Supplementary Material (ESI) for Organic & Biomolecular Chemistry

An anomalous hydration/dehydration sequence for the mild generation of a nitrile oxide

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Contents

Preparation of Nitroisoxazolone 5a

Nitroisoxazolone **5a** was easily prepared from commercially available ethyl nitroacetate by three steps with simple experimental manipulations; 1) condensation of nitroacetate with orthoformate, 2) condensation with hydroxylamine, and 3) *N*-methylation with dimethyl sulfate.

1) Condensation of nitroacetate with orthoformate[1]

To a solution of ethyl nitroacetate (40 mL, 0.36 mol) in acetic anhydride (80 mL), trimethyl orthoformate (58 mL, 0.53 mol) was added, and the resultant mixture was heated at 100 °C for 2 d. The mixture was concentrated under reduced pressure, and the residue was used for next step without further purification.

2) Condensation with hydroxylamine[2]

To a solution of ethyl 3-methoxy-2-nitropropenoate (17.5 g, 100 mmol) in ethanol (175 mL), were added hydroxylamine hydrochloride (7.73 g, 120 mmol) and pyridine (20.2 mL, 250 mmol). The mixture was heated at 60 °C for 3 h. After cooling, pale yellow precipitates were formed and were collected to give pyridinium salt **4a** (14.8 g, 71 mmol, 71% yield).

3) *N*-Methylation with dimethyl sufate[3]

Pyridinium salt **4a** (4.18 g, 20 mmol) was heated with freshly distilled dimethyl sufate (2.3 mL, 24 mmol) without solvent at 65 °C for 3 h. The reaction mixture was cooled to room temperature, and water (100 mL) was added. Generated white precipitates were collected, and recrystallized from acetonitrile to afford isoxazolone **5a** (2.26 g, 15.7 mmol, 79%).

References

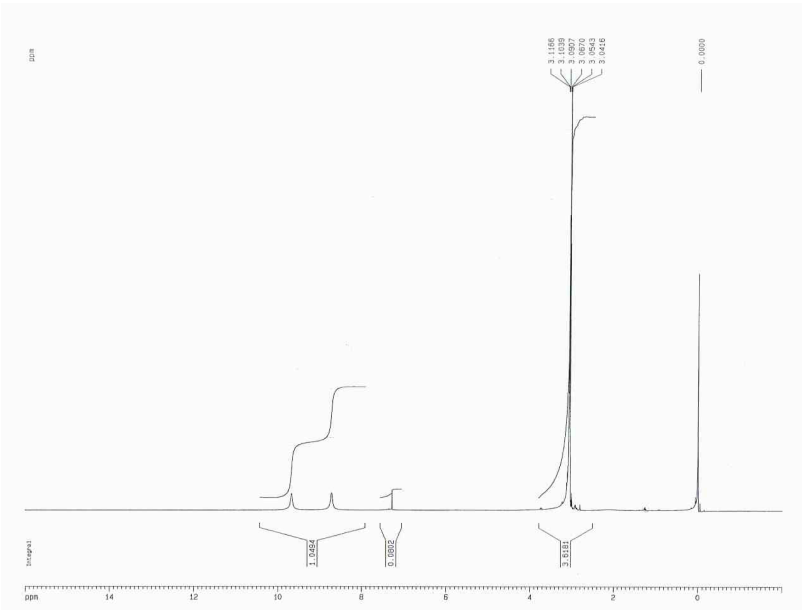
1 M. J. Kamlet, *J. Org. Chem.* 1959, **24**, 714.

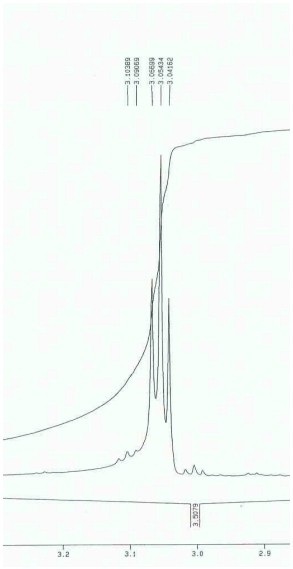
2 N. Nishiwaki, Y. Takada, Y. Inoue, Y. Tohda and M. Ariga, *J. Heterocycl. Chem.* 1995, **32**, 473.

3 N. Nishiwaki M. Nakanishi, T. Hida, Y. Miwa, M. Tamura, K. Hori, Y. Tohda and M. Ariga, *J. Org. Chem.* 2001, **66**, 7535.

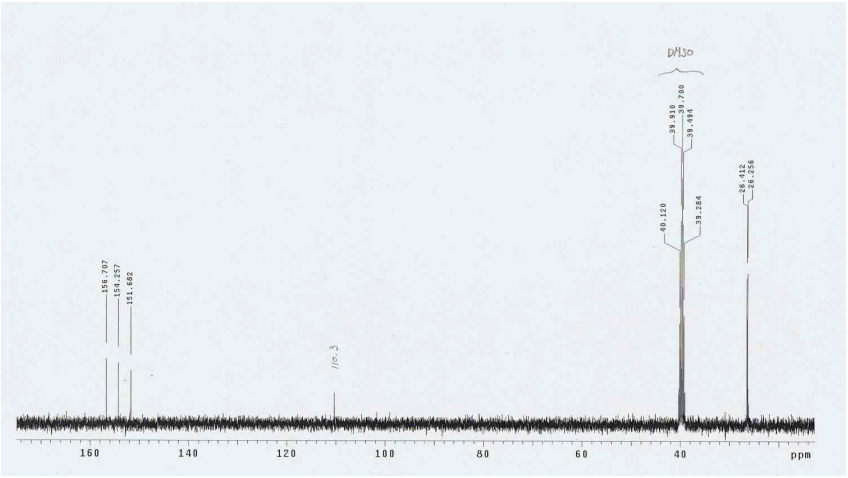
3,4-Bis(*N*-methylcarbamoyl)-1,2,5-oxadiazole 2-oxide (Furoxan) (6)

^{1}H NMR ($CDCl_3$)





^{13}C NMR (DMSO-d_6)



3-(*N*-methylcarbamoyl)-5-phenylisoxazole (8a)

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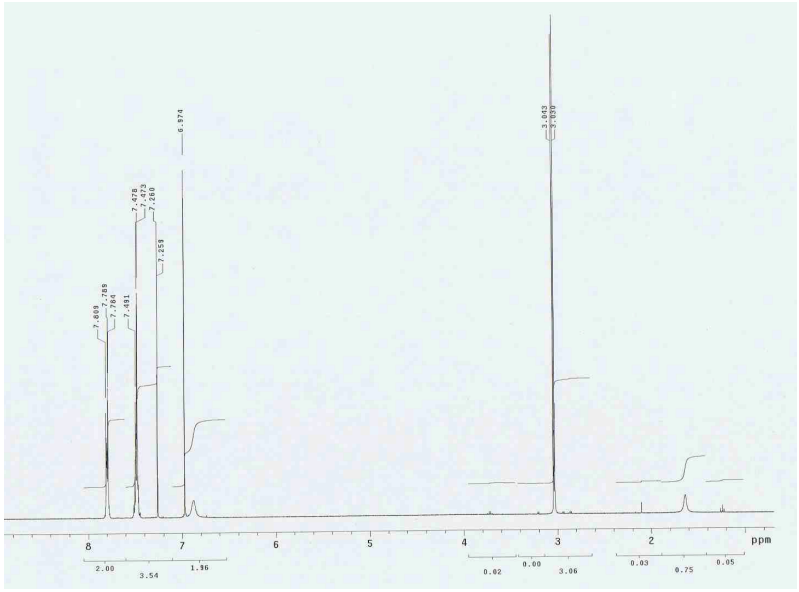

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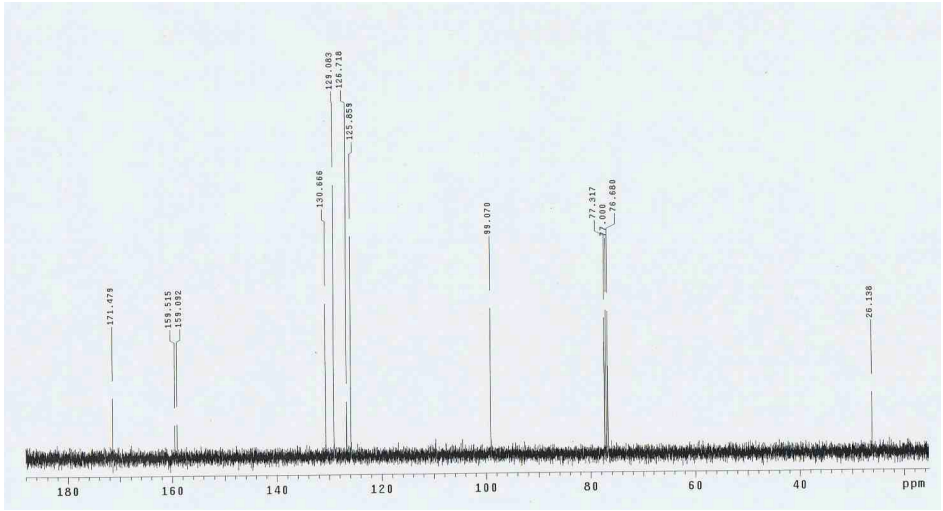

5-Hydroxymethyl-3-(*N*-methylcarbamoyl)isoxazole (8b)

