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Synthesis, Spectral Characterization of Some Novel Schiff's base and its Antibacterial Studies

S. Manikandan *G. Thirunarayanan

Department of Chemistry, Annamalai University, Annamalainagar - 608002, India.

Abstract

(*E*)-4,6-dibromo-N^1-(4-substituted benzylidene)benzene-1,2-diamine **(1-6)** (aryl = C_6H_5, *p*-FC_6H_4, *p*-ClC_6H_4, *p*-BrC_6H_4, *p*-$CH_3C_6H_4$, *p*-$CH_3OC_6H_4$) were synthesized by the condensation of 2-amino-4,6-dibromobenzaldehyde and 4-substituted aniline**.** Schiff bases. All compounds were evaluated for their in vitro antibacterial activity against different strains of *Staphylococcus aureus, Bacillus subtilis, Streptococcus pyogenes, Klebsiella pneumoniae, E.coli* and *Pseudomonas aeruginosa* with *Chloramphenicol* as standard drug. Out of all Schiff's basses, the compound **6** shows good activity against *Klebsiella pneumoniae* strains.

Keywords: Schiff base**,** IR, ^1H and ^{13}C NMR spectra, Antibacterial activities

INTRODUCTION

Schiff's bases have been well-studied region of research in pharmaceuticals and in medicinal fields having remarkable biological activities [1-3], and able to forming stable complexes with transition metals developing new applications in the area of non-linear optical materials [4-8]. Synthesis of privileged Schiff base an economical and environment friendly method is always desirable because Schiff base moieties are of paramount interest in medicinal chemistry due to their antifungal, antimicrobial, antitumor and anticancer properties [9-20]. The Schiff base structural motif is also a building block of pharmaceutics and functional materials. Furthermore, their effective role as therapeutic agents [21] and their remarkable catalytic activity [22,23] have added to their significance. In addition, Schiff bases are used as intermediates in synthesis of organic compounds, pigments, dyes, stabilizers and corrosion inhibitors [24,25]. From this review it makes clear that there are a large number of systems that can be studied by employing a variety of experimental techniques. It is, therefore, quite important to select such systems that can serve as useful prototypes of important and unique properties.

Although pharmaceuticals companies have produced several new antibiotics over the last three decades, antibiotics have increased resistance to these drugs. In general, bacteria have the genetic capacity to resist and buy drugs that treat agents [26]. Such a fact is cause for concern, because of the number of patients in hospitals who have suppressed immunity, and due to new bacterial strains. In recent years, Schiff bases have paid increased attention to fundamentals of fundamental processes. The performance Schiff base derivatives collection is the main goal of drug research. Recent observations, the alternatives Schiff base and heterocyclic, with the possibility of having simple contact with biopolymers; possess potential activity with lower toxicities in the chemotherapeutic approach in man [27]. The usefulness of Schiff's bases has made their synthesis the subject of extensive research. In this article, we report the synthesis and characterizations such as elemental analysis, NMR spectral techniques (^1H, ^{13}C), and antibacterial studies.

EXPERIMENTAL

Material and methods

All chemicals and solvents used were of AnalaR grade. The melting points were taken in open capillaries in an electrical apparatus and are uncorrected. Elemental analyses were carried out on VARIOMICRO V2.2.0 CHN analyser. The FT-IR spectrum of the synthesised compounds was taken in the range of 4000-400 cm^{-1} a AVATAR-330 FT-IR spectrometer (ThermoNicolet) using KBr (pellet form). ^{1}HNMR was recorded on a Bruker 400 MHz NMR and ^{13}CNMR was recorded on a Bruker 100 MHz NMR using $CDCl_3$/DMSO-d_6 as solvent for all the imidazoles.

Antimicrobial activities

The antimicrobial activities of these synthesized title compounds were measured by disc diffusion method [28]. In this experiment there are two each gram positive/ negative and two fungal strains were used for measuring the antibacterial and antifungal activities of these imidazoles.

Gram positive and Gram negative strains like *Staphylococcus aureus, Bacillus subtilis, Streptococcus pyogenes, Klebsiella pneumoniae, E.coli and Pseudomonas aeruginosa* were used for measuring the activities. The *Chloramphenicol* was used as the standard drug.

