

# Access to *N*-carbonyl derivatives of Iminosydnonones by Carbonylimidazolium Activation

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## I. Materials and equipment

*Reactants and solvents:* All chemical products commercially available were purchased from Sigma-Aldrich, Acros and Fluka and used without further purification. Dichloromethane and chloroform were purchased stabilized with amylene.

*Purifications:* Flash chromatography were performed on silica gel (Merck Kieselgel 60, grading 40-63  $\mu\text{m}$ ) or using automate Combiflash<sup>®</sup> Rf Teledyne ISCO with pre-packed column RediSep<sup>®</sup> Rf (grading 35-70  $\mu\text{m}$ ).

*Analysis:*

Reactions were monitored by TLC carried out on silica 0,25 mm (60 F254, Merck) using UV light as visualizing agent and basic aqueous permanganate as developing agent.

<sup>1</sup>H NMR (400 MHz), <sup>13</sup>C NMR (100 MHz) were measured on a Bruker Avance 400 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from residual solvents peaks and coupling constants are reported as Hertz (Hz). Splitting patterns are designated as singlet (s), broad singlet (br. s), doublet (d), triplet (t), quartet (q), quintet (quint), multiplet (m). Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m).

Electrospray mass spectra were obtained using an ESI-Quadripole autopurify, Waters (pump: 2545, mass: ZQ2000) mass Spectrometer.

Infrared spectra (IR) were obtained on a Perkin Elmer system 2000 FT-IR spectrophotometer or a Perkin Elmer UATR TWO FTIR spectrophotometer and are reported as wavelength numbers ( $\text{cm}^{-1}$ ).

Melting points (Mp) were obtained on a BÜCHI Melting Point B-545 and are reported in °C.

Iminosynone chlorhydrate salts **1a,b** were obtained as previously reported.<sup>1</sup>

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<sup>1</sup> Riomet, M.; Decuypere, E.; Porte, K.; Bernard, S.; Plougatel, L.; Kolodych, S.; Audisio, D.; Taran, F. Design and Synthesis of Iminosynones for Fast Click and Release Reactions with Cycloalkynes. *Chem. Eur. J.*, **2018**, *34*, 8535–8541.

## II.Synthetic Procedure and Analytical Data

### General procedures

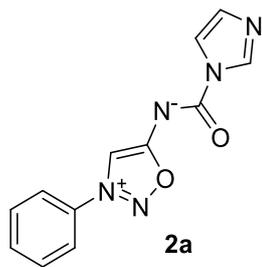
#### **General procedure A for the addition of nucleophiles on iminosydnone-carbonyl-imidazoliums**

To a solution of iminosydnone-carbonyl-imidazolium (0.20 mmol) in DCM (2 mL) were added the nucleophile (0.20 mmol) and triethylamine (0.20–0.40 mmol). The mixture was stirred at room temperature. Once the reaction has reached completion, the solvent was evaporated under reduced pressure.

#### **General procedure B for the addition of nucleophiles on iminosydnone-carbonyl-imidazoliums**

To a solution of iminosydnone-carbonyl-imidazolium (0.20 mmol) in chloroform (2 mL) were added the nucleophile (0.20 mmol) and triethylamine (0.20–0.40 mmol). The mixture was stirred at reflux using a heating block. Once the reaction has reached completion, the solvent was evaporated under reduced pressure.

**(1*H*-imidazole-1-carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (2a)**



$C_{12}H_9N_5O_2$   
**MW:** 255 g.mol<sup>-1</sup>  
**Yield:** 78%  
White solid

To a solution of 1,1'-carbonyldiimidazole (357 mg, 2.20 mmol) in a mixture DMF/MeCN (3 mL/1 mL) was added **1a** (395 mg, 2.00 mmol). The solution was stirred at room temperature for 1 hour before being concentrated under reduced pressure. The crude product was purified by column chromatography (SiO<sub>2</sub>, DCM/MeOH, 98/2) to afford the desired product as a white solid (401 mg, 78%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.40 (s, 1H), 8.30 (s, 1H), 7.80 (m, 2H), 7.70 (m, 1H), 7.62 (m, 2H), 7.55 (s, 1H), 6.95 (s, 1H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 174.9, 154.6, 137.5, 133.5, 133.5, 130.6 (2C), 129.6, 121.5 (2C), 117.2, 104.4.

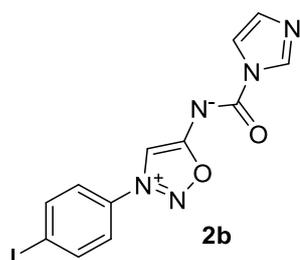
IR (cm<sup>-1</sup>) 1660, 1567, 1466, 1291, 1206, 974, 846, 766.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 256.

Mp. 167–169 °C.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>12</sub>H<sub>10</sub>N<sub>5</sub>O<sub>2</sub> 256.0829; Found 256.0831.

**(1*H*-imidazole-1-carbonyl)(3-(4-iodophenyl)-1,2,3-oxadiazol-3-ium-5-yl)amide (2b)**



$C_{12}H_8IN_5O_2$   
**MW:** 381 g.mol<sup>-1</sup>  
**Yield:** 78%  
Beige solid

To a solution of 1,1'-carbonyldiimidazole (1.78 g, 11.0 mmol) in a mixture DMF/MeCN (15 mL/5 mL) was added **1b** (3.24 g, 10.0 mmol). The solution was stirred at room temperature for 2 hours before being concentrated under reduced pressure. The resulting solid was washed with water and Et<sub>2</sub>O to afford the desired product as a beige solid (2.97 g, 78%).

<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.03 (s, 1H), 8.30 (s, 1H), 8.13(m, 2H), 7.91 (m, 2H), 7.65 (s, 1H), 7.01 (s, 1H).

<sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 174.3, 153.1, 139.0 (2C), 136.8, 133.2, 129.4, 124.3 (2C), 117.3, 106.5, 100.8.

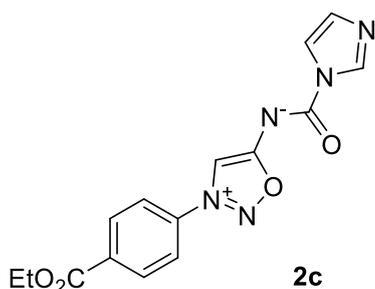
IR (cm<sup>-1</sup>) 1671, 1570, 1374, 1296, 1008, 976.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 382.

Mp. 221–223 °C.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>12</sub>H<sub>9</sub>IN<sub>5</sub>O<sub>2</sub> 381.9795; Found 381.9792.

**(3-(4-(ethoxycarbonyl)phenyl)-1,2,3-oxadiazol-3-ium-5-yl)(1H-imidazole-1-carbonyl)amide (2c)**



C<sub>15</sub>H<sub>13</sub>N<sub>5</sub>O<sub>4</sub>  
MW: 327 g.mol<sup>-1</sup>  
Yield: 61%  
Beige solid

Compound **2b** (1.40 g, 3.67 mmol) was dissolved in a mixture of absolute EtOH (15 mL) and NEt<sub>3</sub> (15 mL). PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (258 mg, 0.367 mmol) was added and the reaction mixture was kept under a CO atmosphere for 5 hours and heated at 80 °C. CO was added to the reaction every 30 min. The solvent was evaporated and the crude mixture was charged on a plug of silica. Impurities were removed by first filtrating with DCM, and then the desired product was obtained by flushing the plug with EtOAc. After evaporation of this filtrate, the product was obtained as a beige solid (729 mg, 61%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.45 (s, 1H), 8.40 (s, 1H), 8.35 (m, 2H), 7.94 (m, 2H), 7.63 (m, 1H), 7.04 (s, 1H), 4.45 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 175.1, 164.3, 154.7, 137.6, 136.3, 135.3, 132.0 (2C), 129.8, 121.7 (2C), 117.3, 104.6, 62.2, 14.3.

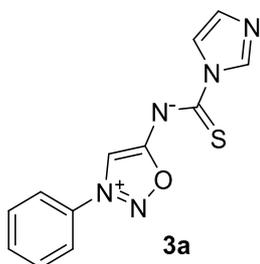
IR (cm<sup>-1</sup>) 1718, 1666, 1575, 1371, 1278, 846, 769.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 328.

Mp. 159–161 °C.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>15</sub>H<sub>14</sub>N<sub>5</sub>O<sub>4</sub> 328.1040; Found 328.1039.

**(1H-imidazole-1-carbonothioyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (3a)**



C<sub>12</sub>H<sub>9</sub>N<sub>5</sub>OS  
MW: 271 g.mol<sup>-1</sup>  
Yield: 81%  
Orange solid

To a solution of 1,1'-thiocarbonyldiimidazole (1.96 g, 11.0 mmol) in anhydrous DCM (10 mL) was added **1a** (1.98 g, 10.0 mmol). The solution was stirred at room temperature overnight before being concentrated under reduced pressure. The crude product was purified by column chromatography (SiO<sub>2</sub> DCM/MeOH, 98/2) to afford the desired product as an orange solid (2.97 g, 81%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.50 (s, 1H), 8.63 (s, 1H), 7.93 (s, 1H), 7.88 (m, 2H), 7.78 (m, 1H), 7.71 (m, 2H), 6.98 (s, 1H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 182.5, 174.6, 137.0, 134.0, 133.5, 130.9 (2C), 129.9, 121.8 (2C), 118.4, 105.3.

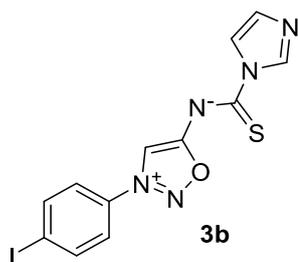
IR (cm<sup>-1</sup>) 1577, 1461, 1376, 1265, 1222, 1023, 735, 657.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 272.

Mp. 167–169 °C.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>12</sub>H<sub>10</sub>N<sub>5</sub>OS 272.0600; Found 272.0599.

**(1H-imidazole-1-carbonothioyl)(3-(4-iodophenyl)-1,2,3-oxadiazol-3-ium-5-yl)amide (3b)**



$C_{12}H_8IN_5OS$   
**MW:** 397 g.mol<sup>-1</sup>  
**Yield:** 65%  
Dark yellow solid

To a solution of 1,1'-thiocarbonyldiimidazole (196 mg, 1.10 mmol) in a mixture DMF/MeCN (1.5 mL/0.5 mL) was added **1b** (324 mg, 1.00 mmol). The solution was stirred at room temperature for 1.5 days before being concentrated under reduced pressure. The resulting solid was washed with water and Et<sub>2</sub>O to afford the desired product as a dark yellow solid (257 mg, 65%).

<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 9.82 (s, 1H), 8.57 (s, 1H), 8.15 (m, 2H), 7.94 (s, 1H), 7.93 (m, 2H), 7.01 (s, 1H).

<sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ 173.7, 139.0 (2C), 136.2, 133.1, 129.6, 124.7 (2C), 118.1, 107.7, 101.2.

One carbon is missing.

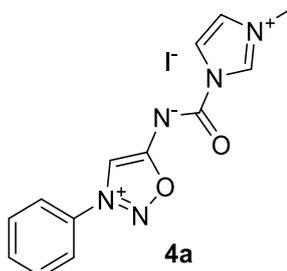
IR (cm<sup>-1</sup>) 1597, 1574, 1462, 1373, 1230, 979.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 398.

Mp. 211–213 °C.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>12</sub>H<sub>9</sub>IN<sub>5</sub>OS 397.9567; Found 397.9567.

**(3-methyl-1H-imidazol-3-ium-1-carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide iodide (4a)**



$C_{13}H_{12}IN_5O_2$   
**MW:** 397 g.mol<sup>-1</sup>  
**Yield:** 98%  
Orange solid

To a solution of **2a** (1.98 g, 7.64 mmol) in anhydrous acetonitrile (20 mL) was added MeI (1.90 mL, 30.6 mmol). The mixture was stirred for 16 hours at room temperature before being concentrated under reduced pressure. The product was obtained as an orange solid (2.98 g, 98%) and was used without any purification.

<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 9.80 (s, 1H), 9.23 (s, 1H), 8.14 (m, 3H), 7.76–7.84 (m, 4H), 3.93 (s, 3H).

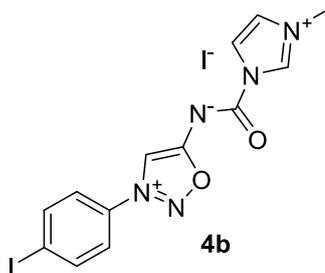
The product is not stable enough in DMSO to afford a <sup>13</sup>C NMR spectrum.

LCMS (ESI) *m/z* [M-Me-Im-I]<sup>+</sup> 188, fragmentation, [M+H]<sup>+</sup> 220, reaction with MeOH used as solvent.

HRMS (ESI-TOF) *m/z* [M-I]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>12</sub>N<sub>5</sub>O<sub>2</sub> 270.0986; Found 270.0983.

Mp. 145 °C–decomp.

**(3-(4-iodophenyl)-1,2,3-oxadiazol-3-ium-5-yl)(3-methyl-1H-imidazol-3-ium-1-carbonyl)amide iodide (4b)**



$C_{13}H_{11}I_2N_5O_2$   
**MW:** 523 g.mol<sup>-1</sup>  
**Yield:** 98%  
Orange solid

To a solution of **2b** (1.52 g, 4.00 mmol) in anhydrous acetonitrile (15 mL) was added MeI (996  $\mu$ L, 16.0 mmol). The mixture was stirred for 16 hours at 40 °C before being concentrated under reduced pressure. The product was obtained as an orange solid (2.05 g, 98%) and was used without any purification.

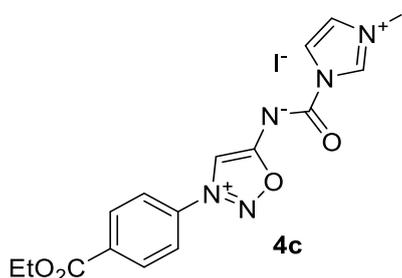
<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  9.79 (s, 1H), 9.26 (s, 1H), 8.16 (m, 2H), 8.13 (m, 1H), 7.94 (m, 2H) 7.80 (m, 1H), 3.93 (s, 3H).

The product is not stable enough in DMSO to afford a <sup>13</sup>C NMR spectrum.

LCMS (ESI)  $m/z$  [M+H]<sup>+</sup> 346, reaction with MeOH used as solvent.

Compound **4b** has no HRMS data or elemental analysis due to the poor stability of the imidazolium sample. The sample was sent out for HRMS analysis but degraded during transportation.

**(3-(4-(ethoxycarbonyl)phenyl)-1,2,3-oxadiazol-3-ium-5-yl)(3-methyl-1H-imidazol-3-ium-1-carbonyl)amide iodide (4c)**



$C_{16}H_{16}IN_5O_4$   
**MW:** 469 g.mol<sup>-1</sup>  
**Yield:** 91%  
Orange solid

To a solution of **2c** (562 mg, 1.72 mmol) in anhydrous acetonitrile (15 mL) was added MeI (430  $\mu$ L, 6.87 mmol). The mixture was stirred for 16 hours at 40 °C before being concentrated under reduced pressure. The product was obtained as an orange solid (736 mg, 91%) and was used without any purification.

<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  9.80 (s, 1H), 9.34 (s, 1H), 8.27–8.34 (m, 4H), 8.14 (m, 1H), 7.80 (m, 1H), 4.40 (q,  $J$  = 7.1 Hz, 2H), 3.93 (s, 3H), 1.37 (t,  $J$  = 7.1 Hz, 3H).

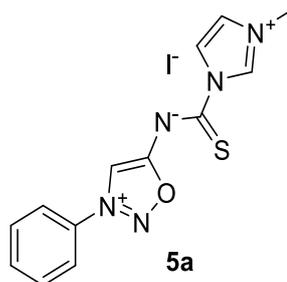
The product is not stable enough in DMSO to afford a <sup>13</sup>C NMR spectrum.

LCMS (ESI)  $m/z$  [M-I]<sup>+</sup> 342.

HRMS (ESI-TOF)  $m/z$  [M-I]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>16</sub>N<sub>5</sub>O<sub>4</sub> 342.1197; Found 342.1201.

Mp. 165 °C–decomp.

**(3-methyl-1H-imidazol-3-ium-1-carbonothioyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide iodide (5a)**



$C_{13}H_{12}IN_5OS$   
**MW:** 413 g.mol<sup>-1</sup>  
**Yield:** 98%  
Orange solid

To a solution of **3a** (2.20 g, 8.10 mmol) in anhydrous acetonitrile (20 mL) was added MeI (2.00 mL, 32.4 mmol). The mixture was stirred for 16 hours at 40 °C before being concentrated under reduced pressure. The product was obtained as an orange solid (3.28 g, 98%) and was used without any purification.

<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 9.98 (s, 1H), 9.97 (s, 1H), 8.37 (s, 1H), 8.18 (m, 2H), 7.77–7.87 (m, 4H), 3.95 (s, 3H).

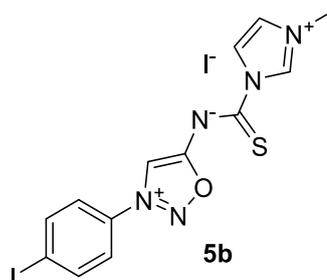
<sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ 175.3, 173.0, 136.1, 133.7, 133.4, 130.4 (2C), 124.2, 123.1 (2C), 119.3, 109.2, 36.5.

LCMS (ESI) *m/z* [M-Me-Im-I]<sup>+</sup> 204, fragmentation

HRMS (ESI-TOF) *m/z* [M-I]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>12</sub>N<sub>5</sub>OS 286.0757; Found 286.0756.

Mp. 184–186 °C.

**(3-(4-iodophenyl)-1,2,3-oxadiazol-3-ium-5-yl)(3-methyl-1H-imidazol-3-ium-1-carbonothioyl)amide iodide (5b)**



$C_{13}H_{11}I_2N_5OS$   
**MW:** 539 g.mol<sup>-1</sup>  
**Yield:** 94%  
Brown solid

To a solution of **3b** (257 mg, 0.65 mmol) in anhydrous acetonitrile (2 mL) was added MeI (161 μL, 2.60 mmol). The mixture was stirred for 16 hours at 40 °C before being concentrated under reduced pressure. The product was obtained as a brown solid (331 mg, 94%) and was used without any purification.

<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 10.00 (s, 1H), 9.97 (s, 1H), 8.37 (m, 1H), 8.19 (m, 2H), 7.96 (m, 2H), 7.80 (m, 1H), 3.93 (s, 3H).

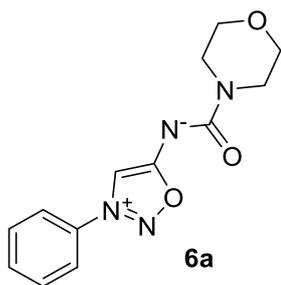
The product is not stable and soluble enough in DMSO to afford a <sup>13</sup>C NMR spectrum.

LCMS (ESI) *m/z* [M-I]<sup>+</sup> 412.

HRMS (ESI-TOF) *m/z* [M-I]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>11</sub>IN<sub>5</sub>OS 411.9724; Found 411.9724.

Mp. 208–209 °C.

**(morpholine-4-carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (6a)**



$C_{13}H_{14}N_4O_3$   
**MW:** 274 g.mol<sup>-1</sup>  
**Yield:** 95%  
Yellow solid

The product was obtained using general procedure **A** from **4a** (79 mg), morpholine (18  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc, from 30/70 to 0/100) to afford the desired product as a yellow solid (52 mg, 95%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.13 (s, 1H), 7.76 (m, 2H), 7.59–7.68 (m, 3H), 3.79 (m, 2H), 3.66 (m, 4H), 3.60 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  173.6, 160.8, 134.2, 132.9, 130.5 (2C), 121.5 (2C), 102.0, 67.1 (2C), 45.5, 43.2.

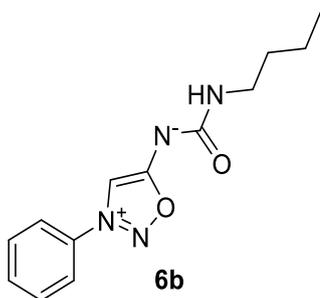
IR (cm<sup>-1</sup>) 1612, 1415, 1254, 1204, 1110, 965, 766.

LCMS (ESI)  $m/z$  [M+H]<sup>+</sup> 275.

HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>15</sub>N<sub>4</sub>O<sub>3</sub> 275.1139; Found 275.1137.

Mp. 168–170 °C.

**(butylcarbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (6b)**



$C_{13}H_{16}N_4O_2$   
**MW:** 260 g.mol<sup>-1</sup>  
**Yield:** 85%  
Yellow solid

The product was obtained using general procedure **A** from **4a** (79 mg), *n*-butylamine (20  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc, from 50/50 to 30/70) to afford the desired product as a yellow solid (44 mg, 85%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.15 (s, 1H), 7.76 (m, 2H), 7.59–7.77 (m, 3H), 5.58 (br.s, 1H), 3.25 (m, 2H), 1.51 (m, 2H), 1.36 (m, 2H), 0.91 (t,  $J$  = 7.3 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  172.7, 161.6, 134.2, 132.8, 130.5 (2C), 121.6 (2C), 102.0, 40.3, 32.3, 20.2, 13.9.

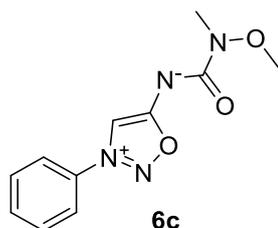
IR (cm<sup>-1</sup>) 3252, 3063, 2927, 1625, 1555, 1299, 965, 737.

LCMS (ESI)  $m/z$  [M+H]<sup>+</sup> 261.

HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>17</sub>N<sub>4</sub>O<sub>2</sub> 261.1346; Found 261.1343.

Mp. 107–109 °C.

**(methoxy(methyl)carbamoyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (6c)**



$C_{11}H_{12}N_4O_3$   
**MW:** 248 g.mol<sup>-1</sup>  
**Yield:** 78%  
Orange oil

The product was obtained using general procedure **A** from **4a** (79 mg), N,O-diméthylhydroxylamine.HCl (19 mg) and triethylamine (56  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as an orange oil (39 mg, 78%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.19 (s, 1H), 7.78 (m, 2H), 7.61–7.70 (m, 3H), 3.76 (s, 3H), 3.30 (s, 3H).

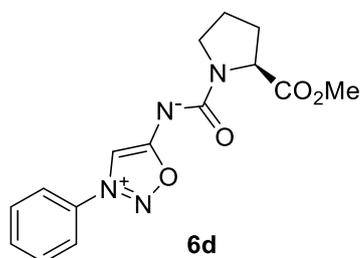
**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  173.9, 162.6, 134.1, 133.0, 130.6 (2C), 121.6 (2C), 102.4, 61.4, 35.5.

**IR (cm<sup>-1</sup>)** 1628, 1583, 1358, 958, 765.

**LCMS (ESI) m/z** [M+H]<sup>+</sup> 249.

**HRMS (ESI-TOF) m/z** [M+H]<sup>+</sup> Calcd for C<sub>11</sub>H<sub>13</sub>N<sub>4</sub>O<sub>3</sub> 249.0982; Found 249.0982.

**(S)-(2-(methoxycarbonyl)pyrrolidine-1-carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (6d)**



$C_{15}H_{16}N_4O_4$   
**MW:** 316 g.mol<sup>-1</sup>  
**Yield:** 88%  
Orange oil

The product was obtained using general procedure **A** from **4a** (79 mg), L-proline methyl ester.HCl (33 mg) and triethylamine (56  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as an orange oil (56 mg, 88%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.16 {8.11} (s, 1H), 7.73 (m, 2H), 7.56–7.67 (m, 3H), 4.43 {4.60} (dd, *J* = 8.5, 3.8 Hz, 1H), 3.71 (s, 3H), 3.52–3.80 (m, 2H), 2.17–2.28 (m, 1H), 1.86–2.05 (m, 3H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  174.1 {174.6}, 173.1 {172.5}, 160.3 {160.3}, 134.1, 132.8 {132.8}, 130.4 (2C), 121.4 {121.5} (2C), 102.3 {102.1}, 58.9 {59.8}, 52.2 {52.1}, 47.5 {46.2}, 30.2 {30.8}, 24.7 {23.8}.

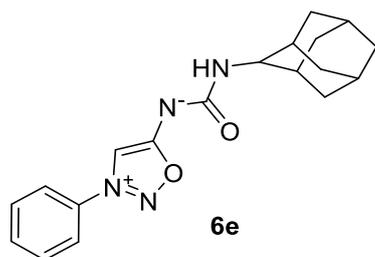
*NMR spectra show the presence of 2 isomers (ratio 1.4/1 at room temperature), minor isomers signals are reported into brackets when they are distinguishable.*

**IR (cm<sup>-1</sup>)** 1740, 1623, 1395, 1199, 957.

**LCMS (ESI) m/z** [M+H]<sup>+</sup> 317.

**HRMS (ESI-TOF) m/z** [M+H]<sup>+</sup> Calcd for C<sub>15</sub>H<sub>17</sub>N<sub>4</sub>O<sub>4</sub> 317.1244; Found 317.1243.

**((1*r*,3*r*,5*r*,7*r*)-adamantan-2-ylcarbamoyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (6e)**



$C_{19}H_{22}N_4O_2$   
**MW:** 338 g.mol<sup>-1</sup>  
**Yield:** 93%  
Yellow solid

The product was obtained using general procedure **A** from **4a** (79 mg), 2-adamantylamine.HCl (38 mg) and triethylamine (56  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc, 50/50) to afford the desired product as a yellow solid (93%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.16 (s, 1H), 7.74 (m, 2H), 7.58–7.67 (m, 3H), 5.87 (br.d,  $J$  = 7.9 Hz, 1H), 3.91 (d,  $J$  = 8.1 Hz, 1H), 1.95 (m, 2H), 1.75–1.87 (m, 8H), 1.70 (m, 2H), 1.59 (m, 1H), 1.56 (m, 1H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  172.4, 160.4, 134.1, 132.9, 130.5 (2C), 121.5 (2C), 102.0, 54.4, 37.7, 37.4 (2C), 32.4 (2C), 31.9 (2C), 27.3, 27.3.

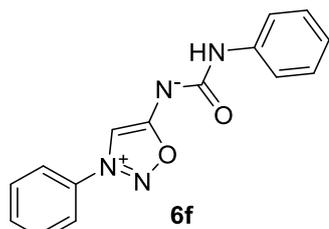
**IR (cm<sup>-1</sup>)** 2904, 1635, 1601, 1495, 1468, 1364.

**LCMS (ESI)  $m/z$  [M+H]<sup>+</sup>** 339.

**HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup>** Calcd for C<sub>19</sub>H<sub>23</sub>N<sub>4</sub>O<sub>2</sub> 339.1816; Found 339.1814.

**Mp.** 70–72 °C.

**(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)(phenylcarbamoyl)amide (6f)**



$C_{15}H_{12}N_4O_2$   
**MW:** 280 g.mol<sup>-1</sup>  
**Yield:** 87%  
Orange solid

The product was obtained using general procedure **A** from **4a** (79 mg), aniline (18  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as an orange solid (49 mg, 87%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.30 (s, 1H), 7.78 (m, 2H), 7.61–7.67 (m, 4H), 7.53 (m, 2H), 7.28 (m, 2H), 7.00 (m, 1H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  173.2, 159.5, 139.6, 134.1, 133.0, 130.5 (2C), 128.9 (2C), 122.7, 121.6 (2C), 118.8 (2C), 102.5.

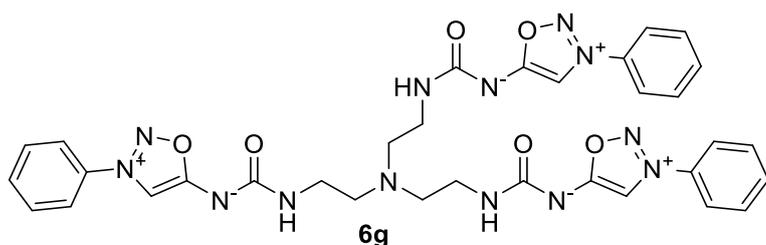
**IR (cm<sup>-1</sup>)** 1643, 1589, 1436, 1310, 962, 756, 680.

**LCMS (ESI)  $m/z$  [M+H]<sup>+</sup>** 281.

**HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup>** Calcd for C<sub>15</sub>H<sub>13</sub>N<sub>4</sub>O<sub>2</sub> 281.1033; Found 281.1033.

**Mp.** 119–121 °C.

**(((nitriлотris(ethane-2,1-diyl))tris(azanediyl))tris(carbonyl))tris((3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide) (6g)**



$C_{33}H_{33}N_{13}O_6$   
**MW:** 707 g.mol<sup>-1</sup>  
**Yield:** 66%  
Yellow solid

The product was obtained using general procedure **B** from **4a** (314 mg), tris(2-aminoethyl)amine (30  $\mu$ L) and triethylamine (84  $\mu$ L). The crude product was diluted in DCM and washed with a saturated solution of  $NH_4Cl$ . The organic layers were combined, dried over  $MgSO_4$  and evaporated. The resulted product purified was purified by column chromatography ( $SiO_2$ , DCM/MeOH, 95/5 then  $NEt_3$ /MeOH/DCM 1/2/97) to afford the desired product as a yellow solid (93 mg, 66%).

**$^1H$  NMR (400 MHz,  $CDCl_3$ )**  $\delta$  8.35 (s, 3H), 7.76 (m, 6H), 7.52–7.1 (m, 9H), 6.58 (br.s, 3H), 3.32 (m, 6H), 2.61 (m, 6H).

**$^{13}C$  NMR (100 MHz,  $CDCl_3$ )**  $\delta$  172.8 (3C), 162.4 (3C), 134.4 (3C), 132.4 (3C), 130.1 (6C), 121.9 (6C), 102.8 (3C), 54.7 (3C), 38.6 (3C).

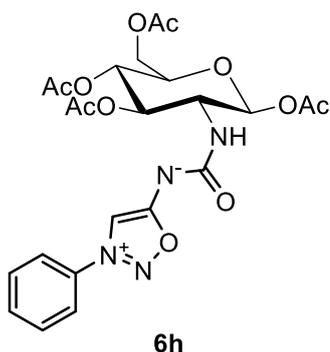
**IR (cm<sup>-1</sup>)** 3266, 1629, 1594, 1470, 1281, 1215, 958, 764.

**LCMS (ESI)  $m/z$  [M+H]<sup>+</sup>** 709; [M+2H]<sup>2+</sup> 355.

**HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup>** Calcd for  $C_{33}H_{34}N_{13}O_6$  708.2750; Found 708.2750.

**Mp.** 179–181 °C.

**(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)(((2S,3R,4R,5S,6R)-2,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2H-pyran-3-yl)carbamoyl)amide (6h)**



$C_{23}H_{26}N_4O_{11}$   
**MW:** 534 g.mol<sup>-1</sup>  
**Yield:** 60%  
Yellow solid

The product was obtained using general procedure **A** from **11a** (79 mg), 1,3,4,6-Tetra-O-acetyl-2-amino-2-deoxy-beta-D-glucopyranose hydrochloride (77 mg) and triethylamine (56  $\mu$ L). The crude product was purified by column chromatography ( $SiO_2$ , Heptane/EtOAc) to afford the desired product as a yellow solid (64 mg, 60%).

**$^1H$  NMR (400 MHz,  $CDCl_3$ )**  $\delta$  8.15 (s, 1H), 7.77 (m, 2H), 7.60–7.70 (m, 3H), 5.95 (d,  $J$  = 8.8 Hz, 1H), 5.92 (d,  $J$  = 9.1 Hz, 1H), 5.47 (dd,  $J$  = 10.3, 9.5 Hz, 1H), 5.09 (dd,  $J$  = 17.8, 8.2 Hz, 1H), 4.30 (dd,  $J$  = 12.4, 2.1 Hz, 1H), 3.97 (dd,  $J$  = 19.4, 9.1 Hz, 1H), 3.89 (ddd,  $J$  = 10.0, 4.5, 2.1 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H).

**$^{13}C$  NMR (100 MHz,  $CDCl_3$ )**  $\delta$  173.2, 170.8, 170.5, 169.7, 169.5, 161.4, 134.1, 133.0, 130.5 (2C), 121.6 (2C), 102.5, 92.5, 72.6, 72.4, 68.6, 61.9, 54.5, 21.1, 20.9, 20.8, 20.8.

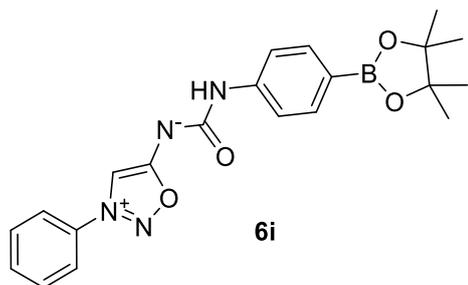
**IR (cm<sup>-1</sup>)** 1744, 1630, 1507, 1366, 1224, 1041.

**LCMS (ESI)  $m/z$  [M+H]<sup>+</sup>** 535.

**HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup>** Calcd for  $C_{23}H_{27}N_4O_{11}$  535.1671; Found 535.1669.

**Mp.** 196–198 °C.

**(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)carbamoyl)amide (6i)**



$C_{21}H_{23}BN_4O_4$   
**MW:** 406 g.mol<sup>-1</sup>  
**Yield:** 63%  
Yellow solid

The product was obtained using general procedure **B** from **4a** (79 mg), 4-aminophenyl boronic acid pinacol ester (44 mg) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a yellow solid (51 mg, 63%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.29 (s, 1H), 7.80 (m, 2H), 7.73 (m, 2H), 7.60–7.70 (m, 4H), 7.54 (m, 2H), 1.32 (s, 12H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  173.2, 159.3, 142.5, 135.9 (2C), 134.0, 133.1, 130.6 (2C), 121.6 (2C), 117.5 (2C), 102.5, 83.6 (2C), 25.0 (4C).

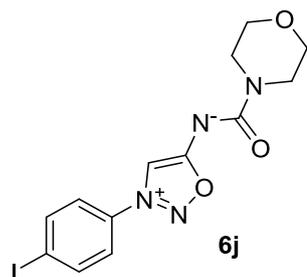
IR (cm<sup>-1</sup>) 2976, 1603, 1578, 1497, 1470, 1355, 1311, 1271, 1237, 1142, 1088, 961.

LCMS (ESI)  $m/z$  [M+H]<sup>+</sup> 407.

HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>24</sub>BN<sub>4</sub>O<sub>4</sub> 407.1885; Found 407.1888.

Mp. 190–192 °C.

**(3-(4-iodophenyl)-1,2,3-oxadiazol-3-ium-5-yl)(morpholine-4-carbonyl)amide (6j)**



$C_{13}H_{13}IN_4O_3$   
**MW:** 400 g.mol<sup>-1</sup>  
**Yield:** 75%  
Dark yellow solid

The product was obtained using general procedure **A** from **4b** (105 mg), morpholine (18  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc, from 50/50 to 10/90) to afford the desired product as a dark yellow solid (60 mg, 75%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.13 (s, 1H), 7.97 (m, 2H), 7.51 (m, 2H), 3.80 (m, 2H), 3.67 (m, 4H), 3.60 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  173.5, 160.7, 139.7 (2C), 133.7, 122.8 (2C), 101.8, 99.3, 67.1 (2C), 45.6, 43.2.

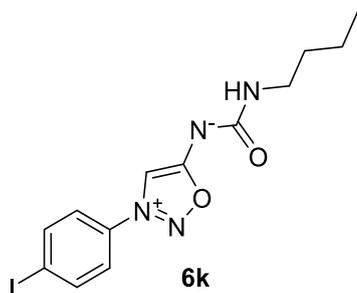
IR (cm<sup>-1</sup>) 1626, 1567, 1275, 1110.

LCMS (ESI)  $m/z$  [M+H]<sup>+</sup> 401.

HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>14</sub>IN<sub>4</sub>O<sub>3</sub> 401.0105; Found 401.0106.

Mp. 210–212 °C.

**(butylcarbamoyl)(3-(4-iodophenyl)-1,2,3-oxadiazol-3-ium-5-yl)amide (6k)**



$C_{13}H_{15}IN_4O_2$   
**MW:** 386 g.mol<sup>-1</sup>  
**Yield:** 80%  
Yellow solid

The product was obtained using general procedure **A** from **4b** (105 mg), *n*-butylamine (20  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a yellow solid (62 mg, 80%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.15 (s, 1H), 7.95 (m, 2H), 7.51 (m, 2H), 5.68 (br.s, 1H), 3.23 (m, 2H), 1.49 (m, 2H), 1.33 (m, 2H), 0.90 (t,  $J$  = 7.3 Hz, 3H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  172.6, 161.7, 139.7 (2C), 133.7, 122.8 (2C), 101.7, 99.1, 40.3, 32.2, 20.2, 13.9.

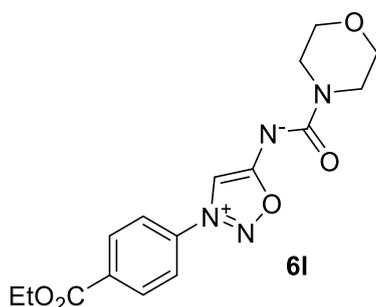
**IR (cm<sup>-1</sup>)** 3277, 1629, 1279, 1216, 955.

**LCMS (ESI)  $m/z$  [M+H]<sup>+</sup>** 387.

**HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup>** Calcd for C<sub>13</sub>H<sub>16</sub>IN<sub>4</sub>O<sub>2</sub> 387.0313; Found 387.0309.

**Mp.** 124–126°C.

**(3-(4-(ethoxycarbonyl)phenyl)-1,2,3-oxadiazol-3-ium-5-yl)(morpholine-4-carbonyl)amide (6l)**



$C_{16}H_{18}N_4O_5$   
**MW:** 346 g.mol<sup>-1</sup>  
**Yield:** 79%  
Yellow solid

The product was obtained using general procedure **A** from **4c** (94 mg), morpholine (18  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc, from 30/70 to 0/100) to afford the desired product as a yellow solid (55 mg, 79%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.29 (m, 2H), 8.21 (s, 1H), 7.86 (m, 2H), 4.41 (q,  $J$  = 7.1 Hz, 2H), 3.79 (m, 2H), 3.66 (m, 4H), 3.59 (m, 2H), 1.40 (t,  $J$  = 7.1 Hz, 3H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  173.5, 164.5, 160.7, 137.0, 134.6, 131.7 (2C), 121.5 (2C), 102.1, 67.1 (2C), 62.1, 45.5, 43.2, 14.3.

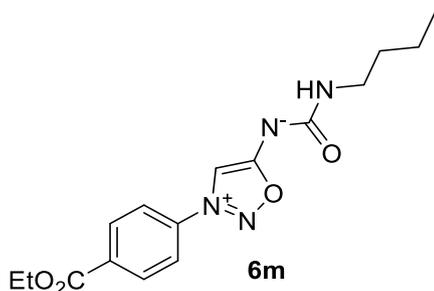
**IR (cm<sup>-1</sup>)** 1724, 1629, 1423, 1276, 1258, 1106, 987, 767.

**LCMS (ESI)  $m/z$  [M+H]<sup>+</sup>** 347.

**HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup>** Calcd for C<sub>16</sub>H<sub>19</sub>N<sub>4</sub>O<sub>5</sub> 347.1350; Found 347.1351.

**Mp.** 192–194 °C.

**(butylcarbamoyl)(3-(4-(ethoxycarbonyl)phenyl)-1,2,3-oxadiazol-3-ium-5-yl)amide (6m)**



$C_{16}H_{20}N_4O_4$   
**MW:** 332 g.mol<sup>-1</sup>  
**Yield:** 86%  
Yellow paste

The product was obtained using general procedure **A** from **4c** (94 mg), *n*-butylamine (20  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc, 50/50) to afford the desired product as a yellow paste (57 mg, 86%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.28 (m, 2H), 8.24 (s, 1H), 7.86 (m, 2H), 5.71 (br.t, *J* = 5.7 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 3.24 (m, 2H), 1.50 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.36 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

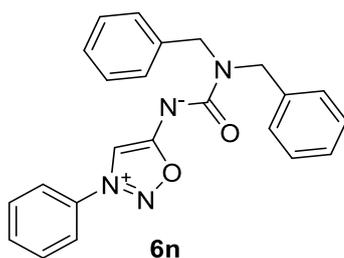
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  172.6, 164.6, 161.5, 137.0, 134.6, 131.7 (2C), 121.6 (2C), 102.1, 62.1, 40.3, 32.2, 20.2, 14.3, 13.9.

IR (cm<sup>-1</sup>) 3279, 1719, 1633, 1533, 1274, 1107, 954, 770.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 333.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>21</sub>N<sub>4</sub>O<sub>4</sub> 333.1557; Found 333.1560.

**(dibenzylcarbamoyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (6n)**



$C_{23}H_{20}N_4O_2$   
**MW:** 384 g.mol<sup>-1</sup>  
**Yield:** 66%  
Yellow paste

The product was obtained using general procedure **A** from **4a** (79 mg), dibenzylamine (38  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc, 50/50) to afford the desired product as a yellow paste (51 mg, 66%).

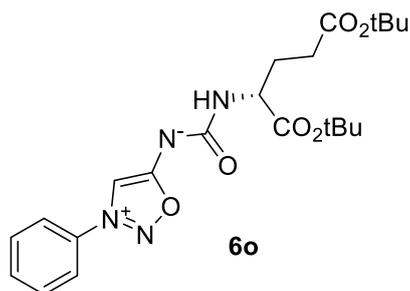
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.19 (s, 1H), 7.72 (m, 2H), 7.54–7.58 (m, 3H), 7.16–7.25 (m, 10H), 4.74 (s, 2H), 4.50 (s, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  173.7, 162.4, 138.8, 138.6, 134.3, 132.8, 130.5 (2C), 128.6 (2C), 128.5(2C), 127.9 (2C), 127.8 (2C), 127.1, 127.0, 121.5 (2C), 102.3, 50.0, 48.1.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 385.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>23</sub>H<sub>21</sub>N<sub>4</sub>O<sub>2</sub> 385.1659; Found 385.1658.

**(R)-((1,5-di-tert-butoxy-1,5-dioxopentan-2-yl)carbamoyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (6o)**



$C_{22}H_{30}N_4O_6$   
**MW:** 446 g.mol<sup>-1</sup>  
**Yield:** 86%  
Yellow paste

The product was obtained using general procedure **A** from **4a** (79 mg), di-tert-butyl D-glutamate hydrochloride (61 mg) and triethylamine (56  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc, 50/50) to afford the desired product as a yellow paste (76 mg, 86%).

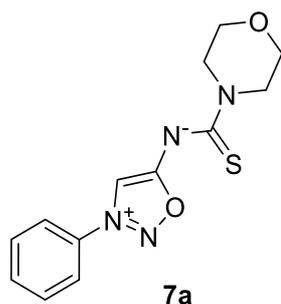
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.10 (s, 1H), 7.73 (m, 2H), 7.58–7.65 (m, 3H), 5.76 (d, *J* = 8.5 Hz, 1H), 4.37 (td, *J* = 8.3 Hz, 5.1 Hz, 1H), 2.25–2.33 (m, 2H), 2.09 (m, 1H), 1.90 (m, 1H), 1.43 (s, 9H), 1.39 (s, 9H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  173.1, 172.3, 171.6, 161.3, 134.1, 132.9, 130.5 (2C), 121.5 (2C), 102.1, 81.9, 80.4, 53.4, 31.7, 28.4, 28.1 (3C), 28.1 (3C).

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 447.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>31</sub>N<sub>4</sub>O<sub>6</sub> 447.2238; Found 447.2232.

**(morpholine-4-carbonothioyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (7a)**



$C_{13}H_{14}N_4O_2S$   
**MW:** 290 g.mol<sup>-1</sup>  
**Yield:** 79%  
Yellow solid

The product was obtained using general procedure **A** from **5a** (83 mg), morpholine (18  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a yellow solid (46 mg, 79%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  9.15 (s, 1H), 7.79 (m, 2H), 7.60–7.70 (m, 3H), 4.25 (m, 2H), 4.10 (m, 2H), 3.72 (m, 2H), 3.66 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  184.5, 173.6, 134.1, 133.0, 130.5 (2C), 121.7 (2C), 102.4, 66.8, 66.8, 49.0, 47.0.

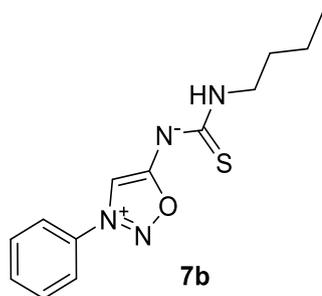
IR (cm<sup>-1</sup>) 1592, 1428, 1217, 1114, 963.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 291.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>15</sub>N<sub>4</sub>O<sub>2</sub>S 291.0910; found 291.0909.

Mp. 209–211 °C.

**(butylcarbamothioyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (7b)**



C<sub>13</sub>H<sub>16</sub>N<sub>4</sub>OS  
MW: 276 g.mol<sup>-1</sup>  
Yield: 69%  
Orange solid

The product was obtained using general procedure **A** from **5a** (79 mg), *n*-butylamine (20 μL) and triethylamine (28 μL). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a orange solid (38 mg, 69%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.22 {9.23} (s, 1H), 7.82 (m, 2H), 7.63–7.73 (m, 3H), 6.98 {6.74} (br.s, 1H), 3.65 {3.52} (m, 2H), 1.63 {1.54} (m, 2H), 1.39 (m, 2H), 0.94 {0.93} (t, *J* = 7.3 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 187.2 {185.6}, 172.8 {174.4}, 134.1 {134.0}, 133.0 {133.1}, 130.5 {130.6} (2C), 121.8 (2C), 102.4 {103.0}, 44.8 {43.9}, 31.0 {31.5}, 20.3 {20.2}, 13.9 {13.9}.

NMR spectra show the presence of 2 isomers (ratio 1.7/1 at room temperature), minor isomer signals are reported into brackets when they are distinguishable.

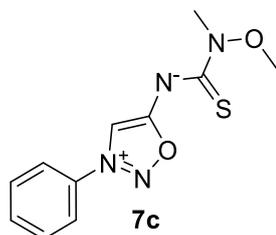
IR (cm<sup>-1</sup>) 3229, 1605, 1594, 1468, 1358, 953, 763.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 277.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>17</sub>N<sub>4</sub>OS 277.1118; Found 277.1115.

Mp. 121–123 °C.

**(methoxy(methyl)carbamothioyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (7c)**



C<sub>11</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>S  
MW: 264 g.mol<sup>-1</sup>  
Yield: 66%  
Yellow solid

The product was obtained using general procedure **B** from **5a** (82 mg), *N,O*-dimethylhydroxylamine.HCl (19 mg) and triethylamine (56 μL). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a yellow solid (35 mg, 66%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.21 (s, 1H), 7.81 (m, 2H), 7.62–7.72 (m, 3H), 3.84 (s, 3H), 3.65 (s, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 183.4, 173.8, 134.1, 133.1, 130.6 (2C), 121.8 (2C), 102.5, 60.7, 38.1.

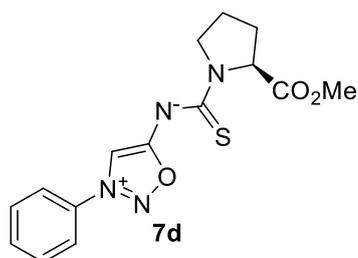
IR (cm<sup>-1</sup>) 1603, 1590, 1359, 131, 955.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 265.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>11</sub>H<sub>13</sub>N<sub>4</sub>O<sub>2</sub>S 265.0754; Found 265.0754.

Mp. 117–120 °C.

**(S)-(2-(methoxycarbonyl)pyrrolidine-1-carbonothioyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (7d)**



$C_{15}H_{16}N_4O_3S$   
**MW:** 332 g.mol<sup>-1</sup>  
**Yield:** 81%  
Orange oil

The product was obtained using general procedure **B** from **5a** (82 mg), L-proline methyl ester.HCl (33 mg) and triethylamine (56  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as an orange oil (54 mg, 81%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  9.14 {9.15} (s, 1H), 7.76 (m, 2H), 7.59–7.69 (m, 3H), 4.79 {4.96} (dd,  $J$  = 8.5, 3.8 Hz, 1H), 3.83–4.01 (m, 2H), 3.71 (s, 3H), 2.24–2.31 (m, 1H), 1.92–2.11 (m, 3H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  183.5 {182.9}, 172.9 {173.2}, 172.3 {173.1}, 134.1, 133.0 {133.0}, 130.5 {130.5} (2C), 121.7 {121.7} (2C), 102.3 {102.5}, 61.6 {63.7}, 52.2, 51.7 {49.9}, 30.6 {30.0}, 23.7 {24.3}.

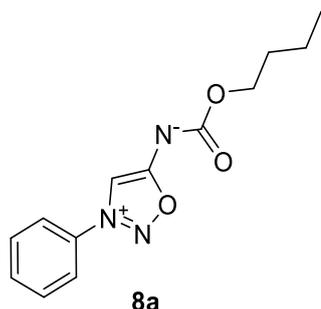
*NMR spectra show the presence of 2 isomers (ratio 1.1/1 at room temperature), minor isomer signals are reported into brackets when they are distinguishable.*

**IR (cm<sup>-1</sup>)** 1738, 1603, 1590, 1403, 1359, 1337, 1201, 957, 764.

**HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup>** Calcd for C<sub>15</sub>H<sub>17</sub>N<sub>4</sub>O<sub>3</sub>S 333.1016; Found 333.1017.

**LCMS (ESI)  $m/z$  [M+H]<sup>+</sup>** 333.

**(butoxycarbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (8a)**



$C_{13}H_{15}N_3O_3$   
**MW:** 261 g.mol<sup>-1</sup>  
**Yield:** 73%  
Beige solid

The product was obtained using general procedure **B** from **4a** (79 mg), *n*-butanol (18  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a beige solid (38 mg, 73%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.09 (s, 1H), 7.77 (m, 2H), 7.63–7.69 (m, 3H), 4.08 (t,  $J$  = 6.7 Hz, 2H), 1.63 (m, 2H), 1.39 (m, 2H), 0.89 (t,  $J$  = 7.4 Hz, 3H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  175.2, 161.9, 133.9, 133.2, 130.7 (2C), 121.6 (2C), 102.8, 65.5, 31.1, 19.3, 13.9.

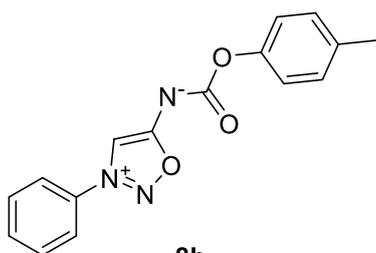
**IR (cm<sup>-1</sup>)** 1645, 1547, 1469, 1356, 1194, 1130, 981, 870, 718.

**LCMS (ESI)  $m/z$  [M+H]<sup>+</sup>** 262.

**HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup>** Calcd for C<sub>13</sub>H<sub>16</sub>N<sub>3</sub>O<sub>3</sub> 262.1186; Found 262.1184.

**Mp.** 83–85 °C.

**(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)((p-tolyloxy)carbonyl)amide (8b)**



$C_{16}H_{13}N_3O_3$   
**MW:** 295 g.mol<sup>-1</sup>  
**Yield:** 65%  
Beige solid

The product was obtained using general procedure **B** from **4a** (79 mg), cresol (22 mg) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a beige solid (39 mg, 65%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.16 (s, 1H), 7.77 (m, 2H), 7.67 (m, 1H), 7.65 (m, 2H), 7.14 (m, 2H), 7.05 (m, 2H), 2.32 (s, 3H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  175.9, 160.8, 149.9, 134.8, 133.9, 133.4, 130.8 (2C), 129.8 (2C), 121.7 (4C), 103.5, 21.0.

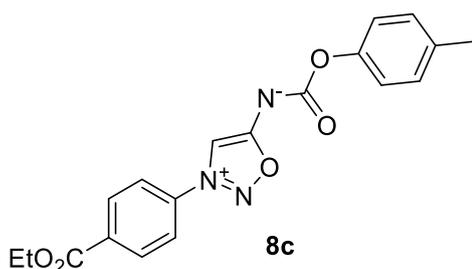
**IR (cm<sup>-1</sup>)** 1671, 1577, 1507, 1365, 1277, 1181, 967, 764.

**LCMS (ESI) *m/z* [M+H]<sup>+</sup>** 296.

**HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup>** Calcd for C<sub>16</sub>H<sub>14</sub>N<sub>3</sub>O<sub>3</sub> 296.1030; Found 296.1031.

**Mp.** 144–146 °C.

**(3-(4-(ethoxycarbonyl)phenyl)-1,2,3-oxadiazol-3-ium-5-yl)((p-tolyloxy)carbonyl)amide (8c)**



$C_{19}H_{17}N_3O_5$   
**MW:** 367 g.mol<sup>-1</sup>  
**Yield:** 60%  
Pale yellow solid

The product was obtained using general procedure **B** from **4c** (94 mg), cresol (22 mg) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a pale yellow solid (44 mg, 60%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.31 (d, *J* = 8.7 Hz, 2H), 8.23 (s, 1H), 7.88 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 2.31 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  175.9, 164.5, 160.8, 149.9, 136.6, 135.1, 134.9, 132.0 (2C), 129.9 (2C), 121.8 (2C), 121.6 (2C), 103.7, 62.3, 21.1, 14.5.

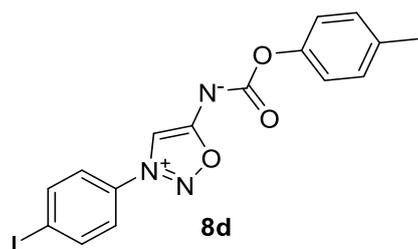
**IR (cm<sup>-1</sup>)** 1717, 1664, 1578, 1276, 1190, 1108, 971, 770.

**LCMS (ESI) *m/z* [M+H]<sup>+</sup>** 368.

**HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup>** Calcd for C<sub>19</sub>H<sub>18</sub>N<sub>3</sub>O<sub>5</sub> 368.1241; Found 368.1244.

**Mp.** 151–153 °C.

**(3-(4-iodophenyl)-1,2,3-oxadiazol-3-ium-5-yl)((p-tolyloxy)carbonyl)amide (8d)**



$C_{16}H_{12}IN_3O_3$   
**MW:** 421 g.mol<sup>-1</sup>  
**Yield:** 63%  
Beige solid

The product was obtained using general procedure **B** from **4b** (105 mg), cresol (22 mg) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc, from 80/20 to 60/40) to afford the desired product as a beige solid (53 mg, 63%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.14 (s, 1H), 7.98 (m, 2H), 7.50 (m, 2H), 7.12 (m, 2H), 7.03 (m, 2H), 2.30 (s, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  175.9, 160.8, 149.9, 140.0 (2C), 134.9, 133.4, 129.9 (2C), 122.9 (2C), 121.6 (2C), 103.3, 100.0, 21.1.

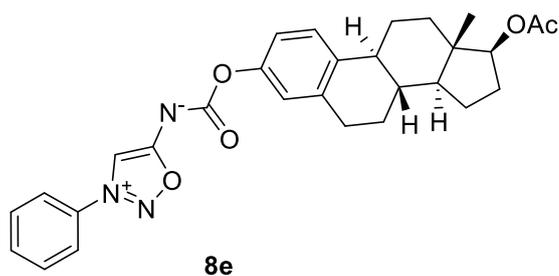
IR (cm<sup>-1</sup>) 1664, 1576, 1507, 1283, 1190, 972.

LCMS (ESI)  $m/z$  [M+H]<sup>+</sup> 422.

HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>13</sub>IN<sub>3</sub>O<sub>3</sub> 421.9996; Found 421.9996.

Mp. 200–202 °C.