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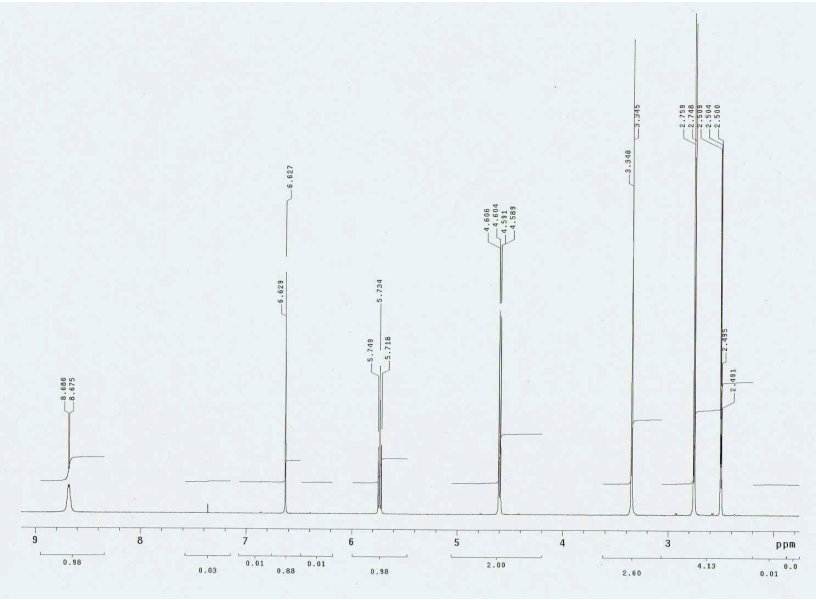

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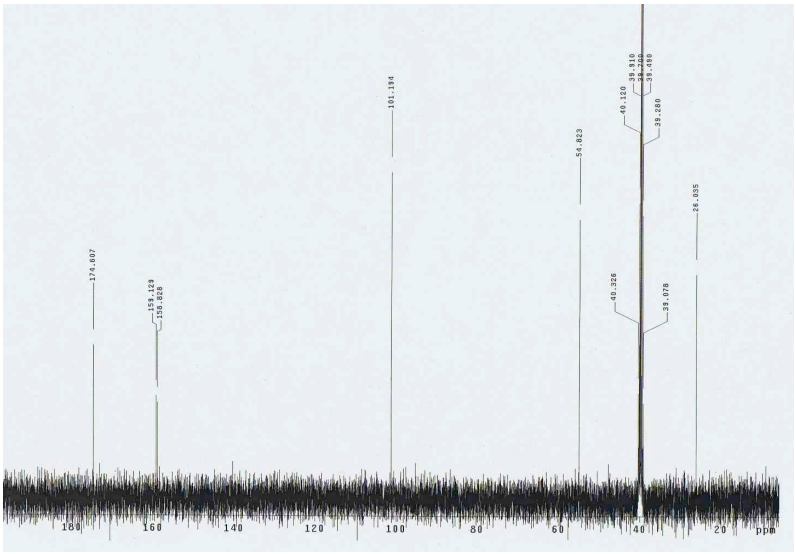

5-Bromomethyl-3-(*N*-methylcarbamoyl)isoxazole (8c)

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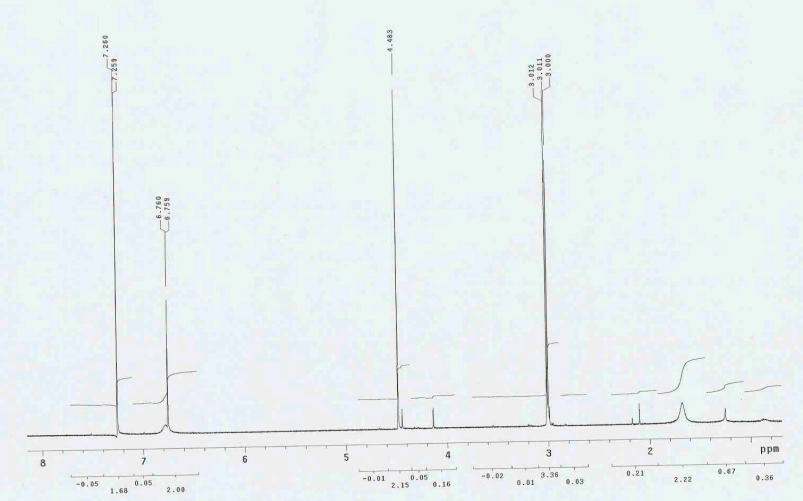

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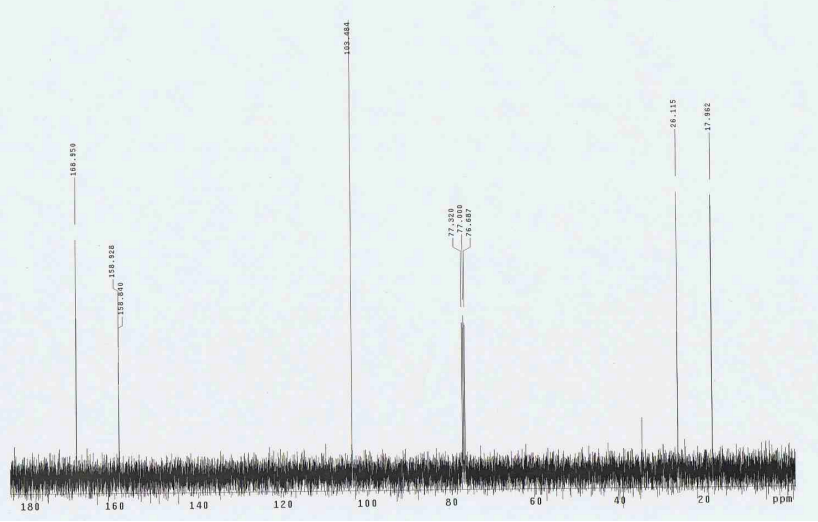

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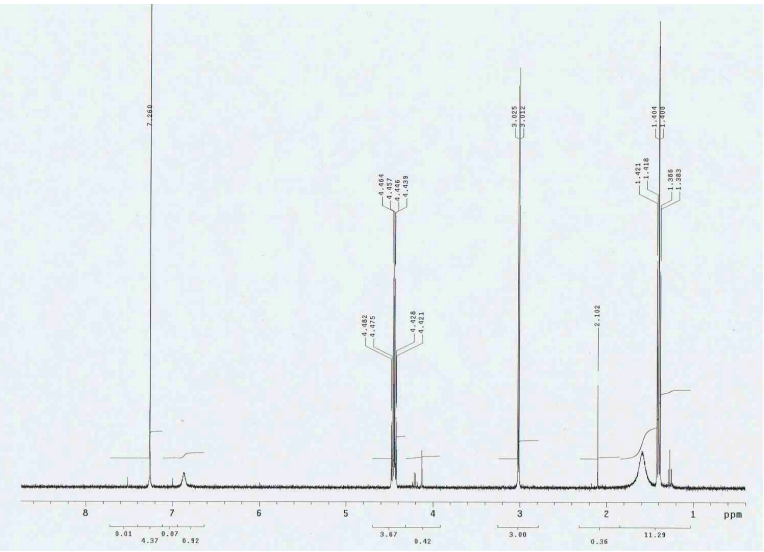

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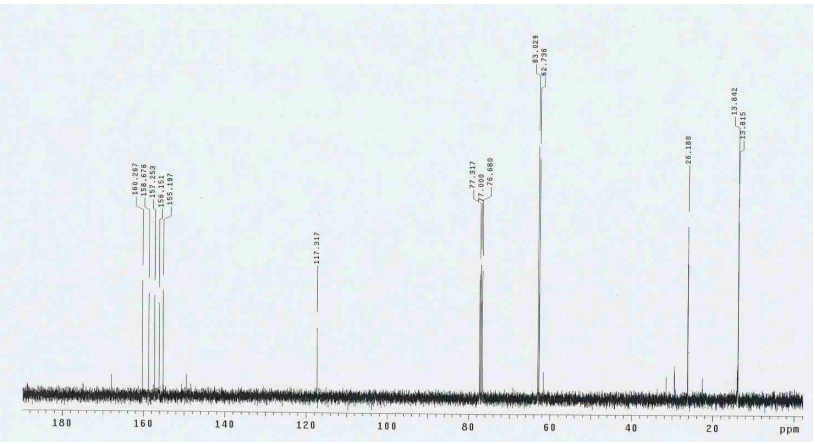

3-(*N*-Methylcarbamoyl)-5-phenyl-2-isoxazoline (11a)

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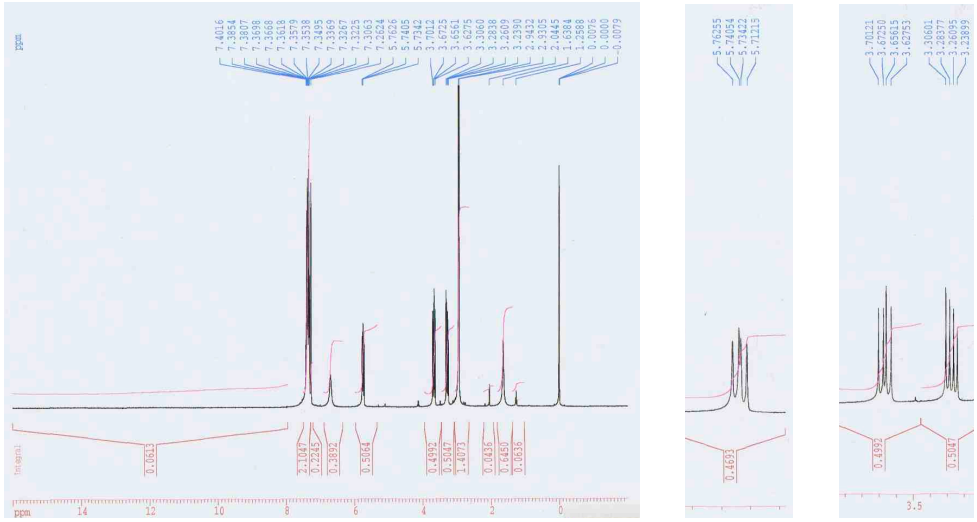
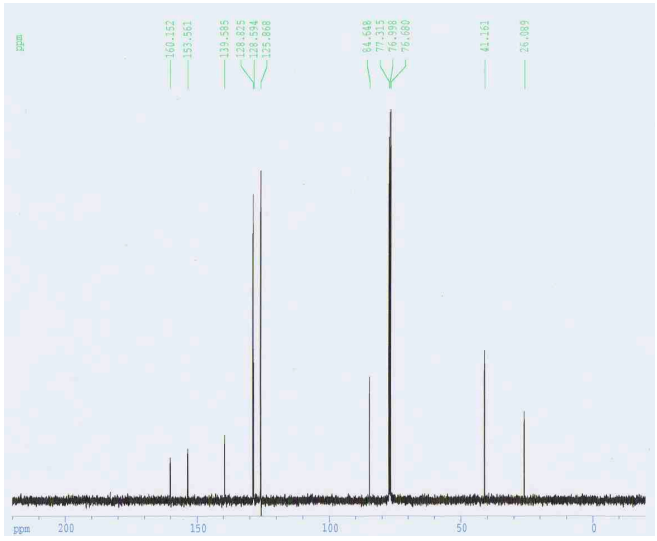


