Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Aerobically-initiated C(sp^3)−H bond amination through the use of activated azodicarboxylates

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Supporting Information

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General Experimental

Chemicals

All reagents were purchased from Aldrich or AlfaAesar and were used as received without further purification unless otherwise stated.

Solvents

Where described below, Petrol refers to petroleum ether (b.p. 40-60 °C).

Chromatography

All reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel plates. Silica get plates were initially examined under short wave UV light and then developed using aqueous potassium permanganate stain. Flash column chromatography was carried out with pre-loaded GraceResolv^{TM} flash cartridges on a Biotage® Isolera Spektra One flash chromatography system.

Spectroscopy

Quoted yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated. ^{1}H NMR spectra were recorded at 600 MHz or 700 MHz and ^{13}C NMR at 151 MHz or 176 MHz on a Bruker Avance III 600 or Bruker Avance Neo 700 spectrometer. The chemical shifts (δ) for ^{1}H and ^{13}C are quoted relative to residual signals of the solvent on the parts per million (ppm) scale. Coupling constants (*J* values) are reported in Hertz (Hz) and are reported as $J_{H\text{-}H}$. Signal multiplicities in ^{13}C NMR were determined using the distortionless enhancement by polarisation transfer (DEPT) spectral editing technique. Many of the compounds formed exist as rotamers, and this leads to broadness in peaks + additional peaks (the stereodynamics of the N−N bond about hydrazide-type molecules is well known in the literature).[1]

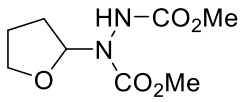
Miscellaneous

Melting points were measured with a Gallenkamp apparatus and are uncorrected.

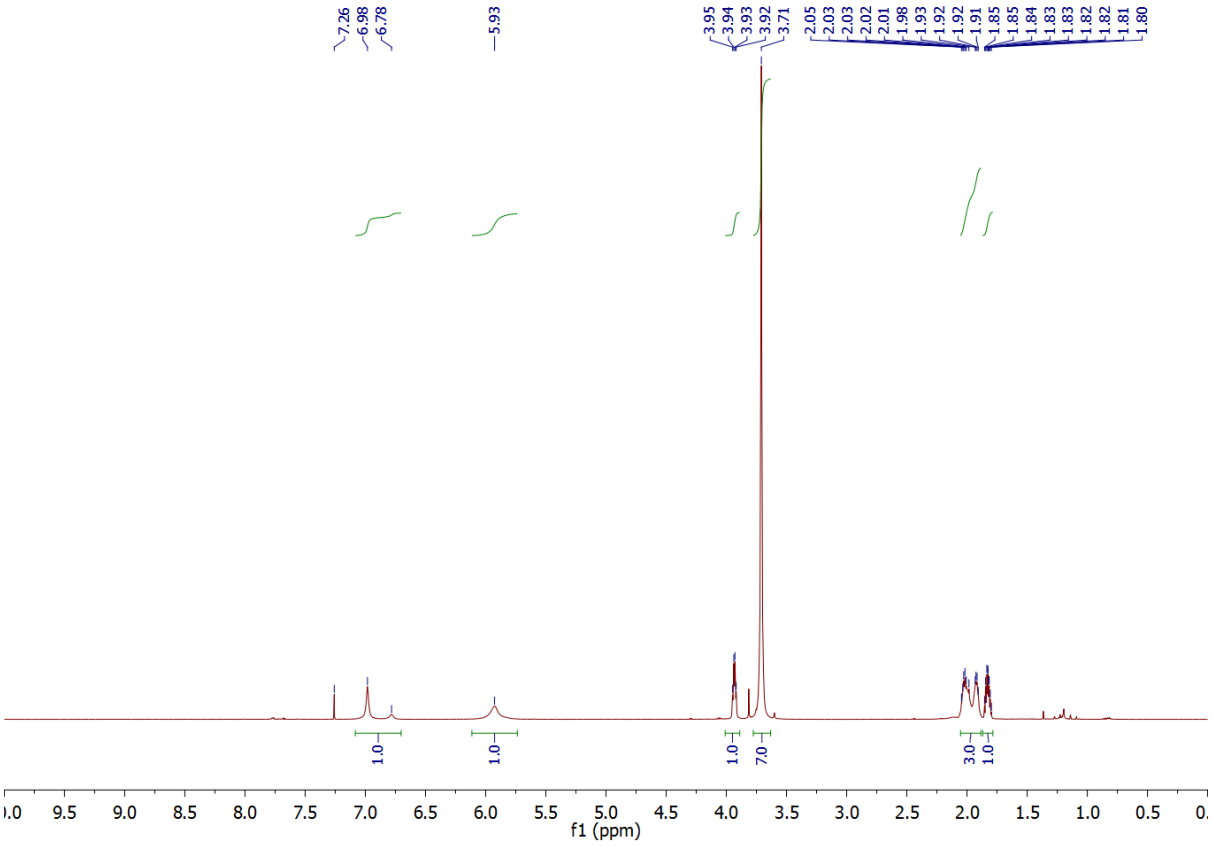
General experimental for the formation of ether hydrazides

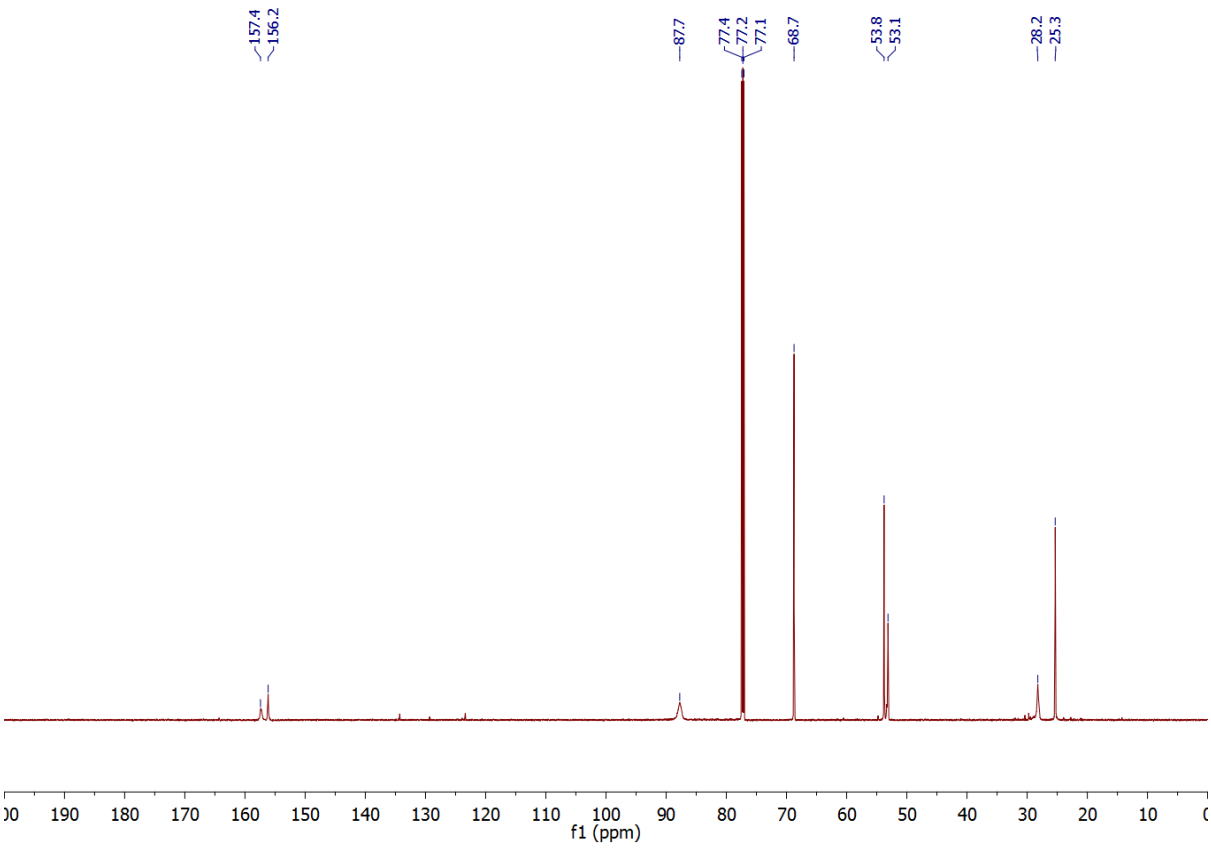
To a solution of azodicarboxylate (1.00 mmol, 1.0 eq.) in fluorinated alcohol (0.5 mL) was added ether (5.00 mmol, 5.0 eq.). The reaction mixture was stirred at 80 °C at 1050 rpm for the time specified below and then poured over saturated aqueous $NaHCO_3$ (20 mL). The resulting mixture was extracted with EtOAc (3 × 15 mL). The combined extracts were dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The resultant crude residue was purified as described below.

Dimethyl 1-(tetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate 6aa[2]



Compound prepared using HFIP as the reaction solvent and a reaction duration of 48 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded dimethyl 1-(tetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate as a clear oil (179 mg, 0.82 mmol, 82%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.99-6.77 (m, NH, 1H), 5.93 (s, 1H), 3.93 (dd, *J* = 7.1, 6.9 Hz, 1H), 3.71 (s, 7H), 2.06-1.89 (m, 3H), 1.86-1.79 (m, 1H); (176 MHz, $CDCl_3$) δ 157.4 (C), 156.2 (C), 87.7 (CH), 68.7 (CH_2), 53.8 (CH_3), 53.1 (CH_3), 28.2 (CH_2), 25.3 (CH_2); IR (thin film) 3306, 2984, 2939, 1750, 1732 cm^{-1}.




157.4
156.2
87.7
77.4
77.2
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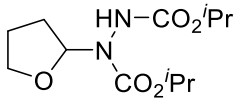
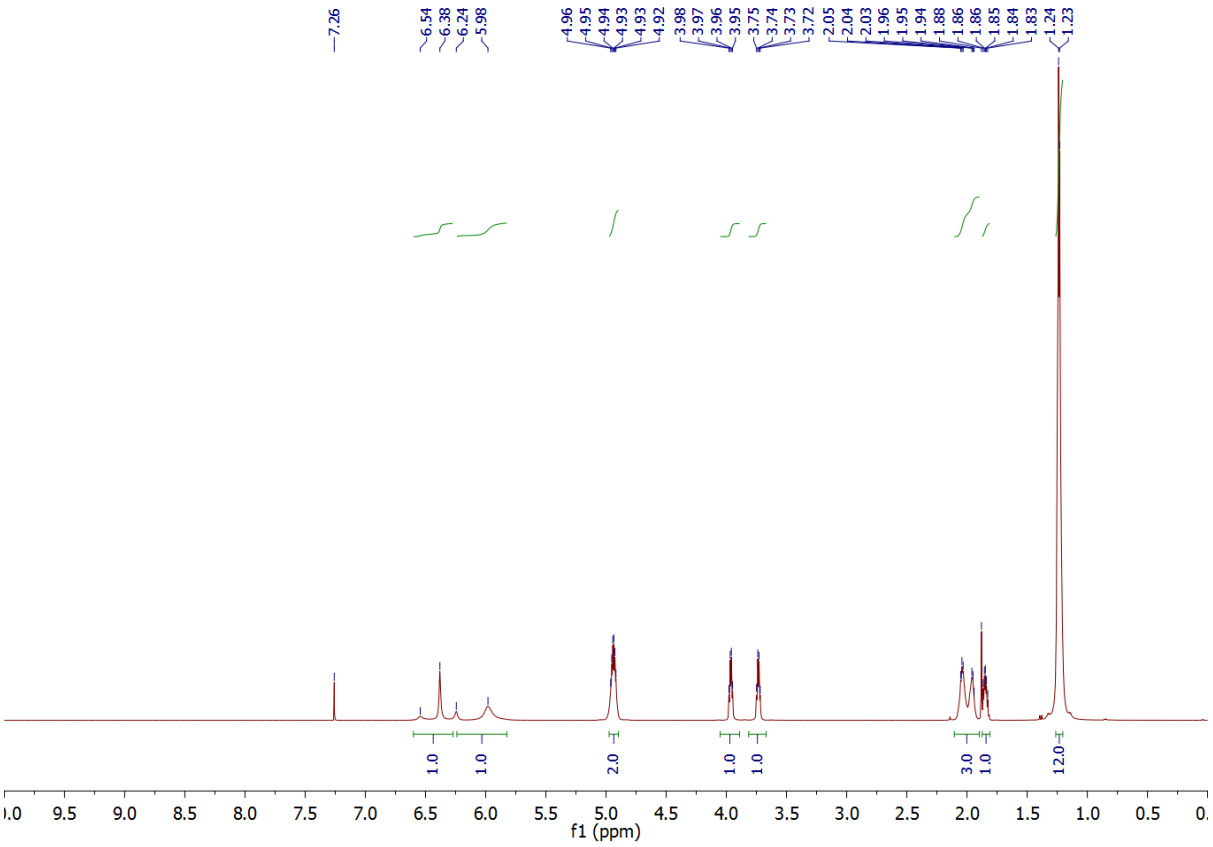
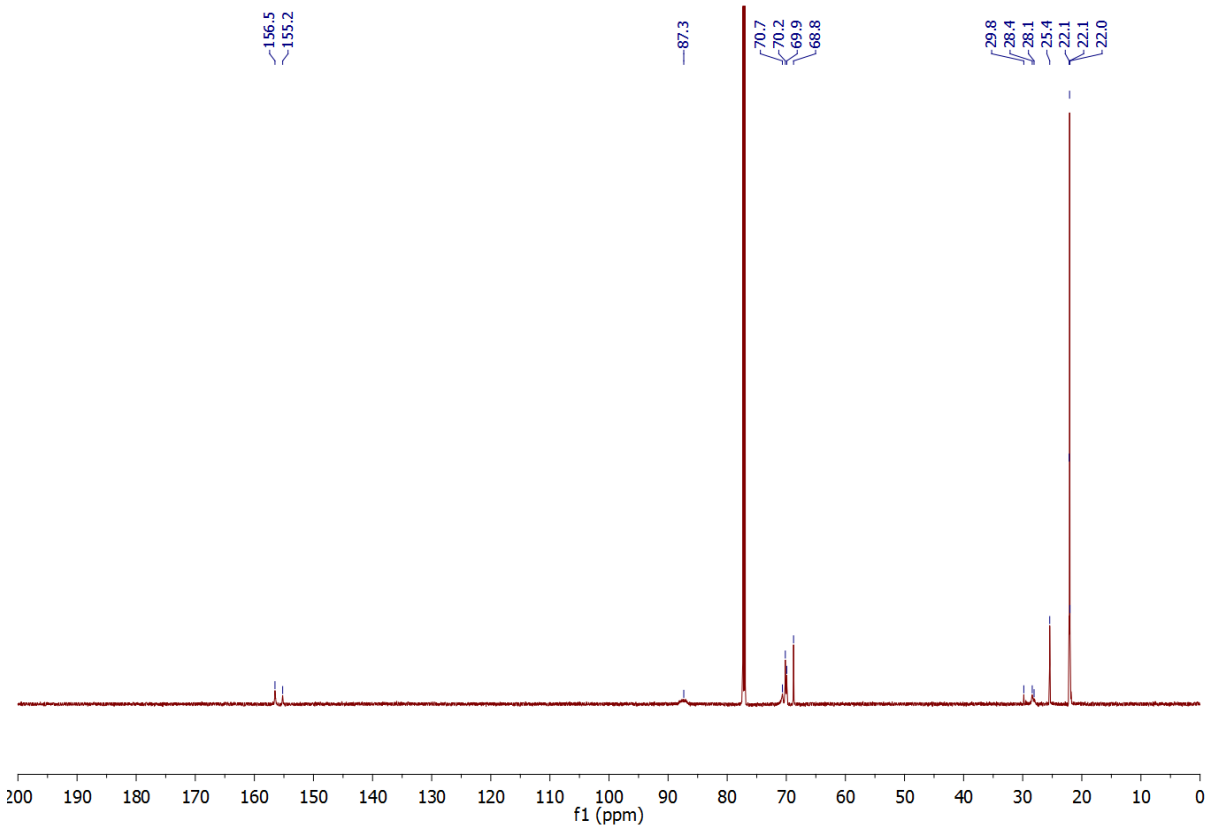
53.8
53.1
28.2
25.3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Diisopropyl 1-benzoylhydrazine-1,2-dicarboxylate 6ab[3]



Compound prepared using HFIP as the reaction solvent and a reaction duration of 48 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-benzoylhydrazine-1,2-dicarboxylate as a white solid (252 mg, 0.920 mmol, 92%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.60-6.28 (m, NH, 1H), 6.25-5.83 (m, 1H), 4.98-4.90 (m, 2H), 3.96 (dt, *J* = 7.0, 7.0 Hz, 1H), 3.73 (dt, *J* = 7.1, 7.1 Hz, 1H), 2.10-1.91 (m, 3H), 1.88-1.82 (m, 1H), 1.23 (d, *J* = 6.3 Hz, 12H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.5 (C), 155.2 (C), 87.3 (CH), 70.7 (CH), 70.2 (CH), 69.9 (CH), 68.8 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 28.4 (CH_2), 28.1 (CH_2), 25.4 (CH_2), 22.1 (CH_3), 22.1 (CH_3), 22.0 (CH_3); IR (solid) 3261, 2974, 2932, 2856, 1731, 1701 cm^{-1}.

