Supporting information for

Enantioselective transformations of 5-hydroxymethylfurfural via Catalytic Asymmetric 1,3-Dipolar Cycloaddition of Azomethine Ylides.

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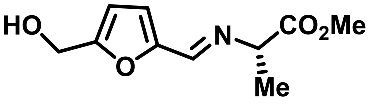
1. General methods

All anaerobic and moisture-sensitive manipulations were carried out in anhydrous solvents and under nitrogen. Dichloromethane, toluene, and tetrahydrofuran were dried over the PureSolv MD purification system. Melting points were taken in open-end capillary tubes. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm silica gel plates (230-400 mesh). Flash column chromatographies were performed using silica gel (230-400 mesh). NMR spectra were recorded on AU-300 MHz instrument and calibrated using residual undeuterated solvent ($CDCl_3$) as internal reference. MS spectra were recorded on a VG *AutoSpec* mass spectrometer. The HPLC chromatograms of the racemic and enantiomerically enriched cycloadducts are also included. α-Iminoesters (**1a-J**) were prepared by condensation of aminoesters hydrochlorides with the corresponding aldehydes, according to literature procedures.[1]

2. Typical procedure for the synthesis of imines

Typical procedure 1: Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneaminopropanoate (1a)

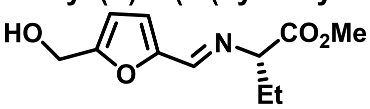


crude **1a**

A suspension of (*S*)-alanine methyl ester hydrochloride (122.8 mg, 0.88 mmol), anhydrous $MgSO_4$ (excess) and Et_3N (0.12 mL, 0.88 mmol) in dry dichloromethane (4.0 mL) was stirred at room temperature for 30 minutes. 5-(Hydroxymethyl)furfural (100 mg, 0.80 mmol) was added and the mixture was stirred at room temperature for 12 hours. Water (10 mL) was added, the organic layer was separated, and the aqueous phase was extracted with dichloromethane (3x10mL). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure to afford **1a** (100 mg, 59%, yellow oil), which was used without further purification in the next reaction step.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 6.76 (d, *J* = 3.5 Hz, 1H), 6.39 (d, *J* = 3.5 Hz, 1H), 4.67 (s, 2H), 4.11 (q, *J* = 6.7 Hz, 1H), 3.74 (s, 3H), 1.53 (d, *J* = 6.0 Hz, 3H).

Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneaminobutanoate (1b)

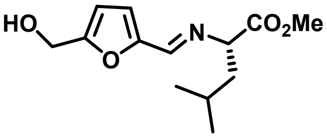


crude **1b**

Following the typical procedure 1, the reaction of (*S*)-methyl 2-aminobutanoate (103.1 mg, 0.88 mmol), $MgSO_4$ (excess), Et_3N (0.12 mL, 0.88 mmol) and 5-(Hydroxymethyl)furfural (100.0 mg, 0.80 mmol) in dichloromethane (5 mL) afforded **1b** (174 mg, 97%, yellow oil).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.92 (s, 1H), 6.69 (d, *J* = 3.4 Hz, 1H), 6.28 (d, *J* = 3.3 Hz, 1H), 4.55 (s, 2H), 3.63 (s, 3H), 2.01 – 1.88 (m, 1H), 1.85 – 1.73 (m, 1H), 0.80 (t, *J* = 7.5 Hz, 3H).

Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneamino)-4-methylpentanoate (1c)

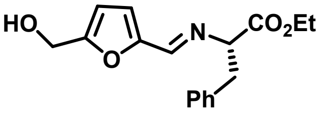


crude **1c**

Following the typical procedure 1, the reaction of (S)-leucine methyl ester hydrochloride (159.9 mg, 0.88 mmol), $MgSO_4$ (excess), Et_3N (0.12 mL, 0.88 mmol) and 5-(Hydroxymethyl)furfural (100.0 mg, 0.80 mmol) in dichloromethane (5 mL) afforded **1c** (200 mg, 99%, yellow oil).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 6.64 (d, *J* = 3.4 Hz, 1H), 6.21 (d, *J* = 3.4 Hz, 1H), 4.48 (s, 2H), 3.85 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.55 (s, 3H), 1.68 – 1.61 (m, 2H), 1.45 – 1.32 (m, 1H), 0.77 (d, *J* = 6.5 Hz, 3H), 0.72 (d, *J* = 6.5 Hz, 3H).

Ethyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneamino-3-phenylpropanoate (1d)

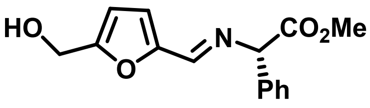


crude **1d**

Following the typical procedure 1, the reaction of (S)-phenylalanine ethyl ester hydrochloride (202.1 mg, 0,88 mmol), $MgSO_4$ (excess), Et_3N (0,12 mL, 0,88 mmol) and 5-(Hydroxymethyl)furfural (100.0 mg, 0.80 mmol) in dichloromethane (5 mL) afforded **1d** (200 mg, 83%, yellow oil).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.40 – 7.21 (m, 5H), 6.76 (d, *J* = 2.5 Hz, 1H), 6.43 (d, *J* = 2.5 Hz, 1H), 4.73 (s, 2H), 4.26 (q, *J* = 7.0 Hz, 2H), 4.18 (dd, *J* = 6.5, 3.8 Hz, 1H), 3.45 (dd, *J* = 13.5, 5.4 Hz, 1H), 3.19 (dd, *J* = 13.5, 8.6 Hz, 1H), 1.31 (t, *J* = 7.0 Hz, 3H).

Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneamino-2-phenylacetate (1e)

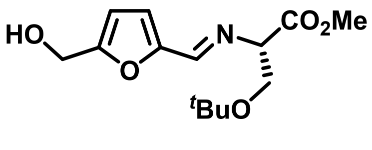


crude **1e**

Following the typical procedure 1, the reaction of (*S*)-2-phenylglycine methyl ester hydrochloride (177.5 mg, 0,88 mmol), $MgSO_4$ (excess), Et_3N (0.12 mL, 0.88 mmol) and 5-(Hydroxymethyl)furfural (100.0 mg, 0.80 mmol) in dichloromethane (5 mL) afforded **1e** (200 mg, 91%, yellow oil).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.46 – 7.40 (m, 2H), 7.37 – 7.30 (m, 3H), 6.75 (d, *J* = 3.4 Hz, 1H), 6.35 (d, *J* = 3.4 Hz, 1H), 4.63 (s, 2H), 3.73 (s, 3H), 3.69 (s, 1H).

Methyl (*S*)-3-(tert-butoxy)-2-(5-(hydroxymethyl)furan-2-yl)methyleneaminopropanoate (1f)

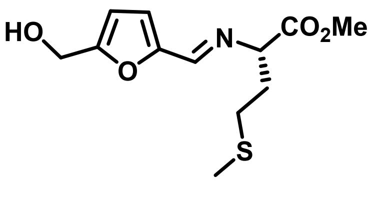


crude **1f**

Following the typical procedure 1, the reaction of *O*-tert-buthyl-(*S*)-serine methyl ester hydrochloride (186.3 mg, 0.88 mmol), $MgSO_4$ (excess), Et_3N (0.12 mL, 0.88 mmol) and 5-(Hydroxymethyl)furfural (100.0 mg, 0.80 mmol) in dichloromethane (5 mL) afforded **1f** (200 mg, 88%, yellow oil).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.92 (s, 1H), 6.67 (d, *J* = 3.4 Hz, 1H), 6.26 (d, *J* = 3.4 Hz, 1H), 4.51 (s, 2H), 3.97 (t, *J* = 6.4 Hz, 1H), 3.79 – 3.73 (m, 1H), 3.62 (s, 3H), 3.50 (t, *J* = 8.0 Hz, 1H), 1.03 (s, 9H).

Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneamino-4-(methylthio)butanoate (1g)

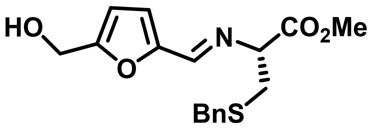


crude **1g**

Following the typical procedure 1, the reaction of (S)-methionine methyl ester hydrochloride (175.7 mg, 0.88 mmol), $MgSO_4$ (excess), Et_3N (0.12 mL, 0.88 mmol) and 5-(Hydroxymethyl)furfural (100.0 mg, 0.80 mmol) in dichloromethane (5 mL) afforded **1g** (200 mg, 92%, yellow oil).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 6.76 (d, *J* = 3.4 Hz, 1H), 6.37 (d, *J* = 3.4 Hz, 1H), 4.64 (s, 2H), 4.13 (dd, *J* = 8.6, 5.0 Hz, 1H), 3.71 (s, 3H), 2.66 – 2.50 (m, 2H), 2.43 – 2.33 (m, 1H), 2.28 – 2.14 (m, 2H), 2.05 (s, 3H).

Methyl (*R*)-3-(benzylthio)-2-(5-(hydroxymethyl)furan-2-yl)methyleneaminopropanoate (1h)

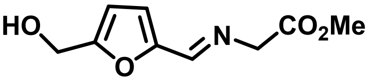


crude **1h**

Following the typical procedure 1, the reaction of *S*-benzyl-(*R*)-cysteine methyl ester hydrochloride (230.4 mg, 0.88 mmol), $MgSO_4$ (excess), Et_3N (0.12 mL, 0.88 mmol) and 5-(Hydroxymethyl)furfural (100.0 mg, 0.80 mmol) in dichloromethane (5 mL) afforded **1h** (250 mg, 94%, yellow oil).

^{1}H NMR-(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.31 – 7.14 (m, 5H), 6.77 (d, *J* = 3.4 Hz, 1H), 6.37 (d, *J* = 3.4 Hz, 1H), 4.63 (s, 2H), 3.89 (dd, *J* = 8.3, 5.3 Hz, 1H), 3.70 (s, 5H), 3.07 (dd, *J* = 13.8, 5.3 Hz, 1H), 2.84 (dd, *J* = 13.8, 8.3 Hz, 1H).

Methyl 2-(5-(hydroxymethyl)furan-2-yl)methyleneaminoacetate (1i)

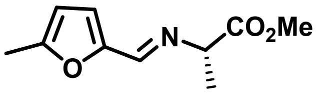


crude **1i**

Following the typical procedure 1, the reaction of glycine methyl ester hydrochloride (110.4 mg, 0.88 mmol), $MgSO_4$ (excess), Et_3N (0.12 mL, 0.88 mmol) and 5-(Hydroxymethyl)furfural (100.0 mg, 0.80 mmol) in dichloromethane (5 mL) afforded **1i** (150 mg, 95%, yellow oil)

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.97 (s, 1H), 6.73 (d, *J* = 3.5 Hz, 1H), 6.32 (d, *J* = 3.5 Hz, 1H), 4.58 (s, 2H), 4.30 (s, 2H), 3.70 (s, 3H).

Methyl (S)-2-((5-methylfuran-2-yl)methyleneamino)propanoate (1j)

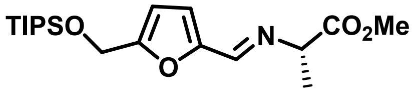


crude **1j**

Following the typical procedure 1, the reaction of (*S*)-alanine methyl ester hydrochloride (455.0 mg, 3.26 mmol), $MgSO_4$ (excess), Et_3N (0.50 mL, 3.58 mmol) and 5-methylfuran-2-carbaldehyde (0.25 mL, 2.51 mmol) in dichloromethane (5 mL) afforded **1j** (350.0 mg, 70%, yellow oil)

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.78 (s, 1H), 6.46 (d, *J* = 2.9 Hz, 1H), 5.85 (d, *J* = 2.9 Hz, 1H), 3.84 (q, *J* = 6.8 Hz, 1H), 3.47 (s, 3H), 2.11 (s, 3H), 1.28 (d, *J* = 6.8 Hz, 3H).

Methyl (S)-2-((5-(triisopropylsilyloxymethyl)furan-2-yl)methyleneamino)propanoate (1k)

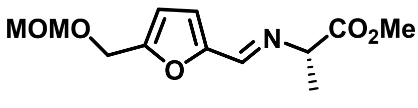


crude **1k**

Following the typical procedure 1, the reaction of (S)-alanine methyl ester hydrochloride (165.0 mg, 1.18 mmol), $MgSO_4$ (excess), Et_3N (0.17 mL, 1.22 mmol) and 5-((triisopropylsilyloxy)methyl)furan-2-carbaldehyde (275.3 mg, 0.97 mmol) in dichloromethane (5 mL) afforded **1k** (250.4 mg, 70%, yellow oil)

^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.30 (s, 1H), 6.43 (d, *J* = 2.5 Hz, 1H), 4.86 (s, 2H), 4.14 (q, *J* = 6.9 Hz, 1H), 3.78 (s, 3H), 1.57 (d, *J* = 6.6 Hz, 3H), 1.23 – 1.17 (m, 3H), 1.15 – 1.06 (m, 18H).

Methyl (S)-2-(5-((methoxymethoxymethyl)furan-2-yl)methyleneamino)propanoate (1l)



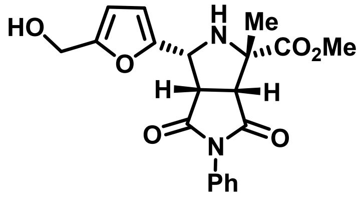
crude **1l**

Following the typical procedure 1, the reaction of (*S*)-alanine methyl ester hydrochloride (135.0 mg, 0.97 mmol), $MgSO_4$ (excess), Et_3N (0.13 mL, 0.95 mmol) and 5-(methoxymethoxymethyl)furan-2-carbaldehyde (128.9 mg, 0,76 mmol) in dichloromethane (5 mL) afforded **1l** (158.3 mg, 81%, yellow oil)

^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 6.72 (d, *J* = 3.2 Hz, 1H), 6.35 (d, *J* = 3.2 Hz, 1H), 4.58 (s, 2H), 4.49 (s, 2H), 4.01 (q, *J* = 6.8 Hz, 1H), 3.63 (s, 3H), 3.29 (s, 3H), 1.43 (d, *J* = 6.8 Hz, 3H).

3. Typical procedure for the asymmetric [3+2] cycloaddition of azomethine ylides

Typical Procedure 2: Methyl (1*S*,3*R*,3*aS*,6*aR*)-3-(5-(hydroxymethyl)furan-2-yl)-1-methyl-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3a)

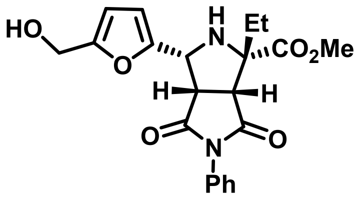


3a

To a suspension of $[Cu(CH_3CN)_4]PF_6$ (8.9 mg, $2.4\cdot10^{-2}$ mmol), (*R*)-Fesulphos (11.9 mg, $2.6\cdot10^{-2}$ mmol), *N*-phenylmaleimide (41.6, 0.24 mmol) and **1a** (50 mg, 0.24 mmol) in anhydrous dichloromethane (5 mL) under argon atmosphere, Et_3N (10 µL, $7.2\cdot10^{-2}$ mmol) was added. The resulting mixture was stirred at room temperature for 12 h, filtered over celite® and the solvent was removed under reduced pressure at the rotary evaporator. The crude mixture was purified by flash chromatography, (heptane:AcOEt 1:1) to afford **3a** (60.0 mg, 65%, white solid),

M.p.: 193-195ºC.
$[\alpha]_D^{20}$:+61.8 (c =0.5 , $CHCl_3$), 95% *ee*.
SFC: Chiralpak IB, CO_2/MeOH from 95-5 to 70/30 in 8 min, flow rate 2 mL/min (λ = 230 nm) t_R: 2.72 min (*2R,3S,3aR,6aS*)-**3a** and 3.02 min (*1S,3R,3aS,6aR*)-**3a**.
^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.35 (m, 3H), 7.26 – 7.20 (m, 2H), 6.34 (d, *J* = 3.3 Hz, 1H), 6.20 (d, *J* = 3.3 Hz, 1H), 4.82 (d, *J* = 8.7 Hz, 1H), 4.42 (s, 2H), 3.86 (s, 3H), 3.64 (t, *J* = 8.3 Hz, 1H), 3.45 (d, *J* = 8.3 Hz, 1H), 1.57 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 174.2, 172.4, 154.7, 149.4, 131.8, 129.3(2C), 128.9, 126.5(2C), 109.6, 108.8, 68.4, 58.1, 57.4, 56.8, 53.1, 50.1, 23.9.
HRMS (ESI+): Calculated for $C_{20}H_{21}N_2O_6$, 385.1394; found, 385.1388.

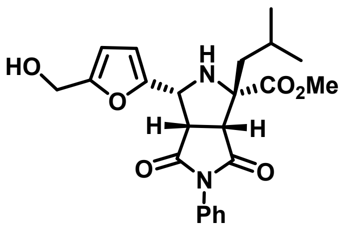
Methyl (*1S,3R,3aS,6aR*)-1-ethyl-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3b)



3b

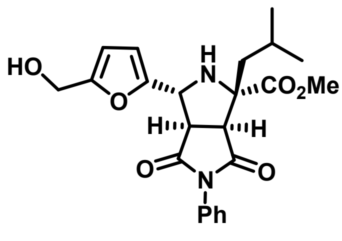
Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (7.5 mg, $2.0 \cdot 10^{-2}$ mmol), (*R*)-Fesulphos (10.1 mg, $2.2 \cdot 10^{-2}$ mmol), *N*-phenylmaleimide (34.6 mg, 0.20 mmol), **1b** (46 mg, 0.20 mmol) and Et_3N (9 µL, $6.0 \cdot 10^{-2}$ mmol) in dichloromethane (5 mL) at 0ºC for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 1:1) the cycloadduct **3b** (58.2 mg, 73%, white solid).
M.p.: 187-189ºC.
$[\alpha]_D^{20}$:+9.9 (c = 1.0, $CHCl_3$), 95% *ee*.
SFC: Chiralpak IB, CO_2/MeOH from 95-5 to 70/30 in 8 min, flow rate 2 mL/min (λ = 254 nm) t_R: 2.73 min (*2R,3S,3aR,6aS*)-**3b** and 3.02 min (*1S,3R,3aS,6aR*)-**3b**.
^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.48 – 7.34 (m, 3H), 7.29 – 7.22 (m, 2H), 6.37 (d, *J* = 3.2 Hz, 1H), 6.23 (d, *J* = 3.2 Hz, 1H), 4.70 (d, *J* = 9.0 Hz, 1H), 4.44 (s, 2H), 3.88 (s, 3H), 3.61 (dd, *J* = 9.0, 7.7 Hz, 1H), 3.46 (d, *J* = 7.7 Hz, 1H), 3.13 (d, *J* = 9.4 Hz, 1H, NH), 2.22 – 2.10 (m, 1H), 1.71 (dq, *J* = 14.2, 7.2 Hz, 1H), 0.94 (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.9, 174.4, 171.7, 154.7, 149.6, 131.8, 129.3(2C), 128.9, 126.5(2C), 109.6, 108.8, 72.5, 57.6, 57.4, 56.6, 52.9, 50.1, 28.7, 8.4.
HRMS (ESI+): Calculated for $C_{21}H_{23}N_2O_6$, 399.1551; found, 399.1549.

Methyl (1*S*,3*R*,3*aS*,6*aR*)-3-(5-(hydroxymethyl)furan-2-yl)-1-isobutyl-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3c)



3c-*endo*-88%

+

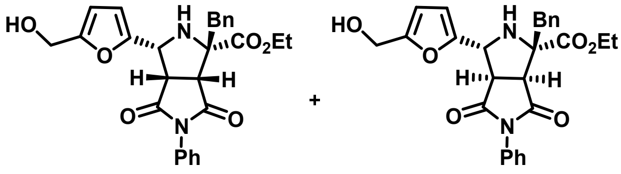


3c-*exo*-12%

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (7.5 mg, $2.0 \cdot 10^{-2}$ mmol), (*R*)-Fesulphos (10.1 mg, $2.2 \cdot 10^{-2}$ mmol), *N*-phenylmaleimide (34.6 mg, 0.20 mmol), **1c** (50 mg, 0.20 mmol) and Et_3N (9 µL, $6.0 \cdot 10^{-2}$ mmol) in dichloromethane (5 mL) at 0ºC for 12 h. The crude mixture was concentrated in vacuo and gave a 85:15 mixture of diastereoisomers **3c-*endo*** and **3c-*exo***. After flash column chromatography (heptane-AcOEt 1:1) a fraction containing 88:12 mixture of **3c-*endo*** and **3c-*exo*** could be isolated (68.2 mg, 80%, white solid).
M.p.: 117-120ºC.
$[\alpha]_D^{20}$:+11.3 (c= 1.0 $CHCl_3$), 98% *ee*.
SFC: Chiralpak IB, CO_2/MeOH from 95-5 to 70/30 in 8 min, flow rate 2 mL/min (λ = 230 nm) t_R: 3.06 min (*2R,3S,3aR,6aS*)-**3c-*endo*** and 3.32 min (*1S,3R,3aS,6aR*)-**3c-*endo***.
^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.31 (m, 3H, **3c-*endo***), 7.26 – 7.17 (m, 2H, **3c-*endo***), 7.12 – 7.09 (m, 3H, **3c-*exo***), 6.59 (s, 1H, **3c-*exo***), 6.41 (d, *J* = 5.6 Hz, 1H, **3c-*exo***), 6.33 (d, *J* = 2.8 Hz, 1H, **3c-*endo***), 6.18 (s, 1H, **3c-*endo***), 4.65 (d, *J* = 8.7 Hz, 1H,

3c-*endo*), 4.54 (d, *J* = 7.2 Hz, 2H, **3c-*exo***), 4.40 (s, 2H, **3c-*endo***), 3.83 (s, 3H, **3c-*endo***), 3.80 (s, 2H, **3c-*exo***), 3.55 (t, *J* = 8.7 Hz, 2H, **3c-*endo***), 3.44 (d, *J* = 7.0 Hz, 2H, **3c-*exo***), 3.35 (d, *J* = 7.2 Hz, 1H, **3c-*endo***), 2.74 (bs, 1H, OH), 2.13 – 1.99 (m, 1H, **3c-*endo***), 1.78 (dd, *J* = 13.2, 6.7 Hz, 1H, **3c-*endo***), 1.60 (dd, *J* = 14.1, 4.8 Hz, 1H, **3c-*endo***), 1.09 – 1.01 (m, 3H. **3c-*exo***), 0.98 (d, *J* = 6.7 Hz, 3H, **3c-*endo***), 0.90 (d, *J* = 1.5 Hz, 3H, **3c-*exo***), 0.86 (d, *J* = 5.8 Hz, 3H. **3c-*endo***).,
^{13}C-NMR (75 MHz, $CDCl_3$, 3c-*endo*) δ 174.6, 174.4, 172.4, 154.8, 149.3, 131.7, 129.2(2C), 128.8, 126.5(2C), 109.5, 108.7, 71.3, 58.0, 57.4, 57.2, 52.7, 50.2, 43.5, 24.8, 24.2, 22.1.
HRMS (ESI+): Calculated for $C_{23}H_{27}N_2O_6$, 427.1864; found, 427.1857.

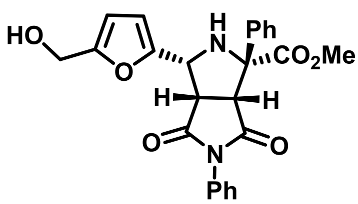
Ethyl (1*S*,3*R*,3*aS*,6*aR*)-1-benzyl-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3d)



3d-*endo*-95% 3d-*exo*-5%

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (6.3 mg, $1.7\cdot10^{-2}$ mmol), (*R*)-Fesulphos (8.6 mg, $1.9\cdot10^{-2}$ mmol), *N*-phenylmaleimide (29.4 mg, 0.17 mmol), **1d** (50 mg, 0.17 mmol) and Et_3N (8 μL, $5.1\cdot10^{-2}$ mmol) in dichloromethane (5 mL) at 0ºC for 12 h. The crude mixture was concentrated in vacuo and gave a 90:10 mixture of diastereoisomers **3d-*endo*** and **3d-*exo***. After flash column chromatography (heptane-AcOEt 1:1) a fraction containing 95:5 mixture of **3d-*endo*** and **3d-*exo*** could be isolated (61.3 mg, 76%, white solid).
M.p.: 90-92ºC.
$[\alpha]_D^{20}$:+133.4 (c = 1.0, $CHCl_3$), 98% *ee*.
SFC: Chiralpak IB, CO_2/MeOH from 95-5 to 70/30 in 8 min, flow rate 2 mL/min (λ = 230 nm) t_R: 3.56 min (*2R,3S,3aR,6aS*)-**3d-*endo*** and 3.78 min (*1S,3R,3aS,6aR*)-**3d-*endo***.
^{1}H-NMR (300 MHz, $CDCl_3$. 3d-*endo*) δ 7.43 – 7.35 (m, 3H), 7.34 – 7.27 (m, 3H), 7.24 – 7.17 (m, 4H), 6.35 (d, *J* = 3.1 Hz, 1H), 6.20 (d, *J* = 3.1 Hz, 1H), 4.86 (s, 1H), 4.45 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.67 – 3.51 (m, 2H), 3.39 (d, *J* = 13.7 Hz, 1H), 3.02 (d, *J* = 13.7 Hz, 1H), 2.06 (bs, 1H, OH), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$, 3d-*endo*) δ 174.6, 174.2, 170.6, 154.7, 150.3, 135.4, 131.8, 130.1(2C), 129.3(2C), 128.8, 128.7(2C), 127.5, 126.5(2C), 109.4, 108.8, 72.2, 62.1, 57.4, 57.3, 55.7, 49.7, 41.3, 14.2.
HRMS (ESI+): Calculated for $C_{27}H_{27}N_2O_6$, 475.1864; found, 475.1858.

Methyl (1*R*,3*R*,3*aS*,6*aR*)-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-1,5-diphenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3e)

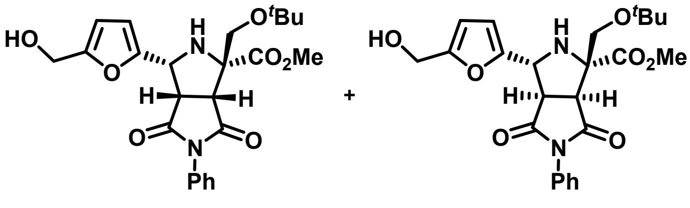


3e

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (6.7 mg, $1.8\cdot10^{-2}$ mmol), (*R*)-Fesulphos (9.2 mg, $2.0\cdot10^{-2}$ mmol), *N*-phenylmaleimide (31.2 mg, 0.18 mmol), **1e** (50 mg, 0.18 mmol) and Et_3N (8 μL, $5.4\cdot10^{-2}$ mmol) in dichloromethane (5 mL) at 0ºC for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 1:1) the cycloadduct **3e** (56.3 mg, 70%, white solid).
M.p.: 146-148ºC.
$[\alpha]_D^{20}$:-7.2 (c=0.5, $CHCl_3$), 97% *ee.*
SFC: Chiralpak IB, CO_2/MeOH from 95-5 to 70/30 in 8 min, flow rate 2 mL/min (λ = 254 nm) t_R: 3.32 min (*2S,3S,3aR,6aS*)-**3e** and 3.54 min (*1R,3R,3aS,6aR*)-**3e**.

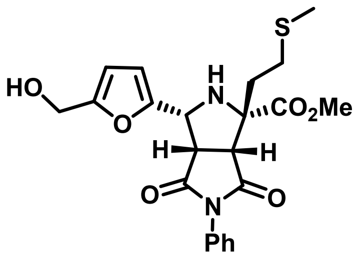
^{1}H-NMR (300 MHz, CDCl$_3$) δ 7.66 – 7.57 (m, 2H), 7.42 – 7.31 (m, 6H), 7.30 – 7.21 (m, 2H), 6.23 (d, *J* = 3.2 Hz, 1H), 6.12 (d, *J* = 3.2 Hz, 1H), 4.36 (bs, 3H), 4.23 (dd, *J* = 7.4, 1.1 Hz, 1H), 3.71 (s, 3H), 3.36 (dd, *J* = 8.9, 7.4 Hz, 1H), 2.61 (bs, 1H, OH).
^{13}C-NMR (75 MHz, CDCl$_3$) δ 175.1, 174.5, 170.7, 154.8, 149.2, 138.0, 131.7, 129.2(2C), 128.9(2C), 128.9, 128.6, 126.8(2C), 126.5(2C), 109.6, 108.6, 73.4, 57.2, 55.2, 53.2, 53.2, 49.9.
HRMS (ESI+): Calculated for $C_{25}H_{23}N_2O_6$, 447.1551; found, 447.1549.

Methyl (1*R*,3*R*,3*aS*,6*aR*)-1-tert-butoxymethyl-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3f)



3f-*endo*-87% + 3f-*exo*-13%

Following the typical procedure 2, the reaction of Cu(CH$_3$CN)$_4$PF$_6$ (6.7 mg, 1.8·10^{-2} mmol), (*R*)-Fesulphos (9.2 mg, 2.0·10^{-2} mmol), *N*-phenylmaleimide (31.2 mg, 0.18 mmol), **1f** (50 mg, 0.18 mmol) and Et$_3$N (8 μL, 5.4·10^{-2} mmol) in dichloromethane (5 mL) at 0ºC for 12 h. The crude mixture was concentrated in vacuo and gave a 86:14 mixture of diastereoisomers **3f-*endo*** and **3f-*exo***. After flash column chromatography (heptane-AcOEt 1:1) a fraction containing 88:12 mixture of **3f-*endo*** and **3f-*exo*** could be isolated (61.0 mg, 73%, white solid).
M.p.: 103-105ºC.
[α]$_D^{20}$:+87.4 (c = 0.5, CH$_2$Cl$_2$), 99% *ee.*
SFC: Chiralpak IC, CO$_2$/MeOH from 95-5 to 60/40 in 8 min, flow rate 2 mL/min (λ=230 nm) t$_R$: 6.24 min (1*S*,3*S*,3*aR*,6*aS*)-**3f-*endo*** and 6.4 min (1*R*,3*R*,3*aS*,6*aR*)-**3f-*endo***.
^{1}H-NMR (300 MHz, CDCl$_3$) δ 7.46 – 7.34 (m, 3H, **3f-*endo***), 7.26 – 7.19 (m, 2H, **3f-*endo***), 7.15 – 7.09 (m, 4H, **3f-*exo***), 6.61 (d, *J* = 5.9 Hz, 1H, **3f-*exo***), 6.46 (d, *J* = 5.9 Hz, 1H, **3f-*exo***), 6.37 (d, *J* = 3.1 Hz, 1H, **3f-*endo***), 6.21 (d, *J* = 3.1 Hz, 1H, **3f-*endo***), 4.99 (d, *J* = 9.2 Hz, 1H, **3f-*endo***), 4.90 (d, *J* = 9.2 Hz, 1H, **3f-*exo***), 4.57 (d, *J* = 7.7 Hz, 1H, **3f-*exo***), 4.46 (s, 2H, **3f-*endo***), 4.19 – 4.05 (m, 4H, **3f-*exo***), 3.90 (d, *J* = 2.4 Hz, 1H, **3f-*exo***), 3.84 (s, 3H, **3f-*endo***), 3.80 (d, *J* = 8.0 Hz, 1H, **3f-*endo***), 3.75 – 3.68 (m, 2H, **3f-*endo***), 3.61 (d, *J* = 7.7 Hz, 1H, **3f-*exo***), 3.51 (d, *J* = 8.0 Hz, 1H, **3f-*endo***), 1.22 (s, 9H, **3f-*endo***).
^{13}C-NMR (75 MHz, CDCl$_3$, 3f-*endo*) δ 175.2, 174.7, 171.0, 154.5, 150.9, 131.9, 129.3(2C), 128.8, 126.5(2C), 109.3, 108.7, 74.0, 71.9, 66.2, 58.4, 57.5, 53.0, 52.8, 50.8, 27.5(3C).
HRMS (ESI+): Calculated for $C_{24}H_{29}N_2O_7$, 457.1969; found, 457.1964.
Methyl (1*S*,3*R*,3*aS*,6*aR*)-3-(5-(hydroxymethyl)furan-2-yl)-1-(2-methylthioethyl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3g)

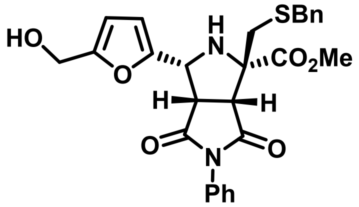


3g

Following the typical procedure 2, the reaction of Cu(CH$_3$CN)$_4$PF$_6$ (6.3 mg, 1.7·10^{-2} mmol), (*R*)-Fesulphos (8.6 mg, 1.9·10^{-2} mmol), *N*-phenylmaleimide (29.4 mg, 0.17 mmol), **1g** (45 mg, 0.17 mmol) and Et$_3$N (8 μL, 5.1·10^{-2} mmol) in dichloromethane (5 mL) at 0ºC for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 1:1) the cycloadduct **3g** (50.6 mg, 67%, white solid).
M.p.: 167-169ºC.
[α]$_D^{20}$:+33.4 (c =0.5 , CHCl$_3$), 88% *ee.*
SFC: Chiralpak IB, CO$_2$/MeOH from 95-5 to 70/30 in 8 min, flow rate 2 mL/min (λ = 230 nm) t$_R$: 3.28 min (*2R,3S,3aR,6aS*)-**3g** and 3.53 min (*1S,3R,3aS,6aR*)-**3g**.
^{1}H-NMR (300 MHz, CDCl$_3$) δ 7.48 – 7.33 (m, 3H), 7.28 – 7.19 (m, 2H), 6.37 (d, *J* = 3.2 Hz, 1H), 6.24 (d, *J* = 3.2 Hz, 1H), 4.74 (d, *J* = 8.9 Hz, 1H), 4.44 (s, 2H), 3.89 (s, 3H), 3.61 (dd, *J* = 8.9, 7.7 Hz, 1H), 3.47 (d, *J* = 7.7 Hz, 1H), 2.72 – 2.60 (m, 1H), 2.53 – 2.34 (m, 2H), 2.14 (s, 3H), 1.95 – 1.83 (m, 1H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ 174.5, 174.0, 171.2, 154.9, 149.0, 131.7, 129.3(2C), 129.0, 126.5(2C), 109.9, 108.9, 71.9, 58.2, 57.6, 57.0, 53.2, 50.4, 35.5, 28.9, 15.9.
HRMS (ESI+): Calculated for $C_{22}H_{25}N_2O_6S$, 445.1428; found, 445.1420.

Methyl (1*S*,3*R*,3*aS*,6*aR*)-1-benzylthiomethyl-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3h)

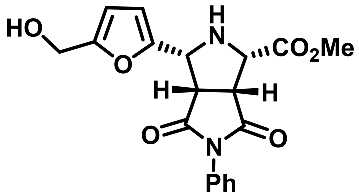


3h

Following the typical procedure 2, the reaction of Cu(CH$_3$CN)$_4$PF$_6$ (5.6 mg, 1.5·10^{-2} mmol), (*R*)-Fesulphos (7.6 mg, 1.7·10^{-2} mmol), *N*-phenylmaleimide (26.0 mg, 0.15 mmol), **1h** (50 mg, 0.15 mmol) and Et$_3$N (7 µL, 4.5·10^{-2} mmol) in dichloromethane (5 mL) at 0ºC for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 1:1) the cycloadduct **3h** (64.6 mg, 85%, white solid).

M.p.: 105-107ºC.
[α]$_D$^{20}:+30.7 (c = 1.0, CHCl$_3$), 86% *ee.*
SFC: Chiralpak IB, CO$_2$/MeOH from 95-5 to 70/30 in 8 min, flow rate 2 mL/min (λ = 210 nm) t$_R$: 5.24 min (*2R,3S,3aR,6aS*)-**3h** and 5.65 min (*1S,3R,3aS,6aR*)-**3h**.
^{1}H-NMR (300 MHz, CDCl$_3$) δ 7.36 – 7.27 (m, 6H), 7.24 – 7.18 (m, 2H), 7.16 – 7.09 (m, 2H), 6.24 (d, *J* = 3.2 Hz, 1H), 6.12 (d, *J* = 3.2 Hz, 1H), 4.36 (bs, 3H), 3.79 (d, *J* = 13.8 Hz, 1H), 3.75 (s, 3H), 3.68 (d, *J* = 13.8 Hz, 1H), 3.40 – 3.33 (m, 1H), 3.29 (d, *J* = 7.7 Hz, 1H), 3.01 (d, *J* = 13.6 Hz, 1H), 2.69 (d, *J* = 13.6 Hz, 1H).
^{13}C-NMR (75 MHz, CDCl$_3$) δ 174.2, 174.0, 170.8, 154.7, 149.5, 138.1, 131.7, 129.3(2C), 129.1(2C), 128.9, 128.8(2C), 127.5, 126.5(2C), 109.5, 108.7, 72.6, 57.4, 57.2, 55.3, 53.1, 49.5, 37.2, 36.4.
HRMS (ESI+): Calculated for $C_{27}H_{27}N_2O_6S$, 507.1584; found, 507.1576.

