

# Supplementary Information

## 5-Nitrofuranyl Derivatives are Reactive Towards Methanolic Media as Exemplified by $^1\text{H}$ , $^{13}\text{C}$ NMR Spectroscopy & Their Colours

Ashley L. Dey, <sup>✦</sup><sup>✉</sup>

<sup>✦</sup> Chemistry Research Laboratory, Department of Chemistry, University of Oxford, 12 Mansfield Road, Oxford, OX1 3TA, United Kingdom

<sup>✉</sup> uccaald@ucl.ac.uk

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# Experimental

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## Materials and Instruments

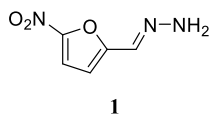
All reagents and solvents in the experiments were of reagent grade quality. They were obtained from commercial sources and used without further purification; unless otherwise stated. Diethyl ether herein is referred to as ether. Water used was from a Millipede Milli-Q EDM Water Purification A10 unit or was HPLC-grade.

High performance liquid chromatography – mass spectrometry (LC-MS) analyses were performed using an Agilent UPLC SQD instrument equipped with a Chromolith<sup>®</sup>, C<sub>18</sub>, 2.1 × 50 mm column. The eluent was 0.1% formic acid (v/v) in water (solvent A)/ acetonitrile (solvent B) over a 5–95% acetonitrile gradient; monitoring at 214 nm over 10 min. Electrospray ionisation mass spectrometry was performed using an Agilent single quadrupole unit equipped with CTC-PAL. High-resolution electrospray mass spectra were obtained on a Waters LCT Premier XE spectrometer. Melting points were determined using a Gallenkamp MFG 595 010 melting point apparatus, and a Reichert Austria hot stage microscope.

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker AVIII HD 400 unit equipped with prodigy N<sub>2</sub> broadband CryoProbe operating at 400 MHz and 101 MHz, respectively, using CDCl<sub>3</sub>, D<sub>2</sub>O, methanol-*d*<sub>4</sub>, acetonitrile-*d*<sub>3</sub> and dimethyl-*d*<sub>6</sub> sulfoxide (DMSO-*d*<sub>6</sub>) as solvents. Chemical shifts (δ) are given in parts per million (ppm) relative to the internal tetramethylsilane (TMS). Coupling constants are given in Hz. The abbreviations s, d, and m correspond to singlet, doublet, and multiplet, respectively.

Reaction products were identified by their NMR, and/or otherwise by LC-MS and HRMS analyses.

**(E)-(5-Nitrofuran-2-yl)methylene hydrazine (1)**

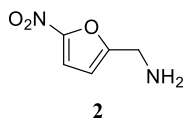


**A:** 5-Nitrofurfural (250 mg, 1.8 mmol) and anhydrous Na<sub>2</sub>SO<sub>4</sub> (50 mg) were placed in a flame-dried reaction vessel, sealed and degassed under argon. Thereto was added anhydrous THF (1.0 ml) and stirred for 2.0 min, followed by addition of hydrazine monohydrate (0.10 ml, 2.0 mmol), and the thus obtained red mixture was stirred under argon at ambient temperature for 24 h. Upon completion – TLC controlled (5.0% methanol in CH<sub>2</sub>Cl<sub>2</sub>; R<sub>f</sub> 0.20) – the dark red cloudy reaction mixture was diluted with deionised water (5.0 ml), and extracted with EtOAc (5.0 × 25 ml). The extracts were combined and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was removed *in vacuo* to afford crude hydrazone **1** (250 mg; 90%) as a red solid, which was further purified by flash column chromatography (EtOAc/cyclohexane, 1:5) to afford the desired product **1** (100 mg; 36%) as needle-like orange crystals; R<sub>f</sub> 0.25 (80% EtOAc in cyclohexane); mp 153–154 °C (from acetonitrile) (lit.<sup>i</sup> 164 °C *dec.*); δ<sub>H</sub> (400 MHz, acetonitrile-*d*<sub>3</sub>) 7.58 (1 H, s, CCHN unsaturated), 7.43 (1 H, d, *J* 3.9, CH-Ar), 6.66 (1 H, d, *J* 3.9, CH-Ar); δ<sub>C</sub> (101 MHz, DMSO-*d*<sub>6</sub>) 108.8 (CH-Ar), 116.1 (CH-Ar), 123.7 (CCHN unsaturated); LC-MS (retention time: 3.87 min) *m/z* (ESI) 156 (*M*<sup>+</sup> + H, 100%); HRMS (ESI) calcd. for C<sub>5</sub>H<sub>5</sub>N<sub>3</sub>O<sub>3</sub> [*M*+H]<sup>+</sup> *m/z* 156.0404, found 156.0403.

