Synthesis and Antibacterial Activities of Some Schiff Bases

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Abstract Schiff bases *p*-hydroxybenzylidene-2-carboxyaniline, *p*-nitrobenzylidene-2-carboxyaniline, *p*-(*N*, *N*-dimethyl)aminobenzylidene-2-carboxyaniline, *N*-(4-hydroxybenzylidene)-benzene-1,2-diamine, *N*-(4-nitrobenzylidene)benzene-1,2-diamine, *N*-(4-(*N*, *N*-dimethylaminobenzylidene)benzene-1,2-diamine, *N*-(4-(*N*, *N*-dimethylamino)benzylidene)naphthalen-1-amine, *N*-(4-nitrobenzylidene)naphthalen-1-amine, *N*-(4-chlorobenzylidene)naphthalen-1-amine, sodium-4-(4-(*N*, *N*-dimethylamino)benzylideneamino)naphthalene-1-sulfonate, sodium -4-(4-nitrobenzylideneamino)naphthalene-1-sulfonate and sodium-4-(4-chlorobenzylideneamino)naphthalene-1-sulfonate obtained by condensation of aniline and naphthylamine derivatives with some aromatic aldehydes were characterized by physical and spectral methods. The biological activity of these products were as antibacterial agents against three species of human pathogenic bacteria such as *Escherichia coli*, *Staphylococcus aureus* and *Klebsiella* sp. Nearly 50% of these compounds showed reasonable activity against the bacterial species investigated and we found that the antibacterial activity is dependent on the molecular structure of the compounds.

Keywords: Schiff bases, Anilines, Naphthylamines, Antibacterial activity.

Introduction

Schiff bases derived from aromatic amines and aromatic aldehydes have a wide variety of applications in many fields, *e.g.*, biological, inorganic and analytical chemistry¹⁻⁴.

Application of many new analytical devices requires the presence of organic reagents as essential compounds of the measuring system. Among the organic reagents actually used, Schiff bases possess excellent characteristics, structural similarities with natural biological substances, relatively simple preparation procedures and the synthetic flexibility that enables design of suitable structural properties^{5,6}. The antibacterial activity is dependent on the molecular structure of the compound, the solvent used and the bacterial species⁷⁻⁹.

The Schiff bases prepared are condensation products of aromatic aldehyde derivatives with aromatic amines derivatives and presented below. In this work the spectroscopic characteristics and antibacterial activity against three species of human pathogenic bacteria such as *Escherichia coli*, *Staphylococcus aureus* and *Klebsiella* sp of these Schiff bases are presented.

Experimental

All chemicals and solvents used for synthesis were of reagent grade. All melting points were taken on a melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu 5000 instrument. ¹H NMR were run on a Jeol 500 MHz instrument using TMS as internal standard, and DMSO as solvent. The spectral analyses were carried out at the NMR laboratory, Alexandria University, Alexandria; the elemental analyses at Microanalytical center Cairo University, Cairo, Egypt

The Schiff bases (**I-VI**) were prepared according to the reported methods¹⁰⁻¹². The procedure is as follows: A solution of the amine derivative (0.01 mol) in absolute ethanol (10 mL) was slowly added to a solution of the aldehyde derivative (0.01 mol) in absolute ethanol (10 mL). After stirring the reaction mixture for 2 h (Compounds **I**, **II** and **III**) and for 5 h at 60-70 °C and cooling (Compounds **IV**, **V** and **VI**), a precipitate was formed which collected by filtration then washed several times with cold ethanol and recrystallised from ethanol.

p-Hydroxybenzylidene-2-carboxyaniline (**I**)

Compound **I** was prepared from anthranilic acid and *p*-hydroxybenzaldehyde; pale orange; m.p. 229.5-230 °C; 1.6 g (70%) yield. IR (KBr, cm⁻¹) $\nu = 3500$ (OH), 2900 (C-H), 1715 (C=O), 1615 (C=N), 1490 (C=C), 1280, 1170 (C-O); ¹H NMR (500 MHz, DMSO); δ (ppm): 6.41-7.66 (8H, m, Ar-H), 8.3 (1H, s, CH=N), 9.70 (1H, s, Ar-OH), 11.00 (1H, s, COOH); C₁₄H₁₁NO₃ (241.2); calcd. C 69.65%, H 4.56%, N 5.80%; found C 68.92%, H 4.52%, N 5.77%.

