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**Supporting information**

# 2-Imidazolidinone Benzofurans as Unexpected Outcome of the Lewis Acid Mediated Nenitzescu Reaction

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# Experimental procedures and characterization data

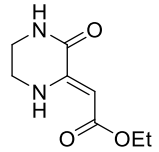
## General information

All chemicals were purchased from Acros Organics, Merck, Alfa Aesar, Fluorochem and TCI Europe. Unless otherwise stated, the reagent was used as received. 1,4-Benzoquinone was purified prior to use by sublimation and stored under inert atmosphere. 2-(4-Ethoxycarbonylphenyl)-1,4-benzoquinone **1d** was synthesised according to a literature procedure.[1] Dry reaction solvents were purchased from commercial sources. Reactions at elevated temperature were heated with an oil bath. Crystallizations were performed by dissolving the product in the appropriate solvent at reflux temperature using a heating mantle. Thin-layer chromatography (TLC) was performed on silica gel 0.20 mm 60 with fluorescent indicator UV254 (pre-coated aluminum sheets) from Merck. Automatic column chromatography was performed using a CombiFlash EZ prep apparatus. Silica used for the MPLC was MP Silica 60 – 200 μm, average pore diameter 60 Å. The stationary phase used for column chromatography was 70-230 mesh silica 60 Å (E.M Merck). NMR spectra were recorded on commercial instruments (Bruker Avance 300 or Bruker Avance III HD 400 and chemical shifts ($\delta$) are reported in parts per million (ppm) referenced to tetramethylsilane ($^1$H NMR $CDCl_3$), or the internal (NMR) solvent signal ($^1$H NMR DMSO-$d_6$ and $^{13}C\{^1H\}$). High-resolution mass spectra were acquired on a quadrupole orthogonal acceleration time-of-flight mass spectrometer (Synapt G2 HDMS, Waters, Milford, MA). Samples were infused at 3 μL/min and spectra were obtained in positive ionization mode with a resolution of 15000 (FWHM) using leucine enkephalin as lock mass. Melting points (not corrected) were determined using a Reichert Thermovar apparatus.

## General procedure 1: Synthesis of piperazinone enaminoesters (5a-d,i)

Piperazinone enaminoesters **5a-e** were synthesised according to a modified literature procedure.[2] The appropriate 1,2-diamine (20 mmol) was added to 8 mL ethanol in a round-bottom flask equipped with a magnetic stirrer and stirred at room temperature under nitrogen atmosphere. A solution of diethyl acetylene dicarboxylate **10** (20 mmol; 3.2 mL) in 8 mL ethanol was added dropwise (0.3 mL/min) using a syringe pump. The reaction was stirred for three hours at room temperature while **5a-e** crystallised from the reaction mixture. After three hours, the reaction mixture was filtered using a vacuum filtration and the precipitate washed with diethyl ether to afford **5a-e** as crystalline solids.

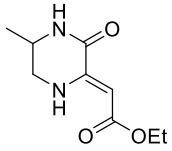
**Ethyl (*Z*)-2-(3-oxopiperazin-2-ylidene)acetate (5a)**



Prepared according to general procedure 1, using ethylenediamine (**10a**;1.202 g; 20 mmol). Crystalline white solid; yield: 2.501 g (68%). Mp: 165 – 167 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.29 (s, 1H), 7.80 (s, 1H), 5.59 (s, 1H), 4.15 (q, $J$ = 7.1 Hz, 2H), 3.55 – 3.49 (m, 2H), 3.45 – 3.40 (m, 2H), 1.27 (t, $J$ = 7.1 Hz, 3H).
$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 170.6, 161.8, 149.0, 86.9, 59.4, 40.3, 39.1, 14.5.
HRMS (ESI-Q-TOF) m/z $[M + Na]^+$ calculated for $C_8H_{12}N_2O_3$: 207.0740; found: 207.0741.

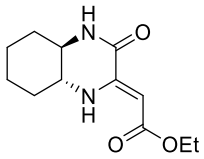
**Ethyl (*Z*)-2-(5-methyl-3-oxopiperazin-2-ylidene)acetate (5b)**



Prepared according to general procedure 1, using 1,2-diaminopropane (racemic mixture) (1.482 g; 20 mmol). Crystalline white solid; yield: 2.530 g (64%). Mp: 154 – 156 °C. Regioselectivity is confirmed by $^1$H – $^1$H COSY NMR analysis (Figure S1).

$^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.24 (s, 1H), 6.31 (s, 1H), 5.63 (s, 1H), 4.15 (q, $J$ = 7.1 Hz, 2H), 3.86 – 3.75 (m, 1H), 3.45 – 3.34 (m, 1H), 3.16 – 3.06 (m, 1H), 1.31 – 1.23 (m, 6H).
$^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 170.7, 161.4, 148.4, 87.0, 59.5, 46.8, 45.7, 18.7, 14.5.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_9H_{14}N_2O_3$: 221.0897; found: 221.0894.

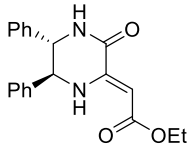
**Ethyl 2-((4a*R*,8a*R*,*Z*)-3-oxooctahydroquinoxalin-2(1*H*)-ylidene)acetate (5c)**



Prepared according to general procedure 1, using (1*R*,2*R*)-1,2-diaminocyclohexane (2.284 g; 20 mmol). Crystalline white solid; yield: 2.810 g (59%). Mp: 194 – 196 °C.

$^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.07 (s, 1H), 7.35 (s, 1H), 5.59 (s, 1H), 4.14 (q, $J$ = 7.1 Hz, 2H), 3.30 – 3.17 (m, 1H), 3.17 – 3.03 (m, 1H), 2.03 – 1.89 (m, 2H), 1.89 – 1.70 (m, 2H), 1.46 – 1.31 (m, 4H), 1.27 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta$ 170.7, 161.8, 149.2, 86.9, 77.6, 77.2, 76.7, 59.4, 55.7, 55.2, 29.8, 29.7, 23.9, 23.6, 14.5.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{12}H_{18}N_2O_3$: 261.1210; found: 261.1208.

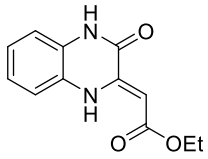
**Ethyl (*Z*)-2-((5*S*,6*S*)-3-oxo-5,6-diphenylpiperazin-2-ylidene)acetate (5d)**



Prepared according to general procedure 1, using (1*S*,2*S*)-1,2-diphenylethylenediamine (4.246 g; 20 mmol). Crystalline white solid; yield: 3.998 g (59%). Mp: 125 – 127 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.36 (s, 1H), 7.26 – 7.11 (m, 6H), 7.04 – 6.94 (m, 4H), 6.14 (s, 1H), 5.76 (s, 1H), 4.63 (d, $J$ = 9.4 Hz, 1H), 4.46 (d, $J$ = 9.4 Hz, 1H), 4.07 (qd, $J$ = 7.1, 0.9 Hz, 2H), 1.21 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 170.5, 160.9, 148.2, 137.2, 136.9, 129.1, 128.9, 128.8, 127.6, 127.5, 88.7, 63.1, 62.1, 59.7, 14.5.
HRMS (ESI-Q-TOF) m/z [M + H]$^+$ calculated for $C_{20}H_{20}N_2O_3$: 337.1547; found: 337.1547.

**Ethyl (*Z*)-2-(3-oxo-3,4-dihydroquinoxalin-2(1*H*)-ylidene)acetate (5i)**



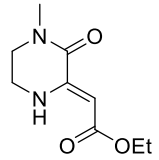
Prepared according to general procedure 1, using 1,2-phenylenediamine (2.163 g; 20 mmol). Crystalline yellow solid; $^1$H NMR contained **5i** and its imine isomer in a 1:0.55 ratio. yield: 3.420 g (74%). Mp: 216 – 218 °C.

Enaminoester **5i**: $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 11.72 (s, 1H), 11.06 (s, 1H), 7.42 – 7.38 (m, 1H), 7.33 – 7.28 (m, 1H), 7.08 – 6.98 (m, 2H), 5.50 (s, 1H), 4.16 (q, $J$ = 7.1 Hz, 2H), 1.24 (t, $J$ = 7.1 Hz, 3H).
Imine-isomer: $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.48 (s, 1H), 7.78 – 7.72 (m, 1H), 7.57 – 7.50 (m, 1H), 7.11 – 6.98 (m, 2H), 4.10 (q, $J$ = 7.2 Hz, 2H), 3.81 (s, 2H), 1.18 (t, $J$ = 7.1 Hz, 3H).
$^1$H NMR and melting point corresponds with literature reports.[3]
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{12}H_{12}N_2O_3$: 255.0740; found: 255.0750.

## General procedure 2: Synthesis of piperazinone enaminoesters (5e-g)

Piperazinone enaminoesters **5e-g** were synthesised according to a modified literature procedure. The appropriate 1,2-diamine (4 mmol) was added to 8 mL ethanol in a round-bottom flask equipped with a magnetic stirrer and stirred at room temperature under nitrogen atmosphere. Diethyl oxaloacetate (4 mmol; 753 mg) was added and the reaction mixture was stirred overnight. Purification of the product was done *via* recrystallization (**5f, g**) or extraction crystallization (**5e**).

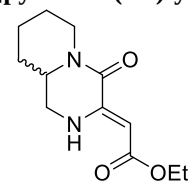
**Ethyl (*Z*)-2-(4-methyl-3-oxopiperazin-2-ylidene)acetate (5e)**



Prepared according to general procedure 2, using *N*-methyl(ethylene-1,2-diamine) (296 mg; 4 mmol). Purification was done by diluting the reaction mixture with ethyl acetate (100 mL), extraction with water (3 x 100 mL) and brine (100 mL). The organic phase was dried over $MgSO_4$, filtered and solvent was removed under reduced pressure. The crude reaction mixture was crystallised in diethyl ether to obtain **5e**. Crystalline white solid; yield: 380 mg (48%). Mp: 152 – 154 °C.

$^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.31 (s, 1H), 5.66 (s, 1H), 4.14 (q, $J$ = 7.1 Hz, 2H), 3.55 – 3.47 (m, 2H), 3.47 – 3.40 (m, 2H), 3.09 (s, 3H), 1.27 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta$ 170.9, 159.8, 149.2, 87.2, 59.4, 47.9, 38.8, 35.6, 14.6.
HRMS (ESI-Q-TOF) m/z $[M + Na]^+$ calculated for $C_9H_{14}N_2O_3$: 221.0897; found: 221.0892.

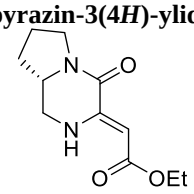
**Ethyl (*Z*)-2-(4-oxohexahydro-2*H*-pyrido[1,2-*a*]pyrazin-3(4*H*)-ylidene)acetate (5f)**



Prepared according to general procedure 2, using piperidin-2-ylmethanamine (racemic mixture) (456 mg; 4 mmol). Purification was done by precipitation in 150 mL water. The precipitate was filtered using a vacuum filtration, dissolved in diethyl ether and dried with $MgSO_4$ to obtain **5f**. White solid; yield: 526 mg (55%) Mp: 77 – 79 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.16 (s, 1H), 5.65 (s, 1H), 4.59 – 4.52 (m, 1H), 4.07 (q, $J$ = 7.1 Hz, 2H), 3.50 – 3.41 (m, 1H), 3.40 – 3.33 (m, 1H), 3.13 – 3.05 (m, 1H), 2.61 – 2.51 (m, 1H), 1.86 – 1.79 (m, 1H), 1.75 – 1.66 (m, 2H), 1.48 – 1.31 (m, 3H), 1.20 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 170.9, 159.6, 149.3, 87.7, 59.4, 54.2, 44.5, 43.3, 30.1, 24.7, 23.0, 14.5.
HRMS (ESI-Q-TOF) m/z $[M + Na]^+$ calculated for $C_{12}H_{18}N_2O_3$: 261.1210; found: 261.1209.

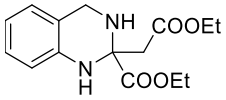
**Ethyl (*S*,*Z*)-2-(4-oxohexahydropyrrolo[1,2-*a*]pyrazin-3(4*H*)-ylidene)acetate (5g)**



Prepared according to general procedure 2, using (S)-pyrrolidin-2-ylmethanamine dihydrochloride (400 mg; 4 mmol) which was neutralised with triethylamine (1.12 mL, 8 mmol). Purification was done by diluting the reaction mixture with ethyl acetate (100 mL) and extraction with water (100 mL) and brine (100 mL). The organic phase was dried over $MgSO_4$, filtered and solvent was removed under reduced pressure. The product was recrystallised in diethylether to obtain **5g**. Crystalline white solid; yield: 642 mg (71%). Mp: 74 – 76 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.28 (s, 1H), 5.60 (s, 1H), 4.21 – 4.08 (m, 2H), 3.87 – 3.78 (m, 1H), 3.69 – 3.52 (m, 3H), 3.10 (t, $J$ = 11.9 Hz, 1H), 2.22 – 2.14 (m, 1H), 2.12 – 2.02 (m, 1H), 1.95 – 1.81 (m, 1H), 1.66 – 1.54 (m, 1H), 1.27 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 170.8, 158.4, 149.1, 86.4, 59.4, 56.4, 45.5, 45.2, 30.5, 22.7, 14.5.
HRMS (ESI-Q-TOF) m/z $[M + Na]^+$ calculated for $C_{11}H_{16}N_2O_3$: 247.1053; found: 247.1051.

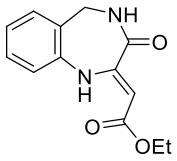
**Ethyl 2-(2-ethoxy-2-oxoethyl)-1,2,3,4-tetrahydroquinazoline-2-carboxylate (S1)**




**S1** was prepared according to a modified literature procedure.[4] In a round-bottom flask equipped with a stirring bar was added 2-aminobenzylamine (1.220 g; 10 mmol) and ethanol (10 mL). A solution of diethyl acetylene dicarboxylate (**10**; 1.6 mL; 10 mmol) in ethanol (1.5 mL) was added dropwise over 30 mL at 0 °C. The reaction mixture was stirred for 1 hour at 0 °C. Afterward, acetic acid (30 µL; 0.5 mmol) was added and the reaction mixture was stirred for 1 hour at 65 °C. Ethanol was evaporated under reduced pressure and the crude reaction mixture was purified *via* flash column chromatography (ethyl acetate/isohexane) to obtain **S1**. Crystalline white solid; yield: 2.450 g (84%). Mp: 67 – 69 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.03 (td, $J$ = 8.0, 1.3 Hz, 1H), 6.89 (d, $J$ = 7.3 Hz, 1H), 6.70 (td, $J$ = 7.4, 1.0 Hz, 1H), 6.60 (d, $J$ = 8.0 Hz, 1H), 4.90 (s, 1H), 4.24 (qd, $J$ = 7.1, 1.8 Hz, 2H), 4.17 (q, $J$ = 7.1 Hz, 2H), 3.99 (d, $J$ = 16.6 Hz, 1H), 3.94 (d, $J$ = 16.6 Hz, 1H), 3.04 (d, $J$ = 15.5 Hz, 1H), 2.85 (d, $J$ = 15.5 Hz, 1H), 1.26 (t, $J$ = 7.1 Hz, 6H).
$^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 171.9, 170.0, 141.5, 127.6, 126.0, 120.3, 118.7, 115.4, 70.8, 62.2, 61.1, 43.6, 42.7, 14.2.
HRMS (ESI-Q-TOF) m/z $[M + Na]^+$ calculated for $C_{15}H_{20}N_2O_4$: 315.1315; found: 315.1308.

**Ethyl (*Z*)-2-(3-oxo-1,3,4,5-tetrahydro-2*H*-benzo[*e*][1,4]diazepin-2-ylidene)acetate (5h)**




**5h** was prepared according to a modified literature procedure.[4] In a round-bottom flask equipped with a magnetic stirrer was added **S1** (2.450 g; 8.4 mmol) and DMF (40 mL). 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU; 3.2 mL; 20 mmol) was added and the reaction was stirred for six hours at 100 °C under nitrogen atmosphere. The reaction mixture was poured into water (500 mL) and extracted with ethyl acetate (3 x 200 mL). Combined organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude reaction mixture was purified using flash column chromatography (ethyl acetate/isohexane) to afford **5i**. White solid; yield: 1.320 g (64%). Mp: 161 – 163 °C. Regioselectivity of **5h** is only analysed in the subsequent reaction product **7h** (figure S2).

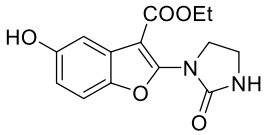
$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 10.66 (s, 1H), 8.22 (t, $J$ = 5.9 Hz, 1H)), 7.29 – 7.23 (m, 1H), 7.15 – 7.10 (m, 1H), 7.06 – 7.00 (m, 2H), 5.47 (s, 1H), 4.26 – 4.17 (m, 4H), 1.31 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 170.5, 165.5, 152.3, 139.6, 130.1, 129.4, 127.8, 124.1, 121.0, 90.5, 59.9, 43.0, 14.5.
HRMS (ESI-Q-TOF) m/z $[M + Na]^+$ calculated for $C_{13}H_{14}N_2O_3$: 269.0897; found: 269.0895.

## General procedure 3: Optimised reaction towards 2-imidazolidinone benzofurans (7a-m, 9)

To a flame-dried reaction tube flask equipped with a stirring bar was added piperazinone enaminoester **5a-i** (0.5 mmol), 1,4-benzoquinone **1a-f** (1.1 mmol) and dry acetonitrile (2 mL). The reaction was stirred at 0 °C and 48% $BF_3{\cdot}OEt_2$ (0.6 mmol; 76 µL) was added dropwise. The reaction mixture was stirred at room temperature for 3 hours. Unless otherwise specified, the solution was diluted with ethyl acetate (50 mL) and extracted with water (3 x 50 mL)

and brine (50 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude mixture was purified using flash column chromatography (ethyl acetate:isohexane) to afford **7a-m** and **9**.

**Ethyl 5-hydroxy-2-(2-oxoimidazolidin-1-yl)benzofuran-3-carboxylate (7a)**

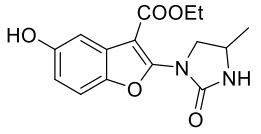



Prepared according to general procedure 3, using **5a** (92 mg; 0.5 mmol) and 1,4-benzoquinone (**1a**; 119 mg; 1.1 mmol). Purified by flash column chromatography. Crystalline white solid; yield: 124 mg (86%). Mp: 190 – 192 °C.

**Large scale synthesis:** To a flame-dried round-bottom flask equipped with a stirring bar was added piperazinone enaminoester **5a** (10 mmol), 1,4-benzoquinone **1a** (22 mmol) and dry acetonitrile (40 mL). The reaction was stirred at 0 °C and 48% $BF_3{\cdot}OEt_2$ (12 mmol; 1.52 mL) was added dropwise over 30 min. The reaction mixture was stirred at room temperature. After 3 hours, 10 mL of water was added and the reaction was stirred for an additional hour. The reaction mixture was placed in the freezer overnight to crystallize. Crystals were filtered and washed with diethyl ether. After recrystallization in ethanol, **7a** was obtained as a crystalline off-white solid. Yield: 1.792 g (62%).

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.38 (s, 1H), 7.37 (s, 1H), 7.35 (d, J = 8.8 Hz, 1H), 7.23 (d, J = 2.4 Hz, 1H), 6.75 (dd, J = 8.8, 2.6 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.01 – 3.94 (m, 2H), 3.54 – 3.46 (m, 2H), 1.32 (t, J = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 162.4, 157.2, 154.3, 153.8, 143.9, 126.6, 113.1, 111.4, 105.7, 101.0, 59.9, 45.4, 37.8, 14.2.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{14}H_{14}N_2O_5$: 313.0795; found: 313.0797.

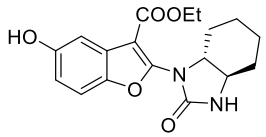
**Ethyl 5-hydroxy-2-(4-methyl-2-oxoimidazolidin-1-yl)benzofuran-3-carboxylate (7b)**




Prepared according to general procedure 3, using **5b** (99 mg; 0.5 mmol) and 1,4-benzoquinone (**1a**; 119 mg; 1.1 mmol). Purified by flash column chromatography. Off-white solid; yield: 117 mg (77%). Mp: 198 – 200 °C.

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.36 (s, 1H), 7.50 (s, 1H), 7.35 (d, $J$ = 8.8 Hz, 1H), 7.24 (d, $J$ = 2.0 Hz, 1H), 6.75 (dd, $J$ = 8.8, 2.2 Hz, 1H), 4.25 (q, $J$ = 7.1 Hz, 2H), 4.07 (t, $J$ = 8.5 Hz, 1H), 3.97 – 3.82 (m, 1H), 3.52 (dd, $J$ = 8.5, 5.9 Hz, 1H), 1.32 (t, $J$ = 7.1 Hz, 3H), 1.23 (d, $J$ = 6.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (75 MHz, DMSO-$d_6$) $\delta$ 162.4, 156.3, 154.3, 153.6, 143.9, 126.6, 113.1, 111.4, 105.7, 101.0, 59.9, 52.3, 45.4, 21.2, 14.2.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{15}H_{16}N_2O_5$: 327.0952; found: 327.0950.

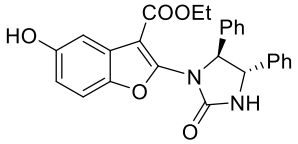
**Ethyl 5-hydroxy-2-((3a*R*,7a*R*)-2-oxooctahydro-1H-benzo[d]imidazol-1-yl)benzofuran-3-carboxylatecarboxylate (7c)**




Prepared according to general procedure 3, using **5c** (119 mg; 0.5 mmol) and 1,4-benzoquinone (**1a**; 119 mg; 1.1 mmol). The precipitate was filtered, washed with diethyl ether and recrystallised in ethanol. Crystalline white solid; yield: 109 mg (63%). Mp: 255 – 257 °C.

$^1$H NMR (400 MHz, DMSO) δ 9.42 (s, 1H), 7.51 (s, 1H), 7.39 (d, $J$ = 8.8 Hz, 1H), 7.27 (d, $J$ = 2.5 Hz, 1H), 6.78 (dd, $J$ = 8.8, 2.6 Hz, 1H), 4.30 – 4.20 (m, 2H), 3.59 (td, $J$ = 11.2, 3.1 Hz, 1H), 3.28 – 3.18 (m, 1H), 1.97 – 1.92 (m, 1H), 1.91 – 1.83 (m, 1H), 1.80 – 1.71 (m, 2H), 1.55 – 1.35 (m, 4H), 1.33 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C NMR (101 MHz, DMSO) δ 162.3, 158.6, 154.3, 153.4, 144.5, 126.5, 113.5, 111.6, 105.8, 103.3, 64.8, 60.0, 58.6, 29.0, 27.7, 23.5, 23.5, 14.2.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{18}H_{20}N_2O_5$: .367.1265; found:367.1264.

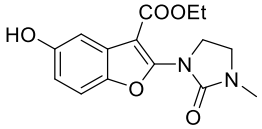
**Ethyl 5-hydroxy-2-((4*S*,5*S*)-2-oxo-4,5-diphenylimidazolidin-1-yl)benzofuran-3-carboxylate (7d)**




Prepared according to general procedure 3, using **5d** (168 mg; 0.5 mmol) and 1,4-benzoquinone (**1a**; 119 mg; 1.1 mmol). Purified by flash column chromatography. White solid; yield: 154 mg (70%). Mp: 121 – 123 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.40 (s, 1H), 8.22 (s, 1H), 7.45 – 7.26 (m, 10H), 7.23 (d, $J$ = 8.9 Hz, 1H), 7.19 (d, $J$ = 2.5 Hz, 1H), 6.70 (dd, $J$ = 8.9, 2.6 Hz, 1H), 5.22 (d, $J$ = 7.9 Hz, 1H), 4.74 (d, $J$ = 8.0 Hz, 1H), 4.32 (q, $J$ = 7.1 Hz, 2H), 1.35 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 162.3, 155.9, 154.3, 152.4, 144.2, 139.7, 137.7, 128.8, 128.8, 128.7, 128.4, 127.2, 126.8, 126.2, 113.4, 111.5, 105.8, 103.5, 69.0, 63.2, 60.2, 14.2.
HRMS (ESI-Q-TOF) m/z [M + H]$^+$ calculated for $C_{26}H_{22}N_2O_5$: 443.1601; found: 443.1595

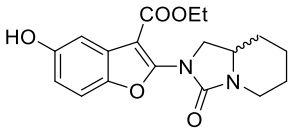
**Ethyl 5-hydroxy-2-(3-methyl-2-oxoimidazolidin-1-yl)benzofuran-3-carboxylatecarboxylate (7e)**




Prepared according to general procedure 3, using **5f** (99 mg; 0.5 mmol) and 1,4-benzoquinone (**1a**; 119 mg; 1.1 mmol). Purified by flash column chromatography. Crystalline off-white solid; yield: 42 mg (28%). Mp: 167 – 169 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.39 (s, 1H), 7.36 (d, $J$ = 8.8 Hz, 1H), 7.24 (d, $J$ = 2.5 Hz, 1H), 6.76 (dd, $J$ = 8.8, 2.6 Hz, 1H), 4.24 (q, $J$ = 7.1 Hz, 2H), 3.94 – 3.88 (m, 2H), 3.58 – 3.49 (m, 2H), 3.33 (s, 3H), 1.29 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 162.2, 155.8, 154.3, 153.8, 143.9, 126.5, 113.2, 111.4, 105.7, 101.2, 59.9, 44.4, 43.1, 30.6, 14.1.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{15}H_{16}N_2O_5$: 327.0952; found:327.0948.

