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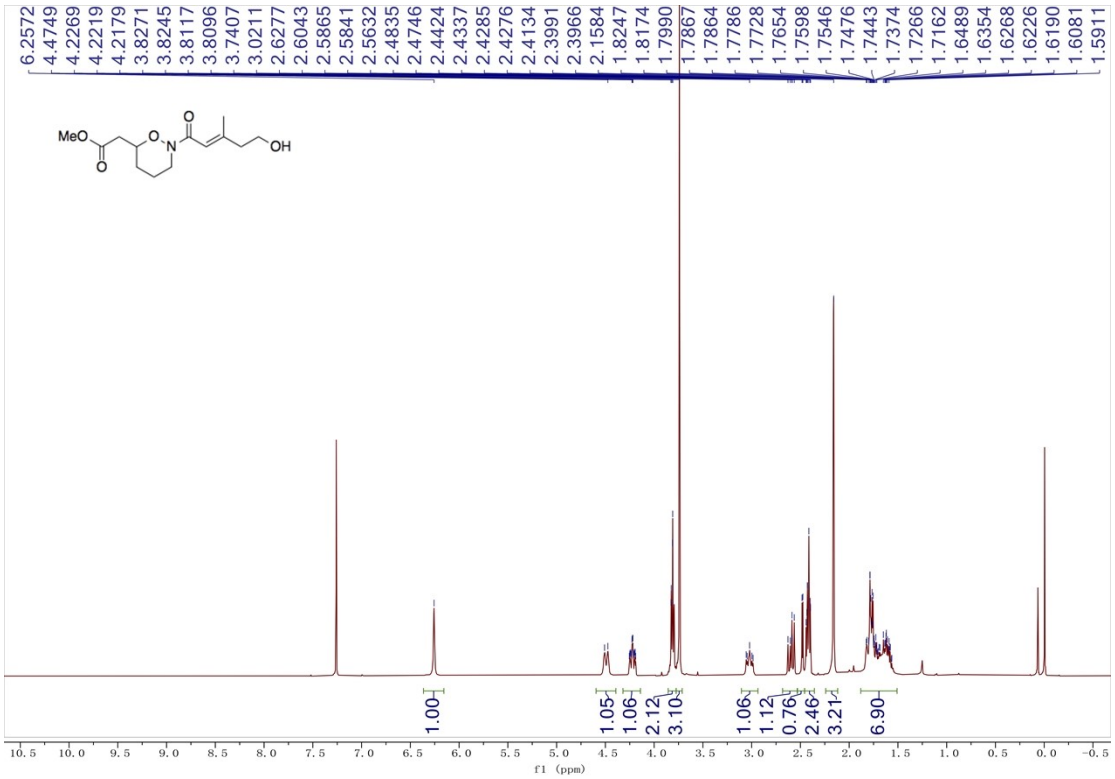
Confirmation of the Structure of (±)-Preisomide by Total Synthesis

Hong Kang Teo, Patcharaporn Sae-Lao and Roderick W. Bates

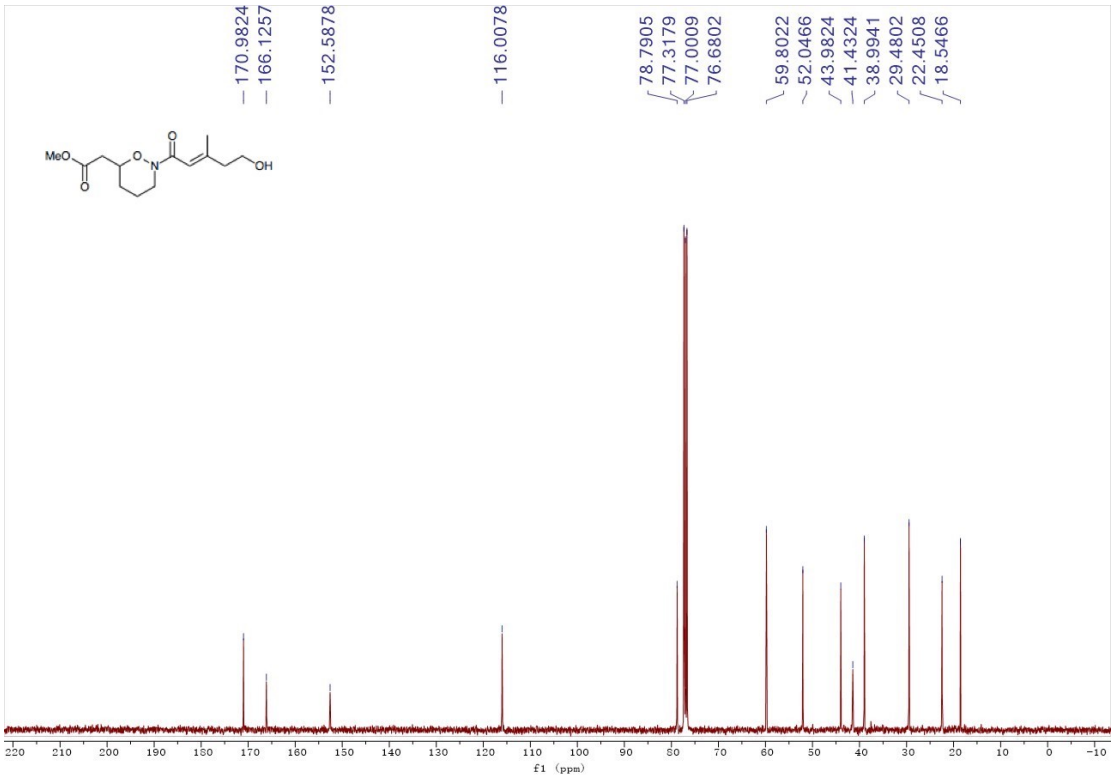
School of Chemistry, Chemical Engineering and Biotechnology,
Nanyang Technological University, 21 Nanyang Link, Singapore 637371

Supplementary Information

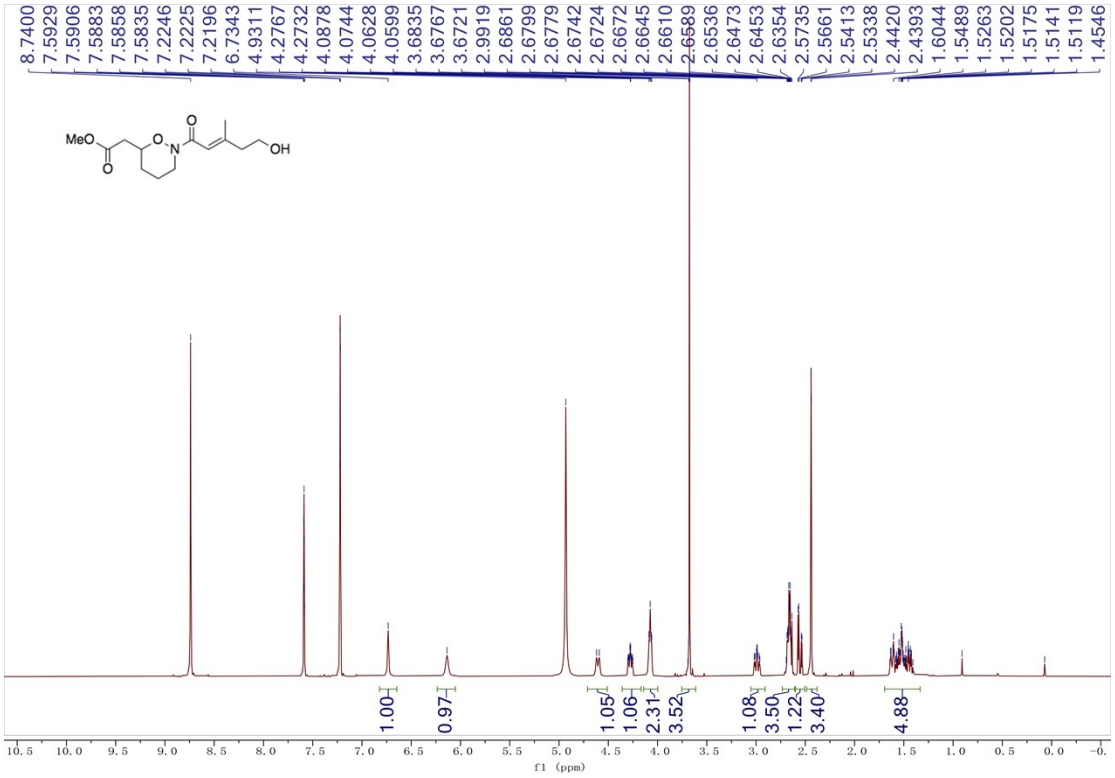
^{1}H and ^{13}C NMR spectra and X-ray structure



