



Synthesis, characterization, crystal structures and antibacterial activities of some Schiff bases with N₂O₂ donor sets

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Abstract

A series of Schiff base compounds were synthesized by the reaction of different 3,5-dihalosalicylaldehyde (halo atoms equal to Cl, Br and I) with polymethylenediamines of varying chain length. The Schiff bases were characterized using FT-IR, UV-Vis, ¹H NMR, ¹³C NMR and mass spectroscopic techniques, and elemental analyses (CHN), and crystal structure of some compounds was determined by X-ray crystallography. The in vitro biological screening effects of the synthesized compounds were tested against different microbial kinds. The results revealed that all compounds were biologically active.

Keywords Schiff base · N₂O₂ donor sets · Crystal structure · Antibacterial activity

Introduction

Compounds containing an azomethine group (–CH=N–) are known as Schiff bases. Their preparation, chemical and physical properties have been studied by many research groups. Schiff bases have different applications in various fields such as electrochemistry, bioinorganic, catalysis, metallic deactivator, separation processes, organic syntheses and environmental chemistry [1–4].

Due to the presence of donor atoms such as nitrogen, oxygen and sulfur in Schiff bases, these compounds are structurally similar to biological systems. In recent years, a considerable number of tetradentate salen-type Schiff base compounds, especially those have a N₂O₂ donor sets, can be used as ligands to obtain metal complexes that can serve as more or less successful models of biological compounds [5–7] and as catalyst in organic reactions [8, 9]. These compounds have been broadly examined for their antibacterial

[10–12], antifungal [13–15], anticancer [16], antitubercular [17, 18], antiviral [19], anti-inflammatory [20, 21], anticonvulsant [22, 23], antimalarial [24] and antitumor [25] activity. Structure–activity relationship (SAR) of Schiff bases has been studied by a lot of researchers [26]. On the basis of these studies, unsubstituted salicylaldehyde has only low activity. In some cases, the effect of substituents is dramatic. The presence of functional groups such as halogen, hydroxyl or nitro may cause higher activity, but the effects are not easily predictable nor can they be extrapolated from one microbe to another [27, 28].

In the current work, we synthesized nine new Schiff bases derived from various primary diamines and 3,5-dichlorosalicylaldehyde, 3,5-dibromosalicylaldehyde and 3,5-diiodosalicylaldehyde (Fig 1). The compounds were characterized using FT-IR, UV-Vis, ¹H NMR, ¹³C NMR, mass spectroscopic technique, elemental analyses (CHN) and single-crystal X-ray diffraction. The in vitro biological activities of the compounds were evaluated against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli* and *Pseudomonas aeruginosa*.

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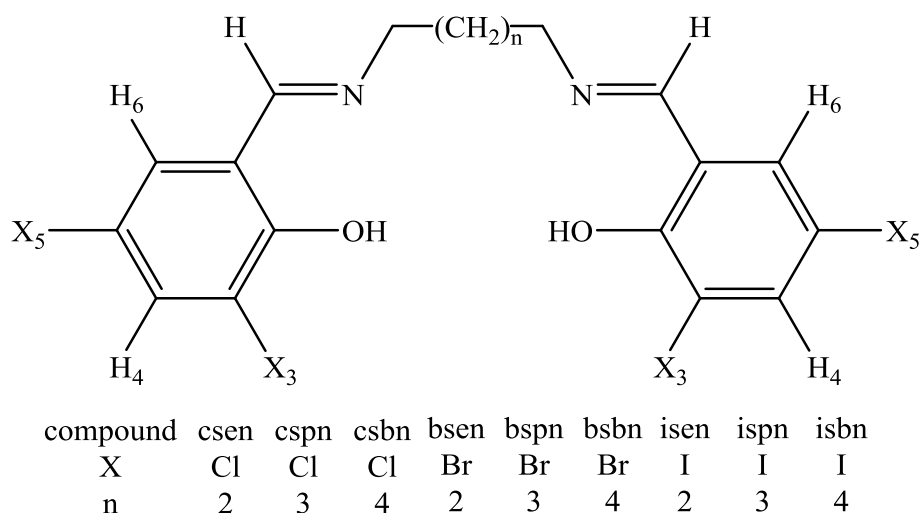
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Experimental

Materials and physical measurements

All chemicals were of reagent grade and used without further purification. Melting points were determined in open

Fig. 1 Structural formula of the Schiff base compounds



capillaries and are uncorrected. The ^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded at ambient temperature by a BRUKER AVANCE 400 MHz spectrometer using CDCl_3 as solvent. The chemical shift values (δ) are given in ppm. Infrared spectra were recorded using KBr disks on an FT-IR Prestige21 spectrophotometer in the range of $4000\text{--}400\text{ cm}^{-1}$. The mass spectra were obtained on an Agilent Technologies 5975C instrument. The C, H and N microanalyses were obtained with a Thermo Finnigan Flash EA 1112 elemental analyzer. Electronic spectra were recorded on a UV-Vis Cary 50 instrument. The X-ray data for the compounds were collected at room temperature on a Bruker Smart APEX CCD diffractometer ($\text{Mo K}\alpha = 0.71073\text{ \AA}$). Full spheres of reciprocal lattice were scanned by 0.3° steps in omega with a crystal-to-detector distance of 5 cm. Cell refinement and data reduction were performed with the help of the SAINT program [29]. Corrections for absorption were made with the multiscan method and SADABS program [29]. The structures were solved with direct methods using SHELXS, and structure refinement on F2 was carried out with the SHELXL-2014/7 program. All non-hydrogen atoms were refined using anisotropic displacement parameters [30]. All calculations were done with PLATON [31].

General procedure for the synthesis of Schiff bases

To a stirred ethanolic (25 mL) solution of 3,5-dihalosalicylaldehyde (2 mmol) was added an ethanolic (25 mL) solution of the diamine (1 mmol). The reaction mixture was refluxed for 1–3 h at $80\text{--}90^\circ\text{C}$ in a water bath. The resulting solution was cooled to room temperature, and the resulting precipitate was collected by suction filtration and washed with cold ethanol ($3 \times 10\text{ mL}$) to afford the desired Schiff base. Single crystals of the **isen**, **bspn** and **isbn** suitable for X-ray

diffraction experiments were obtained by slow evaporation of the hot ethanolic solution of the compounds.