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155.2
87.3
70.7
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68.8
29.8
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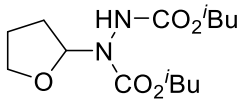
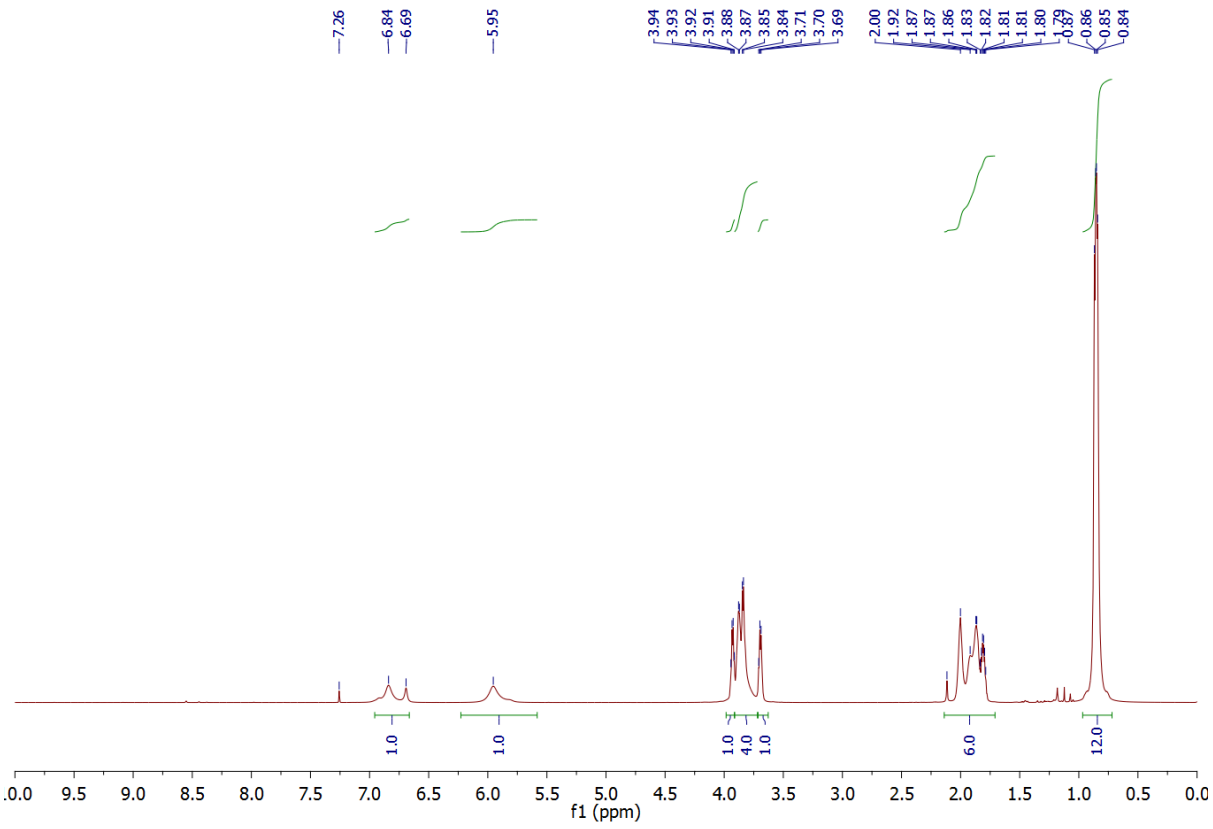
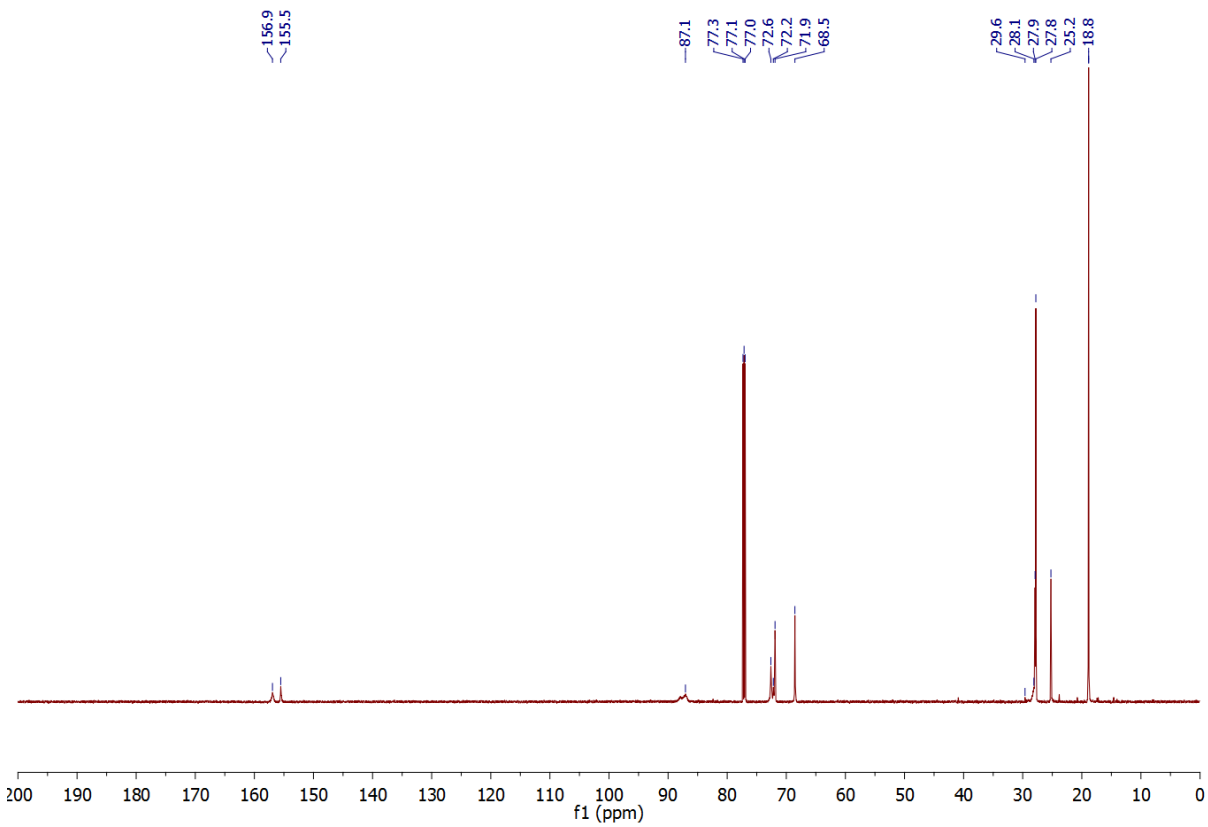
28.1
25.4
22.1
22.1
22.0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Diisobutyl 1-(tetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate 6ac



Compound prepared using HFIP as the reaction solvent and a reaction duration of 48 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisobutyl 1-(tetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate as a white solid (266 mg, 0.880 mmol, 88%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.96-6.66 (m, NH, 1H), 6.22-5.65 (m, 1H), 3.93 (dt, *J* = 6.6, 6.6 Hz, 1H), 3.91-3.72 (m, 4H), 3.70 (dt, *J* = 6.6, 6.6 Hz, 1H), 2.13-1.78 (m, 6H), 0.92-0.78 (m, 12H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 156.9 (C), 155.5 (C), 87.1 (CH), 72.6 (CH_2), 72.2 (CH_2), 71.9 (CH_2), 68.5 (CH_2), 29.6 (CH_2), 28.1 (CH_2) 27.9 (CH), 27.8 (CH), 25.2 (CH_2), 18.8 (CH_3); IR (solid) 3280, 2972, 2935, 2861, 1738, 1711 cm^{-1}. LRMS (ESI) 303 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{14}H_{27}N_2O_5$ $[M+H]^+$ 303.1915; observed 303.1917.

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72.2
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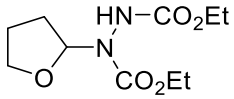
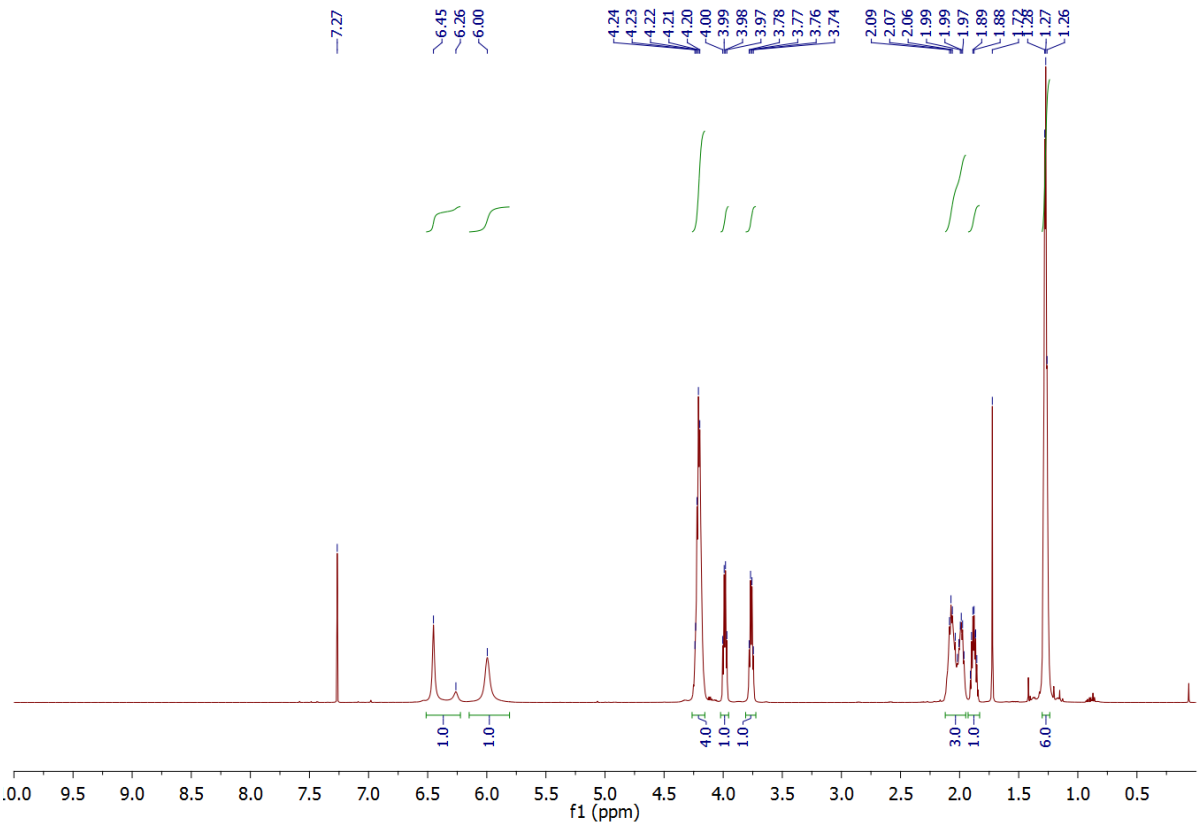
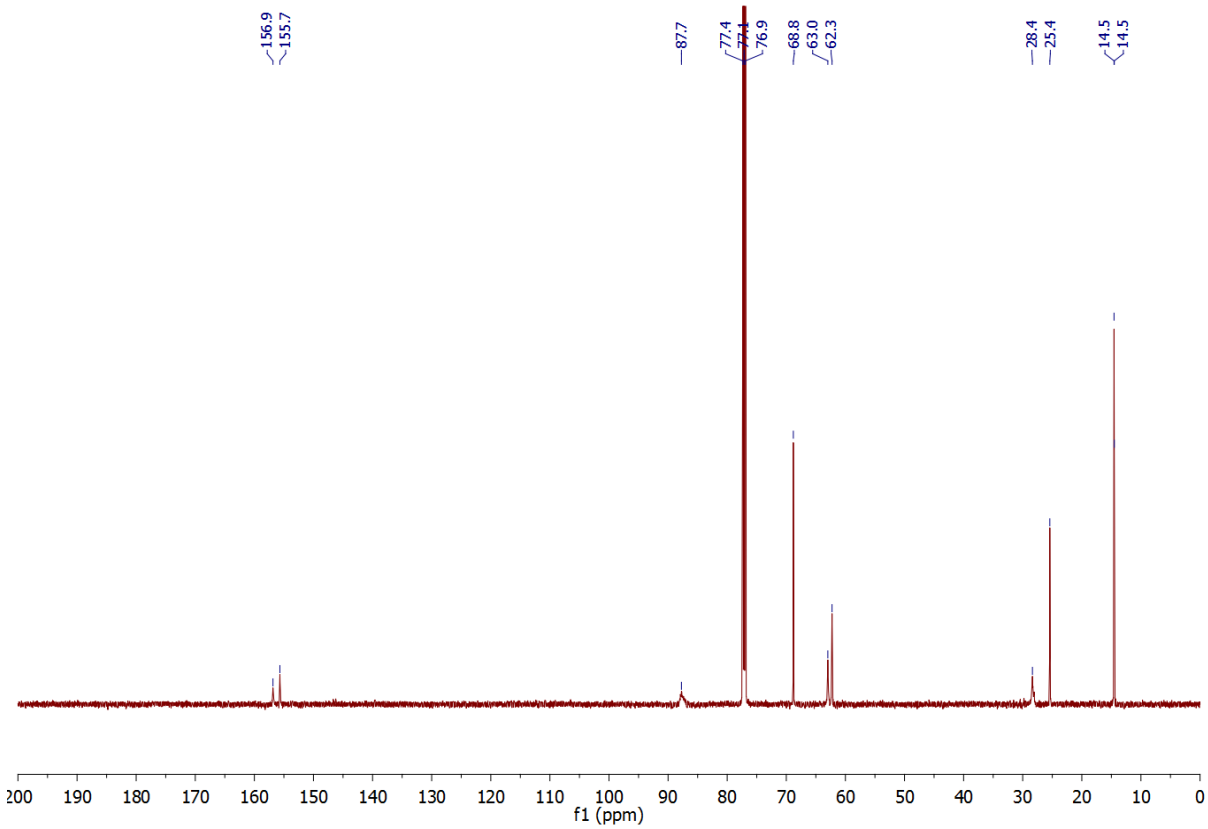
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Diethyl 1-(tetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate 6ad[2]



Compound prepared using HFIP as the reaction solvent and a reaction duration of 48 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diethyl 1-(tetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate as a clear oil (232 mg 0.940 mmol, 94%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.50-6.18 (m, NH, 1H), 6.12-5.87 (m, 1H), 4.25-4.19 (m, 4H), 3.99 (dt, *J* = 7.1, 7.1 Hz, 1H), 3.76 (dt, *J* = 7.1, 7.1 Hz, 1H), 2.09-1.94 (m, 3H), 1.91-1.84 (m, 1H), 1.30-1.24 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.9 (C), 155.7 (C), 87.7 (CH), 68.8 (CH_2), 63.0 (CH_2), 62.3 (CH_2), 28.4 (CH_2), 25.4 (CH_2), 14.5 (CH_3), 14.5 (CH_3); IR (thin film) 3282, 2982, 2972, 2875, 1718 cm^{-1}.

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63.0
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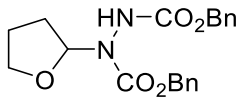
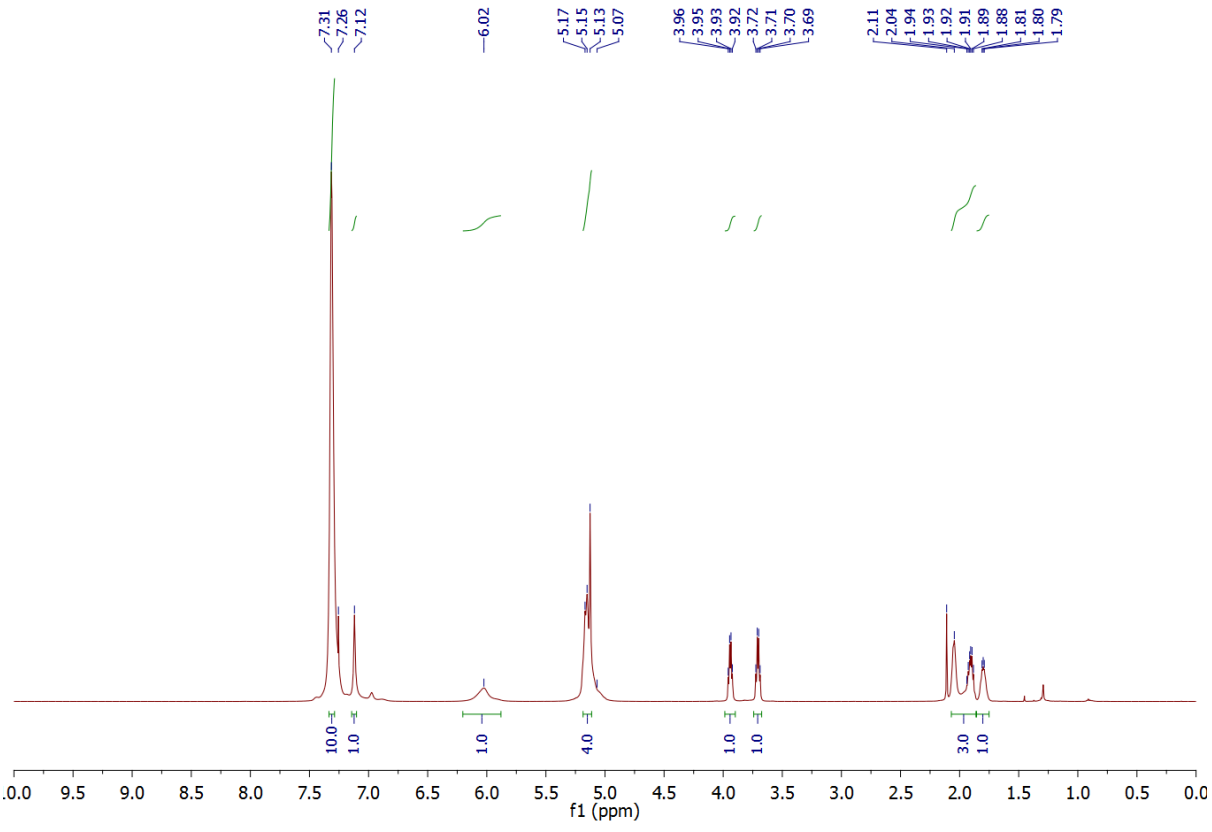
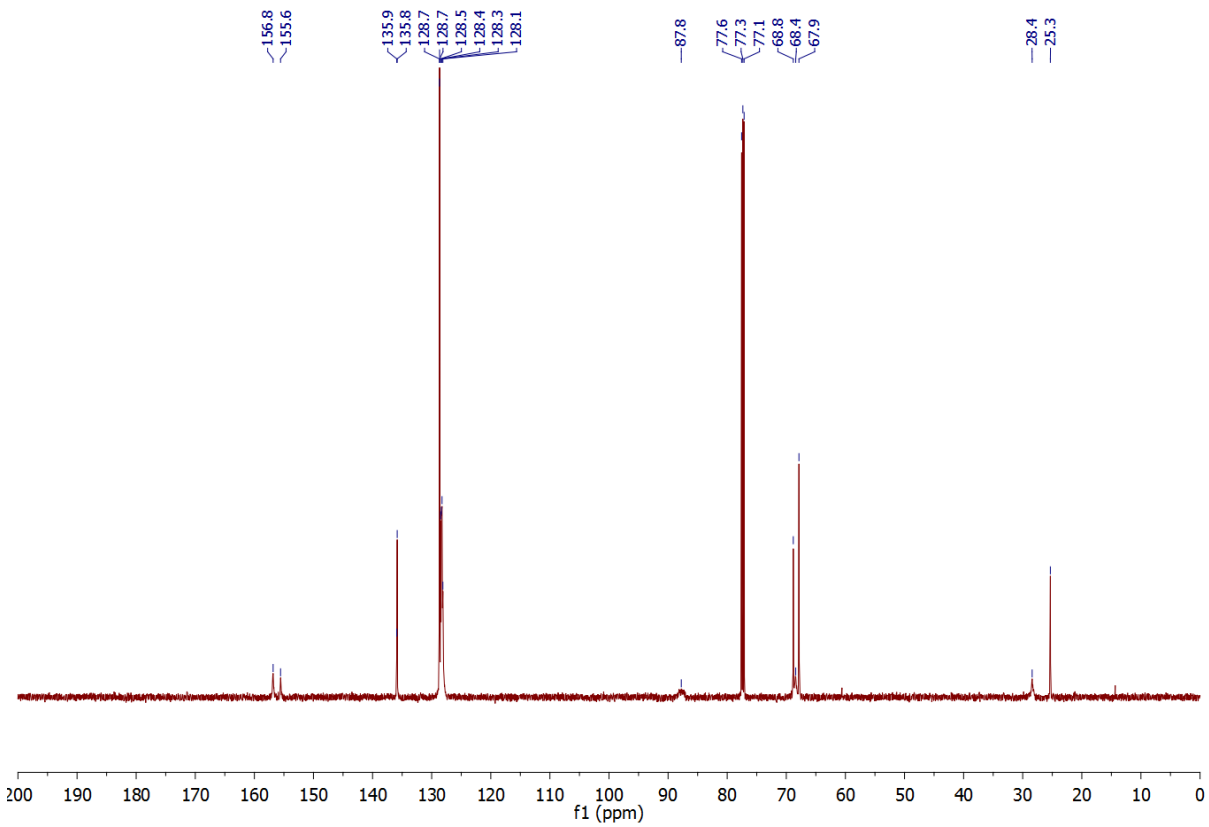
28.4
25.4
14.5
14.5
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Dibenzyl 1-(tetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate 6ae[2]



Compound prepared using HFIP as the reaction solvent and a reaction duration of 48 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded dibenzyl 1-(tetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate as a white solid (267 mg, 0.720 mmol, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.26 (m, 10H), 7.12 (br s, NH, 1H), 6.02 (s, 1H), 5.20-5.09 (m, 4H), 3.94 (dt, *J* = 7.1, 7.1 Hz, 1H), 3.71 (dt, *J* = 7.1, 7.1 Hz, 1H), 2.08-1.86 (m, 3H), 1.84-1.75 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.8 (C), 155.6 (C), 135.9 (C), 135.8 (C), 128.7 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 87.8 (CH), 68.8 (CH_2), 68.4 (CH_2), 67.9 (CH_2), 28.4 (CH_2), 25.3 (CH_3); IR (solid) 3287, 3067, 3034, 2970, 2894, 1742, 1706, 1686 cm^{-1}.