**B:** 5-Nitrofurfural (2.5 g, 18 mmol) and anhydrous Na<sub>2</sub>SO<sub>4</sub> (300 mg, 1.8 mmol) were intimately mixed and cooled in an ice-bath, thereto was added THF (10 ml), followed by hydrazine monohydrate (1.0 ml, 20 mmol). The thus obtained red mixture was stirred for 2.0 h, and then purified by flash column chromatography (EtOAc/cyclohexane, 1:5) to afford the desired product **1** (1.7 g, 62%) as an orange solid. This product was identical to that obtained from the preceding procedure as judged by <sup>1</sup>H and <sup>13</sup>C NMR, melting point, LC-MS and HRMS.

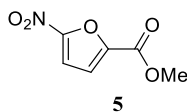
<sup>i</sup> R. Hull, *GB816886 (A)*, Imp. Chem. Ind., Imp. Chem. House, Millbank, London, SW1, 1959.

## 5-Nitrofuran-2-yl methanamine (**2**)



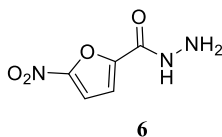
5-Nitrofurfural (250 mg, 1.8 mmol) and sodium triacetoxyborohydride (570 mg, 2.7 mmol) were degassed under argon and cooled in an ice-bath, 0.50 M ammoniacal 1,4-dioxane (4.0 ml, 2.0 mmol) was added therein, followed by glacial AcOH (5.0 drops). The thus obtained dark red mixture was stirred at ambient temperature for 2.0 h. The neutral slurry (pH ~ 7.5) was purified by flash column chromatography (methanol/CH<sub>2</sub>Cl<sub>2</sub>, 1:9) to afford the desired amine **2** (210 mg; 78%) as an orange oil; *R<sub>f</sub>* 0.20 (80% EtOAc in cyclohexane); δ<sub>H</sub> (400 MHz, acetonitrile-*d*<sub>3</sub>) 7.36 (1 H, d, *J* 3.7, *CH*-Ar), 6.59 (1 H, d, *J* 3.7, *CH*-Ar), 4.56 (2 H, s, α-*CH*<sub>2</sub>); δ<sub>C</sub> (101 MHz, acetonitrile-*d*<sub>3</sub>) 57.3 (α-*CH*<sub>2</sub>), 111.4 (*CH*-Ar), 113.9 (*CH*-Ar), 160.0 (2 × *C*-Ar); LC-MS (retention time: 3.38 min) *m/z* (ESI) 144 (*M*<sup>+</sup> + H, 100%); HRMS (ESI) calcd. for C<sub>5</sub>H<sub>6</sub>N<sub>2</sub>O<sub>3</sub> [*M*+H]<sup>+</sup> *m/z* 143.0451, found 143.0452.

