Supporting Information for

Ru(II)-Catalyzed Regioselective Oxidative Heck Reaction with Internal Olefins that Tolerated Strongly Coordinating Heterocycles

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A. General information

^{1}H and ^{13}C NMR spectra were recorded on BRUKER DRX-400 spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 7.26, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); dt (doublets of triplet); dq (doublets of quartet). Coupling constants are reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 77.0, triplet). Gas chromatograph mass spectra were obtained with a SHIMADZU model GCMS–QP 5000 spectrometer. HRMS was carried out on a MAT 95XP (Thermo). Nitrile starting materials are purchased from Energy Chemical, and were used as received.

B. General procedure

B-1. General reaction procedure for the synthesis of benzimidates:

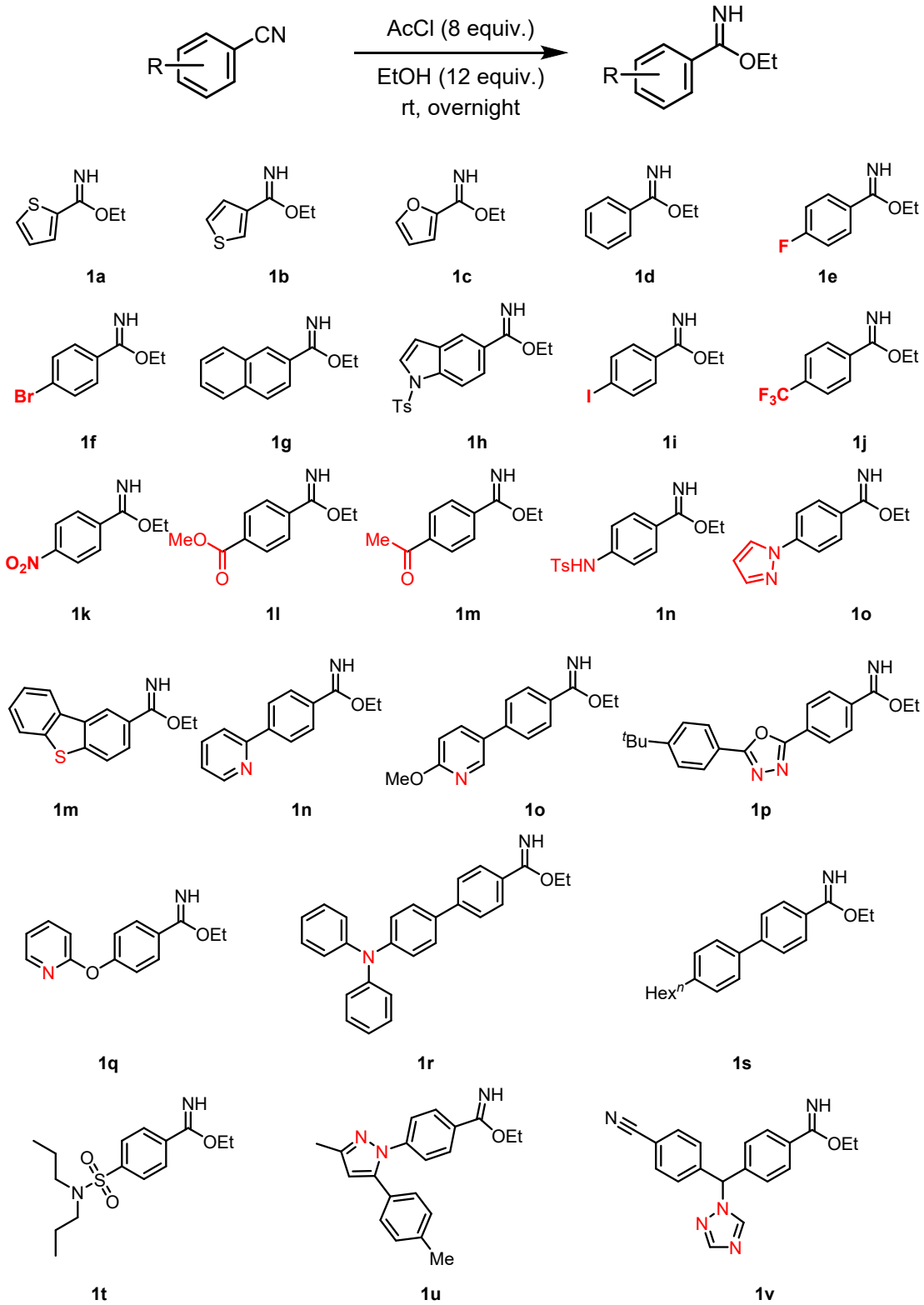


Fig SI-1. Synthesis of benzimidate esters.

General procedure for the synthesis of benzimidate esters: 1) To a stirred solution of a nitrile (1 equiv.) and an alcohol (12 equiv.), AcCl was added (8 equiv.) dropwise at 0 ℃. The Schlenk tube was stoppered tightly and the stirring was continued at 25 ℃. After the reaction was complete monitored by TLC, the volatiles were removed under reduced pressure to isolate the benzimidate hydrochloride. Then slowly mixed benzimidate hydrochloride and saturated aqueous $NaHCO_3$ solution inice bath, until gas evolution had ceased. The product was extracted into Et_2O and theorganic solution was washed with H_2O and brine and concentrated under reducedpressure to obtain the benzimidates.

For this oxidative Heck reaction with internal olefins, the following figure summarized the internal and terminal olefins used in this work (**Fig SI-2**):

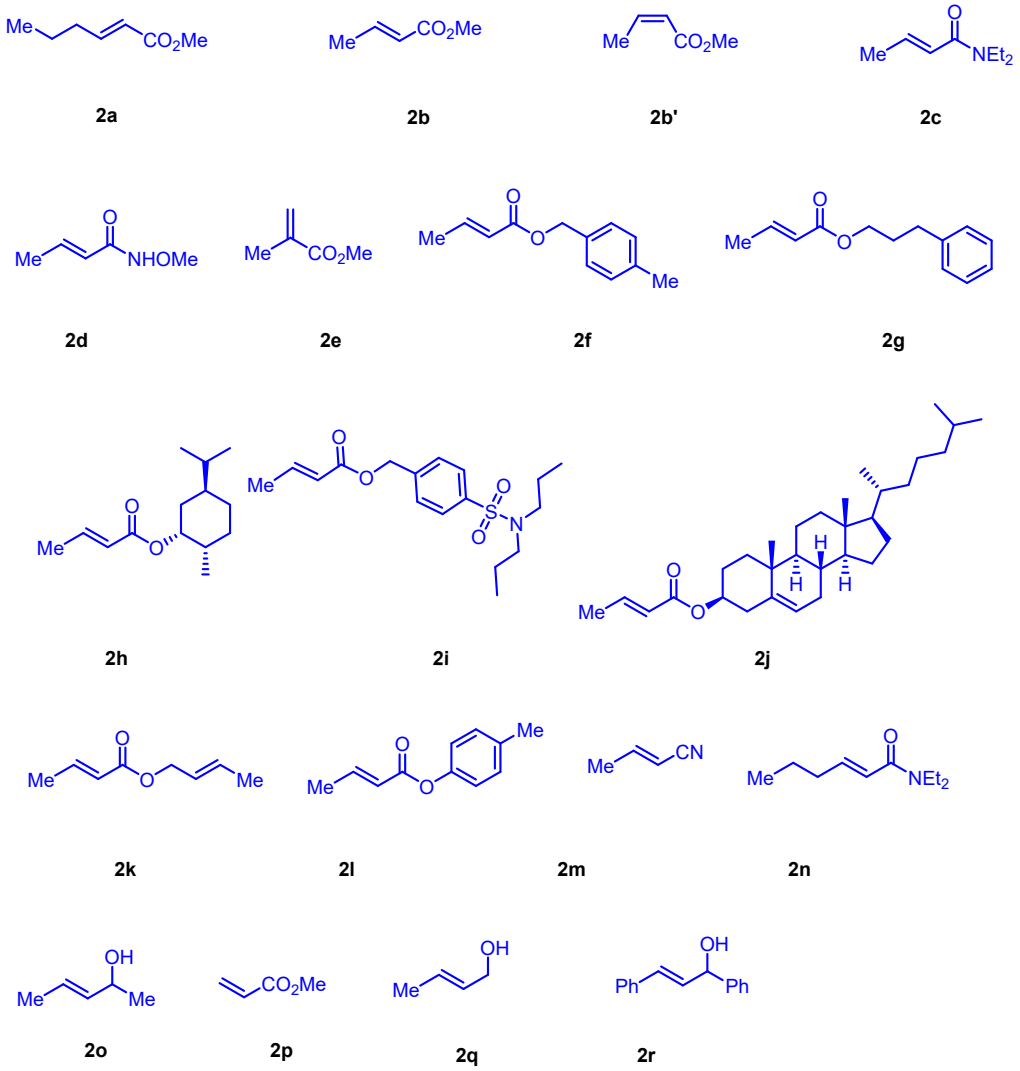


Fig SI-2. Olefins that used in this oxidative Heck reaction.

B-2. General procedure for the Ru(II)-catalyzed oxidative Heck with internal olefins.

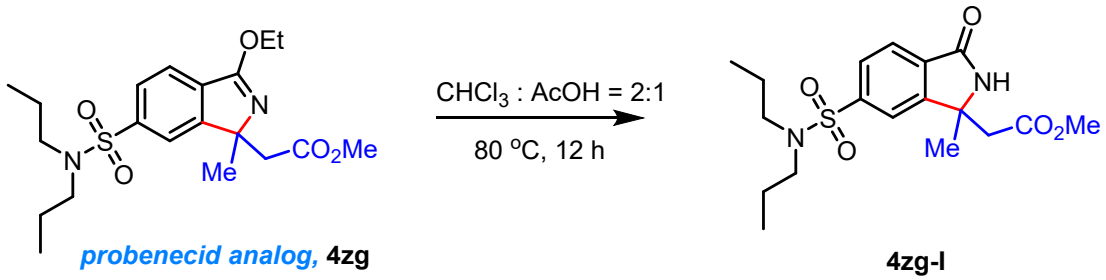
An oven-dried 10 mL Schlenk Tube was charged with **1** (0.1 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (2.4 mg, 0.004 mmol), $AgNTf_2$ (6.2 mg, 0.016 mmol), NaOAc (2.4 mg, 0.03 mmol) and Na_2CO_3•H_2O_2 (31.4 mg, 0.2 mmol) in sequence, followed by adding internal olefins **2** (0.2 mmol) in GVL (0.5 mL) through syringe. The resulting reaction mixture was stirred at 100 ºC for 12 h and then diluted with ethyl acetate and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the desired annulation product **3, 4, 5**.

Identical reaction conditions were also used for the oxidative Heck reaction of N-OPiv oximes **6** with internal olefins, furnishing isoquinolines **7**.

C. Synthetic applications

1) Site-selective modification of probenecid analogue:

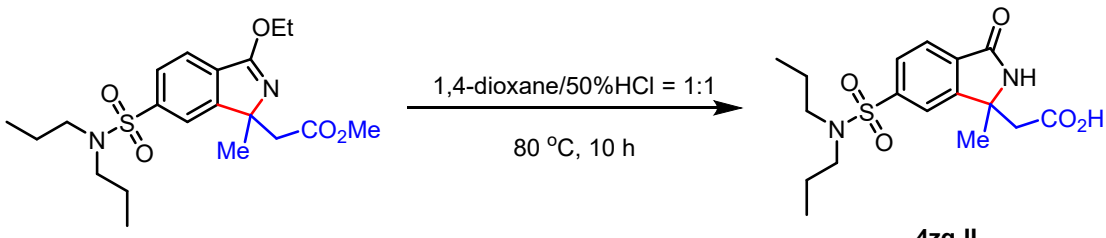
1*H*-Isoindole derivative **4zg** (40.1 mg, 0.1 mmol) was taken in a 10 mL sealed tube and dissolved with 1 mL of $CHCl_3$ and 0.5 mL of AcOH. Then, the reaction mixture was heated at 80 ℃ for 12 h. After cooling to ambient temperature, the solution was concentrated under the reduced pressure. The crude residue was purified through a silica gel column using petroleum ether and ethyl acetate as eluent to give pure **4w-I** (35.9 mg, 94%) (**Figure SI-3**).



probenecid analog, **4zg** **4zg-I**

Figure SI-3. Mild hydrolysis with AcOH of isoindole products.

1*H*-Isoindole derivative **4zg** (40.1 mg, 0.1 mmol) was taken in a 10 mL round bottom flask and dissolved with 1.0 mL of 1,4-dioxane and 1.0 mL of 6 N HCl. Then, the reaction mixture heated at 80 ℃ for 10 h. After cooling to ambient temperature, water was poured into the reaction mixture and extracted with ethyl acetate. The organic layer was washed with brine solution and dried over Na_2SO_4. The solution was concentrated under the reduced pressure. The crude residue was purified through a silica gel column using DCM and ethyl acetate as eluent to give pure **4zg-II** (35.3 mg, 96%) (**Fig SI-4**).



probenecid analog, **4zg** **4zg-II**

Figure SI-4. Hydrolysis of the product with HCl of isoindole products.

2) Site-selective modification of celecoxib analog :

To further demonstrate the synthetic potential of this tranformation, we selected a Celecoxib analog as the model substrate, a phamaceutical molecule that contained multiple reactive C–H bonds. Delightfully, by sequential decoration of nitrile functionality to the corresponding imidate ester as the key directing group, oxidative Heck reaction with internal olefin proceeded smoothly to give product **4x** with great siteselectivity, which thus override the limitation of strongly coordinating pyrazole heterocycle (**Figure SI-5**).

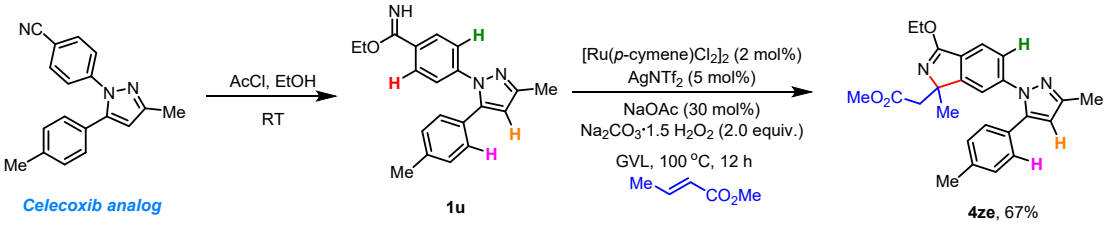


Figure SI-5. Siteselective modification of celecoxib analog via oxidative Heck reaction with internal olefin.

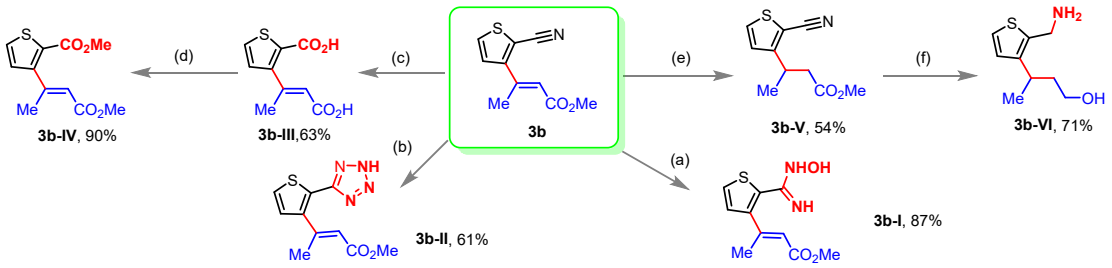
3) Diversification of the obtained thiophene-derived products.

Considering the synthetic potential of polyfunctionalized thiophene derivatives toward biologically active molecules and materials, and the readily transformable nitrile and ester functionality in the obtained products, we performed further diversification of the obtained thiophene products (**Figure SI-6**).

As summarized in **Figure SI-6**, nitrile functionality in the product **3b** could undergo nucleophilic addition with NH_2OH, giving to N-hydroxyacetimidamide **3b-I**, which served as a versatile synthon towards rapid delivery of heterocycles. [3+2] Cycloaddition of nitrile with azide gave tetrazole **3b-II**.

Hydrolysis proceeded smoothly to give di-carboxylic acid **3b-III**. Further esterification led to di-ester product **3b-IV**, which could be regarded as 2-ester

thiophene enabled oxidative Heck reaction with internal olefin, a challenging transformation remained.



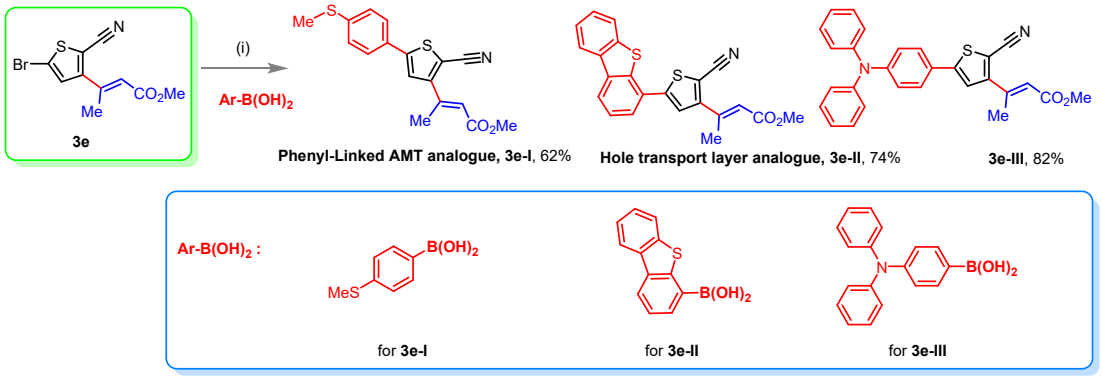
Conditions: (a) **3b** (0.1 mmol), NaOAc (2.0 equiv.), NH_2OH•HCl (2.0 equiv.), MeOH/H_2O (1.0 mL/1.0 mL), 90 ℃, 2 h; (b) **3b** (0.1 mmol), NaN_3 (4.0 equiv.), NH_4Cl (2.0 equiv.), DMF (1.0 mL), N_2, 120 ℃, 24 h ; (c) **3b** (0.1 mmol), NaOH aequous solution (3 equiv., 3M), 80 ℃, 15 h; (d) **3b-V** (0.05 mmol), K_2CO_3 (2.0 equiv.), MeI (2.0 equiv.), THF (1.0 mL), 40 ℃, 5 h; (e) **3b** (0.1 mmol), Pd/C (0.005 mmol), H_2 (1 atm), EtOH (2.0 mL), 40 ℃, 5 h ; (f) **3b-I** (0.05 mmol), $LiAlH_4$ (6 equiv), Et_2O (1.0 mL), rt, 5 h.

Figure SI-6. Diversification of the obtained multiple functionalized thiophene product **3b**.

The obtained thiophene product **3b** could readily undergo selective reduction of C–C double bond into alkyl group via Pd/C catalysis with nitrile remained intact, giving **3b-V**. Further reduction of **3b-V** using $LiAlH_4$, leading to product **3b-VI**, in which both nitrile and ester functionality were reduced into primary amine and alcohol, respectively.

Further diversifications of thiophene product via Suzuki coupling were conducted, with thioether-substituted arylboronic acid, **3e-I** was obtained, which was a phenyl-linked AMT analogue.

While performing cross-coupling with dibenzo[b,d]thiophene, triphenylamine-derived arylboronic acids with **3e**, D-A type hole transport layer analogues **3e-II**, **3e-III** were obtained in good yield (**Figureure SI-7**).

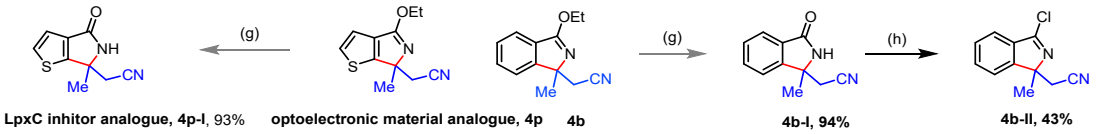


Conditions: (i) **3e** (0.10 mmol), $Pd(PPh_3)_4$ (0.005 mmol), K_2CO_3 (0.4 mmol), Ar-$B(OH)_2$ (0.12 mmol), EtOH/H_2O/Toluene = (0.3 mL/ 0.4 mL/ 1.0 mL), 95 ℃, 12 h.

Figure SI-7. Diversification of thiophene product via Suzuki coupling.

To further demonstrate the synethetic application, the obtained isoindole product **4b** could be readily transformed into benzolactam **4b-I**. Further treatment with $SOCl_2$ enabled the conversion of the carbonyl group to the C−Cl bond, affording **4b-II**, could undergo coupling reactions for the further synthesis (**Figureure SI-8**).

Significantly, thieno[2,3-c]pyrrole **4p** that bearing nitrile substituted quaternary carbon center could be readily obtained, which was an optoelectronic material analogue. While further hydrolysis of **4p** gave the corresponding thieno[2,3-c]pyrrole **4p-I**, which is a LpxC inhitor analogue.



LpxC inhitor analogue, 4p-I, 93% **optoelectronic material analogue, 4p** **4b** **4b-I, 94%** **4b-II, 43%**

Conditions: (g) isoindole **4** (0.1 mmol), $CHCl_3$: AcOH = 2 :1 (1 mL/0.5 mL), 80℃, 12 h; (h) **4b-I** (0.05 mmol), $SOCl_2$ (2.0 equiv.), DMF (8 μL), 50 ℃, 2 h.

Figure SI-8. Diversification of the obtained isoindoline products.

To sum up, the obtained olefin-substituted thiophene nitriles **3** were versatile synthons for the rapid construction of molecular libraries of polyfunctional thiophenes, including various functionality substituted thiophenes. Thus, this transformation could be regarded as imidate esters directed C–H alkylation, weak coordinating, nativte functionality including carboxylic acids, esters, amines, as well as N-hydroxyacetimidamides and tetrazoles directed oxidative Heck reaction with internal olefins, which remained challenging and underexplored.

D. Preliminary mechanistic studies

To shed light into this transformation, some preliminary mechanistic studes were conducted. First, the use of terminal olefin **2b** for the oxidative Heck reaction with N-phenyl pyrazole proceeded smoothly, under standard Ru(II) catalysis (**Figureure SI-9**). While the use of internal olefin **2a** that features steric hindrance under this Ru(II)-catalyzed conditions, only trace amount of the desired product **3a-I** was obtained.

It was postulated that the low binding affinity of internal olefin with steric hindrance, which weaked the corresponding interaction of metal catalyst and olefin coupling partners, and thus, leadint to sluggish migratory insertion of steric olefins into the in situ generated cyclometalated organometallic intermediate.

The overall observations indicated that terminal olefins exhibited match reactivity for metal-catalyzed directed C–H olefination. While the steric olefin partners showed mismatch reactivity for oxidative Heck reaction, leading to undesired reactivity.

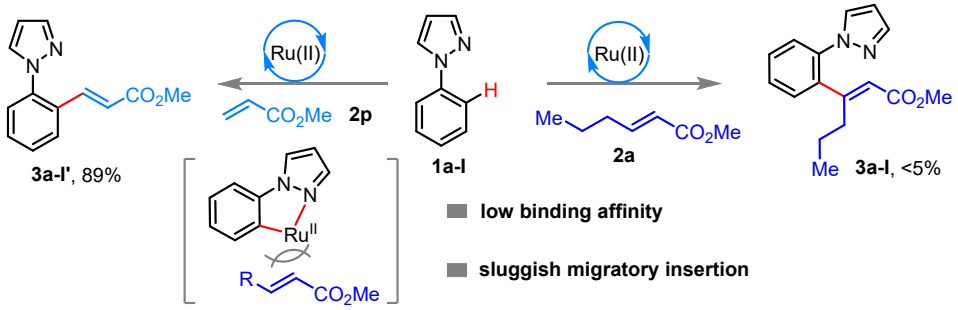
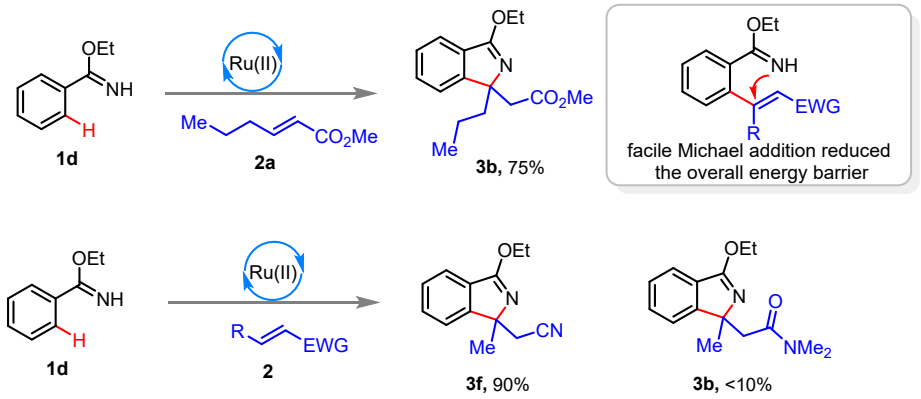


Figure SI-9. Match and mismatch reactivity of terminal and internal olefins for oxidative Heck reaction.

Intriguingly, imidate ester 1b could well assist this oxidative Heck reaction with internal olefin **2a**, leading to isoindole product **3b** (**Figureure SI-10**). It was proposed that the subsequent facile Michael addition reduced the energy barrier for the steric hindrance of internal olefins, and thus, facilitating the oxidative Heck reaction cascade.

Control experiments using different electron-withdrawing groups substituted internal olefins as coupling partners revealed that the corresponding nitrile exhibited even better reactivity, while alkenyl amides gave only trace amount of the desired oxidative Heck product. These observations further support that the subsequent transformation, e.g., facile Michael addtion, served as one crucial driving force to facilitate oxidative Heck reaction with internal olefins.



Figureure SI-10. Facile Michael addition facilitated oxidative Heck reaction with internal olefins.

As a control experiment, the use terminal methyl acrylate, a typical coupling partner in Heck reaction, proceeded smoothly in this oxidative Heck reaction of imidate ester substituted aryl pyrazole, and C–H olefination took place at ortho site to pyrazole. This observation indicated that pyrazole exhibited directing priority to imidate ester in this oxidative Heck reaction (**Figureure SI-11**).

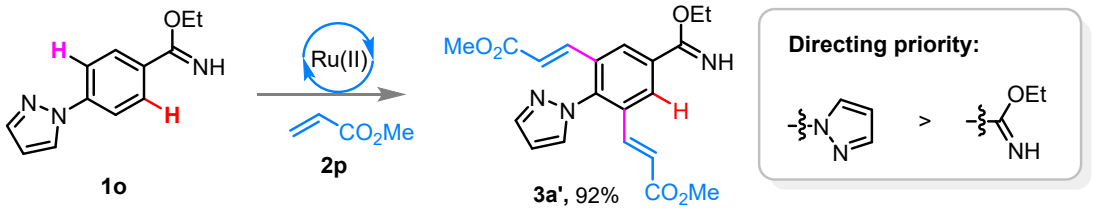


Figure SI-11. Directing priority of pyrazole vs. imidat ester for oxidative Heck reaction.

To further illustrate the reactivity of various electron-withdrawing groups substituted internal olefins for the regioselective oxidative Heck reaction of imidate ester substituted N-aryl pyrazole (**Figure SI-12**). And ester, nitrile substituted internal olefins could serve as amenable coupling partners for the oxidative Heck reaction, and overcome the limitation of strongly coordinating heterocycles.

Significantly, it was envisaged that match and mismatch effect of steric hindrance of internal olefins, and the subsequent facile Michael addition facilitated this oxidative Heck reaction with internal olefins that tolerated strongly coordinating heterocycles.

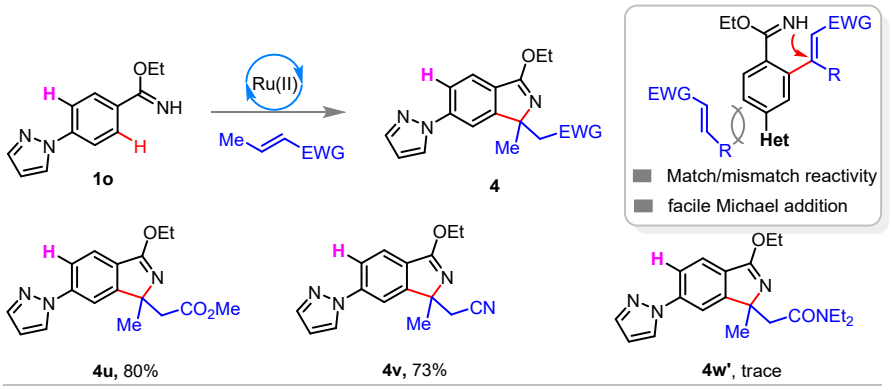


Figure SI-12. Oxidative Heck reaction that override the limitation of strongly coordinating heterocycles.

These results inspired us further investigate electronic nonbiased internal olefin, allylic alcohol, for the oxidative Heck reaction with pyrazole substituted arylimidate ester, and delightfully, indene **5a** was obtained with the release of ethanol and water. N-OPiv oxime ester showed great reactivity and regioselectivity for this oxidative Heck reaction with internal olefins.

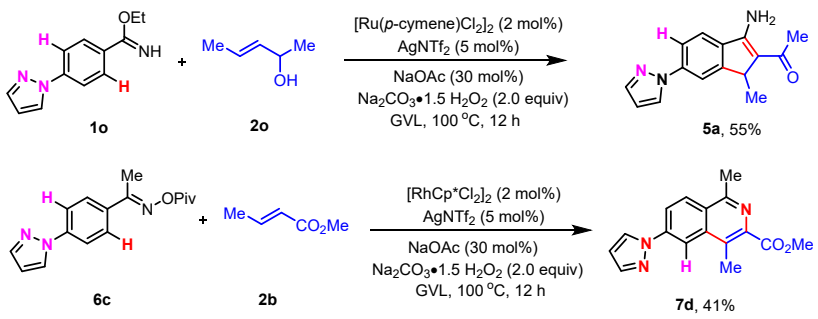


Figure SI-13. Regioselective oxidative Heck reaction that tolerated strongly coordinating heterocycles.

Taking imidate that contained pyrazole substrate **1o** as an example, it was speculated that competing C-H metalation enabled by imidate and pyrazole might proceed reversibly. Subsequently, for pyrazole moiety, which directed C-H metalation to give species **5-A**, however, further olefin migration would be elusive, due to the steric hindrance issue. While for imidate ester moiety, sequential olefin insertion and base induced nucleophilic substitution would give indene amine product **5**, together the release of EtOH.

Thus, the choice of X-type imidate esters, and further interaction of organometallic species with internal olefins, e.g., further cyclization together with the release of small molecules (alcohol, water), and the thermodynamically stable products would favor the overall process. Similarly, for N-OPiv oximes, further formal [4+2] cyclization and aromatization proceeded to give products **7** (**Figure 14**).

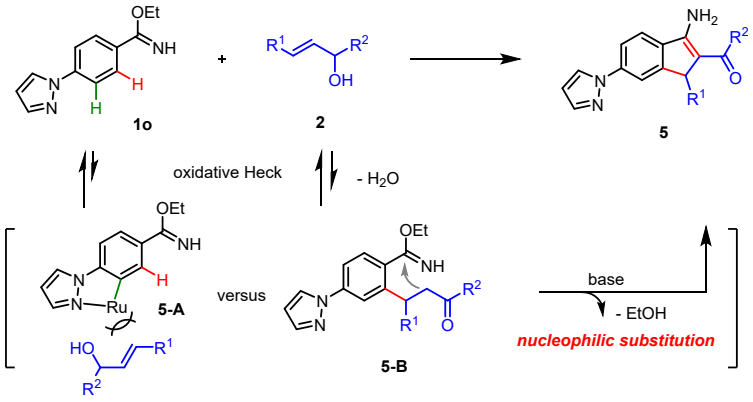


Figure SI-14. Regioselective oxidative Heck reaction with internal allylic alcohols that tolerated strongly coordinating heterocycles.

Further investigations of various X-type nitrogen-directing groups for the competing coordination in the directed oxidative Heck reaction with internal olefins were performed (**Figure SI-15**), and the results revealed that :

1) for N-pyrazole substituted arylamidine substrate, oxidative Heck reaction with internal olefin **2b** took place at undesired position.

2) for N-pyrazole substituted N-OMe arylamide substrate, oxidative Heck reaction with internal olefin **2b** could not proceed, and showed no catalytic reactivity, which probably due to the coordinative saturation of pyrazole to the metal catalyst.

3) Notably, for N-pyrazole substituted arylamidate, oxidative Heck reaction with internal olefin **2b** took place at the desired C–H position, in which imidate ester outcompeted heterocycles.

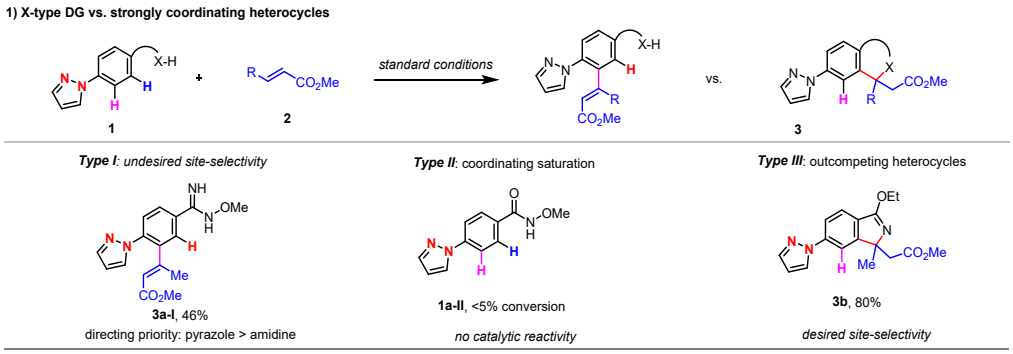


Figure SI-15. Competing coordination in oxidative Heck reaction with internal olefins : strongly coordinating N-heterocycles versus X-type N-directing groups.

To sum up, there are three typical reaction types for the competing coordination of heterocycles versus directing groups for the transition-metal catalyzed C–H functionalizations (**Figure SI-16**),

Type I : strongly coordinating heterocycles showed directing priority to various directing groups, and thus, leading to undesired site-selectivity in the C–H functionalization ;

For this oxidative Heck reaction with internal olefins, arylamidine could assist this oxidative Heck reaction with internal olefins. However, for N-pyrazole substituted arylamidine substrate, undesired site-selectivity was observed, in which C–H olefination took place at the ortho position to the pyrazole.

Type II : strongly coordinating heterocycles led to metal catalyst poisoning, due to the coordinative saturation of metal catalyst, and thus, leading metal catalyst deactivation and recovery of the starting maerials.

Type III : desired regioselective C–H functionalization that override the limitation of strongly coordinationg heterocycles.

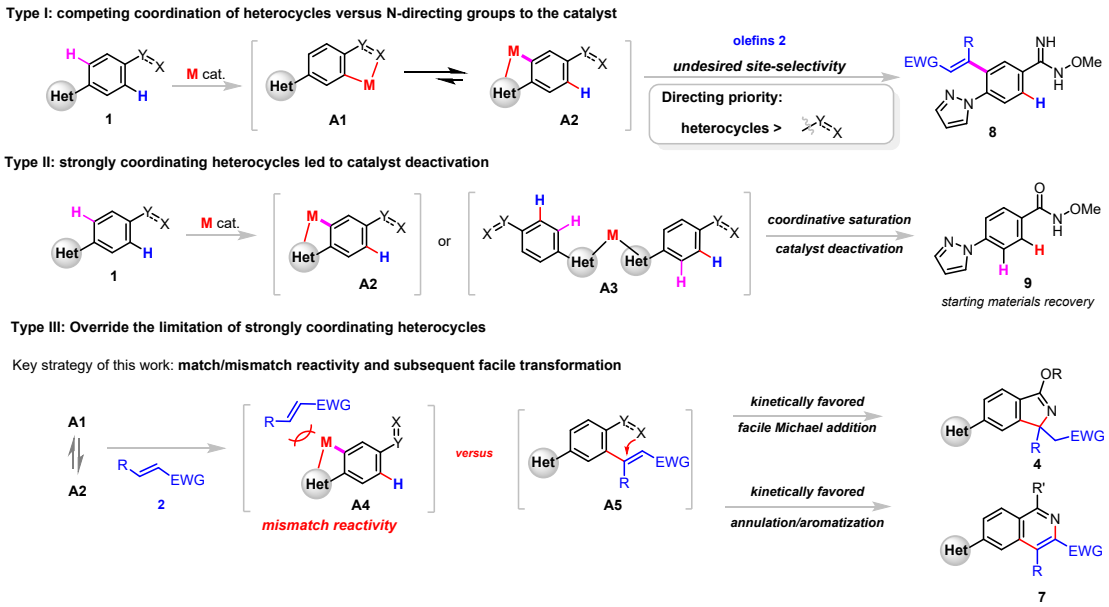
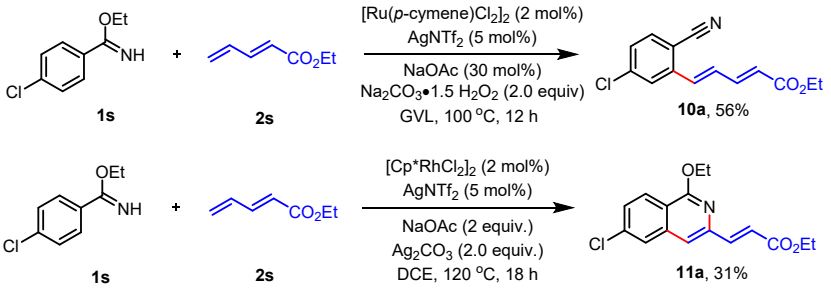


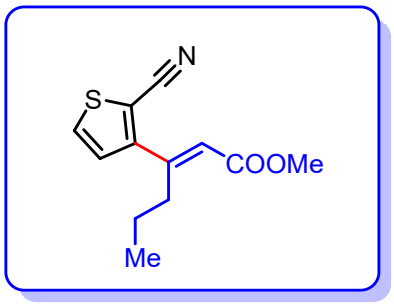
Figure SI-16. Competing coordination of strongly coordinating N-heterocycles with X-type N-directing groups for this oxidative Heck reaction with internal olefins.

For this oxidative Heck reaction with internal olefins, we found that by exploring 'match/mismatch effect', and subsequent facile transformation, including Michael addition, and annulation/aromatization as the key driving forces, which could reduce the overall energy barrier, and thus, leading to oxidative Heck reaction with internal olefins that overrided the strongly coordinating heterocycles.

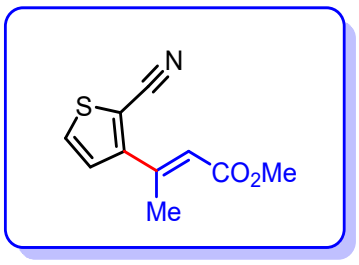
We have also investigated other olefins, such as dienes for this imidate esters enabled oxidative Heck reaction, intriguingly, oxidative Heck reaction of dienyl ester with imidate ester delivered nitrile-substituted arylnitrile **10a**. The use of Rh(III) catalysis led to the dehydrogenative annulation of arylimidate ester with diene, which afforded olefin-substituted isoquinoline **11a**. For details, please see the Supporting Information in the revised Manuscript.



E. Analytical data for the obtained products:

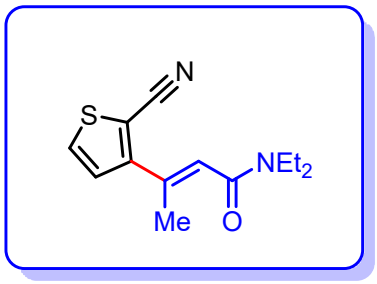


Methyl (*E*)-3-(2-cyanothiophen-3-yl)hex-2-enoate (3a), slightly white solid (18 mg, 76% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 70 ℃. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56 (d, J = 5.2 Hz, 1H), 7.13 (d, J = 5.2 Hz, 1H), 6.19 (s, 1H), 3.75 (s, 3H), 3.08-3.04 (m, 2H), 1.48-1.42 (m, 2H), 0.94 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.0, 152.2, 151.9, 132.0, 127.6, 120.9, 113.8, 106.5, 51.4, 33.4, 22.0, 13.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{12}H_{14}NO_2S$: 236.0740, Found: 236.0744.

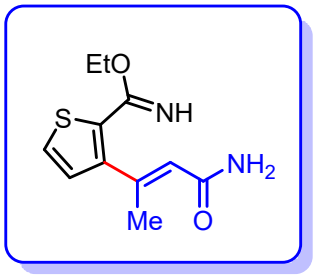


Methyl (*E*)-3-(2-cyanothiophen-3-yl)but-2-enoate (3b), slightly white solid (16 mg, 78% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 73 ℃. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.55 (d, J = 5.2 Hz, 1H), 7.14 (d, J = 5.2 Hz, 1H), 6.24 (s, 1H), 3.72 (s, 3H), 2.56 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.3, 152.4, 147.2, 132.1,

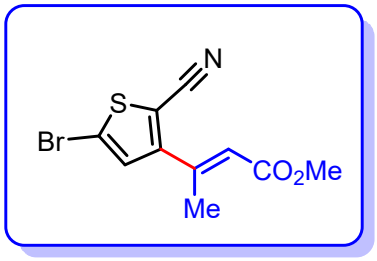
127.5, 120.7, 114.0, 106.1, 51.4, 18.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{10}H_{10}NO_2S$: 208.0427, Found: 208.0422.



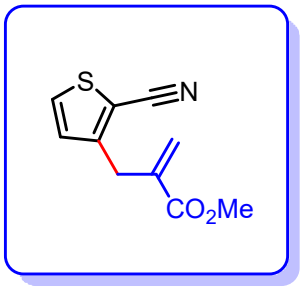
(*E*)-3-(2-Cyanothiophen-3-yl)-*N*, *N*-diethylbut-2-enamide (3c), slightly yellow liquid (13 mg, 54% yield, chromatography on silica gel, eluent: PE/EA = 3:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.53 (d, *J* = 5.2 Hz, 1H), 7.15 (d, *J* = 5.2 Hz, 1H), 6.55 (d, *J* = 1.2 Hz, 1H), 3.50-3.44 (m, 4H), 2.30 (d, *J* = 1.2 Hz, 3H), 1.22-1.17 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.4, 153.1, 138.0, 131.9, 127.5, 124.7, 114.6, 104.6, 39.7, 14.4, 13.1.HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{13}H_{17}N_2OS$: 249.1056, Found: 249.1055.



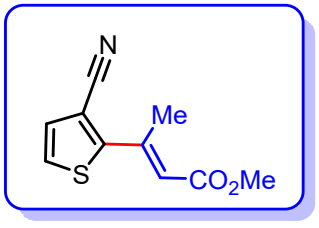
Ethyl (*E*)-3-(4-amino-4-oxobut-2-en-2-yl)thiophene-2-carbimidate (3d), slightly yellow liquid (14 mg, 57% yield, chromatography on silica gel, eluent: PE/EA = 3:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.61 (d, *J* = 5.2 Hz, 1H), 7.33 (d, *J* = 5.2 Hz, 1H), 6.51 (s, 1H), 4.49 (q, *J* = 7.2 Hz, 2H), 2.39 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 180.2, 173.4, 158.0, 143.9, 138.7, 130.6, 127.9, 127.8, 64.1, 23.5, 14.1. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{11}H_{15}N_2O_2S$: 239.0849, Found: 239.0846.



Methyl (*E*)-3-(5-bromo-2-cyanothiophen-3-yl)but-2-enoate (3e), slightly white solid (22 mg, 78% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 75 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.13 (s, 1H), 6.24 (d, J = 1.2 Hz, 1H), 3.76 (s, 3H), 2.54 (d, J = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.0, 152.9, 146.2, 130.3, 121.3, 119.6, 112.8, 107.0, 51.51, 18.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{10}H_9BrNO_2S$: 285.9532, Found: 285.9536.

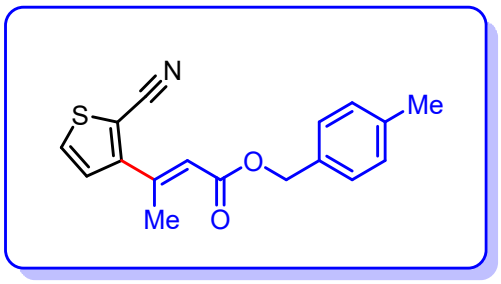


Methyl 2-((2-cyanothiophen-3-yl)methyl)acrylate (3f), slightly yellow oid (15 mg, 61% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.49 (d, J = 4.8 Hz, 1H), 7.01 (d, J = 5.2 Hz, 1H), 6.31 (s, 1H), 5.65 (d, J = 0.8 Hz, 1H), 3.81 (s, 2H), 3.77 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.7, 150.4, 137.4, 131.9, 129.3, 127.8, 114.0, 107.1, 52.3, 32.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{10}H_{10}NO_2S$: 208.0427, Found: 208.0425.

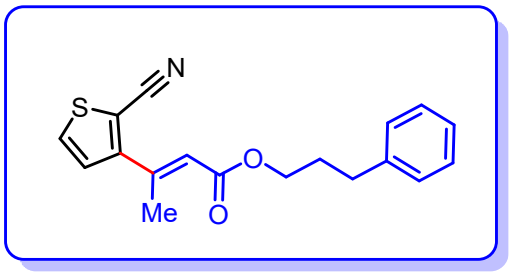


Methyl (*E*)-3-(3-cyanothiophen-2-yl)but-2-enoate (3g), slightly white solid (15 mg, 72% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 73 ℃. ^{1}H NMR**

(400 MHz, $CDCl_3$) δ 7.56 (d, J = 5.2 Hz, 1H), 7.15 (d, J = 5.2 Hz, 1H), 6.26 (d, J = 1.6 Hz, 1H), 3.74 (s, 3H), 2.57 (d, J = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.4, 152.37, 147.3, 132.08, 127.5, 120.7, 114.0, 106.1, 51.4, 18.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{10}NO_2S$: 208.0427, Found: 208.0422.

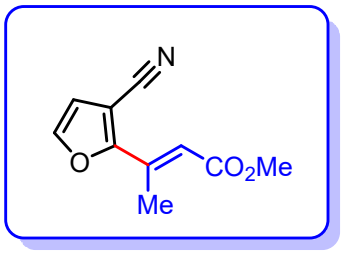


4-Methylbenzyl (*E*)-3-(2-cyanothiophen-3-yl)but-2-enoate (3h), slightly white solid (22 mg, 73% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 71 ℃. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (d, J = 5.2 Hz, 1H), 7.29 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 5.2 Hz, 1H), 6.30 (d, J = 1.2 Hz, 1H), 5.17 (s, 2H), 2.62 (d, J = 1.2 Hz, 3H), 2.36 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.7, 152.4, 147.5, 138.1, 132.8, 131.9, 129.2, 129.1, 128.4, 127.5, 120.9, 113.9, 106.1, 66.1, 21.2, 18.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}NO_2S$: 298.0896, Found: 298.0897.

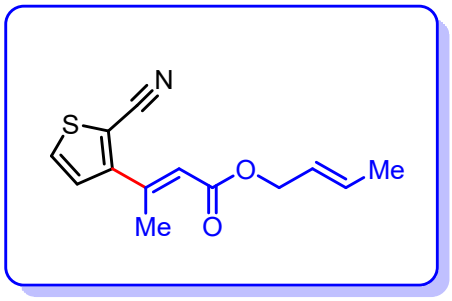


Phenylpropyl (*E*)-3-(2-cyanothiophen-3-yl)but-2-enoate (3i), slightly white solid (23 mg, 75% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 69 ℃. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.55 (d, J = 5.2 Hz, 1H), 7.29-7.27 (m, 1H), 7.21-7.16 (m, 5H), 6.28 (d, J = 0.8 Hz, 1H), 4.19 (t, J = 6.4 Hz, 2H), 2.73 (t, J = 8.0 Hz, 2H), 2.60 (d, J = 0.8 Hz, 3H), 2.04-2.00 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.0, 152.5, 147.1, 141.2, 132.0, 128.5, 128.4, 127.6, 126.0, 121.1, 114.0, 106.1, 63.7, 32.2, 30.2,

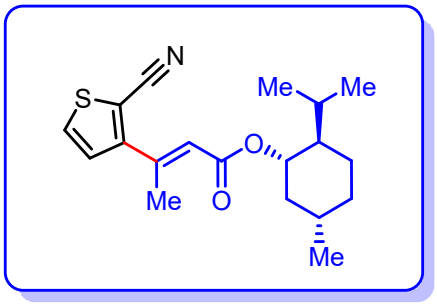
18.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{18}H_{18}NO_2S$: 312.1053, Found: 312.1055.



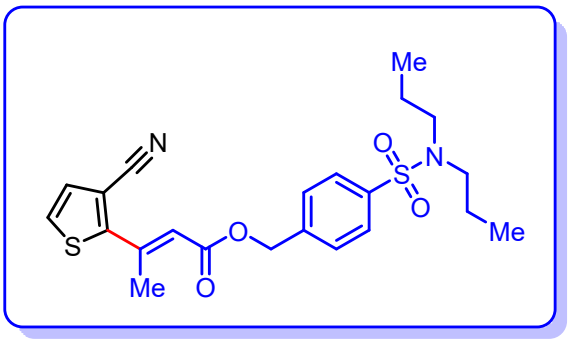
Methyl (*E*)-3-(3-cyanofuran-2-yl)but-2-enoate (3j), slightly yellow solid (15 mg, 77% yield, chromatography on silica gel, eluent: PE/EA = 10:1), m. p: 73 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 2.0 Hz, 1H), 6.65 (d, J = 2.0 Hz, 1H), 6.27 (d, J = 1.2 Hz, 1H), 3.76 (s, 3H), 2.58 (d, J = 1.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 147.3, 143.2, 138.2, 123.5, 119.7, 111.8, 110.4, 51.5, 17.2. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{10}H_{10}NO_3$: 192.0655, Found: 192.0654.



***(E)*-But-2-en-1-yl (*E*)-3-(2-Cyanothiophen-3-yl)but-2-enoate (3k),** slightly white solid (16 mg, 66% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 71℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.55 (d, J = 5.2 Hz, 1H), 7.15 (d, J = 5.2 Hz, 1H), 6.27 (d, J = 1.6 Hz, 1H), 5.88-5.79 (m, 1H), 5.67-5.60 (m, 1H), 4.60 (d, J = 6.4 Hz, 2H), 2.60 (s, 3H), 1.75-1.73 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 165.7, 152.4, 147.2, 131.9, 127.5, 125.0, 121.0, 113.9, 106.1, 65.1, 18.6, 17.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{13}H_{14}NO_2S$: 248.0740, Found: 248.0744.

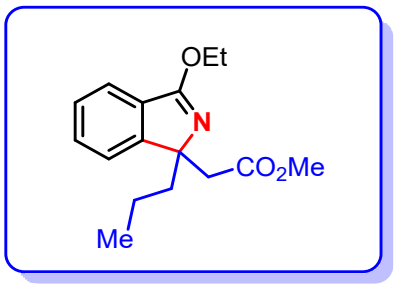


(1*S*, 2*R*, 5*S*)-2-Isopropyl-5-methylcyclohexyl (*E*)-3-(2-cyanothiophen-3-yl) but-2-enoate (3l), slightly white solid (21 mg, 65% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 68 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.54 (d, *J* = 5.2 Hz, 1H), 7.16 (d, *J* = 5.2 Hz, 1H), 6.24 (d, *J* = 1.2 Hz, 1H), 4.80-4.74 (m, 1H), 2.60 (d, *J* = 1.2 Hz, 3H), 2.06-2.03 (m, 1H), 1.92-1.88 (m, 1H), 1.70-1.64 (m, 2H), 1.47-1.45 (m, 1H), 1.25 (s, 2H), 1.07-1.01 (m, 2H), 0.90 (t, *J* = 6.8 Hz, 6H), 0.78 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 165.6, 152.6, 146.7, 131.8, 127.6, 121.6, 74.2, 47.03, 41.0, 34.3, 31.5, 26.3, 23.5, 22.0, 20.8, 18.6, 16.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{26}NO_2S$: 332.1679, Found: 332.1677.

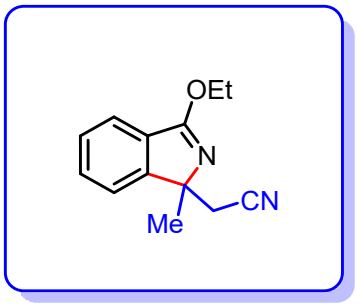


(*N*,*N*-Dipropylsulfamoyl) benzyl (*E*)-3-(2-cyanothiophen-3-yl) but-2-enoate (3m), slightly white solid (32 mg, 71% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 69 ℃.^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.79 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 5.2 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 1.71 (d, *J* = 5.2 Hz, 1H), 6.34 (d, *J* = 1.2 Hz, 1H), 5.25 (s, 2H), 3.05 (t, *J* = 7.6 Hz, 4H), 2.60 (d, *J* = 1.2 Hz, 3H), 1.57-1.51 (m, 4H), 0.85 (d, *J* = 7.2 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 165.4, 152.1, 148.5, 140.4, 139.8, 132.2, 128.3, 127.5, 127.3, 120.2, 113.9, 65.0, 50.1, 22.1, 18.8, 11.2.

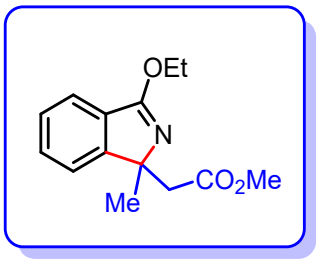
HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{27}N_2O_4$: 447.1407, Found: 447.1405.



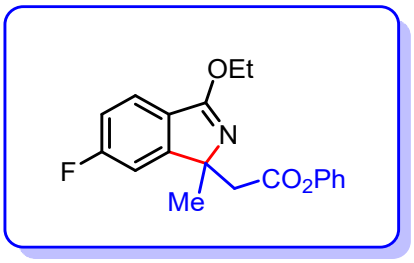
Methyl 2-(3-ethoxy-1-propyl-1*H*-isoindol-1-yl)acetate (4a), slightly yellow liquid (21 mg, 75% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83-.80 (m, 1H), 7.48 (d, J = 7.2 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.44-7.41 (m, 1H), 7.38-7.34 (m, 1H), 4.48-4.42 (m, 2H), 3.48 (s, 2H), 2.92 (d, J = 14.8 Hz, 1H), 2.81 (d, J = 14.4 Hz, 1H), 2.10-1.92 (m, 4H), 1.44 (t, J = 6.8 Hz, 3H), 1.7 (t, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.7, 154.8, 132.0, 129.2, 128.6, 127.5, 127.3, 120.6, 72.9, 63.9, 51.2, 43.3, 40.4, 14.4, 14.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}NO_3$: 276.1594, Found:276.1595.



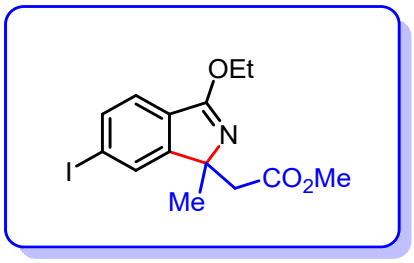
2-(3-Ethoxy-1-methyl-1*H*-isoindol-1-yl)acetonitrile (4c), slightly yellow liquid (21 mg, 92% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.57-7.51 (m, 2H), 7.47-7.43 (m, 1H), 7.42-7.38 (m, 1H), 4.49-4.40 (m, 2H), 2.89 (d, J = 16.4 Hz, 1H), 2.64 (d, J = 16.4 Hz, 1H), 1.58 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.6, 154.2, 132.0, 129.9, 128.4, 121.3, 121.2, 117.2, 68.7, 64.2, 28.9, 24.4, 14.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{15}O_2S$: 215.1179, Found: 215.1177.



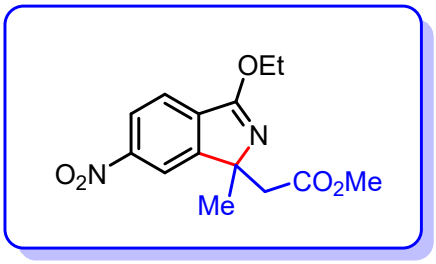
Methyl 2-(3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4d), slightly yellow liquid (22 mg, 91% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.49 (d, J = 7.2 Hz, 1H), 7.44 (d, J = 7.2 Hz, 1H), 7.41-7.34 (m, 2H), 4.48-4.40 (m, 2H), 3.51 (s, 3H), 2.89 (d, J = 14.4 Hz, 1H), 2.75 (d, J = 14.4 Hz, 1H), 1.55 (s, 3H), 1.43 (t, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.7, 167.8 156.2, 132.1, 129.3, 127.5, 121.5, 120.8, 69.9, 63.9, 51.2, 43.6, 25.3, 14.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}NO_3$: 248.1281, Found: 248.1283.



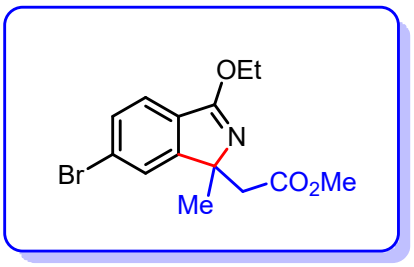
Phenyl 2-(3-ethoxy-6-fluoro-1-methyl-1*H*-isoindol-1-yl)acetate (4e), slightly yellow liquid (27 mg, 83% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 (dd, J = 5.2 Hz, 8.4 Hz, 1H), 7.31-7.27 (m, 2H), 7.25-7.24 (m, 1H), 7.06 (td, J = 1.6 Hz, 7.6 Hz, 17.2 Hz, 1H), 6.84-6.82 (m, 2H), 4.49-4.41 (m, 2H), 3.13 (d, J = 14.4 Hz, 1H), 3.04 (d, J = 14.4 Hz, 1H), 1.61 (s, 3H), 1.42 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.5, 167.2, 165.4, 162.9 (d, J = 250 Hz), 158.7, 158.6, 150.4, 129.3, 128.5, 125.8, 122.4, 122.3, 121.4, 115.4, 115.1, 109.7, 109.5, 69.7, 64.2, 43.7, 25.7, 14.4. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -110.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{19}FNO_3$: 328.1343, Found: 328.1346.



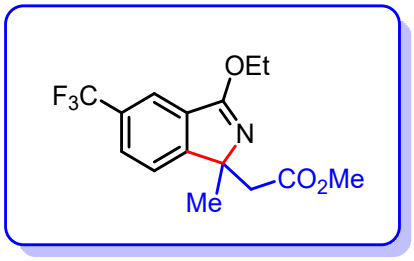
Methyl 2-(3-ethoxy-6-iodo-1-methyl-1*H*-isoindol-1-yl)acetate (4f), slightly yellow liquid (32 mg, 87% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (s, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 4.45-4.37 (m, 2H), 3.53 (s, 3H), 2.87 (d, J = 14.8 Hz, 1H), 2.73 (d, J = 14.8 Hz, 1H), 1.52 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.4, 167.2, 158.4, 136.7, 131.8, 131.1, 122.2, 96.5, 69.9, 64.1, 51.3, 43.3, 25.21, 14.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{17}INO_3$: 374.0248, Found: 374.0244.



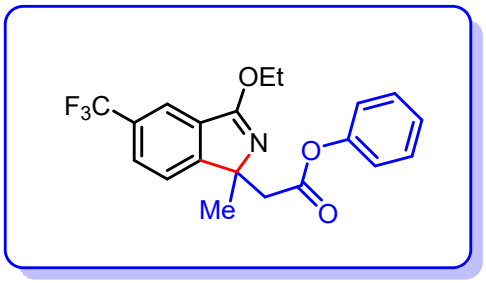
Methyl 2-(3-ethoxy-1-methyl-6-nitro-1*H*-isoindol-1-yl)acetate (4g), slightly yellow liquid (26 mg, 88% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.30 (s, 1H), 8.27 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 4.50-4.42 (m, 2H), 3.53 (s, 3H), 3.00 (d, J = 15.2 Hz, 1H), 2.84 (d, J = 15.2 Hz, 1H), 1.58 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.1, 166.4, 157.6, 148.7, 137.4, 123.8, 121.4, 116.9, 70.4, 64.6, 51.4, 42.9, 25.2, 14.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{17}N_2O_5$: 293.1132, Found: 293.1131.



Methyl 2-(6-bromo-3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4h), slightly yellow liquid (28 mg, 85% yield, chromatography on silica gel, eluent: PE/EA = 10:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.61(d, J = 1.2 Hz, 1H), 7.47 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 4.44-4.39 (m, 2H), 3.53 (s, 3H), 2.88 (d, J = 14.4 Hz, 1H), 2.73 (d, J = 14.4 Hz, 1H), 1.52 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.4, 167.0, 158.3, 131.2, 131.0, 125.2, 124.4, 122.0, 69.9, 64.2, 51.3, 43.2, 25.2, 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{17}BrNO_3$: 326.0386, Found: 326.0388.

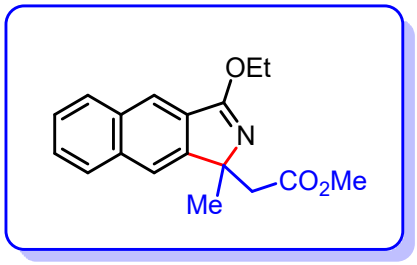


Methyl 2-(3-ethoxy-1-methyl-5-(trifluoromethyl)-1*H*-isoindol-1-yl)acetate (4i), slightly yellow liquid (28 mg, 89% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.76 (s, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 4.50-4.42 (m, 2H), 3.53 (s, 3H), 2.76 (d, J = 14.8 Hz, 1H), 2.80 (d, J = 14.8 Hz, 1H), 1.56 (s, 3H), 1.45 (t, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.4, 166.8, 159.8, 130.5, 127.0 (q, J = 30.0 Hz), 126.4 (q, J = 3.0 Hz), 124.8 (q, J = 270.0 Hz), 122.1 (q, J = 4.0 Hz), 70.3, 64.3, 51.4, 43.2, 25.2, 14.3. **^{19}F NMR (376 MHz, $CDCl_3$) δ** -62.0 (3F). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{17}F_3NO_3$: 316.1155, Found: 316.1156.

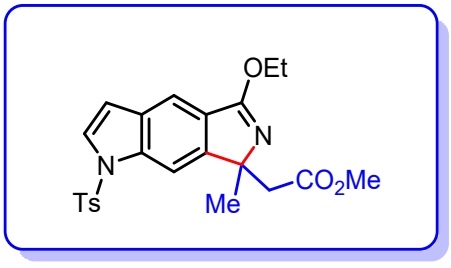


Phenyl 2-(3-ethoxy-1-methyl-5-(trifluoromethyl)-1*H*-isoindol-1-yl)acetate (4j), slightly yellow liquid (29 mg, 76% yield, chromatography on silica gel, eluent: PE/EA

= 10:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.80 (s, 1H), 7.70-7.64 (m, 2H), 7.31-7.25 (m, 2H), 7.16 (t, J = 7.6 Hz, 1H), 6.82-6.81 (m, 2H), 4.52-4.46 (m, 2H), 3.19 (d, J = 14.8 Hz, 1H), 3.09 (d, J = 14.8 Hz, 1H), 1.64 (s, 3H), 1.45 (t, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 168.3, 167.0 159.5, 150.3, 133.1, 130.7, 130.4, 129.3,127.0 (q, J = 30.0 Hz), 126.4 (q, J = 3.0 Hz), 124.8 (q, J = 270.0 Hz), 122.3 (q, J = 4.0 Hz), 70.4, 64.4, 43.4, 25.8, 14.3. **^{19}F NMR (376 MHz, $CDCl_3$) δ** -62.0 (3F). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{19}FNO_3$: 378.1312, Found: 378.1313.

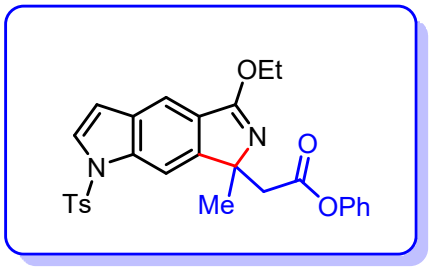


Methyl 2-(3-ethoxy-1-methyl-1*H*-benzo[f]isoindol-1-yl)acetate (4k), slightly yellow liquid (24 mg, 80% yield, chromatography on silica gel, eluent: PE/EA = 10:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.00 (s, 1H), 7.94 (d, J = 6.8 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.84 (s, 1H), 7.54-7.50 (m, 2H), 4.57-4.45 (m, 2H), 3.52 (s, 3H), 3.00 (d, J = 14.8 Hz, 1H), 2.86 (d, J = 14.8 Hz, 1H), 1.65 (s, 3H), 1.49 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.8, 167.6, 151.2, 134.0, 133.0, 131.1, 129.1, 128.4, 127.0, 125.9, 120.2, 120.1, 69.6, 64.1, 51.2, 44.2, 26.4, 14.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{20}NO_3$: 298.1438, Found: 298.1437.

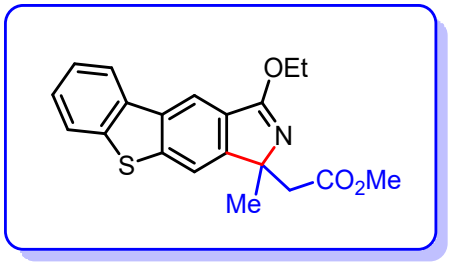


Methyl 2-(5-ethoxy-7-methyl-1-tosyl-1,7-dihydropyrrolo[3,4-f]indol-7-yl)acetate (4l), slightly yellow liquid (32 mg, 72% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.10 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.60 (s, 1H), 7.56 (d, J = 3.6 Hz, 1H), 7.20 (d, J = 7.6 Hz, 2H), 6.87 (d, J = 3.6 Hz, 1H),

4.48-4.39 (m, 2H), 3.54 (s, 3H), 2.99-2.87 (m, 2H), 2.79-2.74 (m, 2H), 2.31(s, 3H), 1.59 (s, 3H), 1.42 (t, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.7, 167.3, 152.7, 145.1, 136.0, 135.0, 130.8, 129.8, 128.4, 127.3, 126.8, 113.5, 109.6, 107.2, 69.4, 63.9, 51.3, 44.2, 38.6, 26.0, 21.4, 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{23}H_{25}N_2O_5S$: 441.1479, Found: 441.1479.

