Synthesis and characterization of some new heterocyclic compounds

Maysoon T.Tawfiq
University of Baghdad
College of Education for Pure Science-Ibn-AlHaitham,

Abstract

This work includes preparing of some new derivatives of pyrimidine ,pyrazolidine, and isoxazolidine from the reaction between tetraethyl 2,2' -(1E,1E')- biphenyl ll-4, 4' -diylbis(diazene-1,2-diyl)dimalonate(1) and ammonia derivatives in dry ethanol to obtain the six membered hetero rings: 5,5'-(1*E*,1*E*') biphenyl-4,4'-diylbis (diazo-1,2-diyl)bis(2-mercaptopyrimidine-4,6-diol)(2) ; 5,5'-(1*E*,1*E*') biphenyl-4,4'-diylbis(diazo-1,2-diyl)dipyrimidine-2,4,6-triol(3);5,5'-(1*E*,1*E*')-biphenyl-4,4'-diylbis (diazo-1,2-diyl)bis(2-aminopyridine-4,6-diol)(4); and five membered hetero ring: 4,4' -(1*E*,1*E*')-biphenyl-4,4'-diylbis(diazene-1,2-diyl)dipyrazolidine-3,5-dione(5);4,4'-(1*E* , 1*E*')-biphenyl-4,4'-diylbis(diazene-1,2-diyl)bis(1-phenylpyrazolidine-3,5-dione)(6); 4,4'-(1*E*,1*E*')-biphenyl-4,4'-diylbis (diazene-1,2-diyl)diisoxazolidine-3,5-dione)(7).

The prepared compounds were characterized by spectral methods FT-IR ,^{1}H-NMR and measurement of some of its physical properties ; and the reaction was followed by TLC.

Key word: Heterocyclic compounds, Pyrimidine, Pyrazolidine, Isoxazolidine, Azo compounds.

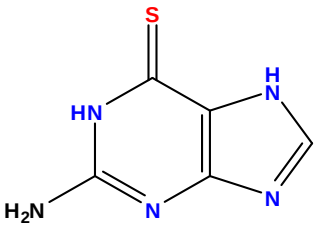
Introduction

Heterocyclic systems are widespread occurrence in nature, particularly in such natural products as nucleic acids, plant alkaloids and chlorophyll[1]. Heterocyclic compounds are considered one of an important type of organic compounds due to their application in drugs and industrial studies. A variety of atoms, such as N, O, S, P, Si and As can be incorporated into the ring structures[2].

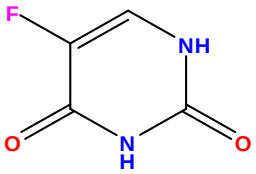
Azo compounds are Considered as starting materials to preparation of heterocyclic compounds[3], they are very important class of chemical compounds receiving attention in scientific research. They are highly colored and have been used as dyes and pigments for a long time [4,5]. Furthermore, they have been studied widely because of their excellent

thermal and optical properties in applications such as optical recording medium[6-9] toner[10,11] ink-jet printing[12,13] and oil-soluble lightfast dyes[14].

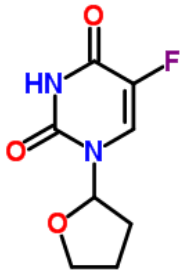
Pyrimidine and pyrazole derivatives are well known for their pharmacological activities. Various drugs containing pyrimidine nucleus were synthesized and used as anticancer agents like 5-Fluorouracil, Tegafur and Thioguanine[15].



thioguanine



5- fluorouracil



tegafur

Pyrazoles and their variously substituted derivatives are important biological agents and a significant amount of research activity has been directed towards this class. In particular, they are used as antitumor [16], antibacterial and antifungal, antiviral, antiparasitic, anti-tubercular and insecticidal agents [17-25]. Some of these compounds have also anti-inflammatory, anti-diabetic, anesthetic and analgesic properties [26-29].

Nitrogen containing heterocycles with an oxygen atom are considered as an important class of compounds in medicinal chemistry because of their diversified biological applications. The exploitation of a simple molecule with different functionalities for the synthesis of heterocycles is a worthwhile contribution in the chemistry of heterocycles[30].

Isoxazoles have been reported to possess diverse biological activities like anti inflammatory [31], antibacterial[32], antifungal[33], antibiotic[34]. anticonvulsant[35], antitubercular[36], anxeolytic[37] properties. In the last decades a number of pyrazole and isoxazole derivatives have been introduced in clinical practice. The therapeutic effectiveness of these agents has been bounded by a number of limiting factors. Due to this, the development of novel, selective, potent and safe agents remains in high

priority in medicinal chemistry research. The structures of the compounds have been established analytically. These structures can help the medicinal chemists to use them as intermediates to design various drug candidates possessing a number of pharmacological activities[36,37].

Experimental

1- Melting point were measured by hot stage **Gallen Kemp** melting point apparatus and were uncorrected.

2- FT.IR spectra were recorded by **SHIMADZU** FT.IR 8300 spectrophotometer in the range (4000-600) cm^{-1} using KBr disk.

3- 1H-NMR spectra were recorded by **BRUKER**-400 MHz operating at 300 MHz with tetra methyl silane as internal stadared in DMSO-d^6 as a solvent at Chemistry Department , AL- Bayt University,Jordan.

4- Thin Lyer Chromatography (TLC) was carried out using Fertigfollen precoated sheets type Polygram silg,and the plates were developed with iodine vapor.

1- Synthesis of : tetraethyl - 2,2' - (1*E*,1*E* ')-biphenyl-4,4'-diylbis (diazene- 1,2-diyl)dimalonate (1).

Benzidine (0.01 mol, 1.84 g) was mixed with(10 mL conc. hydrochloric acid + 10 mL water) , the mixture was stirred and cooled at (0-5)C^0 for (30 min.) . The amine was diazotized by adding solution of sodium nitrite(0.02 mol , 1.38 g) in (20 ml) of water dropwise at (0 – 5)C^0 and stirred for (40 min.) at this temperature.

The diazo obtained was added slowly to a vigorously stirred solution of diethylmalonate (3mL) in ethanol (25 mL) and 10% sodium hydroxide. The reaction mixture was then stirred for (2) hours at (0-5 C^0) and then kept in refrigerator overnight. The resulting product was filtered, washed with water, dried and recrystallized from ethanol to give the titled compound as dark brown solid crystals (m.p 159 – 161C^0, yield 65%).

2- Synthesis of : 5,5' -(1*E*,1*E* ')-biphenyl-4,4' - diylbis(diazene-1,2-diyl)bis(2-mercaptopyrimidine-4,6-diol)(2).

Compound [1] (0.0025mol, 1.315gm.) was dissolved in (15mL) of absolute ethanol. To this mixture a solution of thiourea (0.005mol,0.38gm) in (10mL) absolute ethanol was added dropwise .The reaction mixture was stirred for (30 min.) then refluxed for (12-14 hours) on water bath . The solvent evaporated and the formed light brown crystals was crystallized from appropriate solvents , The end of the reaction was checked by (TLC)., (m.p 125-127 C^0 ,yield 74%).

3- synthesis of : 5,5' -(1*E*,1*E* ')-biphenyl-4,4' - diylbis(diazene-1,2-diyl)dipyrimidine-2,4,6-triol) (3).

This compound was prepared by the same procedure in (2) despite using urea (0.005 mol. ,0.3gm) instead of thiourea to obtain compound [3], (mp 117-120 C^0, yield 57%).

4- synthesis of : 5,5' -(1*E*,1*E* ')-biphenyl-4,4' - diylbis(diazene-1,2-diyl)bis(2-aminopyrimidine-4,6-diol) (4).

This compound was prepared by the same procedure in (2) despite using quanidine hydrochloride (0.005 mol. ,0.475gm) and anhydrous sodium acetate (0.005 mol, 0.41 gm) instead of thiourea to obtain compound [4], (mp 185-187C^0, yield 67%).

5- synthesis of : 4,4' -(1*E*,1*E* ')-biphenyl-4,4 'diylbis(diazene-1,2-diyl)dipyrazolidine-3,5- dione) (5).

Compound [1] (0.0025mol, 1.315gm.) was dissolved in (15mL) of absolute ethanol. To this mixture a solution of hydrazine hydrate (0.005mol, 0.25gm , 0.242mL) in (10mL) absolute ethanol was added dropwise .The reaction mixture was stirred for (30 min.) then refluxed for (14 hours) on water bath . The solvent evaporated and the formed colored crystals was crystallized from appropriate solvents,The end of the reaction was checked by (TLC), m.p 217-219 C^0,yield 61%).

6- synthesis of : 4,4' -(1*E*,1*E* ')-biphenyl-4,4 ' -diylbis(diazene-1,2-diyl)bis(1-phenylpyrazolidine-3,5-dione) (6).

This compound was prepared by the same procedure in (5) despite using phenyl hydrazine (0.005 mol. , 0.54 gm) instead of hydrazine hydrate to obtain compound [6], (mp 291-294 C^0, yield 59%).

7- synthesis of : 4,4' -(1*E*,1*E* ')-biphenyl-4,4 ' -diylbis(diazene-1,2-diyl)diisoxazolidine -3,5 -dione (7).

Compound [1] (0.0025mol, 1.315gm.) was dissolved in (15mL) of absolute ethanol. To this mixture a solution of hydroxylamine hydrochloride (0.005mol, 0.345 gm) and anhydrous sodium acetate (0.005 mol, 0.41gm) in (20mL) absolute ethanol was added dropwise .The reaction mixture was stirred for (30 min.) then refluxed for (14 hours) on water bath . The solvent evaporated and the formed colored crystals was crystallized from appropriate solvents , The end of the reaction was checked by (TLC)., (m.p 219-221 C^0 ,yield 55 %).

