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Synthesis and Antimicrobial Evaluation of Novel Azo Compounds Bearing Imidazolyl Moiety

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ABSTRACT:

Novel imidazolyl bearing azo compounds were synthesized by the reaction of Schiff base with diazonium salts of different aromatic amines. All the newly synthesized azo compounds were characterized by different spectroscopic techniques and elemental analyses. All the compounds were evaluated for their antimicrobial activity.

KEYWORDS: Imidazolyl, Azo compounds, Schiff base, Antimicrobial activity

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INTRODUCTION:

Azo compounds have wide utility in the textile & paper industries and as coloring agents for foods and cosmetics industries[1].

Azo compounds have been reported as important structural motifs in the medicinal field. Prontosil is a known azo-sulfonamide compound clinically used as an antibacterial. Literature survey revealed many research articles reporting their wide spectrum of biological activities such as antibacterial, antifungal, pasticidal, antiviral, anti-inflammatory etc.[2-7]. The imidazole ring is a constituent of several important compounds necessary for human body functions, including purine, histamine, histidine, biotin etc. They display variety of biological activities[8] and many imidazole containing compounds are in clinical use, e.g. metronidazole and nitrosoimidazole, cimetidine, azomycin etc.

In light of the interesting variety of biological activities seen in compounds containing azo linkage and imidazolyl compounds; and as a continuation of our efforts in synthesizing bioactive heterocycles[9-11], it was thought worthwhile to synthesize a series of novel azo compounds bearing Imidazolyl moiety and screen them for antimicrobial activity.

MATERIALS AND METHODS

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on SHIMADZU-FT-IR-8400 [Fourier transform–infrared (FT-IR)]. The IR spectra were taken using KBr pellets. 1H NMR were recorded on Bruker AMX spectrometer. Elemental analysis was carried out using Heraus CHN rapid analyzer. All the chemicals were commercial products and were used without further purification.

Procedure for the Synthesis of 4-(4-hydroxybenzylidene)-1-{4-[(4-chloro benzylidene)amino]phenyl}-2-phenyl-imidazol-5-one (2)

In a 250 ml flask (equipped with reflux condenser), a mixture of 1-(4-aminophenyl)-4-(4-hydroxybenzylidene)-2-phenyl-imidazol-5-one (0.01 M), 4-chloro benzaldehyde (0.01 M) and absolute alcohol (30 ml) was placed and 1 to 2 drops of hydrochloric acid was added. The resulting mixture was then heated on water bath for 6 hours and then cooled. The precipitates thus obtained were filtered off and re-crystallized from absolute alcohol.

General Procedure for the Synthesis of 2-phenyl-1-[4-({(4-chlorophenyl)[aryl diazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-ones (3a-h)

To a solution of aryl amines (0.01 M) in glacial acetic acid (10 ml), concentrated hydrochloric acid (3 ml) was added at 0 to 5^0C. To this mixture, a solution of $NaNO_2$ (1 g in 5 ml of water) was added. The diazonium salt solution thus prepared was added dropwise to a solution of compound 4-(p-hydroxybenzylidene)-1-{4-[(4-chlorobenzylidene)amino]phenyl}-2-phenyl-imidazol-5-one **(2)** (0.01 M) in methanol (40 ml) with constant stirring at 0^0C temperature. The reaction mixture was kept at room temperature for one day and then poured into crushed ice. The resulting solid was washed with water and the obtained product was crystallized from absolute ethanol.

2-phenyl-1-[4-({(4-chlorophenyl)[phenyldiazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-one 3a: Yield 58%. mp 157-159 °C. ^{1}H NMR δ 5.51 (s, 1H, =CH), 6.76-7.53 (m, 22H, Ar-H), 8.51 (s, 1H, OH). MS: m/z 582. Anal. Calcd. for $C_{35}H_{24}ClN_5O_2$: C, 72.22; H, 4.16; N, 12.03; Found: C, 72.19; H, 4.13; N, 12.01.

