Synthesis And Study The Biological Activity of Some Schiff-Bases Derived From 2-Aminothiazole or 2-Aminobenzothiazole and Vanillin Derivatives

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Abstract

Two series of 1,n-alkylene glycol di[4{N(2¯-thiazolylazo-methinyl)}2-methoxy] phenyl ether and 1,n-alkylene glycol di[4{N(2¯-benzo-thiazolylazomethinyl)}2-methoxy]phenyl ether were synthesized via reactions 2-aminothiazole and 2-aminobenzothiazole with dialdehyde , (which are synthesized from reaction vanillin with 1,n-dibromo or chloro alkane in the basic media) . The new compounds characterized by elemental analysis (of some of theme) , physical and spectral data .All the schiff-bases have been screened for their antifungal and antibacterial activity against Aspergillus niger , Escherichia coli (G-) and Staphylococcus aureus (G+) . All compounds were found to be active antibacterial and antifungal (except $[III]_{12}$ was not show any antifungal activity).

Introduction

The chemistry of 2-aminothiazoles and their derivatives has attracted the attention of chemists , since they exhibit important biological activity in medicinal chemistry (1) . 2-Aminothiazoles are known mainly as biologically active compounds such as: antifungi , antibacterial (2,3) and anti-inflammatory (4) . And as an intermediates in the synthesis of antibioties , well known sulfa drugs , and some dyes (5). 2-Aminobenzothiazoles and their derivatives has multiple

applications, they have a broad spectrum of biological activities (6-8) . And as intermediates for dyes (9) , and also show very intensive antitumor activity (10). On the other hand , bis-benzothiazoles and substituted bis-benzothiazoles are frequently fluorescent compounds and therefore convenient for fluorimetric measurements , which could serve as a potential method for detection of binding the biologically active compounds on DNA(11) . Schiff-bases containing benzothiazoles moiety show microbiological activity . The compounds $[1]_{a,b}$ exhibited antibacterial activity against Bacellus subtilis as (G+) bacteria(12)but not show any significant antifungal activity .

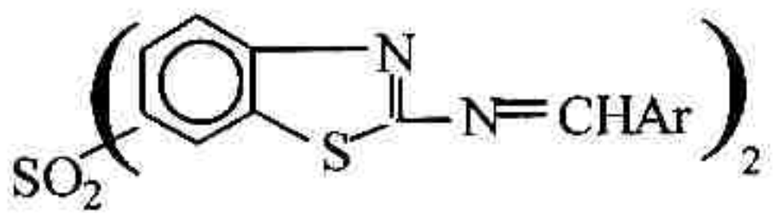
Schiff-bases derived from vanillin and 4-aminoantipyrine showed antibacterial activity against P. Pseudoalcaligenes , Vulgaris , Freundii , S. Subfava and B.megaterum(13) .

According to above facts , we decided to synthesize Schiff-bases compounds derived from 2-aminothiazole or 2-aminobenzothiazole and vanillin derivatives .

Experimental

Chemicals: Most of chemicals used were supplied from Aldrich , Merck and BDH chemicals Co. and were used are received .

Techniques: Melting points were determined by using an (Electro thermal) melting point apparatus and are uncorrected. IR spectra were



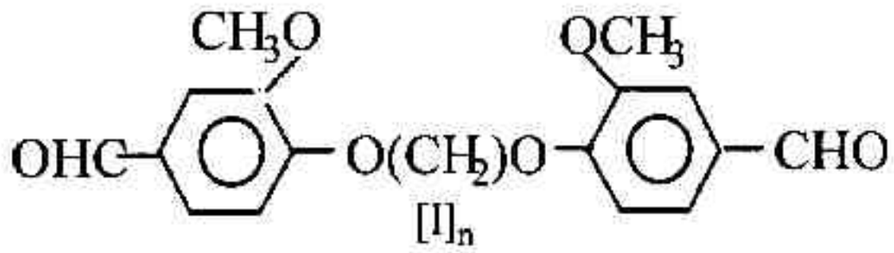
$[1]_{a,b}$

Ar = C_6H_5 - $[1]_a$ or P-$MeOC_6H_4$- $[1]_b$

recorded on a PYE-UNICAME sp 1712 infrared spectrophotometer (KBr disc) and the UV spectra were performed on a Shimadzu UV-visible- 160 spectrophotometer . Elemental analysis were carried out by using Caro-Erba 5500 elemental analyzer .

Synthesis

- n-Alkyleneglycol di (4-formyl-2-methoxy) phenyl ether [I]$_n$

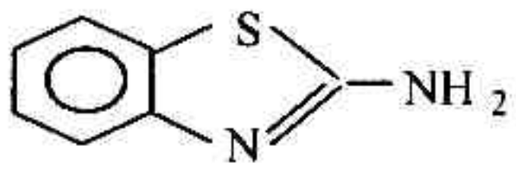


n=2,3,4,10 and 12

In a 100 mL flask , 3-methoxy-4-hydroxybenzaldehyde (2.44 gm , 0.02 mol) was dissolved in 15 mL of dry N,N - dimethylformamide (DMF).