Results and Discussion

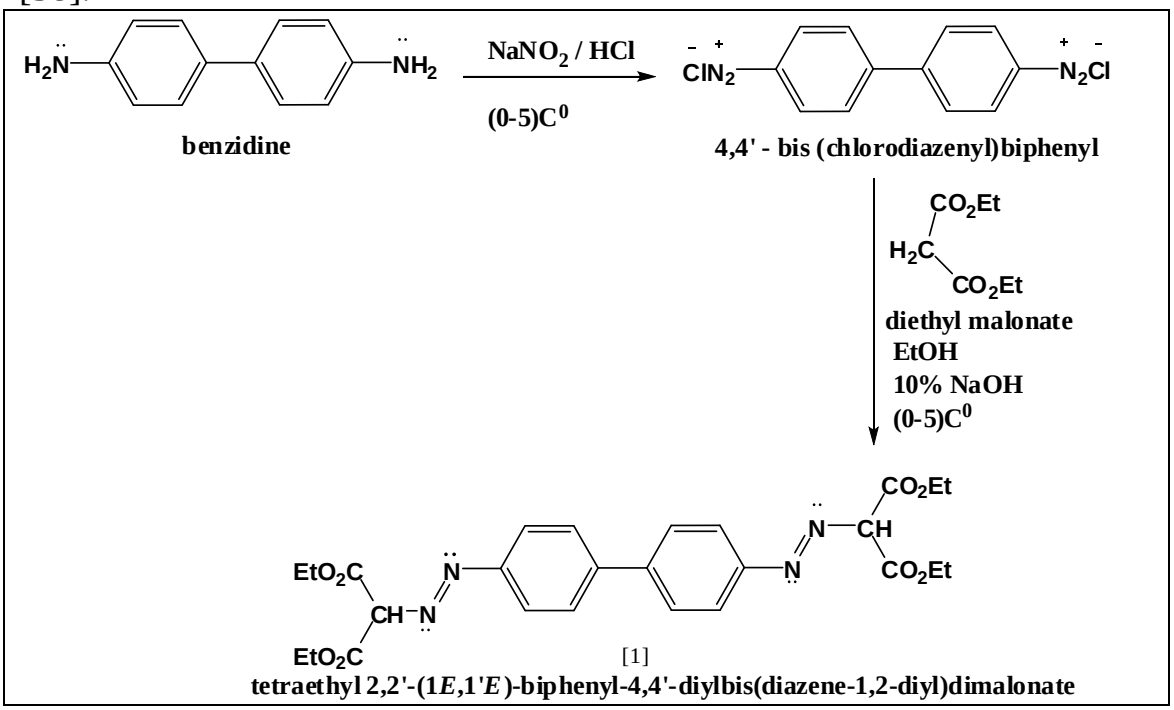
The infrared study of the important methods in identification of absorbed peaks of the resulting functional groups effective and which are found within the structural formula of the compounds prepared.,

The difference in the intensity of the main functional groups of absorption peaks is an indication of the occurrence of interaction.

The first step in scheme (1) involved synthesis of tetraethyl-2,2' -(1*E*,1*E*') -biphenyl-4,4' -diylbis(diazene-1,2-diyl)dimalonate (1) by diazotization of benzidine , then coupling with diethylmalonate in (10%

NaOH + EtOH) at (0-5)C^0 ; The compound was characterized by FT.IR, H^1NMR and physical properties (table-1 and 2).

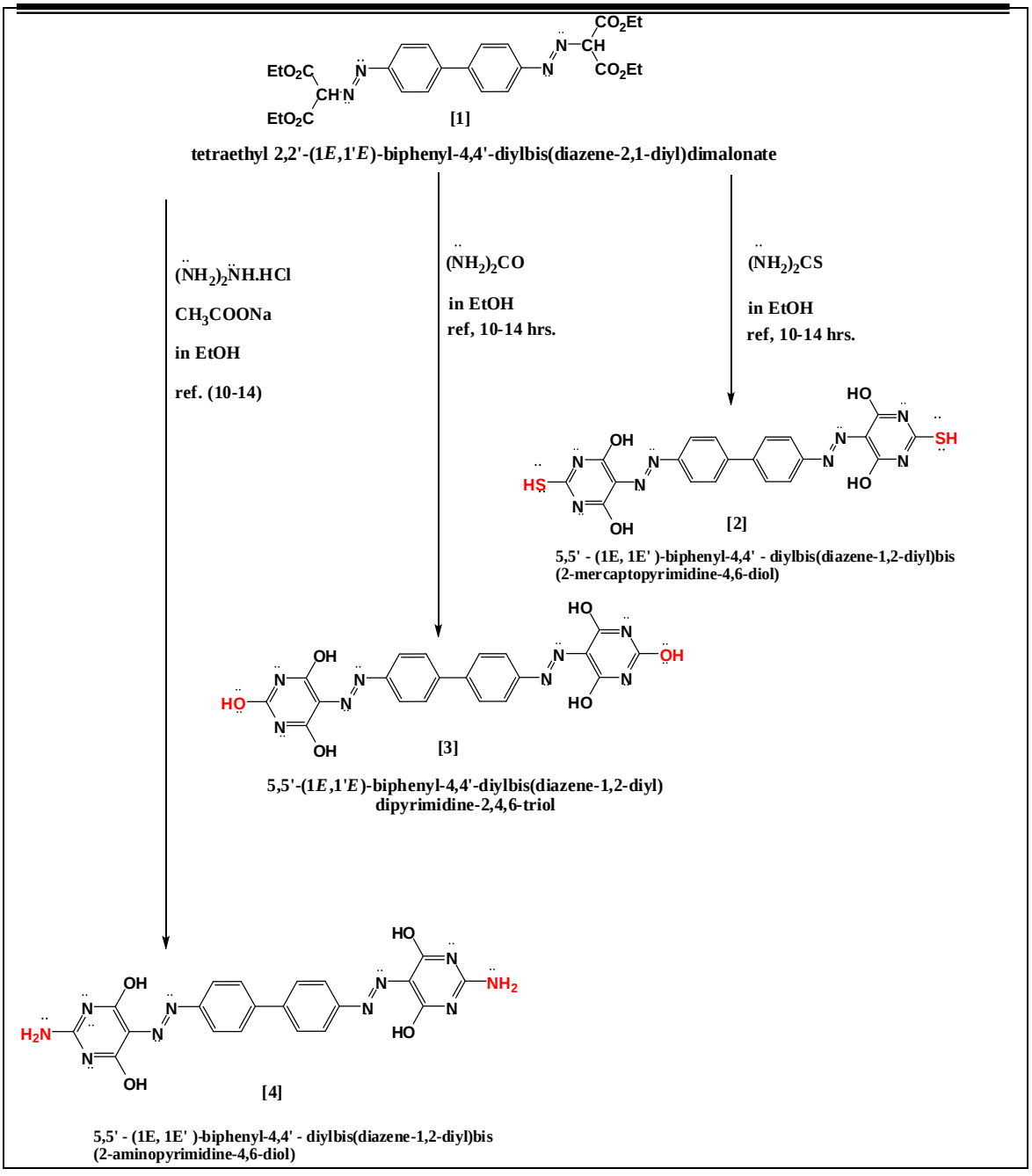
The FT.IR spectrum of compound (1), showed disappearance of stretching band of (NH_2) group at (3400-3600)cm^{-1} and appearance of stretching bands of (C=O ester) group at (1749)cm^{-1} , (C-O ester) group at (1396)cm^{-1} , and (C-H ali) group at (2877-2985)cm^{-1}, (Table- 2), (Fig.1) [38].



Scheme (1)

The H^1-NMR spectrum of compound (1), (fig.8) shows the following characteristic chemical shifts: Protons of (CH_3) groups at **δ**(2.505)ppm , proton of (CH) groups at **δ**(3.39)ppm , protons of (CH_2) groups at **δ**(6.67)ppm , and Protons of aromatic rings appeared at the range **δ**(7.60-9.72)ppm.