2-phenyl-1-[4-({(4-chlorophenyl)[3-methylphenyldiazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-one 3b: Yield 65%. mp 196-198 °C. ^{1}H NMR δ 2.07 (s, 3H, CH_3), 5.54 (s, 1H, =CH), 6.52-7.51 (m, 21H, Ar-H), 8.47 (s, 1H, OH). MS: m/z 596. Anal. Calcd. for $C_{36}H_{26}ClN_5O_2$: C, 72.54; H, 4.40; N, 11.75; Found: C, 72.51; H, 4.38; N, 11.72.

2-phenyl-1-[4-({(4-chlorophenyl)[4-methylphenyldiazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-one 3c: Yield 61%. mp 178-180 °C. ^{1}H NMR δ 2.12 (s, 3H, CH_3), 5.57 (s, 1H, =CH), 6.48-7.57 (m, 21H, Ar-H), 8.50 (s, 1H, OH). MS: m/z 596. Anal. Calcd. for $C_{36}H_{26}ClN_5O_2$: C, 72.54; H, 4.40; N, 11.75; Found: C, 72.52; H, 4.38; N, 11.73.

2-phenyl-1-[4-({(4-chlorophenyl)[2-nitrophenyldiazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-one 3d: Yield 58%. mp 164-166 °C. ^{1}H NMR δ 5.62 (s, 1H, =CH), 6.48-7.90 (m, 21H, Ar-H), 8.43 (s, 1H, OH). MS: m/z 627. Anal. Calcd. for $C_{35}H_{23}ClN_6O_4$: C, 67.04; H, 3.70; N, 13.40; Found: C, 67.01; H, 3.67; N, 13.38.

2-phenyl-1-[4-({(4-chlorophenyl)[3-nitrophenyldiazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-one 3e: Yield 62%. mp 155-157 °C. ^{1}H NMR δ 5.57 (s, 1H, =CH), 6.39-7.87 (m, 21H, Ar-H), 8.41 (s, 1H, OH). MS: m/z 627. Anal. Calcd. for $C_{35}H_{23}ClN_6O_4$: C, 67.04; H, 3.70; N, 13.40; Found: C, 67.02; H, 3.67; N, 13.37.

2-phenyl-1-[4-({(4-chlorophenyl)[4-nitrophenyldiazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-one 3f: Yield 55%. mp 188-190 °C. ^{1}H NMR δ 5.48 (s, 1H, =CH), 6.48-7.77 (m, 21H, Ar-H), 8.48 (s, 1H, OH). MS: m/z 627. Anal. Calcd. for $C_{35}H_{23}ClN_6O_4$: C, 67.04; H, 3.70; N, 13.40; Found: C, 67.01; H, 3.67; N, 13.37.

2-phenyl-1-[4-({(4-chlorophenyl)[3-chlorophenyldiazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-one 3g: Yield 61%. mp 192-194 °C. ^{1}H NMR δ 5.51 (s, 1H, =CH), 6.31-7.42 (m, 21H, Ar-H), 8.50 (s, 1H, OH). MS: m/z 616. Anal. Calcd. for $C_{35}H_{23}Cl_2N_5O_2$: C, 68.19; H, 3.76; N, 11.36; Found: C, 68.16; H, 3.74; N, 11.33.

