**Supplementary Information (37 pp) for**

# Dipolar Cycloadditions of HMF- based nitrones: stepwise and multicomponent reactions, stereochemical outcome and structural scope

Lianjie Wang, Charlie Verrier, Mohammed Ahmar, Yves Queneau*

[1]*Université de Lyon, Institut de Chimie et Biochimie Moléculaires et Supramoléculaires, ICBMS, UMR 5246 CNRS, Université Lyon 1, INSA Lyon, CPE Lyon, Bâtiment Edgar Lederer, 1 rue Victor Grignard, 69622 Villeurbanne Cedex, France*

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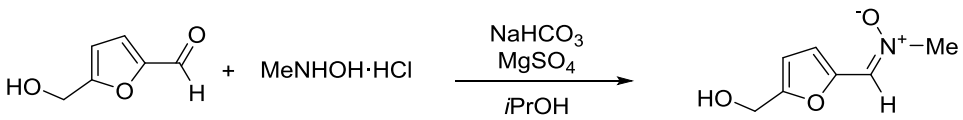
# 1. General methods

The reagents were bought from Aldrich and used directly without purification. HMF was purchased from Carbosynth, GMF was prepared as previously reported from isomaltulose which was a gift from Cargill. The reactions were monitored by TLC, on Silica Gel 60 F254 (Merck), and detection was carried out with UV light (254 nm) and 1% potassium permanganate solution in water containing 1% $NaHCO_3$. Silica gel (Kieselgel 60, 70-230 mesh ASTM, Merck) was employed for column chromatography. The $^{1}H$ NMR (300 MHz, 400 or 500 MHz) and $^{13}C$ NMR (75 MHz, 100 MHz or 125 MHz) spectra were recorded with Brucker ALS300, DRX300 and DRX400 spectrometers. Chemical shifts are given in ppm. Coupling constants are expressed in Hertz and splitting pattern abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. High resolution mass spectra were obtained using an electro spray technique in positive mode, with a Thermo-Finnigan MAT 95 XL spectrometer.

# 2. Synthetic procedures

### 2.1. Procedure for the stepwise approach

2.1.1. Preparation of the nitrone

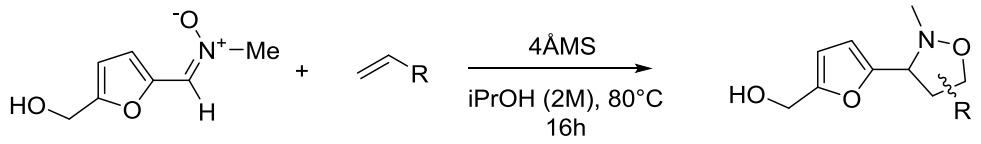



In a dry round bottom flask were placed HMF (1 equiv.), *N*-methyl hydroxylamine hydrochloride (1.2 equiv.), $NaHCO_3$ (1.5 equiv.), anhydrous $MgSO_4$ (2 equiv.), and. anhydrous isopropanol was added ([HMF] = 0.2M), and the solution was stirred at room temperature for 16h. The reaction mixture was then filtered on celite, using isopropanol to rinse the flask and the celite. The solvent was removed under reduced pressure to give the pure nitrone **1a** as a yellowish powder.

The same procedure was applied to HMF and *N*-benzyl and *N-tert*-butyl hydroxylamines, and to DBDPS-HMF and *N*-methyl hydroxylamine leaing to nitrones **1b**, **1c** and **1d**, respectively.

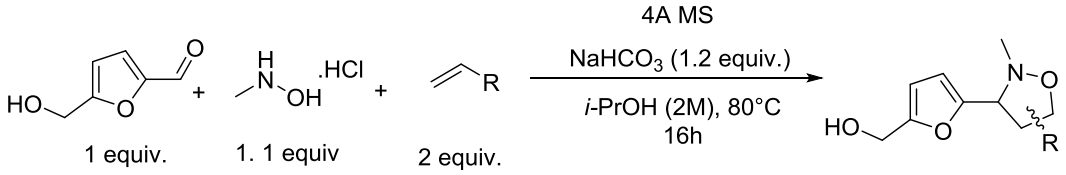
In the case of GMF, EtOH was used as the solvent, leading to **1e**.

2.1.2. Cycloadditions




In a dry MW tube were placed nitrone (1mmol), dipolarophile (2 equiv.), 4 Å molecular sieves (5 pellets), *i*-PrOH (0.5 mL). The tube was sealed and placed at 80°C for 16h. The crude mixture was diluted in EtOAc and filtered through a short column of silica, rinsing with EtOAc. The filtrate was concentrated under reduced pressure, and the crude mixture was then subjected to flash chromatography yielding the pure HMF-derived isoxazolidine as a mixture of isomers.

## 2.2. Procedure for the multicomponent approach




In a dry MW tube were placed HMF (1 mmol), *N*-methylhydroxylamine hydrochloride (1.1 mmol), 4 Å molecular sieves (5 pellets), $NaHCO_3$ (1.2 equiv.), *i*-PrOH (0.5 mL) and the alkene (dipolarophile, 2 equiv.). The tube was sealed and placed at 80°C for 16h. The crude mixture was diluted in EtOAc and filtered through a pad of silica, rinsing with EtOAc. The filtrate was concentrated under reduced pressure, internal standard was added (1,3,5-trimethoxybenzene, 0.33 mmol, 0.33 equiv) and crude NMR yield was measured. The crude mixture was then subjected to flash chromatography yielding the pure HMF-derived isoxazolidine as a mixture of isomers.

## 3. Figures supporting the study if the stereochemical outcome of the reaction

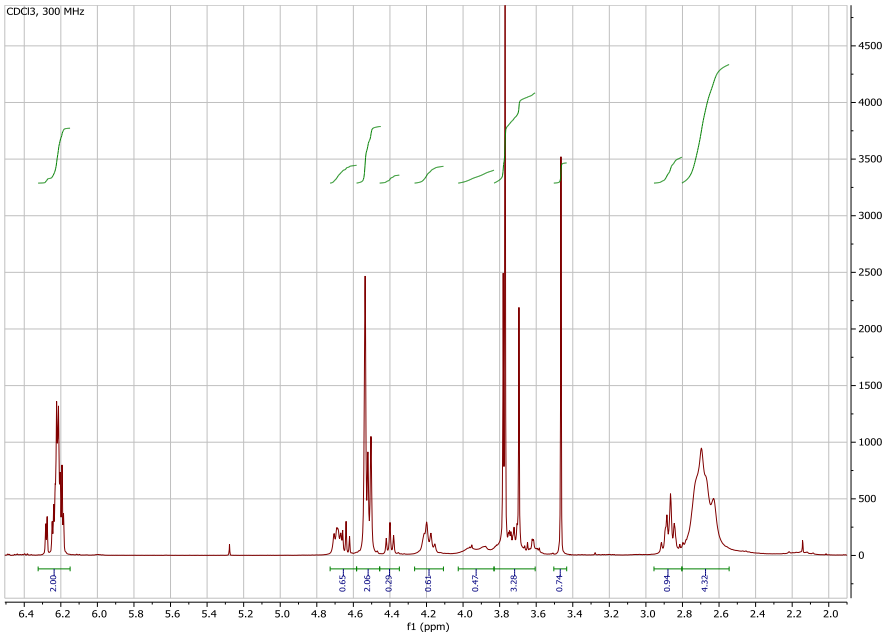



**Figure S1**. $^{1}$H NMR spectra of the crude mixture **2**/**2'** in $CDCl_3$ at room temperature. Most signals are broad due to the presence of rotamers

**Slow equilibrium beetween two rotamers observed by NMR at 25 °C**

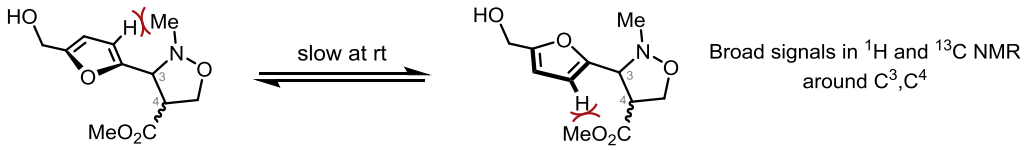



**Figure S2**. Slow equilibrium between **2** and **2'** in $CDCl_3$ at room temperature.

NMR analysis in DMSO at 90°C (fig. S3) shows well defined signals and coupling constant could be measured. Figure 1b shows the signals of each pair of regio-isomers, that could be confirmed by 2D NMR analysis.

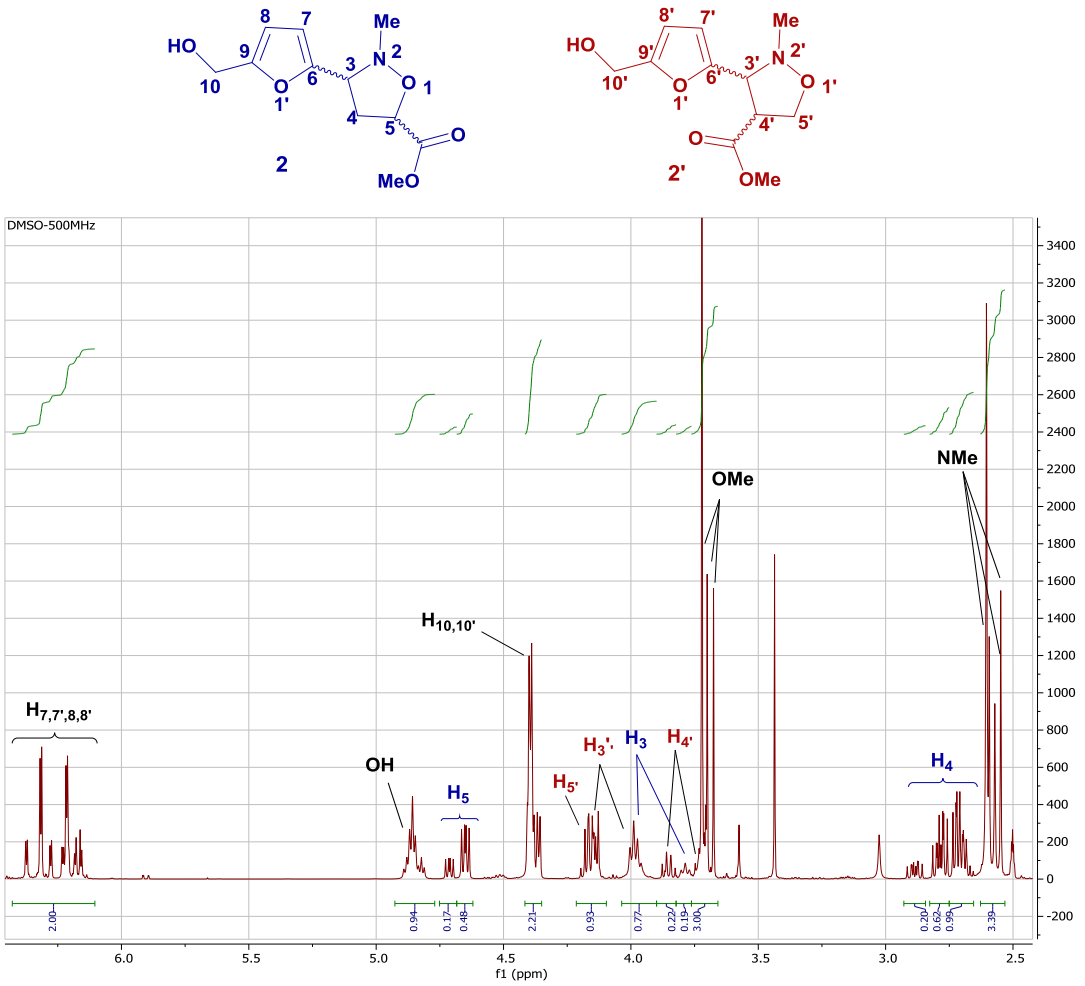



**Figure S3**. $^{1}$H NMR spectra of the crude mixture in DMSO at 90°C. Attribution of signals of **2** and **2'.**

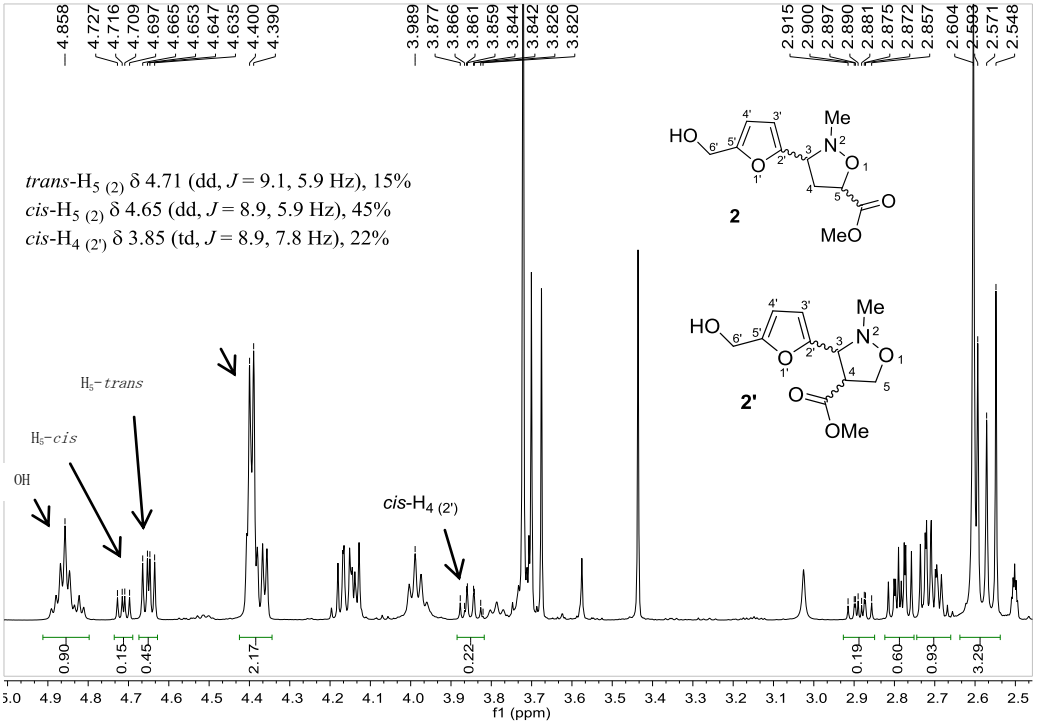



**Figure S4**. Specific signals of **2** and **2'** in $^{1}$H NMR spectrum used for estimating the selectivity by integration measurements

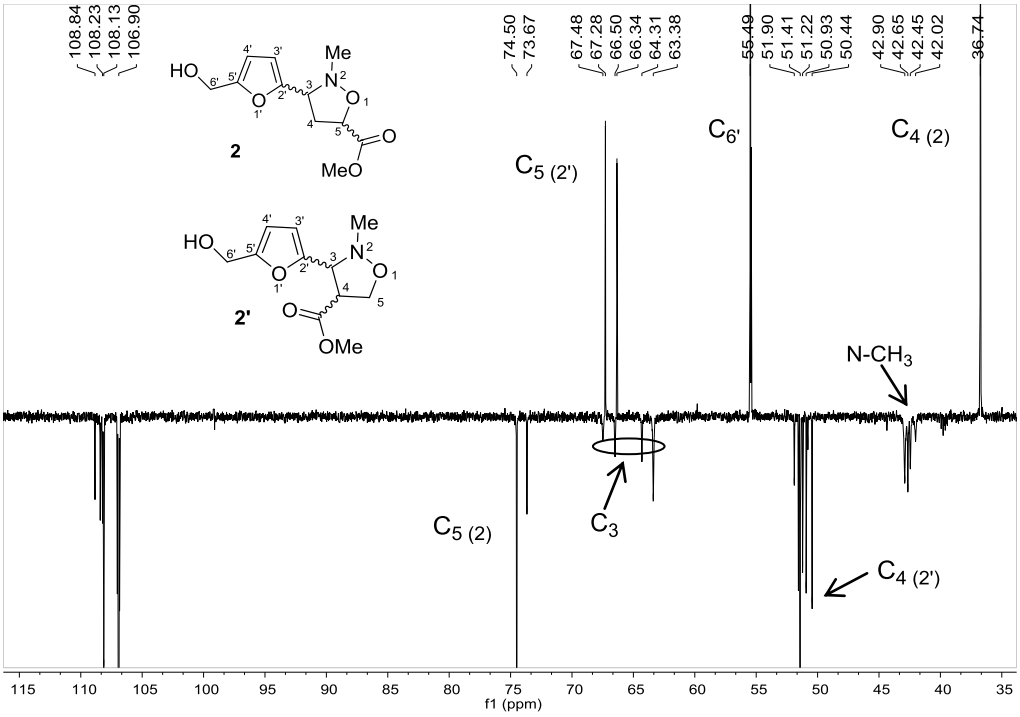



**Figure S5**. $^{13}$C DEPT NMR spectrum of **2** and **2'** showing the presence of four isomers ($C_3$ signals)

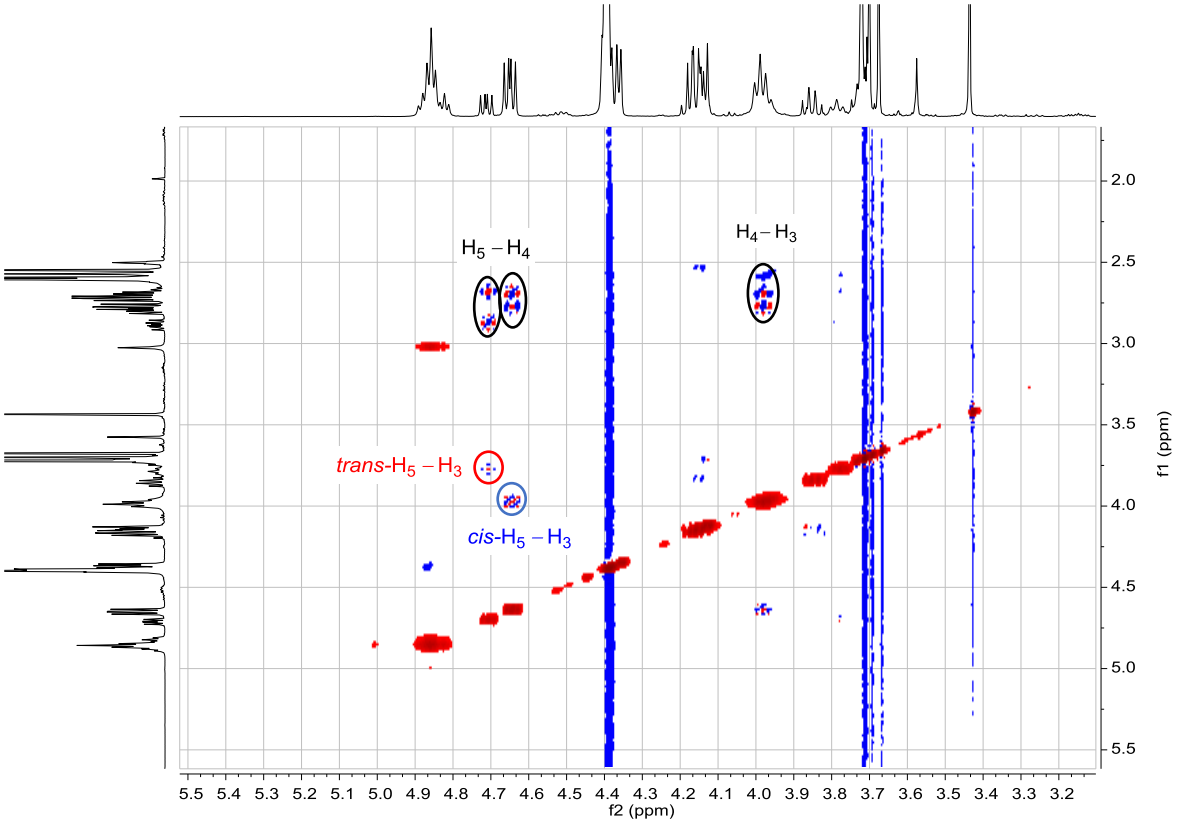



**Figure S6**. 2D NOESY spectrum showing the NOE effect between $H_3$ and $H_5$ on both stereoisomers of **2** showing a cis relationship between $H_3$ and $H_5$ for the major isomer

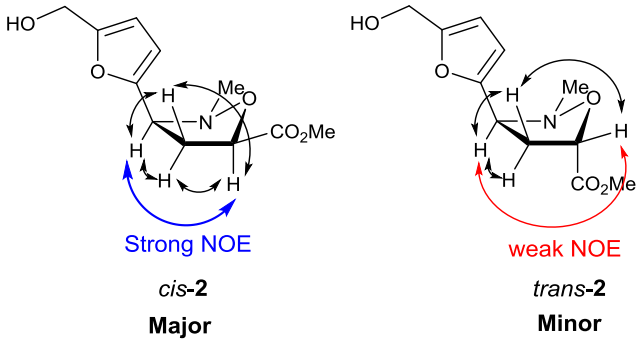
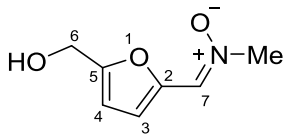



**Figure S7**. Structure of *cis* and *trans* **2** with 2D NOESY indications on the relationship between $H_3$ and $H_5$

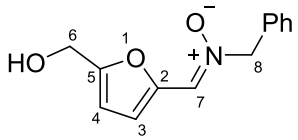
## 4. Characterization of Products

(Z)-1-(5-(Hydroxymethyl)furan-2-yl)-*N*-methylmethanimine oxide **1a**



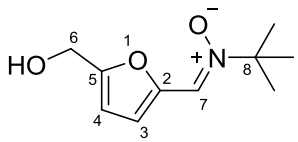
$^1$H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 3.4 Hz, 1H, $H_3$), 7.56 – 7.40 (m, 1H, $H_7$), 6.49 – 6.30 (m, 1H, $H_4$), 4.62 (s, 2H, $H_6$), 3.81 (s, 3H, N-$CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 155.7 ($C_5$), 146.5 ($C_2$), 126.5 ($C_7$), 116.5 ($C_3$), 110.4 ($C_4$), 57.6 ($C_6$), 52.9 ($CH_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_7H_9NNaO_3$ 178.0475; Found 178.0472.

