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Synthesis, Characterization and Antimicrobial Activity of Some Isatin Based Schiff Base Compounds.

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ABSTRACT

Isatin are known for their various biological activities. In this present study various Schiff bases were synthesized, characterized and evaluated for their antimicrobial activity. The compounds were prepared by reacting indole-2,3-dione and 5-substituted indole-2,3-dione with 2-amino-5-chlorobenzophenone to give Schiff base. All the synthesized compounds were characterized by various methods like TLC, MP, FTIR, ^{1}H NMR, ^{13}C NMR, Elemental analysis. The compounds have been evaluated for their antimicrobial activity.

Key words: Isatin, Schiff bases, FTIR, NMR, Kirby – Bauer disc diffusion method

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INTRODUCTION

1-H-indole-2,3-dione, (Isatin) and derivatives possess a broad range of biological and pharmacological properties and are widely used as starting materials for the synthesis of a broad range of heterocyclic compounds and substrates for drug synthesis. One of the next frequently encountered heterocyclic compounds in medicinal chemistry is isatin and its derivatives have gained unique importance due to the broad spectrum of pharmacological activities which are reflected by their use as antimicrobial [1-6], anticonvulsant [7,8], analgesic [9,10], anti-inflammatory [10], anticancer [11,12], antitubercular [13], antiviral [14-16], anti-HIV [17] activities. Schiff bases are used as substrates in the preparation of a number of industrial and biological active compounds via ring closure, cycloaddition and replacement reactions [18]. Moreover, Schiff bases derived from various heterocycles have been reported to possess cytoxic [19], anticonvulsant [20], antiproliferative [21], antimicrobial [22], anticancer [23], and antifungal activities [24]. In generally Schiff bases are reported to possess antimicrobial activities. The literatures survey revealed that introduction of electron-withdrawing groups at positions 5, 6 and 7 greatly increased activities from that of isatin, with substitution at the 5th position being most favorable. This is not surprising, as C-5 substitution has previously been associated with increased biological activity for a range of indole–base compounds [25,26] and the presence of substituted aromatic ring at 3rd position has been reported to be associated with antimicrobial properties [27,28]. The various substituent at 3rd position of the isatin which were reported are various substituted phenyl ring moisties [29,30], heterocyclic rings [31-33] and aliphatic system [34]. In the present study is a series of some different schiff bases are synthesized from 5–substituted isatin with 2–Amino–5–chlorobenzophenone. The melting points were taken in open capillaries and are uncorrected. IR spectra were recorded in KBr on Shimadzu Spectrometer, ^{1}H NMR, ^{13}C NMR in DMSO-D_6 on Bruker NMR Spectrometer and elemental analysis. The synthesized compounds have been evaluated for their antimicrobial activity.

MATERIAL AND METHODS

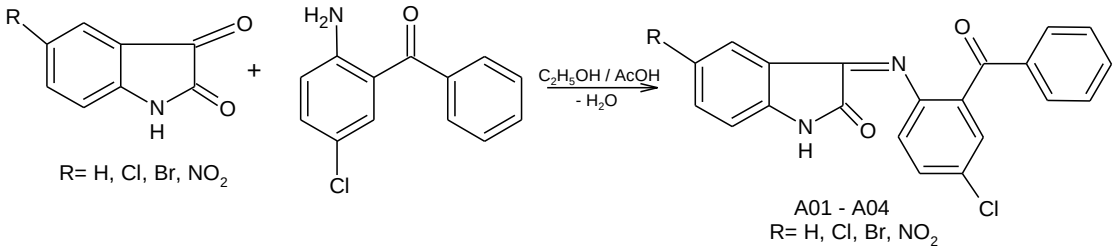
All solvents, reagents and catalysts were of analytical grade and used without further purification. The melting points were determined were uncorrected. The purity of compounds was confirmed by thin layer chromatography.

EXPERIMENTAL METHODS

General method for Synthesis of 3-[(2-benzoyl-4-chlorophenyl)imino]-5-substituted-1,3-dihydro-2*H*-indol-2-one (A01–A04)

0.01mole of equimolar mixture of 2–amino–5–chlorobenzophenone and substituted isatin were dissolved in 20mL of ethanol with few drops of acetic acid. It is reacted under refluxing conditions. After six hour of refluxing the reaction mixture was transferred into the 100 mL beaker. After the completion of reaction the content was cooled and kept a overnight. The separated product was filtered and recrystallized from ethanol.

Scheme of Preparation



RESULT AND DISCUSSION

The synthesized compounds were confirmed by physical parameter of colour, melting point and % yield. The structure of synthesized compounds has been characterized based on IR, ^{1}H NMR, ^{13}C NMR spectra and elemental analysis.

3-[(2-benzoyl-4-chlorophenyl)imino]-1,3- dihydro-2H-indol-2-one (A01):

Bright Orange crystal, 79% yield, mp 212–12^{0}C, IR (KBr) cm^{-1}: 3418 (NH), 3190 (aromatic CH), 1729 (Aromatic C=O), 1615 (C=N), 1535 (aromatic C=C), 1324 (C-N), 763 (Cl-substitution). ^{1}H NMR (DMSO-d6) δ: 11.0 (s, 1H, -NH), 7.0–7.6 (m, 12H, Ar-H), ^{13}C NMR (DMSO-d6) δ: 196 (Aromatic C=O), 184 (NH-C=O), 159 (C=N), 112–150 (Aromatic C). Anal. Calcd. for $C_{21}H_{13}ClN_2O_2$: C, 69.84; H,3.60; N, 7.76; Found: C, 69.64; H,3.69; N, 7.80.

