

## (Supporting Information)

### A Metathesis Based Approach to the Synthesis of 2-Pyridones and Pyridines

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#### Experimental Section

##### General Details

Proton nuclear magnetic resonance spectra (NMR) were recorded at 400 MHz. <sup>13</sup>C NMR spectra were recorded at 100 MHz. Infrared spectra (IR) were recorded as evaporated films or KBr discs. Electrospray ionisation (ESI) was performed using tetraoctylammonium bromide as the lock mass. Chemical ionisation (CI) was performed at an ionisation voltage of 60 eV and a source temperature of 150 °C using amyl acetate as the lock mass and NH<sub>3</sub> as CI gas. All solvents and reagents requiring purification were purified using standard laboratory techniques according to methods published by Perrin, Armarego, and Perrin (Pergamon Press, 1966) apart from CH<sub>2</sub>Cl<sub>2</sub>, toluene, THF and Et<sub>2</sub>O which were dried by filtration through an activated alumina purification column. Petrol refers to petroleum ether in the boiling range 40–60 °C.

##### General Procedures

###### Procedure A: Formation of *O*-benzyl oxime ethers

Pyridine (1.1 eq.) was added drop-wise to a stirred solution of *O*-benzylhydroxylamine hydrochloride (1.3 eq.) and aldehyde (1.0 eq.) in methanol or ethanol (4 mL/mmol) and the mixture was heated at reflux for 4 h. The solvent was removed under reduced pressure, and the remaining solid residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (20 mL/mmol) and washed with water (20 mL/mmol). The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL/mmol × 3) and the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography.

###### Procedure B: Zinc mediated formation of amines

Zinc dust (1.8 eq.) was added portion-wise to a biphasic solution of oxime (1.0 eq.) and allyl bromide (1.4 eq.) in THF (0.8 mL/mmol) and sat. aq. NH<sub>4</sub>Cl solution (4.3 mL/mmol). The reaction mixture was stirred at room temperature until TLC analysis indicated that the starting material was consumed, and the aqueous layer was extracted with EtOAc (15 mL/mmol × 3). The organic layers

were dried over  $\text{MgSO}_4$ , and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography.

#### Procedure C: Formation of $\alpha,\beta$ -unsaturated amides

Acryloyl chloride (1.5 eq.) was added drop-wise to a stirred solution of amine (1.0 eq.) and triethylamine (2.0 eq.) in  $\text{CH}_2\text{Cl}_2$  (10 mL/mmol) at room temperature, and stirring was continued until TLC analysis indicated that the starting material was consumed. The mixture was diluted with  $\text{CH}_2\text{Cl}_2$  (10 mL/mmol), washed with 1.0 M aq. HCl solution (5 mL/mmol) and sat. aq.  $\text{NaHCO}_3$  solution (5 mL/mmol), then dried over  $\text{MgSO}_4$ . The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography.

#### Procedure D: Ring closing metathesis

Hoveyda-Grubbs second generation catalyst (5-10 mol%) was added to a stirred solution of  $\alpha,\beta$ -unsaturated amide (1.0 eq.) in  $\text{CH}_2\text{Cl}_2$ /toluene (25 mL/mmol), and the mixture was heated at 40 °C/95 °C until TLC analysis indicated that the starting material was consumed. The solvent was removed under reduced pressure, and the remaining black residue was purified by flash column chromatography.

#### Procedure E: Aromatisation of dihydropyridones

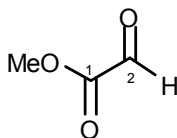
1,8-Diazabicyclo[5.4.0]undec-7-ene (5.0 eq.) was added to a stirred solution of dihydropyridone (1.0 eq.) in THF (2 mL/mmol), and stirring was continued at room temperature until TLC analysis indicated that the starting material was consumed. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography.

#### Procedure F: Formation of pyridines

Potassium bis(trimethylsilyl)amide solution (0.5 M in toluene, 2.0 eq.) was added drop-wise to a stirred solution of pyridone (1.0 eq.) and *N*-(5-chloro-2-pyridyl)triflimide (2.0 eq.) in THF (10 mL/mmol) at  $-78$  °C. The brown mixture was stirred at  $-78$  °C for 1 h, before allowing it to warm to room temperature over 3 h. The resulting solution was diluted with hexane (20 mL/mmol) and washed with sat. aq.  $\text{Na}_2\text{CO}_3$  solution (10 mL/mmol). The organic layer was dried over  $\text{Na}_2\text{SO}_4$ , and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography.

### Experimental Procedures

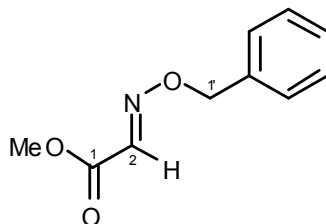
#### Methyl 2-oxoacetate **37**<sup>1</sup>



Ozone was bubbled through a solution of dimethyl maleate (5.22 mL, 41.7 mmol) in  $\text{CH}_2\text{Cl}_2$  (75 mL) at  $-78$  °C for 2 h, then the remaining blue solution was purged with oxygen for 5 min. Dimethyl sulfide (3.39 mL, 45.9 mmol) was added drop-wise at  $-78$  °C, and the reaction mixture was allowed to warm to room temperature. The solvent was removed under reduced pressure, and the remaining oil was purified by distillation under vacuum (b.p. 50 °C at 30 mmHg) to give the title compound **37** as a colourless oil (5.12 g, 70%) which was used immediately in the next step.

$\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.94 (3H, s, OMe), 9.41 (1H, s, C(2)H);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 53.2 (OMe), 159.8 (C(1)), 183.4 (C(2)). All data agreed with those previously published.<sup>2</sup>

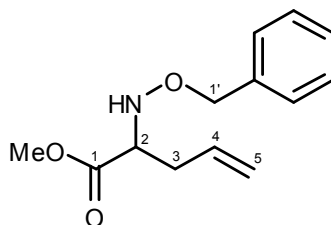
**(E)-Methyl 2-(benzyloxyimino)acetate **6**<sup>3</sup>**



Aldehyde **37** (5.00 g, 56.8 mmol) was subjected to general procedure **A** using methanol and purified by flash column chromatography (petrol) to give the title compound **6** as a colourless oil (8.24 g, 75%).

$\nu_{\max}$  (thin film)/cm<sup>-1</sup> 3033m, 2954s, 1725s, 1600s, 1497m, 1439s, 1369s, 1328s, 1274s, 1208s, 1082s, 1045s, 1002s, 923s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 3.86 (3H, s, OMe), 5.30 (2H, s, C(1')H<sub>2</sub>), 7.34–7.40 (5H, m, Ph), 7.57 (1H, s, C(2)H);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 52.5 (OMe), 78.1 (C(1')), 128.5 (Ph), 128.6 (Ph), 128.6 (Ph), 135.9 (*i*-Ph), 140.9 (C(2)), 162.4 (C(1)). All data agreed with those previously published.<sup>3</sup>

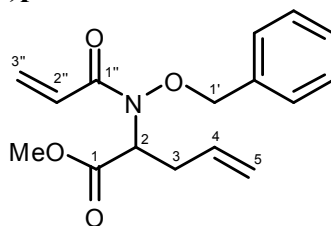
**Methyl 2-(benzyloxyamino)pent-4-enoate **7**<sup>3</sup>**



Oxime **6** (300 mg, 1.55 mmol) was subjected to general procedure **B** and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **7** as a colourless oil (346 mg, 100%).

$\nu_{\max}$  (thin film)/cm<sup>-1</sup> 3264br m, 3032w, 2953m, 1743s, 1642w, 1496m, 1436m, 1365m, 1202s, 993s, 913s, 743s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.32–2.37 (2H, m, C(3)H<sub>2</sub>), 3.70 (1H, t, *J* 7.0, C(2)H), 3.75 (3H, s, OMe), 4.72 (2H, s, C(1')H<sub>2</sub>), 5.06–5.13 (2H, m, C(5)H<sub>2</sub>), 5.73 (1H, ddt, *J* 17.0, 10.5, 7.0, C(4)H), 5.96 (1H, br s, NH), 7.27–7.36 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 33.9 (C(3)), 52.0 (OMe), 63.3 (C(2)), 76.2 (C(1')), 118.2 (C(5)), 127.8 (Ph), 128.3 (Ph), 128.5 (Ph), 133.0 (C(4)), 137.6 (*i*-Ph), 173.6 (C(1)). All data agreed with those previously published.<sup>3</sup>

**Methyl 2-(N-(benzyloxy)acrylamido)pent-4-enoate **8****

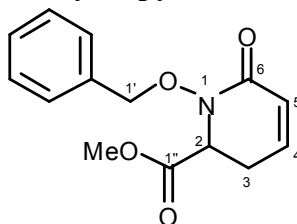


Amine **7** (280 mg, 1.26 mmol) was subjected to general procedure **C** and purified by flash column chromatography (8:1 petrol:EtOAc) to give the title compound **8** as a colourless oil (313 mg, 86%).

$\nu_{\max}$  (thin film)/cm<sup>-1</sup> 2952s, 1746s, 1665s, 1620s, 1410s, 1229s, 986s, 920s, 787s, 744s, 699s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.75–2.89 (2H, m, C(3)H<sub>2</sub>), 3.77 (3H, s, OMe), 4.93 (1H, d, *J* 10.5, C(1')H), 5.02 (1H, d, *J* 10.5, C(1')H), 5.04–5.07 (1H, m, C(2)H), 5.11 (1H, dd, *J* 10.5, 1.0, C(5)H), 5.18 (1H, dd, *J* 17.0, 1.0, C(5)H), 5.78 (1H, dd, *J* 10.5, 2.0, C(3'')H), 5.82 (1H, ddt, *J* 17.0, 10.5, 7.0, C(4)H), 6.45 (1H, dd, *J* 17.0, 2.0, C(3'')H), 6.73 (1H, dd, 17.0, 10.5, C(2'')H), 7.38–7.41 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 32.6 (C(3)), 52.5 (OMe), 60.7 (C(2)), 79.0 (C(1')), 118.4 (C(5)), 126.0 (C(2'')), 128.7 (Ph), 129.0 (Ph), 129.0 (Ph), 130.2 (C(3'')), 133.6 (C(4)), 134.3 (*i*-Ph), 168.3 (C(1'')), 170.3 (C(1));

$m/z$  312 (100%,  $\text{MNa}^+$ ), 290 (30%,  $\text{MH}^+$ ), 236 (10%), 218 (10%); HRMS (ESI)  $\text{C}_{16}\text{H}_{19}\text{NNaO}_4$  ( $\text{MNa}^+$ ) requires 312.1206, found 312.1207 (−0.18 ppm).

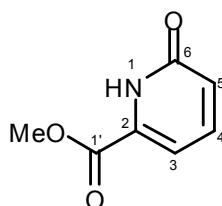
### Methyl 1-(benzyloxy)-6-oxo-1,2,3,6-tetrahydropyridine-2-carboxylate **10**



Amide **8** (300 mg, 1.04 mmol) was subjected to general procedure **D** using 5 mol% Hoveyda-Grubbs second generation catalyst in  $\text{CH}_2\text{Cl}_2$  at 40 °C and purified by flash column chromatography (2:1 petrol:EtOAc) to give the title compound **10** as a colourless oil (271 mg, 98%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  2954m, 1750s, 1692s, 1389m, 1210s, 1080m, 998m, 809m, 757m, 699m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.62–2.66 (2H, m, C(3) $\text{H}_2$ ), 3.73 (3H, s, OMe), 3.94–3.98 (1H, m, C(2)H), 4.96 (1H, d,  $J$  11.0, C(1')H), 5.04 (1H, d,  $J$  11.0, C(1')H), 5.94 (1H, ddd,  $J$  10.0, 2.0, 1.0, C(5)H), 6.34–6.46 (1H, m, C(4)H), 7.35–7.46 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 29.4 (C(3)), 52.8 (OMe), 62.3 (C(2)), 77.4 (C(1')), 125.3 (C(5)), 128.5 (Ph), 128.8 (Ph), 129.8 (Ph), 135.6 (*i*-Ph), 137.1 (C(4)), 165.1 (C(6)), 170.8 (C(1'));  $m/z$  284 (100%,  $\text{MNa}^+$ ), 262 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{14}\text{H}_{15}\text{NNaO}_4$  ( $\text{MNa}^+$ ) requires 284.0893, found 284.0894 (−0.14 ppm).

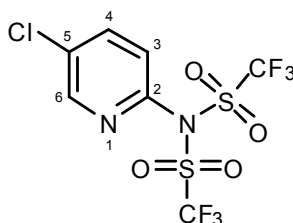
### Methyl 6-oxo-1,6-dihydropyridine-2-carboxylate **11**



Dihydropyridone **10** (85 mg, 0.33 mmol) was subjected to general procedure **E** and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **11** as a white solid (47 mg, 94%).

m.p. 100–103 °C (lit. 108–110 °C)<sup>4</sup>;  $\nu_{\text{max}}$  (KBr disk)/ $\text{cm}^{-1}$  3305br s, 1725s, 1661s, 1613s, 1543s, 1440s, 1352s, 1308s, 1194s, 1132s, 1062s, 1005s, 891s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.94 (3H, s, OMe), 6.83 (1H, dd,  $J$  9.5, 1.0, C(5)H), 6.97 (1H, dd,  $J$  7.0, 1.0, C(3)H), 7.45 (1H, dd,  $J$  9.5, 7.0, C(4)H), 11.28 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 51.3 (OMe), 109.6 (C(3)), 126.9 (C(5)), 133.9 (C(2)), 139.7 (C(4)), 161.4 (C(6)), 163.1 (C(1'));  $m/z$  176 (100%,  $\text{MNa}^+$ ); HRMS (ESI)  $\text{C}_7\text{H}_7\text{NNaO}_3$  ( $\text{MNa}^+$ ) requires 176.0318, found 176.0318 (−0.73 ppm). All data agreed with those previously published.<sup>4</sup>

### *N*-(5-Chloropyridin-2-yl)-1,1,1-trifluoro-*N*-(trifluoromethylsulfonyl)methanesulfonamide **12**<sup>5</sup>

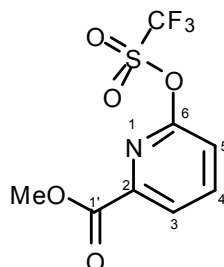


A solution of trifluoromethanesulfonic anhydride (9.15 mL, 54.4 mmol) in  $\text{CH}_2\text{Cl}_2$  (20 mL) was added dropwise *via* a cannula to a stirred solution of 2-amino-5-chloropyridine (3.33 g, 25.9 mmol) and pyridine (2.09 mL, 25.9 mmol) in  $\text{CH}_2\text{Cl}_2$  (100 mL) at −78 °C. The mixture was stirred for 2 h at this temperature, before warming to room temperature and stirring for a further 19 h. The reaction

mixture was quenched with cold water (20 mL) and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL × 4). The combined organic layers were washed with cold 10% aq. NaOH solution (20 mL), cold water (20 mL) and sat. aq. NaCl solution (20 mL) and dried over MgSO<sub>4</sub>. The solvent was removed under reduced pressure and the crude product was purified by Kugelrohr distillation (100 °C at 0.15 mmHg) to give the title compound **12** as a yellow solid (6.56 g, 64%).

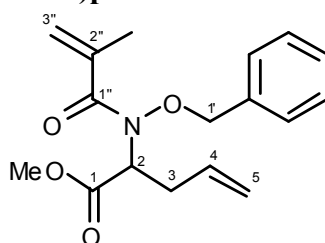
$\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 7.43 (1H, d, *J* 8.5, C(3)H), 7.91 (1H, dd, *J* 8.5, 2.5, C(4)H), 8.59 (1H, d, *J* 2.5, C(6)H);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 116.0 (q, *J*<sub>CF</sub> 326.0, CF<sub>3</sub>), 126.2 (C(3)), 135.8 (C(5)), 139.3 (C(4)), 143.8 (C(2)), 149.4 (C(6)). All data agreed with those previously published.<sup>5</sup>

### Methyl 6-(trifluoromethylsulfonyloxy)picolinate **13**



Pyridone **11** (47 mg, 0.31 mmol) was subjected to general procedure **F** and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **13** as a colourless oil (61 mg, 70%).  $\nu_{\text{max}}$  (thin film)/cm<sup>-1</sup> 2963s, 1736s, 1417s, 1261s, 1021s, 799s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 4.01 (3H, s, OMe), 7.42 (1H, dd, *J* 8.5, 1.0, C(5)H), 8.07 (1H, app t, *J* 8.5, C(4)H), 8.21 (1H, dd, *J* 8.5, 1.0, C(3)H);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 53.2 (OMe), 118.6 (q, *J*<sub>CF</sub> 321.0, CF<sub>3</sub>), 119.0 (C(5)), 125.4 (C(3)), 142.0 (C(4)), 147.3, 155.1 (C(2), C(6)), 163.8 (C(1')); *m/z* 308 (10%, MNa<sup>+</sup>), 286 (100%, MH<sup>+</sup>), 272 (20%); HRMS (ESI) C<sub>8</sub>H<sub>6</sub>F<sub>3</sub>NO<sub>5</sub>S (MNa<sup>+</sup>) requires 285.9992, found 285.9999 (−2.74 ppm).

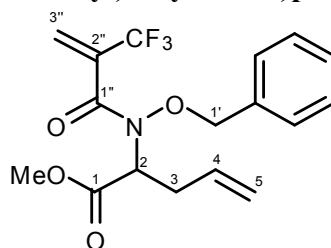
### Methyl 2-(*N*-(benzyloxy)methacrylamido)pent-4-enoate **14a**



Amine **7** (300 mg, 1.28 mmol) was subjected to general procedure **C** using methacryloyl chloride (188  $\mu$ L, 1.92 mmol) and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **14a** as a colourless oil (320 mg, 83%).

$\nu_{\text{max}}$  (thin film)/cm<sup>-1</sup> 2953s, 1746s, 1673s, 1498s, 1436s, 1372s, 1207s, 996s, 920s, 752s, 698s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.00 (3H, app t, *J* 1.5, Me), 2.76–2.82 (2H, m, C(3)H<sub>2</sub>), 3.76 (3H, s, OMe), 4.91 (1H, d, *J* 10.0, C(1')H), 4.92–4.97 (1H, m, C(2)H), 4.97 (1H, d, *J* 10.0, C(1')H), 5.16 (1H, ddd, *J* 10.5, 3.0, 1.0, C(5)H), 5.19 (1H, ddd, *J* 17.0, 3.0, 1.0, C(5)H), 5.32–5.34 (1H, m, C(3'')H), 5.41–5.43 (1H, m, C(3'')H), 5.80 (1H, ddt, *J* 17.0, 10.5, 6.5, C(4)H), 7.32–7.40 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 19.9 (Me), 32.5 (C(3)), 52.6 (OMe), 61.5 (C(2)), 78.2 (C(1')), 118.2, 118.6 (C(3''), C(5)), 128.5 (Ph), 128.7 (Ph), 129.1 (Ph), 133.6 (C(4)), 134.7 (*i*-Ph), 140.3 (C(2'')), 170.1 (C(1'')), 173.2 (C(1)); *m/z* 326 (100%, MNa<sup>+</sup>), 304 (70%, MH<sup>+</sup>), 218 (20%); HRMS (ESI) C<sub>17</sub>H<sub>21</sub>NNaO<sub>4</sub> (MNa<sup>+</sup>) requires 326.1363, found 326.1364 (−0.47 ppm).

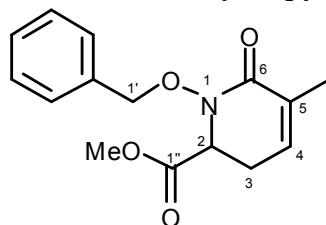
### Methyl 2-(*N*-(benzyloxy)-2-(trifluoromethyl)acrylamido)pent-4-enoate **14b**



A solution of amine **7** (526 mg, 2.40 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added drop-wise to a stirred solution of trifluoromethyl acrylic acid (336 mg, 2.40 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at –40 °C. *N*-(3-Dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (495 mg, 2.40 mmol) was added portion-wise to the mixture at –40 °C, and stirring was continued at 0 °C for 16 h. The solution was diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL), and the organic layer was washed with 1.0 M aq. HCl solution (10 mL), and sat. aq. NaHCO<sub>3</sub> solution (10 mL). The organic layer was dried over MgSO<sub>4</sub>, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (15:1 petrol:EtOAc) to give the title compound **14b** as a colourless oil (495 mg, 58%).

$\nu_{\max}$  (thin film)/cm<sup>–1</sup> 2935s, 1747s, 1674s, 1499s, 1436s, 1140s, 995s, 923s, 742s, 698s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.77–2.90 (2H, m, C(3)H<sub>2</sub>), 3.78 (3H, s, OMe), 4.88–4.92 (1H, m, C(2)H), 4.88 (1H, d, *J* 10.0, C(1')H), 4.95 (1H, dd, *J* 10.0, C(1')H), 5.15 (1H, dd, *J* 10.5, 1.5, C(5)H), 5.20 (1H, dd, *J* 17.5, 1.5, C(5)H), 5.82 (1H, ddt, *J* 17.5, 10.5, 6.5, C(4)H), 6.08 (1H, s, C(3'')H), 6.23 (1H, s, C(3'')H), 7.26–7.40 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 32.4 (C(3)), 52.6 (OMe), 60.4 (C(2)), 78.5 (C(1')), 118.7 (C(5)), 121.3 (q, *J*<sub>CF</sub> 273.5, CF<sub>3</sub>), 126.3 (q, *J*<sub>CF</sub> 5.5, C(3'')), 126.6 (Ph), 129.0 (Ph), 129.1 (Ph), 133.1 (C(4)), 133.9 (*i*-Ph), 136.2 (q, *J*<sub>CF</sub> 43.5, C(2'')), 165.0, 169.5 (C(1), C(1'')); *m/z* 358 (100%, MH<sup>+</sup>); HRMS (ESI) C<sub>17</sub>H<sub>19</sub>F<sub>3</sub>NO<sub>4</sub> (MH<sup>+</sup>) requires 358.1261, found 358.1262 (–0.50 ppm).

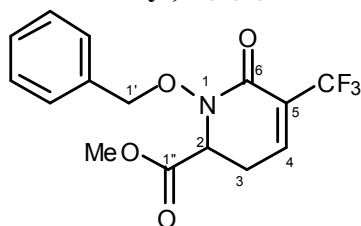
### Methyl 1-(benzyloxy)-5-methyl-6-oxo-1,2,3,6-tetrahydropyridine-2-carboxylate **15a**



Amide **14a** (124 mg, 0.44 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in CH<sub>2</sub>Cl<sub>2</sub> at 40 °C and purified by flash column chromatography (5:2 petrol:EtOAc) to give the title compound **15a** as a colourless oil (107 mg, 88%).

$\nu_{\max}$  (thin film)/cm<sup>–1</sup> 2954s, 1752s, 1687s, 1649s, 1497s, 1435s, 1377s, 1214s, 1077s, 1029s, 905s, 854s, 823s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.89–1.91 (3H, m, Me), 2.49–2.67 (2H, m, C(3)H<sub>2</sub>), 3.72 (3H, s, OMe), 3.97 (1H, dd, *J* 7.0, 3.0, C(2)H), 4.96 (1H, d, *J* 11.0, C(1')H), 5.04 (1H, d, *J* 11.0, C(1')H), 6.08–6.12 (1H, m, C(4)H), 7.34–7.46 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 16.6 (Me), 28.5 (C(3)), 52.7 (OMe), 62.7 (C(2)), 77.5 (C(1')), 128.4 (Ph), 128.7 (Ph), 129.7 (Ph), 131.1 (C(4)), 131.9 (*i*-Ph), 135.7 (C(5)), 166.8 (C(1'')), 171.1 (C(6)); *m/z* 298 (30%, MNa<sup>+</sup>), 276 (100%, MH<sup>+</sup>); HRMS (ESI) C<sub>15</sub>H<sub>17</sub>NNaO<sub>4</sub> (MNa<sup>+</sup>) requires 298.1050, found 298.1050 (–0.10 ppm).

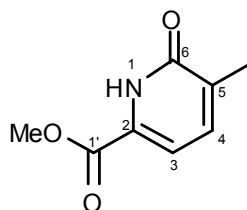
### Methyl 1-(benzyloxy)-6-oxo-5-(trifluoromethyl)-1,2,3,6-tetrahydropyridine-2-carboxylate **15b**



Amide **14b** (150 mg, 0.42 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in toluene (200 mL) at 95 °C and purified by flash column chromatography (3:1 petrol:EtOAc) to give the title compound **15b** as a colourless oil (103 mg, 75%).

$\nu_{\max}$  (thin film)/cm<sup>-1</sup> 2958m, 1749s, 1699s, 1399s, 1305s, 1138s, 1056m, 975m, 917m, 884m, 825m, 753m, 700m;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.76–2.81 (2H, m, C(3)H<sub>2</sub>), 3.75 (3H, s, OMe), 4.05 (1H, t, *J* 5.0, C(2)H), 4.98 (1H, d, *J* 11.0, C(1')H), 5.06 (1H, d, *J* 11.0, C(1')H), 6.97 (1H, app s, C(4)H), 7.35–7.47 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 28.0 (C(3)), 53.1 (OMe), 61.4 (C(2)), 77.8 (C(1')), 120.8 (q, *J*<sub>CF</sub> 272.5, CF<sub>3</sub>), 122.1 (C(5)), 128.6 (Ph), 129.0 (Ph), 129.8 (Ph), 135.1 (*i*-Ph), 139.2 (q, *J*<sub>CF</sub> 4.5, C(4)), 160.6, 169.9 (C(1''), C(6)); *m/z* 352 (100%, MNa<sup>+</sup>), 323 (20%), 307 (10%); HRMS (ESI) C<sub>15</sub>H<sub>15</sub>F<sub>3</sub>NO<sub>4</sub> (MH<sup>+</sup>) requires 330.0948, found 330.0950 (−0.73 ppm).

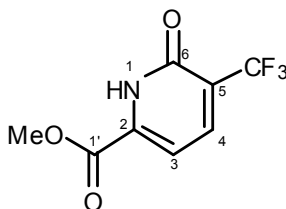
### Methyl 5-methyl-6-oxo-1,6-dihydropyridine-2-carboxylate **16a**



Dihydropyridone **15a** (100 mg, 0.36 mmol) was subjected to general procedure **E** and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **16a** as a white solid (53 mg, 89%).

m.p. 115–118 °C;  $\nu_{\max}$  (KBr disk)/cm<sup>-1</sup> 2947br s, 1726s, 1646s, 1617s, 1434s, 1293s, 1199s, 1122s, 1017s, 806s, 753s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.20 (3H, d, *J* 1.0, Me), 3.93 (3H, s, OMe), 6.91 (1H, d, *J* 7.0, C(3)H), 7.30 (1H, dq, *J* 7.0, 1.0, C(4)H), 10.32 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 17.2 (Me), 53.1 (OMe), 109.8 (C(3)), 131.2 (C(2)), 136.7 (C(5)), 137.2 (C(4)), 161.6 (C(6)), 162.7 (C(1')); *m/z* 190 (100%, MNa<sup>+</sup>); HRMS (ESI) C<sub>8</sub>H<sub>9</sub>NNaO<sub>3</sub> (MNa<sup>+</sup>) requires 190.0475, found 190.0475 (−0.31 ppm).

### Methyl 6-oxo-5-(trifluoromethyl)-1,6-dihydropyridine-2-carboxylate **16b**

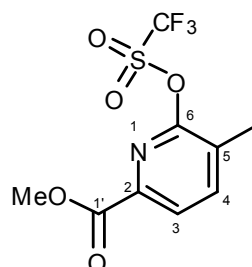


Dihydropyridone **15b** (77 mg, 0.23 mmol) was subjected to general procedure **E** and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **16b** as a white solid (34 mg, 65%).

m.p. 144–148 °C;  $\nu_{\max}$  (KBr disk)/cm<sup>-1</sup> 2963m, 1738s, 1666s, 1620s, 1577w, 1485w, 1439m, 1354w, 1319s, 1297s, 1218m, 1131s, 1096m, 1034m;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 4.02 (3H, s, OMe), 7.03 (1H, d, *J* 7.0, C(3)H), 7.88 (1H, d, *J* 7.0, C(4)H), 10.74 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 53.8 (OMe), 107.2 (C(3)), 122.0 (q, *J*<sub>CF</sub> 267.0, CF<sub>3</sub>), 126.2, 137.1 (C(2), C(5)), 139.4 (q, *J*<sub>CF</sub> 5.0, C(4)), 158.3,

160.3 (C(1'), C(6));  $\delta_F$  (400 MHz,  $CDCl_3$ )  $-66.4$  ( $CF_3$ );  $m/z$  222 (100%,  $MH^+$ ); HRMS (ESI)  $C_8H_7F_3NO_3$  ( $MH^+$ ) requires 222.0373, found 222.0377 ( $-2.22$  ppm).

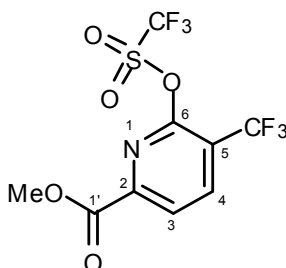
### Methyl 5-methyl-6-(trifluoromethylsulfonyloxy)picolinate **17a**



Pyridone **16a** (10 mg, 0.06 mmol) was subjected to general procedure **F** and purified by flash column chromatography (20:1 petrol:EtOAc) to give the title compound **17a** as a colourless oil (17 mg, 94%).