Methyl (1*S*,3*R*,3*aS*,6*aR*)-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3i)

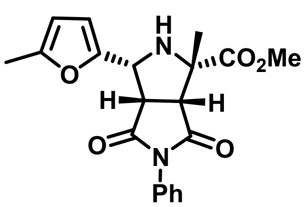


3i

Following the typical procedure 2, the reaction of Cu(CH$_3$CN)$_4$PF$_6$ (9.3 mg, 2.5·10^{-2} mmol), (*R*)-Fesulphos (12.8 mg, 2.8·10^{-2} mmol), *N*-phenylmaleimide (43.3 mg, 0.25 mmol), **1i** (50 mg, 0.25 mmol) and Et$_3$N (11 µL, 7.5·10^{-2} mmol) in dichloromethane (5 mL) at room temperature for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 1:1) the cycloadduct **3i** (65.0 mg, 70%, white solid).

M.p.: 130-132ºC.
[α]$_D$^{20}:+41.0 (c =0.1 , CHCl$_3$), >99% *ee*.
HPLC: Chiralpak IC, hexane/iPrOH 40/60 in 30 min, flow rate 1 mL/min (λ = 254 nm), t$_R$: 10.69 min (*1S,3R,3aS,6aR*)-**3i** and 16.42 min (*1R,3S,3aR,6aS*)-**3i**.
^{1}H-NMR (300 MHz, CDCl$_3$) δ 7.47 – 7.32 (m, 3H), 7.26 – 7.22 (m, 2H), 6.36 (d, *J* = 3.1 Hz, 1H), 6.23 (d, *J* = 3.1 Hz, 1H), 4.64 (d, *J* = 8.8 Hz, 1H), 4.50 (s, 2H), 4.11 (d, *J* = 6.3 Hz, 1H), 3.87 (s, 3H), 3.75 (t, *J* = 7.4 Hz, 1H), 3.59 (t, *J* = 8.3 Hz, 1H), 2.78 (bs, 1H, OH).
^{13}C-NMR (75 MHz, CDCl$_3$) δ 174.9, 174.1, 169.9, 154.7, 149.4, 131.8, 129.3(2C), 128.9, 126.5(2C), 109.4, 108.8, 62.5, 59.3, 57.5, 52.7, 49.6, 49.6.
HRMS (ESI+): Calculated for $C_{19}H_{19}N_2O_6$, 371.1238; found, 371.1239.

Methyl (1*S*,3*R*,3*aS*,6*aR*)-3-(5-methylfuran-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3j)

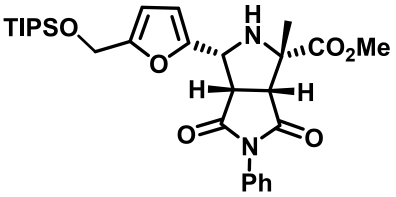


3j

Following the typical procedure 2, the reaction of Cu(CH$_3$CN)$_4$PF$_6$ (4.8 mg, 1.3·10^{-2} mmol), (*R*)-Fesulphos (6.9 mg, 1.5·10^{-2} mmol), *N*-phenylmaleimide (22.5 mg, 0.13 mmol), **1j** (25 mg, 0.13 mmol) and Et$_3$N (5 µL, 3.9·10^{-2} mmol) in

dichloromethane (5 mL) at room temperature for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 3:1) the cycloadduct **3j** (40.5 mg, 86%, white solid).
M.p.: 171-174ºC.
[α]$_D^{20}$:+42.0 (c =0.5, $CHCl_3$), 96% *ee*.
HPLC: Chiralpak IBN, hexane/iPrOH 70/30 in 30 min, flow rate 1 mL/min (λ = 230 nm), t_R: 9.24 min (*1R,3S,3aR,6aS*)-**3j** and 12.96 min (*1S,3R,3aS,6aR*)-**3j**.
^{1}H-NMR (300 MHz, $CDCl_3$) *δ* 7.50 – 7.38 (m, 4H), 7.29 – 7.24 (m, 1H), 6.34 (d, J = 3.2 Hz, 1H), 5.98 – 5.93 (m, 1H), 4.86 (t, J = 9.5 Hz, 1H), 3.92 (s, 3H), 3.68 (t, J = 7.7 Hz, 1H), 3.54 (d, J = 7.7 Hz, 1H), 3.35 (d, *J* = 10.1 Hz, 1H, NH), 2.23 (s, 3H), 1.63 (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$) *δ* 174.8, 174.0, 172.4, 152.8, 147.2, 131.9, 129.2 (2C), 128.8, 126.5(2C), 110.0, 106.7, 68.4, 58.5, 57.2, 53.1, 50.3, 24.0, 13.8.
HRMS (ESI+): Calculated for $C_{20}H_{21}N_2O_5$, 369.1445; found, 369.1440.

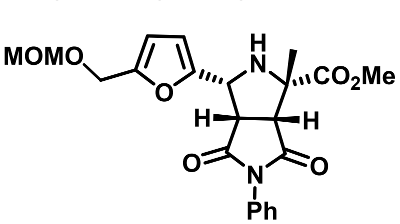
Methyl (1*S*,3*R*,3*aS*,6*aR*)-4,6-dioxo-5-phenyl-3-(5-(triisopropylsilyloxymethyl)furan-2-yl)octahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3k)



3k

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (2.7 mg, 7.2·10^{-3} mmol), (*R*)-Fesulphos (3.6 mg, 7.8·10^{-3} mmol), *N*-phenylmaleimide (12.1 mg, 6.9·10^{-2} mmol), **1i** (25 mg, 6.8·10^{-2} mmol) and Et_3N (5 µL, 2.0·10^{-2} mmol) in dichloromethane (5 mL) at room temperature for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 2:1) the cycloadduct **3i** (21.4 mg, 60%, yellow solid).
M.p.: 110-112ºC.
[α]$_D^{20}$:+15.2 (c =1.0 , $CHCl_3$), 97% *ee*.
HPLC: Chiralpak IBN, hexane/iPrOH 80/20 in 30 min, flow rate 1 mL/min (λ = 250 nm), t_R: 7.10 min (*1R,3S,3aR,6aS*)-**3k** and 8.48 min (*1S,3R,3aS,6aR*)-**3k.**
^{1}H-NMR (300 MHz, $CDCl_3$) *δ* 7.44 – 7.34 (m, 3H), 7.25 – 7.18 (m, 2H), 6.35 (d, *J* = 3.2 Hz, 1H), 6.20 (d, *J* = 3.2 Hz, 1H), 4.82 (dd, *J* = 11.0, 9.0 Hz, 1H), 4.58 (d, *J* = 4.4 Hz, 2H), 3.86 (s, 3H), 3.63 (dd, *J* = 9.0, 7.7 Hz, 1H), 3.46 (d, *J* = 7.7 Hz, 1H), 3.28 (d, *J* = 11.0 Hz, 1H, NH), 1.57 (s, 3H), 1.15 – 0.95 (m, 18H).
^{13}C-NMR (75 MHz, $CDCl_3$) *δ* 174.7, 173.7, 172.1, 155.3, 148.2, 131.9, 129.1(2C), 128.7, 126.4(2C), 109.6, 107.4, 68.4, 58.7, 58.3, 57.0, 53.0, 50.31, 24.0, 18.0(6C), 12.1(3C).
HRMS (ESI+): Calculated for $C_{29}H_{41}N_2O_6Si$, 541.2728; found, 541.2723.

Methyl (1*S*,3*R*,3*aS*,6*aR*)-3-(5-((methoxymethoxy)methyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3l)

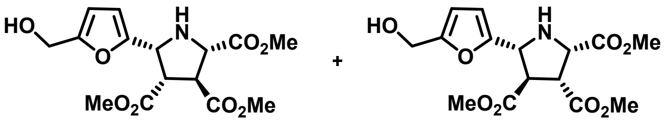


3l

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (4.3 mg, 1.1·10^{-2} mmol), (*R*)-Fesulphos (5.9 mg, 1.3·10^{-2} mmol), *N*-phenylmaleimide (20.3 mg, 0.11 mmol), **1l** (30 mg, 0.11 mmol) and Et_3N (11 µL, 7.5·10^{-2} mmol) in dichloromethane (5 mL) at room temperature for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 3:1) the cycloadduct **3l** (30.2 mg, 60%, yellow solid).
M.p.: 154-157ºC
.**[α]$_D^{20}$:**+87.6 (c =0.5, $CHCl_3$), 97% *ee*.
HPLC: Chiralpak IBN, hexane/iPrOH 70/30 in 30 min, flow rate 1 mL/min (λ = 230 nm), t_R: 14.50 min (*1R,3S,3aR,6aS*)-**3l** and 18.54 min (*1S,3R,3aS,6aR*)-**3l.**
^{1}H-NMR (300 MHz, $CDCl_3$) *δ* 7.47 – 7.31 (m, 3H), 7.25 (d, *J* = 5.3 Hz, 2H), 6.37 (d, *J* = 3.2 Hz, 1H), 6.29 (d, *J* = 3.2 Hz, 1H), 4.84 (t, *J* = 9.1 Hz, 1H), 4.57 (d, *J* = 6.7 Hz, 1H), 4.51 (d, *J* = 6.7 Hz, 1H), 4.43 (d, *J* = 5.5 Hz, 2H), 3.86 (s, 3H), 3.64 (d, *J* = 8.6 Hz, 1H), 3.47 (d, *J* = 7.8 Hz, 1H), 3.34 (s, 3H), 1.58 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ 174.8, 173.8, 172.3, 151.9, 149.8, 131.8, 129.2(2C), 128.8, 126.6(2C), 110.7, 109.5, 95.0, 68.5, 60.7, 58.2, 56.9, 55.5, 53.1, 50.3, 24.0.
HRMS (ESI+): Calculated for $C_{22}H_{25}N_2O_7$, 429.1656; found, 429.1659.

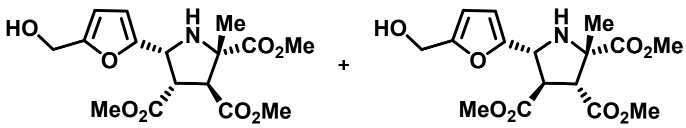
Trimethyl (2*S*,3*S*,4*S*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)pyrrolidine-2,3,4-tricarboxylate (9)



9-*endo*-90% **9-*exo*-10%**

Following the typical procedure 2, the reaction of Cu(CH$_3$CN)$_4$PF$_6$ (8.9 mg, 2.4·10^{-2} mmol), (*R*)-Fesulphos (11.9 mg, 2.6·10^{-2} mmol), dimethyl fumarate (34.6 mg, 0.24 mmol), **1i** (48 mg, 0.24 mmol) and Et$_3$N (10 μL, 7.0·10^{-2} mmol) in THF (5 mL) at room temperature for 12 h. The crude mixture was concentrated in vacuo and gave a 80:20 mixture of diastereoisomers **9-*endo*** and **9-*exo***. After flash column chromatography (heptane-AcOEt 1:2) a fraction containing 90:10 mixture of **9-*endo*** and **9-*exo*** could be isolated (41.5 mg, 51%, yellow oil).
[α]$_D$^{25}: +21.4 (c=0.5, CHCl$_3$), 93% *ee.*
HPLC: Chiralpak IBN, hexane/iPrOH 70/30 in 15 min, flow rate 1 mL/min (λ = 230 nm), t$_R$: 6.07 min (*2S,3S,4S,5R*)-**9** and 7.01 min (*2R,3R,4R,5S*)-**9**.
^{1}H-NMR (300 MHz, CDCl$_3$) δ 6.30 (d, *J* = 3.3 Hz, 1H, **9-*exo***), 6.23 (d, *J* = 3.2 Hz, 1H, **9-*exo***), 6.20 (d, *J* = 3.2 Hz, 1H, **9-*endo***), 6.18 (d, *J* = 3.2 Hz, 1H, **9-*endo***), 4.66 (d, *J* = 8.0 Hz, 1H, **9-*endo***), 4.58 (s, 2H, **9-*exo***), 4.51 (s, 2H, **9-*endo***), 4.18 (d, *J* = 7.2 Hz, 1H, **9-*endo***), 3.80 (s, 3H, **9-*endo***), 3.77 (s, 3H, **9-*endo***), 3.73 (s, 3H, **9-*exo***), 3.70 (d, *J* = 1.9 Hz, 1H, **9-*endo***), 3.61 (t, *J* = 7.2 Hz, 1H, **9-*endo***), 3.52 (s, 3H, **9-*endo***), 2.41 (s, 1H, OH).
^{13}C-NMR (75 MHz, CDCl$_3$, 9-*endo*) δ 172.9, 172.7, 171.4, 154.2, 151.6, 108.6, 108.4, 62.7, 59.0, 57.2, 52.9, 52.8, 52.5, 52.4, 49.6.
HRMS (ESI+): Calculated for $C_{15}H_{20}NO_8$, 342.1183; found, 342.1180.

Trimethyl (2*S*,3*S*,4*S*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)-2-methylpyrrolidine-2,3,4-tricarboxylate (10)

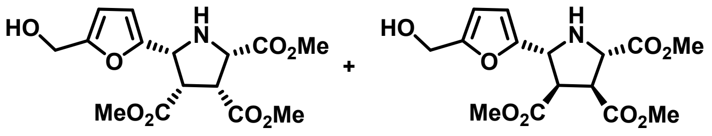


10-*endo*-90% **10-*exo*-10%**

Following the typical procedure 2, the reaction of Cu(CH$_3$CN)$_4$PF$_6$ (7.5 mg, 2.0·10^{-2} mmol), (*R*)-Fesulphos (10.1 mg, 2.2·10^{-2} mmol), dimethyl fumarate (28.9 mg, 0.20 mmol), **1a** (43 mg, 0.20 mmol) and Et$_3$N (9 μL, 6.0·10^{-2} mmol) in THF (5 mL) at room temperature for 12 h. The crude mixture was concentrated in vacuo and gave a 85:15 mixture of diastereoisomers **10-*endo*** and **10-*exo***. After flash column chromatography (heptane-AcOEt 1:1) a fraction containing 90:10 mixture of **10-*endo*** and **10-*exo*** could be isolated (40.0 mg, 56%, yellow oil).
[α]$_D$^{20}: +19.0, (c=0.5, CHCl$_3$), 80% *ee*.
HPLC: Chiralpak IBN, hexane/iPrOH 80/20 in 30 min, flow rate 0.8 mL/min (λ = 210 nm), t$_R$: 8.56 min (*2S,3S,4S,5R*)-**10-*endo*** and 9.11 min (*2R,3R,4R,5S*)-**10-*endo***.
6.22 (d, *J* = 3.2 Hz, 1H), 6.19 (d, *J* = 3.3 Hz, 1H), 4.54 (s, 2H), 3.70 (s, 3H), 3.67 (s, 3H), 3.64 (s, 3H),
^{1}H-NMR (300 MHz, CDCl$_3$) δ 6.22 (d, *J* = 3.3 Hz, 1H, **10-*exo***), 6.19 (d, *J* = 3.3 Hz, 1H, **10-*exo***), 6.13 (d, *J* = 3.3 Hz, 1H, **10-*endo***), 6.11 (d, *J* = 3.3 Hz, 1H, **10-*endo***), 4.71 (d, *J* = 8.1 Hz, 1H, **10-*endo***), 4.54 (s, 2H, **10-*exo***), 4.47 (s, 2H, **10-*endo***), 4.09 (d, *J* = 10.3 Hz, 1H, **10-*endo***), 3.85 (dd, *J* = 10.3, 8.1 Hz, 1H, **10-*endo***), 3.76 (s, 3H, **10-*endo***), 3.74 (s, 3H, **10-*endo***), 3.70 (s, 3H, **10-*exo***), 3.67 (s, 3H, **10-*exo***), 3.64 (s, 3H, **10-*exo***), 3.51 (s, 3H, **10-*endo***), 2.47 (bs, OH, **10-*endo* + 10-*exo***), 1.31 (s, 3H, **10-*endo***), 1.24 (s, 3H, **10-*exo***).

^{13}C-NMR (75 MHz, $CDCl_3$, 9-*endo*) δ 175.7, 171.6, 171.0, 154.0, 153.3, 108.4, 108.3, 66.8, 57.4, 56.6, 53.2, 52.4, 52.3, 51.8, 51.1, 23.3.
HRMS (ESI+): Calculated for $C_{16}H_{22}NO_8$, 356.1340; found, 356.1341.

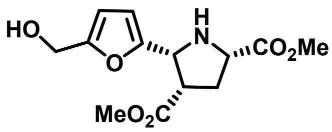
Trimethyl (2*S*,3*R*,4*S*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)pyrrolidine-2,3,4-tricarboxylate (11)



11-*endo*-85% 11-*exo*-15%

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (5.6 mg, $1.5\cdot10^{-2}$ mmol), (*R*)-Fesulphos (7.8 mg, $1.7\cdot10^{-2}$ mmol), dimethyl maleate (38 μL, 0.30 mmol), **1i** (30 mg, 0.15 mmol) and Et_3N (7 μL, $4.5\cdot10^{-2}$ mmol) in THF (5 mL) at room temperature for 12 h. The crude mixture was concentrated in vacuo and gave a 80:20 mixture of diastereoisomers **11-*endo*** and **11-*exo***. After flash column chromatography (heptane-AcOEt 1:2) a fraction containing 85:15 mixture of **11-*endo*** and **11-*exo*** could be isolated (24.0 mg, , 47%, yellow oil).
$[\alpha]_D^{20}$: +21.0 (c=0.5, $CHCl_3$), 83% *ee.*
HPLC: Chiralpak IBN, hexane/iPrOH 70/30 in 30 min, flow rate 1 mL/min (λ = 230 nm), t_R: 8.87 min (2*R*,3*S*,4*R*,5*S*)-**11-*endo*** and 12.28 min (2*S*,3*R*,4*S*,5*R*)-**11-*endo***.
^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.26 (d, *J* = 3.3 Hz, 1H, **11-*endo***), 6.20 (d, *J* = 3.3 Hz, 1H, **11-*endo***), 6.06 – 6.00 (m, 2H, **11-*exo***), 5.18 (d, *J* = 6.7 Hz, 1H, **11-*exo***), 4.85 (d, *J* = 6.9 Hz, 1H, **11-*exo***), 4.52 (s, 2H, **11-*endo***), 4.47 (d, *J* = 7.1 Hz, 1H, **11-*endo***), 4.36 (s, 2H, **11-*exo***), 4.28 (d, *J* = 6.8 Hz, 1H, **11-*exo***), 4.11 (d, *J* = 8.9 Hz, 1H, **11-*endo***), 3.78 (s, 3H, **11-*endo***), 3.83 (s, 3H, **11-*exo***), 3.76 – 3.72 (m, 1H, **11-*exo***), 3.71 (s, 3H, **11-*exo***), 3.68 (s, 3H, **11-*endo***), 3.66 – 3.61 (m, 1H, **11-*endo***), 3.53 – 3.49 (m, 1H, **11-*endo***), 3.49 (s, 3H, **11-*endo***), 3.39 (s, 3H, **11-*exo***), 2.63 (bs, 1H, OH).
^{13}C-NMR (75 MHz, $CDCl_3$) δ 171.2 (**11-*exo***), 171.1 (**11-*endo***), 170.9 (**11-*endo***), 170.6 (**11-*endo***), 170.5 (**11-*exo***), 169.8 (**11-*exo***), 154.0 (**11-*endo***), 152.6 (**11-*exo***), 150.7 (**11-*endo***), 147.6 (**11-*exo***), 112.5 (**11-*exo***), 108.6 (**11-*endo***), 108.4 (**11-*endo***), 61.9 (**11-*endo***), 60.0 (**11-*exo***), 59.5 (**11-*endo***), 58.7 (**11-*exo***), 57.4 (**11-*endo***), 57.3 (**11-*exo***), 52.9 (**11-*exo***), 52.7 (**11-*endo***), 52.5 (**11-*exo***), 52.3 (**11-*endo***), 52.0 (**11-*endo***), 51.9 (**11-*exo***), 51.6 (**11-*exo***), 51.1 (**11-*endo***), 50.6 (**11-*endo***), 48.8 (**11-*exo***).
HRMS (ESI+): Calculated for $C_{15}H_{20}NO_8$, 342.1183; found, 342.1179.

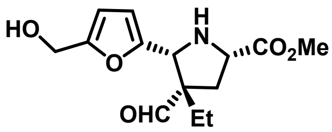
Dimethyl (2*S*,4*S*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)pyrrolidine-2,4-dicarboxylate (12)



12

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (5.6 mg, $1.5\cdot10^{-2}$ mmol), (*R*)-Fesulphos (7.8 mg, $1.7\cdot10^{-2}$ mmol), methyl acrylate (28 μL, 0.30 mmol), **1i** (30 mg, 0.15 mmol) and Et_3N (7 μL, $4.5\cdot10^{-2}$ mmol) in THF (5 mL) at 0ºC for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 1:1) the cycloadduct **12** (21.2 mg, 51%, yellow oil).
$[\alpha]_D^{20}$: +22.8 (c=0.5, $CHCl_3$), 88% *ee.*
HPLC: Chiralpak IBN, hexane/iPrOH 70/30 in 15 min, flow rate 1 mL/min (λ = 230 nm), t_R: 5.54 min (2*R*,4*R*,5*S*)-**12** and 6.59 min (2*S*,4*S*,5*R*)-**12**.
^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.19 (d, *J* = 3.3 Hz, 1H), 6.16 (d, *J* = 3.3 Hz, 1H), 4.52 (d, *J* = 7.3 Hz, 1H), 4.48 (s, 2H), 3.94 (t, *J* = 8.1 Hz, 1H), 3.77 (s, 3H), 3.50 (s, 3H), 3.26 (q, *J* = 7.3 Hz, 1H), 2.61 (bs, 1H, OH), 2.41 (td, *J* = 8.1, 1.5 Hz, 2H).
^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.4, 172.8, 154.0, 152.6, 108.4, 108.2, 59.3, 59.2, 57.3, 52.6, 52.1, 48.4, 32.1.
HRMS (ESI+): Calculated for $C_{13}H_{18}NO_6$, 284.1129; found, 284.1123.

Methyl (2*S*,4*S*,5*R*)-4-ethyl-4-formyl-5-(5-(hydroxymethyl)furan-2-yl)pyrrolidine-2-carboxylate (13)



13

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (5.6 mg, $1.5·10^{-2}$ mmol), (*R*)-Fesulphos (7.8 mg, $1.7·10^{-2}$ mmol), 2-ethylacrolein (30 µL, 0.30 mmol), **1i** (30 mg, 0.15 mmol) and Et_3N (7 µL, $4.5·10^{-2}$ mmol) in DCM (5 mL) at room temperature for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 2:3) the cycloadduct **13** (17.4 mg, 41%, yellow oil).

$[\alpha]_D^{25}$: +14.0 (c=0.5, $CHCl_3$), 91% *ee.*

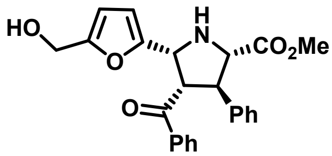
HPLC: Chiralpak IBN, hexane/iPrOH 70/30 in 30 min, flow rate 1 mL/min (λ = 230 nm), t_R: 4.76 min (2*S*,4*S*,5*R*)-**13** and 7.73 min (2*R*,4*R*,5*S*)-**13**.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 9.15 (s, 1H), 6.27 (d, *J* = 3.2 Hz, 1H), 6.20 (d, *J* = 3.2 Hz, 1H), 4.52 (s, 2H), 4.13 (s, 1H), 3.96 (dd, *J* = 9.9, 5.6 Hz, 1H), 3.77 (s, 3H), 2.58 (dd, *J* = 13.4, 5.6 Hz, 1H), 2.10 – 1.93 (m, 2H), 1.58 (dq, *J* = 14.7, 7.5 Hz, 1H), 0.84 (t, *J* = 7.5 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 204.0, 174.2, 154.7, 150.1, 109.3, 108.4, 65.2, 61.3, 58.3, 57.2, 52.6, 34.1, 26.4, 9.8.

HRMS (ESI+): Calculated for $C_{14}H_{20}NO_5$, 282.1336; found, 282.1334.

Methyl (2*S*,3*R*4*S*,5*R*)-4-benzoyl-5-(5-(hydroxymethyl)furan-2-yl)-3-phenylpyrrolidine-2-carboxylate (14)



14

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (5.6 mg, $1.5·10^{-2}$ mmol), (*R*)-Fesulphos (7.8 mg, $1.7·10^{-2}$ mmol), *trans* chalcone (31.2 mg, 0.15 mmol), **1i** (30 mg, 0.15 mmol) and Et_3N (7 µL, $4.5·10^{-2}$ mmol) in THF (5 mL) at 0ºC for 12 h, afforded, after purification by silica gel flash chromatography (heptane-AcOEt 2:1) the cycloadduct **14** (27.4 mg, 45%, yellow oil).

$[\alpha]_D^{20}$: -32.0 (c=0.5, $CHCl_3$), 80% *ee.*

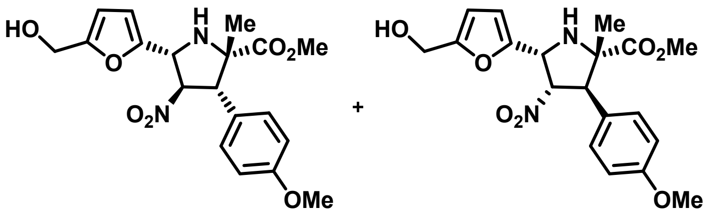
HPLC: Chiralpak IBN, hexane/iPrOH 70/30 in 30 min, flow rate 1 mL/min (λ = 230 nm), t_R: 5.07 min (2*R*,3*S*,4*R*,5*S*)-**14** and 11.17 min (2*S*,3*R*,4*S*,5*R*)-**14**.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.77 – 7.72 (m, 2H), 7.50 – 7.43 (m, 2H), 7.41 – 7.30 (m, 6H), 6.05 (d, *J* = 3.3 Hz, 1H), 5.97 (d, *J* = 3.3 Hz, 1H), 4.99 (d, *J* = 8.1 Hz, 1H), 4.45 (t, *J* = 7.6 Hz, 1H), 4.27 (d, *J* = 4.9 Hz, 2H), 4.23 – 4.16 (m, 1H), 4.12 (d, *J* = 8.1 Hz, 1H), 3.73 (s, 3H), 2.45 (bs, 1H, OH).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 198.0, 174.0, 153.6, 152.0, 141.2, 136.9, 133.2, 129.0(2C), 128.5(2C), 128.3(2C), 127.9(2C), 127.3, 108.8, 108.3, 67.3, 60.4, 59.3, 57.2, 52.6, 51.3.

HRMS (ESI+): Calculated for $C_{24}H_{24}NO_5$, 406.1649; found, 406.1642.

Methyl (2*S*,3*R*,4*R*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)-3-(4-methoxyphenyl)-2-methyl-4-nitropyrrolidine-2-carboxylate (15)



15-*exo*-85% **15-*endo*-15%**

Following the typical procedure 2, the reaction of $Cu(CH_3CN)_4PF_6$ (5.2 mg, $1.4·10^{-2}$ mmol), (*R*)-Fesulphos (6.9 mg, $1.5·10^{-2}$ mmol), *trans*-4-methoxy-*β*-nitrostyrene (25.1, 0.14 mmol), **1a** (30 mg, 0.14 mmol) and Et_3N (6 µL, $4.2·10^{-2}$ mmol) in THF (5 mL) at -10ºC for 12 h. The crude mixture was concentrated in vacuo and gave a 80:20 mixture of diastereoisomers **15-*exo*** and **15-**

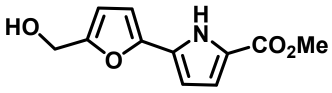
endo. After flash column chromatography (heptane-AcOEt 2:1) a fraction containing 85:15 mixture of **15-*exo*** and **15-*endo*** could be isolated (25.0 mg, , 46%, yellow solid).
M.p.: 140-142ºC
$[\alpha]_D^{20}$: -17.8, (c=0.5, $CHCl_3$) 95% *ee.*
HPLC: Chiralpak IBN, hexane/iPrOH 70/30 in 30 min, flow rate 1 mL/min (λ = 230 nm), t_R: 7.50 min (2*R*,3*S*,4*S*,5*S*)-**15** and 9.86 min (2*S*,3*R*,4*R*,5*R*)-**15**.
^{1}H-NMR (300 MHz, $CDCl_3$) *δ* 7.20 (d, *J* = 8.7 Hz, 2H, **15-*exo***), 7.14 (d, *J* = 8.7 Hz, 2H, **15-*endo***), 6.89 (d, *J* = 8.7 Hz, 2H, **15-*exo***), 6.86-6.83 (m, 2H, **15-*endo***), 6.41 (d, *J* = 3.2 Hz, 1H, **15-*endo***), 6.32 (d, *J* = 3.2 Hz, 1H, **15-*exo***), 6.29 (d, *J* = 3.3 Hz, 1H, **15-*endo***), 6.22 (d, *J* = 3.3 Hz, 1H, **15-*exo***), 5.57 (dd, *J* = 8.1, 7.3 Hz, 1H, **15-*exo***), 5.51 – 5.43 (m, 1H, **15-*endo***), 5.00 (d, *J* = 7.1 Hz, 1H, **15-*exo***), 4.87 (d, *J* = 9.0 Hz, 1H, **15-*endo***), 4.61 (d, *J* = 8.3 Hz, 1H, **15-*exo***), 4.57 (s, 1H, **15-*endo***), 4.55 (s, 2H, **15-*exo***), 4.41 (d, *J* = 7.9 Hz, 1H, **15-*endo***), 3.83 (s, 3H, **15-*exo***), 3.80 (s, 3H, **15-*exo***), 3.79 (s, 3H, **15-*endo***), 2.19 (s, 1H, OH), 1.14 (s, 3H, **15-*endo***), 1.08 (s, 3H, **15-*exo***). Contains Acetone and Ethyl Acetate.
^{13}C-NMR (75 MHz, $CDCl_3$, 15-*exo*) *δ* 175.8, 159.4, 154.7, 149.8, 129.9(2C), 127.2, 114.3(2C), 109.7, 108.8, 92.6, 68.2, 58.6, 57.5, 55.4, 53.8, 53.1, 23.9.
HRMS (ESI+): Calculated for $C_{19}H_{23}N_2O_7$, 391.1500; found, 391.1494.

4. Preparation of racemic products for HPLC analysis.

The racemic pyrrolidines were prepared according to the general procedure, but using PPh_3 as ligand. The samples for HPLC analysis were dissolved in isopropyl alcohol and used as quickly as possible to minimize the formation of decomposition products.

5. Additional transformations

Typical Procedure 3: Methyl 5-(5-(hydroxymethyl)furan-2-yl)-*1H*-pyrrole-2-carboxylate (17)



17

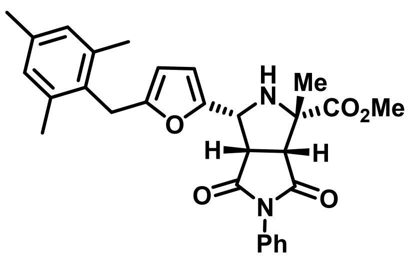
To a suspension of $[Cu(CH_3CN)_4]PF_6$ (18.6 mg, $5.0{\cdot}10^{-2}$ mmol), PPh_3 (14.4 mg, $5.5{\cdot}10^{-2}$ mmol), *trans*-1,2-bis(phenylsulfonyl)ethylene (**16**, 154.2, 0.50 mmol) and **1i** (100 mg, 0.50 mmol) in anhydrous THF (5 mL) under argon atmosphere, Et_3N (21 μL, $1.5{\cdot}10^{-1}$ mmol) was added. The resulting mixture was stirred at room temperature for 5 h and DBU (0.15 mL, 1.02 mmol) was added. After stirring for 30 min the resulting mixture was filtered over celite® and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography, (heptane:AcOEt 3:1) to afford **17** (50.0 mg, 47%, brown oil).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 9.65 (bs, 1H, NH), 6.90 (dd, J = 3.9, 2.3 Hz, 1H), 6.45 (d, J = 3.3 Hz, 1H), 6.41 (dd, J = 3.9, 2.3 Hz, 1H), 6.33 (d, J = 3.3 Hz, 1H), 4.65 (s, 2H), 3.86 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 161.7, 153.4, 146.8, 128.4, 122.4, 116.9, 110.0, 107.2, 106.1, 57.3, 51.7.

HRMS (ESI+): Calculated for $C_{11}H_{12}NO_4$, 222.0761; found, 222.0756.

Typical Procedure 4: (±)-Methyl 1-methyl-4,6-dioxo-5-phenyl-3-(5-(2,4,6-trimethylbenzyl)furan-2-yl)octahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (18)



18

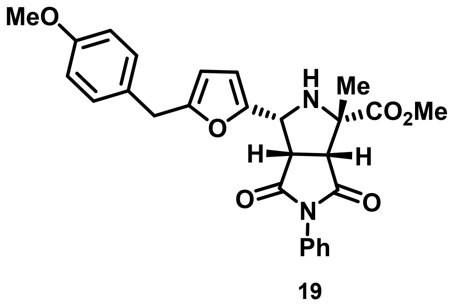
To a suspension of compound **3a** (77 mg, 0.20 mmol), in DCE/HF*i*P (1 mL:1.2 mL), mesitylene (0.29 mL, 2.0 mmol) and $NOBF_4$ (50 μL, $1.0{\cdot}10^{-2}$ mmol , 0.2 M in sulfolane[2]) were added. The mixture was stirred at 80ºC for 1,5 h and the solvent was evaporated under reduced pressure. The crude mixture was purified by flash chromatography, (heptane:AcOEt 2:1) to afford **18** (65.3 mg, 67%, colorless oil).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.51 – 7.41 (m, 2H), 7.39 – 7.26 (m, 3H), 6.82 (s, 2H), 6.23 (d, J = 3.1 Hz, 1H), 5.51 (d, J = 2.2 Hz, 1H), 4.82 (d, J = 9.1 Hz, 1H), 3.89 (s, 3H), 3.83 (d, J = 16.7 Hz, 1H), 3.70 – 3.61 (m, 2H), 3.49 (d, J = 7.8 Hz, 1H), 2.25 (s, 3H), 2.11 (s, 6H), 1.59 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.8, 173.7, 172.4, 155.0, 147.3, 137.1(2C), 136.1, 132.0, 131.0, 129.1(2C), 128.9(2C), 128.8, 126.45(2C), 109.9, 106.3, 68.6, 58.5, 57.1, 53.1, 50.5, 28.4, 24.1, 21.0, 19.7(2C).

HRMS (ESI+): Calculated for $C_{29}H_{31}N_2O_5$, 487.2227; found, 487.2224.

(±)-Methyl 3-(5-(4-methoxybenzyl)furan-2-yl)-1-methyl-4,6-dioxo-5-phenyloctahydropyrrolo[3,4-c]pyrrole-1-carboxylate (19)



19

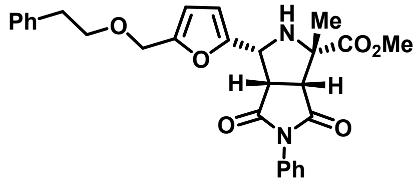
Following the typical procedure 4, the reaction of **3a** (77 mg, 0.20 mmol), anisole (0.22 mL, 2.0 mmol) and $NOBF_4$ (50 µL, 1.0·10^{-2} mmol , 0.2 M) in DCE/HF*i*P (1 mL:1.2 mL) at 80ºC for 1.5 h afforded, after purification by silica gel flash chromatography (heptane-AcOEt 1:1) the cycloadduct **19** (50.3 mg, 53%, yellow oil).

^{1}H-NMR (300 MHz, $CDCl_3$) *δ* 7.40 – 7.33 (m, 3H), 7.22 – 7.15 (m, 2H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 8.5 Hz, 2H), 6.31 (d, *J* = 3.2 Hz, 1H), 5.88 (d, *J* = 3.2 Hz, 1H), 4.82 (d, *J* = 9.0 Hz, 1H), 3.86 (s, 3H), 3.81 (s, 2H), 3.76 (s, 3H), 3.65 (dd, *J* = 9.0, 7.7 Hz, 1H), 3.47 (d, *J* = 7.7 Hz, 1H), 1.58 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.8, 173.8, 172.3, 158.4, 155.7, 147.9, 129.7(2C), 129.4, 129.2(2C), 128.7, 126.6, 126.5(2C), 114.0(2C), 109.8, 107.4, 68.5, 58.4, 57.1, 55.4, 53.1, 50.4, 33.6, 24.1.

HRMS (ESI+): Calculated for $C_{27}H_{27}N_2O_6$, 475.1864; found, 475.1859.