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135.8
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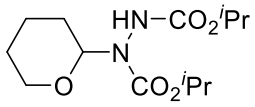
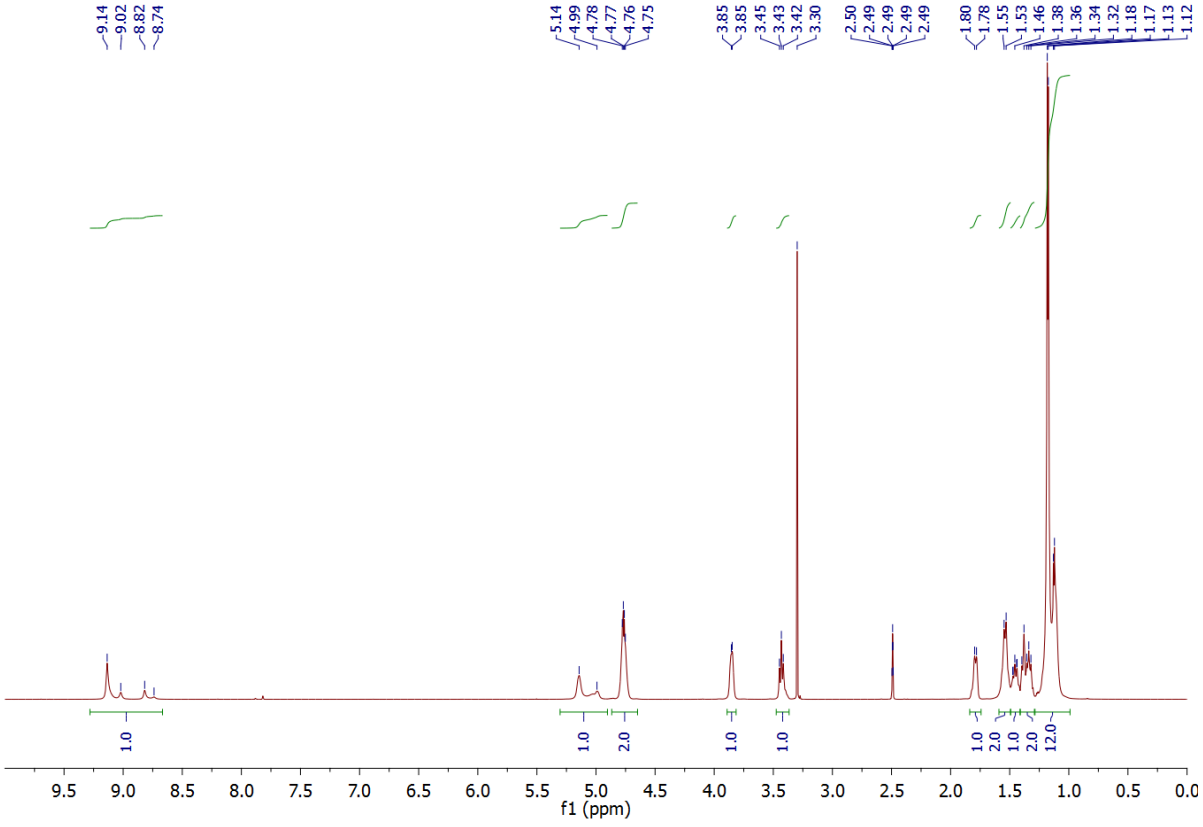
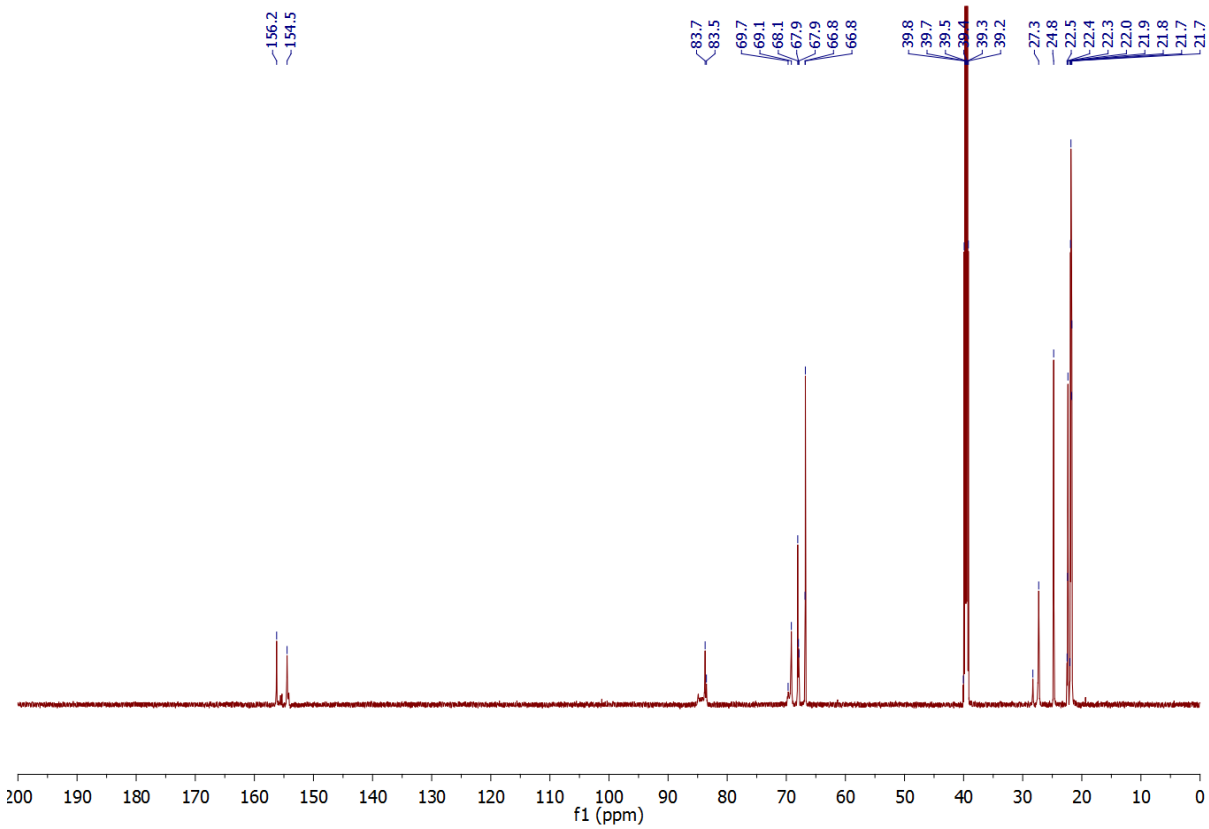
77.3
77.1
68.8
68.4
67.9
28.4
25.3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Diisopropyl 1-(tetrahydro-2*H*-pyran-2-yl)hydrazine-1,2-dicarboxylate 6bb



Compound prepared using HFIP as the reaction solvent and a reaction duration of 72 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(tetrahydro-2*H*-pyran-2-yl)hydrazine-1,2-dicarboxylate as a white solid (202 mg, 0.700 mmol, 70%). ^{1}H NMR (700 MHz, DMSO-d$_6$) δ 9.17-8.70 (m, NH, 1H), 5.18-4.95 (m, 1H), 4.81-4.72 (m, 2H), 3.88 (m, 1H), 3.46-3.38 (m, 1H), 1.83-1.75 (m, 1H), 1.59-1.50 (m, 2H), 1.59-1.41 (m, 1H), 1.40-1.28 (m, 2H), 1.26-1.02 (m, 12H); ^{13}C NMR (176 MHz, DMSO-d$_6$) δ 156.2 (C), 154.5 (C), 83.7 (CH), 83.5 (CH), 69.7 (CH), 69.1 (CH), 68.1 (CH_2), 67.9 (CH), 66.8 (CH_2), 66.8 (CH_2), 28.3 (CH_2), 27.3 (CH_2), 24.8 (CH_2) 22.5 (CH_2), 22.4 (CH_2), 22.3 (CH_2), 22.0 (CH_3), 21.9 (CH_3), 21.8 (CH_3), 21.7 (CH_3), 21.7 (CH_3); IR (solid) 3255, 2983, 2937, 2873, 1740, 1716 cm^{-1}. LRMS (ESI) 289 (100, [M+H]$^+$); HRMS (ESI) calcd for $C_{13}H_{25}N_2O_5$ [M+H]$^+$ 289.1938; observed 289.1941.




156.2
154.5
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83.5
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68.1
67.9
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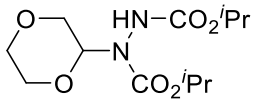
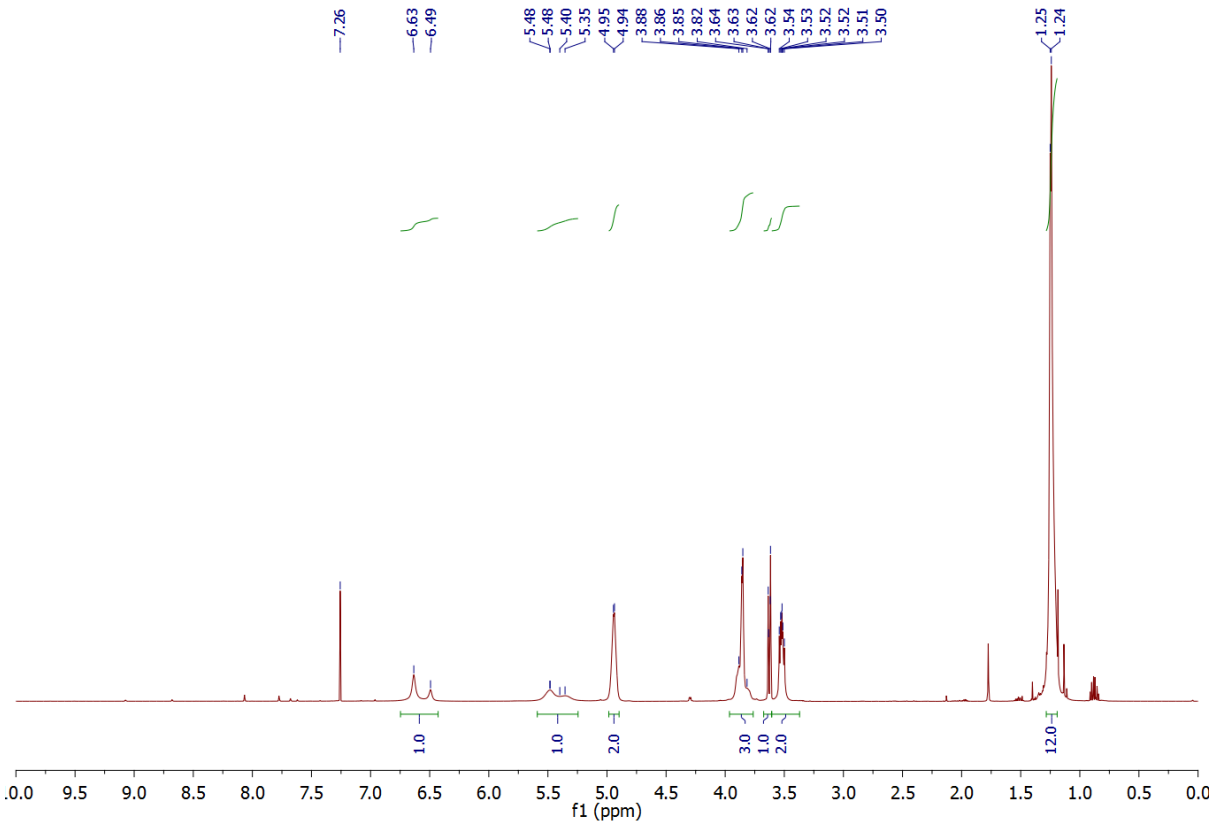
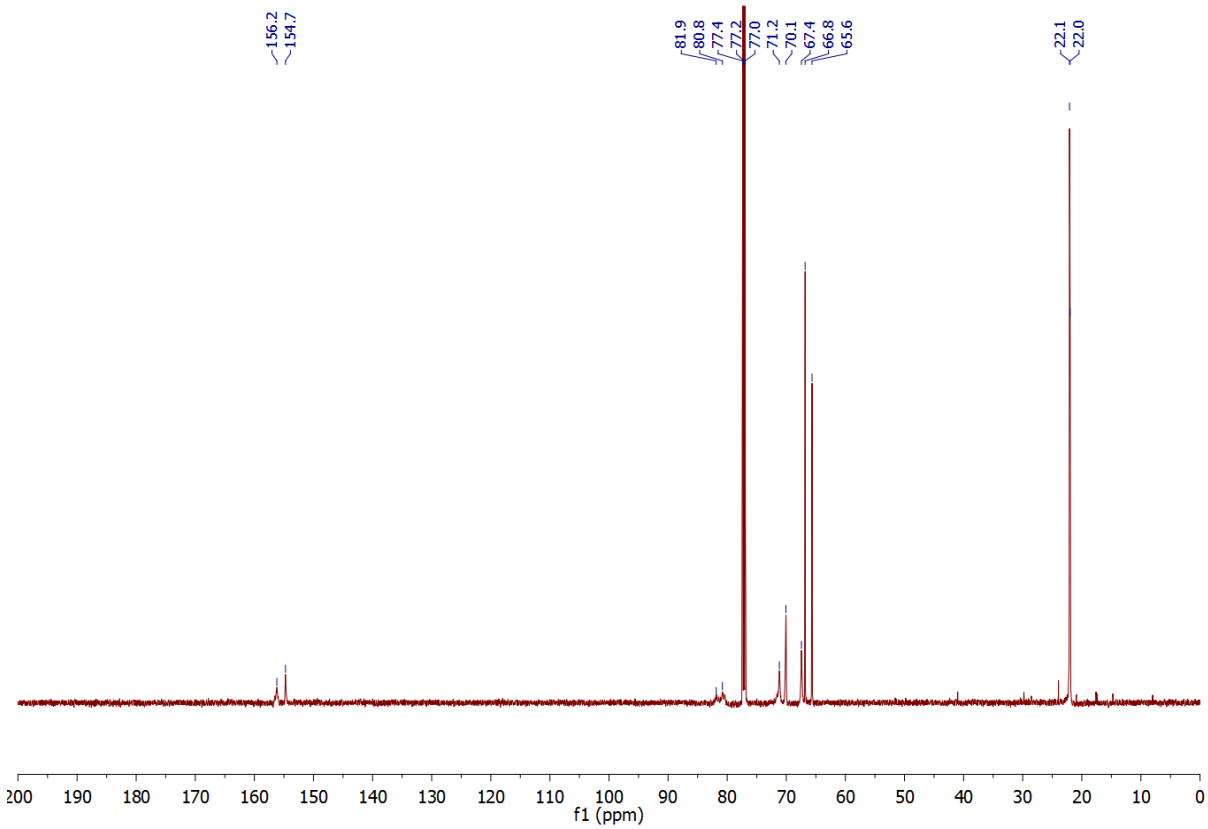
66.8
66.8
39.8
39.7
39.5
39.4
39.3
39.2
27.3
24.8
22.5
22.4
22.3
22.0
21.9
21.8
21.7
21.7
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Diisopropyl 1-(1,4-dioxan-2-yl)hydrazine-1,2-dicarboxylate 6cb[4]



Compound prepared using HFIP as the reaction solvent and a reaction duration of 72 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(1,4-dioxan-2-yl)hydrazine-1,2-dicarboxylate as a white solid (206 mg, 0.710 mmol, 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.75-6.45 (m, NH, 1H), 5.58-5.25 (m, 1H), 4.98-4.90 (m, 2H), 3.92-3.76 (m, 3H), 3.65-3.61 (m, 1H), 3.56-3.47 (m, 2H), 1.28 (d, *J* = 5.8 Hz, 12H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.2 (C), 154.7 (C), 81.9 (CH), 80.8 (CH), 71.2 (CH), 70.1 (CH), 67.4 (CH_2), 66.8 (CH_2), 65.6 (CH_2), 22.1 (CH_3), 22.0 (CH_3); IR (solid) 3264, 2980, 2936, 2873, 1735, 1716 cm^{-1}.

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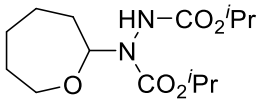
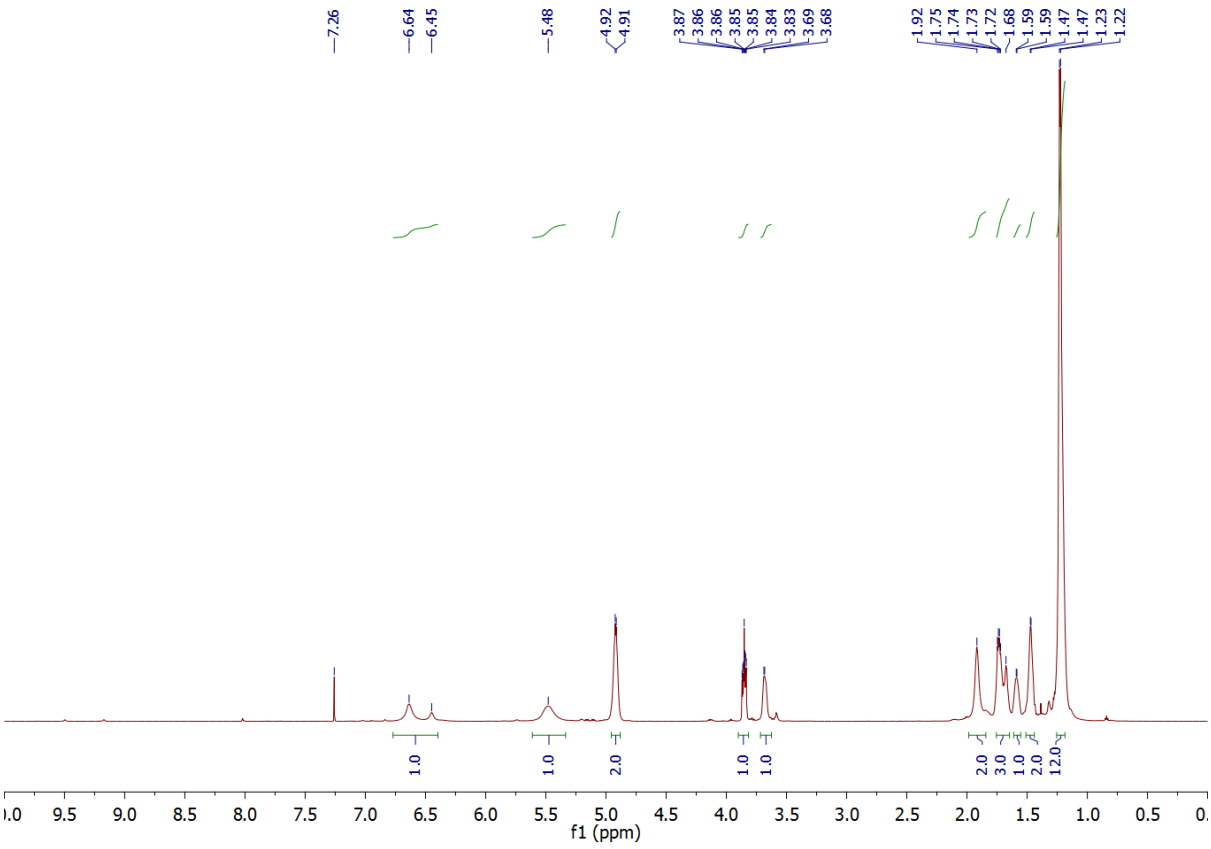
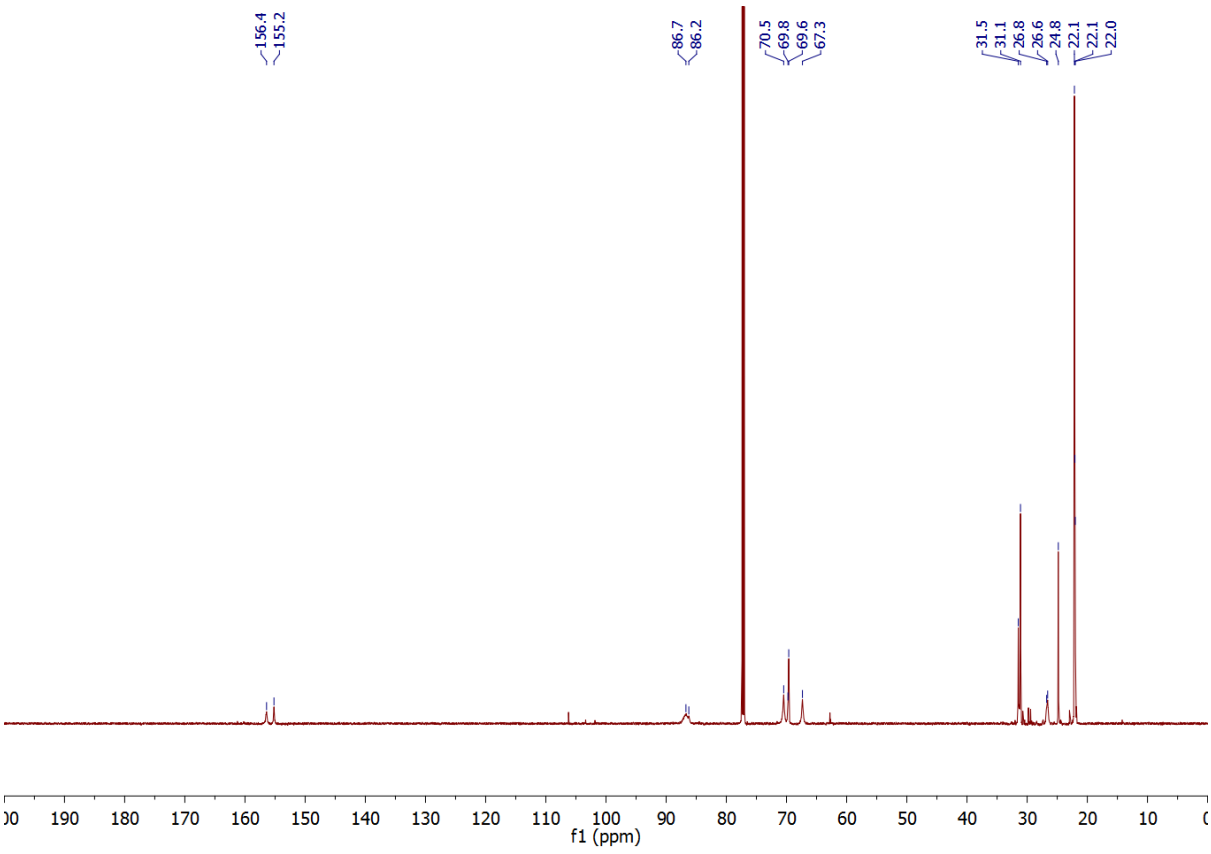
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Diisopropyl 1-(oxepan-2-yl)hydrazine-1,2-dicarboxylate 6db