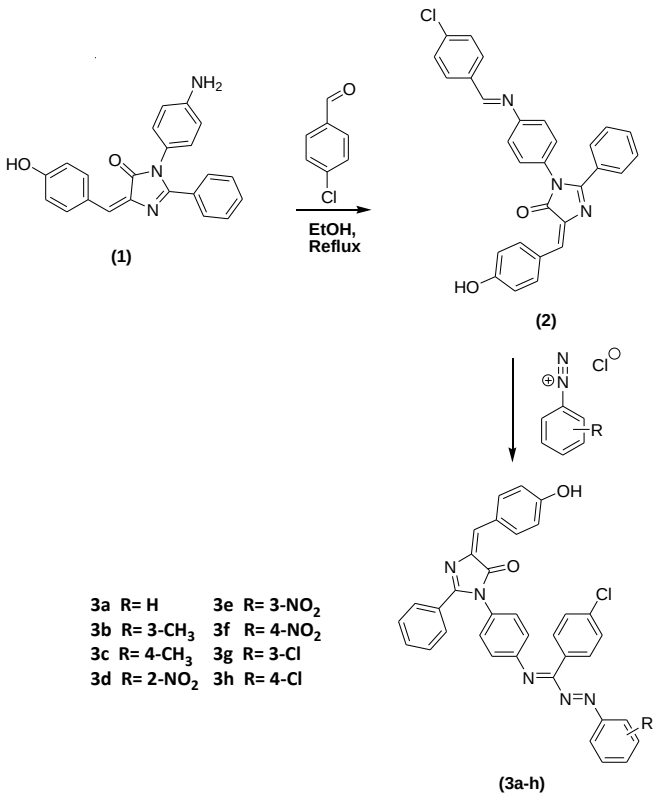
2-phenyl-1-[4-({(4-chlorophenyl)[4-chlorophenyldiazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-one 3h: Yield 58%. mp 196-198 °C. ^{1}H NMR δ 5.45 (s, 1H, =CH), 6.48-7.49 (m, 21H, Ar-H), 8.53 (s, 1H, OH). MS: m/z 616. Anal. Calcd. for $C_{35}H_{23}Cl_2N_5O_2$: C, 68.19; H, 3.76; N, 11.36; Found: C, 68.16; H, 3.72; N, 11.34.

RESULTS AND DISCUSSION

Chemistry

The synthesis of 4-(4-hydroxybenzylidene)-1-{4-[(4-chloro benzylidene)amino]phenyl}-2-phenyl-imidazol-5-one **(2)**

was accomplished by refluxing 1-(4-aminophenyl)-4-(4-hydroxybenzylidene)-2-phenyl-imidazol-5-one **(1)** and 4-chorobenzaldehyde using ethanol as solvent, which was then reacted with different diazonium salts to furnish the title compounds 2-phenyl-1-[4-({(4-chlorophenyl)[aryldiazenyl]methylene}amino)phenyl]-4-(p-hydroxybenzylidene)-imidazol-5-ones **(3a-h) (Scheme 1)**.



Scheme 1. Synthesis of azo compounds (3a-h)

All the newly synthesized azo compounds **(3a-h)** were characterized by different spectroscopic techniques and elemental analyses. The purity of the compounds was controlled by TLC. The spectral data of all the newly synthesized compounds were in full agreement with the proposed structures.

Biological screening

The compounds **(3a-h)** were evaluated for their antibacterial activity against Escherichia coli, Staphylococcus aureus and antifungal activity against Candida albicans using the cup-plate method. After 24 h of incubation at 37 °C, the zones of inhibition were measured in mm. The activities were compared with those of some known drugs, viz. Penicillin, Kanamycin and Amphotericin B. The results are summarized in **Table 1**.

CONCLUSION

To summarize, a series of novel azo compounds bearing imidazolyl moiety was synthesized. The newly synthesized heterocycles exhibited moderate to promising antimicrobial activity against standard strains. These results make them interesting lead molecules for further synthesis of related heterocycles and their biological evaluation.

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Table-1. **Antimicrobial Evaluation of azo compounds (3a-h)**

Compound	**Antibacterial Activity**		**Antifungal Activity**
	E. coli	S. aureus	C. albicans
3a	14	17	17
3b	18	13	13
3c	17	18	14
3d	-	14	14
3e	13	16	13
3f	16	14	17
3g	14	-	12
3h	16	18	18
Penicillin	18	20	-
Kanamycin	19	24	-
Amphotericin B	-	-	21