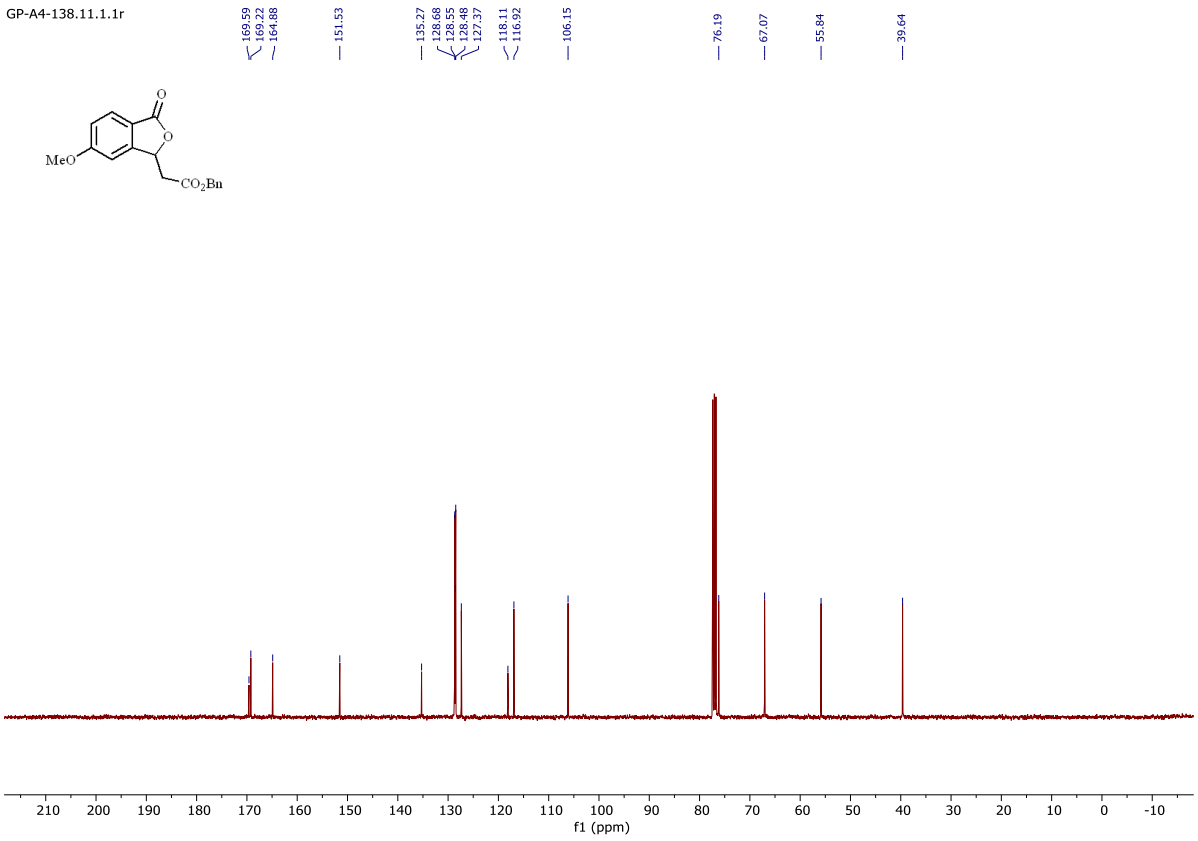
(3f) (^{13}C NMR 101 MHz, $CDCl_3$)



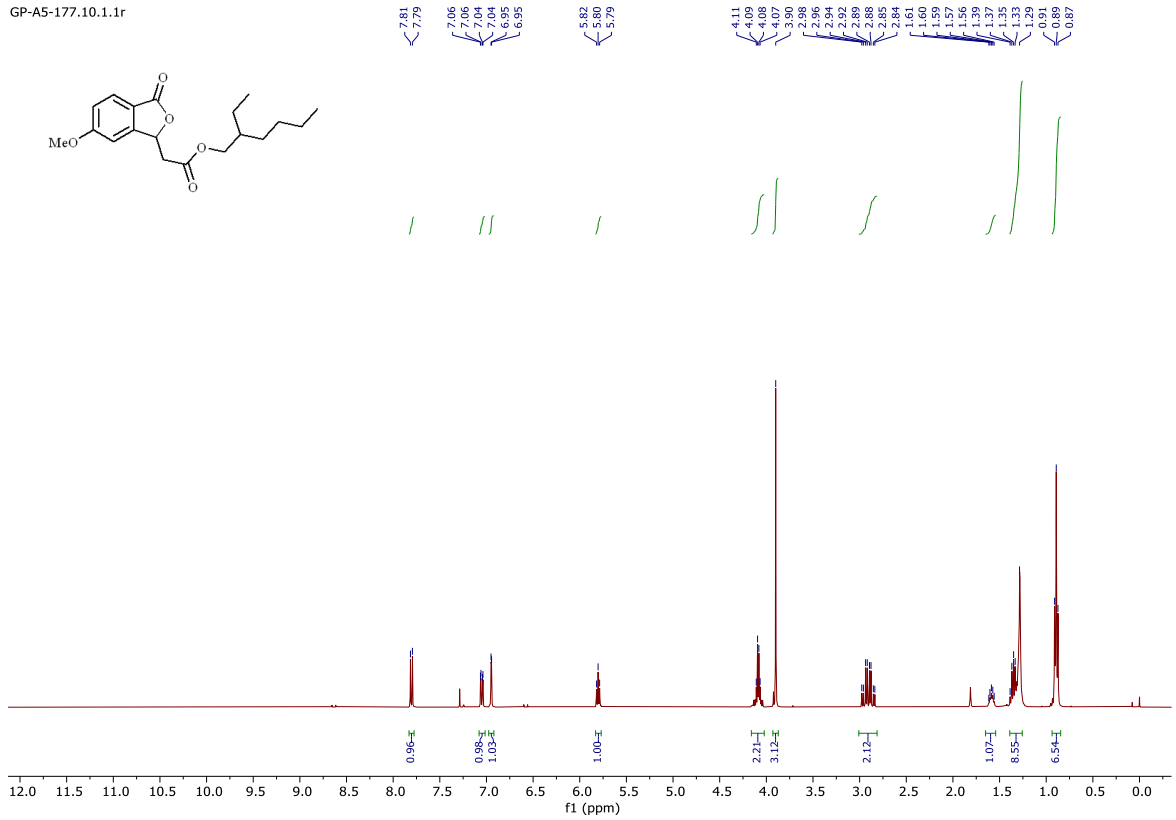
(3g) (^{1}H NMR 400 MHz, $CDCl_3$)



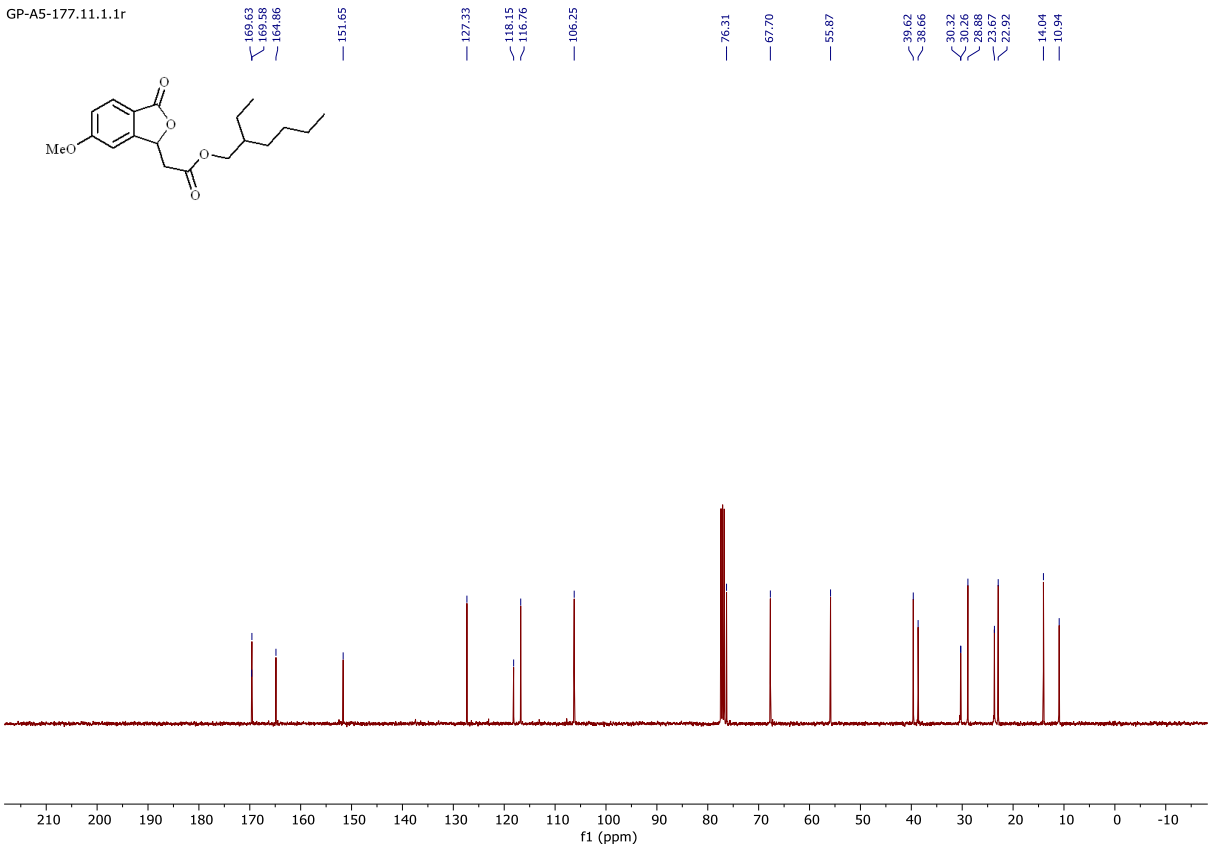
(3g) (^{13}C NMR 101 MHz, $CDCl_3$)



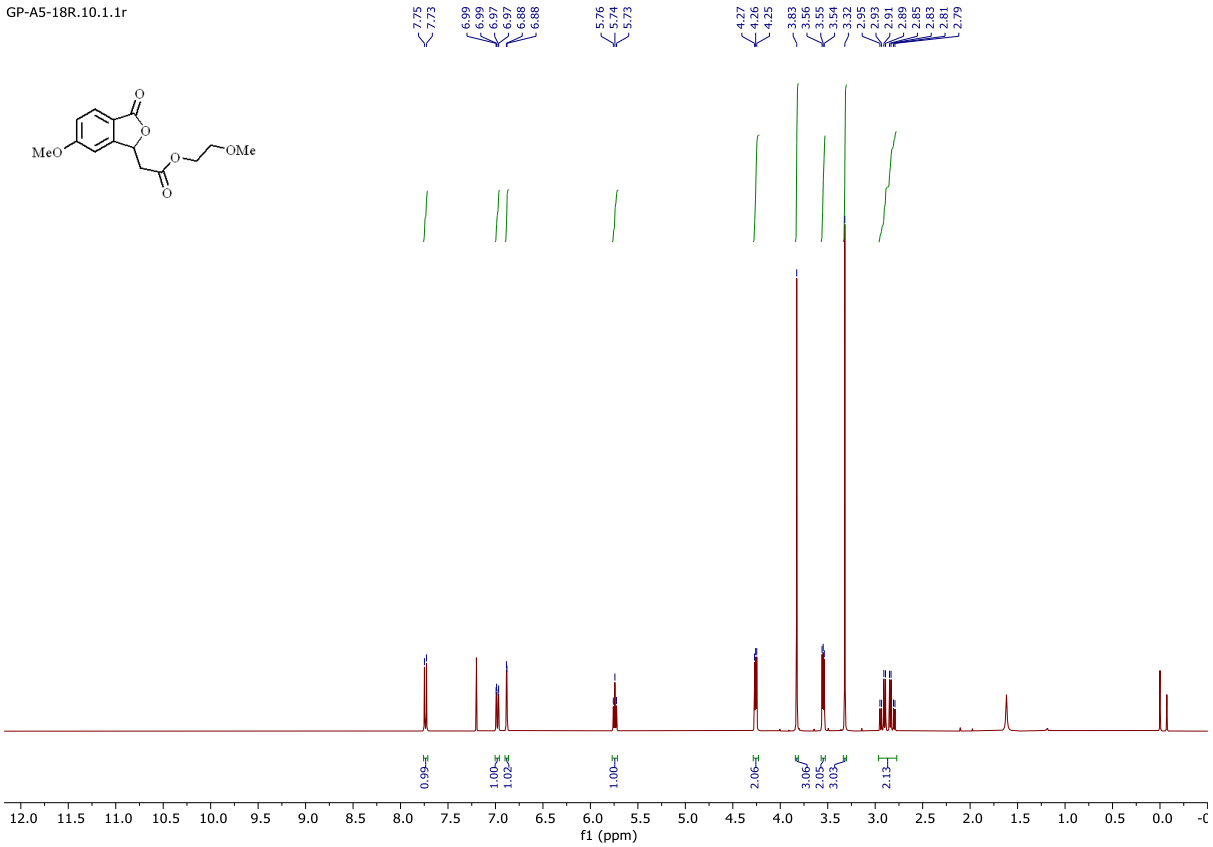
(3h) (^{1}H NMR 400 MHz, $CDCl_3$)



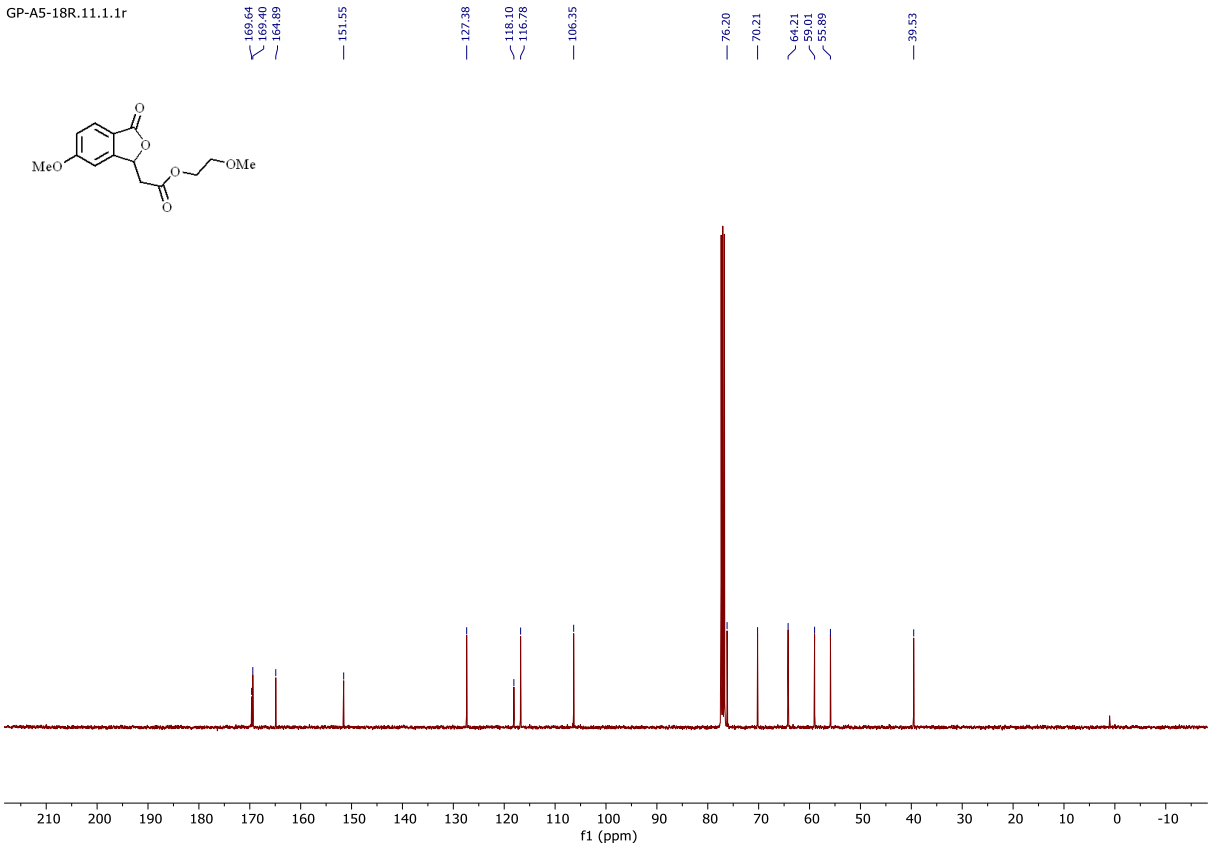
(3h) (^{13}C NMR 101 MHz, $CDCl_3$)



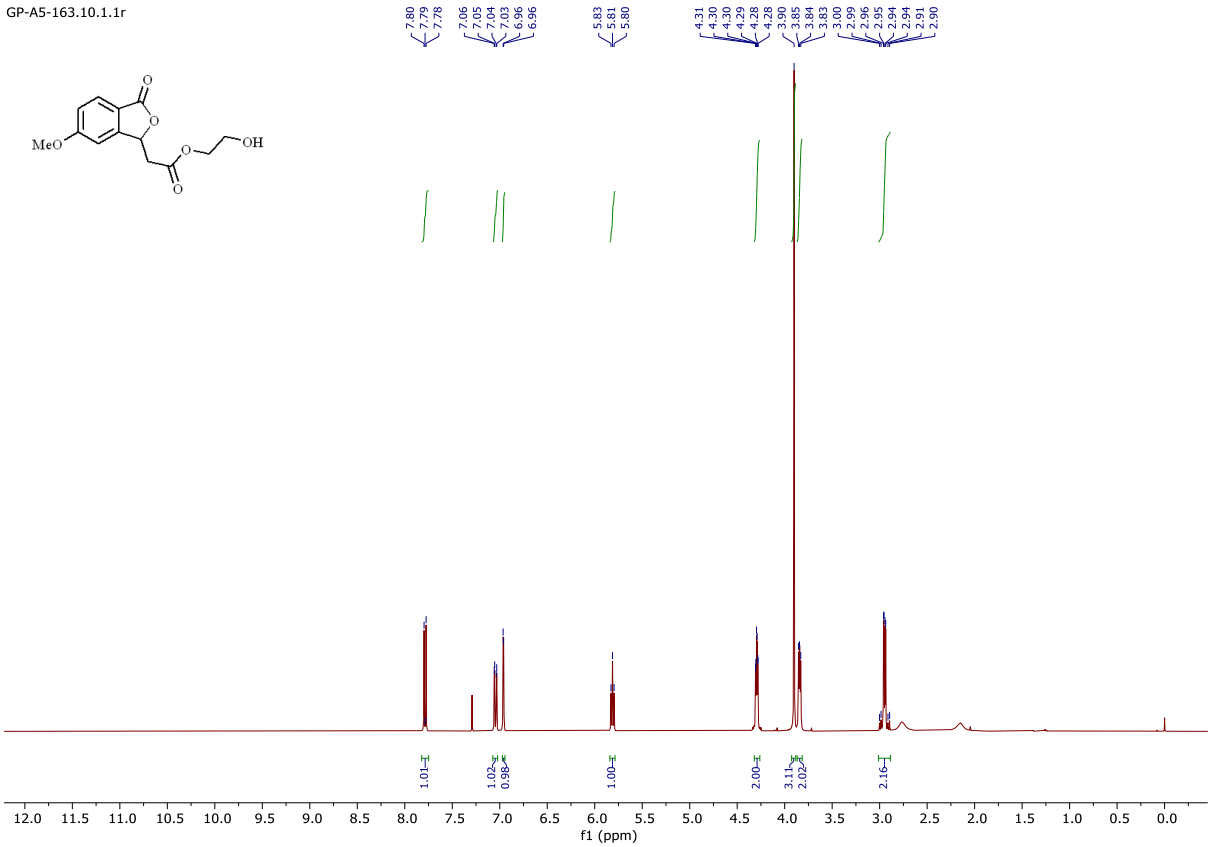
(3i) (^{1}H NMR 400 MHz, $CDCl_3$)



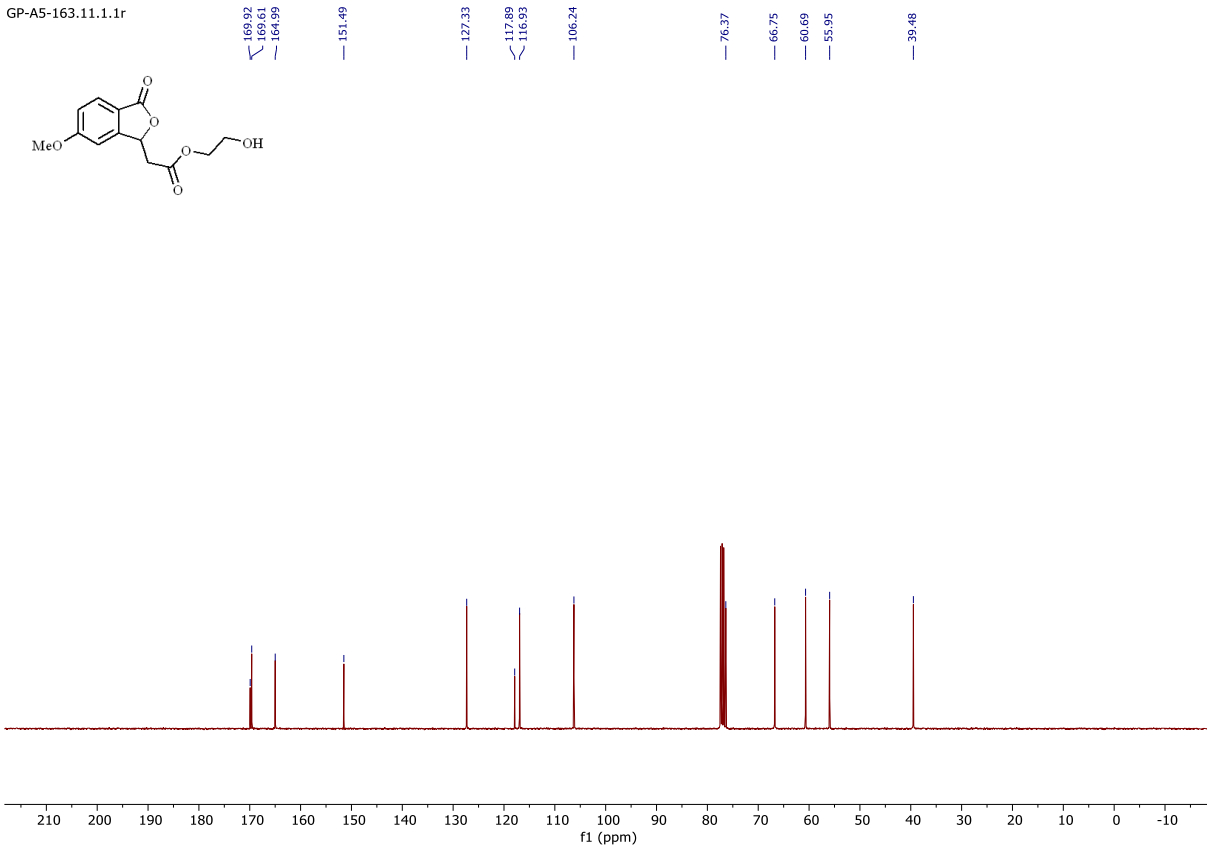
(3i) (^{13}C NMR 101 MHz, $CDCl_3$)



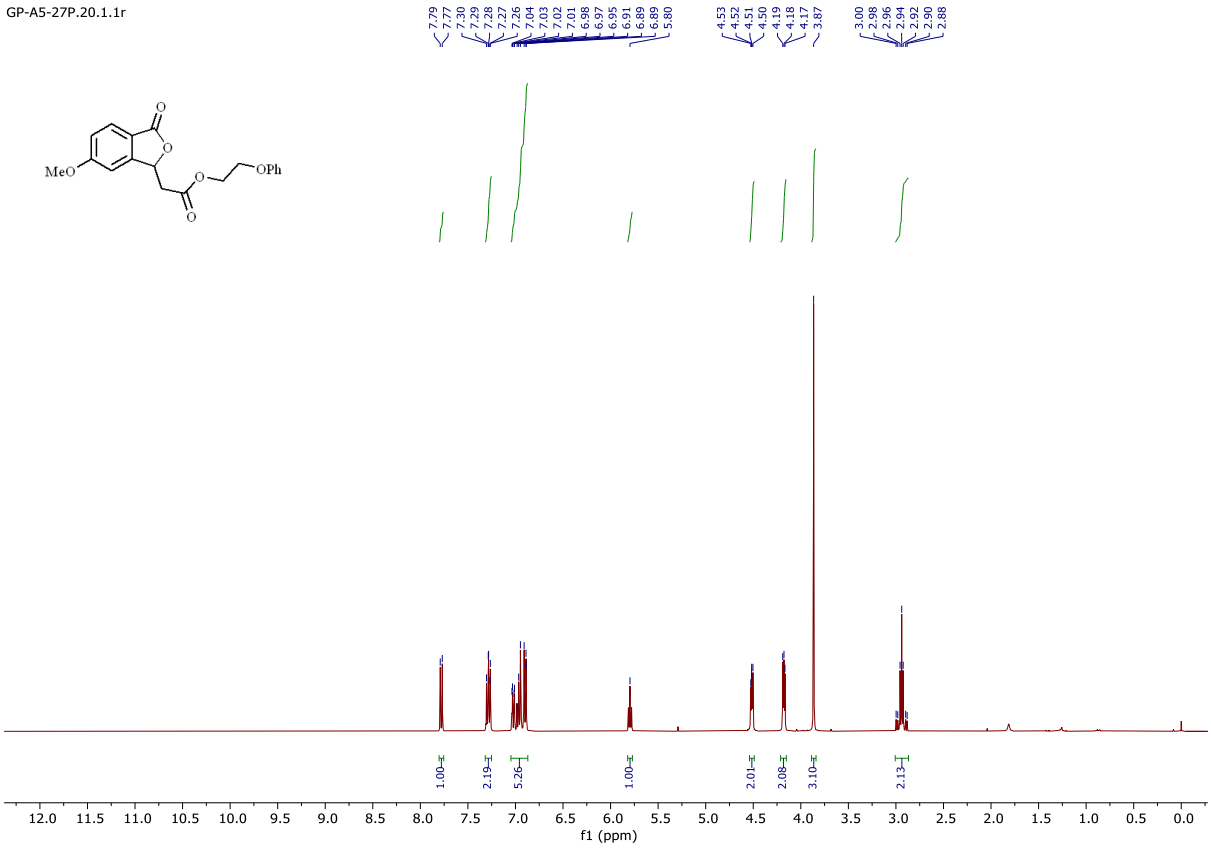
(3j) (^{1}H NMR 400 MHz, $CDCl_3$)



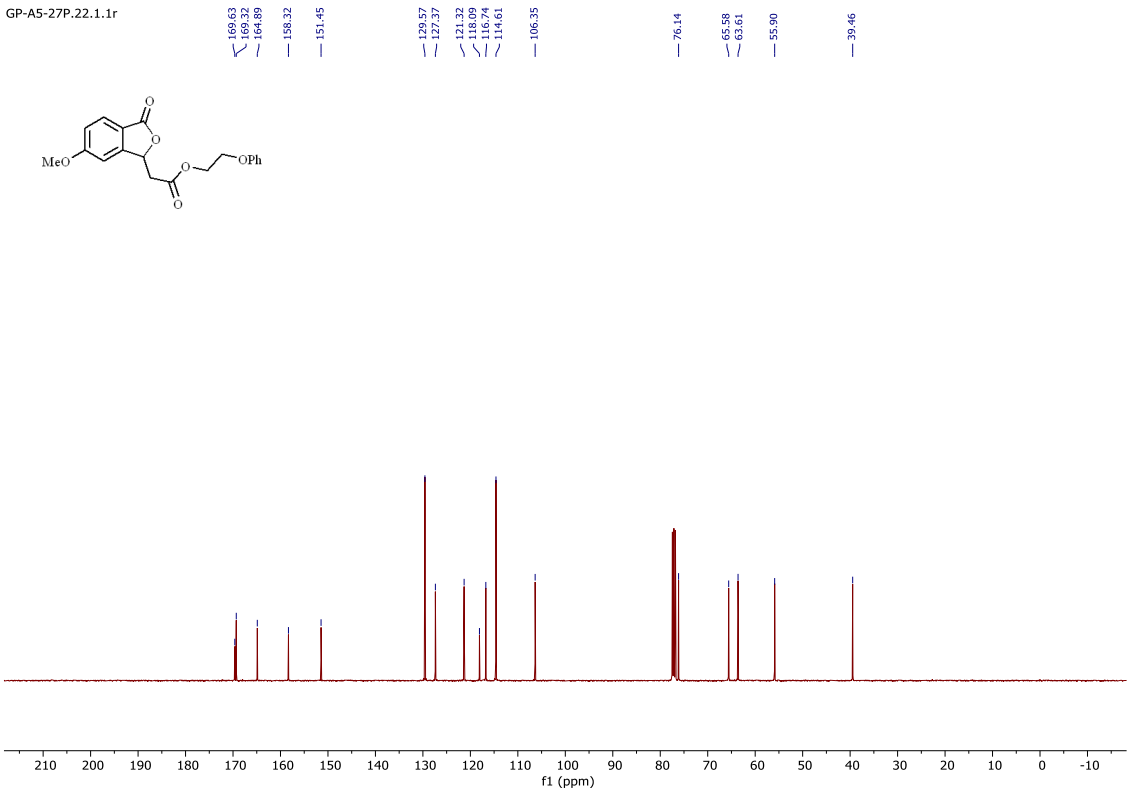
(3j) (^{13}C NMR 101 MHz, $CDCl_3$)



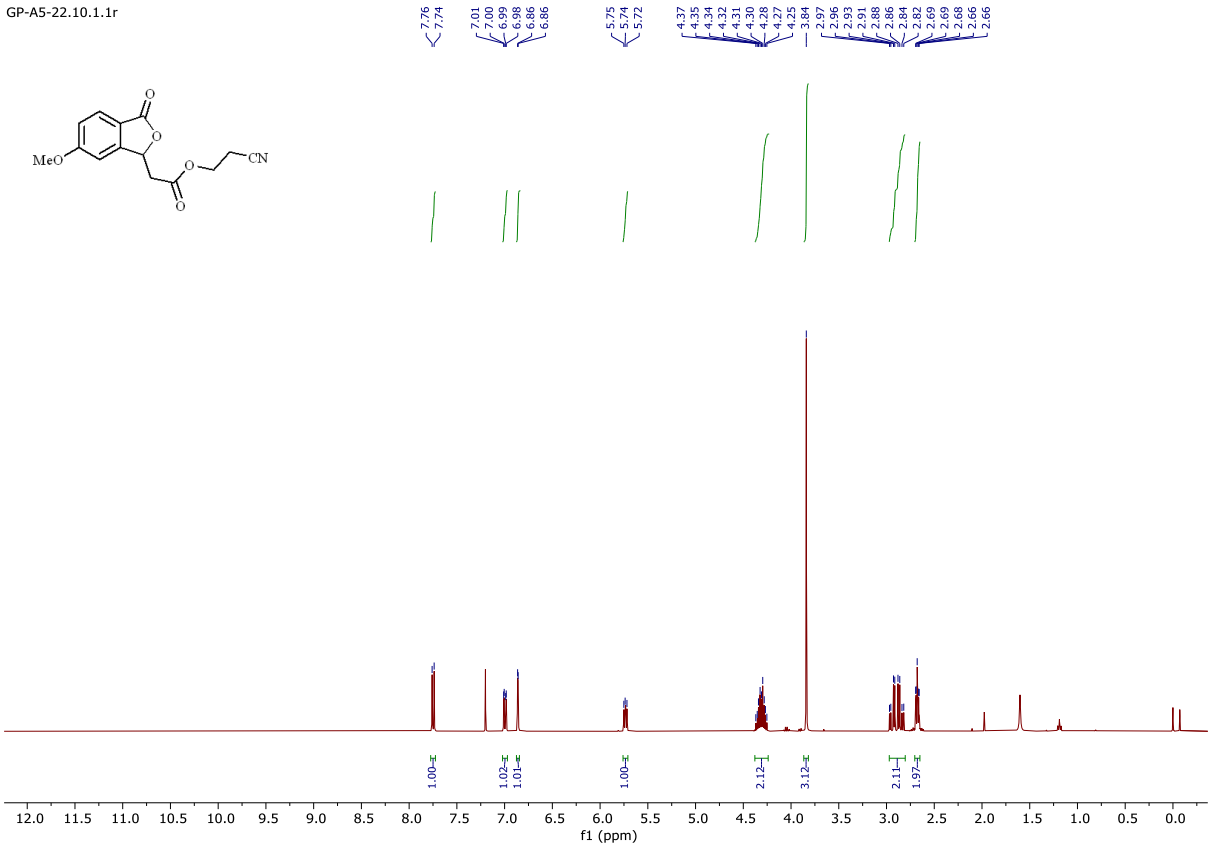
(3k) (^{1}H NMR 400 MHz, $CDCl_3$)



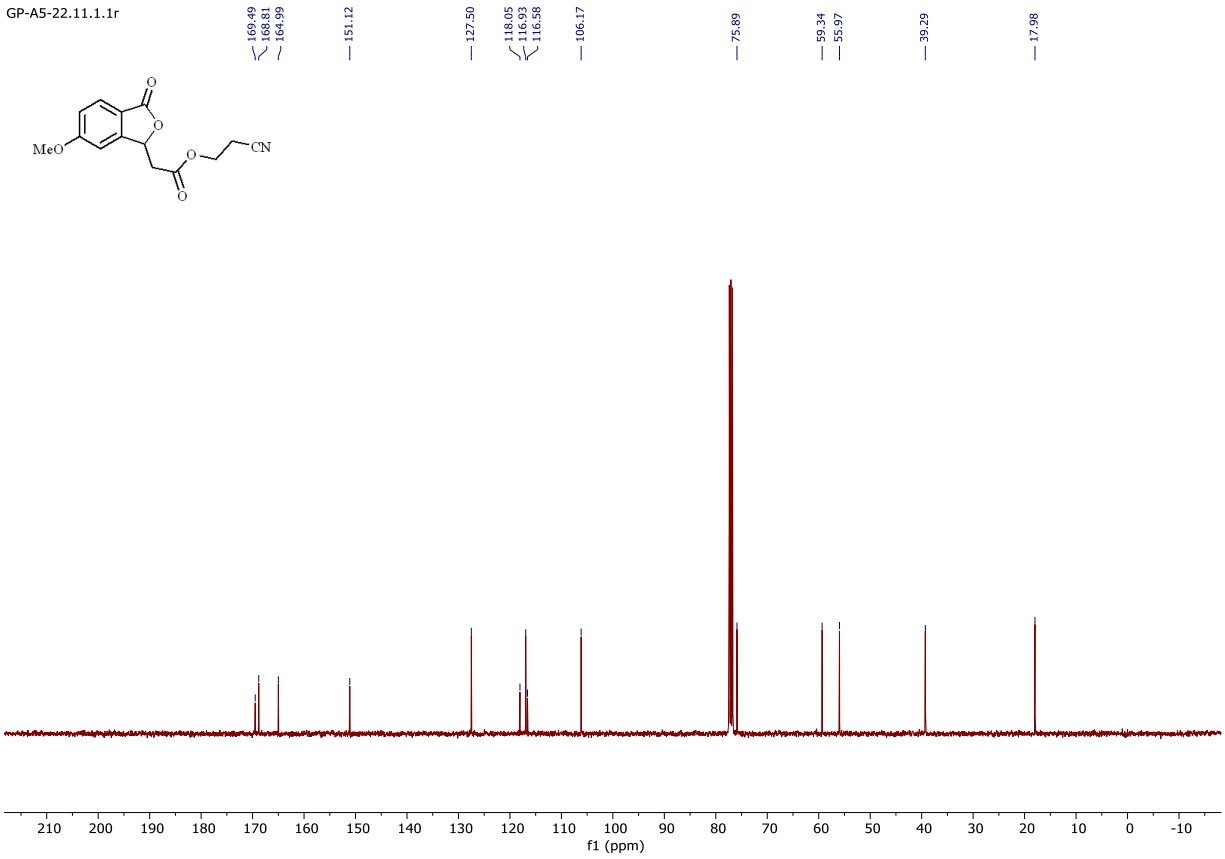
(3k) (^{13}C NMR 101 MHz, $CDCl_3$)



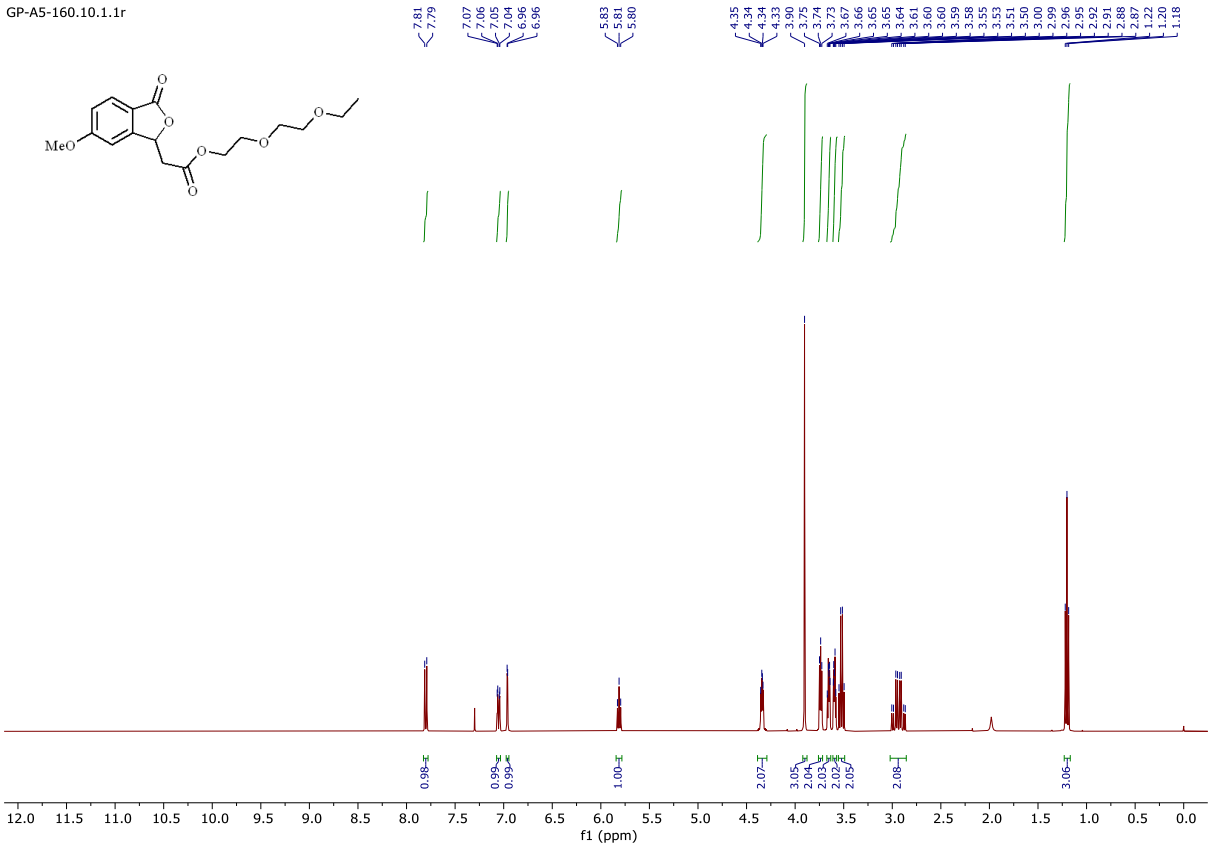
(3l) (^{1}H NMR 400 MHz, $CDCl_3$)



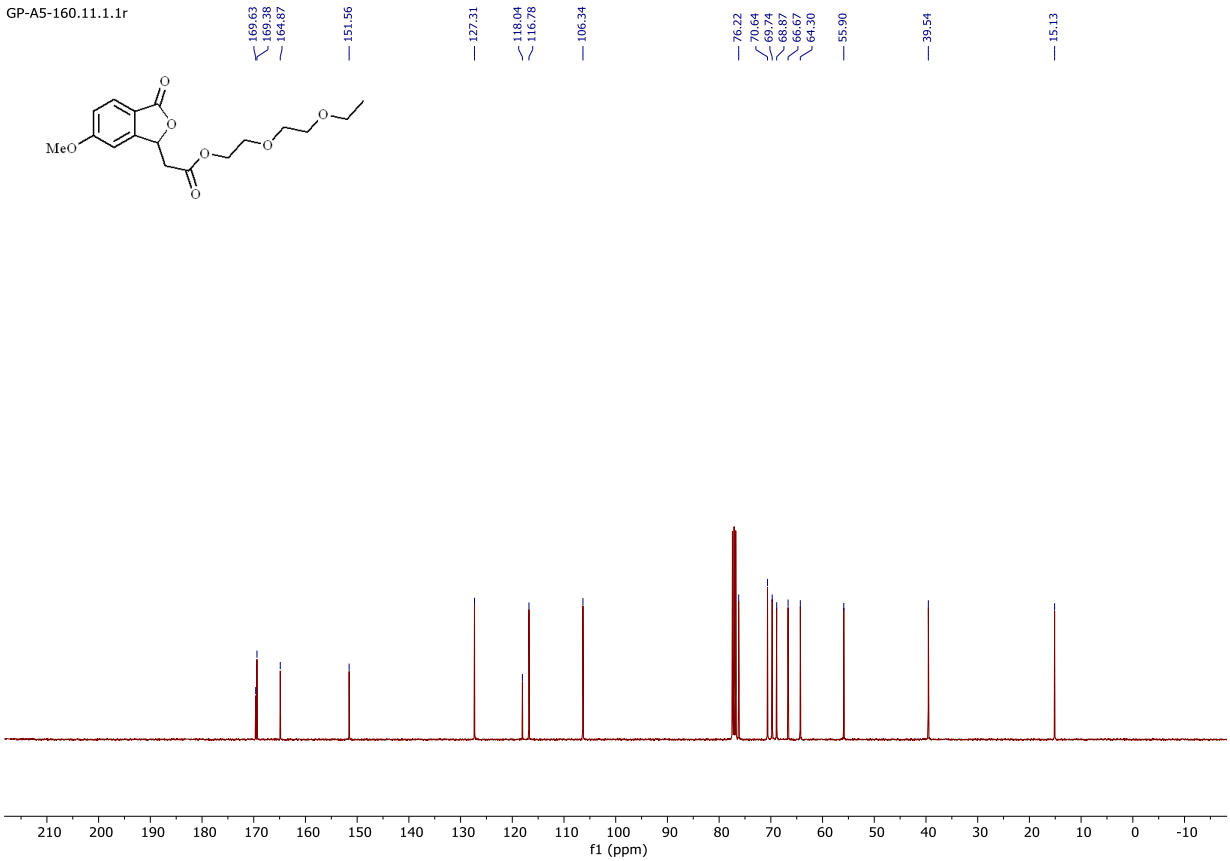
(3l) (^{13}C NMR 101 MHz, $CDCl_3$)



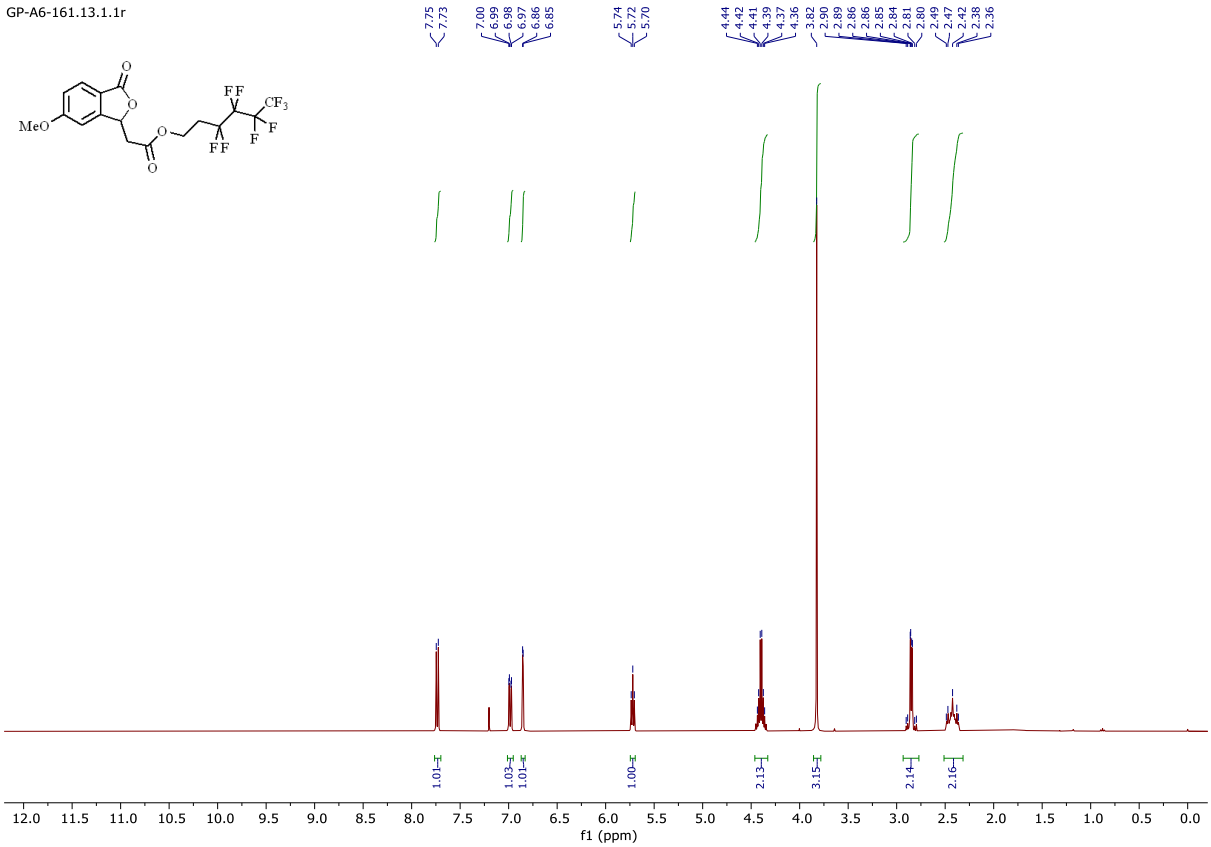
(3m) (^{1}H NMR 400 MHz, $CDCl_3$)