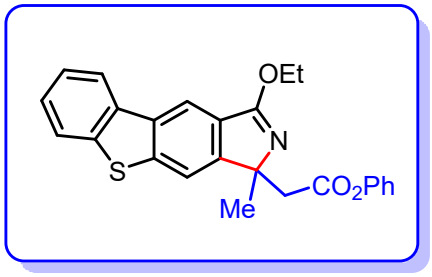


Phenyl 2-(5-ethoxy-7-methyl-1-tosyl-1,7-dihydropyrrolo[3,4-f]indol-7-yl)acetate (4m), slightly yellow liquid (39 mg, 78% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.10 (s, 1H), 7.79 (d, J = 8.0 Hz, 2H), 7.64 (s, 1H), 7.60 (d, J = 3.6 Hz, 1H), 7.18 (t, J = 8.0 Hz, 2H), 7.09 (t, J = 7.2 Hz, 3H), 6.99 (d, J = 8.0 Hz, 2H), 6.70 (d, J = 3.6 Hz, 1H), 4.50-4.37 (m, 2H), 3.23 (d, J = 14.4 Hz, 1H), 8.13 (d, J = 10.0 Hz, 1H), 2.16 (s, 3H), 1.68 (s, 2H), 1.42 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 168.36, 167.5, 152.2, 150.4, 145.0, 136.0, 134.7, 131.0, 129.7, 129.1, 128.6, 127.4, 126.6, 125.4, 121.3, 113.5, 109.6, 107.3, 69.5, 64.0, 44.4, 26.6, 21.4, 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{28}H_{27}N_2O_5S$: 503.1635, Found: 503.1633.

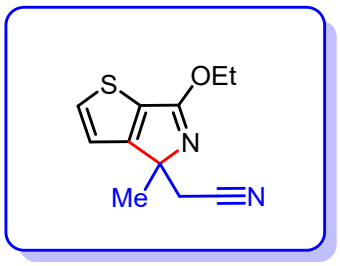


Methyl 2-(1-ethoxy-3-methyl-3*H*-benzo[4,5]thieno[2,3-f]isoindol-3-yl)acetate (4n), slightly yellow liquid (25 mg, 75% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.25 (s, 1H), 8.21-8.18 (m, 1H), 7.9 (s, 1H), 7.85-7.82 (m, 1H), 7.48-7.7.45 (m, 2H), 4.56-4.49 (m, 2H), 3.53 (s, 3H), 3.00 (d, J =

14.8 Hz, 1H), 3.24 (d, J = 14.4 Hz, 1H), 1.64 (s, 3H), 1.51 (t, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.7, 167.4, 154.5, 141.6, 139.6, 135.3, 135.2, 129.8, 126.9, 124.6, 122.9, 121.6, 116.0, 113.5, 69.4, 64.1, 51.3, 43.8, 25.8, 14.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{18}NO_3S$: 340.1002, Found: 340.1001.

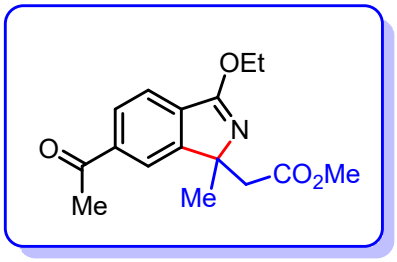


Phenyl 2-(1-ethoxy-3-methyl-3*H*-benzo[4,5]thieno[2,3-f]isoindol-3-yl)acetate (4o), slightly yellow liquid (32 mg, 78% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.27(d, J = 0.8 Hz, 1H), 8.21-8.19 (m, 1H), 7.99(d, J = 0.8 Hz, 1H), 7.84-7.83 (m, 1H), 7.48-7.7.45 (m, 2H), 7.28-7.24 (m, 2H), 7.13 (t, J = 7.2 Hz, 3H), 6.83 (d, J = 7.6 Hz, 2H), 4.59-4.51 (m, 2H), 3.24 (d, J = 14.4 Hz, 1H), 3.11 (d, J = 14.4 Hz, 1H), 1.70 (s, 3H), 1.50 (t, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 168.7, 167.6, 154.2, 150.4, 141.7, 139.7, 135.5, 135.1, 129.9, 129.3, 126.9, 125.7, 124.6, 122.9, 121.7, 121.4, 116.1, 113.7, 69.6, 64.2, 44.1, 26.1, 14.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}NO_3S$: 416.1315, Found: 416.1313.

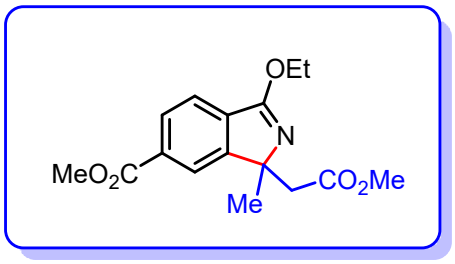


2-(6-Ethoxy-4-methyl-4*H*-thieno[2,3-c]pyrrol-4-yl)acetonitrile (4p), slightly yellow liquid (12 mg, 56% yield, chromatography on silica gel, eluent: PE/EA = 8:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.52 (d, J = 4.8 Hz, 1H), 7.13 (d, J = 4.8 Hz, 1H), 4.44-4.38 (m, 2H), 2.92 (d, J = 16.4 Hz, 1H), 2.56 (d, J = 17.2 Hz, 1H), 1.60 (s, 3H), 1.42 (t, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.0, 134.1, 119.9, 117.2, 100.5, 66.5, 64.7,

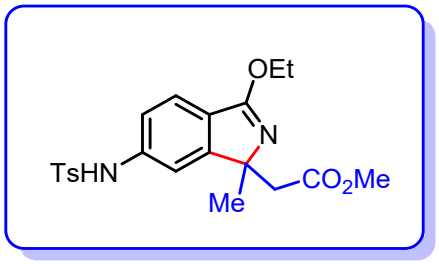
28.5, 23.8, 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{11}H_{13}OS$: 221.0743, Found: 221.0741.



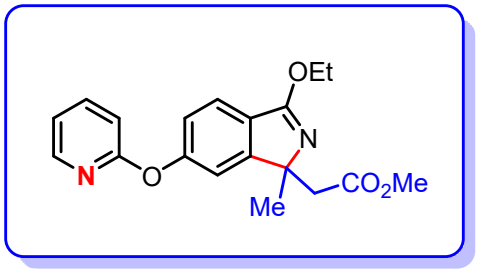
Methyl 2-(6-acetyl-3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4q), slightly yellow liquid (24 mg, 83% yield, chromatography on silica gel, eluent: PE/EA = 10:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.01 (s, 1H), 7.95 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 4.50-4.38 (m, 2H), 3.50 (s, 3H), 2.94 (d, J = 14.4 Hz, 1H), 2.81 (d, J = 14.8 Hz, 1H), 2.63 (s, 3H), 1.55 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 197.9, 170.4, 167.1, 156.6, 137.6, 136.0, 128.4, 121.0, 120.8, 70.2, 64.2, 51.2, 43.2, 26.9, 25.3, 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{20}NO_4$: 290.1387, Found: 290.1388.



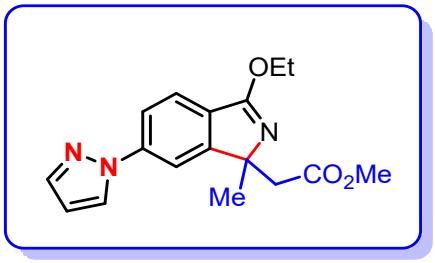
Methyl 3-ethoxy-1-(2-methoxy-2-oxoethyl)-1-methyl-1*H*-isoindole-6-carboxylate (4r), slightly yellow liquid (27 mg, 87% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.08-8.05 (m, 2H), 7.95 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 4.83-4.38 (m, 2H), 3.92 (s, 3H), 3.50 (s, 3H), 2.93 (d, J = 15.2 Hz, 1H), 2.83 (d, J = 14.4 Hz, 1H), 1.55 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.3, 167.2, 166.6, 156.8, 136.1, 130.9, 130.1, 129.5, 122.4, 122.7, 70.1, 64.2, 52.2, 51.2, 43.3, 25.4, 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{20}NO_5$: 306.1336, Found: 306.1333.



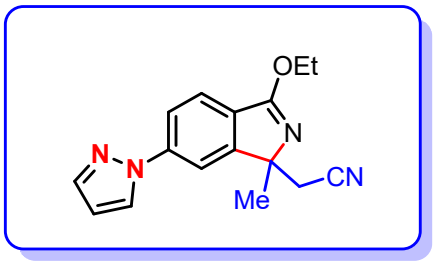
Methyl 2-(3-ethoxy-1-methyl-6-((4-methylphenyl)sulfonamido)-1*H*-isoindol-1-yl)acetate (4s), slightly yellow liquid (33 mg, 79% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, DMSO-d6) δ** 9.65 (s, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 6.24 (dd, *J* = 2.0 Hz, 8.4 Hz, 1H), 3.54-4.46 (m, 2H), 2.02 (d, *J* = 14.4 Hz, 1H), 1.83 (d, *J* = 14.4 Hz, 1H), 1.52 (s, 3H), 0.53 (s, 3H), 0.51 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, DMSO-d6) δ** 169.9, 166.1, 157.9, 143.4, 139.2, 136.4, 129.6, 127.2, 126.8, 121.0, 119.1, 112.9, 69.4, 63.4, 50.9, 42.9, 25.3, 20.9, 14.2. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{25}N_2O_5S$: 417.1479, Found: 417.1477.



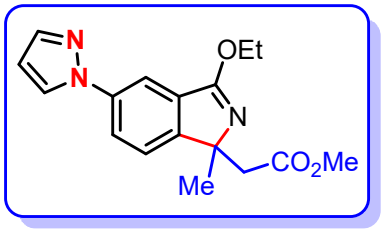
Methyl 2-(3-ethoxy-1-methyl-6-(pyridin-2-yloxy)-1H-isoindol-1-yl)acetate (4t), slightly yellow liquid (34 mg, 71% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.20 (dd, *J* = 1.2 Hz, 4.4 Hz, 1H), 7.73-7.70 (m, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 2.0 Hz, 1H), 7.12 (dd, *J* = 2.0 Hz, 8.4 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 4.50-4.39 (m, 2H), 3.53 (s, 3H), 2.88 (d, *J* = 14.4 Hz, 1H), 2.73 (d, *J* = 14.8 Hz, 1H), 1.58 (s, 3H), 1.43 (t, *J* =6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.7, 167.3, 163.4, 158.2, 155.8, 147.8, 139.6, 134.1, 128.5, 121.9, 120.5, 118.9, 116.5, 114.7, 111.9, 69.7, 64.0, 51.3, 43.6, 25.2, 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{19}H_{21}N_2O_4$: 341.1496, Found: 341.1499.



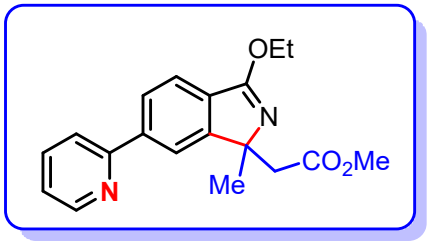
Methyl 2-(3-ethoxy-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl) acetate (4u), slightly yellow liquid (25 mg, 80% yield, chromatography on silica gel, eluent: PE/EA = 5:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.98 (d, *J* = 2.4 Hz, 1H), 7.86 (d, *J* = 1.6 Hz, 1H), 7.74 (d, *J* = 1.6 Hz, 1H), 7.68 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 6.48 (t, *J* = 2.0 Hz, 1H), 4.52-4.35 (m, 2H), 2.96 (d, *J* = 14.8 Hz, 1H), 2.84 (d, *J* = 14.8 Hz, 1H), 1.58 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.5, 167.2, 158.0, 141.5, 141.1, 130.3, 127.1, 121.7, 118.5, 112.6, 108.0, 69.9, 64.1, 51.3, 43.4, 25.5, 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{20}N_3O_3$: 314.1499, Found: 314.1498.



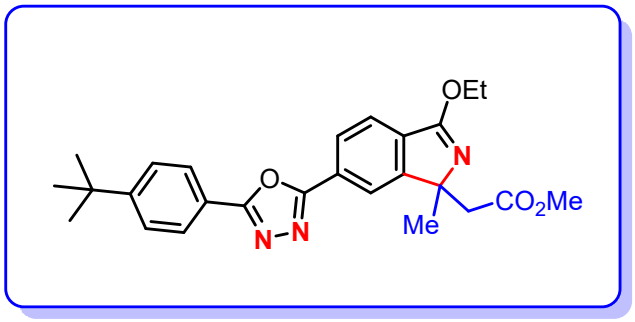
2-(3-Ethoxy-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl)acetonitrile (4v), slightly yellow liquid (23 mg, 83% yield, chromatography on silica gel, eluent: PE/EA = 5:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.98 (d, *J* = 2.4 Hz, 1H), 7.86 (d, *J* = 1.6 Hz, 1H), 7.74 (d, *J* = 1.6 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 6.48 (t, *J* = 2.0 Hz, 1H), 4.52-4.35 (m, 2H), 2.96 (d, *J* = 14.4 Hz, 1H), 2.84 (d, *J* = 14.4 Hz, 1H), 1.58 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 168.6, 154.2, 141.8, 132.0, 130.3, 127.1, 121.7, 118.5, 112.6, 108.0, 68.7, 64.2, 28.9, 24.4, 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{17}N_4O$: 281.1397, Found: 281.1399.



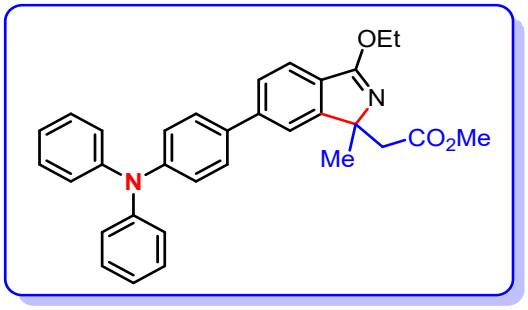
Methyl 2-(3-ethoxy-1-methyl-5-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl)acetate (4w), slightly yellow liquid (32 mg, 79% yield, chromatography on silica gel, eluent: PE/EA = 8:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.98 (d, J = 2.4 Hz, 1H), 7.96 (d, J = 1.6 Hz, 1H), 7.73 (d, J = 1.6 Hz, 1H), 7.69-7.66 (m, 1H), 7.55 (d, J = 8.0 Hz, 1H), 6.49-6.48(m, 1H), 4.48-4.40 (m, 2H), 3.52 (s, 3H), 2.96 (d, J =14.8 Hz, 1H), 2.36 (d, J = 14.8 Hz, 1H), 1.58 (s, 3H), 1.44 (t, J = 2.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.7, 167.1, 154.1, 141.2, 140.1, 133.6, 126.9, 122.50, 120.6, 111.6, 107.8, 69.9, 64.2, 51.3, 43.6, 25.4, 14.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{20}N_3O_3$: 314.1499, Found: 314.1497.



Methyl 2-(3-ethoxy-1-methyl-6-(pyridin-2-yl)-1*H*-isoindol-1-yl)acetate (4x), slightly yellow liquid (17 mg, 53% yield, chromatography on silica gel, eluent: PE/EA = 5:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.76-7.74 (m, 1H), 7.73 (d, J = 4.4 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.59 (s, 2H), 4.50-4.45 (m, 2H), 3.55 (s, 3H), 2.99 (d, J = 14.4 Hz, 1H), 2.80 (d, J = 14.4 Hz, 1H), 1.61 (s, 3H), 1.46 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.7, 167.4, 157.3, 145.4, 140.5, 132.6, 128.2, 128.0, 127.2, 121.7, 121.4, 120.6, 111.3, 64.2, 51.4, 43.5, 25.4, 14.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}N_2O_3$: 325.1547, Found: 325.1544.

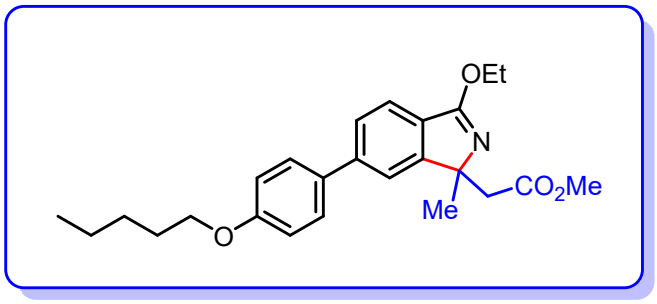


Methyl 2-(6-(5-(4-(*tert*-butyl)phenyl)-1,3,4-oxadiazol-2-yl)-3-ethoxy-1-methyl-1H-isoindol-1-yl)acetate (4y), slightly yellow liquid (29 mg, 64% yield, chromatography on silica gel, eluent: PE/EA = 5:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.22 (s, 1H), 8.16 (d, J = 0.8 Hz, 1H), 8.09 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.4 Hz, 2H), 4.452-4.45 (m, 2H), 3.53 (s, 3H), 3.02 (d, J = 14.8 Hz, 1H), 2.92 (d, J = 14.8 Hz, 1H), 1.62 (s, 3H), 1.47 (t, J = 7.2 Hz, 3H), 1.38 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.3, 167.2, 165.0, 164.4, 157.1, 155.6, 126.9, 126.7, 126.1, 121.6, 120.9, 119.9, 51.4, 43.3, 35.1, 31.1, 25.5, 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{25}H_{28}N_3O_4$: 434.2074, Found: 434.2075.

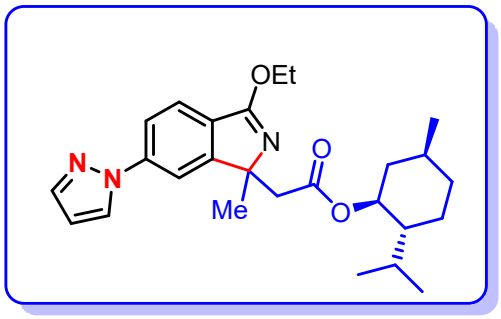


Methyl 2-(6-(4-(diphenylamino) phenyl)-3-ethoxy-1-methyl-1*H*-isoindol-1-yl) acetate (4z), slightly yellow liquid (36 mg, 73% yield, chromatography on silica gel, eluent: PE/EA = 5:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.65 (s, 1H), 7.57-7.54 (m, 2H), 7.52-7.48 (m, 2H), 7.28-7.24 (m, 4H), 7.15-7.12 (m, 6H), 7.03 (t, J = 7.2 Hz, 1H), 4.51-4.41 (m, 2H), 3.54 (s, 3H), 2.96 (d, J = 14.8 Hz, 1H), 2.81 (d, J = 14.4 Hz, 1H), 2.03 (s, 3H), 1.45 (t, J = 7.2 Hz, 3H), 1.25 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.6, 167.6, 156.8, 147.5, 147.4, 142.0, 134.4, 130.5, 129.2, 128.0, 126.2, 124.4,

123.5, 123.0, 121.0, 119.7, 69.8, 63.9, 60.2, 51.1, 43.5, 25.3, 20.9, 14.3, 14.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{31}N_2O_3$: 491.2329, Found: 491.2328.

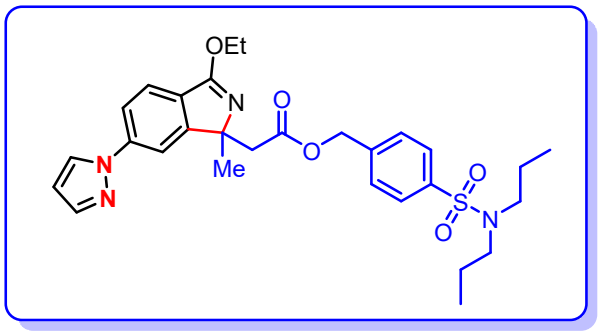


Methyl 2-(3-ethoxy-1-methyl-6-(4-(pentyloxy)phenyl)-1*H*-isoindol-1-yl)acetate (4za), slightly yellow liquid (27 mg, 67% yield, chromatography on silica gel, eluent: PE/EA = 5:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.61 (s, 1H), 7.55-7.54 (m, 1H), 7.53-7.50 (m, 3H), 6.98- 6.95 (m, 2H), 4.50-4.41 (m, 2H), 3.99 (t, J = 6.4 Hz, 2H), 3.53 (s, 3H), 2.94 (d, J = 14.4 Hz, 1H), 2.79 (d, J = 14.4 Hz, 1H), 1.84 -1.77 (m, 2H), 1.60 (s, 3H), 1.45 (t, J = 7.2 Hz, 3H), 1.42-1.36 (m, 2H), 0.94 (t, J = 7.21 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.7, 167.6, 159.0, 156.9, 142.2, 133.0, 130.5, 128.4, 126.3, 120.9, 119.8, 114.7, 69.8, 68.0, 63.9, 51.2, 43.6, 28.7, 28.1, 25.3, 22.4, 14.3, 13.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{32}NO_4$: 410.2326, Found: 410.2322.

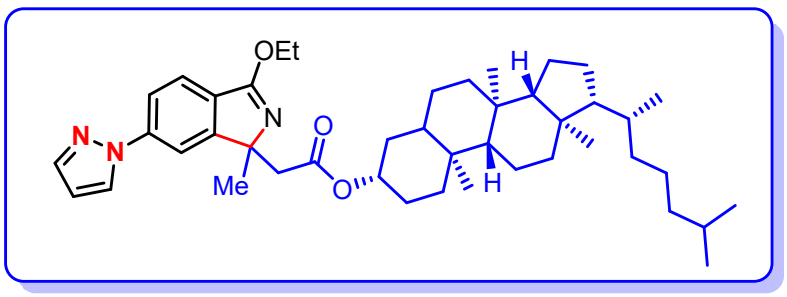


(1*S*, 2*R*, 5*S*)-2-Isopropyl-5-methylcyclohexyl 2-(3-ethoxy-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl)acetate (4zb), slightly yellow liquid (33 mg, 76% yield, chromatography on silica gel, eluent: PE/EA = 5:1) **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.95 (d, J = 2.4 Hz, 1H), 7.89-7.75 (m, 2H), 7.72 (d, J = 1.6 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 6.47 (t, J = 2.4 Hz, 1H), 4.46-4.42 (m, 2H), 2.99-2.90 (m, 2H), 2.20 (s, 1H), 1.96-1.92 (m, 2H), 1.83-1.79 (m, 2H), 1.69-1.61 (m, 3H), 1.55 (d, J = 1.6 Hz, 3H), 1.46-

1.42 (m, 3H), 1.27-1.22 (m, 3H), 0.80-0.75 (m, 6H), 0.62-0.59 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 169.6, 167.2, 154.3, 141.2, 140.0, 133.8, 126.9, 122.4, 120.5, 111.5, 111.45, 107.8, 77.4, 77.0, 76.7, 46.7, 44.1, 40.6, 34.1, 32.7, 31.2, 30.8, 26.4, 23.1, 21.9, 20.7, 16.0. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{26}H_{36}N_3O_3$: 438.2751, Found: 438.2755.

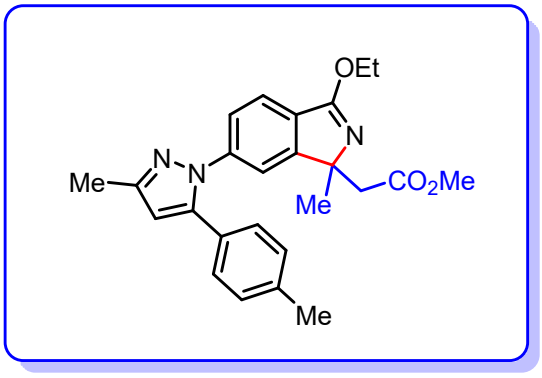


4-(*N*,*N*-Dipropylsulfamoyl)benzyl 2-(3-ethoxy-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl) acetate (4zc), slightly yellow liquid (37 mg, 68% yield, chromatography on silica gel, eluent: PE/EA = 5:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.97 (d, J = 6.4 Hz, 1H), 7.86 (d, J = 0.8 Hz, 1H), 7.73 (d, J = 1.6 Hz, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.61-7.59 (m, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.23 (d, J = 4.4 Hz, 2H), 6.49 (t, J = 2.0 Hz, 1H), 4.95 (d, J = 8.4 Hz, 2H), 4.42-4.37 (m, 2H), 3.04-3.00 (m, 6H), 1.56 (s, 3H), 1.55-1.51 (m, 4H), 1.41 (t, J = 4.4 Hz, 3H), 0.84 (t, J = 7.2 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 169.4, 167.2, 157.7, 141.5, 141.0, 140.1, 139.6, 130.1, 128.1, 127.1, 127.0, 121.7, 118.2, 112.5, 108.1, 69.9, 64.8, 64.1, 50.0, 43.5, 25.9, 22.0, 14.3, 11.1. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{29}H_{37}N_4O_5S$: 553.2479, Found: 553.2477.

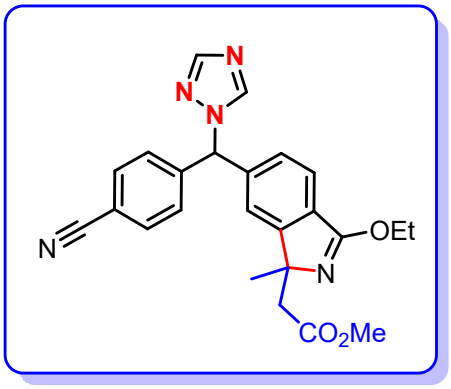


(3*S*, 8*R*, 9*R*, 10*S*, 13*R*, 14*R*, 17*R*)-8, 10, 13-Trimethyl-17-((*R*)-6-methylheptan- 2-yl)hexadecahydro-1*H*-cyclopenta[a]phenanthren-3-yl 2-(3-ethoxy-1-methyl-6-

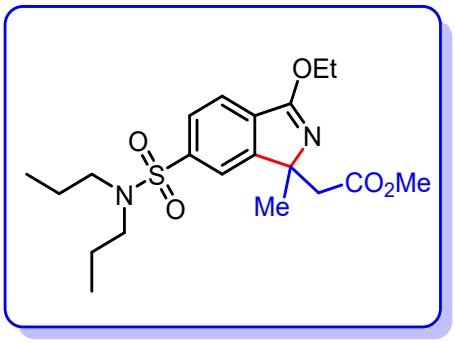
(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl) acetate (4zd), slightly yellow liquid (49 mg, 72% yield, chromatography on silica gel, eluent: PE/EA = 5:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.99 (d, J = 2.4 Hz, 1H), 7.86 (d, J = 1.2 Hz, 1H), 7.75 (d, J = 1.6 Hz, 1H), 7.69-7.67 (m, 1H), 7.55 (d, J = 8.0 Hz, 1H), 6.49 (t, J = 2.0 Hz, 1H), 5.28-5.24 (m, 1H), 4.50-4.39 (m, 2H), 2.97 (d, J = 18.4 Hz, 1H), 2.89-2.85 (m, 1H), 2.24-2.07 (m, 2H), 2.06 (d, J = 10.7 Hz, 1H), 1.97-1.91 (m, 1H), 1.84-1.71 (m, 1H), 1.62 (d, J = 6.8 Hz, 1H), 1.58 (s, 2H), 1.47-1.42 (m, 3H), 1.32 (d, J = 5.6 Hz, 2H), 1.25 (d, J = 7.2 Hz, 2H), 1.14-0.98 (m, 4H), 0.93-0.89 (m, 3H), 0.87-0.84 (m, 2H), 0.65 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 169.3, 167.2, 158.13, 141.5, 141.08, 139.6, 130.5, 127.1, 122.5, 121.6, 118.4, 112.8, 108.07, 73.8, 70.1, 64.2, 56.6, 56.1, 50.0, 44.2, 42.3, 39.7, 39.5, 37.8, 37.7, 36.9, 36.5, 36.2, 35.8, 33.9, 31.8, 28.2, 28.0, 27.5, 25.9, 25.6, 24.9, 24.3, 23.8, 22.8, 22.6, 21.0, 19.21, 18.7, 14.5, 14.2, 11.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{44}H_{66}N_3O_3$: 684.5099, Found: 684.5096.



Methyl 2-(3-ethoxy-1-methyl-6-(3-methyl-5-(*p*-tolyl)-1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl)acetate (4ze), slightly yellow liquid (28 mg, 67% yield, chromatography on silica gel, eluent: PE/EA = 5:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.41 (d, J = 8.0 Hz, 1H), 7.32 (s, 1H),7.28 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 7.10 (s, 1H), 7.07 (s, 3H), 6.29 (s, 1H), 4.47-4.38 (m, 2H), 3.49 (s, 3H), 7.75 (dd, J = 10.8 Hz, 20.0 Hz, 2H), 2.39 (s, 3H), 2.32 (s, 3H), 1.44 (s, 3H), 1.43-1.38 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.3, 167.2, 157.1, 149.8, 144.1, 141.1, 138.1, 129.1, 128.6, 124.6, 121.0, 118.3, 107.9, 69.8, 64.1, 51.2, 43.3, 25.3, 21.2, 14.3, 13.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{25}H_{28}N_3O_3$: 418.2125, Found: 418.2126.

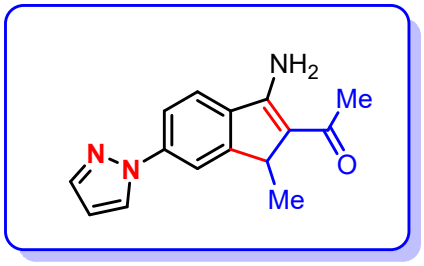


Methyl 2-(6-((4-cyanophenyl)(1*H*-1,2,4-triazol-1-yl)methyl)-3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4zf), slightly yellow liquid (20 mg, 47% yield, chromatography on silica gel, eluent: PE/EA = 5:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.06 (d, *J* = 2.0 Hz, 1H), 8.05-8.03 (m, 1H), 7.97 (d, *J* = 12.4 Hz, 1H), 7.51 (q, *J* = 4.0 Hz, 1H), 7.27 (s, 1H), 7.18-7.16 (m, 1H), 6.87 (s, 1H), 4.44 (q, *J* = 8.0 Hz, 1H), 3.93 (s, 1H), 3.46 (d, *J* = 4.8 Hz, 1H), 2.89 (dd, *J* = 14.4 Hz, 1.2 Hz, 1H), 2.72 (dd, *J* = 14.4 Hz, 3.2 Hz, 1H), 1.51 (d, *J* = 6.0 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.5, 167.1, 166.3, 157.2, 142.5, 138.5, 130.5, 130.2, 129.9, 128.8, 128.3, 128.1, 127.9, 121.8, 121.7, 99.7, 70.1, 67.5, 64.3, 52.3, 51.3, 25.2, 14.3, 14.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{24}N_5O_3$: 430.1874, Found: 430.1877.

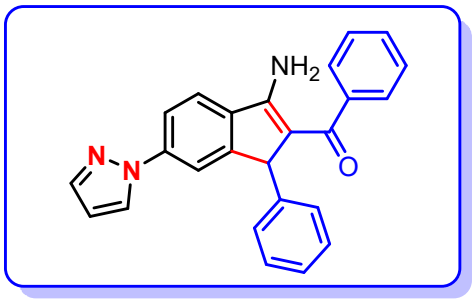


Methyl 2-(6-(*N*, *N*-dipropylsulfamoyl)-3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4zg), slightly yellow liquid (34 mg, 82% yield, chromatography on silica gel, eluent: PE/EA = 8:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.88 (d, *J* = 0.8 Hz, 1H), 7.82 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.60 (dd, *J* = 8.0 Hz, 0.4 Hz, 1H), 4.48-4.42 (m, 2H), 3.51 (s, 3H), 3.13–3.05 (m, 4H), 2.95 (d, *J* = 14.8 Hz, 1H), 2.80 (d, *J* = 14.8 Hz, 1H), 1.56 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.2, 166.8, 157.0, 141.2,

135.5, 126.8, 121.3, 120.4, 70.3, 64.4, 51.3, 49.7, 43.2, 25.2, 21.7, 14.3, 11.1. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{20}H_{31}N_2O_5S$: 411.1948, Found: 411.1949.

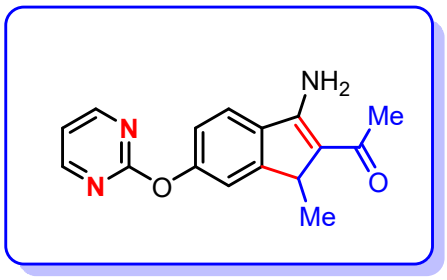


1-(3-Amino-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-inden-2-yl)ethan-1-one (5a), slightly yellow liquid (14 mg, 55% yield, chromatography on silica gel, eluent: PE/EA = 3:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.00 (t, J = 2.0 Hz, 1H), 7.83 (d, J = 2.0 Hz, 1H), 7.77 (d, J = 1.6 Hz, 1H), 7.70 (dd, J = 2.0 Hz, 8.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 6.51 (t, J = 2.0 Hz, 1H), 3.85 (q, J = 7.2 Hz, 1H), 2.31 (s, 3H), 1.50 (d, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 195.1, 152.4, 141.5, 134.1, 127.0, 121.9, 120.6, 118.6, 117.8, 115.0, 112.8, 108.1, 41.2, 29.3, 19.1. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{16}N_3O_1$: 254.1288, Found: 254.1289.

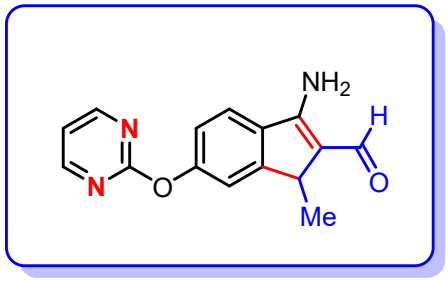


(3-Amino-1-phenyl-6-(1*H*-pyrazol-1-yl)-1*H*-inden-2-yl)(phenyl)methanone (5b), slightly yellow solid (25 mg, 65% yield, chromatography on silica gel, eluent: PE/EA = 1:1), **m. p: 140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.87 (d, J = 2.4 Hz, 1H), 7.76 (dd, J = 2.0 Hz, 8.4 Hz, 1H), 7.68 (d, J = 2.0 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 2.0 Hz, 1H), 7.32 -7.28 (m, 2H), 7.25-7.18 (m, 3H), 6.99-6.95 (m, 3H), 6.78-6.74 (m, 2H), 6.43 (t, J = 2.0 Hz, 1H), 5.11 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 193.5, 159.8,

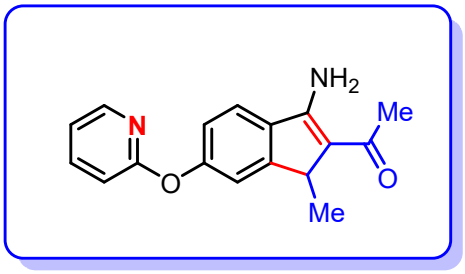
152.2, 142.2, 141.5, 140.2, 134.0, 129.2, 128.1, 127.7, 127.6, 127.0, 126.5, 126.3, 53.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{20}N_3O$: 378.1601, Found: 378.1608.



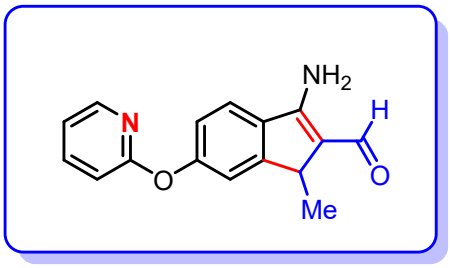
(1-Amino-1-methyl-6-(pyrimidin-2-yloxy)-1*H*-inden-2-yl)ethan-1-one (5c), slightly yellow liquid (21 mg, 75% yield, chromatography on silica gel, eluent: PE/EA = 2:1). **^{1}H NMR (400 MHz, $CDCl_3$)** ***δ*** 8.58 (d, *J* = 4.8 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.29 (d, *J* = 2.0 Hz, 1H), 7.22 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H), 7.07 (t, *J* = 4.8 Hz, 1H), 3.83 (q, *J* = 6.8 Hz, 1H), 2.29 (s, 1H), 1.44 (d, *J* = 7.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** ***δ*** 195.1, 165.3, 159.8, 156.6, 154.6, 152.6, 133.3, 120.6, 117.7, 116.4, 114.5, 41.1, 28.2, 19.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}N_3O_2$: 282.1237, Found: 282.1239.



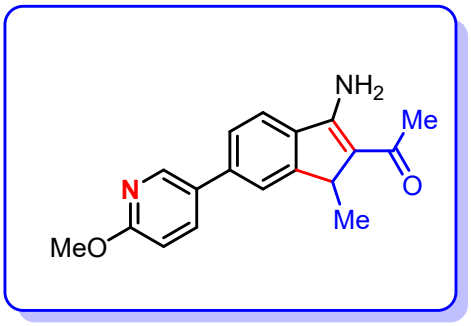
3-Amino-1-methyl-6-(pyrimidin-2-yloxy)-1*H*-indene-2-carbaldehyde (5d), slightly yellow liquid (20 mg, 75% yield, chromatography on silica gel, eluent: PE/EA = 2:1). **^{1}H NMR (400 MHz, $CDCl_3$)** ***δ*** 9.58 (s, 1H), 8.59 (d, *J* = 4.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 2.0 Hz, 1H), 7.24-7.22 (m, 1H), 7.08 (t, *J* = 4.8 Hz, 1H), 3.89 (q, *J* = 7.2 Hz, 1H), 1.46 (d, *J* = 7.2 Hz, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** ***δ*** 186.5, 165.2, 159.8, 157.2, 154.9, 153.4, 133.0, 121.1, 120.8, 117.7, 116.5, 39.7, 18.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}N_3O_2$: 268.1081, Found: 268.1087.



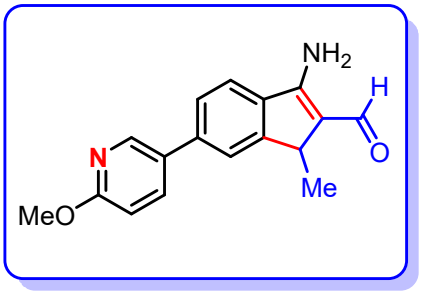
1-(3-Amino-1-methyl-6-(pyridin-2-yloxy)-1*H*-inden-2-yl)ethan-1-one (5e), slightly yellow liquid (21 mg, 74% yield, chromatography on silica gel, eluent: PE/EA = 2:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.20 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 7.74-7.70 (m, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.21 (d, J = 2.0 Hz, 1H), 7.13 (dd, J = 8.4 Hz, 2.0 Hz, 1H), 7.05-7.02 (m, 1H), 6.96 (d, J = 8.0 Hz, 1H), 3.78 (q, J = 7.2 Hz, 1H), 2.28 (s, 3H), 1.42 (d, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 194.8, 163.4, 156.2, 152.8, 147.7, 139.6, 132.3, 120.8, 119.9, 118.9, 116.9, 111.9, 40.9, 28.0, 19.05. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{17}N_2O_2$: 282.1285, Found: 282.1287.



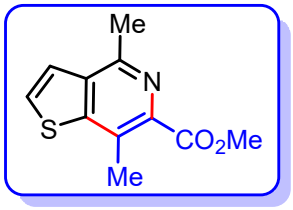
3-Amino-1-methyl-6-(pyridin-2-yloxy)-1*H*-indene-2-carbaldehyde (5f), slightly yellow liquid (20 mg, 75% yield, chromatography on silica gel, eluent: PE/EA = 2:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 9.55 (s, 1H), 8.21 (dd, J = 4.8 Hz, 2.0 Hz, 1H), 7.76-7.71 (m, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.17-7.14 (m, 1H), 7.04 (dd, J = 2.0 Hz, 8.4 Hz, 1H), 7.08 (t, J = 4.8 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 3.86 (t, J = 7.2 Hz, 1H), 1.45 (d, J = 7.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 176.9, 163.3, 157.5, 156.6, 153.5, 147.7, 139.69, 132.0, 121.0, 120.1, 119.0, 117.0, 112.0, 39.7, 18.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}N_2O_2$: 267.1128, Found: 267.1122.



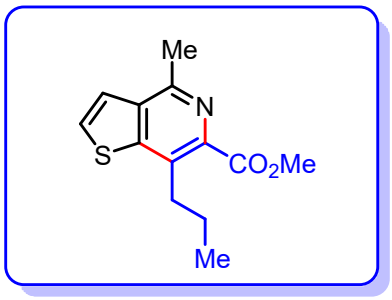
1-(3-Amino-6-(6-methoxypyridin-3-yl)-1-methyl-1*H*-inden-2-yl)ethan-1-one (5g), slightly yellow liquid (23.0 mg, 77% yield, chromatography on silica gel, eluent: PE/EA = 2:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.41 (d, J = 2.4 Hz, 1H), 7.81 (dd, J = 2.4 Hz, 8.8 Hz, 1H), 7.67-7.65 (m, 1H), 7.57 (s, 1H), 7.47-7.45 (d, J = 1.6 Hz, 1H), 6.84-6.82 (m, 1H), 3.98 (s, 3H), 3.85-3.81 (m, 1H), 2.30 (s, 3H), 1.47 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 206.8, 159.1, 159.0, 151.4, 142.9, 134.35, 133.1, 132.9, 128.5, 128.2, 126.4, 125.5, 122.2, 121.1, 120.0, 119.9, 114.8, 114.8, 68.1, 28.9, 28.2, 22.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}N_2O_2$: 295.1441, Found: 295.1441.



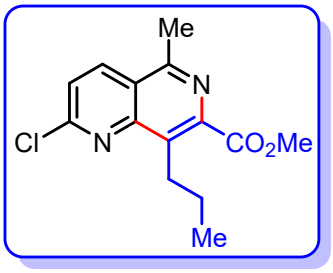
3-Amino-6-(6-methoxypyridin-3-yl)-1-methyl-1*H*-indene-2-carbaldehyde (5h), slightly yellow liquid (21mg, 75% yield, chromatography on silica gel, eluent: PE/EA = 2:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 9.59 (s, 1H), 8.42 (d, J = 2.0 Hz, 1H), 7.83 (m, 1H), 7.60 (s, 1H), 7.55 (d, J = 7.2 Hz, 1H), 6.84 (d, J = 8.8 Hz, 1H), 3.99 (d, J = 0.8 Hz, 3H), 3.92 (q, J = 7.2 Hz, 1H), 1.50 (d, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 163.9, 157.5, 152.3, 145.2, 140.2, 137.5, 134.86, 132.0, 129.7, 128.4, 125.7, 122.31, 120.6, 111.0, 39.7, 18.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{17}N_2O_2$: 381.1285, Found: 381.1288.



Methyl 4,7-dimethylthieno[3,2-*c*]pyridine-6-carboxylate (7a), slightly yellow liquid (22.1 mg, 74% yield, chromatography on silica gel, eluent: PE/EA = 3:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.64 (d, *J* = 5.6 Hz, 1H), 7.51 (d, *J* = 5.6 Hz, 1H), 4.00 (s, 3H), 2.86 (s, 3H), 2.81 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) *δ*** 167.3, 151.4, 150.1, 139.1, 136.3, 129.9, 128.3, 123.3, 52.8, 22.8, 18.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{12}NO_2S$: 222.0583, Found: 222.0589.

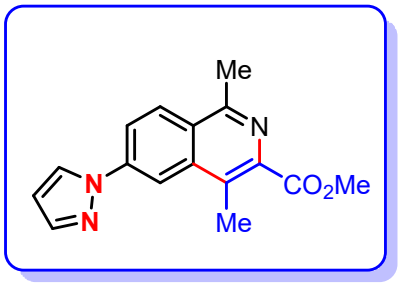


Methyl 4-methyl-7-propylthieno[3,2-c]pyridine-6-carboxylate (7b), slightly yellow liquid (13 mg, 54% yield, chromatography on silica gel, eluent: PE/EA = 3:1). **^{1}H NMR (400 MHz, $CDCl_3$) *δ*** 8.05 (d, *J* = 2.8 Hz, 1H), 7.92 (d, *J* = 3.2 Hz, 1H), 3.98 (s, 3H), 3.21 -3.16 (m, 2H), 2.83 (s, 3H), 1.79-1.73 (m, 2H), 1.06 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) *δ*** 167.9, 153.4, 140.0, 135.0, 131.8, 122.2, 119.9, 77.5, 77.2, 76.8, 52.6, 31.9, 24.0, 22.9, 14.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{12}NO_2S$: 250.0896, Found: 250.0898.

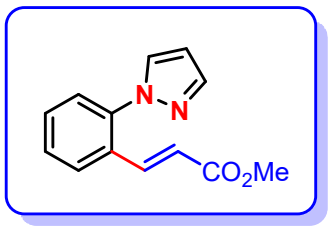


Methyl 2-chloro-5-methyl-8-propyl-1,6-naphthyridine-7-carboxylate (7c), slightly yellow liquid (27.8 mg, 63% yield, chromatography on silica gel, eluent: PE/EA = 3:1). **^{1}H NMR (400 MHz, $CDCl_3$) *δ*** 8.35 (d, *J* = 8.8 Hz, 1H), 7.53 (d, *J* = 8.8 Hz, 1H), 4.02

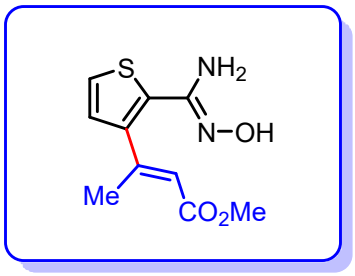
(s, 3H), 3.38-3.28 (m, 2H), 2.93 (s, 3H), 1.75-1.66 (m, 2H), 1.02 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 167.4, 156.9, 154.8, 150.5, 145.2, 136.8, 134.1, 124.5, 122.0, 52.9, 28.6, 24.5, 22.0, 14.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{16}ClN_2O_2$: 279.0895, Found: 279.0901.



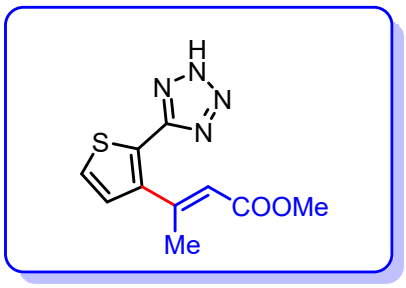
Methyl 1, 4-dimethyl-6-(1*H*-pyrazol-1-yl)isoquinoline-3-carboxylate (7d), slightly yellow liquid (28.1 mg, 63% yield, chromatography on silica gel, eluent: PE/EA = 3:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.40 (d, J = 2.0 Hz, 1H), 8.25 (d, J = 8.8 Hz, 1H), 8.13 (d, J = 2.4 Hz, 1H), 8.06 (dd, J = 9.2 Hz, 2.0 Hz, 1H), 7.83 (d, J = 1.2 Hz, 1H), 6.58-6.56 (m, 1H), 4.03 (s, 3H), 3.27-3.23 (m, 2H), 2.98 (s, 3H), 1.81-1.77 (m, 2H), 1.01 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 168.0, 156.4, 142.2, 141.5, 140.9, 136.9, 128.1, 127.67, 127.1, 126.0, 120.0, 112.9, 108.7, 52.8, 22.5, 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{16}N_3O_2$: 282.1237, Found: 382.1235.



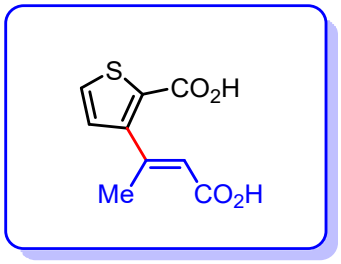
Methyl (*E*)-3-(2-(1*H*-pyrazol-1-yl)phenyl)acrylate (3a-I'), slightly yellow liquid (20 mg, 89% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.75 (d, J = 0.4 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.60 (dd, J = 9.2, 6.8 Hz, 2H), 7.45-7.43 (m, 2H), 7.41-7.37 (m, 1H), 6.46 (t, J = 2.1 Hz, 1H), 6.34 (d, J = 0.4 Hz, 1H), 6.34 (d, J = 1.6 Hz, 1H), 3.72 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.7, 141.21, 140.2, 139.7, 131.2, 130.5, 129.8, 128.3, 127.58, 126.1, 120.2, 107.1, 51.6.



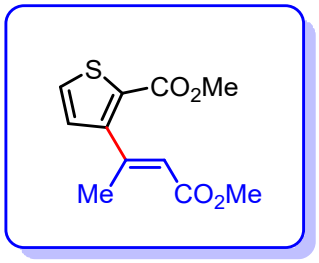
Methyl (*E*)-3-(2-((*Z*)-*N*'-hydroxycarbamimidoyl)thiophen-3-yl)but-2-enoate (3b-I), slightly yellow liquid (21 mg, 87% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.27 (d, J = 4.8 Hz, 1H), 6.95 (d, J = 5.2 Hz, 1H), 6.02-6.01 (m, 1H), 4.91 (s, 2H), 3.74 (s, 3H), 2.50 (d, J = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.8, 151.7, 147.6, 142.6, 128.7, 126.1, 119.6, 51.3, 19.9. HRMS (ESI-TOF) m/z: [M + H]+ Calcd for $C_{10}H_{13}N_2O_3S$: 241.0641, Found: 241.0644.



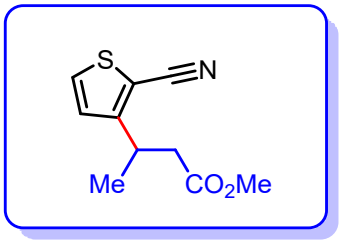
Methyl (*E*)-3-(2-(2*H*-tetrazol-5-yl)thiophen-3-yl)but-2-enoate (3b-II), slightly yellow solid (15 mg, 61% yield, chromatography on silica gel, eluent: PE/EA = 1:1), **m. p: 86 ℃.^{1}H NMR (400 MHz, CD_3OD)** δ 7.49 (d, J = 5.2 Hz, 1H), 7.13 (d, J = 5.2 Hz, 1H), 5.87 (d, J = 1.2 Hz, 1H), 3.67 (s, 3H), 2.33 (d, J = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 167.2, 152.3, 142.6, 128.2, 125.7, 118.3, 50.0, 18.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}N_4O_2S$: 251.0597, Found: 251.0599.



(*E*)-3-(1-Carboxyprop-1-en-2-yl)thiophene-2-carboxylic acid (3b-III), slightly yellow liquid (13 mg, 63% yield, chromatography on silica gel, eluent: PE/EA = 1:1). **^{1}H NMR (400 MHz, CD_3OD) δ** 7.63 (d, J = 5.2 Hz, 1H), 6.98 (d, J = 5.2 Hz, 1H), 5.78 (d, J = 1.2 Hz, 1H), 2.44 (d, J = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD) δ** 168.2, 163.1, 153.3, 152.5, 150.1, 130.9, 129.3, 119.0, 19.2. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_9H_9O_4S$: 213.0216, Found: 213.0211.

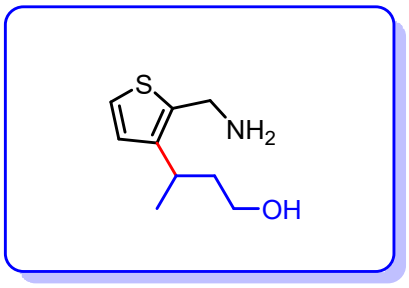


Methyl (*E*)-3-(4-methoxy-4-oxobut-2-en-2-yl)thiophene-2-carboxylate (3b-IV), slightly white solid (13 mg, 90% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 70 ℃.^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.46 (d, J = 5.2 Hz, 1H), 6.92 (d, J = 4.8 Hz, 1H), 5.86 (d, J = 1.2 Hz, 1H), 3.85 (s, 3H), 3.75 (s, 3H), 2.49 (d, J = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.6, 161.9, 152.9, 150.2, 130.8, 129.6, 119.1, 52.2, 51.1, 29.7, 20.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{11}H_{13}O_4S$: 241.0529, Found: 241.0527.

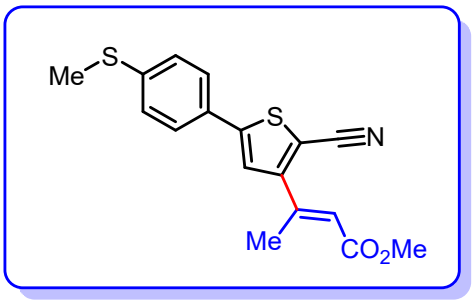


Methyl 3-(2-cyanothiophen-3-yl)butanoate (3b-V), slightly yellow liquid (11 mg, 54% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz,**

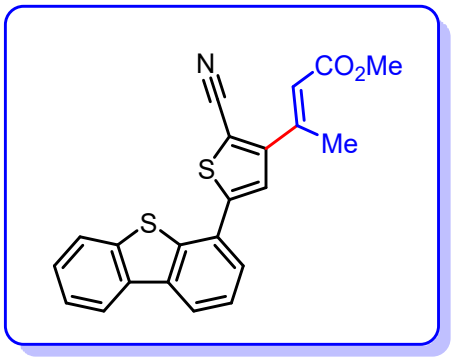
$CDCl_3$) δ 7.50 (d, J = 5.2 Hz, 1H), 7.00 (d, J = 5.2 Hz, 1H), 3.67-3.62 (m, 4H), 2.64 (d, J = 7.2 Hz, 2H), 1.34 (d, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 171.5, 157.0, 132.2, 126.3, 113.8, 105.2, 51.7, 41.4, 31.6, 21.0. HRMS (ESI-TOF) m/z: [M + H]+ Calcd for $C_{10}H_{12}NO_2S$: 210.0583, Found: 210.0588.



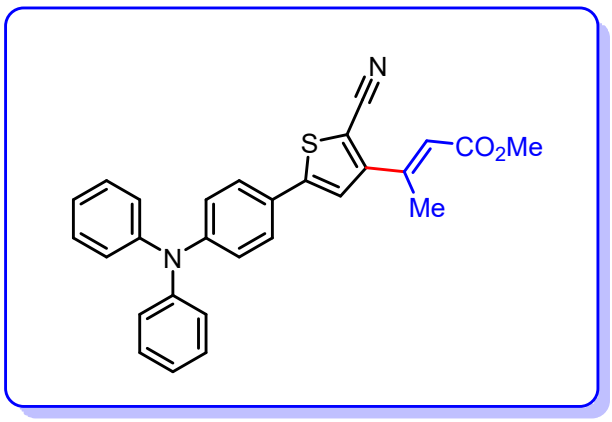
3-(2-(Aminomethyl)thiophen-3-yl)butan-1-ol (3b-VI), slightly yellow liquid (13 mg, 71% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.16 (d, J = 5.2 Hz, 1H), 6.90 (d, J = 5.2 Hz, 1H), 4.03-3.94 (m, 2H), 3.45-3.40 (m, 1H), 3.32-3.26 (m, 1H), 3.09-3.03 (m, 1H), 2.01-1.93 (m, 2H), 1.24 (d, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 144.1, 135.7, 126.5, 123.4, 58.3, 41.7, 37.8, 28.3, 22.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_9H_{16}NOS$: 186.0947, Found: 186.0946.



Methyl (*E*)-3-(2-cyano-5-(4-(methylthio)phenyl)thiophen-3-yl)but-2-enoate (3e-I), slightly yellow solid (13 mg, 62% yield, chromatography on silica gel, eluent: PE/EA = 10:1),**m. p: 74 ℃.**^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 9.2 Hz), 7.28 (d, J = 7.2 Hz), 7.26 (s, 1H), 6.32 (d, J = 0.8 Hz), 3.78 (s), 2.62 (d, J = 1.2 Hz), 2.52 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.40, 153.19, 147.45, 147.12, 141.39, 128.32, 126.51, 126.47, 122.41, 120.60, 114.10, 103.67, 51.47, 18.55, 15.25. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_9H_9N_2OS$: 199.0430, Found: 199.0433.

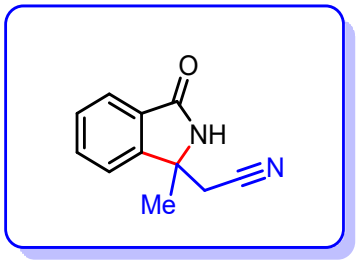


Methyl (*E*)-3-(2-cyano-5-(dibenzo[b,d]thiophen-4-yl)thiophen-3-yl)but-2-enoate (3e-II), slightly yellow solid (29 mg, 74% yield, chromatography on silica gel, eluent: PE/EA = 8:1), **m. p: 74 ℃.^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.23-8.17 (m, 1H), 7.91-7.88 (m, 1H), 7.65-7.62 (m, 1H), 7.56 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.54-7.51 (m, 1H), 6.41-6.37 (m, 1H), 3.80 (s, 2H), 2.69 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.4, 147.3, 137.1, 127.5, 126.8, 125.3, 125.2, 125.02, 122.71, 122.6, 121.9, 120.8, 113.9, 51.5, 18.63. HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{22}H_{16}NO_2S_2$: 390.0617, Found: 390.0616.

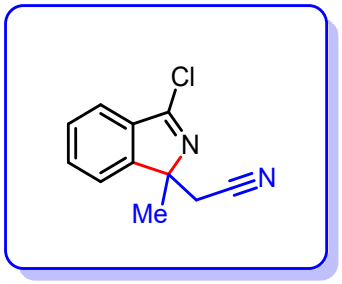


Methyl (*E*)-3-(2-cyano-5-(4-(diphenylamino)phenyl)thiophen-3-yl)but-2-enoate (3e-III), slightly yellow solid (37 mg, 82% yield, chromatography on silica gel, eluent: PE/EA = 10:1), **m. p: 75 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.41 (d, *J* = 8.8 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 4H), 7.18 (s, 1H), 7.12 (d, *J* = 8.4 Hz, 4H), 7.08 (d, *J* = 7.2 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.31 (d, *J* = 1.2 Hz, 1H), 3.77 (s, 3H), 2.61 (d, *J* = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.4, 153.1, 150.8, 149.3, 147.6, 146.8, 129.5, 129.4, 127.1, 125.2, 125.1, 125.0, 124.8, 124.0, 122.2, 121.6, 120.4, 114.3, 102.8, 51.4, 18.5.

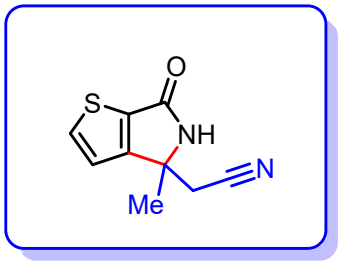
HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{28}H_{23}N_2O_2S$: 451.1475, Found: 451.1477.



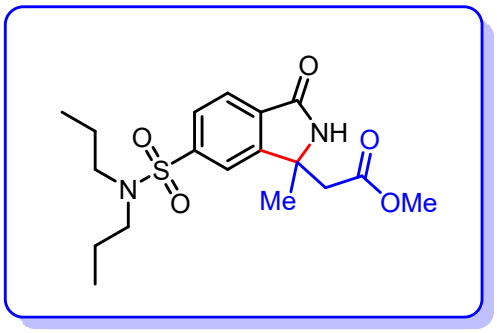
2-(1-Methyl-3-oxoisoindolin-1-yl)acetonitrile (4b-I), slightly yellow liquid (17 mg, 94% yield, chromatography on silica gel, eluent: PE/EA = 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** ***δ*** 8.39 (s, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.64-7.60 (m, 1H), 7.57 (d, *J* = 7.6 Hz, 1 H), 7.52 (td, *J* = 7.4, 1.2 Hz, 1H), 2.92 (d, *J* = 16.6 Hz, 1H), 2.83 (d, *J* = 16.6 Hz, 1H), 1.72 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** ***δ*** 168.6, 150.5, 133.0, 129.6, 127.7, 125.9, 124.8, 115.9, 58.7, 30.2, 25.1. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{11}H_{11}N_2O$: 187.0866, Found: 187.0869.



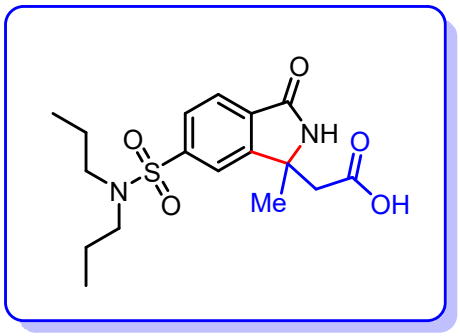
2-(3-Chloro-1-methyl-1*H*-isoindol-1-yl)acetonitrile (4b-II), slightly yellow liquid (9 mg, 43% yield, chromatography on silica gel, eluent: PE/EA = 10:1).**^{1}H NMR (400 MHz, $CDCl_3$)** ***δ*** 7.85 (d, *J* = 7.6 Hz, 1H), 7.66-7.61 (m, 1H), 7.58 (s, 1H), 7.53 (dd, *J* = 7.2 Hz, 0.8 Hz, 1H), 2.87 (d, *J* = 3.6 Hz, 1H), 2.85 (s, 1H), 1.75 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** ***δ*** 166.3, 160.2, 150.3, 134.0, 130.9, 127.1, 126.8, 125.2, 115.0, 61.9, 27.1, 23.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{11}H_{10}ClN_2$: 205.0527, Found: 205.0531.



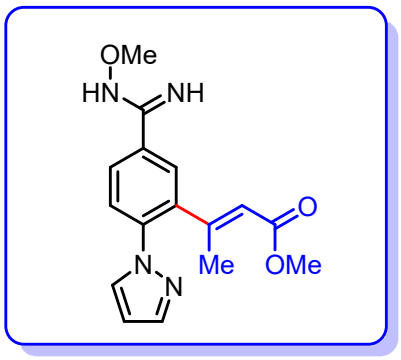
2-(4-Methyl-6-oxo-5,6-dihydro-4*H*-thieno[2,3-c]pyrrol-4-yl)acetonitrile (4p-I), slightly yellow liquid (18 mg, 93% yield, chromatography on silica gel, eluent: PE/EA = 2:1).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.75 (d, *J* = 4.8 Hz, 1H), 7.15 (d, *J* = 4.8 Hz, 1H), 6.83 (s, 1H), 2.85 (d, *J* = 16.4 Hz, 1H), 2.78 (d, *J* = 16.4 Hz, 1H), 1.74 (s, 4H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 164.9, 159.5, 137.2, 134.4, 119.6, 116.1, 58.3, 29.9, 24.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_9H_9N_2OS$: 199.0430, Found: 199.0433.



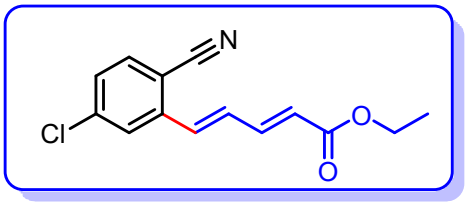
Methyl 2-(6-(*N*,*N*-dipropylsulfamoyl)-1-methyl-3-oxoisoindolin-1-yl)acetate (4zg-I), slightly yellow liquid (36 mg, 94% yield, chromatography on silica gel, eluent: PE/EA = 3:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.95 (d, *J* = 8.0 Hz, 1H), 7.90 (dd, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.86 (s, 1H), 3.74 (s, 3H), 3.15-3.08 (m, 4H), 3.00 (d, *J* = 16.4 Hz, 1H), 2.53 (d, *J* = 16.4 Hz, 1H), 1.64 (s, 3H), 1.58-1.52 (m, 4H), 0.86 (t, *J* = 7.2 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.7, 167.1, 151.6, 144.3, 134.1, 127.3, 125.1, 120.2, 59.2, 52.2, 49.8, 43.7, 24.9, 21.8, 11.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{27}N_2O_5S$: 383.1635, Found: 383.1639.



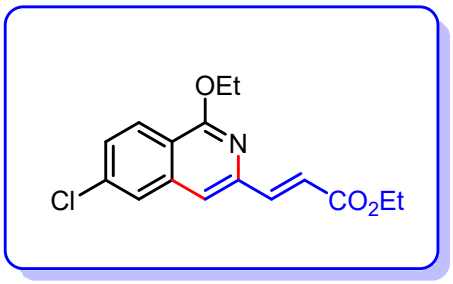
2-(6-(*N*,*N*-Dipropylsulfamoyl)-1-methyl-3-oxoisoindolin-1-yl)acetic acid (4zg-II), slightly yellow liquid (35 mg, 96% yield, chromatography on silica gel, eluent: PE/EA = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.70 (s, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 1.6 Hz, 1H), 7.89 (s, 1H), 3.15-3.11 (m, 3H), 3.07 (d, J = 16.4 Hz, 1H), 2.55 (d, J = 16.4 Hz, 1H), 2.10 (s, 4H), 1.55 (t, J = 8.8 Hz, 4H), 0.86 (t, J = 7.2 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 176.4, 173.7, 152.0, 144.7, 133.7, 127.4, 125.2, 120.2, 61.6, 49.7, 42.8, 24.6, 21.8, 11.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{25}N_2O_5S$: 369.1479, Found: 369.1483.



Methyl (*E*)-3-(5-(N-methoxycarbamimidoyl)-2-(1*H*-pyrazol-1-yl)phenyl)but-2-enoate (4u-I), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, J = 2.0, 8.4 Hz, 1H), 8.01 (d, J = 2.0 Hz, 1H), 7.74 (d, J = 1.6 Hz, 1H), 7.68 (d, J = 2.4 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 6.47-6.46 (m, 1H), 6.04 (d, J = 1.2 Hz, 1H), 3.95 (s, 3H), 3.75 (s, 3H), 2.01 (d, J = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.4, 165.9, 155.7, 141.7, 141.2, 137.7, 131.0, 130.5, 130.5, 129.4, 125.5, 120.5, 108.0, 52.4, 51.2, 18.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{19}N_4O_3$: 315.1452, Found: 315.1455.



Ethyl (2*E*, 4*E*)-5-(5-chloro-2-cyanophenyl)penta-2,4-dienoate (10a), ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.70 (d, *J* = 2.0 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.45 (dd, *J* = 11.2 Hz, 15.6 Hz, 1H), 7.36 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.16 (d, *J* = 15.6 Hz, 1H), 7.01 (dd, *J* = 11.2, 15.6 Hz, 1H), 6.12 (d, *J* = 15.2 Hz, 1H), 4.25 (q, *J* =7.2 Hz, 2H), 2.01 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) *δ*** 166.2, 142.5, 140.7, 139.6, 134.3, 133.4, 131.8, 129.0, 126.0, 125.2, 116.7, 110.1, 60.7, 14.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{13}ClNO_2$: 262.0629, Found: 262.0633.

