Supporting Information for

Palladium (II)/Lewis Acid Catalyzed Oxidative Olefination of 2-Benzamidopyridine 1-Oxide with Acrylates: Synthesis of Isoindolinones

Dharmik M. Patel,[a, b] Raj N. Patel,[a, b] Nileshkumar B. Rathod,[a, b] Sachinkumar D. Patel,[a, b] Dinesh G. Thakur,[a, b] Mahesh A. Sonawane,[a, b] Subhash Chandra Ghosh*,[a, b]

[a]Marine Natural Products and Bio-Polymers Division, Central Salt and Marine Chemicals Research Institute (CSIR), G. B. Marg, Bhavnagar-364002

[b]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India

E-mail: scghosh@csmcri.res.in; schandra1976@gmail.com

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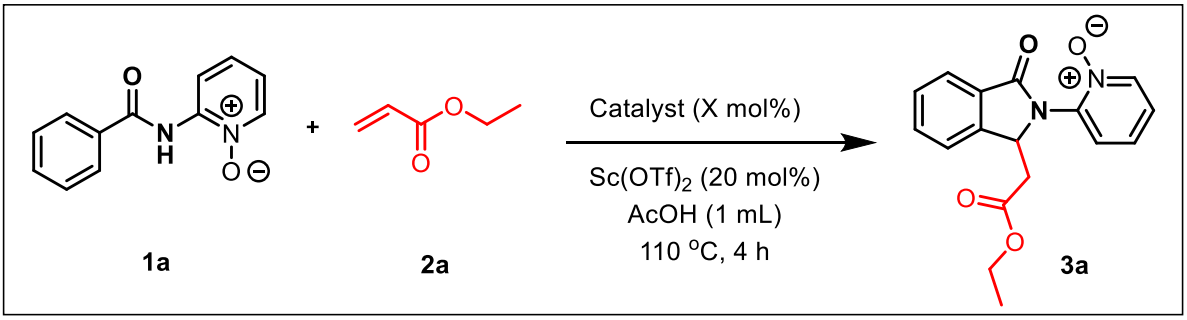
1. General information

All reactions were carried out in oven-dried glassware under standard reaction conditions and all reagents were purchased from Sigma-Aldirch, Spectrochem and TCI Chemical and used without further purification unless otherwise noted. All solvents were dried by the standard reported procedures and stored over activated molecular sieves. Reactions were monitored using thin-layer chromatography (TLC) on commercial silica gel plates. Visualization of the developed plates was performed under UV light (254 nm). Flash column chromatography was performed on silica gel (200-400 mesh). ^{1}H and ^{13}C NMR was recorded on a 600/151 MHz, 500/126 MHz, 400/100 MHz, or 200/50 MHz NMR spectrometer (as mentioned). Chemical shifts are reported in ppm referenced to an internal tetramethylsilane standard $CDCl_3$ (δ 7.26) & DMSO-D_6 (δ 2.50) for ^{1}H NMR. Chemical shifts of ^{13}C NMR are reported relative to $CDCl_3$ (δ 77.16) & DMSO-D_6 (δ 39.52). The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants, J, were reported in Hertz unit (Hz). High resolution mass spectra (HRMS) were obtained on an ESI-LC-MS/MS Spectrometer. X-ray structure data was recorded by Bruker D8 Quest instrument.

2. Optimization of reaction conditions:

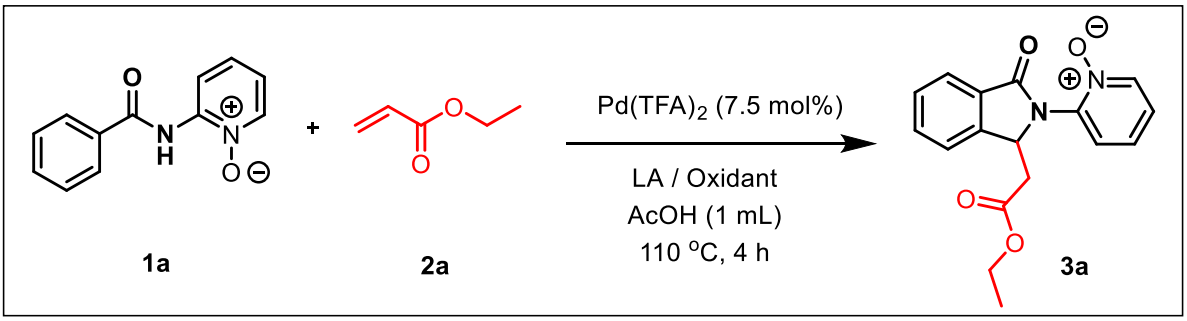
2.1 Table S1: Optimization of Catalyst:



Entry	Catalyst	Lewis acid (20 mol%)	Solvent (1 mL)	Time (h)	Yield (%)
1	$Pd(OAc)_2$(10 mol%)	$Sc(OTf)_3$	AcOH	4	38
2	$PdCl_2$(10 mol%)	$Sc(OTf)_3$	AcOH	4	51
3	$Pd(TFA)_2$(10 mol%)	$Sc(OTf)_3$	AcOH	4	66
4	**$Pd(TFA)_2$(7.5mol%)**	**$Sc(OTf)_3$**	**AcOH**	**4**	**66**
5	$Co(acac)_3$(10 mol%)	$Sc(OTf)_3$	AcOH	4	NR
6	$Cu(TFA)_2$(10 mol%)	$Sc(OTf)_3$	AcOH	4	NR

[a]Reaction conditions: **1a** (0.25 mmol), Catalyst (x mol%), **2a** (2 equiv.), $Sc(OTf)_3$ (20 mol %), AcOH(1 mL) at 110 °C in a Small glass Seal tube under air.

2.2 Table S2: Optimization of Lewis acid:

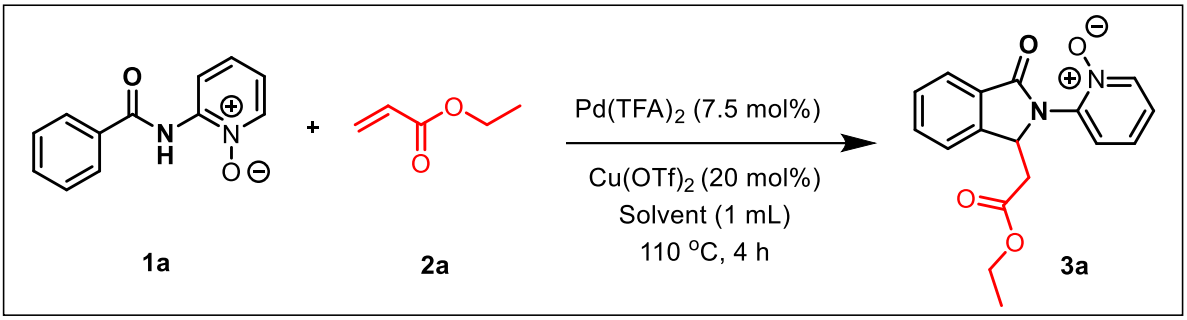


Entry	Catalyst (7.5 mol%)	Lewis acid/Oxidant	Solvent (1 mL)	Time (h)	Yield (%)
1	$Pd(TFA)_2$	AgTFA(1.5 eq)	AcOH	4	26
2	$Pd(TFA)_2$	$Sc(OTf)_3$ (20 mol%)	AcOH	4	66

3	**$Pd(TFA)_2$**	**$Cu(OTf)_2$(20 mol%)**	**AcOH**	**4**	**75**
4	$Pd(TFA)_2$	$Zn(OTf)_2$(20 mol%)	AcOH	4	50
5	$Pd(TFA)_2$	$Yb(OTf)_3$(20 mol%)	AcOH	4	36
6	$Pd(TFA)_2$	$ZnCl_2$(20 mol%)	AcOH	4	46
6	$Pd(TFA)_2$	-	AcOH	4	21

[a]Reaction conditions: 1a (0.25 mmol), $Pd(TFA)_2$ (7.5 mol%), 2a (2 equiv.), LA/Oxidant (X mol %), AcOH(1 mL) at 110 °C in a Small glass Seal tube under air..

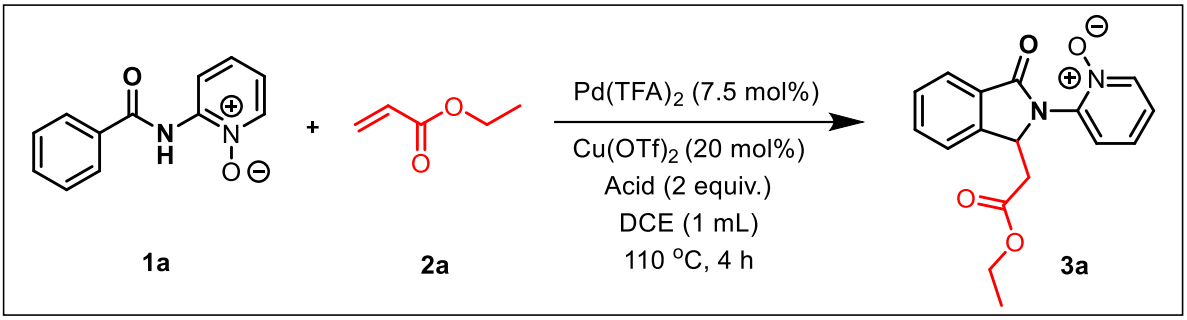
2.3 Table S3: Optimization of Solvent:



Entry	Catalyst (7.5 mol%)	Lewis acid (20 mol%)	Solvent (1 mL)	Time (h)	Yield (%)
1	$Pd(TFA)_2$	$Cu(OTf)_2$	TFE	4	NR
2	$Pd(TFA)_2$	$Cu(OTf)_2$	AcOH	4	75
3	**$Pd(TFA)_2$**	**$Cu(OTf)_2$**	**PivOH**	**4**	**64**
4	$Pd(TFA)_2$	$Cu(OTf)_2$	HFIP	4	Trace
5	$Pd(TFA)_2$	$Cu(OTf)_2$	DCE	4	Trace
6	$Pd(TFA)_2$	$Cu(OTf)_2$	TFA	4	20
7	**$Pd(TFA)_2$**	**$Cu(OTf)_2$**	**AcOH**	**2**	**76**

Reaction conditions: 1a (0.25 mmol), 2a (2 equiv.), $Pd(TFA)_2$ (7.5 mol%), $Cu(OTf)_2$ (20 mol%), Solvent (1 mL) at 110 °C in a Small glass Seal tube under air.

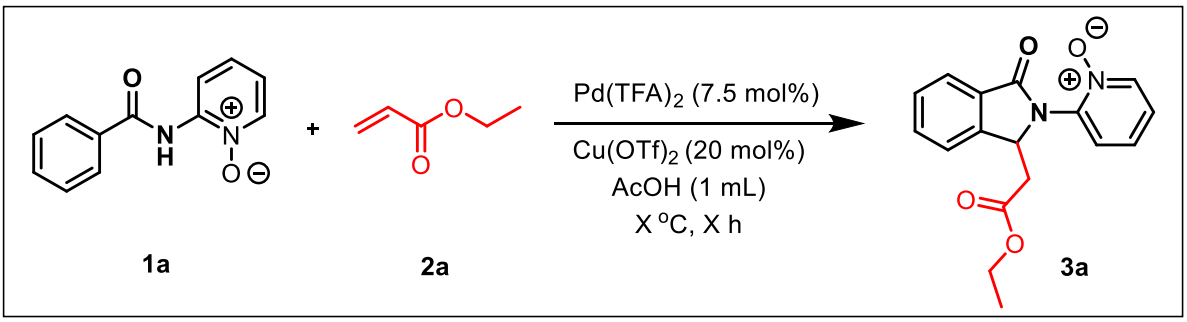
2.4 Table S4: Optimization of Acid:



Entry	Catalyst (7.5 mol%)	Lewis acid (20 mol%)	Acid (2 equiv.)	Time (h)	Yield (%)
1	$Pd(TFA)_2$	$Cu(OTf)_2$	2,4,6 trimethyl benzoic acid	4	31
2	$Pd(TFA)_2$	$Cu(OTf)_2$	Trifluoroacetic acid	4	22
3	**$Pd(TFA)_2$**	**$Cu(OTf)_2$**	**AcOH**	**4**	**64**
4	$Pd(TFA)_2$	$Cu(OTf)_2$	Adamantanecarboxylic acid	4	61
5	**$Pd(TFA)_2$**	**$Cu(OTf)_2$**	**PivOH**	**4**	**61**
6	$Pd(TFA)_2$	$Cu(OTf)_2$	Trichloroacetic acid	4	Trace

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (2 equiv.), $Pd(TFA)_2$ (7.5 mol%), $Cu(OTf)_2$ (20 mol %), Acid (2 equiv.), DCE (1 mL) at 110 °C in a Small glass Seal tube under air.

2.5 Table S5: Optimization of Time and Temperature

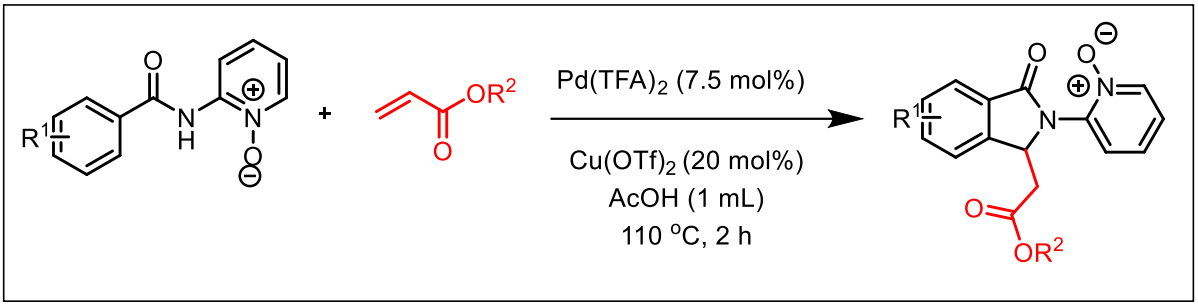


Entry	Catalyst (7.5 mol%)	Lewis acid (20 mol%)	Temp (°C)	Time (h)	Yield (%)
1	$Pd(TFA)_2$	$Cu(OTf)_2$	100	4	62
2	$Pd(TFA)_2$	$Cu(OTf)_2$	80	4	32
3	$Pd(TFA)_2$	$Cu(OTf)_2$	RT	12	NR

4	**$Pd(TFA)_2$**	**$Cu(OTf)_2$**	**110**	**2**	**76**
5	$Pd(TFA)_2$	$Cu(OTf)_2$	120	2	71
6	$Pd(TFA)_2$	$Cu(OTf)_2$	110	12	69

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (2 equiv.), $Pd(TFA)_2$ (7.5 mol%), $Cu(OTf)_2$ (20 mol %), AcOH(1 mL) at T °C in a Small glass tube under air.

3. Experimental procedure for annulation reaction:

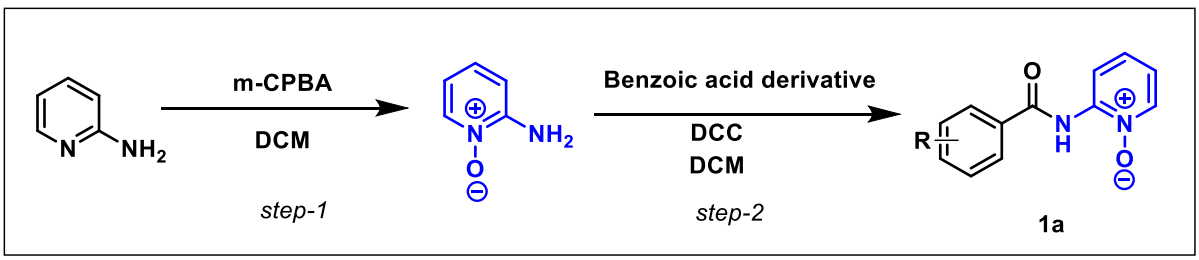


General procedure:

An oven-dried small glass reaction tube equipped with a magnetic stir bar was charged with 2-benzamidopyridine 1-oxide **1a** (53 mg, 0.25 mmol), $Pd(TFA)_2$ (6 mg, 7.5 mol%), and $Cu(OTf)_2$ (18 mg, 20 mol%), acetic acid (1 mL) was added to it via syringe. Then ethyl acrylate **2a** (53 µl, 0.50 mmol) was added to the reaction tube and sealed with a screw cap, and placed on a heating block at 110 °C for 2 h. After completion of the reaction, as monitored by TLC, the reaction mixture was transferred to a vessel, quenched with aqueous $NaHCO_3$ solution, and extracted with ethyl acetate (2x 25 ml). The ethyl acetate layer was washed with water and brine solution and dried over Na_2SO_4, the solvent was removed under reduced pressure and residue was purified by flash chromatography DCM: MeOH (3: 1) to isolate 2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (59 mg, **3a**) in 76% yield.

4. Synthesis of Starting Materials:

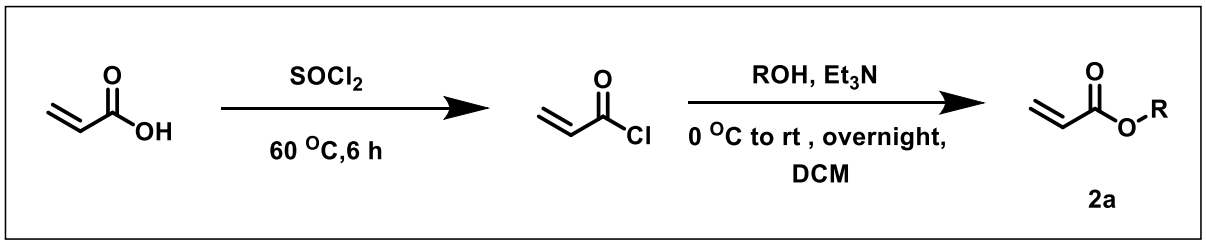
4.1 Procedures for the Synthesis of Benzamide:



Step-1*:* 2-amino pyridine *N*-oxide was prepared by a reported procedure[1]. The 2-aminopyridine (30 mmol) and Acetone (0.1 M) were dissolved in anhydrous CH_2Cl_2 (40 mL) in a 100 mL round-bottom flask, followed by the addition of m-CPBA (1.1 equiv) in two portions at 0 ^oC. The mixture was allowed to be gradually warmed to room temperature and stirred overnight. After completion, the solvent was removed in vacuo and the resulting mixture was purified by column chromatography to afford the product as a yellow solid.

Step-2*:* The benzoic acid derivative (6 mmol), 2-aminopyridine 1-oxide (6.6 mmol,1.1 equiv) and DMAP (0.6 mmol, 0.1 equiv.) were dissolved in anhydrous CH_2Cl_2 (30 mL) in a 100 mL round-bottom flask, followed by dropwise addition of DCC (1.2 equiv) in CH_2Cl_2 (30 mL) was added dropwise manner to the solution at 0 ^oC under an inert atmosphere. The mixture was allowed to be gradually warmed to room temperature and stirred overnight. After completion, the reaction was quenched with water (20 mL). The resulting mixture was extracted with DCM (3 × 20 mL) and the combined organic solvent was dried by Na_2SO_4 and solvent was removed in vacuo and the resulting mixture was purified by column chromatography to afford the product(**1a**) as a white solid (90%). All the Benzamide substrates were prepared following the above procedure.

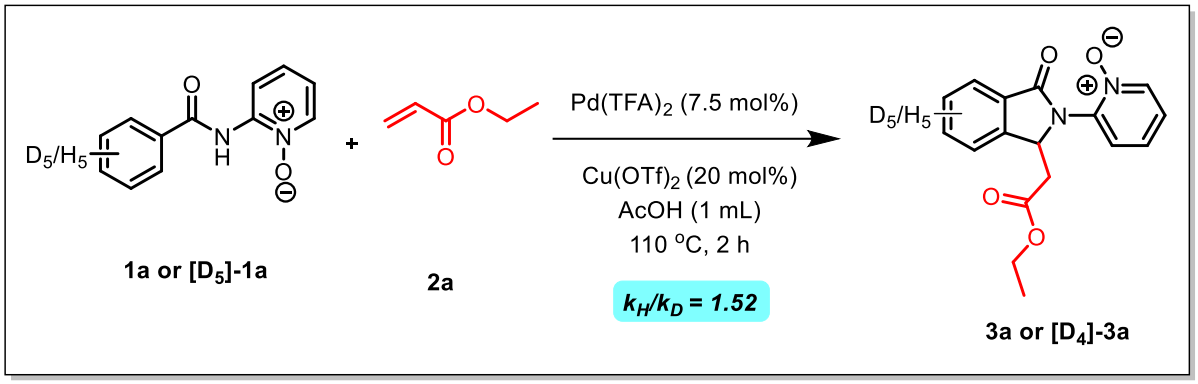
4.2 Procedures for the Synthesis of Acrylate.



Acrylate Derivatives was prepared by a reported procedure[2] with some modification. In a round bottom flask, acrylic acid (1 equiv, 3 mmol) was taken and cooled at 0 ^oC, then $SOCl_2$ (1.2 equiv, 3.6 mmol) was added dropwise and the mixture was stirred at 60°C for 6 hours. After that DCM (3 mL) was added, followed by Et_3N (1.5 equiv, 4.5 mmol) and Derivative of alcohol or phenol (1 equiv, 3 mmol) at 0 ^oC. The mixture was gradually warmed to room temperature and stirred overnight. After completion, the reaction was quenched with water (10 mL). The resulting mixture was extracted with DCM (3 × 15 mL) and the combined organic solvent was dried by Na_2SO_4 and solvent was removed in vacuo and the resulting mixture was purified by column chromatography to afford the product(**2a**) as a colorless liquid (88 %). All Acrylate substrates were prepared following the above procedure.

5. Control experiments study for a mechanism

5.1 Kinetic isotope (KIE) effect:



Two separate oven-dried small glass seal tubes were charged with a magnetic stir bar, **1a** or [D_5]-**1a** (1.0 equiv., 0.25 mmol), $Pd(TFA)_2$ (7.5 mol%), $Cu(OTf)_2$ (20 mol%), were dissolved in AcOH (1 mL). Then Ethyl acrylate **2a** (0.50 mmol) was added to the small glass seal tube and stirred at 110 °C under air. An aliquot of 0.1 mL was periodically withdrawn using a syringe with a long needle, then diluted with ethyl acetate and quenched with $NaHCO_3$ solution. The separated organic layer was passed through a small bed of Na_2SO_4, evaporated, diluted with MeOH, and then injected for HPLC analysis to determine the conversion and yield of the desired product.

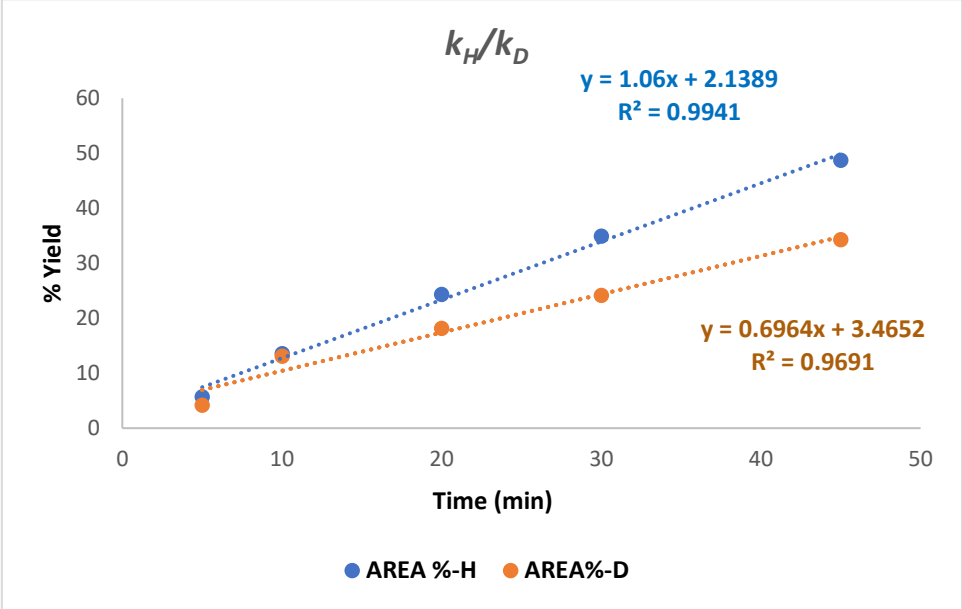
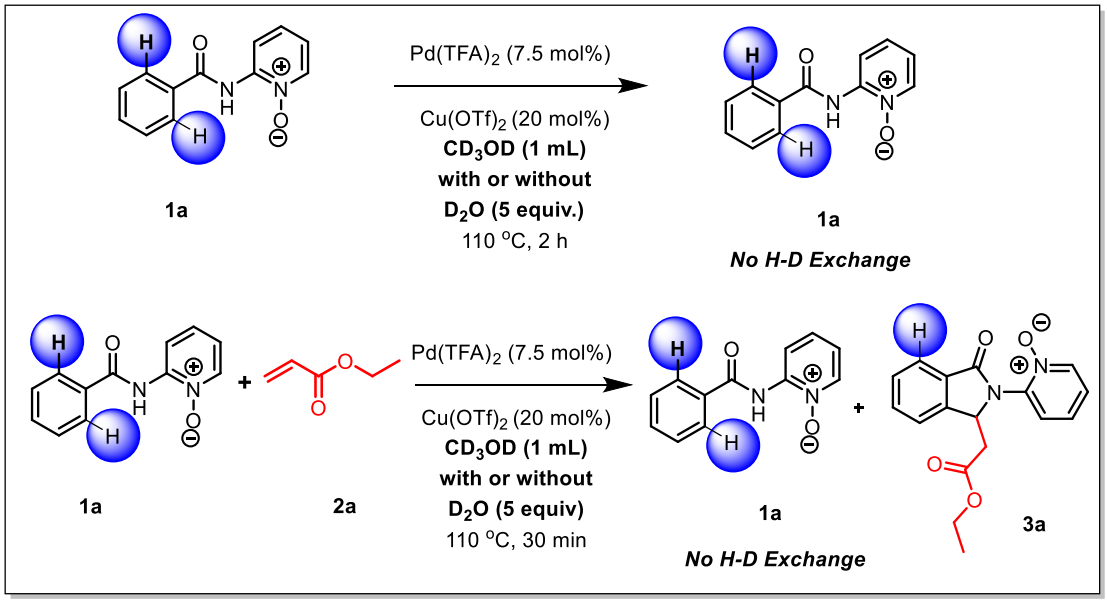


Figure S1 KIE studies

5.2 Deuterium exchange experiment:

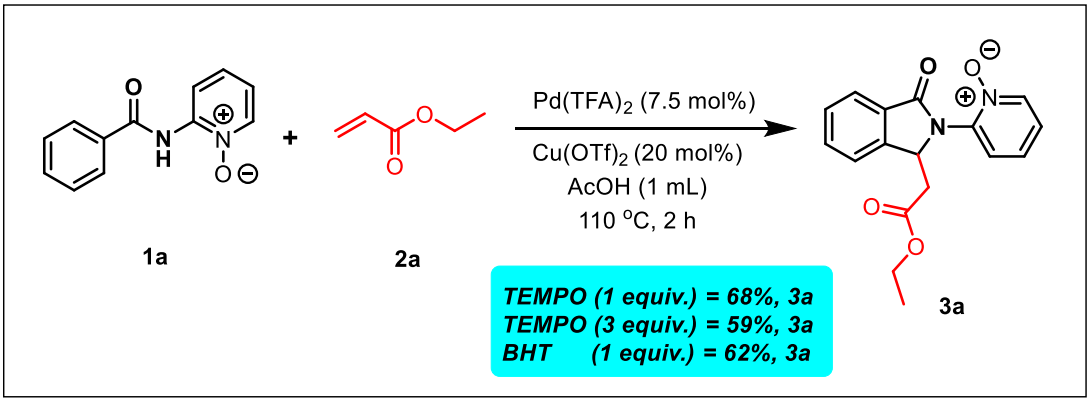
We conducted a deuterium exchange experiment to determine whether C-H activation and functionalization are reversible or irreversible processes. We used D_2O (5 equiv.) as the deuterium source, while also testing without D_2O and utilizing the deuterated solvent D_4-AcOH. The experiment was carried out under standard conditions, both in the absence of a

coupling partner and in its presence. However, we observed no deuterium incorporation in any of the cases.



5.3 Control experiment in the presence of radical inhibitor:

An oven dry the small glass seal tube equipped with a magnetic stir bar was charged with 2-benzamidopyridine 1-oxide **1a** (53 mg, 0.25 mmol), $Pd(TFA)_2$ (6 mg, 7.5 mol%), $Cu(OTf)_2$ (18 mg, 20 mol%) and TEMPO(2,2,6,6-tetramethylpiperidin-1-yl)oxyl)(1 equiv, 39 mg or 3 equiv,117 mg) or BHT (2,6-di-tert-butyl-4-methylpheno)(3 equiv,165 mg), were dissolved in AcOH (1 mL). Then Ethyl acrylate **2a** (53 µl, 0.50 mmol) was added to the small glass seal tube and stirred at 110 °C for 2 h under air. After completion of the reaction, as monitored by TLC, the reaction mixture was quenched with aqueous $NaHCO_3$ solution, 25 mL ethyl acetate, and 15 mL water were added over it, the organic phase was separated and water phase was re-extracted with ethyl acetate (3× 10 mL). The combined organic phase was washed with brine, dried over Na_2SO_4, and the solvent was removed under reduced pressure and residue was purified by flash chromatography CH_2Cl_2/acetone (2:1) to isolate 2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide(**3a**) 68 %, 53 mg (1 equiv. TEMPO), 59 %, 46 mg (3 equiv. TEMPO) and 52 %, 40 mg (3 equiv. BHT)



5.4 UV-vis spectra of the catalyst characterizations

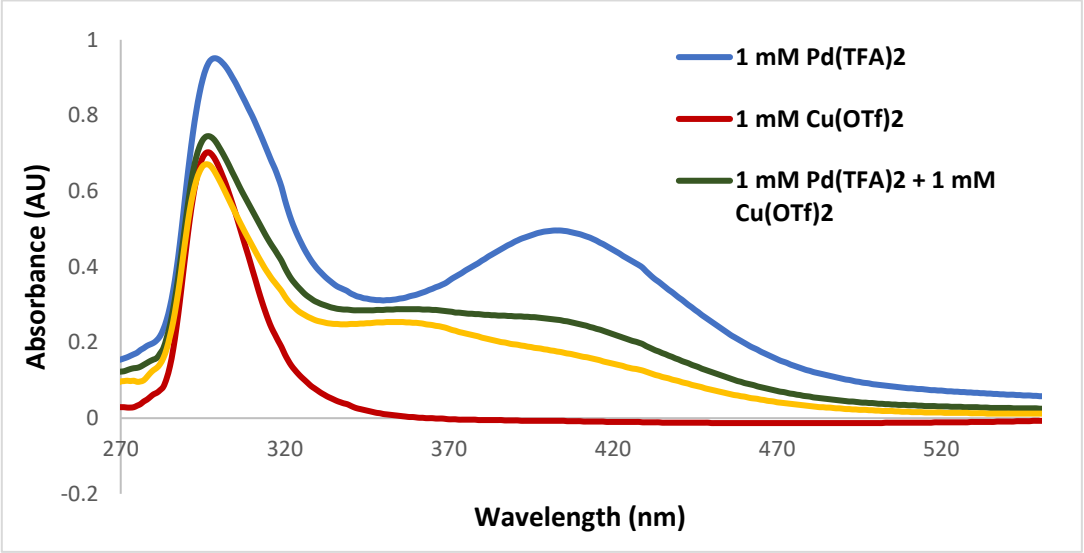


Figure S2 UV-vis spectra of the Pd(II)/Cu(II) catalyst in AcOH. Conditions: solvent, AcOH, 1 mM Pd(II), 1-2 mM Sc(III), room temperature.

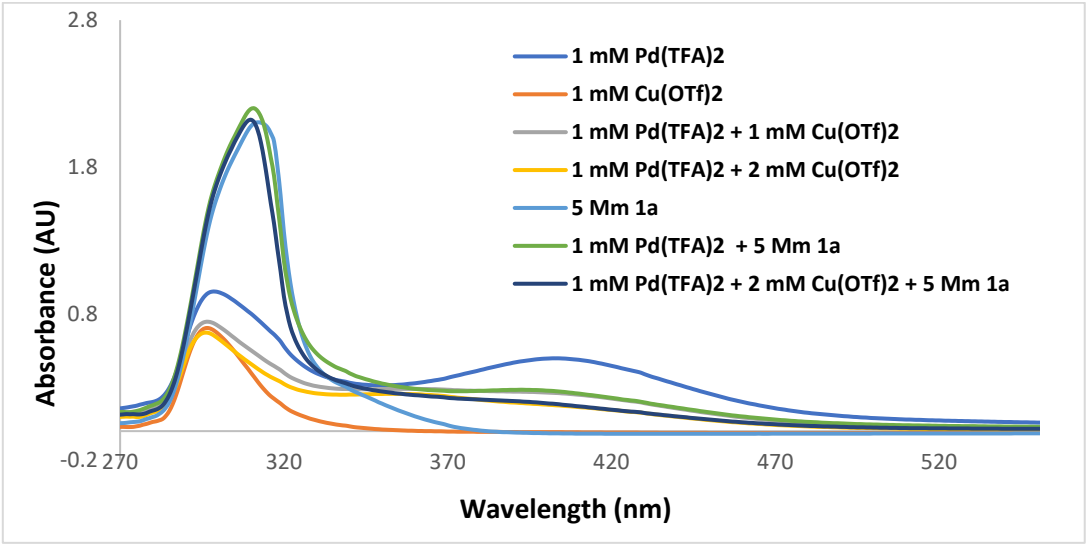
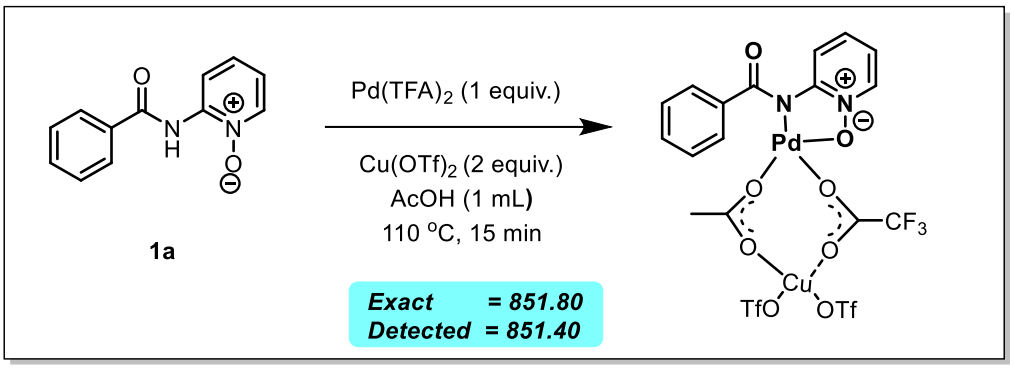


Figure S3 UV-vis spectra of the Pd(II)/Cu(II) catalyst in AcOH. Conditions: solvent, AcOH, 1 mM Pd(II), 1-2 mM Cu(II), 5 mM 1a, room temperature.

5.5 Detection of plausible intermediates via ESI-MS



An oven dry the small glass seal tube equipped with a magnetic stir bar was charged with 2-benzamidopyridine 1-oxide **1a** (53 mg, 0.25 mmol), $Pd(TFA)_2$ (83 mg, 1 equiv.), $Cu(OTf)_2$ (90 mg, 2 equiv.) were dissolved in AcOH (1 mL). The vessel was heated in oil bath at 110 °C. After 15 min little aliquot was taken out and the HRMS was recorded which shows the formation reaction intermediates.