(Z)-*N*-Benzyl-1-(5-(hydroxymethyl)furan-2-yl)methanimine oxide **1b**



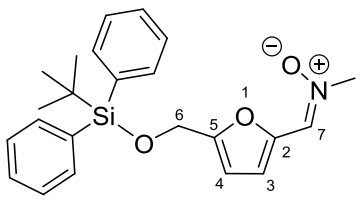
$^1$H NMR (300 MHz, DMSO-$d_6$) δ 8.22 (s, 1H, $H_7$), 7.52 – 7.43 (m, 3H, $H_3$ & Ph), 7.42 – 7.32 (m, 3H, Ph), 6.44 (d, *J* = 3.3 Hz, 1H, $H_4$), 5.05 (s, 2H, $H_8$), 4.43 (s, 2H, $H_6$). $^{13}$C NMR (75 MHz, DMSO-$d_6$) δ 156.7 ($C_5$), 146.3 ($C_2$), 134.6, 129.0, 128.4, 128.3 ($C_{Ph}$), 124.4 ($C_7$), 114.4 ($C_3$), 109.1 ($C_4$), 68.2 ($C_8$), 55.7 ($C_6$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{13}H_{14}NO_3$ 232.0968; Found 232.0966.

(Z)-*N*-tert-Butyl-1-(5-(hydroxymethyl)furan-2-yl)methanimine oxide **1c**



$^1$H NMR (300 MHz, $CDCl_3$) δ 7.70 (s, 1H, $H_7$), 7.67 (d, *J* = 3.4 Hz, 1H, $H_3$), 6.41 (dd, *J* = 3.4, 0.6 Hz, 1H, $H_4$), 4.62 (s, 2H, $H_6$), 1.57 (s, 9H, $C(CH_3)_3$). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 155.2 ($C_5$), 147.4 ($C_2$), 121.6 ($C_7$), 115.8 ($C_3$), 110.2 ($C_4$), 69.8 ($C_8$), 57.5 ($C_6$), 28.1 ($C(\underline{C}H_3)_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{10}H_{15}NNaO_3$ 220.0944; Found 220.0940.

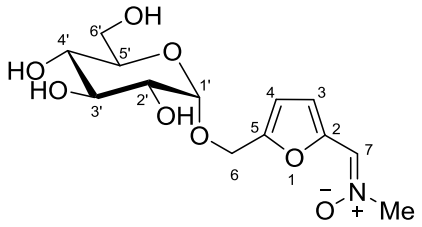
(Z)-1-(5-(((tert-Butyldiphenylsilyl)oxy)methyl)furan-2-yl)-*N*-methylmethanimine oxide **1d**



$^1$H NMR (300 MHz, $CDCl_3$) δ 7.76 – 7.62 (m, 5H, $H_3$&$H_{Ph}$), 7.51 – 7.32 (m, 7H, $H_7$&$H_{Ph}$), 6.43 – 6.23 (m, 1H, $H_4$), 4.66 (s, 2H, $H_6$), 3.81 (s, 3H, N-$CH_3$), 1.06 (s, 9H, $C(CH_3)_3$). $^{13}$C NMR (75 MHz, $CDCl_3$)

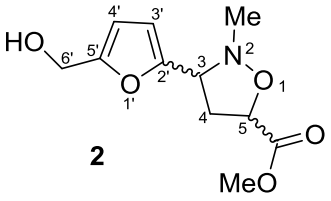
δ 155.5 ($C_5$), 146.2 ($C_2$), 135.7, 133.2, 129.9, 127.8 ($C_{Ph}$), 126.3 ($C_7$), 116.3 ($C_3$), 110.0 ($C_4$), 59.0 ($C_6$), 52.7 (N-$CH_3$), 26.8 (C($\underline{C}H_3)_3$), 19.3 ($\underline{C}(CH_3)_3$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{23}H_{28}NO_3Si$ 394.1833; Found 394.1834.

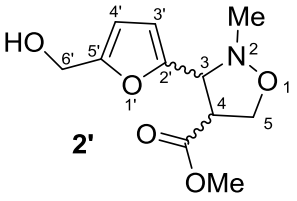
(Z)-*N*-Methyl-1-(5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)methanimine oxide **1e**




$^1$H NMR (300 MHz, MeOD) δ 7.99 (s, 1H, $H_7$), 7.65 (d, *J* = 3.5 Hz, 1H, $H_3$), 6.67 (d, *J* = 3.5 Hz, 1H, $H_4$), 4.93 (d, *J* = 3.7 Hz, 1H, $H_{1'}$), 4.73 (d, *J* = 13.2 Hz, 1H, $H_{6a}$), 4.63 (d, *J* = 13.2 Hz, 1H, $H_{6b}$), 3.84 (s, 3H, N-$CH_3$), 3.80 (dd, *J* = 11.8, 2.4 Hz, 1H, $H_{6'a}$), 3.75 – 3.57 (m, 3H, $H_{6'b}$, $H_{3'}$, $H_{5'}$), 3.44 (dd, *J* = 9.8, 3.7 Hz, 1H, $H_{2'}$), 3.39 – 3.29 (m, 1H, $H_{4'}$). $^{13}$C NMR (75 MHz, MeOD) δ 154.0 ($C_5$), 146.4 ($C_2$), 128.7 ($C_7$), 117.1 ($C_3$), 111.7 ($C_4$), 98.2 ($C_{1'}$), 73.5 ($C_{3'}$), 72.6 ($C_{5'}$), 72.0 ($C_{2'}$), 70.3 ($C_{4'}$), 61.1 ($C_{6'}$), 60.7 ($C_6$), 51.1 ($CH_3$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{13}H_{20}NO_8$ 318.1183; Found 318.1178.

Methyl 3-(4 and 5-(hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carboxylate **2**+**2'**

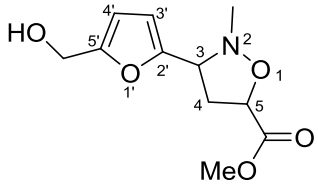



Mixture of isomers. HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{11}H_{16}NO_5$ 242.1023; Found 242.1030.

See section 3 for details in NMR of various streoisomers.

Data for the major isomer cis-**2** (Fig S3): Methyl *cis*-3-(5-(hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carboxylate **2**



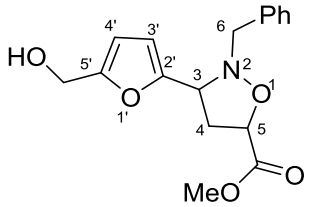

$^1$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.31 (d, *J* = 3.1 Hz) and 6.21 (d, *J* = 3.1 Hz, 2H, $H_{3'}$&$H_{4'}$), 4.94 – 4.76 (m, 1H, OH), 4.71 (dd, *J* = 9.1, 5.9 Hz) and 4.65 (dd, *J* = 8.9, 5.9 Hz, $H_5$), 4.39 (d, *J* = 5.0 Hz, 2H, C$\underline{H}_2$OH), 3.99 (t, *J* = 7.4 Hz), and 3.78 (1H, $H_3$), 3.72 (s, 3H, $CO_2C\underline{H}_3$), 2.88 (ddd, *J* = 12.5, 9.1, 7.6 Hz) and 2.78 (ddd, *J* = 12.6, 8.9, 7.0 Hz) and 2.75 – 2.67 (m,$H_4$), 2.60 (s, 3H, N-C$\underline{H}_3$). $^{13}$C

NMR (125 MHz, DMSO-$d_6$) δ 170.8 (<u>C</u>=O), 155.2 ($C_{5'}$), 150.1 ($C_{2'}$), 108.1 ($C_{3'}$), 106.9 ($C_{4'}$), 74.5 ($C_5$), 64.3 and 63.4 ($C_3$), 55.5 ($\underline{C}H_2OH$), 51.4 ($CO_2\underline{C}H_3$), 42.9 (N-$\underline{C}H_3$), 36.8 ($C_4$).

Methyl 2-benzyl-3-(4 and 5-(hydroxymethyl)furan-2-yl)isoxazolidine-5-carboxylate **3**

Mixture of isomers. HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{17}H_{20}NO_5$ 318.1336; found 318.1337.

Signals extracted from the spectrum of the mixture for the major isomer: Methyl 2-benzyl-3-(5-(hydroxymethyl)furan-2-yl)isoxazolidine-5-carboxylate **3**

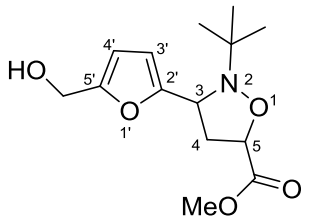



$^1$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 7.43 – 7.13 (m, 5H, $H_{Ph}$), 6.33 (d, $J$ = 3.1 Hz , $H_{3'}$) & 6.21 (d, $J$ = 3.2 Hz, $H_{4'}$), 4.77 (dd, $J$ = 9.1, 5.8 Hz), 4.69 (dd, $J$ = 8.5, 6.4 Hz) ($H_5$), 4.46 – 4.35 (m, 2H, $C\underline{H}_2OH$), 4.28 (t, $J$ = 6.8 Hz, $H_3$), 3.97 (s, 2H, $H_6$), 3.71 (s, 3H, $CO_2C\underline{H}_3$), 2.87 – 2.69 (m, 2H, $H_4$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 170.9 (<u>C</u>=O), 155.1 ($C_{5'}$), 150.5 ($C_{2'}$), 137.3, 128.1, 127.4, 126.3 ($C_{Ph}$), 108.0 ($C_{3'}$), 106.9 ($C_{4'}$), 74.8, 73.9 ($C_5$), 65.4, 64.2, 62.1, 61.6 ($C_3$), 59.5, 58.9, 58.8, 58.5 ($C_6$), 55.5 ($\underline{C}H_2OH$), 51.4 ($CO_2\underline{C}H_3$), 36.6 ($C_4$).

Methyl 2-(tert-butyl)-3-(4 and 5-(hydroxymethyl)furan-2-yl)isoxazolidine-5-carboxylate **4**

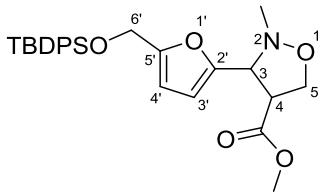
Mixture of isomers. HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{14}H_{22}NO_5$ 284.1492; found 284.1496.

Signals extracted from the spectrum of the mixture for the major isomer: Methyl 2-(tert-butyl)-3-(5-(hydroxymethyl)furan-2-yl)isoxazolidine-5-carboxylate **4**




$^1$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.23 (d, $J$ = 3.1 Hz, 1H, $H_{3'}$), 6.17 (d, $J$ = 3.2 Hz, 1H, $H_{4'}$), 4.67 (dd, $J$ = 8.5, 5.2 Hz) & 4.62 – 4.52 (m) (1H, $H_5$), 4.44 – 4.29 (m, 3H, $C\underline{H}_2OH$ & $H_3$), 3.72 (s, 3H, $CO_2C\underline{H}_3$), 2.86 – 2.72 (m), 2.62 – 2.46 (m) (2H, $H_4$), 1.08 (s, 9H, $C(CH_3)_3$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 169.9 ($\underline{C}O_2CH_3$), 154.4 ($C_{5'}$), 153.6 ($C_{2'}$), 106.8, 106.7 ($C_{3'}$&$C_{4'}$), 74.0 ($C_5$), 66.3 ($C_3$), 57.9 ($\underline{C}(CH_3)_3$), 55.5 ($\underline{C}H_2OH$), 51.3 ($CO_2\underline{C}H_3$), 39.2 ($C_4$), 25.3 ($C(\underline{C}H_3)_3$).

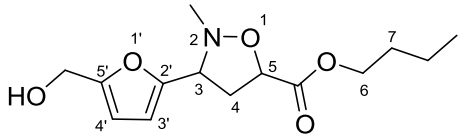
Methyl 3-(4-(((tert-butyldiphenylsilyl)oxy)methyl)furan-2-yl)-2-methylisoxazolidine-4-carboxylate **5**




This compound could be isolated from the mixture of isomers by chromatography on silica gel. $^{1}$H NMR (400 MHz, DMSO-$d_6$, 90°C) δ 7.72 – 7.58 (m, 4H, $H_{Ph}$), 7.51 – 7.34 (m, 6H, $H_{Ph}$), 6.38 (d, $J$ = 3.2 Hz, 1H, $H_{3'}$), 6.21 (d, $J$ = 3.2 Hz, 1H, $H_{4'}$), 4.70 (s, 2H, $H_{6'}$), 4.13 (d, $J$ = 6.7 Hz, 2H, $H_5$), 3.98 (d, $J$ = 7.1 Hz, 1H, $H_3$), 3.72 – 3.61 (m, 4H, $H_4$&$CO_2C\underline{H}_3$), 2.57 (s, 3H, N-C$\underline{H}_3$), 1.04 (s, 9H, C(C$\underline{H}_3$)$_3$). $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 172.3 (C=O), 154.1 ($C_{5'}$), 150.8 ($C_{2'}$), 135.5, 133.7, 130.2, 128.2 ($C_{Ph}$), 109.7 ($C_{3'}$), 109.0 ($C_{4'}$), 68.2 ($C_5$), 59.0 ($C_{6'}$), 52.8 ($C_3$), 52.5 ($C_4$), 42.9 (N-$\underline{C}H_3$), 27.1 (C($\underline{C}H_3$)$_3$), 19.3 ($\underline{C}$(CH$_3$)$_3$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{27}H_{34}NO_5Si$ 480.2201; Found 480.2200.

Butyl 3-(4 and 5-(hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carboxylate **6**

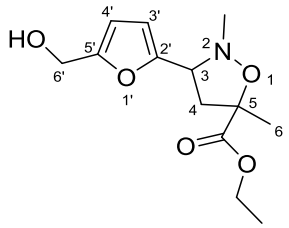
Mixture of isomers. HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{14}H_{21}NNaO_5$ 306.1312; Found 306.1308.




Signals extracted from the spectrum of the mixture for the major isomer: Butyl 3-(5-(hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carboxylate **6**

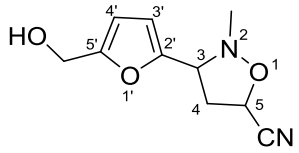
$^{1}$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.34, 6.29, 6.24, 6.22, 6.20, 6.16, and 6.13 (6d, $J$ = 3.2 Hz, 2H, $H_{3'}$ & $H_{4'}$), 4.66 & 4.60 (dd, $J$ = 8.9, 5.8 Hz, 1H, $H_5$), 4.42 – 4.29 (4s, 2H, C$\underline{H}_2$OH), 4.20 – 4.05 (m, 2H, $H_6$), 3.98 (t, $J$ = 7.3 Hz, 1H, $H_3$), 2.87 (ddd, $J$ = 12.5, 9.1, 7.7 Hz), 2.77 (ddd, $J$ = 12.7, 9.0, 7.0 Hz) and 2.66 (dddd, $J$ = 12.5, 9.4, 7.9, 5.9 Hz, 2H, $H_4$), 2.61 – 2.49 (4s, 3H, N-$\underline{C}H_3$), 1.64 – 1.49 (m, 2H, $H_7$), 1.41 – 1.26 (m, 2H, $CO_2(CH_2)_2C\underline{H}_2CH_3$), 0.93 – 0.75 (m, 3H, $CO_2(CH_2)_3C\underline{H}_3$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 171.5, 171.2, 170.9, 169.8 (C=O), 155.6, 155.23, 155.21, 154.9 ($C_{5'}$), 150.4, 150.3, 149.52, 149.47 ($C_{2'}$), 109.2, 108.8, 108.50, 108.47 ($C_{3'}$), 107.5, 107.40, 107.39, 107.3 ($C_{4'}$), 75.0, 74.1 ($C_5$), 64.5 ($C_6$), 63.7 ($C_3$), 55.7 ($\underline{C}H_2$OH), 43.3, 43.0, 42.7, 42.3 (N-$\underline{C}H_3$), 37.0 ($C_4$), 30.0 ($C_7$) , 18.4 ($CO_2(CH_2)_2\underline{C}H_2CH_3$), 13.1 ($CO_2(CH_2)_3\underline{C}H_3$).

Ethyl 3-(5-(hydroxymethyl)furan-2-yl)-2,5-dimethylisoxazolidine-5-carboxylate **7**



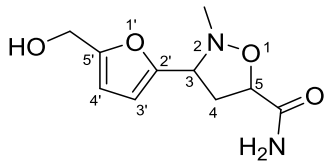
$^{1}$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.30 (d, $J$ = 3.2 Hz) and 6.26 (d, $J$ = 3.1 Hz) and 6.21 (t, $J$ = 3.3 Hz, 2H, $H_{3'}$&$H_{4'}$), 4.91 – 4.56 (m, 1H, OH), 4.38 (s, 2H, $H_{6'}$), 4.23 – 4.08 (m, 2H, $CO_2C\underline{H}_2CH_3$), 3.94 (t, $J$ = 7.9 Hz) and 3.73 (t, $J$ = 8.5 Hz, 1H, $H_3$), 2.57 (s, 3H, N-C$\underline{H}_3$), 3.03 (dd, $J$ = 12.6, 9.0 Hz, 3H) and 2.43 (td, $J$ = 12.4, 8.3 Hz, 2H, $H_4$), 1.44 (s, 3H, $H_6$), 1.24 (dt, $J$ = 9.6, 7.0 Hz, 3H, $CO_2CH_2C\underline{H}_3$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 173.1 (C=O), 155.2 ($C_{5'}$), 149.6 ($C_{2'}$), 108.2 ($C_{3'}$), 106.9 ($C_{4'}$), 80.4 ($C_5$), 64.8 ($C_3$), 60.0 ($CO_2\underline{C}H_2CH_3$), 55.4 ($C_{6'}$), 43.8 ($C_4$), 43.0 (N-$\underline{C}H_3$), 23.6 ($C_6$), 13.4 ($CO_2CH_2\underline{C}H_3$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{13}H_{20}NO_5$ 270.1336; Found 270.1333.

3-(5-(Hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carbonitrile **8**



This compound could be isolated from the mixture of isomers by chromatography on silica gel. $^{1}$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.39 (d, $J$ = 3.2 Hz, 1H, $H_{3'}$), 6.25 (d, $J$ = 3.2 Hz, 1H, $H_{4'}$), 5.19 (dd, $J$ = 9.2, 4.2 Hz, 1H, $H_5$), 4.89 (brs, 1H), 4.41 (s, 2H, C$\underline{H}_2$OH), 3.77 (t, $J$ = 8.2 Hz, 1H, $H_3$), 3.04 (ddd, $J$ = 12.8, 9.2, 8.4 Hz, 1H, $H_{4,a}$), 2.70 (ddd, $J$ = 12.6, 8.0, 4.2 Hz, 1H, $H_{4,b}$), 2.66 (s, 3H, N-$\underline{C}H_3$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 155.6 ($C_{5'}$), 148.5 ($C_{2'}$), 119.3 (CN), 108.9 ($C_{3'}$), 107.1 ($C_{4'}$), 63.9 ($C_3$), 63.3 ($C_5$), 55.4 ($\underline{C}H_2$OH), 42.3 (N-$\underline{C}H_3$), 38.8 ($C_4$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{10}H_{12}N_2NaO_3$ 231.0740; found 231.0748.

3-(5-(Hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carboxamide **9**

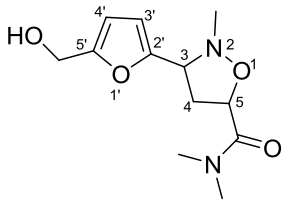


This compound was able to isolate from the mixture of isomers by chromatography on silica gel. $^{1}$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.87 (brs, 2H), 6.28 (d, $J$ = 3.1 Hz, 1H, $H_{3'}$), 6.20 (d, $J$ = 3.2 Hz, 1H, $H_{4'}$), 4.44 (dd, $J$ = 9.4, 5.7 Hz, 1H, $H_5$), 4.38 (s, 2H, C$\underline{H}_2$OH), 3.73 (t, $J$ = 8.1 Hz, 1H, $H_3$), 2.86 (ddd, $J$ = 12.5, 9.3, 7.7 Hz, 1H, $H_{4,a}$), 2.64 (s, 3H, N-C$\underline{H}_3$), 2.58 (ddd, $J$ = 12.5, 8.6, 5.7 Hz, 1H, $H_{4,b}$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 173.6 ($\underline{C}ONH_2$), 155.2 ($C_{5'}$), 149.8 ($C_{2'}$), 108.2 ($C_{3'}$), 106.9 ($C_{4'}$),

74.9 ($C_5$), 64.5 ($C_3$), 55.4 ($\underline{C}H_2OH$), 42.8 (N-$\underline{C}H_3$), 37.3 ($C_4$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{10}H_{15}N_2O_4$ 227.1026; found 227.1030.