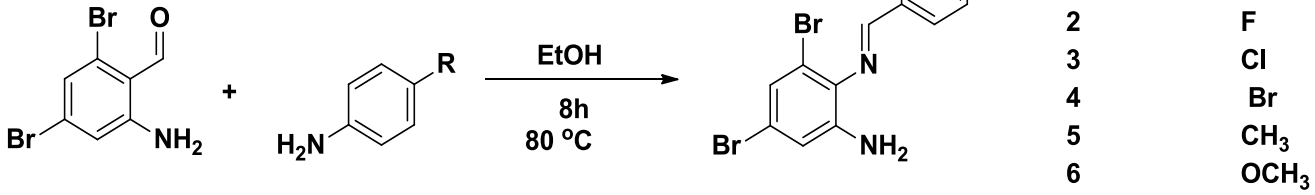
Nutrient agar plates were prepared under sterile conditions and incubated overnight to notice contamination. Regarding 0.2 ml of working stock culture was transferred into separate nutrient agar plates and spread thoroughly by a glass spreader. Whatmann No. 1 discs (6 mm in diameter) were impregnated with the test compounds dissolved in DMSO (200 mg/ml) for on the subject of half an hour. Commercially available drug disc (*Chloramphenicol* 40µg /disc) was used as positive reference standard. Negative controls were also prepared by impregnating the disc of same size in DMSO solvent. The discs were positioned on the inoculated agar plates and incubated at 37 ± 1 C for about 18-24 h. Antibacterial activity was evaluated by measuring the zone of inhibition against the test organism.

Synthesis of phenyl (*E*)-4,6-dibromo-N^1-(4-substituted benzylidene)benzene-1,2-diamine (IBPBD)

After mixing the ethanolic solution (50 ml) of 2-amino-4,6-dibromobenzaldehyde with 4-substituted aniline in ethanol (50 ml), the **IBPBD** was easily synthesized by refluxing the solution. At water bath temperature, reflux was continued for *ca*. 8 h. The crystalline solid formed was collected by vacuum filtration and washed in absolute ethanol. The product was dried at room temperature. **Scheme 1** shows a schematic picture representing the synthesis of molecule.

RESULTS AND DISCUSSION

The new (*E*)-4,6-dibromo-N^1-(4-substituted benzylidene) benzene-1,2-diamine (**1**-**6**) were prepared through the condensation of 2-amino-4,6-dibromobenzaldehyde, 4-substituted aniline in ethanol. In this reaction the yield obtained was in the interval 83-95%. The synthesized Schiff bases were characterized by their elemental analysis and FT-IR, ^{1}H and ^{13}C NMR spectral data. The physical constants and elemental analyses data of title compounds are shown in **Table 1**.



Scheme 1 Representation of the synthesis of the Schiff bases

Table 1 Physical constants, yields and analytical data of compounds **1-6**

Entry	X	M.F	M.W	Yield (%)	M.p (°C)	Found (Calcd.) (%)		
						C	H	N
1	H	$C_{13}H_{10}Br_2N_2$	354.04	92	134-136	44.10 (44.08)	2.85 (2.79)	7.91 (7.89)
2	F	$C_{13}H_9Br_2FN_2$	372.03	95	164-266	41.97 (41.90)	2.44 (2.39)	7.53 (7.49)
3	Cl	$C_{13}H_9Br_2ClN_2$	388.48	93	182-184	40.19 (40.14)	2.34 (2.31)	7.21 (7.19)
4	Br	$C_{13}H_9Br_3N_2$	432.94	90	196-198	36.07 (36.02)	2.10 (2.09)	6.47 (6.41)
5	CH_3	$C_{14}H_{12}Br_2N_2$	368.07	85	114-116	45.68 (45.52)	3.29 (3.19)	7.67 (7.61)
6	OCH_3	$C_{14}H_{12}Br_2N_2O$	384.07	83	106-108	43.78 (43.72)	2.85 (2.80)	7.91 (7.80)

IR spectral analysis

The IR spectral data of compounds **1-6** are given in **Table 2.** The IR spectrum of compound **1** is shown in **Figure 1**. The N-H stretching vibration [29,30] appears as a strong and broad band in the region 3500-3100 cm^{-1}. Thirunarayanan et al. [31] synthesized oxazine amines derivatives and reported assigned N-H stretching in the region 3532-3559 cm^{-1}. For the title compounds, the strong band in the region 3264.03-3448.71 cm^{-1} are assigned to N-H stretching. Generally, aromatic compounds commonly exhibit multiple weak bands in the region 3150-2930 cm^{-1} [32]. Therefore, the IR bands in the region 3044.76-3064.40 cm^{-1}. The C-H stretching in alkanes occurs at lower frequencies than those of aromatic ring. The CH_3 stretching is expected at 2980-2870 cm^{-1} [33] and usually the bands are weak. The band *ca.* 2930 cm^{-1} is attributed to methyl (CH_3) group in compounds **5** and **6**.

Thirunarayanan et al. [33] assigned C=N stretching in the region 1548-1579 cm^{-1} in phenazine derivatives. In this case, the carbonyl C=N stretching appeared in the region 1613.46-1637.18 cm^{-1}. The appearance of C=N band is the preliminary evidence for the formation of Schiff bases. The ring C=C vibrations, known as semicircle stretching usually occur in the interval 1400-1625 cm^{-1} [34]. Hence in the present investigation, the FT-IR band identified in the region 1519.98-1412.74cm^{-1}. The band ascribed at 1393.13- 1244.06 cm^{-1} in FT-IR spectra had band designated to C-H in- plane bending vibrations. The bands in the range 1179.78-693.07 cm^{-1} are due to the aromatic C-H out-of-plane bending vibrations.