6,6'((*1E, 1'E*)(ethane-1,2-diylbis(azanylylidene))bis(methanylylidene))bis(2,4-dichlorophenol) or **c_{sen}** was prepared using ethane-1,2-diamine and 3,5-dichlorosalicylaldehyde: Yield 373.6 mg (92%). m.p.: 216°C . UV-Vis (λ_{max} , nm): 429, 335, 262. IR (KBr): 3061m, 2912m, 2850m, 1635s, 1446s, 1362m, 1275m, 1207m, 1176m, 1042m, 854m, 731m, 696m, 563m, cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , δ): 13.99 (*br*, 2H, $-\text{OH}$), 8.31 (*s*, 2H, $\text{H}-\text{C}=\text{N}$), 7.43 (*d*, 2H, $J=2.4$, H-6), 7.17 (*d*, 2H, $J=2.4$, H-4), 4.03 (*s*, 4H, $=\text{N}-\text{CH}_2-\text{C}$). ^{13}C NMR (100 MHz, CDCl_3 , δ): 166.21, 157.79, 132.27, 129.85, 122.70, 121.55, 119.26, 57.70. MS (m/z): calculated for $[\text{C}_{16}\text{H}_{12}\text{Cl}_4\text{N}_2\text{O}_2]^+$ 406.08, observed 406.0. Combustion analysis for $\text{C}_{16}\text{H}_{12}\text{Cl}_4\text{N}_2\text{O}_2$: Calculated. C 47.32, H 2.98, N 6.90; found C 47.21, H 2.92, N 6.25.

6,6'((*1E, 1'E*)(propane-1,3-diylbis(azanylylidene))bis(methanylylidene))bis(2,4-dichlorophenol) or **c_{spn}** was prepared using propane-1,3-diamine and 3,5-dichlorosalicylaldehyde: Yield 365.5 mg (87%). m.p.: 186°C . UV-Vis (λ_{max} , nm): 429, 333, 262. IR (KBr): 3071m, 2947m, 2858m, 1631s, 1458s, 1363m, 1292m, 1219s, 1182s, 1066m, 1001m, 974m, 869m, 731m, 569m, 482m, cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , δ): 14.37 (*br*, 2H, $-\text{OH}$), 8.34 (*s*, 2H, $\text{H}-\text{C}=\text{N}$), 7.44 (*d*, 2H, $J=2.4$, H-6), 7.18 (*d*, 2H, $J=2.4$, H-4), 3.81 (*t*, 4H, $J=6.4$, $=\text{N}-\text{CH}_2-\text{C}$), 2.17 (*q*, 2H, $J=6.4$, $=\text{N}-\text{C}-\text{CH}_2$). ^{13}C NMR (100 MHz, CDCl_3 , δ): 164.44, 157.37, 131.93, 129.04, 122.55, 121.61, 118.87, 55.02, 30.82. MS (m/z): calculated for $[\text{C}_{17}\text{H}_{14}\text{Cl}_4\text{N}_2\text{O}_2]^+$ 420.11, observed 420.0. Combustion analysis for $\text{C}_{17}\text{H}_{14}\text{Cl}_4\text{N}_2\text{O}_2$: Calculated. C 48.60, H 3.36, N 6.67; found C 48.83, H 3.28, N 6.76.

6,6'((*1E, 1'E*)(butane-1,4-diylbis(azanylylidene))bis(methanylylidene))bis(2,4-dichlorophenol) or **c_{sbn}** was prepared using ethane-1,2-diamine and 3,5-dibromosalicylaldehyde: Yield 356.0 mg (82%). m.p.: 216°C . UV-Vis

(λ_{\max} , nm): 428, 334, 264. IR (KBr): 3068m, 2914m, 2852m, 1636s, 1462s, 1355m, 1288, 1211m, 1161m, 1035m, 957m, 740m, 686m, 555m, cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , δ): 14.58 (*br*, 2H, $-\text{OH}$), 8.28 (*s*, 2H, $\text{H}-\text{C}=\text{N}$), 7.43 (*d*, 2H, $J=2.4$, H-6), 7.16 (*d*, 2H, $J=2.4$, H-4), 3.71 (*t*, 4H, $J=6.0$, $=\text{N}-\text{CH}_2-\text{C}$), 1.85 (*q*, 2H, $J=6.0$, $=\text{N}-\text{C}-\text{CH}_2$). ^{13}C NMR (100 MHz, CDCl_3 , δ): 167.34, 157.65, 134.54, 129.48, 127.34, 119.48, 117.65, 53.34, 27.34. MS (m/z): calculated for $[\text{C}_{18}\text{H}_{16}\text{Cl}_4\text{N}_2\text{O}_2]^+$ 434.14, observed 434.0. Combustion analysis for $\text{C}_{18}\text{H}_{16}\text{Cl}_4\text{N}_2\text{O}_2$: Calculated. C 49.80, H 3.71, N 6.45; found C 49.98, H 3.66, N 6.43.

6,6'((*IE, I'E*)(ethane-1,2-diylbis(azanylylidene))bis(methanylylidene))bis(2,4-dibromophenol) or **bsen** was prepared using ethane-1,2-diamine and 3,5-dibromosalicylaldehyde: Yield 467.1 mg (80%). m.p.: 238 °C. UV–Vis (λ_{\max} , nm): 431, 335, 264. IR (KBr): 3099m, 3054m, 2939m, 1623s, 1596m, 1531m, 1508m, 1434m, 1251s, 978m, 854m, 822m, 748m, 569m, 513w, cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , δ): 14.15 (*br*, 2H, $-\text{OH}$), 8.27 (*s*, 2H, $\text{H}-\text{C}=\text{N}$), 7.72 (*d*, 2H, $J=2.4$, H-6), 7.34 (*d*, 2H, $J=2.4$, H-4), 4.00 (*s*, 4H, $=\text{N}-\text{CH}_2-\text{C}$). ^{13}C NMR (100 MHz, CDCl_3 , δ): 166.84, 162.02, 138.23, 134.33, 118.90, 114.34, 106.60, 55.60. MS (m/z): calculated for $[\text{C}_{16}\text{H}_{12}\text{Br}_4\text{N}_2\text{O}_2]^+$ 583.90, observed 583.80. Combustion analysis for $\text{C}_{16}\text{H}_{12}\text{Br}_4\text{N}_2\text{O}_2$: Calculated. C 32.91, H 2.07, N 4.80; found C 32.21, H 1.99, N 4.50.