3-(4 and 5-(Hydroxymethyl)furan-2-yl)-N,N,2-trimethylisoxazolidine-5-carboxamide **10**

Mixture of isomers. HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{12}H_{19}N_2O_4$ 255.1339; found 255.1339.

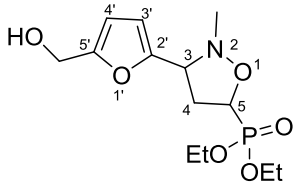



Signals extracted from the spectrum of the mixture for the major isomer: 3-(5-(Hydroxymethyl)furan-2-yl)-N,N,2-trimethylisoxazolidine-5-carboxamide **10**

$^1$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.31 (d, $J$ = 3.2 Hz, 1H, $H_{3'}$), 6.21 (d, $J$ = 3.1 Hz, 1H, $H_{4'}$), 4.89 (dd, $J$ = 8.5, 5.6 Hz, 1H, $H_5$), 4.41 (s, 2H, $C\underline{H}_2OH$), 3.90 (t, $J$ = 7.6 Hz, 1H, $H_3$), 3.10 – 2.81 (m, 7H, $H_{4,a}$ & CON($C\underline{H}_3$)$_2$), 2.63 – 2.53 (m, 4H, $H_{4,b}$ & N-$C\underline{H}_3$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 168.2 ($\underline{C}ONMe_2$), 155.1 ($C_{5'}$), 150.6 ($C_{2'}$), 107.9 ($C_{3'}$), 106.9 ($C_{4'}$), 73.8 ($C_5$), 64.3 ($C_3$), 55.6 ($\underline{C}H_2OH$), 43.0 (N-$\underline{C}H_3$), 35.6 ($C_4$ & CON$\underline{Me}_2$).

Diethyl (3-(4 and 5-(hydroxymethyl)furan-2-yl)-2-methylisoxazolidin-5-yl)phosphonate **11**

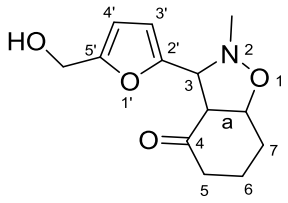
Mixture of isomers. HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{13}H_{22}NNaO_6P$ 342.1077; found 342.1081.




Signals extracted from the spectrum of the mixture for the major isomer: Diethyl (3-(5-(hydroxymethyl)furan-2-yl)-2-methylisoxazolidin-5-yl)phosphonate **11**

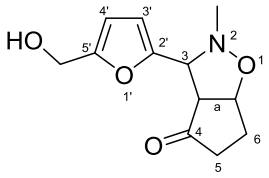
$^1$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.39 (d, $J$ = 3.2 Hz) & 6.32 (t, $J$ = 3.6 Hz) & 6.24 – 6.19 (m) ($H_{3'}$ & $H_{4'}$), 4.45 (dd, $J$ = 8.6, 1.7 Hz) 4.33 (td, $J$ = 7.2, 3.7 Hz) ($H_5$), 4.40 (s, 2H, $C\underline{H}_2OH$), 4.17 – 4.06 (m, 4H, PO(O$C\underline{H}_2CH_3$)$_2$), 4.00 (d, $J$ = 12.8 Hz), 3.97 – 3.91 (m), 2.78 – 2.64 (m, $H_3$&$H_4$), 2.58 (s, 3H, N-$C\underline{H}_3$), 1.33 – 1.25 (m) & 1.26 – 1.14 (m) (PO(OCH$_2$C$\underline{H}_3$)$_2$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 155.4 , ($C_{5'}$), 149.8 ($C_{2'}$), 108.2 ($C_{3'}$), 106.9 ($C_{4'}$), 71.8, 70.5 ($C_5$), 65.63 , 63.92 ($C_3$) 62.0 – 61.1 (PO(O$\underline{C}H_2CH_3$)$_2$), 55.5 ($\underline{C}H_2OH$), 43.3 (N-$\underline{C}H_3$), 34.9 ($C_4$), 15.7 (ddd, $J$ = 21.8, 5.4, 2.8 Hz, PO(OCH$_2$$\underline{C}H_3$)$_2$).

3-(5-(Hydroxymethyl)furan-2-yl)-2-methylhexahydrobenzo[d]isoxazol-4(2H)-one **12**



$^{1}$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.30 (d, $J$ = 3.1 Hz, 1H, $H_{3'}$), 6.21 (d, $J$ = 3.1 Hz, 1H, $H_{4'}$), 4.57 (dt, $J$ = 7.2, 4.7 Hz, 1H, $H_{7a}$), 4.40 (s, 2H, C$\underline{H}_2$OH), 4.10 (d, $J$ = 5.6 Hz, 1H, $H_3$), 3.49 – 3.42 (m, 1H, $H_{3a}$), 2.58 (s, 3H, N-$CH_3$), 2.46 (dt, $J$ = 16.0, 8.0 Hz, 1H, $H_{5,a}$), 2.35 (dt, $J$ = 16.1, 5.4 Hz, 1H, $H_{5,b}$), 2.08 – 1.96 (m, 1H, $H_{7,a}$), 1.91 – 1.81 (m, 2H, $H_6$), 1.79 – 1.72 (m, 1H, $H_{7,b}$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 207.8 (C=O), 155.1 ($C_{5'}$), 150.8 ($C_{2'}$), 108.1 ($C_{3'}$), 106.9 ($C_{4'}$), 76.7 ($C_{7a}$), 65.7 ($C_3$), 58.6 ($C_{3a}$), 55.5 (C$\underline{H}_2$OH), 43.1 (N-$\underline{C}H_3$), 39.0 ($C_5$), 25.4 ($C_7$), 18.6 ($C_6$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{13}H_{18}NO_4$ 252.1230; found 252.1230.

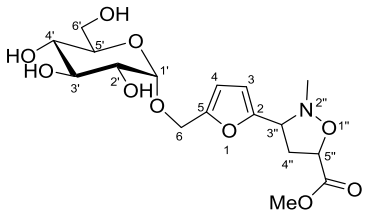
3-(5-(Hydroxymethyl)furan-2-yl)-2-methylhexahydro-4H-cyclopenta[d]isoxazol-4-one **13**



$^{1}$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.34 (d, $J$ = 3.1 Hz, 1H, $H_{3'}$), 6.23 (d, $J$ = 3.1 Hz, 1H, $H_{4'}$), 4.85 (t, $J$ = 5.7 Hz, 1H, $H_{6a}$), 4.41 (s, 2H, C$\underline{H}_2$OH), 3.72 (d, $J$ = 5.2 Hz, 1H, $H_3$), 3.37 – 3.27 (m, 1H, $H_{3a}$), 2.53 (s, 3H, N-$CH_3$), 2.51 – 2.45 (m, 1H, $H_{5,a}$), 2.30 (dddd, $J$ = 18.3, 9.5, 3.2, 1.5 Hz, 1H, $H_{5,b}$), 2.23 – 2.13 (m, 1H, $H_{6,a}$), 2.09 – 2.01 (m, 1H, $H_{6,b}$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 216.0 (C=O), 155.5 ($C_{5'}$), 149.6 ($C_{2'}$), 108.7 ($C_{3'}$), 107.0 ($C_{4'}$), 79.4 ($C_{6a}$), 68.4 ($C_3$), 59.8 ($C_{3a}$), 55.5 (C$\underline{H}_2$OH), 42.1 (N-$\underline{C}H_3$), 34.7 ($C_5$), 24.0 ($C_6$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{12}H_{16}NO_4$ 238.1074; found 238.1076.

Methyl 2-methyl-3-(4 and 5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)isoxazolidine-5-carboxylate **14**

Mixture of isomers. HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{17}H_{26}NO_{10}$ 404.1551; found 404.1560.

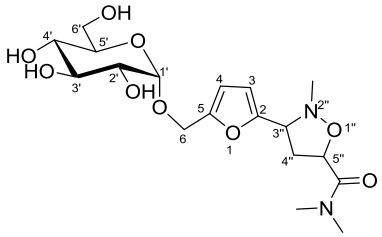


Signals extracted from the spectrum of the mixture for the major isomer: Methyl 2-methyl-3-(5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)isoxazolidine-5-carboxylate **14**

$^1$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.41 – 6.27 (m, 2H, $H_3$ & $H_4$), 4.80 – 4.76 (m, 1H, $H_{1'}$), 4.72 (dd, $J$ = 9.1, 5.9 Hz) and 4.66 (dd, $J$ = 8.9, 5.9 Hz) ($H_{5''}$), 4.53 – 4.43 (m, 2H, $H_6$), 4.08 – 3.99 (m, 1H, $H_{3''}$), 3.73 (s, 3H, $CO_2C\underline{H}_3$), δ 3.68 – 3.63 (m), 3.62 – 3.57 (m), 3.56 – 3.50 (m), 3.49 – 3.43 (m) (4H, $H_{3'}$, $H_{5'}$, $H_{6'}$), 3.27 (dd, $J$ = 10.2, 4.2 Hz, $H_{2'}$), 3.16 (t, $J$ = 9.3 Hz, 1H, $H_{4'}$), 2.83 – 2.69 (m, 1H, $H_{4''}$), 2.56 (s, 3H, N-$CH_3$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 170.8 ($\underline{C}$=O), 151.1 ($C_2$ & $C_5$), 109.5, 107.8 ($C_3$ & $C_4$), 97.5 ($C_{1'}$), 74.5 ($C_{5''}$), 73.1, 72.5, 71.7 ($C_{3'}$ & $C_{2'}$ & $C_{5'}$), 70.3 ($C_{4'}$), 67.2 , 66.3 ($C_{3''}$), 60.9 ($C_{6'}$), 60.28 ($C_6$), 51.4 ($CO_2\underline{C}H_3$), 42.1 (N-$CH_3$), 36.7 ($C_{4''}$).

*N*,*N*,2-Trimethyl-3-(4 and 5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)isoxazolidine-5-carboxamide **15**

Mixture of isomers. HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{18}H_{29}N_2O_9$ 417.1868; found, 417.1864.

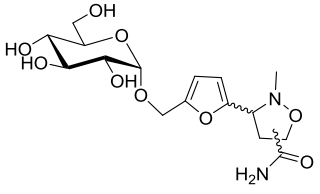



Signals extracted from the spectrum of the mixture for the major isomer: *N*,*N*,2-Trimethyl-3-(5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)isoxazolidine-5-carboxamide **15**

$^1$H NMR (500 MHz, DMSO-$d_6$, 90°C) δ 6.48 – 6.15 (m, 2H, $H_3$&$H_4$), 4.91 (dd, $J$ = 8.5, 5.9 Hz, 1H, $H_{5''}$), 4.80 (t, $J$ = 4.4 Hz, 1H, $H_{1'}$), 4.59 (d, $J$ = 13.1 Hz, 1H, $H_{6,a}$), 4.48 (dd, $J$ = 13.1, 1.6 Hz, 1H, $H_{6,b}$), 4.02 – 3.89 (m, 1H, $H_{3''}$), 3.67 (dd, $J$ = 11.4, 2.6 Hz, 1H, $H_{6',a}$), 3.57 – 3.41 (m, 3H, $H_{6',b}$, $H_{3'}$, $H_{5'}$), 3.29 (dd, $J$ = 9.6, 3.7 Hz, 1H, $H_{2'}$), 3.18 (t, $J$ = 9.2 Hz, 1H, $H_{4'}$), 3.00 – 2.83 (m, 6H, CON($C\underline{H}_3$)$_2$), 2.59 (s, 4H, N-$C\underline{H}_3$, $H_{4''}$). $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 170.7, 169.4, 169.1, 168.9 ($\underline{C}$ON($CH_3$)$_2$), 152.6, 151.9 ($C_2$, $C_5$), 110.4, 108.9 ($C_3$, $C_4$), 98.5 ($C_{1'}$), 74.6 ($C_{5''}$), 74.5, 74.0, 73.3, 72.6, 71.2 ($C_{3'}$ & $C_{5'}$ & $C_{2'}$ & $C_{4'}$), 68.9, 65.0 ($C_{3''}$), 61.8 ($C_{6'}$), 61.3 ($C_6$), 44.0 (N-$\underline{C}H_3$), 36.4 (CON($\underline{C}H_3$)$_2$ & $C_{4''}$).

2-Methyl-3-(4 and 5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)isoxazolidine-5-carboxamide **16**

Mixture of isomers. HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{16}H_{25}N_2O_9$ 389.1555; found 389.1542.

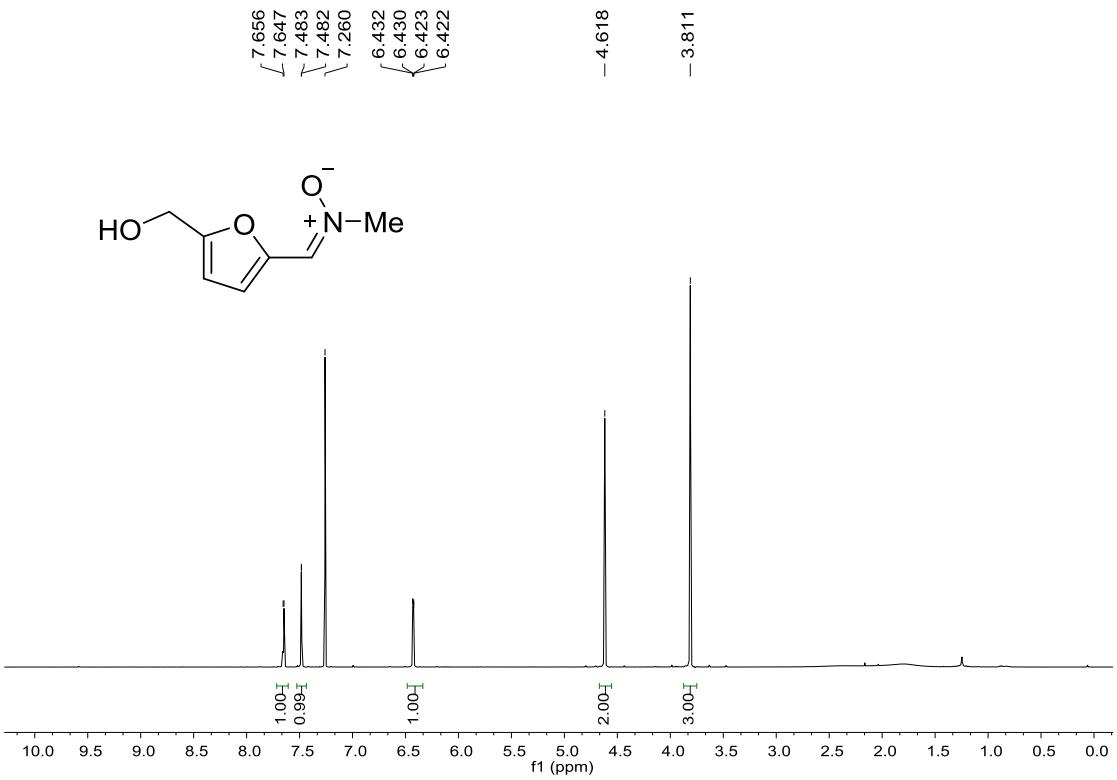


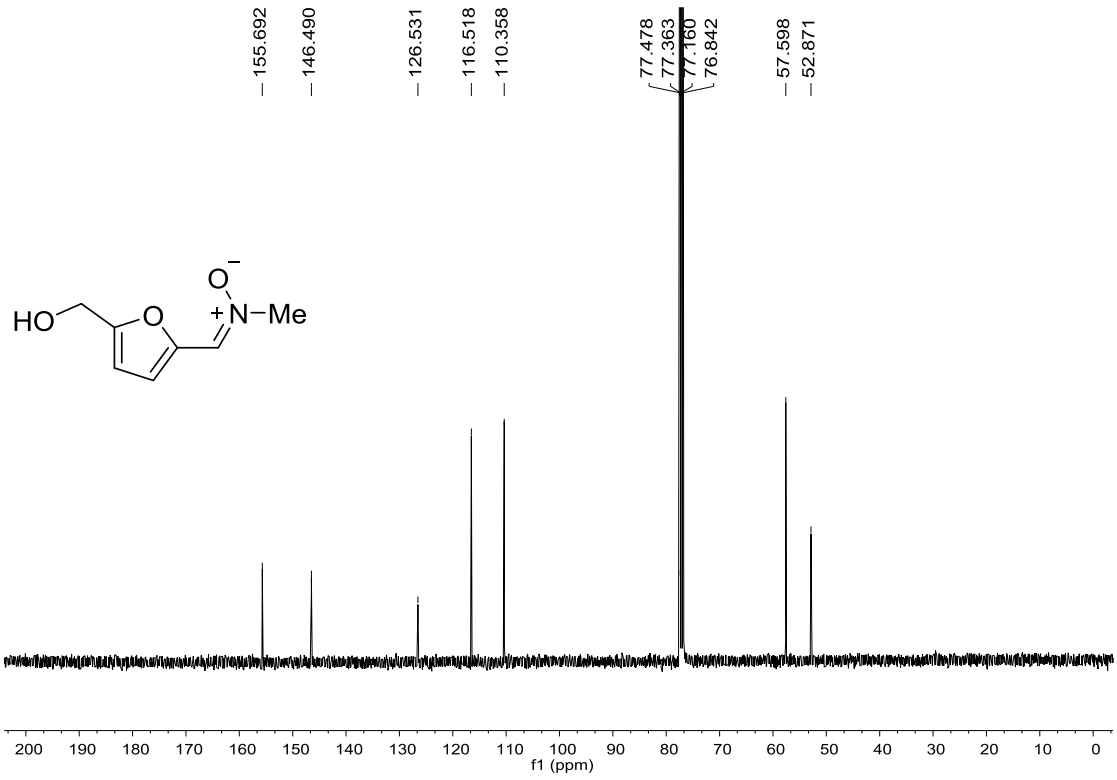
Signals extracted from the spectrum of the mixture for the major isomer: 2-Methyl-3-(5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)isoxazolidine-5-carboxamide **16**

This compound was able to isolate from the mixture of isomers by chromatography on silica gel. $^{1}$H NMR (400 MHz, DMSO-$d_6$, 90°C) δ 6.39 – 6.36 (m) & 6.35 (d, $J$ = 3.2 Hz) (2H, $H_3$ & $H_4$), 4.77 (dd, $J$ = 5.3, 3.6 Hz, 1H, $H_{1'}$), 4.57 (d, $J$ = 13.2 Hz, 1H, $H_{6,a}$), 4.50 – 4.37 (m, 2H, , $H_{6,b}$ & $H_{5''}$), 4.22 – 4.11 (m, 1H) (m, 1H, $H_{3''}$), 3.68 – 3.59 (m, 1H, $H_{6', a}$), 3.58 – 3.37 (m, 3H, $H_{6', b}$, $H_{3'}$, $H_{5'}$), 3.27 (dd, $J$ = 9.7, 3.7 Hz, 1H, $H_{2'}$), 3.21 – 3.10 (m, 1H, $H_{4'}$), 2.70 (dd, $J$ = 9.0, 6.9 Hz, 1H, $H_{4'', a}$), 2.61 (s, 3H, N-$CH_3$), 2.59 – 2.53 (m, 1H, $H_{4'', b}$). $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 173.2 ($\underline{C}ONH_2$), 152.2, 152.0 ($C_2$, $C_5$), 110.4, 109.1 ($C_3$, $C_4$), 100.0, 98.5 ($C_{1'}$), 76.6 ($C_{5''}$), 73.9, 73.4, 72.5, 71.2 ($C_{3'}$& $C_{5'}$& $C_{2'}$& $C_{4'}$), 69.3 ($C_{3''}$), 61.7 ($C_{6'}$), 61.2 ($C_6$), 43.6 (N-$\underline{C}H_3$), 38.0 ($C_{4''}$).