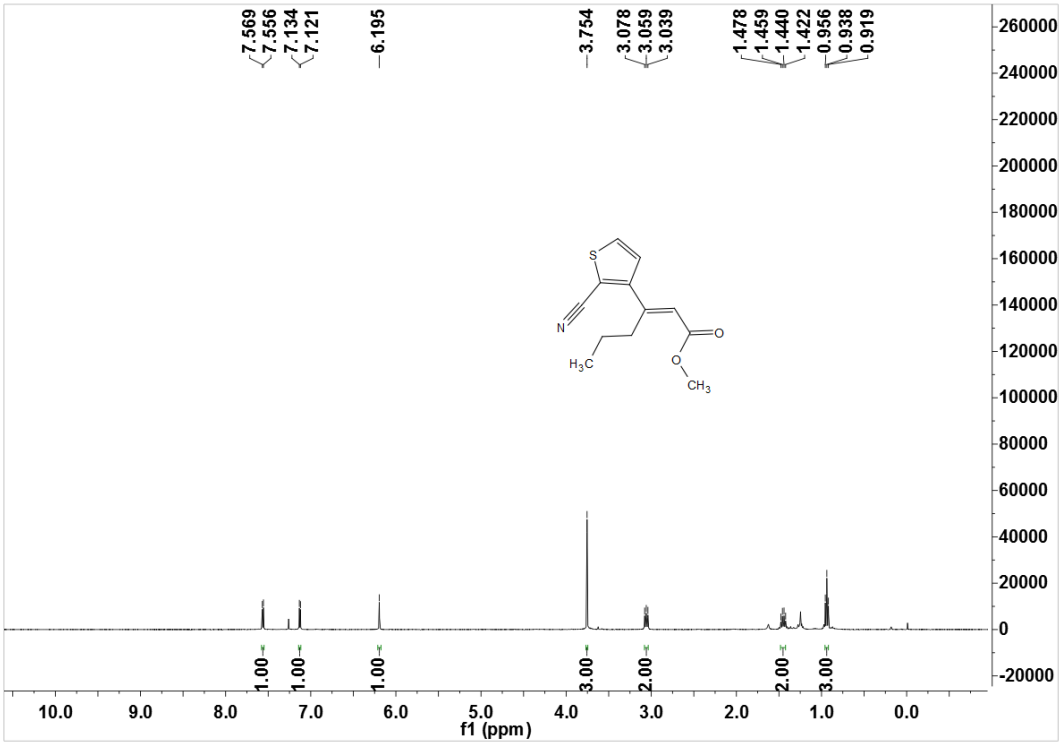


Ethyl (*E*)-3-(6-chloro-1-ethoxyisoquinolin-3-yl)acrylate (11a), ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.18 (dd, *J* = 8.8 Hz, 1H), 7.71 (d, *J* = 2.0 Hz, 1H), 7.64 (d, *J* = 14.4 Hz, 1H), 7.47 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.18 (s, 1H), 7.01 (d, *J* = 14.4 Hz, 1H), 4.62 (dd, *J* = 7.2 Hz, 14.0 Hz, 2H), 4.29 (dd, *J* = 7.2 Hz, 14.4 Hz, 2H), 1.51 (t, *J* = 7.2 Hz, 3H), 1.37 (t, *J* = 3.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) *δ*** 167.2, 160.1, 145.2, 143.3, 138.9, 137.1, 128.2, 126.3, 125.8, 121.4, 183.9, 116.5. 62.3, 60.5, 14.4, 14.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}ClNO_3$: 306.0891, Found: 306.0896.

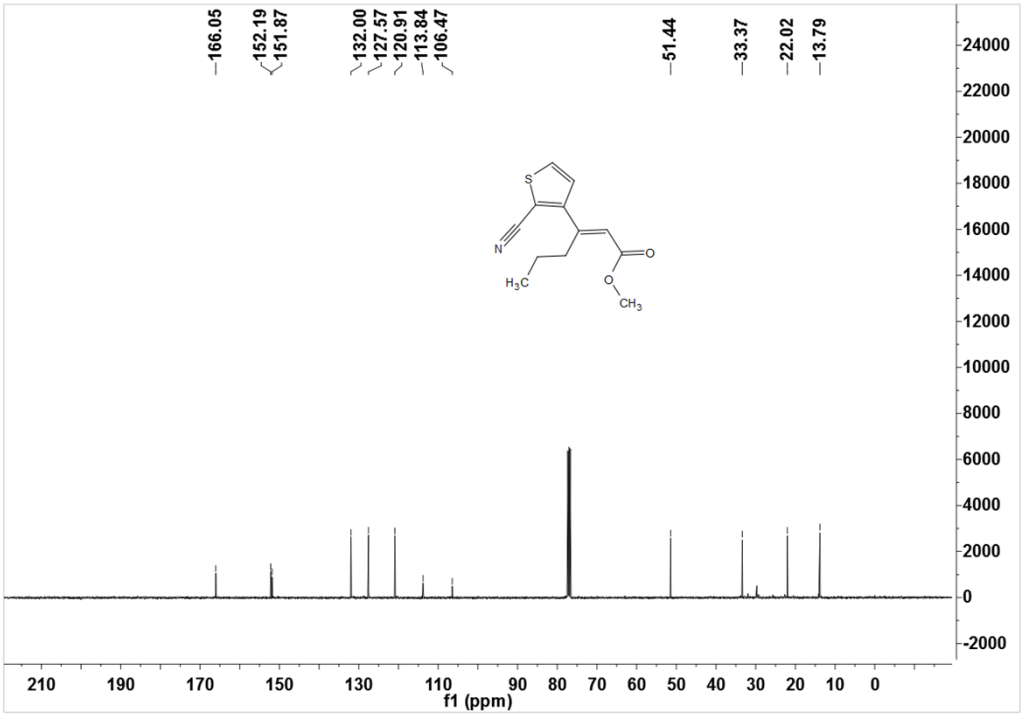
F. NMR spectra

Methyl (*E*) -3-(2-cyanothiophen-3-yl)hex-2-enoate (3a)

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

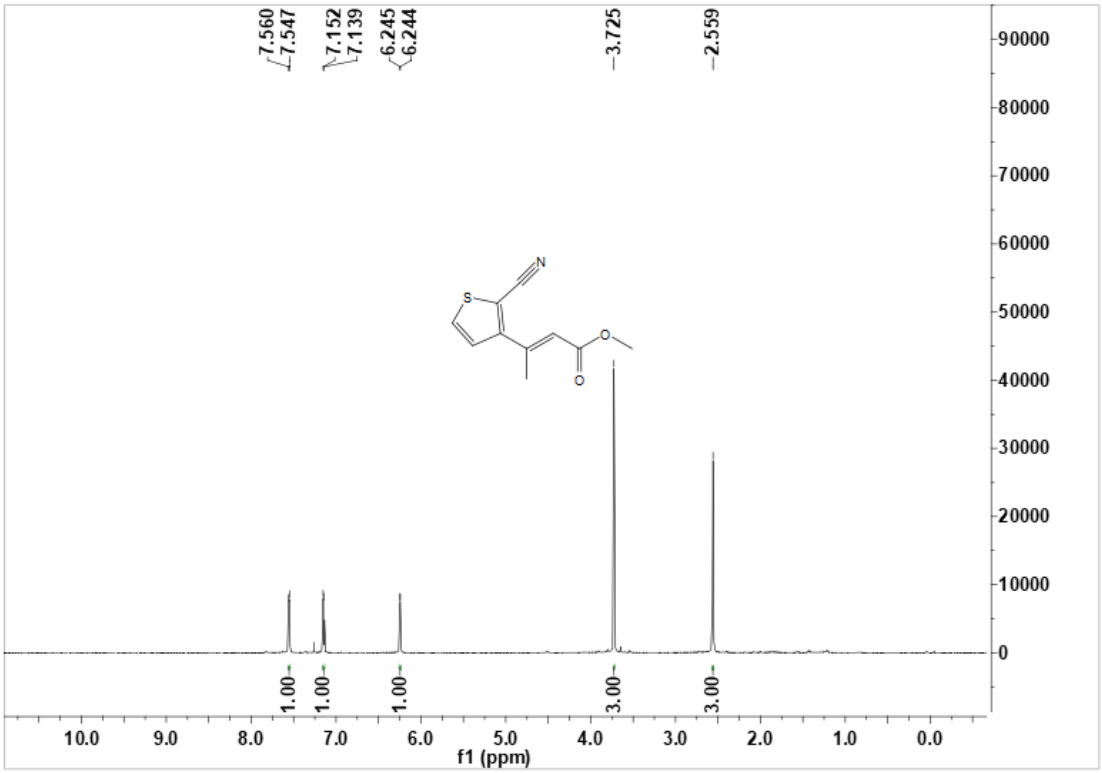


^{13}C NMR (100 MHz, $CDCl_3$)

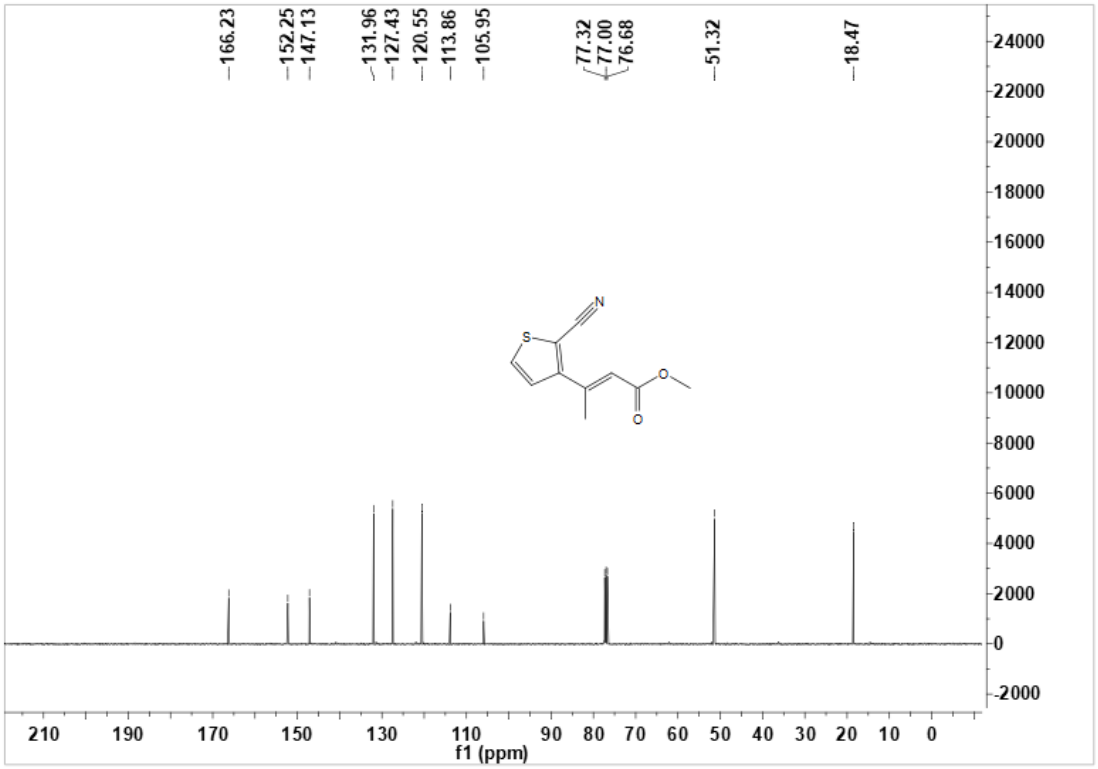


Methyl (*E*)-3-(2-cyanothiophen-3-yl)but-2-enoate (3b)

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

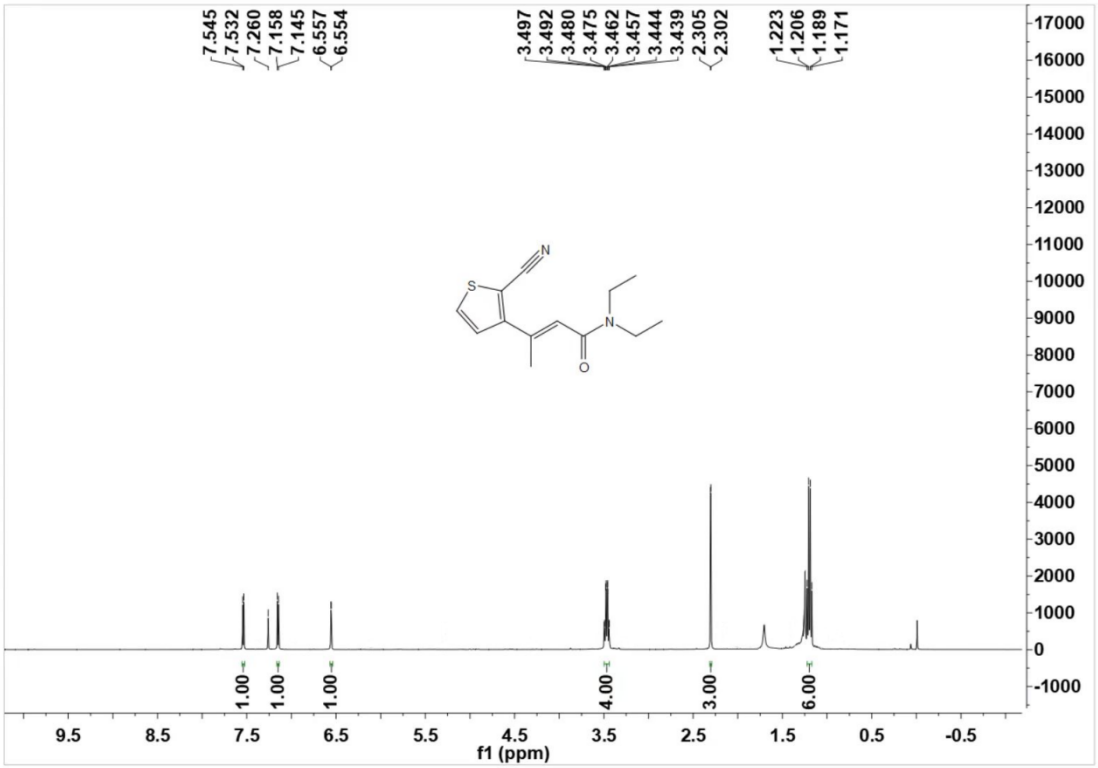


^{13}C NMR (100 MHz, $CDCl_3$)

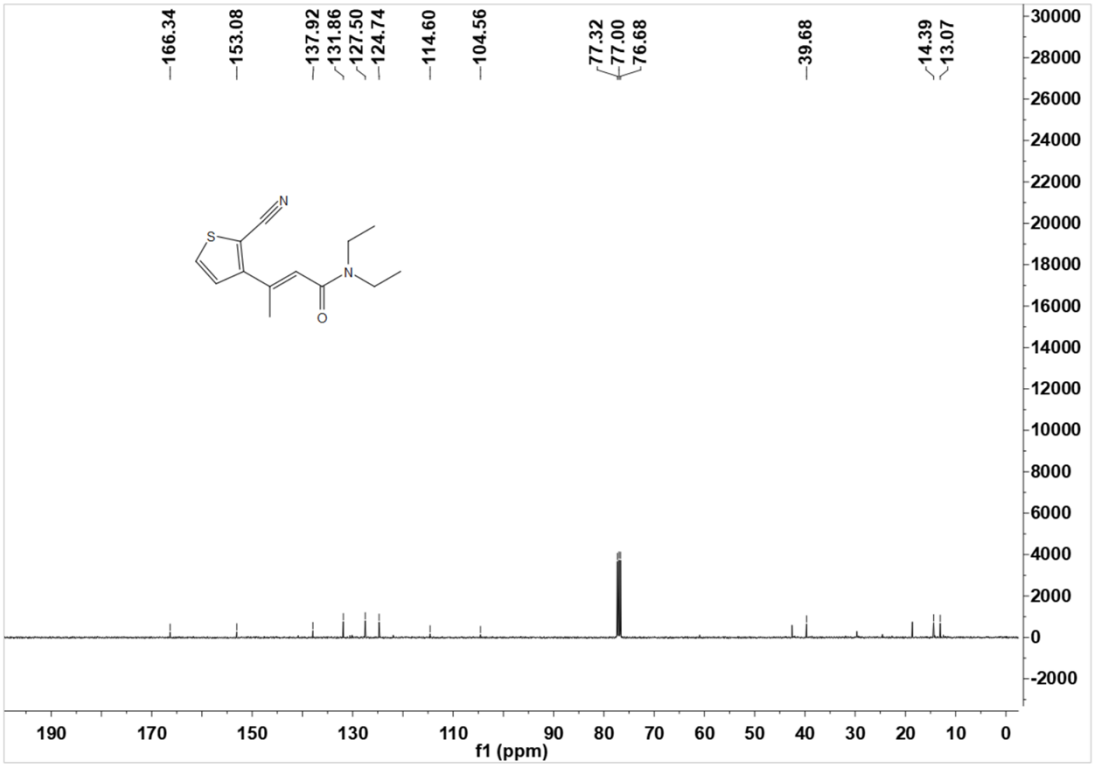


(*E*)-3-(2-Cyanothiophen-3-yl)-*N*, *N*-diethylbut-2-enamide (3c)

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

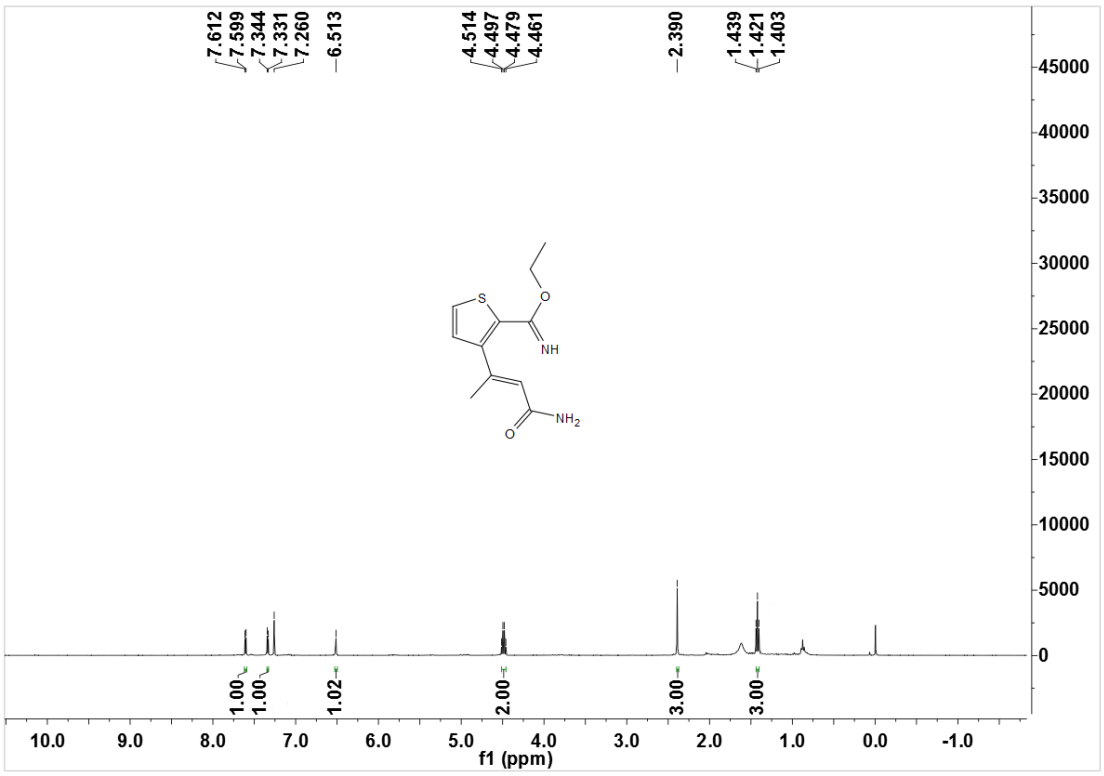


^{13}C NMR (100 MHz, $CDCl_3$)

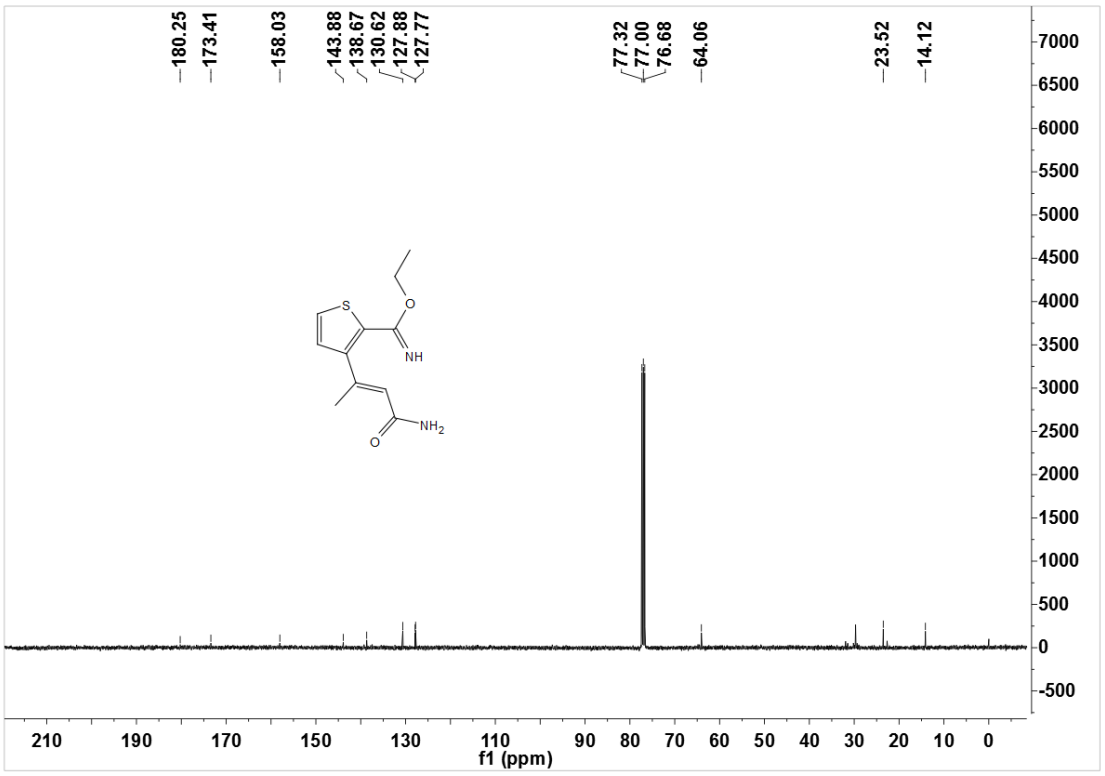


Ethyl (*E*)-3-(4-amino-4-oxobut-2-en-2-yl)thiophene-2-carbimidate (3d)

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

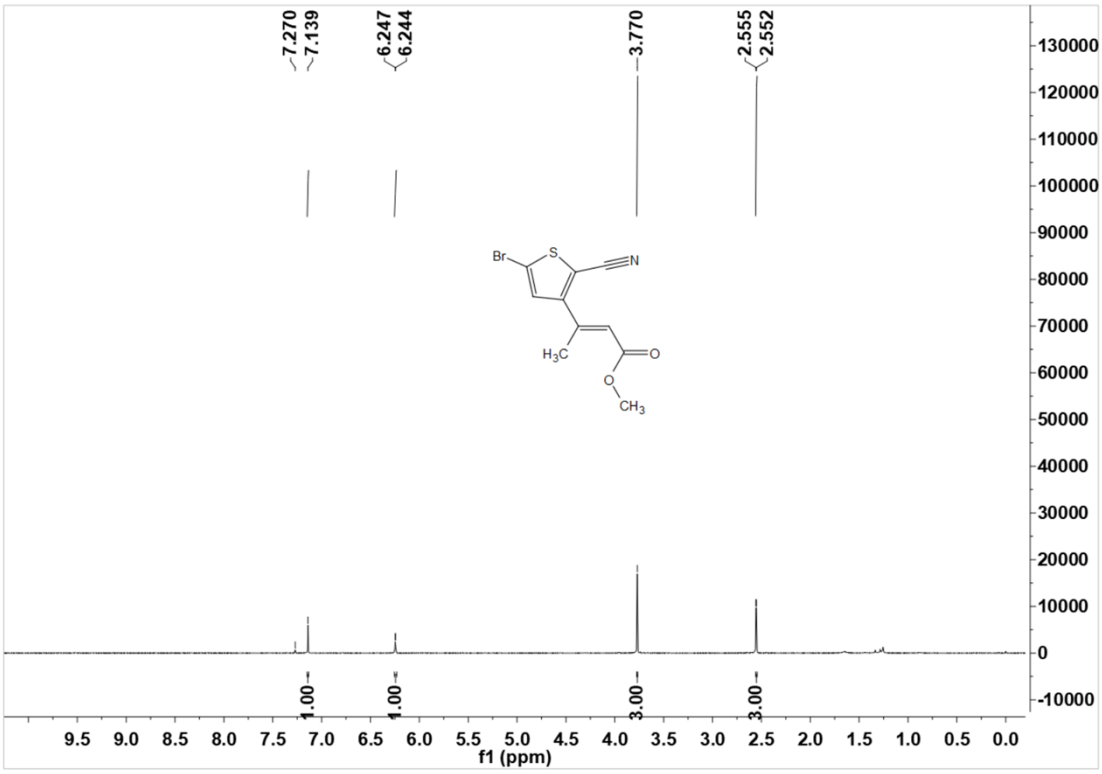


^{13}C NMR (100 MHz, $CDCl_3$)

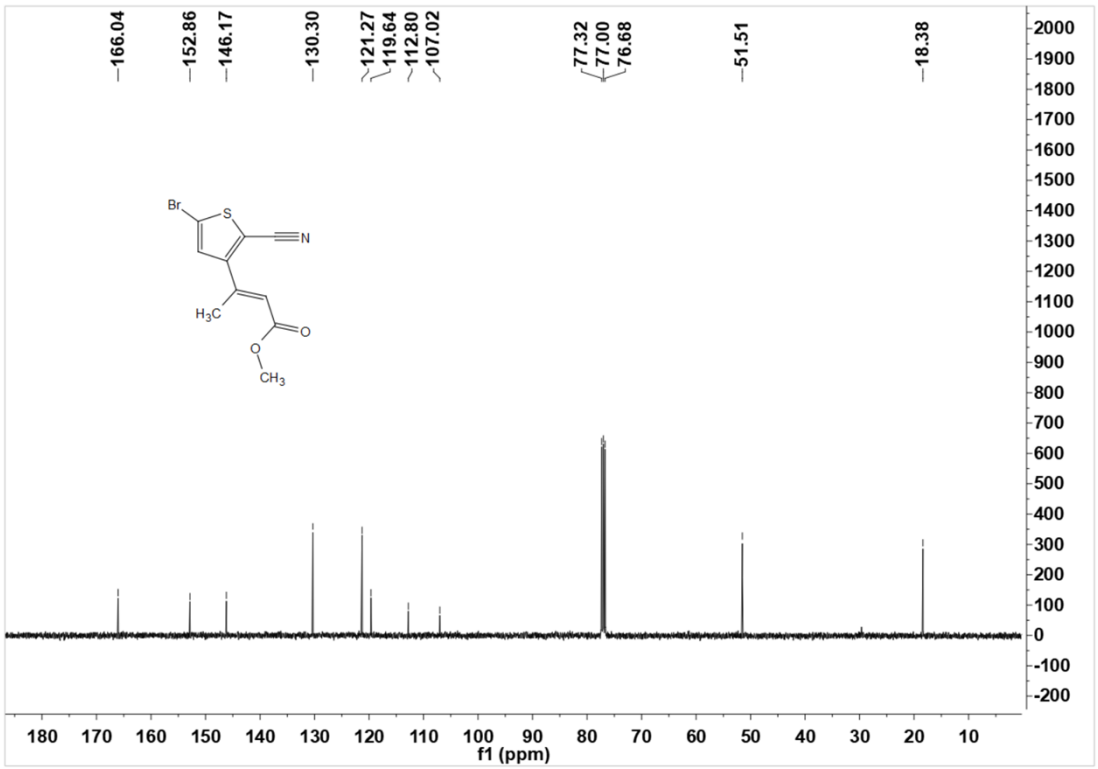


Methyl (*E*)-3-(5-bromo-2-cyanothiophen-3-yl)but-2-enoate (3e)

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

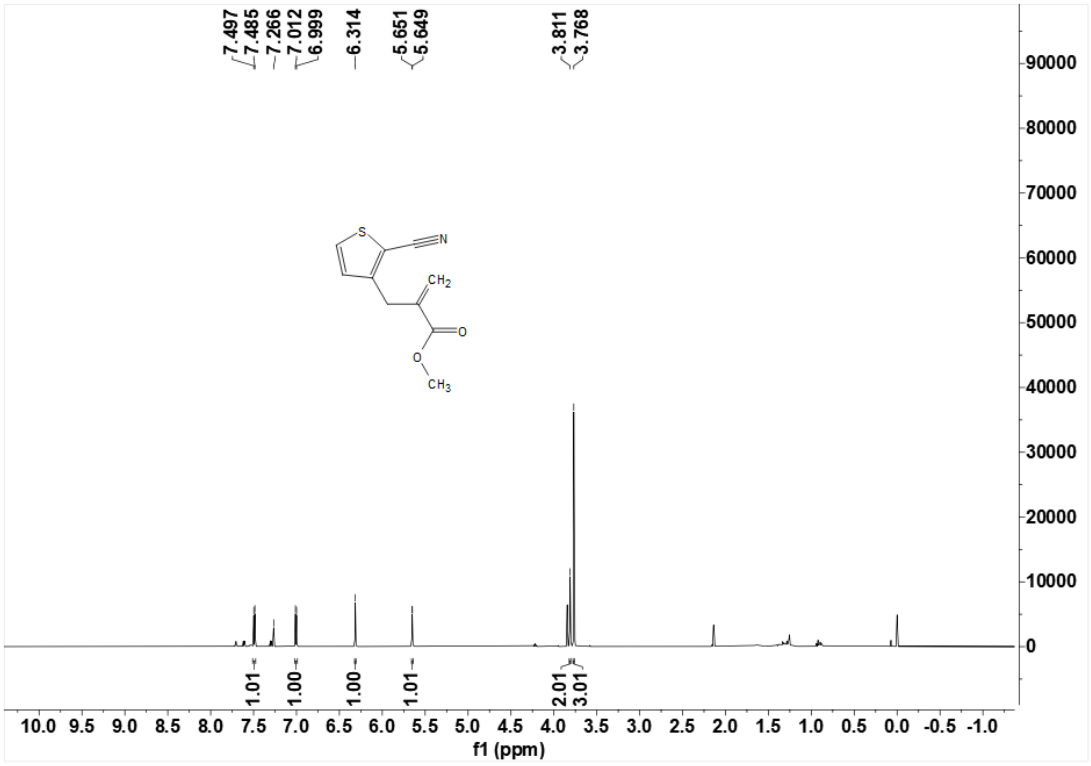


^{13}C NMR (100 MHz, $CDCl_3$)

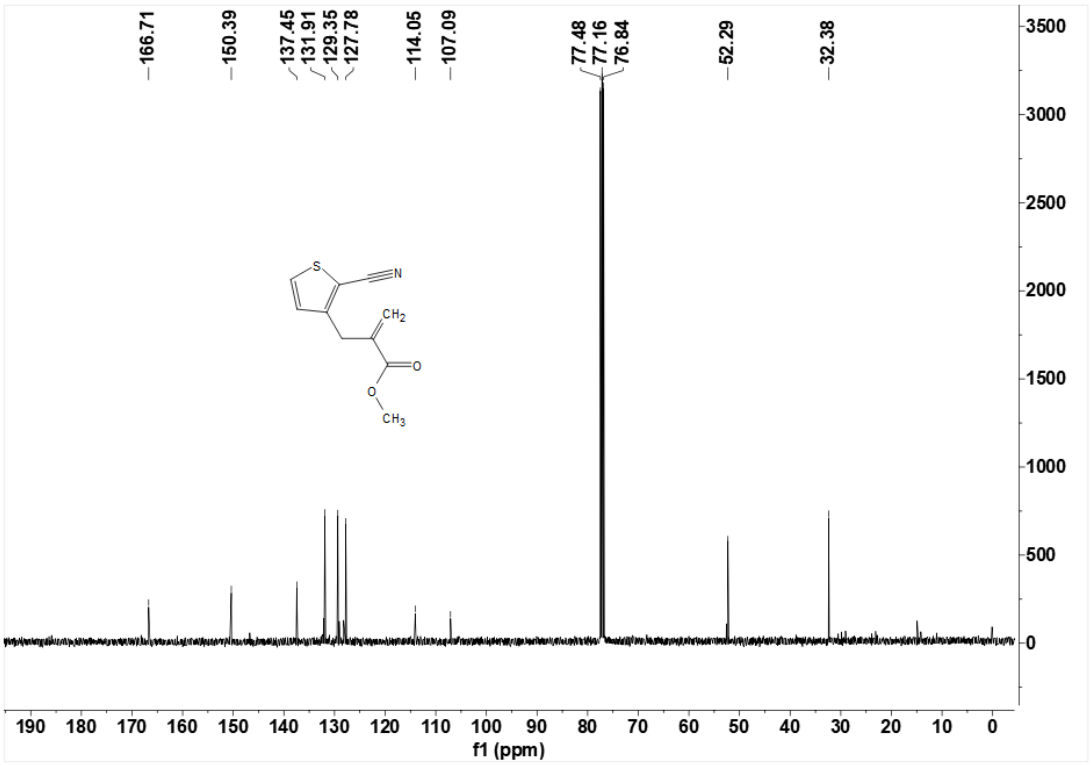


Methyl 2-((2-cyanothiophen-3-yl)methyl)acrylate (3f)

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

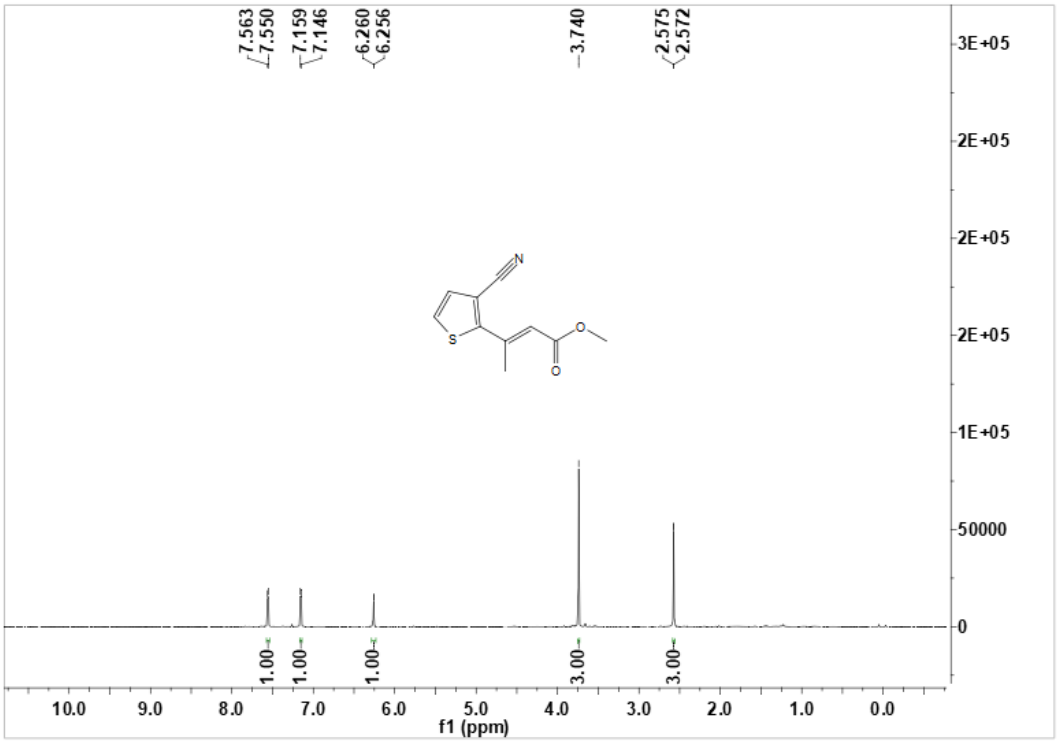


^{13}C NMR (100 MHz, $CDCl_3$)

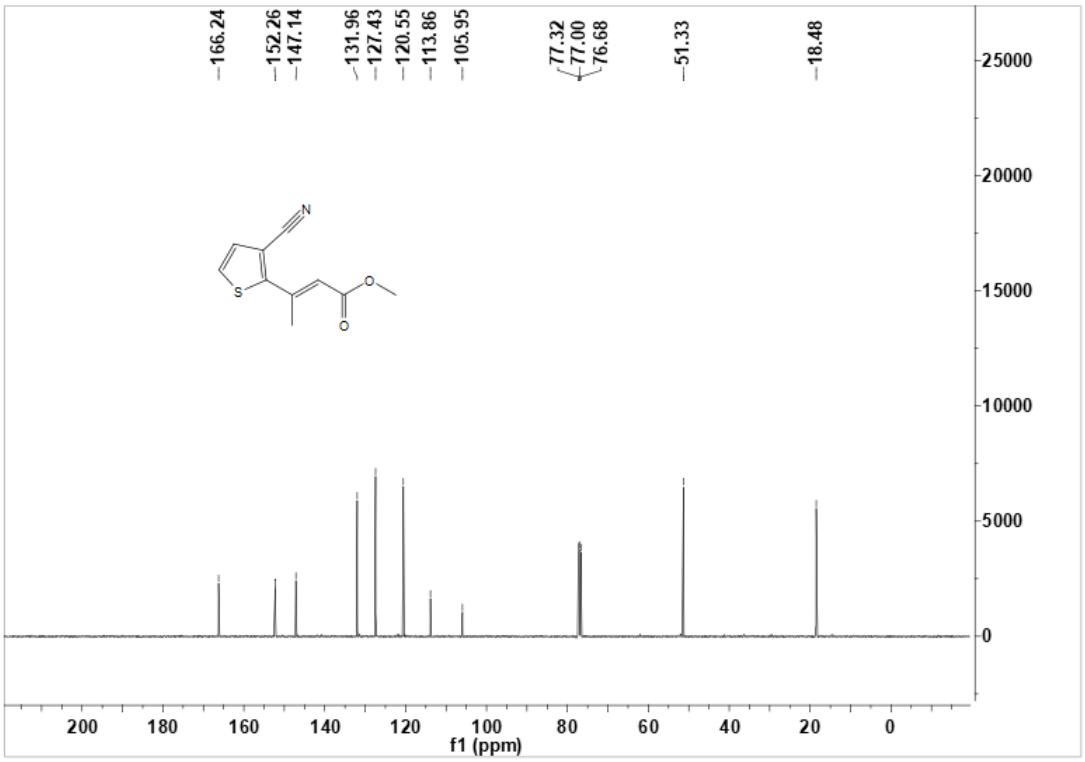


Methyl (*E*)-3-(3-cyanothiophen-2-yl)but-2-enoate (3g)

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

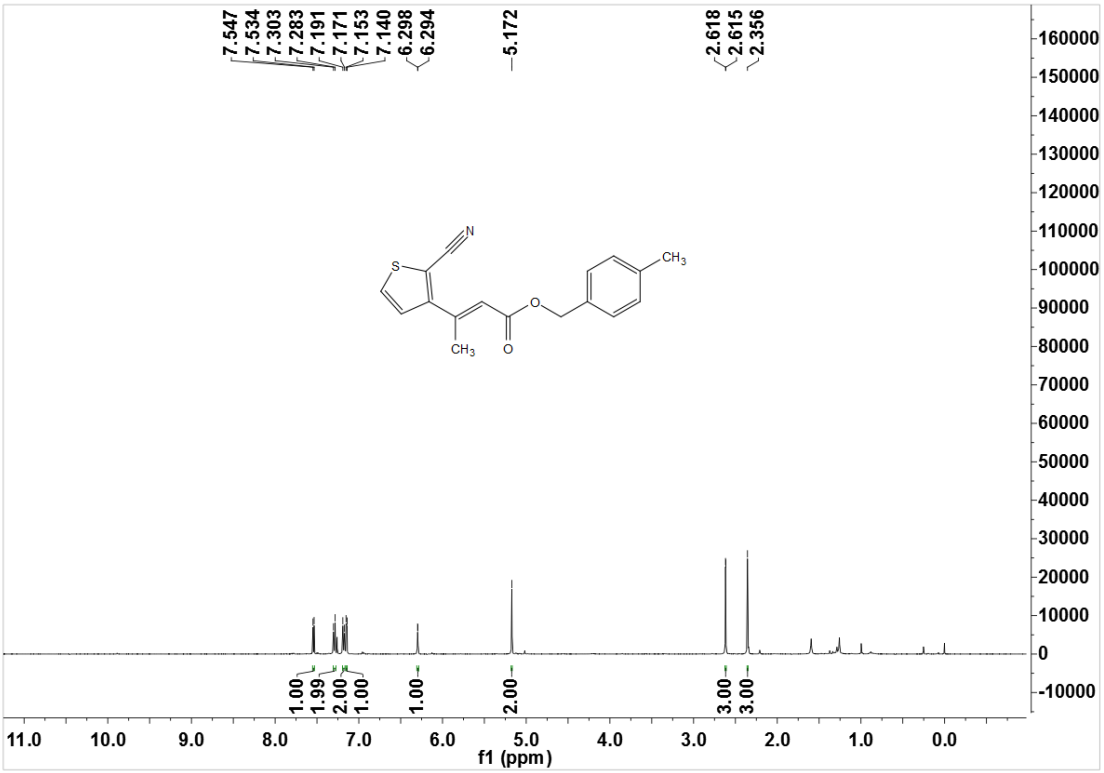


^{13}C NMR (100 MHz, $CDCl_3$)

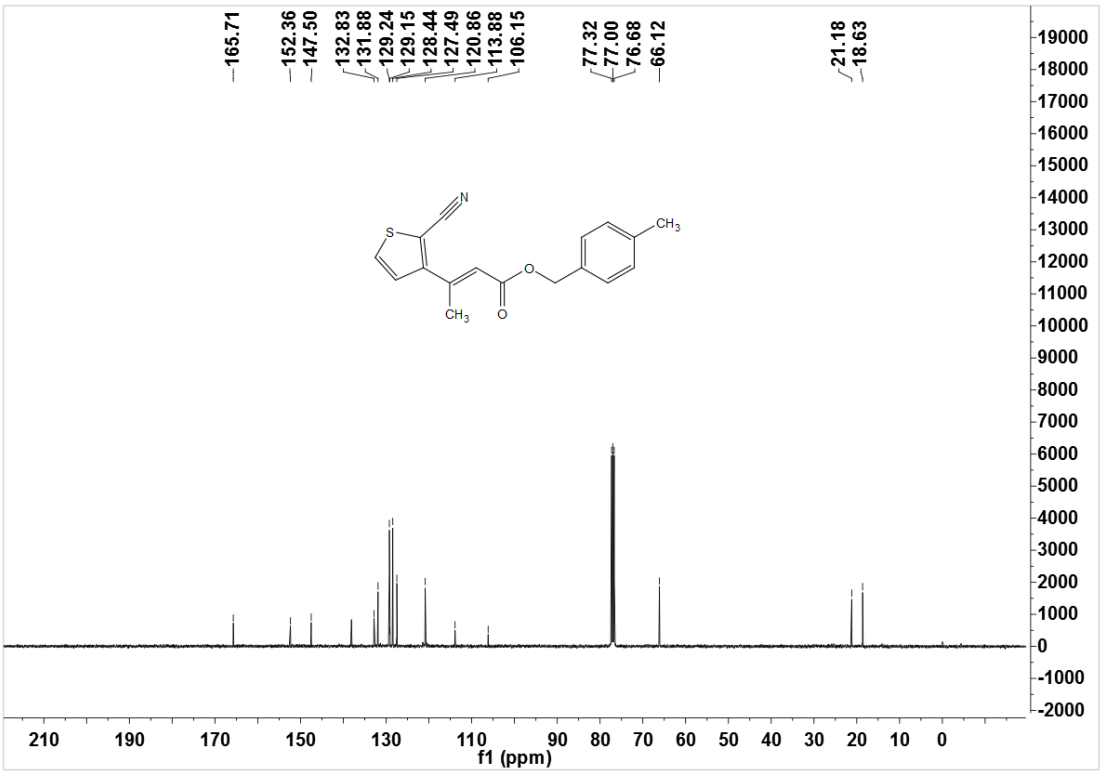


Methylphenethyl (*E*)-3-(2-cyanothiophen-3-yl)but-2-enoate (3h)

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

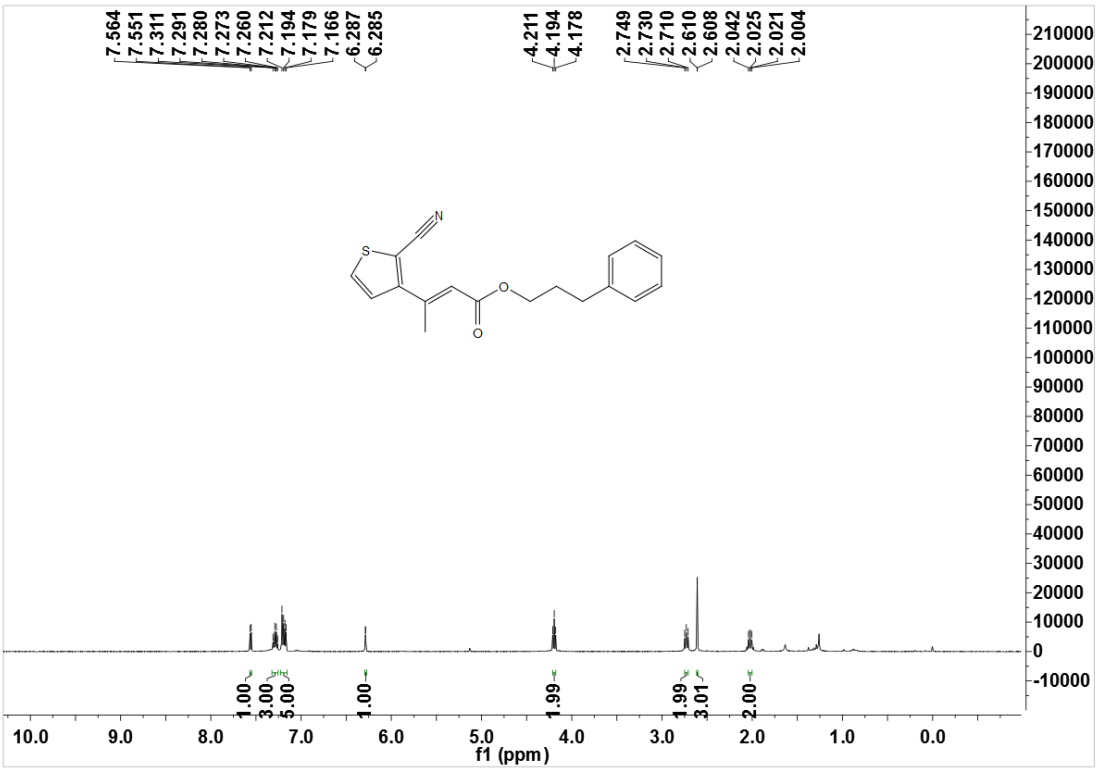


^{13}C NMR (100 MHz, $CDCl_3$)

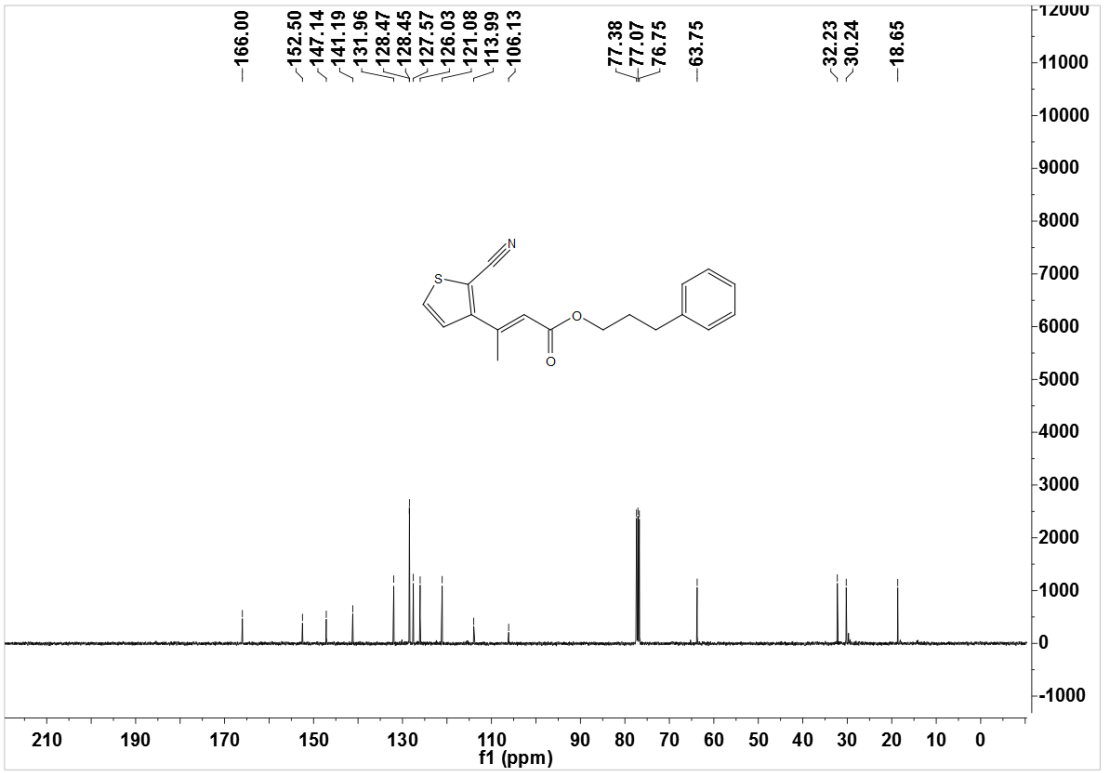


Phenylpropyl (*E*)-3-(2-cyanothiophen-3-yl)but-2-enoate (3i)

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

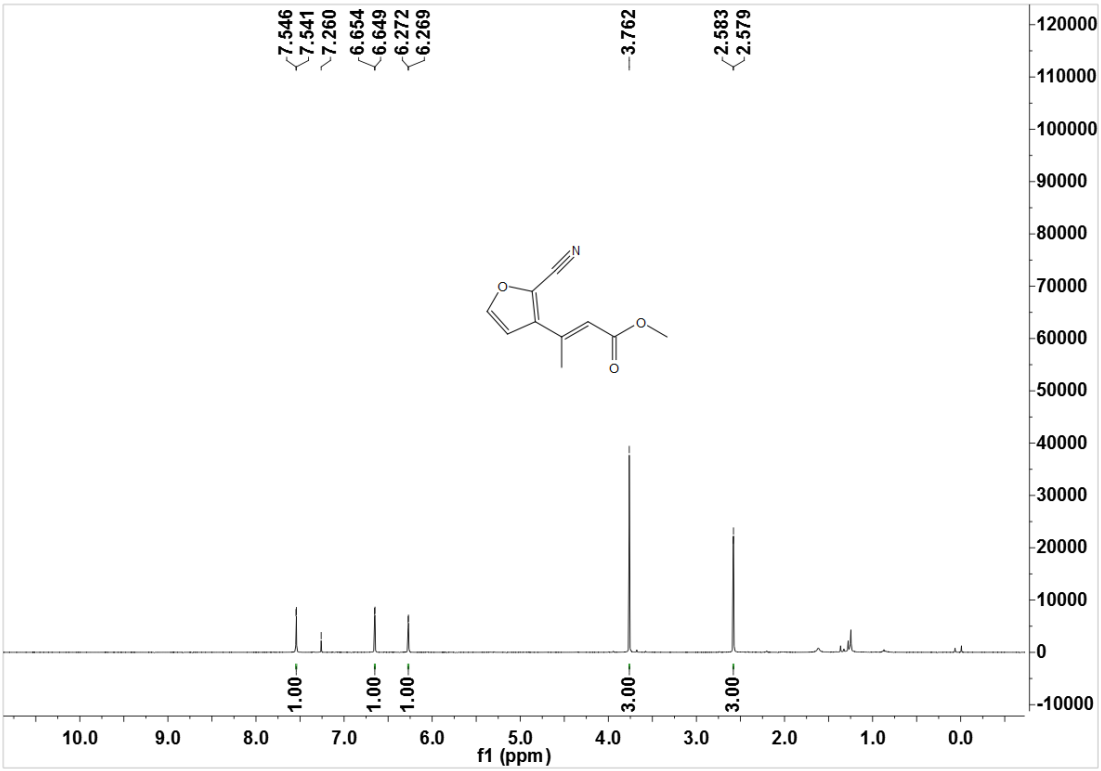


^{13}C NMR (100 MHz, $CDCl_3$)

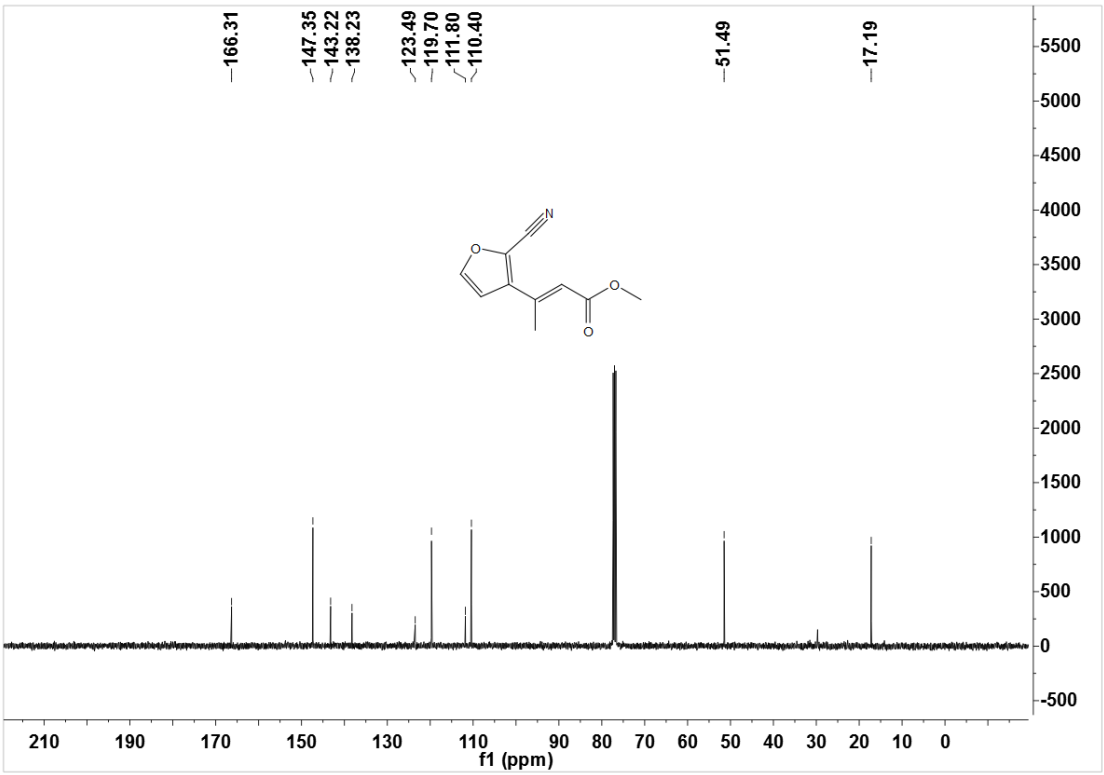


Methyl (*E*)-3-(3-cyanofuran-2-yl)but-2-enoate (3j)

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

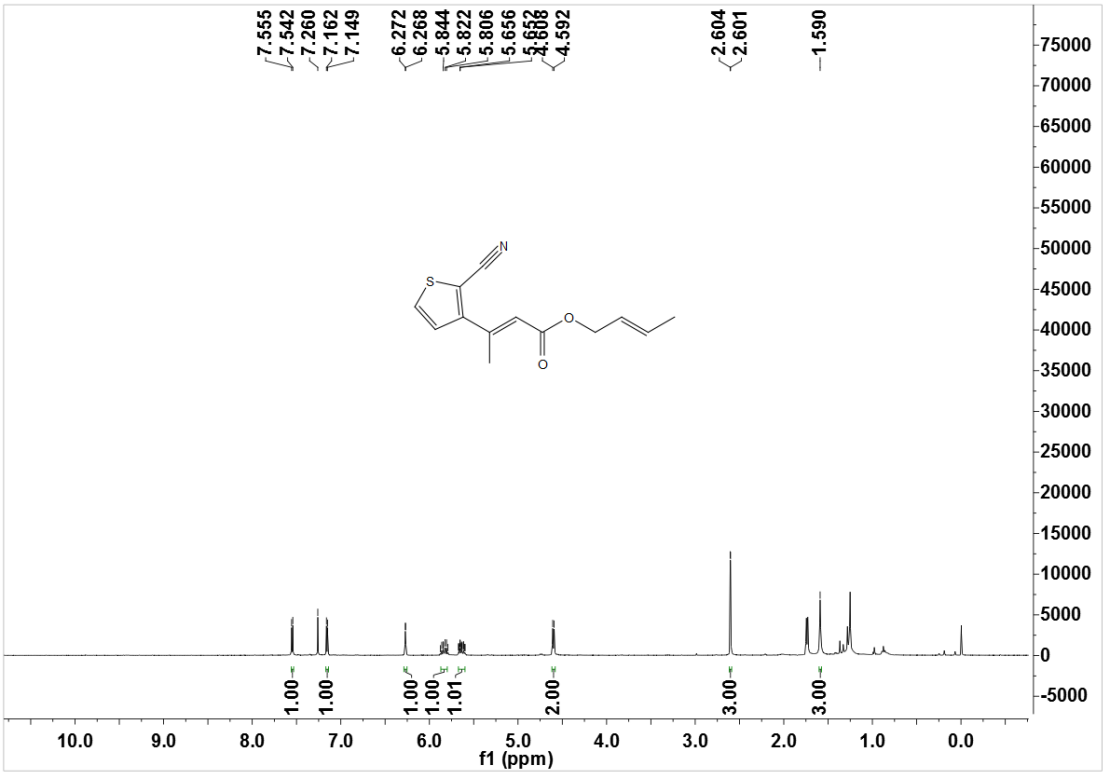


^{13}C NMR (100 MHz, $CDCl_3$)

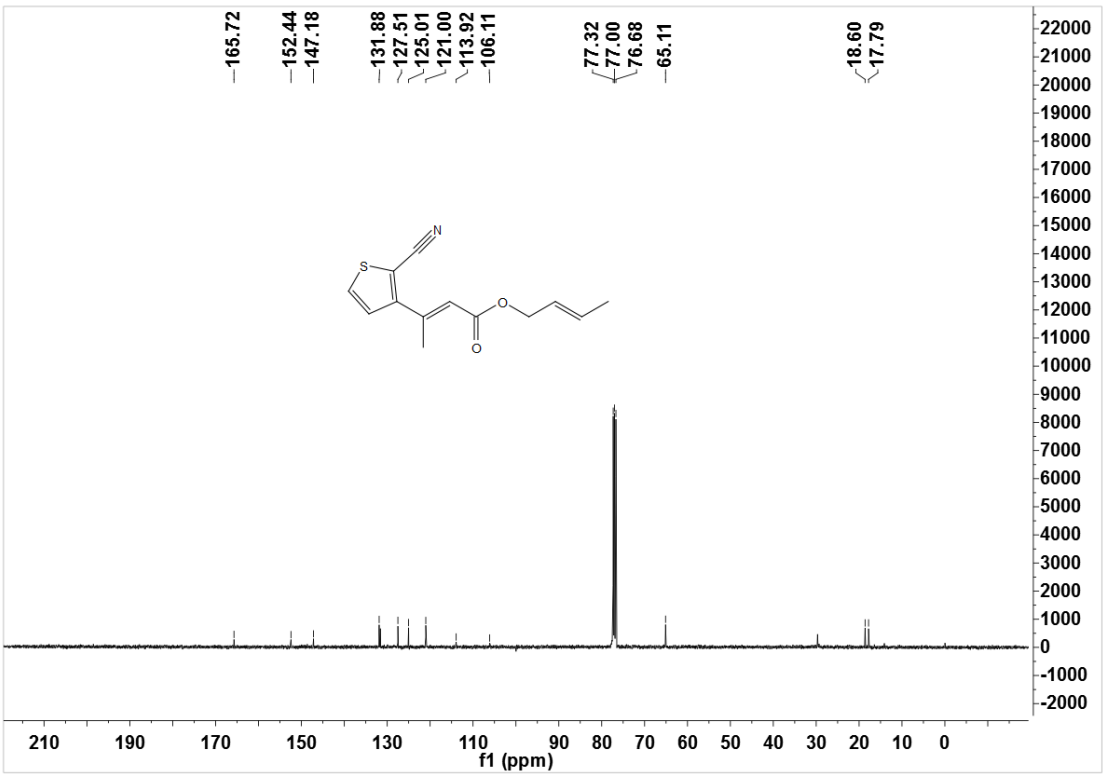


(E)-But-2-en-1-yl (*E*)-3-(2-Cyanothiophen-3-yl)but-2-enoate (3k)

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

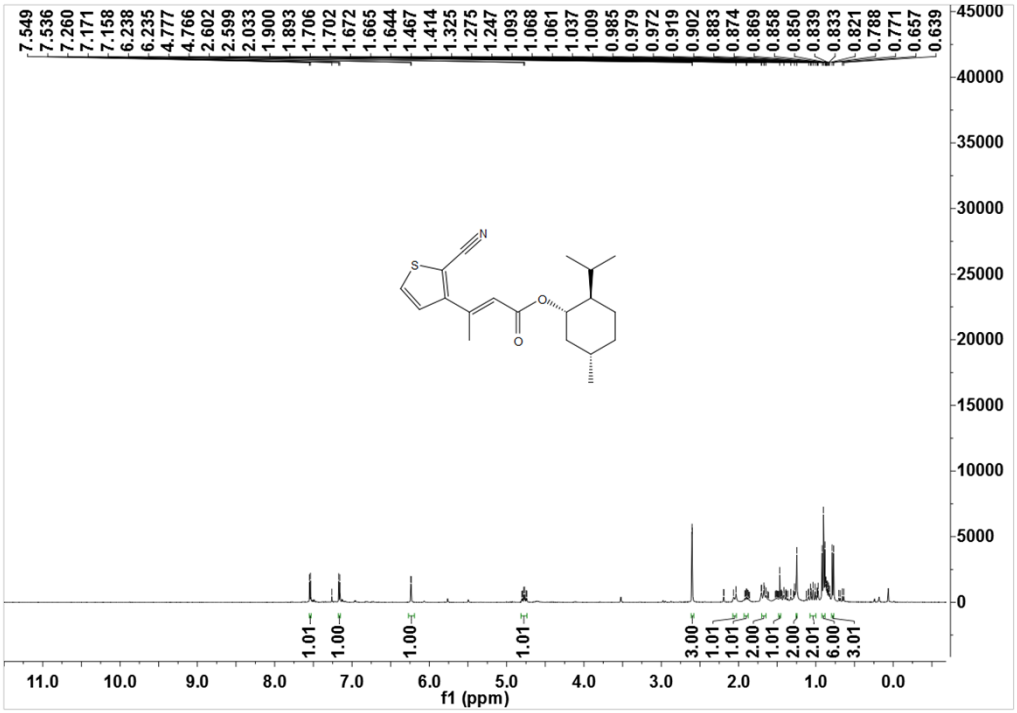


^{13}C NMR (100 MHz, $CDCl_3$)

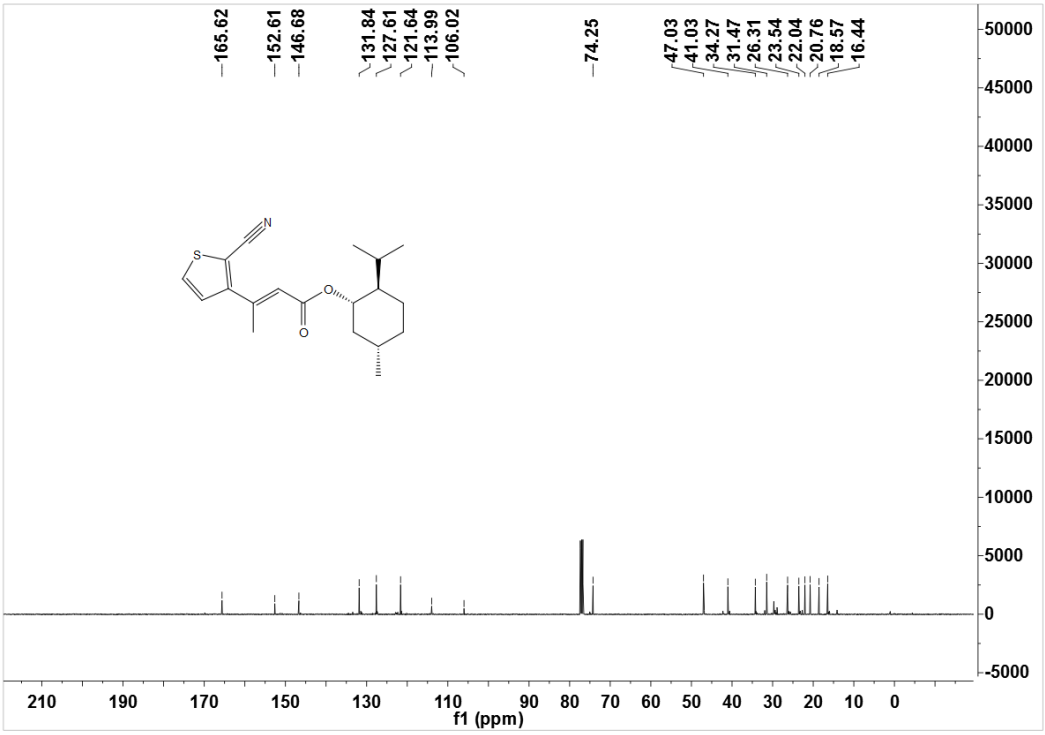


(1*S*, 2*R*, 5*S*)-2-Isopropyl-5-methylcyclohexyl, (*E*)-3-(2-cyanothiophen-3-yl) but-2-enoate (3l)

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

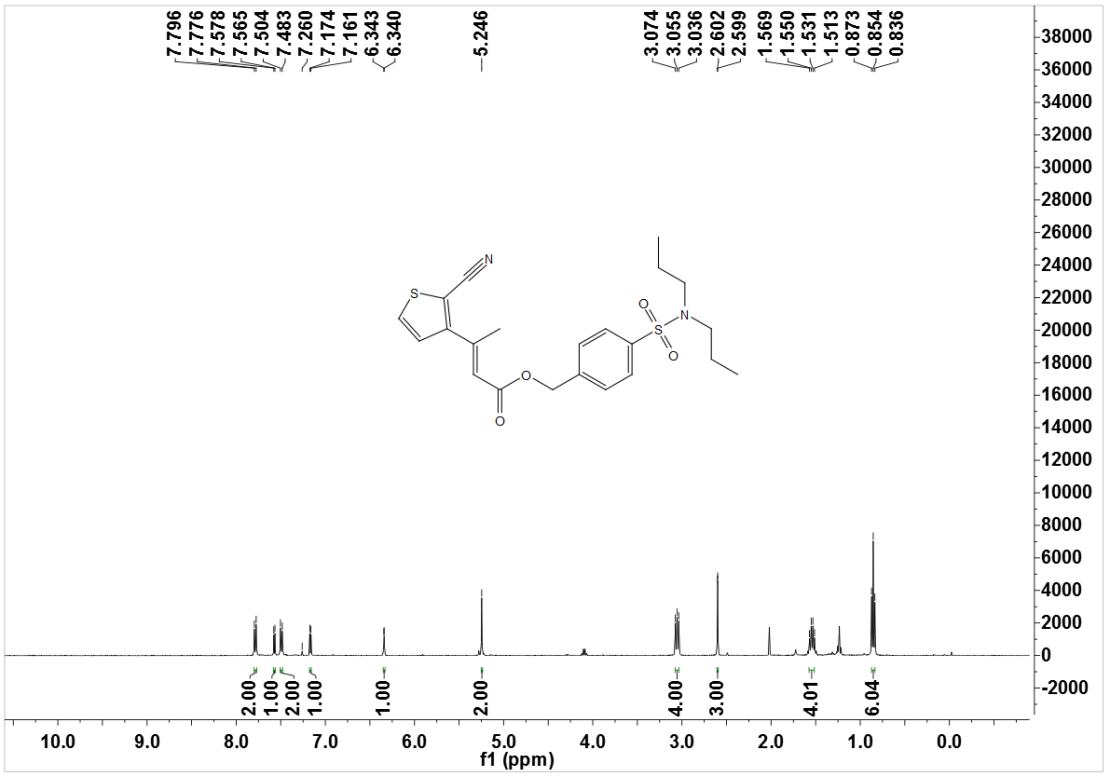


^{13}C NMR (100 MHz, $CDCl_3$)