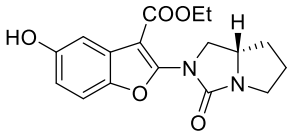
**Ethyl 5-hydroxy-2-(3-oxohexahydroimidazo[1,5-*a*]pyridin-2(3*H*)-yl)benzofuran-3-carboxylate (7f)**




Prepared according to general procedure 3, using **5g** (119 mg; 0.5 mmol) and 1,4-benzoquinone (**1a**; 119 mg; 1.1 mmol). Purified by flash column chromatography. Crystalline off-white solid; yield: 64 mg (37%). Mp: 207 – 209 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.40 (s, 1H), 7.35 (d, $J$ = 8.8 Hz, 1H), 7.24 (d, $J$ = 2.5 Hz, 1H), 6.76 (dd, $J$ = 8.8, 2.6 Hz, 1H), 4.25 (qd, $J$ = 7.1, 1.3 Hz, 2H), 4.02 (t, $J$ = 8.5 Hz, 1H), 3.78 – 3.64 (m, 2H), 3.55 (dd, $J$ = 8.8, 5.9 Hz, 1H), 2.79 (td, $J$ = 12.7, 3.2 Hz, 1H), 1.87 – 1.81 (m, 2H), 1.67 – 1.58 (m, 1H), 1.51 – 1.33 (m, 3H), 1.30 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 162.3, 154.3, 154.2, 153.7, 144.0, 126.6, 113.3, 111.4, 105.8, 101.4, 60.0, 52.4, 49.6, 40.7, 30.4, 24.3, 22.6, 14.2.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{18}H_{20}N_2O_5$: 367.1265; found: 367.1264.

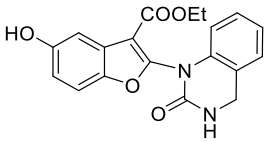
**Ethyl (*S*)-5-hydroxy-2-(3-oxotetrahydro-1*H*-pyrrolo[1,2-c]imidazol-2(3*H*)-yl)benzofuran-3-carboxylate (7g)**



Prepared according to general procedure 3, using **5h** (112 mg; 0.5 mmol) and 1,4-benzoquinone (**1a**; 119 mg; 1.1 mmol). Purified by flash column chromatography. Crystalline white solid; yield: 61 mg (37%). Mp: 156 – 157 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.42 (s, 1H), 7.37 (d, $J$ = 8.8 Hz, 1H), 7.24 (d, $J$ = 2.5 Hz, 1H), 6.77 (dd, $J$ = 8.8, 2.5 Hz, 1H), 4.25 (q, $J$ = 7.1 Hz, 2H), 4.06 (t, $J$ = 8.8 Hz, 1H), 3.94 – 3.85 (m, 2H), 3.48 (dt, $J$ = 11.0, 7.9 Hz, 1H), 3.09 – 3.03 (m, 1H), 2.09 – 1.81 (m, 3H), 1.55 – 1.43 (m, 1H), 1.30 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 162.2, 158.4, 154.4, 153.0, 144.0, 126.4, 113.4, 111.5, 105.8, 101.5, 60.0, 56.5, 48.5, 45.0, 30.4, 24.8, 14.2.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{17}H_{18}N_2O_5$: 353.1108; found: 353.1105.

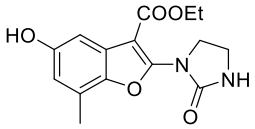
**Ethyl 5-hydroxy-2-(2-oxo-3,4-dihydroquinazolin-1(2H)-yl)benzofuran-3-carboxylate (7h)**



Prepared according to general procedure 3, using **5h** (123 mg; 0.5 mmol) and 1,4-benzoquinone (**1a**; 119 mg; 1.1 mmol). Regioselectivity of **7h** and consequently **5h** is confirmed by $^1$H – $^1$H COSY NMR analysis (Figure S2). Crystalline white solid; yield: 68 mg (39%). Mp: 249 – 251 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.57 (s, 1H), 7.74 (s, 1H), 7.52 (d, $J$ = 8.9 Hz, 1H), 7.39 (d, $J$ = 2.5 Hz, 1H), 7.26 (d, $J$ = 7.4 Hz, 1H), 7.17 – 7.09 (m, 1H), 7.06 – 7.00 (m, 1H), 6.91 (dd, $J$ = 8.9, 2.6 Hz, 1H), 6.30 (d, $J$ = 7.9 Hz, 1H), 4.51 (s, 2H), 4.17 (q, $J$ = 7.1 Hz, 2H), 1.12 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 161.5, 154.6, 152.2, 151.4, 145.4, 138.0, 128.0, 126.2, 125.9, 123.0, 119.3, 114.9, 113.6, 112.3, 108.0, 106.2, 60.2, 42.1, 13.8.
HRMS (ESI-Q-TOF) m/z [M + H]$^+$ calculated for $C_{19}H_{16}N_2O_5$: 375.0952; found: 375.0944

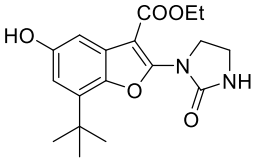
**Ethyl 5-hydroxy-7-methyl-2-(2-oxoimidazolidin-1-yl)benzofuran-3-carboxylatecarboxylate (7i)**



Prepared according to general procedure 3, using **5a** (92 mg; 0.5 mmol) and 2-methyl-1,4-benzoquinone (**1b**; 135 mg; 1.1 mmol). Purified by flash column chromatography. Off white solid; yield: 108 mg (71%). Mp: 186 – 188 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.26 (s, 1H), 7.33 (s, 1H), 7.06 (d, $J$ = 2.2 Hz, 1H), 6.60 (d, $J$ = 1.7 Hz, 1H), 4.24 (q, $J$ = 7.1 Hz, 2H), 3.99 – 3.93 (m, 2H), 3.52 – 3.46 (m, 2H), 2.34 (s, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 162.4, 157.5, 154.2, 153.6, 143.1, 126.0, 121.2, 114.2, 103.3, 101.9, 59.9, 45.6, 37.8, 14.6, 14.1.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{15}H_{16}N_2O_5$: 327.0952; found: 327.0948.

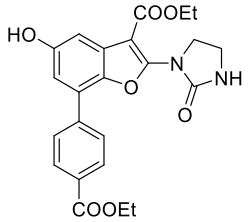
**Ethyl 7-(*tert*-butyl)-5-hydroxy-2-(2-oxoimidazolidin-1-yl)benzofuran-3-carboxylate (7j)**



Prepared according to a modified general procedure 3, using **5a** (92 mg; 0.5 mmol) and 2-*tert*-butyl-1,4-benzoquinone (**1c**; 180 mg; 1.1 mmol). The precipitate was filtered, washed with diethyl ether and recrystallised in ethanol. Crystalline white solid; yield: 134 mg (77%). Mp: 247 – 249 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.25 (s, 1H), 7.36 (s, 1H), 7.09 (d, $J$ = 2.3 Hz, 1H), 6.64 (d, $J$ = 2.3 Hz, 1H), 4.23 (q, $J$ = 7.1 Hz, 2H), 4.04 – 3.97 (m, 2H), 3.54 – 3.48 (m, 2H), 1.39 (s, 9H), 1.30 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 162.5, 157.1, 154.0, 152.9, 142.0, 134.5, 127.1, 110.2, 103.3, 100.35, 59.8, 45.4, 37.7, 33.8, 29.5, 14.2.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{18}H_{22}N_2O_5$: 369.1421; found: 369.1416.

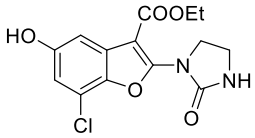
**Ethyl 7-(4-(ethoxycarbonyl)phenyl)-5-hydroxy-2-(2-oxoimidazolidin-1-yl)benzofuran-3-carboxylate (7k)**




Prepared according to general procedure 3, using **5a** (92 mg; 0.5 mmol) and 2-(4-ethoxycarbonylphenyl)-1,4-benzoquinone (**1d**; 282 mg; 1.1 mmol). Purified by flash column chromatography. Off-white solid; yield: 130 mg (59%). Mp: 193 – 194 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.62 (s, 1H), 8.08 (d, $J$ = 8.4 Hz, 2H), 7.95 (d, $J$ = 8.4 Hz, 2H), 7.41 (s, 1H), 7.32 (d, $J$ = 2.3 Hz, 1H), 7.02 (d, $J$ = 2.3 Hz, 1H), 4.34 (q, $J$ = 7.1 Hz, 2H), 4.27 (q, $J$ = 7.1 Hz, 2H), 4.05 – 3.97 (m, 2H), 3.54 – 3.47 (m, 2H), 1.38 – 1.30 (m, 6H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 165.4, 162.3, 157.0, 154.7, 154.0, 141.0, 139.7, 129.6, 129.2, 128.4, 127.9, 123.4, 112.1, 106.2, 100.7, 60.8, 60.0, 45.4, 37.7, 14.2.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{23}H_{22}N_2O_7$: 461.1319; found: 461.1309.

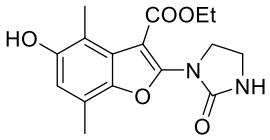
**Ethyl 7-chloro-5-hydroxy-2-(2-oxoimidazolidin-1-yl)benzofuran-3-carboxylate (7l)**




Prepared according to general procedure 3, using **5a** (92 mg; 0.5 mmol) and 2-chloro-1,4-benzoquinone (**1e**; 156 mg; 1.1 mmol). After 3 hours, 0.1 mL of water was added and the reaction was stirred for an additional hour. The product crystallised from the reaction mixture and was filtered off and washed with diethyl ether. Crystalline white solid; yield: 92 mg (57%). Mp: 215 – 217 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.80 (s, 1H), 7.46 (s, 1H), 7.20 (d, $J$ = 2.3 Hz, 1H), 6.85 (d, $J$ = 2.3 Hz, 1H), 4.25 (q, $J$ = 7.1 Hz, 2H), 4.03 – 3.97 (m, 2H), 3.54 – 3.47 (m, 2H), 1.31 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 161.9, 156.9, 154.9, 154.4, 139.6, 128.1, 114.9, 112.9, 105.0, 101.5, 60.2, 45.4, 37.8, 14.1.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{14}H_{13}ClN_2O_5$: 347.0405; found: 347.0405.

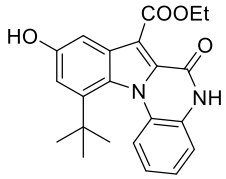
**Ethyl 5-hydroxy-4,7-dimethyl-2-(2-oxoimidazolidin-1-yl)benzofuran-3-carboxylate (7m)**




Prepared according to general procedure 3, using **5a** (92 mg; 0.5 mmol) and 2,5-dimethyl -1,4-benzoquinone (**1f**; 150 mg; 1.1 mmol). Purified by flash column chromatography. Crystalline white solid; yield: 18 mg (11%). Mp: 206 – 207 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.99 (s, 1H), 7.33 (s, 1H), 6.64 (s, 1H), 4.17 (q, $J$ = 7.1 Hz, 2H), 3.99 – 3.92 (m, 2H), 3.53 – 3.46 (m, 2H), 2.31 (s, 3H), 2.27 (s, 3H), 1.26 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 163.4, 157.5, 151.4, 151.1, 142.8, 125.0, 117.5, 113.5, 112.5, 102.8, 60.1, 45.2, 37.6, 14.4, 14.0, 12.0.
HRMS (ESI-Q-TOF) m/z [M + Na]$^+$ calculated for $C_{16}H_{18}N_2O_5$: 341.1108; found: 341.1095.

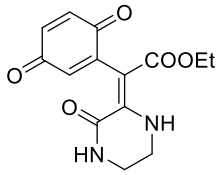
**Ethyl 11-(*tert*-butyl)-9-hydroxy-6-oxo-5,6-dihydroindolo[1,2-*a*]quinoxaline-7-carboxylate (9)**




Prepared according to general procedure 3, using **5e** (116 mg; 0.5 mmol) and 2-*tert*-butyl-1,4-benzoquinone (**1c**; 180 mg; 1.1 mmol). After column chromatography, **9** crystallised and was filtered off. Crystalline yellow solid; yield: 57 mg (36%). Mp: 258 – 260 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.40 (s, 1H), 9.02 (s, 1H), 7.76 (d, $J$ = 8.0 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.35 – 7.28 (m, 2H), 6.98 (d, $J$ = 2.4 Hz, 1H), 6.54 (d, $J$ = 2.5 Hz, 1H), 4.49 (q, $J$ = 7.0 Hz, 2H), 1.43 (s, 9H), 1.40 (t, $J$ = 7.1 Hz, 3H).
$^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$) $\delta$ 160.6, 153.5, 153.4, 152.0, 139.5, 133.6, 132.1, 131.5, 129.6, 129.4, 128.2, 123.2, 115.1, 108.0, 103.7, 91.8, 68.3, 33.7, 29.6, 15.0.
HRMS (ESI-Q-TOF) m/z [M + H]$^+$ calculated for $C_{22}H_{22}N_2O_4$: 379.1652; found: 379.1651

**Ethyl-2-(3,6-dioxocyclohexa-1,4-dien-1-yl)-2-(3-oxopiperazin-2-ylidene)acetate (8)**




Prepared according to a modified literature procedure.[5] In a round-bottom flask equipped with a magnetic stirrer was added 1,4-benzoquinone (**1a**; 640 mg; 6 mmol), **5a** (553 mg; 3 mmol), ethanol (5 mL) and acetic acid (1 mL). The reaction was stirred for six hours. The reaction was placed in the freezer overnight to crystallize. The crystals were filtered off and washed with cold diethyl ether to obtain **8**. Crystalline red solid; yield: 616 mg (71 %). Mp: 195 – 198 °C. $^1$H NMR and melting point corresponds with literature reports.[6]

## One-pot two step reaction towards 2-imidazolidinone benzofuran 7a

In a round-bottom flask equipped with a magnetic stirrer was added ethylenediamine (**10a**; 34 µL; 0.5 mmol) and ethanol (1.5 mL). The solution was cooled to 0 °C and diethyl acetylene dicarboxylate (**11**; 80 µL; 0.5 mmol) in ethanol (0.5 mmol) was added dropwise (0.05 mL/min) using a syringe pump. After addition, the reaction was stirred at room temperature. After one hour, solvent was removed under reduced pressure. To the crude piperazinone enaminoesters **5a** was added dry acetonitrile (2 mL) and 1,4-benzoquinone (**1a**; 119 mg; 1.1 mmol). The suspension was cooled to 0 °C and 48% $BF_3{\cdot}OEt_2$ (0.6 mmol; 76 µL) was added dropwise. The reaction was stirred at room temperature. After three hours, the reaction was diluted with ethyl acetate (50 mL) and extracted with water (3 x 50 mL) and brine (50 mL), dried over $MgSO_4$, filtered and solvent was removed under reduced pressure. The crude mixture was purified by flash column chromatography to obtain 98 mg of **7a** (68%).

# $^{1}H - {}^{1}H$ COSY analysis

**Figure S1. $^{1}H - {}^{1}H$ COSY analysis of 5b**

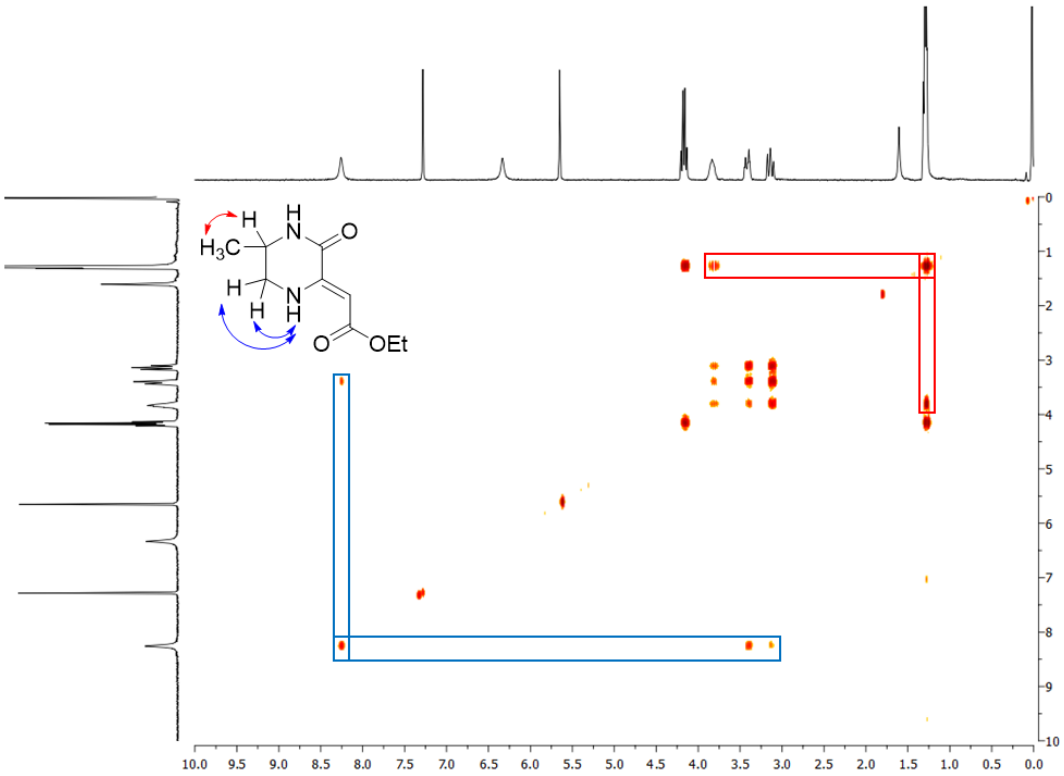
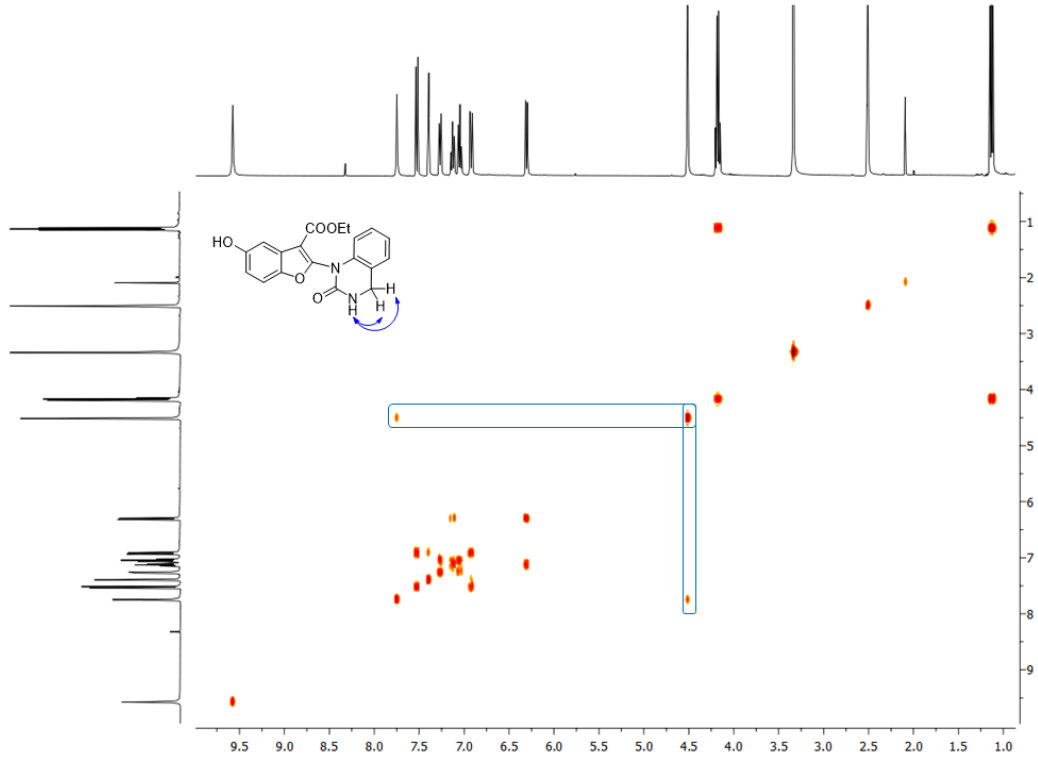
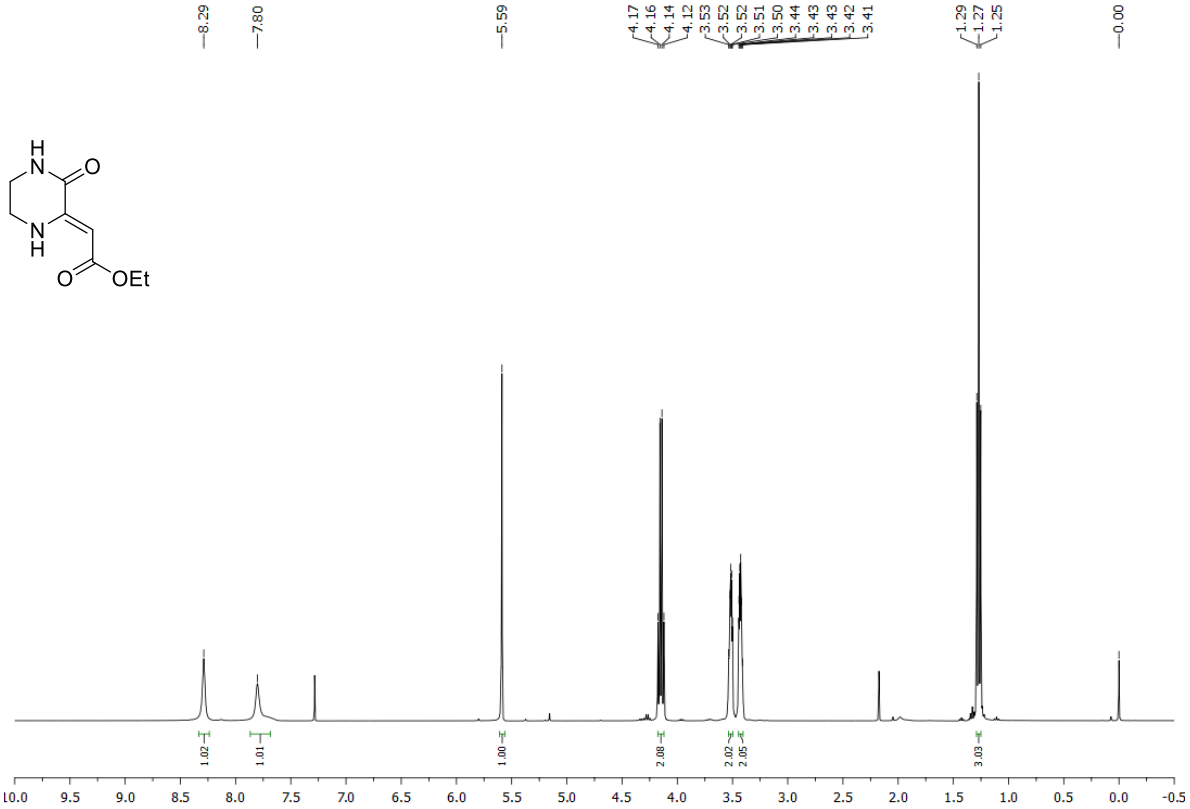



