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SCHIFF BASES: FACILE SYNTHESIS, SPECTRAL CHARACTERIZATION AND BIOCIDAL STUDIES

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ABSTRACT: A family of Schiff bases was synthesized by the reactions of o-aminobenzoic acid and Knovenegal condensate of β-ketoesters in 1:1 ratio. The newly synthesized Schiff bases were characterized by Elemental analyses and spectral (FT-IR, UV–Vis and ^{1}H-NMR) studies and the structures have been proposed tentatively. These compounds were subjected to study their biocidal efficacy against S. epidermidis, E. coli, B. cinerea and A. niger.

Keywords: Schiff base, β-ketoesters, Knovenegal condensate, Biocidal.

INTRODUCTION

Schiff bases, named after Hugo Schiff [1], are formed when any primary amine reacts with an aldehyde or a ketone under specific conditions. Structurally, a Schiff base (also known as imine or azomethine) is a nitrogen analogue of an aldehyde or ketone in which the carbonyl group (>C=O) has been replaced by an imine or azomethine group. Schiff bases are some of the most widely used organic compounds. Schiff bases have also been shown to exhibit a broad range of biological activities, including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic properties [2,3]. Imine or azomethine groups are present in various natural, natural-derived, and non-natural compounds. The imine group present in such compounds has been shown to be critical to their biological activities [4–6]. The first preparation of imines was reported in the 19th century by Schiff (1864). Since then a variety of methods for the synthesis of imines have been described [7]. The classical synthesis reported by Schiff involves the condensation of a carbonyl compound with an amine under azeotropic distillation [8]. Molecular sieves are then used to completely remove water formed in the system [9]. In the 1990s an in situ method for water elimination was developed, using dehydrating solvents such as tetramethyl orthosilicate or trimethyl orthoformate [10,11]. In 2004, Chakraborti et al. [12] demonstrated that the efficiency of these methods is dependent on the use of highly electrophilic carbonyl compounds and strongly nucleophilic amines. They proposed as an alternative the use of substances that function as Bronsted-Lowry or Lewis acids to activate the carbonyl group of aldehydes, catalyze the nucleophilic attack by amines, and dehydrate the system, eliminating water as the final step [12]. The main aim of the production and synthesis of any antimicrobial compound is to inhibit the causal microbe without any side effects on the patients. In addition, it is worthy to stress here on the basic idea of applying any chemotherapeutic agent which depends essentially on the specific control of only one biological function and not multiple ones. The chemotherapeutic agent affecting only one function has a highly sounding application in the field of treatment by anticancer, since most anticancers used in the present time affect both cancerous diseased cells and healthy ones which in turns affect the general health of the patients. Therefore, there is a real need for having a chemotherapeutic agent which controls only one function. In this paper, we discuss the synthesis, spectral characterization and biocidal efficiency of series Schiff base compounds.

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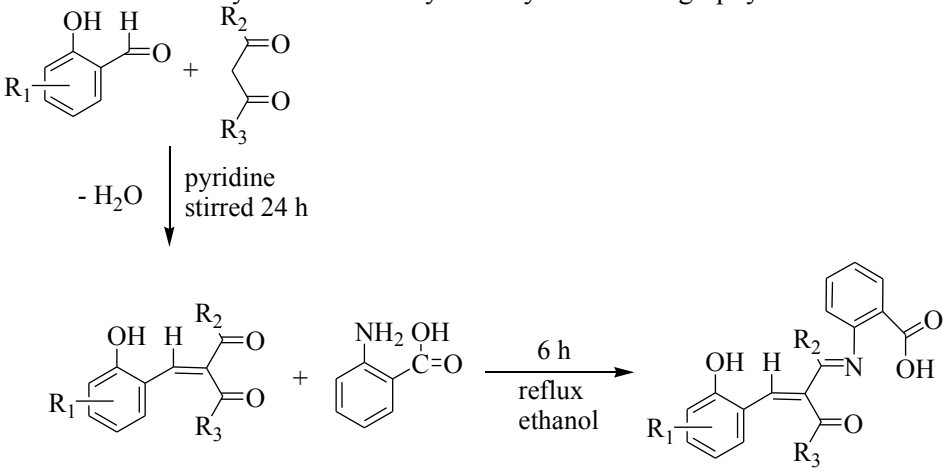
Experimental

Physical Measurements

All the reagents used were of analar or chemically pure grade. Solvents were purified and dried according to standard procedures. Biocidal studies were carried out according to reported procedures [13]. Melting points were recorded on a Veego VMP-DS melting point apparatus and are uncorrected. The micro analyses were performed using Vario EL III CHNS analyzer at Cochin University, Kerala, India. Mass spectra were recorded at IIT Madras. FT-IR spectra were recorded in KBr pellets in the region 400–4000 cm^{-1} using Shimadzu instrument. ^{1}H-NMR spectra for the ligands were recorded in Indian Institute of Science, Bangalore. Electronic spectra were recorded in CH_2Cl_2 with a Systronics Double beam UV–Vis Spectrophotometer-2202 in the range 200–800 nm.

