Supporting Information for

Synthesis of Cyclic Imides from Nitriles and Diols Using Hydrogen Transfer as a Substrate-Activating Strategy

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Contents

General considerations

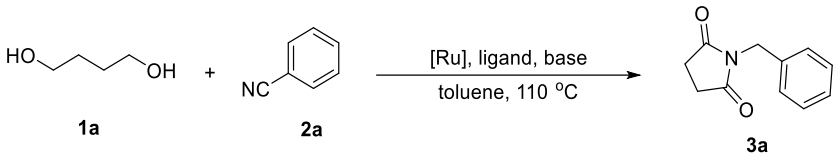
Unless otherwise noted, all reactions were carried out using standard Schlenk techniques or in an argon-filled glove box. All anhydrous solvents were purchased from commercial suppliers and degassed with dry argon before usage. NMR spectra were recorded in $CDCl_3$, and residue solvent signals were used as references. GC analyses were carried out using dodecane as an internal standard. $RuH_2(PPh_3)_4$,[1] $RuH_2(CO)(PPh_3)_3$,[2] and other metal reagents were prepared by literature procedures or purchased from commercial suppliers. Compound **4** was prepared according to the reported procedure.[3] Compounds **5**, **6**, **7**, and **8** were purchased from commercial suppliers and used as received without further purifications.

General procedure for the synthesis of cyclic imides

$RuH_2(PPh_3)_4$ (28.8 mg, 0.025 mmol), **4** (5.8 mg, 0.025mmol), NaH (2.4 mg, 0.10 mmol), and benzene (1.2 mL) were added to oven dried 4 mL vial equipped with septum screw cap inside a glove box. If solid nitrile (0.50 mmol) or diol (0.55 mmol) substrates were used, they were also added to the reaction mixture inside the glove box. Liquid nitrile or diol substrates were added into the vial using micro-syringe under Ar flow after the vial was taken out of the glove box. The septum of vial cap was pierced with 22 gauge needle connected to a manifold under inert atmosphere to make an open system. The mixture was heated to reflux for 18~24 h before being cooled to room temperature. All the volatiles were removed under vacuum. Purification of the crude products was performed with silica gel column chromatography using hexane and ethyl acetate solvent mixture as an eluent to afford the corresponding cyclic imide.

Optimization table

Table S1. Evaluation of Catalysts for Cyclic Imide Synthesis



Entry	Ru complex	Ligand	Base	Time(h)	Yield (%)[b]
1	$RuHCl(CO)(PPh_3)_3$	**4**	NaH	48	17
2	$RuCl_2(PPh_3)_3$	**4**	NaH	48	12
3	$RuH_2(CO)(PPh_3)_3$	**4**	NaH	48	58
4	Milstein cat.	-	-	24	0
5	$[Ru(benzene)Cl_2]_2$	**4**, CH_3CN	NaH	24	0
6	$[Ru(p\text{-}cymene)Cl_2]_2$	**4**, pyridine	NaH	24	0
7	$RuH_2(PPh_3)_4$	**4**	NaH	24	61

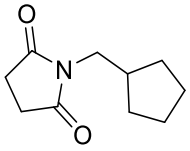
[a]Reaction conditions: **1a** (0.55 mmol, 1.1 equiv), **2a** (0.50 mmol, 1.0 equiv), [Ru] (5 mol %), ligand (5 mol %), NaH (20 mol %), toluene (0.6 mL), 110 °C in an open system under argon atmosphere. [b]Determined by GC.

GC analysis for reaction intermediate detection

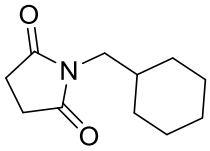
$RuH_2(PPh_3)_4$ (14.4 mg, 0.0125 mmol), **4** (2.9 mg, 0.0125 mmol), NaH (1.2 mg, 0.05 mmol), and benzene (0.6 mL) were added to oven dried 4 mL vial equipped with septum screw cap inside the glove box. **1a** (24.5 μL, 0.275 mmol), **2a** (26.0 μL, 0.25 mmol) were added into the vial using micro-syringe under Ar flow after the vial was taken out of the glove box. The septum of vial cap was pierced with 22 gauge needle connected to a manifold under inert atmosphere to make an open system. The each single mixture was heated to reflux for 10 min, 20 min, 30 min, 1 h, 2 h, 3 h, 4 h, 5 h, and 6 h, respectively, before being cooled to room temperature. The sample was diluted with dichloromethane, filtered with celite, analyzed with GC. The respective response factor was obtained by the GC analysis of a series of samples of known concentration, plotting the ratio of the areas, $A_{sample}/A_{standard}$ of each versus the ratio of the concentrations, [Sample]/[Standard]. Average data of independent 4 runs were plotted for the reaction profile in Figure 1.

Characterization of cyclic imides

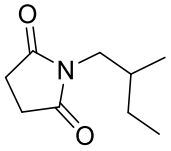
The reaction was performed in 0.50 mmol scale. All reported compounds, **3a**[4] (white solid, 68.3 mg, 0.361 mmol, 72%), **3b**[5] (white solid, 92.8 mg, 0.427 mmol, 86%), **3e**[6] (brown oil, 95.1 mg, 0.411 mmol, 82%), **3g**[7] (white solid, 80.5 mg, 0.367 mmol, 74%), **3j**[8] (colorless oil, 70.5 mg, 0.385 mmol, 77%), **3k**[5] (colorless oil, 95.1 mg, 0.348 mml, 70%), **3p**[9] (colorless oil, 96.4 mg, 0.363 mmol, 73%) were identified by spectral comparison with literature data.



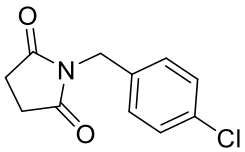
1-(Cyclopentylmethyl)-2,5-pyrrolidinedione (3c): yellow oil (69.8 mg, 0.385 mmol, 77%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 3.45 (d, *J* = 7.8 Hz, 2 H), 2.70 (s, 4 H), 2.26 (spt, *J* = 1.0 Hz, 1 H), 1.71 - 1.62 (m, 4 H), 1.57 - 1.46 (m, 2 H), 1.26 - 1.17 (m, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 177.4, 43.4, 38.2, 30.2, 28.0, 24.7; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{10}H_{16}NO_2$, 182.1181; found: 182.1178.



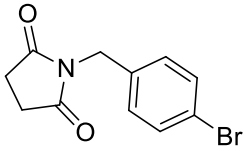
1-(Cyclohexylmethyl)-2,5-pyrrolidinedione (3d): white crystalline solid (78.4 mg, 0.402 mmol, 80%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 3.35 (d, *J* = 7.3 Hz, 2 H), 2.71 (s, 4 H), 1.74 - 1.66 (m, 3 H), 1.66 - 1.57 (m, 3 H), 1.22 - 1.12 (m, 3 H), 1.01 - 0.90 (m, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 177.5, 44.9, 36.1, 30.7, 28.1, 26.1, 25.6; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{11}H_{18}NO_2$, 196.1338; found: 196.1334.



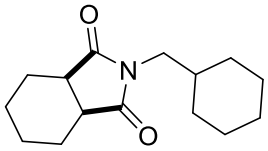
1-(2-Methylbutyl)-2,5-pyrrolidinedione (3f): dark brown oil (61.1 mg, 0.361 mmol, 72%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 3.40 (dd, *J* = 6.6, 13.0 Hz, 1 H), 3.32 (dd, *J* = 8.1, 13.0 Hz, 1 H), 2.70 (s, 4 H), 1.87 - 1.76 (m, 1 H), 1.40 - 1.29 (m, 1 H), 1.18 - 1.07 (m, 1 H), 0.90 (t, *J* = 7.3 Hz, 3 H), 0.83 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (75MHz, $CDCl_3$) δ = 177.4, 44.7, 33.2, 28.0, 26.9, 16.7, 11.0; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_9H_{16}NO_2$, 170.1181; found: 170.1177.



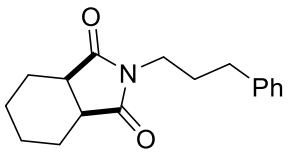
1-(4-Chlorobenzyl)-2,5-pyrrolidinedione (3h): white crystalline solid (74.8 mg, 0.334 mmol, 67%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 7.35 - 7.32 (m, *J* = 8.8 Hz, 1 H), 7.29 - 7.26 (m, *J* = 8.3 Hz, 1 H), 4.62 (s, 2 H), 2.71 (s, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 176.7, 134.2, 134.0, 130.5, 128.8, 41.7, 28.2; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{11}H_{11}ClNO_2$, 224.0478; found: 224.0480.



1-(4-Bromobenzyl)-2,5-pyrrolidinedione (3i): white crystalline solid (78.5 mg, 0.293 mmol, 59%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 7.44 (d, *J* = 8.3 Hz, 2 H), 7.28 (d, *J* = 8.3 Hz, 2 H), 4.60 (s, 2 H), 2.71 (s, 4 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 176.70, 134.67, 131.78, 130.76, 122.13, 41.77, 28.19; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{11}H_{11}BrNO_2$, 267.9973; found: 267.9975.

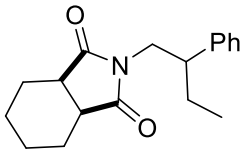


2-(Cyclohexylmethyl)-*cis*-hexahydro-1H-isoindole-1,3(2H)-dione (3l): white crystalline solid (104.4 mg, 0.419 mmol, 84%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 3.32 (d, *J* = 7.3 Hz, 2 H), 2.87 - 2.80 (m, 2 H), 1.92 - 1.82 (m, 2 H), 1.79 - 1.73 (m, 2 H), 1.73 - 1.66 (m, 3 H), 1.66 - 1.56 (m, 3 H), 1.51 - 1.37 (m, 4 H), 1.27 - 1.09 (m, 3 H), 1.01 - 0.89 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 180.10, 44.54, 39.66, 36.26, 30.76, 26.21, 25.61, 23.90, 21.72; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{15}H_{24}NO_2$, 250.1807; found: 250.1801.

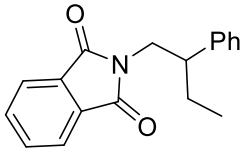


2-(3-Phenylpropyl)-*cis*-hexahydro-1H-isoindole-1,3(2H)-dione (3m): colorless oil (116.6 mg, 0.430 mmol, 86%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 7.30 - 7.26 (m, 2 H), 7.20 - 7.15 (m, 3 H), 3.54 (t, *J* = 7.3 Hz, 2 H), 2.81 - 2.73 (m, 2 H), 2.63 (t, *J* = 7.3 Hz, 2 H), 1.95 - 1.88 (m, 2 H), 1.88

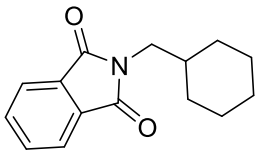
- 1.79 (m, 2 H), 1.76 - 1.67 (m, 2 H), 1.50 - 1.34 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 179.66, 140.95, 128.29, 128.18, 125.89, 39.55, 38.20, 33.11, 28.98, 23.61, 21.47; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{17}H_{22}NO_2$, 272.1651; found: 272.1655.



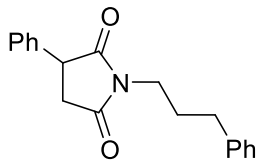
2-(2-Phenylbutyl)-*cis*-hexahydro-1H-isoindole-1,3(2H)-dione (3n): colorless oil (114.9 mg, 0.403 mmol, 81%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 7.26 - 7.21 (m, 2 H), 7.19 - 7.12 (m, 3 H), 3.81 (dd, *J* = 10.3, 13.2 Hz, 1 H), 3.55 (dd, *J* = 6.4, 13.2 Hz, 1 H), 3.18 - 3.08 (m, 1 H), 2.67 - 2.55 (m, 2 H), 1.73 - 1.55 (m, 4 H), 1.55 - 1.46 (m, 1 H), 1.38 - 1.29 (m, 1 H), 1.26 - 1.08 (m, 4 H), 0.79 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) Major rotamer: δ = 179.6, 141.2, 128.3, 128.3, 126.8, 45.0, 43.5, 39.5, 27.1, 23.4, 21.6, 11.8; Minor rotamer: δ = 179.8, 141.2, 128.3, 128.3, 126.8, 45.0, 43.5, 39.2, 27.1, 23.7, 11.8; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{18}H_{24}NO_2$, 286.1807; found: 286.1799.



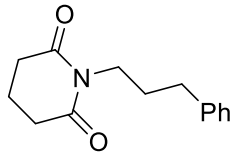
2-(2-Phenylbutyl)isoindoline-1,3-dione (3o): colorless oil (83.7 mg, 0.300 mmol, 60%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 7.81 - 7.75 (m, 2 H), 7.69 - 7.64 (m, 2 H), 7.26 - 7.14 (m, 5 H), 3.92 - 3.79 (m, 2 H), 3.14 - 3.04 (m, 1 H), 1.80 - 1.60 (m, 2 H), 0.79 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.3, 141.4, 133.8, 131.9, 128.3, 128.0, 126.7, 123.1, 46.1, 43.8, 26.2, 11.8; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{18}H_{18}NO_2$, 280.1338; found: 280.1337.



2-(Cyclohexylmethyl)isoindoline-1,3-dione (3q): white crystalline solid (85.0 mg, 0.349 mmol, 70%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 7.86 - 7.81 (m, 2 H), 7.72 - 7.68 (m, 2 H), 3.52 (d, *J* = 7.3 Hz, 2 H), 1.84 - 1.75 (m, 1 H), 1.75 - 1.59 (m, 5 H), 1.26 - 1.11 (m, 3 H), 1.07 - 0.94 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.7, 133.8, 132.1, 123.1, 44.1, 37.0, 30.7, 26.2, 25.6; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{15}H_{18}NO_2$, 244.1338; found: 244.1333.



