Synthesis and study the biological activity of some new derivatives of 1,2,4-triazole compounds

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Abstract:

Some derivatives of triazoles have been synthesized . These derivatives (Schiff's bases) were resulted from the reaction of (3-(4-methoxy phenyl)-4-amino-5-mercapto-1,2,4-triazole and the corresponding substituted benzaldehydes in presence of glacial acetic acid . The chemical structures of the products were characterized by IR and UV spectra, elemental analysis C.H.N and the biological activity were studied against different kinds of bacteria.

تحضير ودراسة الفعالية البايولوجية لبعض المشتقات الجديدة من مركبات 4,2,1-ترايازول .

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المستخلص

تم تحضير بعض مشتقات الترايازولات . وهذه المشتقات (قواعد شيف) ناتجة من تفاعل (3-(بارا -ميثوكسي فنيل)-4-امين 5- مركبتو- 4,2,1-ترايازول مع بنزلديهايدات معوضة مختلفة بوجود حامض الخليك الثلجي . التركيب الكيميائي للنواتج تم تشخيصه بواسطة اطياف الاشعه تحت الحمراء IR و فوق البنفسجيه UV واجراء التحليل العنصري C.H.N كما تم دراسة الفعاليـــة البايولوجيـــة ضد انواع مختلفة من البكتريا .

Key words: Synthesis ,Biological activity, Derivatives , 1,2,4-triazole, Compounds

Introduction

Different substituted triazoles and other heterocyclic compounds have been synthesized and received much attention for their pharmacological properties [1-8] , Thus , different derivatives of triazole were found to be as useful as medicaments especially in the treatment of inflammatory and autoimmune diseases , tumors as N-(1-oxyl-2,2,5,5-tetramethylpyrrolin-3-yl)-N'-(mercapto-1,2,4-triazol-4-yl)ureas and N-(3-aryl-5-mercapto-1,2,4-triazol-4-yl)-(1-oxyl-2,2,5,5-tetramethylpyrrolin-3-yl)acidamide [9]. Triazoles and related compounds exhibited antifungal as 4-allyl/amino-5-aryl-1,2,4-triazoles [10] and 4-substituted aryl-5-(1-phenyl-5-methyl-1,2,3-triazol-4-yl)-1,2,4-triazol-3-thiones [11-12], antiviral as 1-beta-D-ribofuranosyl-1,2,4-triazole-3-carboxamide [13], bacteriostatic such as 4,4'-bis(1,2,4-triazole [10,14] and insecticidal activities such as 3-(3-thiophenyl)-4-amino-5-mercapto 1,2,4-triazole [15] . Keeping this in view, we have synthesized some Schiff's bases of triazole ring.

Experimental

Materials

Melting points were determined by using as "Electrothermal", melting points apparatus and remain uncorrected. The IR pectra were recorded on a shimadzu infrared spectrophotometer in KBr discs (υ in cm^{-1}). Melting points , crystallization solvents and percentage yields are listed in Table (I) . UV specra were recorded on shimadzu Table (II). Elemental analysis (C.H.N) was performed by micro analytical uniton corlo Erba model (1106) Table (III).

1) Preparation of 4-methoxyphenyl methyl benzoate (anisate) by [16] .

A mixture of 4-methoxybenzoic acid (0.1 Mole) , excess of methanol and concentrated sulphuric acid (4-5 mls) was refluxed for 4-5 hrs with stirring . After that the solvent was distilled under vacuum, the product washed by sodium bicarbonate , extracted by diethyl ether (30 mls) and dryed by anhydrous magnesium sulfate . (Melting Point (M.p) = 49-51 °C , Yield = 85 %) .

2) Preparation of 4-Methoxy benzoyl hydrazine (anisoyl hydrazide)(2) [17] .