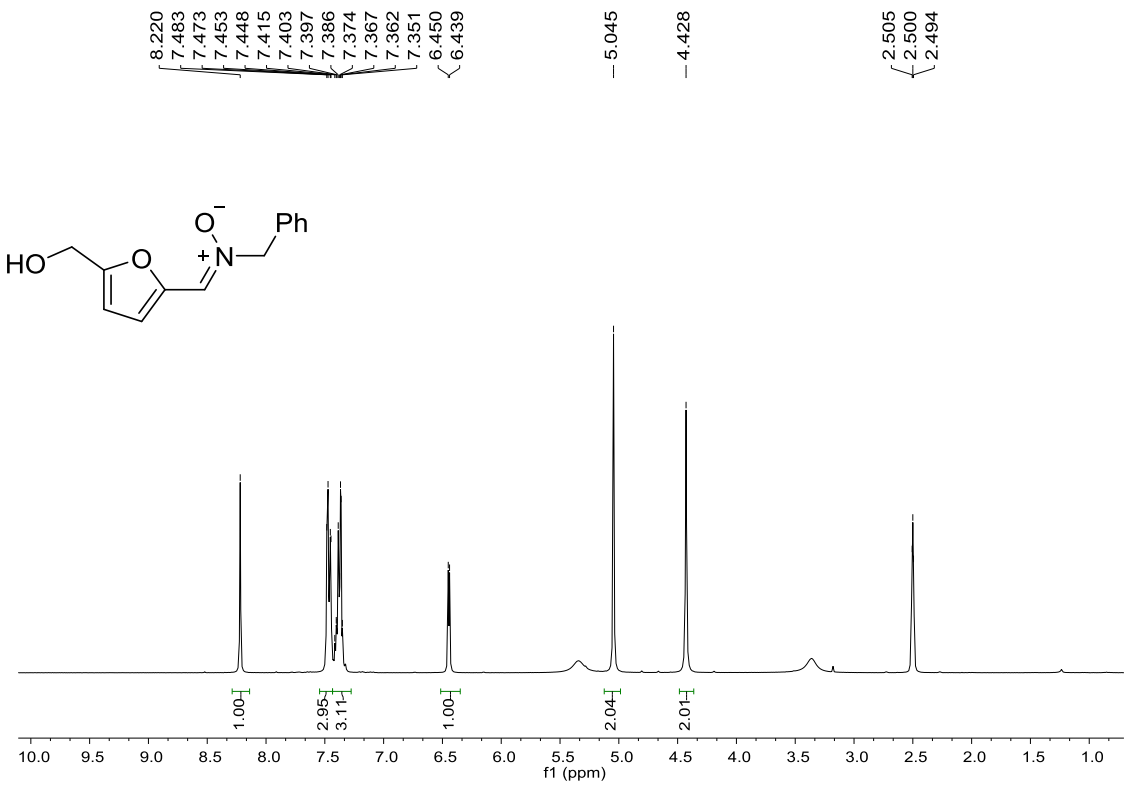
## 5. NMR Spectra of isoxazolidine products

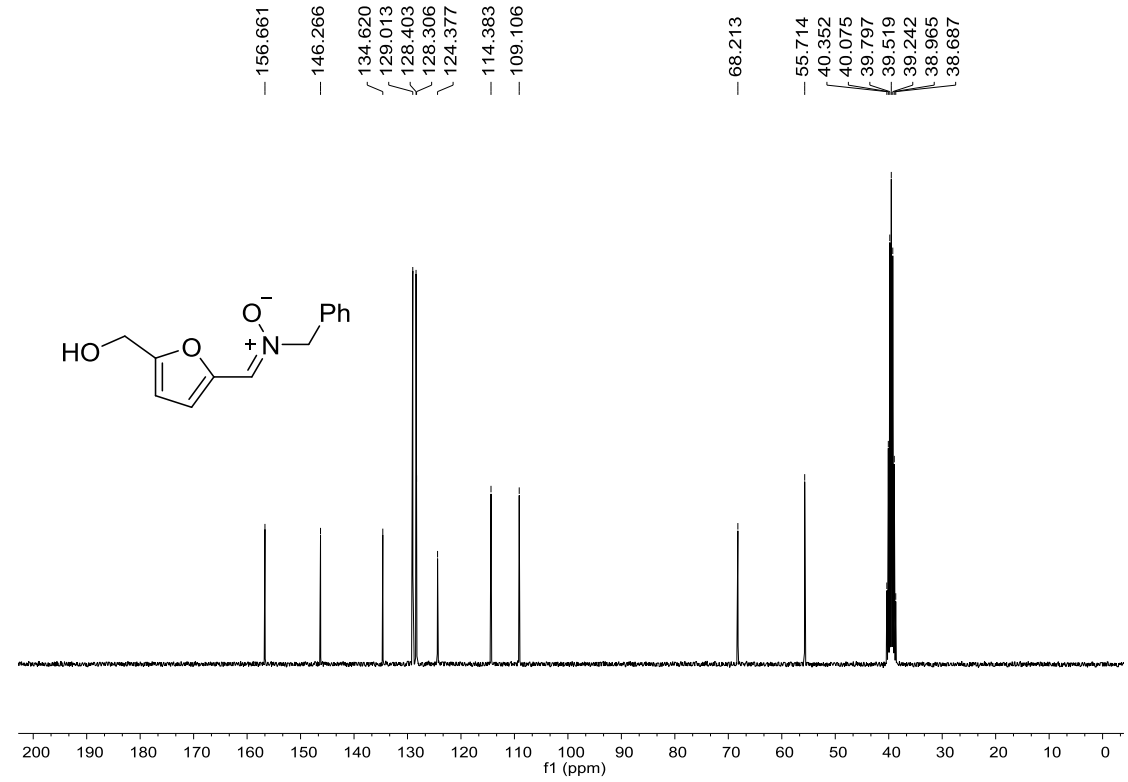
(Z)-1-(5-(Hydroxymethyl)furan-2-yl)-*N*-methylmethanimine oxide **1a**



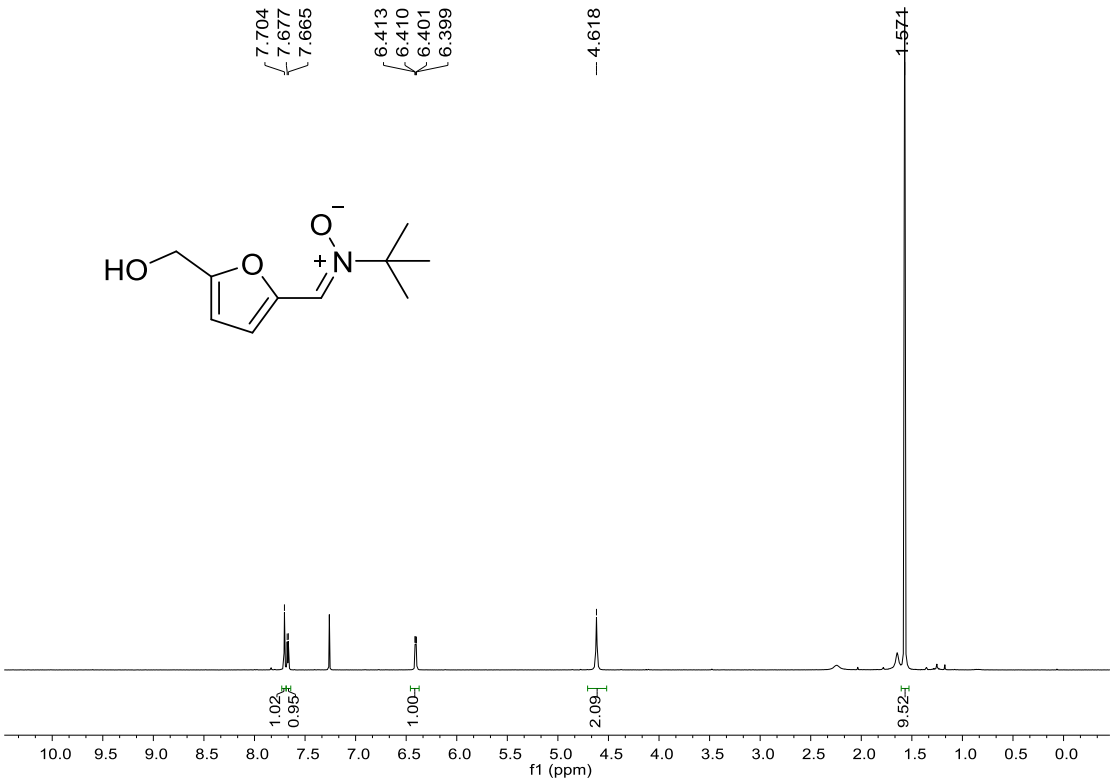



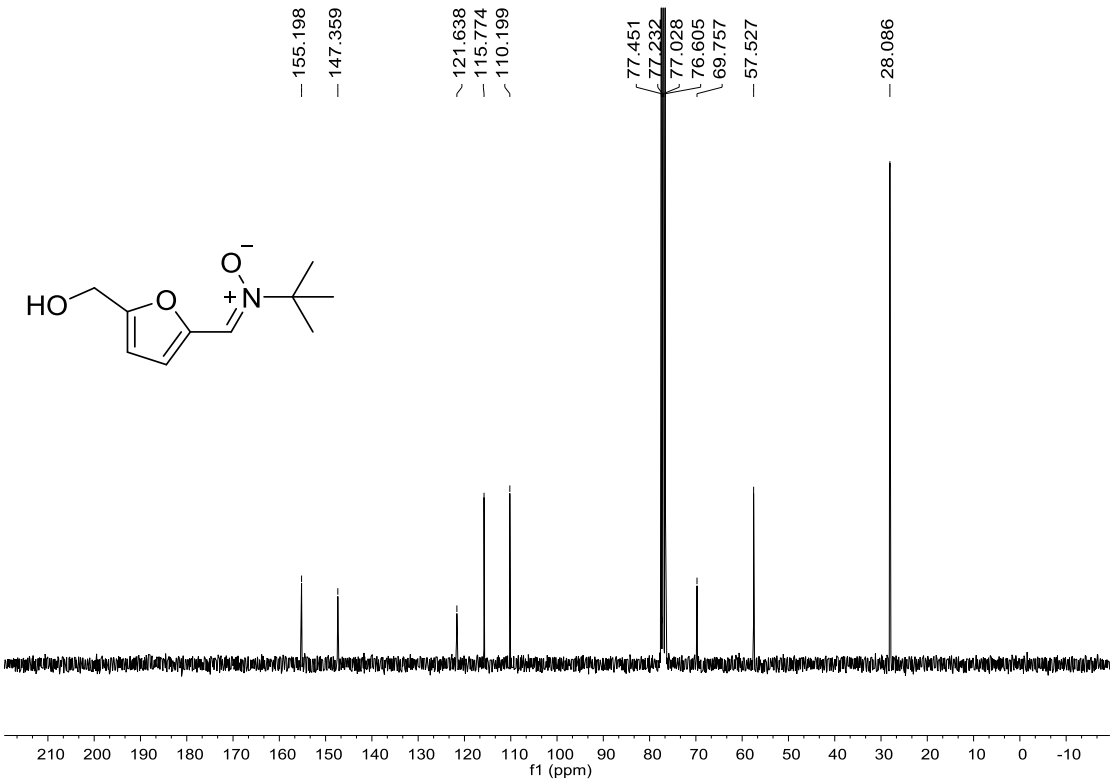
(Z)-*N*-Benzyl-1-(5-(hydroxymethyl)furan-2-yl)methanimine oxide **1b**



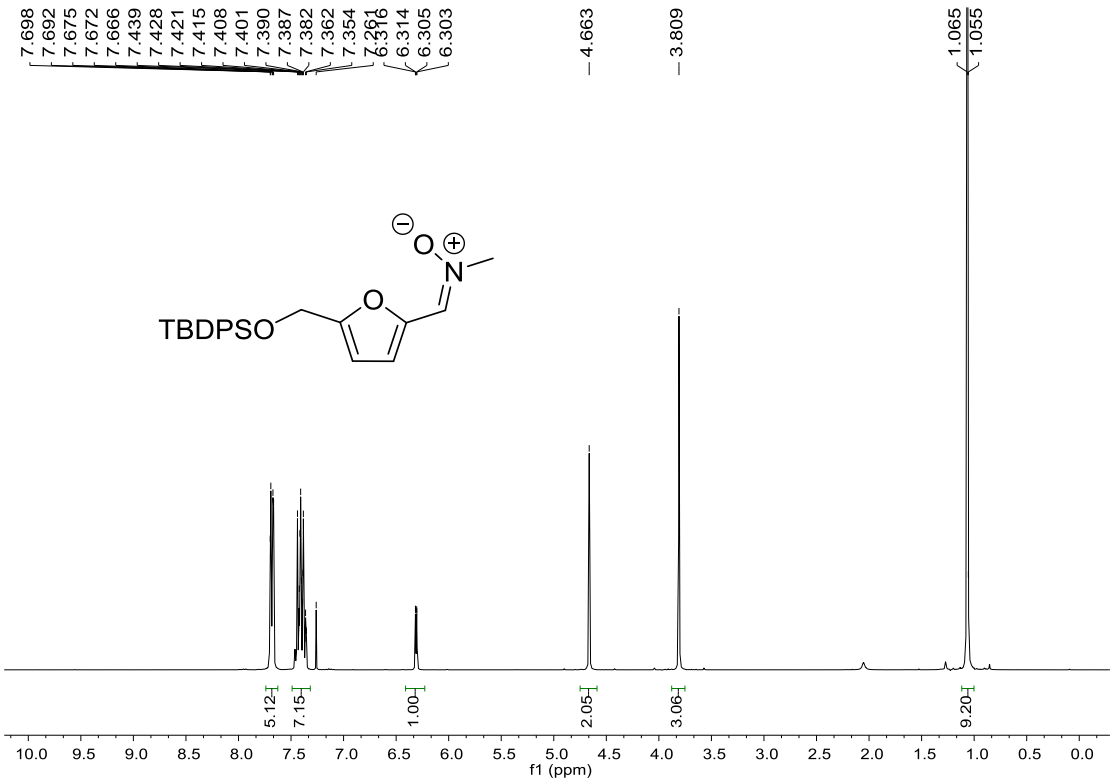



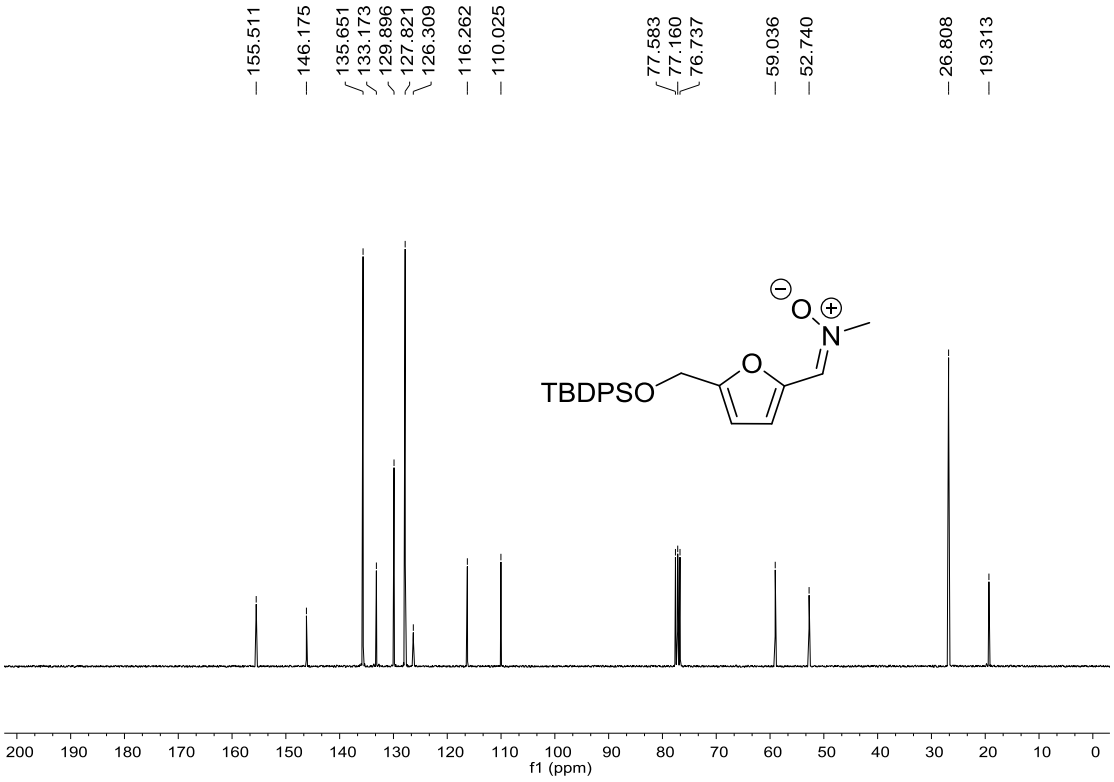
(Z)-*N*-tert-Butyl-1-(5-(hydroxymethyl)furan-2-yl)methanimine oxide **1c**



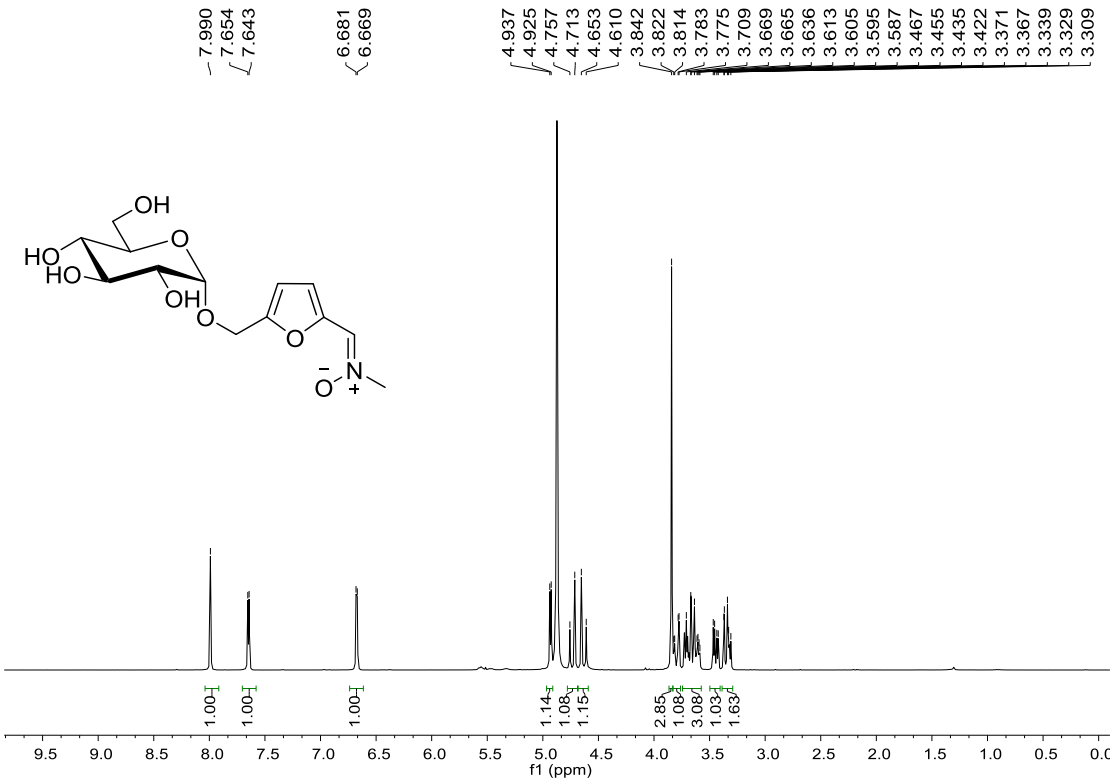



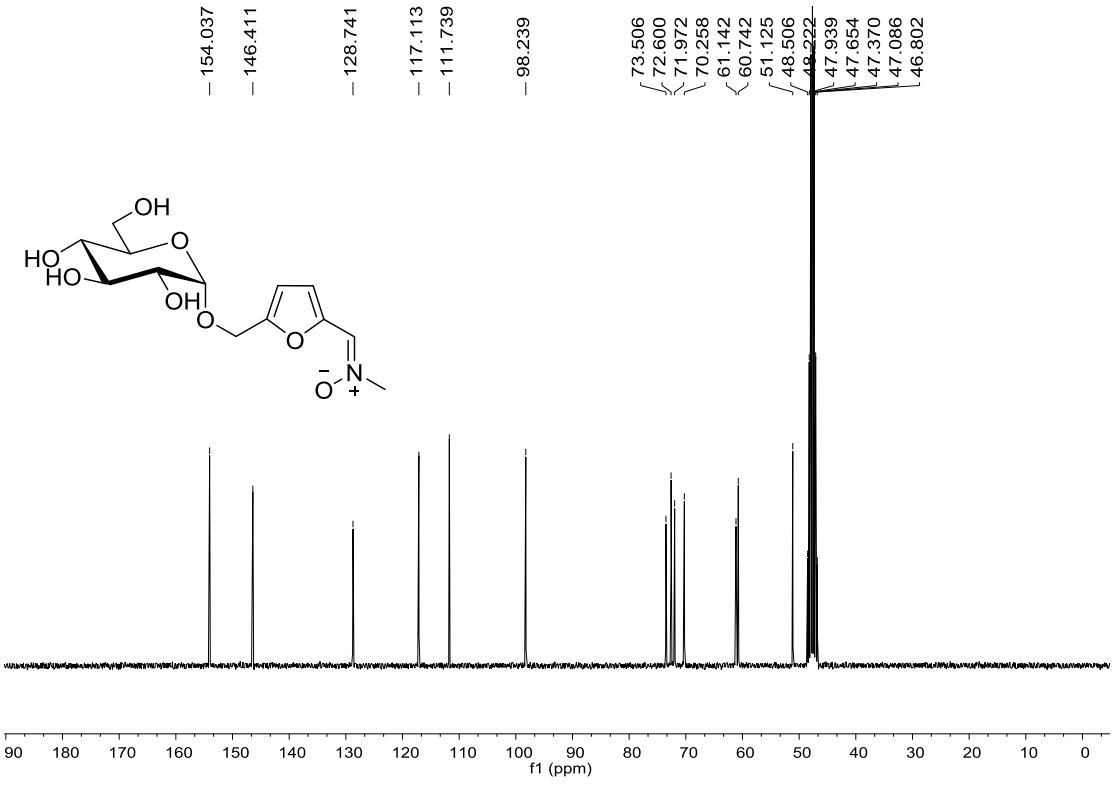
(Z)-1-(5-(((tert-Butyldiphenylsilyl)oxy)methyl)furan-2-yl)-*N*-methylmethanimine oxide **1d**