p-Nitrobenzylidene-2-carboxyaniline (**II**)

Compound **II** was prepared from anthranilic acid and *p*-nitrobenzaldehyde; yellow-white; m.p. 172-174 °C; 1.7 g (62%) yield. IR (KBr, cm⁻¹) $\nu = 3500$ (OH), 2900 (C-H), 1720 (C=O), 1610 (C=N), 1480 (C=C), 1495, 1320 (N=O), 1285, 1170 (C-O); ¹H NMR (500 MHz, DMSO);

δ (ppm): 6.35-8.28 (8H, m, Ar-H), 8.30 (1H, s, CH=N), 10.11 (1H, s, COOH); $C_{14}H_{10}N_2O_4$ (270.2): calcd. C 62.17%, H 3.70%, N 10.36%; found C 61.88%, H 3.65%, N 10.03%.

p-(*N,N*-dimethyl)aminobenzylidene-2-carboxyaniline (**III**)

Compound **III** was prepared from anthranilic acid and *p*-(*N,N*-dimethylamino)benzaldehyde; pale green; m.p. 198 °C; 2.0 g (75%) yield. IR (KBr, cm^{-1}) ν = 3500 (OH), 2910 (C-H), 1725 (C=O), 1615 (C=N), 1355 (C-N), 1475 (C=C), 1280, 1170 (C-O); 1H NMR (500 MHz, DMSO); δ (ppm): 2.89 (6H, s, N-(CH₃)₂), 6.41-7.62 (8H, m, Ar-H), 8.29 (1H, s, CH=N), 9.57 (1H, s, Ar-OH); $C_{16}H_{16}N_2O_2$ (268.2): calcd. C 71.58%, H 5.96%, N 10.43%; found C 70.42%, H 5.81%, N 9.33%.

N-(4-Hydroxybenzylidene)-benzene-1,2-diamine (**IV**)

It was prepared from *o*-phenylenediamine and *p*-hydroxybenzaldehyde; cotton pale brown; m.p. 148 °C; 1.3 g (64%) yield. IR (KBr, cm^{-1}) ν = 3400, 3300 (N-H), 3000 (O-H), 3010 (C-H), 1600 (C=N), 1445 (C=C), 1360 (C-N); 1H NMR (500 MHz, DMSO); δ (ppm): 5.00 (2H, s, -NH₂), 6.41-7.70 (8H, m, Ar-H), 8.38 (1H, s, CH=N), 10.47 (1H, s, Ar-OH); $C_{13}H_{12}N_2O$ (212.2): calcd. C 73.51%, H 5.65%, N 13.19%; found C 73.01%, H 5.42%, N 12.87%.

N-(4-Nitrobenzylidene)-benzene-1,2-diamine (**V**)

It was prepared from *o*-phenylenediamine and *p*-nitrobenzaldehyde; pale brown; m.p. 317-318 °C; 1.9 g (81%) yield. IR (KBr, cm^{-1}) ν = 3400, 3300 (N-H), 3010 (C-H), 1615 (C=N), 1440 (C=C), 1365 (C-N), 1510, 1330 (N=O); 1H NMR (500 MHz, DMSO); δ (ppm): 5.00 (2H, s, -NH₂), 6.40-8.1 (8H, m, Ar-H), 8.38 (1H, s, CH=N); $C_{13}H_{11}N_3O_2$ (241.2): calcd. C 64.67%, H 4.56%, N 17.41%; found C 63.28%, H 4.22%, N 15.96%.

N-(4-(*N,N*-Dimethylaminobenzylidene)-benzene-1,2-diamine (**VI**)

It was prepared from *o*-phenylenediamine and *p*-(*N,N*-dimethyl)benzaldehyde; yellow; m.p. 141-142 °C; 0.4 g (16%) yield. IR (KBr, cm^{-1}) ν = 3460, 3370 (N-H), 2900, 2800 (C-H), 1600 (C=N), 1440 (C=C), 1360 (C-N); 1H NMR (500 MHz, DMSO); δ (ppm): 2.86 (6H, s, -N-(CH₃)₂), 4.97 (2H, s, -NH₂), 6.40-7.66 (8H, m, Ar-H), 8.31 (1H, s, CH=N); $C_{15}H_{17}N_3$ (239.2): calcd. C 75.25%, H 7.10%, N 17.55%; found C 74.90%, H 6.58%, N 17.04%.

