

One Pot Synthesis of 2-Hydroxy Pyrrolidine derivatives

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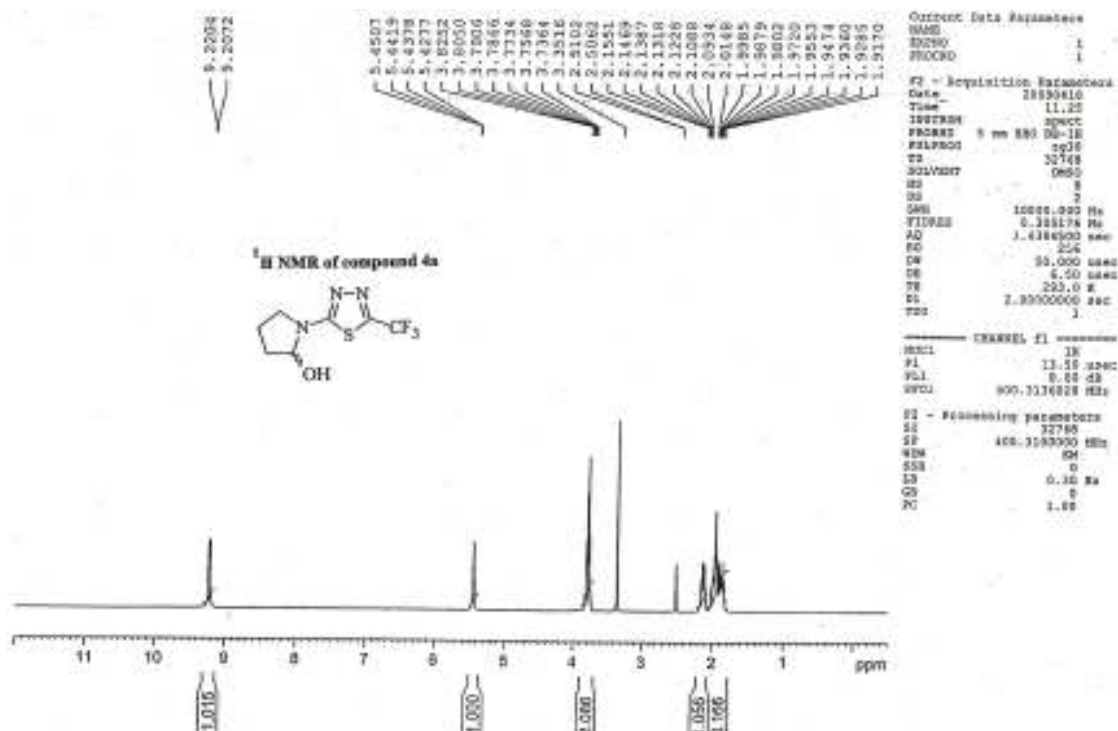
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Science, Kuvempu University, Shankaraghatta, Karnataka, 577451, India.*

³*Bioorganics and Applied Materials Pvt. Ltd., Bangalore, India*

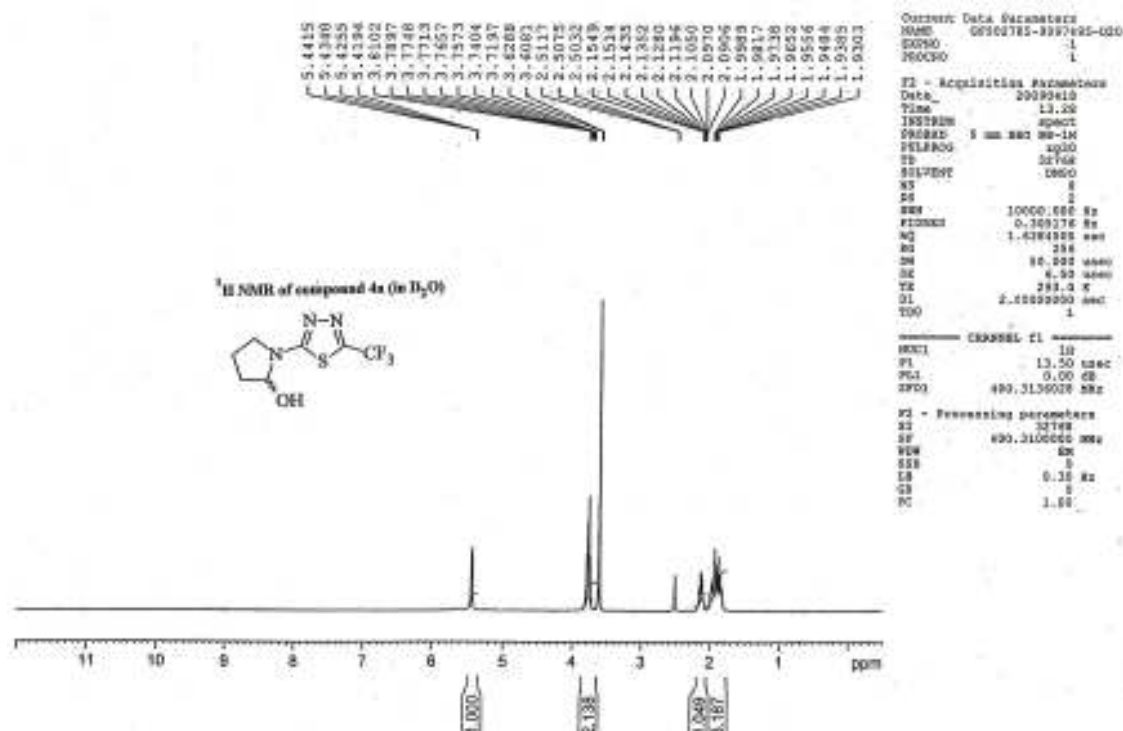
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1. ¹H-NMR Spectrum of 1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl] pyrrolidin-2-ol 4a.

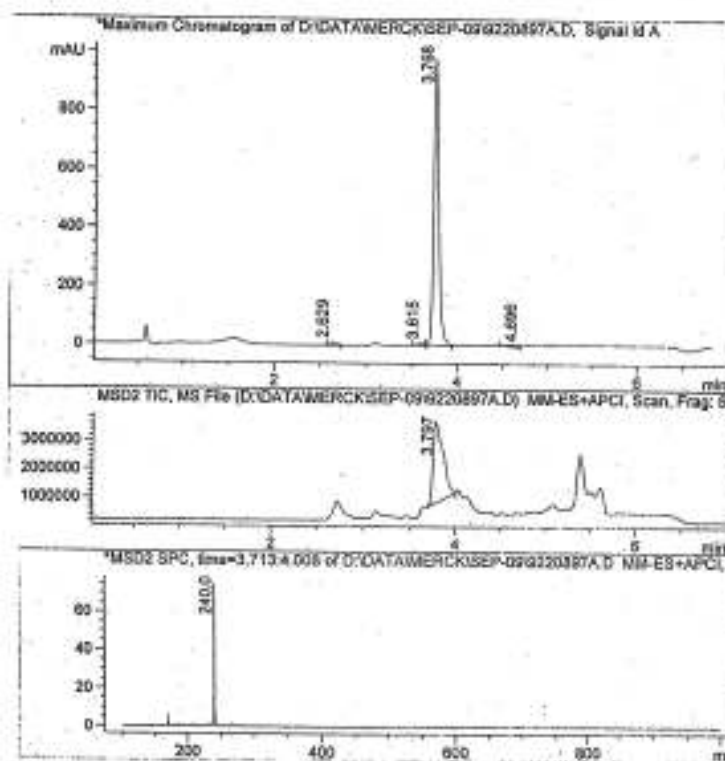


2. ¹H-NMR Spectrum of 1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl] pyrrolidin-2-ol 4a in D₂O.

LC/MS REPORT

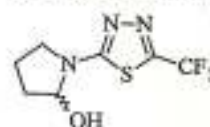
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 Injection vol : 2.0ul

Method info : A-0.1%HOAc;B-MEOW Flow: 1.2ml/min,
 Column-Atlantis dC18 (50X4.6mm-5µm,) POSITIVE MODE
 TIME (MIN) : 0--4.0 4.0--5.0 5.0--5.5 5.5--7.0
 8B 10-95 95 95-10 10



Peak No	RT min	Area	Area %
1	2.63	66.97	1.66
2	3.62	46.44	1.15
3	3.77	3854.17	95.83
4	4.70	54.44	1.35

Mass spectrum of 4a



Mass Calcd m/z = 239.0
 Found m/z = 240.0 (M+1)

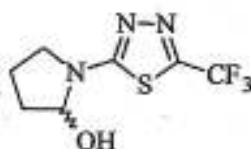
3. Mass Spectrum of 1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl] pyrrolidin-2-ol 4a

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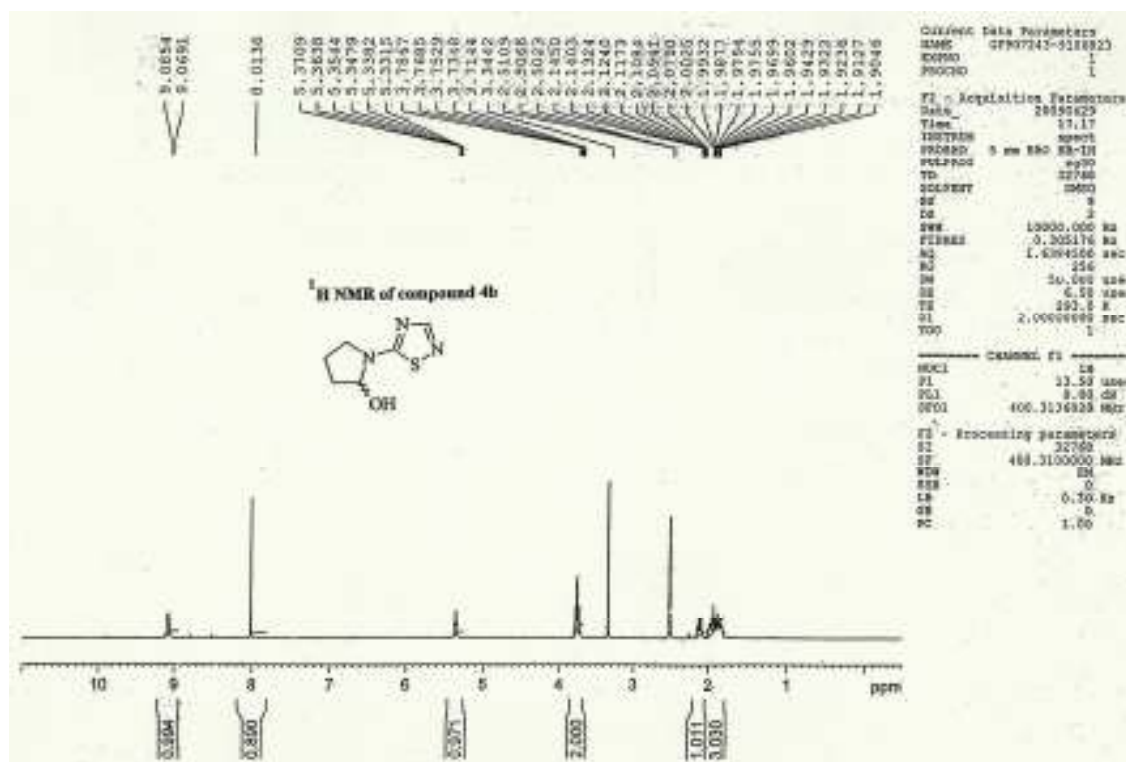
Statistic report