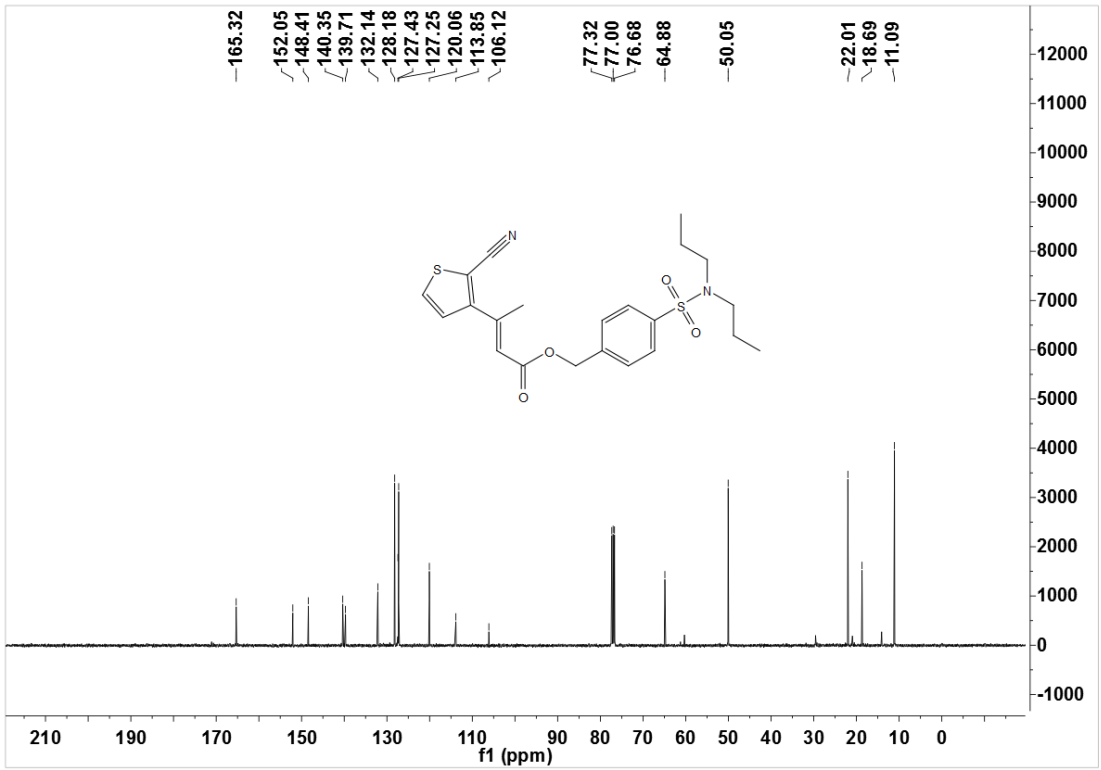


(*N*, *N*-Dipropylsulfamoyl) benzyl (*E*)-3-(2-cyanothiophen-3-yl) but-2-enoate (3m)

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

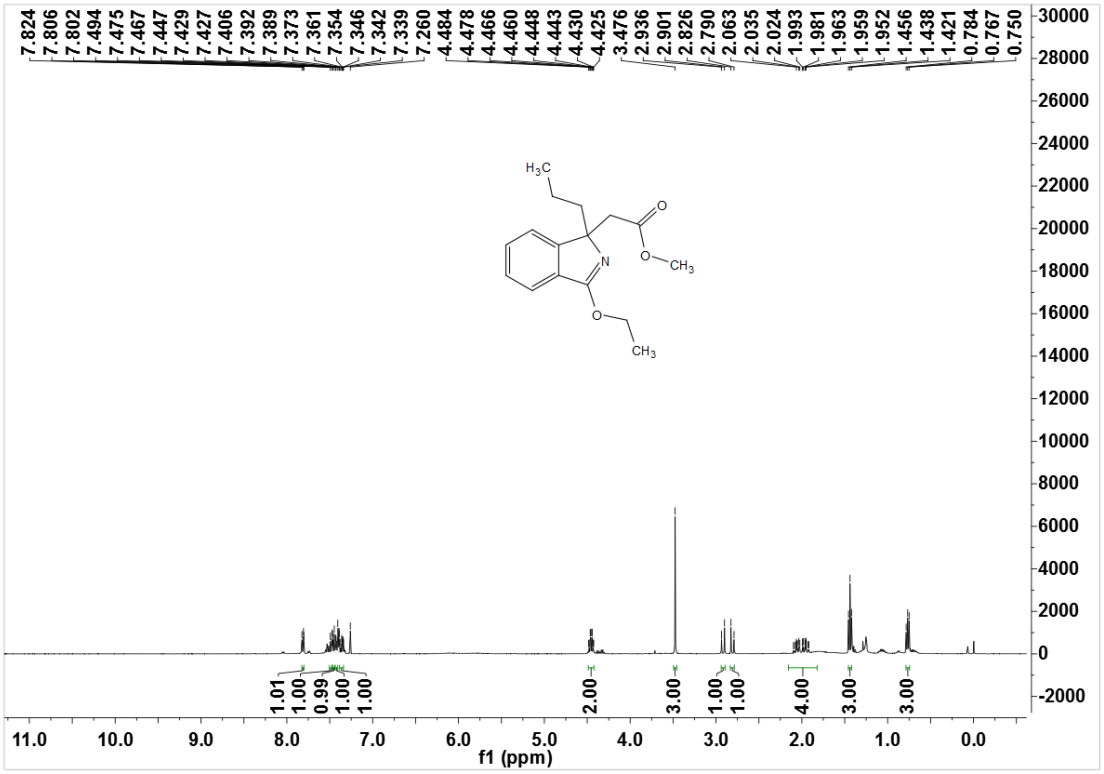


^{13}C NMR (100 MHz, $CDCl_3$)

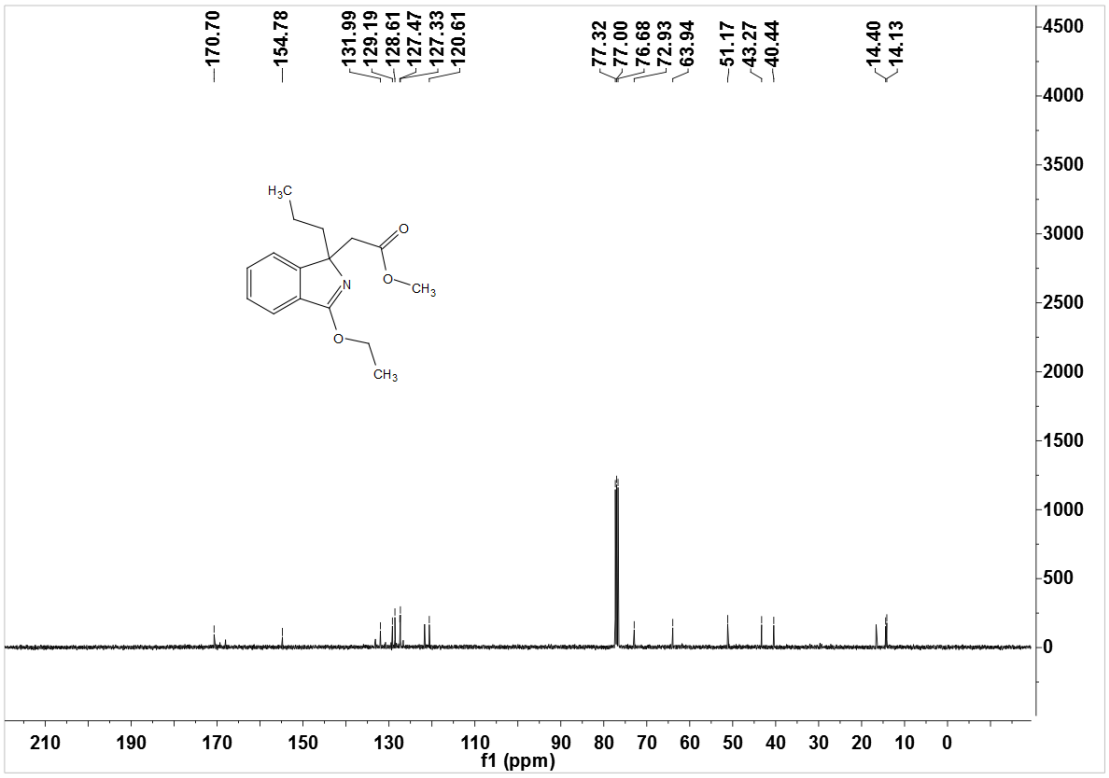


Methyl 2-(3-ethoxy-1-propyl-1*H*-isoindol-1-yl)acetate (4a)

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

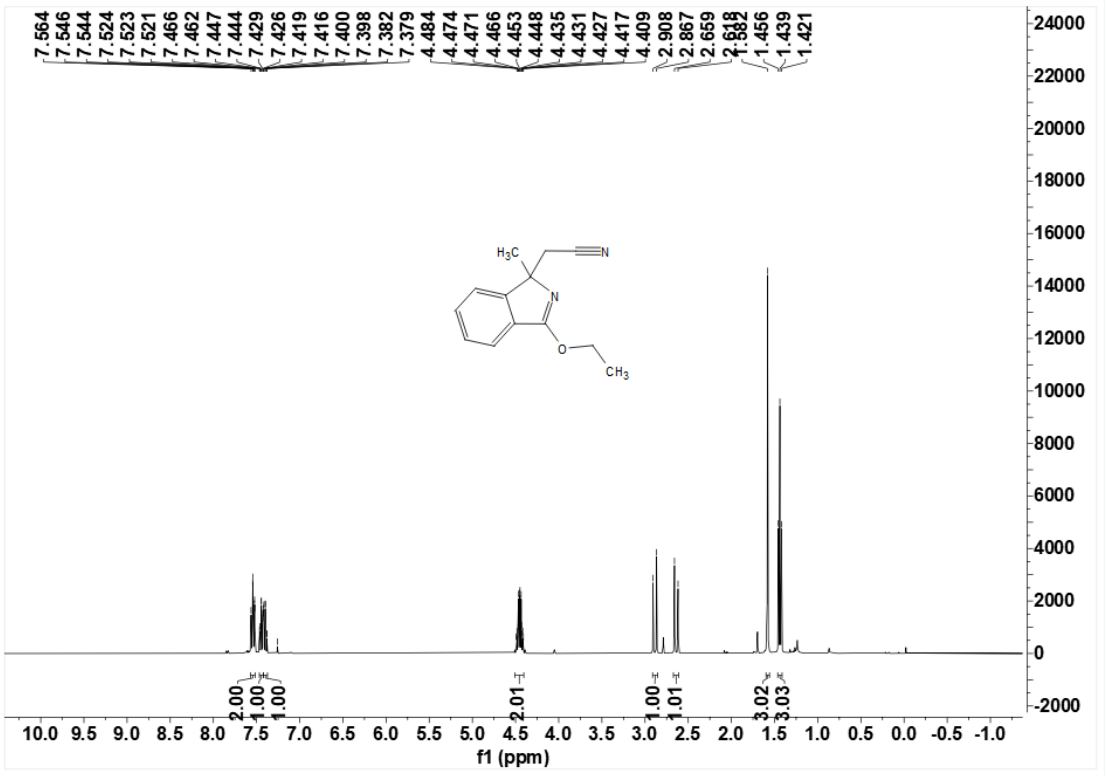


^{13}C NMR (100 MHz, $CDCl_3$)

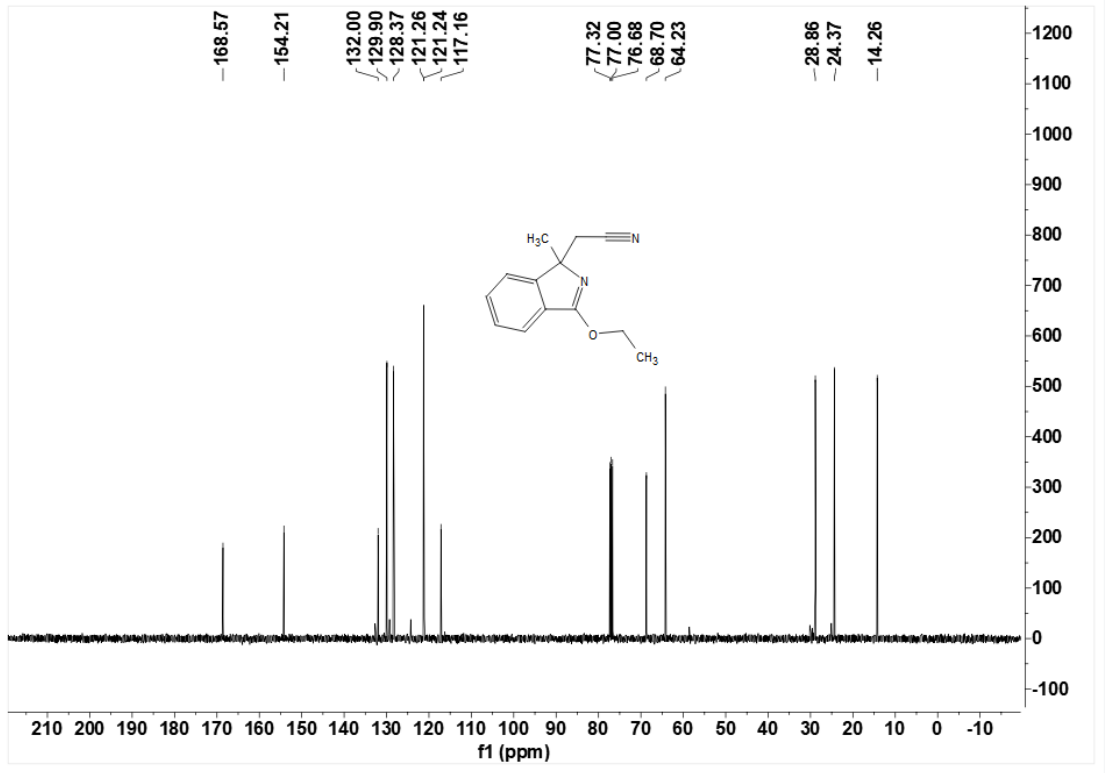


2-(3-Mthoxy-1-methyl-1H-isoindol-1-yl)acetonitrile (4c)

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

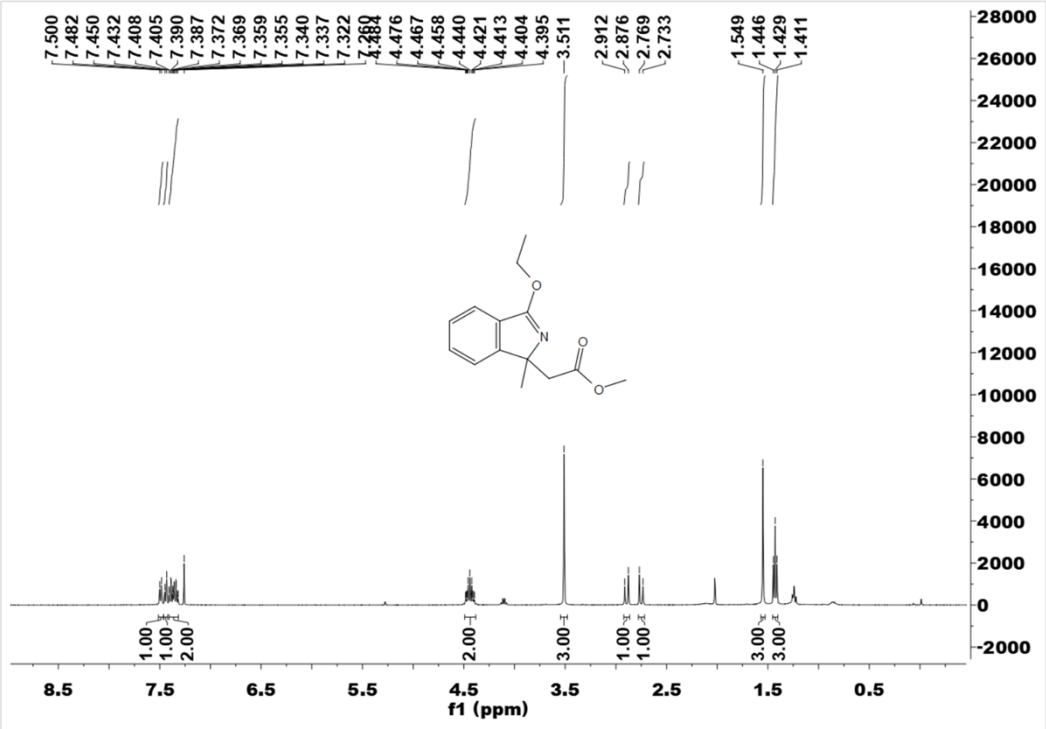


^{13}C NMR (100 MHz, $CDCl_3$)

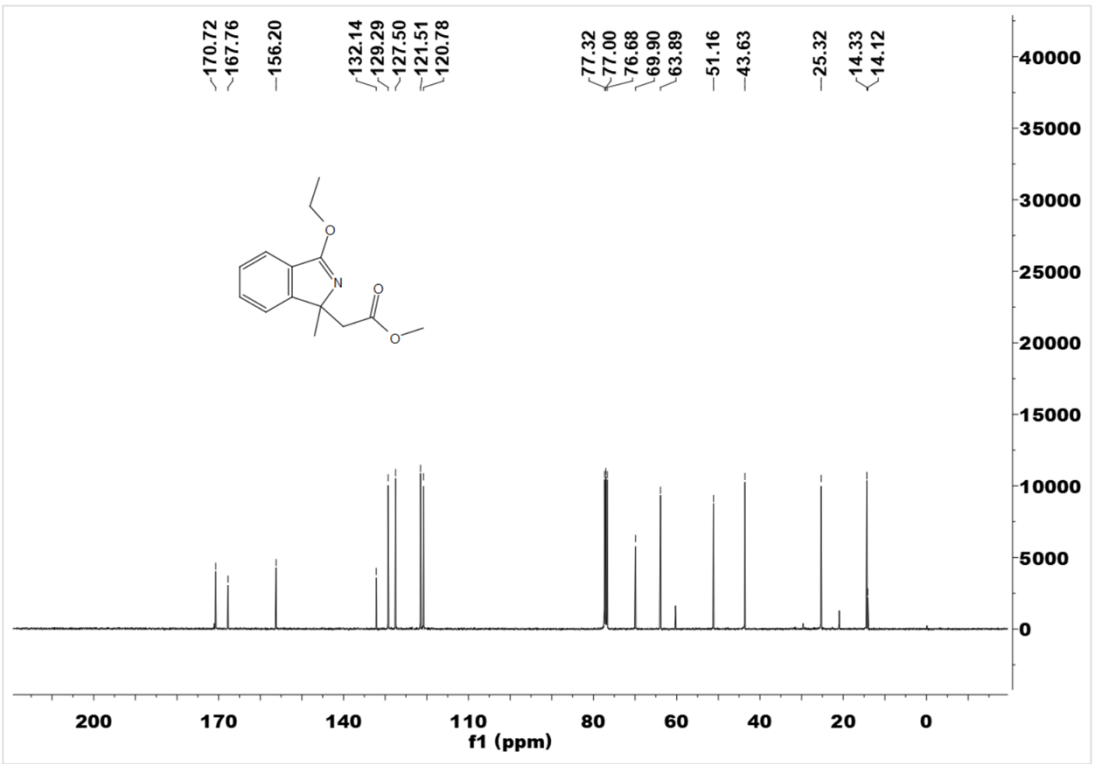


Methyl 2-(3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4d)

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

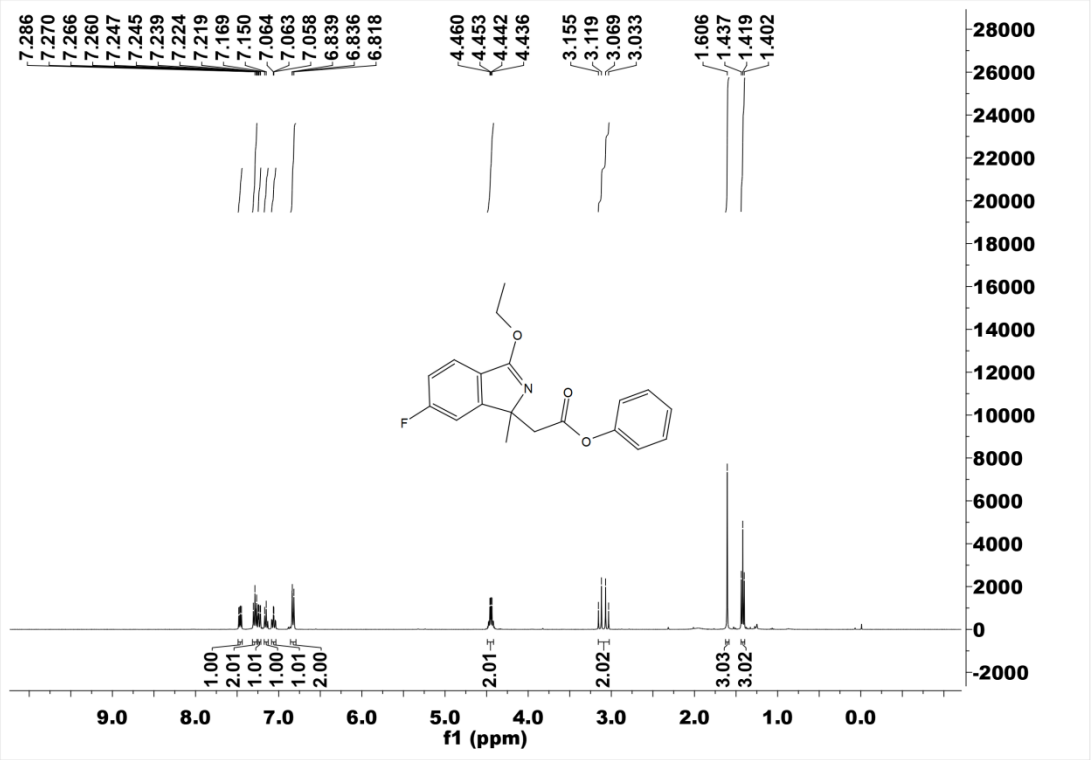


^{13}C NMR (100 MHz, $CDCl_3$)

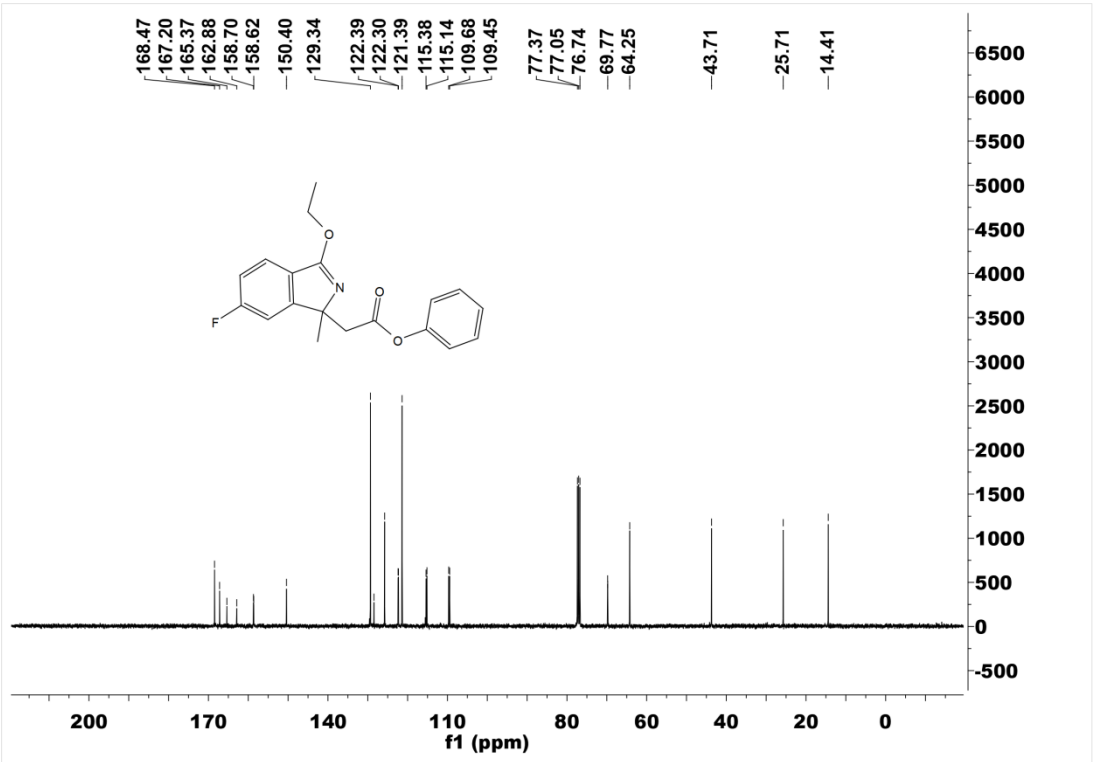


Phenyl 2-(3-ethoxy-6-fluoro-1-methyl-1H-isoindol-1-yl)acetate (4e)

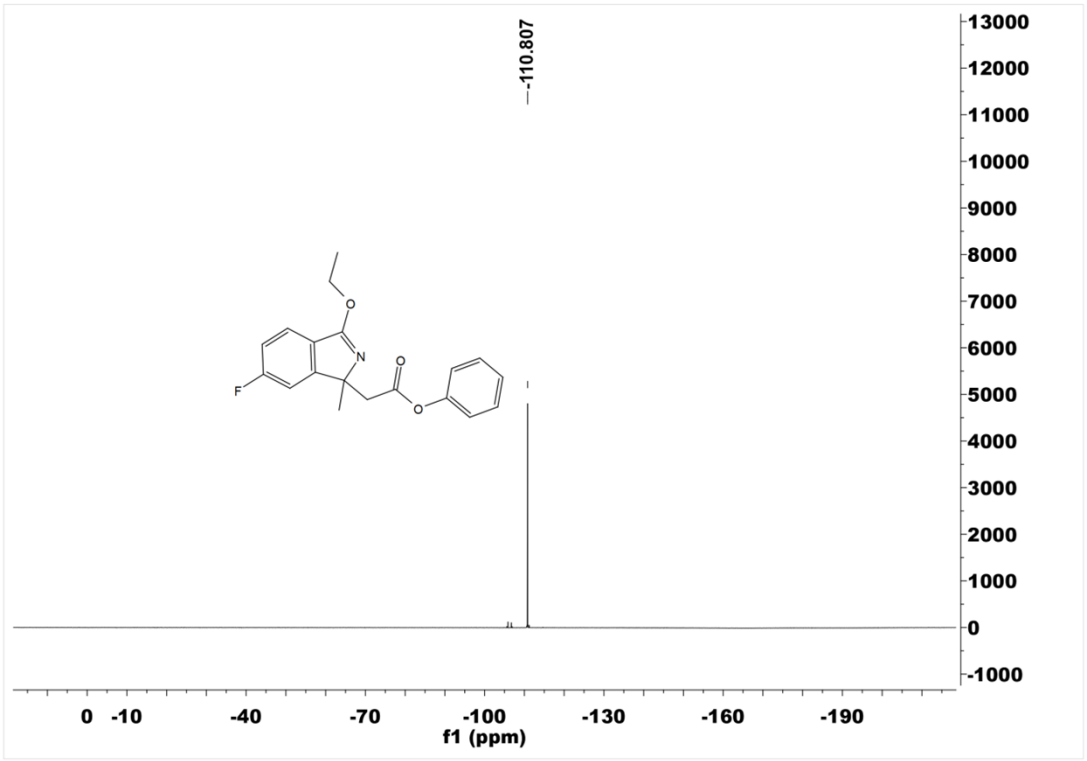
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

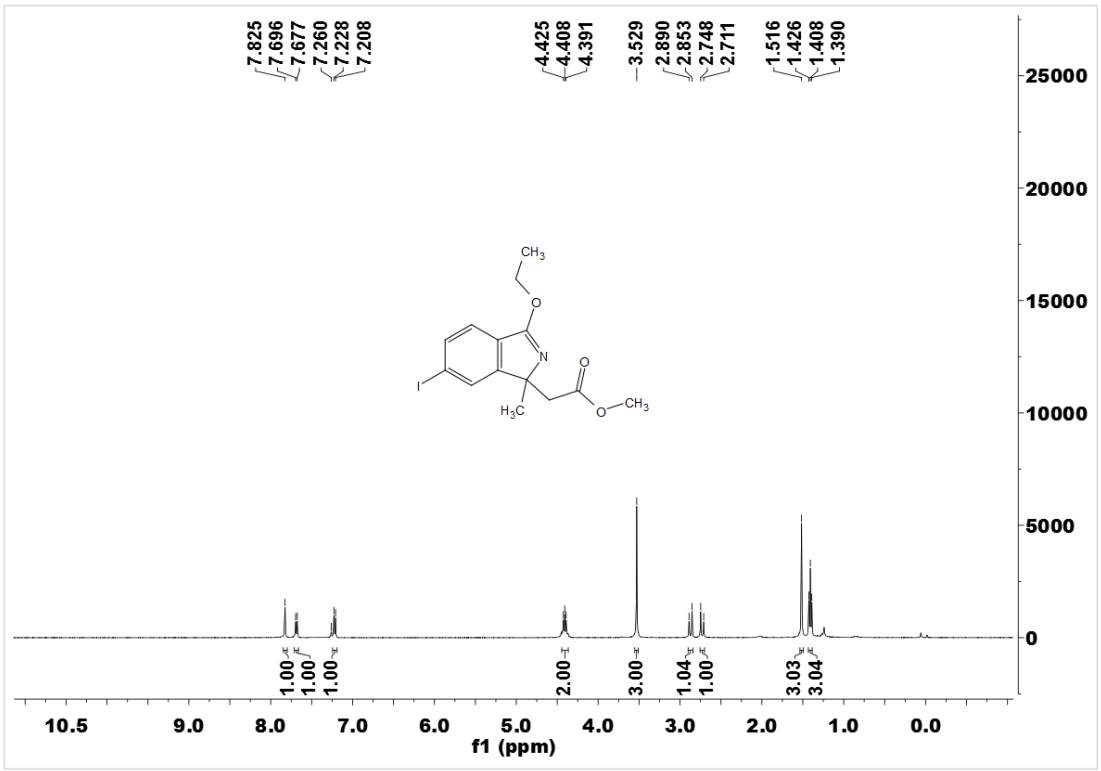


^{19}F NMR (376 MHz, $CDCl_3$)

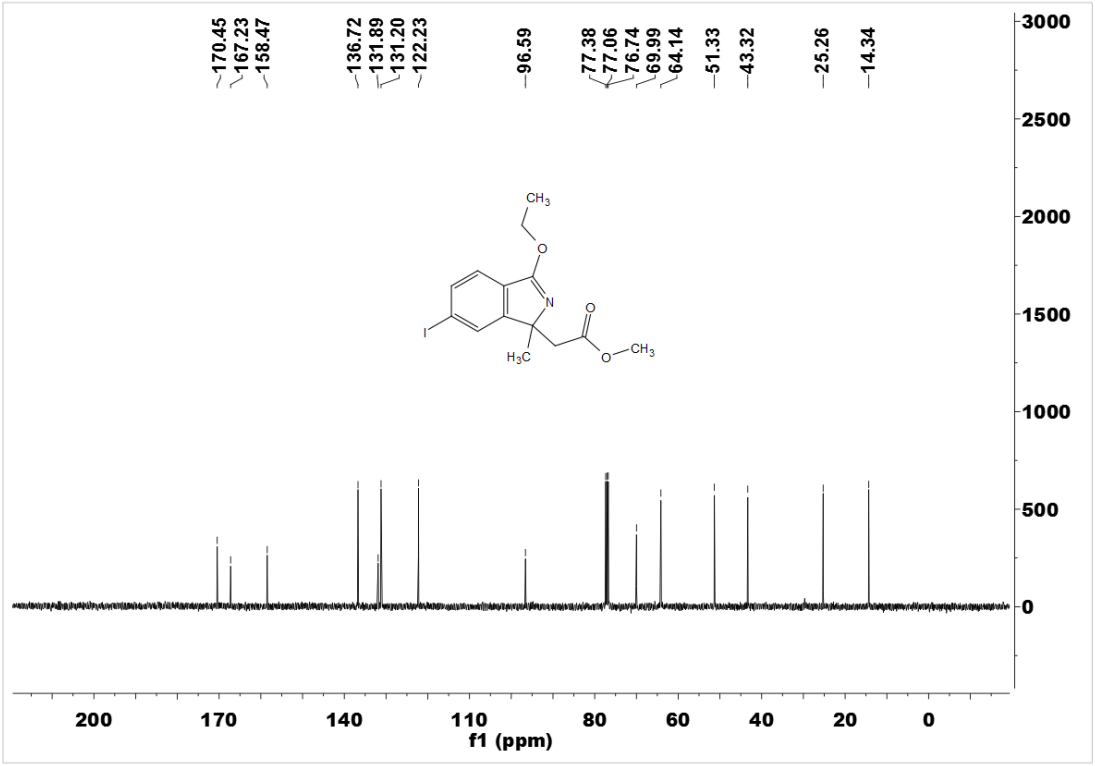


Methyl 2-(3-ethoxy-6-iodo-1-methyl-1*H*-isoindol-1-yl)acetate (4f)

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

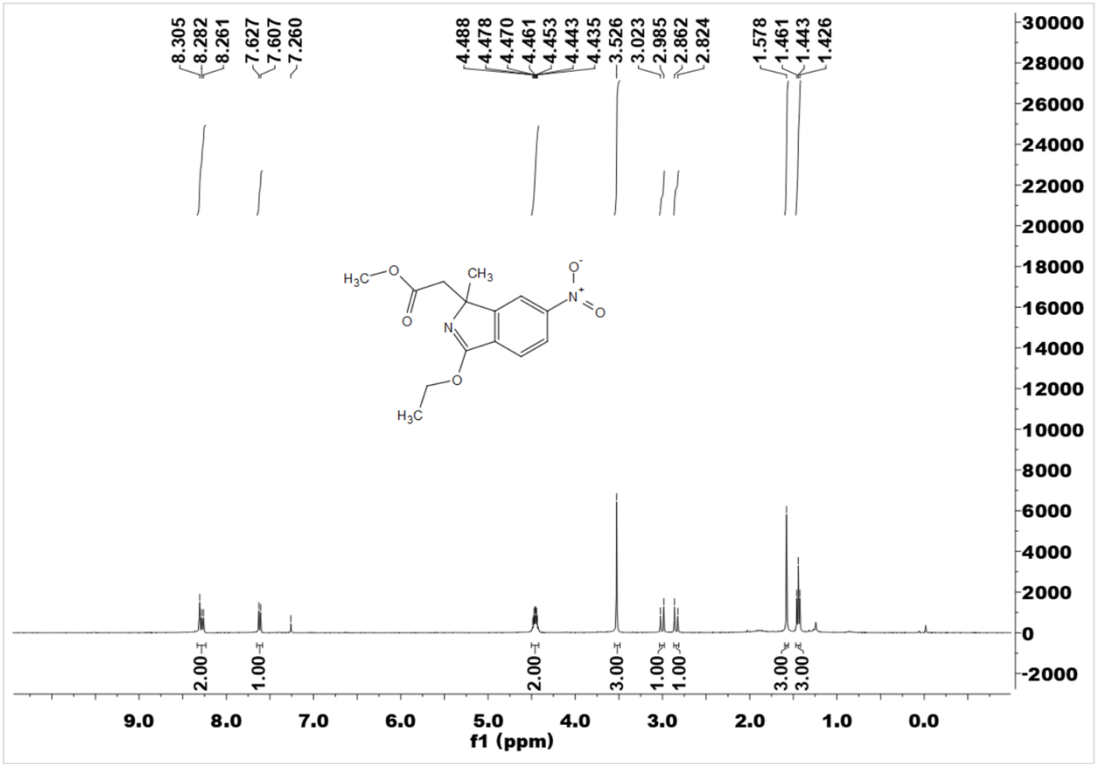


^{13}C NMR (100 MHz, $CDCl_3$)

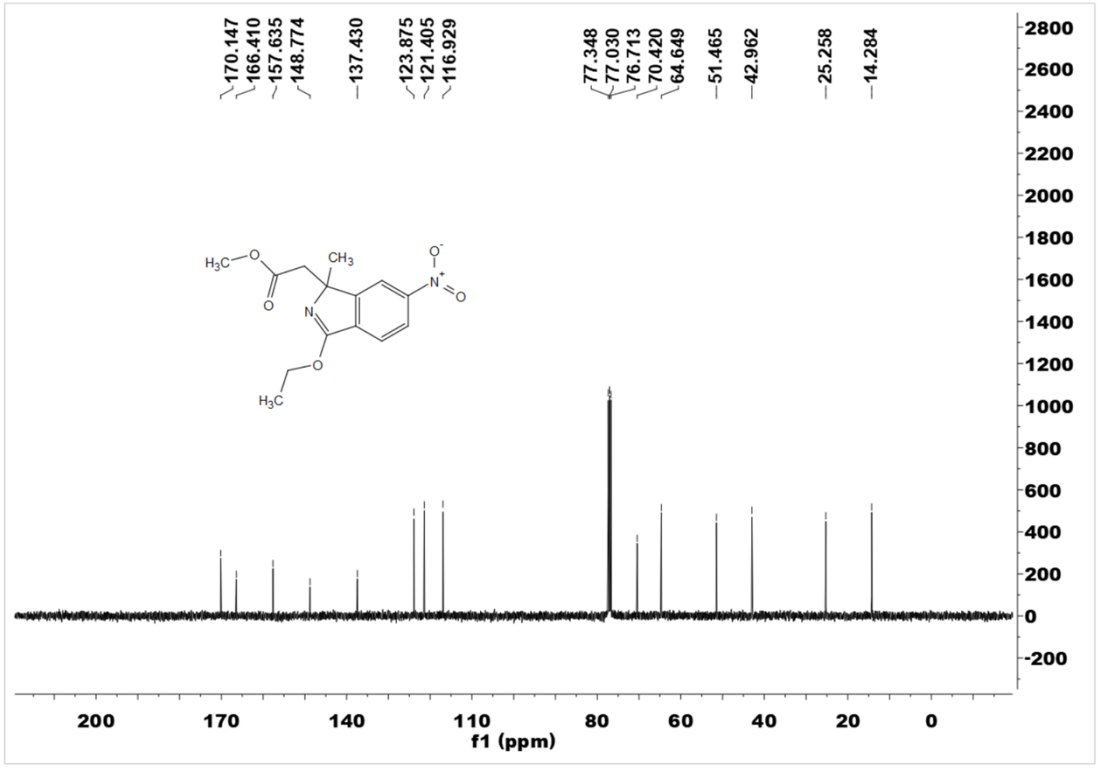


Methyl 2-(3-ethoxy-1-methyl-6-nitro-1*H*-isoindol-1-yl)acetate (4g)

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

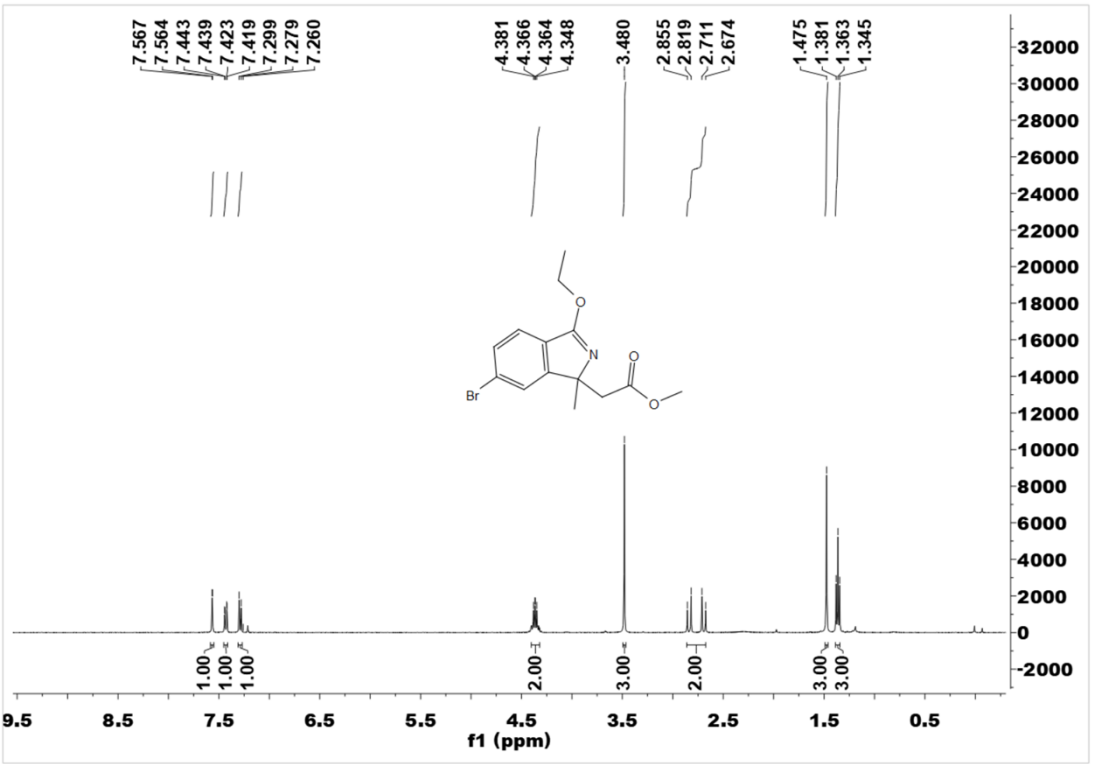


^{13}C NMR (100 MHz, $CDCl_3$)

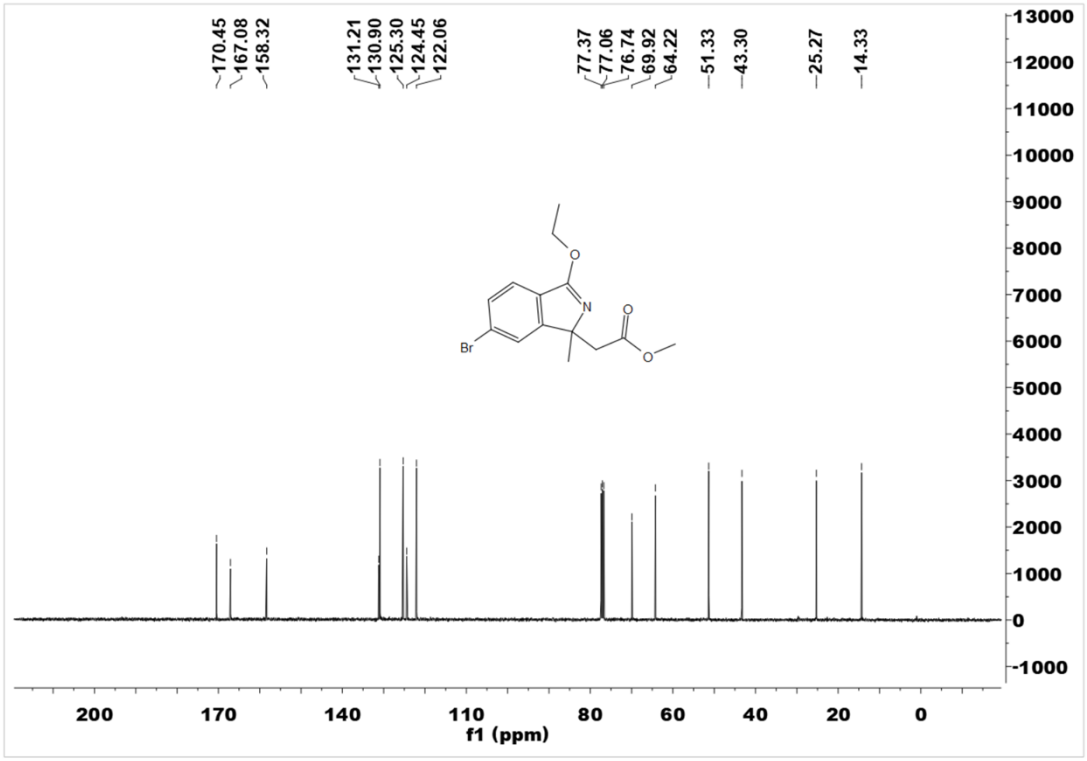


Methyl 2-(6-bromo-3-ethoxy-1-methyl-1H-isoindol-1-yl)acetate (4h)

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

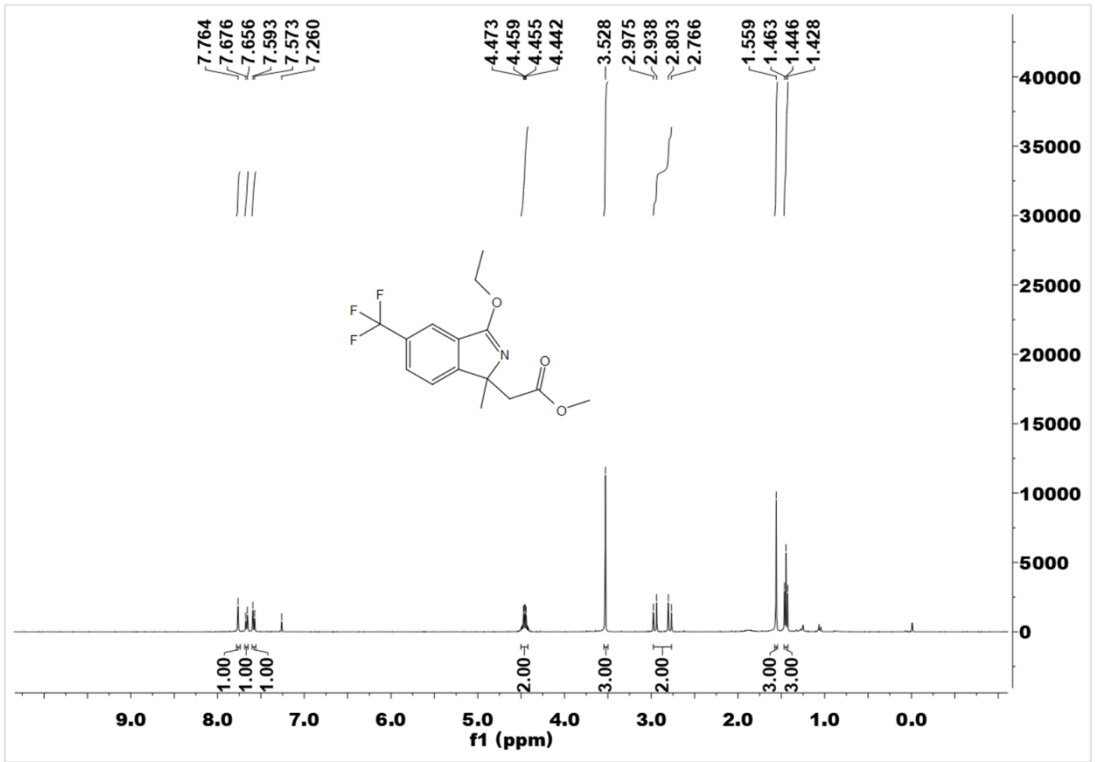


^{13}C NMR (100 MHz, $CDCl_3$)

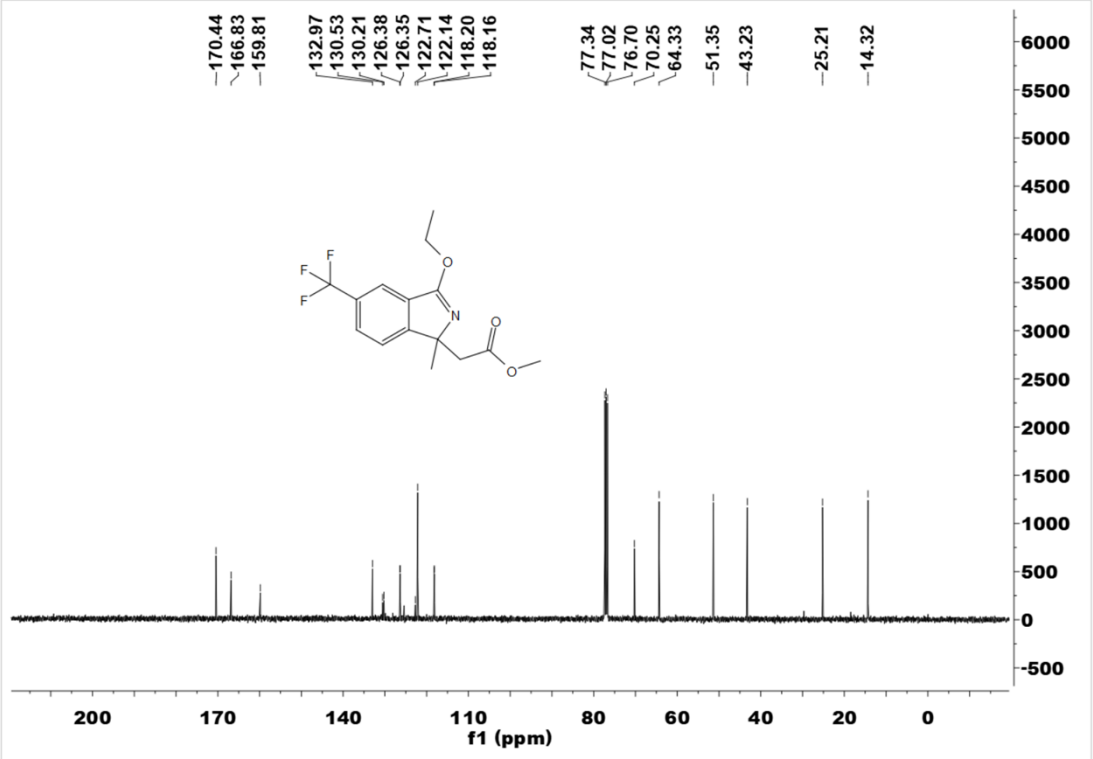


Methyl 2-(3-ethoxy-1-methyl-5-(trifluoromethyl)-1*H*-isoindol-1-yl)acetate (4i)

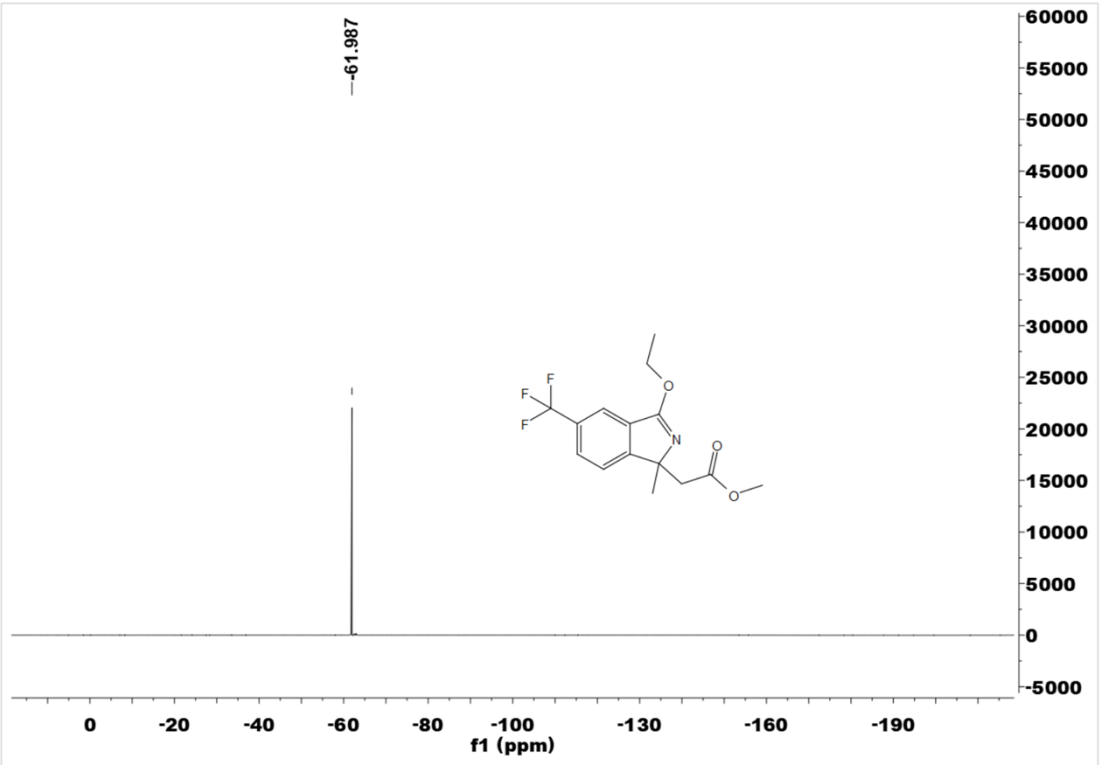
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

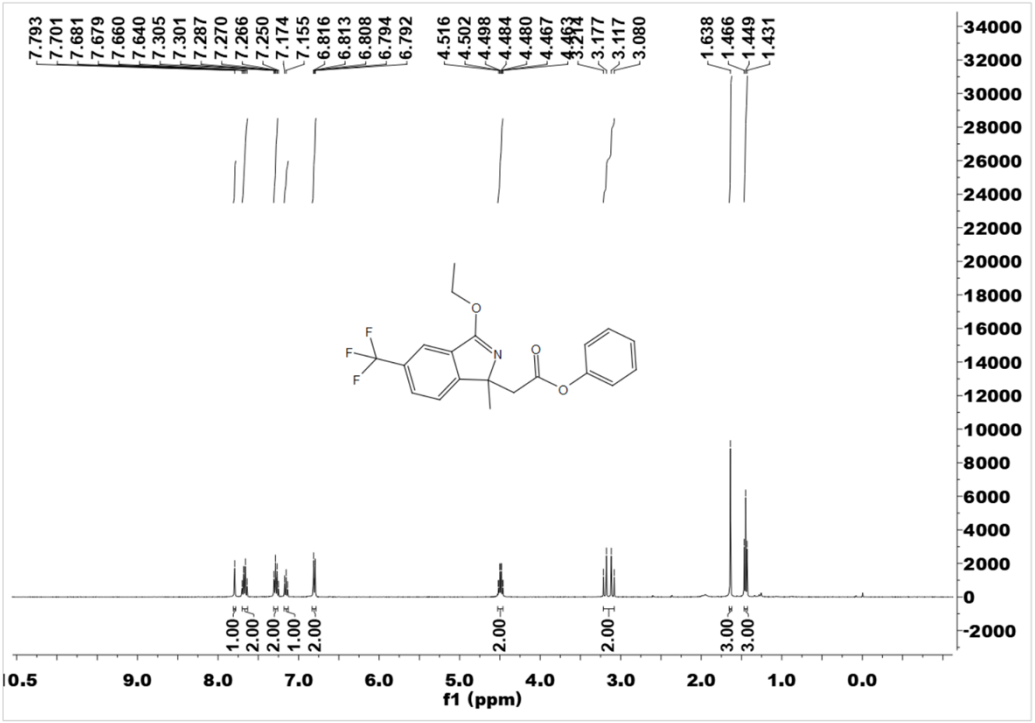


^{19}F NMR (376 MHz, $CDCl_3$)

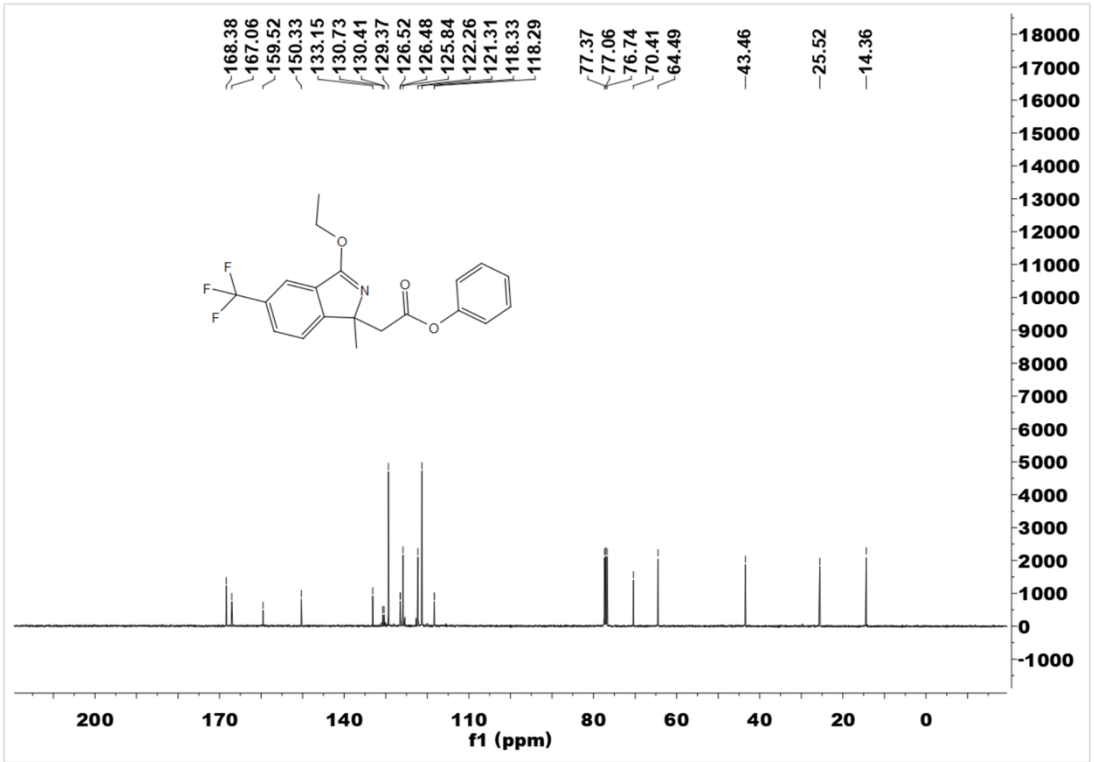


Phenyl 2-(3-ethoxy-1-methyl-5-(trifluoromethyl)-1*H*-isoindol-1-yl)acetate (4j)

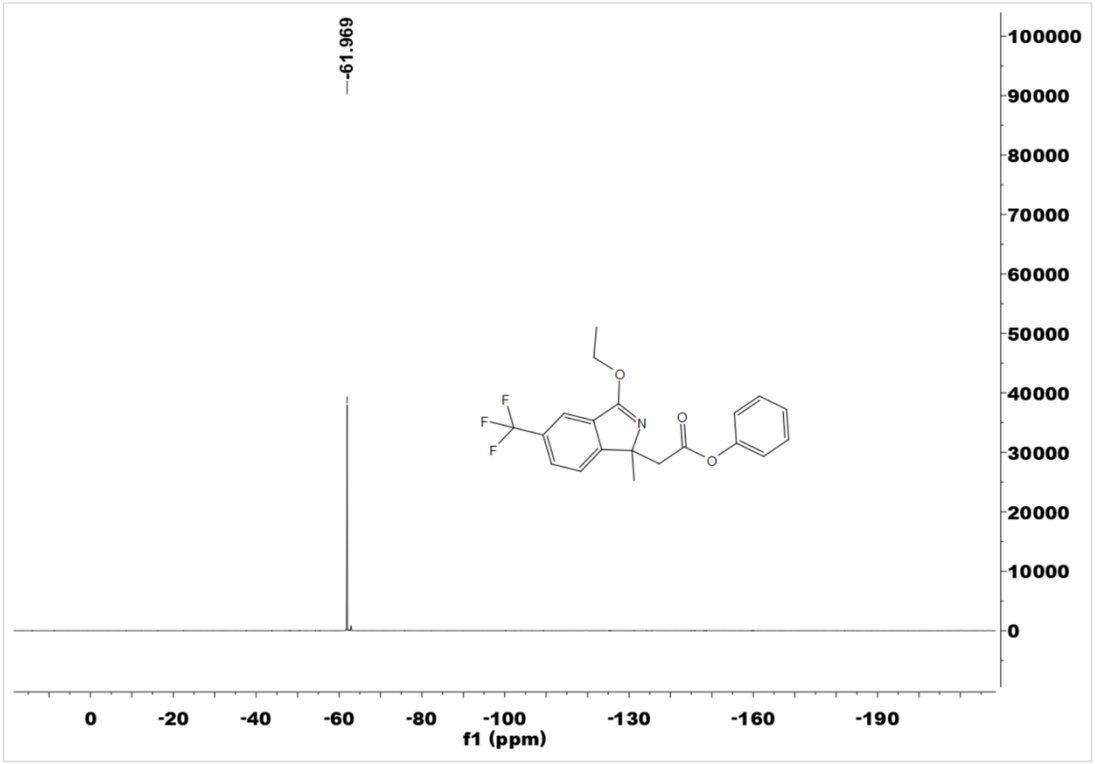
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

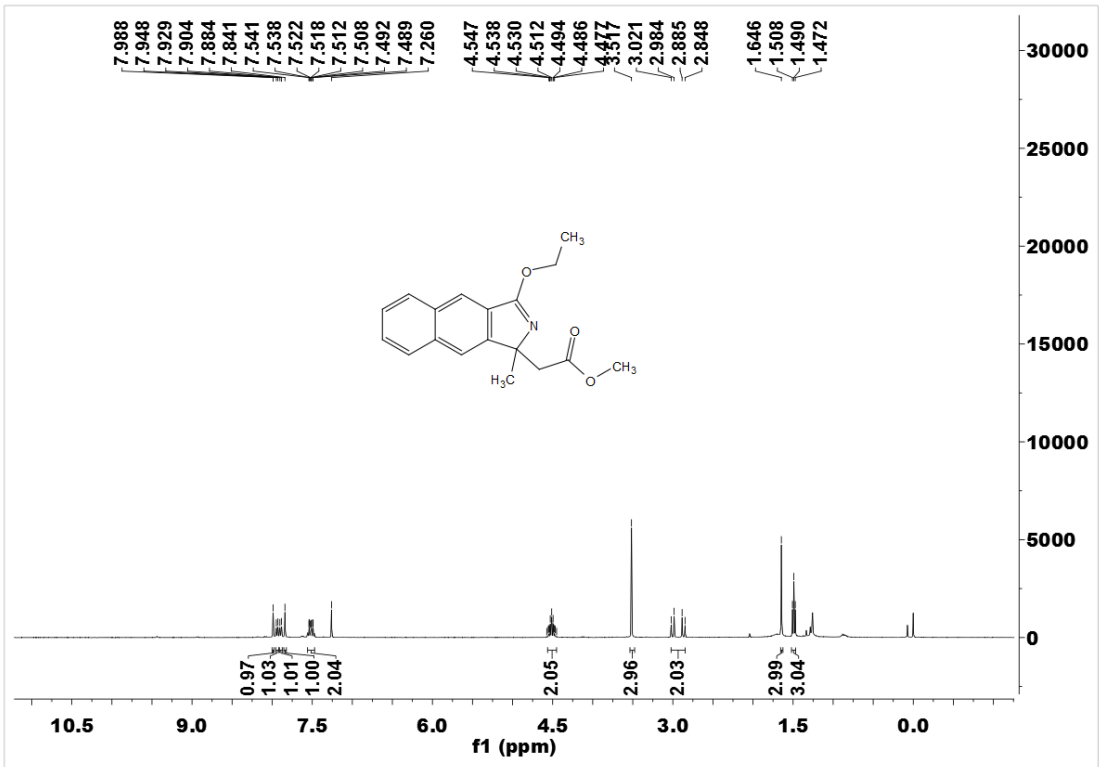


^{19}F NMR (376 MHz, $CDCl_3$)

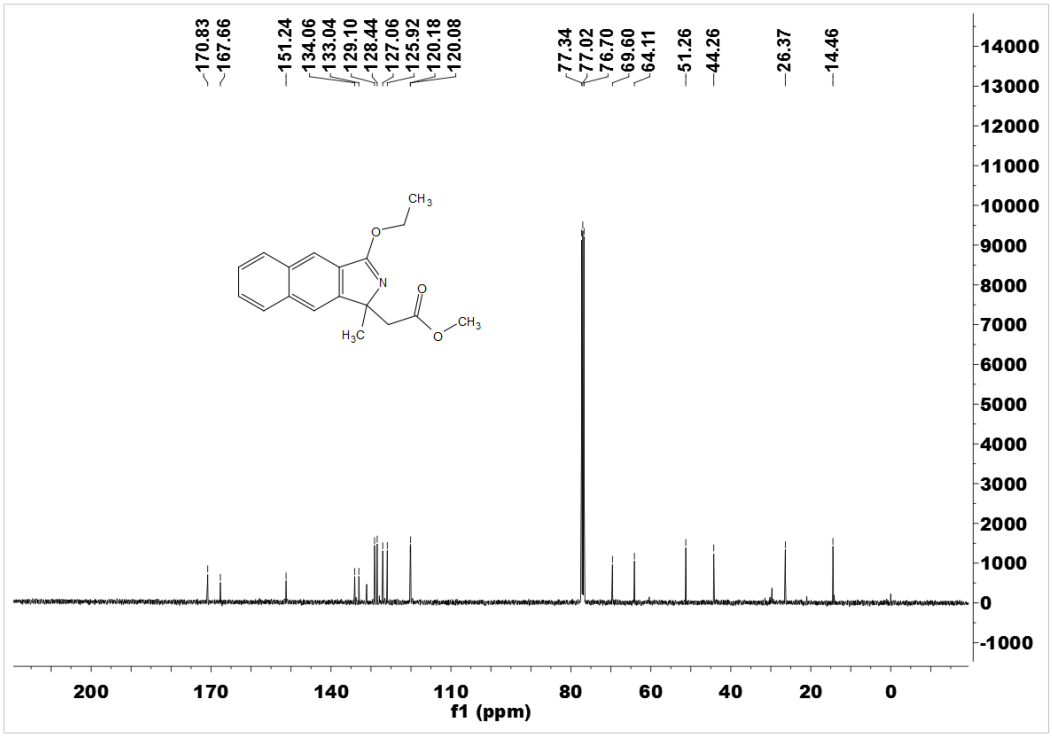


Methyl 2-(3-ethoxy-1-methyl-1*H*-benzo[f]isoindol-1-yl)acetate (4k)