^{13}C NMR ($CDCl_3$)



3-(*N*-Methylcarbamoyl)-5-propyl-2-isoxazoline (11b)

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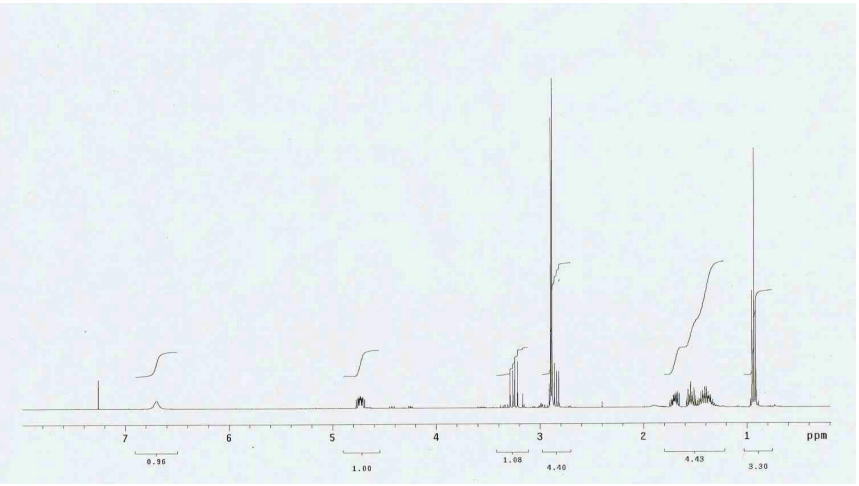
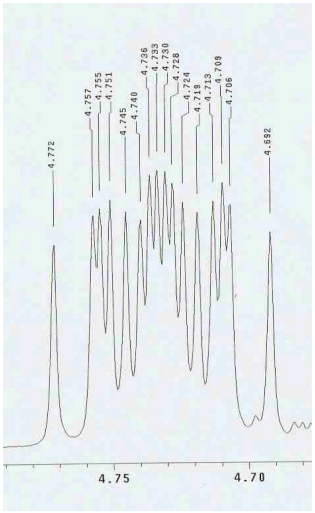
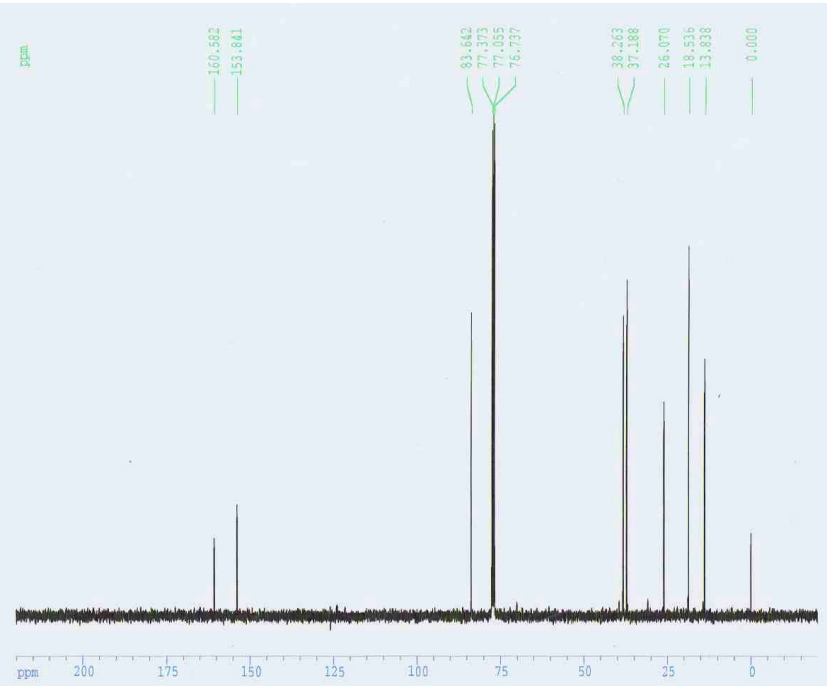


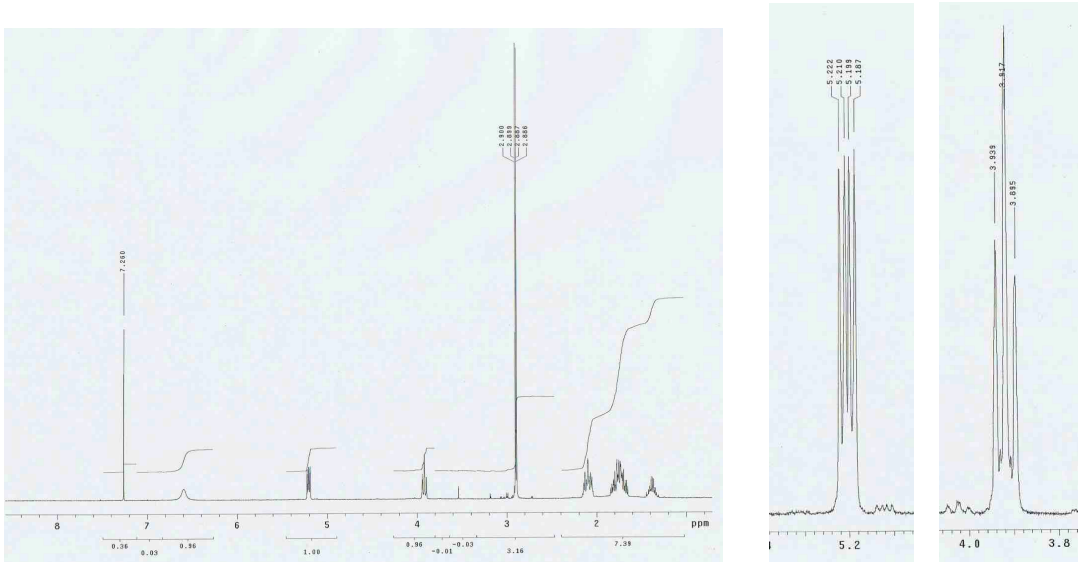


^{13}C NMR ($CDCl_3$)

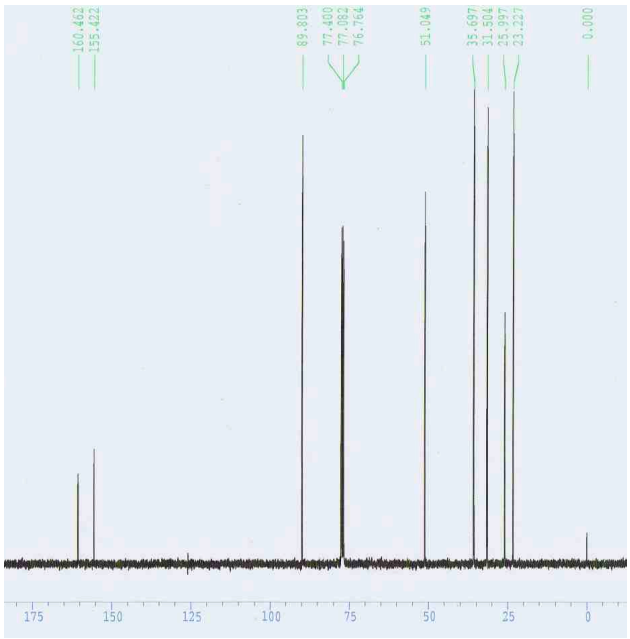


3-(*N*-Methylcarbamoyl)-3a,5,6,6a-tetrahydro-4*H*-cyclopent[*d*]isoxazole (11c)

^{1}H NMR ($CDCl_3$)

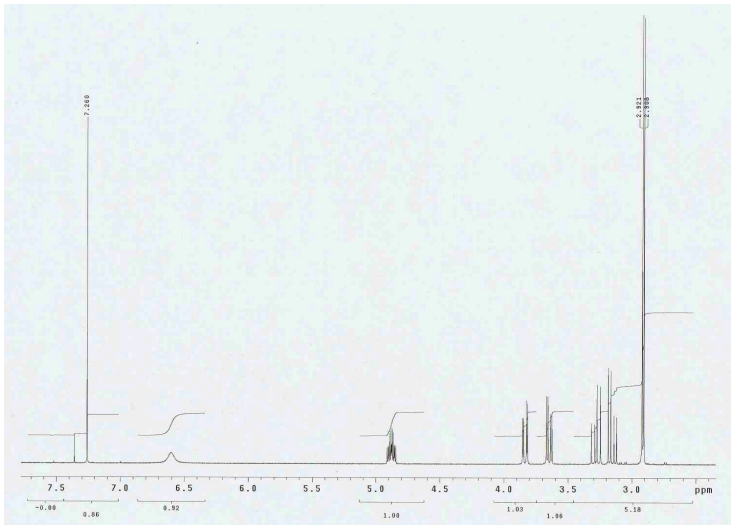


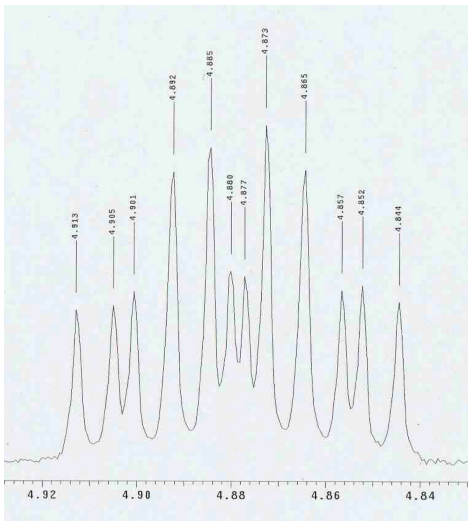
^{13}C NMR ($CDCl_3$)