Typical Procedure 5: (±)-Methyl 1-methyl-4,6-dioxo-3-(5-(phenethoxymethyl)furan-2-yl)-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (20)



20

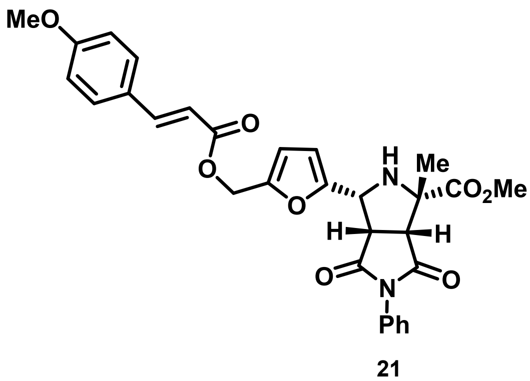
To a suspension of $Yb(OTf)_3$ (16.1 mg, 2.6·10^{-2} mmol) and **3a** (100 mg, 0.26 mmol) in anhydrous MeCN (2 mL) under argon atmosphere, a solution of phenylethyl alcohol (0.16 mL, 1.3 mmol) was added. The resulting mixture was stirred at 80ºC for 12 h. The resulting mixture was cooled and filtered over celite® and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography, (heptane:AcOEt 2:1) to afford **20** (60.0 mg, 47%, yellow oil).

^{1}H-NMR (300 MHz, $CDCl_3$) *δ* 7.47 – 7.31 (m, 4H), 7.25 – 7.12 (m, 6H), 6.37 (d, *J* = 3.2 Hz, 1H), 6.23 (d, *J* = 3.2 Hz, 1H), 4.87 (d, *J* = 9.0 Hz, 1H), 4.35 (q, *J* = 13.2 Hz, 2H), 3.87 (s, 3H), 3.68 (dd, *J* = 9.0, 7.7 Hz, 1H), 3.57 – 3.45 (m, 3H), 2.77 (t, *J* = 7.3 Hz, 2H), 1.61 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) *δ* 174.8, 173.7, 172.3, 152.5, 149.5, 139.0, 131.8, 129.2(2C), 129.1(2C), 128.8, 128.4(2C), 126.6(2C), 126.3, 110.4, 109.5, 70.8, 68.6, 64.8, 58.2, 56.9, 53.1, 50.3, 36.2, 24.0.

HRMS (ESI+): Calculated for $C_{28}H_{29}N_2O_6$, 489.2020; found, 489.2014.

Typical Procedure 6: (±)-Methyl 3-(5-(*E*)-3-(4-methoxyphenyl)acryloyloxymethylfuran-2-yl)-1-methyl-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (21)



21

A suspension of *trans*-4-methoxycinnamic acid (46.3 mg, 0.26 mmol), **3a** (100 mg, 0.26 mmol), *N*,*N'*-dicyclohexylcarbodiimide (60.0, 0.29), 4-(dimethylamino)pyridine (3.2 mg, 2.6·10^{-2} mmol) in DCM (3 mL) was stirred at room temperature for 12 h. The resulting mixture was filtered and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography, (heptane:AcOEt 3:1) to afford **21** (109.0 mg, 77%, white solid).

M.p. 134-136ºC

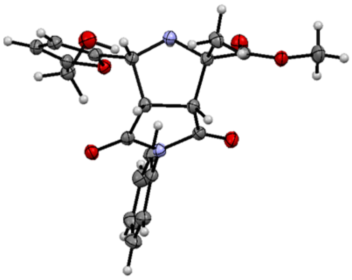
^{1}H-NMR (300 MHz, $CDCl_3$) *δ* 7.62 (d, *J* = 16.0 Hz, 1H), 7.44 – 7.34 (m, 2H), 7.33 – 7.27 (m, 2H), 7.25 – 7.20 (m, 2H), 7.05 (d, *J* = 7.7 Hz, 1H), 6.99 – 6.97 (m, 1H), 6.92 (dd, *J* = 7.7, 2.4 Hz, 1H), 6.41 (s, 2H), 6.32 (d, *J* = 16.0 Hz, 1H), 5.06 (d, *J* = 1.6 Hz, 2H), 4.86 (d, *J* = 9.0 Hz, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.69 (dd, *J* = 9.0, 7.7 Hz, 1H), 3.49 (d, *J* = 7.7 Hz, 1H), 1.60 (s, 3H).

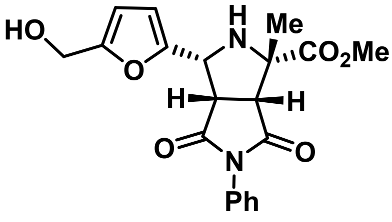
^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.7, 173.7, 172.2, 166.4, 159.9, 150.3, 150.0, 145.4, 135.7, 131.8, 129.8, 129.2(2C), 128.8, 126.4(2C), 121.0, 117.8, 116.4, 113.0, 111.8, 109.8, 68.4, 58.0, 58.0, 56.8, 55.3, 53.0, 50.1, 23.9.
HRMS (ESI+): Calculated for $C_{30}H_{29}N_2O_8$, 545.1918; found, 545.1911.

6. Stereochemical assignment of the products

The relative configuration of **3a** was unequivocally established by X-ray crystal structure analysis.

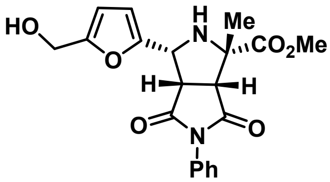
X-ray structure of 3a





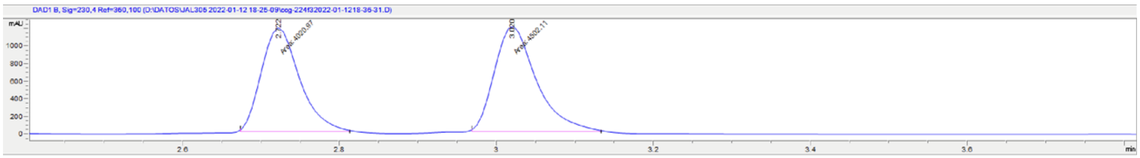
(+) 3a

7. HPLC chart



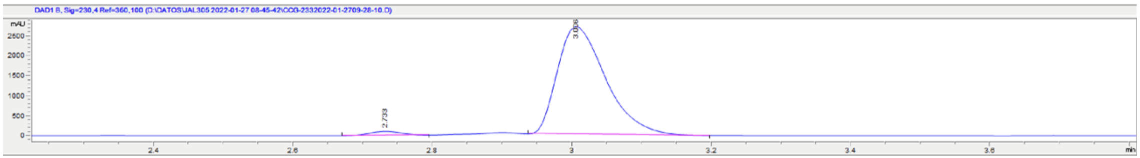
3a

(±)-**3a**

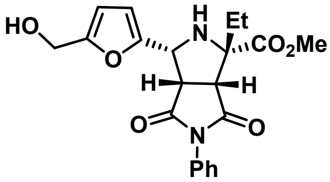


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.722	MM	4021	1195.8	0.056	47.177	0.779
2	3.02	MM	4502.1	1218.7	0.0616	52.823	0.717

(+)-**3a**; 95% *ee*

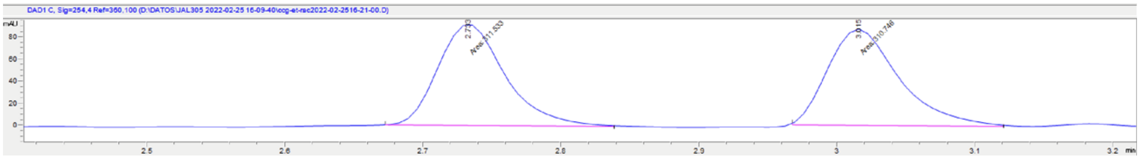


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.733	BB	317.3	102	0.0503	2.374	0.963
2	3.006	BB	13046.5	2729.7	0.0758	97.626	0.589



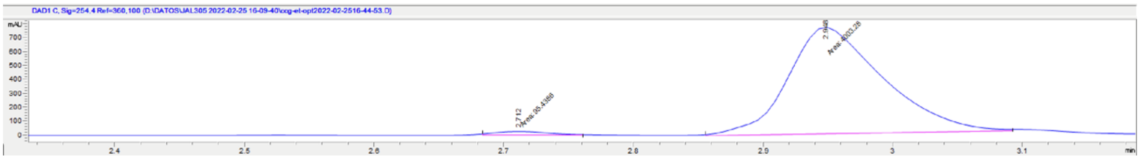
3b

(±)-**3b**

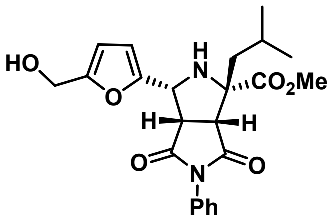


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.733	MM	311.5	92	0.0565	50.063	0.79
2	3.015	MM	310.7	86.9	0.0596	49.937	0.717

(+)-**3b**; 95% *ee*

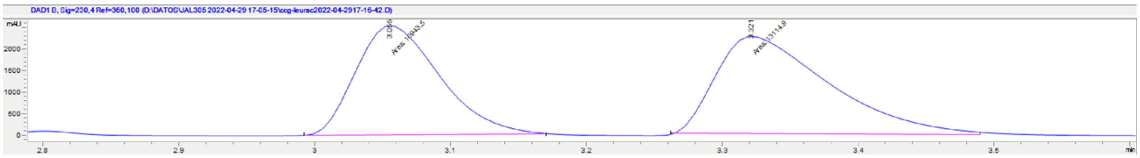


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.712	MM	95.4	31.4	0.0507	2.328	0.634
2	2.948	MM	4003.3	779.9	0.0856	97.672	0.649



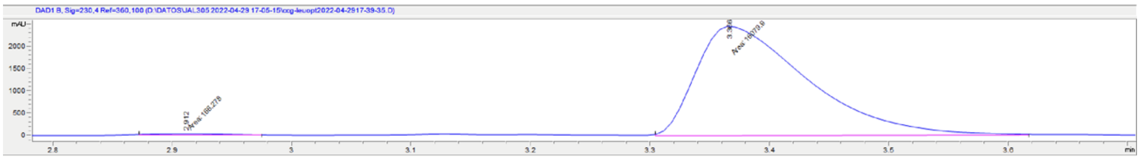
3c

(±)-**3c**

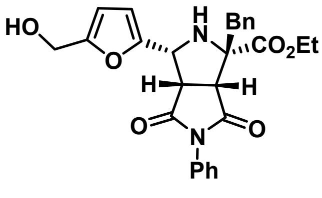


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.055	MM	10943.5	2558.4	0.0713	45.487	0.677
2	3.321	MM	13114.9	2277	0.096	54.513	0.455

(+)-**3c**; 98% *ee*

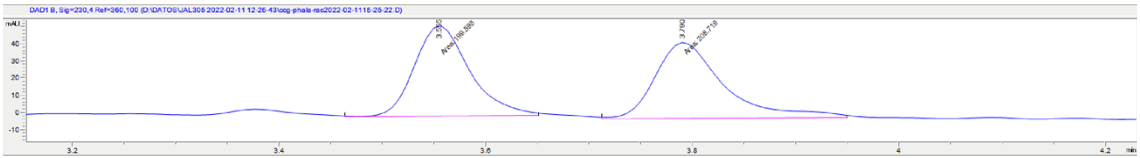


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.912	MM	166.3	36	0.0769	1.023	0.708
2	3.366	MM	16079.9	2479.4	0.1081	98.977	0.42



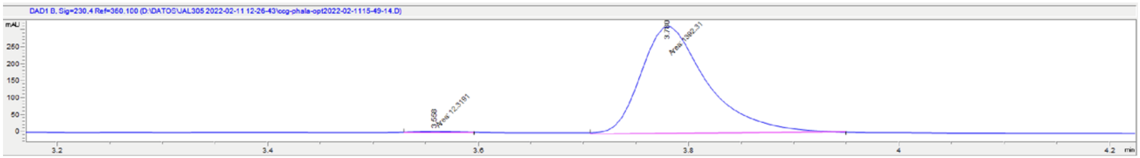
3d

(±)-**3d**

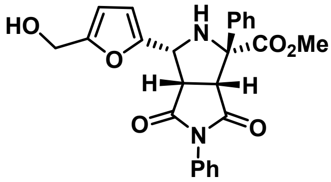


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.555	MM	199.6	53.3	0.0624	48.883	0.796
2	3.79	MM	208.7	44.8	0.0776	51.117	0.652

(+)-**3d**; 98% *ee*

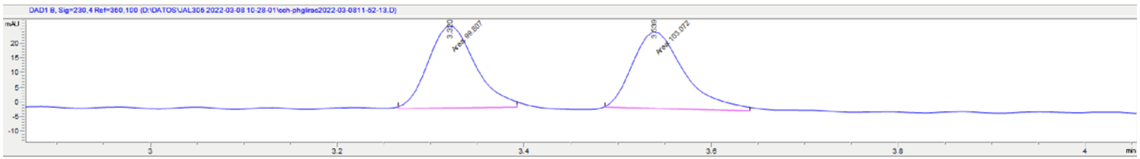


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.558	MM	12.3	4.2	0.0487	0.877	0.858
2	3.78	MM	1392.3	319	0.0728	99.123	0.668



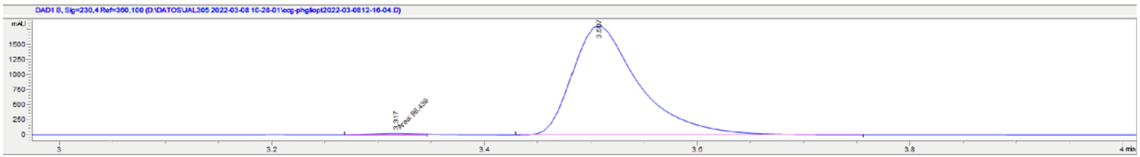
3e

(±)-**3e**

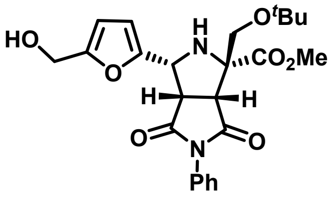


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.32	MM	99.8	28.5	0.0584	49.195	0.82
2	3.539	MM	103.1	26.6	0.0646	50.805	0.706

(-)-**3e**; 98% *ee*

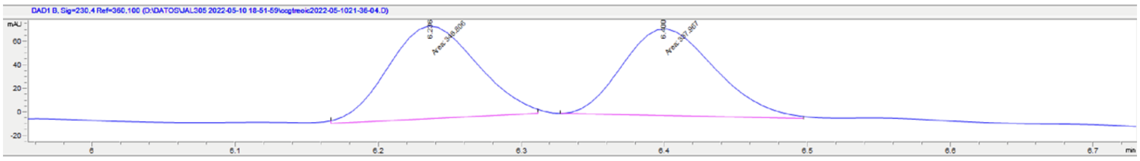


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.317	MM	96.4	28.4	0.0567	1.217	1.162
2	3.507	BB	7827.2	1820.8	0.0642	98.783	0.599



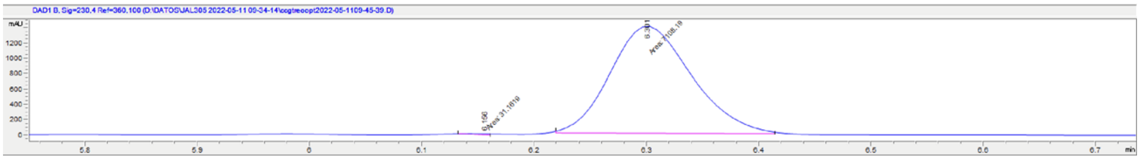
3f

(±)-**3f**

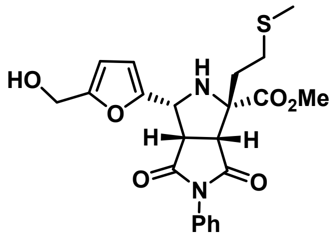


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.236	MM	346.8	79.9	0.0724	50.645	0.899
2	6.4	MM	338	74.6	0.0755	49.355	0.785

(+)-**3f**; 99% *ee*

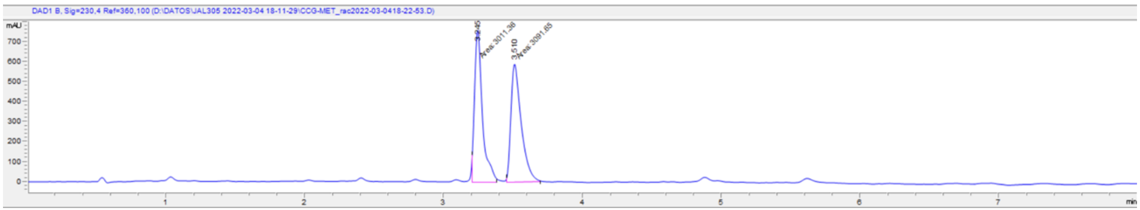


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.156	MM	31.2	22.3	0.0233	0.436	0.229
2	6.301	MM	7108.2	1412	0.0839	99.564	0.809



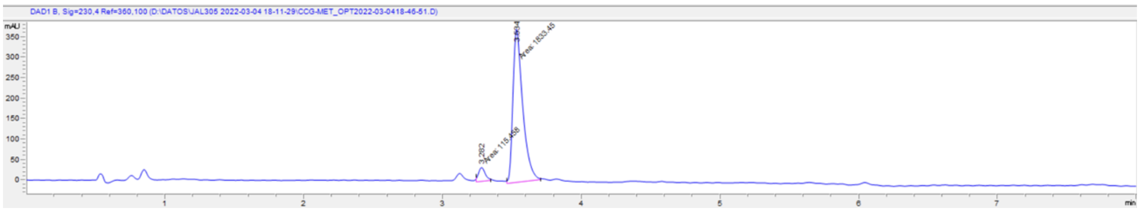
3g

(±)-**3g**

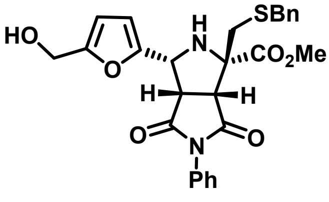


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.245	MM	3011.4	773	0.0649	49.342	0.616
2	3.51	MM	3091.6	598	0.0862	50.658	0.528

(+)-**3g**; 88% *ee*

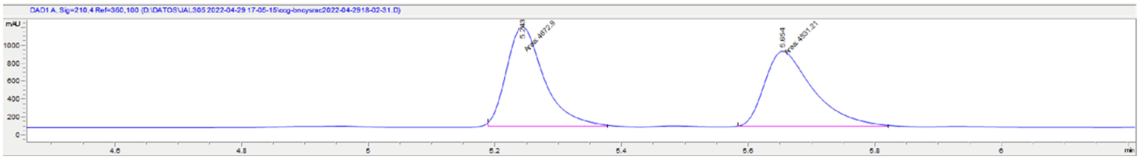


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.282	MM	115.5	34.4	0.0559	5.924	0.731
2	3.534	MM	1833.4	373.6	0.0818	94.076	0.581



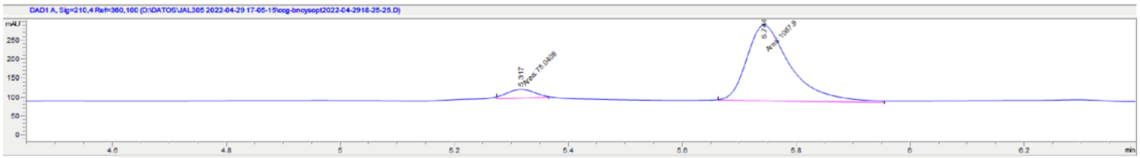
3h

(±)-**3h**

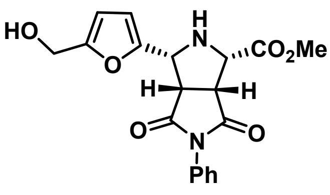


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.243	MM	4672.9	1132.1	0.0688	50.770	0.692
2	5.654	MM	4531.2	848.7	0.089	49.230	0.572

(+)-3h; 86% *ee*

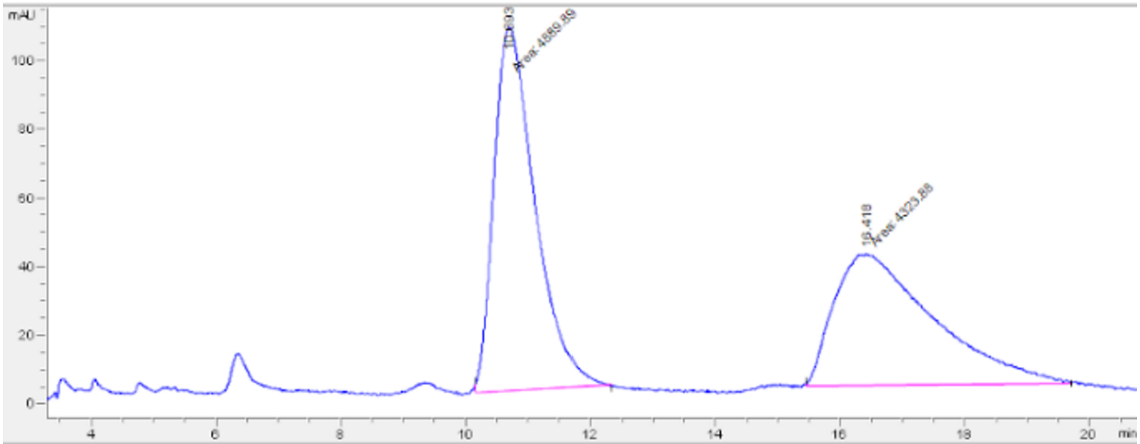


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.317	MM	78	23.6	0.0551	6.810	0.976
2	5.744	MM	1067.9	200.3	0.0889	93.190	0.622



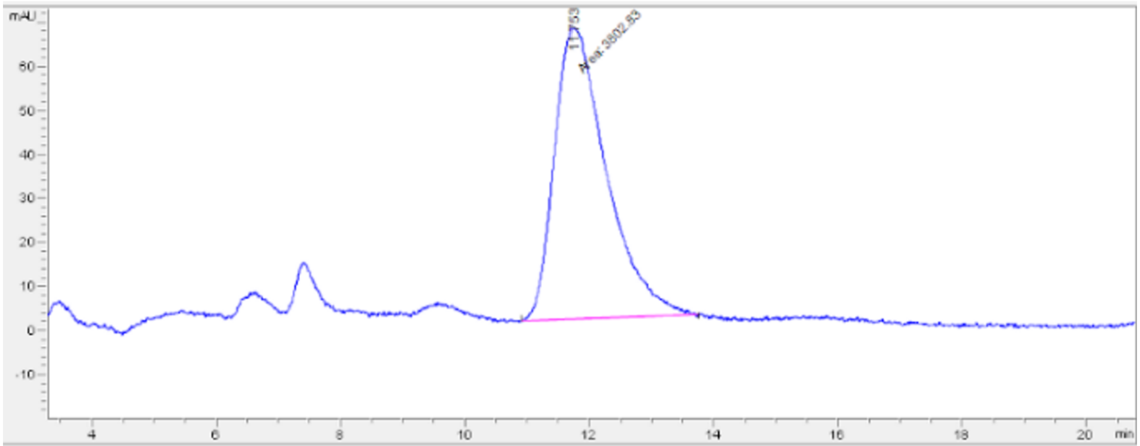
3i

(±)-**3i**

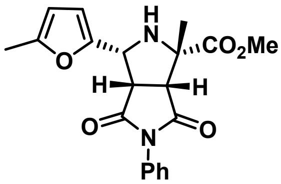


#	Time	Area	Height	Width	Area%	Symmetry
1	10.693	4889.9	106.3	0.7667	53.072	0.555
2	16.418	4323.9	38.7	1.8614	46.928	0.462

(+)-**3i**; >99% *ee*

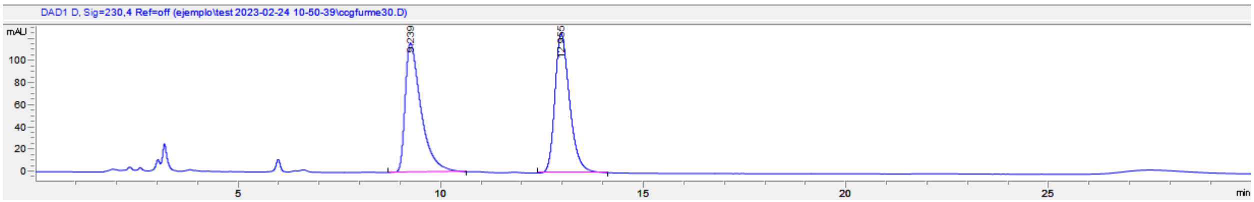


#	Time	Area	Height	Width	Area%	Symmetry
1	11.753	3802.8	66.2	0.9569	100.000	0.592



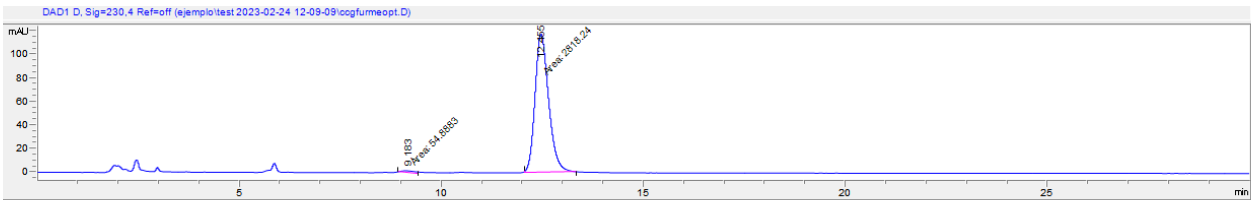
3j

(±)-**3j**

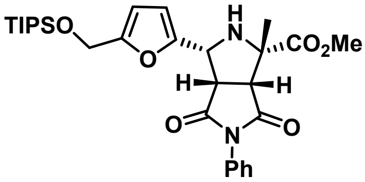


#	Time	Area	Height	Width	Area%	Symmetry
1	9.239	3184.5	116.8	0.3662	49.932	0.468
2	12.955	3193.2	125.9	0.3329	50.068	0.688

(+)-**3j**

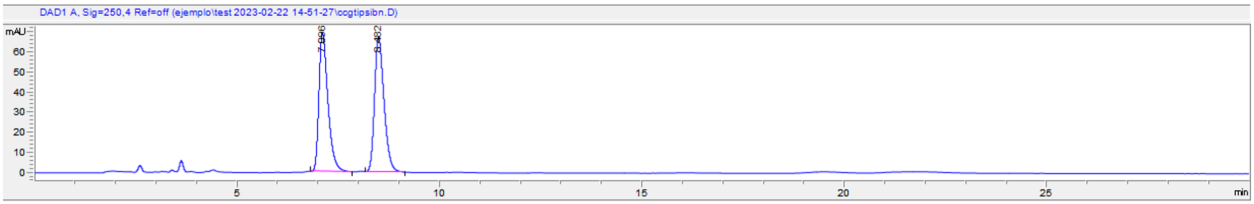


#	Time	Area	Height	Width	Area%	Symmetry
1	9.183	54.9	2.2	0.4185	1.910	0.862
2	12.455	2818.2	118.9	0.395	98.090	0.763



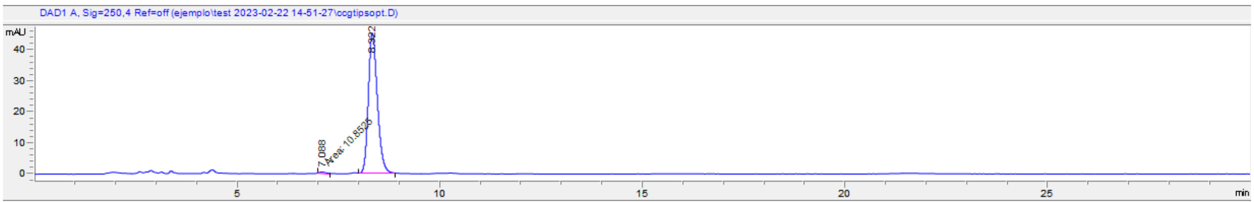
3k

(±)-**3k**

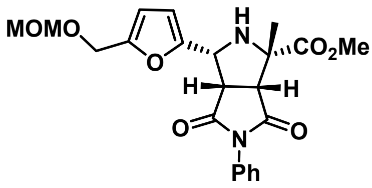


#	Time	Area	Height	Width	Area%	Symmetry
1	7.096	1068.9	68.8	0.2277	49.681	0.597
2	8.482	1082.7	66.9	0.2319	50.319	0.699

(+)-**3k**

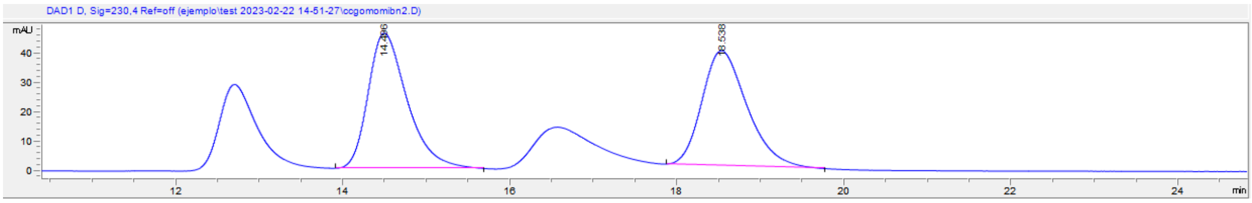


#	Time	Area	Height	Width	Area%	Symmetry
1	7.088	10.9	7.9E-1	0.2287	1.545	0.464
2	8.322	691.6	44.9	0.2225	98.455	0.752



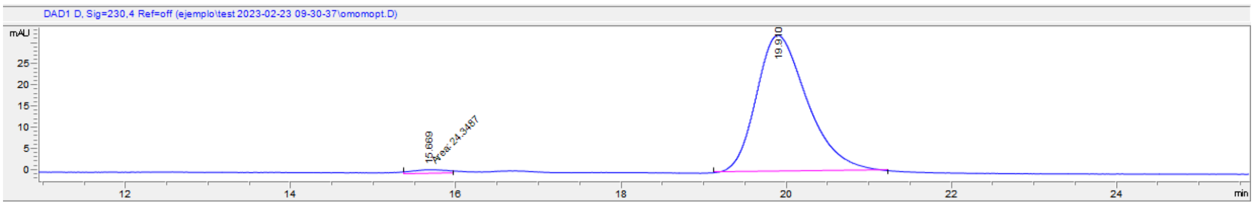
3l

(±)-**3l**

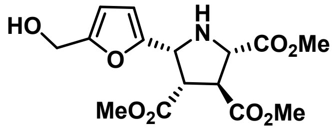


#	Time	Area	Height	Width	Area%	Symmetry
1	14.496	1506	46.4	0.3809	50.403	0.695
2	18.538	1481.9	39.3	0.4476	49.597	0.763

(+)-**3l**

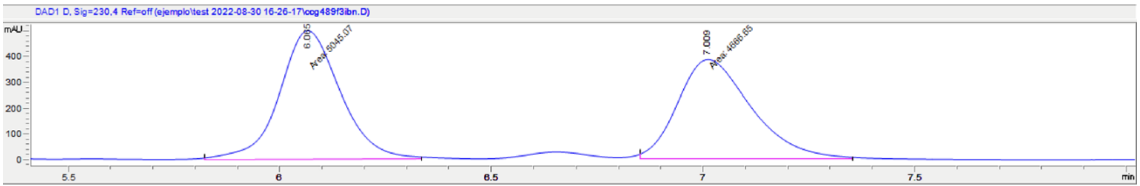


#	Time	Area	Height	Width	Area%	Symmetry
1	15.669	24.3	8.6E-1	0.4714	1.712	1.035
2	19.91	1397.7	32.4	0.5049	98.288	0.752



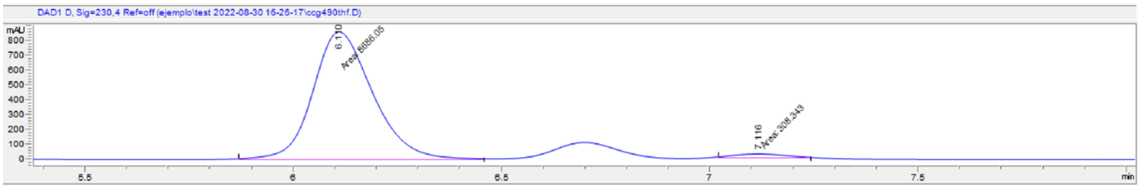
9

(±)-**9**

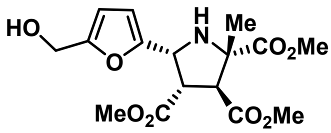


#	Time	Area	Height	Width	Area%	Symmetry
1	6.065	5045.1	500.8	0.1679	51.948	0.87
2	7.009	4666.6	385.8	0.2016	48.052	0.689

(+)-9; 93% *ee*

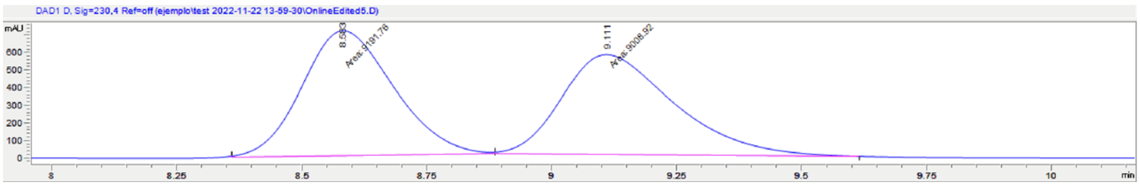


#	Time	Area	Height	Width	Area%	Symmetry
1	6.11	8686	862.6	0.1678	96.572	0.762
2	7.116	308.3	31.8	0.1614	3.428	0.826



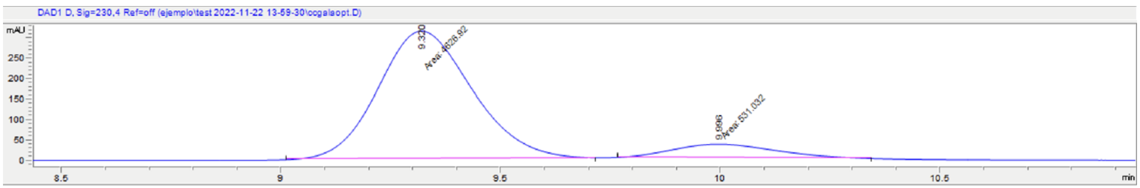
10

(±)-**10**

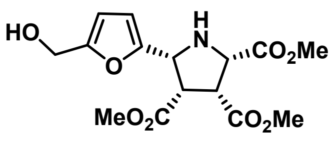


#	Time	Area	Height	Width	Area%	Symmetry
1	8.583	9191.8	718	0.2134	50.502	0.803
2	9.111	9008.9	573.7	0.2617	49.498	0.632

(+)-10; 79% *ee*

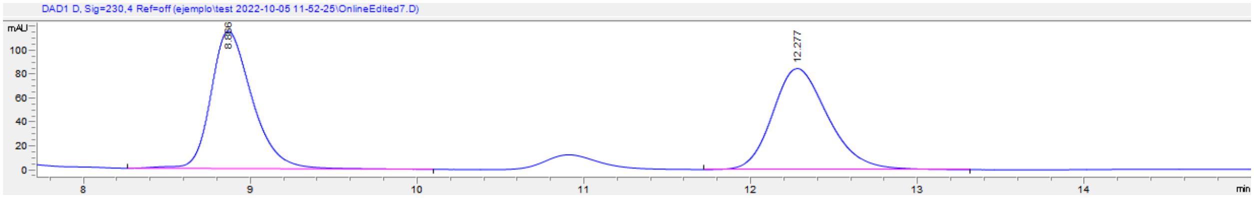


#	Time	Area	Height	Width	Area%	Symmetry
1	9.32	4626.9	311.1	0.2479	89.705	0.832
2	9.996	531	33	0.2685	10.295	0.8



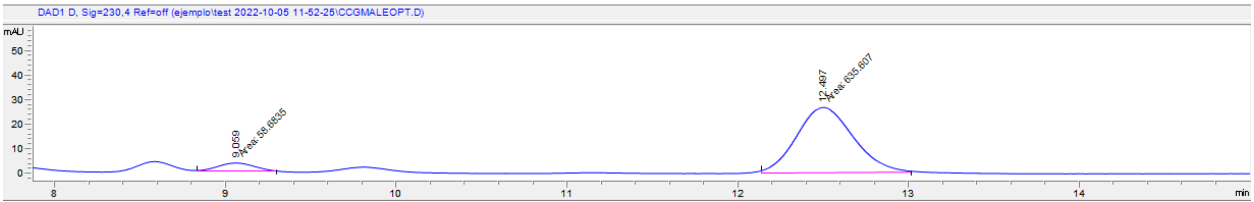
11

(±)-**11**

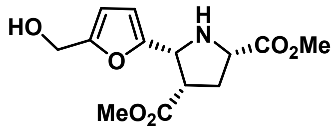


#	Time	Area	Height	Width	Area%	Symmetry
1	8.866	1998.9	115.9	0.2597	50.330	0.706
2	12.277	1972.7	85.2	0.3497	49.670	0.763

