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Synthesis, Characterization And Biological Activity Of Schiff Bases Of Acetylacetone

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Abstract:
In the present study new Schiff base compounds derived from acetyl acetone with amines such as with aniline, 2 amino phenol, para anisidine and hydrazine hydrate. The Schiff base compounds were characterized by IR, and 1H NMR spectroscopy. The Schiff base ligands have also been tested in vitro for their antibacterial and anti fungal activity. The experimental results suggest that Schiff base ligands are more potent in anti bacterial and anti fungal activities.

Key words*: Schiff bases, acetylacetone, aniline, 2 amino phenol, para anisidine, hydrazine hydrate and Antibacterial activity; Antifungal activity.*

1.Introduction

In organic synthesis, Schiff base reactions are useful in making carbon nitrogen bonds compounds containing azomethine group (-CH=N-).

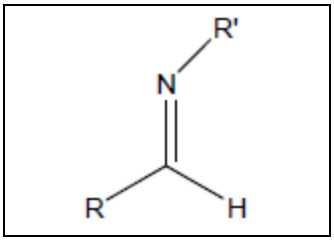

Figure 1

They are usually formed by condensation of a primary amine with a carbonyl compound, the general formula of Schiff bases R1R2C=N-R3, where R1, R2, R3 is maybe an aliphatic or an aromatic group. Schiff's bases are usually synthesized from the condensation of primary amines and active carbonyl groups by nucleophilic addition forming a hemiaminal, followed by a dehydration to generate an imine.

The possibility of having a lone pair of electrons in either π or sp2 hybridized orbital or trigonally hybridized nitrogen in the C=N group is of the fundamental chemical and biological importance.

Mechanistically, the formation of an imine involves two steps. First, the amine nitrogen acts as a nucleophile, attacking the electrophilic carbonyl carbon of aldehydes or ketones. In the next step, the nitrogen is deprotonated, and the electrons from this N-H bond push the oxygen off of the carbon, leaving a compound with a C=N double bond (an imine) and a water molecule displaced.

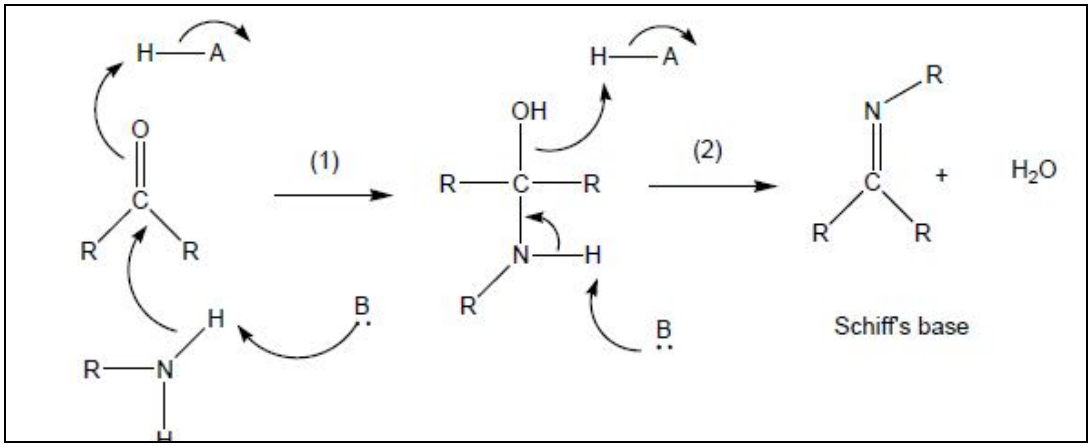

Figure 2

The field of Schiff base complexes has been fast developing on account of the wide variety of possible structures for the ligands depending upon the aldehydes and amines. Schiff bases are considered as a very important class of organic compounds, which have wide applications in many biological aspects [1].

In recent years, they have gained significant interest in the area of drug research and development owing to their broad bioactivities like insecticidal [2], antibacterial [3], antituberculosis [4], antimicrobial [5] and anticonvulsant [6] activities.

Schiff bases also serve as a backbone for the synthesis of various heterocyclic compounds. Imines play an important role in many biochemical reactions because some of the enzymes use an amine group of an amino acid to react with an aldehyde or ketone to form an imine linkage.

Studies of a new kind of chemotherapeutic Schiff bases are now attracting the attention of biochemists [7-10].

The present aim of the work is to synthesize a Schiff base derived from acetylacetone and primary amine derivatives such as aniline, para anisidine, 2 amino phenol and hydrazine hydrate and to characterize them and study their antibacterial and anti fungal activities.

2.Experimental

2.1.Reagents And Apparatus

All the chemicals used were of AnalaR grade and procured from Sigma-Aldrich and Fluka. The IR spectra were recorded on Jusco 300 instrument in KBr pellets. 1H NMR spectra of ligands in CDCl3 solution were recorded on a Bruker DT- 400MHz spectrometer, and chemical shifts are indicated in ppm relative to tetramethylsilane. Mass spectra were recorded using a KRATOS MS50TC spectrometer.

