Available online at http://qu.edu.iq/journalsc/index.php/JOPS

Al-Qadisiyah Journal Of Pure Science (QJPS)

Vol. xx, No. xx, pp. xx –xx, Month-Year

ISSN 2411-3514 ONLINE

ISSN 1997-2490PRINTED

…Synthesis and Characterization and evaluation of biological activities of some new pyrroline compounds

May Jalil Abed

Lecturermay79@gmail.com

Department of chemistry Collage of medicine Al-Qadisiya university

---

Abstract

The chemical preparation of pyrroline compounds through series reactions with acetic anhydride, then iodine in methanol .,periodic acid finally with some derivatives of aniline .,These new derivatives were characterized by I.R,H^{1}NMR , spectra and element analysis data (C.H.N) ,melting point and the yield of the final new compound

Key words: Pyrroline compounds, aza sugar, Schiff bases, pyrrol compounds ,heterocyclic compounds.

Available online at http://qu.edu.iq/journalsc/index.php/JOPS

Al-Qadisiyah Journal Of Pure Science (QJPS)

Vol. xx, No. xx, pp. xx –xx, Month-Year

ISSN 2411-3514 ONLINE

ISSN 1997-2490PRINTED

Introduction

The heterocyclic compound 2-Acetyl-1-Pyrroline(ACPY) is a major compound contributing to the characteristic popcorn-like aroma in aromatic rice varieties. ACPY was not only identified as a key component contributing to the aromatic rice flavours(1) but was also shown to be a major component of the volatile oil of Pandanus amaryllifolius (2) The steroidal alkaloid veracintine, isolated from the above-ground part of Veratrum album ssp. Lobelianum (3) was found to be biologically active; its antileukemic effect is subject to the presence of pyrroline ring (2). Preparation of some simple models having the pyrroline ring was stimulated by the need to study the biological properties in more detail(4).Also the volitle compound 2-Acetyl pyrroline(2AP)is generated during the growing season in the plant and can be found in the leaves and stems as well as in the rice kernel (5). The maximum 2AP concentration is variety dependent (4) and occurs four or five weeks after heading (WAH) and decreases to 20% of maximum at seven or eight WAH (6).. Furthermore, 2AP concentration decreases with storage time and temperature (7). Consequently, even rice of the same variety grown under the same conditions may show a significant difference in 2AP concentration due to differences in harvest date and postharvest handling. Several methods have been developed for the isolation and concentration of 2AP in aromatic rice samples for subsequent analysis by gas chromatography with nitrogen-phosphorus, flame ionization, or mass spectrometry as a detector. These methods include concentration of 2AP in rice by purge and trap (8), steam distillation/solvent extraction (9), solvent extraction followed by direct injection (10), solid-phase microextraction (SPME) (11) and headspace analysis (12). Recently, SPME has shown the presence of 2AP in a single kernel of aromatic rice(13)

Experimental

1-Materials and methods

In this research our chemicals which are used from (BDH,Fluka and Merck).,All solvents were dried and distilled before used according to the standard procedures .

Melting point were measured on a start melting point apparatus. IR spectra were taken using KBr disk and film on Testcan Shimadzu FTIR 8000 series. Elemental analysis were calculated by C.H.N analyzer type Euro vector,EA 3000 A Itali., The H^1NMR spectra were taken on Burker, Ultra shield 300 MHz ,Switzear land using TMS as internal standard.

Reaction progress were monitored by T.L.C technique using silica gel coated plates type liner K(20x20) m.m Watman company, in the presence (benzene:methanol) (8:2)

2-Synthesis

Synthesis of derivative (P3)[N-ethyl phenyl -5,6-O-isopropylidine-aza-ascorbic acid]:

This derivative prepared by mixing (8.1 gm,0.0253 mole) of isopropylidine-N-2-phenyl ethyl gluconamide in a solution of pyridine (20 ml) and acetic anhydride (25 ml,0.026 mole) and continuous stirring at room temp for one day, then extracted with chloroform (25ml),then with

(0.05 HCl) (50 ml).,We get a brown crystals after evaporated the solvent.

Synthesis of derivative (P4)[N-ethel phenyl-aza-ascorbic acid]:

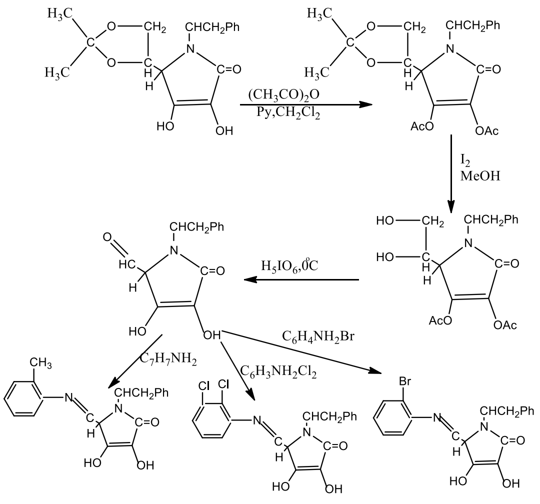
It was prepared by added (1.82 gm, 0.0146 mole)of iodine dissolved in (30 ml)methanol into a solution of (6.9 gm, 0.0171 mole) of P3 in (40 ml) chloroform., The final mixture refluxed for 1 hr .,Cooled, filtered and recrystallised from ethanol to get a milky crystals.

Synthesis of derivative P5[N-ethyl phenyl-5-formyl-3,4 dihydroxy-2-one-pyrolline:

A solution of iodine (3.13 gm ,0.0137 mole) of periodic acid dissolved in 25 ml distilled water added to (5 gm,0.0137 mole)of P4 gradually through 30 min at (0 C)., Then we added (0.5 ml) ethylene glycol, the final mixture extracted with ethyl acetate (30 ml x3) and evaporated the organic layer to get a white crystals .

Synthesis of Schiff bases derivatives (PT,PCl,PBr).

The last derivatives were synthesized by condensation of (4.2 gm ,0.017 mole)of P5 in (30 ml) of absolute ethanol with (0.017 mole) of different amines (ortho toludune, 2-bromo aniline ,2,3-di chloro aniline). The mixture refluxed for ≈ 3 hr and then filtered recrystallised from ethanol to obtain a new Schiff bases which are respectively N-phenyl ethyl -5-(2- methyl pheniline imine)-3,4-di hydroxyl-2-N-pyrroline derivative (PT) ,N- phenyl ethyl -5-(2,3-di chloro pheniline imine)-3,4-di hydroxyl-2-N-pyrroline derivative (PCl) ,N- phenyl ethyl -5-(2-Bromo pheniline imine)-3,4-di hydroxyl-2-N-pyrroline derivative (PBr)



Fig(1):Methods of preparation of new pyrolline derivatives

Results and Discussion

The total synthesis of new pyrroline derivatives was achieved in four steps with an overall yield of 80%. The preparation of these derivative required a modification of the published substrate . Besides using diethyl ether instead of Pyridine as a solvent, our procedure allowed the reaction to stir at room temperature overnight, instead of 3 hr in earlier reports. This was due to the observation by thin-layer chromatography

and characterized by FTIR, H^{1}NMR and the C.H.N elements

FTIR spectroscopic for new prepared derivative(P3) fig (3) show bipartite peak at 1650 Cm^{-1} into two peaks one of them due to estric carbonyl and the other for lactonic carbonyl groups(14) , the (P4) derivative fig (4) show streaching peak in 3400 Cm^{-1} for hydroxyl group and weak peak in 2810 Cm^{-1} for CH$_2$ group (15) ,While (P5) derivative fig (5) show weak stretching peak in 2765 Cm^{-1} for aldehyde group and another stretching peak in 3400 Cm^{-1} for hydroxyl group .,The final new three derivatives (PT,PCl,PBr) respectively fig(6,7,8) show strong peak in 3300-3400 Cm^{-1} for hydroxyl groups and a sharp peak in 1500-1600 Cm^{-1} for methen groups(16).