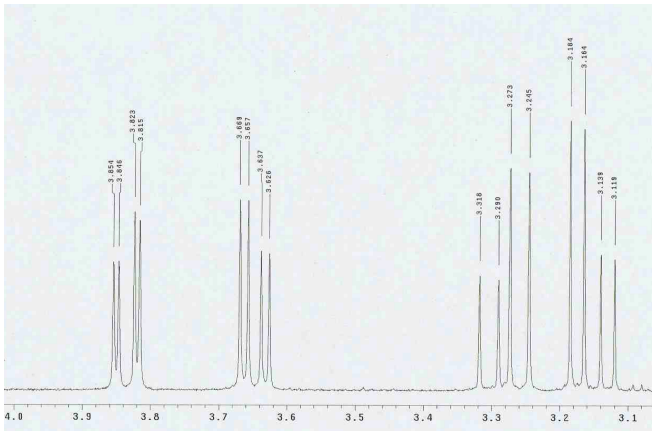


5-Hydroxymethyl-3-(*N*-methylcarbamoyl)-2-isoxazoline (11d)

^{1}H NMR ($CDCl_3$)







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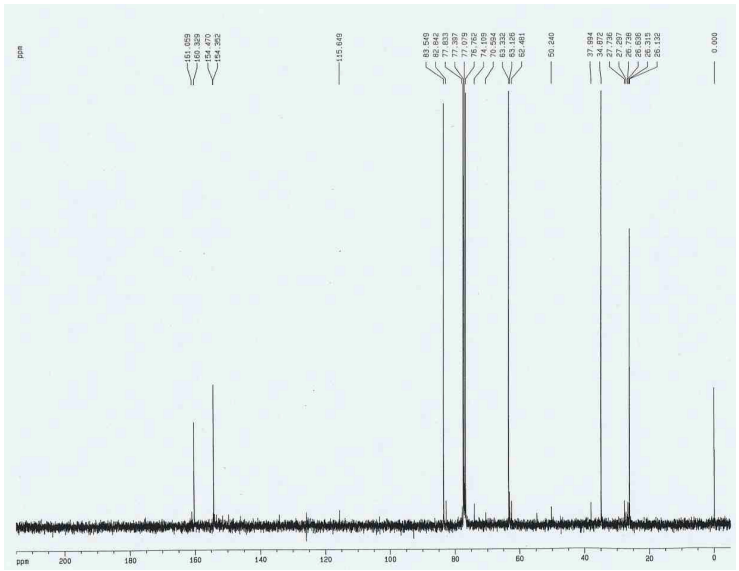
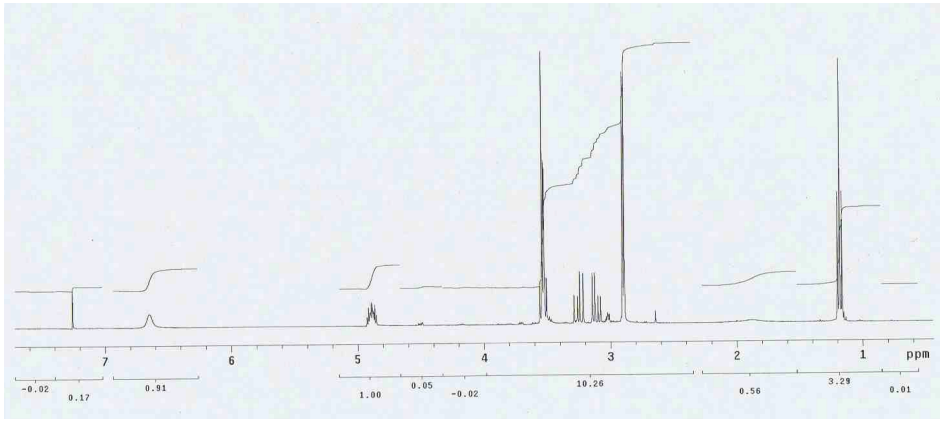
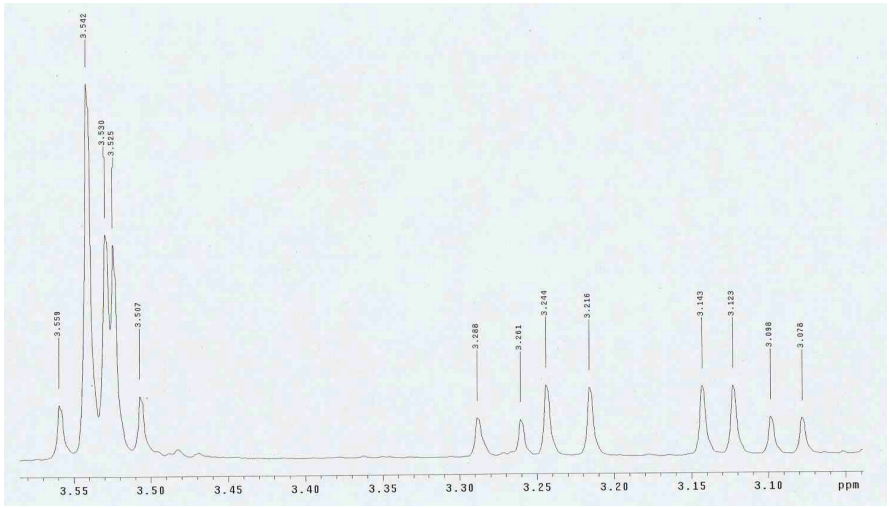


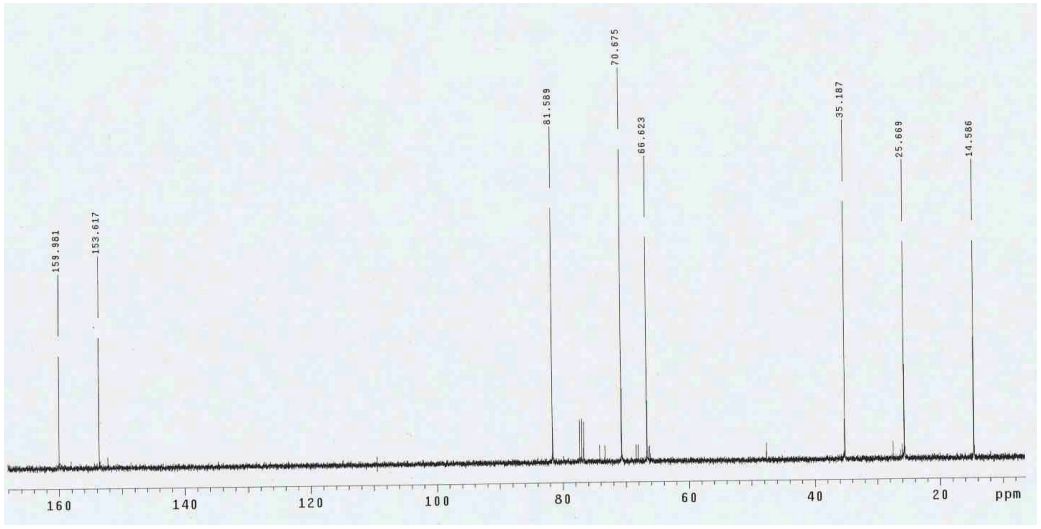
5-Ethoxymethyl-3-(*N*-methylcarbamoyl)-2-isoxazoline (11e)

^{1}H NMR ($CDCl_3$)



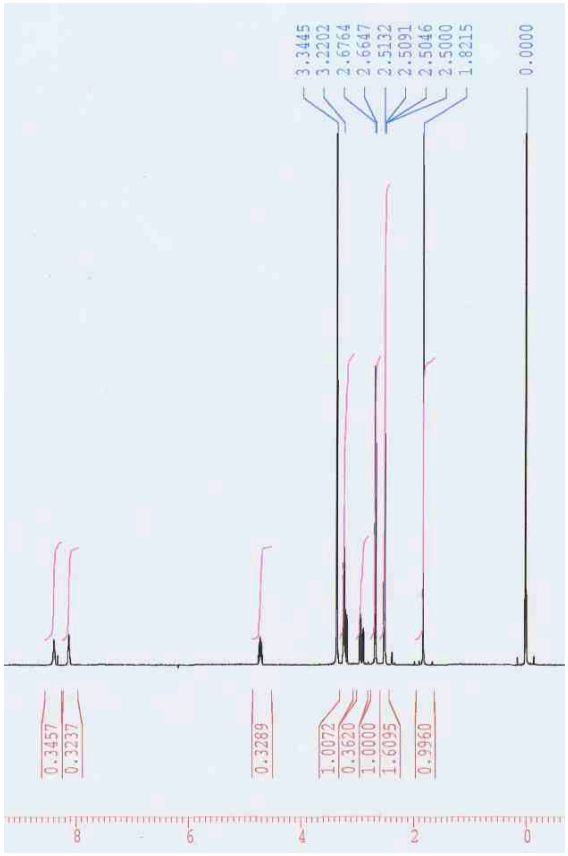


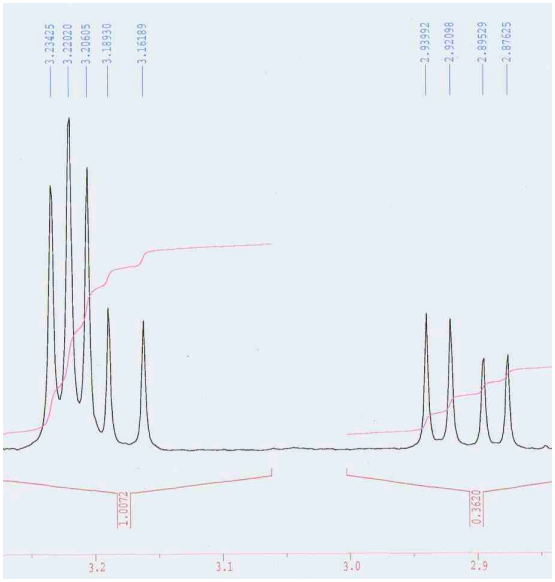
^{13}C NMR ($CDCl_3$)