(+)-11; 83% *ee*

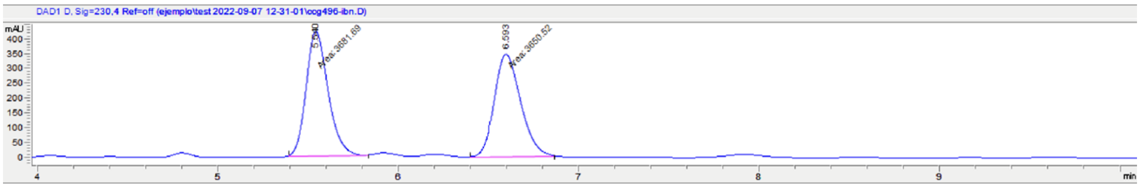


#	Time	Area	Height	Width	Area%	Symmetry
1	9.059	58.7	3.7	0.267	8.452	1.006
2	12.497	635.6	27.1	0.3912	91.548	0.852



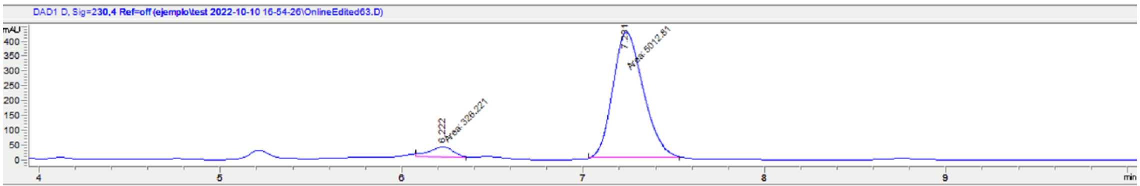
12

(±)-**12**

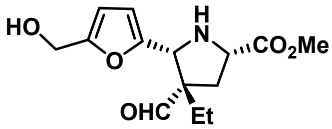


#	Time	Area	Height	Width	Area%	Symmetry
1	5.54	3681.7	427.6	0.1435	50.213	0.769
2	6.593	3650.5	352.3	0.1727	49.787	0.773

(+)-12; 88 % *ee*

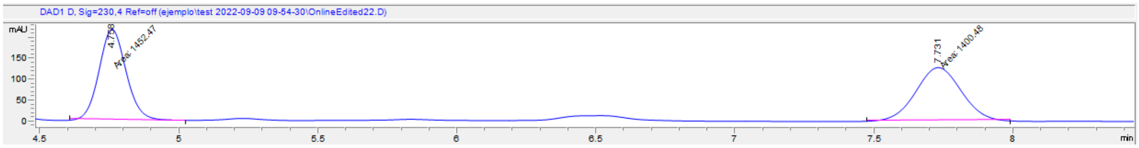


#	Time	Area	Height	Width	Area%	Symmetry
1	6.222	326.2	34.4	0.1579	6.110	1.077
2	7.231	5012.8	428.7	0.1949	93.890	0.746



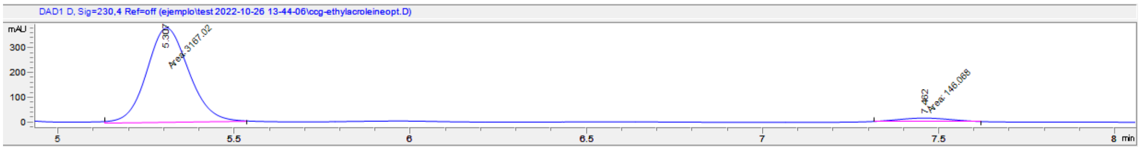
13

(±)-**13**

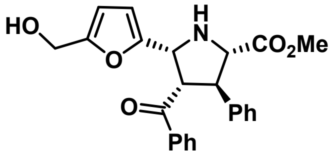


#	Time	Area	Height	Width	Area%	Symmetry
1	4.758	1452.5	215.5	0.1123	50.911	0.88
2	7.731	1400.5	125.4	0.1861	49.089	0.98

(+)-13; 91% *ee*

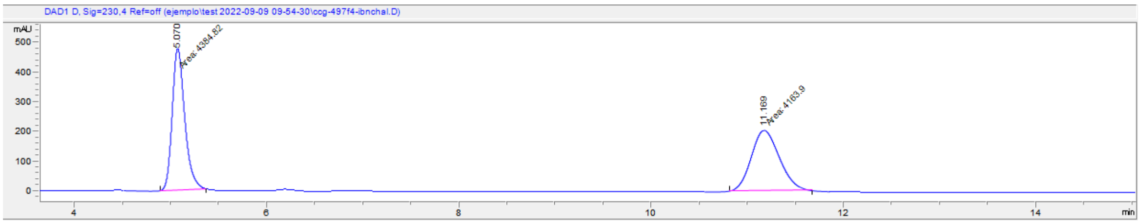


#	Time	Area	Height	Width	Area%	Symmetry
1	5.307	3167	377.4	0.1399	95.591	0.86
2	7.462	146.1	14	0.1741	4.409	0.744



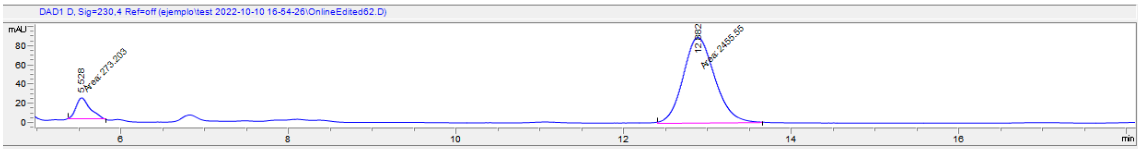
14

(±)-**14**

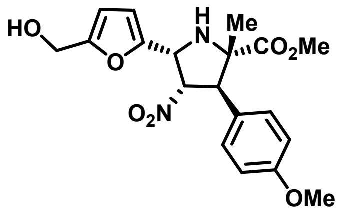


#	Time	Area	Height	Width	Area%	Symmetry
1	5.07	4384.8	478.6	0.1527	51.292	0.749
2	11.169	4163.9	203.7	0.3406	48.708	0.828

(-)-14; 80% ee

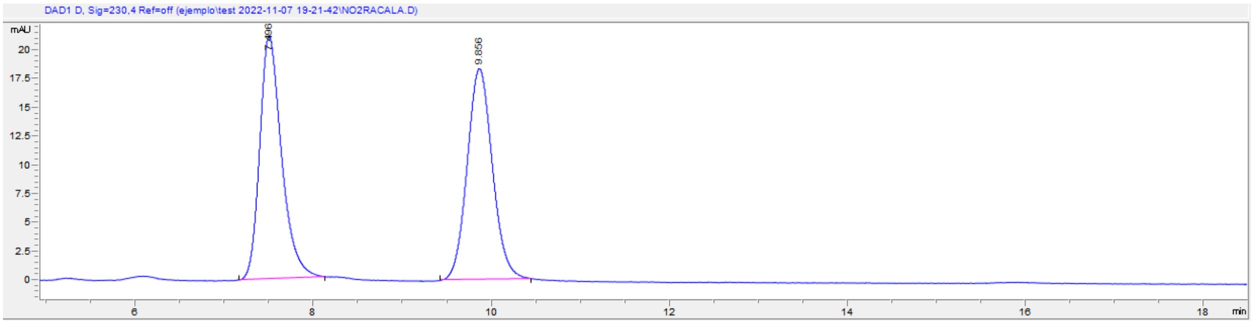


#	Time	Area	Height	Width	Area%	Symmetry
1	5.528	273.2	22.7	0.201	10.012	0.62
2	12.882	2455.6	91.6	0.4469	89.988	0.834



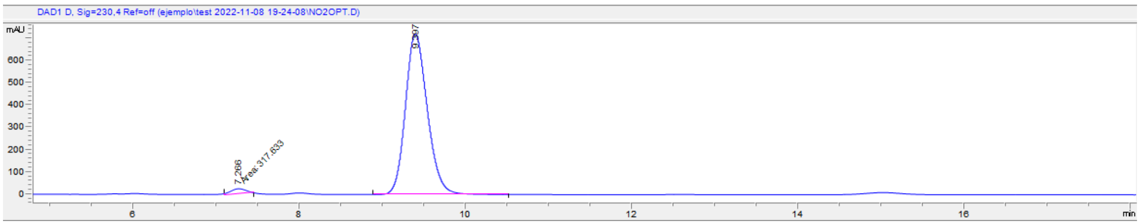
15

(±)-**15**



#	Time	Area	Height	Width	Area%	Symmetry
1	7.496	359.9	21.1	0.2062	49.907	0.72
2	9.856	361.2	18.3	0.2316	50.093	0.904

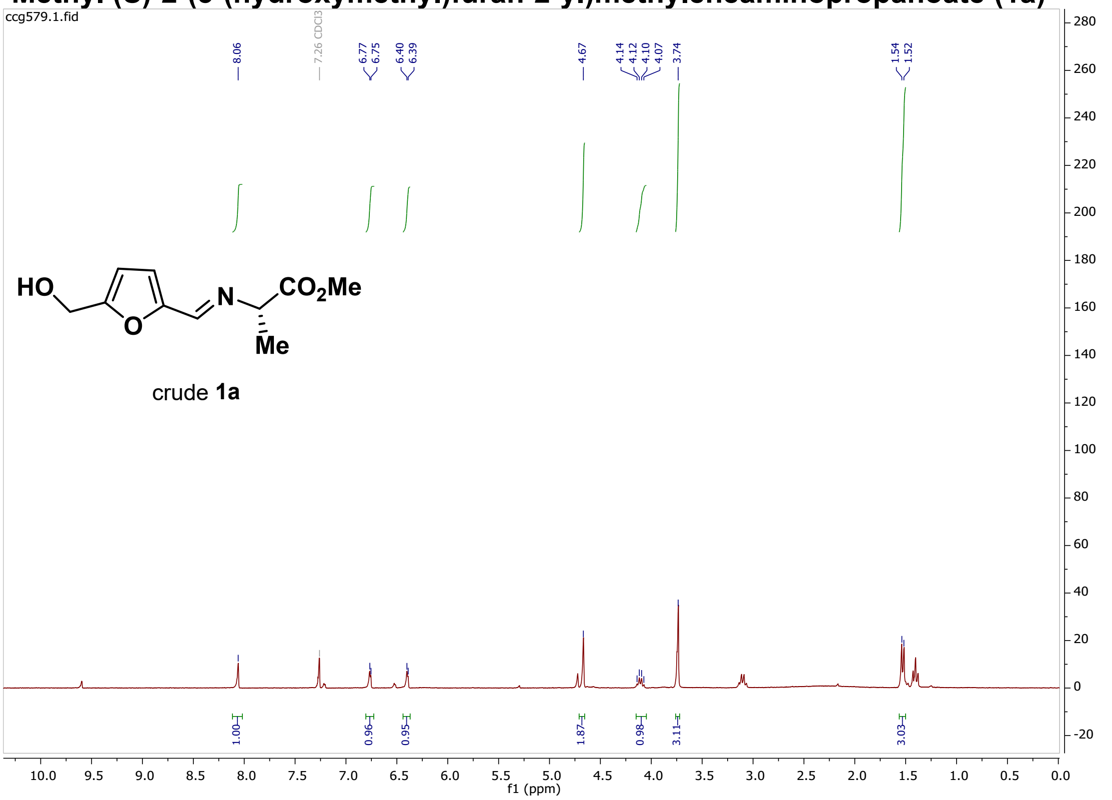
(-)-15; 95% *ee*



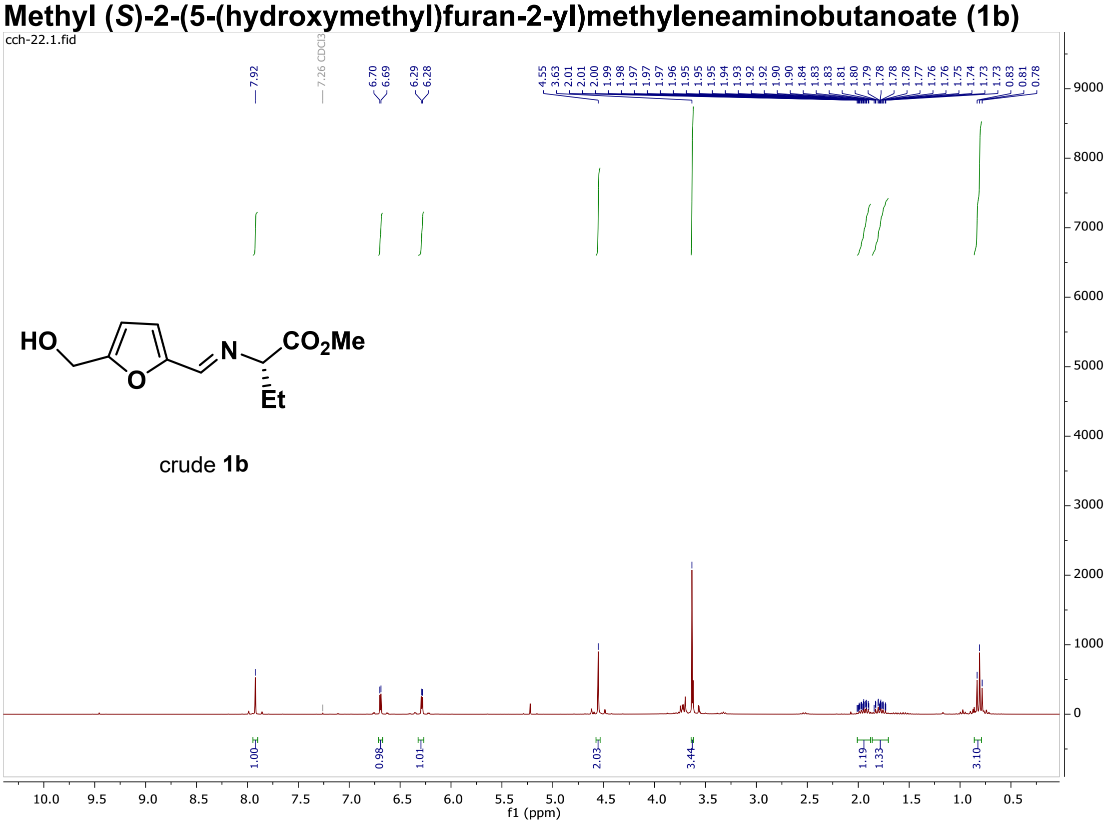
#	Time	Area	Height	Width	Area%	Symmetry
1	7.266	317.6	24.3	0.2176	2.335	1.245
2	9.397	13285.7	725.1	0.2773	97.665	0.786

8. NMR Spectra collection

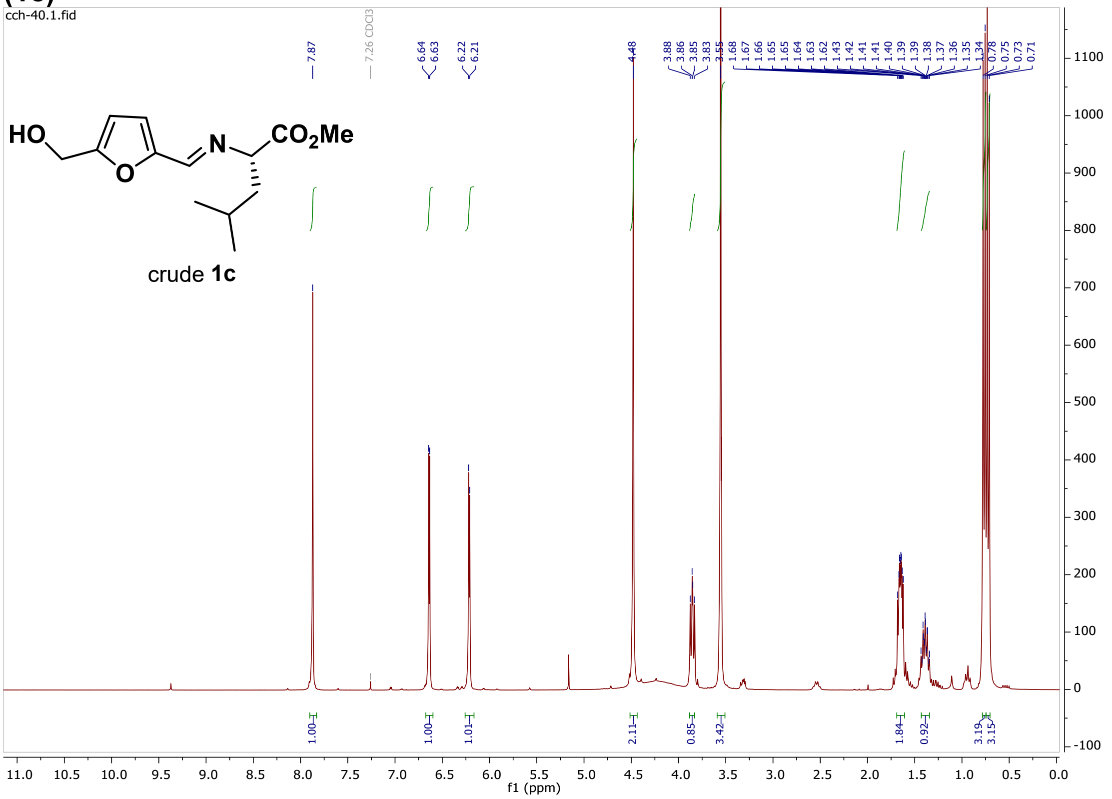
Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneaminopropanoate (1a)



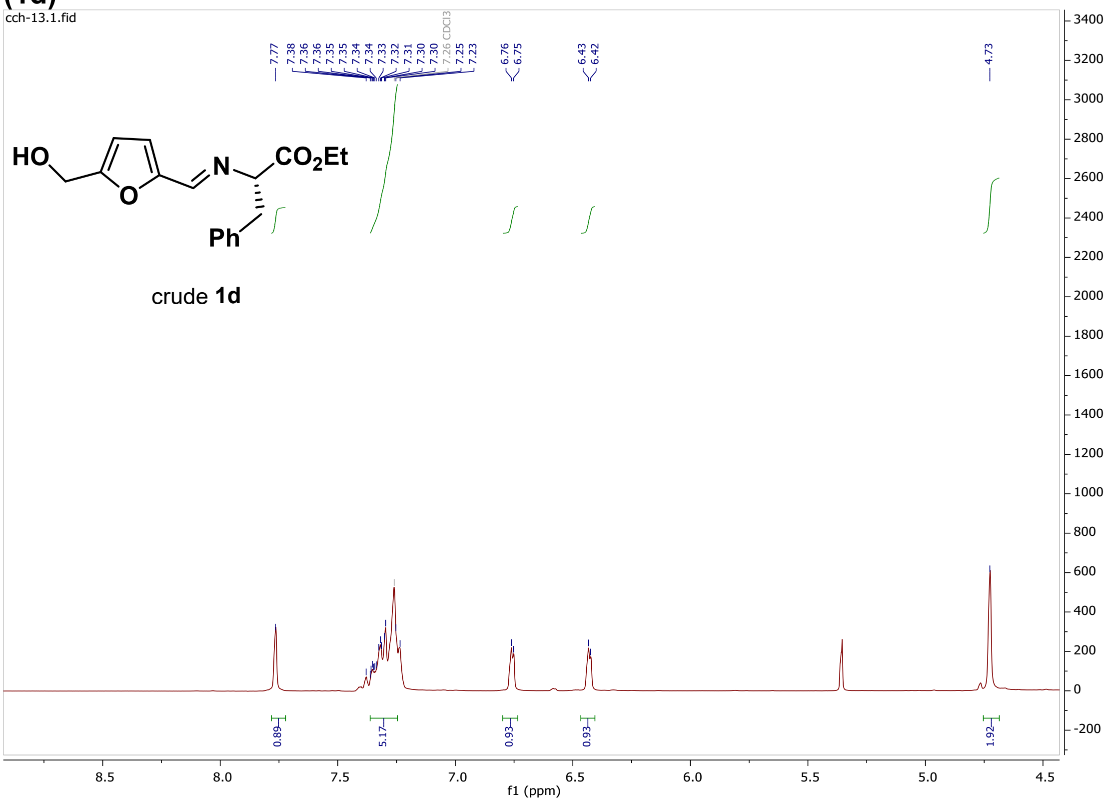
Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneaminobutanoate (1b)



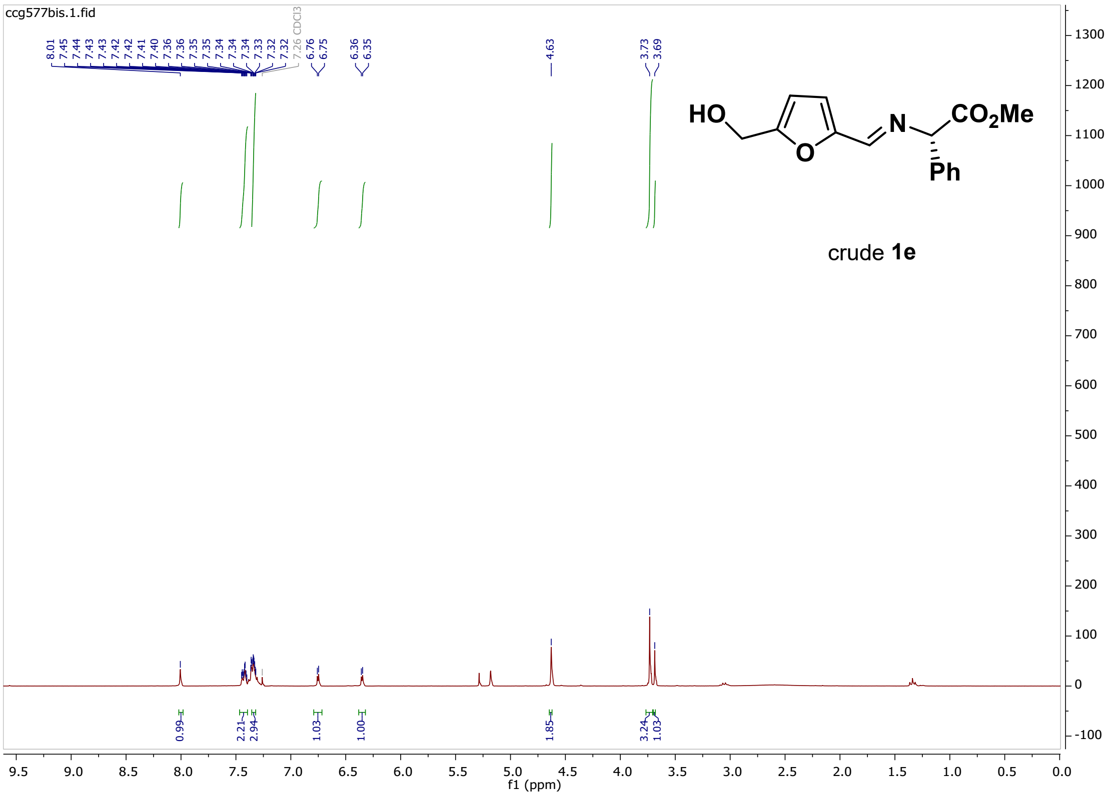
Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneamino)-4-methylpentanoate (1c)



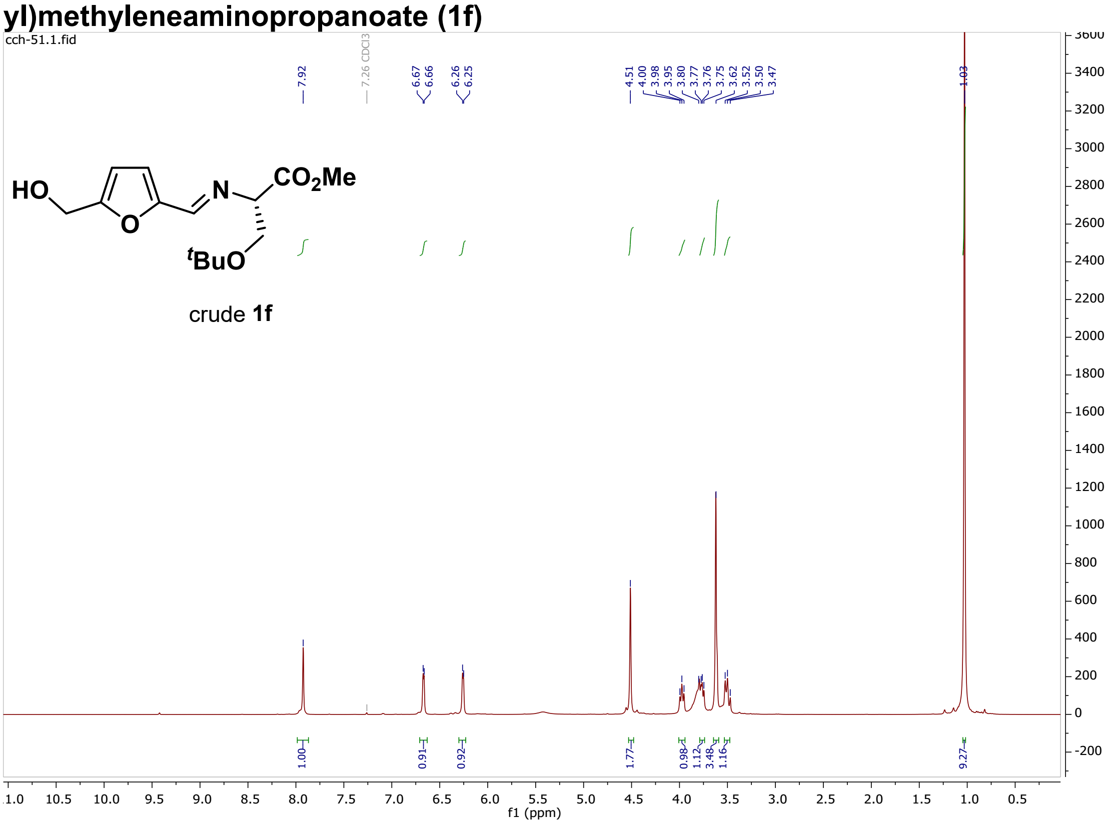
Ethyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneamino-3-phenylpropanoate (1d)



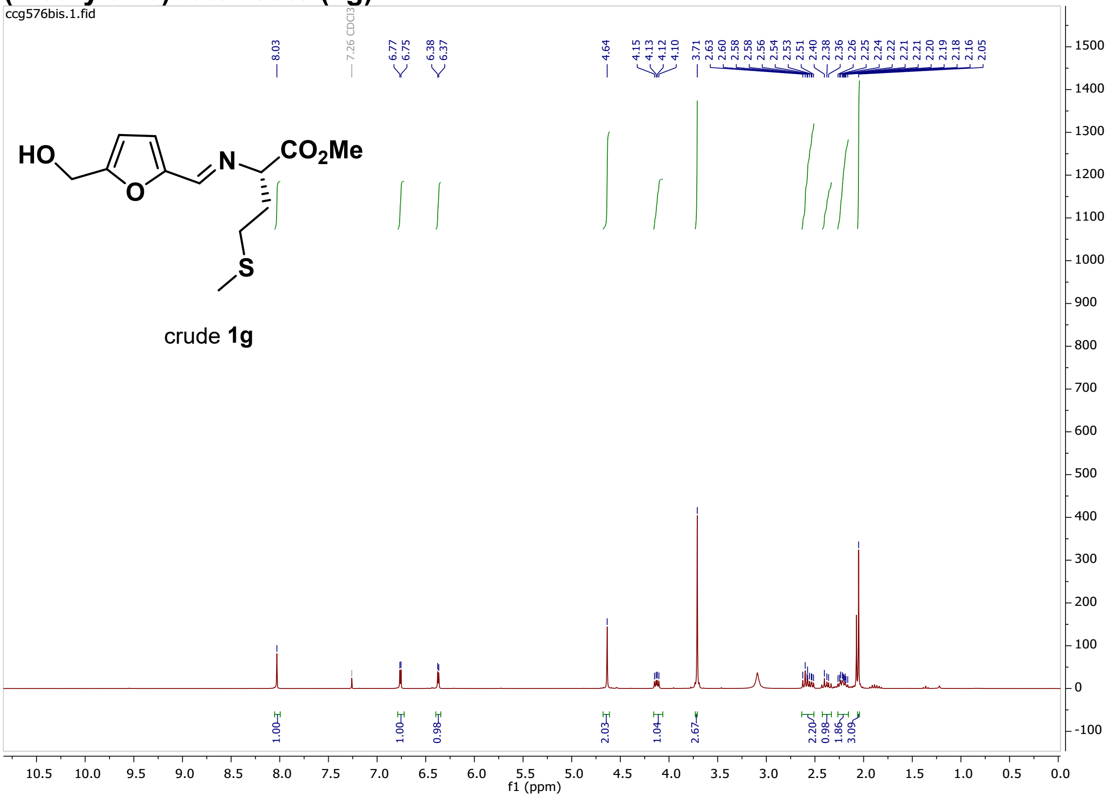
Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneamino-2-phenylacetate (1e)



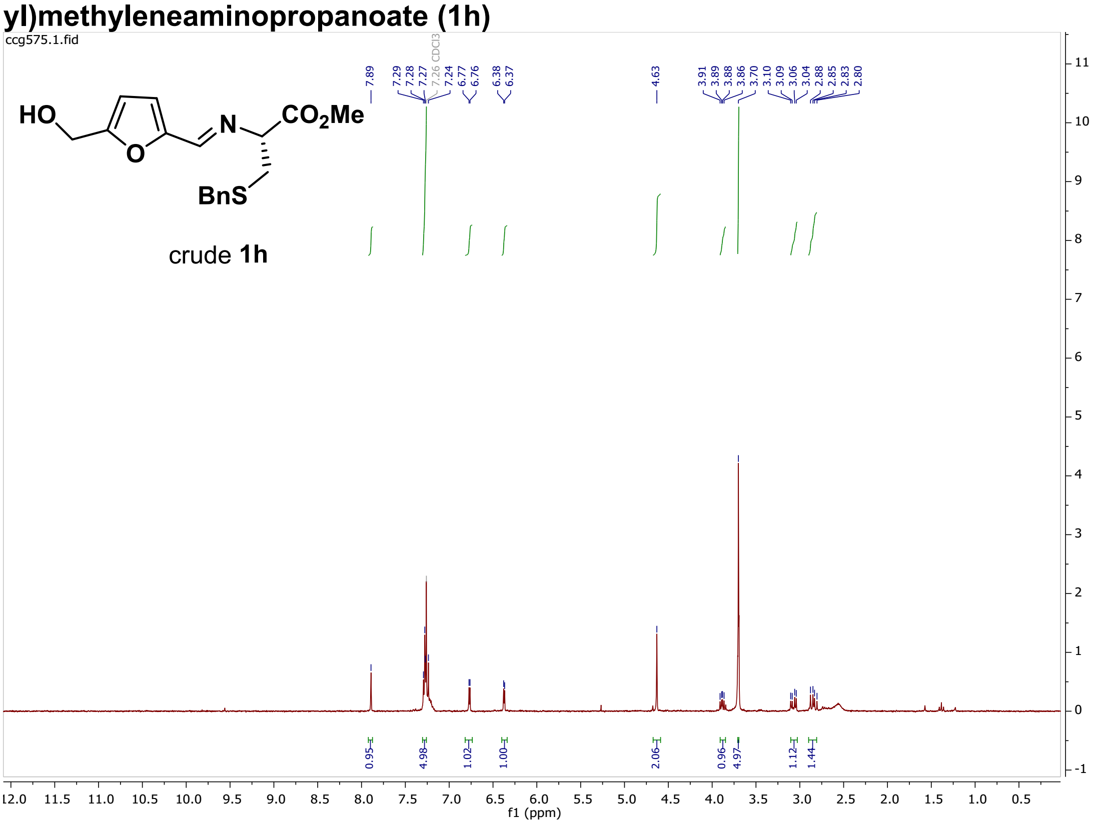
Methyl (*S*)-3-(tert-butoxy)-2-(5-(hydroxymethyl)furan-2-yl)methyleneaminopropanoate (1f)



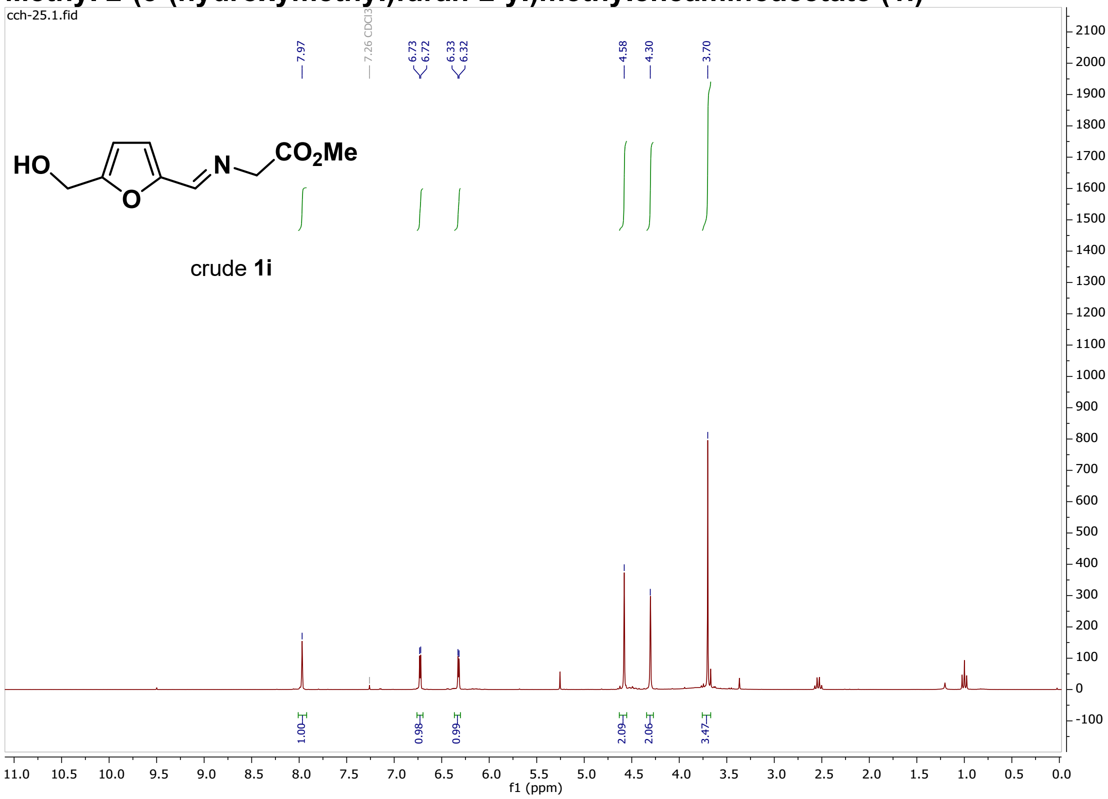
Methyl (*S*)-2-(5-(hydroxymethyl)furan-2-yl)methyleneamino-4-(methylthio)butanoate (1g)



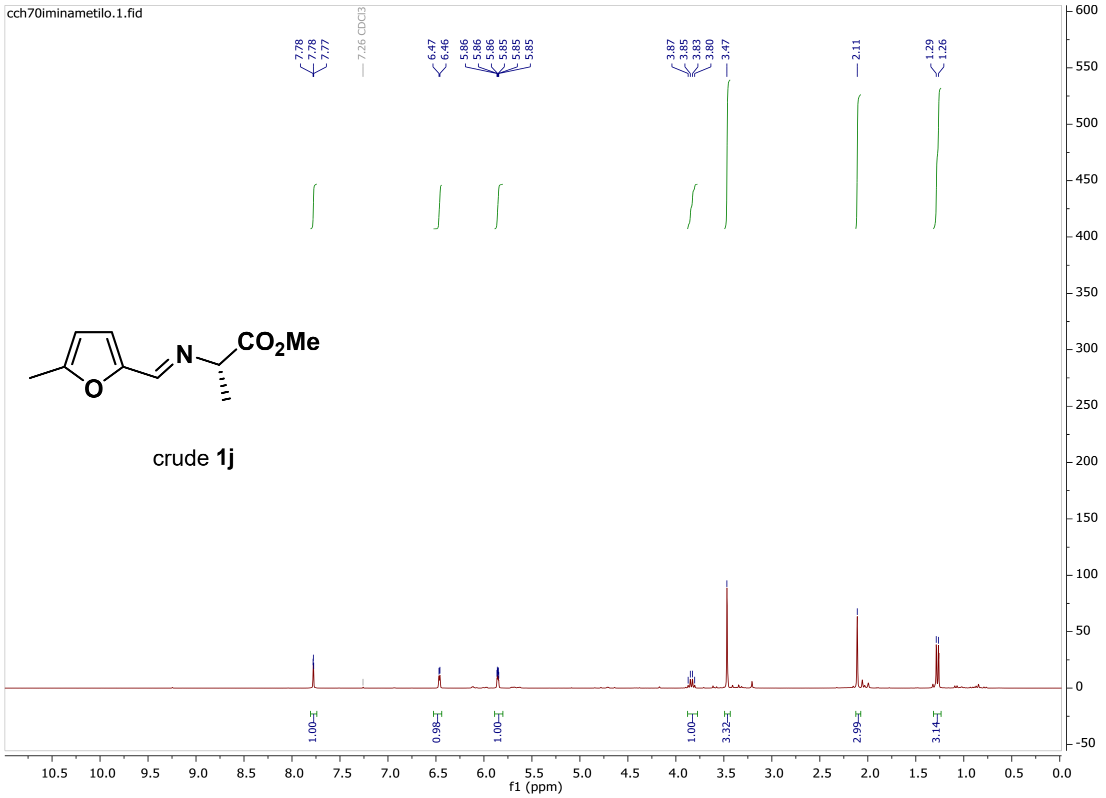
Methyl (*R*)-3-(benzylthio)-2-(5-(hydroxymethyl)furan-2-yl)methyleneaminopropanoate (1h)