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12 GI948070.9199955	35.29	3.443	17.50	13.672
13 GI948070.9199955	35.68	3.284	17.87	15.628
Mean value [%]	35.49	3.364	17.68	14.650
Deviation, abs. [%]	0.27	0.112	0.26	1.384
Delta [%]	0.39	0.158	0.37	1.957

Elemental analysis of compound 4a



4. Elemental Analysis of 1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl] pyrrolidin-2-ol 4a

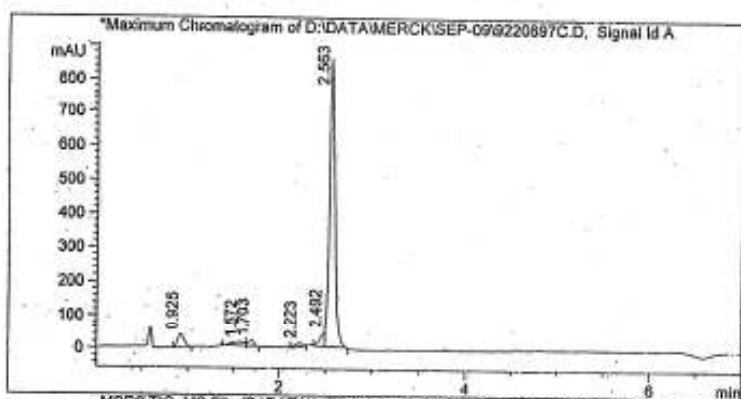


5. ¹H-NMR Spectrum of 1-(1,2,4-thiadiazol-5-yl)pyrrolidin-2-ol 4b.

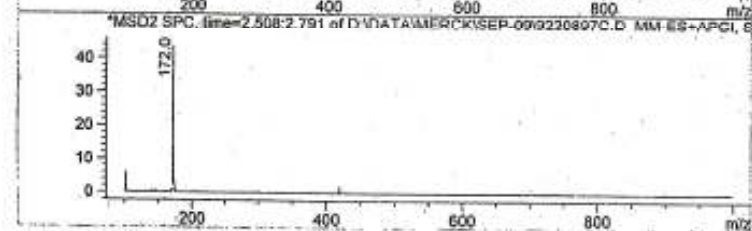
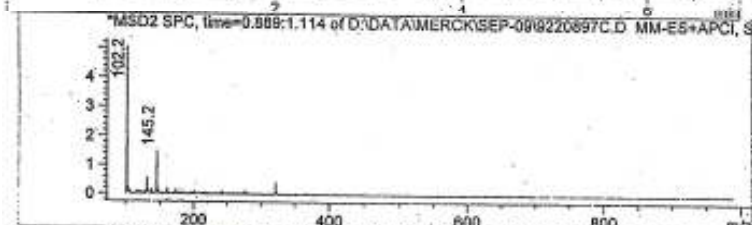
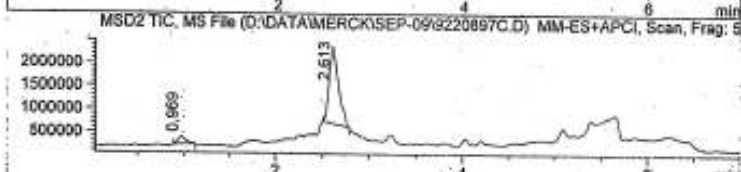
LC/MS REPORT

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 Injection vol : 2.0ul

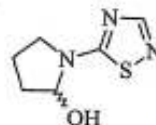
Method info : A-0.1% HCOOH; B-MEOH Flow: 1.2ml/min,
 Column-Atlantis dC18 (50X4.6mm-5µm,) POSITIVE MODE
 TIME (MIN) : 0--4.0 4.0--5.0 5.0--5.5 5.5-7.0
 %B : 10-95 95 95-10 10



Peak No	RT min	Area	Area %
1	0.92	205.61	4.95
2	1.57	118.73	2.86
3	1.70	77.00	1.85
4	2.22	70.65	1.70
5	2.49	148.52	3.58
6	2.56	3532.57	85.06

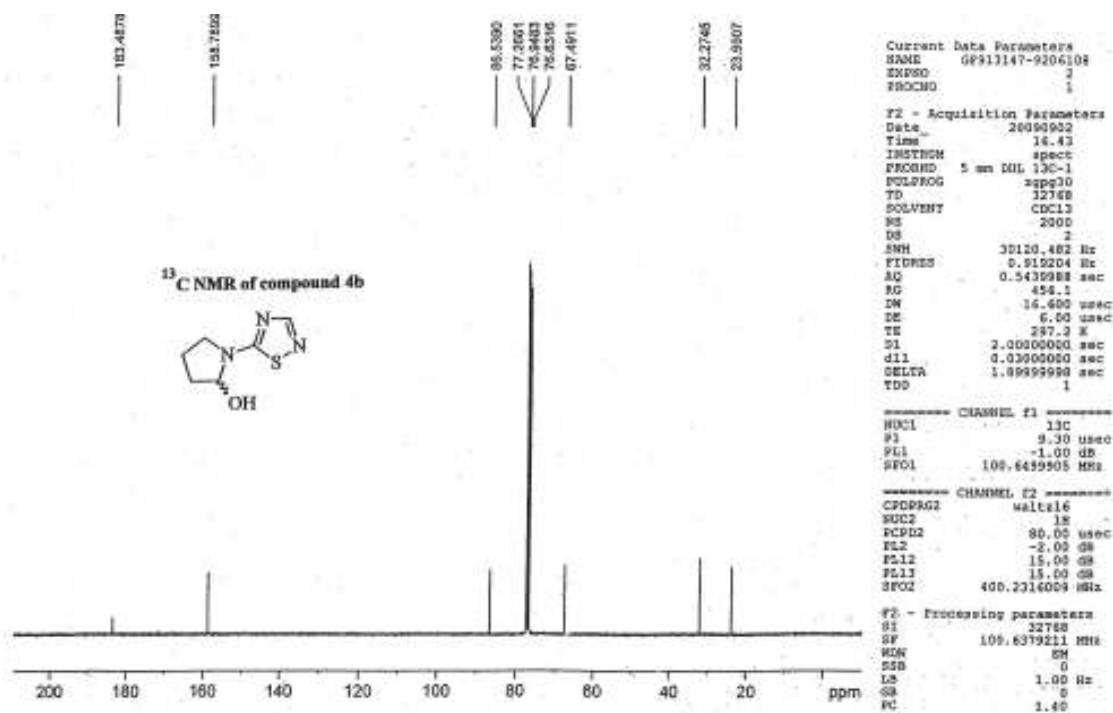


Mass spectrum of 4b



Mass Calcd m/z = 171.0
 Found m/z = 172.0 (M+1)

6. Mass Spectrum of 1-(1,2,4-thiadiazol-5-yl)pyrrolidin-2-ol 4b.



7. ¹³C Spectrum of 1-(1,2,4-thiadiazol-5-yl)pyrrolidin-2-ol 4b.

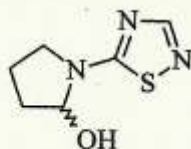
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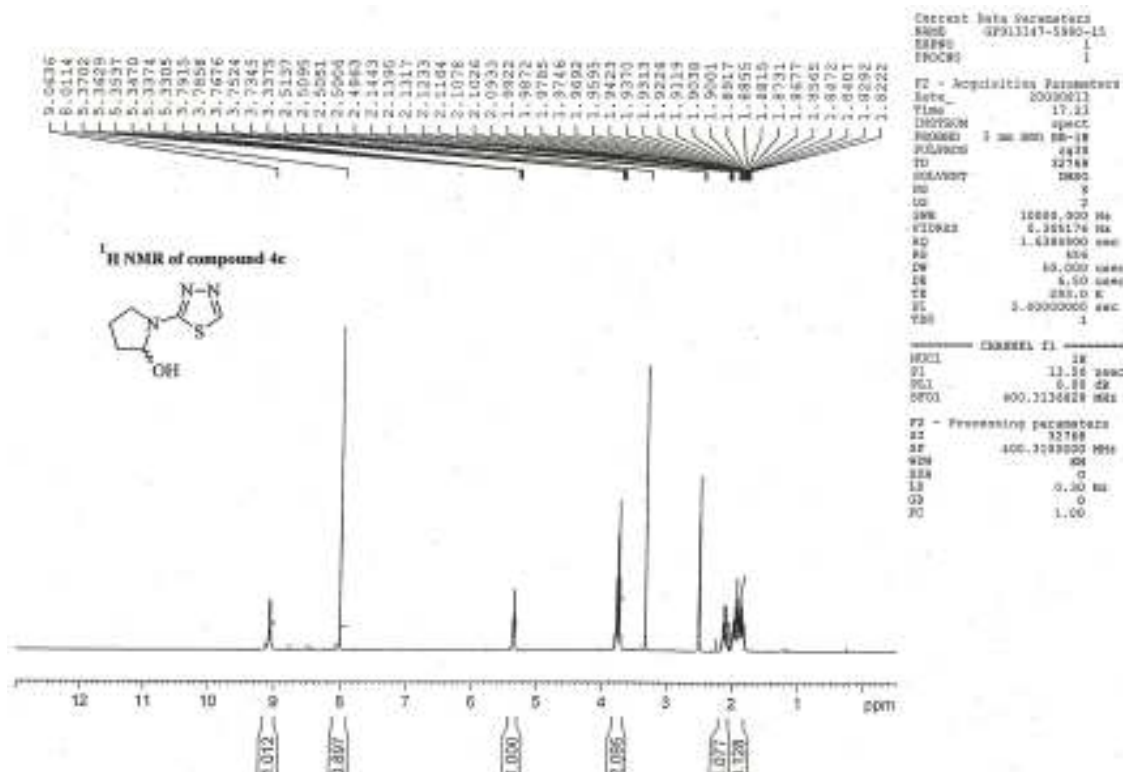
Statistic report