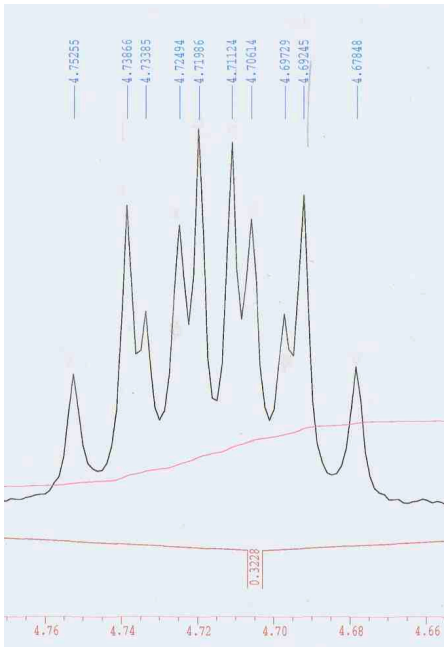


5-Acetylaminomethyl-3-(*N*-methylcarbamoyl)-2-isoxazoline (11g)

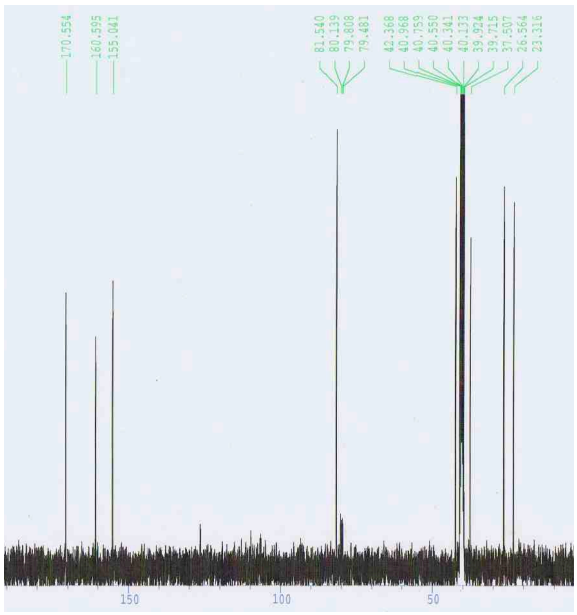
^{1}H NMR ($CDCl_3$)







^{13}C NMR ($CDCl_3$)



5-Ethoxy-3-(*N*-methylcarbamoyl)-2-isoxazoline (11h)

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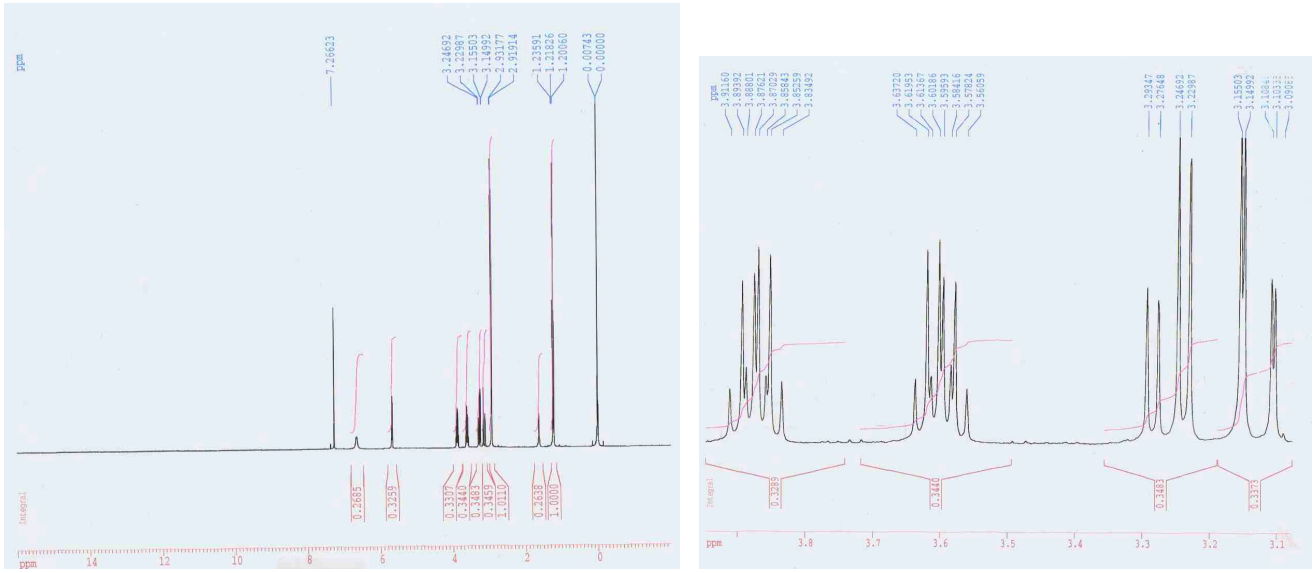
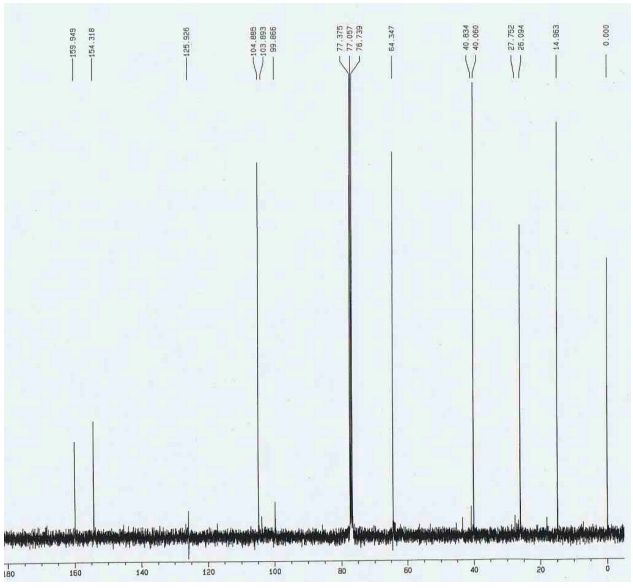
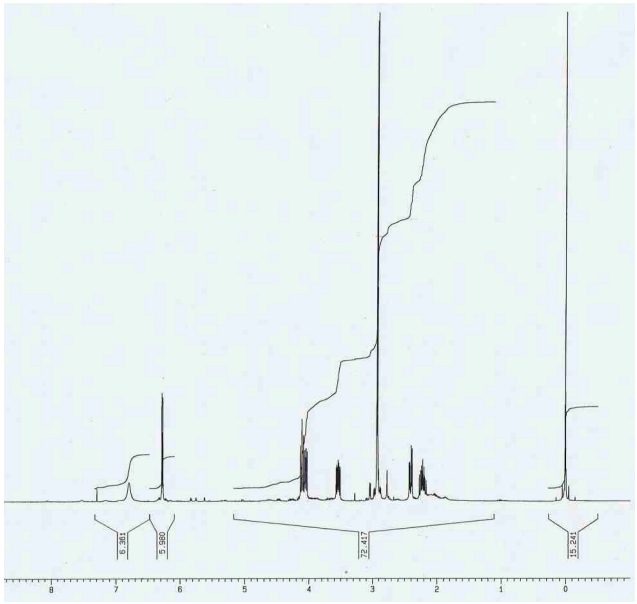


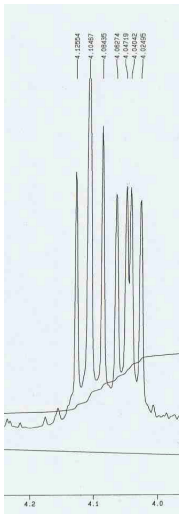
^{13}C NMR ($CDCl_3$)

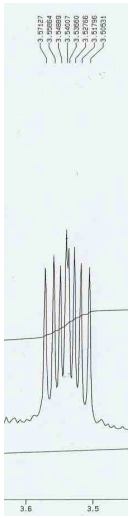


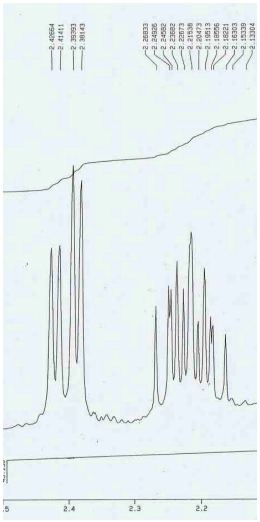
3-(*N*-Methylcarbamoyl)-3a,4,5,6a-tetrahydrofuro[3,2-*d*]isoxazole (11i)

^{1}H NMR ($CDCl_3$)