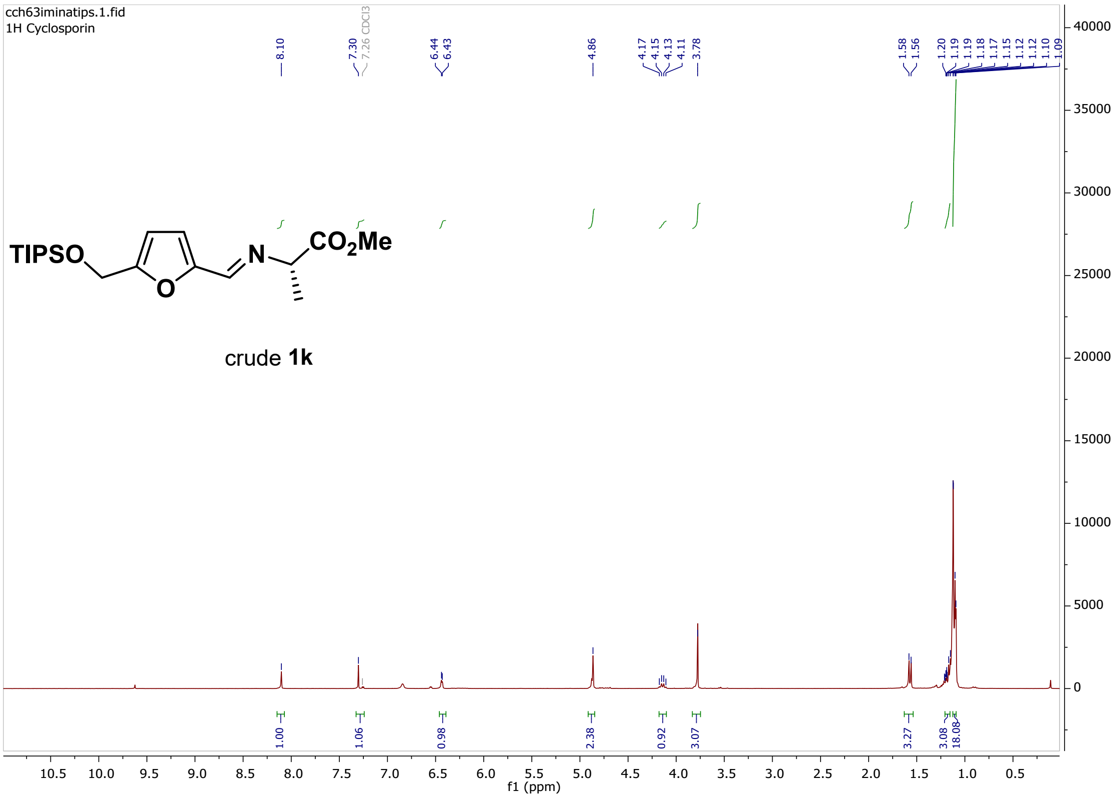
Methyl 2-(5-(hydroxymethyl)furan-2-yl)methyleneaminoacetate (1i)



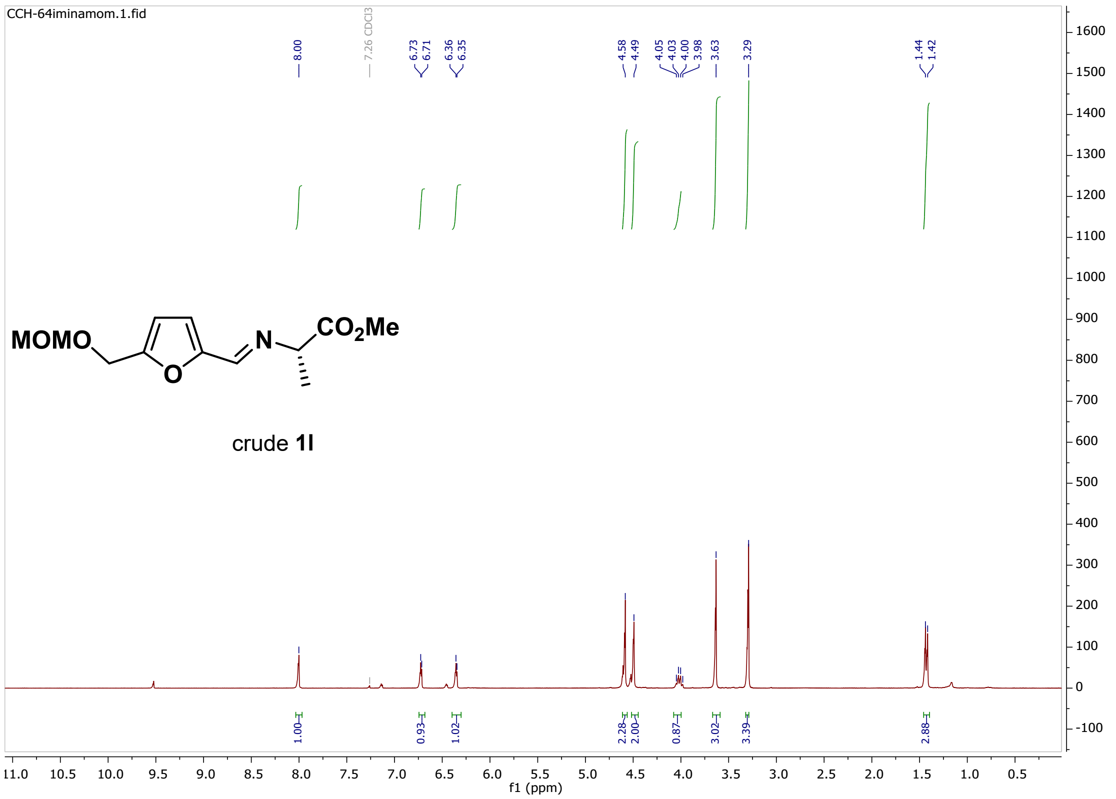
Methyl (S)-2-((5-methylfuran-2-yl)methyleneamino)propanoate (1j)



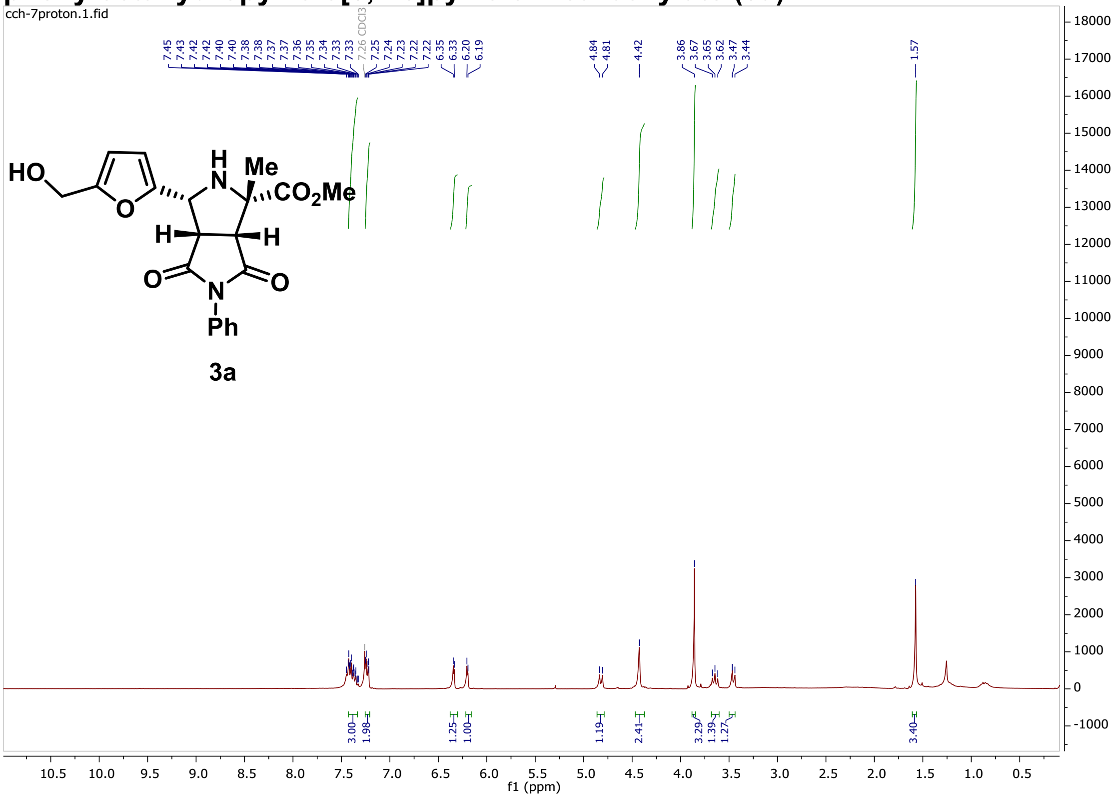
Methyl (S)-2-((5-(triisopropylsilyloxymethyl)furan-2-yl)methyleneamino)propanoate (1k)

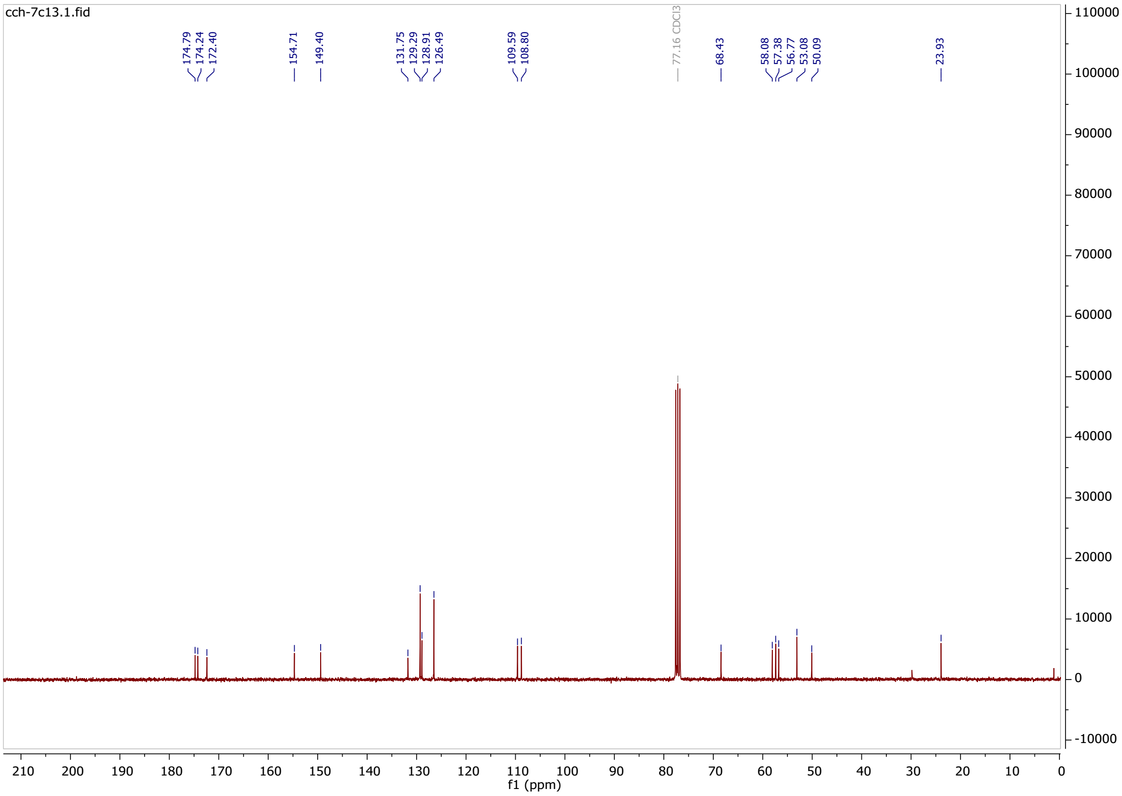


Methyl (S)-2-(5-((methoxymethoxymethyl)furan-2-yl)methyleneamino)propanoate (1l)

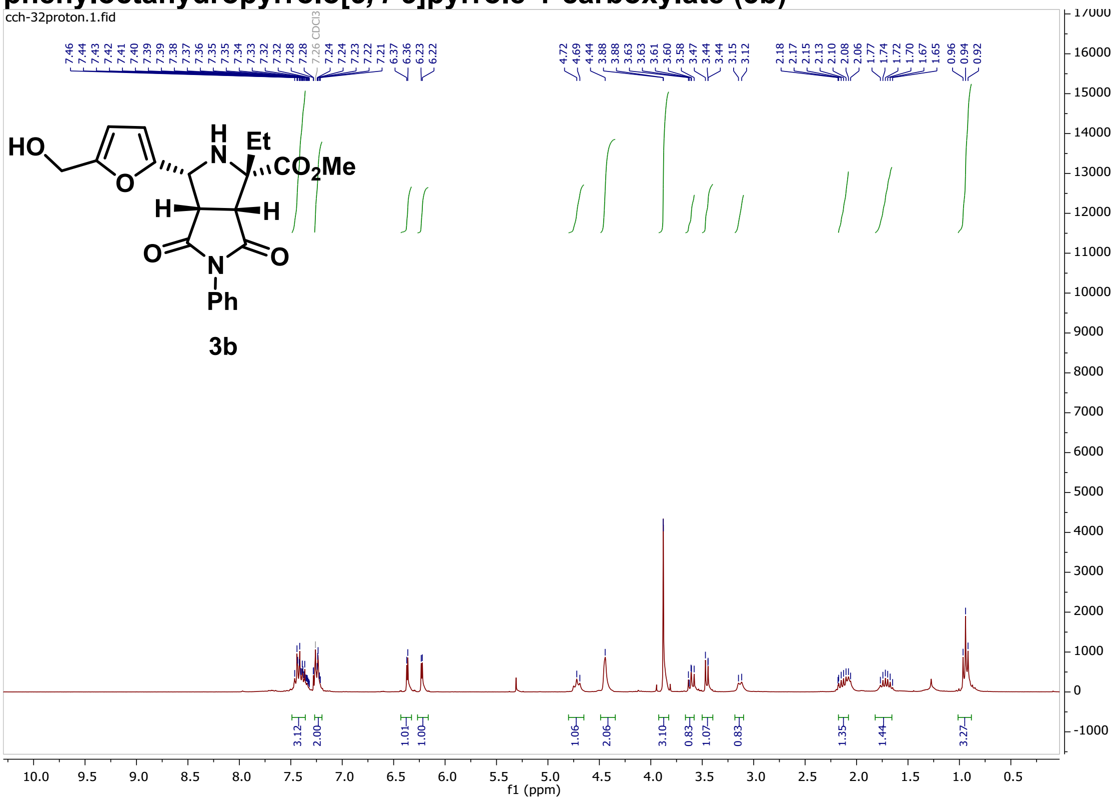


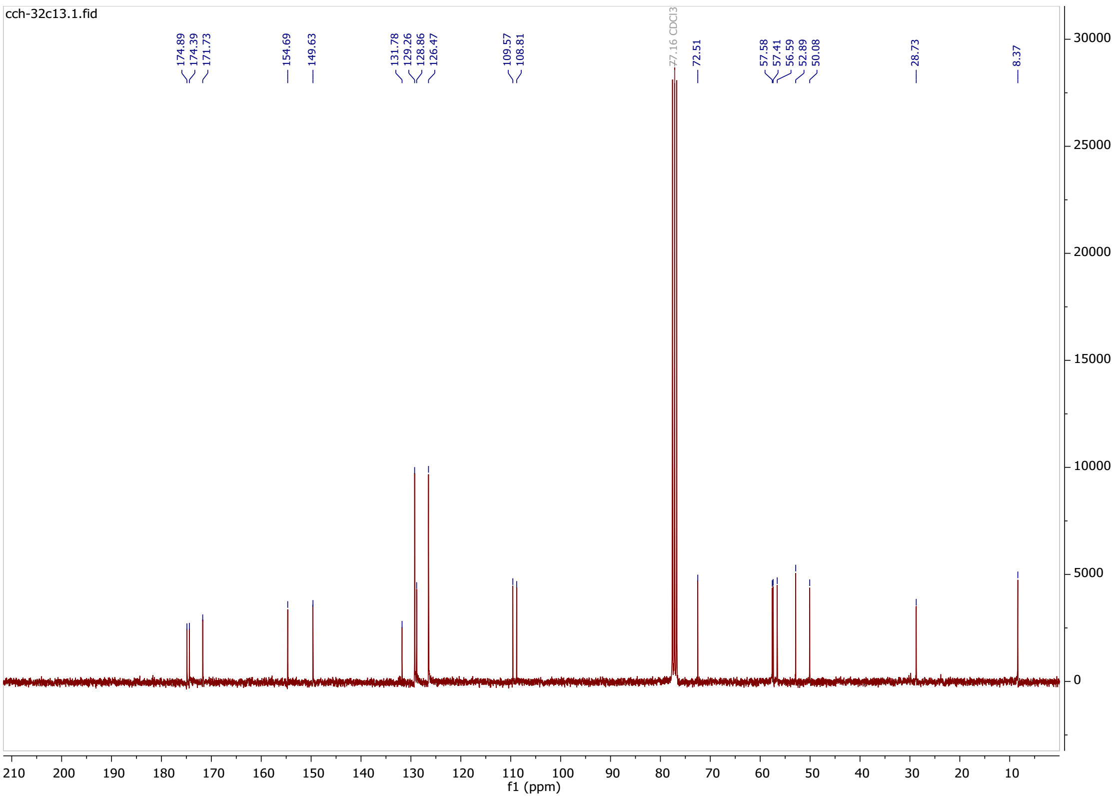
Methyl (1*S*,3*R*,3a*S*,6a*R*)-3-(5-(hydroxymethyl)furan-2-yl)-1-methyl-4,6-dioxo-5-phenyloctahydropyrrolo[3,4-c]pyrrole-1-carboxylate (3a)



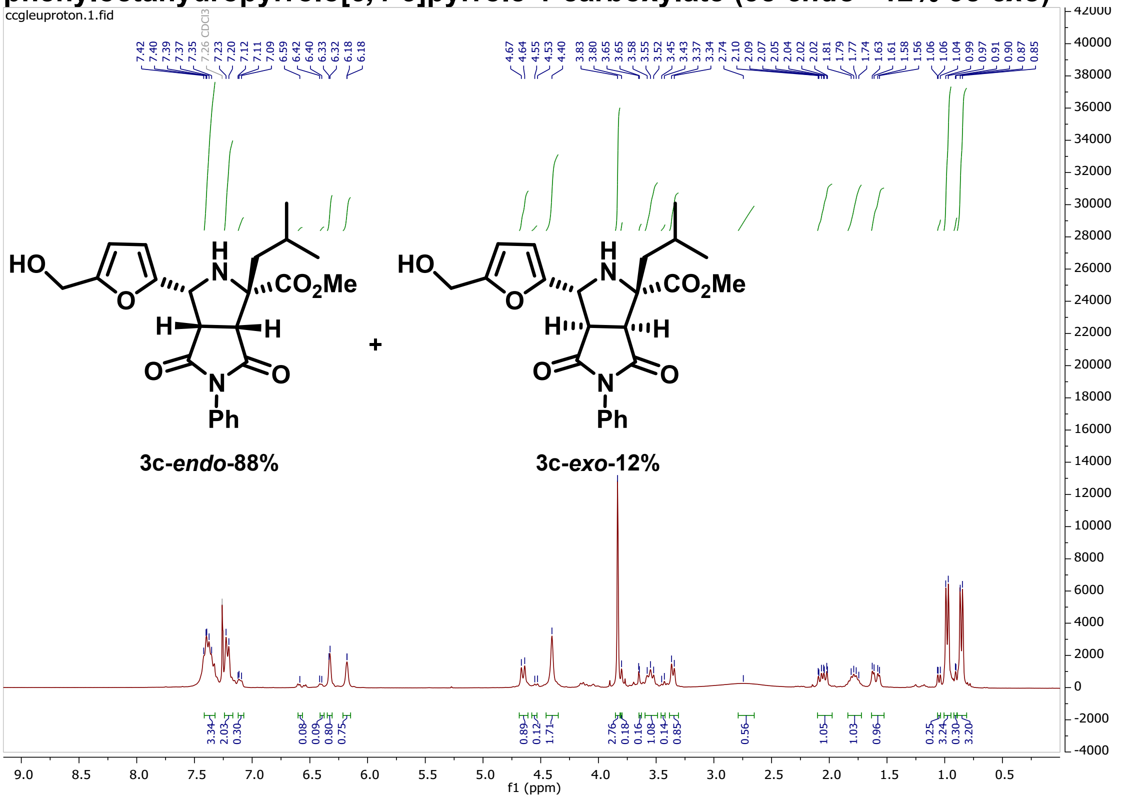


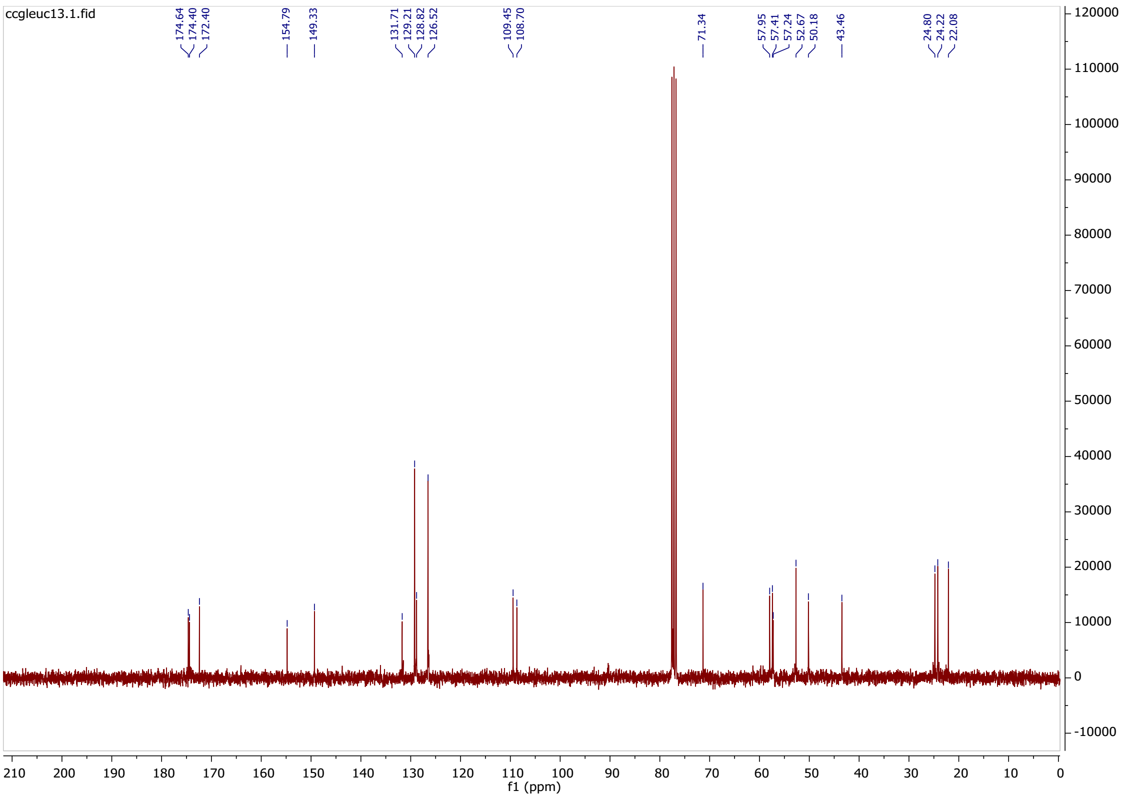
Methyl (*1S,3R,3aS,6aR*)-1-ethyl-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3b)



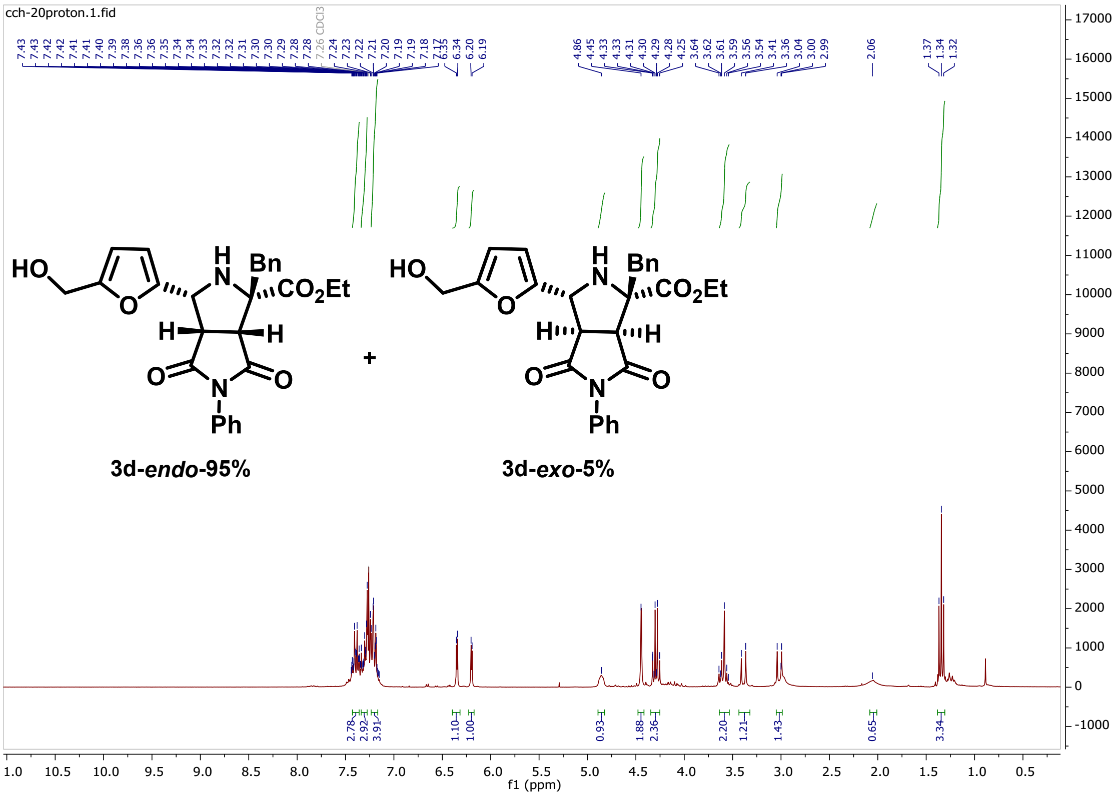


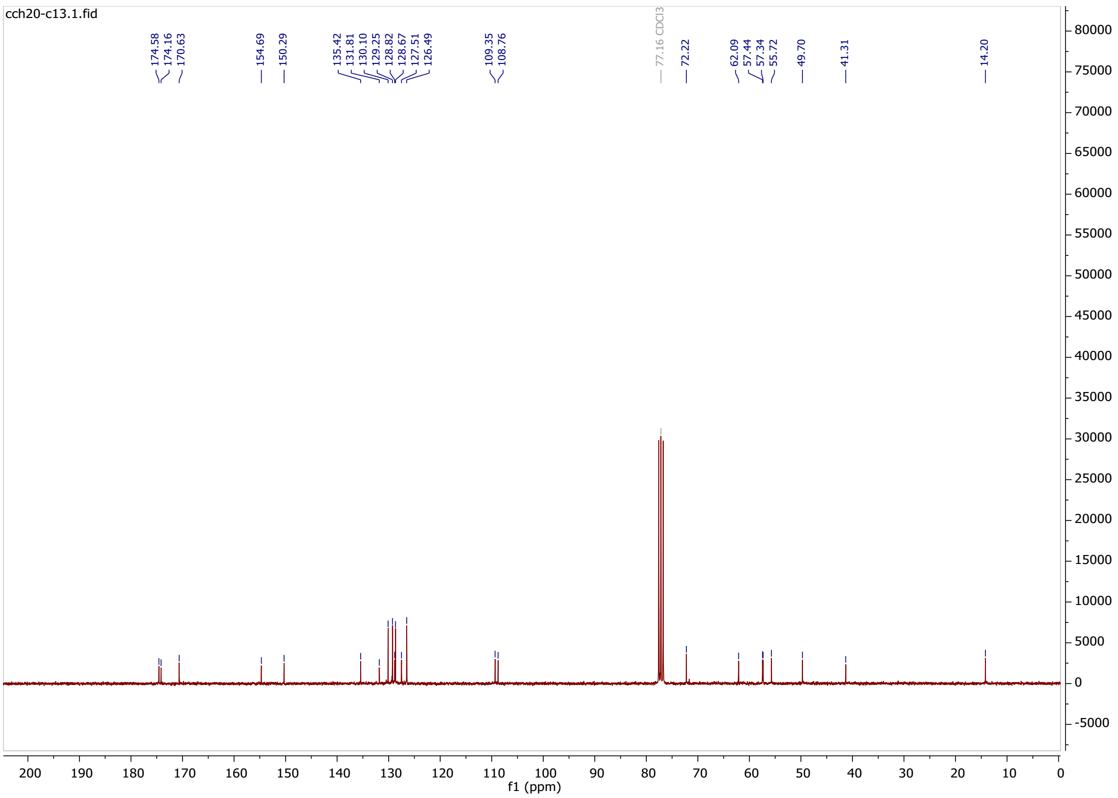
Methyl (1*S*,3*R*,3a*S*,6a*R*)-3-(5-(hydroxymethyl)furan-2-yl)-1-isobutyl-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3c-*endo*+ 12% 3c-*exo*)



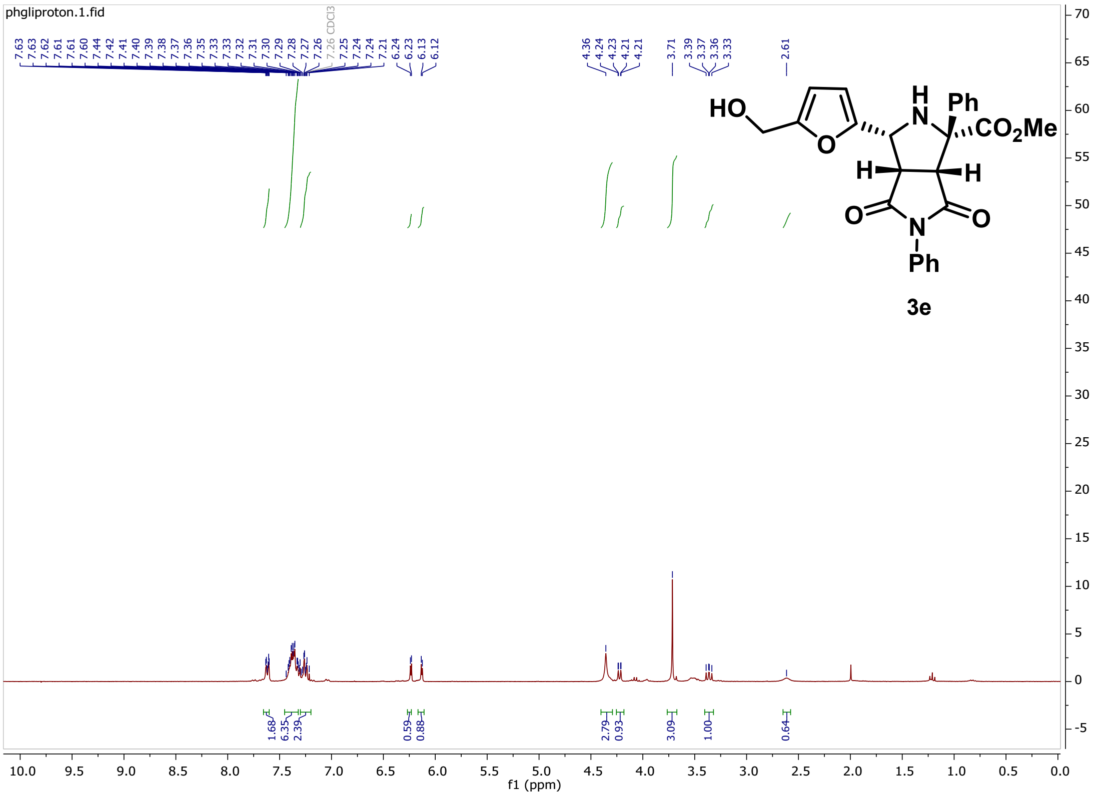


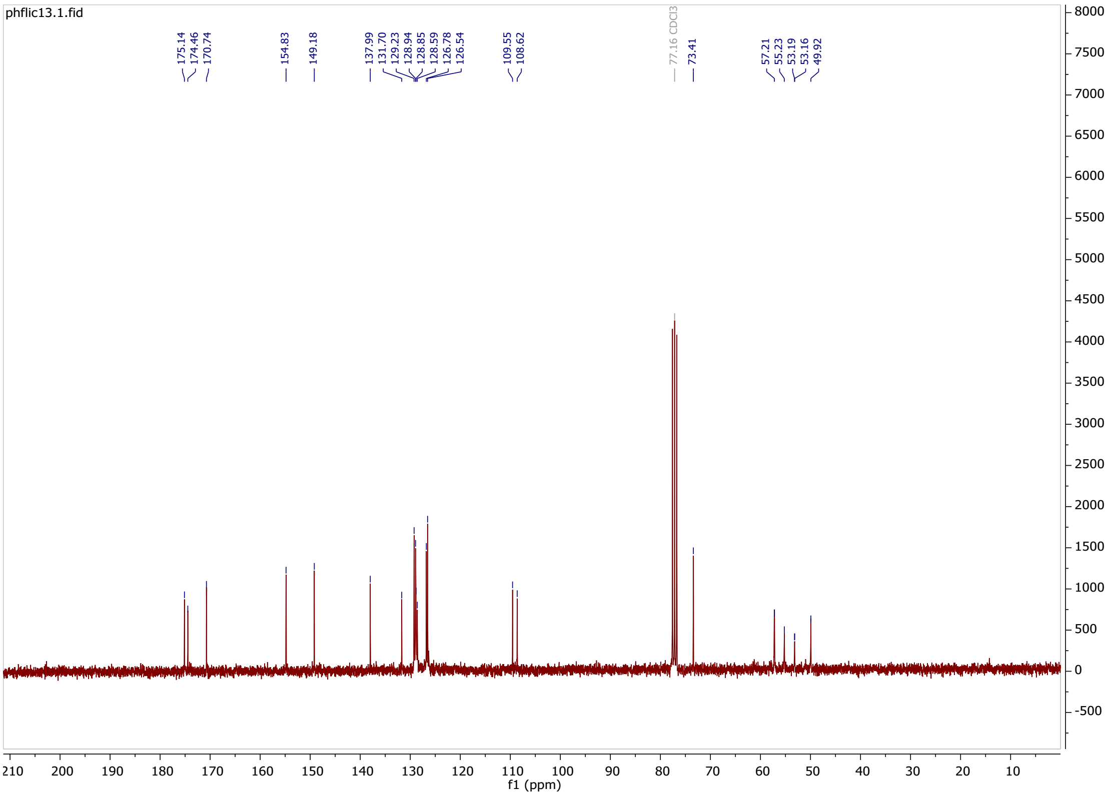
Ethyl (1*S*,3*R*,3a*S*,6a*R*)-1-benzyl-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3d-*endo*+ 7% 3d-*exo*)