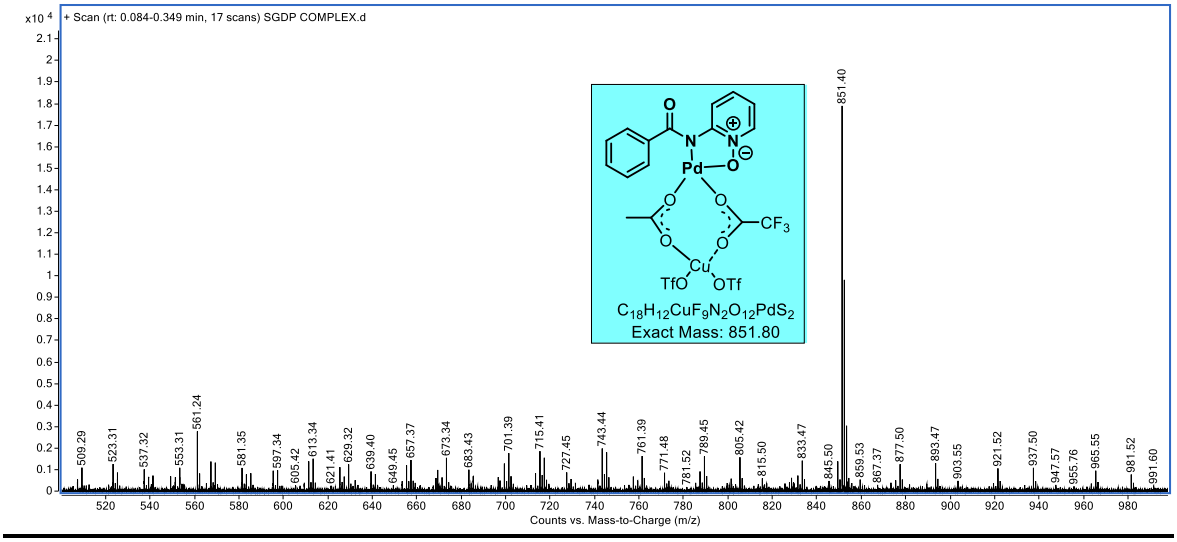
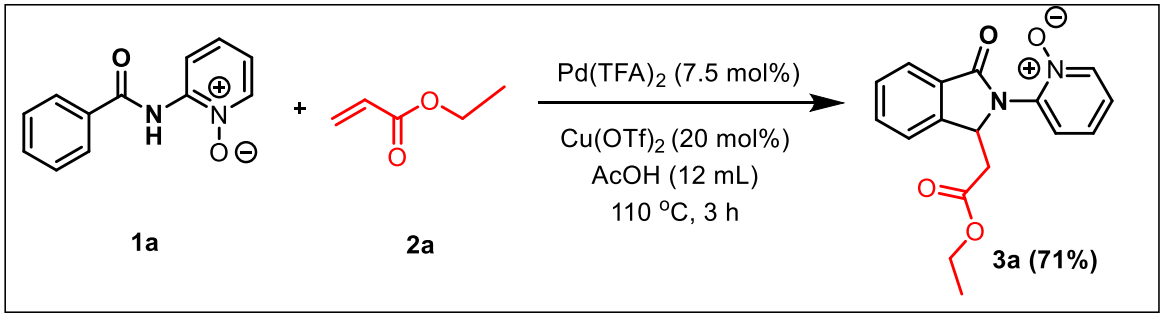


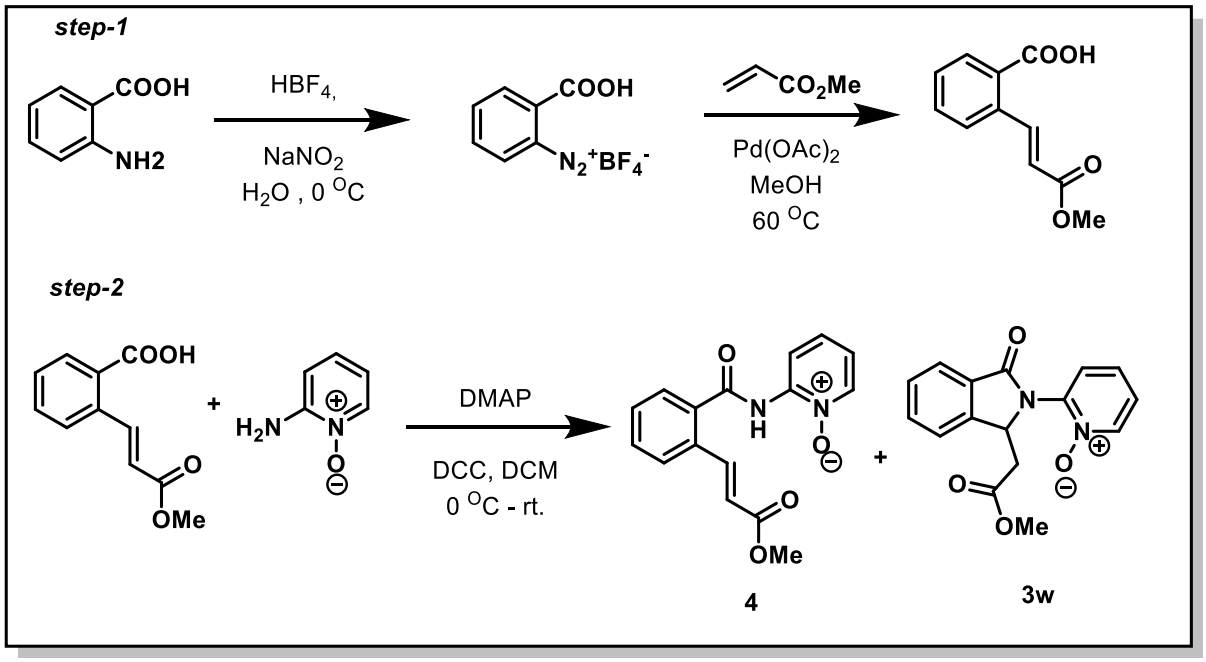
Figure S3 Identification of organometallic complex by ESI-MS

6. Gram scale synthesis



Procedure: An oven-dry 50 mL RBF equipped with a magnetic stir bar was charged with 2-benzamidopyridine 1-oxide **1a** (1.07 gm, 5 mmol), $Pd(TFA)_2$ (124 mg, 7.5 mol%), $Cu(OTf)_2$ (361 mg, 20 mol%), were dissolved in AcOH (12 mL). Then Ethyl acrylate **2a** (1.06 mL, 0.50 mmol) was added to RBF and R at reflux at 110 ^oC for 3 h. After completion of the reaction, as monitored by TLC, the reaction mixture was quenched with aqueous $NaHCO_3$ solution, 250 mL ethyl acetate, and 150 mL water were added over it, the organic phase was separated and water phase was re-extracted with ethyl acetate (3× 150 mL). The combined organic phase was washed with brine, dried over Na_2SO_4, and the solvent was removed under reduced pressure and residue was purified by flash chromatography CH_2Cl_2/acetone (3:1)) to isolate 2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (1.11gm, **3a**) in 71% yield.

7. Synthesized methods for intermediate compounds



Step-1

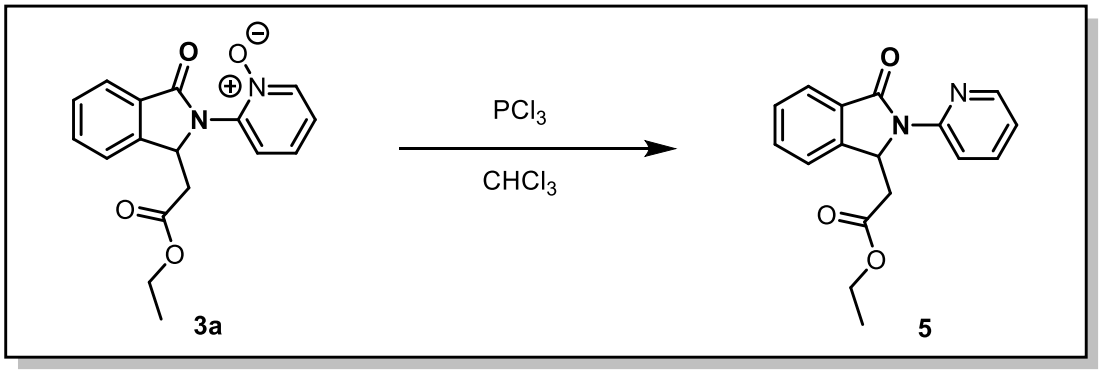
An oven-dry 50 mL RBF equipped with a magnetic stir bar was charged with Anthranilic acid (1.0 g, 7.30 mmol) in 42% HBF_4 (3.8 mL, 18.25 mmol) at 0 ^oC, followed by dropwise addition of a solution of $NaNO_2$ (1.0 g, 14.6 mmol) in water (5 mL). The reaction mixture was stirred for 1 h at 0 ^oC. Subsequently, methanol (1 mL), methyl acrylate (1.0 mL, 10.95 mmol), and Pd(OAc)2 (33 mg, 0.15 mmol) were added to the mixture, which was then heated in an oil bath at 60 ^oC 2 h. The mixture was then extracted with diethyl ether, and the extract was washed with saturated aqueous $NaHCO_3$, dried by Na_2SO_4 and solvent was removed under reduced pressure. The resultant residue was 2-(3-methoxy-3-oxoprop-1-en-1-yl)benzoic acid (1.08 gm, 72%) obtained as a white solid.

Step-2

The resultant residue was 2-(3-methoxy-3-oxoprop-1-en-1-yl)benzoic acid (5 mmol), 2-aminopyridine 1-oxide (5.5 mmol,1.1 equiv.) and DMAP (0.5 mmol, 0.1 equiv.) were dissolved in anhydrous CH_2Cl_2 (30 mL) in a 100 mL round-bottom flask, followed by dropwise addition of DCC (6 mmol, 1.2 equiv.) in CH_2Cl_2 (30 mL) was added dropwise manner to the solution at 0 ^oC under an inert atmosphere. The mixture was allowed to be gradually warmed to room temperature and stirred overnight. After completion, the reaction was quenched with water (20 mL). The resulting mixture was extracted with DCM (3 × 30 mL) and the combined organic solvent was dried by Na_2SO_4 and solvent was removed in vacuo and the resulting mixture was purified by column chromatography to afford the product **4** as a white solid (66%) and **3w** as a Yellow Solid (21%)

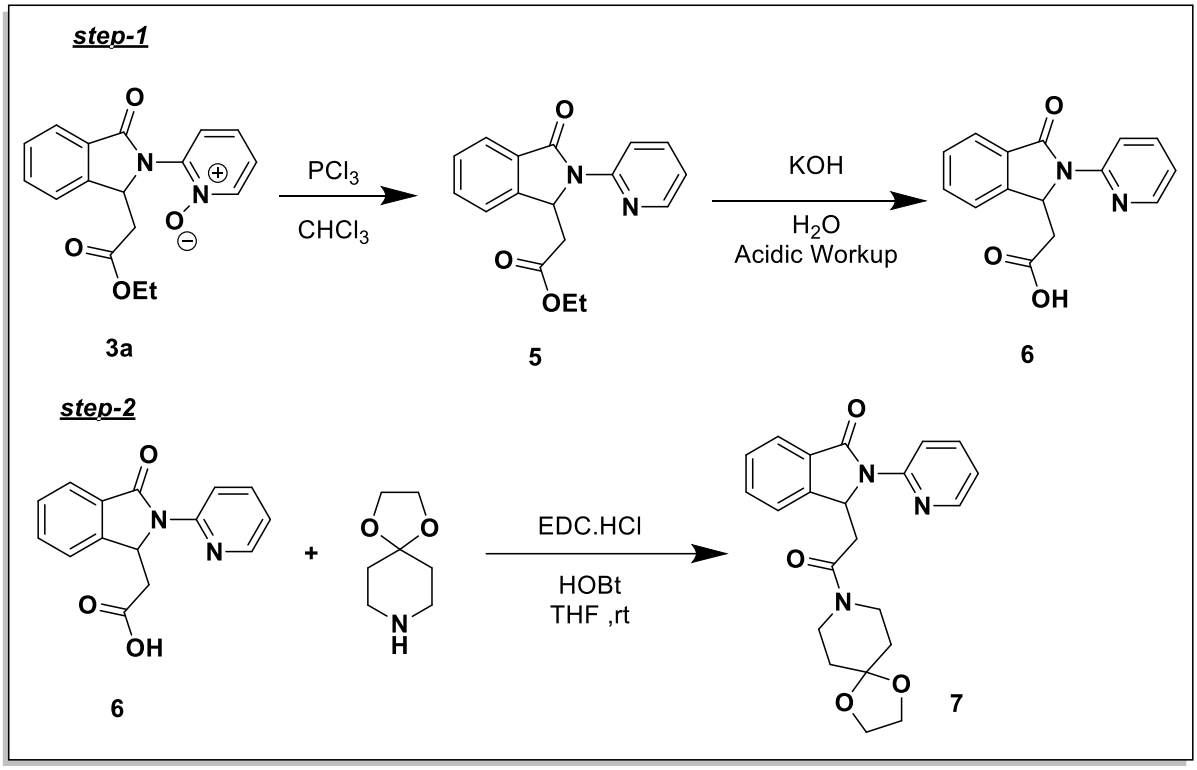
8. Post-synthetic modification

8.1 Deoxygenation of product:



A 100 mL oven-dried reaction flask was equipped with a magnetic stir bar. PCl_3 (3 mmol, in 20 mL of $CHCl_3$) was added dropwise to a solution of **3a** (1 mmol) in $CHCl_3$ (20 mL). The solution was stirred at 0 °C for 1 hour and monitored by TLC. The residue was treated with 5% NaOH until the pH reached 7. Then, the resulting mixture was extracted with 25 mL of ethyl acetate and dried over Na_2SO_4. The deoxygenation compound **5** was purified by flash column chromatography HEX:EA (3:2) to isolate **5** as a yellowish-white solid in 90% yield

8.2 Synthesis of bioactive molecules



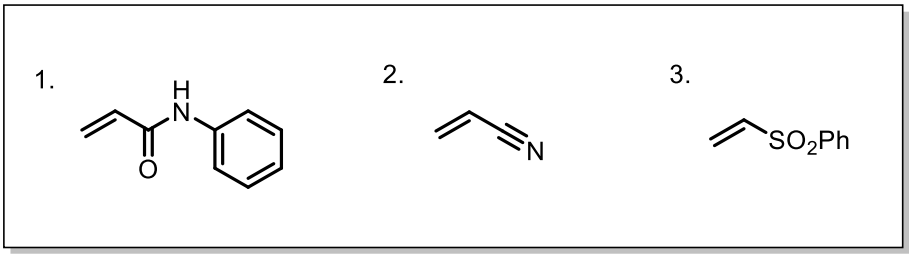
Step-1

A 100 mL oven-dried reaction flask was equipped with a magnetic stir bar. PCl_3 (3 mmol, in 20 mL of $CHCl_3$) was added dropwise to a solution of **3a** (1 mmol) in $CHCl_3$ (20 mL). The solution was stirred at 0 °C for 1 hour and monitored by TLC. The residue was treated with 5% NaOH until the pH reached 7, then it was extracted with 25 mL of ethyl acetate, dried over Na_2SO_4, and purified by flash column chromatography using a 3:2 mixture of hexane and ethyl acetate to obtain compound 5. The resulting product (**5**) was treated with KOH (1.0 equiv.) and heated in an oil bath at 100 °C for 3 hours. The reaction mixture was diluted with water, maintaining the pH between 2 and 3 using concentrated HCl. Following this step, the mixture was diluted with 30 mL of $CHCl_3$, and the layers were separated. The organic layer was washed with a saturated aqueous brine solution and dried over Na_2SO_4. Finally, the organic layer was concentrated under reduced pressure to obtain compound (**6**) with 85% yield

Step-2

The crude material (**6**) was treated with HOBt (1.0 equiv.), EDC-HCl (1.0 equiv.), and 1,4-dioxa-8-azaspiro[4.5]decane (1.0 equiv.) in THF at room temperature for 10 hours. The progress of the reaction was monitored using TLC analysis. Once the starting material was completely consumed, it was extracted with 25 mL DCM, The organic layer was washed with an aqueous saturated brine solution and then dried over Na_2SO_4 and concentrated under reduced pressure. The crude material obtained was purified by column chromatography on silica gel, using a mixture of hexane and ethyl acetate in a 2:3 ratio to get 76 % yield of the final product, 3-(2-oxo-2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)ethyl)-2-(pyridin-2-yl)isoindolin-1-one (**7**).

9. Unreactive Michael acceptors.



10. X-Ray Crystallographic Data.

Procedure for Crystal Growth

In a glass vial (5 mL) 40-50 mg of pure compound was taken and dissolved with 1-2 mL solvent (Ethyl acetate and MeOH). On the mouth of the glass vial, a loose screw cap was placed on top of the vial and it was kept for slow evaporation at room temperature. After a couple of days or so, small crystals were begun to form. X-ray structure data was recorded by Bruker D8 Quest instrument.

10.1 Table-S6: Crystal Data and Refinement Parameters for 3p

Identification code	**3p**
Empirical formula	$C_{17}H_{14}BrFN_2O_4$
Formula weight	409.21
Temperature/K	298
Crystal system	triclinic
Space group	P-1
a/Å	8.9400(5)
b/Å	9.2953(5)
c/Å	11.9582(7)
α/°	84.896(2)
β/°	72.675(2)
γ/°	61.415(2)
Volume/Å3	831.31(8)
Z	2
ρcalcg/cm3	1.635
μ/mm-1	2.508

F(000)	412.0
Crystal size/mm3	0.28 × 0.25 × 0.06
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5 to 61.316
Index ranges	-12 ≤ h ≤ 12, -13 ≤ k ≤ 13, -17 ≤ l ≤ 17
Reflections collected	58517
Independent reflections	5132 [Rint = 0.0622, Rsigma = 0.0324]
Data/restraints/parameters	5132/0/227
Goodness-of-fit on F2	1.040
Final R indexes [I>=2σ (I)]	R1 = 0.0414, wR2 = 0.1016
Final R indexes [all data]	R1 = 0.0657, wR2 = 0.1184
Largest diff. peak/hole / e Å-3	0.76/-0.62
CCDC	2292973

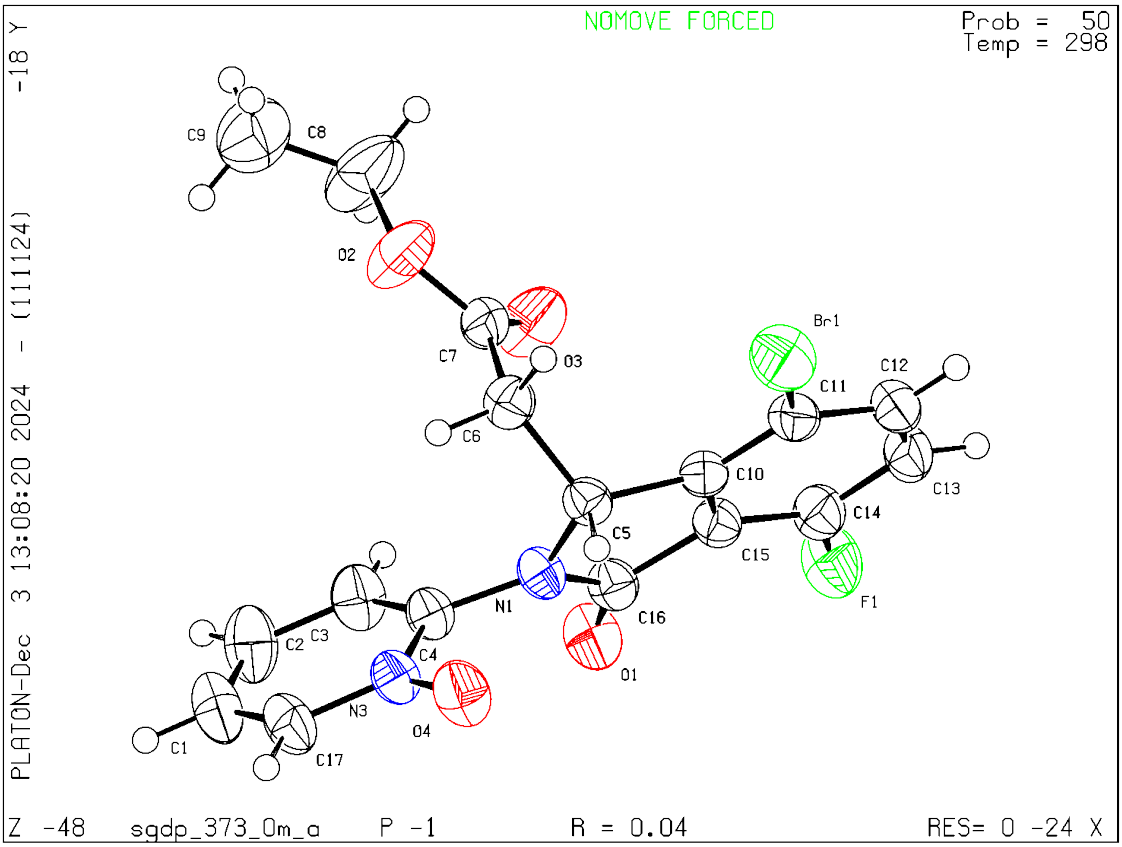


Fig. **S4** The thermal ellipsoid plot of the organic compound **3p** with atom numbering scheme (50% probability for the thermal ellipsoids) Crystal growth from solvent ethyl acetate.

10.2 Table-S7: Crystal Data and Refinement Parameters for 3w

Identification code	**3w**
Empirical formula	$C_{16}H_{14}N_2O_4$
Formula weight	298.29
Temperature/K	298
Crystal system	monoclinic
Space group	P21/n
a/Å	7.3356(4)
b/Å	12.1862(6)
c/Å	16.2134(8)
α/°	90
β/°	94.601(2)
γ/°	90
Volume/Å3	1444.70(13)
Z	4
ρcalcg/cm3	1.371
μ/mm-1	0.100
F(000)	624.0
Crystal size/mm3	0.48 × 0.28 × 0.08
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.186 to 61.146
Index ranges	-10 ≤ h ≤ 10, -17 ≤ k ≤ 17, -23 ≤ l ≤ 23
Reflections collected	98968
Independent reflections	4433 [Rint = 0.0768, Rsigma = 0.0293]
Data/restraints/parameters	4433/0/200
Goodness-of-fit on F2	1.153
Final R indexes [I>=2σ (I)]	R1 = 0.0540, wR2 = 0.1501
Final R indexes [all data]	R1 = 0.0664, wR2 = 0.1694
Largest diff. peak/hole / e Å-3	0.49/-0.35
CCDC	2292970

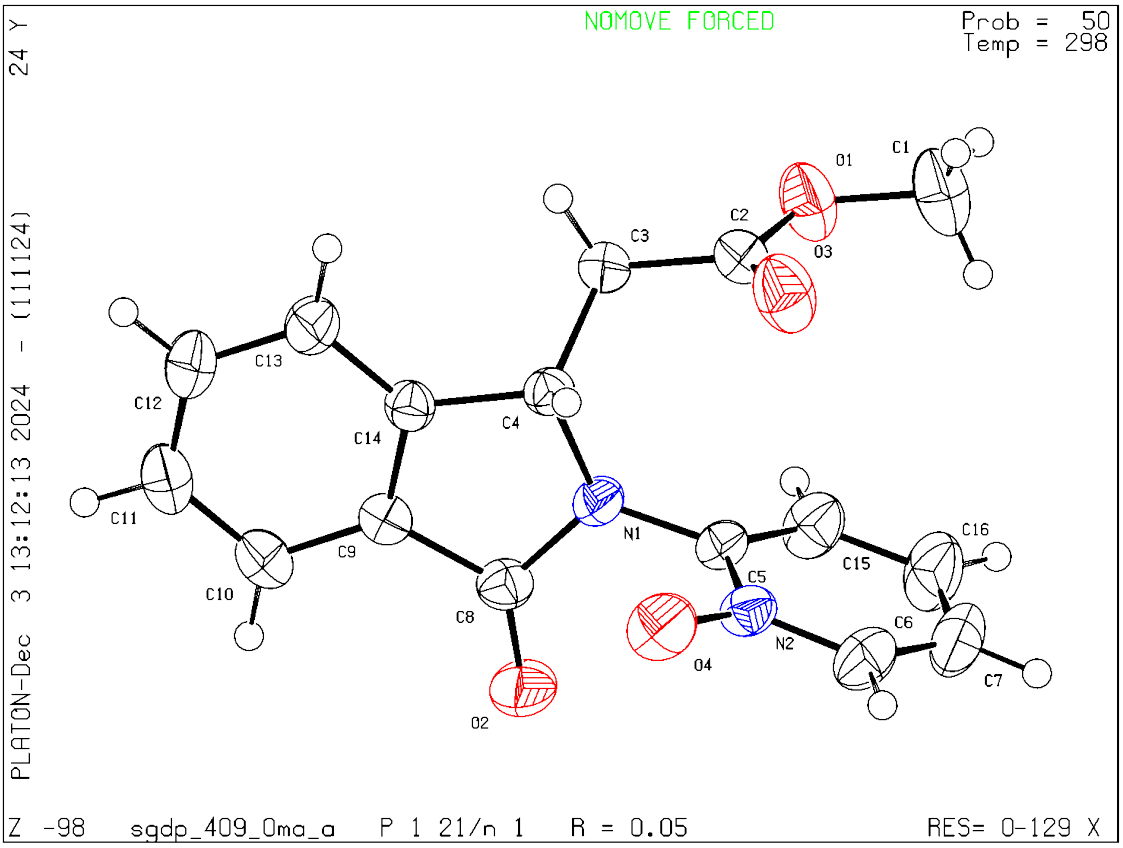


Fig. **S5** The thermal ellipsoid plot of the organic compound **3w** with atom numbering scheme (50% probability for the thermal ellipsoids) Crystal growth from solvent ethyl acetate.

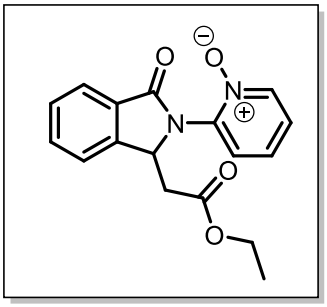
11. References.

1. R. N. Patel, D. M. Patel, N. B. Rathod, D. G. Thakur, S. D. Patel, S. Tothadi and S. C. Ghosh, Cobalt-Catalyzed, 2-Aminopyridine-N-Oxide-Directed C(sp^2)–H Bond Functionalization with Maleimides: Facile Access to Isoindolone Spirosuccinimides, *Eur J Org Chem*, 2023, **26**, e202300669. https://doi.org/10.1002/ejoc.202300669

2. J. Zhang, S. Zhang and H. Zou, Acid- and Base-Switched Palladium-Catalyzed γ-C(sp^3)–H Alkylation and Alkenylation of Neopentylamine, *Org. Lett.*, 2021, **23**, 3466–3471. https://doi.org/10.1021/acs.orglett.1c00903

12. Spectroscopic Data of Synthesized Compounds

12.1. Spectral characterization data



2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3a)

Physical appearance: Yellow semi-solid.

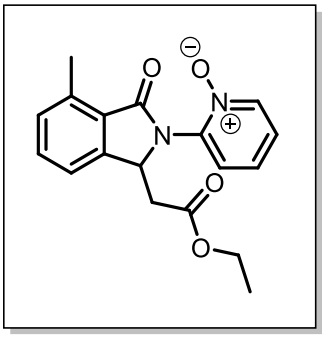
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 76 % (59 mg)

^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.31 (dd, *J* = 6.6, 1.5 Hz, 1H), 7.92 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.71 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.63 (td, *J* = 7.5, 1.1 Hz, 1H), 7.54 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.50 (t, *J* = 7.1 Hz, 1H), 7.38 (td, *J* = 7.8, 1.4 Hz, 1H), 7.25 – 7.21 (m, 1H), 6.48 (t, *J* = 5.3 Hz, 1H), 3.94 – 3.83 (m, 2H), 2.83 (dd, *J* = 16.0, 4.8 Hz, 1H), 2.64 (dd, *J* = 16.0, 5.7 Hz, 1H), 1.00 (t, J = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-D) δ 169.2, 168.0, 144.8, 142.5, 140.5, 133.2, 130.7, 128.7, 126.7, 126.5, 124.6, 123.9, 122.9, 60.8, 56.6, 37.2, 13.9

HRMS: calcd. for $C_{17}H_{16}N_2O_4H$: 313.1188, found: 313.1190.



2-(1-(2-ethoxy-2-oxoethyl)-4-methyl-3-oxoisoindolin-2-yl)pyridine 1-oxide (3b)

Physical appearance: Pale Yellow liquid

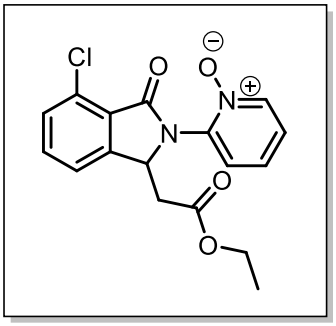
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 70 % (57 mg)

^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.35 (d, *J* = 6.6 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.28 – 7.19 (m, 2H), 6.35 (s, 1H), 3.87 (dq, *J* = 13.8, 7.1 Hz, 2H), 2.79 (dd, *J* = 16.0, 4.6 Hz, 1H), 2.69 (s, 3H), 2.63 (dd, *J* = 16.0, 5.2 Hz, 1H), 0.99 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-D) δ 169.3, 168.7, 145.4, 142.7, 140.6, 138.8, 132.7, 130.6, 127.7, 127.1, 126.8, 123.8, 120.2, 60.7, 55.9, 37.4, 17.6, 13.9.

HRMS: calcd. for $C_{18}H_{18}N_2O_4Na$ $[M+Na]^+$: 349.1164, found: 349.1161.



2-(4-chloro-1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3c)

Physical appearance: Pale semi-solid.

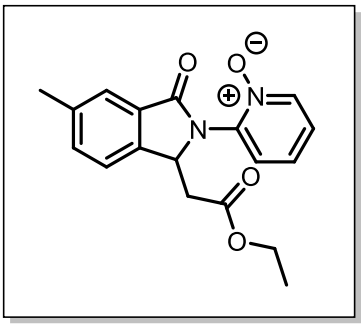
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 61 % (53 mg)

^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.28 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 1H), 7.45 (dd, *J* = 7.6, 3.8 Hz, 2H), 7.34 (s, 1H), 7.27 (d, *J* = 7.6 Hz, 1H), 6.47 (s, 1H), 3.92 (qd, *J* = 7.2, 4.3 Hz, 2H), 2.82 (dd, *J* = 16.1, 3.4 Hz, 1H), 2.64 (dd, *J* = 16.1, 4.5 Hz, 1H), 1.04 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-D) δ 169.0, 165.6, 147.4, 142.2, 140.6, 133.8, 132.6, 130.3, 126.9, 126.6, 126.3, 123.9, 121.3, 60.9, 55.3, 37.2, 14.0.

HRMS: calcd. for $C_{17}H_{15}ClN_2O_4Na$ $[M+Na]^+$: 369.618, found: 369.0615.



2-(1-(2-ethoxy-2-oxoethyl)-5-methyl-3-oxoisoindolin-2-yl)pyridine 1-oxide (3f)

Physical appearance: Yellow liquid

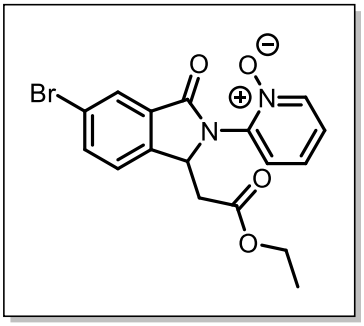
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 58 % (47 mg)

^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.33 (dd, *J* = 6.5, 1.5 Hz, 1H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.70 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.39 (td, *J* = 7.7, 1.4 Hz, 1H), 7.32 (s, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 7.24 (ddd, *J* = 7.3, 6.4, 1.8 Hz, 1H), 6.42 (t, *J* = 5.2 Hz, 1H), 3.94 – 3.82 (m, 2H), 2.80 (dd, *J* = 16.0, 4.9 Hz, 1H), 2.62 (dd, *J* = 16.0, 5.7 Hz, 1H), 2.47 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-D) δ 169.3, 168.1, 145.2, 144.2, 142.5, 140.5, 129.7, 128.0, 126.9, 126.7, 124.4, 123.8, 123.3, 60.8, 56.5, 37.3, 22.2, 14.0.

HRMS: calcd. for $C_{18}H_{18}N_2O_4H$: 327.1345, found: 327.1336.



2-(5-bromo-1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3g)

Physical appearance: Yellow liquid

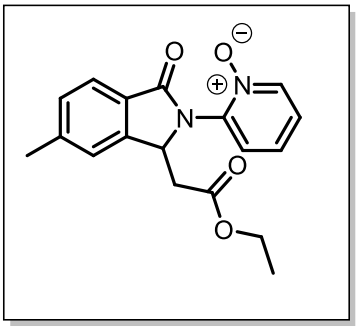
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 54 % (53 mg)

^{1}H NMR (500 MHz, CHLOROFORM-D) δ 8.31 (d, *J* = 6.2 Hz, 1H), 8.06 (d, *J* = 1.7 Hz, 1H), 7.75 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.69 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.26 (m, 1H), 6.45 (t, *J* = 5.2 Hz, 1H), 4.04 – 3.84 (m, 2H), 2.83 (dd, *J* = 16.2, 4.6 Hz, 1H), 2.62 (dd, *J* = 16.2, 5.9 Hz, 1H), 1.05 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-D) δ 169.0, 166.6, 143.5, 142.1, 140.6, 136.2, 132.8, 127.7, 126.6, 126.5, 124.6, 124.2, 122.8, 61.0, 56.4, 36.9, 14.1.

HRMS: calcd. for $C_{17}H_{15}BrN_2O_4Na$ $[M+Na]^+$: 413.0113, found: 413.0121.



2-(3-(2-ethoxy-2-oxoethyl)-5-methyl-1-oxoisoindolin-2-yl)pyridine 1-oxide (3h)

Physical appearance: Yellow semi-solid

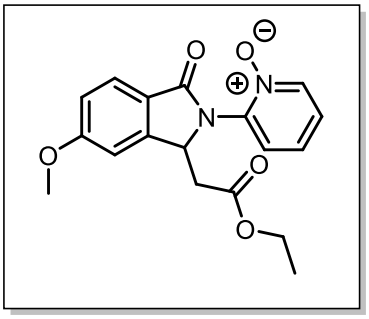
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 79 % (64 mg)

^{1}H NMR (600 MHz, CHLOROFORM-*D*) δ 8.54 (d, *J* = 8.5 Hz, 1H), 8.41 (dt, *J* = 4.8, 2.0 Hz, 1H), 7.83 – 7.69 (m, 2H), 7.49 – 7.29 (m, 2H), 7.11 – 7.01 (m, 1H), 5.94 (dt, *J* = 7.6, 3.7 Hz, 1H), 4.09 (dqt, *J* = 10.8, 7.4, 3.6 Hz, 2H), 3.33 (ddd, *J* = 15.8, 6.8, 3.7 Hz, 1H), 2.76 (td, *J* = 16.2, 7.9 Hz, 1H), 2.47 (d, *J* = 9.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-*D*) δ 169.3, 168.2, 142.1, 138.8, 134.7, 134.3, 130.8, 128.9, 126.5, 124.7, 123.7, 122.6, 122.1, 60.8, 56.4, 37.3, 21.4, 14.0.

HRMS: calcd. for $C_{18}H_{18}N_2O_4Na$ $[M+Na]^+$: 349.1164, found: 349.1168.



2-(3-(2-ethoxy-2-oxoethyl)-5-methoxy-1-oxoisoindolin-2-yl)pyridine 1-oxide (3i)

Physical appearance: Yellow liquid

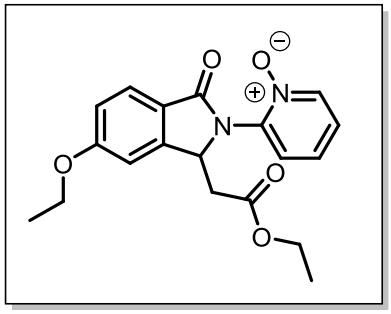
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 70 % (60 mg)

^{1}H NMR (600 MHz, CHLOROFORM-*D*) δ 8.25 (d, *J* = 6.4 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.64 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.18 (td, *J* = 7.6, 1.9 Hz, 1H), 6.96 (dq, *J* = 4.0, 2.2 Hz, 2H), 6.38 (t, *J* = 5.3 Hz, 1H), 3.94 – 3.78 (m, 5H), 2.75 (dd, *J* = 16.1, 4.8 Hz, 1H), 2.57 (dd, *J* = 16.1, 6.0 Hz, 1H), 0.99 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-*D*) δ 169.2, 167.7, 164.1, 147.4, 142.6, 140.4, 126.5, 126.0, 123.7, 123.1, 115.5, 107.5, 60.8, 56.3, 55.8, 37.4, 14.0.

HRMS: calcd. for $C_{18}H_{18}N_2O_5Na$ $[M+Na]^+$: 365.1113, found: 365.1121.



2-(5-ethoxy-3-(2-ethoxy-2-oxoethyl)-1-oxoisoindolin-2-yl)pyridine 1-oxide (3j)

Physical appearance: Yellow liquid

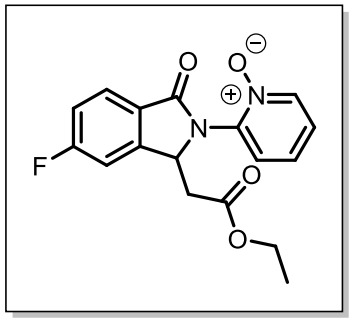
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 69 % (61 mg)

^{1}H NMR (600 MHz, CHLOROFORM-*D*) δ 8.35 – 8.17 (m, 1H), 7.88 – 7.76 (m, 1H), 7.76 – 7.68 (m, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.16 (m, 1H), 7.00 (d, *J* = 7.9 Hz, 2H), 6.46 (t, *J* = 5.3 Hz, 1H), 4.12 (q, *J* = 7.0 Hz, 2H), 4.03 – 3.79 (m, 2H), 2.79 (dd, *J* = 16.0, 4.0 Hz, 1H), 2.62 (dd, *J* = 16.1, 5.2 Hz, 1H), 1.45 (t, *J* = 7.0 Hz, 3H), 1.04 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-*D*) δ 169.3, 167.7, 163.5, 147.4, 140.5, 126.4, 126.4, 126.1, 123.5, 122.9, 115.9, 107.9, 64.2, 60.8, 56.3, 37.4, 14.7, 14.0.

HRMS: calcd. for $C_{19}H_{21}N_2O_5H$: 357.1450, found: 357.1444.



2-(3-(2-ethoxy-2-oxoethyl)-5-fluoro-1-oxoisoindolin-2-yl)pyridine 1-oxide (3k)

Physical appearance: Yellow liquid

Eluent: (CH_2Cl_2/acetone 2:1)

Yield: 60 % (49 mg)

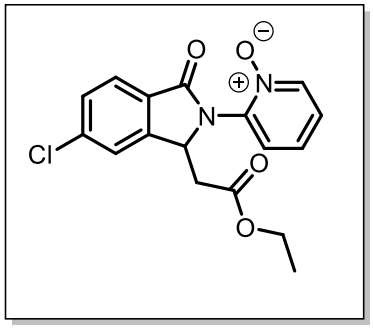
^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.29 (d, *J* = 6.4 Hz, 1H), 7.91 (dd, *J* = 8.4, 5.0 Hz, 1H), 7.67 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.24 (td, *J* = 7.2, 6.3, 2.3 Hz,

2H), 7.20 (td, *J* = 8.6, 2.9 Hz, 1H), 6.47 (t, *J* = 5.4 Hz, 1H), 4.03 – 3.86 (m, 2H), 2.81 (dd, *J* = 16.1, 4.6 Hz, 1H), 2.62 (dd, *J* = 16.2, 6.2 Hz, 1H), 1.04 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-D) δ 169.0, 166.9, 166.1 (d, C−F, $^{1}J_{C-F}$ = 252.6Hz), 147.5 (d, C−F, $^{3}J_{C-F}$ = 9.8 Hz), 142.1, 140.5 (d, C−F, $^{3}J_{C-F}$ = 6.9 Hz), 126.9, 126.8, 126.5, 126.3, 124.0, 116.6 (d, C−F, $^{2}J_{C-F}$ = 23.4 Hz), 110.5 (d, C−F, $^{2}J_{C-F}$ = 24.4Hz), 61.0, 56.2, 37.00, 14.00.