The H^{1}NMR spectra for(P3) derivative fig (9) show singlet signal at δ=2.5 ppm for the solvent used and singlet signal at δ=2.9 ppm for protons of acetyl group and singlet signal at δ=0.9 ppm for protons of methyl groups and doublet signal at δ=0.5 ppm for protons of ethyl group that attached to nitrogen atom(17) and another doublet signal at δ=1.4 ppm for the proton that attached to oxygen atom and triplet signal at δ=1.0 ppm for the proton that attached to another oxygen atom and multiplet signal at δ=7.0-7.3 ppm for protons of aromatic ring(18).The (P4) derivative fig (10) show new singlet signal at δ=4.1 ppm due to protons of hydroxyl groups and disappearance of methyl group signal .,The (p5) derivative fig (11) show singlet signal at δ=9.1 ppm for proton of aldehyde group(19) .,The (PT) derivative fig (12) show singlet signal at δ=0.6 ppm due to protons of methyl group and doublet signal at δ=1.1 ppm for protons of ethyl group that attach to nitrogen atom and singlet signal at δ=3.3 ppm for protons of hydroxyl group(20) and multiplet signal at δ=7.1-7.3 ppm due to protons of aromatic rings and singlet signal at δ= 8.2 for proton of imine group .,The(PCl) derivative fig (13) show disappearance of signal of methyl group and movement in the signal of protons of phenyl ring into δ=7.5 ppm because of the effect of halide groups (21)

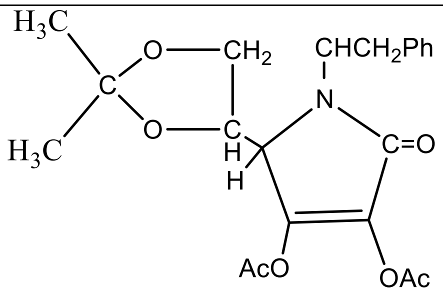
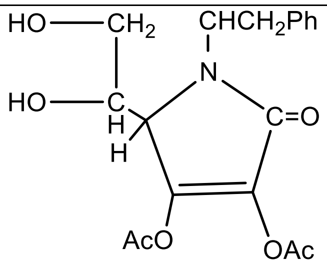
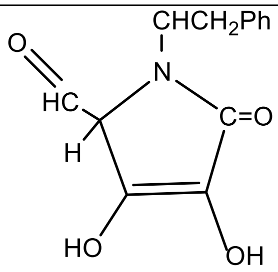
Available online at http://qu.edu.iq/journalsc/index.php/JOPS

Al-Qadisiyah Journal Of Pure Science
(QJPS)
Vol. xx, No. xx, pp. xx –xx, Month-Year

ISSN 2411-3514 ONLINE

ISSN 1997-2490PRINTED

Table -1:Some physical properties of a new pyrolline derivatives

No.	Structure	M.F	MWt.	M.P C°	Yield%
P3		**$C_{21}H_{25}O_7N$**	**403**	**190**	**85**
P4		**$C_{18}H_{21}O_7N$**	**363**	**150**	**72**
P5		**$C_{13}H_{13}O_4N$**	**247**	**100**	**84**

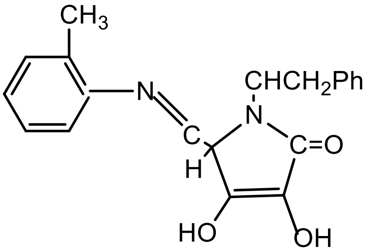
PT		**C20H20O3N2**	**336**	**150**	**82**

Table -2:Some physical properties of a new pyrolline derivatives

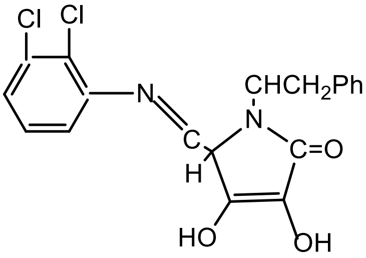
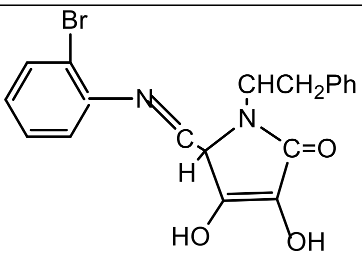
No.	**Structure**	**M.F**	**MWt.**	**M.P** **C°**	**Yield%**
PCl		**$C_{19}H_{16}O_3N_2Cl_2$**	**390**	**170**	**81**
PBr		**$C_{19}H_{17}O_3N_2Br$**	**401**	**180**	**82**

Table -3:Analytical data and R_f of a new pyrolline derivatives

No.	**Structure**	**R_f**	**C%**	**H%**	**N%**	**S%**
			Calc.	**Calc.**	**Calc.**	**Calc.**
			Found	**Found**	**Found**	**Found**

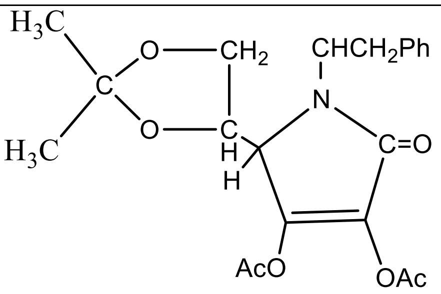
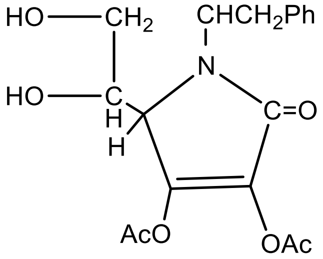
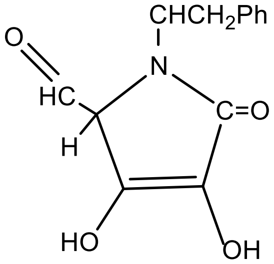
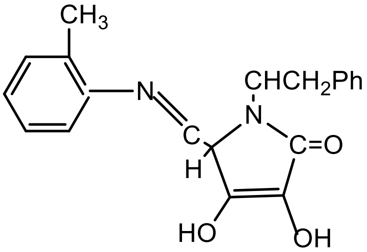
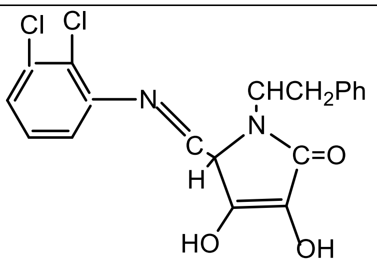
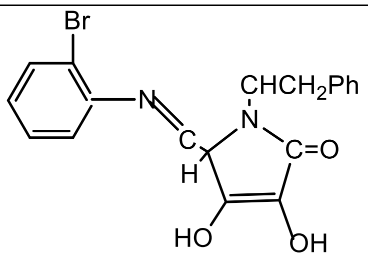
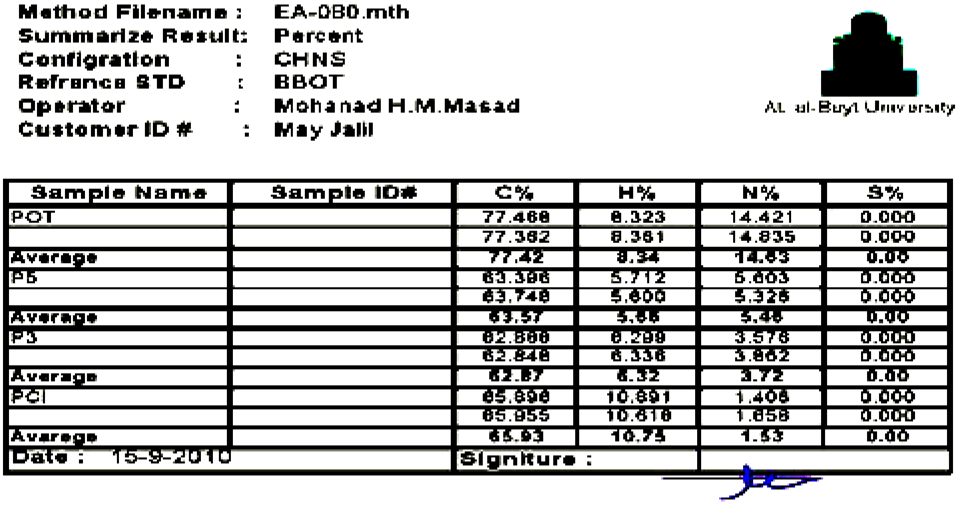
P3		**0.89**	**62.888** **62.848**	**6.299** **6.336**	**3.576** **3.862**	**0.00** **0.00**
P4		**0.81**				