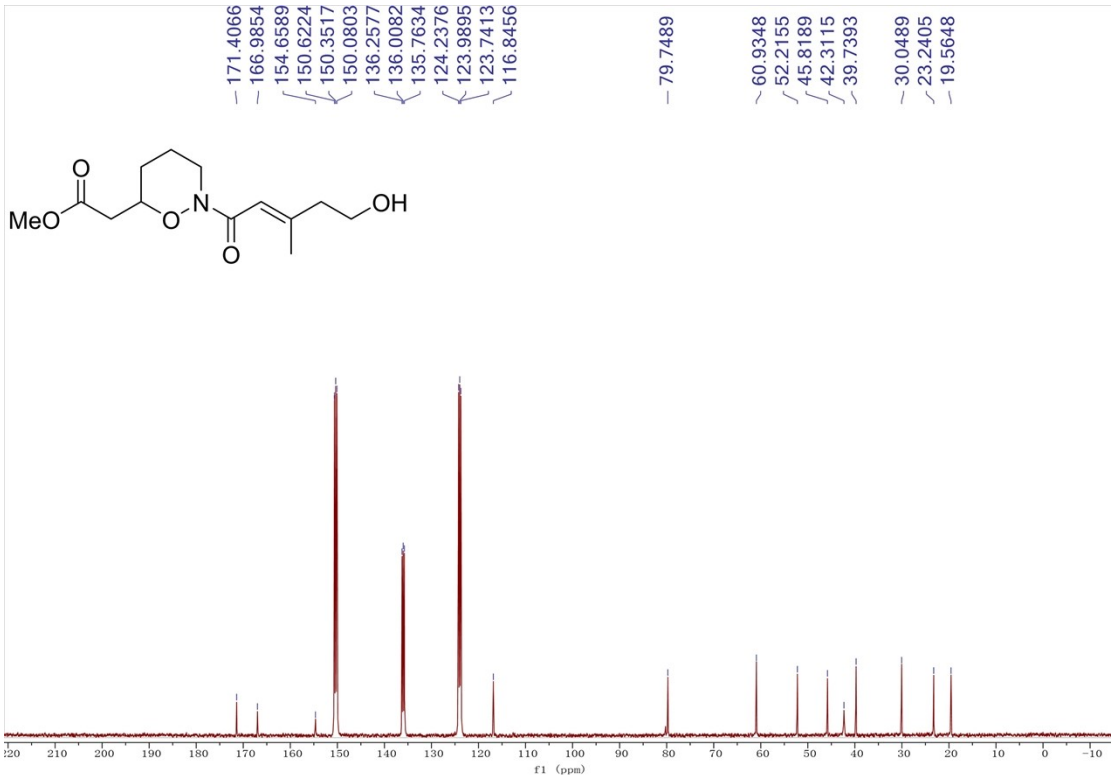
^{1}H NMR spectrum of preisomide **1** ($CDCl_3$, 500 MHz)



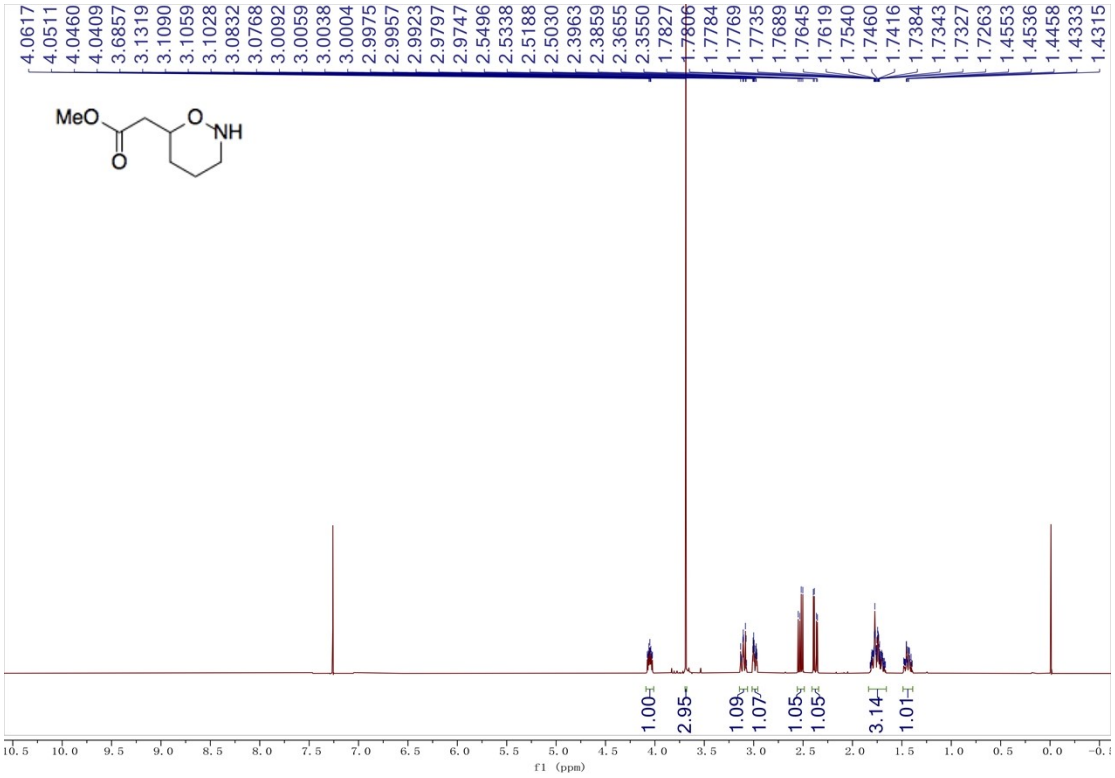
^{13}C NMR spectrum of preisomide **1** ($CDCl_3$, 100 MHz)



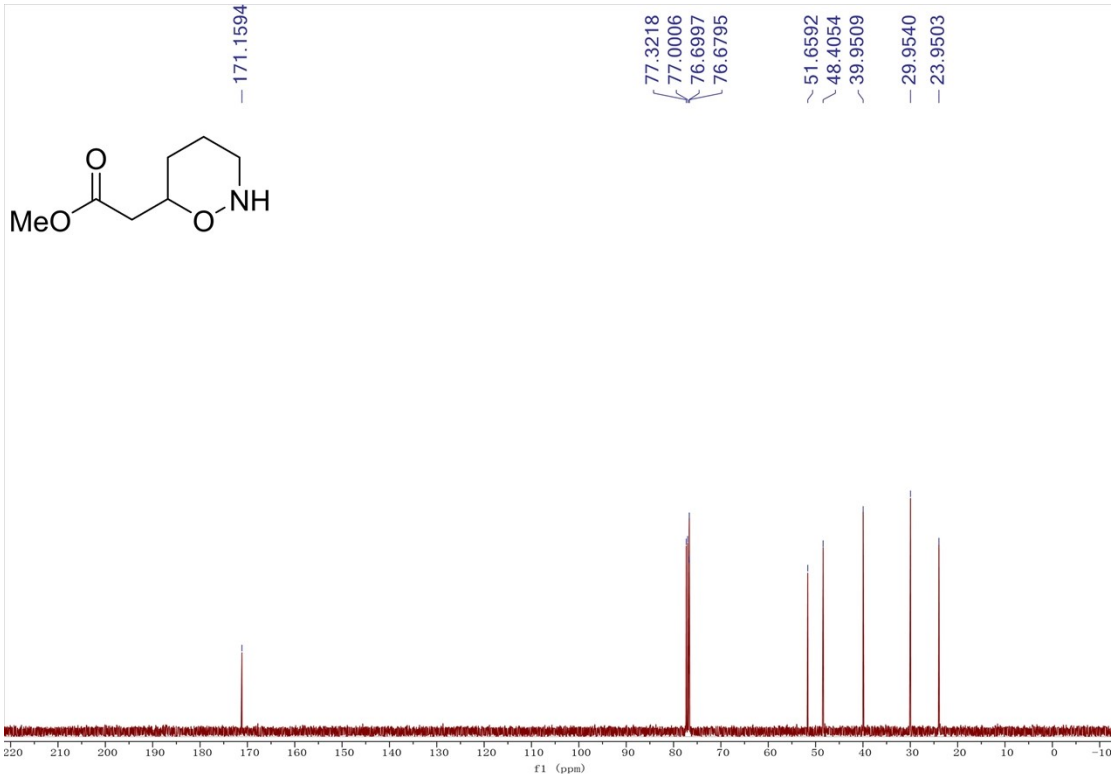
^{1}H NMR spectrum of preisomide **1** (d5-pyridine, 500 MHz)



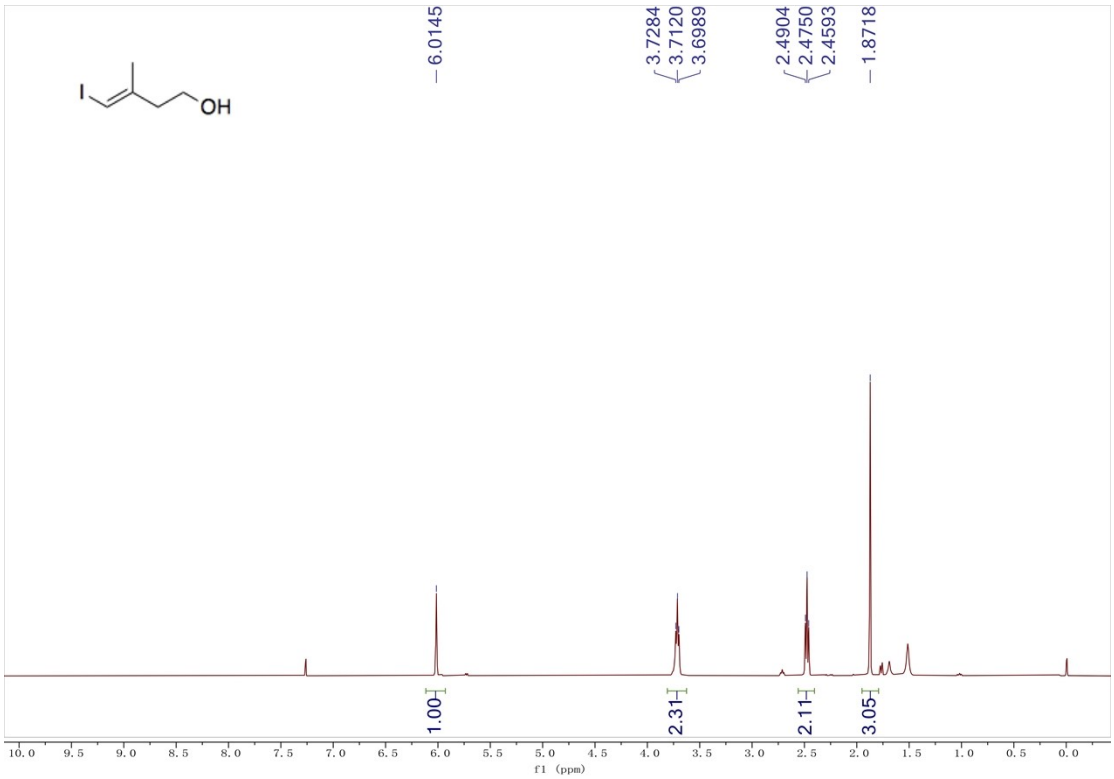
^{13}C NMR spectrum of preisomide **1**(d5-pyridine, 100 MHz)