**Figure S2. $^{1}H - {}^{1}H$ COSY analysis of 7h**

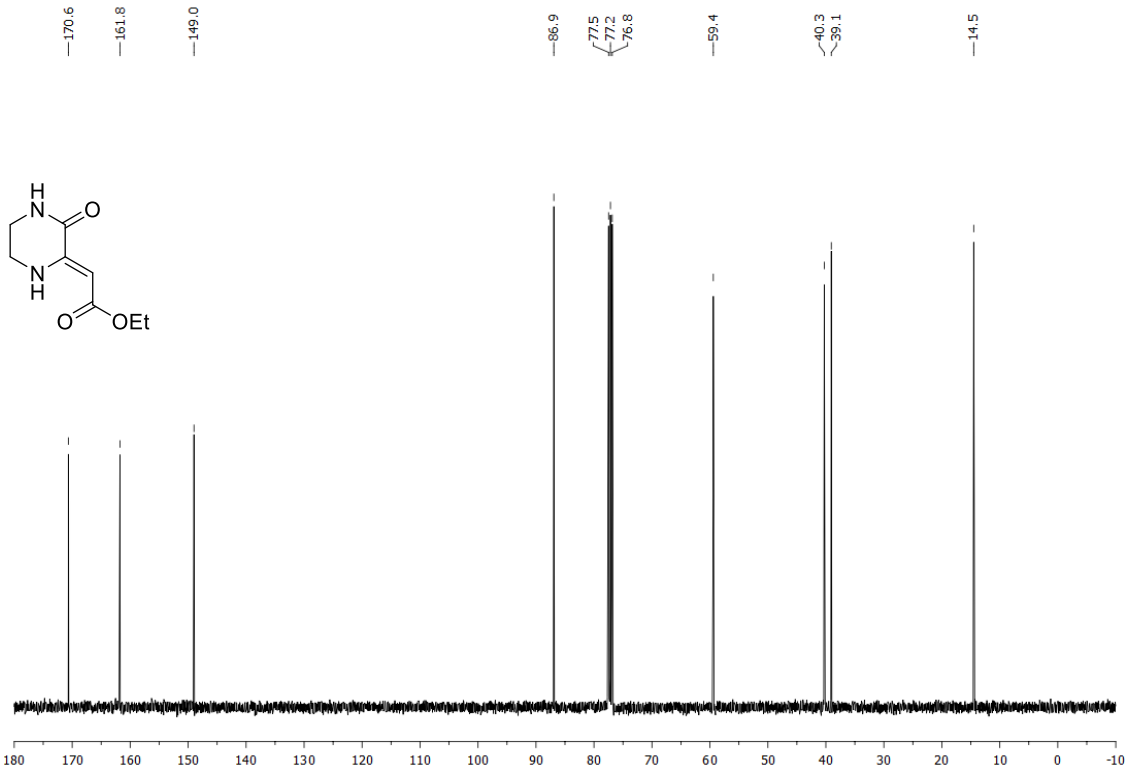


# $^{1}H$ and $^{13}C\{^{1}H\}$ NMR spectra

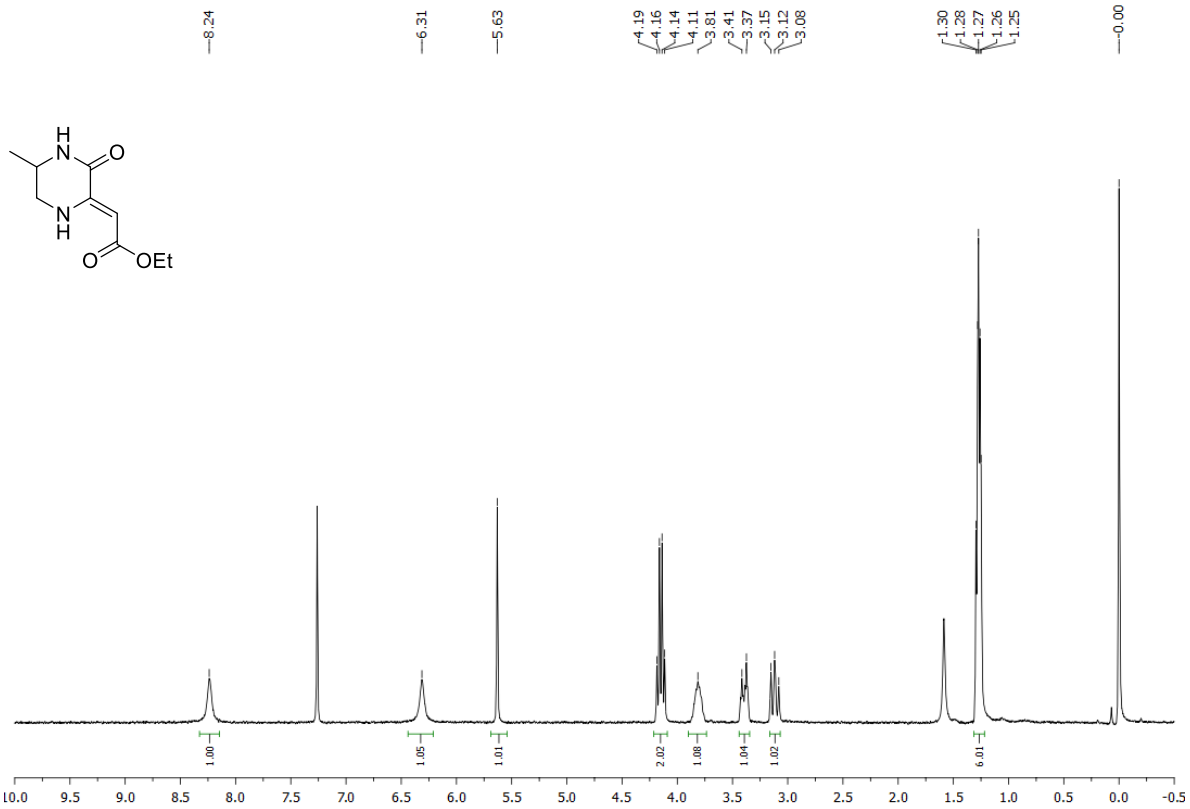
**5a** ($^{1}H$ NMR, 400 MHz, $CDCl_3$)



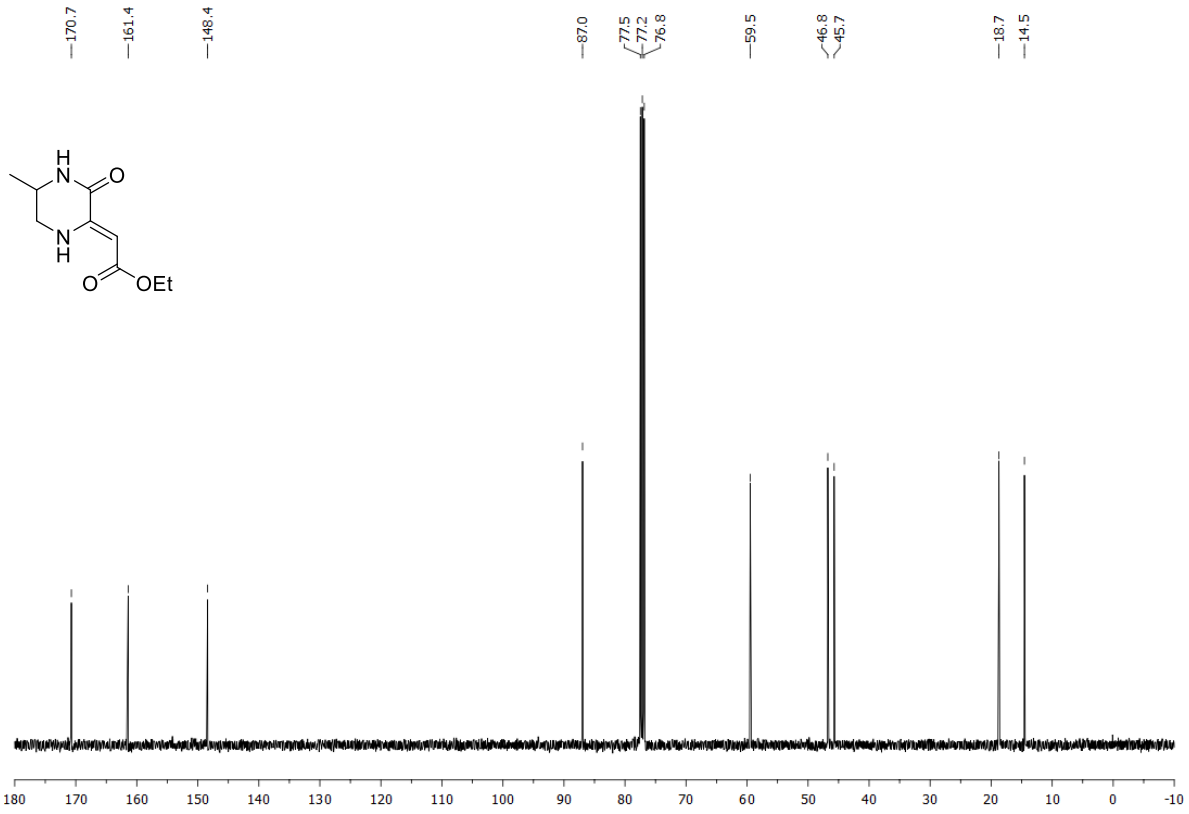

**5a** ($^{13}C\{^{1}H\}$ NMR, 101 MHz, $CDCl_3$)



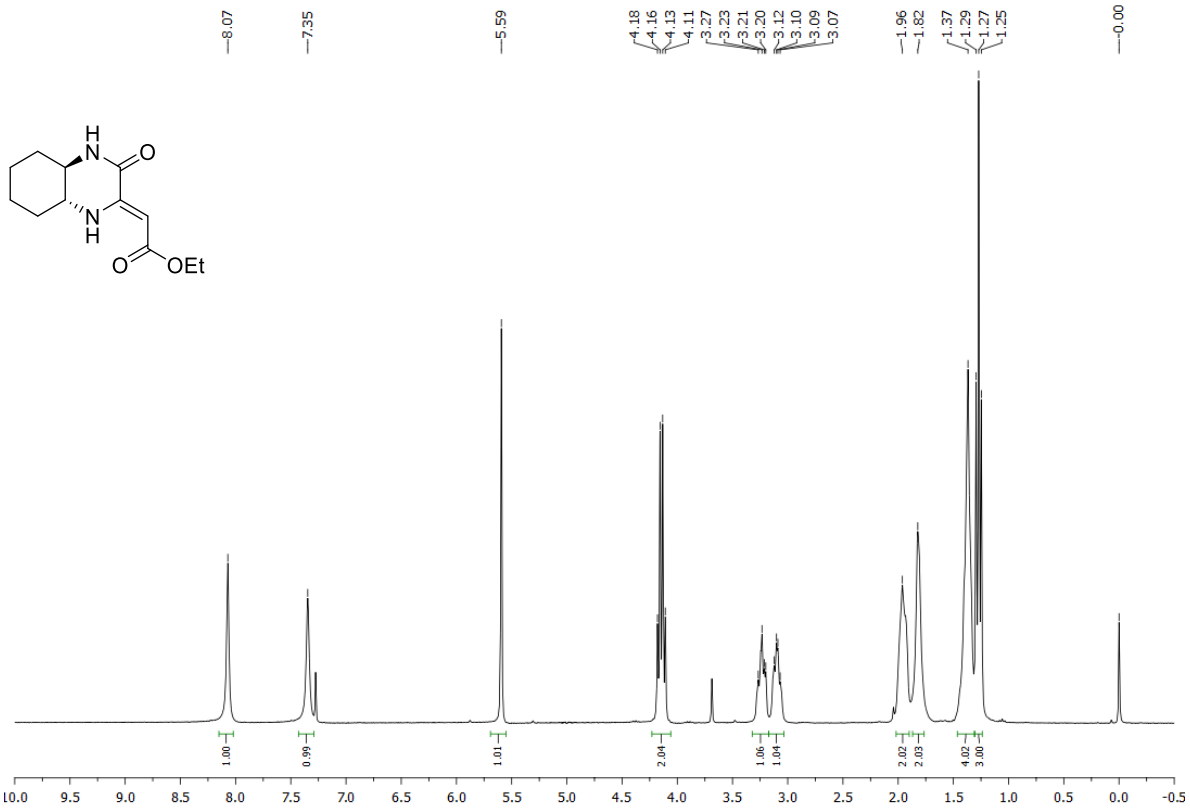
**5b** ($^{1}$H NMR, 300 MHz, $CDCl_3$)



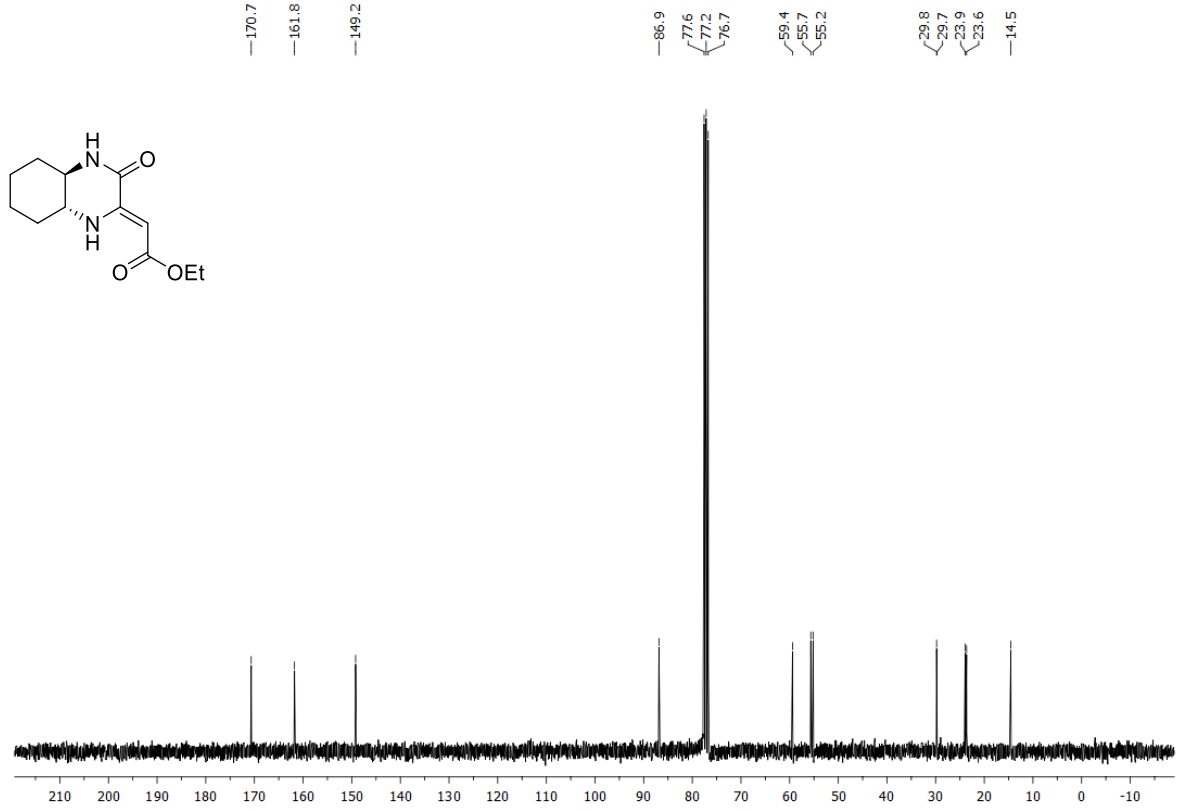

**5b** ($^{13}$C{$^{1}$H} NMR, 101 MHz, $CDCl_3$)



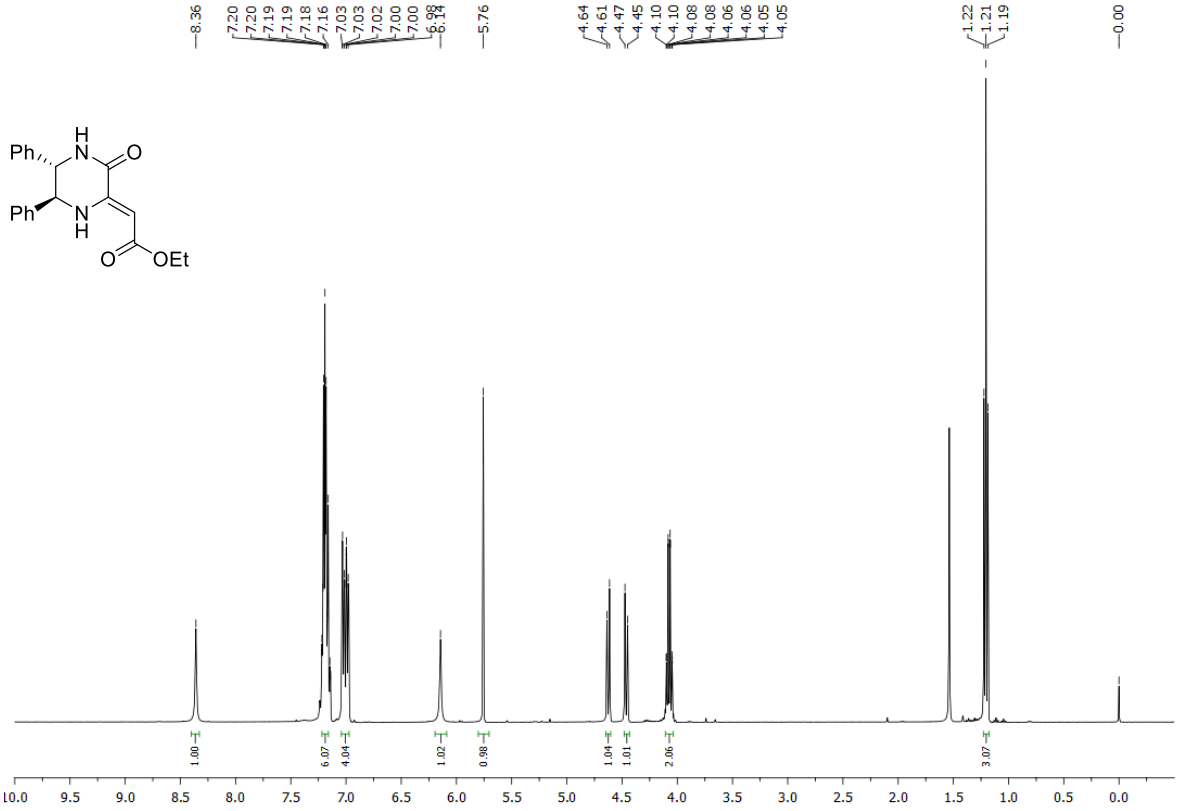
**5c** ($^{1}$H NMR, 300 MHz, $CDCl_3$)



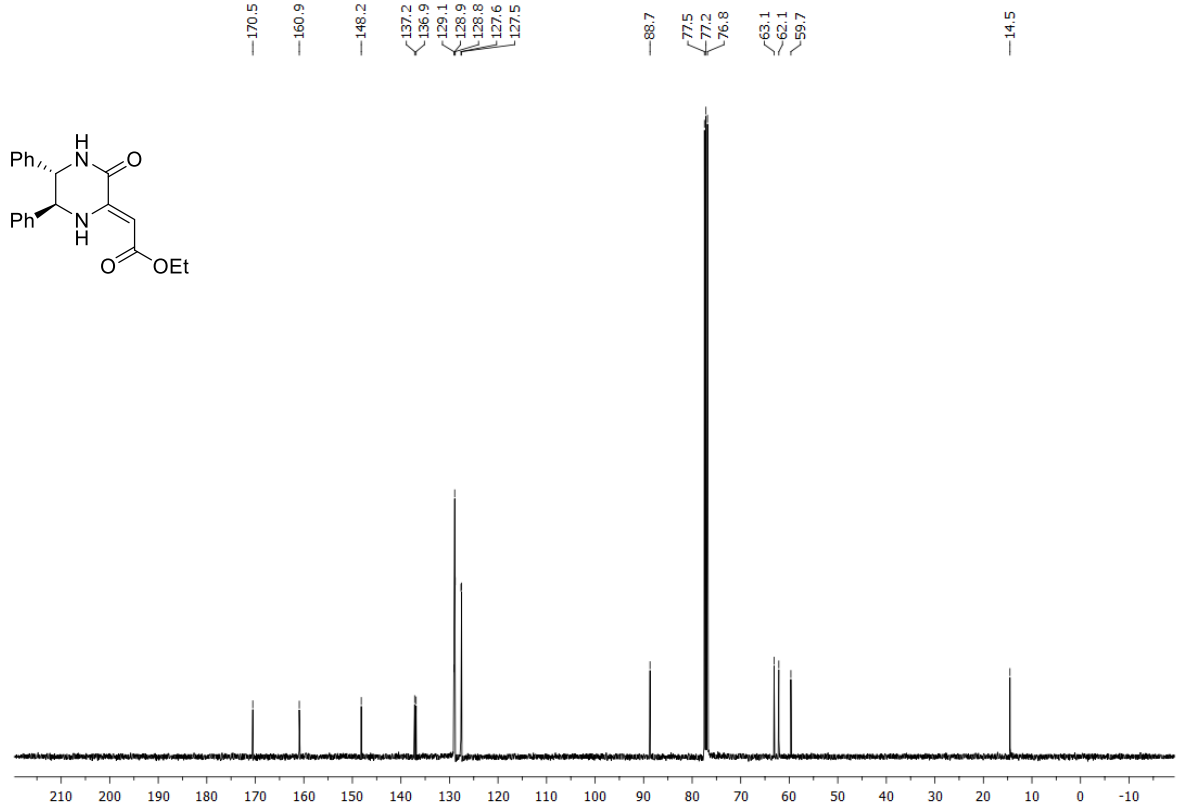

**5c** ($^{13}C\{^{1}H\}$ NMR, 75 MHz, $CDCl_3$)



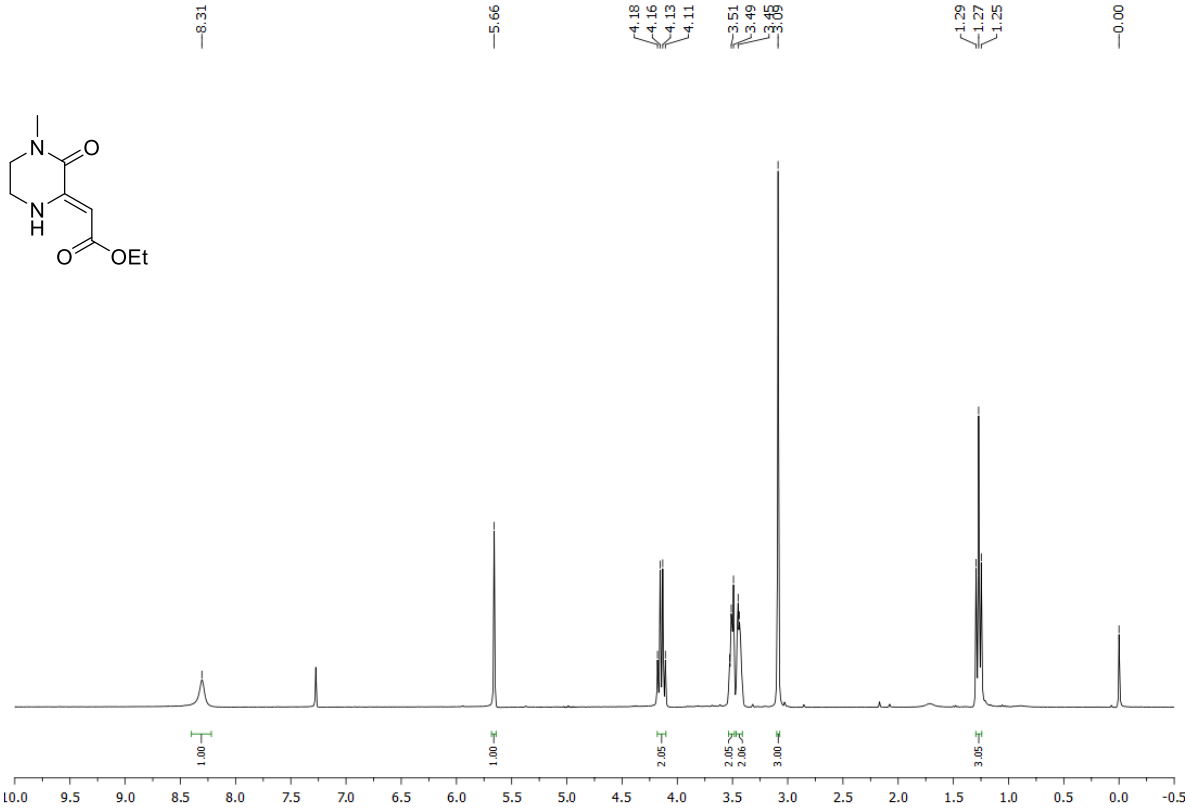
**5d** ($^{1}$H NMR, 400 MHz, $CDCl_3$)