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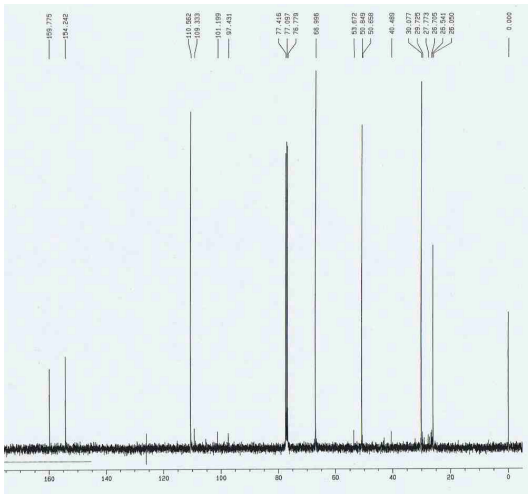

5-Ethoxycarbonyl-3-(*N*-methylcarbamoyl)-2-isoxazoline (11j)

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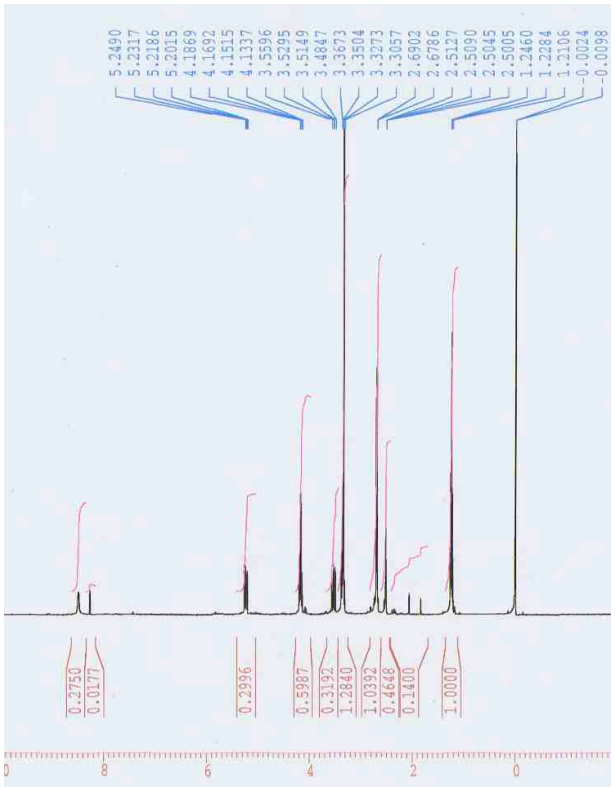

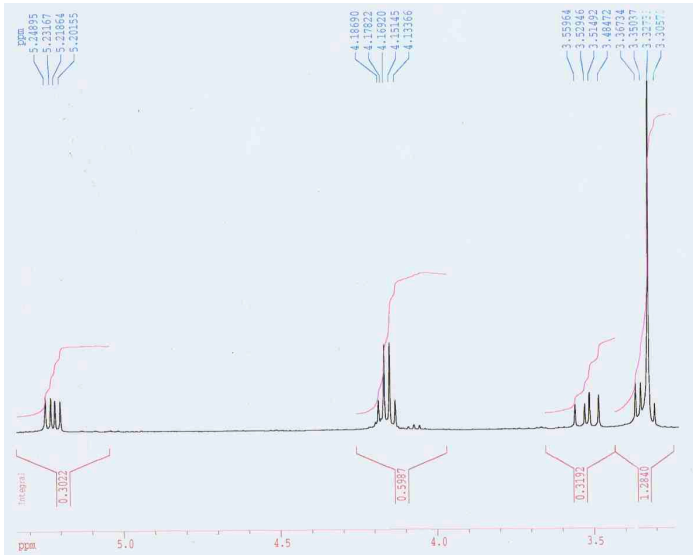

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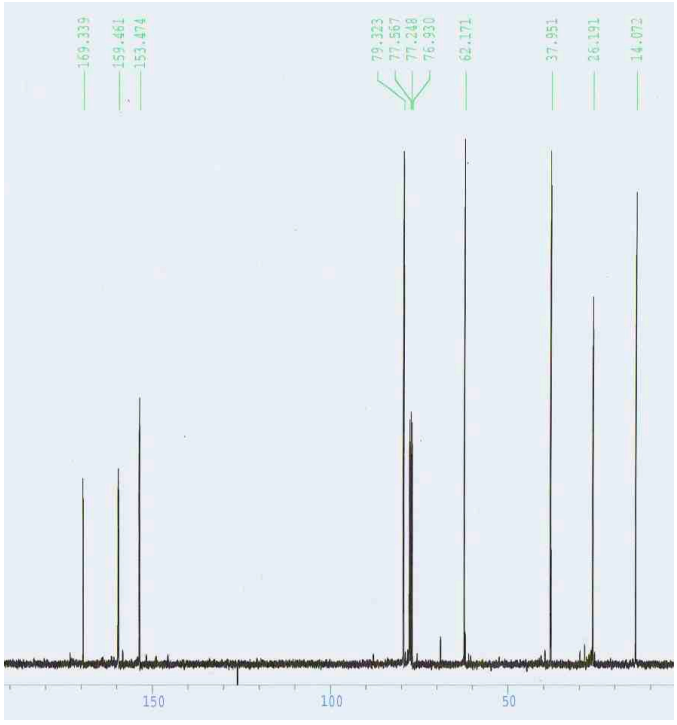
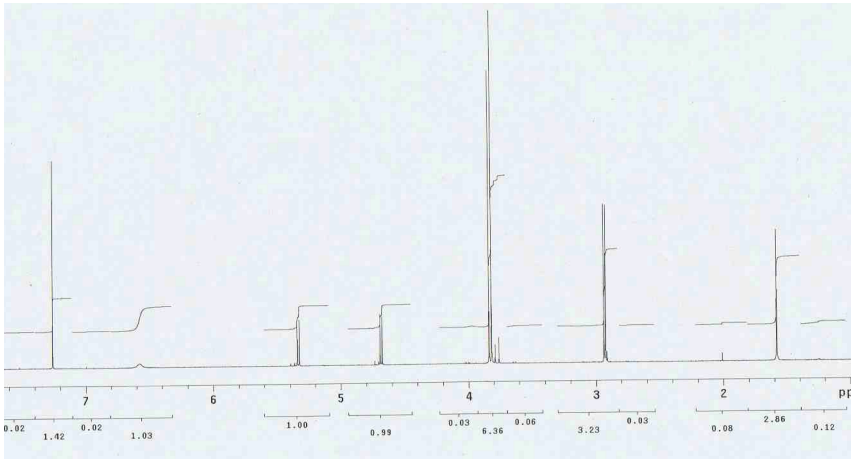
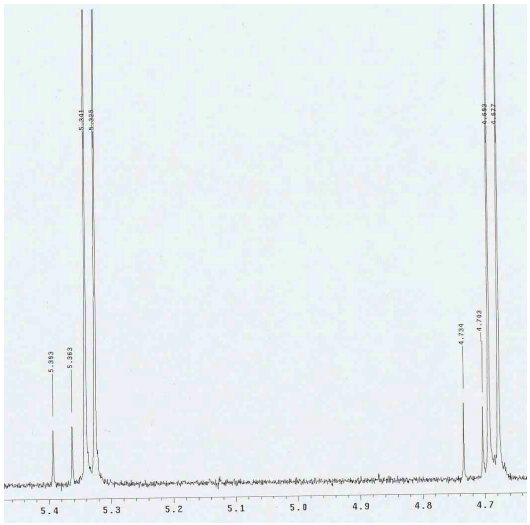


4,5-Bis(methoxycarbonyl)-3-(*N*-methylcarbamoyl)-2-isoxazoline (11k)

^{1}H NMR ($CDCl_3$)





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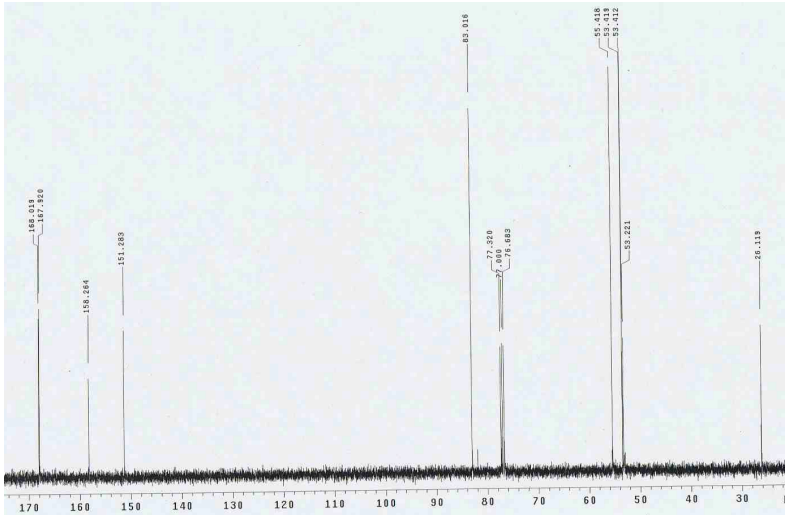
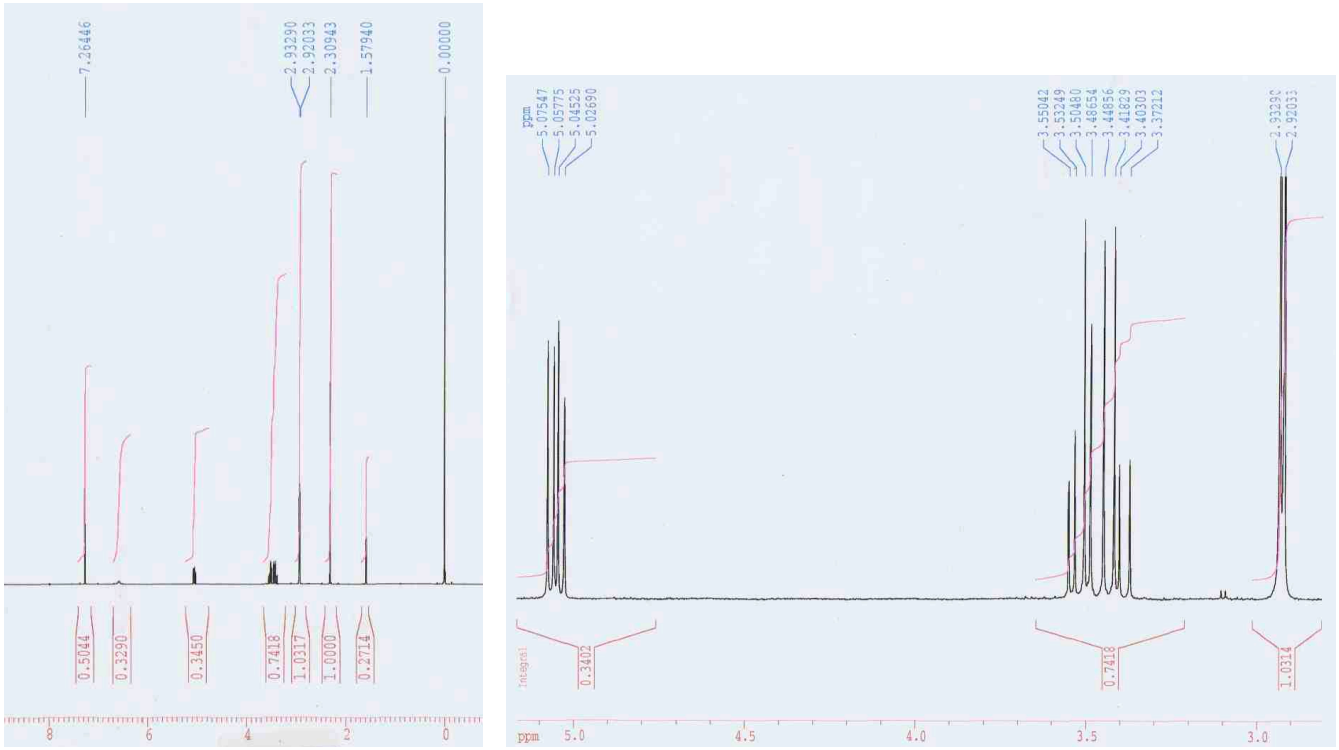


