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Spectral Characterization and Antimicrobial Activity of Some Schiff Bases Derived from 4-Methyl-2-aminophenol

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A series of *N*-(5-methyl-2-hydroxyphenyl)-(2/3/4/5-substituted)-benzaldimines (**I**—**XIII**) were synthesized using appropriate synthetic route. Their structures were characterized by FT-IR, UV-Visible, ESI-MS, ^{1}H- and ^{13}C-NMR spectroscopic techniques and analytical methods. The crystal structure of *N*-(5-methyl-2-hydroxyphenyl)-3,4-dimethoxybenzaldimine (**XIII**) was determined by X-ray diffraction at room temperature. Relationship between the melting points and the structures of the compounds were examined. Antibacterial activities of the compounds were evaluated against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Proteus mirabilis*. Antifungal activities were reported for *Candida albicans*. Some of the Schiff bases showed considerable antimicrobial activity against *S. aureus* and *C. albicans*.

Keywords Schiff bases, methylhydroxyphenyl, spectroscopy, X-ray diffraction, antimicrobial

Introduction

Schiff bases are some of the most widely used organic compounds. They are used as pigments and dyes, catalysts, intermediates in organic synthesis, and as polymer stabilizers.[1,2] They are also used as substrates in the preparation of a number of industrial and biologically active compounds *via* ring closure, cycloaddition, and replacement reactions.[3,4]

Schiff bases are widely applicable in analytical determination, using reactions of condensation of primary amines and carbonyl compounds in which the azomethine bond is formed (determination of compounds with an amino or carbonyl group); using complex formation reactions (determination of amines, carbonyl compounds and metal ions); or utilizing the variation in their spectroscopic characteristics following changes in pH and solvent.[5-9] They exhibit a broad range of biological activities, including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, antipyretic, and herbicide properties.[1,10,11] On the other hand, it was reported that some Schiff bases have antitumor activity.[12-20] 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.[21-24] Schiff bases have also been extensively used as ligands in coordination chemistry because of their excellent donor abilities and chelating agents.[25-30]

In this study, keeping in view the facts mentioned above, we synthesized thirteen benzaldimine Schiff bases (Scheme 1) derived from 4-methyl-2-aminophenol with various salicyl- and dimethoxy-benzaldehyde derivatives and characterized them by using analytical and spectroscopic techniques. Antibacterial and antifungal activities of the Schiff bases were evaluated by the disk diffusion method against six bacteria and *C. albicans* as fungus.

Experimental

Chemistry and apparatus

All chemicals and solvents are of reagent grade and were used without further purification. Elemental data were obtained with a Thermo Finnigan Flash EA 1112 analyzer. Melting points were determined using an Electro thermal melting-point apparatus. ^{1}H NMR and ^{13}C NMR spectra were run on a Varian Unity Inova 500 NMR spectrometer. The residual DMSO-d_6 signal was also used as an internal reference. FT-IR spectra were recorded in KBr disks on a Mattson 1000 FT-IR spectrometer. UV-Visible spectra were performed on a Perkin Elmer Lambda 25 UV/Visible Spectrometer. The Electron Spray Ionization-Mass Spectrometry (ESI-MS) analyses were carried out in positive ion modes using a Thermo Finnigan LCQ Advantage MAX LC/MS/MS.

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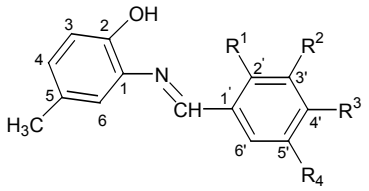
Scheme 1



Compound	R^1	R^2	R^3	R^4	Yield/%	m.p./℃
I	OH	H	H	H	60	165
II	OH	CH_3	H	H	90	181
III	OH	H	H	CH_3	81	185
IV	OH	OCH_3	H	H	88	203
V	OH	H	OCH_3	H	76	214
VI	OH	H	H	Cl	65	174
VII	OH	H	H	Br	73	185
VIII	OH	Cl	H	Cl	86	261
IX	OH	Br	H	Cl	94	253
X	OH	OCH_3	H	Br	80	238
XI	OCH_3	H	OCH_3	H	66	98
XII	H	OCH_3	H	OCH_3	55	72
XIII	H	OCH_3	OCH_3	H	80	137

Synthesis of the Schiff bases

The Schiff bases were prepared by condensation reaction of 4-methyl-2-aminophenol (246 mg; 2 mmol) with appropriate salicylaldehyde (*e.g.* 3-methylsalicylaldehyde for **II**, 272 mg; 2 mmol) in 10 mL of ethanol. This mixture was then refluxed with stirring for 3 h and the solution was allowed at the room temperature to crystallize the Schiff bases. The crystalline product was dissolved in ethanol and filtered for recrystallization. The filtrate was kept at room temperature for 2—3 d to slow evaporation. After this period the crystals suitable for X-ray diffraction study were formed. The single crsytals were filtered and dried at room temperature.

The structures of the compounds were confirmed by FT-IR, UV-vis, ^{1}H NMR and ^{13}C NMR, mass spectrometry techniques and elemental analysis. The compounds **I**—**V** and **VIII**—**XIII** are the new compounds (except **VI** and **VII**) and IR, UV and NMR spectra of the compounds are given as Supporting Information.

N-(5-methyl-2-hydroxyphenyl)-2-hydroxybenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-salicyl-aldimine (**I**): m.p. 165 ℃; color: orange-red; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 13.78 (s, 1H, OH-2'), 9.43 (s, 1H, OH), 8.94 (s, 1H, CH=N), 7.59 (dd, J=1.6, 7.3 Hz, 1H, H-6'), 7.36 (dt, br, J=1.6, 7.3 Hz, 1H, H-4'), 7.16 (d, J=1.6, 1H, H-6), 6.93 (m, 3H, H-4+H-3'+H-5'), 6.84 (d, J=7.8 Hz, H-3), 2.24 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 162.07 (CH=N), 133.42 (C-4'), 132.93 (C-6'), 129.15 (C-4), 120.57 (C-6), 119.37 (C-5'), 117.37 (C-3), 117.09 (C-3'), 20.85 (CH_3), 161.47 (C-2'), 149.51 (C-2), 135.22 (C-1), 129.01 (C-5), 120.25 (C-1'); IR (KBr) v: 3426, 2909, 1632, 1622, 1523, 1490, 1284, 1231, 1191, 1145, 1009, 823, 770, 561 cm^{-1}; UV-vis (MeOH) λ_{max}: 446, 354, 350, 269, 231, 220 nm; MS (70 eV) m/z (%): 228 ([M+1]$^+$, 100), 229 ([M+2]$^+$, 15.1). Anal. calcd for $C_{14}H_{13}NO_2$: C 74.00, H 5.77, N 6.16; found C 73.82, H 5.86, N 6.28.