## Methyl 5-nitrofuran-2-carboxylate (**5**)



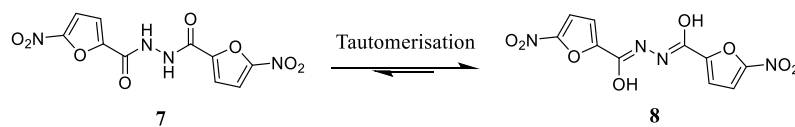
A pressure vessel was charged with 5-nitro-2-furonyl chloride (0.36 g, 2.0 mmol), thereto was added methanol (20 ml) at ambient temperature. The thus obtained clear reaction mixture was sealed and stirred at 70 °C overnight. The resulting reaction mixture was concentrated *in vacuo*, saturated NaHCO<sub>3(aq)</sub> (5.0 ml) was added and extracted with EtOAc (5.0 × 25 ml). The extracts were combined, washed with brine (2.0 × 20 ml), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was removed *in vacuo* to afford crude ester **5** (0.34 g; 99%) as a white solid, which was further purified by flash column chromatography (EtOAc/cyclohexane, 1:4) to afford the desired ester **5** (0.33 g; 95%) as a white fluff; R<sub>f</sub> 0.20 (10% EtOAc in cyclohexane); δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 7.35 – 7.28 (2 H, m, 2 × CH-Ar), 3.97 (3 H, s, O-CH<sub>3</sub>); δ<sub>C</sub> (101 MHz, CDCl<sub>3</sub>) 53.1 (O-CH<sub>3</sub>), 111.6 – 119.0 (2 × CH-Ar), 120.2 – 144.9 (2 × C-Ar), 157.6 (C=O methyl ester); LC-MS (retention time: 5.90 min) *m/z* (ESI) 172 (*M*<sup>+</sup> + H, 100%).

## 5-Nitrofuran-2-carbohydrazide (**6**)



Ester **5** (0.34 g, 2.0 mmol) and anhydrous Na<sub>2</sub>SO<sub>4</sub> (50 mg) were placed in a flame-dried reaction vessel, sealed and degassed under argon. There to was added anhydrous THF (2.0 ml) and stirred for 2.0 min, followed by addition of hydrazine monohydrate (0.11 ml, 2.2 mmol), and the thus obtained tarry mixture was stirred under argon at 0 °C overnight. Upon completion – TLC controlled (80% EtOAc in cyclohexane; R<sub>f</sub> 0.25) – the resulting reaction mixture was diluted with deionised water (5.0 ml), and extracted with EtOAc (5.0 × 25 ml). The extracts were combined, washed with brine (2.0 × 50 ml), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was removed *in vacuo* to afford crude carbohydrazide **6** (0.31 g; 90%) as a dark green solid, which was further purified by flash column chromatography (EtOAc) to afford the desired carbohydrazide **6** (0.29 g; 85%) as a yellow powder; R<sub>f</sub> 0.30 (EtOAc); δ<sub>H</sub> (400 MHz, acetonitrile-*d*<sub>3</sub>) 8.54 (1 H, s, CONH), 7.44 (1 H, d, *J* 3.9, CH-Ar), 7.18 (1 H, d, *J* 3.9, CH-Ar), 4.16 (2 H, s, NHNH<sub>2</sub>); δ<sub>C</sub> (101 MHz, acetonitrile-*d*<sub>3</sub>) 113.6 – 116.2 (2 × CH-Ar), 148.6 (2 × C-Ar), 157.7 (C=O carbohydrazide); LC-MS (retention time: 3.07 min) *m/z* (ESI) 172 (*M*<sup>+</sup> + H, 100%), 155 (10); HRMS (ESI) calcd. for C<sub>5</sub>H<sub>4</sub>N<sub>3</sub>O<sub>4</sub> [*M*-H] *m/z* 170.0207, found 170.0207.