5-Acetyl-3-(*N*-methylcarbamoyl)-2-isoxazoline (11l)

^{1}H NMR ($CDCl_3$)



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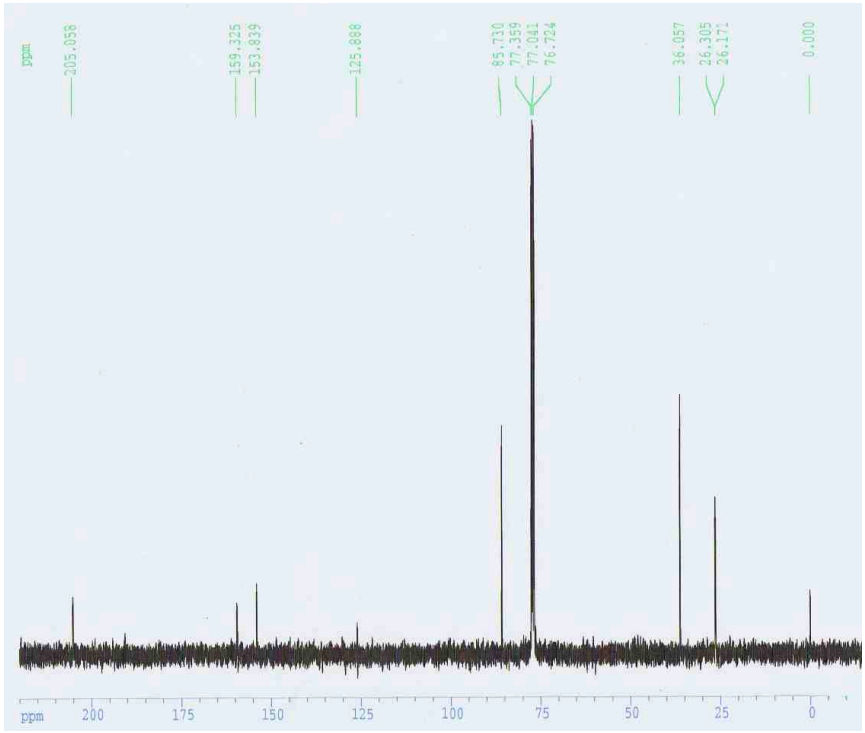

1-Methoxy-1-methylamino-2-nitroethene (17)

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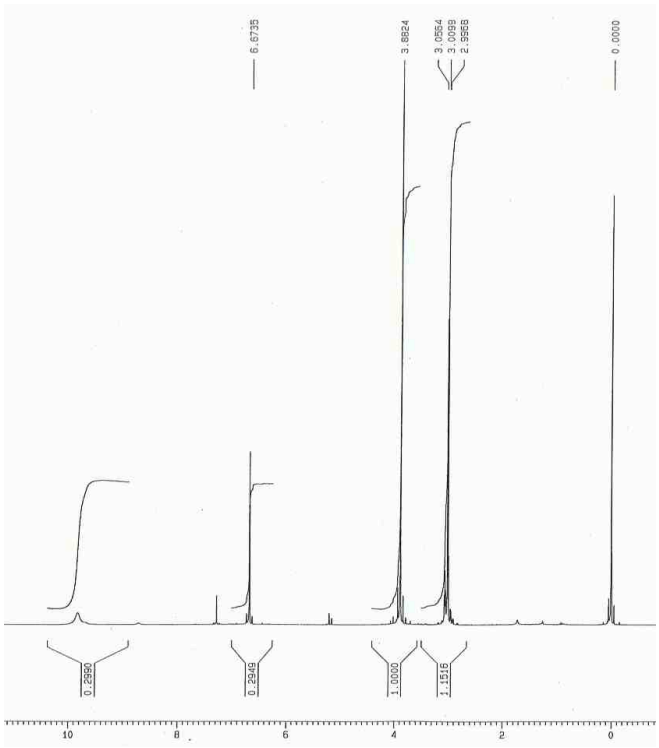
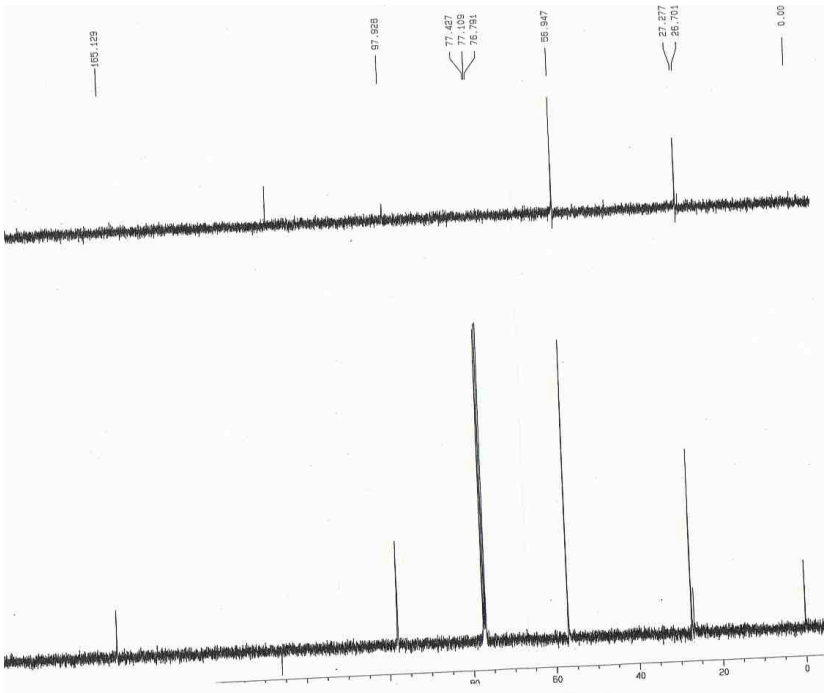


^{13}C NMR ($CDCl_3$)



Methyl 4-Aza-2-nitro-3-oxopentanoate (3d)

