



Research article

Synthesis, characterization, spectroscopic studies and biological evaluation of Schiff bases derived from 1-hydroxy-2-acetonaphthanone

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ABSTRACT

The four Schiff bases (**I** - **IV**) were synthesized by the condensation reaction of 1-(1-hydroxynaphthalen-2-yl)ethanone, 1-(4-chloro-1-hydroxynaphthalen-2-yl)ethanone and 1-(4-bromo-1-hydroxynaphthalen-2-yl)ethanone with propane-1,3-diamine and pentane-1,3-diamine. The structural analysis is done by UVvis., FT-IR, ¹H NMR, ¹³C NMR, LCMS and elemental analyses. These compounds were assayed for antibacterial (*Escherichia coli* and *Salmonella Typhi*) activity and antioxidant (2,2-Diphenyl-1-Picryl Hydrazyl(DPPH) and Hydroxyl radical scavenging method) activity. The antibacterial and antioxidant activities of synthesized Schiff bases exhibited better degrees of inhibitory effects. Among these, Schiff base 2,2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-chloronaphthalen-1-ol) (**II**) exhibited excellent antibacterial activity with MICs of 0.12, 0.25, 0.5 and 1 mg/ml against *E. coli* and *Salmonella Typhi*. Furthermore, two Schiff bases such as, 2,2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol) (**I**) and 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-bromonaphthalen-1-ol) (**IV**) exhibited promising antioxidant activity.

1. Introduction

Schiff bases contains azomethine (-C=N-) linkage and are usually derived by the condensation of carbonyl compounds (aldehydes/ketones) with primary aliphatic/aromatic/heteroaromatic amines. Schiff bases are known for their antitumor [1, 2, 3, 4, 5, 6, 7, 8], antifungal [9, 10, 11, 12, 13], antiviral [14], antibacterial [9, 10, 11, 12, 15, 16, 17] and anticancer [18, 19] activities. Schiff bases find many applications including acid catalyst [20, 21, 22, 23], reduction catalyst [24, 25], oxidation catalyst [26, 27, 28, 29, 30, 31], dye [32, 33] and it also exhibit special liability towards metal ions [34, 35, 36, 37]. The intermolecular hydrogen bonding ability and proton transfer equilibria of Schiff bases offer them excellent bioactivity [38]. Metal complexes derived from Schiff bases have been used as insecticides, pesticides, bactericides and fungicides [39, 40]. Furthermore, metal complexes of Schiff bases harbouring hetero atoms such as N, S, O etc. exhibit several bio potencies [41] including antitumor [42, 43], antioxidant [44], antibacterial [45, 46], antimicrobial [47] antifungal [48], anticancer [49, 50, 51], antiviral [52], anti-inflammatory [53] and anti-HIV [54] activities. Infections with Gram-negative bacteria are especially worrisome than that of Gram-positive bacteria [55]. Considering the magnitude of ever-growing antibacterial resistance, it is necessary to discover novel Schiff bases with

resistance improved pharmacological profile. We chose to synthesize a library of Schiff bases from 1-hydroxy-2-acetonaphthanone and diamines having 3-carbon spacer since it offers tetradentate and flexible nature to the new Schiff bases [56, 57, 58, 59, 60].

In present work, we report here in synthesis, characterization, antibacterial and antioxidant activity of four new Schiff bases derived from 1-(1-hydroxynaphthalen-2-yl)ethanone, 1-(4-chloro-1-hydroxynaphthalen-2-yl)ethanone and 1-(4-bromo-1-hydroxynaphthalen-2-yl)ethanone with propane-1,3-diamine and pentane-1,3-diamine. The structures of these Schiff bases were confirmed by UV, FT-IR, ¹H-NMR, ¹³C NMR, and Mass spectroscopic tools, and additionally by Elemental analysis.

2. Experimental

Chemicals were obtained from AURA, SPECTROCHEM & TCI and were used as received without any further purification.

2.1. Synthesis

The tetradentate Schiff base, 2,2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol) (**I**) and 2,2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-chloronaphthalen-

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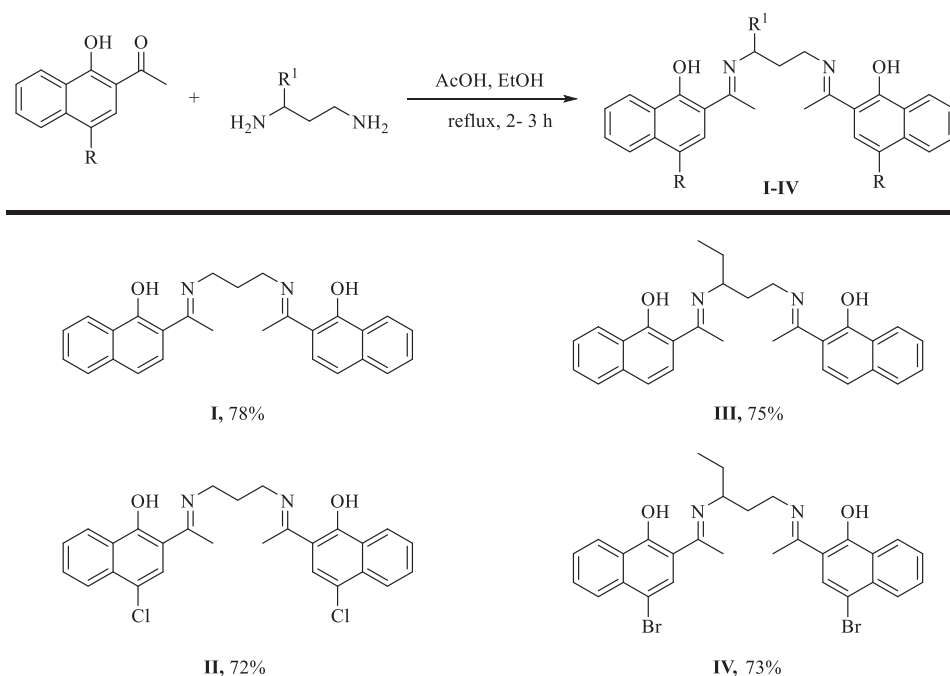


Fig. 1. Synthesis and structure of Schiff bases (I-IV).

Table 1

Antibacterial activity of given Schiff bases (I-IV).

Compounds	<i>E. coli</i>	<i>Salmonella Typhi</i>
Penicillin (10 µg/disc)	09	12
I	05	06
II	10	11
III	07	08
IV	08	05
DMSO	–	–

Bold showing reference drug numbers.

Table 2

MICs of given Schiff bases (I-IV).

Code No. of Compound	Name of pathogens							
	<i>Escherichia coli</i> (mg/mL)				<i>Salmonella Typhi</i> (mg/mL)			
	1.0	0.5	0.25	0.12	1.0	0.5	0.25	0.12
I	+	+	+	+	–	+	+	+
II	–	–	–	–	–	–	–	–
III	–	–	+	+	–	–	+	+
IV	–	–	+	+	+	+	+	+
Penicillin (10 µg/mL)	–	–	–	–	–	–	–	+

The positive sign (+) indicate growth on plate; negative sign (–) indicate no growth on plate.

Table 3

Antioxidant activity of given Schiff bases (I-IV).

Compounds	DPPH (%)	OH (%)
Ascorbic Acid	85.42 ± 0.78	–
α-Tocopherol	–	82.50 ± 0.84
I	74.28 ± 0.36	70.77 ± 0.31
II	65.19 ± 0.15	55.50 ± 0.15
III	62.89 ± 0.55	61.93 ± 0.15
IV	78.56 ± 0.45	71.28 ± 0.17

Bold showing reference drug numbers.

1-ol) (**II**) were synthesized as 1:2 M ratio by the refluxing propane-1,3-diamine (10 mmol) with 1-(1-hydroxynaphthalen-2-yl)ethanone (20

mmol) and 1-(4-chloro-1-hydroxynaphthalen-2-yl)ethanone (20 mmol) respectively, also the tetradentate Schiff base, 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol) (**III**) and 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-bromonaphthalen-1-ol) (**IV**) were synthesized by the refluxing pentane-1,3-diamine (10 mmol) with 1-(1-hydroxynaphthalen-2-yl)ethanone (20 mmol) and 1-(4-bromo-1-hydroxynaphthalen-2-yl)ethanone (20 mmol). In each reaction 2–3 drops of acetic acid added and absolute ethanol (10 ml) was used as a solvent, the reaction mixture was refluxed for 2–3 h. After completion of heating, reaction mixture was cooled for overnight, the Product was filtered, washed with water and recrystallized with absolute ethanol. The purity of the product was checked by TLC and melting point.

2.1.1. 2,2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol) (I) Yield 307.7 mg, 78 %, colour - Yellow, M.P. 153–155 °C

FT-IR (KBr, cm⁻¹): 3485(νOH), 1726(νC = N), 1587(νN–H), 1552(νC = C), 1022(νC–N–C).

¹H NMR (CDCl₃) (ppm) δ: 13.52(s, Ar-OH, 2H), 8.50 (d, J = 7.4Hz, 2H), 7.61 (d, J = 7.3Hz, 2H), 7.55(dd, J = 4.8Hz, J = 1.4Hz, 2H), 7.50(dd, J = 5.4, J = 2.1Hz, 2H), 7.40(dd, J = 7.3Hz, J = 1.3Hz, 2H), 6.85(dd, J = 6.3Hz, J = 4.7Hz, 2H), 3.83(t, J = 4.6Hz, -CH₂, 4H), 2.47(s, -CH₃, 6H), 2.40–2.31(m, J = 4.6Hz, -CH₂, 2H).

¹³C NMR (CDCl₃) (ppm) δ: 175.2(–C=N–), 171.6(C–O), 137.2–108.8(Ar–C–), 42.2(–N–CH₂–), 29.4(HC–C–CH₂–), 14.5(–N=C–CH₃).

ESIMS (m/z): 411.20 (29.2 %).

2.1.2. 2,2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-chloronaphthalen-1-ol) (II) Yield 328.9 mg, 72 %, colour - Brown, M.P. 158–160 °C

FT-IR (KBr, cm⁻¹): 3399(νOH), 1724(νC = N), 1585(νN–H), 1525(νC = C), 1072(νC–N–C).

¹H NMR (CDCl₃) (ppm) δ: 14.02(s, Ar-OH, 2H), 8.53(dd, J = 7.3Hz, J = 1.0Hz, 2H), 7.77(dd, J = 5.3Hz, J = 3.1Hz, 2H), 7.67(dd, J = 6.3Hz, J = 1.2Hz, 2H), 7.26 (s, 2H), 6.84(dd, J = 6.9Hz, J = 3.6Hz, 2H), 3.84(t, J = 4.5Hz, -CH₂, 4H), 2.50(s, -CH₃, 6H), 2.40–2.33(m, J = 4.5Hz, -CH₂, 2H).

¹³C NMR (CDCl₃) (ppm) δ: 175.2(–C=N–), 171.7(C–O), 137.1–108.2(Ar–C–), 132.4(C–X), 42.1(–N–CH₂–), 29.2(HC–C–CH₂–),

Table 4

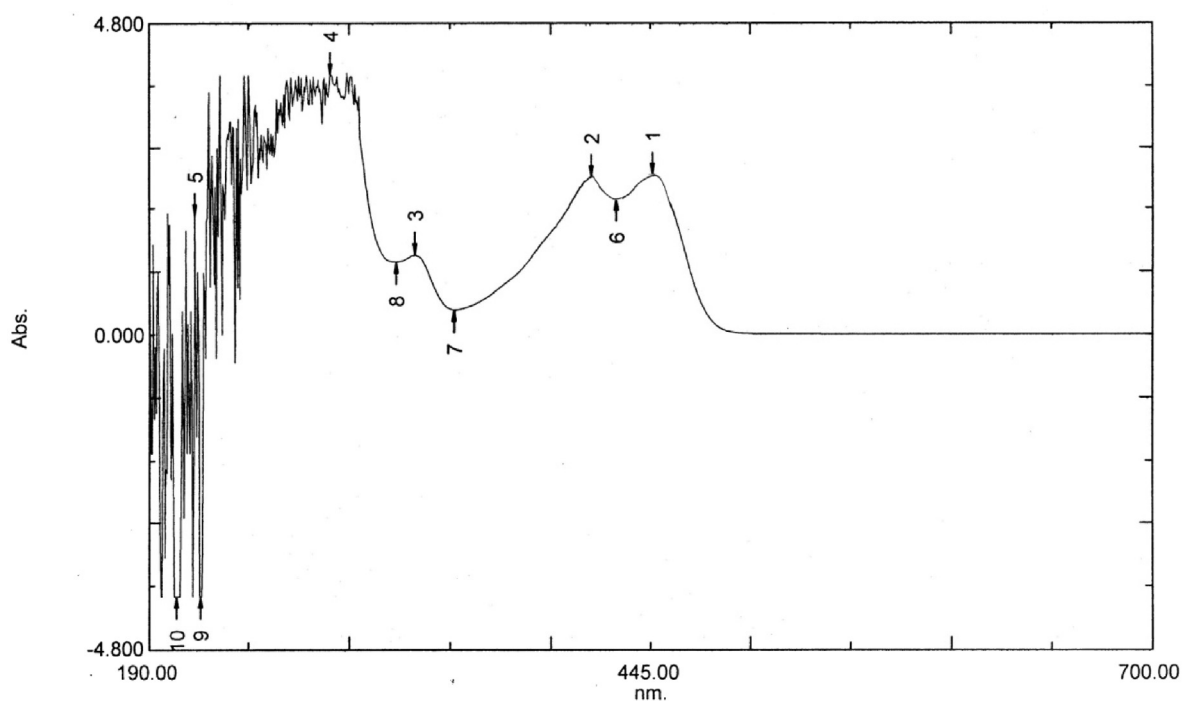
Analytical And Physical data of given Schiff bases (I-IV).