Compound prepared using HFIP as the reaction solvent and a reaction duration of 96 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl diisopropyl 1-(oxepan-2-yl)hydrazine-1,2-dicarboxylate as a white solid (187 mg, 0.620 mmol, 62%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.76-6.40 (m, 1H), 5.60-5.35 (m, 1H), 4.97-4.87 (m, 2H), 3.88-3.82 (m, 1H), 3.71-3.63 (m, 1H), 1.98-1.85 (m, 2H), 1.75-1.65 (m, 3H), 1.51-1.44 (m, 2H), 1.25-1.18 (d, *J* = 5.9 Hz, 12H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.4 (C), 86.7 (CH), 86.2 (CH), 70.5 (CH), 69.8 (CH_2), 69.6 (CH), 67.3 (CH_2), 31.5 (CH_2), 31.1 (CH_2), 26.8 (CH_2), 26.8 (CH_2), 24.8 (CH_2), 22.1 (CH_3), 22.1 (CH_3), 22.0 (CH_3); IR (solid) 3293, 2979, 2928, 2863 1740, 1715 cm^{-1}. LRMS (ESI) 303 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{14}H_{27}N_2O_5$ $[M+H]^+$ 303.1915; observed 303.1918.

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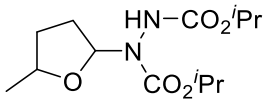
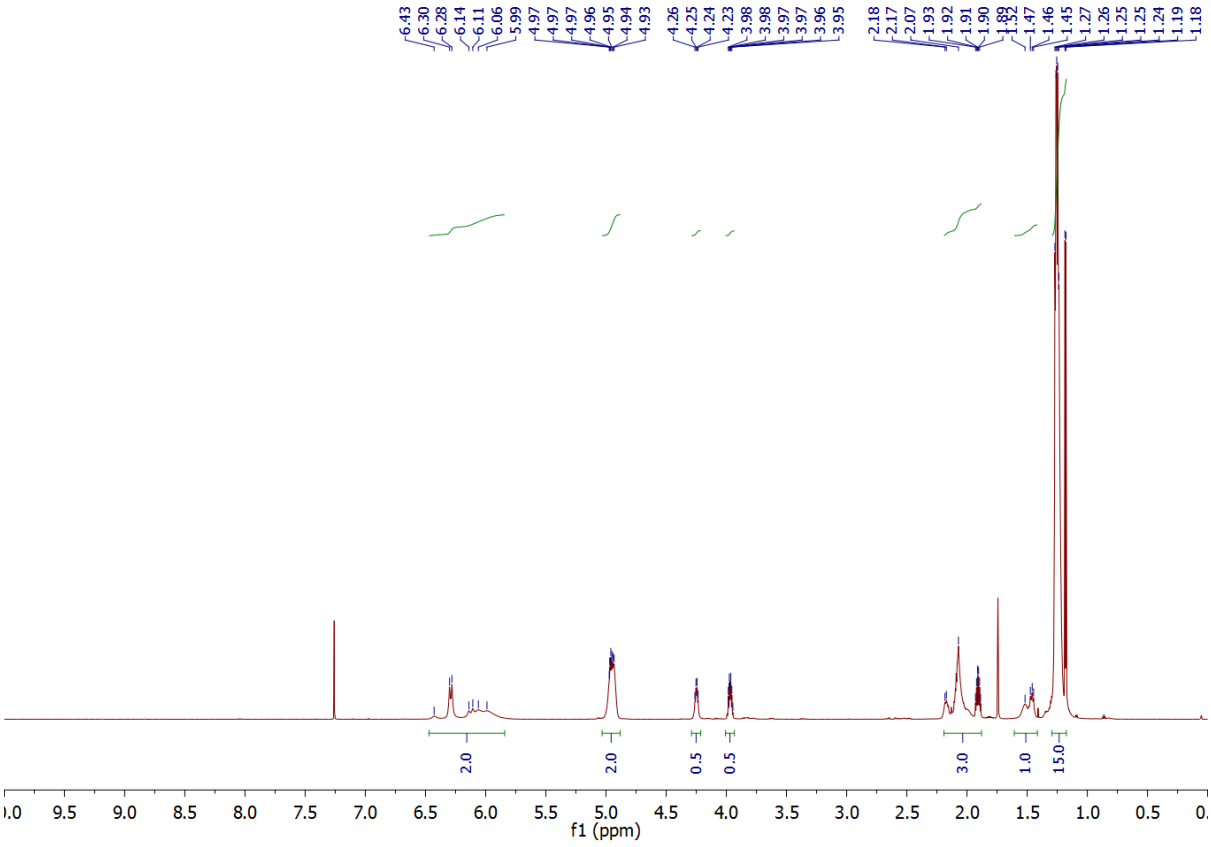
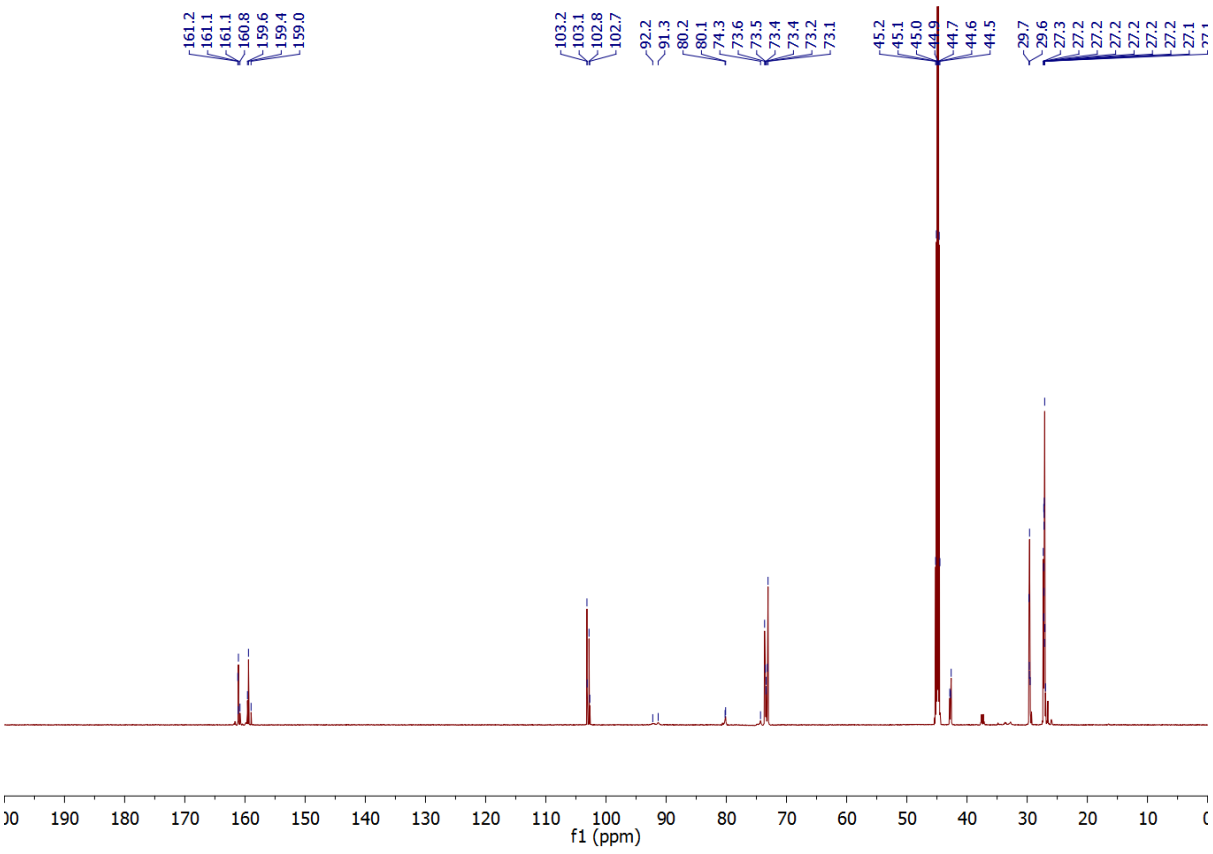
86.7
86.2
70.5
69.8
69.6
67.3
31.5
31.1
26.8
26.6
24.8
22.1
22.1
22.0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Diisopropyl 1-(5-methyltetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate 6eb

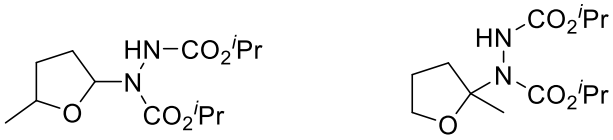


Compound prepared using HFIP as the reaction solvent and a reaction duration of 48 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(5-methyltetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate as a clear oil (58.0 mg, 0.200 mmol, 20%). ^{1}H NMR (700 MHz, $CDCl_3$, diastereomers (1:1)) δ 6.48-5.85 (m, 2H), 4.98-4.92 (m, 2H), 4.27-4.22 (m, 0.5H), 4.00-3.94 (m, 0.5H), 2.22-1.88 (m, 3H), 1.55-1.41 (m, 1H), 1.30-1.17 (m, 15H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 156.5 (C), 155.2 (C), 86.8 (CH), 70.6 (CH), 70.1 (CH), 70.0 (CH), 69.9 (CH), 69.8 (CH), 33.1 (CH_2), 32.5 (CH_2), 28.7 (CH_2), 22.2 (CH_3), 22.1 (CH_2) 22.1 (CH_3), 22.1 (CH_3), 22.0 (CH_3), 21.4 (CH_3), 21.0 (CH_3); IR (thin film) 3251, 2986, 2942, 2867, 1732, 1713 cm^{-1}. LRMS (ESI) 303 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{13}H_{25}N_2O_5$ $[M+H]^+$ 303.1915; observed 303.1918.

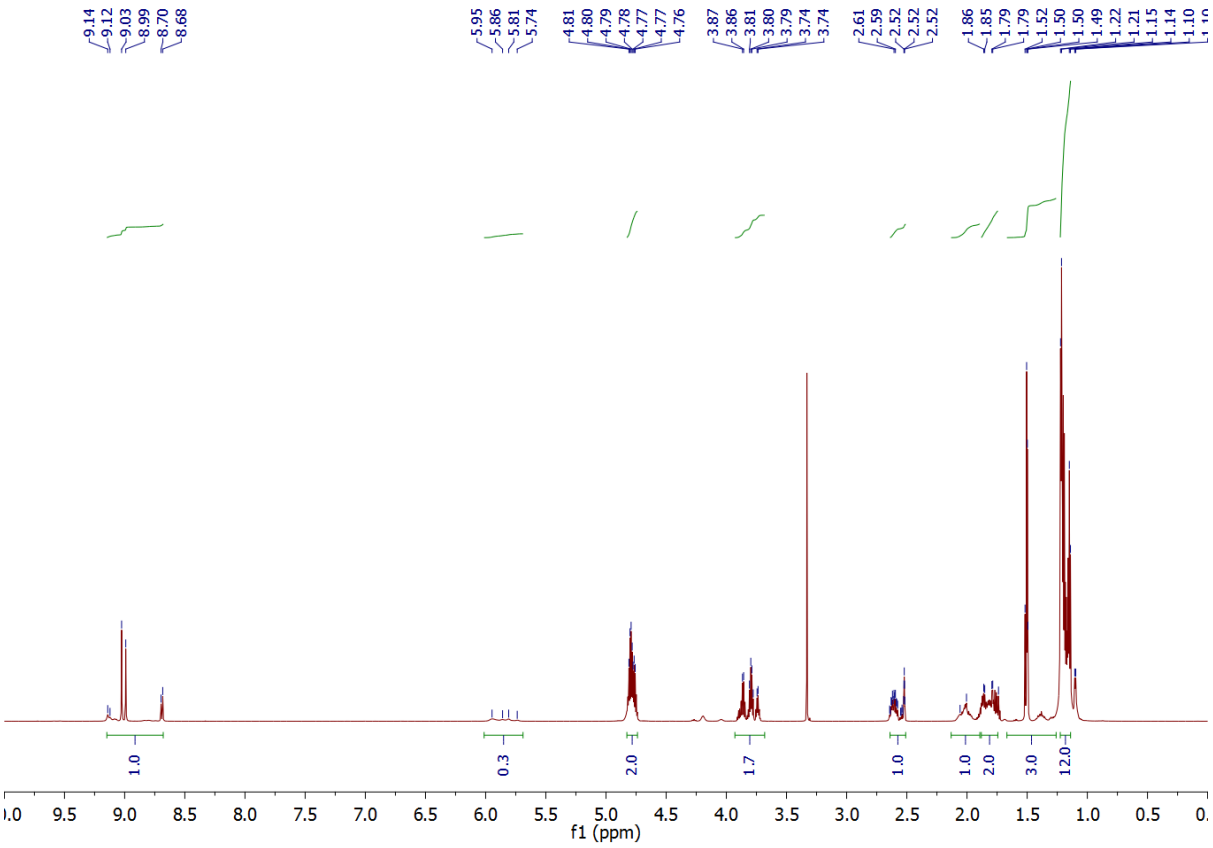


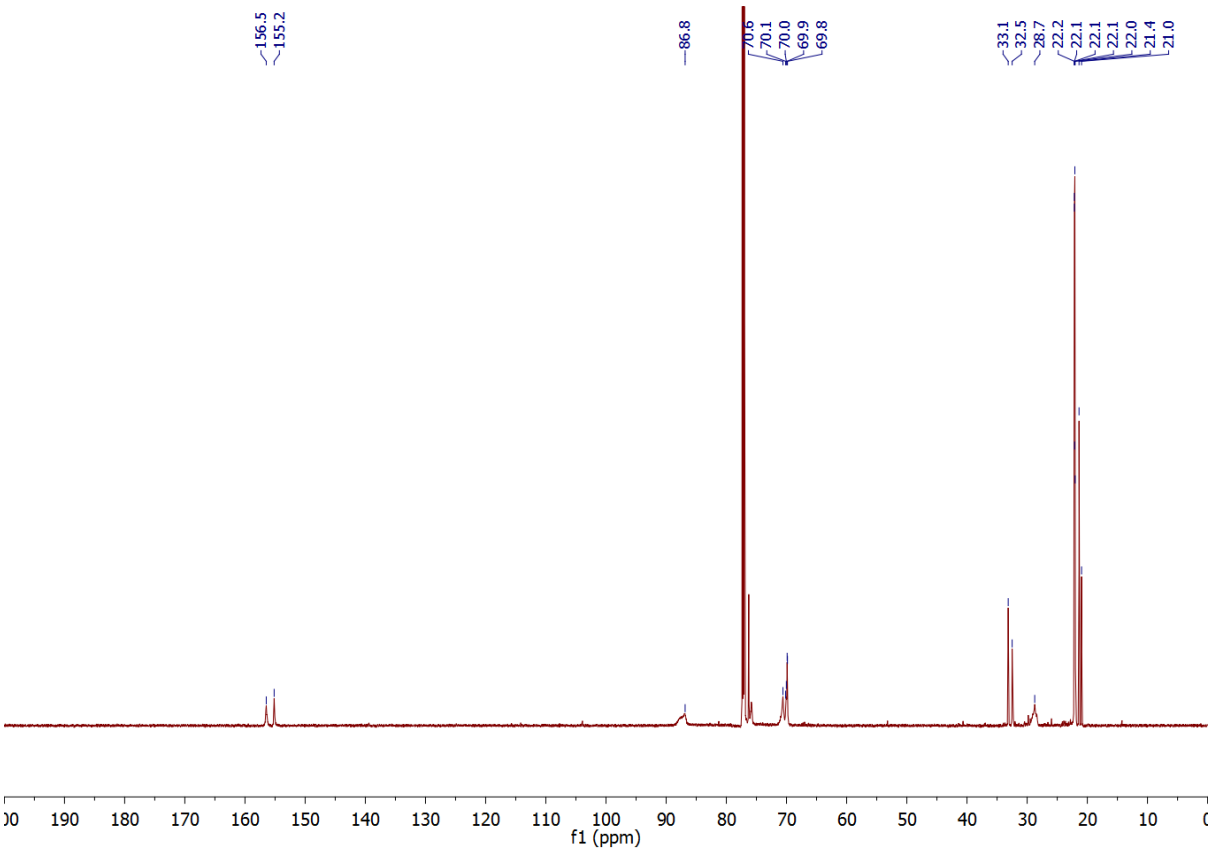

161.2
161.1
161.1
160.8
159.6
159.4
159.0
103.2
103.1
102.8
102.7
92.2
91.3
80.2
80.1
74.3
73.6
73.5
73.4
73.4
73.2
73.1
45.2
45.1
45.0
44.9
44.7
44.6
44.5
29.7
29.6
27.3
27.2
27.2
27.2
27.2
27.2
27.2
27.1
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

(30:70) Regioisomeric mixture of diisopropyl 1-(5-methyltetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate 6eb and diisopropyl 1-(2-methyltetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate 6fb

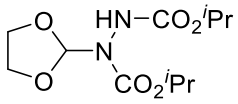


Compounds prepared without the use of fluorinated alcohol as the reaction solvent and a reaction duration of 48 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded an inseparable mixture of regioisomers diisopropyl 1-(5-methyltetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate **6eb** and diisopropyl 1-(2-methyltetrahydrofuran-2-yl)hydrazine-1,2-dicarboxylate **6fb** as a clear oil (196 mg, 0.68 mmol, 68%). ^{1}H NMR (700 MHz, DMSO-d_6, regioisomers (3:7) δ 9.14-8.68 (m, NH, 1H), 5.96-5.73 (m, 0.3H), 4.83-4.74 (m, 2H), 3.89-3.72 (m, 1.7H), 2.62-2.50 (m, 1H), 2.10-1.73 (m, 1H), 1.65-1.30 (m, 3H), 1.24-1.10 (m, 12H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 161.2 (C), 161.1 (C), 161.1 (C), 160.8 (C), 159.6 (C), 159.4 (C), 159.0 (C), 103.2 (C), 103.1 (C), 102.8 (C), 102.7 (C), 92.3 (CH), 91.3 (CH), 80.2 (CH), 80.1 (CH), 74.3 (CH_2), 73.6 (CH), 73.5 (CH), 73.4 (CH_2), 73.4 (CH), 73.2 (CH_2), 73.1 (CH_2), 42.9 (CH_2), 42.7 (CH_2), 42.6 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 27.3 (CH_2), 27.2 (CH_2), 27.2 (CH_2), 27.2 (CH_2), 27.2 (CH_2), 27.2 (CH_2), 27.2 (CH_2), 27.1 (CH_2), 27.1 (CH_2), 27.1 (CH_2), 27.1 (CH_2), 26.9 (CH_2);); IR (thin film) 3247, 2986, 2937, 2920, 2863, 1735, 1714 cm^{-1}.

