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Synthesis of some New 1,2,4-Triazole derivatives

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A R T I C L E I N F O

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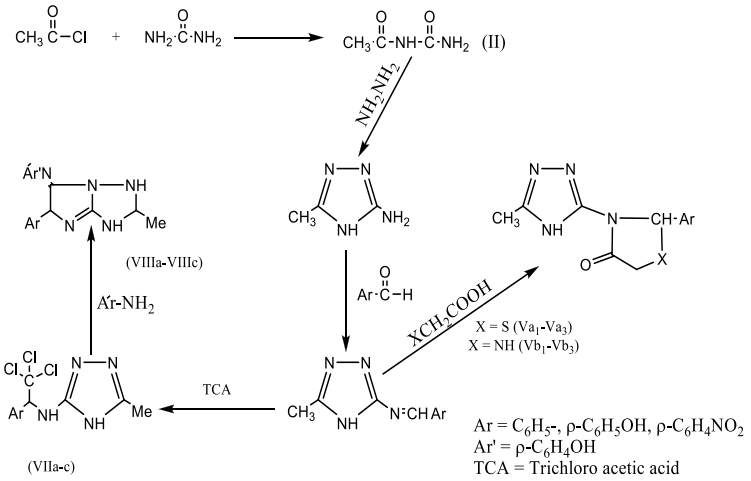
A B S T R A C T

In the present work, compound 3-arylidene amino-5-methyl-1,2,4-triazole (IIIa-c), required as starting material obtained in one-pot reaction by condensing 5-methyl-3-amino-1,2,4-triazole with different aromatic aldehydes. The required 5-methyl-3-amino-1,2,4-triazole was prepared from treatment of acetyl urea (I) with hydrazine hydrate, the compounds (IIIa-c) were converted to the corresponding [3-[5-methyl-1,2,4-triazol-2-yl]-2-arylthiazolidine-4-one (Va1-a3) and imidazoleine-4-one (Vb1-b3) by reacted it with thioglycolic acid and Glycine in absolute ethanol. The compounds (IIa-c) were converted also to 2-methyl-5-arylamino-5,6,-dihydroimidozo[2,1-b]-1,2,4-triazole (VIIIa-VIIIc) reacted with TCA then with aniline derivatives. The linear pathway strategy of all these synthesized compounds can be summarized in scheme (1).



Scheme (1)

Introduction:

The 1,3,4-tiazole derivatives are an important and frequent insecticidal, agrochemical structure feature of many biologically active compounds such as cytochrome Pu50 enzyme inhibitors(1) and peptide analog inhibitors(2). Recently, much attention has been focused on 4H-1,2,4-triazole derivatives for their broad-spectrum activities such as fungicidal, herbicidal, anticonvulsants and plant growth regulatory activities(3-5).

Further, the disubstituted 1,2,4-triazole derivatives were also reported to show antifungal, insecticidal, herbicidal and anti-inflammatory properties which similar to 4H-1,2,4-triazole derivatives(6-8), promoted by the above observations that the combination of two or more heterocyclic systems enhances the biological profile many-fold than its parent nuclei, we consider or synthesis some compounds bearing 4H-1,2,4-triazole in a molecular framework. Thiazolidinones and their derivatives have

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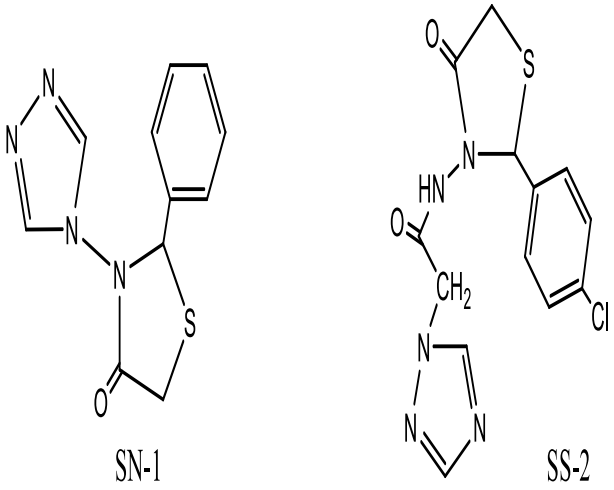
been reported having fungicidal, insecticidal and pharmacological activities(9-11), some of them showed similar activity(12-13) such as (SN-2) and (SS-2), (scheme 2).



Scheme (2)

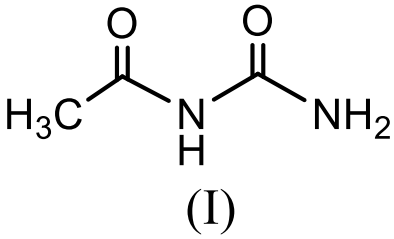
Experimental:

Melting points were determined in open capillary tubes on a Galekamp melting point apparatus and are uncorrected. The IR spectra (KBr disks) were recorded with Shimadzu Fourier Transform Infrared spectrophotometer FT-IR 8400 S(KBr) scale (4000-400) cm-1.