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

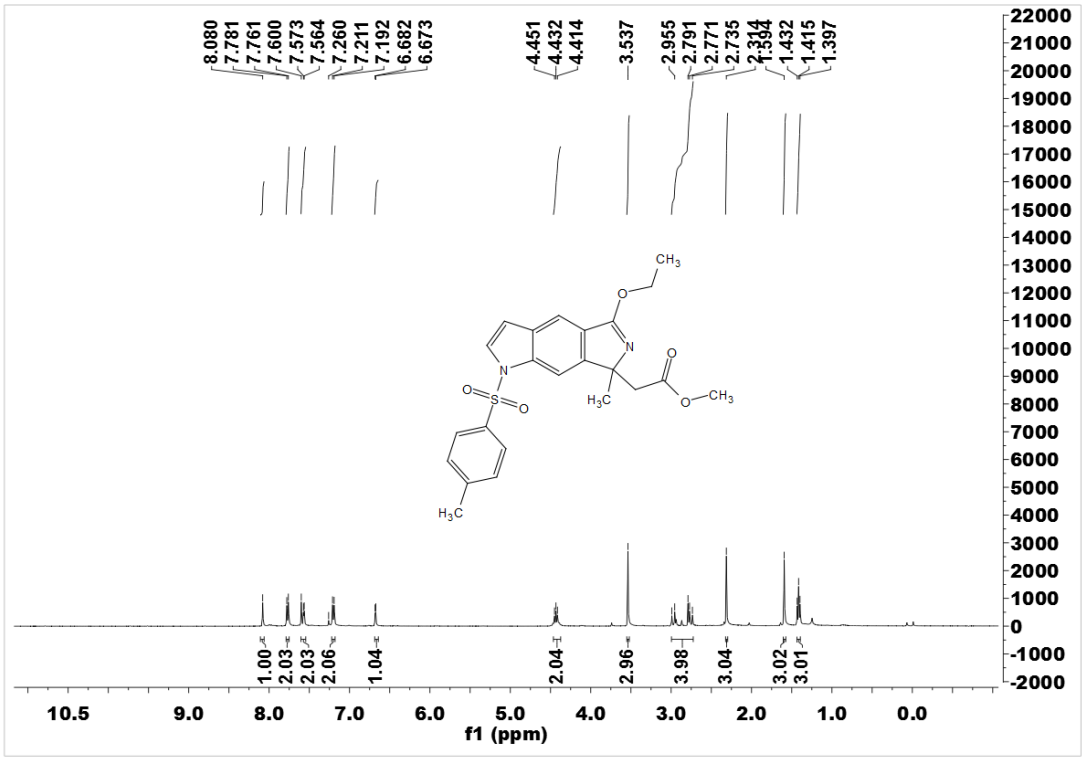


^{13}C NMR (100 MHz, $CDCl_3$)

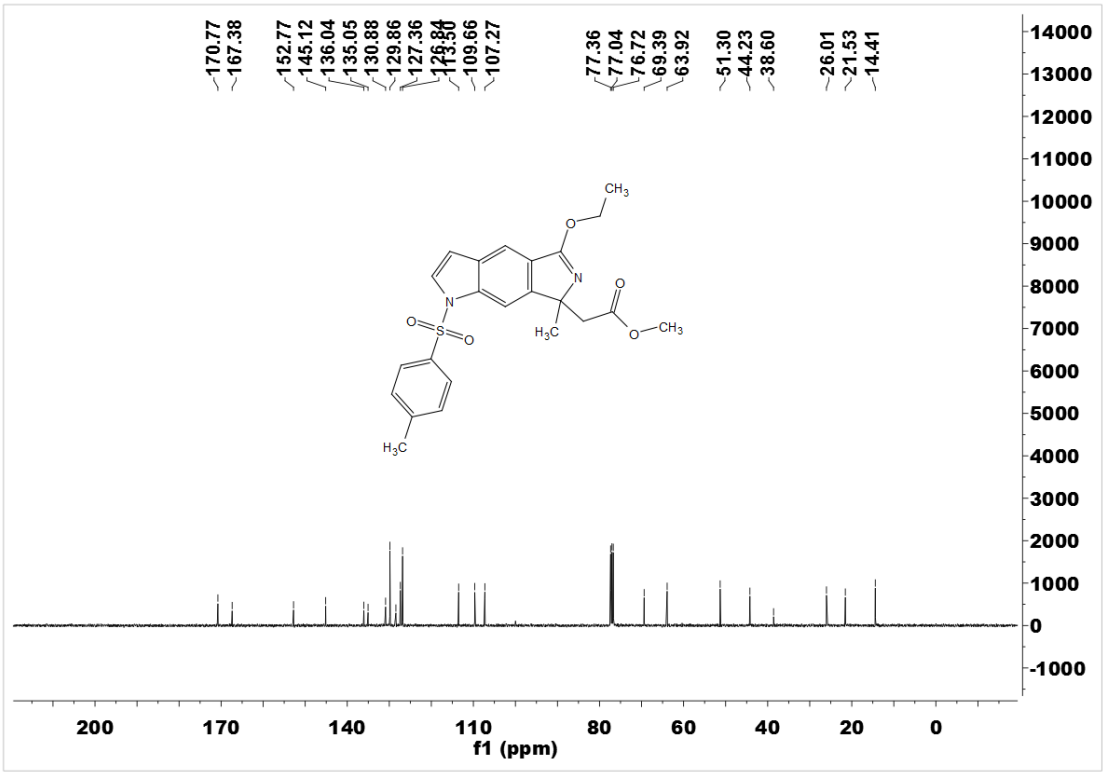


Methyl 2-(1-ethoxy-3-methyl-3*H*-benzo[4,5]thieno[2,3-f]isoindol-3-yl)acetate (4l)

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

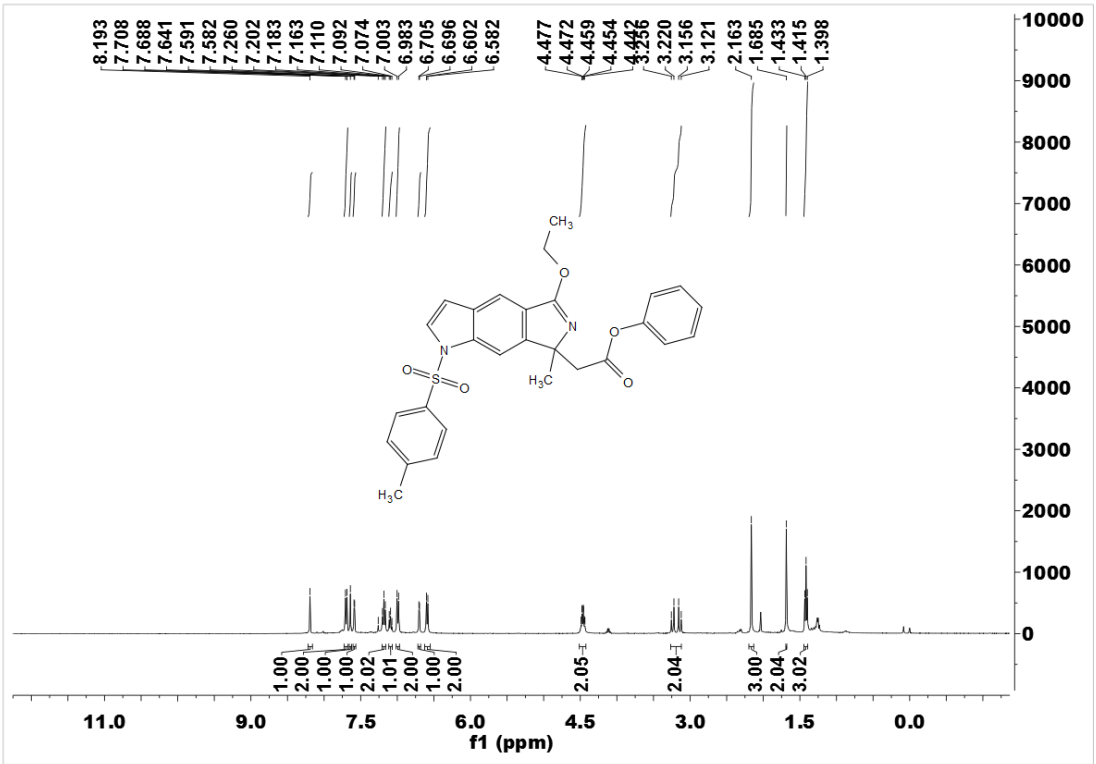


^{13}C NMR (100 MHz, $CDCl_3$)

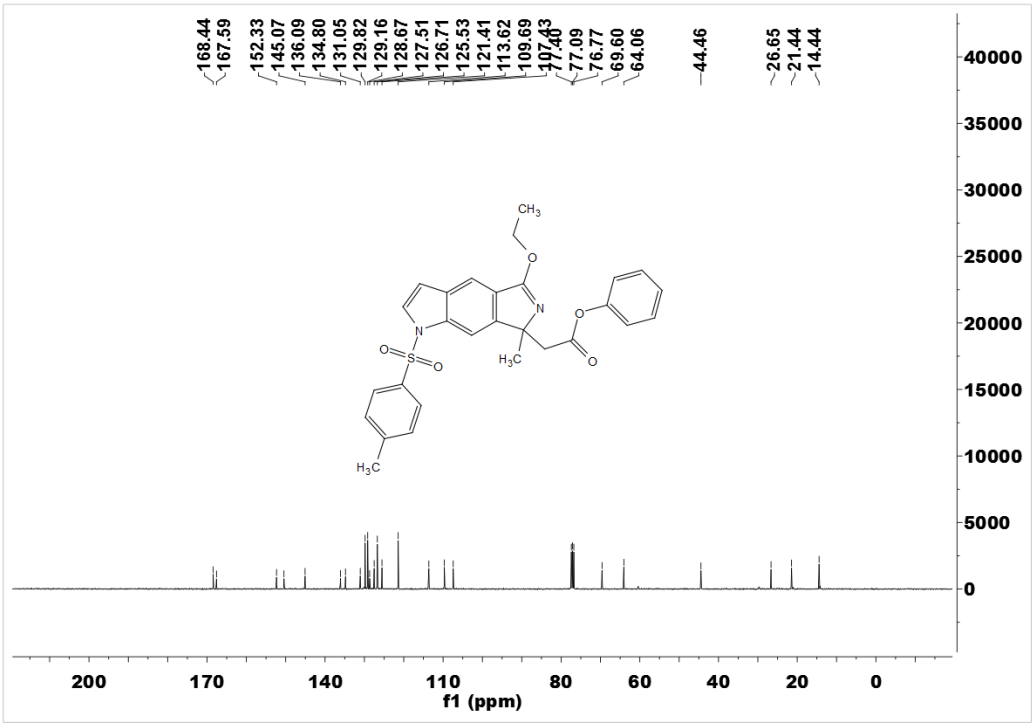


Phenyl 2-(1-ethoxy-3-methyl-3*H*-benzo[4,5]thieno[2,3-f]isoindol-3-yl)acetate (4m)

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

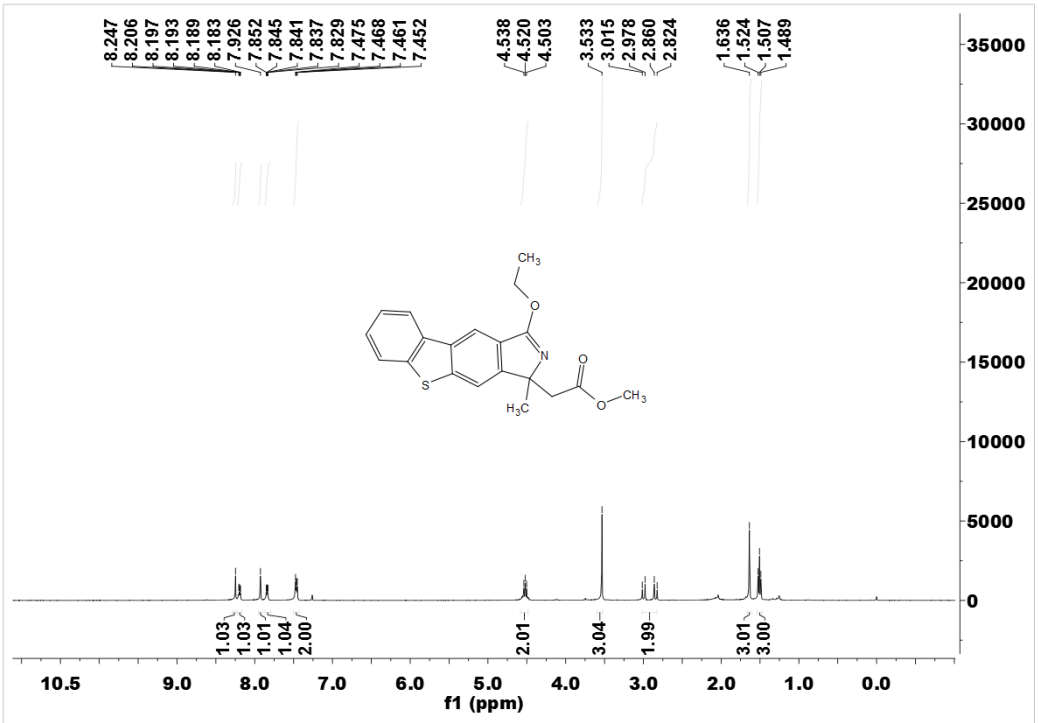


^{13}C NMR (100 MHz, $CDCl_3$)

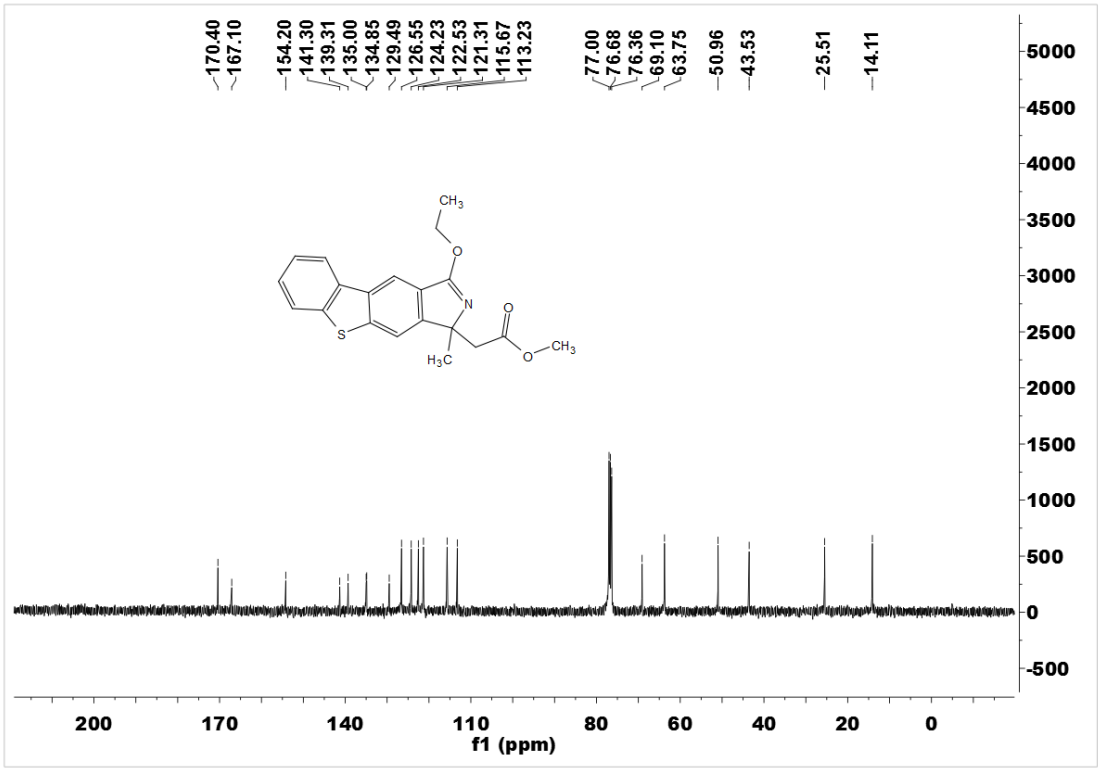


Methyl 2-(5-ethoxy-7-methyl-1-tosyl-1,7-dihydropyrrolo[3,4-f]indol-7-yl)acetate (4n)

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

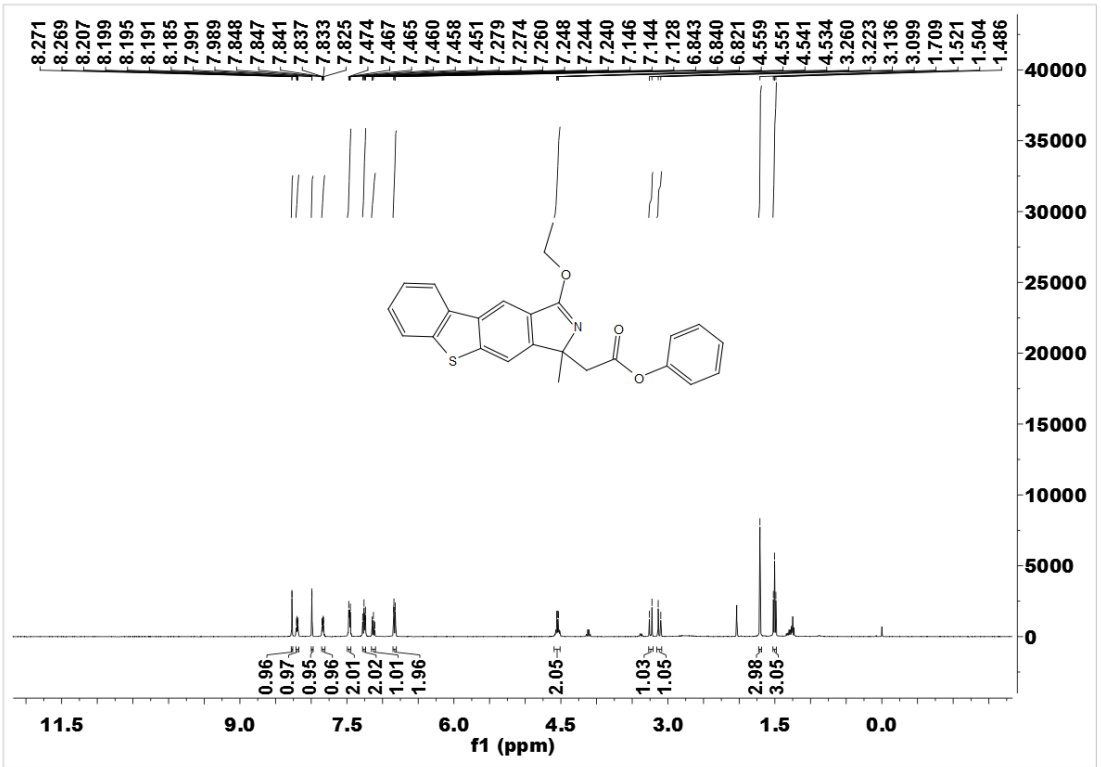


^{13}C NMR (100 MHz, $CDCl_3$)

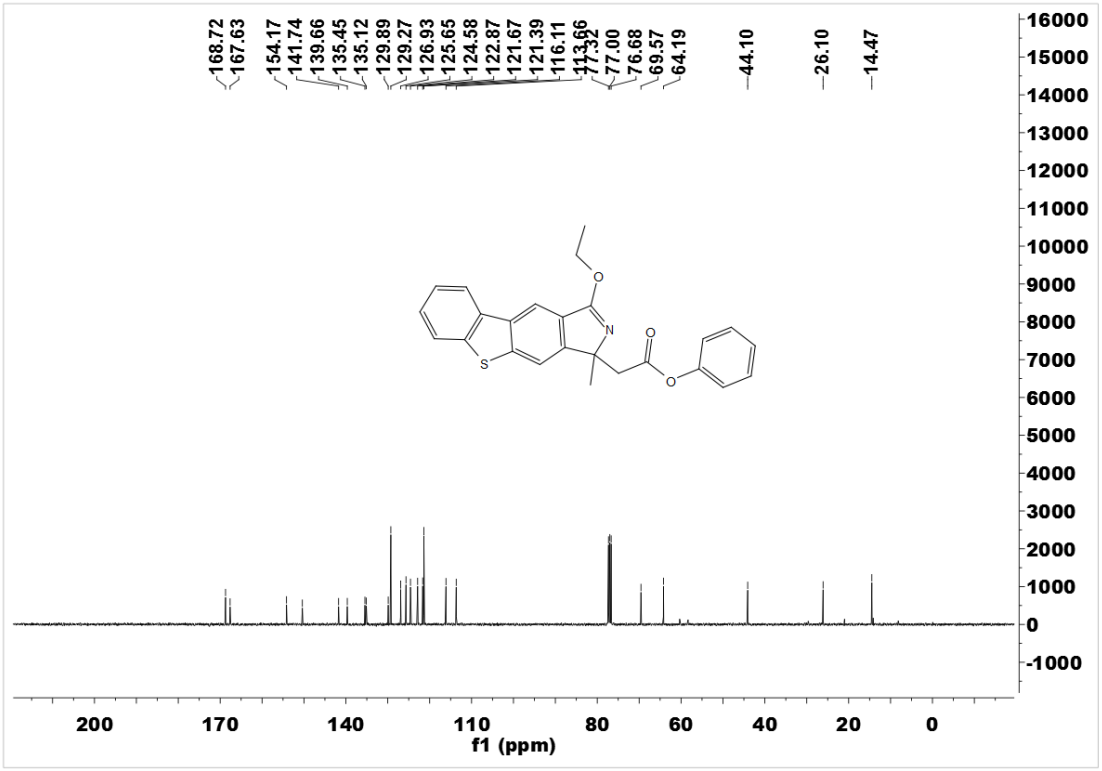


Phenyl 2-(1-ethoxy-3-methyl-3*H*-benzo[4,5]thieno[2,3-f]isoindol-3-yl)acetate (4o)

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

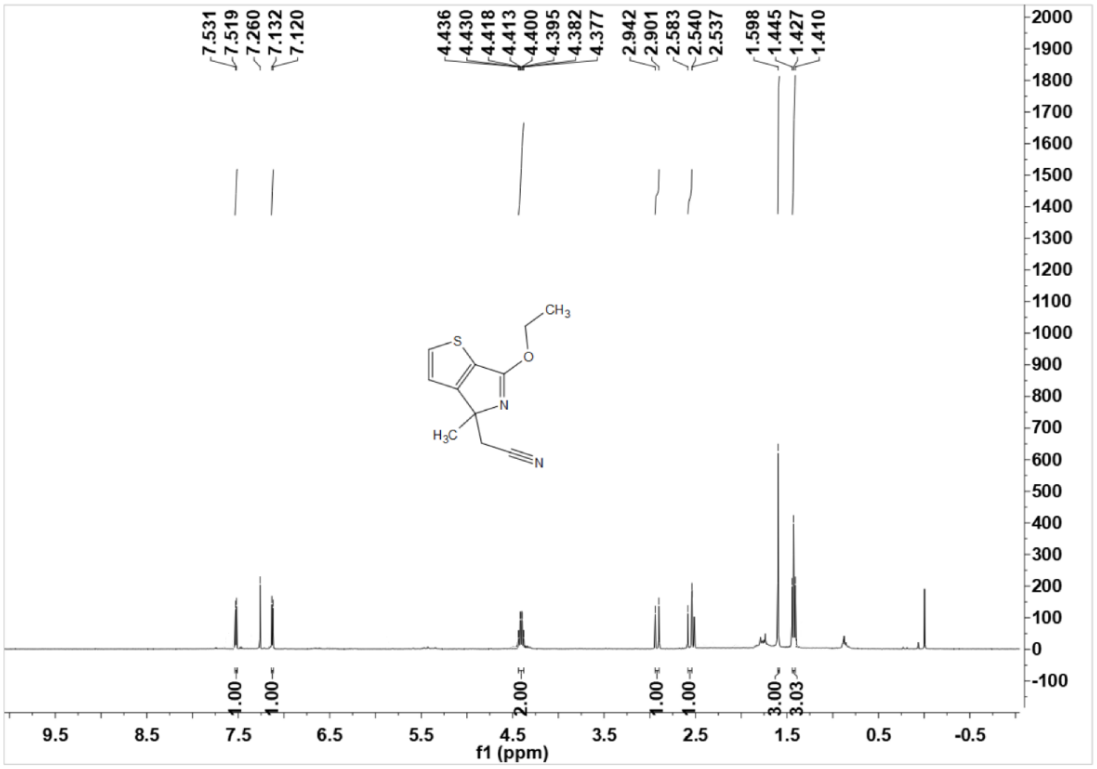


^{13}C NMR (100 MHz, $CDCl_3$)

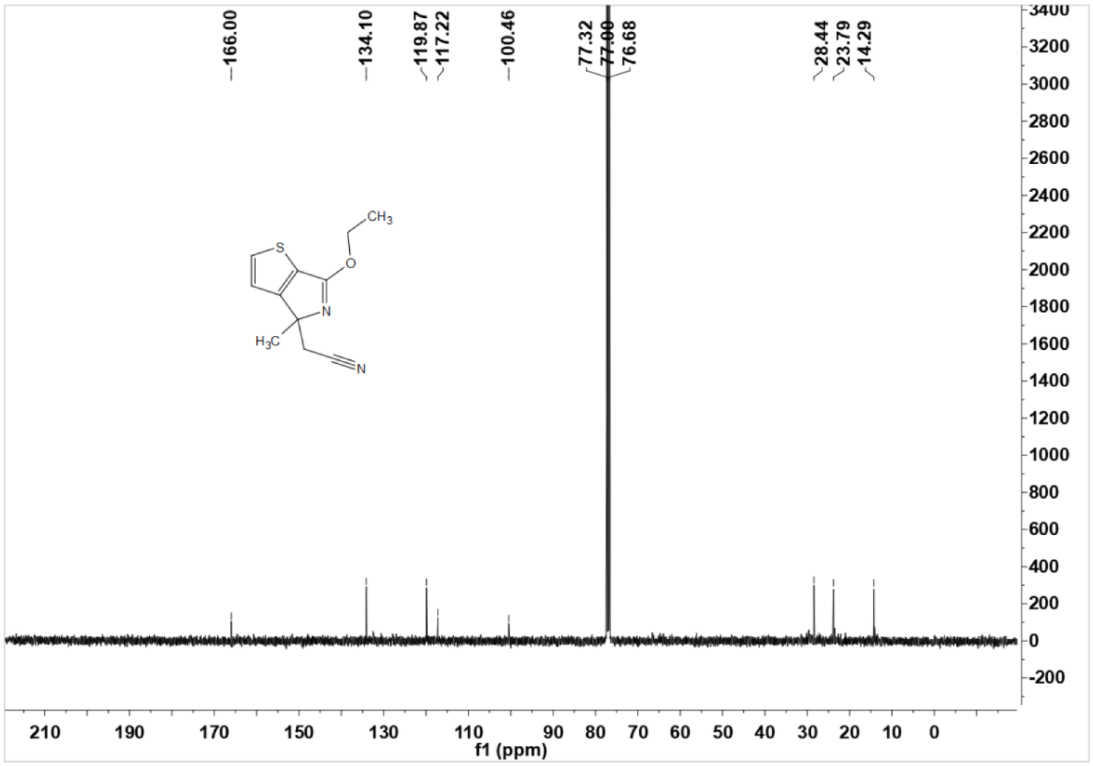


Methyl 2-(6-acetyl-3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4p),

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

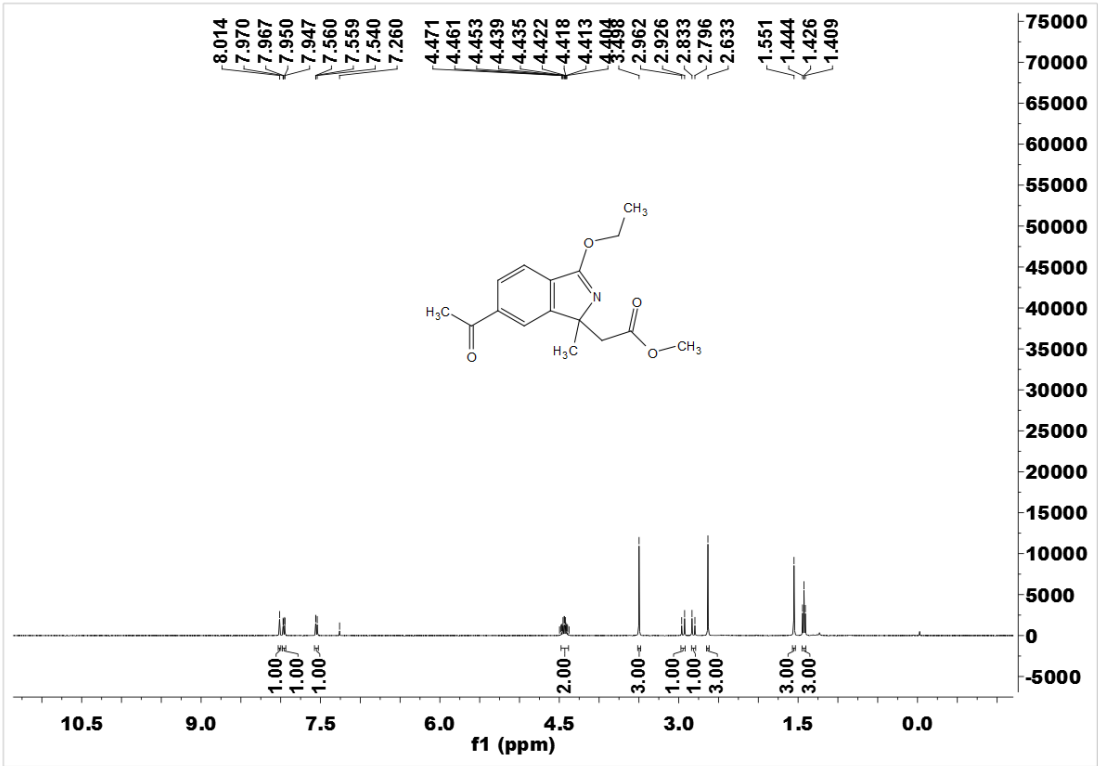


^{13}C NMR (100 MHz, $CDCl_3$)

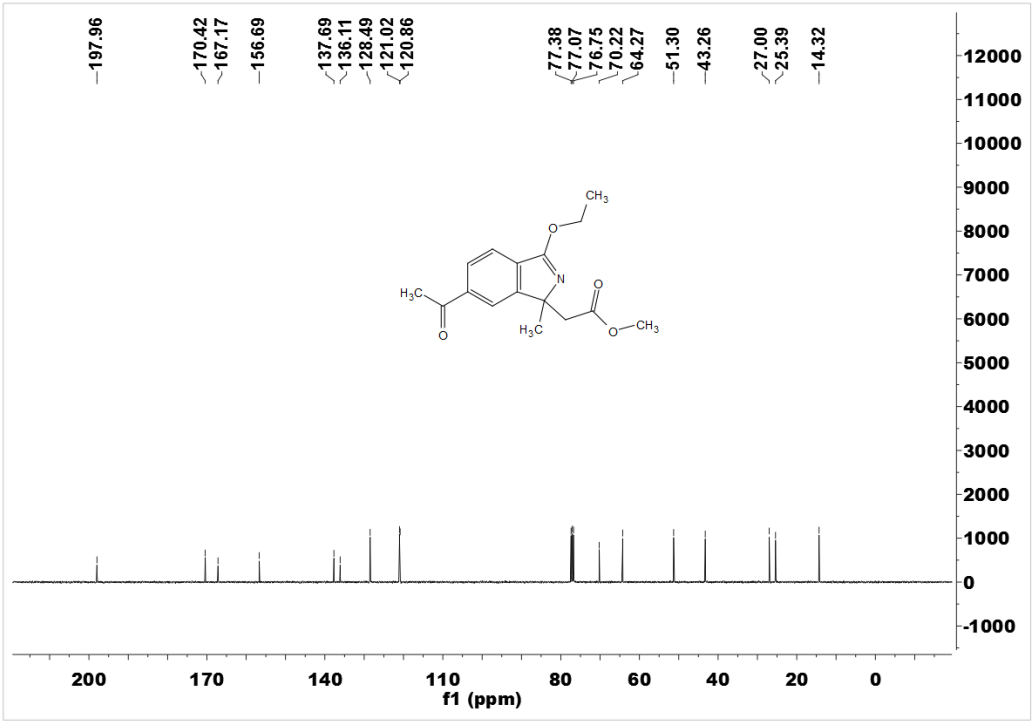


Methyl 2-(6-acetyl-3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4q)

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

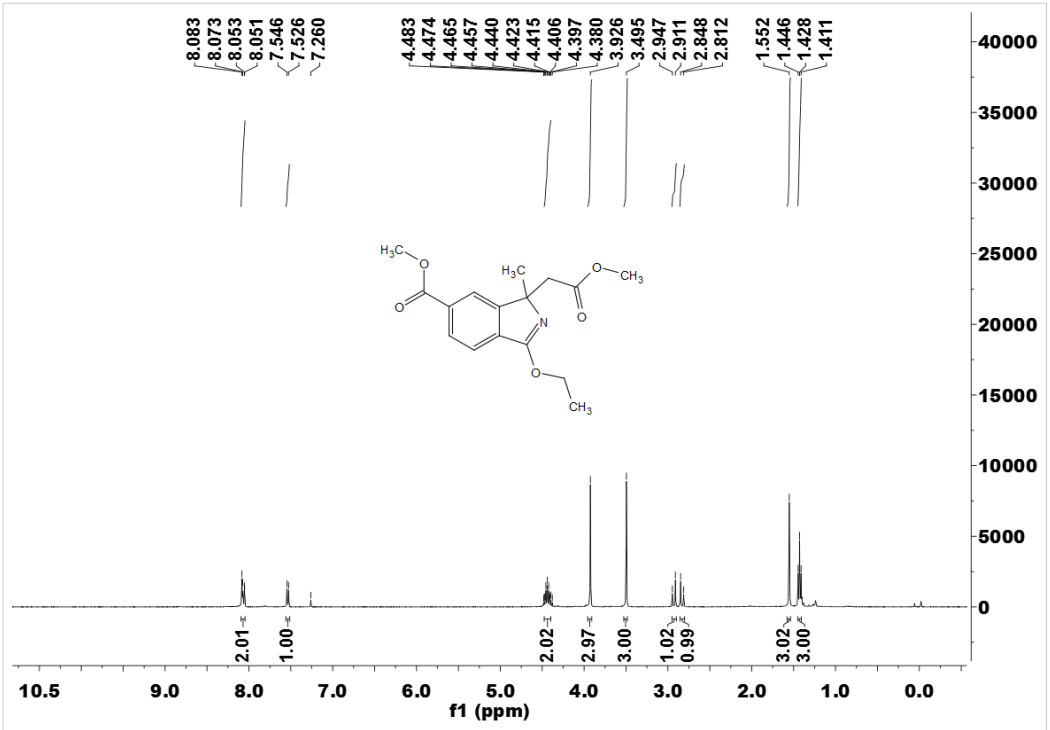


^{13}C NMR (100 MHz, $CDCl_3$)

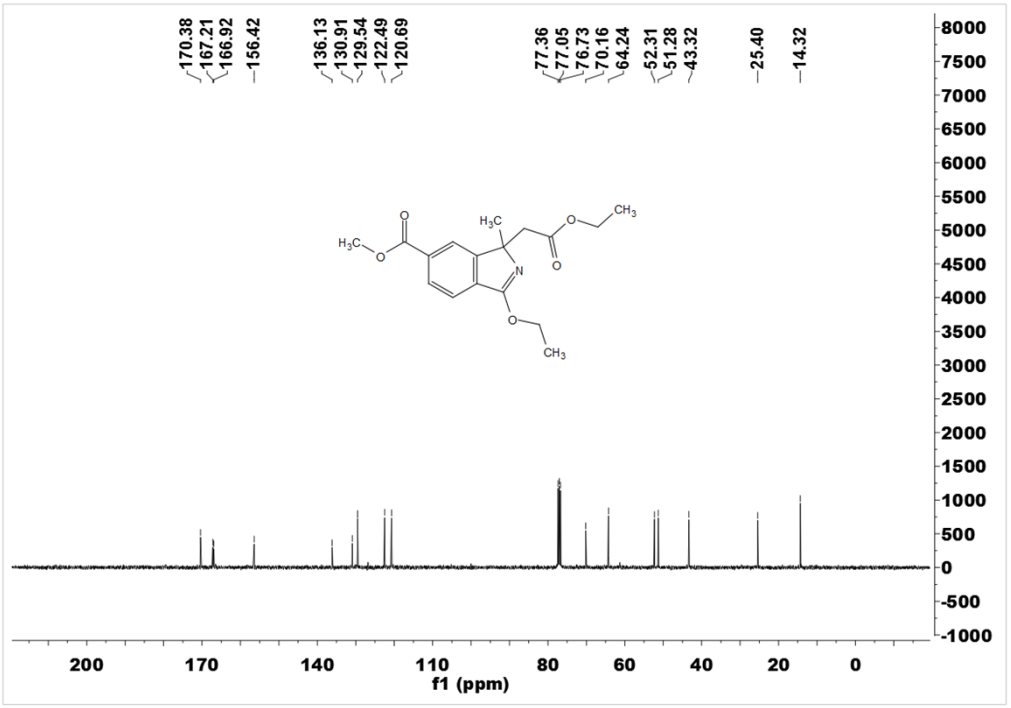


Methyl 3-ethoxy-1-(2-methoxy-2-oxoethyl)-1-methyl-1*H*-isoindole-6-carboxylate (4r)

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

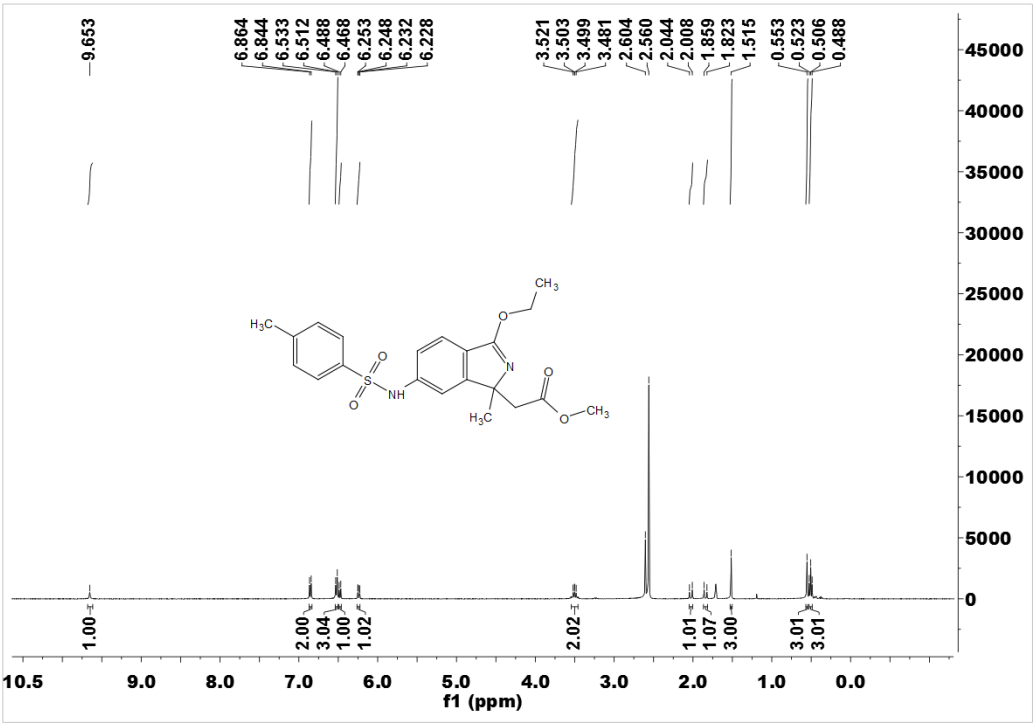


^{13}C NMR (100 MHz, $CDCl_3$)

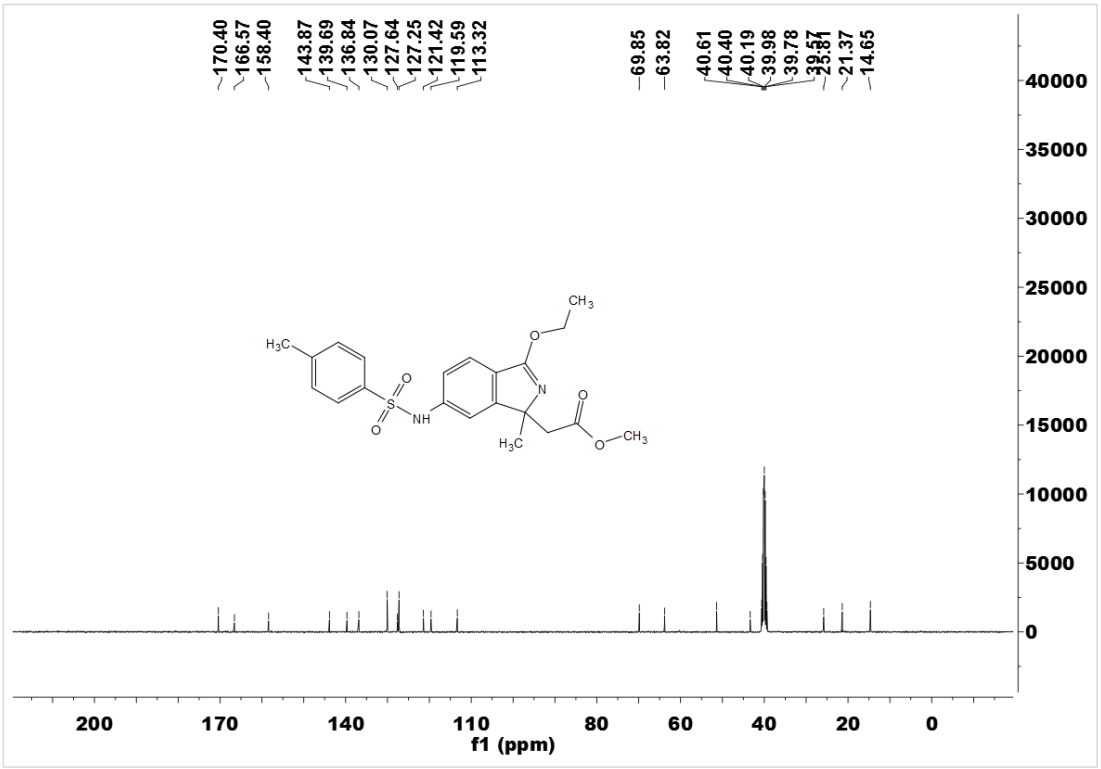


Methyl 2-(3-ethoxy-1-methyl-6-((4-methylphenyl)sulfonamido)-1*H*-isoindol-1-yl)acetate (4s)

^{1}H NMR (400 MHz, DMSO-d6)

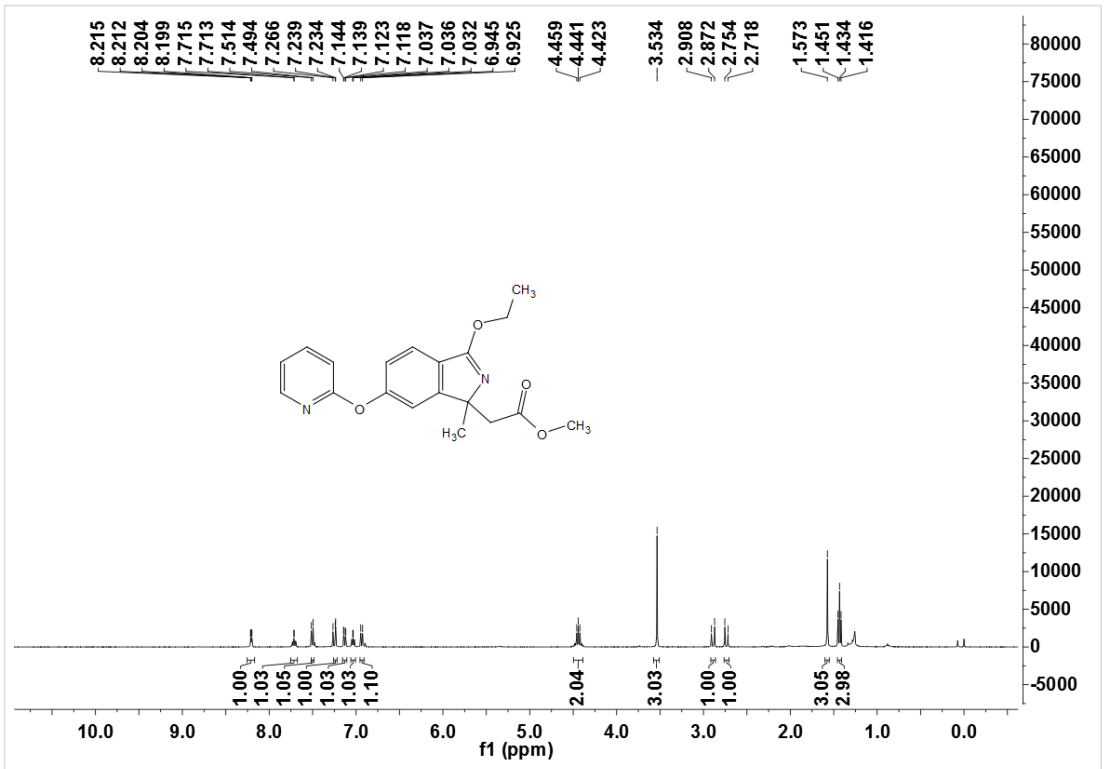


^{13}C NMR (100 MHz, DMSO-d6)

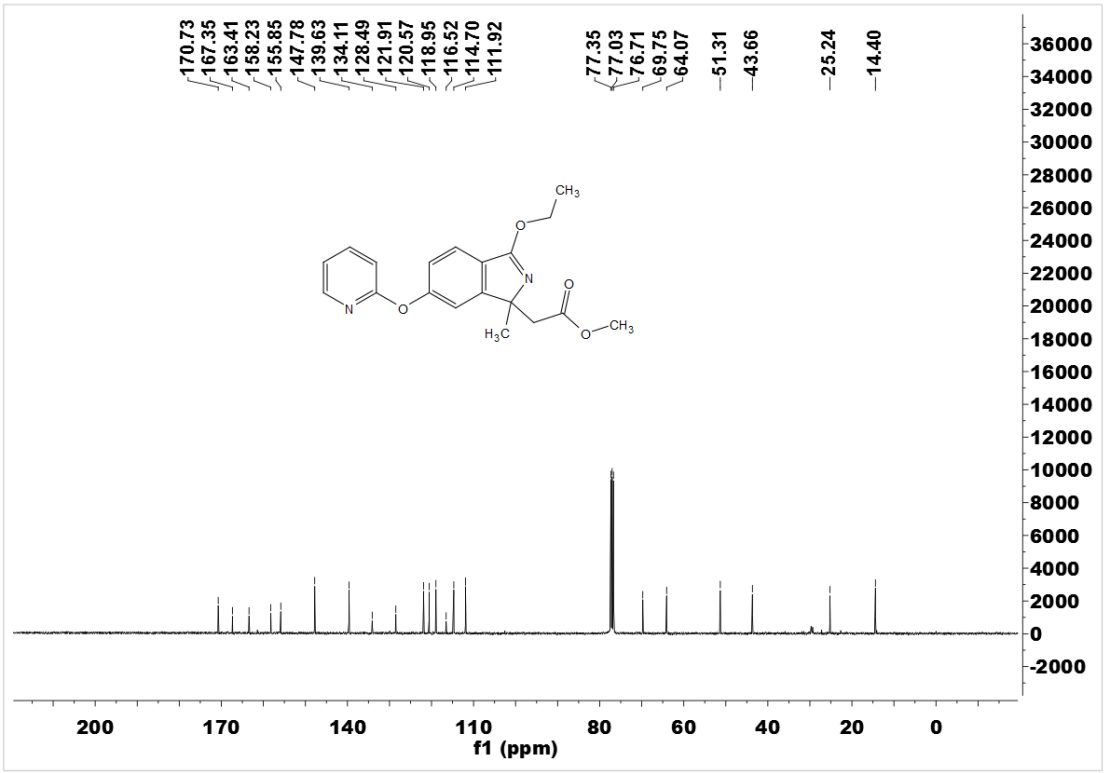


Methyl 2-(3-ethoxy-1-methyl-6-(pyridin-2-yloxy)-1*H*-isoindol-1-yl)acetate (4t)

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

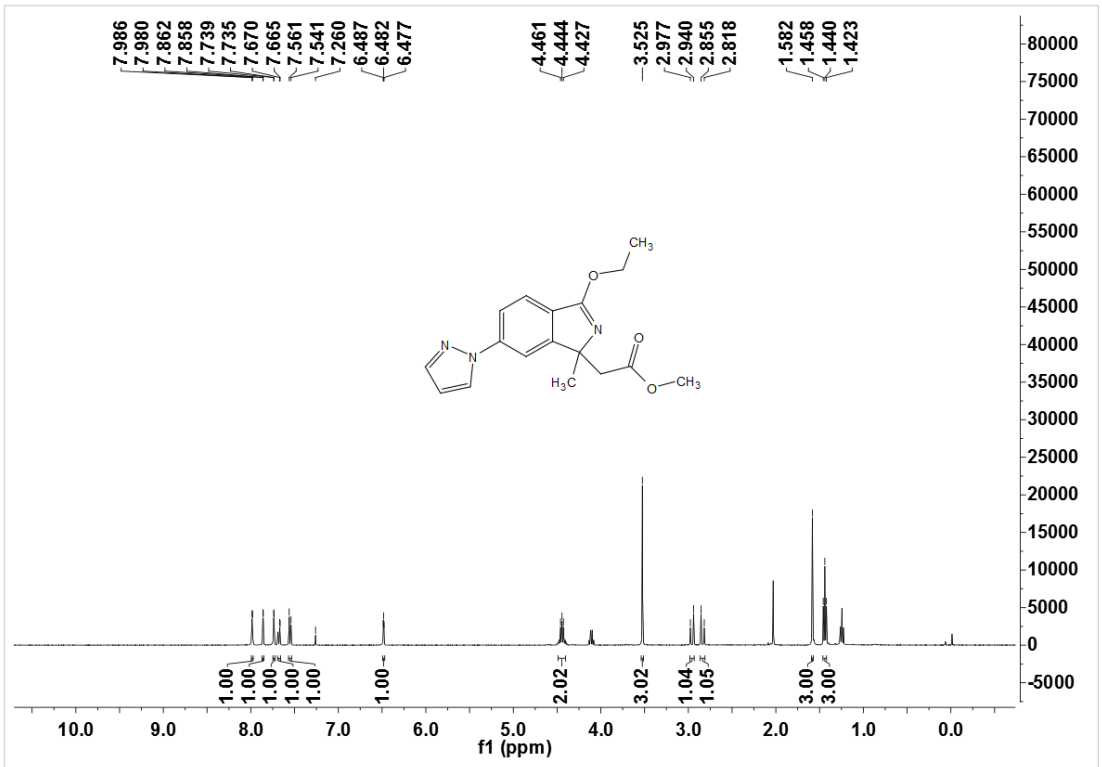


^{13}C NMR (100 MHz, $CDCl_3$)

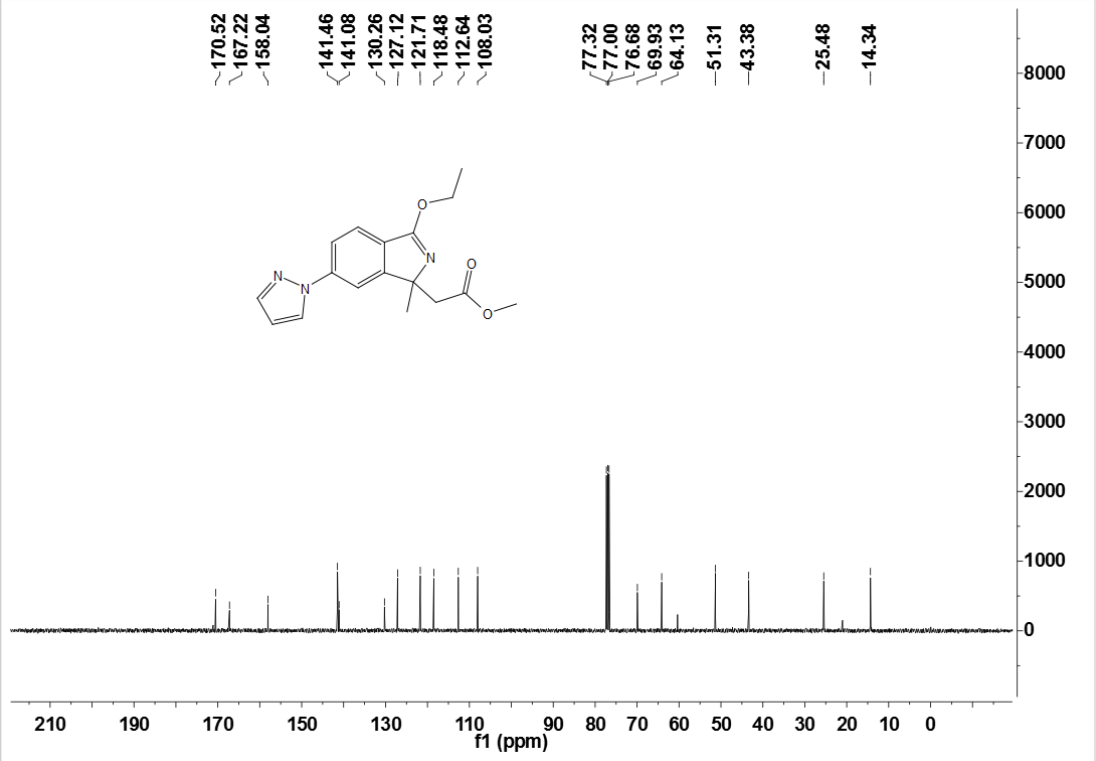


Methyl 2-(3-ethoxy-1-methyl-5-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl)acetate (4u)

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

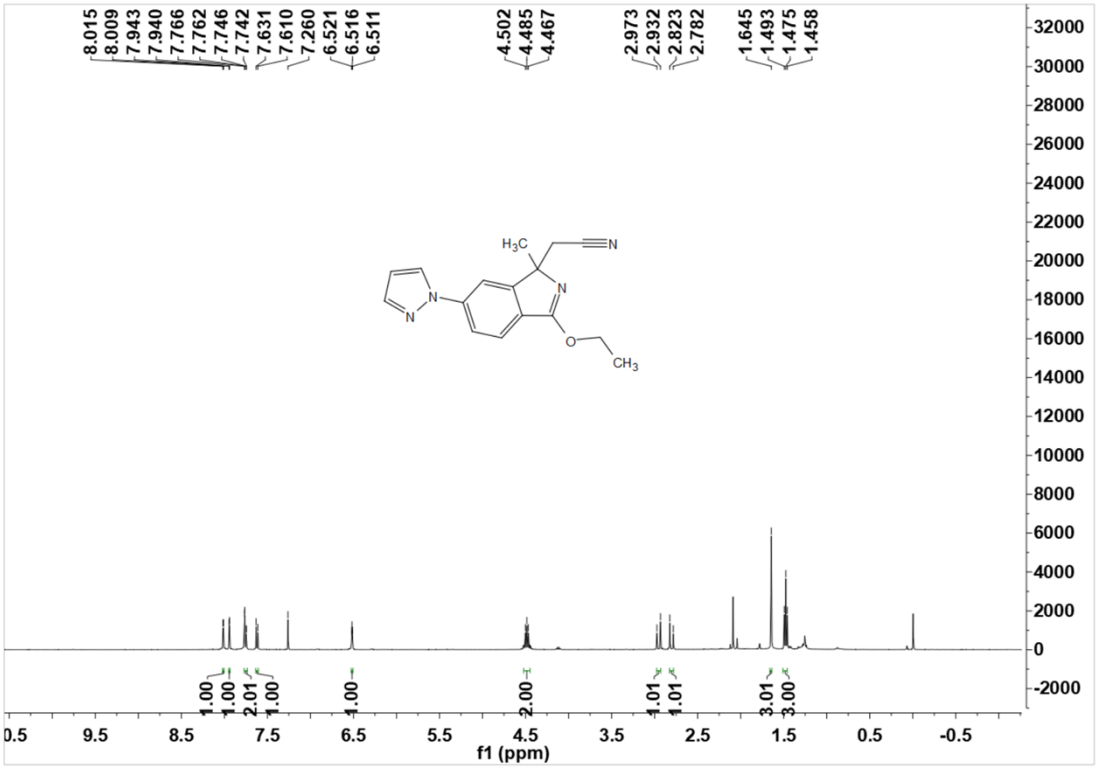


^{13}C NMR (100 MHz, $CDCl_3$)

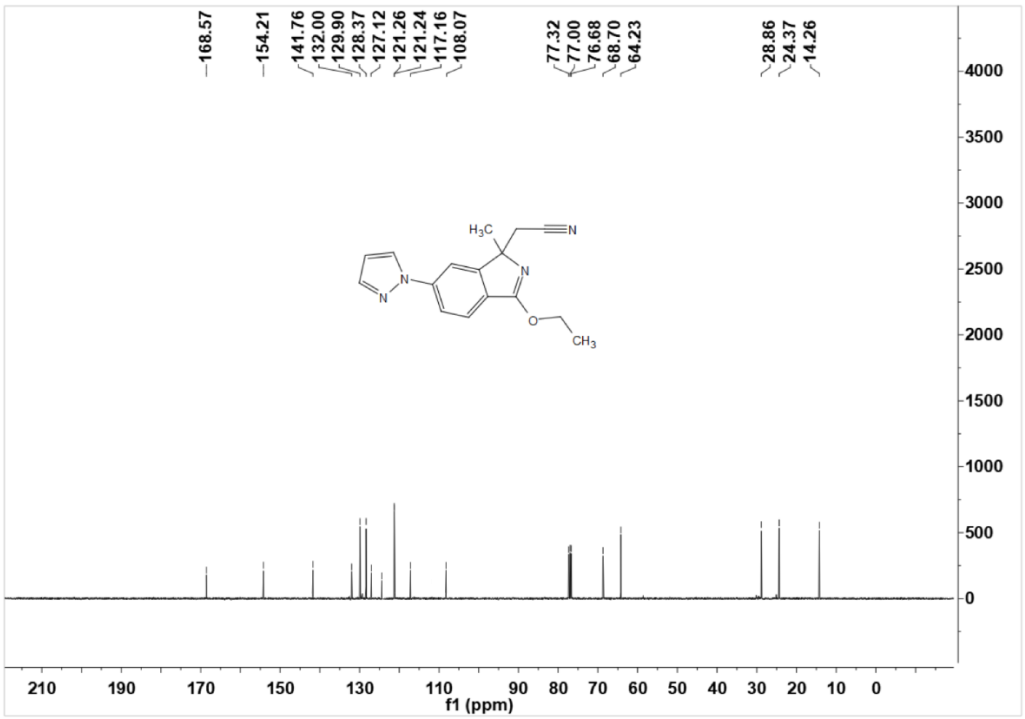


2-(3-Ethoxy-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl)acetonitrile (4v)

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

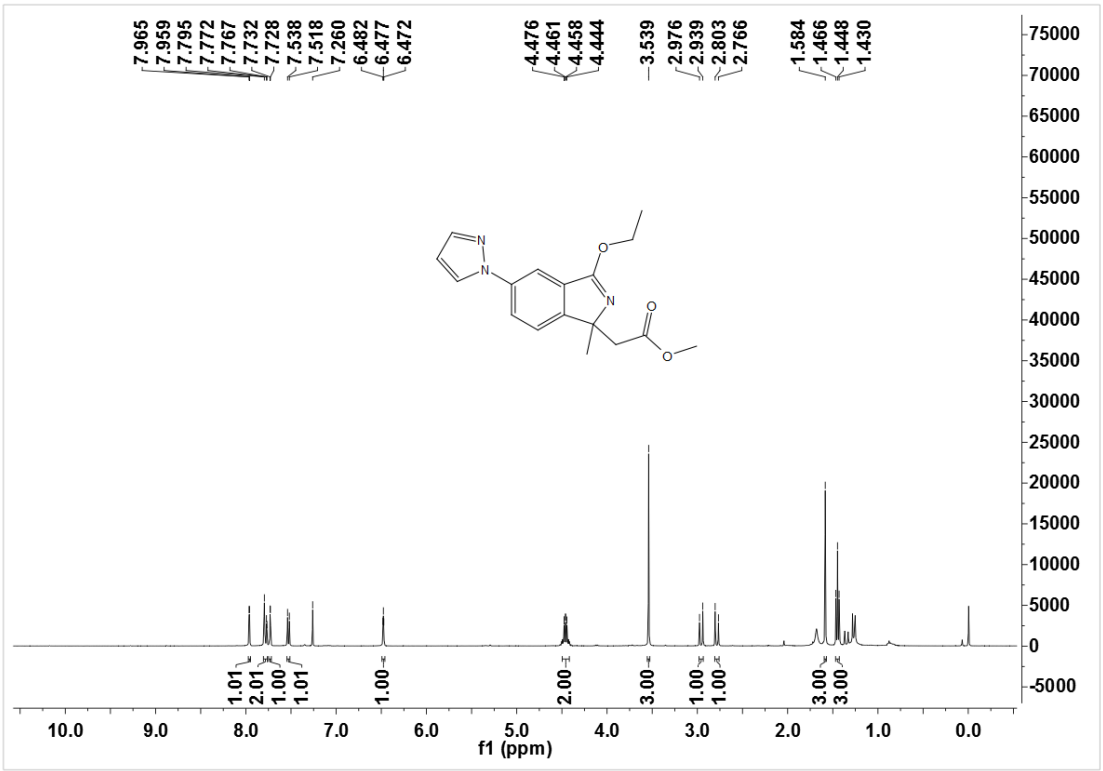


^{13}C NMR (100 MHz, $CDCl_3$)

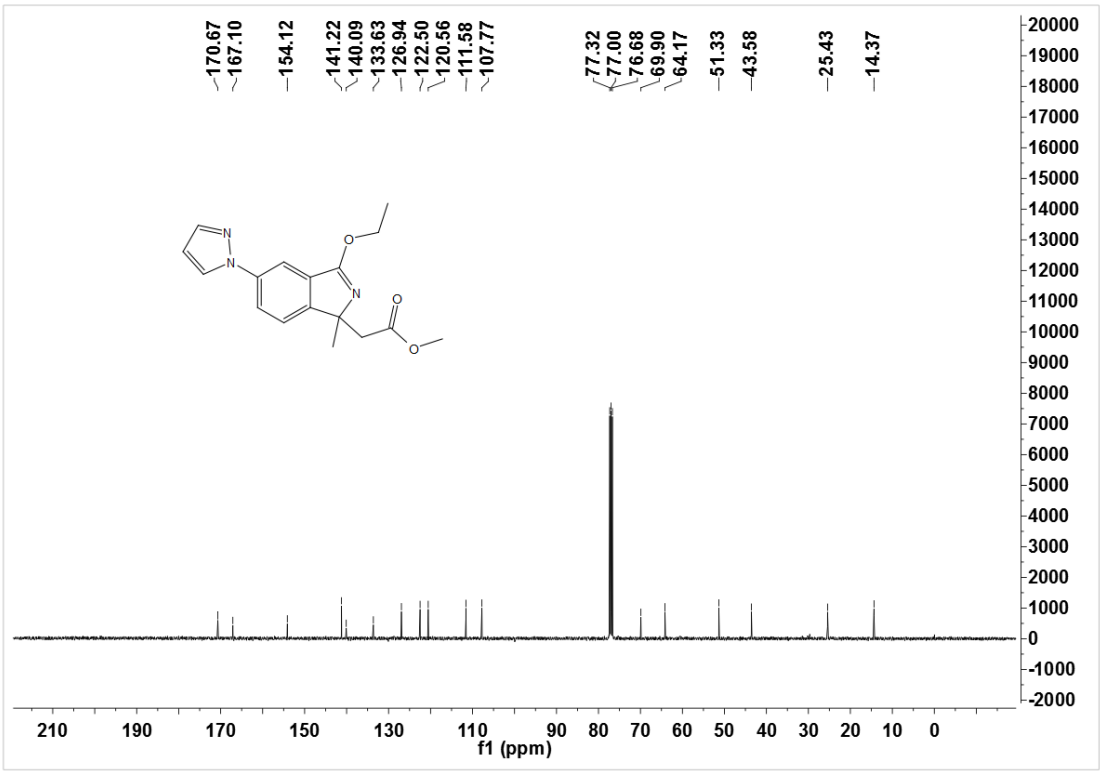


Methyl 2-(3-ethoxy-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl) acetate (4w)

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

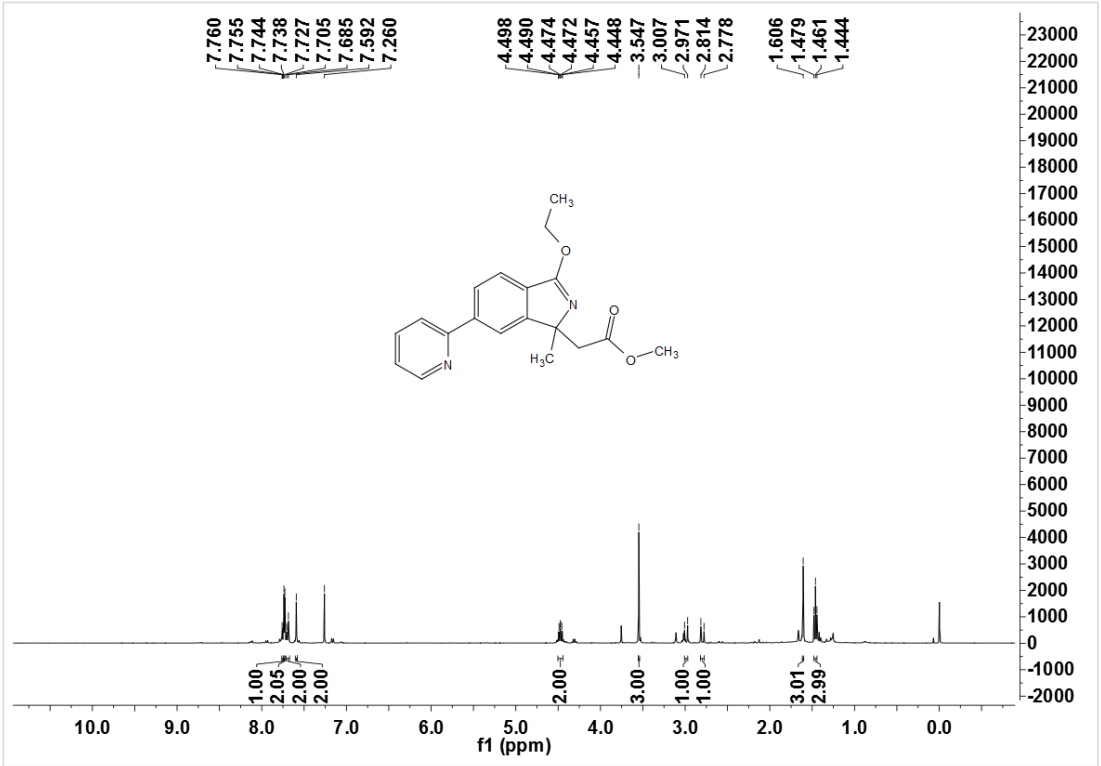


^{13}C NMR (100 MHz, $CDCl_3$)