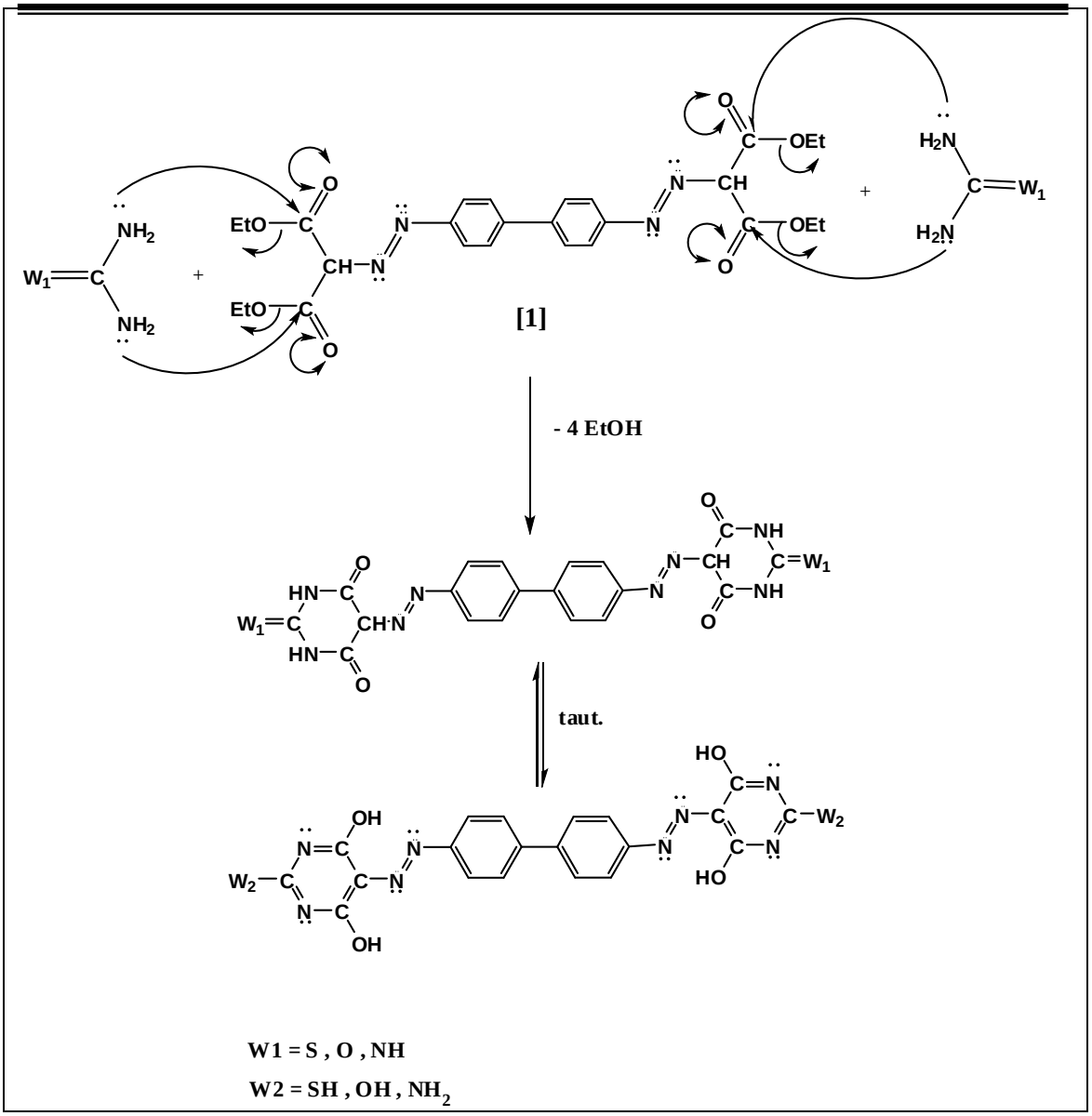
Compounds (2),(3) and (4) were prepared from reaction of compound(1) with thiourea or urea or quinidine hydrochloride in absolute ethanol, as shown in scheme
(2). The reaction was reflexed in water bath for (10-14 hrs.)



Scheme (2)

These compounds suffered tautomerization phenomenon to give aromatic compounds (pyrimidine derivatives).

The suggested mechanism of the reaction is shown in scheme below**:**

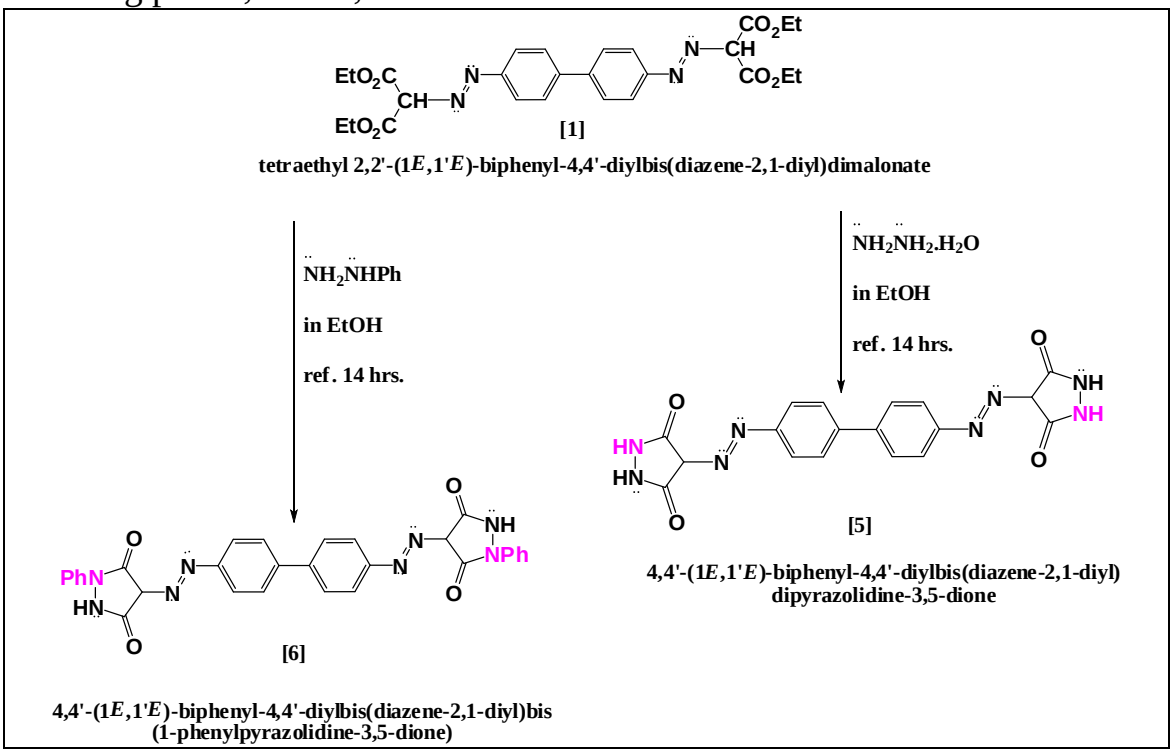


Scheme(3) Mechanism steps for the prepared compounds (2,3, and 4).

The structure of these prepared aromatic compounds were confirmed through the disappearance of absorption bands of (C=O ester) group at (1749)cm^{-1} and (C-H aliphatic) group at (2877-2985) cm^{-1} , and appearance of strong stretching bands of (O-H) group at (3404-3446)cm^{-1}, (C=N endo) group at (1616-1680)cm^{-1}, (S-H) group at (2359)cm^{-1} for compound (2) , and sym. and asym. (NH_2) group at (3242)cm^{-1} for compound (4), (Table -2) ,(Figs. 2,3, and 4); While the H^1NMR spectrum of compound (4),(Fig.9), shows the following characteristic shifts : **δ**(3.301)ppm due to protons of (NH_2) , **δ**(7.43- 8.133)ppm due to protons of aromatic ring, and **δ**(9.11) ppm due to protons of (phenolic OH); Besides the melting points , colors and TLC.

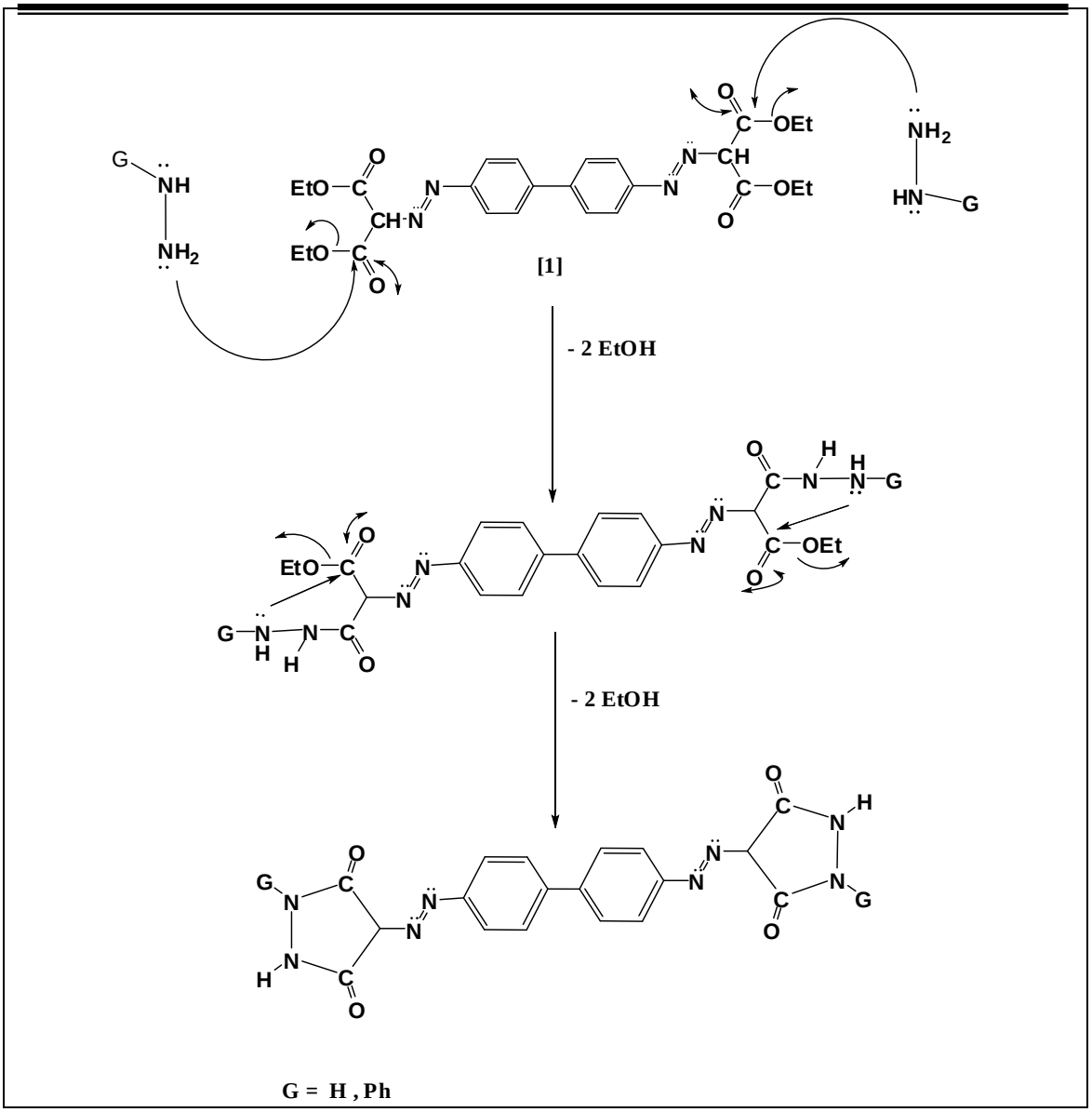
Pyrazolidine derivatives (5), and (6)were prepared by reaction of compound (1) with hydrazine hydrate or *N*-phenylhydrazine in absolute ethanol, as shown in scheme(4). The reaction was reflexed in water bath for (14 hrs.).