Uv spectra were recorded on Shimadzu (Uv-Visible) spectrophotometer Uv-1650 PC, Ethanol (95%) scale (200-800) nm. Micro Analysis (CHN) were recorded in Jordon and TLC chromatograms were eluted by the following solvent system Ethanol : water (2:1).

General procedure:

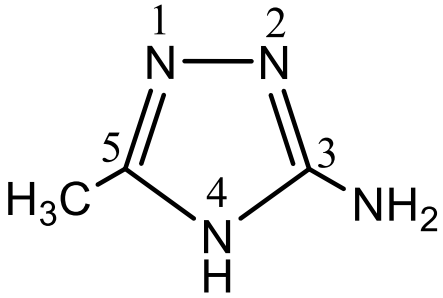
1- Synthesis of ((1-acetyl urea)) (I)



(I)

To a stirring of compound Acetyl chloride (0.01 mole) in dry benzene (15ml), a mixture of urea (0.01 mole) and benzene (10ml) was added drop wise. After that, the mixture was refluxed for 1 hour, after cooling; the excess of benzene was removed under vacuum. The product was collected as an oily compound.

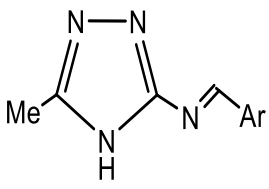
2- Synthesis of ((3-amino-5-methyl-1,2,4-triazole)) (II)



(II)

A mixture of (0.01 mole) of 1-acetyl urea (I), (0.01 mole) of hydrazine, 15ml of 30% aqueous sodium hydroxide and 25ml of ethanol was taken in a beaker. The beaker was then placed in a microwave for 10 minutes [14], then the mixture was cooled to room temperature and the solution was poured into 125ml of water, mixes thoroughly and allowed to stand for 15 minutes. Then the solution was filtered under suction and the filtrate acidified with concentrated hydrochloric acid, cooled in ice water, filtered and recrystallized from ethanol and water. Yield 75%, m.p. 146-148 °C .

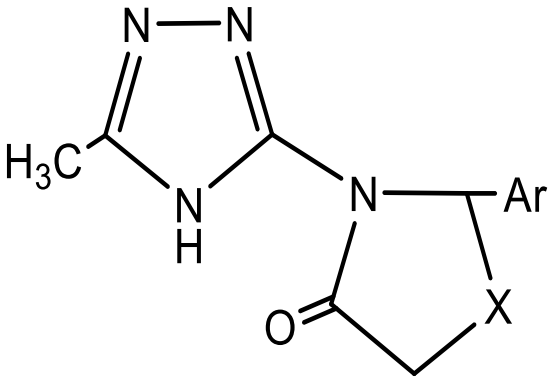
3- Synthesis of ((3-arylidene amino-5-methyl-1,2,4-triazole))



(IIIa-IIIc) Ar = C_6H_5-, ρ-C_6H_4OH, ρ-$C_6H_4NO_2$

These compounds were prepared by the general procedure, Schiff's bases reaction [16]: Mixture of II (0.01mole) and aromatic aldehydes (0.01mole) was refluxed in ethanol containing few drops of acidified for 4hr, after cooling; the precipitated solid was collected by filtration.

4- Synthesis of ((3-[5-methyl-1,2,4-triazol-2-yl]-2-arylthiazolidine))

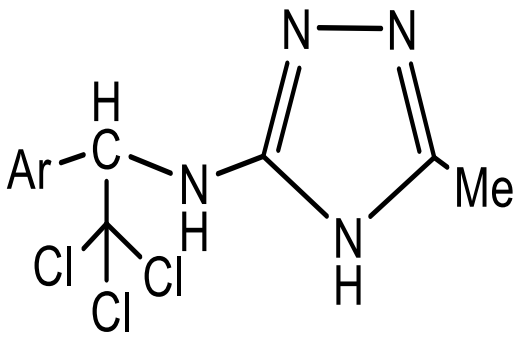


$(Va_1\text{-}Va_3)$ $Va_{1\text{-}3}$, X = S

$(Vb_1\text{-}Vb_3)$ $Vb_{1\text{-}3}$, X = N

A mixture of individual derivatives (IIIa-IIIc) (0.01 mole) and thioglycolic acid or glycine (0.01 mole) in dry toluene (30 ml) was refluxed in absolute ethanol (30ml) for 4hr. After cooling the precipitate solid was filtered off and recrystallized from ethanol.The physical data of compounds (Va1-Va3) and (Vb1-Vb3) are given in table (1).

5- Synthesis of ((2-[1-aryl-2,2,2-trichloroethyl]-3-amino-5-methyl-1,2,4-triazole))



These compounds were prepared as follows [17]: A mixture of compounds (IIIa-IIIc) (0.01 mole) and trichloroacetic acid (TCA) (0.01 mole) was refluxed in benzene (100ml) for 2hr. Then the benzene was distilled out. The residue thus obtained was triturated with ethanol water mixture (2:1 v/v) and recrystallized from ethanol.

The physical data of compounds (VIIa-VIIc) are given in table (1).