2.2.Synthesis Of 4-(Phenylimino)Pentan-2-One

To a hot methanolic (25 mL) solution of aniline (3.85 g, 50 mmol), a hot methanolic (25 mL) solution of acetylacetone (5 g, 50mmol) was added dropwise with constant stirring. This solution was refluxed at 70-75 °C for 2 h and then for 24 h at room temperature. On cooling white coloured 4-(phenylimino)pentan-2-one was precipitated out. It was filtered, washed with cold water, and dried yield 89% (2.63g), mp 198-200 °C,

1H NMR (CDCl3, δ ppm: 1.2 (s, 6H), 5.8(s, 2H), 6.4-7.3(d,, 4H), 9.2(s, 2H).

Selected IR data (KBr, υ cm-1): 1670 υ (C=O), 1608 υ(C=N), 1489υ(C=C).

Mass: m/z 175

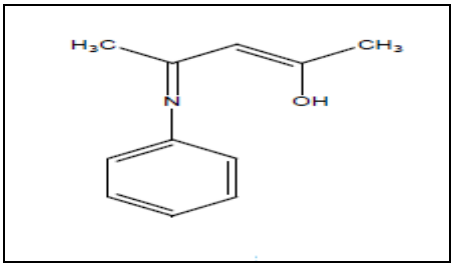

Figure 3

Synthesis of 4-(2-hydroxyphenylimino)pentan-2-one
Methanolic (25 mL) solution of 2-aminophenol (2.675 g, 25 mmol), was added dropwise to hot methanolic (25 mL) solution of acetylacetone (2.5 g, 25 mmol) with constant stirring. This solution was refluxed at 70-75 °C for 2 h. On cooling white coloured 4-(2-hydroxyphenylimino)pentan-2-one was precipitated out. It was filtered, washed with cold water, and dried. Yield 81% (1.91g), mp 200-202 °C,
1H NMR (CDCl3, δ ppm: 1.2 (s, 6H), 5.8(s, 2H),13.2 (s, H), 6.4-7.3(d, 4H).
Selected IR data (KBr, υ cm-1): 1628 υ(C=O), 1608 υ(C=N), 1332(C-O).
Mass: m/z 191

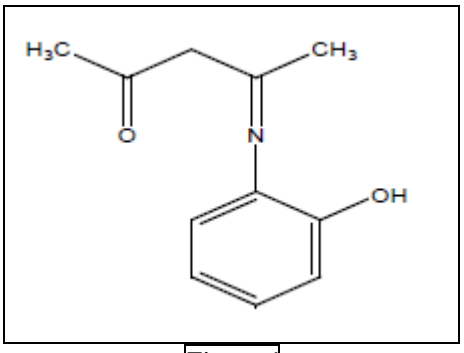

Figure 4

Synthesis of bis(acetylacetone) hydrzinediimine
1.2 g (2.0 mmol) of hydrazine hydrate (98% 2cc) was added dropwise with constant stirring to 4.0 g(4.0 mmol)of acetylacetone. The mixture was refluxed for about 4 h on a water bath. The solid reaction product was dissolved in a 1:1 mixture of ethyl acetate and dichloromethane by heating. After recrystallization two times from the hexane, colorless needle-like crystals of bis(acetylacetone) hydrzinediimine precipitated, filtered and dried. 2.8g(63% yield), mp 119-121°C.
1HNMR (CDCl3): CH3 (1.3), CH2(s 2.6) and NH2 (s 6.82)
IR (KBr, υ cm-1): 3250(NH2), 1612 (C=N),
MS:m/z 128

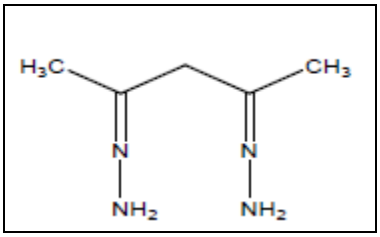

Figure 5

Synthesis of compound 4 4-(4-methoxyphenylimino)pentan-2-one
Methanolic (20 ml) solution of *p*-anisidine (10 mmole) and acetylacetone (10 mmole) and the mixture was refluxed for about 4 h on a water bath in presence of few drops of piperidine as condensing agent. The reaction mixture on ice-cooling gave 4-(4-methoxyphenylimino) pentan-2-one an orange-yellow solid precipitated, filtered and dried. Yield: 60% (m.p. 86°C).
1H NMR CDCl3 OH (13.2), Phenyl (6.4–7.3), imine (5.8) methoxy (3.7), methyl (1.6 and 1.2)
IR(KBr, υ cm-1) 3190 (enolisable OH group) 1620 (C=N)
Mass:m/z 205