These structures were confirm through FT.IR spectra ,H^1NMR spectrum, melting points, colors, and TLC.



Scheme (4)

The suggested mechanism of the reaction is shown in scheme below**:**

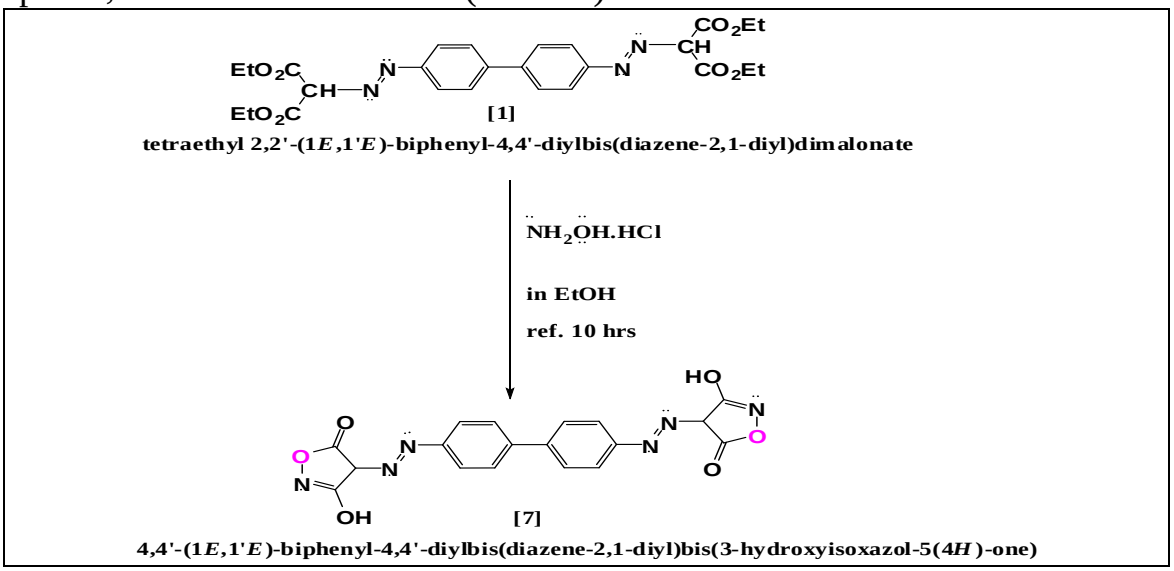


Scheme(5) Mechanism steps for the prepared compounds (5 and 6)

The FT.IR spectrum of compound (5),showed disappearance of stretching band at (1749)cm^{-1} due to (C=O ester) group , and appearance of stretching bands of (C=O ketone) group at (1638)cm^{-1}, and (N-H) group at (3446)cm^{-1} ,(Table-2),(Figs.5and6) [38].

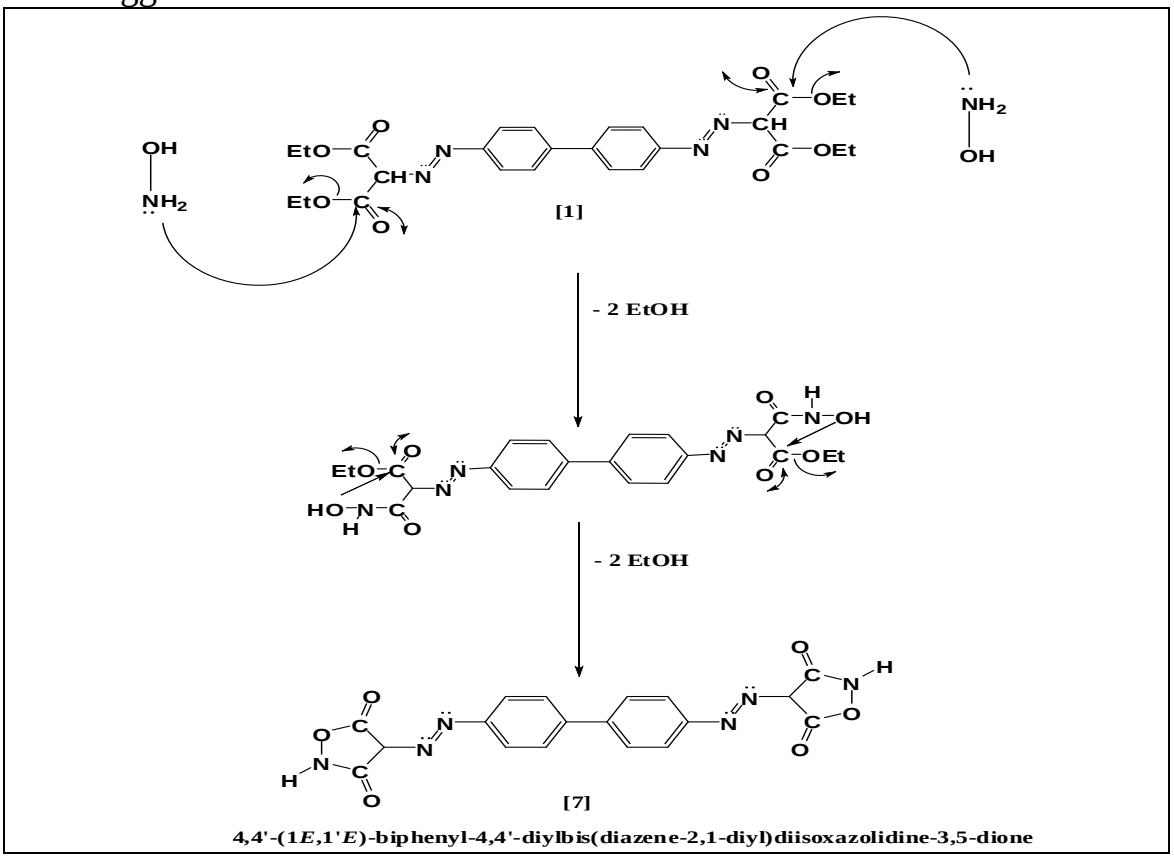
The H^1NMR spectrum of compound (5) (Fig.10), shows the following characteristic shifts**:** **δ**(3.351)ppm due to protons of (CH) , **δ**(6.81- 7.78)ppm due to protons of aromatic rings, and **δ**(7.89)ppm due to protons of (NH).

Isoxazolidine derivative (7) was prepared by reaction of compound (1) with hydroxylamine hydrochloride in absolute ethanol as shown in scheme (6). The reaction was reflexed in water bath for (10 hrs.) . The product was characterized by FT.IR spectroscopy, H^1NMR, and melting point , TLC were determined (Table-1).



Scheme (6)

The suggested mechanism of the reaction is shown in scheme below**:**



Scheme(7) Mechanism steps for the prepared compounds (5 and 6)

The FT.IR spectrum of compound (7) showed appearance of (C=O ketone) group at (1710)cm^{-1} , (C=N endo) at (1554)cm^{-1} ; the absorption band at (3456)cm^{-1} refere to (N-H) group in isoxazolidine ring, (Table-2) (Fig.7) [38].

The H^1NMR spectrum of compound (7) (Fig.11), shows the following characteristic shifts**: δ(** 3.33)ppm due to protons of (CH) , **δ(**7.45- 8.14)ppm due to protons of aromatic rings, and **δ**(8.16)ppm due to protons of (NH).