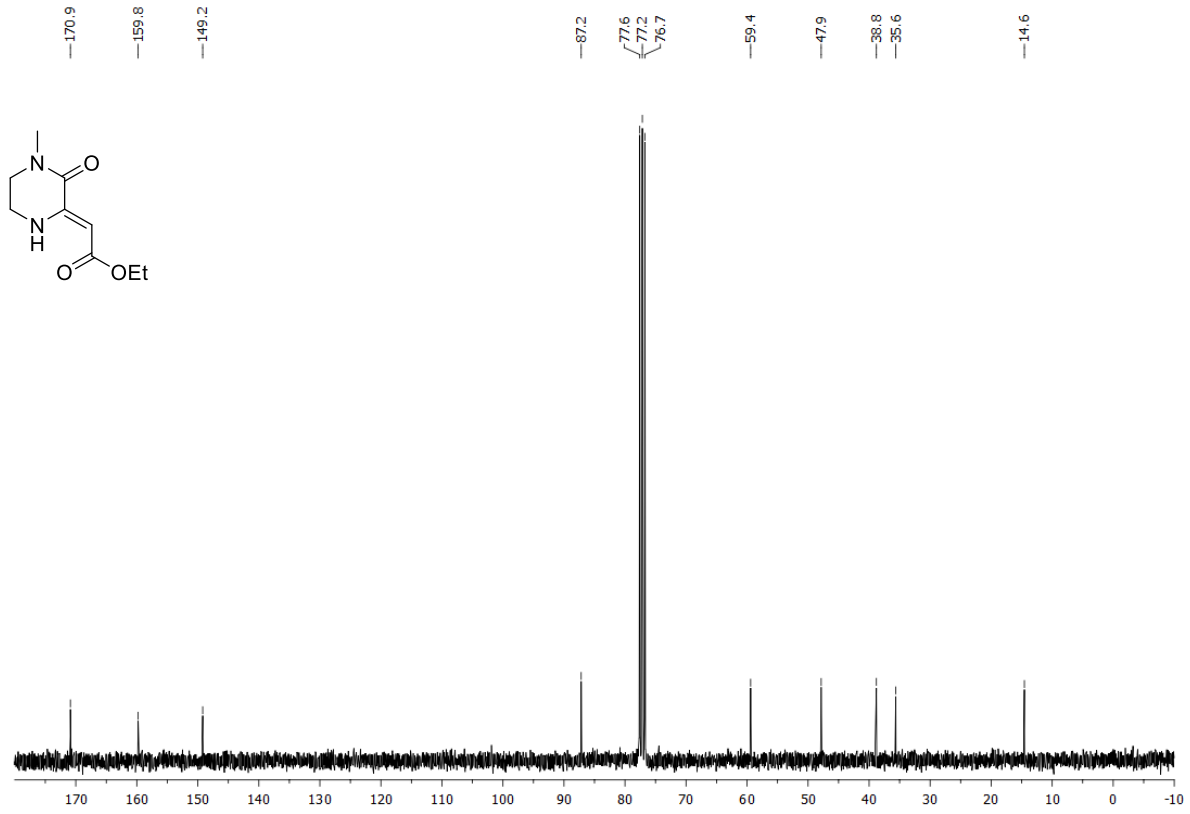

**5d** ($^{13}$C{$^{1}$H} NMR, 101 MHz, $CDCl_3$)



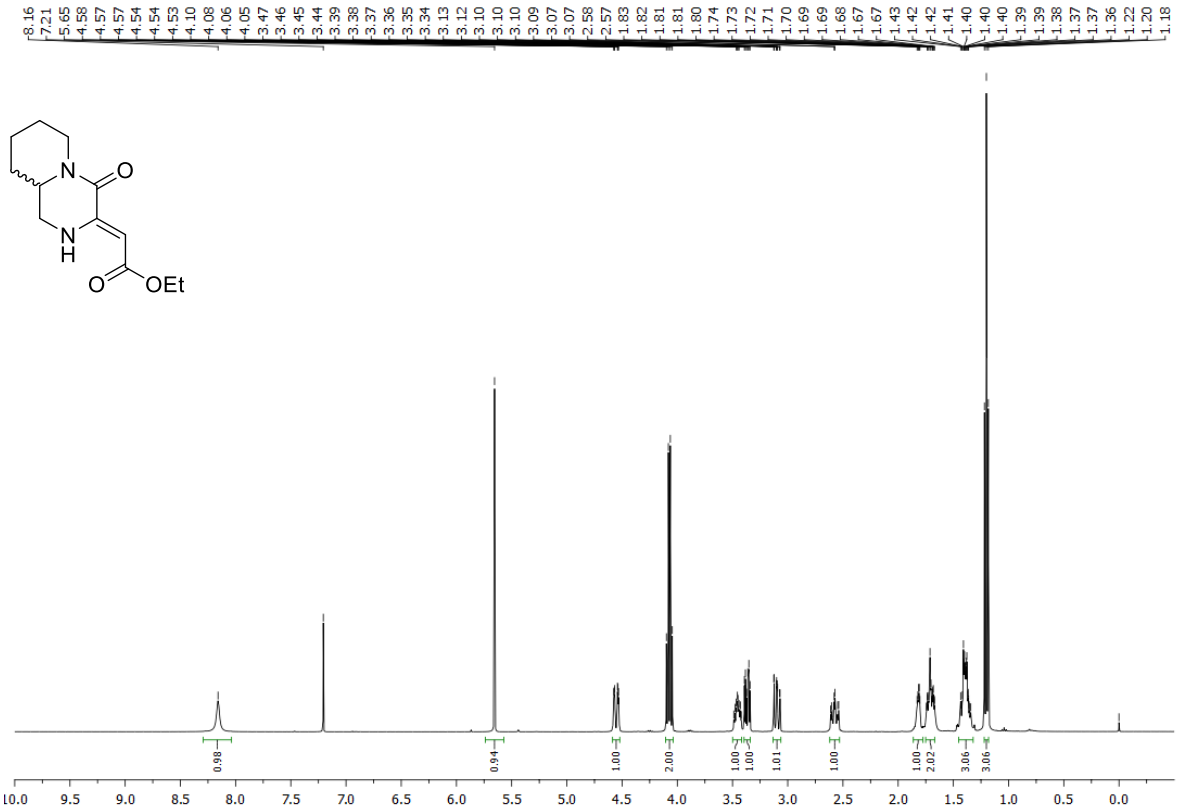
**5e** ($^1$H NMR, 300 MHz, $CDCl_3$)



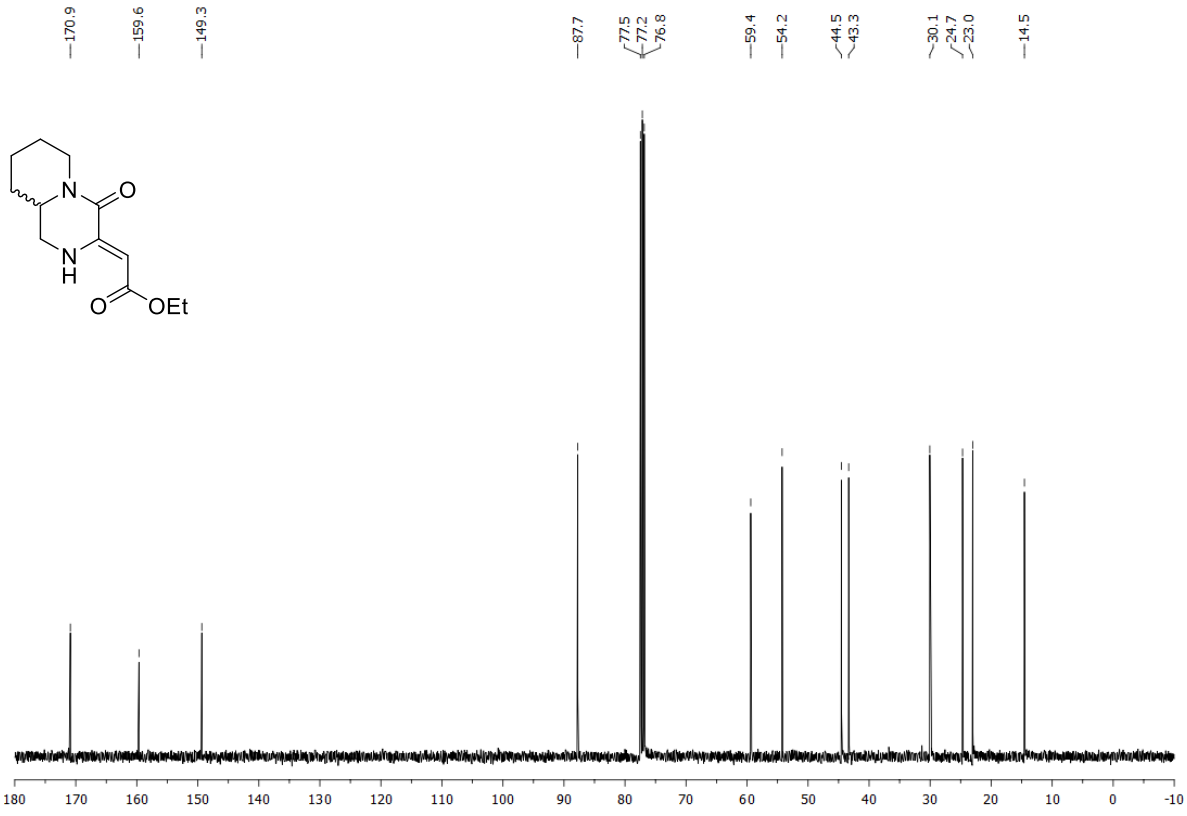

**5e** ($^{13}C\{^1H\}$ NMR, 75 MHz, $CDCl_3$)



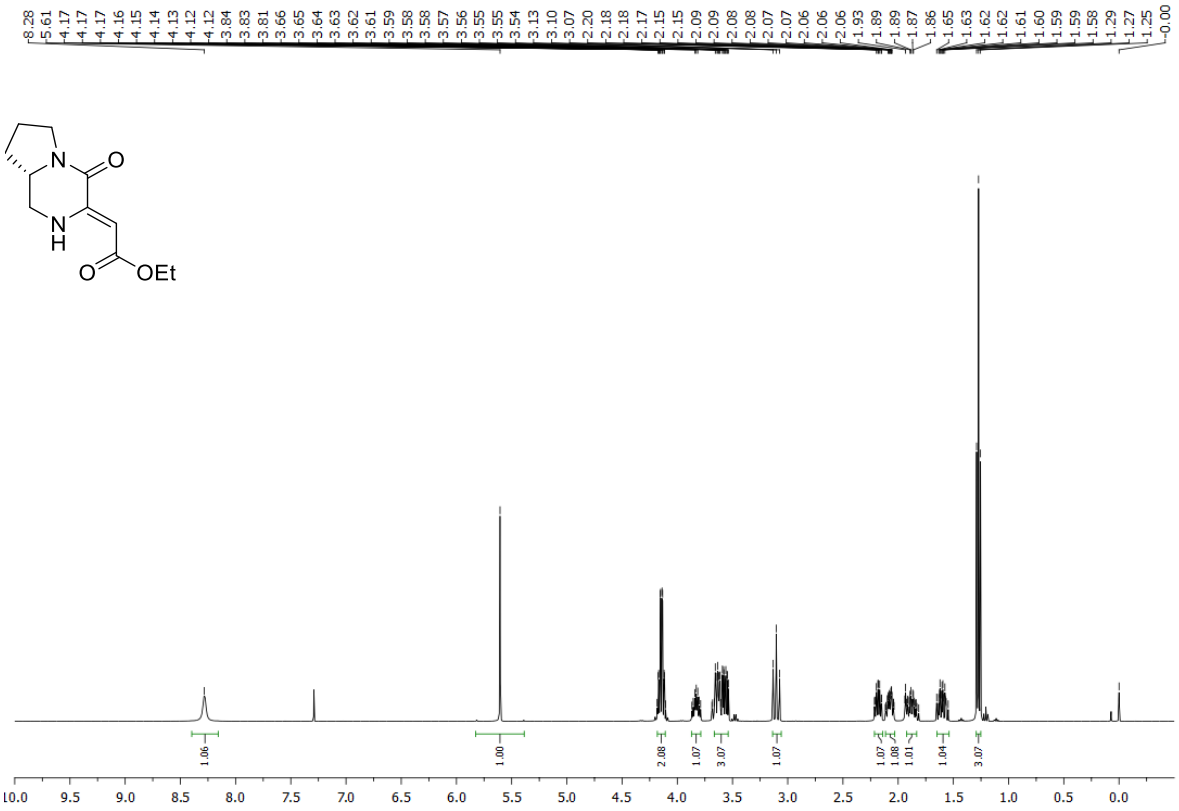
**5f** ($^{1}$H NMR, 400 MHz, $CDCl_3$)



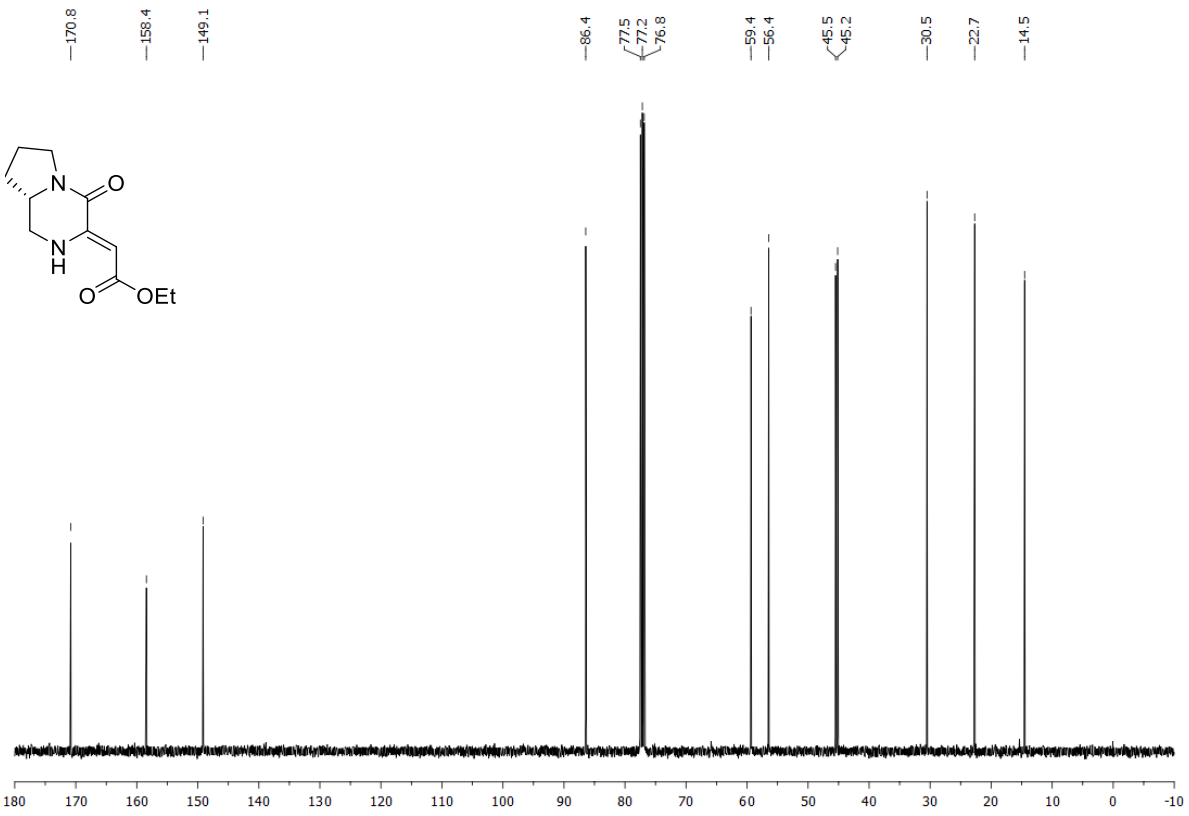

**5f** ($^{13}$C{$^{1}$H} NMR, 75 MHz, $CDCl_3$)



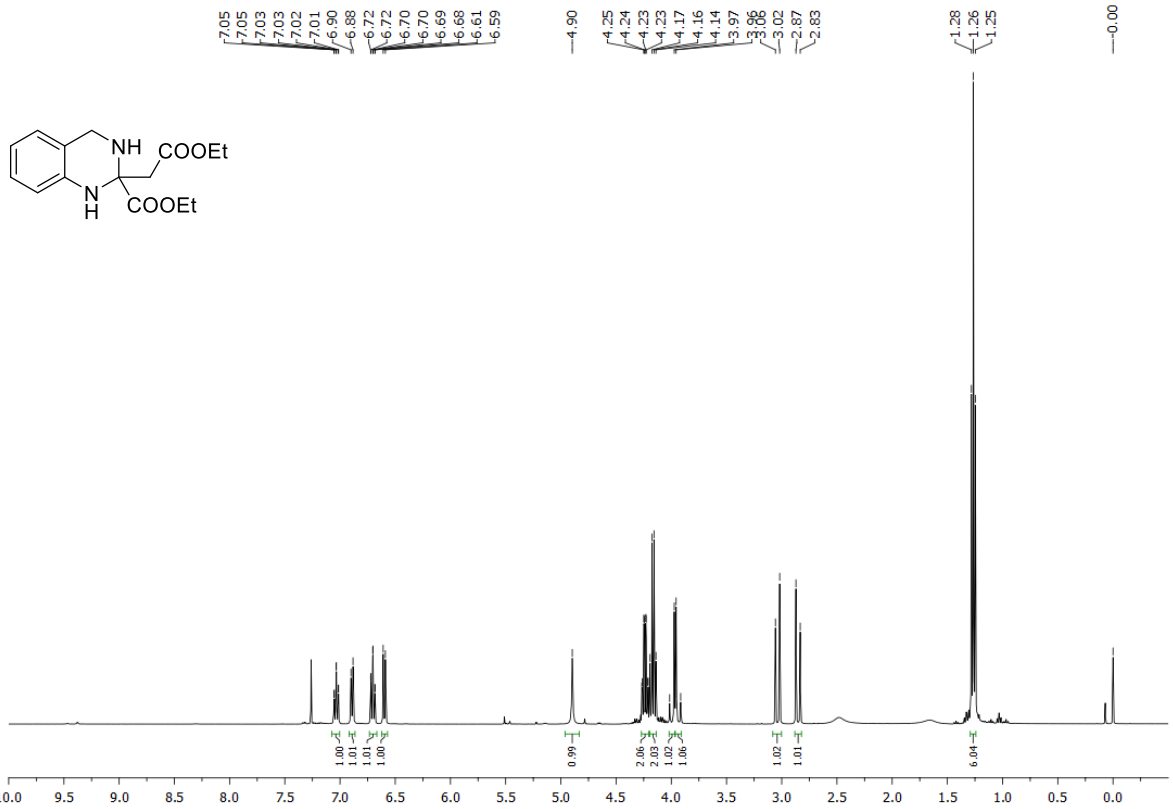
**5g** ($^1$H NMR, 400 MHz, $CDCl_3$)



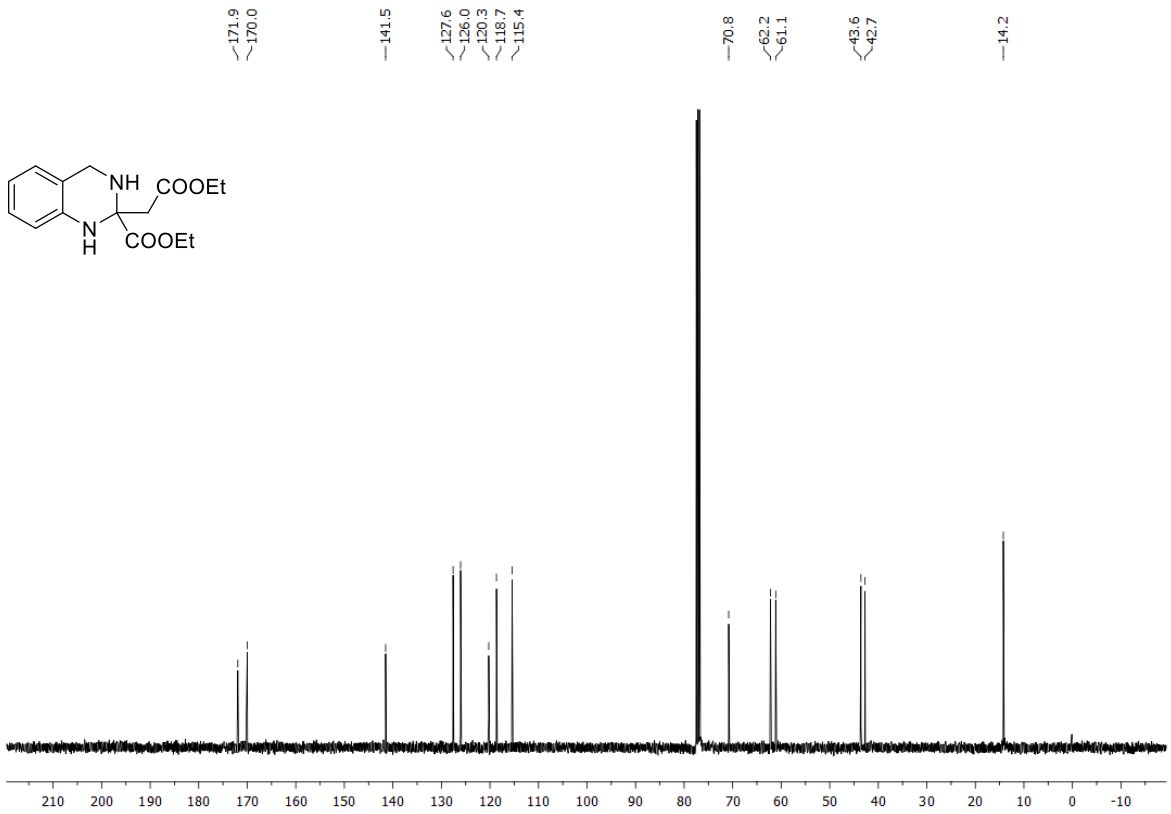

**5g** ($^{13}C\{^1H\}$ NMR, 101 MHz, $CDCl_3$)



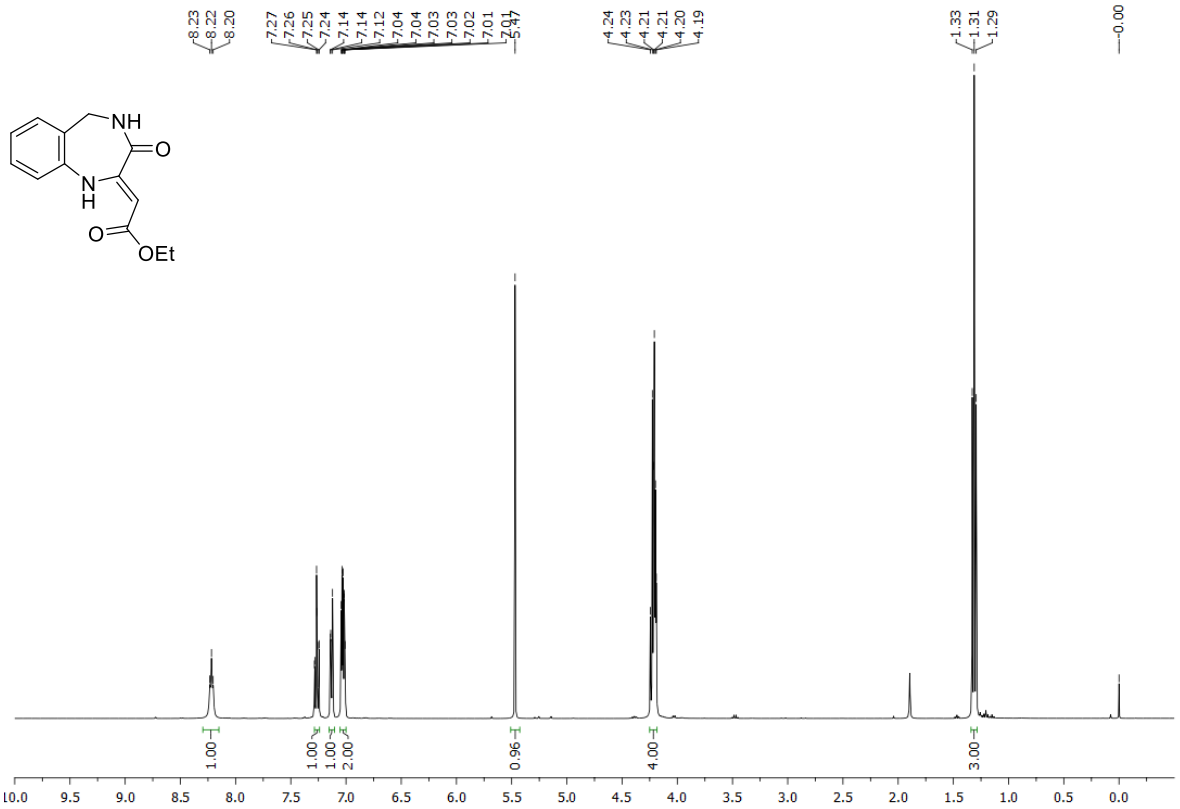
**S1** ($^{1}$H NMR, 400 MHz, $CDCl_3$)