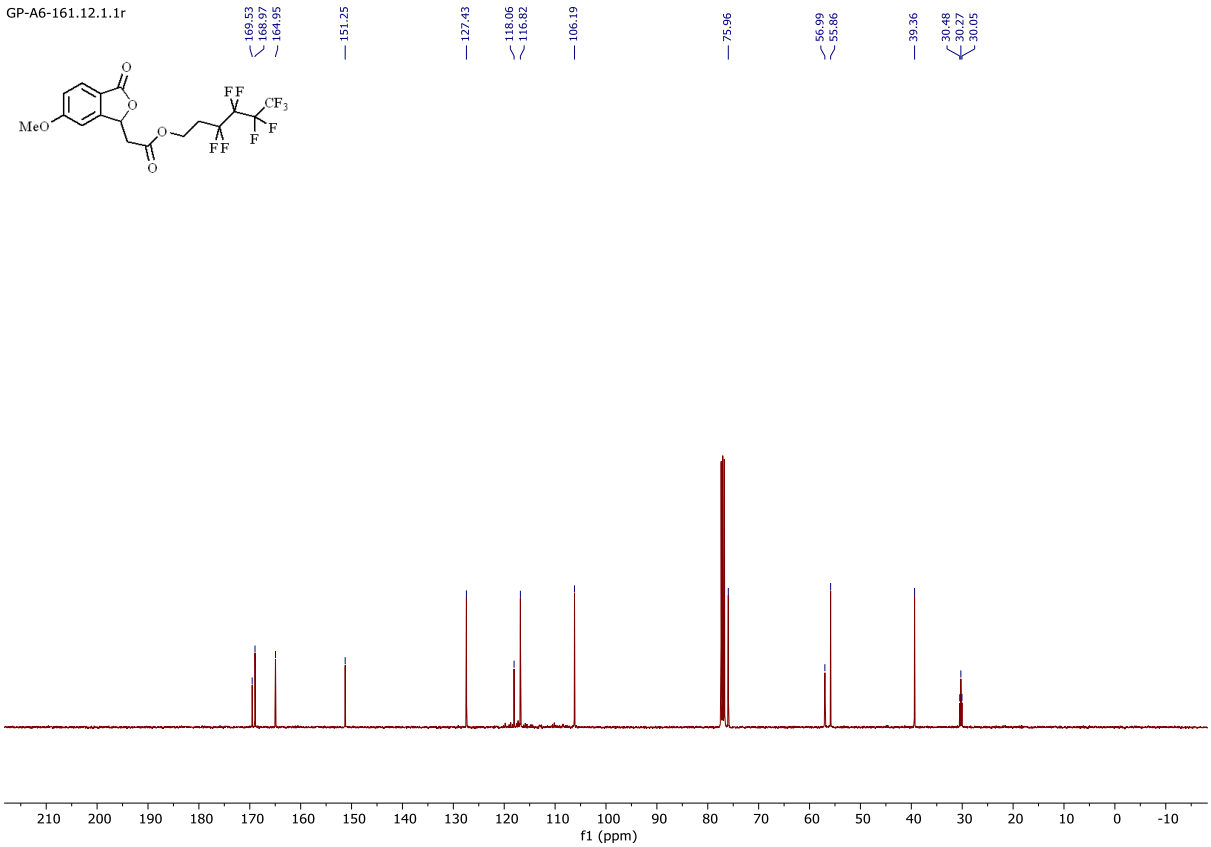
(3m) (^{13}C NMR 101 MHz, $CDCl_3$)



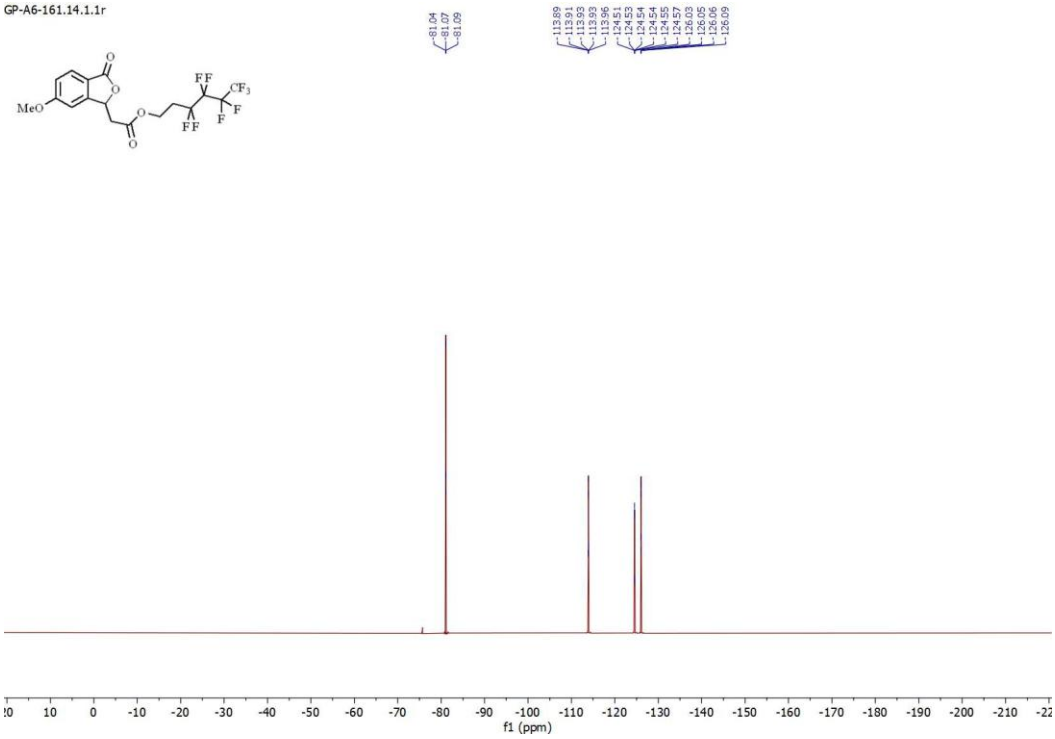
(3n) (^{1}H NMR 400 MHz, $CDCl_3$)



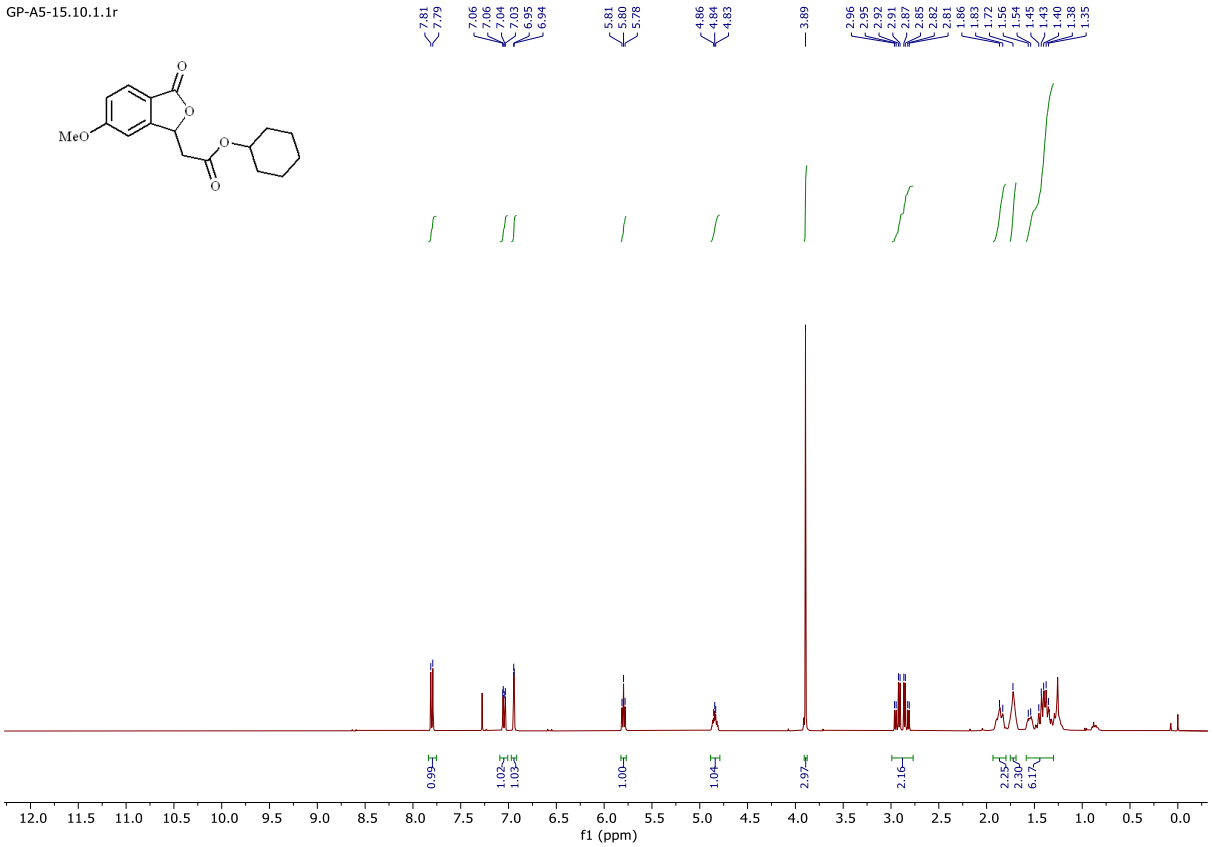
(3n) (^{13}C NMR 101 MHz, $CDCl_3$)



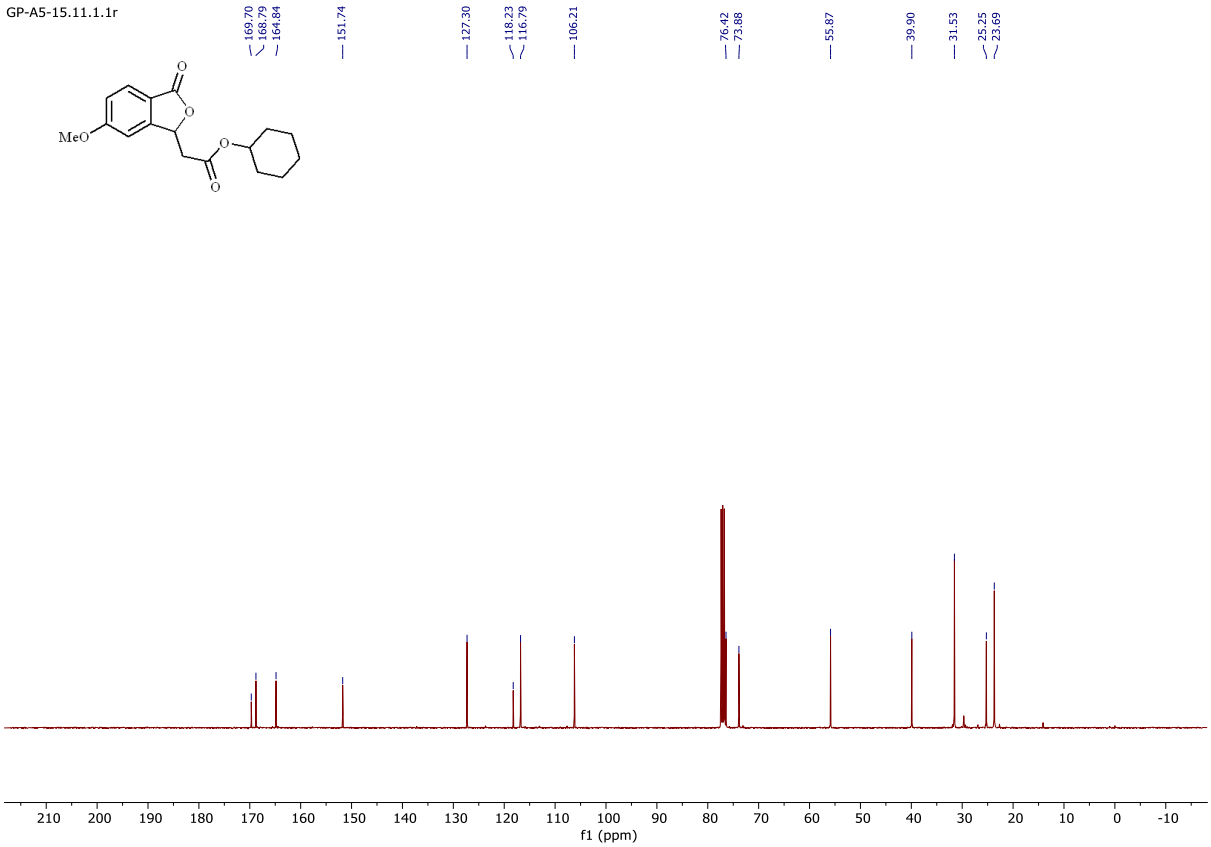
(3n) (^{19}F NMR 377 MHz, $CDCl_3$)



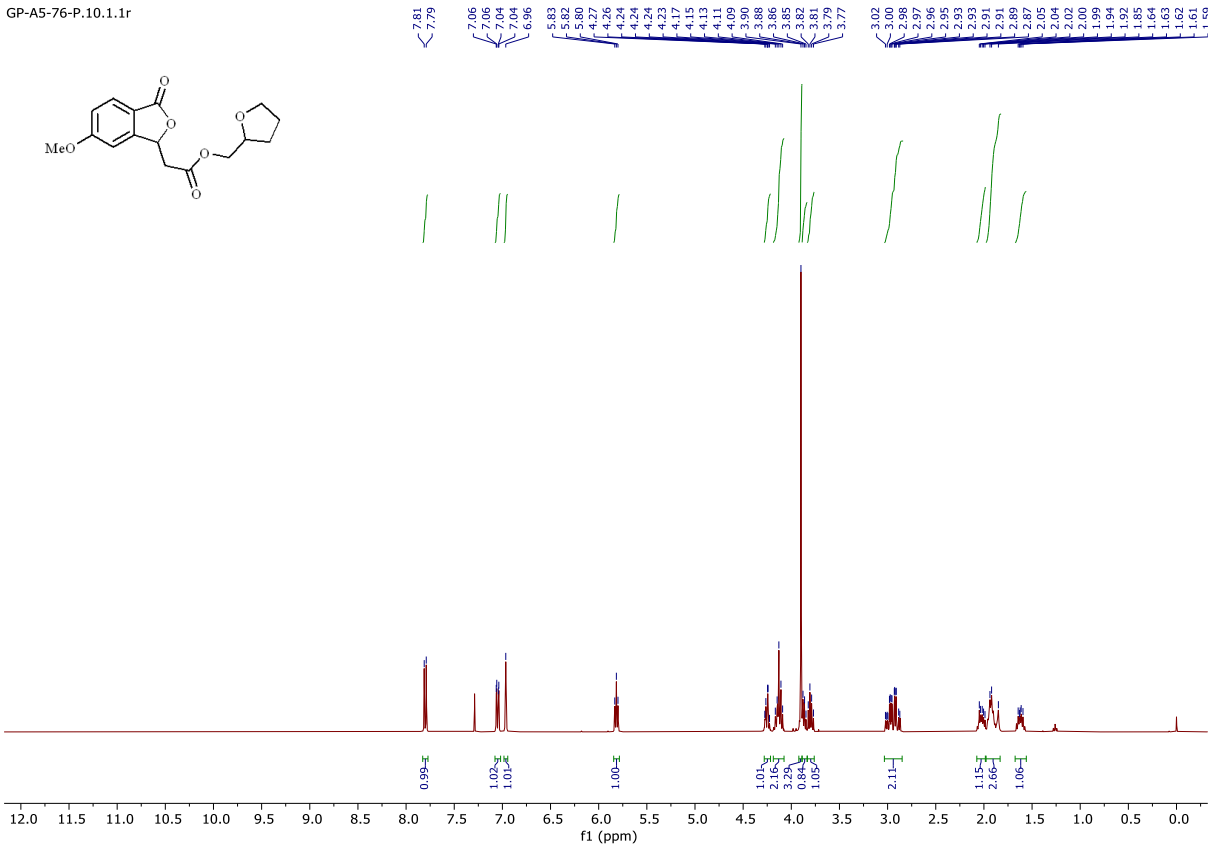
(3o) (^{1}H NMR 400 MHz, $CDCl_3$)



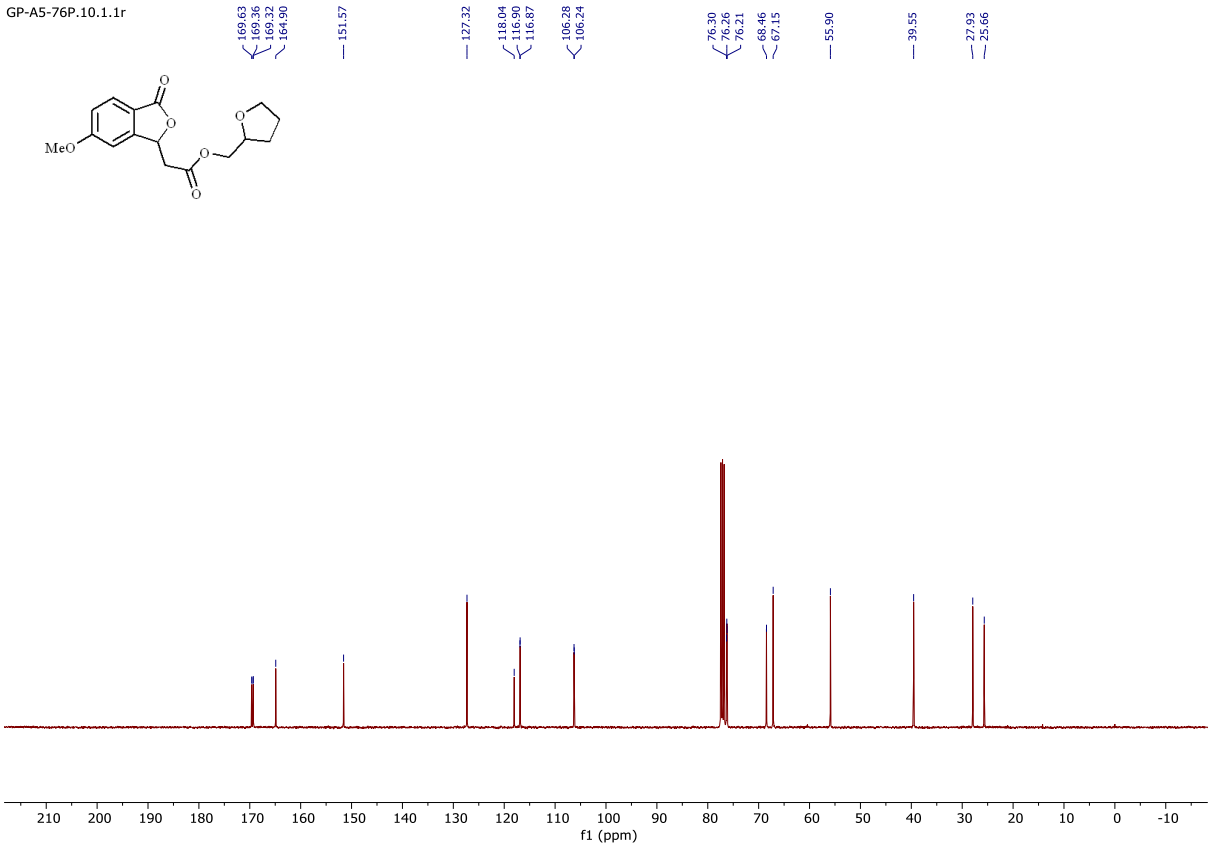
(3o) (^{13}C NMR 101 MHz, $CDCl_3$)



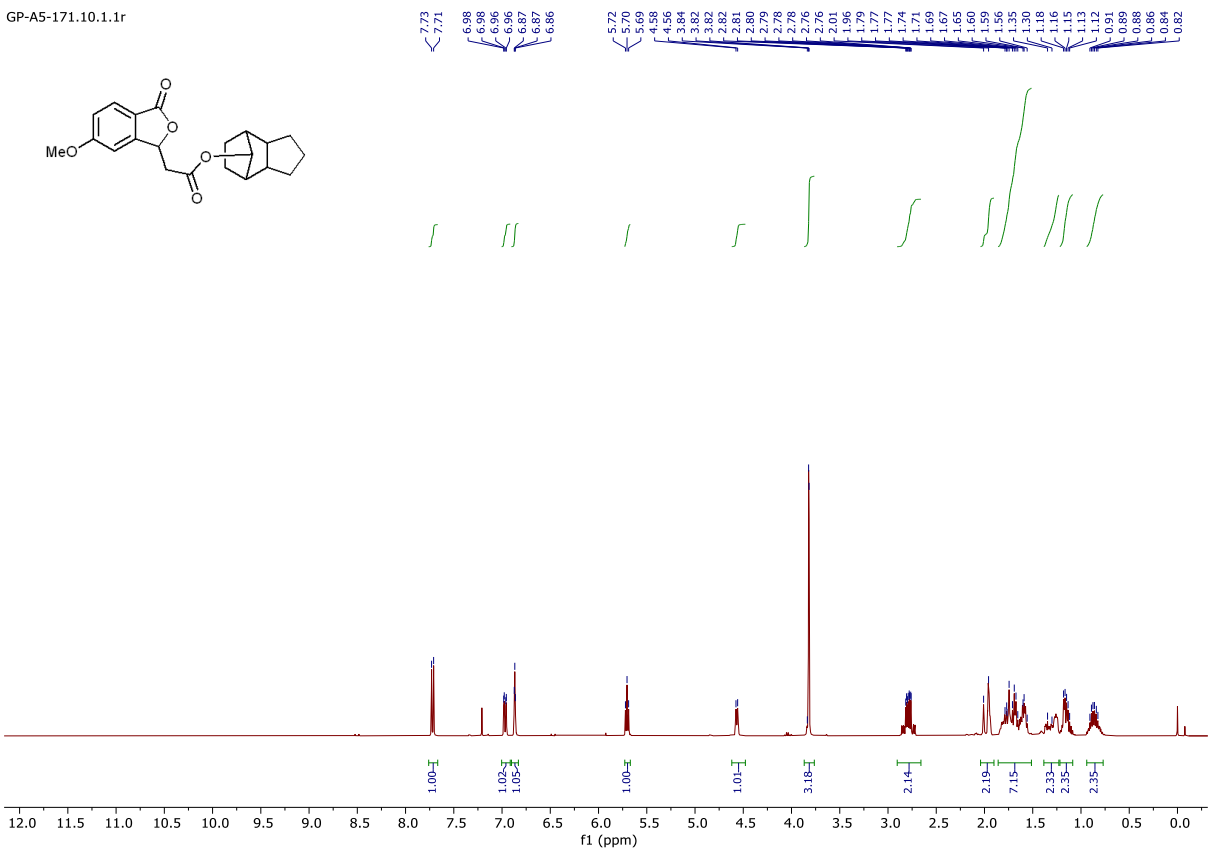
(3p) (^{1}H NMR 400 MHz, $CDCl_3$)



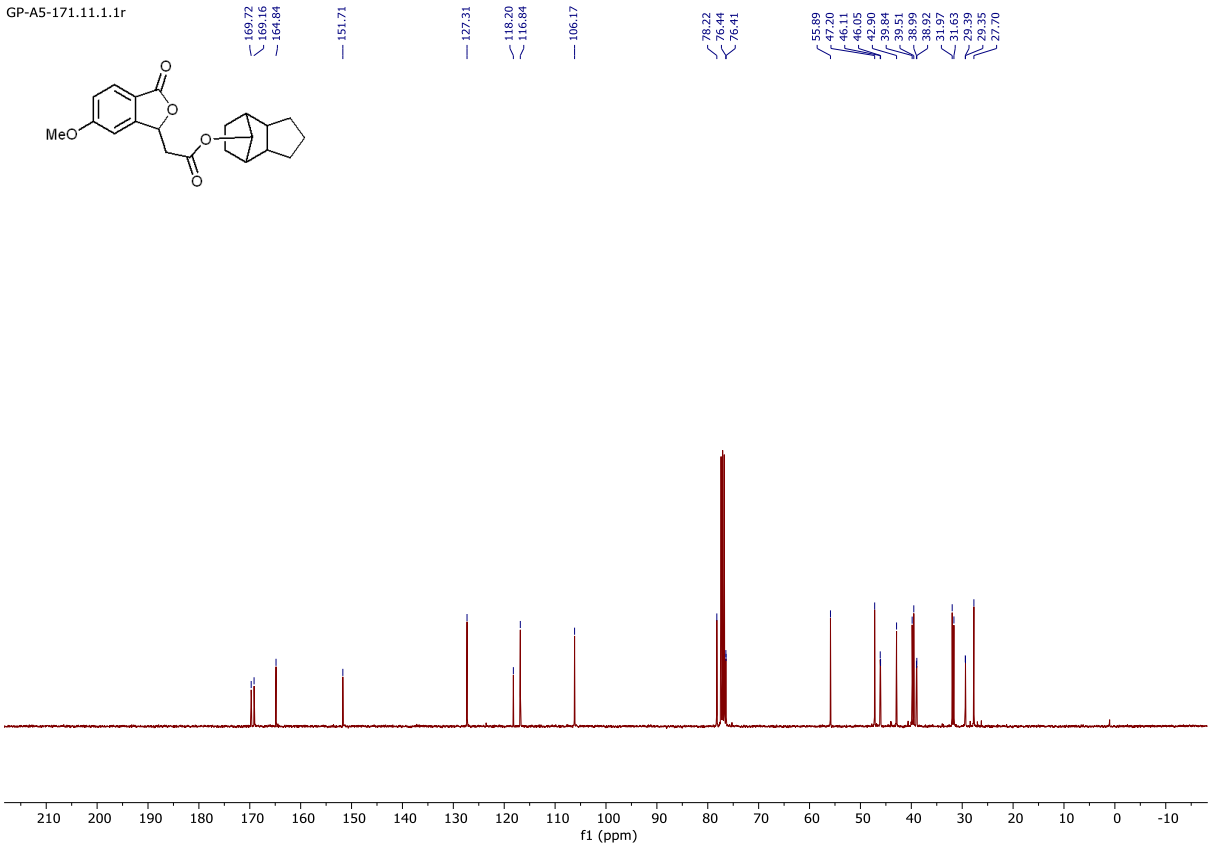
(3p) (^{13}C NMR 101 MHz, $CDCl_3$)



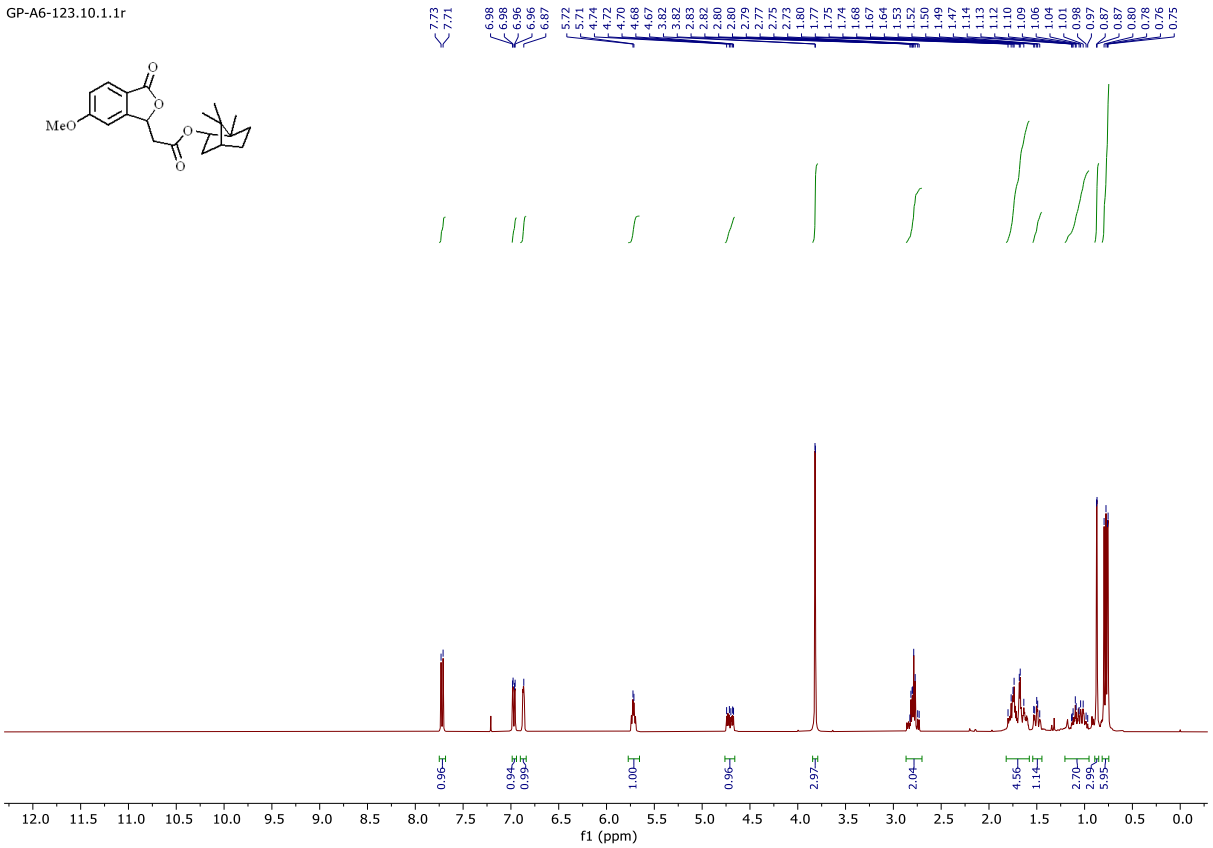
(3q) (^{1}H NMR 400 MHz, $CDCl_3$)



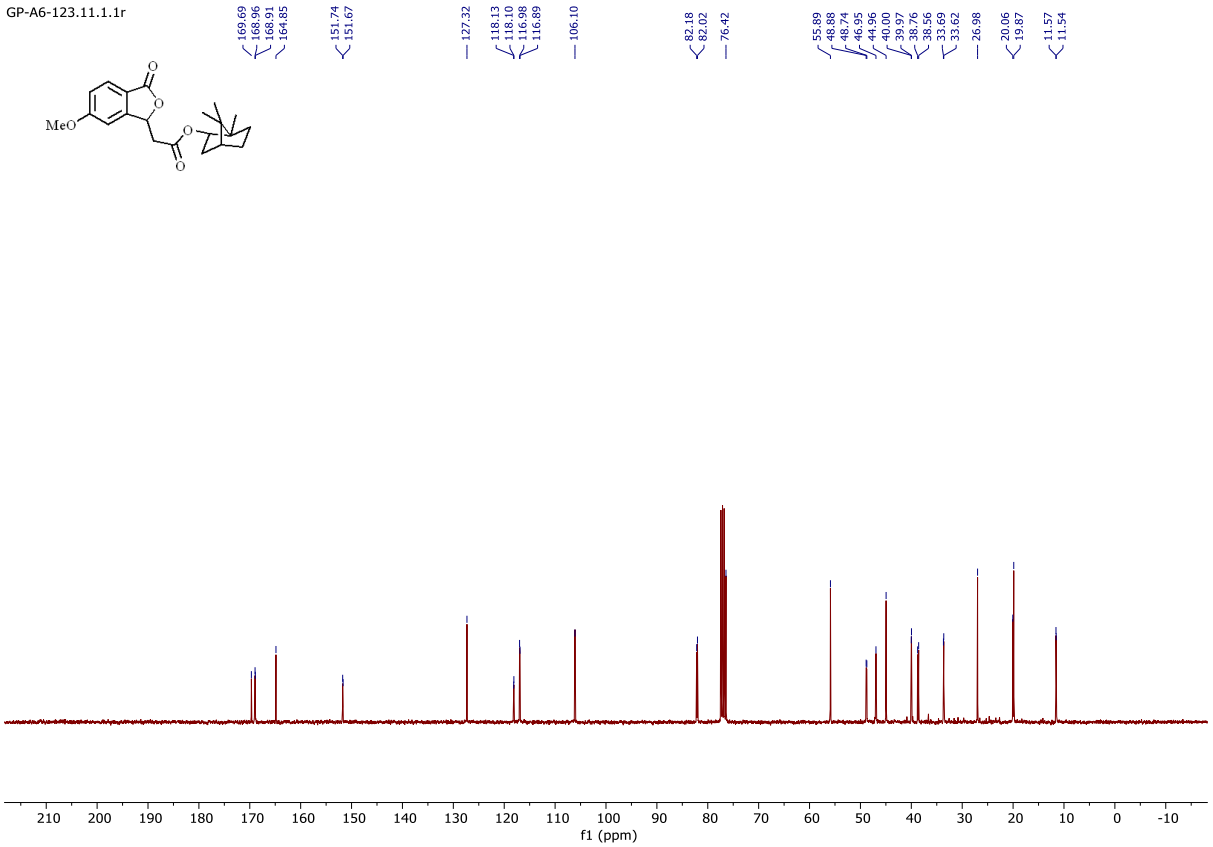
(3q) (^{13}C NMR 101 MHz, $CDCl_3$)



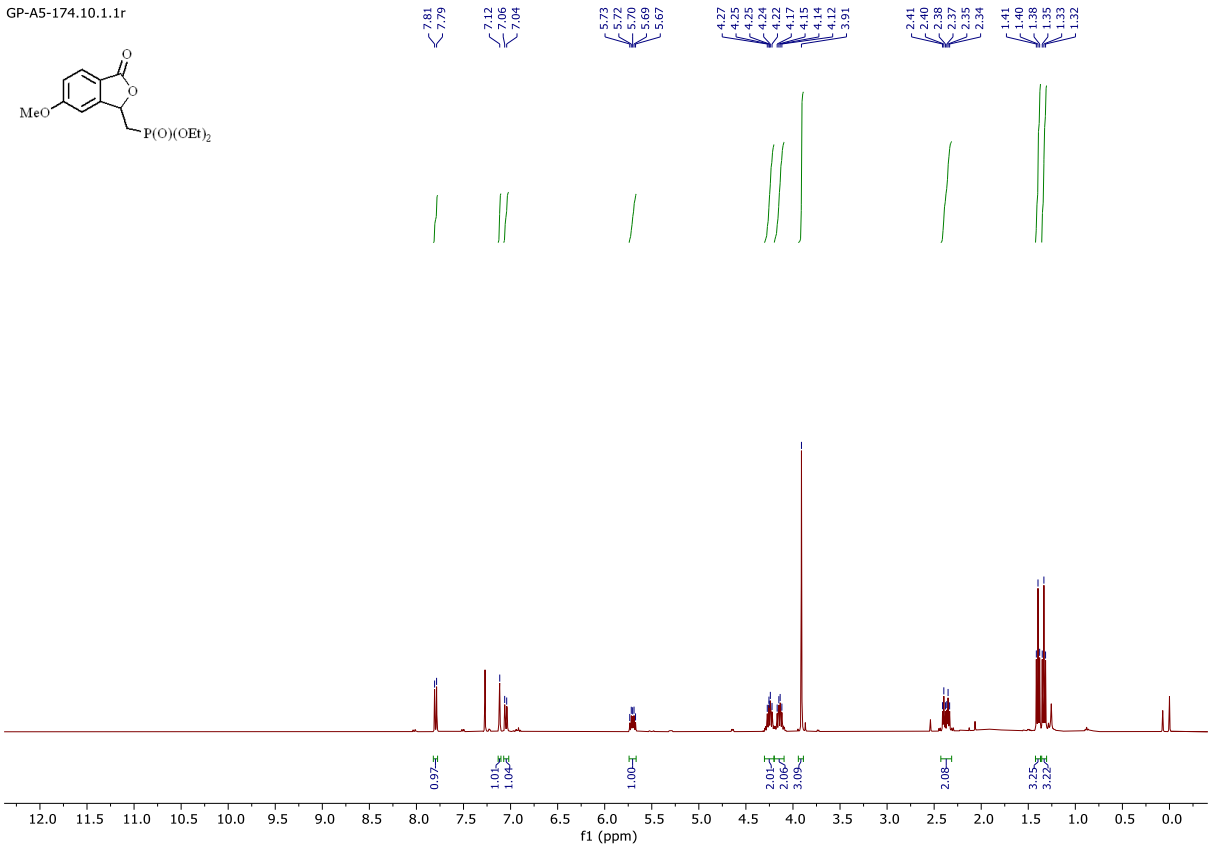
(3r) (^{1}H NMR 400 MHz, $CDCl_3$)



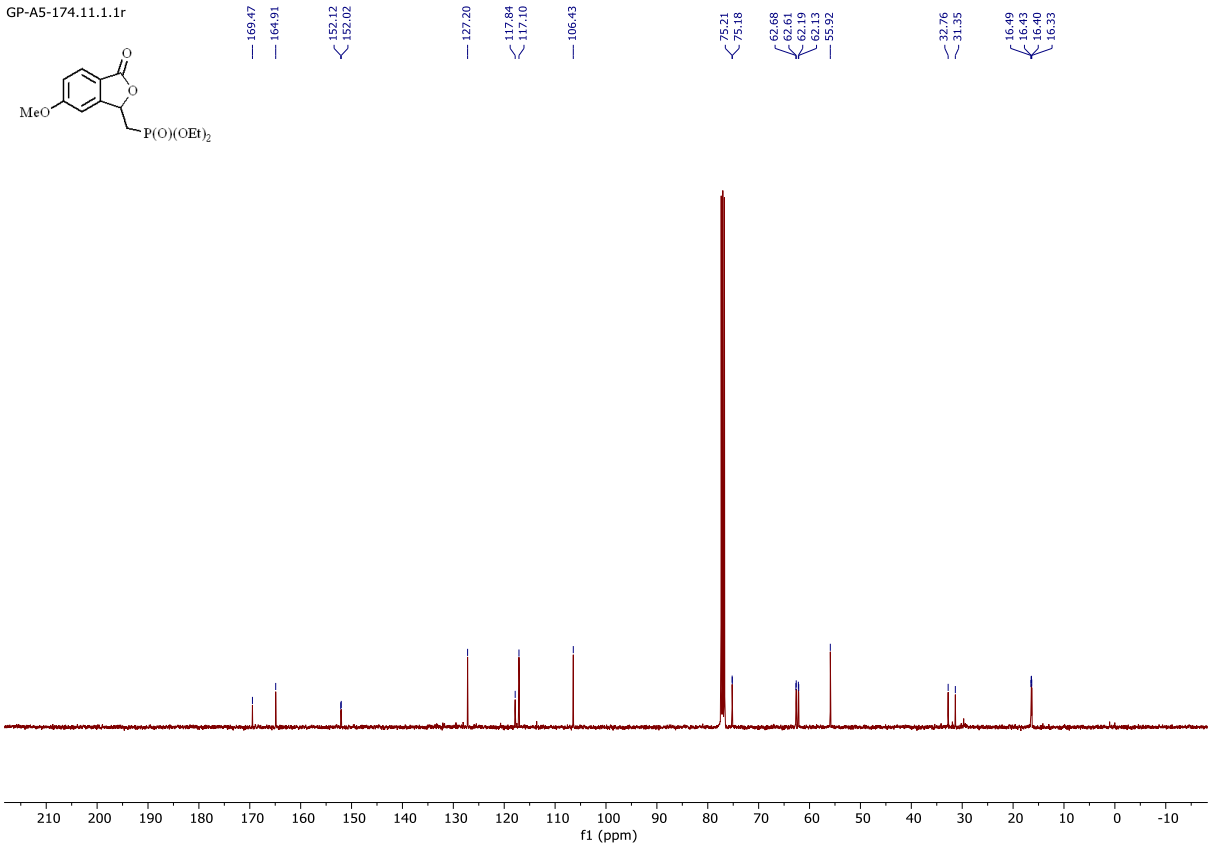
(3r) (^{13}C NMR 101 MHz, $CDCl_3$)



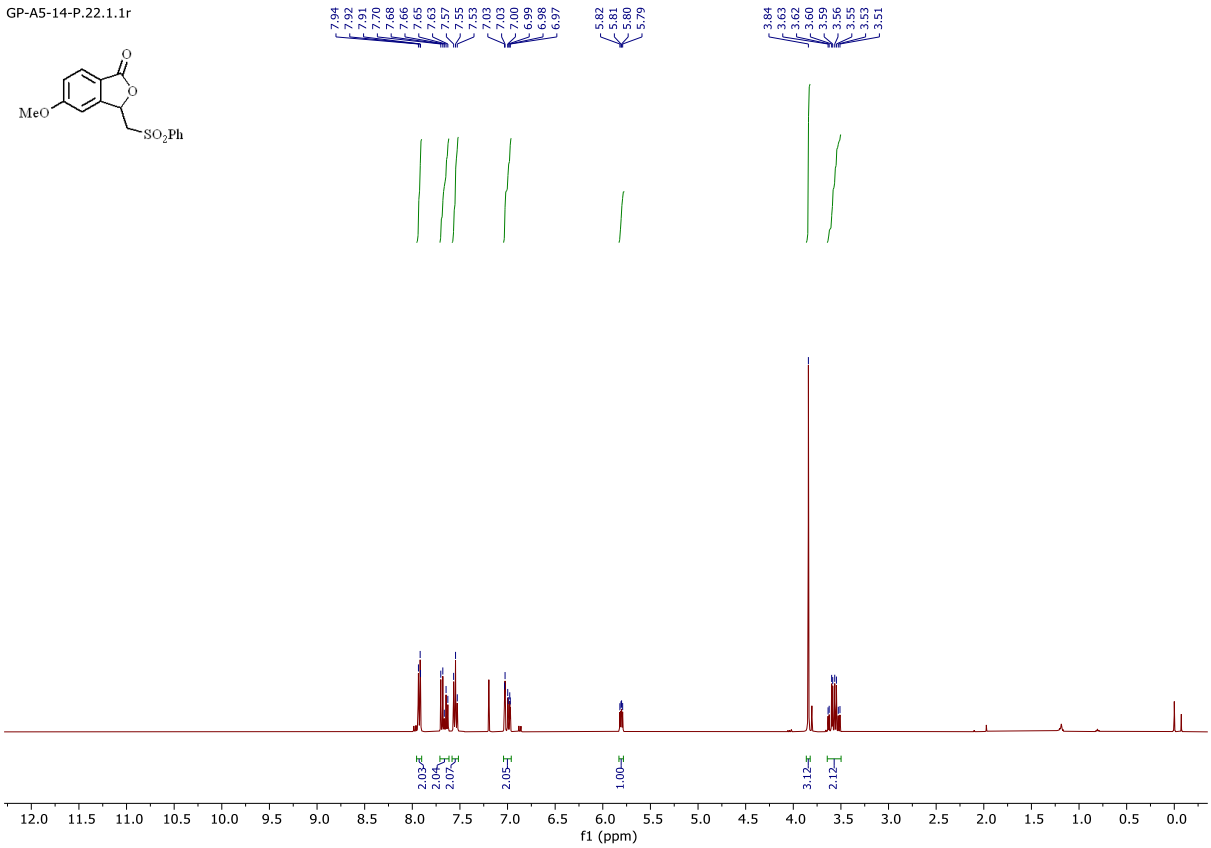
(3s) (^{1}H NMR 400 MHz, $CDCl_3$)