Name	C [%]	H [%]	N [%]	S [%]
16 GF913706-9204586	42.12	5.081	25.13	17.800
17 GF913706-9204586	41.99	5.131	25.06	18.452
Mean value [%]	42.06	5.106	25.10	18.126
Deviation, abs. [%]	0.09	0.036	0.05	0.461
Delta [%]	0.13	0.051	0.08	0.652

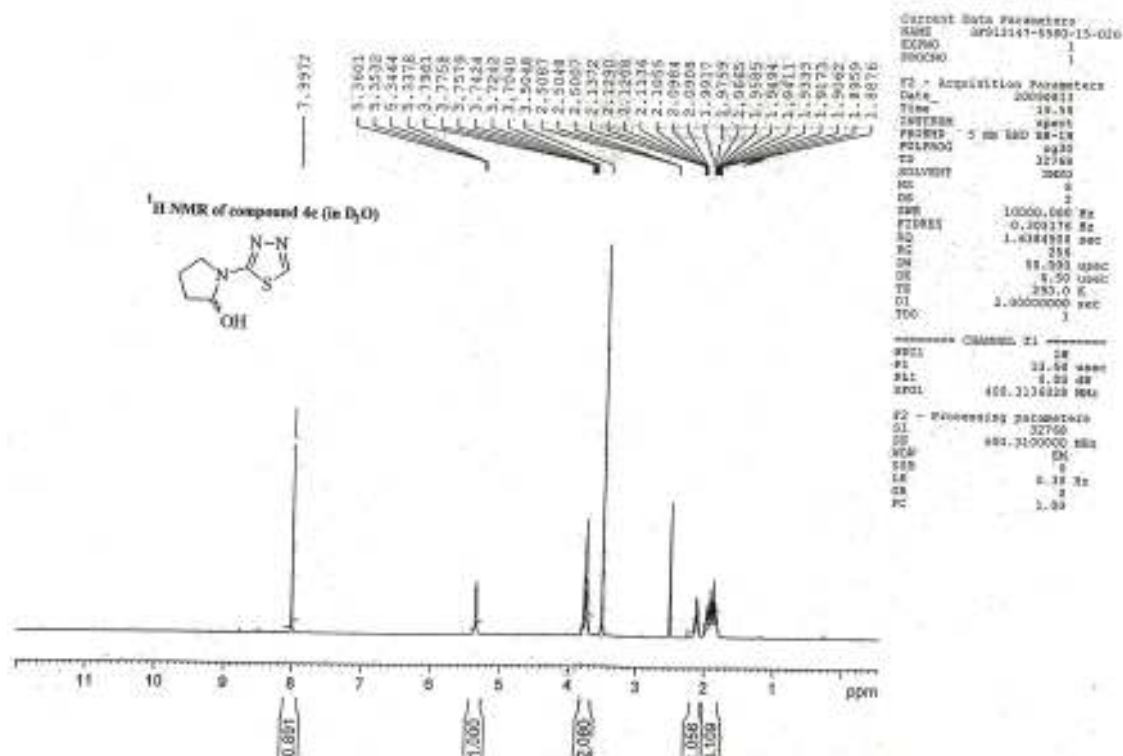
Elemental analysis of compound 4b



8. Elemental Analysis of 1-(1,2,4-thiadiazol-5-yl)pyrrolidin-2-ol 4b.



9. ¹H-NMR Spectrum of 1-(1,3,4-thiadiazol-2-yl)pyrrolidin-2-ol 4c.

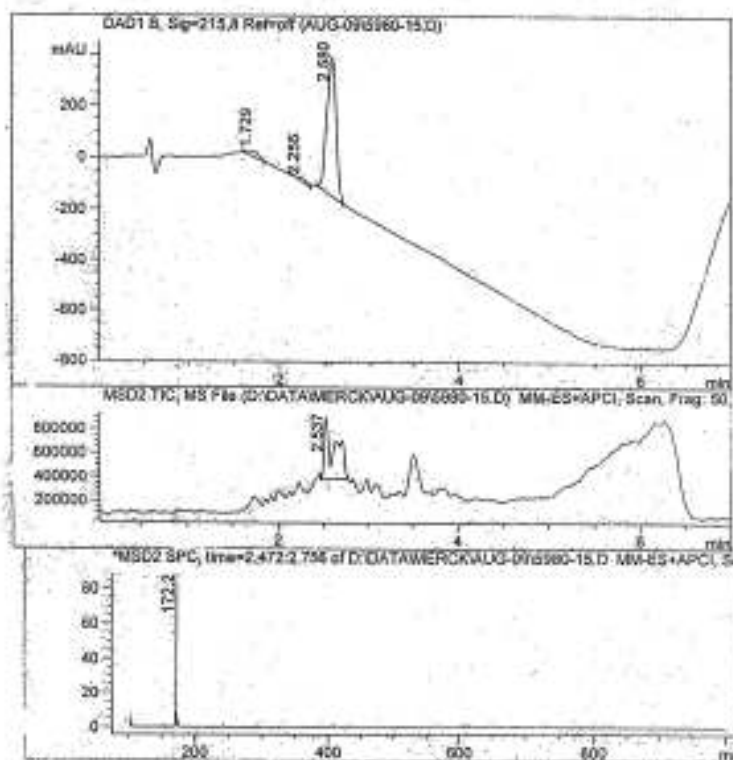


10. ¹H-NMR Spectrum of 1-(1,3,4-thiadiazol-2-yl)pyrrolidin-2-ol 4c in D₂O.

LC/MS REPORT

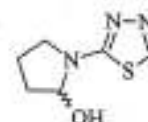
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Method info : A=0.1% HCOOH; B=MEOH Flow: 1.2ml/min.
 Column: Atlantis dC18 (50x4.6mm-5µm,) POSITIVE MODE
 TIME (MIN) : 0--4.0 4.0--5.0 5.0--5.5 5.5--7.0
 %B : 10-95 95 95-10 10



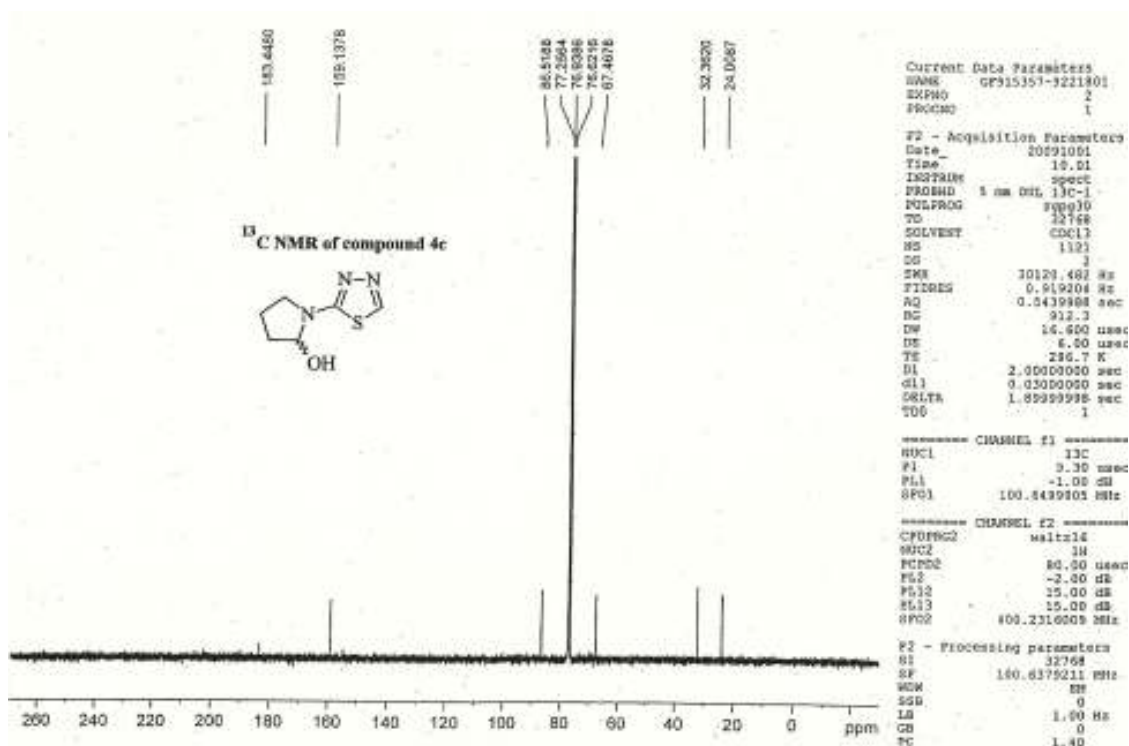
Peak No	RT min	Area	Area %
1	1.73	159.09	3.92
2	2.26	104.63	2.58
3	2.58	1793.50	93.50

Mass spectrum of 4c



Mass Calcd m/z = 171.0
 Found m/z = 172.0 (M+1)

11. Mass Spectrum of 1-(1,3,4-thiadiazol-2-yl)pyrrolidin-2-ol 4c.



12. ¹³C Spectrum of 1-(1,3,4-thiadiazol-2-yl)pyrrolidin-2-ol 4c.