$\nu_{max}$  (thin film)/ $cm^{-1}$  2960s, 1731s, 1571s, 1420s, 1212s, 911s, 844s;  $\delta_H$  (400 MHz,  $CDCl_3$ ) 2.47 (3H, s, Me), 3.98 (3H, s, OMe), 7.86 (1H, d,  $J$  8.0, C(4)H), 8.10 (1H, d,  $J$  8.0, C(3)H);  $\delta_C$  (100 MHz,  $CDCl_3$ ) 16.1 (Me), 53.0 (OMe), 118.6 (q,  $J_{CF}$  264.0,  $CF_3$ ), 125.4 (C(3)), 129.6 (C(5)), 142.7 (C(4)), 144.6, 154.1 (C(2), C(6)), 164.0 (C(1'));  $m/z$  322 (30%,  $MNa^+$ ), 300 (100%,  $MH^+$ ), 286 (50%), 268 (20%), 242 (10%); HRMS (ESI)  $C_9H_9F_3NO_5S$  ( $MH^+$ ) requires 300.0148, found 300.0149 ( $-0.19$  ppm).

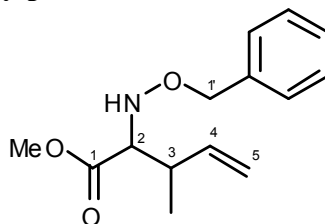
### Methyl 5-(trifluoromethyl)-6-(trifluoromethylsulfonyloxy)picolinate **17b**



Pyridone **16b** (17 mg, 0.08 mmol) was subjected to general procedure **F** and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **17b** as a white solid (18 mg, 67%).

m.p. 57–60 °C;  $\nu_{max}$  (KBr disk)/ $cm^{-1}$  2936s, 2360s, 1736s, 1432s, 1148s, 1039s, 832s;  $\delta_H$  (400 MHz,  $CDCl_3$ ) 4.04 (3H, s, OMe), 8.28 (1H, d,  $J$  8.5, C(3)H), 8.32 (1H, d,  $J$  8.5, C(4)H);  $\delta_C$  (100 MHz,  $CDCl_3$ ) 53.5 (OMe), 118.4 (q,  $J_{CF}$  320.5,  $CF_3$ ), 120.4 (q,  $J_{CF}$  35.5, C(5)), 120.9 (q,  $J_{CF}$  273.5,  $CF_3$ ), 124.5 (C(3)), 139.6 (q,  $J_{CF}$  5.0, C(4)), 149.7, 151.7 (C(2), C(6)), 162.8 (C(1'));  $m/z$  376 (20%,  $MNa^+$ ), 242 (100%); HRMS (ESI)  $C_9H_6F_6NO_5S$  ( $MH^+$ ) requires 353.9865, found 353.9866 ( $-0.04$  ppm).

### Methyl 2-(benzyloxyamino)-3-methylpent-4-enoate **18a**



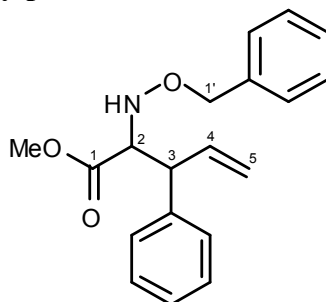
Oxime **6** (600 mg, 3.17 mmol) was subjected to general procedure **B** using crotyl bromide (457  $\mu$ L, 4.44 mmol) and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title



compound **18a** as a colourless oil (740 mg, 94%) and a mixture of diastereoisomers which were not separated (ca. 4:1 from  $^1\text{H}$  NMR). The  $^1\text{H}$  and  $^{13}\text{C}$  NMR data provided is for the major diastereoisomer.

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3266w, 3031w, 2952m, 1741s, 1641w, 1469w, 1454m, 1364m, 1253m, 1205s, 1271m, 996m, 918m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 1.04 (3H, d,  $J$  7.0, Me), 2.38 (1H, app sextet,  $J$  7.0, C(3)H), 3.47–3.55 (1H, m, C(2)H), 3.73 (3H, s, OMe), 4.69 (2H, s, C(1')H<sub>2</sub>), 4.98–5.06 (2H, m, C(5)H<sub>2</sub>), 5.66 (1H, ddd,  $J$  17.0, 10.5, 7.0, C(4)H), 5.97 (1H, br s, NH), 7.28–7.37 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 17.0 (Me), 38.9 (C(3)), 51.6 (OMe), 68.1 (C(2)), 76.0 (C(1')), 115.8 (C(5)), 127.8 (Ph), 128.2 (Ph), 128.6 (Ph), 137.7 (*i*-Ph), 139.0 (C(4)), 173.6 (C(1));  $m/z$  272 (100%,  $\text{MNa}^+$ ); HRMS (ESI)  $\text{C}_{14}\text{H}_{19}\text{NNaO}_3$  ( $\text{MNa}^+$ ) requires 272.1257, found 272.1257 (+0.18 ppm).

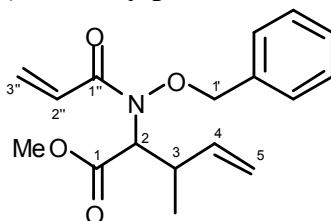
### Methyl 2-(benzyloxyamino)-3-phenylpent-4-enoate **18b**



Oxime **6** (174 mg, 1.04 mmol) was subjected to general procedure **B** using cinnamyl bromide (288 mg, 1.46 mmol) and purified by flash column chromatography (8:1 petrol:EtOAc) to give the title compound **18b** as a colourless oil (227 mg, 70%) and as a single diastereoisomer (which was unassigned).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3063m, 3030m, 2951m, 1741s, 1638m, 1601m, 1495s, 1453s, 1338m, 1242s, 1203s, 993s, 923m, 748s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.46–3.54 (1H, m, C(3)H), 3.72 (3H, s, OMe), 3.97 (1H, d,  $J$  8.5, C(2)H), 4.58 (1H, d,  $J$  11.5, C(1')H), 4.62 (1H, d,  $J$  11.5, C(1')H), 5.06–5.13 (2H, m, C(5)H<sub>2</sub>), 5.77 (1H, br s, NH), 5.98 (1H, ddd,  $J$  17.0, 10.0, 9.0, C(4)H), 7.11–7.35 (10H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 50.6 (C(3)), 51.8 (OMe), 68.0 (C(2)), 76.2 (C(1')), 117.1 (C(5)), 127.1 (Ph), 127.7 (Ph), 127.8 (Ph), 128.2 (Ph), 128.7 (Ph), 128.7 (Ph), 136.9 (C(4)), 137.4 (*i*-Ph), 139.4 (*i*-Ph), 173.1 (C(1));  $m/z$  334 (100%,  $\text{MNa}^+$ ), 312 (10%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{19}\text{H}_{21}\text{NNaO}_3$  ( $\text{MNa}^+$ ) requires 334.1414, found 334.1414 (+0.02 ppm).

### Methyl 2-(*N*-(benzyloxy)acrylamido)-3-methylpent-4-enoate **19a**

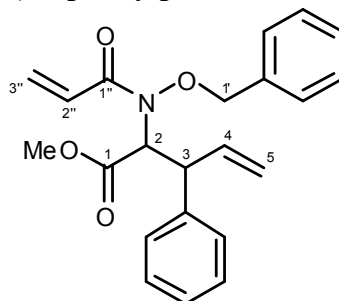


Amine **18a** (300 mg, 1.20 mmol) was subjected to general procedure **C** and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **19a** as a colourless oil (365 mg, 90%) and a mixture of diastereoisomers which were not separated (ca. 4:1 from  $^1\text{H}$  NMR). The  $^1\text{H}$  and  $^{13}\text{C}$  NMR data provided is for the major diastereoisomer.

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  2952w, 1745s, 1667s, 1621w, 1407s, 1313w, 1240m, 1202m, 985m, 919w, 786w;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 1.06 (3H, d,  $J$  7.0, Me), 3.05–3.21 (1H, m, C(3)H), 3.74 (3H, s, OMe), 4.85–5.20 (5H, m, C(1')H<sub>2</sub>, C(2)H, C(5)H<sub>2</sub>), 5.74–5.84 (2H, m, C(3'')H, C(4)H), 6.48 (1H, dd,  $J$  17.0, 2.0, C(3'')H), 6.78 (1H, dd,  $J$  17.0, 10.5, C(2'')H), 7.35–7.45 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 17.2 (Me), 37.6 (C(3)), 52.0 (OMe), 64.2 (C(2)), 79.0 (C(1')), 116.3 (C(5)), 125.8 (C(2'')),

128.7 (Ph), 128.9 (Ph), 129.2 (Ph), 130.5 (C(3'')), 134.2 (*i*-Ph), 139.1 (C(4)), 168.0, 170.3 (C(1), C(1''));  $m/z$  326 (100%,  $MNa^+$ ), 235 (30%), 180 (20%); HRMS (ESI)  $C_{17}H_{22}NO_4$  ( $MH^+$ ) requires 304.1543, found 304.1545 (−0.44 ppm).

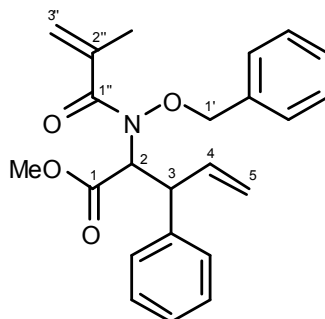
### Methyl 2-(*N*-(benzyloxy)acrylamido)-3-phenylpent-4-enoate **19b**



Amine **18b** (100 mg, 0.32 mmol) was subjected to general procedure **C** and purified by flash column chromatography (8:1 petrol:EtOAc) to give the title compound **19b** as a colourless oil (114 mg, 97%) and as a single diastereoisomer (which was unassigned).

$\nu_{\max}$  (thin film)/ $cm^{-1}$  3032w, 2951w, 1746s, 1669s, 1621m, 1495w, 1454m, 1406s, 1309m, 1237s, 1198m, 1173m, 986m, 921w;  $\delta_H$  (400 MHz,  $CDCl_3$ ) 3.79 (3H, s, OMe), 4.30 (1H, dd,  $J$  8.5, 11.0, C(3)H), 4.69 (1H, d,  $J$  10.0, C(1')H), 4.96 (1H, d,  $J$  10.0, C(1')H), 5.11–5.22 (2H, m, C(5)H<sub>2</sub>), 5.52–5.58 (2H, m, C(2)H, C(3'')H), 5.98–6.08 (1H, m, C(4)H), 6.19–6.35 (2H, m, C(2'')H, C(3'')H), 7.15–7.42 (10H, m, Ph);  $\delta_C$  (100 MHz,  $CDCl_3$ ) 49.3 (C(3)), 52.2 (OMe), 62.9 (C(2)), 78.7 (C(1')), 117.3 (C(5)), 125.6 (C(2'')), 127.0 (Ph), 128.4 (Ph), 128.6 (Ph), 128.7 (Ph), 128.8 (Ph), 129.0 (Ph), 129.9 (C(3'')), 134.4 (*i*-Ph), 137.4 (C(4)), 139.0 (*i*-Ph), 168.4, 170.1 (C(1), C(1''));  $m/z$  388 (100%,  $MNa^+$ ), 366 (20%,  $MH^+$ ); HRMS (ESI)  $C_{22}H_{24}NO_4$  ( $MH^+$ ) requires 366.1700, found 366.1702 (−0.51 ppm).

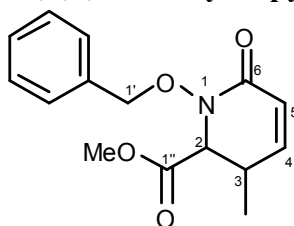
### Methyl 2-(*N*-(benzyloxy)methacrylamido)-3-phenylpent-4-enoate **19c**



Amine **18b** (150 mg, 0.51 mmol) was subjected to general procedure **C** using methacryloyl chloride (74  $\mu$ L, 0.76 mmol) and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **19c** as a colourless oil (135 mg, 74%) and as a single diastereoisomer (which was unassigned).

$\nu_{\max}$  (thin film)/ $cm^{-1}$  2952w, 1746s, 1666s, 1495w, 1454m, 1376m, 1256m, 1197m, 991w, 919m, 746w;  $\delta_H$  (400 MHz,  $CDCl_3$ ) 1.97 (3H, dd,  $J$  1.5, 1.0, Me), 3.81 (3H, s, OMe), 4.28 (1H, dd,  $J$  11.0, 8.0, C(3)H), 4.70 (1H, d,  $J$  9.5, C(1')H), 4.93 (1H, d,  $J$  9.5, C(1')H), 5.12 (1H, app dt,  $J$  10.5, 1.0, C(5)H), 5.17 (1H, app dt,  $J$  17.0, 1.0, C(5)H), 5.46 (1H, d,  $J$  11.0, C(2)H), 5.68–5.70 (1H, m, C(3'')H), 5.99 (1H, ddd,  $J$  17.0, 10.5, 8.0, C(4)H), 6.24–6.25 (1H, m, C(3'')H), 7.16–7.40 (10H, m, Ph);  $\delta_C$  (100 MHz,  $CDCl_3$ ) 18.9 (Me), 49.4 (C(3)), 49.4 (C(2)), 52.2 (OMe), 78.0 (C(1')), 117.3 (C(5)), 127.1 (Ph), 127.6 (C(3'')), 128.5 (Ph), 128.5 (Ph), 128.6 (Ph), 128.6 (Ph), 129.1 (Ph), 138.9 (C(4)), 134.7, 137.3, 140.0 (C(2'')), *i*-Ph  $\times$  2), 170.1, 172.1 (C(1), C(1''));  $m/z$  402 (100%,  $MNa^+$ ), 380 (10%,  $MH^+$ ); HRMS (ESI)  $C_{23}H_{26}NO_4$  ( $MH^+$ ) requires 380.1856, found 380.1857 (−0.26 ppm).

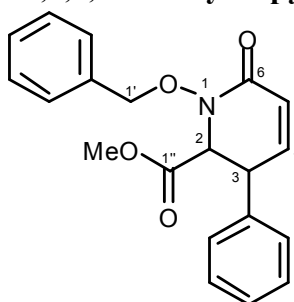
### Methyl 1-(benzyloxy)-3-methyl-6-oxo-1,2,3,6-tetrahydropyridine-2-carboxylate **20a**



Amide **19a** (300 mg, 0.99 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in  $\text{CH}_2\text{Cl}_2$  at 40 °C and purified by flash column chromatography (2:1 petrol:EtOAc) to give the title compound **20a** as a brown oil (265 mg, 97%) and a mixture of diastereoisomers which were not separated (ca. 4:1 from  $^1\text{H}$  NMR). The  $^1\text{H}$  and  $^{13}\text{C}$  NMR data provided is for the major diastereoisomer.

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3033w, 2953w, 1748s, 1694s, 1624w, 1497m, 1454m, 1384w, 1207s, 1133w, 1052w, 989m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 1.07 (3H, d,  $J$  7.5, Me), 2.98–3.06 (1H, m, C(3)H), 3.70 (3H, s, OMe), 3.96 (1H, d,  $J$  8.5, C(2)H), 4.92 (1H, d,  $J$  11.0, C(1')H), 5.02 (1H, d,  $J$  11.0, C(1')H), 5.98 (1H, dd,  $J$  10.0, 3.0, C(5)H), 6.11–6.15 (1H, m, C(4)H), 7.30–7.45 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 15.8 (Me), 33.8 (C(3)), 52.3 (OMe), 67.5 (C(2)), 77.3 (C(1')), 123.7 (C(5)), 129.5 (Ph), 129.6 (Ph), 129.7 (Ph), 135.6 (*i*-Ph), 142.8 (C(4)), 165.9, 169.2 (C(1''), C(6));  $m/z$  298 (100%,  $\text{MNa}^+$ ), 207 (60%); HRMS (ESI)  $\text{C}_{15}\text{H}_{18}\text{NO}_4$  ( $\text{MH}^+$ ) requires 276.1230, found 276.1229 (+0.34 ppm).

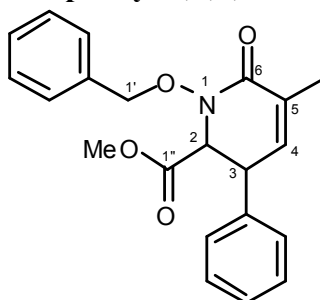
### Methyl-1-(benzyloxy)-6-oxo-3-phenyl-1,2,3,6-tetrahydropyridine-2-carboxylate **20b**



Amide **19b** (95 mg, 0.26 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in toluene at 95 °C and purified by flash column chromatography (3:1 petrol:EtOAc) to give the title compound **20b** as a brown oil (51 mg, 59%) and as a single diastereoisomer (which was unassigned).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3032m, 2951m, 1746s, 1696s, 1629m, 1494m, 1454m, 1384m, 1206s, 1057m, 1002m, 913m, 839m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.32 (3H, s, OMe), 4.13 (1H, d,  $J$  7.5, C(2)H), 4.20 (1H, dt,  $J$  7.5, 2.5, C(3)H), 5.00 (1H, d,  $J$  11.0, C(1')H), 5.07 (1H, d,  $J$  11.0, C(1')H), 6.16 (1H, dd,  $J$  10.0, 2.5, C(5)H), 6.49 (1H, dd,  $J$  10.0, 2.5, C(4)H), 7.01–7.05 (2H, m, Ph), 7.29–7.36 (3H, m, Ph), 7.40–7.50 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 45.4 (C(3)), 52.0 (OMe), 68.7 (C(2)), 77.5 (C(1')), 125.3 (C(5)), 128.2 (Ph), 128.5 (Ph), 128.7 (Ph), 128.8 (Ph), 128.8 (Ph), 129.8 (Ph), 135.6 (*i*-Ph), 136.5 (*i*-Ph), 139.9 (C(4)), 165.8, 168.6 (C(1''), C(6));  $m/z$  360 (100%,  $\text{MNa}^+$ ), 338 (80%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{20}\text{H}_{19}\text{NNaO}_4$  ( $\text{MNa}^+$ ) requires 360.1206, found 360.1207 (−0.33 ppm).

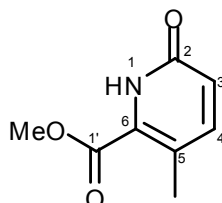
### Methyl-1-(benzyloxy)-5-methyl-6-oxo-3-phenyl-1,2,3,6-tetrahydropyridine-2-carboxylate **20c**



Amide **19c** (125 mg, 0.33 mmol) was subjected to general procedure **D** 10 mol% Hoveyda-Grubbs second generation catalyst in toluene at 95 °C and purified by flash column chromatography (2:1 petrol:EtOAc) to give the title compound **20c** as a white solid (82 mg, 71%) and as a single diastereoisomer (which was unassigned).

m.p. 123–125 °C;  $\nu_{\text{max}}$  (KBr disk)/ $\text{cm}^{-1}$  2952w, 1736s, 1683s, 1651m, 1454m, 1392m, 1213m, 1035m, 812m, 737m, 696m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.04 (3H, app t,  $J$  1.5, Me), 3.31 (3H, s, OMe), 4.12–4.19 (2H, m, C(2)H, C(3)H), 5.00 (1H, d,  $J$  11.0, C(1')H), 5.07 (1H, d,  $J$  11.0, C(1')H), 6.22–6.25 (1H, m, C(4)H), 7.03–7.07 (2H, m, Ph), 7.28–7.49 (8H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 16.8 (Me), 44.7 (C(3)), 51.9 (OMe), 69.0 (C(2)), 77.4 (C(1')), 128.0 (Ph), 128.2 (Ph), 128.5 (Ph), 128.6 (Ph), 128.7 (Ph), 129.7 (Ph), 132.0 (C(5)), 134.2 (C(4)), 135.8 (*i*-Ph), 137.2 (*i*-Ph), 167.5 (C(6)), 168.9 (C(1''));  $m/z$  374 (90%,  $\text{MNa}^+$ ), 352 ( $\text{MH}^+$ , 100%), 283 (10%); HRMS (ESI)  $\text{C}_{21}\text{H}_{22}\text{NO}_4$  ( $\text{MH}^+$ ) requires 352.1543, found 352.1544 (–0.06 ppm).

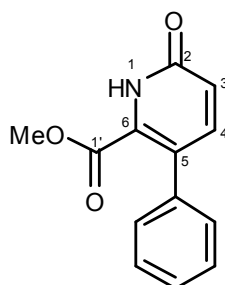
### Methyl 3-methyl-6-oxo-1,6-dihydropyridine-2-carboxylate **21a**



Dihydropyridone **20a** (250 mg, 0.91 mmol) was subjected to general procedure **E** and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **21a** as a white solid (142 mg, 93%).

m.p. 120–123 °C;  $\nu_{\text{max}}$  (KBr disk)/ $\text{cm}^{-1}$  2953s, 1724s, 1655s, 1598s, 1445s, 1315s, 1254s, 1193s, 1097s, 912s, 857s, 784s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.41 (3H, s, Me), 3.96 (3H, s, OMe), 6.73 (1H, d,  $J$  9.0, C(3)H), 7.30 (1H, d,  $J$  9.0, C(4)H), 9.97 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 18.3 (Me), 53.1 (OMe), 121.5 (C(5)), 126.5 (C(3)), 129.4 (C(6)), 145.5 (C(4)), 161.5, 161.9 (C(1'), C(2));  $m/z$  190 (100%,  $\text{MNa}^+$ ); HRMS (ESI)  $\text{C}_8\text{H}_9\text{NNaO}_3$  ( $\text{MNa}^+$ ) requires 190.0475, found 190.0474 (+0.53 ppm).

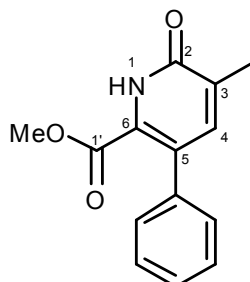
### Methyl 6-oxo-3-phenyl-1,6-dihydropyridine-2-carboxylate **21b**



Dihydropyridone **20b** (35 mg, 0.10 mmol) was subjected to general procedure **E** and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **21b** as a white solid (22 mg, 92%).

m.p. 130–132 °C;  $\nu_{\text{max}}$  (KBr disk)/ $\text{cm}^{-1}$  3054s, 1723s, 1664s, 1612s, 1591s, 1490s, 1446s, 1430s, 1312s, 1241s, 1086s, 1037s, 1011s, 980s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.69 (3H, s, OMe), 6.83 (1H, d, *J* 9.0, C(3)H), 7.22–7.27 (2H, m, Ph), 7.37–7.42 (4H, m, C(4)H, Ph  $\times$  3), 10.45 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 53.0 (OMe), 125.1 (C(5)), 126.6 (C(3)), 128.0 (Ph), 128.2 (Ph), 128.7 (Ph), 130.2 (C(6)), 137.2 (*i*-Ph), 144.3 (C(4)), 161.8 (C(2)), 162.0 (C(1')); *m/z* 252 (100%,  $\text{MNa}^+$ ), 230 (80%,  $\text{MH}^+$ ), 202 (30%), 170 (20%); HRMS (ESI)  $\text{C}_{13}\text{H}_{11}\text{NNaO}_3$  ( $\text{MNa}^+$ ) requires 252.0631, found 252.0630 (+0.41 ppm).

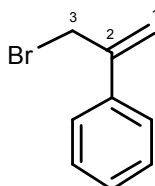
### Methyl 5-methyl-6-oxo-3-phenyl-1,6-dihydropyridine-2-carboxylate **21c**



Dihydropyridone **20c** (20 mg, 0.06 mmol) was subjected to general procedure **E** and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **21c** as a white solid (13 mg, 93%).

m.p. 164–168 °C;  $\nu_{\text{max}}$  (KBr disk)/ $\text{cm}^{-1}$  3012s, 1732s, 1668s, 1431s, 1319s, 1278s, 1241s, 1188s, 1071s, 761s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.24 (3H, d, *J* 1.0, Me), 3.69 (3H, s, OMe), 7.22–7.28 (3H, m, Ph), 7.36–7.42 (3H, m, C(4)H, Ph), 9.99 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 16.9 (Me), 52.8 (OMe), 125.7 (C(5)), 127.3 (C(3)), 127.8 (Ph), 128.1 (Ph), 128.7 (Ph), 136.0 (C(6)), 137.5 (*i*-Ph), 141.4 (C(4)), 161.8, 161.9 (C(1'), C(2)); *m/z* 266 (90%,  $\text{MNa}^+$ ), 244 (100%,  $\text{MH}^+$ ), 212 (30%), 184 (20%); HRMS (ESI)  $\text{C}_{14}\text{H}_{14}\text{NO}_3$  ( $\text{MH}^+$ ) requires 244.0968, found 244.0972 (–1.60 ppm).

### (3-Bromoprop-1-en-2-yl)benzene **22**<sup>6</sup>

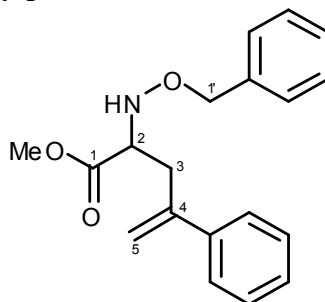


*N*-Bromosuccinimide (8.90 g, 50.0 mmol) was added to a solution of  $\alpha$ -methylstyrene (10.5 mL, 80.0 mmol) in  $\text{CCl}_4$  (5 mL), and the mixture was heated to 170 °C until the solids had dissolved and the exothermic reaction had subsided. The reaction mixture was allowed to cool for 3 h and the precipitate was removed by filtration. The solvent was removed under reduced pressure, and the

resulting orange oil was purified by flash column chromatography (petrol) to give the title compound **22** as a colourless oil (5.10 g, 52%).

$\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 4.41 (2H, s, C(3) $\text{H}_2$ ), 5.51 (1H, s, C(1)H), 5.58 (1H, s, C(1)H), 7.23–7.55 (5H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 34.2 (C(3)), 117.2 (C(1)), 126.1 (Ph), 128.3 (Ph), 128.5 (Ph), 137.6 (*i*-Ph), 144.2 (C(2)). All data agreed with those previously published.<sup>6</sup>

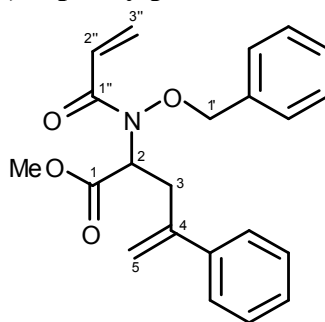
### Methyl 2-(benzyloxyamino)-4-phenylpent-4-enoate **23**



Oxime **6** (300 mg, 1.55 mmol) was subjected to general procedure **B** using allyl bromide **22** and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **23** as a colourless oil (228 mg, 47%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3060s, 3030s, 2951s, 1741s, 1453s, 1212s, 780s, 699s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.80 (2H, app dt,  $J$  7.5, 1.5, C(3) $\text{H}_2$ ), 3.66 (3H, s, OMe), 3.71–3.79 (1H, m, C(2)H), 4.66 (2H, s, C(1') $\text{H}_2$ ), 5.12–5.13 (1H, m, C(5)H), 5.35–5.36 (1H, m, C(5)H), 5.92 (1H, br s, NH), 7.27–7.39 (10H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 35.4 (C(3)), 51.9 (OMe), 62.5 (C(2)), 76.2 (C(1')), 115.7 (C(5)), 126.2 (Ph), 127.8 (Ph), 127.8 (Ph), 128.3 (Ph), 128.4 (Ph), 128.5 (Ph), 137.6, 139.8, 143.7 (C(4), *i*-Ph  $\times$  2), 173.8 (C(1));  $m/z$  334 (100%,  $\text{MNa}^+$ ), 279 (60%), 201 (30%), 195 (20%); HRMS (ESI)  $\text{C}_{19}\text{H}_{21}\text{NNaO}_3$  ( $\text{MNa}^+$ ) requires 334.1414, found 334.1415 (−0.49 ppm).

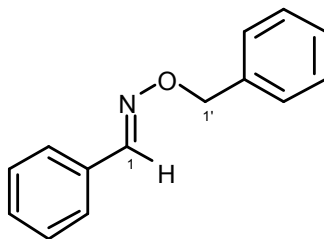
### Methyl 2-(*N*-(benzyloxy)acrylamido)-4-phenylpent-4-enoate **24**



Amine **23** (40 mg, 0.13 mmol) was subjected to general procedure **C** and purified by flash column chromatography (8:1 petrol:EtOAc) to give the title compound **24** as a colourless oil (41 mg, 91%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3032w, 2952m, 1744s, 1663s, 1621m, 1495w, 1410m, 1314s, 1263s, 985s, 908m, 845w;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.26 (1H, dd,  $J$  15.0, 10.5, C(3)H), 3.40 (1H, dd,  $J$  15.0, 4.5, C(3)H), 3.76 (3H, s, OMe), 4.79 (1H, d,  $J$  10.5, C(1')H), 4.85 (1H, d,  $J$  10.5, C(1')H), 4.89 (1H, dd,  $J$  10.5, 4.5, C(2)H), 5.20 (1H, s, C(5)H), 5.39 (1H, s, C(5)H), 5.74 (1H, dd,  $J$  10.5, 2.0, C(3'')H), 6.43 (1H, dd,  $J$  17.0, 2.0, C(3'')H), 6.66 (1H, dd,  $J$  17.0, 10.5, C(2'')H), 7.21–7.44 (10H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 33.9 (C(3)), 52.6 (OMe), 60.6 (C(2)), 78.6 (C(1')), 115.9 (C(5)), 126.1 (C(2'')), 126.3 (Ph), 127.8 (Ph), 128.5 (Ph), 128.6 (Ph), 128.9 (Ph), 129.0 (Ph), 129.9 (C(3'')), 134.2, 140.0, 143.9 (C(4), *i*-Ph  $\times$  2), 167.8, 170.2 (C(1), C(1''));  $m/z$  388 (80%,  $\text{MNa}^+$ ), 387 (100%), 366 (20%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{22}\text{H}_{24}\text{NO}_4$  ( $\text{MH}^+$ ) requires 366.1700, found 366.1700 (−0.13 ppm).

