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Synthesis of Some New Schiff Bases Derived From Symmetrical 4-Amino-1,2,4-Triazole

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Abstract **- In this paper the synthesis of some Schiff bases, namely 4-(substituted benzylidene amino)-4H-1,2,4-triazoles (3a-g) derivatives by the reaction of symmetrical substituted 4-amino-1,2,4-triazole (2) and appropriate substituted ketons in presence of acetic acid. The synthesized compounds were characterized on the bases of their physical properties and spectroscopic data. Some of these compounds were tested for biological activities as antibacterial and antifungal agents and showed a significance to moderate activity.**

Keywords **- Benzilic acid, Schiff bases , 4-amino-1,2,4-triazole.**

I. INTRODUCTION

Triazoles are heterocyclic organic compounds having a five-memberd ring molecular structure containing three nitrogen atoms. The chemistry of triazole derivatives have been of interest due to its useful application in medicine [1], agriculture [2] and industry [3]. Substituted 1,2,4-triazoles are of great utility in synthetic organic chemistry, as a consequence, various methods have been used and described in the literature[4-7]. Compounds containing 4-amino- 1,2,4-triazole moiety have received considerable attention among chemists because molecules with these structural features have been found to display a wide range of biological activities, such as antifungal [8], antibacterial, antimicrobial [9,10]. In view of these facts and as a continuation of our search for new biological agents, in this paper we report, the synthesis of new Schiff bases and by the reaction of new 4-amino-3,5-bis(diphenyl hydroxymethyl)-1,2,4-triazole with different ketones in hot acetic acid. Some of them were evaluated for their biological activities.

II. EXPERIMENTAL SETUP

Melting points were determined on an electro thermal 9300 melting point apparatus and are uncorrected. IR spectra were recorded on a Bruker optics (FT-IR) spectrophotometer Co. using KBr-disk. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker 300-MHz spectrometer using TMS as an internal standard and DMSO-d_6 as a solvent. UV spectra were delivered by Shimadzu UV-Visible recording UV-160 spectrophotometer. The methyl benzilate (2) was prepared by the usual esterfication method, benzilic acid hydrazide (3) was prepared using reported method [11]starting from methyl benzilate.

A. Prepration of 4-amino-3,5-bis(diphenyl hydroxy methyl)-1,2,4-triazole (4)[12]:

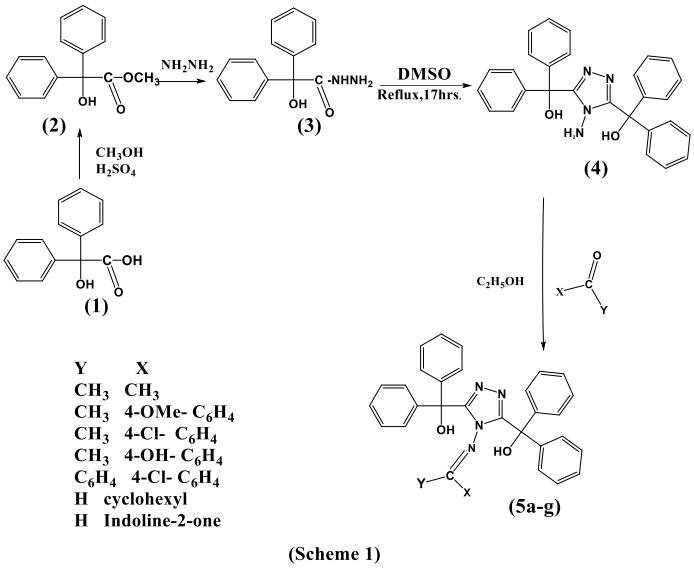
Benzilic acid hydrazide (3) (0.968 g, 0.004 mole) was dissolved in (10ml) dimethyl sulfoxide, the mixture was refluxed for (17 h.) ,then distilled under a reduced pressure, cooled, then (10 ml) of water was added. The reaction mixture was stirred at room temperature for (12 h.), The resulting solid was filtered, dried and recrystallized from aqueous ethanol to give the corresponding compound (4) as a pale yellow powder (1.07 g, 60%) (m.p. 140-142˚C)