3-Phenyl-1-(3-phenylpropyl)-2,5-pyrrolidinedione (3r): colorless oil (74.2 mg, 0.253 mmol, 51 %); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 7.42 - 7.33 (m, 3 H), 7.33 - 7.27 (m, 2 H), 7.25 - 7.14 (m, 5 H), 3.93 - 3.85 (m, 1 H), 3.66 - 3.60 (m, 2 H), 3.10 (dd, *J* = 9.3, 12.7 Hz, 1 H), 2.76 (dd, *J* = 4.6, 18.3 Hz, 1 H), 2.66 (t, *J* = 7.6 Hz, 2 H), 2.05 - 1.93 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 177.7, 176.1, 140.9, 137.2, 129.2, 128.4, 128.3, 127.9, 127.3, 126.0, 45.8, 38.9, 37.1, 33.2, 28.8; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{19}H_{20}NO_2$, 294.1494; found: 294.1487.



1-(3-Phenylpropyl)-2,6-piperidinedione (3s): black oil (49.6 mg, 0.214 mmol, 43%); ^{1}H NMR (499 MHz, $CDCl_3$) δ = 7.28 - 7.24 (m, 2 H), 7.20 - 7.14 (m, 3 H), 3.83 (t, *J* = 7.8 Hz, 2 H), 2.64 (t, *J* = 7.8 Hz, 2 H), 2.57 (t, *J* = 6.6 Hz, 4 H), 1.92 - 1.80 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.42, 141.42, 128.25, 128.17, 125.79, 39.44, 33.20, 32.77, 28.97, 17.00; HRMS–FAB (*m/z*) $[M+H]^+$ calcd for $C_{14}H_{18}NO_2$, 232.1338; found: 232.1339.

References

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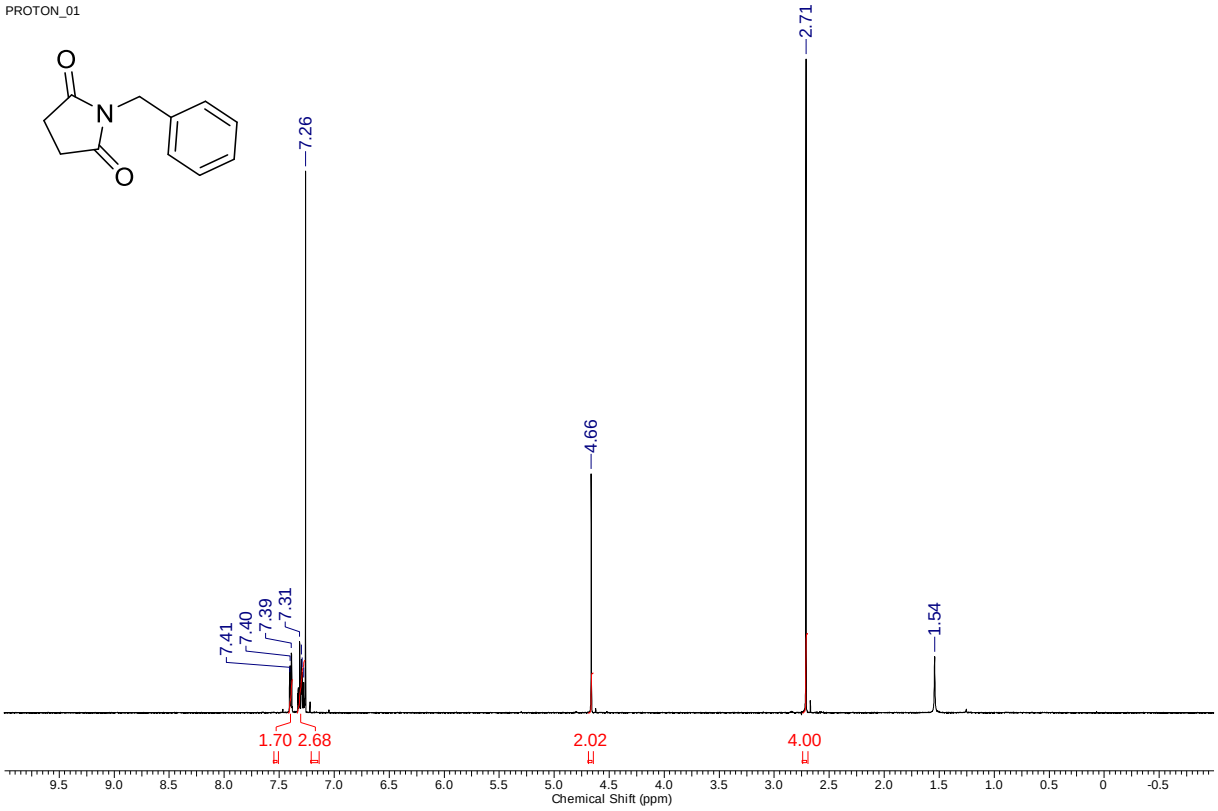
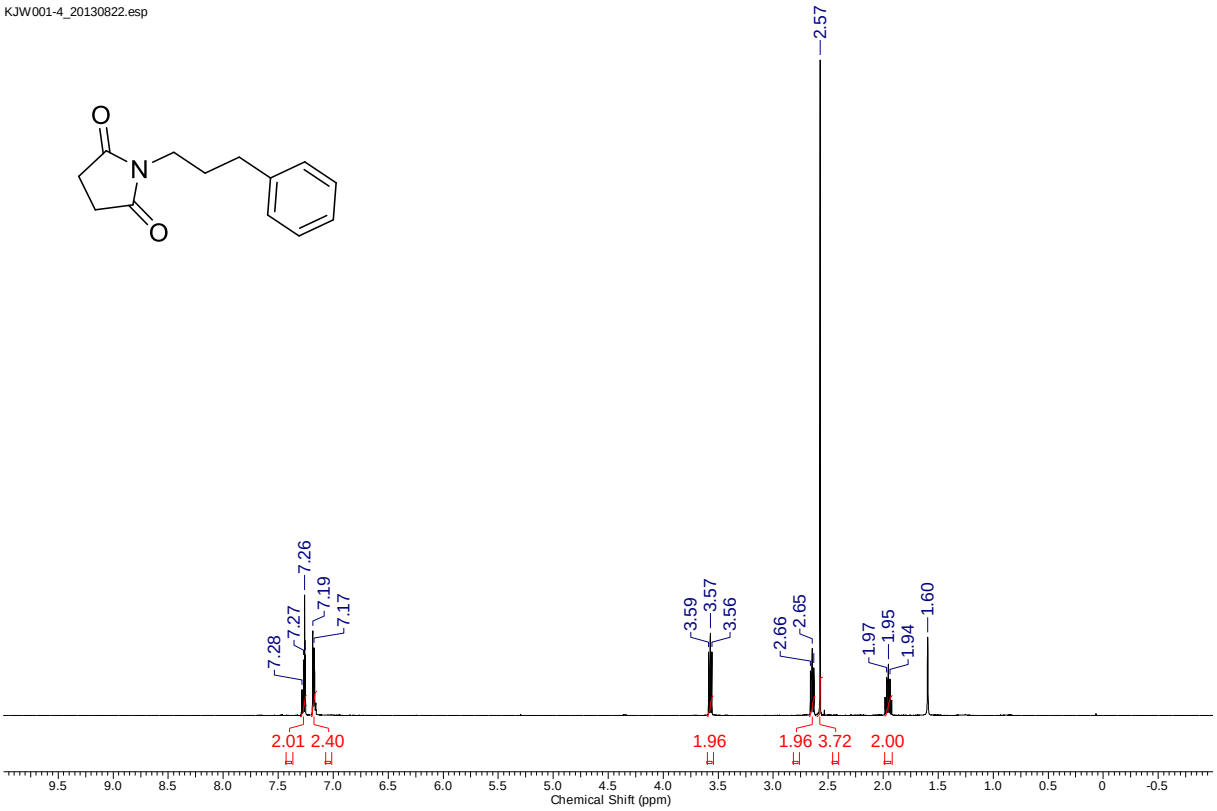
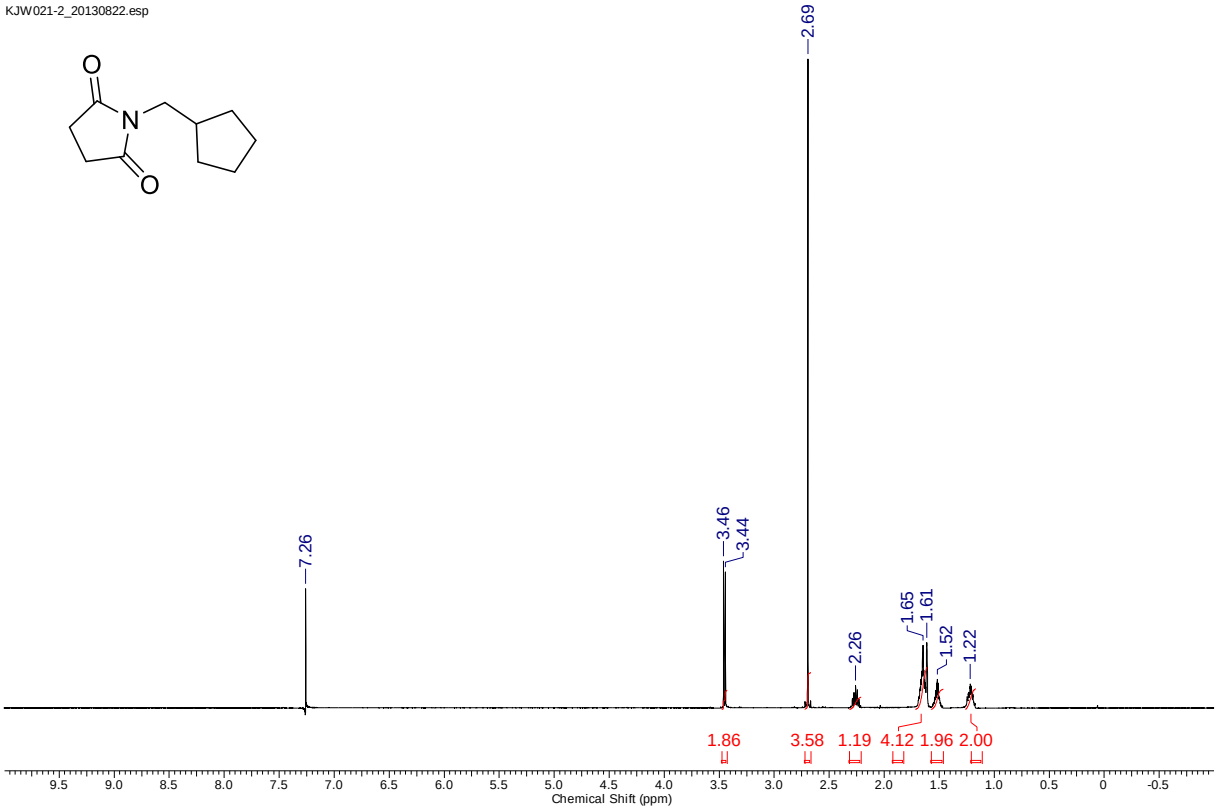
^{1}H NMR (**3a)** ($CDCl_3$)



^{1}H NMR (**3b)** ($CDCl_3$)



^{1}H NMR (**3c)** ($CDCl_3$)



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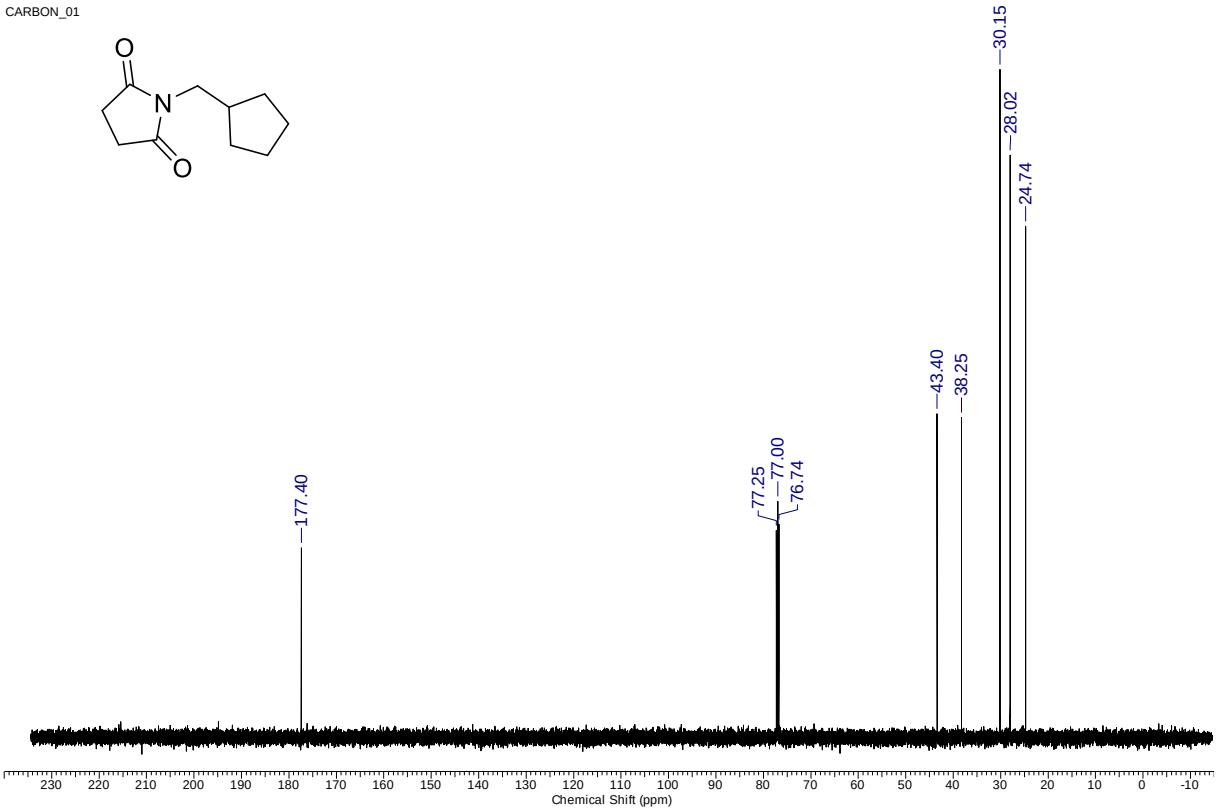