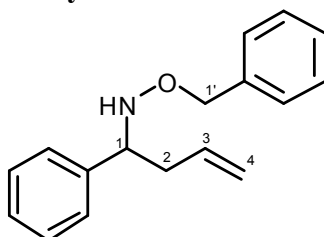
**(*E*)-Benzaldehyde *O*-benzyl oxime **38**<sup>3</sup>**



Benzaldehyde (305  $\mu$ L, 3.00 mmol) was subjected to general procedure **A** using ethanol and purified by flash column chromatography (petrol) to give the title compound **38** as a colourless oil (589 mg, 93%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3063s, 3030s, 2927s, 1495s, 1447s, 1367s, 1341s, 1211s, 1081s, 1020s, 946s, 915s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 5.23 (2H, s, C(1')H<sub>2</sub>), 7.30–7.62 (10H, m, Ph), 8.15 (1H, s, C(1)H);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 76.4 (C(1')), 127.1 (Ph), 128.0 (Ph), 128.4 (Ph), 128.4 (Ph), 128.7 (Ph), 129.0 (Ph), 129.8 (*i*-Ph), 132.2 (*i*-Ph), 149.0 (C(1)). All data agreed with those previously published.<sup>3</sup>

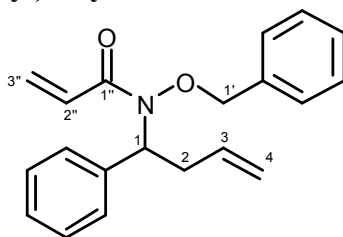
***O*-Benzyl-*N*-(1-phenylbut-3-enyl)hydroxylamine **39****



Boron trifluoride diethyl etherate (721  $\mu$ L, 5.69 mmol) was added to a stirred solution of oxime **38** (400 mg, 1.80 mmol) in toluene (5 mL) at  $-78^\circ\text{C}$ , and the mixture was stirred for 15 min. Allyl magnesium bromide (5.70 mL, 1.0 M in  $\text{Et}_2\text{O}$ , 5.69 mmol) was added drop-wise to the reaction mixture over 15 min, and stirring was continued for 14 h. The reaction was quenched at  $-78^\circ\text{C}$  with water (10 mL), and the mixture was allowed to warm to room temperature. The aqueous layer was extracted with  $\text{Et}_2\text{O}$  (20 mL  $\times$  3), and the combined organic layers were dried over  $\text{K}_2\text{CO}_3$  and concentrated under reduced pressure. The resulting yellow oil was purified by flash column chromatography (25:1 petrol: $\text{Et}_2\text{O}$ ) to give the title compound **39** as a colourless oil (431 mg, 90%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3031s, 2914s, 1641s, 1495s, 1454s, 1361s, 994s, 916s, 751s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.40–2.60 (2H, m, C(2)H<sub>2</sub>), 4.08 (1H, t,  $J$  7.0, C(1)H), 4.55 (1H, d,  $J$  11.0, C(1')H), 4.62 (1H, d,  $J$  11.0, C(1')H), 5.02–5.11 (2H, m, C(4)H<sub>2</sub>), 5.66–5.77 (1H, m, C(3)H), 5.81 (1H, br s, NH), 7.21–7.40 (10H, m, Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 38.5 (C(2)), 65.0 (C(1)), 76.8 (C(1')), 117.7 (C(4)), 127.5 (Ph), 127.7 (Ph), 127.8 (Ph), 127.8 (Ph), 128.3 (Ph), 128.5 (Ph), 134.8 (C(3)), 137.7 (*i*-Ph), 141.5 (*i*-Ph);  $m/z$  276 (100%,  $\text{MNa}^+$ ); HRMS (ESI)  $\text{C}_{17}\text{H}_{19}\text{NNaO}$  ( $\text{MNa}^+$ ) requires 276.1359, found 276.1358 (+0.38 ppm).

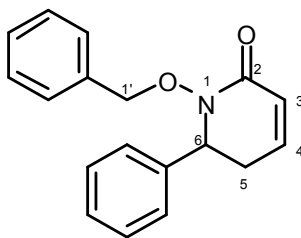
***N*-(Benzyloxy)-*N*-(1-phenylbut-3-enyl)acrylamide **26a****



Amine **39** (280 mg, 1.11 mmol) was subjected to general procedure **C** and purified by flash column chromatography (4:1 petrol: $\text{Et}_2\text{O}$ ) to give the title compound **26a** as a white solid (337 mg, 99%).

m.p. 45–48 °C;  $\nu_{\max}$  (KBr disk)/cm<sup>-1</sup> 3030s, 2885s, 1651s, 1499s, 1453s, 1408s, 1376s, 1311s, 1232s, 1133s, 971s, 910s, 854s, 785s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.80–3.07 (2H, m, C(2)H<sub>2</sub>), 4.22 (1H, d,  $J$  9.5, C(1')H), 4.60 (1H, d,  $J$  9.5, C(1')H), 5.07 (1H, dd,  $J$  10.5, 1.0, C(4)H), 5.17 (1H, dd,  $J$  17.0, 1.0, C(4)H), 5.74–5.86 (3H, m, C(1)H, C(3)H, C(3'')H), 6.49 (1H, dd,  $J$  17.0, 2.0, C(3'')H), 6.71 (1H, dd,  $J$  17.0, 10.5, C(2'')H), 7.19–7.23 (2H, m, Ph), 7.32–7.43 (6H, m, Ph), 7.53–7.57 (2H, m, Ph);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 34.6 (C(2)), 59.8 (C(1)), 79.4 (C(1')), 118.1 (C(4)), 126.8 (C(2'')), 128.1 (Ph), 128.6 (Ph), 128.6 (Ph), 128.7 (Ph), 128.8 (Ph), 128.9 (Ph), 129.7 (C(3'')), 134.3 (*i*-Ph), 134.4 (C(3)), 138.8 (*i*-Ph), 167.8 (C(1''));  $m/z$  330 (100%, MNa<sup>+</sup>), 266 (90%), 238 (20%); HRMS (ESI) C<sub>20</sub>H<sub>21</sub>NNaO<sub>2</sub> (MNa<sup>+</sup>) requires 330.1465, found 330.1464 (+0.01 ppm).

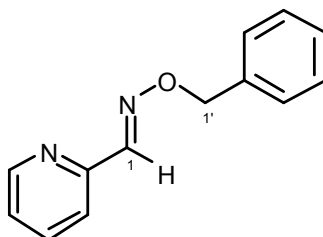
### 1-(Benzyloxy)-6-phenyl-5,6-dihydropyridin-2(1H)-one **27a**



Amide **26a** (133 mg, 0.43 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in toluene at 95 °C and purified by flash column chromatography (2:1 petrol:EtOAc) to give the title compound **27a** as a white solid (105 mg, 87%).

m.p. 84–86 °C;  $\nu_{\max}$  (KBr disk)/cm<sup>-1</sup> 3030s, 2946s, 2885s, 1683s, 1623s, 1455s, 1384s, 1364s, 1289s, 1124s, 1065s, 1008s, 984s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.68 (1H, dddd,  $J$  18.0, 7.0, 4.0, 2.0, C(5)H), 2.82 (1H, dddd,  $J$  18.0, 7.0, 4.0, 2.0, C(5)H), 4.64 (1H, app t,  $J$  7.0, C(6)H), 4.78 (1H, d,  $J$  10.5, C(1')H), 5.03 (1H, d,  $J$  10.5, C(1')H), 6.00 (1H, dt,  $J$  9.5, 2.0, C(3)H), 6.42 (1H, dt,  $J$  9.5, 4.0, C(4)H), 7.17–7.39 (10H, m, Ph);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 34.1 (C(5)), 63.8 (C(6)), 77.3 (C(1')), 124.8 (C(3)), 127.0 (Ph), 128.0 (Ph), 128.3 (Ph), 128.5 (Ph), 128.6 (Ph), 129.6 (Ph), 135.4 (*i*-Ph), 138.3 (C(4)), 139.2 (*i*-Ph), 165.8 (C(2));  $m/z$  302 (100%, MNa<sup>+</sup>), 211 (40%); HRMS (ESI) C<sub>18</sub>H<sub>17</sub>NNaO<sub>2</sub> (MNa<sup>+</sup>) requires 302.1151, found 302.1151 (+0.02 ppm).

### (*E*)-Picolinaldehyde *O*-benzyl oxime **40**

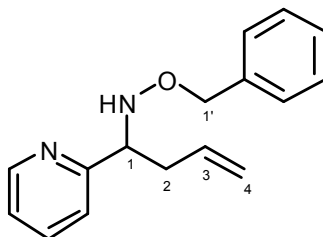


Pyridine-2-carboxaldehyde (1.00 g, 9.34 mmol) was subjected to general procedure **A** using ethanol and purified by flash column chromatography (petrol) to give the title compound **40** as a colourless oil (1.98 g, 100%).

$\nu_{\max}$  (thin film)/cm<sup>-1</sup> 3032w, 1584m, 1566w, 1496w, 1468m, 1454m, 1434m, 1366m, 1331w, 1201w, 1017s, 990s, 941s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 5.28 (2H, s, C(1')H<sub>2</sub>), 7.23–7.46 (6H, m, Ph × 5, Ar), 7.69 (1H, td,  $J$  8.0, 1.5, Ar), 7.80 (1H, d,  $J$  8.0, Ar), 8.25 (1H, s, C(1)H), 8.61 (1H, d,  $J$  5.0, Ar);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 76.8 (C(1')), 121.0 (Ar), 123.9 (Ar), 128.0 (Ph), 128.3 (Ph), 128.4 (Ph), 136.4 (Ar), 137.2 (*i*-Ph), 149.6 (Ar), 149.6 (C(1)), 151.6 (*i*-Ar);  $m/z$  213 (100%, MH<sup>+</sup>), 132 (20%); HRMS (ESI) C<sub>13</sub>H<sub>13</sub>N<sub>2</sub>O (MH<sup>+</sup>) requires 213.1022, found 213.1021 (−0.74 ppm).



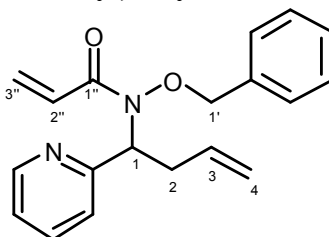
***O*-Benzyl-*N*-(1-(pyridin-2-yl)but-3-enyl)hydroxylamine **41****



Oxime **40** (1.00 g, 4.71 mmol) was subjected to general procedure **B** and purified by flash column chromatography (gradient of 0–50% EtOAc in cyclohexane) to give the title compound **41** as a colourless oil (1.20 g, 81%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  2913w, 1640w, 1591m, 1571m, 1473m, 1453m, 1434s, 1363m, 1292w, 1207w, 994s, 914s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.46–2.52 (2H, m, C(2) $\text{H}_2$ ), 4.17 (1H, t,  $J$  7.0, C(1)H), 4.63 (1H, d,  $J$  11.5, C(1')H), 4.68 (1H, d,  $J$  11.5, C(1')H), 4.99–5.07 (2H, m, C(4) $\text{H}_2$ ), 5.72 (1H, ddt,  $J$  17.0, 10.0, 7.0, C(3)H), 6.22 (1H, br s, NH), 7.15–7.19 (1H, m, Ar), 7.24–7.34 (6H, m, Ph  $\times$  5, Ar), 7.64 (1H, td,  $J$  7.5, 1.5, Ar), 8.59 (1H, d,  $J$  5.0, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 37.3 (C(2)), 65.7 (C(1)), 76.2 (C(1')), 117.5 (C(4)), 122.2 (Ar), 122.5 (Ar), 127.7 (Ph), 128.2 (Ph), 128.4 (Ar), 134.5 (C(3)), 136.1 (Ar), 137.9 (*i*-Ph), 149.4 (Ar), 161.1 (*i*-Ar);  $m/z$  255 (100%,  $\text{MH}^+$ ), 164 (10%), 132 (20%); HRMS (ESI)  $\text{C}_{16}\text{H}_{19}\text{N}_2\text{O}$  ( $\text{MH}^+$ ) requires 255.1492, found 255.1491 (–0.49 ppm).

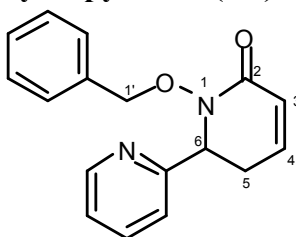
***N*-(Benzyloxy)-*N*-(1-(pyridin-2-yl)but-3-enyl)acrylamide **26b****



Amine **41** (949 mg, 3.74 mmol) was subjected to general procedure **C** and purified by flash column chromatography (gradient of 0–50% EtOAc in cyclohexane) to give the title compound **26b** as a colourless oil (880 mg, 77%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3066w, 1658s, 1589s, 1571m, 1472w, 1454w, 1433m, 1410s, 1371m, 1228m, 1134w, 985s, 917m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.00–3.17 (2H, m, C(2) $\text{H}_2$ ), 4.58 (1H, d,  $J$  10.0, C(1')H), 4.70 (1H, d,  $J$  10.0, C(1')H), 5.04–5.09 (1H, m, C(4)H), 5.14–5.21 (1H, m, C(4)H), 5.75 (1H, dd,  $J$  10.5, 2.0, C(3'')H), 5.77–5.91 (2H, m, C(1)H, C(3)H), 6.46 (1H, dd,  $J$  17.0, 2.0, C(3'')H), 6.76 (1H, dd,  $J$  17.0, 10.5, C(2'')H), 7.21–7.37 (6H, m, Ph  $\times$  5, Ar), 7.51 (1H, d,  $J$  8.0, Ar), 7.69 (1H, td,  $J$  8.0, 1.5, Ar), 8.64 (1H, d,  $J$  5.0, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 33.8 (C(2)), 62.3 (C(1)), 79.2 (C(1')), 117.8 (C(4)), 122.8 (Ar), 123.7 (Ar), 126.6 (C(2'')), 128.5 (Ph), 128.8 (Ph), 129.0 (Ph), 129.6 (C(3'')), 134.4 (*i*-Ph), 134.5 (C(3)), 136.7 (Ar), 148.9 (Ar), 158.4 (*i*-Ar), 167.6 (C(1''));  $m/z$  309 (100%,  $\text{MH}^+$ ), 201 (70%), 132 (20%); HRMS (ESI)  $\text{C}_{19}\text{H}_{21}\text{N}_2\text{O}_2$  ( $\text{MH}^+$ ) requires 309.1598, found 309.1595 (–0.85 ppm).

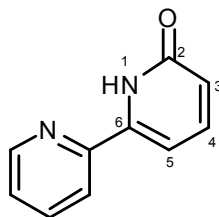
### 1-(Benzyloxy)-6-(pyridin-2-yl)-5,6-dihydropyridin-2(1H)-one **27b**



Amide **26b** (150 mg, 0.49 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in toluene at 95 °C and purified by flash column chromatography (gradient of 0–100% EtOAc in cyclohexane) to give the title compound **27b** as a brown oil (100 mg, 74%).

$\nu_{\max}$  (thin film)/cm<sup>-1</sup> 2927w, 1682s, 1620m, 1589m, 1471w, 1454w, 1436m, 1392m, 1325w, 1291w, 1248w, 1134w, 994m;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.80 (1H, ddt, *J* 18.0, 7.0, 3.0, C(5)H), 2.98 (1H, dt, *J* 18.0, 4.0, C(5)H), 4.66 (1H, dd, *J* 7.0, 4.0, C(6)H), 4.95 (1H, d, *J* 11.0, C(1')H), 5.04 (1H, d, *J* 11.0, C(1')H), 5.93 (1H, dd, *J* 10.0, 3.0, C(3)H), 6.32 (1H, ddd, *J* 10.0, 4.0, 3.0, C(4)H), 7.19 (1H, dd, *J* 7.5, 4.0, Ar), 7.26 (1H, d, *J* 7.5, Ar), 7.31–7.35 (5H, m, Ph), 7.64 (1H, td, *J* 7.5, 1.5, Ar), 8.55 (1H, app d, *J* 4.0, Ar);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 31.7 (C(5)), 64.1 (C(6)), 76.9 (C(1')), 121.2 (Ar), 122.2 (Ar), 124.3 (C(3)), 128.0 (Ph), 128.3 (Ph), 129.3 (Ph), 135.1 (*i*-Ph), 136.3 (Ar), 137.9 (C(4)), 149.0 (Ar), 158.0 (*i*-Ar), 164.7 (C(2)); *m/z* 281 (100%, MH<sup>+</sup>); HRMS (ESI) C<sub>17</sub>H<sub>17</sub>N<sub>2</sub>O<sub>2</sub> (MH<sup>+</sup>) requires 281.1285, found 281.1283 (–0.67 ppm).

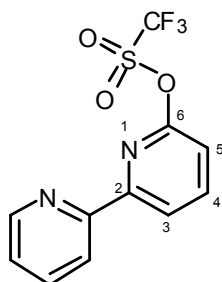
### 6-(Pyridin-2-yl)pyridin-2(1H)-one **28b**



Dihydropyridone **27b** (98 mg, 0.35 mmol) was subjected to general procedure **E** with heating to 50 °C and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **28b** as a white solid (48 mg, 80%).

m.p. 117–119 °C (lit. 115–116 °C)<sup>7</sup>;  $\nu_{\max}$  (KBr disk)/cm<sup>-1</sup> 3055w, 1648s, 1599s, 1465s, 1455s, 1291w, 1245w, 1155m, 994m, 778s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 6.64 (1H, dd, *J* 9.0, 1.0, C(3)H), 6.81 (1H, dd, *J* 7.0, 1.0, C(5)H), 7.33–7.39 (1H, m, Ar), 7.49 (1H, dd, *J* 9.0, 7.0, C(4)H), 7.80–7.85 (2H, m, Ar), 8.66 (1H, dt, *J* 5.0, 1.0, Ar), 10.72 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 102.7 (C(5)), 119.6 (Ar), 122.0 (C(3)), 124.5 (Ar), 137.3 (Ar), 140.5 (C(4)), 141.7 (C(6)), 147.8 (*i*-Ar), 149.2 (Ar), 162.8 (C(2)); *m/z* 173 (100%, MH<sup>+</sup>); HRMS (ESI) C<sub>10</sub>H<sub>9</sub>N<sub>2</sub>O (MH<sup>+</sup>) requires 173.0709, found 173.0710 (–0.44 ppm). All data agreed with those previously published.<sup>7</sup>

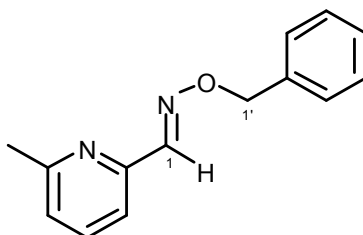
## 2,2'-Bipyridin-6-yl trifluoromethanesulfonate **29b**



Pyridone **28b** (20 mg, 0.12 mmol) was subjected to general procedure **F** and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **29b** as a colourless oil (30 mg, 86%).

$\nu_{\max}$  (thin film)/ $\text{cm}^{-1}$  3067w, 1603s, 1586s, 1556s, 1422s, 1313s, 1212s, 1135s, 1086m, 1046m, 994m, 913s, 828s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 7.18 (1H, d,  $J$  8.0, C(5)H), 7.36 (1H, ddd,  $J$  8.0, 5.0, 1.5, Ar), 7.85 (1H, td,  $J$  8.0, 1.5, Ar), 8.01 (1H, t,  $J$  8.0, C(4)H), 8.35 (1H, dd,  $J$  8.0, 1.5, Ar), 8.54 (1H, d,  $J$  8.0, C(3)H), 8.68 (1H, dd,  $J$  5.0, 1.5, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 114.6 (C(5)), 118.7 (q,  $J_{\text{CF}}$  320.5,  $\text{CF}_3$ ), 121.0 (Ar), 121.5 (C(3)), 124.6 (Ar), 137.2 (Ar), 141.8 (C(4)), 149.3 (Ar), 153.7, 155.4, 155.9 (C(2), C(6), *i*-Ar);  $m/z$  327 (40%,  $\text{MNa}^+$ ), 305 (100%,  $\text{MH}^+$ ), 182 (30%); HRMS (ESI)  $\text{C}_{11}\text{H}_7\text{F}_3\text{N}_2\text{NaO}_3\text{S}$  ( $\text{MNa}^+$ ) requires 327.0022, found 327.0026 (−1.31 ppm).

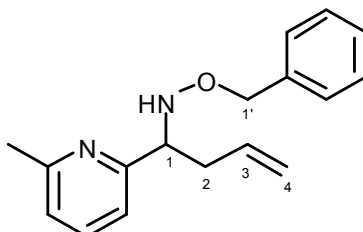
## (*E*)-6-Methylpicolinaldehyde *O*-benzyl oxime **42**



6-Methyl-2-pyridine carboxaldehyde (1.00 g, 8.25 mmol) was subjected to general procedure **A** using ethanol and purified by flash column chromatography (gradient of 0–50% EtOAc in cyclohexane) to give the title compound **42** as a colourless oil (1.87 g, 100%).

$\nu_{\max}$  (thin film)/ $\text{cm}^{-1}$  2925w, 1586m, 1572m, 1496w, 1456s, 1366m, 1329w, 1248w, 1209w, 1155w, 1025s, 945s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.57 (3H, s, Me), 5.27 (2H, s, C(1')H<sub>2</sub>), 7.10–7.14 (1H, m, Ar), 7.30–7.45 (5H, m, Ph), 7.54–7.64 (2H, m, Ar), 8.23 (1H, s, C(1)H);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 24.7 (Me), 77.0 (C(1')), 118.4 (Ar), 123.9 (Ar), 128.3 (Ph), 128.6 (Ph), 128.7 (Ph), 136.9 (Ar), 137.7 (*i*-Ph), 150.4 (C(1)), 151.4 (*i*-Ar), 158.7 (*i*-Ar);  $m/z$  227 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}$  ( $\text{MH}^+$ ) requires 227.1179, found 227.1177 (+0.85 ppm).

## *O*-Benzyl-*N*-(1-(6-methylpyridin-2-yl)but-3-enyl)hydroxylamine **43**

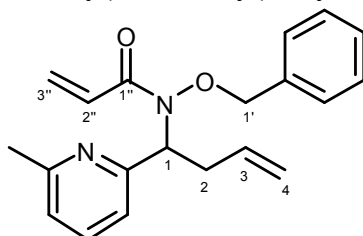


Oxime **42** (500 mg, 2.21 mmol) was subjected to general procedure **B** and purified by flash column chromatography (gradient of 0–25% EtOAc in cyclohexane) to give the title compound **43** as a colourless oil (500 mg, 84%).

$\nu_{\max}$  (thin film)/ $\text{cm}^{-1}$  2919m, 1640w, 1592s, 1576m, 1495w, 1455s, 1363m, 1207w, 1155w, 994s, 913s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.44–2.50 (2H, m, C(2)H<sub>2</sub>), 2.54 (3H, s, Me), 4.13 (1H, t,  $J$  7.0, C(1)H),

4.64 (1H, d,  $J$  11.0, C(1')H), 4.68 (1H, d,  $J$  11.0, C(1')H), 4.98–5.08 (2H, m, C(4)H<sub>2</sub>), 5.73 (1H, ddt,  $J$  17.5, 10.5, 7.0, C(3)H), 6.24 (1H, br s, NH), 7.02 (1H, d,  $J$  7.5, Ar), 7.09 (1H, d,  $J$  7.5, Ar), 7.24–7.34 (5H, m, Ph), 7.51 (1H, t,  $J$  7.5, Ar);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 24.5 (Me), 37.4 (C(2)), 65.8 (C(1)), 76.2 (C(1')), 117.4 (C(4)), 119.2 (Ar), 121.8 (Ar), 127.7 (Ph), 128.2 (Ph), 128.4 (Ph), 134.9 (C(3)), 136.3 (Ar), 135.0 (*i*-Ph), 158.0 (*i*-Ar), 160.5 (*i*-Ar);  $m/z$  269 (100%, MH<sup>+</sup>); HRMS (ESI) C<sub>17</sub>H<sub>21</sub>N<sub>2</sub>O (MH<sup>+</sup>) requires 269.1648, found 269.1645 (+1.33 ppm).

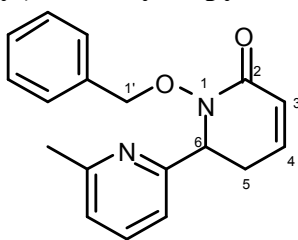
### ***N*-(Benzyloxy)-*N*-(1-(6-methylpyridin-2-yl)but-3-enyl)acrylamide 26c**



Amine **43** (480 mg, 1.79 mmol) was subjected to general procedure **C** and purified by flash column chromatography (gradient of 0–50% EtOAc in cyclohexane) to give the title compound **26c** as a colourless oil (544 mg, 94%).

$\nu_{\text{max}}$  (thin film)/cm<sup>-1</sup> 3066w, 2924w, 1658s, 1619m, 1591m, 1576m, 1455s, 1410s, 1372m, 1313m, 1259m, 1156w, 986s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.57 (3H, s, Me), 2.96–3.16 (2H, m, C(2)H<sub>2</sub>), 4.68 (1H, d,  $J$  10.0, C(1')H), 4.73 (1H, d,  $J$  10.0, C(1')H), 5.03–5.07 (1H, m, C(4)H), 5.16 (1H, ddd,  $J$  17.0, 3.0, 1.5, C(4)H), 5.69–5.76 (1H, m, C(1)H), 5.74 (1H, dd,  $J$  11.0, 2.0, C(3'')H), 5.84 (1H, ddt,  $J$  17.0, 10.5, 7.0, C(3)H), 6.45 (1H, dd,  $J$  17.0, 2.0, C(3'')H), 6.77 (1H, dd,  $J$  17.0, 11.0, C(2'')H), 7.07 (1H, d,  $J$  7.5, Ar), 7.28 (1H, d,  $J$  7.5, Ar), 7.30–7.39 (5H, m, Ph), 7.56 (1H, t,  $J$  7.5, Ar);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 24.5 (Me), 34.2 (C(2)), 62.8 (C(1)), 79.1 (C(1')), 117.7 (C(4)), 120.5 (Ar), 122.1 (Ar), 126.8 (C(2'')), 128.5 (Ph), 128.7 (Ph), 129.0 (Ph), 129.3 (C(3'')), 134.7 (*i*-Ph), 134.9 (C(3)), 136.7 (Ar), 157.6 (*i*-Ar), 157.8 (*i*-Ar), 167.5 (C(1''));  $m/z$  323 (100%, MH<sup>+</sup>), 215 (20%); HRMS (ESI) C<sub>20</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> (MH<sup>+</sup>) requires 323.1754, found 323.1749 (+1.44 ppm).

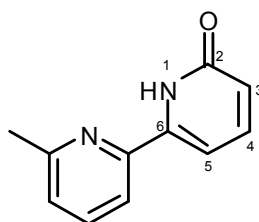
### **1-(Benzyloxy)-6-(6-methylpyridin-2-yl)-5,6-dihydropyridin-2(1*H*)-one 27c**



Amide **26c** (200 mg, 0.62 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in toluene at 95 °C and purified by flash column chromatography (gradient of 0–100% EtOAc in cyclohexane) to give the title compound **27c** as a brown oil (168 mg, 92%).

$\nu_{\text{max}}$  (thin film)/cm<sup>-1</sup> 2943w, 1680s, 1620m, 1593m, 1575m, 1458m, 1419w, 1388m, 1317w, 1205w, 1079w, 992w;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.51 (3H, s, Me), 2.78 (1H, app ddt,  $J$  18.5, 7.5, 3.0, C(5)H), 2.99–3.02 (1H, m, C(5)H), 4.62 (1H, dd,  $J$  7.5, 3.5, C(6)H), 4.96 (1H, d,  $J$  11.0, C(1')H), 5.05 (1H, d,  $J$  11.0, C(1')H), 5.92 (1H, ddd,  $J$  10.0, 3.0, 1.0, C(3)H), 6.30 (1H, ddd,  $J$  10.0, 5.0, 3.0, C(4)H), 7.04 (1H, d,  $J$  7.5, Ar), 7.06 (1H, d,  $J$  7.5, Ar), 7.31–7.35 (5H, m, Ph), 7.52 (1H, t,  $J$  7.5, Ar);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 24.4 (Me), 32.2 (C(5)), 64.5 (C(6)), 77.3 (C(1')), 118.4 (Ar), 122.1 (Ar), 124.7 (C(3)), 128.4 (Ph), 128.6 (Ph), 129.7 (Ph), 135.5 (*i*-Ph), 136.8 (Ar), 138.3 (C(4)), 157.6 (*i*-Ar), 158.2 (*i*-Ar), 165.0 (C(2));  $m/z$  295 (100%, MH<sup>+</sup>), 187 (20%); HRMS (ESI) C<sub>18</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub> (MH<sup>+</sup>) requires 295.1441, found 295.1438 (+1.01 ppm).

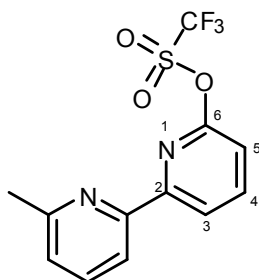
### 6-(6-Methylpyridin-2-yl)pyridin-2(1H)-one **28c**



Dihydropyridone **27c** (150 mg, 0.51 mmol) was subjected to general procedure **E** with heating to 50 °C and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **28c** as a white solid (60 mg, 63%).

m.p. 84–86 °C;  $\nu_{\text{max}}$  (KBr disk)/ $\text{cm}^{-1}$  3315w, 2925w, 1651s, 1602s, 1572m, 1375w, 1301w, 1235w, 1158w, 1100w, 994w;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.76 (3H, s, Me), 6.61 (1H, dd,  $J$  9.0, 1.0, C(3)H), 6.78 (1H, dd,  $J$  7.0, 1.0, C(5)H), 7.19 (1H, d,  $J$  7.5, Ar), 7.47 (1H, dd,  $J$  9.0, 7.0, C(4)H), 7.61 (1H, d,  $J$  7.5, Ar), 7.69 (1H, t,  $J$  7.5, Ar), 10.81 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 24.3 (Me), 102.6 (C(5)), 116.7 (Ar), 121.8 (C(3)), 124.2 (C(4)), 137.5 (Ar), 140.6 (Ar), 141.9, 146.9, 158.4 (C(6),  $i$ -Ar  $\times$  2), 162.9 (C(2));  $m/z$  187 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}$  ( $\text{MH}^+$ ) requires 187.0871, found 187.0872 (+0.50 ppm).