## 5-Nitro-*N'*-(5-nitrofuran-2-carbonyl)furan-2-carbohydrazide (**7**) & (**8**)

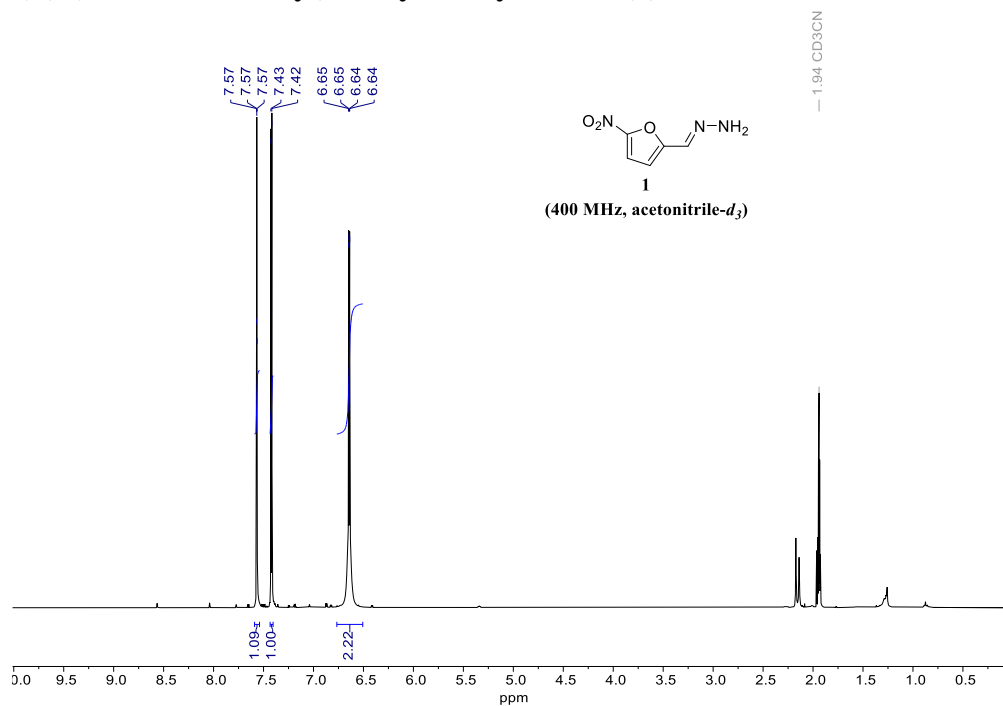


5-Nitro-2-furyl chloride (0.18 g, 1.0 mmol) and anhydrous Na<sub>2</sub>SO<sub>4</sub> (50 mg) were placed in a flame-dried reaction vessel, sealed and degassed under argon. Thereto was added anhydrous THF (10 ml) and stirred for 2.0 min, followed by addition of hydrazine monohydrate (49 μl, 1.0 mmol), and the thus obtained red mixture was stirred under argon at 20 °C overnight. Upon completion – TLC controlled (60% EtOAc in cyclohexane; R<sub>f</sub> 0.25) – the dark red cloudy reaction mixture which was acidic to Congo red, was diluted with deionised water (5.0 ml), and washed with EtOAc (5.0 × 25 ml). Thereto was added saturated NaHCO<sub>3aq</sub> to adjust the pH to ~ 7.0 (*caution! effervescent*), and the aqueous was extracted with EtOAc (6.0 × 25 ml). The extracts were combined and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was removed *in vacuo* to afford crude carbohydrazide **7** (250 mg; 81%) as a dark orange solid, which was further purified by flash column chromatography (EtOAc/cyclohexane, 2:1) to afford the desired product **7** or/and **8** (200 mg; 65%) as a coral pink solid; R<sub>f</sub> 0.25 (80% EtOAc in cyclohexane); mp 180–185 °C *dec.* (from methanol); δ<sub>H</sub> (400 MHz, DMSO-*d*<sub>6</sub>) 7.74 (2 H, d, *J* 3.9, 2 × *CH*-Ar), 7.34 (2 H, d, *J* 3.9, 2 × *CH*-Ar); δ<sub>C</sub> (101 MHz, DMSO-*d*<sub>6</sub>) 113.8 – 114.9 (2 × *CH*-Ar), 149.9 – 151.3 (2 × *C*-Ar), 154.0 (*C*=O carbohydrazide); LC-MS (retention time: 5.08 min) *m/z* (ESI) 311 (*M*<sup>+</sup> + H, 100%), 172 (50), 141 (16).