6,6'((*IE, I'E*)(propane-1,3-diylbis(azanylylidene))bis(methanylylidene))bis(2,4-dibromophenol) or **bspn** was prepared using propane-1,3-diamine and 3,5-dibromosalicylaldehyde: Yield 466.4 mg (78%). m.p.: 160 °C. UV–Vis (λ_{\max} , nm): 430, 335, 259. IR (KBr): 3064m, 2943m, 2850m, 1632s, 1560m, 1514m, 1444s, 1360m, 1286m, 1221m, 1167m, 1067m, 1036m, 999m, 872w, 849m, 740m, 687m, 561w, 474w, 419w, cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , δ): 14.52 (*br*, 2H, $-\text{OH}$), 8.29 (*s*, 2H, $\text{H}-\text{C}=\text{N}$), 7.73 (*d*, 2H, $J=2.4$, H-6), 7.33 (*d*, 2H, $J=2.4$, H-4), 3.79 (*t*, 4H, $J=6.4$, $=\text{N}-\text{CH}_2-\text{C}$), 2.16 (*q*, 2H, $J=6.4$, $=\text{N}-\text{C}-\text{CH}_2$). ^{13}C NMR (100 MHz, CDCl_3 , δ): 166.16, 163.53, 138.28, 134.38, 118.53, 115.17, 105.41, 52.35, 30.51. MS (m/z): calculated for $[\text{C}_{17}\text{H}_{14}\text{Br}_4\text{N}_2\text{O}_2]^+$ 597.93, observed 597.90. Combustion analysis for $\text{C}_{17}\text{H}_{14}\text{Br}_4\text{N}_2\text{O}_2$: Calculated. C 34.15, H 2.36, N 4.69; found C 34.04, H 2.28, N 4.57.

6,6'((*IE, I'E*)(butane-1,4-diylbis(azanylylidene))bis(methanylylidene))bis(2,4-dibromophenol) or **bsbn** was prepared using butane-1,4-diamine and 3,5-dibromosalicylaldehyde: Yield 428.4 mg (70%). m.p.: 207 °C. UV–Vis (λ_{\max} , nm): 429, 336, 261. IR (KBr): 3064m, 2945m, 2916m, 2846m, 1632s, 1560m, 1514m, 1452s, 1366m, 1286m, 1196m, 1163m, 1043m, 874m, 686m, 474w, cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , δ): 14.74 (*br*, 2H, $-\text{OH}$), 8.24 (*s*, 2H, $\text{H}-\text{C}=\text{N}$), 7.72 (*d*, 2H, $J=2.4$, H-6), 7.34 (*d*, 2H, $J=2.4$, H-4), 3.71 (*t*, 4H, $J=6.0$,

$=\text{N}-\text{CH}_2-\text{C}$), 1.85 (*q*, 2H, $J=6.0$, $=\text{N}-\text{C}-\text{CH}_2$). ^{13}C NMR (100 MHz, CDCl_3 , δ): 165.92, 164.89, 138.52, 134.54, 117.77, 115.90, 104.22, 53.46, 27.34. MS (m/z): calculated for $[\text{C}_{18}\text{H}_{16}\text{Br}_4\text{N}_2\text{O}_2]^+$ 611.95, observed 611.9. Combustion analysis for $\text{C}_{18}\text{H}_{16}\text{Br}_4\text{N}_2\text{O}_2$: Calculated. C 55.33, H 2.67, N 4.58; found C 54.97, H 2.61, N 4.47.

6,6'((*IE, I'E*)(ethane-1,2-diylbis(azanylylidene))bis(methanylylidene))bis(2,4-diiodophenol) or **isen** was prepared using ethane-1,2-diamine and 3,5-diiodosalicylaldehyde: Yield 578.9 mg (75%). m.p.: 236 °C. UV–Vis (λ_{\max} , nm): 439, 343, 260. IR (KBr): 3053m, 2881m, 1630s, 1580m, 1458m, 1437s, 1352m, 1285m, 1209m, 1153m, 1032m, 966m, 868m, 741m, 552m, cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , δ): 14.49 (*br*, 2H, $-\text{OH}$), 8.48 (*s*, 2H, $\text{H}-\text{C}=\text{N}$), 8.04 (*d*, 2H, $J=2.0$, H-6), 7.72 (*d*, 2H, $J=2.0$, H-4), 4.01 (*s*, 4H, $=\text{N}-\text{CH}_2-\text{C}$). ^{13}C NMR (100 MHz, CDCl_3 , δ): 166.66, 164.66, 148.99, 141.15, 118.73, 92.51, 77.69, 55.43. MS (m/z): calculated for $[\text{C}_{16}\text{H}_{12}\text{I}_4\text{N}_2\text{O}_2]^+$ 771.90, observed 771.9. Combustion analysis for $\text{C}_{16}\text{H}_{12}\text{I}_4\text{N}_2\text{O}_2$: Calculated. C 24.90, H 1.57, N 3.63; found C 24.99, H 1.69, N 3.55.

6,6'((*IE, I'E*)(propane-1,3-diylbis(azanylylidene))bis(methanylylidene))bis(2,4-diiodophenol) or **ispn** was prepared using propane-1,3-diamine and 3,5-diiodosalicylaldehyde: Yield 534.4 mg (68%). m.p.: 176 °C. UV–Vis (λ_{\max} , nm): 437, 343, 258. IR (KBr): 3049m, 2292m, 2851m, 1624s, 1582m, 1456m, 1435s, 1357m, 1319m, 1285m, 1271m, 1215m, 1155s, 1095m, 1060m, 987m, 964m, 871m, 850m, 738m, 657m, 547m, cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , δ): 14.40 (*br*, 2H, $-\text{OH}$), 8.19 (*s*, 2H, $\text{H}-\text{C}=\text{N}$), 8.08 (*d*, 2H, $J=2.0$, H-6), 7.52 (*d*, 2H, $J=2.0$, H-4), 3.79 (*t*, 4H, $J=6.4$, $=\text{N}-\text{CH}_2-\text{C}$), 2.16 (*q*, 2H, $J=6.4$, $=\text{N}-\text{C}-\text{CH}_2$). ^{13}C NMR (100 MHz, CDCl_3 , δ): 166.07, 165.94, 149.01, 141.26, 118.21, 93.76, 76.33, 52.19, 30.52. MS (m/z): calculated for $[\text{C}_{17}\text{H}_{14}\text{I}_4\text{N}_2\text{O}_2]^+$ 785.93, observed 785.90. Combustion analysis for $\text{C}_{17}\text{H}_{14}\text{I}_4\text{N}_2\text{O}_2$: Calculated. C 25.98, H 1.80, N 3.56; found C 26.09, H 1.91, N 3.45.

6,6'((*IE, I'E*)(butane-1,4-diylbis(azanylylidene))bis(methanylylidene))bis(2,4-diiodophenol) or **isbn** was prepared using butane-1,4-diamine and 3,5-dibromosalicylaldehyde: Yield 480.0 mg (60%). m.p.: 196 °C. UV–Vis (λ_{\max} , nm): 434, 343, 261. IR (KBr): 3053m, 2940m, 2856w, 1634s, 1580m, 1477m, 1439m, 1352m, 1219m, 1182m, 1128m, 1041m, 1016m, 912m, 866m, 759m, 657m, cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , δ): 14.72 (*br*, 2H, $-\text{OH}$), 8.13 (*s*, 2H, $\text{H}-\text{C}=\text{N}$), 8.06 (*d*, 2H, $J=2.0$, H-6), 7.50 (*d*, 2H, $J=2.0$, H-4), 3.69 (*t*, 4H, $J=6.8$, $=\text{N}-\text{CH}_2-\text{C}$), 1.83 (*q*, 2H, $J=6.8$, $=\text{N}-\text{C}-\text{CH}_2$). ^{13}C NMR (100 MHz, CDCl_3 , δ): 167.24, 165.66, 149.19, 141.45, 117.68, 94.88, 75.39, 53.40, 27.37. MS (m/z): calculated for $[\text{C}_{18}\text{H}_{16}\text{I}_4\text{N}_2\text{O}_2]^+$ 799.96, observed 799.9. Combustion

analysis for $C_{18}H_{16}I_4N_2O_2$: Calculated. C 27.03, H 2.02, N 3.50; found C 27.14, H 2.03, N 3.63.