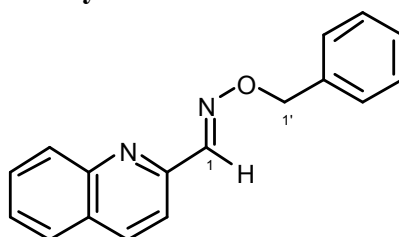
### 6'-Methyl-2,2'-bipyridin-6-yl trifluoromethanesulfonate **29c**



Pyridone **28c** (30 mg, 0.16 mmol) was subjected to general procedure **F** and purified by flash column chromatography (12:1 cyclohexane:EtOAc) to give the title compound **29c** as a colourless oil (45 mg, 88%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  2927w, 1591s, 1559s, 1427s, 1318w, 1214s, 1136s, 1087m, 1074m, 996m, 933s, 863s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.63 (3H, s, Me), 7.15 (1H, dd,  $J$  8.0, 1.0, C(5)H), 7.21 (1H, d,  $J$  8.0, Ar), 7.72 (1H, t,  $J$  8.0, Ar), 7.98 (1H, t,  $J$  8.0, C(4)H), 8.14 (1H, d,  $J$  8.0, Ar), 8.56 (1H, dd,  $J$  8.0, 1.0, C(3)H);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 24.5 (Me), 114.3 (C(5)), 118.5 (Ar), 118.7 (q,  $J_{\text{CF}}$  318.5,  $\text{CF}_3$ ), 121.0 (C(3)), 124.2 (Ar), 137.3 (Ar), 141.6 (C(4)), 153.1, 155.3, 156.2, 158.2 (C(2), C(6),  $i$ -Ar  $\times$  2);  $m/z$  319 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{12}\text{H}_9\text{F}_3\text{N}_2\text{NaO}_3\text{S}$  ( $\text{MNa}^+$ ) requires 341.0178, found 341.0178 (+1.62 ppm).

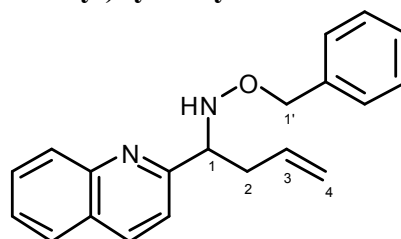
### (*E*)-Quinoline-2-carbaldehyde *O*-benzyl oxime **44**



2-Quinoline carboxaldehyde (800 mg, 5.10 mmol) was subjected to general procedure **A** using ethanol and purified by flash column chromatography (gradient of 0–25% EtOAc in cyclohexane) to give the title compound **44** as a white solid (1.05 g, 78%).

m.p. 50–53 °C;  $\nu_{\max}$  (KBr disk)/ $\text{cm}^{-1}$  2929m, 1599s, 1503s, 1454m, 1427m, 1367m, 1208w, 1200s, 942s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 5.33 (2H, s, C(1')H<sub>2</sub>), 7.32–7.50 (5H, m, Ph), 7.56 (1H, t,  $J$  8.0, Ar), 7.73 (1H, t,  $J$  8.0, Ar), 7.81 (1H, d,  $J$  8.0, Ar), 7.99 (1H, d,  $J$  8.0, Ar), 8.09 (1H, d,  $J$  8.0, Ar), 8.13 (1H, d,  $J$  8.0, Ar), 8.41 (1H, s, C(1)H);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 77.4 (C(1')), 118.6 (Ar), 127.6 (Ar), 128.1 (Ar), 128.5 (Ph), 128.6 (*i*-Ar), 128.8 (Ph), 128.9 (Ph), 129.9 (Ar), 130.2 (Ar), 136.7 (Ar), 137.7 (*i*-Ph), 148.4 (*i*-Ar), 150.8 (C(1)), 152.6 (*i*-Ar);  $m/z$  263 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}$  ( $\text{MH}^+$ ) requires 263.1179, found 263.1177 (+0.69 ppm).

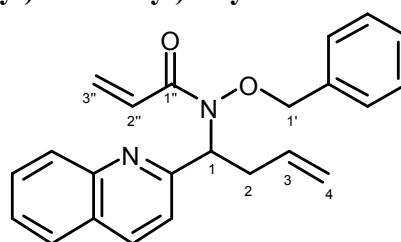
#### ***O*-Benzyl-*N*-(1-(quinolin-2-yl)but-3-enyl)hydroxylamine 45**



Oxime **44** (588 mg, 2.24 mmol) was subjected to general procedure **B** and purified by flash column chromatography (gradient of 0–25% EtOAc in cyclohexane) to give the title compound **45** as a colourless oil (307 mg, 45%).

$\nu_{\max}$  (thin film)/ $\text{cm}^{-1}$  2913w, 1599m, 1503s, 1454m, 1427m, 1362m, 1305w, 1208w, 987s, 915s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.51–2.65 (2H, m, C(2)H<sub>2</sub>), 4.38–4.45 (1H, m, C(1)H), 4.67 (1H, d,  $J$  12.0, C(1')H), 4.71 (1H, d,  $J$  12.0, C(1')H), 5.02–5.14 (2H, m, C(4)H<sub>2</sub>), 5.81 (1H, ddt,  $J$  17.0, 10.5, 7.0, C(3)H), 6.39 (1H, br s, NH), 7.23–7.32 (5H, m, Ph), 7.49 (1H, d,  $J$  8.0, Ar), 7.50–7.56 (1H, m, Ar), 7.69–7.74 (1H, m, Ar), 7.82 (1H, dd,  $J$  8.0, 1.0, Ar), 8.10–8.14 (2H, m, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 37.5 (C(2)), 66.3 (C(1)), 76.2 (C(1')), 117.8 (C(4)), 120.3 (Ar), 126.1 (Ar), 124.5 (Ar), 127.6 (*i*-Ar), 127.6 (Ph), 128.2 (Ph), 128.3 (Ph), 129.3 (Ar), 129.3 (Ar), 134.5 (C(3)), 136.2 (Ar), 137.9 (*i*-Ph), 147.8 (*i*-Ar), 161.9 (*i*-Ar);  $m/z$  305 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}$  ( $\text{MH}^+$ ) requires 305.1648, found 305.1646 (+0.83 ppm).

#### ***N*-(Benzyloxy)-*N*-(1-(quinolin-2-yl)but-3-enyl)acrylamide 26d**

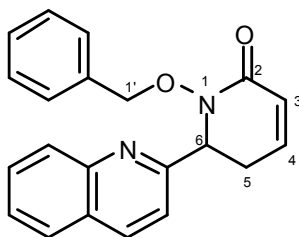


Amine **45** (238 mg, 0.78 mmol) was subjected to general procedure **C** and purified by flash column chromatography (gradient of 0–25% EtOAc in cyclohexane) to give the title compound **26d** as a colourless oil (249 mg, 89%).

$\nu_{\max}$  (thin film)/ $\text{cm}^{-1}$  3064w, 1657s, 1618m, 1600m, 1566w, 1502m, 1410s, 1356m, 1223m, 984m, 916m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.16–3.30 (2H, m, C(2)H<sub>2</sub>), 4.58 (1H, d,  $J$  9.5, C(1')H), 4.67 (1H, d,  $J$  9.5, C(1')H), 5.05–5.10 (1H, m, C(4)H), 5.18–5.25 (1H, m, C(4)H), 5.77 (1H, dd,  $J$  10.5, 2.0, C(3'')H), 5.91 (1H, ddt,  $J$  17.0, 10.0, 7.0, C(3)H), 5.99 (1H, t,  $J$  7.0, C(1)H), 6.49 (1H, dd,  $J$  17.0, 2.0, C(3'')H), 6.80 (1H, dd, 17.0, 10.5, C(2'')H), 7.24–7.32 (5H, m, Ph), 7.51–7.56 (1H, m, Ar), 7.62 (1H, d,  $J$  8.5, Ar), 7.69–7.74 (1H, m, Ar), 7.81 (1H, d,  $J$  8.5, Ar), 8.12 (1H, d,  $J$  8.5, Ar), 8.14 (1H, d,  $J$  8.5, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 34.2 (C(2)), 63.2 (C(1)), 79.7 (C(1')), 118.3 (C(4)), 122.1 (Ar), 127.0 (C(2'')), 127.9 (Ar), 127.9 (Ar), 128.0 (Ar), 129.0 (Ar), 129.9 (Ar), 129.2 (Ar), 129.5 (Ar), 129.9 (C(3'')), 130.1 (*i*-Ar), 134.8 (*i*-Ph), 135.3 (C(3)), 137.0 (Ar), 148.0 (*i*-Ar), 159.1 (*i*-Ar), 168.2

(C(1''));  $m/z$  359 (100%,  $MH^+$ ); HRMS (ESI)  $C_{23}H_{23}N_2O_2$  ( $MH^+$ ) requires 359.1754, found 359.1753 (+0.42 ppm).

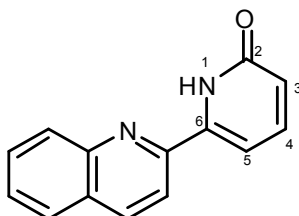
### 1-(Benzyloxy)-6-(quinolin-2-yl)-5,6-dihydropyridin-2(1H)-one **27d**



Amide **26d** (185 mg, 0.52 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in toluene at 95 °C and purified by flash column chromatography (gradient of 0–100% EtOAc in cyclohexane) to give the title compound **27d** as a brown oil (167 mg, 98%).

$\nu_{\max}$  (thin film)/ $cm^{-1}$  3060w, 1680s, 1618m, 1597m, 1503m, 1428m, 1391m, 1306m, 1135m, 1079m, 986m;  $\delta_H$  (400 MHz,  $CDCl_3$ ) 2.86 (1H, ddt,  $J$  18.5, 7.0, 3.0, C(5)H), 3.06–3.14 (1H, m, C(5)H), 4.82 (1H, dd,  $J$  7.0, 3.0, C(6)H), 4.96 (1H, d,  $J$  11.0, C(1')H), 5.05 (1H, d,  $J$  11.0, C(1')H), 5.93 (1H, dd,  $J$  10.0, 3.0, C(3)H), 6.31 (1H, ddd,  $J$  10.0, 5.5, 3.0, C(4)H), 7.24–7.31 (5H, m, Ph), 7.39 (1H, d,  $J$  8.5, Ar), 7.45–7.50 (1H, m, Ar), 7.63–7.68 (1H, m, Ar), 7.76 (1H, d,  $J$  7.5, Ar), 7.98 (1H, d,  $J$  8.5, Ar), 8.08 (1H, d,  $J$  8.5, Ar);  $\delta_C$  (100 MHz,  $CDCl_3$ ) 26.8 (C(5)), 65.0 (C(6)), 77.2 (C(1')), 119.2 (Ar), 124.7 (C(3)), 126.4 (Ar), 127.3 (*i*-Ar), 127.5 (Ar), 128.3 (Ar), 128.6 (Ar), 128.9 (Ar), 129.6 (Ar), 129.7 (Ar), 135.4 (*i*-Ar), 136.7 (Ar), 138.4 (C(4)), 147.6 (*i*-Ar), 159.1 (*i*-Ar), 165.1 (C(2));  $m/z$  331 (100%,  $MH^+$ ); HRMS (ESI)  $C_{21}H_{19}N_2O_2$  ( $MH^+$ ) requires 331.1441, found 331.1439 (+0.57 ppm).

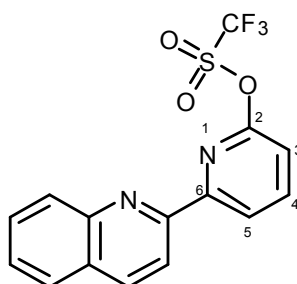
### 6-(Quinolin-2-yl)pyridin-2(1H)-one **28d**



Dihydropyridone **27d** (125 mg, 0.38 mmol) was subjected to general procedure **E** with heating to 50 °C and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **28d** as a white solid (60 mg, 71%).

m.p. 143–146 °C;  $\nu_{\max}$  (KBr disk)/ $cm^{-1}$  3314w, 1650s, 1604s, 1590s, 1506m, 1448m, 1291w, 1238w, 1146w, 997m, 805s;  $\delta_H$  (400 MHz,  $CDCl_3$ ) 6.68 (1H, d,  $J$  9.0, C(3)H), 6.93 (1H, d,  $J$  7.0, C(5)H), 7.51 (1H, dd,  $J$  9.0, 7.0, C(4)H), 7.58 (1H, t,  $J$  8.5, Ar), 7.73–7.78 (1H, m, Ar), 7.82 (1H, d,  $J$  8.5, Ar), 7.84 (1H, d,  $J$  8.5, Ar), 8.05 (1H, d,  $J$  8.5, Ar), 8.24 (1H, d,  $J$  8.5, Ar), 11.02 (1H, br s, NH);  $\delta_C$  (100 MHz,  $CDCl_3$ ) 104.6 (C(5)), 117.0 (Ar), 123.2 (C(3)), 128.0 (Ar), 128.2 (Ar), 128.6 (*i*-Ar), 129.9 (Ar), 131.1 (Ar), 138.0 (Ar), 141.0 (C(4)), 142.1, 147.4, 147.5 (C(6), *i*-Ar  $\times$  2), 163.3 (C(2));  $m/z$  223 (100%,  $MH^+$ ); HRMS (ESI)  $C_{14}H_{11}N_2O$  ( $MH^+$ ) requires 223.0866, found 223.0866 (+0.04 ppm).

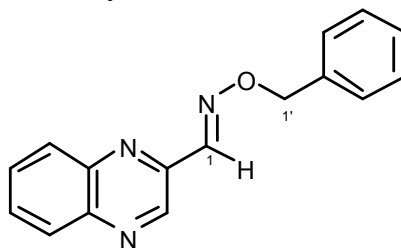
### 6-(Quinolin-2-yl)pyridin-2-yl trifluoromethanesulfonate **29d**



Pyridone **28d** (8 mg, 0.04 mmol) was subjected to general procedure **F** and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **29d** as a white solid (8 mg, 62%).

m.p. 102–105 °C;  $\nu_{\max}$  (KBr disk)/cm<sup>-1</sup> 2926w, 1603s, 1553m, 1503s, 1425s, 1217s, 1173m, 1132s, 1072m, 956s, 911s, 861s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 7.24 (1H, dd, *J* 8.0, 1.0, C(3)H), 7.60 (1H, ddd, *J* 8.0, 7.0, 1.0, Ar), 7.77 (1H, *J* 8.0, 7.0, 1.0, Ar), 7.88 (1H, dd, *J* 8.0, 1.0, Ar), 8.07 (1H, t, *J* 8.0, C(4)H), 8.15–8.19 (1H, m, Ar), 8.31 (1H, d, *J* 8.0, Ar), 8.48 (1H, d, *J* 8.0, Ar), 8.80 (1H, dd, *J* 8.0, 1.0, C(5)H);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 115.0 (C(3)), 118.7 (q, *J*<sub>CF</sub> 320.5, CF<sub>3</sub>), 118.8 (Ar), 121.7 (C(5)), 127.3 (Ar), 127.7 (Ar), 128.5 (*i*-Ar), 129.8 (Ar), 129.9 (Ar), 137.2 (Ar), 141.7 (C(4)), 148.7 (*i*-Ar), 153.7, 155.4, 156.1 (C(2), C(6), *i*-Ar); *m/z* 377 (40%, MNa<sup>+</sup>), 355 (100%, MH<sup>+</sup>); HRMS (ESI) C<sub>15</sub>H<sub>9</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub>S (MNa<sup>+</sup>) requires 377.0178, found 377.0179 (−0.33 ppm).

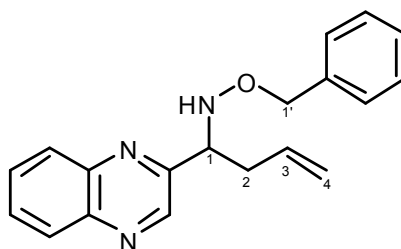
### (*E*)-Quinoxaline-2-carbaldehyde *O*-benzyl oxime **46**



2-Quinoxalinecarboxaldehyde (1.00 g, 6.32 mmol) was subjected to general procedure **A** using ethanol and purified by flash column chromatography (gradient of 0–25% EtOAc in cyclohexane) to give the title compound **46** as a white solid (1.60 g, 97%).

m.p. 100–103 °C;  $\nu_{\max}$  (KBr disk)/cm<sup>-1</sup> 2928w, 1613w, 1592w, 1552w, 1492m, 1454w, 1369w, 1321w, 1208w, 1126w, 1080w, 1020s;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 5.36 (2H, s, C(1')H<sub>2</sub>), 7.33–7.50 (5H, m, Ph), 7.75–7.80 (2H, m, Ar), 8.05–8.14 (2H, m, Ar), 8.38 (1H, s, C(1)H), 9.39 (1H, s, Ar);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 77.5 (C(1')), 128.3 (Ph), 128.6 (Ph), 128.6 (Ph), 129.4 (Ar), 129.4 (Ar), 130.3 (Ar), 130.4 (Ar), 136.8 (*i*-Ph), 142.0 (*i*-Ar), 142.3 (*i*-Ar), 143.2 (Ar), 146.8 (*i*-Ar), 148.4 (C(1)); *m/z* 264 (100%, MH<sup>+</sup>); HRMS (ESI) C<sub>16</sub>H<sub>14</sub>N<sub>3</sub>O (MH<sup>+</sup>) requires 264.1131, found 264.1128 (+1.32 ppm).

### *O*-Benzyl-*N*-(1-(quinoxalin-2-yl)but-3-enyl)hydroxylamine **47** and *N*-(Benzyloxy)-*N*-(1-(quinoxalin-2-yl)but-3-enyl)acrylamide **26e**

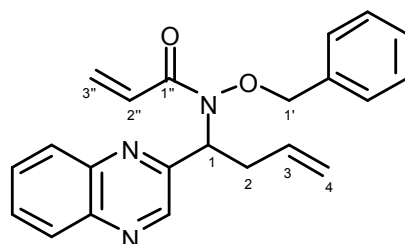


Indium powder (864 mg, 1.14 mmol) was added to a stirred solution of allyl bromide (1.63 mL, 18.8 mmol) in water (10 mL) at room temperature. After 30 minutes, oxime **46** (300 mg, 1.14 mmol) was



added to the grey slurry and the mixture was stirred for a further 4 h. The reaction was quenched with a sat. aq.  $\text{NH}_4\text{Cl}$  (50 mL) solution and stirred for 1 h. The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (20 mL  $\times$  4) and the combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ . The solvent was removed under reduced pressure and the crude product **47** was used immediately without further purification.

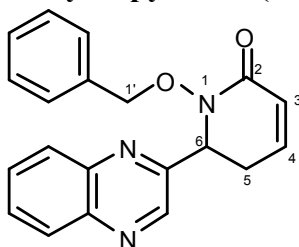
$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  2915w, 1640w, 1561w, 1493m, 1454w, 1435w, 1365m, 1295w, 1207w, 1126w, 990m, 918m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.63 (2H, app t,  $J$  7.0, C(2) $\text{H}_2$ ), 4.45 (1H, app q,  $J$  7.0, C(1)H), 4.65 (1H, d,  $J$  12.0, C(1')H), 4.70 (1H, d,  $J$  12.0, C(1')H), 5.06–5.15 (2H, m, C(4) $\text{H}_2$ ), 5.80 (1H, ddt,  $J$  17.0, 10.0, 7.0, C(3)H), 6.27 (1H, d,  $J$  7.0, NH), 7.22–7.31 (5H, m, Ph), 7.74–7.82 (2H, m, Ar), 8.08–8.15 (2H, m, Ar), 8.91 (1H, s, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 36.9 (C(2)), 64.4 (C(1)), 76.4 (C(1')), 118.5 (C(4)), 127.8 (Ph), 128.3 (Ph), 128.4 (Ph), 129.2 (Ar), 129.2 (Ar), 129.5 (Ar), 129.9 (Ar), 133.7 (C(3)), 137.5 (*i*-Ph), 142.1 (*i*-Ar), 142.1 (*i*-Ar), 145.1 (Ar), 156.6 (*i*-Ar);  $m/z$  306 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{19}\text{H}_{20}\text{N}_3\text{O}$  ( $\text{MH}^+$ ) requires 306.1601, found 306.1597 (+1.33 ppm).



Amine **47** was immediately subjected to general procedure **C** and purified by flash column chromatography (gradient of 0–50% EtOAc in cyclohexane) to give the title compound **26e** as a colourless oil (362 mg, 88% over two steps).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3066w, 1661s, 1619m, 1615w, 1493m, 1454w, 1410s, 1365m, 1241m, 1218m, 1126w, 985s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.13–3.25 (2H, m, C(2) $\text{H}_2$ ), 4.58 (1H, d,  $J$  10.0, C(1')H), 4.73 (1H, d,  $J$  10.0, C(1')H), 5.06–5.10 (1H, m, C(4)H), 5.20 (1H, ddd,  $J$  17.0, 3.0, 1.0, C(4)H), 5.78 (1H, dd,  $J$  10.5, 2.0, C(3''H)), 5.87 (1H, ddt,  $J$  17.0, 10.0, 6.5, C(3)H), 6.03 (1H, dd,  $J$  8.0, 7.0, C(1)H), 6.47 (1H, dd,  $J$  17.0, 2.0, C(3''H)), 6.76 (1H, dd,  $J$  17.0, 10.5, C(2''H)), 7.20–7.29 (5H, m, Ph), 7.72–7.79 (2H, m, Ar), 8.06–8.12 (2H, m, Ar), 8.98 (1H, s, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 33.4 (C(2)), 60.9 (C(1)), 79.7 (C(1')), 118.5 (C(4)), 126.3 (C(2'')), 128.6 (Ph), 128.9 (Ph), 128.9 (Ph), 129.3 (Ar), 129.4 (Ar), 129.9 (Ar), 130.1 (Ar), 130.2 (C(3'')), 134.1 (C(3)), 134.1 (*i*-Ph), 141.7 (*i*-Ar), 141.9 (*i*-Ar), 145.0 (Ar), 153.6 (*i*-Ar), 168.1 (C(1''));  $m/z$  360 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{22}\text{H}_{22}\text{N}_3\text{O}_2$  ( $\text{MH}^+$ ) requires 360.1707, found 360.1702 (+1.33 ppm).

### 1-(Benzyloxy)-6-(quinoxalin-2-yl)-5,6-dihydropyridin-2(1H)-one **27e**

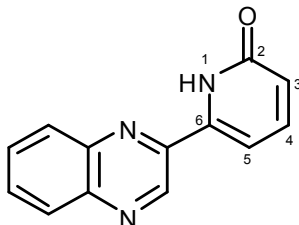


Amide **26e** (80 mg, 0.22 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in toluene at 95 °C and purified by flash column chromatography (gradient of 0–100% EtOAc in cyclohexane) to give the title compound **27e** as a brown oil (70 mg, 95%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3062w, 1689s, 1621w, 1493m, 1454w, 1369w, 1254w, 1211w, 1129w, 1079w, 992w;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.88 (1H, ddt,  $J$  18.5, 7.0, 3.0, C(5)H), 3.07 (1H, dtd,  $J$  18.5, 5.0, 1.0, C(5)H), 4.86 (1H, dd,  $J$  7.0, 5.0, C(6)H), 4.93 (1H, d,  $J$  11.0, C(1')H), 5.06 (1H, d,  $J$  11.0, C(1')H), 6.00 (1H, ddd,  $J$  10.0, 3.0, 1.0, C(3)H), 6.39 (1H, ddd,  $J$  10.0, 5.0, 3.0, C(4)H), 7.26–7.29 (5H, m,

Ph), 7.72–7.79 (2H, m, Ar), 7.99–8.04 (1H, m, Ar), 8.07–8.12 (1H, m, Ar), 8.83 (1H, s, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 31.9 (C(5)), 63.5 (C(6)), 77.6 (C(1')), 125.1 (C(3)), 128.4 (Ph), 128.7 (Ph), 129.2 (Ph), 129.3 (Ar), 129.6 (Ar), 130.0 (Ar), 130.3 (Ar), 135.3 (*i*-Ph), 138.1 (C(4)), 141.7 (*i*-Ar), 142.2 (*i*-Ar), 144.0 (Ar), 153.4 (*i*-Ar), 165.4 (C(2));  $m/z$  332 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{20}\text{H}_{18}\text{N}_3\text{O}_2$  ( $\text{MH}^+$ ) requires 332.1394, found 332.1391 (+0.66 ppm).

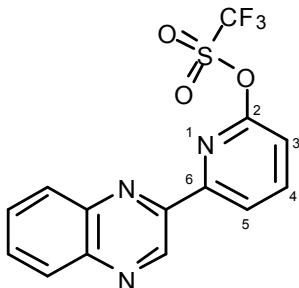
#### 6-(Quinoxalin-2-yl)pyridin-2(1H)-one **28e**



Dihydropyridone **27e** (49 mg, 0.17 mmol) was subjected to general procedure **E** with heating to 50 °C and purified by flash column chromatography (gradient of 0–10% MeOH in EtOAc) to give the title compound **28e** as a white solid (35 mg, 95%).

m.p. 193–196 °C;  $\nu_{\text{max}}$  (KBr disk)/ $\text{cm}^{-1}$  3005w, 2680w, 1664m, 1605m, 1575m, 1551m, 1448s, 1413m, 1370m, 1349m, 1271m, 1145w;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 6.77 (1H, dd,  $J$  9.5, 1.0, C(3)H), 7.12 (1H, dd,  $J$  7.0, 1.0, C(5)H), 7.58 (1H, dd,  $J$  9.5, 7.0, C(4)H), 7.81–7.89 (2H, m, Ar), 8.08–8.18 (2H, m, Ar), 9.35 (1H, s, Ar), 10.63 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 105.1 (C(5)), 124.1 (C(3)), 129.3 (Ar), 129.4 (Ar), 131.1 (Ar), 131.4 (Ar), 139.7, 140.3 (C(4)), 140.9, 141.4 (Ar), 142.3, 142.5 (C(6), *i*-Ar  $\times$  3), 162.6 (C(2));  $m/z$  224 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{13}\text{H}_{10}\text{N}_3\text{O}$  ( $\text{MH}^+$ ) requires 224.0824, found 224.0827 (+1.30 ppm).

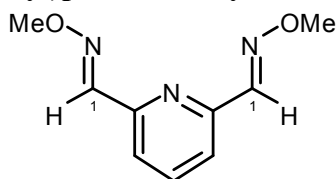
#### 6-(Quinoxalin-2-yl)pyridin-2-yl trifluoromethanesulfonate **29e**



Pyridone **28e** (25 mg, 0.11 mmol) was subjected to general procedure **F** and purified by flash column chromatography (10:1 petrol:EtOAc) to give the title compound **29e** as a white solid (28 mg, 70%).

m.p. 105–108 °C;  $\nu_{\text{max}}$  (KBr disk)/ $\text{cm}^{-1}$  2990w, 2938w, 1642m, 1423s, 1381m, 1320m, 1226s, 1132s, 977s, 924s, 870s;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 7.31 (1H, dd,  $J$  8.0, 1.0, C(3)H), 7.81–7.85 (2H, m, Ar), 8.11 (1H, t,  $J$  8.0, C(4)H), 8.14–8.20 (2H, m, Ar), 8.72 (1H, dd,  $J$  8.0, 1.0, C(5)H), 9.84 (1H, s, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 115.9 (C(3)), 118.7 (q,  $J_{\text{CF}}$  321.0,  $\text{CF}_3$ ), 122.0 (C(5)), 129.4 (Ar), 129.7 (Ar), 130.5 (Ar), 130.8 (Ar), 141.6, 142.0 (C(4)), 142.9, 143.7 (Ar), 147.8, 154.2, 155.4 (C(2), C(6), *i*-Ar  $\times$  3);  $m/z$  356 (100%,  $\text{MH}^+$ ); HRMS (ESI)  $\text{C}_{14}\text{H}_8\text{F}_3\text{N}_3\text{NaO}_3\text{S}$  ( $\text{MNa}^+$ ) requires 378.0131, found 378.0129 (+0.51 ppm).

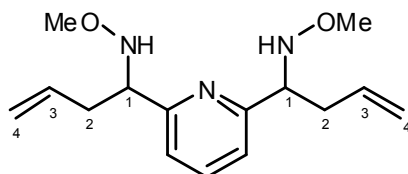
**(1*E*,1*E*)-6-((*E*)-(Methoxyimino)methyl)picolinaldehyde *O*-methyl oxime 30**



Pyridine (1.32 mL, 16.3 mmol) was added drop-wise to a stirred solution of *O*-methylhydroxylamine hydrochloride (1.61 g, 19.3 mmol) and 2,6-pyridine cardoxaldehyde (1.00 g, 7.41 mmol) in ethanol (30 mL) and the mixture was heated at reflux for 4 h. The solvent was removed under reduced pressure, and the remaining solid residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) and washed with water (50 mL). The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (50 mL × 3) and the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (20:1 petrol:EtOAc) to give the title compound **30** as a white solid (1.35 g, 94%).

m.p. 53–56 °C;  $\nu_{\max}$  (KBr disk)/cm<sup>-1</sup> 2937m, 1599w, 1569m, 1458m, 1323w, 1184w, 1153w, 1058s, 954w, 918s, 808w;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 3.99 (6H, s, OMe × 2), 7.63–7.76 (3H, m, Ar), 8.13 (2H, s, C(1)H × 2);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 62.4 (OMe), 120.9 (Ar), 136.7 (Ar), 148.9 (C(1)), 151.6 (*i*-Ar);  $m/z$  216 (100%, MNa<sup>+</sup>), 194 (90%, MH<sup>+</sup>), 163 (20%), 137 (20%); HRMS (ESI) C<sub>9</sub>H<sub>11</sub>N<sub>3</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) requires 216.0743, found 216.0743 (+0.31 ppm).