**(((8R,9S,13S,14S,17S)-17-acetoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)oxy)carbonyl(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (8e)**



$C_{29}H_{31}N_3O_5$   
**MW:** 501 g.mol<sup>-1</sup>  
**Yield:** 62%  
Beige solid

The product was obtained using general procedure **B** from **4a** (79 mg),  $\beta$ -estradiol-17-acetate (63 mg) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a beige solid (62%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.14 (s, 1H), 7.75 (m, 2H), 7.69 (m, 1H), 7.62 (m, 2H), 7.22 (d,  $J$  = 8.7 Hz, 1H), 6.92 (dd,  $J$  = 8.7, 2.4 Hz, 1H), 6.87 (d,  $J$  = 2.4 Hz, 1H), 4.65 (t,  $J$  = 8.6 Hz, 1H), 2.82 (m, 2H), 2.18 (m, 2H), 2.03 (s, 3H), 1.85 (m, 2H), 1.23–1.55 (m, 7H), 0.79 (s, 3H).

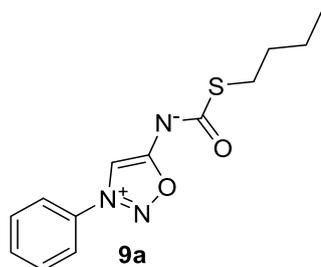
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  175.8, 171.3, 160.9, 149.9, 137.9, 137.2, 133.9, 133.4, 130.7 (2C), 126.3, 121.9, 121.6 (2C), 119.1, 103.5, 82.8, 49.9, 44.1, 43.0, 38.4, 37.0, 29.7, 27.7, 27.2, 26.2, 23.4, 21.4, 12.2.

IR (cm<sup>-1</sup>) 2928, 1731, 1674, 1589, 1227, 1192, 989, 970.

HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup> Calcd for C<sub>29</sub>H<sub>31</sub>N<sub>3</sub>O<sub>5</sub> 502.2336; Found 502.2338.

Mp. 97–99 °C.

**((butylthio)carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (9a)**



$C_{13}H_{15}N_3O_2S$   
**MW:** 277 g.mol<sup>-1</sup>  
**Yield:** 32%  
Yellow paste

The product was obtained using general procedure **B** from **4a** (79 mg), *n*-butanethiol (21  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a yellow paste (18 mg, 32%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.24 (s, 1H), 7.80 (m, 2H), 7.72 (m, 1H), 7.66 (m, 2H), 2.88 (t, *J* = 7.4 Hz, 2H), 1.64 (m, 2H), 1.43 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H).

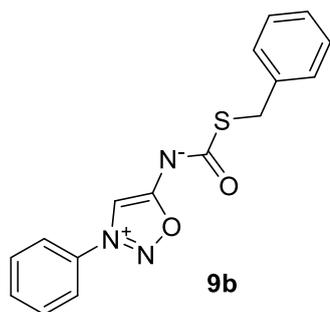
**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  178.1, 171.6, 133.4 (2C), 130.8 (2C), 121.7 (2C), 104.1, 32.5, 30.6, 22.3, 13.9.

**IR (cm<sup>-1</sup>)** 1621, 1556, 1359, 1242, 1148, 964, 848, 760.

**LCMS (ESI) *m/z* [M+H]<sup>+</sup>** 278.

**HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup>** Calcd for C<sub>13</sub>H<sub>16</sub>N<sub>3</sub>O<sub>2</sub>S 278.0958; Found 278.0959.

**((benzylthio)carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (9b)**



$C_{16}H_{13}N_3O_2S$   
**MW:** 311 g.mol<sup>-1</sup>  
**Yield:** 51%  
Yellow paste

The product was obtained using general procedure **B** from **4a** (79 mg), benzyl mercaptan (24  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a yellow paste (32 mg, 51%).

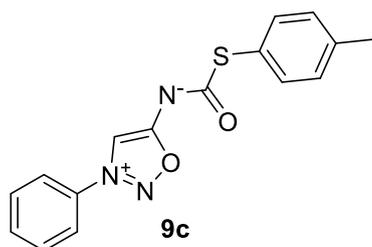
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.23 (s, 1H), 7.77 (m, 2H), 7.70 (m, 1H), 7.64 (m, 2H), 7.37 (m, 2H), 7.27 (m, 2H), 7.19 (m, 1H), 4.12 (s, 2H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  177.1, 171.6, 138.7, 133.3, 130.6 (2C), 128.8 (2C), 128.4 (2C), 126.9, 121.5 (2C), 104.1, 35.2.

**LCMS (ESI) *m/z* [M+H]<sup>+</sup>** 312.

**HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup>** Calcd for C<sub>16</sub>H<sub>14</sub>N<sub>3</sub>O<sub>2</sub>S 312.0801; Found 312.0806.

**(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)((*p*-tolylthio)carbonyl)amide (9c)**



$C_{16}H_{13}N_3O_2S$   
**MW:** 311 g.mol<sup>-1</sup>  
**Yield:** 53%  
Yellow solid

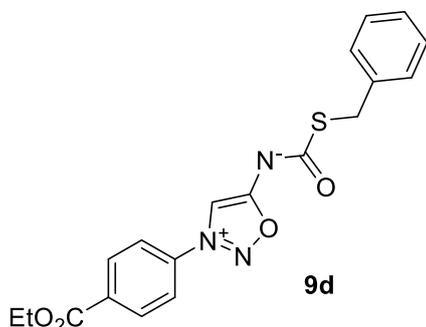
The product was obtained using general procedure **B** from **4a** (79 mg), *p*-thiocresol (21  $\mu$ L) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a yellow solid (33 mg, 53%).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.20 (s, 1H), 7.72 (m, 3H), 7.62 (m, 2H), 7.42 (d,  $J = 8.1$  Hz, 2H), 7.18 (d,  $J = 8.1$  Hz, 2H), 2.34 (s, 3H).

The product was not stable enough to afford a  $^{13}\text{C NMR}$  spectrum.

HRMS (ESI-TOF)  $m/z$   $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{16}\text{H}_{14}\text{N}_3\text{O}_2\text{S}$  312.0801; Found 312.0806.

**((benzylthio)carbonyl)(3-(4-(ethoxycarbonyl)phenyl)-1,2,3-oxadiazol-3-ium-5-yl)amide (9d)**



$\text{C}_{19}\text{H}_{17}\text{N}_3\text{O}_4\text{S}$   
MW: 383  $\text{g}\cdot\text{mol}^{-1}$   
Yield: 47%  
Yellow solid

The product was obtained using general procedure **B** from **4c** (94 mg), benzyl mercaptan (24  $\mu\text{L}$ ) and triethylamine (28  $\mu\text{L}$ ). The crude product was purified by column chromatography ( $\text{SiO}_2$ , Heptane/EtOAc, 50/50) to afford the desired product as a yellow solid (36 mg, 47%).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.30 (d,  $J = 8.2$  Hz, 2H), 8.30 (s, 1H), 7.87 (d,  $J = 8.7$  Hz, 2H), 7.35 (m, 2H), 7.26 (m, 2H), 7.19 (m, 1H), 4.43 (q,  $J = 7.2$  Hz, 2H), 4.12 (s, 2H), 1.42 (t,  $J = 7.2$  Hz, 3H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  177.4, 171.7, 164.5, 138.8, 136.6, 135.2, 132.0 (2C), 129.0 (2C), 128.6 (2C), 127.1, 121.8 (2C), 104.4, 62.3, 35.4, 14.5.

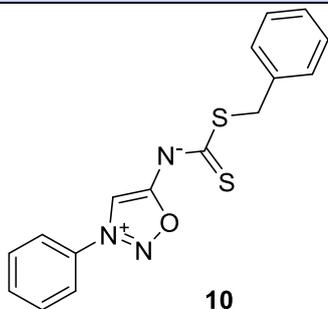
IR ( $\text{cm}^{-1}$ ) 1719, 1560, 1276, 1150, 845, 768.

LCMS (ESI)  $m/z$   $[\text{M}+\text{H}]^+$  384.

HRMS (ESI-TOF)  $m/z$   $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{19}\text{H}_{18}\text{N}_3\text{O}_4\text{S}$  384.1013; Found 384.1016.

Mp. 129–131  $^\circ\text{C}$ .

**((benzylthio)carbonothioyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (10)**



$\text{C}_{16}\text{H}_{13}\text{N}_3\text{OS}_2$   
MW: 327  $\text{g}\cdot\text{mol}^{-1}$   
Yield: 56%  
Brown paste

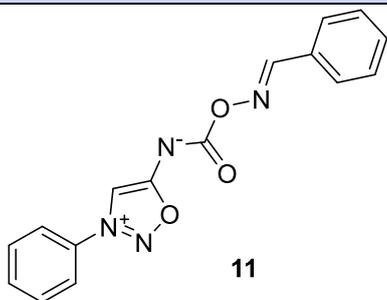
The product was obtained using general procedure **B** from **5a** (82 mg), benzyl mercaptan (24  $\mu\text{L}$ ) and triethylamine (28  $\mu\text{L}$ ). The crude product was purified by column chromatography ( $\text{SiO}_2$ , Heptane/EtOAc) to afford the desired product as a brown paste (36 mg, 56%).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.43 (s, 1H), 7.82 (m, 2H), 7.65–7.74 (m, 3H), 7.39 (m, 2H), 7.27 (m, 2H), 7.22 (m, 1H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  209.8, 171.5, 137.6, 133.9, 133.8, 130.9 (2C), 129.4 (2C), 128.6 (2C), 127.1, 122.0 (2C), 104.7, 40.7.

HRMS (ESI-TOF)  $m/z$   $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{16}\text{H}_{13}\text{N}_3\text{OS}_2$  328.0573; Found 328.0577.

**(E)-(((benzylideneamino)oxy)carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (11)**



C<sub>16</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub>  
MW: 308 g.mol<sup>-1</sup>  
Yield: 66%  
White solid

The product was obtained using general procedure **B** from **4a** (79 mg), benzaldehyde oxime (24 mg) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a white solid (41 mg, 66%).

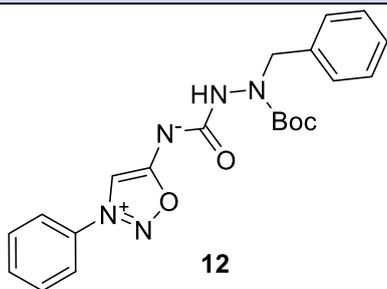
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.39 (s, 1H), 8.27 (s, 1H), 7.81 (m, 2H), 7.61–7.72 (m, 5H), 7.34–7.42 (m, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  175.5, 160.2, 154.3, 133.8, 133.4, 131.2, 131.0, 130.7 (2C), 128.8 (2C), 128.3 (2C), 121.7 (2C), 103.5.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 309.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>13</sub>N<sub>4</sub>O<sub>3</sub> 309.0982; Found 309.0984.

**(2-benzyl-2-(tert-butoxycarbonyl)hydrazine-1-carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (12)**



C<sub>21</sub>H<sub>23</sub>N<sub>5</sub>O<sub>4</sub>  
MW: 409 g.mol<sup>-1</sup>  
Yield: 65%  
Yellow solid

The product was obtained using general procedure **B** from **4a** (79 mg), tert-butyl 1-benzylhydrazine-1-carboxylate<sup>2</sup> (22 mg) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a yellow solid (53 mg, 65%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.18 (s, 1H), 7.76 (m, 2H), 7.66 (m, 3H), 7.35 (s, 1H), 7.26–7.29 (m, 4H), 7.23 (br.s, 1H), 4.70 (s, 2H), 1.47 (s, 9H).

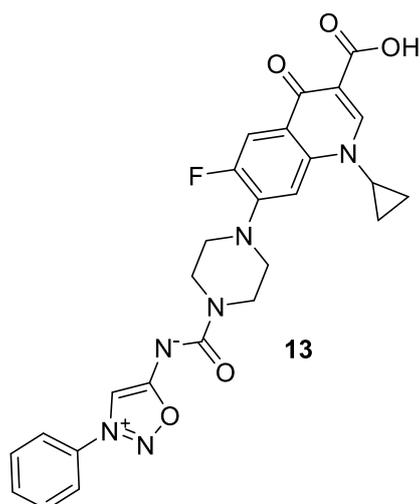
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  173.3, 155.7, 155.3, 137.4, 133.9, 133.0, 130.5 (2C), 128.4 (4C), 127.3, 121.5 (2C), 102.7, 80.9, 54.6, 28.3 (3C).

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 410.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>24</sub>N<sub>5</sub>O<sub>4</sub> 410.1823; Found 410.1821.

<sup>2</sup> tert-butyl 1-benzylhydrazine-1-carboxylate was synthesized according to a reported procedure J. Kim, H. Song, S. B. Park, *Eur. J. Org. Chem.* **2010**, 3815–3822

**(4-(3-carboxy-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl)piperazine-1-carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (13)**



$C_{26}H_{23}FN_6O_5$   
**MW:** 518  $g \cdot mol^{-1}$   
**Yield:** 68%  
Yellow solid

The product was obtained using general procedure **A** from **4a** (79 mg), ciprofloxacin (66 mg) and triethylamine (28  $\mu$ L). After completion, methanol was added to the reaction. Water was then added and the mixture was filtered to afford the desired product as a yellow solid (71 mg, 68%).

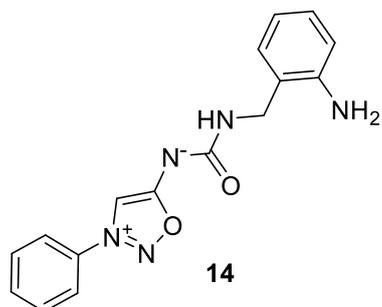
**$^1H$  NMR (400 MHz,  $CDCl_3$ )**  $\delta$  11.71 (br.s, 1H), 8.84 (s, 1H), 8.83 (s, 1H), 7.91–8.00 (m, 3H), 7.85 (m, 1H), 7.76 (m, 2H), 7.47 (d,  $J = 7.0$  Hz, 1H), 3.92 (m, 4H), 3.65 (tt,  $J = 7.1, 4.1$  Hz, 1H), 3.46 (m, 4H), 1.45 (m, 2H), 1.19 (m, 2H).

**$^{13}C$  NMR (100 MHz,  $CDCl_3$ )**  $\delta$  176.3, 169.6, 167.6, 160.0 (q,  $J = 40$  Hz), 155.3, 152.8, 150.4, 148.3, 146.0 (q,  $J = 10$  Hz), 139.6, 135.3, 132.6, 131.5 (2C), 122.2 (2C), 115.3 (q,  $J = 285$  Hz), 112.5 (q,  $J = 22$  Hz), 107.0, 105.7, 49.3 (2C), 44.3 (2C), 36.4, 8.4.

**LCMS (ESI)  $m/z$   $[M+H]^+$**  519.

**HRMS (ESI-TOF)  $m/z$   $[M+H]^+$**  Calcd for  $C_{26}H_{24}FN_6O_5$  519.1787; Found 519.1791.

**((2-aminobenzyl)carbamoyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (14)**



$C_{16}H_{15}N_5O_2$   
**MW:** 309  $g \cdot mol^{-1}$   
**Yield:** 68%  
Yellow solid

The product was obtained using general procedure **A** from **4a** (79 mg), 2-aminobenzylamine (27 mg) and triethylamine (31  $\mu$ L). After completion, methanol was added to the reaction. Water was then added and the mixture was filtered to afford the desired product as a yellow solid (42 mg, 68%).

**$^1H$  NMR (400 MHz,  $DMSO-d_6$ )**  $\delta$  8.39 (s, 1H), 8.03 (m, 2H), 7.66–7.76 (m, 3H), 7.43 (br.t,  $J = 6.4$  Hz, 1H), 6.99 (d,  $J = 7.2$  Hz, 1H), 6.93 (dd,  $J = 7.9, 7.2$  Hz, 1H), 6.59 (d,  $J = 7.9$  Hz, 1H), 6.47 (dd,  $J = 7.9, 7.2$  Hz, 1H), 5.18 (br.s, 2H), 4.11 (d,  $J = 6.4$  Hz, 2H).

**$^{13}C$  NMR (100 MHz,  $DMSO-d_6$ )**  $\delta$  172.0, 161.2, 146.3, 133.9, 132.6, 130.2 (2C), 129.4, 127.6, 123.4, 122.2 (2C), 115.5, 114.4, 102.4, 40.5.

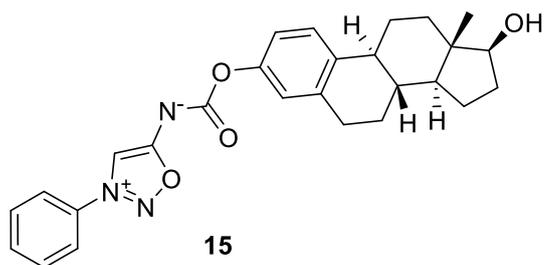
**IR ( $cm^{-1}$ )** 3266, 1632, 1552, 1285, 967, 761.

**LCMS (ESI)  $m/z$   $[M+H]^+$**  310.

**HRMS (ESI-TOF)  $m/z$   $[M+H]^+$**  Calcd for  $C_{16}H_{16}N_5O_2$  310.1299; Found 310.1296.

**Mp.** 187–189  $^{\circ}C$ .

**(((8*R*,9*S*,13*S*,14*S*,17*S*)-17-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)carbonyl(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (15)**



$C_{27}H_{29}N_3O_4$   
MW: 459 g.mol<sup>-1</sup>  
Yield: 53%  
Beige solid

The product was obtained using general procedure **B** from **4a** (79 mg),  $\beta$ -estradiol (60 mg) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, Heptane/EtOAc) to afford the desired product as a beige solid (38 mg, 53%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.14 (s, 1H), 7.77 (m, 2H), 7.70 (m, 1H), 7.64 (m, 2H), 7.25 (d, *J* = 8.7 Hz, 1H), 6.94 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.88 (d, *J* = 2.5 Hz, 1H), 3.7 (t, *J* = 8.4 Hz, 1H), 2.84 (m, 2H), 2.30 (m, 1H), 2.19 (m, 1H), 2.09 (m, 1H), 1.92 (m, 1H), 1.85 (m, 1H), 1.64–1.72 (m, 1H), 1.13–1.51 (m, 8H), 0.74 (s, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  175.9, 161.0, 149.9, 138.1, 137.4, 133.9, 133.5, 130.8 (2C), 126.3, 121.9, 121.7 (2C), 119.1, 103.5, 82.1, 50.2, 44.4, 43.4, 38.7, 36.9, 30.7, 29.8, 27.3, 26.4, 23.3, 11.2.

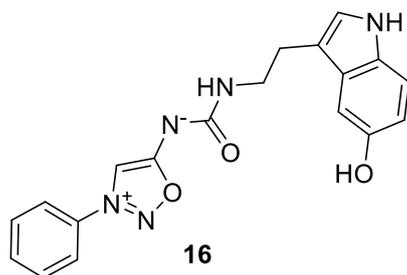
IR (cm<sup>-1</sup>) 3387, 2924, 1670, 1586, 1493, 1290, 1224, 1192, 973.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 460.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>27</sub>H<sub>30</sub>N<sub>3</sub>O<sub>4</sub> 460.2231; Found 460.2227.

Mp. 179–181 °C.

**((2-(5-hydroxy-1*H*-indol-3-yl)ethyl)carbamoyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (16)**



$C_{19}H_{17}N_5O_3$   
MW: 363 g.mol<sup>-1</sup>  
Yield: 53%  
Red solid

The product was obtained using general procedure **A** from **4a** (79 mg), serotonin.HCl (40 mg) and triethylamine (56  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, DCM/MeOH, from 100/0 to 95/5) and then (C18-grefted silica, H<sub>2</sub>O/MeCN + TFA 1%, from 95/5 to 0/100, gradient 2% MeCN/min) to afford the desired product as a red solid (36 mg, 53%).

<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  10.54 (s, 1H), 9.10 (s, 1H), 8.11 (m, 2H), 7.81 (m, 1H), 7.75 (m, 2H), 7.67 (br.s 1H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.07 (d, *J* = 1.9 Hz, 1H), 6.86 (d, *J* = 2.4 Hz, 1H), 6.6 (dd, *J* = 8.6, 2.4 Hz, 1H), 3.41 (m, 2H), 2.82 (br.t, *J* = 6.6 Hz, 2H).

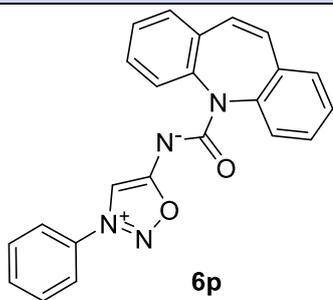
<sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  167.9, 154.0, 150.2, 133.5, 133.1, 130.8, 130.4 (2C), 127.9, 123.2, 122.6 (2C), 111.7, 111.3, 110.5, 105.8, 102.2, 40.5, 25.5.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 364.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>18</sub>N<sub>5</sub>O<sub>3</sub> 364.1404; Found 364.1401.

Mp. 189–191 °C.

**(5H-dibenzo[b,f]azepine-5-carbonyl)(3-phenyl-1,2,3-oxadiazol-3-ium-5-yl)amide (6p)**



$C_{23}H_{16}N_4O_2$   
**MW:** 380 g.mol<sup>-1</sup>  
**Yield:** 58%  
Yellow solid

The product was obtained using general procedure **B** from **4a** (79 mg), iminostilbene (39 mg) and triethylamine (28  $\mu$ L). The crude product was purified by column chromatography (SiO<sub>2</sub>, cyclohexane/EtOAc, 60/40) to afford the desired product as a yellow solid (44 mg, 58%).

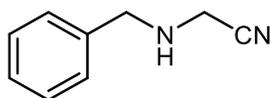
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.15 (s, 1H), 7.67 (d,  $J$  = 8.0 Hz, 2H), 7.63-7.59 (m, 1H), 7.55 (d,  $J$  = 7.8 Hz, 2H), 7.53-7.50 (m, 2H), 7.42 (m, 2H), 7.36-7.33 (m, 2H), 7.28 (m, 2H), 6.92 (s, 2H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  173.6, 161.2, 141.9, 141.4, 134.7, 134.1, 132.9, 130.6, 130.5 (3C), 129.8 (2C), 129.3, 129.1, 129.0 (2C), 128.9, 127.0, 126.8, 121.4 (2C), 102.8.

**IR (cm<sup>-1</sup>):** 1630, 1578, 1489, 1325, 1303, 1194, 966, 762, 730.

**HRMS (ESI-TOF)  $m/z$  [M+H]<sup>+</sup>** Calcd for C<sub>23</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub> 381.1346; Found 381.1345.

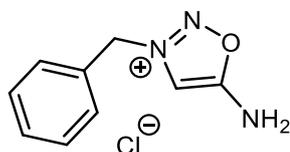
**Mp.** 158-159 °C

**2-(benzylamino)acetonitrile (S1)**

$C_9H_{10}N_2$   
**MW:** 146 g.mol<sup>-1</sup>  
**Yield:** 99%  
Yellow oil

To a suspension of phenylmethanamine (1.20 g, 11.2 mmol) and N,N-Diisopropylethylamine (1.77 g, 13.8 mmol) in MeCN (10 mL) was added 2-bromoacetonitrile (1 g, 7.5 mmol) at room temperature and the reaction mixture was stirred at room temperature for 16 hours. LCMS showed that the material was converted to the product completely. The organic solvent were removed under reduced pressure and the residue was taken up in ethyl acetate, then organic layer were washed with water and brine and dried over anhydrous MgSO<sub>4</sub>. The solvent was removed under reduced pressure. Purification of the crude mixture by flash column chromatography using (9/1) to (7/3) of heptane/ethyl acetate gave the desired product as a yellow oil (1.09 g, 99%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.35 (d, *J* = 4.5 Hz, 4H), 7.33 – 7.27 (m, 1H), 3.94 (s, 2H), 3.57 (s, 2H), 1.63 (s, 1H).  
The spectral data ( <sup>1</sup>H-NMR) was consistent with reported one: *Haihua Yu, Li Xiao, Xicheng Yang, Liming Shao; Chem. Commun., 2017,53, 9745-9748*

**(1H-imidazole-1-carbonyl)(3-(4-iodophenyl)-1,2,3-oxadiazol-3-ium-5-yl)amide (S2)**

$C_{12}H_8IN_5O_2$   
**MW:** 212 g.mol<sup>-1</sup>  
**Yield:** 67%  
White solid

To a solution of 2-(benzylamino)acetonitrile **S1** (0.5 g, 3.42 mmol) in THF (1.5 mL), tert-butyl nitrite (1.21 mL, 10.26 mmol) was added. The solution was stirred at room temperature for 2 hours. Then, a solution of HCl (4M) in dioxane was added (2.4 mL) and the reaction mixture was stirred overnight at room temperature under argon. Et<sub>2</sub>O was added and the precipitate was collected by filtration, washed with Et<sub>2</sub>O, washed with Et<sub>2</sub>O to afford the product as a white powder (486 mg, 67%).

<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 9.67 (s, 2H), 8.10 (s, 1H), 7.56 (d, *J* = 9.6 Hz, 2H), 7.47 (s, 3H), 5.89 (s, 2H).

<sup>13</sup>C NMR (101 MHz, DMSO-d<sub>6</sub>) δ 169.2, 131.3, 129.7, 129.4 (2C), 129.1 (2C), 103.0, 56.4.

IR (cm<sup>-1</sup>) 1671, 1570, 1374, 1296, 1008, 976.

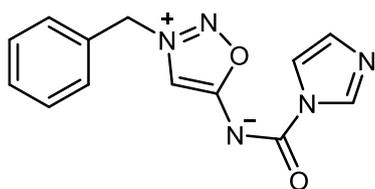
LCMS (ESI) *m/z* [M+H]<sup>+</sup> 176.5.

HRMS (ESI-TOF) *m/z* [M-Cl]<sup>+</sup> Calcd for C<sub>12</sub>H<sub>8</sub>IN<sub>5</sub>O<sub>2</sub> 176.0819; Found 176.0818.

Mp. 127-129 °C.

IR (cm<sup>-1</sup>) 2946, 1669, 1667, 1467, 1172, 912, 693.

**(3-benzyl-1,2,3-oxadiazol-3-ium-5-yl)(1H-imidazole-1-carbonyl)amide (S3)**



$C_{13}H_{11}N_5O_2$   
**MW:** 269 g.mol<sup>-1</sup>  
**Yield:** 67%  
White solid

To a solution of 1,1'-carbonyldiimidazole (368 mg, 2.27 mmol) in a mixture DMF/MeCN (4 mL/1.5 mL) was added **S2** (400 mg, 2.00 mmol). The solution was stirred at room temperature for 4 hour before being concentrated under reduced pressure. The crude product was purified by column chromatography (SiO<sub>2</sub>, DCM/MeOH, 98/2) to afford the desired product as a white solid (454 mg, 89%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  8.33 (t, *J* = 1.0 Hz, 1H), 7.82 (s, 1H), 7.57 (t, *J* = 1.4 Hz, 1H), 7.55 – 7.46 (m, 3H), 7.46 – 7.39 (m, 2H), 7.01 (dd, *J* = 1.5, 1.0 Hz, 1H), 5.58 (s, 2H).

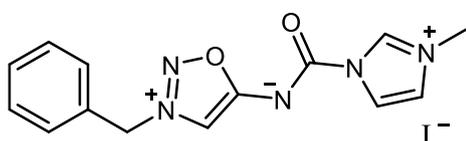
**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**  $\delta$  175.0, 154.7, 137.5, 130.9, 130.0 (2C), 129.8, 129.1 (2C), 129.0, 117.2, 105.6, 57.7.

**IR (cm<sup>-1</sup>)** 1660, 1557, 1366, 1288, 1193, 1051, 746, 699.

**HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup>** Calcd for C<sub>13</sub>H<sub>12</sub>N<sub>5</sub>O<sub>2</sub> 270.0988; Found 270.0986.

**Mp.** 140-142 °C.

**(3-benzyl-1,2,3-oxadiazol-3-ium-5-yl)(3-methyl-1H-imidazol-3-ium-1-carbonyl)amide iodide (S4)**



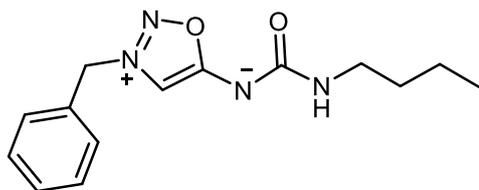
$C_{14}H_{14}IN_5O_2$   
**MW:** 411 g.mol<sup>-1</sup>  
Orange oil

To a solution of **S3** (67 mg, 0.248 mmol) in anhydrous acetonitrile (0.6 mL) was added MeI (61.73  $\mu$ L, 0.99 mmol). The mixture was stirred for 16 hours at 30 °C before being concentrated under reduced pressure. The product was obtained as an orange oil and was used without any purification as it is not stable enough to undergo purification. The crude was utilized directly in the subsequent step.

*The product is not stable enough in DMSO to afford <sup>1</sup>H and <sup>13</sup>C NMR spectra.*

**LCMS (ESI) *m/z* [M+H]<sup>+</sup>** 285.

**(3-benzyl-1,2,3-oxadiazol-3-ium-5-yl)(butylcarbamoyl)amide (6p)**



C<sub>14</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub>  
MW: 274 g.mol<sup>-1</sup>  
Yield: 42%  
Yellow solid

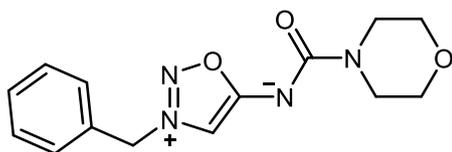
To a solution of crude **S4** (75 mg, 263.81 μmol) in CHCl<sub>3</sub> (2.65 mL, stabilized on amylene) were added *n*-butylamine (26 μL, 263.81 μmol) and trimethylamine (71.3 μL, 527.61 μmol). The reaction mixture was left stirring under argon at 30 °C for 16 h. The crude product was purified by column chromatography (SiO<sub>2</sub>, Hept/AcOEt, 6/4 to 2/8) to afford the desired product as a yellow solid (30.4 mg, 42%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.58 (s, 1H), 7.44 (d, *J* = 3.3 Hz, 3H), 7.38 (d, *J* = 9.6 Hz, 2H), 5.38 (s, 2H), 5.29 (bs, 1H), 3.19 (dd, *J* = 13.1, 6.9 Hz, 2H), 1.45 (dd, *J* = 14.7, 7.6 Hz, 2H), 1.36 – 1.30 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 172.7, 161.7, 130.3, 130.0, 129.6 (2C), 129.0 (2C), 103.1, 56.8, 40.1, 32.1, 20.1, 13.8.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>12</sub>N<sub>5</sub>O<sub>2</sub> 275.1502; Found 275.1506.

**(3-benzyl-1,2,3-oxadiazol-3-ium-5-yl)(morpholine-4-carbonyl)amide (6q)**



C<sub>14</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>  
MW: 288 g.mol<sup>-1</sup>  
Yield: 35%  
Yellow paste

To a solution of **S4** (155 mg, 377 μmol) in CHCl<sub>3</sub> (4 mL, stabilized on amylene) were added morpholine (33 μL, 377 μmol) and trimethylamine (105 μL, 754 μmol). The reaction mixture was left stirring under argon at 30 °C for 16 h. The crude product was purified by column chromatography (SiO<sub>2</sub>, Hept/AcOEt, 5/5 to 100% AcOEt) to afford the desired product as a yellow paste (38 mg, 35%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.58 (s, 1H), 7.47 – 7.39 (m, 3H), 7.37 (dd, *J* = 7.6, 2.0 Hz, 2H), 5.40 (s, 2H), 3.76 (s, 2H), 3.65 – 3.60 (m, 4H), 3.55 (s, 2H).

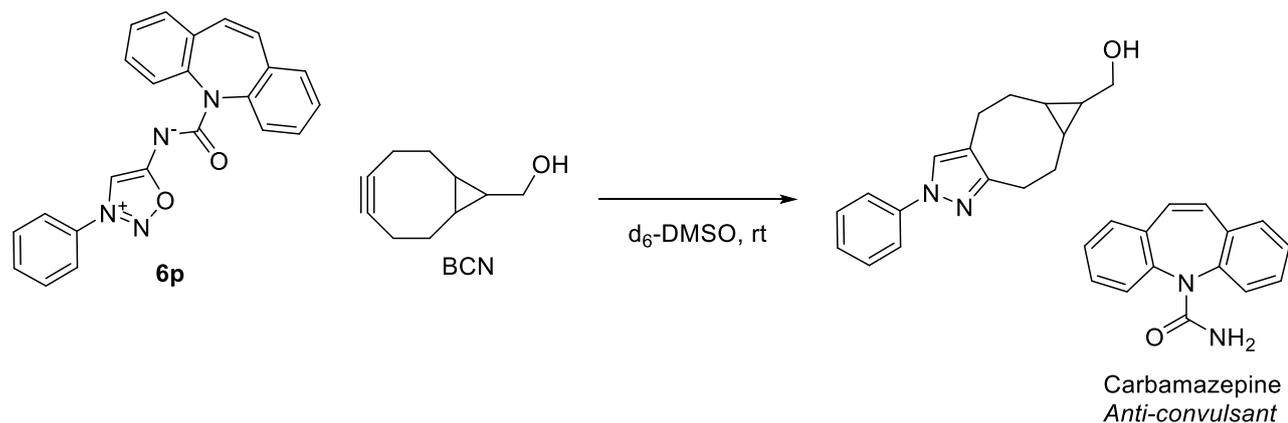
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 173.6, 160.7, 130.4, 129.9, 129.7 (2C), 129.0 (2C), 103.2, 66.9 (2C), 56.9, 45.4, 42.9.

IR (cm<sup>-1</sup>) 2851, 1619, 1407, 1252, 1112, 989, 706.

LCMS (ESI) *m/z* [M+H]<sup>+</sup> 290.

HRMS (ESI-TOF) *m/z* [M+H]<sup>+</sup> Calcd for C<sub>14</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub> 289.1298; Found 289.1295.

### III. Click & Release kinetics



The compound **6p** (3.7 mg, 0.097 mmol, 1 eq.) was solubilised in  $d_6$ -DMSO (0.4 mL) and Tri-methoxybenzene was added as an internal standard (0.5 mg, 0.0032 mmol, 0.33 eq.). The NMR of this solution was referenced as the SM measurement. Then BCN (2.2 mg, 0.034 mmol, 1.5 eq.) was added and the reaction was followed by NMR measurement. The experiment shown complete conversion of the starting material after 6h. The final products were obtained with 96% (carbamazepine) NMR yield.

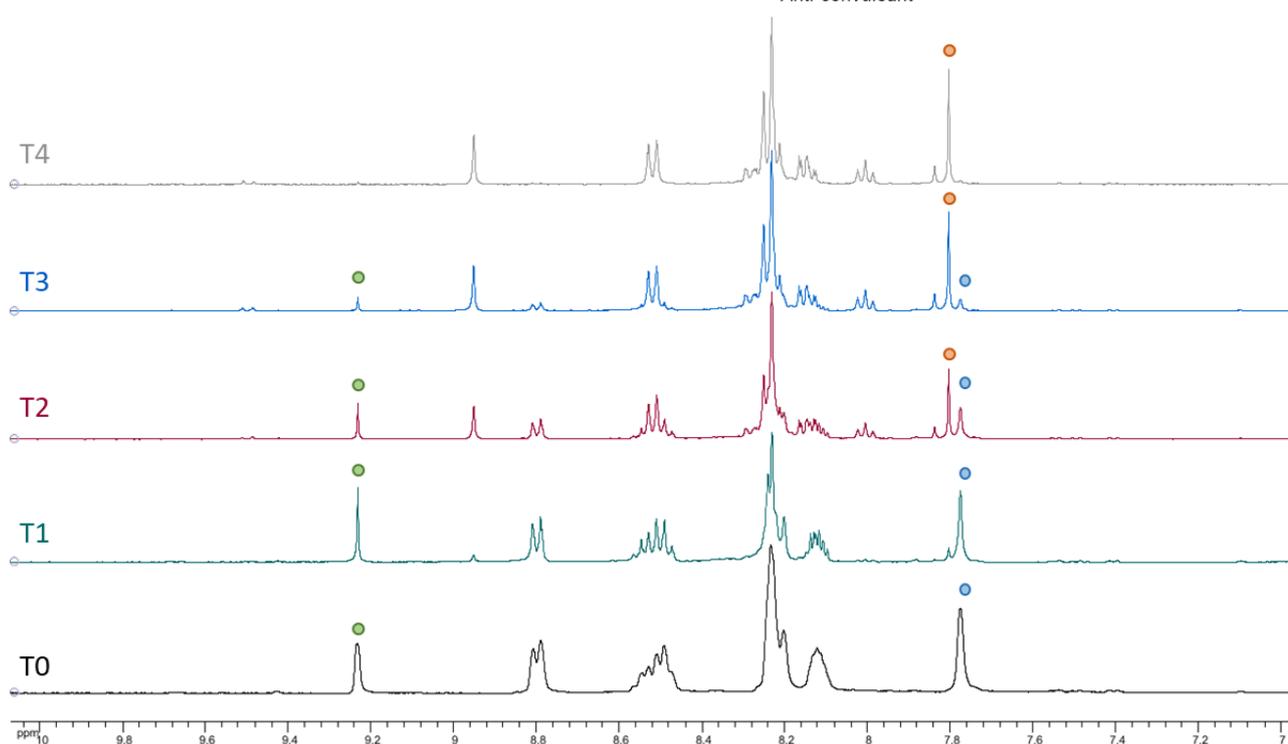
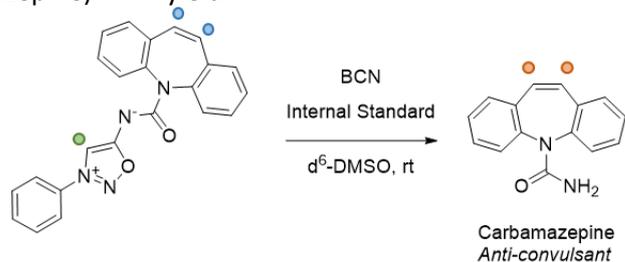


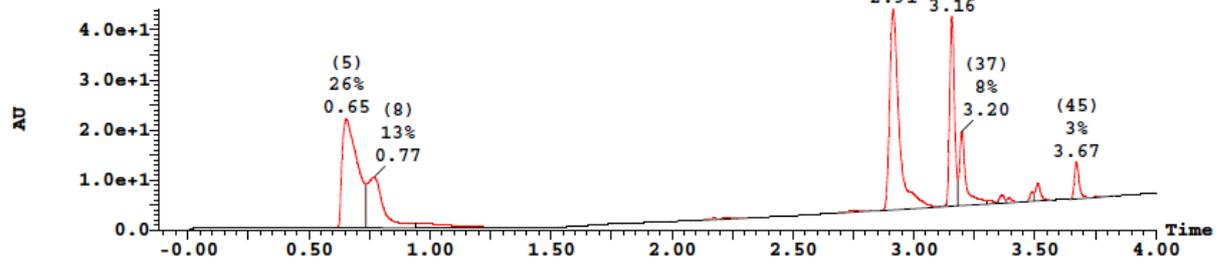
Figure S1: NMR analysis of the drug release in  $d_6$ -DMSO. zoom on the aromatic area **T1: 5 min, T2: 60 min, T3: 170 min, T4: 360 min**



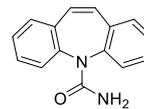
LC-MS analysis

Sample 52 Vial 2:A,4 ID KP-4-105-click File KP-4-105-click Date 28-Mar-2019 Time 19:50:04 Description

3: UV Detector: TAC :Wavelength Range: (220 - 400) Smooth (SG, 2x2) (31) (34) 4.415e+1  
 Range: 4.415e+1

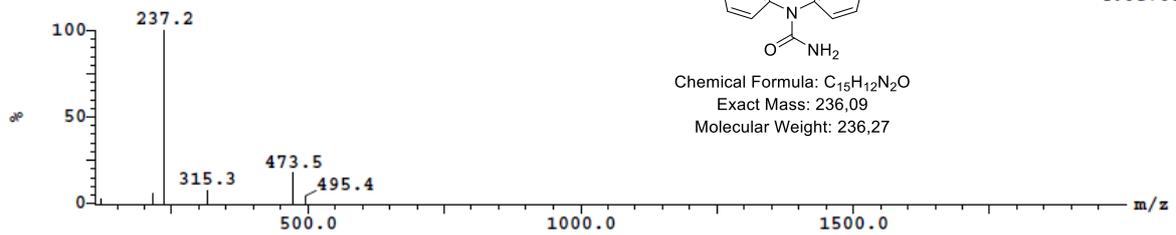


Peak ID Compound Time Mass Found  
 31  
 31: (Time: 2.91) Combine (391:405- (316:323+492:499))

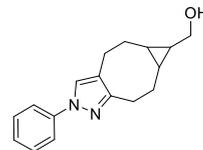


Chemical Formula: C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O  
 Exact Mass: 236,09  
 Molecular Weight: 236,27

1:MS ES+  
 4.0e+007

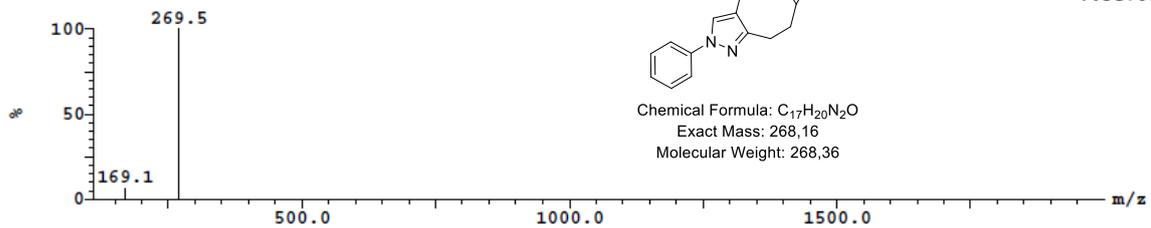


Peak ID Compound Time Mass Found  
 34  
 34: (Time: 3.16) Combine (424:438- (349:356+502:509))



Chemical Formula: C<sub>17</sub>H<sub>20</sub>N<sub>2</sub>O  
 Exact Mass: 268,16  
 Molecular Weight: 268,36

1:MS ES+  
 7.3e+007

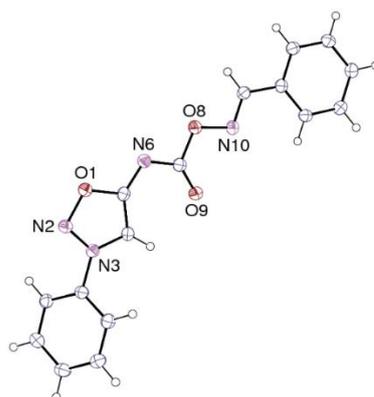


## IV. Crystallography

The crystals were obtained by vapour diffusion of a DCM/Et<sub>2</sub>O system.

**Crystallography.** The data for compound **11** were collected at 100(2) K on a Nonius Kappa-CCD area detector diffractometer<sup>3</sup> using graphite-monochromated Mo K $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The crystal was introduced into a glass capillary with a protective coating of Paratone-N oil (Hampton Research). The unit cell parameters were determined from ten frames, then refined on all data. The data (combinations of  $\varphi$ - and  $\omega$ -scans with a minimum redundancy of 4 for 90% of the reflections) were processed with HKL2000,<sup>4</sup> with no correction for absorption effects. The structure was solved by intrinsic phasing with SHELXT<sup>5</sup> and refined by full-matrix least-squares on  $F^2$  with SHELXL-2014.<sup>6</sup> All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were introduced at calculated positions and were treated as riding atoms with an isotropic displacement parameter equal to 1.2 times that of the parent atom.

**Crystal data for compound 11.** C<sub>16</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub>,  $M = 308.30$ , monoclinic, space group  $P2_1/c$ ,  $a = 9.8228(8)$ ,  $b = 17.1390(13)$ ,  $c = 8.9017(5) \text{ \AA}$ ,  $\beta = 103.987(5)$ ,  $V = 1454.19(18) \text{ \AA}^3$ ,  $Z = 4$ ,  $D_c = 1.408 \text{ g cm}^{-3}$ ,  $\mu = 0.101 \text{ mm}^{-1}$ ,  $F(000) = 640$ . Refinement of 208 parameters on 2738 independent reflections out of 46295 measured reflections ( $R_{\text{int}} = 0.069$ ) led to  $R_1 = 0.037$ ,  $wR_2 = 0.095$ ,  $S = 1.060$ ,  $\Delta\rho_{\text{max}} = 0.18$ ,  $\Delta\rho_{\text{min}} = -0.18 \text{ e \AA}^{-3}$ .



View of compound **11**. Hydrogen atoms are omitted, except for those bound to nitrogen atoms. Displacement ellipsoids are drawn at the 50% probability level.

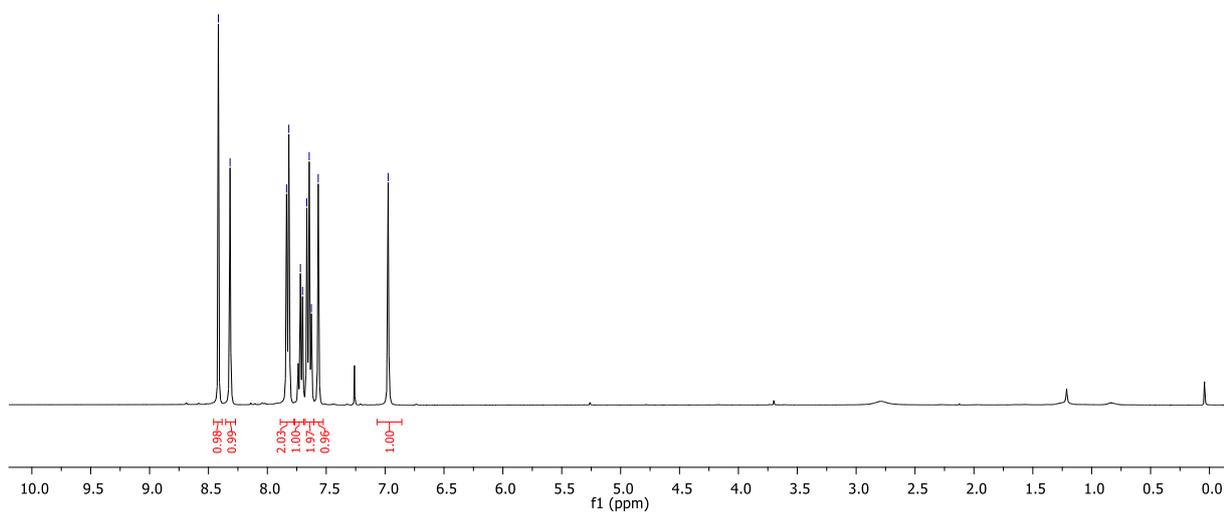
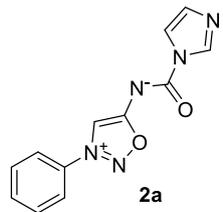
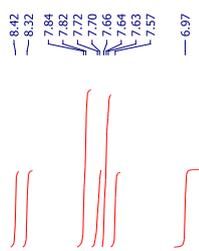
<sup>3</sup> Hooft, R. W. W. *COLLECT*, Nonius BV: Delft, The Netherlands, 1998.

<sup>4</sup> Otwinowski, Z.; Minor, W. Processing of X-Ray Diffraction Data Collected in Oscillation Mode. *Methods Enzymol.* **1997**, *276*, 307–326.

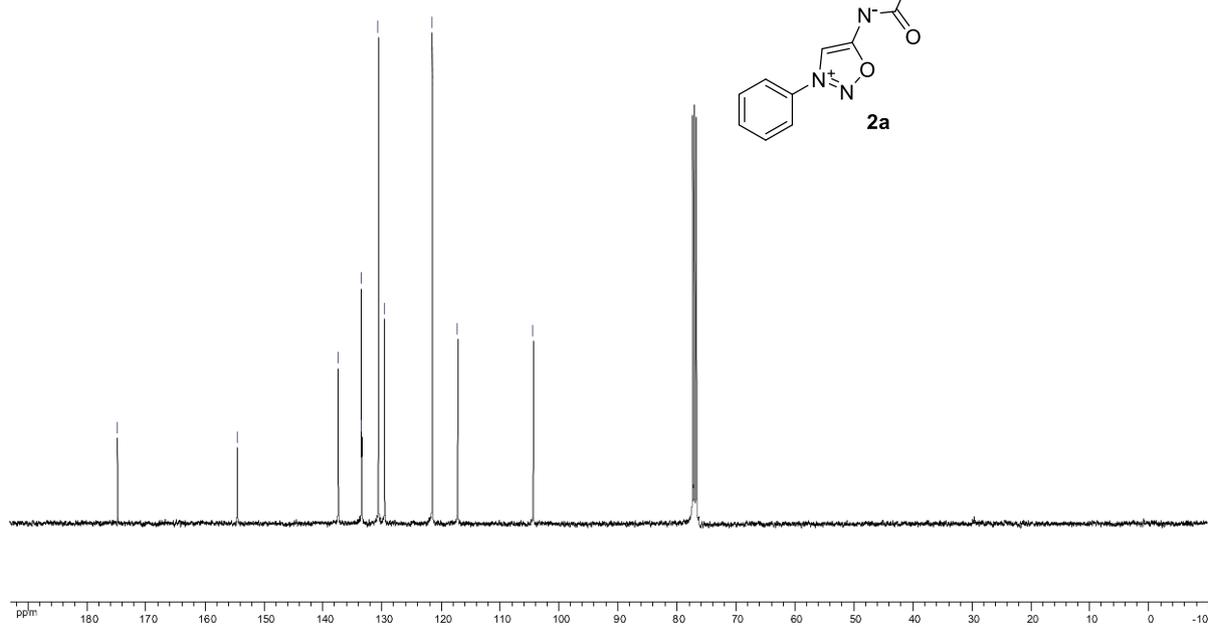
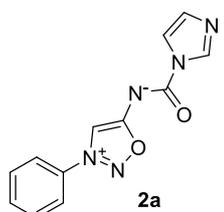
<sup>5</sup> Sheldrick, G. M. SHELXT – Integrated Space-Group and Crystal-Structure Determination. *Acta Crystallogr., Sect. A* **2015**, *71*, 3–8.

<sup>6</sup> Sheldrick, G. M. Crystal Structure Refinement with SHELXL. *Acta Crystallogr., Sect. C* **2015**, *71*, 3–8.