Compound	Molecular formula	Colour	Yield %	M.P. (°C)	Elemental Analysis (Cal.) (%)			
					C	H	N	X(halogen)
I	C ₂₇ H ₂₆ O ₂ N ₂	Yellow	78	153–155	79.02	6.34	6.82	–
II	C ₂₇ H ₂₄ O ₂ N ₂ Cl ₂	Brown	72	158–160	67.78	5.02	5.85	14.64
III	C ₂₉ H ₃₀ O ₂ N ₂	Yellow	75	172–174	77.67	6.69	6.25	–
IV	C ₂₉ H ₂₈ O ₂ N ₂ Br ₂	Pale Yellow	73	178–180	58.38	4.69	4.69	26.84

Spectrum Peak Pick Report

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 Measuring Mode: Absorbance
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[Attachment Properties]

Attachment: None

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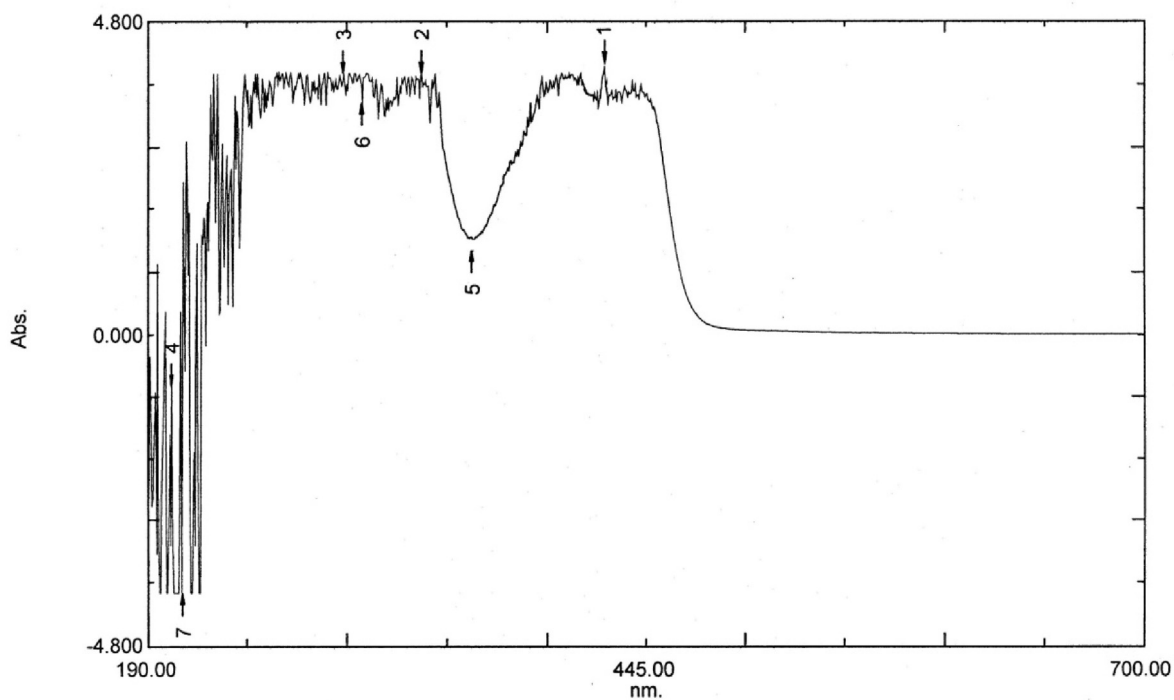
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4	⬆	283.00	4.000	
5	⬆	213.50	1.818	
6	⬇	435.50	2.294	
7	⬇	345.00	0.374	
8	⬇	315.50	1.113	
9	⬇	216.50	-4.000	
10	⬇	204.00	-4.000	

Fig. 2. UV- Vis. Spectrum of 2, 2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

Spectrum Peak Pick Report

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Data Set: v5 - RawData



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3	⬆	290.50	4.000	
4	⬆	202.50	-0.801	
5	⬆	360.70	1.731	
6	⬆	300.00	3.546	
7	⬆	207.50	-4.000	

Fig. 3. UV- Vis. Spectrum of 2, 2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-chloronaphthalen-1-ol).

14.4(-N=C-CH₃).

ESIMS (*m/z*): 480.12 (63.9 %)

2.1.3. 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol) (**III**) Yield 298.6 mg, 75 %, colour - Yellow, M.P.

172–174 °C

FT-IR (KBr, cm⁻¹): 3485(νOH), 1725(νC = N), 1593(νN-H), 1562(νC = C), 1022(νC-N-C).

¹H NMR (CDCl₃) (ppm) δ: 13.50(s, Ar-OH, 2H), 8.50 (d, J = 7.6Hz, 2H), 7.61 (d, J = 7.2Hz, 2H), 7.50 (dd, J = 4.6Hz, J = 1.2Hz, 2H), 7.46(dd, J = 5.3Hz, J = 1.4Hz, 2H), 7.26(dd, J = 7.3Hz, J = 1.3Hz, 2H), 6.80(dd, J = 7.3Hz, J = 4.7Hz, 2H), 4.32(t, J = 4.6Hz, -CH₂, 2H), 3.71–3.69(m, J = 4.6Hz, -CH, 1H), 2.44(s, -CH₃, 3H), 2.40(s, -CH₃, 3H), 2.21(q, J = 4.3Hz, -CH₂, 2H), 1.86–1.82(m, J = 4.1Hz, -CH₂, 2H), 1.02(t, J =

4.1Hz, -CH₃, 3H).

¹³C NMR (CDCl₃) (ppm) δ: 175.2(-C=N-), 171.1(C-O), 137.2–106.5(Ar-C-), 54.1(-N-C-H), 41.8(-N-CH₂-), 34.6(HC-C-CH₂-), 29.4(H₃C-C-CH-), 14.4(-N=C-CH₃), 10.3(C-CH₂-CH-).

ESIMS (*m/z*): 439.2 (31.4 %).

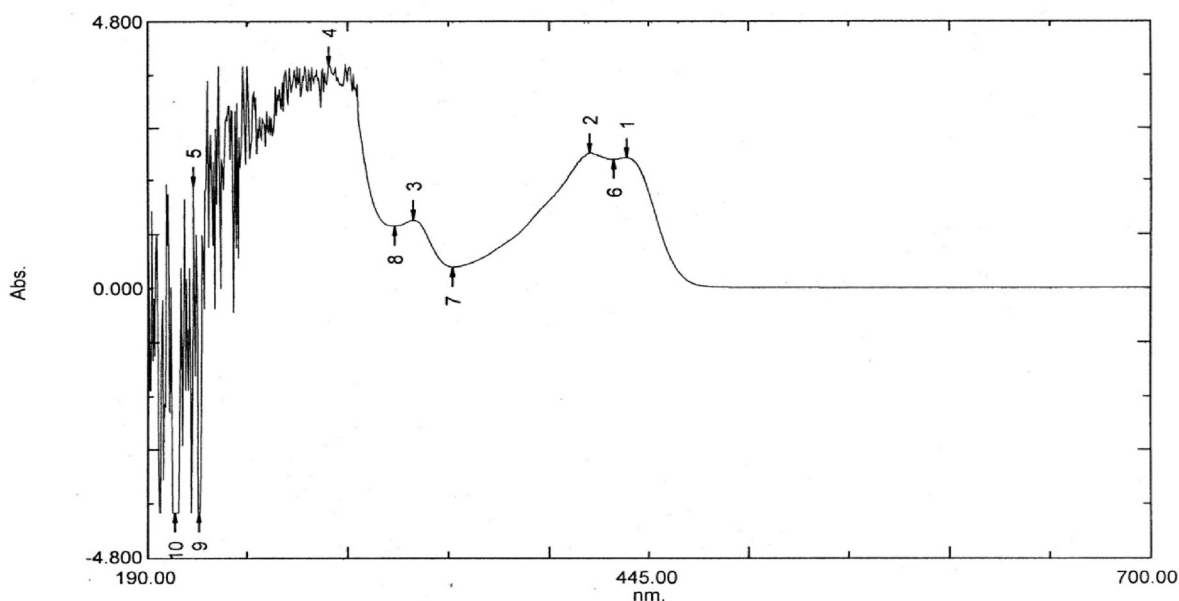
2.1.4. 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-bromonaphthalen-1-ol) (**IV**) Yield 417.1 mg, 73 %, colour - Pale yellow, M.P. 178–180 °C

FT-IR (KBr, cm⁻¹): 3467(νOH), 1730(νC = N), 1590(νN-H), 1562(νC = C), 1080(νC-N-C). ¹H NMR (CDCl₃) (ppm) δ: 13.82(s, Ar-OH, 2H), 8.52(dd, J = 7.1Hz, J = 2.4Hz, 2H), 7.95(dd, J = 6.3Hz, J = 3.1Hz, 2H), 7.65(dd, J = 6.8Hz, J = 1.2Hz, 2H), 7.26(s, 2H), 6.83(dd, J = 7.3Hz, J = 3.1Hz, 2H), 4.39(t, J = 4.5Hz, -CH₂, 2H), 3.70–3.72(m, J =

Spectrum Peak Pick Report

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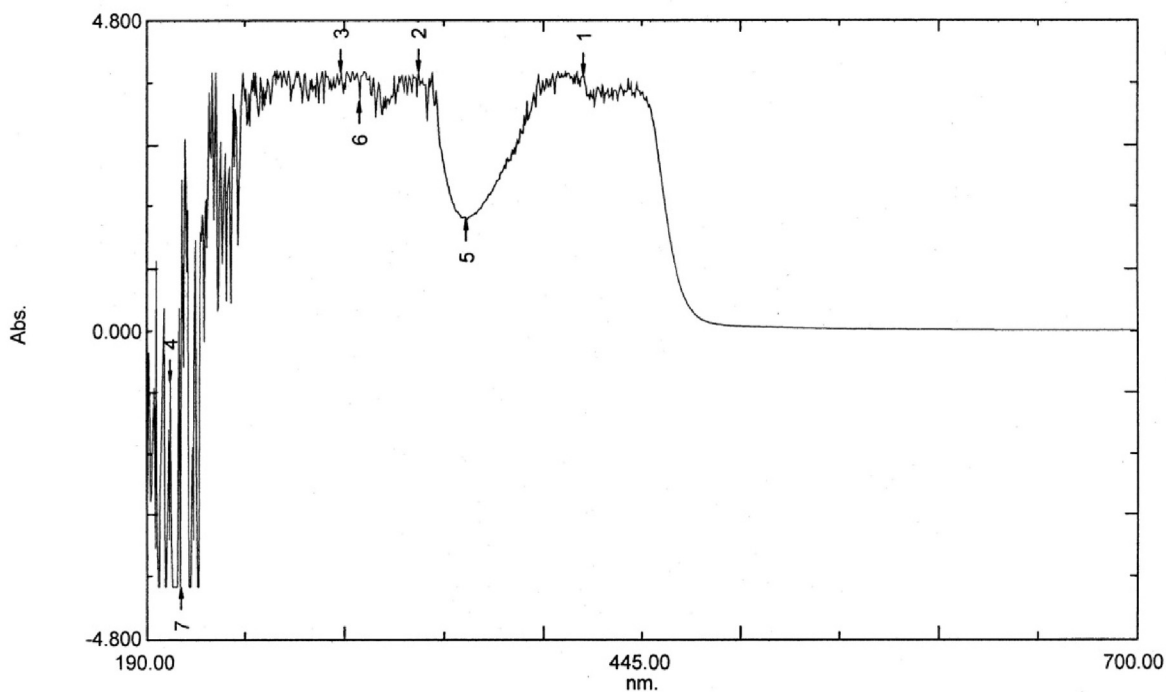
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5	Ⓢ	213.50	1.818	
6	Ⓢ	427.50	2.294	
7	Ⓢ	345.00	0.374	
8	Ⓢ	315.50	1.113	
9	Ⓢ	216.50	-4.000	
10	Ⓢ	204.00	-4.000	

Fig. 4. UV- Vis. Spectrum of 2, 2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

Spectrum Peak Pick Report

11/27/2018 12:24:31 PM

Data Set: v3 - RawData



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 Measuring Mode: Absorbance
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 Light Source Change Wavelength: 360.0 nm
 S/R Exchange: Normal

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 Attachment: None

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 Average: Disabled

[Sample Preparation Properties]
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2	⬆	330.00	4.000	
3	⬆	290.50	4.000	
4	⬆	202.50	-0.801	
5	⬆	354.50	1.731	
6	⬆	300.00	3.546	
7	⬆	207.50	-4.000	

Fig. 5. UV- Vis. Spectrum of 2, 2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-bromonaphthalen-1-ol).