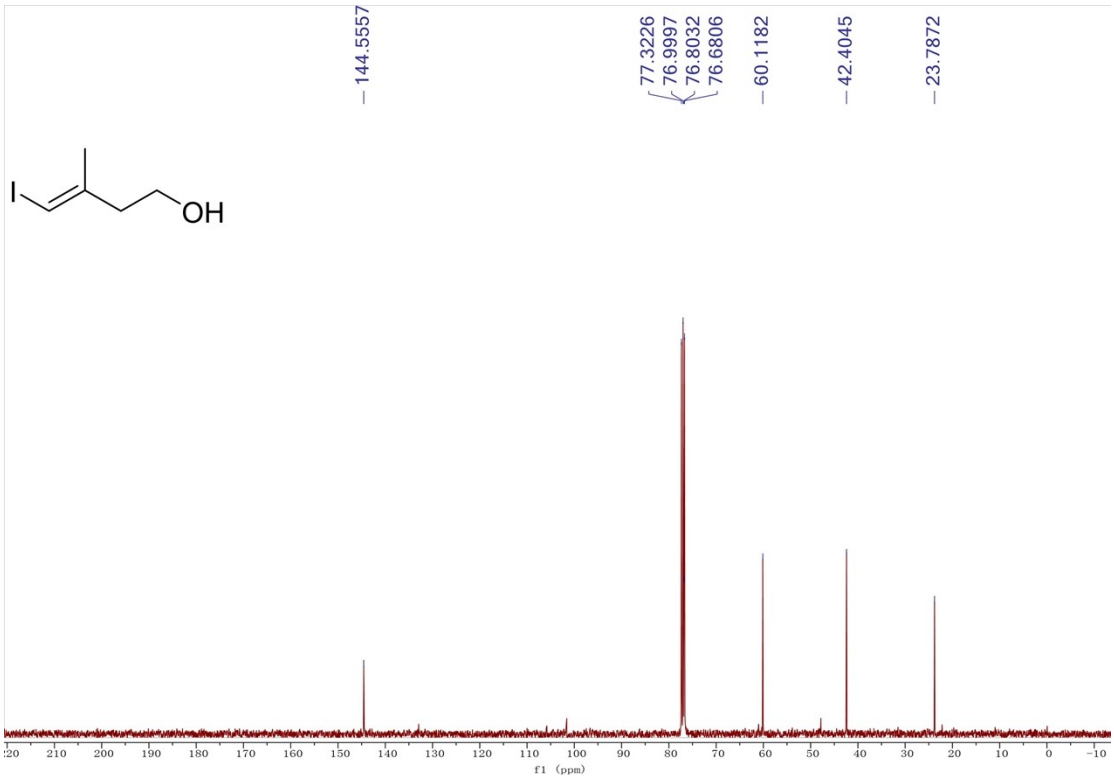
^{1}H NMR spectrum of tetrahydrooxazine **2** ($CDCl_3$, 500 MHz)



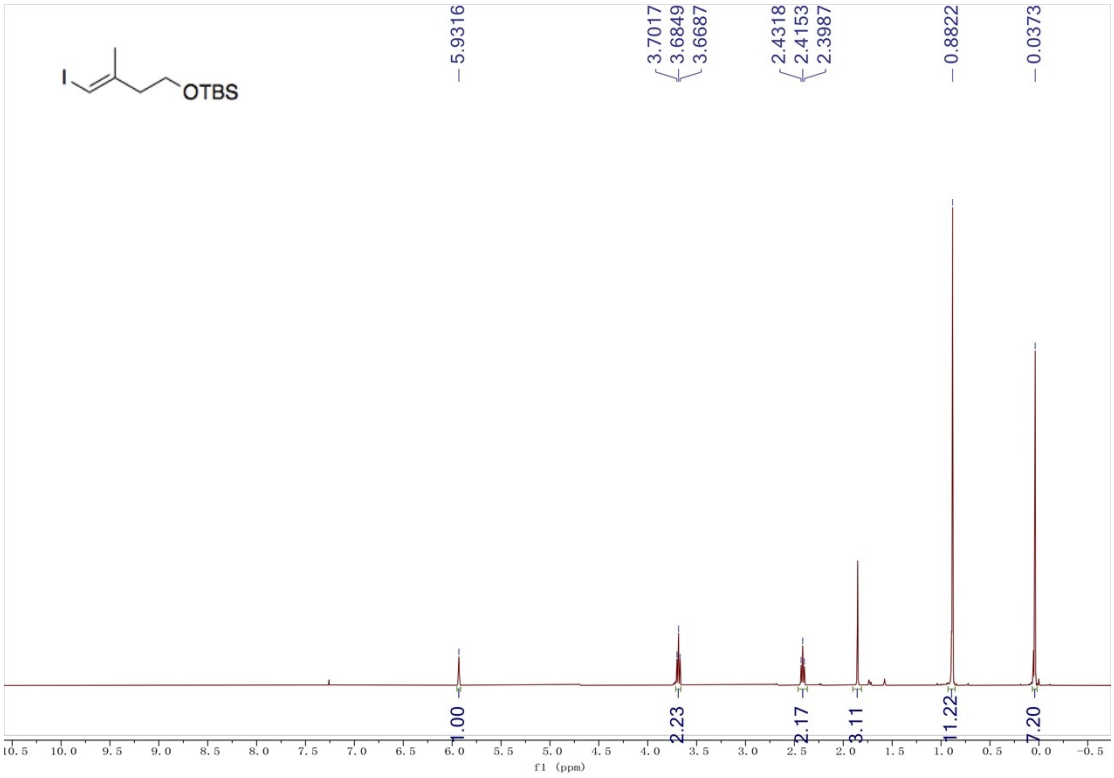
^{13}C NMR spectrum of tetrahydrooxazine **2** ($CDCl_3$, 100 MHz)



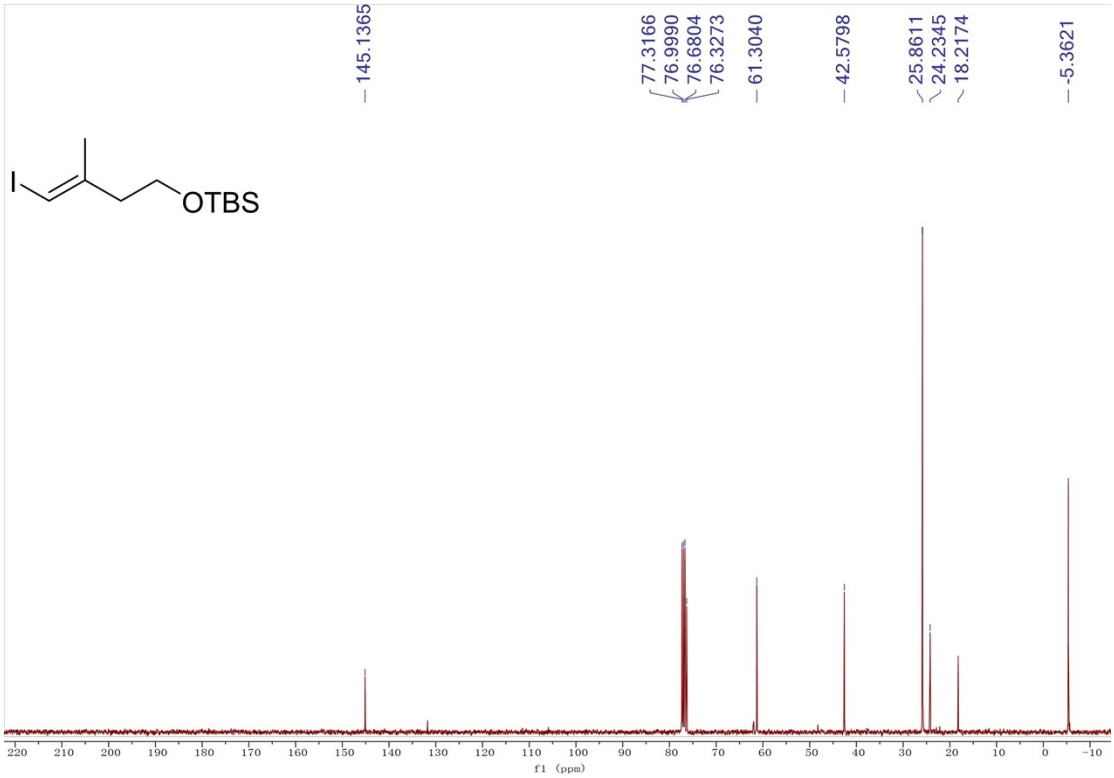
^{1}H NMR spectrum of iodide **5** ($CDCl_3$, 400 MHz)