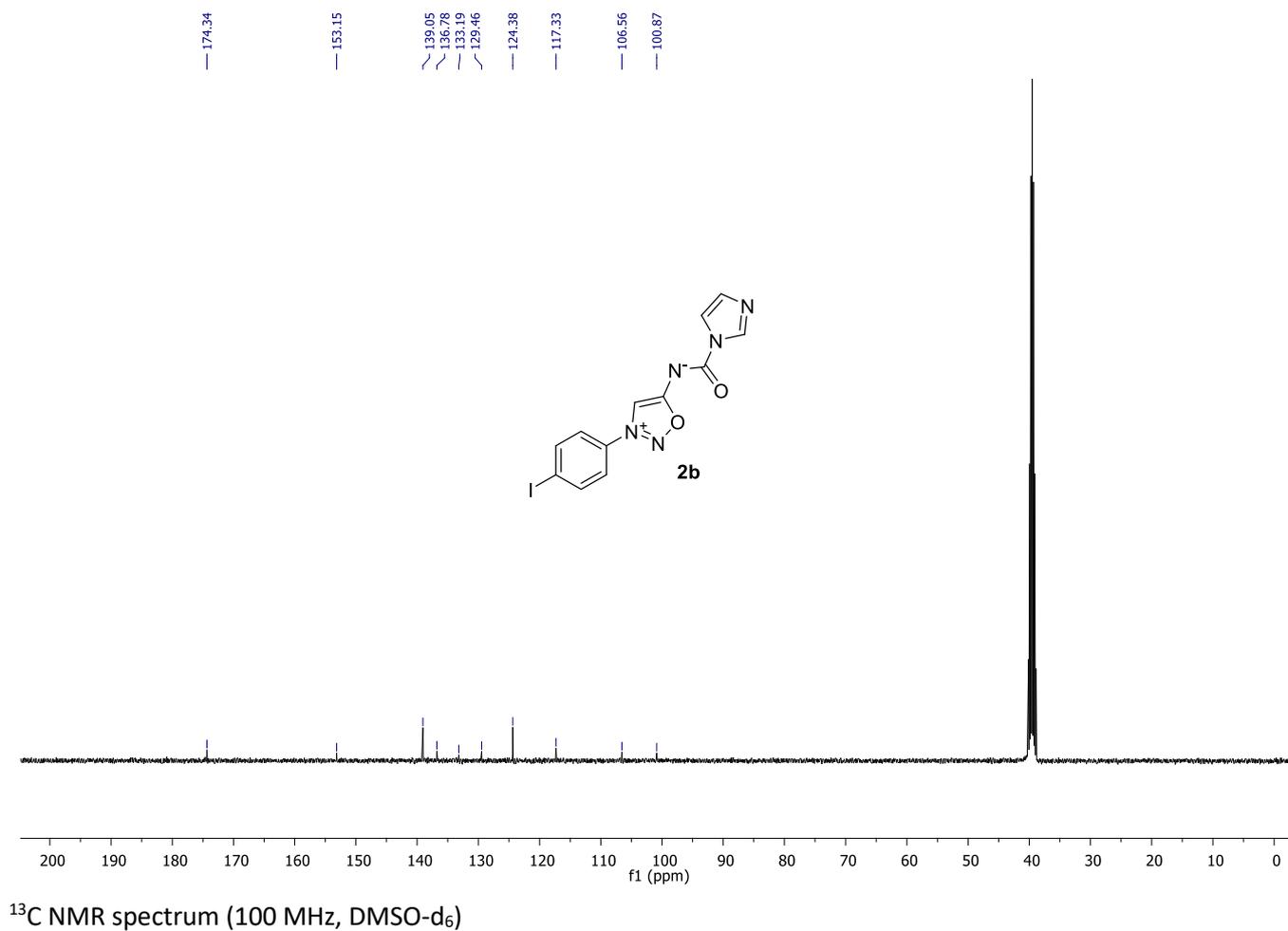
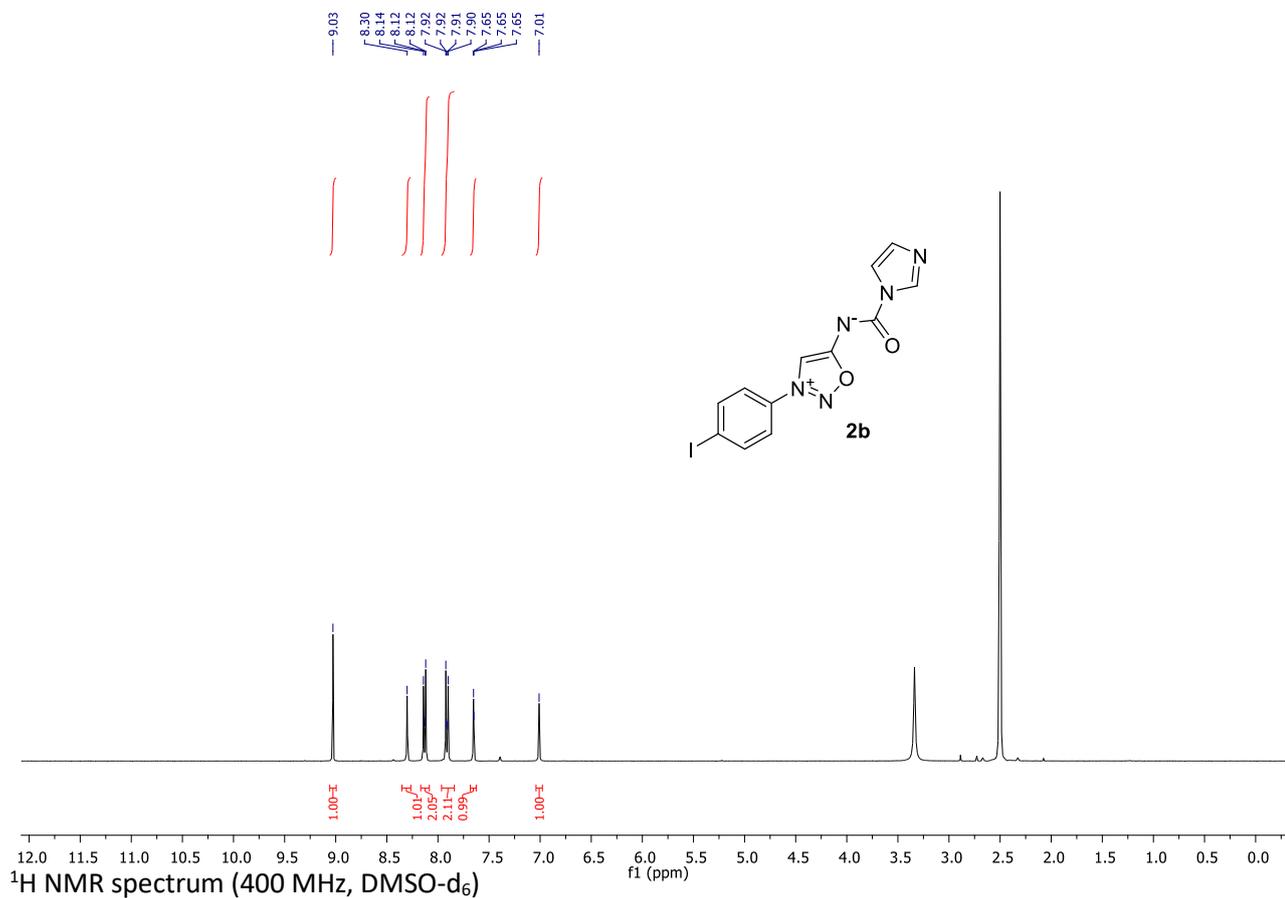
# V. NMR Spectra

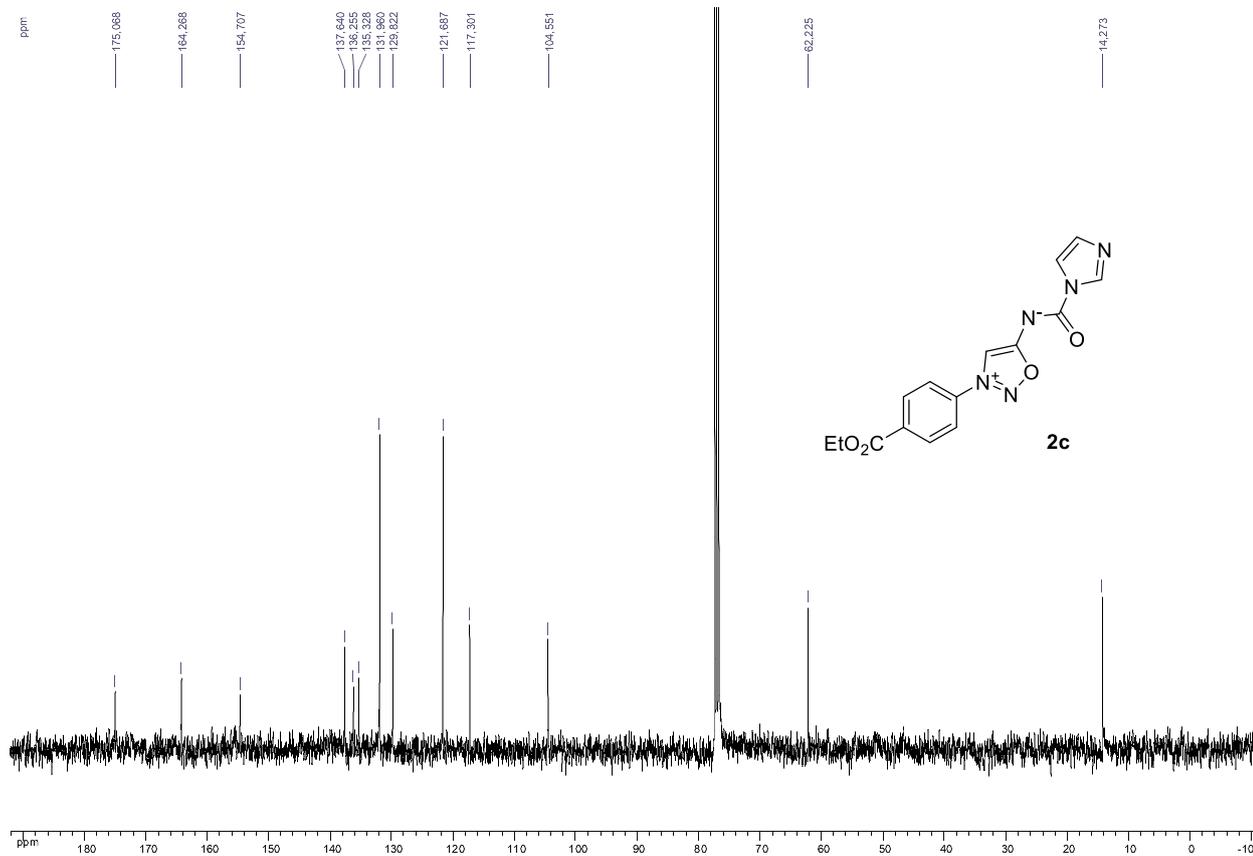
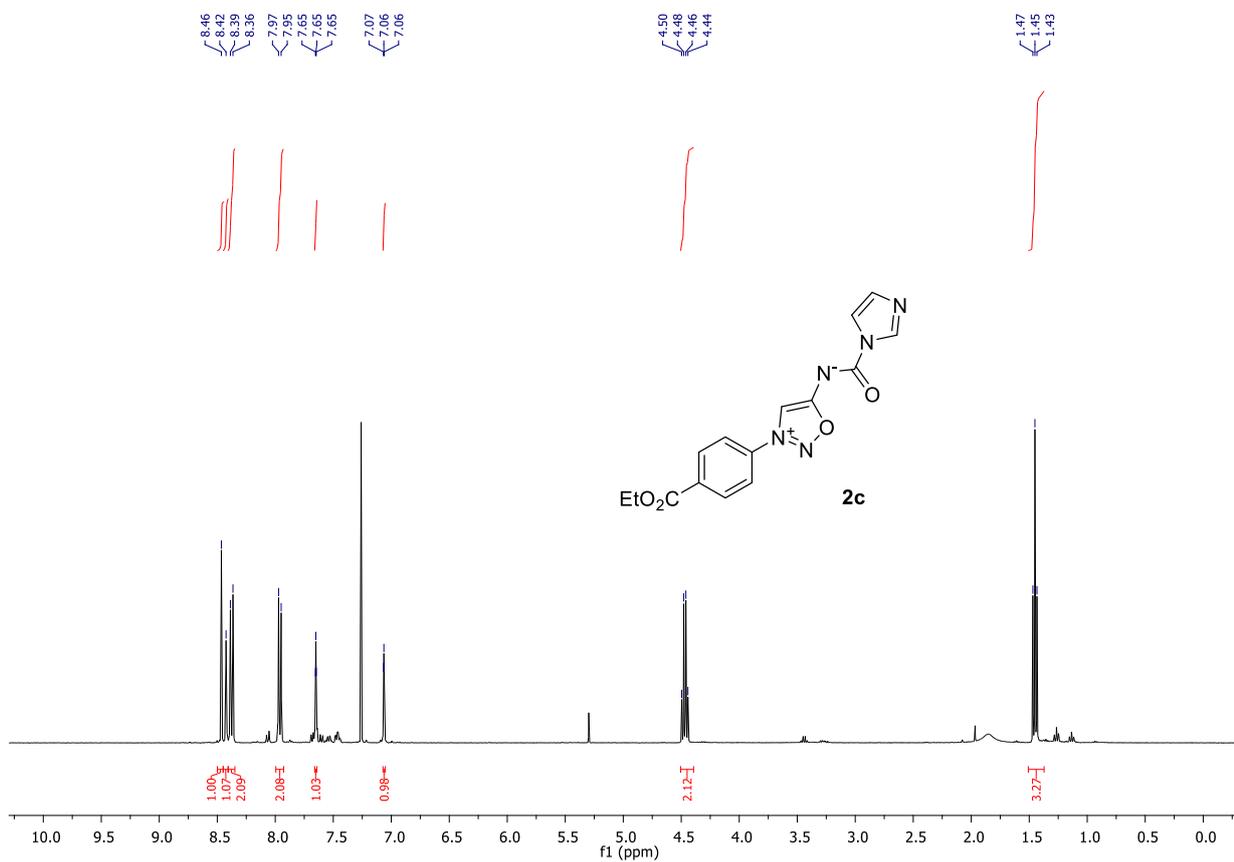


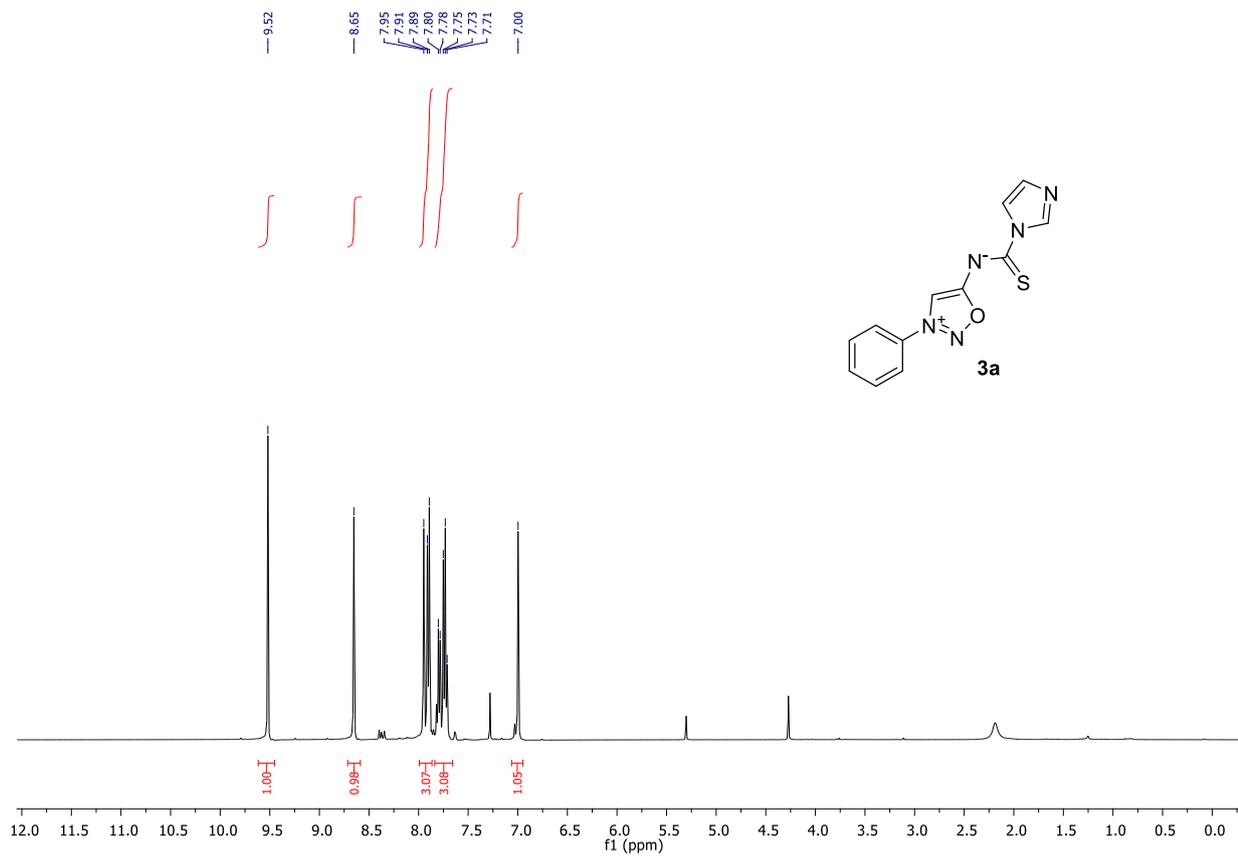
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



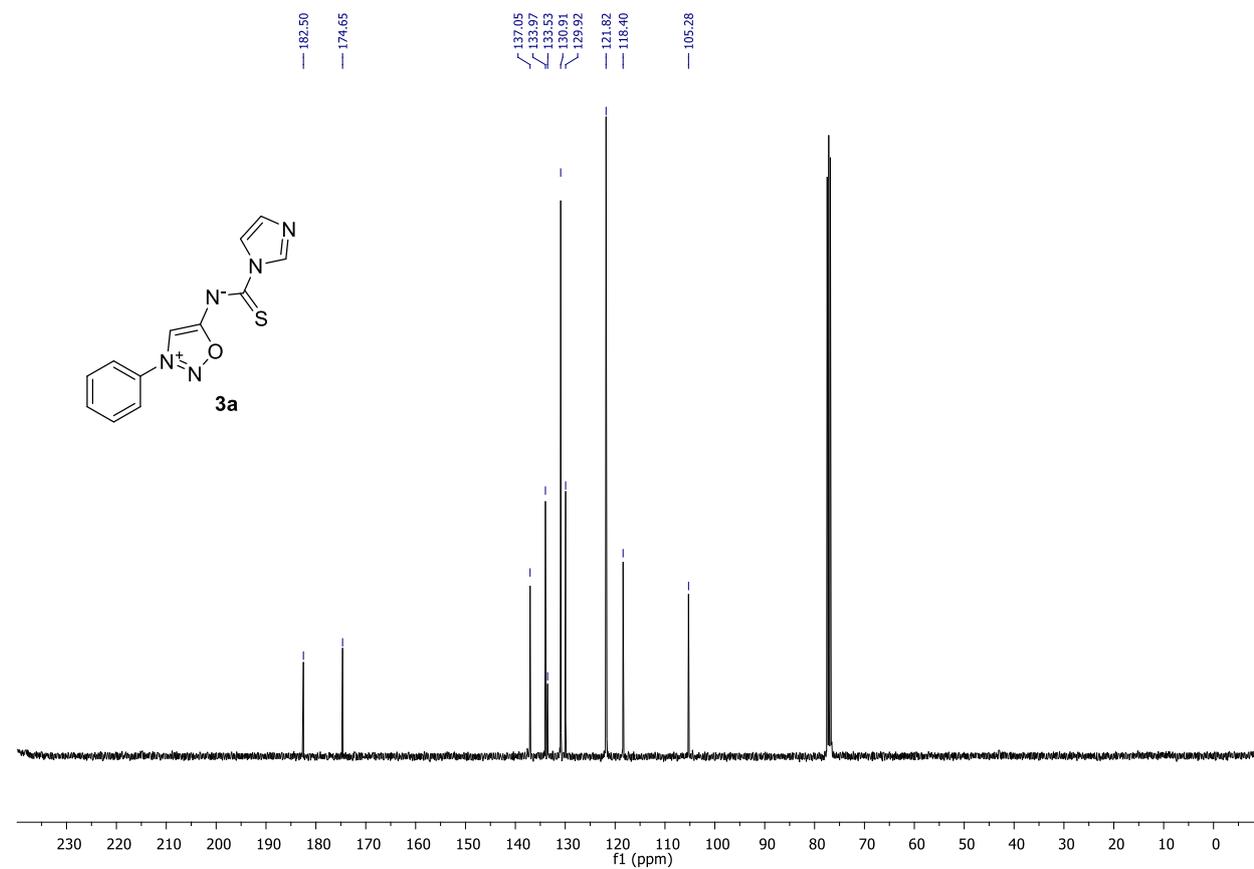
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



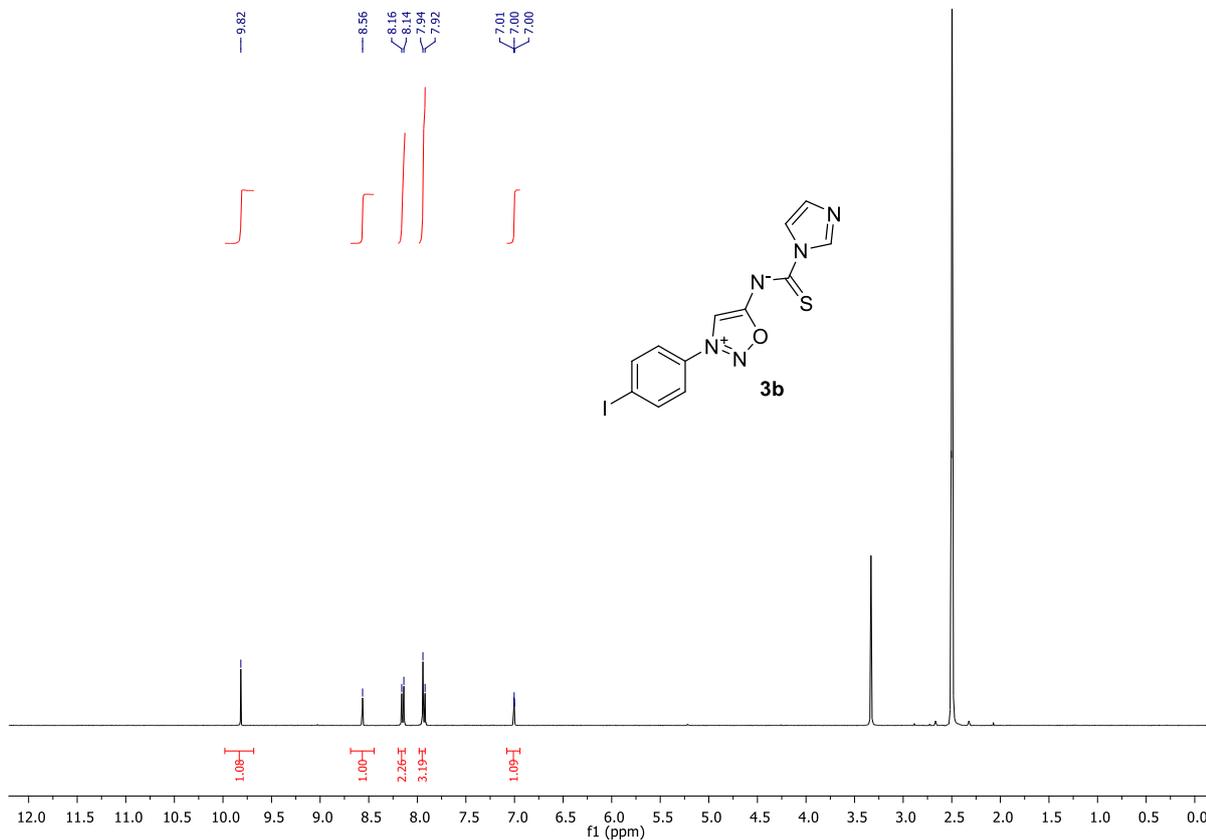




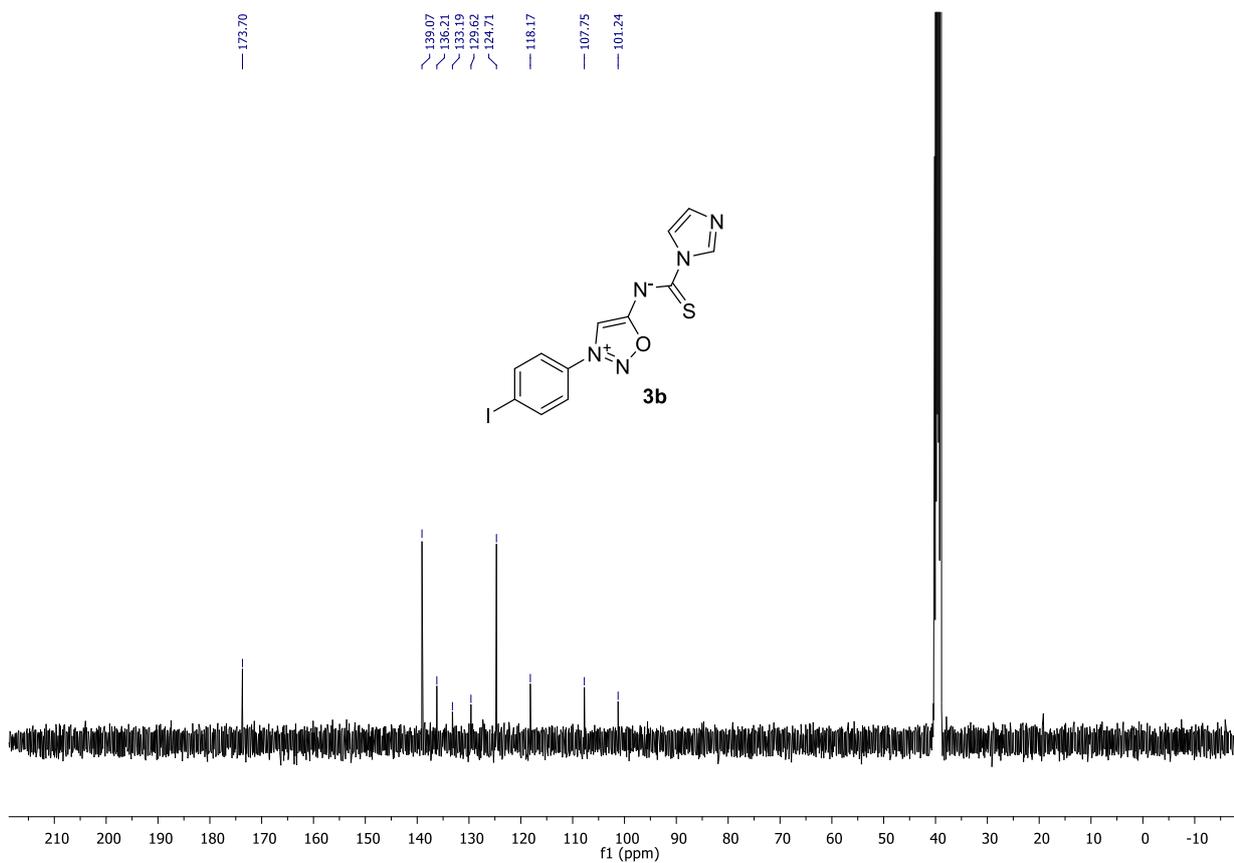
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



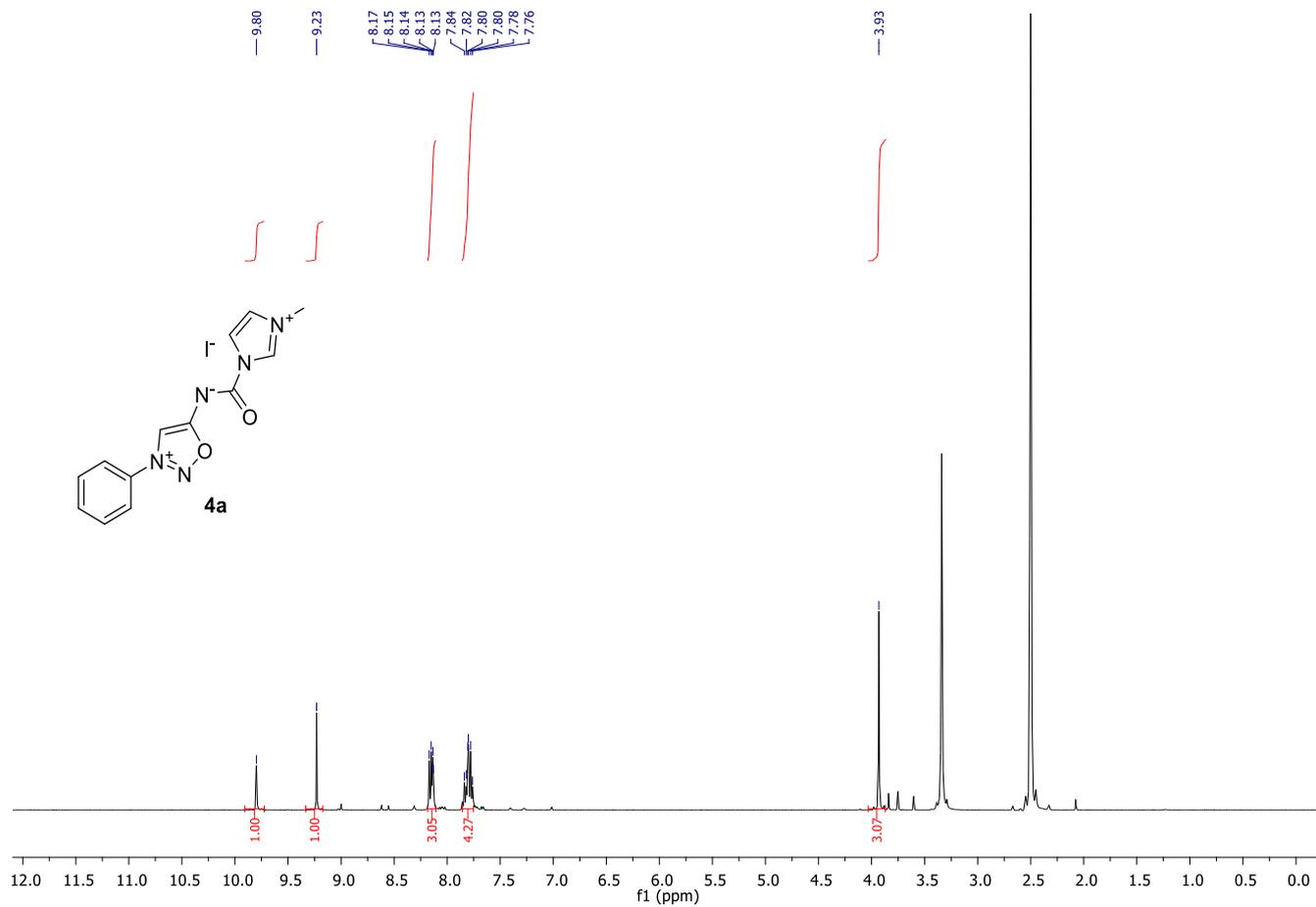
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



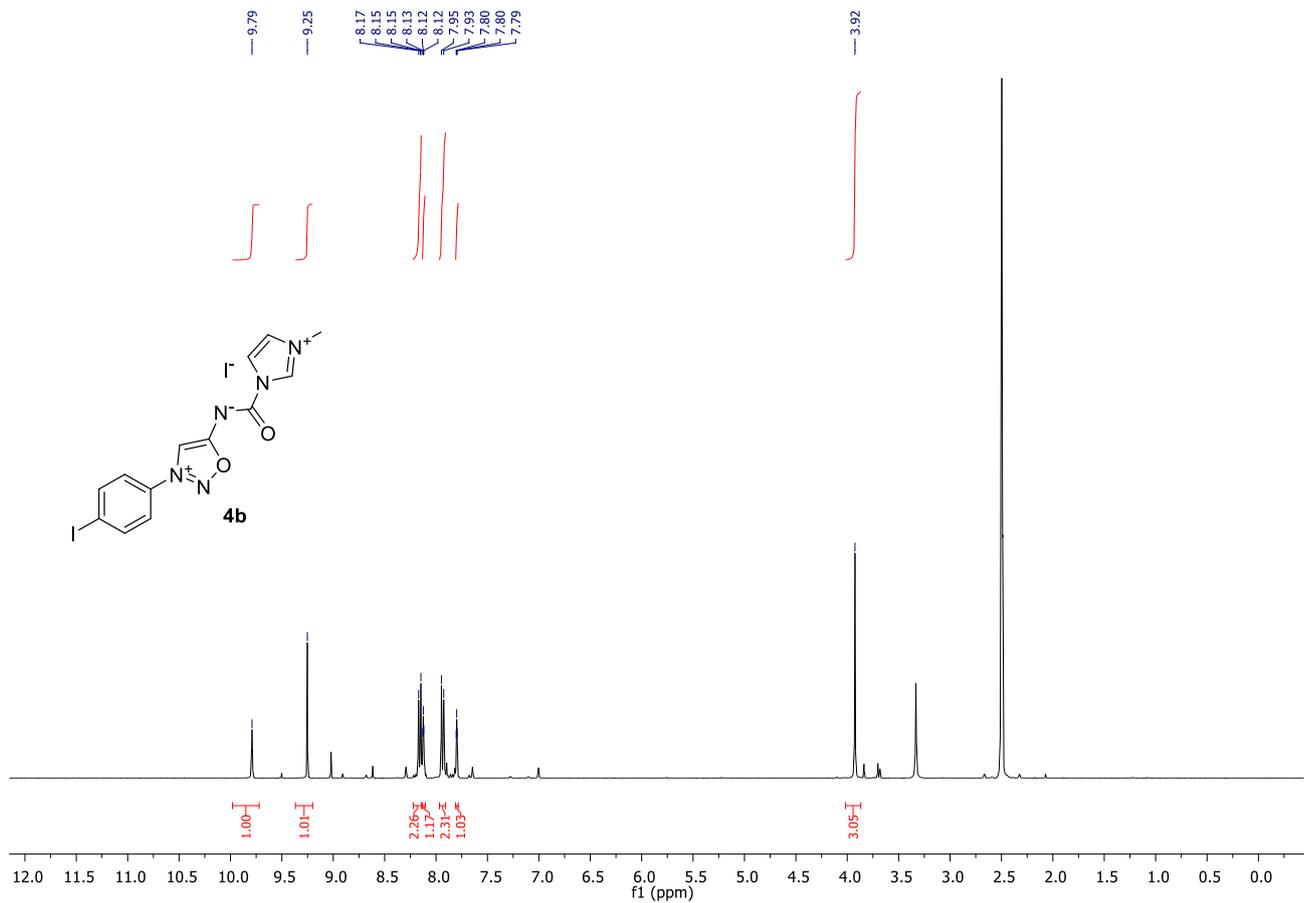
<sup>1</sup>H NMR spectrum (400 MHz, DMSO-d<sub>6</sub>)



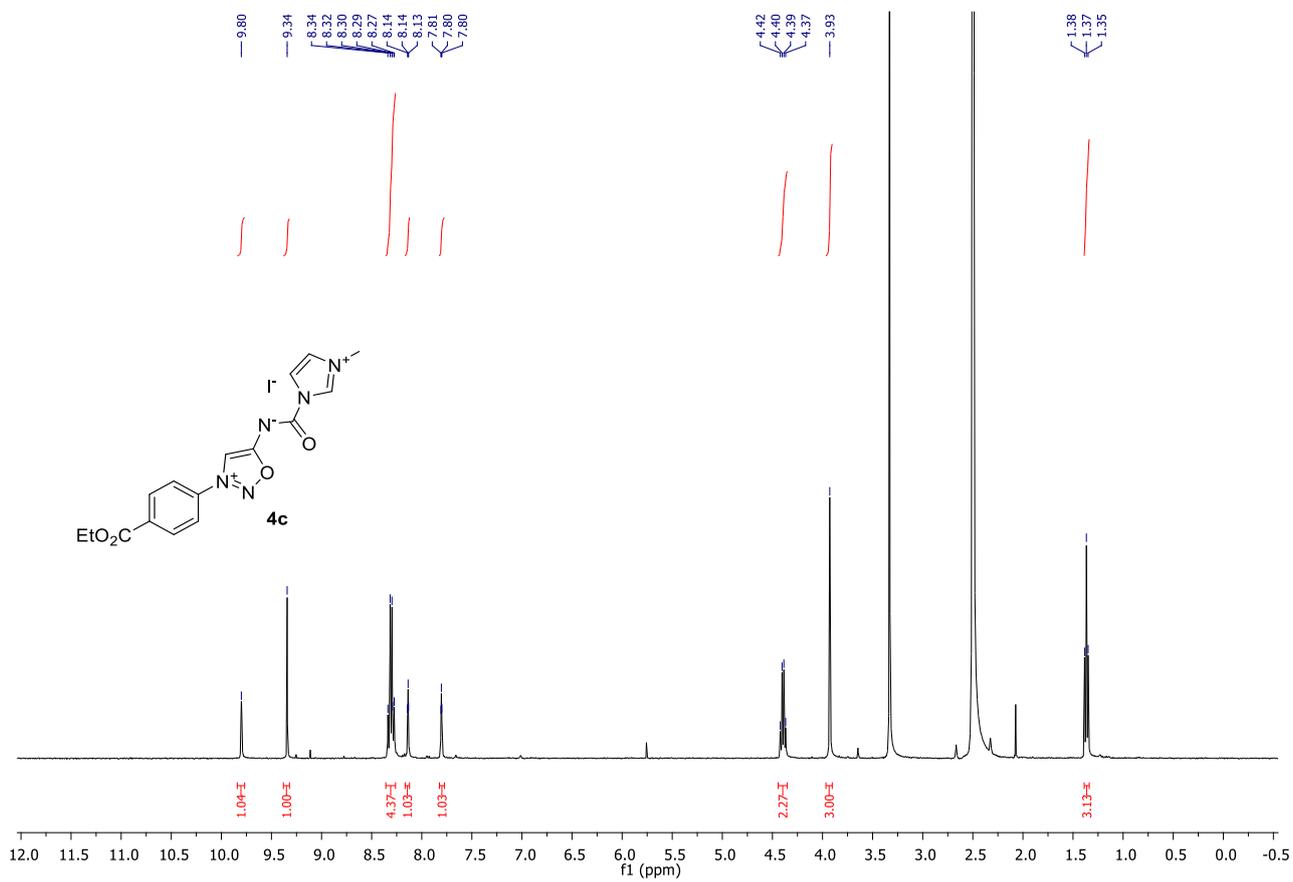
<sup>13</sup>C NMR spectrum (100 MHz, DMSO-d<sub>6</sub>)



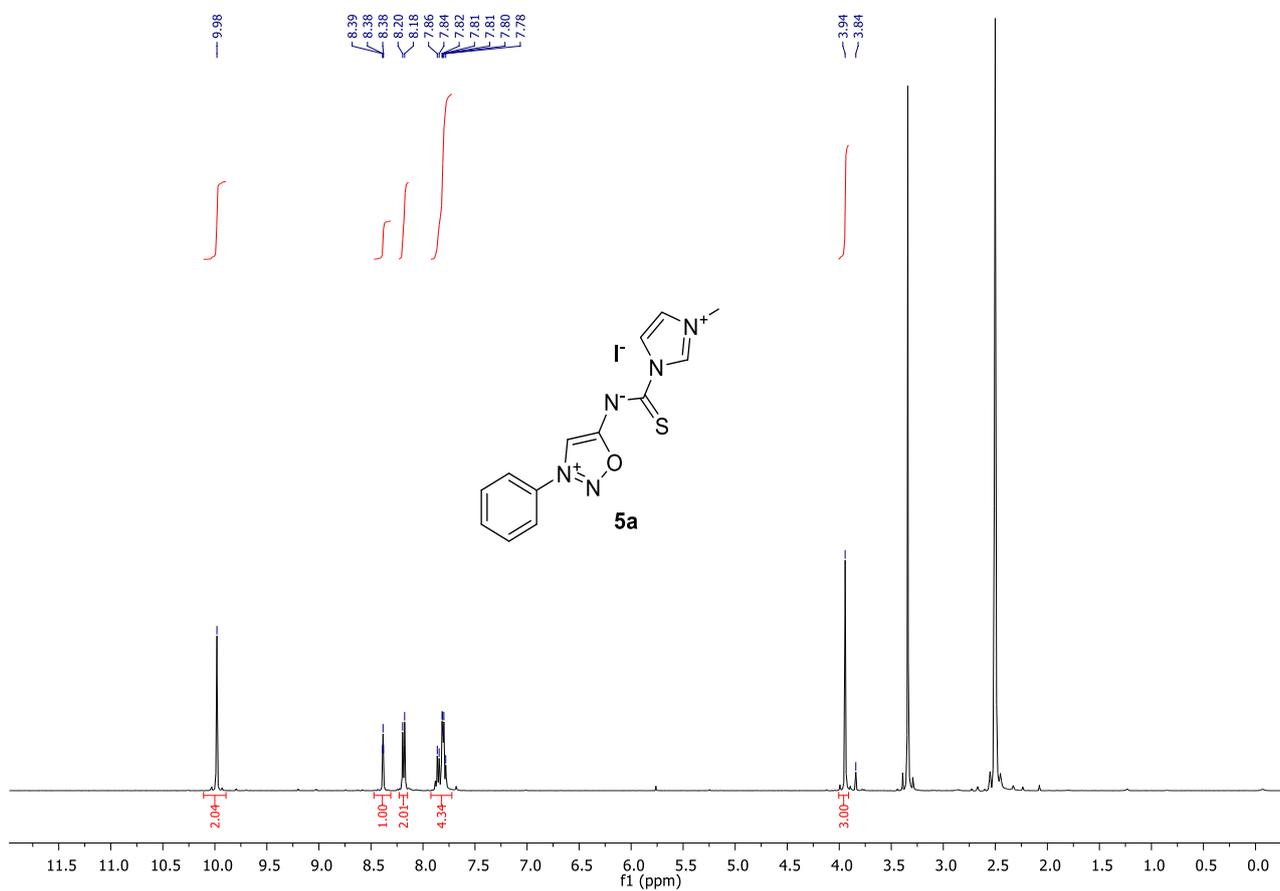
<sup>1</sup>H NMR spectrum (400 MHz, DMSO-d<sub>6</sub>)



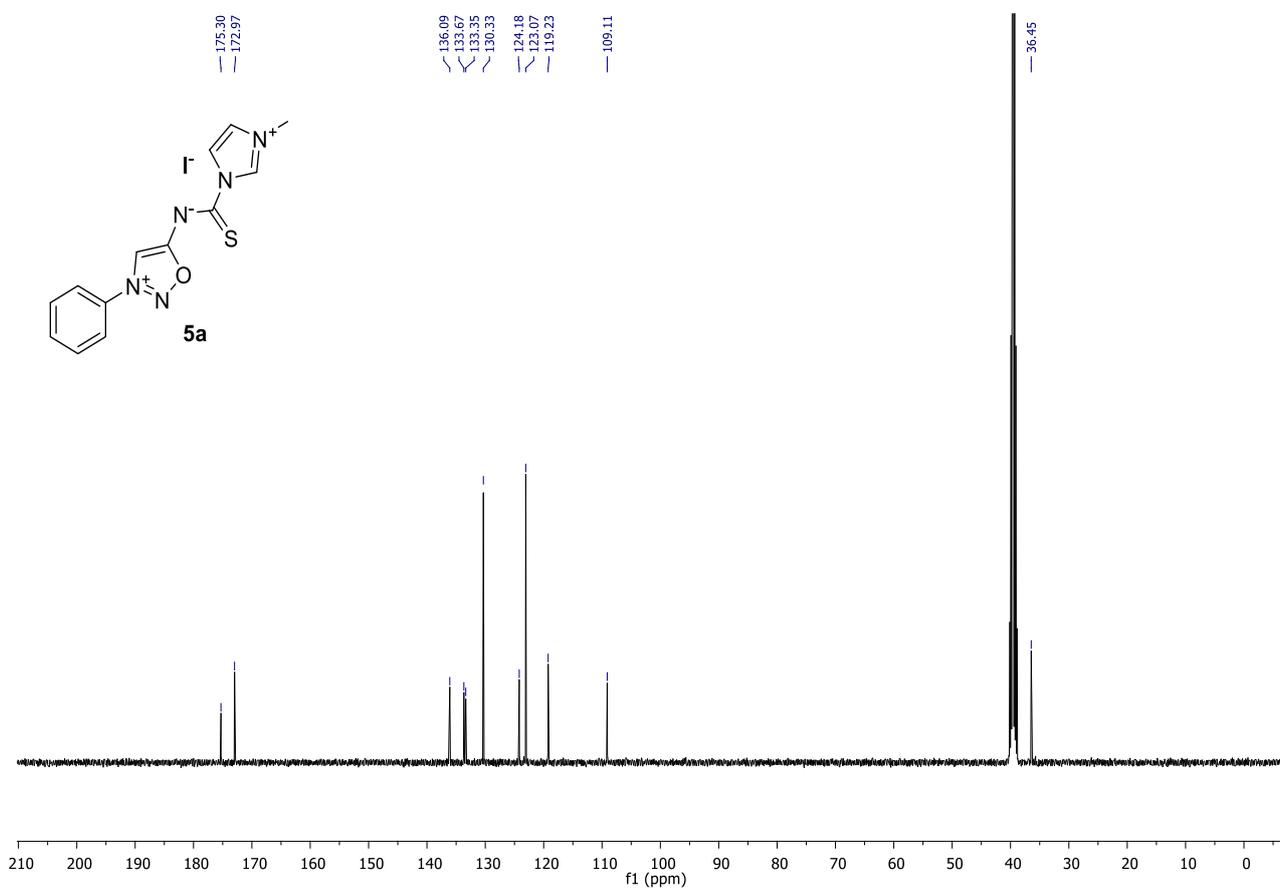
<sup>1</sup>H NMR spectrum (400 MHz, DMSO-d<sub>6</sub>)



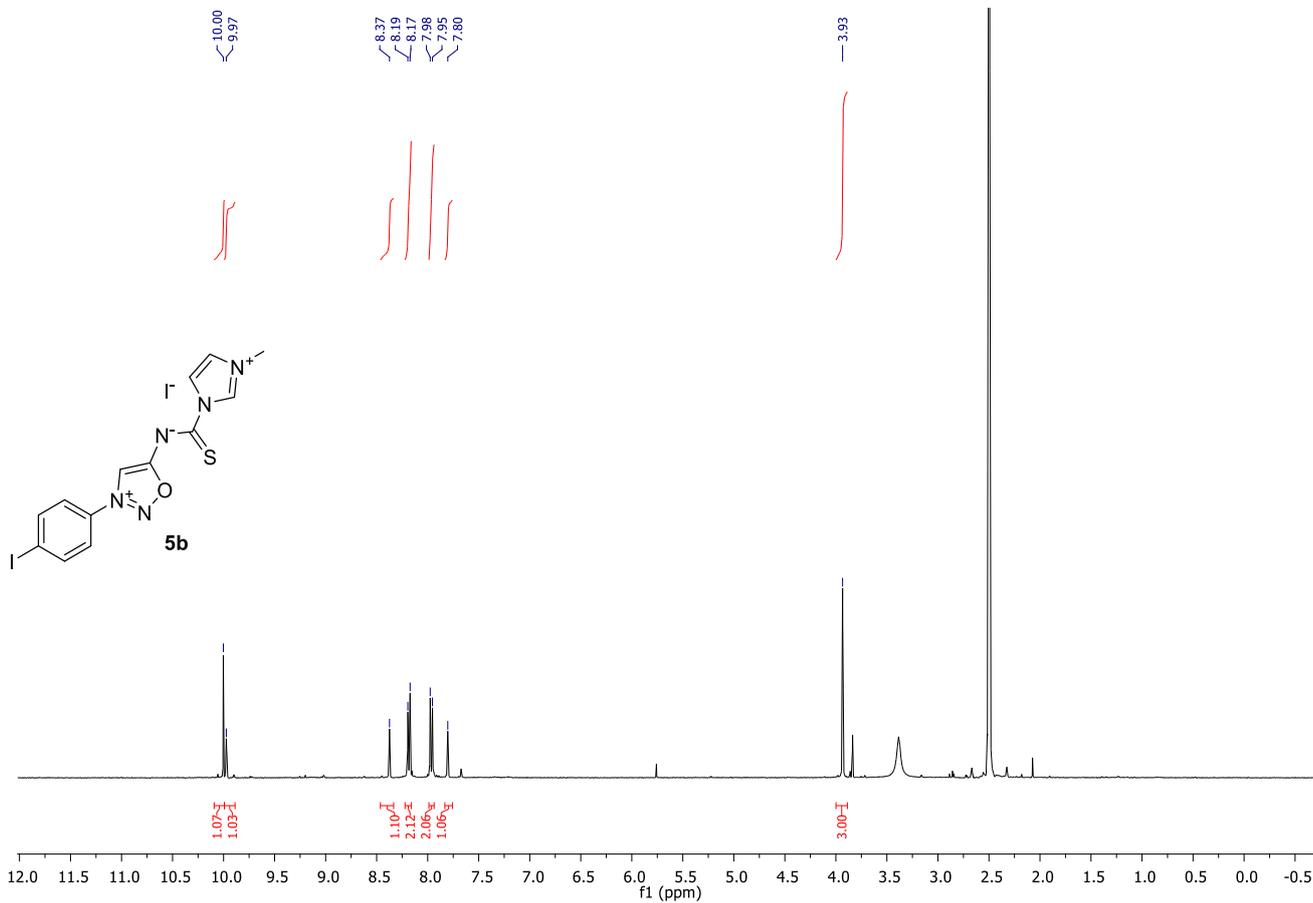
<sup>1</sup>H NMR spectrum (400 MHz, DMSO-d<sub>6</sub>)



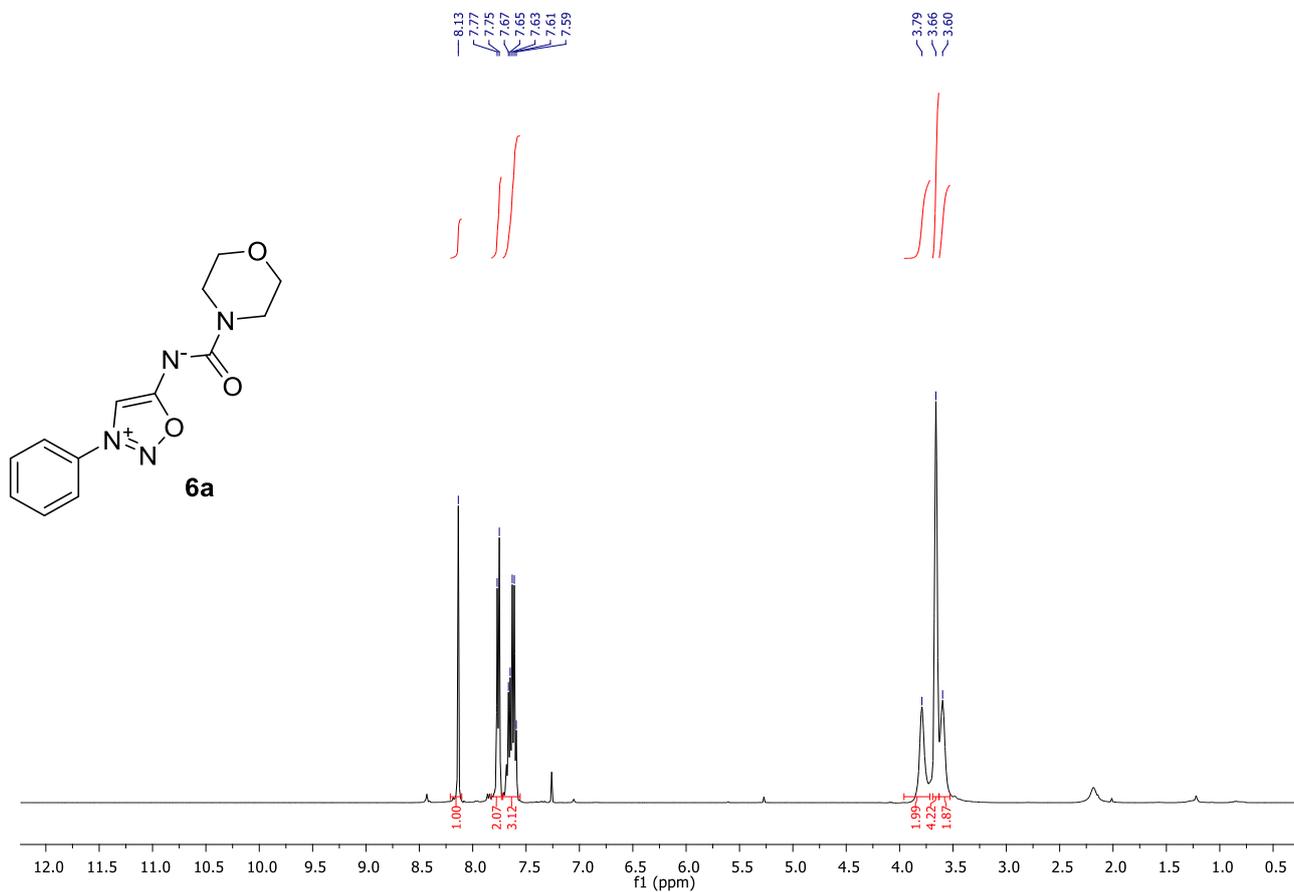
<sup>1</sup>H NMR spectrum (400 MHz, DMSO-d<sub>6</sub>)



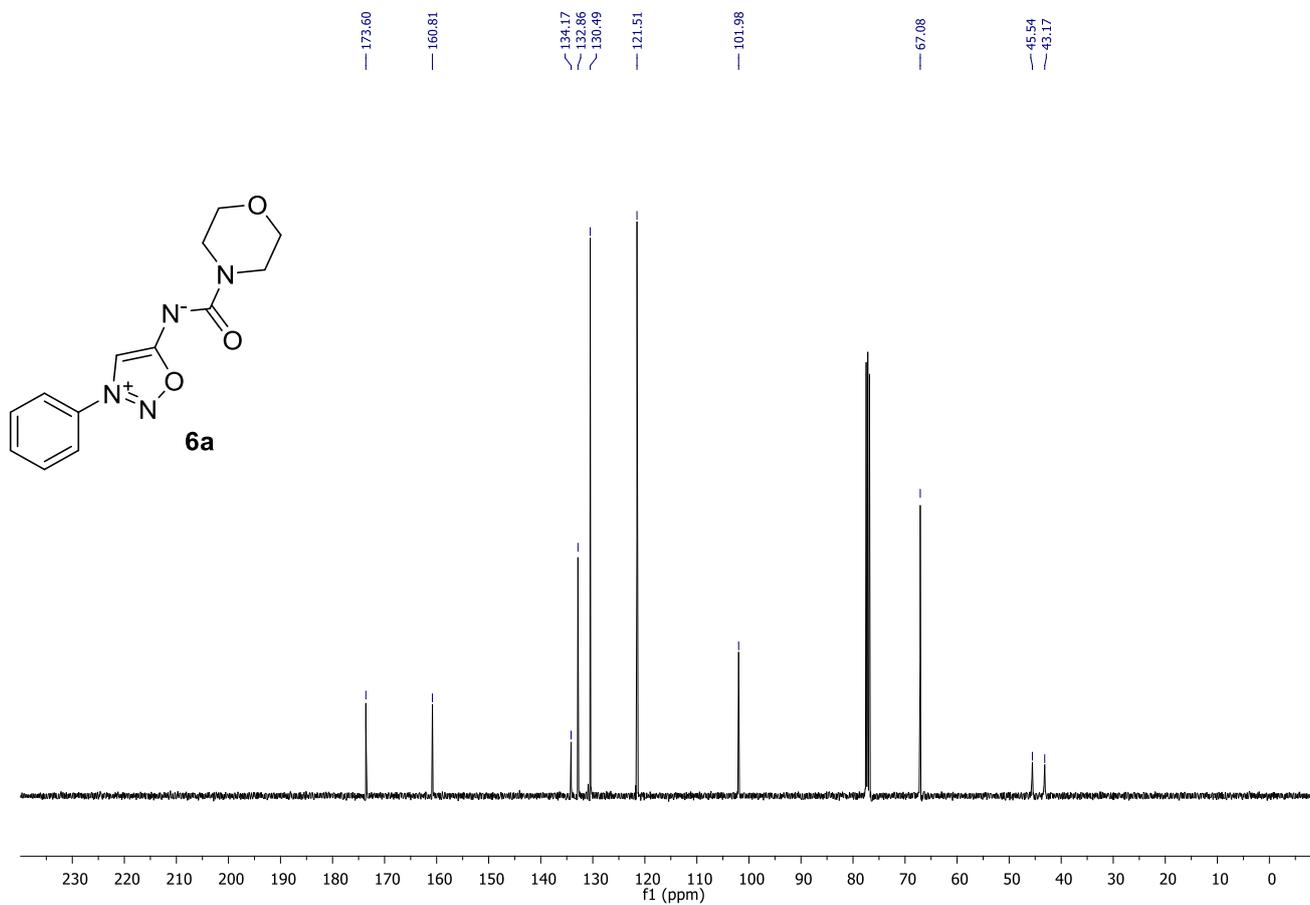
<sup>13</sup>C NMR spectrum (100 MHz, DMSO-d<sub>6</sub>)



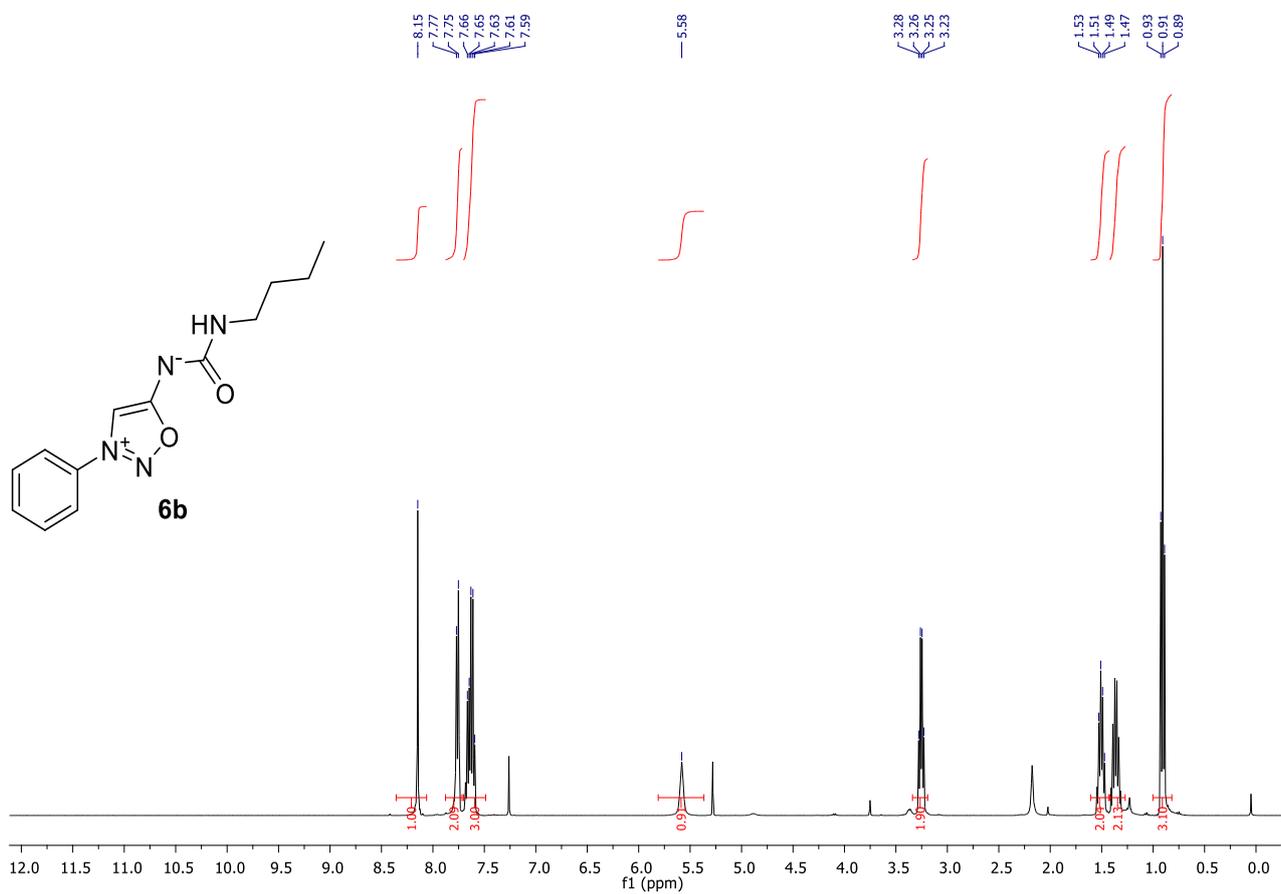
<sup>1</sup>H NMR spectrum (400 MHz, DMSO-d<sub>6</sub>)