Biological activity evaluation

The in vitro antibacterial activity of the synthesized Schiff bases was investigated against the standard strains of two Gram-positive (*Staphylococcus aureus* PTCC1431, *Bacillus cereus* PTCC1015) and two Gram-negative (*Escherichia coli* PTCC1394, *Pseudomonas aeruginosa* PTCC1074) bacteria. In order to compare the results, ampicillin (10 mg/disk) and erythromycin (15 mg/disk) were used as standard antibacterial drugs. The compounds were dissolved in DMSO at $50 \mu\text{g mL}^{-1}$ concentration. Bacteria culture Petri dishes treated with the test compounds were incubated for 24 h at 37°C . Inhibition zone (mm) around the specimens was used to indicate antibacterial activity of each of compounds. Each test was performed in triplicate.

Results and discussion

All the Schiff base compounds are stable at room temperature and are non-hygroscopic. The compounds are insoluble in water, ethanol and methanol but are soluble in DMSO.

FT-IR spectra

The infrared spectrum provided valuable information for identifying the nature of the functional groups. For example, FT-IR spectrum of csen is shown in Fig. 2. The IR spectra of the Schiff bases show strong intensity absorption bands at $1623\text{--}1636 \text{ cm}^{-1}$ assigned to $\text{C}=\text{N}$ stretching mode of the azomethine [32]. The presence of aromatic rings has been identified by their characteristic ring vibrations at $1500\text{--}1400$, $1100\text{--}1050$ and $900\text{--}700 \text{ cm}^{-1}$ regions [33–35]. In all compounds, the absence of characteristic bands of unreacted carbonyl groups $\nu(\text{C}=\text{O})$ and primary amine $\nu(\text{NH}_2)$ confirms the formation of the proposed Schiff base structure. A band in the $1250\text{--}1290 \text{ cm}^{-1}$ due to $\text{C}-\text{O}$ phenolic group was also observed in these compounds [36].

UV-Vis spectra

The UV-visible absorption spectra were obtained in DMSO (10^{-4} M) at room temperature. Earlier papers emphasis that the electronic absorption bands of the salicylaldehyde-type Schiff base comprise of three bands [37]. The compounds exhibit three main peaks in the about 261, 337 and 432 nm. The $250\text{--}300 \text{ nm}$ bands are due to the $\pi \rightarrow \pi^*$ transitions of the aromatic rings. It is shown in Fig. 3. The bands at the $300\text{--}350 \text{ nm}$ range involve $\pi \rightarrow \pi^*$ transitions of the $\text{C}=\text{N}$ chromophore group. The longer wavelength bands over ca.

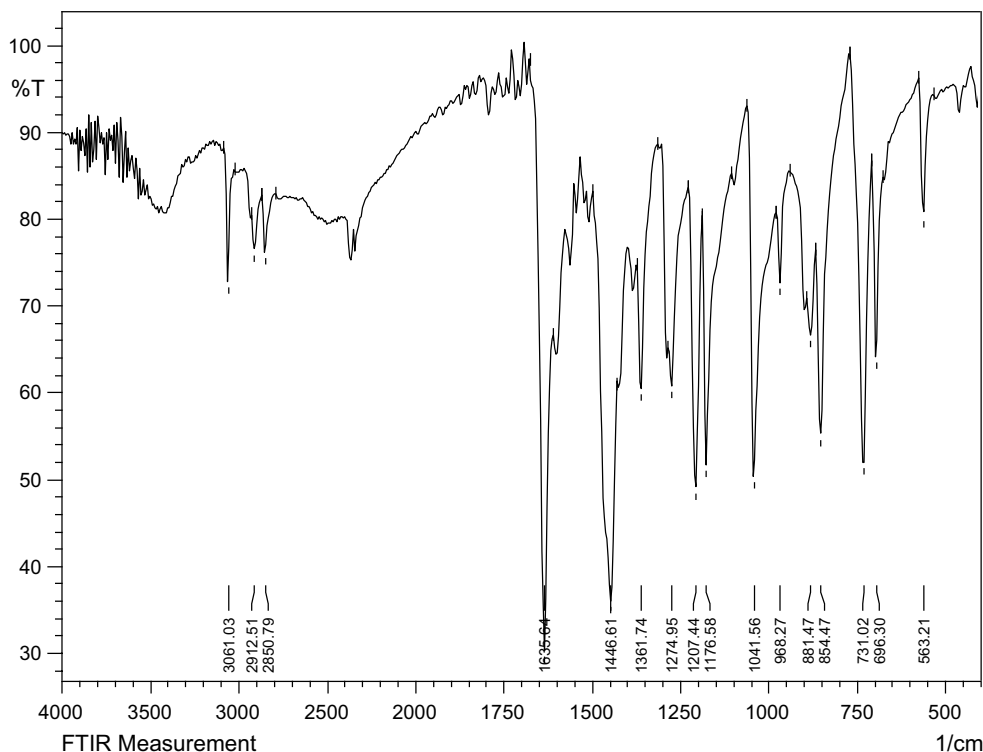


Fig. 2 FTIR spectrum of csen

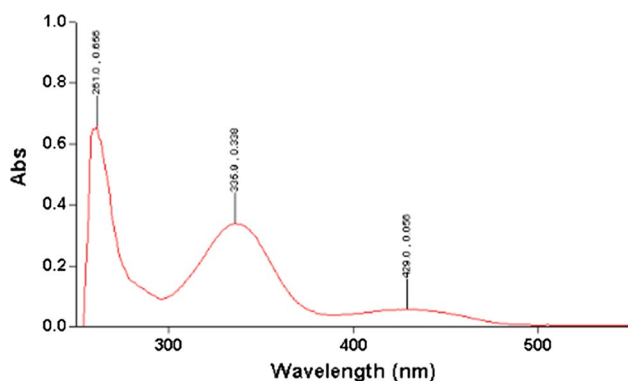


Fig. 3 UV-Vis. spectrum of **csen**

400 nm can be assigned to the intramolecular charge transfer interactions ($n \rightarrow \pi^*$ transition) of the non-bonding electrons present on the nitrogen of the azomethine group in the Schiff base compounds [38, 39].