6- Synthesis of ((2-aryl-5-arylamino-5,6-dihydroimidazo[2,1-b]-1,2,4-triazole)) (VIIIa-VIIIf)

These compounds were prepared as followed (18): To a stirred suspension of compounds (IIIa-IIIc) (0.002 mole) and aniline derivatives (0.002 mole) in dioxane (20ml) was added TEA (0.001 mole) and the mixture was refluxed for 4hr. the reaction mixture was then cooled, poured in water (50ml). And the product obtained was recrystallized from ethanol to give compounds (VIIIa-VIIIf). The physical data of compounds (VIIIa-VIIIc) are given in table (1).

Results and discussion

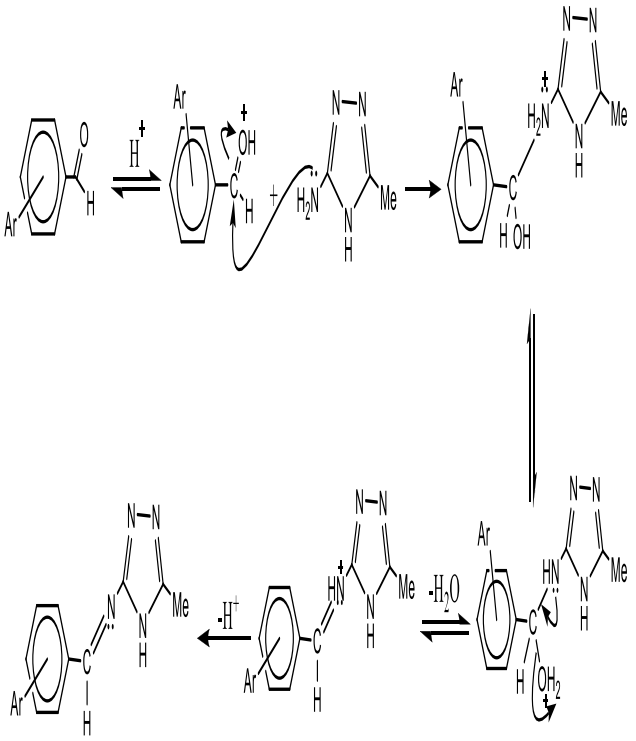
Compound acetyl chloride was reacted with urea to give acetyl urea (I), which cyclized to triazole ring through the reaction of acetyl urea (I) and hydrazine afforded 2-amino-5-methyl-1,2,4-triazole in 75% yield [14]. The analytical and spectral data are in accordance with the structure assigned. The FT-IR spectrum showed the disappearance of band due to carbonyl (C=O) at the region (1674-1650) cm^{-1} and amino group appearance of bands in the region (1643-1612) cm^{-1}, due to stretching vibration of (C=N) group, appeared bands in the region (1226-1328) cm^{-1} and (3282-3207) cm^{-1} were due to (ν-NH_2) and (ν-NH) stretching vibration respectively. The analytical and

spectral data are in accordance with the structure assigned.

The Schiff bases compounds (IIIa-c) were synthesized from 3-amino-1,2,4-triazole with different substituted benzaldehydes. The reaction was followed by the disappearance of (C=O) absorption band of aldehyde and of NH_2 at 3500 cm^{-1}, and the appearance of the azomethane (CH=N) stretching at 1646 cm^{-1} combined with the disappearance of NH_2 stretching band.

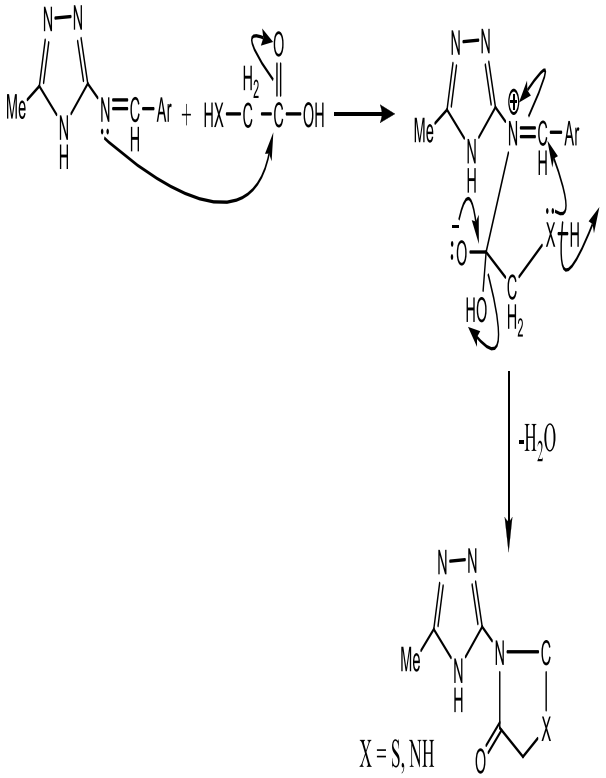
The structures of these Schiff bases were identified from their UV and IR spectra table (2).

The mechanism of this condensation is known and acid catalyzed, it may be outlined at follows (in scheme 2).