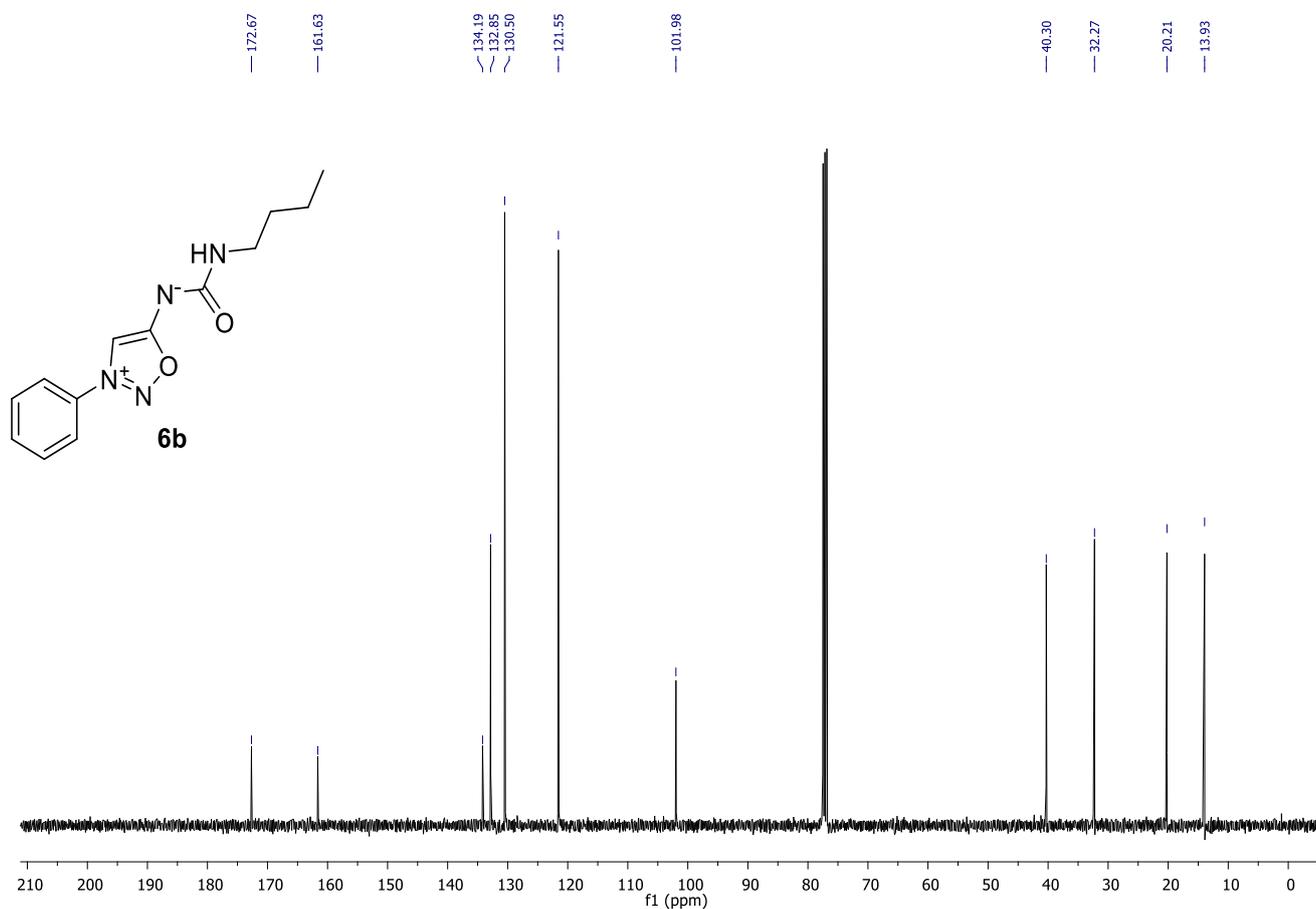
$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ )



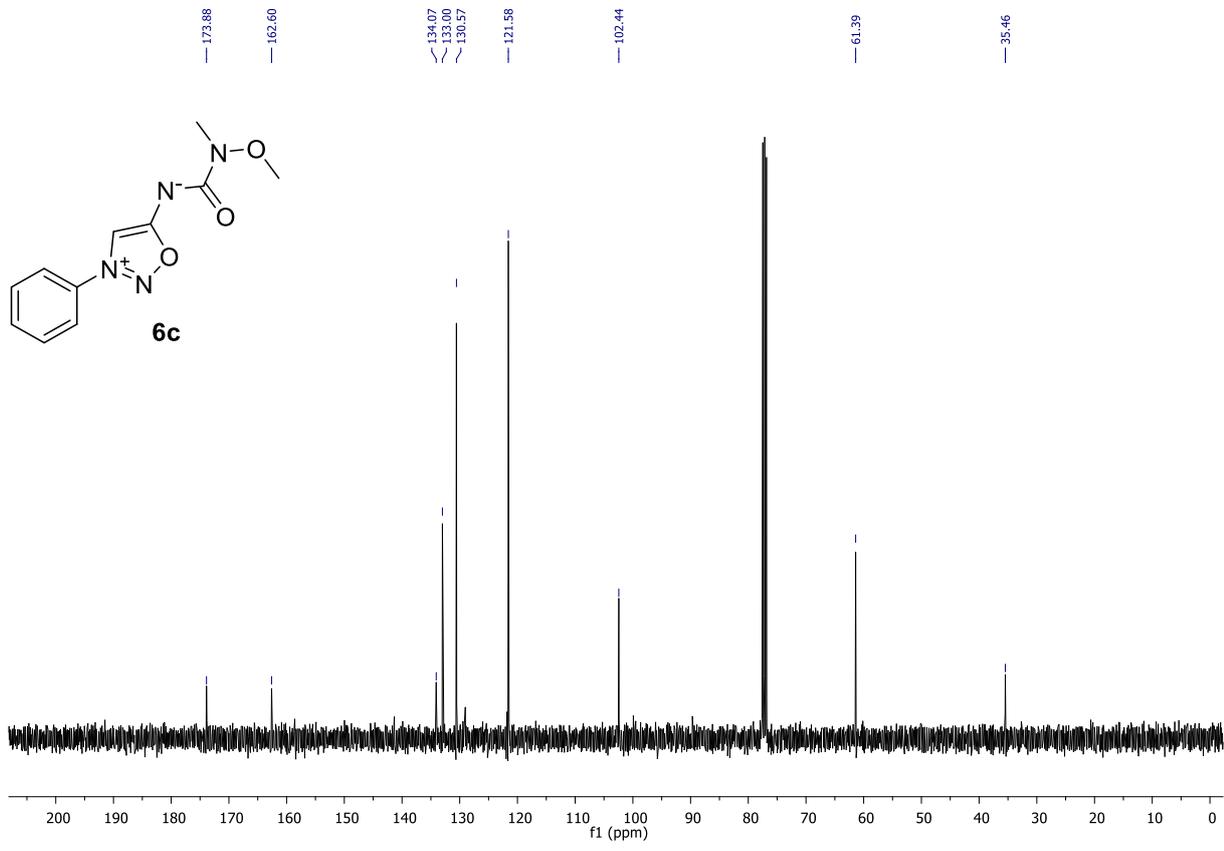
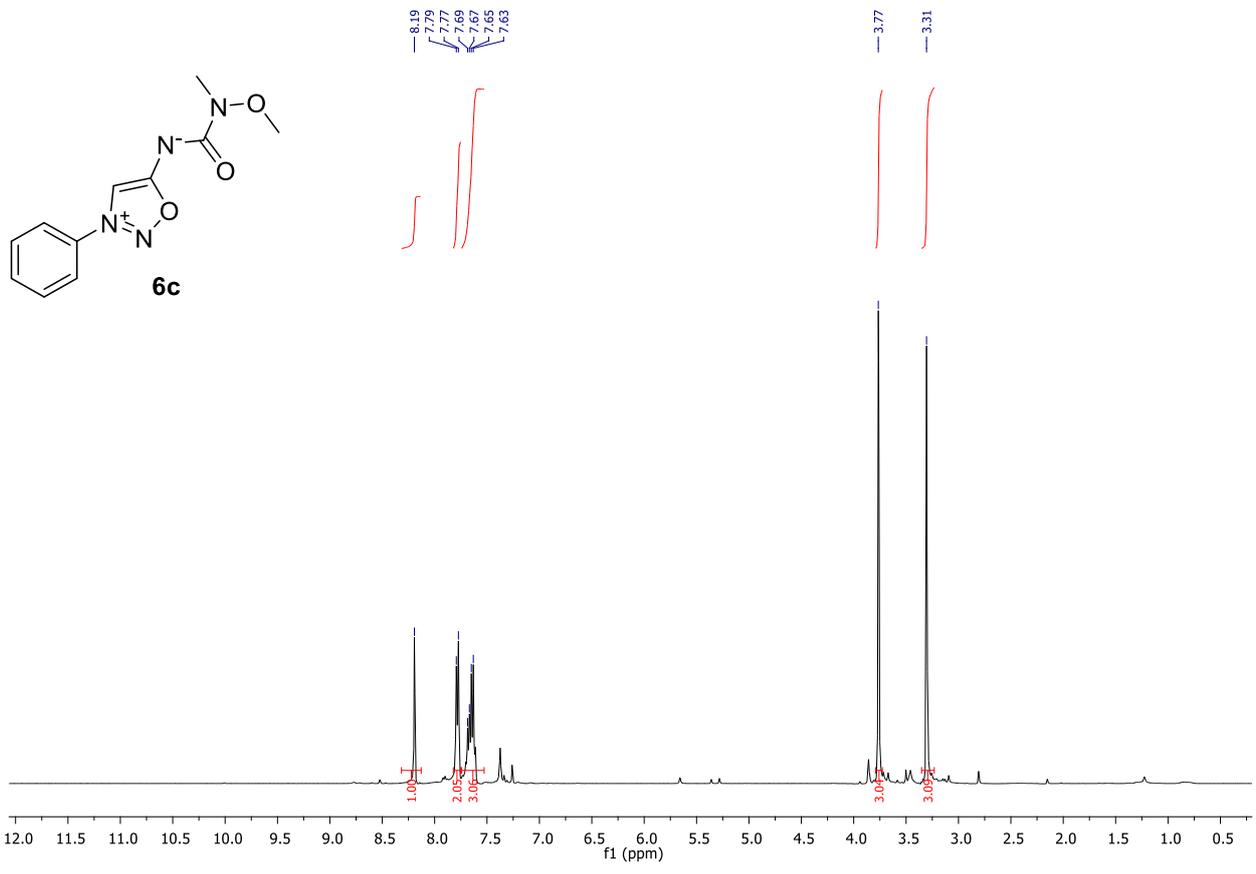
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ )

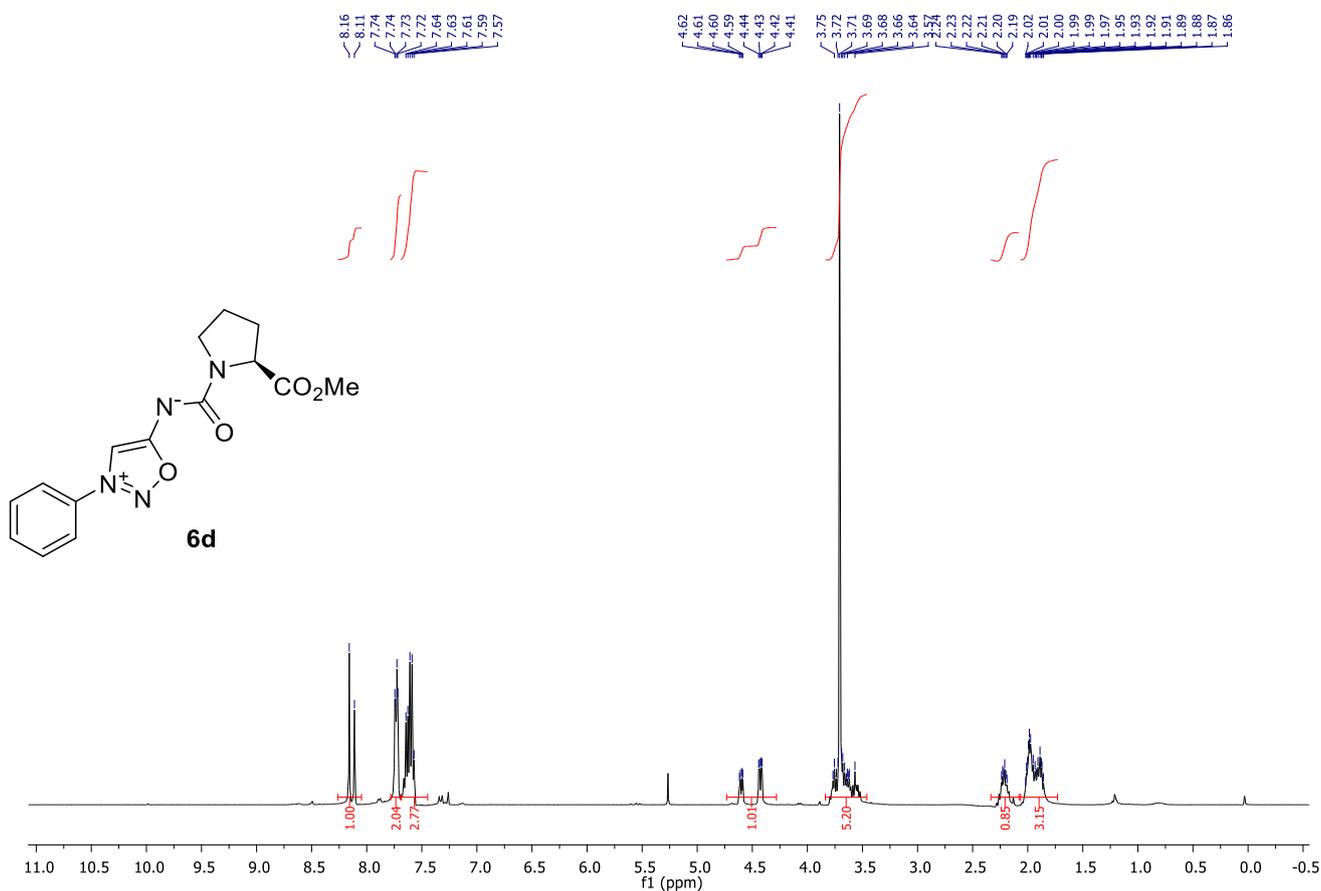


$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ )

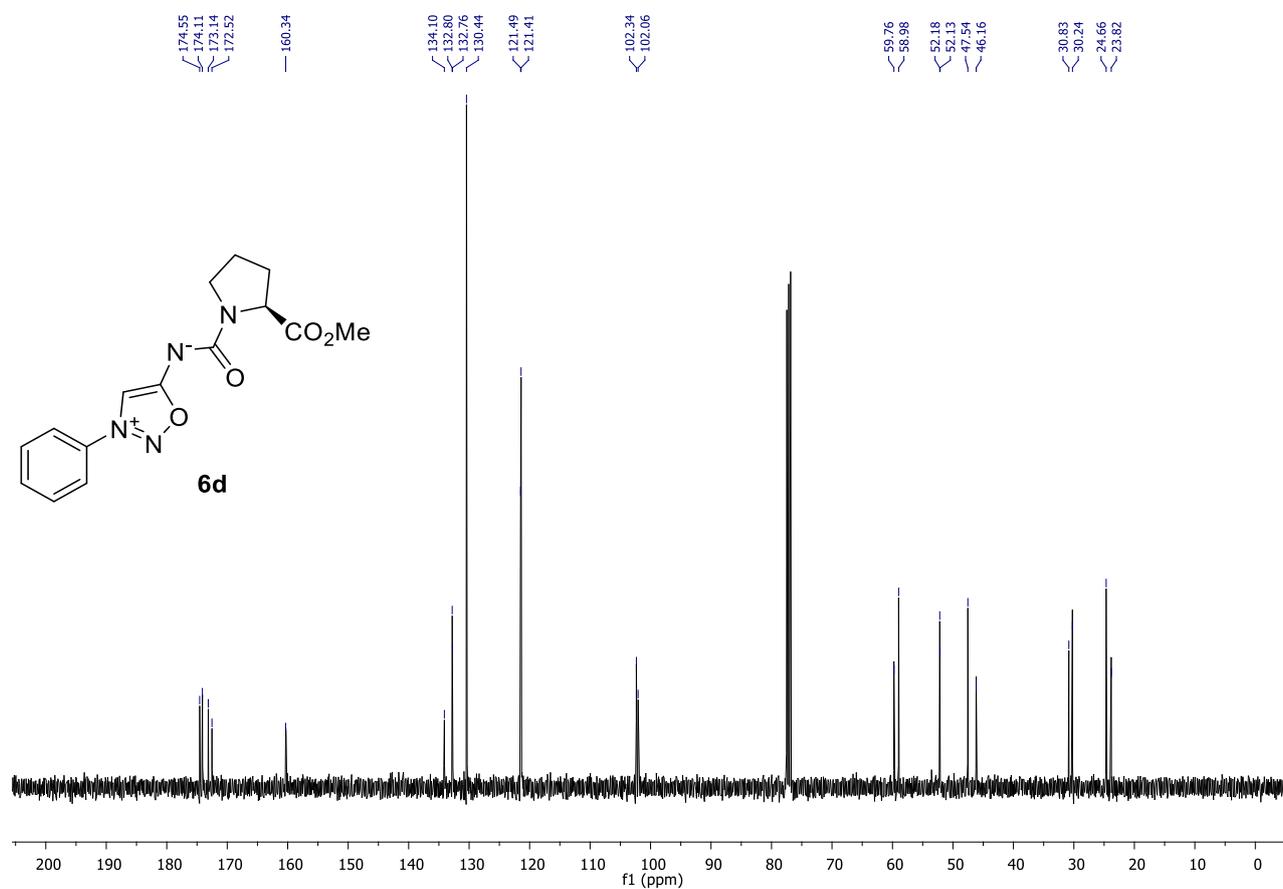


$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ )

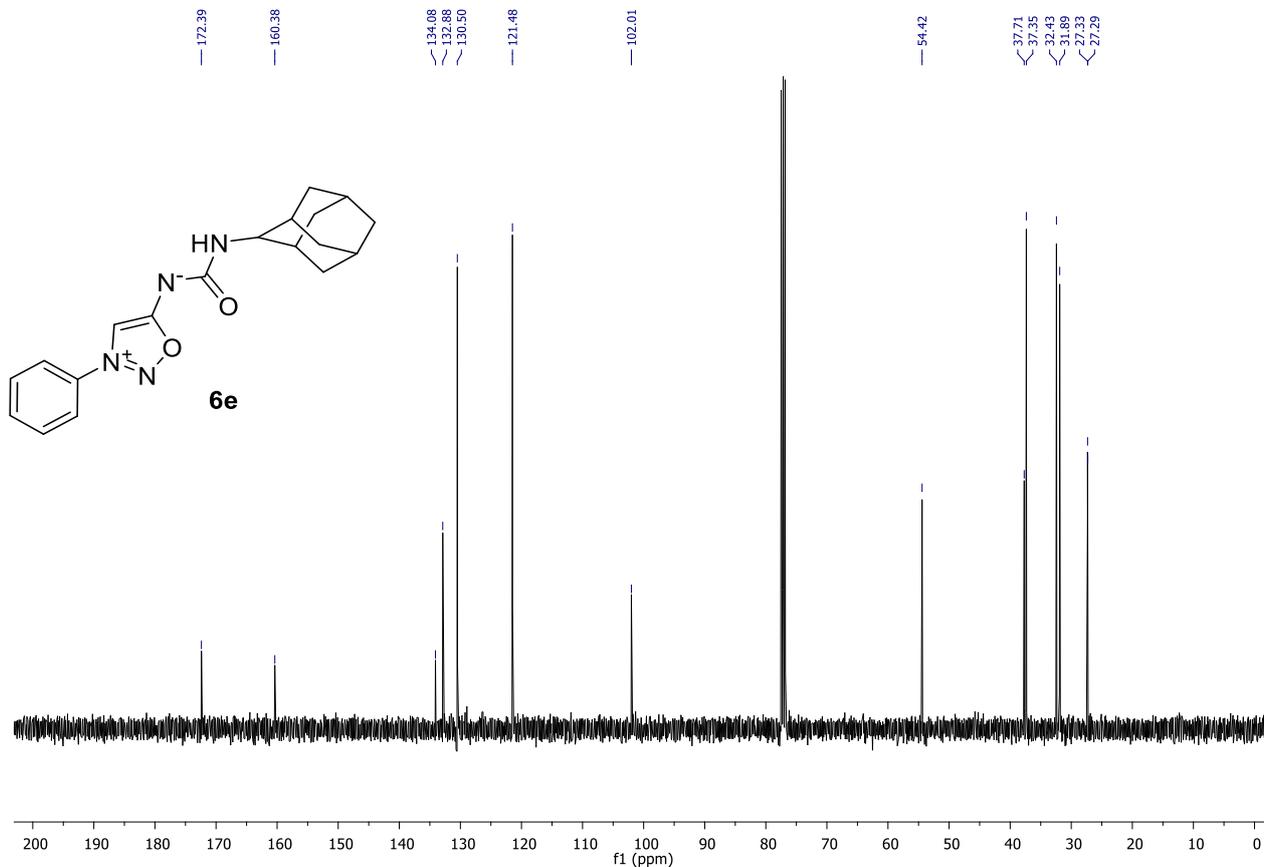
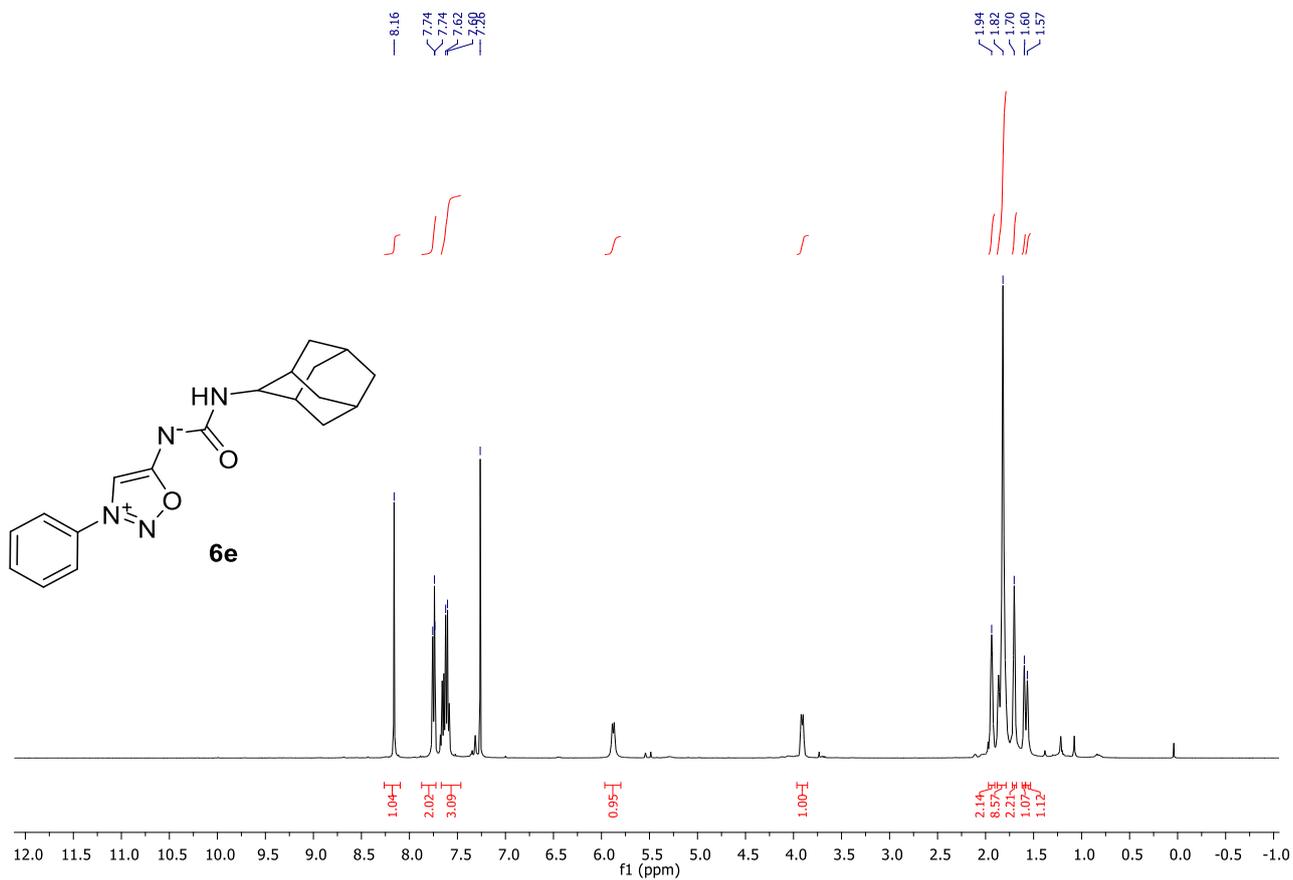


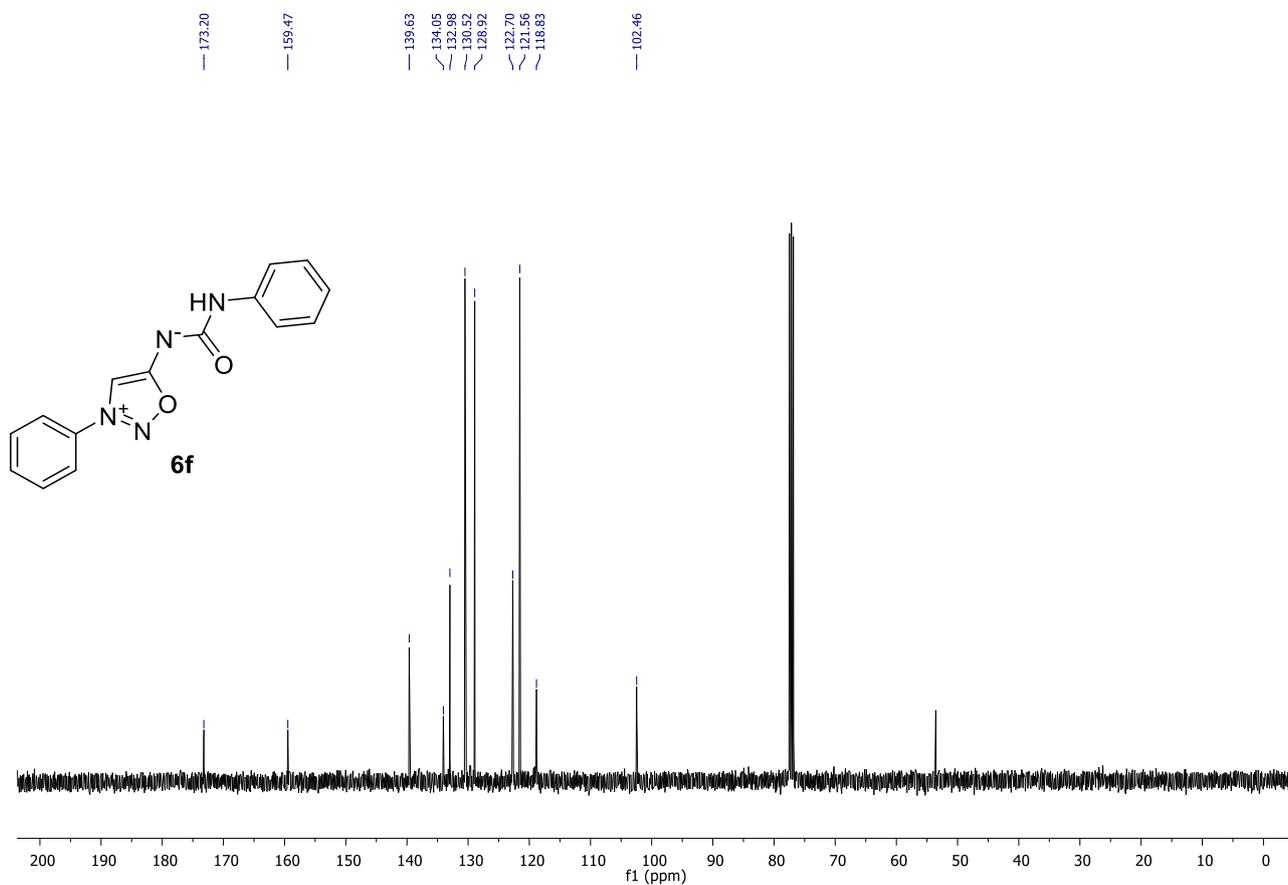
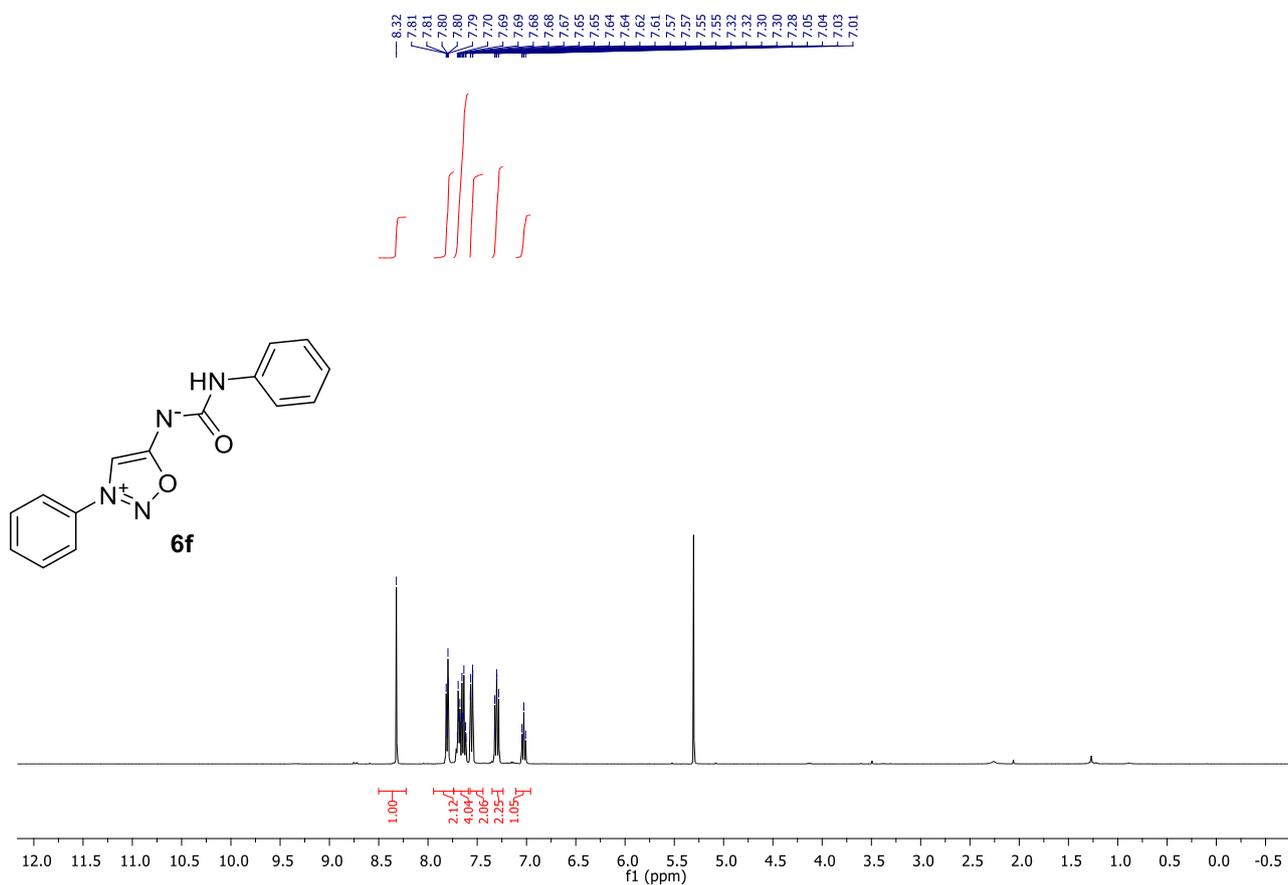


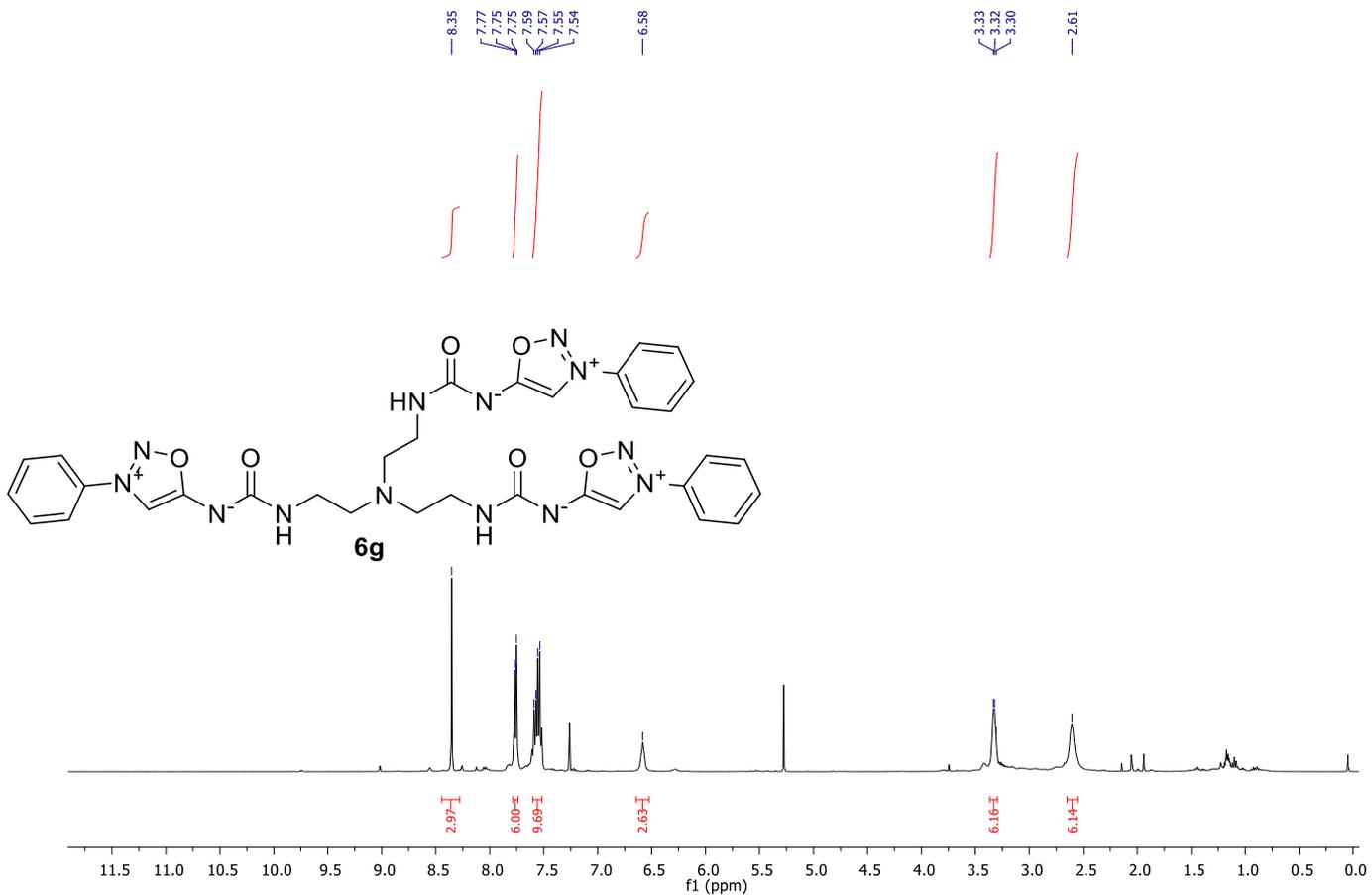
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



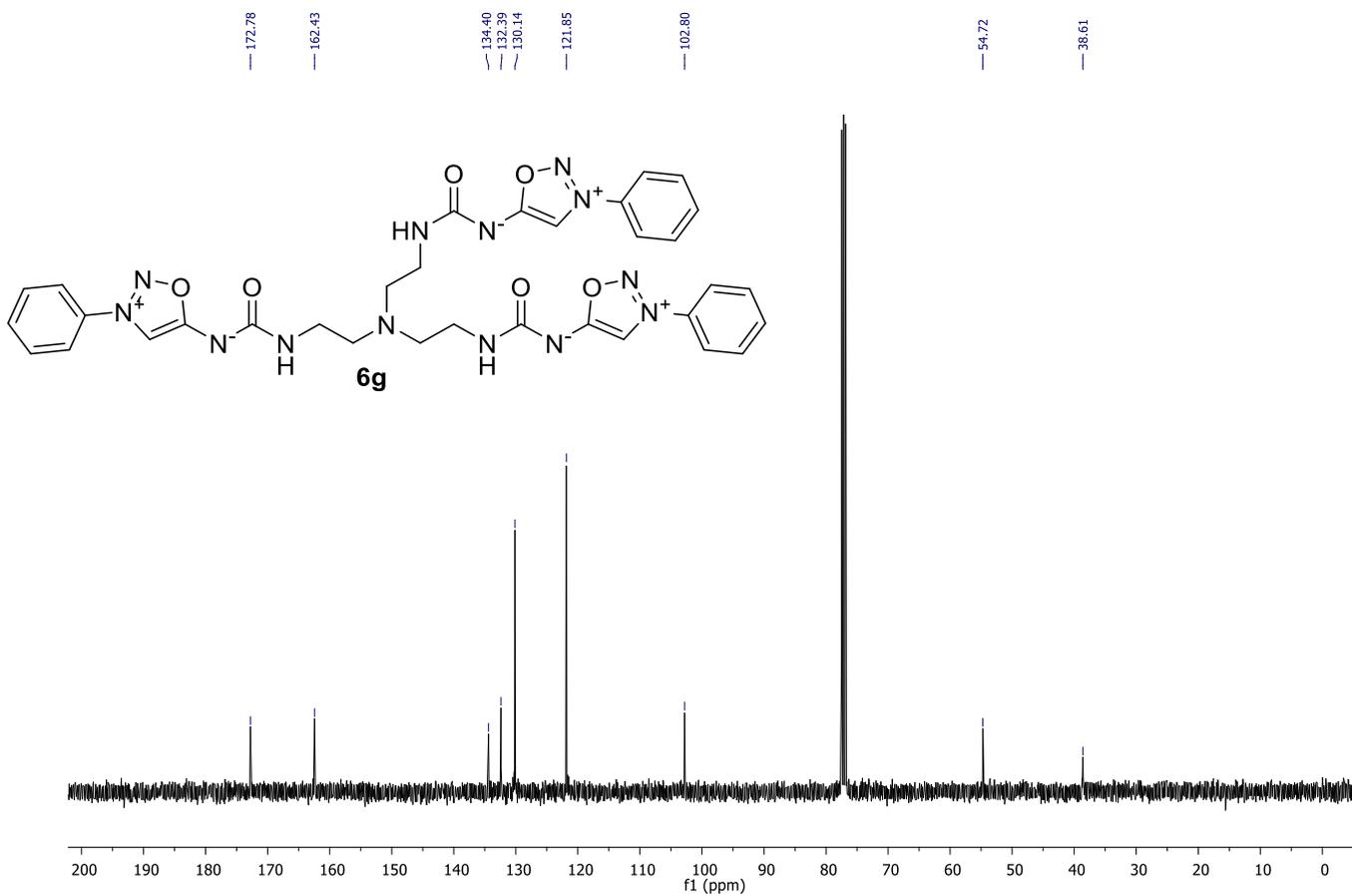
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



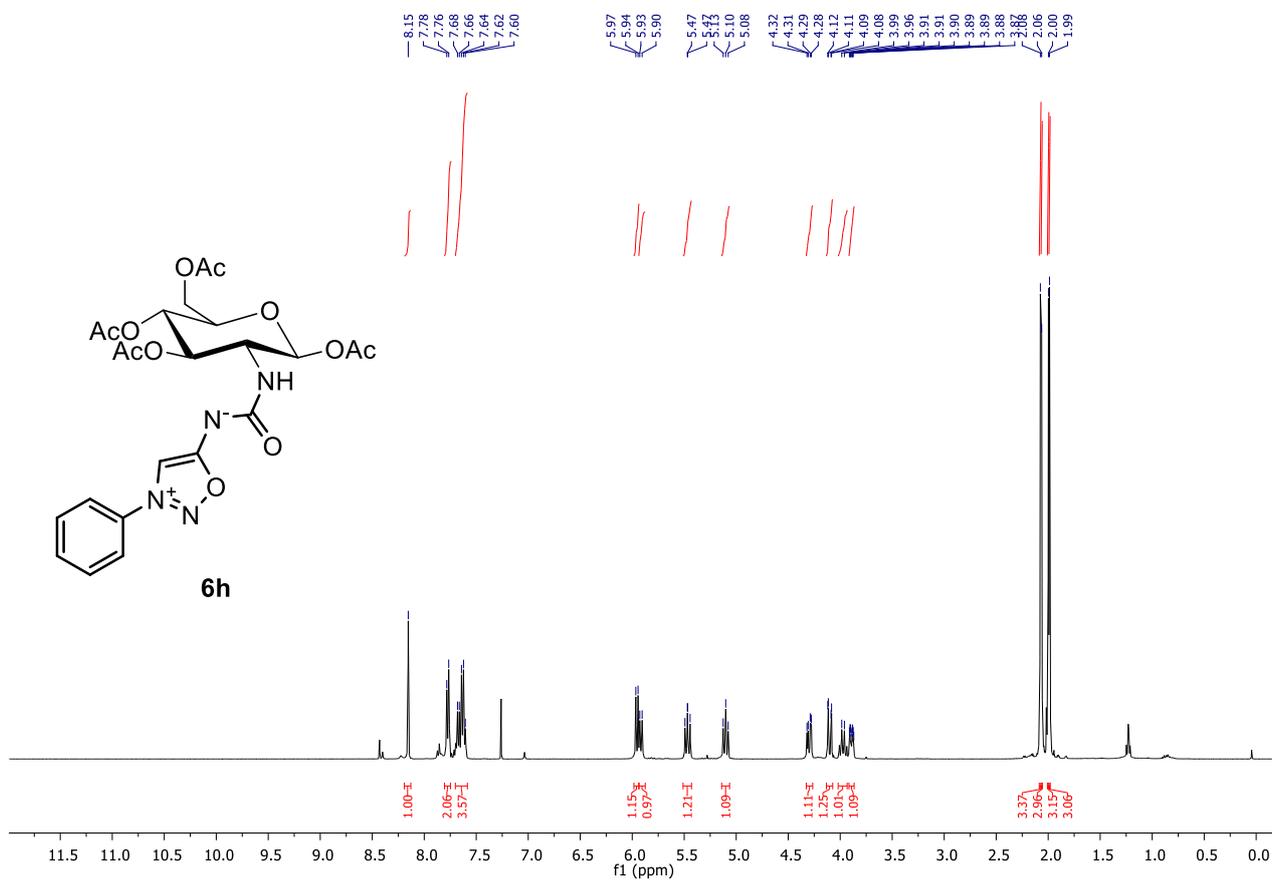




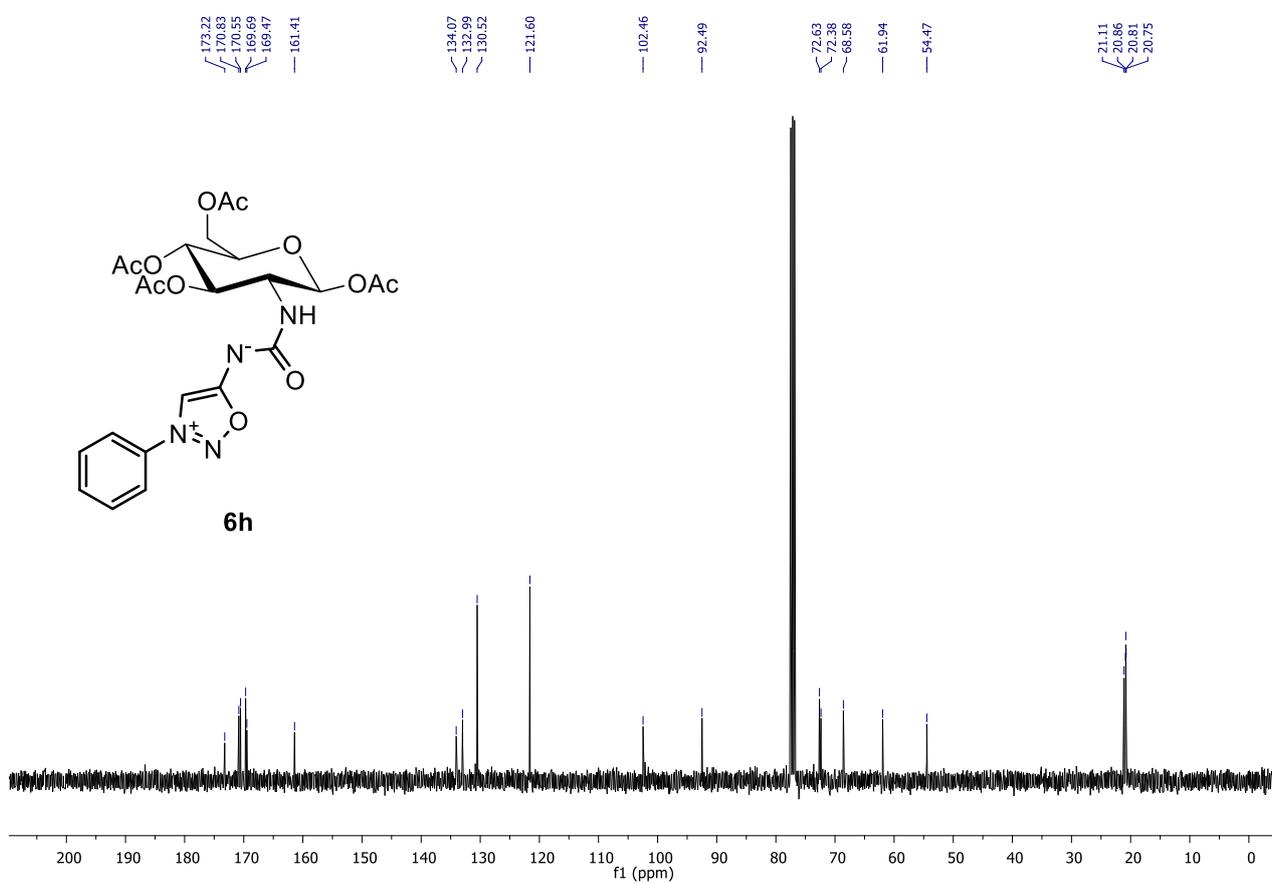
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



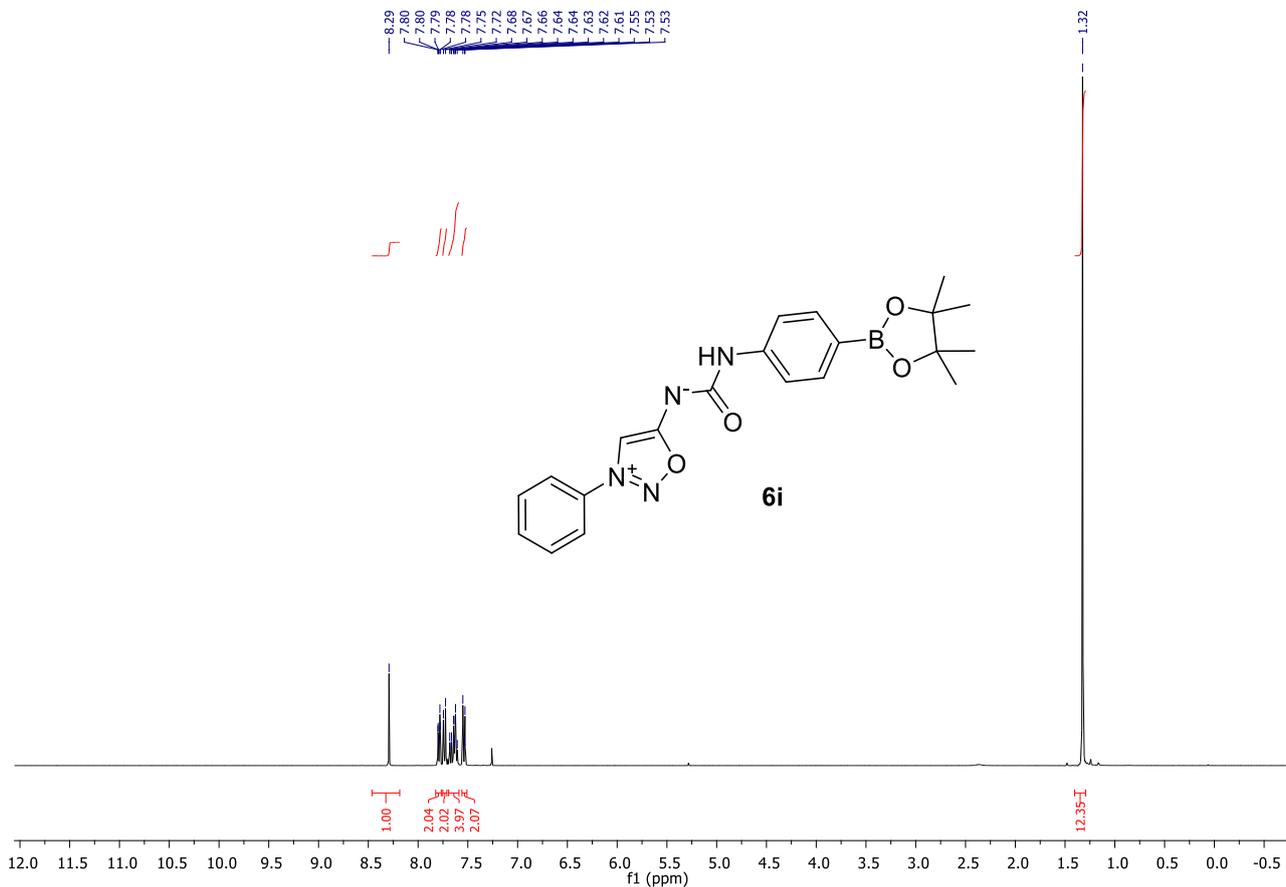
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



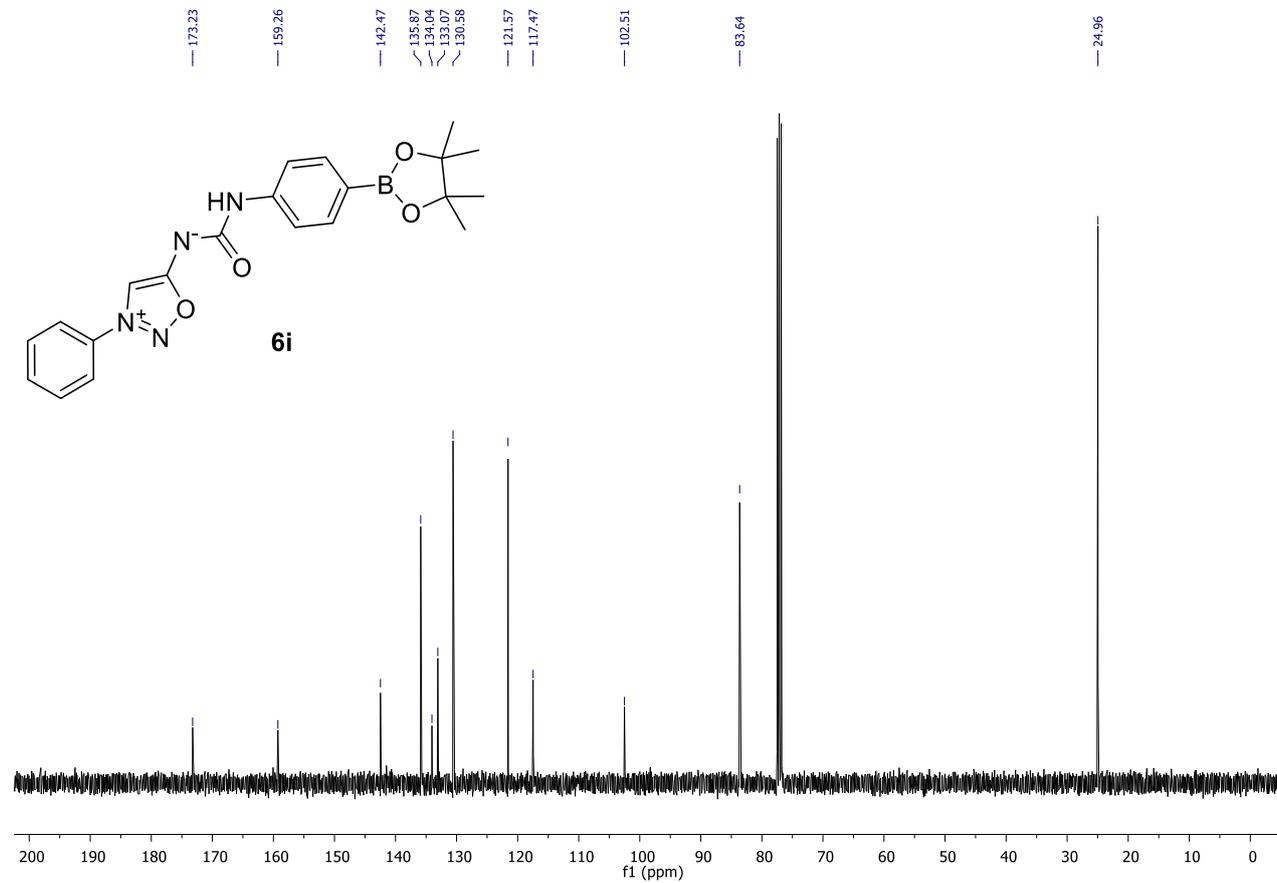
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



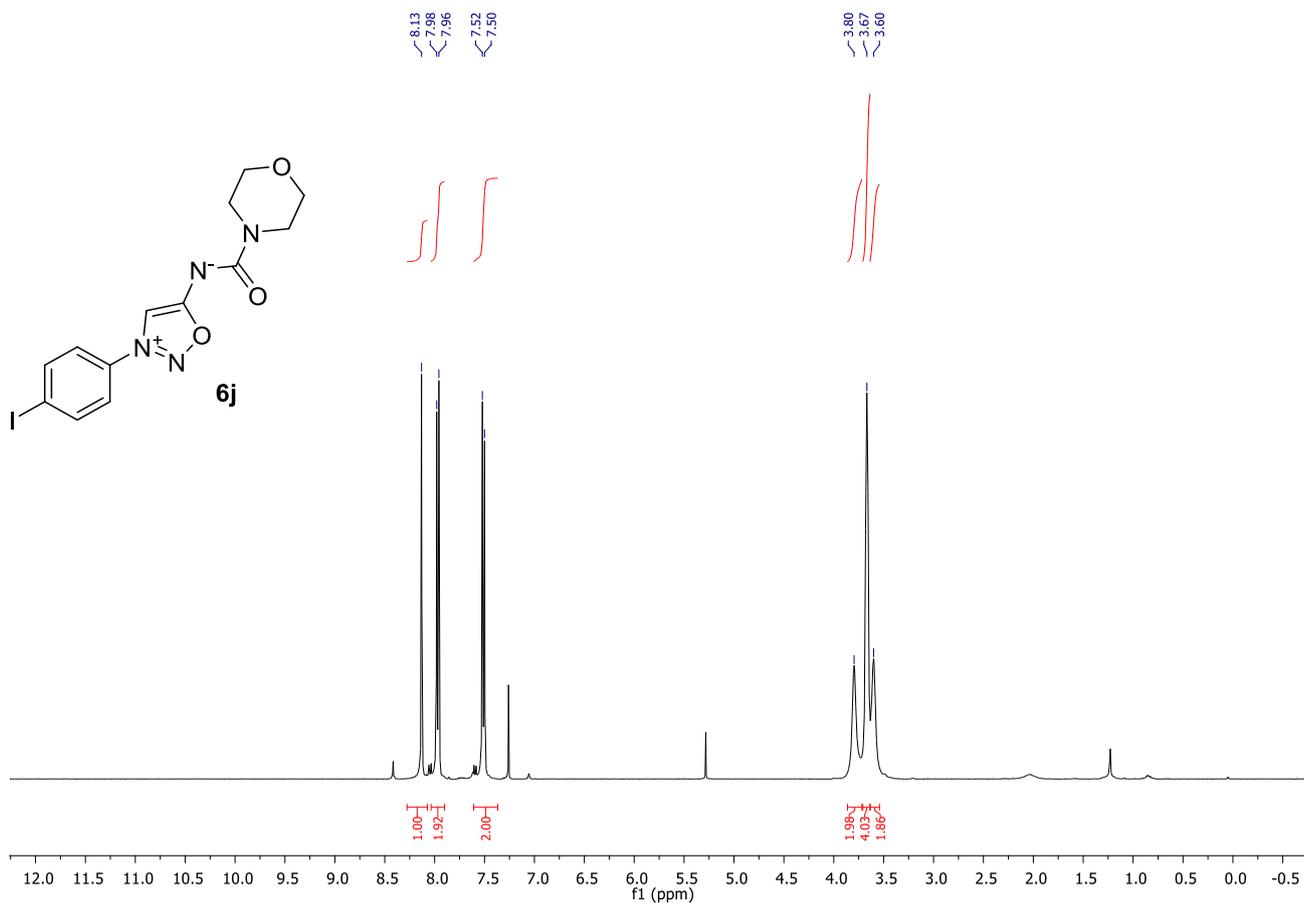
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