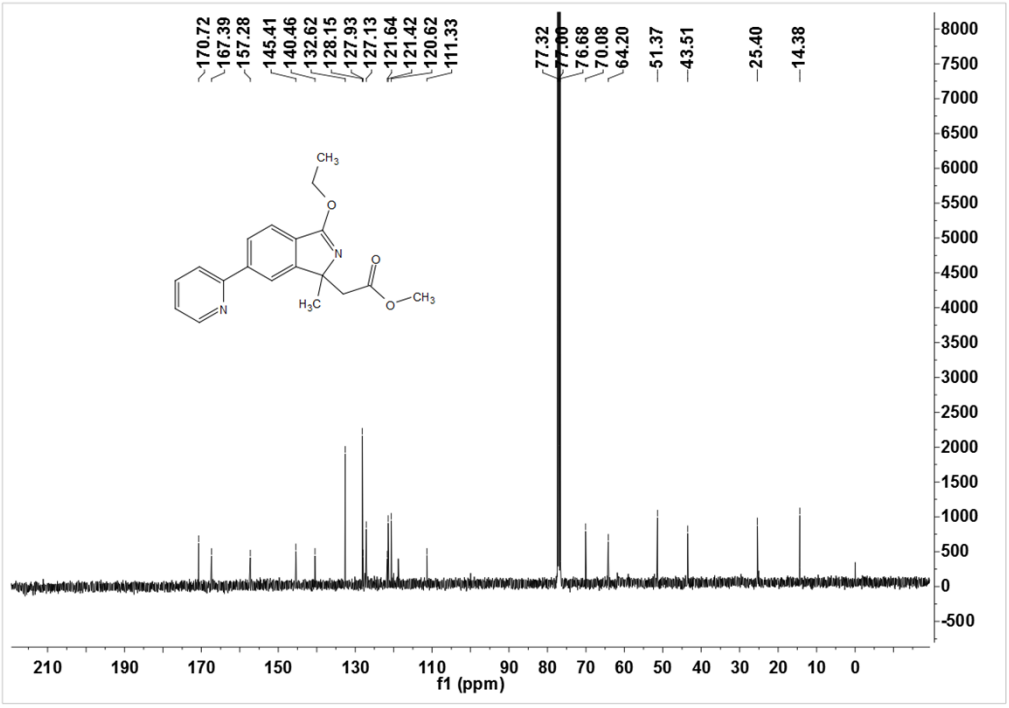


Methyl 2-(3-ethoxy-1-methyl-6-(pyridin-2-yl)-1*H*-isoindol-1-yl)acetate (4x)

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

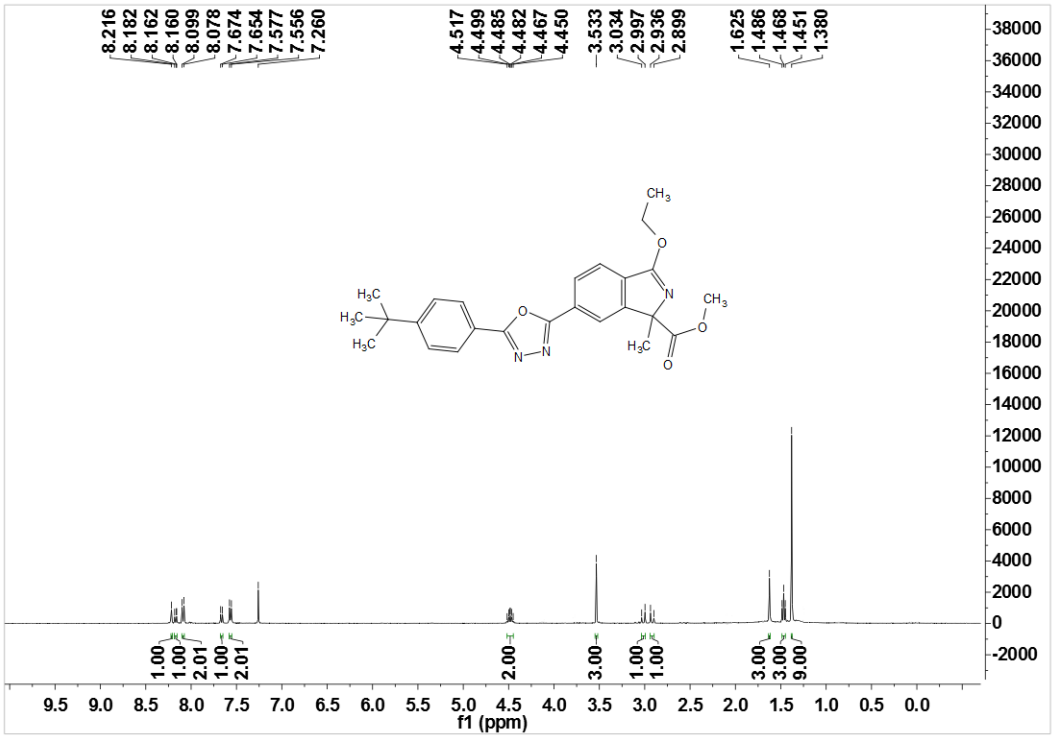


^{13}C NMR (100 MHz, $CDCl_3$)

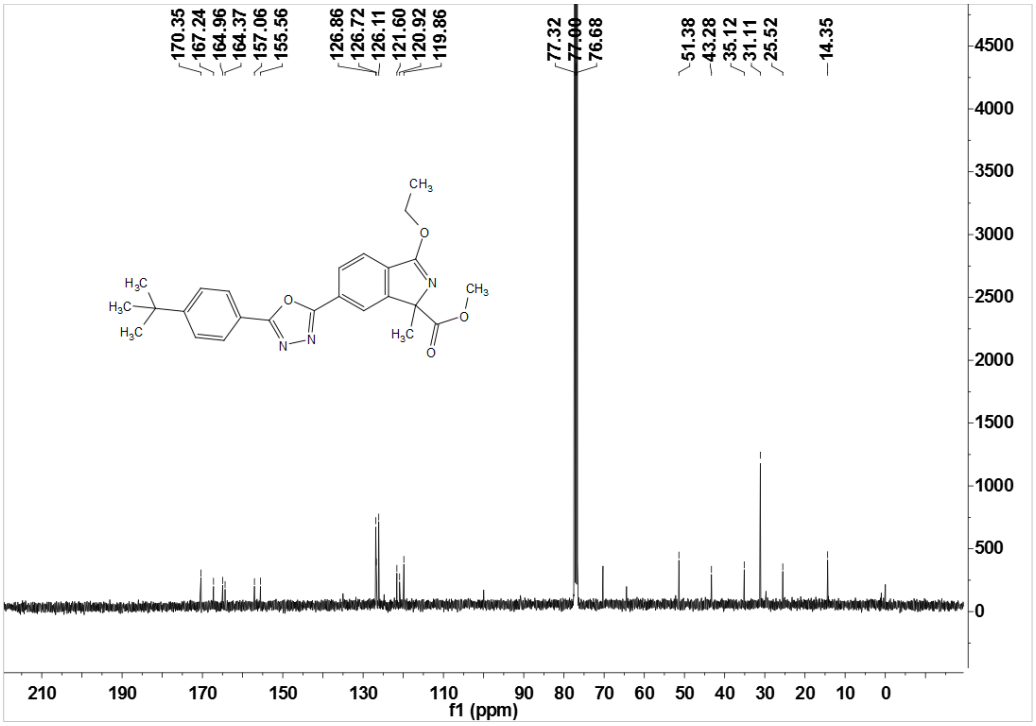


Methyl 6-(5-(4-(*tert*-butyl)phenyl)-1,3,4-oxadiazol-2-yl)-3-ethoxy-1-methyl-1*H*-isoindole-1-carboxylate (4y)

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

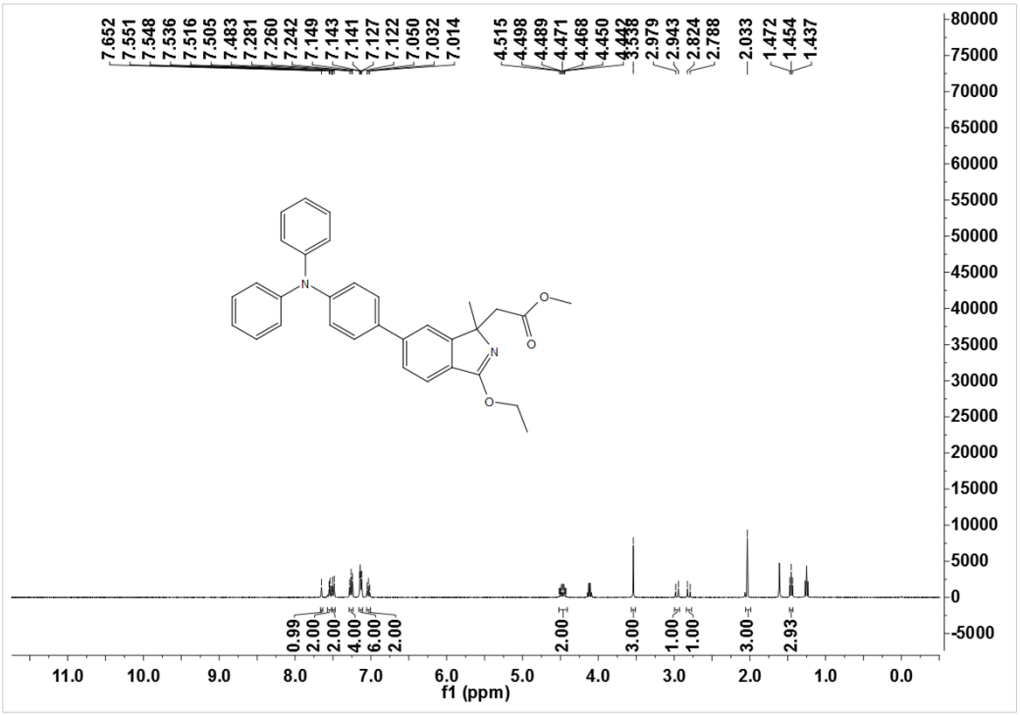


^{13}C NMR (100 MHz, $CDCl_3$)

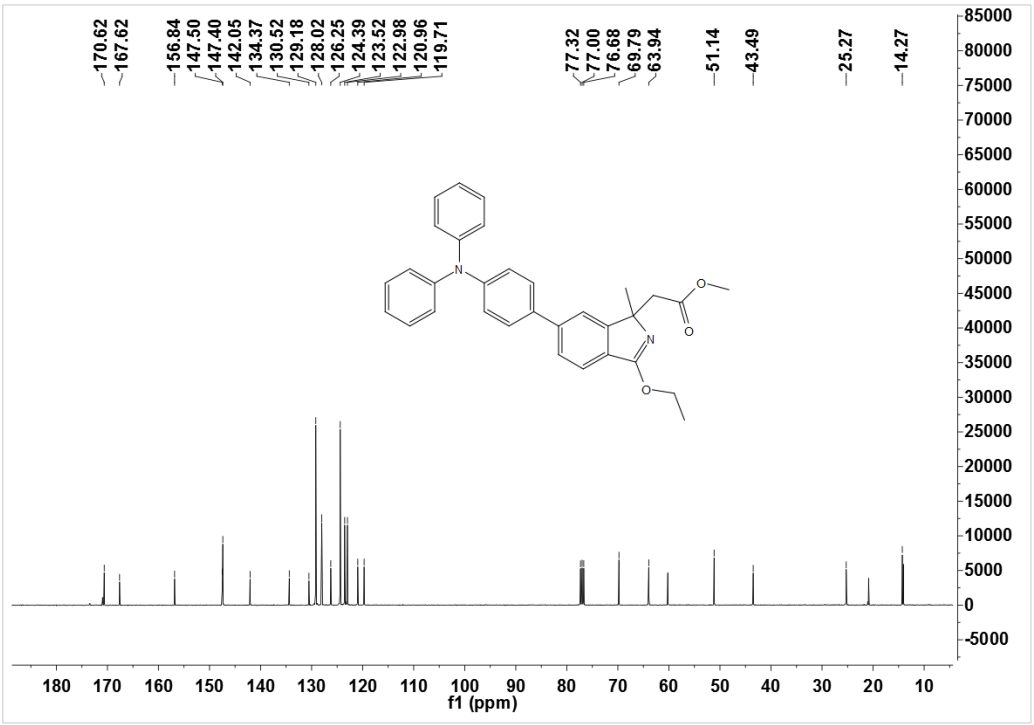


Methyl 2-(6-(4-(diphenylamino) phenyl)-3-ethoxy-1-methyl-1*H*-isoindol-1-yl) acetate (4z)

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

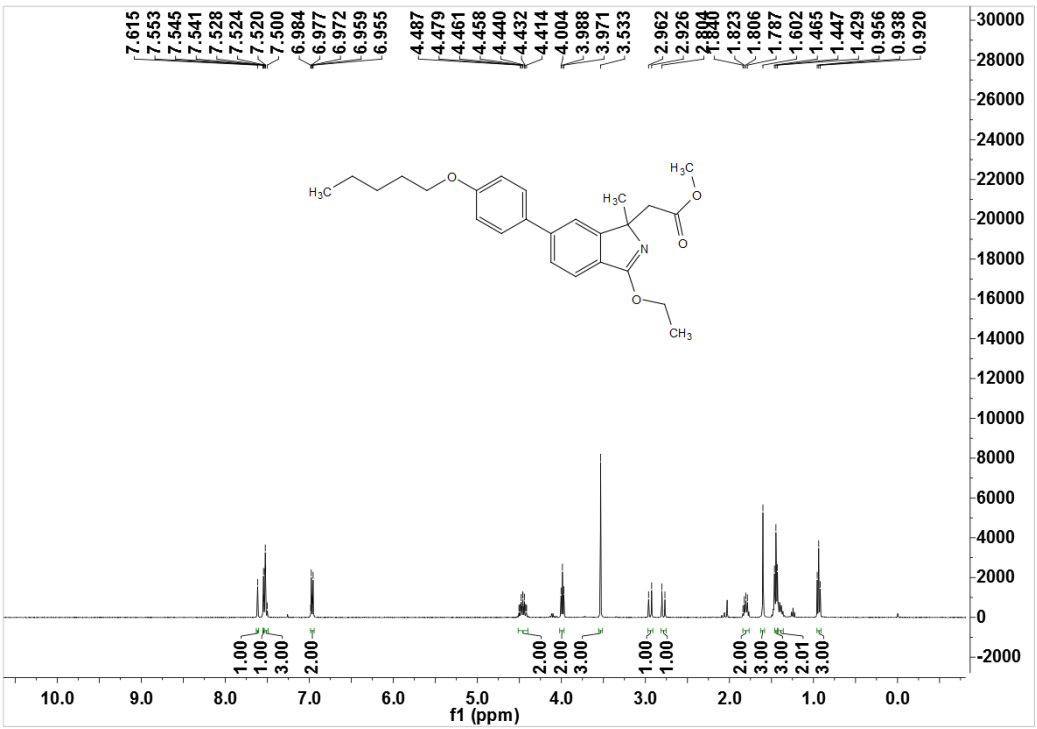


^{13}C NMR (100 MHz, $CDCl_3$)

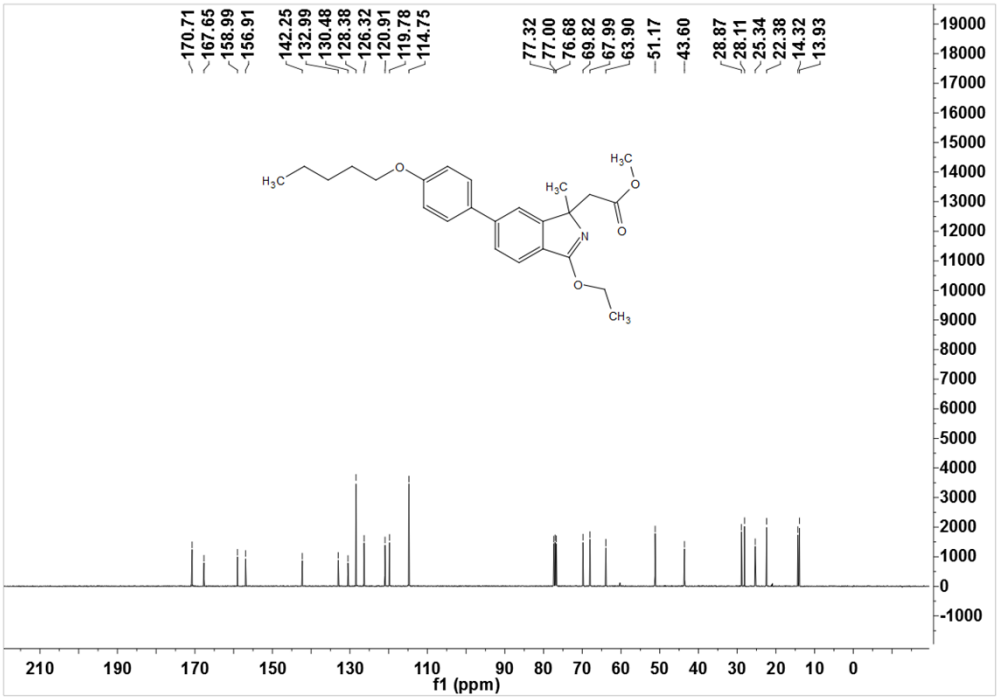


Methyl 2-(3-ethoxy-1-methyl-6-(4-(pentyloxy)phenyl)-1*H*-isoindol-1-yl)acetate (4za)

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

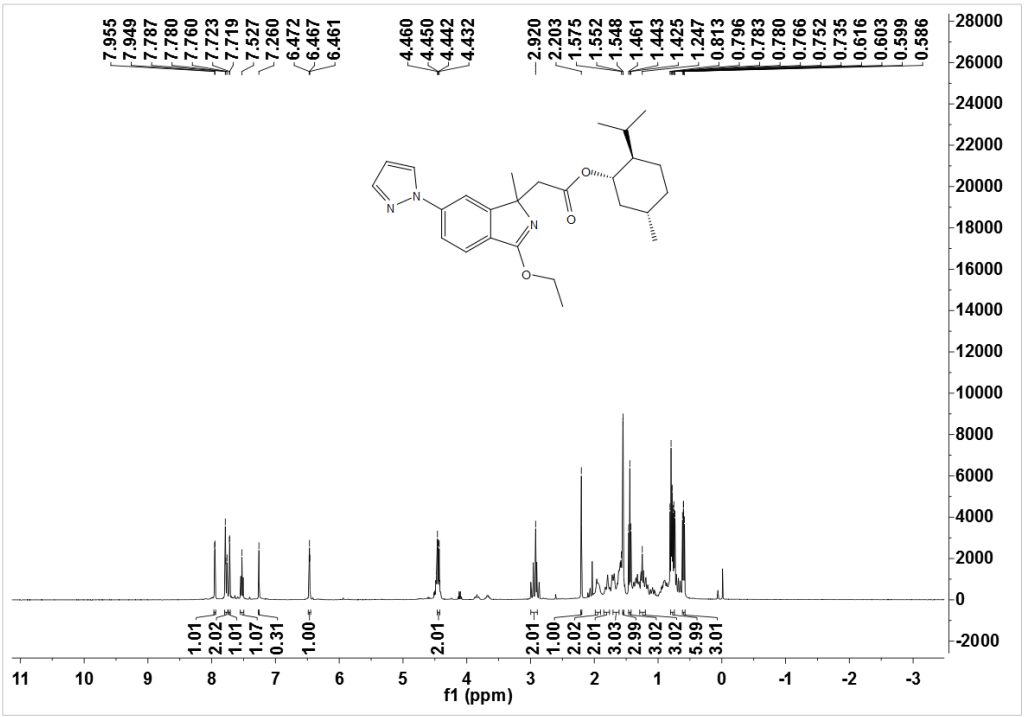


^{13}C NMR (100 MHz, $CDCl_3$)

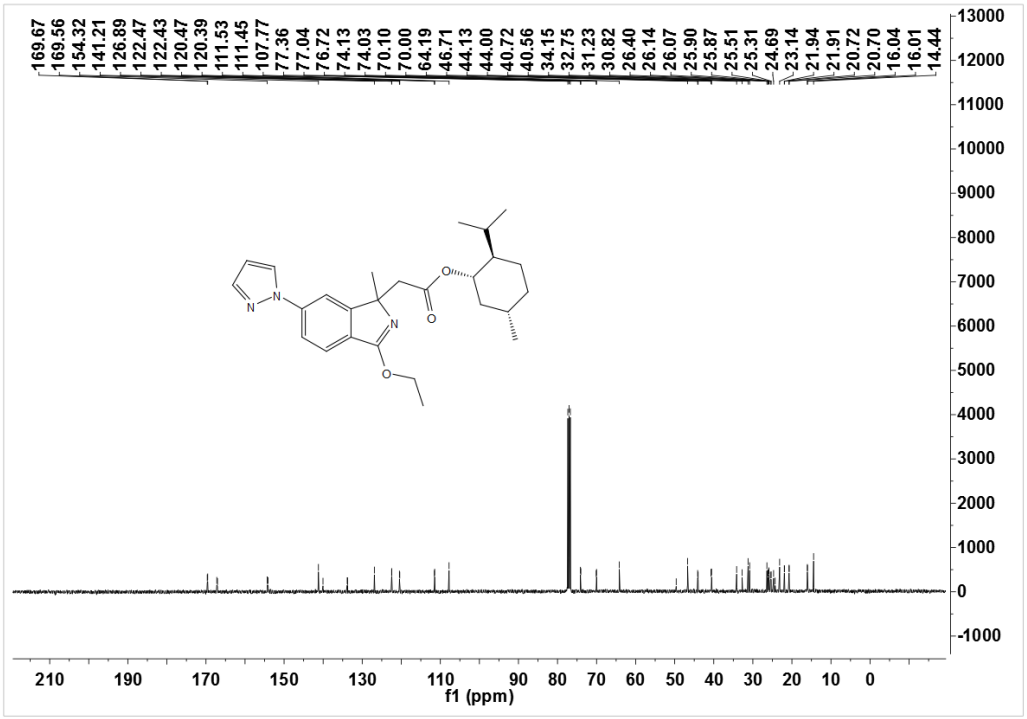


(1*S*, 2*R*, 5*S*)-2-Isopropyl-5-methylcyclohexyl 2-(3-ethoxy-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl)acetate (4zb)

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

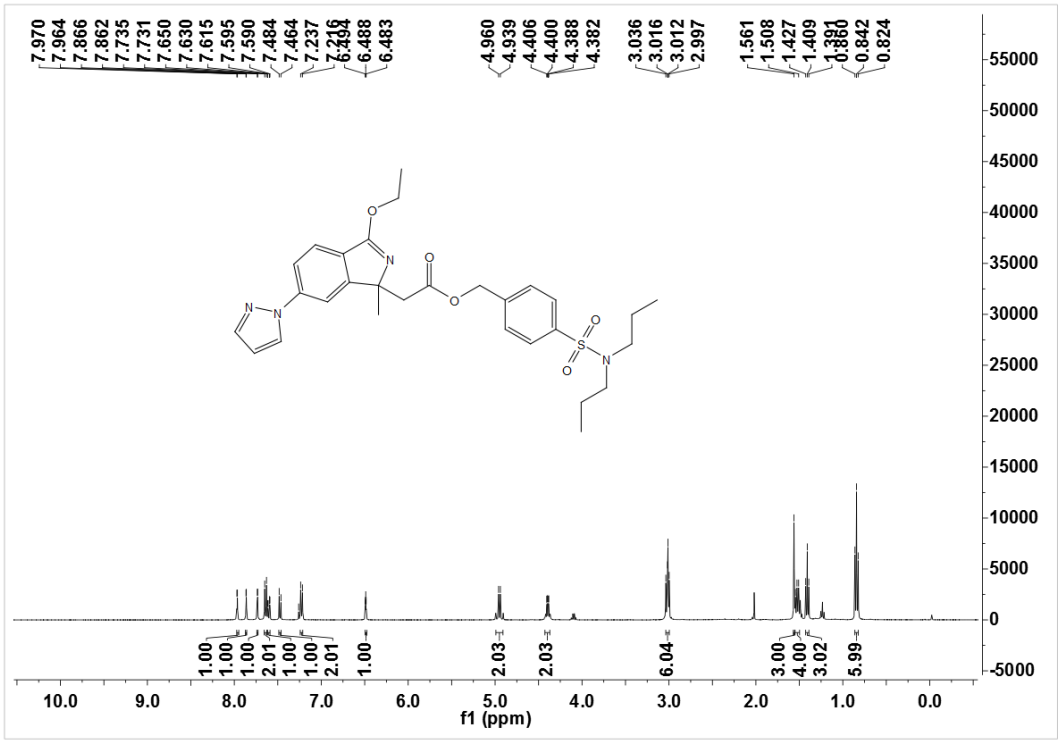


^{13}C NMR (100 MHz, $CDCl_3$)

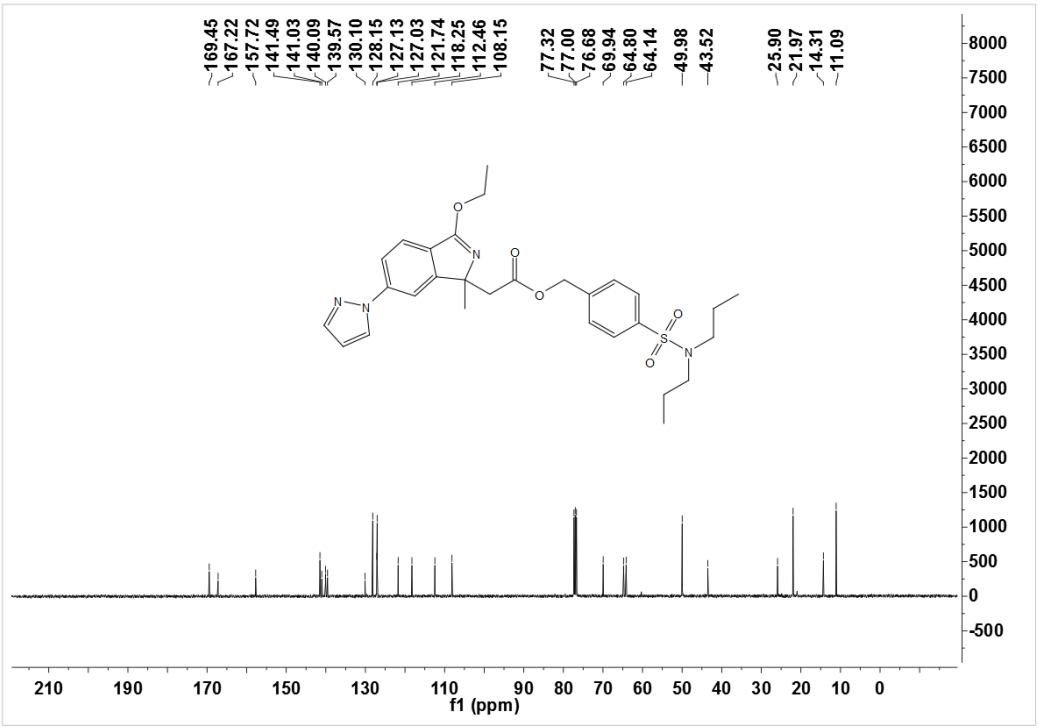


4-(*N*,*N*-Dipropylsulfamoyl)benzyl 2-(3-ethoxy-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl) acetate (4zc)

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

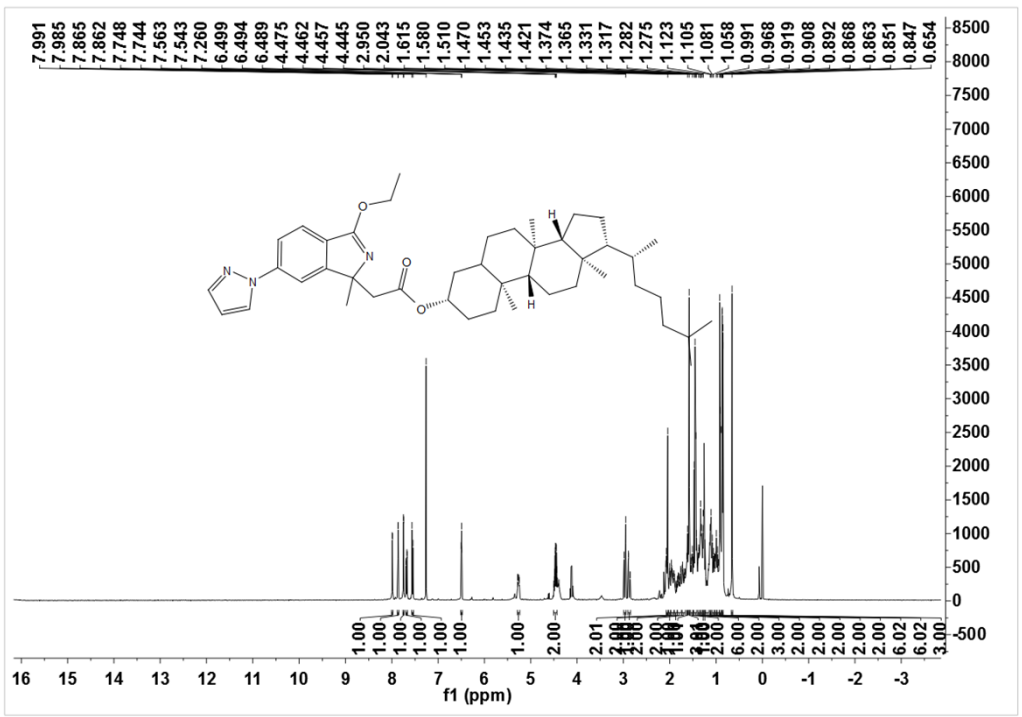


^{13}C NMR (100 MHz, $CDCl_3$)

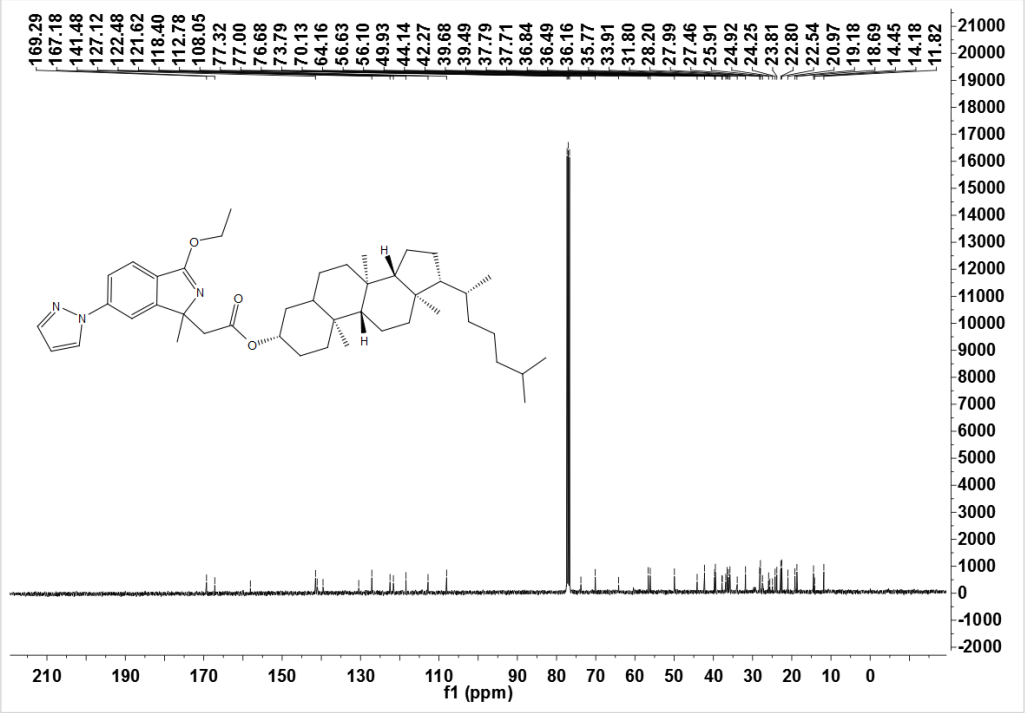


(3*S*, 8*R*, 9*R*, 10*S*, 13*R*, 14*R*, 17*R*)-8, 10, 13-Trimethyl-17-((*R*)-6-methylheptan- 2-yl)hexadecahydro-1*H*-cyclopenta[a]phenanthren-3-yl 2-(3-ethoxy-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl) acetate (4zd)

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

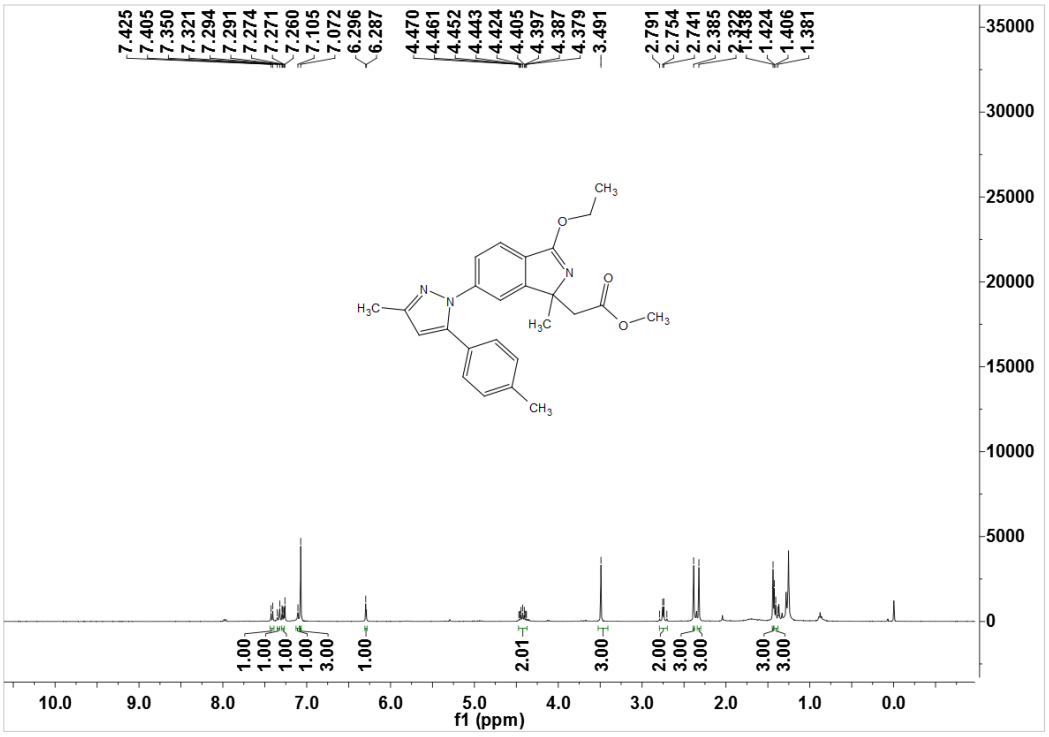


^{13}C NMR (100 MHz, $CDCl_3$)

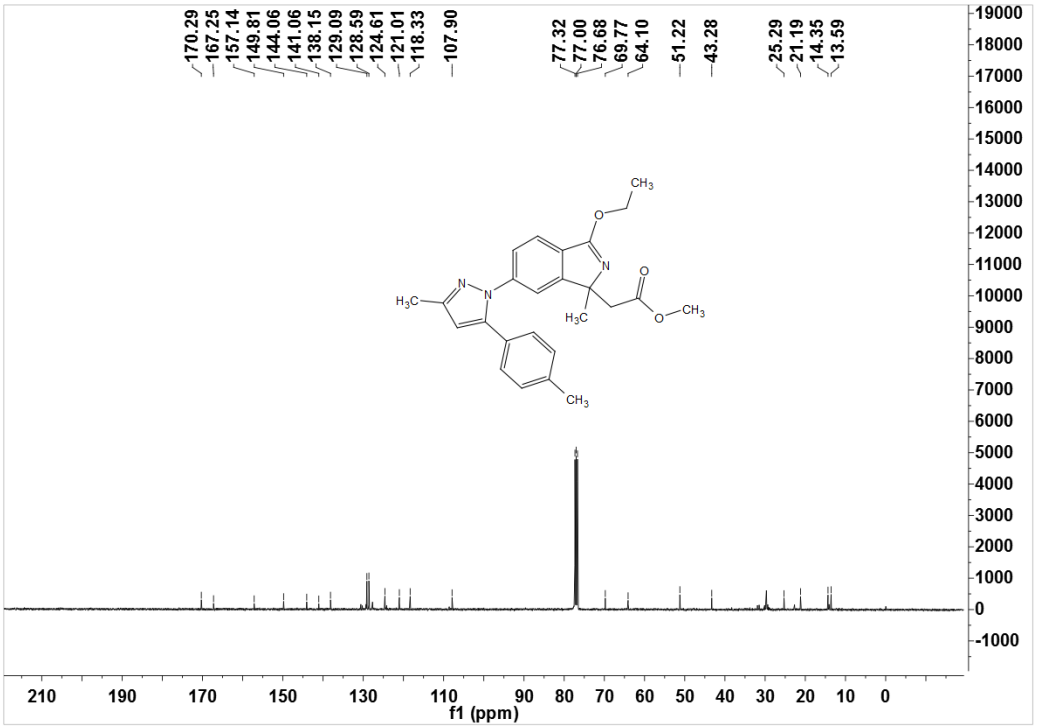


Methyl 2-(3-ethoxy-1-methyl-6-(3-methyl-5-(*p*-tolyl)-1*H*-pyrazol-1-yl)-1*H*-isoindol-1-yl)acetate (4ze)

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

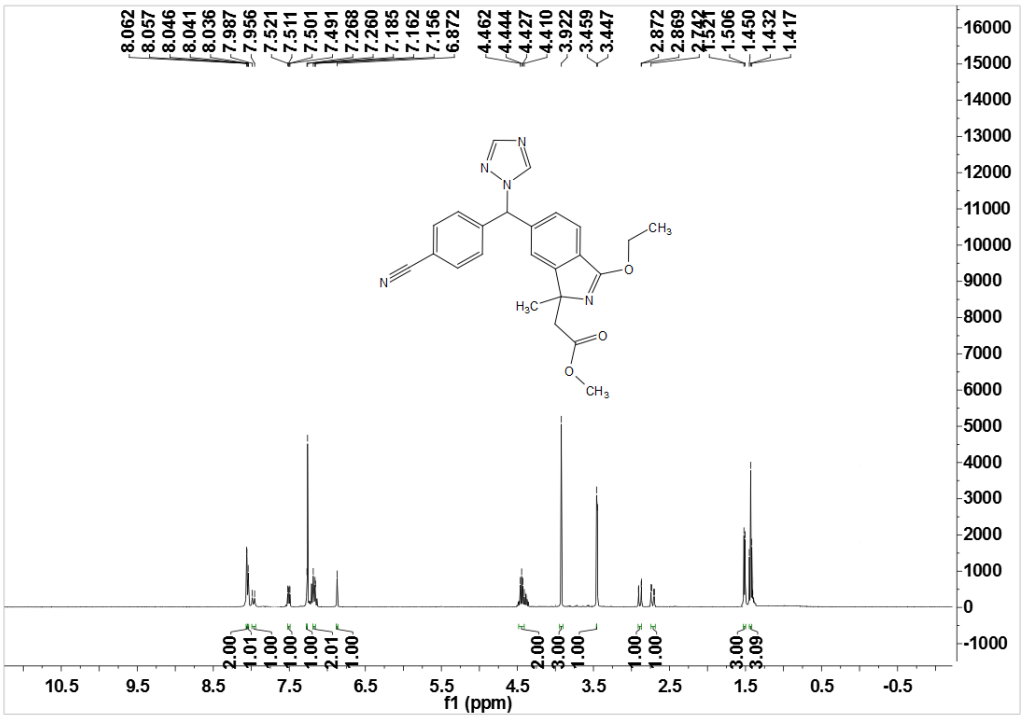


^{13}C NMR (100 MHz, $CDCl_3$)

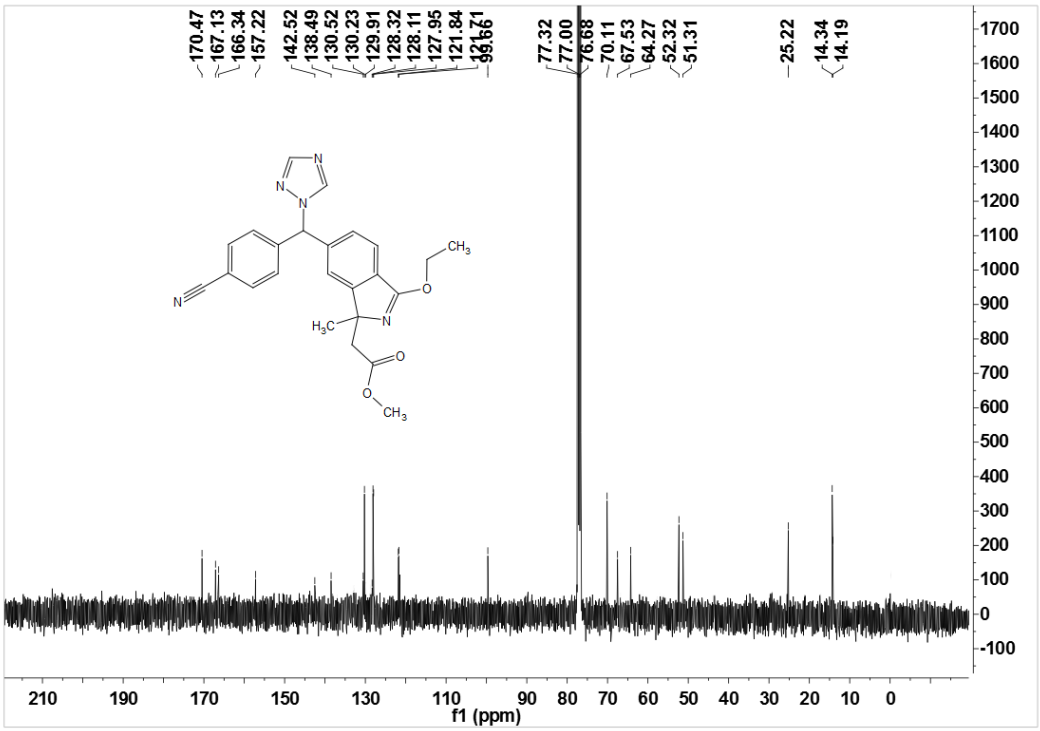


Methyl2-(6-((4-cyanophenyl)(1*H*-1,2,4-triazol-1-yl)methyl)-3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4zf)

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

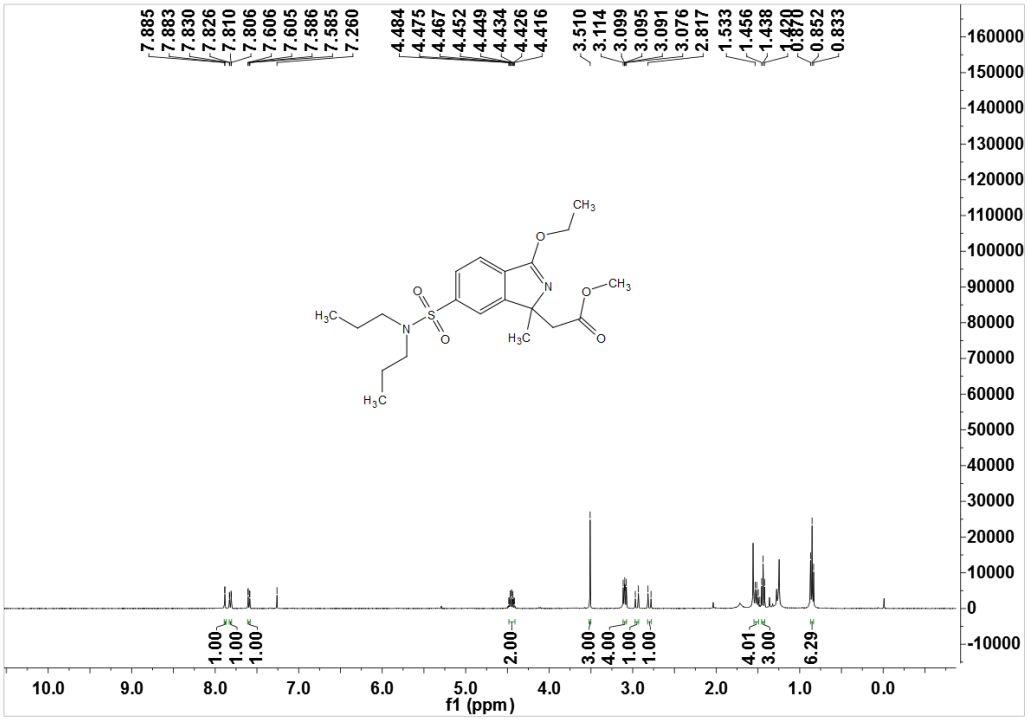


^{13}C NMR (100 MHz, $CDCl_3$)

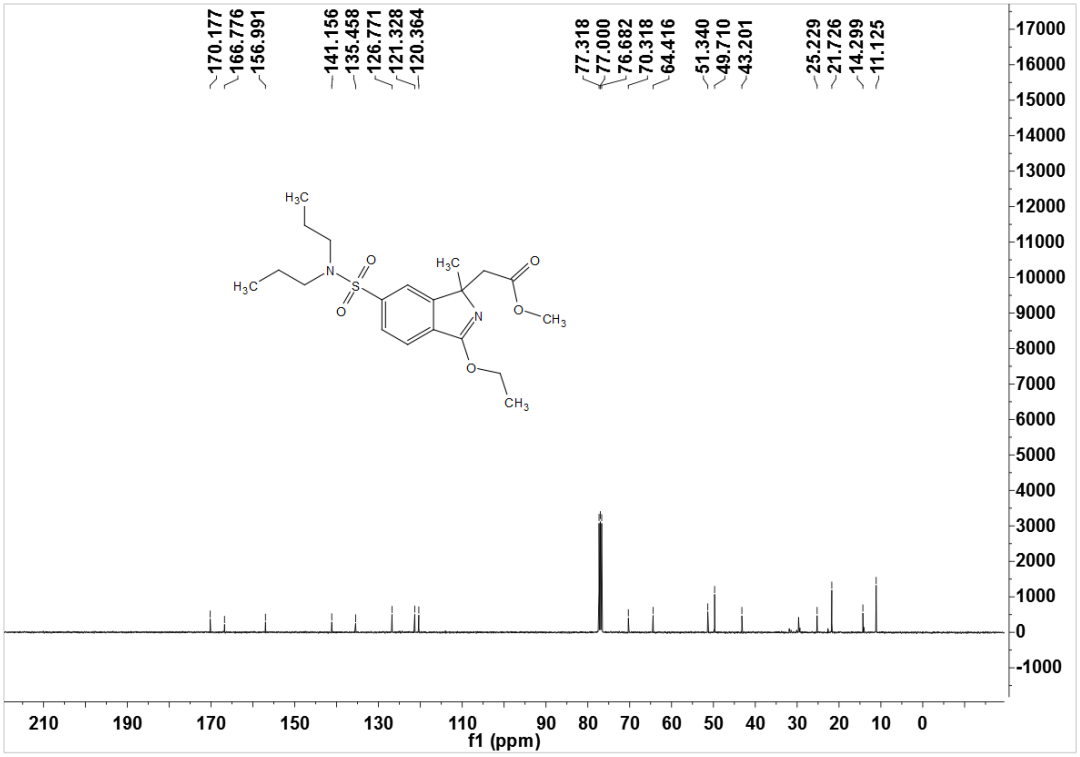


Methyl 2-(6-(*N*,*N*-dipropylsulfamoyl)-3-ethoxy-1-methyl-1*H*-isoindol-1-yl)acetate (4zg)

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

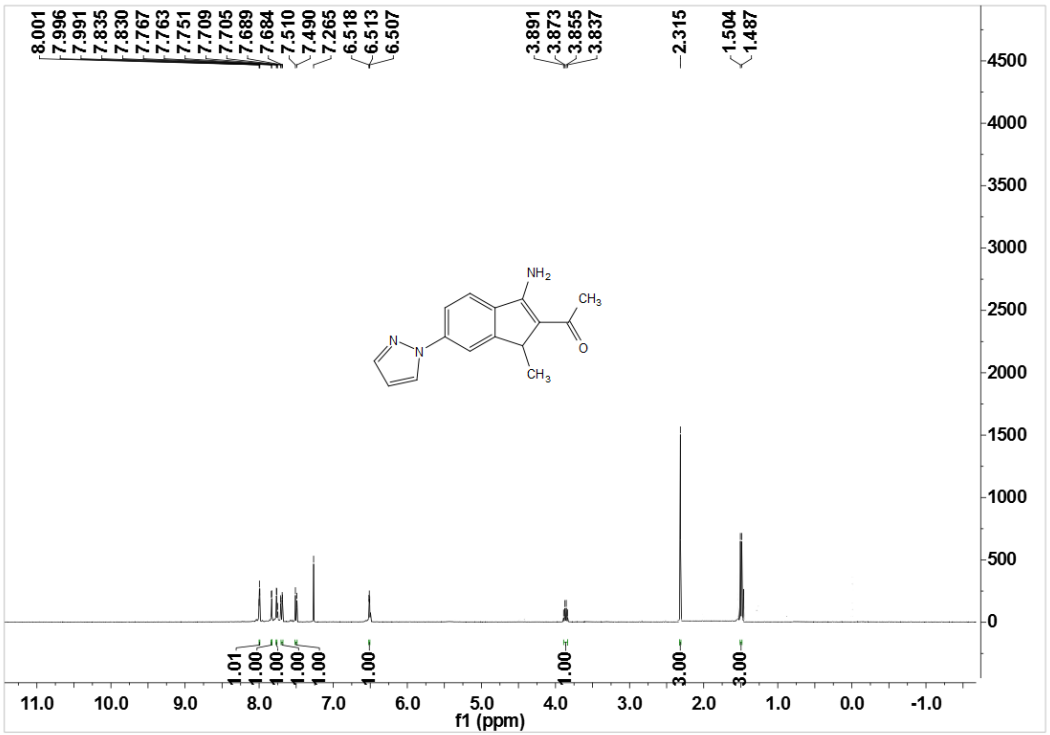


^{13}C NMR (100 MHz, $CDCl_3$)

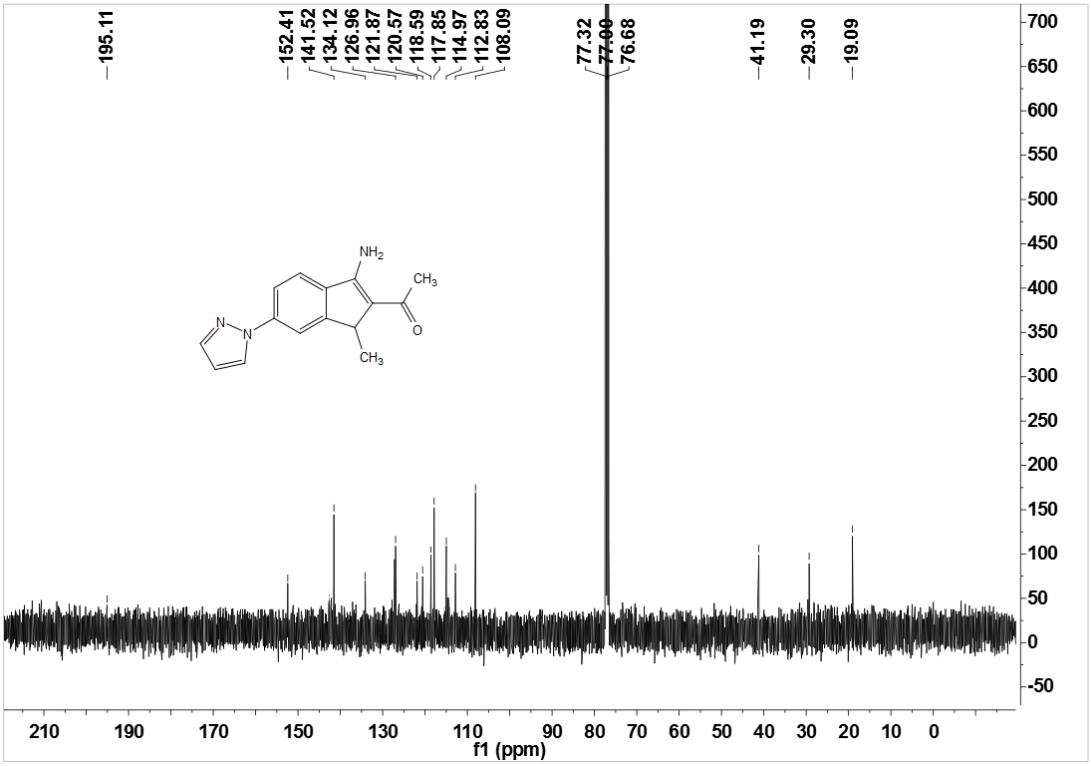


1-(3-Amino-1-methyl-6-(1*H*-pyrazol-1-yl)-1*H*-inden-2-yl)ethan-1-one (5a)

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

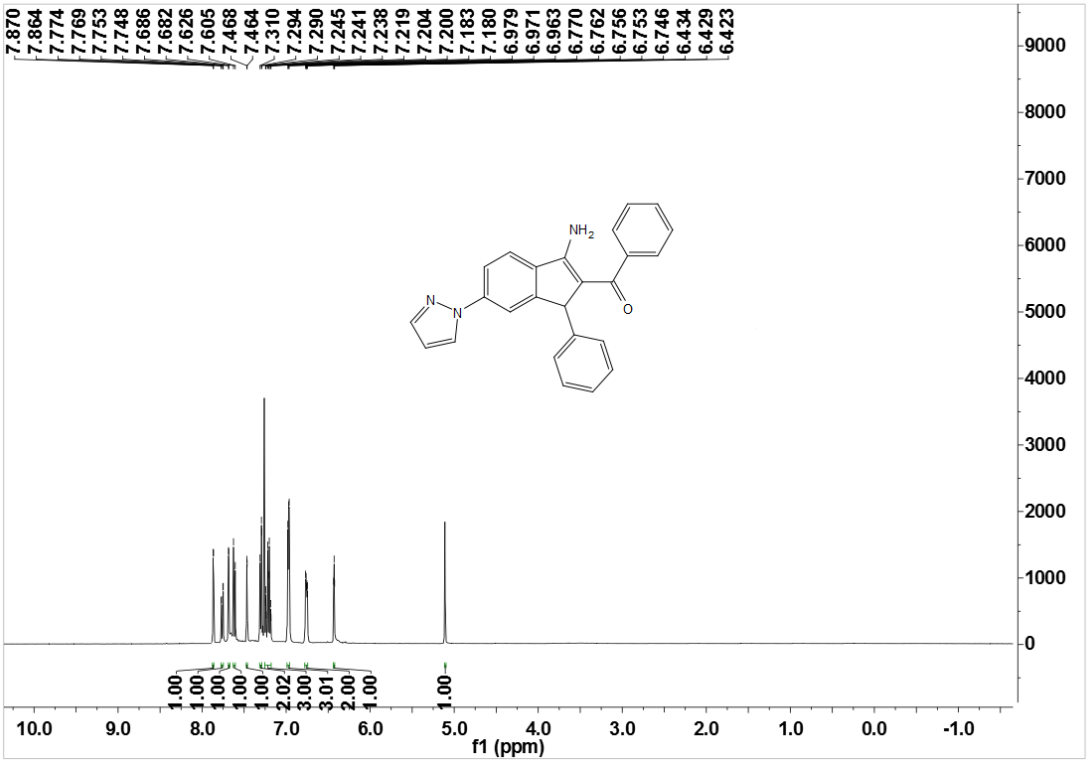


^{13}C NMR (100 MHz, $CDCl_3$)

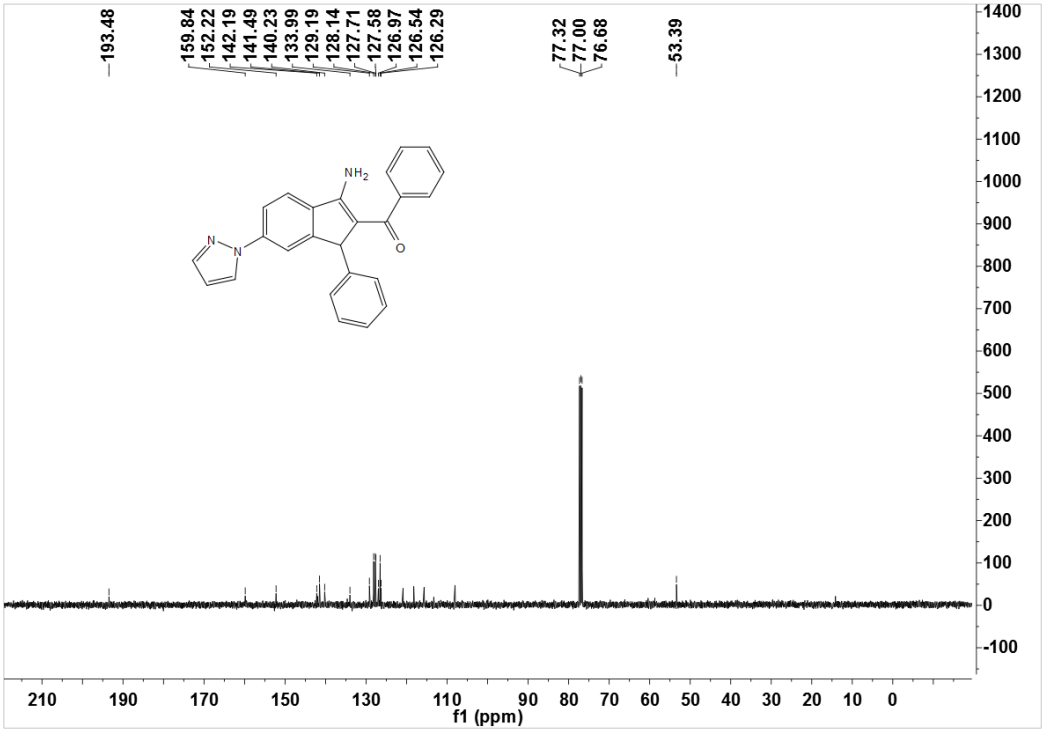


(3-Amino-1-phenyl-6-(1*H*-pyrazol-1-yl)-1*H*-inden-2-yl)(phenyl)methanone (5b)

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

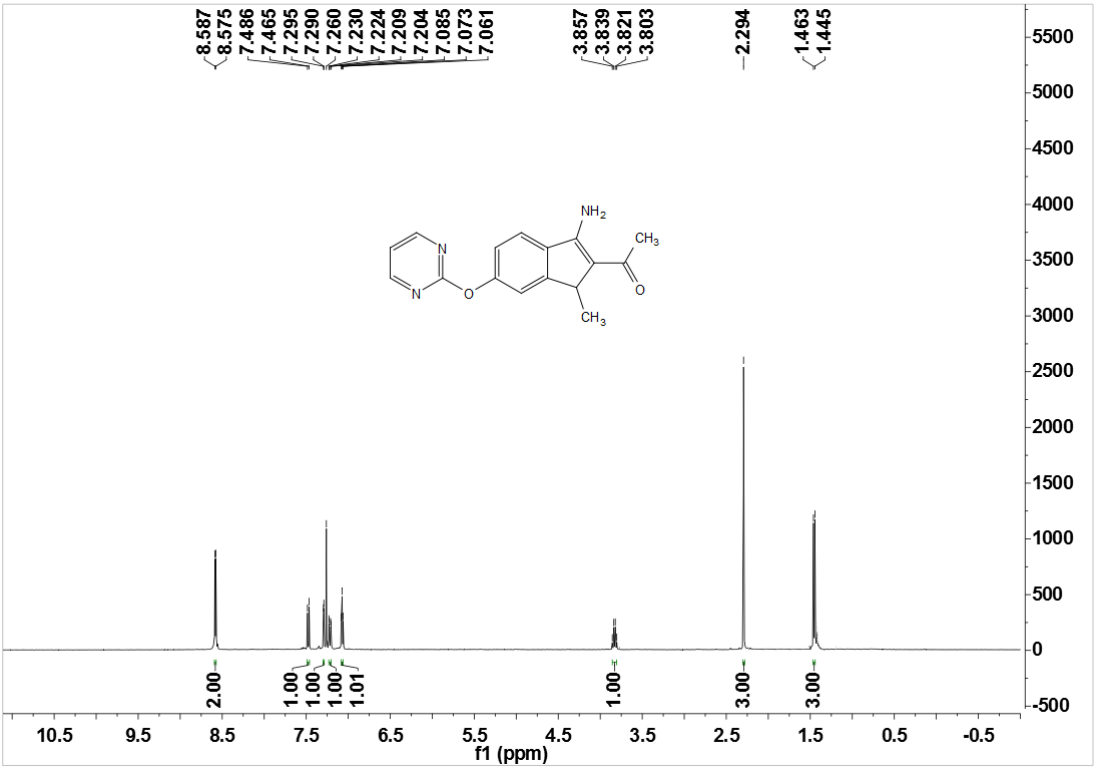


^{13}C NMR (100 MHz, $CDCl_3$)

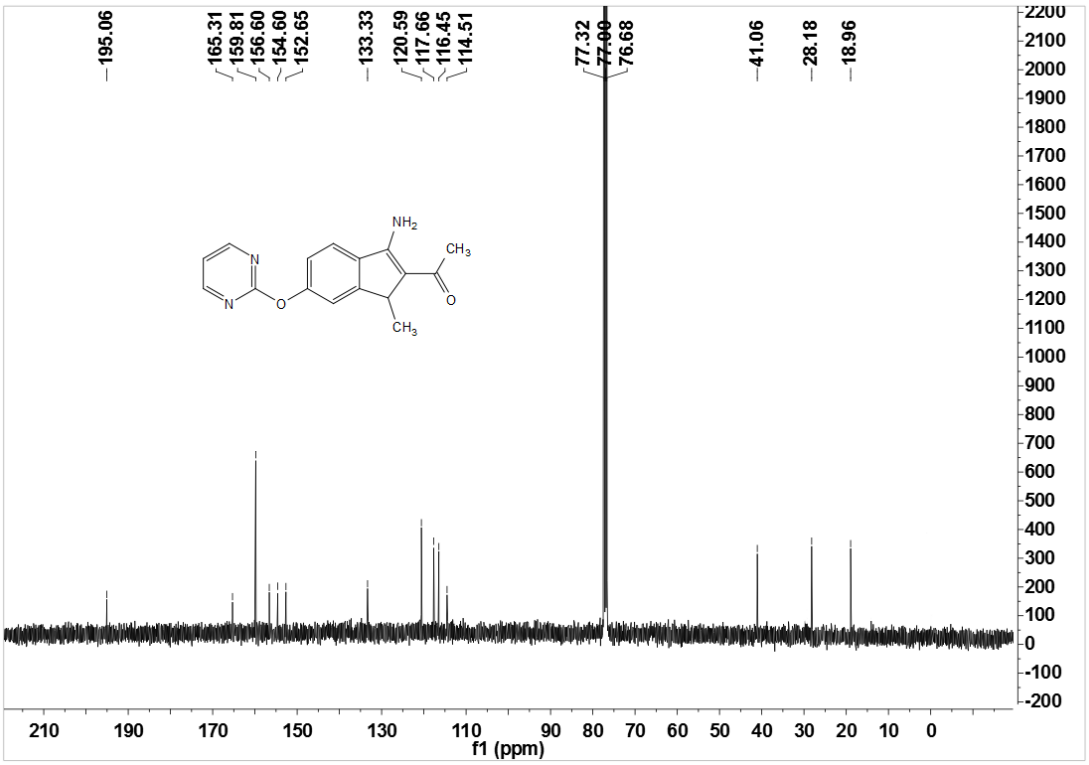


(1-Amino-1-methyl-6-(pyrimidin-2-yloxy)-1*H*-inden-2-yl)ethan-1-one (5c)

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

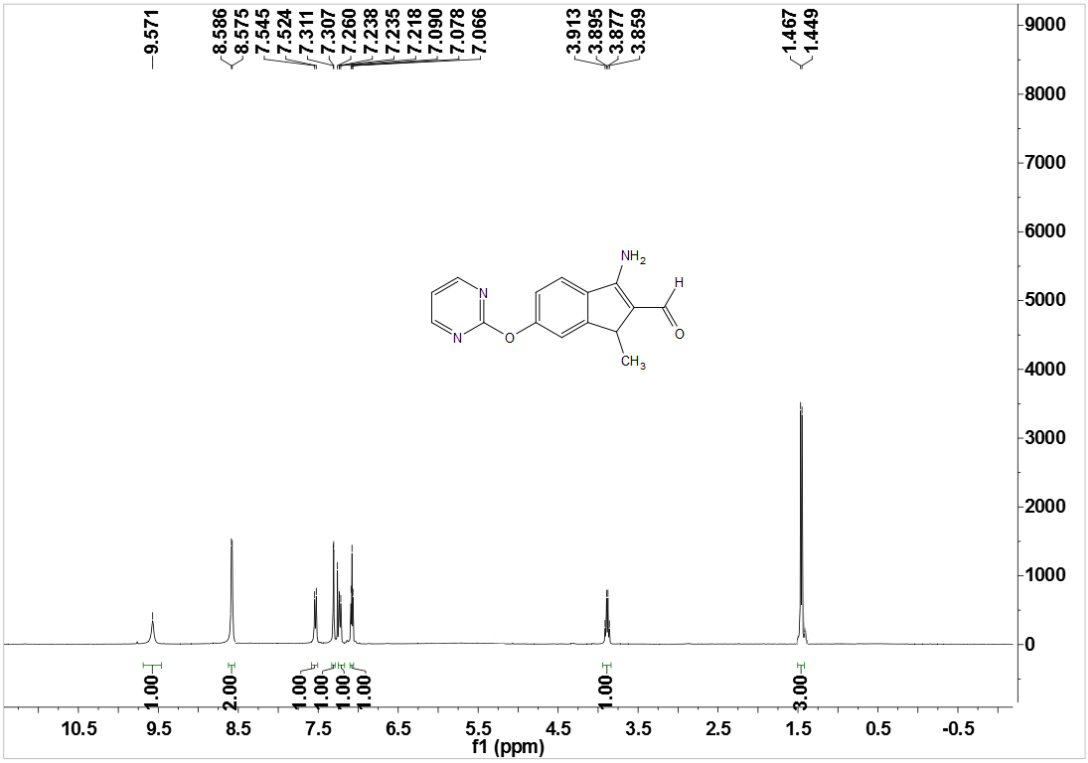


^{13}C NMR (100 MHz, $CDCl_3$)