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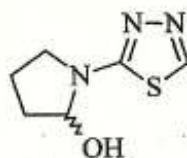
analytic functional testing

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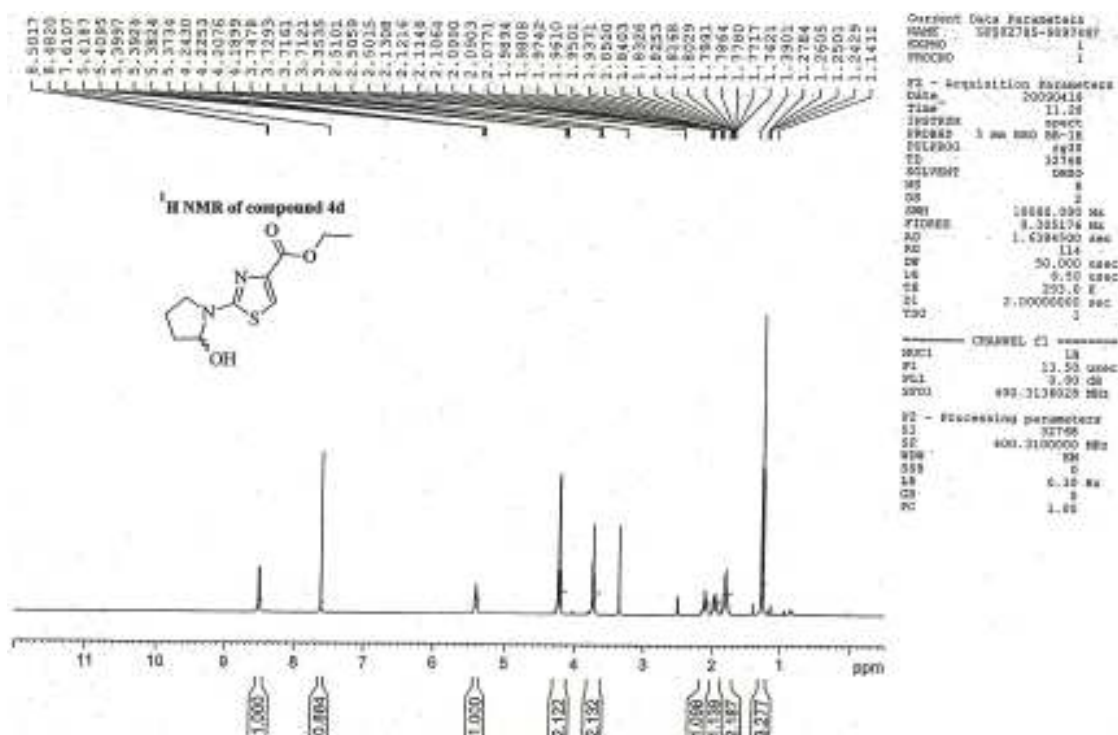
Statistic report

Name	C [%]	H [%]	N [%]	S [%]
16 GF913706-9204586	42.12	5.081	25.13	17.800
17 GF913706-9204586	41.99	5.131	25.06	18.452
Mean value [%]	42.06	5.106	25.10	18.126
Deviation, abs. [%]	0.09	0.036	0.05	0.461
Delta [%]	0.13	0.051	0.08	0.652

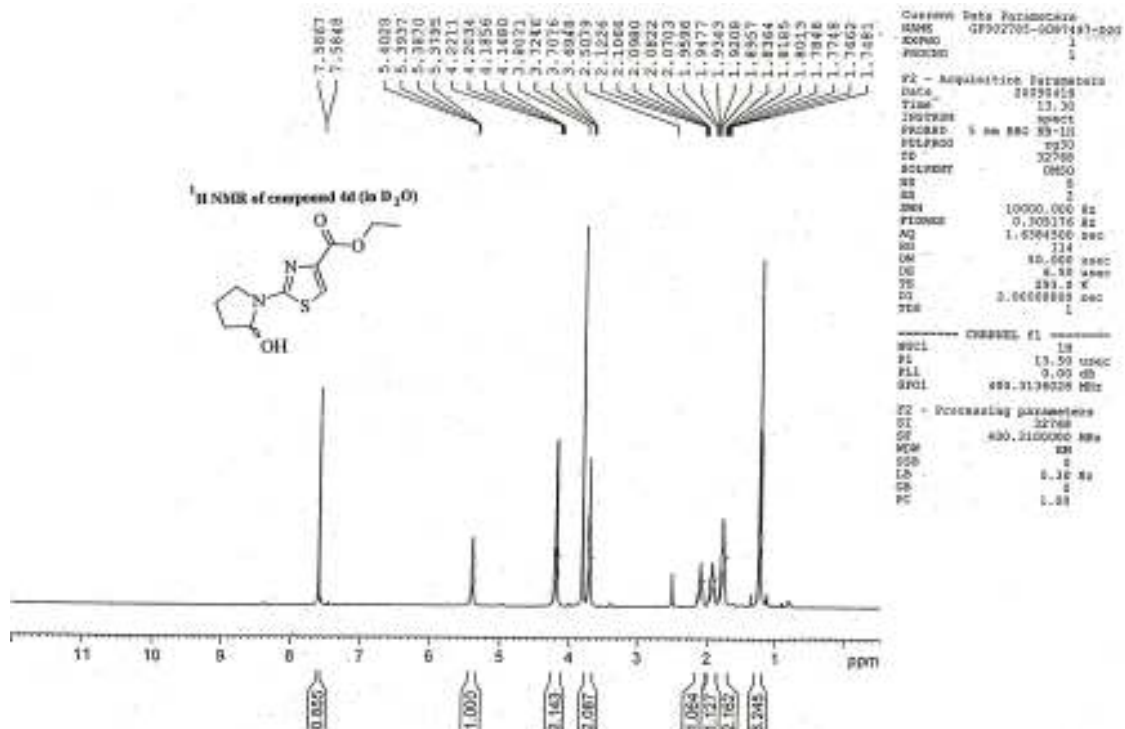
Elemental analysis of compound 4c



13. Elemental Analysis of 1-(1,3,4-thiadiazol-2-yl)pyrrolidin-2-ol 4c.



14. ¹H-NMR Spectrum of Ethyl 2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazol e-4-carboxylate 4d.



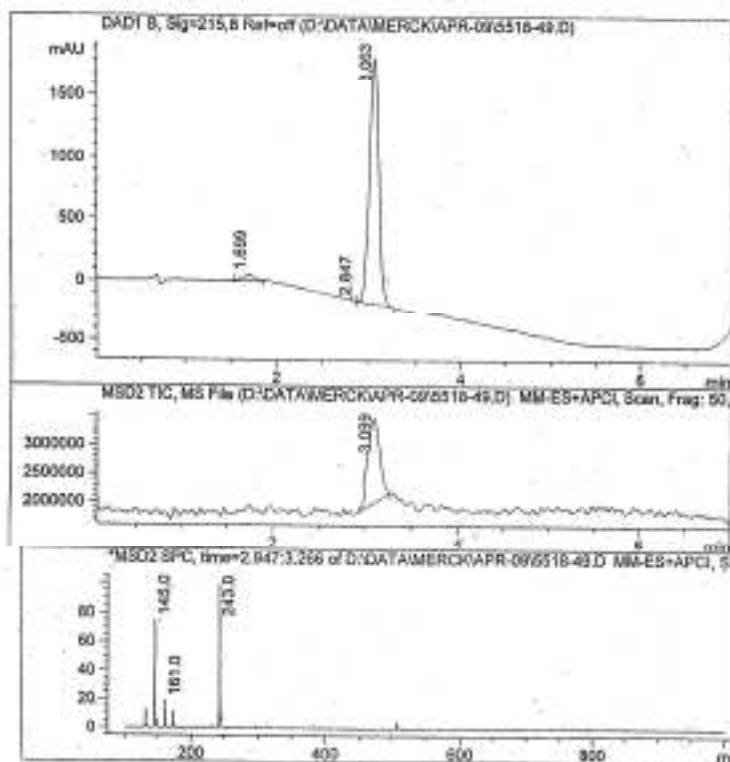
15. ¹H-NMR Spectrum of Ethyl 2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazol e-4-carboxylate 4d in D₂O.

MM : 1.000

LC/MS REPORT

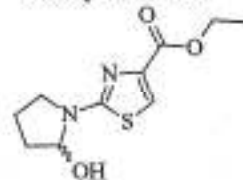
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Injection vol : 2.0ul

Method info : A-0.1%HOAC;B-MEOW Flow: 1.2ml/min,
Column-Atlantis dC18 (50X4,6mm-5um,) POSITIVE MODE
TIME (MIN) : 0--4.0 4.0--5.0 5.0--5.5 5.5-7.0
IN 10-95 95 95-10 10



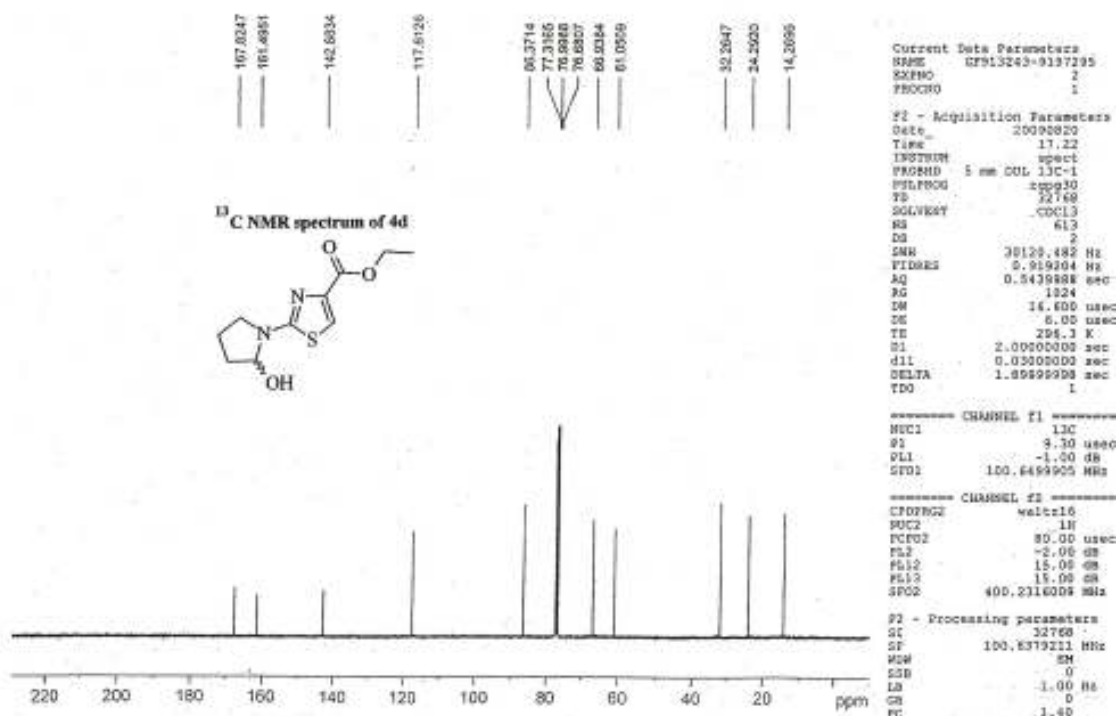
Peak No	RT min	Area	Area %
1	1.70	501.27	13.46
2	2.85	18.85	0.13
3	3.06	13954.60	96.41

Mass spectrum of 4d



Mass Calcd m/z = 242.0
Found m/z = 243.0 (M+1)

16. Mass Spectrum of Ethyl 2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazol e-4-carboxylate 4d.



17. ¹³C Spectrum of Ethyl 2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazol e-4-carboxylate 4d.