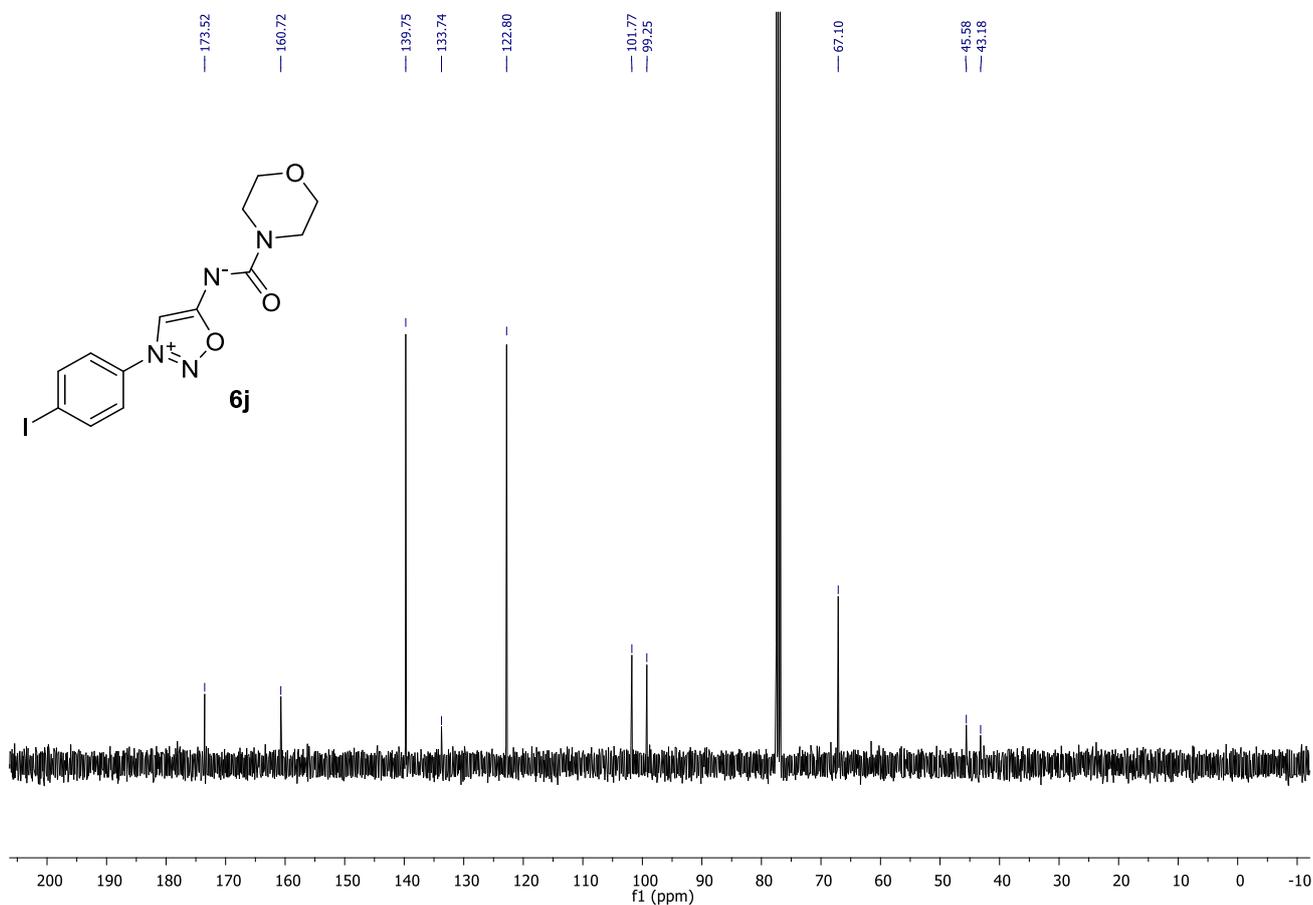
$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ )



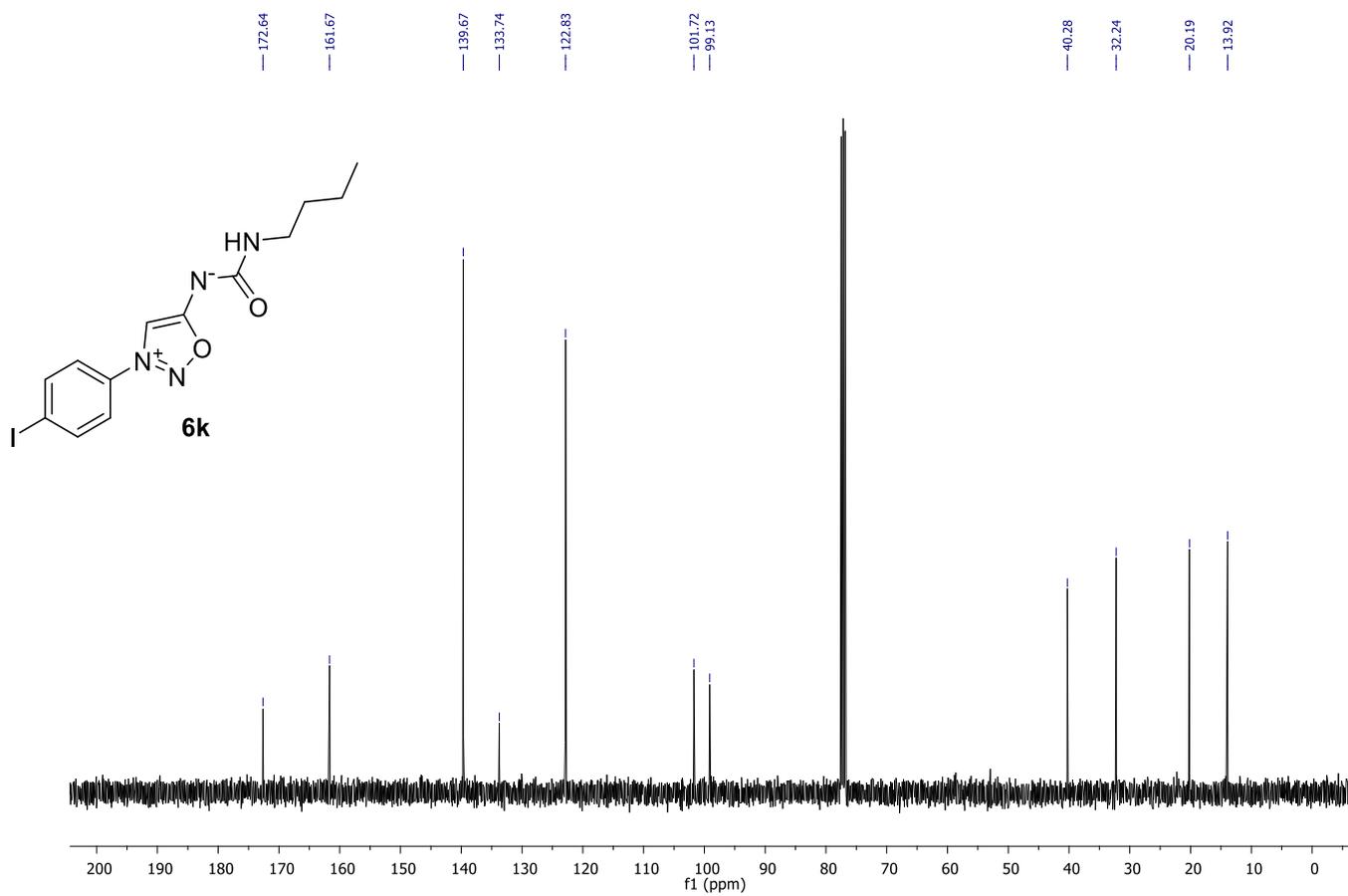
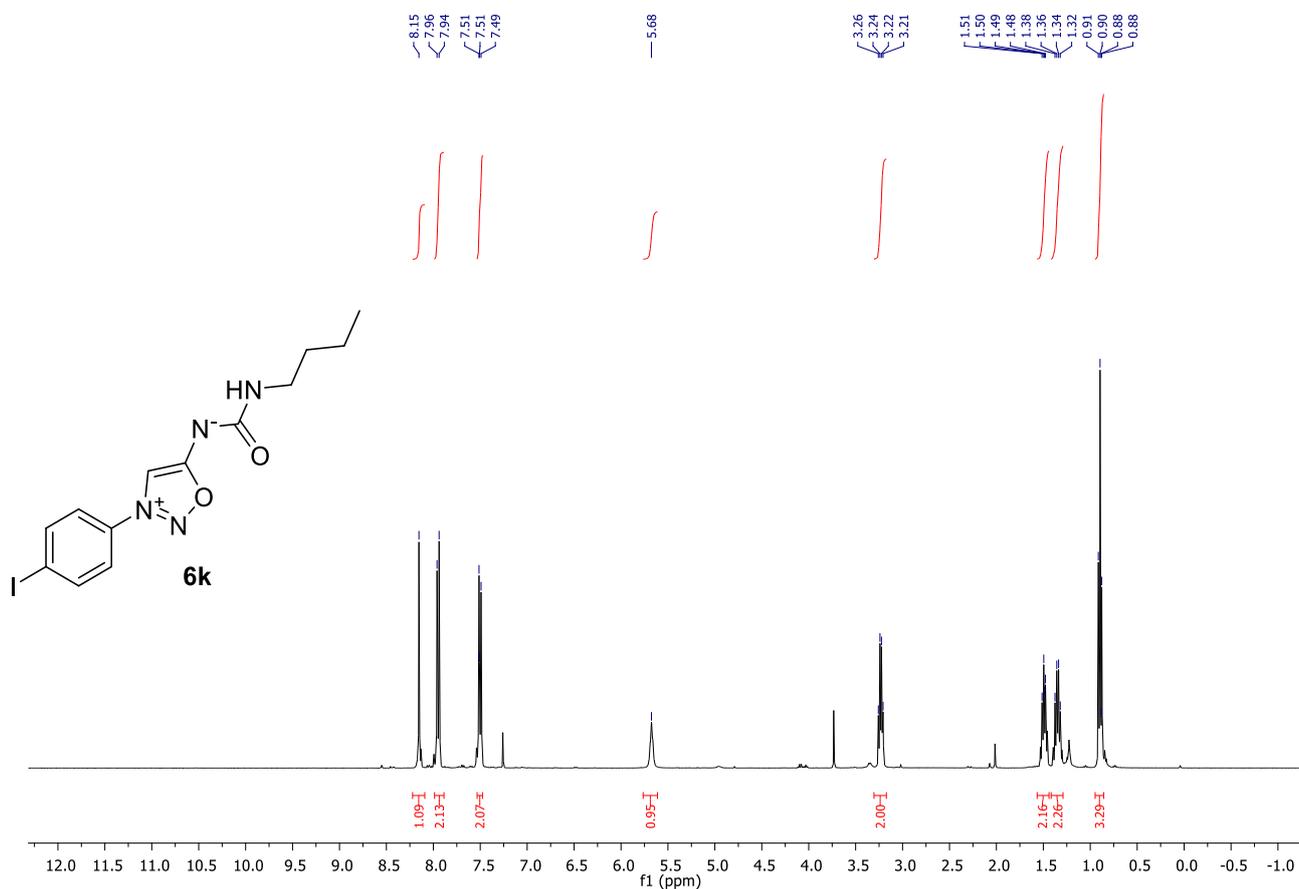
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ )

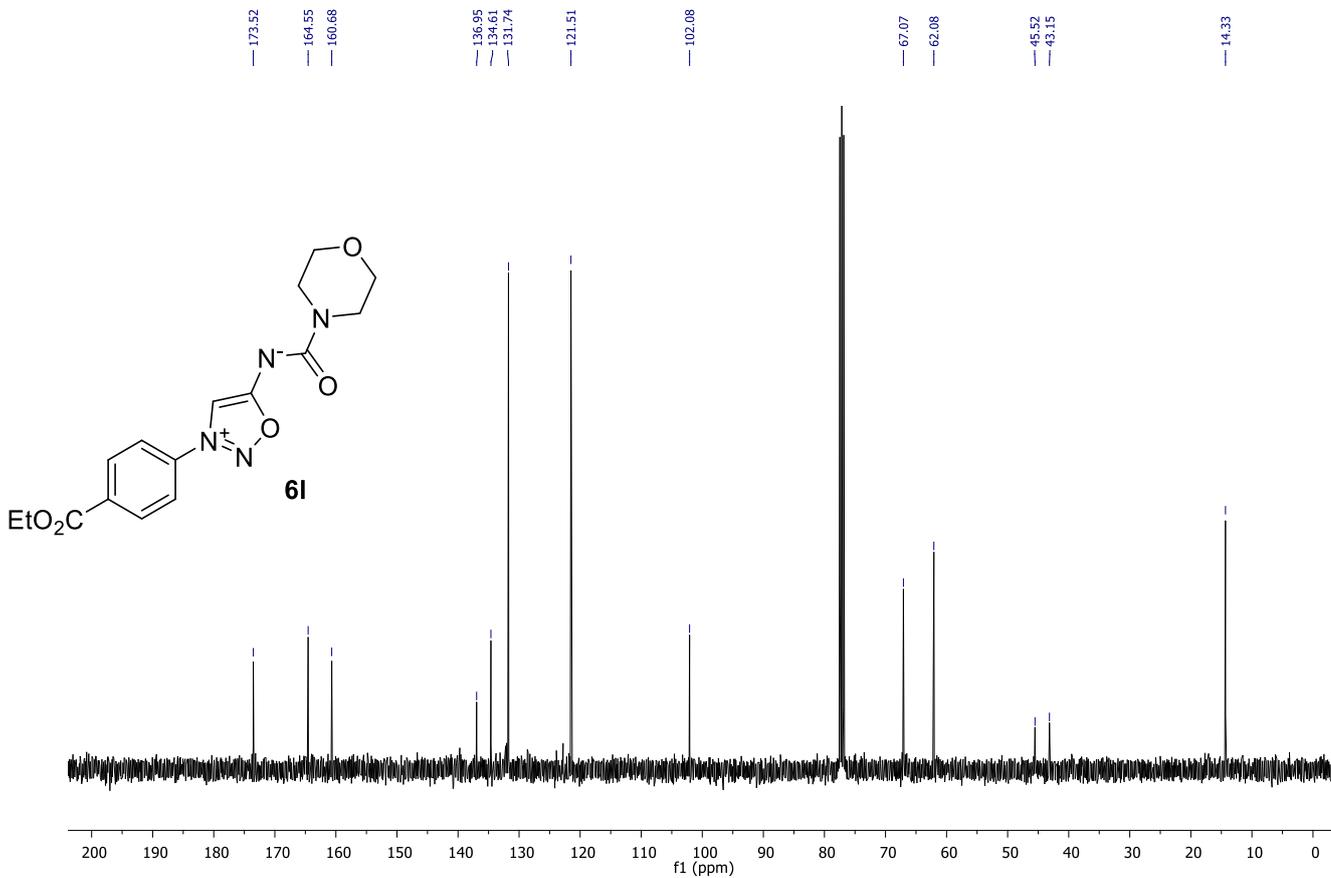
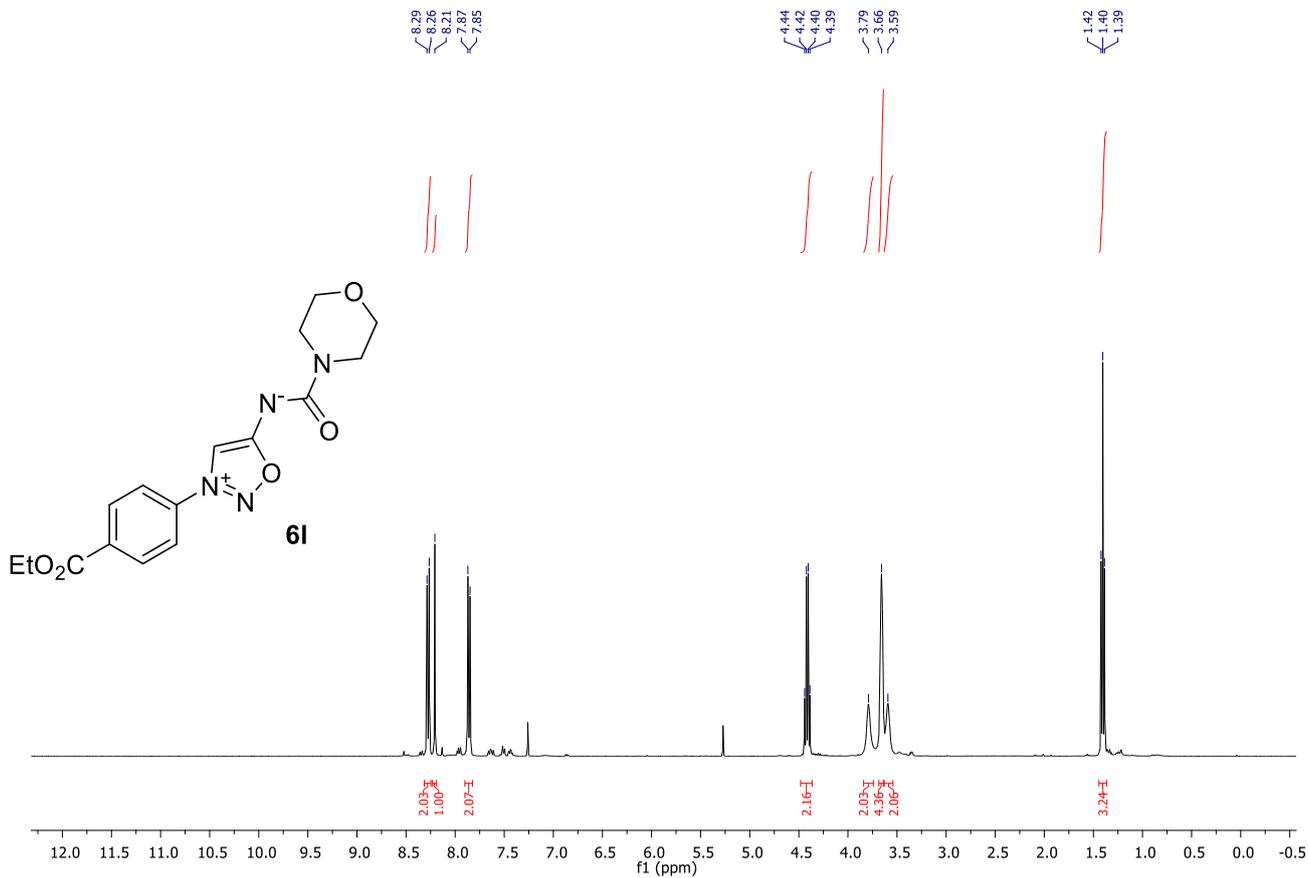


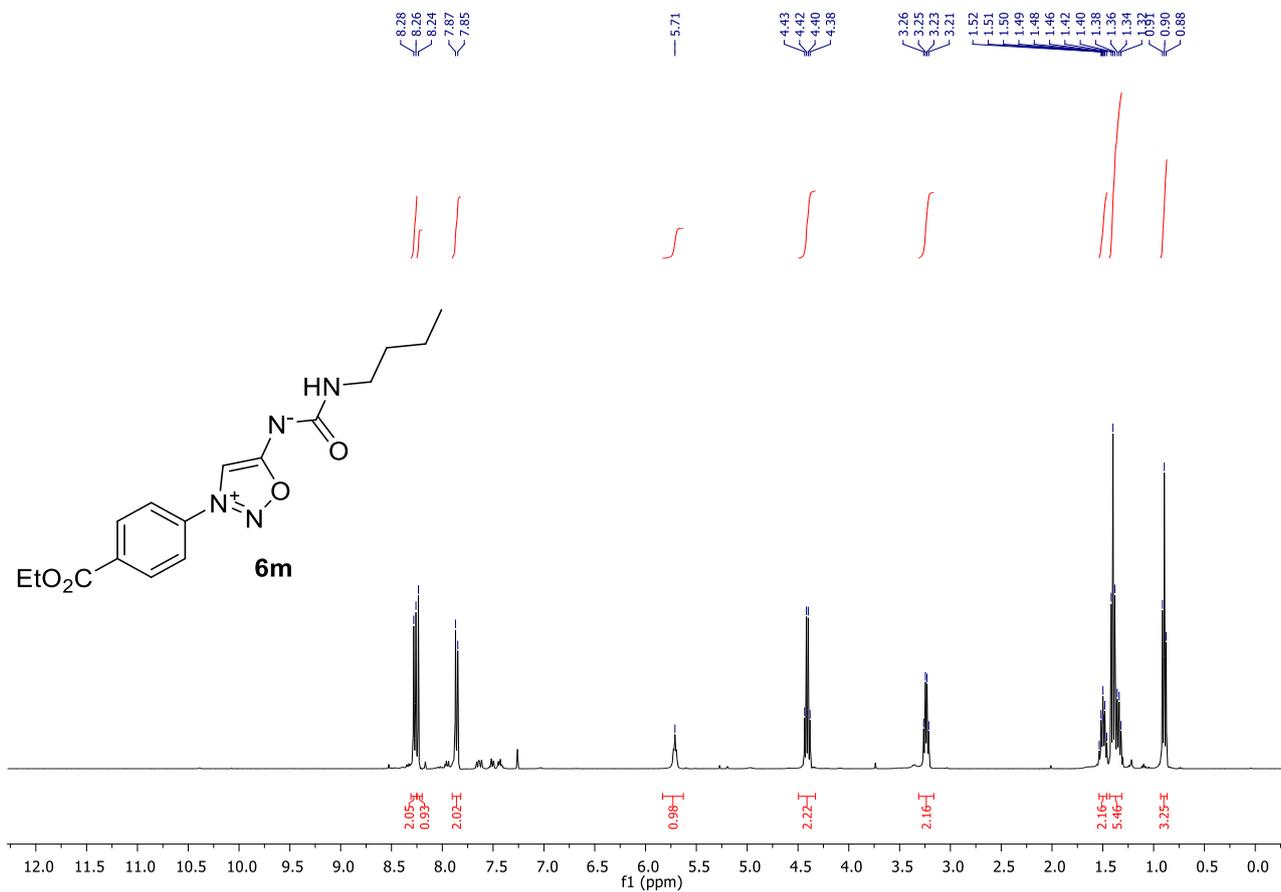
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



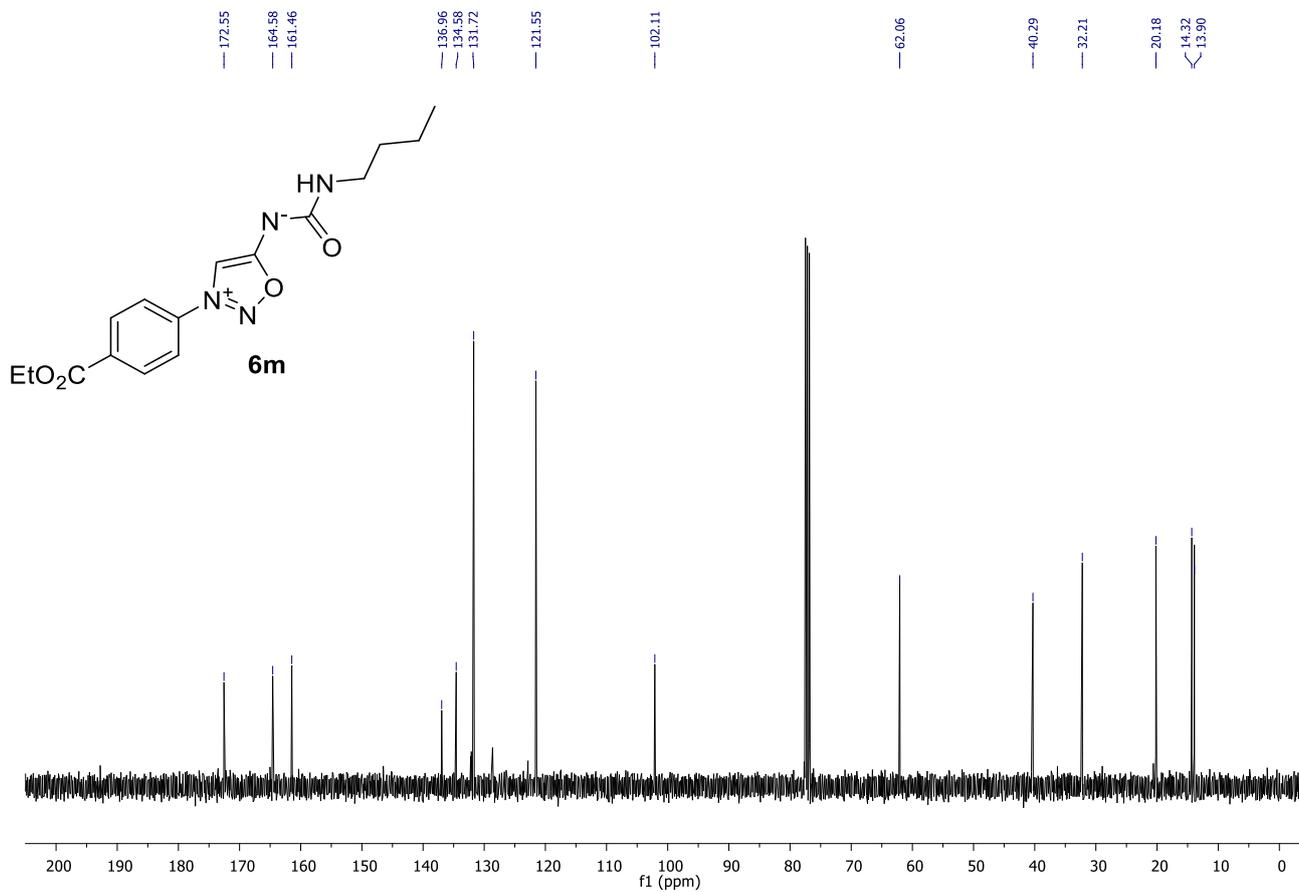
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



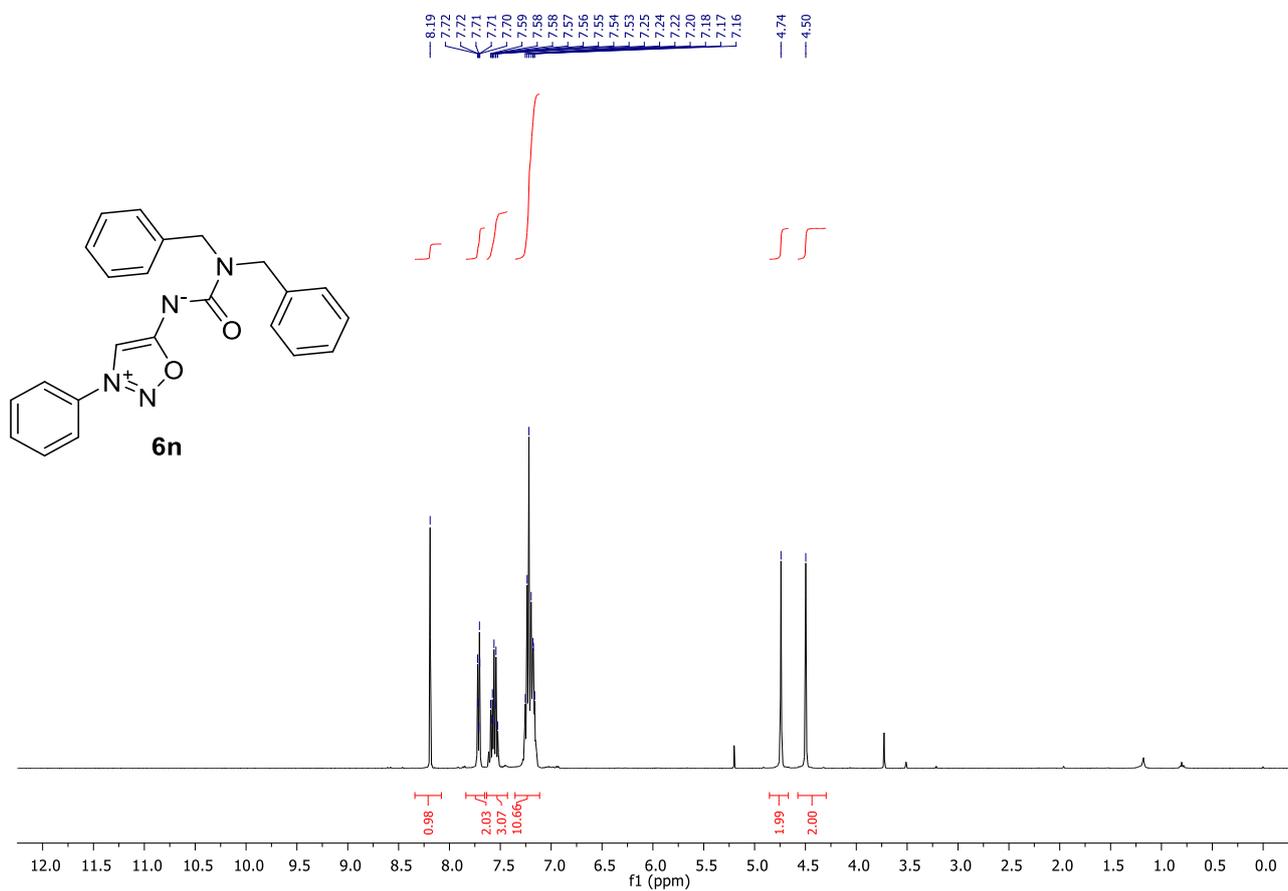




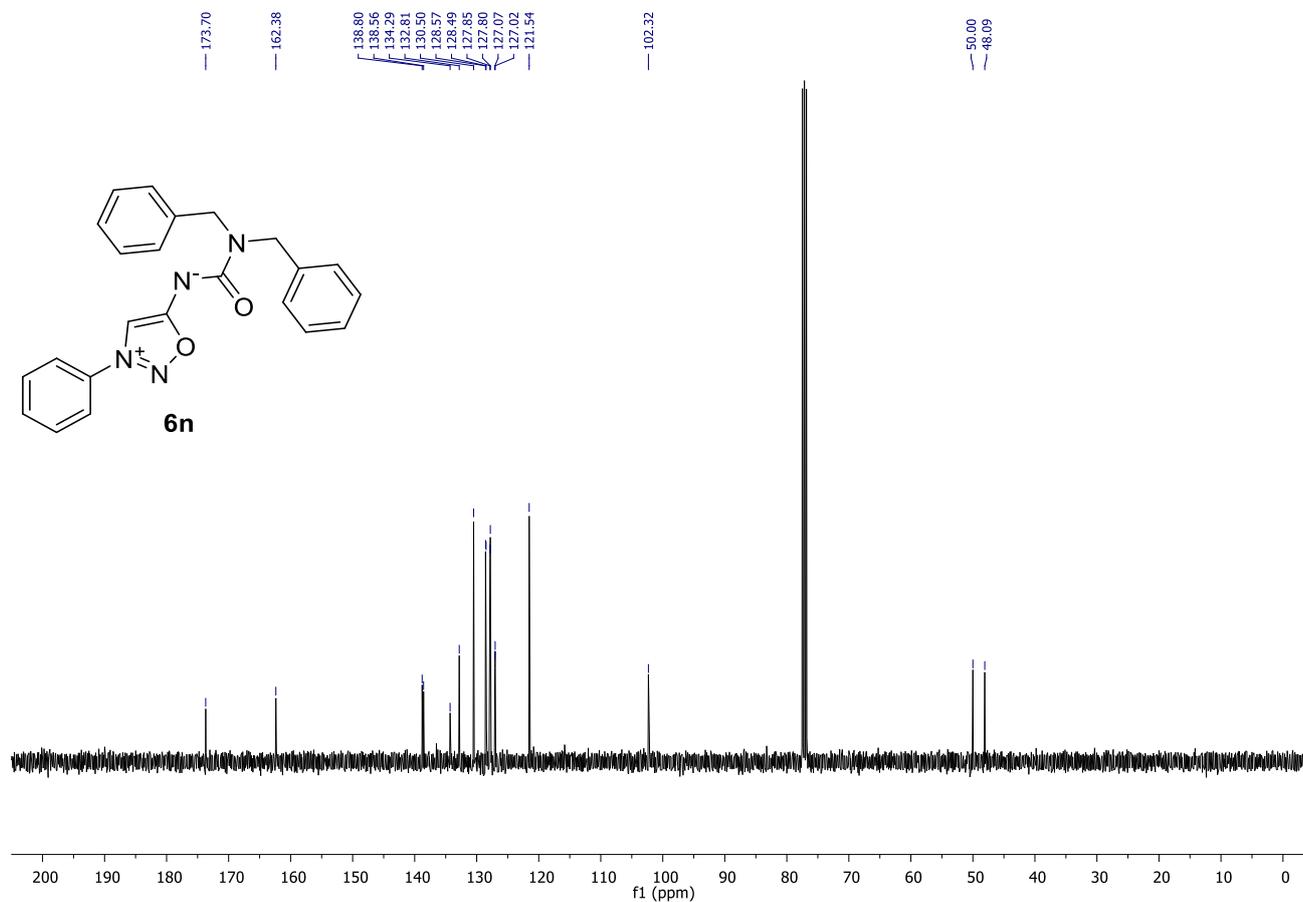
$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ )



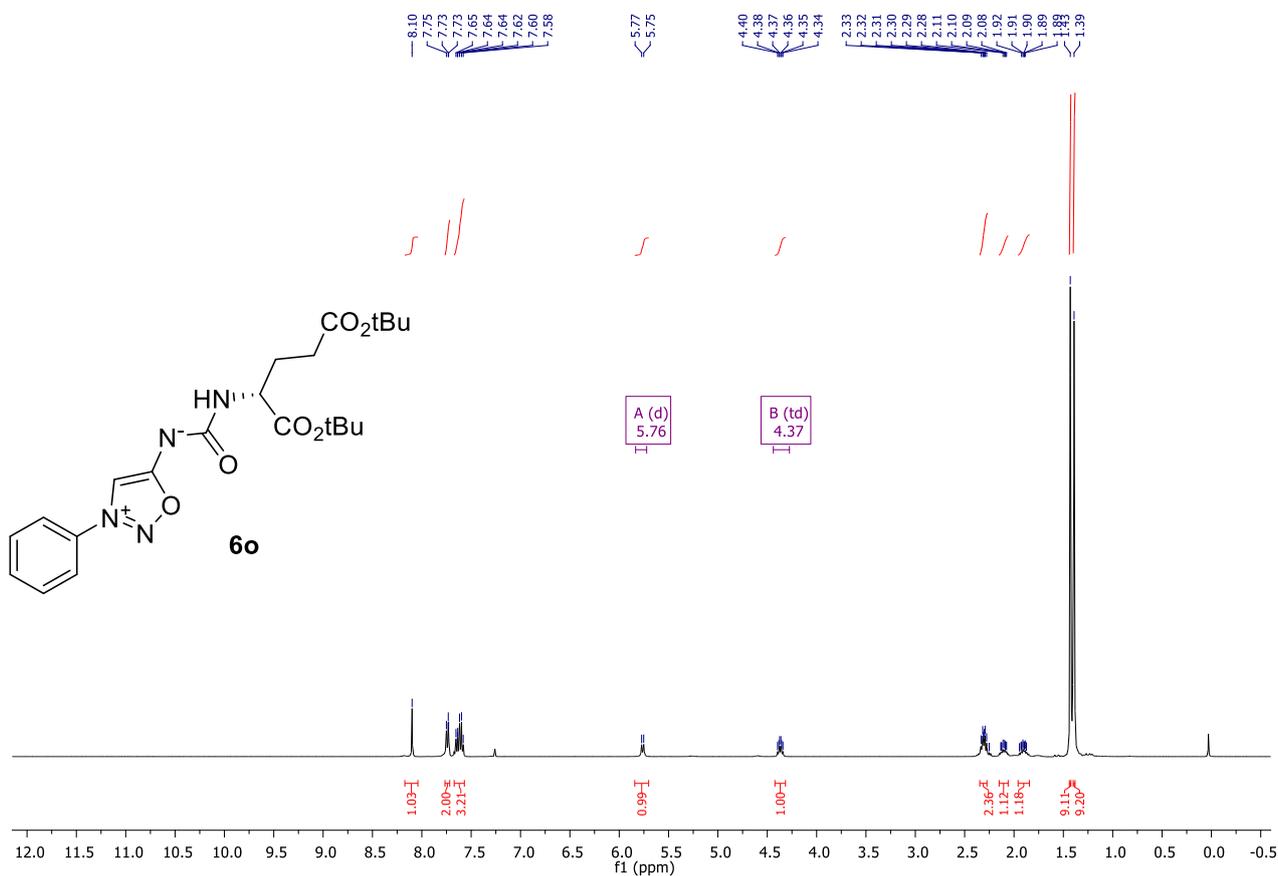
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ )



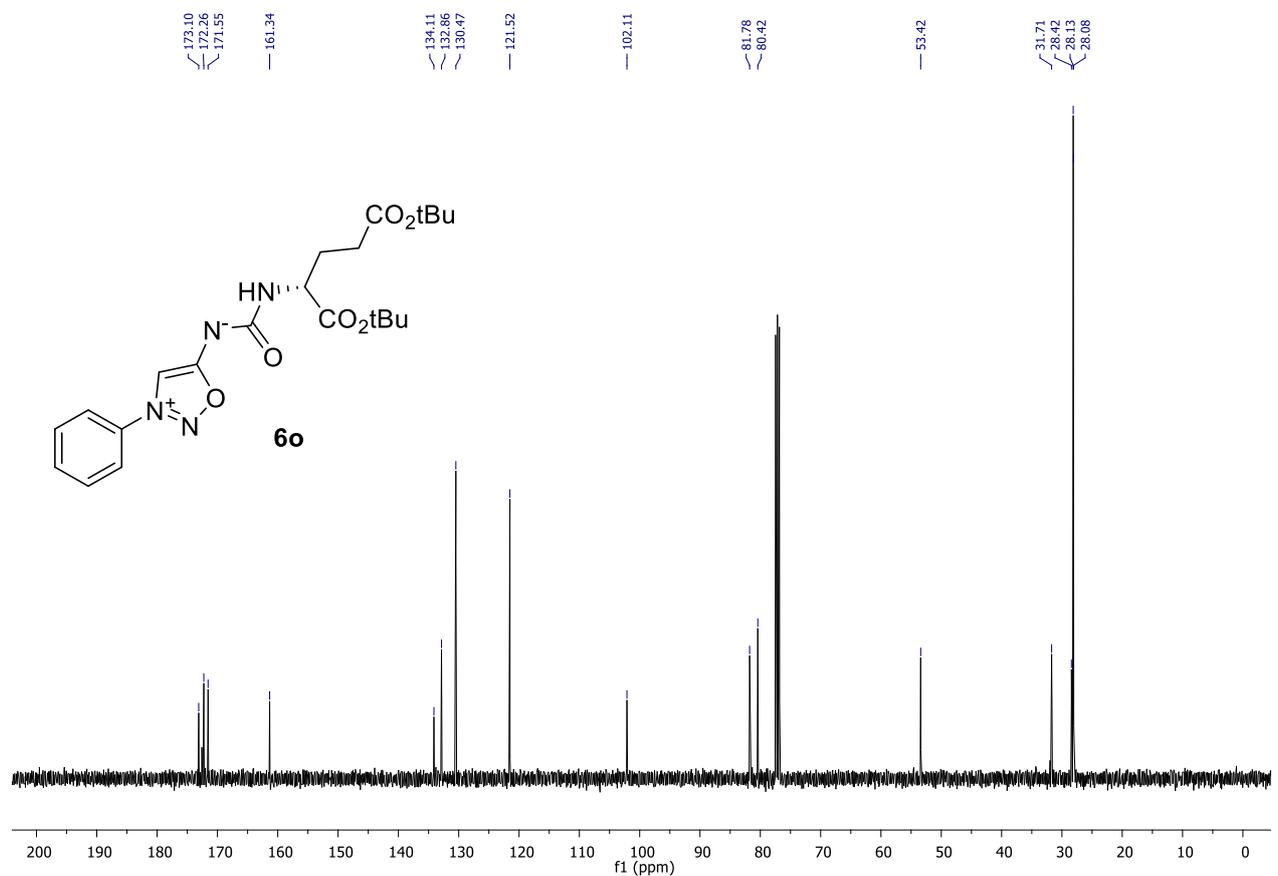
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)

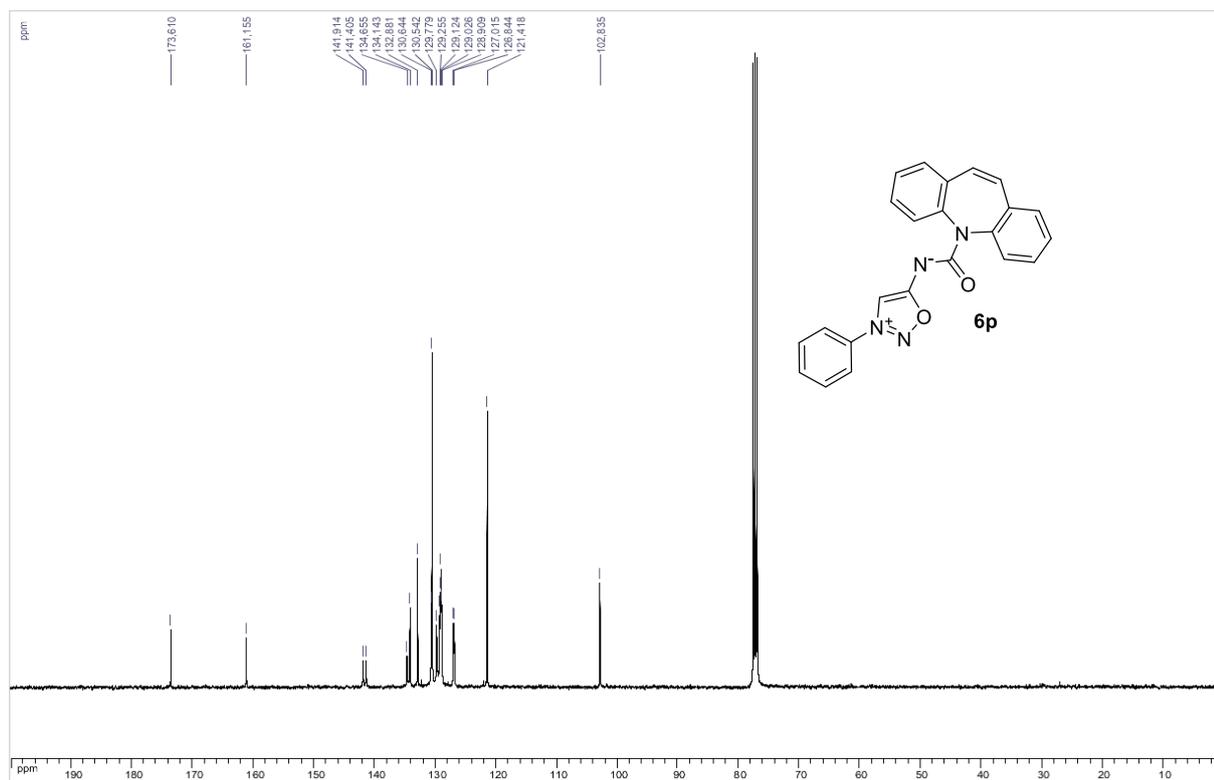
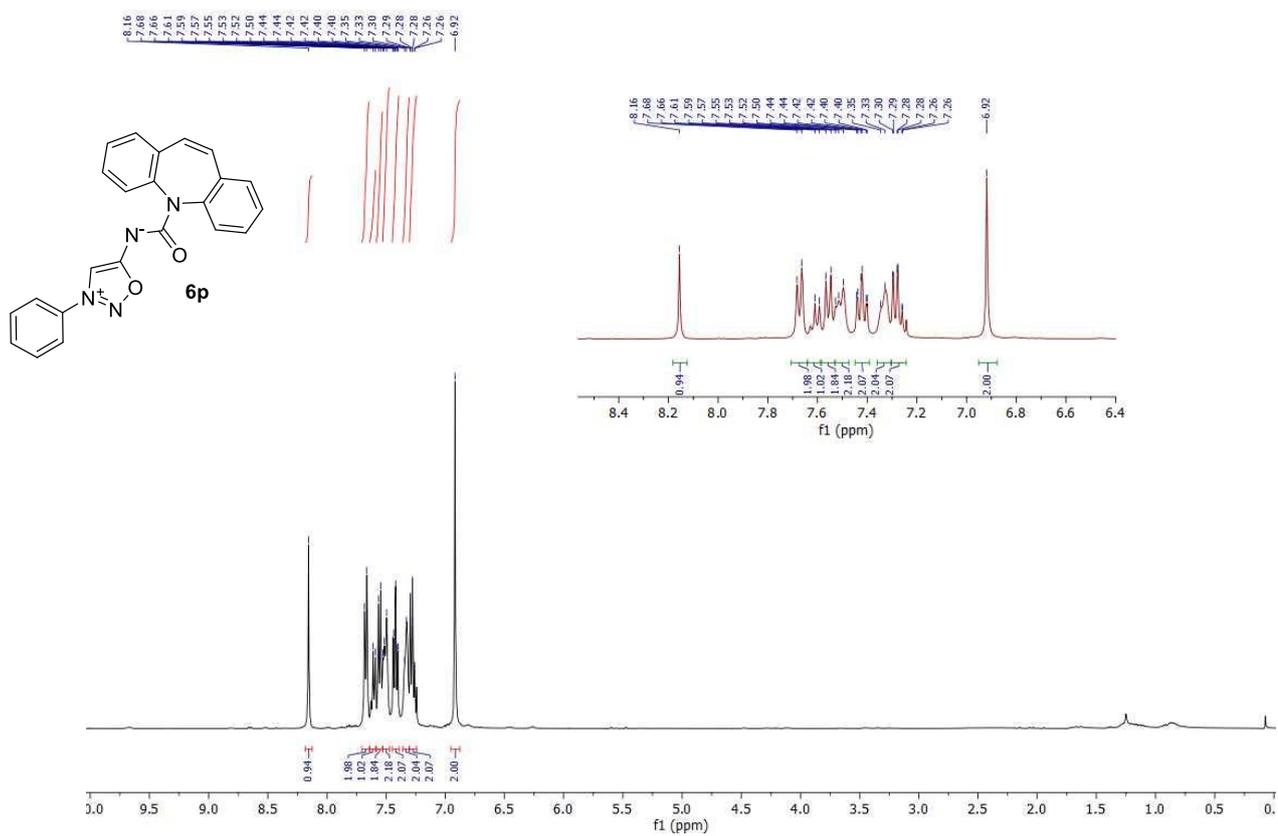


$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ )

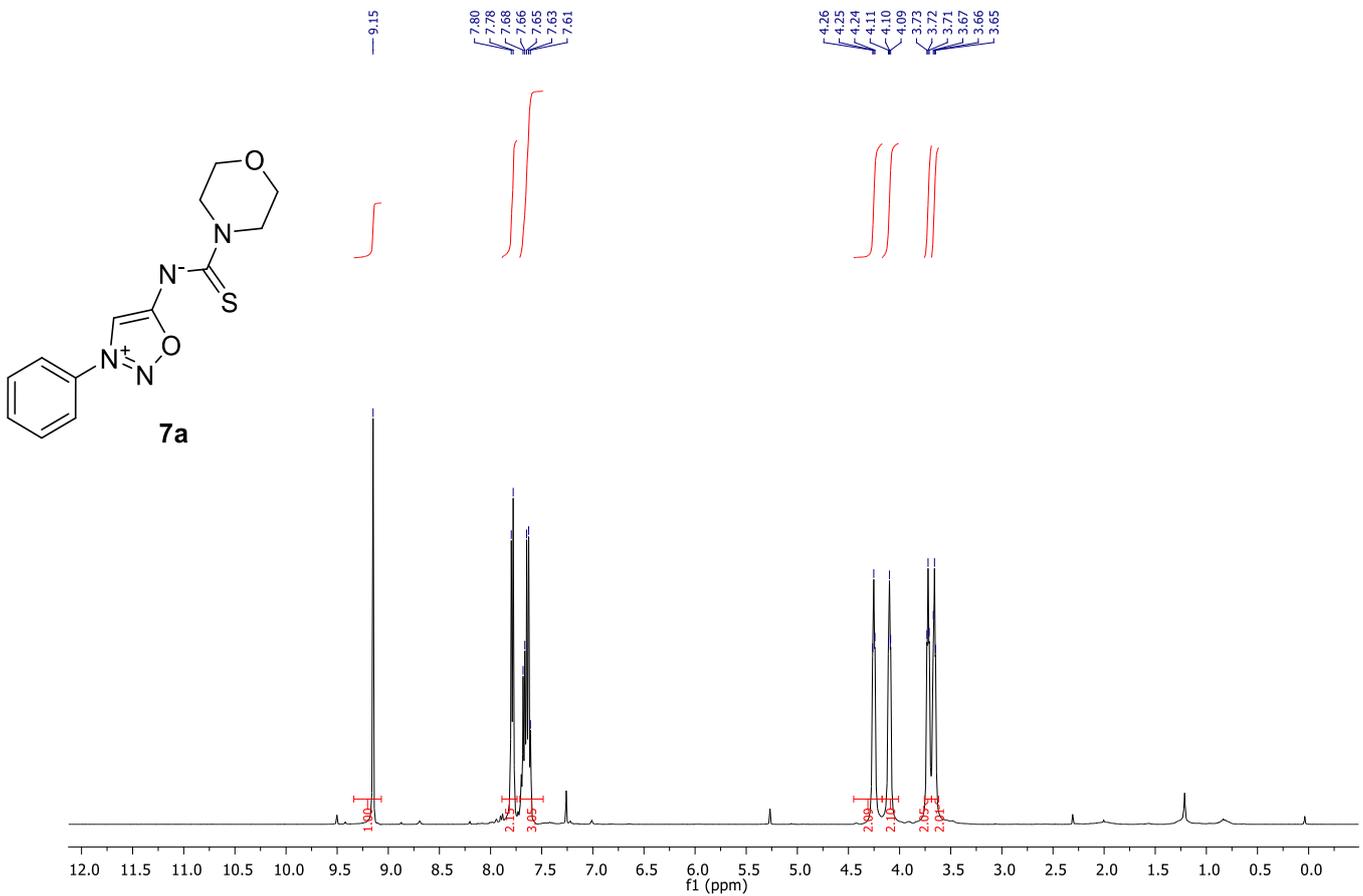


$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ )

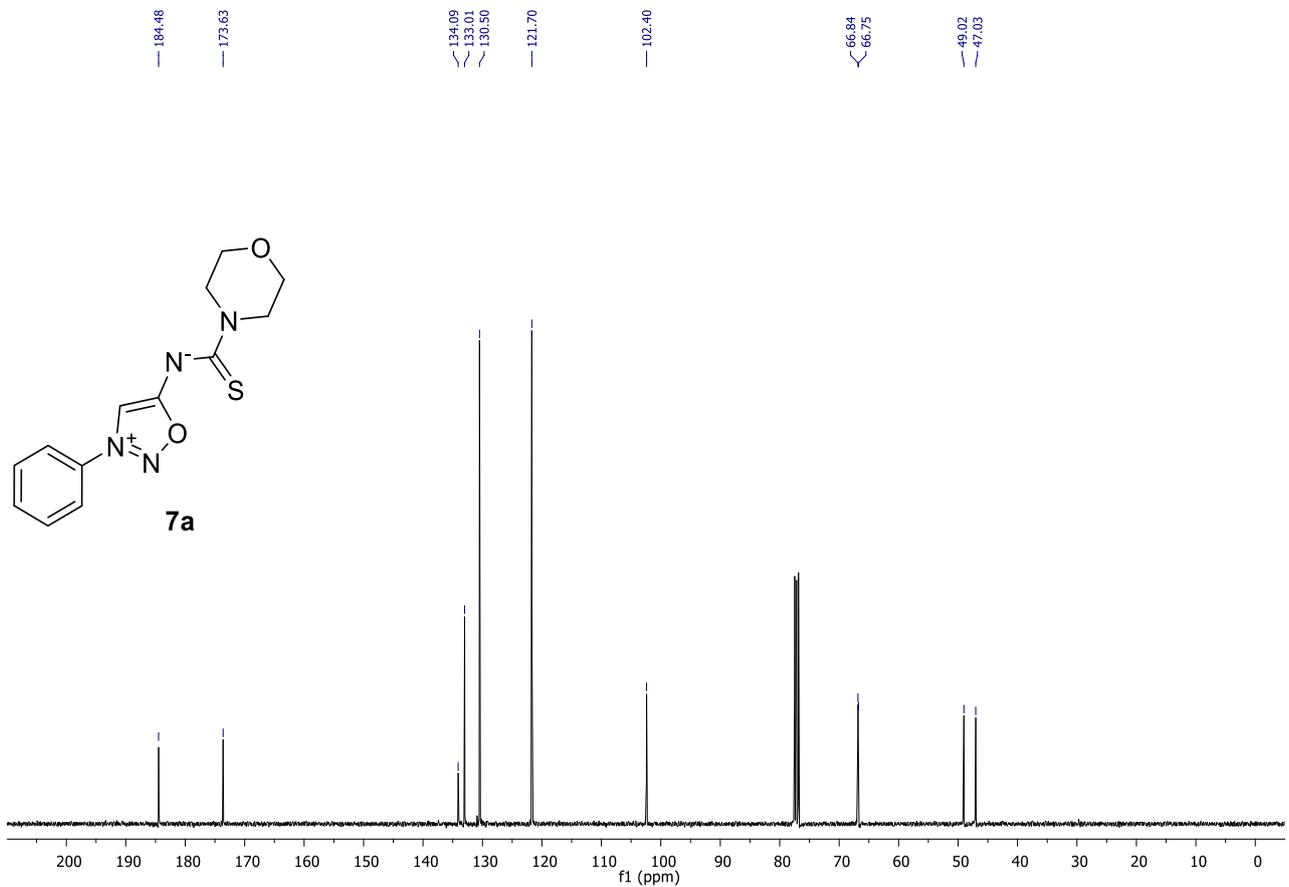
$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ )



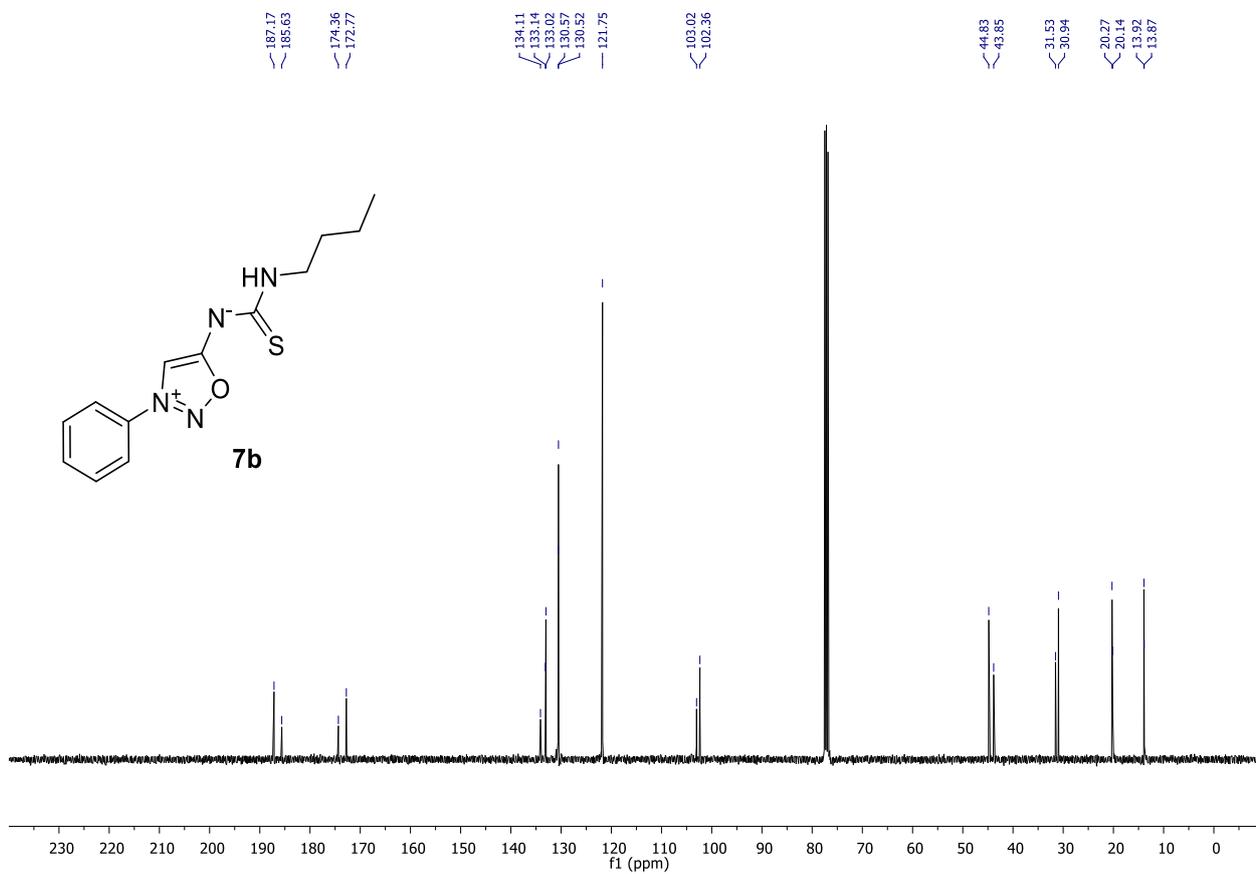
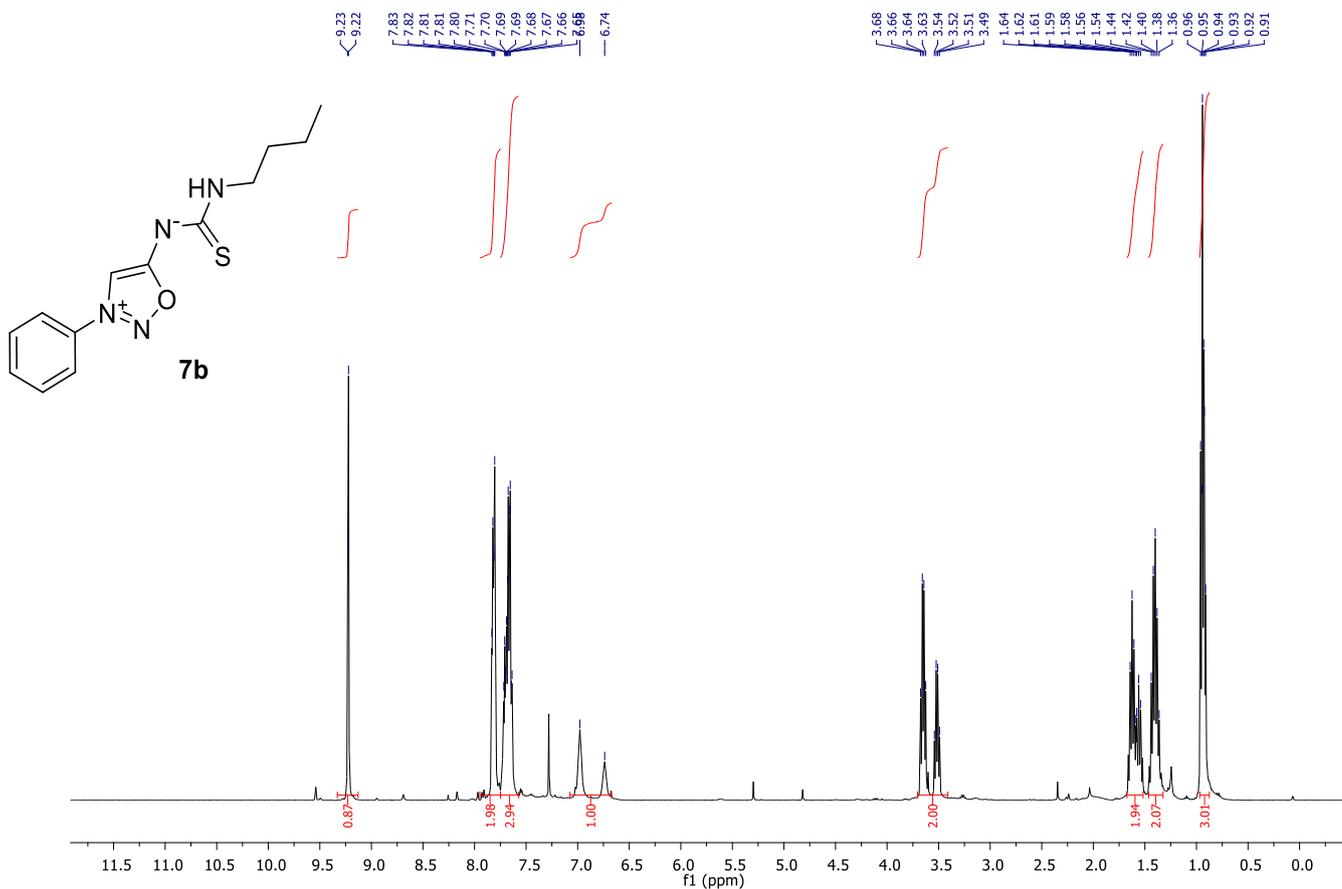
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ )

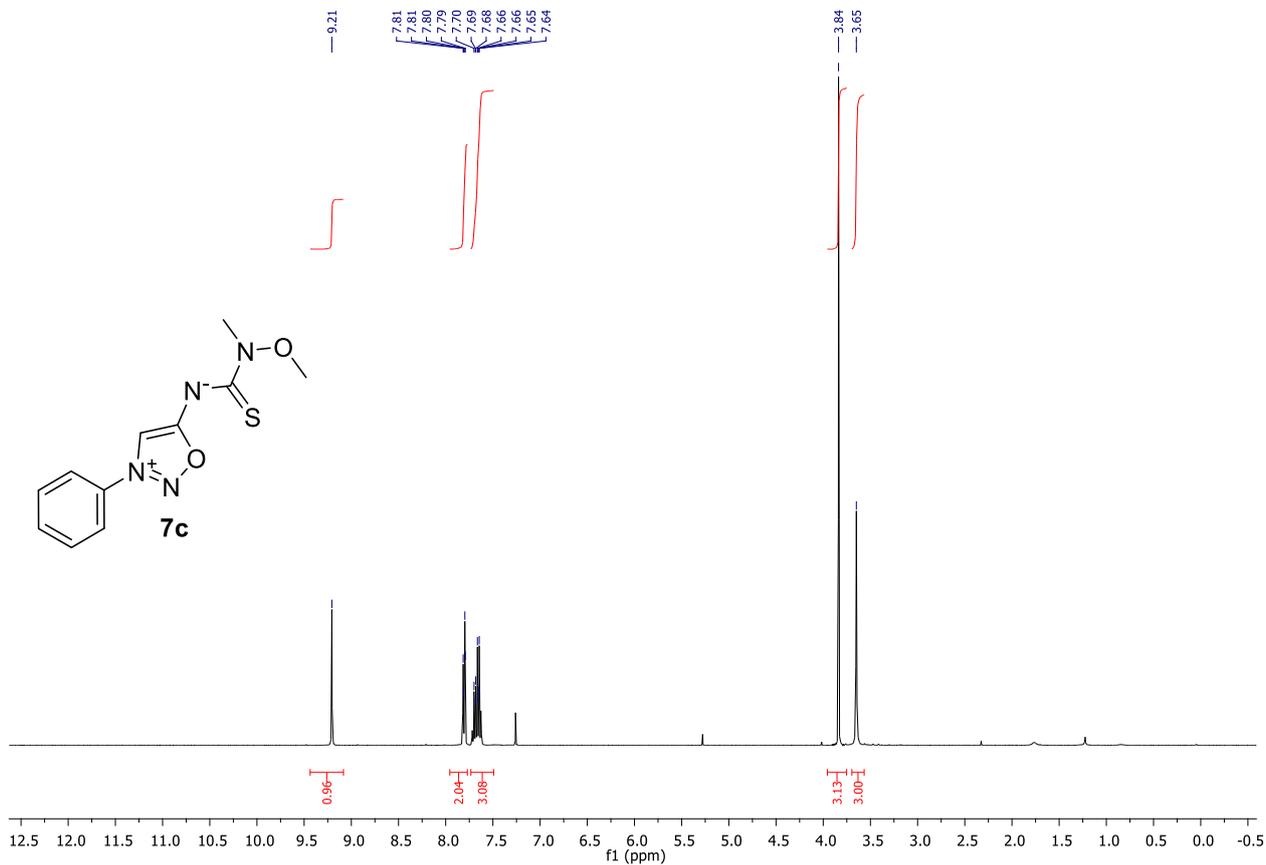


$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ )

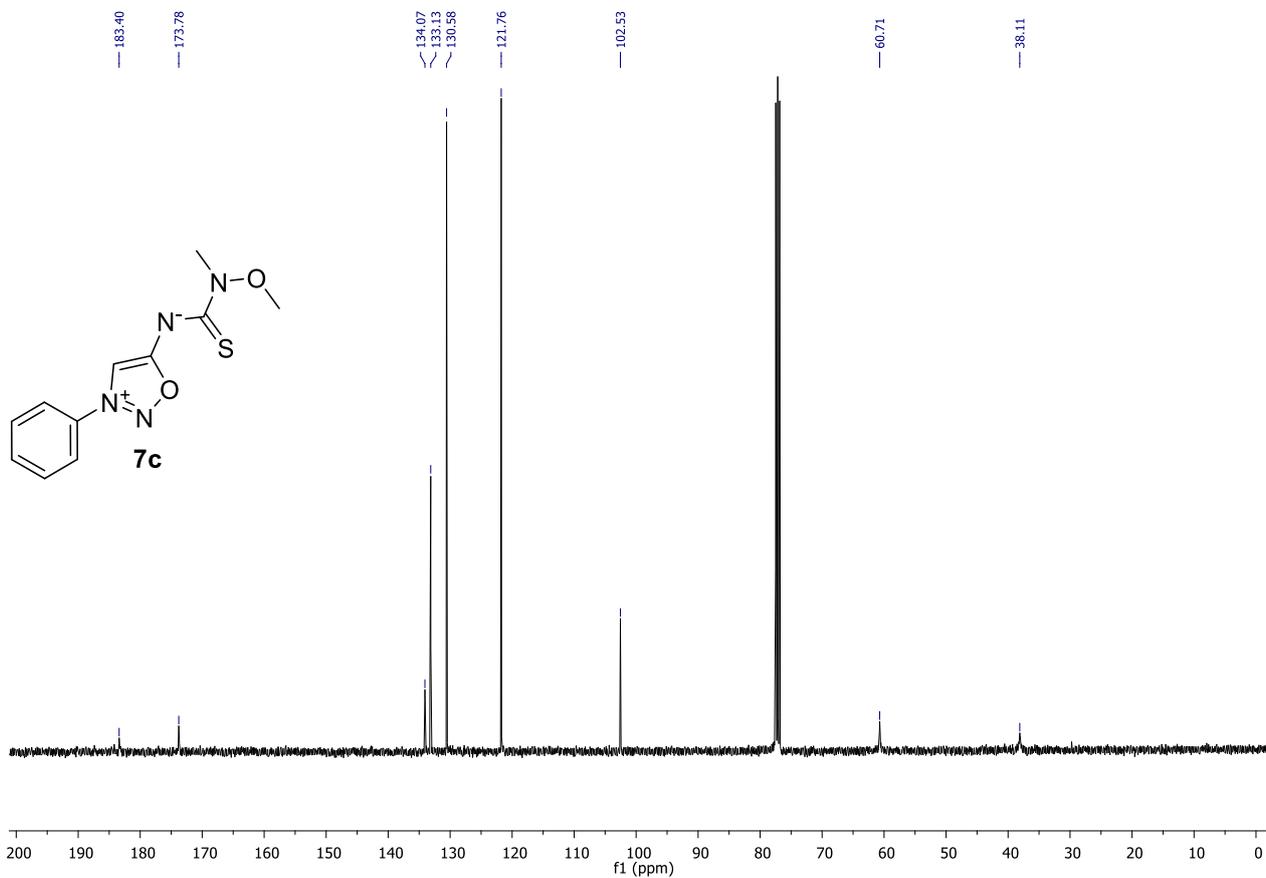


$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ )

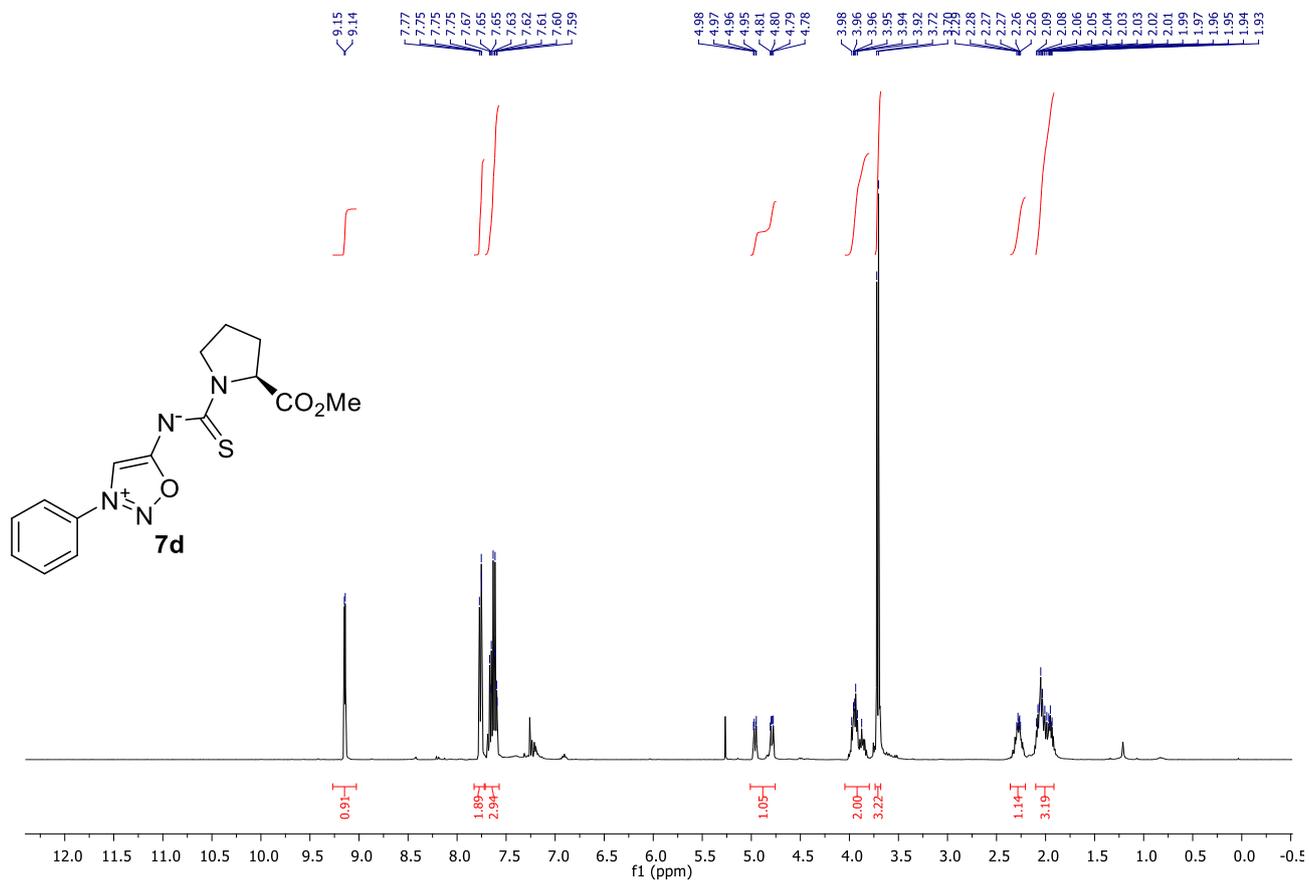




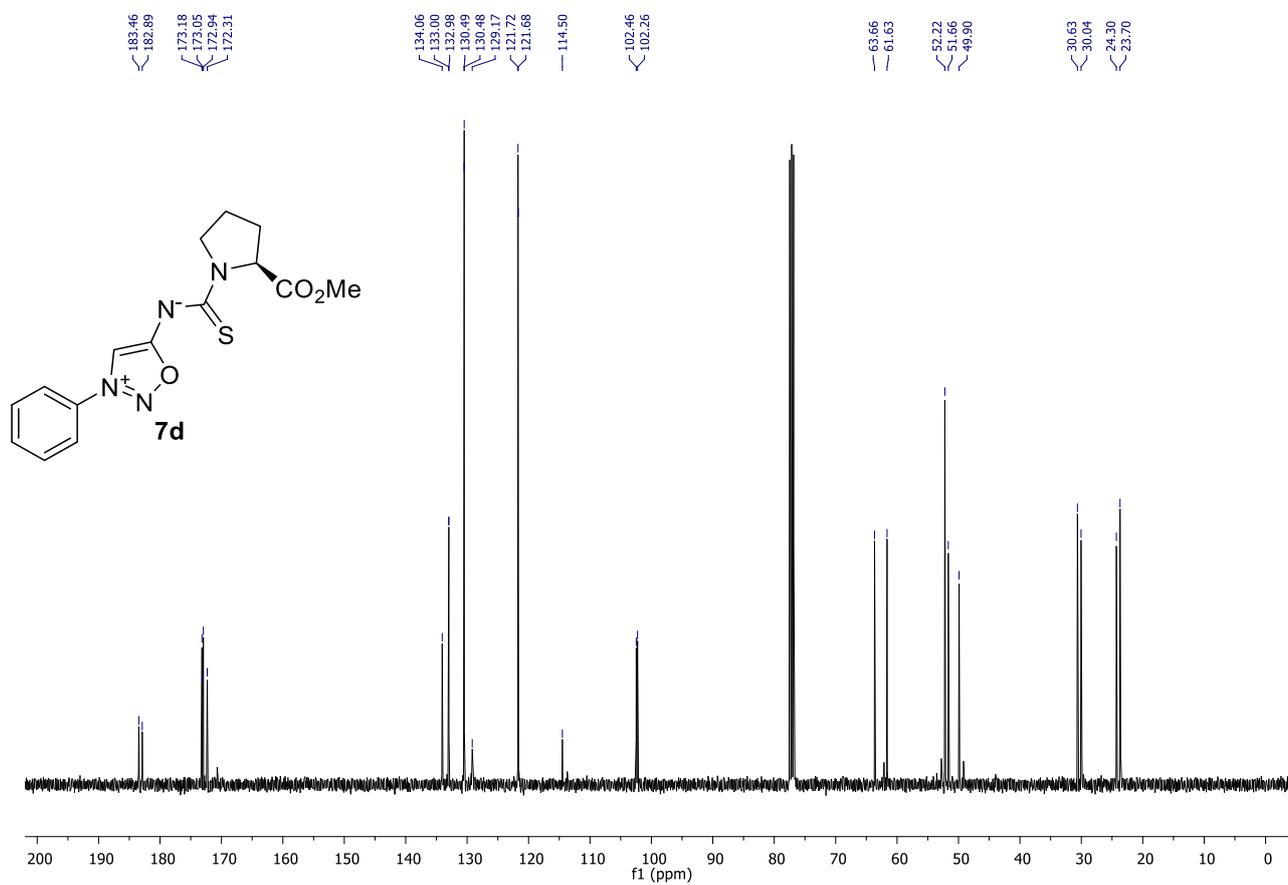
$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ )



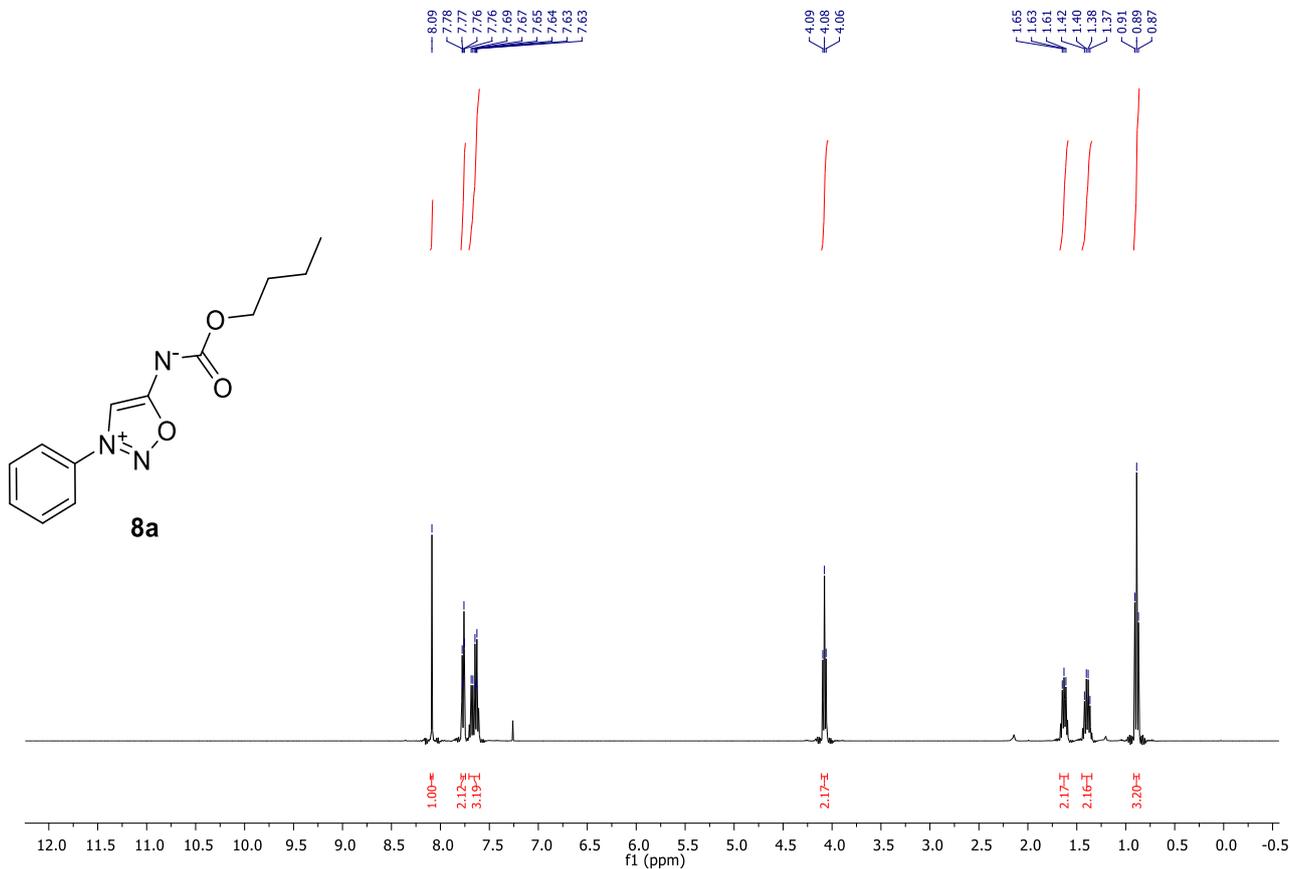
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ )



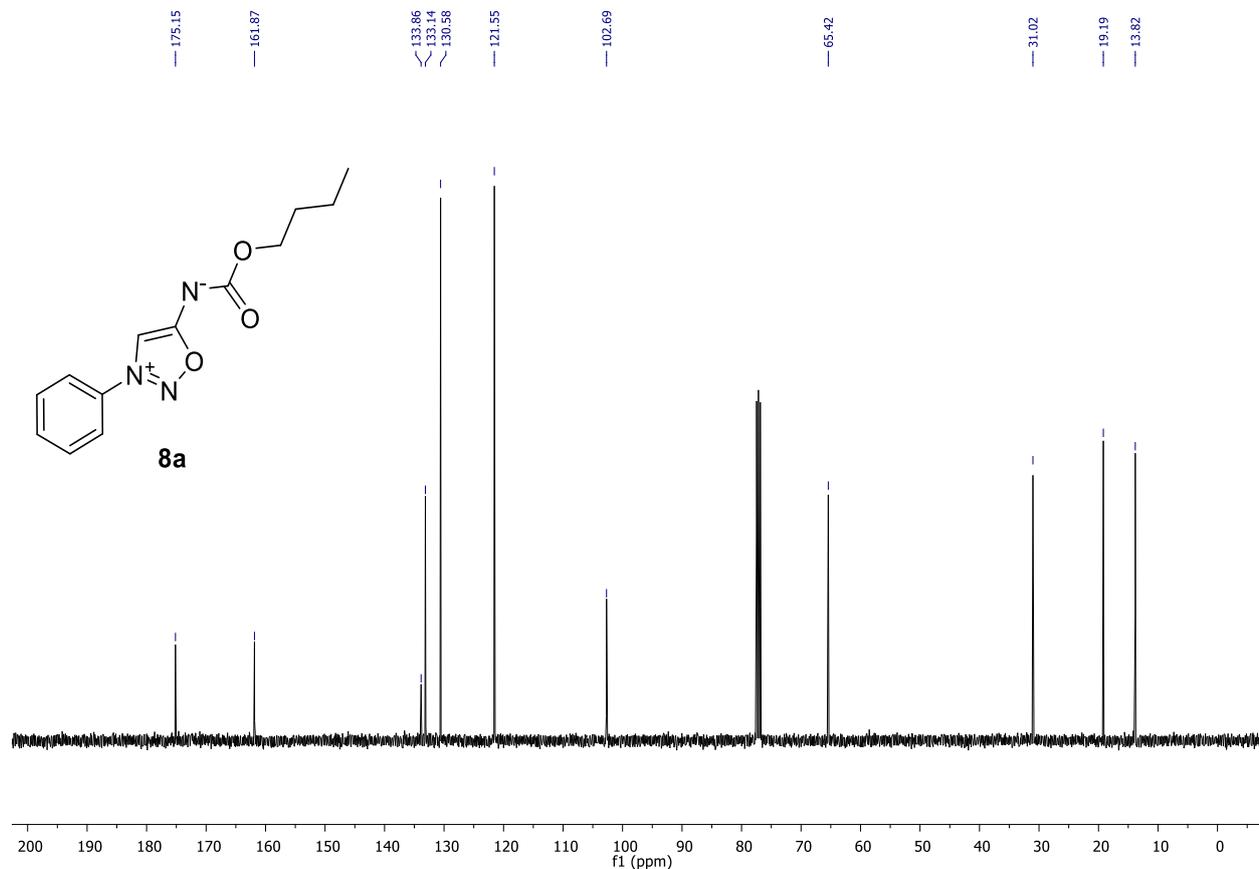
**<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)**



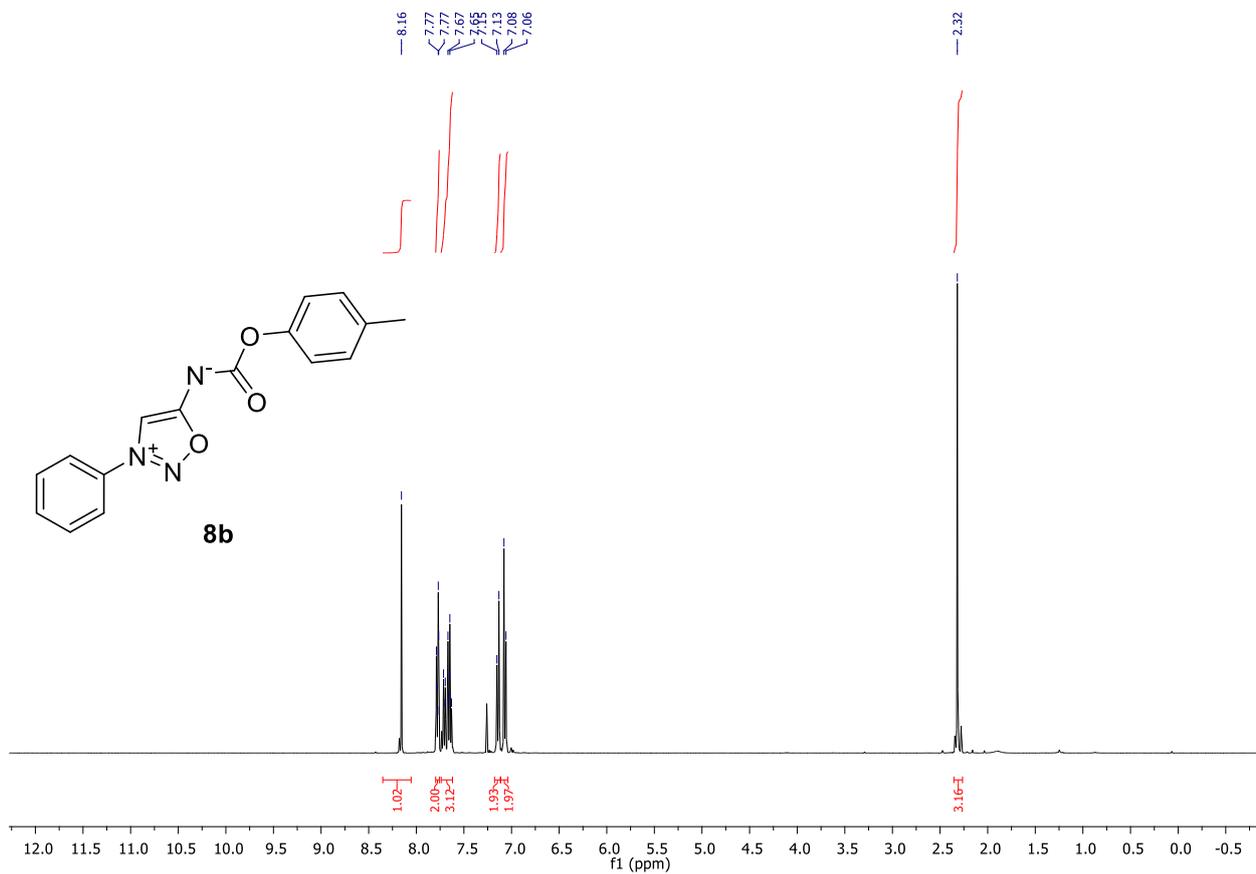
**<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)**



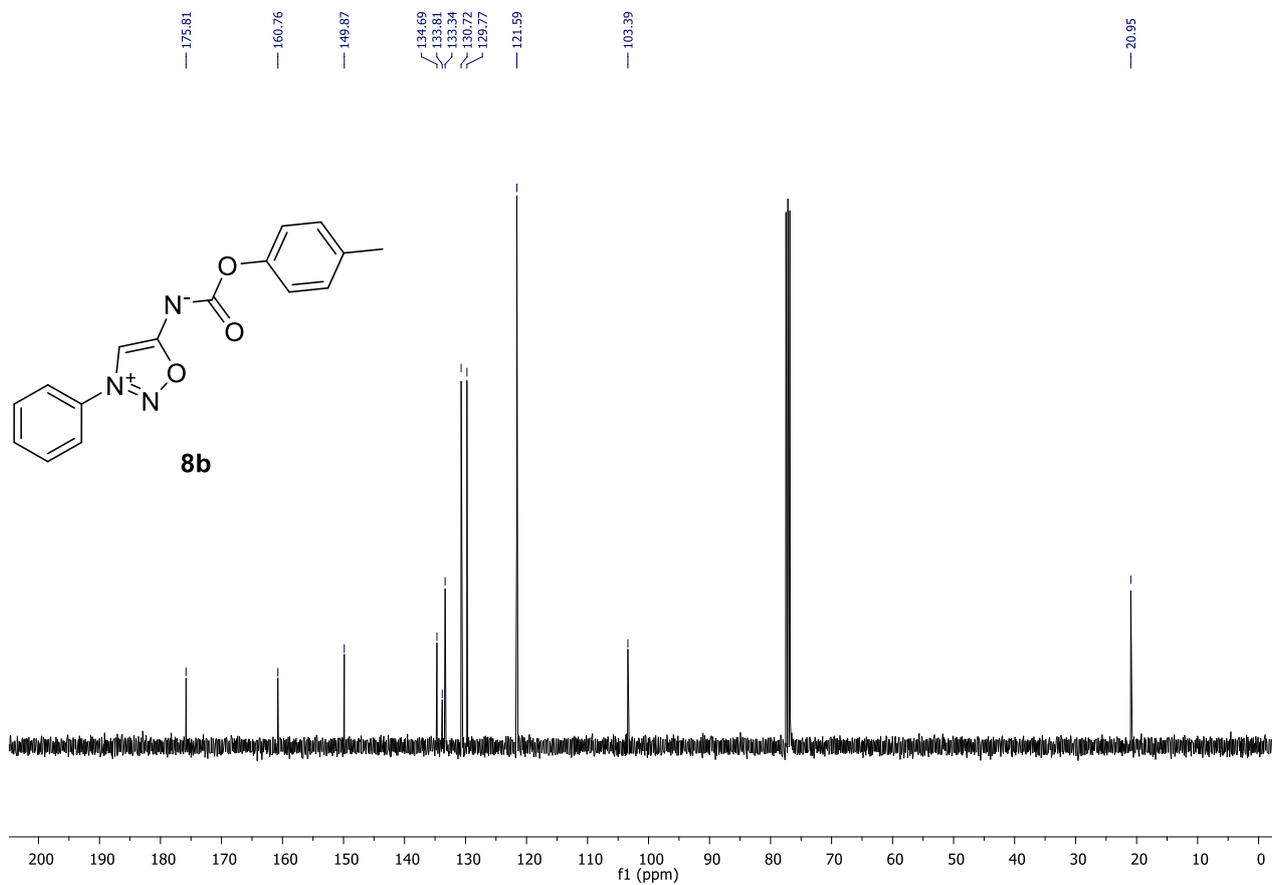
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



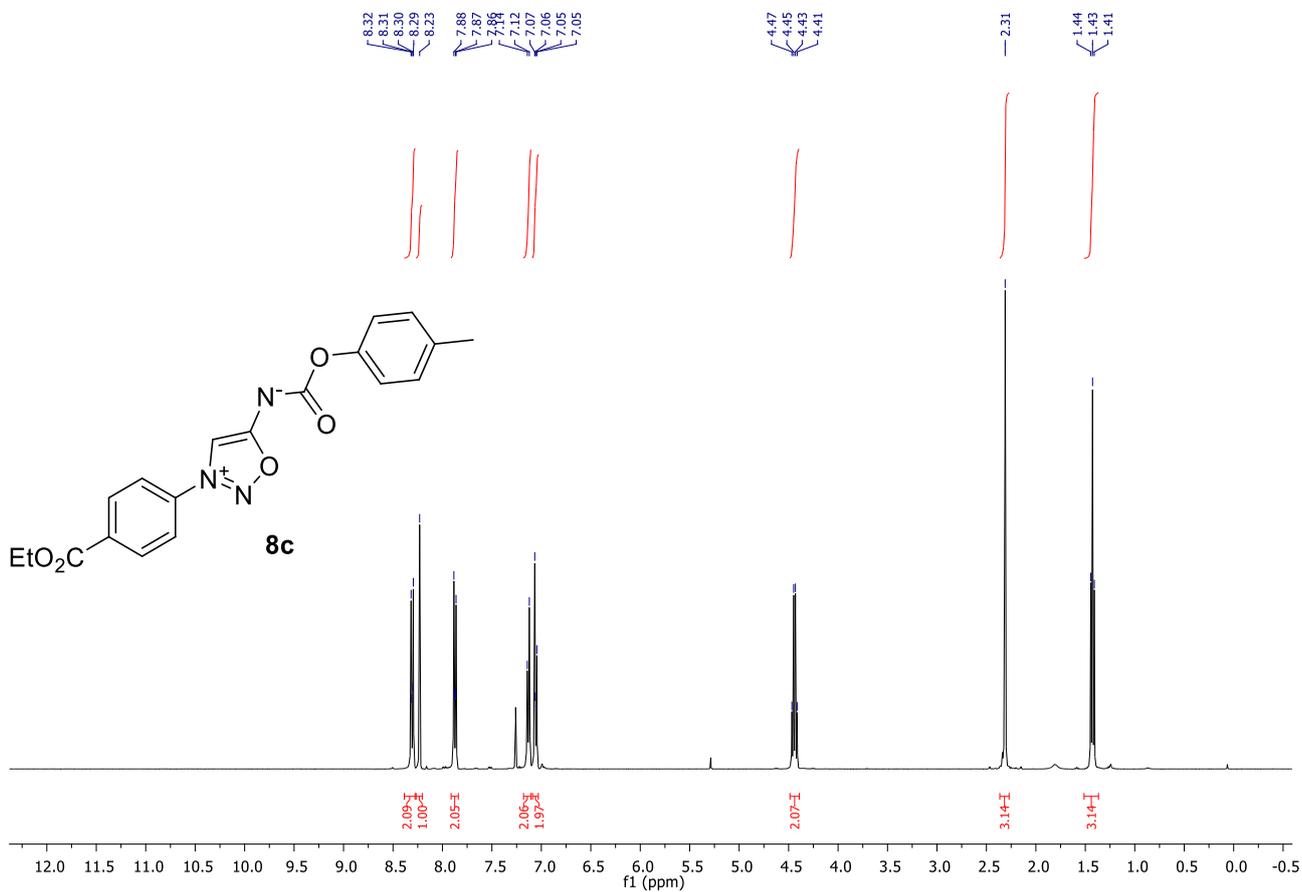
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



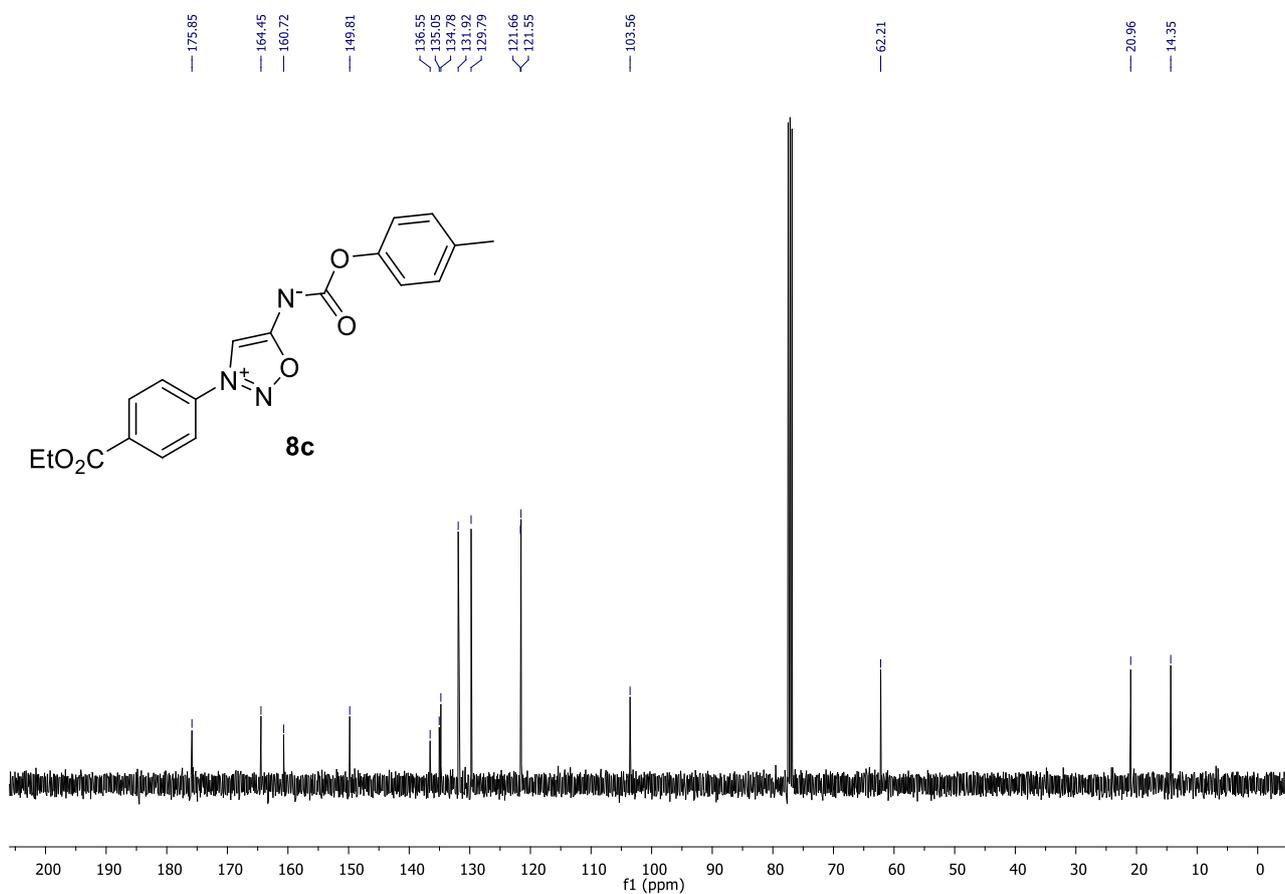
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



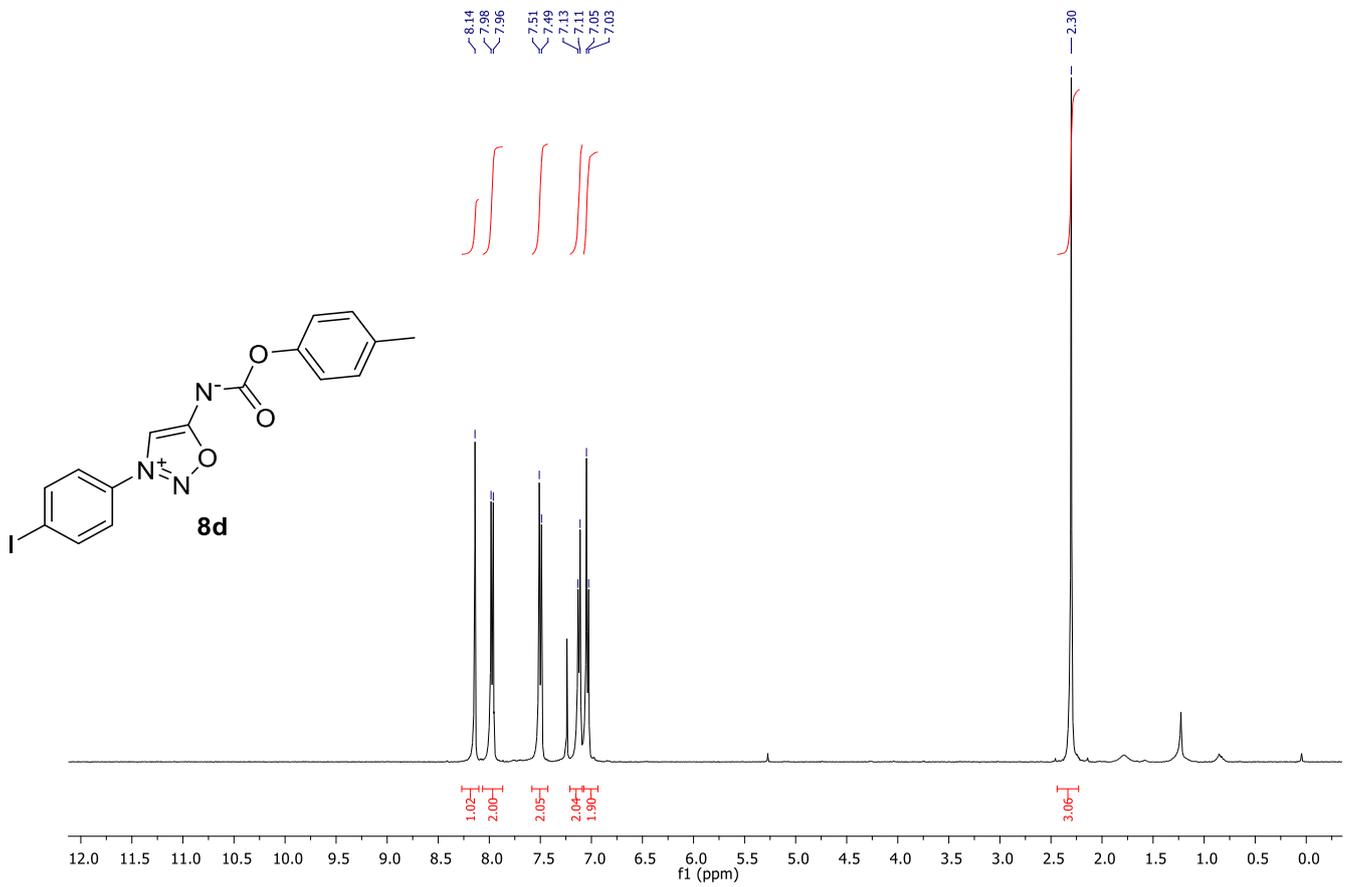
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



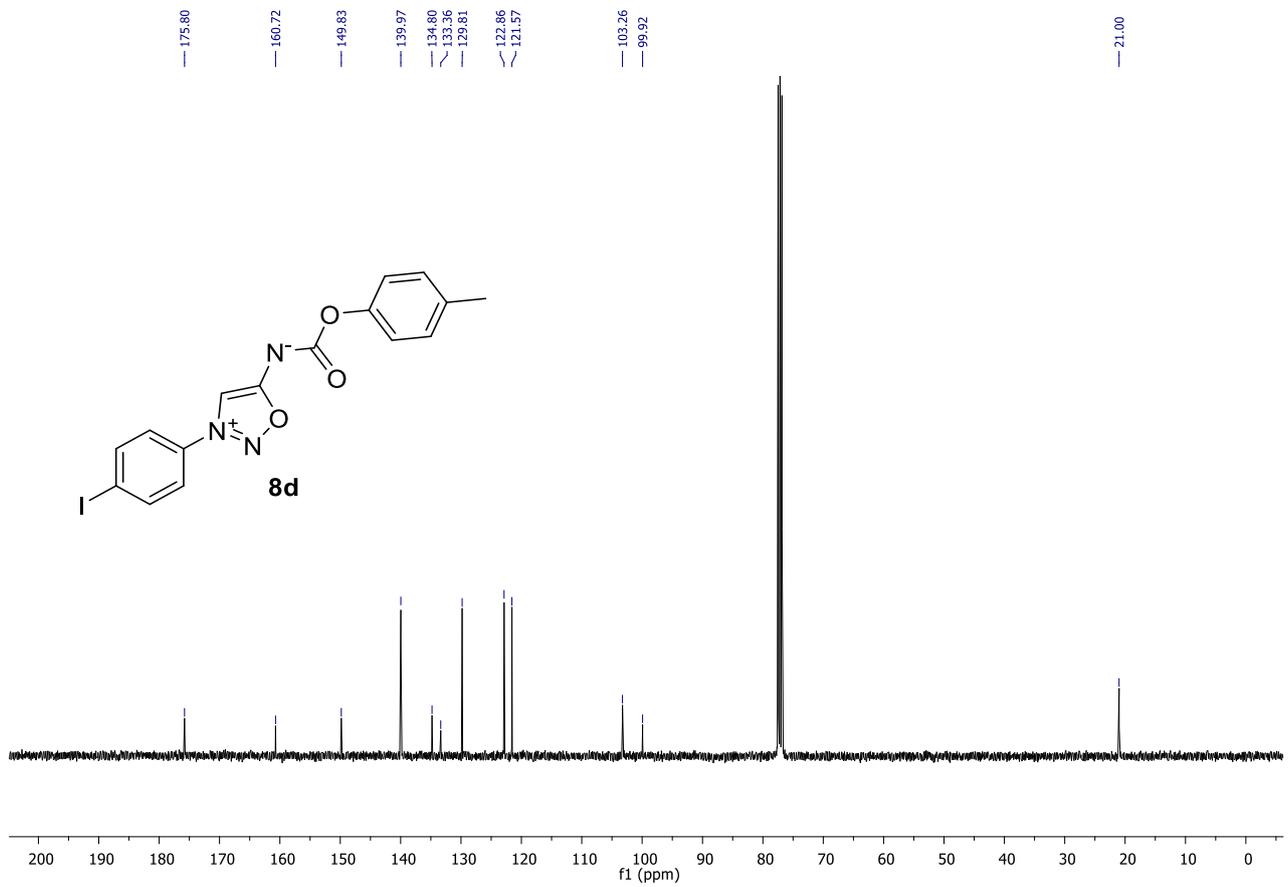
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



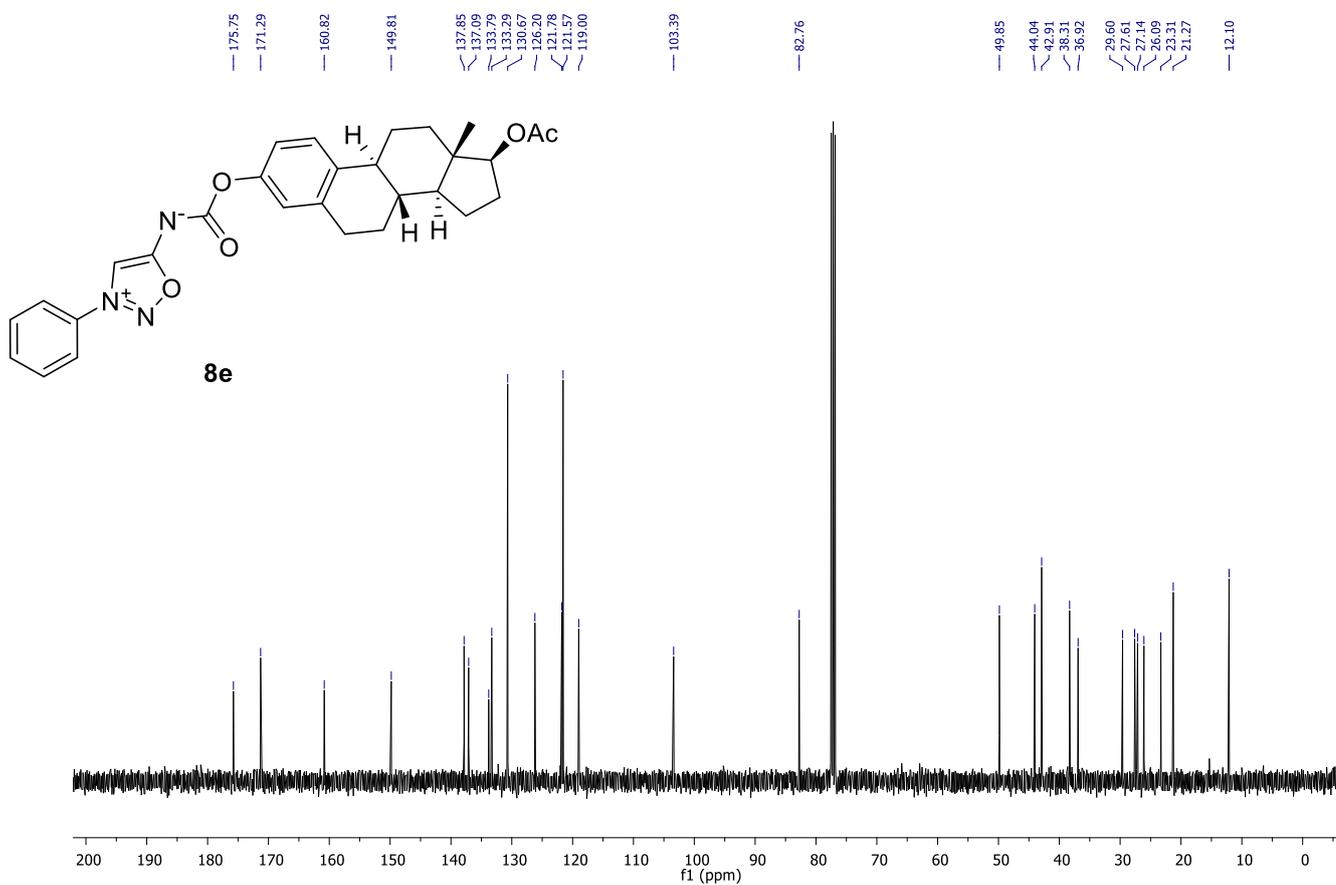
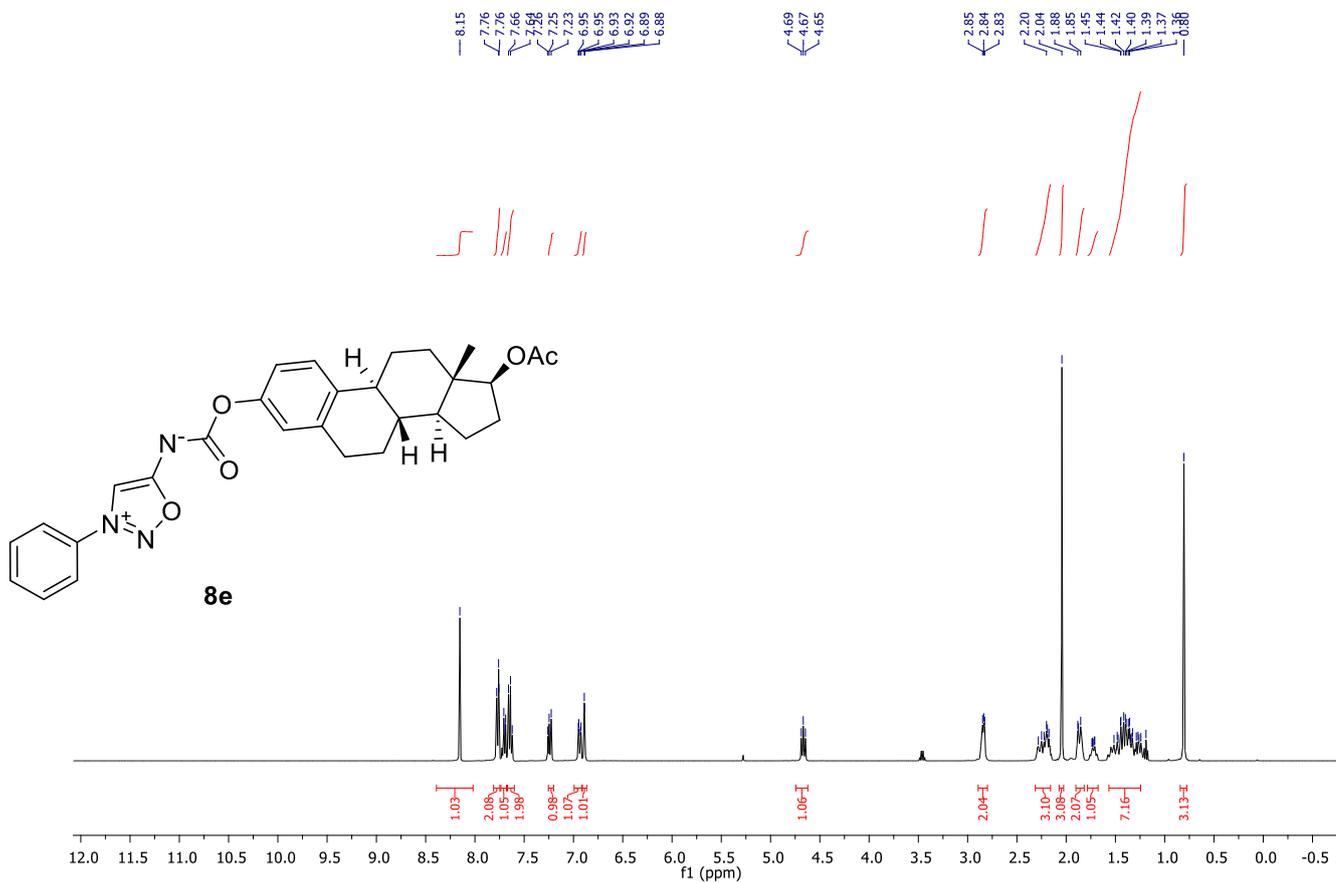
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)