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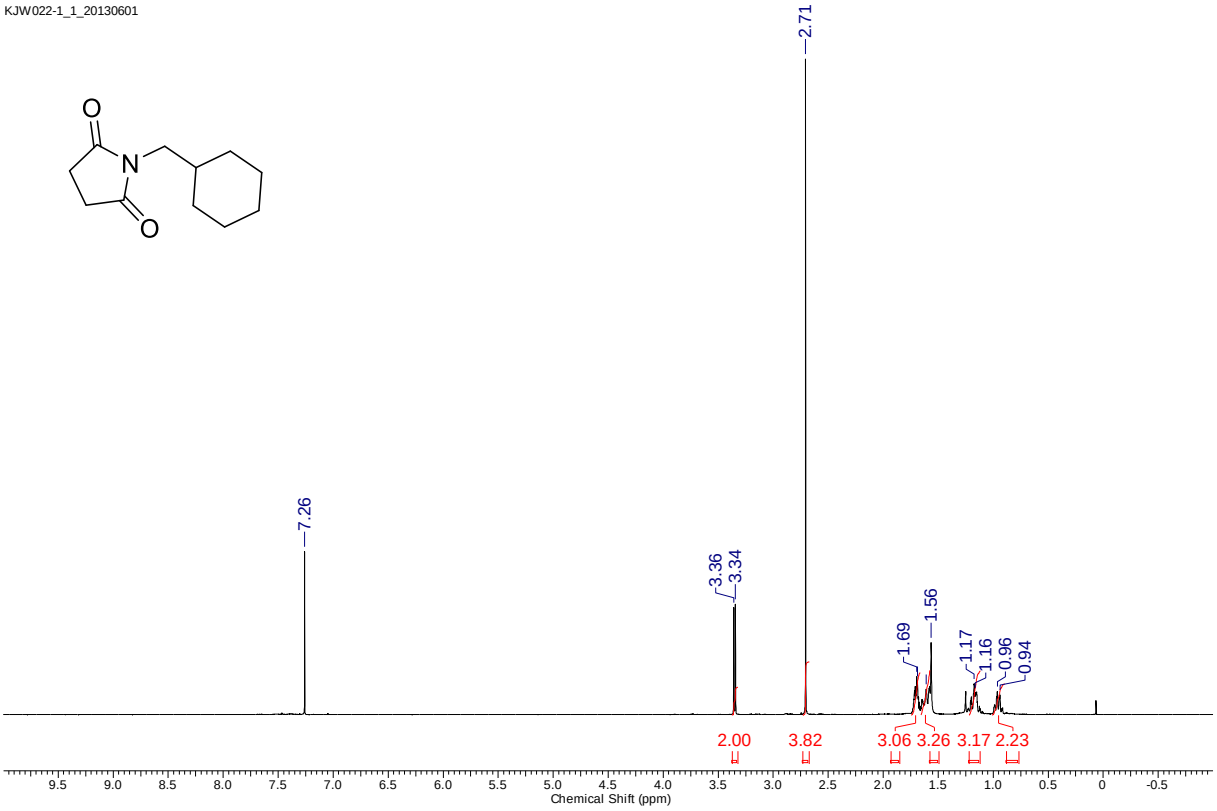
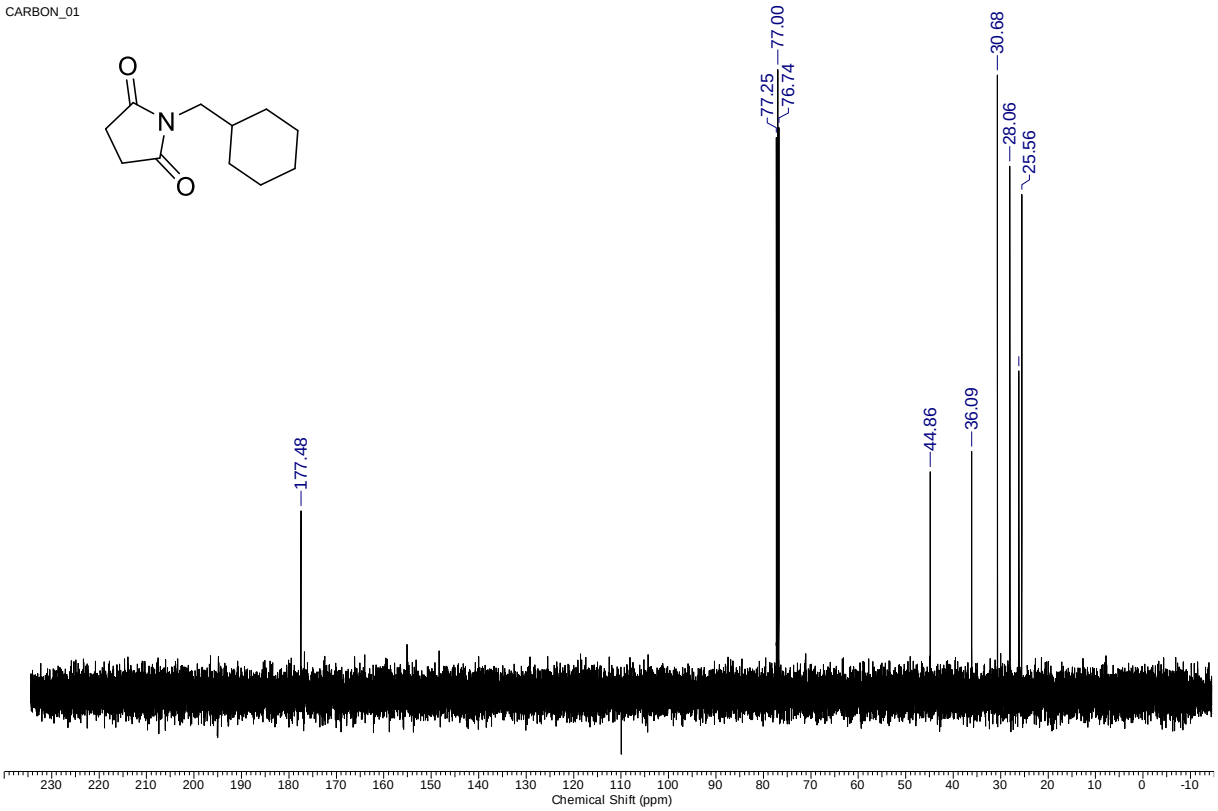


^{13}C NMR (**3d)** ($CDCl_3$)



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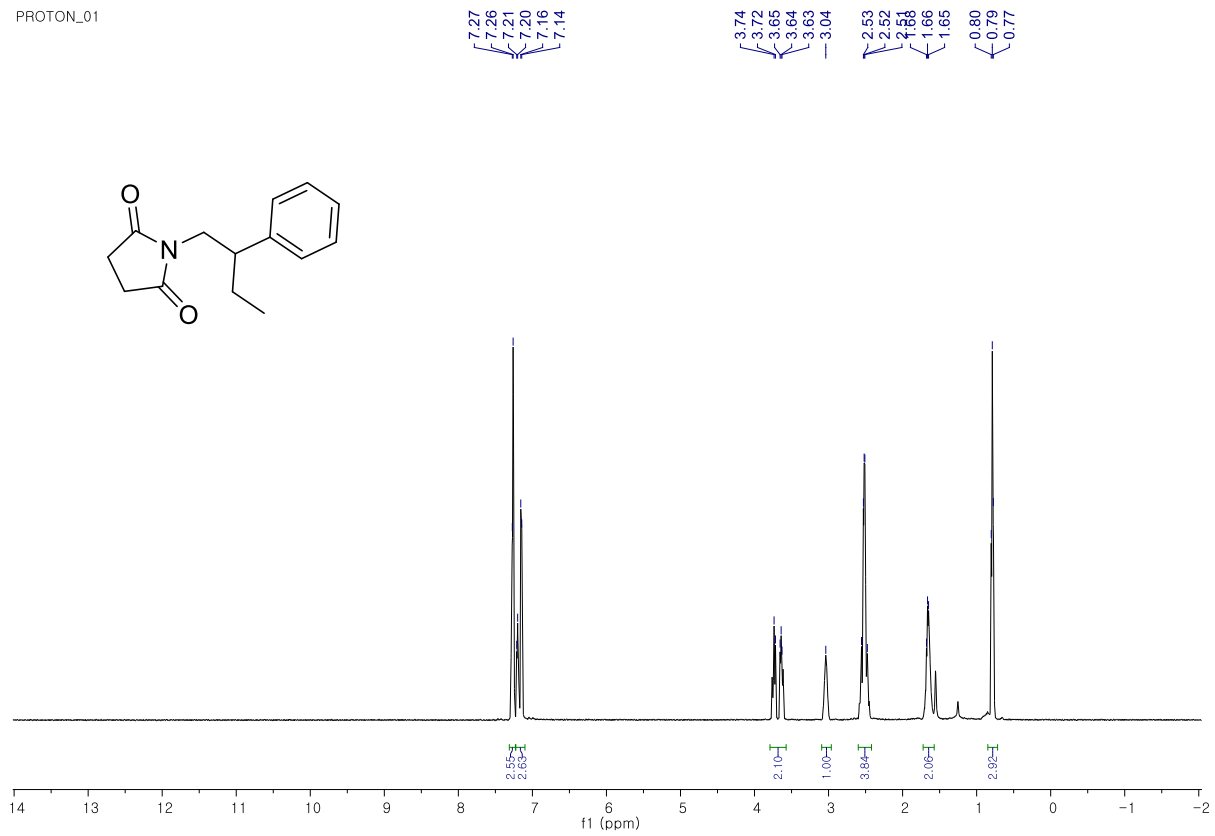
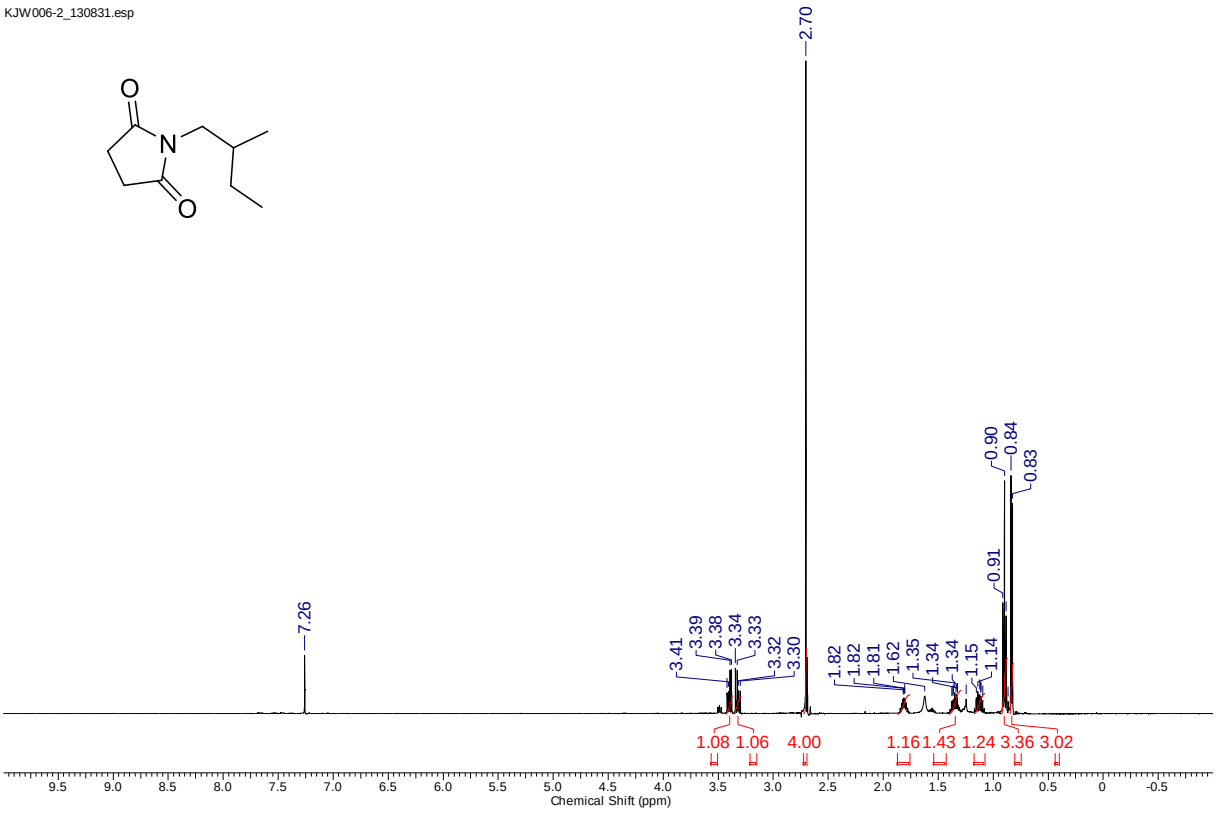
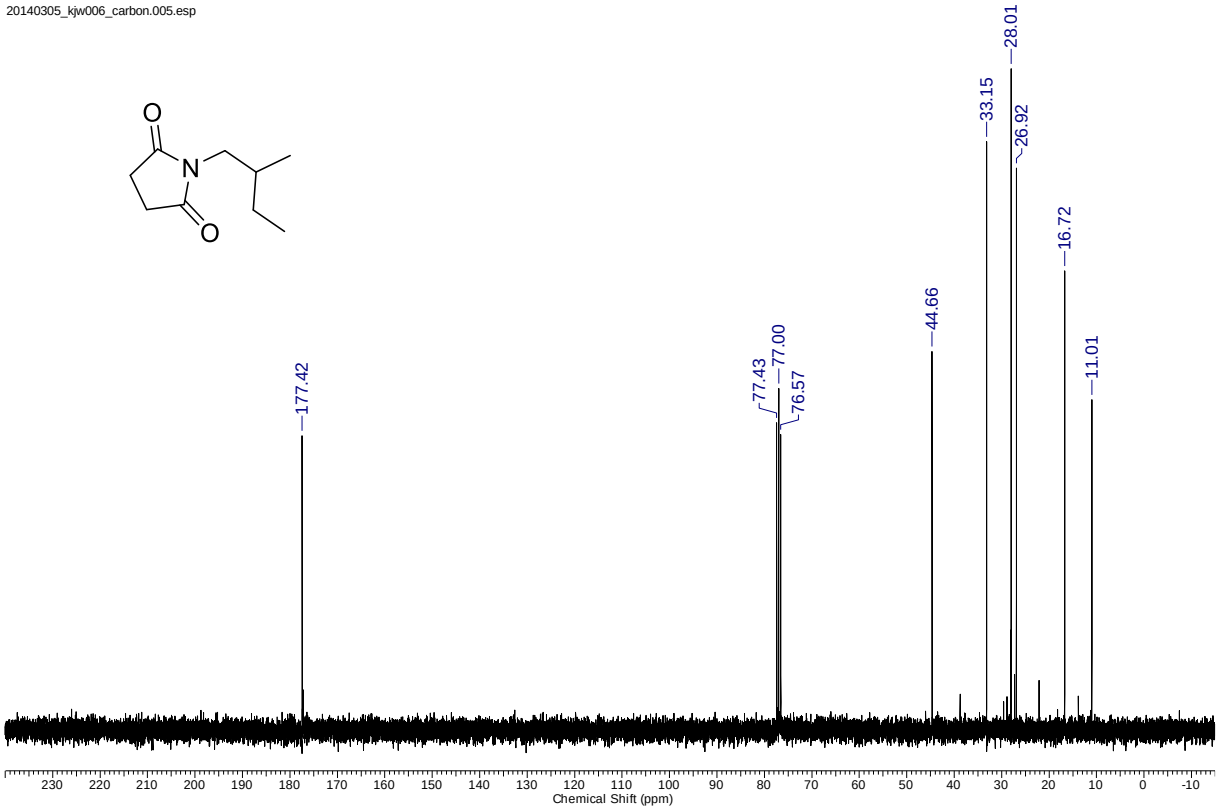