(Z)-*N*-Methyl-1-(5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)methanimine oxide **1e**

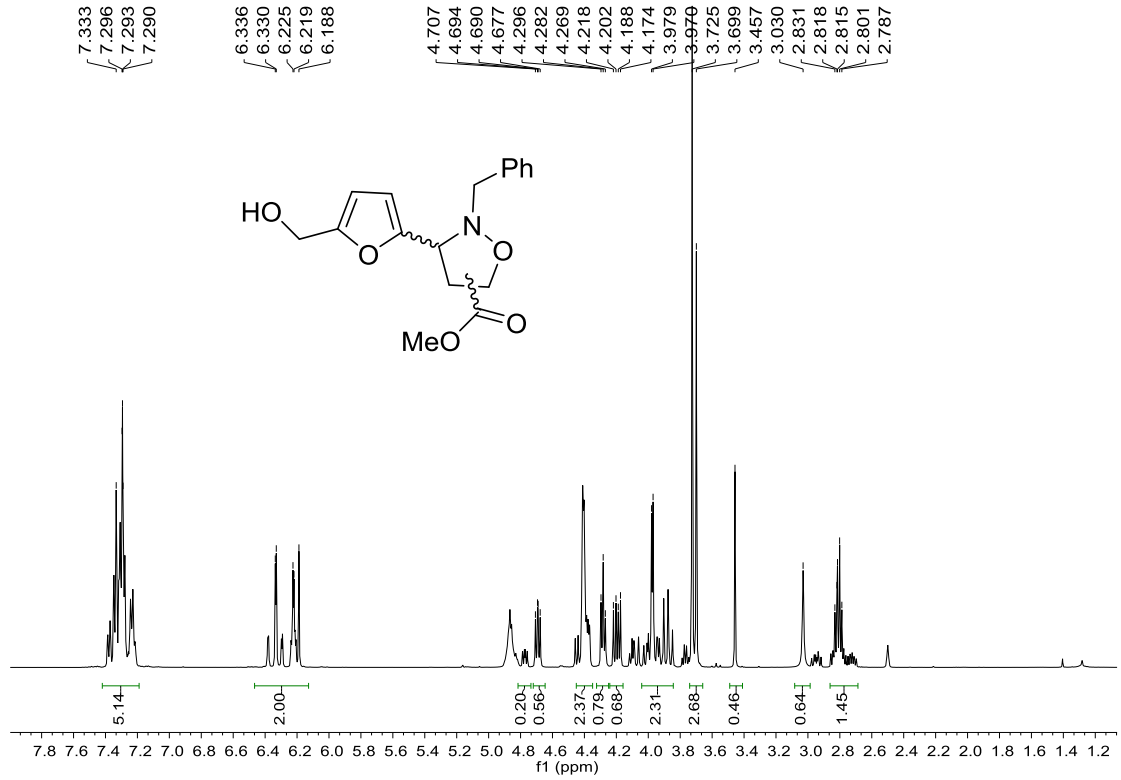


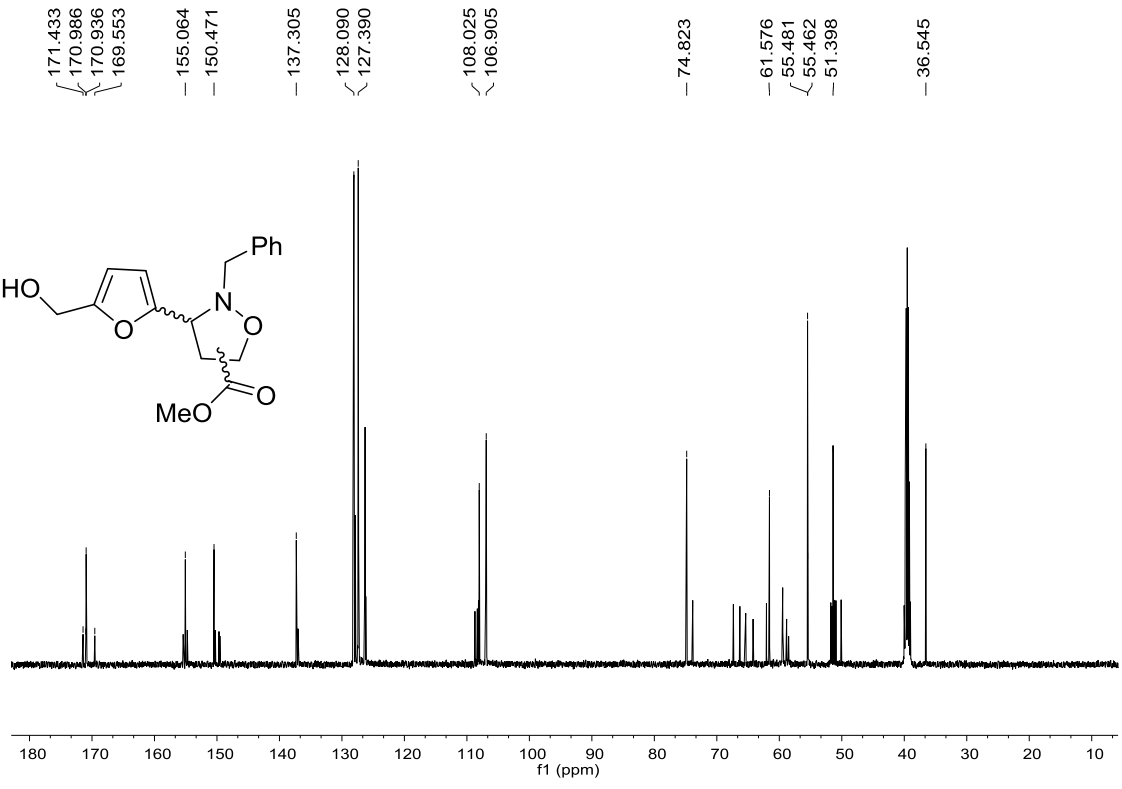



Methyl 3-(4 and 5-(hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carboxylate **2+2'**

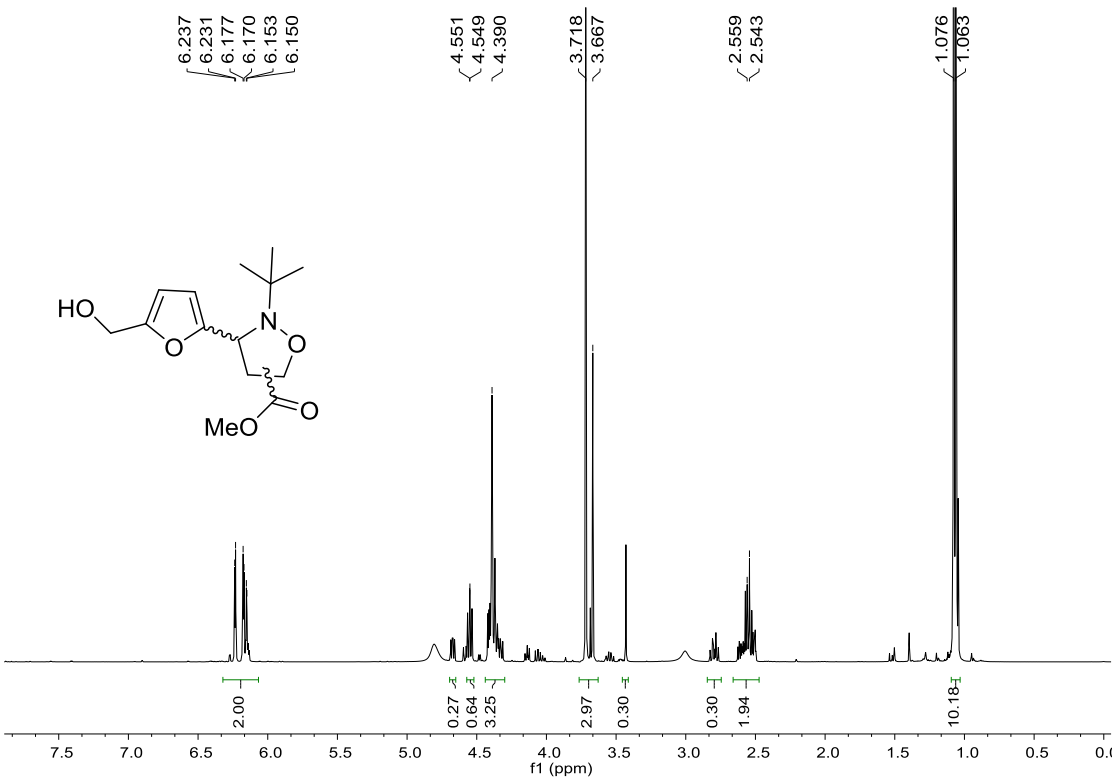
**See section 3**

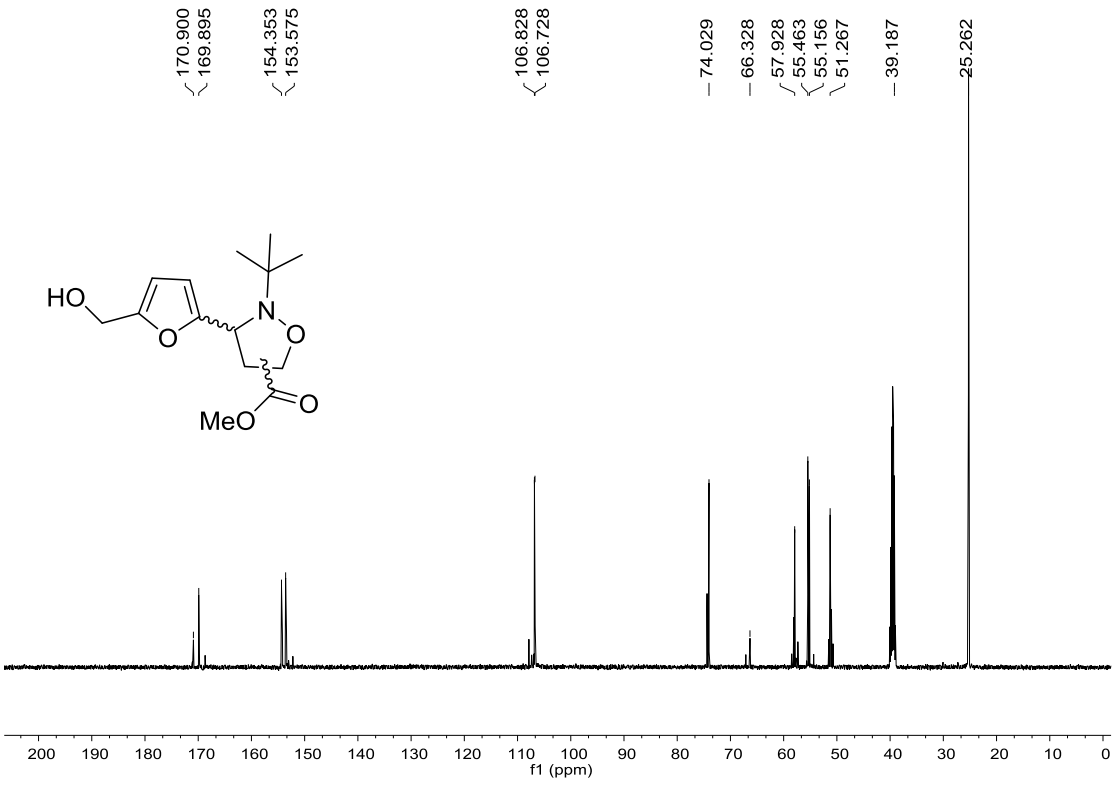
Methyl 2-benzyl-3-(4 and 5-(hydroxymethyl)furan-2-yl)isoxazolidine-5-carboxylate **3**



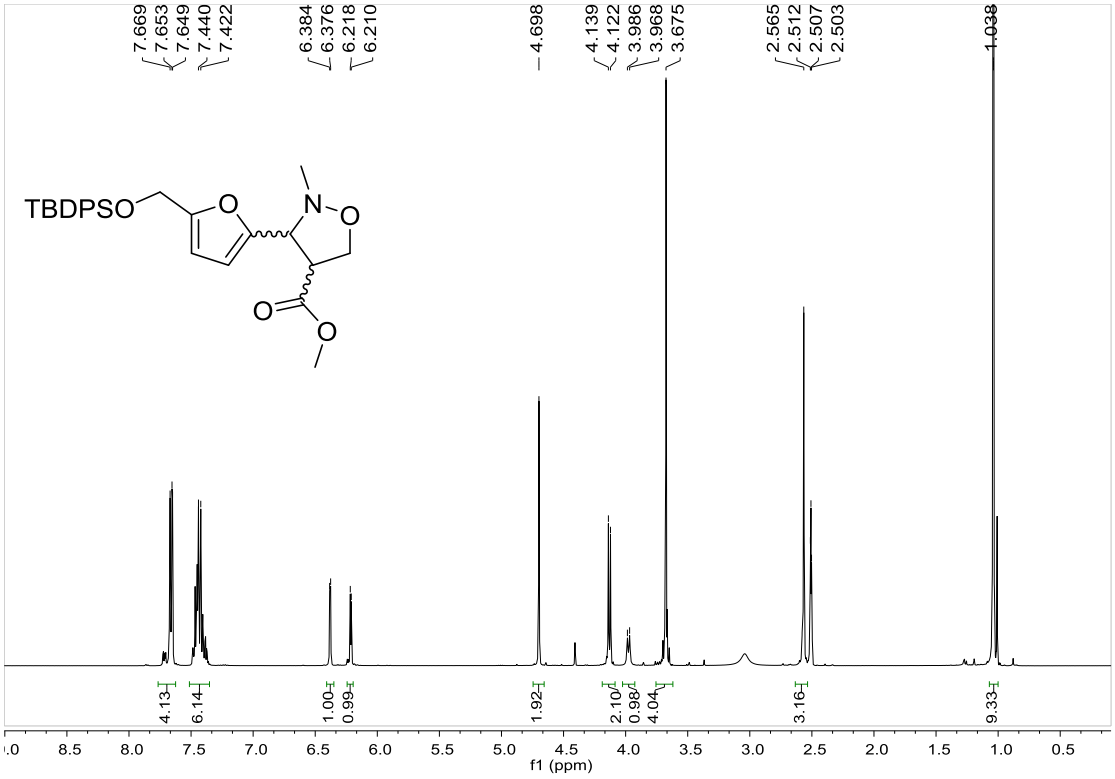



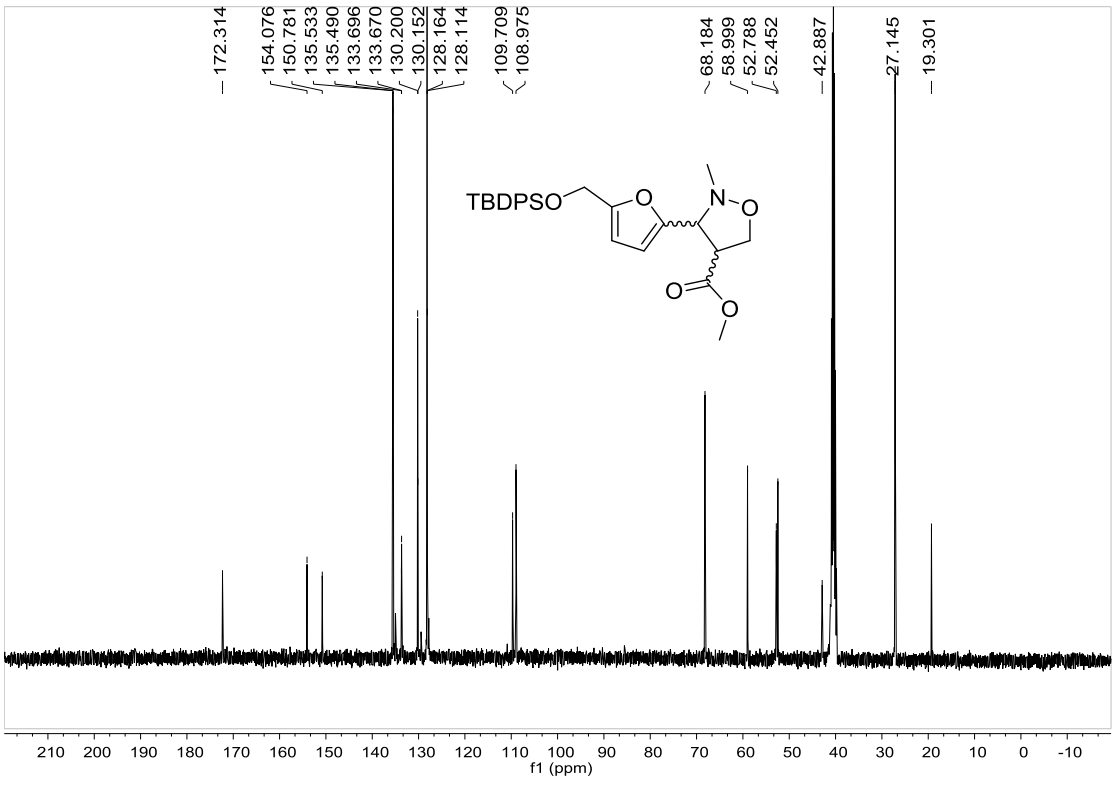
Methyl 2-(tert-butyl)-3-(4 and 5-(hydroxymethyl)furan-2-yl)isoxazolidine-5-carboxylate **4**



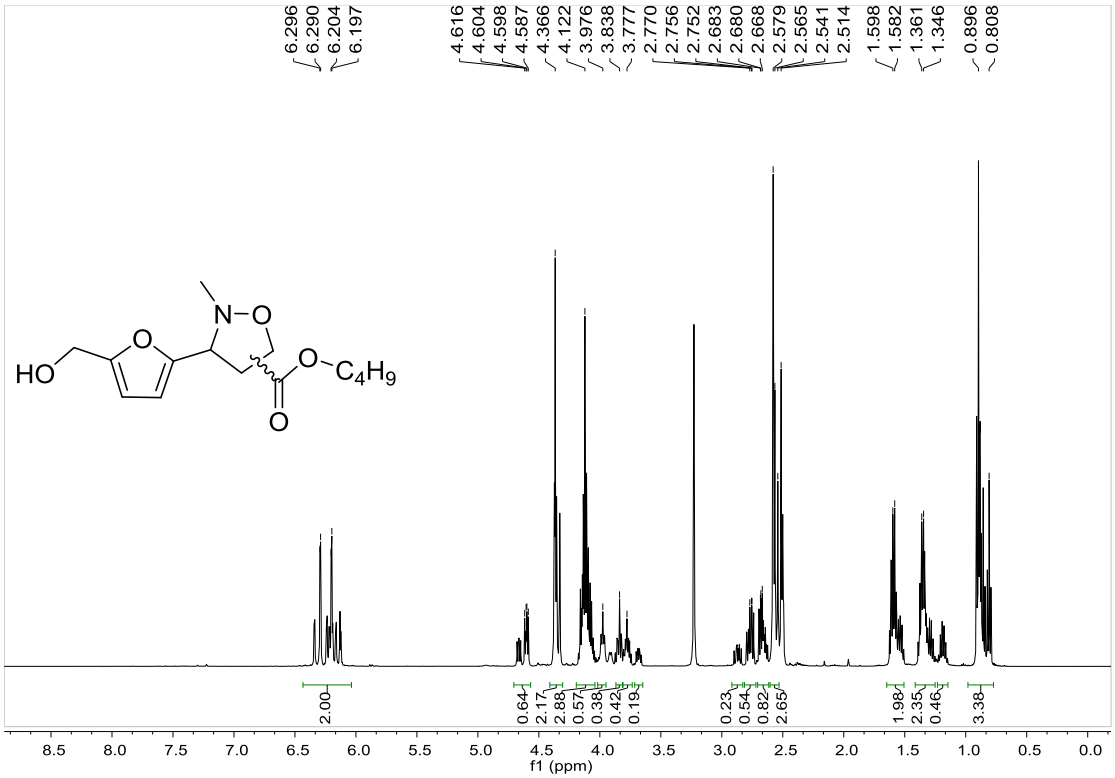



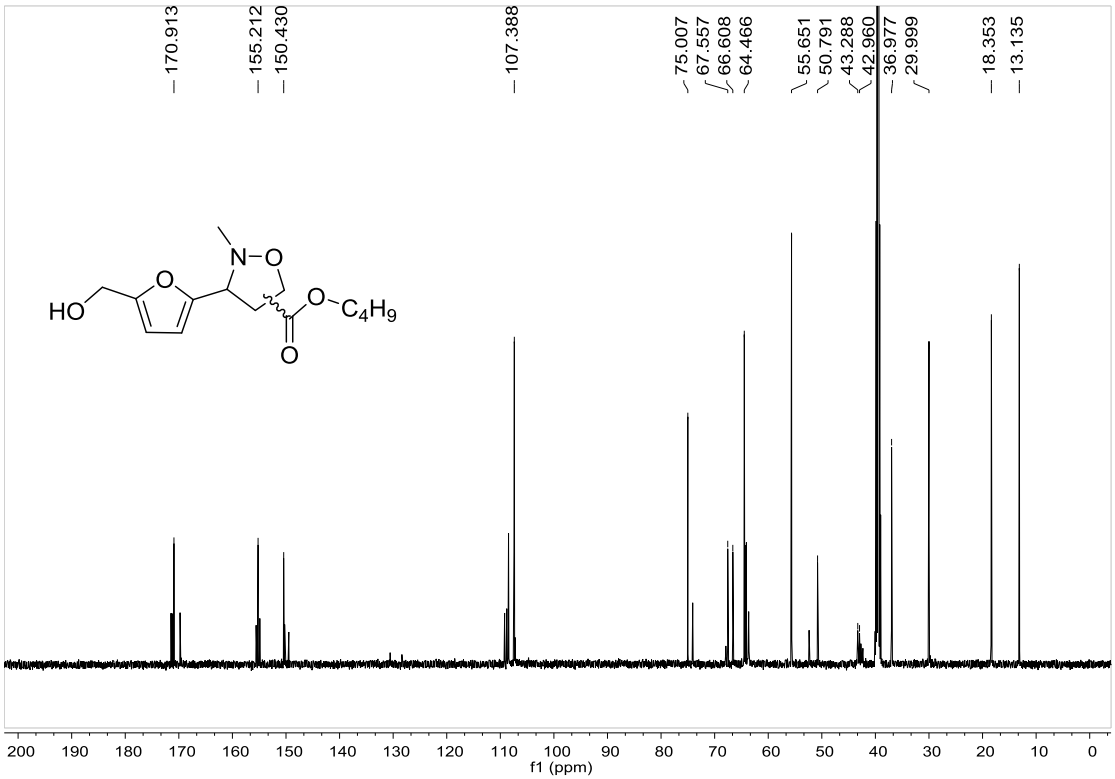
Methyl 3-(5-(((tert-butyldiphenylsilyl)oxy)methyl)furan-2-yl)-2-methylisoxazolidine-4-carboxylate **5**