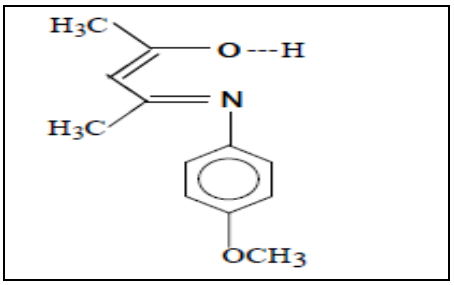

Figure 6

3.Biological Activity

3.1.Antibacterial

The in vitro biological screening effects of the investigated compounds were tested against the bacteria Bacillus subtilis. Paper discs of Whatman filter paper no. 1 were cut and sterilized in an autoclave. The paper discs were saturated with 10 µl of the compounds dissolved in DMSO solution or DMSO as negative control and was placed aseptically in the Petri dishes containing Nutrient agar media inoculated with the above mentioned two bacteria separately. The petridishes were incubated at 37^0C and the inhibition zones were recorded after 24 h of incubation.

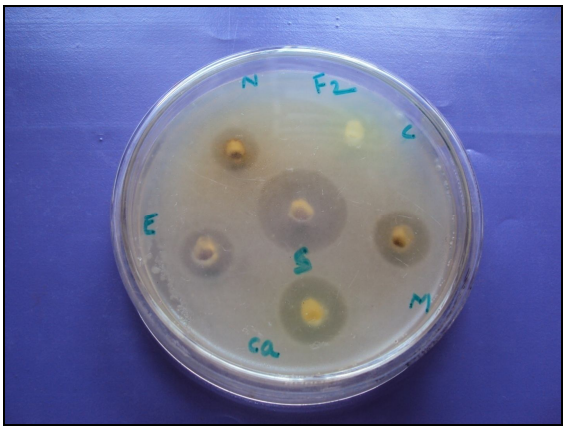

Figure 7

Ca: standard drug amoxycillin
M:bis(acetylacetone)hydrzinediimine
S: 4-(2-hydroxyphenylimino)pentan-2-one
N: 4-(4-methoxyphenylimino)pentan-2-one
E: 4-(phenylimino)pentan-2-one

3.2.Antifungal

The Schiff base complexes were screened for their antifungal activity against fungi viz. candida. Filter paper discs of 5 mm in size, prepared by using Whatman filter paper no. 1 (sterilized in an autoclave) was saturated with 10 µl of the compounds dissolved in DMSO solution . The fungal culture plates were inoculated and incubated at 25± 2^0C for 48 h. The plates were then observed and the diameters of the inhibition zones (in mm) were measured and tabulated.

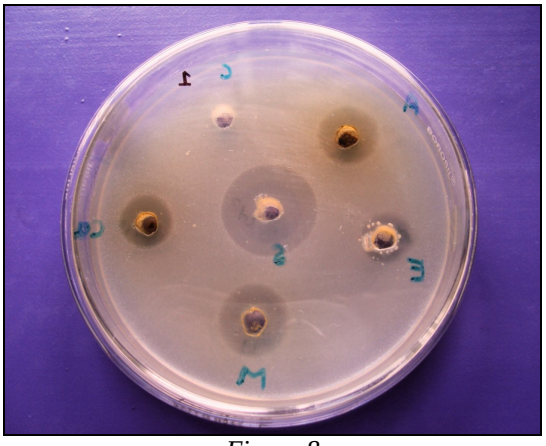

Figure 8

Ca: standard drug moconazole
N: 4-(4-methoxyphenylimino)pentan-2-one
S: 4-(2-hydroxyphenylimino)pentan-2-one
E: 4-(phenylimino)pentan-2-one
M: bis(acetylacetone) hydrzinediimine

4.Results And Discussion

Structures of compounds have been elucidated by IR, Proton NMR and Mass Spectral measurements. Schiff bases shows IR absorption peak at 1615-1530 cm-1 (C=N stretching). All the compounds show NMR signals for different kinds of protons at their respective positions.

The synthesized all four Schiff bases were found to be more active than standard antibacterial drug against Bacillus subtilis. The synthesized compound 4-(2-hydroxyphenylimino) pentan-2-onecterial) showed more active against Bacillus subtilis compared to other Schiff bases.

The synthesized compound 4-(2-hydroxyphenylimino)pentan-2-one ---S) showed more active than standard drug amoxicillin.

The synthesized all four Schiff bases were found to be more active than standard antifungal drug against candida. The synthesized Schiff base 4-(2-hydroxyphenylimino)pentan-2-one ---S) showed more active against candida compared to other Schiff bases.

5.Conclusion

Hence, further study of a synthesized Schiff base compound 4-(2-hydroxyphenylimino)pentan-2-one in antimicrobial and anti fungal activities may become fruitful.

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