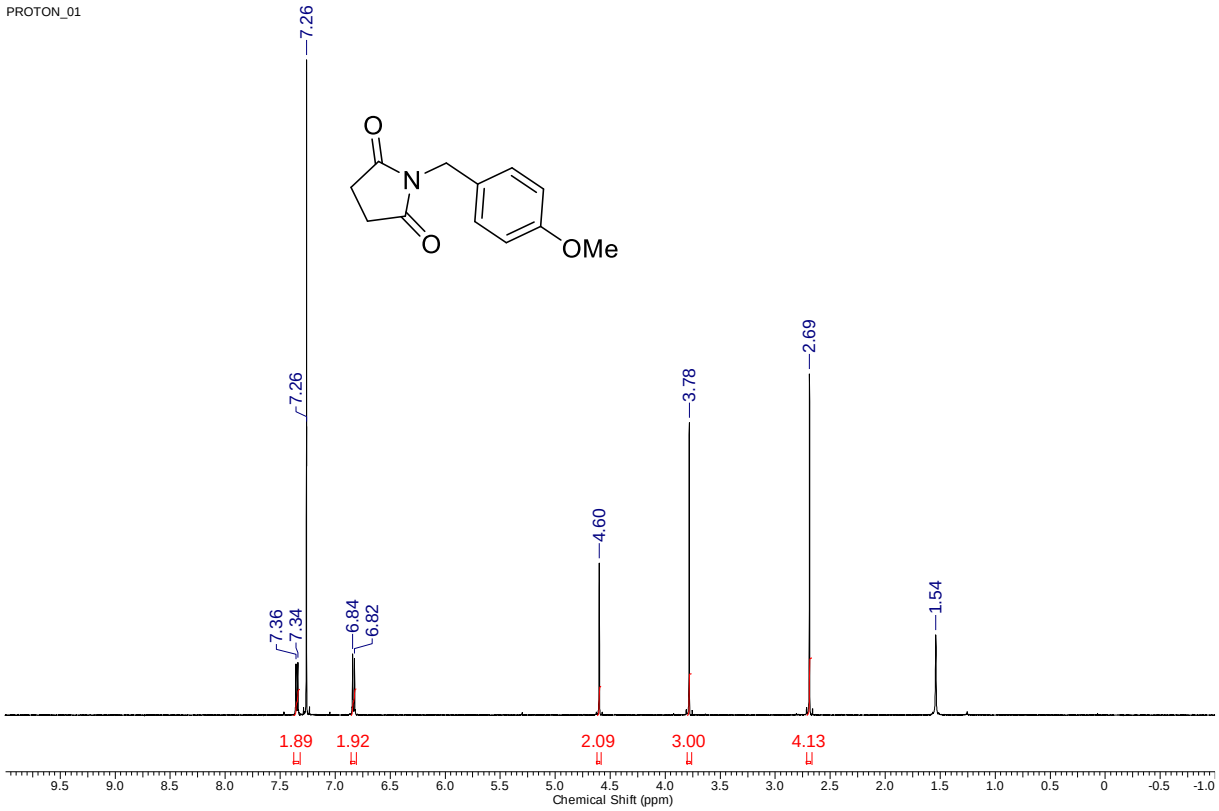
^{1}H NMR (**3f)** ($CDCl_3$)



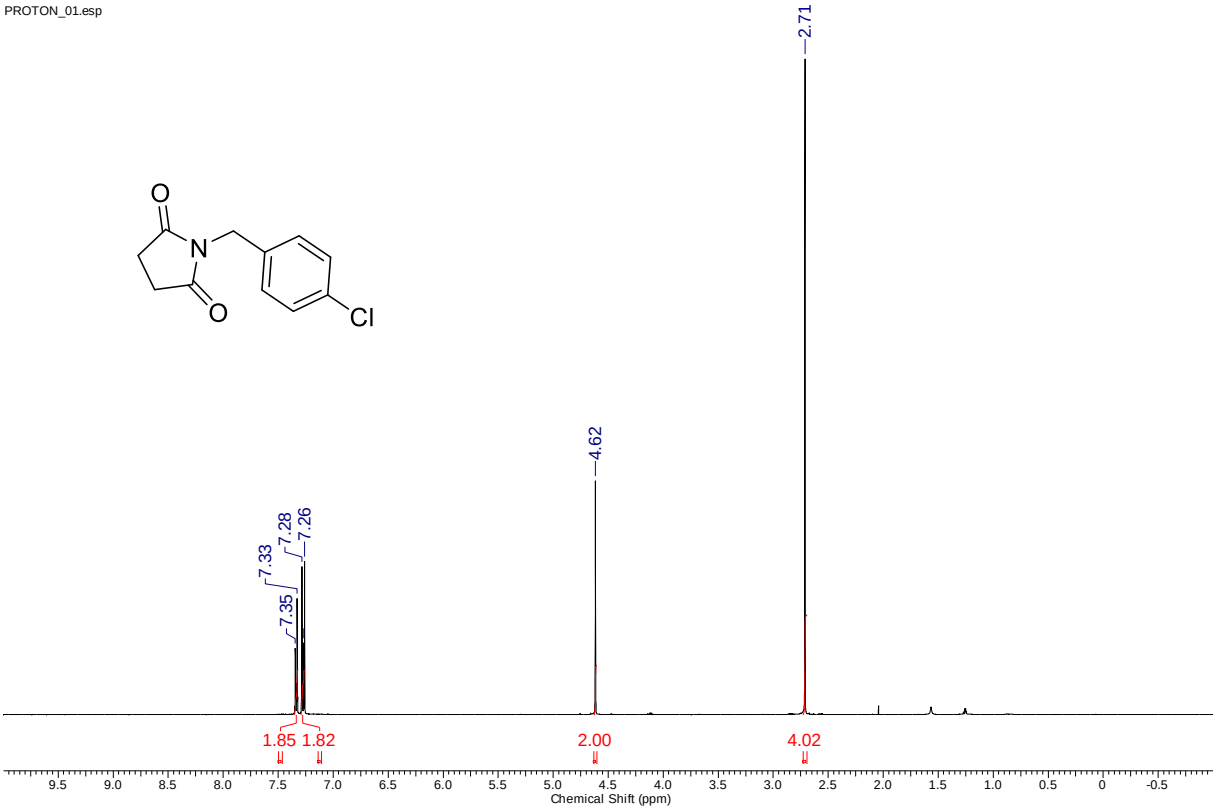
^{13}C NMR (**3f)** ($CDCl_3$)



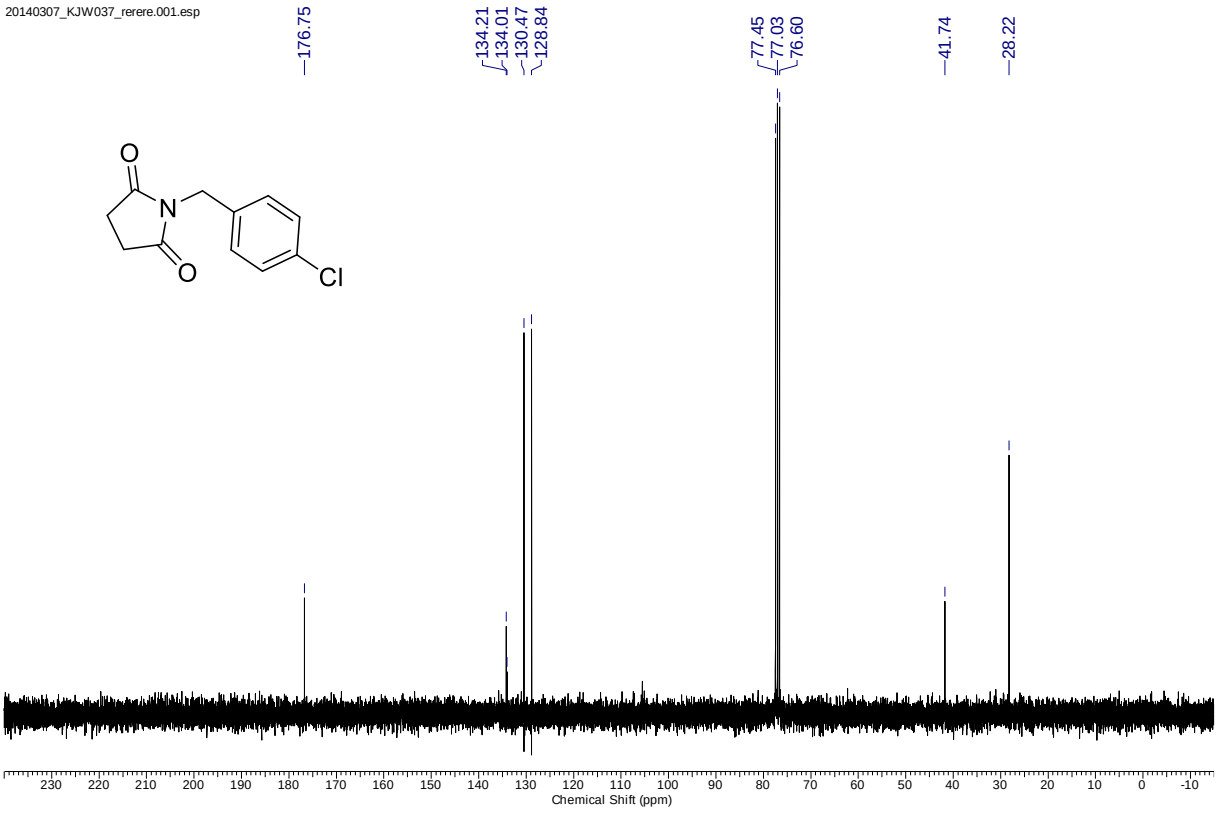
^{1}H NMR (**3g)** ($CDCl_3$)



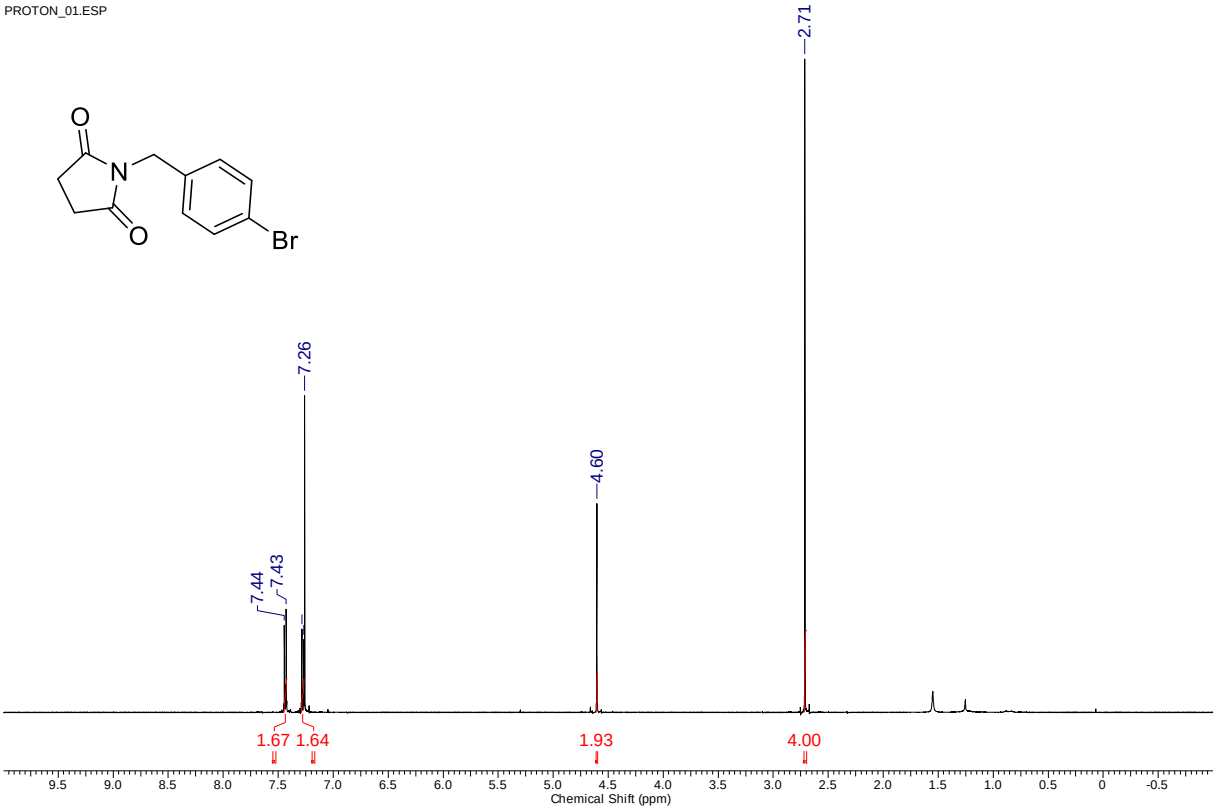
^{1}H NMR (**3h)** ($CDCl_3$)