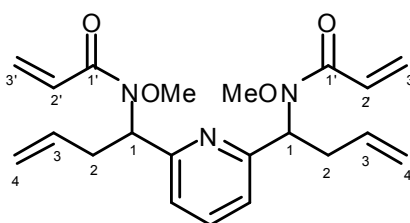
***N,N*-(1,1'-(Pyridine-2,6-diyl)bis(but-3-ene-1,1-diyl))bis(*O*-methylhydroxylamine) 31**



Oxime **30** (300 mg, 1.55 mmol) was subjected to general procedure **B** and purified by flash column chromatography (4:1 petrol:EtOAc) to give the title compound **31** as a colourless oil (431 mg, 52%) and as a single diastereoisomer (which was unassigned).

$\nu_{\max}$  (thin film)/cm<sup>-1</sup> 3075m, 2978m, 2937m, 2808m, 1640m, 1592m, 1575m, 1440m, 1155m, 994m;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.50 (4H, tt,  $J$  7.0, 1.0, C(2)H<sub>2</sub> × 2), 3.48 (6H, s, OMe × 2), 4.17 (2H, t,  $J$  7.0, C(1)H × 2), 4.99–5.08 (4H, m, C(4)H<sub>2</sub> × 2), 5.74 (2H, ddt,  $J$  17.0, 10.0, 7.0, C(3)H × 2), 6.13 (2H, br s, NH × 2), 7.19 (2H, d,  $J$  7.5, Ar × 2), 7.61 (1H, t,  $J$  7.5, Ar);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 37.3 (C(2)), 61.8 (OMe), 65.1 (C(1)), 117.5 (C(4)), 121.0 (Ar), 134.6 (C(3)), 136.5 (Ar), 160.5 (*i*-Ar);  $m/z$  278 (100%, MH<sup>+</sup>), 248 (50%), 231 (30%); HRMS (ESI) C<sub>15</sub>H<sub>24</sub>N<sub>3</sub>O<sub>2</sub> (MH<sup>+</sup>) requires 278.1863, found 278.1863 (−0.09 ppm).

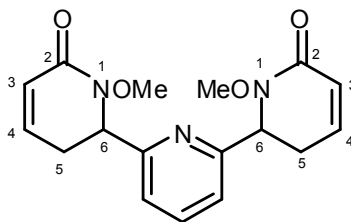
***N,N*-(1,1'-(Pyridine-2,6-diyl)bis(but-3-ene-1,1-diyl))bis(*N*-methoxyacrylamide) 32**



Amine **31** (276 mg, 1.00 mmol) was subjected to general procedure **C** and purified by flash column chromatography (4:1 petrol:EtOAc) to give the title compound **32** as a colourless oil (288 mg, 84%) and as a single diastereoisomer (which was unassigned).

$\nu_{\max}$  (thin film)/ $\text{cm}^{-1}$  2938w, 1726w, 1660s, 1616w, 1410s, 1362w, 1246w, 987m, 918w, 786w;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.97–3.03 (4H, m,  $\text{C}(2)\text{H}_2 \times 2$ ), 3.54 (6H, s,  $\text{OMe} \times 2$ ), 5.03–5.08 (2H, m,  $\text{C}(4)\text{H} \times 2$ ), 5.16 (2H, ddd,  $J$  17.0, 3.0, 1.5,  $\text{C}(4)\text{H} \times 2$ ), 5.71 (2H, t,  $J$  7.5,  $\text{C}(1)\text{H} \times 2$ ), 5.79 (2H, dd,  $J$  10.0, 2.0,  $\text{C}(3')\text{H} \times 2$ ), 5.82 (2H, ddt,  $J$  17.0, 10.0, 7.0,  $\text{C}(3)\text{H} \times 2$ ), 6.45 (2H, dd,  $J$  17.0, 2.0,  $\text{C}(3')\text{H} \times 2$ ), 6.72 (2H, dd,  $J$  17.0, 10.0,  $\text{C}(2')\text{H} \times 2$ ), 7.32 (2H, d,  $J$  8.0, Ar), 7.63 (1H, t,  $J$  8.0, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 33.7 ( $\text{C}(2)$ ), 61.7 ( $\text{C}(1)$ ), 65.0 ( $\text{OMe}$ ), 117.7 ( $\text{C}(4)$ ), 122.3 (Ar), 126.4 ( $\text{C}(2')$ ), 129.7 ( $\text{C}(3')$ ), 134.7 ( $\text{C}(3)$ ), 137.2 (Ar), 157.3 (*i*-Ar), 167.3 ( $\text{C}(1')$ );  $m/z$  408 (100%,  $\text{MNa}^+$ ), 386 (70%,  $\text{MH}^+$ ), 355 (40%); HRMS (ESI)  $\text{C}_{21}\text{H}_{27}\text{N}_3\text{NaO}_4$  ( $\text{MNa}^+$ ) requires 408.1894, found 408.1893 (+0.29 ppm).

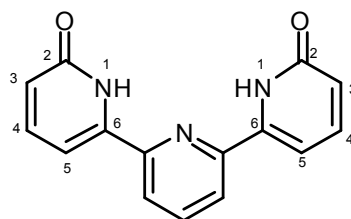
### 6,6-(Pyridine-2,6-diyl)bis(1-methoxy-5,6-dihydropyridin-2(1*H*)-one) **48**



Amide **32** (117 mg, 0.30 mmol) was subjected to general procedure **D** using 10 mol% Hoveyda-Grubbs second generation catalyst in  $\text{CH}_2\text{Cl}_2$  at 40 °C and purified by flash column chromatography (1:1 EtOAc:acetone) to give the title compound **48** as a colourless oil (100 mg, 100%) and as a single diastereoisomer (which was unassigned).

$\nu_{\max}$  (thin film)/ $\text{cm}^{-1}$  2936m, 1682s, 1620m, 1457m, 1315m, 1136m, 1086m, 995m, 913m, 859m, 809m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.93–3.08 (4H, m,  $\text{C}(5)\text{H}_2 \times 2$ ), 3.75 (6H, s,  $\text{OMe} \times 2$ ), 5.01 (2H, dd,  $J$  7.0, 3.5,  $\text{C}(6)\text{H} \times 2$ ), 5.86 (2H, dd,  $J$  9.5, 1.5,  $\text{C}(3)\text{H} \times 2$ ), 6.28 (2H, ddd,  $J$  9.5, 5.0, 3.0,  $\text{C}(4)\text{H} \times 2$ ), 7.11 (2H, d,  $J$  8.0, Ar), 7.58 (1H, t,  $J$  8.0, Ar);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 32.5 ( $\text{C}(5)$ ), 62.6 ( $\text{C}(6)$ ), 62.8 ( $\text{OMe}$ ), 120.3 (Ar), 124.6 ( $\text{C}(3)$ ), 137.4 (Ar), 138.1 ( $\text{C}(4)$ ), 157.8 (*i*-Ar), 165.1 ( $\text{C}(2)$ );  $m/z$  352 (90%,  $\text{MNa}^+$ ), 330 (100%,  $\text{MH}^+$ ), 300 (40%); HRMS (ESI)  $\text{C}_{17}\text{H}_{19}\text{N}_3\text{NaO}_4$  ( $\text{MNa}^+$ ) requires 352.1268, found 352.1268 (−0.24 ppm).

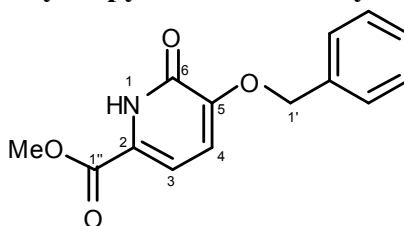
### 6,6-(Pyridine-2,6-diyl)dipyridin-2(1*H*)-one **33**



Dihydropyridone **48** (96 mg, 0.29 mmol) was subjected to general procedure **E** with heating to 50 °C and purified by flash column chromatography (50:45:5 *i*-PrOH:EtOAc:20% aq.  $\text{NH}_3$  solution) to give the title compound **33** as a white solid (43 mg, 56%).

m.p. >350 °C;  $\nu_{\max}$  (KBr disk)/ $\text{cm}^{-1}$  3444w, 1652s, 1588s, 1469m, 1246w, 1164w, 988m, 930w, 790s, 618w;  $\delta_{\text{H}}$  (400 MHz, DMSO) 6.52 (2H, d,  $J$  9.0,  $\text{C}(3)\text{H} \times 2$ ), 7.10 (2H, d,  $J$  7.0,  $\text{C}(5)\text{H} \times 2$ ), 7.61 (2H, dd,  $J$  9.0, 7.0,  $\text{C}(4)\text{H} \times 2$ ), 8.06–8.22 (3H, m, Ar);  $\delta_{\text{C}}$  (100 MHz, DMSO) 104.5 ( $\text{C}(5)$ ), 121.6 ( $\text{C}(3)$ ), 121.6 (Ar), 139.3 (Ar), 140.8 ( $\text{C}(4)$ ), 142.7, 148.9 ( $\text{C}(6)$ , *i*-Ar), 163.0 ( $\text{C}(2)$ );  $m/z$  288 (40%,  $\text{MNa}^+$ ), 266 (40%,  $\text{MH}^+$ ), 191 (100%), 170 (100%), 149 (80%), 127 (50%); HRMS (ESI)  $\text{C}_{15}\text{H}_{11}\text{N}_3\text{NaO}_2$  ( $\text{MNa}^+$ ) requires 288.0743, found 288.0744 (−0.32 ppm).

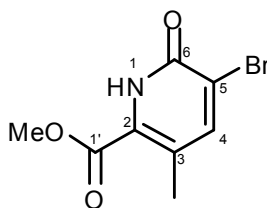
### Methyl 5-(benzyloxy)-6-oxo-1,6-dihydropyridine-2-carboxylate **35**



Bromine (188  $\mu\text{L}$ , 1.35 mmol) was added drop-wise to a stirred solution of cyclic amide **10** (70 mg, 0.27 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) at 0  $^\circ\text{C}$ . Stirring was continued at room temperature for 1 h before removing the solvent under reduced pressure. The resulting residue was dissolved in THF (5 mL) and DBU (404  $\mu\text{L}$ , 2.77 mmol) was added drop-wise. The solution was stirred at room temperature for 16 h, before filtering through a plug of silica eluting with EtOAc to give the title compound **35** as a colourless oil (51 mg, 74%).

$\nu_{\text{max}}$  (thin film)/ $\text{cm}^{-1}$  3034w, 2955w, 1740s, 1674s, 1590m, 1546w, 1496w, 1436m, 1398w, 1279s, 1206m, 1132m, 1014w, 961w, 912w;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 3.86 (3H, s, OMe), 5.41 (2H, s, C(1')H<sub>2</sub>), 6.49 (1H, d,  $J$  6.5, C(3)H), 6.83 (1H, d,  $J$  6.5, C(4)H), 7.25–7.58 (5H, m Ph);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 53.2 (OMe), 78.6 (C(1')), 107.9 (C(3)), 126.0 (C(4)), 128.5 (Ph), 129.2 (Ph), 130.1 (Ph), 133.7, 137.2, 138.8 (C(2), C(5),  $i$ -Ph), 158.8, 160.4 (C(1''), C(6));  $m/z$  318 (100%,  $\text{MNH}_4^+\cdot\text{MeCN}$ ), 282 (70%,  $\text{MNa}^+$ ), 175 (50%); HRMS (ESI)  $\text{C}_{14}\text{H}_{14}\text{NO}_4$  ( $\text{MH}^+$ ) requires 260.0917, found 260.0916 (+0.48 ppm).

### Methyl 5-bromo-3-methyl-6-oxo-1,6-dihydropyridine-2-carboxylate **36**



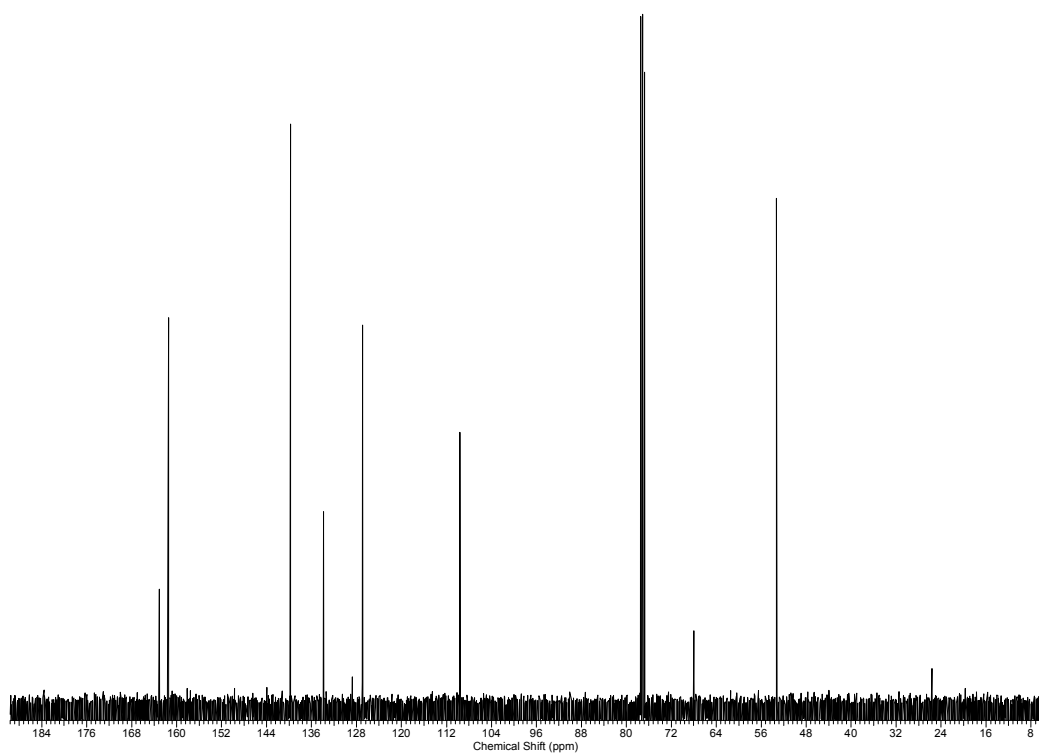
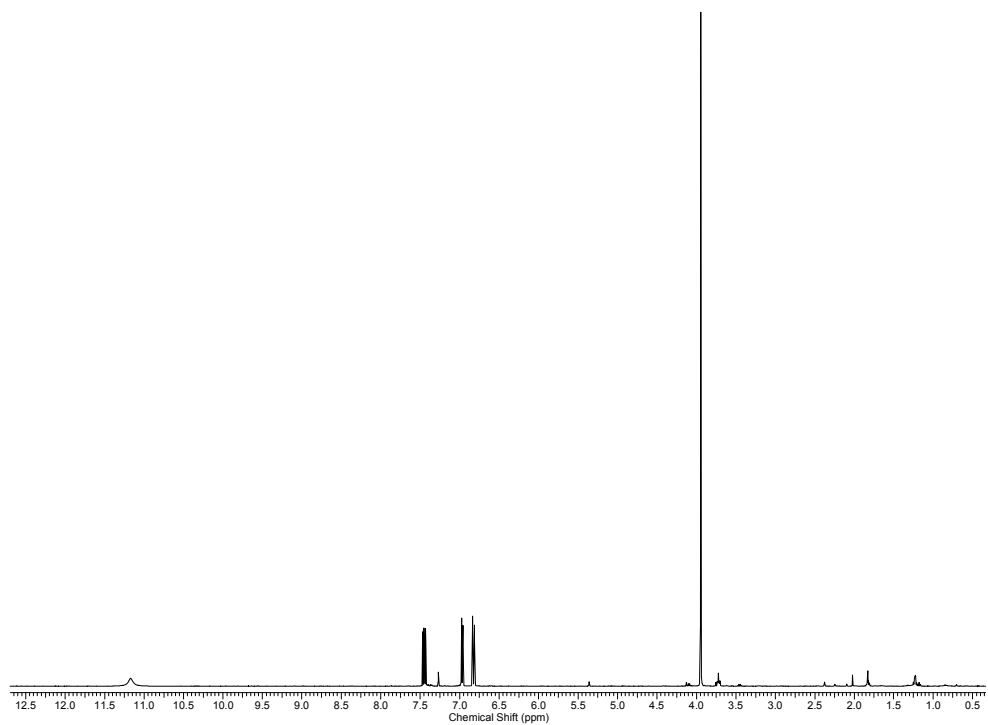
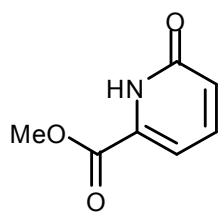
*N*-Bromosuccinimide (83 mg, 0.39 mmol) was added to a solution of pyridone **20a** (60 mg, 0.36 mmol) in MeCN (10 mL) and the mixture was heated at reflux for 3 h. The reaction mixture was cooled to room temperature, and the precipitate was filtered and washed with cold  $\text{CH}_2\text{Cl}_2$  to give the title compound **36** as a white solid (62 mg, 70%).

m.p. 186–188  $^\circ\text{C}$ ;  $\nu_{\text{max}}$  (KBr disk)/ $\text{cm}^{-1}$  2945m, 1727s, 1657s, 1434m, 1312m, 1277m, 1238w, 1116m, 951w, 896w, 800w;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 2.43 (3H, s, Me), 3.98 (3H, s, OMe), 7.75 (1H, s, C(4)H), 10.50 (1H, br s, NH);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 18.1 (Me), 53.2 (OMe), 121.9, 123.1 (C(3), C(5)), 129.1 (C(2)), 146.9 (C(4)), 157.9, 161.5 (C(1'), C(6));  $m/z$  246 (100%,  $\text{MH}^+$ ), 220 (70%), 218 (60%), 216 (50%); HRMS (ESI)  $\text{C}_8\text{H}_9\text{BrNO}_3$  ( $\text{MH}^+$ ) requires 245.9760, found 245.9762 (−0.75 ppm).

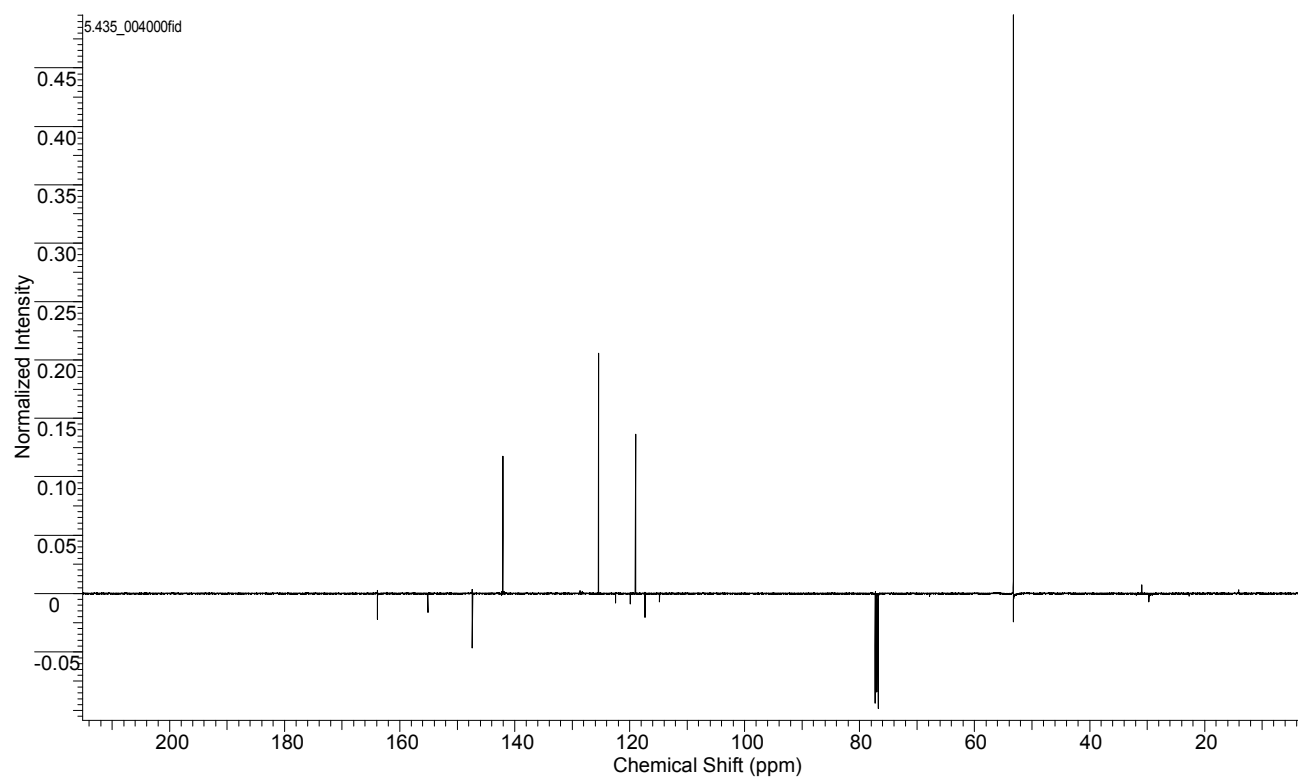
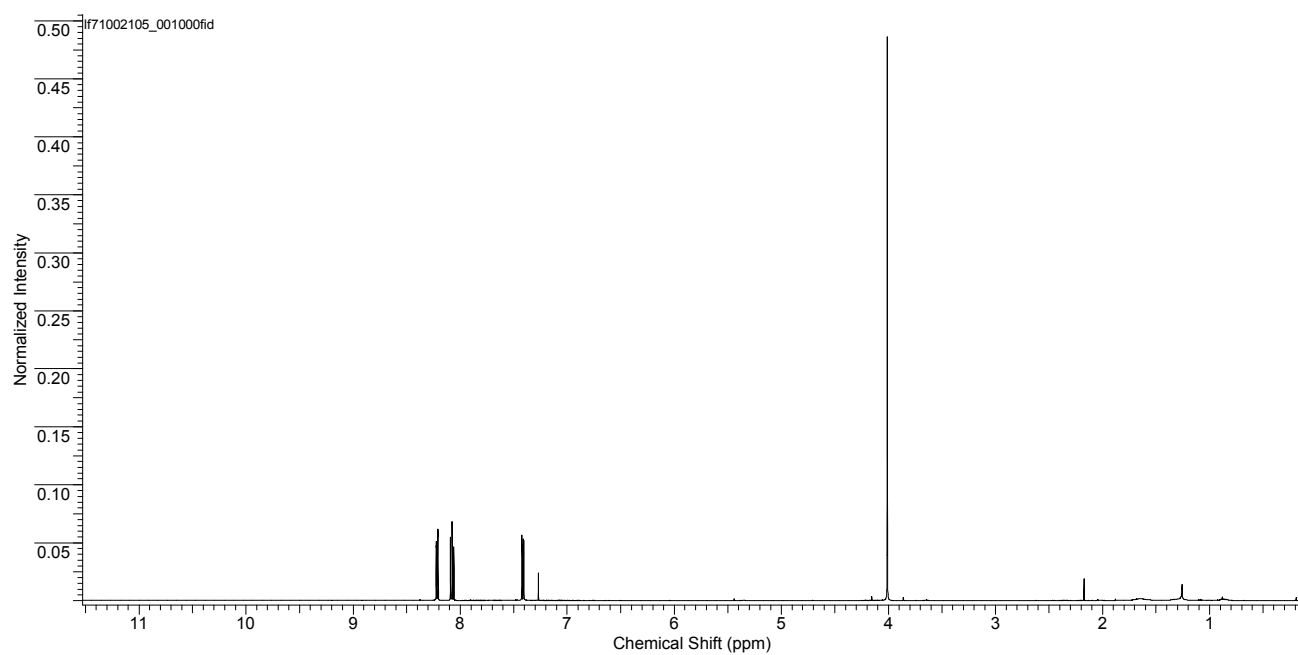
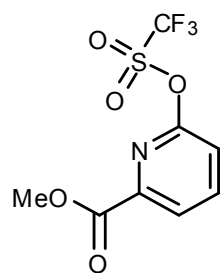
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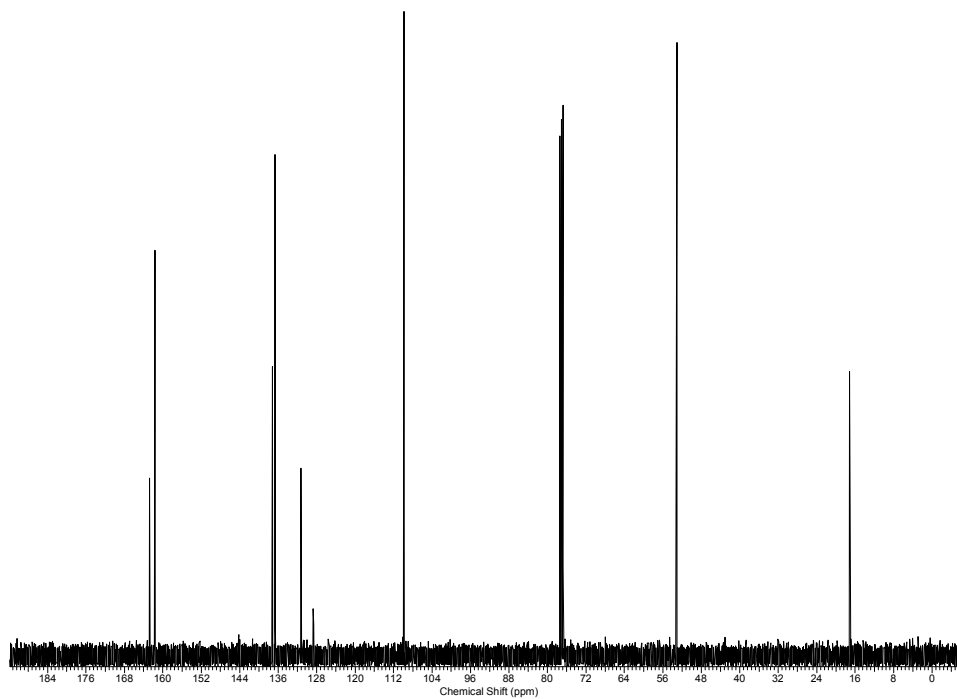
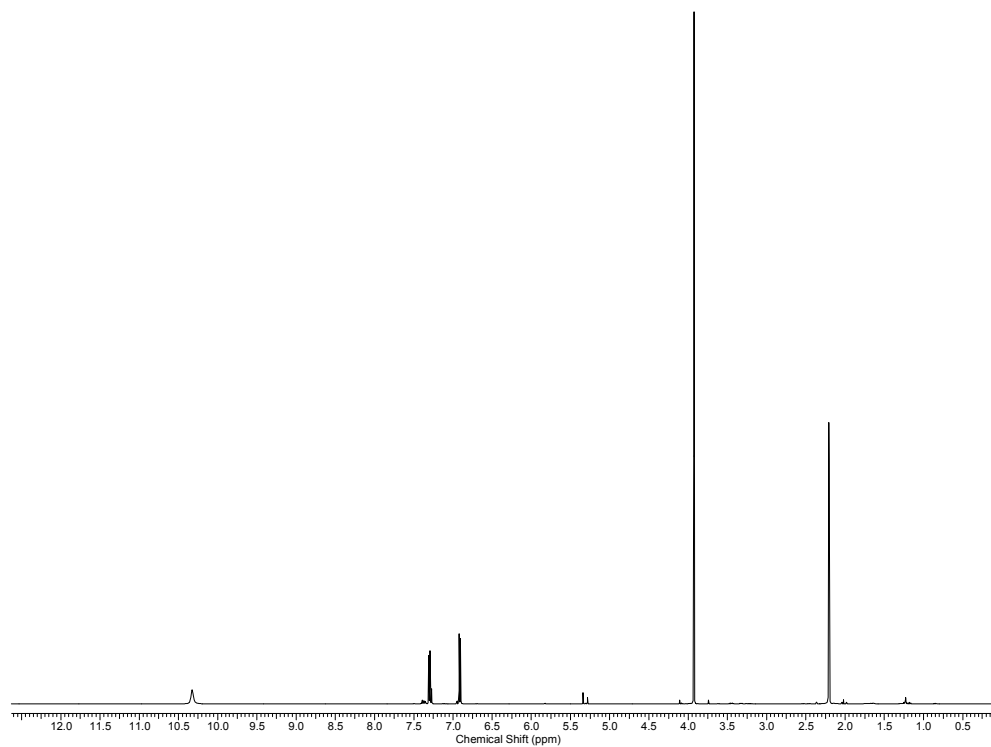
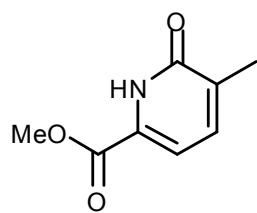
# Methyl 6-oxo-1,6-dihydropyridine-2-carboxylate 11