Hydrazine hydrate (0.1 Mole) was added to a solution of 4-methoxy methyl benzoate (0.1 Mole) in ethanol (20 ml.) with continuous stirring and heating . Stirring and reflux was continued for 3hrs. and the precipitated solid was filtered , recrystallised , washed with water and finally dried. (M.p = 93-95 °C , Yield = 80%) .

3) Preparation of 3-(4-Methoxy phenyl)- 4-amino-5-mercapto-1,2,4-triazol (3) [18] .

Carbon disulphide (0.1 Mole) was added to a solution of 4-Methoxy benzoyl hydrazine (2)(0.1 Mole) and potassium hydroxide (0.1 Mole) in ethanol (25 ml.) with continuous stirring at room temperature . Stirring was continued for 5 hrs. and then the precipitated solid was filtered , washed with ether , dried and suspended in hydrazine hydrate 98 % (10 ml.) and heated under reflux for 2 hrs. On cooling, the mixture was diluted with water (100 ml.) and filtered , then the filtrate was neutralized with 10 % HCl . The separated crude products was filtered , dried and crtstallized .

M.p = 145-7 °C , Yield = 85 % . IR : 1340 cm^{-1}(C=S) , 1610 cm^{-1} (C=N) , 2700 cm^{-1} (SH) , 3114 cm^{-1} (NH ,

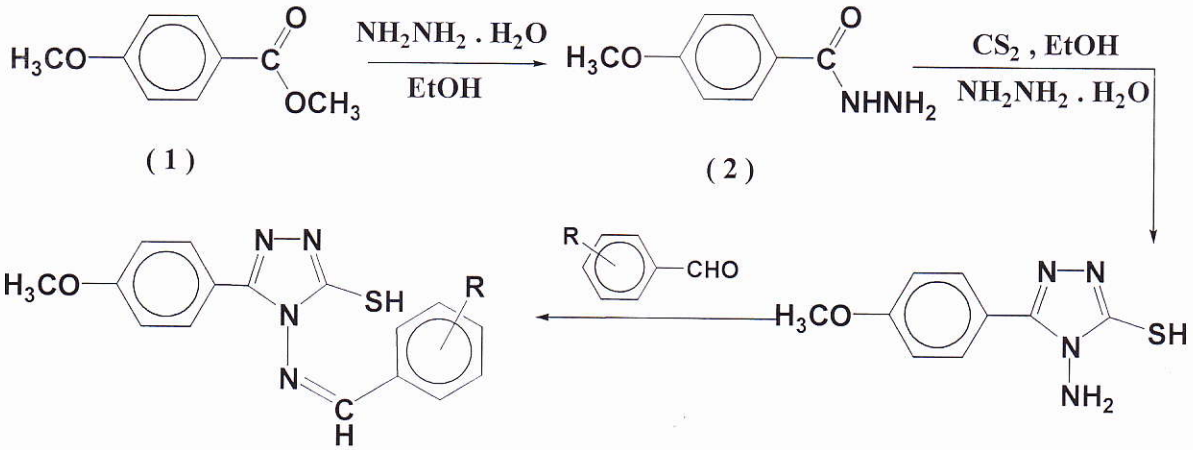
thion form) and 3200 cm^{-1} (NH_2).UV : 361 nm , 278 nm, 275 nm [19] .

4) Preparation of 3-(4-Methoxy phenyl)-4-arylideneamino-5-mercapto- 1,2,4-triazol (4-9) .

A mixture of substituted benzaldehydes (0.1 Mole), absolute ethanol (20 ml.) and 3-(4-methoxy phenyl)4-arylideneamino 5-Mercapto-1,2,4-triazole (3)(0.1 Mole) with (1-2) drops of glacial acetic acid was refluxed for 1hr. with continuous stirring . After cooling to room temperature the precipitate was filtered , dried and recrystallized from ethanol, (Table I).