N-(5-Methyl-2-hydroxyphenyl)-2-hydroxy-3-methylbenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-3-methylsalicylaldimine (**II**): m.p. 181 ℃; color: dirty yellow; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 9.47 (s, 1H, OH), 8.93 (s, 1H, CH=N), 7.40 (d, br, J=7.8 Hz, 1H, H-6'), 7.25 (d, br, J=7.3 Hz, 1H, H-6), 7.18 (d, br, J=1.5 Hz, 1H, H-4'), 6.92 (dd, J=8.3, 1.9 Hz, 1H, H-4), 6.84 (m, 2H, H-3+H-5'), 2.24 (s, 3H, 5-CH_3), 2.20 (s, 3H, 3'-CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 162.33 (CH=N), 134.21 (C-4'), 130.76 (C-6'), 129.10 (C-4), 120.51 (C-6), 118.82 (C-5'), 177.10 (C-3), 20.86 (5-CH_3), 15.98 (3'-CH_3), 159.96 (C-2'), 149.52 (C-2), 135.00 (C-1), 129.00 (C-5), 125.81 (C-3'), 119.29 (C-1'); IR (KBr) v: 3426, 3032, 2915, 1614, 1546, 1514, 1293, 1232, 1039, 813, 761 cm^{-1}; UV-vis (MeOH) λ_{max}: 452, 354, 270, 262, 218, 212 nm; MS (70 eV) m/z (%): 242 ([M+1]$^+$, 31.0), 241 ([M]$^+$, 100). Anal. calcd for $C_{15}H_{15}NO_2$: C 74.67, H 6.27, N 5.81; found C 74.96, H 6.41, N 5.70.

N-(5-Methyl-2-hydroxyphenyl)-2-hydroxy-5-methylbenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-5-methylsalicylaldimine (**III**): m.p. 185 ℃; color: dark orange; UV-vis (MeOH) λ_{max}: 458, 359, 326, 269, 262, 213 nm; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 13.44 (s, 1H, OH-2'), 9.41 (s, 1H, OH), 8.87 (s, 1H, CH=N), 7.38 (d, J=1.9 Hz, 1H, H-6'), 7.18 (dd, J=8.3, 1.9 Hz, 1H, H-4'), 7.13 (d, J=1.5 Hz, 1H, H-6), 6.91 (dd, J=8.3 Hz, 1H, H-3'), 6.82 (m, 2H, H-3+H-4), 2.26 (s, 3H, 5-CH_3), 2.23 (s, 3H, 5'-CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 162.06 (CH=N), 134.18 (C-4'), 132.70 (C-6'), 129.03 (C-4), 120.64 (C-6), 117.17 (C-3), 117.06 (C-3'), 20.86 (5-CH_3), 20.66 (5'-CH_3), 159.17 (C-2'), 149.47 (C-2), 135.46 (C-1), 128.99 (C-5), 127.90 (C-5'), 119.93 (C-1'); IR (KBr) v: 3426, 2915, 1635, 1522, 1502, 1466, 1285, 1252, 1200, 1168, 1108, 1095, 822, 592 cm^{-1}; MS (70 eV) m/z (%): 242 ([M+1]$^+$, 100). Anal. calcd for $C_{15}H_{15}NO_2$: C 74.67, H 6.27, N 5.81; found C 74.56, H 6.38, N 5.94.

N-(5-Methyl-2-hydroxyphenyl)-2-hydroxy-3-methoxybenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-3-methoxysalicylaldimine (**IV**): m.p. 203 ℃; color: orange-red; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 14.07 (s, 1H, OH-2'), 9.49 (s, 1H, OH), 8.93 (s, 1H, CH=N), 7.18 (s, br, 1H, H-6), 7.16 (d, J=7.8 Hz, 1H, H-6'), 7.05 (d, J=7.8 Hz, 1H, H-4), 6.92 (d, br, J=8.3 Hz, 1H, H-4'), 6.84 (s, br, 1H, H-5'), 6.82 (d, J=7.8 Hz, 1H, H-3), 3.79 (s, 3H, OCH_3), 2.23 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 161.89 (CH=N), 129.16 (C-4), 124.47 (C-6), 120.42 (C-6'), 118.54 (C-3), 117.07 (C-5'), 115.88 (C-4'), 56.56 (OCH_3), 20.86 (CH_3), 152.69 (C-2'), 149.38 (C-3'), 148.9 (C-2), 134.67 (C-1), 129.02 (C-5), 119.94 (C-1'); IR (KBr) v: 3450, 2927,

1614, 1510, 1461, 1457, 1349, 1208, 1172, 1047, 813, 745, 721, 576 cm^{-1}; UV-vis (MeOH) λ_{max}: 460, 355, 309, 268, 262, 230, 213 nm; MS (70 eV) *m/z* (%): 257 ($[M]^+$, 100). Anal. calcd for $C_{15}H_{15}NO_3$: C 70.02, H 5.88, N 5.44; found C 70.02, H 5.96, N 5.42.

N-(5-Methyl-2-hydroxyphenyl)-2-hydroxy-4-methoxybenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-4-methoxysalicylaldimine (**V**): m.p. 214 ℃; color: dark yellow; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 14.41 (s, 1H, OH-2'), 9.46 (s, 1H, OH), 8.82 (d, J=1.6 Hz, 1H, CH=N), 7.43 (d, J=8.8 Hz, 1H, H-6'), 7.16 (d, J=1.6 Hz, 1H, H-6), 6.88 (dd, J=8.8, 1.6 Hz, 1H, H-4), 6.82 (d, J=8.3 Hz, 1H, H-3), 6.44 (dd, J=8.8, 2.6 Hz, 1H, H-5'), 6.37 (d, J=2.6 Hz, 1H, H-3'), 3.78 (s, 3H, OCH_3), 2.23 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 160.24 (CH=N), 134.51 (C-6'), 128.39 (C-4), 120.03 (C-6), 116.93 (C-3), 107.17 (C-5'), 101.77 (C-3'), 56.04 (OCH_3), 20.90 (CH_3), 166.51 (C-4'), 164.50 (C-2'), 148.80 (C-2), 134.15 (C-1), 129.04 (C-5), 113.73 (C-1'); IR (KBr) *v*: 3440, 2938, 1625, 1609, 1523, 1486, 1457, 1315, 1290, 1237, 1221, 1127, 1022, 797, 609, 569 cm^{-1}; UV-vis (MeOH) λ_{max}: 452, 425, 357, 342, 309, 256, 214 nm; MS (70 eV) *m/z* (%): 257 ($[M]^+$, 100). Anal. calcd for $C_{15}H_{15}NO_3$: C 70.02, H 5.88, N 5.44; found C 69.90, H 5.84, N 5.50.