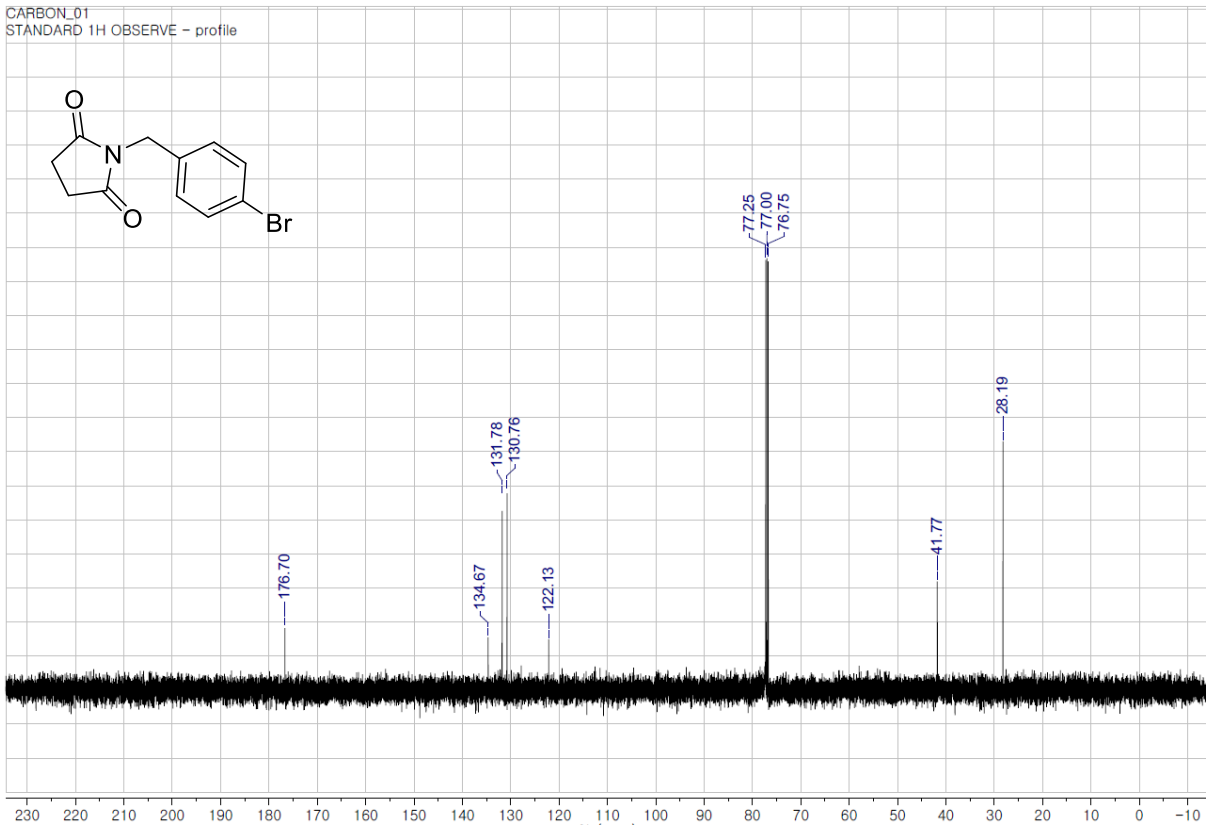
^{13}C NMR (**3h)** ($CDCl_3$)



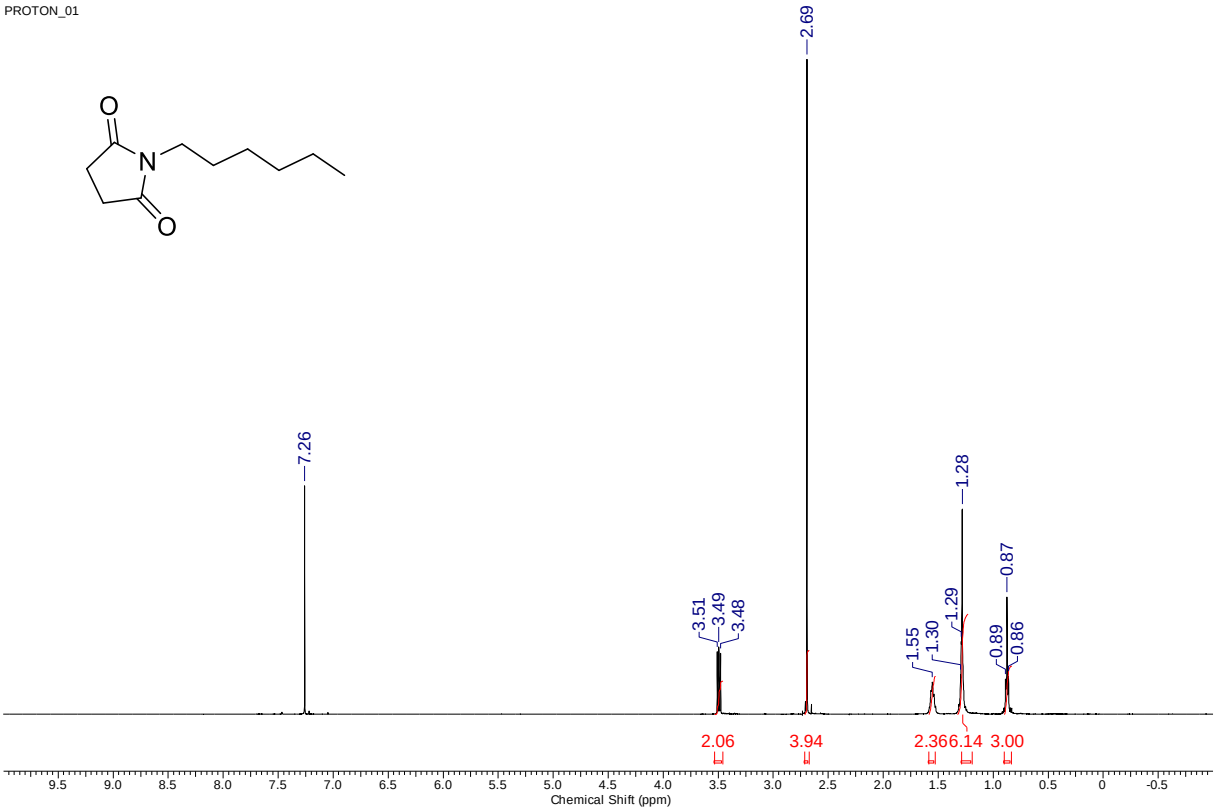
^{1}H NMR (**3i**) ($CDCl_3$)



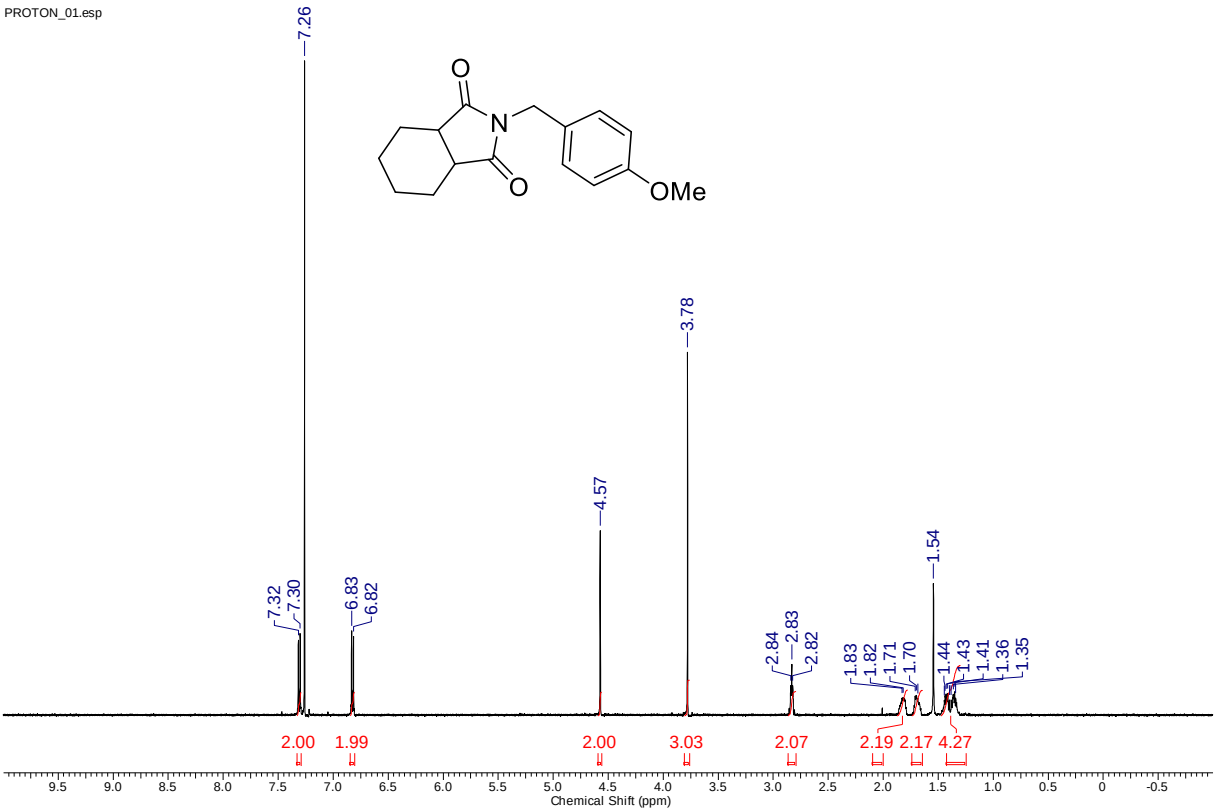
^{13}C NMR (**3i**) ($CDCl_3$)



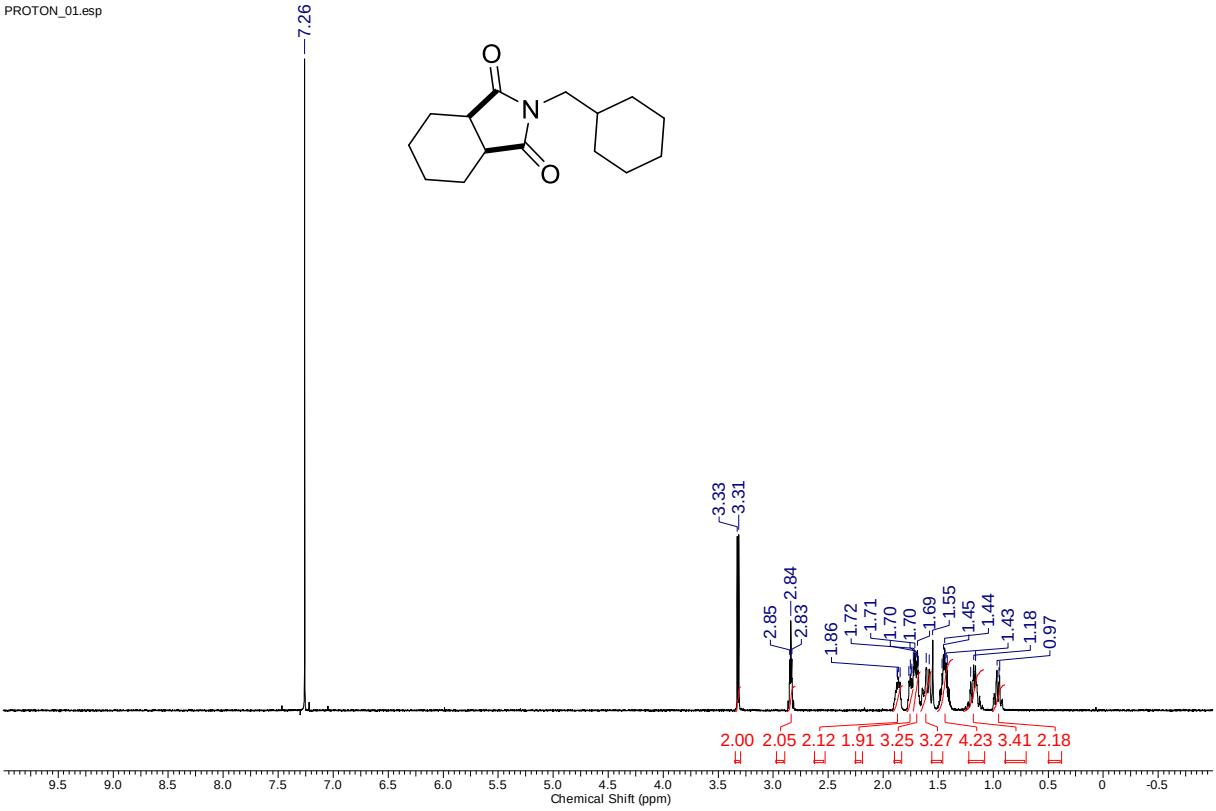
^{1}H NMR (**3j)** ($CDCl_3$)