The Schiff bases (**VII-XII**) were prepared according to the reported methods¹⁰⁻¹². The procedure is as follows: A solution of the amine derivative (0.01 mol) in absolute ethanol (10 mL), (with 0.01 mol NaOH for compounds **IV-VI**), was slowly added to a solution of the aldehyde derivative (0.01 mol) in absolute ethanol (10 mL). After stirring the reaction mixture for 2 h (Compounds **I, II** and **III**) and for 5-10 h at 60-70 °C and cooling (Compounds **IV, V** and **VI**), a precipitate was formed which collected by filtration then washed several times with cold ethanol and recrystallised from ethanol.

N-(4-(*N,N*-Dimethylamino)benzylidene)naphthalene-1-amine (**VII**)

It was prepared from 1-naphthylamine and *p*-(*N,N*-dimethylamino)benzaldehyde; yellow; m.p. 112-114 °C; 2.1 g (76%) yield. IR (KBr, cm^{-1}) ν = 3050 (=C-N), 3020 (=C-H), 2900 (C-H), 1600 (C=N), 1480 (C=C), 1300 (C-N); 1H NMR (500 MHz, DMSO); δ (ppm): 2.84 (6H, s, -NMe₂), 6.63-7.71 (11H, m, Ar-H), 8.32 (1H, s, CH=N); $C_{19}H_{18}N_2$ (274.3): calcd. C 83%, H 6.5%, N 10.2%; found C 82.8%, H 6.45%, N 10.03%.

N-(4-Nitrobenzylidene)naphthalene-1-amine (**VIII**)

It was prepared from 1-naphthylamine and *p*-nitrobenzaldehyde; dark yellow; m.p. 164-165 °C; 2.3 g (85%) yield. IR (KBr, cm^{-1}) ν = 3020 (=C-H), 1600 (C=N), 1480 (C=C), 1510, 1330

(N=O); ^1H NMR (500 MHz, DMSO); δ (ppm): 7.26-8.27 (11H, m, Ar-H), 8.86 (1H, s, CH=N); $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}_2$ (276.3): calcd. C 74%, H 4.3%, N 10.1%; found C 72.9%, H 4.25, N 9.77%.

N-(4-Chlorobenzylidene)naphthalene-1-amine (**IX**)

It was prepared from 1-naphthylamine and *p*-chlorobenzaldehyde; pale yellow; m.p. 103-105 °C; 2.08 g (78%) yield. IR (KBr, cm^{-1}) ν = 3020 (=C-H), 1620 (C=N), 1480 (C=C), 1100-1035 (C-Cl); ^1H NMR (500 MHz, DMSO); δ (ppm): 7.1-7.9 (11H, m, Ar-H), 8.64 (1H, s, CH=N); $\text{C}_{17}\text{H}_{12}\text{NCl}$ (265.7): calcd. C 77%, H 4.5%, N 5.3%; found C 76.5%, H 4.49%, N 5.26%.

Sodium-4-(4-(*N,N*-dimethylamino)benzylideneamino)naphthalene-1-sulfonate (**X**)

It was prepared from 4-amino-1-naphthalenesulfonic acid and *p*-(*N,N*-dimethylamino)benzaldehyde; green-yellow; m.p. > 370 °C; 3.6 g (96%) yield. IR (KBr, cm^{-1}) ν = 3600-3100, 1250-1150 (S=O), 3020 (=C-H), 1600 (C=N), 1480 (C=C), 1310 (C-N), 650 (S-O); ^1H NMR (500 MHz, DMSO); δ (ppm): 2.89 (6H, s, -NMe₂) 6.68-8.50 (10H, m, Ar-H), 8.37 (1H, s, CH=N). $\text{C}_{19}\text{H}_{17}\text{N}_2\text{O}_3\text{SNa}$ (377.4): calcd. C 60%, H 4.5%, N 7.4%; found C 59.6%, 4.43%, N 7.33%.