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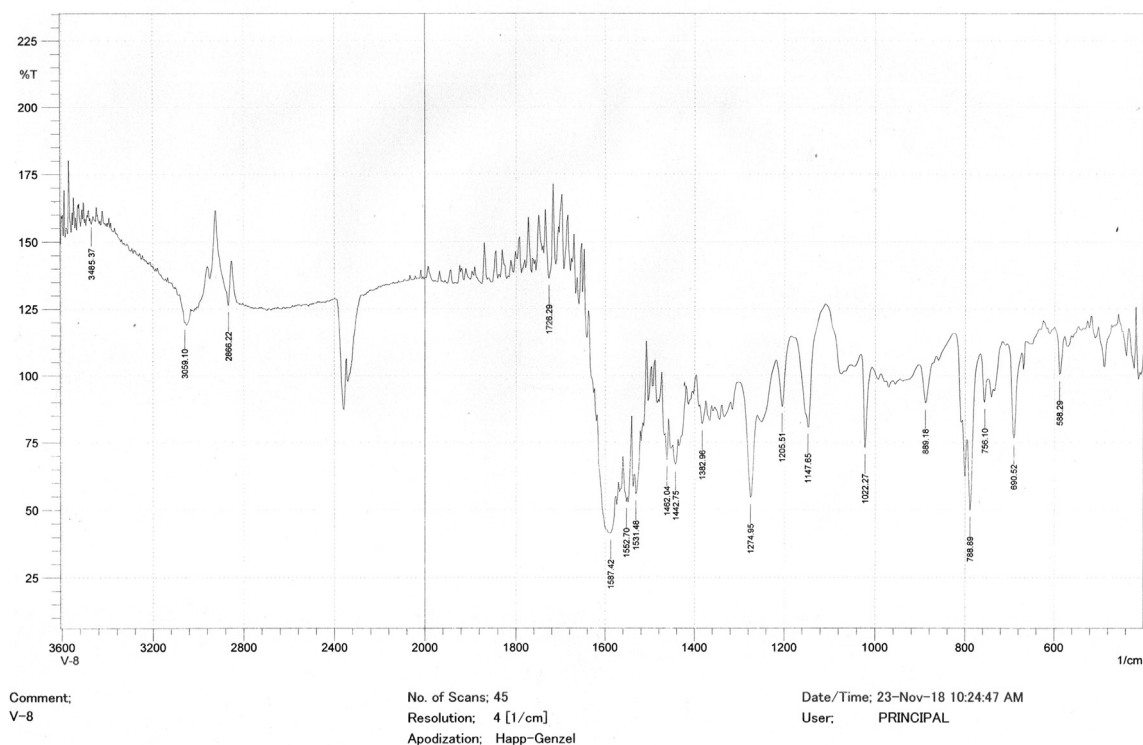


Fig. 6. FT-IR spectrum of 2, 2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

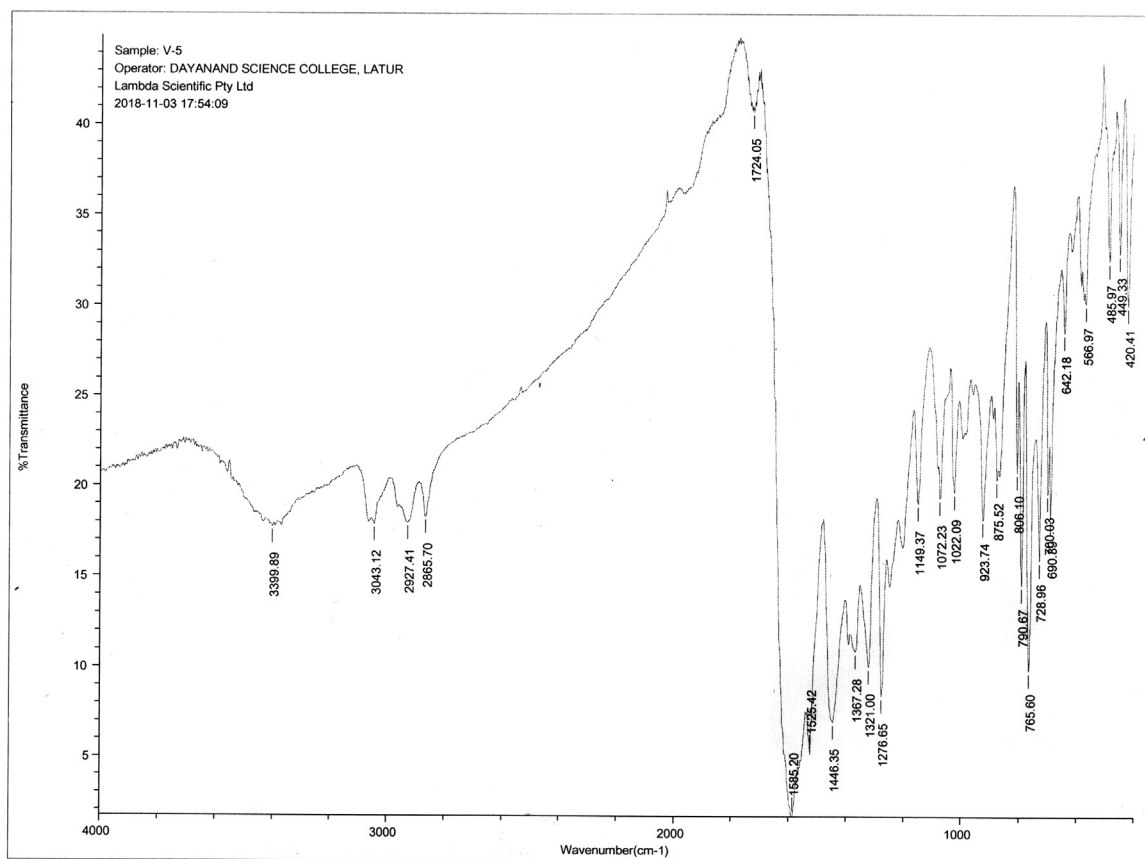


Fig. 7. FT-IR spectrum of 2, 2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-chloronaphthalen-1-ol).

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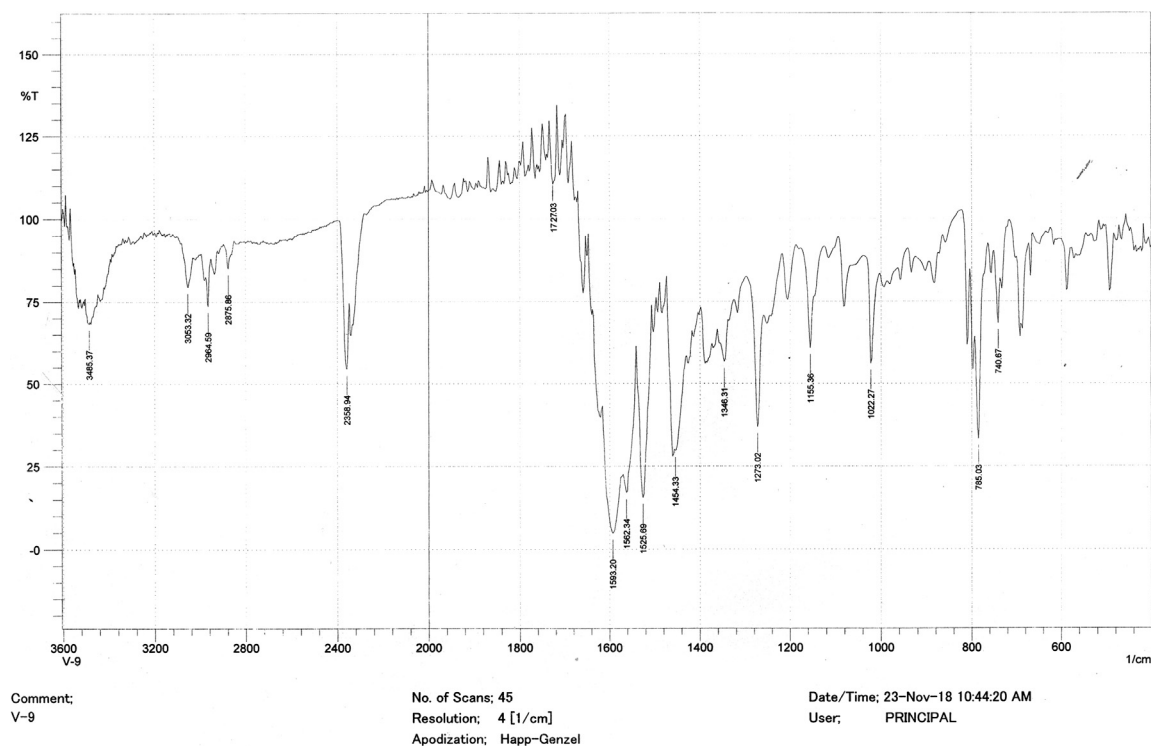


Fig. 8. FT-IR spectrum of 2, 2'-(pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

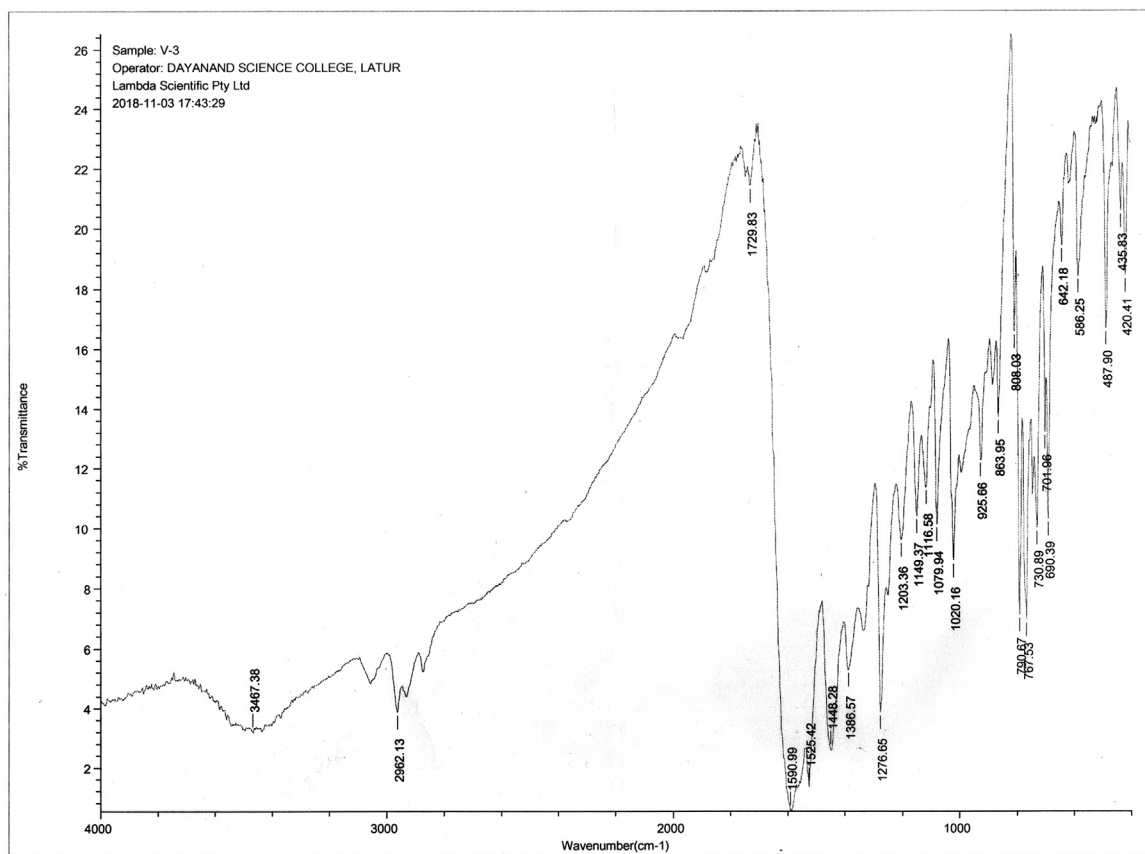


Fig. 9. FT-IR spectrum of 2, 2'-(pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-bromonaphthalen-1-ol).