Table -4:Analytical data and R_f of a new pyrolline derivatives

No.	**Structure**	**R_f**	**C%** **Calc.** **Found**	**H%** **Calc.** **Found**	**N%** **Calc.** **Found**	**S%** **Calc.** **Found**
P5		**0.78**	**63.396** **63.748**	**5.712** **5.600**	**5.603** **5.326**	**0.00** **0.00**
PT		**0.72**	**77.468** **77.362**	**8.323** **8.361**	**14.421** **14.835**	**0.00** **0.00**

PCl		**0.69**	**65.896** **65.955**	**10.891** **10.618**	**1.406** **1.658**	**0.00** **0.00**
PBr		**0.61**				

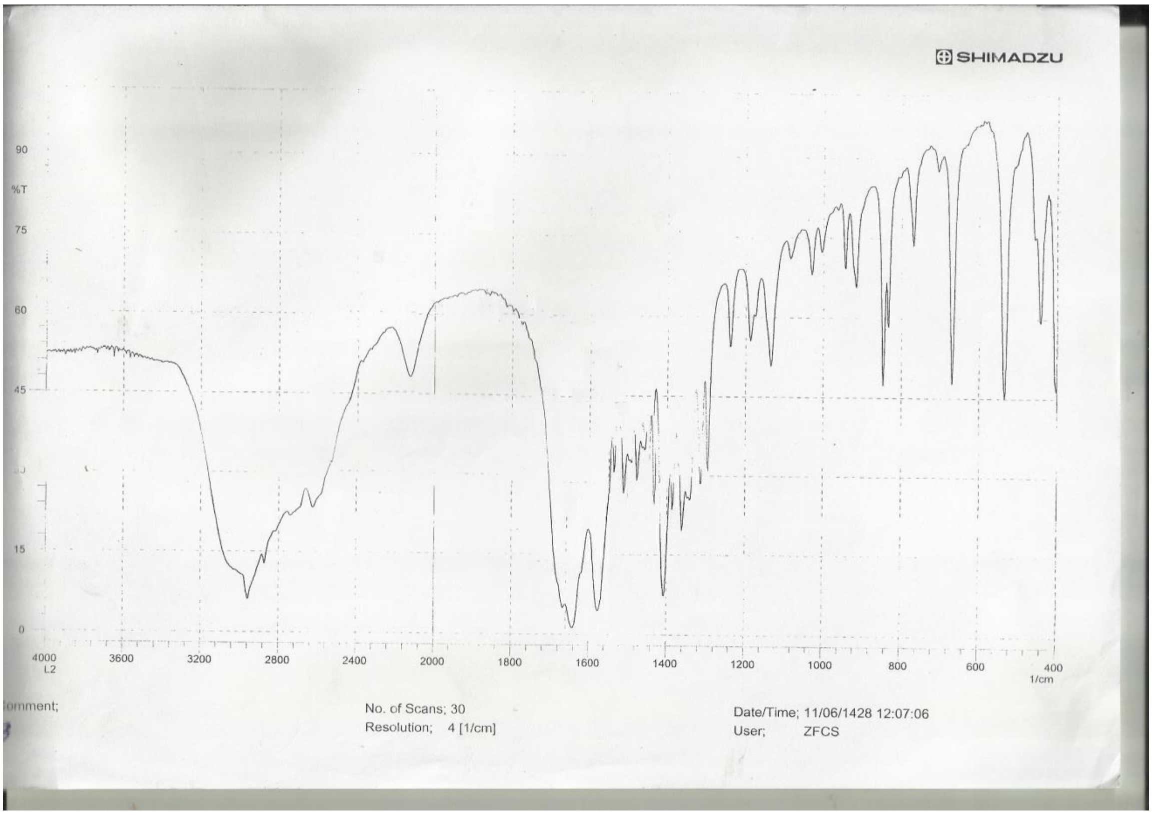


Method Filename : EA-080.mth
Summarize Result: Percent
Configration : CHNS
Refrance STD : BBOT
Operator : Mohanad H.M.Masad
Customer ID # : May Jalil

Sample Name	Sample ID#	C%	H%	N%	S%
POT		77.468	8.323	14.421	0.000
		77.362	8.361	14.835	0.000
Average		77.42	8.34	14.63	0.00
P5		63.396	5.712	5.603	0.000
		63.748	5.600	5.326	0.000
Average		63.57	5.66	5.46	0.00
P3		62.888	6.299	3.576	0.000
		62.848	6.336	3.862	0.000
Average		62.87	6.32	3.72	0.00
PCl		65.896	10.891	1.406	0.000
		65.955	10.618	1.658	0.000
Avarege		65.93	10.75	1.53	0.00

Date : 15-9-2010
Signiture :