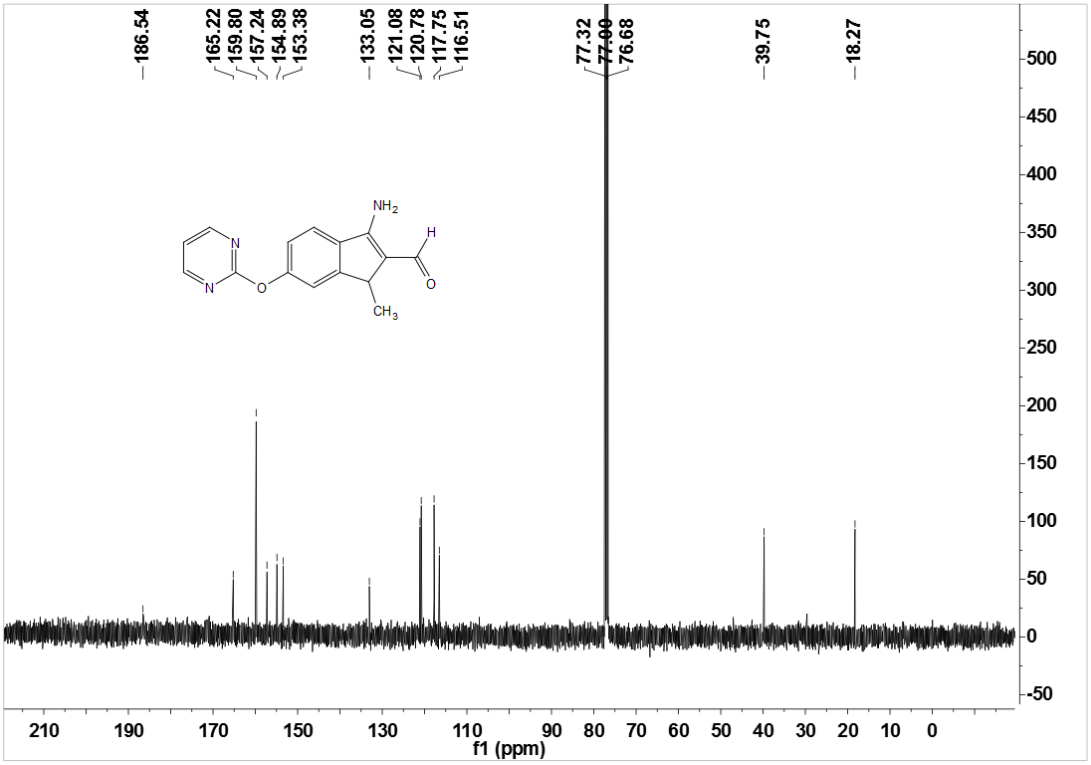


3-Amino-1-methyl-6-(pyrimidin-2-yloxy)-1*H*-indene-2-carbaldehyde (5d)

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

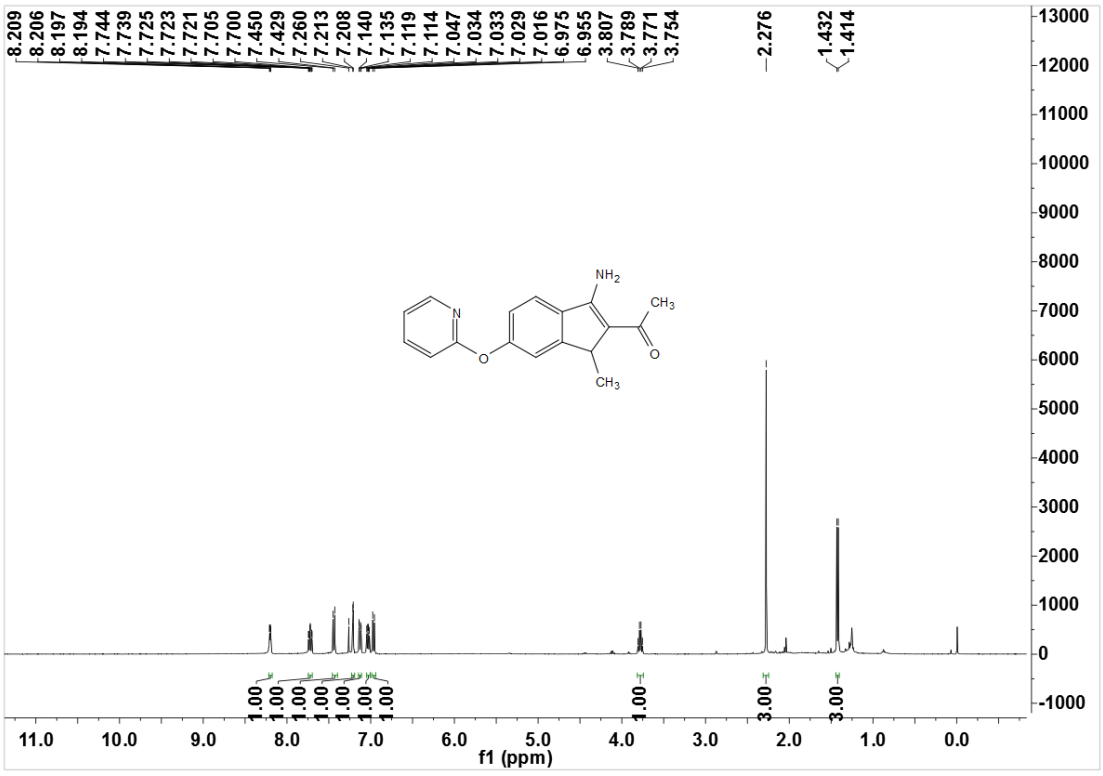


^{13}C NMR (100 MHz, $CDCl_3$)

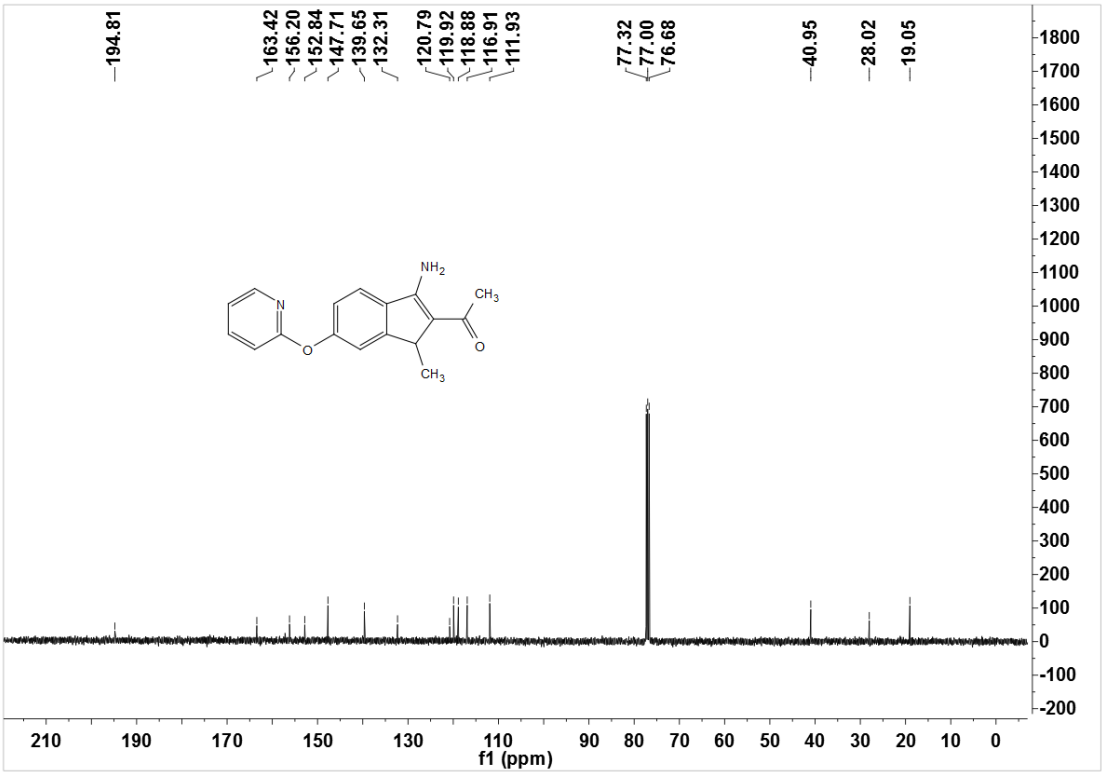


1-(3-Amino-1-methyl-6-(pyridin-2-yloxy)-1*H*-inden-2-yl)ethan-1-one (5e)

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

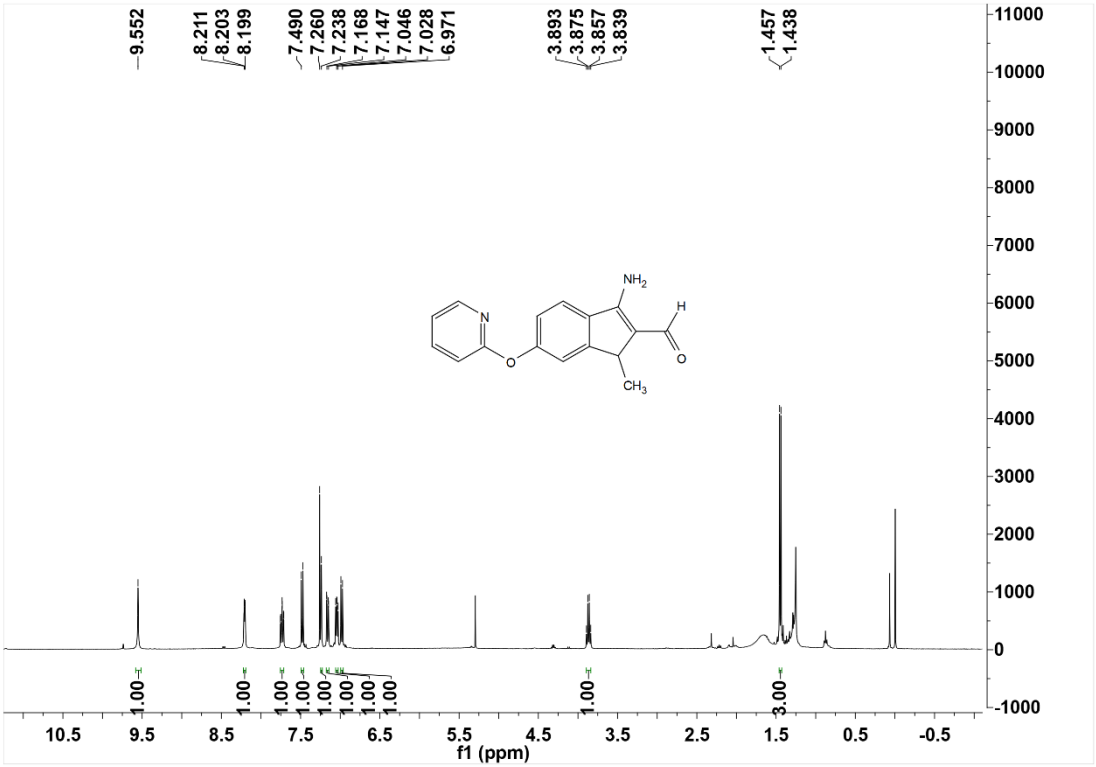


^{13}C NMR (100 MHz, $CDCl_3$)

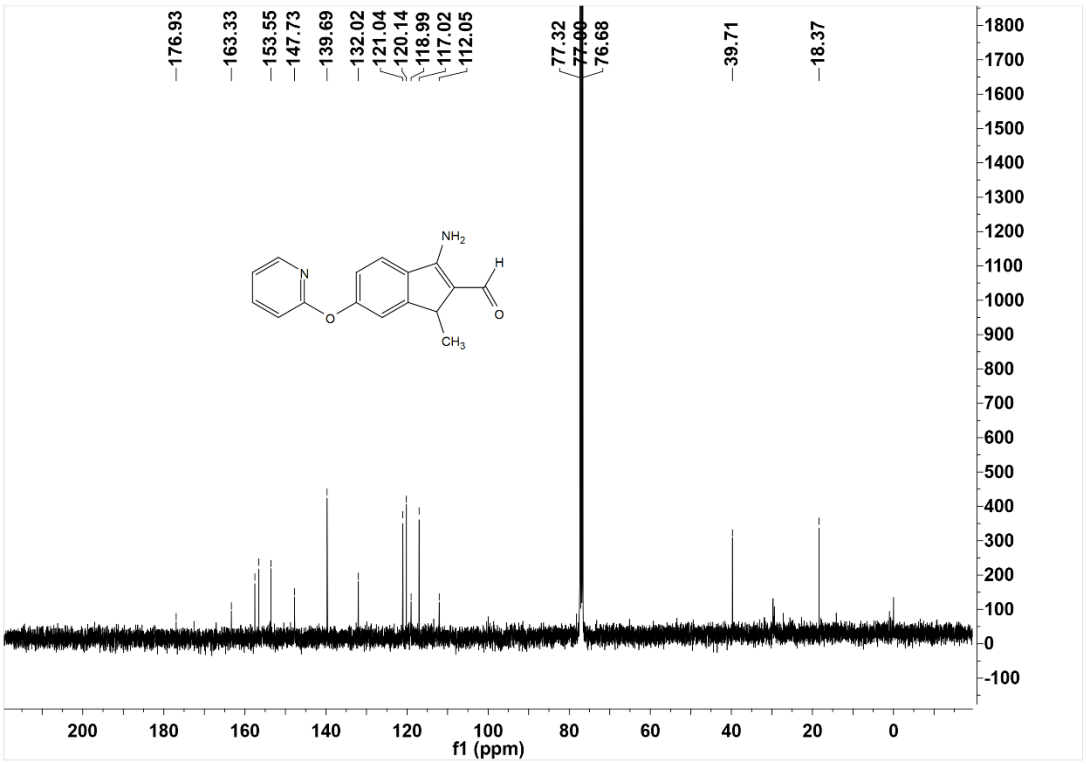


3-Amino-1-methyl-6-(pyridin-2-yloxy)-1*H*-indene-2-carbaldehyde (5f)

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

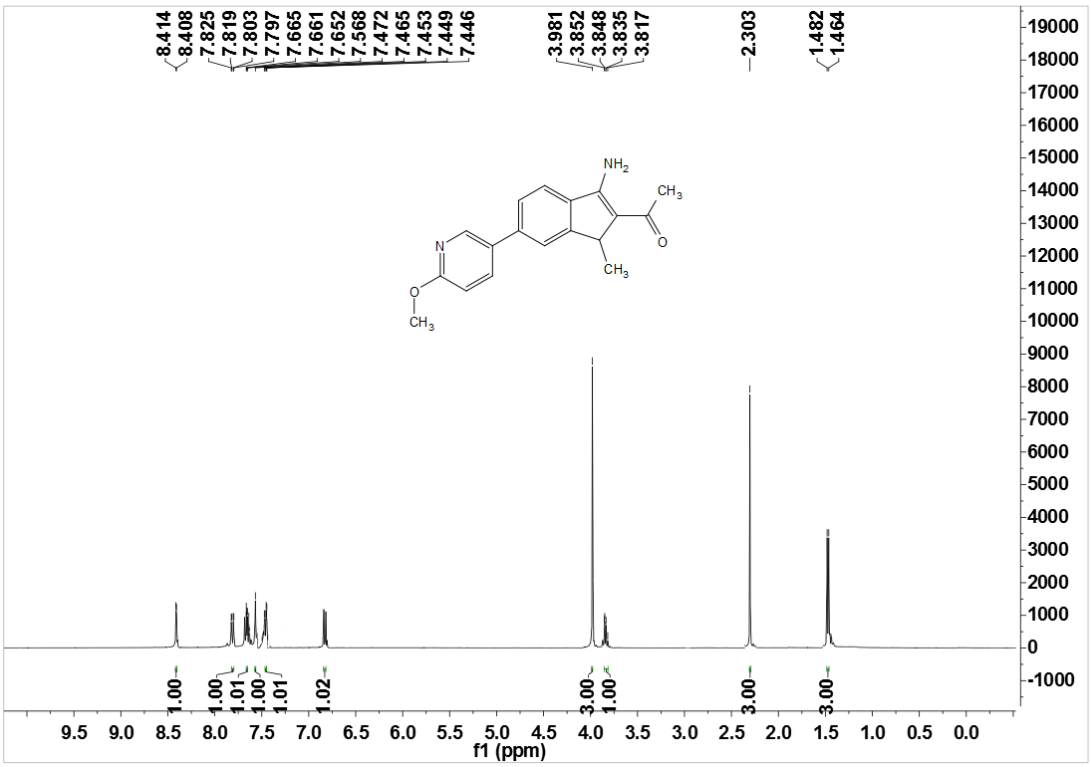


^{13}C NMR (100 MHz, $CDCl_3$)

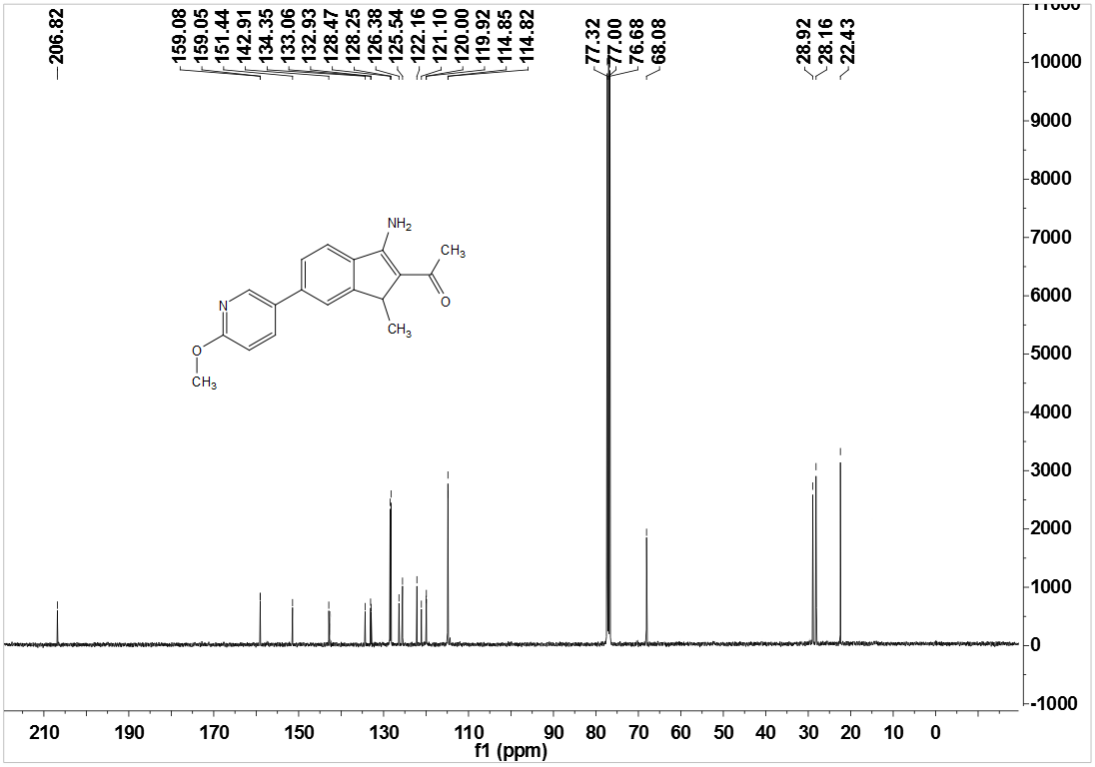


1-(3-Amino-6-(6-methoxypyridin-3-yl)-1-methyl-1*H*-inden-2-yl)ethan-1-one (5g)

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

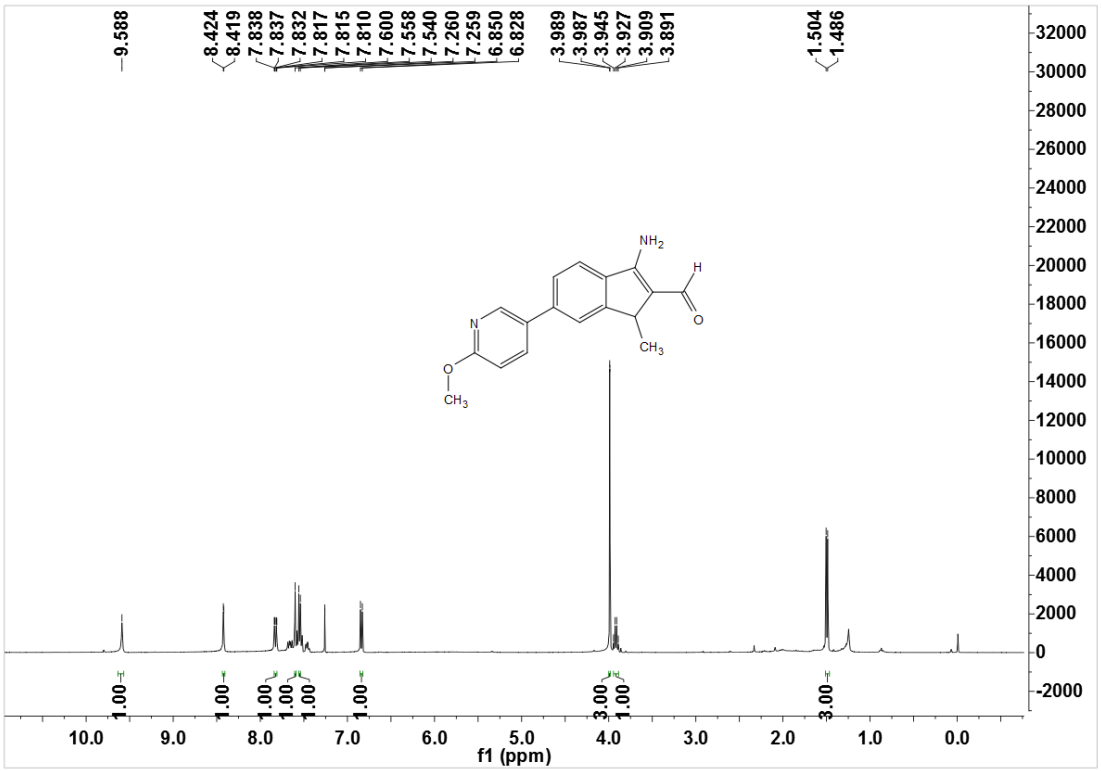


^{13}C NMR (100 MHz, $CDCl_3$)

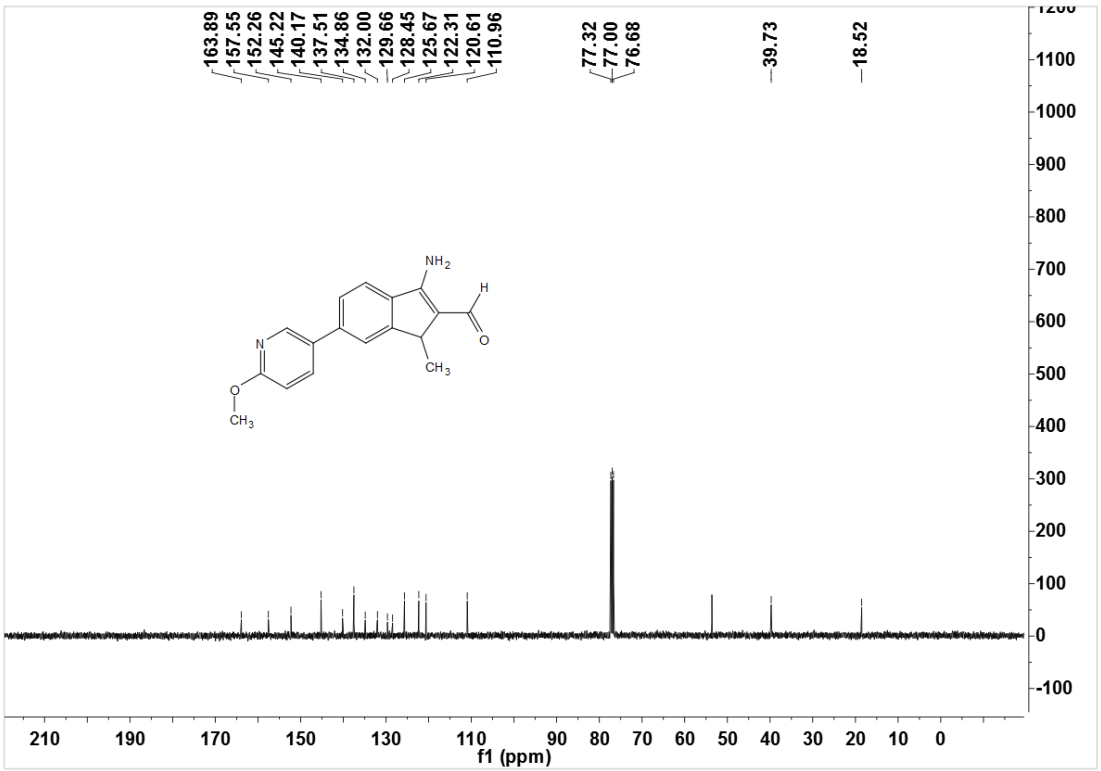


3-Amino-6-(6-methoxypyridin-3-yl)-1-methyl-1*H*-indene-2-carbaldehyde (5h)

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

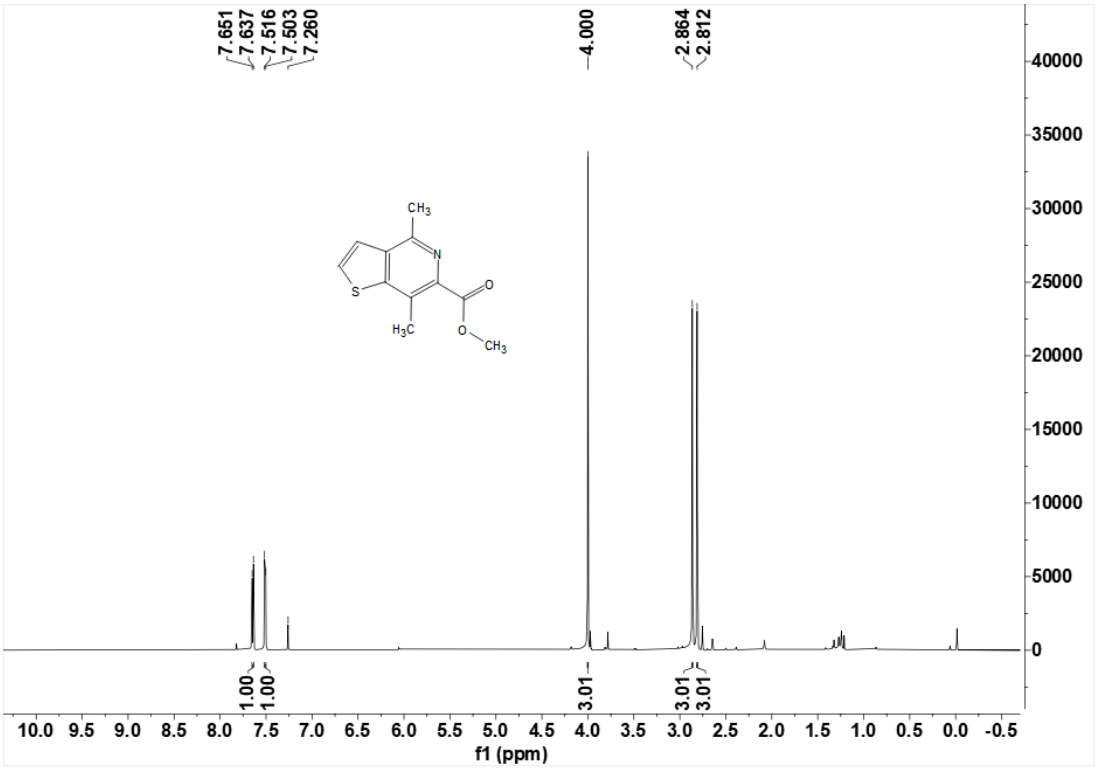


^{13}C NMR (100 MHz, $CDCl_3$)

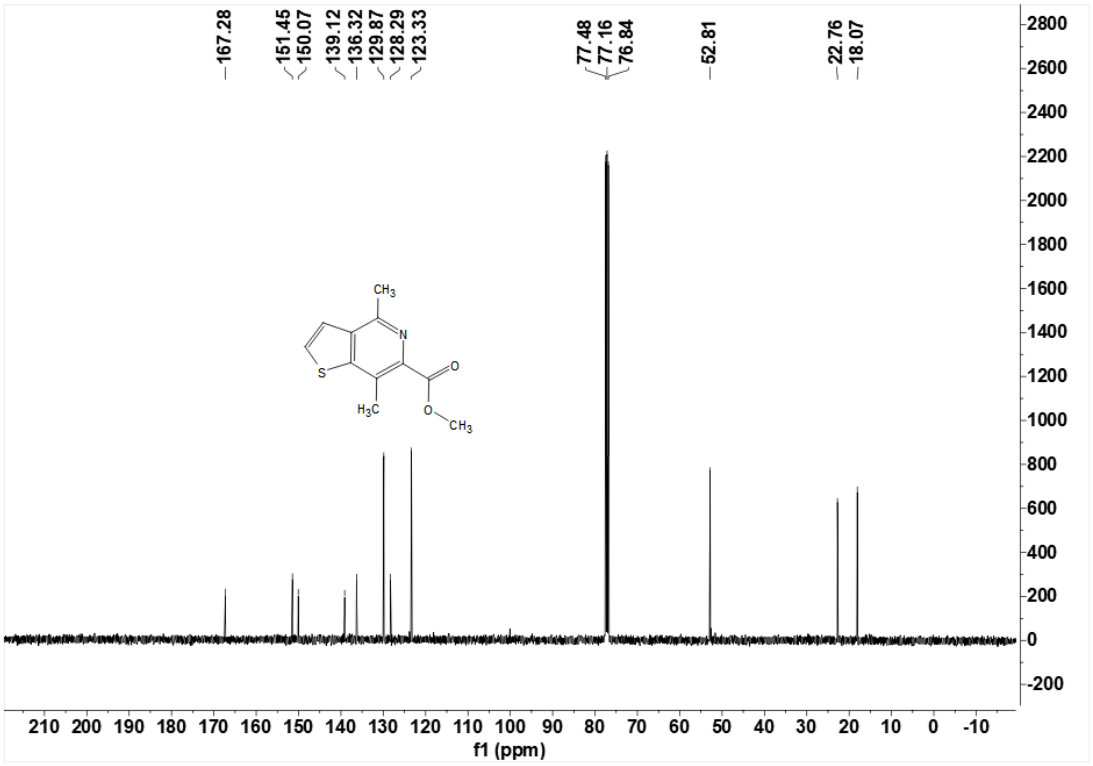


Methyl 4,7-dimethylthieno[3,2-*c*]pyridine-6-carboxylate (7a)

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

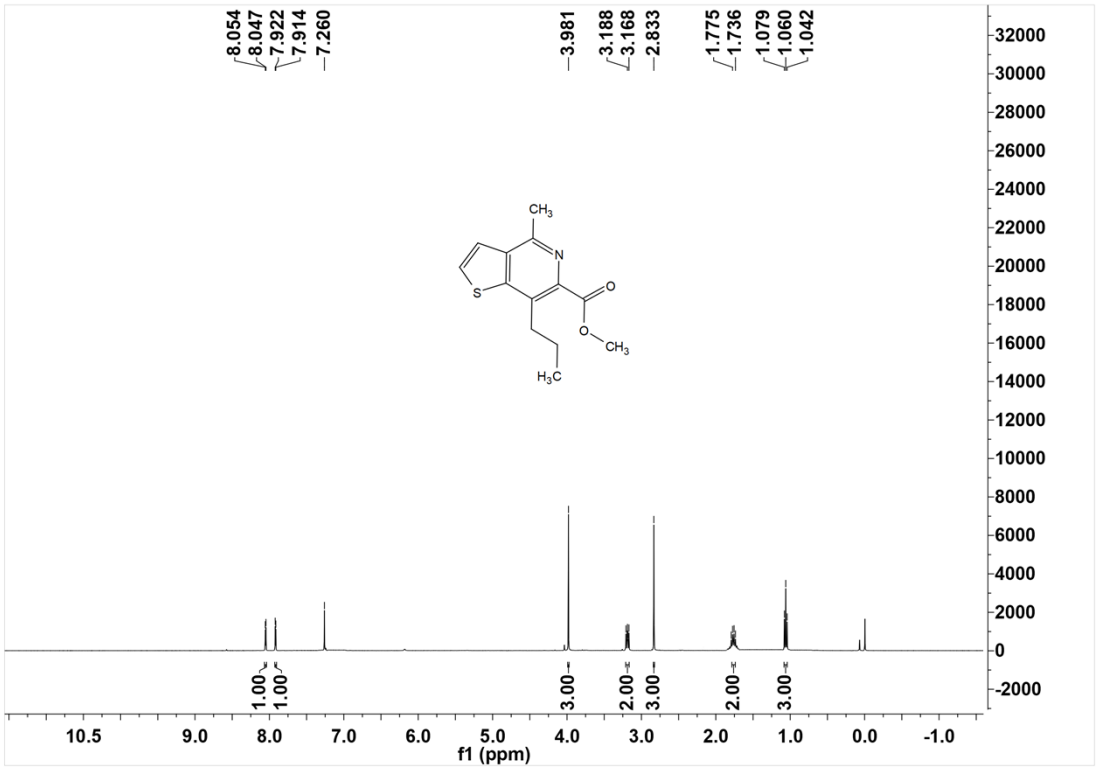


^{13}C NMR (100 MHz, $CDCl_3$)

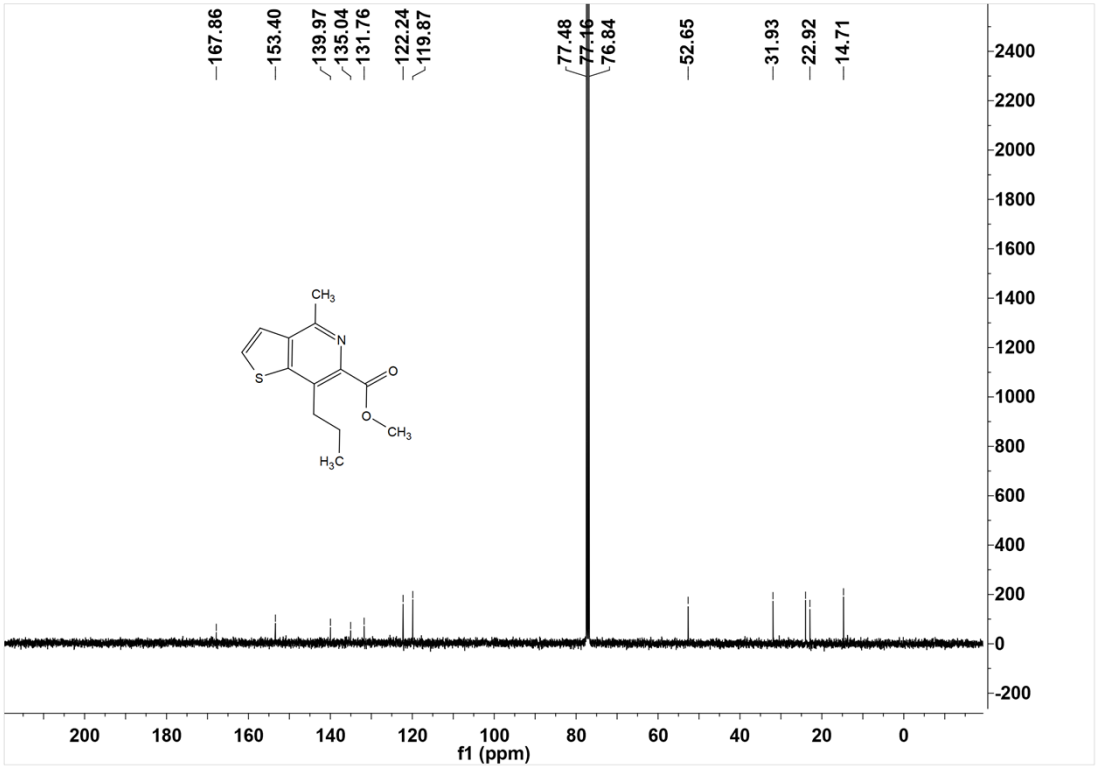


Methyl 4-methyl-7-propylthieno[3,2-c]pyridine-6-carboxylate (7b)

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

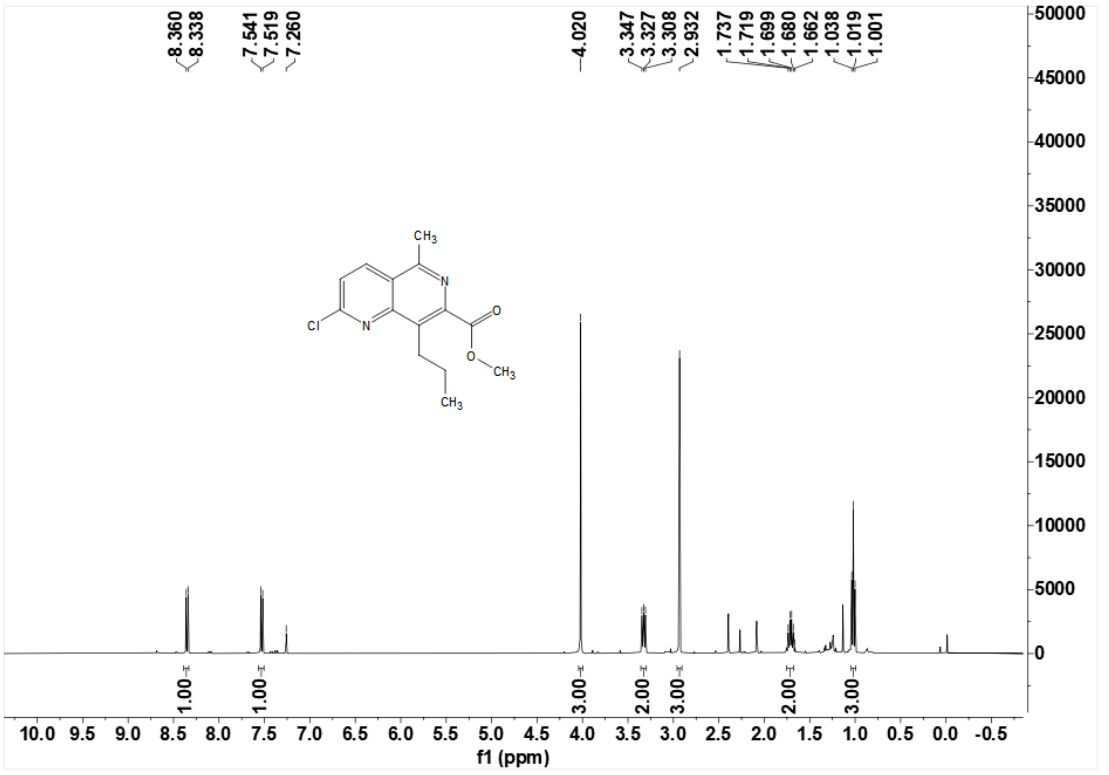


^{13}C NMR (100 MHz, $CDCl_3$)

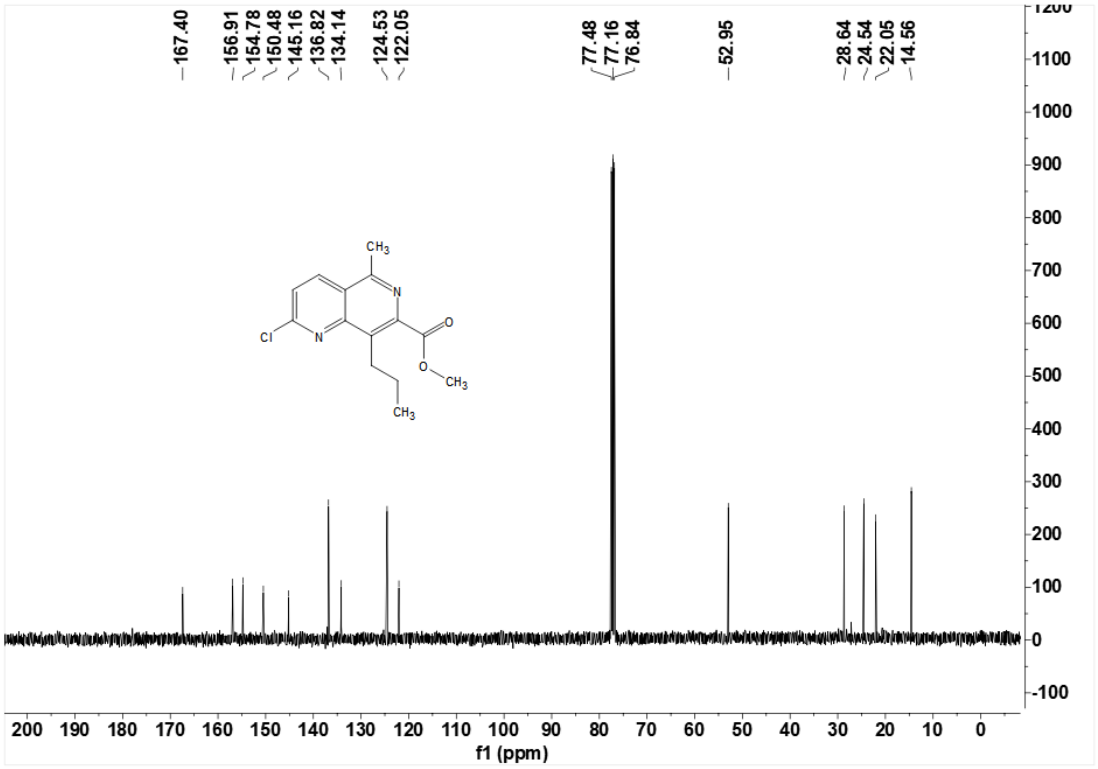


Methyl 2-chloro-5-methyl-8-propyl-1,6-naphthyridine-7-carboxylate (7c)

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

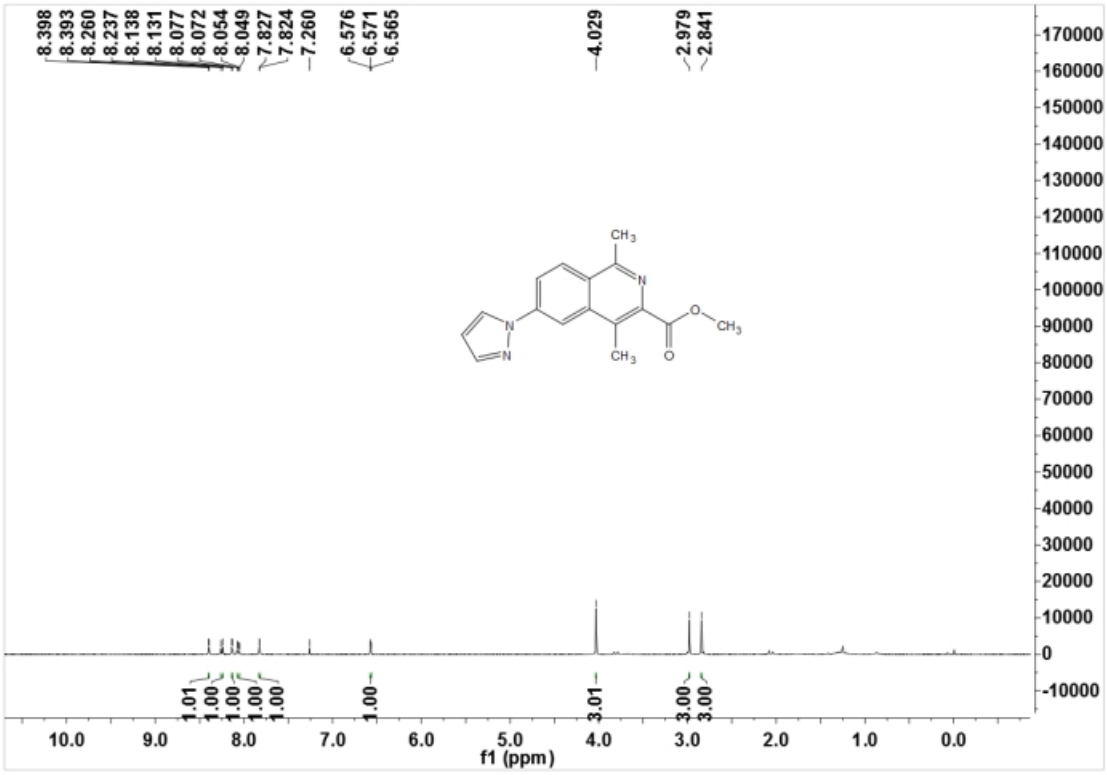


^{13}C NMR (100 MHz, $CDCl_3$)

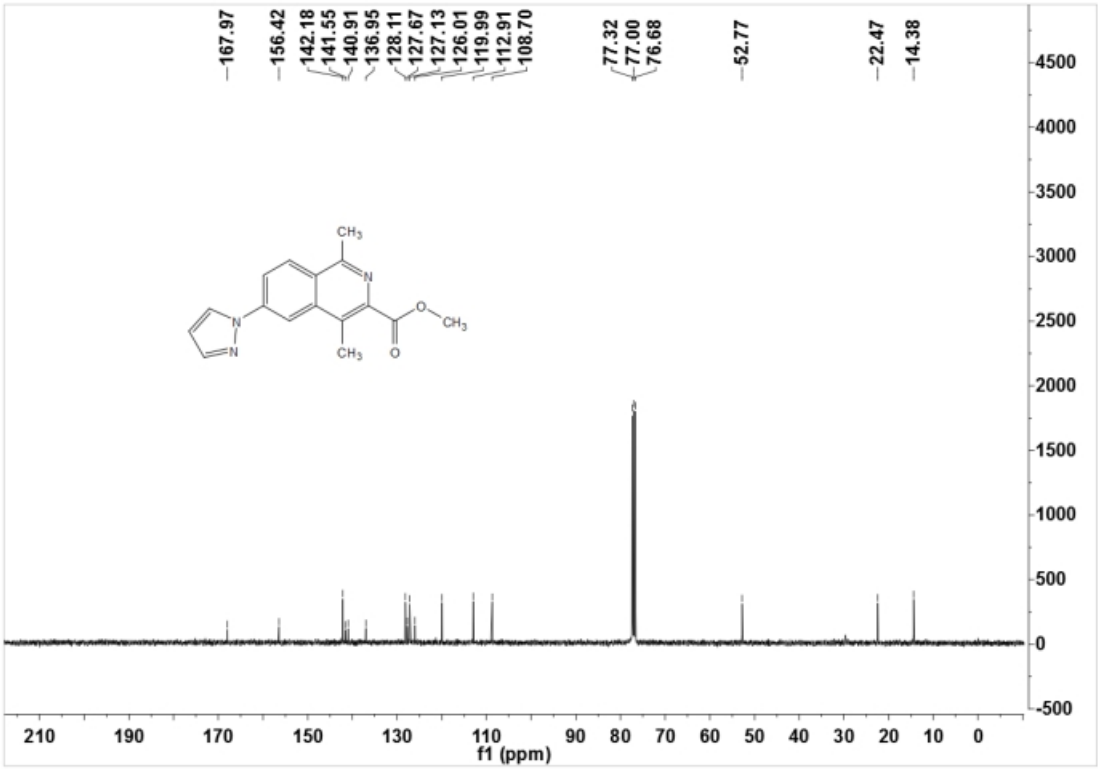


Methyl 1,4-dimethyl-6-(1*H*-pyrazol-1-yl)isoquinoline-3-carboxylate (7d)

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

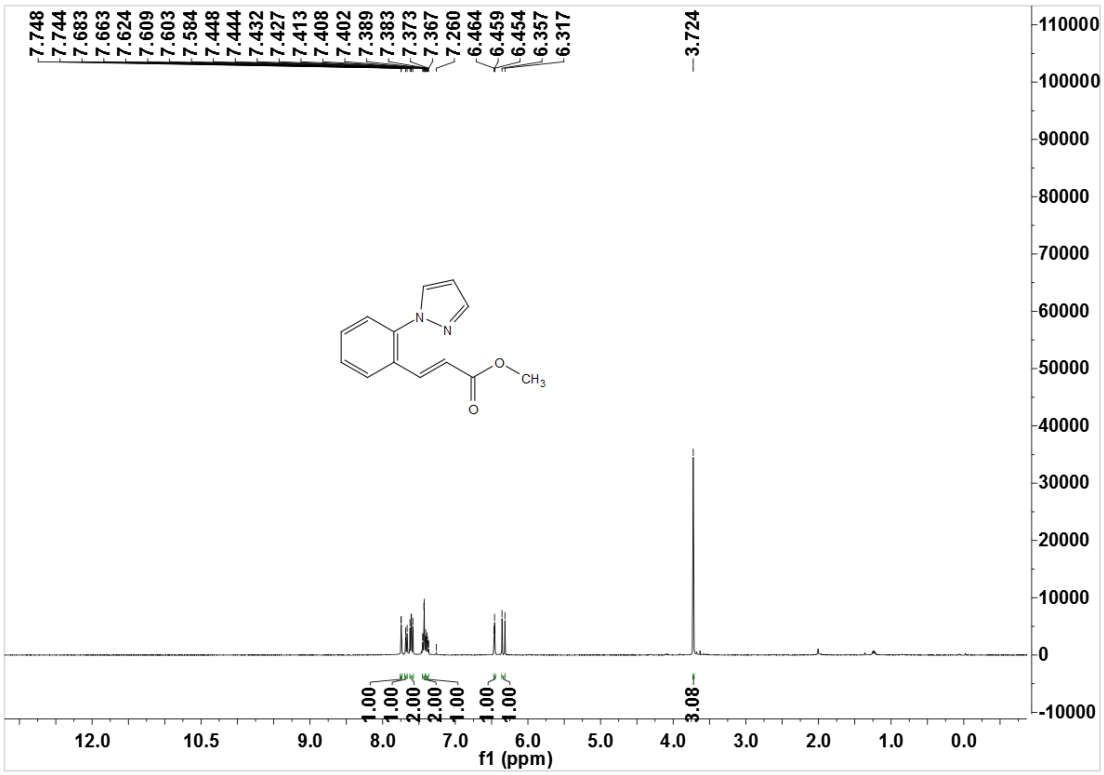


^{13}C NMR (100 MHz, $CDCl_3$)

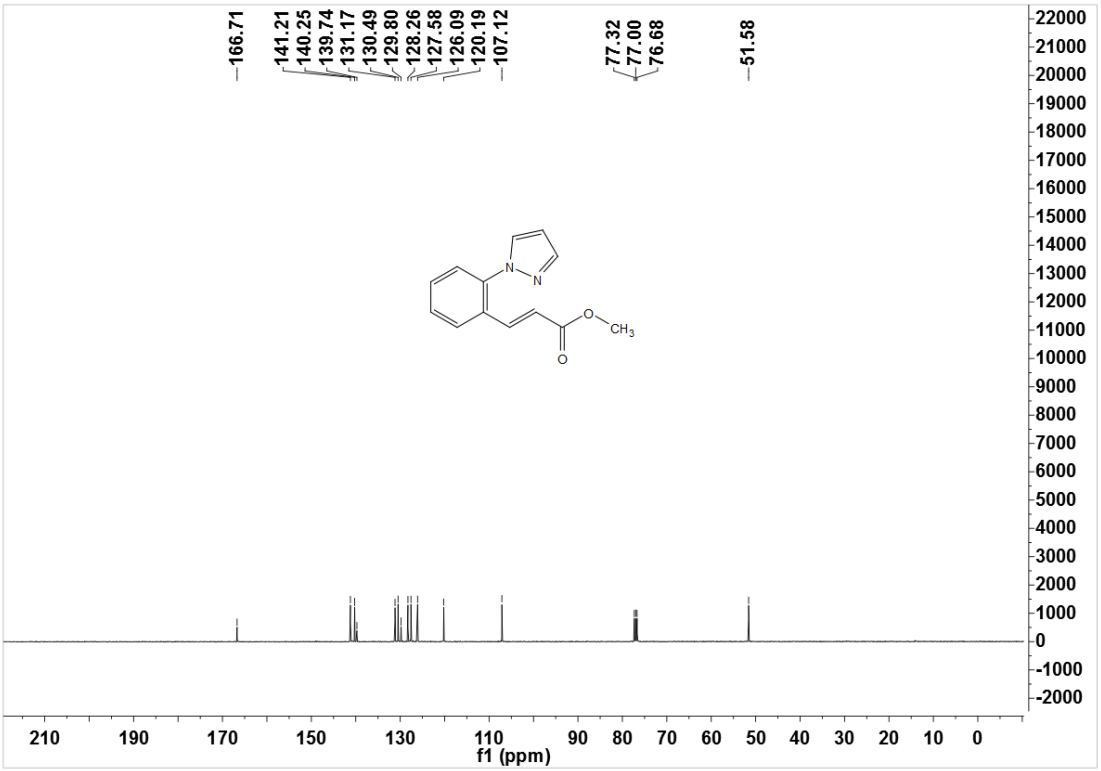


Methyl (*E*)-3-(2-(1*H*-pyrazol-1-yl)phenyl)acrylate (3a-I')

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



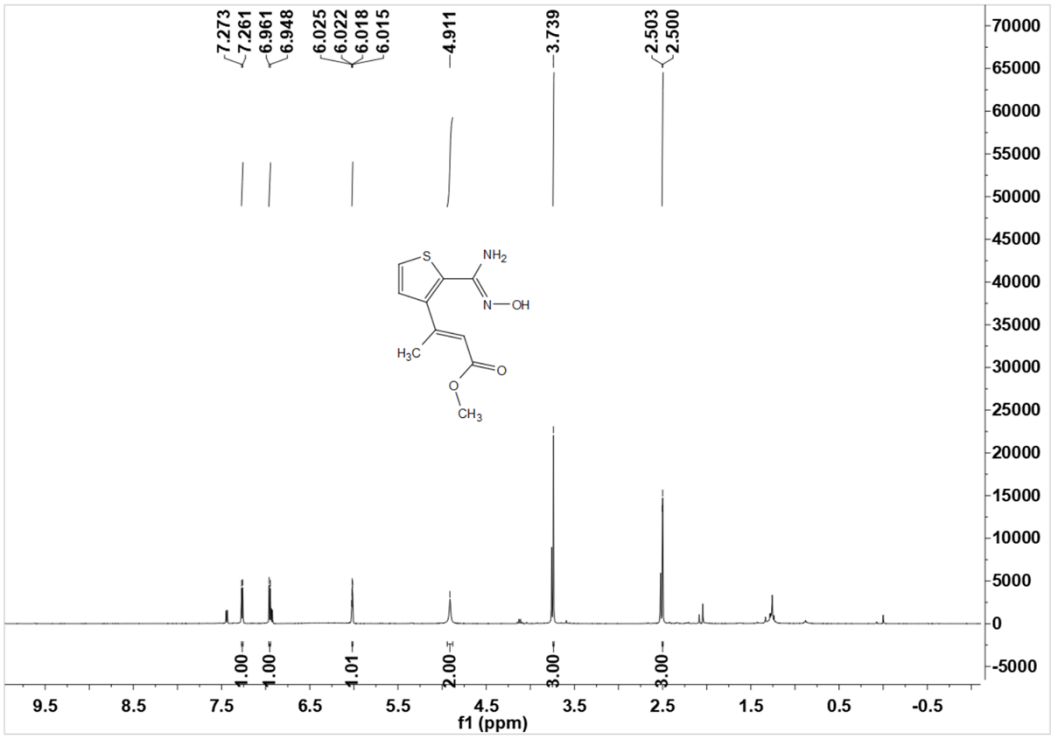
^{13}C NMR (100 MHz, $CDCl_3$)



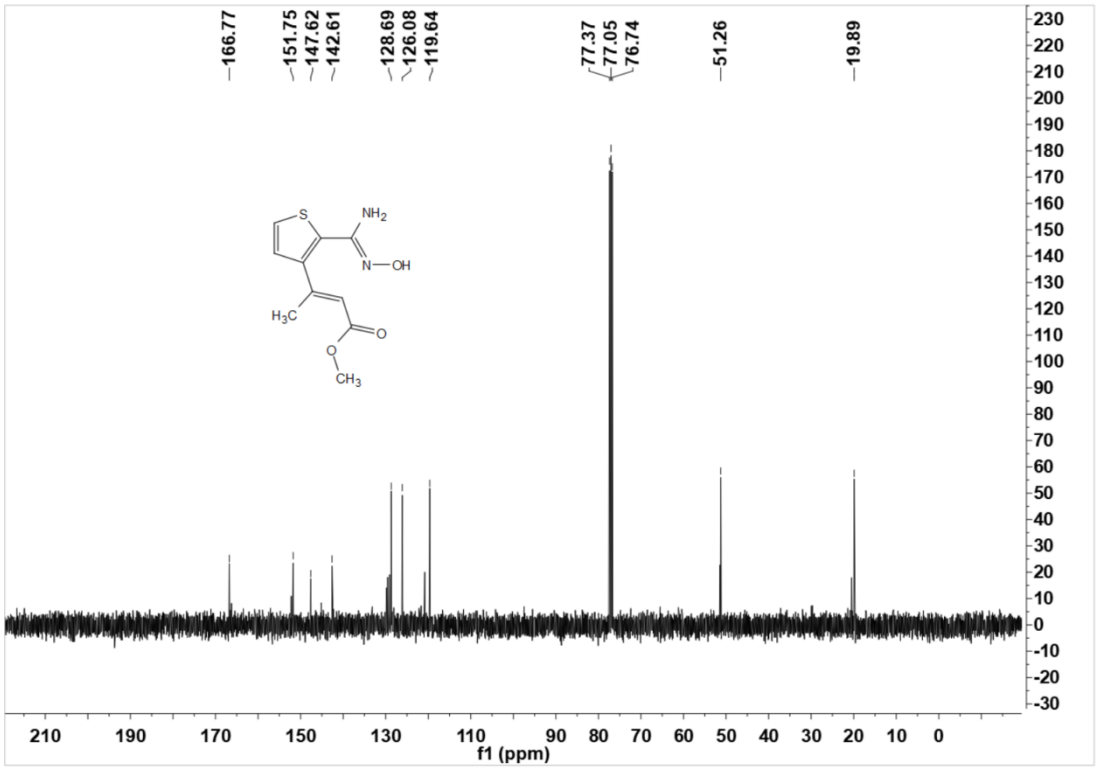
Methyl (*E*)-3-(2-((*Z*)-N'-hydroxycarbamimidoyl)thiophen-3-yl)but-2-enoate

(3b-I)

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

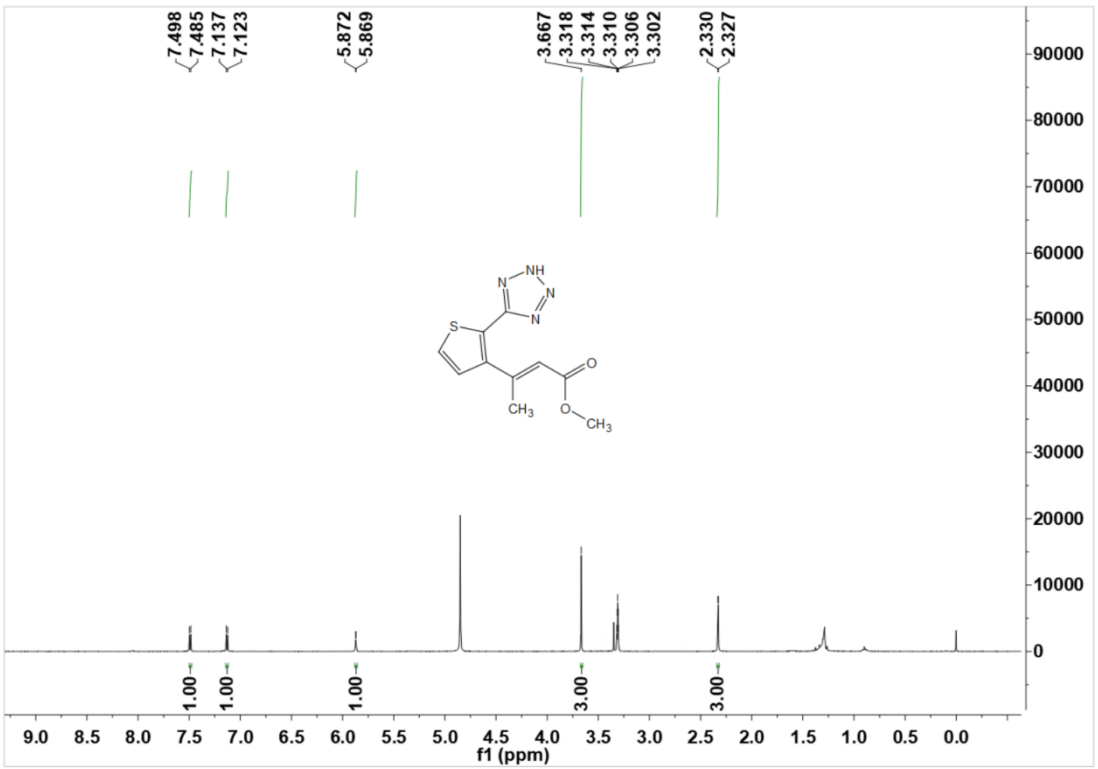


^{13}C NMR (100 MHz, $CDCl_3$)

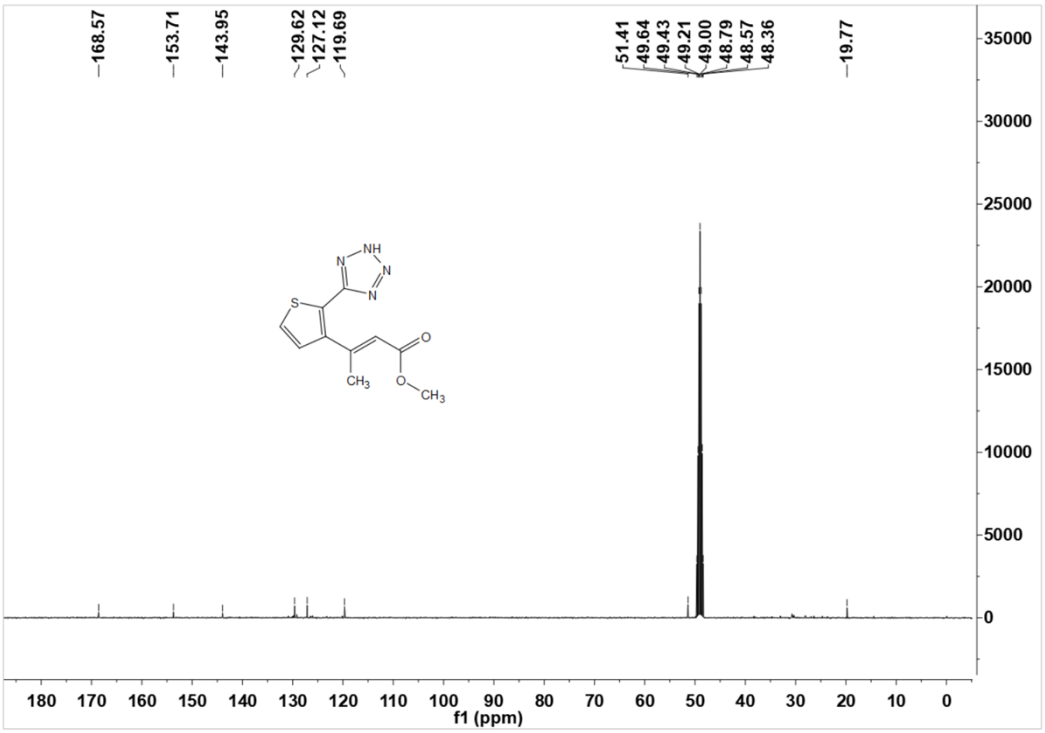


Methyl (*E*)-3-(2-(2*H*-tetrazol-5-yl)thiophen-3-yl)but-2-enoate (3b-II)

^{1}H NMR (400 MHz, CD_3OD)

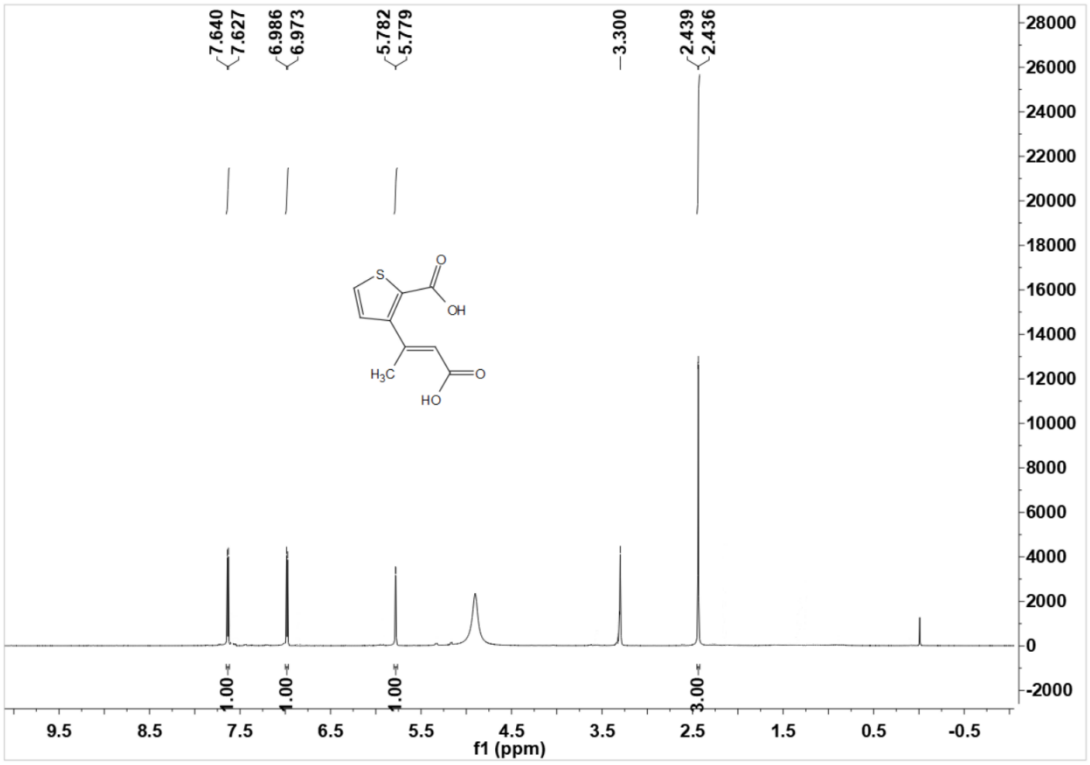


^{13}C NMR (100 MHz, CD_3OD)

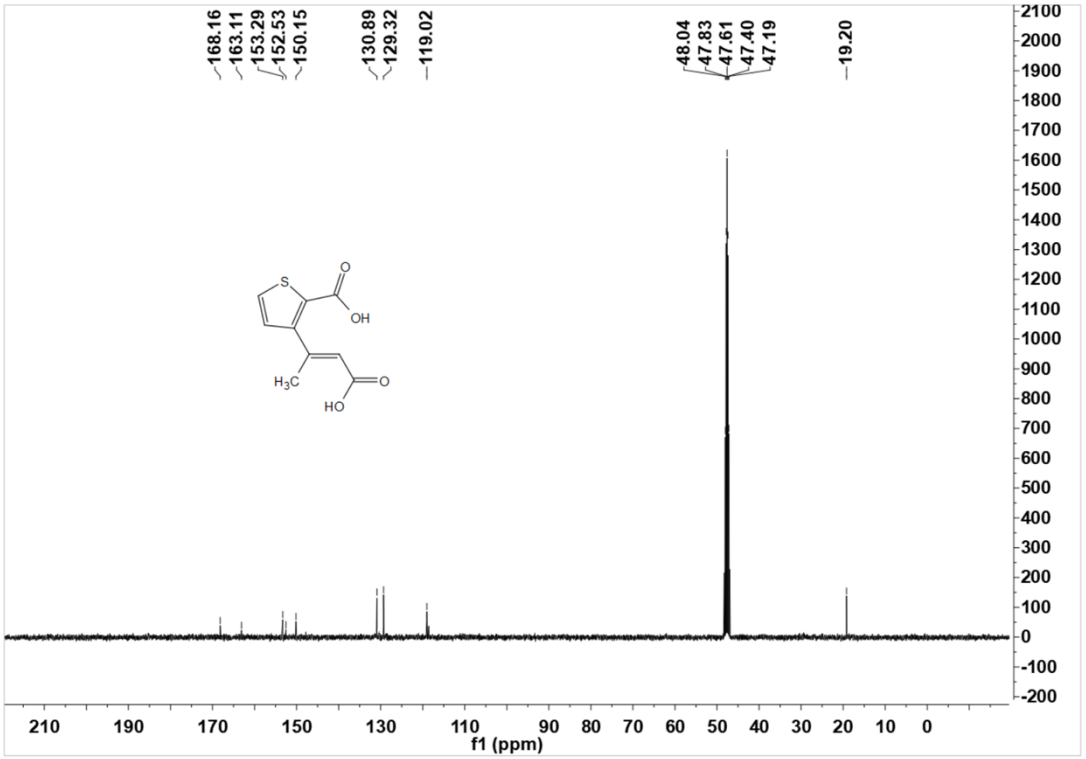


(*E*)-3-(1-Carboxyprop-1-en-2-yl)thiophene-2-carboxylic acid (3b-III)