Table 5

Spectroscopic data (IR) of given Schiff bases (I-IV).

Compound	$\nu(\text{O-H})$	$\nu(\text{CH})_{\text{Ar}}$	$\nu(-\text{CH}=\text{N}-)$	$\delta(\text{N-H})$	$\nu(\text{C}=\text{C})$	$\nu(\text{C}-\text{O})$	$\nu(\text{C}-\text{N}-\text{C})$	$\nu(\text{C}-\text{X})$
I	3485	2910–2866	1726	1587	1552	1147–1383	1022	–
II	3399	2927–2865	1724	1585	1525	1149–1367	1072	806,875
III	3485	2964–2875	1727	1593	1562	1155–1346	1022	–
IV	3467	2962–2800	1730	1590	1562	1149–1386	1080	808, 863

4.6Hz, -CH₂1H), 2.45(s, -CH₃, 3H), 2.40(s, -CH₃, 3H), 2.37(q, J = 4.3Hz, -CH₂, 2H), 1.87–1.89(m, J = 4.1Hz, -CH₂, 2H), 1.02(t, J = 4.1Hz, -CH₃, 3H).

¹³C NMR (CDCl₃) (ppm) δ : 175.2(-C=N-), 170.7(C=O), 137.1–105.9(Ar-C-), 135.0(-C-X), 54.1(-N-C-H), 41.7(-N-CH₂-), 34.6(HC-C-CH₂-), 29.4(H₃C-C-CH-), 14.4(-N=C-CH₃), 10.2(-C-CH₂-CH-).

ESIMS (m/z): 598.05 (48.6 %).

2.2. Characterization

All synthesised products are confirmed by their characterization. In laboratory, thin layer chromatography (TLC) is used to check the purity of product. TLC was carried out on 0.25-mm E Merck gel plates (60F-254) and spot were visualized by UV light. Melting points were determined on a digital apparatus Kofler Banc. The elemental analysis was carried out by using Perkin-Elmer 240 elemental analyzer. The UV-Visible spectra were recorded in chloroform between 190–700 nm using UV-1800 series spectrophotometer with the light source wavelength 360 nm. A Perkin Elmer Spectrum one FT-IR spectrometer with the diffuse reflectance attachment (Miracle Attenuated Total Reflectance Attachment) at a 4 cm⁻¹ resolution in the region 4000–600 cm⁻¹ was employed to record the infrared spectrum to analyze the functional groups present in the

Schiff bases compounds. NMR spectra were obtained with Bruker Avance III HD 300 operating at 300 MHz (1H), 50 MHz (13C) at 21 °C. Chemical shifts referenced to ext. TMS (1H, 13C). Coupling constants are given in Hz. Mass spectra were taken on LC-MS (ESI) mass or GC-MS mass spectrometer at 70 eV.

2.3. Biological activity

2.3.1. Antibacterial activity (in vitro)

The synthesized Schiff bases (I–IV) were screened *in vitro* for their antibacterial activity, Kirby-Bauer method was followed for disc diffusion method. *In vitro* antibacterial activity was screened by using Mueller Hinton Agar (MHA) obtained from Himedia (Mumbai). The MHA plates were prepared by pouring 15 ml of molten media into sterile petriplates. The plates were allowed to solidify for 5 min and 0.1 % inoculums suspension was swabbed uniformly and the Inoculums were allowed to dry for 5 min. The concentration of compounds were set at (10 µg/disc) were loaded on 5 mm sterile individual discs. The loaded discs were placed on the surface of medium and the compound was allowed to diffuse for 5 min and the plates were kept for incubation at 37 °C for 24 h. Penicillin (10 µg/disc) was used as positive control. At the end of incubation, inhibition zones formed around the disc were measured with transparent

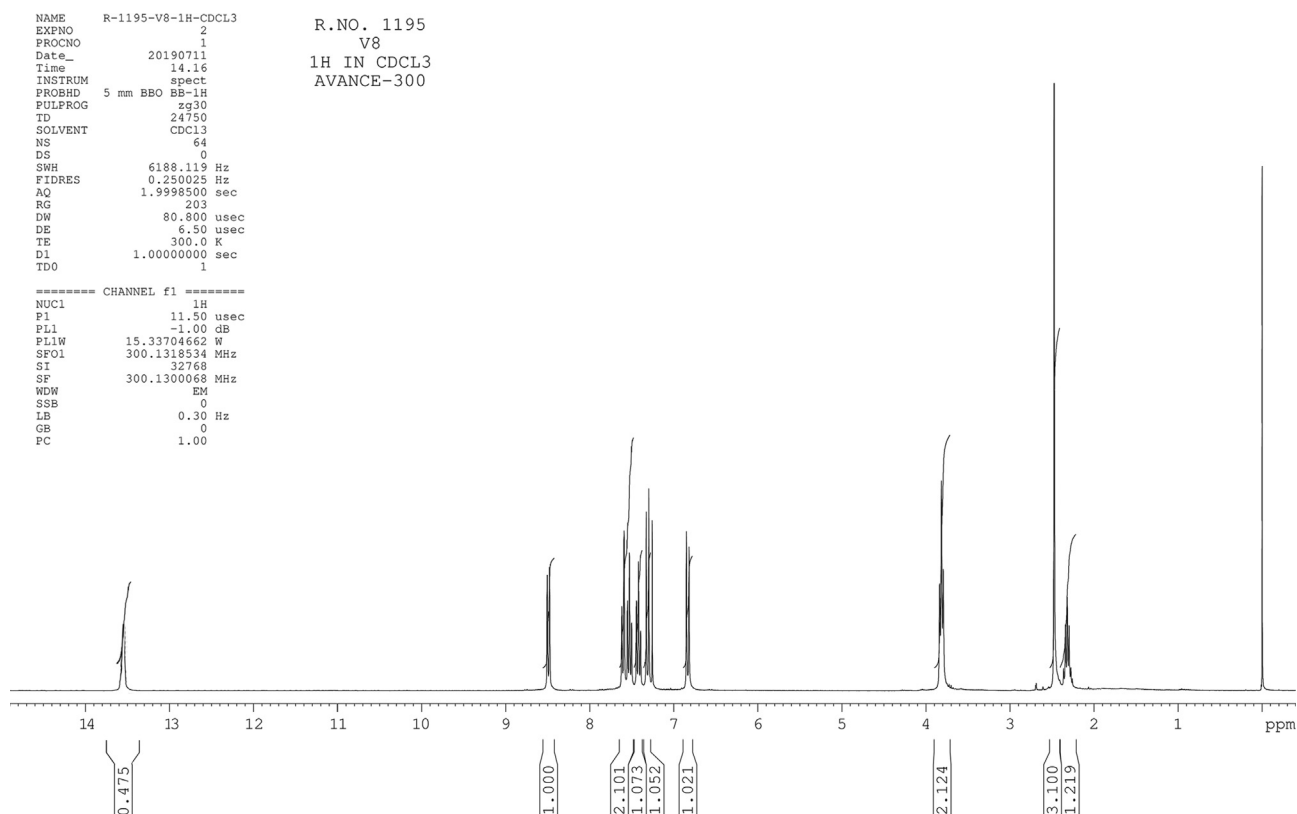


Fig. 10. ¹H NMR spectrum of 2,2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

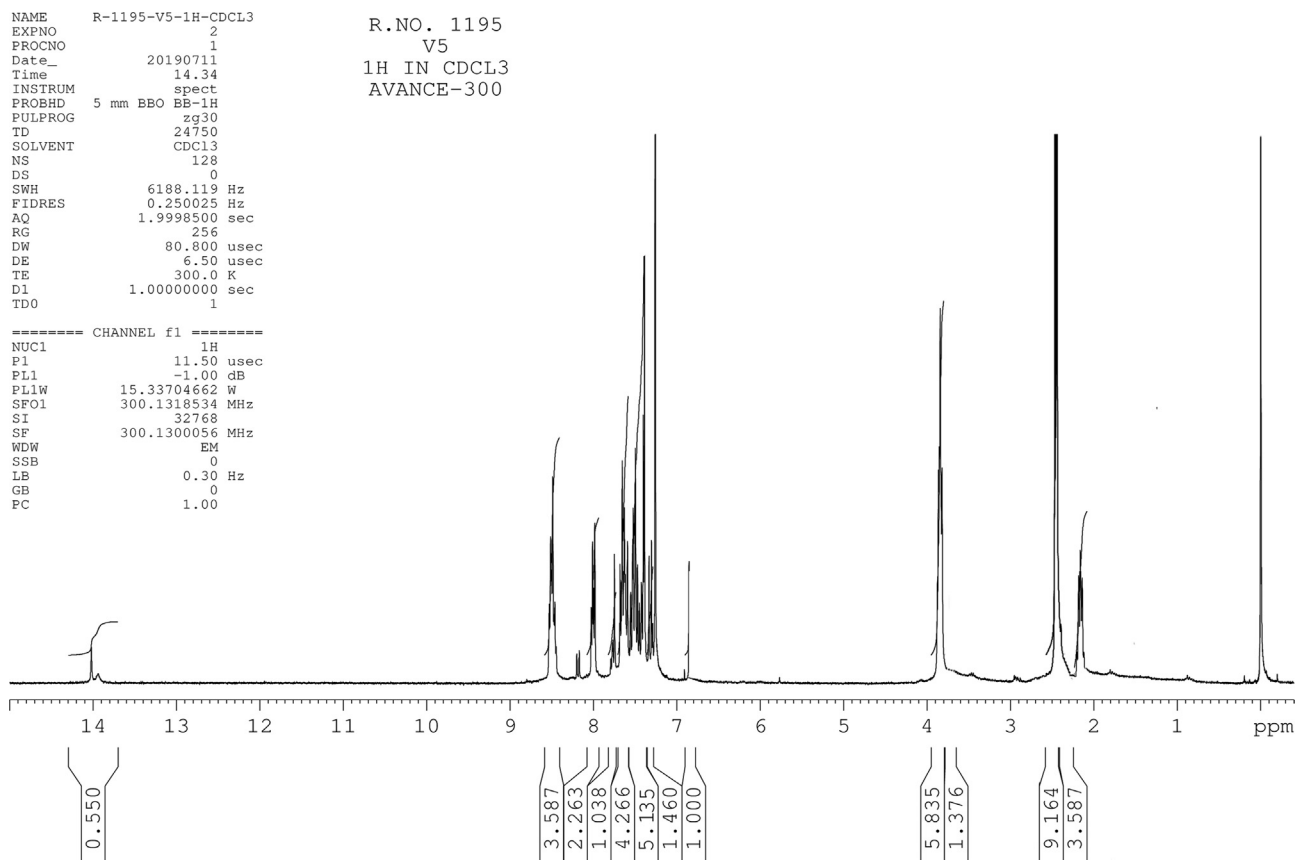


Fig. 11. ^1H NMR spectrum of 2,2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-chloronaphthalen-1-ol).