Fig-2: Element analysis for pyrolline compounds

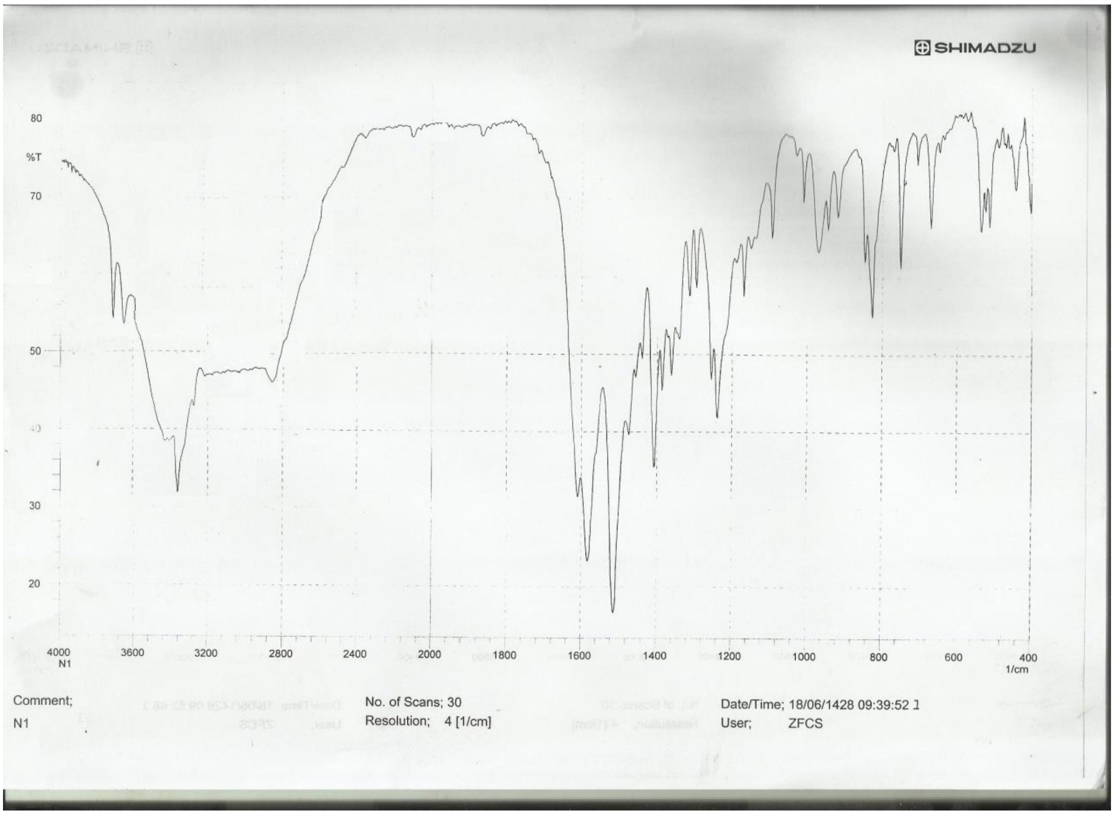


Comment;

No. of Scans; 30
Resolution; 4 [1/cm]

Date/Time; 11/06/1428 12:07:06
User; ZFCS

Fig-3:FTIR spectra for P3 derivative



Comment;
N1

No. of Scans; 30
Resolution; 4 [1/cm]

Date/Time; 18/06/1428 09:39:52 1
User; ZFCS

Fig-4:FTIR spectra for P4 derivative

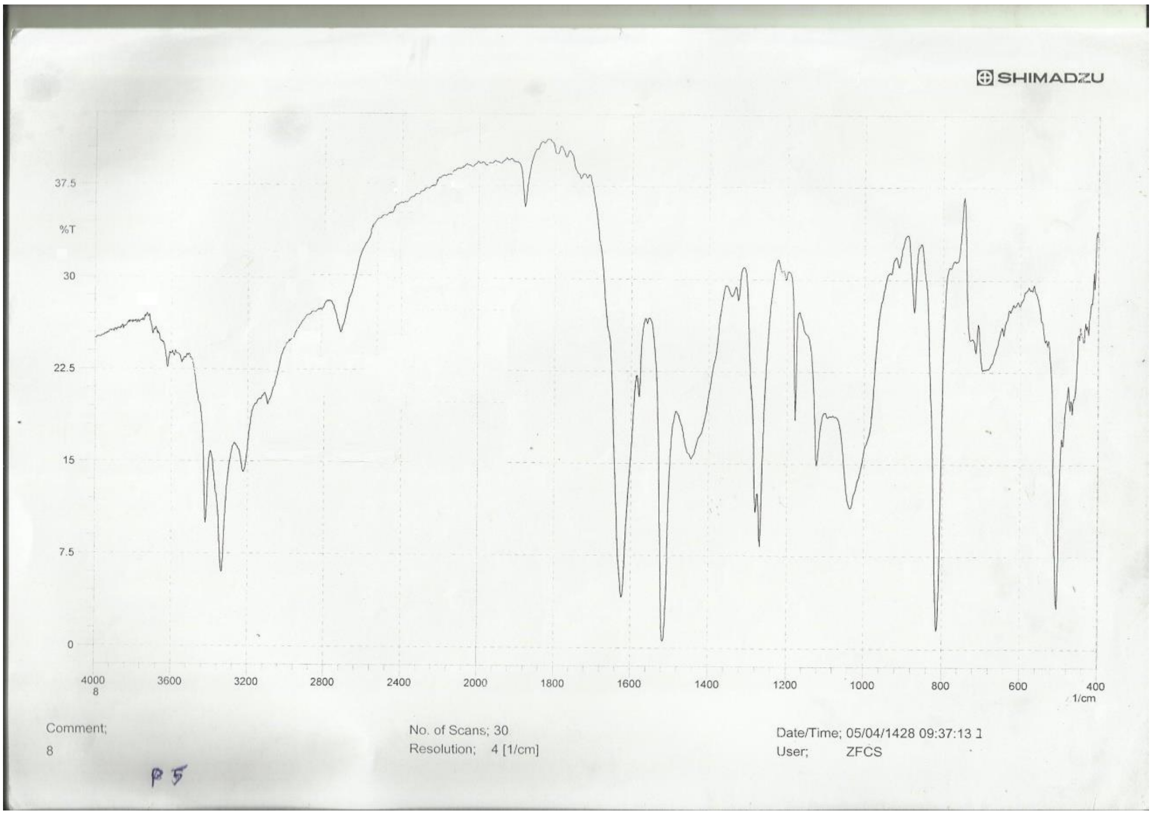


Fig-5:FTIR spectra for P5 derivative

Available online at http://qu.edu.iq/journalsc/index.php/JOPS

Al-Qadisiyah Journal Of Pure Science (QJPS)
Vol. xx, No. xx, pp. xx –xx, Month-Year