Scheme (3)

The reaction of Schiff bases with thioglycolic acid or glycine is a sort of cycloaddition reaction. These reactions were followed the attack of the azomethane nitrogen at the carbonyl group of the thioglycolic acid or glycine forming iminium cation, however iminium cation was unstable, so the SH or NH_2 attacked (N^+=C) moiety and afford more stable covalently bonded compounds (Va_1-a_3) and (Vb_1-b_3). The mechanism of the reaction may be outlined as follow [19]:



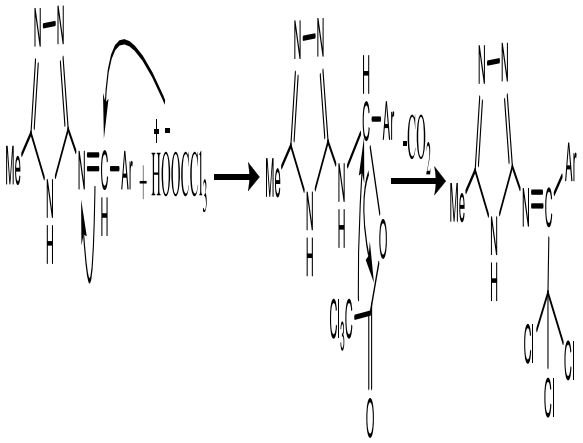
Scheme (4)

The reaction was followed by the disappearance of absorption stretching bands at (1623-1635) cm^{-1} for (νCH=N) and appearance of new absorption bands at (1699-1720) cm^{-1} for (C=O) and appearance of absorption bands at (1207-1250) cm^{-1}, and (713-760) cm^{-1}which were attributed to (C-N) and (S-C), (N-H) moieties respectively. Other information bands are listed in table (2).

The prepared Schiff bases were introduced in reaction with trichloroacetic acid (TCA), in suitable solvent in the second step to obtain 2-[1-aryl-2,2,2-

trichloroethylamino-5-methyl-1,2,4-triazole) (VIIa-VIIc).

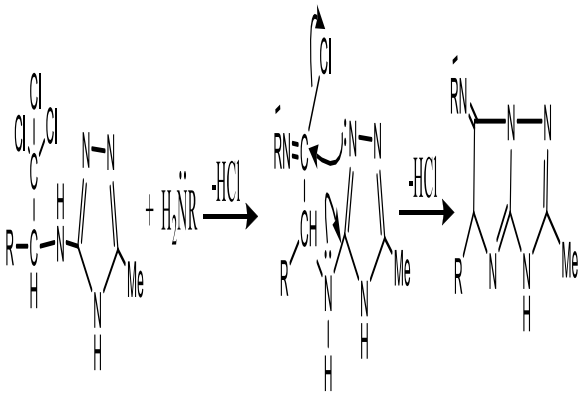
Mechanism of this reaction involved nucleophilic attack of oxygen of acidic on carbon atom of isomethane group in triazole as shown in scheme (5):



Scheme (5)

This reaction was followed by disappearance of absorption stretching bands at (1620-1640) cm^{-1} for (CH=N) and appearance of exhibited significant band around (3300 and 1615) cm^{-1} due to (N-H) and cyclic (C=N) groups, a band also appears in 850 cm^{-1} due to (C-Cl). UV spectra of compounds (VIIa-c) have λ_{max}(290-343) nm due to the ($\pi\rightarrow\pi^*$) and ($n\rightarrow\pi^*$) transition which appears at shorter wave length because of less conjugation between benzene ring and hetero aromatic ring, the spectral study (IR and UV) data in table (3).

The intermediates (VIIa-VIIc) treated with different primary aryl amines in dioxane (reaction time varied from 3 to 5 hr.). The mechanism for this reaction shows, that the reaction is second order a nucleophilic addition with losing of 3HCl molecules:

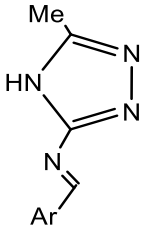


Scheme (6)

The informed compounds were characterized using spectral (IR, UV) and (C.H.N) analysis. IR spectrum showed disappearance of (*ν*C-Cl) band at (860-910) cm^{-1}. And appearing of new strong band at (1670) cm^{-1} due to exocyclic (C=N) group.

The UV spectra of the prepared compounds compounds, have λ_{max} at (215-260, 290-310, 308-312) nm due to ($n\rightarrow\pi^*$) transitions, and λ_{max} at (194-204) nm due to ($\pi\rightarrow\pi^*$) transition, these transitions appeared at longer wavelength because of the additional aromatic system.

Table (1): physical data of the synthesized compounds.

No.comp	Structure	Ar	Ar′	m.p.°C	Yield%	Color	R_f
IIIa		C_6H_5-	---	182-184	63%	White-yellow	0.83
IIIb		*p*-OHC_6H_4-	---	190-192	58%	White-yellow	0.60
IIIc		*p*-$NO_2C_6H_4$-	---	168-170	68%	White-yellow	0.73