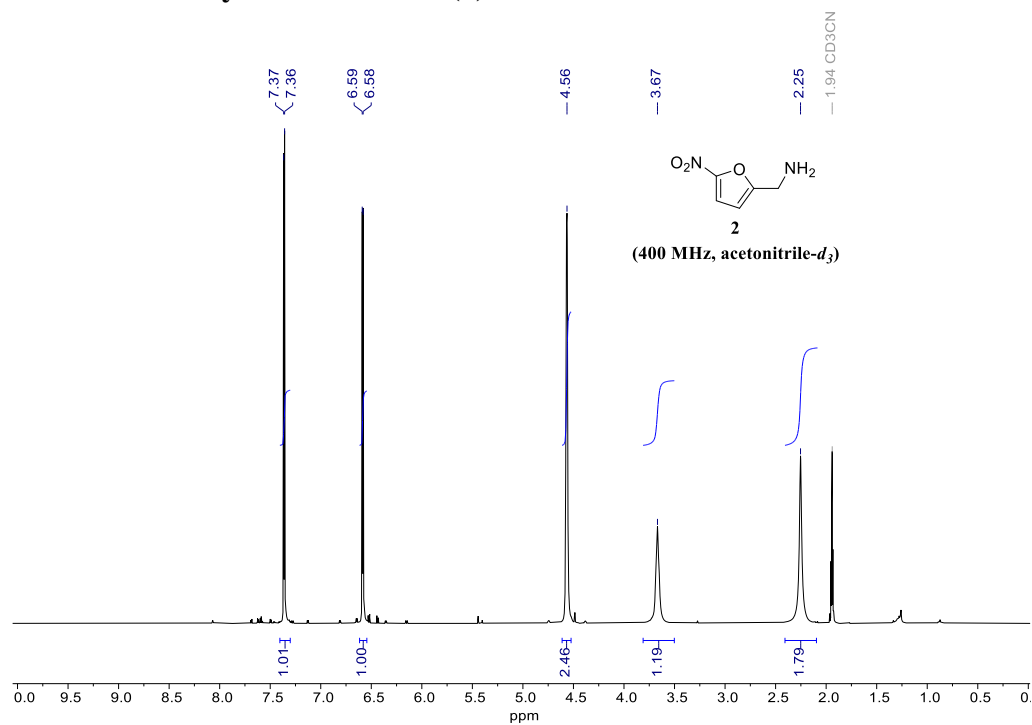


# $^1\text{H}$ NMR Spectra

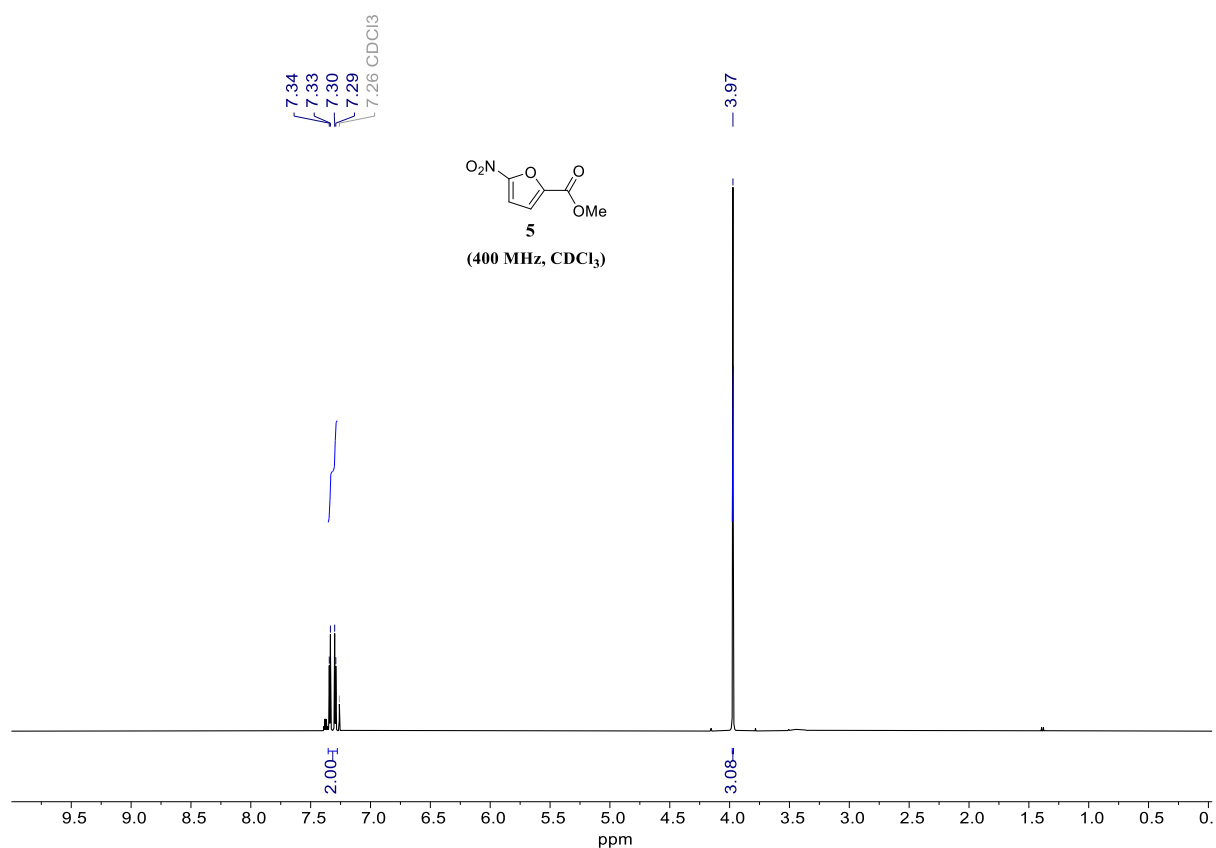
**(E)-(5-Nitrofur-2-yl)methylene hydrazine (1)**



