

Synthesis and Study the Biological Activity of new Derivatives of Schiff bases Containing bis triazole group

Ibtisam k. Jassim¹, Fawzi H. Jumaa² and Gazwan H. Abed Elwahab Al-Somaidai³

¹Department of Chemistry, College of Education-Ibn-Alhatham, University of Baghdad, Baghdad, Iraq.

²Department of Chemistry, College of Education for Woman, University of Tikrit, Tikrit, Iraq .

³Department of Chemistry, College of Science, University of Tikrit, Tikrit, Iraq .

Key words: Antibacterial Activity, synthesized, Triazoles.

Abstract :

Various Substituted bis-triazoles from terephthalic acid have been synthesized by the preparation of bis 1,4-(3-mercapto-4-amino-1,2,4-triazolo-5-yl)benzene . This compound was reacted with different aldehydes . The structures of these derivatives were characterized from (IR , UV)spectra , elements analysis , melting points and the reaction was followed by TLC .The biological activity were studied against different kinds of bacteria .

Introduction :

5-Mercapto- 4H-1,2,4-triazole analoges possess wide spectrum of biological activity such as hypogcemic [1,2], antifluminatory activities [3,4]. Bousche et al have reported that the major effect of triazole , on fungi is inhibition of sterbt 14- α -demethylase , a microsomaicy tochrane P-rs dependent enzyme system . Triazoles thus impetus the biosynthesis of ergosterol for the cytoplasmic membrane and lead to the accumulation of 14- α -methylsienois [5].

Some other triazole derivatives show fungicidal effect (oral or Intra-Vaginal) [6-9] antibacterial agent and shown inhibition against 5-lipoxynase, cyclooxygenase [9-10] and anti-inflammatory [11-12].

Here we have synthesized some bis-triazole with it's derivatives as antibacterial agents.

Experimental :

Materials:

Different substituted benzaldehydes were BDH analar grade solvents and other chemicals used of analar grade . Melting points were determined on a electrothermal melting point apparatus and are uncorrected. The I.R spectra were recorded on Pye-Unicam spectrophotometer as KBr wafers in 4000-500 cm^{-1} range. The UV absorption spectra were measured in ethanol as a solvent by philips UV/Vis scanning spectrophotometer PV 8720. $^1\text{H-NMR}$ spectrum for starting material was record in $\text{DMSO } d_6$ on Hitachi Perkin-Elmer 60 MHz with using TMS as the internal reference (chemical shift in δ -PPM). Elemental analysis (C.H.N) was performed by micro analytical unton corlo Erba model (1106).

1. Preparation of Terephthalic Acid (I) [13].

p-xylene (0.01mole) and sodium carbonate (0.005 mole) suspended in boiling water (75-80 mls) then powdered potassium permanganate (0.03 mole) was introduce and refluxing mixture (1-4 hrs). Cool and acidify with sulphuric acid (10%). The mixture heated under reflux for (30 min.) then cooled. Manganese dioxide removed by addition of a little sodium bisulphate. The precipitate filtered and re-crystallized from ethanol.

2. Preparation of Methyl Terephthalate(II) [13].

A mixture of Terephthalic Acid (0.1 Mole), excess of methanol and concentrated sulphuric acid (5-6 mls) was refluxed for 6-7 hrs with stirring . After that the solvent was distilled under vacuum, the product washed by sodium bicarbonate solution then with diethyl ether (40 mls). (M.p)= 141-143 $^{\circ}\text{C}$, Yield = 85 %).

3. Preparation of Terephthalic Acid dihydrazide (III) [13].

Dissolve Methyl Terephthalate (0.1 mole) with hydrazine hydrate 98 % (0.3 mole) in absolute ethanol (40 mls) and refluxing amixture (5-6 hrs), cooling to room temperature , the precipitate was washed , re-crystallized and dried from ethanol. (M.p)= 225-227 $^{\circ}\text{C}$, Yield = 90 %).

4. Preparation of 1,4-(3-mercapto-4-amino-1,2,4-triazol-5-yl)benzene (IV) [14].

Carbon disulfide (8.0 g. , 0.1 mole) was added to a solution of terephthalic acid dihydrazide (19 g. , 0.05 mole) and potassium hydroxide (5.6 , 0.1 mole) in ethanol (50 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 5 hrs. On cooling the mixture was diluted with water (100 ml) and filtered , then neutralized with 10% HCl . The separated crude product was filtered, dried and crystallized . IR : 1342 (C=S) , 1615 (C=N) , 2710 (SH) , 3145 (NH, thione form) and 3230 (NH₂) , $^1\text{H-NMR}$: 1.9 (s , 2H , SH) , 5.75 (s , 4H , NH₂) , 7.10-7.30 (m , 4H , Ar-H) .