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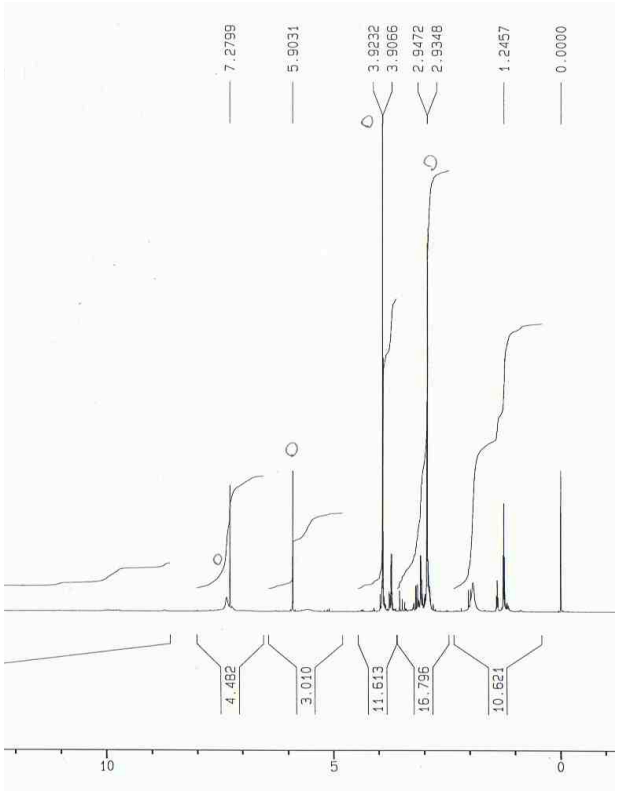
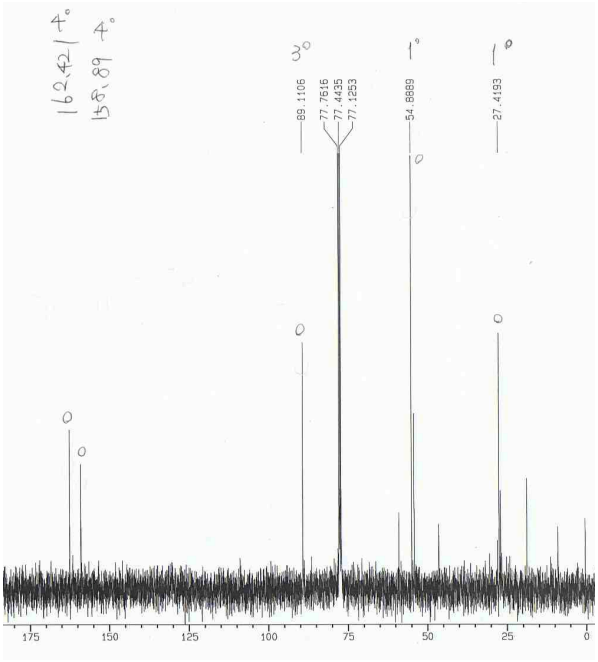
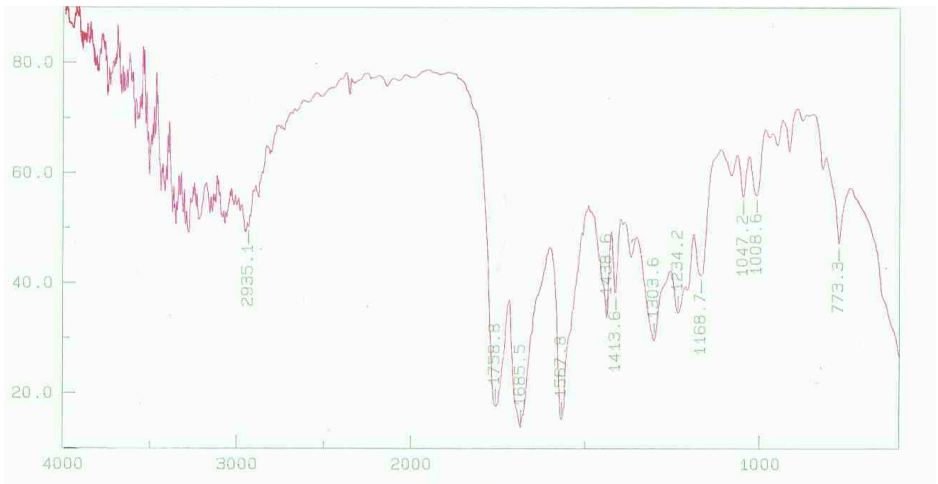


^{13}C NMR ($CDCl_3$)

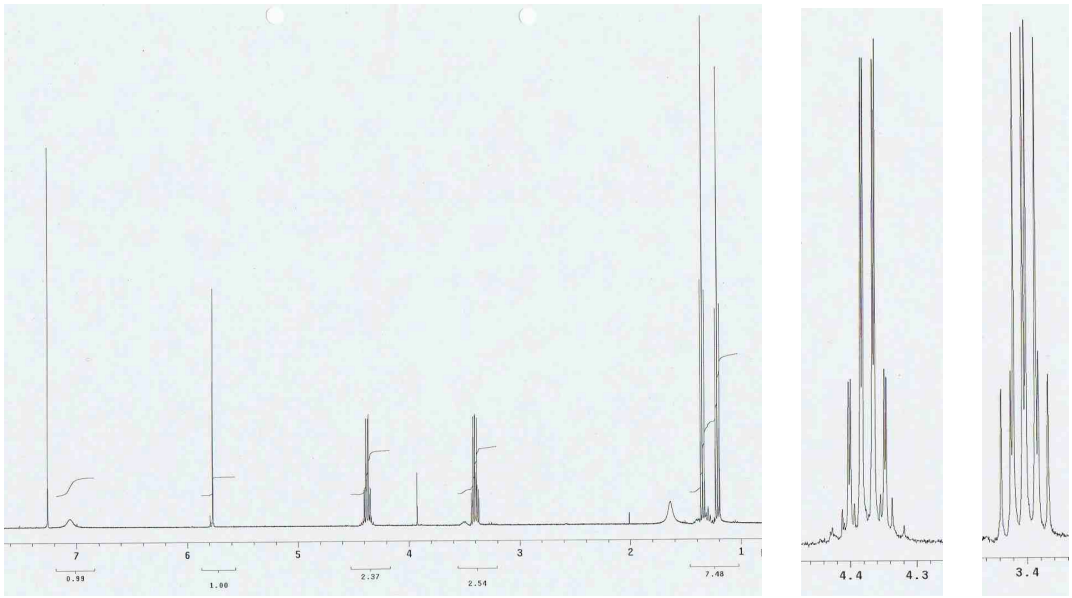


IR (neat)

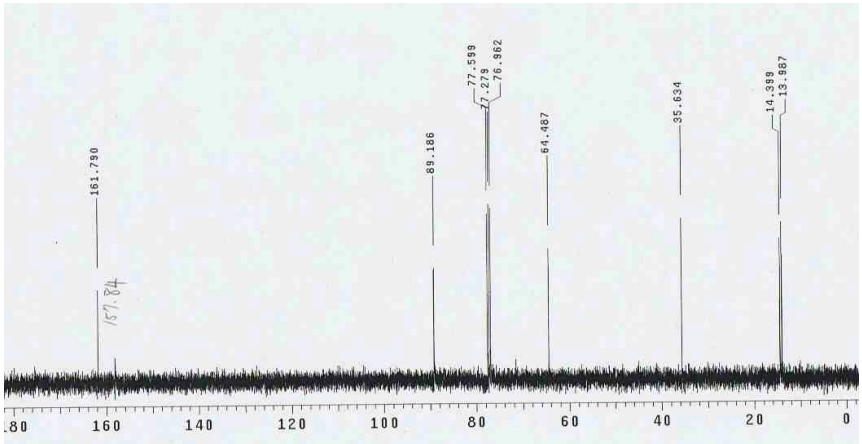


Ethyl 4-Aza-2-nitro-3-oxohexanoate (3e)

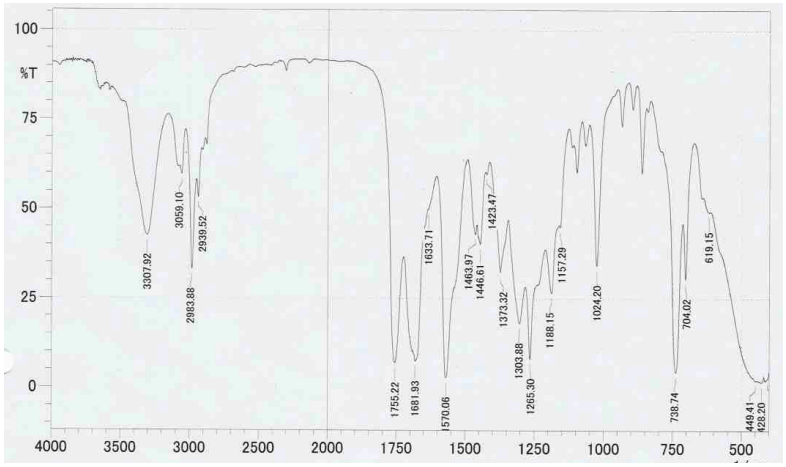
^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)



IR (neat)



Cartesian Coordinates and Energergies of 17'

Cartesian coordinate of 17'				**Sum of electronic and zero-point Energies**
6	-1.475447	-0.475061	-0.149777	HF = -602.1980748
6	-0.021009	-0.024501	-0.023963	
6	0.735248	-0.197525	1.262487	
8	1.712154	0.653988	1.599550	
8	0.424470	-1.089674	2.029846	
7	0.484398	0.558123	-1.101425	
8	-2.269046	0.165859	-0.822402	
8	1.819386	1.084399	-0.943889	
8	0.024627	0.697689	-2.226355	
1	1.957156	1.509696	-1.811984	
1	-1.149699	-1.962538	1.230181	
1	1.933823	1.254427	0.866972	
7	-1.785048	-1.611808	0.522197	
1	-2.764805	-1.857044	0.556092	

Cartesian Coordinates and Energergies of 19

Cartesian coordinate of 19				**Sum of electronic and zero-point Energies**
1	2.050312	0.951611	0.828003	HF = -602.1795791
1	-2.207998	-0.497109	1.176231	
1	3.142087	0.233314	-0.222269	
8	1.048696	-0.115862	-2.066794	
8	2.480677	0.941707	-0.165719	
1	-3.248781	-1.156750	-0.128541	
7	-2.373580	-0.778100	0.203791	
7	0.825958	0.069602	-0.924958	
8	1.196902	0.825324	1.846208	
8	-0.926299	0.161710	2.185204	
6	0.076855	0.360887	1.499753	
6	-0.068245	-0.032625	-0.030714	
6	-1.380365	-0.642518	-0.680439	
8	-1.398649	-0.927163	-1.863727	

Cartesian coordinate of 2d'			**Sum of electronic and zero-point Energies**
6	0.136706	-1.088672	0.000000	HF = -337.2513014
6	-0.291669	0.320996	0.000000	
7	-0.163219	1.486262	0.000000	
7	-0.892596	-1.976740	0.000000	
8	-0.118326	2.691316	0.000000	
1	-1.855057	-1.675846	0.000000	
8	1.318385	-1.393386	0.000000	
1	-0.675304	-2.962860	0.000000	

Cartesian coordinate of H_2O			**Sum of electronic and zero-point Energies**
8	-0.000309	0.065186	0.000000	HF = -76.4127544
1	-0.766961	-0.521011	0.000000	
1	0.771871	-0.513713	0.000000	

Cartesian coordinate of CO_2			**Sum of electronic and zero-point Energies**
8	-0.919365	-0.722613	0.000000	HF = -188.5788251
6	0.000000	0.000000	0.000000	
8	0.919365	0.722613	0.000000	