# Methyl 6-(trifluoromethylsulfonyloxy)picolinate 13

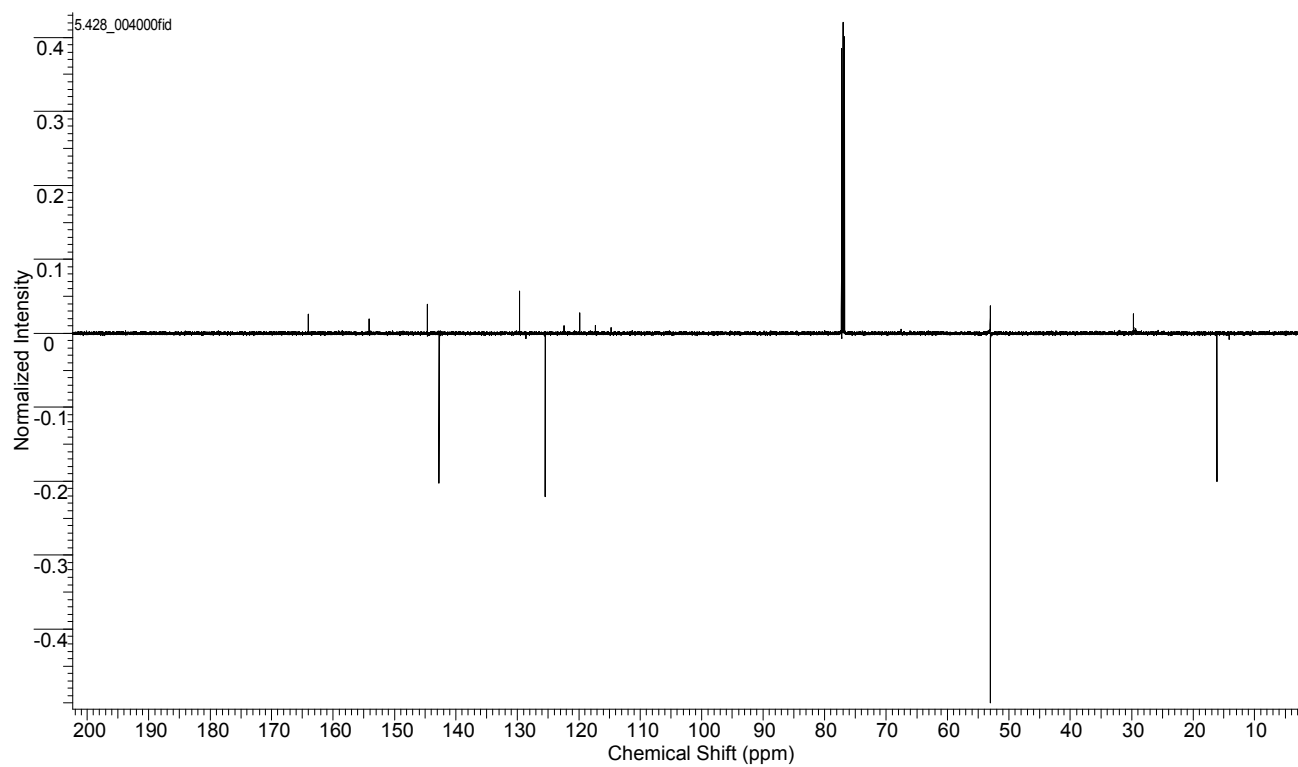
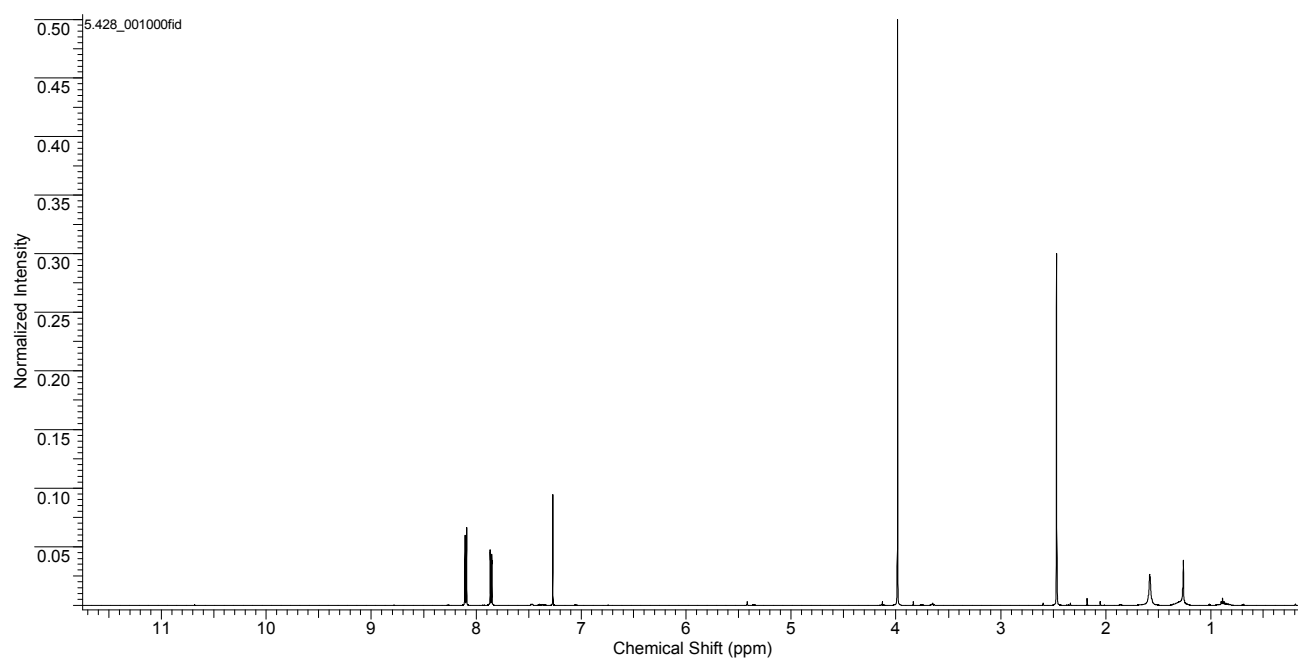
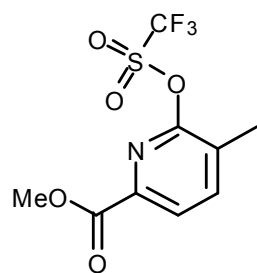


**Methyl 5-methyl-6-oxo-1,6-dihydropyridine-2-carboxylate 16a**

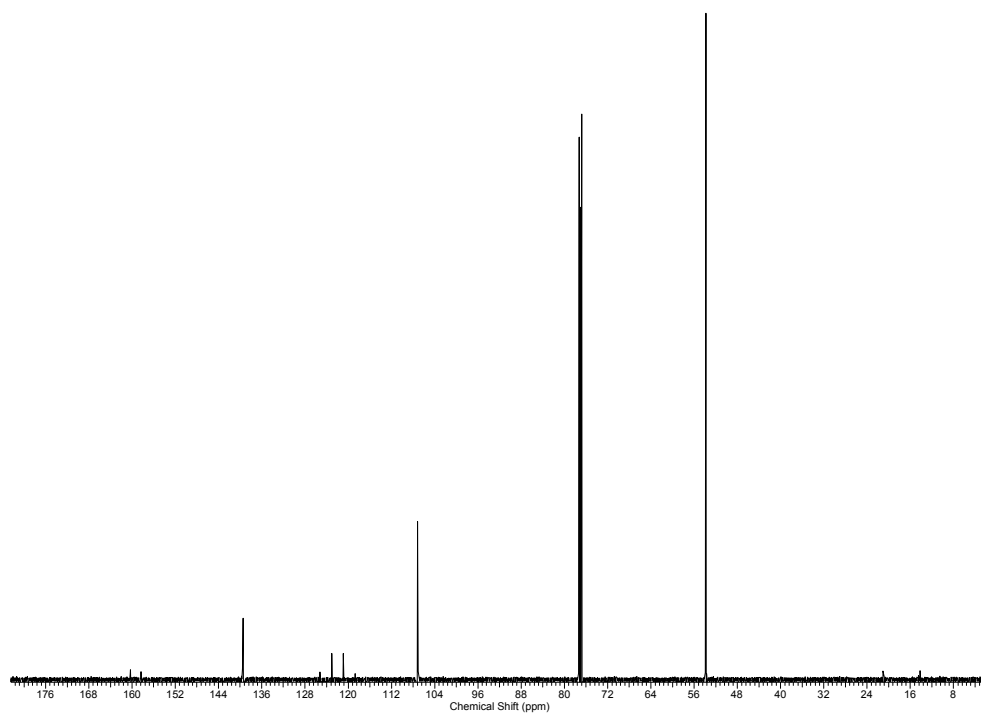
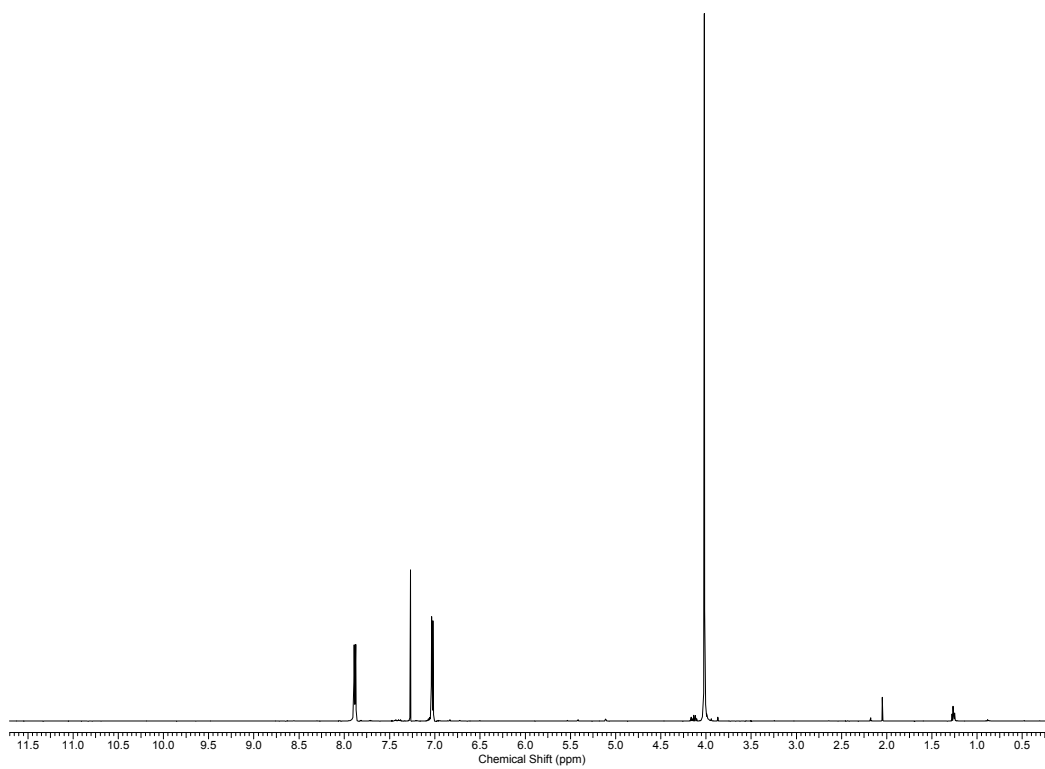
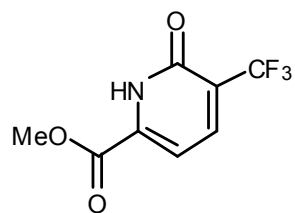




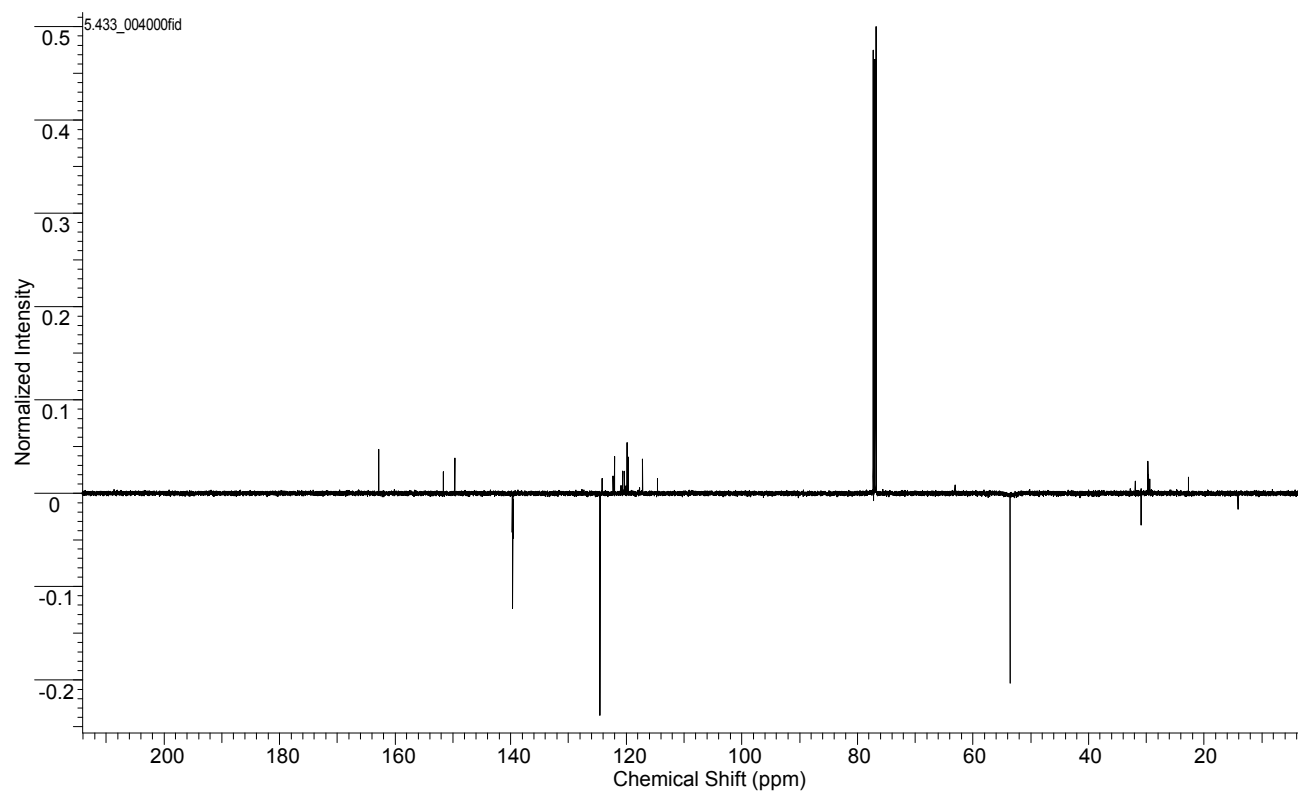
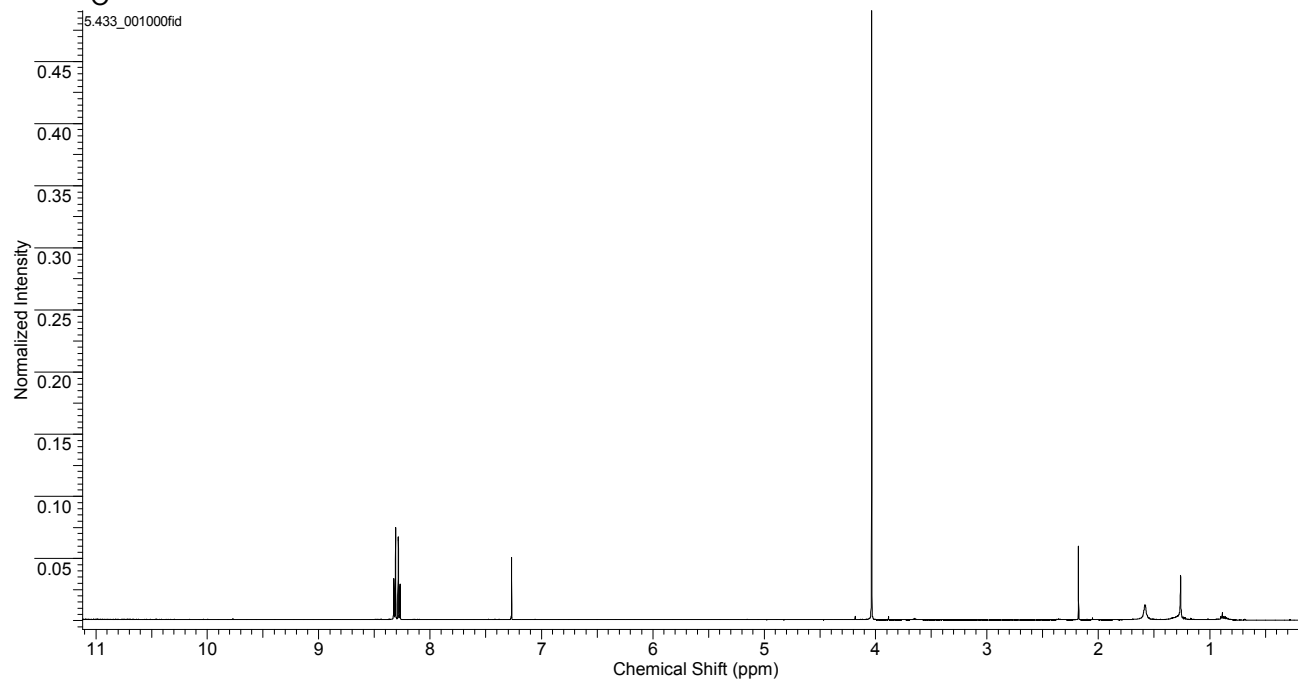
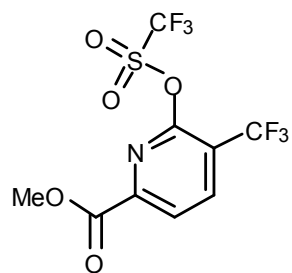
**Methyl 5-methyl-6-(trifluoromethylsulfonyloxy)picolinate 17a**



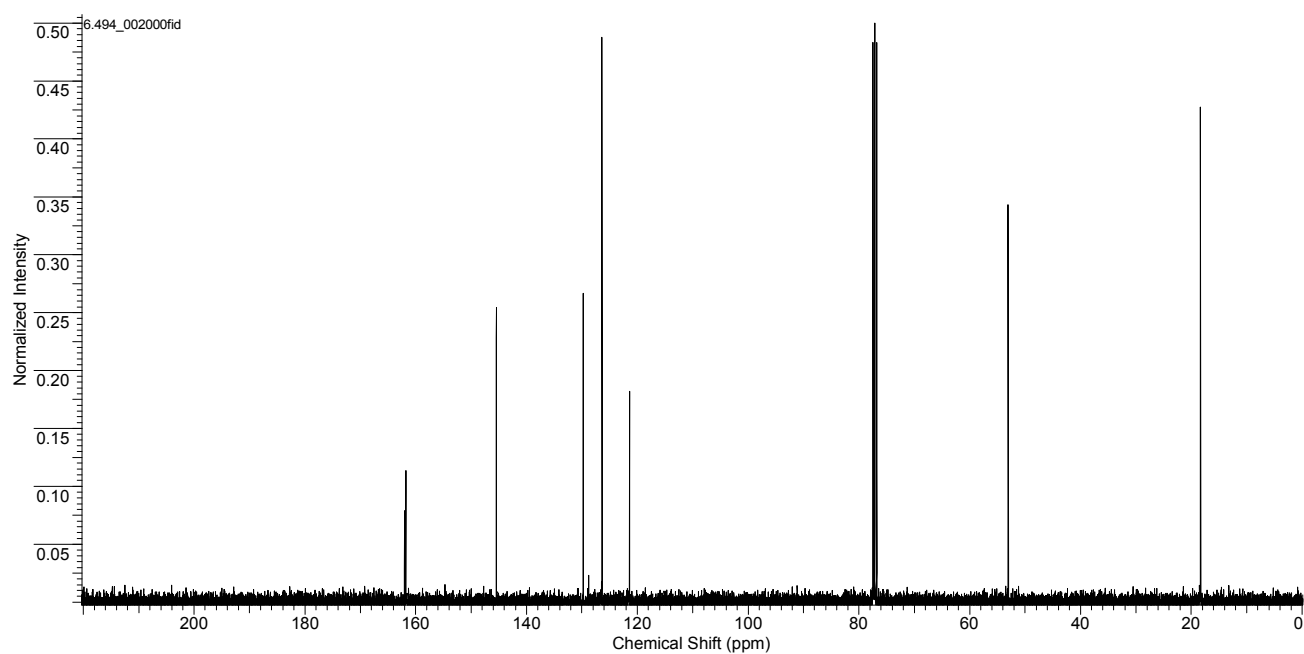
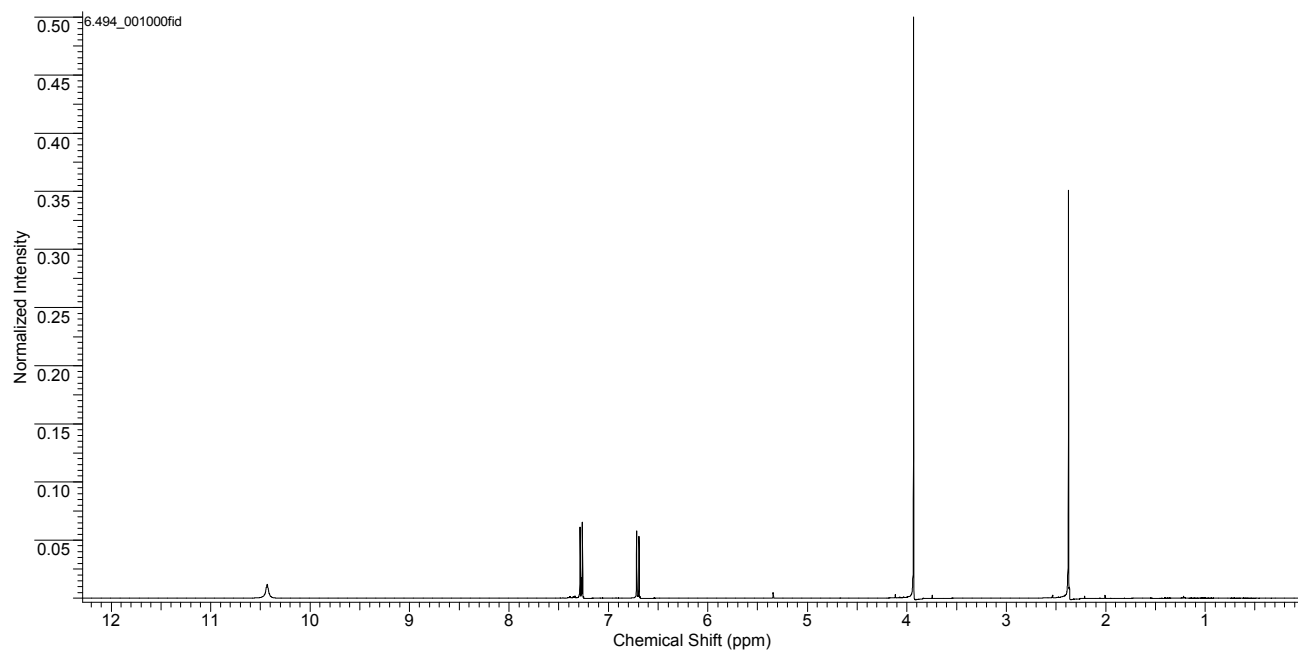
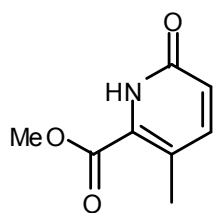
**Methyl 6-oxo-5-(trifluoromethyl)-1,6-dihydropyridine-2-carboxylate 16b**



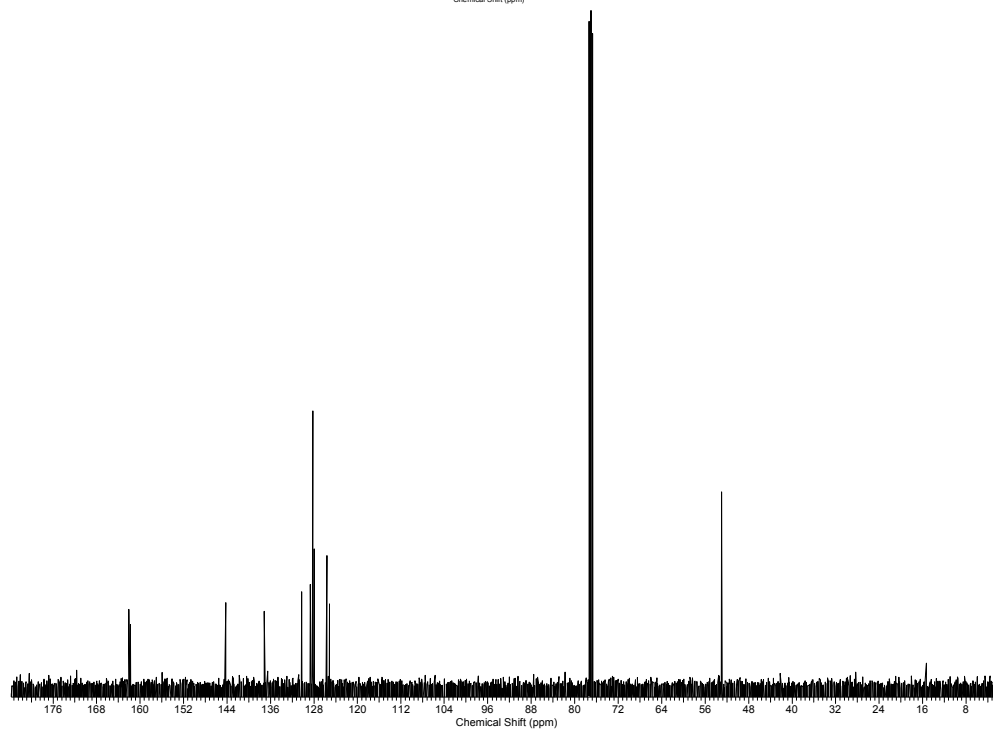
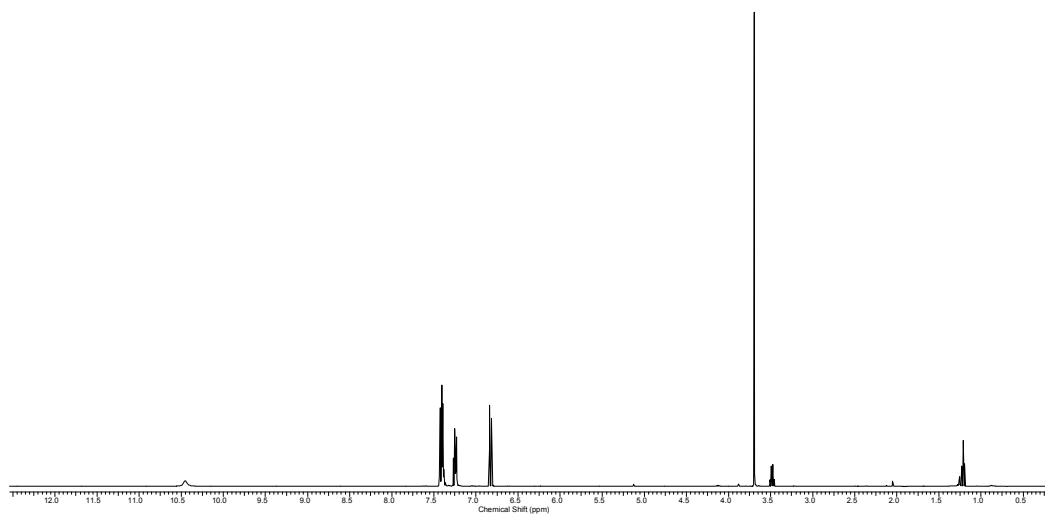
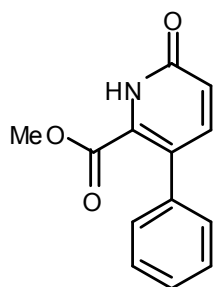
**Methyl 5-(trifluoromethyl)-6-(trifluoromethylsulfonyloxy)picolinate 17b**



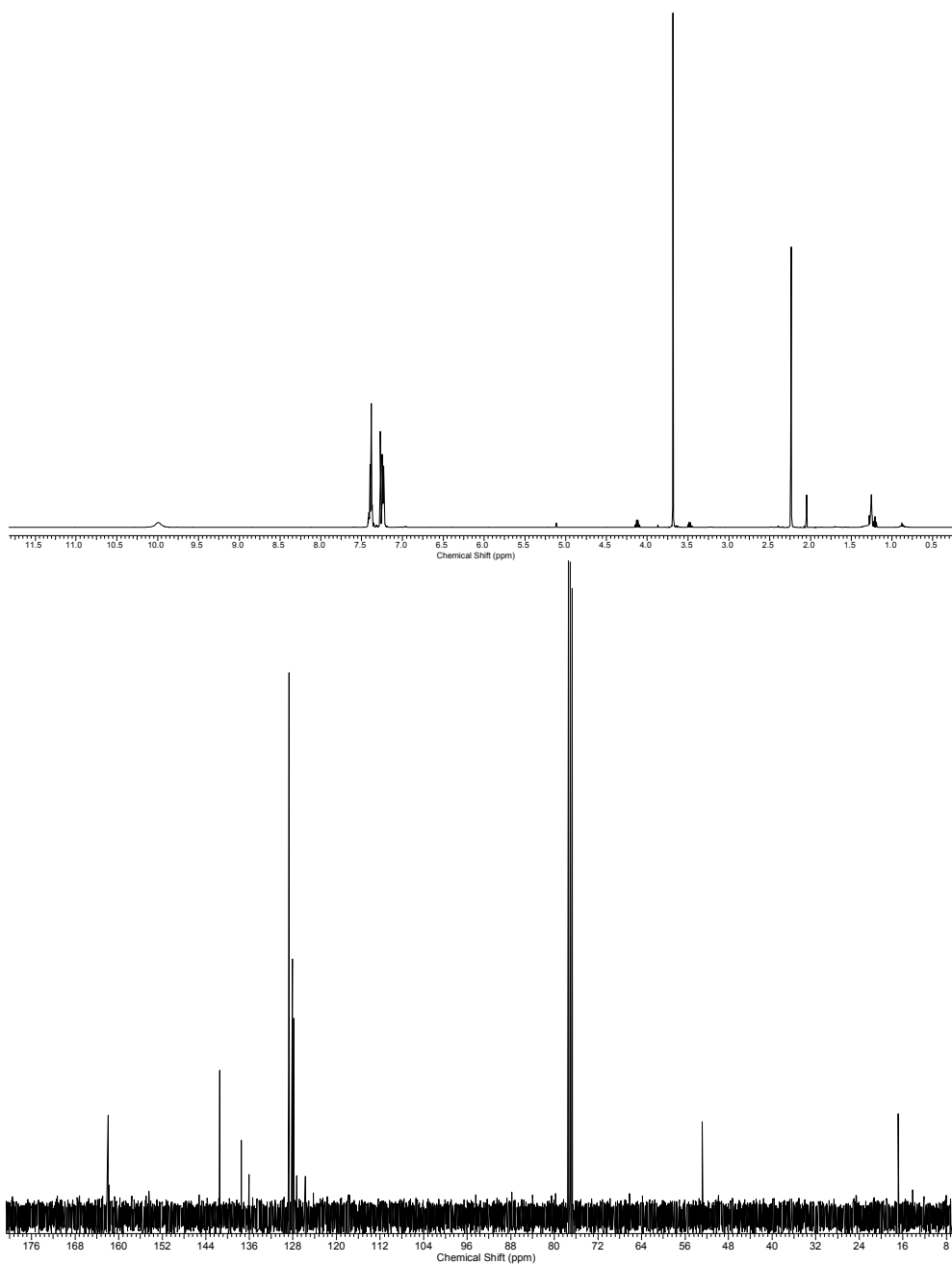
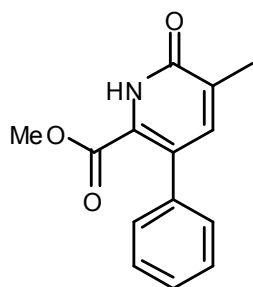
# Methyl 3-methyl-6-oxo-1,6-dihydropyridine-2-carboxylate 21a