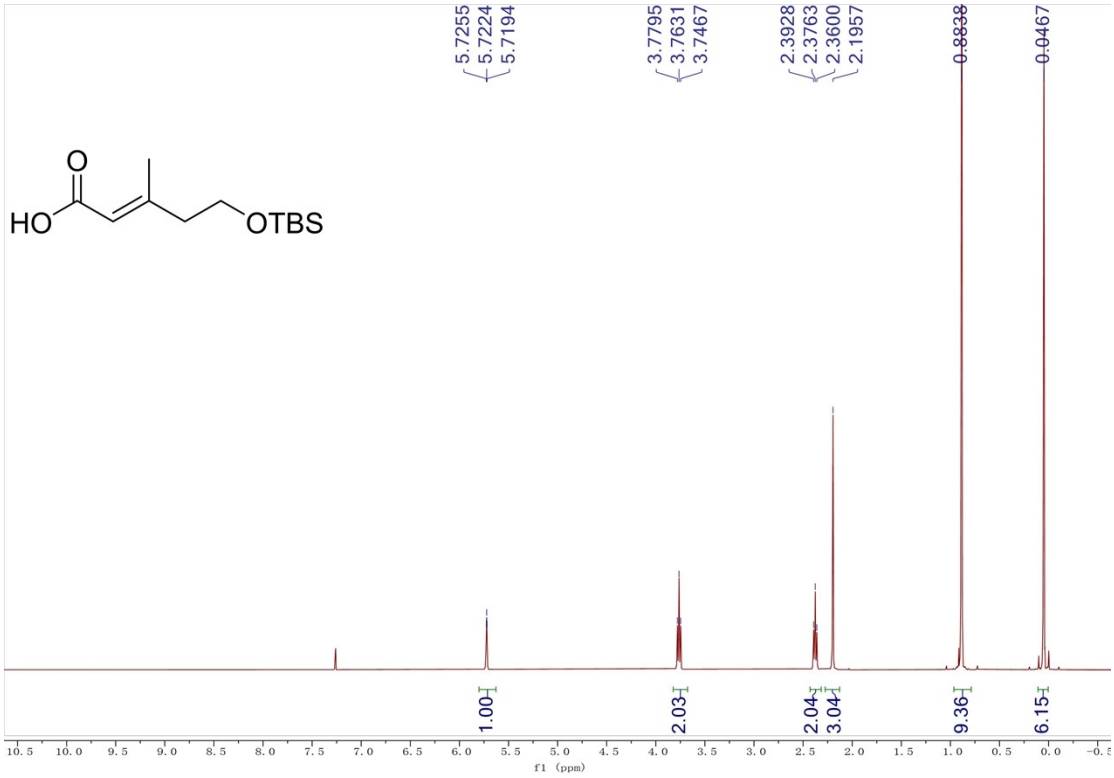
^{13}C NMR spectrum of iodide **5** ($CDCl_3$, 100 MHz)*



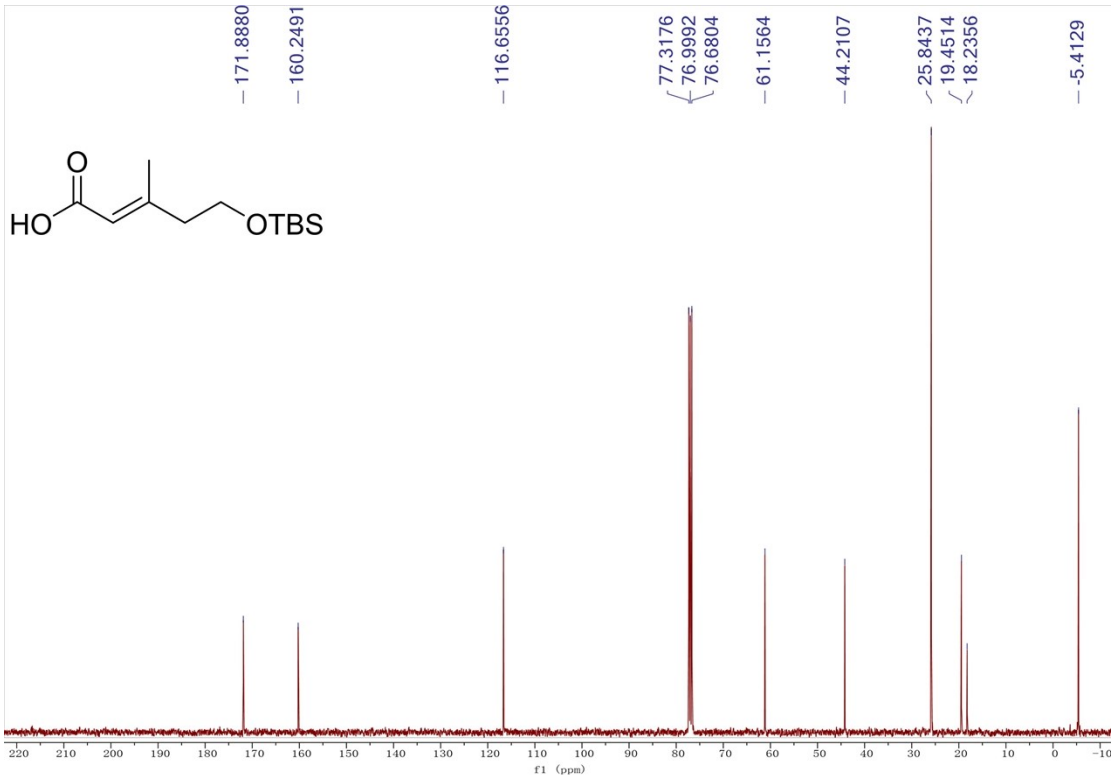
^{1}H NMR spectrum of iodide **6** ($CDCl_3$, 400 MHz)



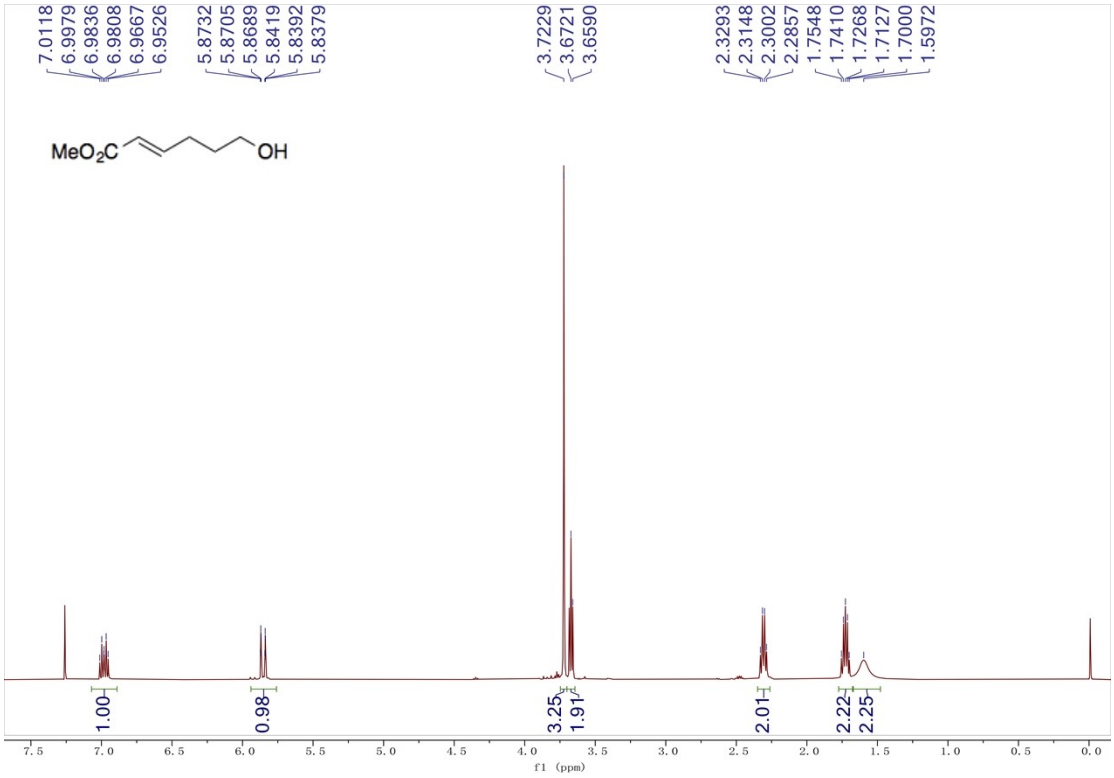
^{13}C NMR spectrum of iodide **6** ($CDCl_3$, 100 MHz)*



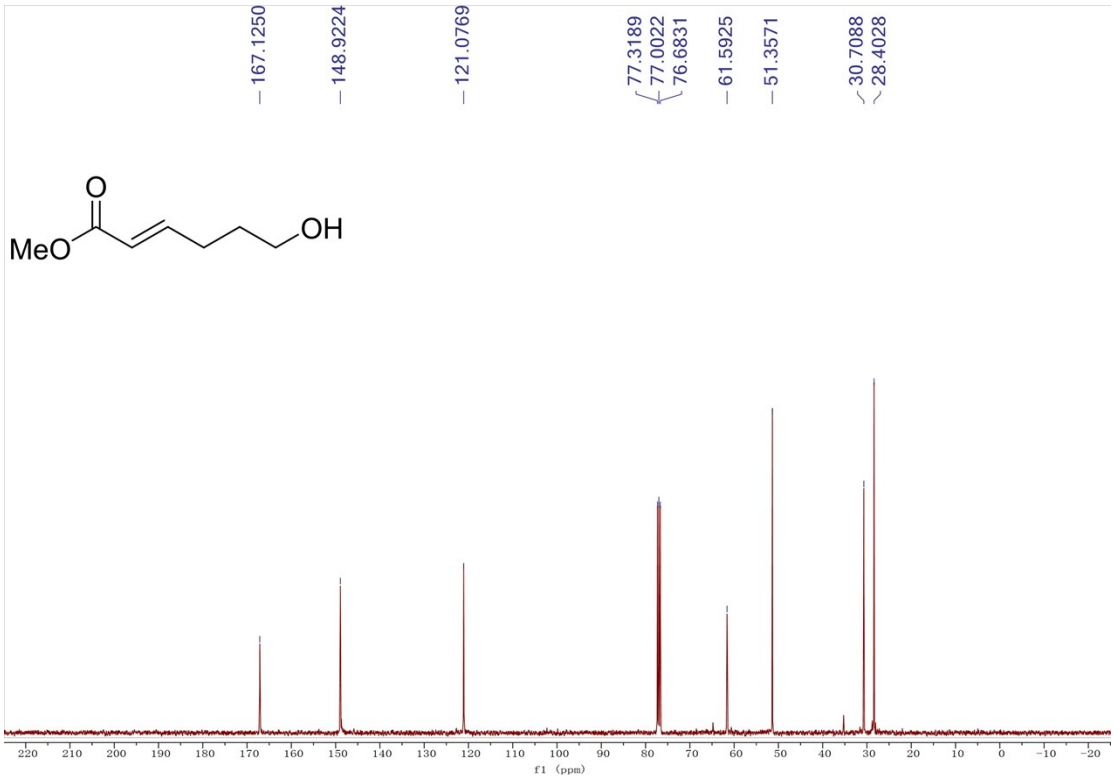
^{1}H NMR spectrum of carboxylic acid **7** ($CDCl_3$, 400 MHz)