ISSN 2411-3514 ONLINE
ISSN 1997-2490PRINTED

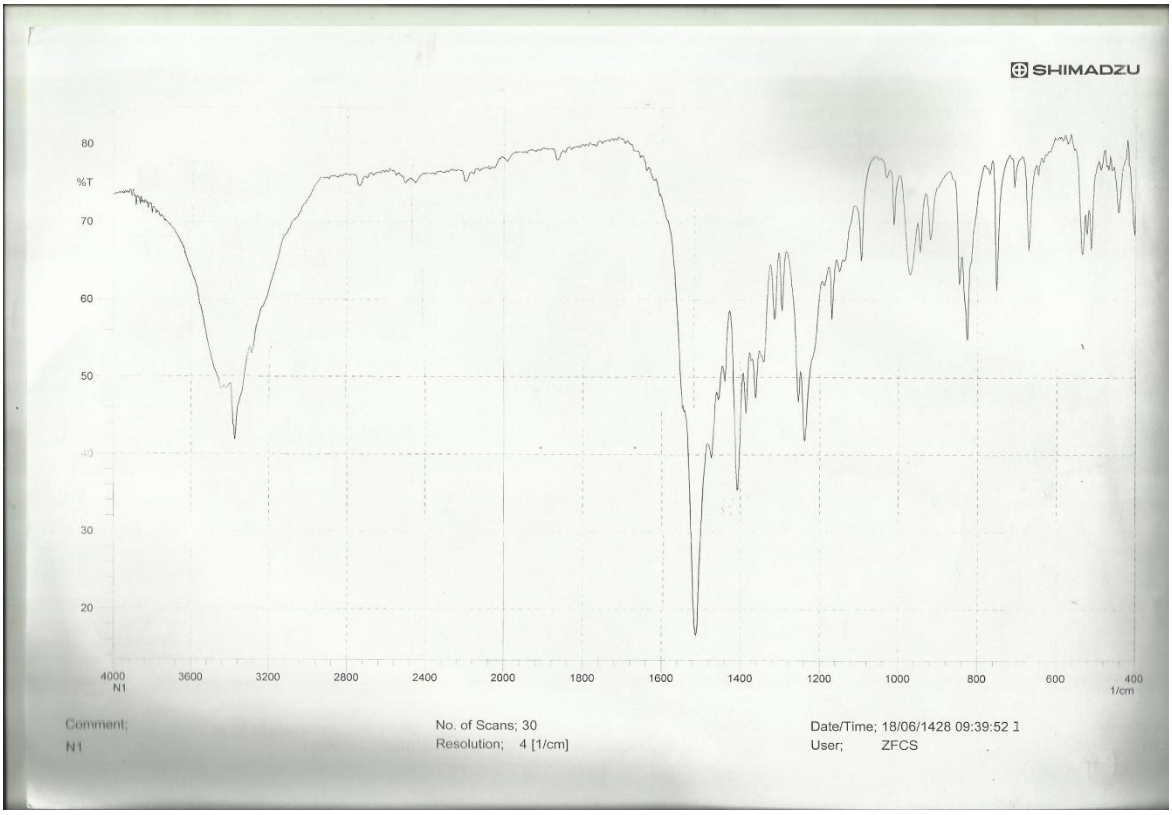


Fig-6:FTIR spectra for PT derivative

Available online at http://qu.edu.iq/journalsc/index.php/JOPS

Al-Qadisiyah Journal Of Pure Science (QJPS)

Vol. xx, No. xx, pp. xx –xx, Month-Year

ISSN 2411-3514 ONLINE

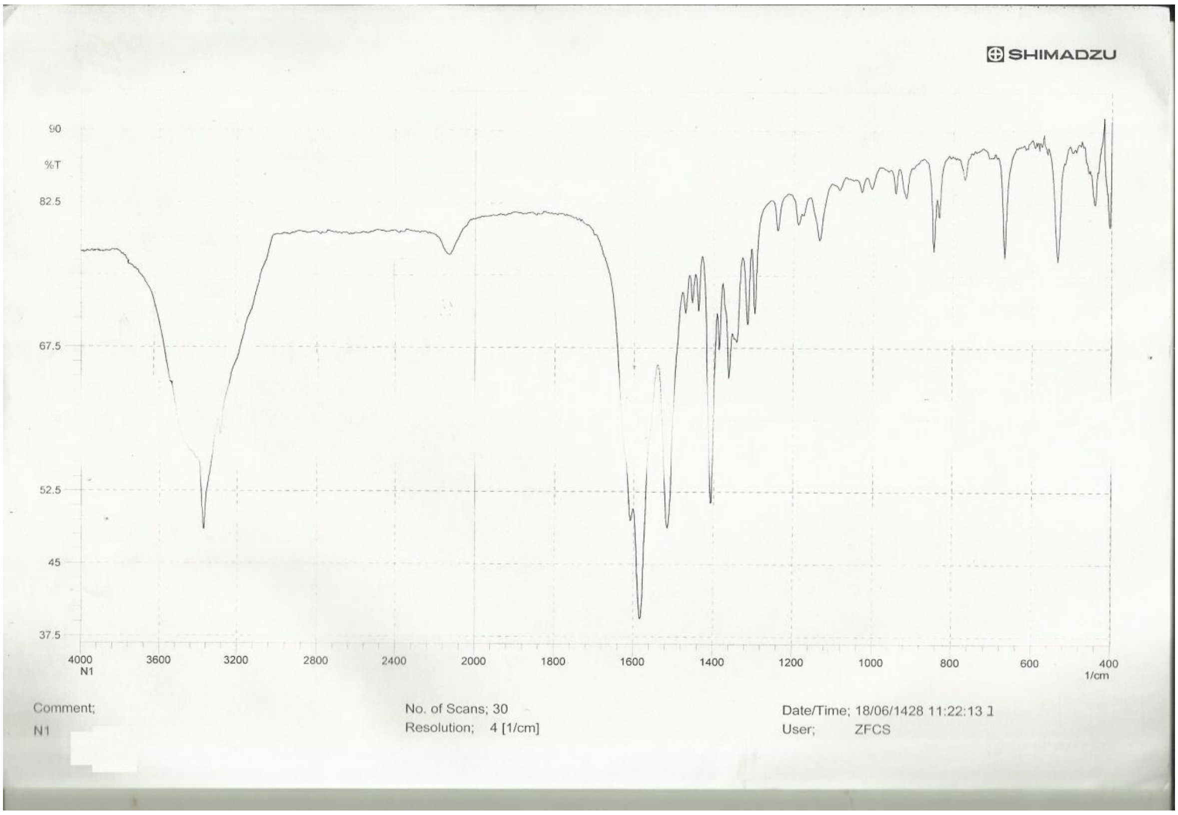
ISSN 1997-2490PRINTED

Comment;
N1

No. of Scans; 30
Resolution; 4 [1/cm]

Date/Time; 10/06/1428 12:39:14
User; ZFCS

Fig-7:FTIR spectra for PCl derivative



Comment;

N1

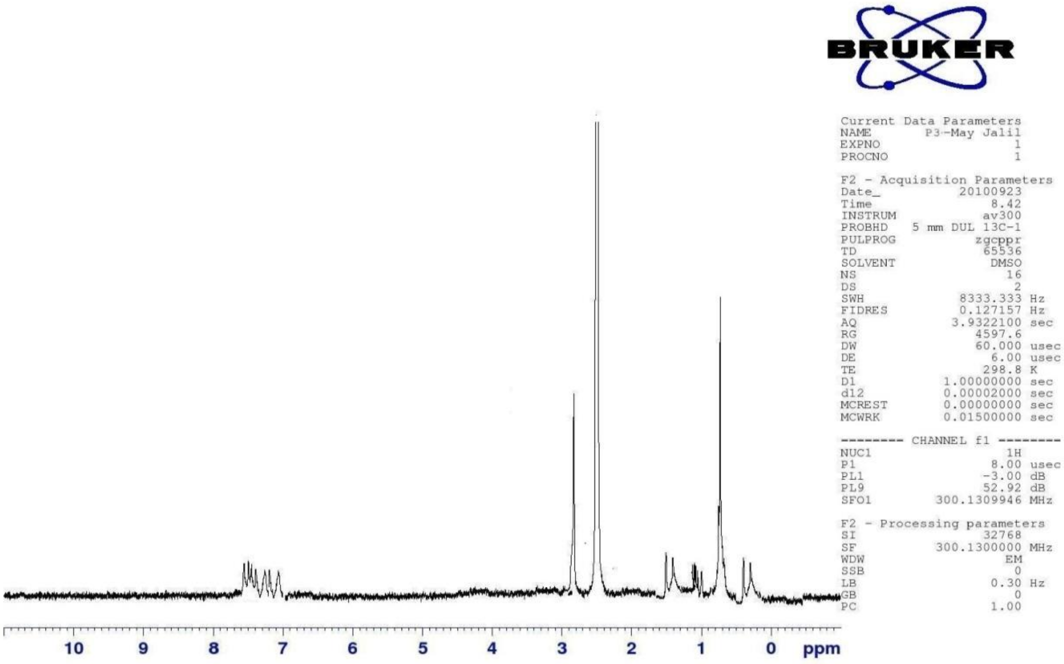
No. of Scans; 30

Resolution; 4 [1/cm]