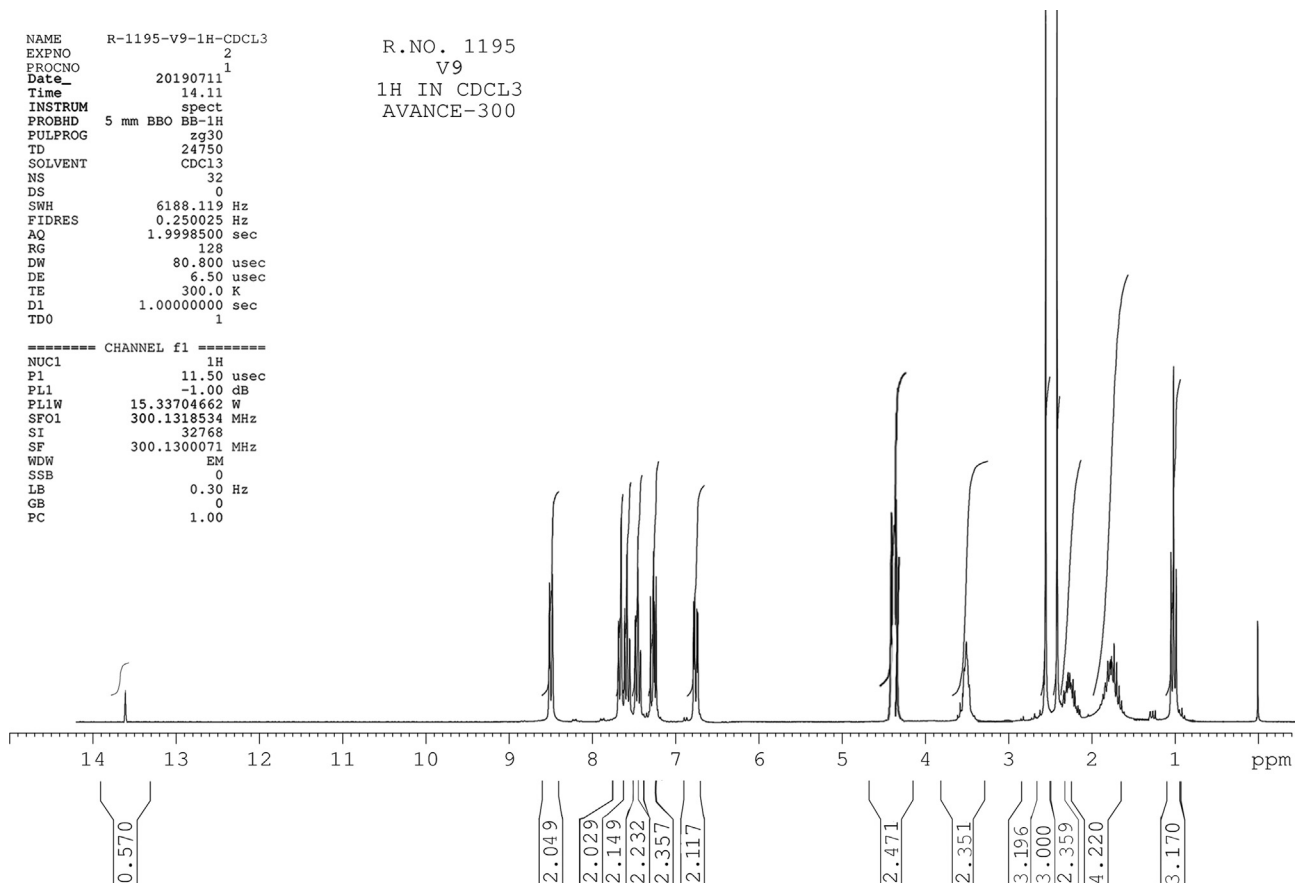


Fig. 12. ^1H NMR spectrum of 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

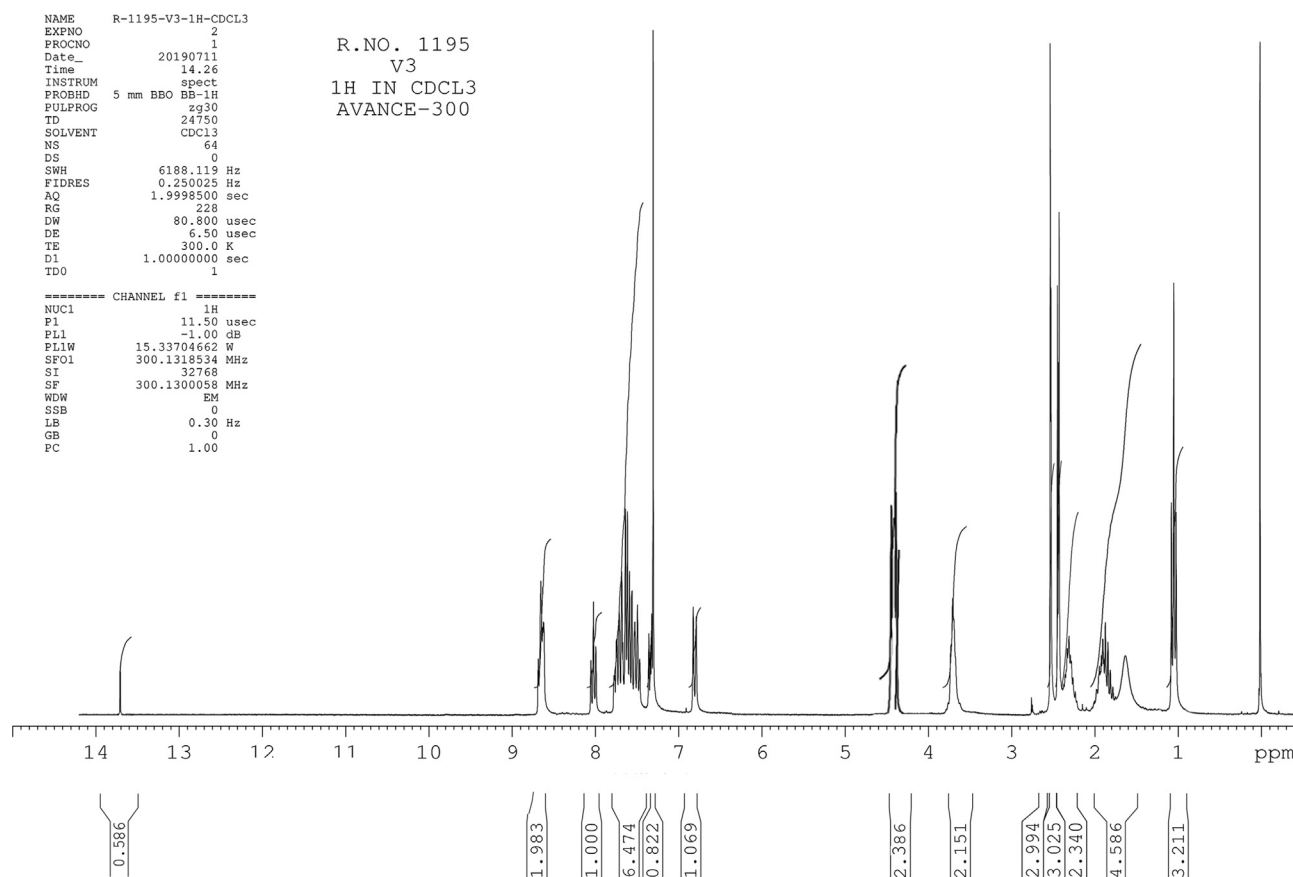


Fig. 13. ^1H NMR spectrum of 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-bromonaphthalen-1-ol).

Table 6

Spectroscopic data (^1H NMR) (δ) of the given Schiff bases (I-IV).

Group	Comp. I	Comp. II	Comp. III	Comp. IV
Ar-O-H	13.52	14.02	13.50	13.82
Ar-H	8.50–6.85	8.53–6.84	8.50–6.80	8.52–6.83
=N-CH ₂ -CH ₂ -CH ₂ -N	3.87	3.84	–	–
N=C-CH ₃	2.47	2.50	2.44,2.40	2.45,2.40
=N-CH ₂ -CH ₂ -CH ₂ -N	2.31	2.33	–	–
CH ₂	–	–	3.69	3.72
=N-CH-CH ₃	–	–	–	–
=N-CH ₂ -CH ₂ -CH-	–	–	4.32	4.39
=N-CH ₂ -CH ₂ -CH-	–	–	2.21	2.37
CH ₃ -CH ₂ -	–	–	1.82	1.89
CH ₃ -CH ₂ -	–	–	1.02	1.02

ruler in millimetre.

2.3.2. Minimum inhibitory concentration (MIC)

The determination of minimum inhibitory concentration (MIC) were carried out by micro dilution method using serially diluted (2 fold) plant extract according to (National Committee for Clinical Laboratory Standards NCCLS, 2000). The crude extracts were reconstituted in 10 % v/v aqueous dimethyl sulfoxide (DMSO) at various concentrations of 1 mg/ml, 0.5 mg/ml, 0.25 mg/ml and 0.12.5 mg/ml respectively. 1.0 ml of extract and add 1.0 ml of nutrient broth were mixed in a test tube then 100 μL of an 24 h old active cultures of each of bacteria earlier adjusted at 10^6 colony forming unit (CFU/mL) were added in each tube. Two control tubes were maintained for each test batch. These included antibiotic control (tube containing extract and growth media) and organism control

(tube containing growth media and inoculums). The lowest concentration of the extract with no detectable bacterial growth (no turbidity) by visual inspection was considered as minimum inhibitory concentration (MIC).

2.3.3. Antioxidant activity

2.3.3.1. 2, 2-Diphenyl-1- Picryl Hydrazyl (DPPH) assay. DPPH (2, 2, Diphenyl-1-Picryl Hydrazyl) radical scavenging assay was carried out as per kato *et al*, 1998 produces with slight modifications. 1ml ethanolic solution of different concentration of newly synthesized Schiff's bases was added to equal volume of 0.1mm ethanolic solution of DPPH. Above solutions were kept for incubation at room temp. The decreases in concentration of DPPH were measured by noting the absorbance at 517nm.

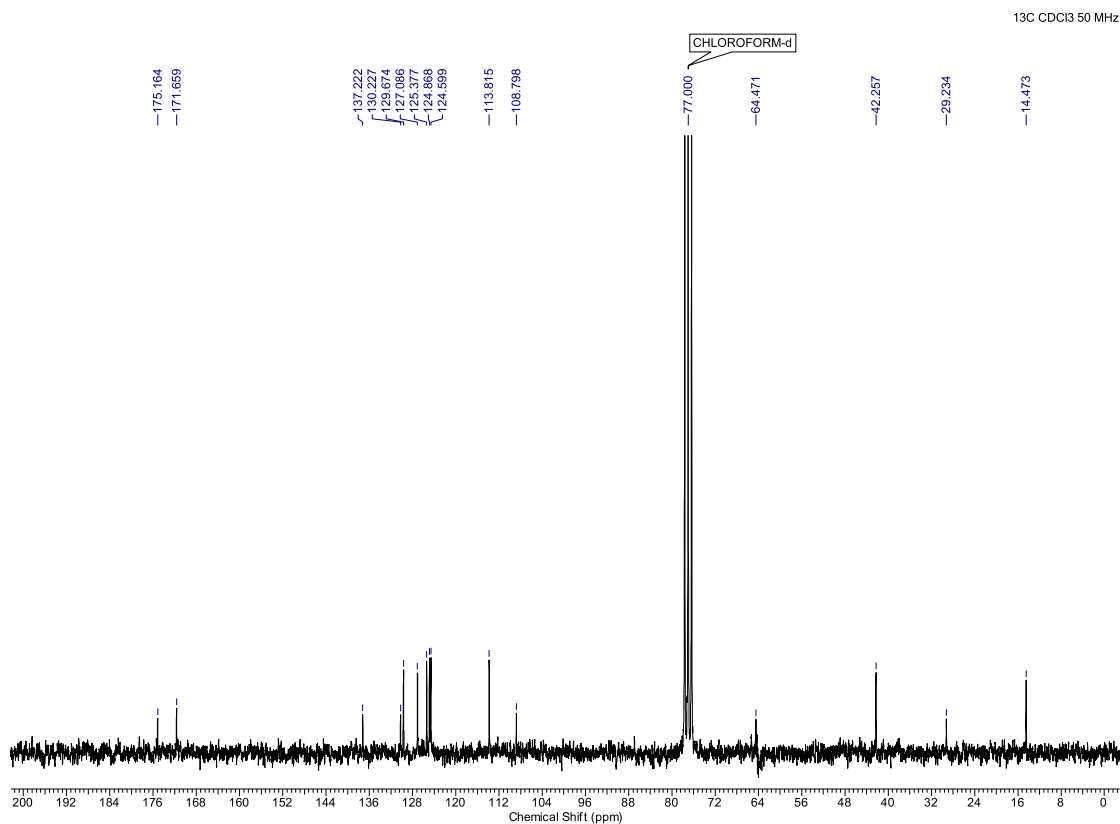


Fig. 14. ^{13}C NMR spectrum of 2, 2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