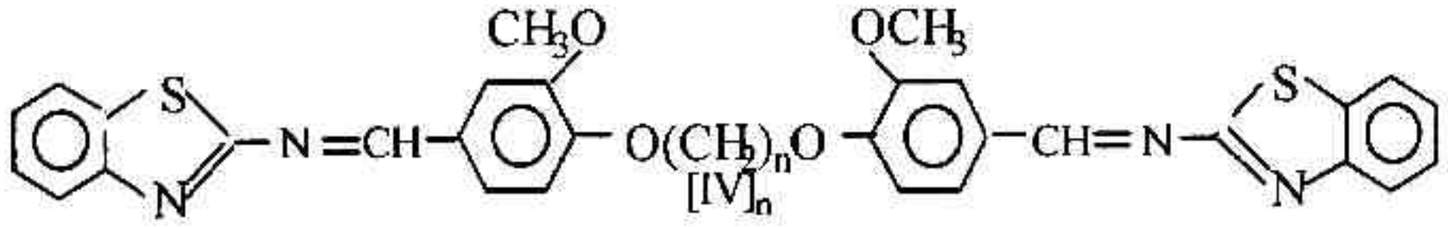
Anhydrous sodium carbonate (2.65 gm , 0.025 mol) and (0.01 mol) of the approprite 1,n-dibromo or chloro alklane were added to the reaction mixture . The stirred mixture was heated under reflux for 4hrs , allowed to cool and Then poured into 400mL of cold water , cooled to 5 °C overnight .The precipitated was formed, filtered and washed with water , dried in air and recrystalized from ethanol(14),(yields 85-94%) .

-Aminobenzothiazoles[II] : was prepared according to the Literature (15) .



[II]

1,n-alkyleneglycol di[4{N(2¯-thiazolylazomethinyl)}2-methoxy]phenyl ether [III]$_n$ and 1,n-alkyleneglycol di[4{N(2¯-benzothiazolylazo-methinyl)}2-methoxy]phenyl ether [IV]$_n$.



A mixture of compound $[I]_n$ (0.01mole) , 2-aminothiazole or 2-amino benzothiazole (0.02mole) , glacial acetic acid (3drops) and absolute ethanol (15 mL) was refluxed for 4 hrs . The mixture was then cooled to room temperature, then pricipitate was formed filtered and recrystallized from chloroform. Physical properties of the synthesized compounds are given in table 1 .

Results and Discussions

1,n-Alkyleneglycol di (4-formyl-2-methoxy) phenyl ether $[I]_n$ were obtained from the reaction of vaniline with 1,n-dibromo or dichloro alkane using DMF as the solvent in basic medium ($NaCO_3$) . The structures of these compounds were characterized by IR spectroscopy. The IR-spectra of these compounds showed the disappearance of a C=H stretching band of 4-hydrobenzaldehyde.

2-Aminobenzothiazoles [II] was synthesized by using the literature (15) . The structure of this compound was identified by IR spectrum , which is showed three prominent bands in the region (3190–3345) cm^{-1} , 1620 cm^{-1} and (2120–2160) cm^{-1} which are attributed to the NH_2 symmetrical and asymmetrical stretching frequency (typical amino NH_2 pair of bands) and a stretching band of C=N and S-C=N parameter of thiazole ring , respectively.

The compounds $[I]_n$ were allowed to react with 2-aminothiazole and 2-aminobenzothiazole in the presence of catalytic amount of glacial acetic acid and absolute ethanol to give Schiff -bases series $[III]_n$ and $[IV]_n$. The structure of these compounds were confirmed on the bases of their melting points Table (1) , elemental analysis for some of them , IR and UV spectra .

Table (2) showed the value of elemental analysis for some of them which are in good agreement with the theoretical data .

IR- absorption bands of these compunds showed the disappearance of two absorption bands due to NH_2 streching of aminothiazol and aminobenzothiazol with the appearance of stretching band in the range (1640–1675) cm^{-1} attribute to the Imine C=N group. It also show a stretching band in the range (2750-2945) cm^{-1} due to alphatic – CH_2- stretching . Table 3 exhibited the characteristic IR absorption bands of these compounds and the UV data (λ_{max}) which are obtained in DMSO (as a solvent) [$C(M)=1\times10^{-3}$] .

Biological Screening : Antibacterial and Antifungal Activity Test.