References

1- R. O. C. Norman; (1974), " Principles of Organic Synthesis ", John Wiley & Sons, Inc. New York, p.313 .
2- H. L. Yalc and K. Losee.;(1966), J. Med. Chem., 9, 478 .
3- Dyes Pigments;(2006), 71 (2) , pp. 90–96
4- J. Koh and A.J. Greaves,;(2001), Dyes Pigments 50, 117-126 .
5- N. Sekar, Colourage; (1999), 46, 63-65 .
6- H.E. Katz, K.D. Singer, J.E. Sohn, C.W. Dirk, L.A. King and H.M. Gordon,;(1987), J. Am. Chem. Soc. 109 (21), 6561-6563 .
7- T. Abe, S. Mano, Y. Yamada and A. Tomotake; (1999), J. Imag. Sci. Tech. 43, 339-344 .
8- T. Chino, M. Yamada and B. KIRKAN, R. GUP; (2002), "Synthesis of New Azo Dyes and Copper(II)., 16(1).
9- S. Wang, S. Shen and H. Xu; (2000), "Dyes Pigments" , 44, pp.195-198 .
10- K. Maho, T. Shintaro, K. Yutaka, W. Kazuo, N. Toshiyuki and T. Mosahiko, Jpn.; (2003), J.Appl.Phys. 42, pp.1068- 1075 .
11- D.W. Rangnekar, V.R. Kanetkar, J.V. Malanker and G.S. Shankarling; (1999), Indian J. Fiber Text. Res. 24, pp. 142-144 .
12- G. Hallas and J.H. Choi; (1999), "Dyes Pigments" , 40, pp.119-129 .
13- P. Gregory, D.R. Waring and G. Hallos; (1990), "The Chemistry and Application of Dyes", Plenum Press, London pp. 18-20..
14- S.S. Kandil; (1998), "Trans. Met. Chem." , 23, pp.461-465 .
15- Jain K. S ,Chitre T. S, Miniyar P. B , Kathiravan M. K, Bendre V. S, Veer V. S, Shahane S. R and Shishoo C.J.; (2006), "Biological and medicinal significance of pyrimidines", Curr. Sc i ; 90; pp. 793-803.
16- Taylor, E.C.; Patel, H.; and Kumar, H.; (1992), "Synthesis of pyrazolo 3,4-dpyrimidine analogues of the potent agent N-4-2-2-amino-4-3H-oxo-7H-pyrrolo2,3-dpyrimidin-5-yl ethylbenzoyl-L-glutamic acid" , Tetrahedron , 48, pp.8089–8100.
17- Abdel-Rahman, A.A.-H.; Abdel-Megied, A.E.-S.; Hawata, M.A.M.; Kasem, E.R.; and Shabaan, M.T.; (2007), "Synthesis and antimicrobial of some chalcones and their derived pyrazoles, pyrazolines,isoxzolines and 5,6-dihydropyrimid ine-2-(1H)-thiones' , Monatsh. Chem. , 138, pp.889–897.
18- Sharshira, E.M.; and Hamada, N.M.; (2011) , "Synthesis and in vitro antimicrobial activity of some pyrazolyl-1-carboxamide derivatives" ,Molecules . 16, pp.7736–7745.

19- Rashad, A.E.; Shamroukh, A.H.; Hegab, M.I.; and Awad, H.M. ;(2005), "Synthesis of some biologically active pyrazoles and C-nucleosides" , . Acta Chim. Slov. , 52, 429–434.
20- Rashad, A.E.; Hegab, M.I.; Abdel-Megeid, R.E.; Micky, J.A.; Abdel-Megeid, and F.M.E.; (2008), "Synthesis and antiviral evaluation of some new pyrazole and fused pyrazolo pyrimidine derivatives" , Bioorg. Med. Chem, 16, pp.7102–7106.
21- Bhat, B.A.; Dhar, K.L.; Saxena, A.K.; and Shanmugavel, M. ; (2005), "Synthesis and biological evaluation of chalcones and their derived pyrazoles as potential cytotoxic agent" , . Bioorg. Med. Chem., 15, pp.3177–3180.
22- Michael, L.E.; David, M.S.;and Prasad, S.S.; (1990), "Chalcones: A new class of antimitotic agents" ,. J. Med. Chem. 33, pp.1948–1954.
23- Kalirajan, R.; Sivakumar, S.U.; Jubie, S.; Gowramma, B.; and Suresh, B.; (2009), "Synthesis and biological evaluation of some heterocyclic derivatives of chalcones" , . Int. J. ChemTech Res. ,1,pp. 27–34.
24- Holla, B.S.; Akberali, P.M.; and Sivanada, M.K.; (2000), "Studies on arylfuran derivatives: Part X. Synthesis and antibacterial properties of arylfuryl-Δ2-pyrazolines." , Farmaco, 55, pp.256–263.
25- Maggio, B.; Daidone, G.; Raffa, D.; Plescia, S.; Mantione, L.; Cutuli, V.M.C.; Mangano, N.G.;and Caruso, A.; (2001), "Synthesis and pharmacological study of ethyl 1-methyl-5-(substituted-3,4-dihydro-4-oxoquinazolin-3-yl)-1H-pyrazole-4-acetates" , . Eur. J. Med. Chem. 36, pp.737–742.
26- Vibhute, Y.B.; and Basser, M.A.; (2003), "Synthesis and activities of a new series of chalcones as antibacterial agents" ,. Ind. J. Chem. , 42B, pp.202–205.
27- Clinton, R.O.; Manson, A.J.; Stonner, F.W.; Beyler, A.L.; Potts, G.O.;and Arnold, A.; (1959), 'Steroidal [3,2-c]pyrazoles" , . J. Am. Chem. Soc. 1959, 81, pp.1513–1514.; Molecules (2012), 17, p. 4970
28- Kalirajan, R.; Palanivelu, M.; Rajamanickam, V.; Vinothapooshan, G.; and Andarajagopal, K. (2997), "Synthesis and biological evaluation of some heterocyclic derivatives chalcones" , . Int. J. Chem. Sci. , 5, pp.73–80.
29- Urmila, G.; Vineeta, S.; Vineeta, K.;and Sanjana, C.; (2005), "Synthesis and antifungal activity of new fluorine containing 4-(substituted phenylazo) pyrazoles and isoxazoles" ,. Indian J. Heterocycl. Chem. 14, pp.265–266.
30- Ngaini Z, Siti M Haris-Fadzillah, Hasnain Hussain and Kamarulzamon Kamoruddin,(2009), World J Chem., , 4(1), pp.09-14.
31- Hans P. and Walter P, (1972), US Patent, , 3668215.,
Dunstan WR and Dymond TS.;(1955), "The action of alkalis on the nitro compounds of the paraffin series Formation of isoxazoles." , (1991), J Chem Soc;59 p.410-433.
32- Hoffer M, US Patent, (1955) , 2721200.
33- Sorithiya S D, Patel V B and Parikh A R,(1997), Indian J Chem., , 36B, p.822.
34- Doyle F P, Betchworth G and Charles J H,(1962) , US Patent, 2996501.
35- Uno H, Kurokawa M, Masuda Y and Nishimura H, ;(1979) , J Med Chem., ,,22,pp.180- 183.
36- Haripara K, Patel S, Joshi A and Paresh H,; (2004), Indian J Heterocycl Chem., ,13, p.221.
37- Wagner E, Becam L and Nowakowska E,;(2004), Bioorg Med Chem., , 12, pp.265-272.
38- R.M.Silverstein and G.C.Bassler,; (1981), " spectrophotometaric identification of organic compounds " , 4th Edition, ,,John and Sons, New York.

Table (1): physical properties of the prepared compounds.

Comp. no.	Molecular formula	Molecular Weight (gm/mol.)	Yield %	M.P. C^0	Color
1	$C_{26}H_{30}N_4O_8$	526	65	159-161	Dark brown
2	$C_{20}H_{14}N_8O_4S_2$	494	74	125-127	Light brown
3	$C_{20}H_{14}N_8O_6$	462	57	117-120	Light brown
4	$C_{20}H_{16}N_{10}O_4$	460	67	185-187	brown
5	$C_{18}H_{14}N_8O_4$	40	61	217-219	radish brown
6	$C_{30}H_{22}N_8O_4$	558	59	291-294	radish brown
7	$C_{18}H_{12}N_6O_6$	408	55	219-221	brown

Comp.	CH aro.	CH ali.	OH	NH_2	SH	C=O ester	C-O ester	C=O ketone	C=C aro.	N=N trans azo	C=N	N-H
[1]	3030	2985, 2937, 2877	-	-	-	1749	1396	-	1473-1448	1681-1602	-	-
[2]	3057	-	3414	-	2359	-	-	-	1483-1448	1647	1674	-
[3]	3032	-	3446	-	-	-	-	-	1485-1442	1641	1680	-
[4]	3145	-	3404	3242	-	-	-	-	1489-1356	1600-1575	1616	-
[5]	3059	2954	-	-	-	-	-	1638	1467	1600	-	3446 In pyrazolidine
[6]	3059	2931	-	-	-	-	-	1675	1452	1602	-	3448 In pyrazolidine
[7]	3061	2939	-	-	-	-	-	1710	1465	1600	-	3456 In isoxazolidine

Table (2): FT.IR spectral data of the prepared compounds.