Results and discussion

The starting materiel, 3-(4-Methoxy phenyl)4-arylideneamino-5-mercapto-1,2,4-triazole (3) was prepared by the method of Reid and Heidel [18], by the interaction of 4-methoxy benzoyl hydrazine (2) with carbon disulphide and potassium hydroxide , followed by cyclization with hydrazine hydrate . Then , the reaction of (3) with deferent aromatic aldehydes in acetic acid afforded the corresponding compounds (4-9) in good yields. The structure of the prepared compounds were confirmed by IR spectral data . Thus , the IR spectrum of (3) showed the presence of (NH_2) group at 3200 ,(NH thion form) at 3140 cm^{-1}, (C=S)1340 cm^{-1}, (C=N)1610 cm^{-1}, (SH)2700 cm^{-1} [19] .Condensation of compound (3) with aryl aldehydes was found to produce the corresponding N-arylidene (4-9) . The IR spectra of the compounds (4-9) showed the presence of C=N at (1600-1650) cm^{-1} with the mercapto group at (2650-2700) $cm^{-1}$and (NH, thion form) at (3130-3180)cm^{-1} ,(Fig. II, Table III). The UV spectra also revealed the presence of n—► π* and π —►π* transitions which confirmed the presence of ion pair of hetero atom and aromatic ring , (Fig. I, Table II) .



(4-9) R = 4-Me , OH , NO_2 , $N(CH_3)_2$, Cl , 2,4-dihydroxy (3)

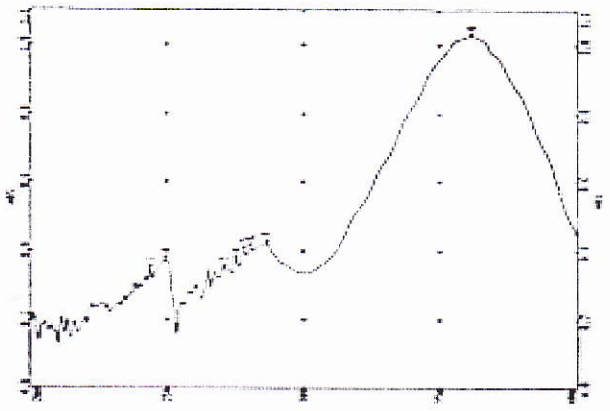


Fig.(I): UV spectrum for the compound (3)

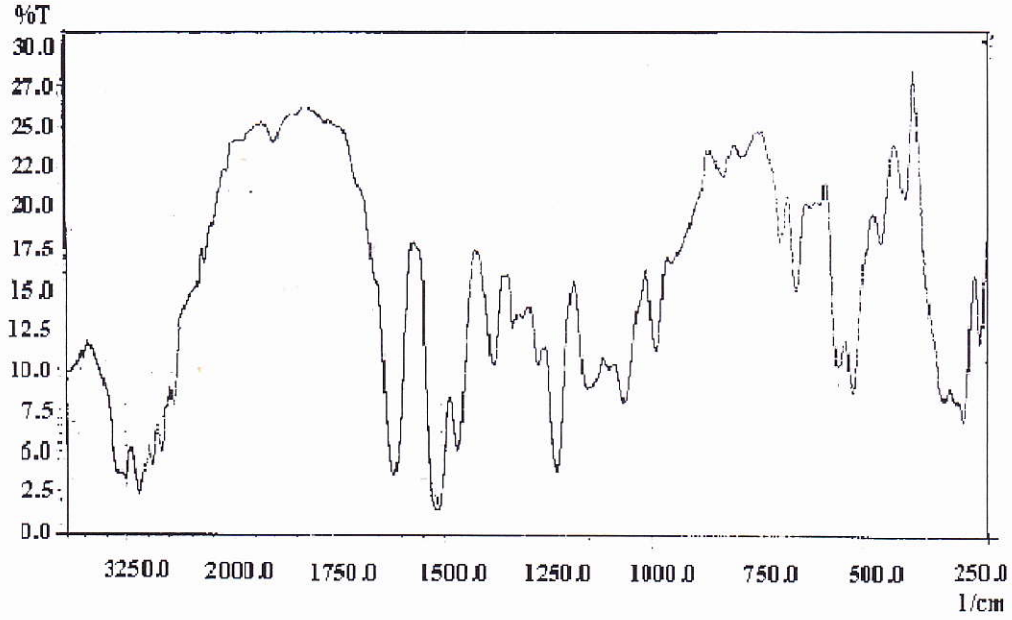


Fig.(II): IR spectrum for the compound (3)