Biologically significant of 2-aminothiazole and 2-amino benzothiazole derivatives are well documented in the Literature . Such as , 2-Alkylthio-5-benzylideneamine-thiazol was shown to be strong antibacterial and antifungal(16) . And N-benzoyl-N-2-benzothiazolyl thioureas have higher activity against E.Coli and S.aureus(15).

The synthesized compounds Table 4 have been screened for their antifungal activity against Aspergillus niger by Poisoned Food technique(17) and antibacterial activity against Escherichia coli(G-) and Staphylococcus aureus(G+) by agar diffusion technique(18) . Each compound was dissolved in DMSO to give a final concentration of 0.01mg/mL . From the data obtained in Table 4, it is clear that all the compounds exhibited biological activity against bacteria (G-) and (G+) but in different range . Also the number of carbon atoms in alkyl group $(CH_2)_n$ affected on these data . Compounds $[III]_n$ (with n= 2,3,4,12) and compounds $[IV]_n$ (with n= 4,12) were found to be highly active against E.Coli, Compounds $[IV]_n$ (with n= 2,3,10) were found to be moderately active . While Compound $[III]_{10}$ was found to be slightly active against this type of bacteria . Compounds $[III]_n$ (with n= 3,12) and compounds $[IV]_n$ (with n= 4,12) were found to be highly active . Compounds $[III]_n$ (with n= 2,4) and $[IV]_n$ (with n=2,3) were found to be moderately active but Compounds $[III]_{10}$ and $[IV]_{10}$ were found to be slightly active against S.aureus . The test against fungi exhibited , all the compounds showed antifungal activity except the compound $[III]_{12}$ which was not show any antifungal activity (Inhibition zone = zero) . Compound $[III]_3$ and compound $[IV]_{12}$ showed very high activity (a complete inhibition), Compound $[III]_2$ and compound $[IV]_n$ (with n=2,4,) showed moderately activity .While Compound$[III]_n$ (n=4,10) and compound [IV] (n=3,10) showed slight activity against Aspergillus nagger .

References

1. Barone, R. ; Chanon, M. and Gallo, R. (1979) . Vol. 34, Part 2 ed., J.V.Metzger, Wiley , New York .
2. Rossignol, J. F. and Stachulski, A.V. (1999) . J. Chem. Research(s) , 44-45.
3. Ramana, M. M. ; Dubhashi, D. S. and D'souza, J. J. (1998). J.Chem. Research (s), 496.

4. Geronikaki, A. ; Hadjiparolou - Litina, D. ; Chatziopoulos, C. and Soloupis, G. (2003) . J. Molecules , 8 , 472-479.
5. Nam, G. ; Lee, J. ; Chi, D. and Kim, J. (1990). Bull. Kor. Chem. Soc., 11, 383 .
6. Russo, F. and Santagati, M. (1976) . Farmaco , Ed. Sci. 31 , 41.
7. Ghoneim, K. M. ; El-Basil, S. ; Osaman, A. N. ; Said, M. M. and Megahed, S. A. (1991). Rev. Roum . Chim. 36 , 1355 .
8. Singh, P. S. and Segal, S. (1988). Indian J. Chem. 27B , 941.
9.Hagen, H. and Kohler, R. D. (1987). Ger. Pat. , 3,528,230 (Chem. Abstr. , 95, 187261, 1981) .
10. El-Sherbeny, M. A. (2000). Arzeneim. Forsch. 50, 848-853.
11. Akyama, S. ; Ochiai, T. ; Nakatsuji, S. ;Nakashima, K. and Ohkura, Y. (1987). Chem. Pharm. Bull. 35 , 3029-3032 .
12. Kandel, M. M. (2001). Journal of the Chinese Chemical .Soc. 48, 37-43.
13. Vaghasiya, Y. k. ; Nair, R. ; Soni, M. ; Baluj, S. and Chanda, S. (2004) . J. Serb. Chem. Soc. 69:(12) , 991-998 .
14. Griffin, A. C. and Havens, S. J. (1981) . J. of polym. Sci. polymer physics Edition , 19 , 951-964 .
15. Sarkis, G. ; Kahait, A. and Abdul Ghani, Z. (1992). Iraq. J. Chem., 26:(1), 81-83 .
16. Jawetz, E. ; Melnick J. L. and Delbory, E. A. (1984). Review of Medical , Microbiology , 16Th , ed., 326.
17. Grand, A. (1988). J. of ethnopharmacology , 22 , 25-31 .
18. Cruickshank, R. ; Duguid, J. P. ; Marmion, B. P. and Swain, R. A. (1975)."Medical Microbiology the Practical of Medical Microbiology " , 12th Ed., Vol.2 , Longman .

Table(1) The physical data of new two series $[III]_n$and $[IV]_n$.