^{19}F NMR (565 MHz, CHLOROFORM-*D*) δ -104.19.

HRMS: calcd. for $C_{17}H_{15}FN_2O_4Na$ $[M+Na]^+$: 353.0914, found: 353.0913.



2-(5-chloro-3-(2-ethoxy-2-oxoethyl)-1-oxoisoindolin-2-yl)pyridine 1-oxide (3l)

Physical appearance: Yellow liquid

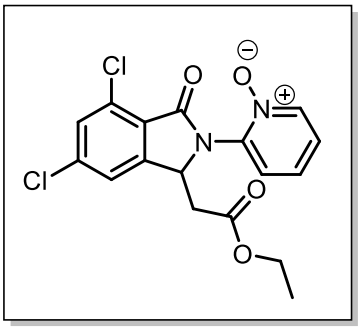
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 51 % (44 mg)

^{1}H NMR (600 MHz, CHLOROFORM-*D*) δ 8.27 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 1.7 Hz, 1H), 7.49 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.33 (d, *J* = 8.8 Hz, 1H), 7.30 – 7.25 (m, 1H), 6.48 (s, 1H), 3.93 (qq, *J* = 10.8, 7.1 Hz, 2H), 2.89 – 2.72 (m, 1H), 2.63 (dd, *J* = 16.1, 4.6 Hz, 1H), 1.04 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-*D*) δ 169.0, 167.0, 146.5, 140.6, 139.7, 138.7, 129.4, 129.3, 126.5, 125.8, 124.0, 123.5, 61.0, 56.2, 36.9, 14.0.

HRMS: calcd. for $C_{17}H_{15}ClN_2O_4Na$ $[M+Na]^+$: 369.618, found: 369.0635.



2-(4,6-dichloro-1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3n)

Physical appearance: Yellow liquid

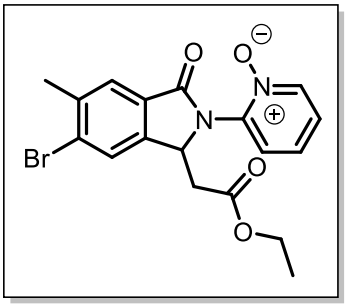
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 66 % (63 mg)

^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.30 (d, *J* = 6.6 Hz, 1H), 7.69 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.46 (q, *J* = 1.7 Hz, 2H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.29 – 7.26 (m, 1H), 6.43 (t, *J* = 5.2 Hz, 1H), 4.10 – 3.69 (m, 2H), 2.80 (dd, *J* = 16.3, 3.7 Hz, 1H), 2.63 (dd, *J* = 16.4, 5.4 Hz, 1H), 1.06 (td, *J* = 7.0, 1.1 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-D) δ 168.8, 164.7, 148.6, 141.8, 140.6, 139.7, 133.3, 130.4, 126.8, 126.6, 125.6, 124.2, 122.0, 61.1, 55.2, 36.8, 14.0.

HRMS: calcd. for $C_{17}H_{14}Cl_2N_2O_4H$: 381.0409, found: 381.0405.



2-(5-bromo-3-(2-ethoxy-2-oxoethyl)-6-methyl-1-oxoisoindolin-2-yl)pyridine 1-oxide (3o)

Physical appearance: Yellow liquid

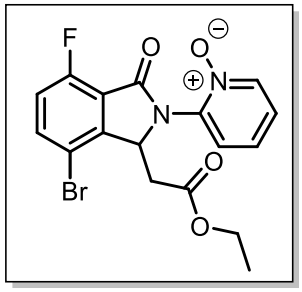
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 62 % (63 mg)

^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.28 (d, *J* = 6.5 Hz, 1H), 7.76 (d, *J* = 13.1 Hz, 2H), 7.68 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.27 – 7.22 (m, 1H), 6.42 (t, *J* = 5.2 Hz, 1H), 4.09 – 3.79 (m, 2H), 2.79 (dd, *J* = 16.3, 4.2 Hz, 1H), 2.60 (dd, *J* = 16.3, 5.8 Hz, 1H), 2.49 (s, 3H), 1.05 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-D) δ 169.0, 167.3, 143.8, 142.4, 140.5, 138.9, 130.6, 130.1, 127.0, 126.5, 126.3, 126.1, 123.9, 60.9, 55.9, 37.0, 23.2, 14.0.

HRMS: calcd. for $C_{18}H_{17}BrN_2O_4Na$ $[M+Na]^+$: 427.0269, found: 427.0267.



Exact Mass: 408.0121

2-(4-bromo-3-(2-ethoxy-2-oxoethyl)-7-fluoro-1-oxoisoindolin-2-yl)pyridine 1-oxide (3p)

Physical appearance: Orange Solid

Eluent: (CH_2Cl_2/acetone 2:1)

Yield: 72 % (73 mg)

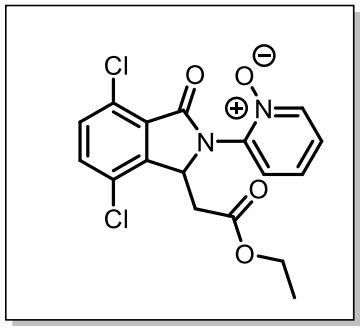
Melting Point: 195 to 200 °C

^{1}H NMR (600 MHz, CHLOROFORM-*D*) δ 8.30 (d, *J* = 6.5 Hz, 1H), 7.78 – 7.66 (m, 2H), 7.37 (t, *J* = 6.7 Hz, 1H), 7.28 (t, *J* = 7.0 Hz, 1H), 7.09 (t, *J* = 8.5 Hz, 1H), 6.44 (t, *J* = 3.9 Hz, 1H), 3.86 (qq, *J* = 10.8, 7.1 Hz, 2H), 3.42 (dd, *J* = 16.2, 3.9 Hz, 1H), 2.68 (dd, *J* = 16.6, 3.4 Hz, 1H), 0.99 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-D) δ 168.7, 163.9, 158.8 (d, C−F, $^1J_{C-F}$ = 262.1Hz), 145.5, 141.7, 140.6, 138.4 (d, C−F, $^3J_{C-F}$ = 7.5Hz), 126.6, 124.2, 120.9 (d, C−F, $^2J_{C-F}$ = 13.4Hz), 118.2, 118.1, 112.1 (d, C−F, $^3J_{C-F}$ = 3Hz), 60.87, 57.20, 33.73, 14.00.

^{19}F NMR (377 MHz, CHLOROFORM-*D*) δ -113.44.

HRMS: calcd. for $C_{17}H_{14}BrFN_2O_4K$$[M+K]^+$: 446.9758, found: 446.9760.



2-(4,7-dichloro-1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3q)

Physical appearance: Yellow Solid

Eluent: (CH_2Cl_2/acetone 3:1)

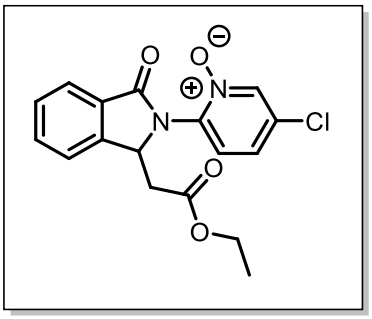
Yield: 71% (67 mg)

Melting Point: 196 to 200 °C

^{1}H NMR (500 MHz, CHLOROFORM-D) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 6.3 Hz, 1H), 7.69 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.28 – 7.23 (m, 1H), 6.42 (t, *J* = 4.1 Hz, 1H), 3.90 – 3.72 (m, 2H), 3.26 (dd, *J* = 16.4, 4.5 Hz, 1H), 2.68 (dd, *J* = 16.4, 3.8 Hz, 1H), 0.94 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-D) δ 168.6, 164.6, 143.5, 141.5 140.3, 134.0, 131.6, 131.0, 129.0, 127.8, 126.6, 126.3, 124.3, 60.7, 55.0, 33.8, 13.8.

HRMS: calcd. for $C_{17}H_{14}Cl_2N_2O_4H$ 381.0409, found: 381.0413.



5-chloro-2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3t)

Physical appearance: Yellow liquid

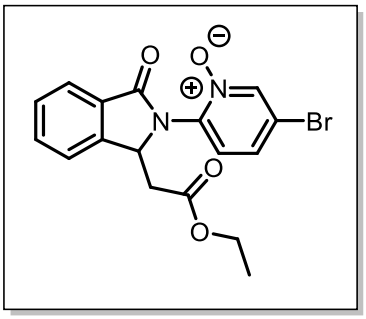
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 71% (61 mg)

^{1}H NMR (600 MHz, DMSO-D_6) δ 8.73 (s, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 5.7 Hz, 2H), 7.63 (q, *J* = 8.9 Hz, 2H), 7.60 – 7.55 (m, 1H), 5.89 (t, *J* = 5.7 Hz, 1H), 3.84 (qq, *J* = 10.9, 7.2 Hz, 2H), 2.88 (d, *J* = 5.7 Hz, 2H), 0.97 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, DMSO-*D_6*) δ 169.5, 167.3, 145.2, 141.2, 139.0, 133.2, 130.9, 130.0, 128.7, 127.3, 126.0, 123.7, 123.5, 60.2, 60.2, 55.9, 36.8, 13.7.

HRMS: calcd. for $C_{17}H_{15}ClN_2O_4Na$ $[M+Na]^+$: 369.0618 found: 369.0634



5-bromo-2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3u)

Physical appearance: Yellow liquid

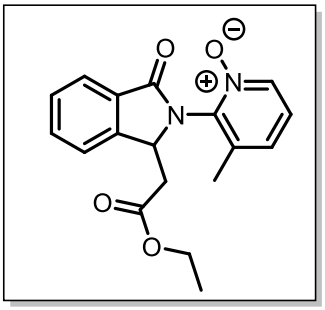
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 69% (67 mg)

^{1}H NMR (600 MHz, CHLOROFORM-*D*) δ 8.44 (d, *J* = 1.7 Hz, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.60 (d, *J* = 9.0 Hz, 1H), 7.56 – 7.47 (m, 3H), 3.98 – 3.79 (m, 2H), 2.83 (dd, *J* = 16.0, 4.9 Hz, 1H), 2.65 (dd, *J* = 16.0, 5.6 Hz, 1H), 1.01 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (151 MHz, DMSO-D_6) δ 169.1, 167.9, 144.7, 141.6, 138.3, 133.3, 130.4, 129.2, 128.7, 126.5, 124.6, 122.9, 117.8, 60.8, 56.6, 37.2, 14.0..

HRMS: calcd. for $C_{17}H_{15}BrN_2O_4H$: 391.0293 found: 391.0301



2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)-3-methylpyridine 1-oxide (3v)

Physical appearance: Yellow liquid

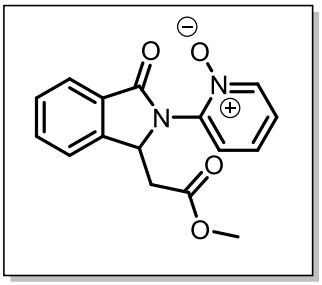
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 68% (55 mg)

^{1}H NMR (500 MHz, CHLOROFORM-*D*) δ 8.19 (d, *J* = 5.9 Hz, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.63 (td, *J* = 7.6, 1.0 Hz, 1H), 7.58 – 7.45 (m, 3H), 7.05 (d, *J* = 4.6 Hz, 1H), 6.52 (t, *J* = 4.8 Hz, 1H), 4.01 – 3.78 (m, 2H), 2.84 (dd, *J* = 15.9, 4.2 Hz, 1H), 2.63 (dd, *J* = 15.9, 5.5 Hz, 1H), 2.41 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-*D*) δ 169.2, 168.0 144.8, 141.6, 139.7, 138.5, 133.2, 130.8, 128.6, 126.9, 124.8, 124.6, 122.9, 60.8, 56.6, 37.2, 20.6, 14.0.

HRMS: calcd. for $C_{18}H_{18}N_2O_4H$: 327.1345 found: 327.1352



2-(1-(2-methoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3w)

Physical appearance: White Solid

Eluent: (CH_2Cl_2/acetone 2:1)

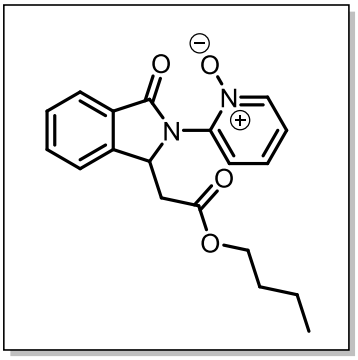
Yield: 74% (55 mg)

Melting Point: 202 to 206 °C

^{1}H NMR (600 MHz, CHLOROFORM-*D*) δ 8.28 (d, *J* = 6.3 Hz, 1H), 7.93 (d, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 10.1 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.51 (dd, *J* = 14.1, 7.5 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.25 (d, *J* = 5.9 Hz, 1H), 6.48 (d, *J* = 5.4 Hz, 1H), 3.47 (s, 3H), 2.82 (dd, *J* = 16.1, 4.0 Hz, 1H), 2.66 (dd, *J* = 16.1, 5.0 Hz, 1H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-*D*) δ 169.7, 168.0, 144.9, 142.8, 140.6, 133.3, 130.6, 128.7, 126.6, 126.4, 124.7, 123.8, 122.8, 56.5, 51.9, 37.2.

HRMS: calcd. for $C_{16}H_{14}N_2O_4Na$ $[M+Na]^+$: 321.0851, found: 321.0855.



2-(1-(2-butoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3x)

Physical appearance: Yellow Semi Solid

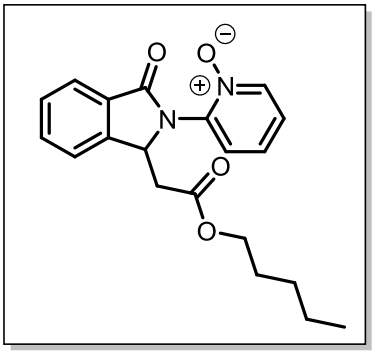
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 71% (61 mg)

^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.30 (d, *J* = 6.3 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.70 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.57 – 7.45 (m, 2H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.25 – 7.22 (m, 1H), 6.47 (t, *J* = 5.2 Hz, 1H), 3.82 (tt, *J* = 7.2, 3.6 Hz, 2H), 2.84 (dd, *J* = 15.7, 4.7 Hz, 1H), 2.64 (dd, *J* = 15.9, 5.9 Hz, 1H), 1.34 (dq, *J* = 13.8, 6.9 Hz, 2H), 1.18 – 1.09 (m, 2H), 0.80 (t, *J* = 7.3 Hz, 3H).

$^{13}C\{^1H\}$ NMR (151 MHz, CHLOROFORM-D) δ 169.3, 168.0, 144.8, 142.5, 140.5, 133.2, 130.7, 128.6, 126.7, 126.4, 124.6, 123.9, 122.8, 64.7, 56.6, 37.13, 30.4, 19.0, 13.6

HRMS: calcd. for $C_{19}H_{20}N_2O_4Na$ $[M+Na]^+$: 341.1501, found: 341.1505.



2-(1-oxo-3-(2-oxo-2-(pentyloxy)ethyl)isoindolin-2-yl)pyridine 1-oxide (3y)

Physical appearance: Yellow Solid

Eluent: (CH_2Cl_2/acetone 3:1)

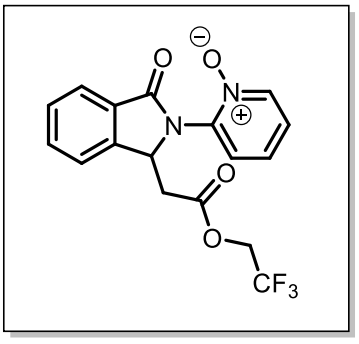
Yield: 71% (63 mg)

Melting Point: 208 to 211 °C

^1H NMR (600 MHz, CHLOROFORM-*D*) δ 8.36 (d, *J* = 6.2 Hz, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.72 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.63 (td, *J* = 7.5, 1.2 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.41 (td, *J* = 7.9, 1.4 Hz, 1H), 7.29 – 7.21 (m, 1H), 6.47 (t, *J* = 5.2 Hz, 1H), 3.82 (td, *J* = 6.9, 1.5 Hz, 2H), 2.85 (dd, *J* = 16.1, 4.6 Hz, 1H), 2.65 (dd, *J* = 16.1, 5.8 Hz, 1H), 1.40 – 1.30 (m, *J* = 6.8 Hz, 2H), 1.24 – 1.17 (m, 2H), 1.12 – 1.05 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H).

$^{13}C\{^1H\}$ NMR (151 MHz, CHLOROFORM-D) δ 169.3, 168.0, 144.8, 142.4, 140.6, 133.3, 130.6, 128.6, 127.1, 126.7, 124.6, 123.9, 122.8, 65.0, 56.7, 37.0, 28.1, 27.9, 22.3, 13.9.

HRMS: calcd. for $C_{20}H_{22}N_2O_4Na$ $[M+Na]^+$: 377.1477, found: 377.1479



2-(1-oxo-3-(2-oxo-2-(2,2,2-trifluoroethoxy)ethyl)isoindolin-2-yl)pyridine 1-oxide (3z)

Physical appearance: White Semi Solid

Eluent: (CH_2Cl_2/acetone 3:1)

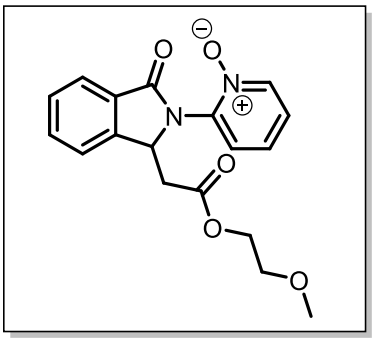
Yield: 68% (62 mg)

^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.32 (d, *J* = 6.8 Hz, 1H), 7.92 (d, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 5.7 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.56 – 7.48 (m, 2H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.31 – 7.21 (m, 1H), 6.53 (t, *J* = 5.1 Hz, 1H), 4.29 – 4.10 (m, 2H), 2.98 (dd, *J* = 16.6, 4.6 Hz, 1H), 2.78 (dd, *J* = 16.5, 5.4 Hz, 1H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-*D*) δ 167.8, 167.7, 144.1, 142.2, 140.6, 133.5, 130.6, 128.9, 127.0, 126.5, 124.8, 124.0, 122.7, 122.3 (q, C–F, $^1J_{C\text{-}F}$ = 352.6 Hz), 60.3 (q, C–F, $^2J_{C\text{-}F}$ = 36.9 Hz), 56.3, 36.3.

^{19}F NMR (377 MHz, $CDCl_3$) δ -73.76.

HRMS: calcd. for $C_{17}H_{13}F_3N_2O_4Na$ $[M+Na]^+$: 389.0725, found: 389.0721



2-(1-(2-(2-methoxyethoxy)-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3aa)

Physical appearance: Yellow liquid

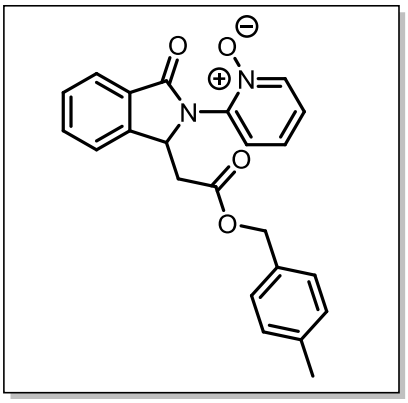
Eluent: (CH_2Cl_2/acetone 3:1)

Yield: 77% (62 mg)

^{1}H NMR (600 MHz, DMSO-D_6) δ 8.44 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.75 (dt, *J* = 14.6, 7.6 Hz, 2H), 7.69 – 7.65 (m, 1H), 7.59 (t, *J* = 7.3 Hz, 1H), 7.50 – 7.45 (m, 2H), 6.01 (t, *J* = 5.6 Hz, 1H), 3.97 – 3.90 (m, 2H), 3.44 (s, 2H), 3.20 (s, 3H), 2.96 (dd, *J* = 16.5, 5.9 Hz, 1H), 2.86 (dd, *J* = 16.4, 5.5 Hz, 1H).

^{13}C{^{1}H} NMR (151 MHz, DMSO-D_6) δ 169.4, 167.3, 145.2, 141.7, 140.1, 133.1, 130.3, 128.6, 127.4, 125.8, 125.4, 123.6, 123.4, 69.4, 63.2, 58.0, 55.7, 36.6.

HRMS: calcd. for $C_{18}H_{18}N_2O_5Na$ $[M+Na]^+$: 365.1113, found: 365.1118



2-(1-(2-((4-methylbenzyl)oxy)-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3ab)

Physical appearance: Yellow Solid

Eluent: (CH_2Cl_2/acetone 3:1)

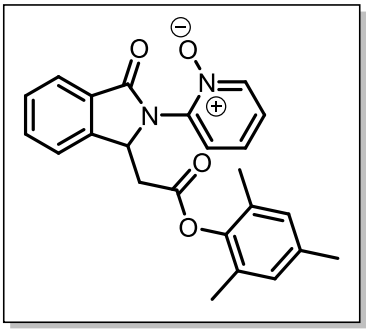
Yield: 68% (62 mg)

Melting Point: 208 to 212 °C

^{1}H NMR (600 MHz, CHLOROFORM-D) δ 8.40 – 8.18 (m, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 9.2 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.22 (dt, *J* = 13.2, 7.2 Hz, 2H), 7.11 (d, *J* = 7.5 Hz, 2H), 7.02 (d, *J* = 7.5 Hz, 2H), 6.49 (t, *J* = 5.5 Hz, 1H), 4.94 – 4.73 (m, 2H), 2.88 (dd, *J* = 16.1, 4.0 Hz, 1H), 2.68 (dd, *J* = 15.9, 5.0 Hz, 1H), 2.34 (s, 3H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-*D*) δ 169.1, 167.9, 144.7, 142.6, 140.6, 138.4, 133.2, 132.2, 130.7, 129.3, 128.8, 128.6, 126.6, 126.5, 124.7, 123.7, 122.8, 66.7, 56.6, 37.2, 21.0.

HRMS: calcd. for $C_{23}H_{20}N_2O_4H$: 389.1501, found: 389.1551



2-(1-(2-(mesityloxy)-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3ac)

Physical appearance: Orange Solid

Eluent: (CH_2Cl_2/acetone 2:1)

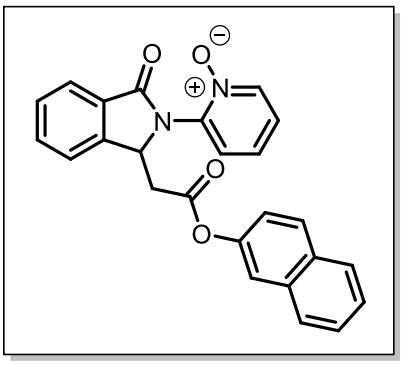
Yield: 72% (72 mg)

Melting Point: 240 to 242 °C

^{1}H NMR (600 MHz, DMSO-D_6) δ 8.39 (dd, *J* = 5.6, 2.1 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.64 – 7.60 (m, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.43 (qd, *J* = 8.9, 7.5, 4.9 Hz, 2H), 6.77 (s, 2H), 6.09 (t, *J* = 4.9 Hz, 1H), 3.38 (dd, *J* = 17.5, 5.5 Hz, 1H), 3.15 (dd, *J* = 17.3, 4.6 Hz, 1H), 2.13 (s, 3H), 1.71 (s, 6H).

^{13}C{^{1}H} NMR (151 MHz, DMSO-D_6) δ 168.4, 168.0, 145.8, 145.6, 142.3, 140.7, 135.3, 133.8, 131.0, 129.7, 129.4, 129.3, 127.8, 126.4, 125.8, 124.2, 124.1, 56.1, 36.0, 20.7, 16.1.

HRMS: calcd. for $C_{24}H_{22}N_2O_4Na$ $[M+Na]^+$: 425.1477, found: 425.1476



2-(1-(2-(naphthalen-2-yloxy)-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3ad)

Physical appearance: Orange Solid

Eluent: (CH_2Cl_2/acetone 3:1)

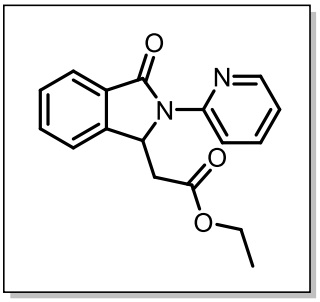
Yield: 74% (72 mg)

Melting Point: 210 to 212 °C

^{1}H NMR (600 MHz, CHLOROFORM-*D*) δ 8.33 (s, 1H), 7.99 (d, *J* = 7.3 Hz, 1H), 7.81 – 7.73 (m, 2H), 7.76 – 7.64 (m, 4H), 7.56 (t, *J* = 6.6 Hz, 1H), 7.48 – 7.39 (m, 2H), 7.35 (s, 1H), 7.24 (d, *J* = 24.6 Hz, 1H), 7.14 (s, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.67 (s, 1H), 3.17 (d, *J* = 14.6 Hz, 1H), 2.96 (d, *J* = 14.3 Hz, 1H).

^{13}C{^{1}H} NMR (151 MHz, CHLOROFORM-*D*) δ 168.0, 147.7, 144.4, 142.5, 140.6, 133.6, 133.5, 131.6, 130.8, 129.6, 129.0, 127.8, 127.73, 127.66, 127.2, 126.8, 126.8, 126.0, 124.8, 124.0, 123.1, 120.5, 118.3, 56.8, 37.3.

HRMS: calcd. for $C_{25}H_{18}N_2O_4H$: 411.1345, found: 411.1349,



ethyl 2-(3-oxo-2-(pyridin-2-yl)isoindolin-1-yl)acetate (5)

Physical appearance: Off White Solid

Eluent: (Hex/EA 3:2)

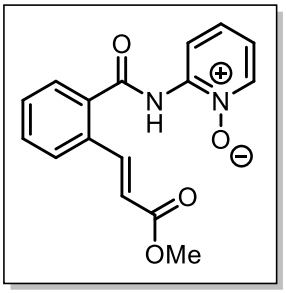
Yield: 91% (426 mg)

Melting Point: 110 to 112 °C

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.55 (dt, *J* = 8.5, 1.0 Hz, 1H), 8.42 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1H), 7.93 (dt, *J* = 7.3, 1.2 Hz, 1H), 7.77 (ddd, *J* = 8.5, 7.4, 2.0 Hz, 1H), 7.65 – 7.46 (m, 3H), 7.08 (ddd, *J* = 7.3, 4.9, 0.9 Hz, 1H), 6.00 (dd, *J* = 7.8, 3.6 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.36 (dd, *J* = 15.8, 3.7 Hz, 1H), 2.79 (dd, *J* = 15.8, 7.8 Hz, 1H), 1.15 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$) δ 170.5, 167.6, 150.9, 147.7, 144.9, 138.0, 132.9, 131.9, 128.7, 124.2, 122.8, 119.5, 115.8, 60.7, 56.5, 38.1, 14.1.

HRMS: calcd. for $C_{17}H_{16}N_2O_3H$: 297.1239 found: 297.1240



(E)-2-(2-(3-methoxy-3-oxoprop-1-en-1-yl)benzamido)pyridine 1-oxide (4)

Physical appearance: White Solid

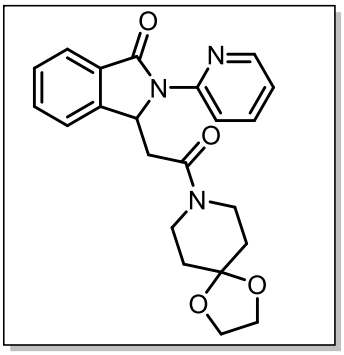
Eluent: (CH_2Cl_2/acetone 2:1)

Yield: 66% (983 mg)

^{1}H NMR (200 MHz, CDCl3) δ 10.54 (s, 1H), 8.69 – 8.57 (m, 1H), 8.30 (d, *J* = 6.4 Hz, 1H), 8.16 (d, *J* = 15.9 Hz, 1H), 7.79 – 7.67 (m, 2H), 7.65 – 7.31 (m, 4H), 7.12 – 7.01 (m, 1H), 6.43 (d, *J* = 15.9 Hz, 1H), 3.80 (s, 3H).

^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$) δ166.8, 166.5, 144.3, 142.1, 137.2, 134.7, 134.4, 131.9, 130.0, 128.39, 128.0, 127.9, 121.1, 119.2, 51.9.

HRMS: calcd. for $C_{16}H_{14}N_2O_4H$: 299.1032 found: 299.1043



3-(2-oxo-2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)ethyl)-2-(pyridin-2-yl)isoindolin-1-one (7)

Physical appearance: White Solid

Eluent: (Hex/EA 2:3)

Yield: 76% (426 mg)

Melting Point: 140 to 142 °C

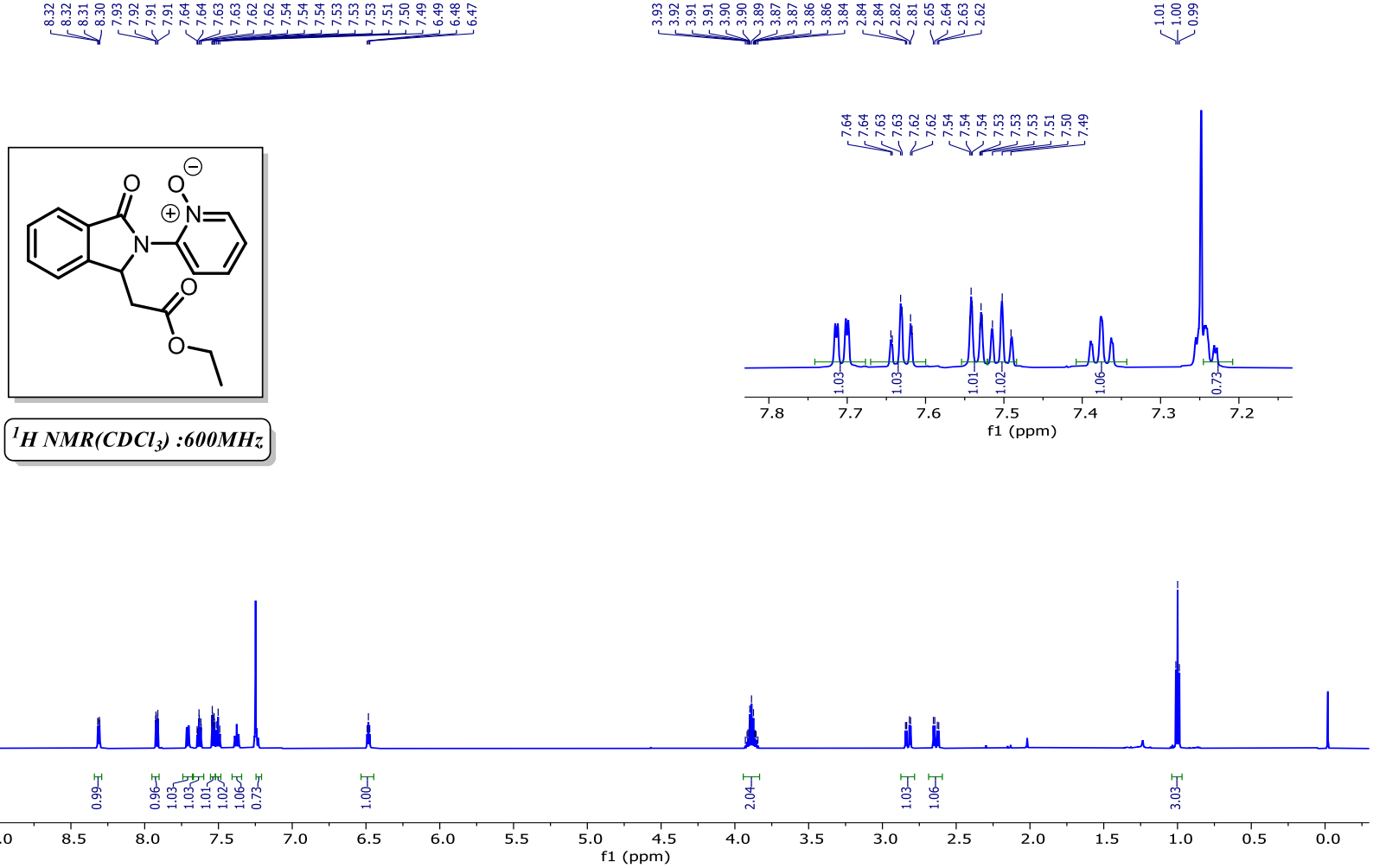
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 8.5 Hz, 1H), 8.47 – 8.37 (m, 1H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.80 – 7.73 (m, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.06 (dd, *J* = 6.8, 5.2 Hz, 1H), 6.11 (dd, *J* = 9.8, 2.9 Hz, 1H), 3.96 (q, *J* = 5.1 Hz, 4H), 3.78 (t, *J* = 5.9 Hz, 2H), 3.61 – 3.42 (m, 3H), 2.42 (dd, *J* = 15.3, 9.8 Hz, 1H), 1.72 (h, *J* = 7.5 Hz, 2H), 1.58 (tt, *J* = 13.2, 7.2 Hz, 2H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.4, 167.8, 151.0, 147.8, 145.9, 138.0, 133.0, 131.5, 128.6, 124.1, 123.9, 119.5, 115.5, 106.8, 64.5, 57.2, 43.6, 40.0, 37.5, 35.6, 34.8.