Date/Time; 18/06/1428 11:22:13 1

User; ZFCS

Fig-8:FTIR spectra for PBr derivative



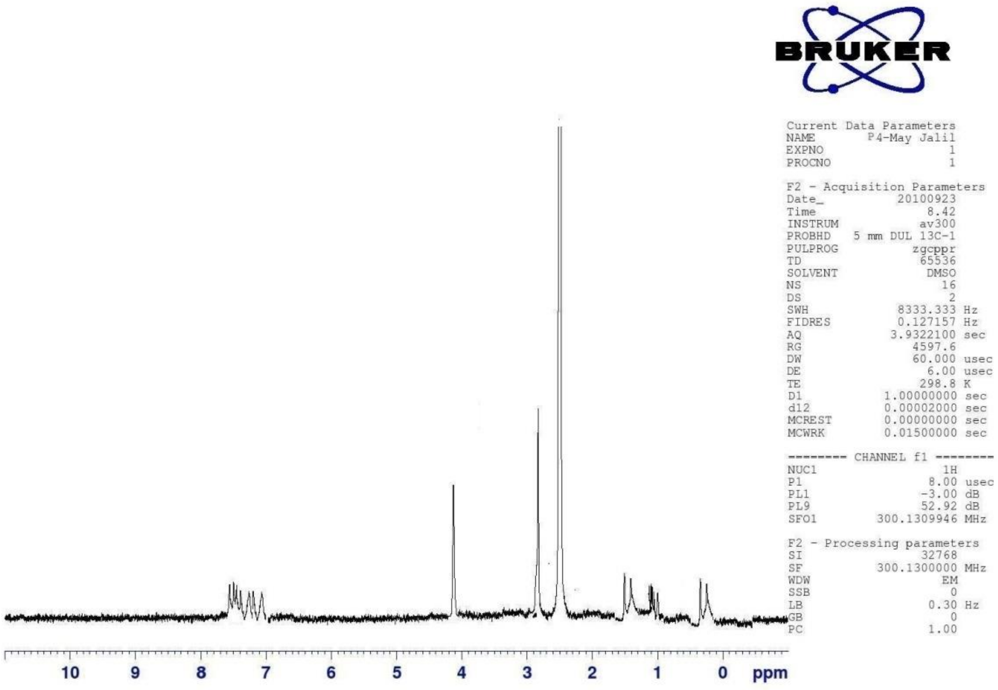
```
Current Data Parameters
NAME        P3-May Jalil
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20100923
Time                8.42
INSTRUM            av300
PROBHD   5 mm DUL 13C-1
PULPROG          zgcppr
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8333.333 Hz
FIDRES          0.127157 Hz
AQ             3.9322100 sec
RG                4597.6
DW                60.000 usec
DE                  6.00 usec
TE                 298.8 K
D1            1.00000000 sec
d12           0.00002000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  8.00 usec
PL1                -3.00 dB
PL9                52.92 dB
SFO1         300.1309946 MHz

F2 - Processing parameters
SI                 32768
SF           300.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

Fig -9 :The H^{1}NMR spectra for P3 derivative



```
Current Data Parameters
NAME          P4-May Jalil
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20100923
Time                  8.42
INSTRUM              av300
PROBHD   5 mm DUL 13C-1
PULPROG             zgcppr
TD                   65536
SOLVENT               DMSO
NS                      16
DS                       2
SWH               8333.333 Hz
FIDRES            0.127157 Hz
AQ               3.9322100 sec
RG                  4597.6
DW                  60.000 usec
DE                    6.00 usec
TE                   298.8 K
D1              1.00000000 sec
d12             0.00002000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                    8.00 usec
PL1                  -3.00 dB
PL9                  52.92 dB
SFO1           300.1309946 MHz

F2 - Processing parameters
SI                   32768
SF             300.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

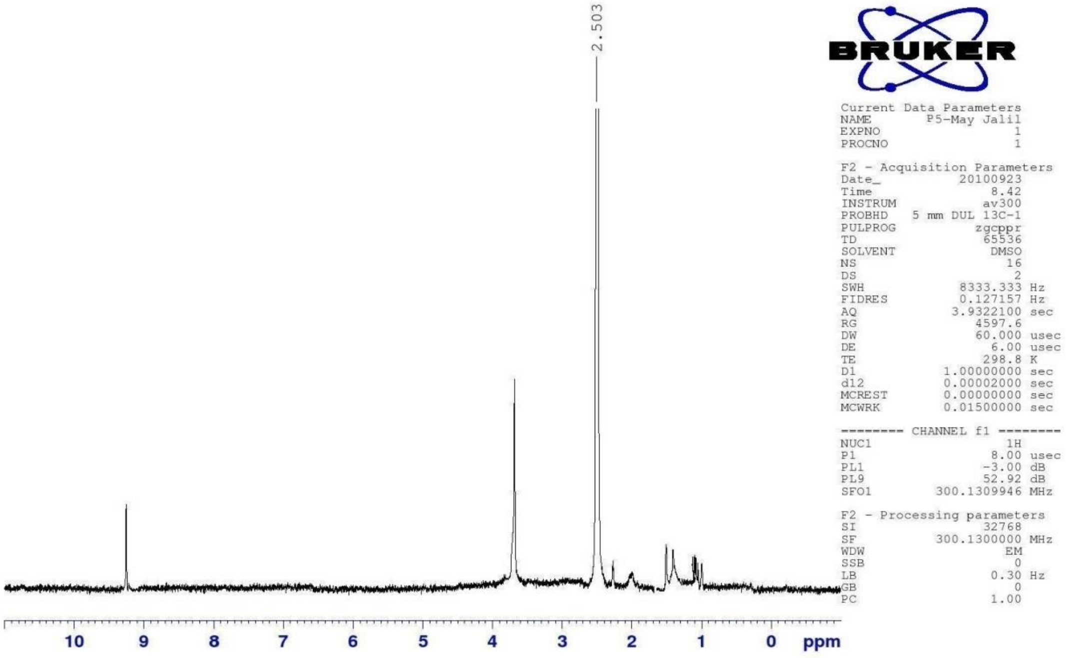
Fig-10 :The H^1NMR spectra for P4 derivative

Available online at http://qu.edu.iq/journalsc/index.php/JOPS

Al-Qadisiyah Journal Of Pure Science
(QJPS)
Vol. xx, No. xx, pp. xx –xx, Month-Year