Synthesis of new Schiff bases

Tridentate Schiff base ligands were synthesized from the reactions of *o*-aminobenzoic acid with Knovenegal condensate of β-ketoesters [14] (2-[3-(2-hydroxy-phenyl)-1-methyl-2-phenoxycarbonyl-allylideneamino]-benzoic acid, 2-[3-(3-hydroxy-naphthalen-2-yl)-1-methyl-2-phenoxycarbonyl-allylideneamino]-benzoic acid in 1:1 molar ratio in ethanolic medium and refluxed for 6 hours and given the Scheme below. Purity was checked by thin-layer chromatography.



SB1 : R_1 = H, R_2 = C_6H_5, R_3 = OC_2H_5; SB2 : R_1 = C_4H_4, R_2 = C_6H_5, R_3 = OC_2H_5;
SB3 : R_1 = H, R_2 = CH_3, R_3 = OC_2H_5; SB4 : R_1 = C_4H_4, R_2 = CH_3, R_3 = OC_2H_5

Scheme. Two stage Synthesis of new Schiff bases

RESULTS AND DISCUSSION

The new compounds are soluble in most of the common organic solvents. Their purity was checked by thin-layer chromatography. The analytical data obtained for all the new compounds agree well with the proposed molecular formulae (Scheme 1) and are listed in Table 1.

Table 1. Analytical data of Schiff bases

Compound	Colour	Melting point (°C)	Emprical formula	Molecular weight	Elemental analysis Calculated (found) (%)		
					C	H	N
SB1	yellow	126	$C_{25}H_{21}NO_5$	415.44	72.28(72.24)	5.10(5.08)	3.37(3.35)
SB2	brown	134	$C_{29}H_{23}NO_5$	465.5	74.83(74.75)	4.98(4.92)	3.01(2.99)

FT-IR Spectra

The IR spectra of the ligands were recorded using KBr pellets and the values are listed in Table 2. For the anthranilic acid moiety, the $\nu_{(OH)}$ absorption observed at 3300 cm^{-1} in the free Schiff base and the $\nu_{(C=O)}$ frequency of the carbonyl was seen as a band at 1719 - 1736 cm^{-1}.

The $\nu_{(C=N)}$ bands appears in the region of 1608- 1619 cm^{-1}. In the free ligands, the asymmetric and symmetric stretching frequency of the ester group was found in the range of 1665 -1681 cm^{-1} and 1463-1489 cm^{-1}. The band appears around 3233-3334 cm^{-1} in the ligands due to phenolic OH.

Table 2. FT-IR spectral and UV-Vis data of new Schiff bases

Compounds	IR spectra (cm^{-1})				UV-Vis λ_{max}(nm)
	$\nu_{asy(COO)}$	$\nu_{sym(COO)}$	$\nu_{C=N}$	ester $\nu_{C=O}$	
SB1	1665	1463	1610	1719	262,300,368,401,432,458,507
SB2	1681	1489	1619	1736	262,296, 370,388

Electronic spectral analysis

Electronic spectra of the two compounds were recorded in chloroform showed four to seven bands in the region 262–507 nm (Table 2). For the ligands, the high intensity bands around 262–368 nm and 370–507 nm has been designated as n– π^* and π – π^* transitions respectively for the electrons localized on the -COO-, >C=N and -COOH group of the Schiff bases.

^{1}H - NMR spectroscopic analysis

The ^{1}H - NMR spectra of the Schiff bases were recorded in chloroform (Table 3 and Fig 1-2). Multiplets are observed around 6.4–7.9 ppm in all the ligands have been assigned to aromatic protons. For COOH and phenolic OH protons in all the ligands showed a singlet in the region 13.0–13.5 ppm and 10.4–10.8 ppm, respectively. For CH protons all the ligands show singlet in the region 4.8 ppm. For ethoxy group methylene and methyl protons shows quartet and triplet in the region 3.1-4.9 ppm and 1.1–3.7 ppm, respectievely.

Table 3. ^{1}H – NMR Spectral data of Schiff bases

Compounds	^{1}H-NMR (ppm)
SB1	4.2 - 4.9 (q, CH_2), 3.1-3.7 (t, CH_3), 4.8 (s, CH), 6.4-7.9 (m, aromatic), 10.8(s, Ph-OH),13.5 (s, COOH)
SB2	3.1 – 3.6 (q, CH_2), 1.1-1.4 (t, CH_3), 4.8 (s, CH), 6.4 – 7.9 (m, aromatic), 10.4 (s, Ph-OH), 13.0 (s, COOH)