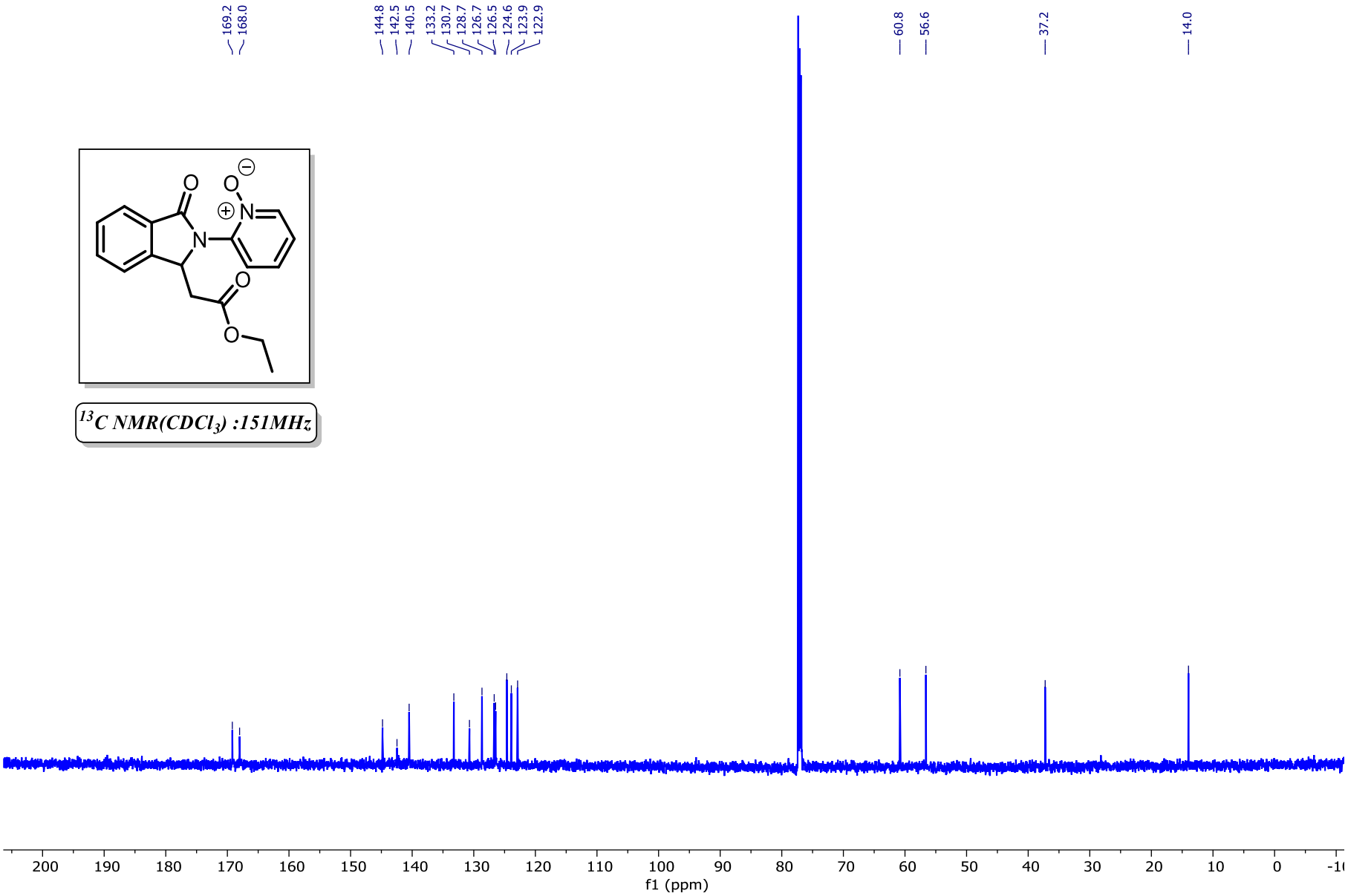
HRMS: calcd. for $C_{22}H_{23}N_3O_4H$:394.1767 found: 394.1751

11.2. ^{1}H, $^{13}C\{^{1}H\}$ and ^{19}F NMR spectra

2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3a)

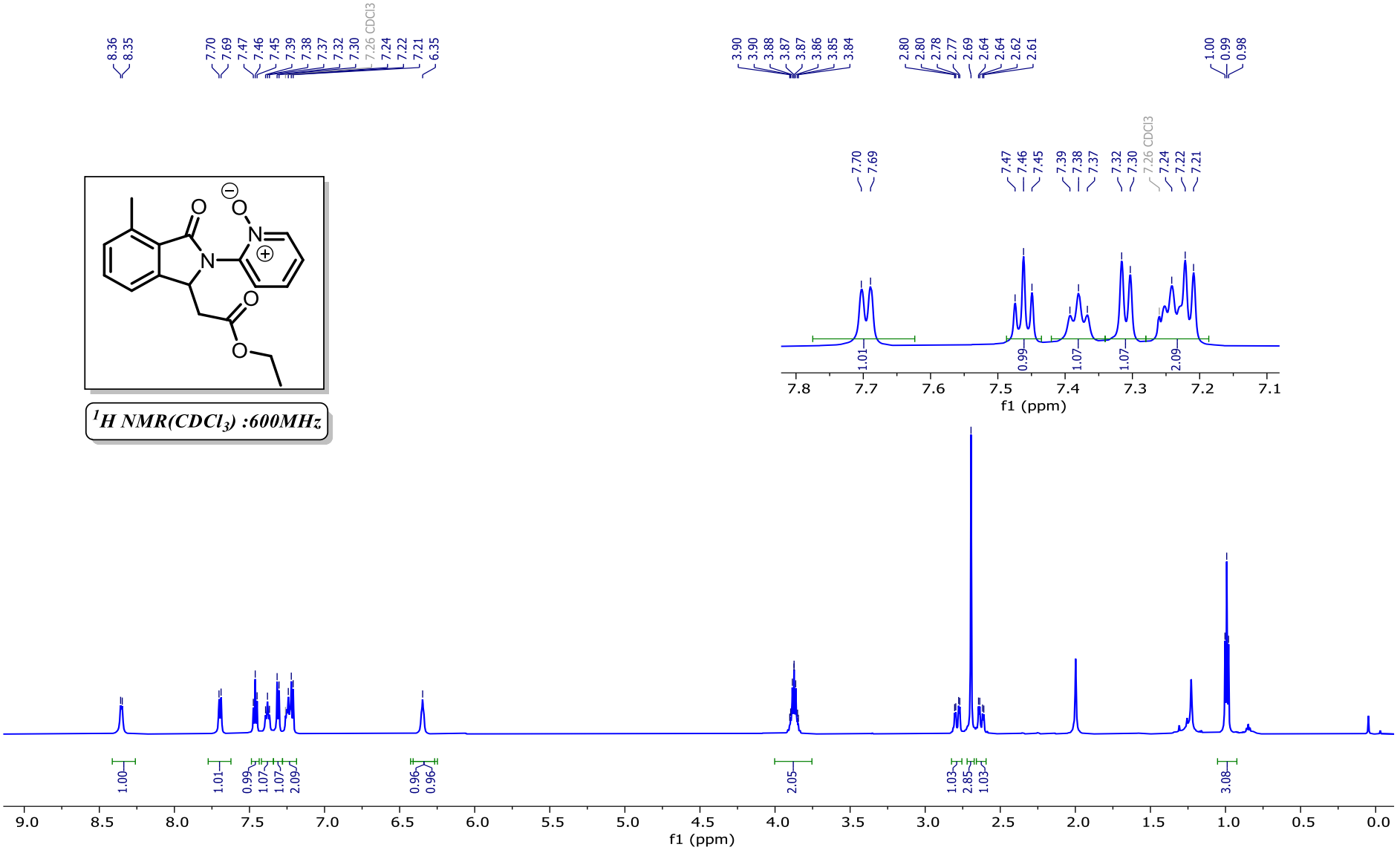


^{1}H NMR($CDCl_3$) :600MHz

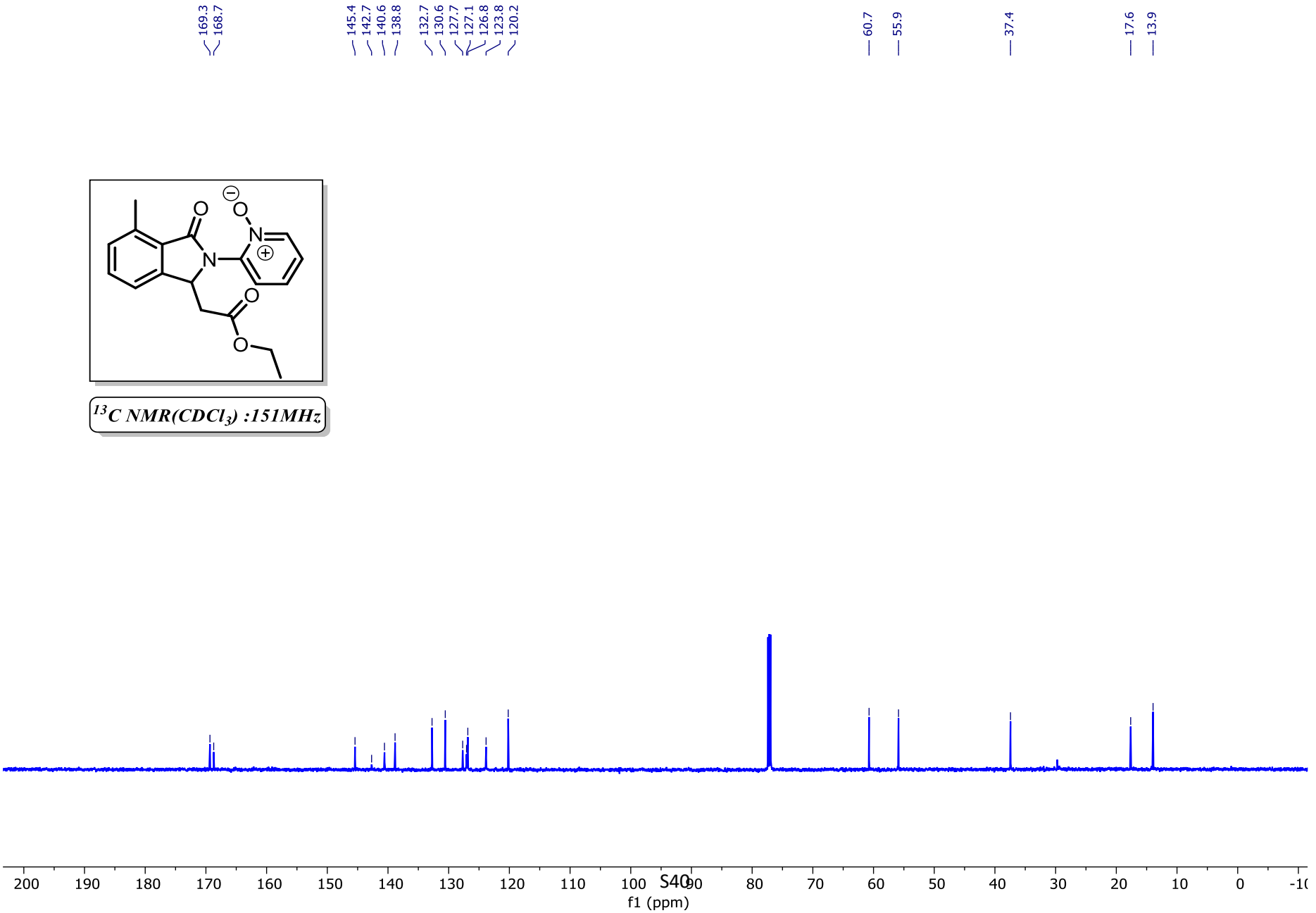


^{13}C NMR($CDCl_3$) :151MHz

2-(1-(2-ethoxy-2-oxoethyl)-4-methyl-3-oxoisoindolin-2-yl)pyridine 1-oxide (3b)

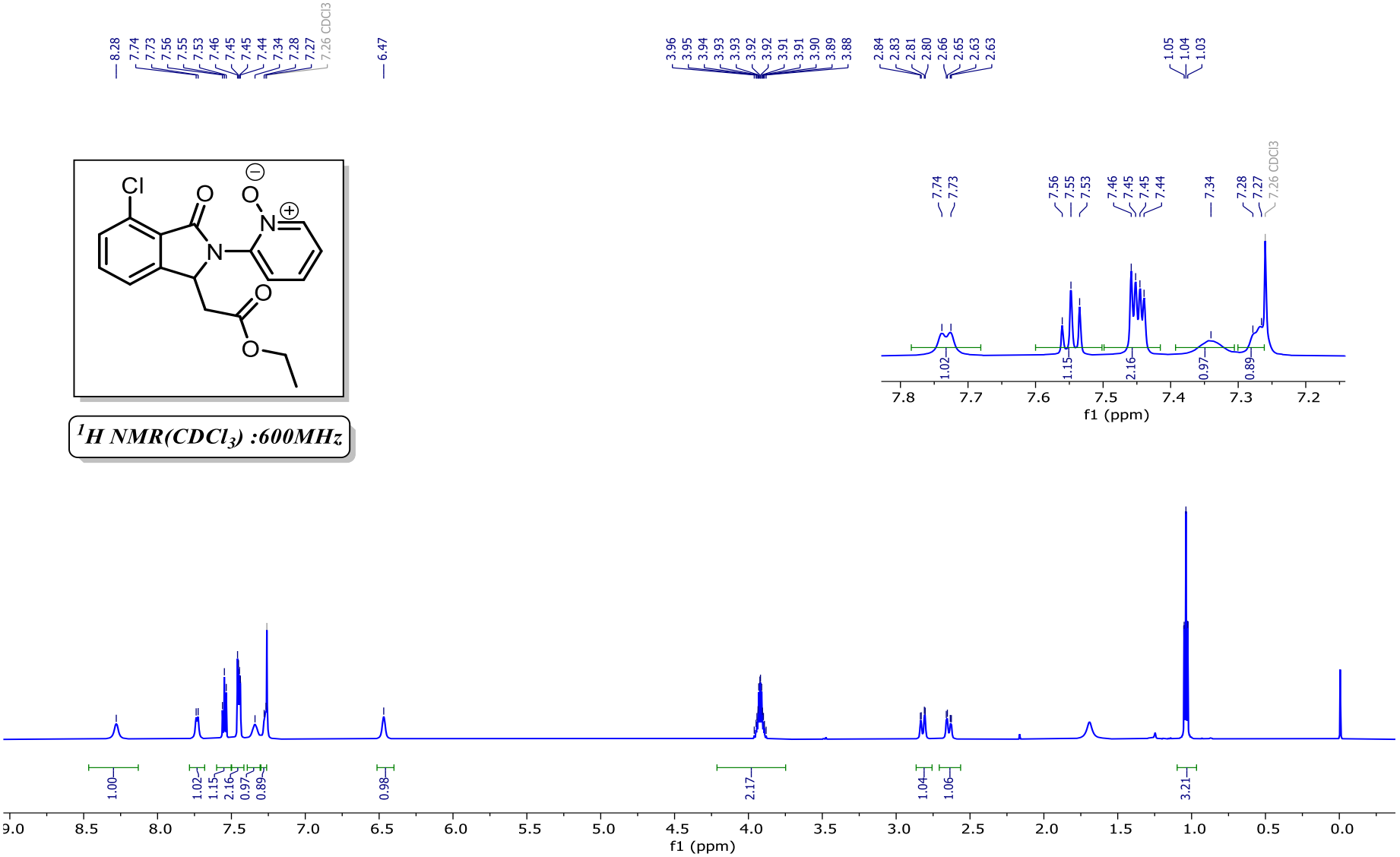


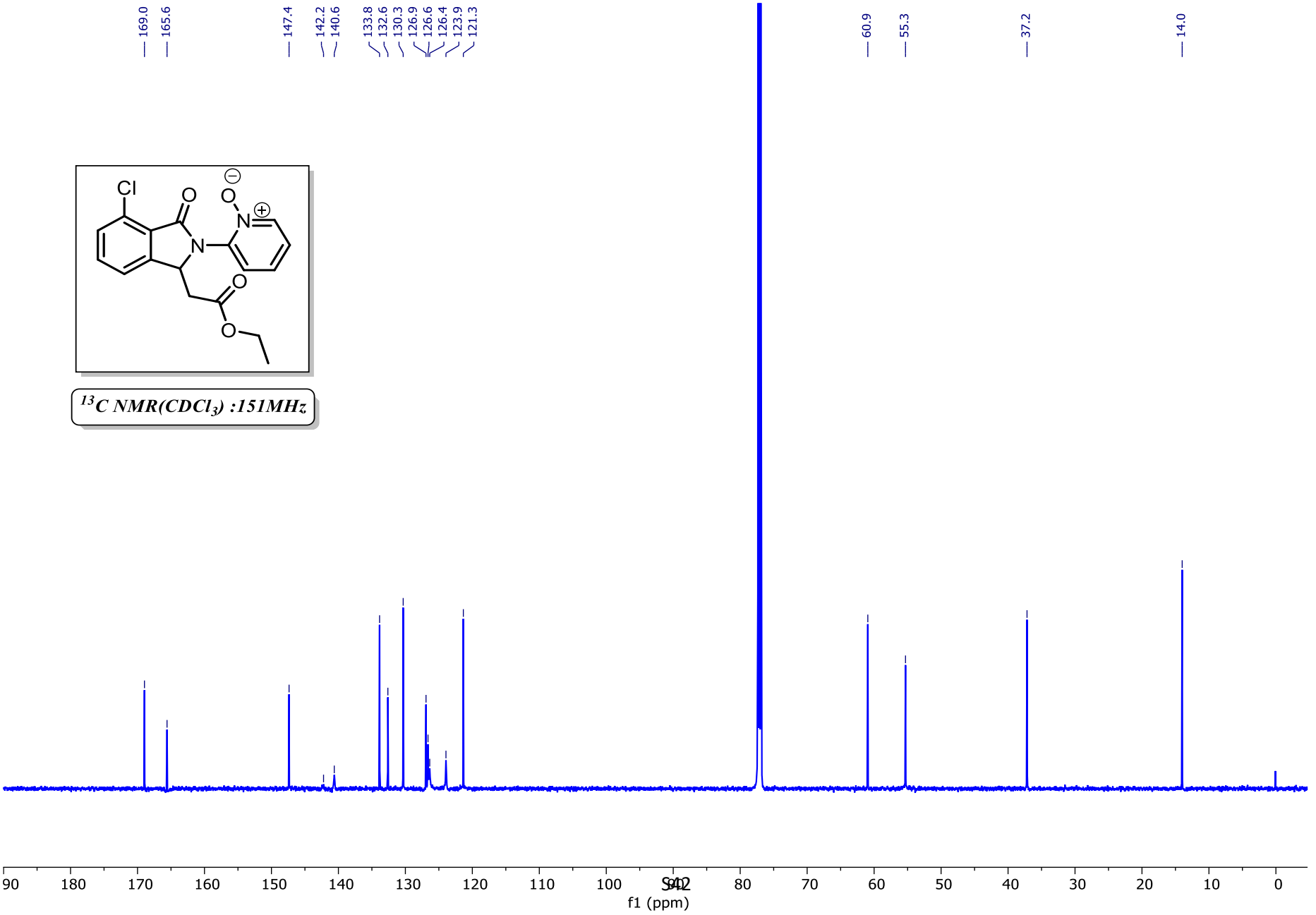
^{1}H NMR($CDCl_3$) :600MHz



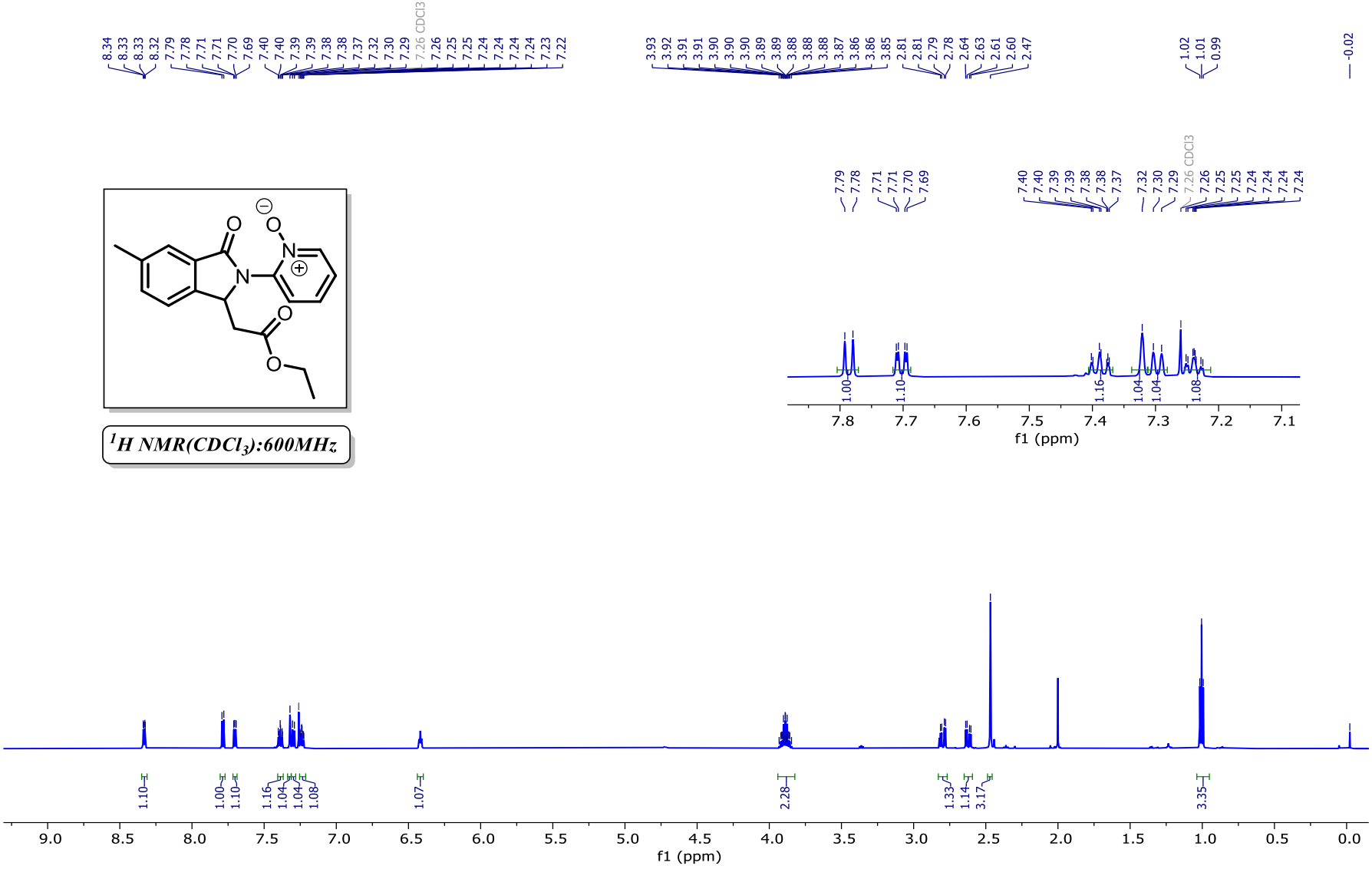
^{13}C NMR($CDCl_3$) :151MHz

2-(4-chloro-1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3c)

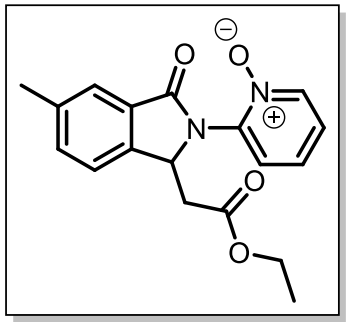



169.0
165.6
147.4
142.2
140.6
133.8
132.6
130.3
126.9
126.6
126.4
123.9
121.3
60.9
55.3
37.2
14.0
Cl
O
O
N
N
O
O
^{13}C NMR($CDCl_3$) :151MHz
90
180
170
160
150
140
130
120
110
100
80
70
60
50
40
30
20
10
0
f1 (ppm)

2-(1-(2-ethoxy-2-oxoethyl)-5-methyl-3-oxoisoindolin-2-yl)pyridine 1-oxide (3f)

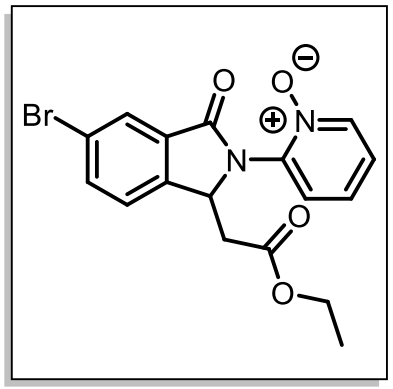


^{1}H NMR($CDCl_3$):600MHz

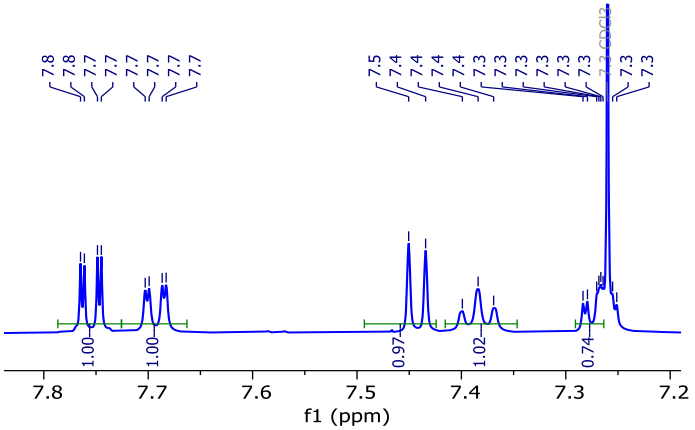


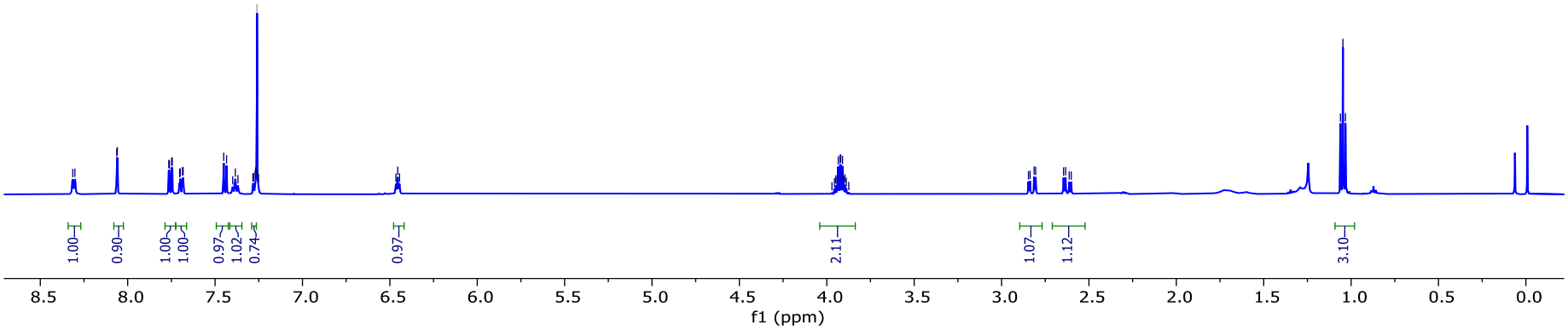
^{13}C NMR($CDCl_3$) :151MHz

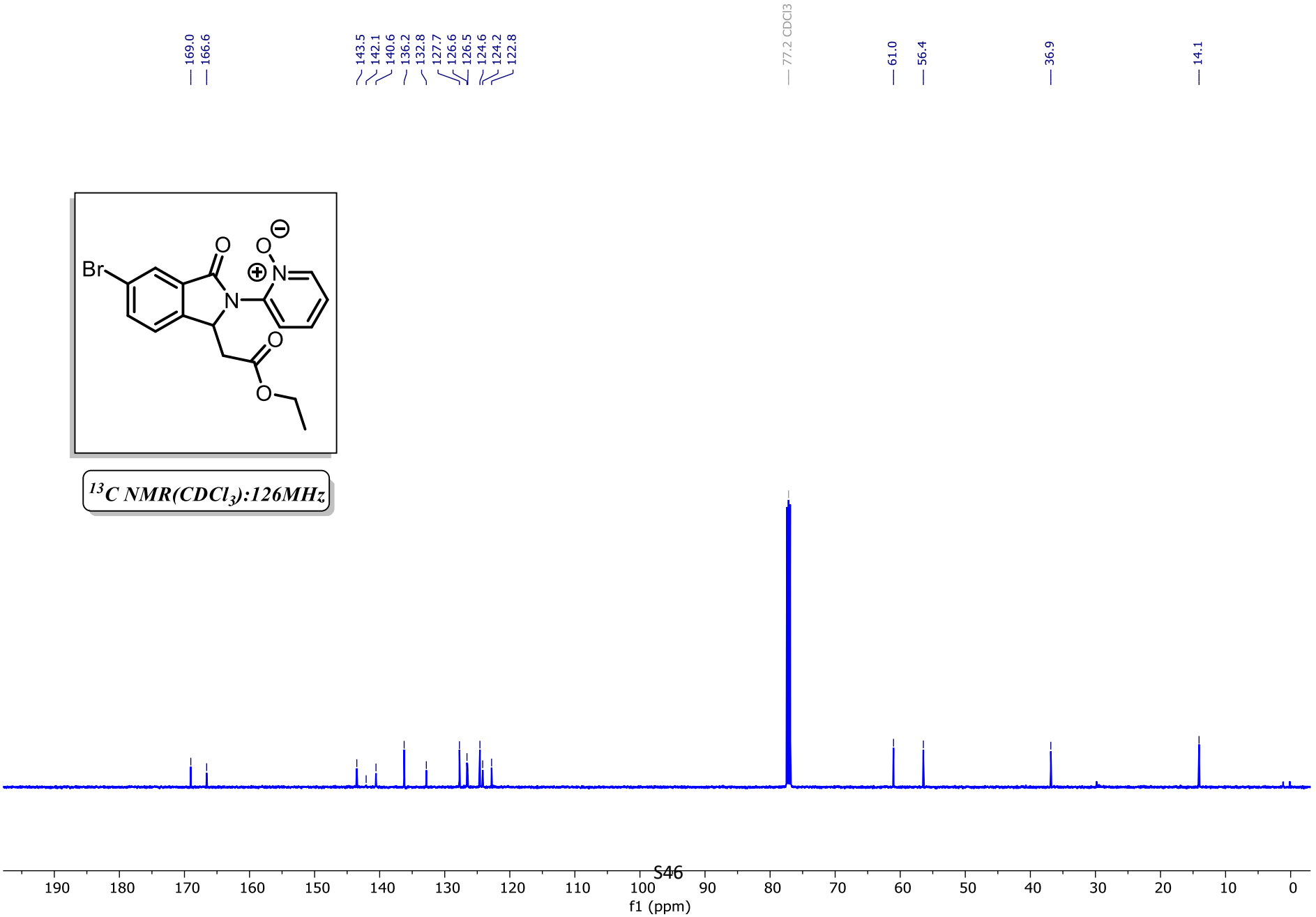
2-(5-bromo-1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3g)



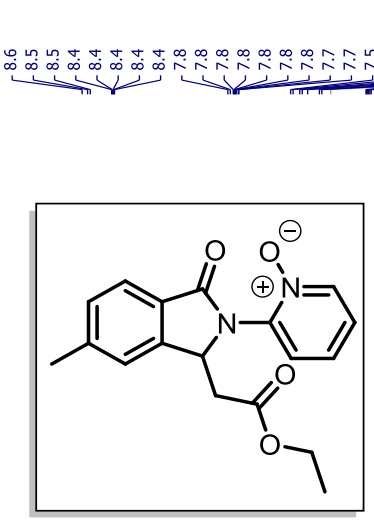
^{1}H NMR($CDCl_3$):500MHz



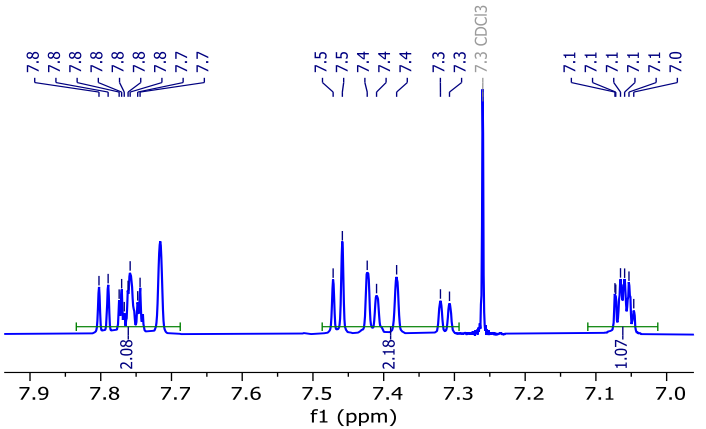


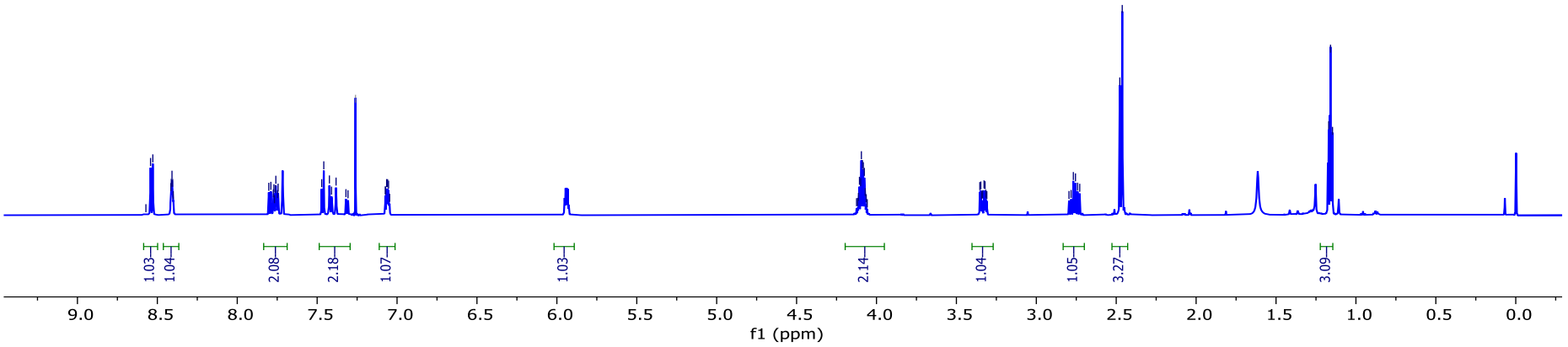

169.0
166.6
143.5
142.1
140.6
136.2
132.8
127.7
126.6
126.5
124.6
124.2
122.8
77.2 CDCl3
61.0
56.4
36.9
14.1
Br
O
O
N
N
O
O
13C NMR(CDCl3):126MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

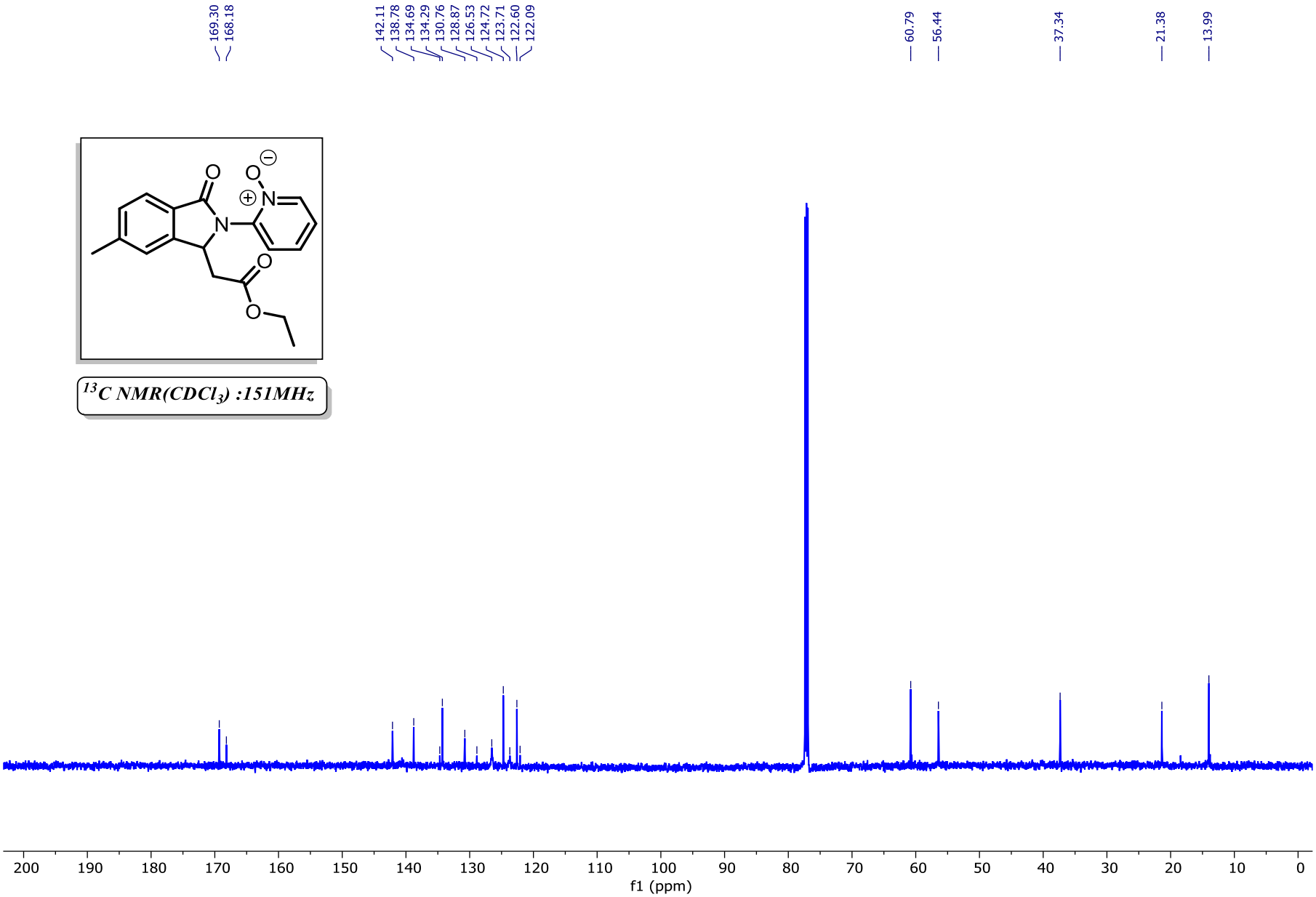
2-(3-(2-ethoxy-2-oxoethyl)-5-methyl-1-oxoisoindolin-2-yl)pyridine 1-oxide (3h)



^{1}H NMR(CDCl$_3$):600MHz

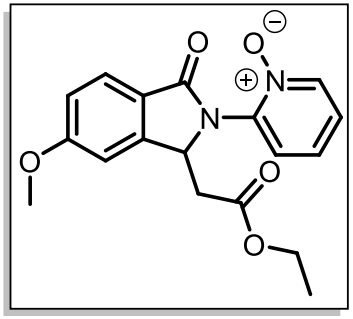




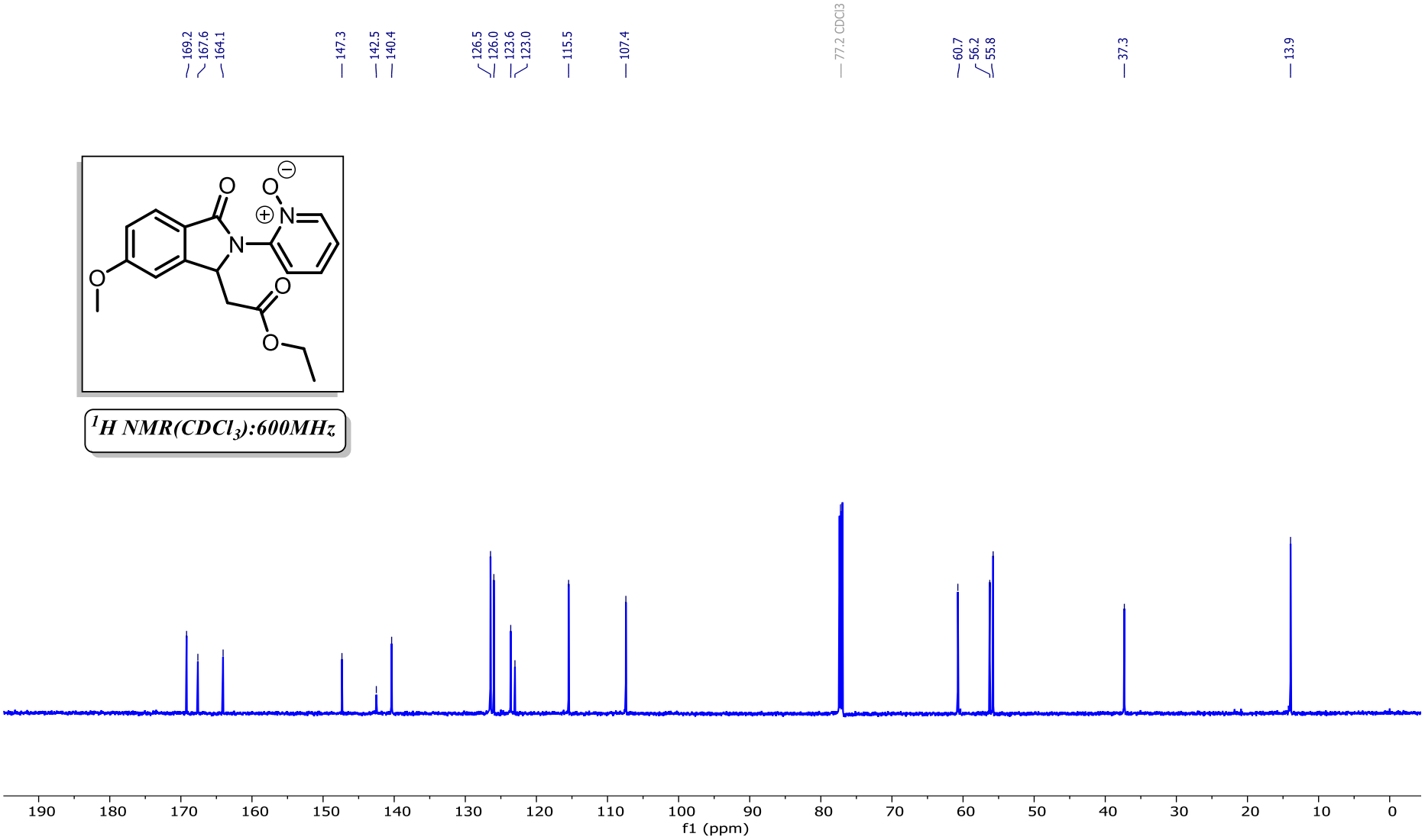


^{13}C NMR($CDCl_3$) :151MHz

2-(3-(2-ethoxy-2-oxoethyl)-5-methoxy-1-oxoisoindolin-2-yl)pyridine 1-oxide (3i)