B. Preparation of 4-(substituted benzylidine amino)-4H-3,5-bis(diphenyl hydroxy methyl) -1,2,4-triazole (5a-g)[13]

The solution of 4-amino-3,5-bis(diphenyl hydroxy methyl)-1,2,4-triazole (4) (0.001 mole, 0.448 gm) in (10 ml) acetic acid was refluxed with an appropriate ketones (0.001 mole) for (6 hrs). The reaction mixture was poured into ice-water with stirring, the precipitated product was filtered off, and washed with water, dried to give a solid product and recrystallized from suitable solvent. The physical and spectral data are listed in (Tables 1 and 2) respectively.

III. RESULTS AND DISSCUSION

1,2,4-Triazole compounds have been found to possess several biological activities[14]. In connection with our continuous interest in the chemistry of benzilic acid. we now report that 4-amino-3,5-bis(diphenyl hydroxy methyl)-1,2,4-triazole (2)was reacted with some ketones to prepare some Schiff bases(5a-g),as shown in scheme1.



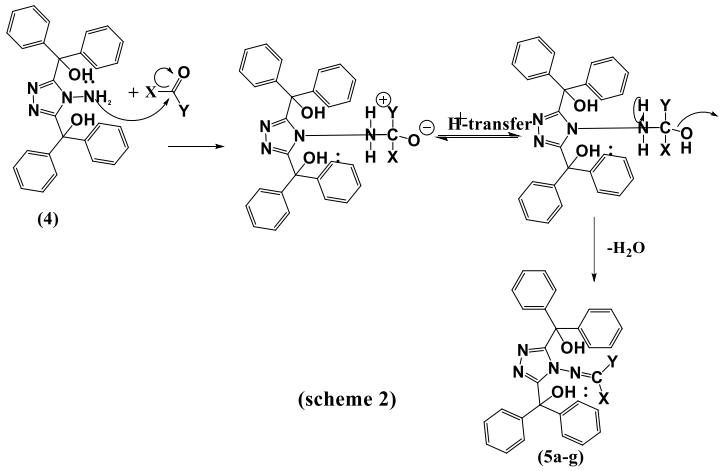
(Scheme 1)

The IR spectrum of the triazole (4) showed broad bands of (OH) group at (3410cm^{-1}), (NH_2) group at (3306cm^{-1}) and a band of (C=N) group at (1651cm^{-1}). The UV spectrum showed λ_{max} ($CHCl_3$) at (318nm) due to ($\pi \rightarrow \pi^*$) transition. This assignment was further supported by ^{1}H-NMR spectrum data which showed multiplet bands at δ(7.05-7.93 ppm) for (20 H) aromatic protons, a singlet bands at (4.51 ppm) for two (OH) protons and broad band at (1.20 ppm) for two(NH_2) proton. The structures of the target compounds (5a-g) and were elucidated using UV, IR, ^{1}H-NMR and ^{13}C-NMR.

The IR spectra for compounds (5a-g)showed the following stretching bands; (1652-1689cm^{-1})due to the (C=N) bond for hetetrocyclic ring ,(1594-1637cm^{-1})due to (C=N)bond for Schiff base, (3298-3326cm^{-1}) for the (O-H) bond (3057-3058cm $^{-1}$)due to(C-H)for methyl group .

The ^{1}H-NMR spectra for compounds (5a)in (DMSO-d_6)which showed multiplet bands in the range(7.0-7.92ppm)due to aromatic parts ,also broad bands at (4.5 ppm) due to two hydroxy group in compound, in addition the singlet peaks at(3.8ppm) for three protons of methoxy group finally singlet peaks at(1.9ppm) due to three protons for methyl group. while compound (5g) showed multiplet bands in the range(6.9-7.6ppm)due to aromatic parts , in addition the singlet peaks at(6.6ppm) for (NH)protons and broad bands at (4.6 ppm) due to two hydroxy group in compound,

^{13}C-NMR Spectra showed peaks for compound (5b)at the following data (14, 55.4, 80, 113.8, 126.9, 126.3, 127.2-129.5, 142.3, 163, 164, 167) while compound(5g) appeared at δ values(80.8, 111, 119.8, 120.9, 122.5, 127.1-127.8, 131.7, 138.4, 142.5, 142.9, 170.6, 178.6) which gave additional support to the results. The reaction proceeded on the following suggested mechanism [15] as shown in scheme2.