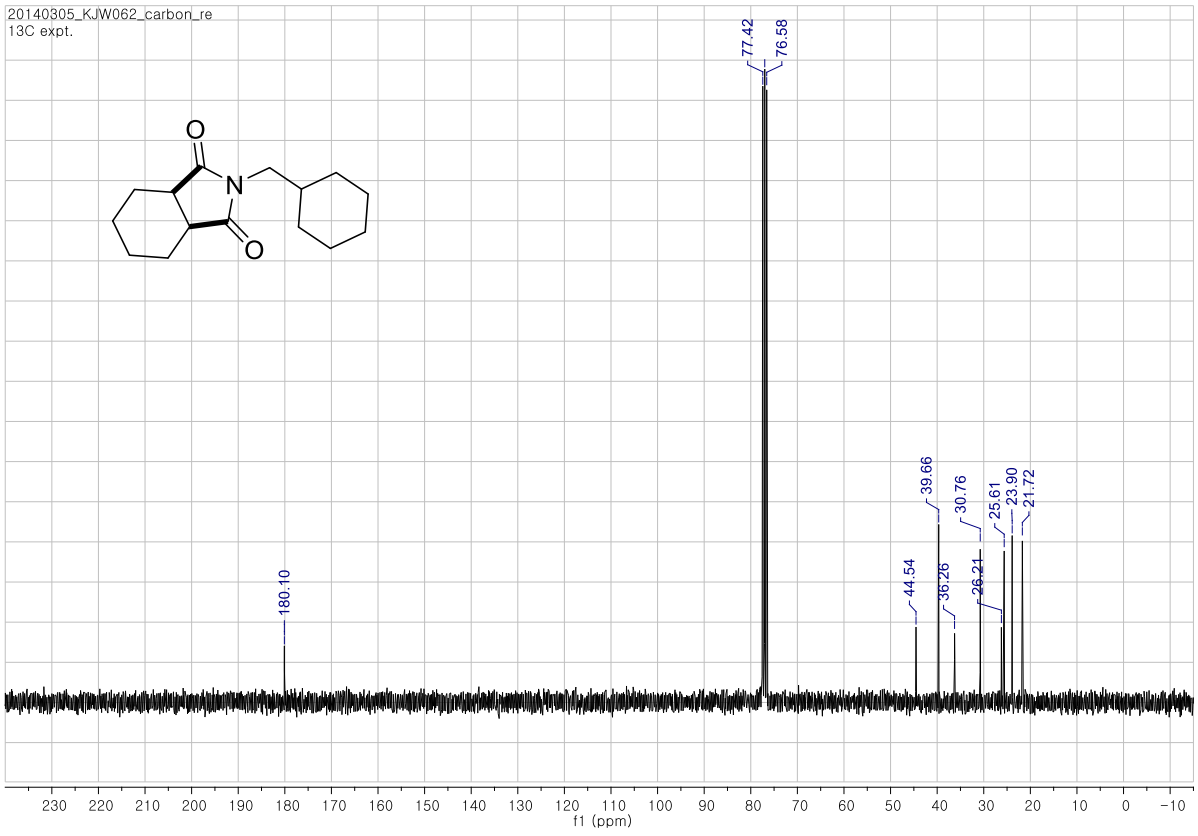
^{1}H NMR (**3k)** ($CDCl_3$)



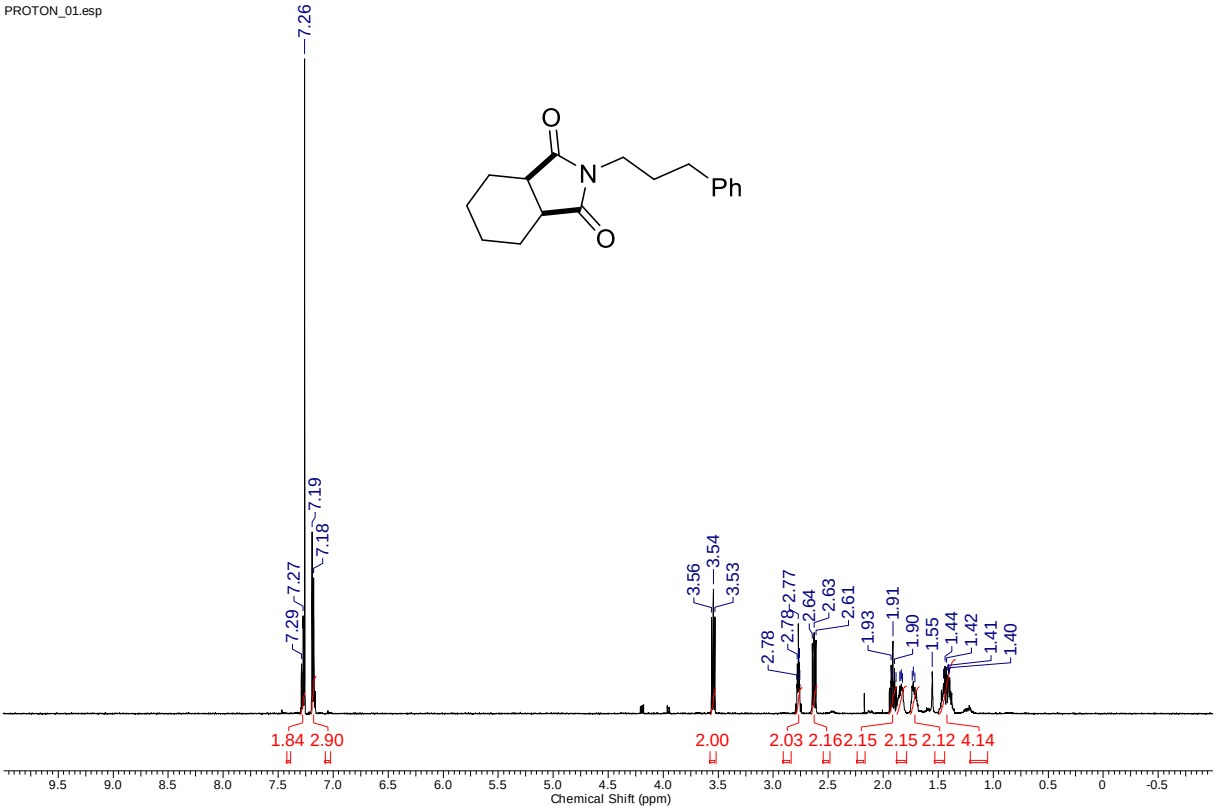
^{1}H NMR (**3l**) ($CDCl_3$)



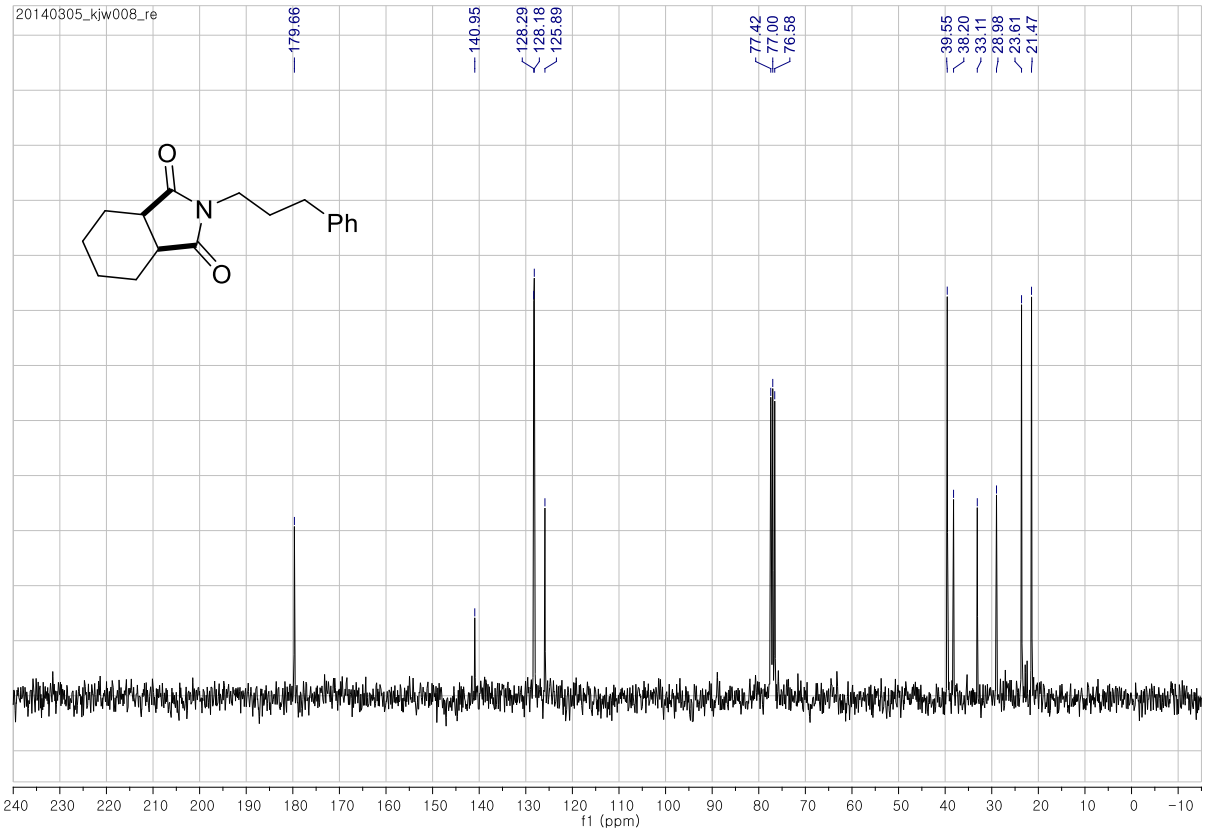
^{13}C NMR (**3l**) ($CDCl_3$)



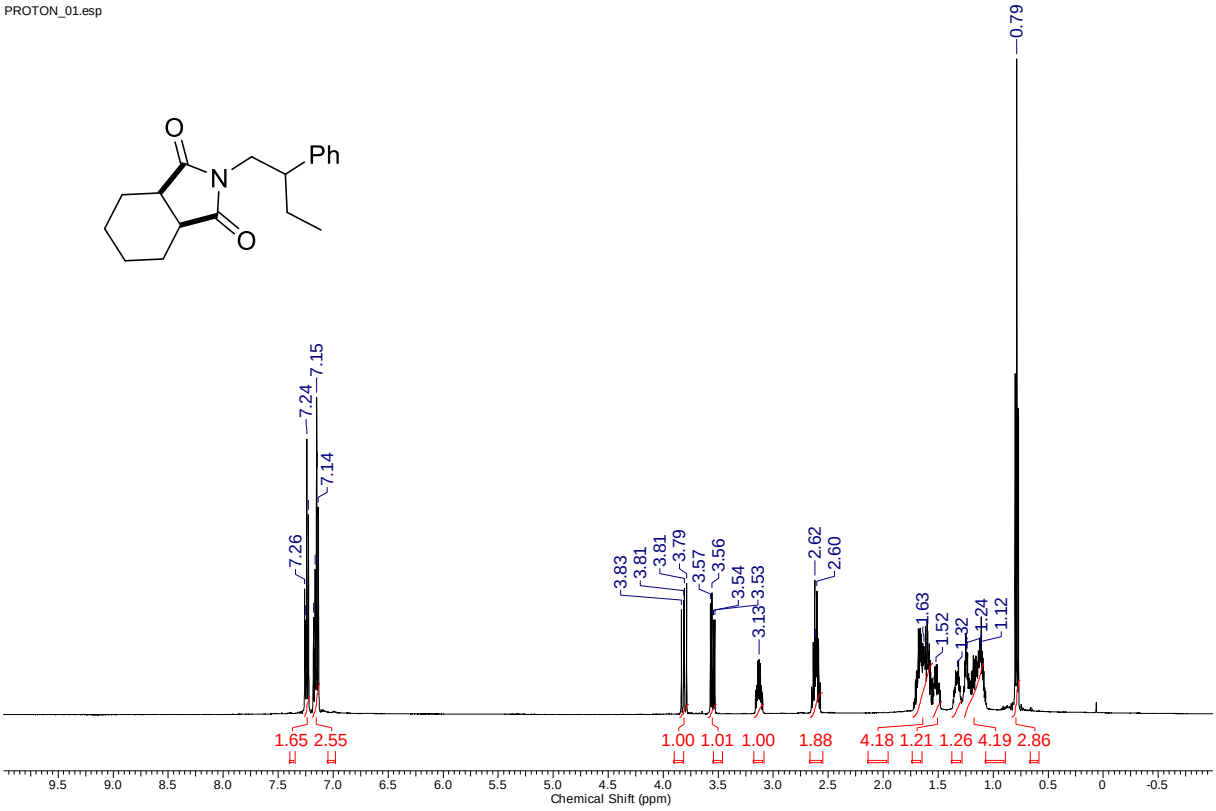
^{1}H NMR (**3m**) ($CDCl_3$)