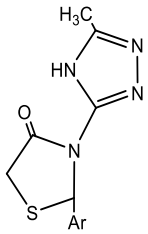
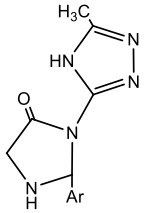
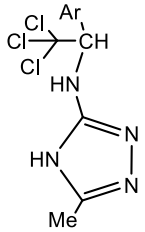
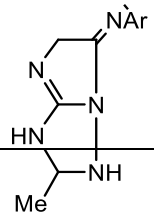
No.comp	Structure	Ar	Ar′	m.p. °C	Yield %	Color	Rf
VIa$_1$		**C_6H_5-**	---	**142-144**	**63%**	**White-**	**0.72**
VIa$_2$		***p*-OHC_6H_4-**	---	**151-153**	**58%**	**Yellow**	**0.37**
VIa$_3$		***p*-$NO_2C_6H_4$-**	---	**160-162**	**54%**	**Yellow**	**0.42**
VIb$_1$		**C_6H_5-**	---	**196-198**	**45%**	**Reddish-yellow**	**0.78**
VIb$_2$		***p*-OHC_6H_4-**	---	**186-188**	**57%**	**White-yellow**	**0.45**
VIb$_3$		***p*-$NO_2C_6H_4$-**	---	**161-163**	**43%**	**Reddish-yellow**	**0.32**
VIIa		**C_6H_5-**	---	**116-118**	**83%**	**Deep yellow**	**0.76**
VIIb		***p*-OHC_6H_4-**	---	**105-107**	**71%**	**Yellow**	**0.53**
VIIc		***p*-$NO_2C_6H_4$-**	---	**123-125**	**76%**	**Pale yellow**	**0.64**
VIIIa$_1$		**C_6H_5-**	***p*-OHC_6H_4-**	**290-292**	**72%**	**White**	**0.96**
VIIIb$_1$		***p*-OHC_6H_4-**	***p*-OHC_6H_4-**	**180-182**	**68%**	**Off white**	**0.72**
VIIIc$_1$		***p*-$NO_2C_6H_4$-**	***p*-OHC_6H_4-**	**206-208**	**61%**	**White-yellow**	**0.74**

Table (2): FT-IR spectra and UV data

Comp. No.	λ_{max} nm	*v*C=N	*v*C=O	*v*N-H	*v*C-N imide	*v*S-H
IIIa	**218,256,339**	**1604**	**---**	**3309**	**1280-1236**	**---**
IIIb	**225,275,325**	**1630**	**---**	**3375**	**1250**	**---**
IIIc	**318,267,334**	**1625**	**---**	**3169**	**1267-1251**	**---**
Va	**220,296,334**	**1620**	**1690**	**3200**	**1250**	**765**
Vb	**219,255,338**	**1600**	**1628**	**3172**	**1282-1228**	**759**
Vc	**218,289,323**	**1640**	**1660**	**3295**	**1265**	**800**
VIa	**215,267,334**	**1625**	**1670**	**3280**	**1240**	
VIb	**215,288,330**	**1600**	**1630**	**3245**	**1255**	
VIc	**222,285,333**	**1595**	**1670**	**3053**	**1249**	**-NO_2 1535, 1305**
VIIa	**205-295**	**1620**	***v*C=C**	**3150**	**C-Harom**	***v*C-Cl**
			1590		**3100-3000**	**860-910**
VIIb	**220-282**	**1623**	**1560**	**3249**	**3050-2987**	
VIIc	**208-215**	**1620**	**1615**	**3300**	**3100-3000**	
VIIIa	**215,300,311**	**1647**	**1589**	**3155**	***v*C-N**	***v*-OCH_3**
					1282	**1166**
VIIIb	**219-290,308**	**1670**	**1600**	**3150**	**1250**	***v*-OH**
						3433
VIIIc	**260-310,312**	**1643**	**1598**	**3109**	**1259**	***v*NO_2**
						1525-1332

Table (3): C.H.N. analysis

Comp. No.		%C	%H	%N
II	$C_3H_5N_4$	37.100 37.109	5.154 5.132	57.730 57.628
IIIa	$C_9H_8N_4$	81.0810 81.0819	5.400 5.400	30.430 30.427
VIa$_1$	$C_{12}H_9ON_4S$	48.868 48.871	4.073 4.069	25.336 25.338
VIb$_1$	$C_{12}H_9ON_5$	53.2019 53.2023	4.433 4.436	34.482 34.485
VIIa	$C_{10}H_{10}N_4Cl_3$	40.955 40.948	3.4129 3.4108	19.1263 19.1270
VIIIa$_1$	$C_{17}H_{12}ON_5$	67.540 67.538	3.973 3.972	23.178 23.181