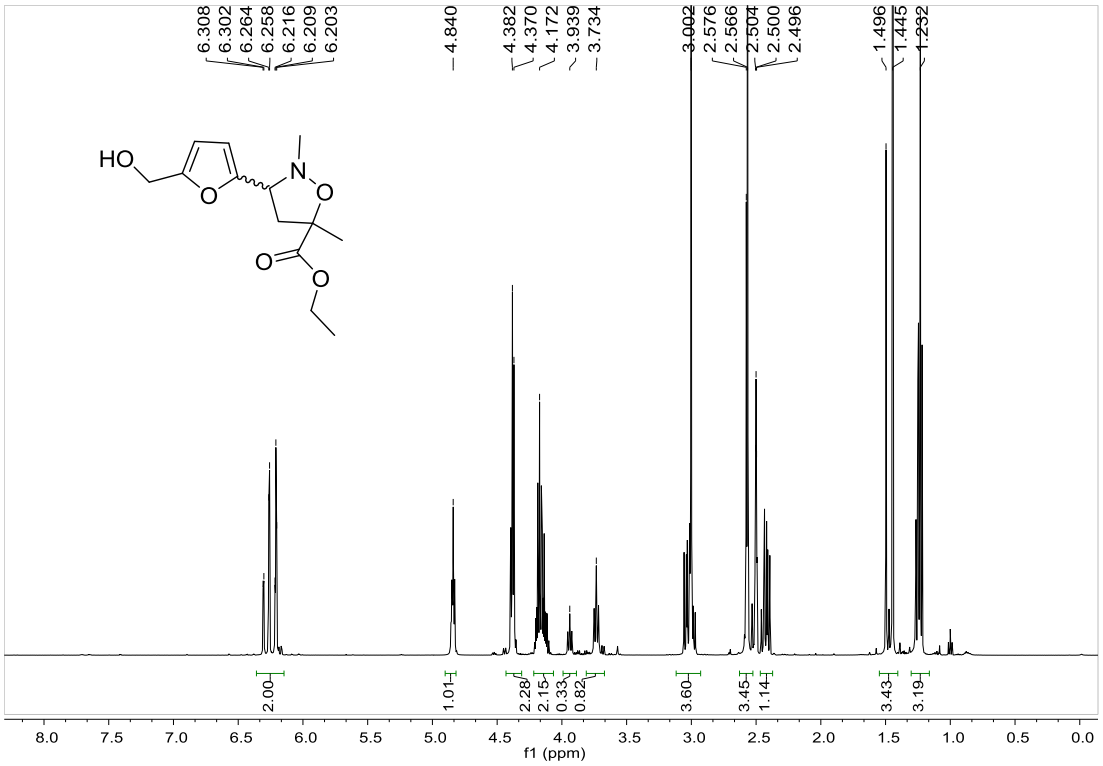



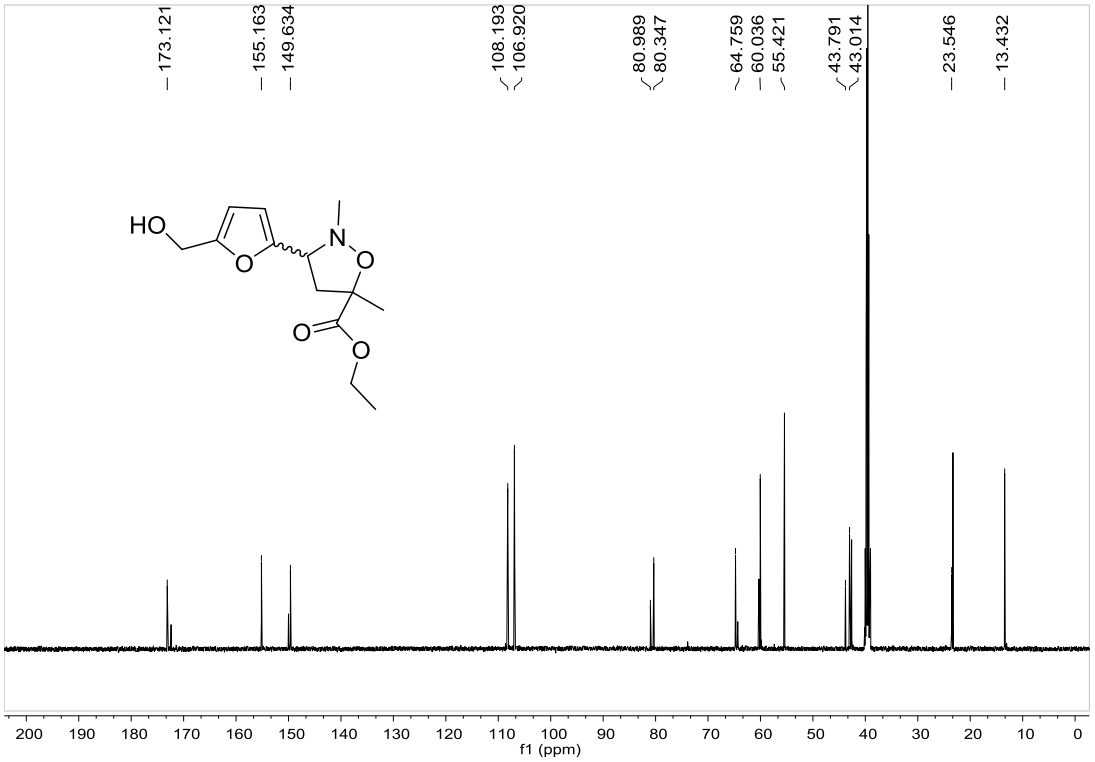
Butyl 3-(4 and 5-(hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carboxylate **6**



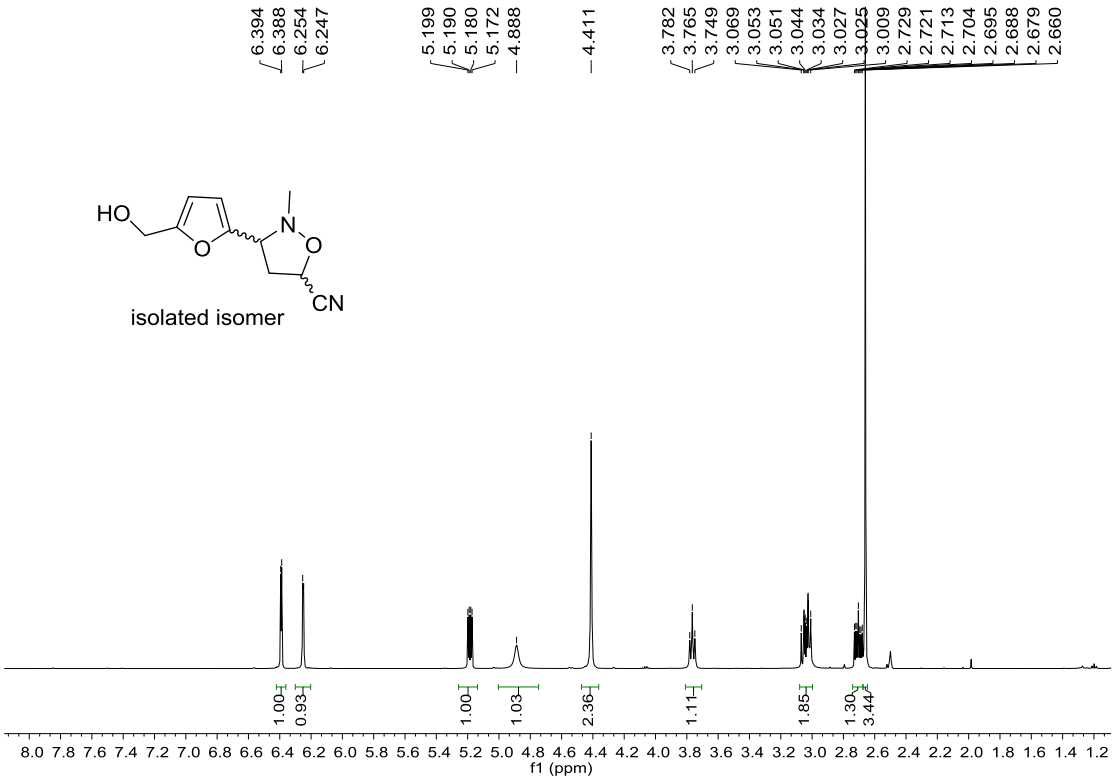



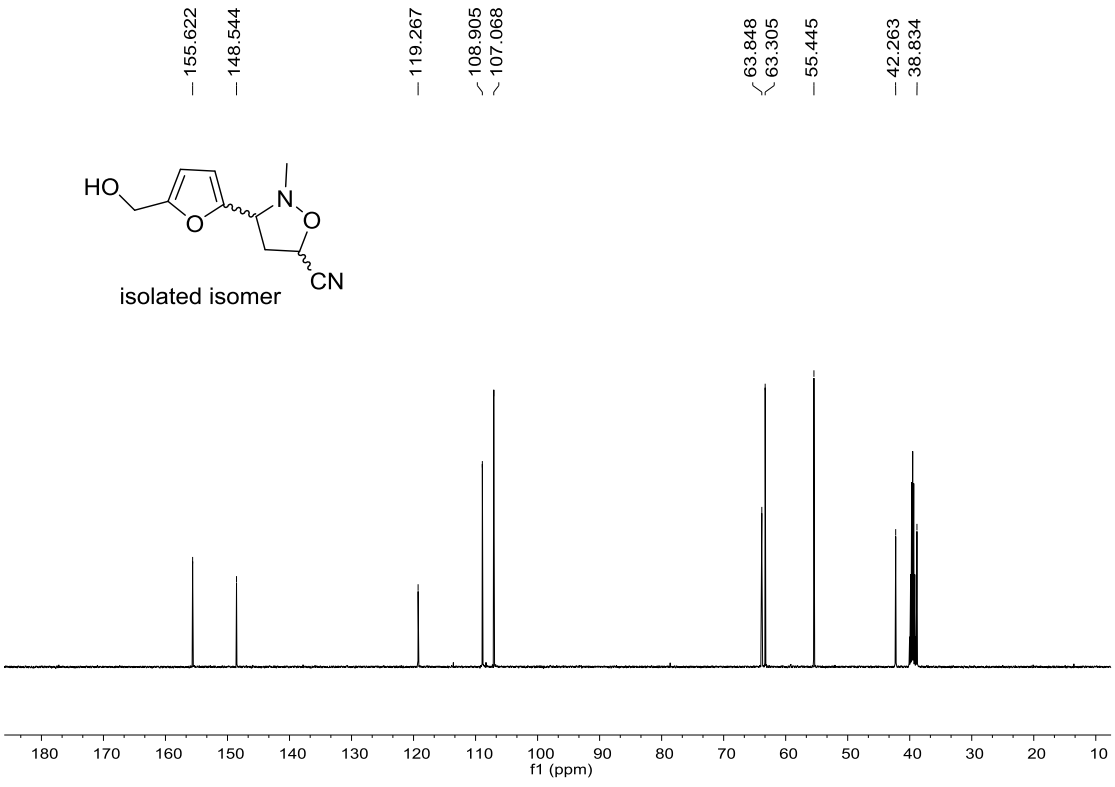
Ethyl 3-(5-(hydroxymethyl)furan-2-yl)-2,5-dimethylisoxazolidine-5-carboxylate **7**



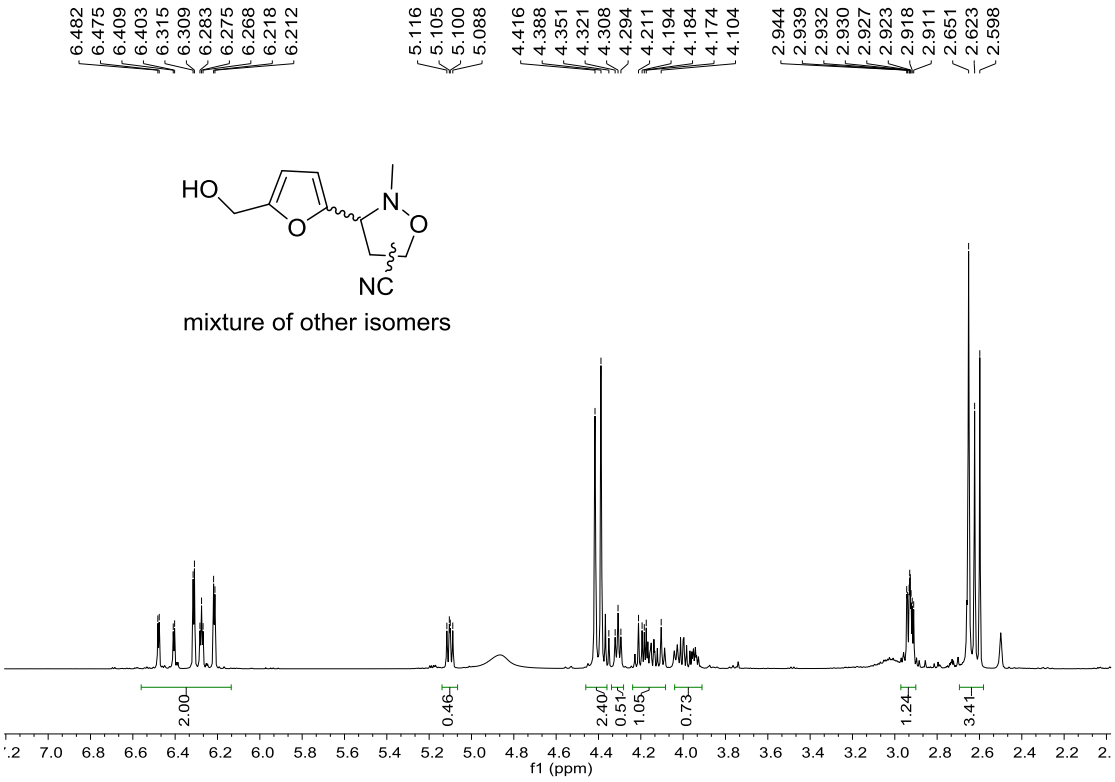



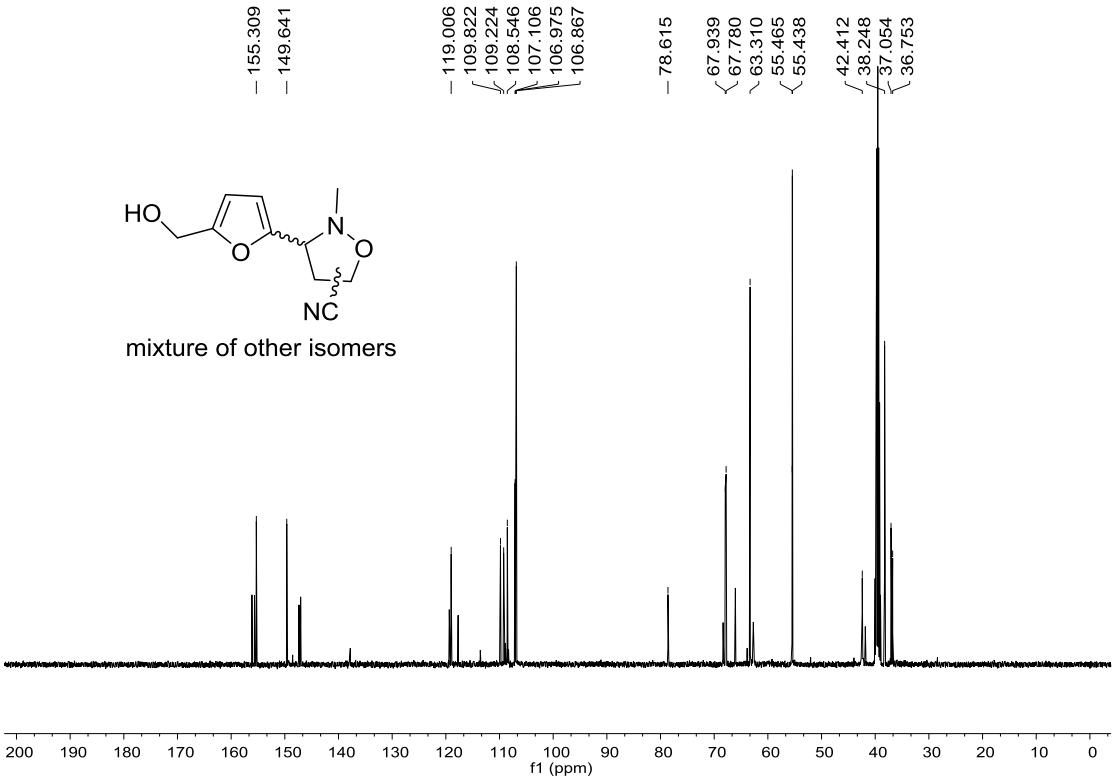
3-(5-(Hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carbonitrile **8**