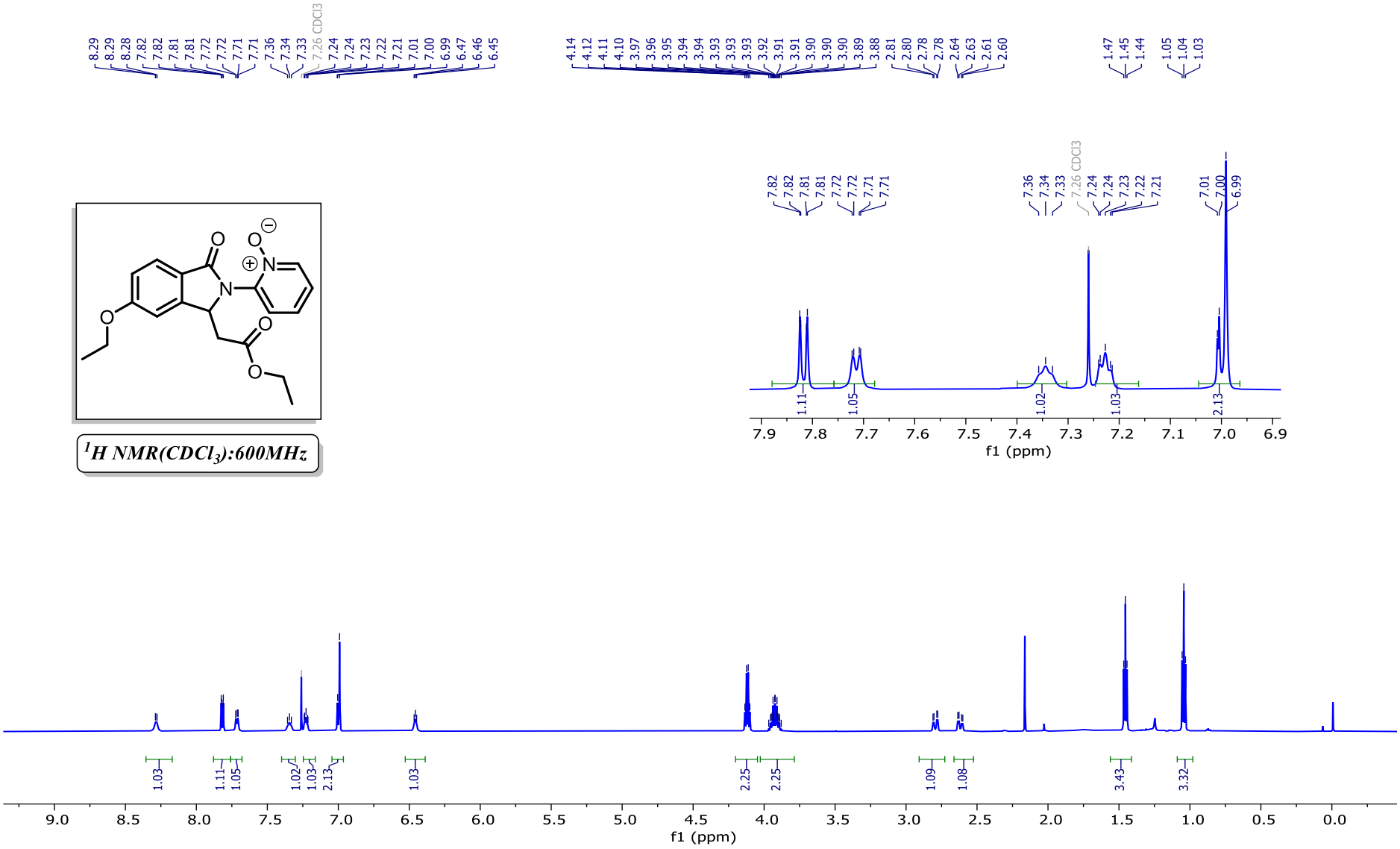


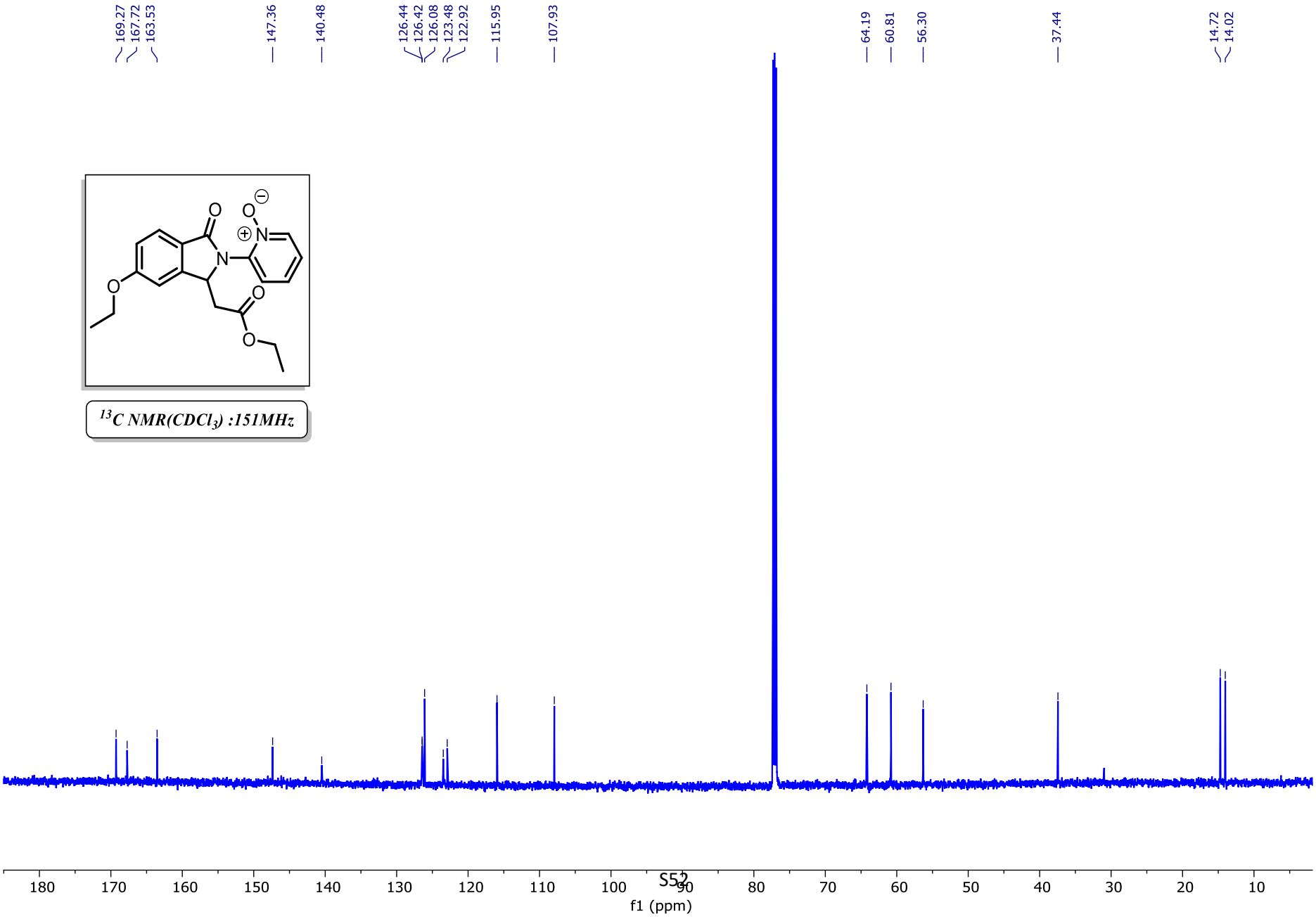
^{1}H NMR($CDCl_3$):600MHz



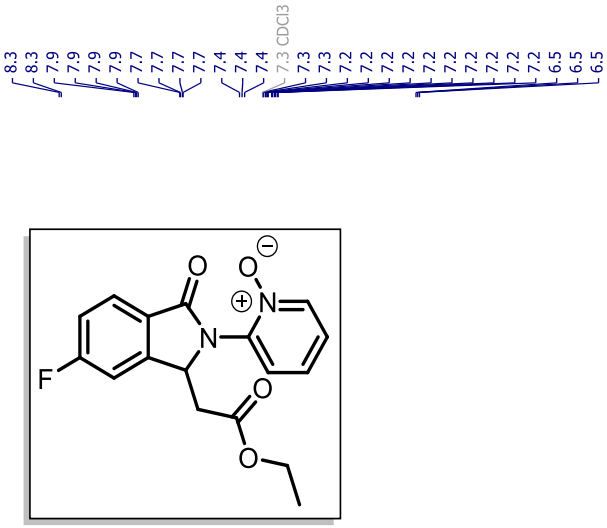
^{1}H NMR(CDCl$_3$):600MHz

2-(5-ethoxy-3-(2-ethoxy-2-oxoethyl)-1-oxoisoindolin-2-yl)pyridine 1-oxide (3j)

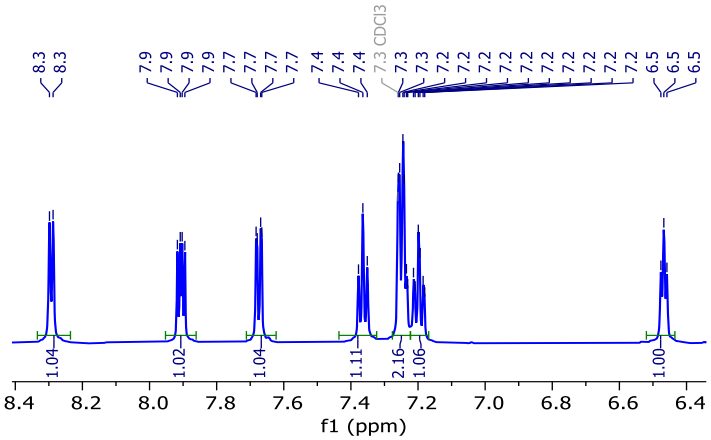


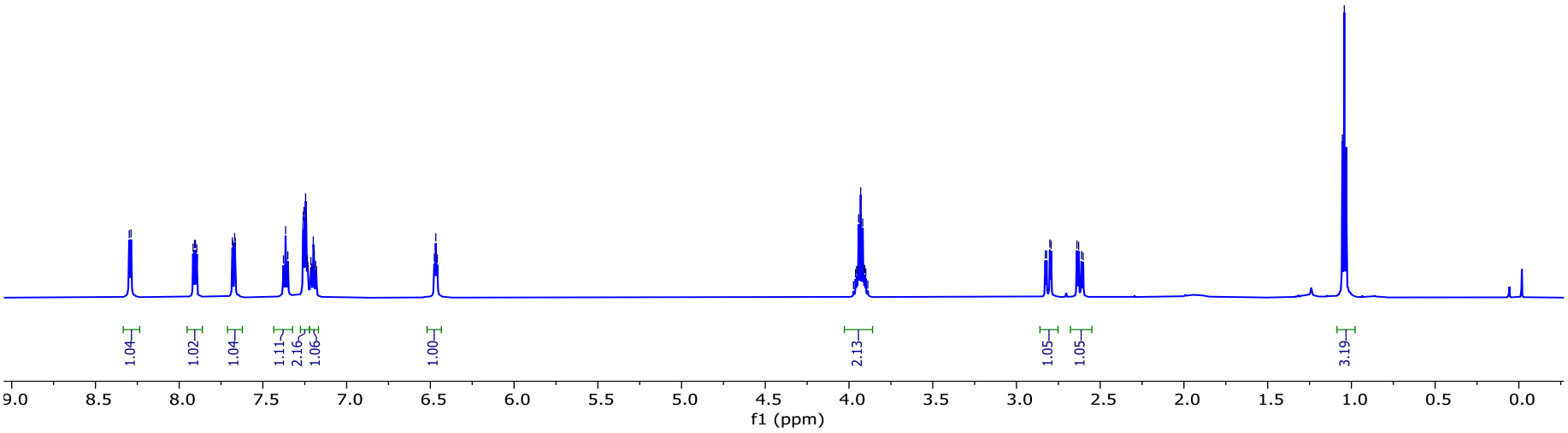

169.27
167.72
163.53
147.36
140.48
126.44
126.42
126.08
123.48
122.92
115.95
107.93
64.19
60.81
56.30
37.44
14.72
14.02
O
O
N
N
O
O
O
O
^{13}C NMR(CDCl$_3$) :151MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

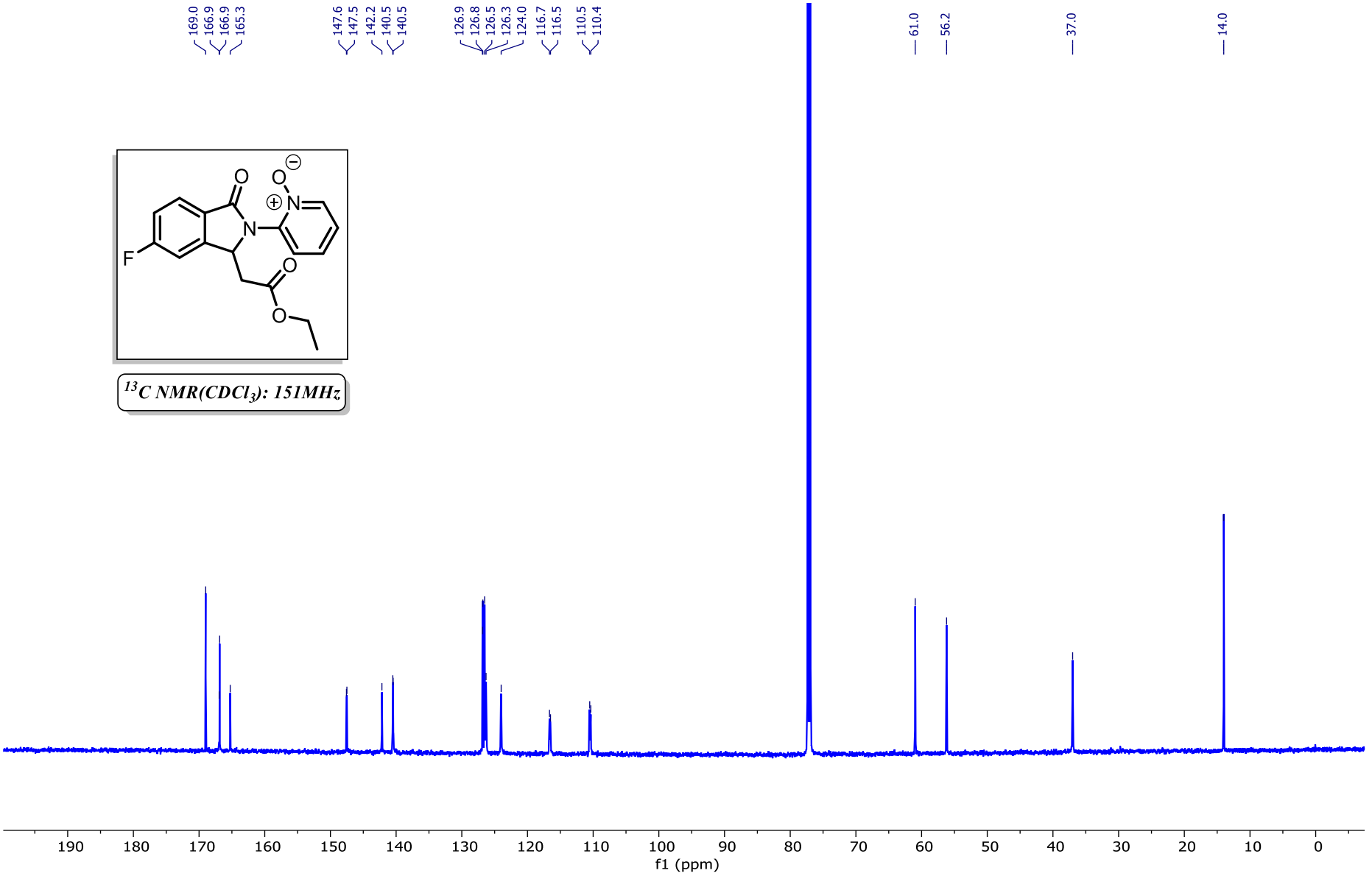
2-(3-(2-ethoxy-2-oxoethyl)-5-fluoro-1-oxoisoindolin-2-yl)pyridine 1-oxide (3k)



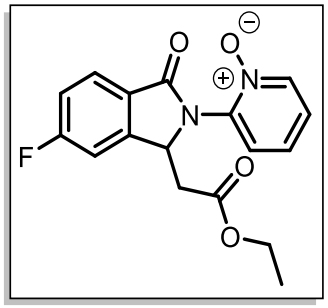
^{1}H NMR($CDCl_3$):600MHz





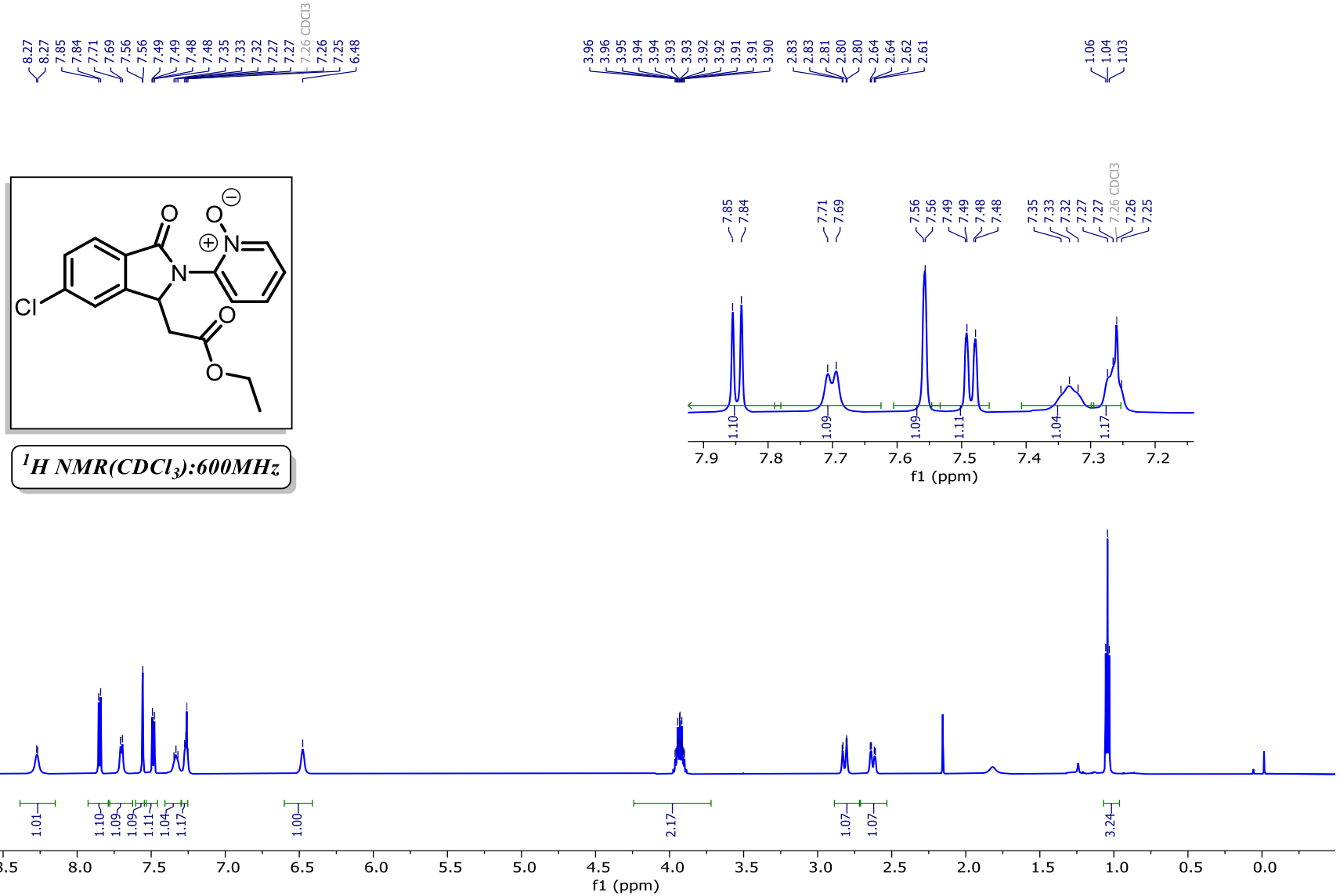


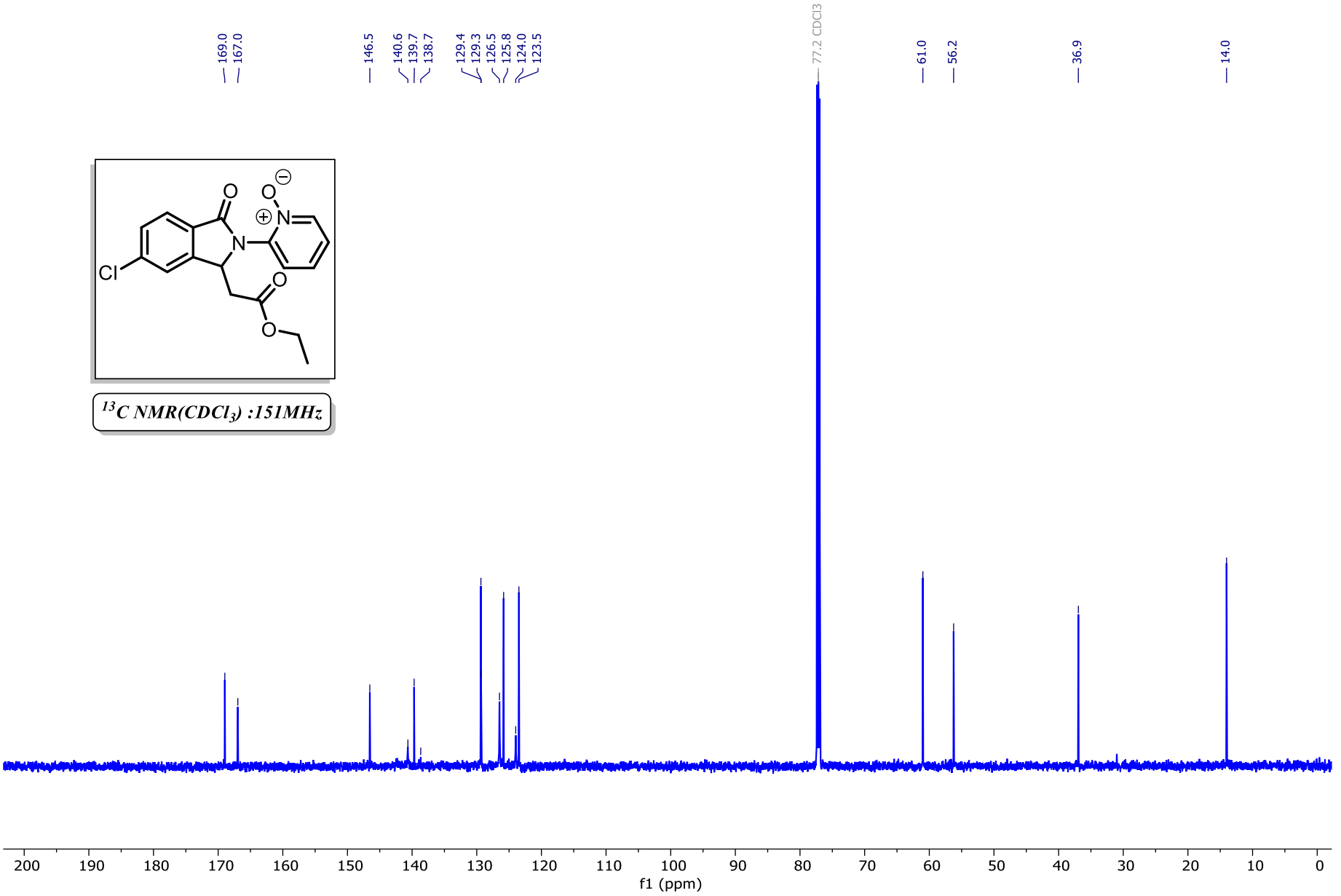
^{13}C NMR($CDCl_3$): 151MHz



^{19}F NMR (565 MHz)

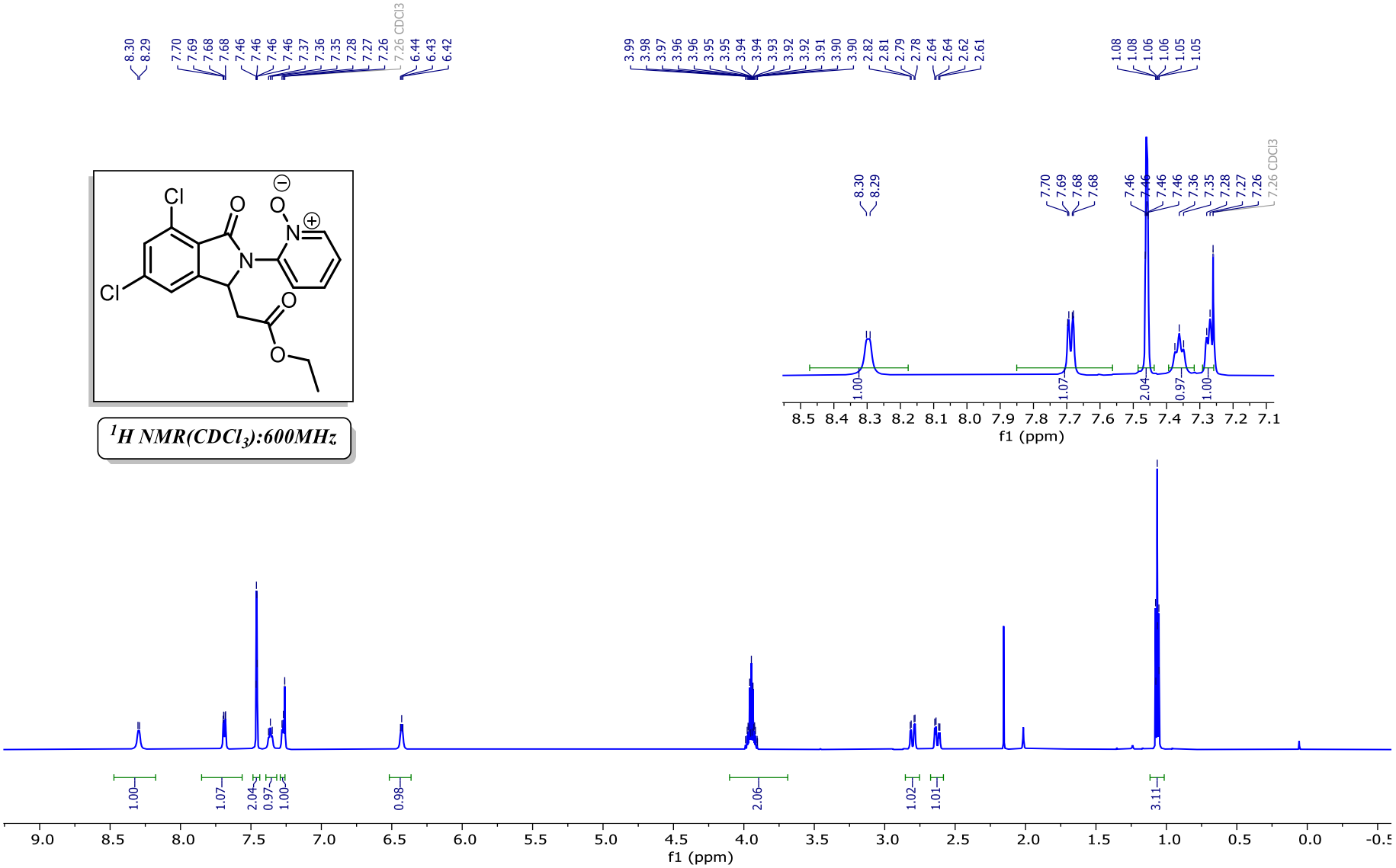
2-(5-chloro-3-(2-ethoxy-2-oxoethyl)-1-oxoisoindolin-2-yl)pyridine 1-oxide (3l)

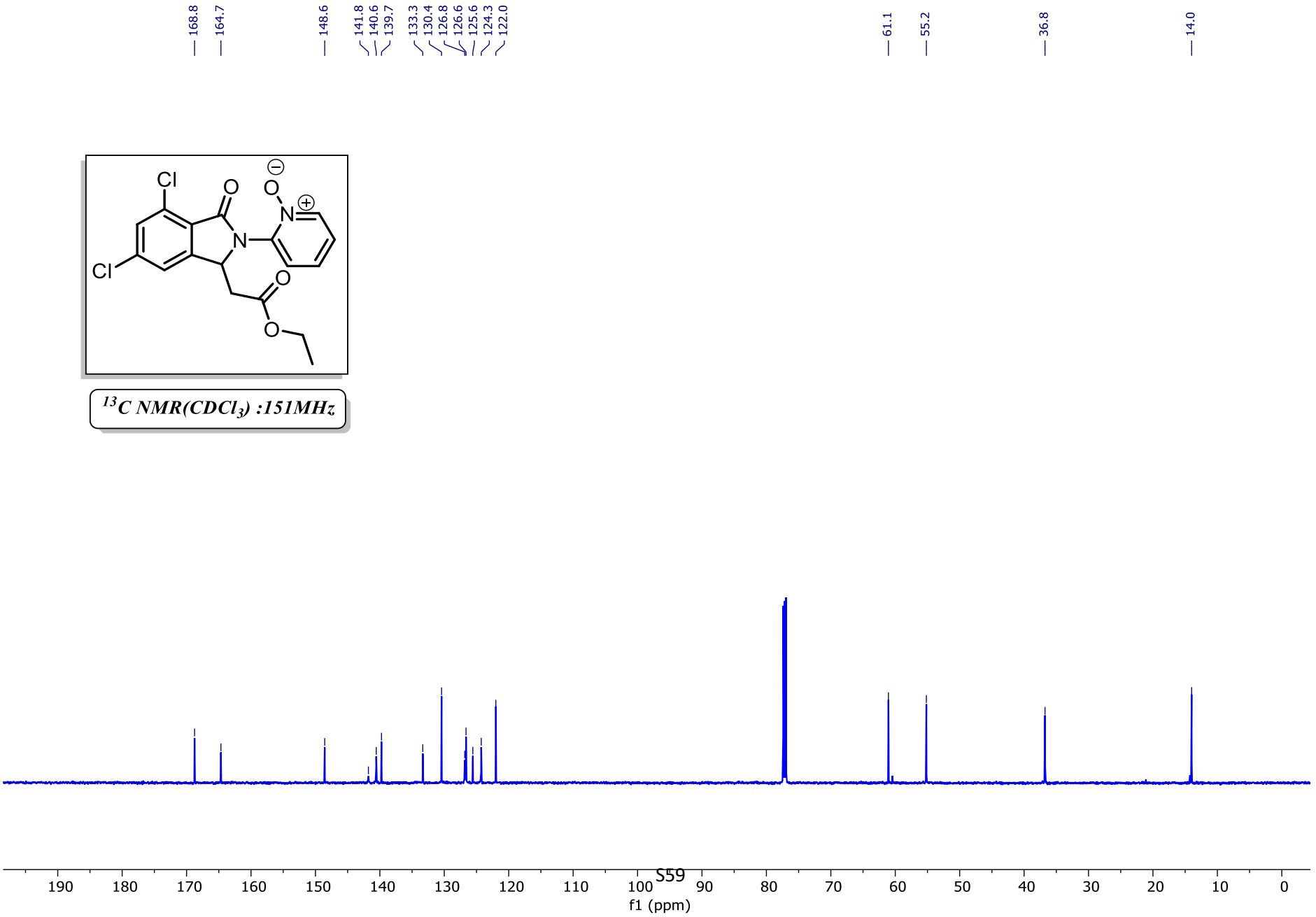




^{13}C NMR($CDCl_3$) :151MHz

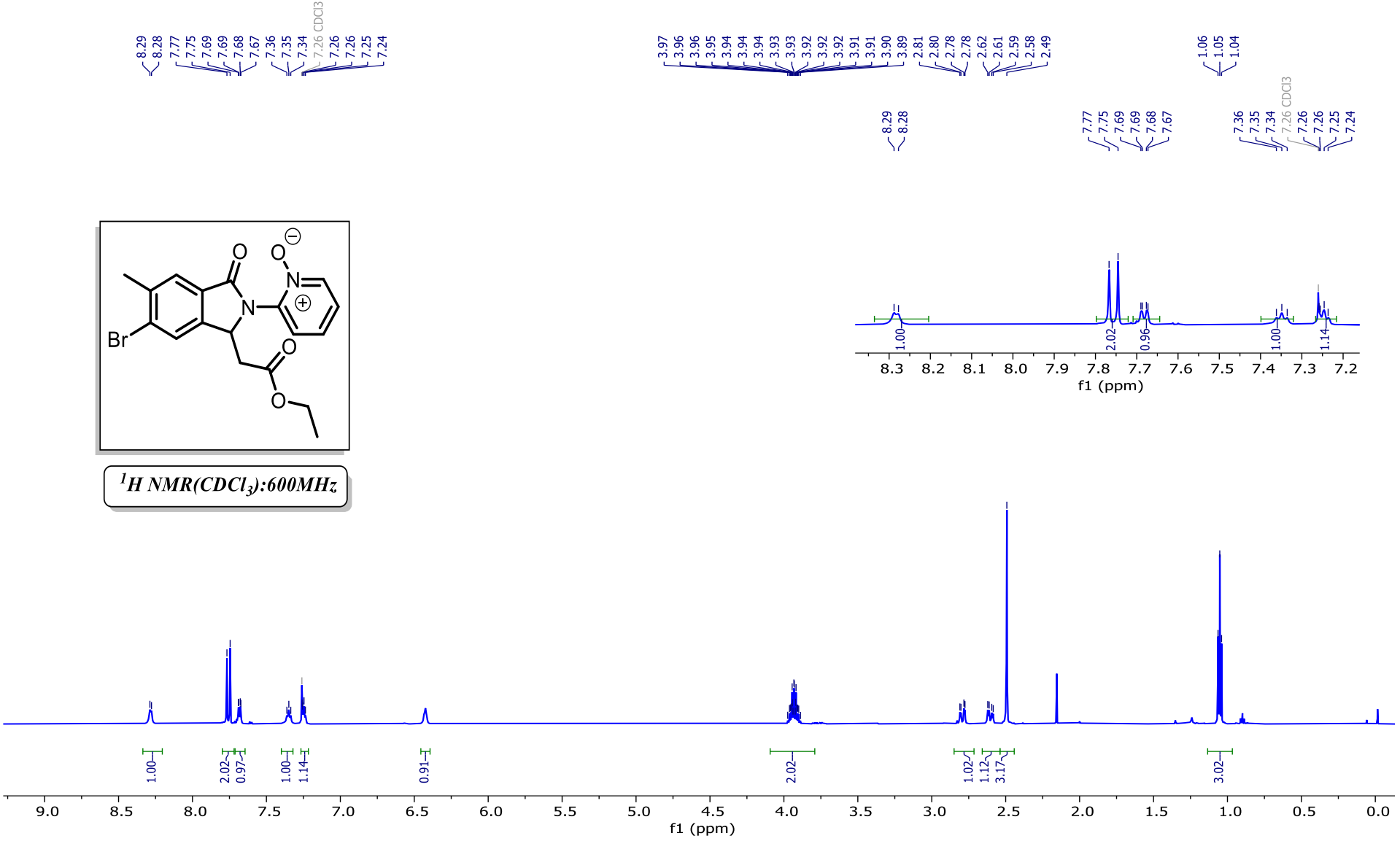
2-(4,6-dichloro-1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3n)