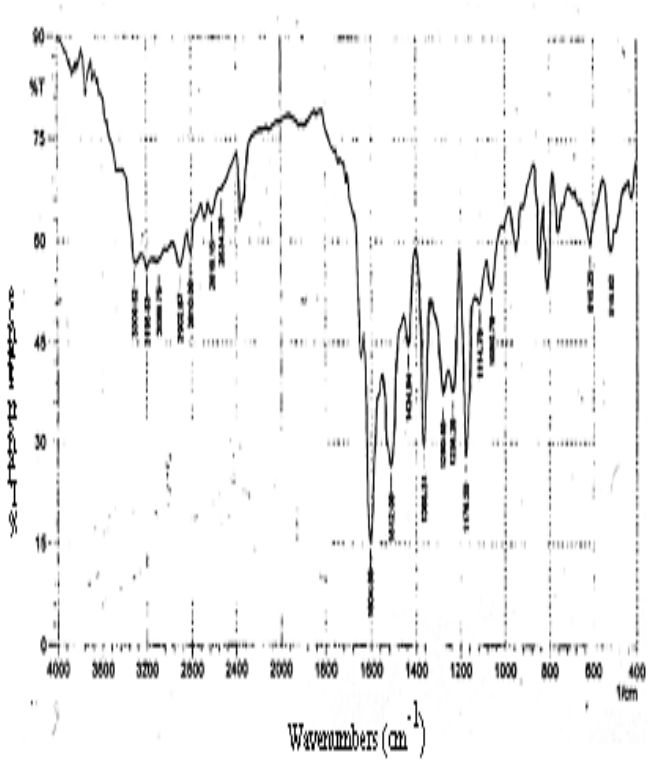


Figure (1) FT-IR spectrum of compound (IIIa)

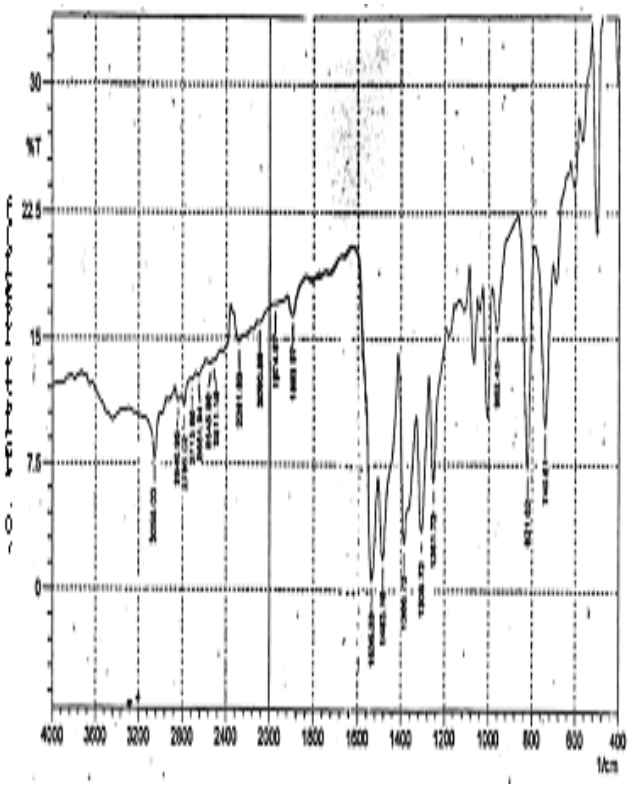


Figure (2) FT-IR spectrum of compound (IIIc)

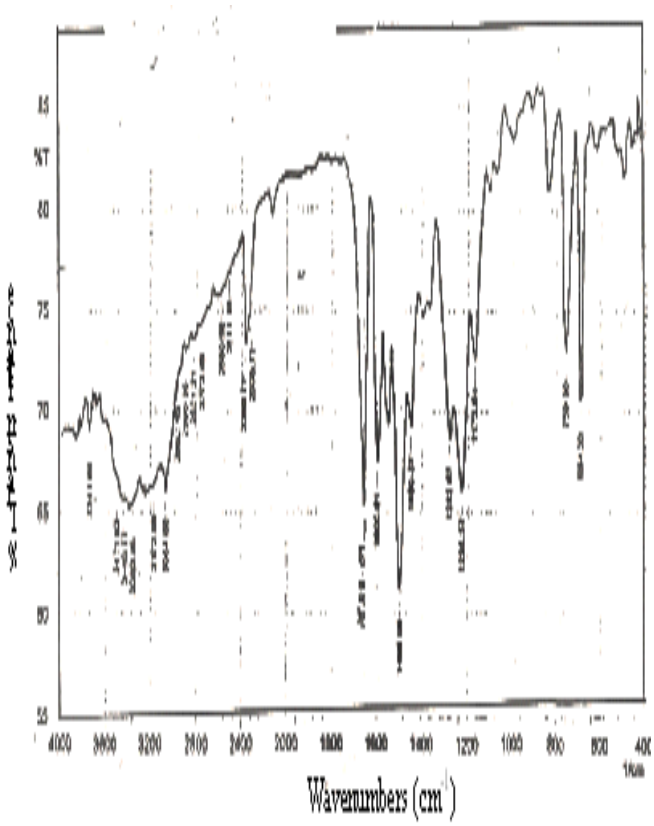


Figure (3) FT-IR spectrum of compound (Vb)