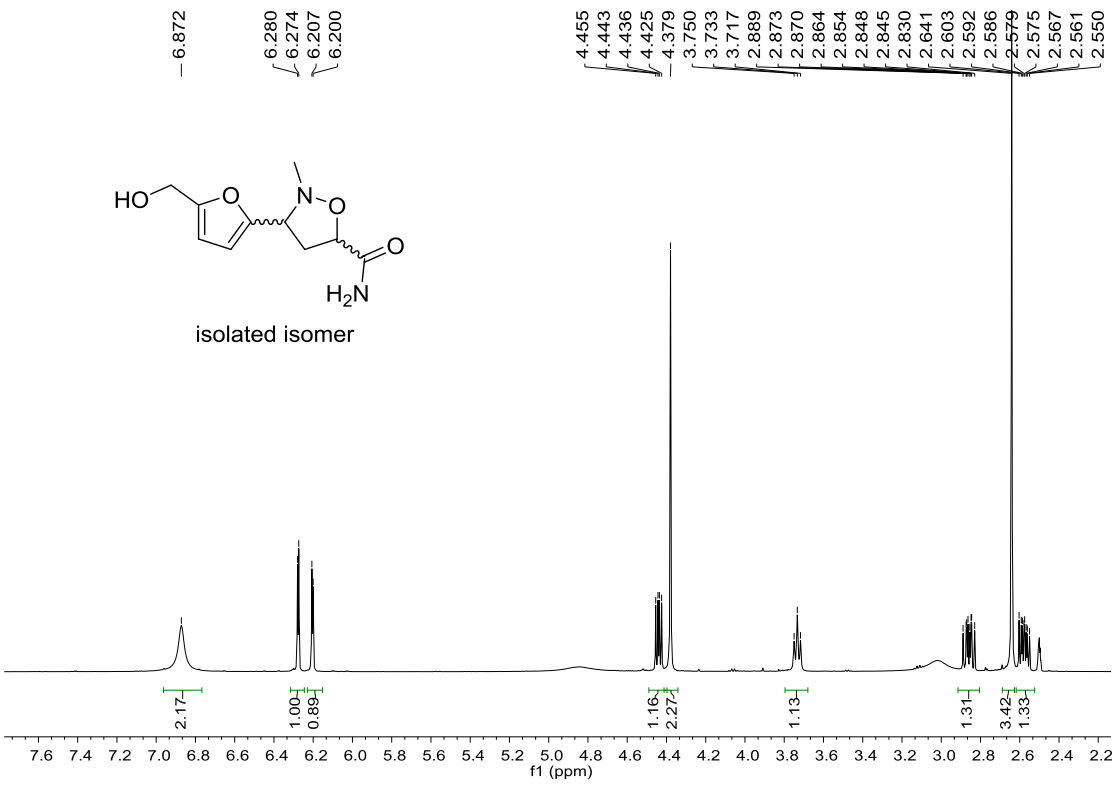



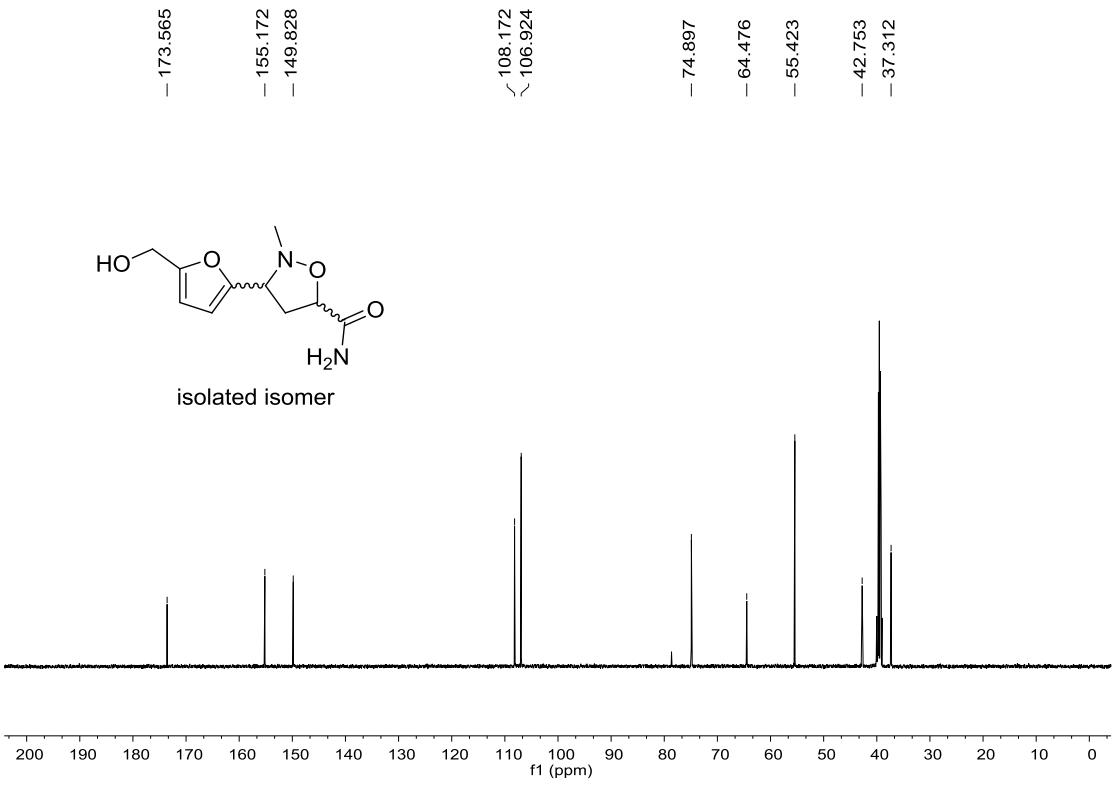
Mixture of 3-(4 and 5-(Hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carbonitrile **8**



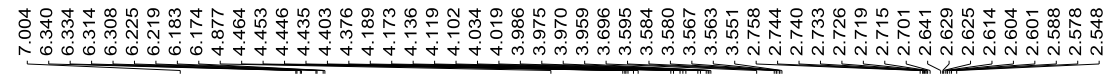



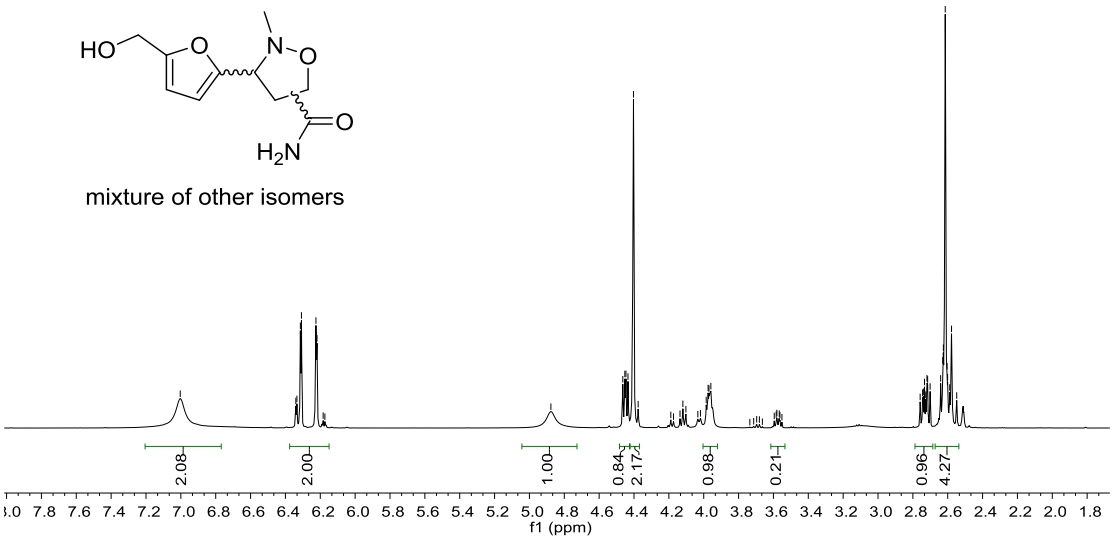
3-(5-(Hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carboxamide **9**

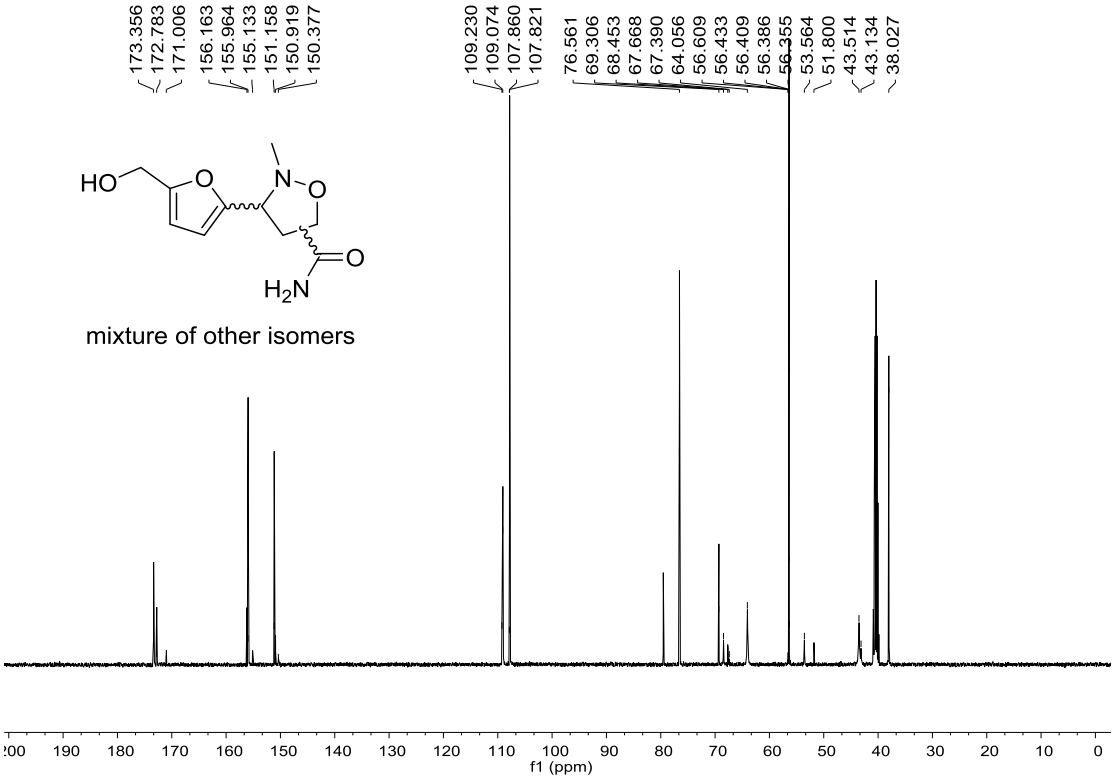


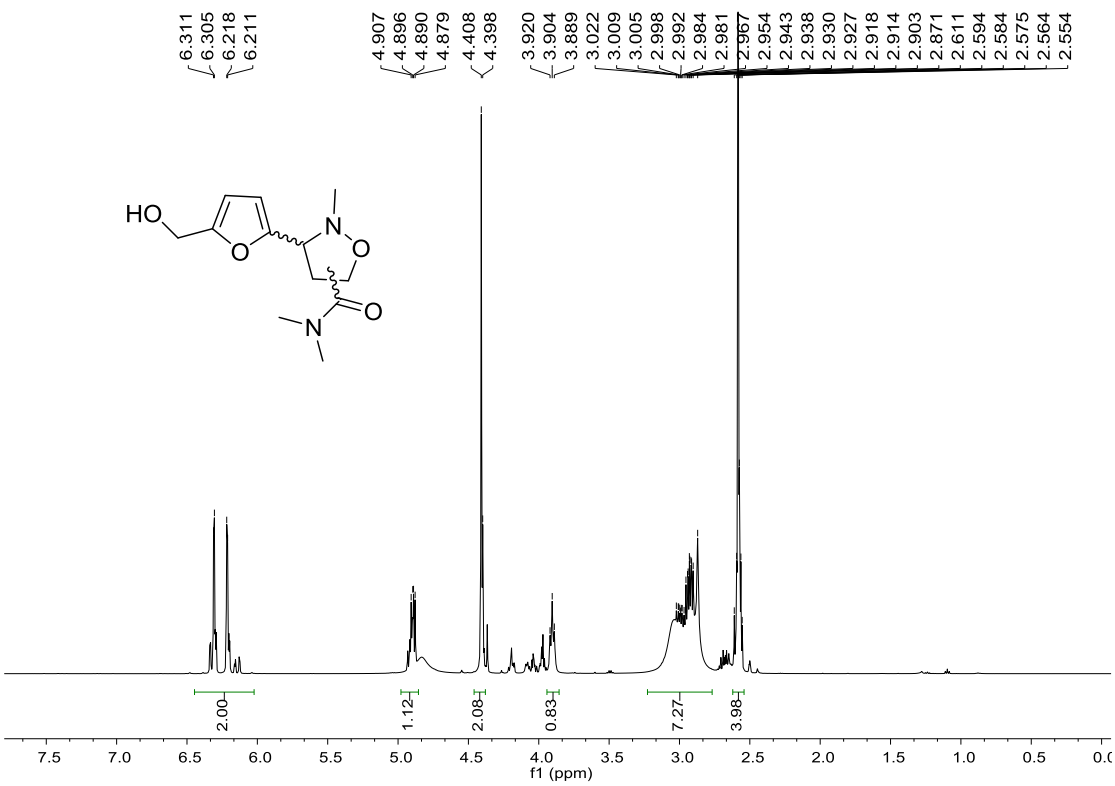
Mixture of 3-(4 and 5-(Hydroxymethyl)furan-2-yl)-2-methylisoxazolidine-5-carboxamide **9**

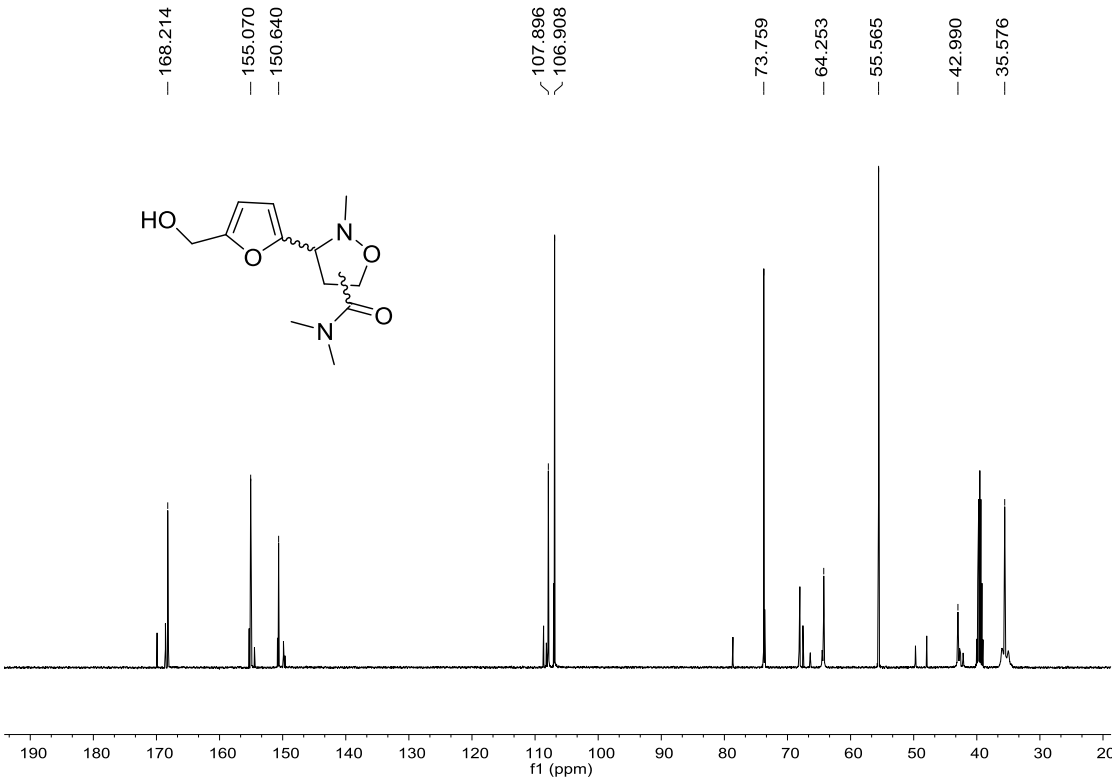


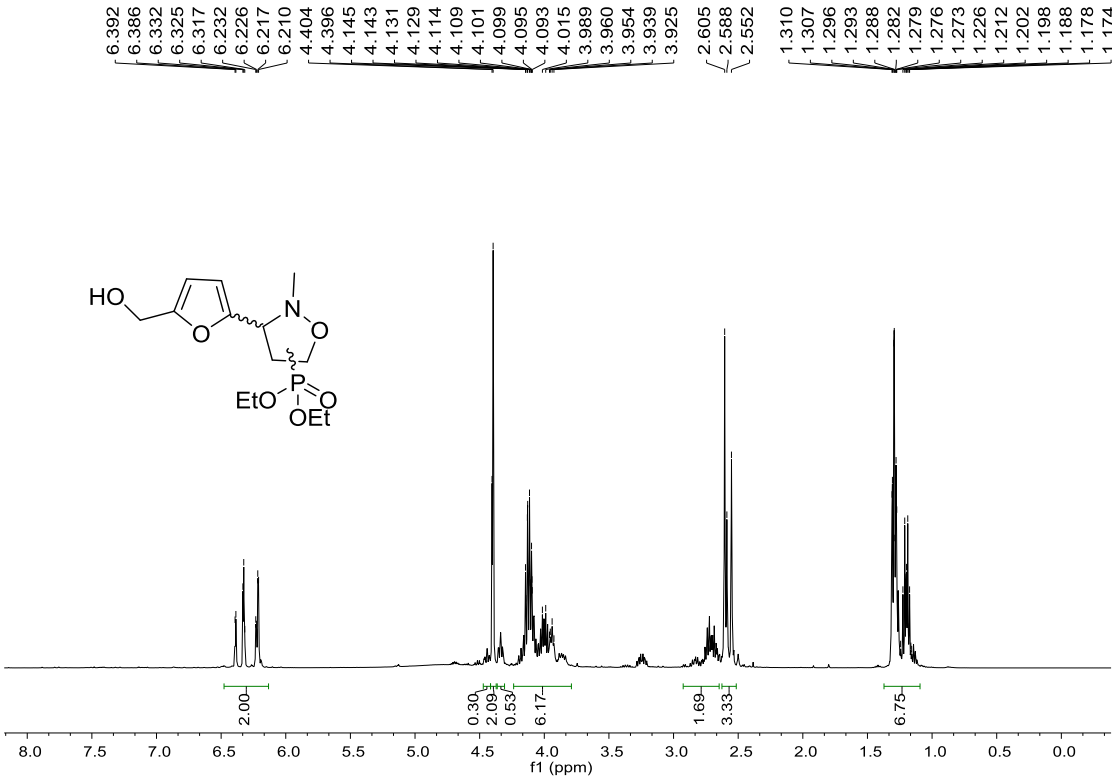



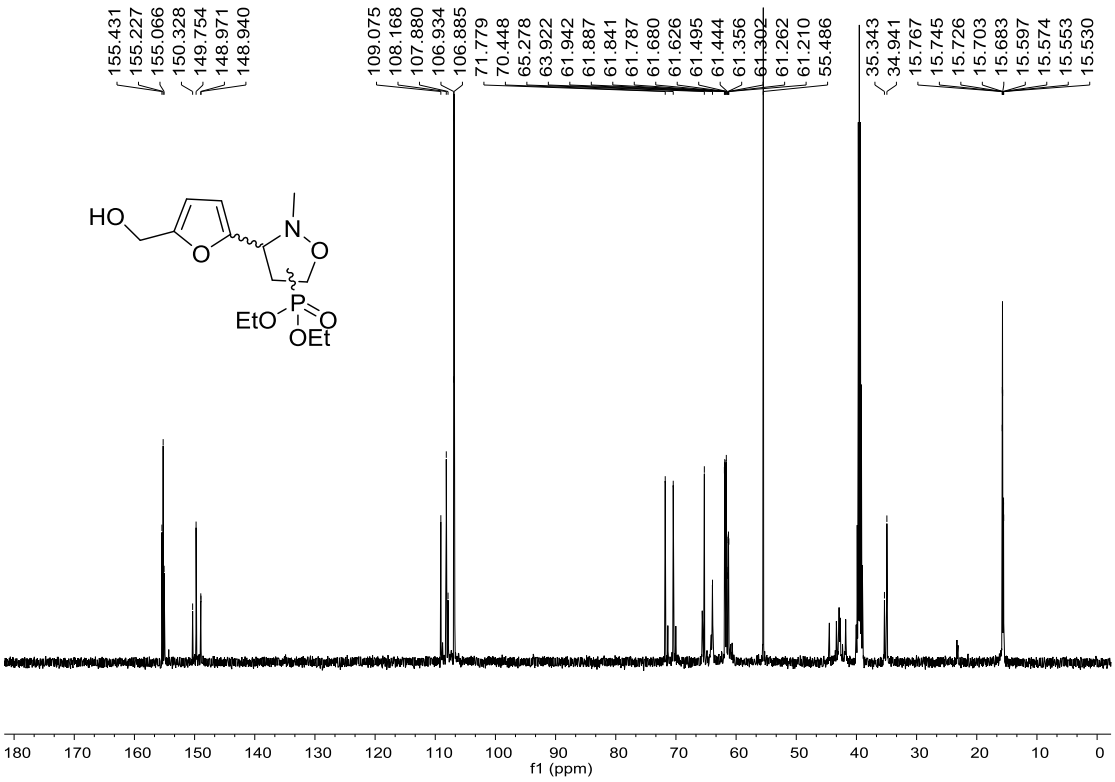
3-(4 and 5-(Hydroxymethyl)furan-2-yl)-N,N,2-trimethylisoxazolidine-5-carboxamide **10**