5. Preparation of Schiff's bases (Va-e).

A hot ethanolic solution of the bis 1,4-(3-mercapto-4-amino-1,2,4-triazol-5-yl)benzene (0.01 mole) was mixed with a solution of the selected aldehyde (0.02 mole) was in 10 ml ethanol with few drops of glacial acetic acid . The resulting mixture was then refluxed for a 60 min. Then, the product was filtered and re-crystallized from suitable solvent . It's m.ps , yield and C.H.N analysis are shown in Tables (1,2) .

Table (1): Physical properties of the products .

Comp. No.	R	M.P $^{\circ}\text{C}$	Yield %	Color	Crystal. Solvent
Va	p-NO ₂	218-20	90	Yellow	Ethanol
Vb	m-NO ₂	185-7	85	=	Ethyl acetate
Vc	3,4-diOH	290-2Dec.	75	=	Ethanol
Vd	4-N(CH ₃) ₂	262-4	80	=	Ethanol
Ve	p-Me	214-6	85	=	Ethanol

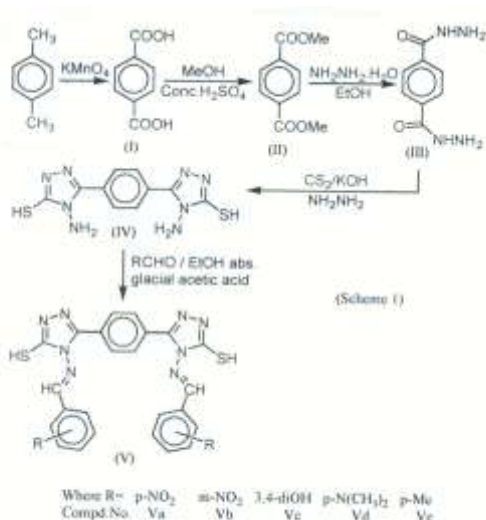
Table (2): Physical properties and C.H.N analysis of the synthesized compounds

Comp. No.	Molecular Weight	Molecular Formula	Caled / found		
			C %	H %	N %
Va	572.58	C ₂₄ H ₁₆ N ₁₀ O ₄ S ₂	50.34 50.31	2.82 2.73	24.46 24.41
Vb	572.58	C ₂₄ H ₁₆ N ₁₀ O ₄ S ₂	50.34 50.29	2.82 2.79	24.46 24.44
Vc	546.58	C ₂₄ H ₁₈ N ₈ O ₄ S ₂	52.74 52.70	3.32 3.27	20.50 20.45
Vd	568.72	C ₂₈ H ₂₈ N ₁₀ S ₂	59.13 59.02	4.96 4.98	24.63 24.64
Ve	510.64	C ₂₆ H ₂₂ N ₈ S ₂	61.15 60.98	4.34 4.36	21.94 21.92

Results and Discussion :

1,4-(3-mercapto-4-amino-1,2,4-triazolo-5-yl)benzene (V) Which used as starting material prepared by a method of Reid and Heindel [15].

The Schiff's bases compounds were synthesized from the starting material and different substituted benzaldehydes (Scheme1).



The structure of these Schiff's bases were identified from their I.R and U.V spectra (Table 3,4). The IR spectra showed the following absorption bands and the corresponding functional group.

The reaction was accompanied by the disappearance of C=O absorption band of NH₂ at 3500 cm⁻¹ and appearance of C=N absorption b and in IR spectra of the products.

Table (3): IR Spectra of the Schiff's bases.

Comp. No.	C=N Imine	S-H	C=C Aromatic	C=S	Others
Va	1616	2700	1590,1600	1340	NO ₂ vs , 1520
Vb	1610	νν..	1540,1590	=	NO ₂ vs , 1520
Vc	1615	νν..	1440,1580	=	OH , 3370
Vd	1610	νν..	1500,1ν..	=	CH ₃ , 2985
Ve	1616	νν..	1500,1600	=	CH ₃ , 2995

Table (4): Ultra Violet spectral data(nm) of Schiff's bases compounds (Va-e)

Comp. No.	λ ₁ max	A ₁	λ ₂ max	A ₂
Va	380	1.38	289	3.41
Vb	840	1.21	239	2.2
Vc	390	2.12	285	0.29
Vd	382	1.27	298	1.43
Ve	355	1.38	279	0.95

Biological Testing:

Antimicrobial activity of the compounds (Va-e) was examined by the agar diffusion method [16] using four different bacterial species i.e *Escherichia coli*, *Staphylococcus aureus* , *Salmonella typhi* and *Pseudomonas aeruginosa* .