N-(5-Methyl-2-hydroxyphenyl)-2-hydroxy-5-chlorobenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-5-chlorosalicylaldimine (**VI**): m.p. 174 ℃; color: orange; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 13.81 (s, 1H, OH-2'), 9.51 (s, 1H, OH), 8.94 (s, 1H, CH=N), 7.70 (d, J=2.4 Hz, 1H, H-6'), 7.38 (dd, J=8.8, 2.7 Hz, 1H, H-4'), 7.16 (s, br, 1H, H-6), 6.94 (m, 2H, H-4+H-3'), 6.84 (d, J=8.2 Hz, 1H, H-3), 2.24 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 160.29 (CH=N), 132.94 (C-4'), 131.52 (C-6'), 129.64 (C-4), 120.41 (C-6), 119.44 (C-3), 117.16 (C-3'), 20.85 (CH_3), 160.36 (C-2'), 149.71 (C-2), 134.71 (C-1), 129.03 (C-5), 122.71 (C-5'), 121.43 (C-1'); IR (KBr) *v*: 3426, 3068, 2916, 1632, 1609, 1516, 1469, 1397, 1254, 1231, 1177, 1128, 1035, 869, 823, 690, 651, 608 cm^{-1}; UV-vis (MeOH) λ_{max}: 458, 364, 268, 26, 232, 216 nm; MS (70 eV) *m/z* (%): 260 ($[M-1]^+$, 100), 261 ($[M]^+$, 7.1), 262 ($[M+1]^+$, 25.5), 263 ($[M+2]^+$, 12.8). Anal. calcd for $C_{14}H_{12}ClNO_2$: C 64.25, H 4.62, N 5.35; found C 64.17, H 4.71, N 5.18.

N-(5-Methyl-2-hydroxyphenyl)-2-hydroxy-5-bromobenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-5-bromosalicylaldimine (**VII**): m.p. 185 ℃; color: orange; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 13.85 (s, 1H, OH-2'), 9.52 (s, 1H, OH), 8.94 (s, 1H, CH=N), 7.83 (d, J=1.9 Hz, H-6'), 7.49 (tt, J=8.8, 1.9, 1.0 Hz, 1H, H-4'), 7.16 (s, 1H, H-6), 6.94 (d, br, J=7.8 Hz, 1H, H-4), 6.89 (d, J=8.8 Hz, 1H, H-3'), 6.84 (d, J=7.8 Hz, 1H, H-3), 2.24 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 160.28 (CH=N), 135.75 (C-4'), 134.48 (C-6'), 129.64 (C-4), 120.39 (C-6), 119.90 (C-3), 117.51 (C-3'), 20.86 (CH_3), 160.75 (C-2'), 149.71 (C-2), 134.68 (C-1), 129.03 (C-5), 122.06 (C-1'), 110.03 (C-5'); IR (KBr) *v*: 3447, 3076, 2911, 1638, 1611, 1522, 1445, 1413, 1381, 1252, 1168, 1124, 1031, 922, 878, 814, 685, 548 cm^{-1}; UV-vis (MeOH) λ_{max}: 458, 363, 268, 262, 242, 213 nm; MS (70 eV) *m/z* (%): 306 ($[M]^+$, 100), 307 ($[M+1]^+$, 18.0), 308 ($[M+2]^+$, 97.1), 309 (9.3, $[M+3]^+$), 311 ($[M+4]^+$, 9.6). Anal. calcd for $C_{14}H_{12}BrNO_2$: C 54.92, H 3.95, N 4.58; found C 55.07, H 4.01, N 4.45.

N-(5-Methyl-2-hydroxyphenyl)-2-hydroxy-3,5-dichlorobenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-3,5-dichlorosalicylaldimine (**VIII**): m.p. 261 ℃; color: dark yellow; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 9.94 (s, 1H, OH), 9.07 (s, 1H, CH=N), 7.64 (d, J=2.4 Hz, 1H, H-4'), 7.60 (d, J=2.9 Hz, 1H, H-6'), 7.33 (s, 1H, H-6), 7.00 (dd, J=8.3, 1.5 Hz, 1H, H-4), 6.89 (d, J=8.3 Hz, 1H, H-3), 2.26 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 159.25 (CH=N), 133.03 (C-4'), 130.98 (C-4), 130.32 (C-6'), 119.87 (C-6), 117.25 (C-3), 20.89 (CH_3), 160.54 (C-2'), 149.31 (C-2), 131.28 (C-1), 129.29 (C-5), 123.81 (C-5'), 120.41 (C-3'), 120.06 (C-1'); IR (KBr) *v*: 3210, 2922, 1638, 1622, 1506, 1350, 1277, 1211, 1148, 1016, 853, 814, 754, 671; UV-vis (MeOH) λ_{max}: 466, 364, 303, 268, 262, 246, 216 nm; MS (70 eV) *m/z* (%): 296 ($[M]^+$, 100), 297 ($[M+1]^+$, 6.5), 298 ($[M+2]^+$, 72.0), 299 ($[M+3]^+$, 18.3), 300 ($[M+4]^+$, 9.9), 301 ($[M+5]^+$, 15.1), 302 ($[M+6]^+$, 4.9). Anal. calcd for $C_{14}H_{11}Cl_2NO_2$: C 56.78, H 3.74, N 4.73; found C 56.64, H 3.61, N 4.68.