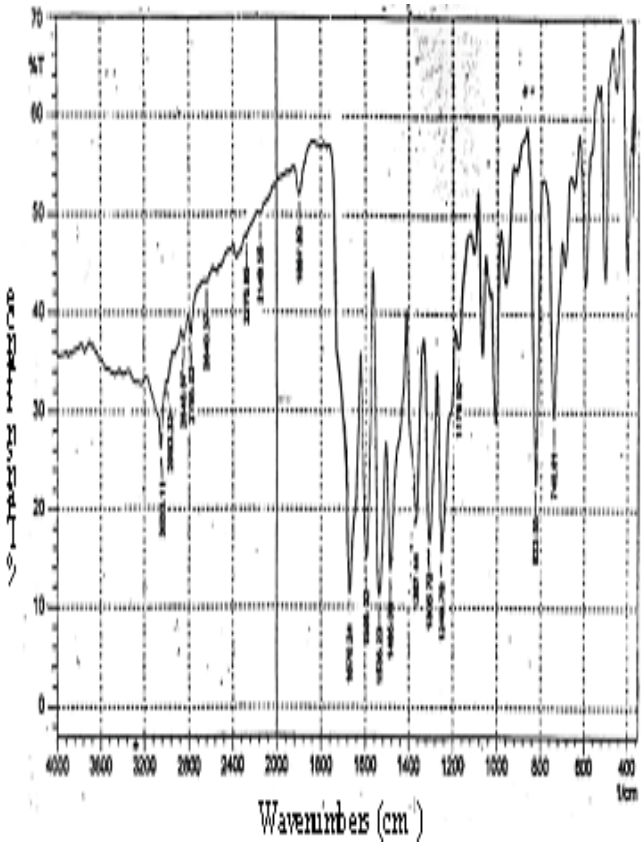


Figure (4) FT-IR spectrum of compound (VIc)

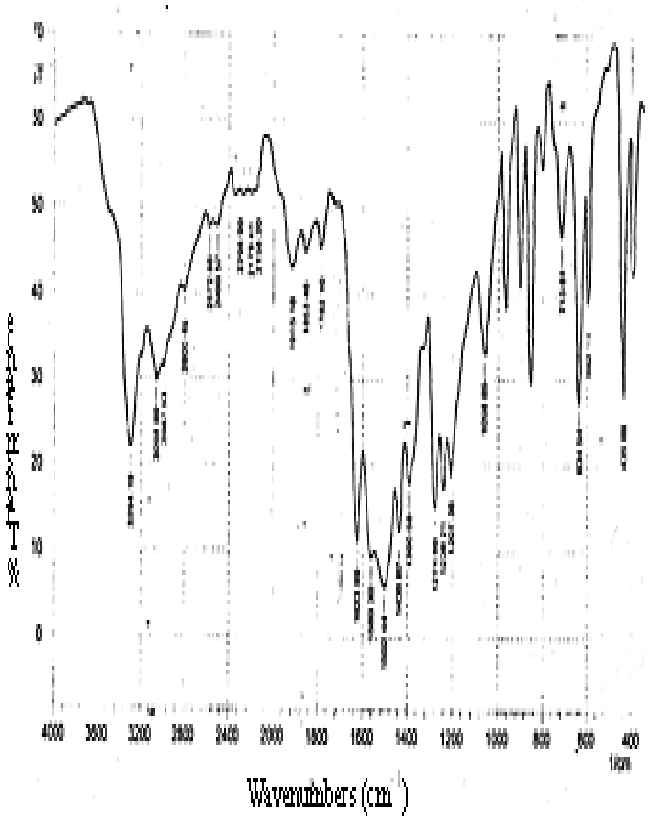


Figure (5) FT-IR spectrum of compound (VIIb)

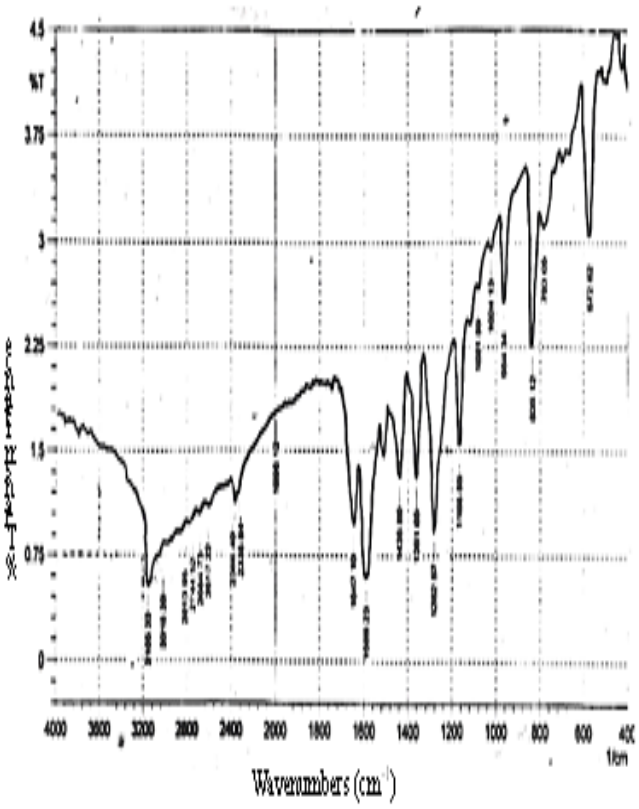


Figure (6) FT-IR spectrum of compound (VIIIa)