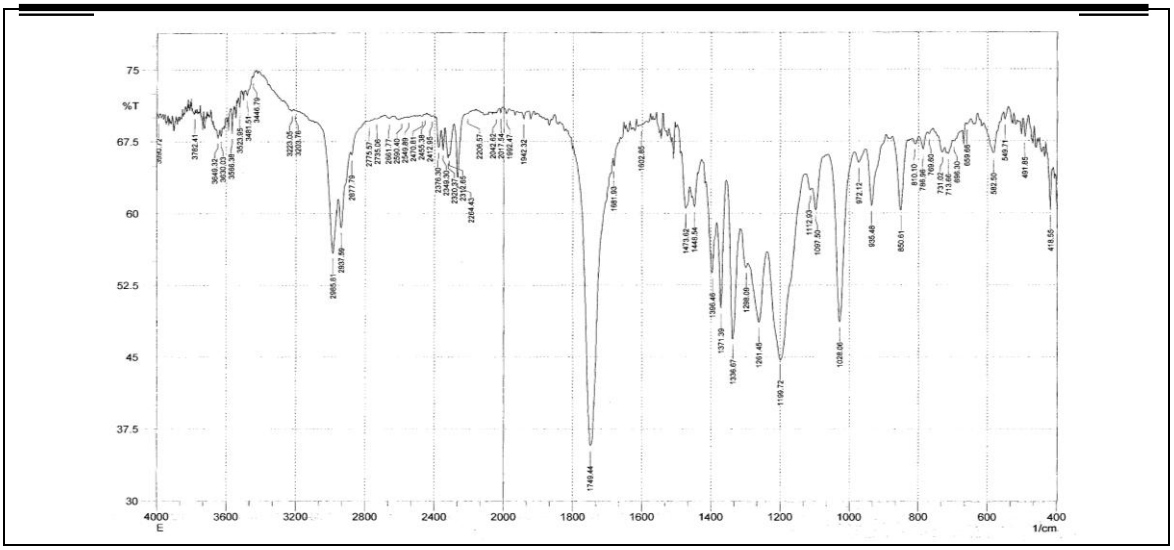


Fig.(1): FT.IR spectrum of compound (1).

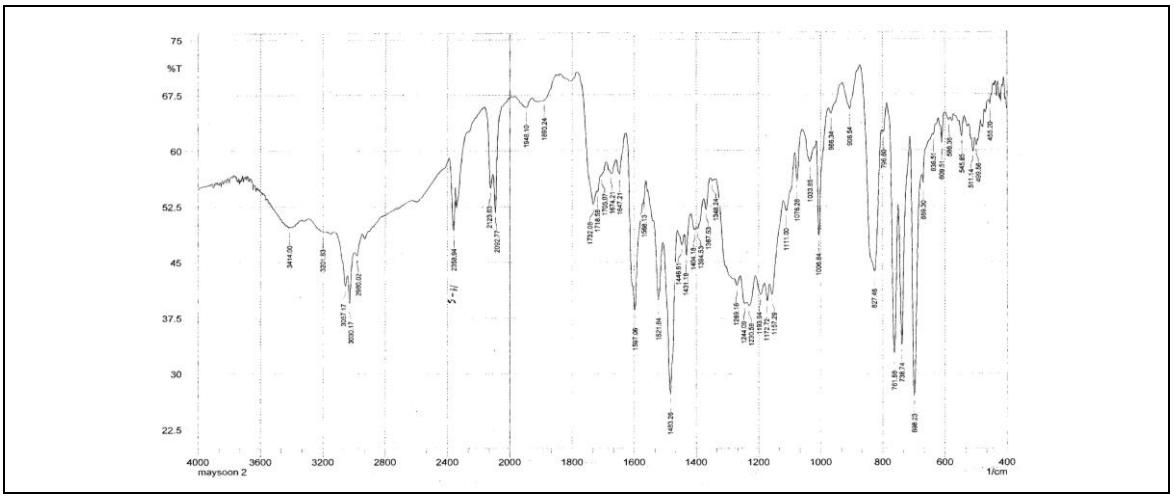


Fig.(2): FT.IR spectrum of compound (2).

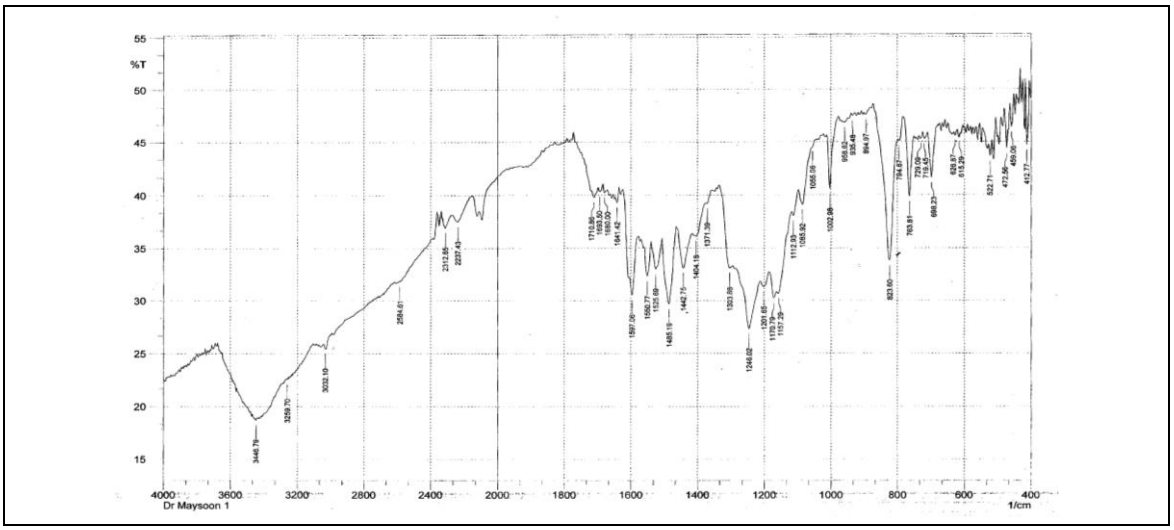


Fig.(3): FT.IR spectrum of compound (3).

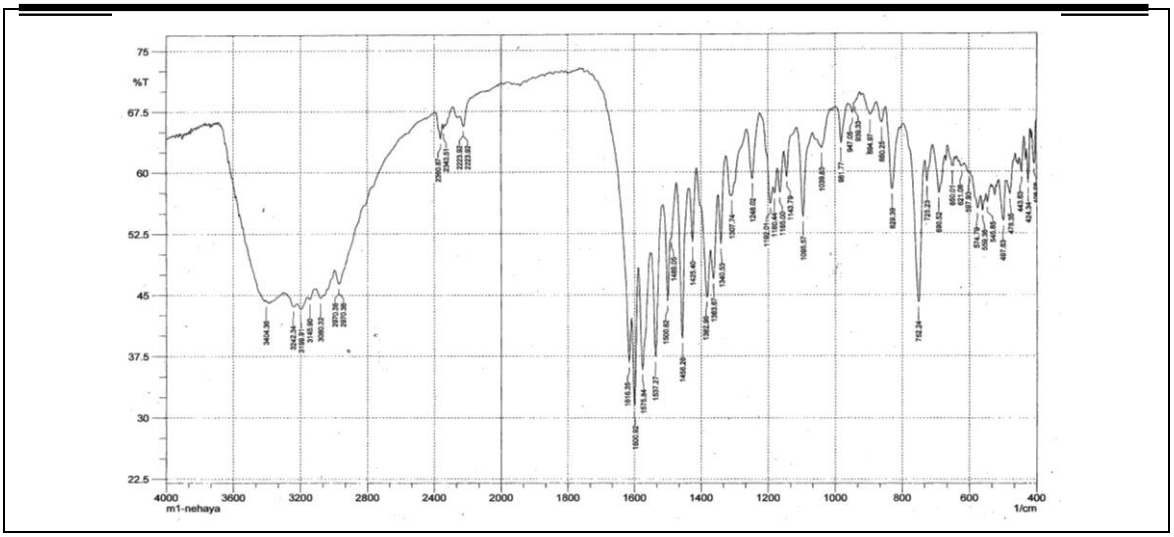


Fig.(4): FT.IR spectrum of compound (4).

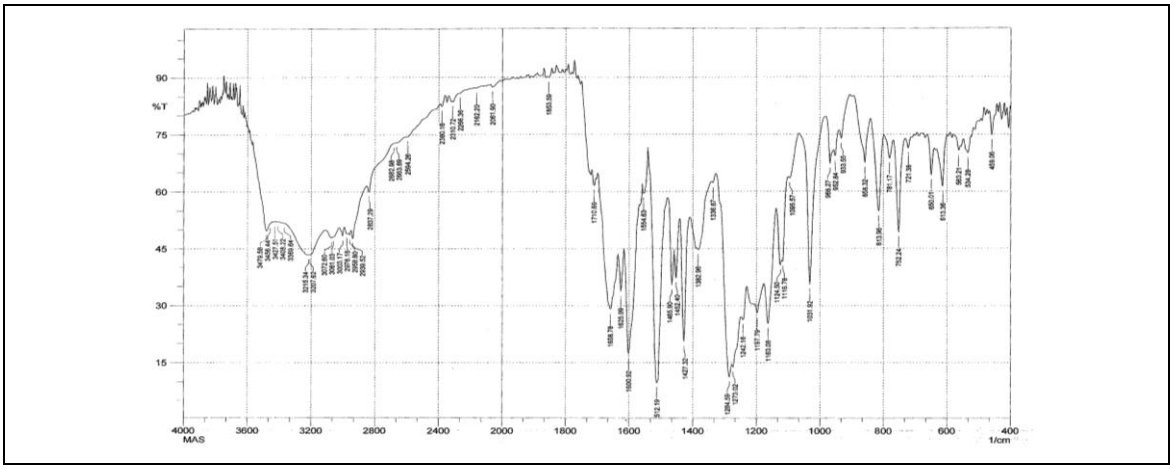


Fig.(5): FT.IR spectrum of compound (5).