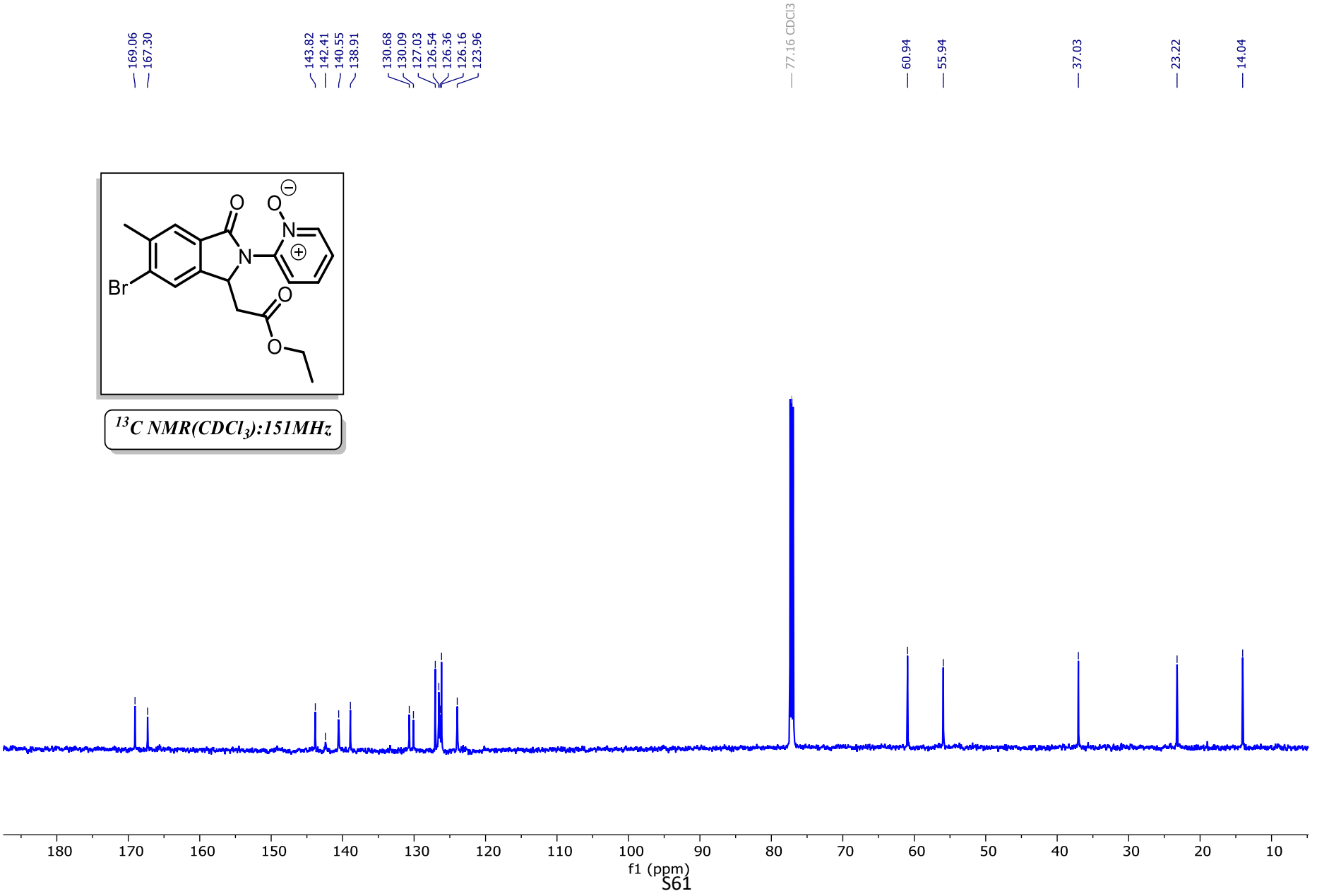




^{13}C NMR($CDCl_3$) :151MHz

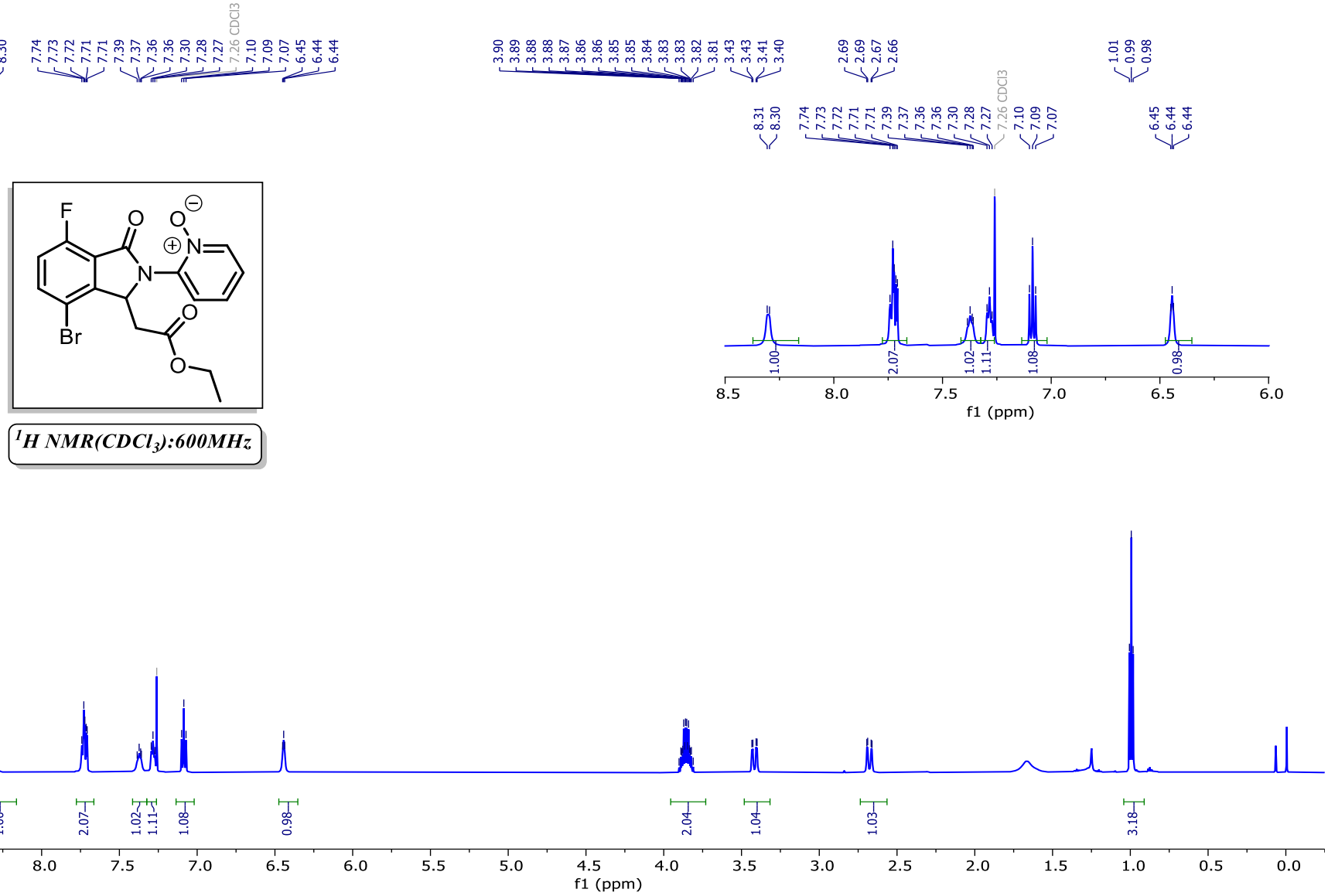
2-(5-bromo-3-(2-ethoxy-2-oxoethyl)-6-methyl-1-oxoisoindolin-2-yl)pyridine 1-oxide (3o)



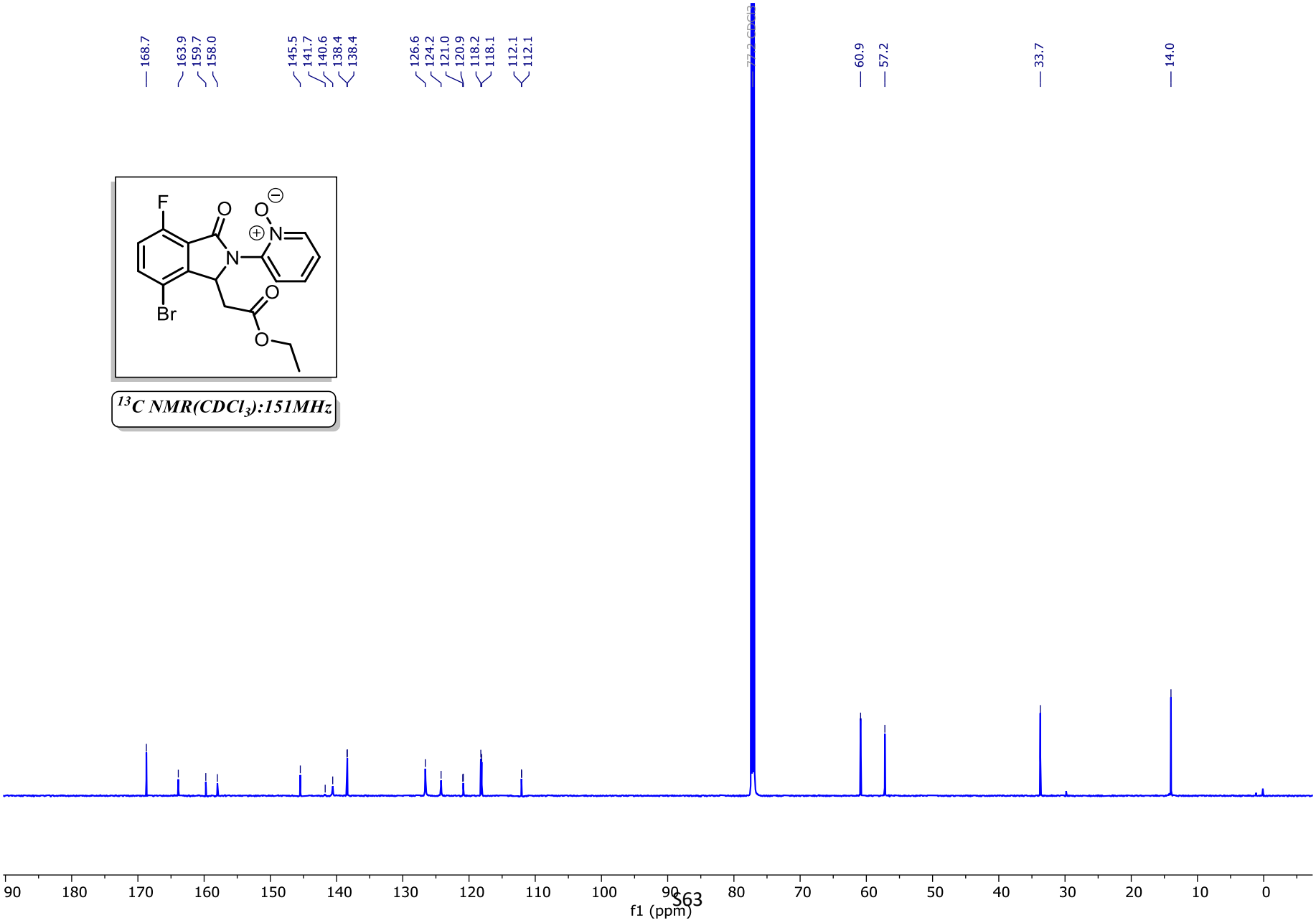


^{13}C NMR($CDCl_3$):151MHz

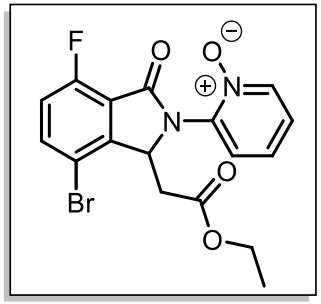
2-(4-bromo-3-(2-ethoxy-2-oxoethyl)-7-fluoro-1-oxoisoindolin-2-yl)pyridine 1-oxide (3p)



^{1}H NMR($CDCl_3$):600MHz

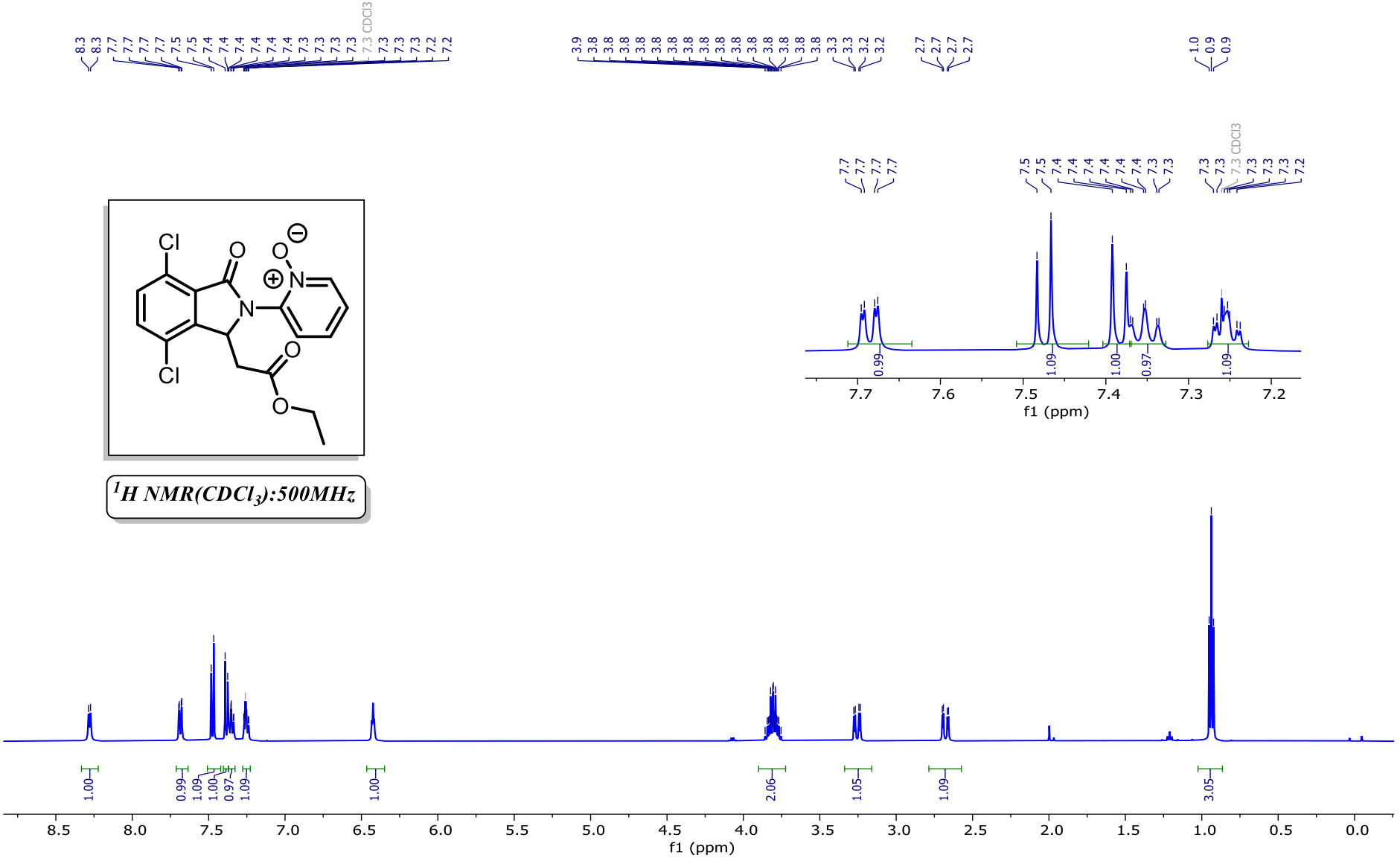


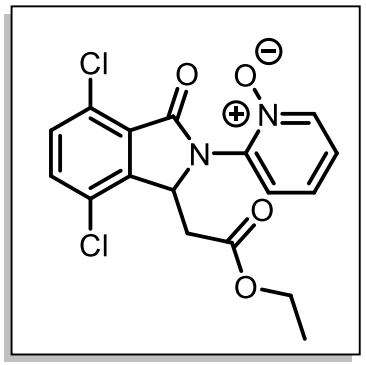
^{13}C NMR($CDCl_3$):151MHz



^{19}F NMR ($CDCl_3$): 377 MHz

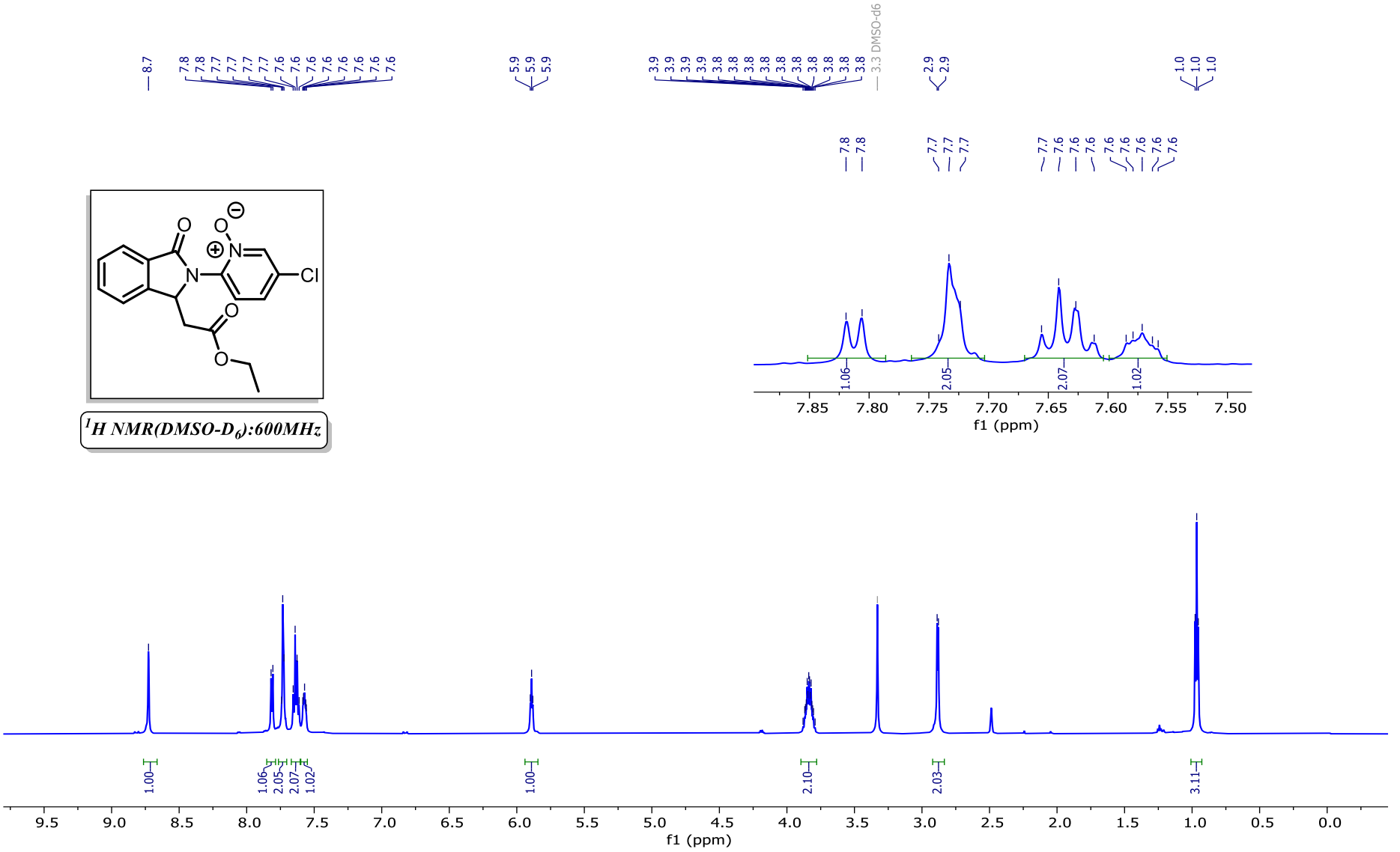
2-(4,7-dichloro-1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3q)



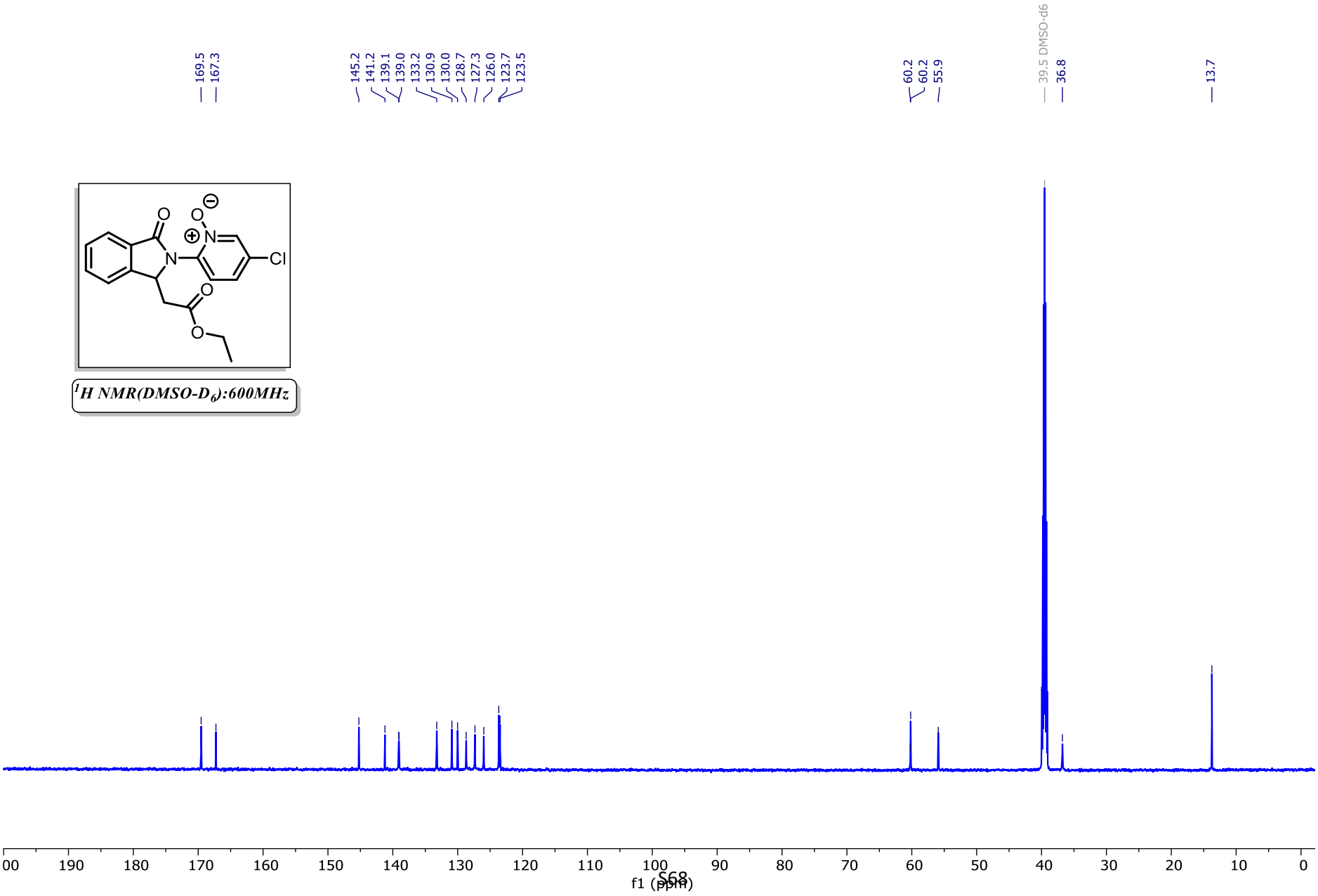


^{13}C NMR($CDCl_3$):126MHz

5-chloro-2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3t)



^{1}H NMR(DMSO-D_6):600MHz


169.5
167.3
145.2
141.2
139.1
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133.2
130.9
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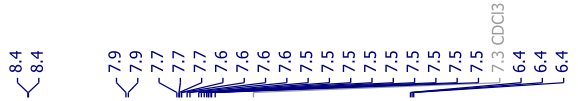
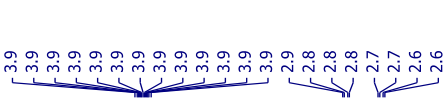
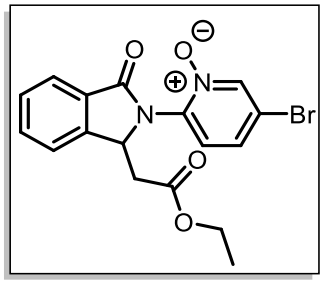
128.7
127.3
126.0
123.7
123.5
60.2
60.2
55.9
39.5 DMSO-d6
36.8
13.7
Cl
^{1}H NMR(DMSO-D$_6$):600MHz
f1 (ppm)

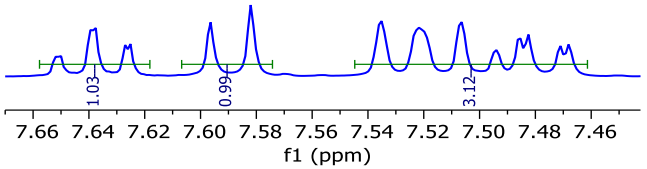
5-bromo-2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3u)

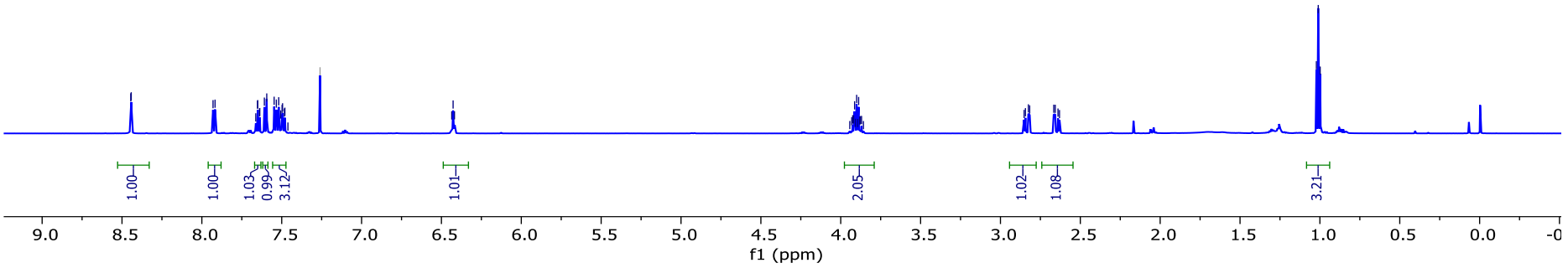


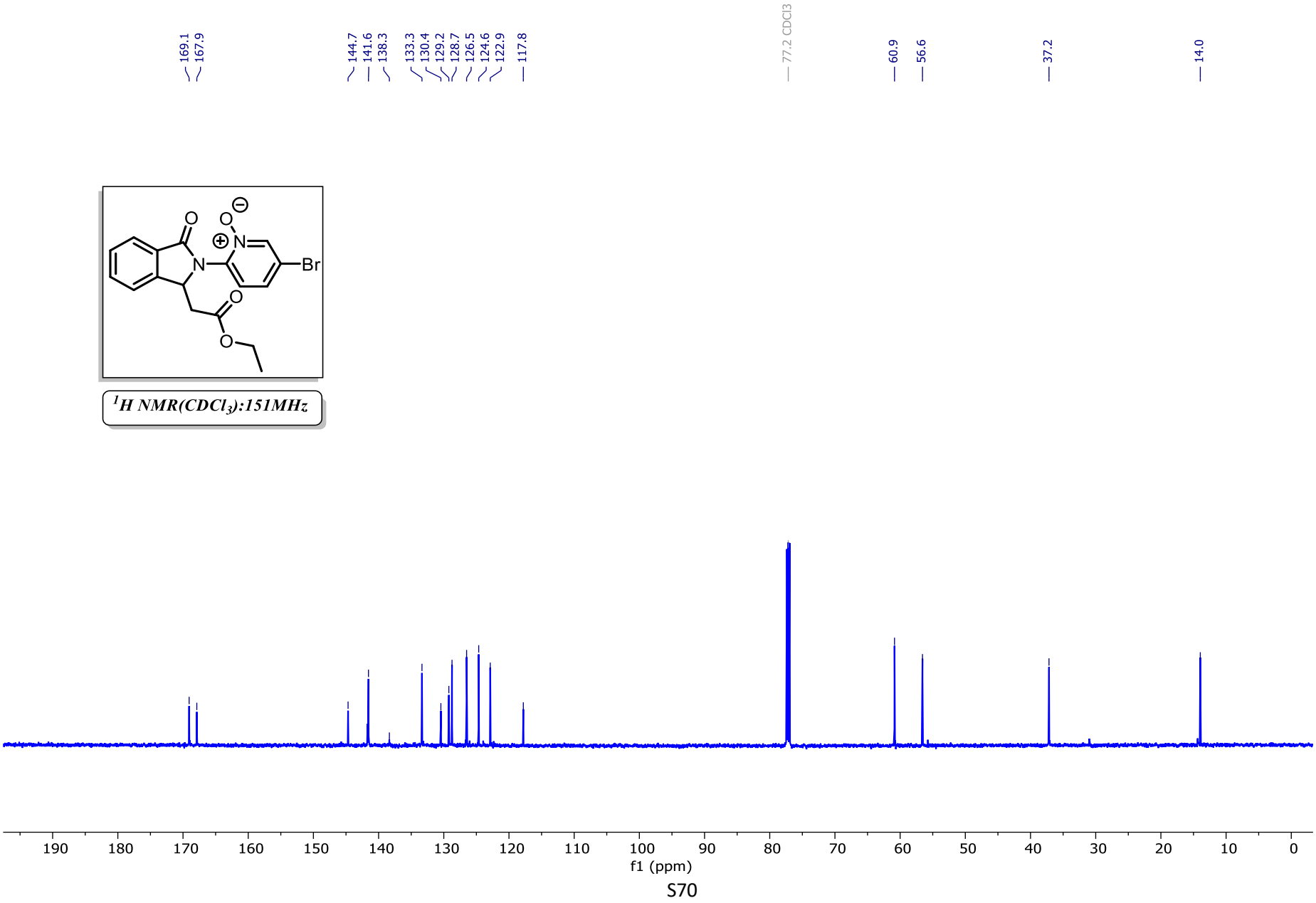




^{1}H NMR($CDCl_3$):600MHz

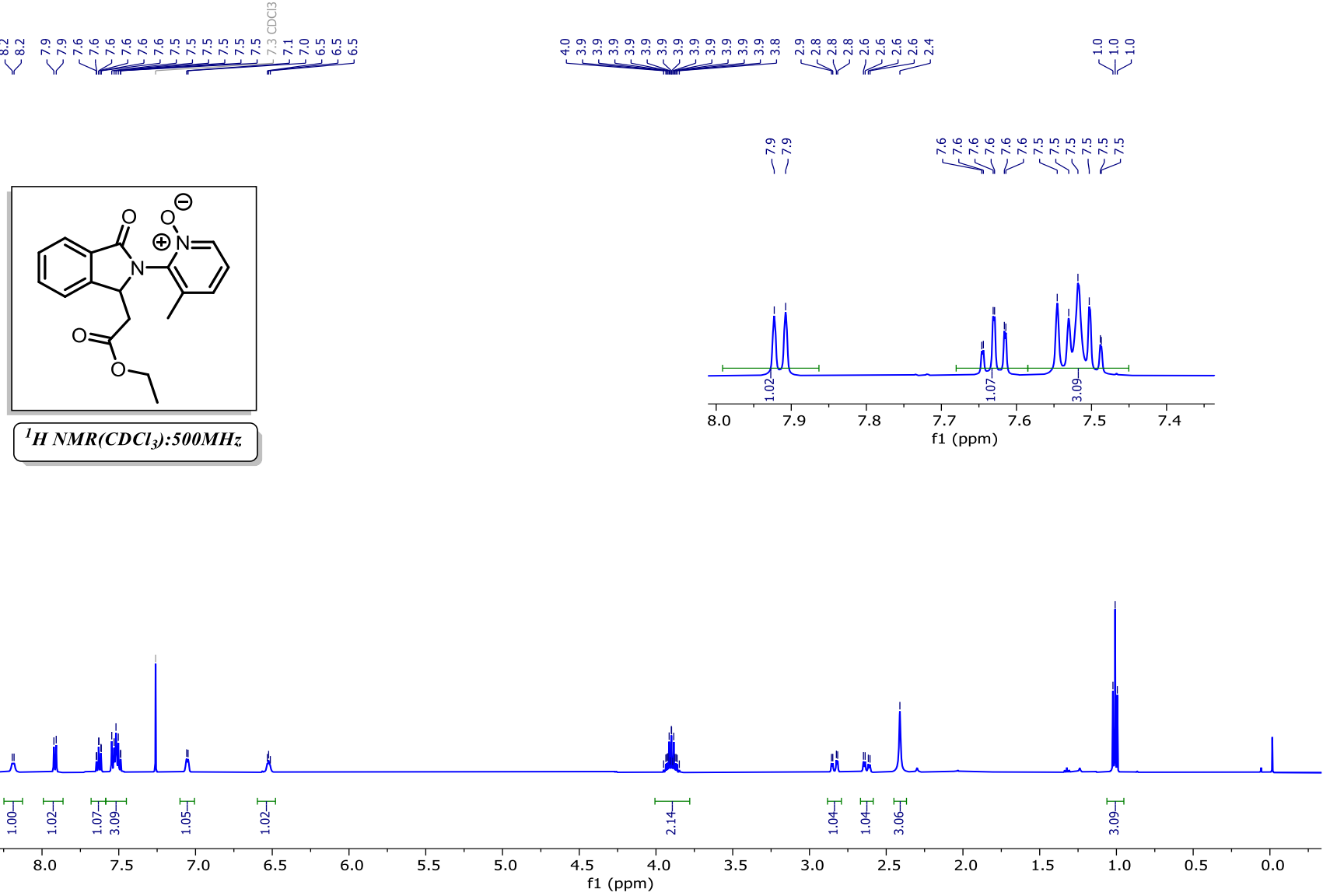




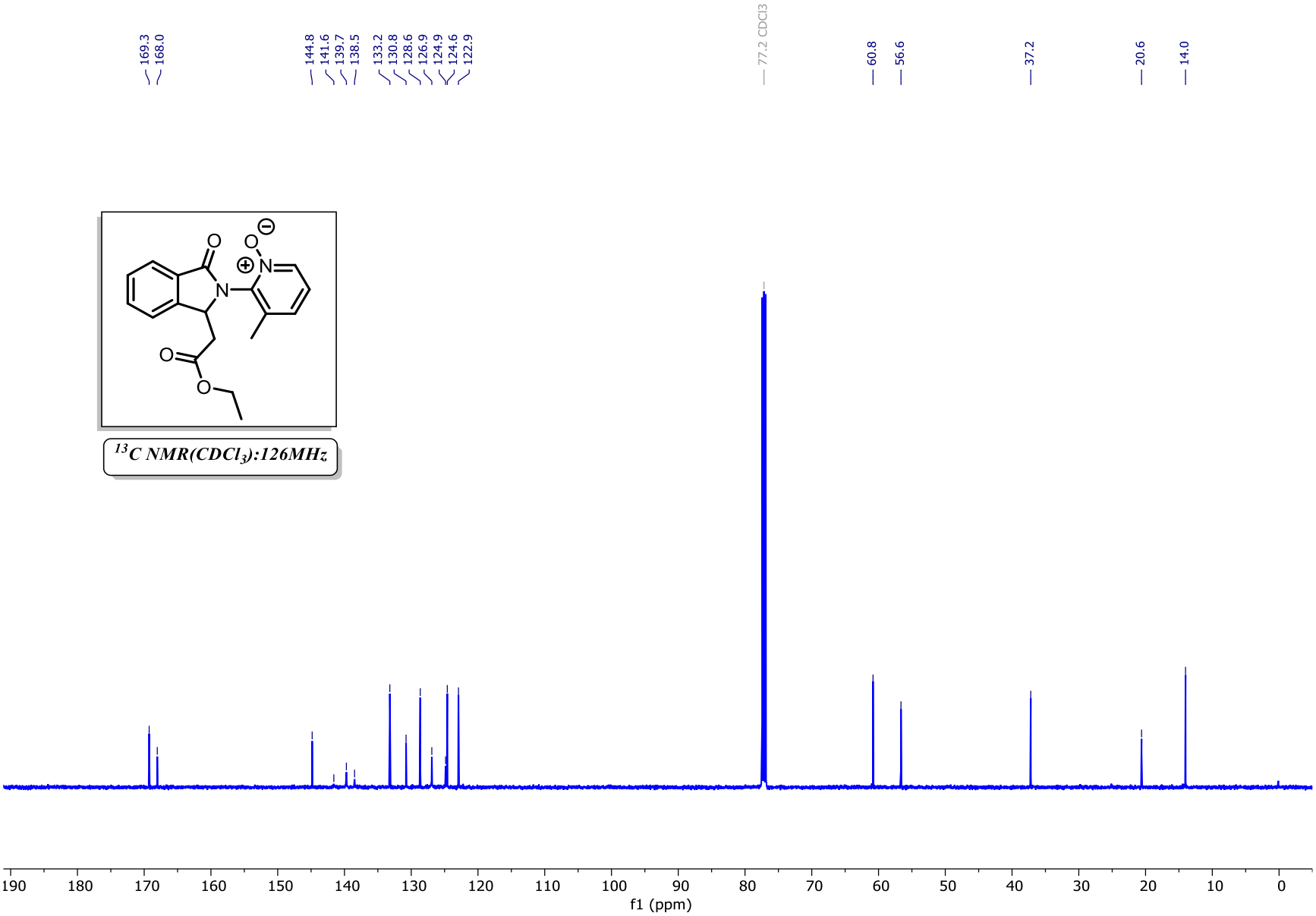


^{1}H NMR($CDCl_3$):151MHz

2-(1-(2-ethoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)-3-methylpyridine 1-oxide (3v)