NMR spectra

The ^1H NMR spectra of the Schiff base compounds were obtained in CDCl_3 at room temperature. The synthesized compounds showed signals of all protons in their expected regions, and the integration curve were equivalent to the total number of the protons deduced from their proposed structure. The chemical shift for the OH protons in the Schiff base compounds is observed in 13.99–14.74 ppm. The signals at $\delta = 8.13$ –8.48 ppm are assigned to the $-\text{C}(\text{H})=\text{N}-$ proton of azomethine [40, 41]. It is known that orthophenolic hydrogen bonding shifts the resonance signal of a proton to lower field (higher frequency). Comparing the ^1H NMR data of the OH protons of salicyl part of the compounds, it can be said that the strongest intramolecular hydrogen bond ($\text{OH} \cdots \text{N}$) is formed in **bsbn**, and the weakest one in **csen**. It is interesting that 13.99 ppm value of the **csen** is lower than those of the other phenolic Schiff bases. This difference means that the phenolic OH proton of **csen** has less acidic character and, consequently, **csen** has weaker intramolecular hydrogen bonding according to the others. The aromatic protons of the Schiff base

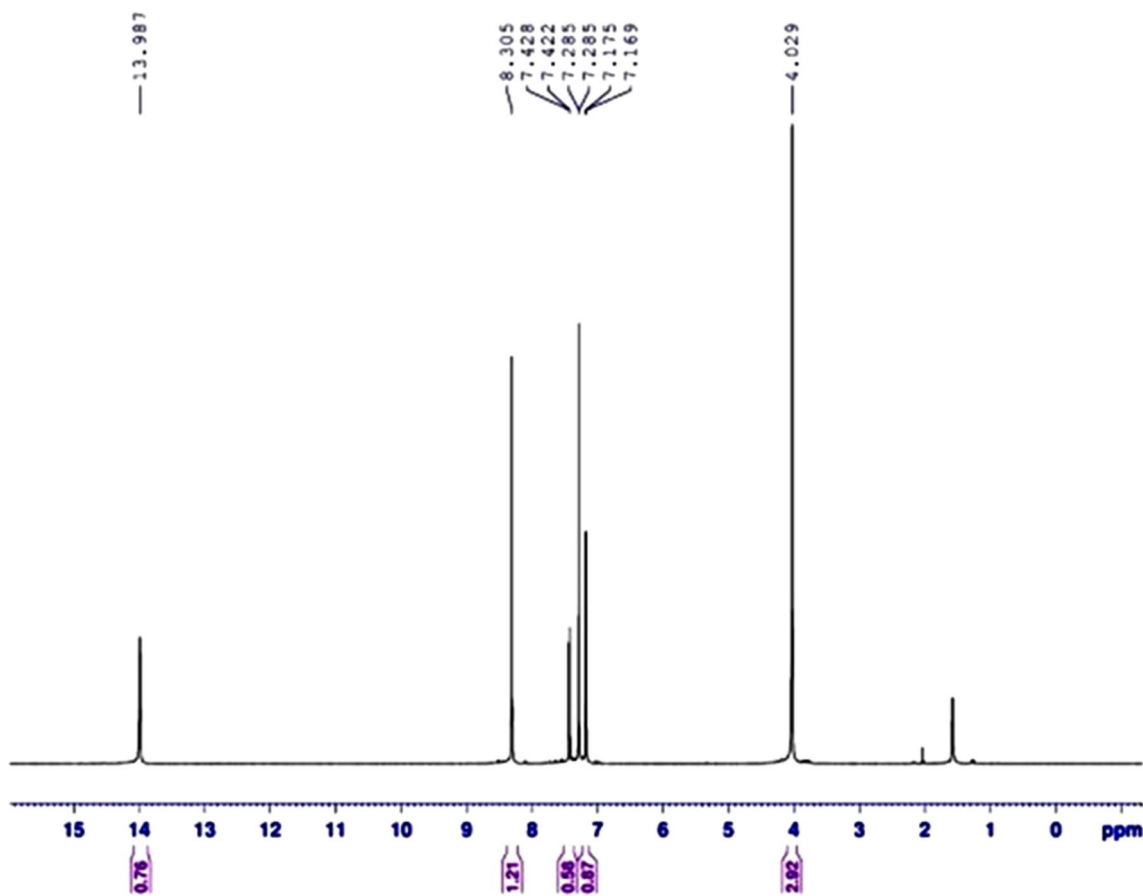


Fig. 4 ^1H NMR spectrum of **csen** in CDCl_3

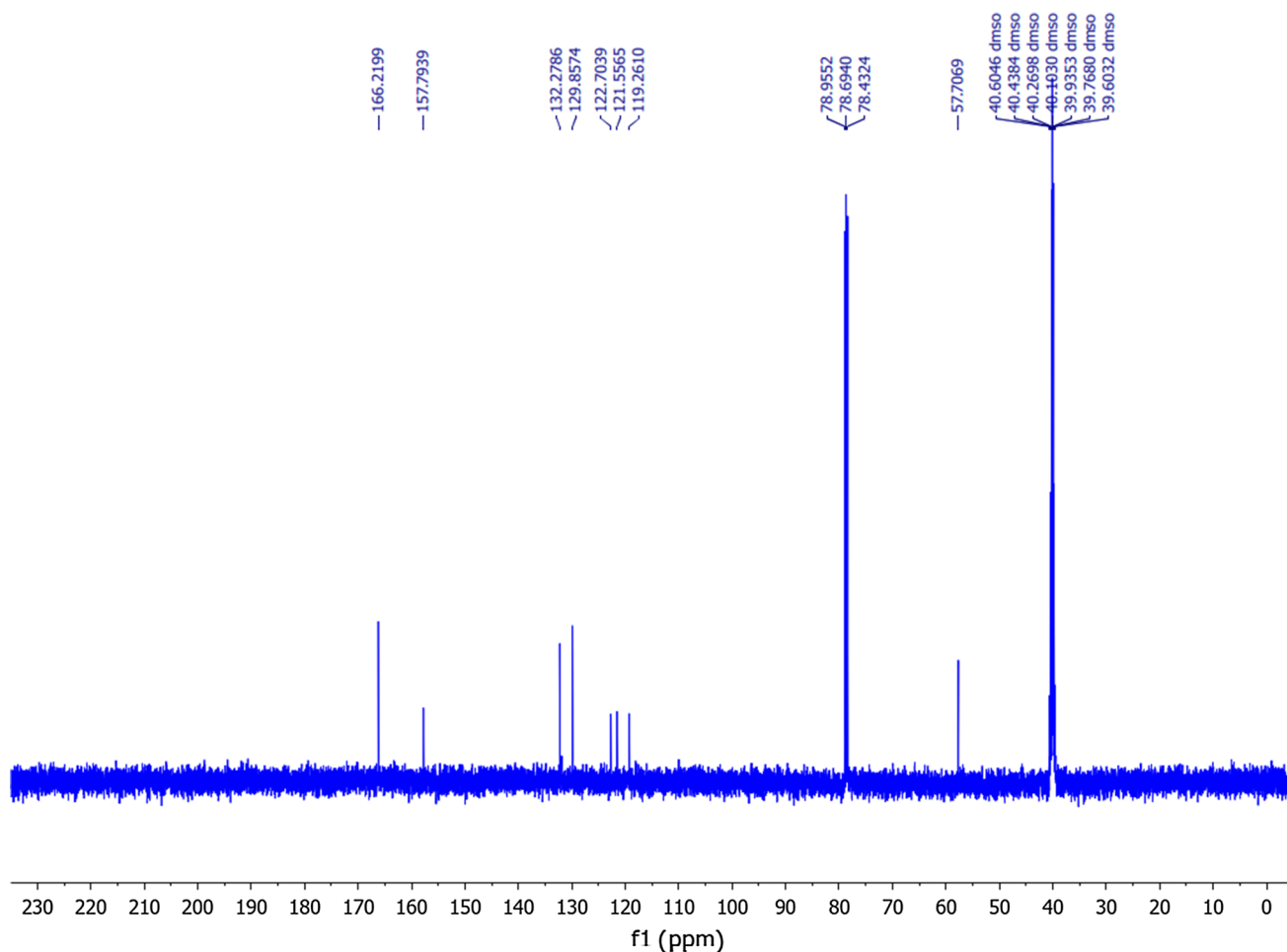


Fig. 5 ^{13}C NMR spectrum of **csen** in CDCl_3

compounds appeared at $\delta = 7.16\text{--}8.08$ ppm. The H-4 signal was observed as a doublet, due to coupling with the H-6, and also the H-6 signal was observed as a doublet, due to coupling with the H-4. The multiples of the aliphatic protons were appeared within the range of 1.83–4.03 ppm.

The ^{13}C NMR spectra of the Schiff base compounds are consistent with the number of carbons in their structures. The peaks observed at 166.22, 167.35, 164.44, 166.85, 166.17, 165.93, 166.66, 166.07 and 167.24 ppm are ascribed to the imine carbon atoms of **csen**, **cspn**, **csbn**, **bsen**, **bspn**, **bsbn**, **isen**, **ispn** and **isbn**, respectively. The existence of these peaks in the spectra of Schiff base compounds supports the presence of the Schiff base in them.

The chemical shift values of the different types of protons and carbons in the **csen** are reported in Figs. 4 and 5, respectively.

Mass Spectra