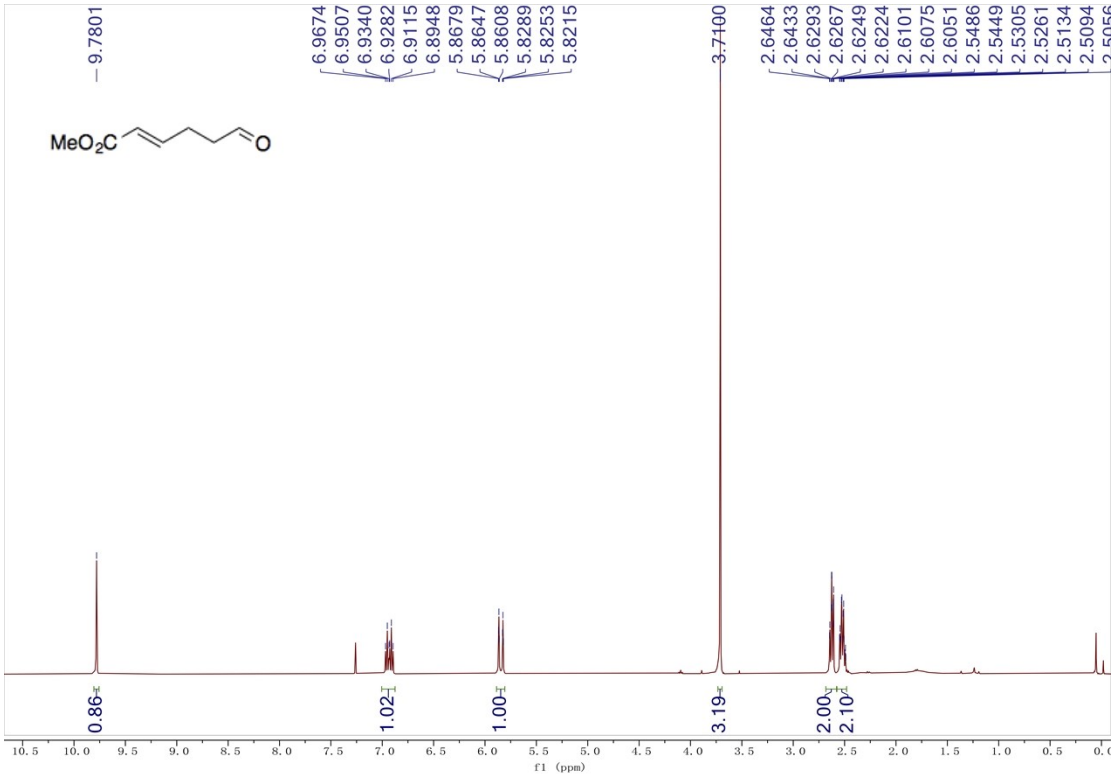
^{13}C NMR spectrum of carboxylic acid **7** ($CDCl_3$, 100 MHz)



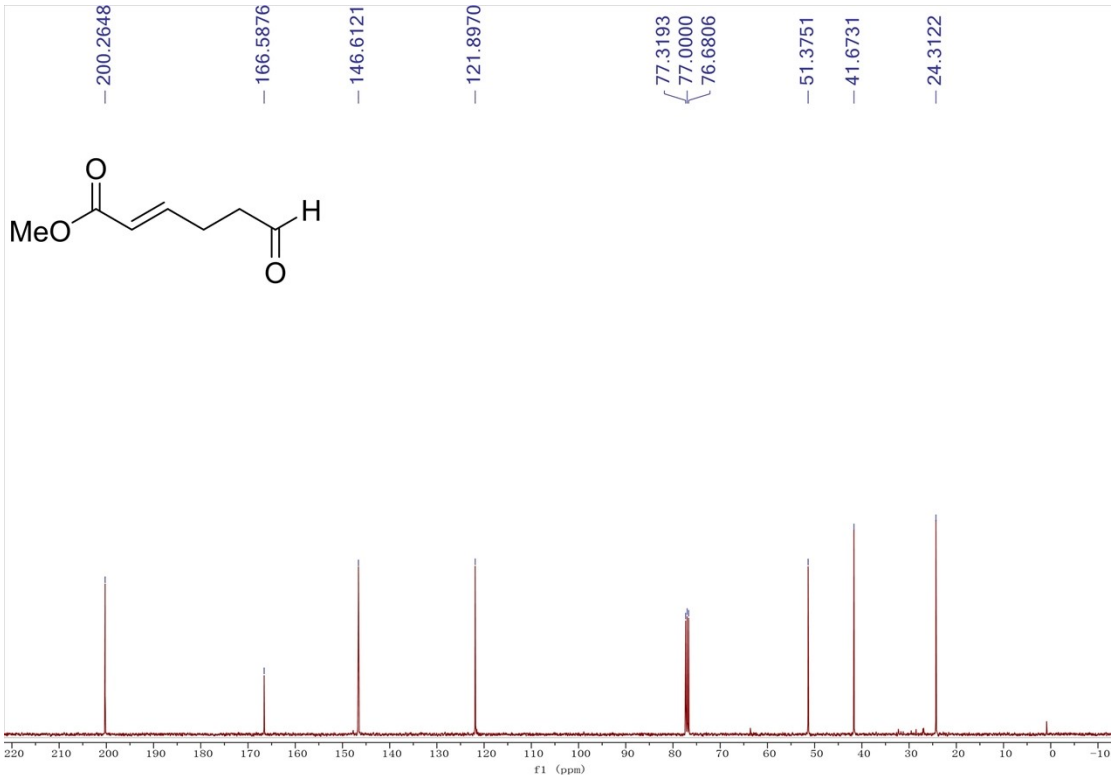
^{1}H NMR spectrum of ester **9** ($CDCl_3$, 500 MHz)



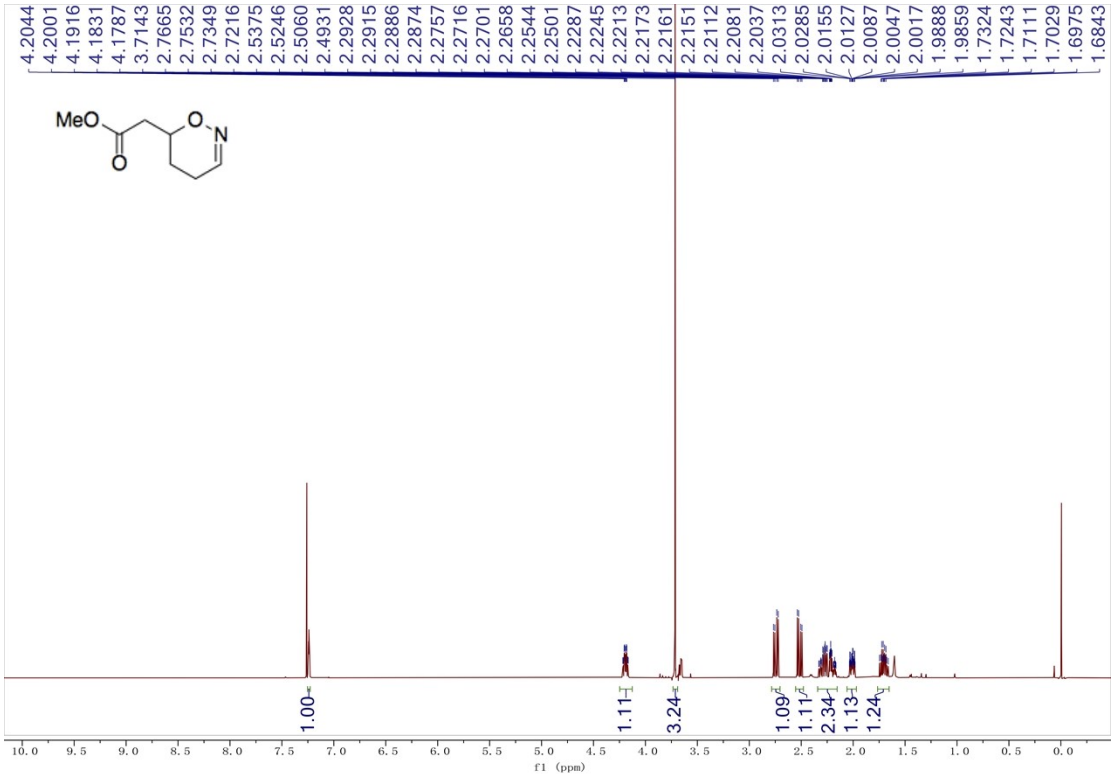
^{13}C NMR spectrum of ester **9** ($CDCl_3$, 100 MHz)