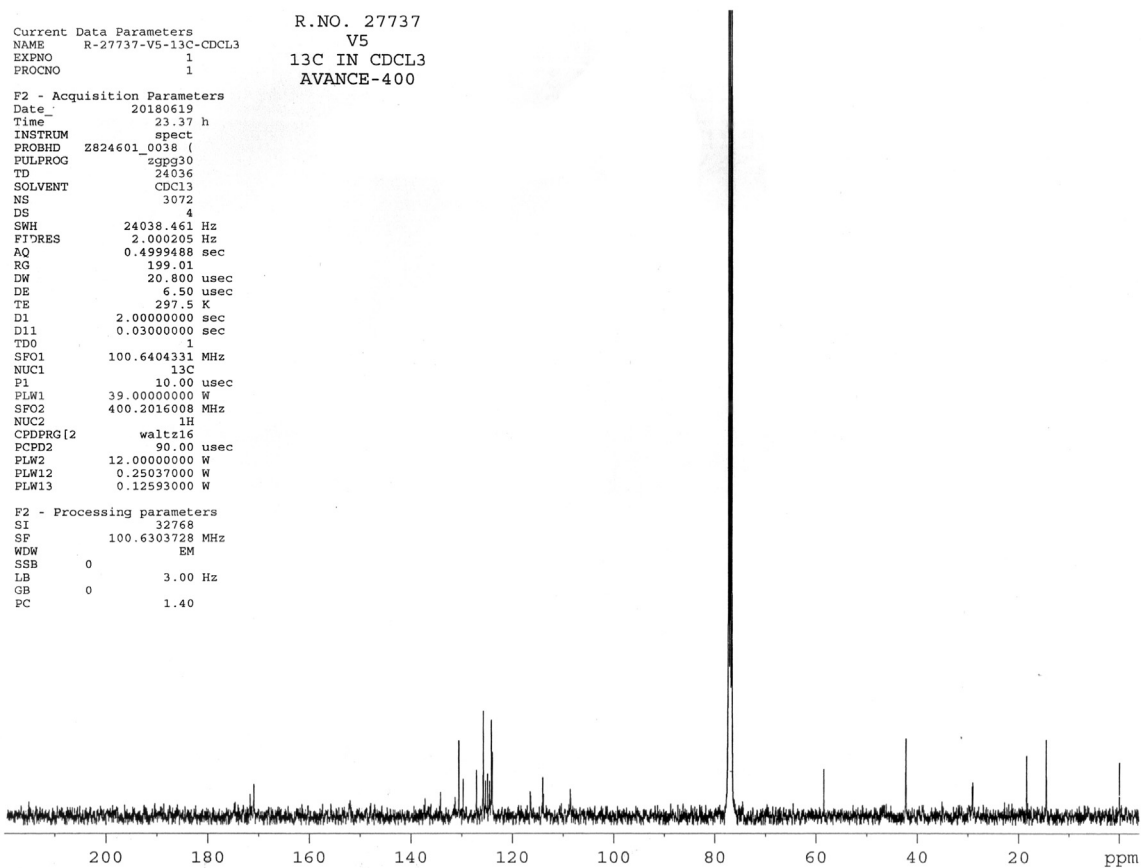


Fig. 15. ^{13}C NMR spectrum of 2,2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-chloronaphthalen-1-ol).

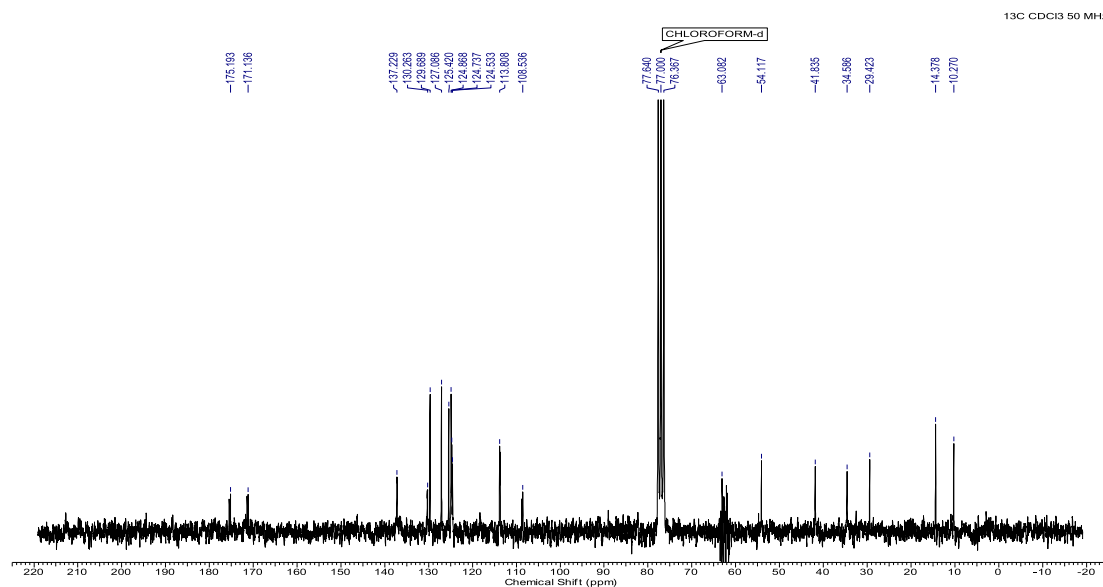


Fig. 16. ^{13}C NMR spectrum of 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

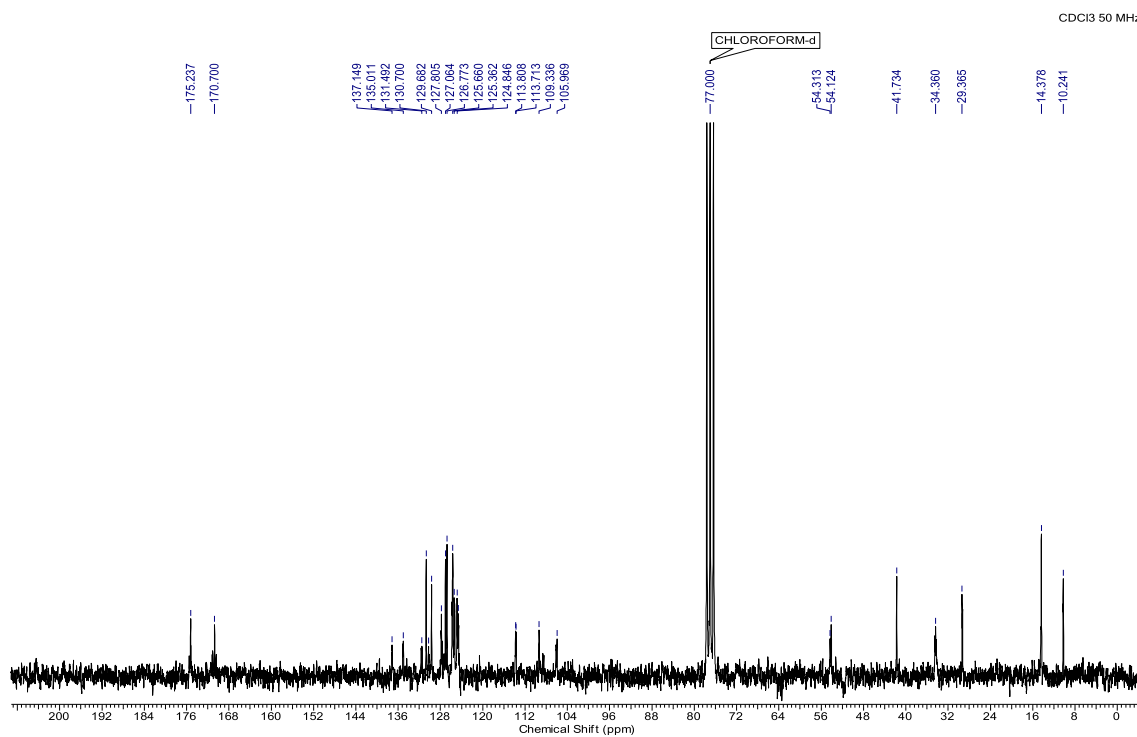


Fig. 17. ^{13}C NMR spectrum of 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-bromonaphthalen-1-ol).

Table 7
Spectroscopic data (^{13}C NMR) (δ) of the given Schiff bases (I-IV).

Group	Comp. I	Comp. II	Comp.III	Comp. IV
-C=N-	175.16	175.20	175.19	175.23
-C-O-H	171.65	171.68	171.13	170.70
Ar-C-	137.10–108.79	137.02–108.19	137.22–106.53	137.14–105.96
C-X	–	132.37	–	135.01
-N-C-H	–	–	54.11	54.12
$\text{-N-CH}_2\text{-}$	42.25	42.10	41.83	41.73
$\text{HC-C-CH}_2\text{-}$	29.40	29.23	34.59	34.60
$\text{CH}_3\text{-C-CH-}$	–	–	29.43	29.36
-N=C-CH_3	14.47	14.40	14.37	14.37
$\text{-C-CH}_2\text{-CH-}$	–	–	10.27	10.24

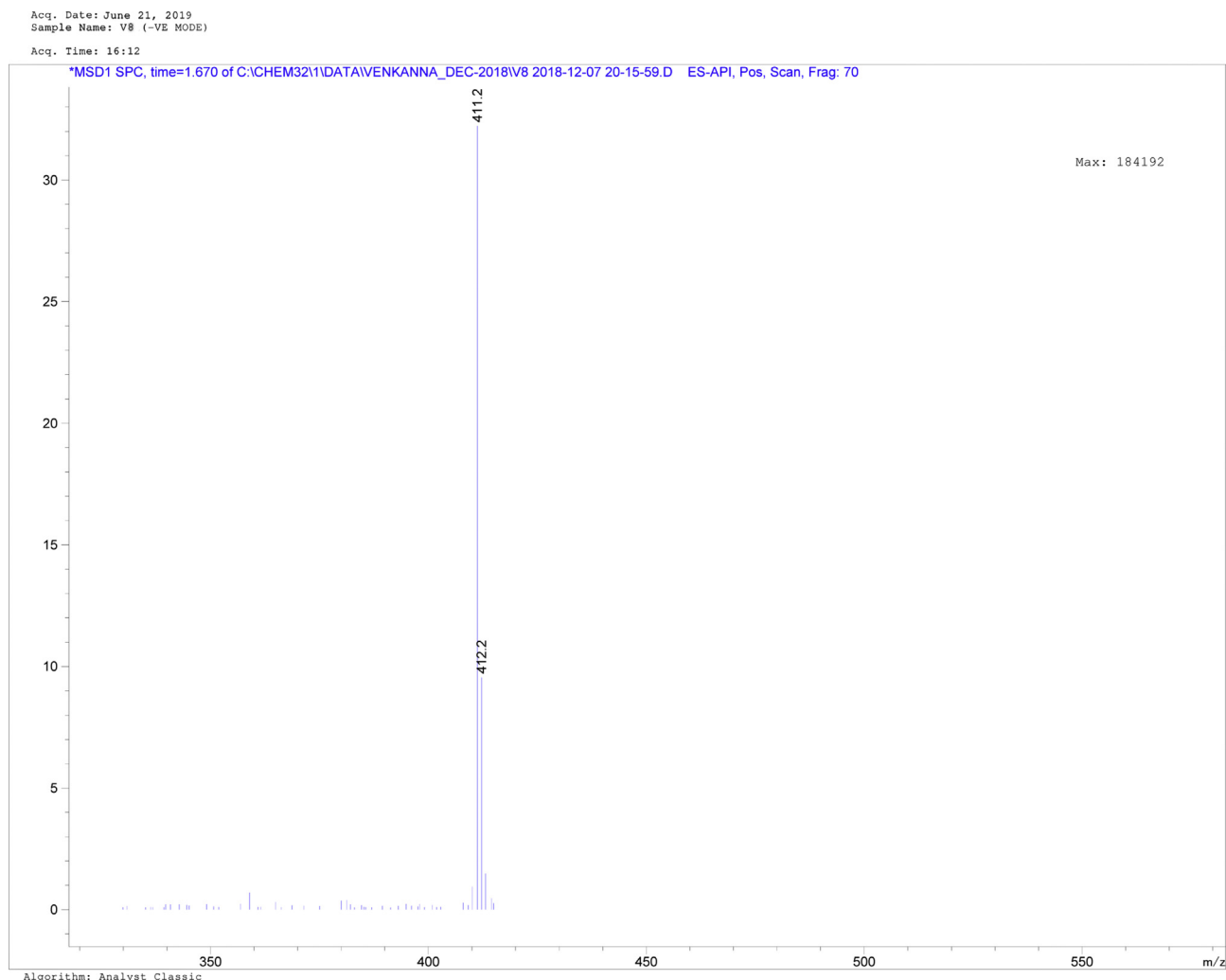


Fig. 18. Mass spectrum of 2, 2'-((propane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

Similar test was performed using ascorbic acid, as an internal standard, instead of Schiff's base.