The formulation of the Schiff base compounds is deduced from analytical data, ^1H and ^{13}C NMR and further supported by mass spectroscopy. The electron impact mass spectra of Schiff base compounds are recorded and investigated at 70 eV of electron energy. The mass spectra of the studied Schiff bases are characterized by low to high relative intensity molecular ion peaks. The mass spectra of the compounds showed molecular ion peaks at m/e 404, 418, 432, 580, 594, 608, 772, 786 and 800 which corresponding to their molecular formula $\text{C}_{16}\text{H}_{12}\text{Cl}_4\text{N}_2\text{O}_2$ (**csen**), $\text{C}_{17}\text{H}_{14}\text{Cl}_4\text{N}_2\text{O}_2$ (**cspn**), $\text{C}_{18}\text{H}_{16}\text{Cl}_4\text{N}_2\text{O}_2$ (**csbn**), $\text{C}_{16}\text{H}_{12}\text{Br}_4\text{N}_2\text{O}_2$ (**bsen**), $\text{C}_{17}\text{H}_{14}\text{Br}_4\text{N}_2\text{O}_2$ (**bspn**), $\text{C}_{18}\text{H}_{16}\text{Br}_4\text{N}_2\text{O}_2$ (**bsbn**), $\text{C}_{16}\text{H}_{12}\text{I}_4\text{N}_2\text{O}_2$ (**isen**), $\text{C}_{17}\text{H}_{14}\text{I}_4\text{N}_2\text{O}_2$ (**ispn**) and $\text{C}_{18}\text{H}_{16}\text{I}_4\text{N}_2\text{O}_2$ (**isbn**), respectively. It is obvious that the molecular ion peaks are in good agreement with their suggested empirical formula as indicated from elemental analyses (Table 1). The low intensities of the molecular

Table 1 Crystal data and refinement parameters for isbn, bspn and isen

Schiff base compound	isbn	bspn	isen
Empirical formula	C ₁₈ H ₁₆ I ₄ N ₂ O ₂	C ₁₇ H ₁₄ Br ₄ N ₂ O ₂	C ₁₆ H ₁₀ I ₄ N ₂ O ₂
Formula weight	799.93	597.94	769.86
Crystal size (mm)	0.300×0.140×0.120	0.350×0.250×0.220	0.250×0.150×0.160
Temperature (K)	296 (2)	296 (2)	296 (2)
Crystal system	Monoclinic	Orthorhombic	Monoclinic
Space group	<i>P2</i> ₁	<i>Fdd2</i>	<i>P2</i> ₁ / <i>c</i>
θ range for data collection (°)	1.336–25.997	2.010–25.992	1.574–27.976
<i>a</i> (Å)	7.5152 (8)	25.8874 (17)	13.0382 (19)
<i>b</i> (Å)	9.3943 (11)	32.562 (2)	10.6131 (16)
<i>c</i> (Å)	15.6191 (17)	4.4186 (3)	7.0982 (10)
α (°)	90	90	90
β (°)	102.663 (4)	90	97.067
γ (°)	90	90	90
<i>V</i> (Å ³)	1075.9 (2)	3724.7 (4)	974.8 (2)
<i>Z</i>	2	8	2
ρ_{calc} (Mg/m ³)	2.469	2.133	2.623
μ (mm ⁻¹)	5.808	8.658	6.405
<i>F</i> (000)	732	2288	696
Index ranges	−9 ≤ <i>h</i> ≤ 9 −11 ≤ <i>k</i> ≤ 9 −19 ≤ <i>l</i> ≤ 19	−31 ≤ <i>h</i> ≤ 31 −40 ≤ <i>k</i> ≤ 40 −5 ≤ <i>l</i> ≤ 5	−17 ≤ <i>h</i> ≤ 17 −13 ≤ <i>k</i> ≤ 13 −9 ≤ <i>l</i> ≤ 9
Reflections collected	8871	7643	2316
Independent reflections	3610 [<i>R</i> (int)=0.0421]	1792 [<i>R</i> (int)=0.0409]	2316 [<i>R</i> (int)=0.05]
Data/restraints/parameters	3610/1/236	1792/1/116	2316/0/110
Goodness-of-fit (GOF)	0.985	1.037	1.090
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> ₁ =0.0363 w <i>R</i> ₂ =0.0575	<i>R</i> ₁ =0.0265 w <i>R</i> ₂ =0.0555	<i>R</i> ₁ =0.0692 w <i>R</i> ₂ =0.2577
Final <i>R</i> indexes (all data)	<i>R</i> ₁ =0.0607 w <i>R</i> ₂ =0.0658	<i>R</i> ₁ =0.0384 w <i>R</i> ₂ =0.0588	<i>R</i> ₁ =0.0865 w <i>R</i> ₂ =0.2731