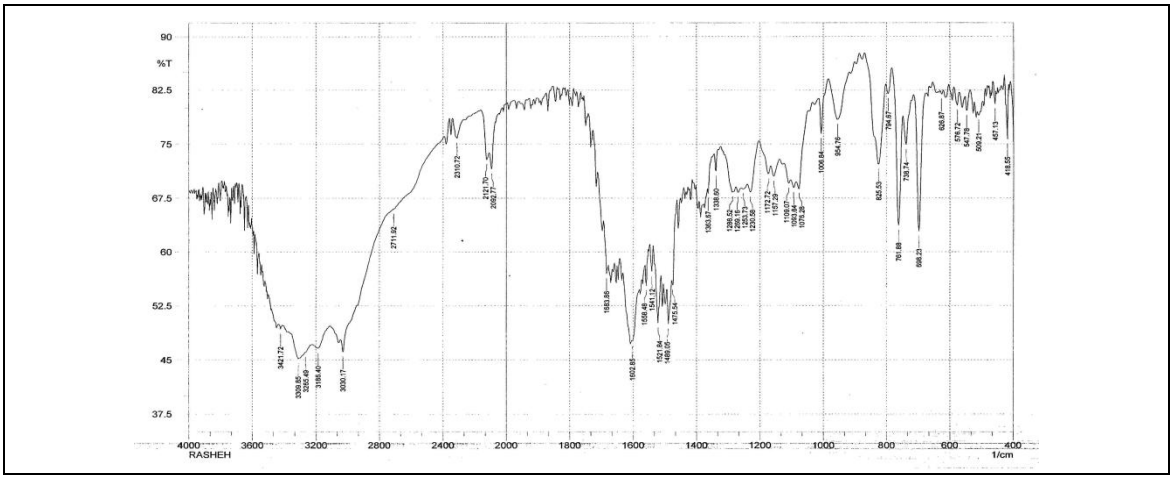


Fig.(6): FT.IR spectrum of compound (6).

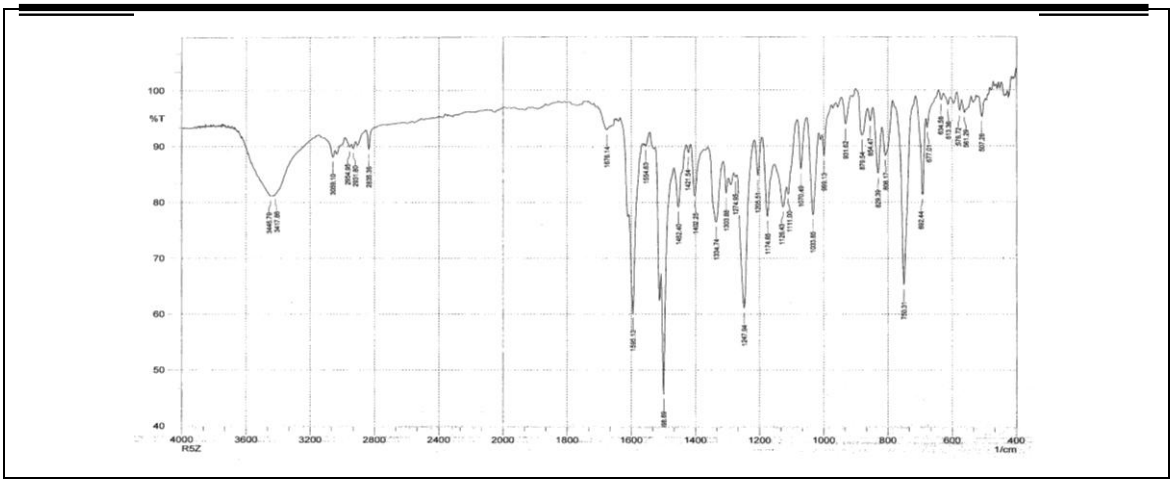


Fig.(7): FT.IR spectrum of compound (7).

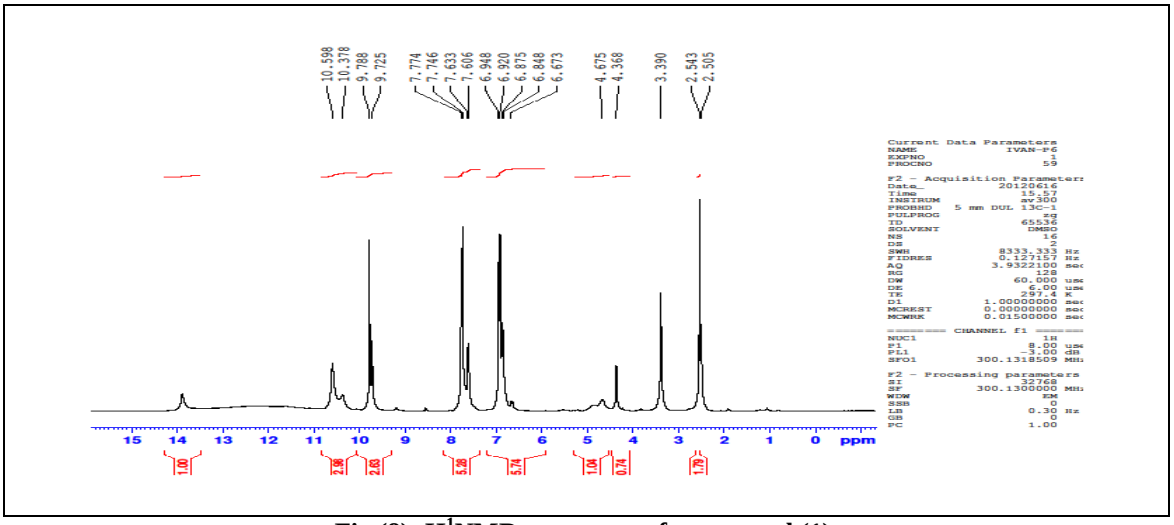


Fig.(8): H^{1}NMR spectrum of compound (1).

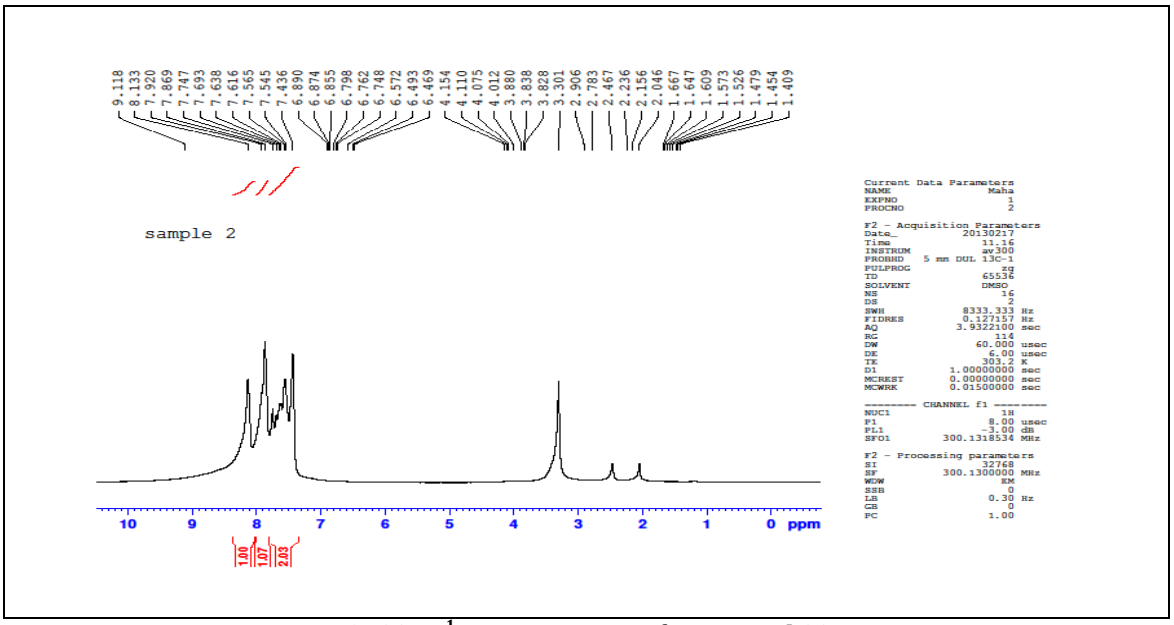


Fig.(9): H^{1}NMR spectrum of compound (4).

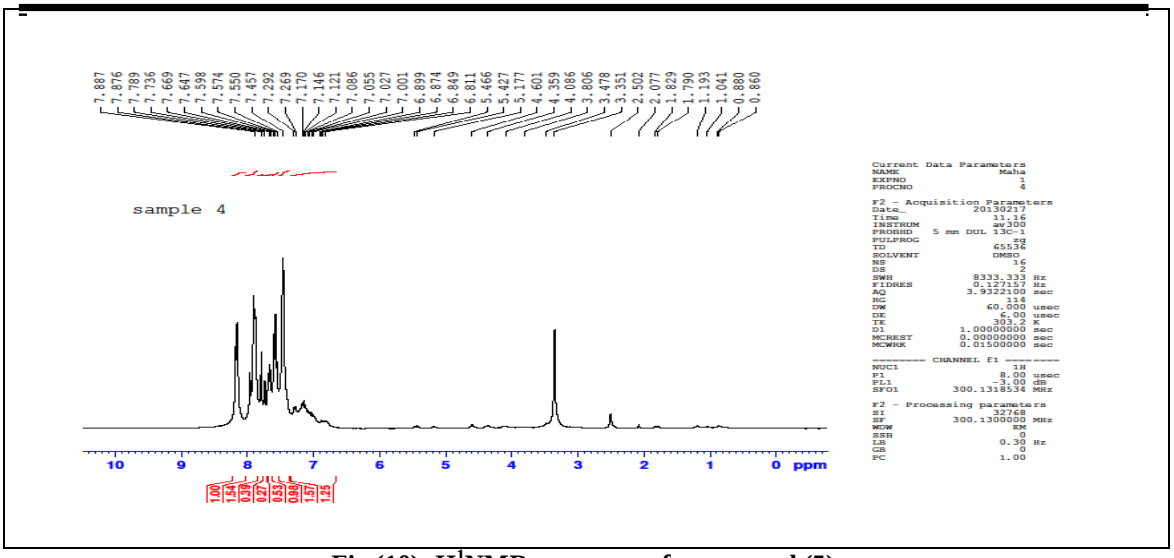


Fig.(10): H[1]NMR spectrum of compound (5).