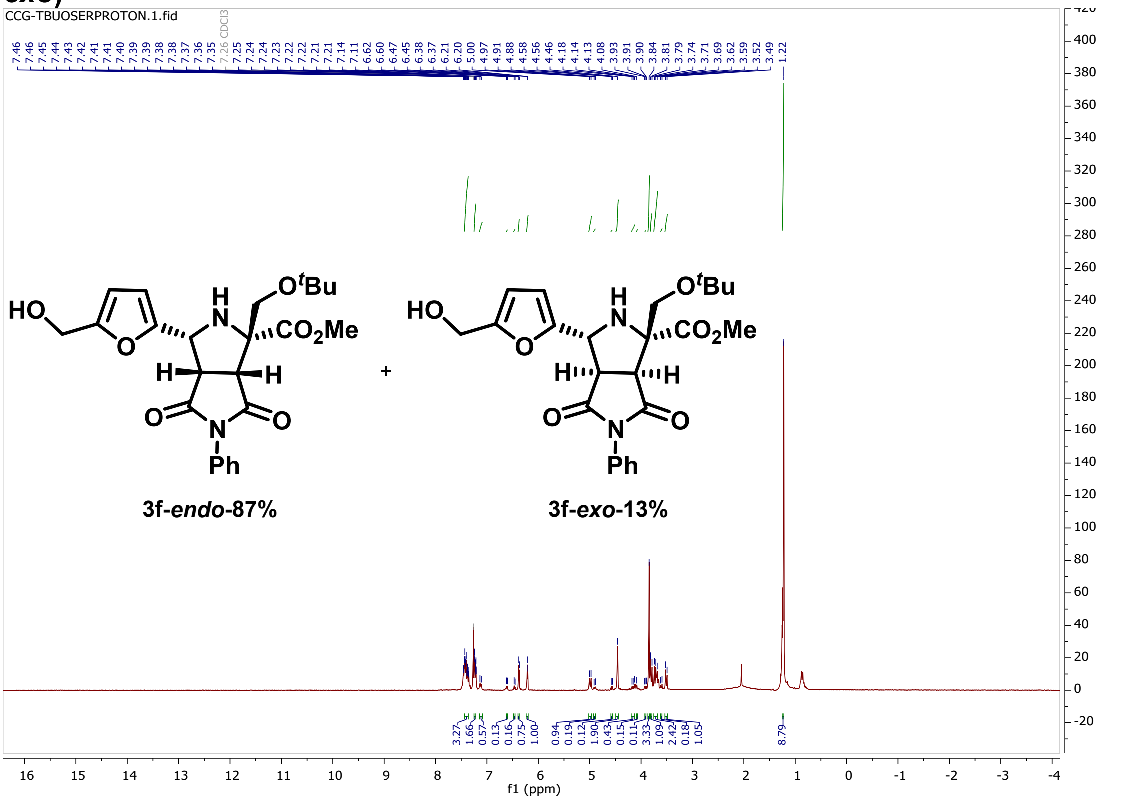


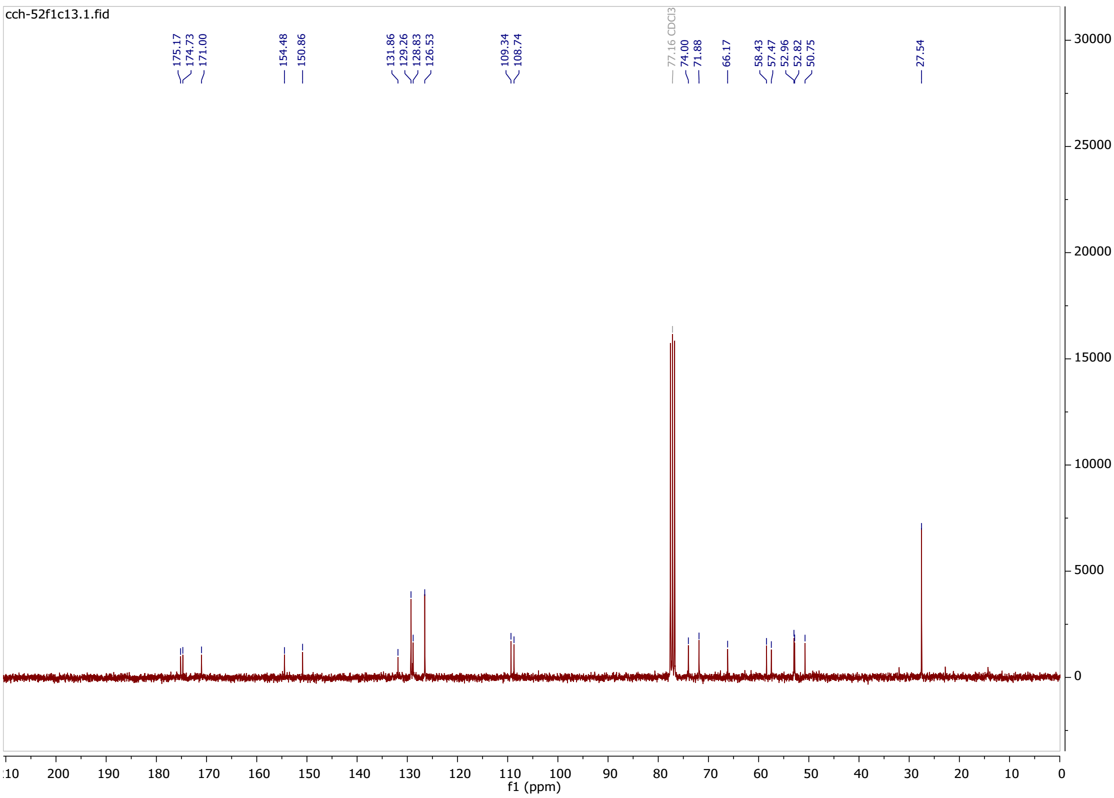
Methyl (1*R*,3*R*,3a*S*,6a*R*)-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-1,5-diphenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3e)



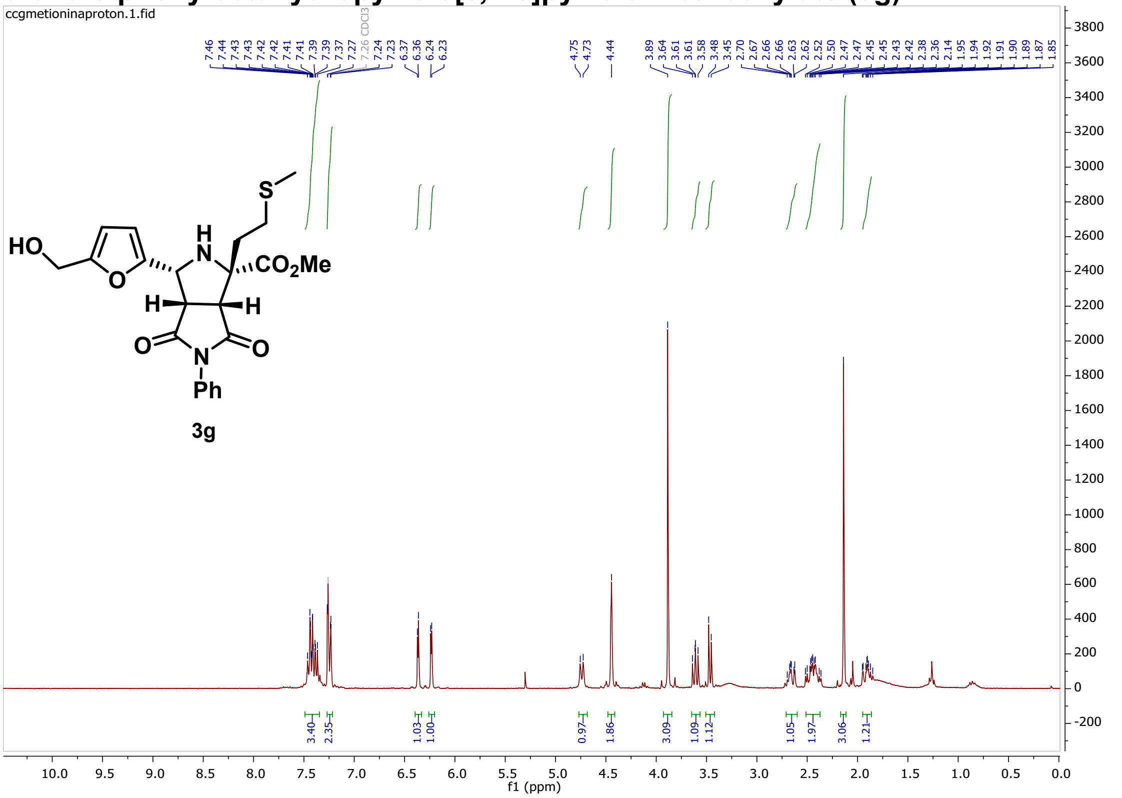


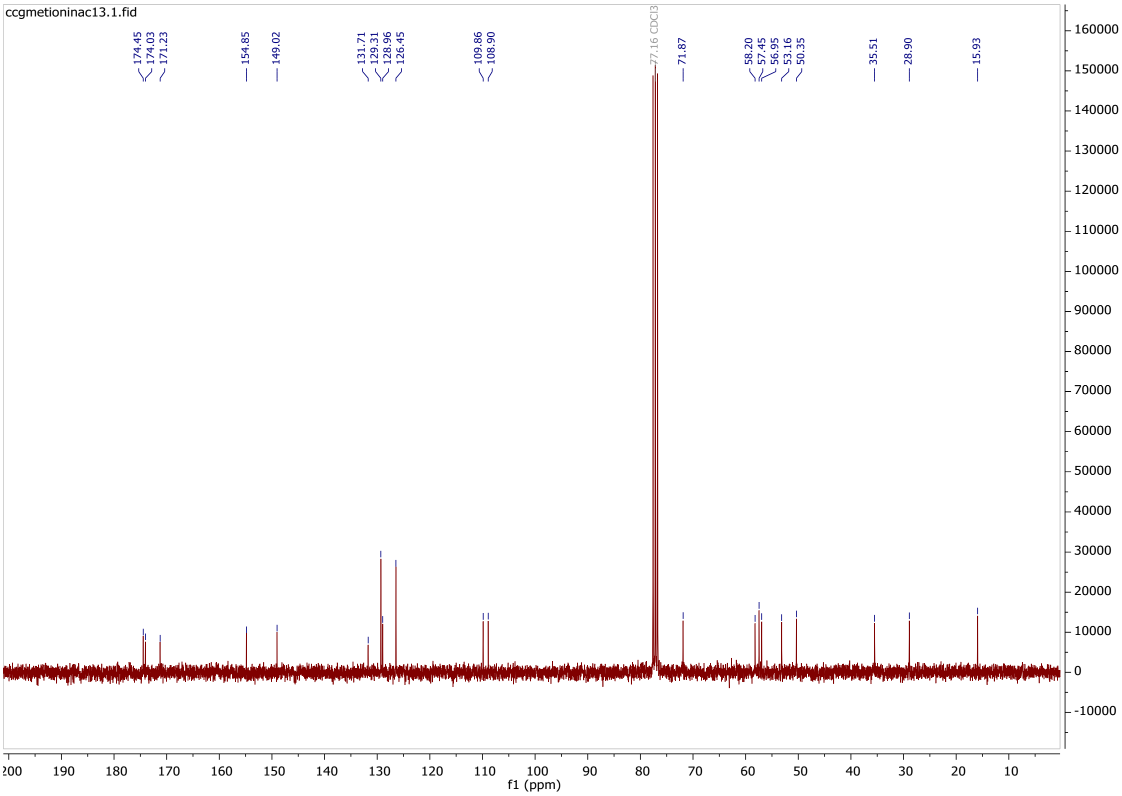
Methyl (1*R*,3*R*,3*aS*,6*aR*)-1-tert-butoxymethyl-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3f-*endo*+ 13% 3f-*exo*)



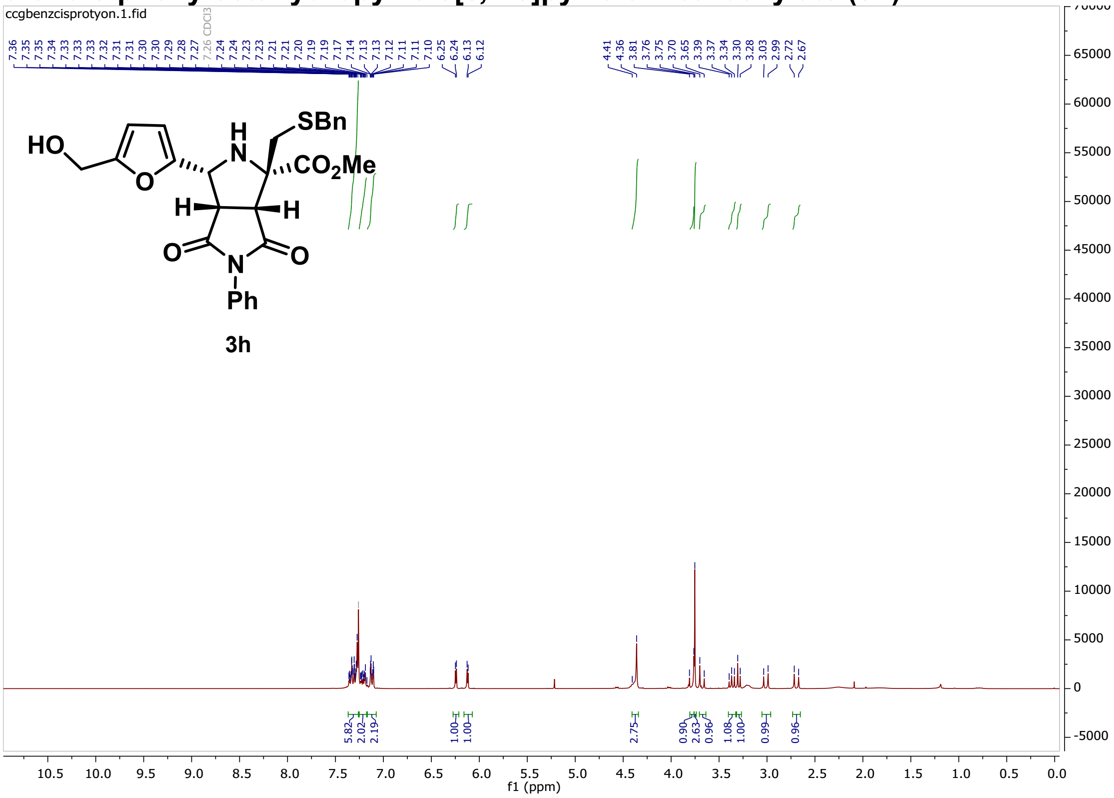


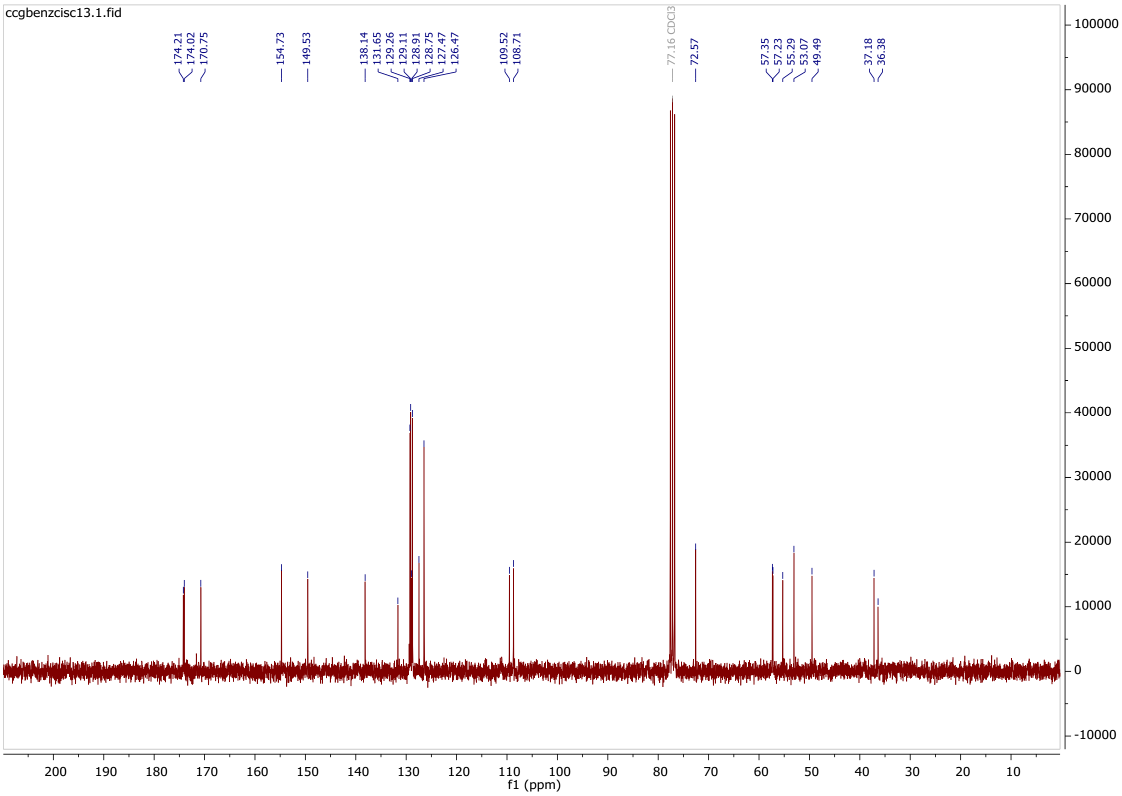
Methyl (1*S*,3*R*,3a*S*,6a*R*)-3-(5-(hydroxymethyl)furan-2-yl)-1-(2-methylthioethyl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3g)



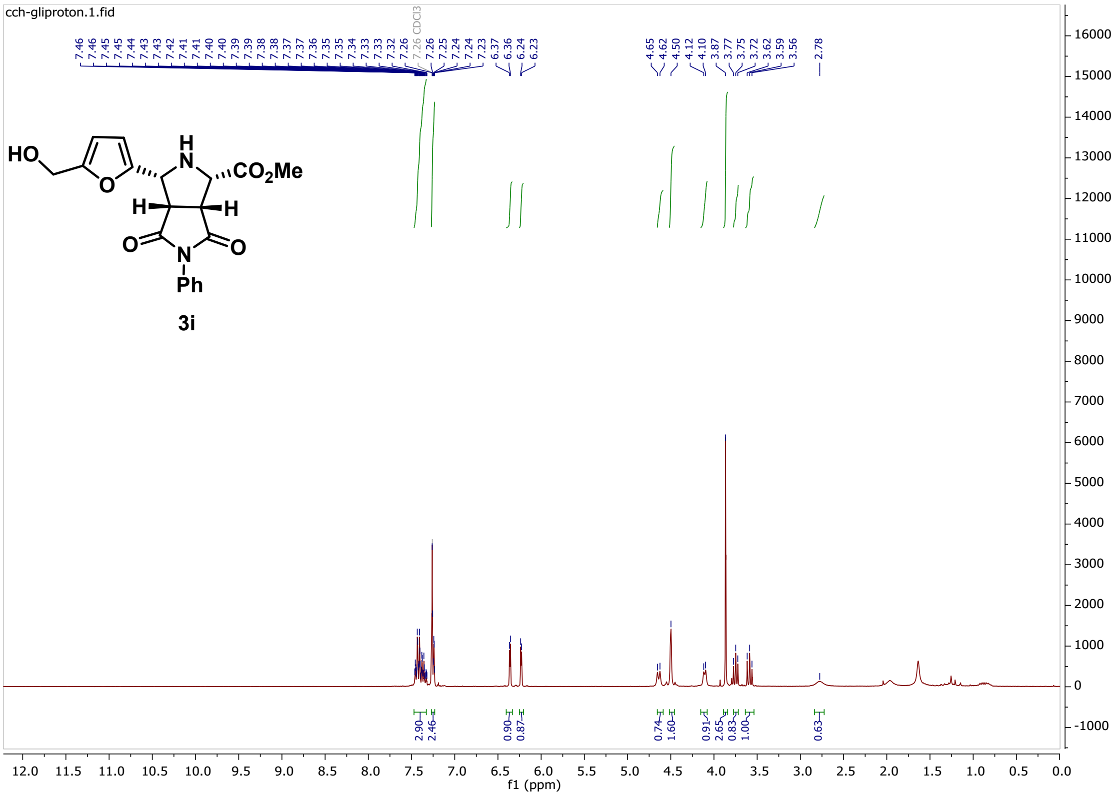


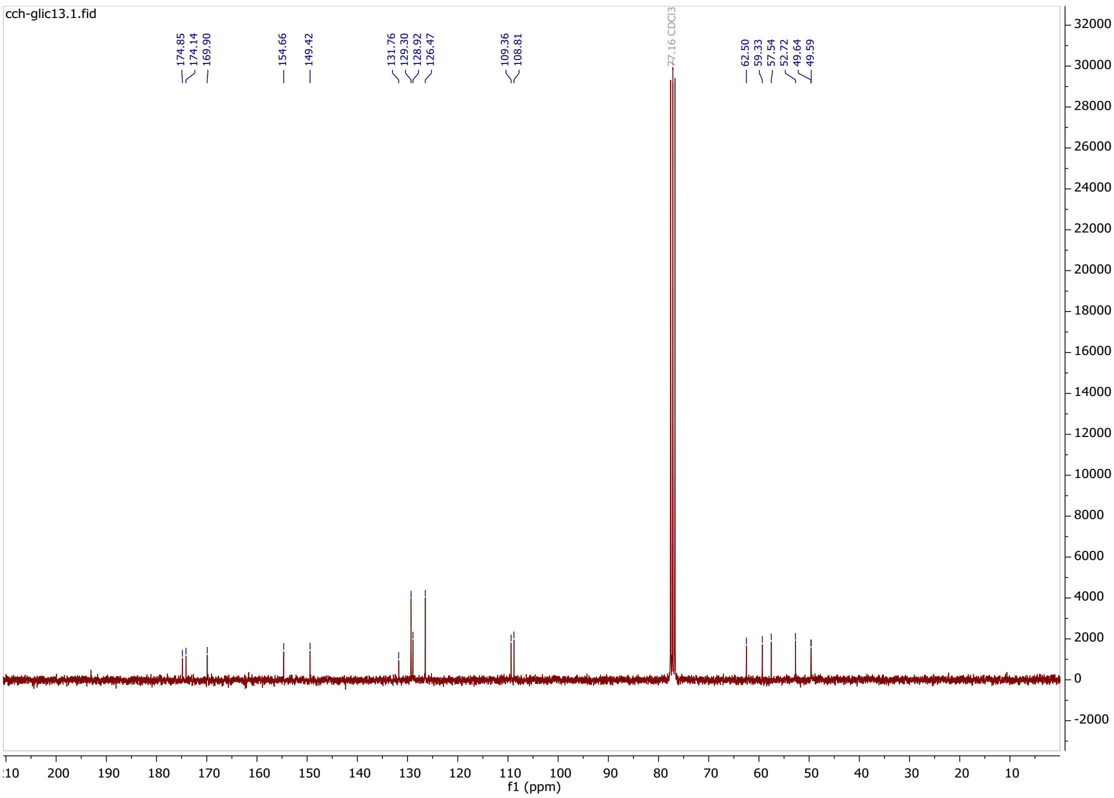
Methyl (1*S*,3*R*,3a*S*,6a*R*)-1-benzylthiomethyl-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (3h)



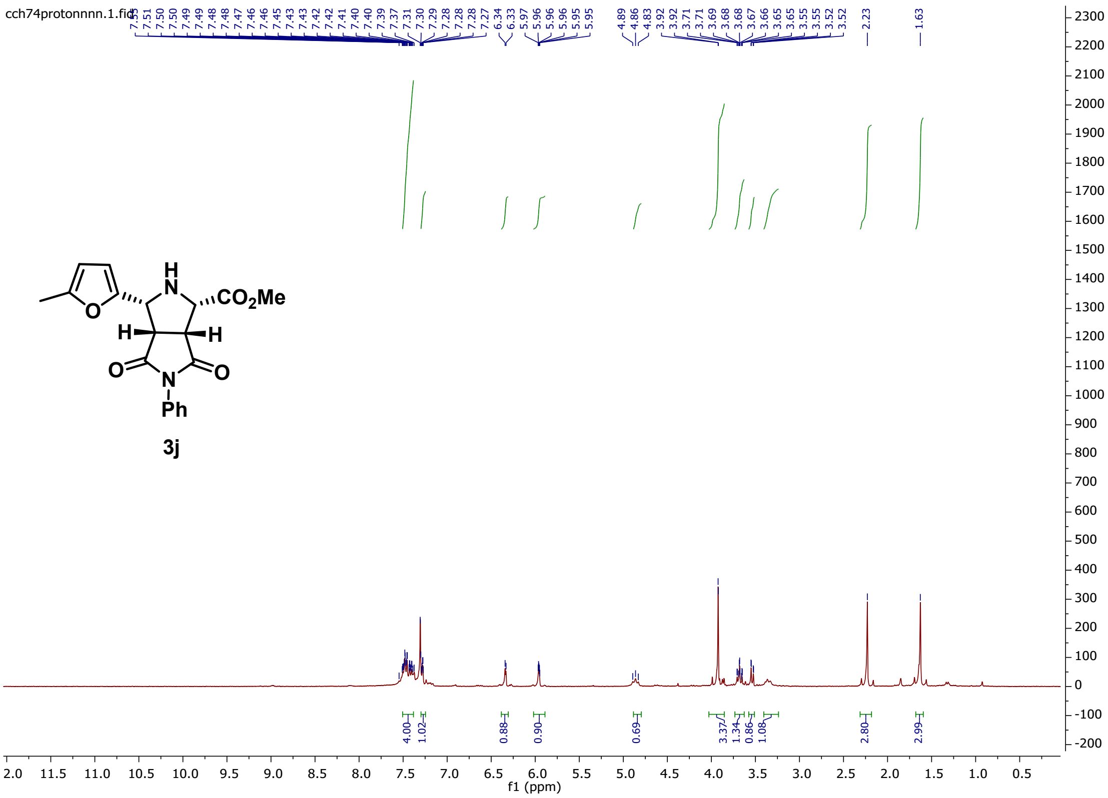


Methyl (1*S*,3*R*,3a*S*,6a*R*)-3-(5-(hydroxymethyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3i)

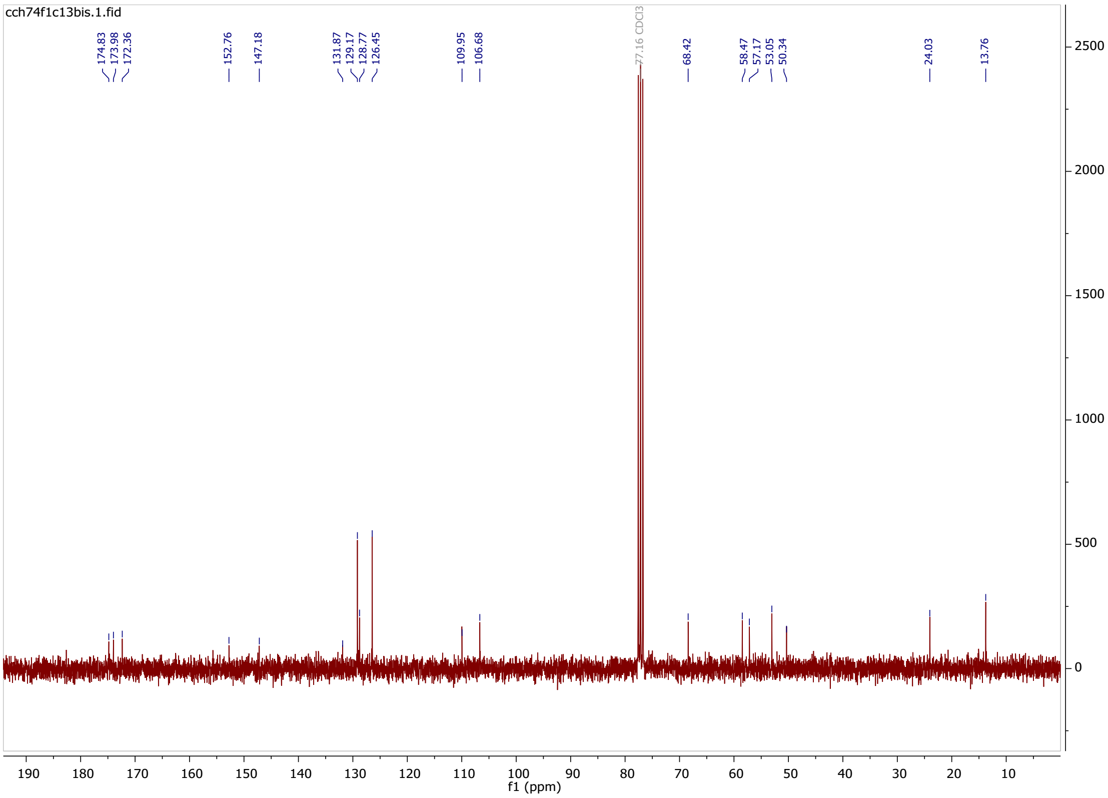




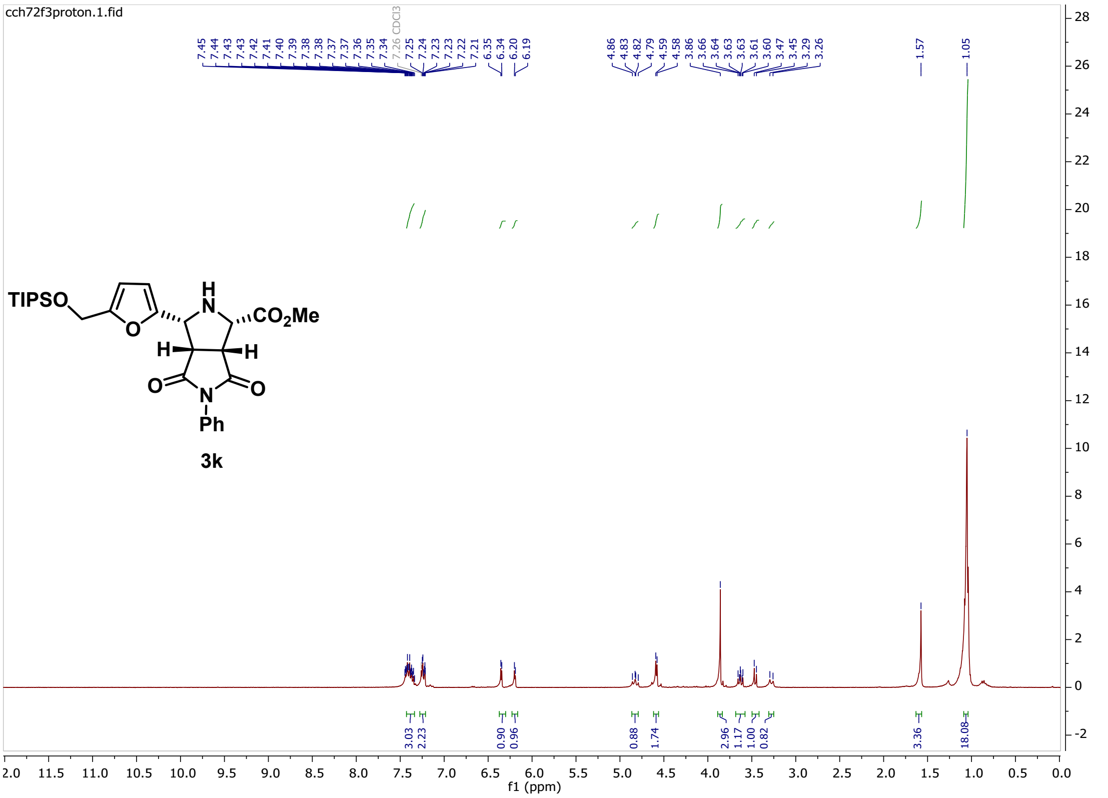
Methyl (1*S*,3*R*,3a*S*,6a*R*)-3-(5-methylfuran-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3j)

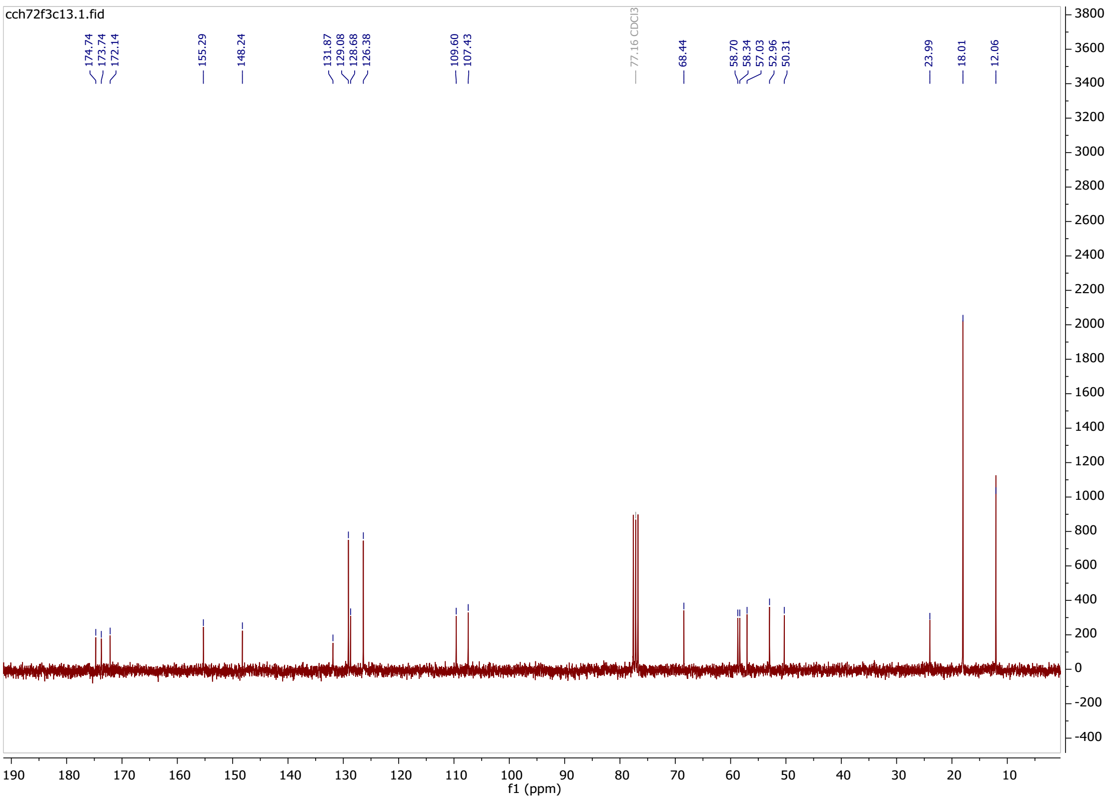


3j

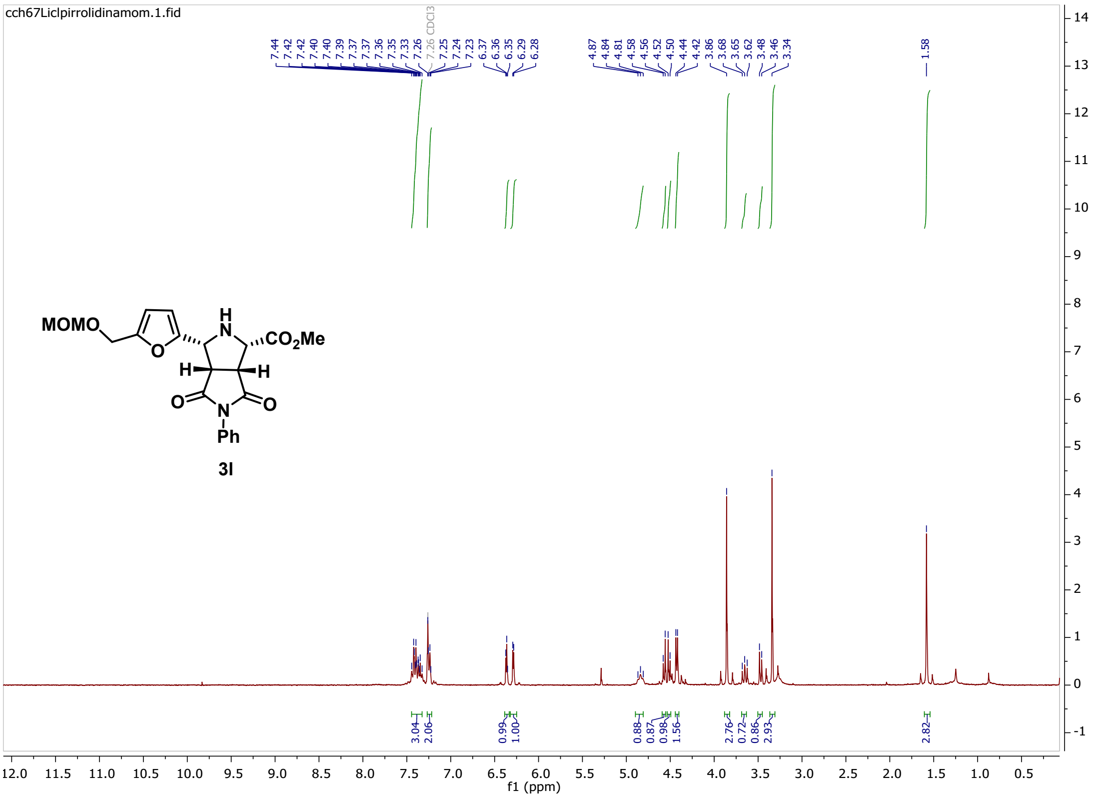


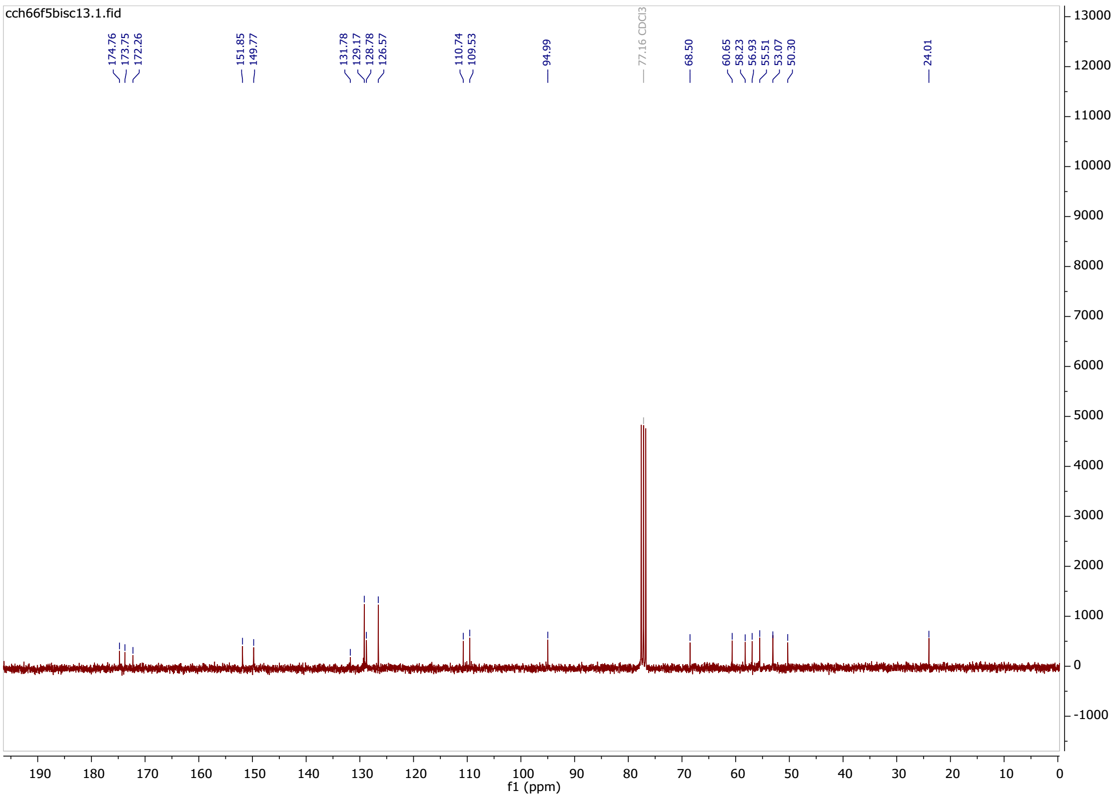
Methyl (1*S*,3*R*,3a*S*,6a*R*)-4,6-dioxo-5-phenyl-3-(5-(triisopropylsilyloxymethyl)furan-2-yl)octahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3k)