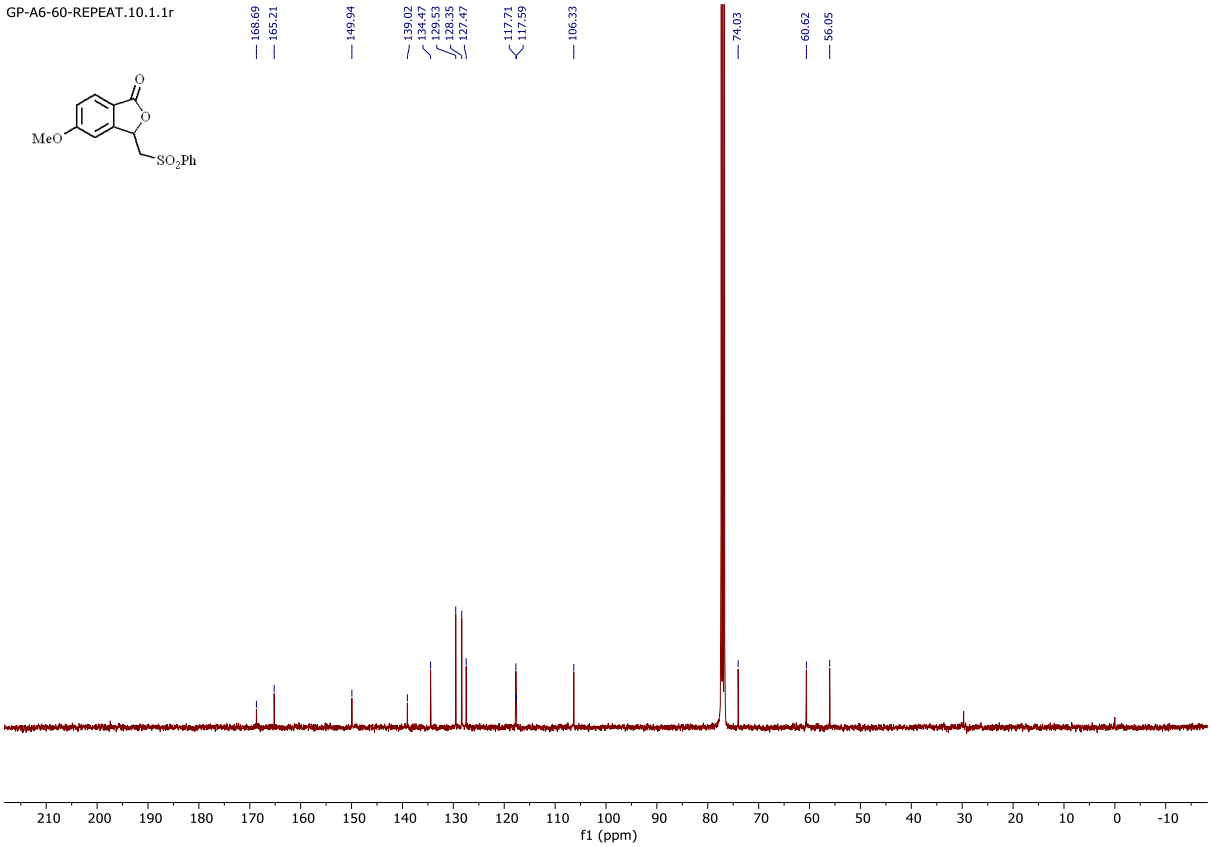
(3s) (^{13}C NMR 101 MHz, $CDCl_3$)



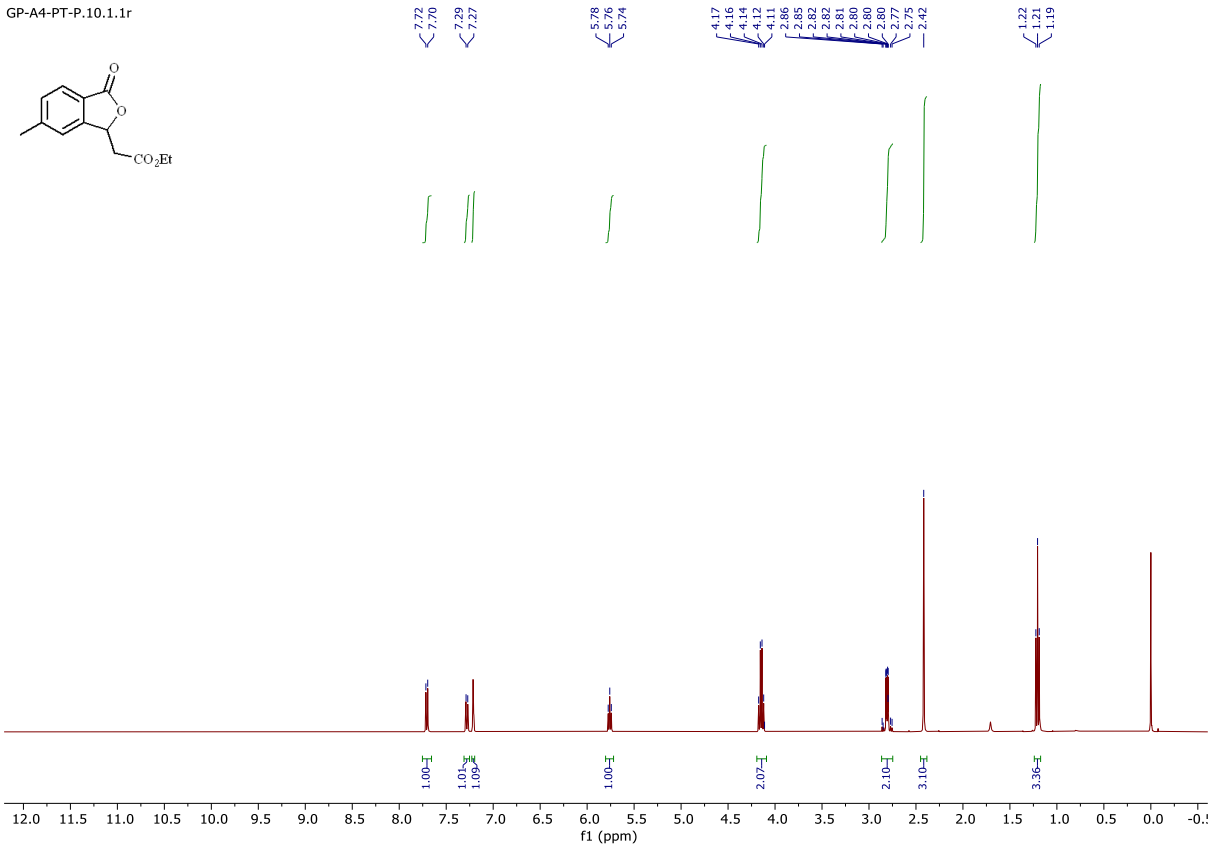
(3t) (^{1}H NMR 400 MHz, $CDCl_3$)



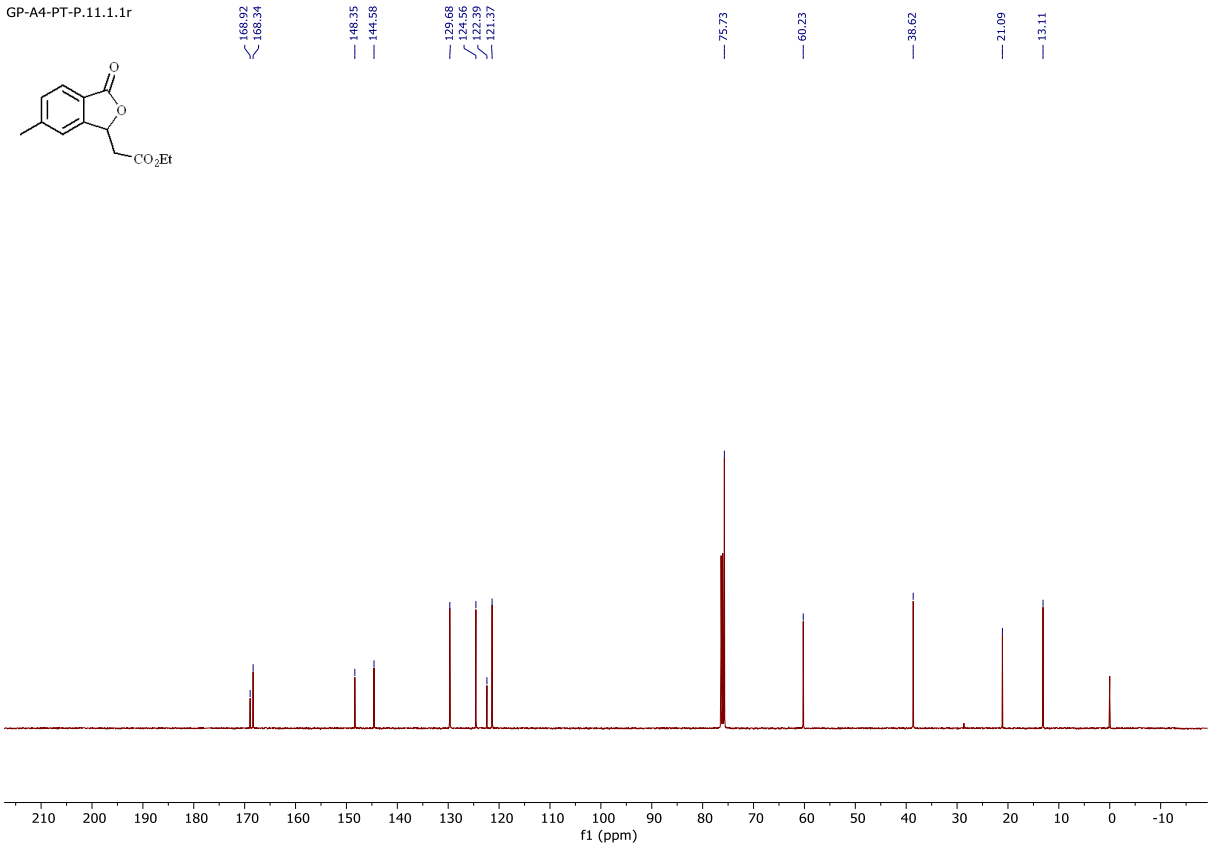
(3t) (^{13}C NMR 101 MHz, $CDCl_3$)



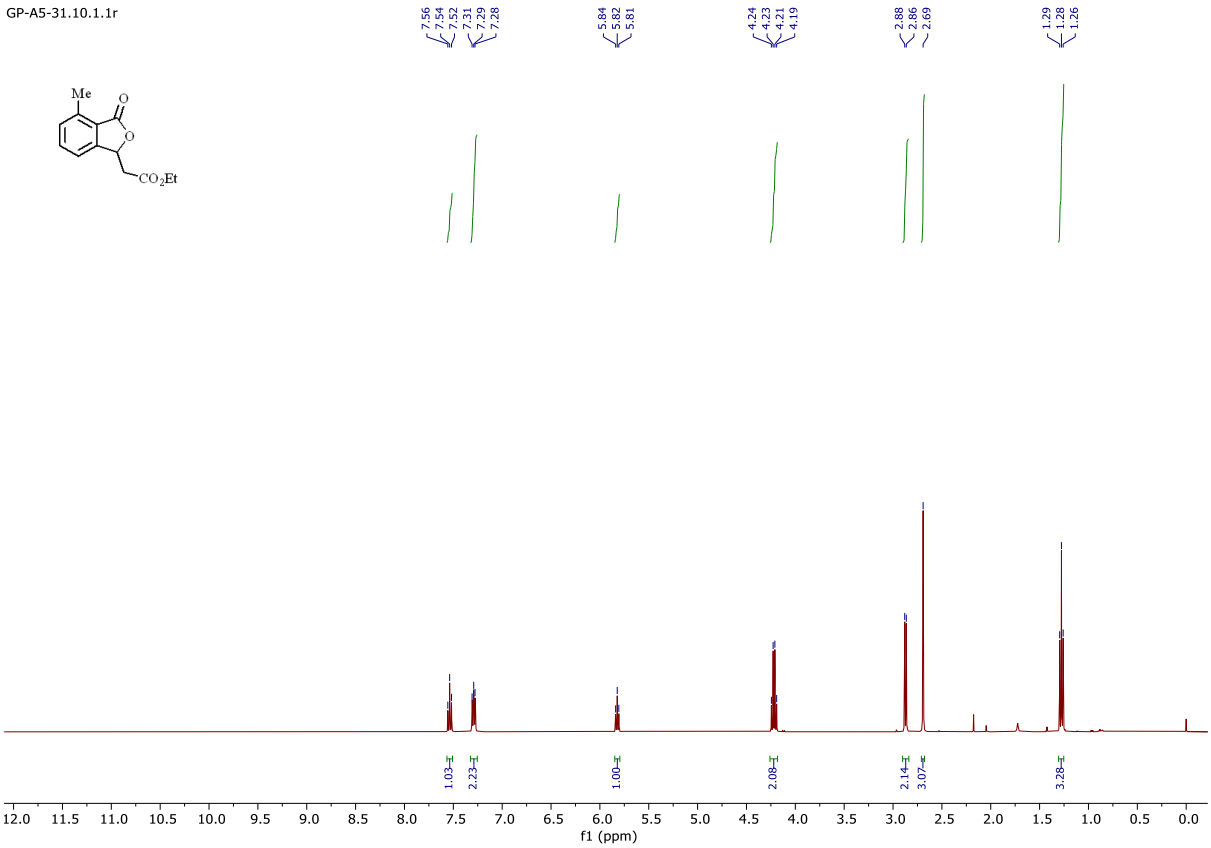
(5a) (^{1}H NMR 400 MHz, $CDCl_3$)



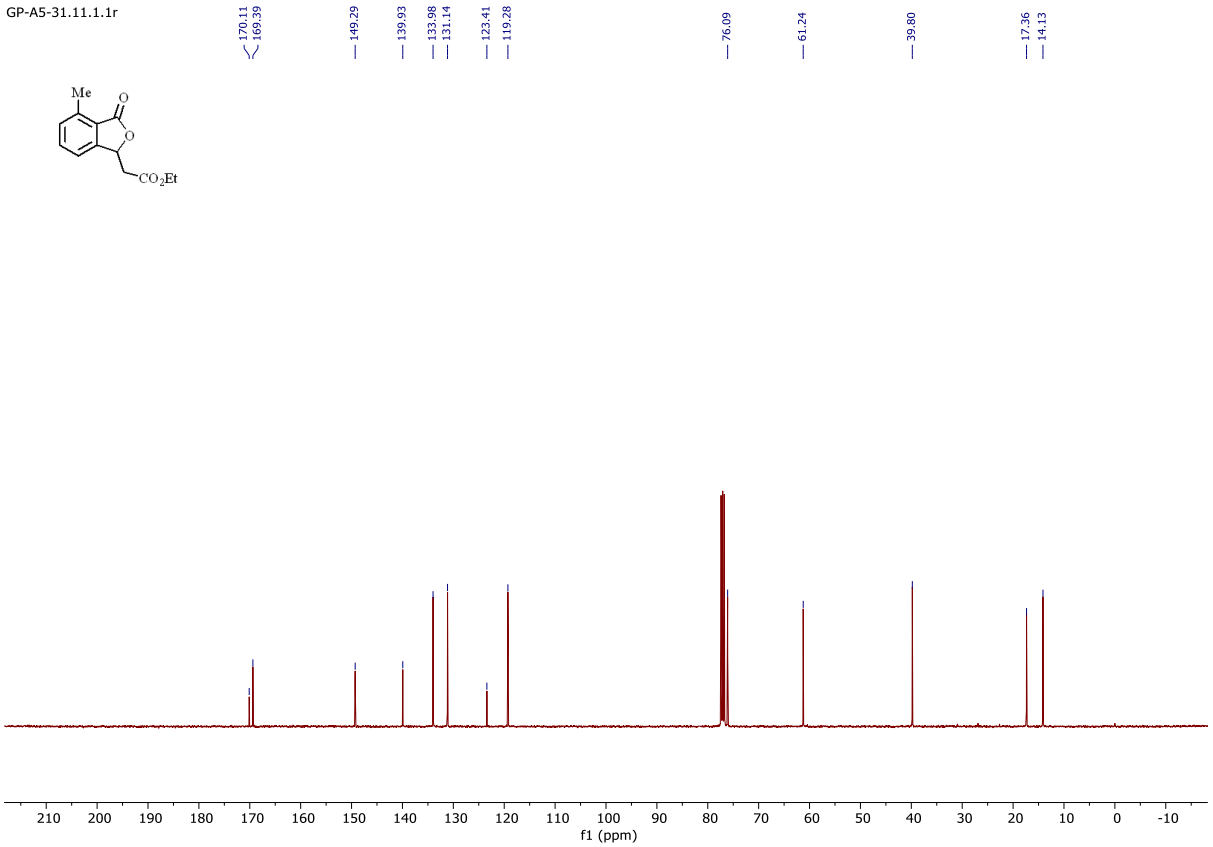
(5a) (^{13}C NMR 101 MHz, $CDCl_3$)



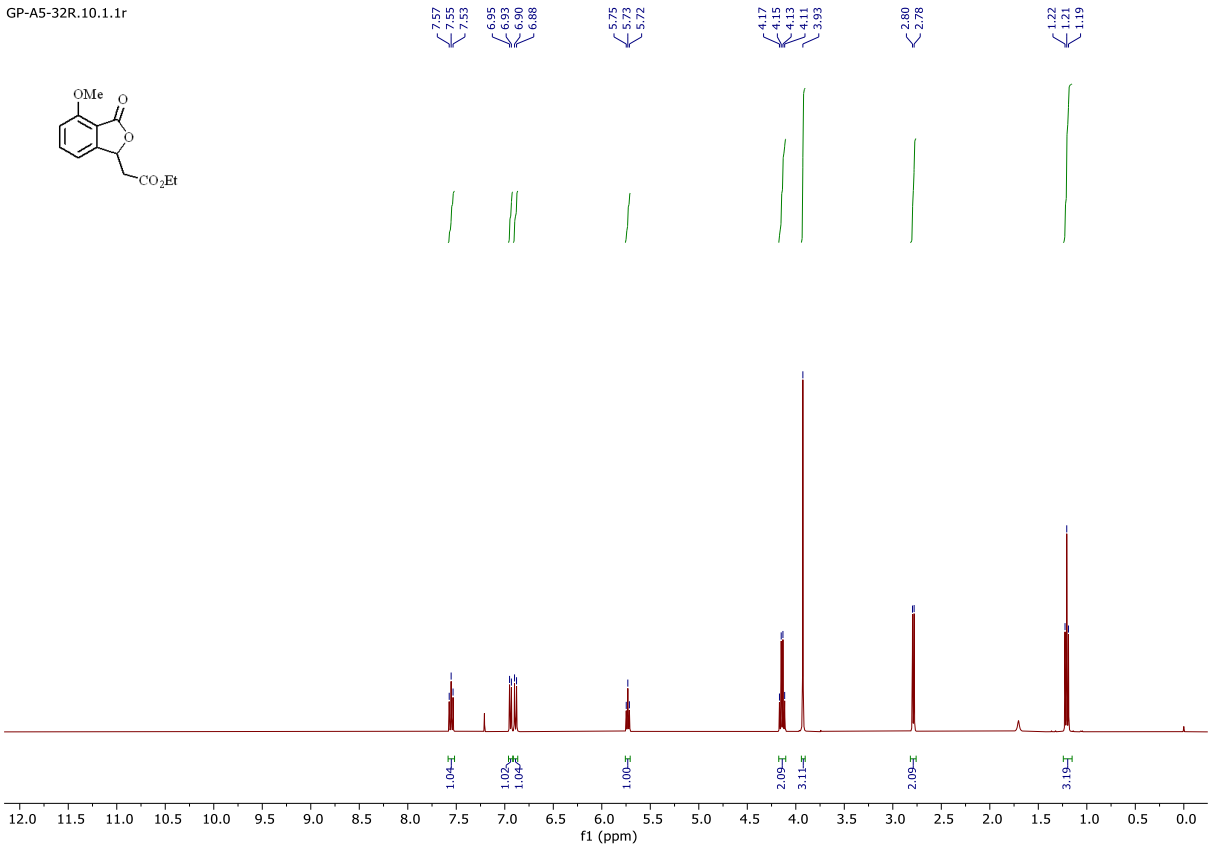
(5b) (^{1}H NMR 400 MHz, $CDCl_3$)



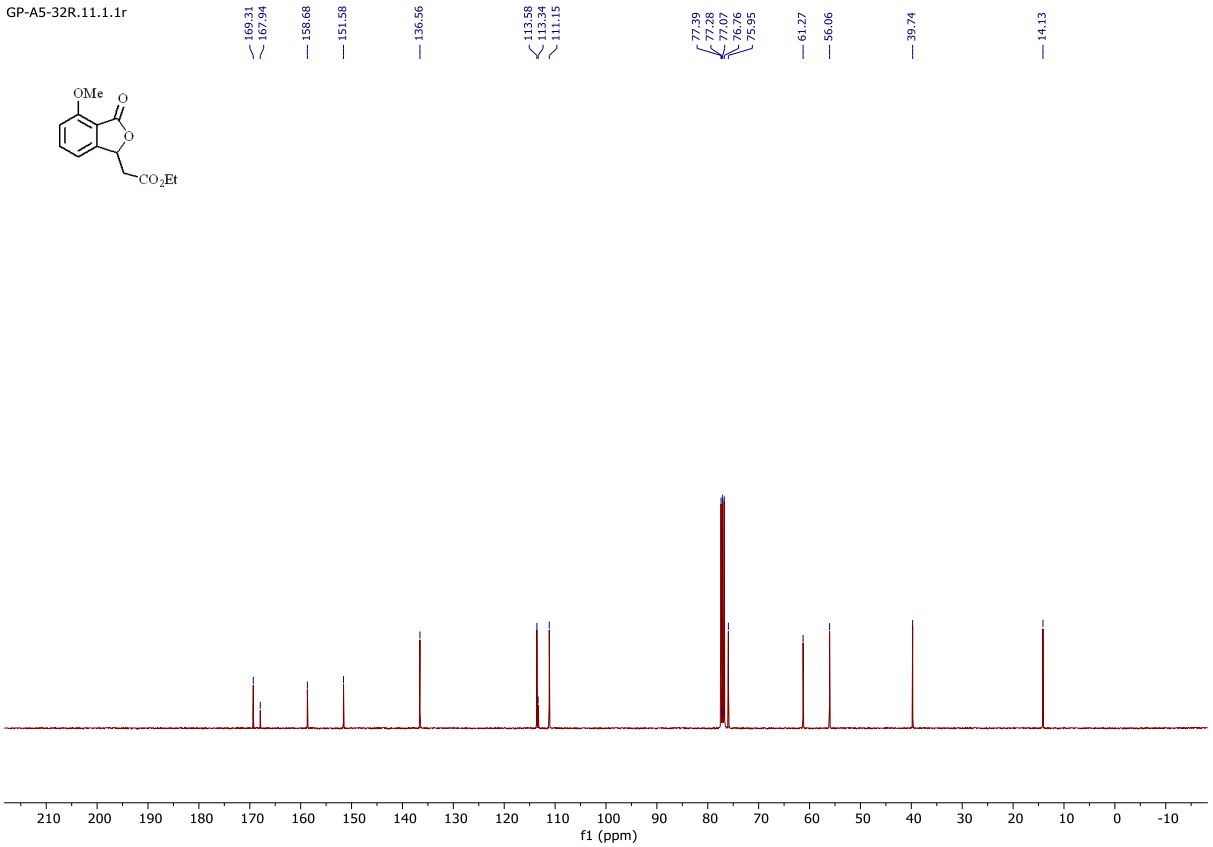
(5b) (^{13}C NMR 101 MHz, $CDCl_3$)



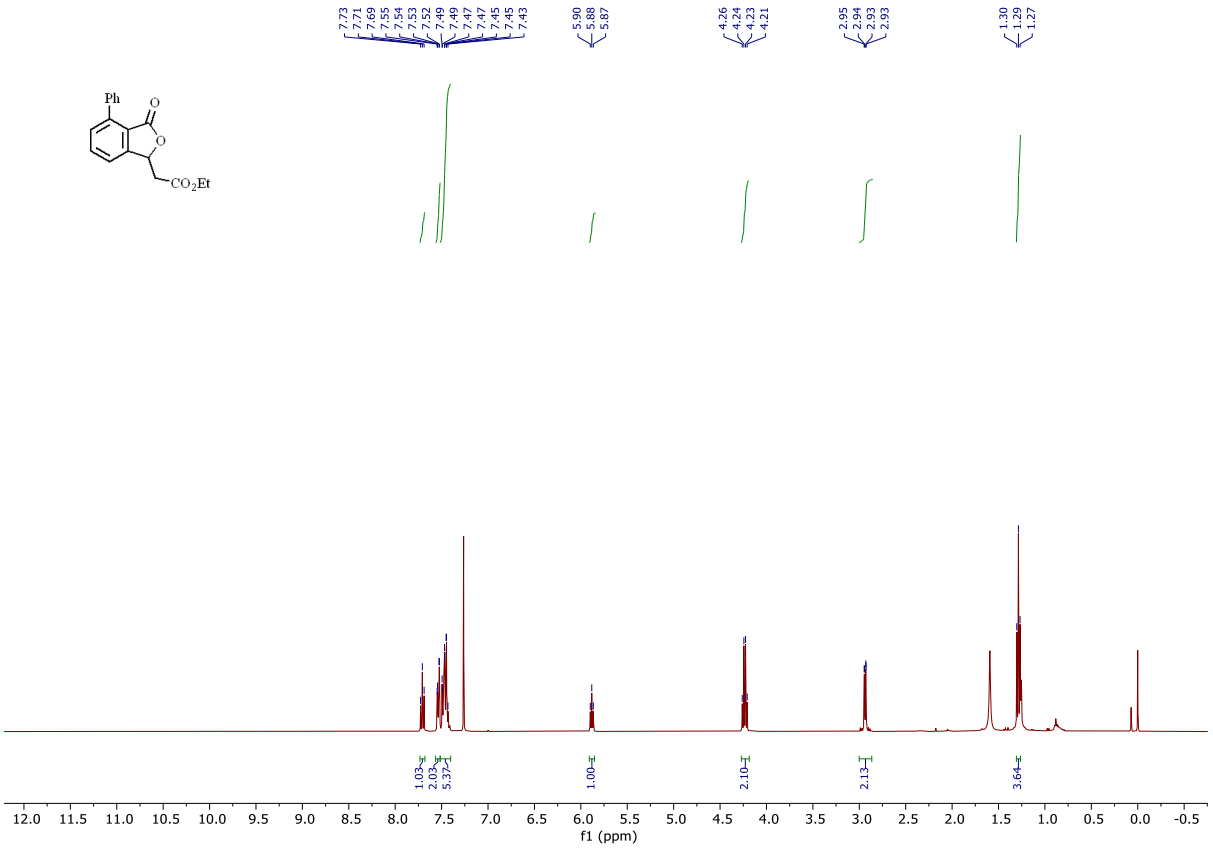
(5c) (^{1}H NMR 400 MHz, $CDCl_3$)



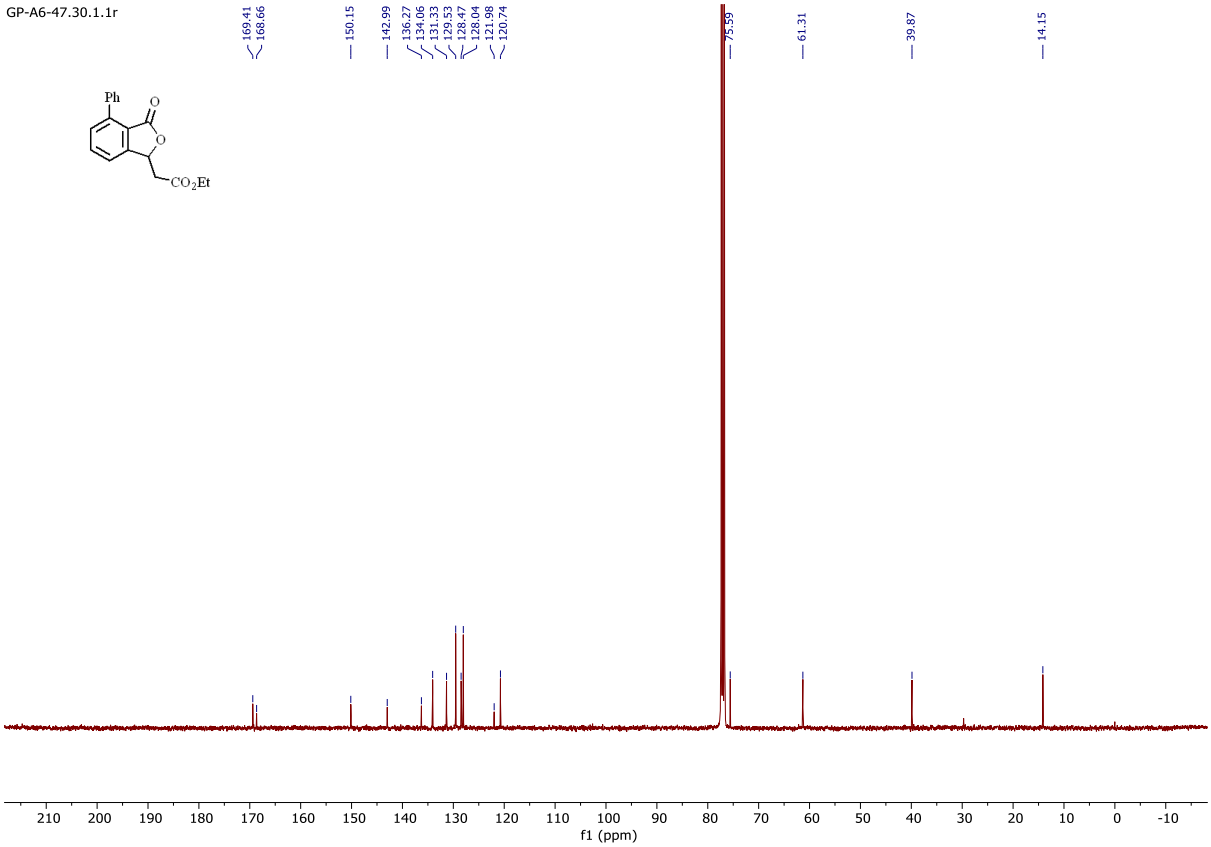
(5c) (^{13}C NMR 101 MHz, $CDCl_3$)



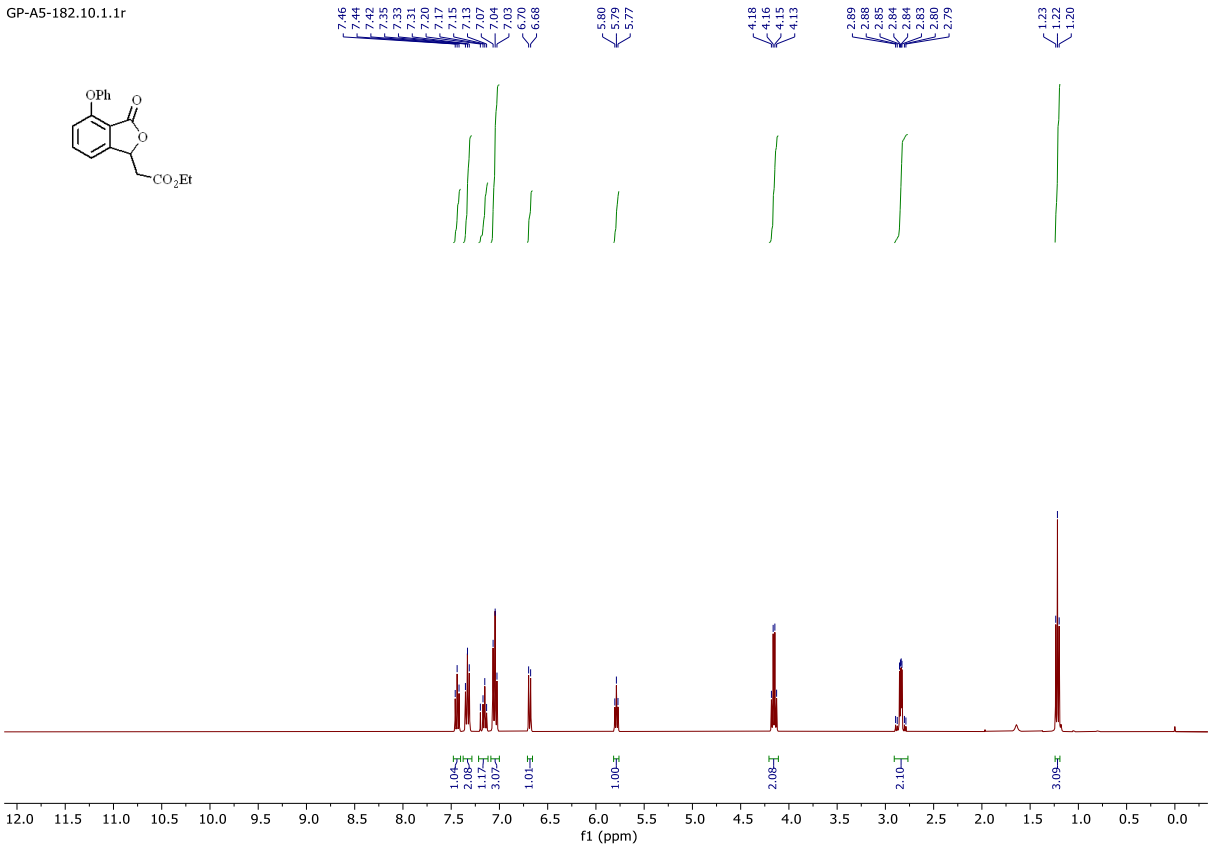
(5d) (^{1}H NMR 400 MHz, $CDCl_3$)



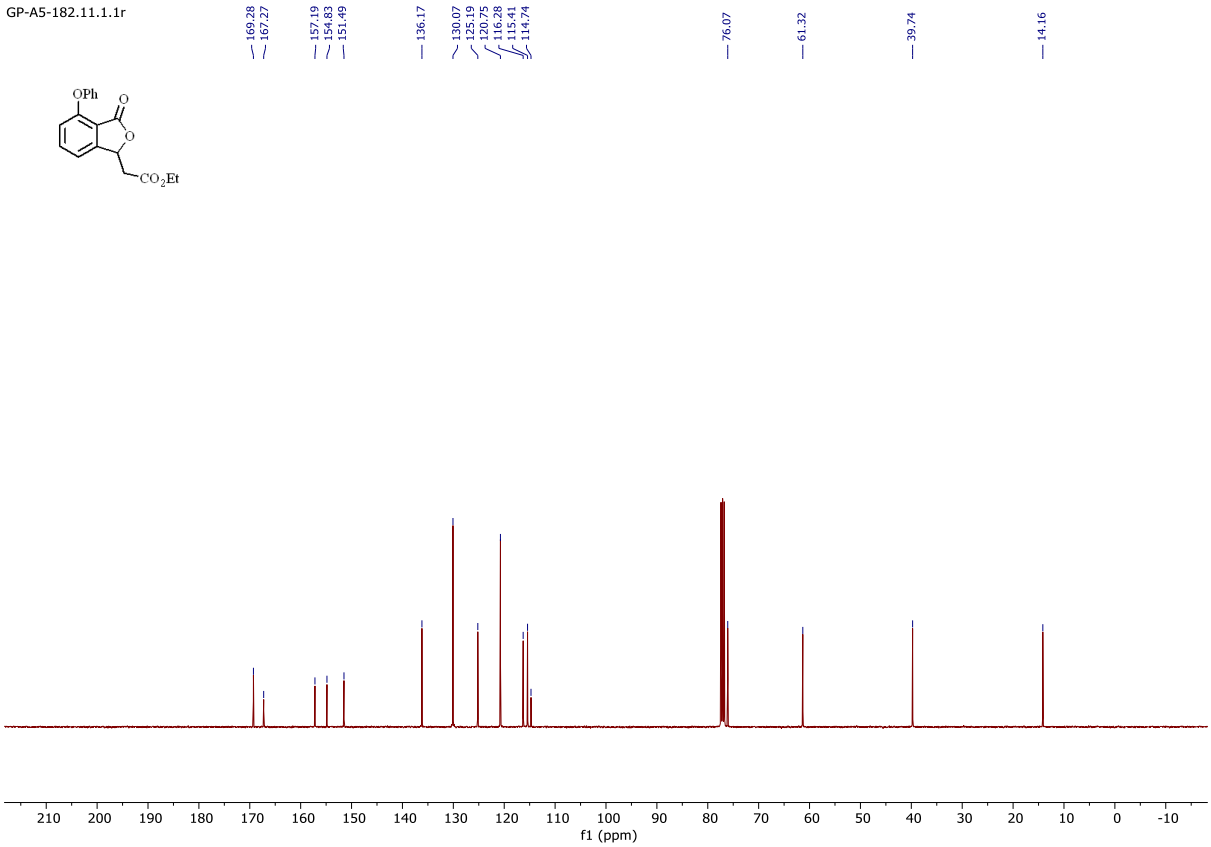
(5d) (^{13}C NMR 101 MHz, $CDCl_3$)



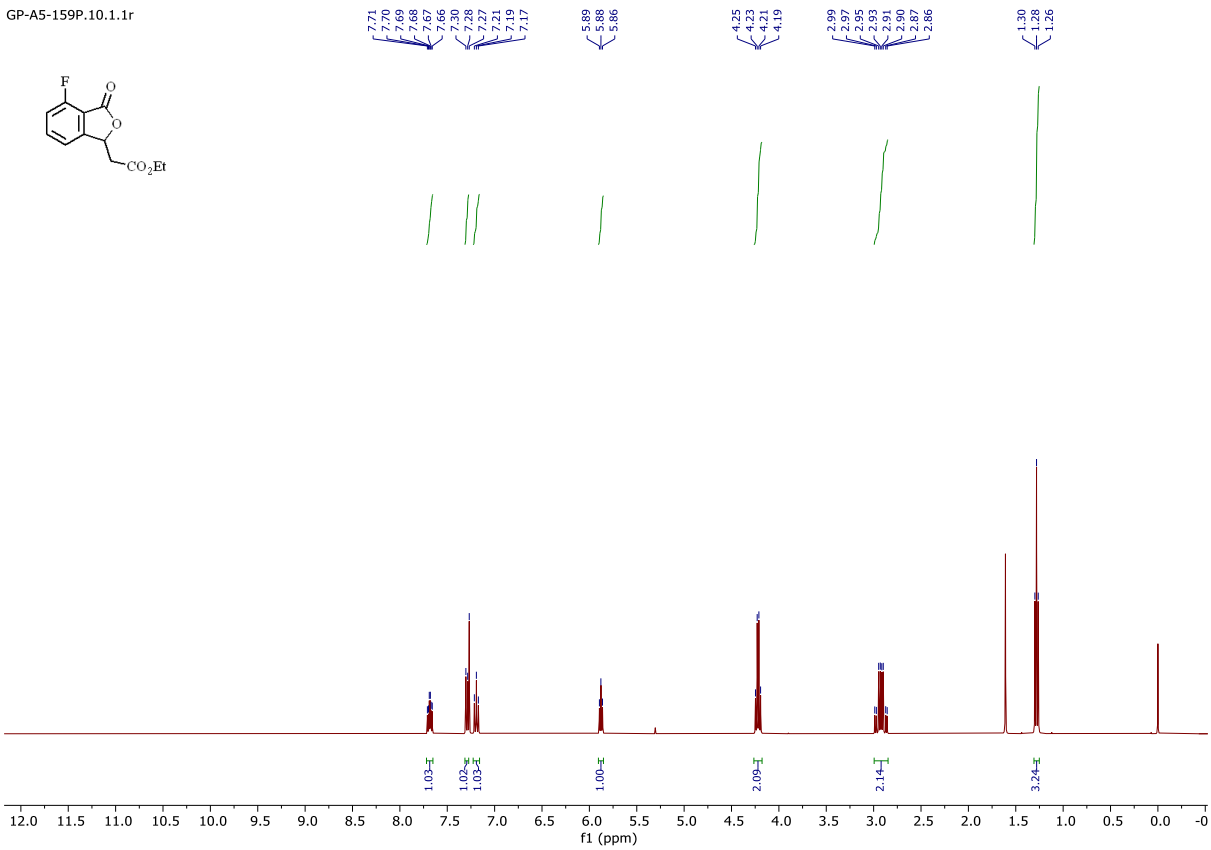
(5e) (^{1}H NMR 400 MHz, $CDCl_3$)



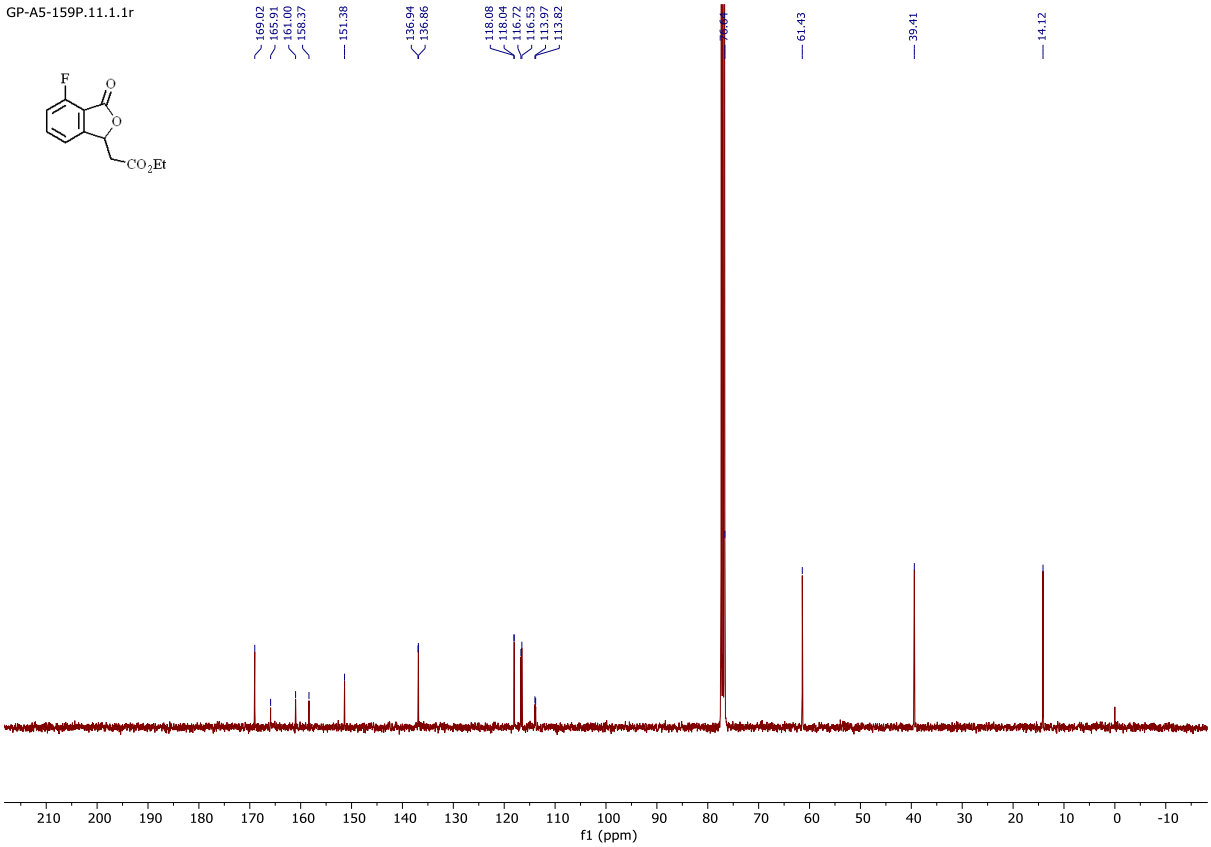
(5e) (^{13}C NMR 101 MHz, $CDCl_3$)