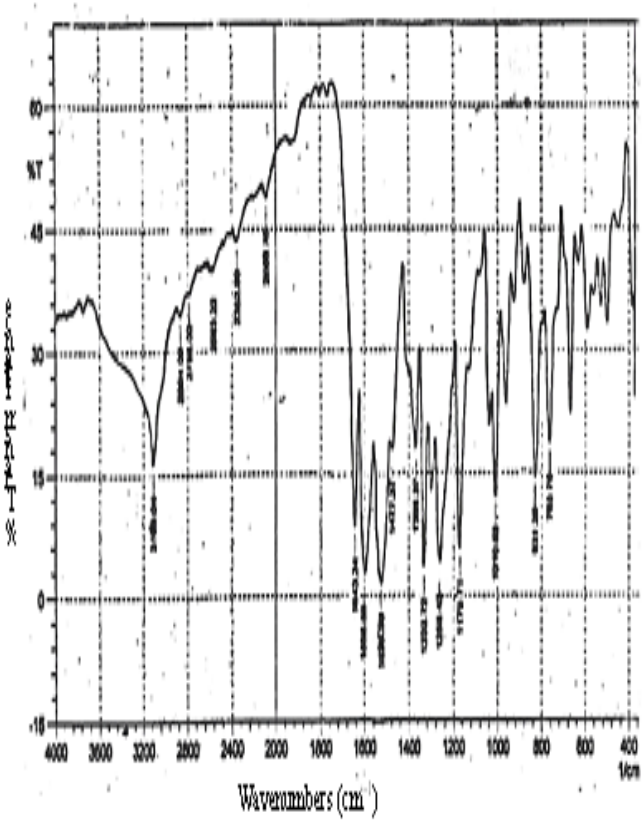


Figure (7) FT-IR spectrum of compound (VIIIc)

References

1- Vanden Bossche H. J. steroid Biochem. Molec. Biol.1992, 42, 45.
2- Meek, T.D.; J. Enzyme Inhib.1992,6,65
3- Toyabek, Nezu M, Shimazu H,Jpn Kokai Tokkyo Kono Jp, 0641086, Chem, Abstr., 1989,121, 94099h
4- Shaber S.J, Flyn K.E, Fujimolo T.T, Eur Pat Ep, 529,973 Chem. Abstr.,1993,119,726122z
5- Stankovsky S, Jedlovaska E, Spirkova K, Collect Czech Chem. Commun.1993. 58, 221
6- Talawar M.B, Laddi U.V, Somannavar Y.S, India J. Heterocyc. Chem, 1995, 4, 297
7- Znang Z.Y, Yan H, Acta Chemica Sinica, 1987, 45, 403.
8- Talawar M.B., Bennar S.C., Kankanwadi S.K., Patil P.A. Indian J. Pharm Sci, 1995, 57, 194
9- Egan AR, Eur, Pat Appl. Ep 478, 195 Chem, Abstr, 1992, 118, 131213d
10- Umehara T. Kohai Tokkoyo Koho Jp, 03, 220, 177, Chem, Abstr, 1992, 118, 21926f
11- Tanikawak, PCT Int Appl. Wo9116, 314 Chem. Abstr. 1992,118, 106307J
12- Siddiqui N, Deepanjali, Arshad F, Arpano R, Indian J. Heterocycl Chem. 2007, 16,403
13- Strirastera S.K, Soumya S, and Srivastara S.D. Indian J. Chem. 2002, 411, 1937
14- Rezki, N., Al-Bayati, R. I. and Sharba, A. K., AL-Mustansiriya J. Sci., 13(2), 47-55 (2002)
15- Vijar Kumar T, Amol Y.G, Kashinath N, and Poul B.N, Organic Chemistry. Indian J. 2009, 5(3), 325
16- K.K. Rajasekhar, V. Shantar Anath, T.S. Nithiyananthan. International J. of Chem. Tech. Research, Vol.2, No.1, PP592-597. Jan. Mar 2010
17- R. Huisgen, Angew Chem. Internat.Edit., 7, 321 (1986)
18- Mynng H. J., Westphal J. F., J. Med. Chem: -5(1), 58-59; (1995)
19- H. I. El-Subbagh, M. Y. Yousif and A. A. El-Eman, J. Arch. Pharm. Rcs. 12(2), 135-137 (1989).

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تحضير بعض مشتقات 1,2,4-Triazole الجديدة

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الخلاصة

يتضمن البحث تحضير المركب 3-اريليدين امينو-5-مثيل-4,2,1-ثايزول (IIIa-c) والتي استخدمت كمادة اولية حيث تم تحضيرها من خلال تكاثف 5-مثيل-3-امينو-4,2,1-ترايزول مع الديهايدات مختلفةاما المركب 5-مثيل-3-امينو-4,2,1-ترايزول فقد تم تحضيره من خلال تفاعل اسيتايل يوريا مع الهيدرازين. المشتقات (IIIa-c) تم تحويلها الى 3-[5-مثيل-4,2,1-ترايزو-2-يل]-2-اريل ثايوزوليدين-4-اون (Va1-b3) و ايمادوزولدين-4-اون (Vb1-b3) بواسطة تفاعل المركبات (IIIa-c) مع حامض الثايوكلايكولك في البنزين والكلايسين في THF.ايضا مركبات شف يمكن تحويلها الى 2-مثيل-5-اريل امينو-6,5-داي هيدروامايدوزو [b-1,2]-4,2,1-ترايزول (VIIIc-VIIIa), بتفاعلها مع TCA ثم مع مشتقات الانيلين.