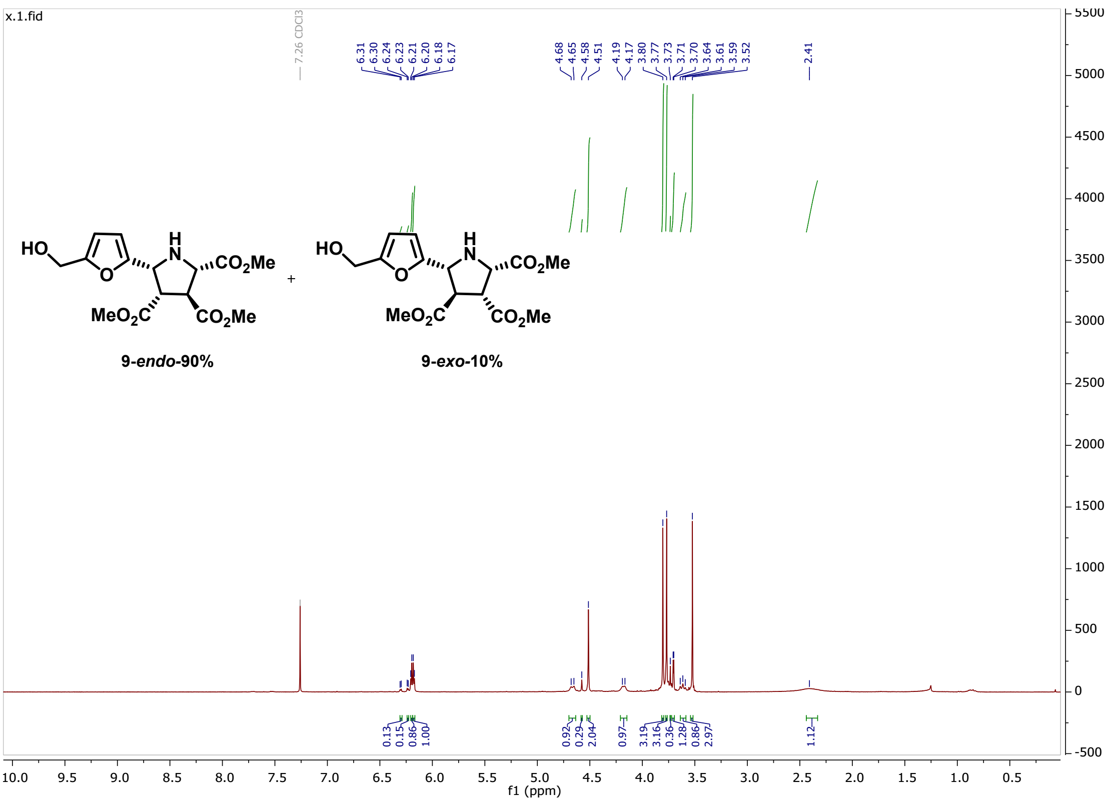


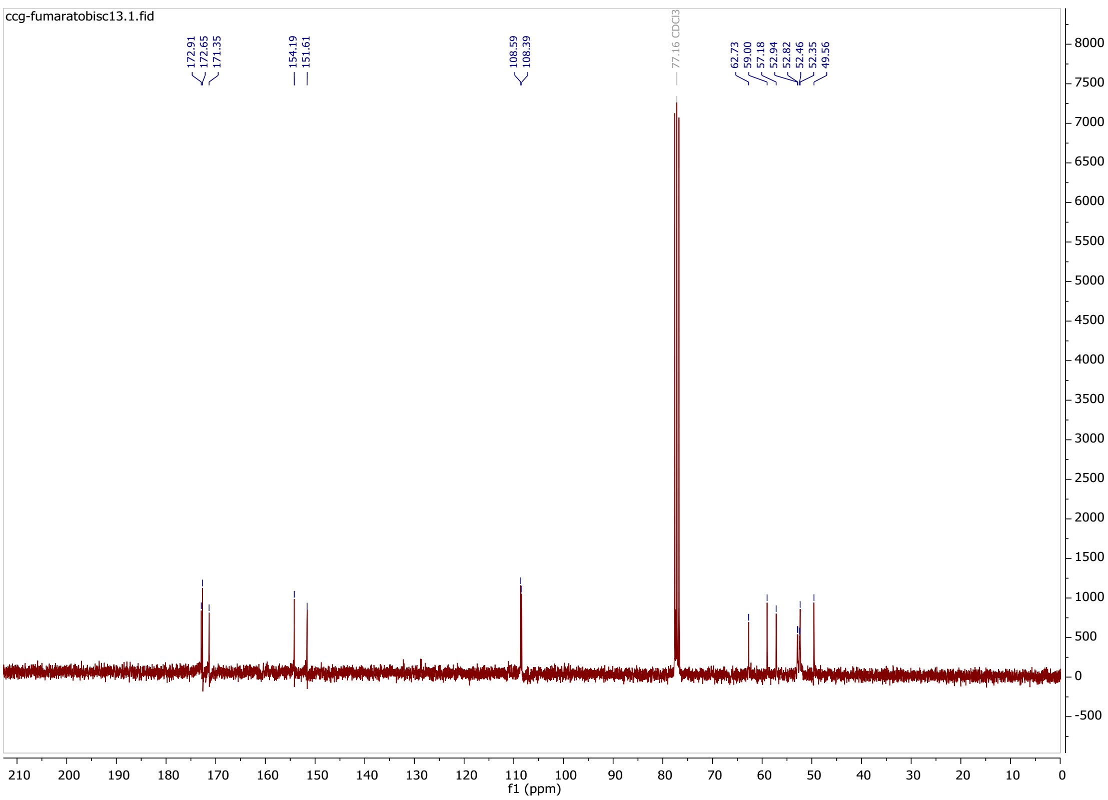
Methyl (1*S*,3*R*,3a*S*,6a*R*)-3-(5-((methoxymethoxy)methyl)furan-2-yl)-4,6-dioxo-5-phenyloctahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3l)



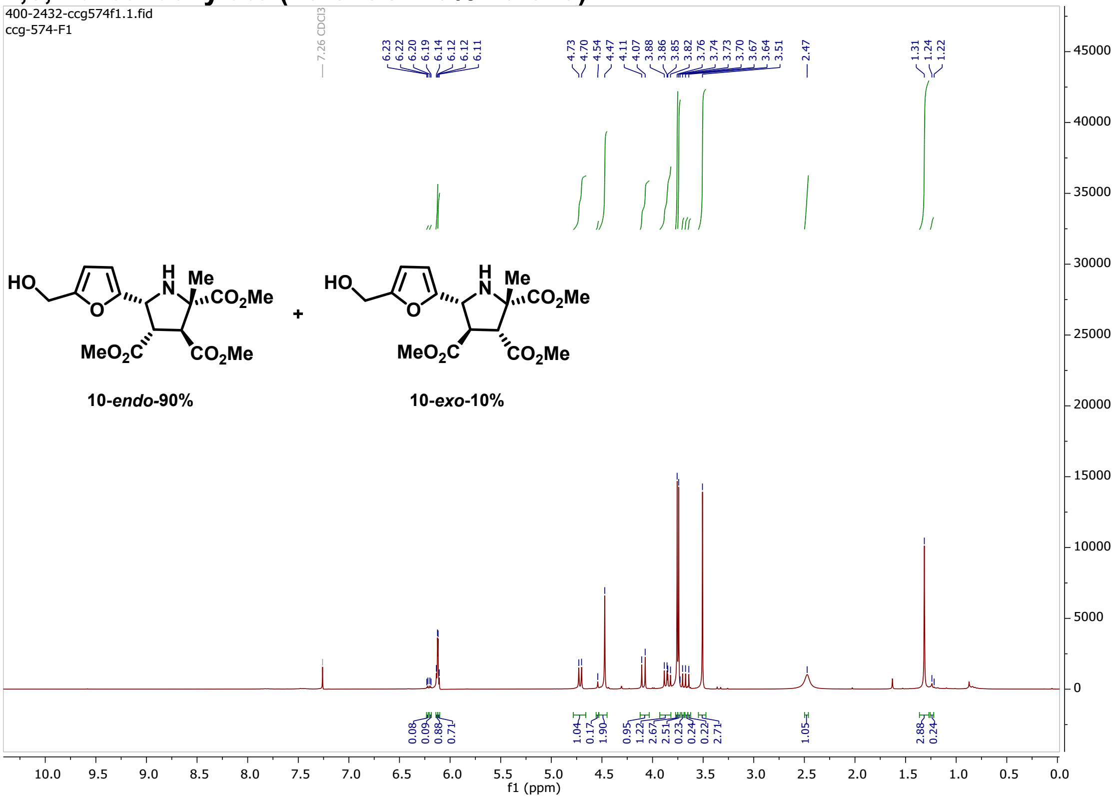


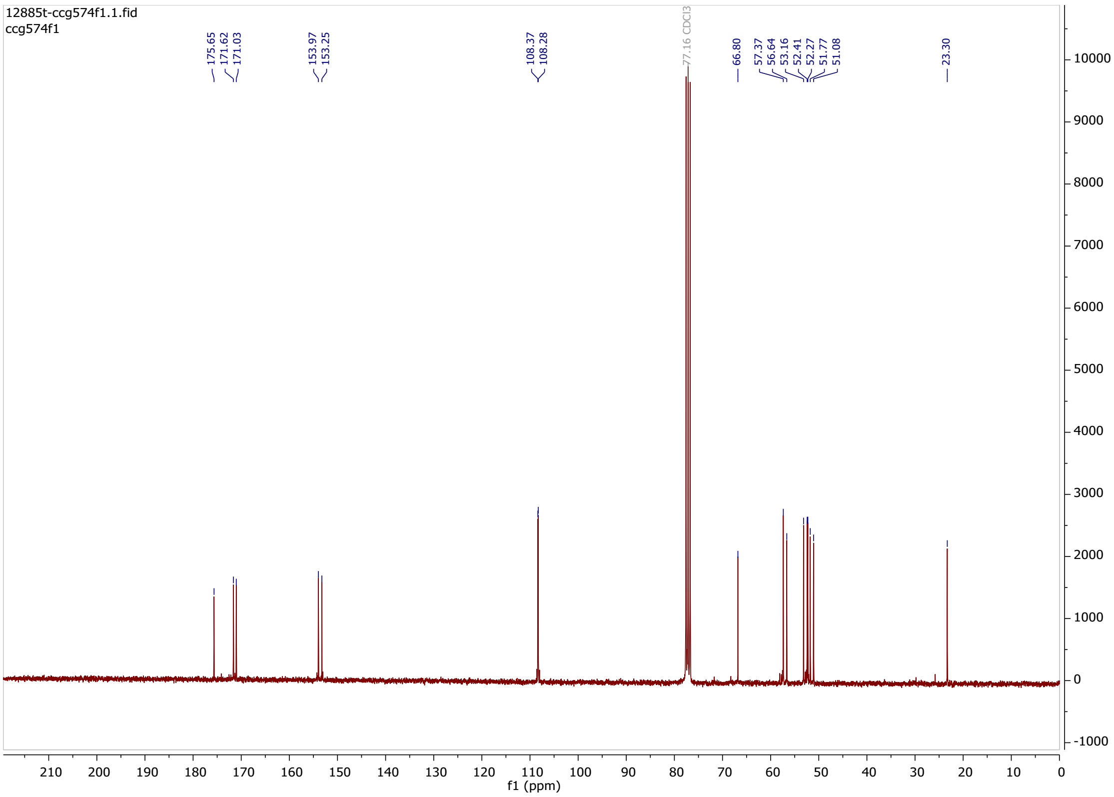
Trimethyl (2*S*,3*S*,4*S*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)pyrrolidine-2,3,4-tricarboxylate (9)



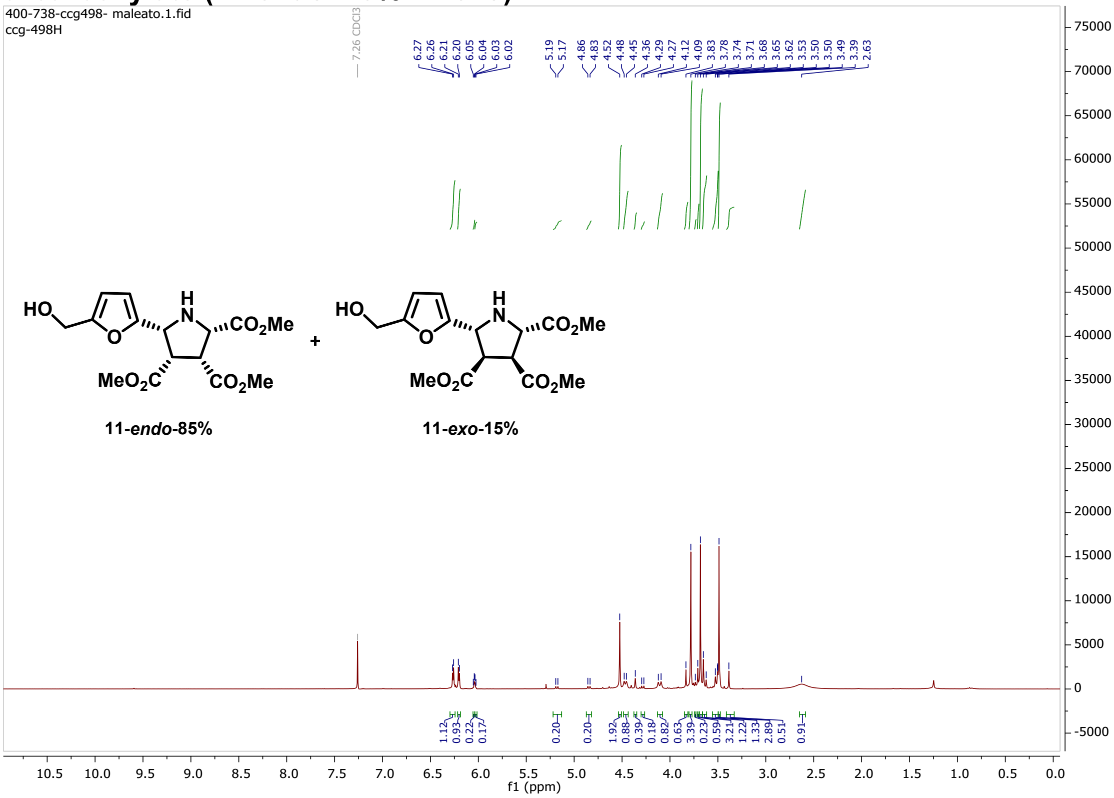


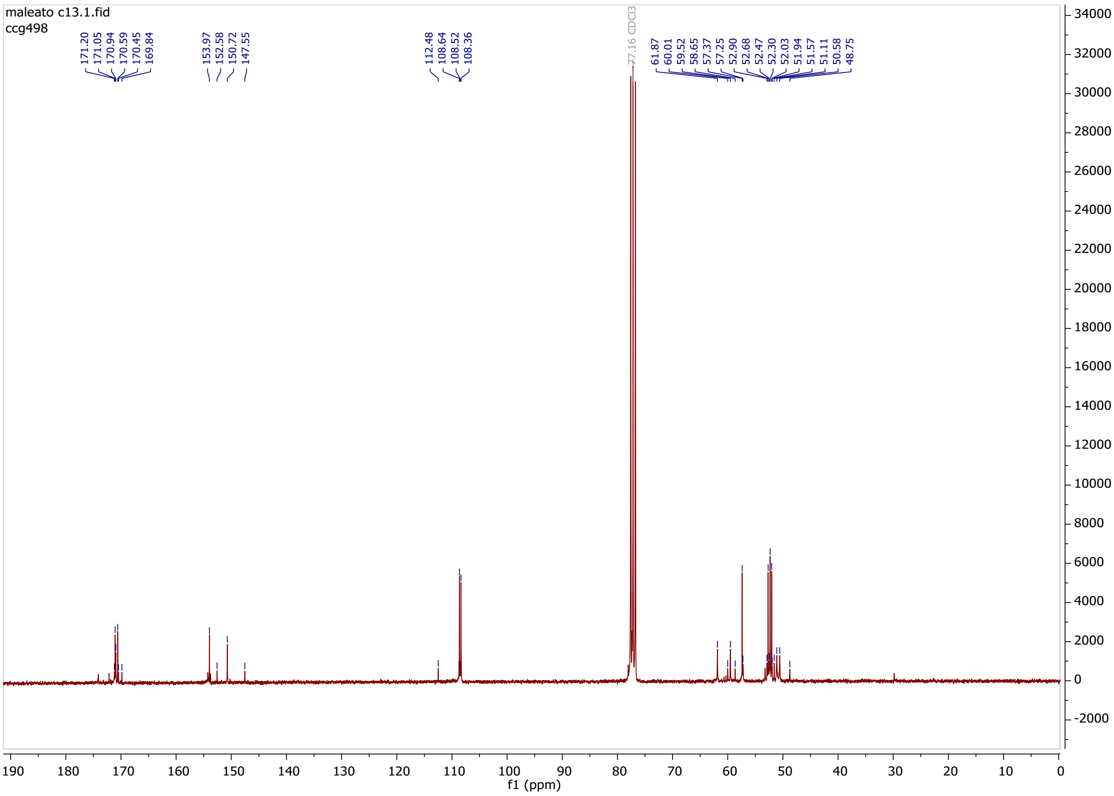
Trimethyl (2*S*,3*S*,4*S*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)-2-methylpyrrolidine-2,3,4-tricarboxylate (10-*endo*+10% 10-*exo*)



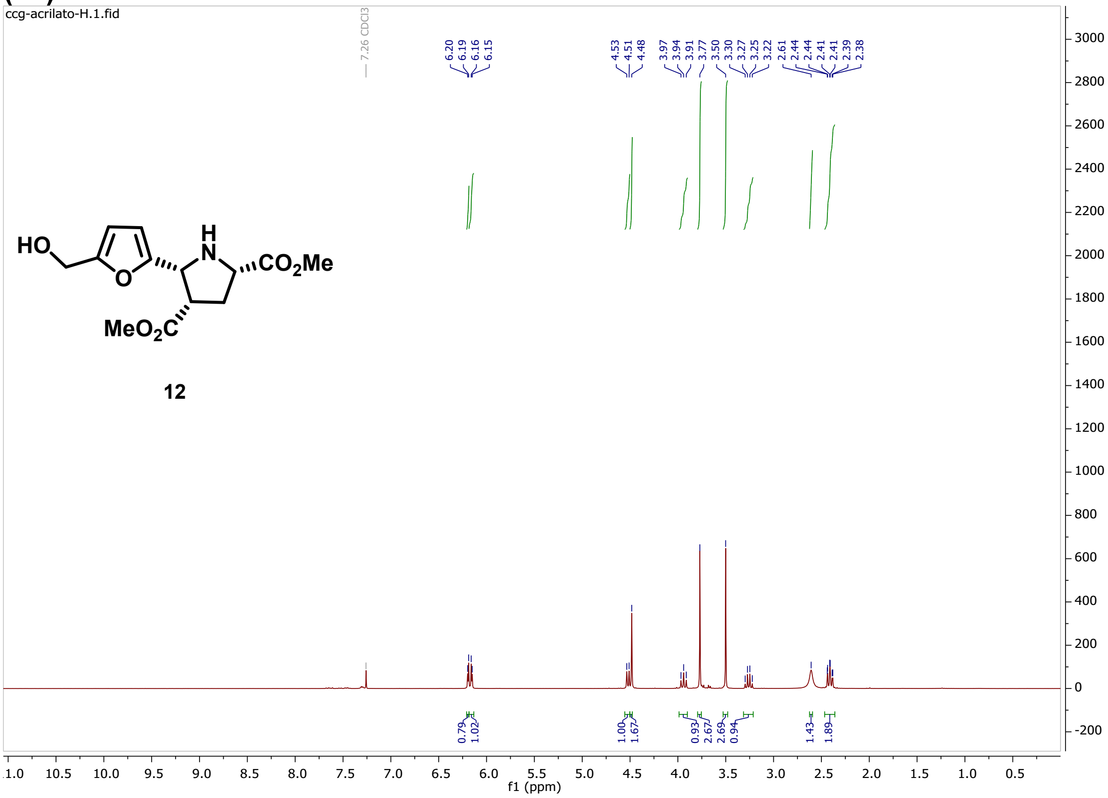


Trimethyl (2*S*,3*R*,4*S*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)pyrrolidine-2,3,4-tricarboxylate (11-*endo*+20% 11-*exo*)

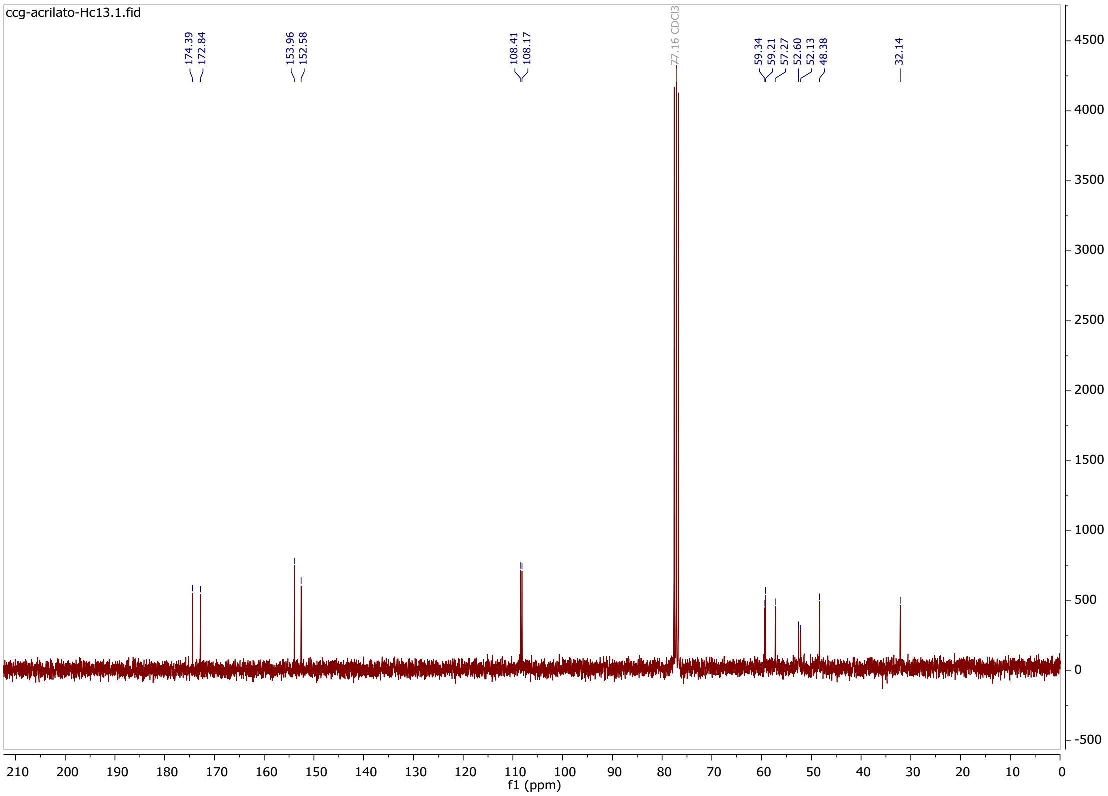




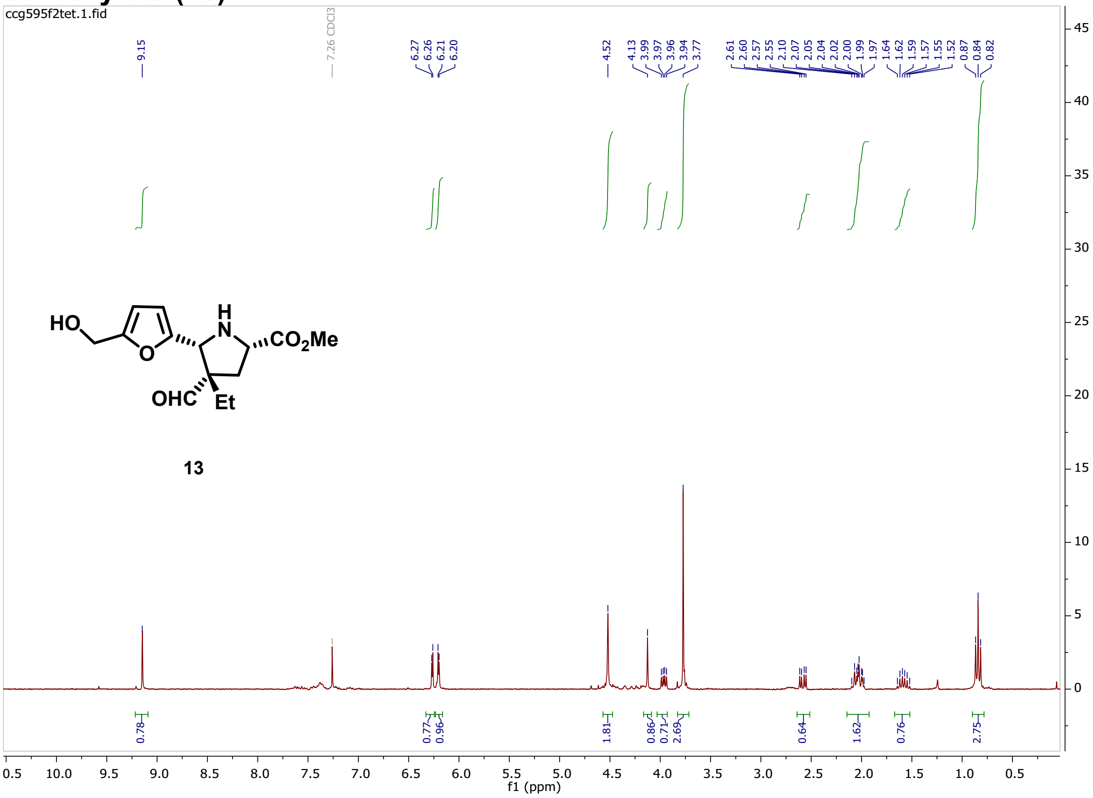
Dimethyl (2*S*,4*S*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)pyrrolidine-2,4-dicarboxylate (12)

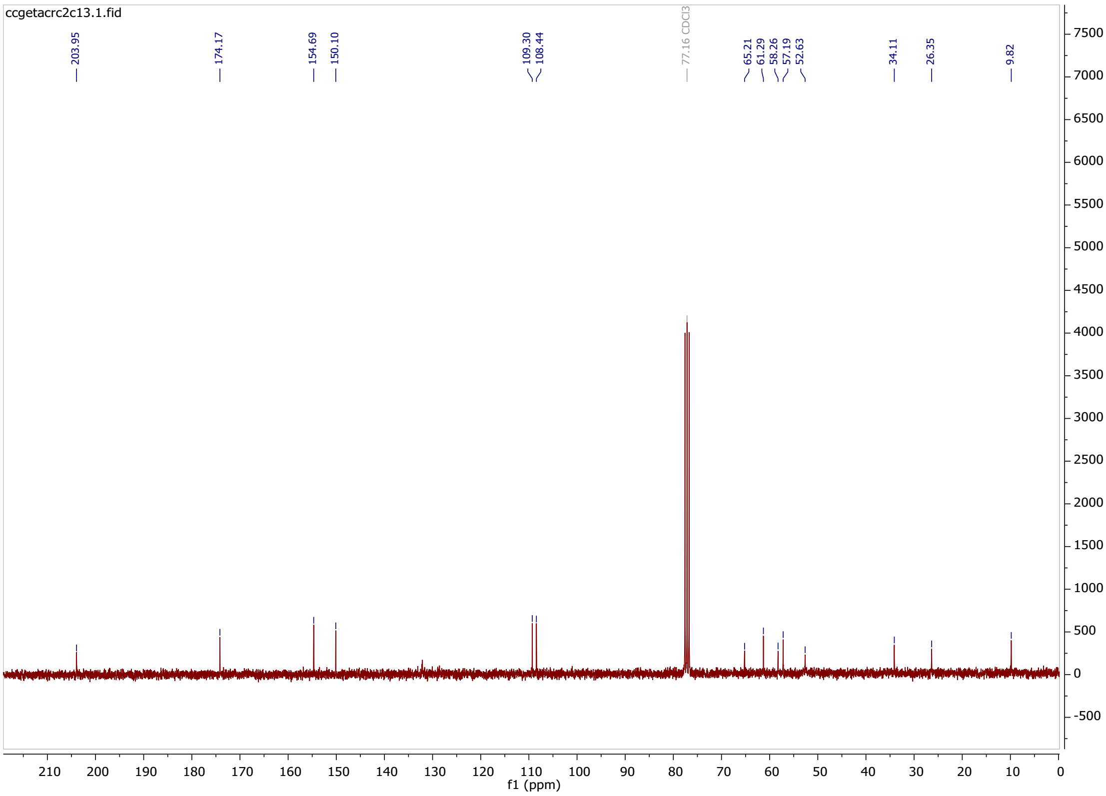


12

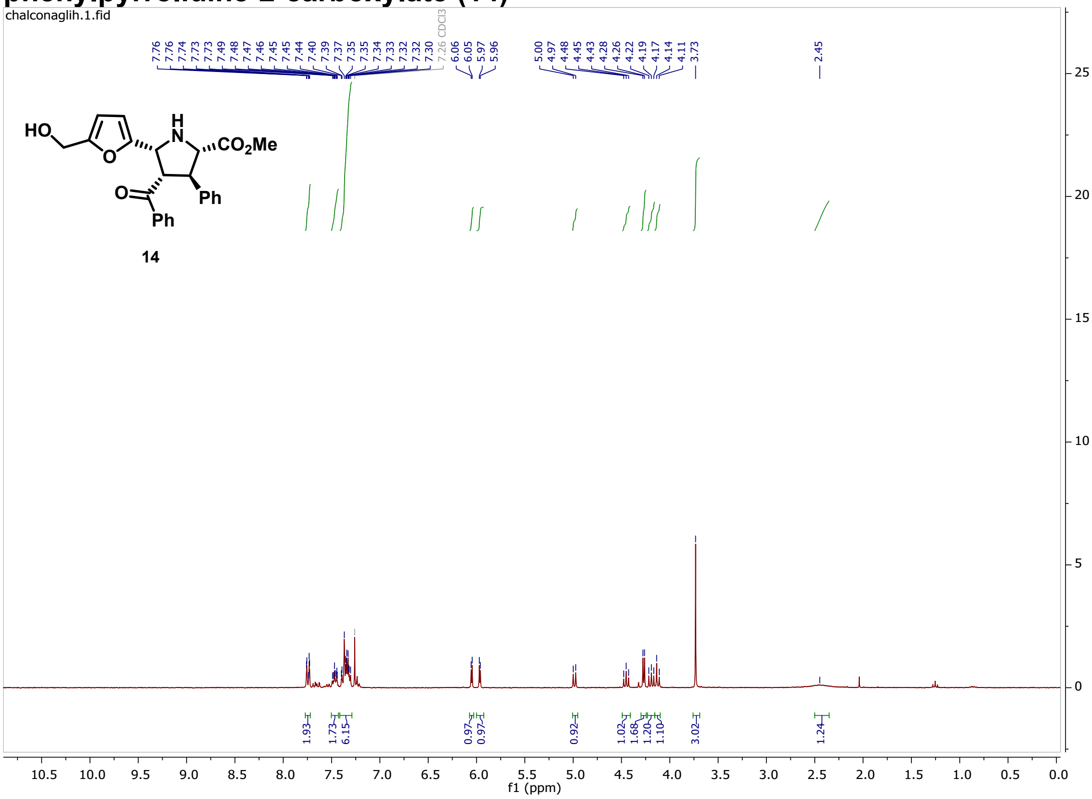


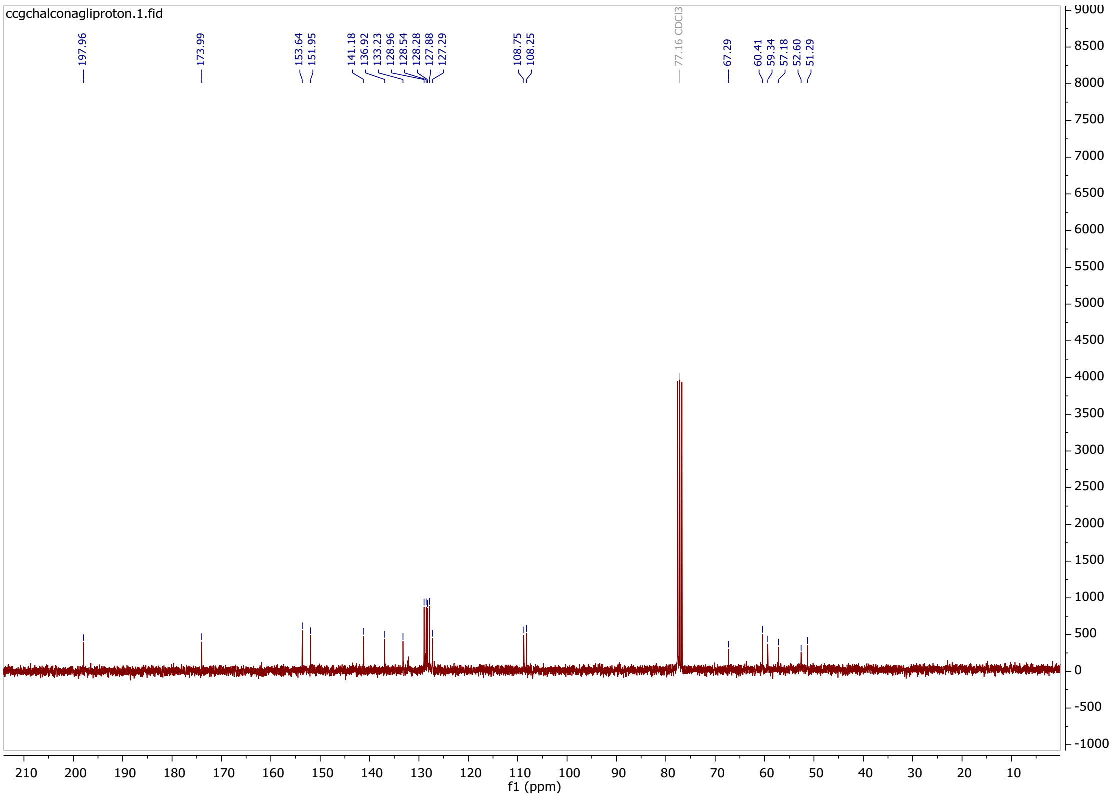
Methyl (2*S*,4*S*,5*R*)-4-ethyl-4-formyl-5-(5-(hydroxymethyl)furan-2-yl)pyrrolidine-2-carboxylate (13)