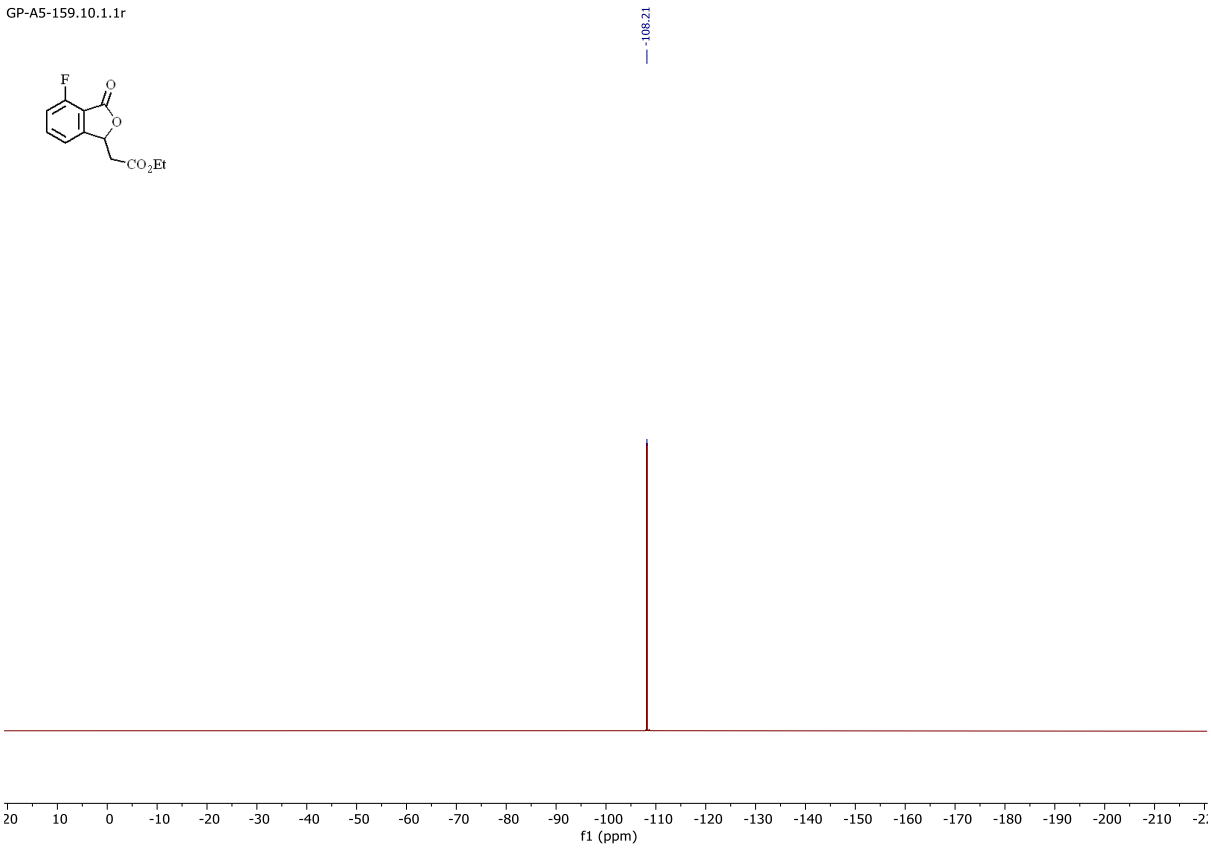
(5f) (^{1}H NMR 400 MHz, $CDCl_3$)



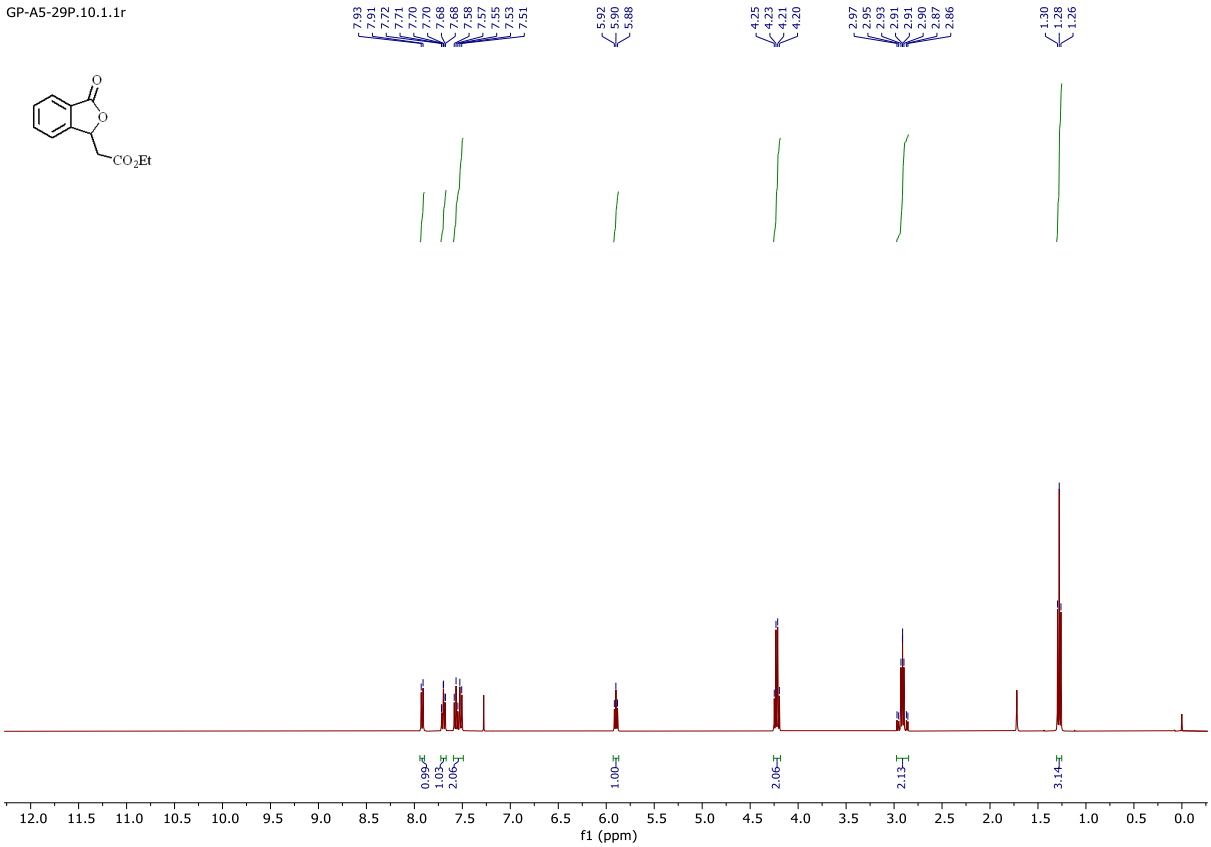
(5f) (^{13}C NMR 101 MHz, $CDCl_3$)



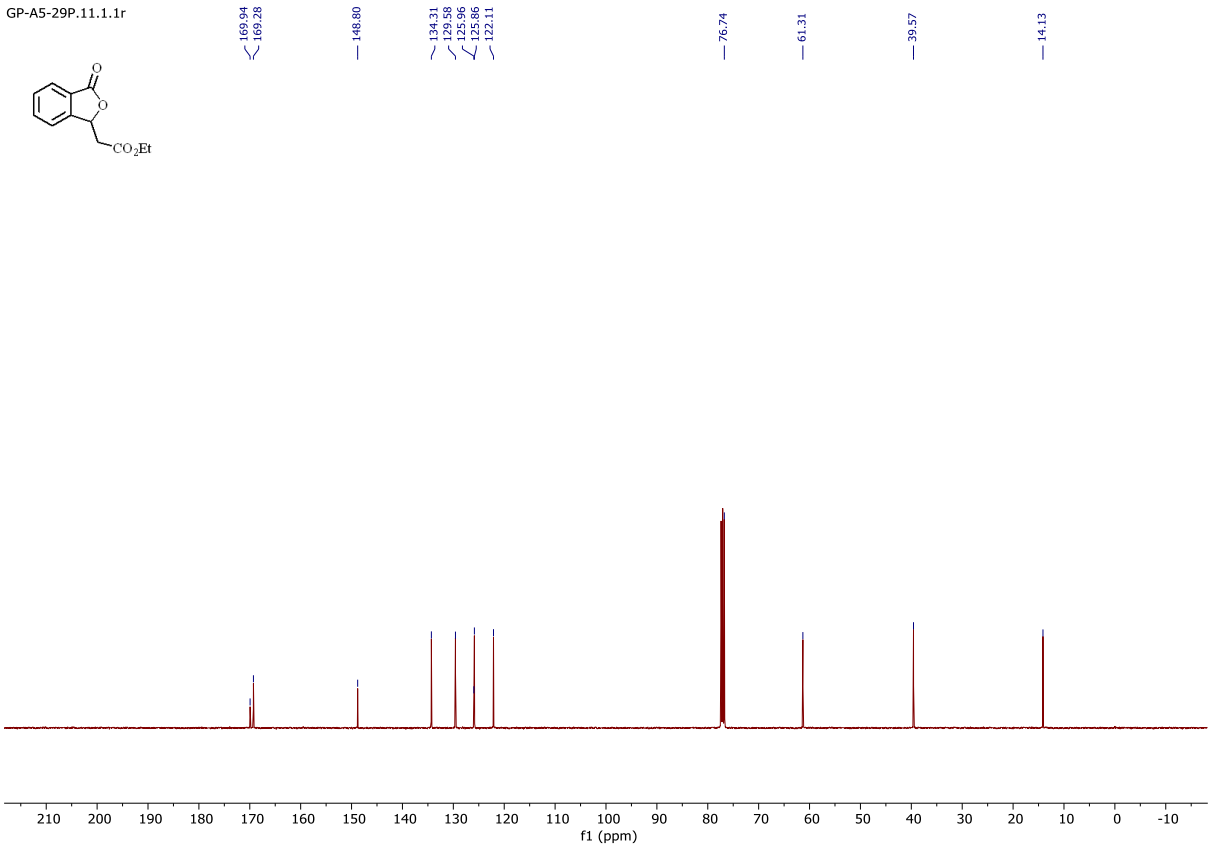
(5f) (^{19}F NMR 377 MHz, $CDCl_3$)



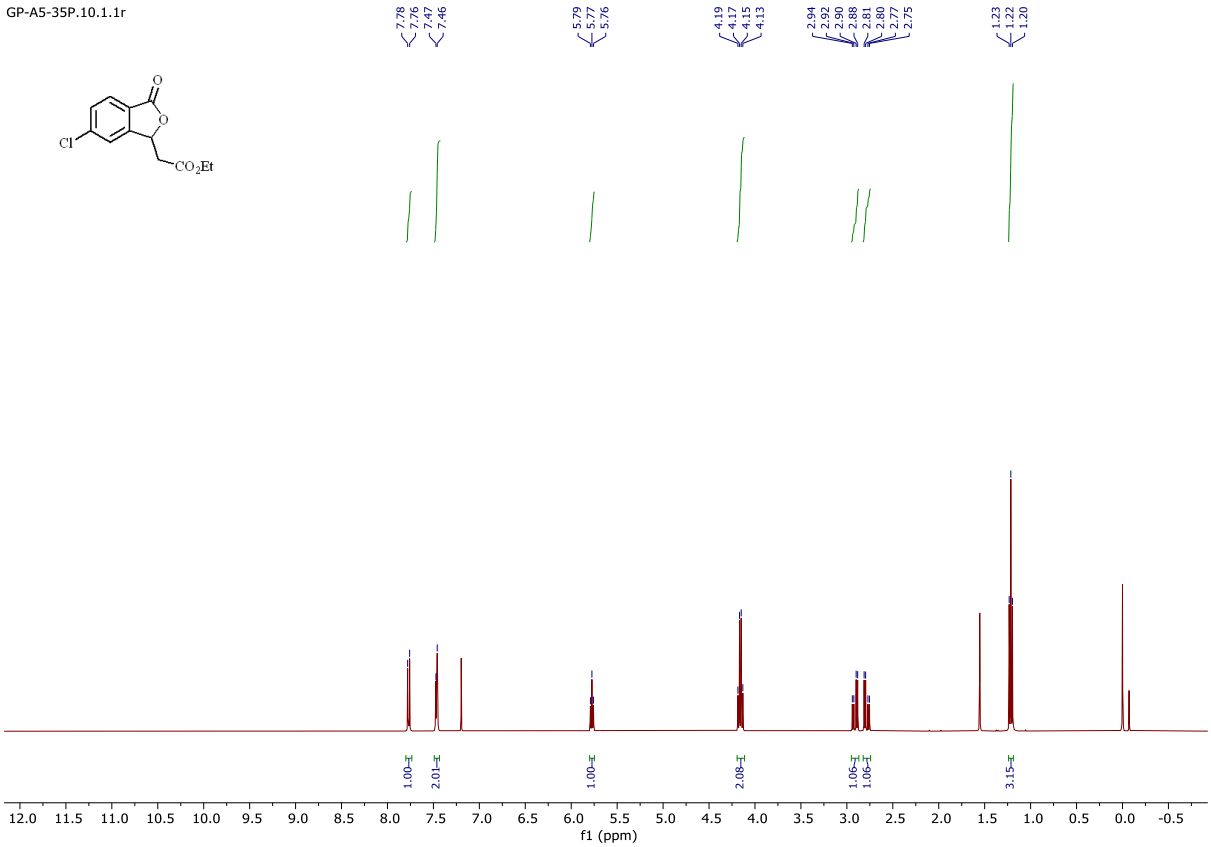
(5g) (^{1}H NMR 400 MHz, $CDCl_3$)



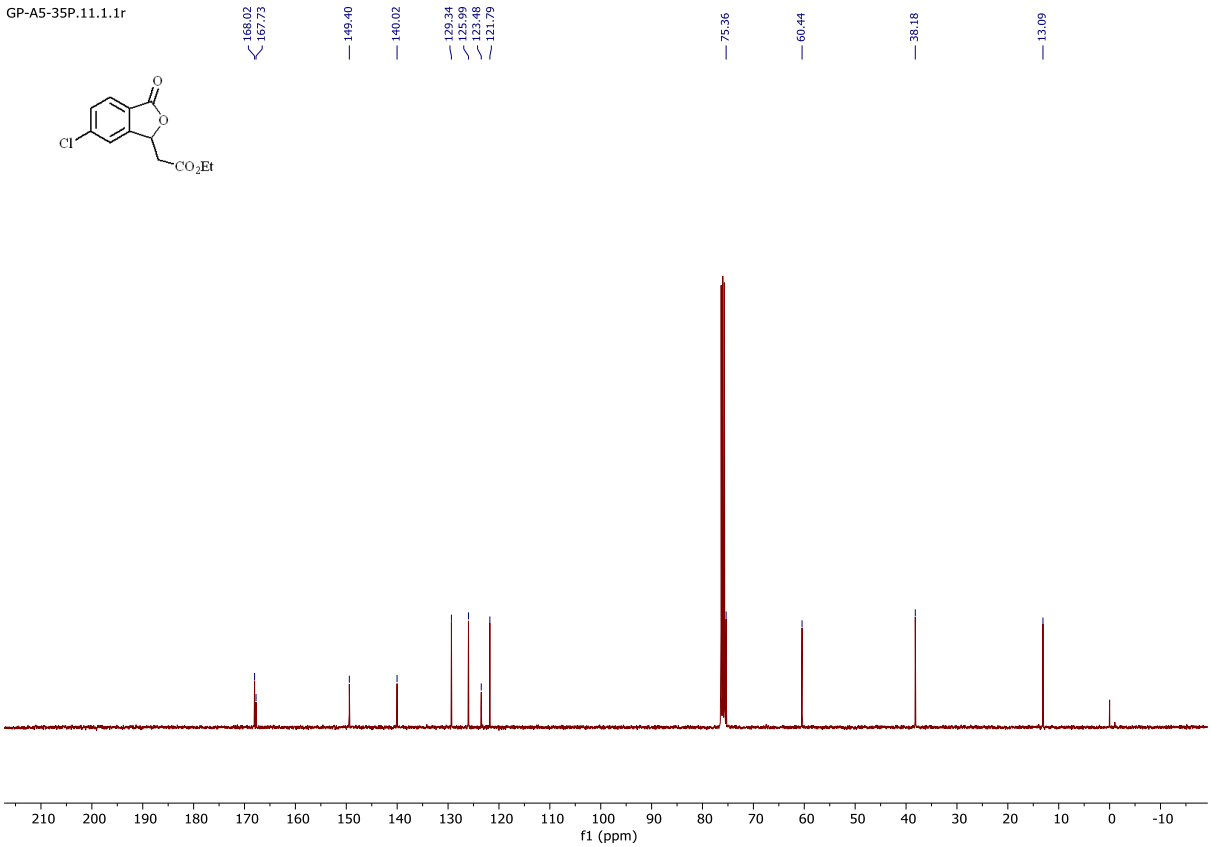
(5g) (^{13}C NMR 101 MHz, $CDCl_3$)



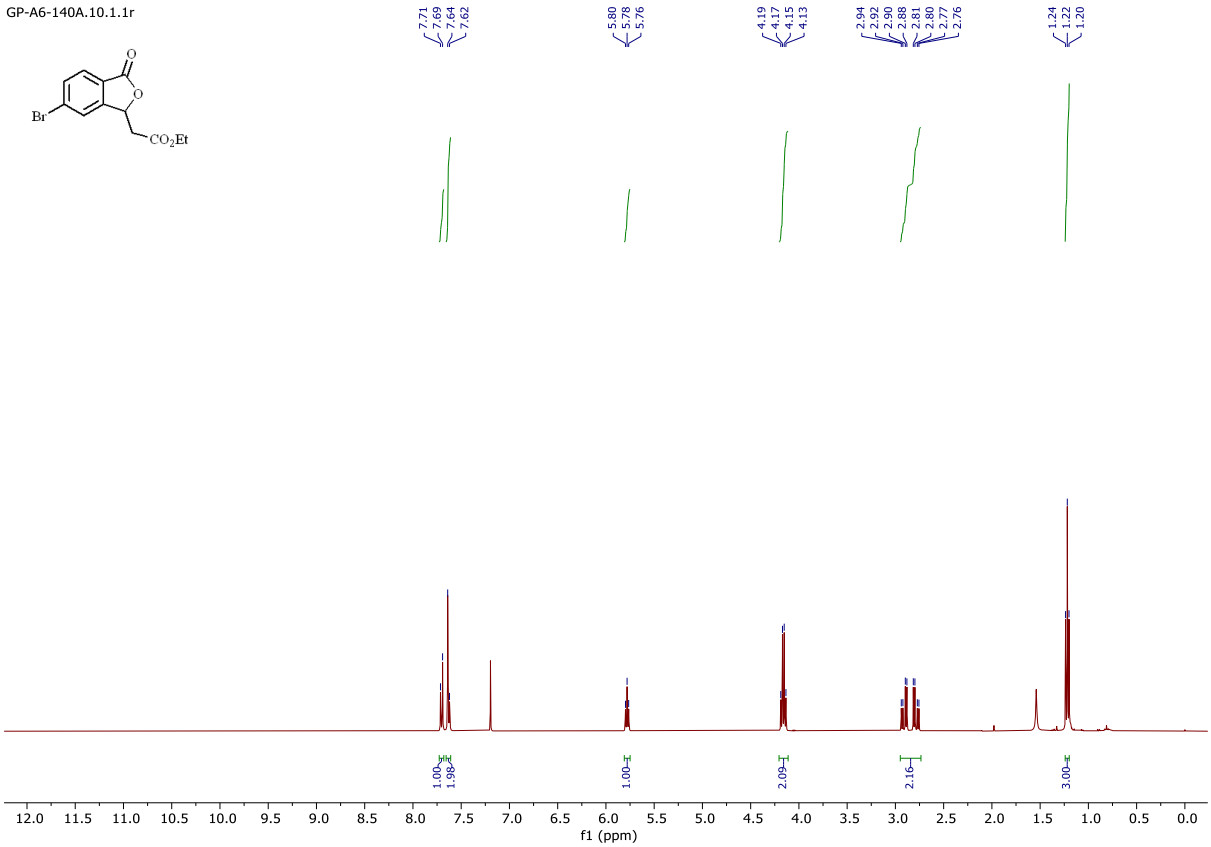
(5h) (^{1}H NMR 400 MHz, $CDCl_3$)



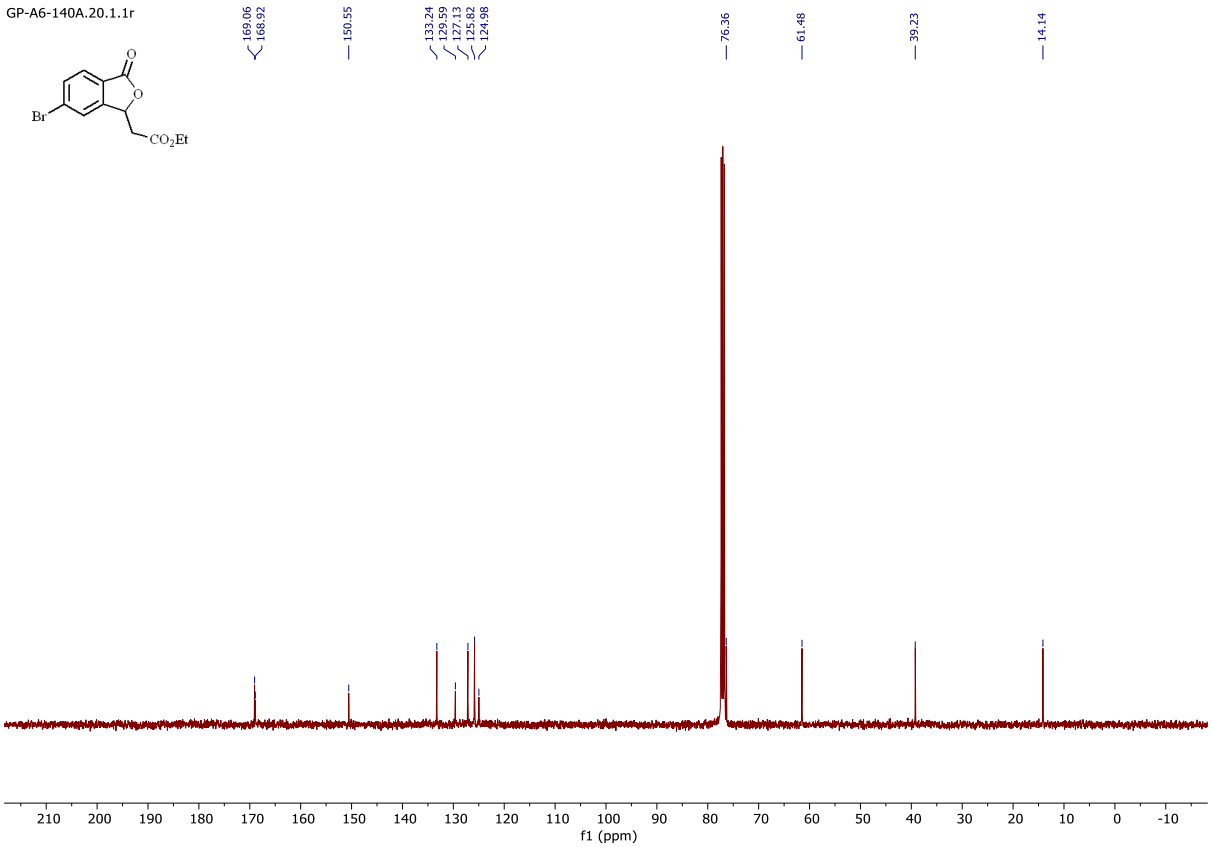
(5h) (^{13}C NMR 101 MHz, $CDCl_3$)



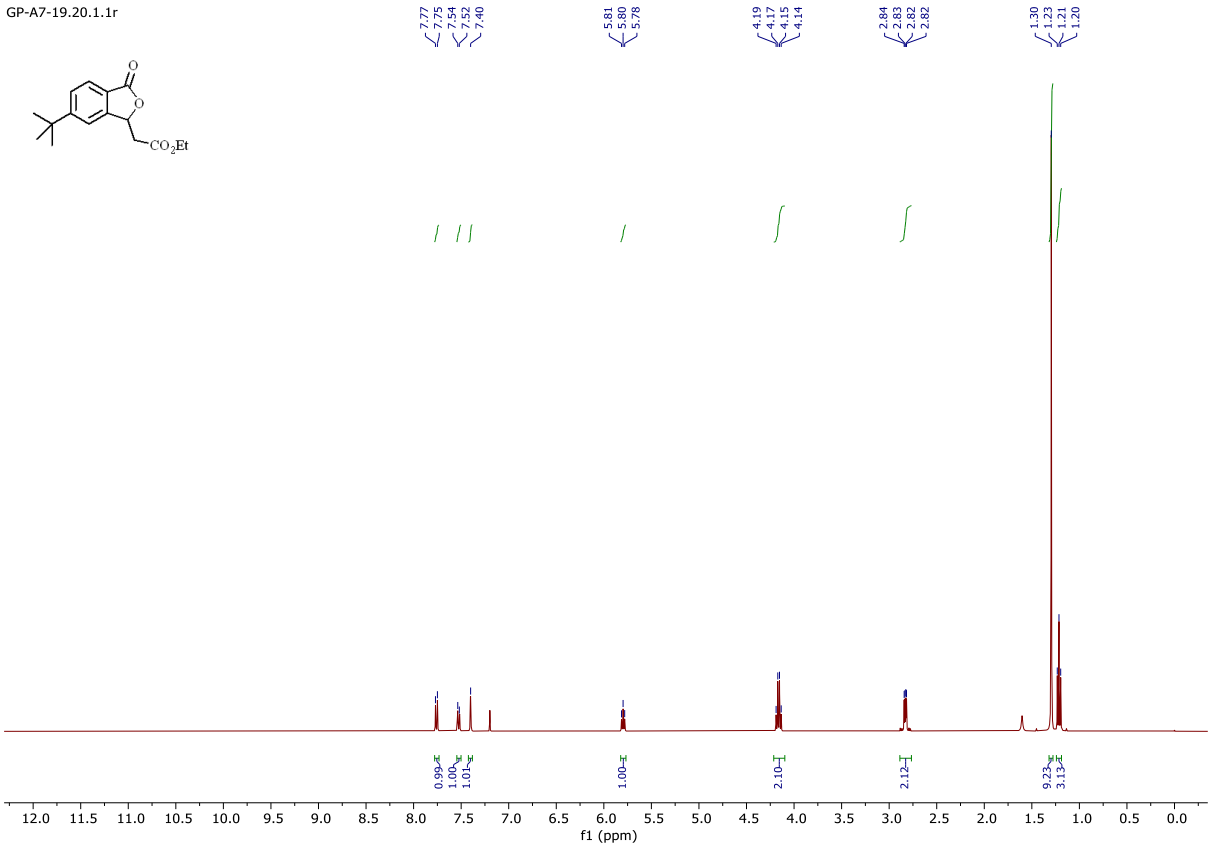
(5i) (^{1}H NMR 400 MHz, $CDCl_3$)



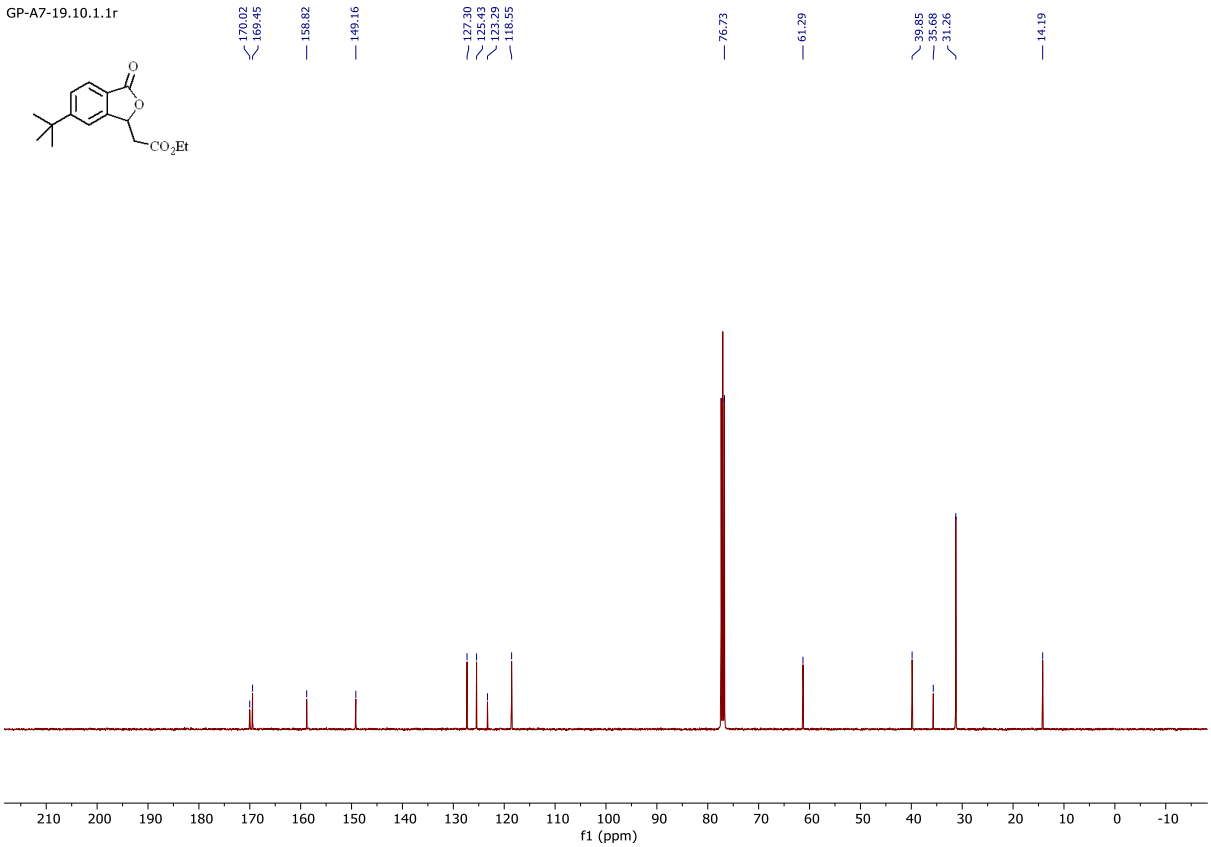
(5i) (^{13}C NMR 101 MHz, $CDCl_3$)



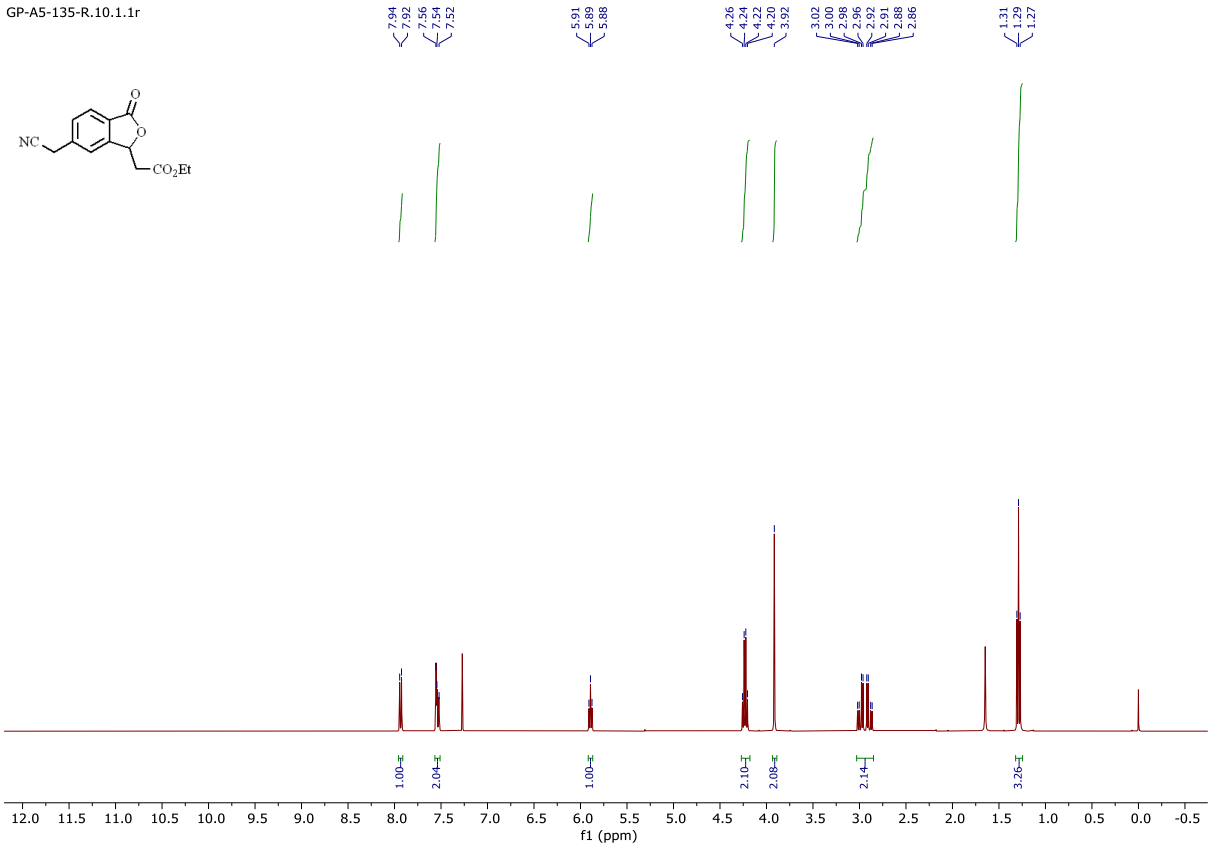
(5j) (^{1}H NMR 400 MHz, $CDCl_3$)



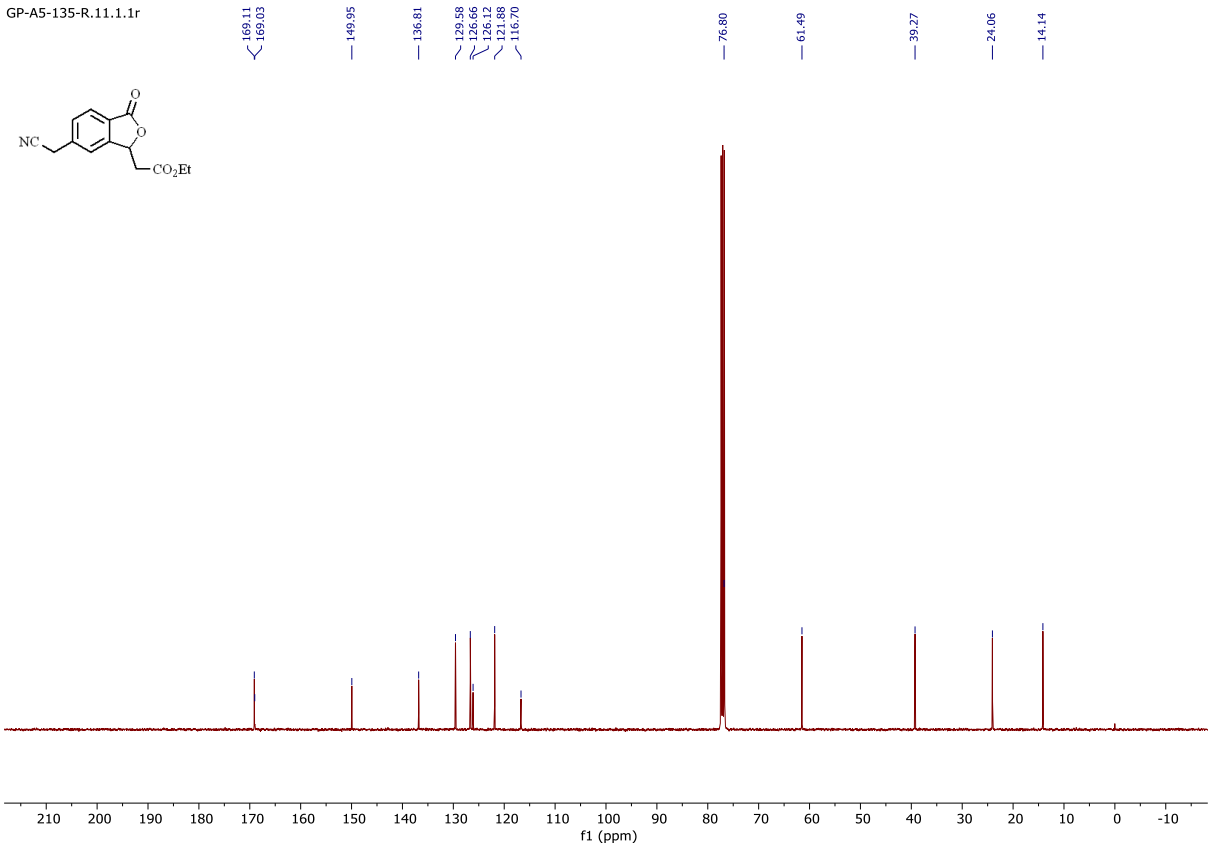
(5j) (^{13}C NMR 101 MHz, $CDCl_3$)



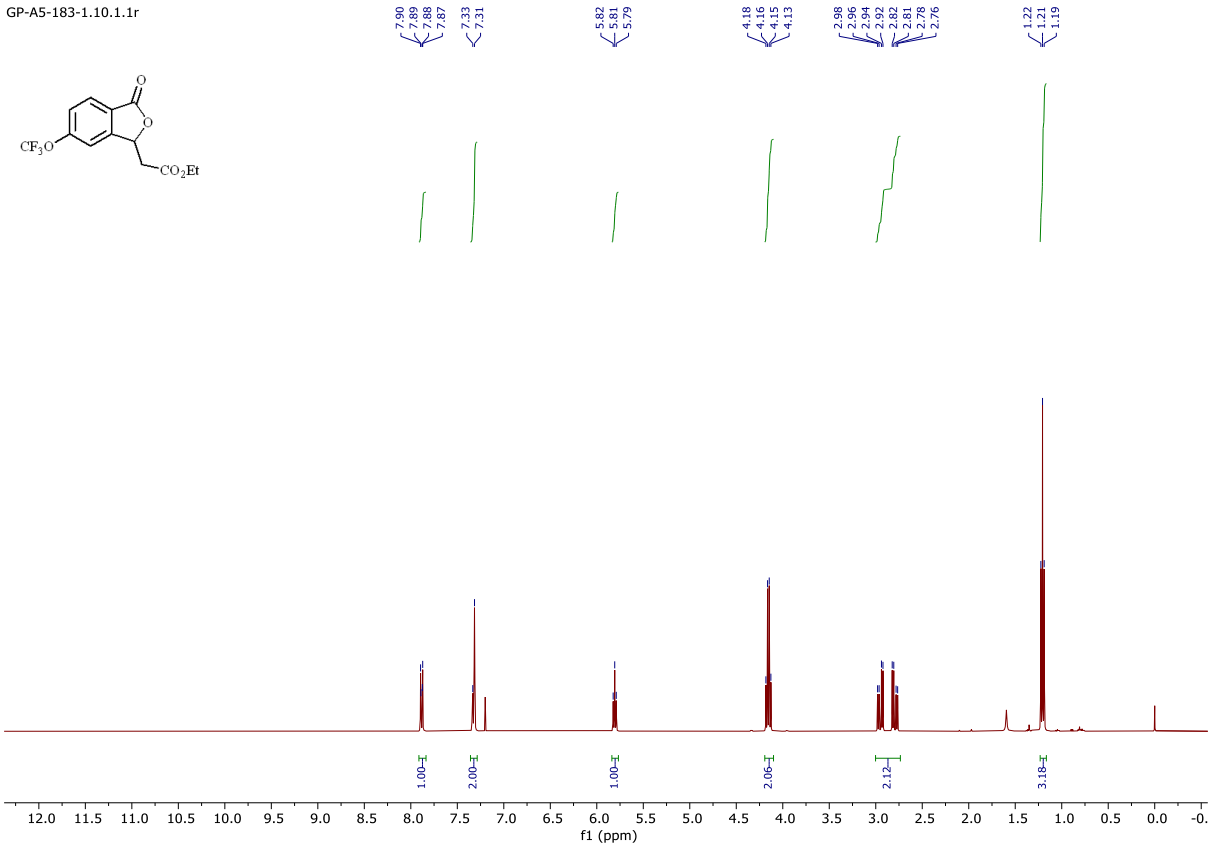
(5k) (^{1}H NMR 400 MHz, $CDCl_3$)



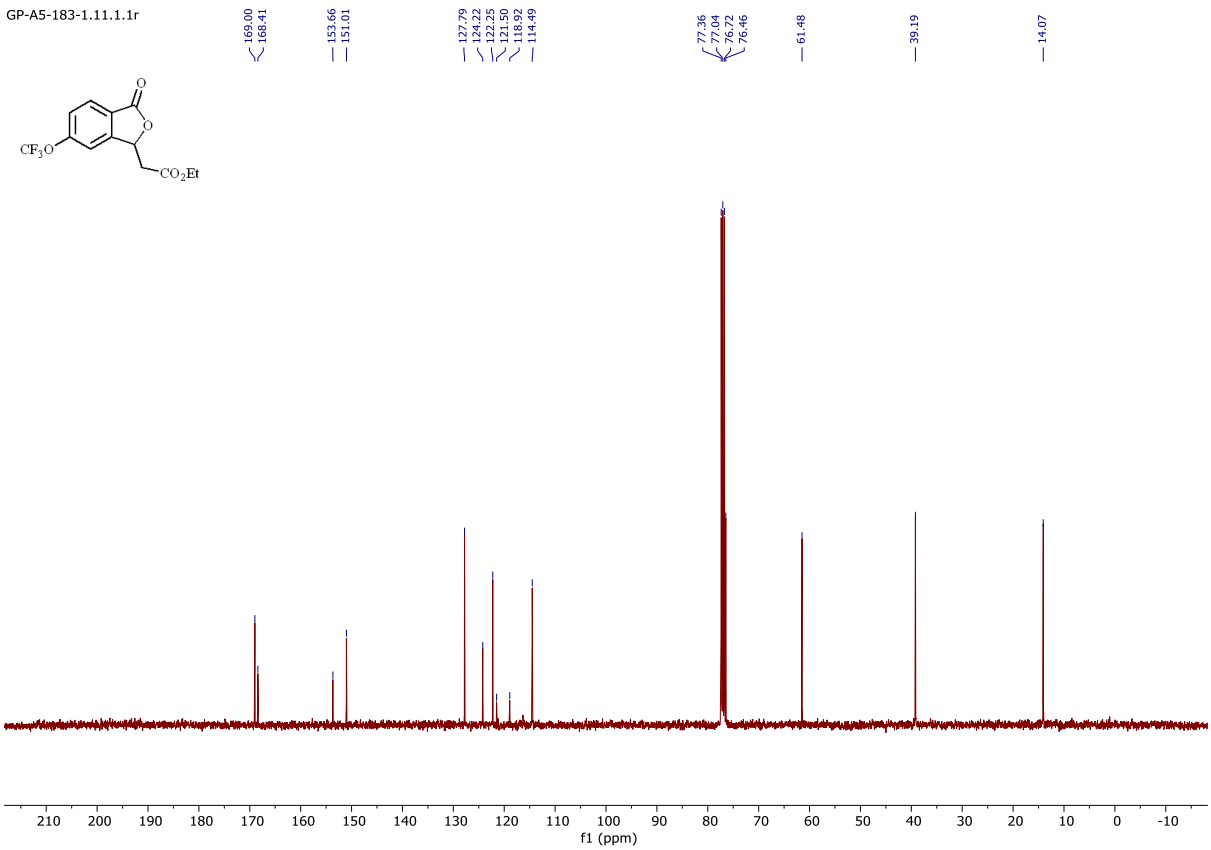
(5k) (^{13}C NMR 101 MHz, $CDCl_3$)



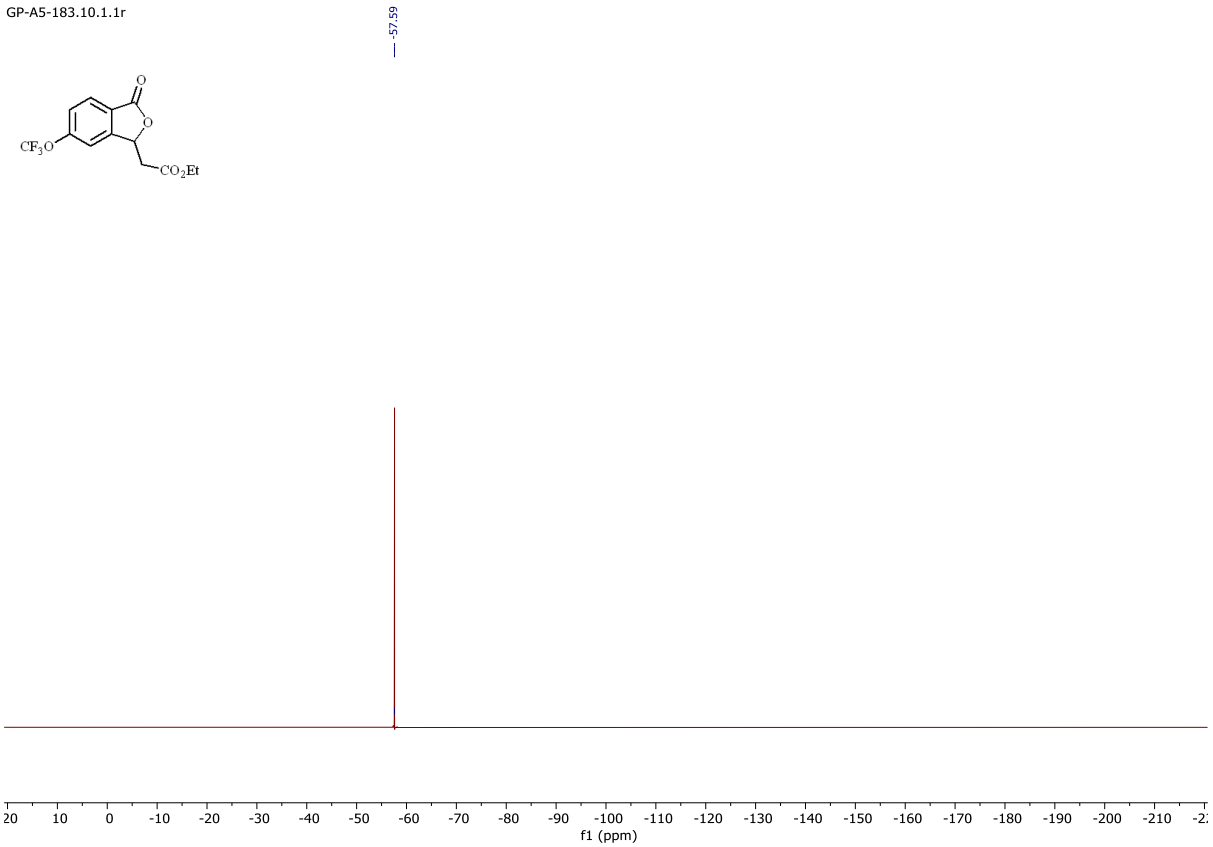
(5l) (^{1}H NMR 400 MHz, $CDCl_3$)