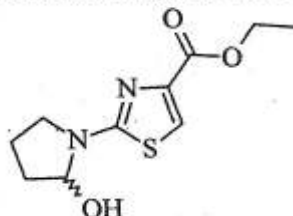
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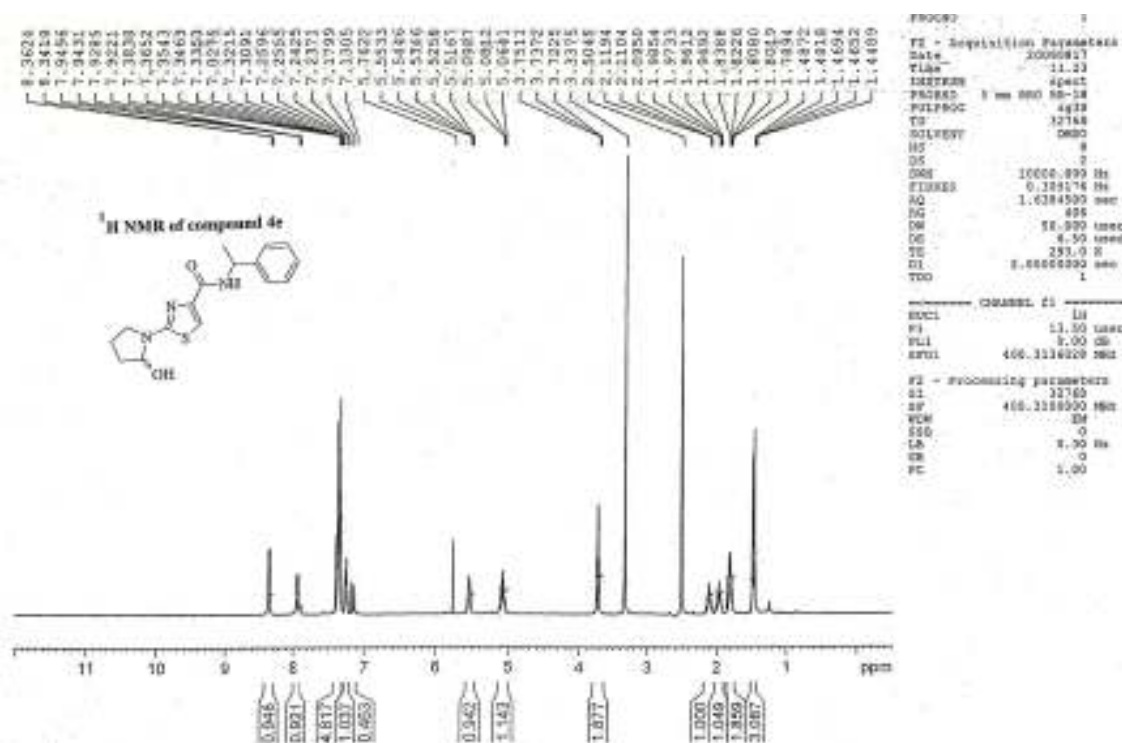
Statistic report

Name	C [%]	H [%]	N [%]	S [%]
19 GF913706-9204586A	48.87	5.568	11.93	13.021
20 GF913706-9204586A	48.87	5.599	11.40	13.456
Mean value [%]	48.87	5.583	11.66	13.239
Deviation, abs. [%]	0.00	0.022	0.37	0.307
Delta [%]	0.00	0.031	0.53	0.434

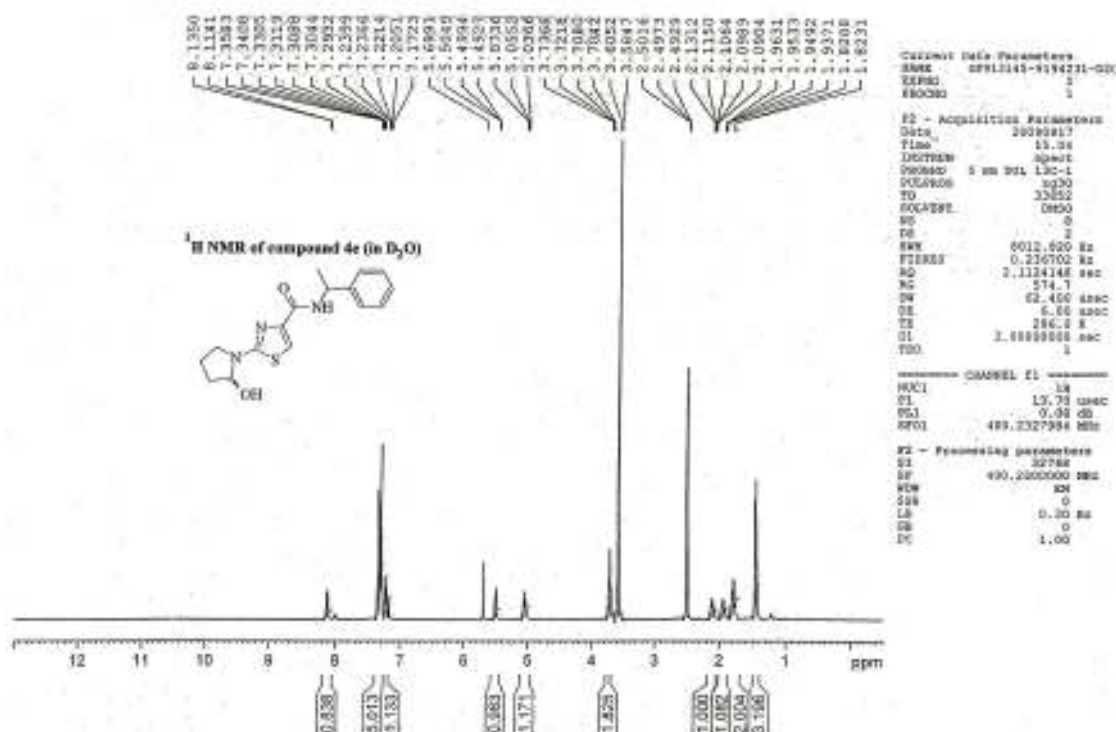
Elemental analysis of compound 4d



18. Elemental Analysis of Ethyl 2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazol e-4-carboxylate 4d.



19. ¹H-NMR Spectrum of 2-(2-hydroxypyrrolidin-1-yl)-*N*-(1-phenyl ethyl)-1,3-thiazole-4-carboxamide 4e.

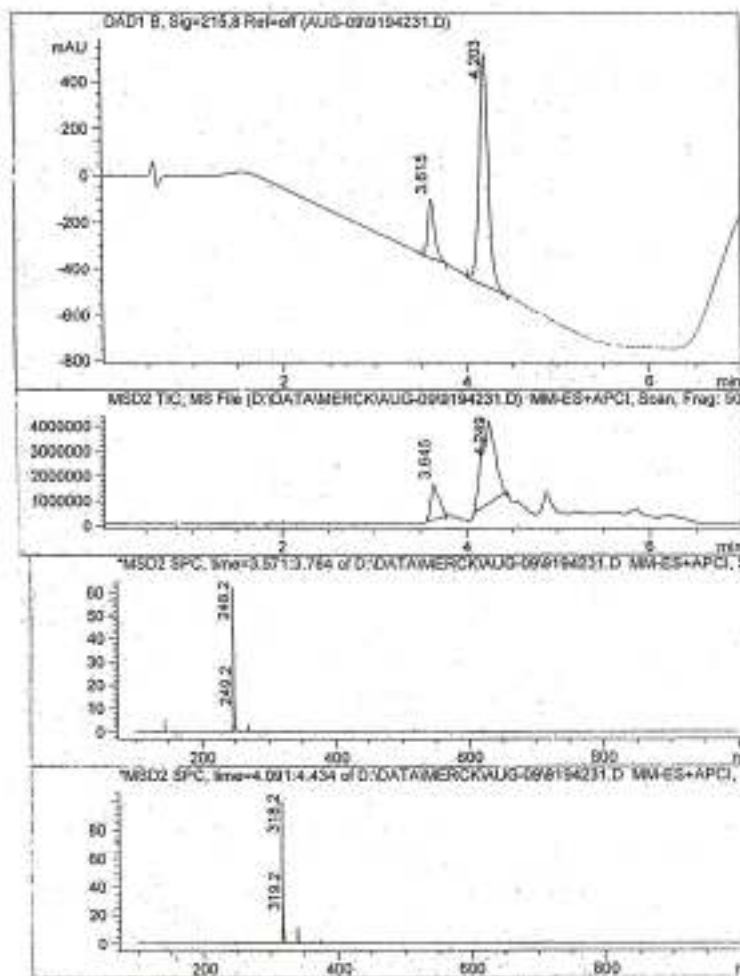


20. ¹H-NMR Spectrum of 2-(2-hydroxypyrrolidin-1-yl)-*N*-(1-phenyl ethyl)-1,3-thiazole-4-carboxamide 4e in D₂O.