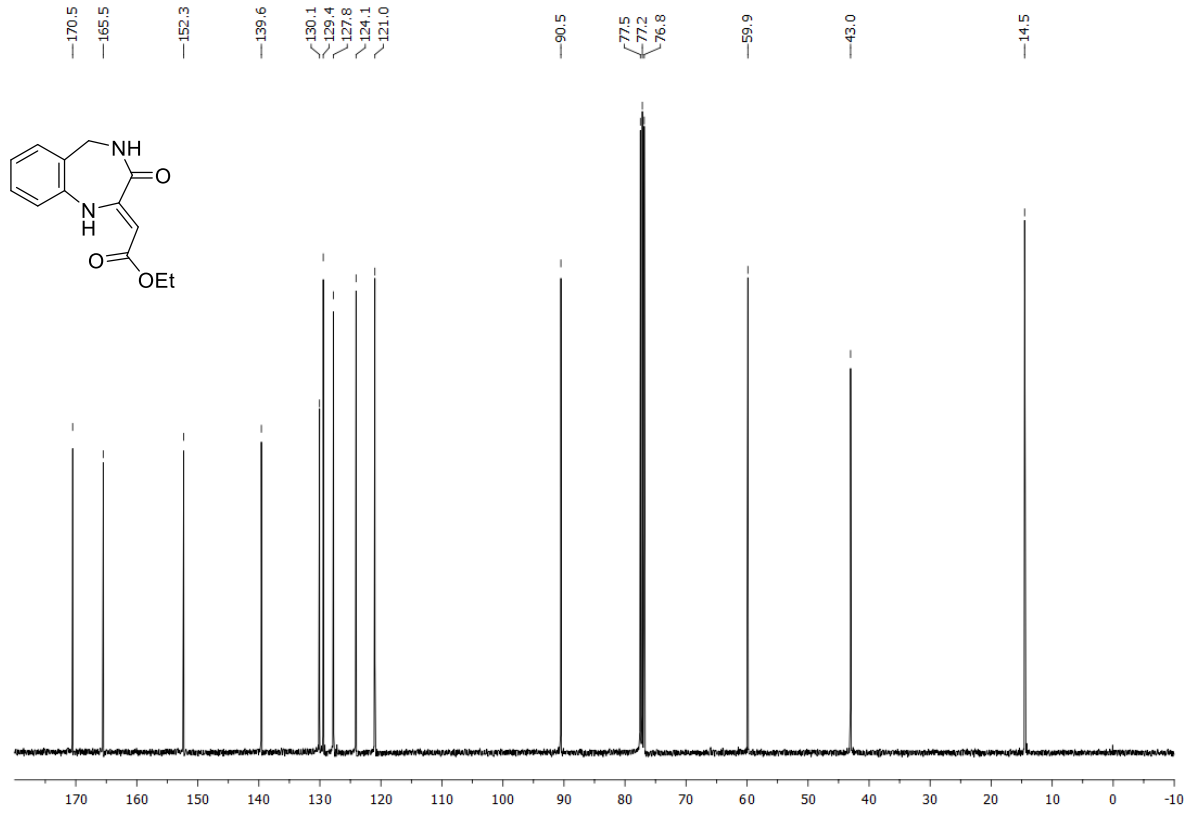

**S1** ($^{13}$C{$^{1}$H} NMR, 101 MHz, $CDCl_3$)



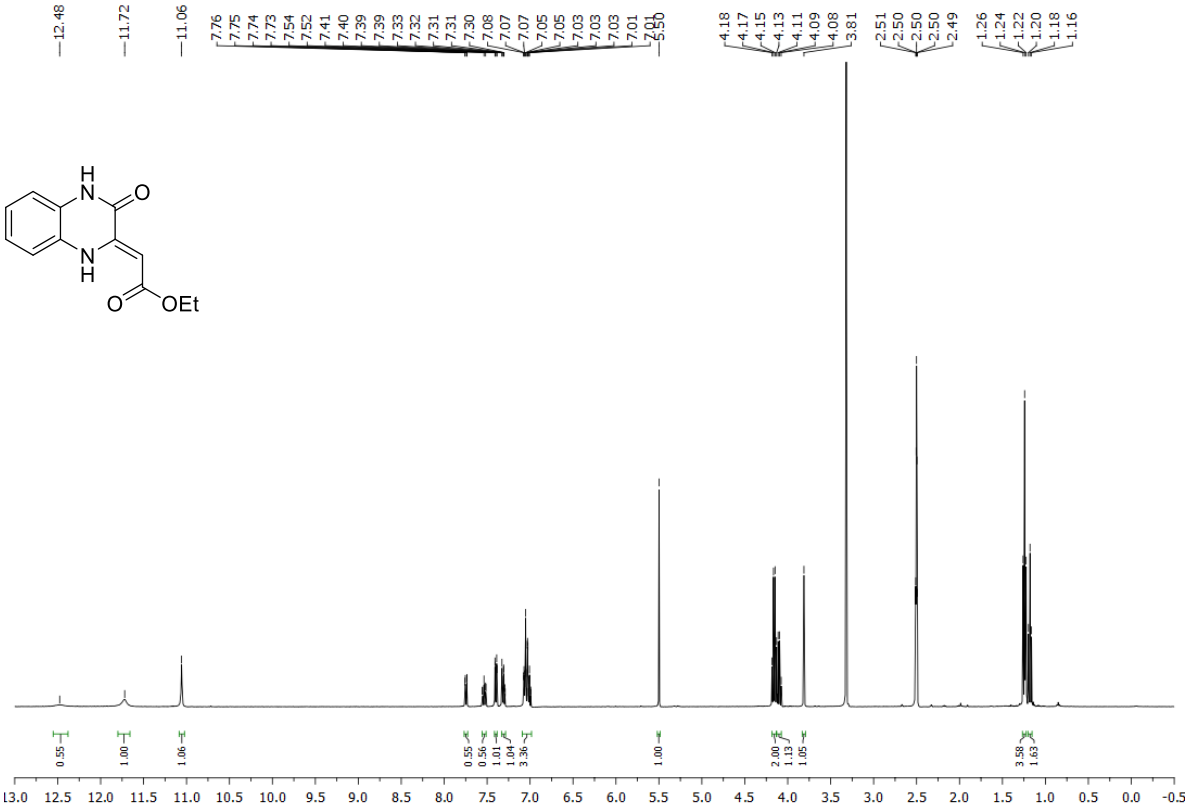
**5h** ($^{1}$H NMR, 400 MHz, $CDCl_3$)



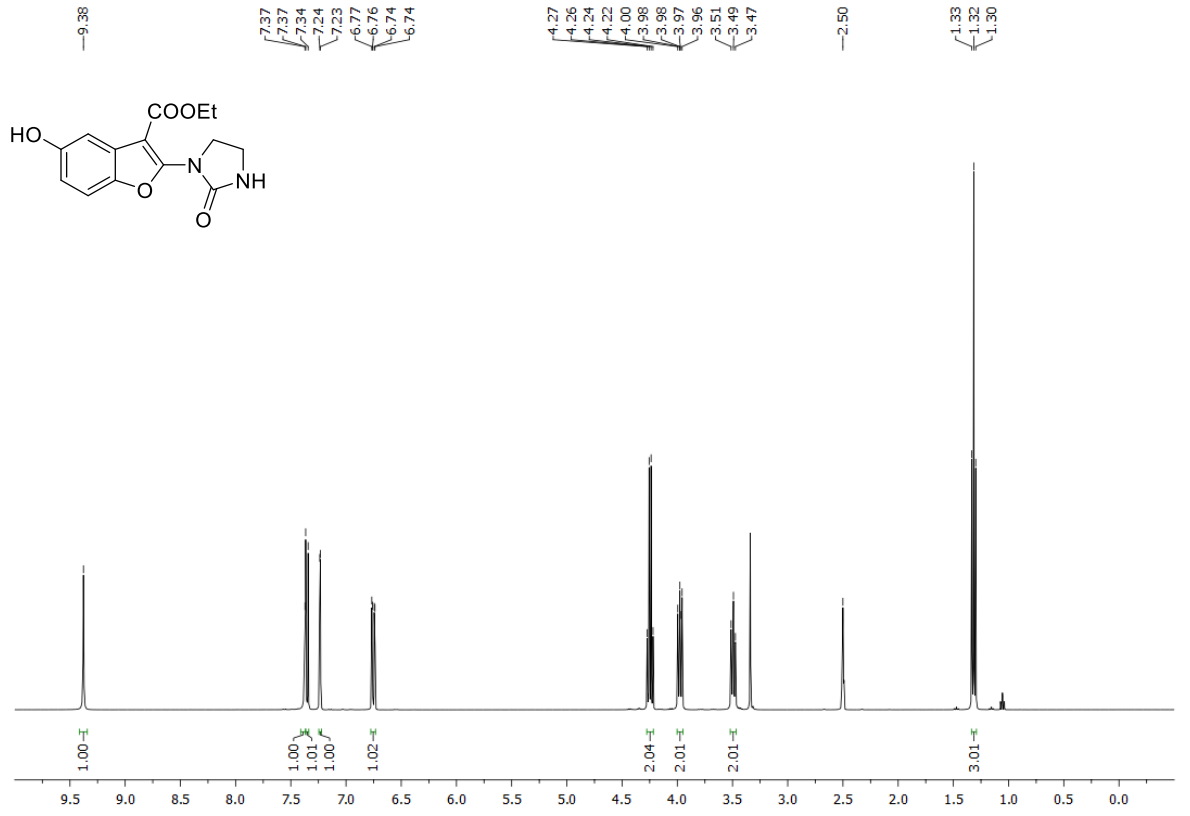

**5h** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



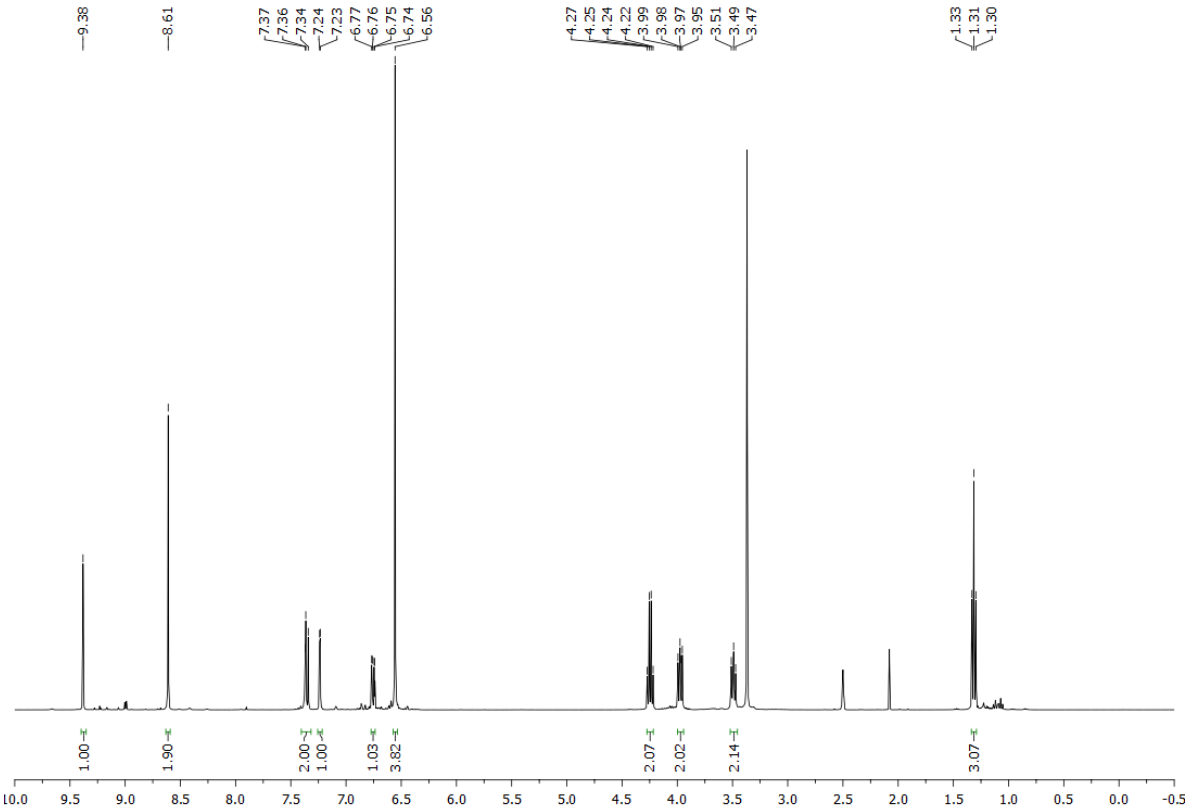
**5i** ($^1$H NMR, 400 MHz, DMSO-$d_6$)



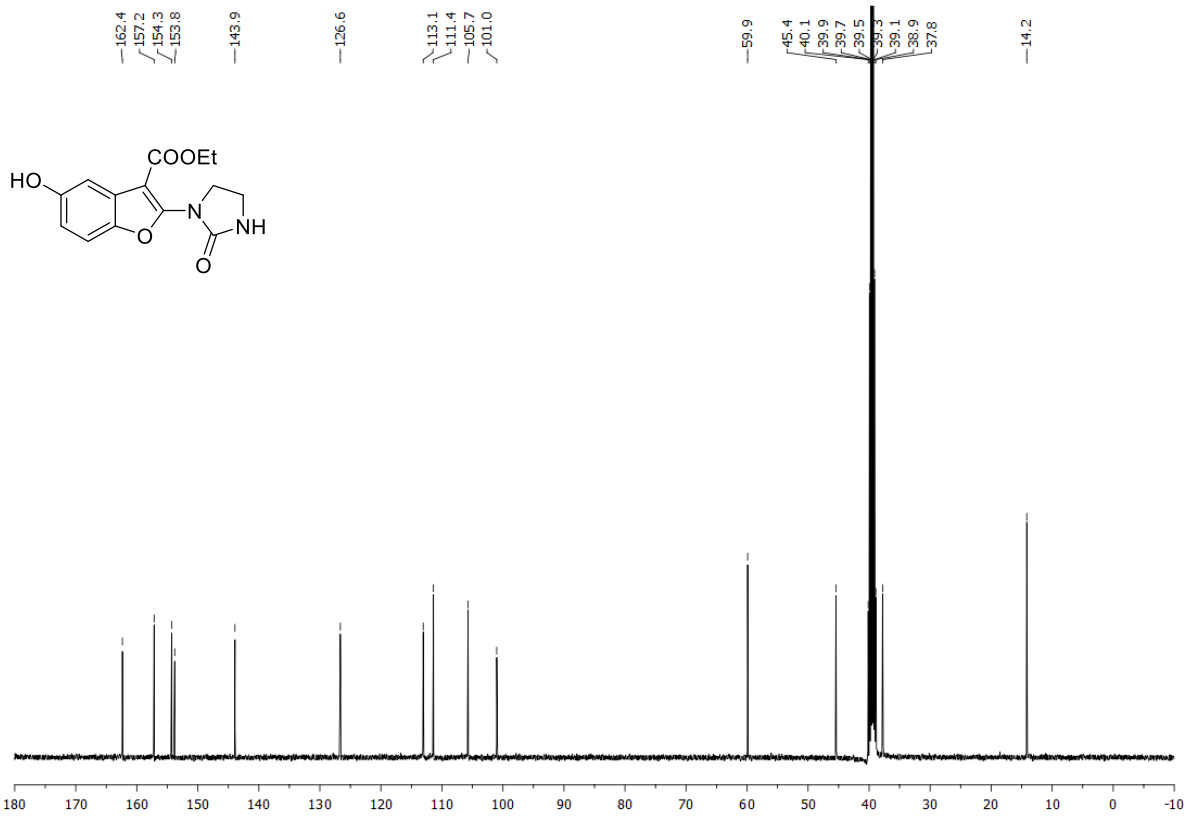

**7a** ($^1$H NMR, 400 MHz, DMSO-$d_6$)



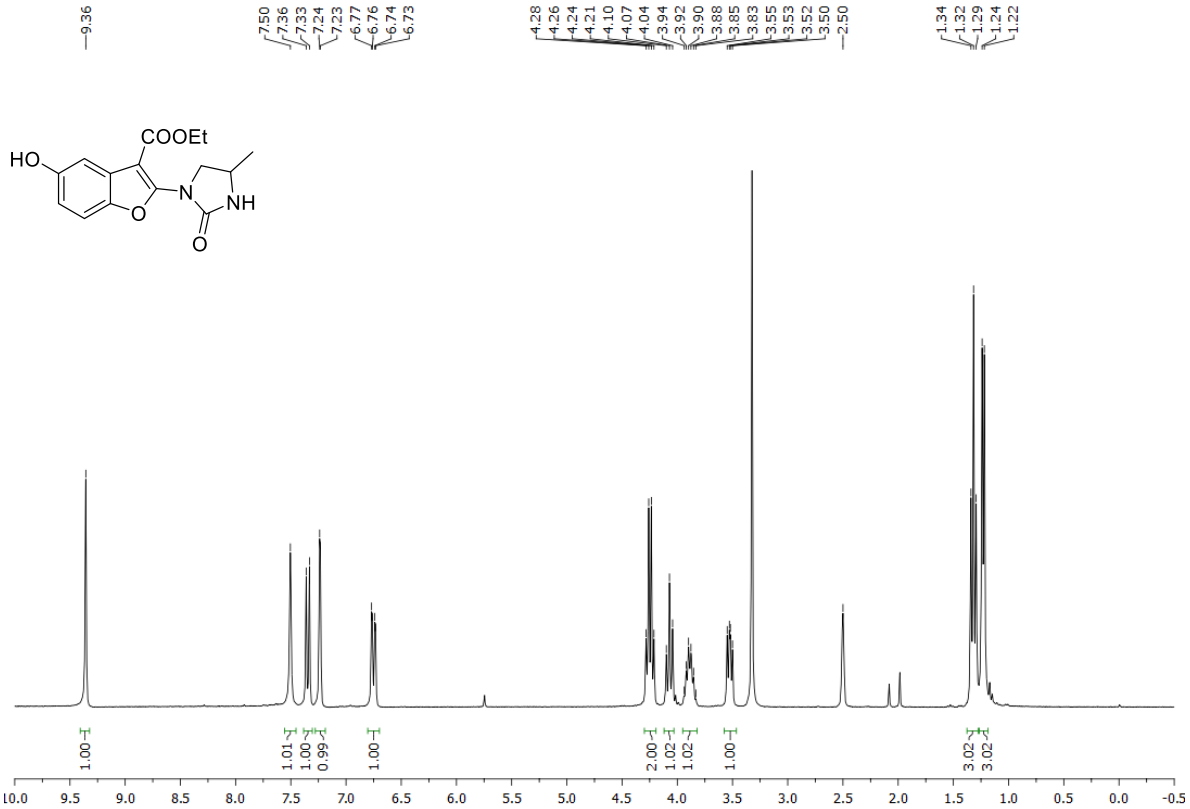
**7a, reaction mixture after extraction** ($^1$H NMR, 400 MHz, DMSO-$d_6$). (Excess BQ is sublimated during drying)



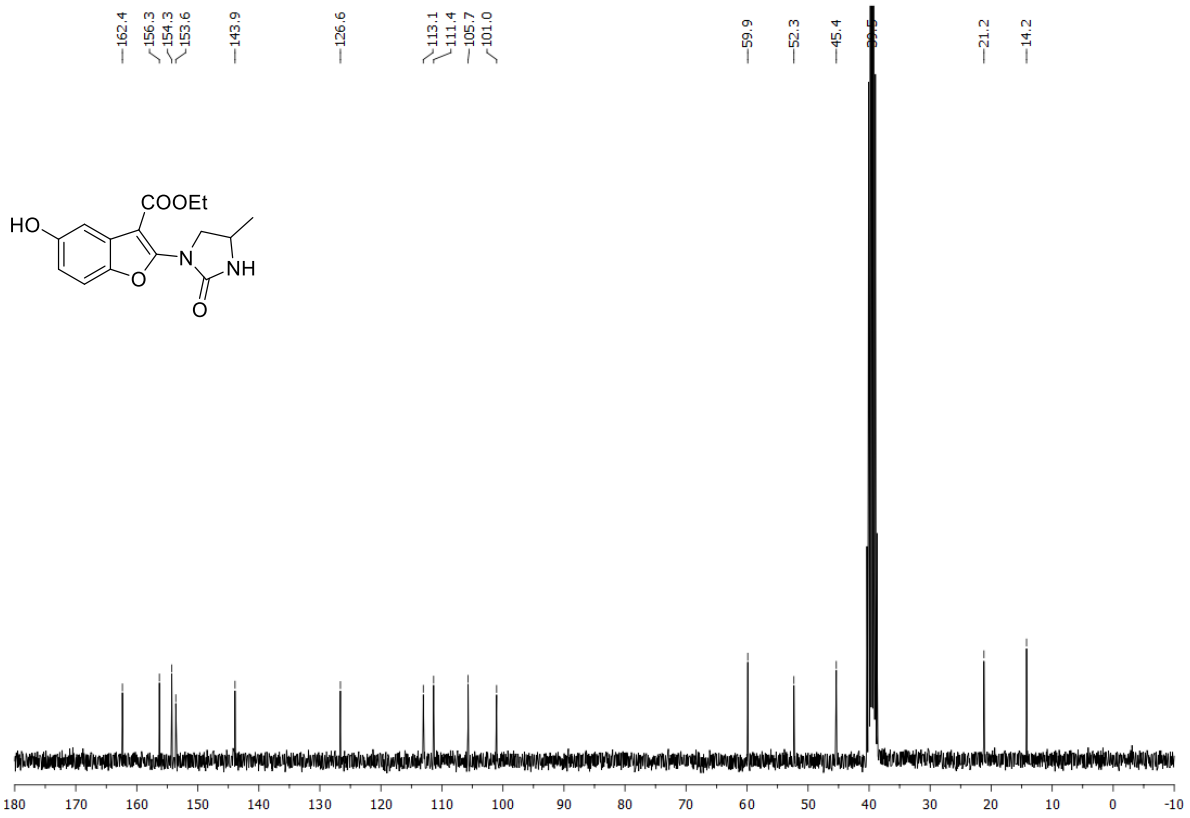

**7a** ($^{13}$C{$^1$H} NMR, 101 MHz, DMSO-$d_6$)



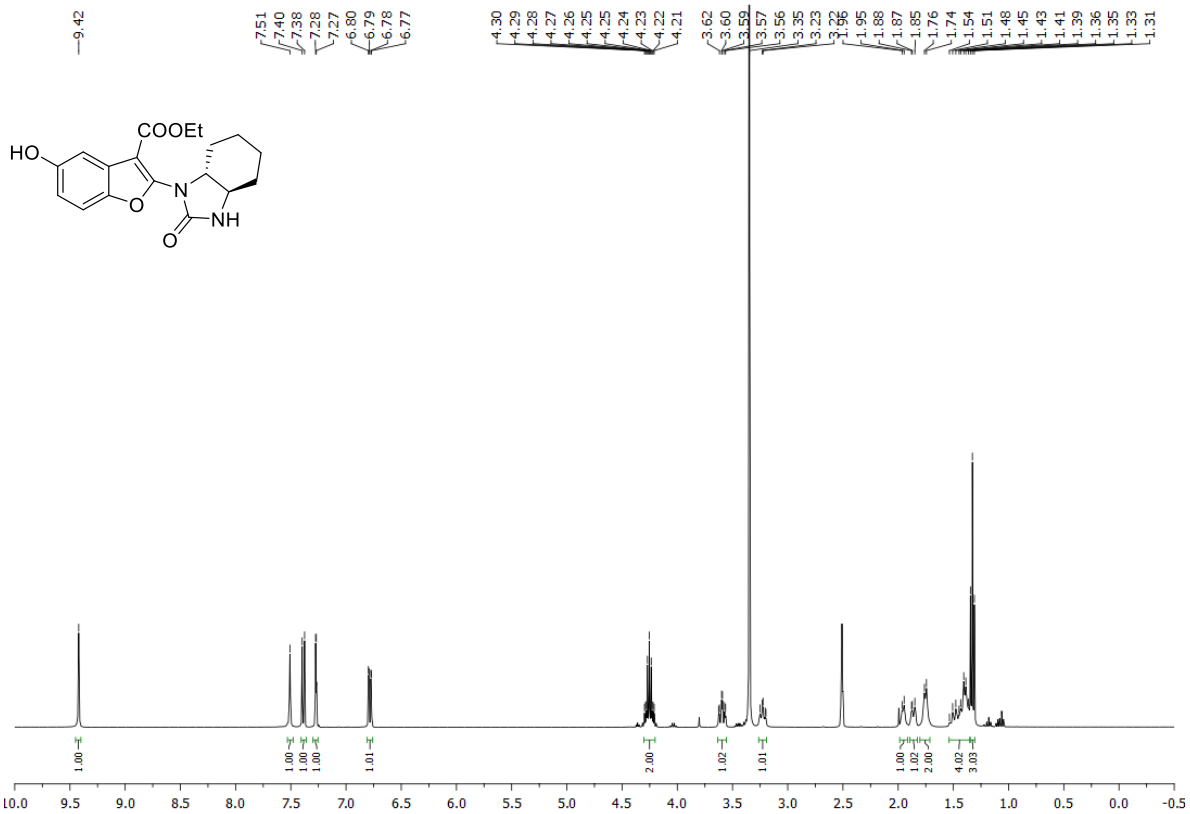
**7b** ($^{1}$H NMR, 300 MHz, DMSO-$d_6$)