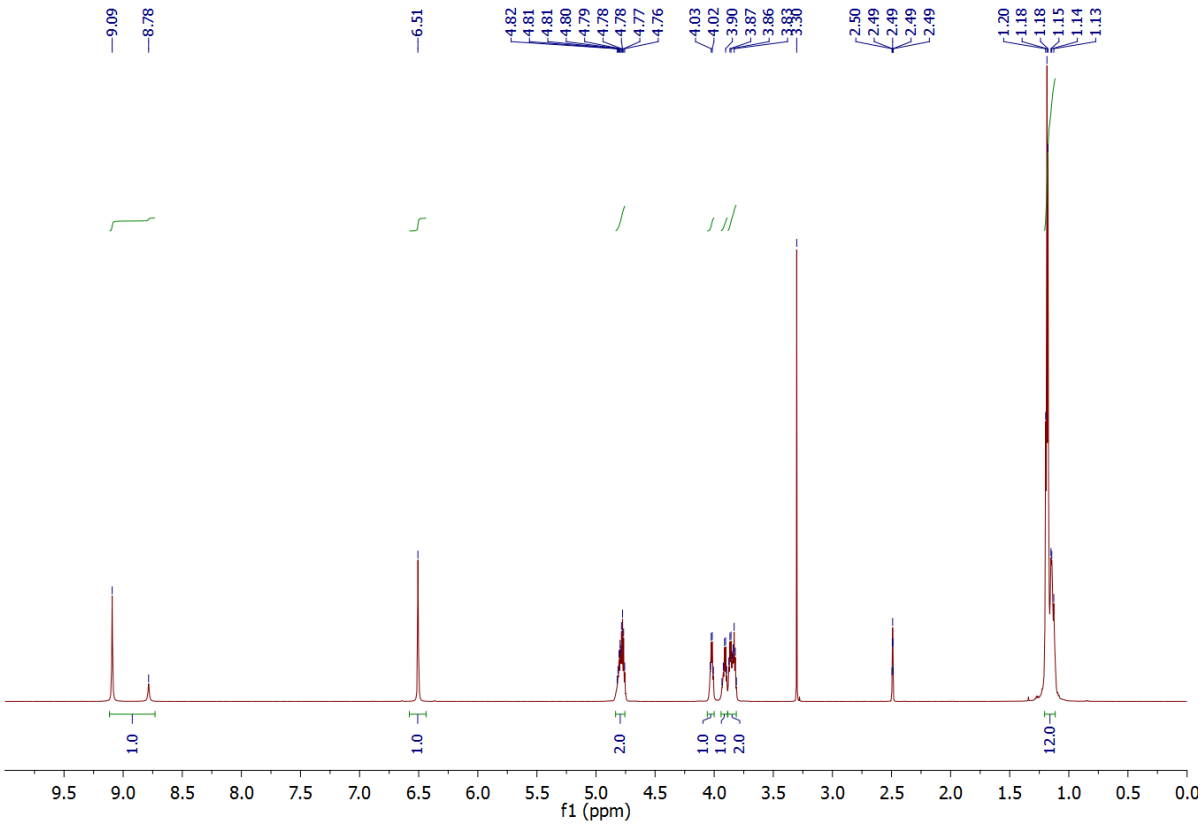

9.14
9.12
9.03
8.99
8.70
8.68
5.95
5.86
5.81
5.74
4.81
4.80
4.79
4.78
4.77
4.77
4.76
3.87
3.86
3.81
3.80
3.79
3.74
3.74
2.61
2.59
2.52
2.52
2.52
1.86
1.85
1.79
1.79
1.52
1.50
1.50
1.49
1.22
1.21
1.15
1.14
1.10
1.0
0.3
2.0
1.7
1.0
1.0
2.0
3.0
12.0
f1 (ppm)

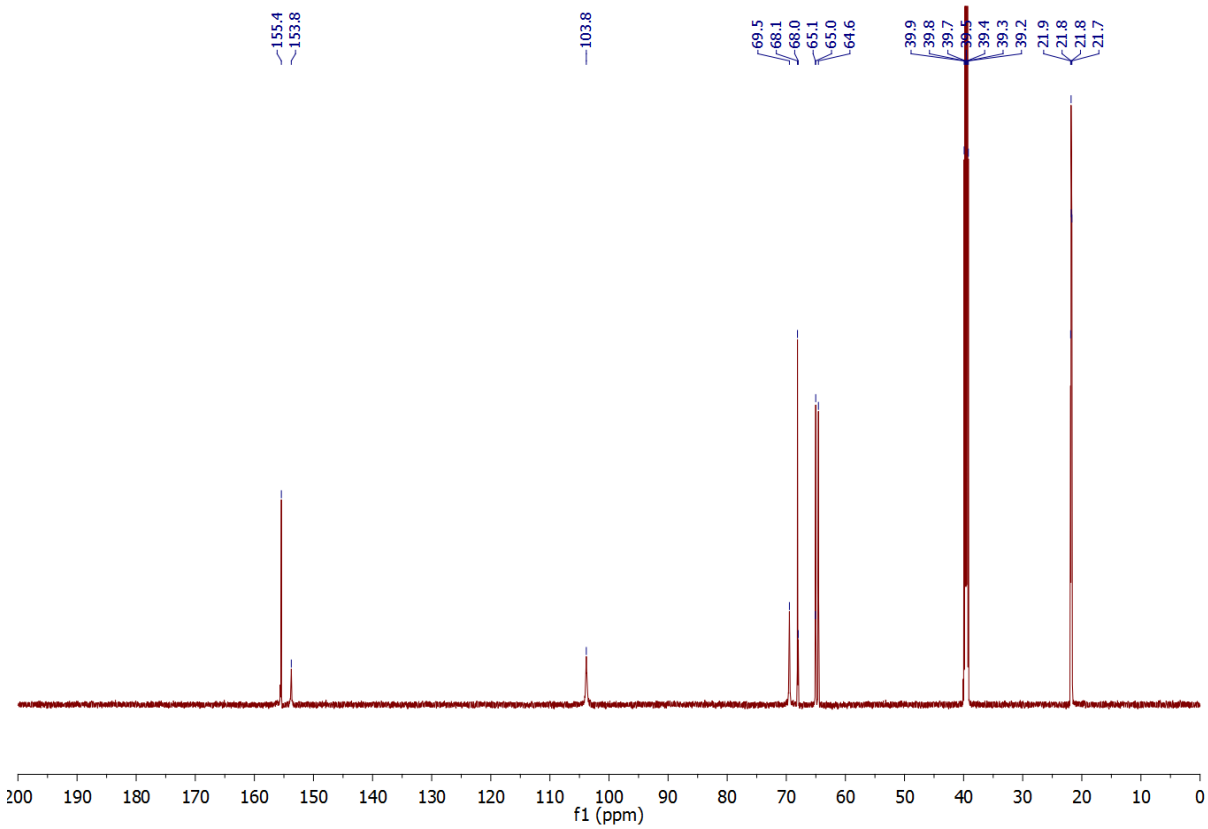

156.5
155.2
86.8
70.6
70.1
70.0
69.9
69.8
33.1
32.5
28.7
22.2
22.1
22.1
22.1
22.0
21.4
21.0
f1 (ppm)

Diisopropyl 1-(1,3-dioxolan-2-yl)hydrazine-1,2-dicarboxylate 6gb

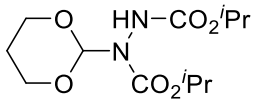


Compound prepared using HFIP as the reaction solvent and a reaction duration of 24 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(1,3-dioxolan-2-yl)hydrazine-1,2-dicarboxylate as a white solid (193 mg, 0.700 mmol, 70%). ^{1}H NMR (700 MHz, DMSO-d_6) δ 9.10-8.77 (m, NH, 1H), 6.51 (s, 1H), 4.84-4.75 (m, 2H), 4.02 (dt, *J* = 6.2, 6.2 Hz, 1H), 3.94-3.89 (m, 1H) 3.88-3.81 (m, 2H), 1.21-1.10 (m, 12H); ^{13}C NMR (176 MHz, DMSO-d_6) δ 155.4 (C), 153.8 (C), 103.8 (CH), 69.5 (CH), 68.1 (CH), 68.0 (CH), 65.1 (CH_2), 65.0 (CH_2), 64.6 (CH_2), 21.9 (CH_3), 21.8 (CH_3), 21.8 (CH_3), 21.7 (CH_3); IR (solid) 3271, 2986, 2937, 2909, 1748, 1691 cm^{-1}. LRMS (ESI) 277 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{11}H_{21}N_2O_6$ $[M+H]^+$ 277.1394; observed 277.1395.

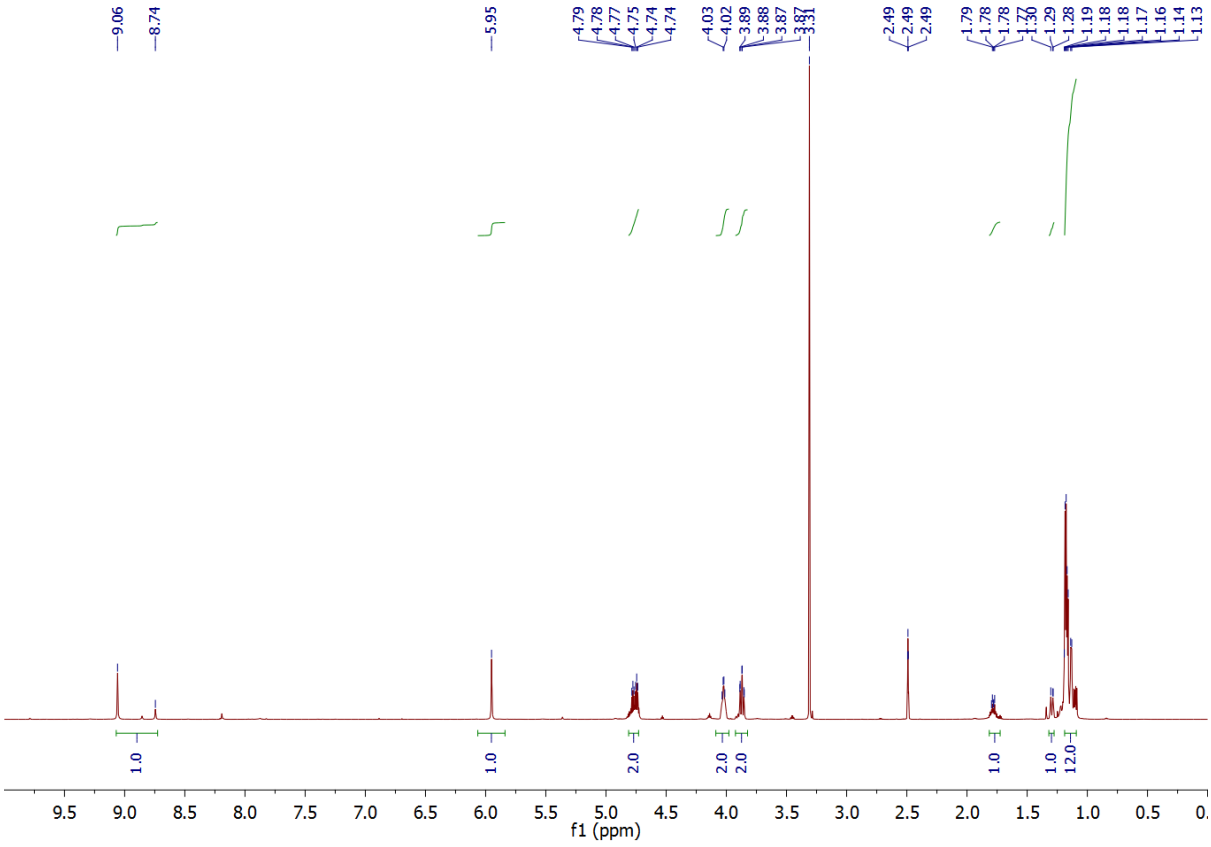


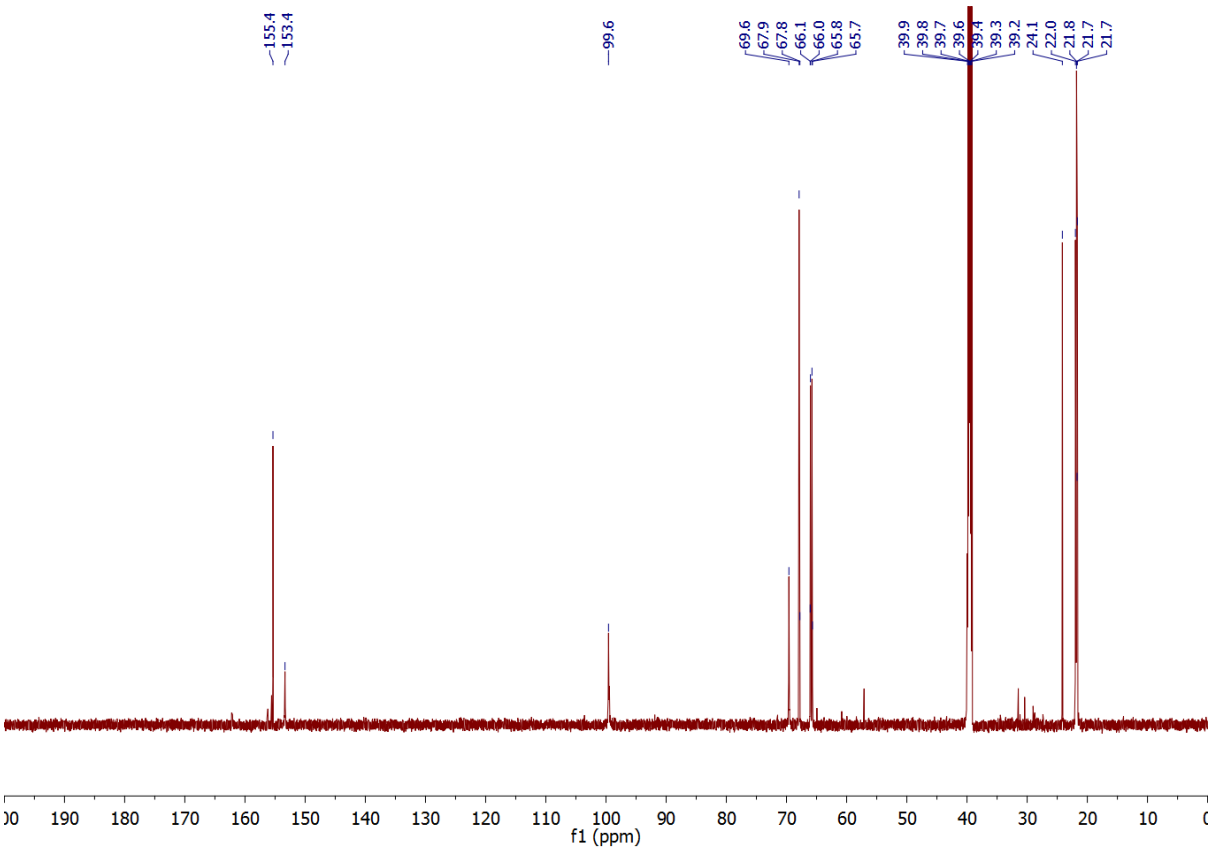

155.4
153.8
103.8
69.5
68.1
68.0
65.1
65.0
64.6
39.9
39.8
39.7
39.5
39.4
39.3
39.2
21.9
21.8
21.8
21.7
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Diisopropyl 1-(1,3-dioxan-2-yl)hydrazine-1,2-dicarboxylate 6hb

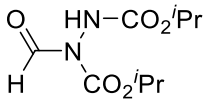


Compound prepared using HFIP as the reaction solvent and a reaction duration of 24 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(1,3-dioxan-2-yl)hydrazine-1,2-dicarboxylate as a white solid (171 mg, 0.590 mmol, 59%). ^{1}H NMR (700 MHz, DMSO-d_6) δ 9.08-8.72 (m, NH, 1H), 5.95 (s, 1H), 4.82-4.71 (m, 2H), 4.02 (dd, *J* = 5.8, 5.1 Hz, 2H), 3.92-3.84 (m, 2H), 1.81-1.72 (m, 1H), 1.32-1.27 (m, 1H), 1.19-1.08 (m, 12H); ^{13}C NMR (176 MHz, DMSO-d_6) δ 155.4 (C), 153.4 (C), 99.6 (CH), 69.6 (CH), 67.9 (CH_2), 67.8 (CH), 66.1 (CH_2), 66.0 (CH_2), 65.8 (CH_2), 65.7 (CH_2), 24.1 (CH_2), 22.0 (CH_3), 21.8 (CH_3), 21.7 (CH_3), 21.7 (CH_3); IR (solid) 3269, 2982, 2943, 2901, 1740, 1698 cm^{-1}. LRMS (ESI) 291 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{12}H_{23}N_2O_6$ $[M+H]^+$ 291.1551; observed 291.1555.