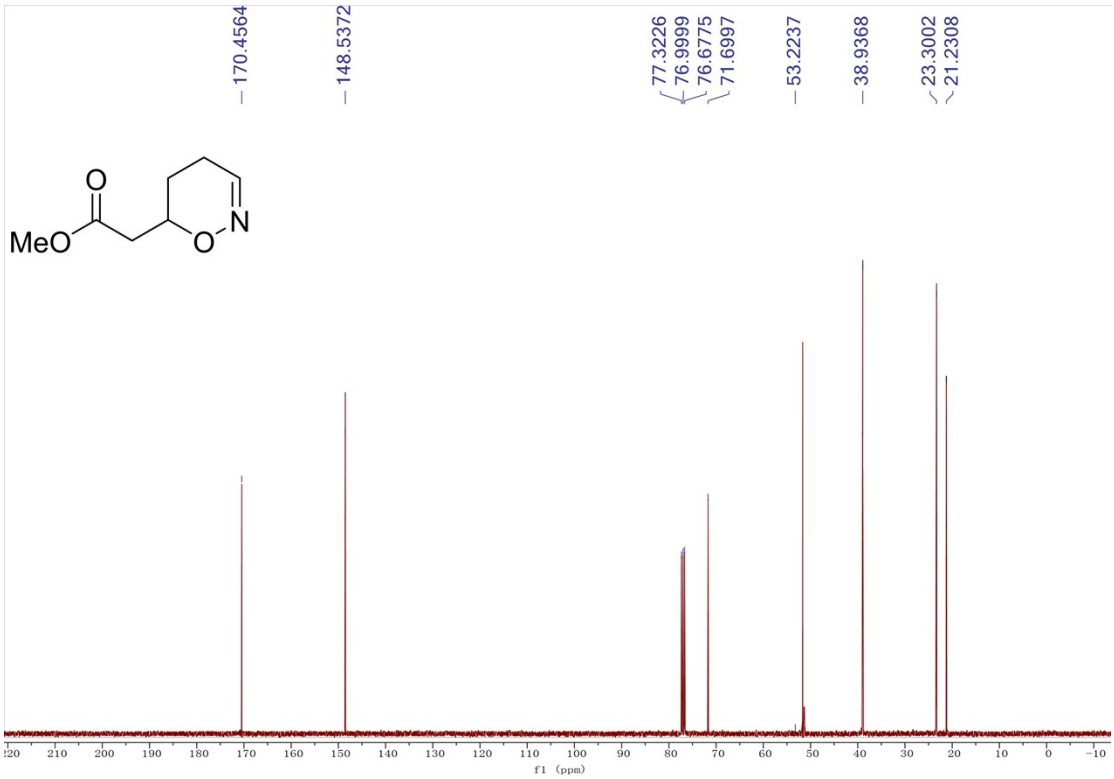
^{1}H NMR spectrum of aldehyde **10** ($CDCl_3$, 400 MHz)



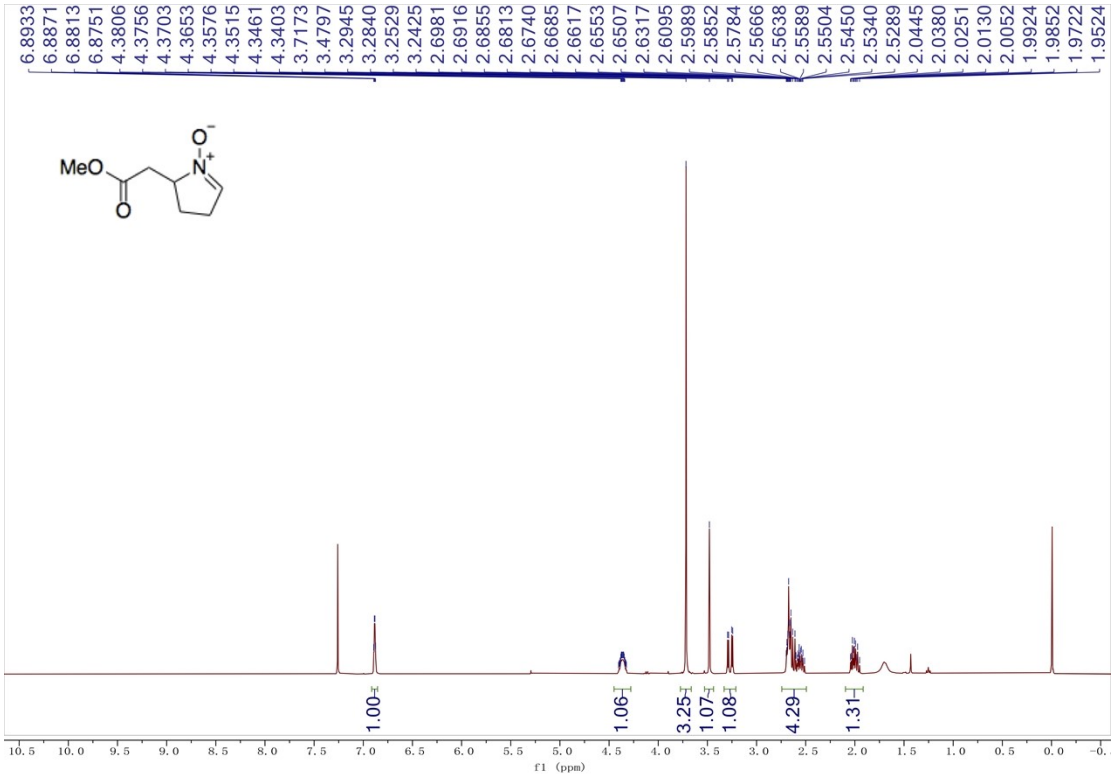
^{13}C NMR spectrum of aldehyde **10** ($CDCl_3$, 100 MHz)



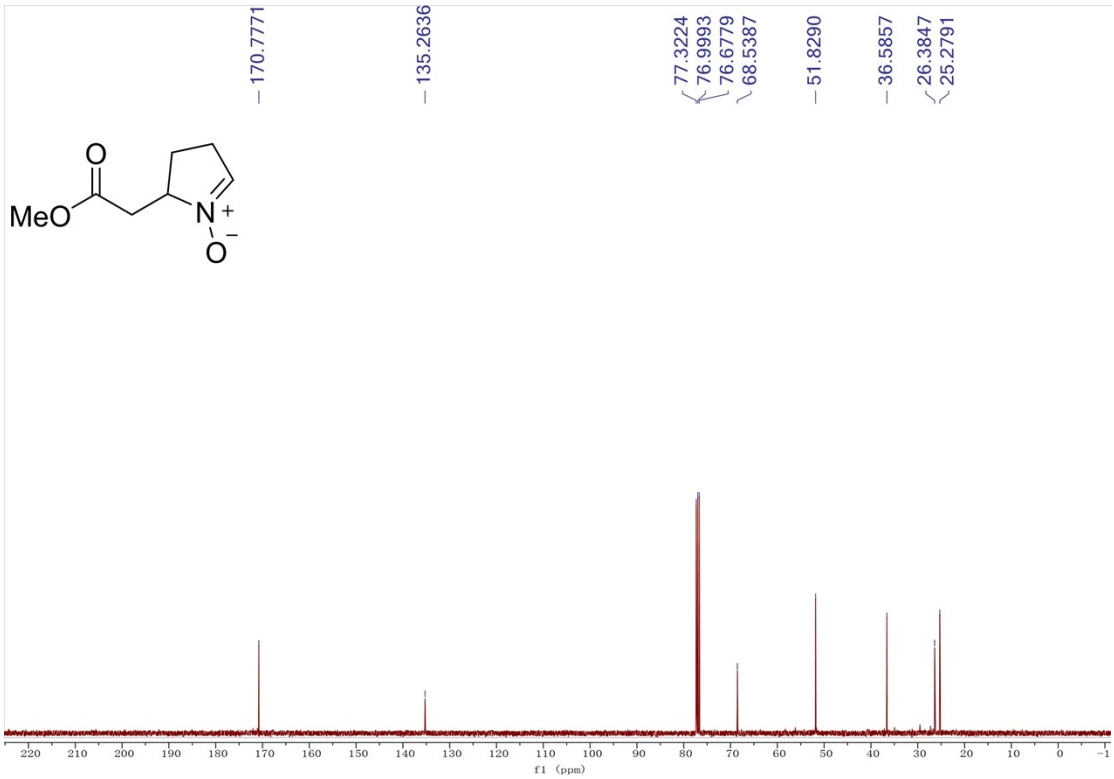
^{1}H NMR spectrum of oxazine **11** ($CDCl_3$, 500 MHz)



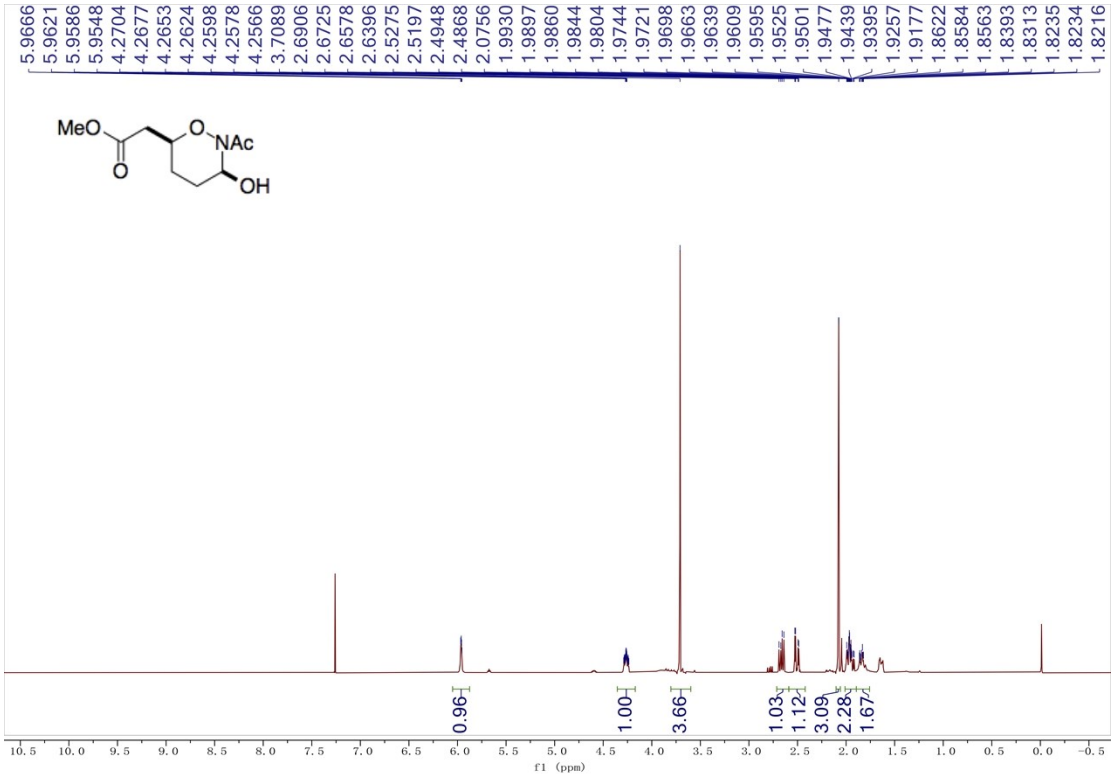
^{13}C NMR spectrum of oxazine **11** ($CDCl_3$, 100 MHz)*