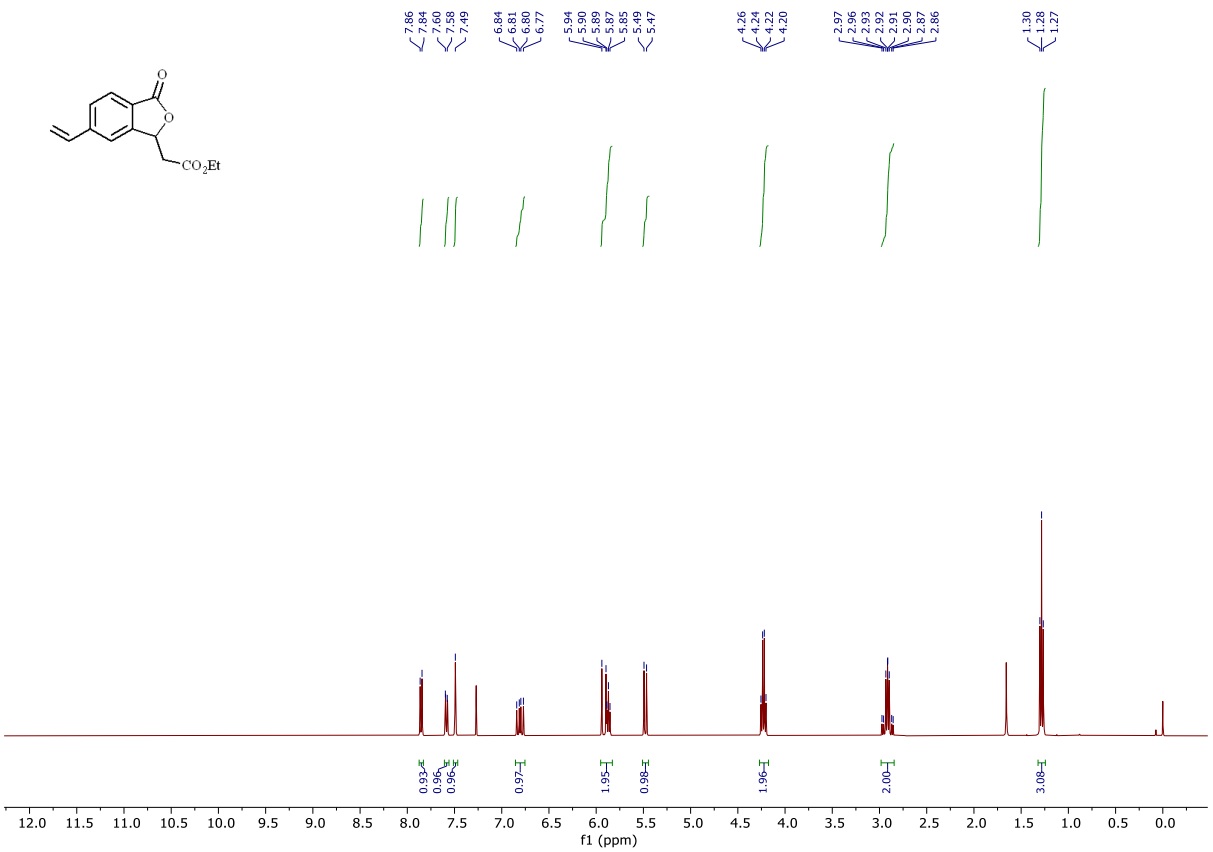
(5l) (^{13}C NMR 101 MHz, $CDCl_3$)



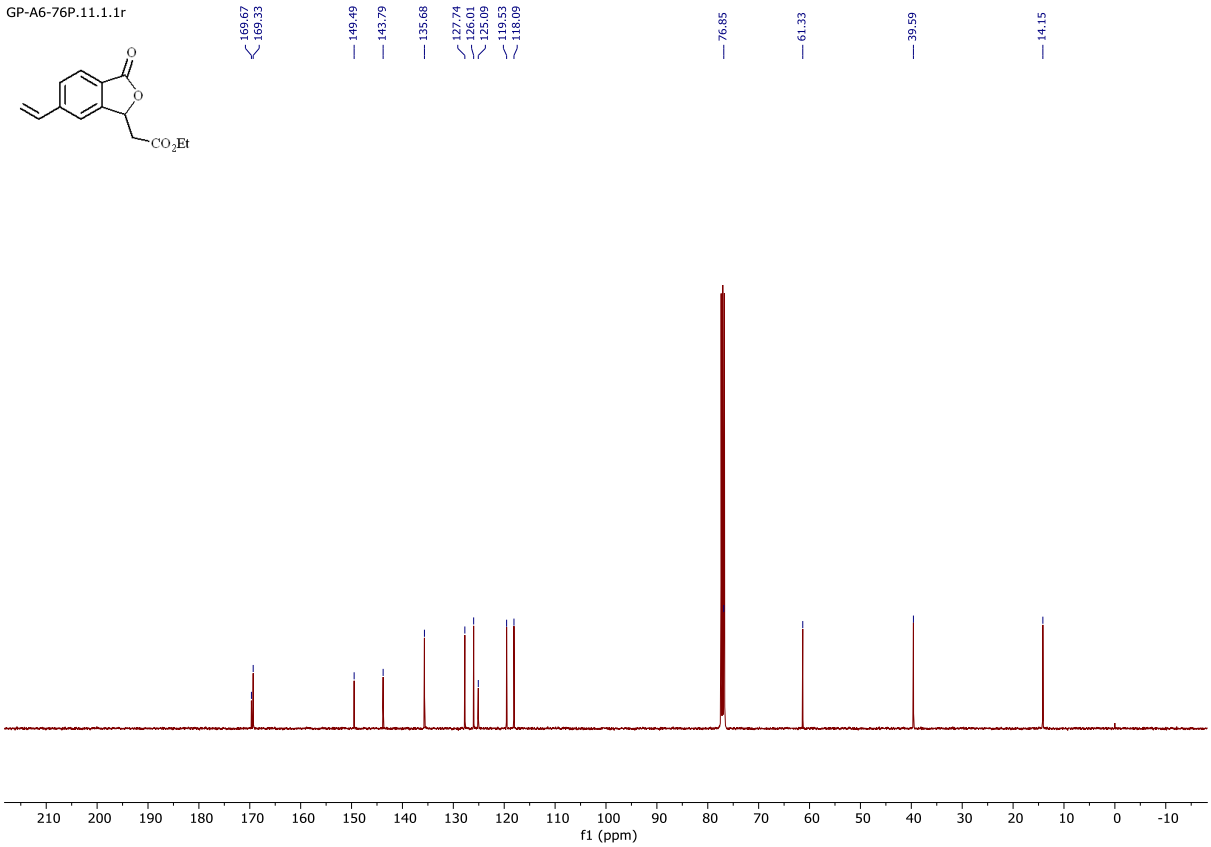
(5l) (^{19}F NMR 377 MHz, $CDCl_3$)



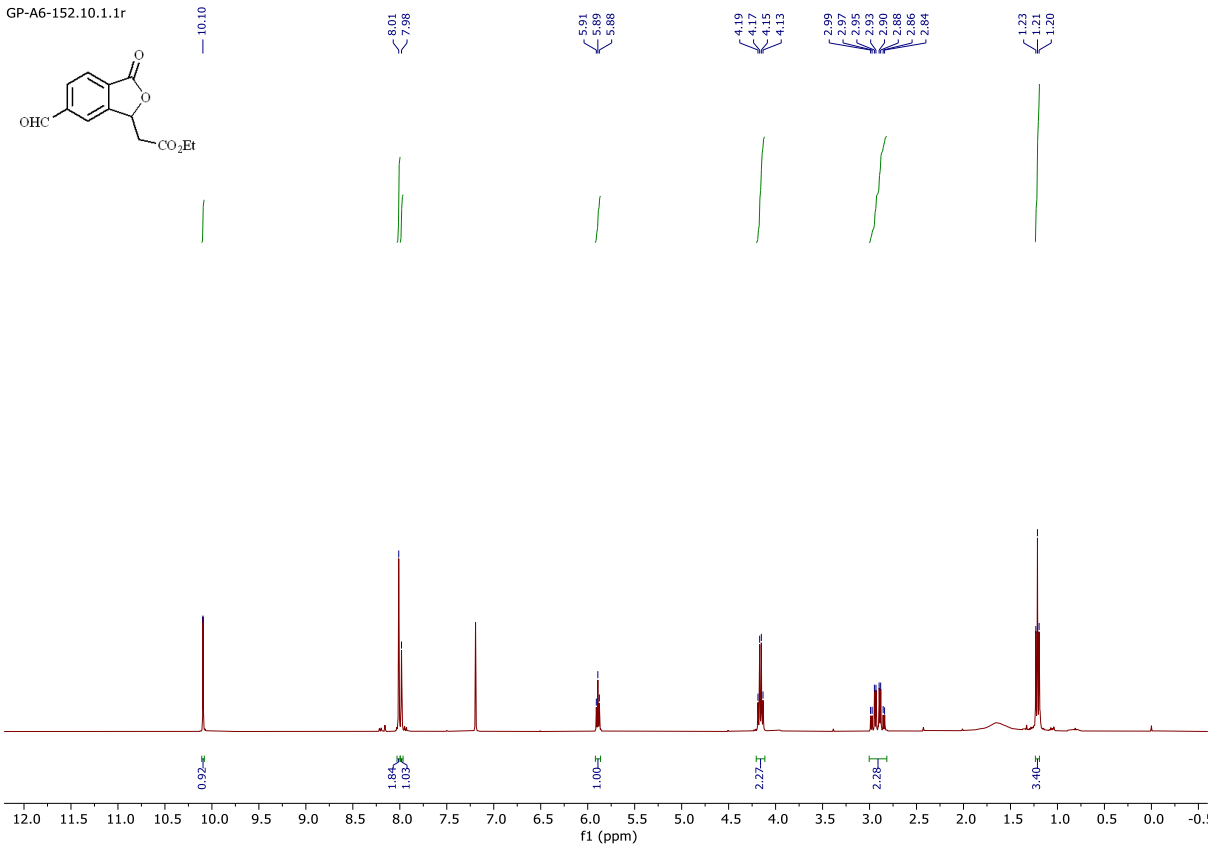
(5m) (^{1}H NMR 400 MHz, $CDCl_3$)



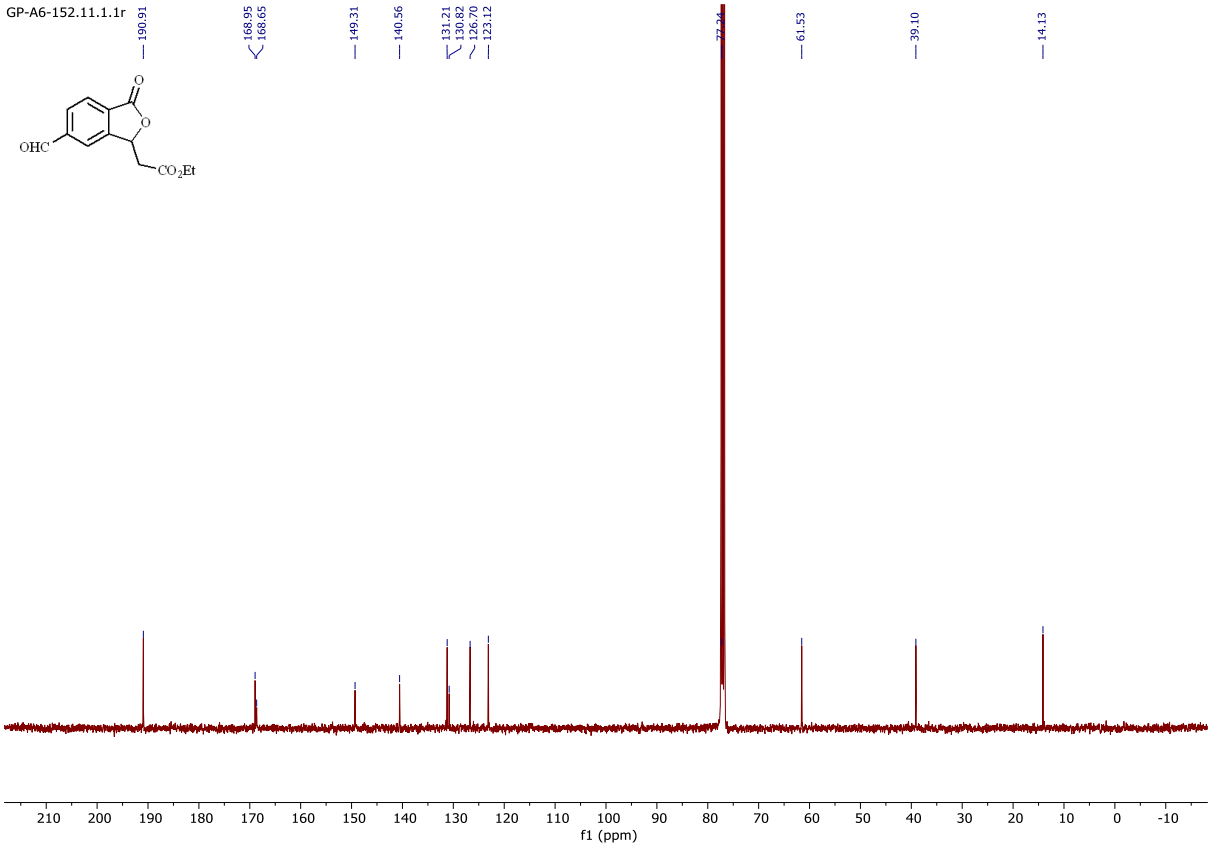
(5m) (^{13}C NMR 101 MHz, $CDCl_3$)



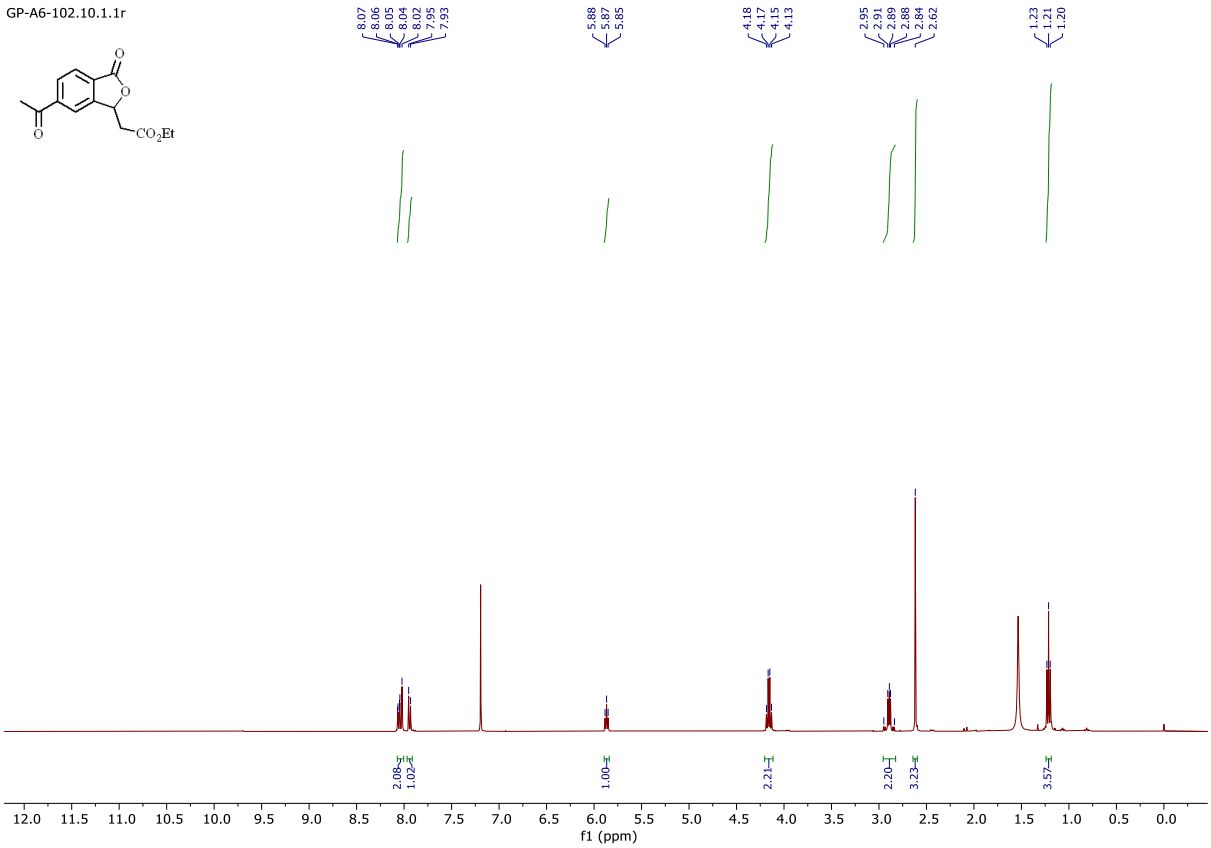
(5n) (^{1}H NMR 400 MHz, $CDCl_3$)



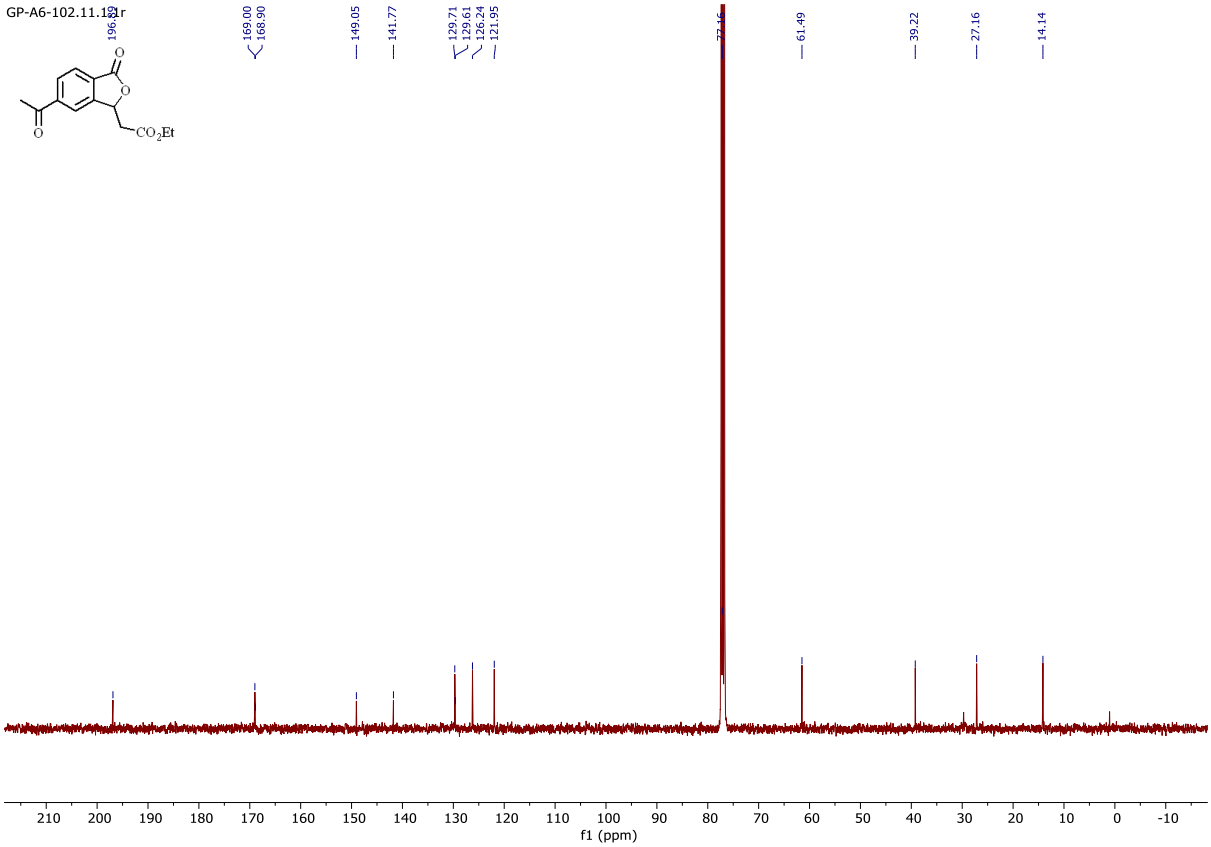
(5n) (^{13}C NMR 101 MHz, $CDCl_3$)



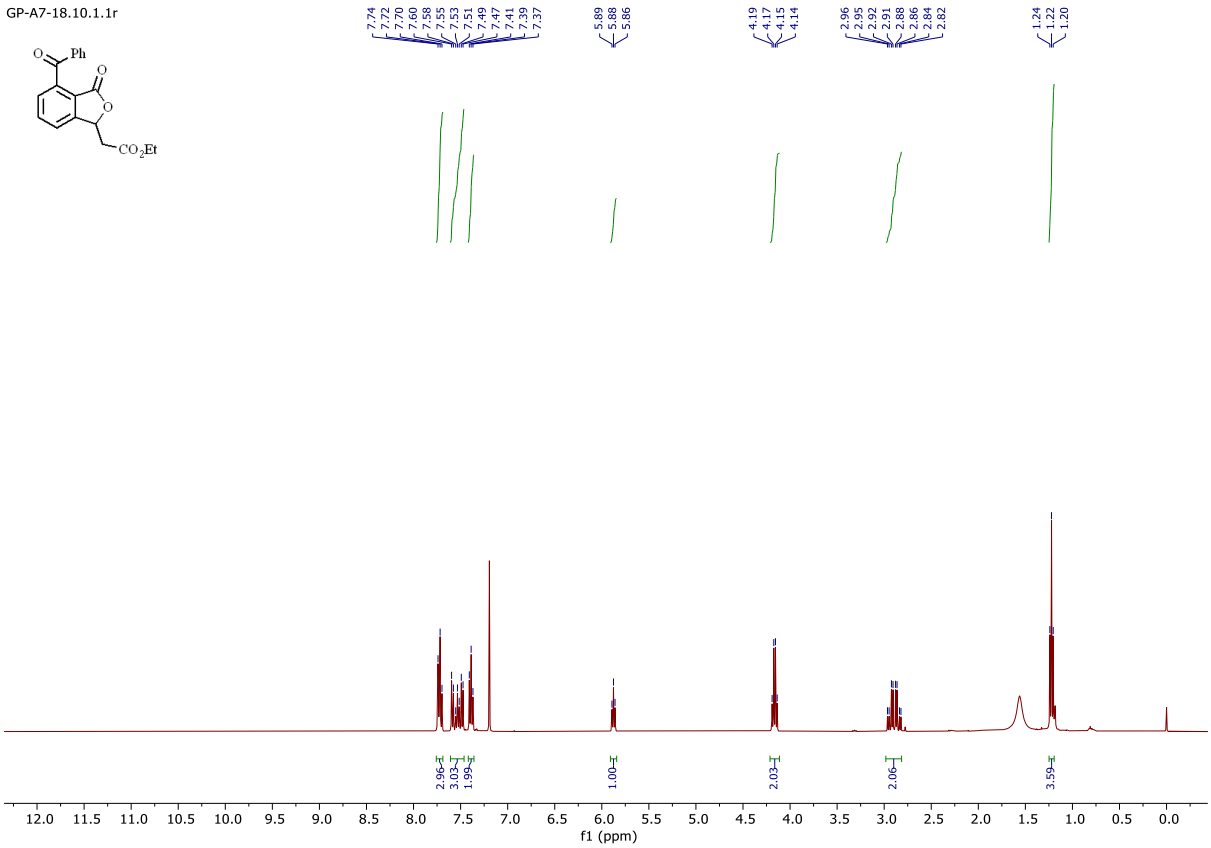
(5o) (^{1}H NMR 400 MHz, $CDCl_3$)



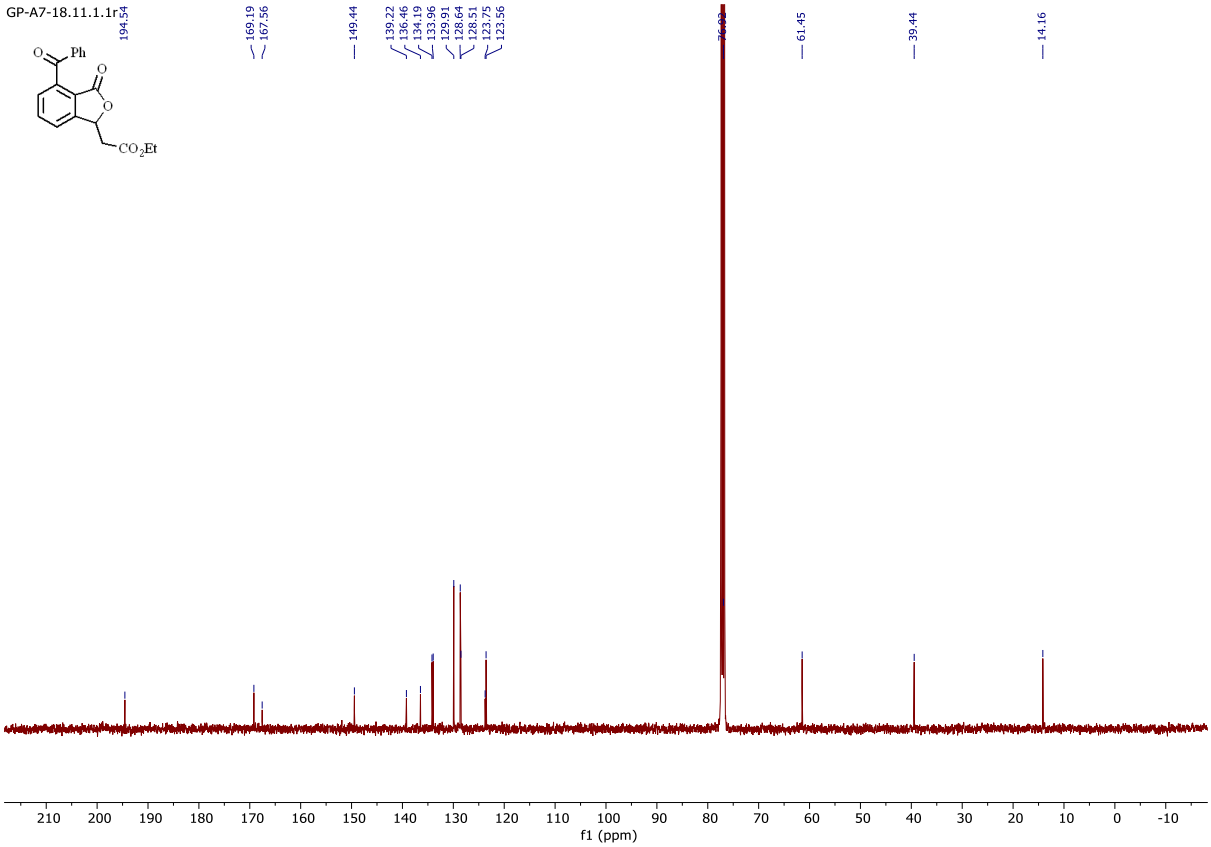
(5o) (^{13}C NMR 101 MHz, $CDCl_3$)



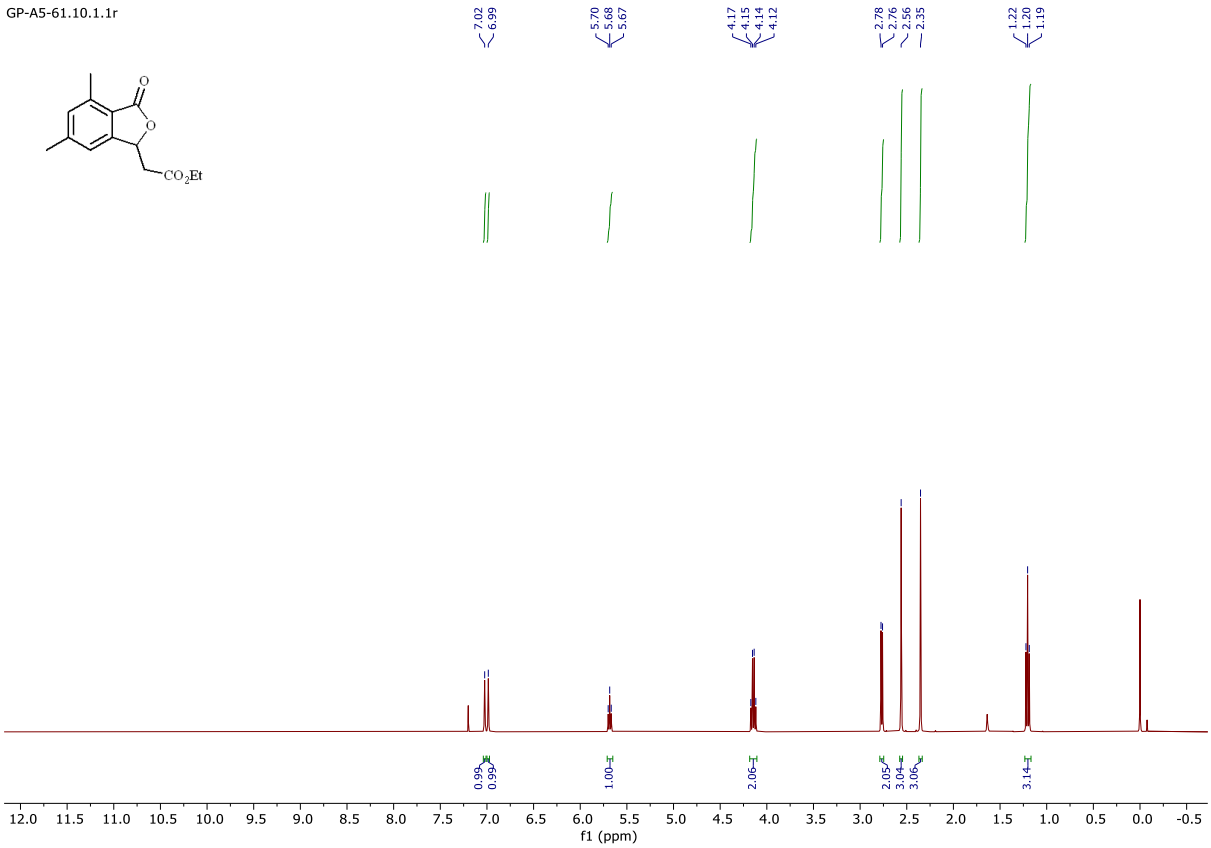
(5p) (^{1}H NMR 400 MHz, $CDCl_3$)



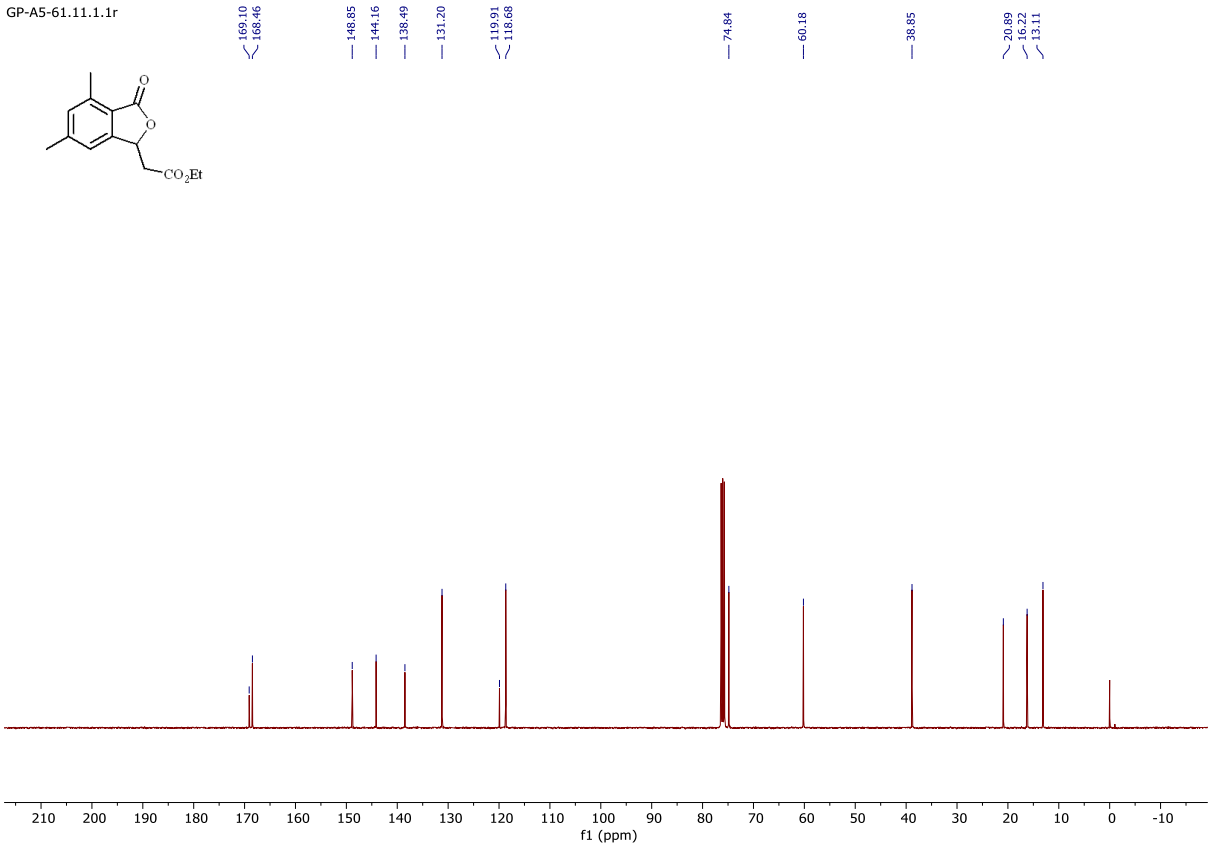
(5p) (^{13}C NMR 101 MHz, $CDCl_3$)



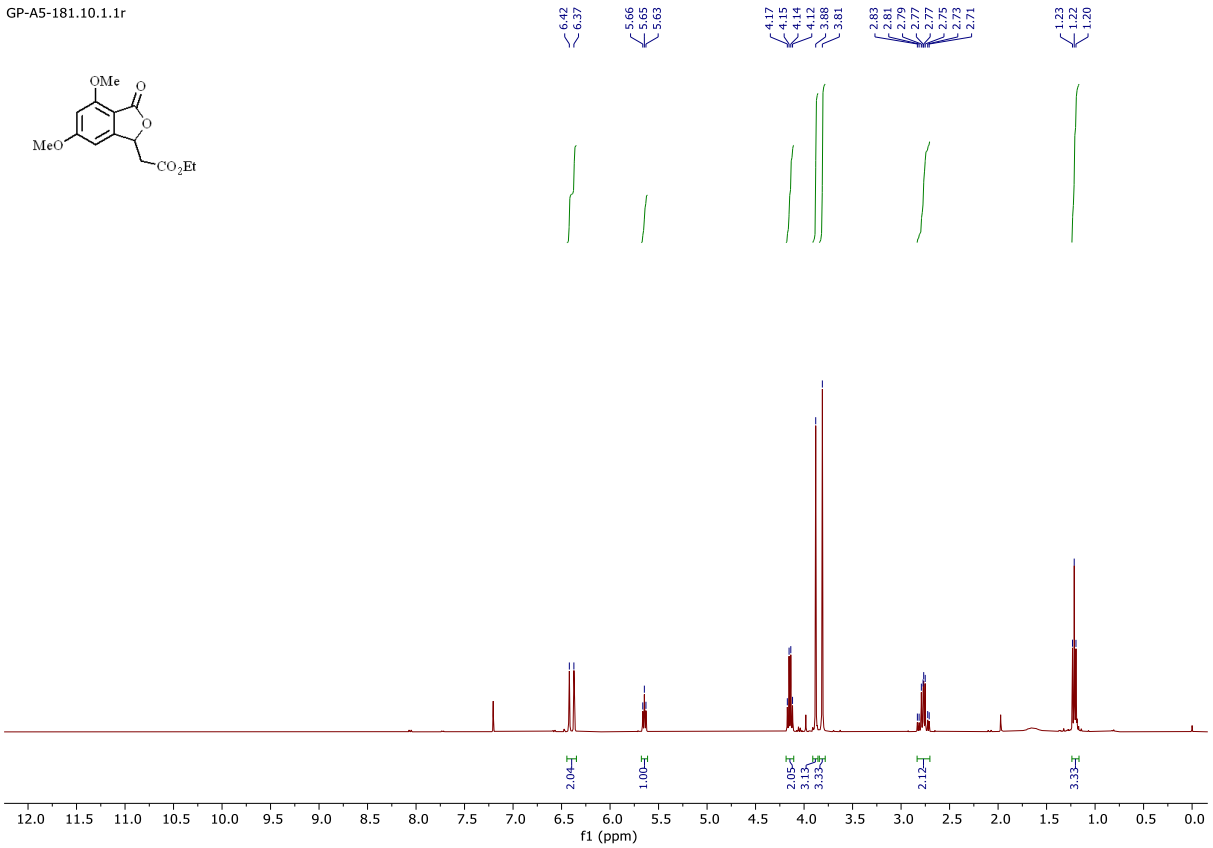
(5q) (^{1}H NMR 400 MHz, $CDCl_3$)



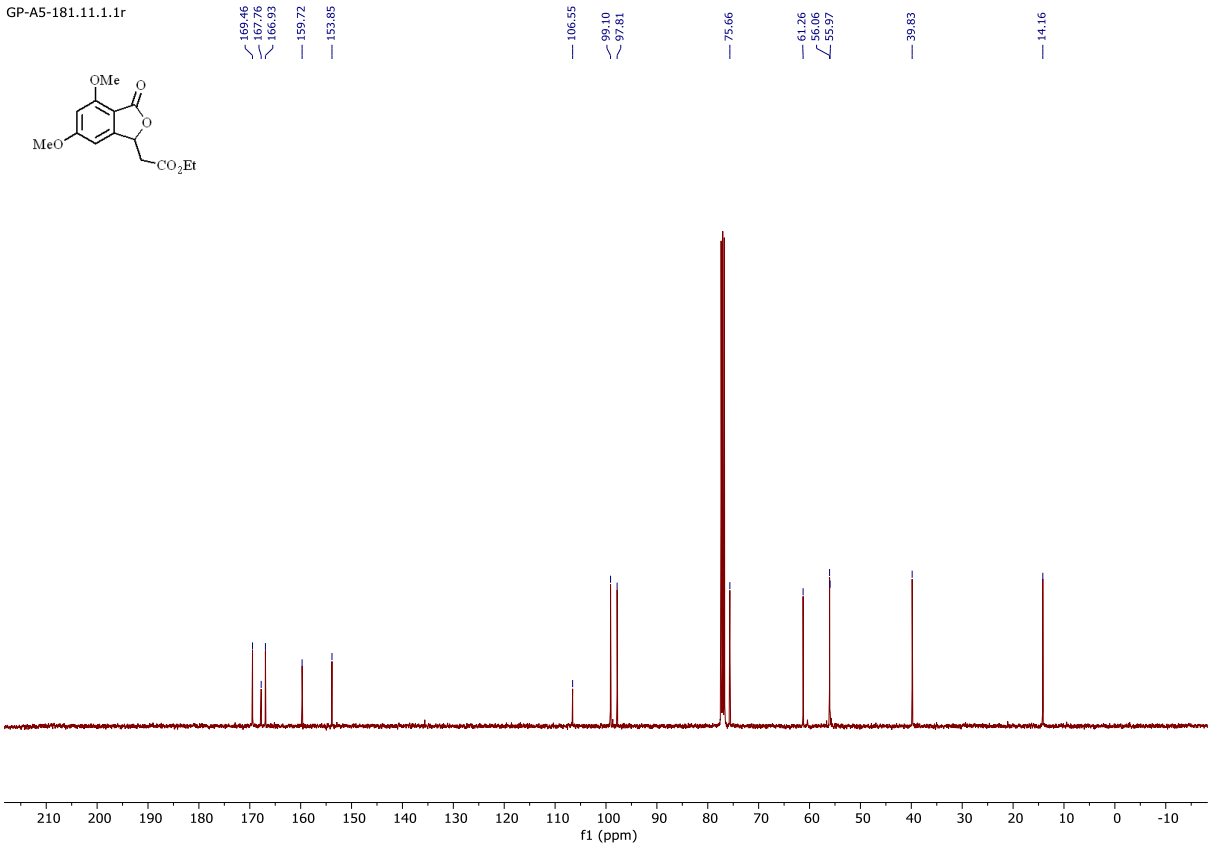
(5q) (^{13}C NMR 101 MHz, $CDCl_3$)



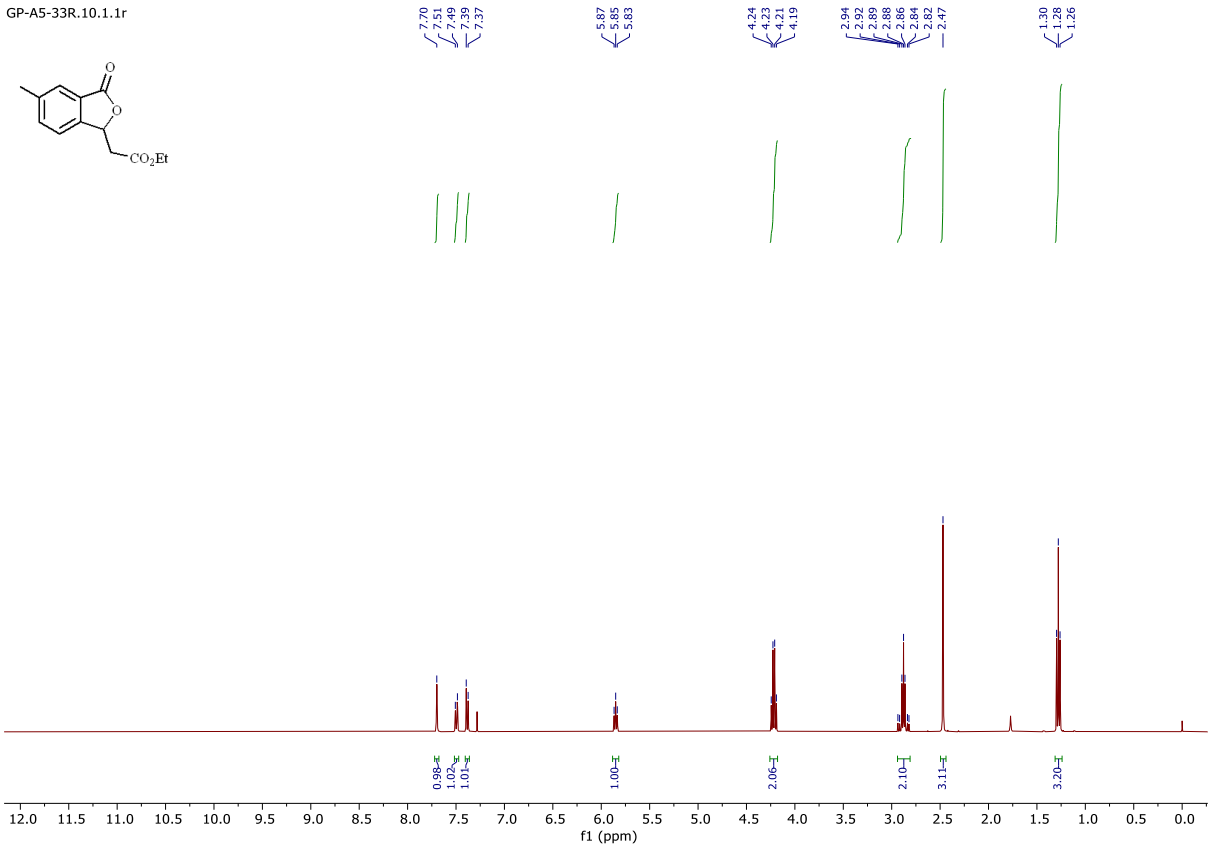
(5r) (^{1}H NMR 400 MHz, $CDCl_3$)