2.3.3.2. Hydroxyl radical scavenging assay. Hydroxyl radical scavenging activities were determined by the earlier reported method (Yu et al., 2004). The reaction cocktail contained 60 μ l of 1 mM, FeCl_3 , 90 μ l of 1 mM 1,10-phenanthroline, 2.4 ml of 0.2 M phosphate buffer (pH 7.8), 150 μ l of 0.17 M H_2O_2 , and 1.5 ml of various concentration of individual compound. Reaction mixture kept at room temperature for 5 min incubation and absorbance was measured at 560 nm using spectrophotometer. The α -Tocopherol was used a reference compound (see Fig. 1).

3. Result and discussion

From various physical parameter and obtained instrumental data we have concluded that, the Schiff bases (I-IV) are coloured solid, partially soluble in ethanol but soluble in methanol, dichloromethane, DMSO, DMF, and CHCl_3 . The purity of compounds was checked by TLC. From spectral data (UV-Vis, FT - IR, ^1H NMR, ^{13}C NMR and LCMS) we predict correct structure of Schiff bases (I-IV). All the synthesized compounds (I-IV) were screened for their antibacterial activity with MICs of 0.12, 0.25, 0.5 and 1 mg/ml against *E. coli* and *Salmonella Typhi* whereas antioxidant activity by DPPH (2, 2, Diphenyl-1-Picryl Hydrazyl) radical scavenging assay and Hydroxyl radical scavenging method. These are formulated in

Tables 1, 2, and 3.

3.1. Elemental analysis

The formations of the Schiff bases (I-IV) were confirmed by their elemental analysis. From elemental analysis we find out the carbon, hydrogen, nitrogen, oxygen and halogen contents of their structures. It is seen in Table 4.

3.2. Spectroscopic studies

3.2.1. UV-Vis. Analysis

The UV-Vis spectra of Schiff bases (I-IV) are presented in Figs. 2, 3, 4, and 5 respectively. The UV-Vis. spectra of four compounds were studied in polar solvent. The electronic absorption spectra of compounds (I-IV) showed bands at 345 nm, 360 nm, 345 nm and 354 nm due to $n \rightarrow \pi^*$ transition of the $\text{C}=\text{N}$ imine group. Here, in compound II & IV there is slightly increase in transition value of imine group this is due to presence of halogen group. The longer wavelength band over 400 nm showed that an intermolecular charge transfer interaction [61, 62].

3.2.2. FT-IR analysis

The IR spectra of Schiff bases (I-IV) synthesized are presented in Figs. 6, 7, 8, and 9 respectively. From Table 5 it is clear that schiff bases I to IV are given strong bands at 1726, 1724, 1727 and 1730 cm^{-1} are due

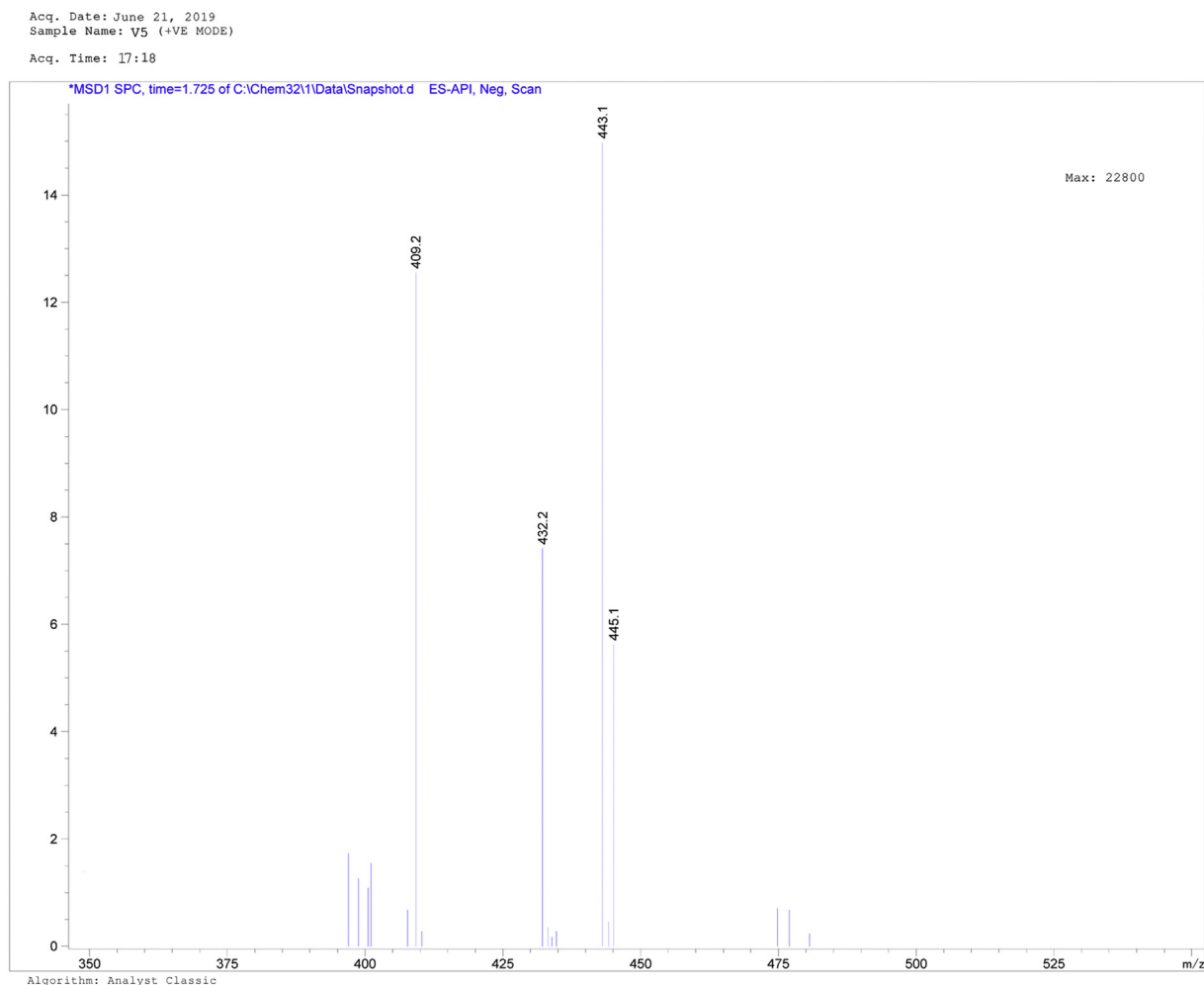


Fig. 19. Mass spectrum of 2,2'-((propane-1,3-diylbis(azanylylidene)))bis(ethan-1-yl-1-ylidene))bis(4-chloronaphthalen-1-ol).

to (C=N) stretching mode of the imine group respectively. The observation of phenolic $\nu(\text{C}-\text{O})$ in range $1147\text{--}1386\text{ cm}^{-1}$ for these compounds it is the evidence for the existence of keto-amine form (N-O...H) intramolecular hydrogen bonding only in the solid state [61]. Two C-X stretching vibrations are seen for compound **II** and **IV** at $806,875\text{ cm}^{-1}$ and $808,863\text{ cm}^{-1}$ respectively, it confirms that these halogens substituted at para position to the aromatic -OH group. It is clear that compounds **II** and **IV** are halogen substituted compounds at aromatic ring [61, 62]. The significant Infrared bands of these compounds are summarised in Table 5.

3.2.3. ^1H NMR analysis

The ^1H NMR spectra of Schiff's bases (**I-IV**) are shown in Figs. 10, 11, 12, and 13 respectively. The various observations are found by these spectral data and they are formulated in Table 6. In compound **I**, **II**, **III** and **IV** presence of singlet in between range of δ 13.50–14.02 ppm is due to phenolic -OH proton. In Comp. **II** the chloride atom present at para position to the aromatic hydroxyl group, it shows singlet at 14.02 ppm due to more acidic proton. Whereas comp. **IV** contains bromide atom at para position to the aromatic hydroxyl group, it shows singlet at 13.82 ppm due to moderate acidic proton. Presence of hydrogen bond between phenolic -OH and nitrogen atoms is stronger in comp. **II** than that of the comp. **IV** having weaker hydrogen bond between phenolic -OH and

nitrogen atom. Presence of singlet at δ 2.47 and 2.50 ppm of 6H due to two -CH₃ confirms formation of compound **I** and **II**. But in compound **III** and **IV** due to different environment they give two peaks. Also the appearance of ethyl group in compound **III** and **IV**, the Presence of quartet of -CH₃ at δ 1.02 and Presence of multiplet of -CH₂ at δ 1.82 and 1.89. The significant ^1H NMR ppm values of these compounds are summarised in Table 6.

3.2.4. ^{13}C NMR analysis

The ^{13}C NMR spectra of Schiff's bases (**I-IV**) are shown in Figs. 14, 15, 16, and 17 respectively. The various observations are seen by these spectral data and they are formulated in Table 7. From the table it is shown that Compounds **I** to **IV** gives signals at δ 175.16, 175.20, 175.19 and 175.20 due to imine carbon, the presence of signals at δ 171.65, 171.68, 171.13 and 170.70 due to carbon bearing oxygen respectively. It is also clear that the compounds **II** and **IV** shows peak at δ 132.37 and 135.01 due to carbon bearing to halogen group. The compounds **III** and **IV** signal shows at δ 54.11 and 54.12 due to -N-C-H group, at δ 29.43 and 29.36 due to CH₃-C-CH- group whereas δ 10.27 and 10.24 due to -C-CH₂-CH- group. From Table 7, it confirms compounds **I** and **III** are have no halogen substituted carbon, it is also clear that the compounds **III** and **IV** are having presence of -N-C-H, CH₃-C-CH-, -C-CH₂-CH- groups. The significant ^{13}C NMR ppm values of these compounds are summarised in

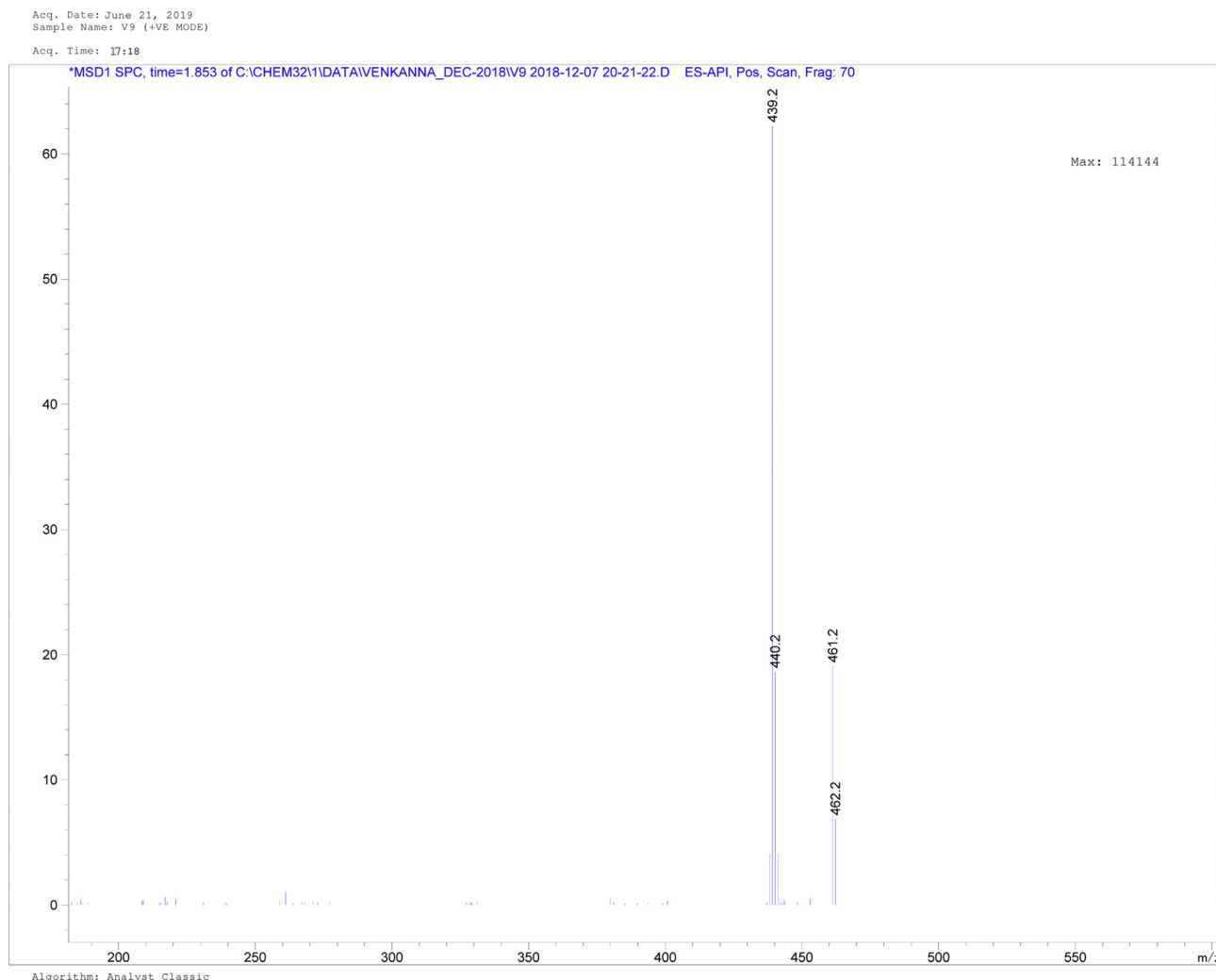


Fig. 20. Mass spectrum of 2, 2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(naphthalen-1-ol).