^{1}H NMR (400 MHz, CD_3OD)

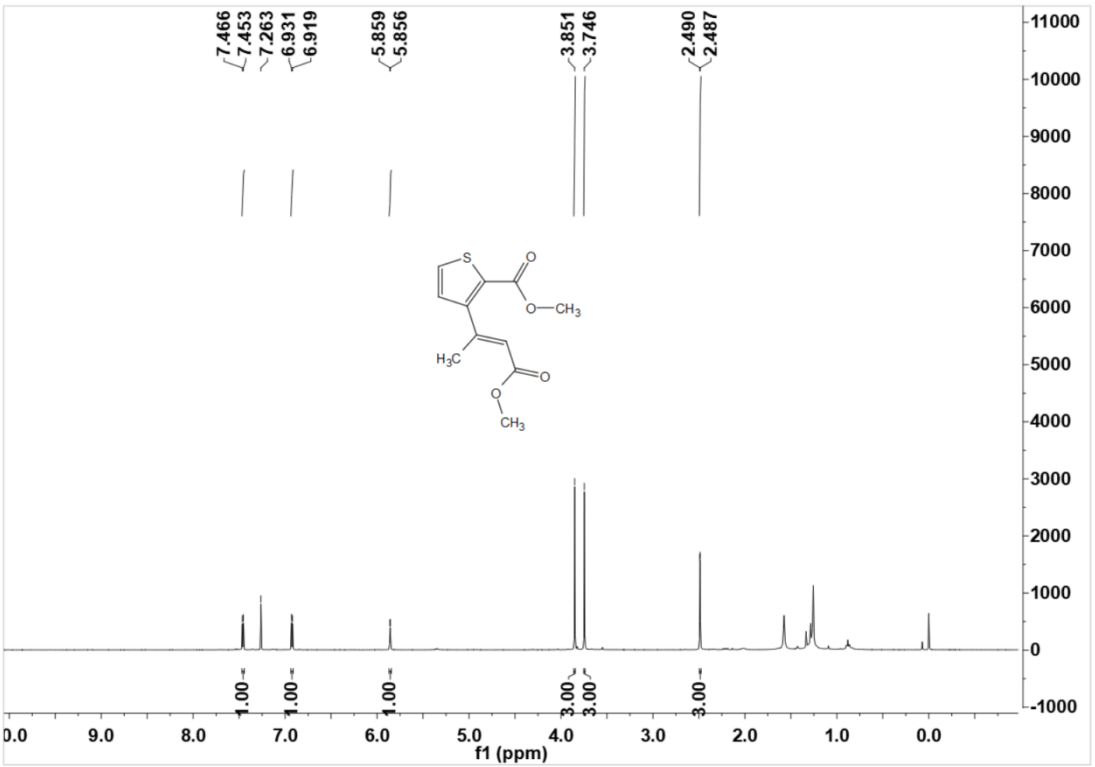


^{13}C NMR (100 MHz, CD_3OD)

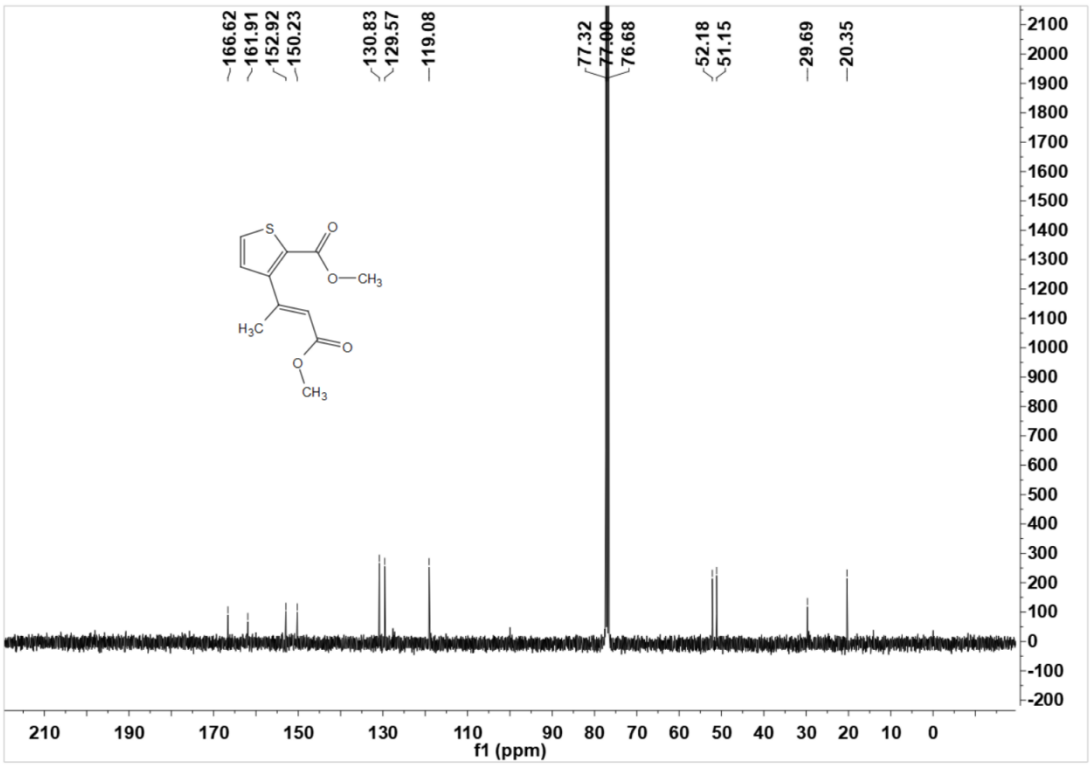


Methyl (*E*)-3-(4-methoxy-4-oxobut-2-en-2-yl)thiophene-2-carboxylate (3b-IV)

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

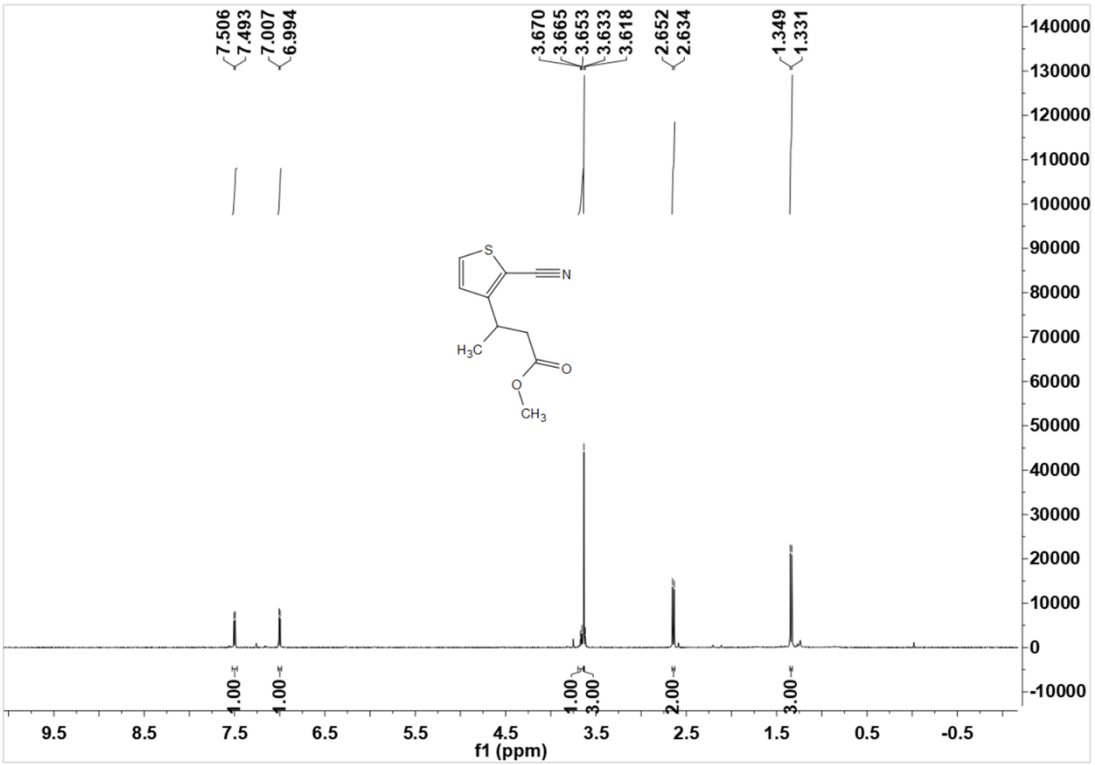


^{13}C NMR (100 MHz, $CDCl_3$)

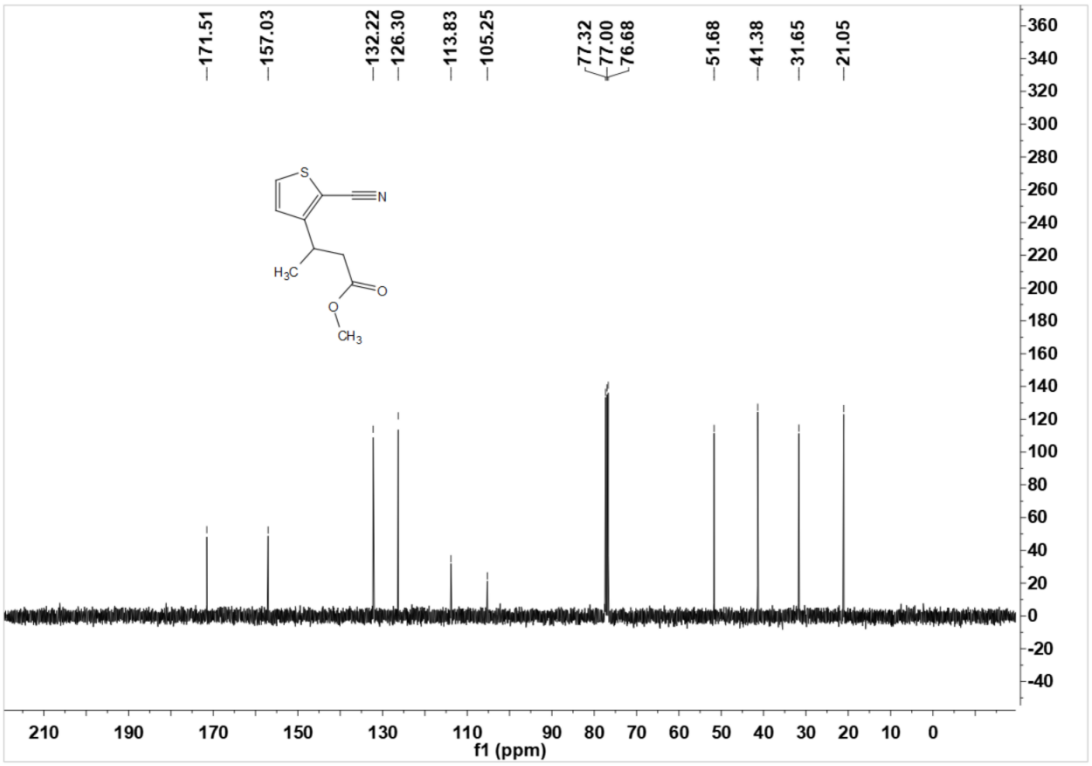


Methyl 3-(2-cyanothiophen-3-yl)butanoate (3b-V)

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

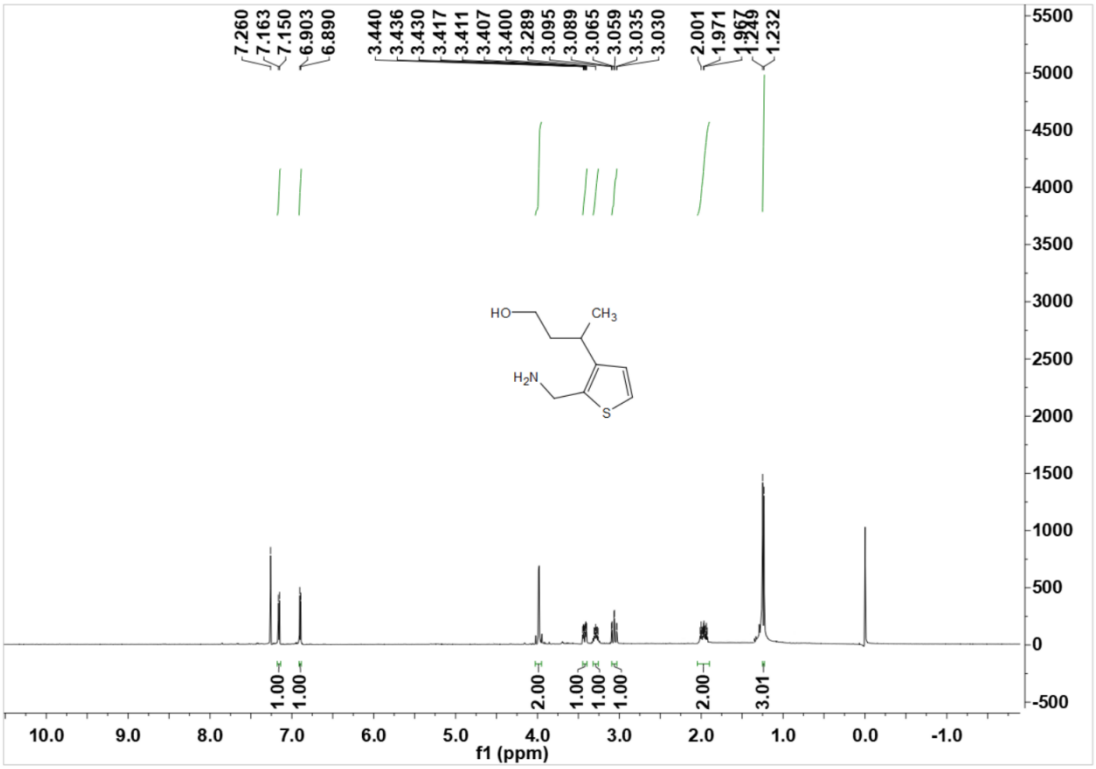


^{13}C NMR (100 MHz, $CDCl_3$)

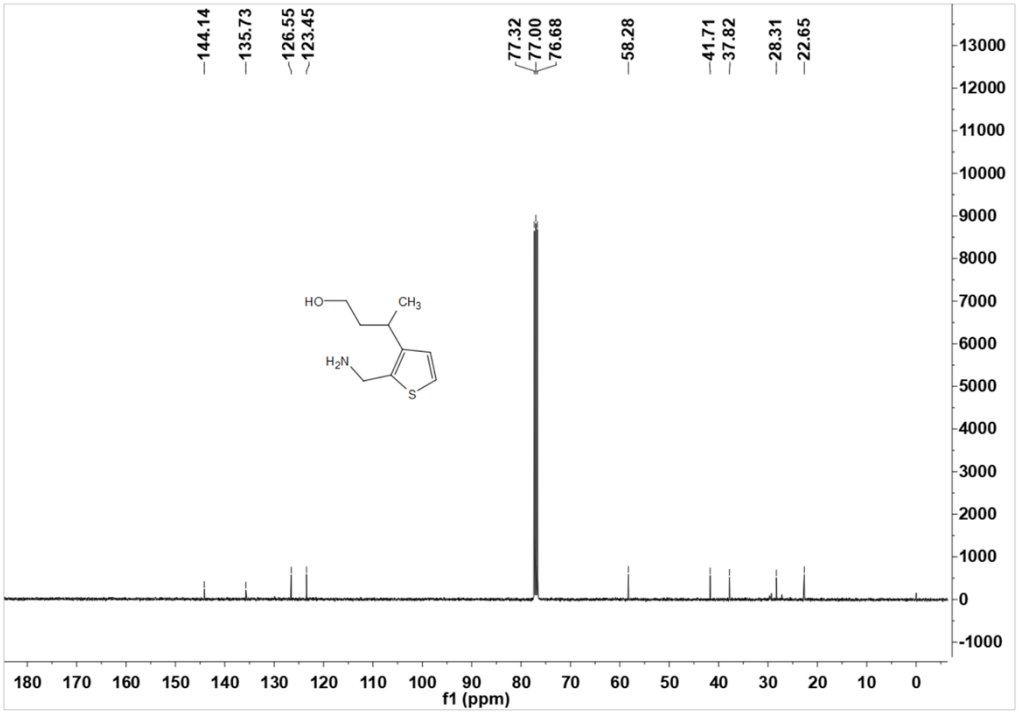


3-(2-(Aminomethyl)thiophen-3-yl)butan-1-ol (3b-VI)

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

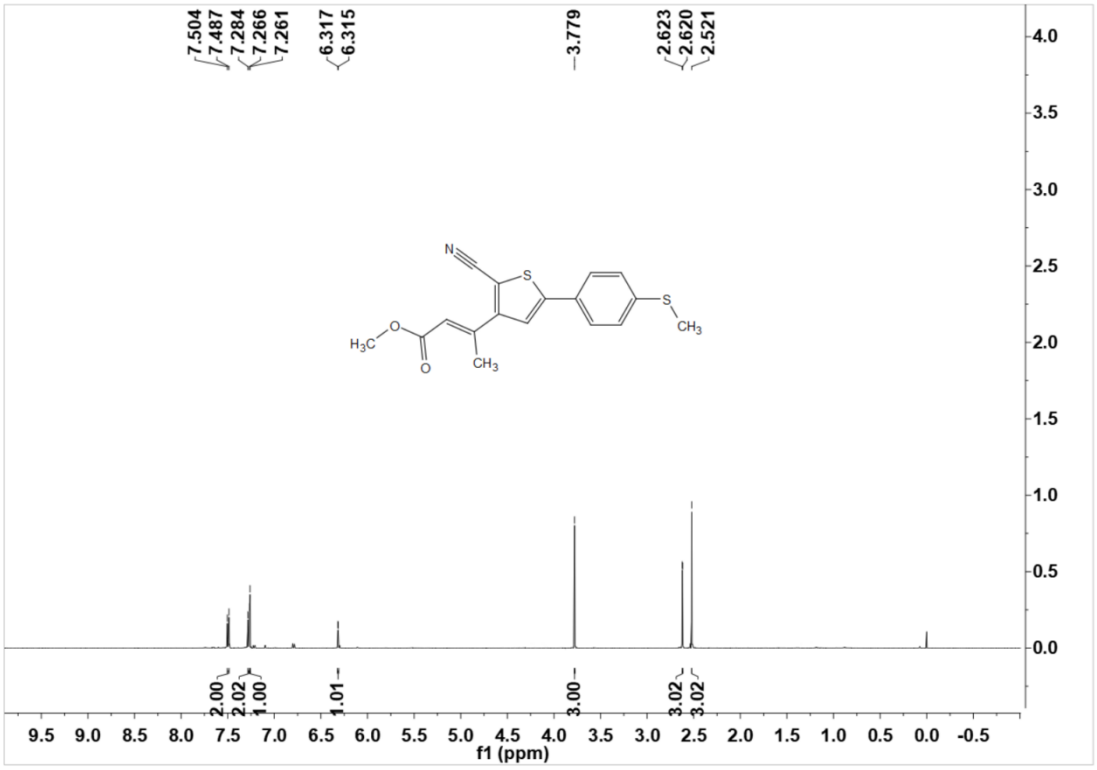


^{13}C NMR (100 MHz, $CDCl_3$)

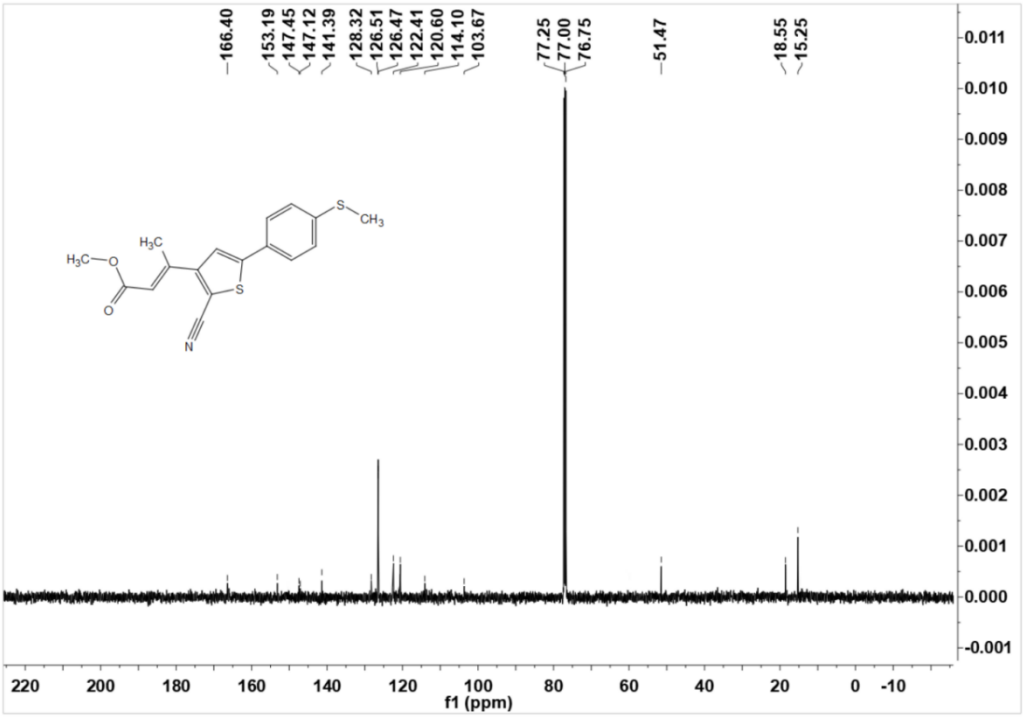


2-(4-Methyl-6-oxo-5,6-dihydro-4*H*-thieno[2,3-c]pyrrol-4-yl)acetonitrile (3e-I)

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

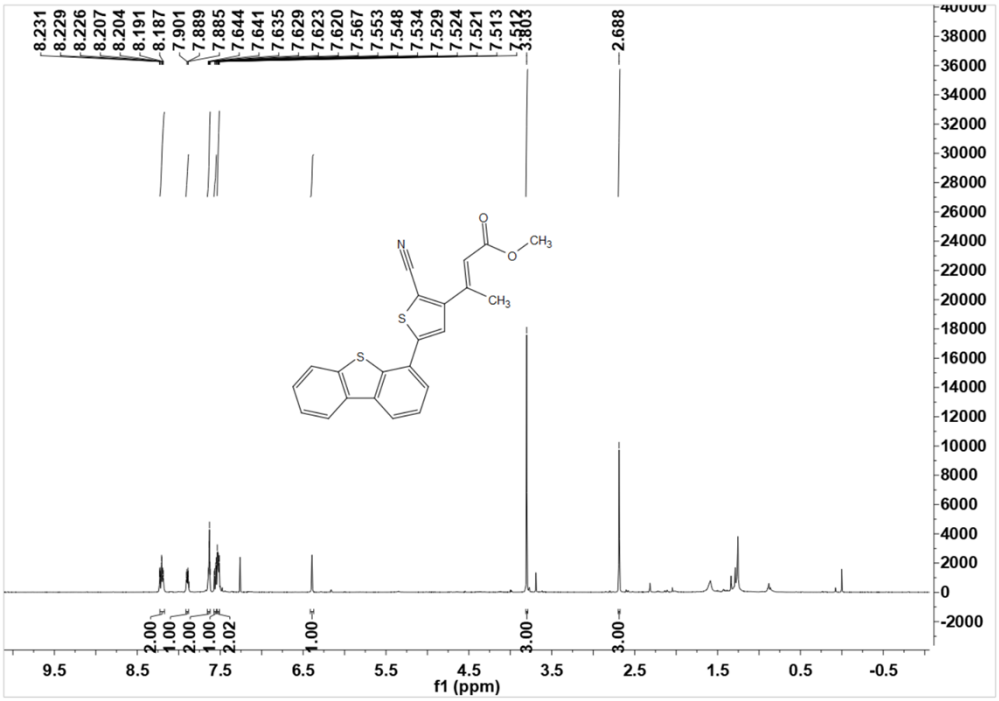


^{13}C NMR (100 MHz, $CDCl_3$)

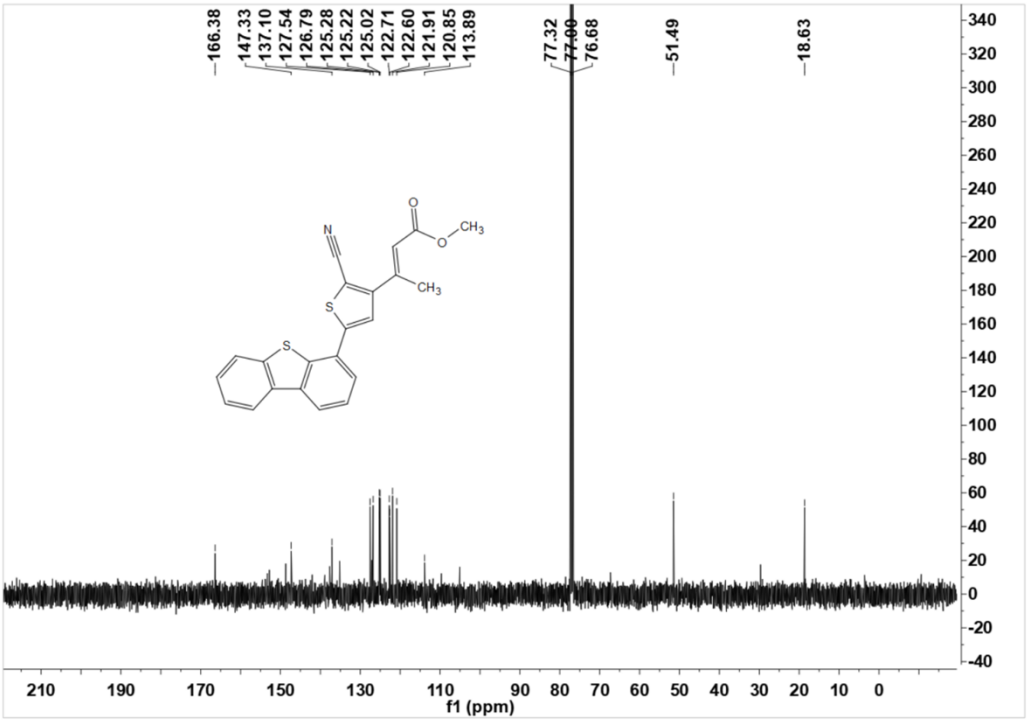


Methyl (*E*)-3-(2-cyano-5-(dibenzo[*b,d*]thiophen-4-yl)thiophen-3-yl)but-2-enoate (3e-II)

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

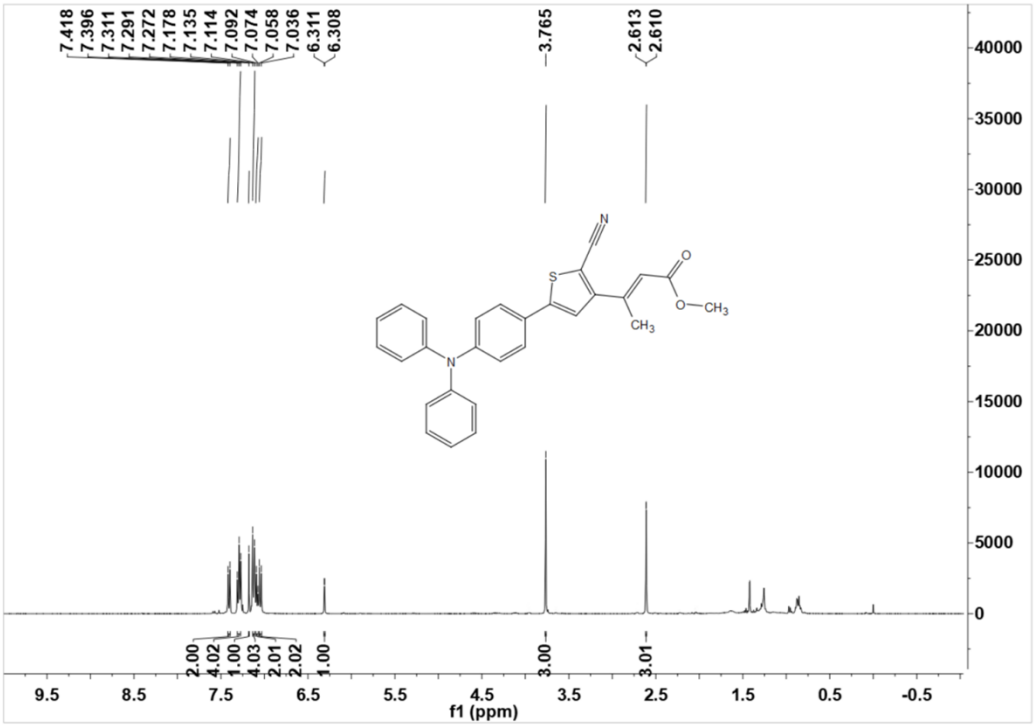


^{13}C NMR (100 MHz, $CDCl_3$)

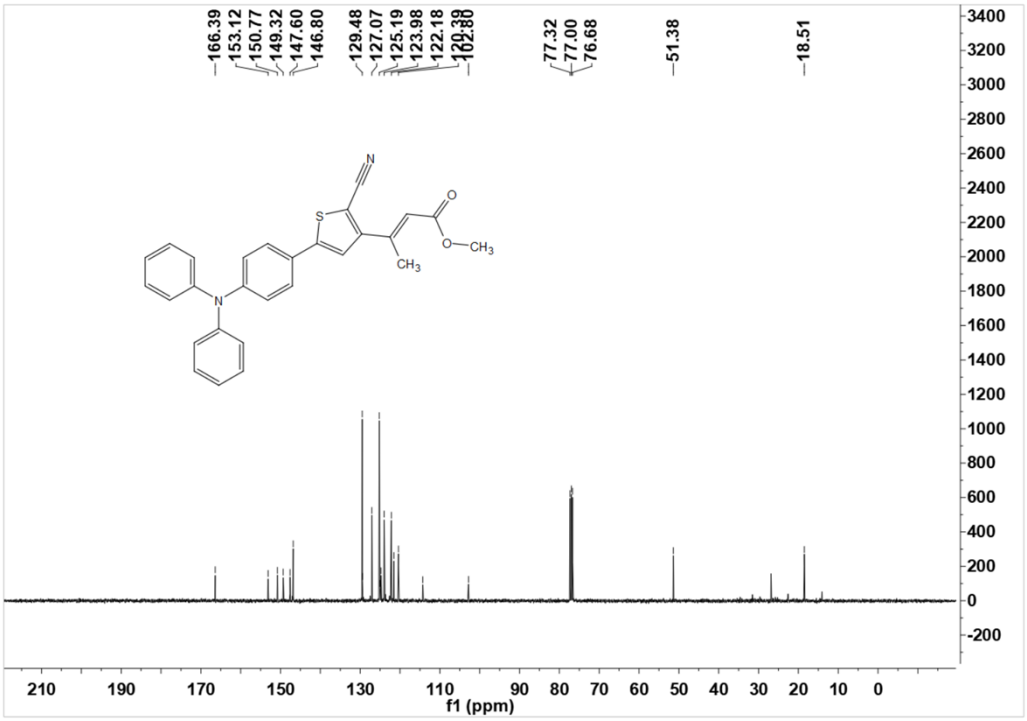


Methyl (*E*)-3-(2-cyano-5-(4-(diphenylamino)phenyl)thiophen-3-yl)but-2-enoate (3e-III)

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

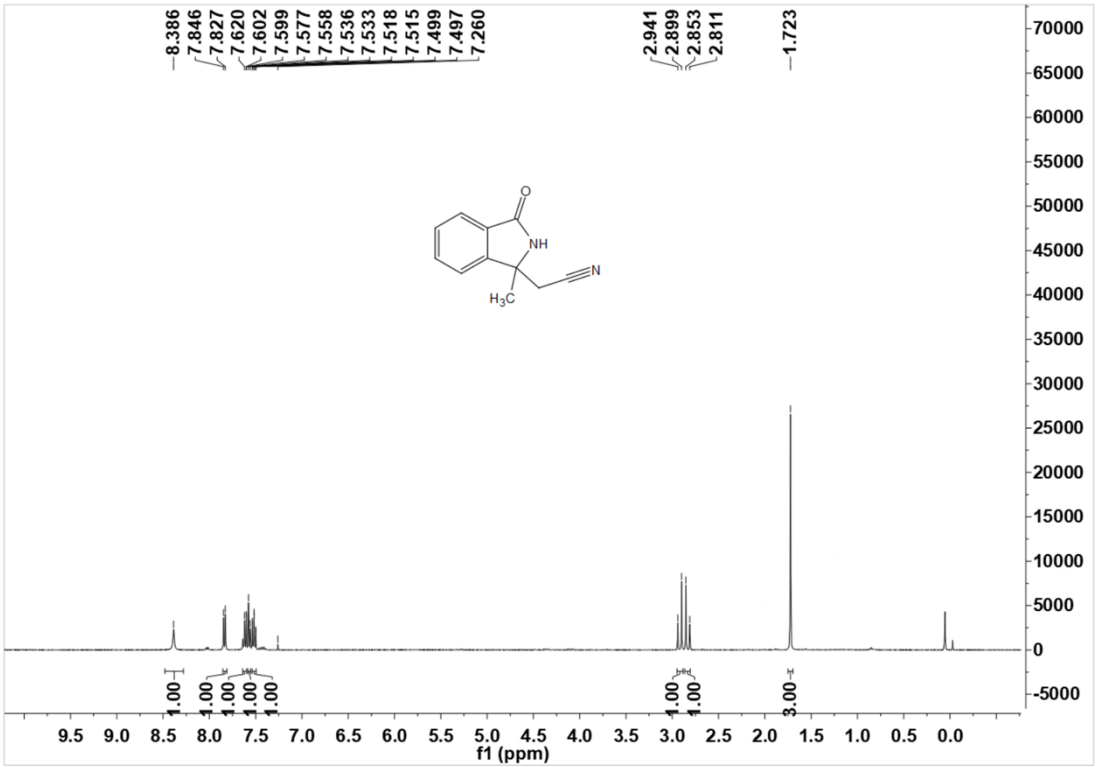


^{13}C NMR (100 MHz, $CDCl_3$)

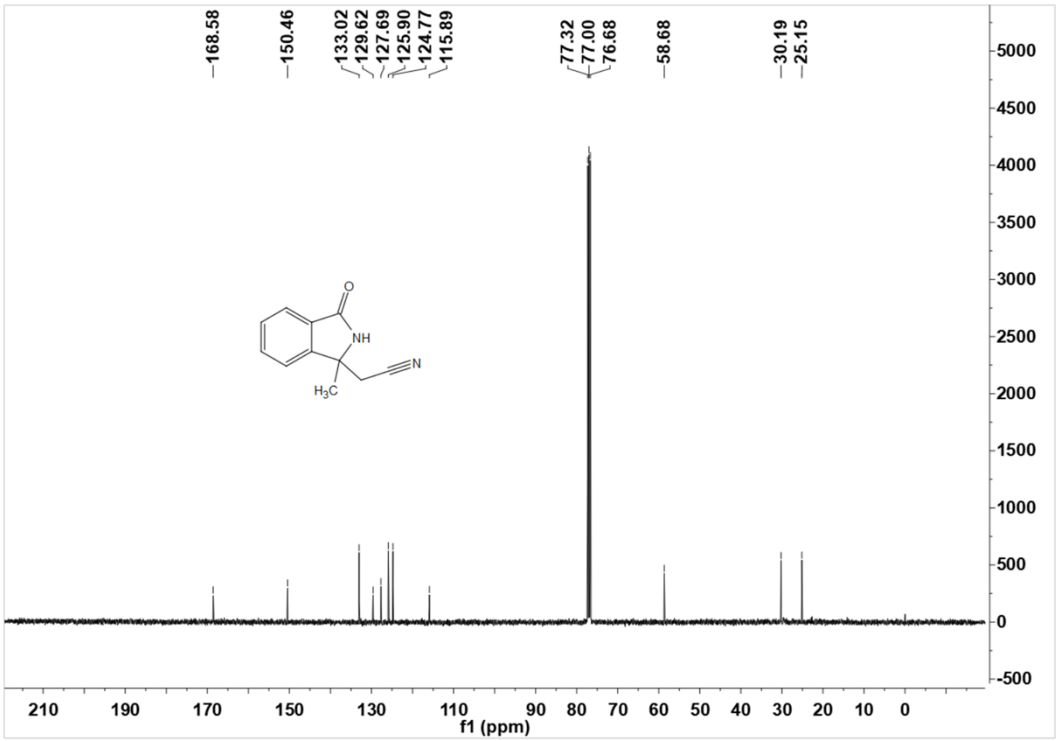


2-(1-Methyl-3-oxoisoindolin-1-yl)acetonitrile (4c-I)

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

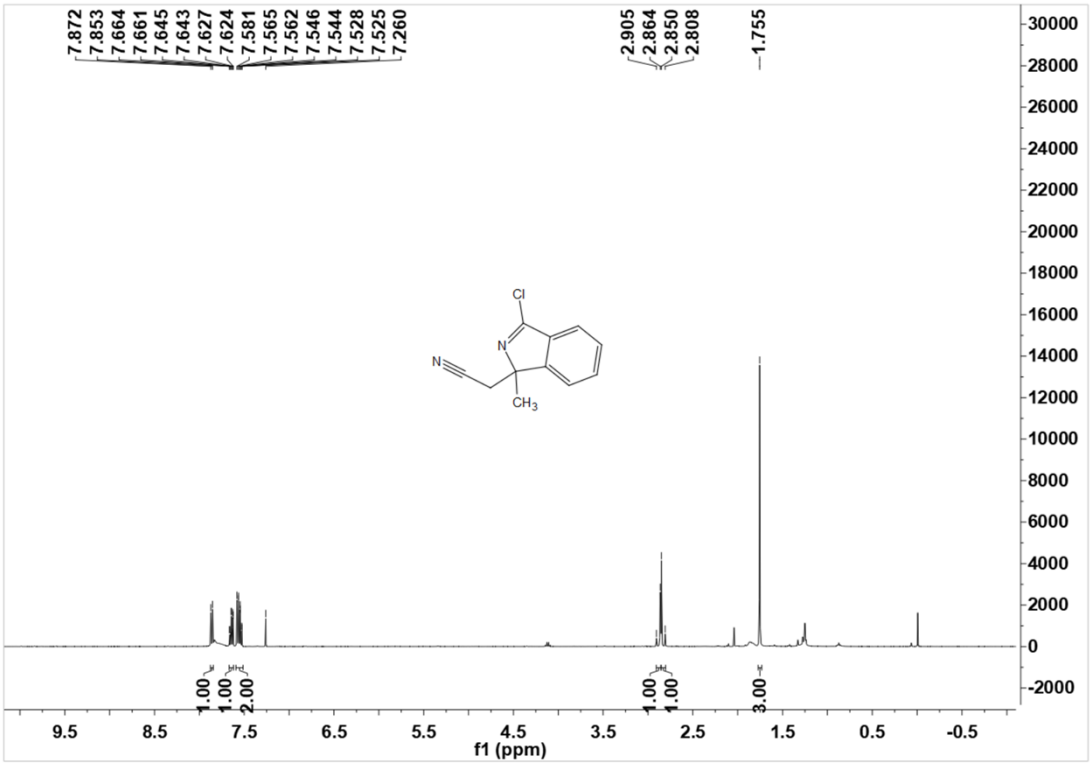


^{13}C NMR (100 MHz, $CDCl_3$)

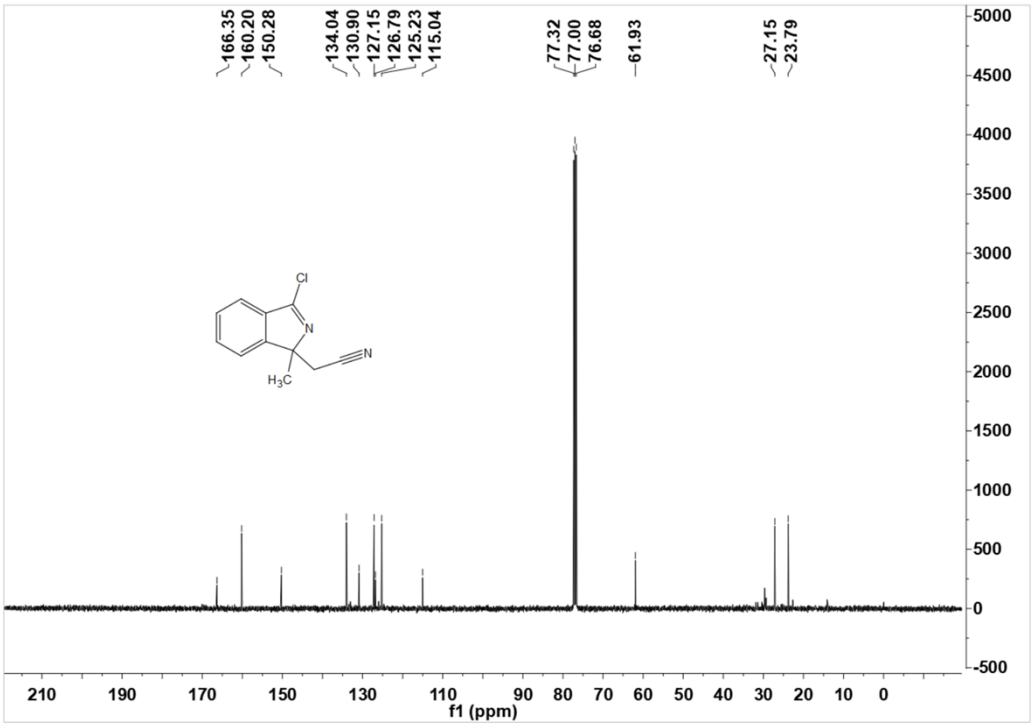


2-(3-Chloro-1-methyl-1*H*-isoindol-1-yl)acetonitrile (4c-II)

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



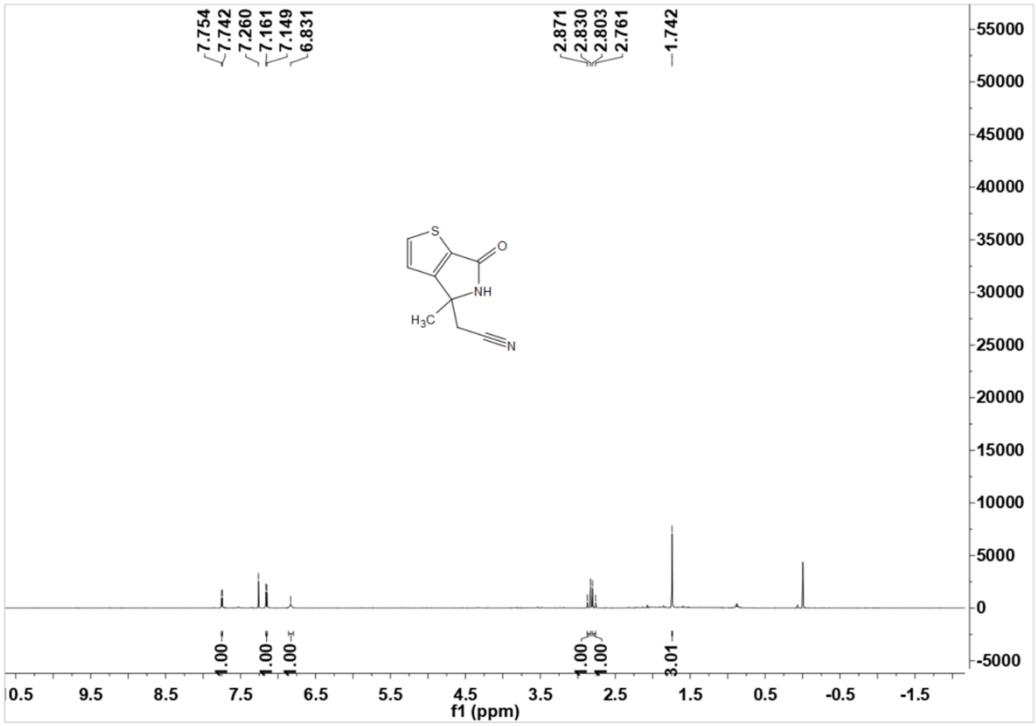
^{13}C NMR (100 MHz, $CDCl_3$)



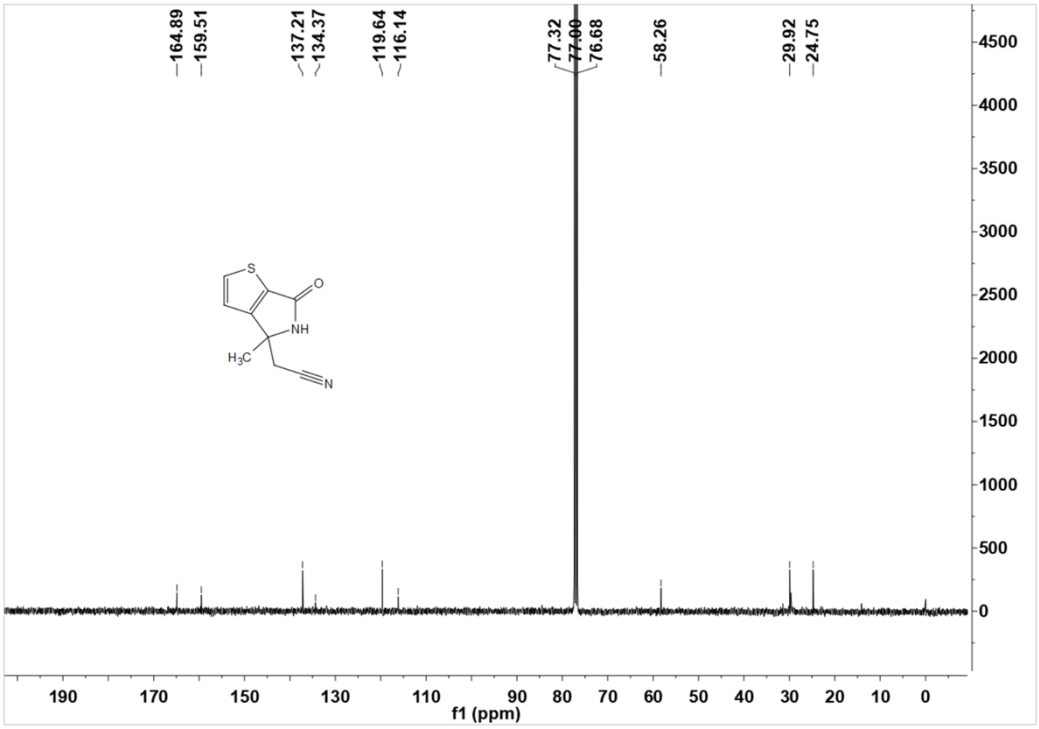
2-(4-Methyl-6-oxo-5,6-dihydro-4*H*-thieno[2,3-c]pyrrol-4-yl)acetonitrile

(4p-I)

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

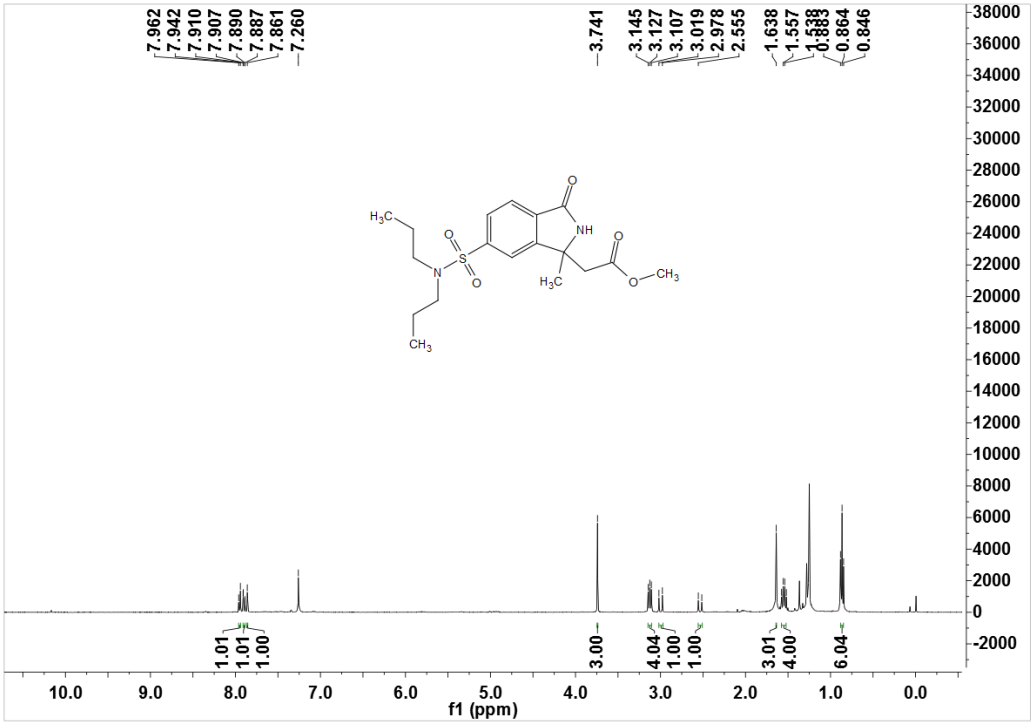


^{13}C NMR (100 MHz, $CDCl_3$)

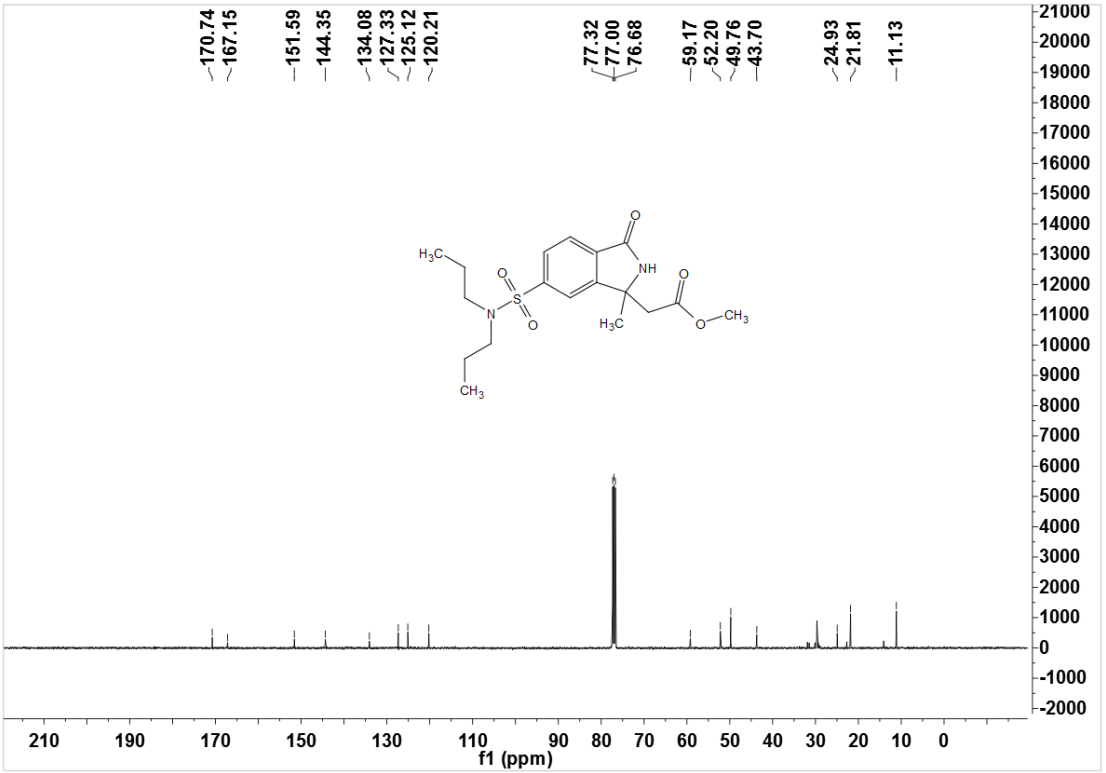


Methyl 2-(6-(*N*, *N*-dipropylsulfamoyl)-1-methyl-3-oxoisoindolin-1-yl)acetate (4zg-I)

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

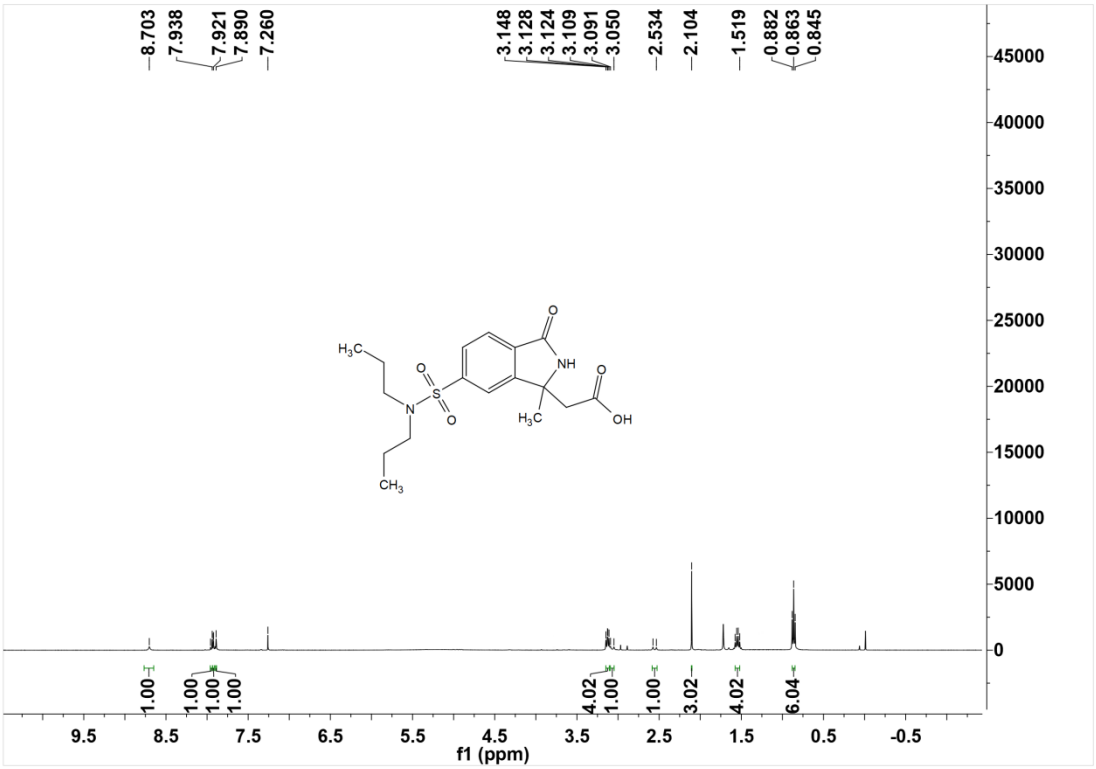


^{13}C NMR (100 MHz, $CDCl_3$)

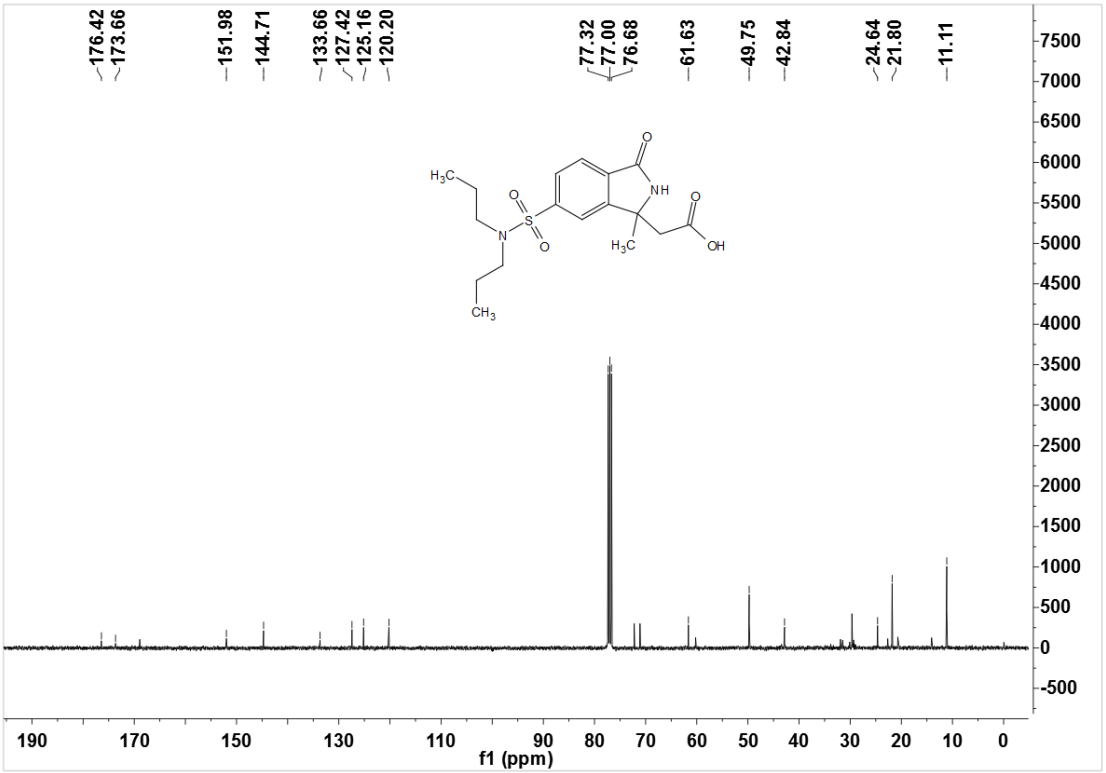


2-(6-(*N*,*N*-dipropylsulfamoyl)-1-methyl-3-oxoisoindolin-1-yl)acetic acid (4zg-II)

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

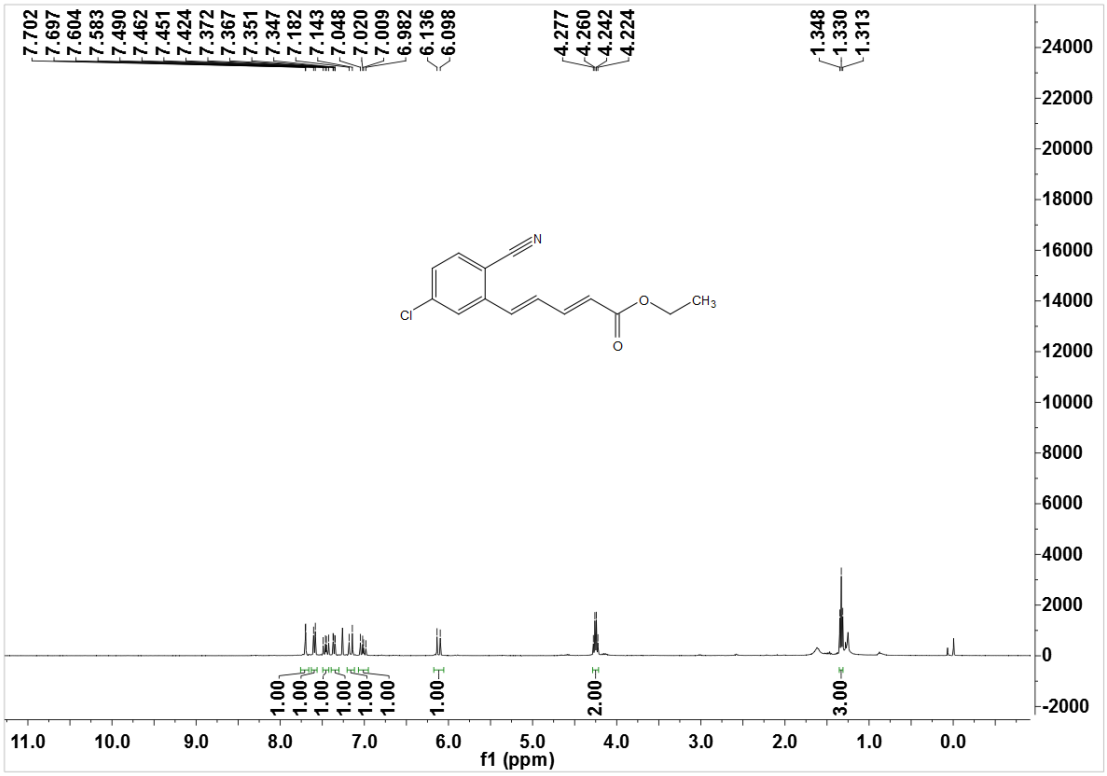


^{13}C NMR (100 MHz, $CDCl_3$)

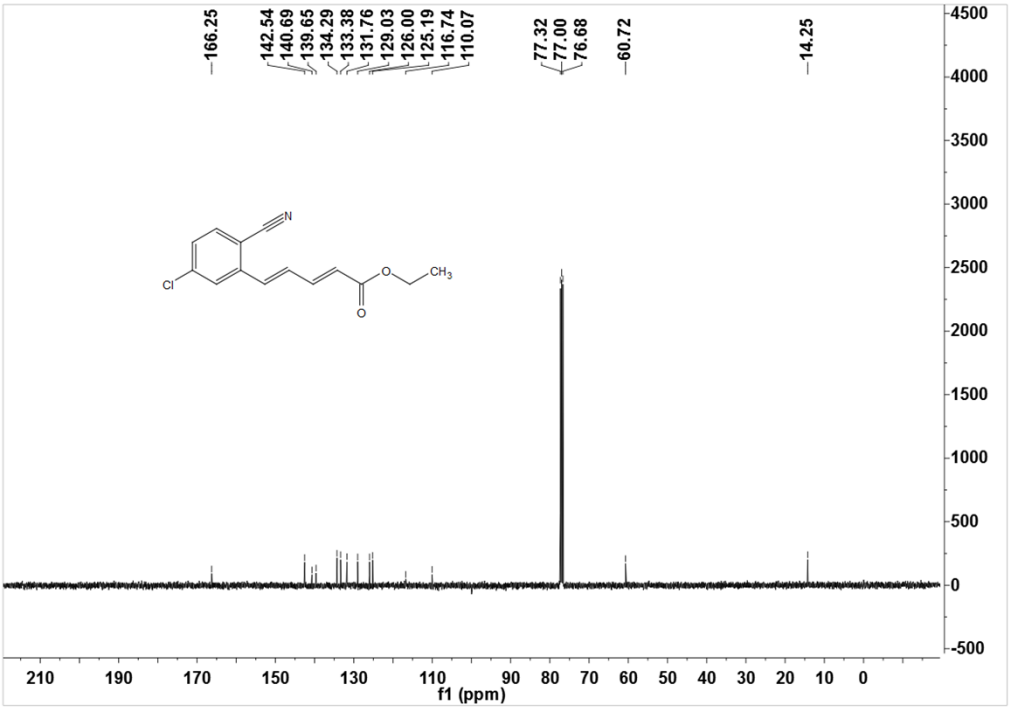


Ethyl (2*E*, 4*E*)-5-(5-chloro-2-cyanophenyl)penta-2,4-dienoate (10a)

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

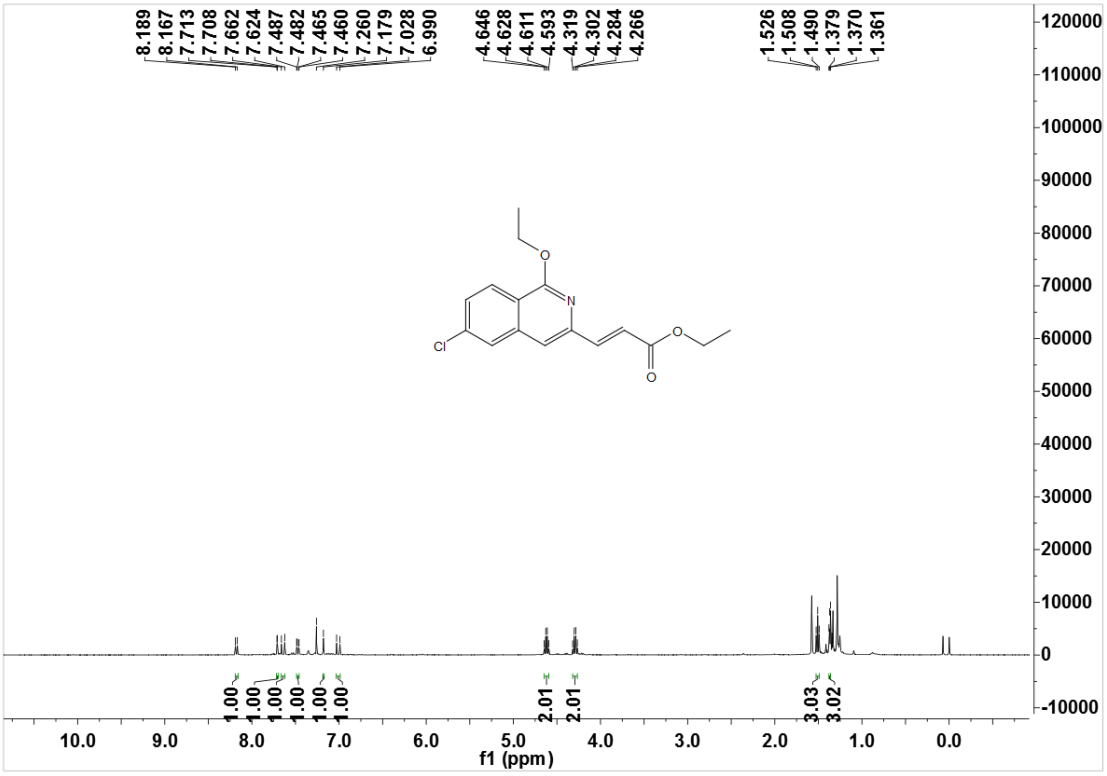


^{13}C NMR (100 MHz, $CDCl_3$)



Ethyl (E)-3-(6-chloro-1-ethoxyisoquinolin-3-yl)acrylate (11a)

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



^{13}C NMR (100 MHz, $CDCl_3$)