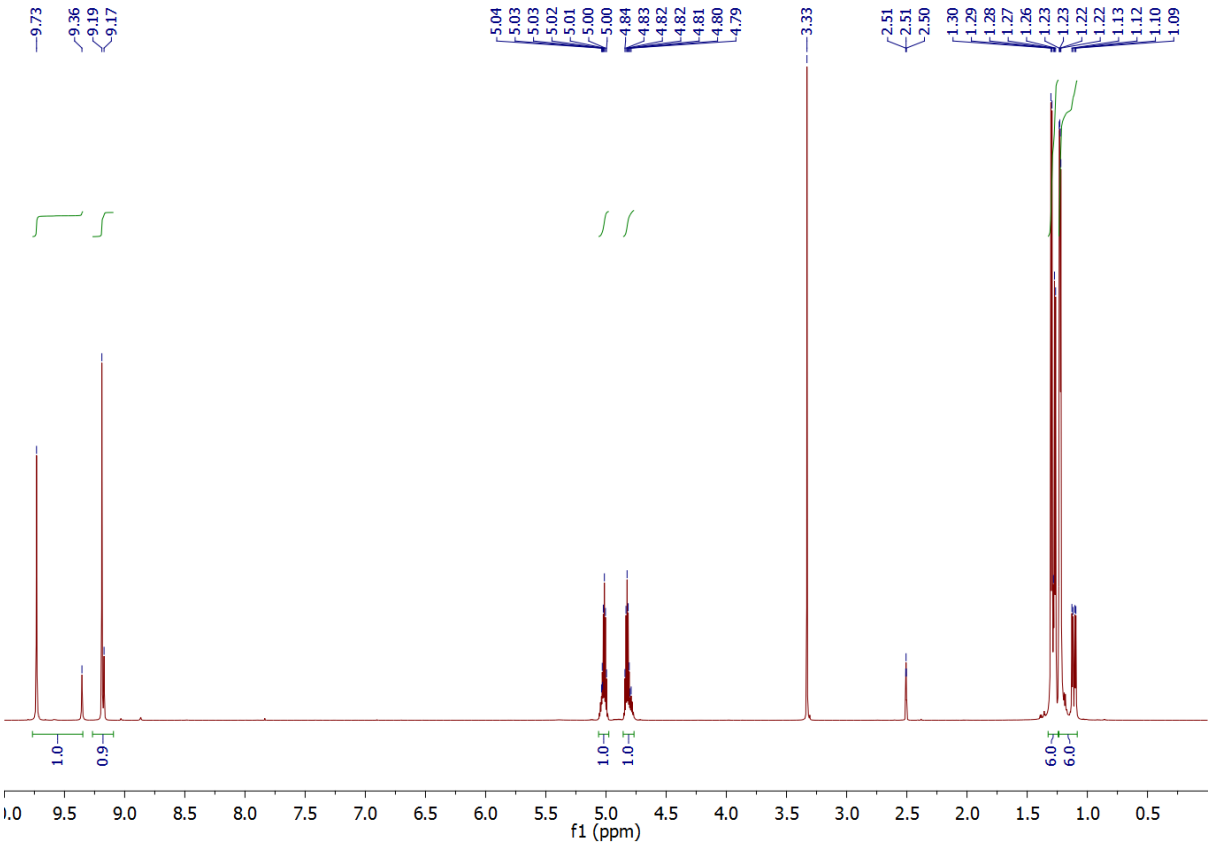


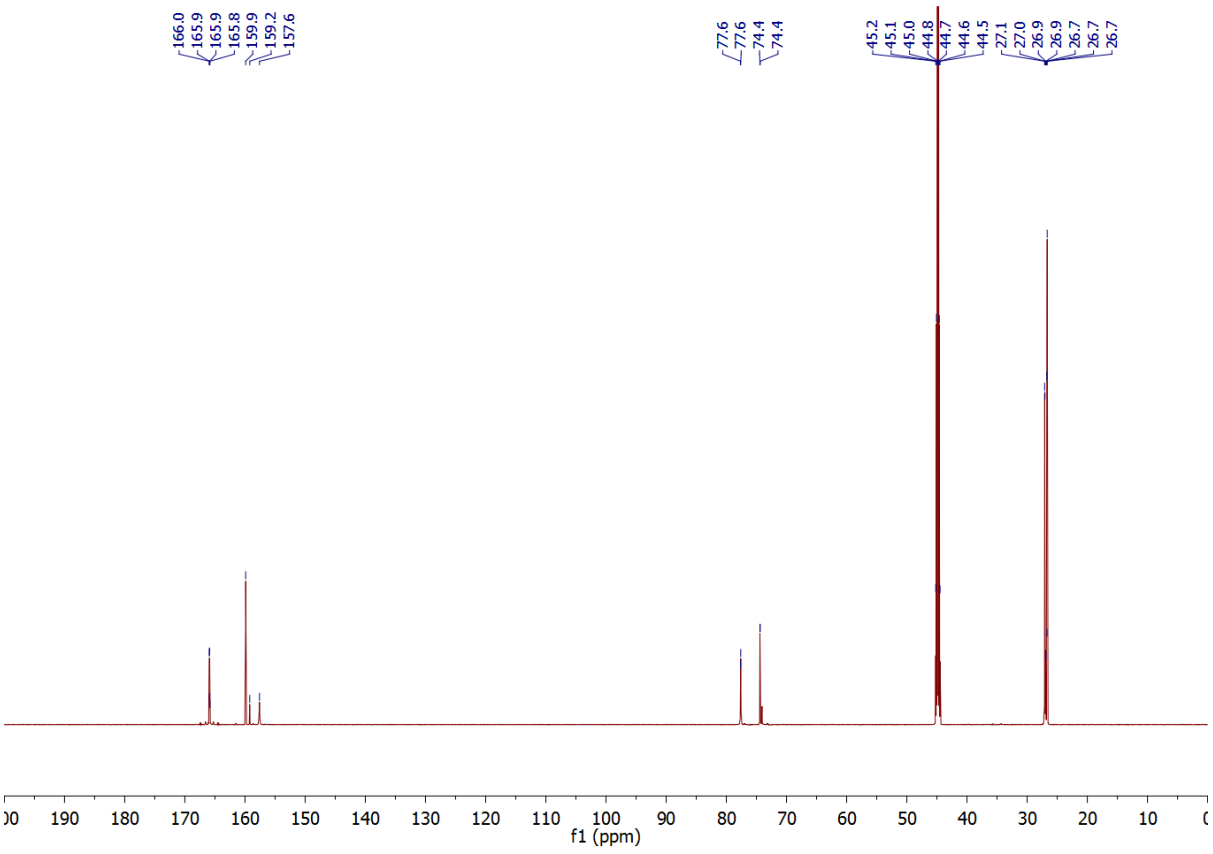

155.4
153.4
99.6
69.6
67.9
67.8
66.1
66.0
65.8
65.7
39.9
39.8
39.7
39.6
39.4
39.3
39.2
24.1
22.0
21.8
21.7
21.7
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Diisopropyl 1-benzoylhydrazine-1,2-dicarboxylatedicarboxylate 6ib

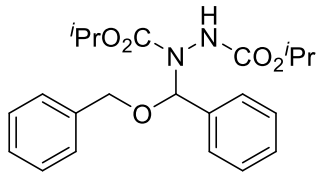


Compound prepared using TFE as the reaction solvent and a reaction duration of 24 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-formylhydrazine-1,2-dicarboxylate as a clear oil (144 mg, 0.620 mmol, 62%). ^{1}H NMR (700 MHz, DMSO-d_6) δ 9.74-9.35 (m, 1H), 9.20-9.16 (m, NH, 1H), 5.06-4.99 (m, 1H), 4.85-4.77 (m, 1H), 1.32-1.25 (m, 6H), 1.23-1.07 (m, 6H); ^{13}C NMR (176 MHz, DMSO-d_6) δ 166.0 (C), 165.9 (C), 165.9 (C), 165.8 (C), 159.9 (C), 159.2 (C), 157.6 (C), 77.6 (CH), 77.6 (CH), 74.4 (CH), 74.4 (CH), 27.1 (CH_3), 27.0 (CH_3), 26.9 (CH_3), 26.9 (CH_3), 26.7 (CH_3), 26.7 (CH_3), 26.7 (CH_3); IR (thin film) 3308, 2981, 2934, 2857, 1730, 1687 cm^{-1}. LRMS (ESI) 233 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_9H_{17}N_2O_5$ $[M+H]^+$ 233.1132; observed 233.1134.

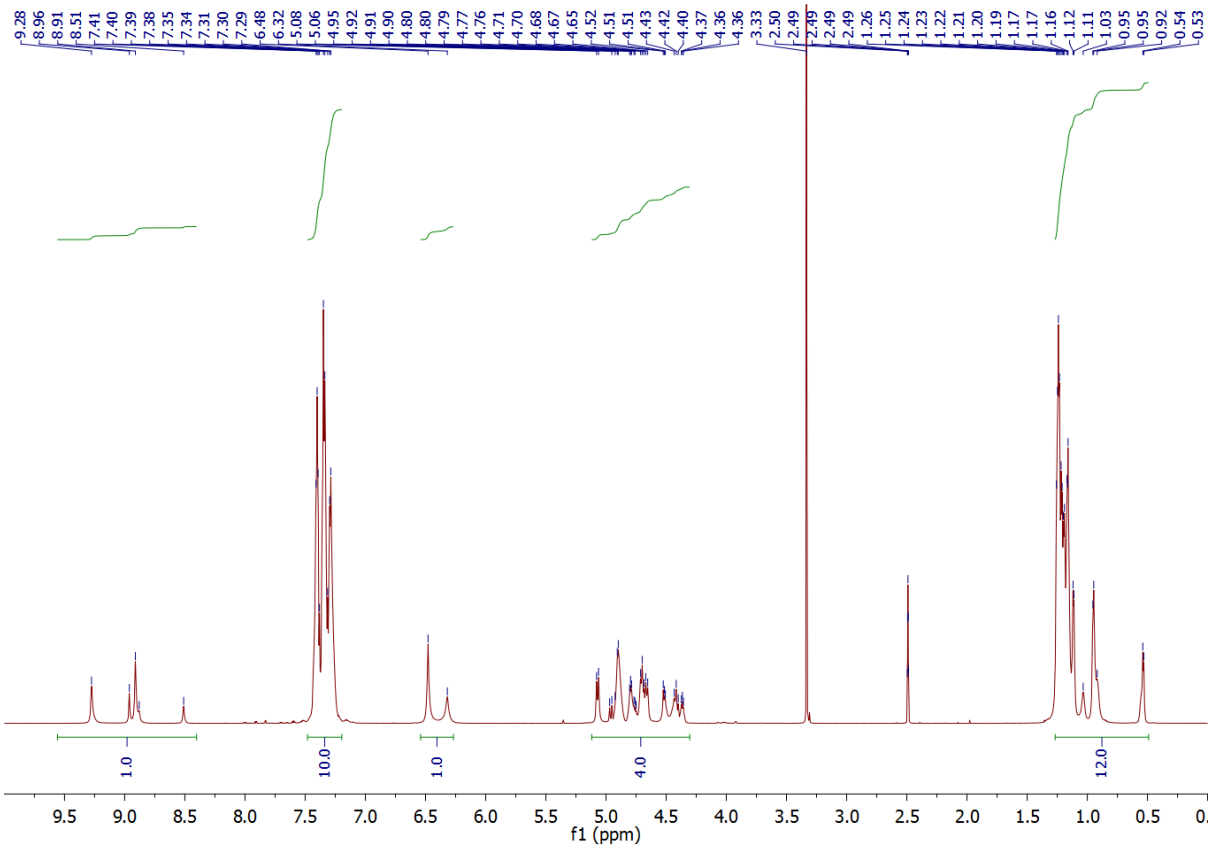



166.0
165.9
165.9
165.8
159.9
159.2
157.6
77.6
77.6
74.4
74.4
45.2
45.1
45.0
44.8
44.7
44.6
44.5
27.1
27.0
26.9
26.9
26.7
26.7
26.7
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Diisopropyl 1-((benzyloxy)(phenyl)methyl)hydrazine-1,2-dicarboxylate 6kb



Compound prepared using HFIP as the reaction solvent and a reaction duration of 72 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-((benzyloxy)(phenyl)methyl)hydrazine-1,2-dicarboxylate as a white solid (252 mg, 0.630 mmol, 63%). ^{1}H NMR (700 MHz, DMSO-d_6, 21 °C) δ 9.29-8.50 (m, NH, 1H), 7.43-7.20 (m, 10H), 6.50-6.25 (m, 1H), 5.10-4.30 (m, 4H), 1.27-0.52 (m, 12H); ^{13}C NMR (176 MHz, DMSO-d_6, 21 °C) δ 156.4 (C), 155.9 (C), 155.7 (C), 155.5 (C), 155.0 (C), 154.9 (C), 154.5 (C), 138.3 (C), 137.8 (C), 137.6 (C), 137.0 (C), 128.2 (CH), 128.1 (CH), 128.0 (CH), 128.0 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.2 (CH), 127.1 (CH), 127.0, (CH), 126.6 (CH), 85.5 (CH), 85.2 (CH), 84.8 (CH), 84.7 (CH), 69.9 (CH), 69.5 (CH), 68.9 (CH), 68.2 (CH), 67.8 (CH), 67.6 (CH), 21.9 (CH_3), 21.9 (CH_3), 21.8 (CH_3), 21.7 (CH_3), 21.7 (CH_3), 20.8 (CH_3); ^{1}H NMR (400 MHz, DMSO-d_6, 120 °C) δ 8.43 (br s, NH, 1H), 7.45-7.40 (m, 4H), 7.38-7.27 (m, 6H), 6.44 (s, 1H), 5.00-4.88 (m, 2H), 4.72-4.66 (m, 2H), 1.30-1.22 (m, 6H), 1.15-0.98 (m, 6H); ^{13}C NMR (101 MHz, DMSO-d_6, 120 °C) δ 156.1 (C), 155.7 (C), 138.7 (C), 137.0 (C), 128.6 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.8 (CH), 127.4 (CH), 87.0 (CH), 70.3 (CH), 68.6 (CH), 22.1 (CH_3), 22.0 (CH_3); IR (solid) 3282, 2984, 2937, 1742, 1699, 1681, 1650 cm^{-1}. LRMS (ESI) 401 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{22}H_{29}N_2O_5$ $[M+H]^+$ 401.2071; observed 401.2076.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7.35
7.34
7.31
7.30
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6.48
6.32
5.08
5.06
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4.92
4.91
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1.24
1.23
1.22
1.21
1.20
1.19
1.17
1.17
1.16
1.12
1.11
1.03
0.95
0.95
0.92
0.54
0.53
1.0
10.0
1.0
4.0
12.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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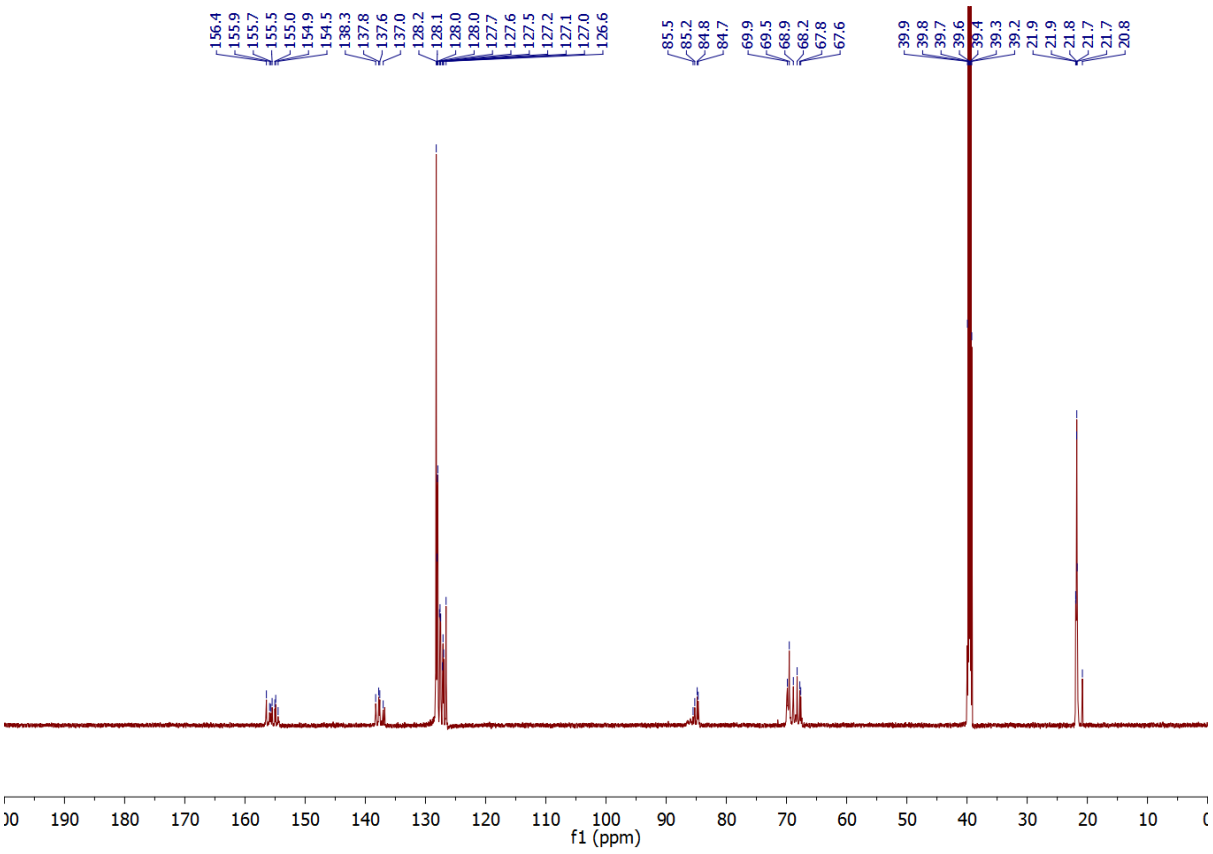
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


156.4
155.9
155.7
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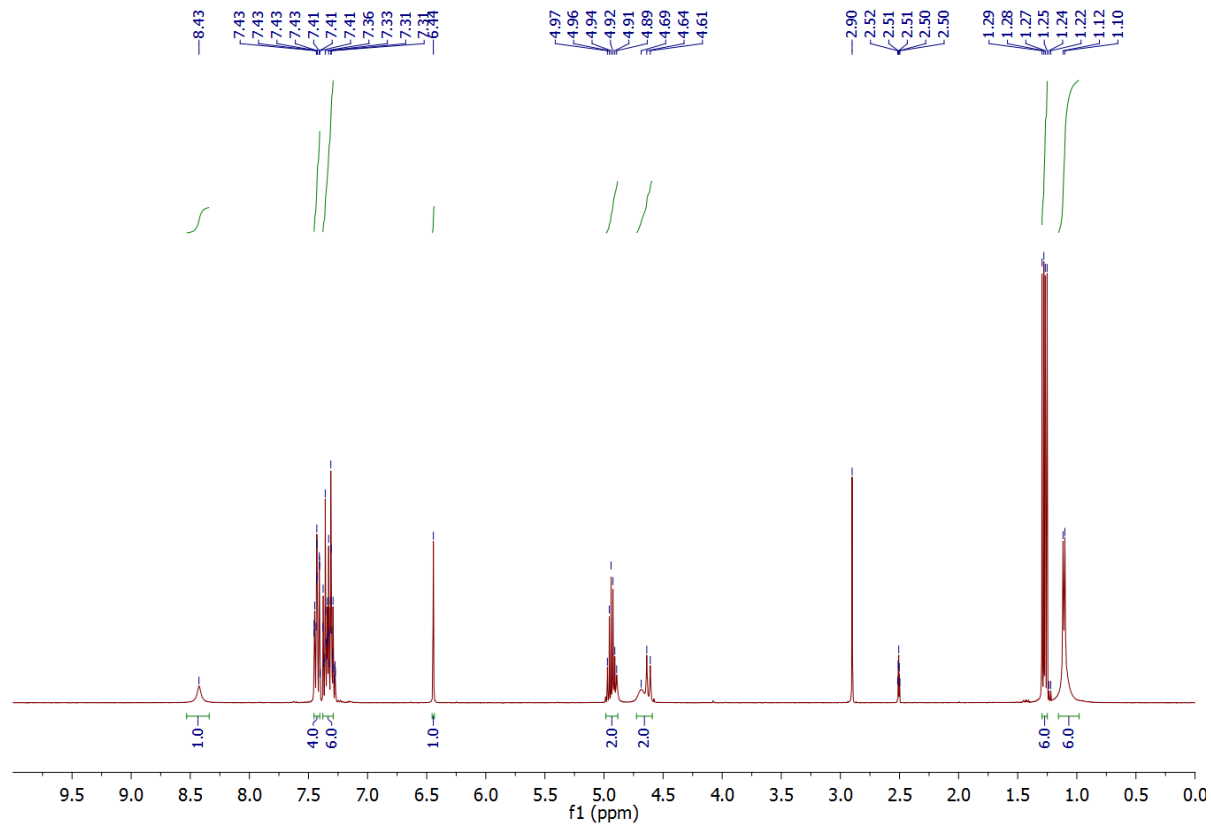
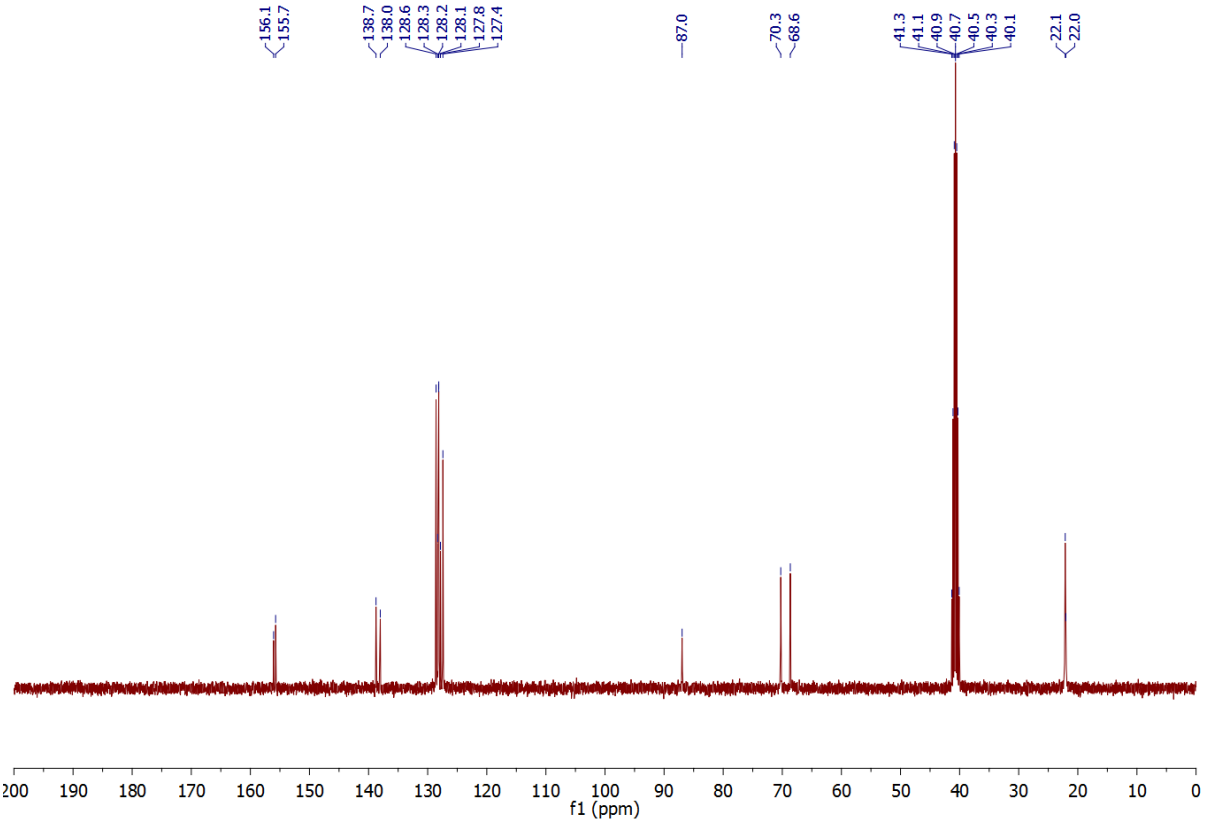
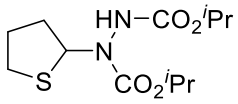
155.0
154.9
154.5
138.3
137.8
137.6
137.0
128.2
128.1
128.0
128.0
127.7
127.6
127.5
127.2
127.1
127.0
126.6
85.5
85.2
84.8
84.7
69.9
69.5
68.9
68.2
67.8
67.6
39.9
39.8
39.7
39.6
39.4
39.3
39.2
21.9
21.9
21.8
21.7
21.7
20.8
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