Sodium-4-(4-nitrobenzylideneamino)naphthalene-1-sulfonate (**XI**)

Was prepared from 4-amino-1-naphthalenesulfonic acid and *p*-nitrobenzaldehyde; dark brown; m.p. > 370 °C; 2.3 g (63%) yield. IR (KBr, cm^{-1}) ν = 3600-3100, 1250-1150 (S=O), 3030 (=C-H), 1600 (C=N), 1460 (C=C), 1510, 1350 (N=O), 650 (S-O); ^1H NMR (500 MHz, DMSO); δ (ppm): 7.20-8.61 (10H, m, Ar-H), 8.68 (1H, s, CH=N) $\text{C}_{17}\text{H}_{11}\text{N}_2\text{O}_5\text{SNa}$ (379.3): calcd. C 54%, H 2.9%, N 7.4%; found C 53.5%, H 2.8%, N 7.2%.

Sodium-4-(4-chlorobenzylideneamino)naphthalene-1-sulfonate (**XII**)

It was prepared from 4-amino-1-naphthalenesulfonic acid and *p*-chlorobenzaldehyde; grey; m.p. > 370 °C; 1.8 g (51%) yield. IR (KBr, cm^{-1}) ν = 3600-3100, 1250-1150 (S=O), 3020 (=C-H), 1620 (C=N), 1470 (C=C), 1100-1035 (C-Cl), 650 (S-O); ^1H NMR (500 MHz, DMSO); δ (ppm): 7.17-8.62 (10H, m, Ar-H), 8.65 (1H, s, CH=N); $\text{C}_{17}\text{H}_{11}\text{NO}_3\text{ClSNa}$ (368.8): calcd. C 55%, H 3%, N 3.8%; found C 54.9%, H 2.98%, N 3.7%.

Antibacterial assay

The antibacterial tests were assayed according to the diffusion method. The strains of bacteria used were *Escherichia coli*, *Staphylococcus aureus* and *Klebsiella* sp. All species were isolated from patients in Al-Jamahiriya hospital, Benghazi, Libya. The identity of all the strains was confirmed. A bacterial suspension was prepared and added to the sterilized nutrient agar (OXID/England) medium before solidification. The medium with bacteria was poured into sterilized Petri dishes under aseptic condition. Different weights of Schiff bases (5 mg, 10 mg and 20 mg) were placed on the surface of the culture and incubated at 37 °C for 24 h. After incubation, the average of inhibition zones was recorded (mm). Antibacterial activity was indicated by the presence of clear inhibition zones around the samples.

Results and Discussion

Schiff bases were prepared in this work through condensation of aniline derivatives and naphthylamine derivatives with some aromatic aldehydes, The IR and NMR spectral data confirmed their molecular structure. They showed different effects on bacterial species.

Table 1 shows the mean of inhibition zone of some Schiff bases which were tested at different concentrations of 5, 10 and 20 mg against several species of human pathogenic bacteria. The results from this study indicated that **I**, **II**, **III**, **XI** and **XII** had antibacterial activities against *Escherichia coli* and *Klebsilla* sp which are known as resistant to most commercial antibiotics used. Also, the compounds **I-III** and **X-XII** had effects on *Staphylococcus aureus*. In contrast, no effect was observed of IV-IX compounds against all bacterial tested.

Table 1. The effect of Schiff bases on bacteria growth

Species of bacteria Samples	Mean of inhibition zone, mm								
	<i>Staphylococcus aureus</i>			<i>Escherichia coli</i>			<i>Klebsilla sp</i>		
	5 mg	10 mg	20 mg	5 mg	10 mg	20 mg	5 mg	10 mg	20 mg
I	10	15	22	10	15	18	10	14	18
II	15	25	35	15	20	25	15	24	30
III	20	25	30	12	16	20	15	18	22
IV	-	-	-	-	-	-	-	-	-
V	-	-	-	-	-	-	-	-	-
VI	-	-	-	-	-	-	-	-	-
VII	-	-	-	-	-	-	-	-	-
VIII	-	-	-	-	-	-	-	-	-
IX	-	-	-	-	-	-	-	-	-
X	7	11	15	-	-	-	-	-	-
XI	22	28	35	18	22	30	15	20	25
XII	9	13	20	4	8	16	10	15	25

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