ISSN 2411-3514 ONLINE

ISSN 1997-2490PRINTED



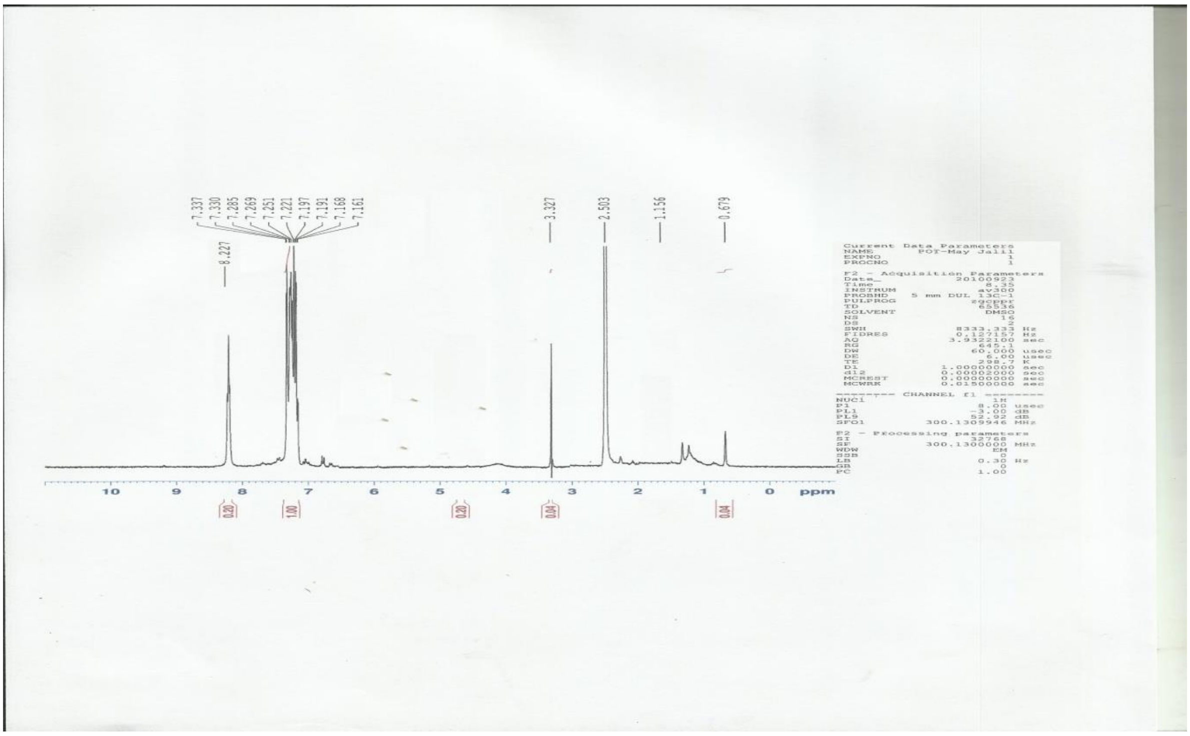
```
Current Data Parameters
NAME          P5-May Jalil
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20100923
Time                  8.42
INSTRUM              av300
PROBHD   5 mm DUL 13C-1
PULPROG             zgcppr
TD                   65536
SOLVENT               DMSO
NS                      16
DS                       2
SWH               8333.333 Hz
FIDRES            0.127157 Hz
AQ               3.9322100 sec
RG                  4597.6
DW                  60.000 usec
DE                    6.00 usec
TE                   298.8 K
D1              1.00000000 sec
d12             0.00002000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                    8.00 usec
PL1                  -3.00 dB
PL9                  52.92 dB
SFO1           300.1309946 MHz

F2 - Processing parameters
SI                   32768
SF             300.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

Fig-11 :The H^1NMR spectra for P5 derivative



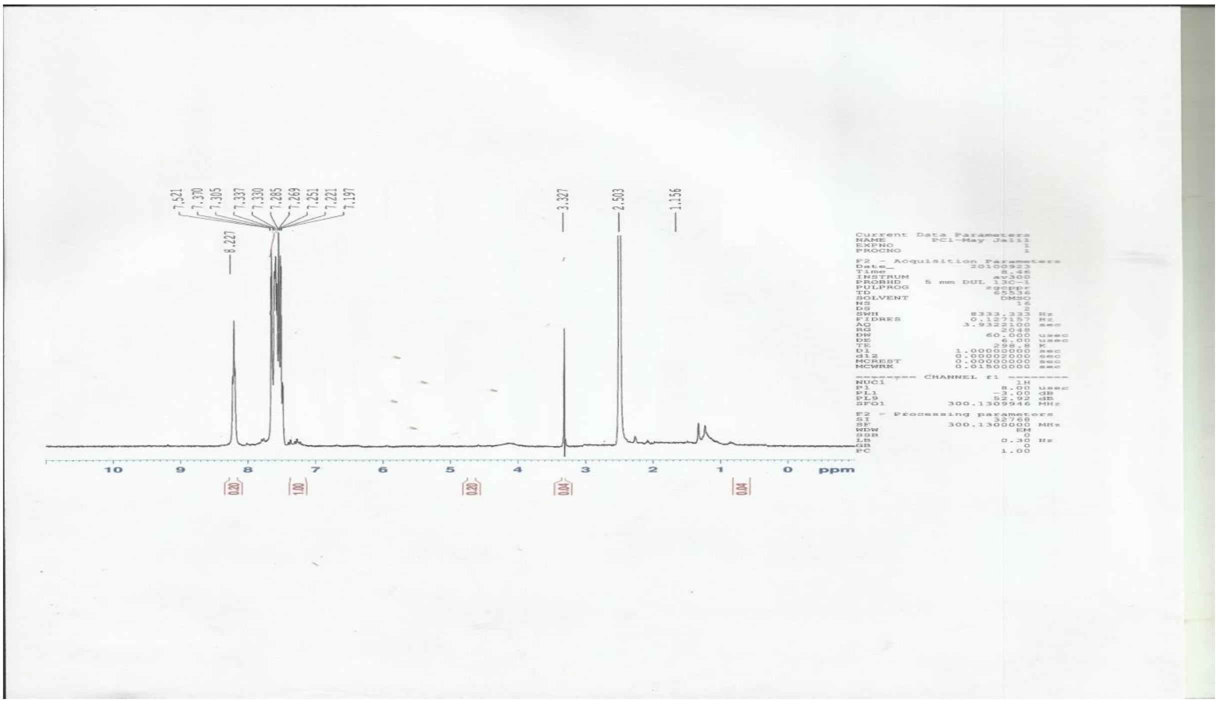
```
Current Data Parameters
NAME          POT-May Jalil
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20100923
Time                   8.35
INSTRUM               av300
PROBHD    5 mm DUL 13C-1
PULPROG              zgcppr
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8333.333 Hz
FIDRES             0.127157 Hz
AQ                3.9322100 sec
RG                    645.1
DW                   60.000 usec
DE                     6.00 usec
TE                    298.7 K
D1               1.00000000 sec
d12              0.00002000 sec
MCREST           0.00000000 sec
MCWRK            0.01500000 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                    8.00 usec
PL1                  -3.00 dB
PL9                  52.92 dB
SFO1           300.1309946 MHz

F2 - Processing parameters
SI                   32768
SF             300.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