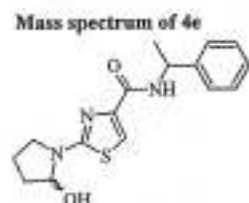
LC/MS REPORT

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 Sample Name : GF913145
 Vial No. : P1-A-06
 Acq Method : D:\METHODS\AT_1090MFA.M
 Injection vol : 2.0ul

Method info : A-0.1%HOOCOH;B-MEOH Flow: 1.2ml/min,
 Column-Atlantis dC18 (50X4.6mm-5µm,) POSITIVE MODE
 TIME (MIN) : 0--4.0 4.0--5.0 5.0--5.5 5.5--7.0
 VB 10-95 95 95-10 10

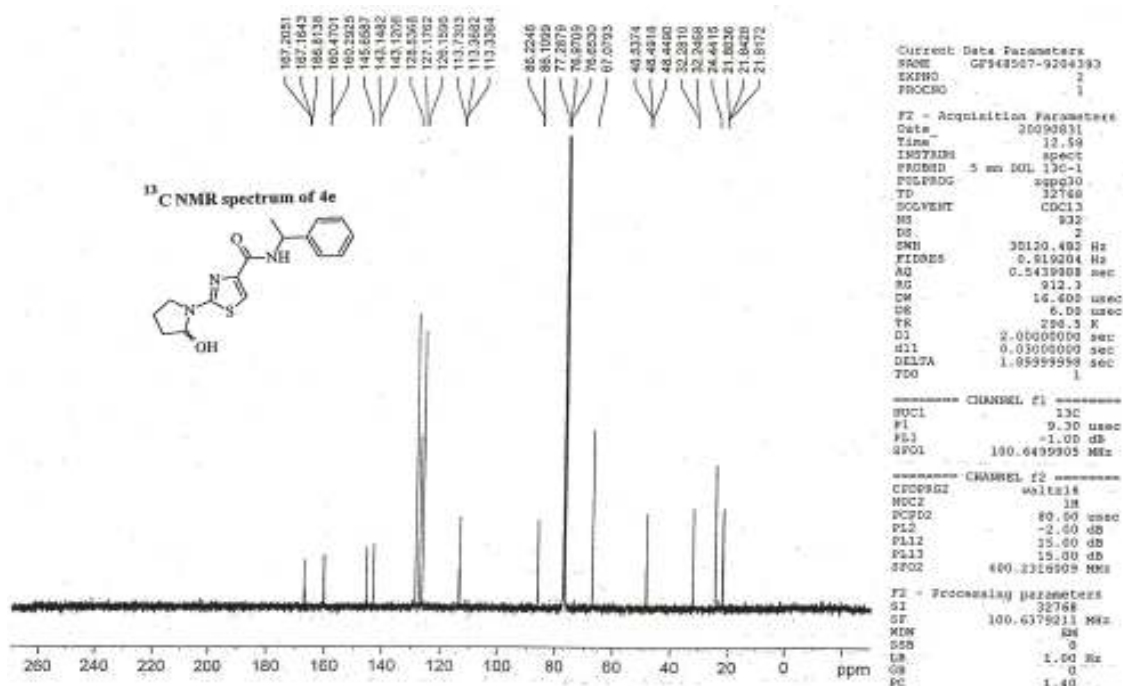


Peak No	RT min	Area	Area %
1	3.62	1293.94	15.95
2	4.20	6820.75	84.05



Mass Calcd m/z = 317.1
 Found m/z = 318.2 (M+1)

21. Mass Spectrum of 2-(2-hydroxypyrrolidin-1-yl)-N-(1-phenyl ethyl)-1,3-thiazole-4-carboxamide 4e.



22. ¹³C Spectrum of 2-(2-hydroxypyrrolidin-1-yl)-N-(1-phenyl ethyl)-1,3-thiazole-4-carboxamide 4e.

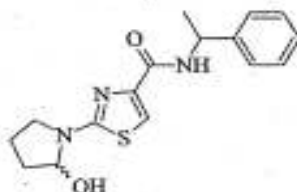
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analytic functional testing
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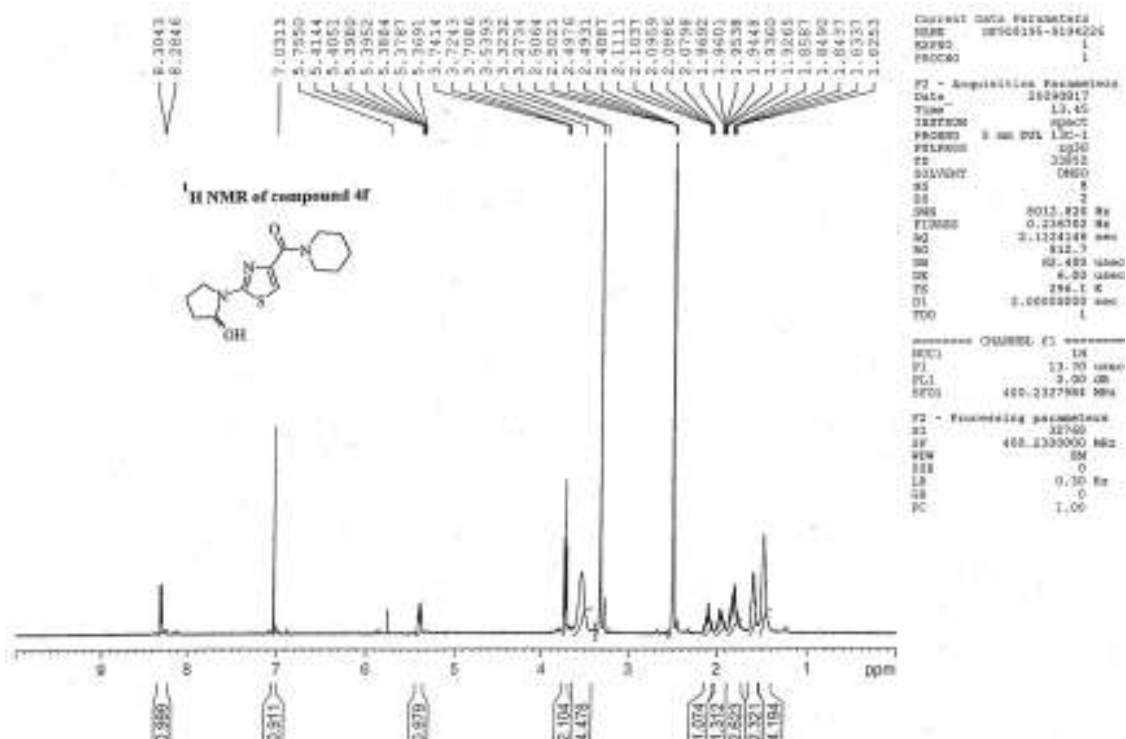
Statistic report

Name	C [%]	H [%]	N [%]	S [%]
26 GI948507-9201886A	57.90	5.822	12.58	10.121
27 GI948507-9201886A	58.82	5.904	12.93	10.064
Mean value [%]	58.36	5.863	12.76	10.093
Deviation, abs. [%]	0.65	0.058	0.25	0.041
Delta [%]	0.92	0.082	0.36	0.057

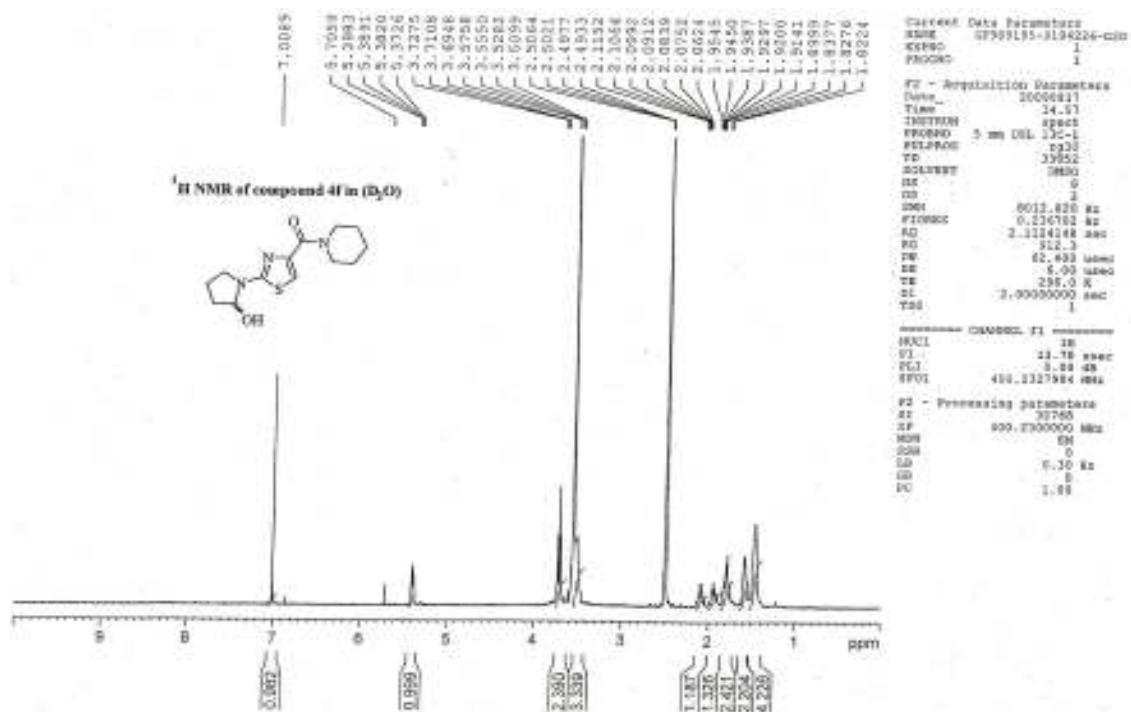
Elemental analysis of compound 4e



23. Elemental Analysis of 2-(2-hydroxypyrrolidin-1-yl)-N-(1-phenyl ethyl)-1,3-thiazole-4-carboxamide 4e.



24. ¹H-NMR Spectrum of [2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazol-4-yl] (piperidin-1-yl)methanone 4f.

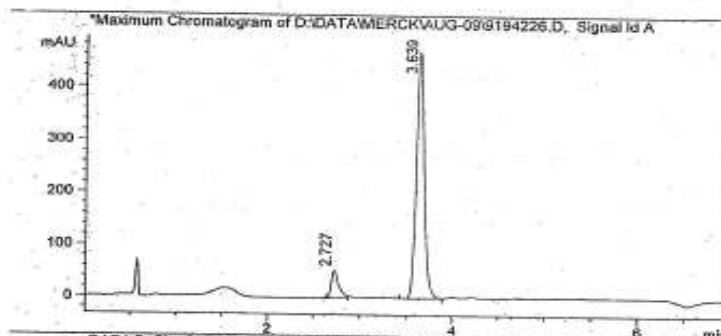


25. ¹H-NMR Spectrum [2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazol-4-yl] (piperidin-1-yl)methanone 4f in D₂O