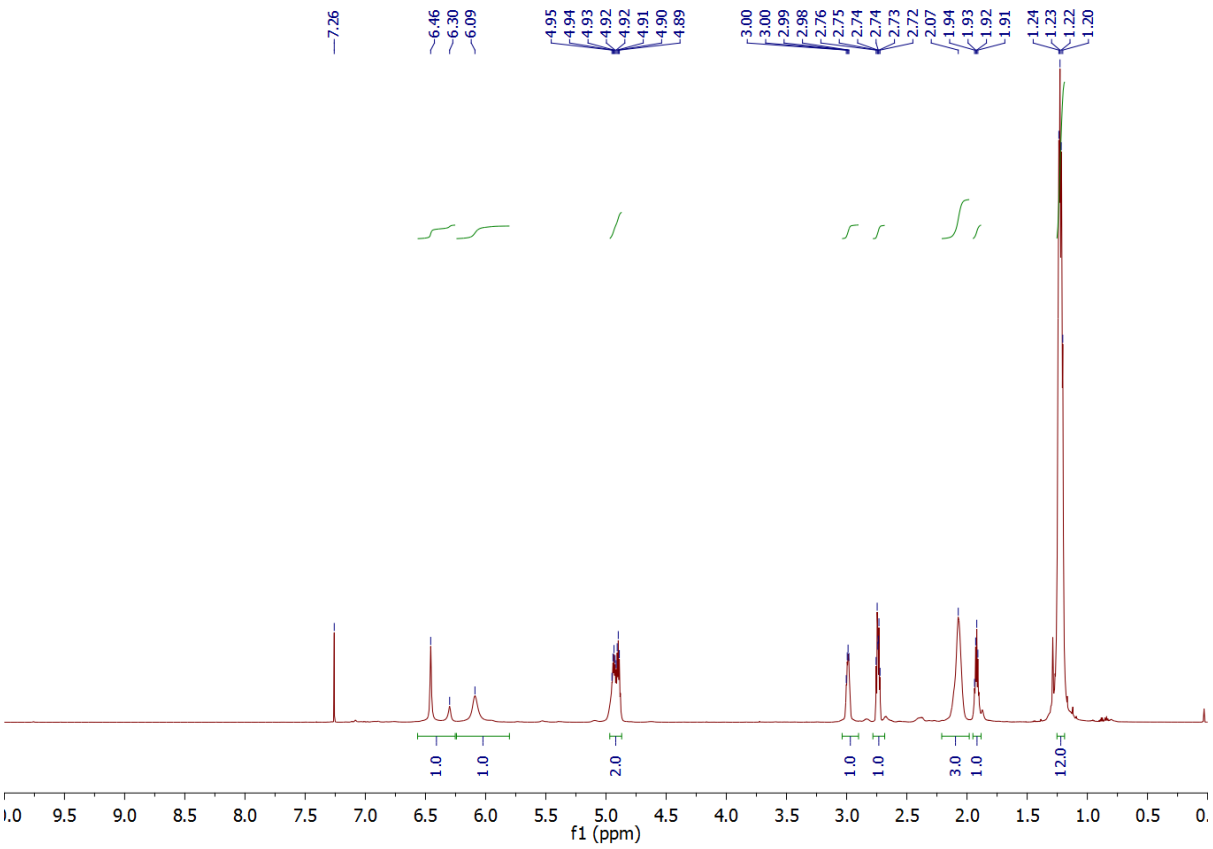

8.43
7.43
7.43
7.43
7.43
7.41
7.41
7.41
7.36
7.33
7.31
7.31
6.44
4.97
4.96
4.94
4.92
4.91
4.89
4.69
4.64
4.61
2.90
2.52
2.51
2.51
2.50
2.50
1.29
1.28
1.27
1.25
1.24
1.22
1.12
1.10
1.0
4.0
6.0
1.0
2.0
2.0
6.0
6.0
f1 (ppm)

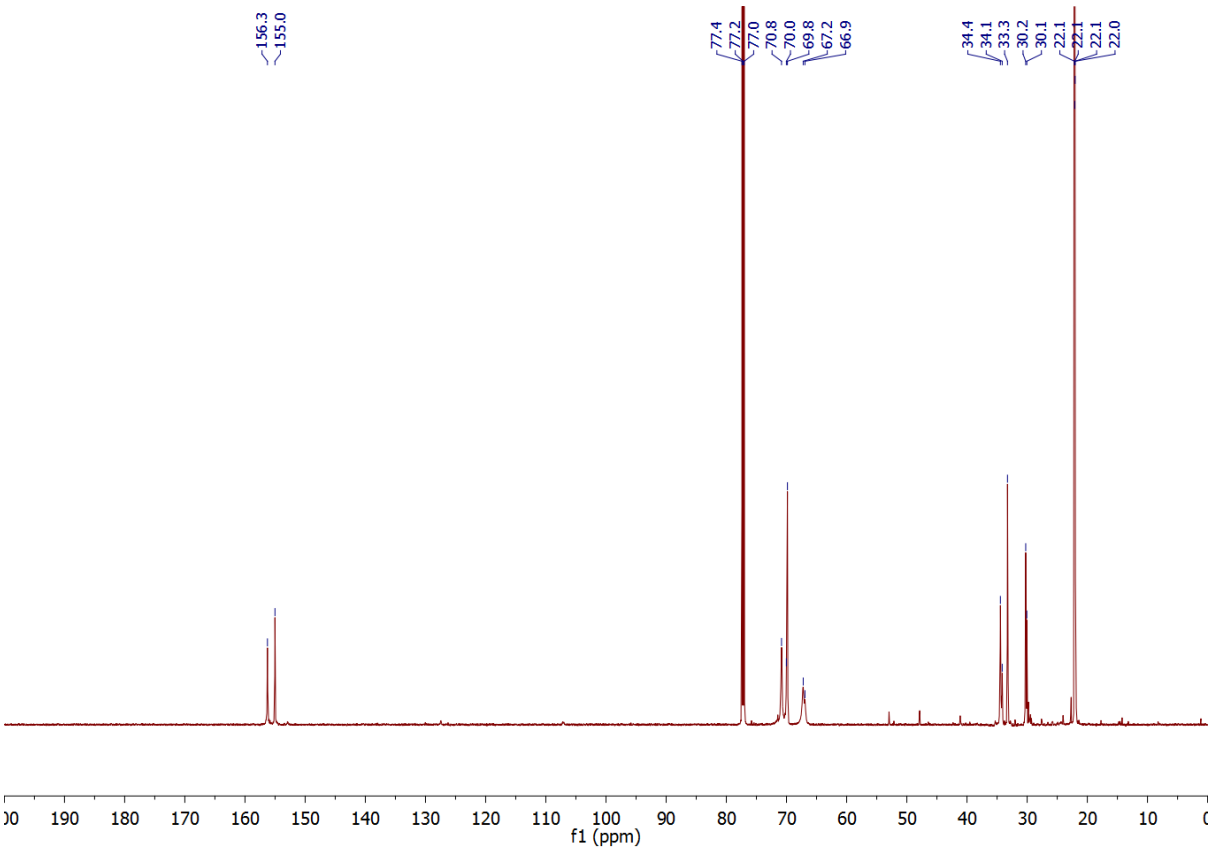

156.1
155.7
138.7
138.0
128.6
128.3
128.2
128.1
127.8
127.4
87.0
70.3
68.6
41.3
41.1
40.9
40.7
40.5
40.3
40.1
22.1
22.0
f1 (ppm)

Diisopropyl 1-(tetrahydrothiophen-2-yl)hydrazine-1,2-dicarboxylate 6lb

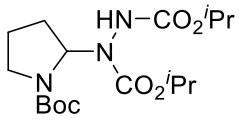


Compound prepared using HFIP as the reaction solvent and a reaction duration of 48 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(tetrahydrothiophen-2-yl)hydrazine-1,2-dicarboxylate as a white solid (142 mg, 0.490 mmol, 49%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.49-6.25 (m, NH, 1H), 6.15-5.90 (s, 1H), 4.99-4.86 (m, 2H), 3.06-2.94 (m, 1H), 2.78-2.68 (m, 1H), 2.14-2.02 (m, 3H), 1.96-1.88 (m, 1H), 1.26-1.19 (m, 12H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 156.3 (C), 155.0 (C), 70.8 (CH), 70.0 (CH), 69.8 (CH), 67.2 (CH), 66.9 (CH), 34.4 (CH_2), 34.1 (CH_2), 33.3 (CH_2), 30.2 (CH_2), 30.1 (CH_2), 22.1 (CH_3), 22.1 (CH_3), 22.1 (CH_3), 22.0 (CH_3); IR (solid) 3284, 2980, 2934, 1739, 1703 cm^{-1}. LRMS (ESI) 401 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{12}H_{23}N_2O_4S$ $[M+H]^+$ 291.1373; observed 291.1373.

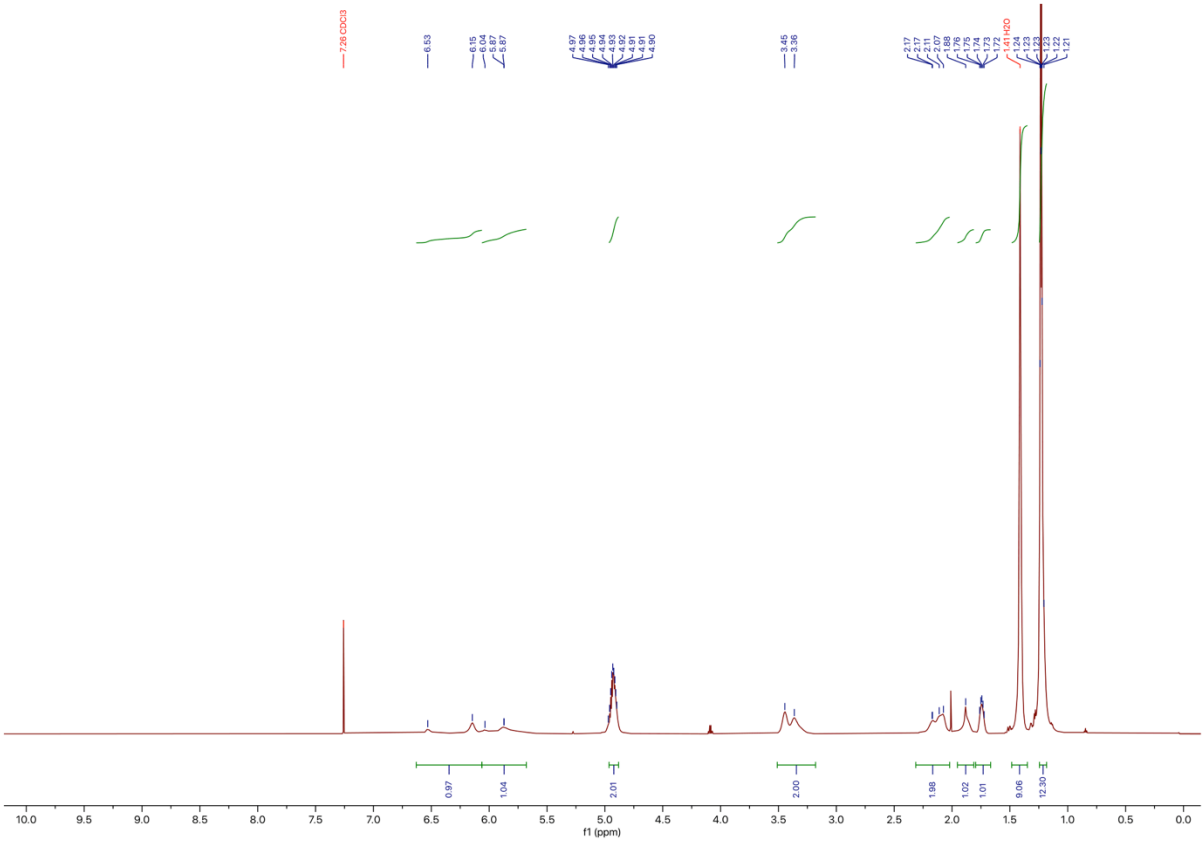


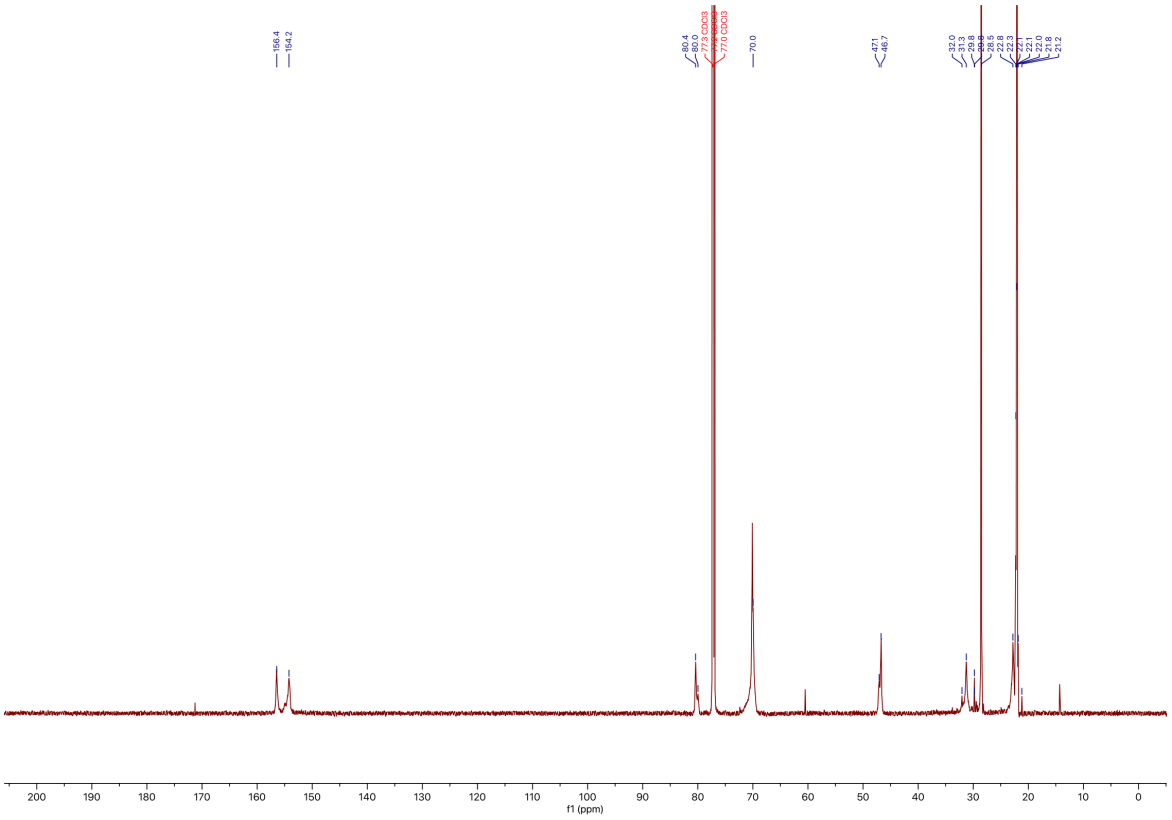

156.3
155.0
77.4
77.2
77.0
70.8
70.0
69.8
67.2
66.9
34.4
34.1
33.3
30.2
30.1
22.1
22.1
22.1
22.0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Diisopropyl 1-(1-(*tert*-butoxycarbonyl)pyrrolidin-2-yl)hydrazine-1,2-dicarboxylate 6mb



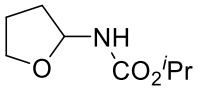
Compound prepared using HFIP as the reaction solvent and a reaction duration of 48 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(1-(*tert*-butoxycarbonyl)pyrrolidin-2-yl)hydrazine-1,2-dicarboxylate as a white solid (302 mg, 0.810 mmol, 81%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.63-6.16 (m, NH, 1H), 6.04-5.87 (m, 1H), 4.97-4.90 (m, 2H), 3.46-3.45 (m, 2H), 2.17-2.07 (m, 2H), 1.88 (m, 1H), 1.74-1.72 (m, 1H), 1.41 (s, 9H), 1.24-1.21 (m, 12H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.4 (C), 154.2 (C), 154.2 (C), 80.4 (C), 80.0 (C), 70.0 (CH), 70.0 (CH), 47.1 (CH), 46.7 (CH), 31.3 (CH_2), 29.8 (CH_2), 28.5 (CH_3), 22.8 (CH_2), 22.3 (CH_3), 22.1 (CH_3), 22.0 (CH_3), 21.8 (CH_3); IR (solid) 3253, 2983, 2945, 2830, 1730, 1710 cm^{-1}. LRMS (ESI) 396 (100, $[M+Na]^+$); HRMS (ESI) calcd for $C_{17}H_{31}N_3O_6Na$ $[M+Na]^+$ 396.2105; observed 396.2105.