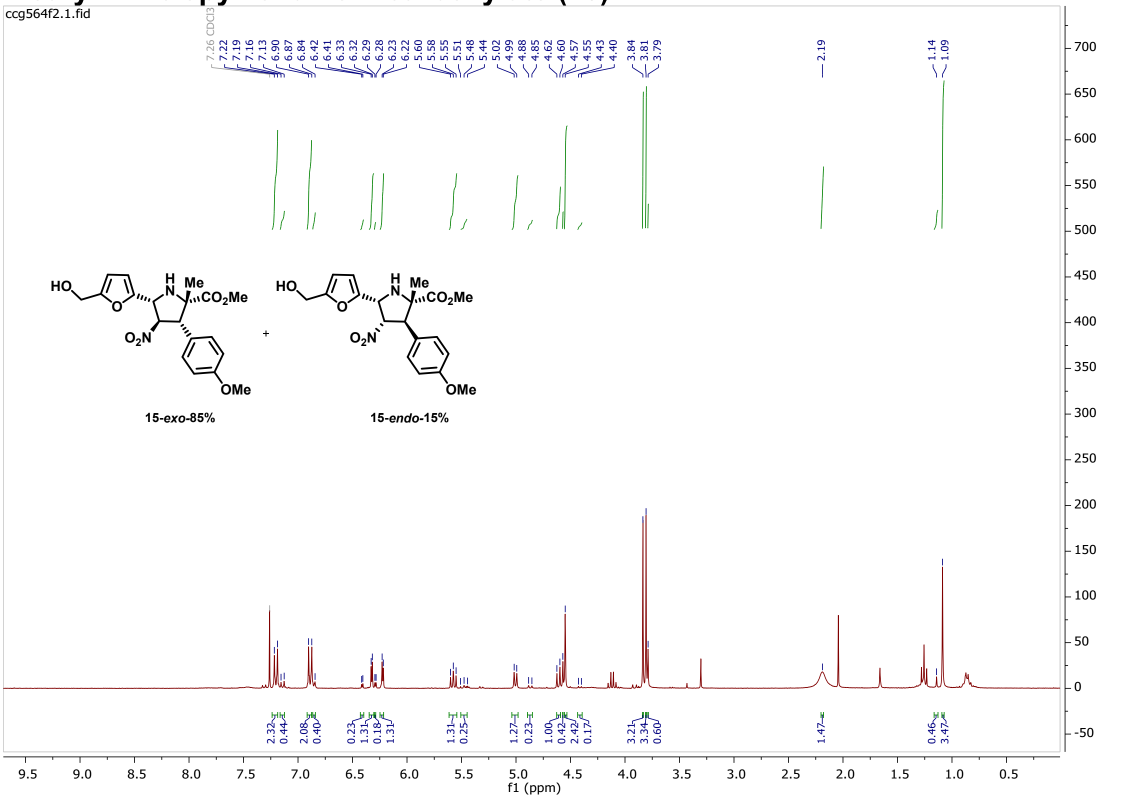


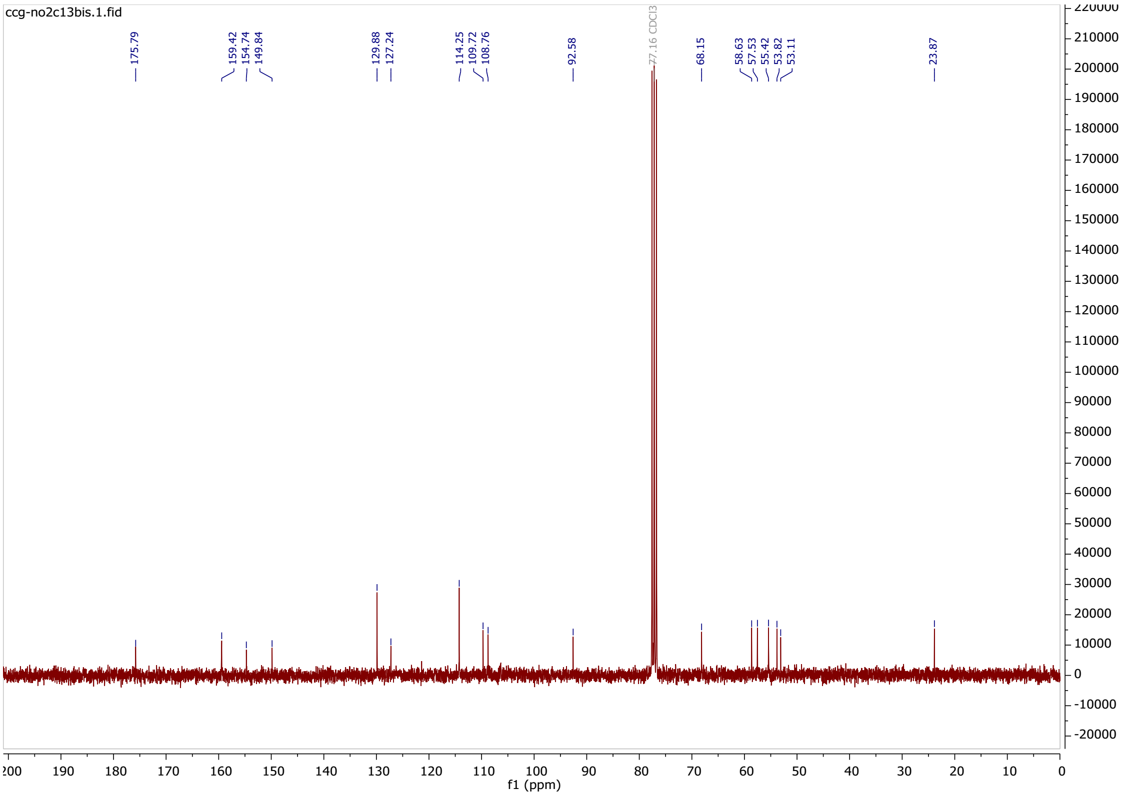
Methyl (2*S*,3*R*,4*S*,5*R*)-4-benzoyl-5-(5-(hydroxymethyl)furan-2-yl)-3-phenylpyrrolidine-2-carboxylate (14)



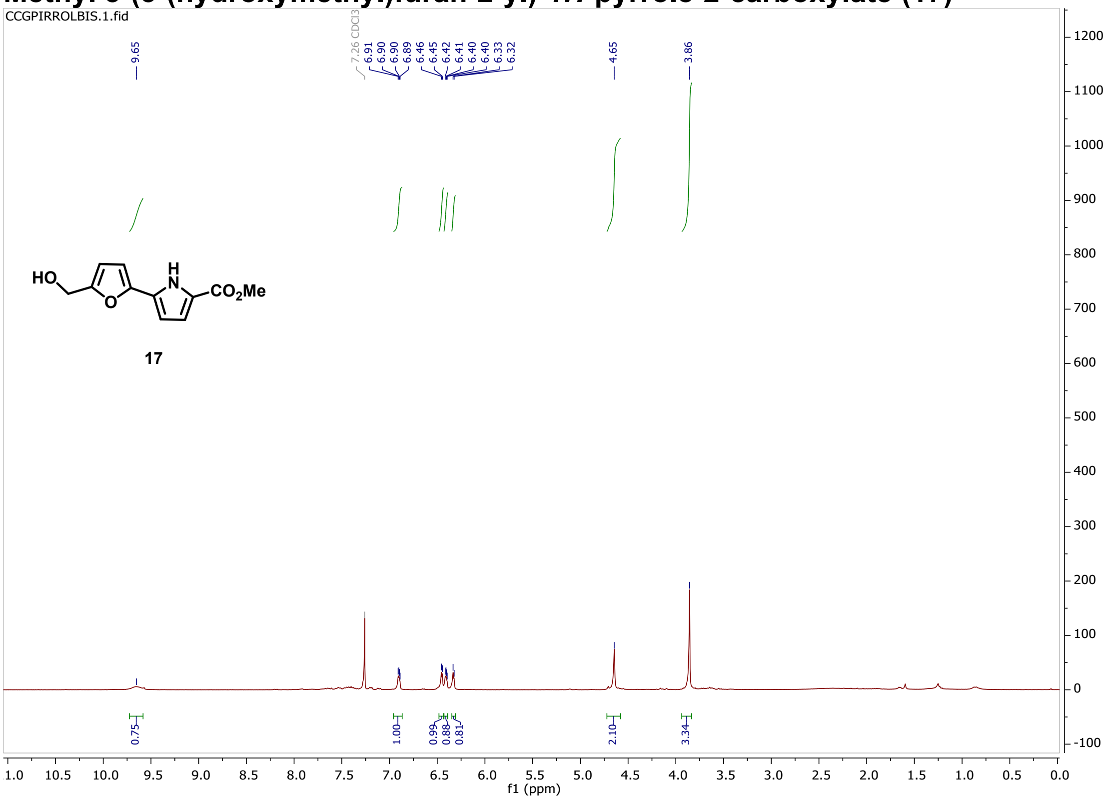


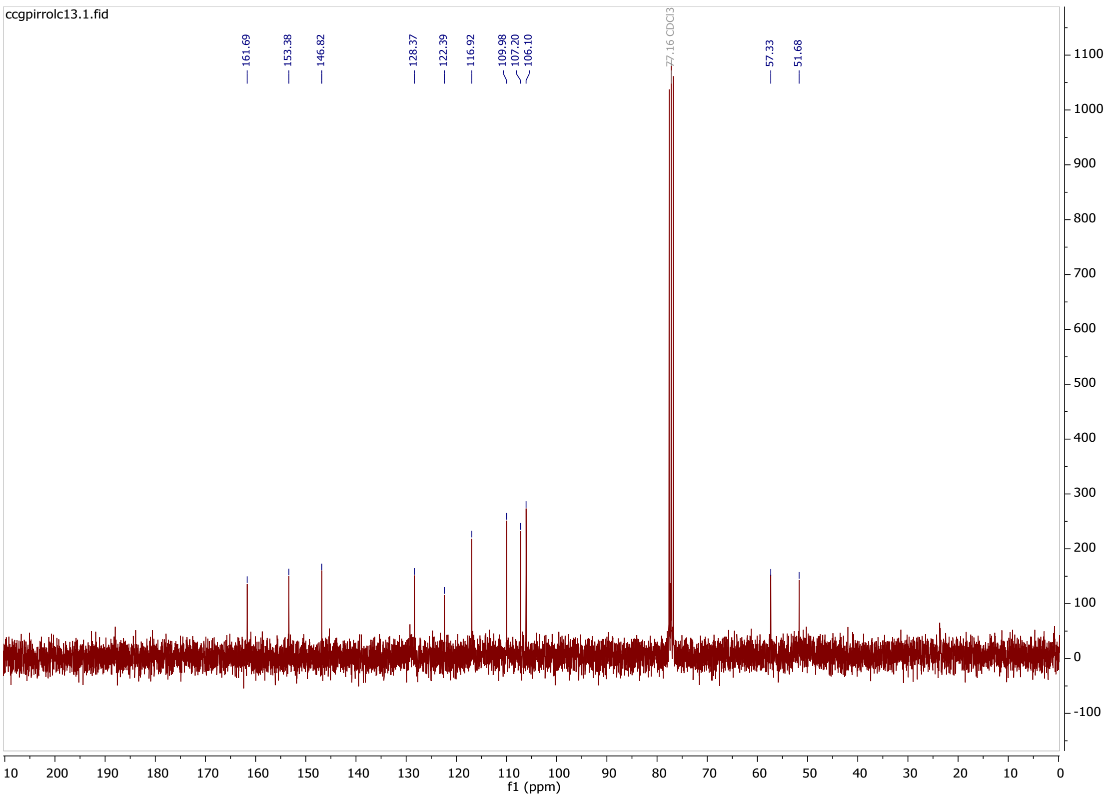
Methyl (2*S*,3*R*,4*R*,5*R*)-5-(5-(hydroxymethyl)furan-2-yl)-3-(4-methoxyphenyl)-2-methyl-4-nitropyrrolidine-2-carboxylate (15)



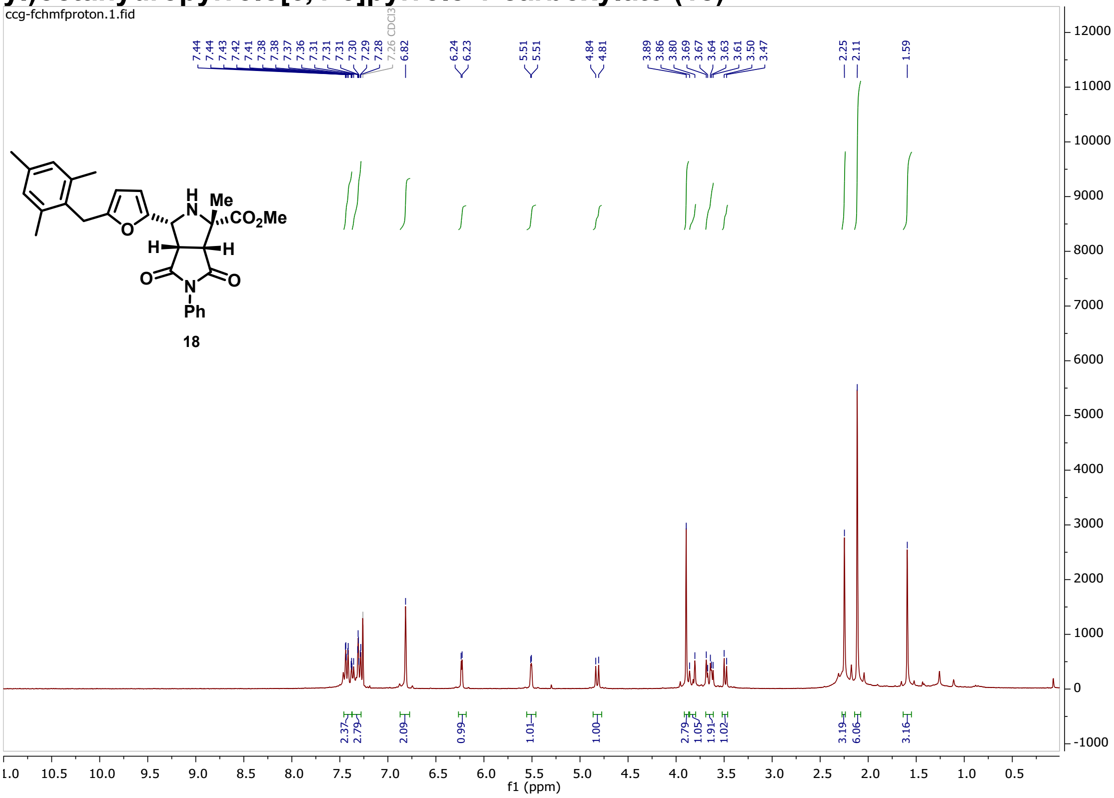


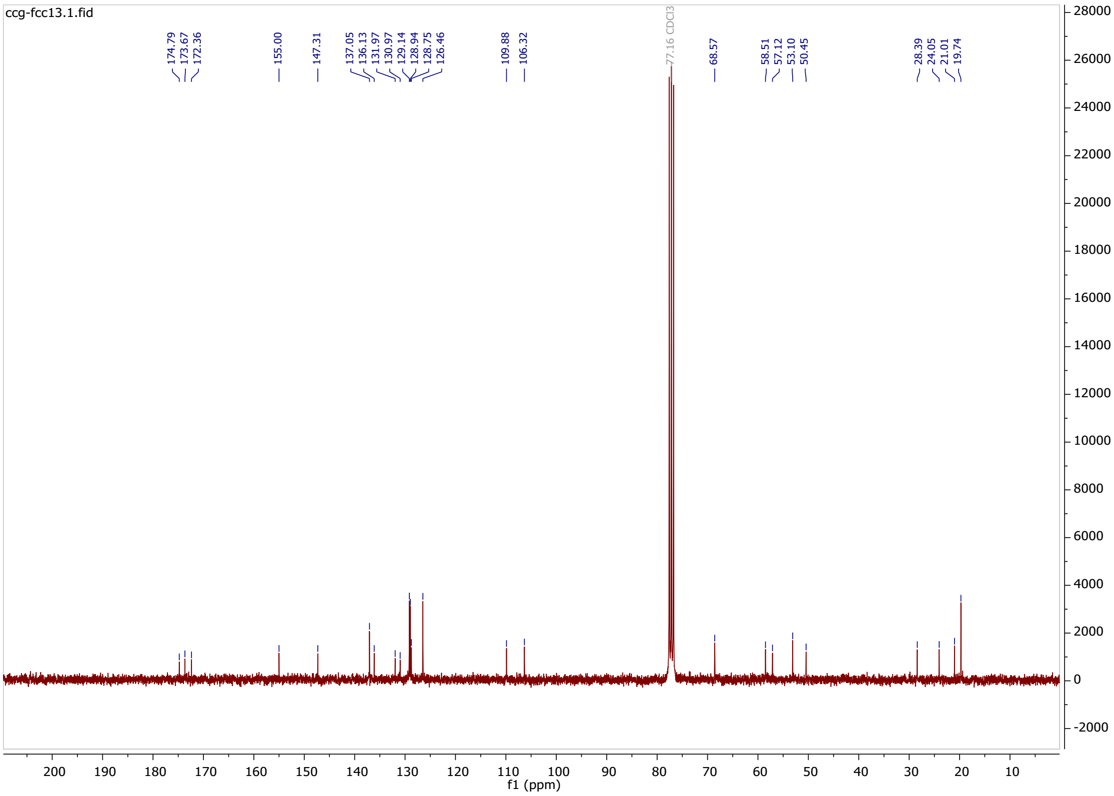
Methyl 5-(5-(hydroxymethyl)furan-2-yl)-*1H*-pyrrole-2-carboxylate (17)



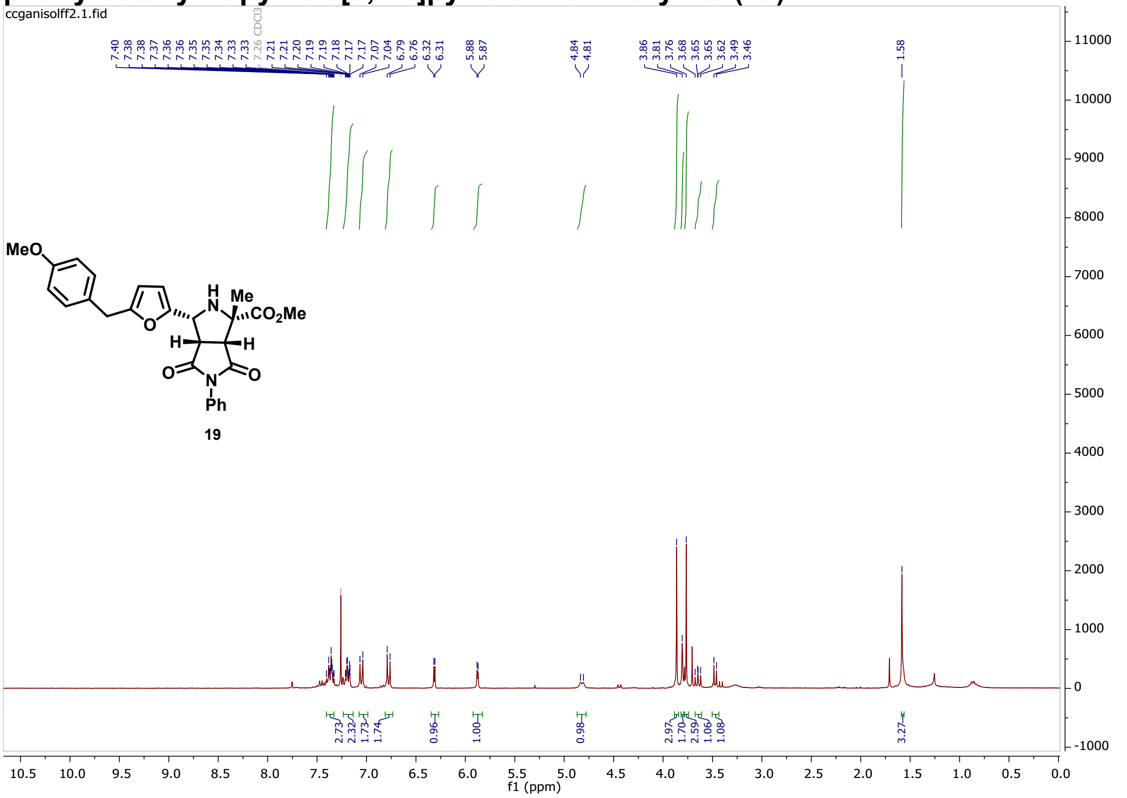


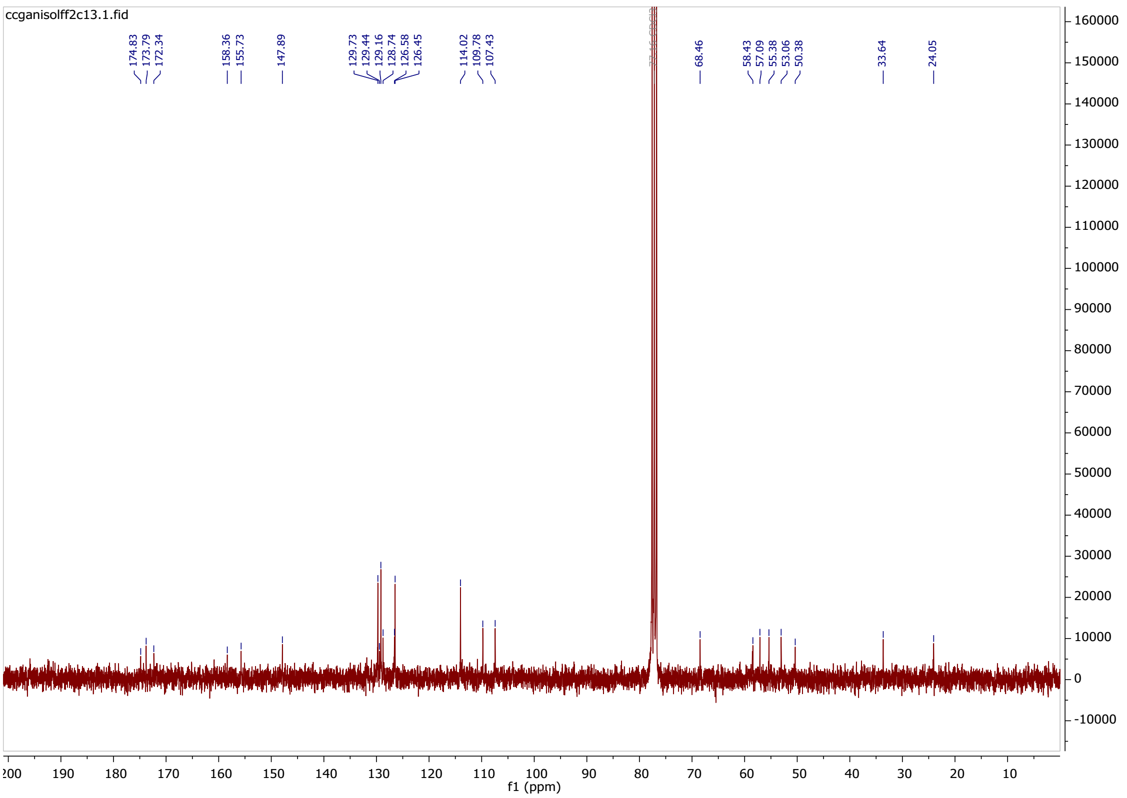
(±)-Methyl 1-methyl-4,6-dioxo-5-phenyl-3-(5-(2,4,6-trimethylbenzyl)furan-2-yl)octahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (18)



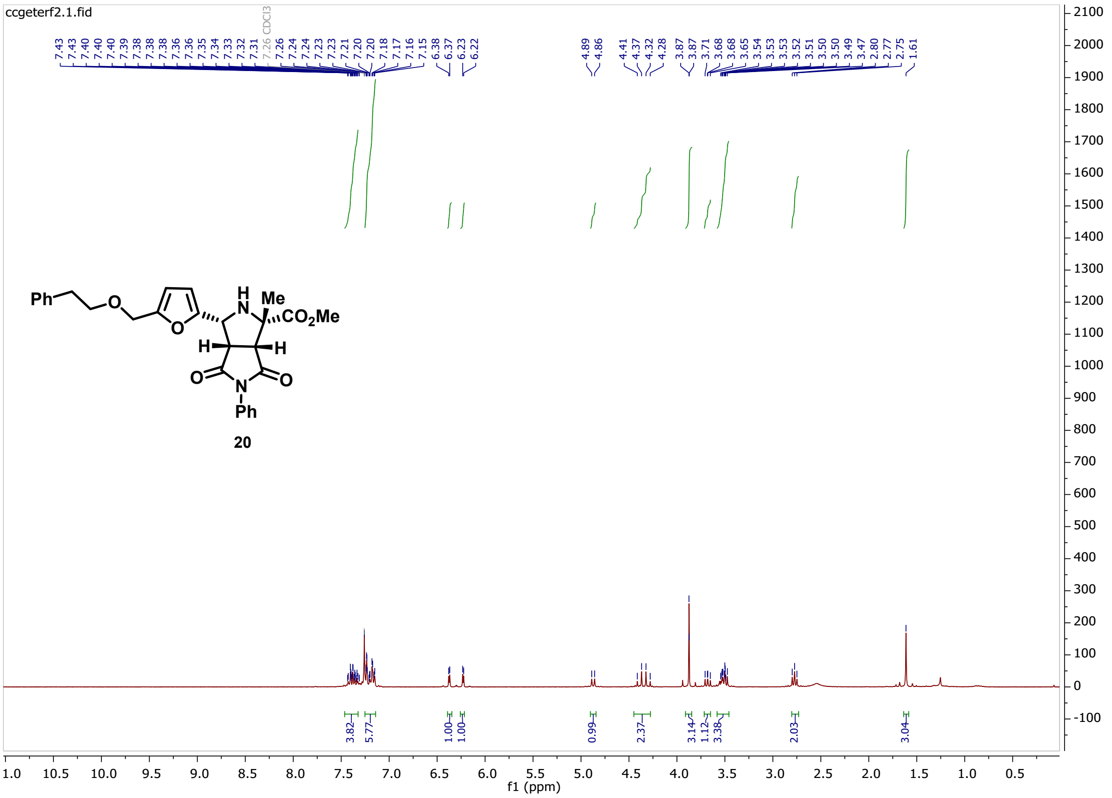


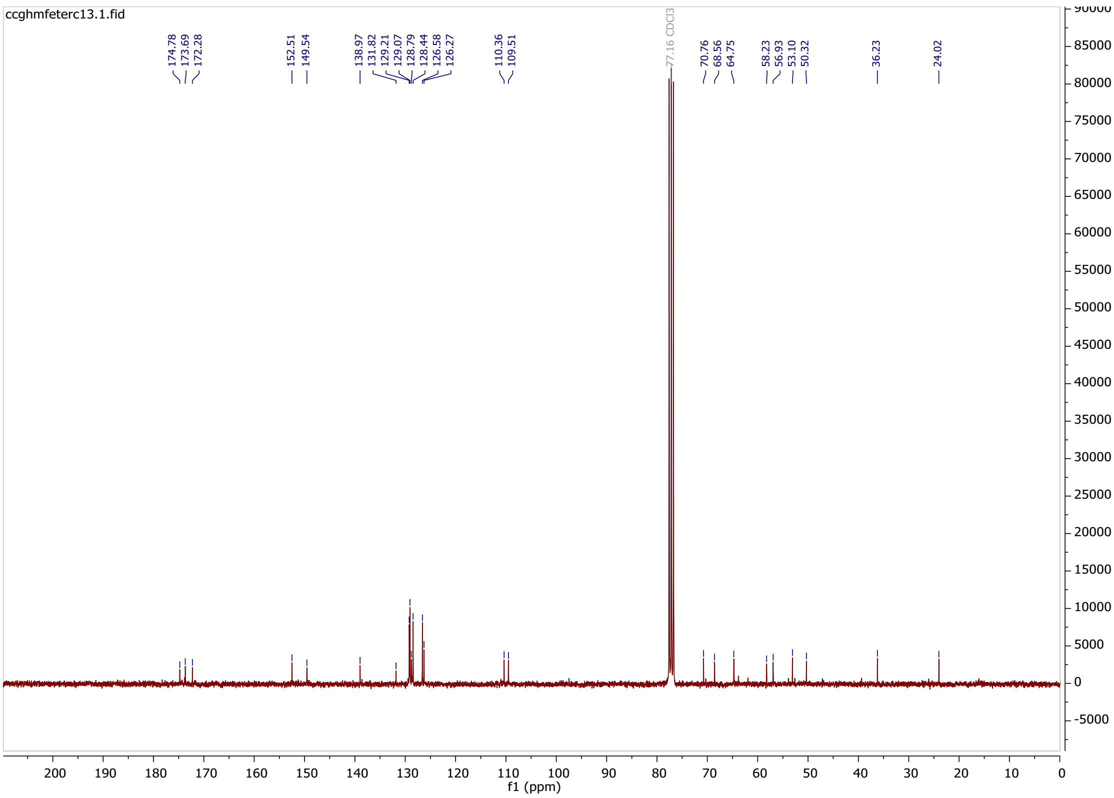
(±)-Methyl 3-(5-(4-methoxybenzyl)furan-2-yl)-1-methyl-4,6-dioxo-5-phenyloctahydropyrrolo[3,4-c]pyrrole-1-carboxylate (19)



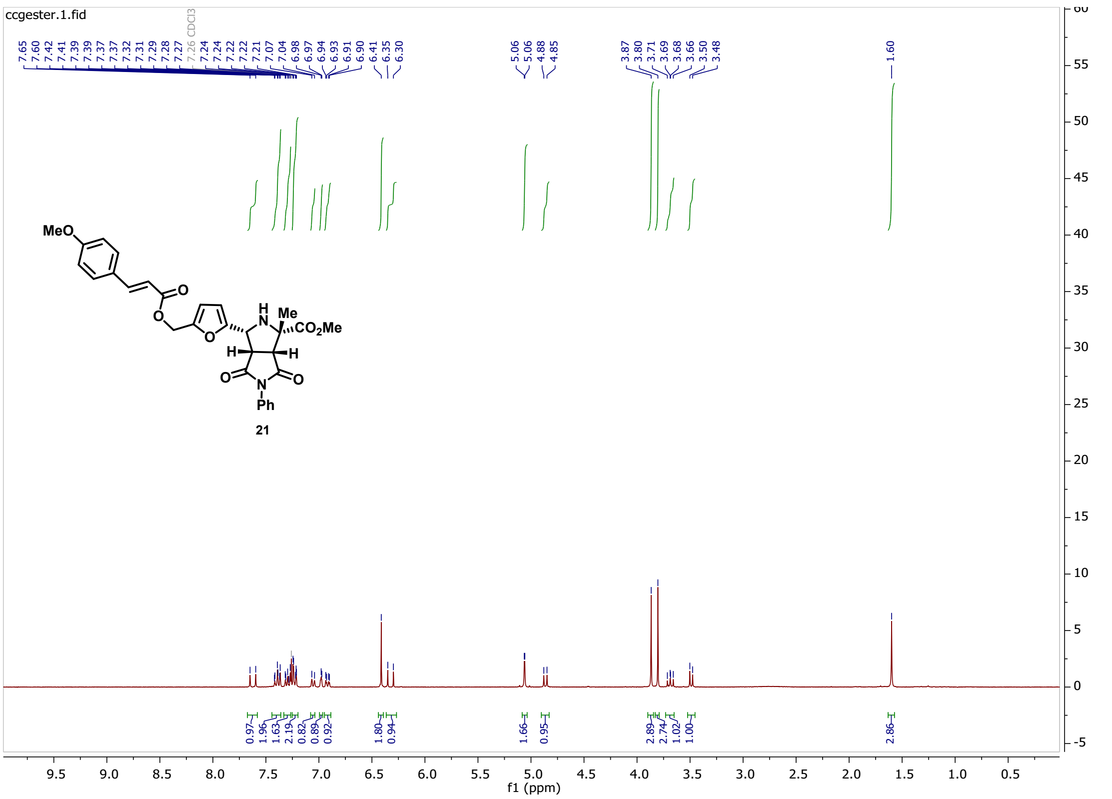


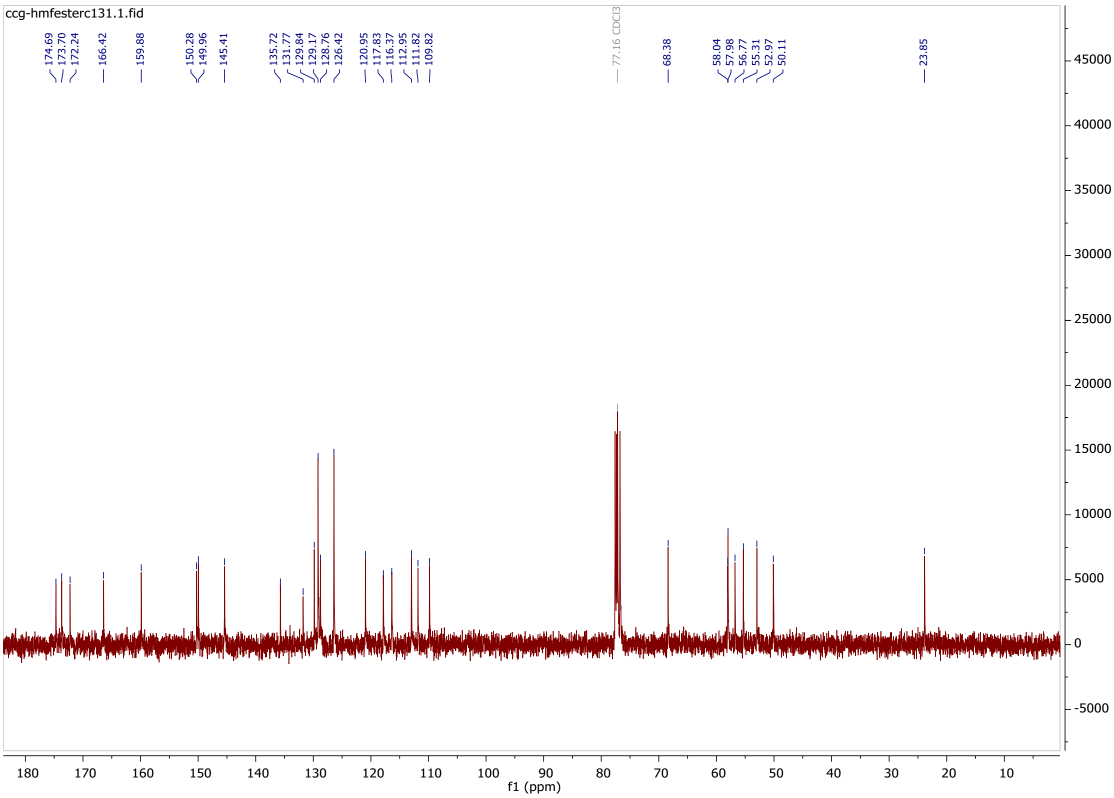
(±)-Methyl 1-methyl-4,6-dioxo-3-(5-(phenethoxymethyl)furan-2-yl)-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (20)





(±)-Methyl 3-(5-(*E*)-3-(4-methoxyphenyl)acryloyloxymethylfuran-2-yl)-1-methyl-4,6-dioxo-5-phenyloctahydropyrrolo[*3,4-c*]pyrrole-1-carboxylate (21)





9. Bibliography

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2. Bering, L., Jeyakumar, K., Antonchick, A. *Org. Lett.* **2018**, 20, 3911–3914.