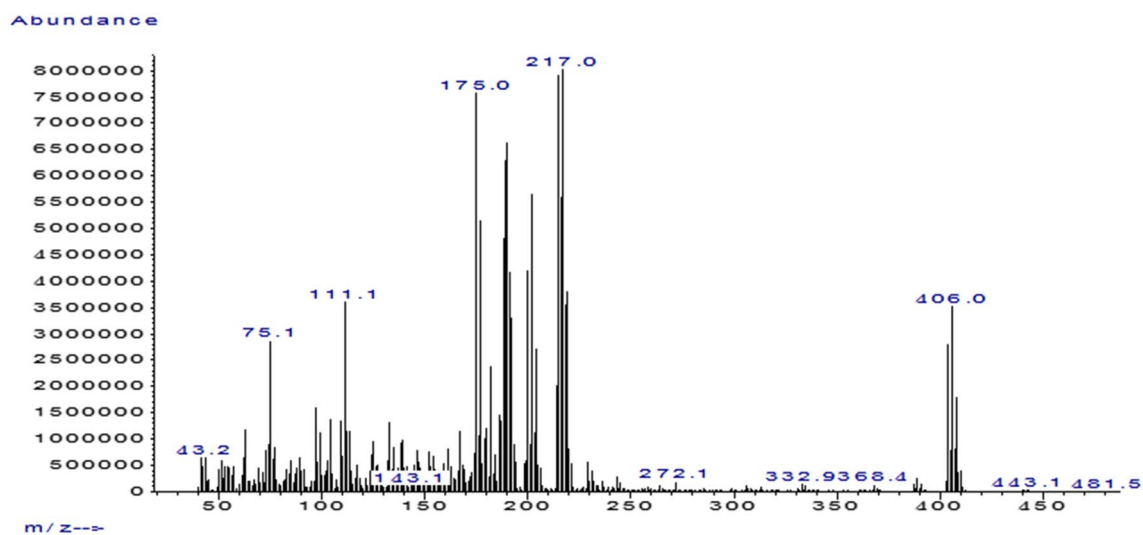
**Fig. 6** Mass spectrum of esen

Table 2 Selected bond lengths (Å) and angles (°) of bspn, isbn and isen

Bond	bspn	Bond	isbn	Bond	isen
Lengths (Å)					
N(1)–C(7)	1.274 (7)	N(1)–C(7)	1.290 (14)	N(1)–C(7)	1.295 (17)
N(1)–C(8)	1.473 (7)	N(1)–C(8)	1.474 (12)	N(1)–C(8)	1.470 (15)
O(1)–C(1)	1.343 (6)	O(1)–C(1)	1.272 (13)	O(1)–C(1)	1.346 (14)
Br(1)–C(2)	1.888 (5)	I(1)–C(2)	2.103 (11)	I(1)–C(4)	2.096 (12)
Angles (°)					
C(7)–N(1)–C(8)	118.7 (5)	C(7)–N(1)–C(8)	122.9 (10)	C(7)–N(1)–C(8)	118.2 (12)
O(1)–C(1)–C(2)	119.9 (5)	O(1)–C(1)–C(2)	122.0 (11)	O(1)–C(1)–C(2)	119.7 (11)
C(1)–C(2)–Br(1)	119.3 (4)	C(1)–C(2)–I(1)	118.1 (9)	C(1)–C(2)–I(2)	119.0 (9)
N(1)–C(7)–C(6)	121.8 (5)	N(1)–C(7)–C(6)	123.6 (11)	N(1)–C(7)–C(6)	121.2 (12)

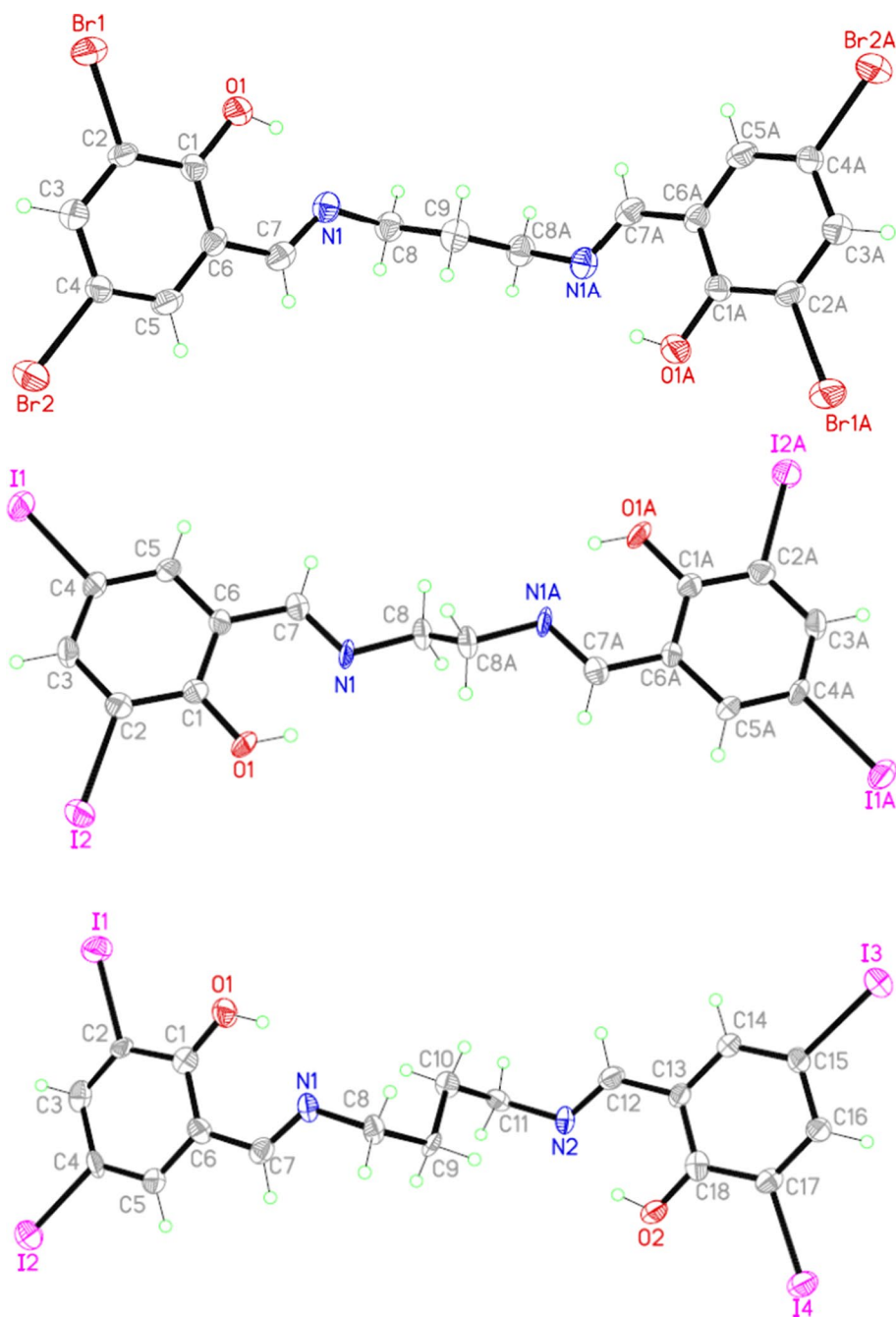
Fig. 7 ORTEP plots of bspn (top), isen (middle) and isbn (down) with atom numbering and ellipsoids probability at 30%