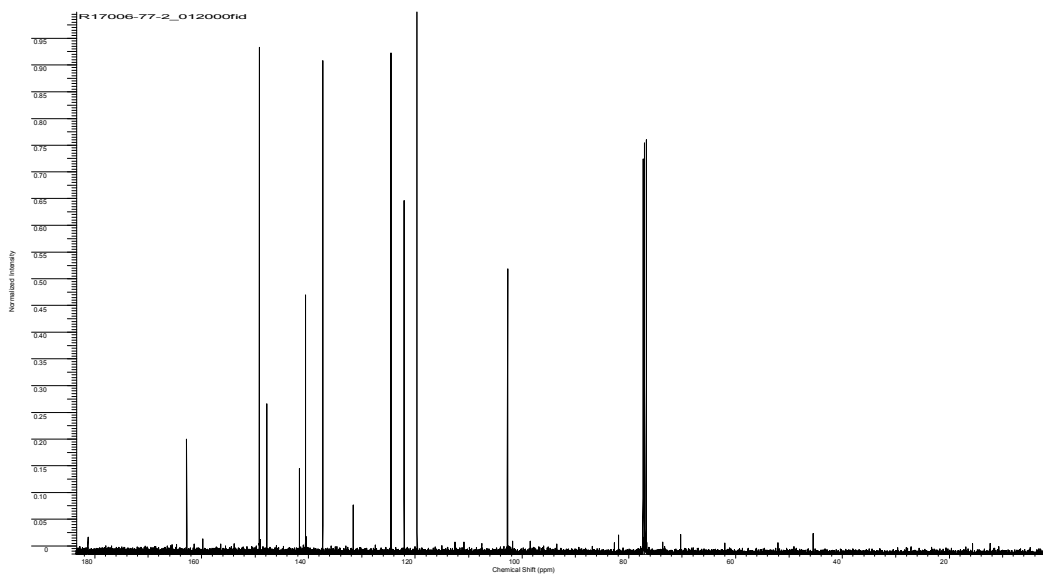
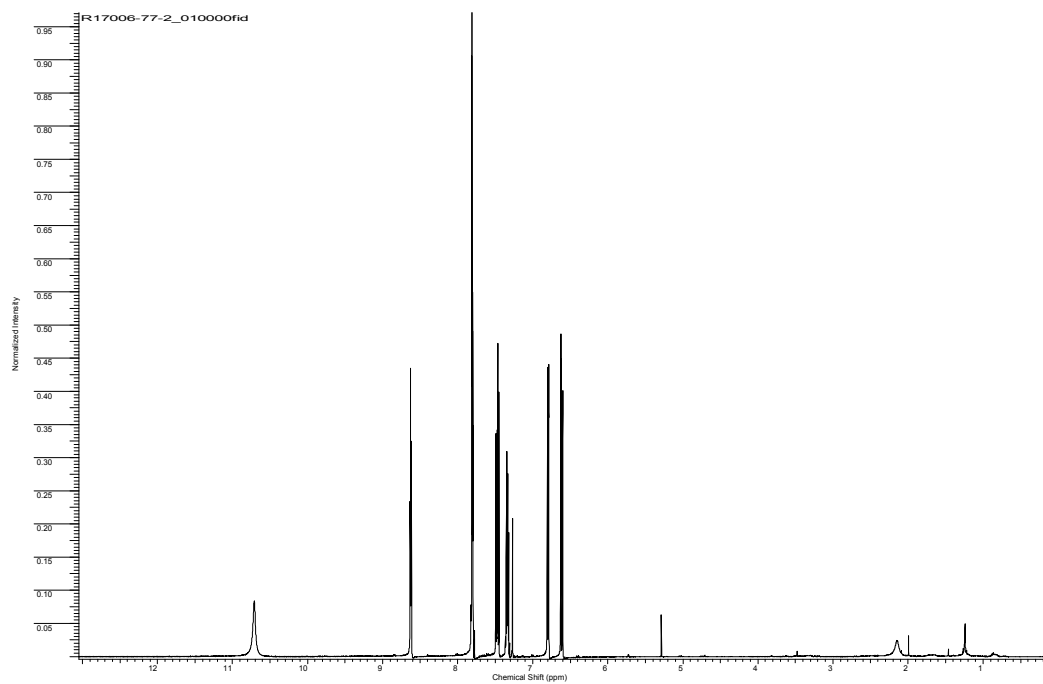
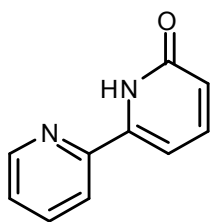
**Methyl 6-oxo-3-phenyl-1,6-dihydropyridine-2-carboxylate 21b**



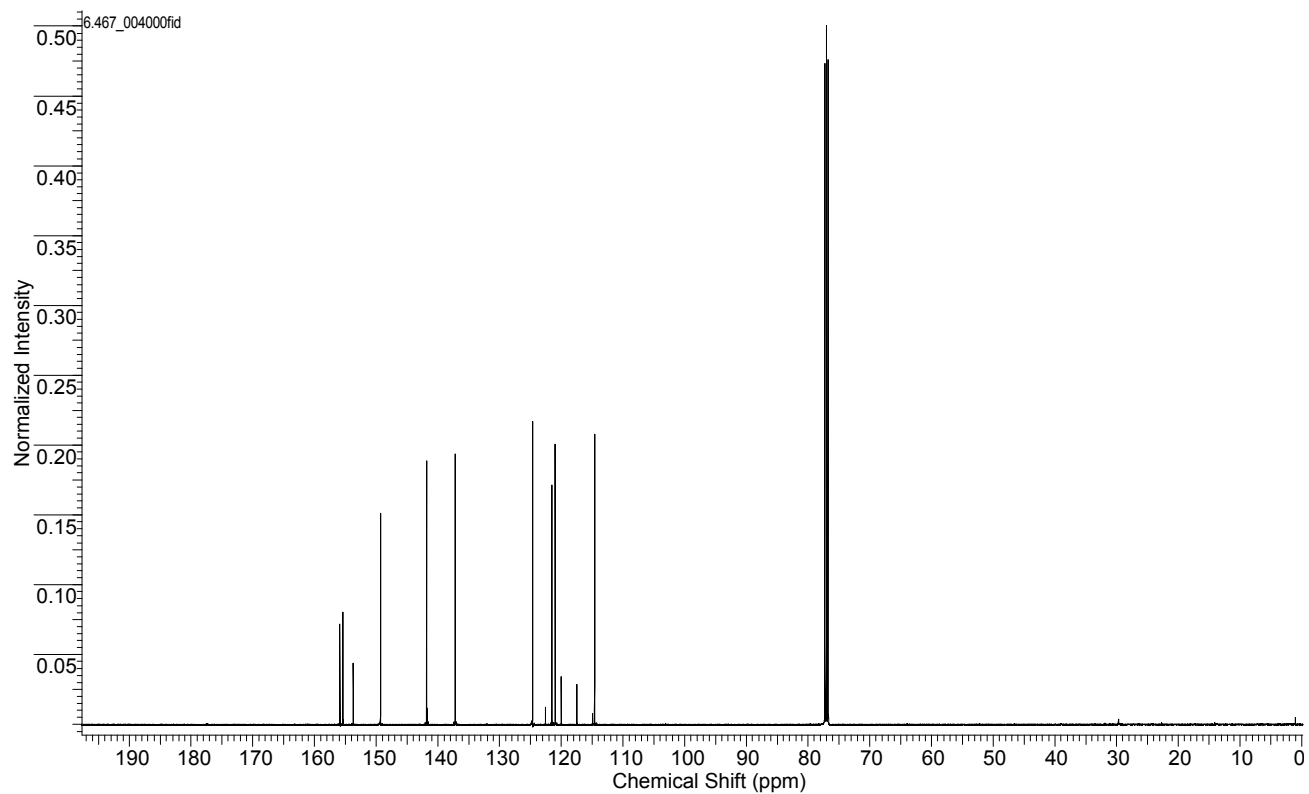
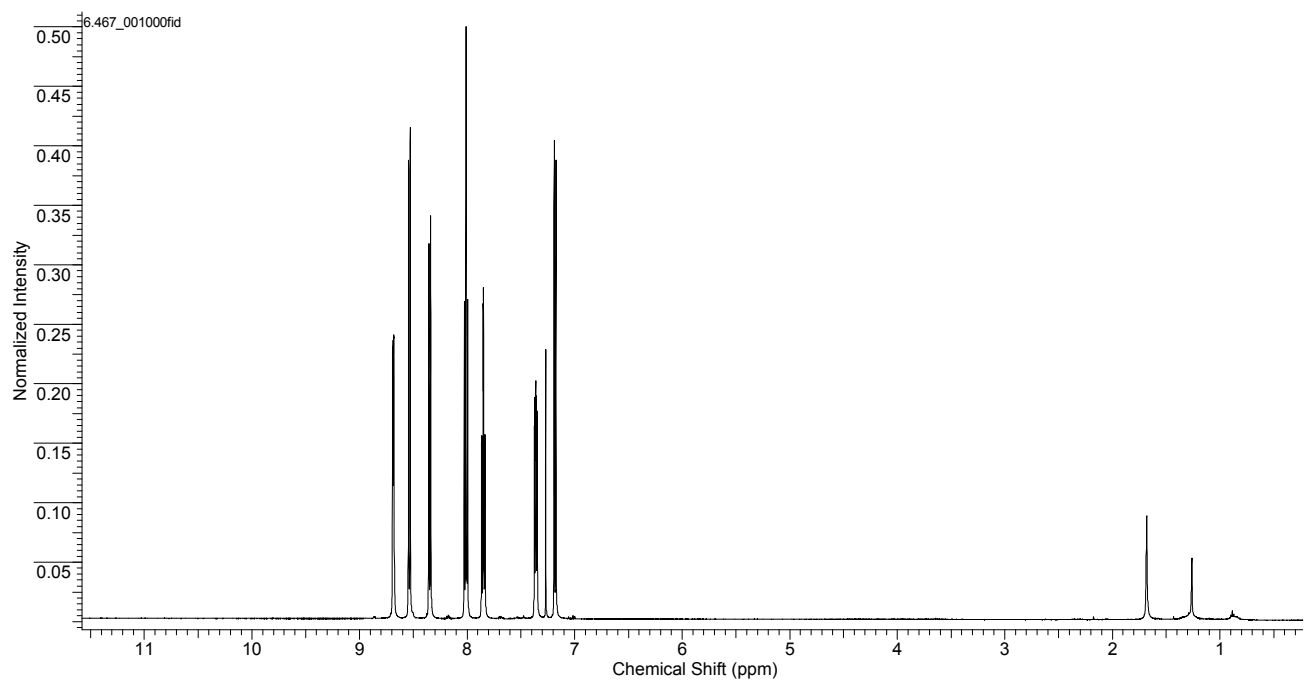
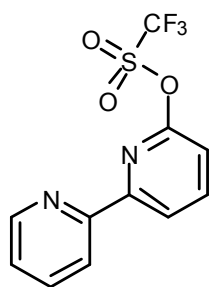
**Methyl 5-methyl-6-oxo-3-phenyl-1,6-dihydropyridine-2-carboxylate 21c**



## 6-(Pyridin-2-yl)pyridin-2(1H)-one 28b

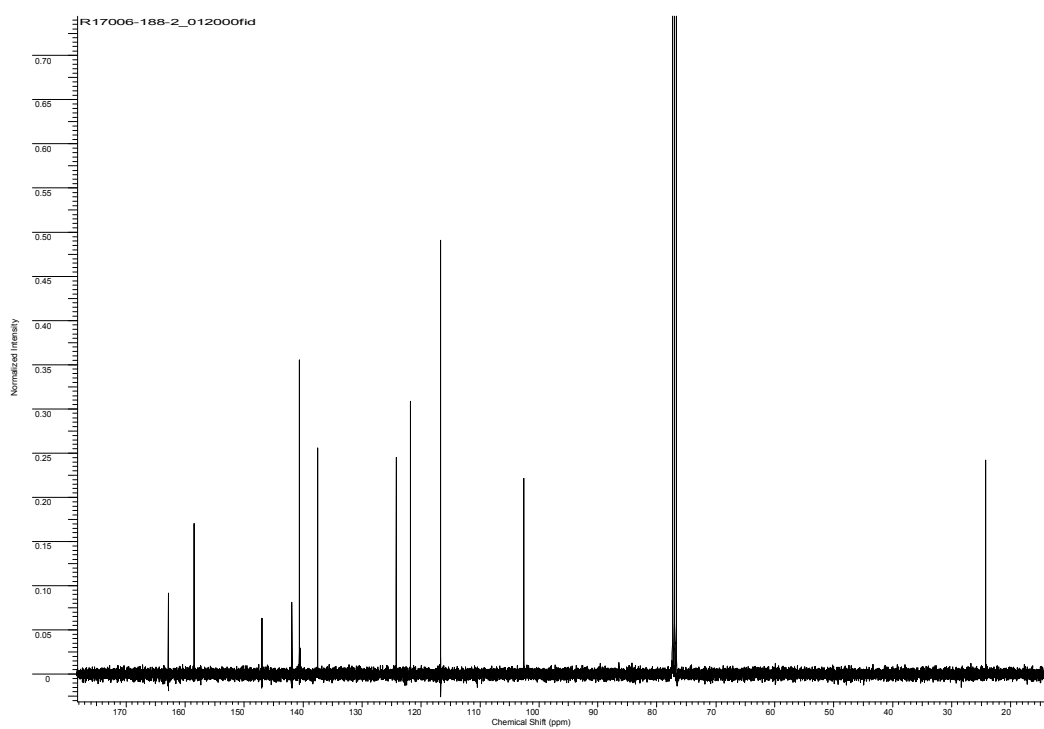
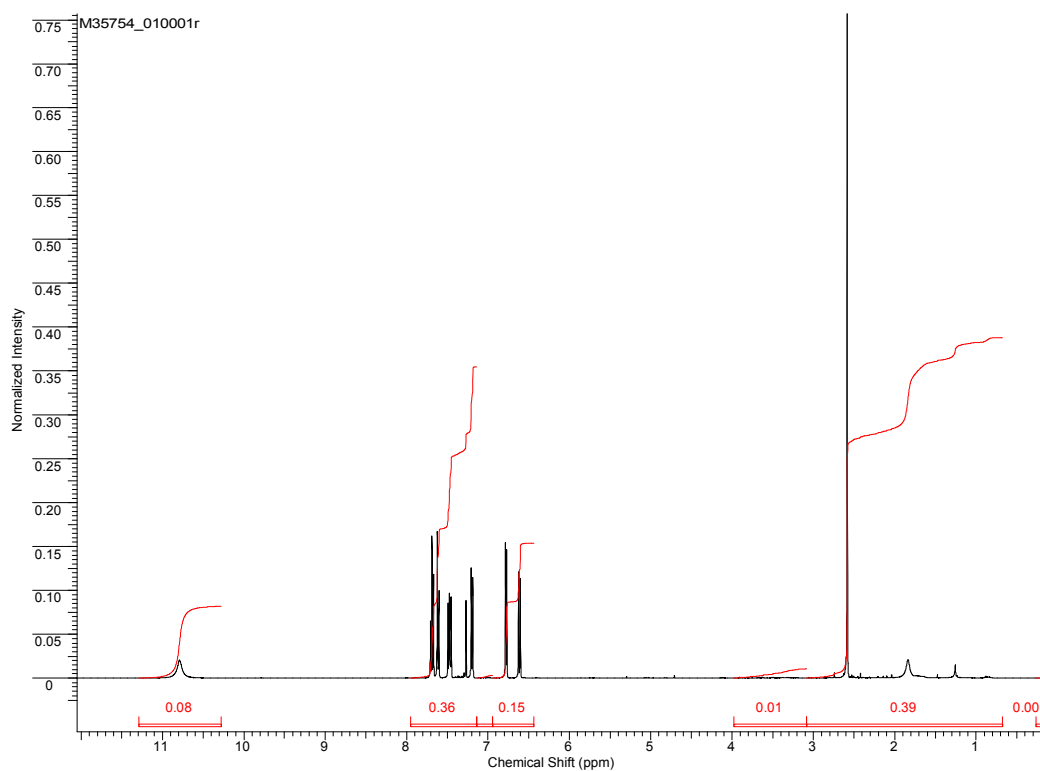
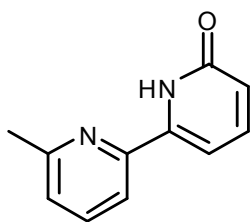


**2,2'-Bipyridin-6-yl trifluoromethanesulfonate 29b**

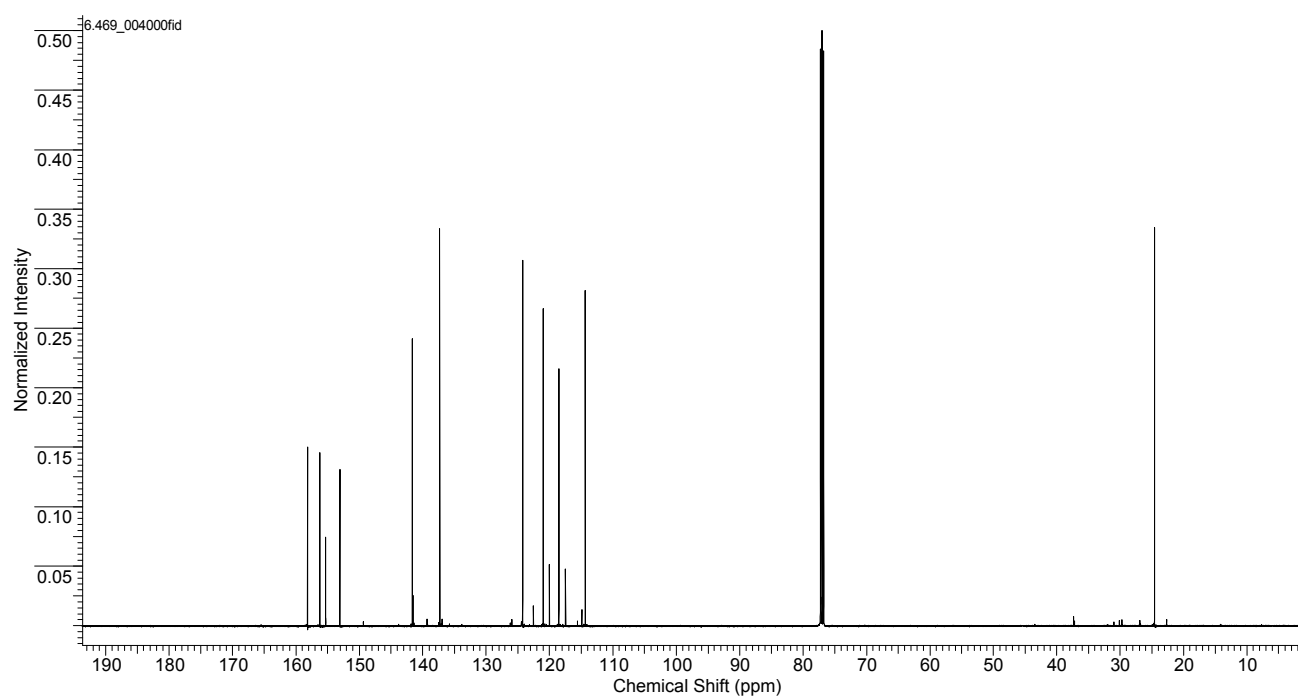
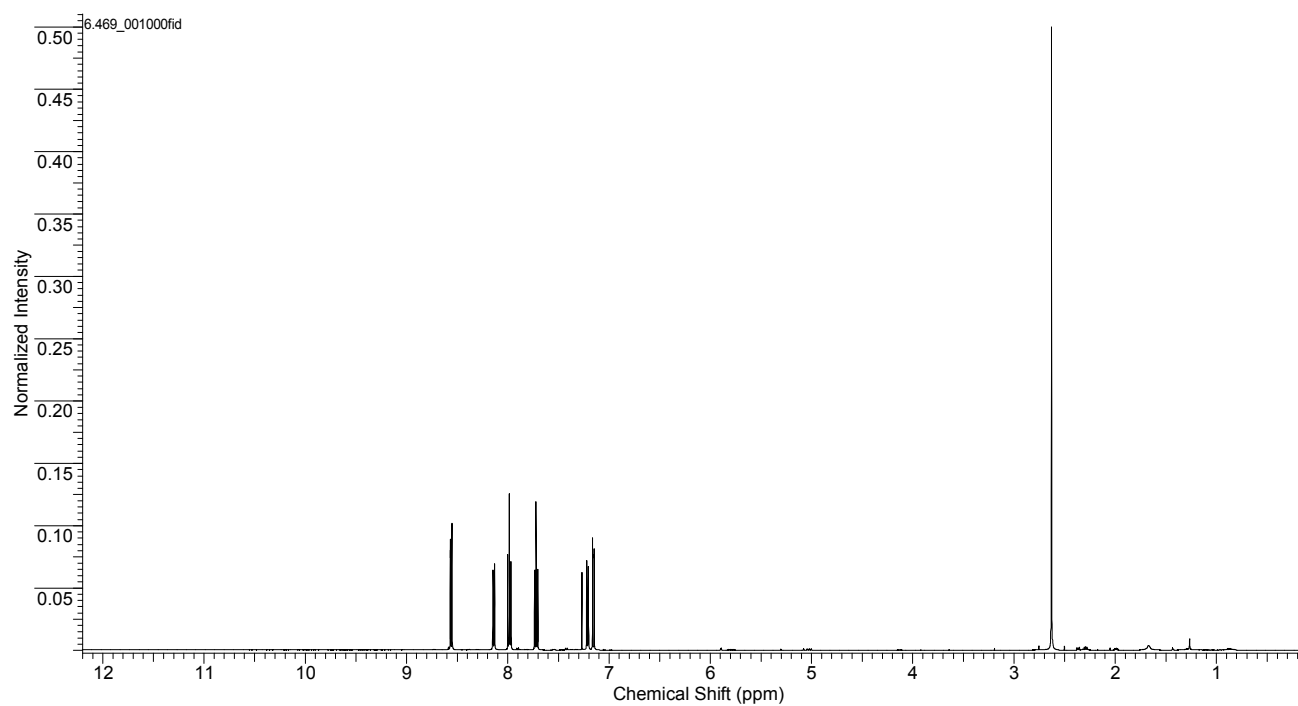
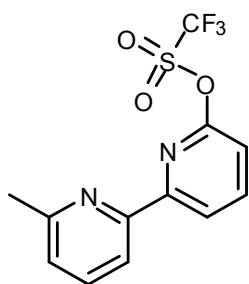




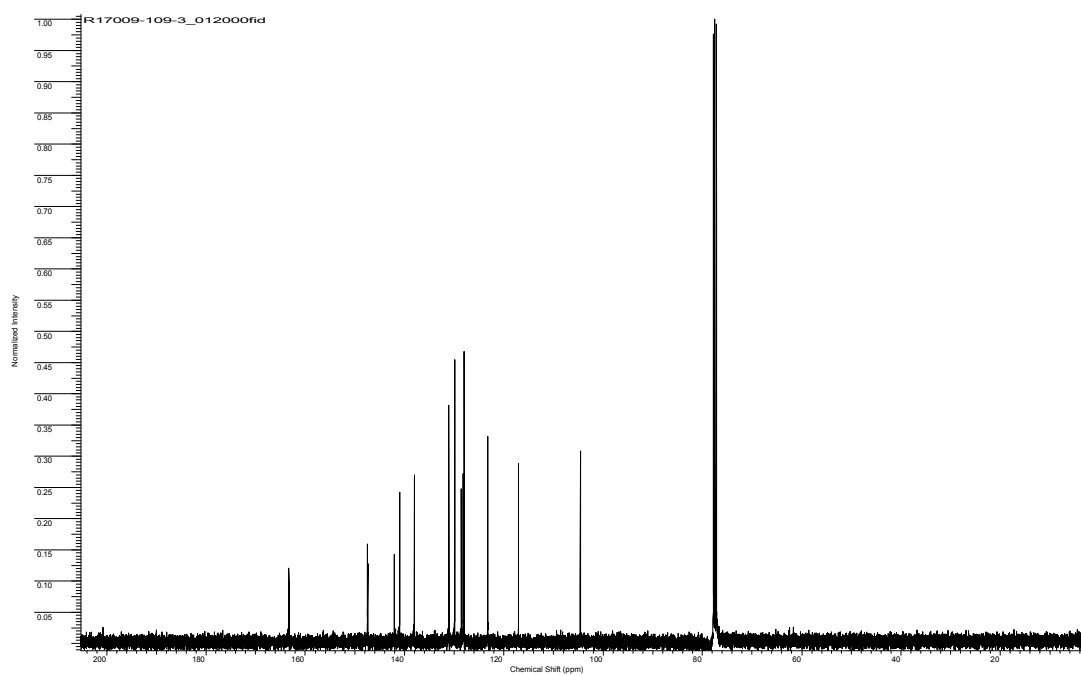
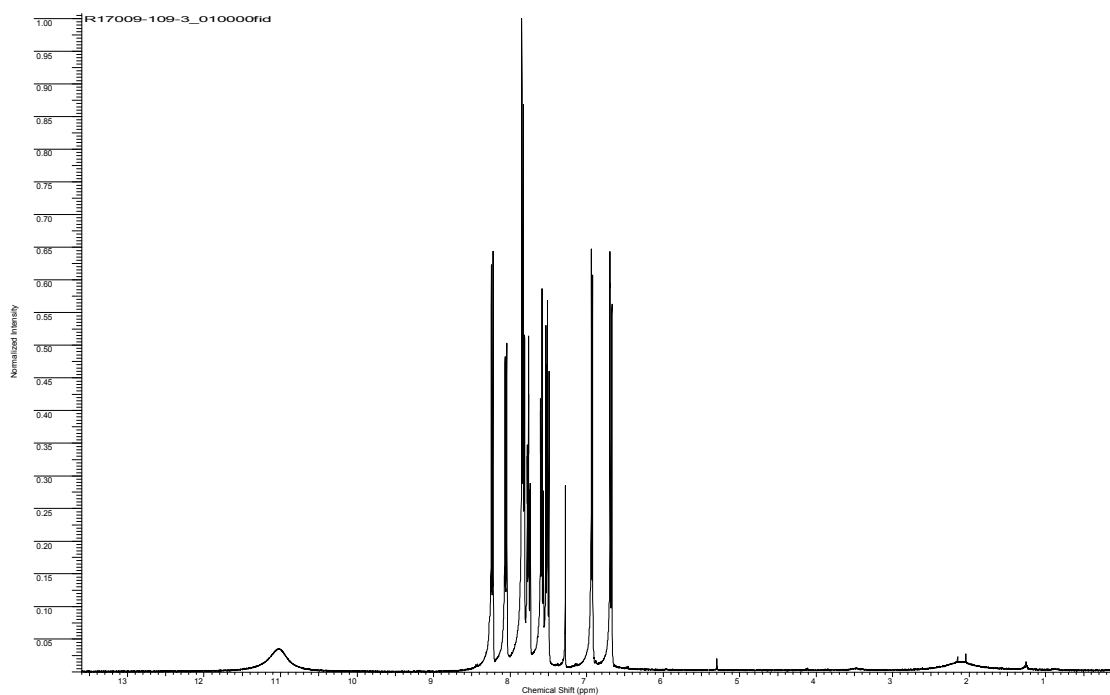
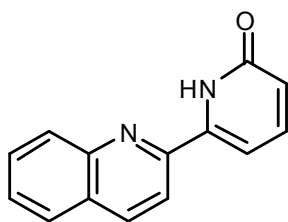
**6-(6-Methylpyridin-2-yl)pyridin-2(1*H*)-one 28c**