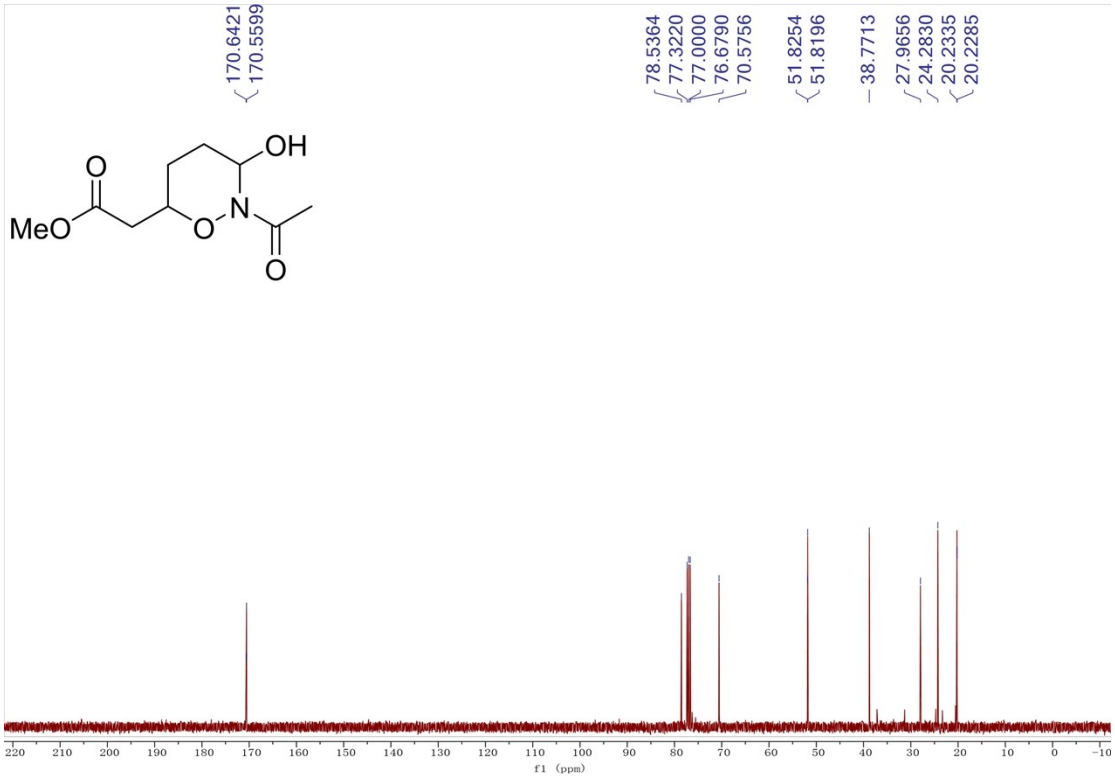
^{1}H NMR spectrum of nitrone **12** ($CDCl_3$, 400 MHz)



^{13}C NMR spectrum of nitrone **12** ($CDCl_3$, 100 MHz)



^{1}H NMR spectrum of aminal **13** ($CDCl_3$, 400 MHz)



^{13}C NMR spectrum of aminal **13** ($CDCl_3$, 100 MHz)

Procedure for the conversion of oxazine 2 to *p*-nitrobenzamide 14

Methyl 2-(2-(4-nitrobenzoyl)-1,2-oxazinan-6-yl)acetate

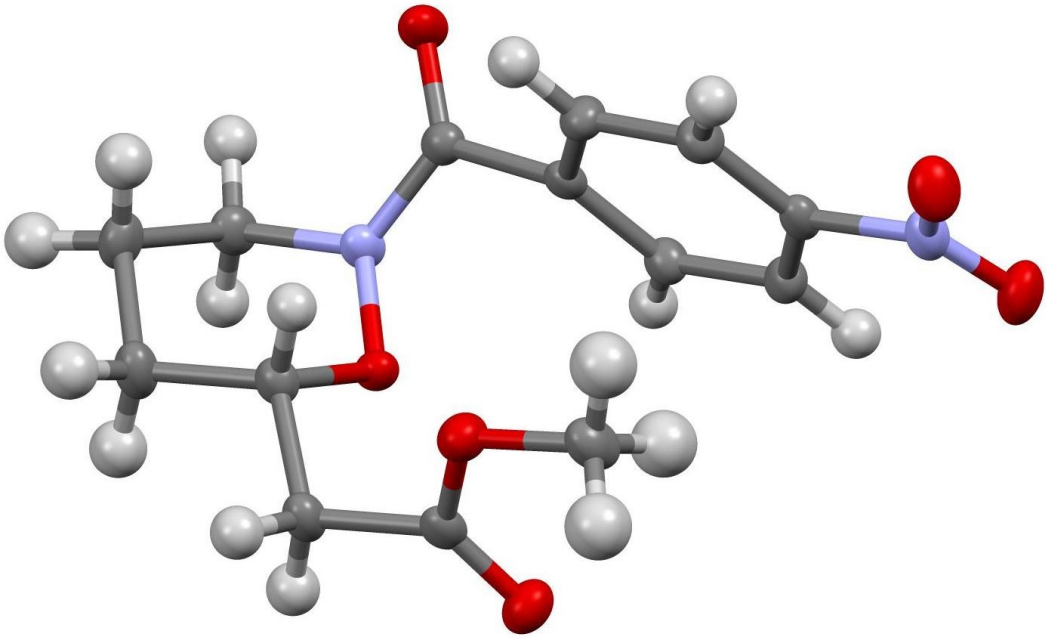
Anhydrous triethylamine (24 μL, 0.178 mmol, 2.0 equiv.) was added to a solution of tetrahydrooxazine **2** (14.2 mg, 0.089 mmol), 4-nitrobenzoic acid (16.4 mg, 0.098 mmol, 1.1 equiv.), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (24.5 mg, 0.128 mmol, 1.2 equiv.) and DMAP (3.2 mg, 0.026 mmol, 0.3 equiv.) in anhydrous tetrahydrofuran (1 mL). The mixture was stirred at room temperature overnight. The white precipitate formed was removed by filtration and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel using 50% ethyl acetate-hexane as the eluent to give *p*-nitrobenzamide **14** as a pale yellow crystalline solid (9.0 mg, 0.029 mmol, 33%), mp 99-102 °C.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.23 (d, *J* = 10.0 Hz, 2H), 7.79 (d, *J* = 10.0 Hz, 2H), 4.57 (br d, *J* = 13.2 Hz, 1H), 4.25 – 4.14 (m, 1H), 3.44 (s, 3H), 3.25 – 3.19 (m, 1H), 2.41 (dd, *J* = 16.1, 8.4 Hz, 1H), 2.34 (dd, *J* = 16.0, 4.3 Hz, 1H), 1.96 – 1.81 (m, 3H), 1.72 – 1.61 (m, 1H).

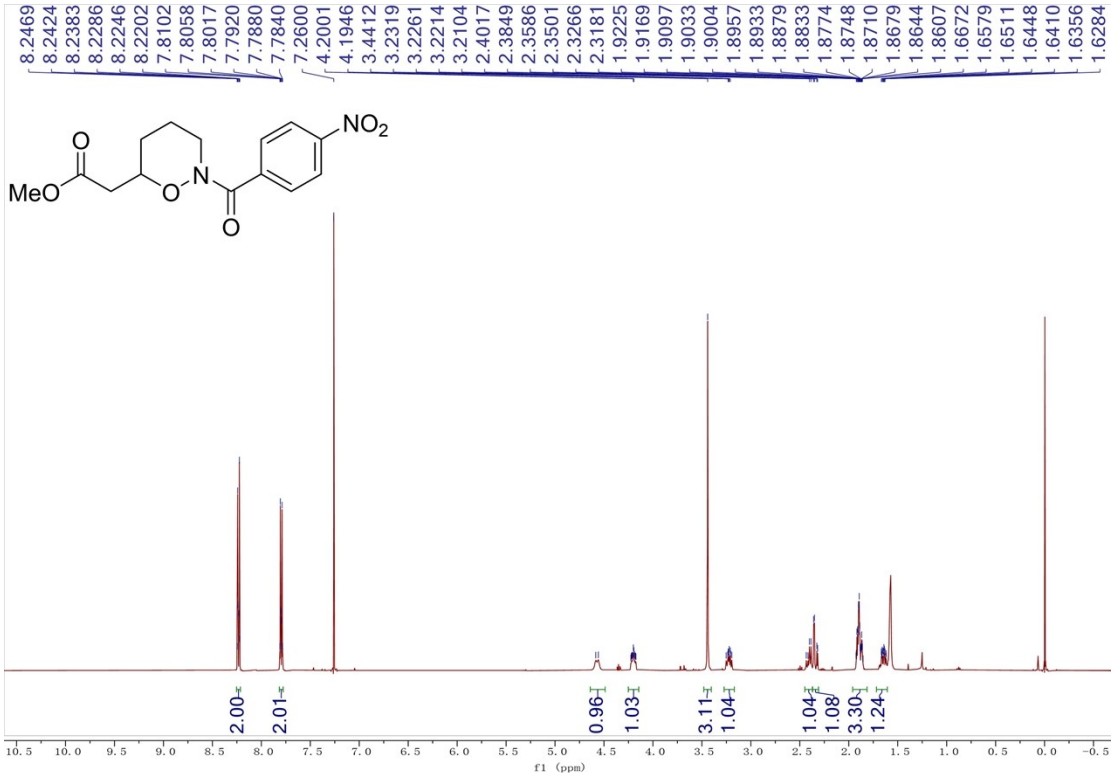
^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.9, 167.0, 148.1, 141.3, 129.8, 123.0, 80.0, 77.2, 52.2, 39.9, 31.1, 23.3.