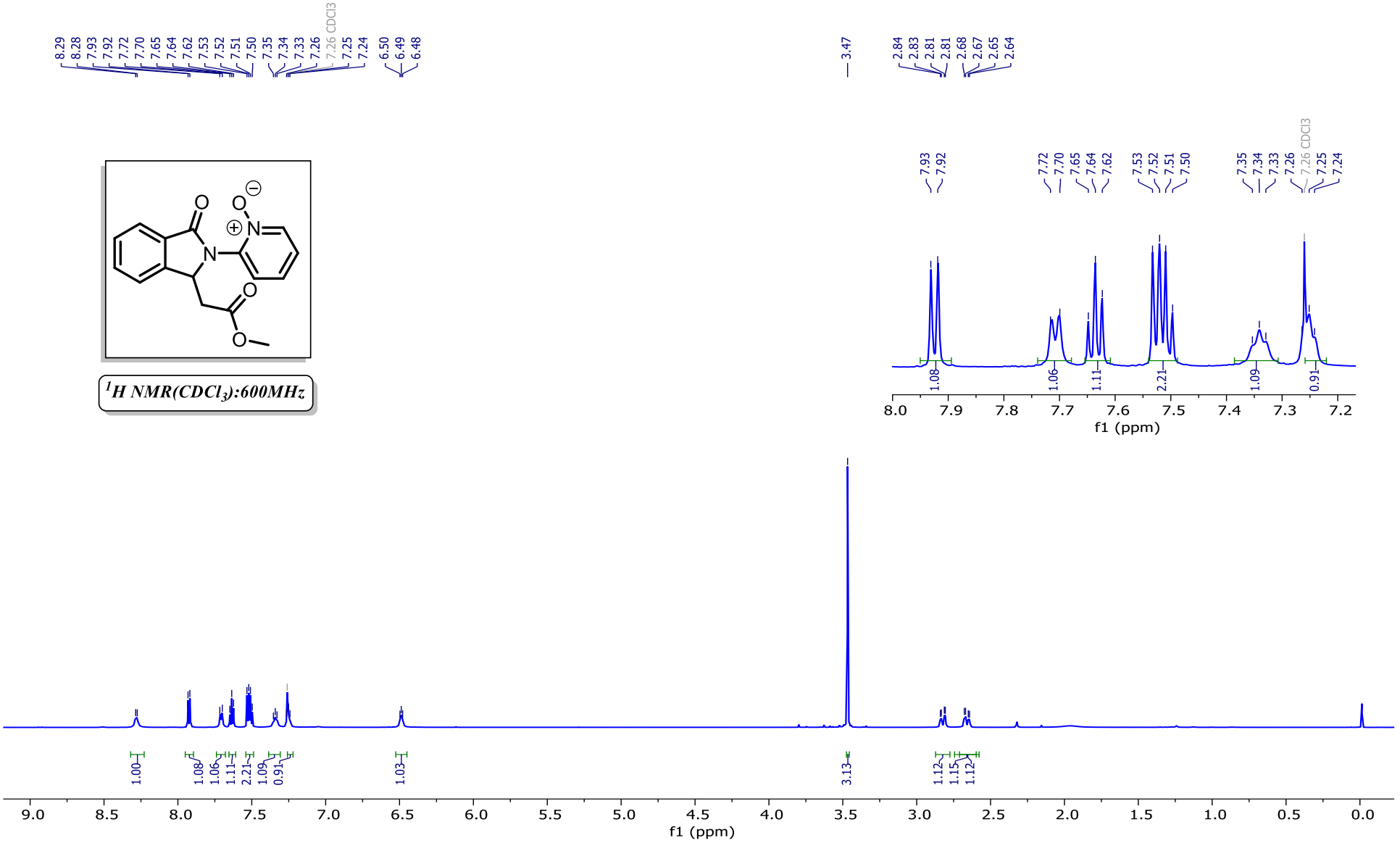


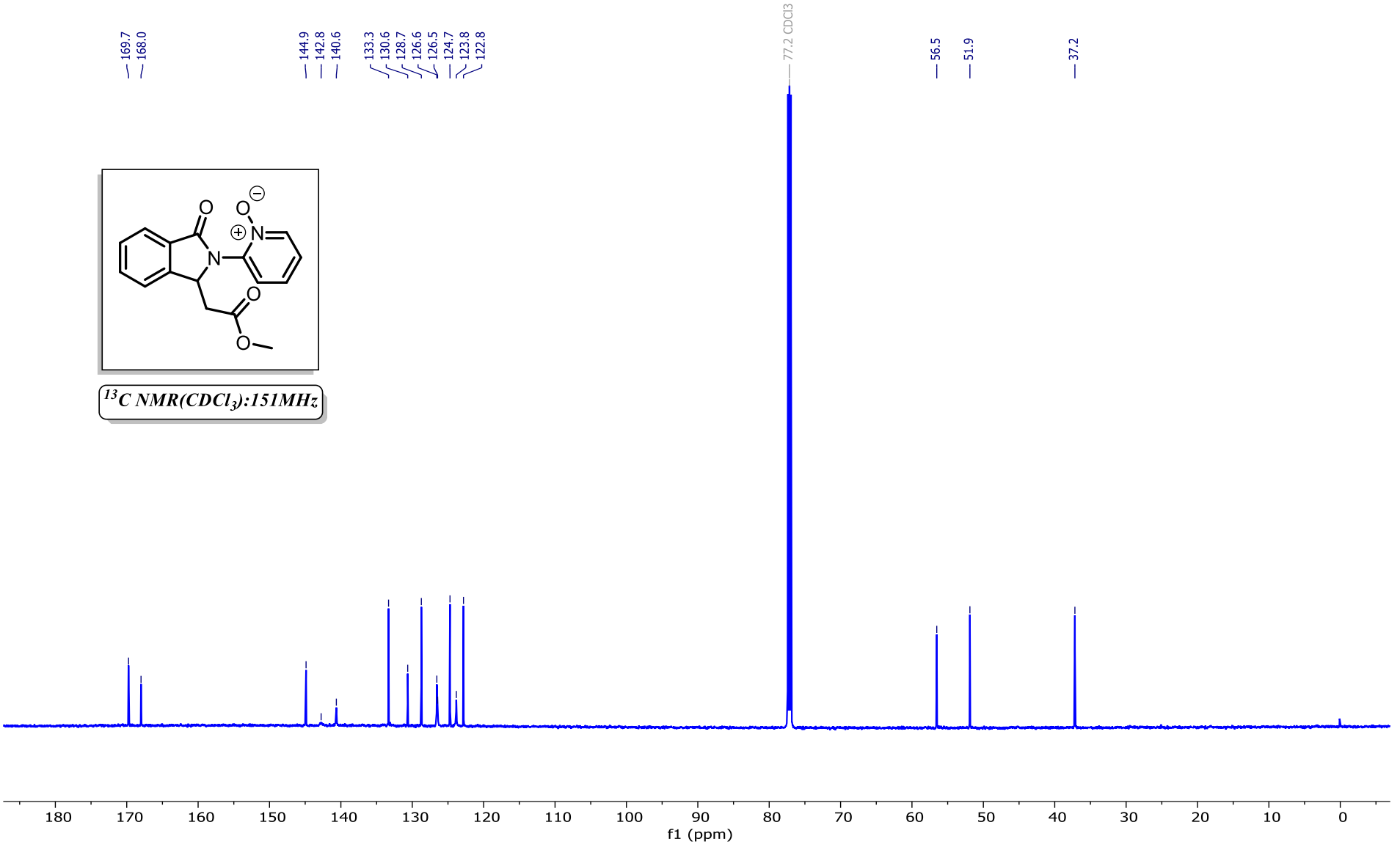
^1H NMR($CDCl_3$):500MHz



^{13}C NMR($CDCl_3$):126MHz

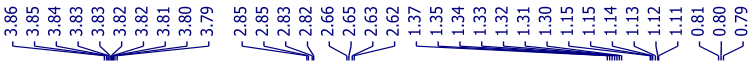
2-(1-(2-methoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3w)

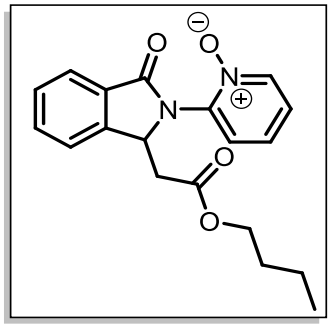


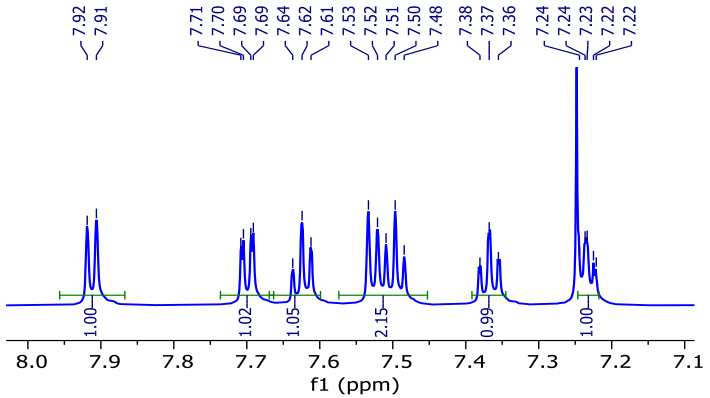


^{13}C NMR($CDCl_3$):151MHz

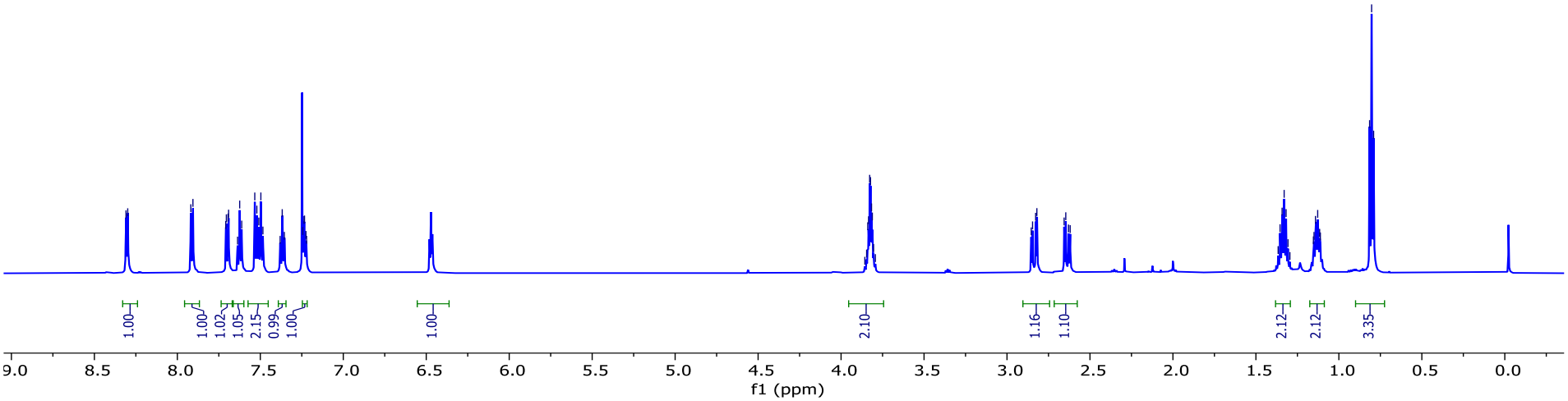
2-(1-(2-butoxy-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3x)

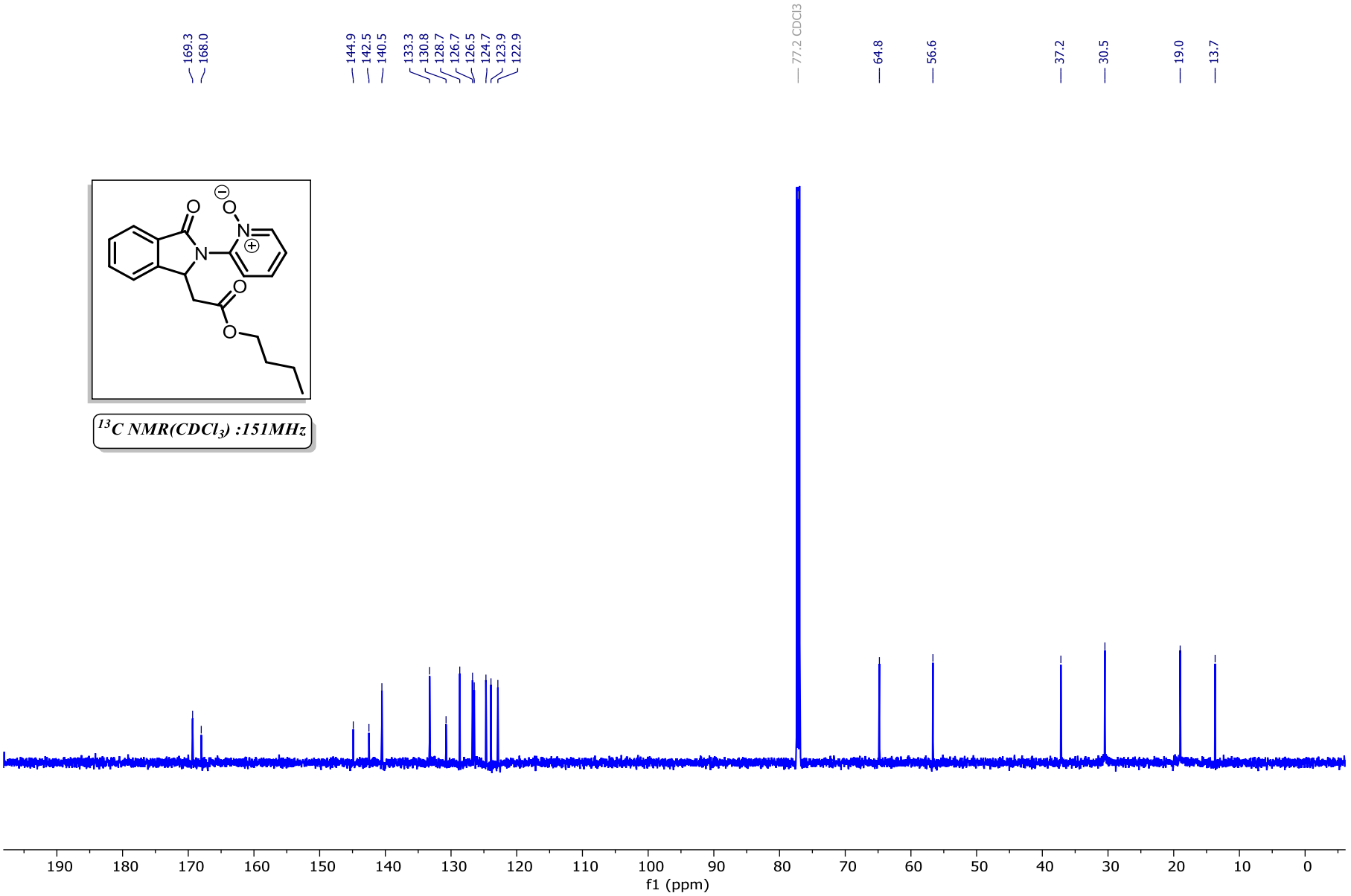






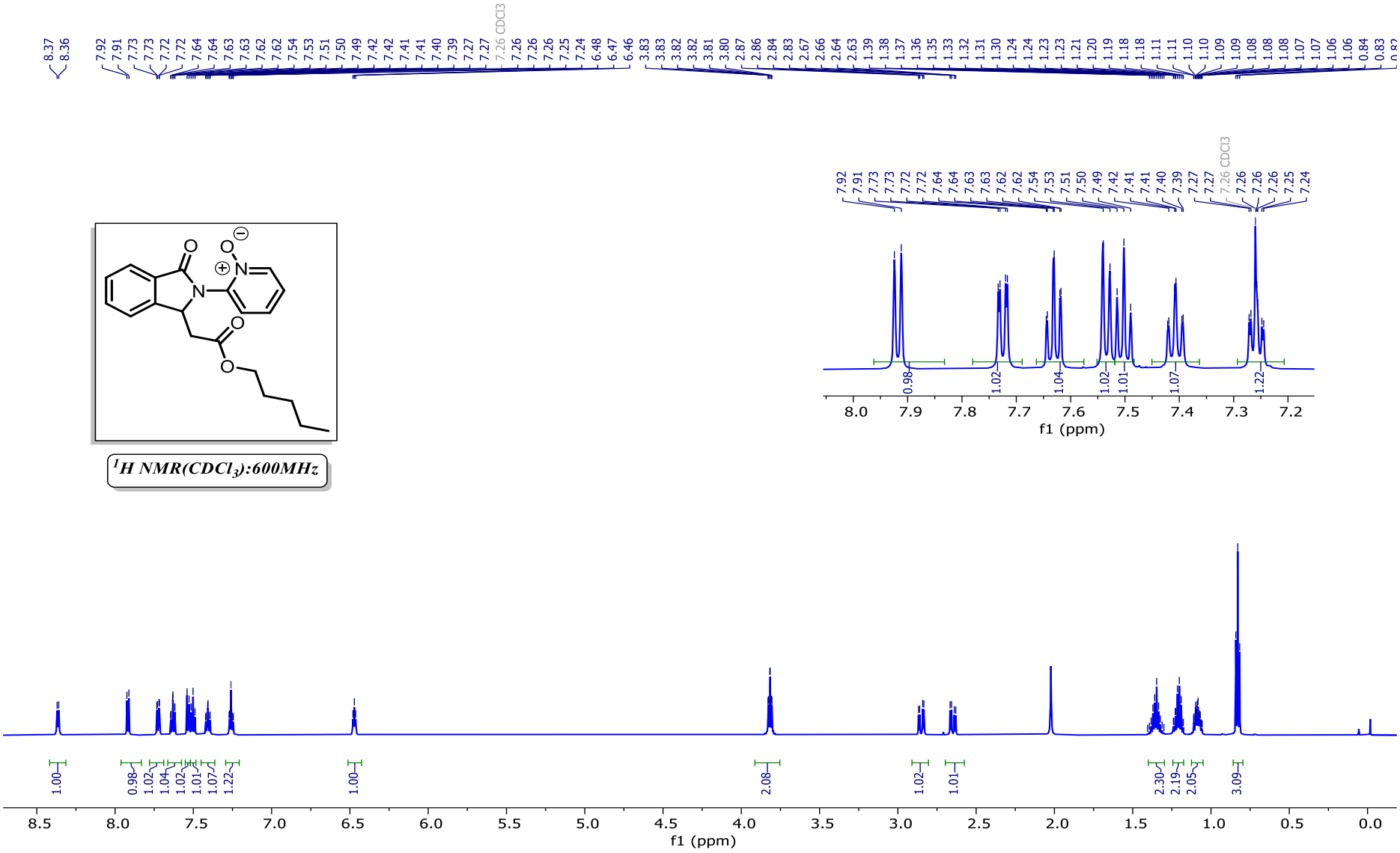
^{1}H NMR(CDCl$_3$):600MHz

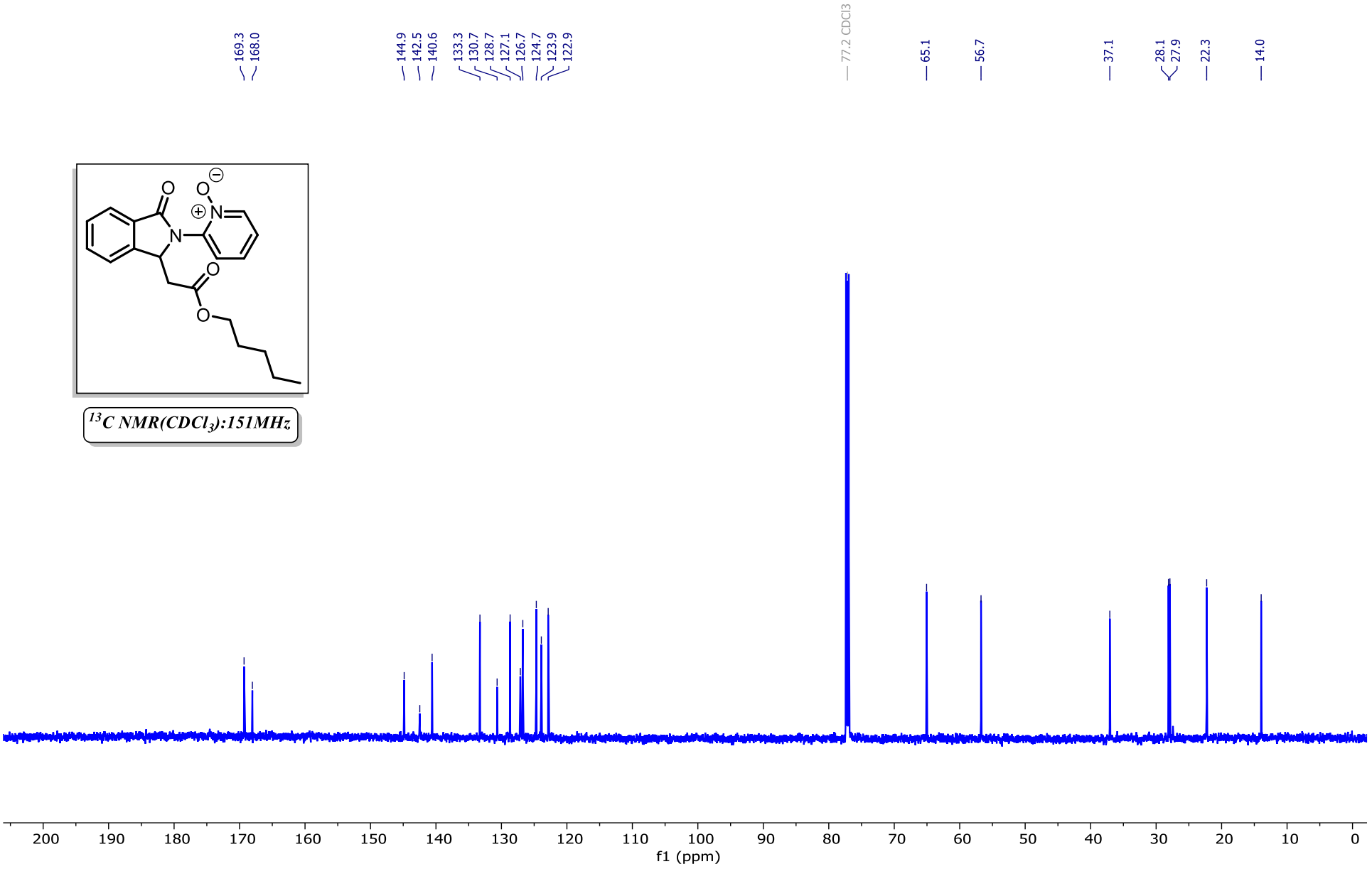




^{13}C NMR($CDCl_3$) :151MHz

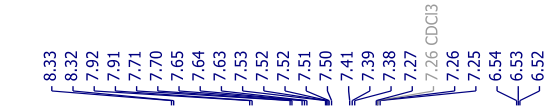
2-(1-oxo-3-(2-oxo-2-(pentyloxy)ethyl)isoindolin-2-yl)pyridine 1-oxide (3y)

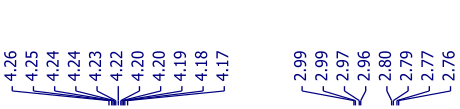


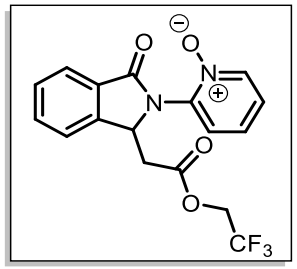


^{13}C NMR($CDCl_3$):151MHz

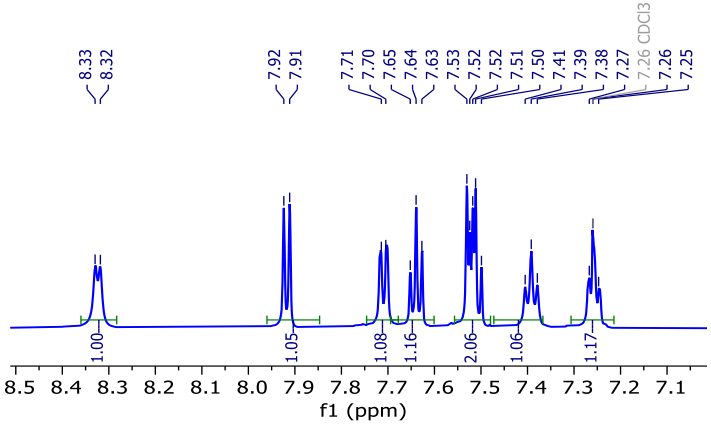
2-(1-oxo-3-(2-oxo-2-(2,2,2-trifluoroethoxy)ethyl)isoindolin-2-yl)pyridine 1-oxide (3z)

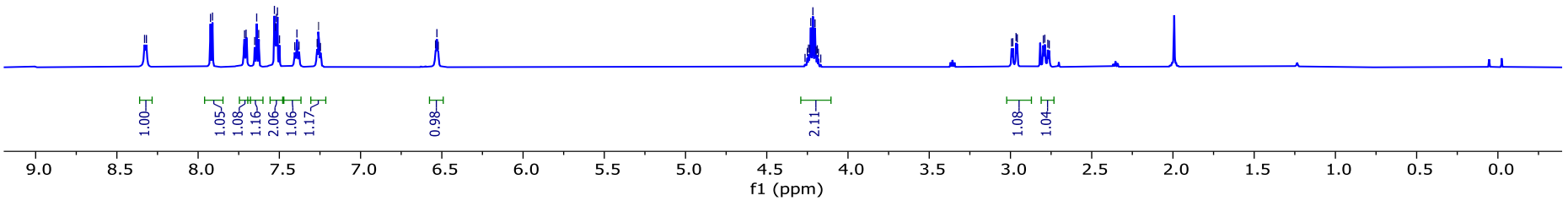


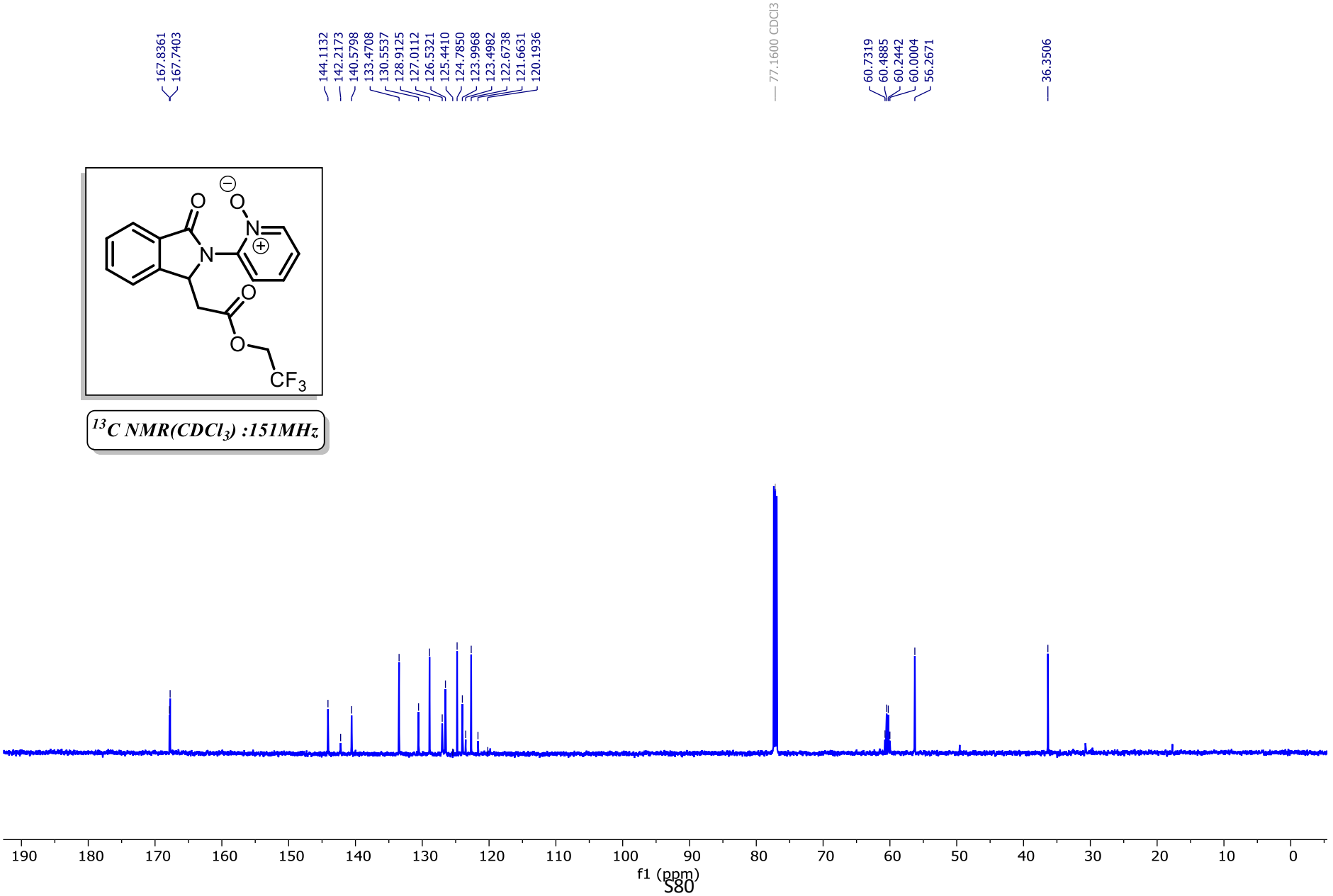




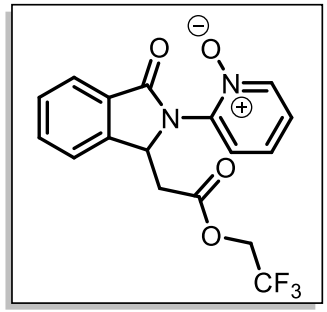
^{1}H NMR($CDCl_3$):600MHz



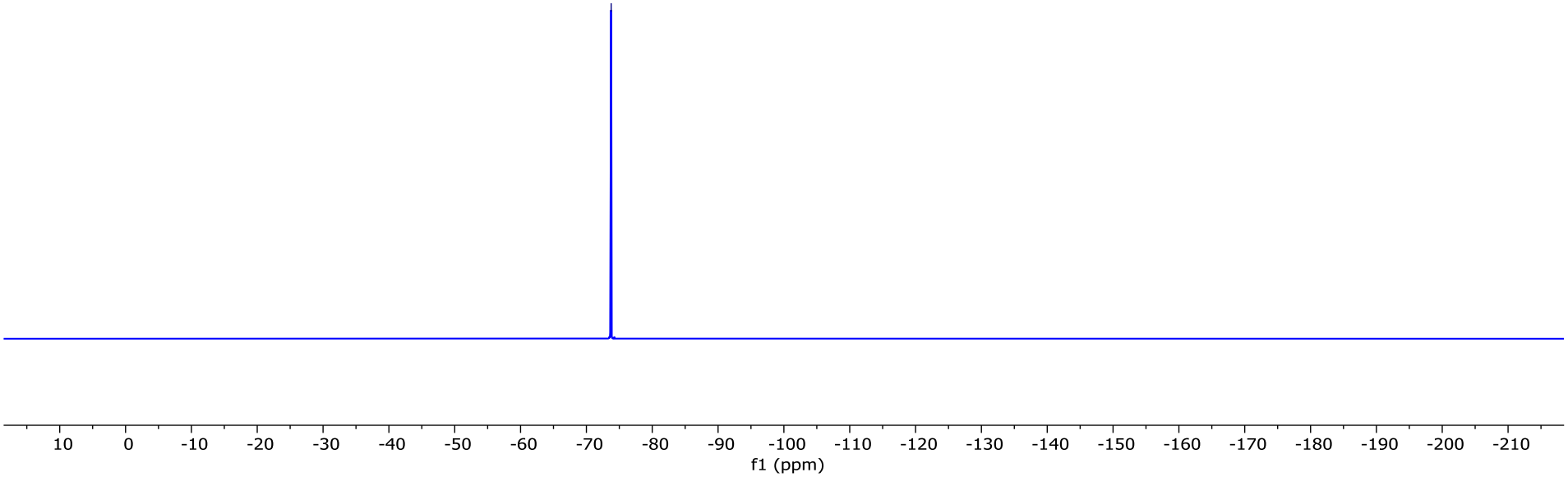




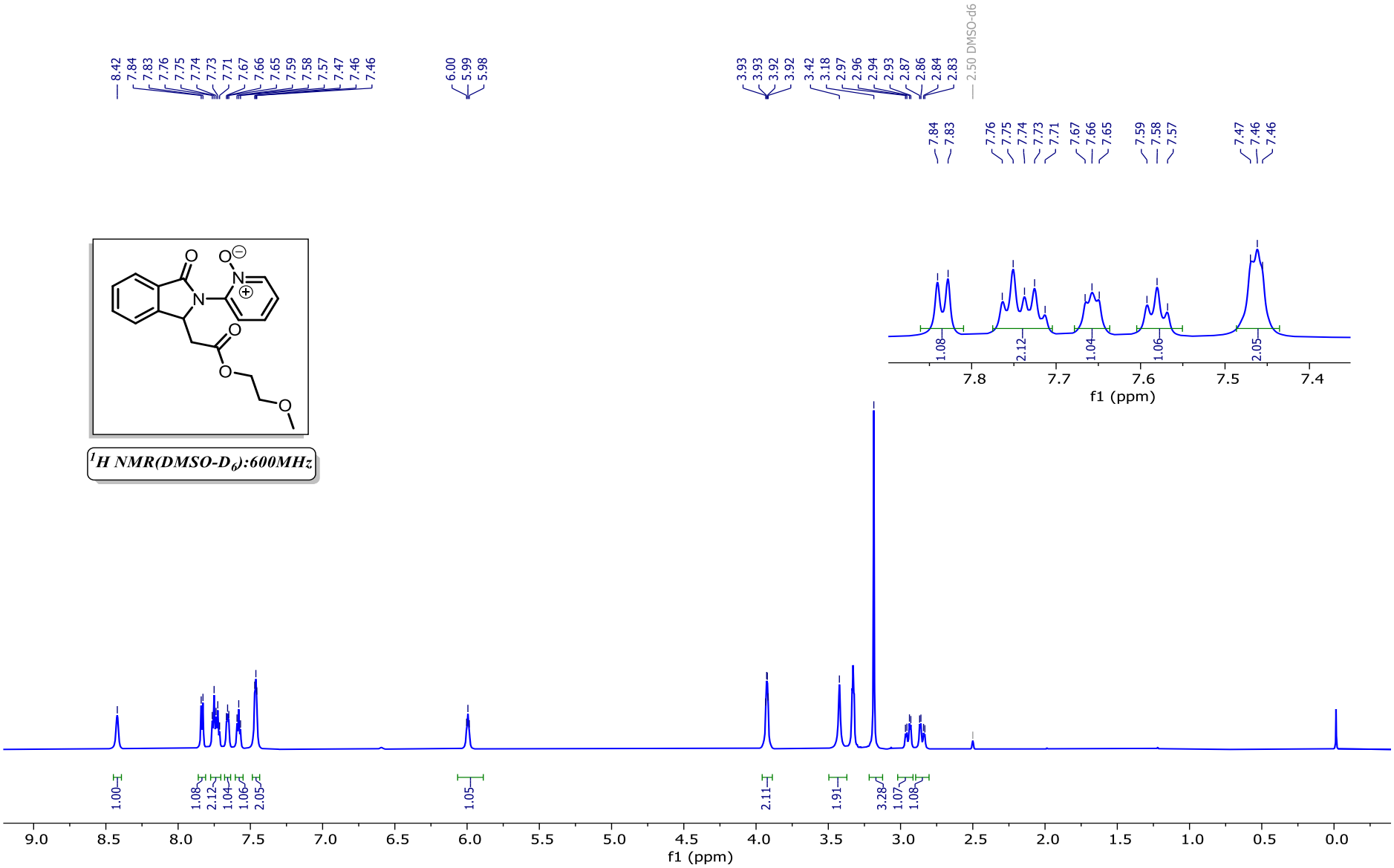
^{13}C NMR($CDCl_3$) :151MHz



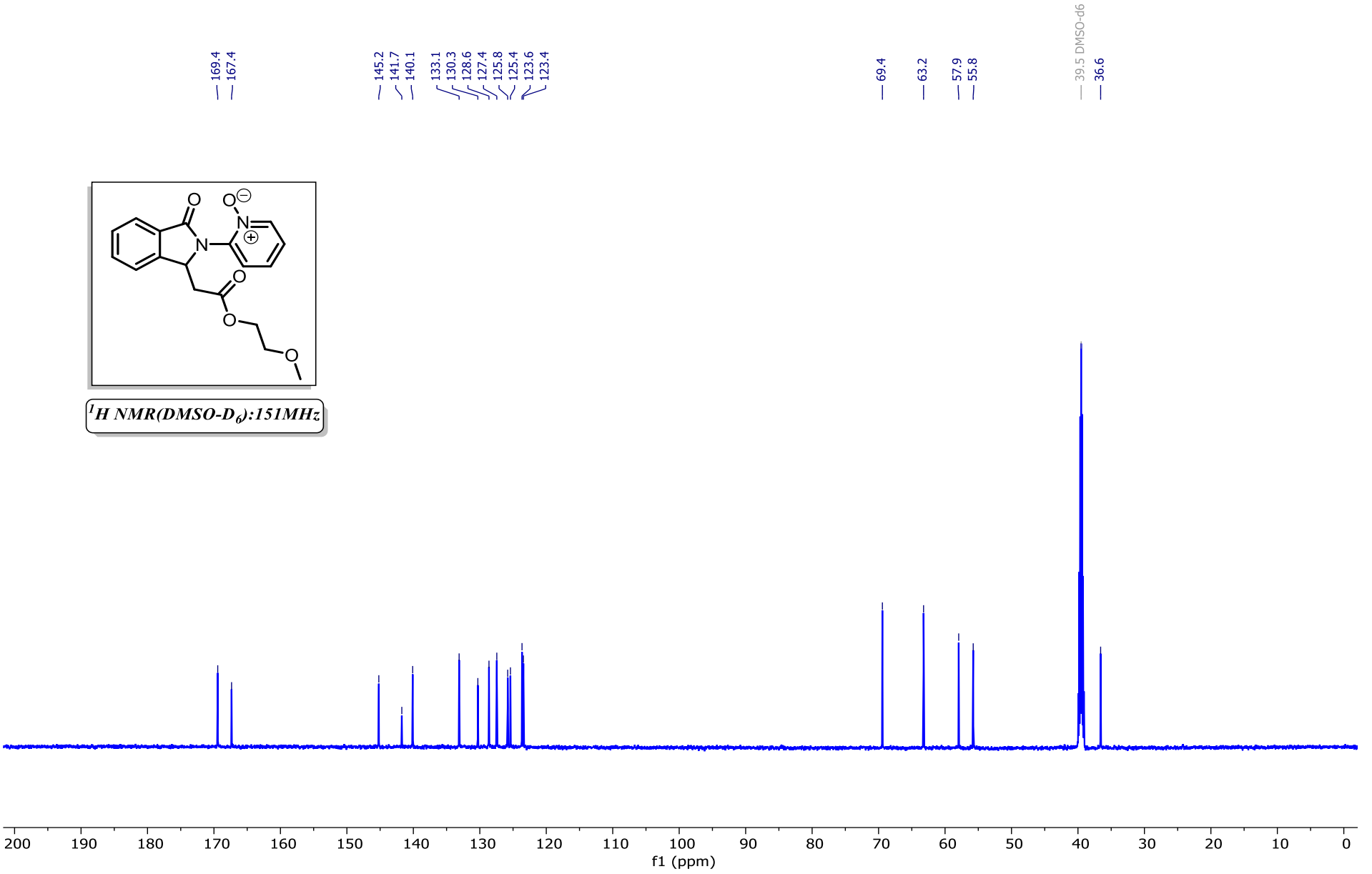
^{19}F NMR(CDCl$_3$) :377MHz



2-(1-(2-(2-methoxyethoxy)-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3aa)