Biological Testing

Antimicrobial activity of the compounds (3-9) was examined by agar diffusion method [20] , using four different species i.e (*Escherichia coli , Staphylococcus aureus , Salmonella typhi ,Pseudomonas. aerugenosa)* .The results indicated that all the assayed compounds showed activity against the tested organisms up to 3.2 Mg/disk .

Among this group of organism *Staph.aureus* and *Ps.aerugenosa* showed higher sensitivity towards the mentioned compounds Table (V).

Table (I) :The physical properties of Schiff's bases compounds (4-9)

Compd.	R	M.P °C	Yield %	Crystal. Solvent
4	4-CH_3	170	68	Ethanol
5	4-OH	200	80	=
6	4-NO_2	115	67	=
7	4-$N(CH_3)_2$	215	75	=
8	4-Cl	150	70	=
9	2,4-di(OH)	75	69	=

Table (II) : Ultra Violet spectral data of Schiff's bases compounds (4-9)

Compd. No.	$\lambda_1$max nm	A_1	$\lambda_2$max nm	A_2	$\lambda_3$max (nm), A_3
4	350	1.08	275	0.85	276 , 1.08
5	381	0.86	285	1.32	----
6	350	1.28	279	1.61	----
7	380	1.15	278	1.23	----
8	380	0.98	281	0.70	----
9	370	1.05	283	0.25	----

Table (III) :IR spectra data (cm^{-1}) of Schiff 's bases compounds (4-9).

Compd. No.	C = N Imine	N-H	C=C Aromatic	SH	Others
4	1610	3140	1500,1575	2650	CH_3 : 2990
5	1620	3160	1500,1550	2700	OH : 3350
6	1650	3145	1490,1560	2680	NO_2 :1520 , 1348
7	1600	3130	1500,1590	2680	CH_3 : 2985
8	1630	3140	1500,1570	2650	-----
9	1625	3180	1500,1580	2580	OH : 3370

Table (IV) :Physical properties and C.H.N analysis of the synthesized compounds

Comp. No.	Molecular Weight	Molecular Formula	Caled / found C %	H %	N %
3	222.27	$C_9H_{10}N_4OS$	48.63 48.63	4.53 4.52	25.21 25.21
4	324.40	$C_{17}H_{16}N_4OS$	62.94 62.93	4.97 4.98	17.27 17.26
5	326.37	$C_{16}H_{14}N_4O_2S$	58.88 58.88	4.32 4.32	17.17 17.16
6	355.37	$C_{16}H_{13}N_5O_3S$	54.08 54.06	3.69 3.70	19.71 19.71
7	353.44	$C_{18}H_{19}N_5OS$	61.17 61.17	5.42 5.41	19.81 19.80
8	344.05	$C_{16}H_{13}ClN_4OS$	55.73 55.73	3.80 3.79	16.25 16.24
9	342.37	$C_{16}H_{14}N_4O_3S$	56.13 56.12	4.12 4.12	16.36 16.36

Table (V) : Antimicrobial activity of the models compounds

No .Compd	*Staph. aureus*	*E. coli*	*Sal.typhi*	*Ps.aerugenosa*
3	++	+	+	+
4	++	±	-	++
5	++	±	-	+
6	+	-	-	±
7	+	+	±	±
8	+	±	-	±
9	++	±	-	++

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