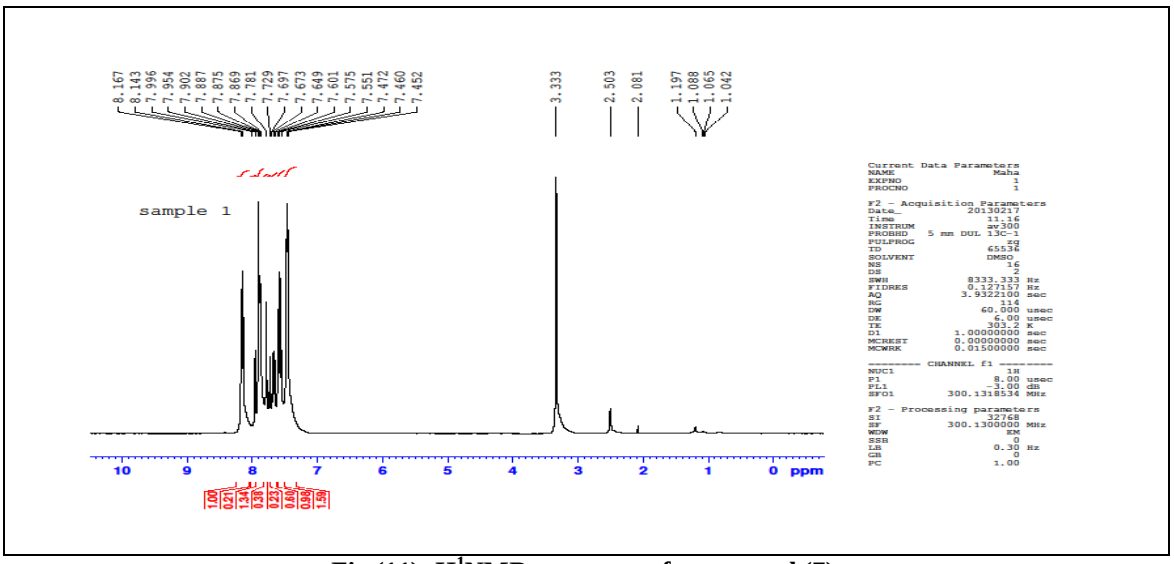
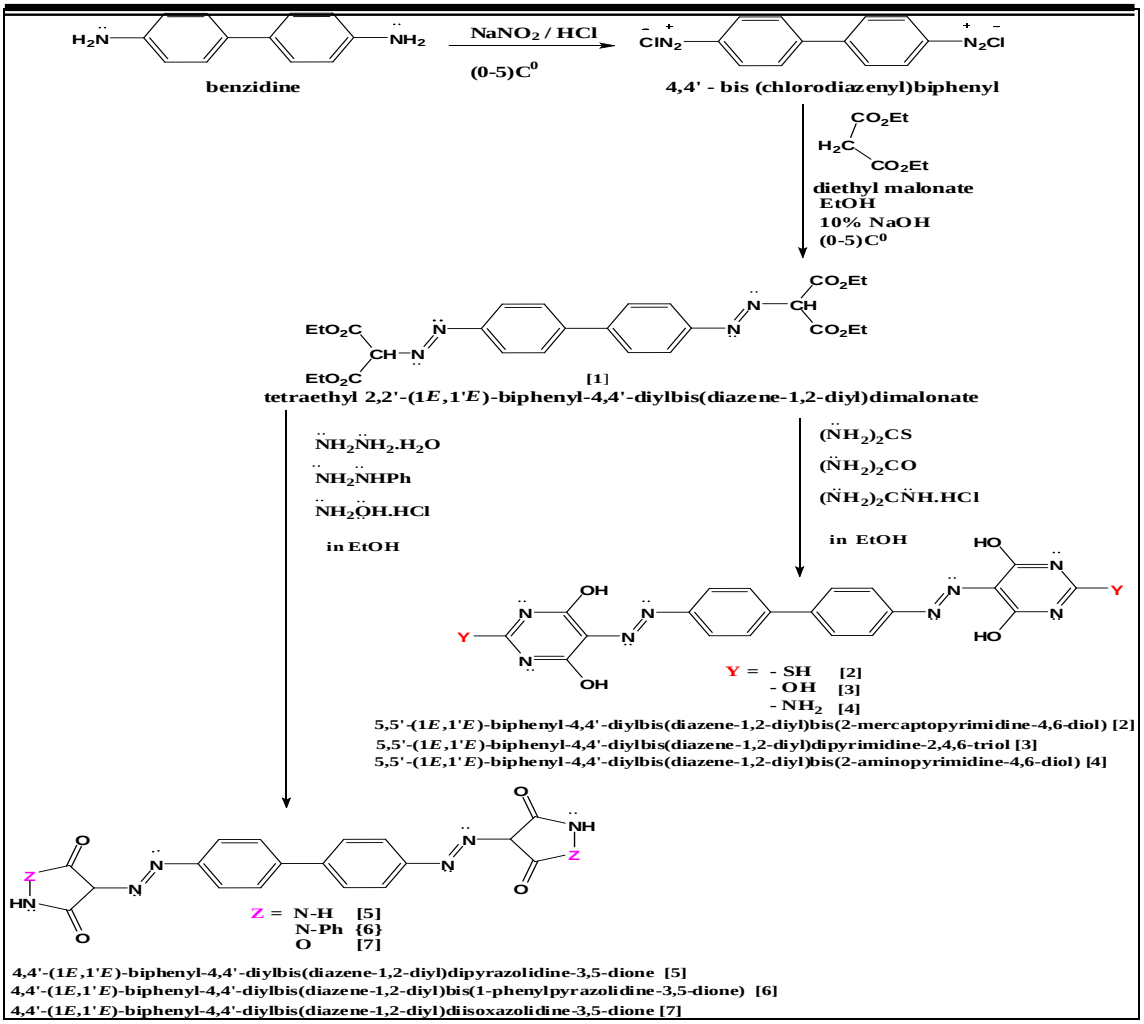


Fig.(11): H[1]NMR spectrum of compound (7).



Scheme (8)

تحضير و تشخيص بعض المركبات الحلقية الغير متجانسة جديدة

ميسون طارق توفيق

قسم الكيمياء , كلية التربية للعلوم الصرفة - ابن الهيثم , جامعة بغداد , بغداد , العراق

الخلاصة

تضمن البحث تحضير مشتقات جديدة للبريميدين و البيرازول و الأيزوكسازول من تفاعل رباعي أثيل 2,2ˉ - (1*E*' ,1*E*) ثنائي فنيل-4,4ˉ - ثنائي يل ثنائي (ثنائي أزين- 2,1- ثنائي يل) ثنائي مالونيت[1] مع مشتقات الأمونيا في مذيب الأيثانول المطلق لتكوين حلقات سداسية غير متجانسة : 5,5ˉ - (1*E*',1*E*)ثنائي فنيل - 4,4ˉ - ثنائي يل ثنائي (ثنائي أزين-2,1 -ثنائي يل) ثنائي (2- مركبتوبريميدين -6,4- ثنائي ول)[2], 5,5ˉ -(1*E*',1*E*- ثنائي فنيل -4,4ˉ - ثنائي يل ثنائي(ثنائي أزين-2,1 - ثنائي يل) ثنائي بريميدين -6,4,2- ثلاثي ول [3] , 5,5ˉ - (1*E*',1*E*)-ثنائي فنيل - 4,4ˉ - ثنائي يل ثنائي (ثنائي أزين -2,1- ثنائي يل) ثنائي (2 - أمينوبريميدين - 6,4 - ثنائي ول)[4], و حلقات خماسية غير متجانسة : 4,4ˉ -(1*E*',1*E*) - ثنائي فنيل - 4,4ˉ - ثنائي يل ثنائي(ثنائي أزين - 2,1 - ثنائي يل) ثنائي بيرازوليدين-5,3 - ثنائي ون [5] : 4,4ˉ - (1*E*',1*E*) - ثنائي فنيل - 4,4ˉ - ثنائي يل ثنائي (ثنائي أزين - 2,1 - ثنائي يل) ثنائي (1- فنيل بيرازوليدين - 5,3 - ثنائي ون) [6] : 4,4ˉ - (1*E*',1*E*) - ثنائي فنيل - 4,4ˉ - ثنائي يل ثنائي (ثنائي أزين - 2,1 - ثنائي يل) ثنائي آيزوزازوليدين -5,3 - ثنائي ون [7] .

تم متابعة التفاعل بواسطة كروموتوغرافيا الطبقة الرقيقة , وشخصت المركبات المحضرة بواسطة أطياف الأشعة تحت الحمراء و طيف الرنين النووي المغناطيسي و قياس درجات انصهار.

الكلمات المفتاحية : المركبات الحلقية غير المتجانسة , بريميدين , بيرازوليدين , ايزوكسازوليدين , مركبات الآزو .