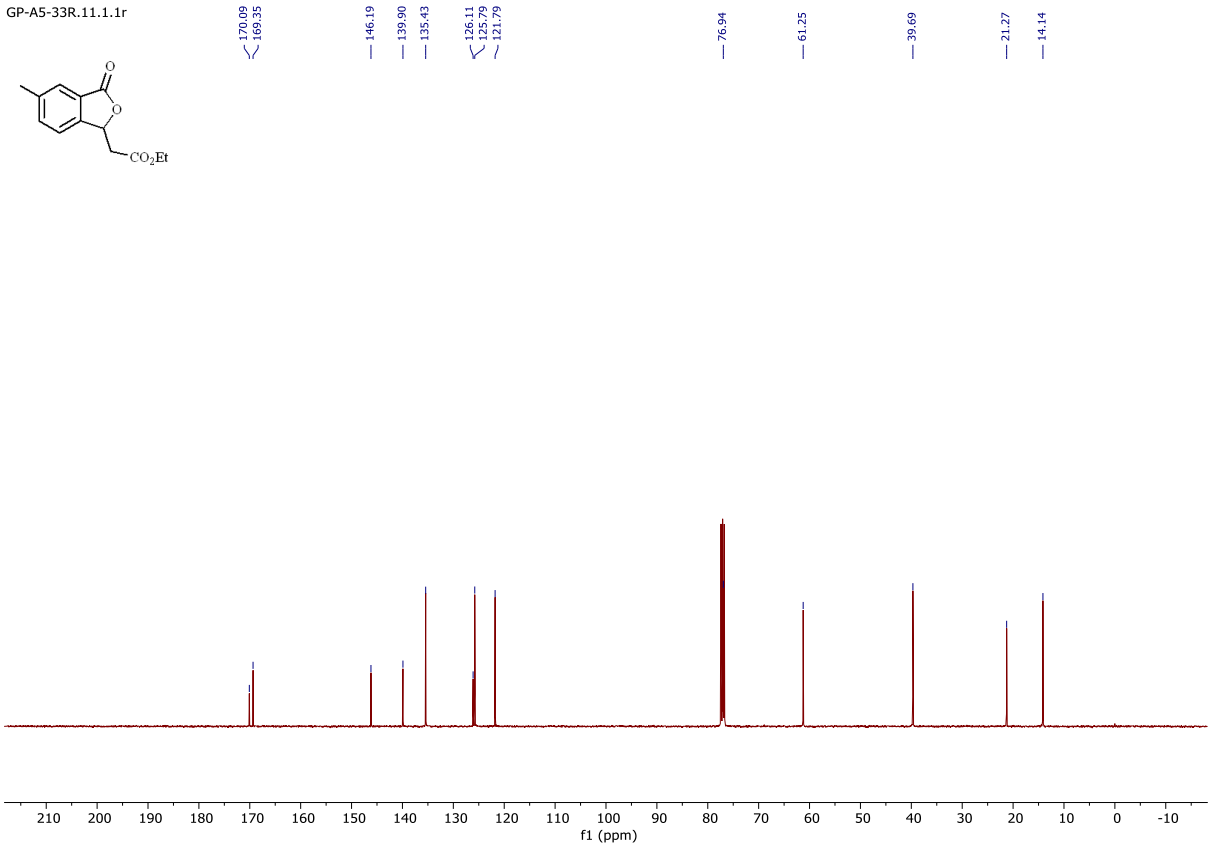
(5r) (^{13}C NMR 101 MHz, $CDCl_3$)



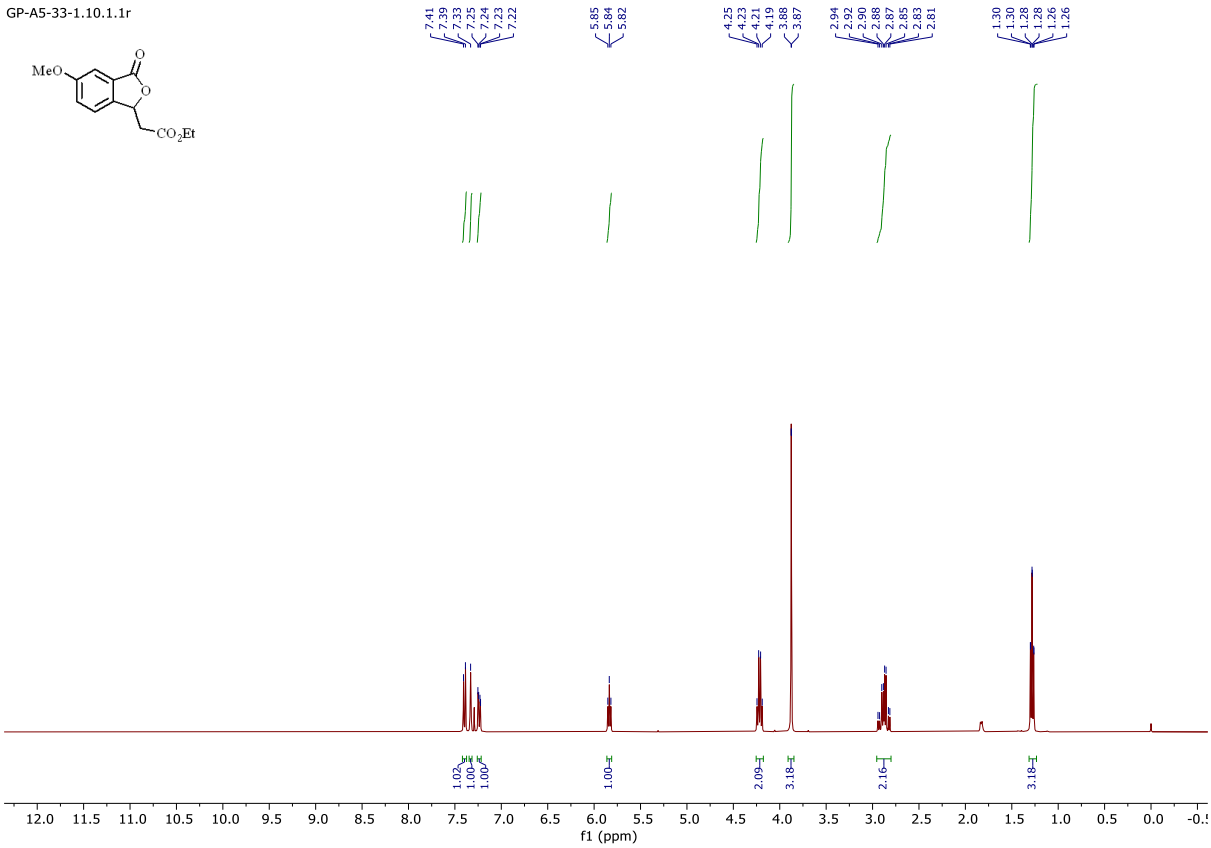
(5s) (^{1}H NMR 400 MHz, $CDCl_3$)



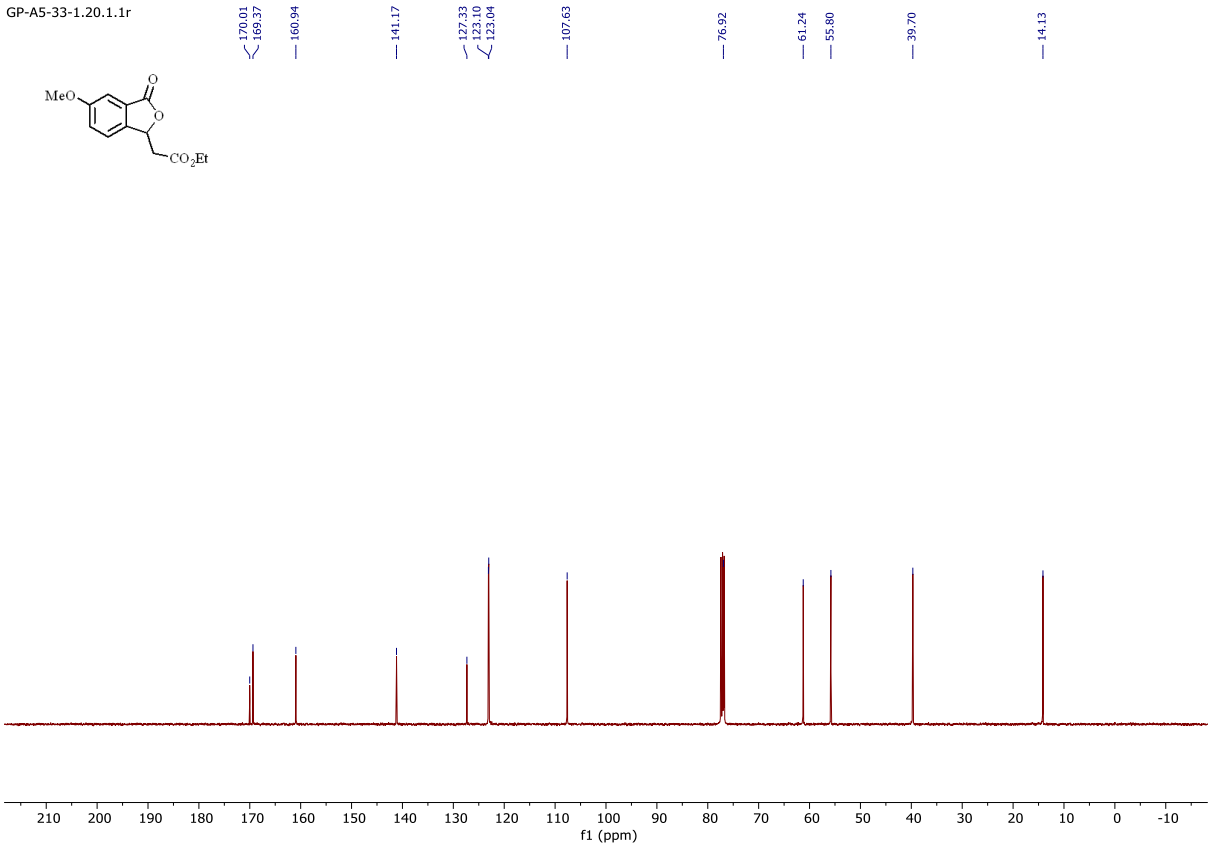
(5s) (^{13}C NMR 101 MHz, $CDCl_3$)



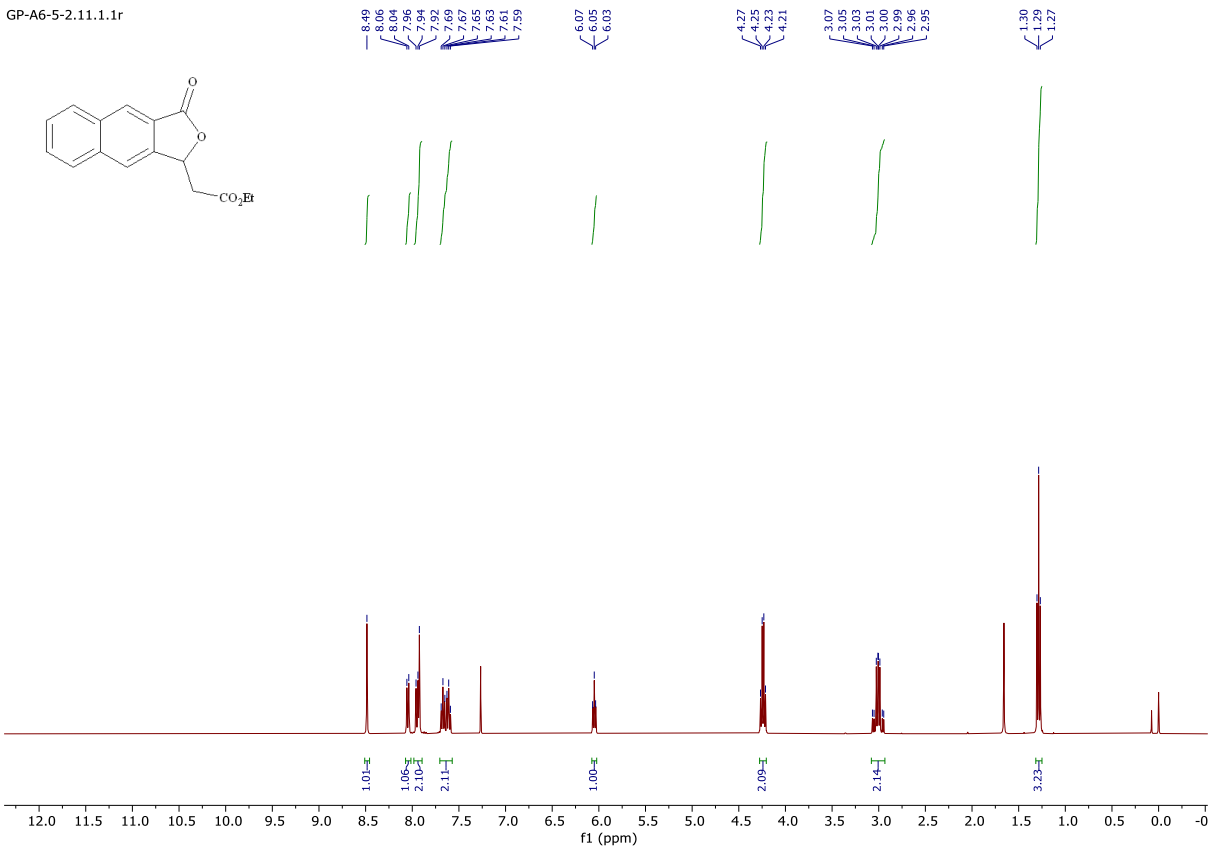
(5t) (^{1}H NMR 400 MHz, $CDCl_3$)



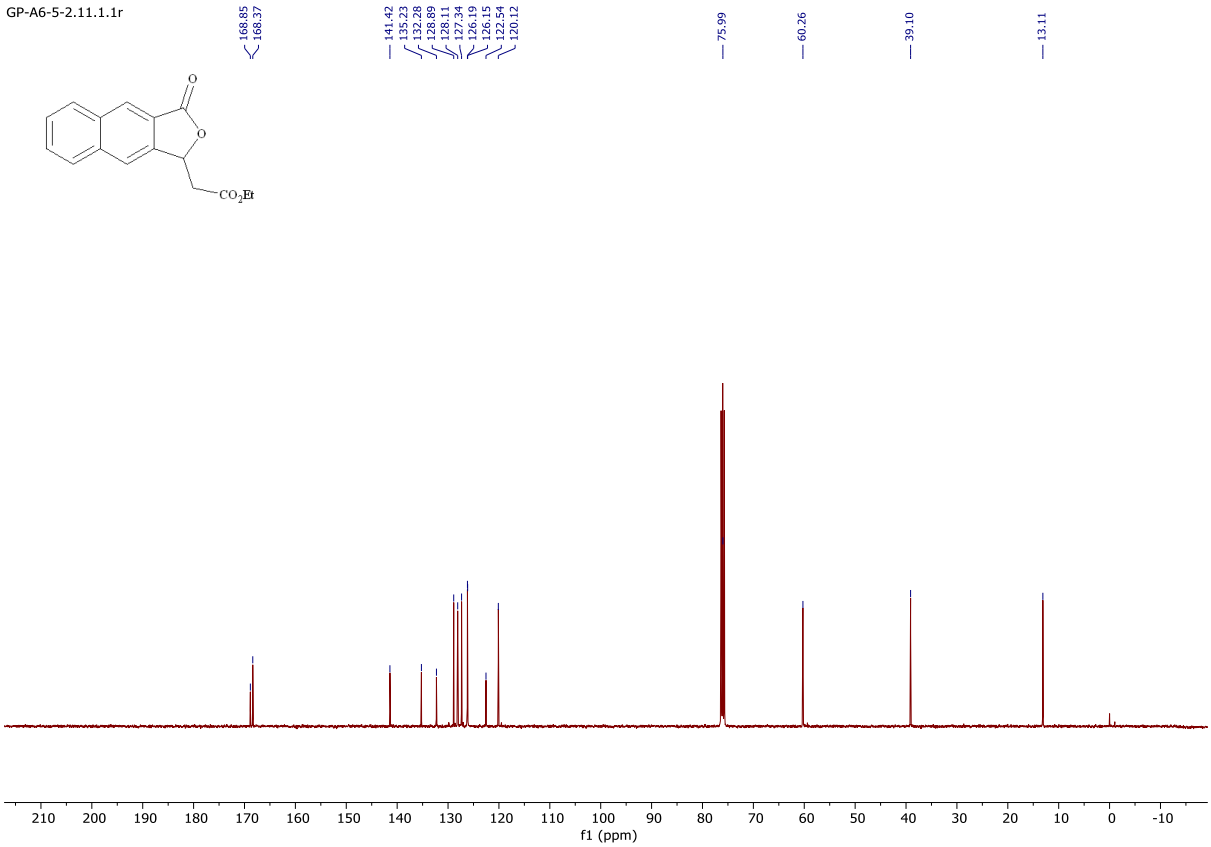
(5t) (^{13}C NMR 101 MHz, $CDCl_3$)



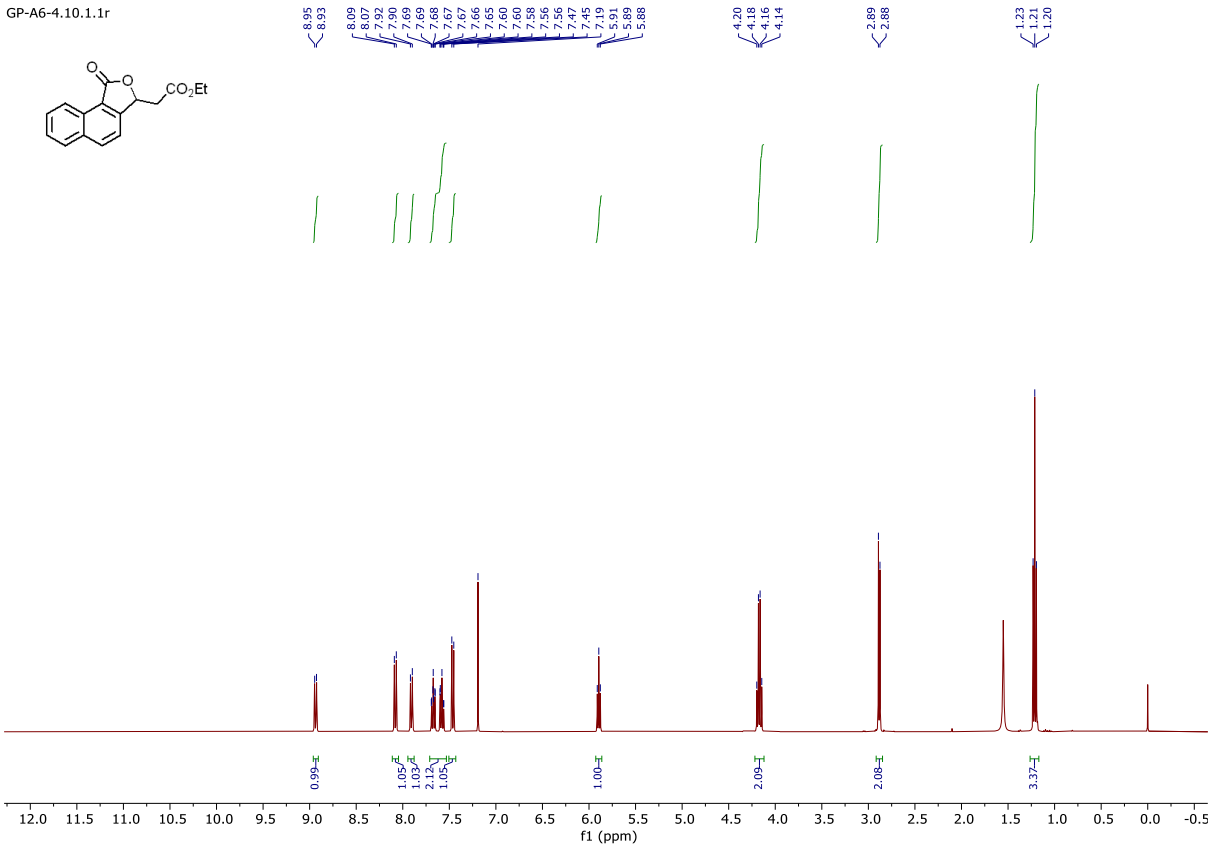
(5u) (^{1}H NMR 400 MHz, $CDCl_3$)



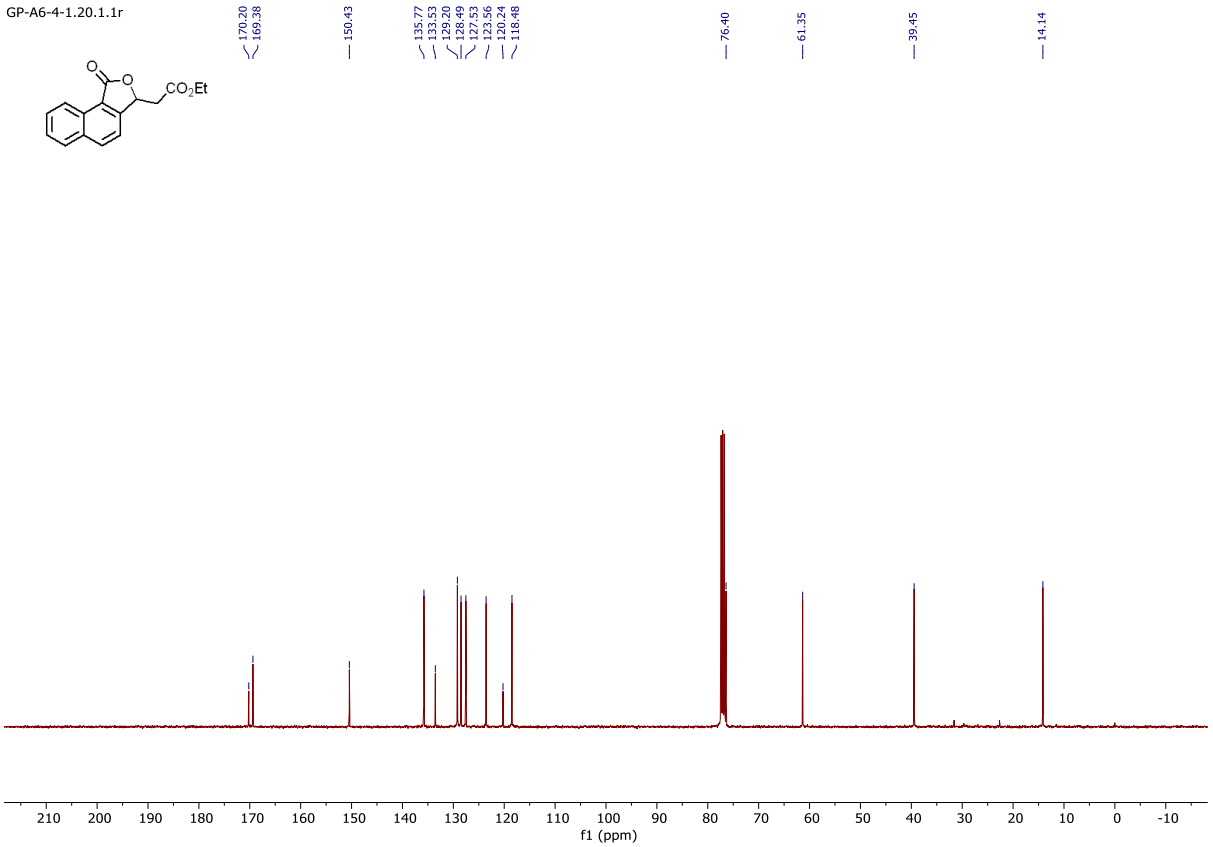
(5u) (^{13}C NMR 101 MHz, $CDCl_3$)



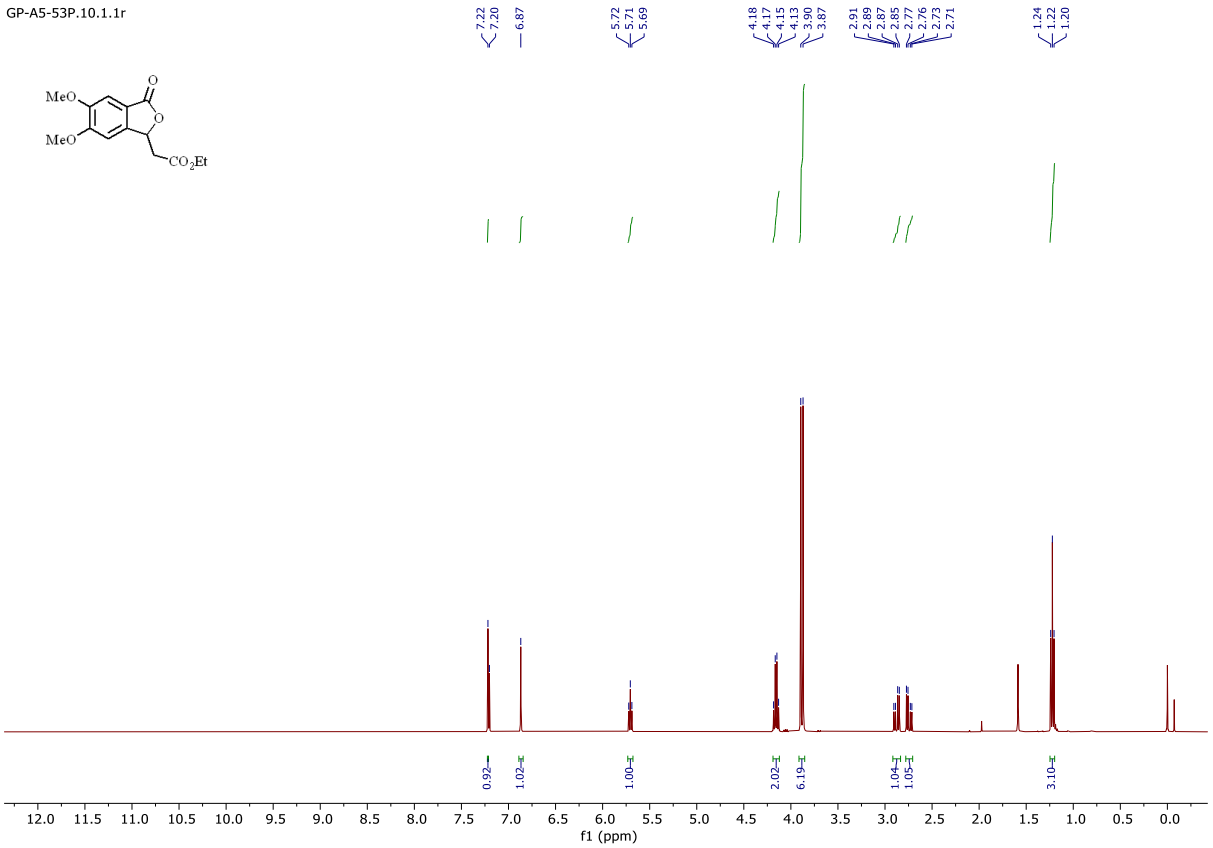
(5v) (^{1}H NMR 400 MHz, $CDCl_3$)



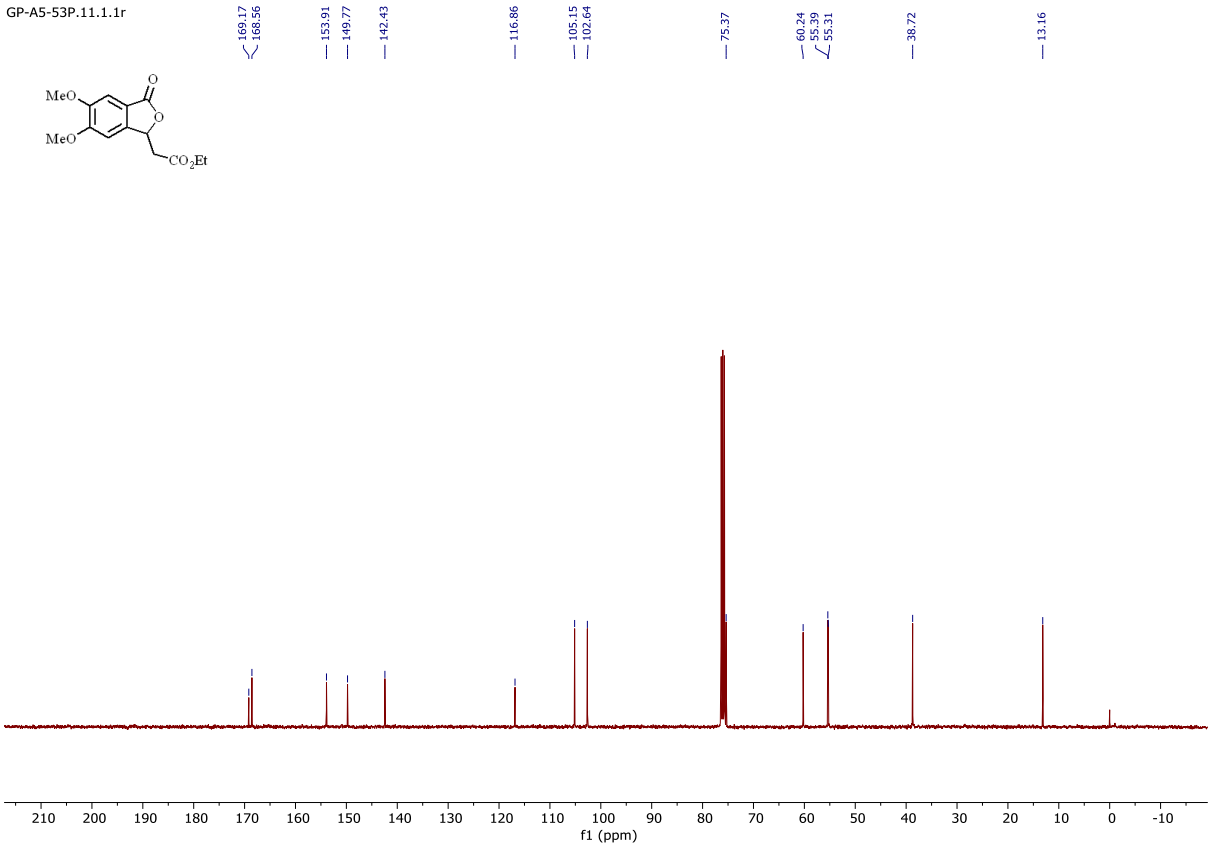
(5v) (^{13}C NMR 101 MHz, $CDCl_3$)



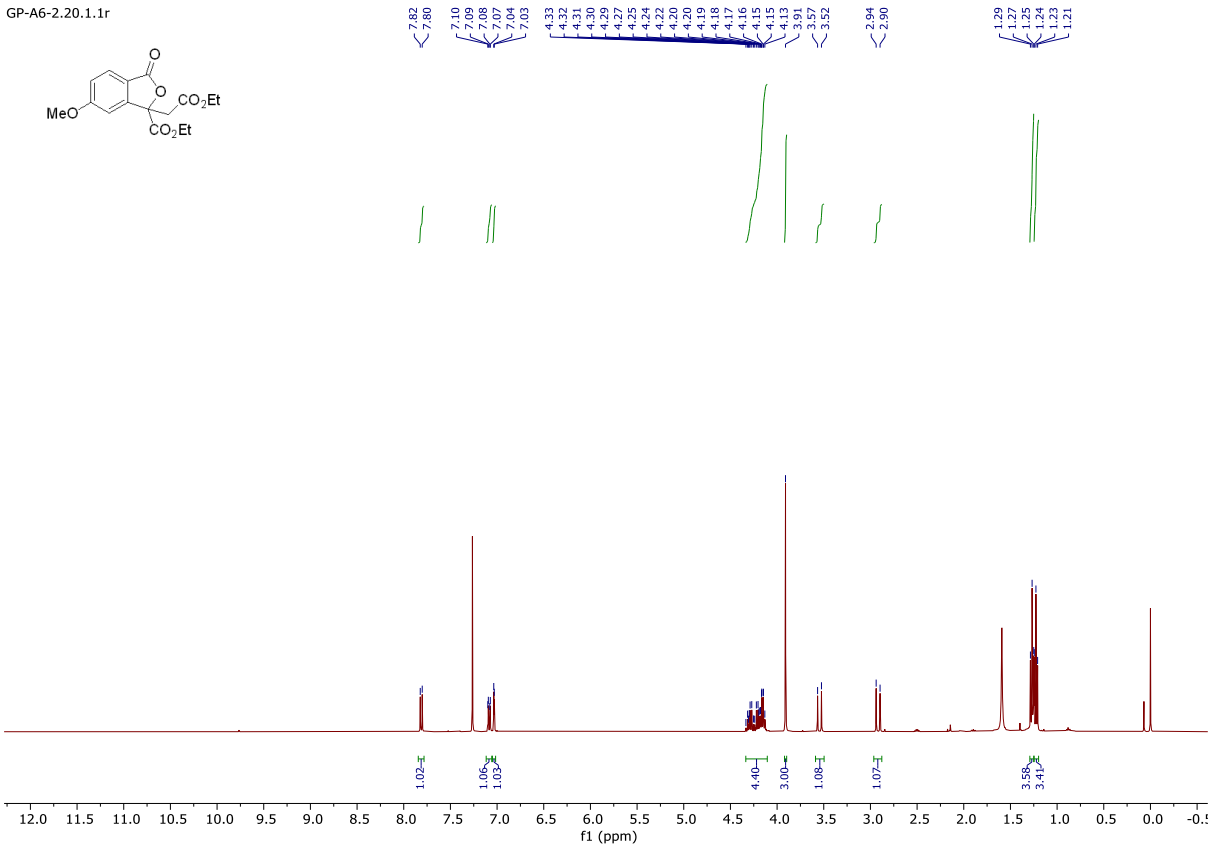
(5w) (^{1}H NMR 400 MHz, $CDCl_3$)



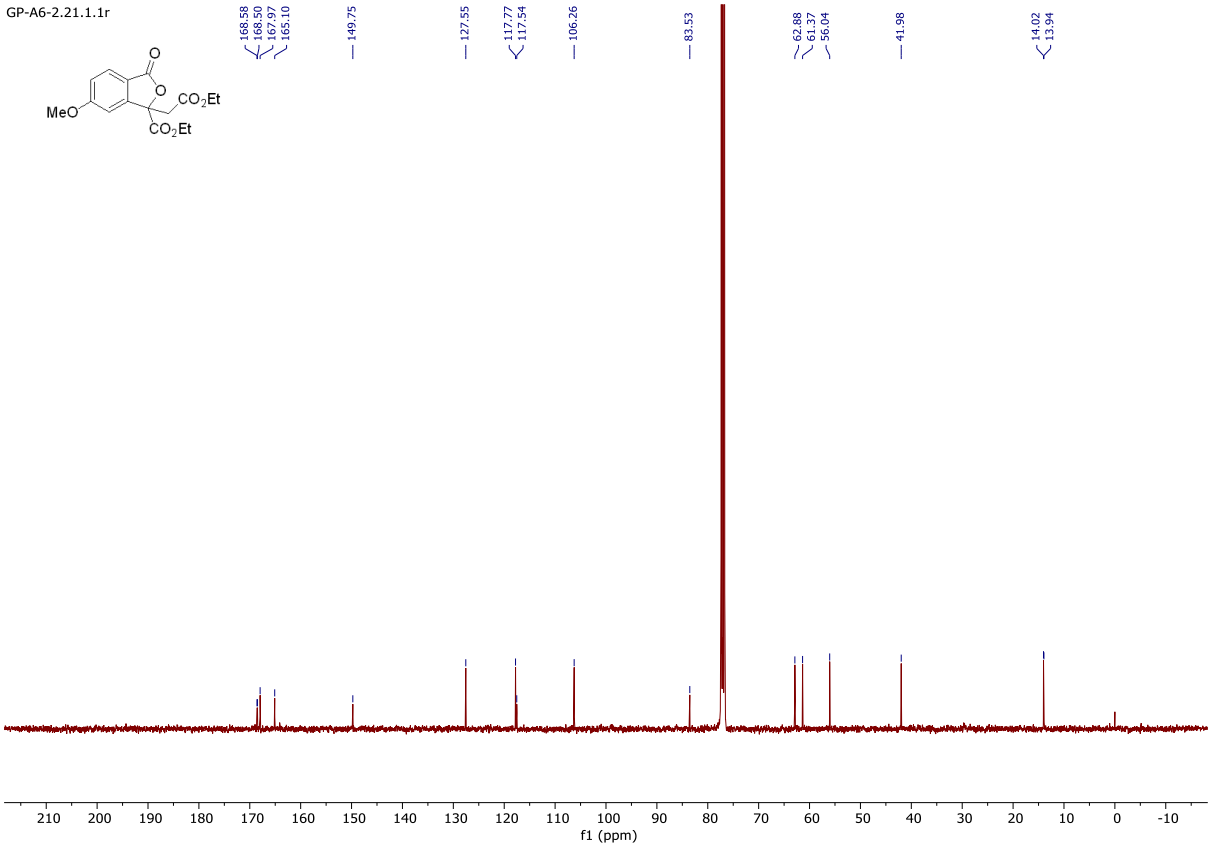
(5w) (^{13}C NMR 101 MHz, $CDCl_3$)



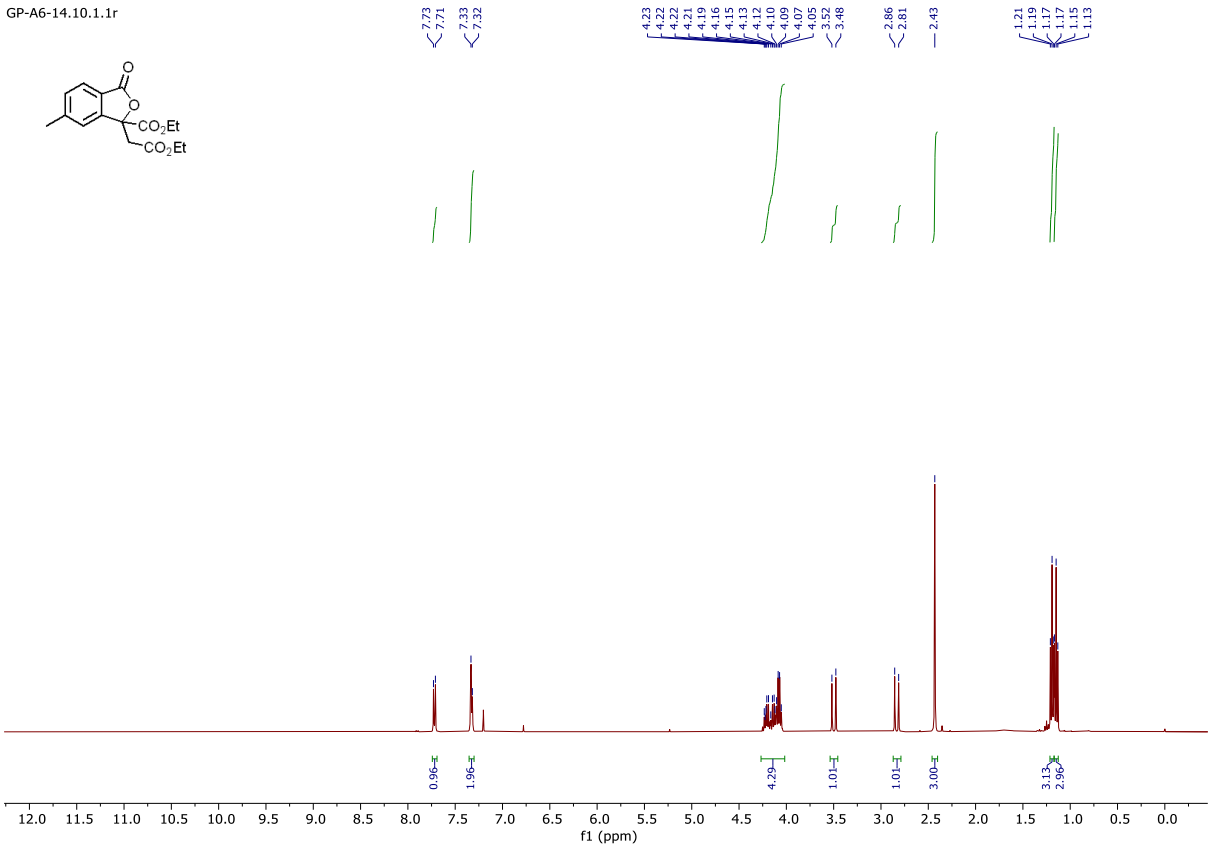
(7a) (^{1}H NMR 400 MHz, $CDCl_3$)



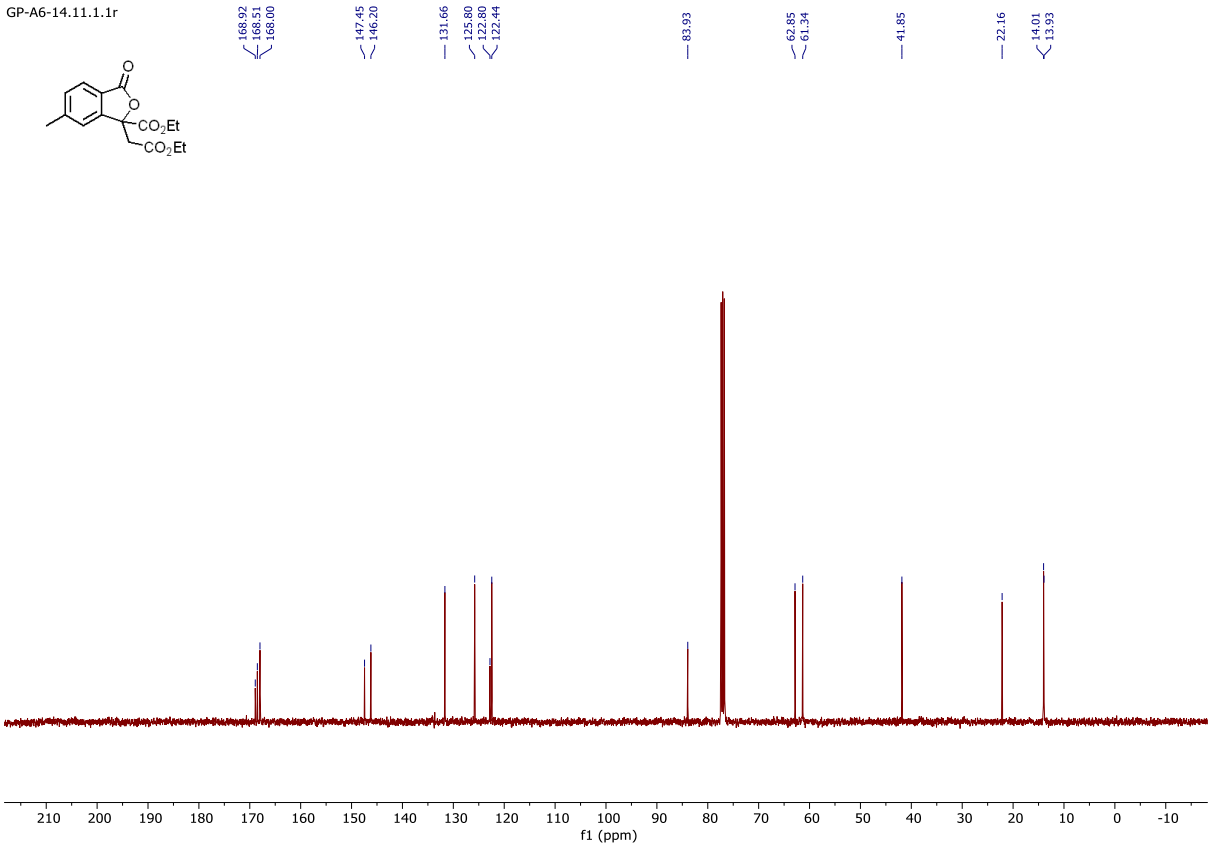
(7a) (^{13}C NMR 101 MHz, $CDCl_3$)