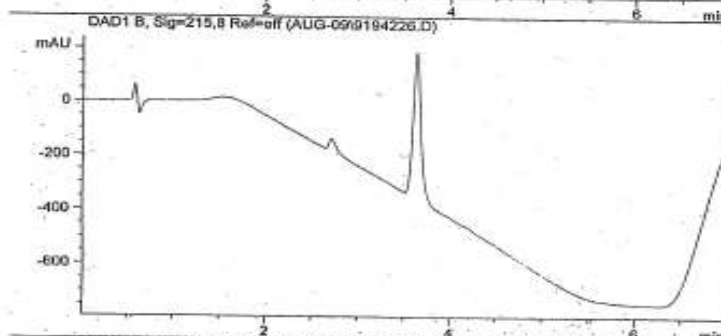
LC/MS REPORT

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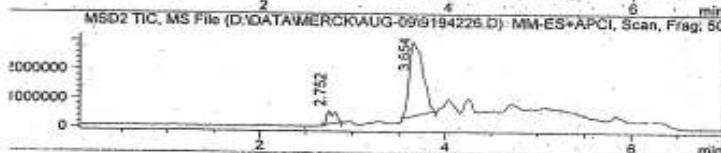
=====
Data file       : D:\DATA\MERCK\AUG-09\9194226.D
Injection Date  : 8/17/2009
Sample Name     : GP913146
Vial No.        : P1-A-08
Acq Method      : D:\METHODS\AT_1090MFA.M
Injection vol    : 2.0ul
=====
Method info     : A-0.1%HOAc/B-MeOH Flow: 1.2ml/min,
                  Column-Atlantis dC18 (50X4.6mm-5µm; ) POSITIVE MODE
                  TIME (MIN) : 0--4.0      4.0--5.0      5.0--5.5      5.5-7.0
                           %B      10-95      95      95-10      10
=====
  
```



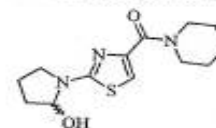
Peak No	RT min	Area	Area %
1	2.73	294.20	9.72
2	3.64	2733.40	90.28



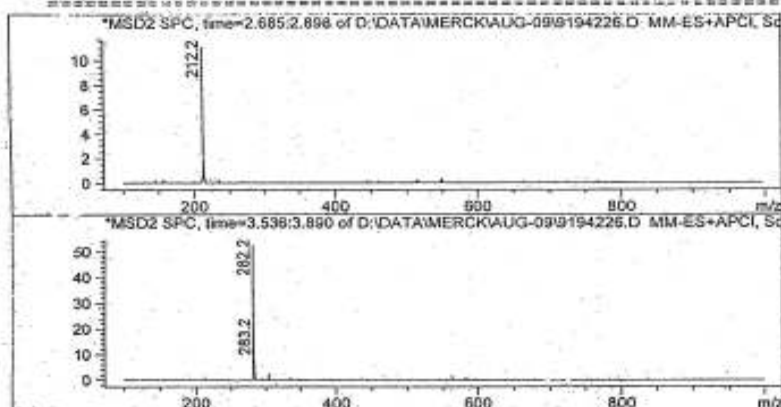
Peak No	RT min	Area	Area %
1	3.64	2733.40	90.28



Mass spectrum of 4f



Mass Calcd m/z = 281.1
Found m/z = 282.2 (M+1)



26. Mass Spectrum of [2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazol-4-yl] (piperidin-1-yl)methanone 4f.

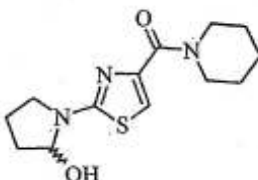
Document: 030909 (VarioMICRO) from: --.-- (modified)

analytic functional testing
varioMICRO CHNS

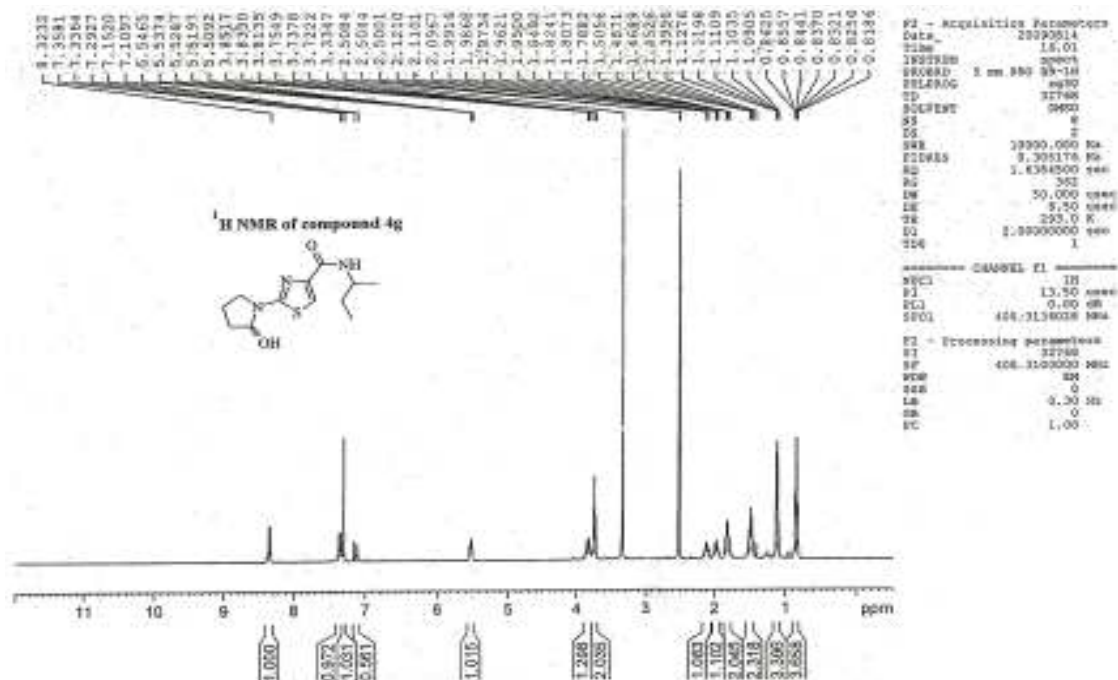
Statistic report

Name	C [%]	H [%]	N [%]	S [%]
18 GF914663-9205240A	54.44	6.639	13.42	10.013
19 GF914663-9205240A	54.80	6.694	13.36	10.134
Mean value [%]	54.62	6.667	13.39	10.073
Deviation, abs. [%]	0.25	0.038	0.04	0.085
Delta [%]	0.36	0.054	0.06	0.121

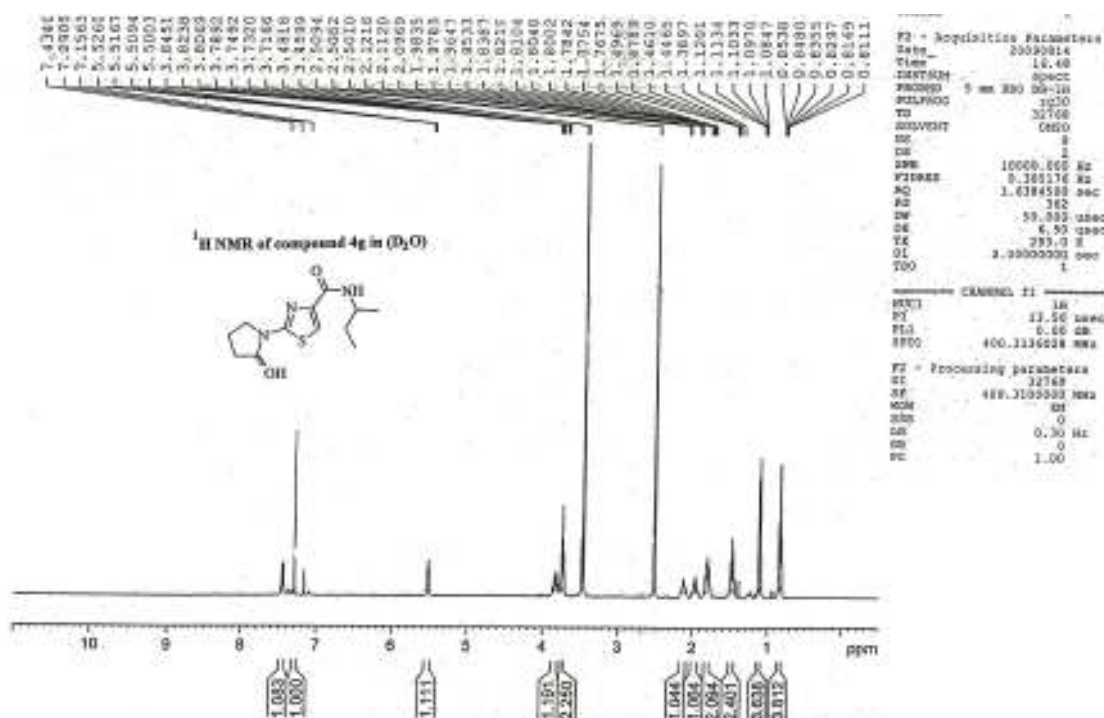
Elemental analysis of compound 4f



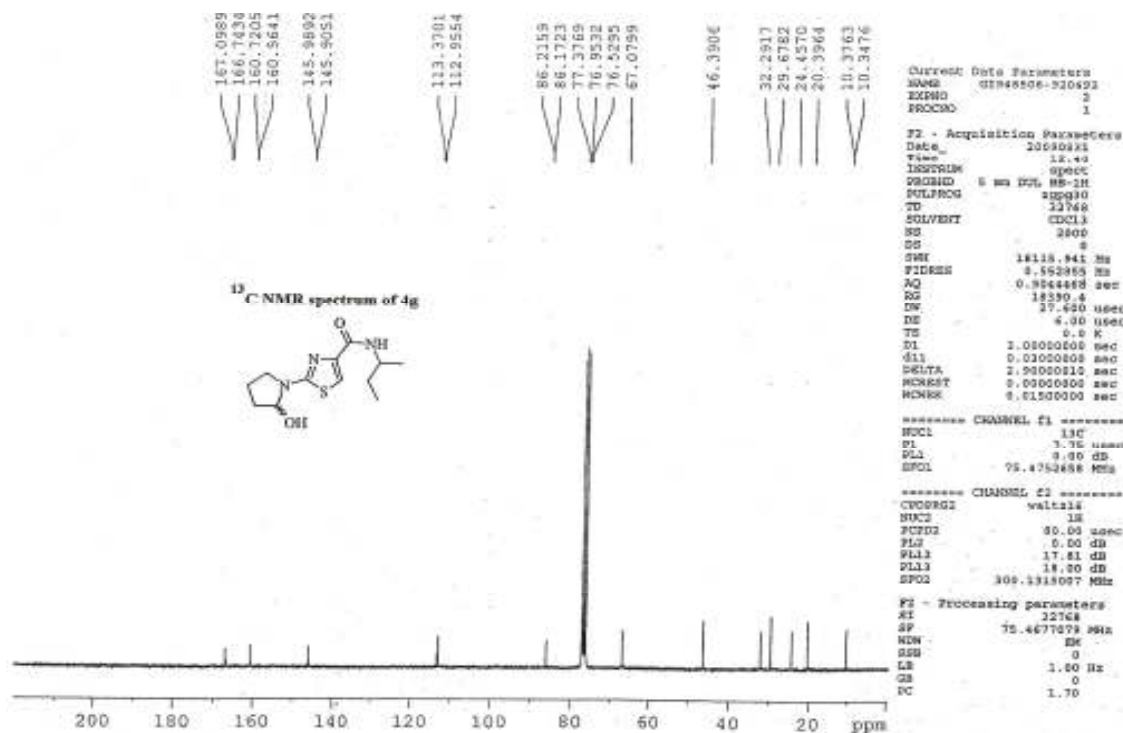
27. Elemental Analysis of [2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazol-4-yl] (piperidin-1-yl)methanone 4f.