N-(5-Methyl-2-hydroxyphenyl)-2-hydroxy-3-bromo-5-chlorobenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-3-bromo-5-chlorosalicylaldimine (**IX**): m.p. 253 ℃; color: orange; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 9.95 (s, 1H, OH), 9.05 (s, 1H, CH=N), 7.77 (d, J=2.9 Hz, 1H, H-6'), 7.64 (d, J=2.4 Hz, 1H, H-6), 7.33 (d, J=1.5 Hz, 1H, H-4'), 7.00 (dd, J=8.3, 1.9 Hz, 1H, H-4), 6.89 (d, J=8.3 Hz, 1H, H3), 2.26 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 159.19 (CH=N), 135.88 (C-4'), 131.65 (C-6'), 130.34 (C-4), 119.90 (C-6), 117.25 (C-3), 20.89 (CH_3), 161.37 (C-2'), 149.32 (C-2), 131.19 (C-1), 129.30 (C-5), 120.85 (C-5'), 119.79 (C-1'), 113.83 (C-3'); IR (KBr) *v*: 3449, 3238, 2915, 1640, 1617, 1501, 1346, 1277, 1208, 1138, 1016, 854, 815, 723, 643, 583 cm^{-1}; UV-vis (MeOH) λ_{max}: 490, 468, 366, 304, 255, 218, 210 nm; MS (70 eV) *m/z* (%): 338 ($[M-2]^+$, 6.85), 339 ($[M-1]^+$, 5.2), 340 ($[M]^+$, 69.2), 341 ($[M+1]^+$, 13.9), 342 ($[M+2]^+$, 100), 343 ($[M+3]^+$, 14.2), 344 ($[M+4]^+$, 22.3). Anal. calcd for $C_{14}H_{11}BrClNO$: C 49.37, H 3.26, N 4.11; found C 49.29, H 3.51, N 4.08.

N-(5-Methyl-2-hydroxyphenyl)-2-hydroxy-3-methoxy-5-bromobenzaldimine; *N*-(5-methyl-2-hydroxyphenyl)-3-methoxy-5-bromosalicylaldimine (**X**): m.p. 238 ℃; color: dark yellow; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 9.61 (s, 1H, OH), 8.93 (s, 1H, CH=N), 7.38 (m, 1H, H-6'), 7.20 (s, br, 1H, H-6), 7.14 (d, br, J=1.9 Hz, 1H, H-4'), 6.94 (d, br, J=1.0 Hz, 1H, H-4), 6.84 (dd, J=8.3, 1.0 Hz, 1H, H-3), 3.81 (s, 3H, OCH_3), 2.24 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 159.97 (CH=N), 129.57 (C-4), 125.81 (C-6), 120.13 (C-6'),

117.89 (C-3), 117.11 (C-4'), 56.87 (OCH_3), 20.87 (CH_3), 153.40 (C-3'), 150.40 (C-2'), 149.37 (C-2), 133.65 (C-1), 129.09 (C-5), 120.61 (C-1'), 108.72 (C-5'); IR (KBr) *v*: 3426, 3071, 2916, 1634, 1622, 1500, 1470, 1360, 1295, 1212, 1016, 876, 824, 777, 591; MS (70 eV) *m/z* (%): 334 ($[M-2]^+$, 100), 335 ($[M-1]^+$, 7.1), 336 ($[M]^+$, 89.2), 337 ($[M+1]^+$, 7.1); UV-vis (MeOH) λ_{max}: 469, 381, 358, 312, 268, 262, 212 nm. Anal. calcd for $C_{15}H_{14}BrNO_3$: C 53.59, H 4.20, N 4.17; found C 53.45, H 4.29, N 4.30.

N-(5-Methyl-2-hydroxyphenyl)-2,4-dimethoxybenzaldimine (**XI**): m.p. 98 ℃; color: milky brown; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 8.81 (s, 1H, OH), 8.55 (s, 1H, CH=N), 8.15 (d, J=8.3 Hz, H-6'), 6.87 (s, 1H, H-6), 6.82 (d, J=8.3 Hz, H-5'), 6.73 (d, J=7.8 Hz, 1H, H-4), 6.64 (s, 1H, H-3'), 6.62 (d, J=8.8 Hz, 1H, H-3), 3.88 (s, 3H, 2'-OCH_3), 3.84 (s, 3H, 4'-OCH_3), 2.21 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 154.00 (CH=N), 129.53 (C-6'), 127.74 (C-4), 119.83 (C-6), 116.22 (C-3), 107.11 (C-5'), 98.64 (C-3'), 56.53 (2'-OCH_3), 56.22 (4'-OCH_3), 20.88 (CH_3), 164.20 (C-4'), 161.36 (C-2'), 149.37 (C-2), 139.12 (C-1), 128.80 (C-5), 118.20 (C-1'); IR (KBr) *v*: 3426, 3086, 2980, 2914, 1621, 1590, 1508, 1469, 1383, 1300, 1277, 1214, 1168, 1112, 1040, 947, 825, 802 cm^{-1}; UV-vis (MeOH) λ_{max}: 358, 321, 280, 270, 240, 216, 210 nm; MS (70 eV) *m/z* (%): 270 ($[M-1]^+$, 100). Anal. calcd for $C_{16}H_{17}NO_3$: C 70.83, H 6.32, N 5.16; found C 70.78, H 6.44, N 5.04.

N-(5-Methyl-2-hydroxyphenyl)-3,5-dimethoxybenzaldimine (**XII**): m.p. 72 ℃; color: light brown; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 8.72 (d, J=1.9 Hz, 1H, OH), 8.62 (s, 1H, CH=N), 7.21 (d, J=1.9, 2H, H-2'+H-6'), 7.02 (s, 1H, H-6), 6.88 (dd, J=8.8, 1.0, 1H, H-4), 6.77 (d, J=8.3 Hz, 1H, H-3), 6.62 (t, J=2.4, 2.4 Hz, 1H, H-4'), 3.81 (s, 6H, 2×OCH_3), 2.22 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 159.33 (CH=N), 128.70 (C-4), 119.93 (C-6), 116.54 (C-3), 107.23 (C-2'+C-6'), 104.24 (C-4'), 56.12 (2×OCH_3), 20.89 (CH_3), 161.30 (C-3'+C-5'), 149.75 (C-2), 139.20 (C-1), 137.73 (C-1'), 128.76 (C-5); IR (KBr) *v*: 3393, 3087, 2932, 2839, 1625, 1599, 1506, 1463, 1430, 1377, 1347, 1291, 1238, 1215, 1158, 1062, 923, 837, 814, 684 cm^{-1}; UV-vis (MeOH) λ_{max}: 369, 348, 279, 269, 262, 233, 217, 210 nm; MS (70 eV) *m/z* (%): 270 ($[M-1]^+$, 100), 271 ($[M]^+$, 11.2). Anal. calcd for $C_{16}H_{17}NO_3$: C 70.83, H 6.32, N 5.16; found C 70.90, H 6.34, N 5.10.