Table 3 Antibacterial activity (zone of inhibition, mm) of synthesized Schiff base compounds

compound	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>B. cereus</i>
cse	14	13	12	19
cspn	15	11	12	16
csbn	12	13	12	18
bsen	12	12	22	19
bspn	14	12	25	26
bsbn	15	13	21	23
isen	12	12	26	22
ispn	13	12	25	21
isbn	11	12	25	22
Erythromycin	16	17	25	24
Ampicillin	11	14	27	26

ion peaks in some of compounds, $[M]^+$, are indicative of the ease of fragmentation of these compounds, and this may reflect of halo atoms present in structures [42]. The mass spectrum of **cse** is shown in Fig. 6.

Crystal structure description

The solid-state structures of **isbn**, **bspn** and **isen** were determined by X-ray diffraction. The crystal data and refinement parameters are summarized in Table 1, and ORTEP plots of **isbn**, **bspn** and **isen** are shown in Fig. 1. Selected bond lengths and angles are summarized in Table 2. The asymmetric unit of **isbn** comprises a potentially tetradentate Schiff base ligand. Pair of the intramolecular O–H...N hydrogen bonds make *S*(6) ring. The compound crystallizes in monoclinic system with *P*2(1) space group. The absolute structure parameter (Flack parameter) was determined successfully. The crystal packing of the compound shows two-dimensional network of connected molecules through the intermolecular C–I... π interactions parallel to *ab*-plane (Fig. 7). The asymmetric unit of **bspn** comprises half of a potentially tetradentate Schiff base ligand. Pair of the intramolecular O–H...N hydrogen bonds make *S*(6) ring. The intermolecular C–H...O interactions link neighboring molecules along the *a*-axis. Similar to **bspn** compound, the asymmetric unit of the **isen** compound comprises half of a potentially tetradentate Schiff base ligand. The crystal is twinned non-merohedrally with a refined ratio of 0.829(7)/0.171(7).

Antimicrobial activity

The in vitro antibacterial activities of the synthesized Schiff base compounds and known drugs such as ampicillin and erythromycin were screened in DMSO against more than medically important Gram-positive and Gram-negative bacteria to increase the chance of antibiotic principles in

the tested materials. The microorganisms used in this work include *Staphylococcus aureus* and *Bacillus cereus* (as Gram-positive bacteria) and *Escherichia coli* and *Pseudomonas aeruginosa* (as Gram-negative bacteria).

The antibacterial activities of the compounds are represented by size of the diameter of inhibition zone in mm and for all Schiff bases are shown in Table 3.

The compounds were tested at the concentrations of $50 \mu\text{g mL}^{-1}$ in DMSO. Antimicrobial activity depends on the nature of bacterial strain, the solvent and chelating ability of the Schiff base. It is believed that Schiff bases act by forming a chelate with the bacterial strain. This may involve hydrogen bonding through the azomethine group with the active centers of cell constituents thus resulting in an interference with normal cell process.

In general, compounds having chloro, bromo or iodo substituent in their structure are having significant antibacterial and antifungal activity. In all nine compounds, the central ligand is salicylaldehyde with different side chains. In **cse**, **cspn** and **csbn**, it is 3,5-dichloro, in **bsen**, **bspn** and **bsbn**, it is 3,5-dibromo, and in **isen**, **ispn** and **isbn**, it is 3,5-diiodo. The diffusion capacity of the compounds and the effect of them against bacteria vary with their structure.

It is observed that the compounds with Br and I substituents have better antimicrobial activity according to the others (as reported in previous articles [43, 44]).

It is evident from Table 3 that all Schiff bases described here were found to be biologically active and showed significantly enhanced antibacterial activity against all of the bacterial species. From the bactericidal activity, it is apparent that the compounds were more toxic toward Gram-positive strains than Gram-negative strains. This difference may be attributed to the fact that the cell wall in Gram-positive bacteria is of a single layer, whereas the Gram-negative cell wall is a multilayered structure.

For *E. coli*, the **cspn** and **bsbn** showed maximum activity followed by **cse** and **bspn**. Against *P. aeruginosa*, **cse** and **csbn** showed maximum activity, and minimum inhibition was observed for **cspn**. For *S. aureus*, **isen** showed maximum inhibition. The **bspn** showed excellent activity against *B. cereus*.

Conclusion

In this paper, a series of symmetrical Schiff bases containing the N_2O_2 unit derived from condensation reaction of various diaminoalkyls with substituted salicylaldehydes have been synthesized. These compounds physically and chemically characterized through elemental analysis (CHN), FT-IR, UV–Vis, ^1H NMR, ^{13}C NMR and mass spectroscopic. The crystal structures of **isen**, **bspn**

and **isbn** were determined by X-ray diffraction at room temperature. They have been crystallized in monoclinic, orthorhombic and monoclinic, respectively. The antimicrobial activity results showed that most of the synthesized Schiff base compounds possess a good antibacterial activity against both Gram-negative and Gram-positive bacteria tested. The structures of the Schiff bases determine an intensification of the antimicrobial activity.

Supplementary data

Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre. CCDCs 1563977, 1563978 and 1563979 and contain the supplementary crystallographic data for **bspn**, **isen** and **isbn**. These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> or from the CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK; Fax: (+44) 01223-336-033; E-mail: deposit@ccdc.cam.ac.

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