The results indicated that all the assayed compounds showed activity against the tested organisms up to 3.2 mg/disc.

Among this group of organism *Staph. aureus* and *Ps. aeruginosa* showed higher sensitivity towards the mentioned compounds (Table 5) .

Table (5): Shows excreasing biological activity for 1,2,4-triazoles and imidazoles independ on the structures .

Comp.No.	<i>Staph. aureus</i>	<i>E. coli</i>	<i>Sal. typhi</i>	<i>Ps. aeruginosa</i>
Va	++	+	-	+
Vb	++	±	±	++
Vc	++	±	-	+
Vd	+	+	+	+
Ve	+	±	-	±

(-) = no inhibition.,(±) = 6-9 mm., (+) = 10-14 mm.,(++) = 15-20 mm .

References :

- Mhesalkar MY. , Shah MH. and Nikam ST (1970) , J. Med. Chem. , 13 , 672-4 .
- Patil RD. , Dimova V. and Biradar JS.(1992) , Indian J. Chem. Sect B-Org. Chem. Incl. Med. Chem. 39 ,12 ,929-935.
- Gasowammi B.N. , Katakya J.C.S. and Baruah J.N. (1986) , J. Heterocycl. Chem. , 23 , 1439 .
- Abdel-Rahman S. Ferwanah (2005) , J. of The Islamic University of Gaza , Series of Natural Studies of Engineering , Vol. 13 , No. 1 , P. 35-45 .
- Bousche VH. , Kaymana E. and Masrunia H. (1999) , Pharmac. Ther , 67 , 1-22 .
- Shaukath A. Khanum , Sheena Shashikanth and Belagur S. Sudna (2003) , Science Asia , 29 , 383-392 .
- Eisa H.M. El-Emam A.A. , Mostafa M.A. and El-Kerdawy M.M. (1988) , J. Chinese Chem. Soc. , 35 , 353-6 .
- Wuy J. , Yang J. , Zhang DZ. And Zhou M. (1997) , Actor Pharmaceutica Sinica , 45 , 20 .
- Westan MC. , Grimshaw JM. And Ludbrook A. (2001) , The Cochran Library , Update Software Ltd. , 2 , r2
- Akio OH. (1956) , Bull. Inst. Chem. Research Kyoto University , 34 , 25 : C.A. (1956) , 50 , 10851b .
- Sengupta A.K. , Gupta A.A. (1983) , Indian J. Chem. , 22b , 263 .
- Mohan J. (1983) , Indian J. Chem. , 22b , 270 .
- Vogel I.A., A (1974) "Text Book of Practical Organic Chemistry" Third Ed., Longman Group Ltd. London .
- Baker W., Haksar C.N., and Meomic J.F.W.(1950), J. Chem. Soc.; 170 .
- Reid J.R., and Heindel N.D. (1976), J. Heterocycl. Chem., 13 ,925 .

16. Bauer A.W., Kirby W.A.M., Sherris J.S., and Turk

M. (1966), Amer.J. Clin. Patho., 45 , 493-496 .

تحضير ودراسة الفعالية البيولوجية لمشتقات جديده من قواعد

شيف الحاوية على مجموعة بس-ترايازول

ابتسام خليفة جاسم^١، فوزي حميد جمعة^٢ و غزوان حسن عبد الوهاب^٣

^١ قسم الكيمياء ، كلية التربية - ابن الهيثم، جامعة بغداد، بغداد، جمهورية العراق

^٢ قسم الكيمياء، كلية التربية للبنات، جامعة تكريت، تكريت، جمهورية العراق

^٣ قسم الكيمياء، كلية العلوم، جامعة تكريت، تكريت، جمهورية العراق

الملخص:

تحت الحمراء IR و فوق البنفسجية UV مع اجراء التحليل
العنصري و قياس درجات الانصهار لها كما تم متابعة التفاعلات
بكروموتوغرافيا الطبقة الرقيقة TLC . الفعالية البيولوجية درست ضد
انواع مختلفة من البكتريا

حضرت انواع مختلفة من الترايازولات الثنائية من حامض الترفثاليك
وذلك من تحضير ثنائي ٤،١-(٣-مركبتو-٤-امينو-٤،١،٢-
ترايازولو-٥-يل) بنزين . ان هذا المركب تم مفاعله مع الديهايدات
مختلفة . التراكييب للمشتقات تم تشخيصها باستعمال طيف الاشعة