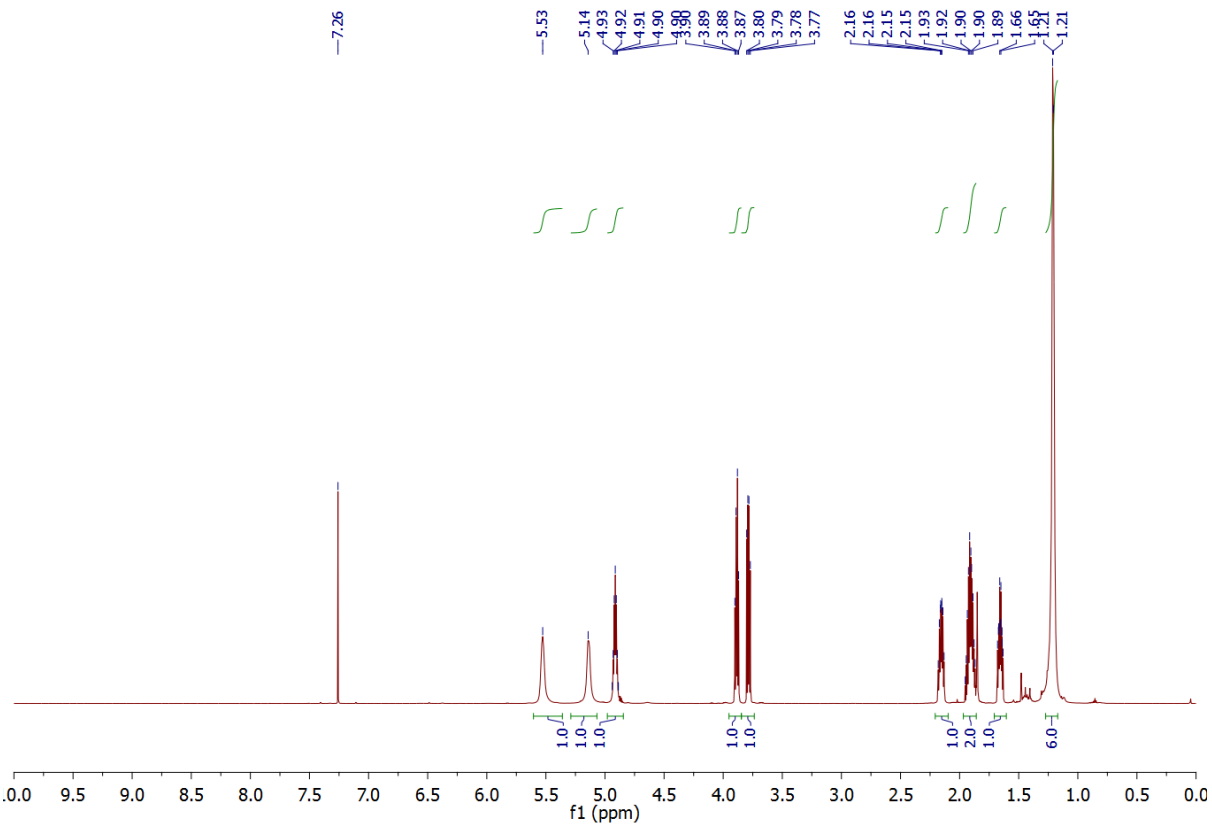

156.4
154.2
80.4
80.0
77.3 CDCl3
77.0
76.7 CDCl3
70.0
47.1
46.7
32.0
31.3
29.8
28.6
28.5
22.8
22.3
22.1
21.9
21.8
21.2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

N−N bond cleavage reaction of ether hydrazide

Isopropyl (tetrahydrofuran-2-yl)carbamate 9



To a stirring solution of sodium hydride (60% mineral oil dispersion, 200 mg, 5.00 mmol, 5 eq.) in anhydrous THF (0.5 mL) was added dropwise a solution of diisopropyl 1-benzoylhydrazine-1,2-dicarboxylate **6ab** (274 mg, 1.00 mmol, 1 eq.) pre-dissolved in anhydrous THF (1.5 mL) under an atmosphere of argon and the reaction mixture was stirred for 5 minutes. After this time, to the reaction mixture was added dropwise *tert*-butyl bromoacetate (162 μL, 1.10 mmol, 1.1 eq.) pre-dissolved in anhydrous THF (0.5 mL). The reaction mixture was then stirred at 25 °C for 16 h and then poured over saturated aqueous NH_4Cl (10 mL). The resulting solution was extracted with EtOAc (3 × 15 mL). The combined extracts were dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded isopropyl (tetrahydrofuran-2-yl)carbamate as a white solid (130 mg, 0.75 mmol, 75%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 5.53 (br s, NH, 1H), 5.14 (app. s, 1H), 4.91 (septet, *J* = 6.2 Hz, 1H), 3.89 (dt, *J* = 7.1, 7.1 Hz, 1H), 3.78 (dt, *J* = 7.1, 7.1 Hz, 1H), 2.19-2.12 (m, 1H), 1.96-1.86 (m, 2H), 1.69-1.62 (m, 1H), 1.21 (d, *J* = 5.0 Hz, 6H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 155.5 (C), 82.2 (CH), 68.5 (CH), 67.1 (CH_2), 31.9 (CH_2), 24.8 (CH_2), 22.2 (CH_3); IR (solid) 3314, 2980, 2933, 2871, 1738, 1683 cm^{-1}. LRMS (ESI) 401 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_8H_{16}NO_3$ $[M+H]^+$ 174.1125; observed 174.1124.


7.26
5.53
5.14
4.93
4.92
4.91
4.90
3.89
3.88
3.87
3.80
3.79
3.78
3.77
2.16
2.16
2.15
2.15
1.93
1.92
1.90
1.90
1.89
1.66
1.21
1.21
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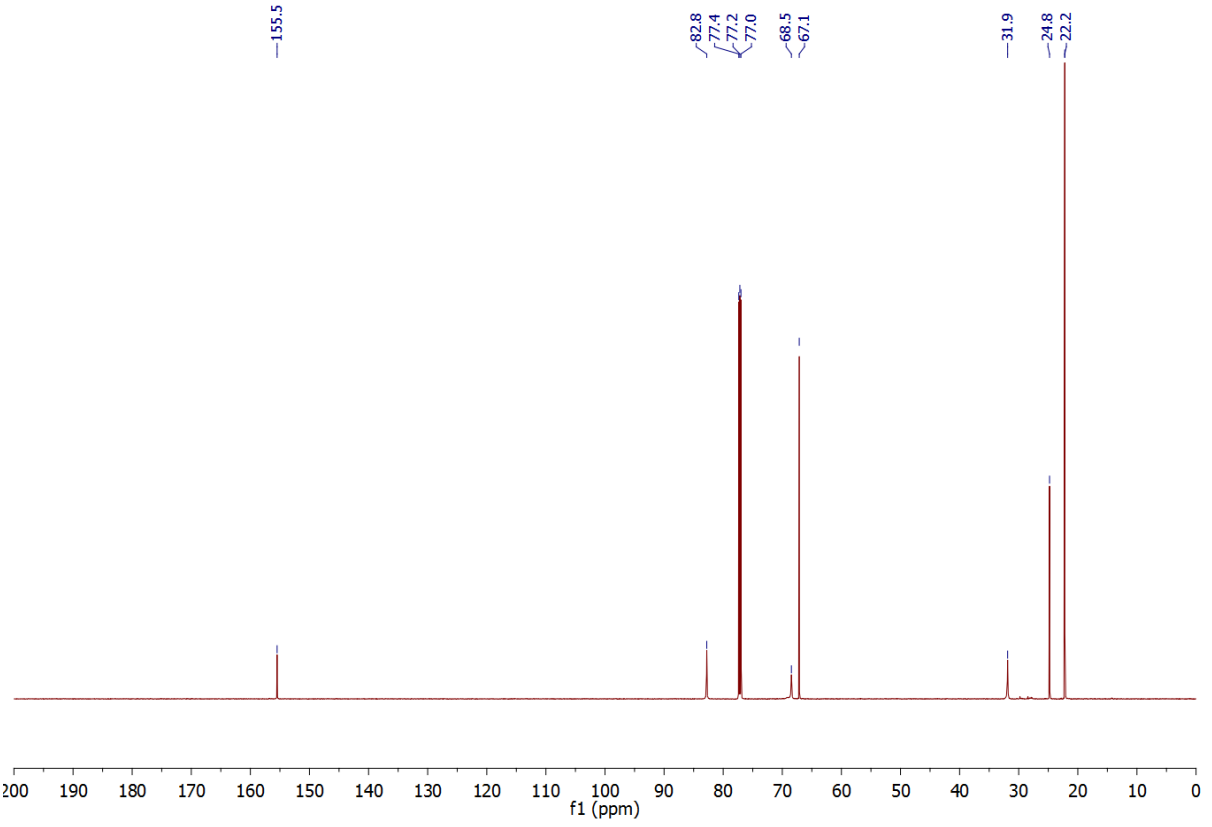
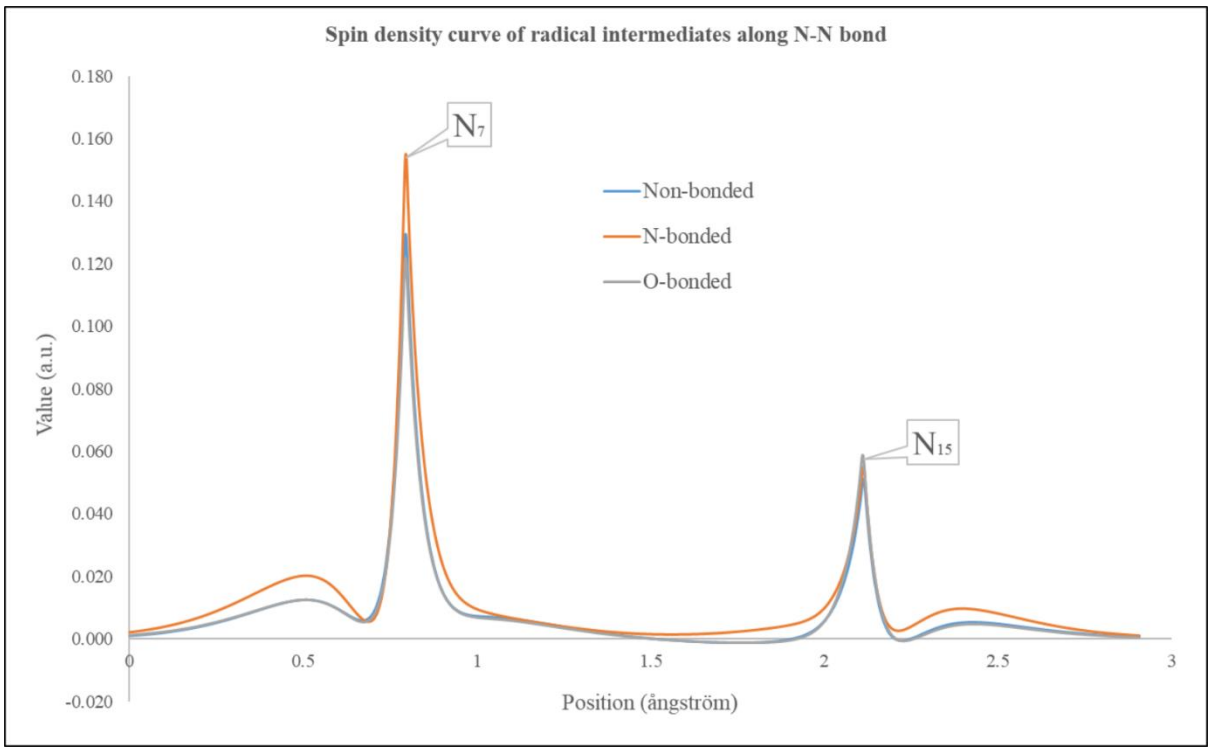
1.0
1.0
1.0
1.0
1.0
2.0
1.0
6.0
f1 (ppm)


155.5
82.8
77.4
77.2
77.0
68.5
67.1
31.9
24.8
22.2
f1 (ppm)

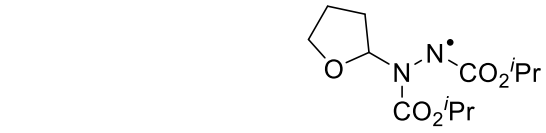
Computational Details

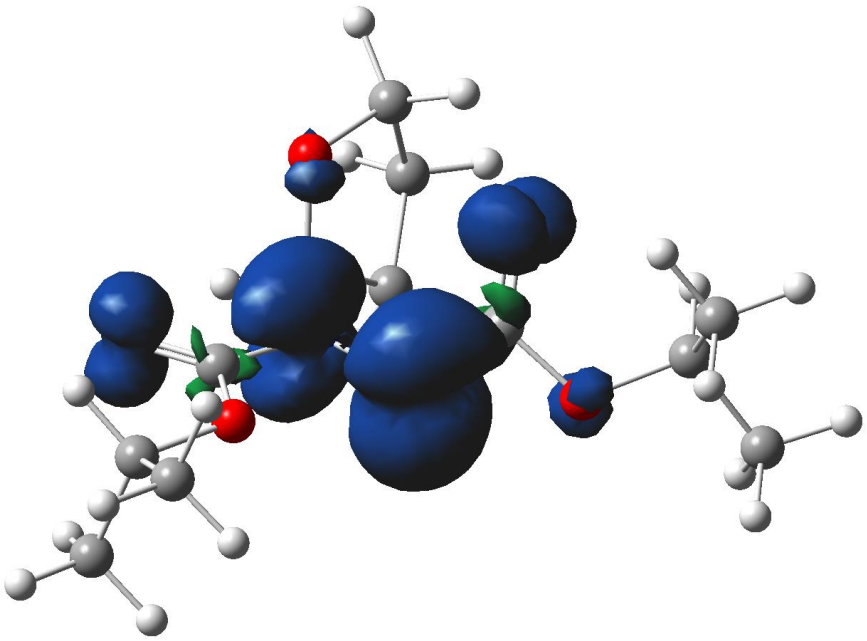
Spartan 14 and Gaussian 09 computational chemistry packages were used for all theoretical calculations. The optimised structures were drawn using the GaussView5 program. All structures were confirmed to be local minima by the absence of negative eigenvalues of the Hesse matrix in the frequency analysis at the same level. No symmetrical or internal coordinate constraints were applied. M06 2X/6-311++G(d,p) model chemistry was used to determine relative electronic energies, thermodynamic properties, and to conduct partial charges and population analysis calculations with the Multiwfn 3.7 suite.[5]

Spin density maps for nitrogen centred radical intermediates

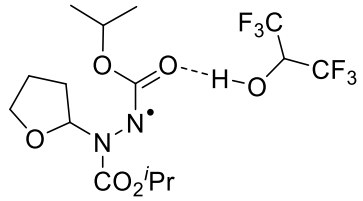


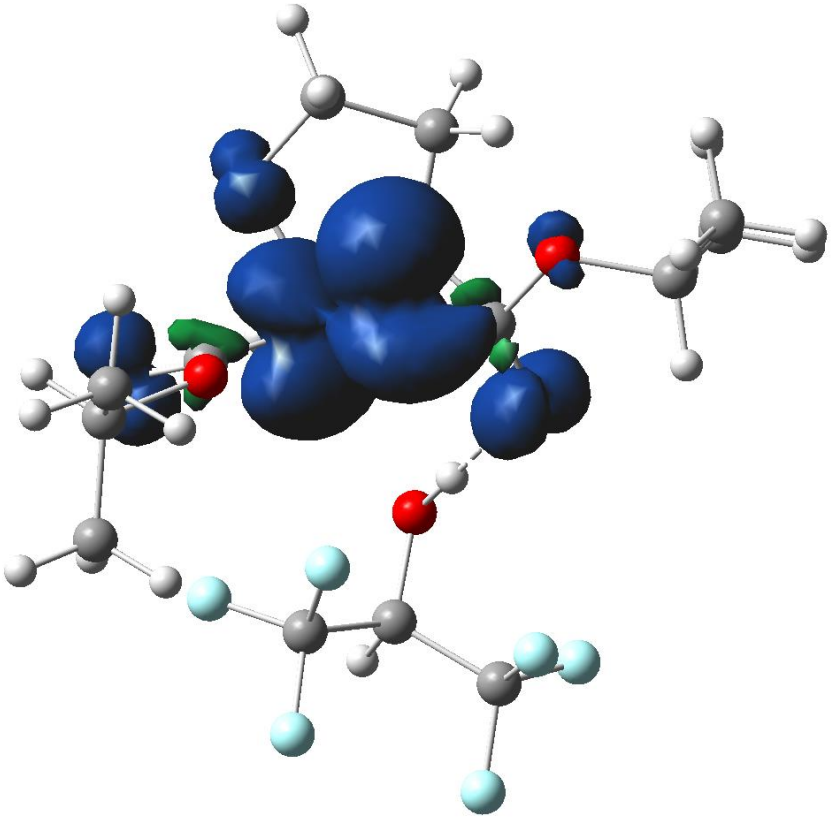
Non-bonded (THF radical attack on DIAD 5b)



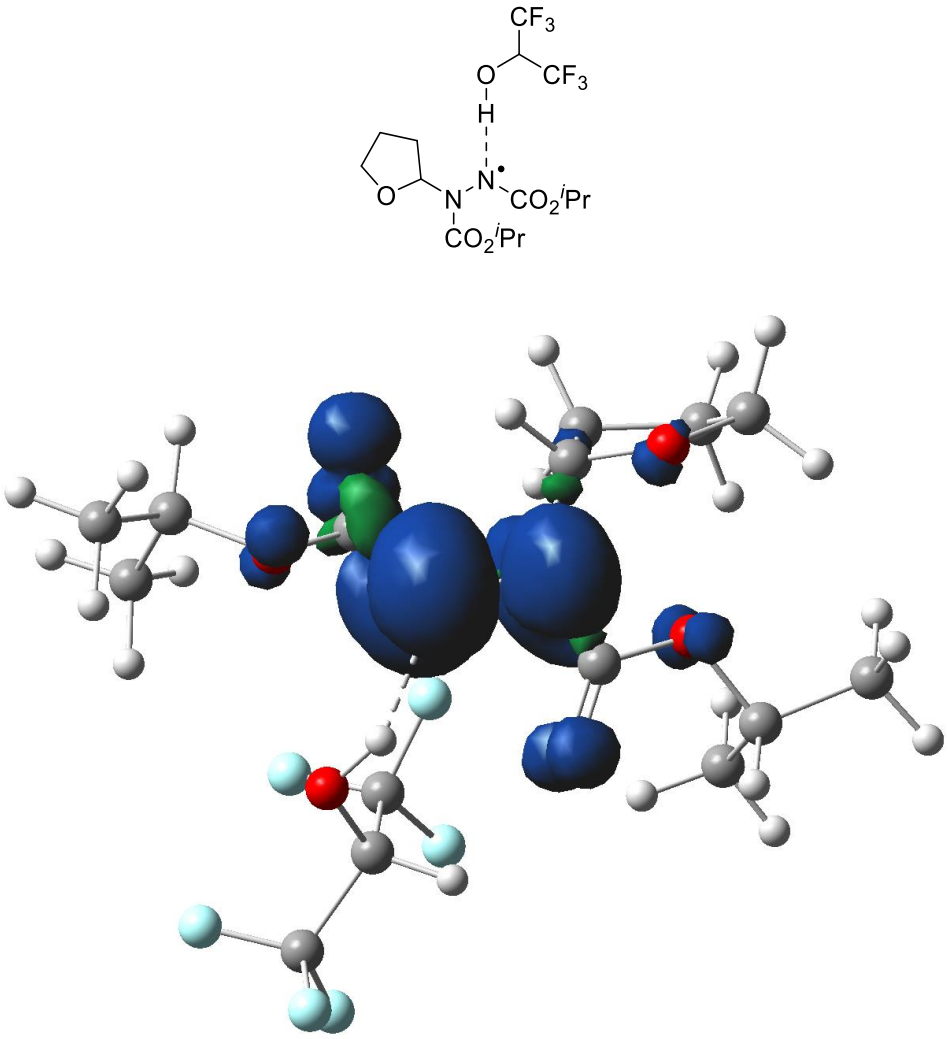


O-bonded (THF radical attack on DIAD 5b^{O})





N-bonded (THF radical attack on DIAD 5b^{N})



References

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2 R. Askani, *Chem. Ber.*, 1965, **98**, 2551–2555.

3 I. Ryu, A. Tani, T. Fukuyama, D. Ravelli, S. Montanaro and M. Fagnoni, *Org. Lett.*, 2013, **15**, 2554–2557.

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5 T. Lu and F. Chen, *J. Comput. Chem.*, 2012, **33**, 580–592.