(scheme 2)

IV BIOLOGICAL ACTIVITY

Antibacterial and antifungal studies

The synthesized compounds were screened for *in vitro* antibacterial and antifungal activity by adopting the disc diffusion method. For antibacterial studies the microorganisms employed were *Esherichia coli, Staphylococcus aurous, Micrococcus, Pseudomonas, Bacillius 11 and Bacillius 12.* While for antifungal, *Microsporumgypseum, Microsporumdestortum, and Trichophytonrubrum* were used as microorganisms. Both antimicrobial studies were assessed by a minimum inhibitory concentration. It is evident that compounds (3b and 3g) possess a very good activity against bacteria Strains like *E. coli* and *Staphylococcu*s. And the compound (3g) possess almost a significant activity against all fungi tested at 1 mg/ml and 2 mg/ml. The remaining compounds showed a moderate activity against other bacteria and fungi tested.

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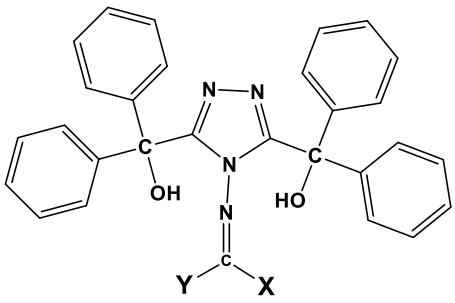
Table I
Physical data for compounds (5a-g)



Comp. No.	X	Y	m.p °C	Yield %	Color	Cryst. solvent
5a	CH_3	CH_3	193-195	42	pale yellow	EtOH+ H_2O
5b	4-MeO-C_6H_4	CH_3	276-278	57	pale yellow	EtOH+ H_2O
5c	4-ClC_6H_4	CH_3	179-181	38	brown	MeOH
5d	4-OHC_6H_4	CH_3	168-170	37	light brown	EtOH
5e	4-ClC_6H_4	C_6H_5	133-135	75	dark brown	EtOH
5f	Cyclohexyl	H	199-201	45	light brown	MeOH
5g	Indoline-2-one	H	93-95	90	pale yellow	EtOH+ H_2O

Table II

Spectral data for compounds (5a-g)

Compd. No.	**UV ($CHCl_3$) λ_{max} nm**	**IR (KBr),(5a-m) υcm^{-1}**			
		C=N cyclic	**C=N Schiff bases**	**OH**	**Others**
5a	310	1636	1652	3318	C-H(CH_3) 3058
5b	302	1594	1653	3326	C-H(CH_3) 3058 Ar-O-CH_3 Ass 1230 Sy. 1166
5c	292	1624	1670	3300	C-H(CH_3) 3057
5d	270	1624	1653	3298	C-H(CH_3) 3057
5e	300	1632	1662	3300	——
5f	266	1635	1662	3300	C-H 3057
5g	306	1637	1689	3305	N-H 3234 C=O 1689

Table III

^{1}H-NMR and ^{13}C-NMR data for compounds (5b & 5g)

Compd. No.	**^{1}H-NMR (δ,ppm)**	**^{13}C-NMR (δ,ppm)**
5b	δ 7.0-7.9 (bs, 24H). δ 3.84(S, 3H, OMe). δ 4.5(bs, 2H,2OH). δ 1.9(s, 3H, Me).	14, 55.4, 80, 113.8, 126.9, 126.3, 127.2-129.5, 142.3, 163, 164, 167
5g	δ 6.9-7.6(m, 24H-arom.) δ 6.6(s, 1H, NH) δ 4.6(bs, 2H,2OH)	80.8, 111, 119.8, 120.9, 122.5, 127.1-127.8, 131.7, 138.4, 142.5, 142.9, 170.6, 178.6