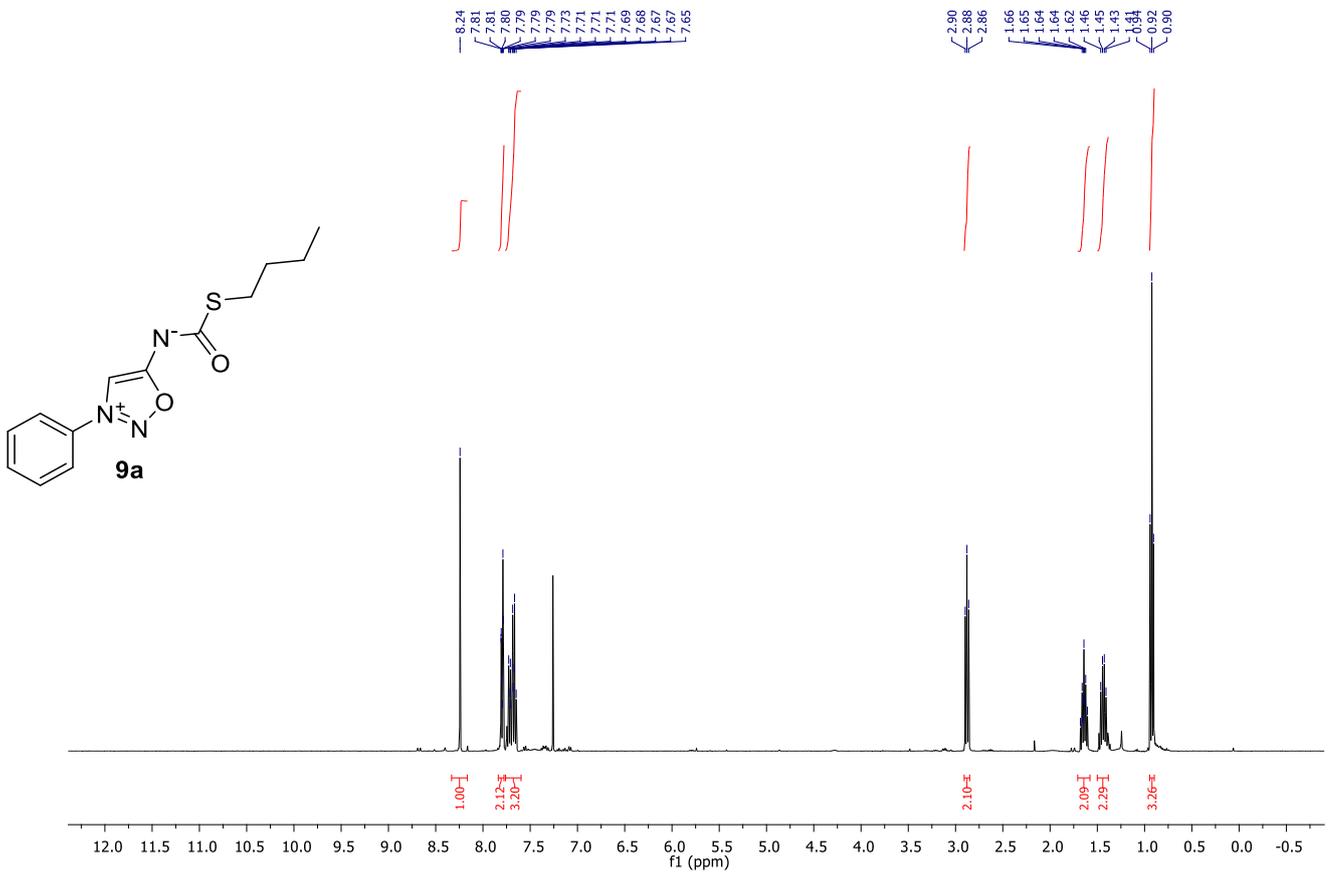


<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)

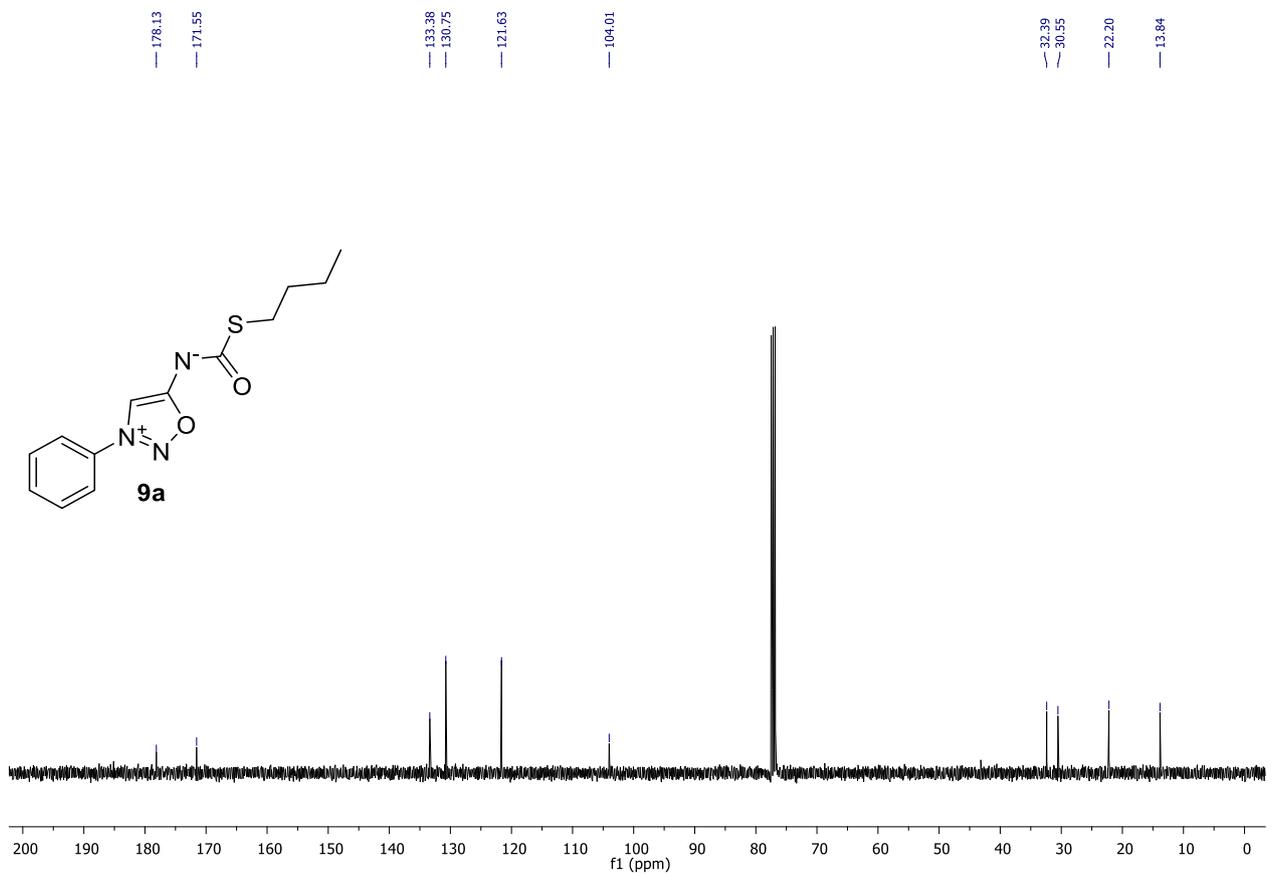


<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)

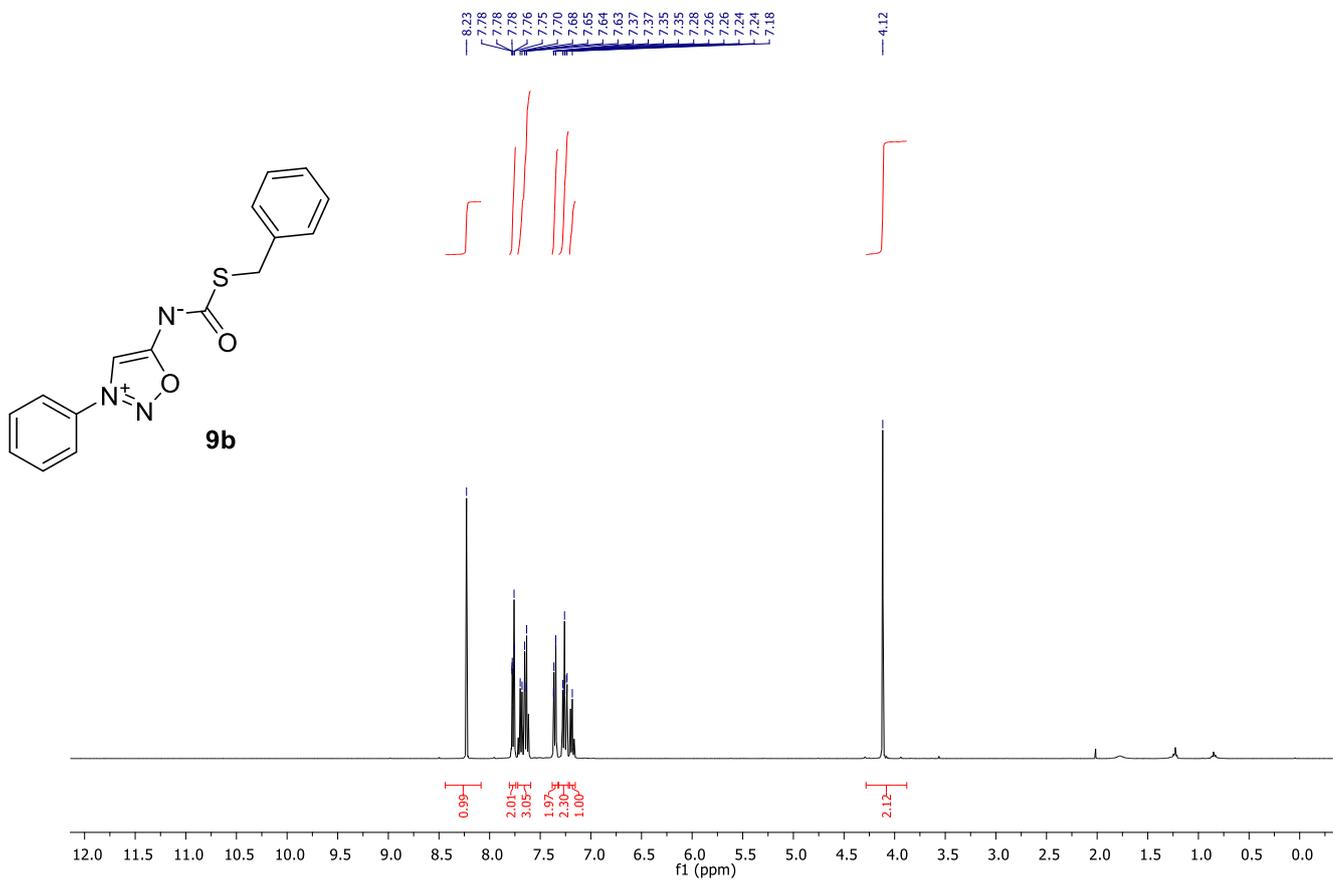




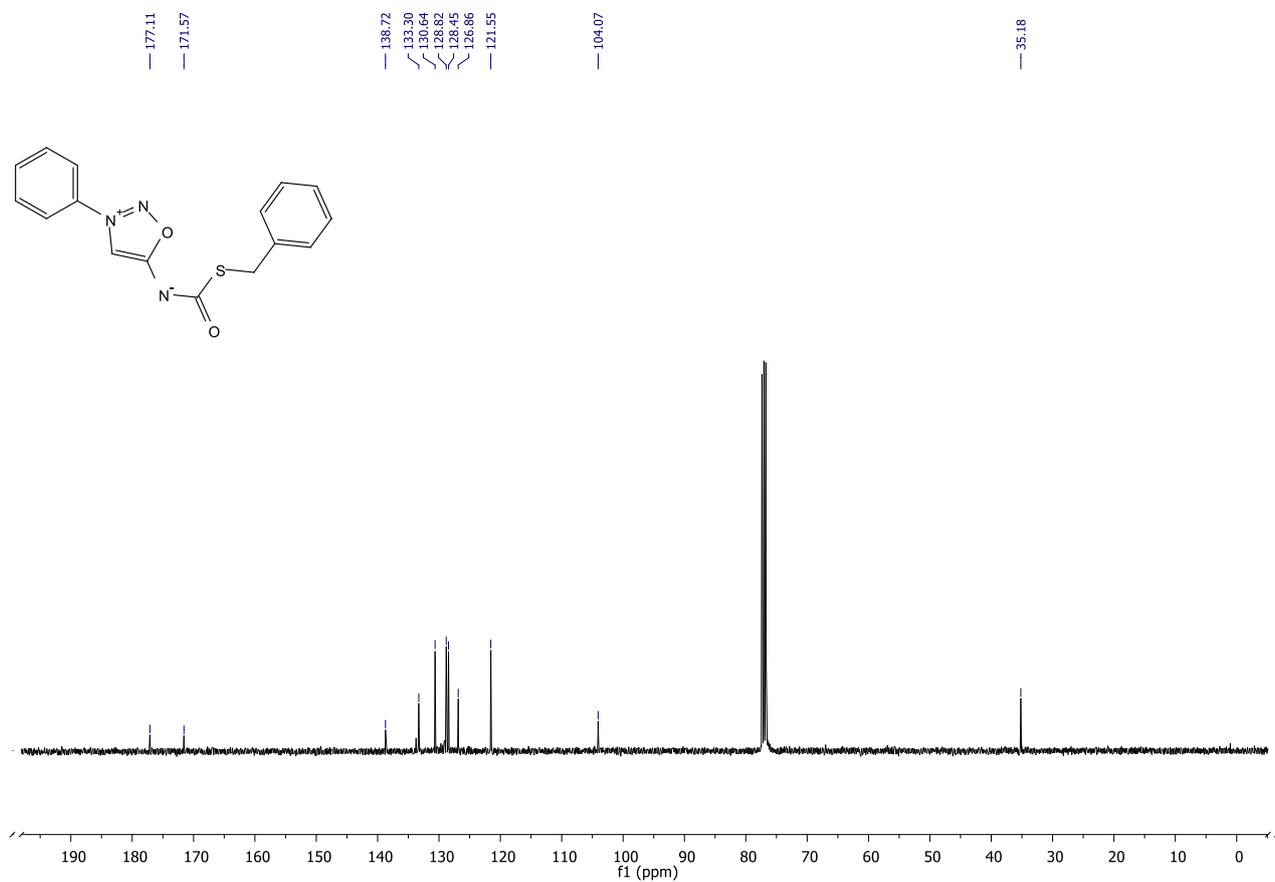
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



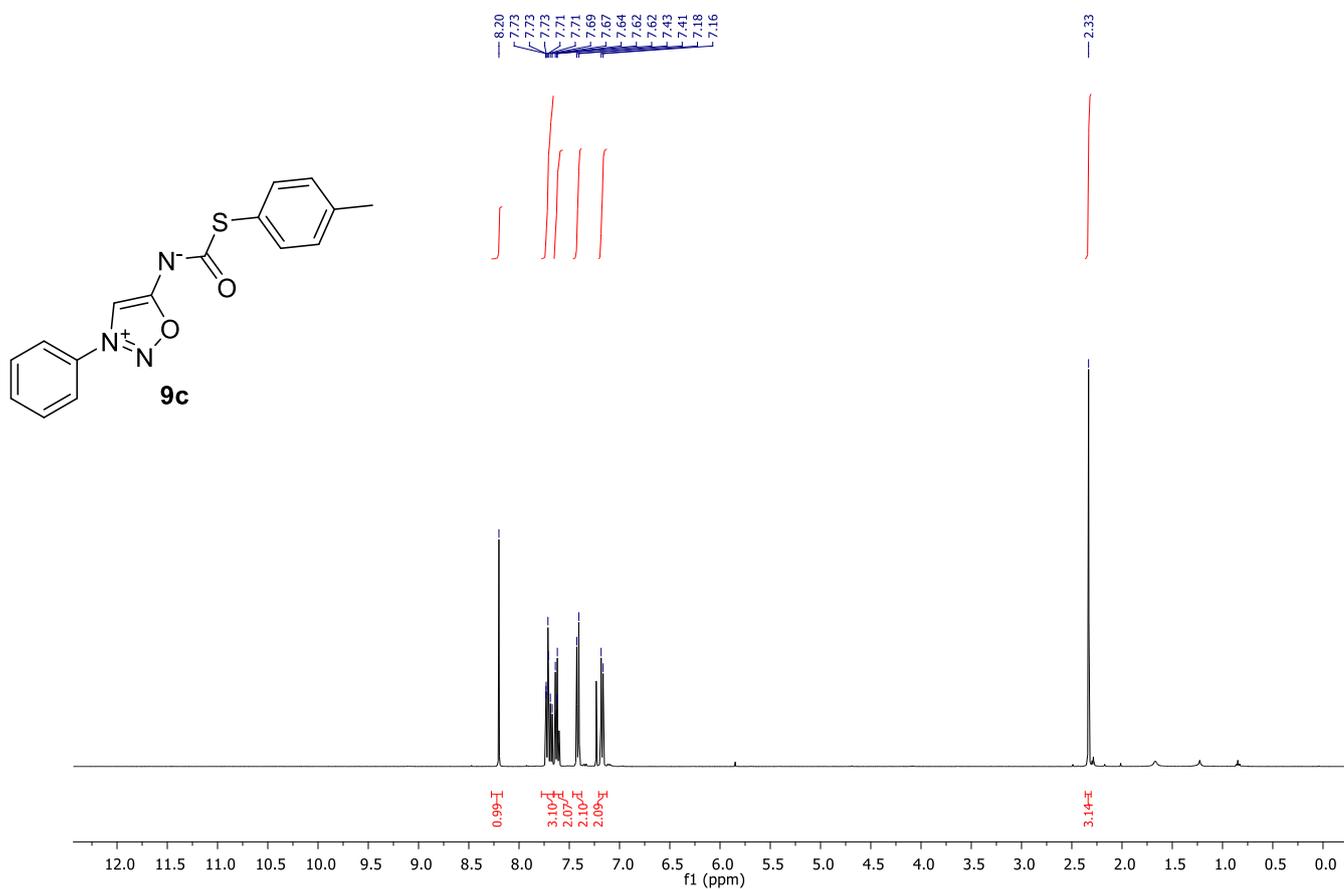
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



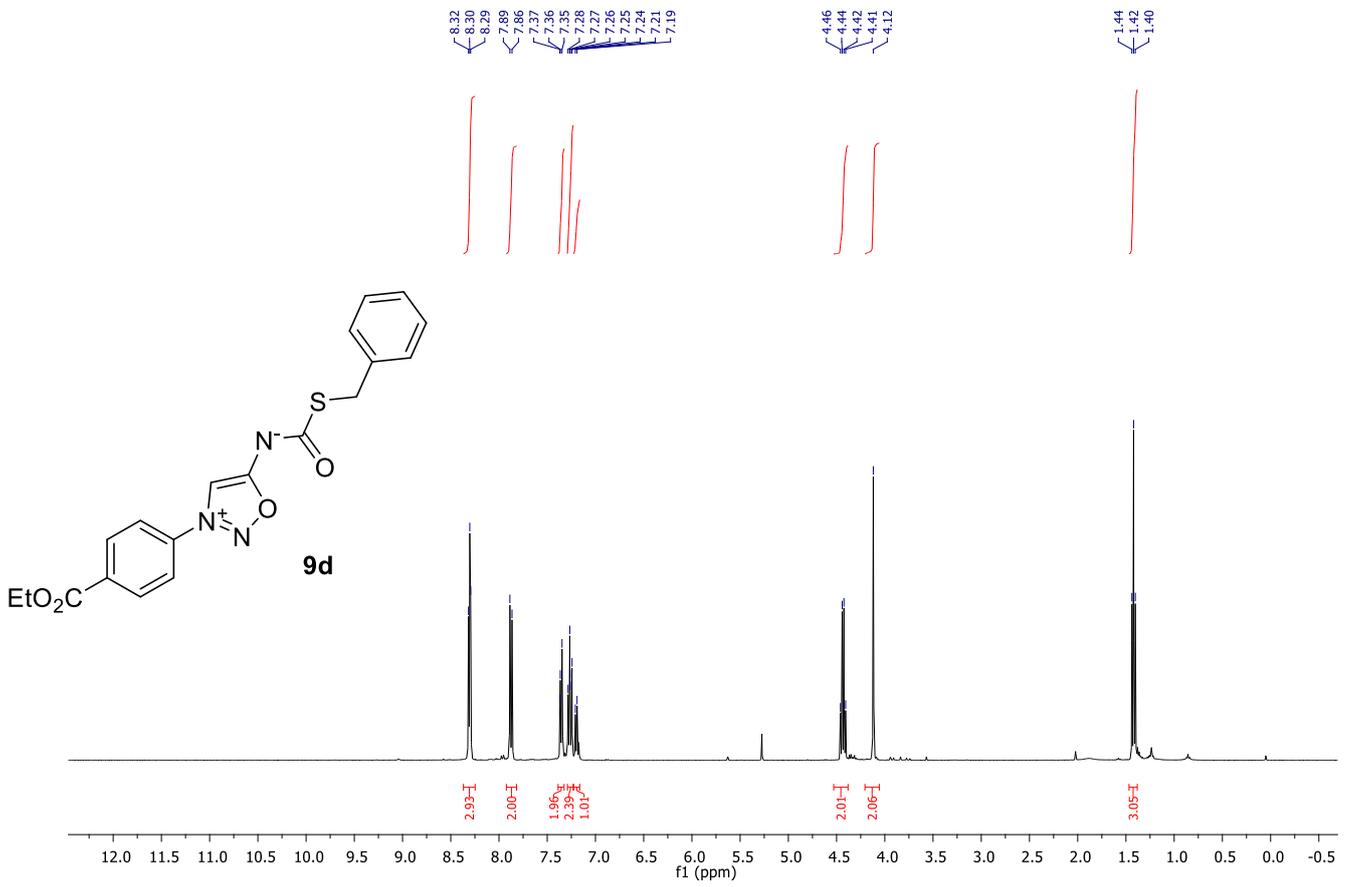
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)



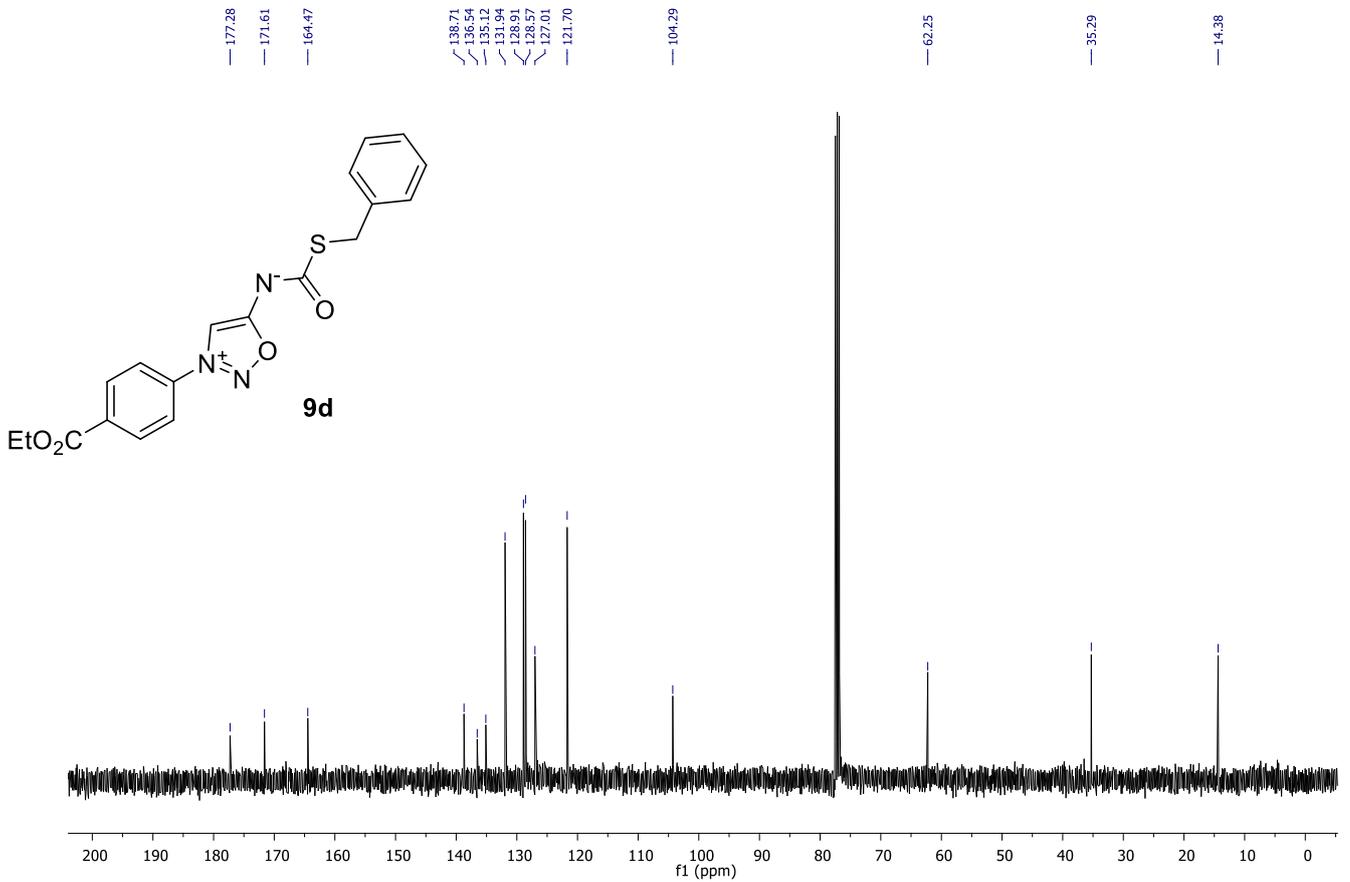
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)



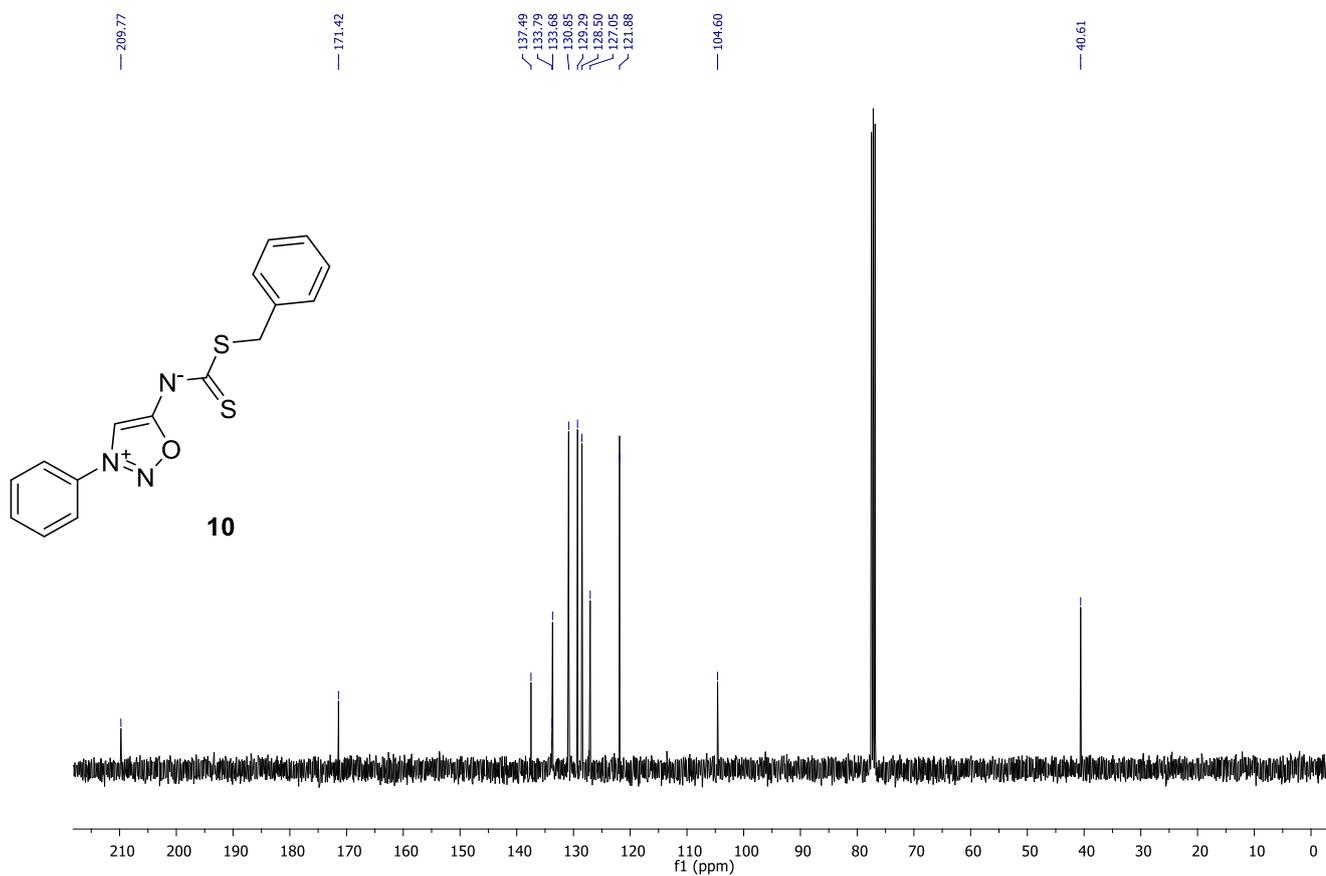
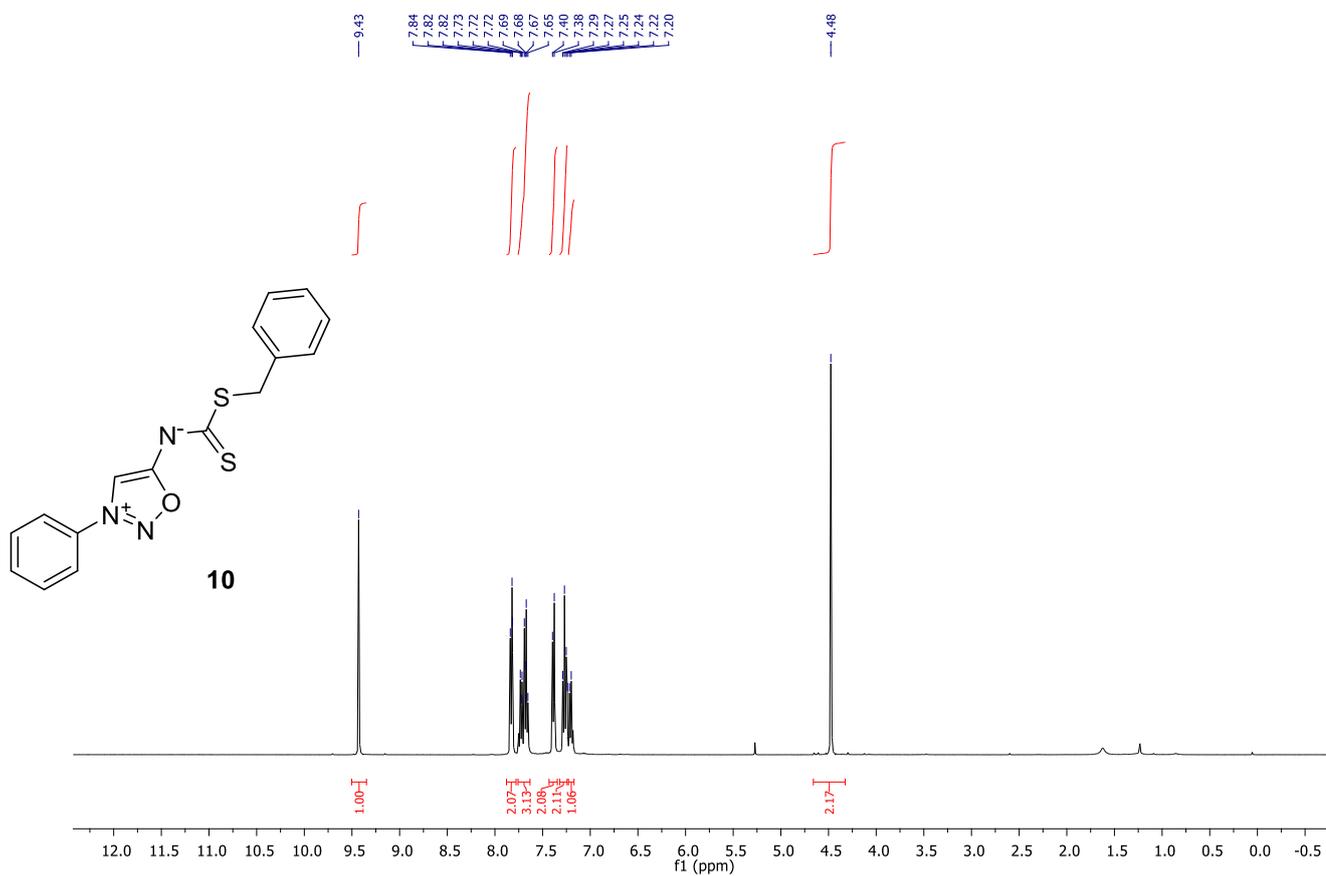
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>)

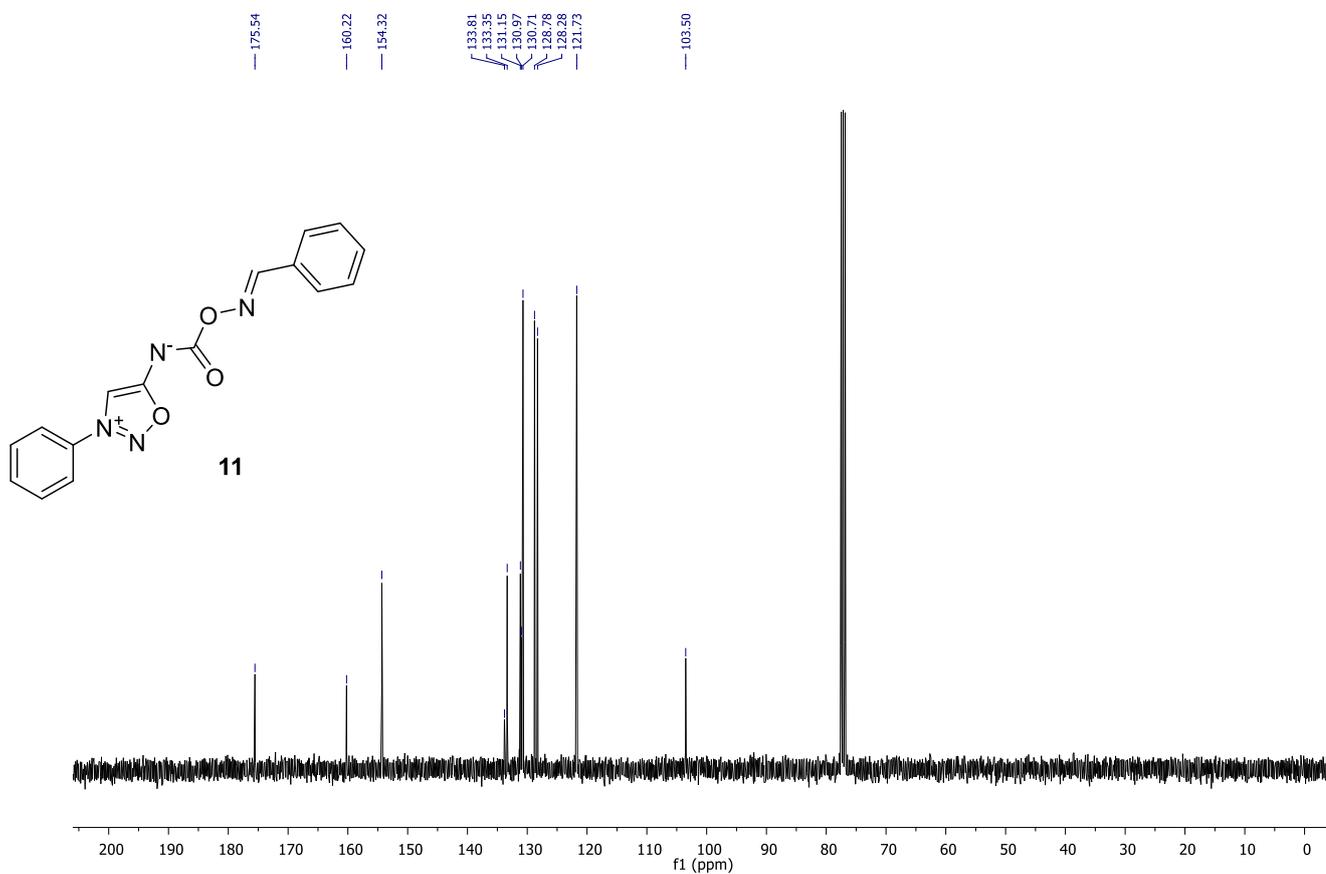
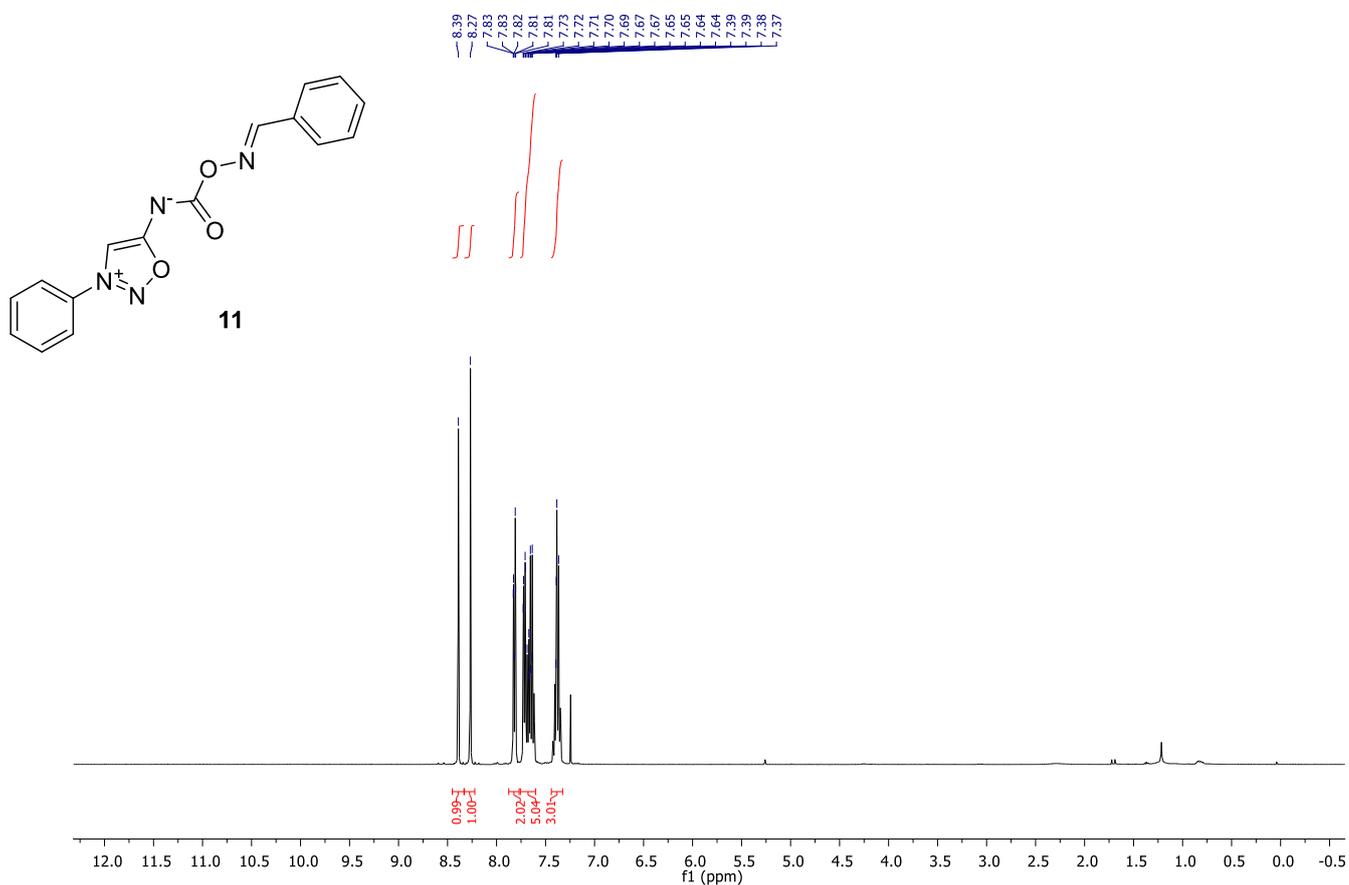


$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ )

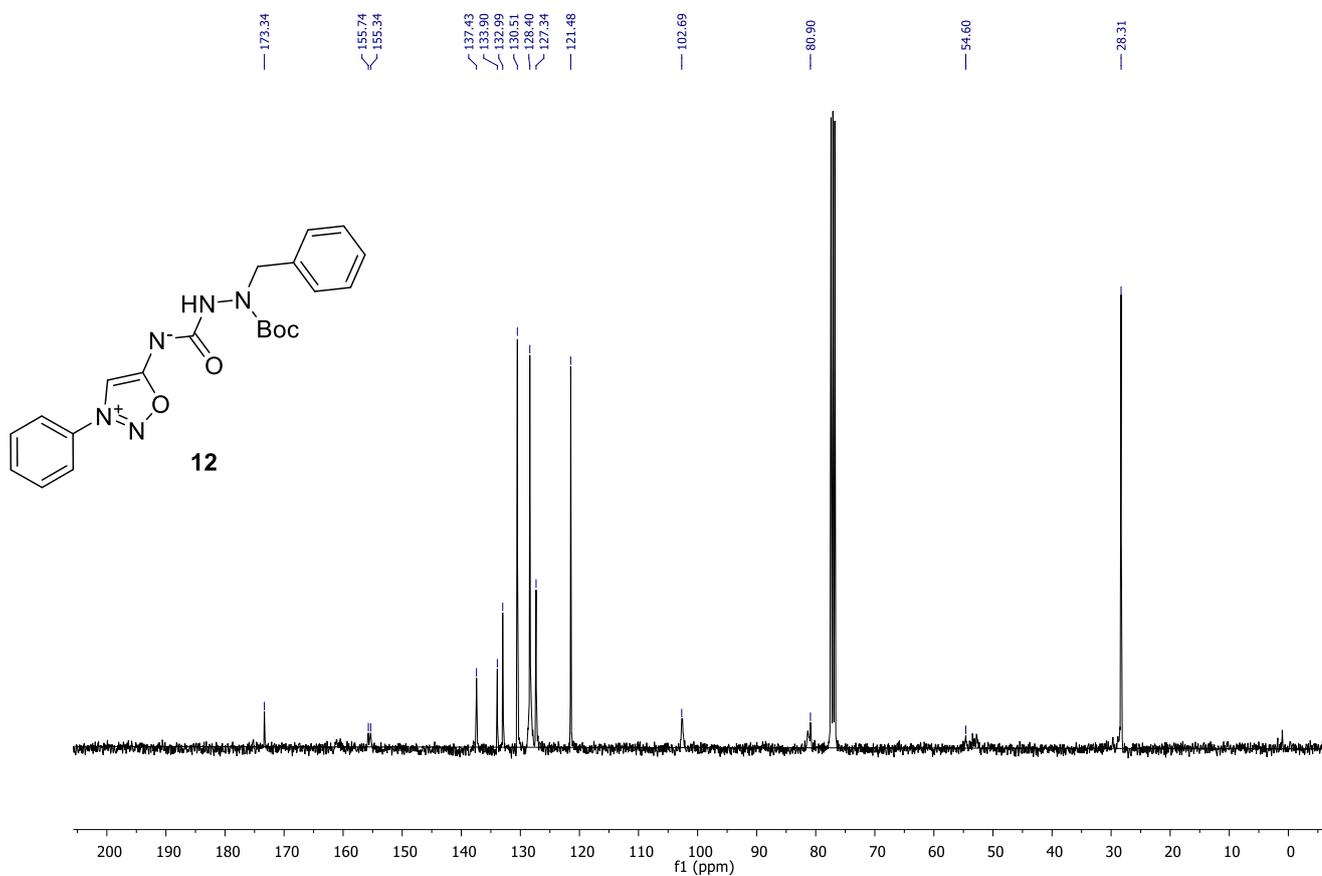
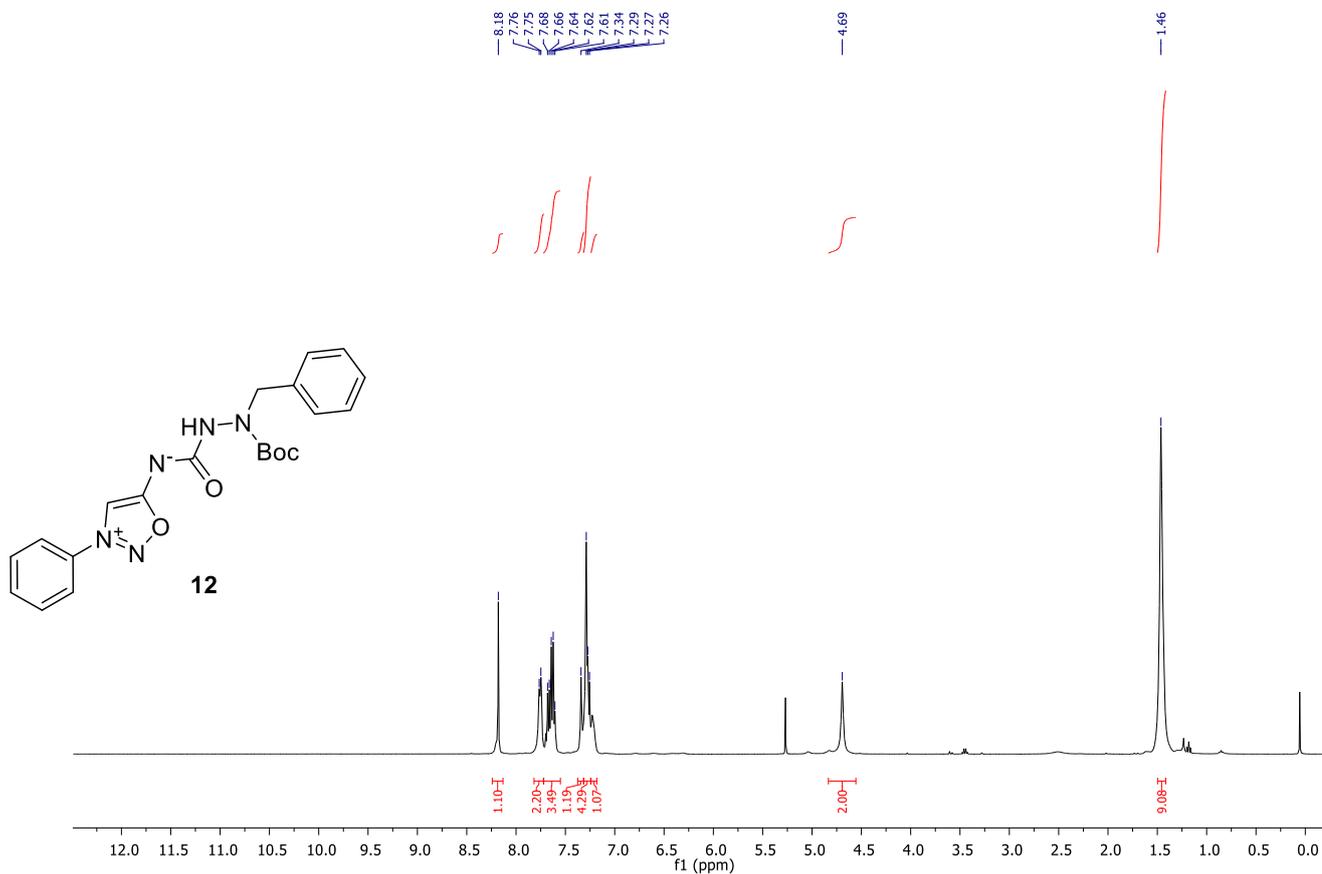


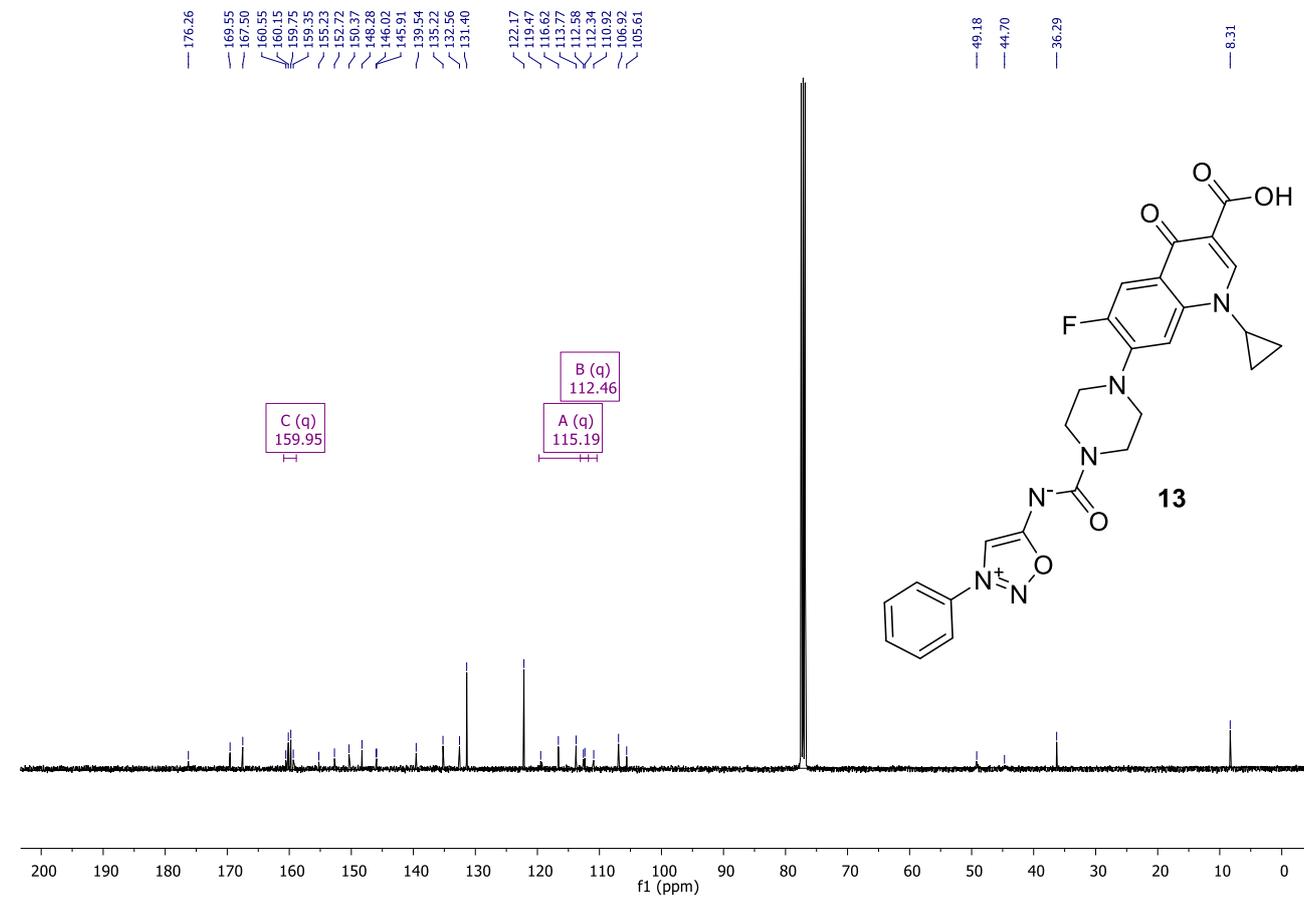
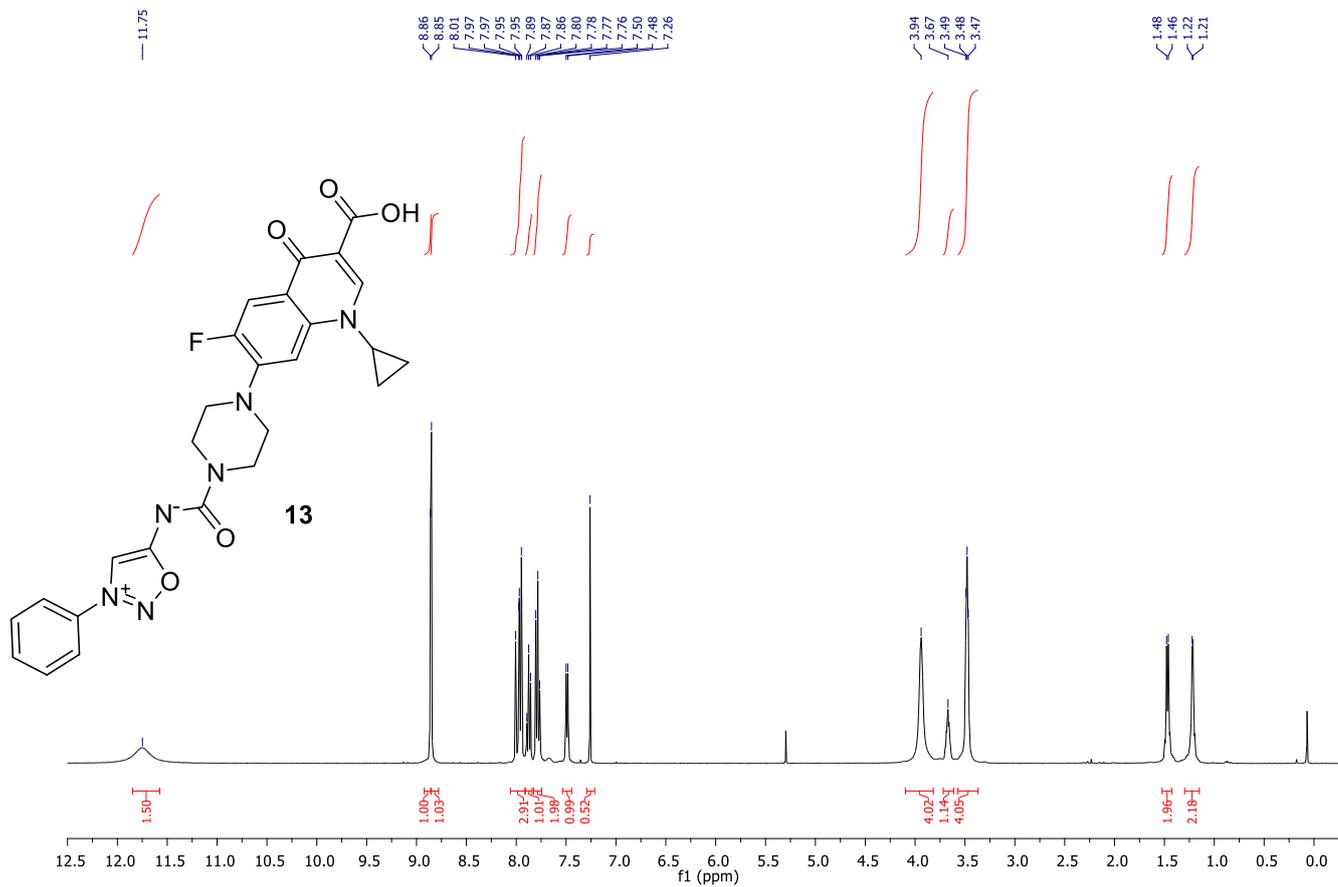
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ )