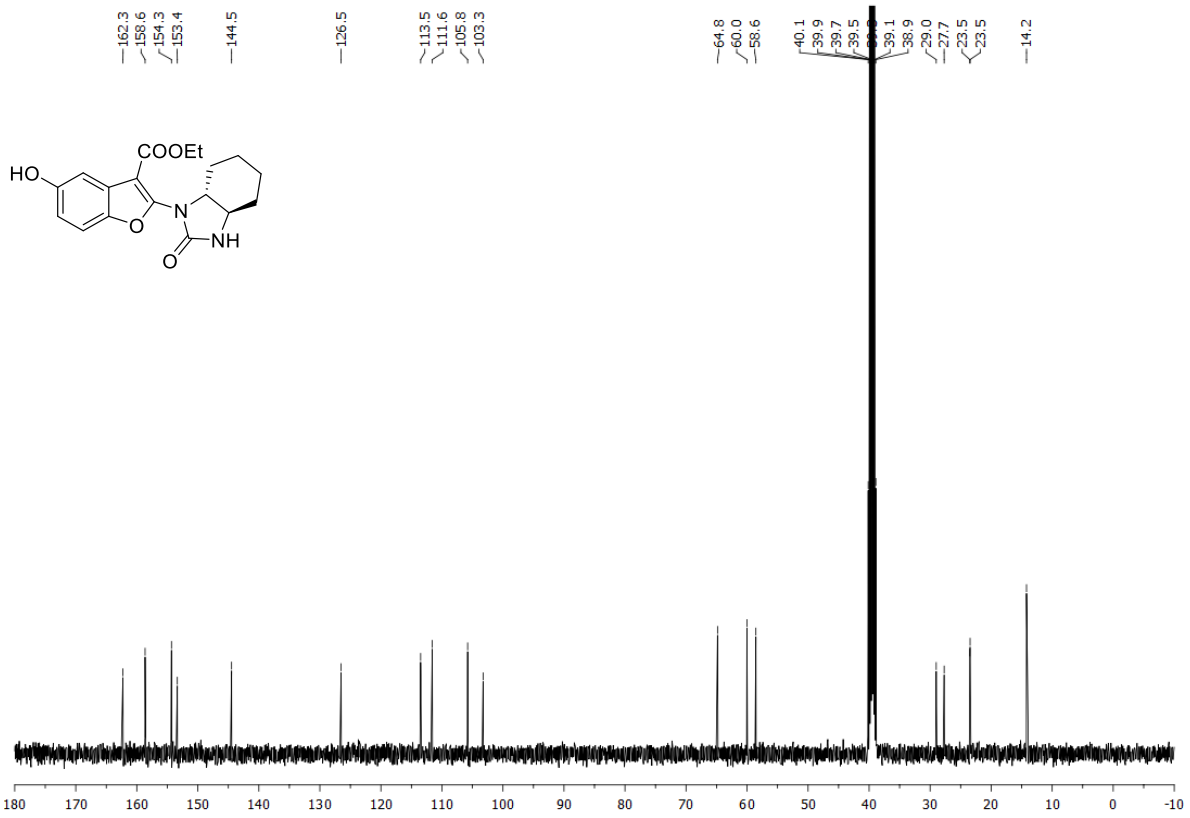

**7b** ($^{13}$C{$^{1}$H} NMR, 75 MHz, DMSO-$d_6$)



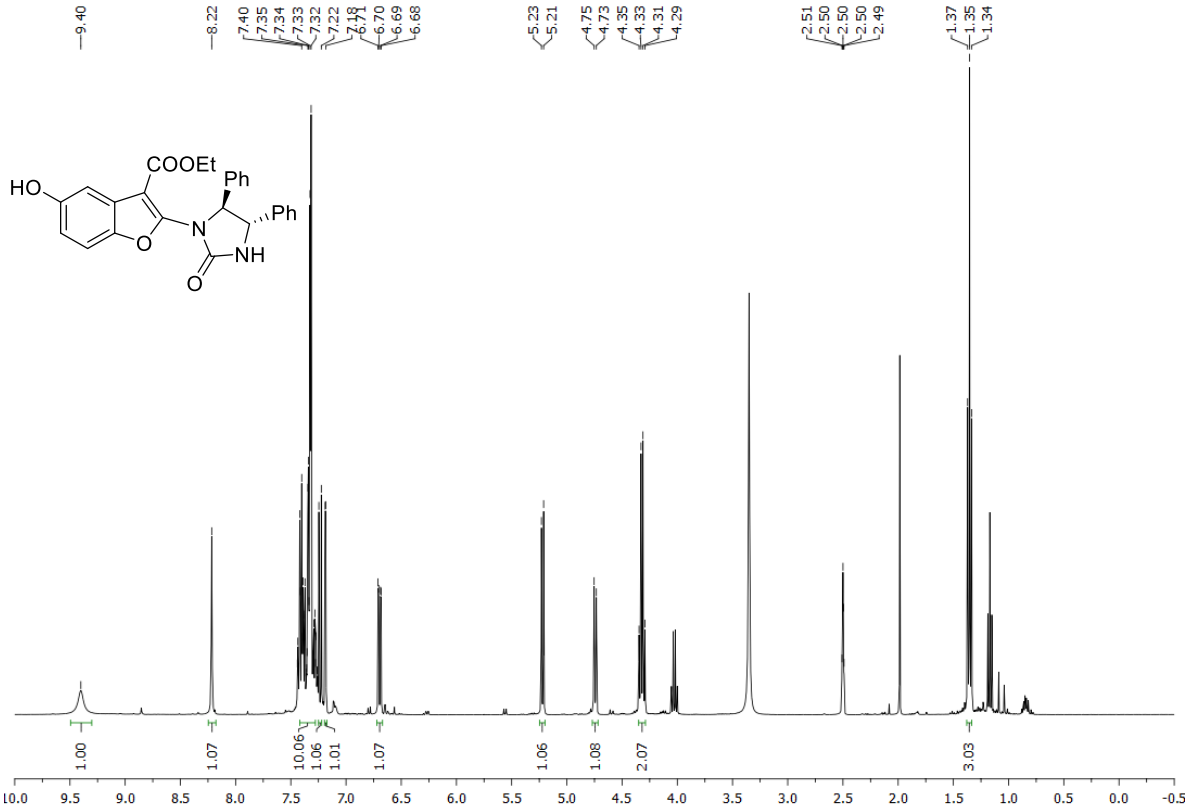
**7c** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



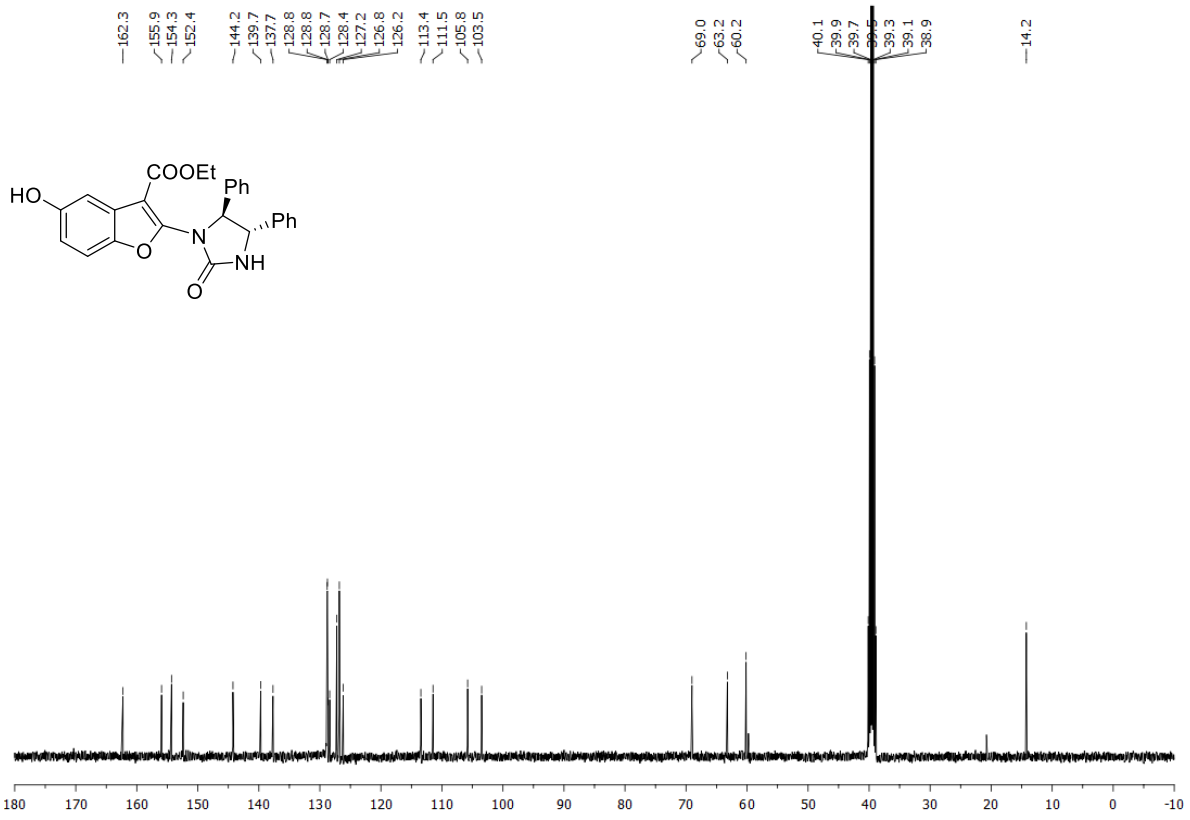

**7c** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



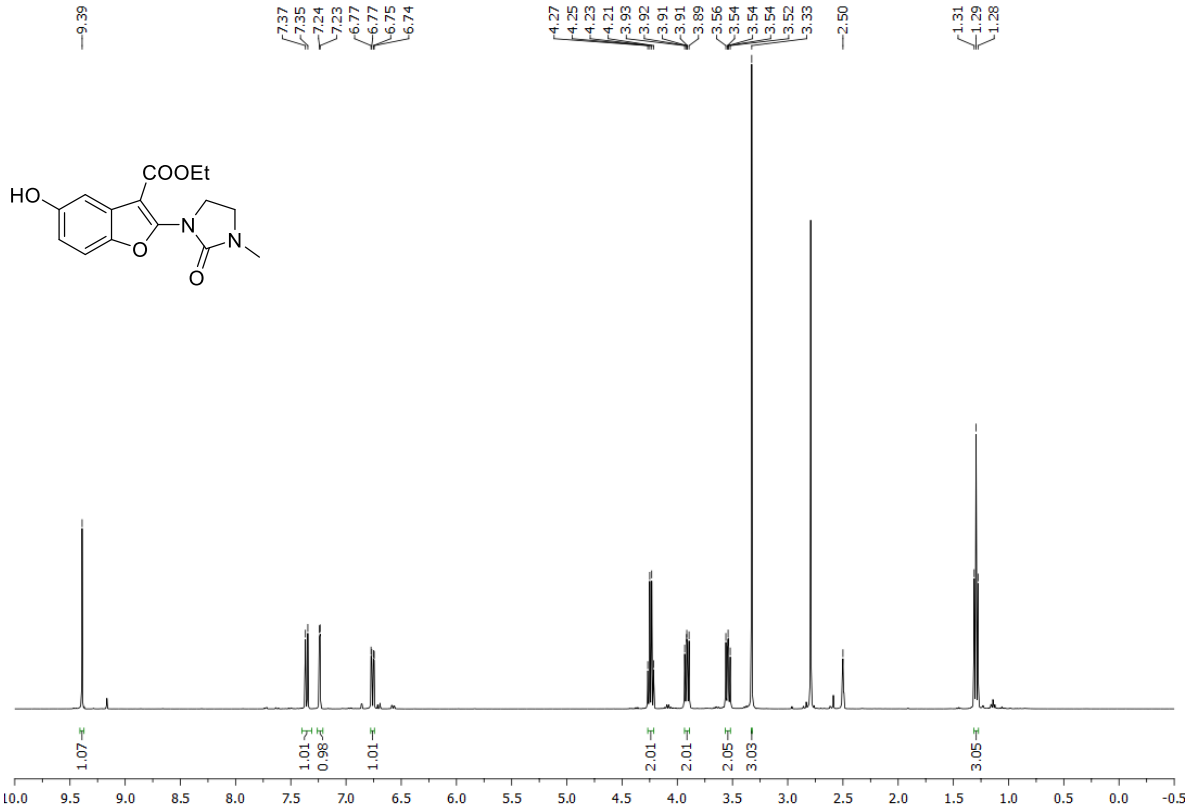
**7d** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



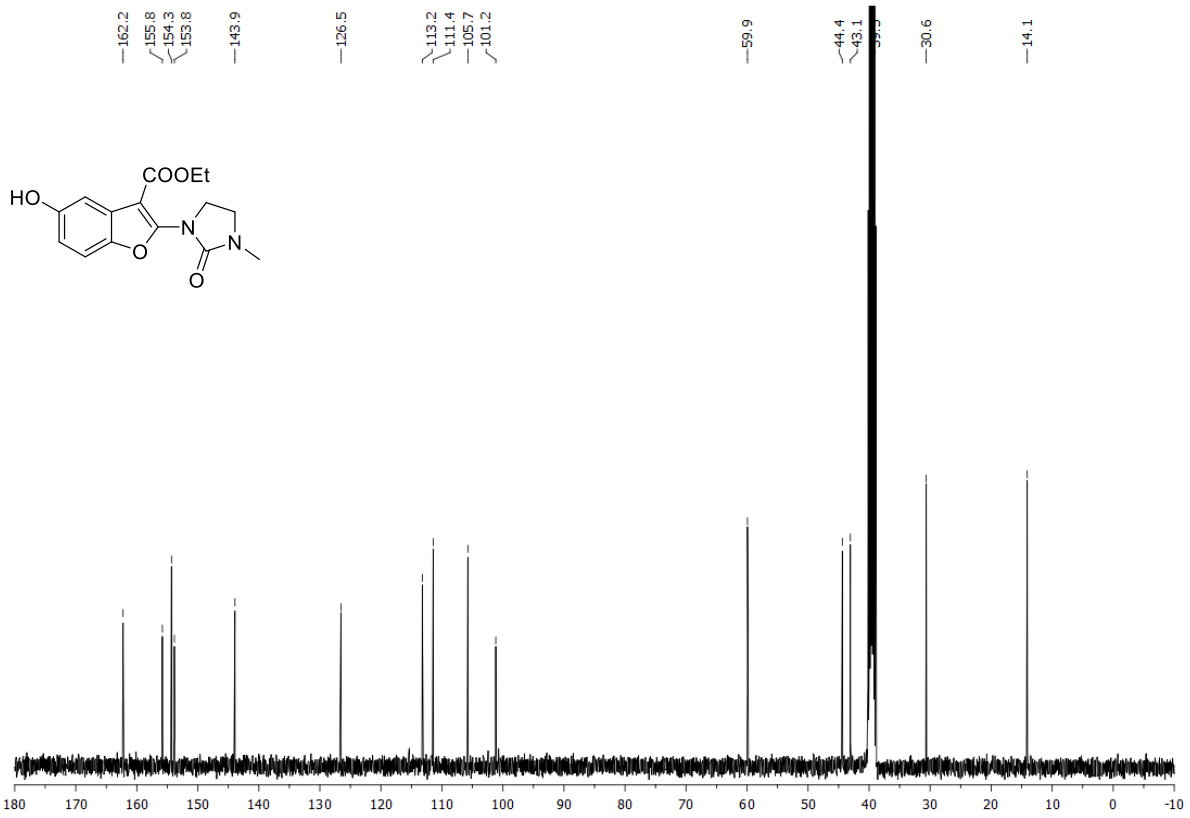

**7d** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



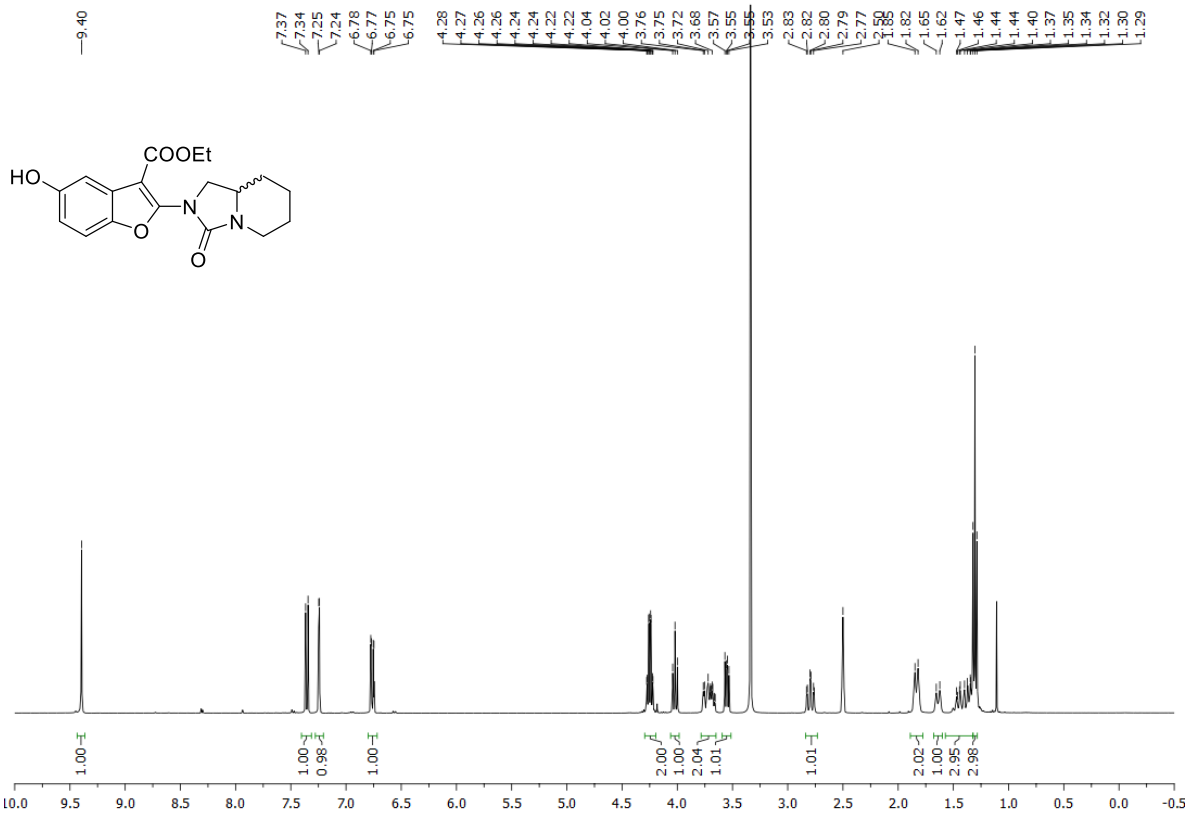
**7e** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



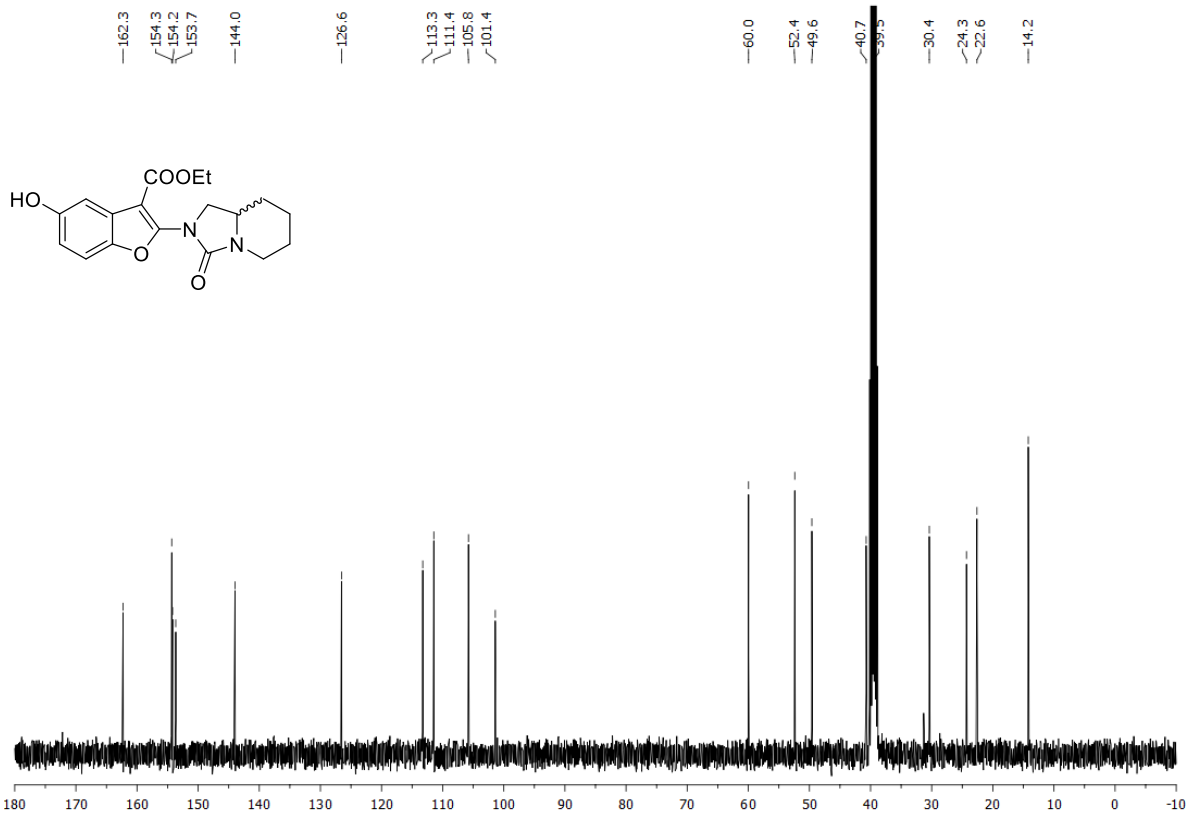

**7e** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



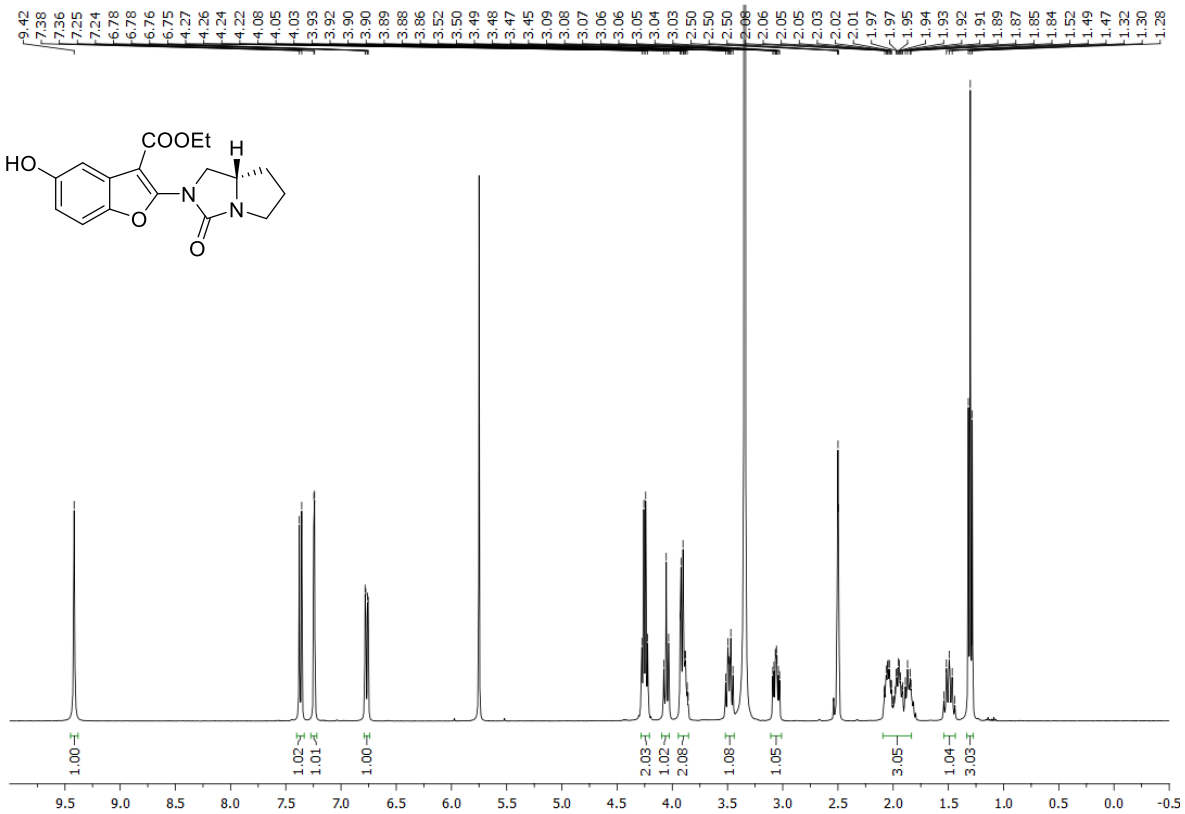
**7f** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