Table 7.

3.2.5. LCMS analysis

The LCMS spectra of Schiff bases (**I-IV**) are shown in Figs. 18, 19, 20, and 21 respectively. Presence of M+1 signal at m/z 411 and m/z 439 confirms formation of Schiff bases **I** and **III** respectively. Similarly, the appearance of M-2Cl signals at m/z 409 and M-2Br signal at m/z 437 as base peak also confirms formation of compounds **II** and **IV** [62, 63].

3.3. Biological activity

3.3.1. Antibacterial activity (in vitro)

Schiff bases (**I-IV**) were evaluated for their antibacterial potencies against pathogenic gram negative bacteria, *E. coli* and *Salmonella Typhi* using penicillin as positive control and solvent DMSO as a negative control and the results are represented in Table 1. Although no define structure-activity relationship could be determined, some conclusions on structural changes that may influence the antibacterial activity can be drawn by the comparison among the structure of compound with different activity (see Figs. 22 and 23).

The biological activity is depending on hydrogen bonding present in that molecule. From the spectral data it confirms, comp. **II** having stronger hydrogen bonding, it is responsible to show good antibacterial

activity against *E. coli* and *Salmonella Typhi*. comp. **IV** having moderate hydrogen bonding, hence it shows moderate antibacterial activity against *E. coli* while it shows less antibacterial activity against *Salmonella Typhi*. Similarly, compound **I** shows less antibacterial activity against *E. coli* and *Salmonella Typhi*.

The hydroxyl group adjacent to imine group is very common feature in Schiff bases; it participates to stabilize by a hydrogen bond the predominant structure of the Schiff bases. Therefore, the hydroxyl substituent may be important group for structure stability.

A hydroxyl group in position 4 is halogenated the Schiff base is more active. When the free hydroxyl group in position 4 Schiff bases not more active. Here, compounds **II** and **IV** inhibited effectively *E. coli*, it may be because of halogen group present at position 4 to the hydroxyl group.

3.3.1.1. Minimum inhibitory concentration (MIC). The minimum inhibitory concentration of synthesized schiff bases were carried out at different concentration i.e. 1.0, 0.5, 0.25, 0.12 mg/ml the result of MIC were given in Table 3. From table it is clear that, the Comp. **II** shows a good inhibition at minimum concentration (0.12 mg/ml) against both organisms. The comp. **III** shows a good inhibition at minimum concentration (0.50 mg/ml) against both organisms. Compound **IV** shows good inhibition at minimum concentration (0.50 mg/ml) against *E. coli*. Comp. **III** and **IV** shows good inhibition at minimum concentration (1.0 mg/ml)

Acq. Date: June 21, 2019
Sample Name: V3 (+VE MODE)

Acq. Time: 16:37

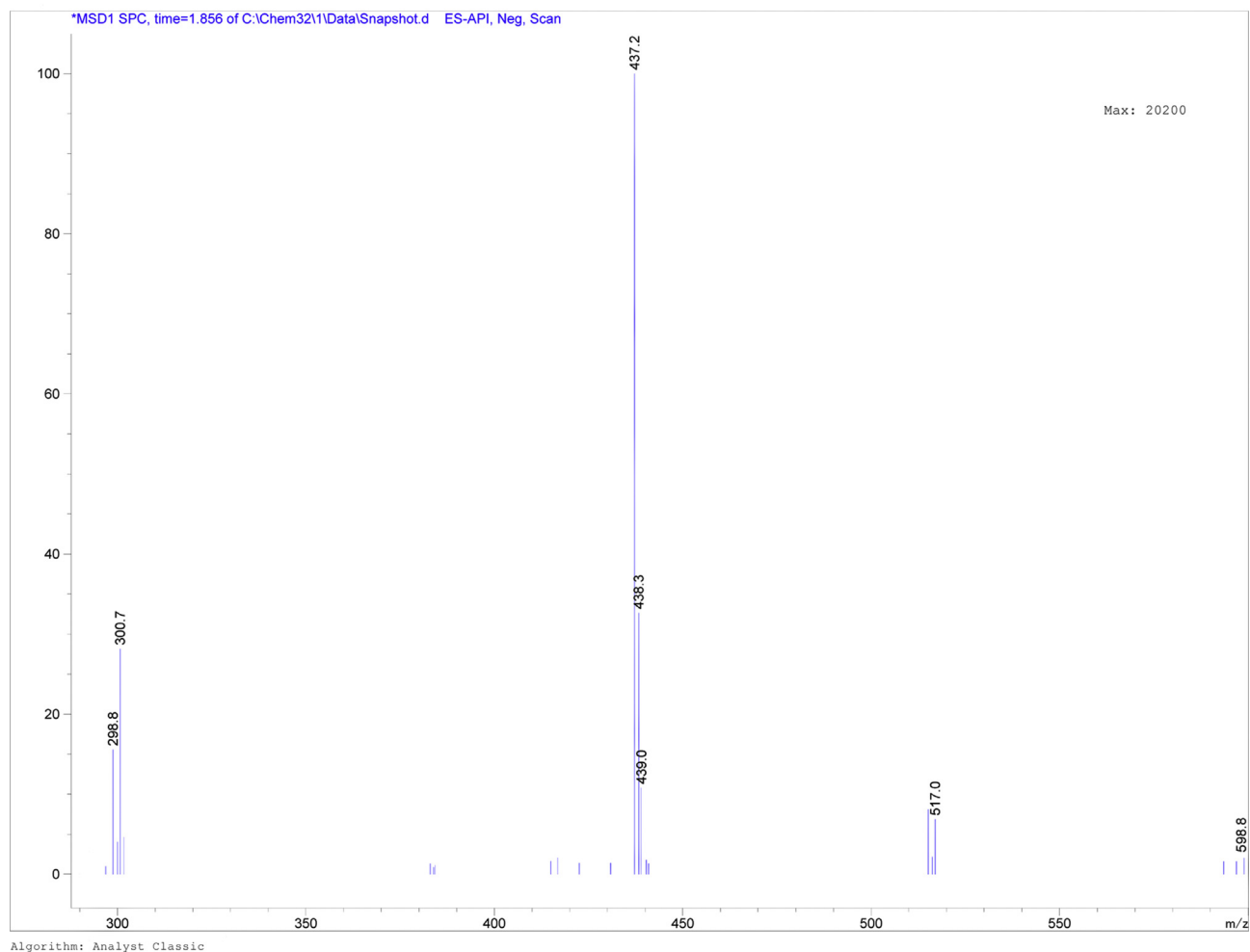


Fig. 21. Mass spectrum of 2,2'-((pentane-1,3-diylbis(azanylylidene))bis(ethan-1-yl-1-ylidene))bis(4-bromonaphthalen-1-ol).

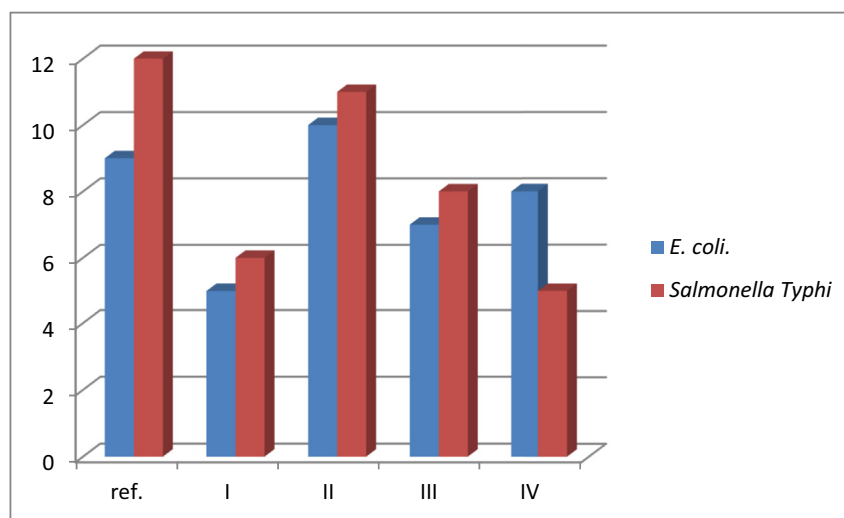


Fig. 22. Graphical Representation of Antibacterial activity of synthesized Schiff bases (I-IV).

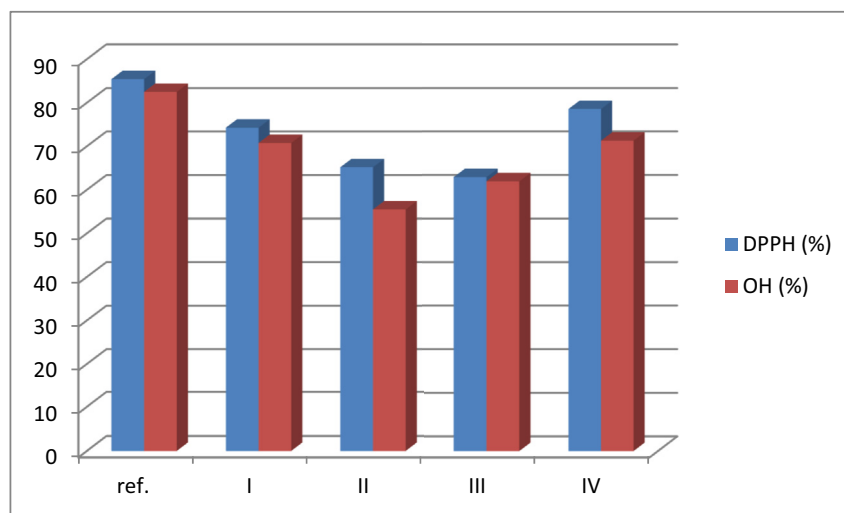


Fig. 23. Graphical Representation of Antioxidant activity of synthesized Schiff bases (I-IV).

against *E. coli*. Comp. I and III shows good inhibition at minimum concentration (1.0 mg/ml) against *Salmonella typhi*.

Comparative study also revealed that the halogen substituent with less number carbon chain has good inhibition against *E. coli* and *Salmonella Typhi*. Inhibition will be reduces if carbon chain extended on halogen substituted compound.

3.3.2. Antioxidant activity (in vitro)

Schiff bases (I-IV) were evaluated for their radical scavenging capacity (antioxidant activity) by DPPH and hydroxyl radical scavenging assay using Ascorbic acid and α -Tocopherol as internal standard respectively, results are showed in Table 3. In both methods used, the compounds I and IV are exhibiting higher activity than II and III. It may be due to compound I is with free hydroxyl group in position 4 and presence of 1,3 propane diamine group also compound IV is with halogenated hydroxyl group in position 4 and 1,3 pentane diamines.

Comparative study also revealed that the halogen substituent with extended carbon chain has good antioxidant activity. Activity will be reduces if free hydroxyl group and halogenated hydroxyl group in position 4 with less number of carbon chain.

4. Conclusion

The current study describes the synthesis of four novel Schiff bases (I-IV) were identified by using melting point, UVvis., IR, ^1H NMR, ^{13}C NMR and LCMS.

It is also assayed for antibacterial and antioxidant activities. Antibacterial activity was studied against Gram-negative pathogenic bacteria with MICs of 0.12, 0.25, 0.5 and 1 mg/ml against *E. coli* and *Salmonella Typhi*. Antioxidant activity was studied by DPPH and hydroxyl radical method.

Among these schiff bases, compound II and IV are having stronger hydrogen bonding than compound I and III. It concludes that compound II shows better antibacterial activity against *E. coli* and *Salmonella Typhi* and compound IV exhibits better radical scavenging activity by both DPPH and hydroxyl radical method. These studies reveal the antibacterial and antioxidant potency of Schiff bases of 1-hydroxyacetophenone.

Declarations

Author contribution statement

Avinash Shinde: Conceived and designed the experiments; Analyzed and interpreted the data.

Bhagwat Vhanale: Performed the experiments; Wrote the paper.

Nagesh Deshmukh: Contributed reagents, materials, analysis tools or data.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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