Com. No.	Formula	M.P(°C)	Yields %	Color
$[III]_2$	$C_{24}H_{26}N_4O_4S_2$	174-175	92	Pale yellow
$[III]_3$	$C_{25}H_{28}N_4O_4S_2$	120-122	84	Pale yellow
$[III]_4$	$C_{26}H_{30}N_4O_4S_2$	118-119	90	Brown
$[III]_{10}$	$C_{32}H_{42}N_4O_4S_2$	104-106	80	Orange
$[III]_{12}$	$C_{34}H_{46}N_4O_4S_2$	76-78	90	Orange
$[IV]_2$	$C_{32}H_{26}N_4O_4S_2$	180-182	90	Pale yallow
$[IV]_3$	$C_{33}H_{28}N_4O_4S_2$	126-128	94	Yellow
$[IV]_4$	$C_{34}H_{30}N_4O_4S_2$	67-69	85	Yellow-green
$[IV]_{10}$	$C_{40}H_{42}N_4O_4S_2$	95-97	88	Yellow
$[IV]_{12}$	$C_{42}H_{46}N_4O_4S_2$	88-89	84	Yellow-green

Table (2) Elemental analysis of the Schiff-base derivatives [VII].

Comp. No.	Theoretical			Experimental		
	C%	H%	N%	C%	H%	N%
$[IV]_2$	64.64	4.37	9.42	64.98	4.66	9.96
$[IV]_{10}$	67.98	5.94	7.93	68.26	5.59	8.24
$[III]_3$	58.59	5.46	10.93	58.89	5.22	10.68
$[III]_{12}$	63.94	7.21	8.77	63.64	7.50	8.98

Table (3) haracteristic IR absorption bands and UV data(λ_{max}) of new two series .

Comp. No.	Characteristic bands IR spectra (cm^{-1})				UV data
	νC-H Aliph.	νC=N Azomethin group	νC=N thiazole ring	νC=C Arom.	λ_{max} (nm) in DMSO as a solvent
$[III]_2$	2750-2880	1645	1620	1565-1575	290
$[III]_3$	2750-2845	1645	1625	1570-1585	292
$[III]_4$	2765-2875	1640	1628	1570-1590	296
$[III]_{10}$	2790-2880	1650	1625	1565-1590	299
$[III]_{12}$	2785-2885	1640	1625	1570-1585	302
$[IV]_3$	2735-2910	1670	1630	1590-1605	297
$[IV]_2$	2730-2940	1675	1630	1590-1610	298
$[IV]_4$	2750-2925	1675	1632	1585-1605	295
$[IV]_{10}$	2745-2940	1670	1635	1585-1610	304
$[IV]_{12}$	2750-2945	1670	1632	1590-1610	305

Table (4) Results of biological activity of the compounds $[III]_n$ and $[IV]_n$.

Comp. No.	E. coli (G-)	S. aureus (G+)	A. niger
$[III]_2$	+++	++	50%
$[III]_3$	+++	+++	100%
$[III]_4$	+++	++	25%
$[III]_{10}$	+	+	25%
$[III]_{12}$	+++	+++	zero%
$[IV]_2$	++	++	75%
$[IV]_3$	++	++	30%
$[IV]_4$	+++		+++55%
$[IV]_{10}$	++	+	25%
$[IV]_{12}$	+++	+++	100%

High active = +++ (inhibition zone > 14mm) , Moderately active = ++ (inhibition zone 10-13mm) Slightly active = + (inhibition zone 6-9mm) , Inactive = - (inhibition zone < 6mm)

تحضير ودراسة الفعالية البايولوجية لبعض من قواعد شف المشتقة من 2- امينوثايازول او2 -امينوبنزوثايازول ومشتقات الفانلين

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الخلاصة

شمل هذا البحث على تحضير سلسلتين من قواعد شف هما السلسلة 1 ، ن الكيلين كلايكول ثنائي [4{ N(2¯ - ثايازولايل ازوميثانيل) }-2-ميثوكسي] فنيل ايثر والسلسلة 1 ، ن الكيلين كلايكول ثنائي [4{ N(2¯ - بنزوثايازولايل ازوميثانيل) }-2ميثوكسي] فنيل ايثر وذلك عن طريق مفاعلة 2 -امينوثايازول و2 -امينوبنزوثايازول مع ثنائي الالديهايد (الذي حضر من مفاعلة الفانلين مع 1 ، ن-ثنائي برومو او كلورو الكان في وسط قاعدي) . شخصت المركبات المحضرة بستعمال التحليل الدقيق للعناصر (للبعض منها) والقياسات الطيفية والفيزياوية . اظهرت جميع المركبات المستعملة فعالية بايولوجية تجاه البكتريا المستخدمة بنوعيها وتجاه الفطر المستعمل باستثناء المركب III_{12}, اذ لم يظهر أي فعالية بايولوجية تجاه الفطر المستعمل فقط.