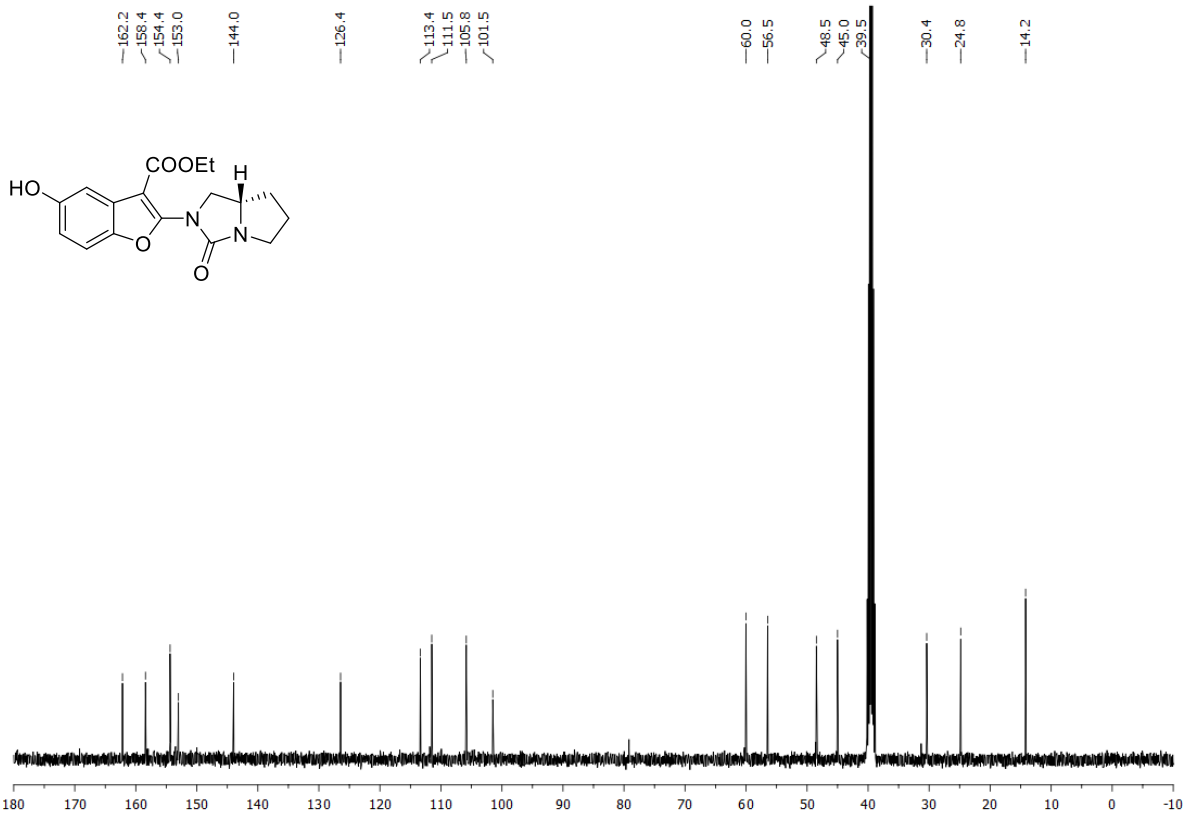

**7f** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



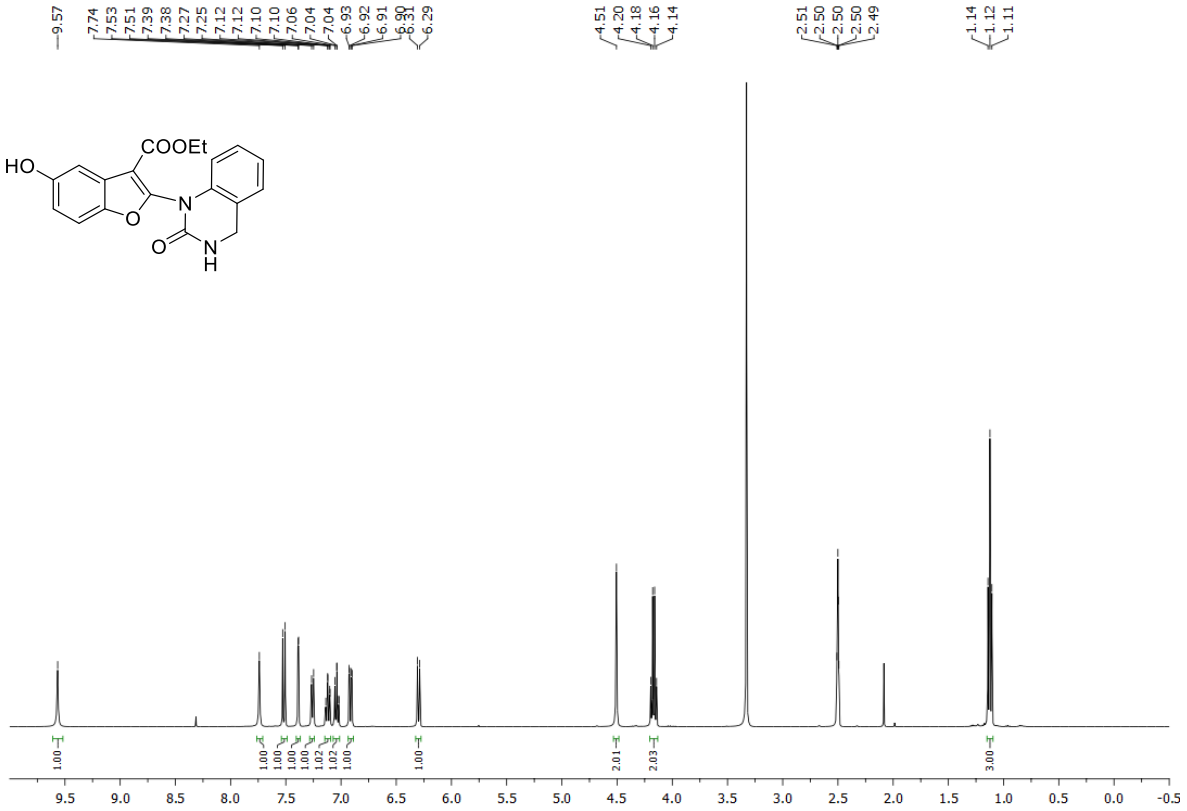
**7g** ($^1$H NMR, 400 MHz, DMSO-$d_6$)



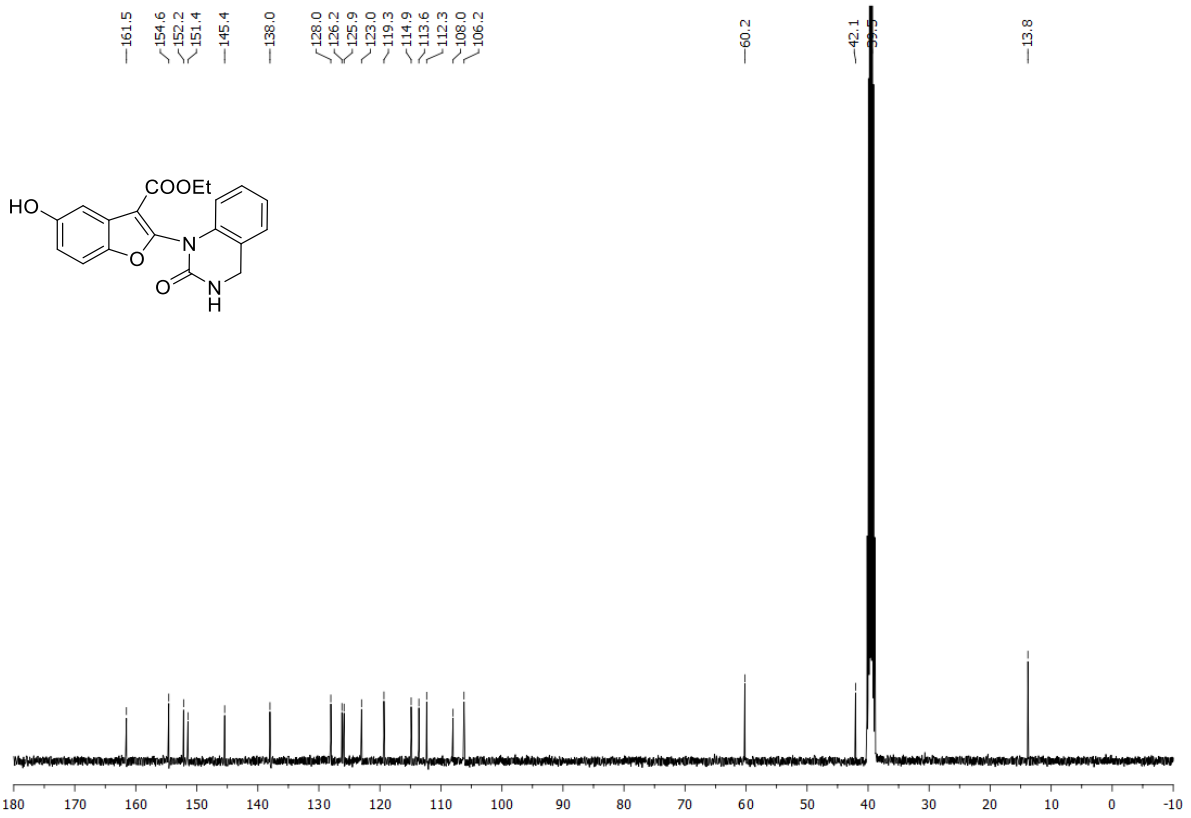

**7g** ($^{13}$C{$^1$H} NMR, 101 MHz, DMSO-$d_6$)



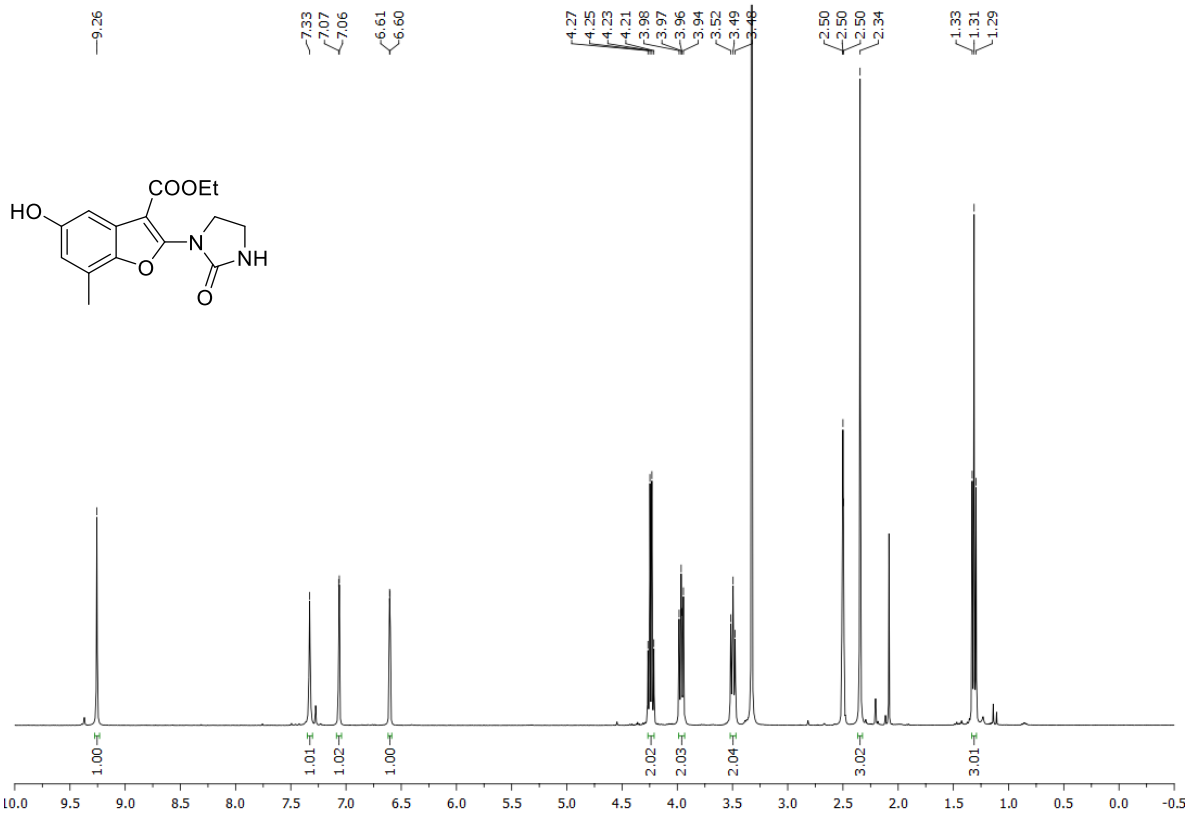
**7h** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



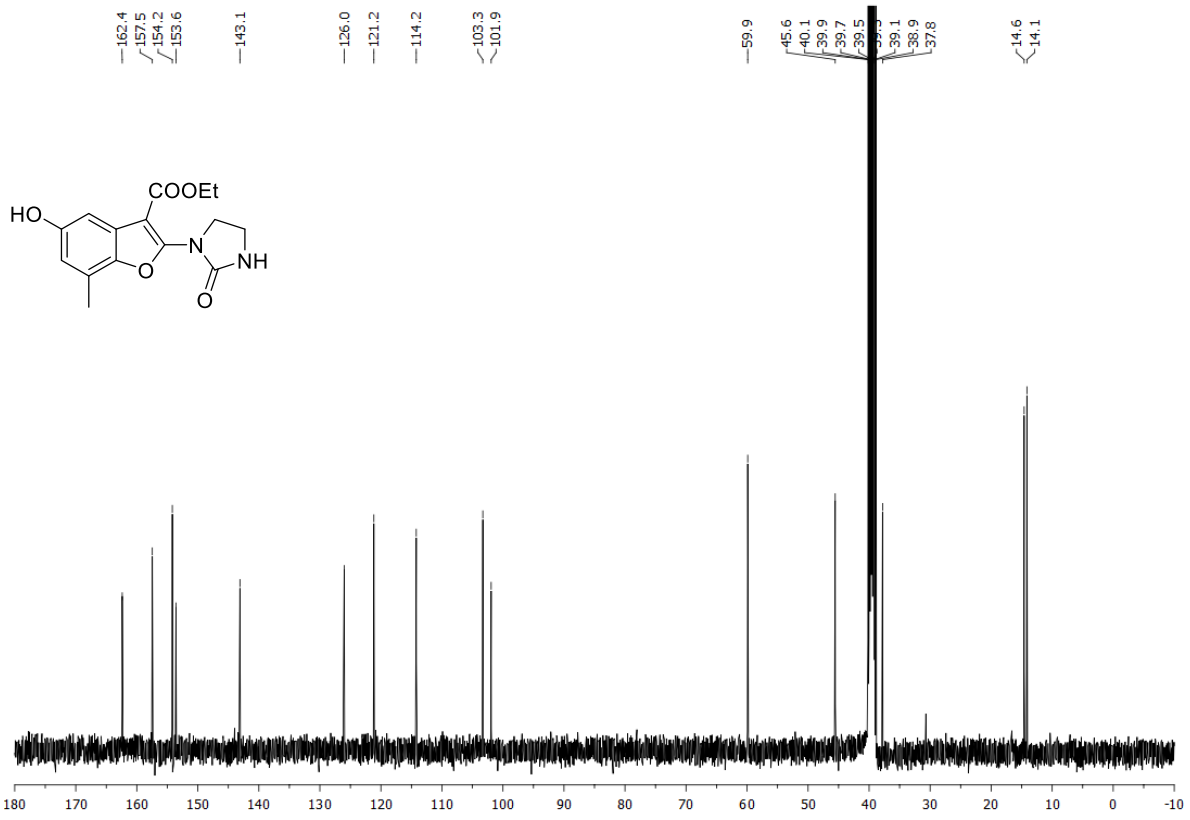

**7h** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



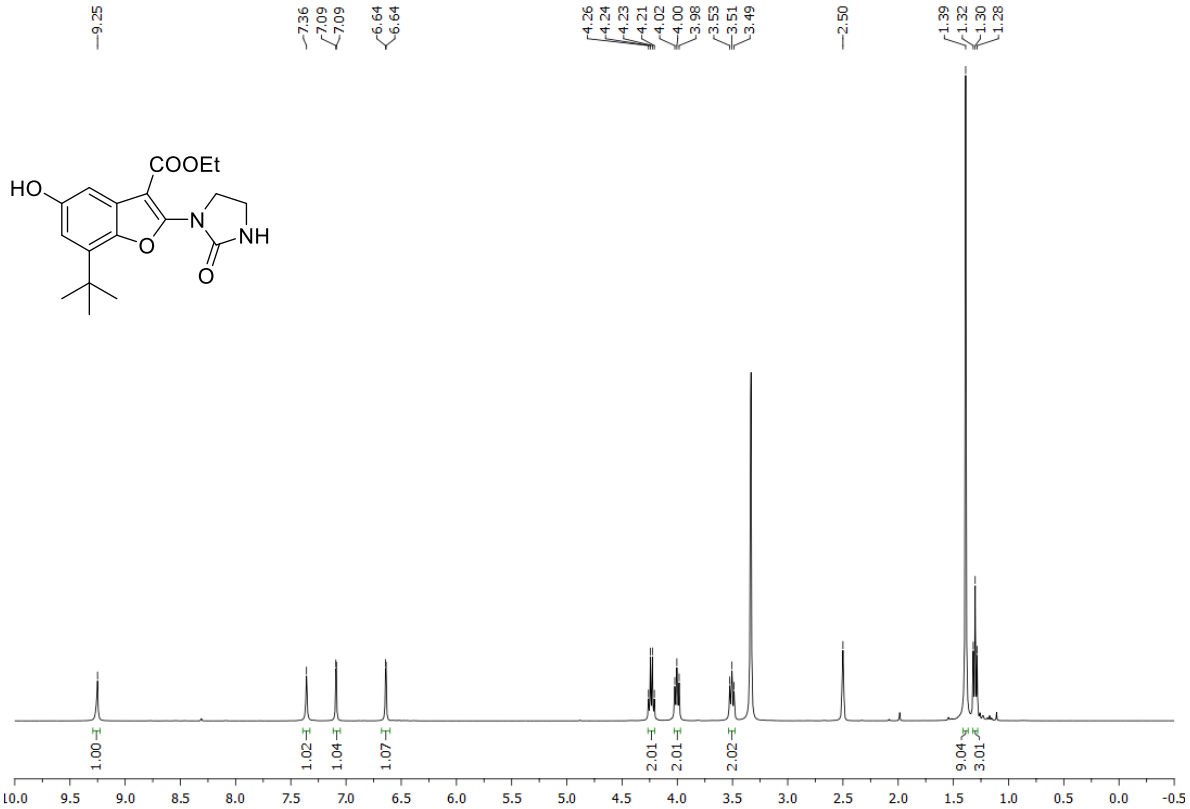
**7i** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



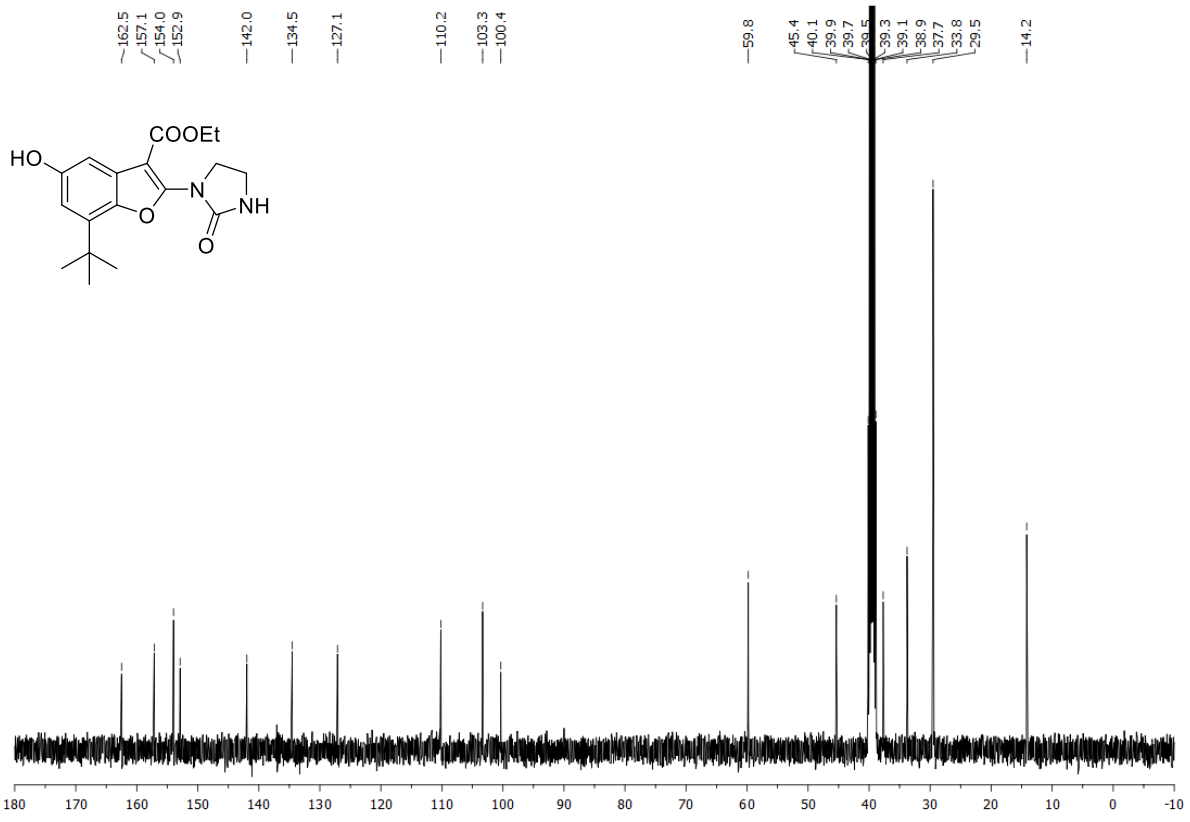

**7i** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



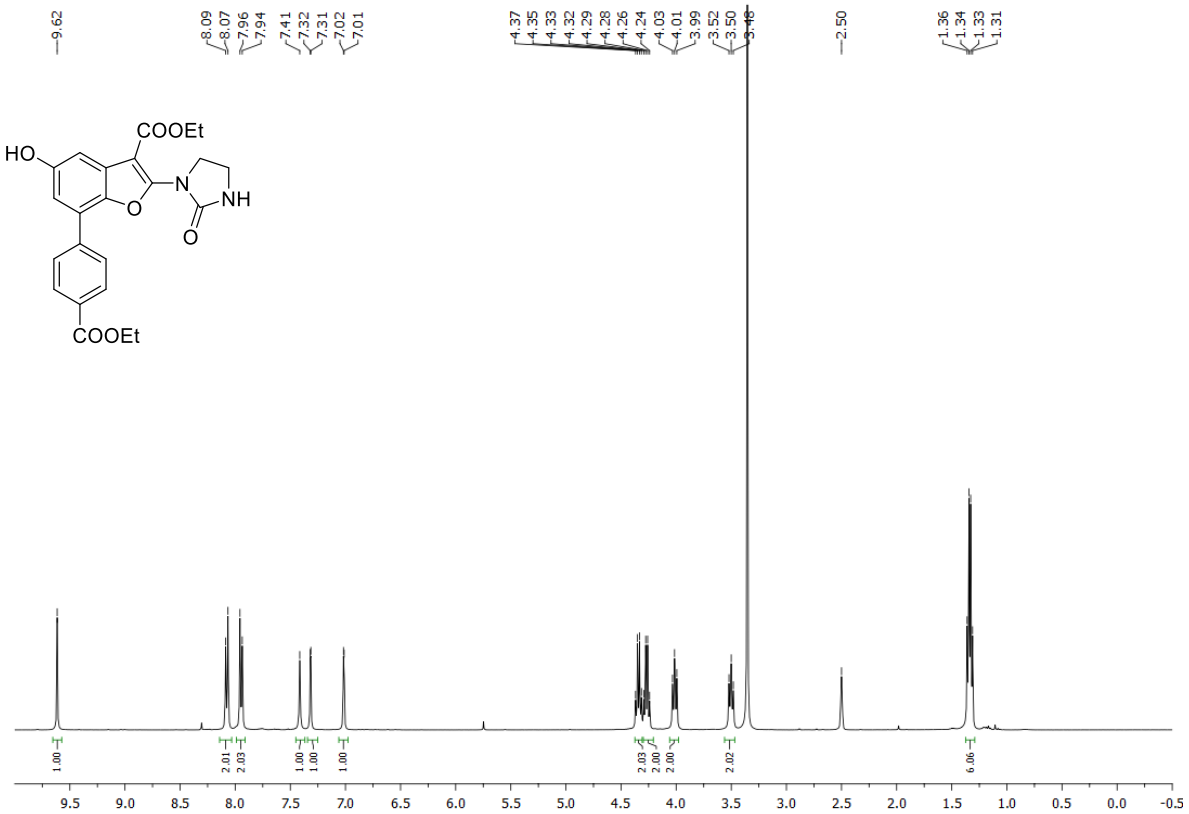
**7j** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