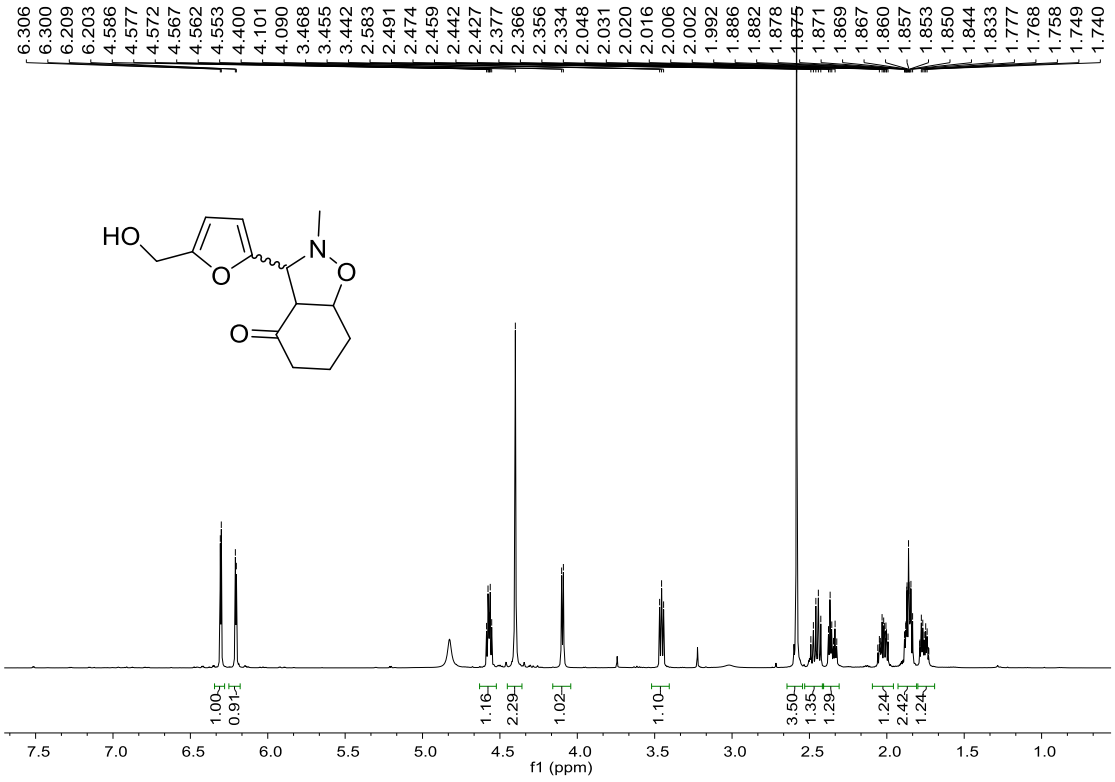



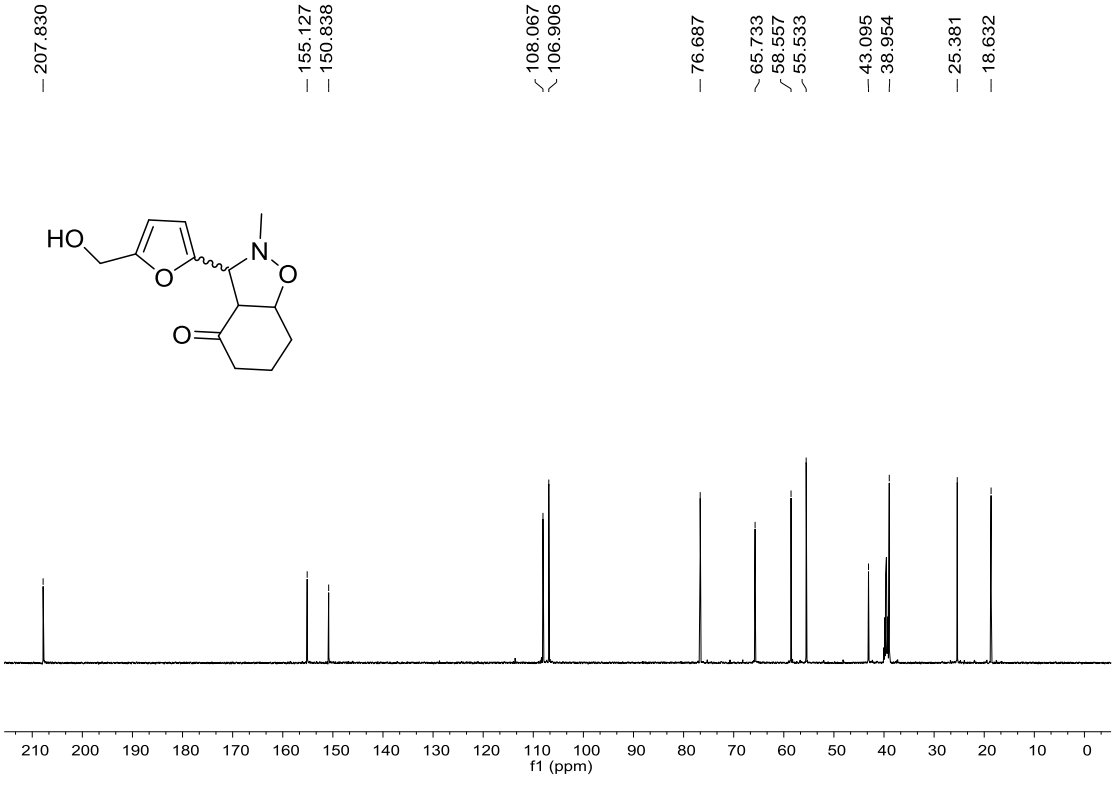
Diethyl (3-(4 and 5-(hydroxymethyl)furan-2-yl)-2-methylisoxazolidin-5-yl)phosphonate **11**



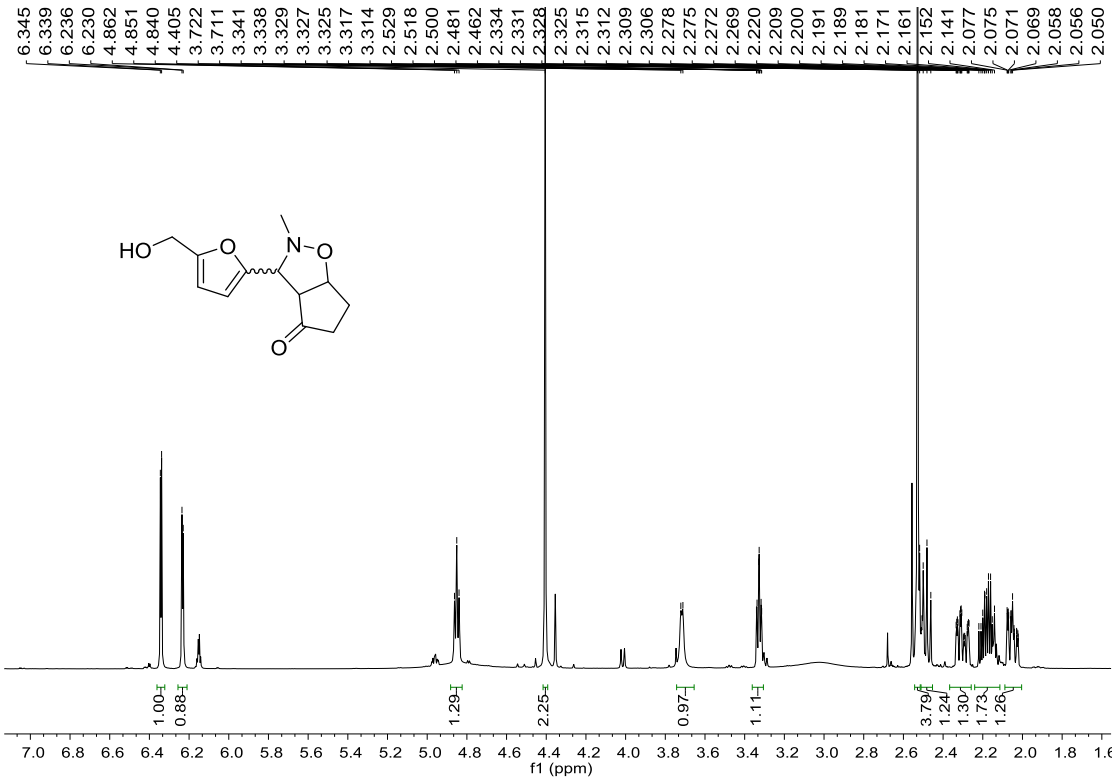



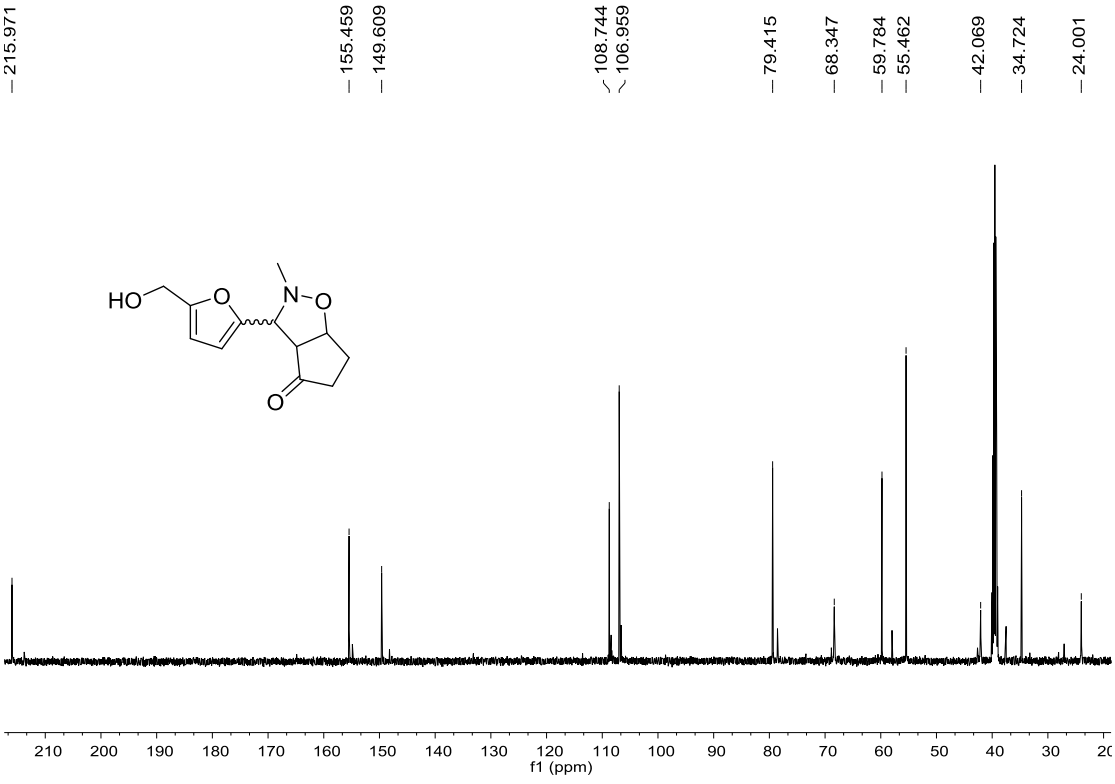
3-(5-(Hydroxymethyl)furan-2-yl)-2-methylhexahydrobenzo[d]isoxazol-4(2H)-one **12**



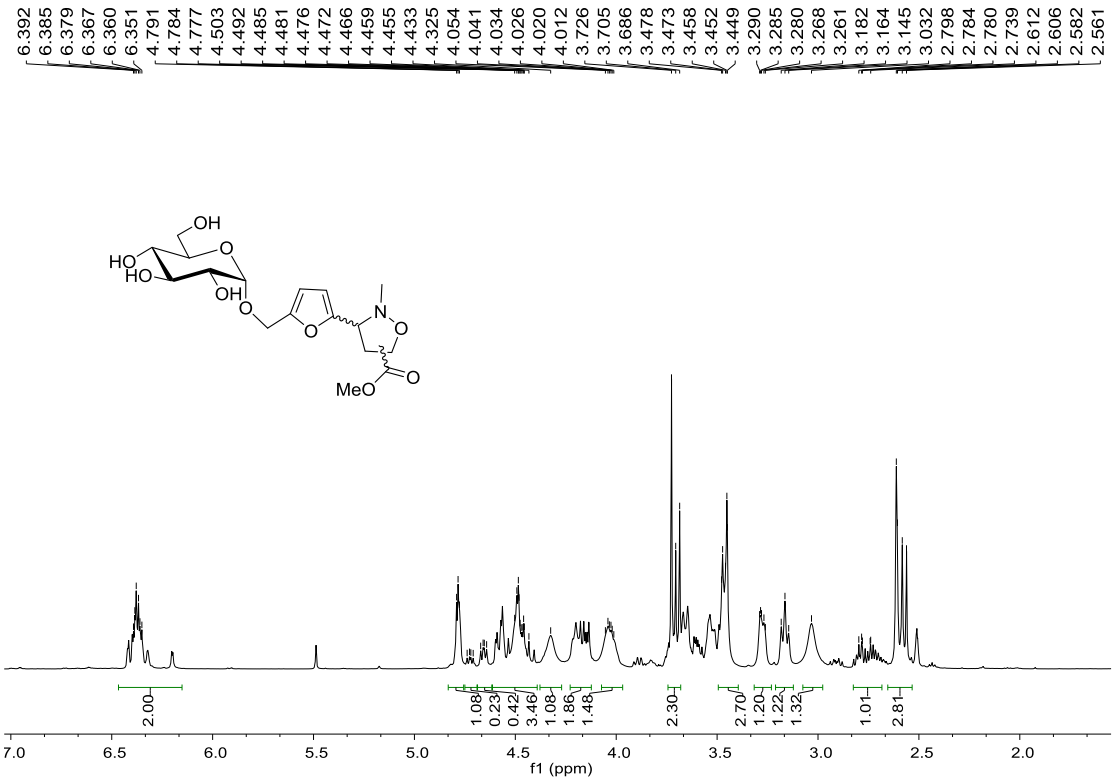



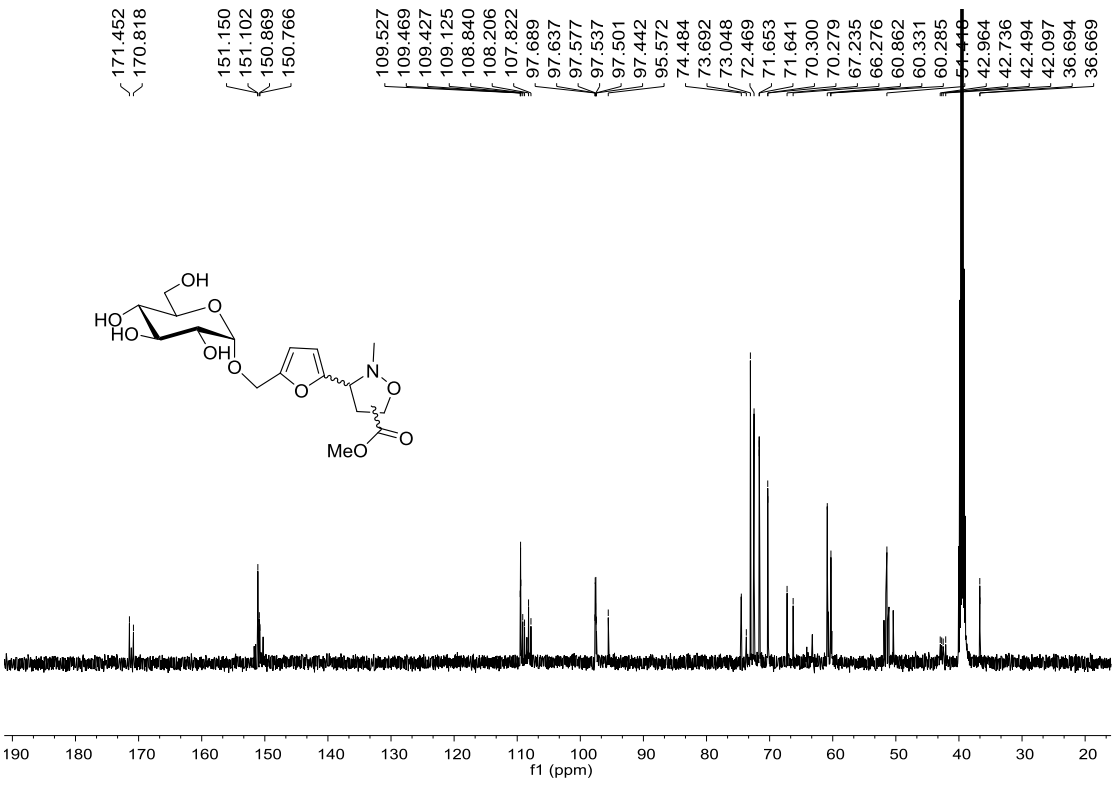
3-(5-(Hydroxymethyl)furan-2-yl)-2-methylhexahydro-4H-cyclopenta[d]isoxazol-4-one **13**



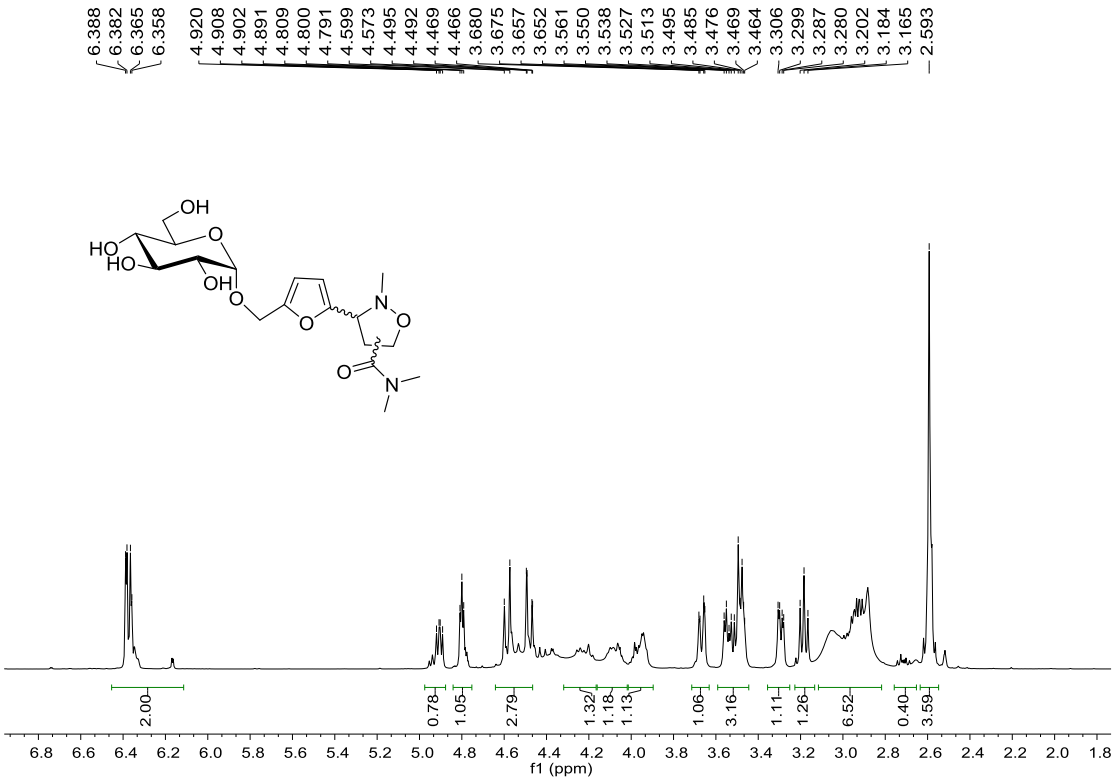



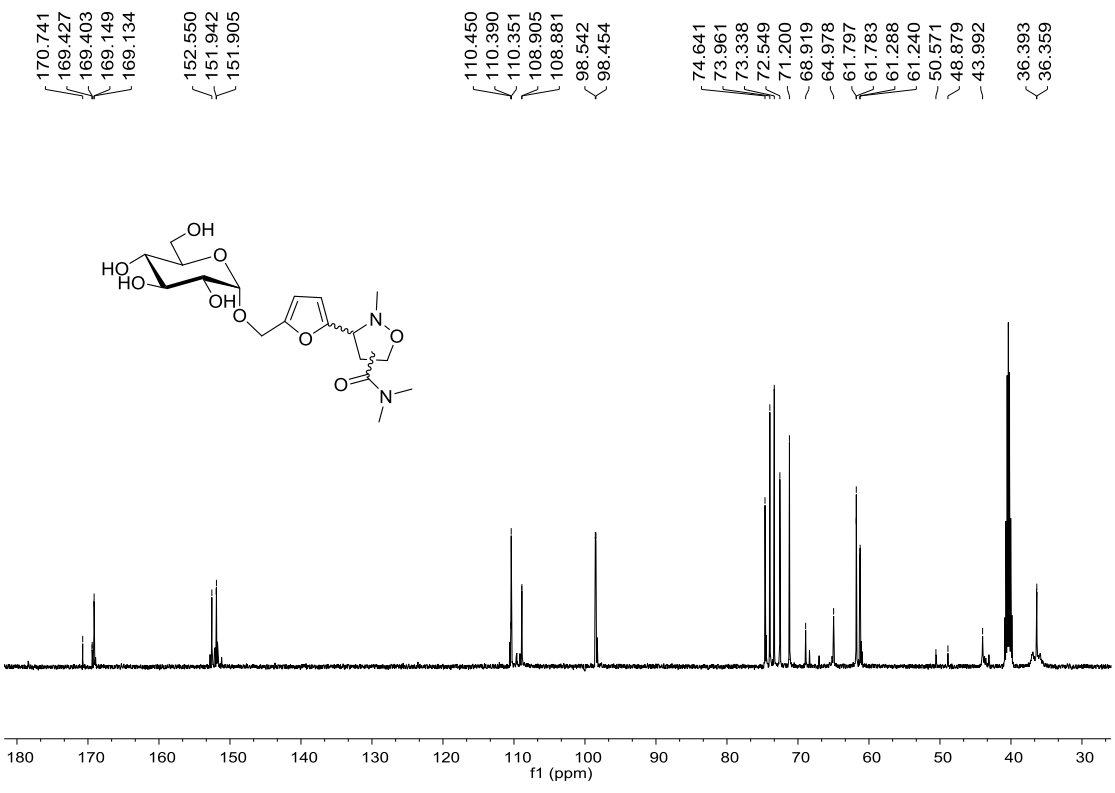
Methyl 2-methyl-3-(4 and 5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)isoxazolidine-5-carboxylate **14**



*N*,*N*,2-Trimethyl-3-(4 and 5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)isoxazolidine-5-carboxamide **15**



2-Methyl-3-(5-(α-D-glucopyranosyloxymethyl)-furan-2-yl)isoxazolidine-5-carboxamide **16**