Fig-12 :The H^{1}NMR spectra for PT derivative



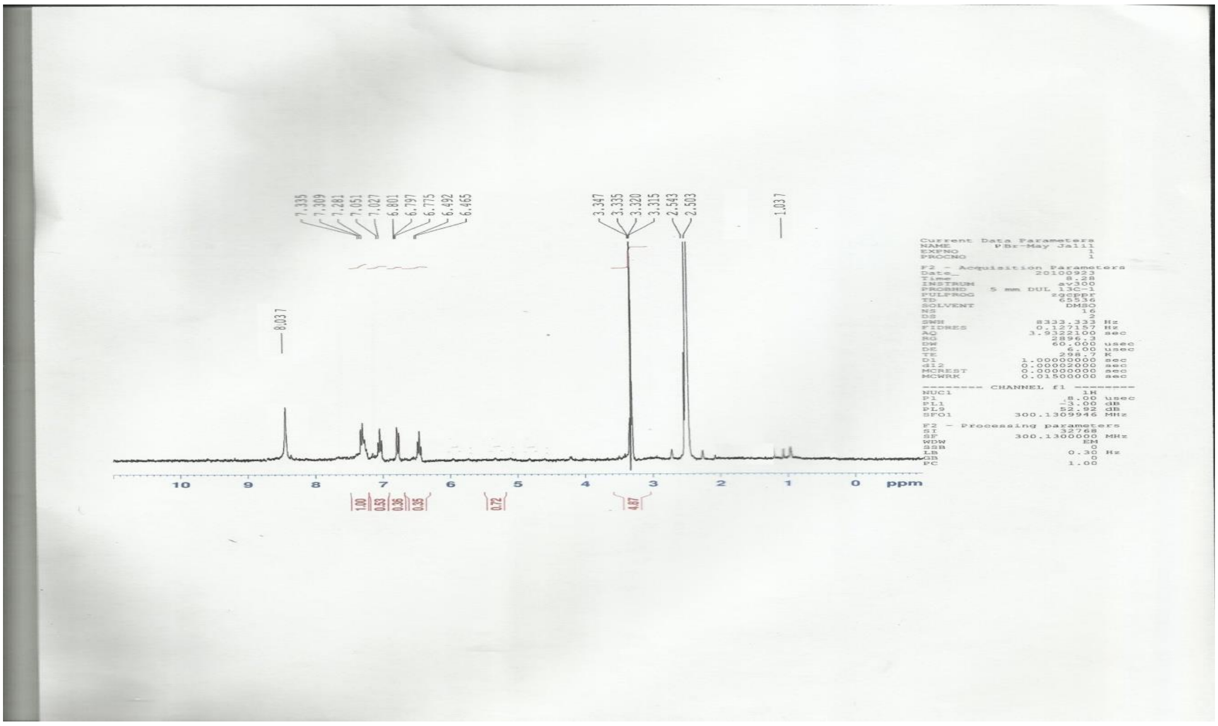
```
Current Data Parameters
NAME          PCl-May Ja111
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20100923
Time                   8.46
INSTRUM               av300
PROBHD     5 mm DUL 13C-1
PULPROG             zgcppr
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8333.333 Hz
FIDRES             0.127157 Hz
AQ                3.9322100 sec
RG                     2048
DW                   60.000 usec
DE                     6.00 usec
TE                    298.8 K
D1               1.00000000 sec
d12              0.00002000 sec
MCREST           0.00000000 sec
MCWRK            0.01500000 sec

======== CHANNEL f1 ========
NUC1                     1H
P1                     8.00 usec
PL1                   -3.00 dB
PL9                   52.92 dB
SFO1            300.1309946 MHz

F2 - Processing parameters
SI                    32768
SF              300.1300000 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Fig-13 :The H^1NMR spectra for PCl derivative



```
Current Data Parameters
NAME          PBr-May Ja111
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20100923
Time                   8.28
INSTRUM               av300
PROBHD     5 mm DUL 13C-1
PULPROG             zgcppr
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8333.333 Hz
FIDRES             0.127157 Hz
AQ                3.9322100 sec
RG                   2896.3
DW                   60.000 usec
DE                     6.00 usec
TE                    298.7 K
D1               1.00000000 sec
d12              0.00002000 sec
MCREST           0.00000000 sec
MCWRK            0.01500000 sec

======== CHANNEL f1 ========
NUC1                     1H
P1                     8.00 usec
PL1                   -3.00 dB
PL9                   52.92 dB
SFO1            300.1309946 MHz

F2 - Processing parameters
SI                    32768
SF              300.1300000 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Fig-14 :The H^1NMR spectra for PBr derivative

References

1-Buttery, R, Turnbaugh, J., and Ling, L. (1988) Contributions of volatiles to rice aroma. J. Agric. Food Chern. 36: 1006-1009.

2- Grimm, C. c, Bergman, C. J., Delgado, J. T., and Bryant, R (2001). Screening for 2-acetyl-l-pyrroline in the headspace of rice using SPMEI GCI MS. J. Agric. Food Chern. 49:245-249

3-Bergman, C., Delgado, J., Bryant, R., Grimm, C; Cadwallder, K., and Webb, B.(2000). A rapid gas chromatographic technique for quantifying 2-acetyl-l-pyrroline and hexanal in rice (Oryza sativa, L.). Cereal Chern. 77:454-458.

4-Buttery, R, Turnbaugh, J., and Ling, L.(1988). Contributions of volatiles to rice aroma. J. Agric. Food Chern. 36: 1006-1009.

5-Ferraris, D., Ko, Y-S., Calvin, D., Chiou, T., Lautar, S., Thomas, B., Wozniak, K., Rojas, C., Kalish, V., and Belyakov, S. (2004). Ketopyrrolidines and ketoazetidines as potent dipeptidyl peptidase.

6-Bergman, C., Delgado, J., Bryant, R., Grimm, C; Cadwallder, K., and Webb, B.(2000). A rapid gas chromatographic technique for quantifying 2-acetyl-l-pyrroline and hexanal in rice (Oryza sativa, L.). Cereal Chern. 77:454-458.

7-Bounphanousay, C; Jaisil, P., Fitzgerald, M., and Hamilton, N. R. S. (2008). Chemical and molecular characterization of fragrance in black glutinous rice from Lao PDR Asian J. Plant Sci. 7:1-7.

8-Buttery, R., Ling, L., and Juliano, B. (1982). 2-Acetyl-l-pyrroline: An important aroma compound in cooked rice. Chern. Ind. 4 Dec.: 958.

9-Johnson, L.F. and Eiroy A. Curl. (1972). Methods for research Ecology of soil-Borne plant pathogens. 426 So, 6th street, Minneapolis, MN 55415:mBurgess publishing Company.

10-Khulbe, R.D.(2001). A Manual of Aquatic Fungi. I Edn., Daya Publishing House, Delhi

11-Laksanalamai, V. and Ilangantileke, S.(1993). Comparison of aroma compound (2-acetyl-1-pyrroline) in leaves from pandan (Pandanus amaryllifolius) and Thai fragrant rice (Khao Dawk Mali-105). Cereal Chemistry.,70 : 381 – 384.

12-Itani, T., Tamaki, M., Hayata, Y, Fushimi, T, and Hashizume, K.(2004). Variation of 2-acetyl-l-pyrroline concentration in aromatic rice grains collected in the same region in Japan and factors affecting its concentration. Plant Prod. Sci. 7: 178-183.

13-Goufo, P., Mei-Yan, D., Wongpomchaii, S., and Xiang-Ru, T. (2010). Factors affecting concentration of the aroma compound 2-acetyl-1-pyrroline in two fragrant rice cultivars grown in South China. Frontiers Agric. China 4: 1-9.

14-T.D.Butters,R.A.Dwek,F.M.Platt,Chem.Rev.2000,100,4683.

15-S.Inouye,T.Tsurouka,T.Ito,T.Niida,Tetrahedron 1968,24,2125.

16-R.Bloch,Chem.Rev 1998,98,11407.

17-R.A.volkmann in comprehensive organic synthesis ,part 1 vol 1 979 p:504.

18-G.B Evans ,R.H.Furneaux, J.Org.Chem 2001,66,5723.

19-P.D.Mehata,synthesis and biological activity studies of some thiazolidinones and azetidinone ,Indian .J.Pharm.Sci.,2006,68 ,101-103.

20-E.S.Canpolat and N.M.Kaya, Studies on mononuclear chelates derived from substituted Schiff base ligand ,Turk .J.Chem 2003,29,409-415.

21-N.Asano,R.J.Nash ,R.J.Molyneaux, G.W.J.Fleet, Tetrahedron :Asymmetry 2000,11,1645.