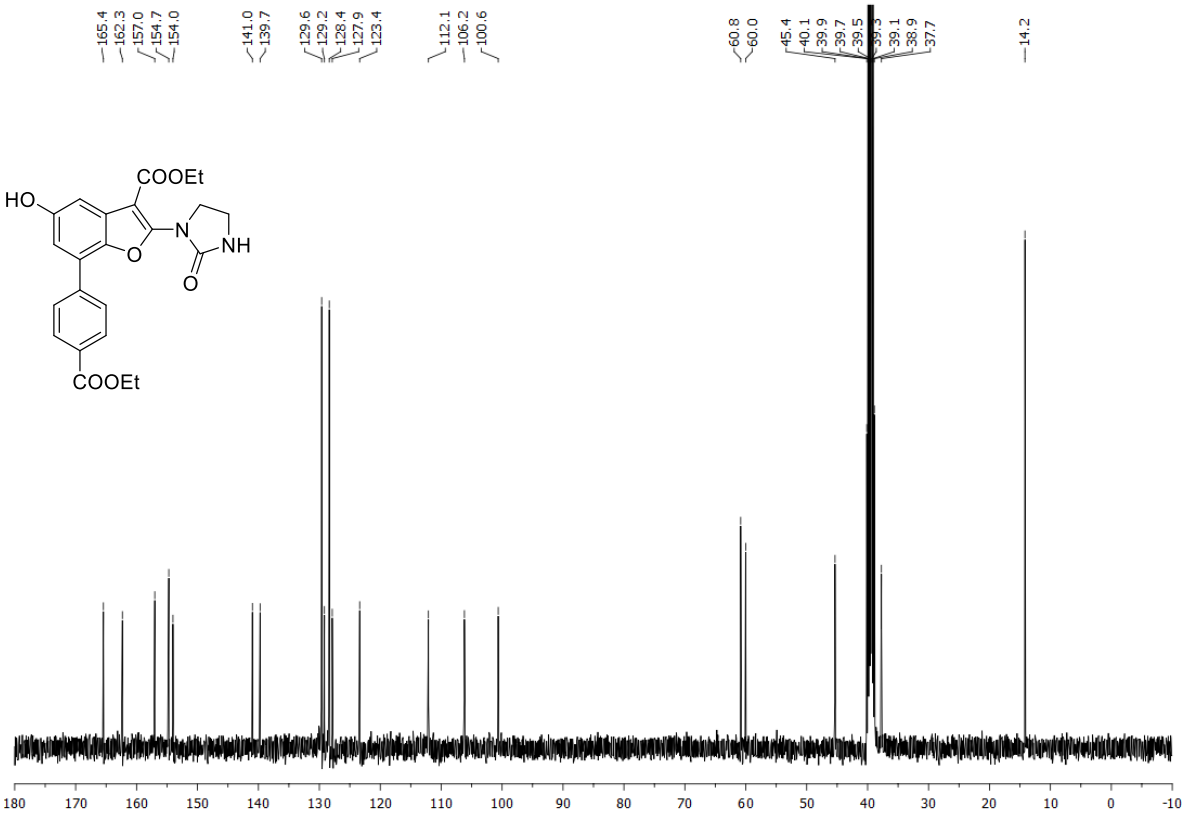

**7j** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



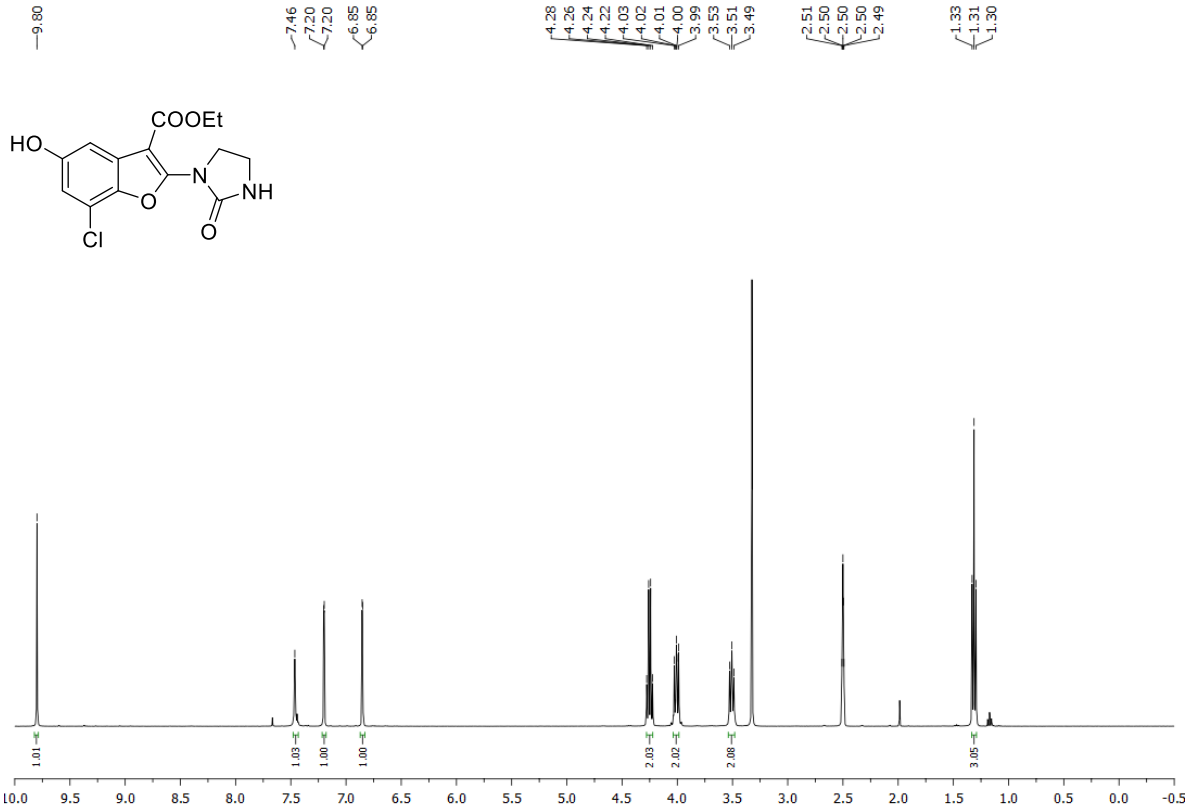
**7k** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



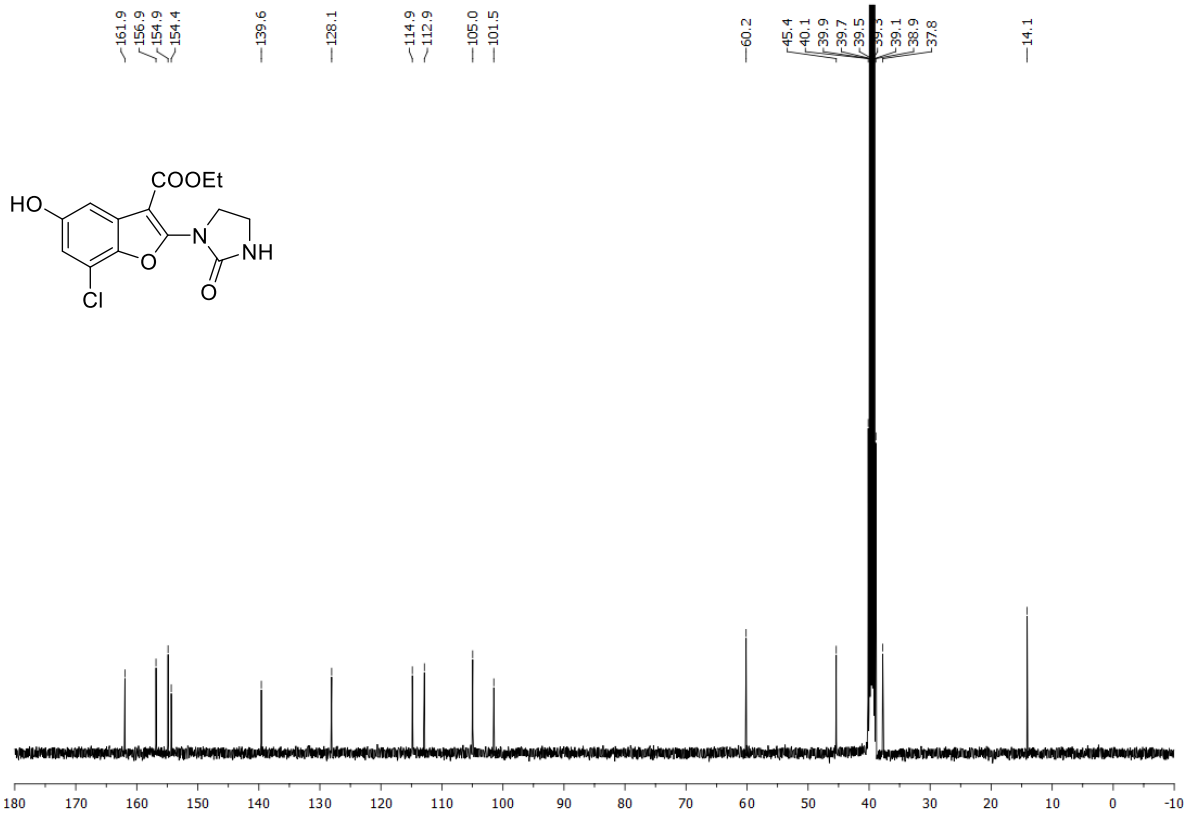

**7k** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



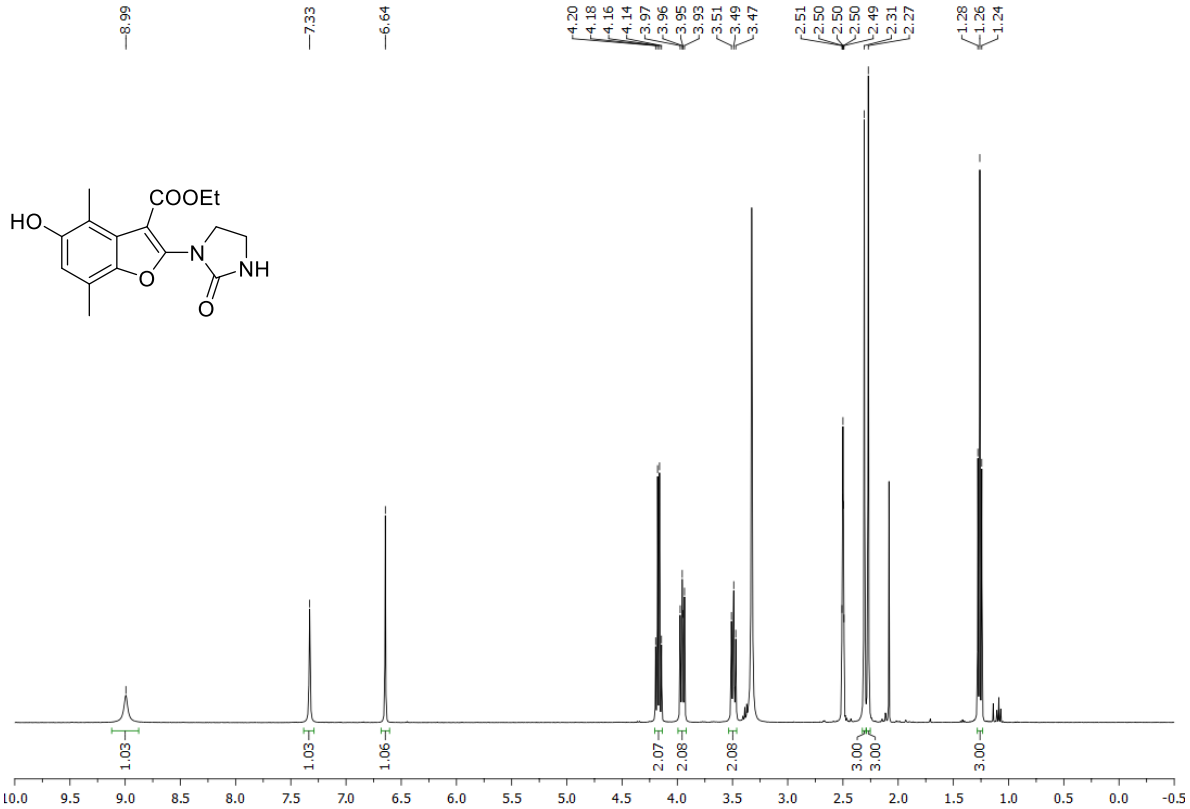
**7l** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



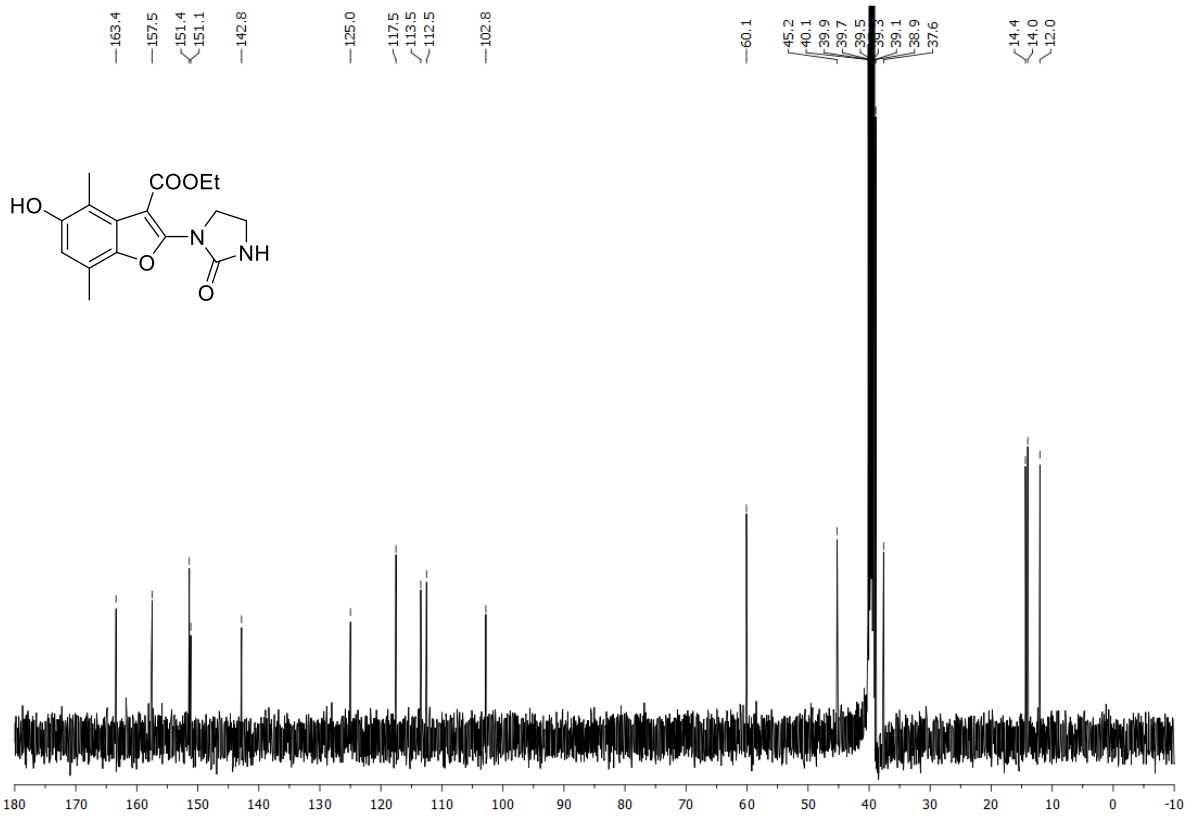

**7l** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



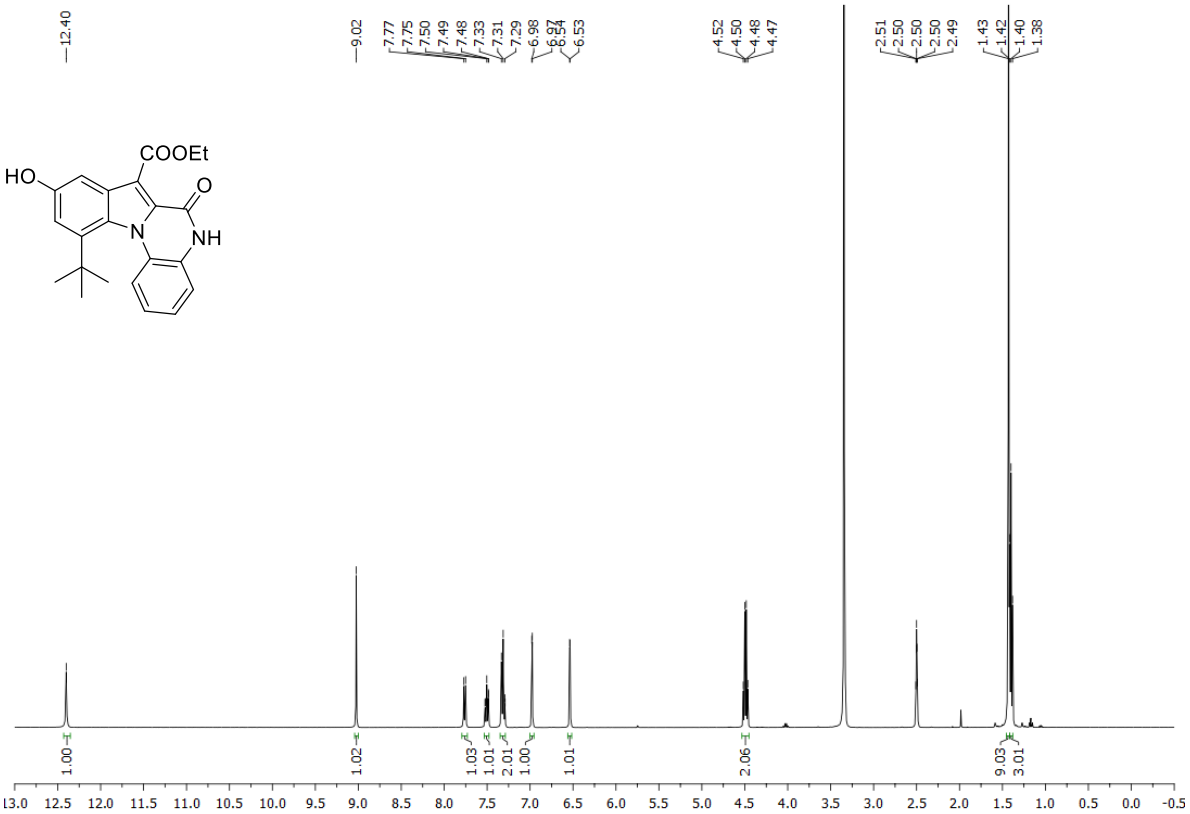
**7m** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)



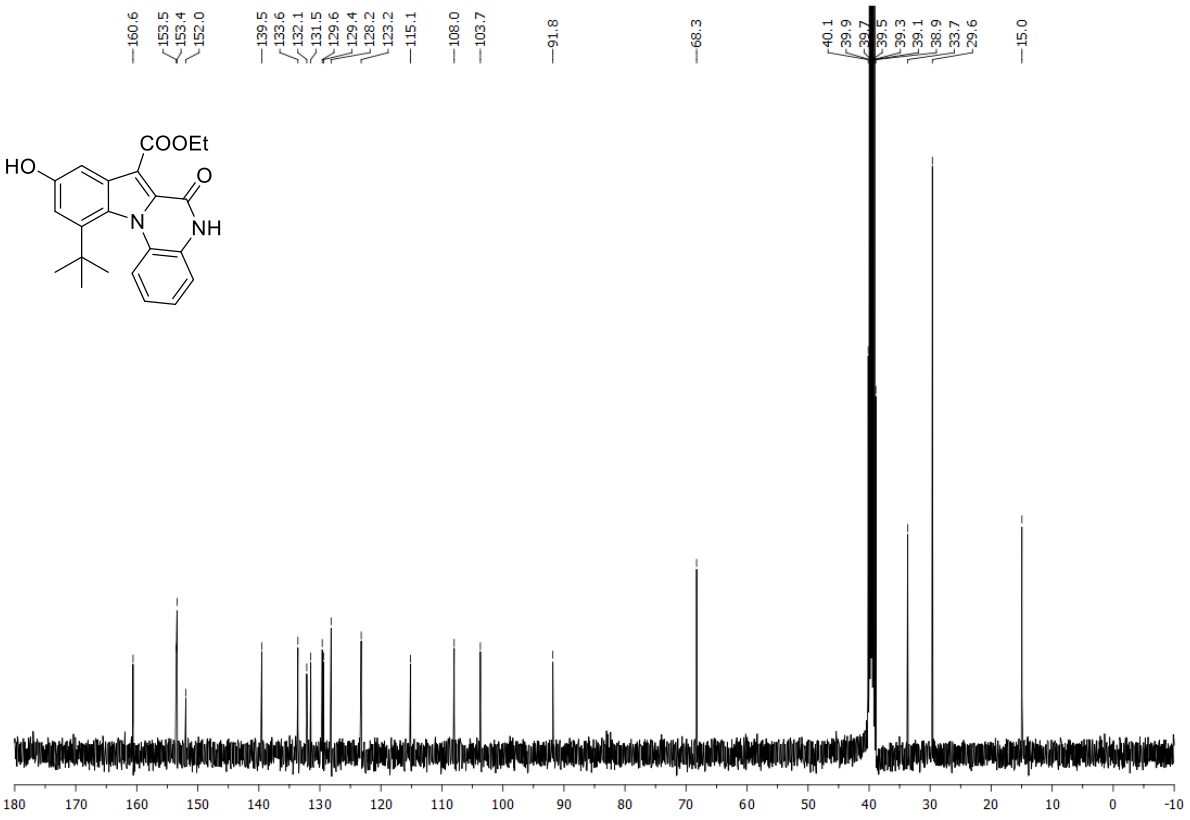

**7m** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



**8** ($^{1}$H NMR, 400 MHz, DMSO-$d_6$)




**8** ($^{13}$C{$^{1}$H} NMR, 101 MHz, DMSO-$d_6$)



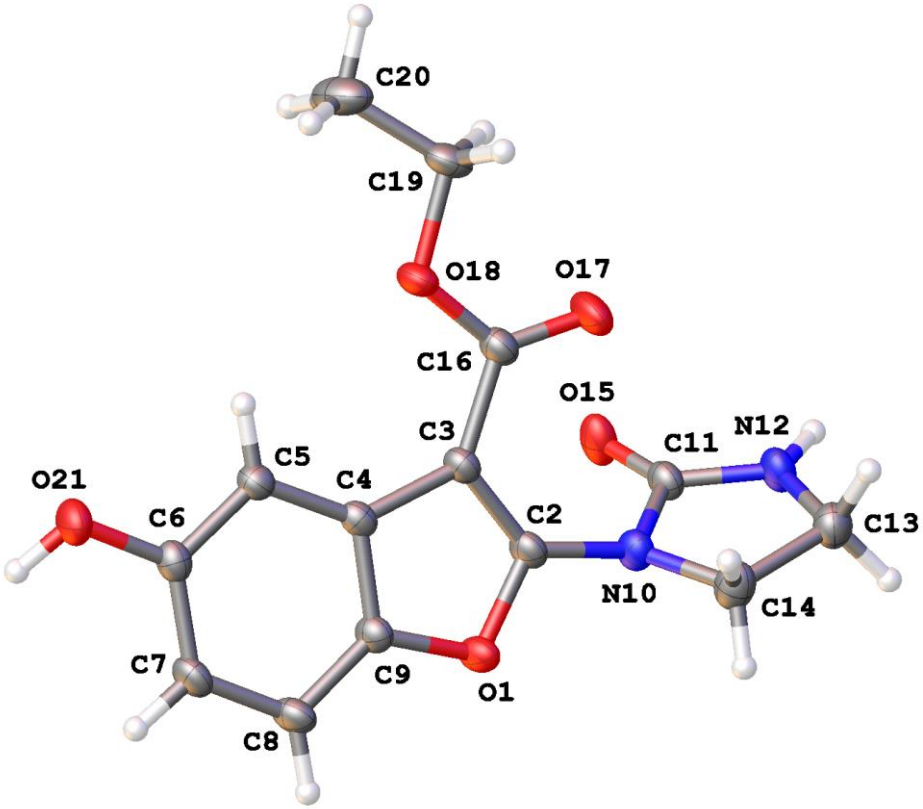
# Single-crystal X-ray structure determination of 7a

Single crystals suitable for X-ray diffraction were obtained by slow evaporation at room temperature from a DMSO-water mixture (1:1 v/v) for **7a**. X-ray intensity data were collected at 294(2) K on an Agilent SuperNova diffractometer with Eos CCD detector using Mo Kα radiation (λ = 0.71073 Å). The images were interpreted and integrated with CrysAlisPRO[7] and the implemented absorption correction was applied. Data frames were processed (unit cell determination, intensity data integration, correction for Lorentz and polarization effects, and empirical absorption correction) using CrysAlis PRO.[7] Using Olex2,[8] the structure was solved with the ShelXT[9] structure solution program using Intrinsic Phasing and refined with the ShelXL[9] refinement package using full-matrix least-squares minimization on $F^2$. Non-hydrogen atoms were refined anisotropically and hydrogen atoms attached to C atoms in the riding mode with isotropic temperature factors fixed at 1.2 times $U_{eq}$ of the parent atoms (1.5 for methyl group). Hydrogen atoms H12 and H21 were located in a difference Fourier map and refined freely. CCDC 2107174 contains the supplementary crystallographic data for this paper and can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/getstructures or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; deposit@ccdc.cam.ac.uk)

**Table S2. Crystal data and structure refinement for 7a.**

| | |
|---|---|
| Empirical formula | $C_{14}H_{14}N_2O_5$ |
| Formula weight | 290.27 |
| Temperature/K | 293(2) |
| Crystal system | triclinic |
| Space group | *P*-1 |
| a/Å | 8.4320(3) |
| b/Å | 8.6450(5) |
| c/Å | 10.0078(5) |
| α/° | 66.339(5) |
| β/° | 84.385(4) |
| γ/° | 81.355(4) |
| Volume/Å3 | 660.03(6) |
| Z | 2 |
| $\rho_{calc}$g/cm3 | 1.461 |
| μ/mm$^{-1}$ | 0.113 |
| F(000) | 304.0 |
| Crystal size/mm$^3$ | 0.4 × 0.3 × 0.25 |
| Radiation | MoKα (λ = 0.71073 Å) |
| 2Θ range for data collection/° | 4.89 to 52.744 |
| Index ranges | $-10 \le h \le 10$, $-10 \le k \le 10$, $-12 \le l \le 12$ |
| Reflections collected | 13643 |
| Independent reflections | 2698 [$R_{int}$ = 0.0265, $R_{sigma}$ = 0.0198] |
| Data/restraints/parameters | 2698/0/200 |
| Goodness-of-fit on $F^2$ | 1.059 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0394, wR2 = 0.0955 |
| Final R indexes [all data] | $R_1$ = 0.0495, wR2 = 0.1039 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.22/-0.16 |

**Figure S3**. Single crystal structure of compound **7a** with thermal ellipsoids at 30% probability level



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