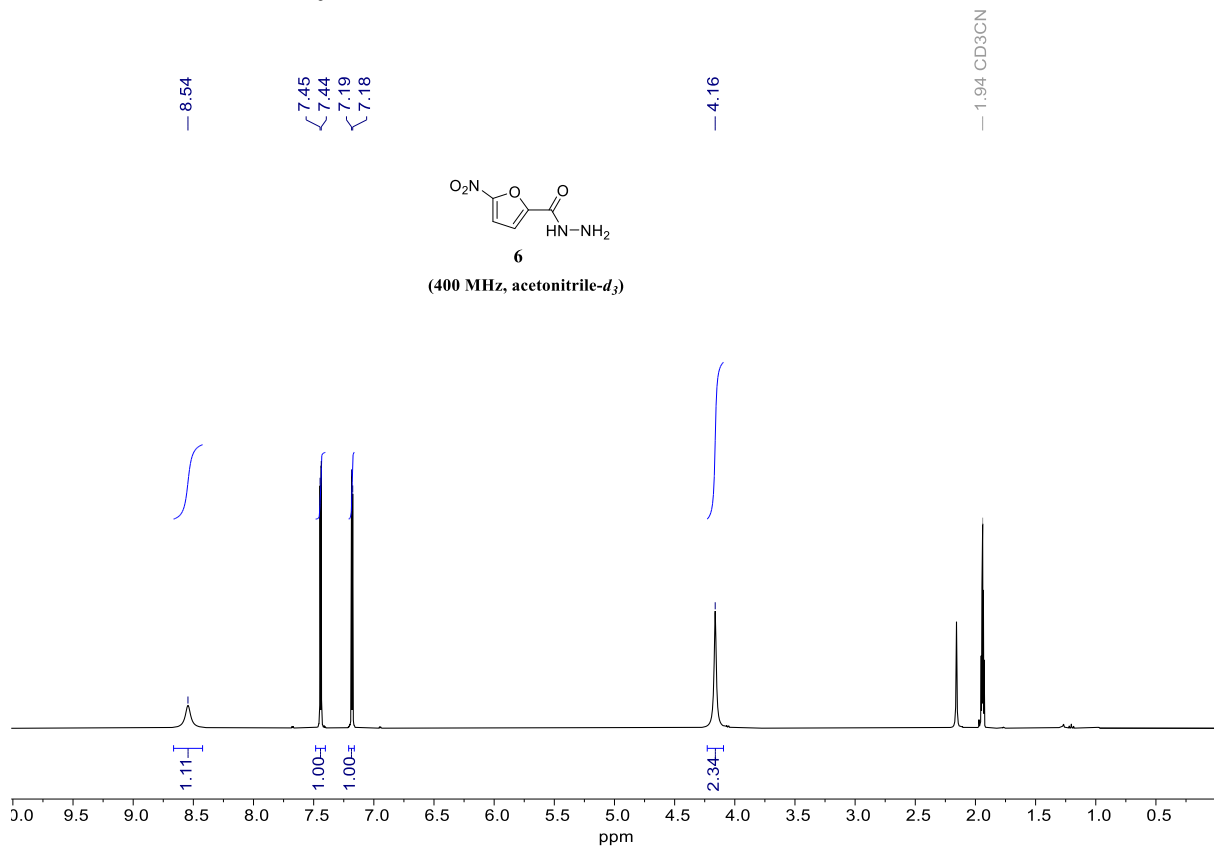
**5-Nitrofur-2-yl methanamine (2)**



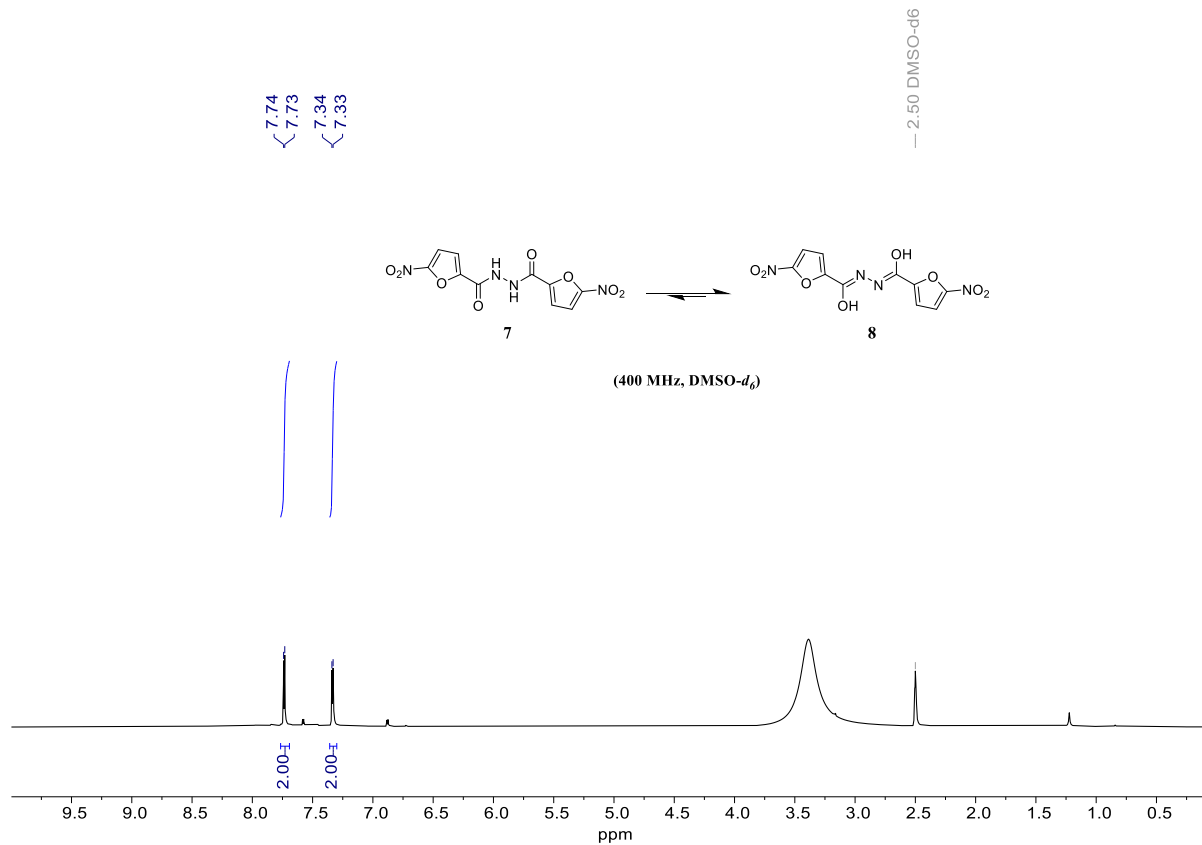
### Methyl 5-nitrofur-2-carboxylate (5)



### 5-Nitrofur-2-carbohydrazide (6)



# 5-Nitro-*N'*-(5-nitrofuran-2-carbonyl)furan-2-carbohydrazide (7) & (8)



# HRMS Spectrum of 1