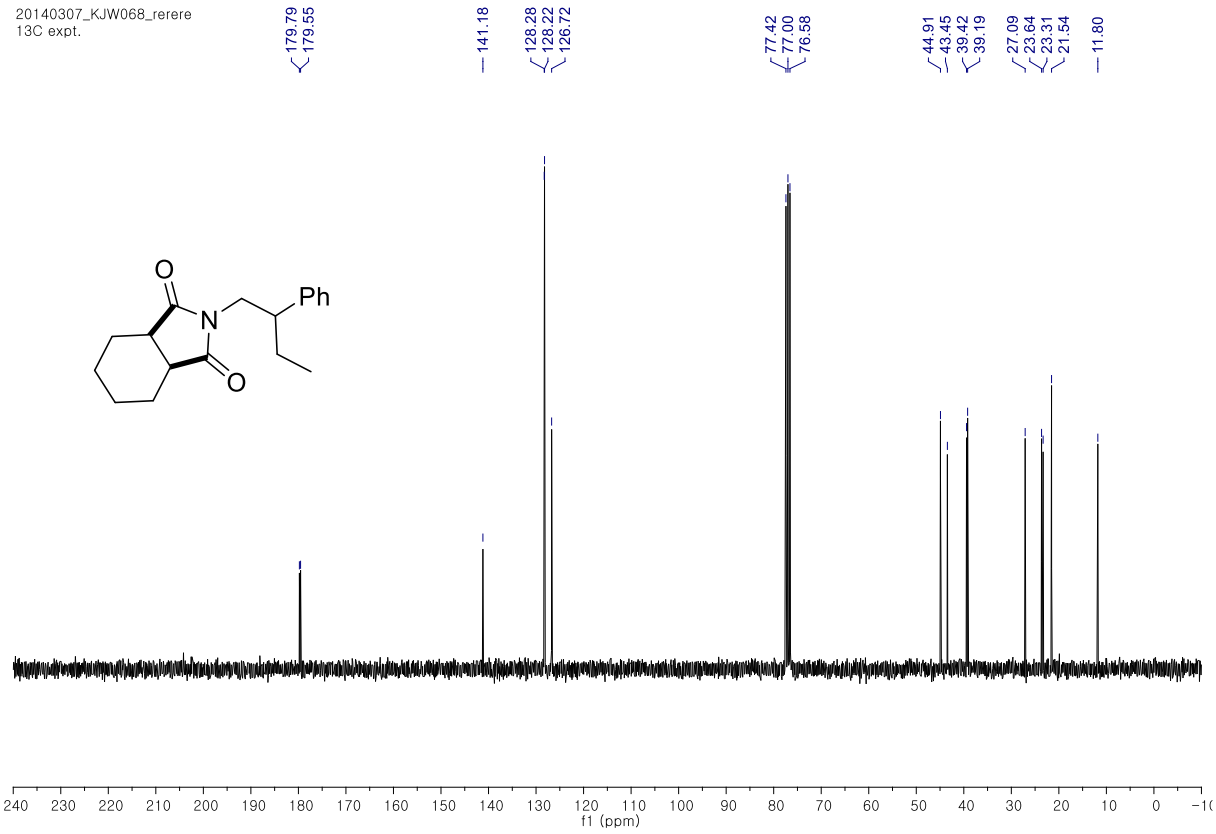
^{13}C NMR (**3m**) ($CDCl_3$)



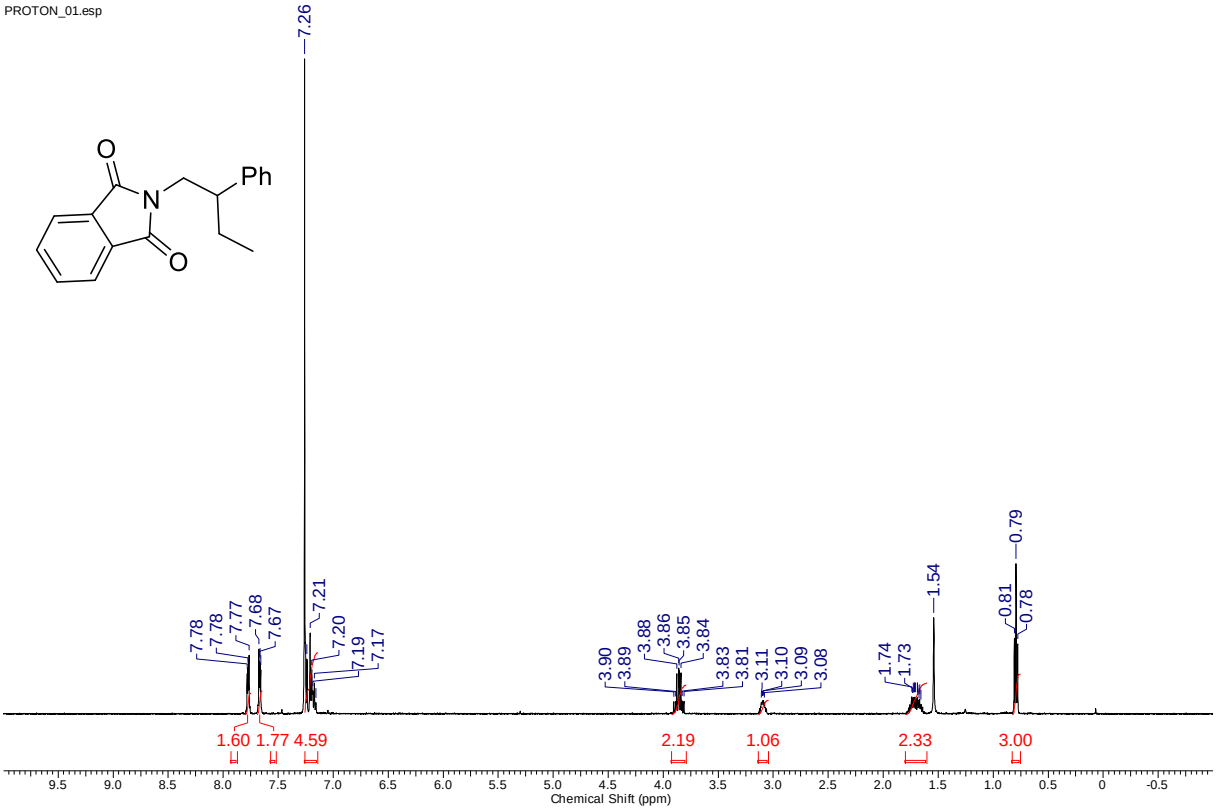
^{1}H NMR (**3n**) ($CDCl_3$)



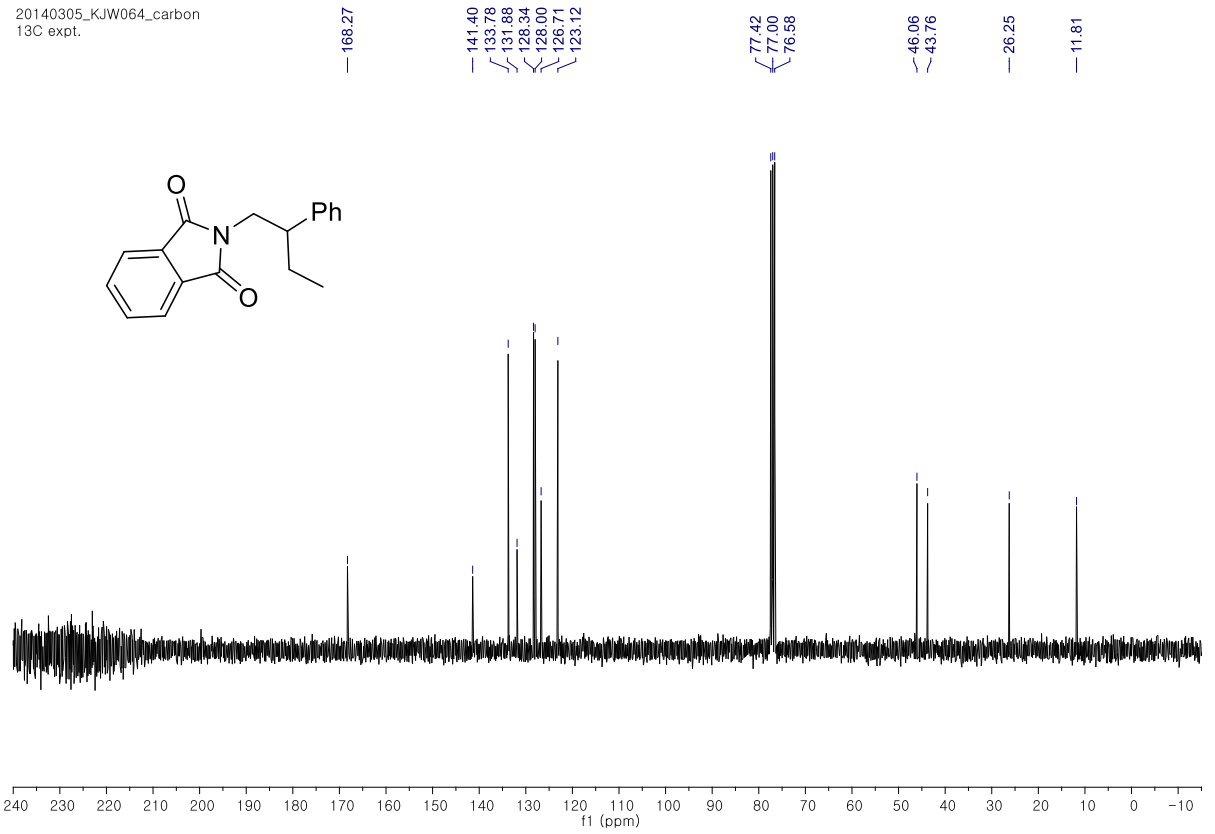
^{13}C NMR (**3n**) ($CDCl_3$)



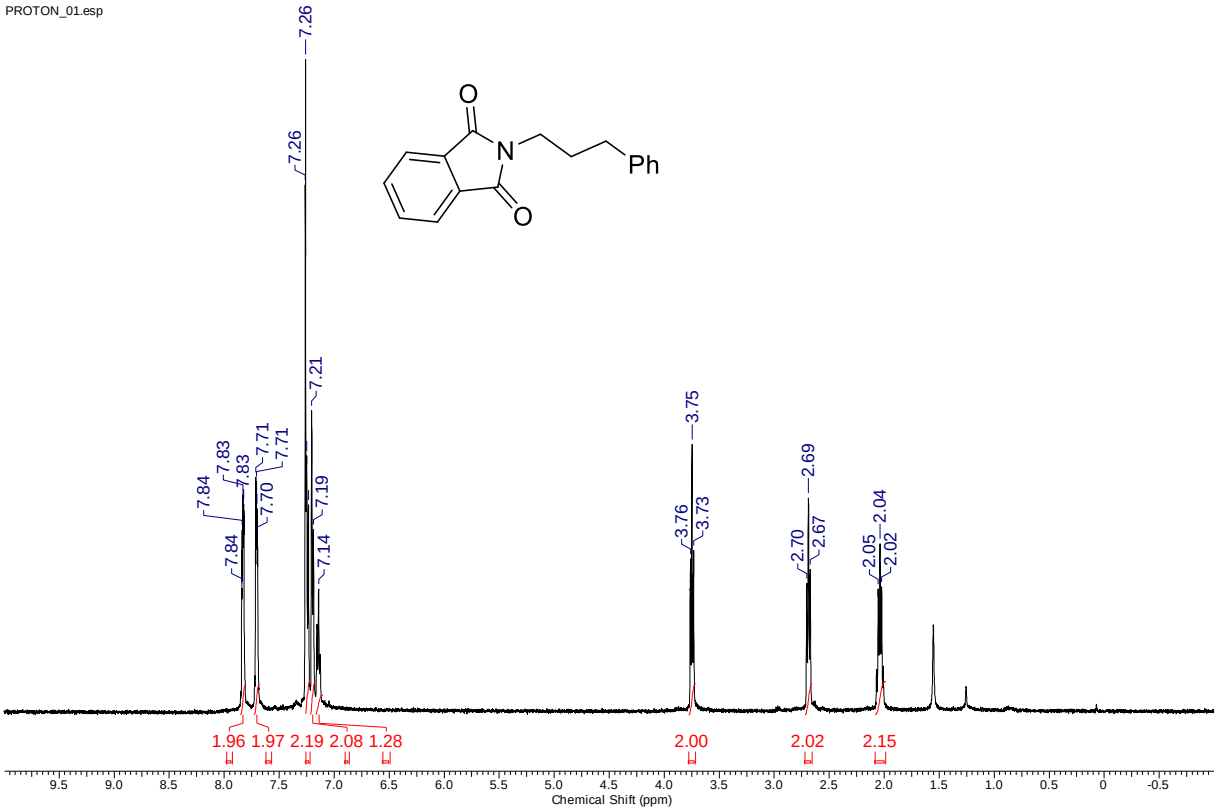
^{1}H NMR (**3o**) ($CDCl_3$)



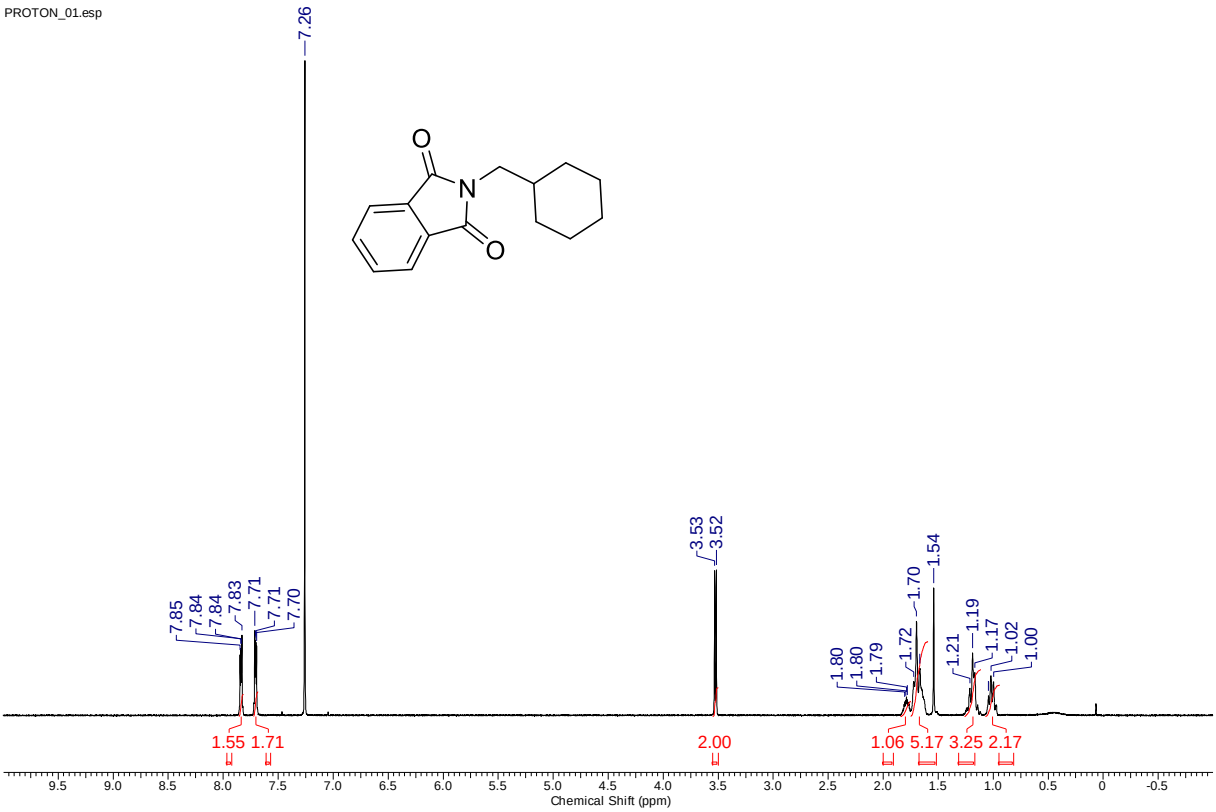
^{13}C NMR (**3o**) ($CDCl_3$)