N-(5-Methyl-2-hydroxyphenyl)-3,4-dimethoxybenzaldimine (**XIII**): m.p. 137 ℃; color: golden yellow; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 8.61 (s, 1H, OH), 8.58 (s, 1H, CH=N), 7.73 (d, J=1.9 Hz, 1H, H-2'), 7.44 (dd, J=8.3, 1.9 Hz, 1H, H-6'), 7.05 (d, J=8.3 Hz, 1H, H-4), 7.00 (d, J=1.5 Hz, 1H, H-6), 6.85 (dd, J=8.3, 1.5 Hz, 1H, H-3), 6.76 (d, J=8.3 Hz, 1H, H-5'), 3.85 (s, 3H, 3'-OCH_3), 3.82 (s, 3H, 4'-OCH_3), 2.22 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 158.91 (CH=N), 128.09 (C-4), 124.83 (C-6'), 119.62 (C-6), 116.28 (C-3), 111.88 (C-2'), 110.62 (C-5'), 56.33 (3'-OCH_3), 56.31 (4'-OCH_3), 20.93 (CH_3), 152.38 (C-4'), 149.74 (C-3'), 149.65 (C-2), 138.12 (C-1), 130.22 (C-5), 128.71 (C-1'); IR (KBr) *v*: 3423, 3056, 2938, 2855, 1624, 1597, 1515, 1465, 1422, 1385, 1276, 1247, 1138, 1023, 884, 808, 613 cm^{-1}; UV-vis (MeOH) λ_{max}: 373, 350, 315, 282, 269, 262, 235, 214 nm; MS (70 eV) *m/z* (%): 270 ($[M-1]^+$, 100). Anal. calcd for $C_{16}H_{17}NO_3$: C 70.83, H 6.32, N 5.16; found C 70.79, H 6.42, N 5.08.

Crystallography

Diffraction measurements were carried out at (20±1) ℃ on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo Kα radiation (μ=0.71070 Å), with a distance of 127.40 mm between the crystal and the detector (Istanbul University Advanced Analyses Laboratory).

For the structure solution, 28178 reflections were collected, 1394 were unique (R_{int}=0.032); equivalent reflections were merged. An empirical absorption correction was applied which resulted in transmission factors ranging from 0.73 to 0.99. The data were corrected for Lorentz and polarization effects.

The structure of **XIII** was solved by direct methods (SIR92) and expanded using Fourier techniques.[31,32] The non-hydrogen atoms were refined anisotropically. H atoms were treated as riding, with C—H=0.95(6) Å and $U_{iso}(H) = 1.2U_{eq}(C)$. All calculations were performed using the CrystalStructure crystallographic software package.[33] Coordinate parameters of the structure were deposited with the CSD, deposition number is CCDC 825167.

Determination of antimicrobial activity

Antimicrobial activities against *Staphylococcus aureus* ATCC 6538, *Staphylococcus epidermidis* ATCC 12228, *Escherichia coli* ATCC 8739, *Klebsiella pneumoniae* ATCC 4352, *Pseudomonas aeruginosa* ATCC 27853, *Proteus mirabilis* ATCC 14153 and *Candida albicans* ATCC 10231 were determined by the micro broth dilutions technique strictly following the National Committee for Clinical Laboratory Standards (NCCLS) recommendations.[34,35] Mueller-Hinton broth for bacteria, and RPMI-1640 medium buffered to pH 7.0 with MOPS for yeast strain were used as the test medium. Serial two-fold dilutions ranging from 5000 to 4.9 μg/mL were prepared in medium. The inoculum was prepared using a 4—6 h broth culture of each bacteria and 24 cultures of yeast strains adjusted to a turbidity equivalent to a 0.5 McFarland standard, diluted in broth media to give a final concentration of 5×10^5 cfu/mL for bacteria and 0.5×10^3 to 2.5×10^3 cfu/mL for yeast in the test tray. The trays were covered and placed in plastic bags to prevent evaporation. The trays containing Mueller-Hinton broth were incubated at 35 ℃ for 18—20 h and the trays containing RPMI-1640 medium were incubated at 35 ℃ for 46—50 h. The minimum inhibitory concentrations (MIC) were defined as the lowest concentration of compound giving complete inhibition of visible growth. Antimicrobial effects of the

solvents were investigated against test microorganisms. According to values of the controls, the results were evaluated.

Results and Discussion

The analytical data and physical properties of the Schiff bases are given in Experimental section. As can be seen from Scheme 1, **XI**, **XII** and **XIII** are structurally isomers. Also, **II** with **III** and **IV** with **V** are isomers. Considering the yields, it can be said that the substituents increase the yields of the compounds **II**—**XIII** (except **XII**) in respect to **I**. The high yields of the compounds **VIII** and **IX**, which have two electronegative groups at R^2 and R^4, are remarkable. Also, the methyl groups at R^2 or R^4 positions increase the yield of the compounds **II** and **III**.

Melting points

It is known that intermolecular hydrogen bonding plays an important role in high melting points of Schiff bases. It is noticed that the compound **I** has the lowest melting point (165 ℃, see Experimental section) among the compounds including salicyl group (except **XI**—**XIII**). Accoding to this observation it can be said that the substituents increase the melting points of the compounds **II**—**X** in respect to the compound **I** in addition to intermolecular hydrogen bonding. The melting points of the compounds **VIII**, **IX** and **X** are higher than those of the others: 261, 253 and 238 ℃, respectively: These compounds contain two electronegative groups with a salicyl ring; Cl, Cl (**VIII**); Br, Cl (**IX**) and OCH_3, Br (**X**). This may mean that Br, Cl and OCH_3 substituents on the salicyl ring cause stronger hydrogen bonding according to the others and consequently, they increase the melting points considerably. It is remarkable that the dimethoxy derivatives (**XI**—**XIII**) have lower melting point than the others. These compounds include only one OH group and they have weaker intermolecular hydrogen bonding, and consequently, their melting points decrease.

The melting points of the Schiff bases in this study are lower than those of 4-chloro-2-aminophenol derivative analogues.[36] This observation leads us to conclude that methyl substituent on hydroxyphenyl ring decreases the melting point of Schiff bases.

FT-IR spectra

FT-IR spectral data of the compounds are given in Experimental section. The bands at around 3400 cm^{-1} can be assigned to ν(OH) in the IR spectra of the all compounds. The medium or strong intensity absorption bands between 1610 and 1640 cm^{-1} are assigned to C=N stretching mode. The presence of aromatic rings has been identified by their characteristic ring vibrations at 1500—1400, 1200—1100 and 930—700 cm^{-1} regions. The absence of bands for characteristic of ν(C=O) and primary amine ν(NH) confirms the formation of the proposed Schiff base framework.