28. ¹H-NMR Spectrum of N-(butan-2-yl)-2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazole-4-carboxamide 4g.



29. ¹H-NMR Spectrum of *N*-(butan-2-yl)-2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazole-4-carboxamide 4g in D₂O.

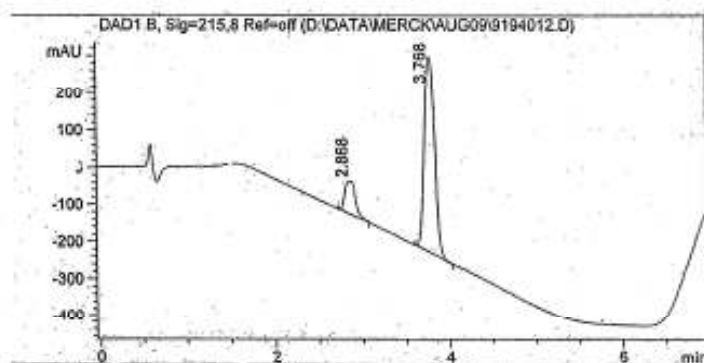


30. ¹³C Spectrum of *N*-(butan-2-yl)-2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazole-4-carboxamide 4g.

LC/MS REPORT

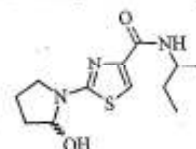
Data file : D:\DATA\MERCK\AUG09\9194012.D
 Injection Date : 8/14/2009
 Sample Name : GF913624
 Vial No : P1-P-02
 Acq Method : C:\CHEM32\1\METHODS\AT_1090MFA.M
 Injection vol : 2.0ul

Method info : A=0.1%HOAc;B-MEOH Flow: 1.2ml/min,
 Column-Atlantis dC18 (50X4.6mm-5µm,) POSITIVE MODE
 TIME (MIN) : 0--4.0 4.0--5.0 5.0--5.5 5.5--7.0
 %B 10-95 95 95-10 10

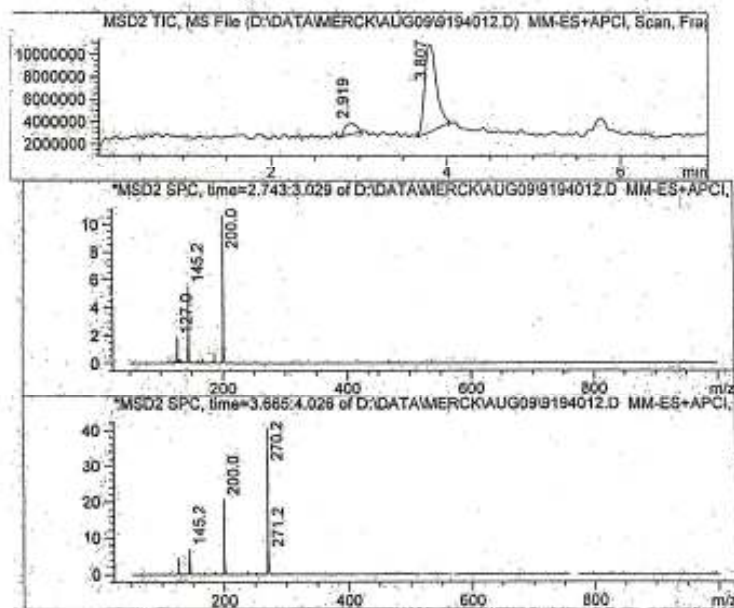


Peak No	RT min	Area	Area %
1	2.87	750.17	14.94
2	3.77	4271.09	85.06

Mass spectrum of 4g



Mass Calcd m/z = 269.1
 Found m/z = 270.2 (M+1)

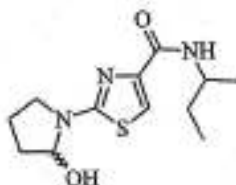


31. Mass Spectrum of *N*-(butan-2-yl)-2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazole-4-carboxamide 4g.

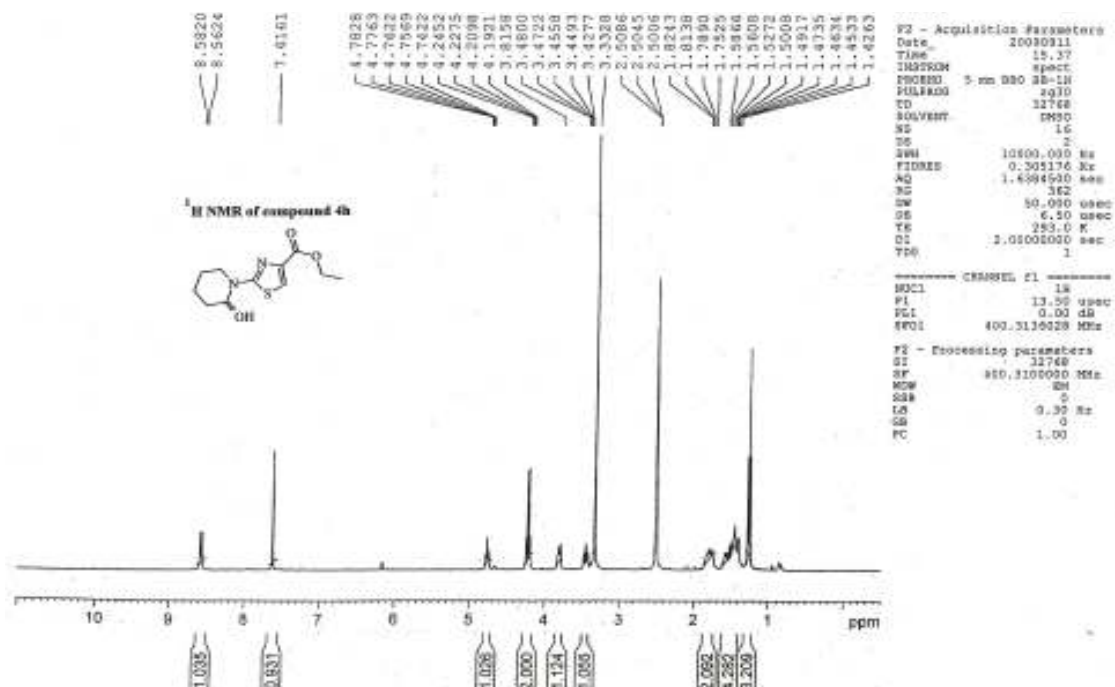
Statistic report

Name	C [%]	H [%]	N [%]	S [%]
20 GF914663-9205240	44.42	6.048	13.26	9.284
21 GF914663-9205240	42.94	5.684	12.08	9.105
Mean value [%]	43.68	5.866	12.67	9.195
Deviation, abs. [%]	1.04	0.257	0.83	0.126
Delta [%]	1.47	0.364	1.18	0.179

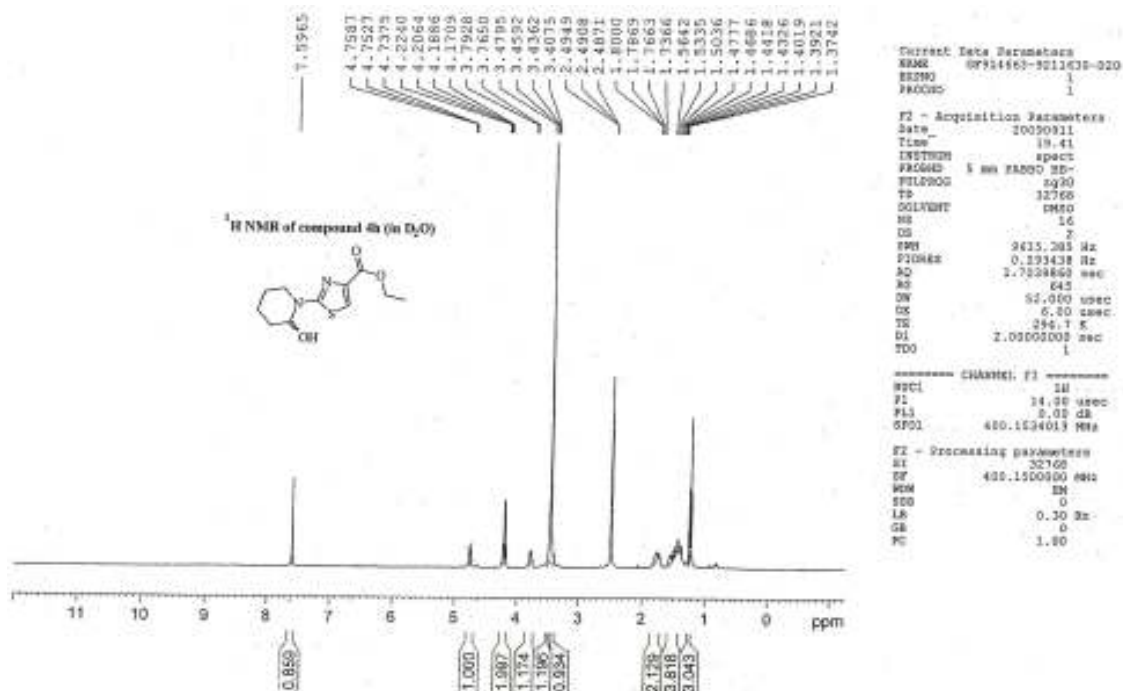
Elemental analysis of compound 4g



32. Elemental Analysis of *N*-(butan-2-yl)-2-(2-hydroxypyrrolidin-1-yl)-1,3-thiazole-4-carboxamide 4g.



33. ¹H-NMR Spectrum of Ethyl-2(2-hydroxypiperidin-1-yl)-1,3-thiazole-4-carboxylate 4h.



34. ¹H-NMR Spectrum of Ethyl-2(2-hydroxypiperidin-1-yl)-1,3-thiazole-4-carboxylate 4h in D₂O.