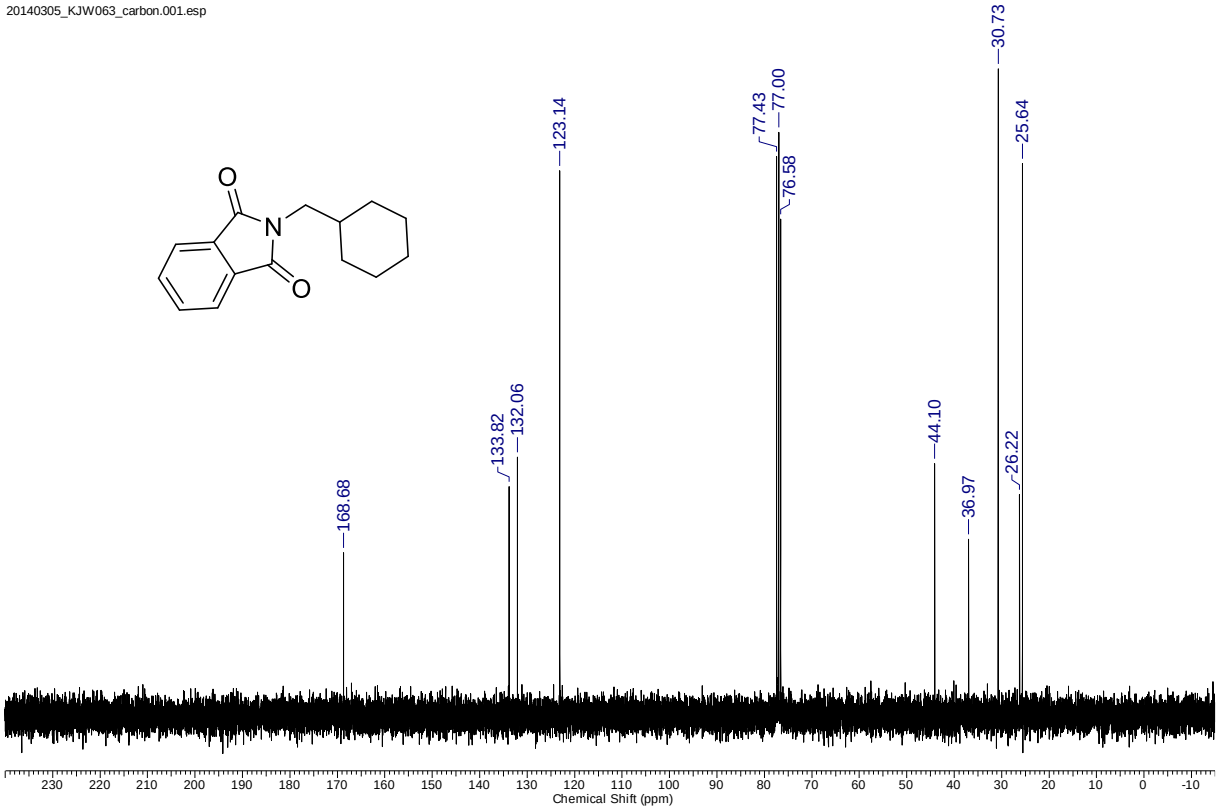
^{1}H NMR (**3p)** ($CDCl_3$)



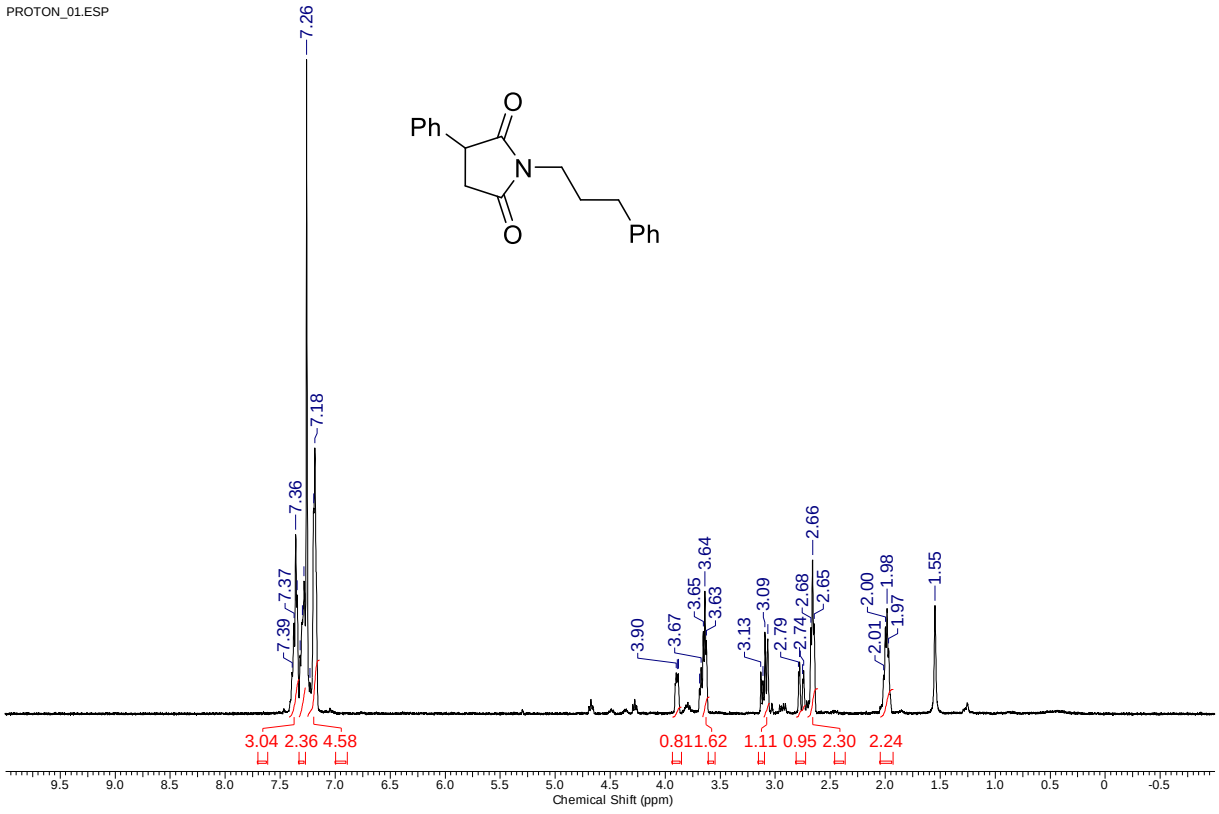
^{1}H NMR (**3q)** ($CDCl_3$)



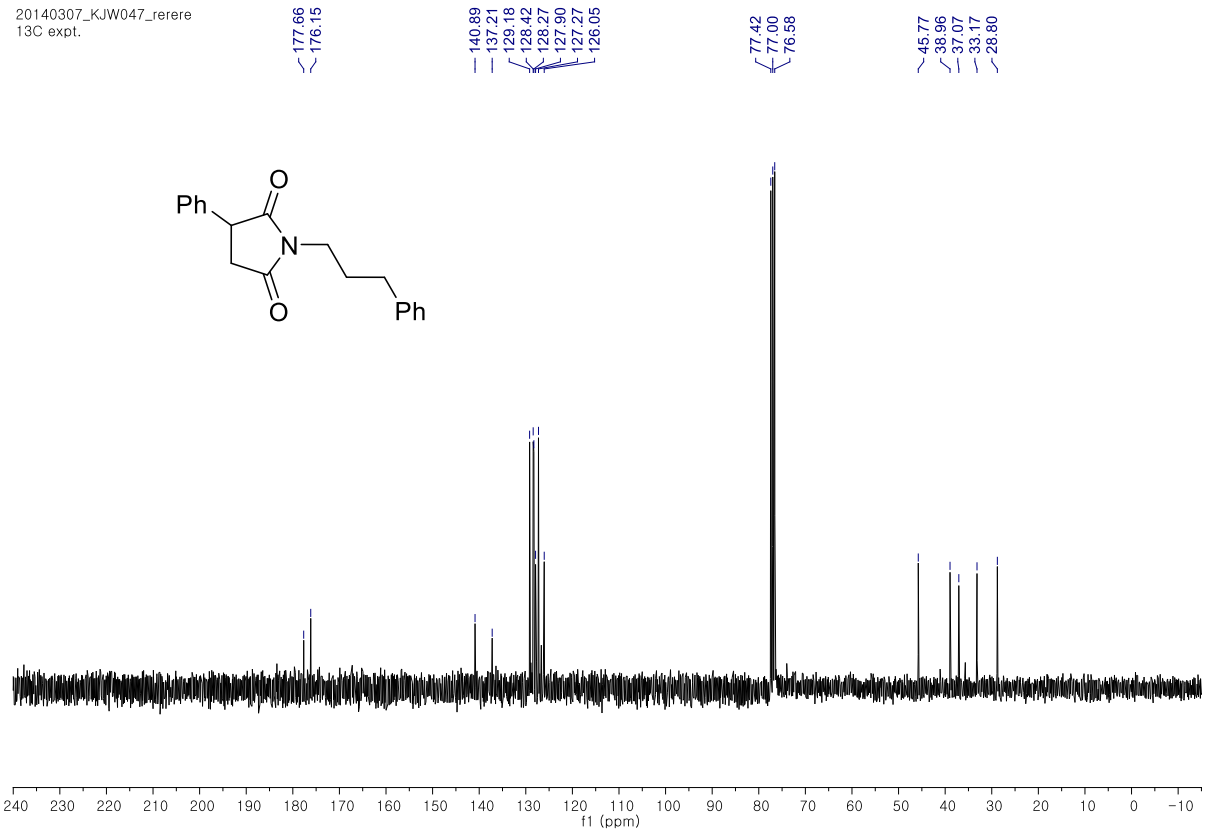
^{13}C NMR (**3q)** ($CDCl_3$)



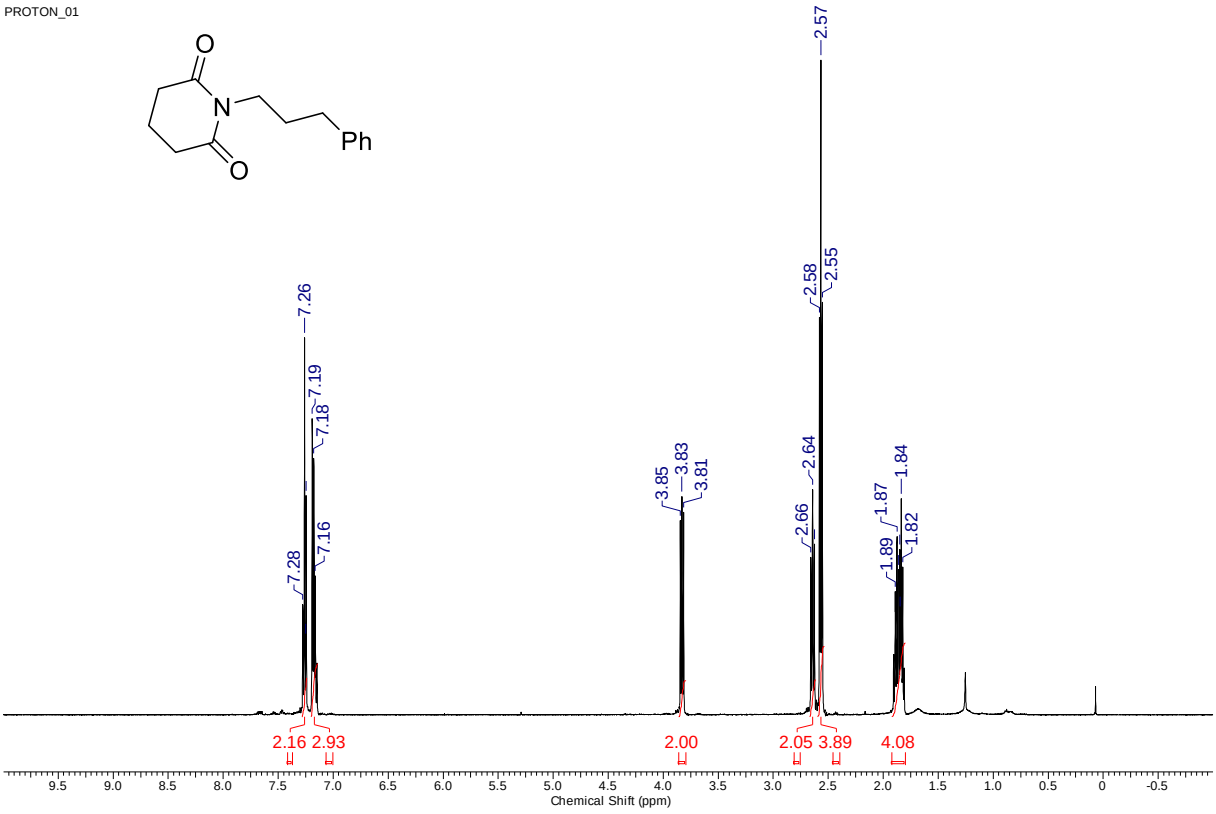
^{1}H NMR (**3r)** ($CDCl_3$)



^{13}C NMR (**3r**) ($CDCl_3$)



^{1}H NMR (**3s**) ($CDCl_3$)



^{13}C NMR **(3s)** ($CDCl_3$)