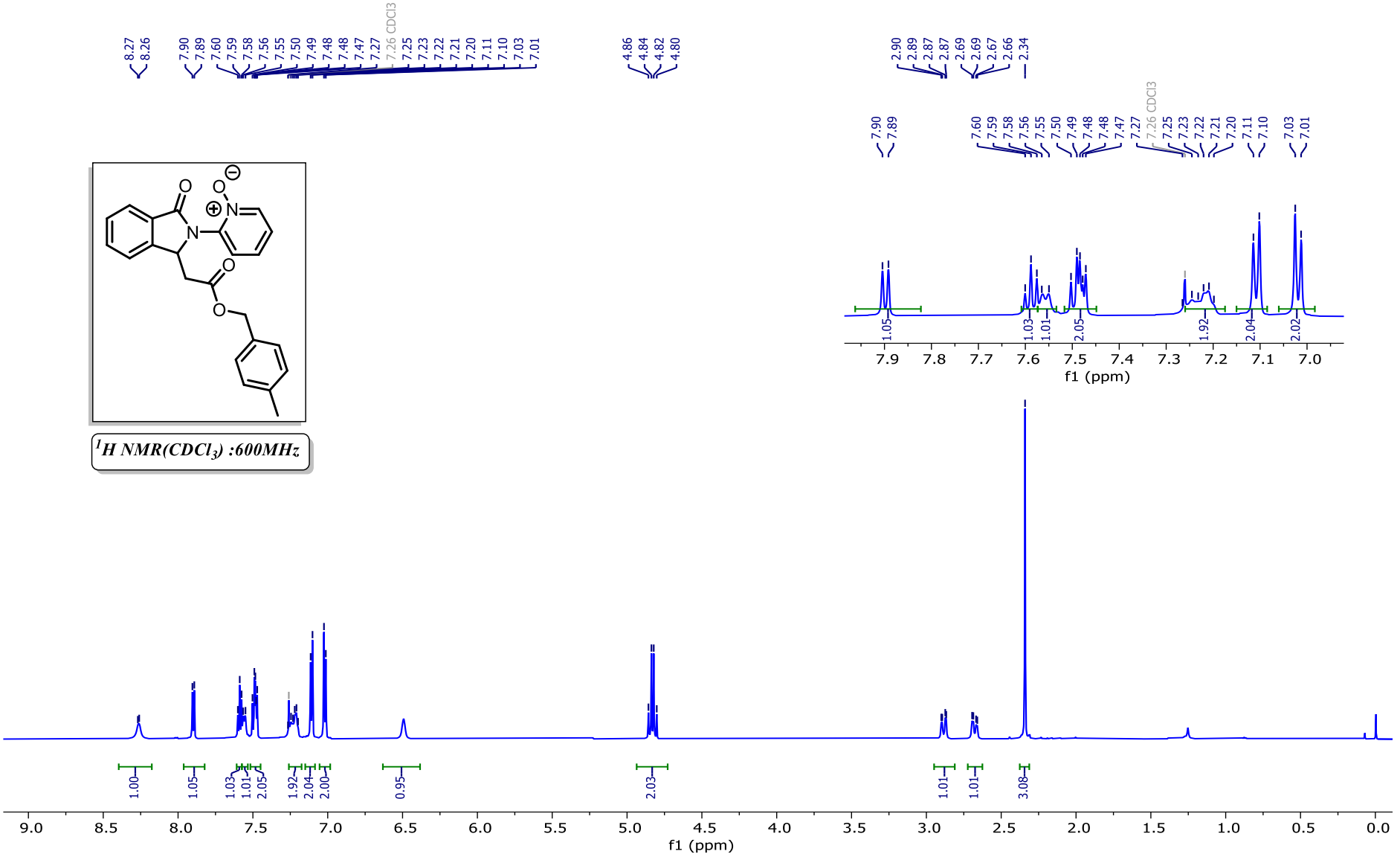


^{1}H NMR(DMSO-D_6):600MHz

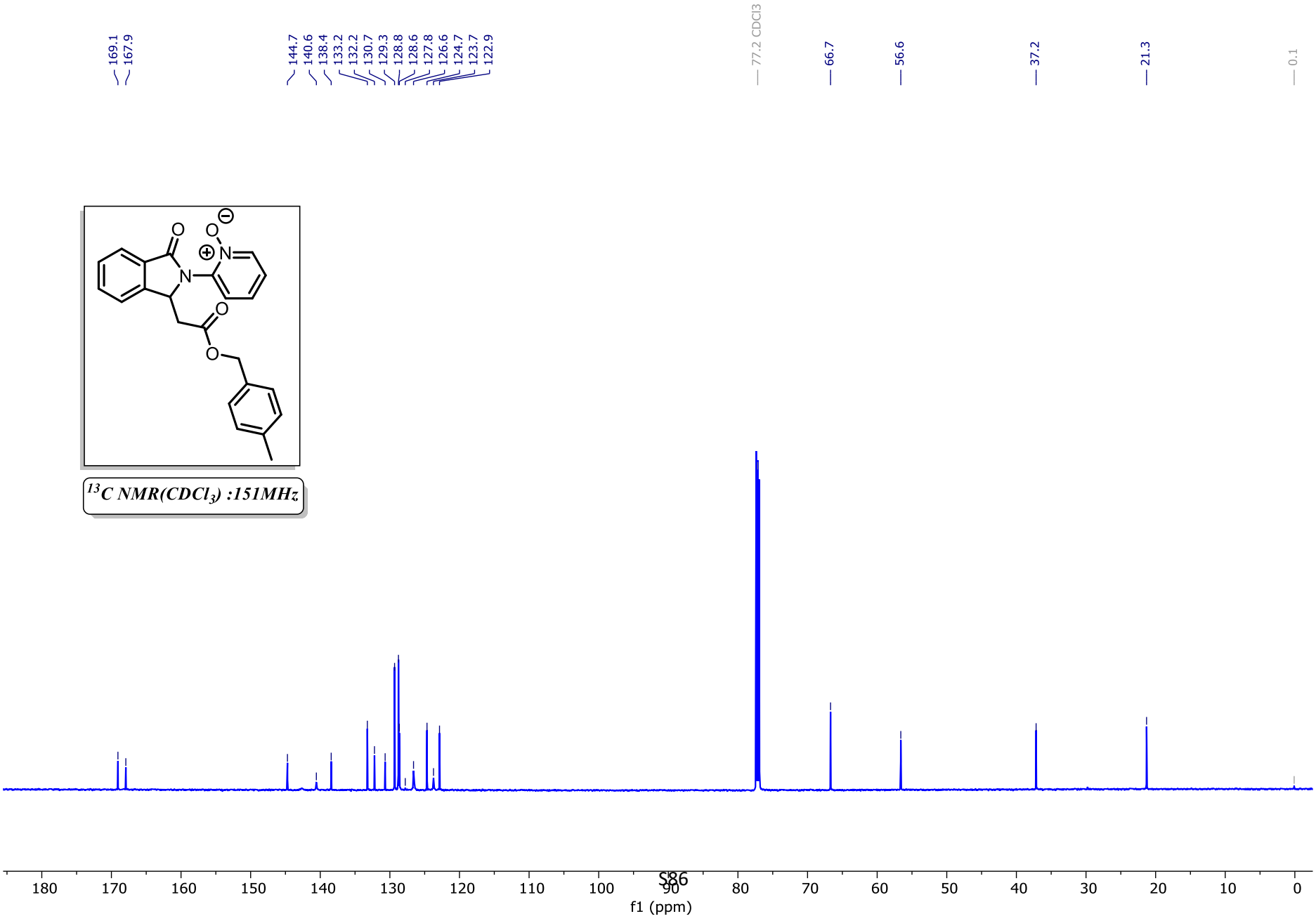


^{1}H NMR(DMSO-D$_6$):151MHz

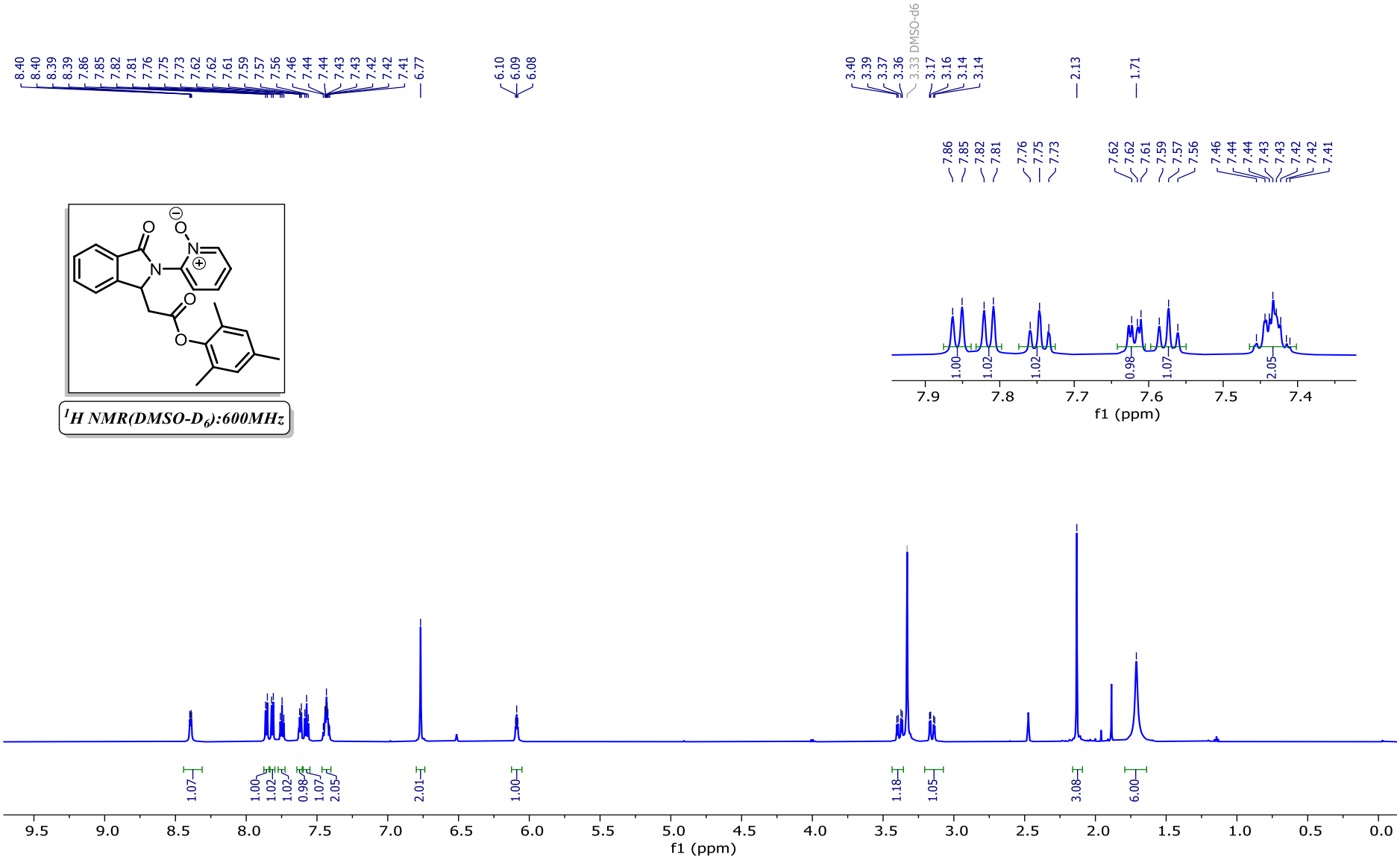
2-(1-(2-((4-methylbenzyl)oxy)-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3ab)



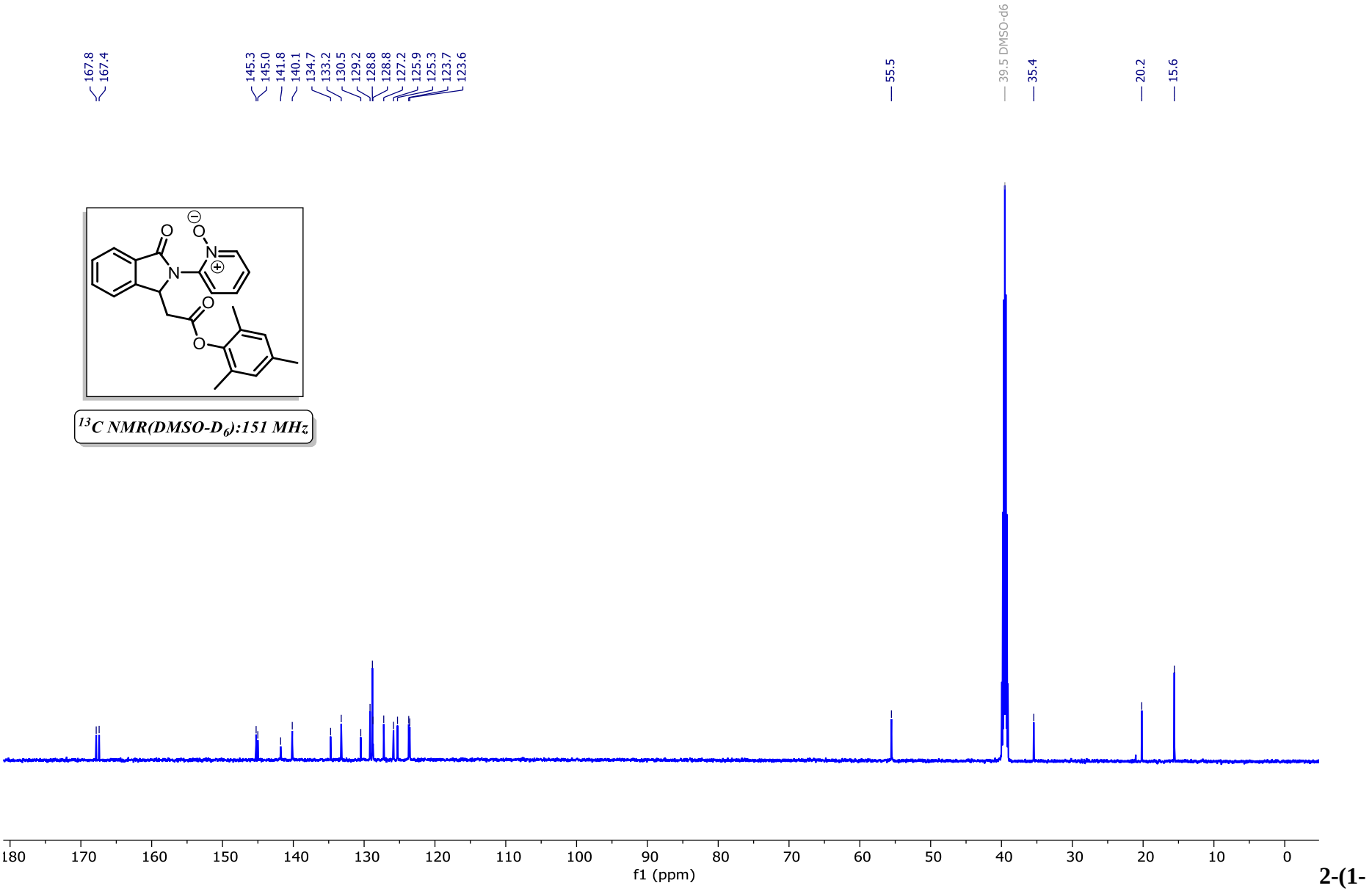
^{1}H NMR($CDCl_3$) :600MHz


169.1
167.9
144.7
140.6
138.4
133.2
132.2
130.7
129.3
128.8
128.6
127.8
126.6
124.7
123.7
122.9
77.2 CDCl3
66.7
56.6
37.2
21.3
0.1
O
O
N
N
O
O
^{13}C NMR($CDCl_3$) :151MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

2-(1-(2-(mesityloxy)-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3ac)



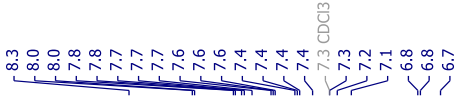
^{1}H NMR(DMSO-D_6):600MHz

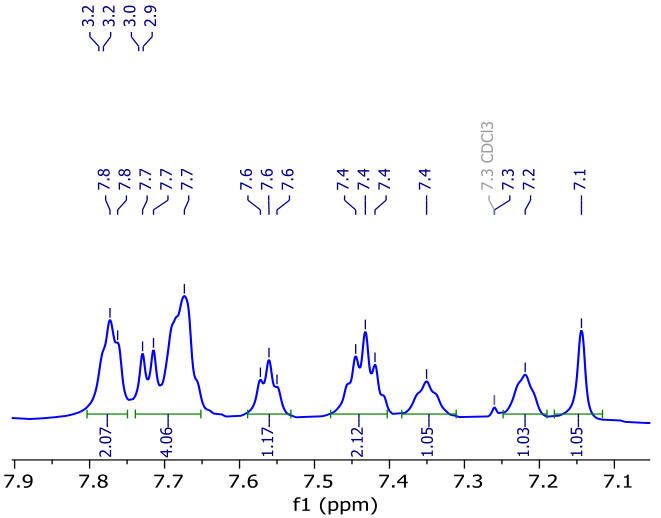


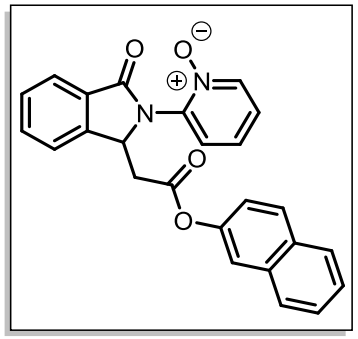
^{13}C NMR(DMSO-D_6):151 MHz

2-(1-

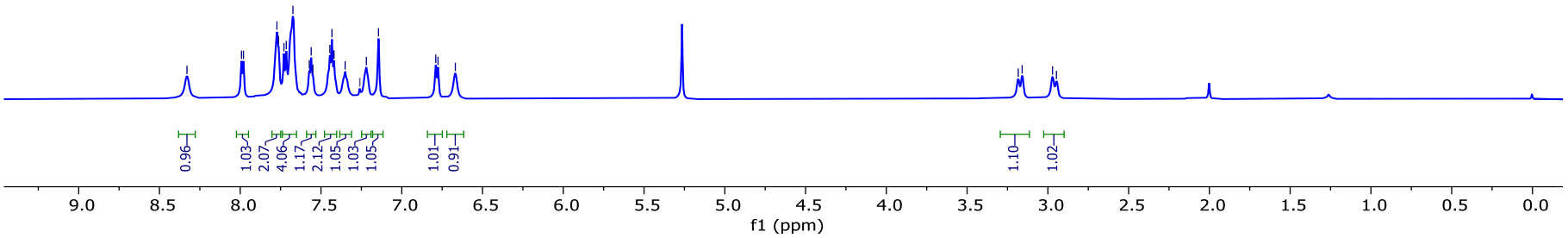
(2-(naphthalen-2-yloxy)-2-oxoethyl)-3-oxoisoindolin-2-yl)pyridine 1-oxide (3ad)

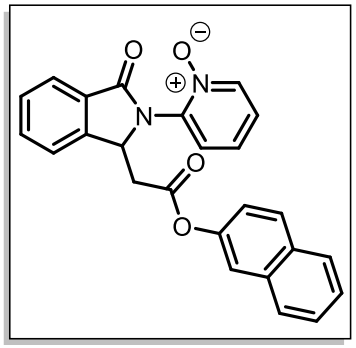






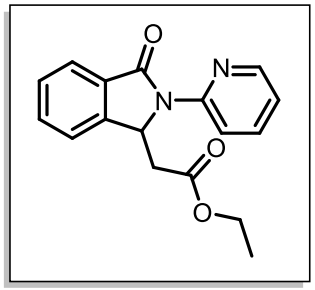
^{1}H NMR($CDCl_3$):600MHz

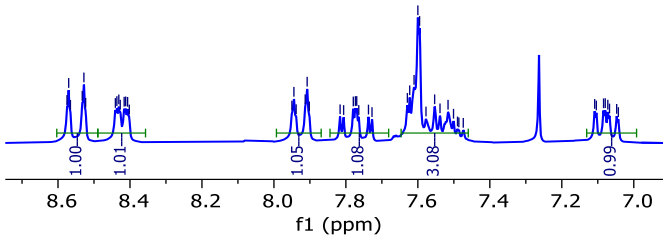




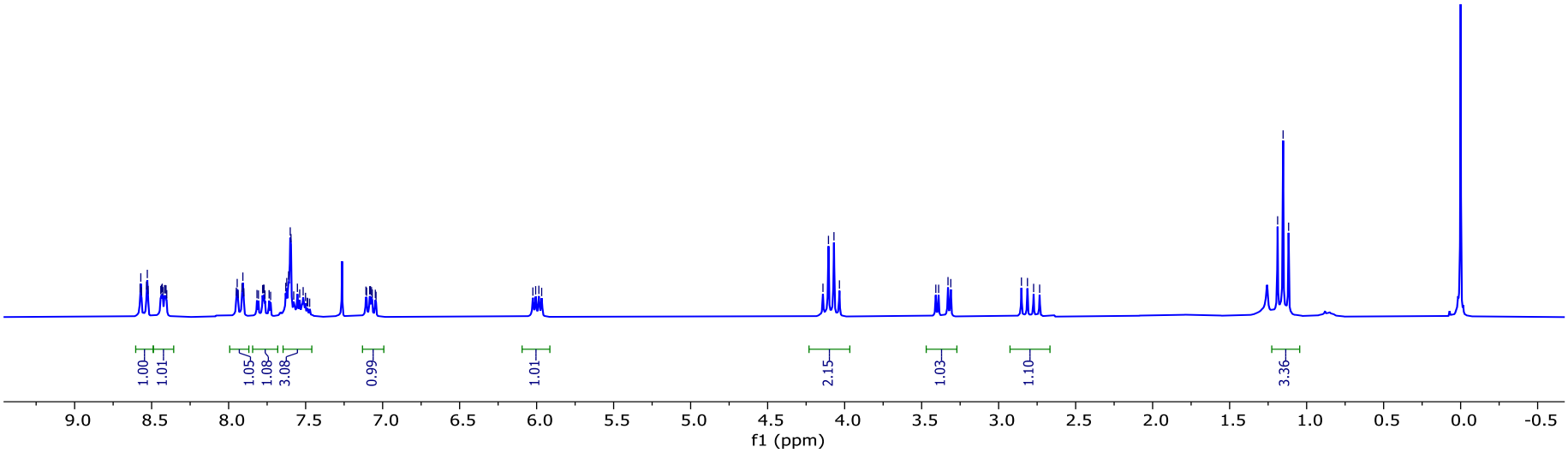
^{13}C NMR($CDCl_3$):151MHz

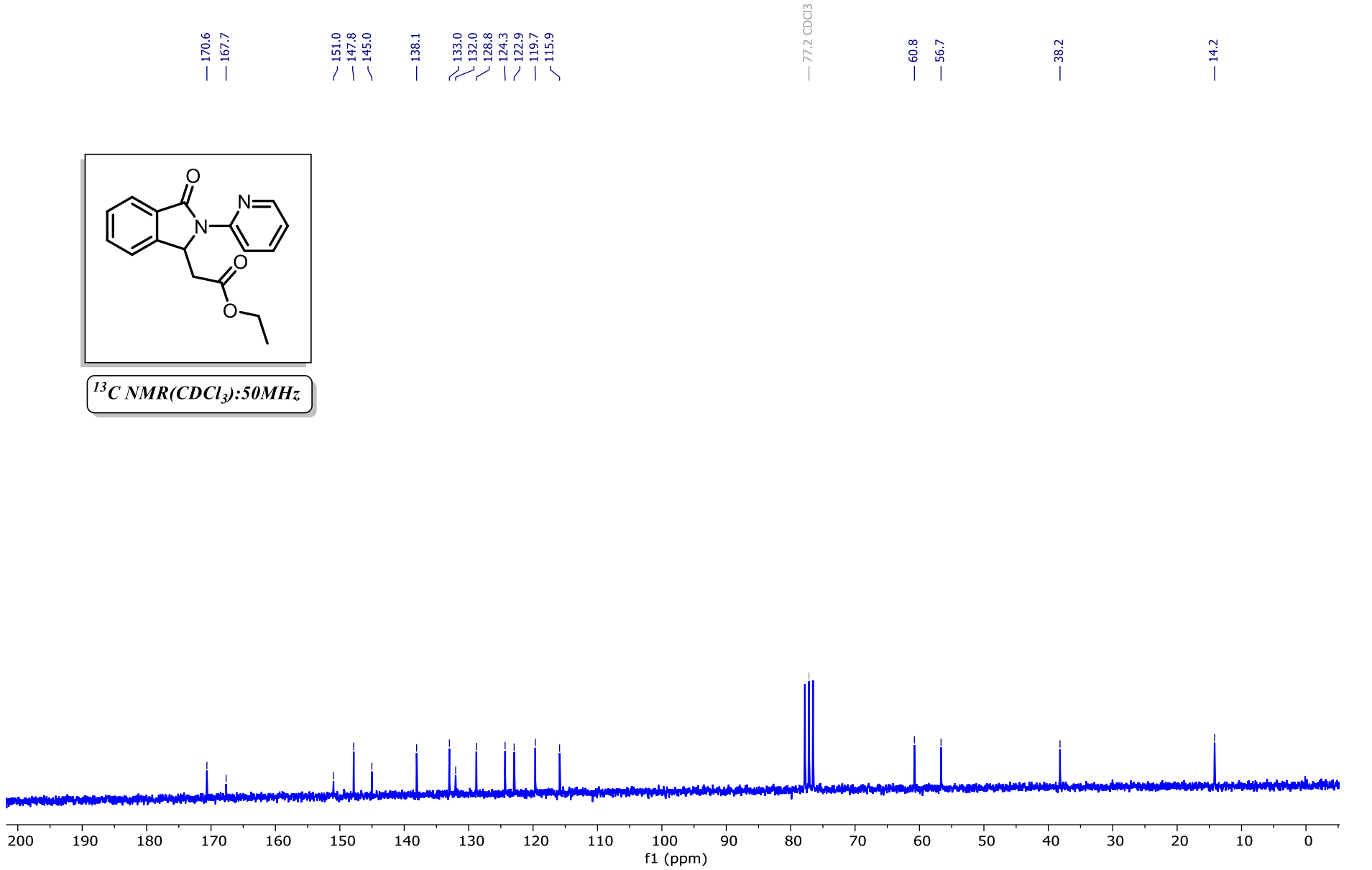
ethyl 2-(3-oxo-2-(pyridin-2-yl)isoindolin-1-yl)acetate (5)





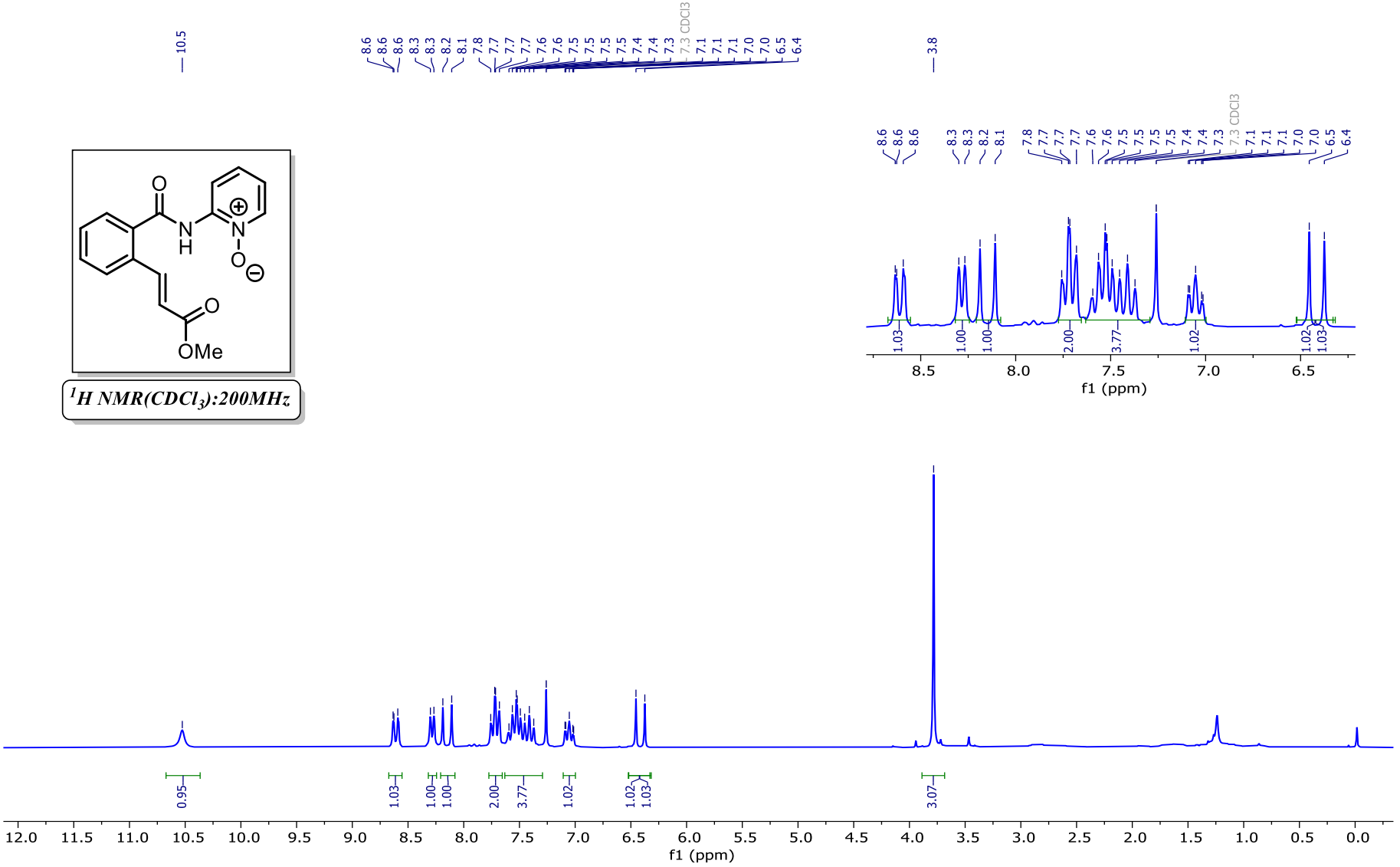
^{1}H *NMR(CDCl$_3$):200MHz*

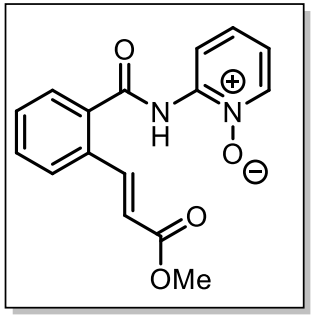




^{13}C NMR($CDCl_3$):50MHz

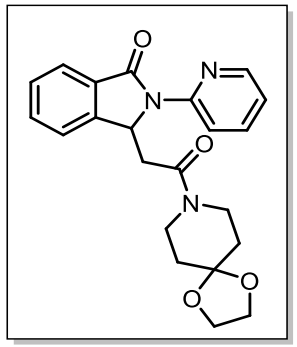
(E)-2-(2-(3-methoxy-3-oxoprop-1-en-1-yl)benzamido)pyridine 1-oxide (4)



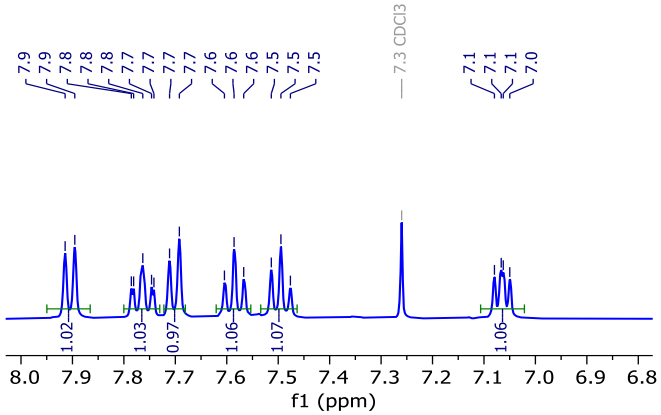


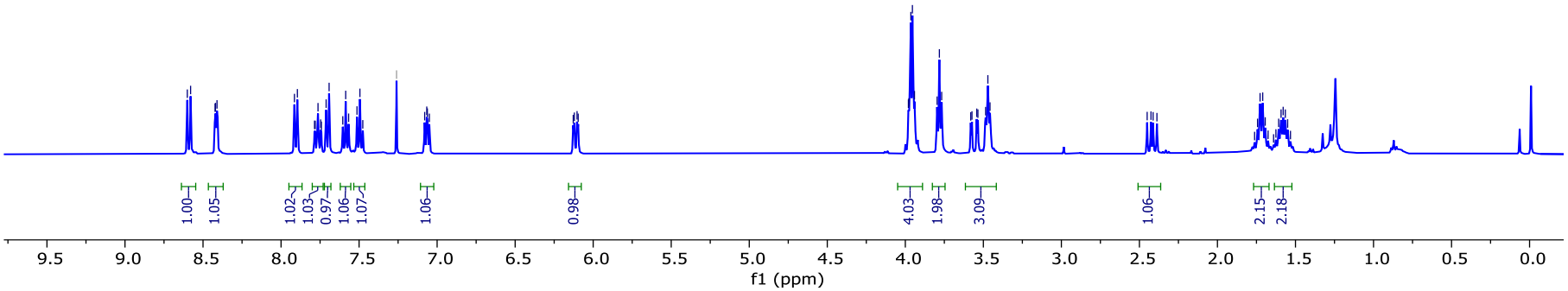
^{13}C NMR($CDCl_3$):50MHz

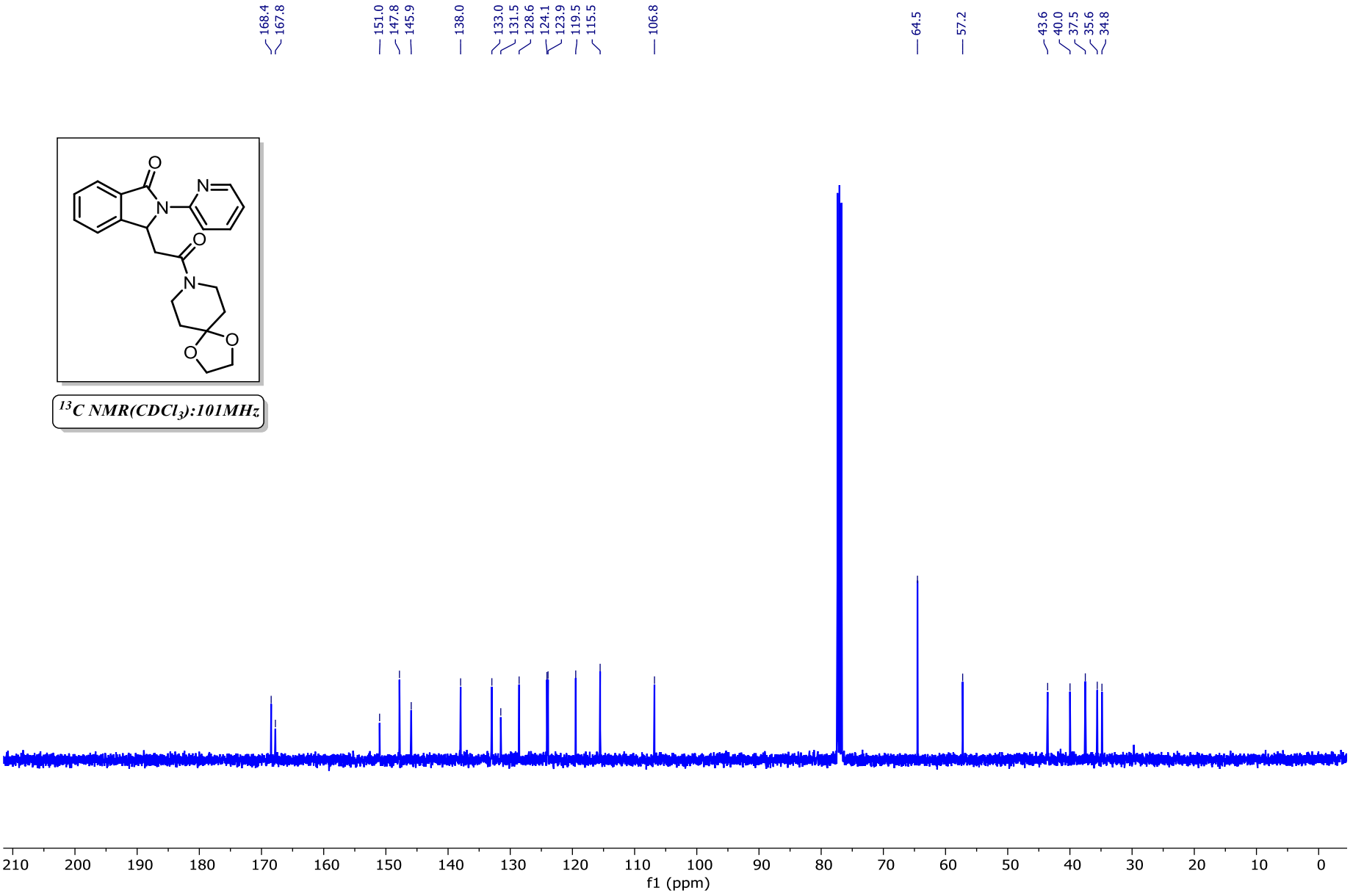
3-(2-oxo-2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)ethyl)-2-(pyridin-2-yl)isoindolin-1-one (7)



^{1}H NMR($CDCl_3$):400MHz







^{13}C NMR($CDCl_3$):101MHz