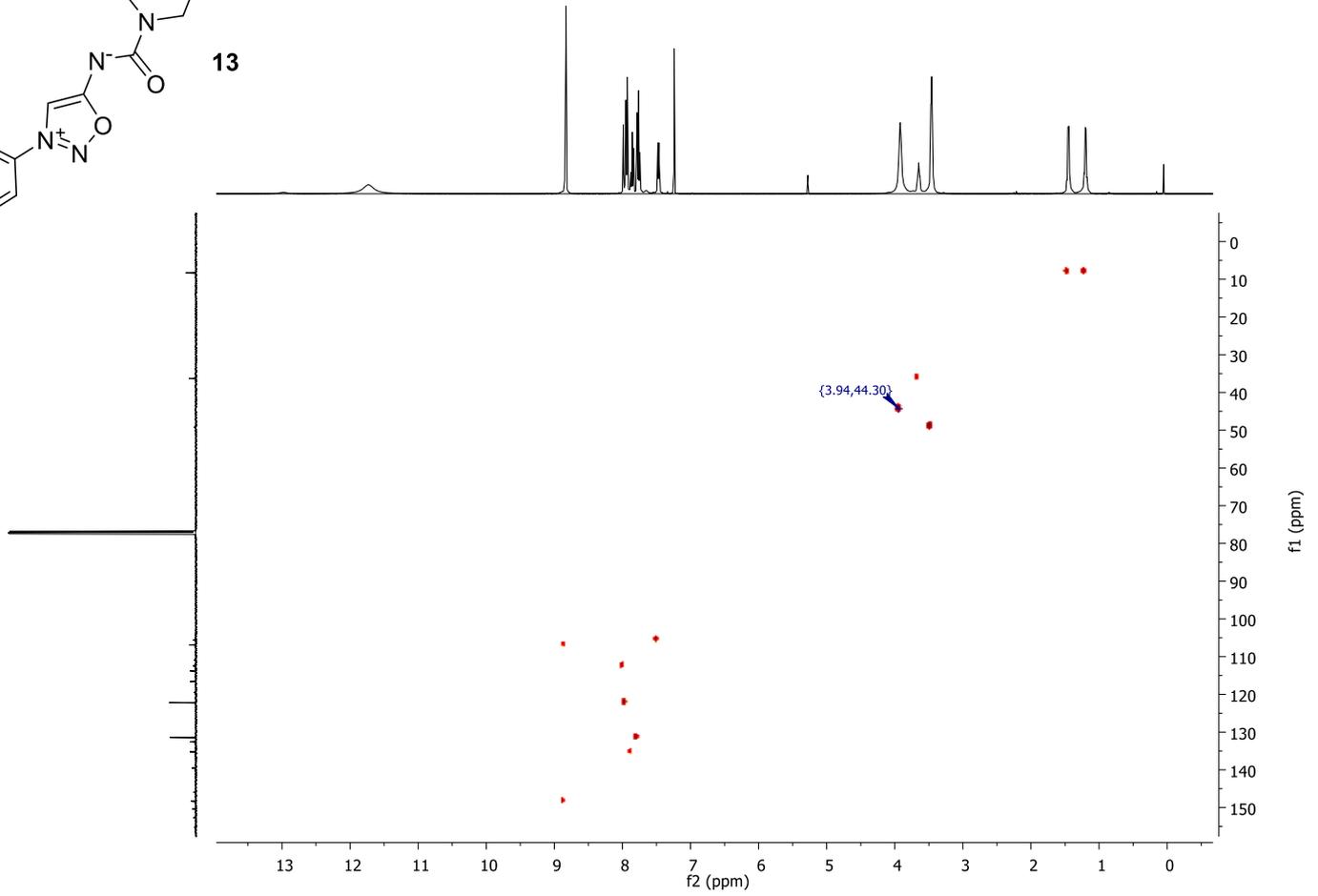
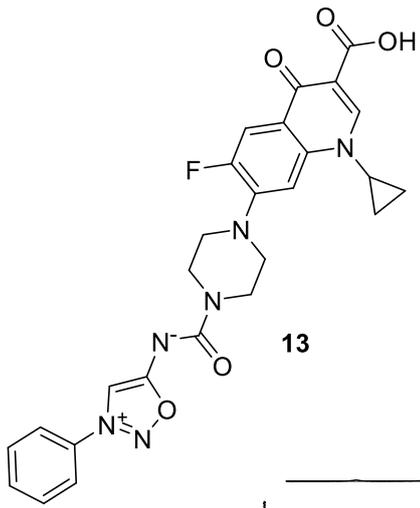


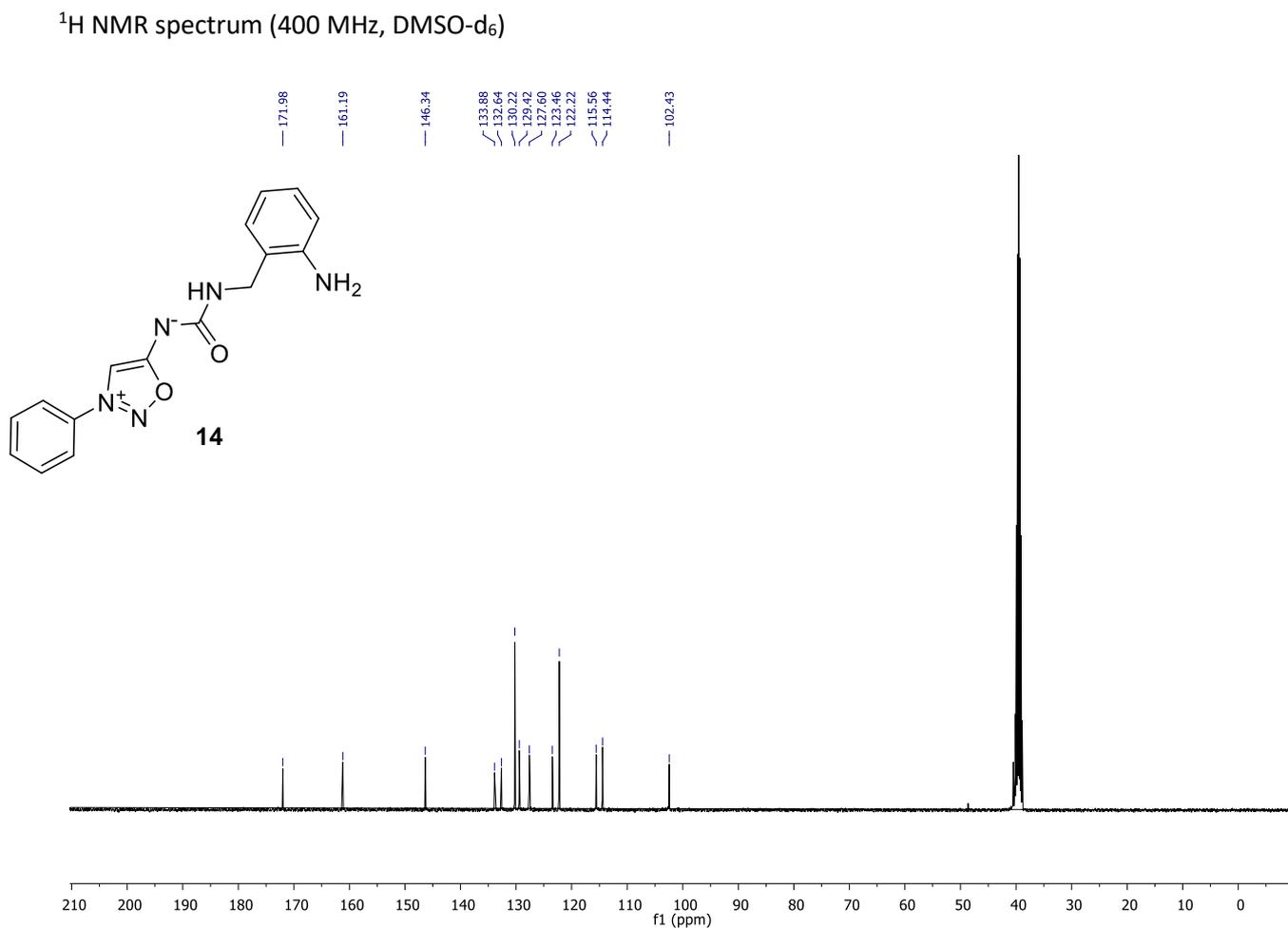
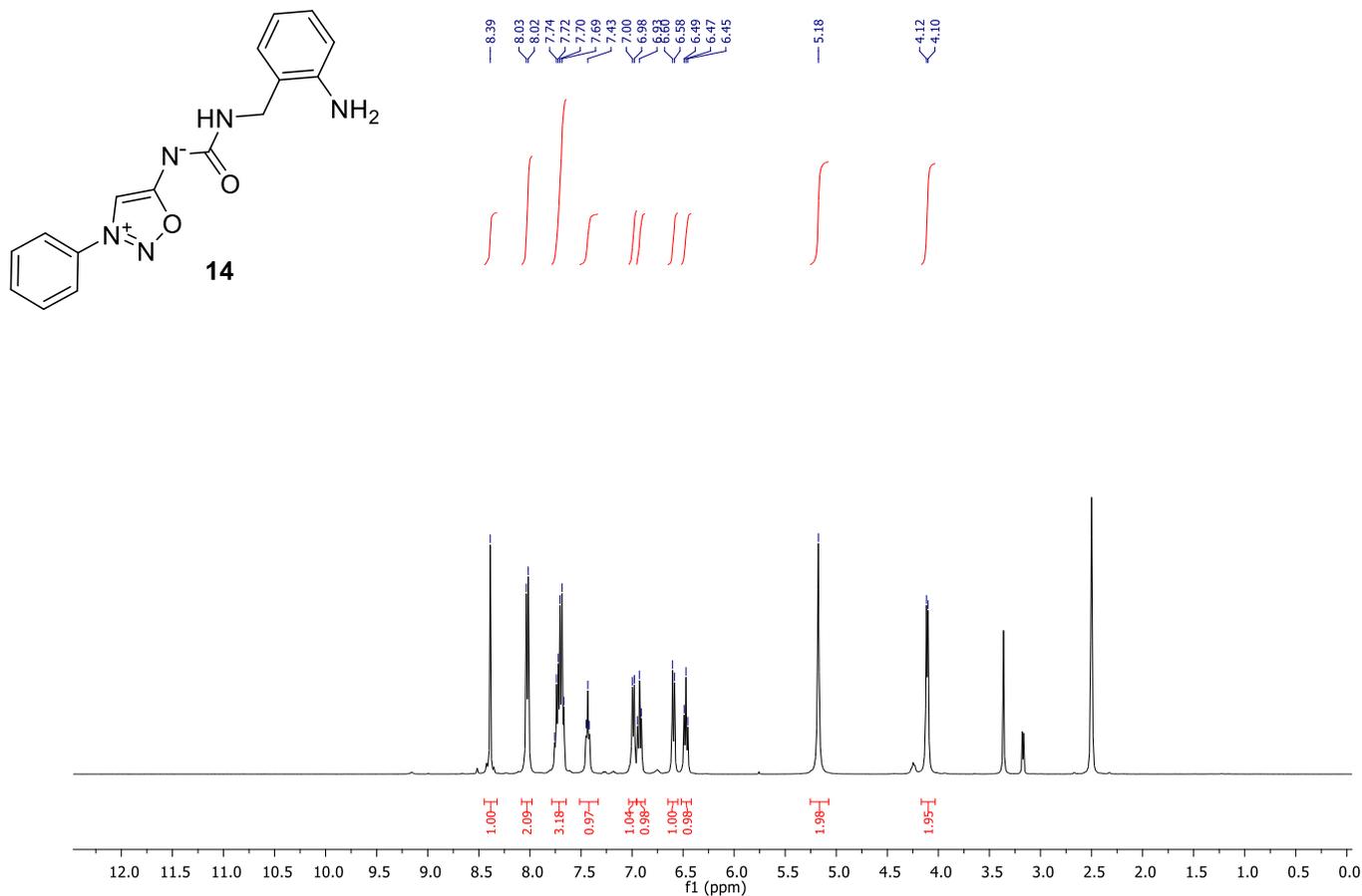


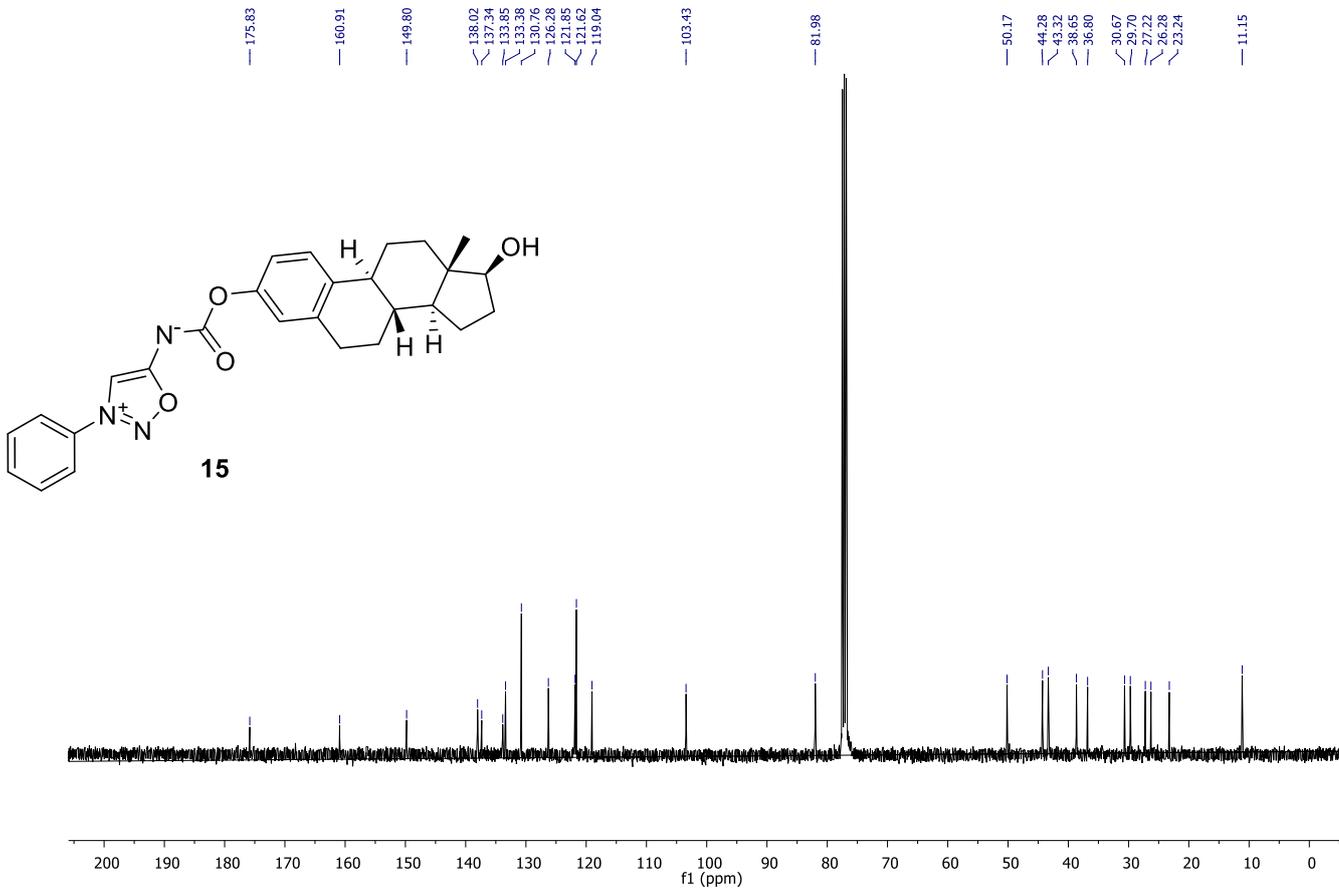
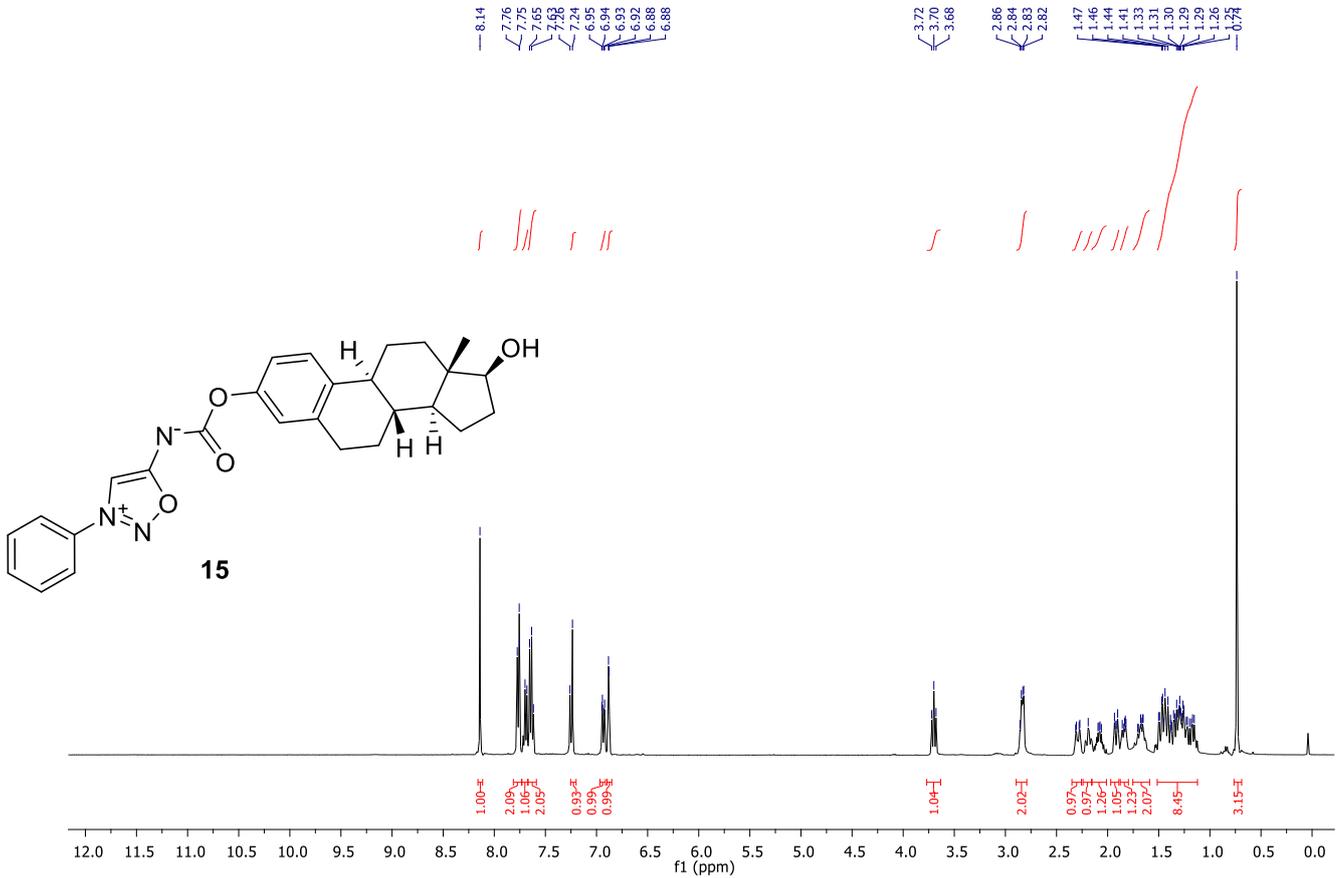
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>)

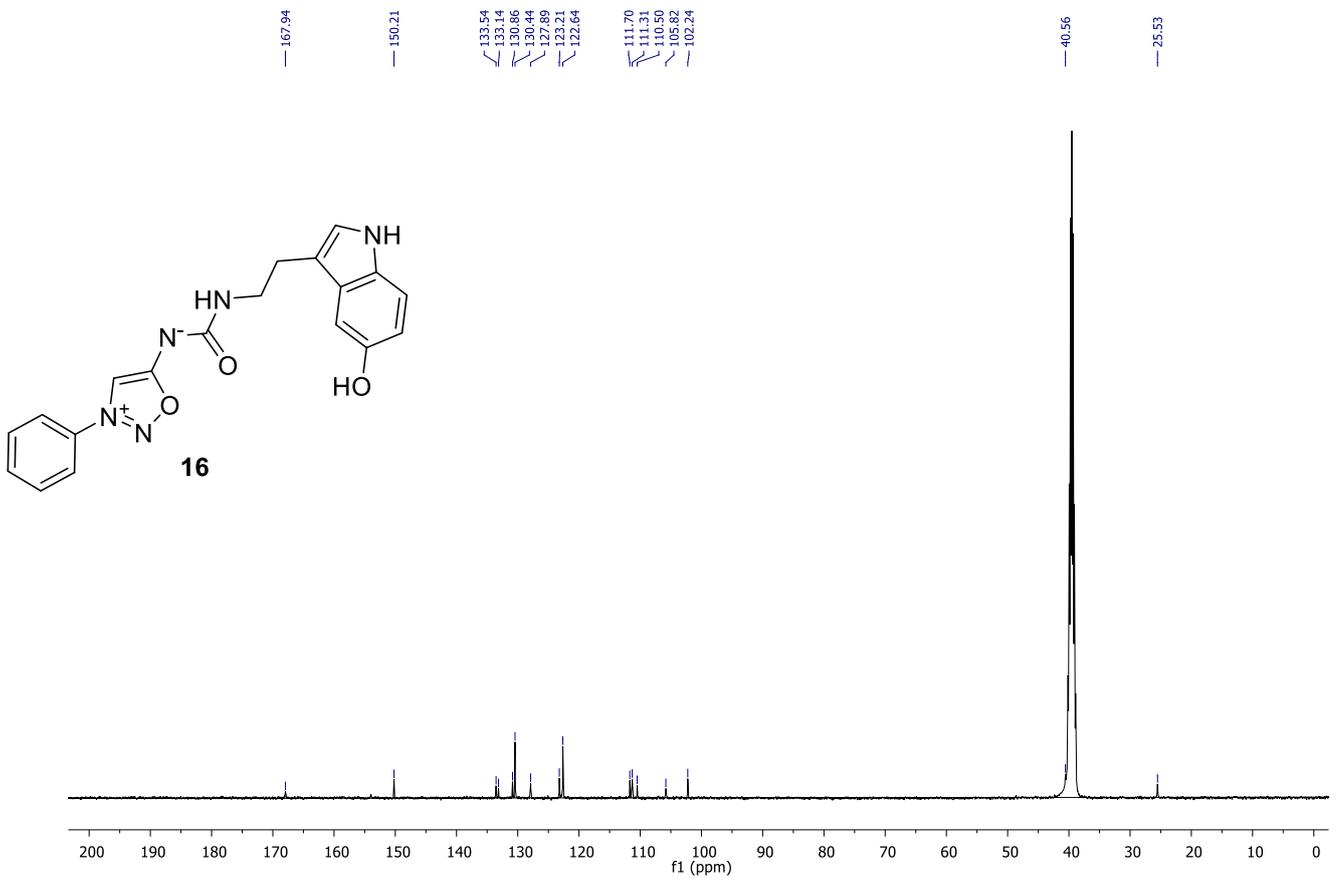
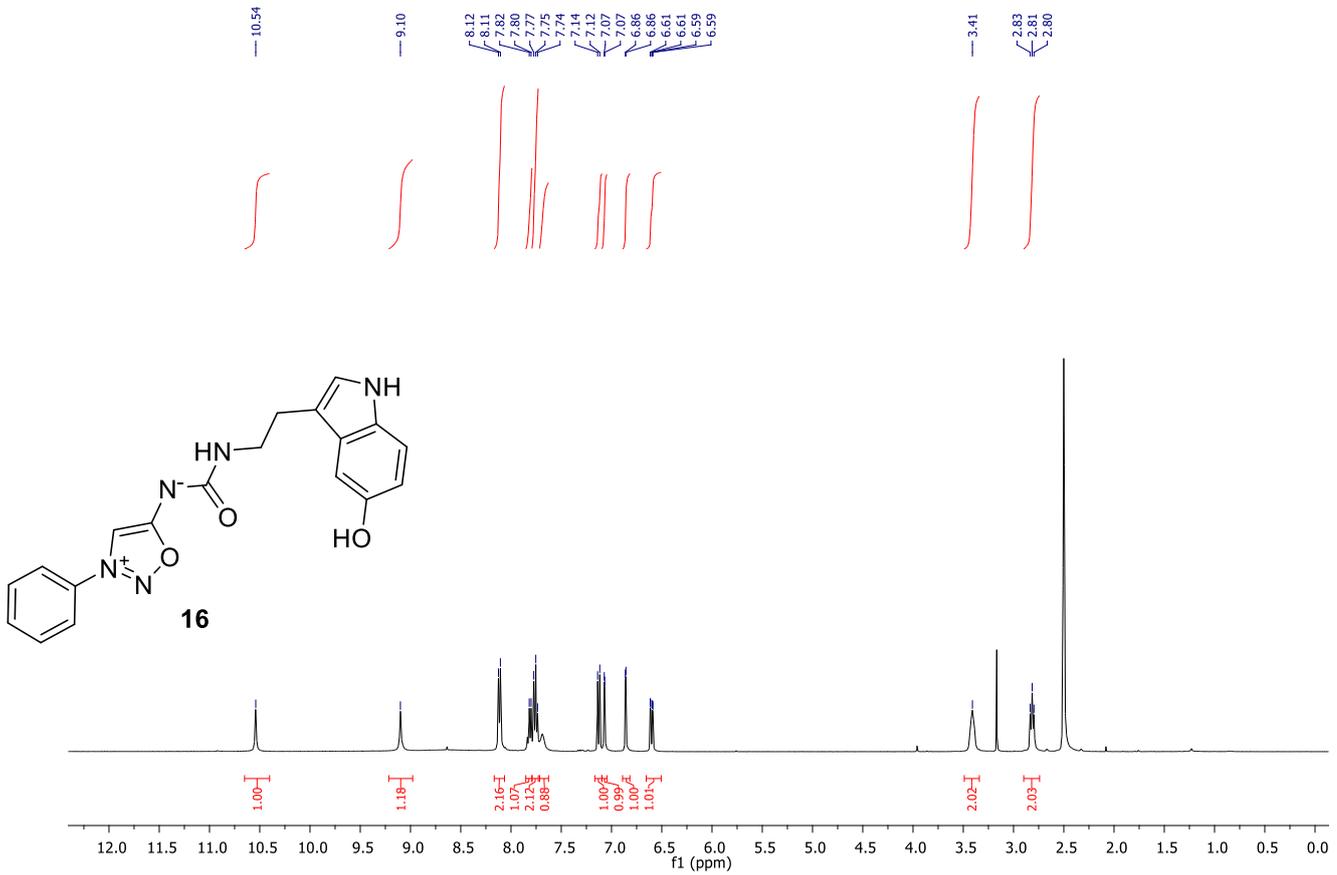




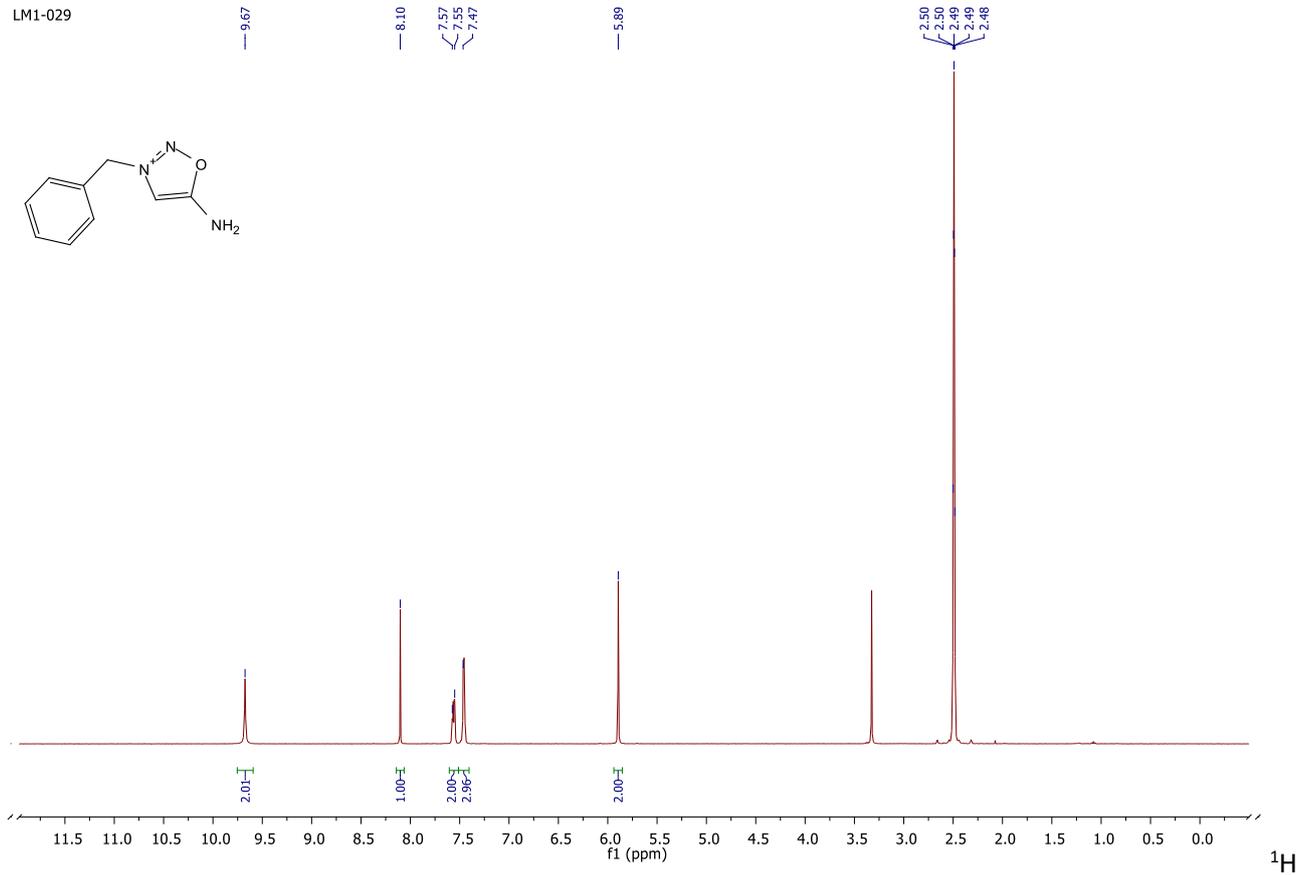




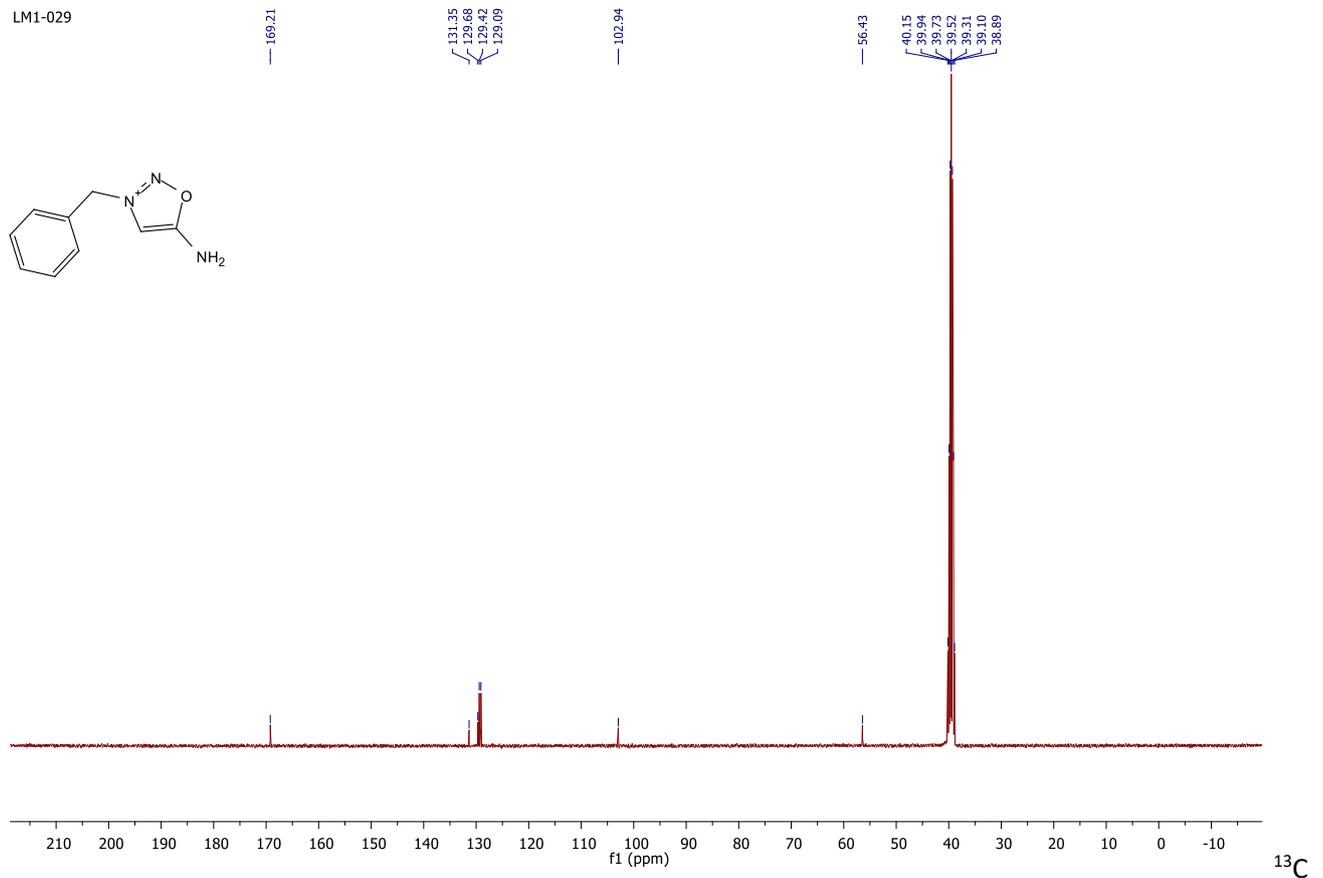


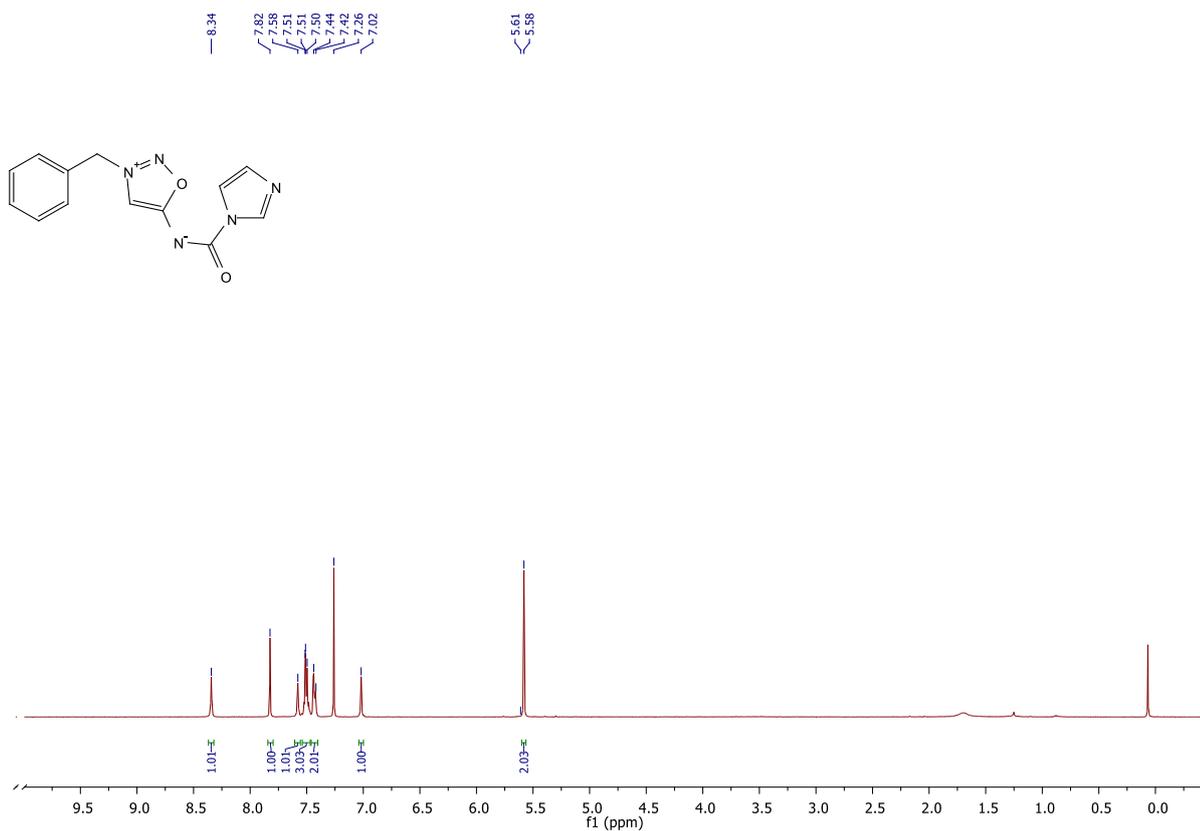


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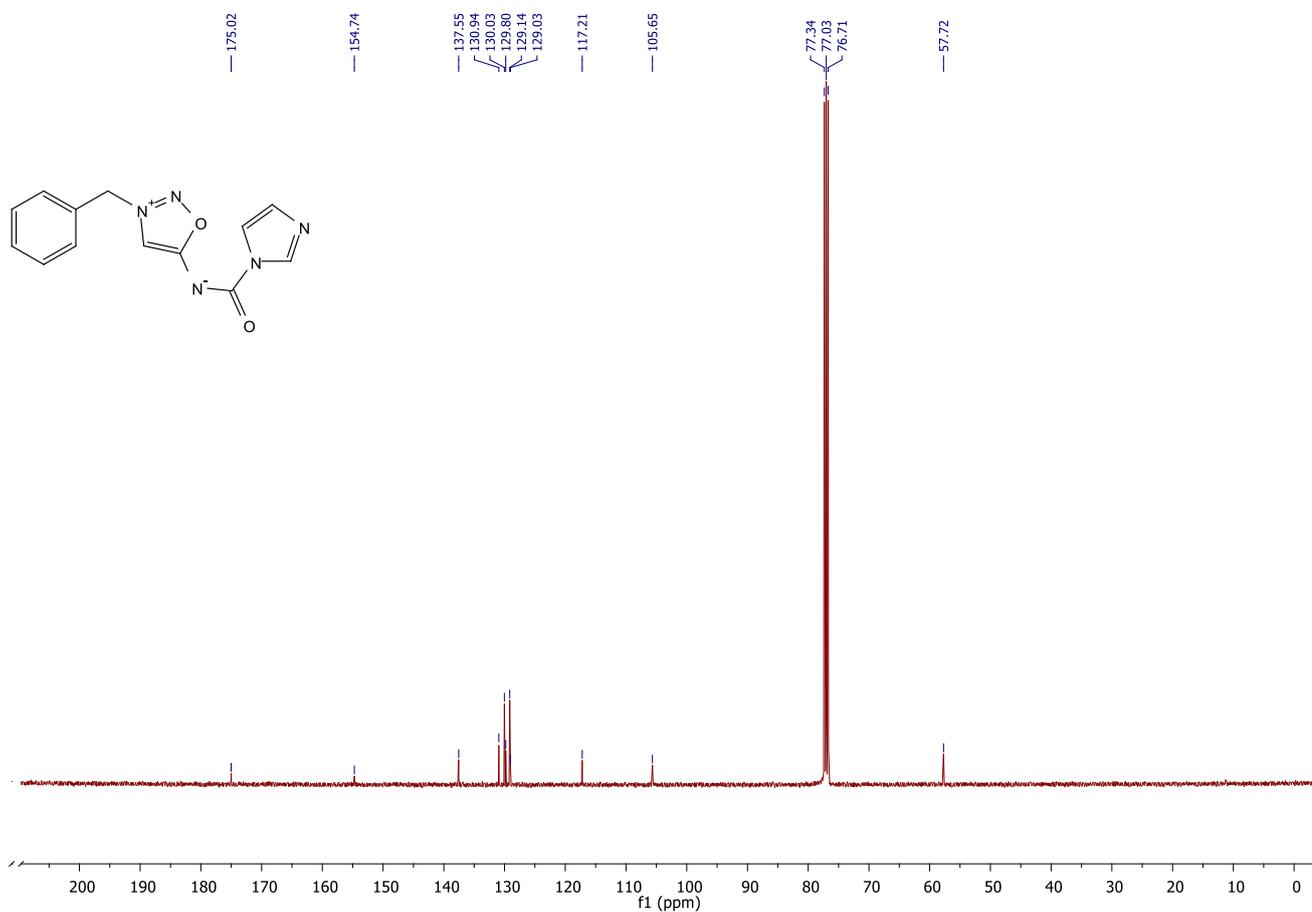
NMR spectrum of **S2** (400 MHz, DMSO-d<sub>6</sub>)

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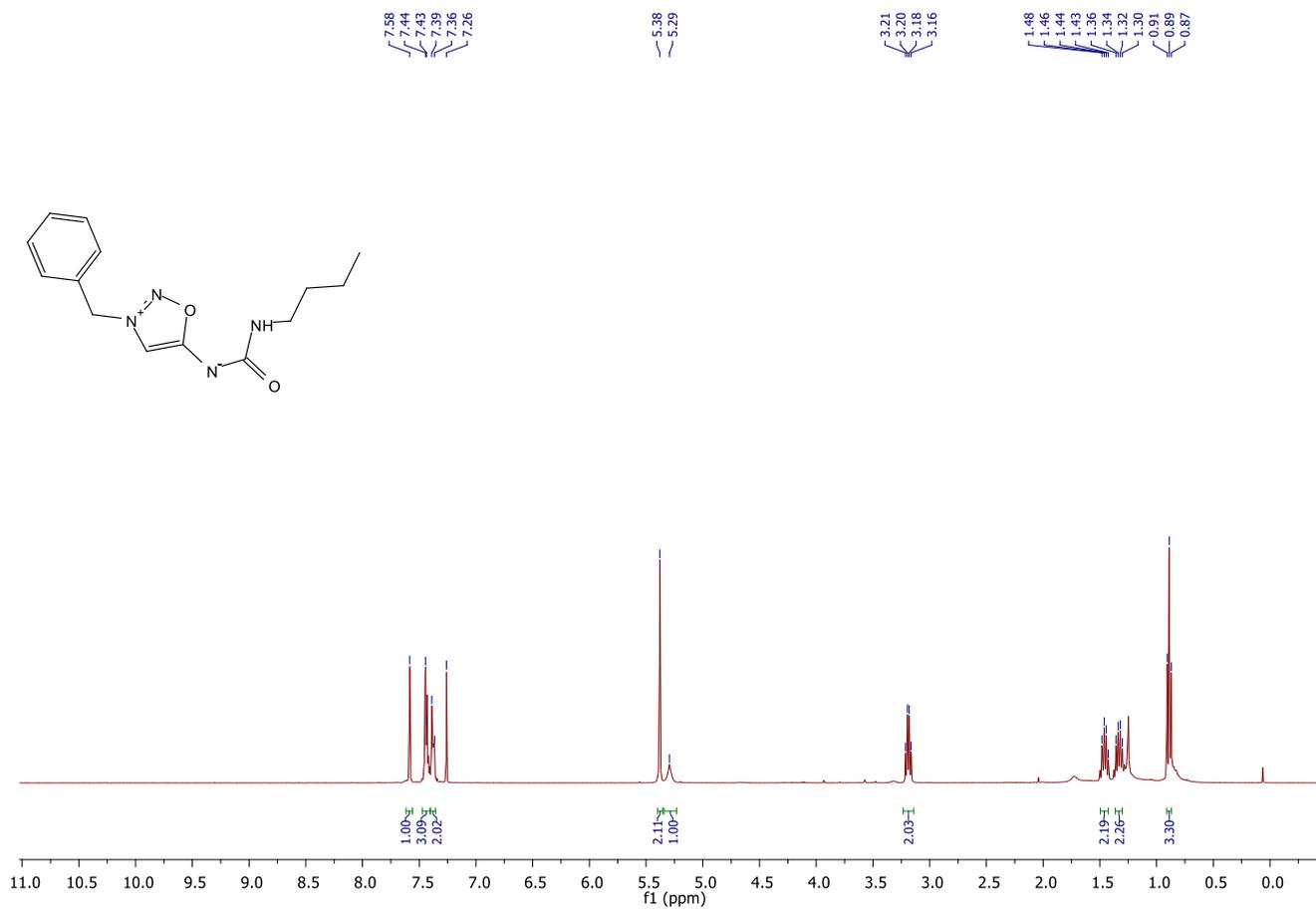
NMR spectrum of **S2** (100 MHz, DMSO-d<sub>6</sub>)



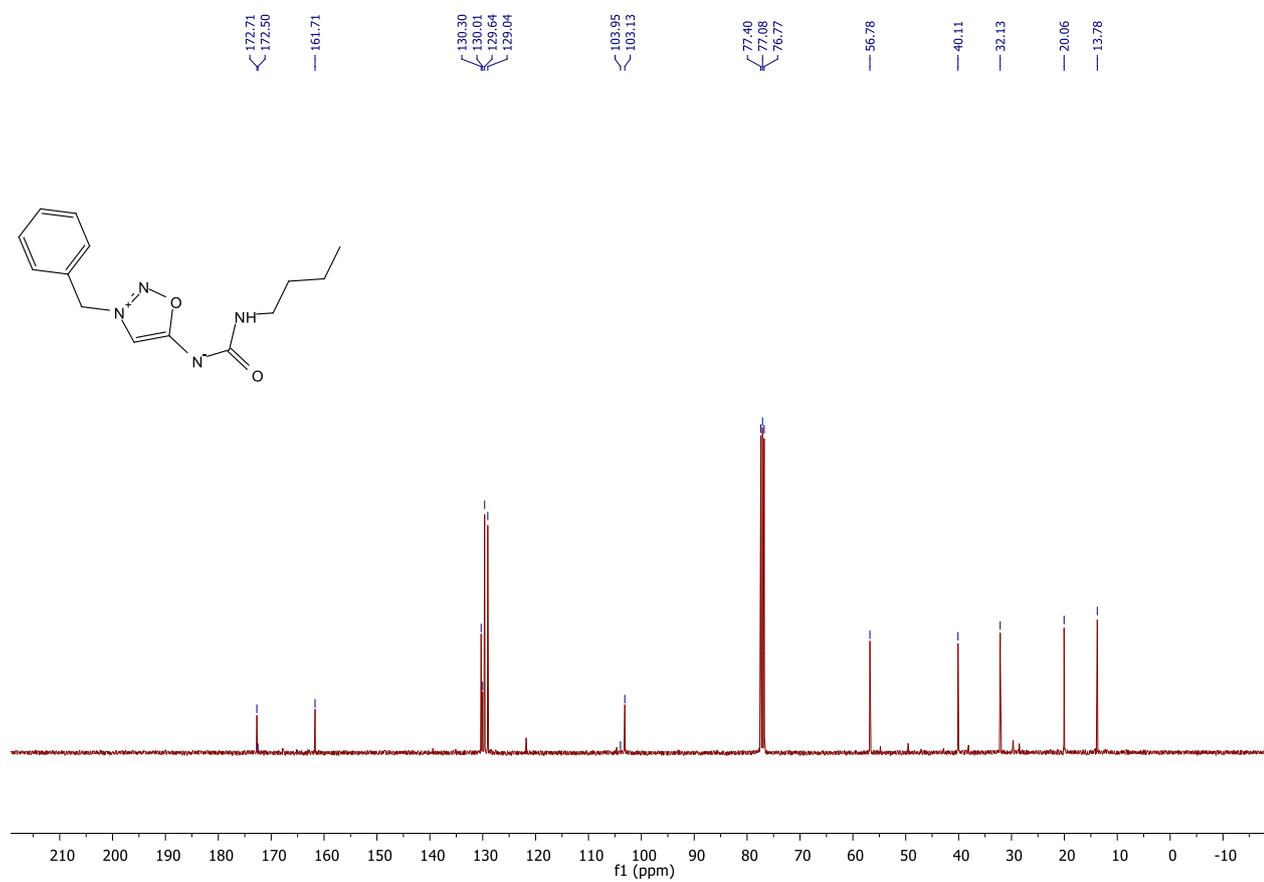
<sup>1</sup>H NMR spectrum of **S3** (400 MHz, CDCl<sub>3</sub>)



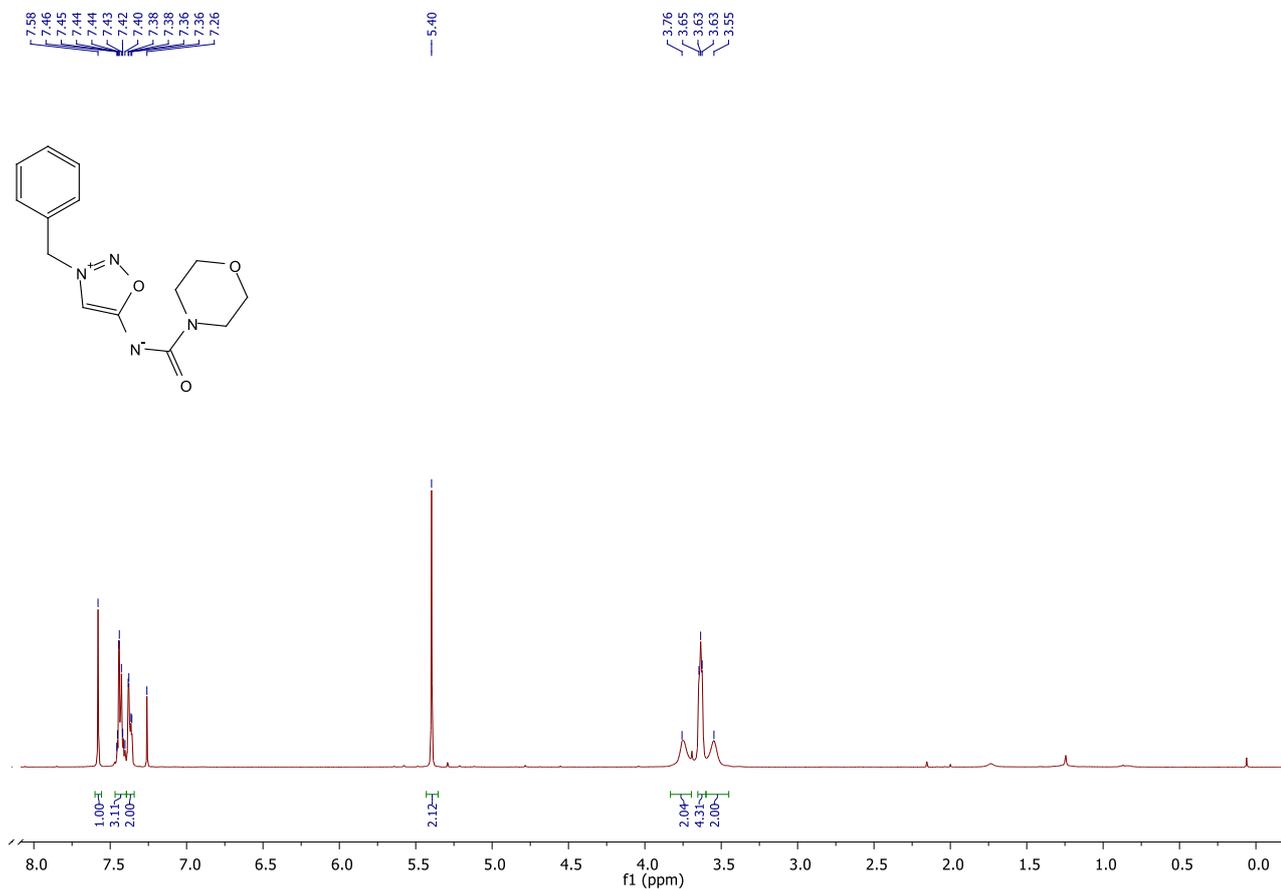
<sup>13</sup>C NMR spectrum of **S3** (100 MHz, CDCl<sub>3</sub>)



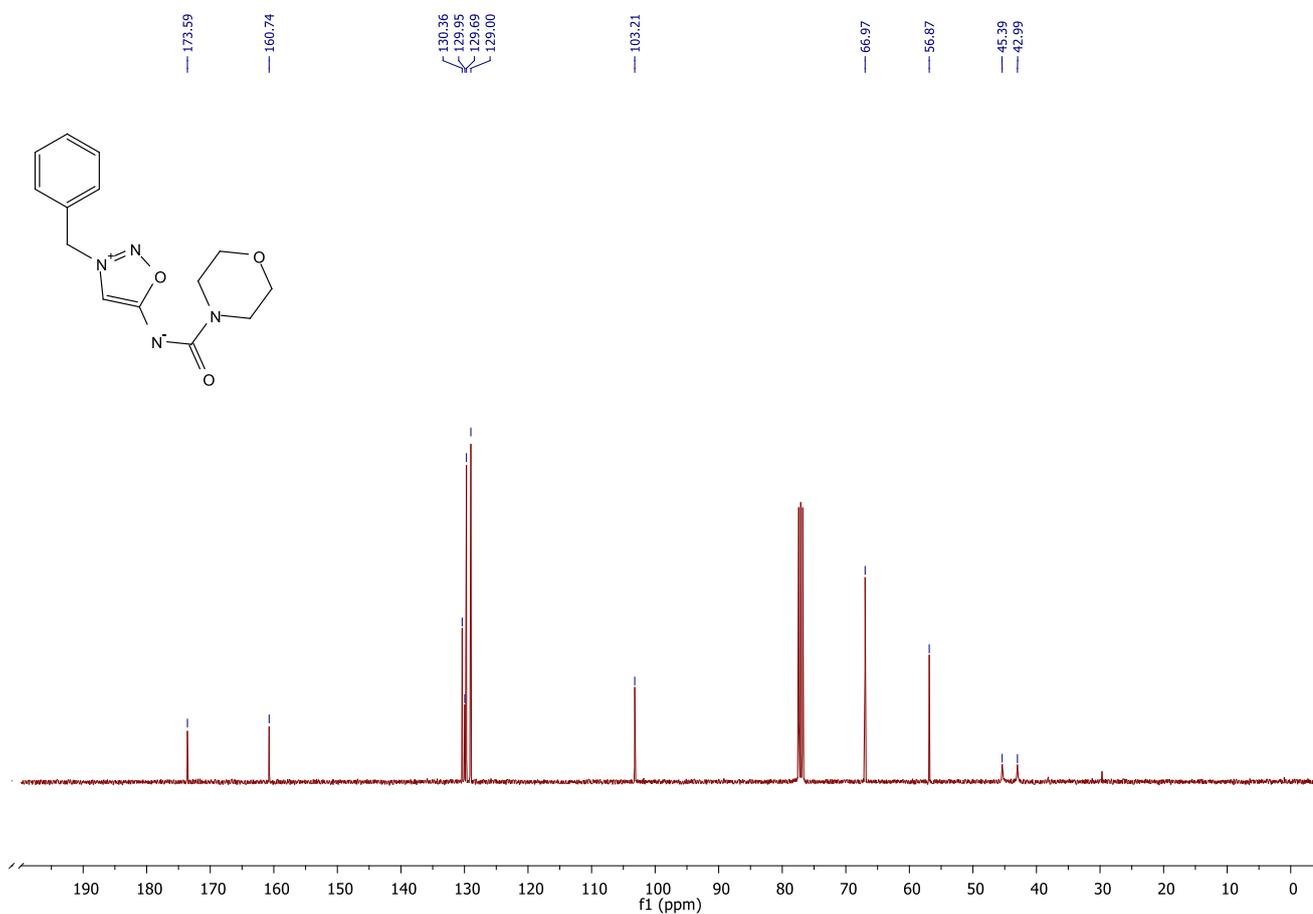
**<sup>1</sup>H NMR spectrum of 6p (400 MHz, CDCl<sub>3</sub>)**



**<sup>13</sup>C NMR spectrum of 6p (100 MHz, CDCl<sub>3</sub>)**



<sup>1</sup>H NMR spectrum of **6q** (400 MHz, CDCl<sub>3</sub>)



<sup>13</sup>C NMR spectrum of **6q** (100 MHz, CDCl<sub>3</sub>)