The C—O stretching vibrations appear in the 1200—1250 cm^{-1} range as strong bands.[37] The C—Cl stretching vibration is seen in the range 600—700 cm^{-1} as medium or weak bands for **VI**, **VIII** and **IX**. The C—Br stretching vibrations are seen at 548, 583 and 591 cm^{-1} as weak bands for the compounds **VII, IX** and **X**.[38]

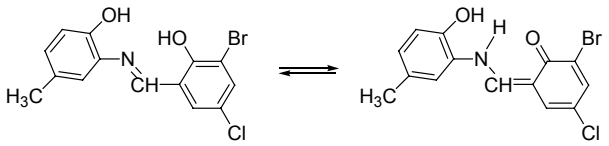
A considerable strong H-bonding is observed in the compounds **I**—**X** with salicyl OH group (weak and broad bands between 2800 and 2400 cm^{-1}), whereas weak H-bonding in the compounds **XI**—**XIII** does not include salicyl OH group, as expected.

UV-Visible spectra

The UV-visible spectral data of the compounds are presented in Experimental section. The UV-visible absorption spectra were obtained in methanol at room temperature. The electronic spectra of the compounds exhibit intense bands in the 200—400 nm region, which may be assignable to n→π* and π→π* transitions. The 210—300 nm bands are due to the π→π* transitions of the aromatic rings. The 300—350 nm bands involve π→π* transitions of the C=N group.

UV-visible spectroscopy is known to be a very sensitive method for studying tautomeric equilibrium in Schiff bases. The two long-wave bands observed in the electronic spectra of the compounds have been assigned to the enol and keto forms (Scheme 2).[39-45] The bands between 350 and 400 nm can be assigned to the enol form whereas the bands above 400 nm are assigned to the keto form.[46-51] According to this, much of the compounds such as **I**—**X**, which have salicyl OH group, have the characteristic keto form band, whereas the others, **XI**—**XIII**, have characteristic enol form band in methanol. The UV-visible spectra of the Schiff bases having the keto form band indicate the existence of the proton transfer equilibrium.

Scheme 2



In the UV-visible spectra above 400 nm, the absorption values of the compounds **VIII**, **IX** and **X**, are higher than the others: 466, 468 and 469 nm, respectively (also, they have higher meting points than the others: see Melting Points section). On the other hand, the salicyl OH protons of these three compounds could not be detected in their ^{1}H NMR spectra. This situation can be explained as follows: These compounds include two electronegative groups at 5-methyl-2-hydroxyphenyl ring. Probably, the strong electronegative groups (Cl, Br, OCH_3) of the hydroxyphenyl ring strengthen the keto form, acidic character of the NH proton is increased and consequently, the absorption maximum

CHINESE JOURNAL OF CHEMISTRY

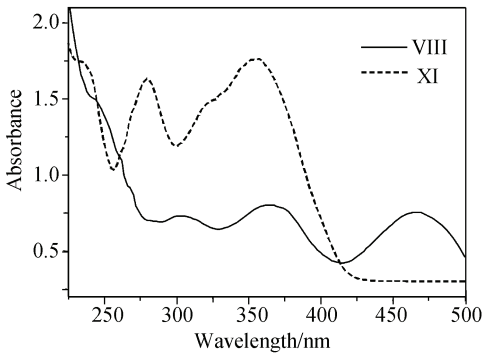


Figure 1 UV-visible spectra of the compounds **VIII** and **XI** in the range of 225—500 nm.

shifts to the higher wavelength.

The UV-visible spectra of the compounds **VIII** and **XI** are shown in Figure 1 to compare Schiff bases which have keto and enol forms, respectively.

Mass spectra

The ESI-MS spectral data of the compounds are given in Experimental section as molecular ions with the relative abundance.

All of the mole peaks of the Schiff bases are determined. It is known that chlorine and bromine have two isotopes, their percent abundance and approximately relative proportions are as follows: ^{35}Cl (75.8%): ^{37}Cl (24.2%) (3 ∶ 1); ^{79}Br (50.7%):^{81}Br (49.3%) (1 ∶ 1). There are a lot of isotopic patterns in the ESI-MS spectra of the compounds **VI**—**X** because of presence of chlorine or bromine atoms. Considering all the compounds, the most isotopic patterns are observed in the spectra of the compounds **VIII** (includes two chlorine atoms) and **IX** (includes a chlorine and a bromine atoms).

NMR spectra

^{1}H NMR spectral data and their assignments are present in Experimental section. The OH protons of 5-methyl-2-hydroxyphenyl ring appear in the δ 8.61—9.95 range, whereas NMR signal values of the salicylaldimine ring OH protons (**I**—**X**, at 2'-position) that form intramolecular hydrogen bonding with the C=N nitrogen atom, vary between δ 13.44 and 14.41. Salicyl OH proton of **II**, **VIII**, **IX** and **X** is not detected in their ^{1}H NMR spectra: It can be said that OH proton of these compounds has more acidic character than the others and consequently, it cannot be detected because of its dissociation.

Azomethine proton appears between δ 8.82 and 9.07 in the compounds **I**—**X** whereas it shifts to higher field, δ 8.55—8.62 range, in the compounds **XI**—**XIII**. Shielding of azomethine proton of the compounds **XI**—**XIII** is increased according to the other compounds because of lack of the salicyl OH group (shifting to the high field). Similarly, also OH protons of the compounds **XI**—**XIII** shift to the higher field because of shielding.

It is observed that azomethine proton of **V** gives a doublet by far interacting with H(6) (J=1.6 Hz). OH proton of **XII** appears as a doublet as a result of far interaction with H(2') (J=1.9 Hz).

The compounds **XI**, **XII** and **XIII** have two methoxy groups. The NMR spectral data show that the methoxy carbon atoms of the compound **XII** are magnetically equivalent. Two methoxy group protons of **XII** give only a signal at δ 3.81 (6H). At the same time, methoxy carbons give only one peak at δ 56.12 in the ^{13}C NMR spectra. According to the APT spectral data, C(2') and C(6') are also magnetically equivalent to each other: They exhibit a single signal at δ 107.23.

^{13}C NMR (APT) spectral data are given in Experimental section with their assignments. All of the carbon atoms were observed and APT spectra of the compounds are straightforward. APT spectrum of **IV** is presented in Figure 2. Azomethine carbons of the compounds appear between δ 154.00 and 162.3. The carbon atoms bonded to the OH group [C(2)] at methyl-hydroxyphenyl ring give signals at the lower δ value (near δ 149) than the carbon atoms that bonded to the other OH group, C(2') (at around δ 160). The methyl carbons of 5-methyl-2-hydroxyphenyl rings are observed near δ 20.9.