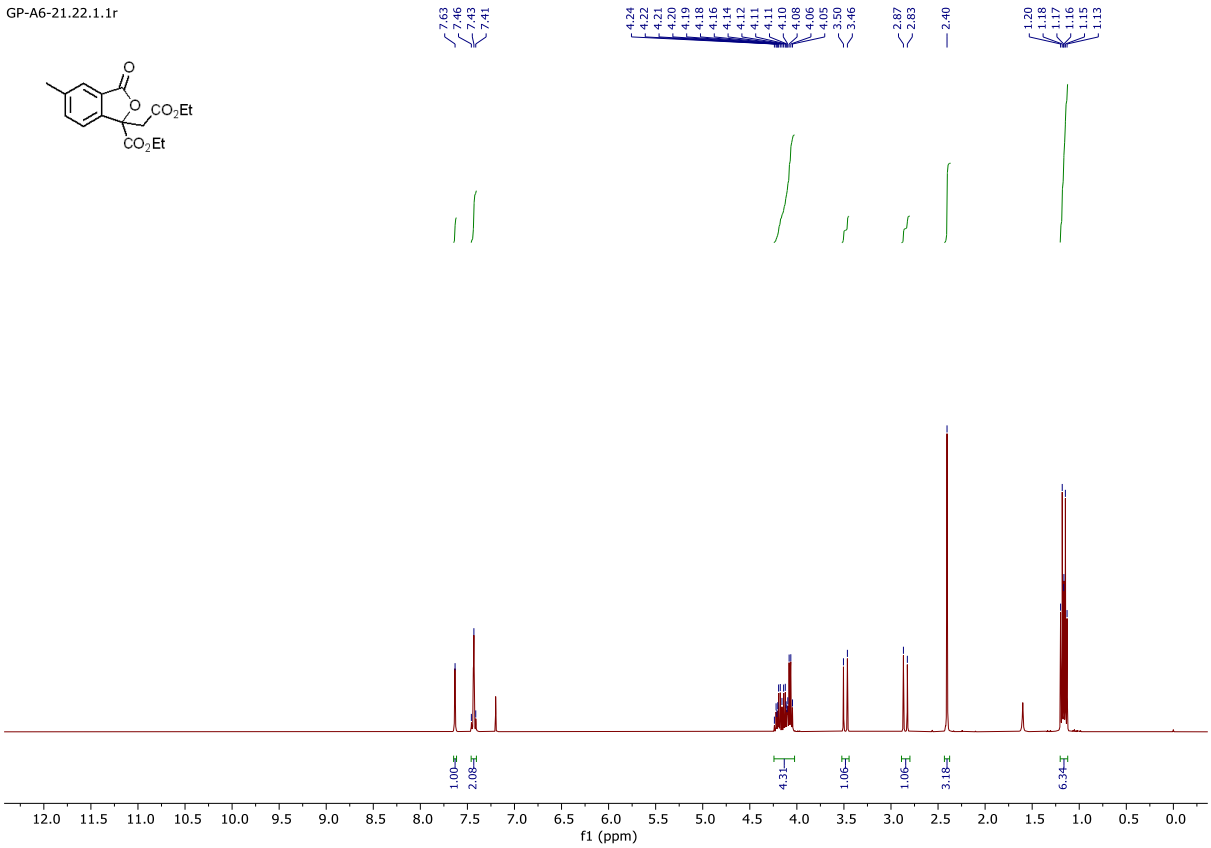
(7b) (^{1}H NMR 400 MHz, $CDCl_3$)



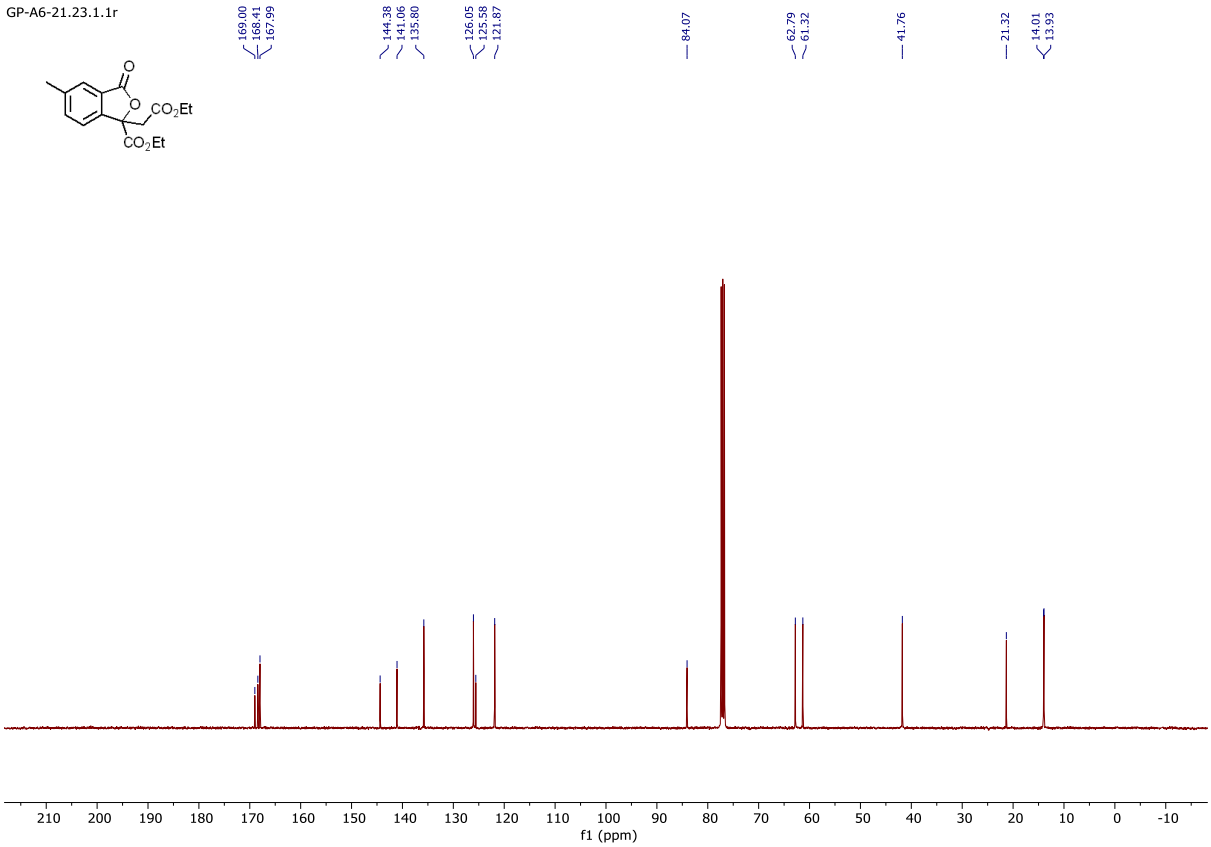
(7b) (^{13}C NMR 101 MHz, $CDCl_3$)



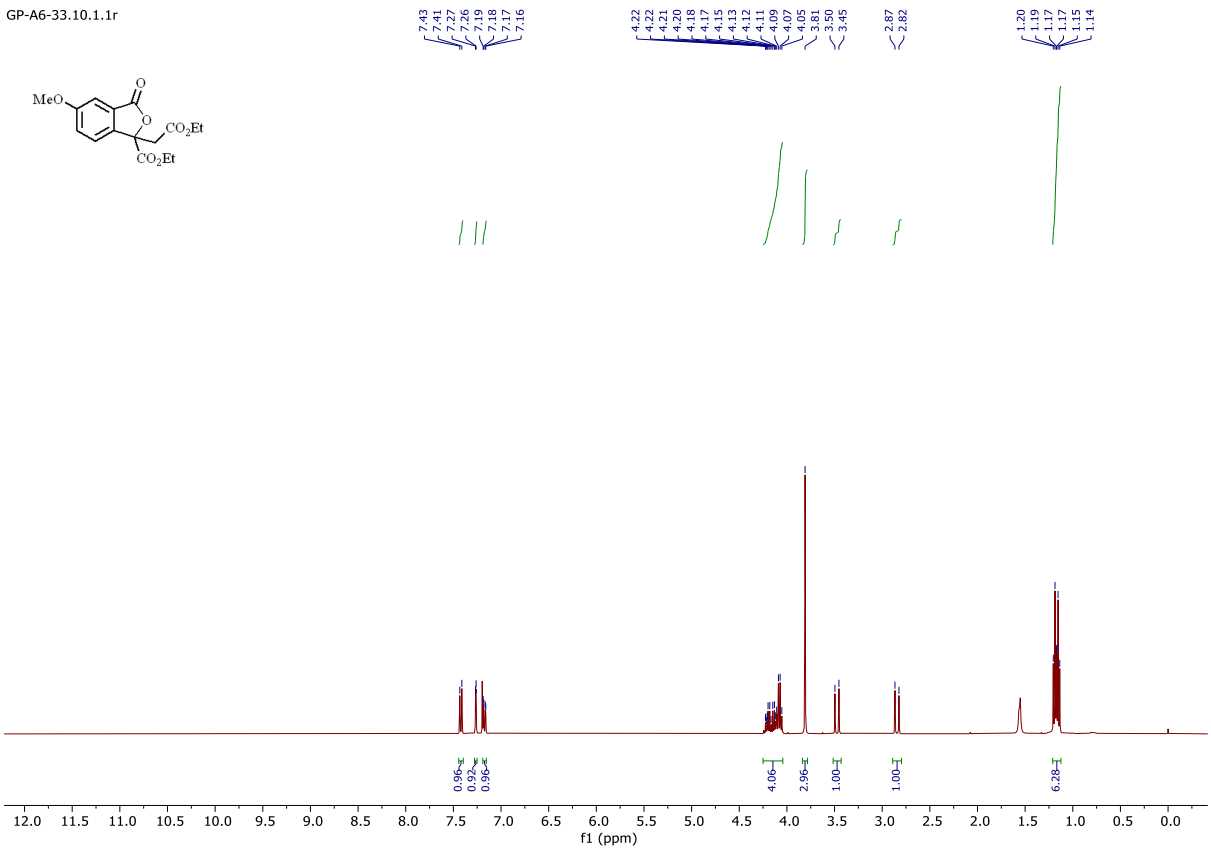
(7c) (^{1}H NMR 400 MHz, $CDCl_3$)



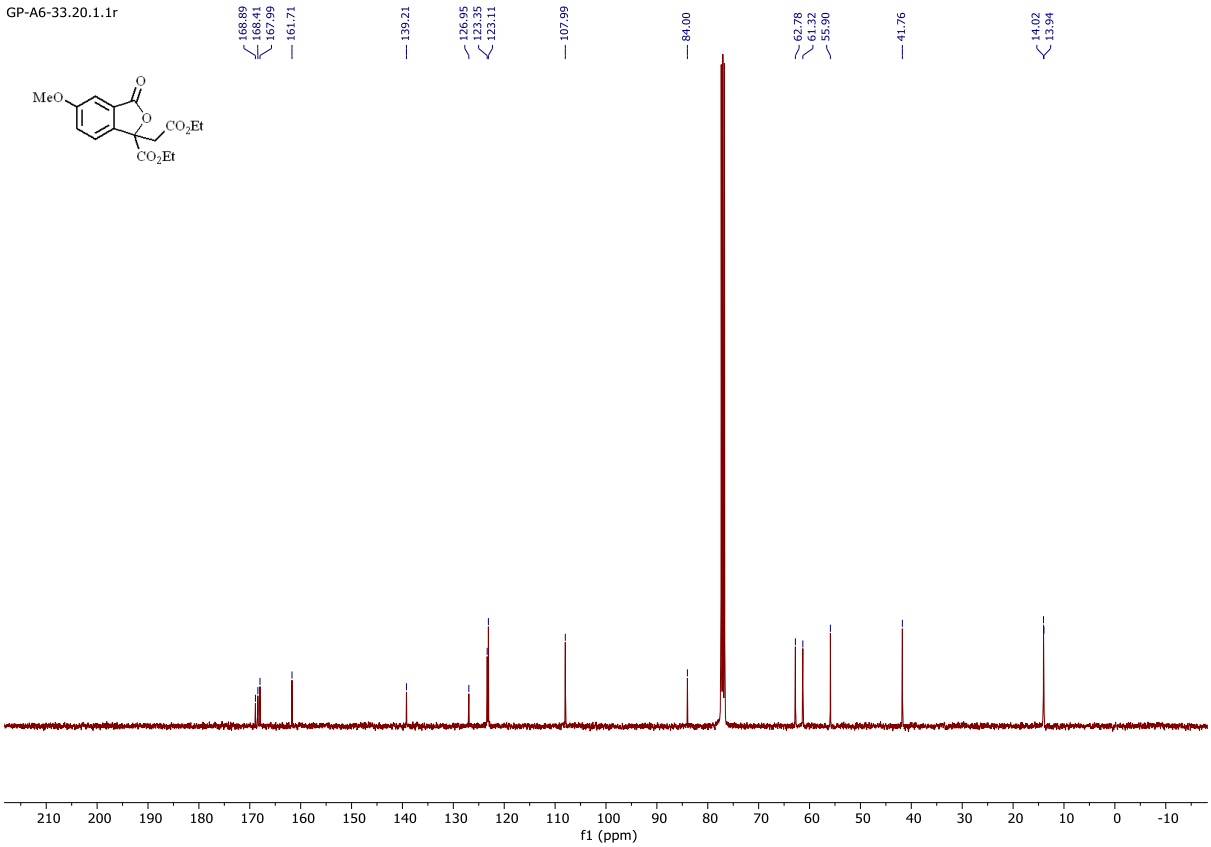
(7c) (^{13}C NMR 101 MHz, $CDCl_3$)



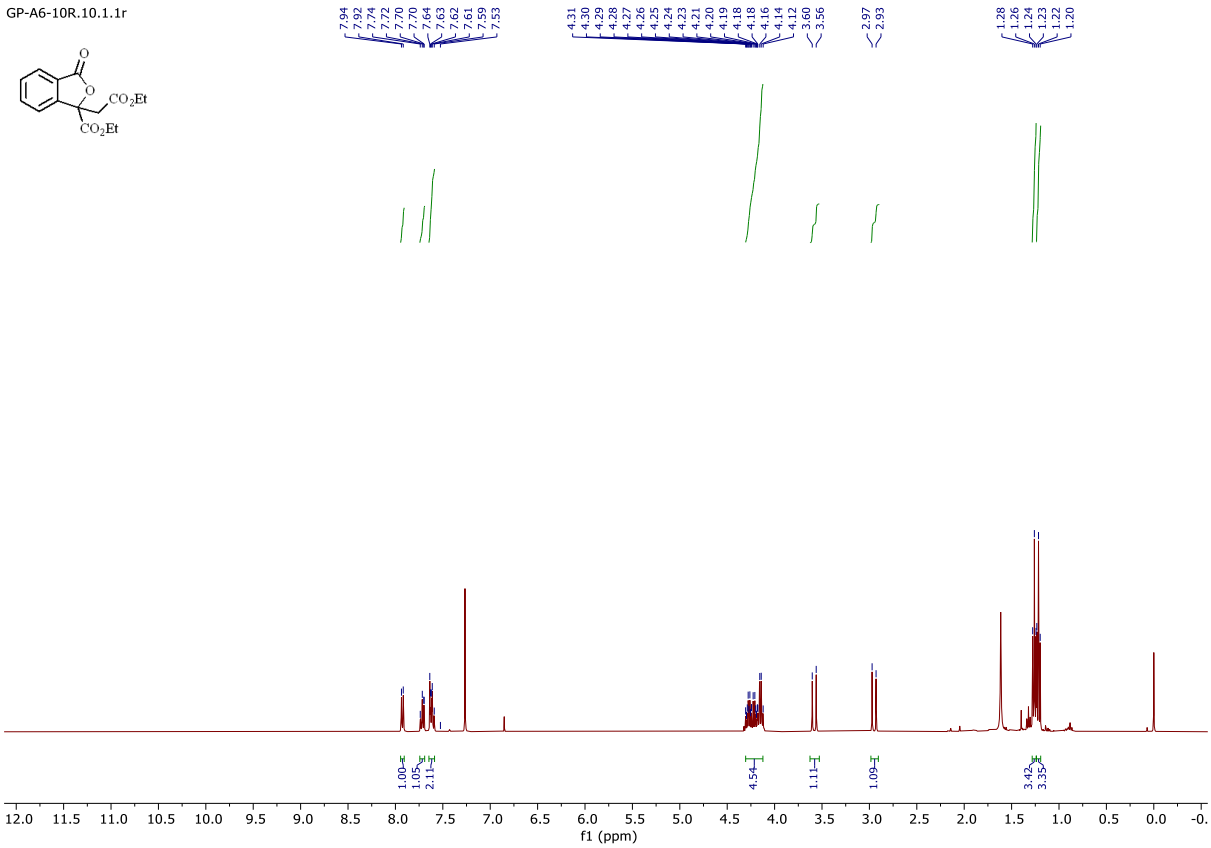
(7d) (^{1}H NMR 400 MHz, $CDCl_3$)



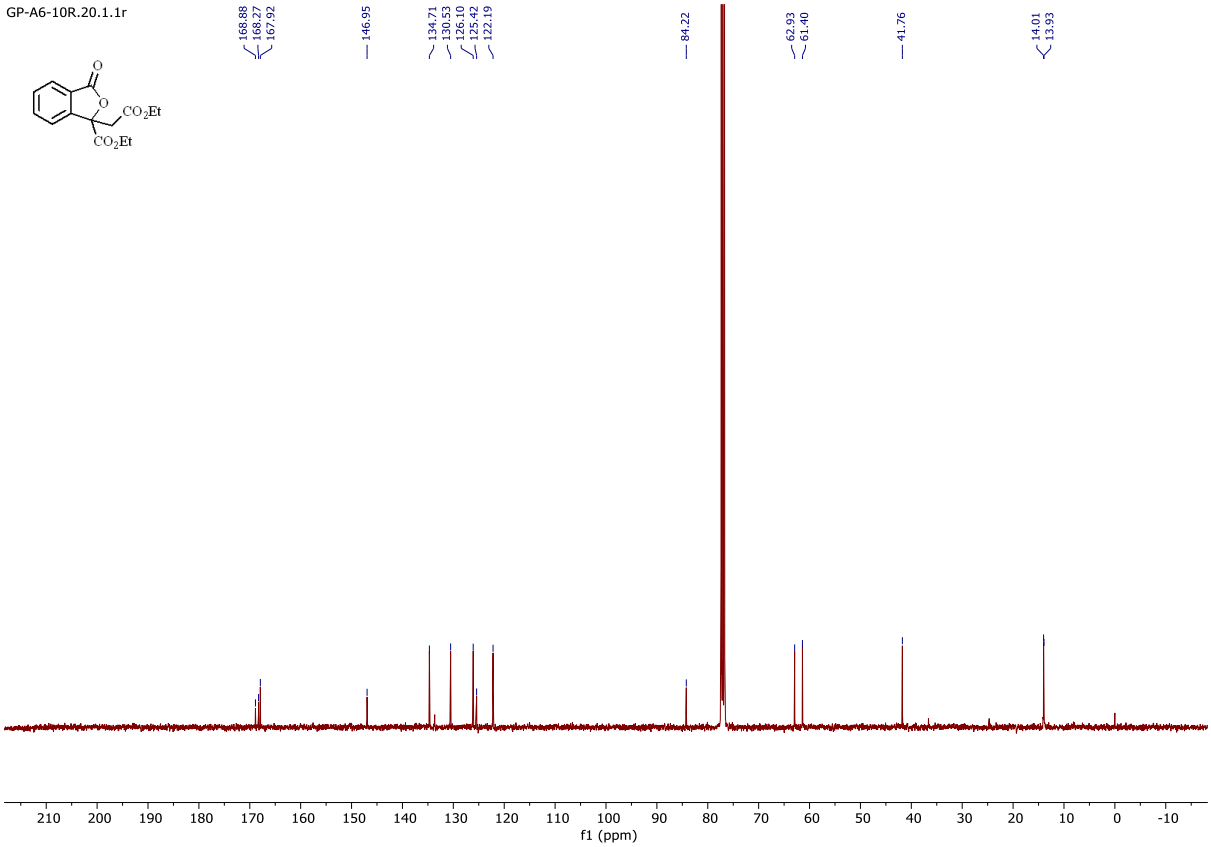
(7d) (^{13}C NMR 101 MHz, $CDCl_3$)



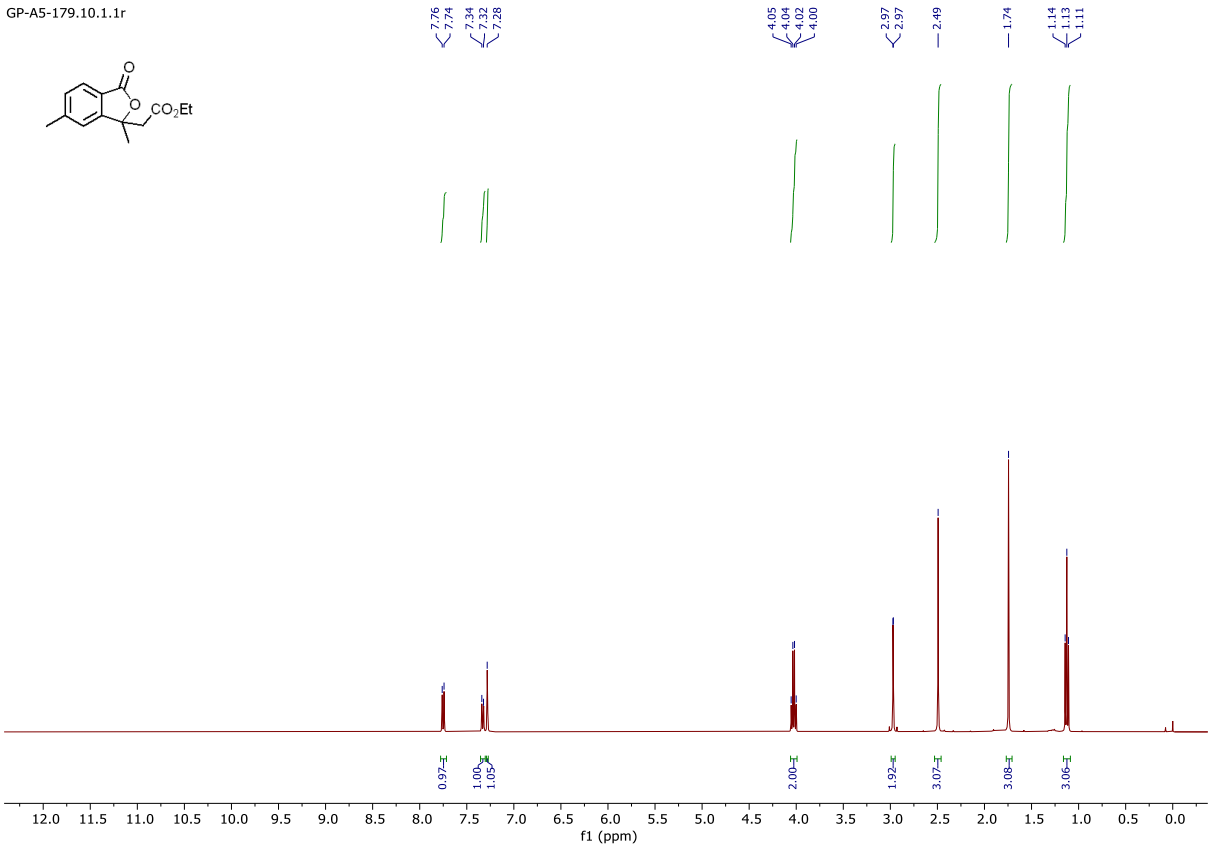
(7e) (^{1}H NMR 400 MHz, $CDCl_3$)



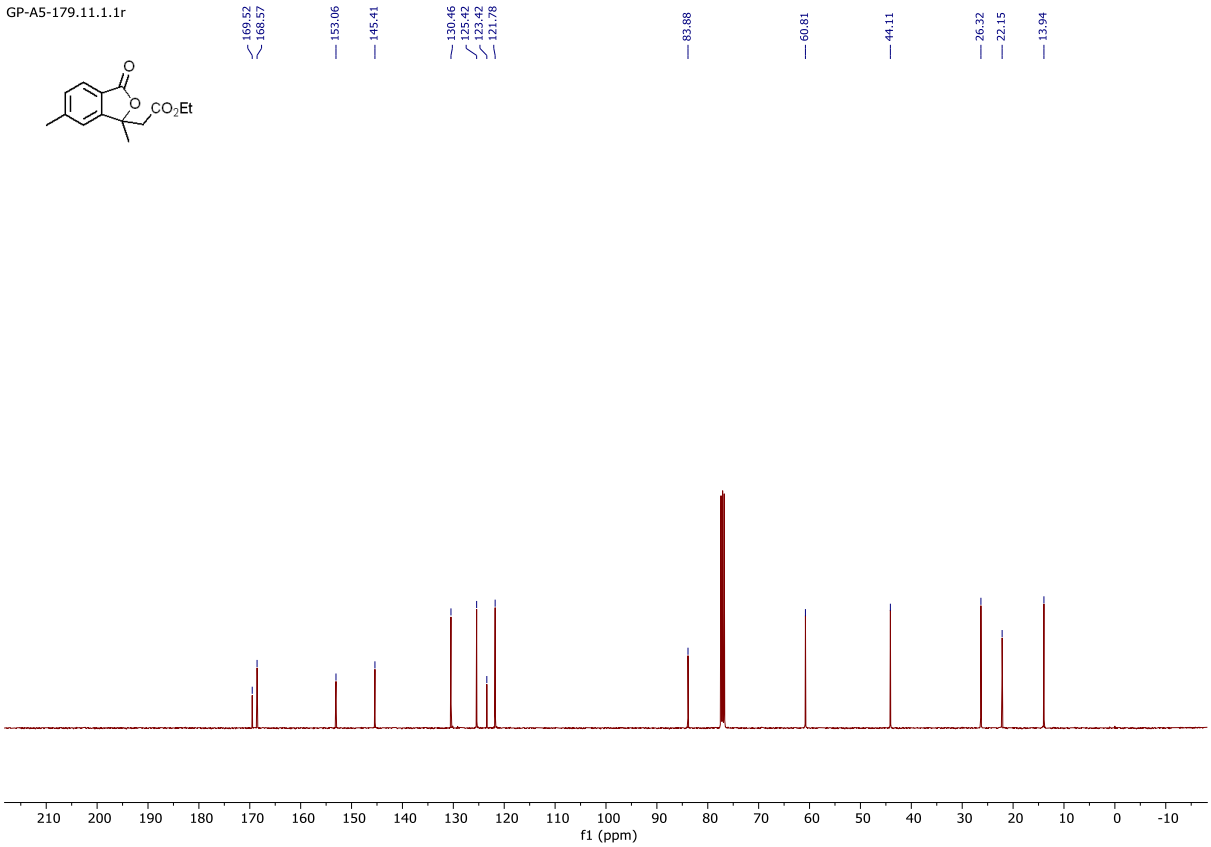
(7e) (^{13}C NMR 101 MHz, $CDCl_3$)



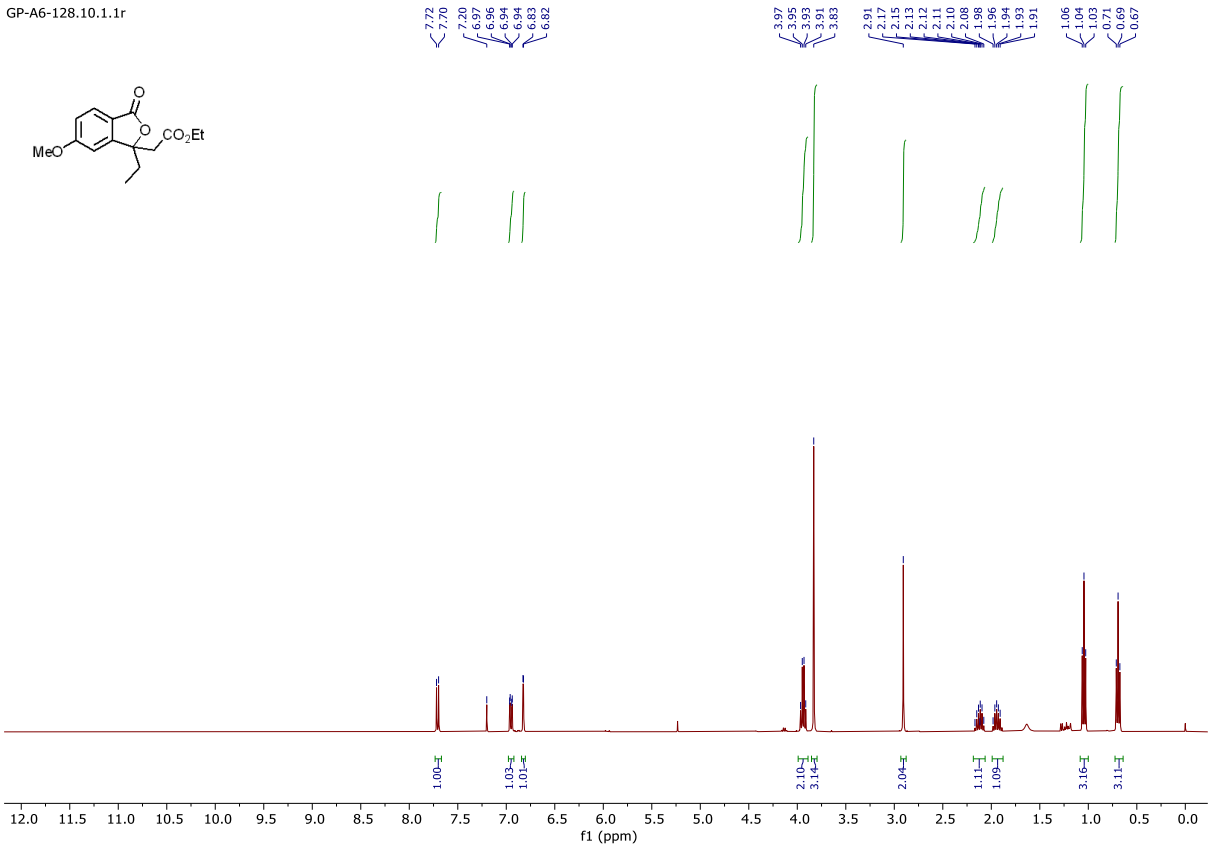
(7f) (^{1}H NMR 400 MHz, $CDCl_3$)



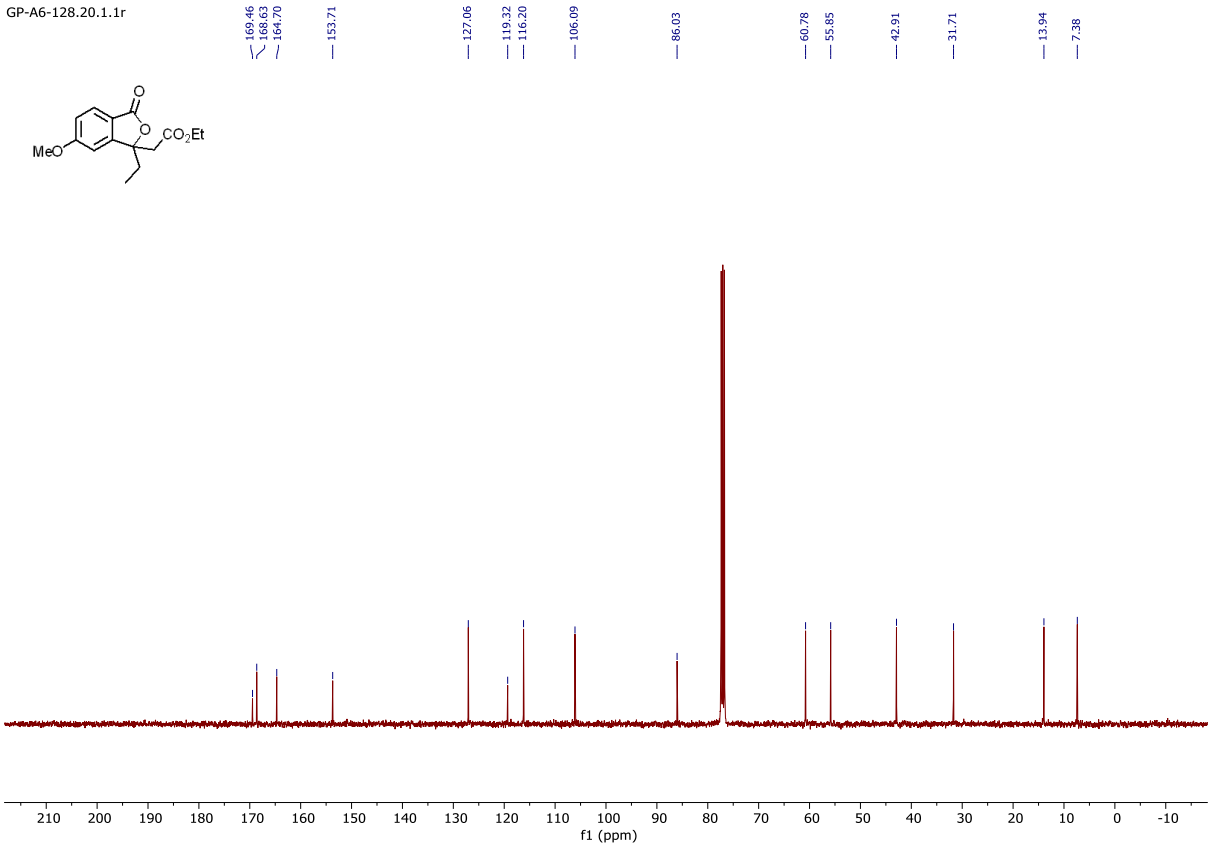
(7f) (^{13}C NMR 101 MHz, $CDCl_3$)



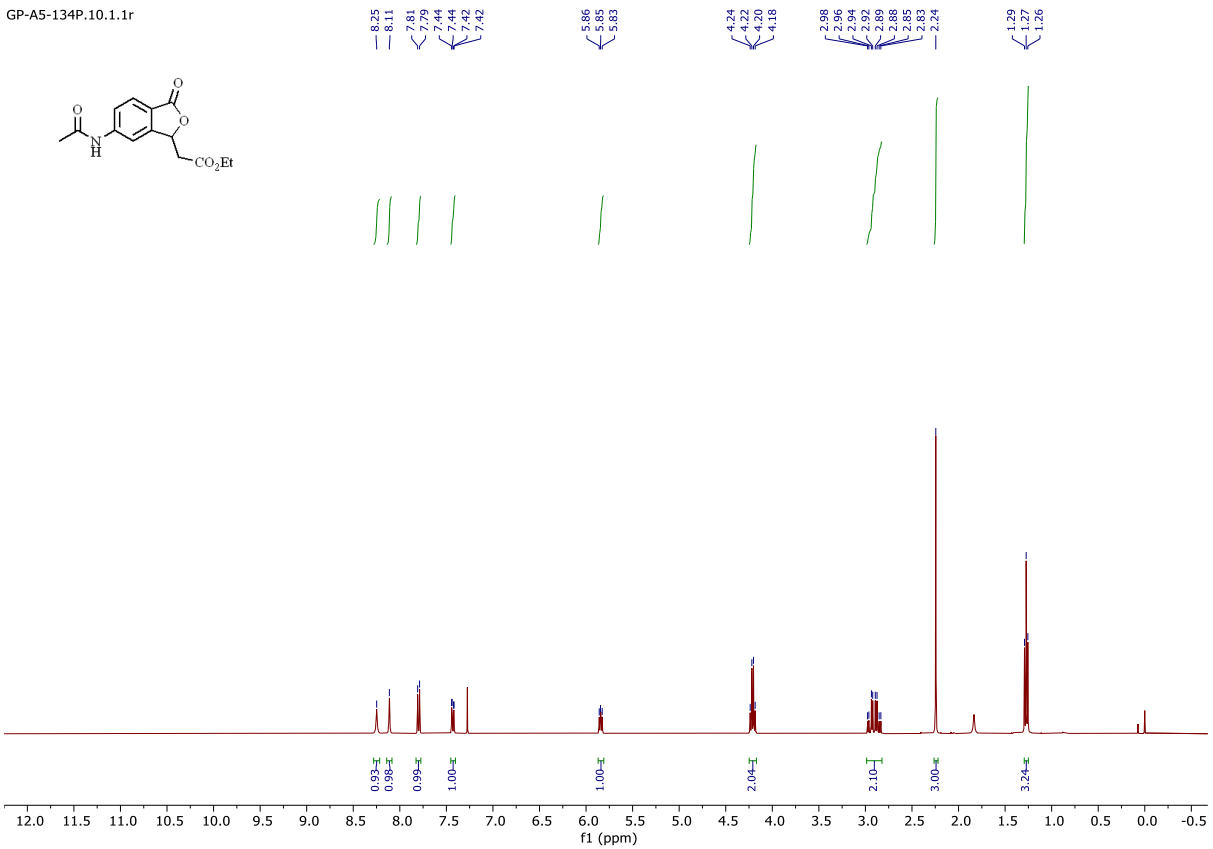
(7g) (^{1}H NMR 400 MHz, $CDCl_3$)



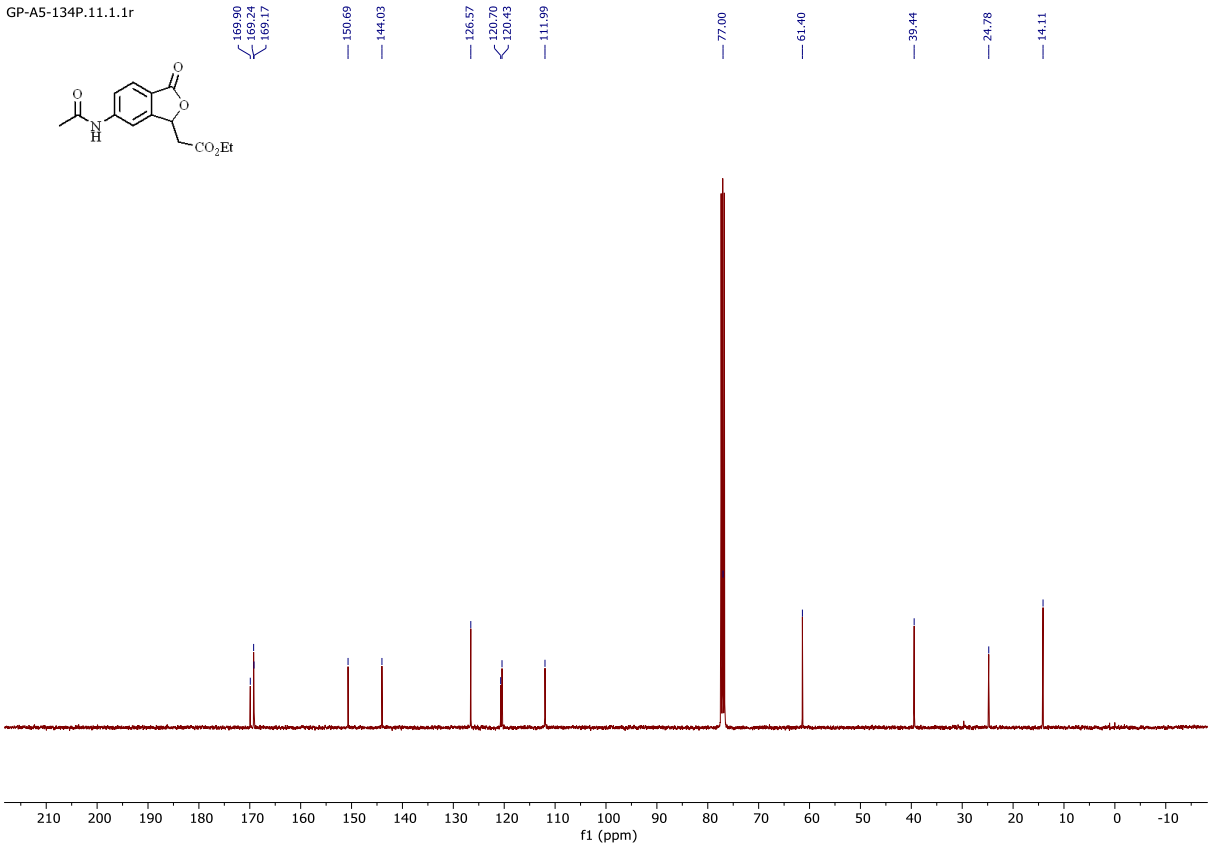
(7g) (^{13}C NMR 101 MHz, $CDCl_3$)



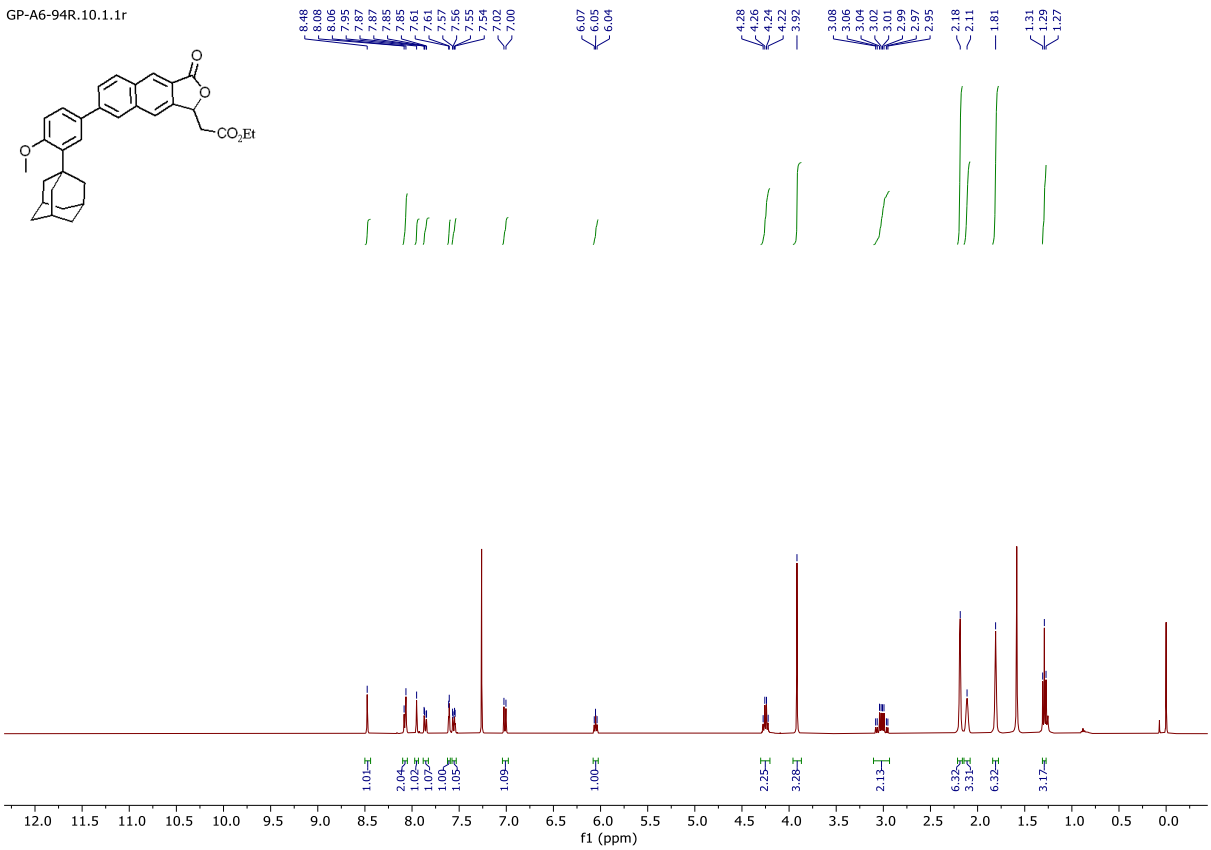
(11a) (^{1}H NMR 400 MHz, $CDCl_3$)



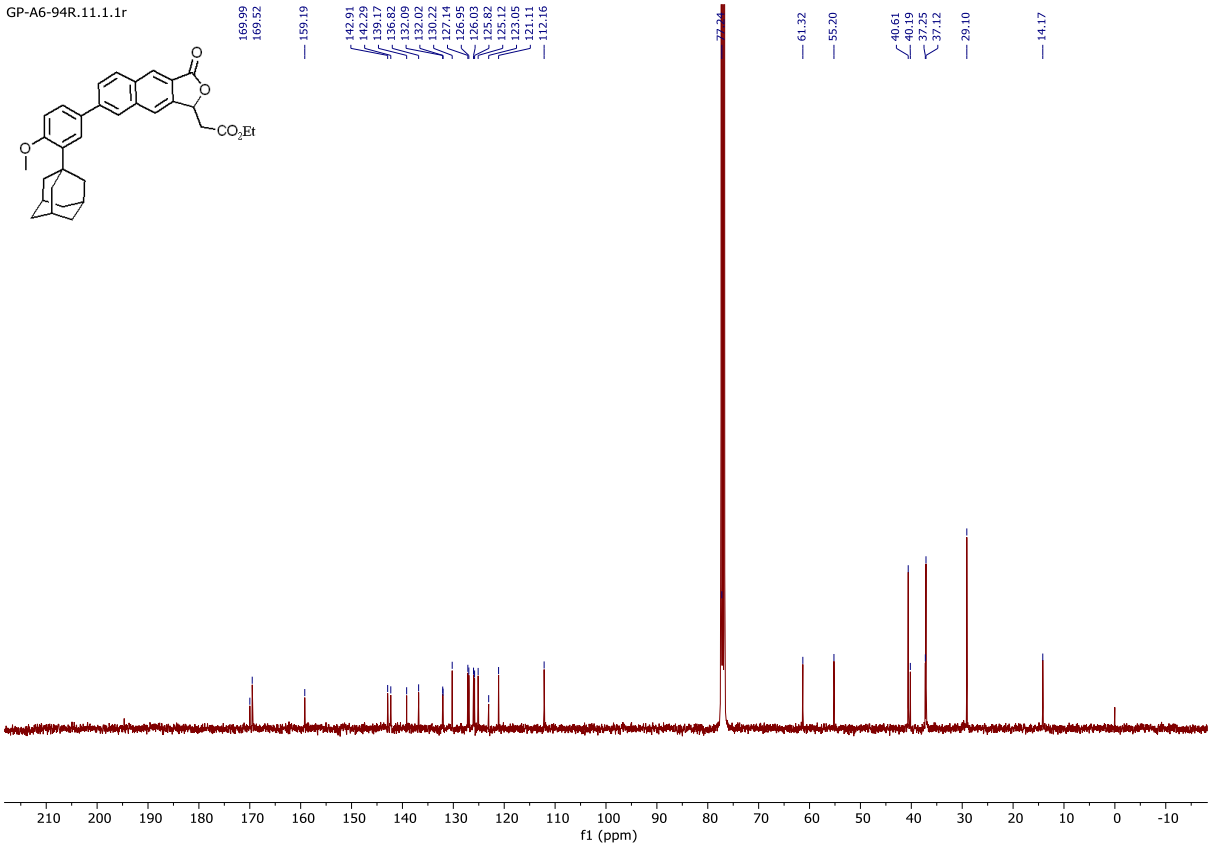
(11a) (^{13}C NMR 101 MHz, $CDCl_3$)