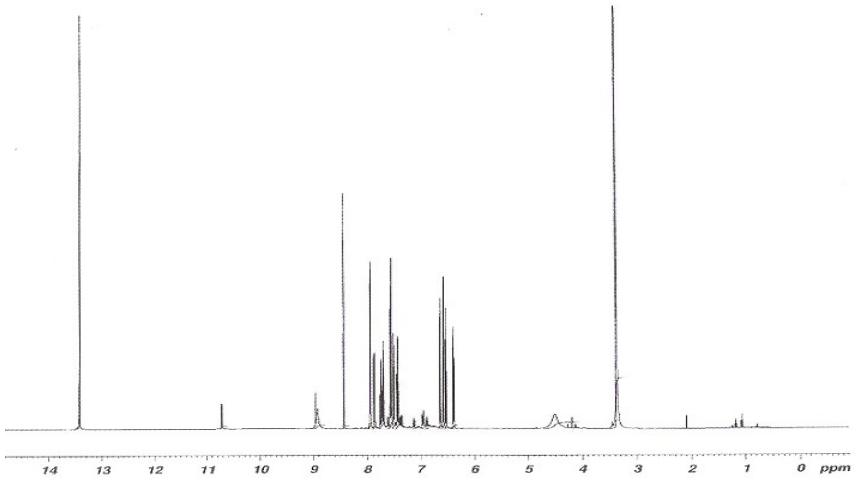


Fig.1. ^{1}H-NMR spectrum of SB1

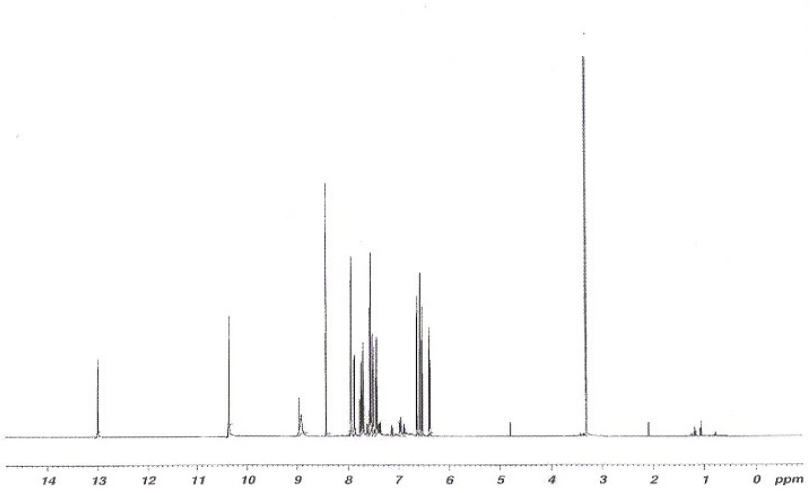


Fig.2. ^{1}H-NMR spectrum of SB2

Biocidal Studies

By testing the antibacterial and antifungal activity of these compounds we used more than one test organism to increase the chance of detecting antibiotic principles in tested materials. The sensitivity of microorganisms to standard antibiotic and free Schiff bases was determined by the assay plates which incubated at 28°C for two days for fungus and at 37°C for one day for bacteria. All of the tested compounds showed a remarkable biological activity against bacteria (*S.epidermis and E. coli*) and fungus (*Botrytis cinerea and Aspergillus niger*) by *Disc diffusion* method at 0.25%, 0.50% and 1% concentration and the results are shown in Table 4. The results indicate that the some of the Schiff bases show greater microbial activity when compared with standard reference (*Ciprofloxacin* and *Co-trimoxazole*) against same microbes under identical experimental conditions. It is known that the membrane of fungus and bacteria are surrounded by an outer membrane containing liphopolysacherides. The newly synthesized Schiff bases seem to be able to combine with the liphophilic layer in order to enhance the membrane permeability of bacteria of bacteria and fungus. The lipid membrane surrounding the cell favors the passage of only lipidsoluble materials; thus the lipophilicity is an important factor that controls the antimicrobial activity. Also the increase in lipophilicity enhances the penetration of Schiff bases into the lipid membranes and thus restricts further growth of the organism [15,16]. The Schiff bases could enhances the antimicrobial effect on both strains probably due to >C=N, -COO-, C_2H_5 and phenyl groups, which interact with the double membrane [17]. The variation in the effectiveness of different compounds against different organisms depends either on the impermeability of the cells of the microbes or on differences in ribosome of microbial cells. The microbial screening was repeated twice and the error limit was found to be 0.2 – 0.5 mm. Most of the Schiff bases show better efficiency when compared with the standard (*Ciprofloxacin* and *Co-trimoxazole*).

Table 4. Biological activity of Schiff bases

Compounds	Antibacterial activity						Antifungal activity					
	S. epidermidis			*E. coli*			*B. cinerea*			*A. niger*		
	0.25	0.5	1	0.25	0.5	1	0.25	0.5	1	0.25	0.5	1
SB1	25	25	25	6	6	7	5	6	6	6	6	7
SB2	6	7	7	23	23	23	7	8	8	23	23	23
Standard	23			22			19			21		
Dichloromethane	No activity						No activity					

Conclusion

A series of new Schiff bases were synthesized and characterized by elemental analyses, mass spectra, spectral (FT-IR, UV–Vis and ^{1}H-NMR) studies. Based on the analytical and spectroscopic studies tentative structure has been proposed for all the Schiff bases. These Schiff bases were subjected to find out their biocidal activity against *S. epidermidis, E. coli*, *B. cinerea and A. niger.* Some of the Schiff bases show higher activity than the respective standards (*Ciprofloxacin* and *Co-trimoxazole*).

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