HRMS (ESI-Quadrupole): m/z: $[M+Na]^+$ Calcd for $[C_{14}H_{16}N_2O_6Na]^+$: 331.0906; found: 331.0903.

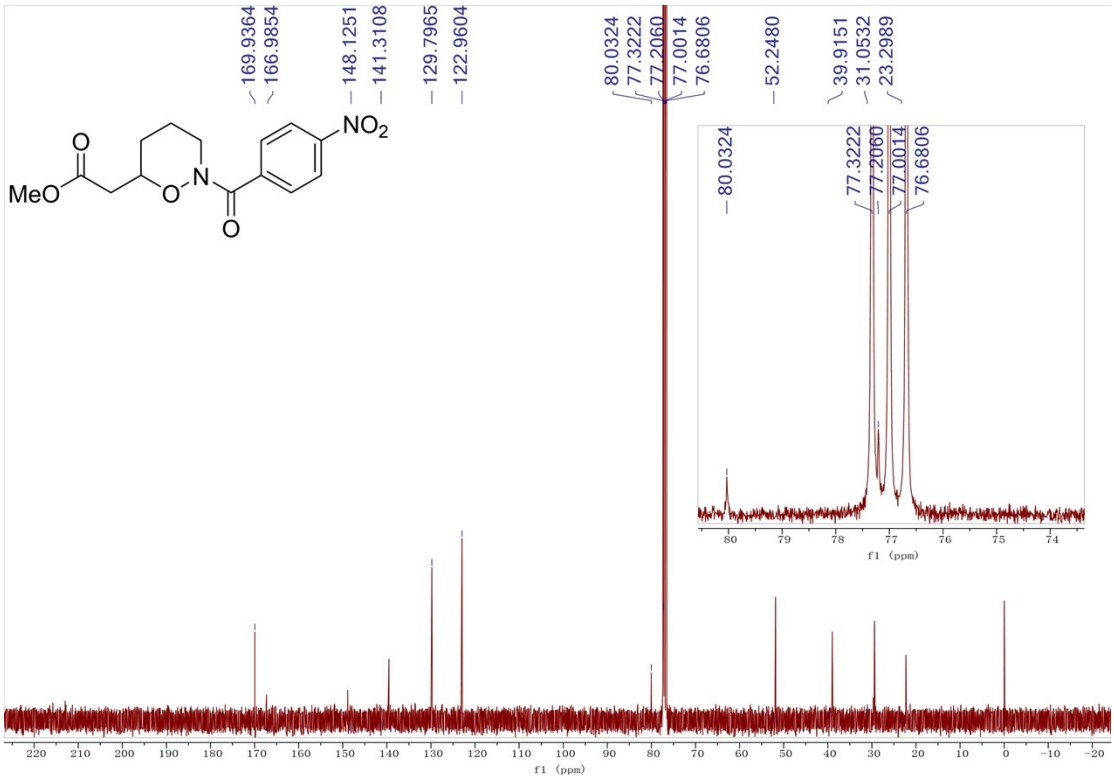
IR (neat, cm^{-1}): 2920, 2850, 1735, 1643, 1600, 1519, 1435, 1345, 1273, 1207, 1188, 1080, 1022, 918, 844, 794, 717, 648.



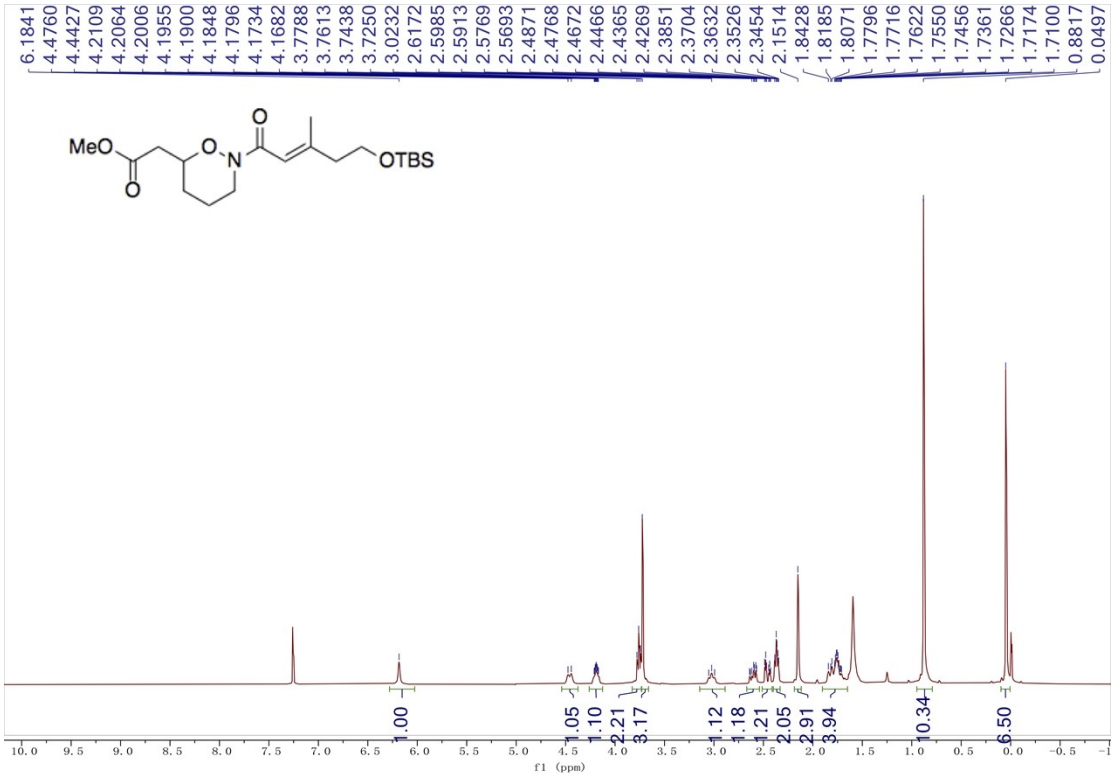
X-ray structure of *p*-nitrobenzamide **14**



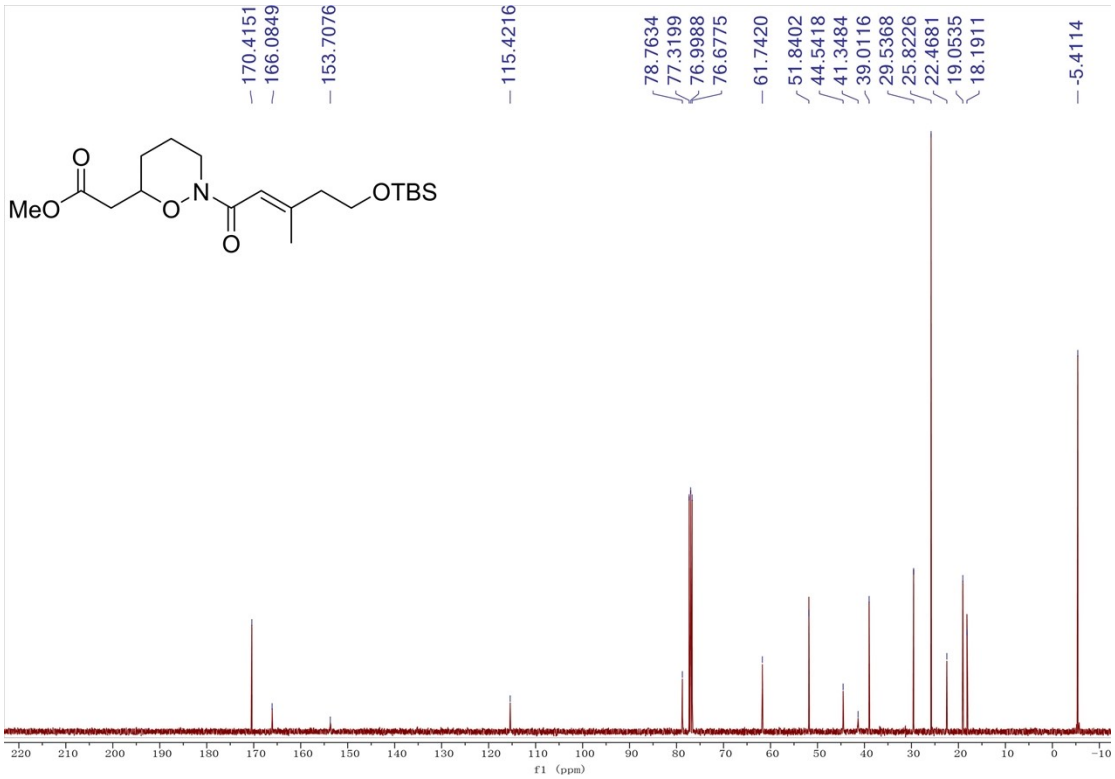
^{1}H NMR spectrum of *p*-nitrobenzamide **14** ($CDCl_3$, 500 MHz)



^{13}C NMR spectrum of *p*-nitrobenzamide **14** ($CDCl_3$, 100 MHz)



^{1}H NMR spectrum of *N*-acyloxazine **15** ($CDCl_3$, 500 MHz)



^{13}C NMR spectrum of *N*-acyloxazine **15** ($CDCl_3$, 100 MHz)

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* the signal at *ca* 100 pm (**5** and **6**) or *ca* 50 ppm (**11**) is an instrument artifact.