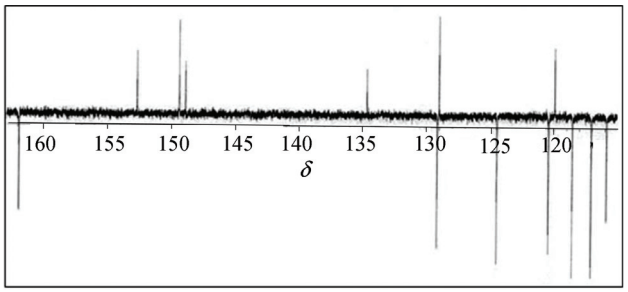


Figure 2 ^{13}C NMR spectrum, obtained with Attached Proton Test (APT) technique, of the compound **IV** between δ 115 and 165 range.

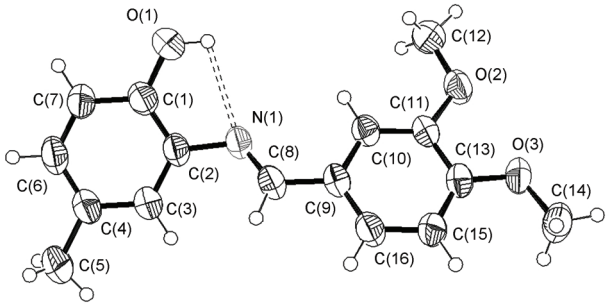


Figure 3 A molecular drawing (ORTEP 3) of the asymmetric unit of the compound **XIII**, showing 50% probability displacement ellipsoids and the atom-numbering scheme. Broken line shows intra-molecular hydrogen bond.

X-ray analysis

The crystal data of the compound **XIII** and the details of data processing are given in Table 1. Table 2

Table 1 Crystal and experimental data for the compound **XIII**

Empirical formula	$C_{16}H_{17}NO_3$
Formula weight	271.32
Temperature	293 K
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	a=7.4750(5) Å, b=7.7954(7) Å c=12.6696(8) Å, β=98.475(4)°
Cell volume	730.20(9) Å^3
Z, Calculated density	2, 1.234 g/cm^3
Absorption coefficient (Mo Kα)	0.85 cm^{-1}
F(000)	288
Crystal size	0.30 mm×0.20 mm×0.10 mm
Linear absorption coefficient (μ)	0.9 cm^{-1}
No. of observations [$I>3.00\sigma(I)$]	1372
Refinement method	Full-matrix least-squares on F
Goodness of fit indicator	1.287
Index range	$-8\leqslant h\leqslant 8$, $-8\leqslant k\leqslant 9$, $-15\leqslant l\leqslant 15$
θ range for data collection	3.0°—25.0°
Data collection	CRYSTALCLEAR
R ($I>3\sigma(I)$)	0.050
R_w ($I>3\sigma(I)$)	0.033
Largest diff. peak and hole	0.14 and −0.17 e$^-$/Å^3

Table 2 Hydrogen-bond geometry [Å, (°)] for **XIII**[a]

D—H···A	D—H	H···A	D···A	D—H···A
O(1)—H(17)···N(1)[1]	0.882(2)	2.397(2)	2.734(3)	103.1(2)
O(1)—H(17)···O(3)[2]	0.882(2)	2.177(2)	2.852(2)	133.0(1)

[a] Symmetry code: 1: $+x,+y,+z$; 2: $-x$, 1/2$+y$,+1$-z$.

contains the hydrogen bond geometry parameters. Selected bond lengths and angles are given in Table 3; some torsion angles are given in Table 4. ORTEP-III view of the molecular structure of **XIII** is given in Figure 3. The unit cell of **XIII** is shown in Figure 4.

Kabak *et al.* reported the crystal structure of the compound **I**.[52] They investigated tautomeric properties and conformations of **I**, and they showed that intramolecular hydrogen bonds occur between the pairs of atoms N(1) and O(1), and N(1) and O(2); the H atom is essentially bonded to the N atom.

In this study, it is observed that O(1)—H(17) bond length (O—H) is 0.882(2) Å and the distance between N(1) and H(17) atoms (C=N···H—O) is 2.397(2) Å (Table 2). This shows that there is a weak interaction (intramolecular hydrogen bonding) between C=N and OH groups because of steric strain. Also, there is intermoleculer hydrogen bonding between H(17) and O(3) atoms (2.177 Å). H(17) forms hydrogen bonding with two electronegative atoms [N(1) and O(3)] as in similar molecules reported,[52,53] and it is closer to O(3) atom according to N(1). The crystal structure is stabilized by intermolecular hydrogen bonds.

Table 3 Selected bond lengths (Å) and angles (°) for **XIII**

O(1)—C(1)	1.358(3)	O(2)—C(11)	1.370(2)
O(2)—C(12)	1.420(3)	O(3)—C(13)	1.357(2)
O(3)—C(14)	1.432(3)	N(1)—C(2)	1.422(2)
N(1)—C(8)	1.262(3)	C(4)—C(5)	1.506(4)
C(4)—C(6)	1.377(4)	C(8)—C(9)	1.462(3)
C(9)—C(10)	1.410(3)	C(9)—C(16)	1.383(3)
C(11)—C(13)	1.408(3)		
C(11)-O(2)-C(12)	118.6(2)	C(13)-O(3)-C(14)	117.2(2)
C(2)-N(1)-C(8)	119.7(2)	C(2)-C(1)-O(19)	121.9(2)
C(7)-C(1)-O(1)	118.2(2)	N(1)-C(2)-C(1)	116.1(2)
C(9)-(C8)-N(1)	123.6(2)	C(13)-C(11)-O(2)	113.9(2)
O(2)-C(11)-C(10)	125.4(2)	C(15)-C(13)-O(3)	125.1(2)
O(3)-(C13)-C(11)	114.9(2)		

Table 4 Selected torsion angles (°) for **XIII**

C(12)-O(2)-C(11)-C(10)	−0.8(3)
C(14)-O(3)-C(13)-C(11)	172.6(2)
C(8)-N(1)-C(2)-C(1)	148.4(2)
C(2)-N(1)-C(8)-C(9)	176.4(2)
O(1)-C(1)-C(2)-C(3)	−178.4(2)
N(1)-C(8)-C(9)-C(10)	4.3(4)
O(2)-C(11)-C(13)-O(3)	−1.1(3)
O(3)-C(13)-C(15)-C(16)	−179.4(2)
C(12)-O(2)-C(11)-C(13)	179.3(2)
C(14)-O(3)-C(13)-C(15)	−7.3(3)
C(8)-N(1)-C(2)-C(3)	−35.8(3)
O(1)-C(1)-C(2)-N(1)	−2.4(4)
O(1)-C(1)-C(7)-C(6)	178.6(2)
N(1)-C(8)-C(9)-C(16)	−175.3(3)
O(2)-C(11)-C(13)-C(15)	178.8(2)

C-N-C bond angle is 119.7(2)° for the C(2)-N(1)-C(8) and C=N bond [C(8)–N(1)] length is 1.262(3) Å. These data are in line with the literature data.[54-58] According to the C(2)-N(1)-C(8)-C(9) torsion angle, 176.4(2)°, the molecule is non-planar and twisted around C—N single bond.