3-[(2-benzoyl-4-chlorophenyl)imino]-5-bromo-1,3-dihydro-2H-indol-2-one (A02):

Yellow crystal, 81% yield, mp 220–21^{0}C, IR (KBr) cm^{-1}: 3418 (NH), 3191 (aromatic CH), 1748 (Aromatic C=O), 1615 (C=N), 1535 (aromatic C=C), 1356 (C-N), 891(Cl-substitution). ^{1}H NMR (DMSO-d6) δ: 11.1 (s, 1H, -NH), 7.1–7.7 (m, 11H, Ar-H), ^{13}C NMR (DMSO-d6) δ: 196 (Aromatic C=O), 183 (NH-C=O), 158 (C=N), 112–150(Aromatic C). Anal. Calcd. for $C_{21}H_{12}BrClN_2O_2$: C, 57.31; H,2.72; N, 6.36; Found: C, 57.34; H,2.76; N, 6.32.

3-[(2-benzoyl-4-chlorophenyl)imino]-5-chloro-1,3-dihydro-2H-indol-2-one (A03):

Yellow crystal, 76% yield, mp 219–220^{0}C, IR (KBr) cm^{-1}: 3419 (NH), 3186 (aromatic CH), 1753 (Aromatic C=O), 1615 (C=N), 1535 (aromatic C=C), 1356 (C-N), 763 (Cl-substitution). ^{1}H NMR (DMSO-d6) δ: 11.0 (s, 1H, -NH), 6.9–7.6 (m, 11H, Ar-H), ^{13}C NMR (DMSO-d6) δ: 196 (Aromatic C=O), 183 (NH-C=O), 159 (C=N), 113–150(Aromatic C). Anal. Calcd. for $C_{21}H_{12}Cl_2N_2O_2$: C, 63.75; H,3.03; N, 7.08; Found: C, 63.71; H,3.05; N, 7.10.

3-[(2-benzoyl-4-chlorophenyl)imino]-5-nitro-1,3-dihydro-2H-indol-2-one (A04):

Bright yellow crystal, 76% yield, mp 208–209^{0}C, IR (KBr) cm^{-1}: 3461 (NH), 3274 (aromatic CH), 1766 (Aromatic C=O), 1620 (C=N), 1534 (aromatic C=C), 1324 (C-N), 763 (Cl-substitution).^{1}H NMR (DMSO-d6) δ: 11.6 (s, 1H, -NH), 6.8–8.4 (m, 12H, Ar-H), ^{13}C NMR (DMSO-d6) δ: 196 (Aromatic C=O), 182 (NH-C=O), 159 (C=N), 112–156 (Aromatic C). Anal. Calcd. for $C_{21}H_{12}ClN_3O_4$: C, 62.09; H,3.20; N, 10.34; Found: C, 62.11; H,3.25; N, 10.31.

Antibacterial Activity

Table 1: Zone of inhibition (mm) of compounds

Sample code	Anti-bacterial activity																Anti-fungal activity			
	Gram positive								Gram negative											
	Staphylococcus				*Bacillus*				*Salmonella*				*Pseudomonas*				*Candida*			
	100 mcg	50 mcg	25 mcg	Std	100 mcg	50 mcg	25 mcg	Std	100 mcg	50 mcg	25 mcg	Std	100 mcg	50 mcg	25 mcg	Std	100 mcg	50 mcg	25 mcg	Std
A01	5	2	-	11	2	1	-	9	3	2	-	9	6	4	3	9	-	-	-	14
A02	8	6	4	5	8	6	5	3	8	5	5	5	8	7	5	10	7	6	4	12
A03	8	7	5	9	9	7	5	9	9	8	7	10	9	8	6	8	7	5	3	21
A04	9	7	5	2	9	7	5	9	6	5	3	10	9	8	5	5	7	5	4	15

The synthesized compounds were tested for their antimicrobial activity by measuring the zone of inhibition on agar plates (Kirby – Bauer Disc diffusion method) with *Staphylococcus.spp, Bacillus.spp*., *Salmonella.spp*, *Pseudomonas.spp.* and *candida. Ampicillin* is used as standard antibiotic drugs. The large zone of inhibition shows the compounds of A04 and A02 in 100mcg concentration against in Gram positive bacteria of *Staphylococcus.spp* and *Bacillus.spp*., Similarly the large zone of inhibition shows the compounds of A04 and A03 in 100mcg concentration against in Gram negative bacteria of *Salmonella.spp*, *Pseudomonas.spp*. Anti fungal activity of synthesized compound shows the moderate activity. Zone of inhibitions are presented in the table (1).

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CONCLUSION

Isatin based Schiff bases were synthesized and the structures of the compounds were established by means of FTIR, ^{1}H NMR, ^{13}C NMR and Elemental analysis. All the compounds were evaluated for antimicrobial activity by Kirby – Bauer Disc diffusion method. All the compounds have shown significant and moderate antibacterial activity. With the suitable molecular modification of these compounds can be proved as potent antimicrobial against in future.

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