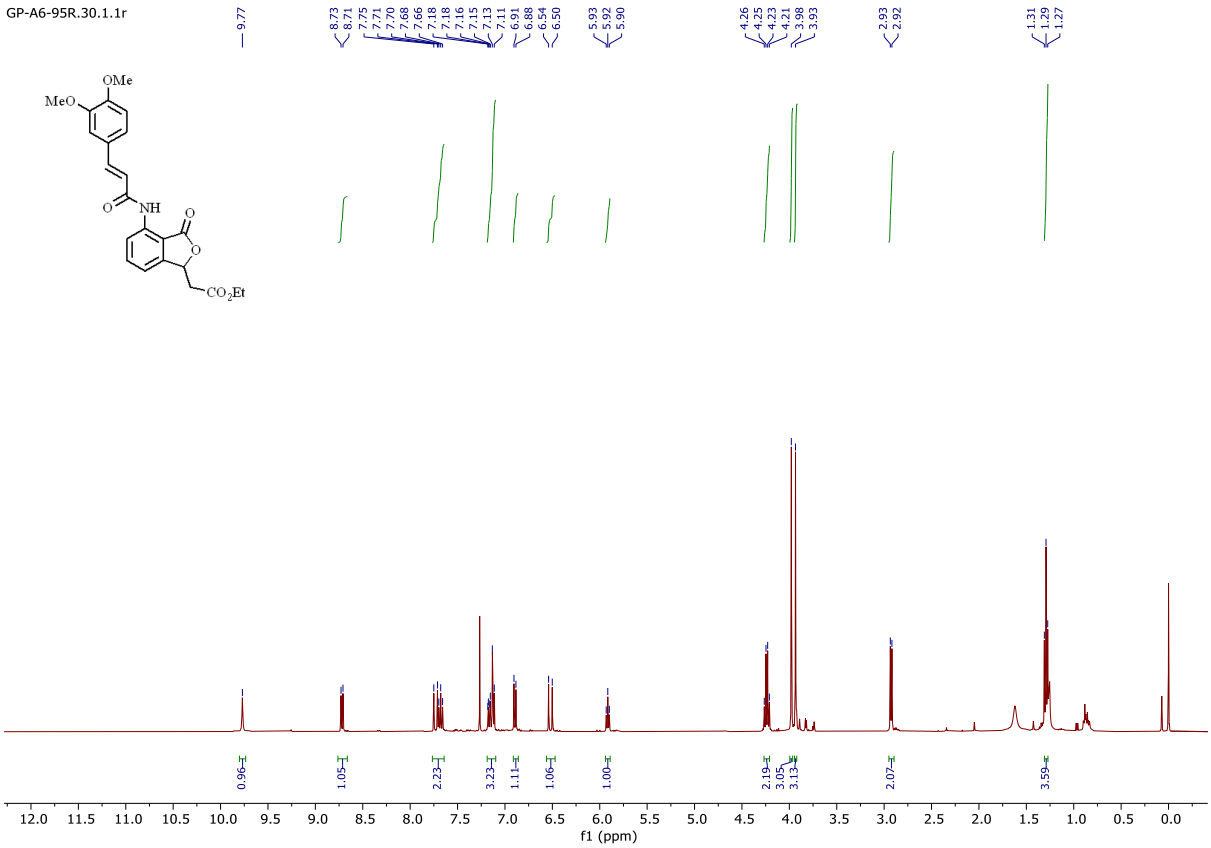
(11b) (^{1}H NMR 400 MHz, $CDCl_3$)



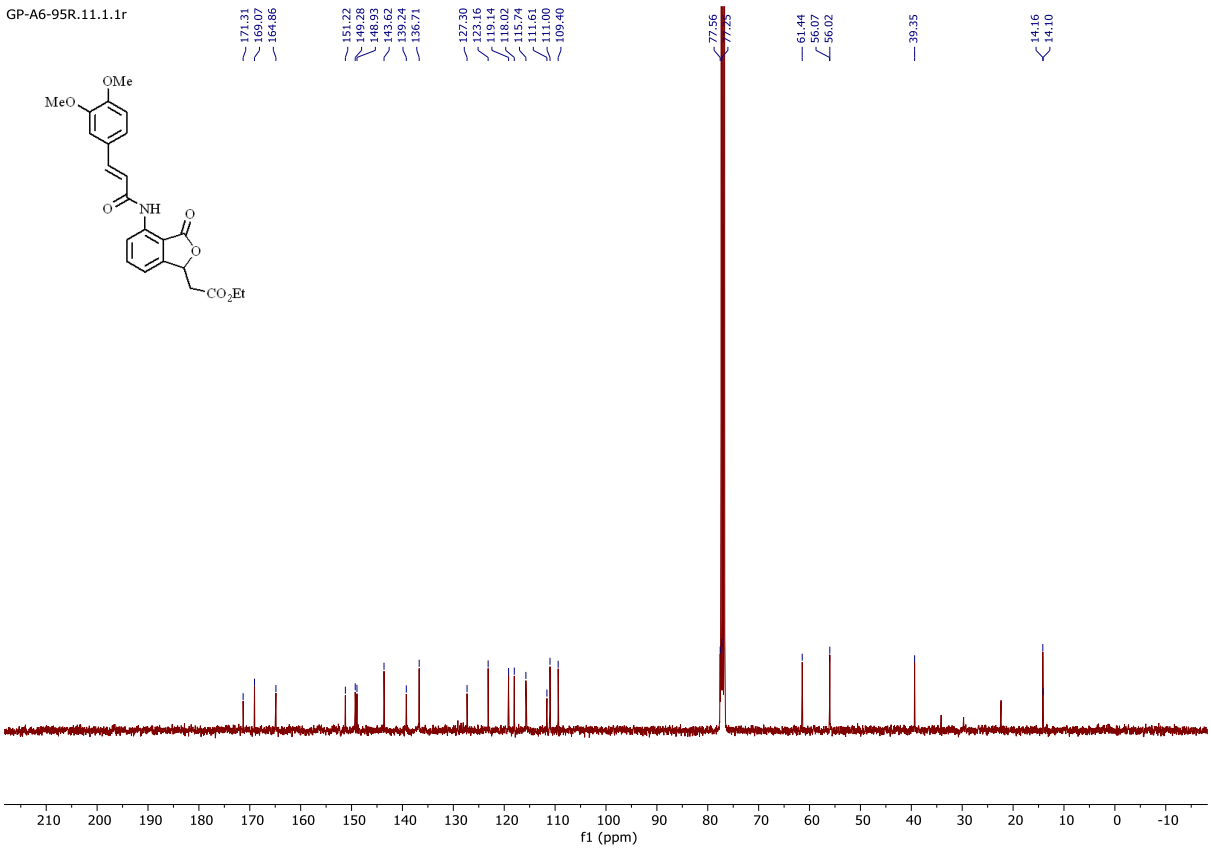
(11b) (^{13}C NMR 101 MHz, $CDCl_3$)



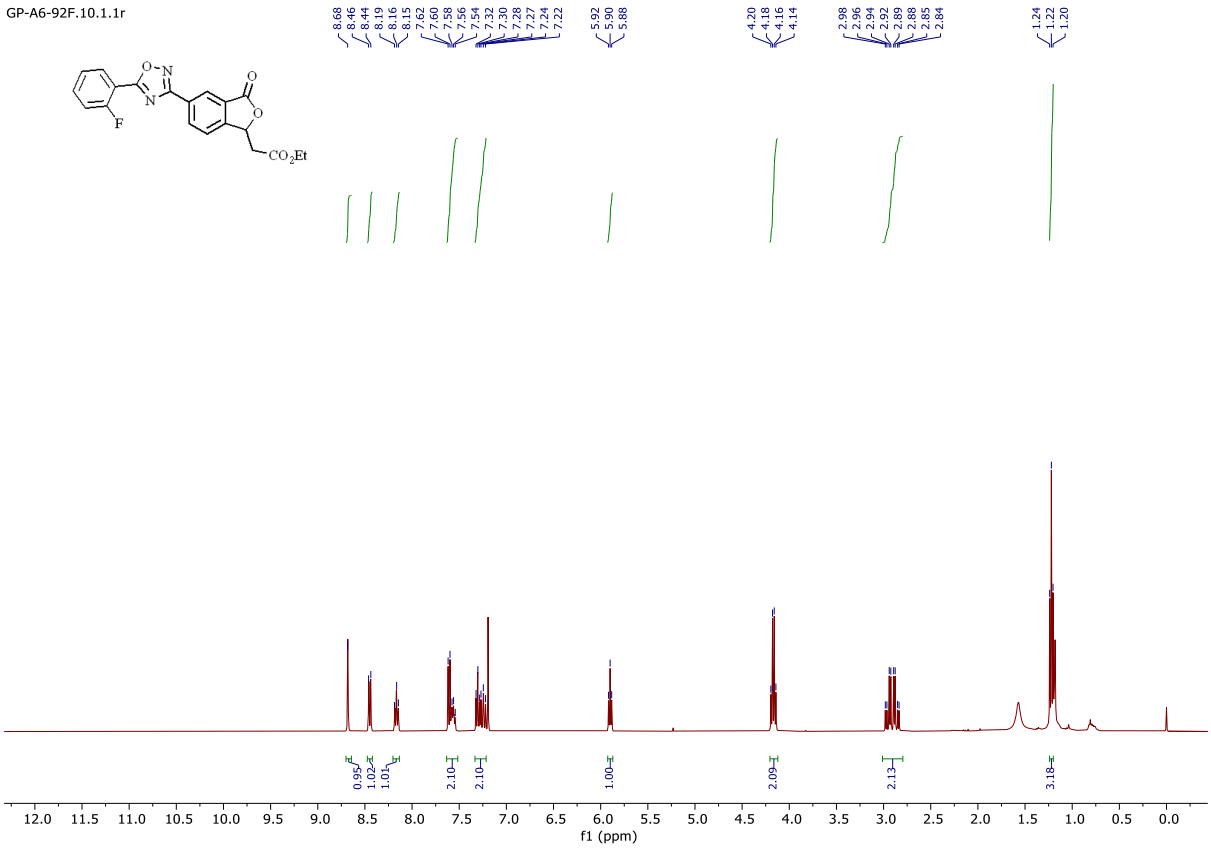
(11c) (^{1}H NMR 400 MHz, $CDCl_3$)



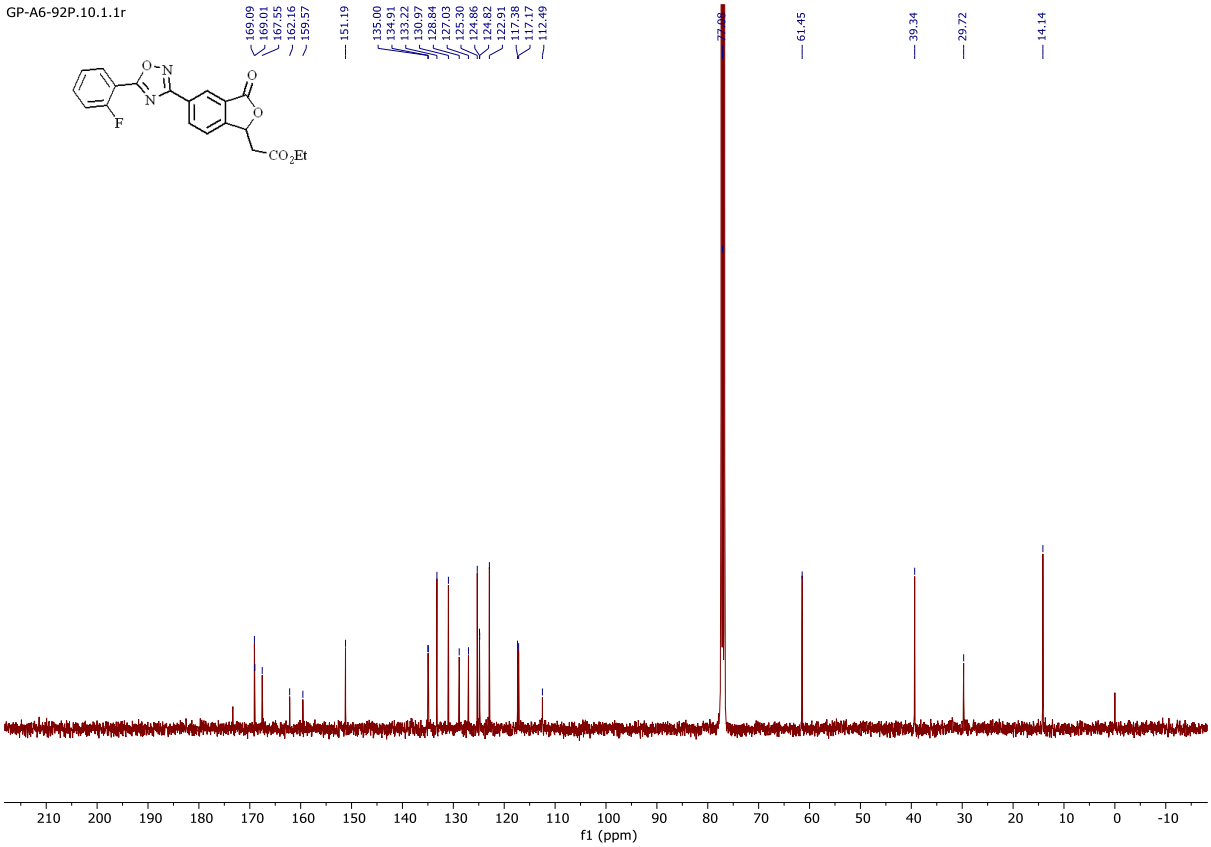
(11c) (^{13}C NMR 101 MHz, $CDCl_3$)



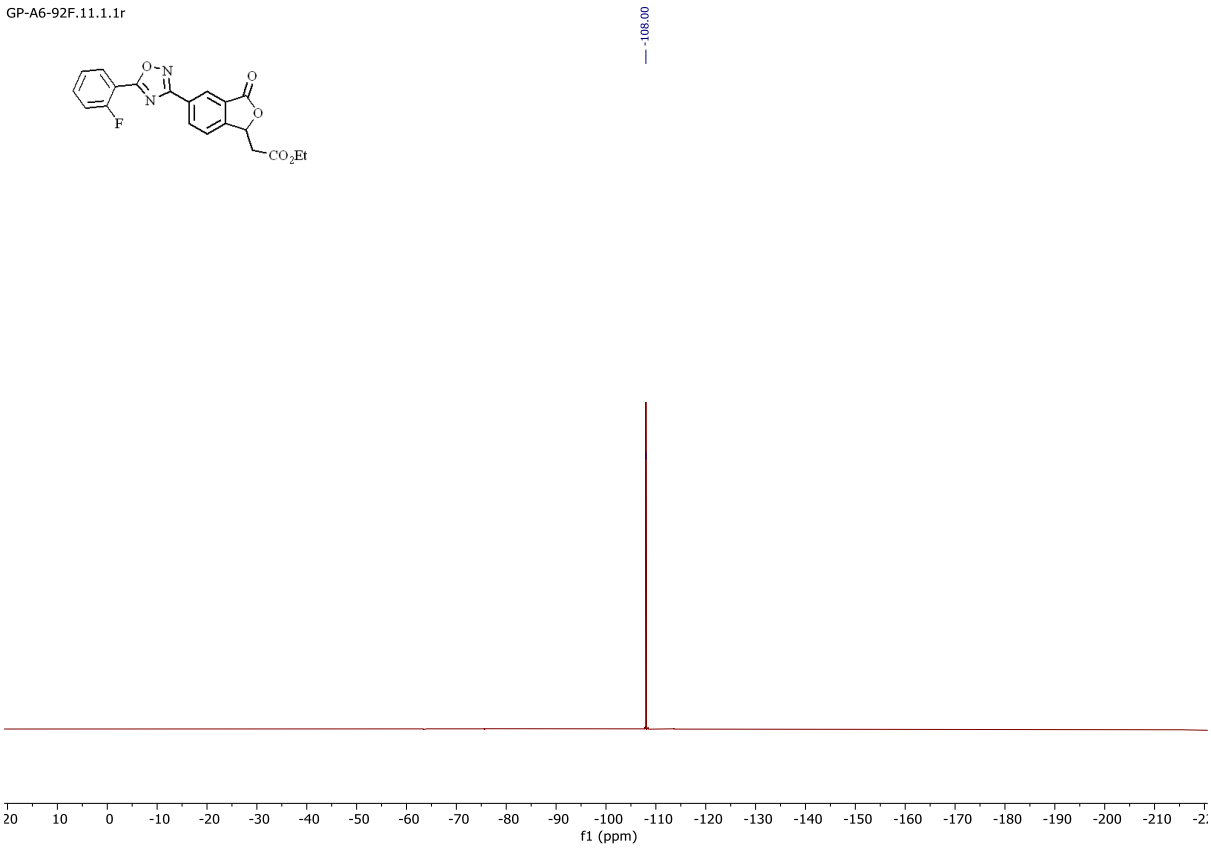
(11d) (^{1}H NMR 400 MHz, $CDCl_3$)



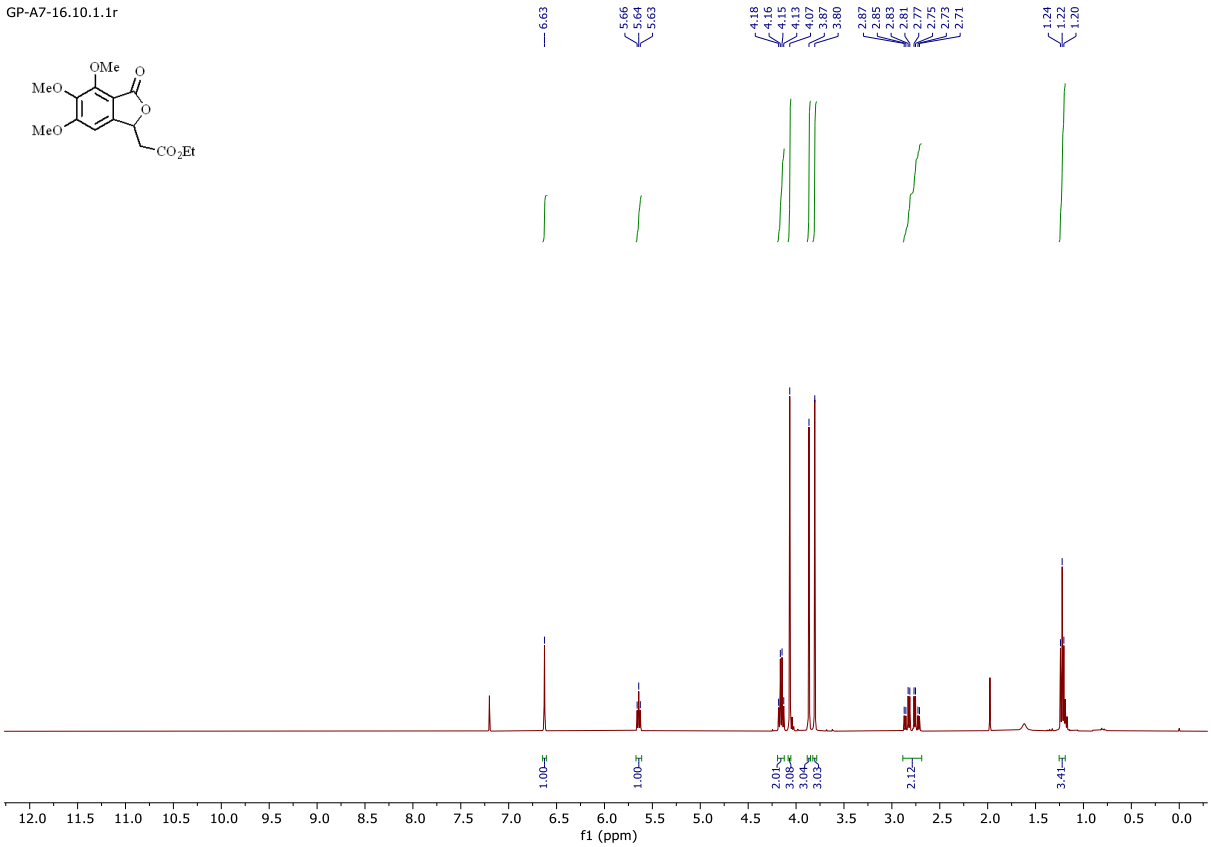
(11d) (^{13}C NMR 101 MHz, $CDCl_3$)



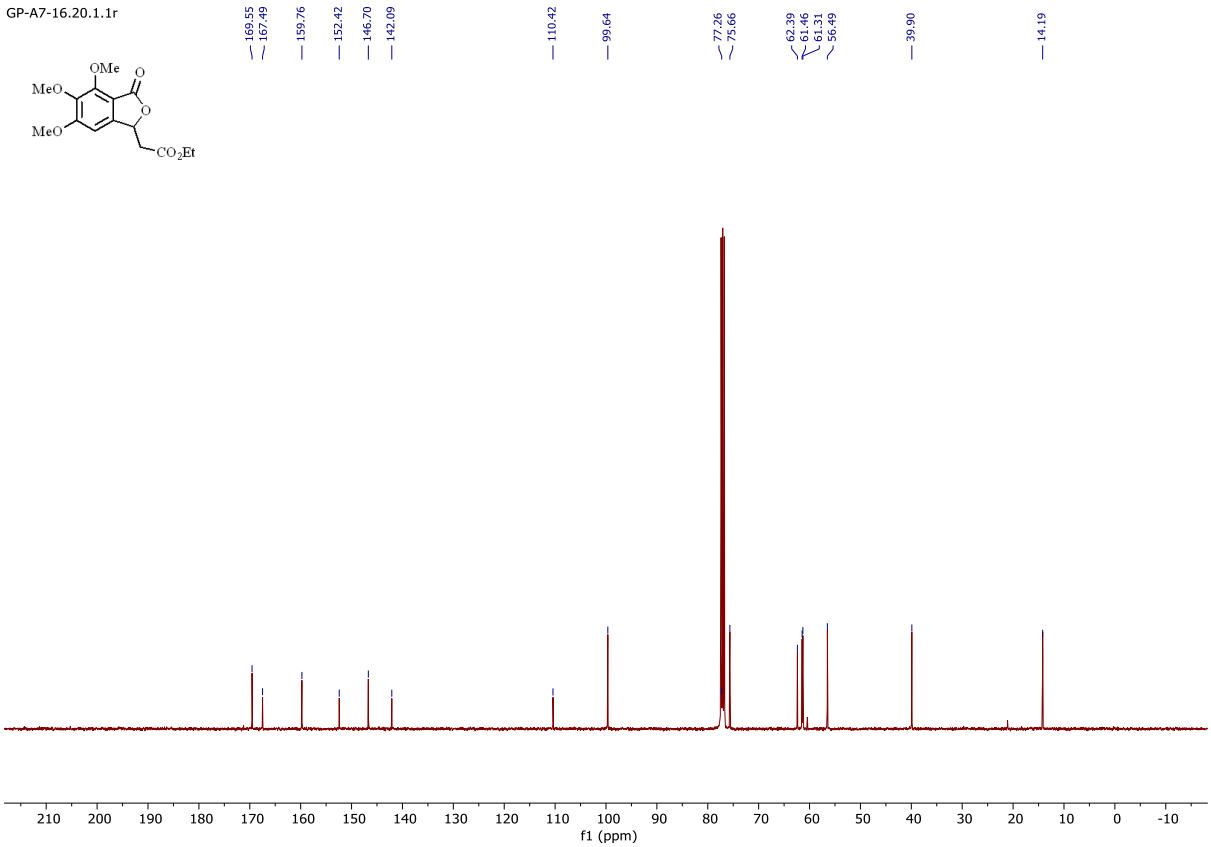
(11d) (^{19}F NMR 377 MHz, $CDCl_3$)



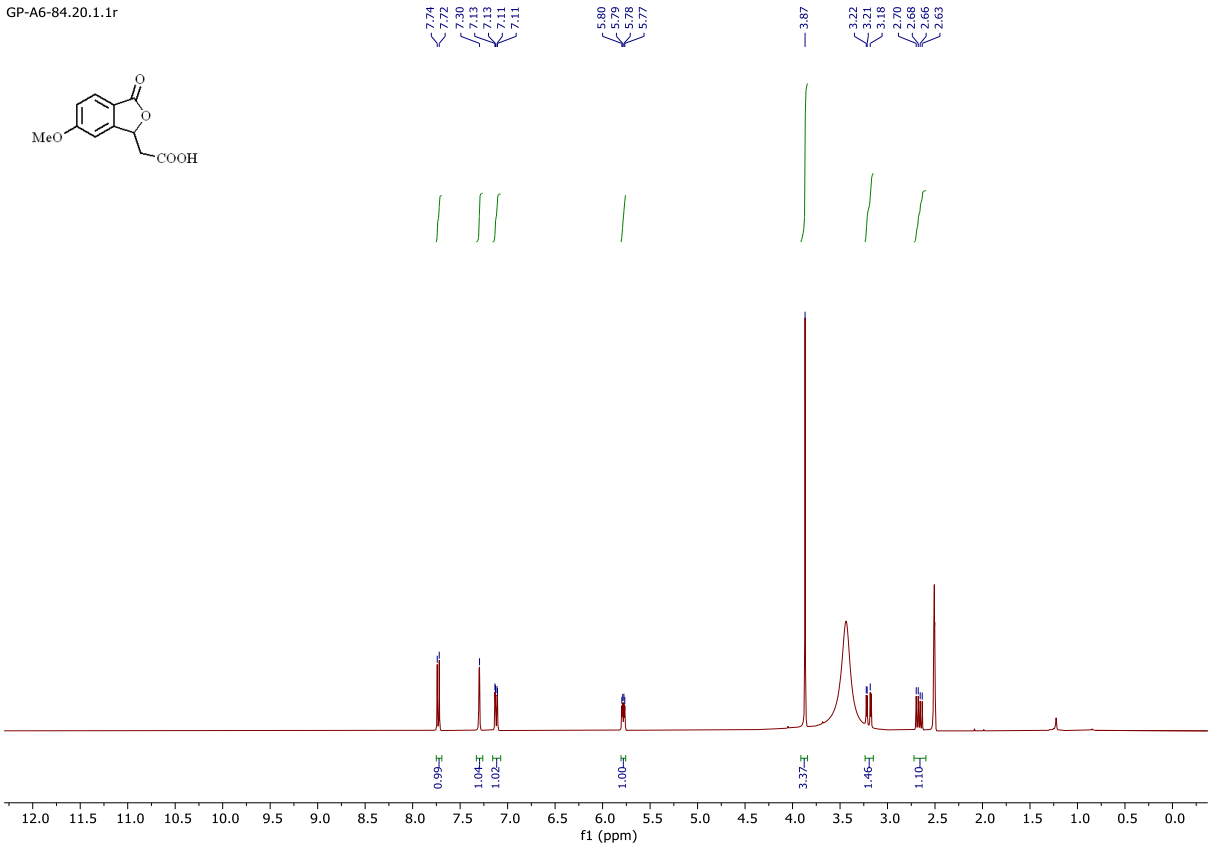
(11e) (^{1}H NMR 400 MHz, $CDCl_3$)



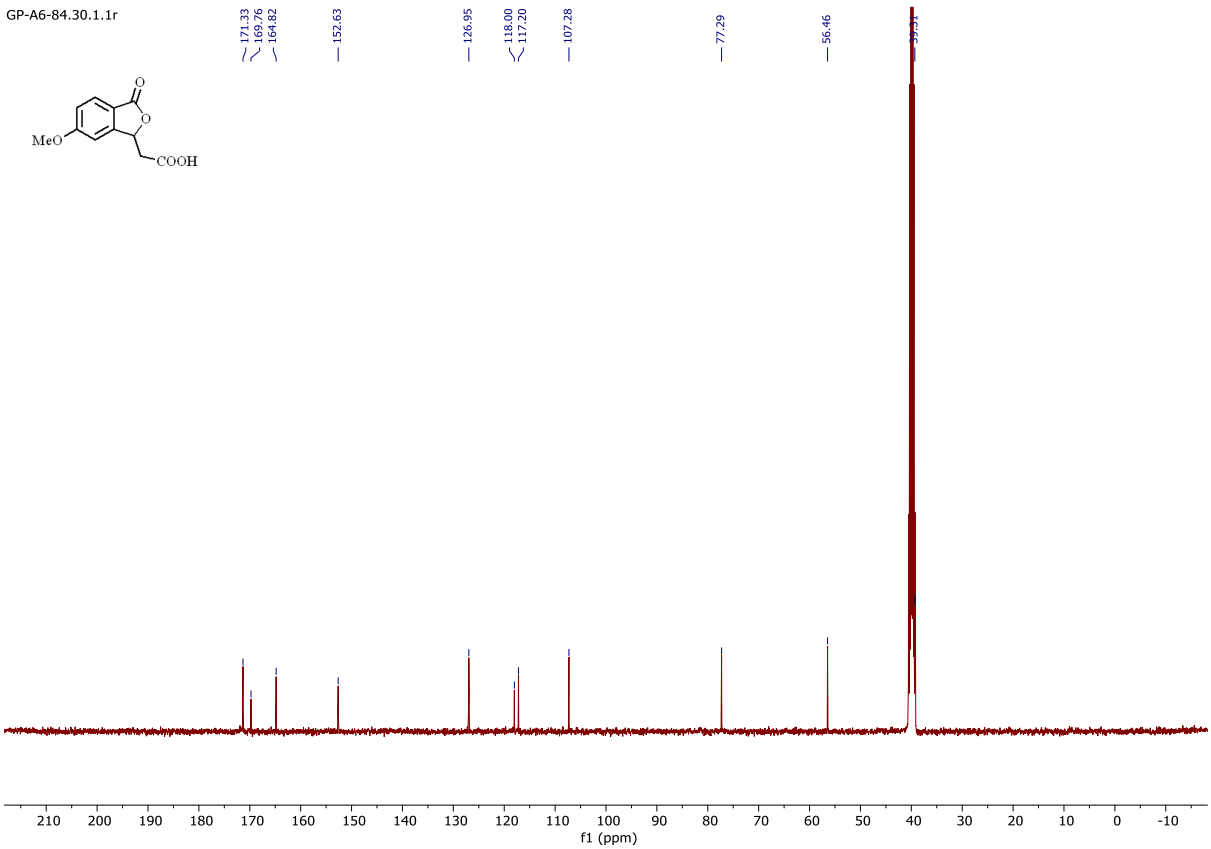
(11e) (^{13}C NMR 101 MHz, $CDCl_3$)



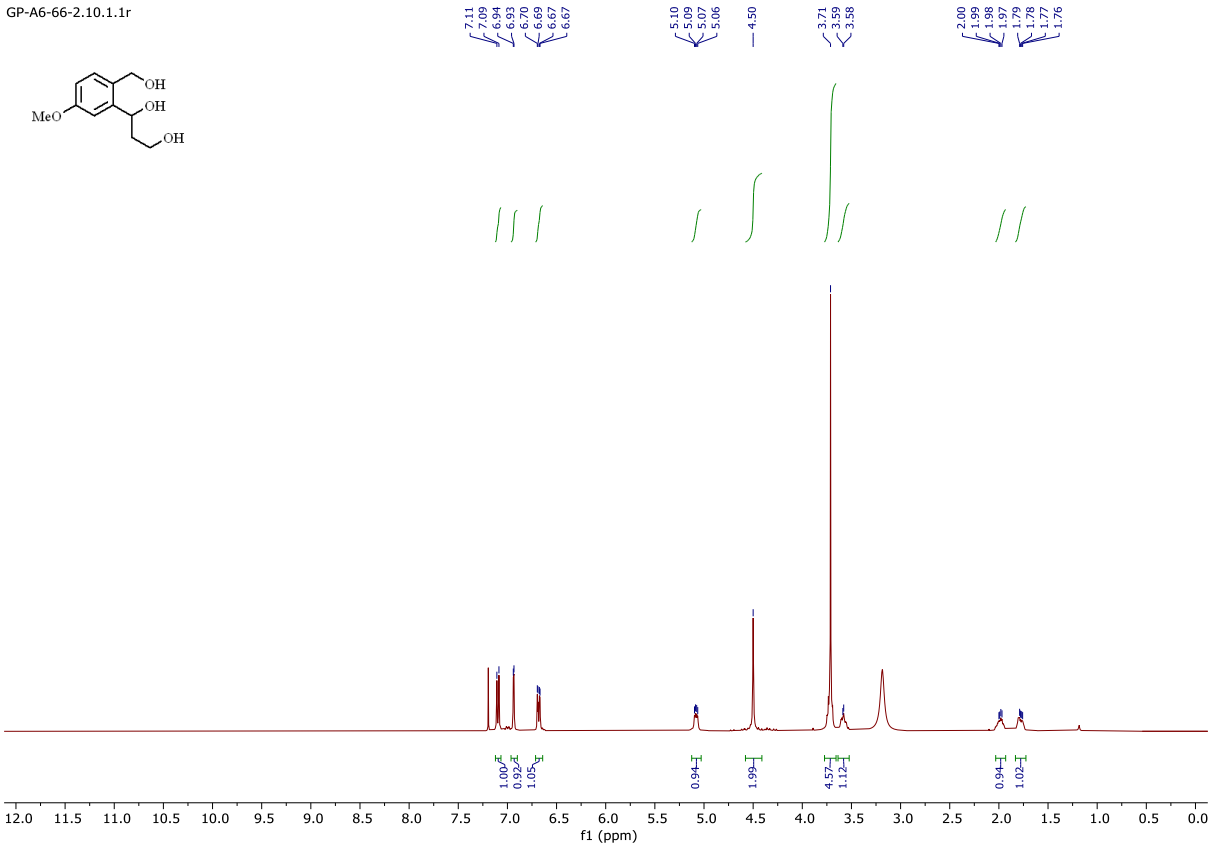
(12a) (^{1}H NMR 400 MHz, $CDCl_3$)



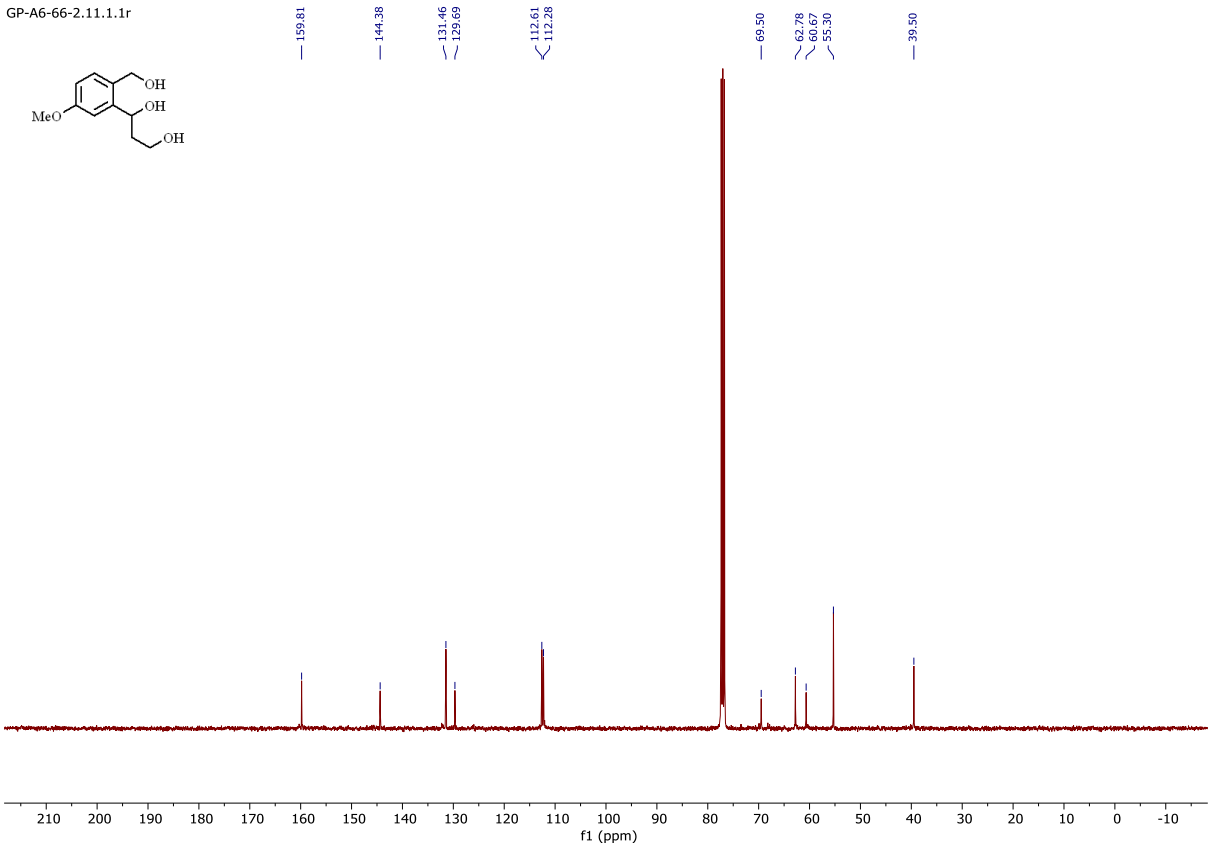
(12a) (^{13}C NMR 101 MHz, DMSO)



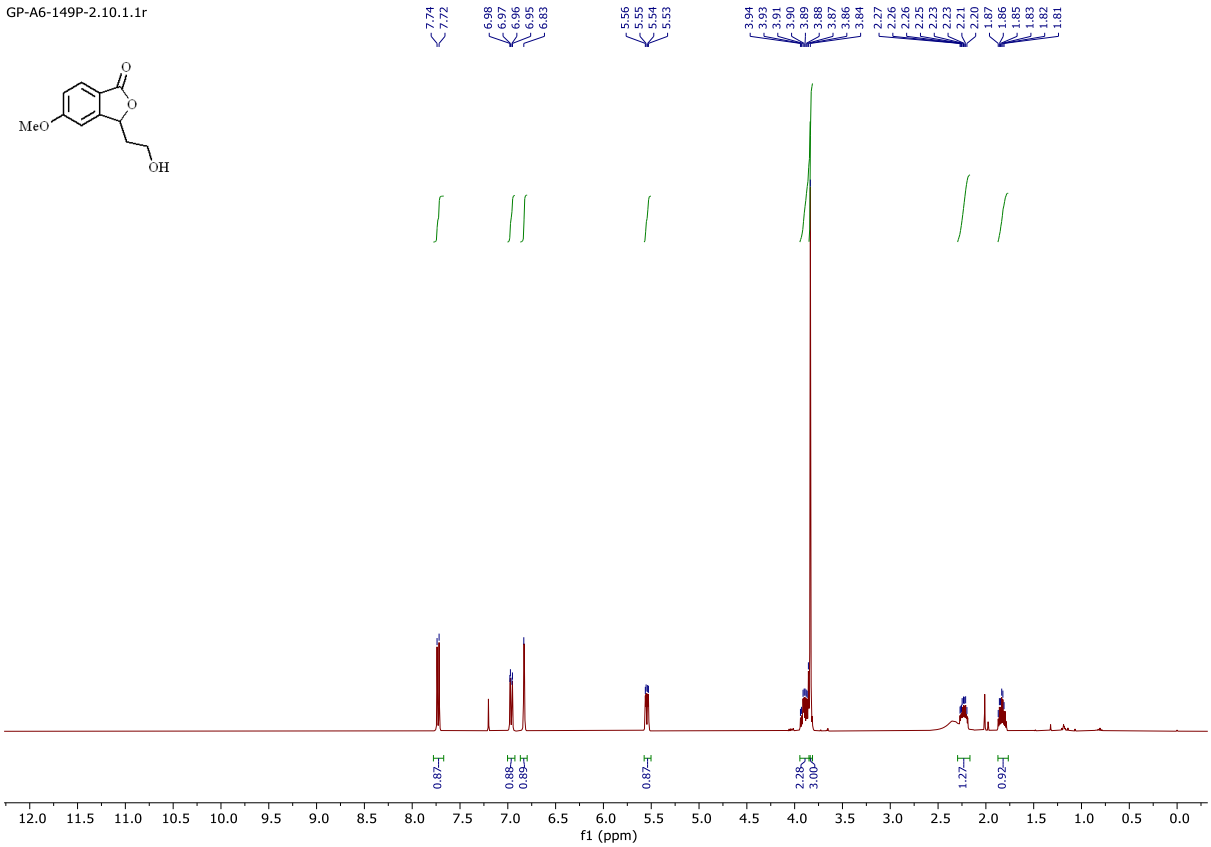
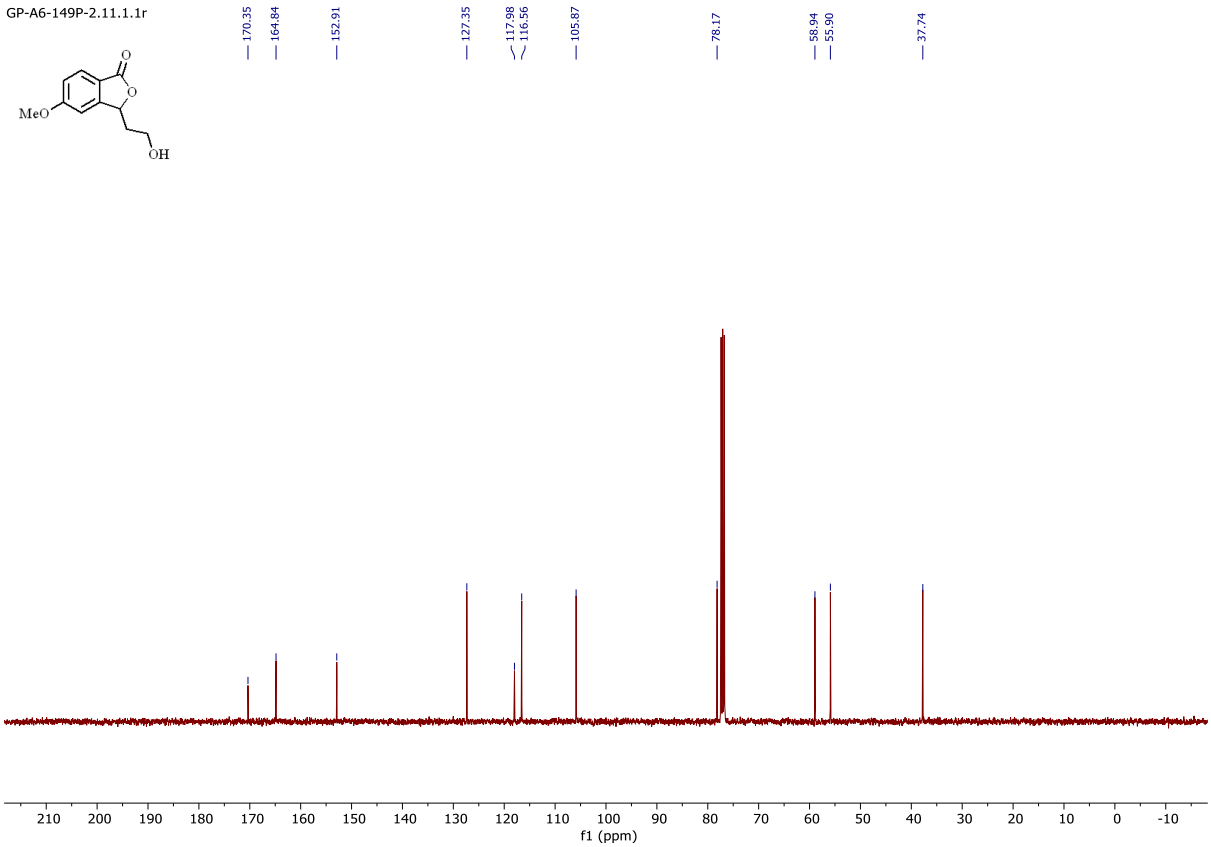
(12b) (^{1}H NMR 400 MHz, $CDCl_3$)



(12b) (^{13}C NMR 101 MHz, $CDCl_3$)



(12c) (^{1}H NMR 400 MHz, $CDCl_3$)



(12c) (^{13}C NMR 101 MHz, $CDCl_3$)