Antimicrobial activity

The results concerning *in vitro* antimicrobial activity of the compounds together with MIC values of compared antibiotic and antifungal reagents are presented in Table 5.

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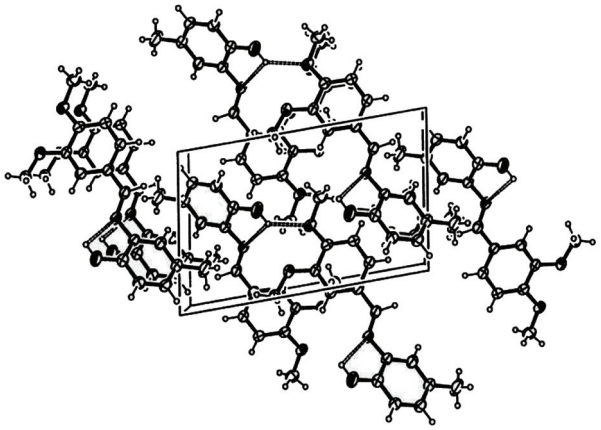

Figure 4 A packing diagram (view along the *b* axis) of the compound **XIII**. Hydrogen bonds are shown as dashed lines.

Table 5 *In vitro* antimicrobial activities of the compounds **I**—**XIII** (MIC, μg/mL)

Compound	Microorganisms[a]		
	Sa	*Kp*	*Ca*
III	156	—[b]	—
IV	—	312	—
V	—	—	156
VI	—	—	156
VII	156	—	625
VIII	—	—	312
IX	19.5	—	312
X	—	—	78
XI	156	312	—
XIII	156	—	—
Ciprofloxacin	0.125	0.0625	—
Cefuroxime sodium	—	—	—
Ceftazidime	—	4.9	—
Clotrimazole	—	—	4.9
Fluconazole	—	—	1.0

[a] *Sa*: *Staphylococcus aureus* ATCC 6538 (Gram+). *Kp*: *Klebsiella pneumoniae* ATCC 4352 (Gram−). *Ca*: *Candida albicans* ATCC 10231. [b] —: Antimicrobial activity was not detected.

At a glance of Table 5, it can be seen that most of the compounds are effective toward *S. aureus* and *C. albicans*. This observation can be evaluated as a selective activity.

It is observed that the compounds **IX** (includes Br and Cl substituents) and **X** (includes Br and OCH_3) have a little better antimicrobial activity according to the others. It is possible to say that this activity is caused by bromine atom. It is known that some compounds that contain bromine substituent have various biological activities. For example, bronopol (2-bromo-2-nitropropane-1,3-diol) has a broad spectrum of antibacterial and antifungal activities and is widely used as a preservatives in drugs and cosmetics.[59,60] There are a lot of studies that reported bromine containing compounds have antibacterial and antifungal activities.[61-65]

It is observed that the compounds **I**, **II** and **XII** have no any activity on the test microorganisms. On the other hand, all of the compounds did not show significant activity (or they have very low activity) toward *S. epidermidis*, *E. coli*, *P. aeruginosa* and *P. mirabilis.*

Conclusions

It is known that salicylaldimines have strong intramolecular hydrogen bonding between azomethine (HC = N) nitrogen and salicyl OH hydrogen atoms.[54,55,66-69] In this study the intramolecular hydrogen bonding is proved by spectroscopic methods. For example, the weak or broad bands between 2800 and 2400 cm^{-1} in the IR spectra of the compounds **I**—**X** demonstrate the formation of intramolecular hydrogen bonding between salicyl OH hydrogen and C = N nitrogen atoms of the Schiff bases. Appearing of the NMR signal of the benzaldimine OH hydrogen above δ 12.50 is related with the intramolecular hydrogen bonding. In UV-visible spectra, the bands between 350 and 400 nm indicate enol form and the absorptions above 400 nm show keto form.

Our study results are in line with the literature although there are very limited studies on antimicrobial activities of similar compounds. For example, it was reported that (*E*)-4-chloro-2-[(4-fluorobenzylimino)-methyl]phenol showed the most favorable antimicrobial activity against *B. subtilis*, *E. coli*, *P. fluorescence*, *S. aureus* and *A. niger*.[70] In our previous studies some *N*-(5-chloro-2-hydroxyphenyl)-phenylaldimines including methoxy group and some *N*-(5-chloro-2-hydroxyphenyl)-(3/4/5-substituted)-salicylaldimines showed considerable activity toward *S. aureus*, *S. epidermidis* and *C. albicans*.[36,71] In this study, some of the Schif bases show similar antimicrobial activity to those of the literature. For example, it is observed that most of the compounds are effective on two microorganisms mentioned above (*S. aureus* and *C. albicans*).

The crystal structure of *N*-(5-methyl-2-hydroxyphenyl)-3,4-dimethoxybenzaldimine (**XIII**) is determined by X-ray diffraction at room temperature. It crystallizes in monoclinic system, and space group $P2_1$. Unit-cell dimensions are as follows: a=7.4750(5) Å, b=7.7954(7) Å, c=12.6696(8) Å, V=730.20(9) $Å^3$, Z=2. Non-planar title compound has a weak intramolecular hydrogen bonding between C=N nitrogen and OH hydrogen atoms.

As a conclusion, it can be said that the moderate and selective antimicrobial activities of the Schiff bases against *S. aureus*, *K. pneumoniae* and *C. albicans* encouraged further investigation on similar compounds.

Supplementary Material

Crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Centre (CCDC 825167). Copies of the

data can be obtained free of charge upon application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [e-mail: deposit@ccdc.cam.ac.uk].

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