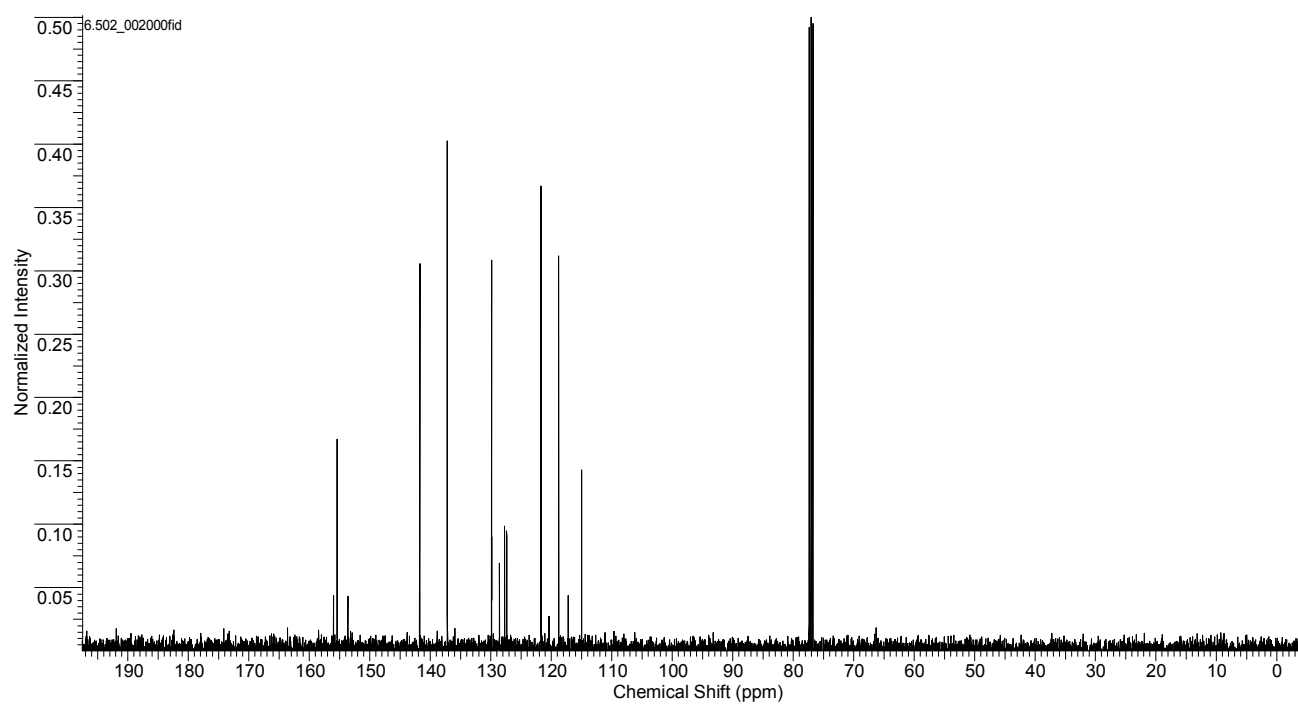
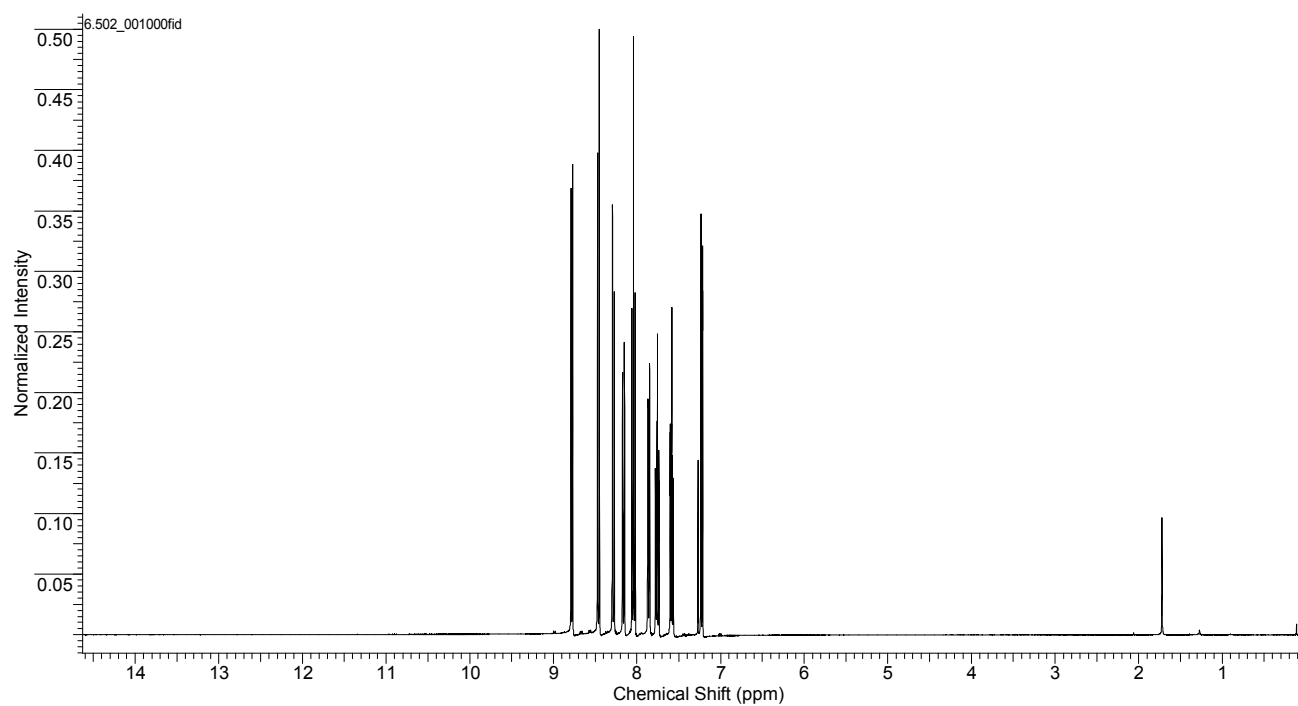
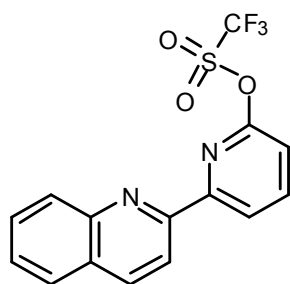
**6'-Methyl-2,2'-bipyridin-6-yl trifluoromethanesulfonate 29c**



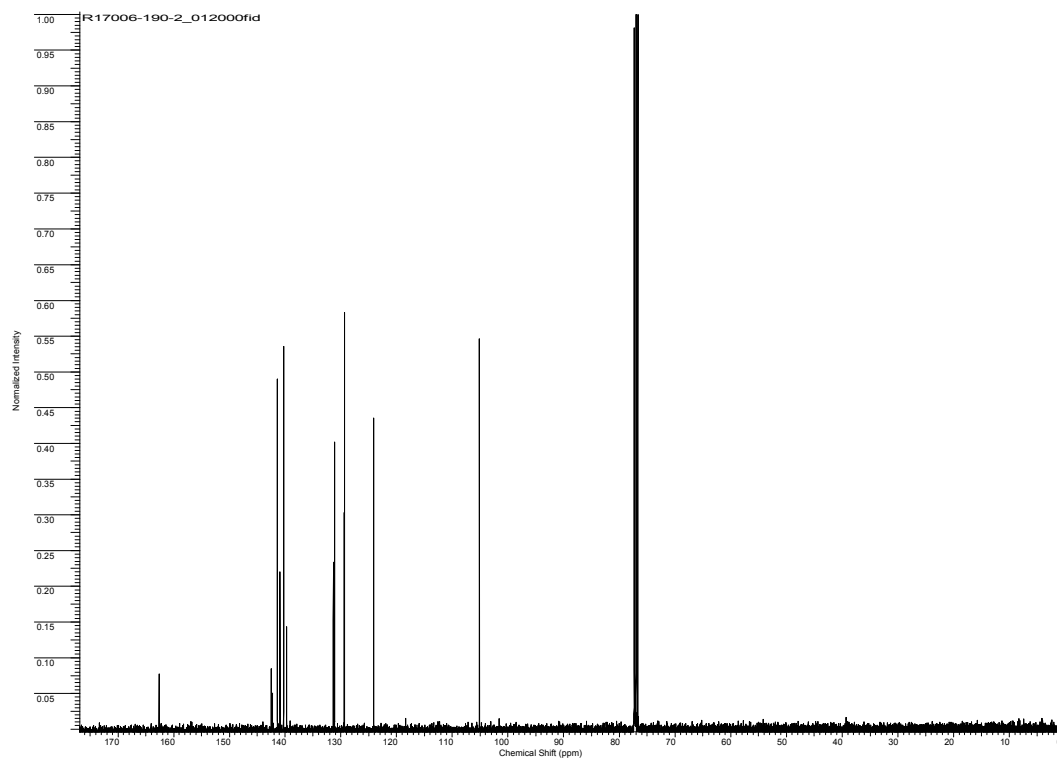
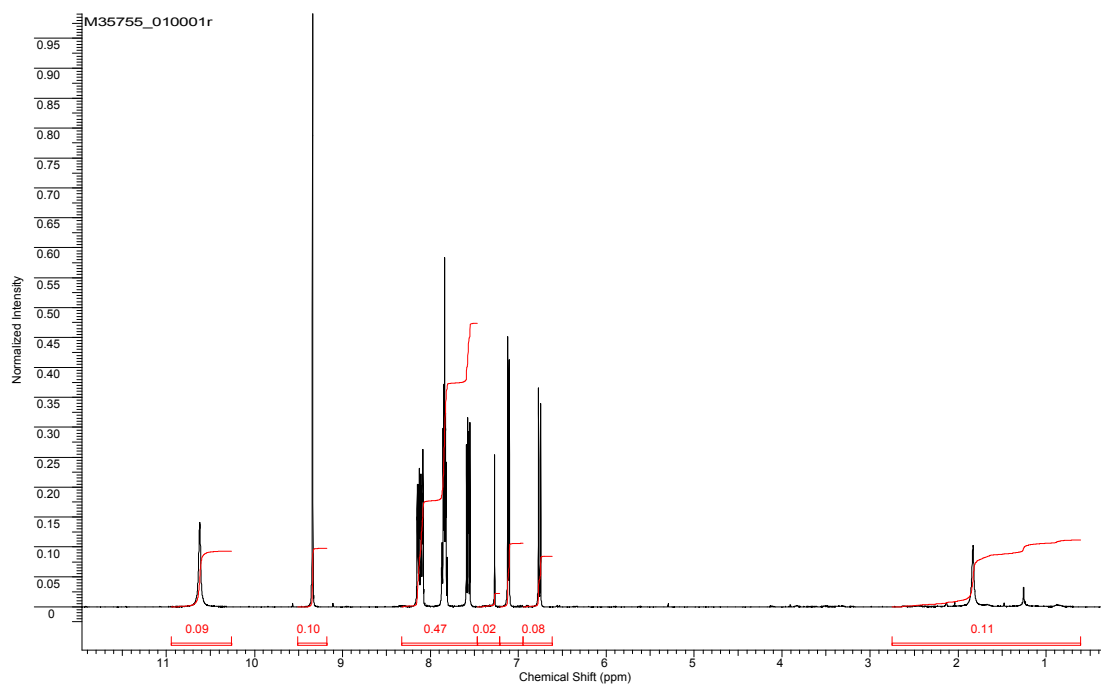
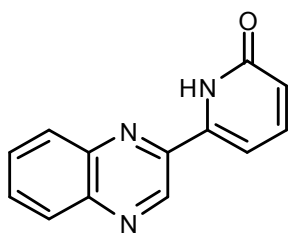
# 6-(Quinolin-2-yl)pyridin-2(1H)-one 28d



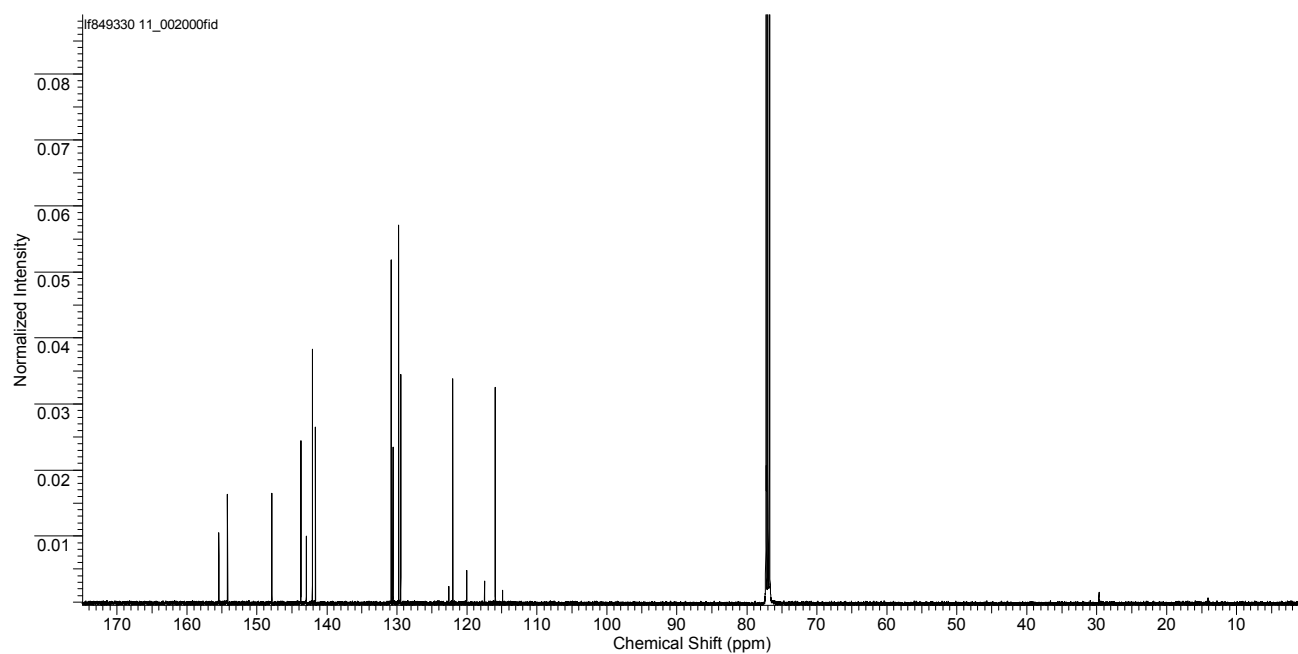
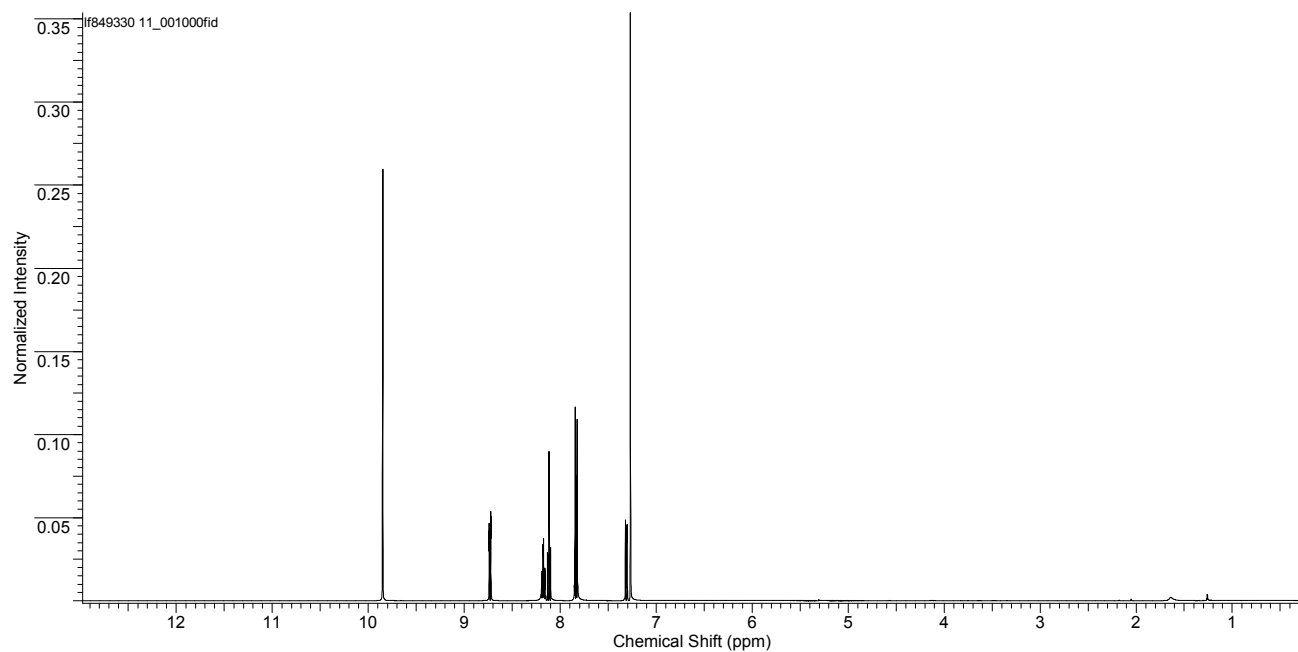
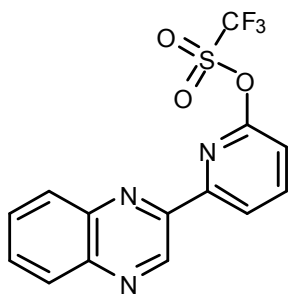
**6-(Quinolin-2-yl)pyridin-2-yl trifluoromethanesulfonate 29d**



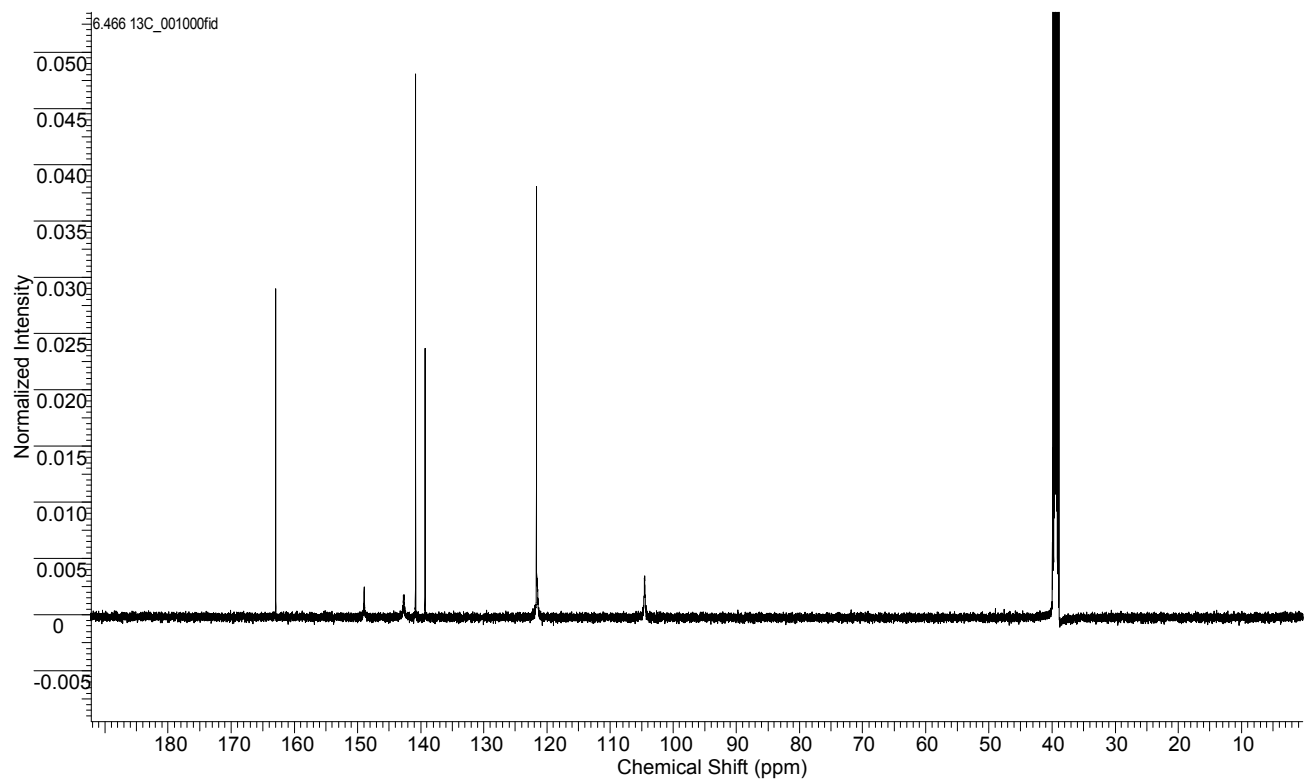
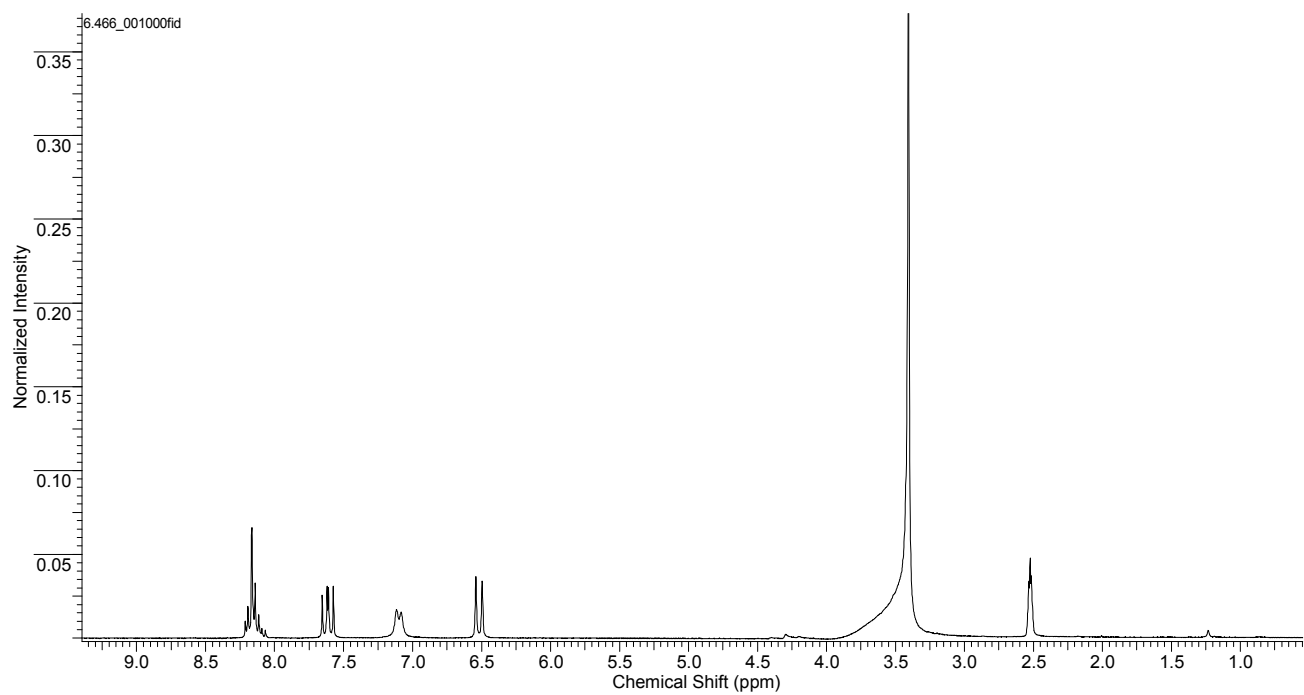
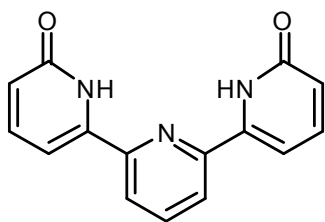
**6-(Quinoxalin-2-yl)pyridin-2(1H)-one 28e**



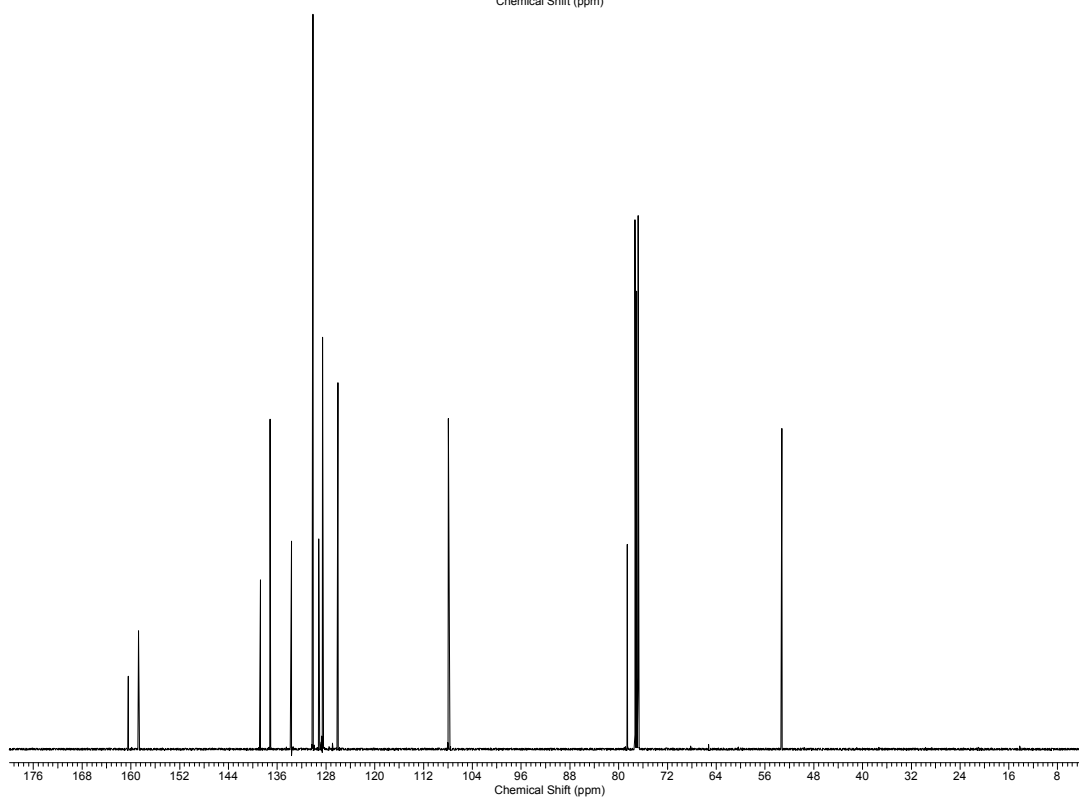
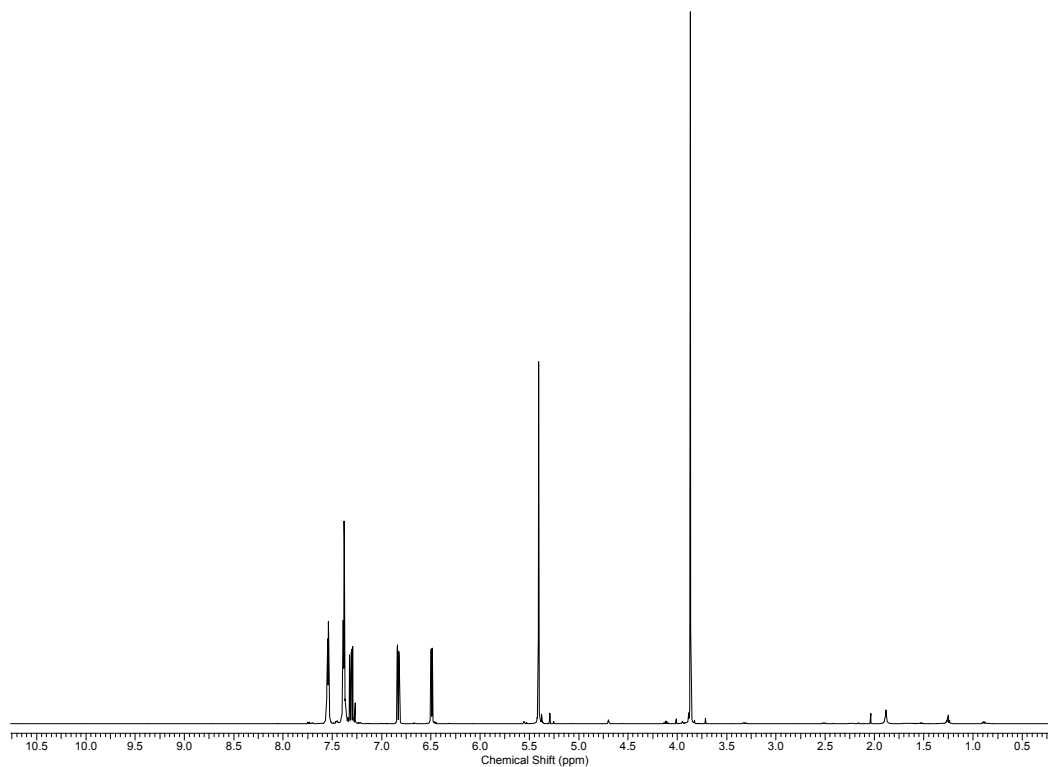
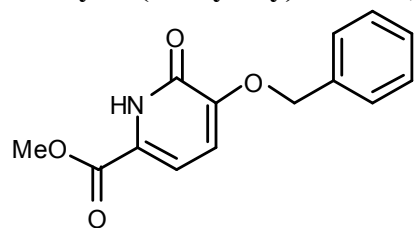
**6-(Quinoxalin-2-yl)pyridin-2-yl trifluoromethanesulfonate 29e**



**6,6-(Pyridine-2,6-diyl)dipyridin-2(1*H*)-one 33**



**Methyl 5-(benzyloxy)-6-oxo-1,6-dihydropyridine-2-carboxylate 35**





**Methyl 5-bromo-3-methyl-6-oxo-1,6-dihydropyridine-2-carboxylate 36**