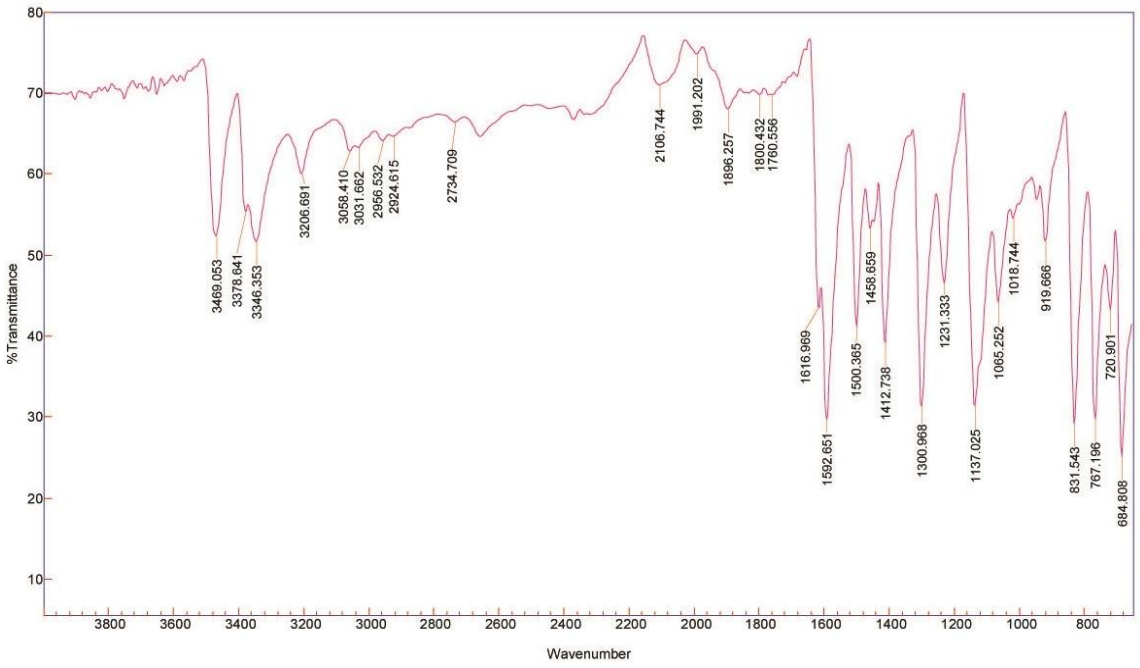


Figure 1. FT-IR spectrum of compound **1**

Table 2. FT-IR spectral data of compounds **1-6**

Assignments	**1**	**2**	**3**	**4**	**5**	**6**
	H	**F**	**Cl**	**Br**	**CH_3**	**OCH_3**
ν_{N-H}	3378.64	3264.03	3361.96	3329.22	3448.71	3391.30
ν_{ArC-H}	3058.41	3064.40	3044.76	3046.79	3046.00	3065.55
	2956.53	2930.55	2930.00	2929.49	2976.32	2988.00
ν_{AliC-H}	-	-	-	-	2929.95	2931.68
$\nu_{C=N}$	1616.97	1613.46	1633.99	1635.59	1636.35	1637.18
$\nu_{C=C}$	1500.37	1493.22	1519.63	1516.82	1519.98	1467.28
	1458.66	1455.08	1477.66	1491.54	1491.75	1426.12
	1412.74		1444.97	1445.31	1443.56	
β_{C-H}	1300.97	1309.16	1325.86	1321.27	1393.13	1378.04
	1231.33	1252.54	1299.38	1304.82	1299.79	1319.47
				1248.41	1244.06	1286.25
Γ_{C-H}	1137.02-720.90	1177.990-714.12	1111.43-695.25	1129.06-693.07	1129.44-762.19	1179.78-705.94
ν_{C-Br}	684.80	640.48	638.24	643.05	642.18	-

NMR spectral analysis

The ^{1}H NMR spectrum of compound **1** is shown in **Figure 2**. The chemical shift values of title Schiff bases are given **Table 3.** The aromatic protons in the compound **1** are appeared in the interval 7.22-8.29 ppm.The upfield signal in the region 4.07-4.90 ppm is assigned to N-H proton present in compounds **1-6**. The methine proton (N=C**H**) signal appeared in the interval 8.31-8.52 ppm. In compound **6**, the methoxy proton signal appeared at 3.39 ppm. The upfield signal at 2.36 ppm corresponds to methyl proton in compound **5**.

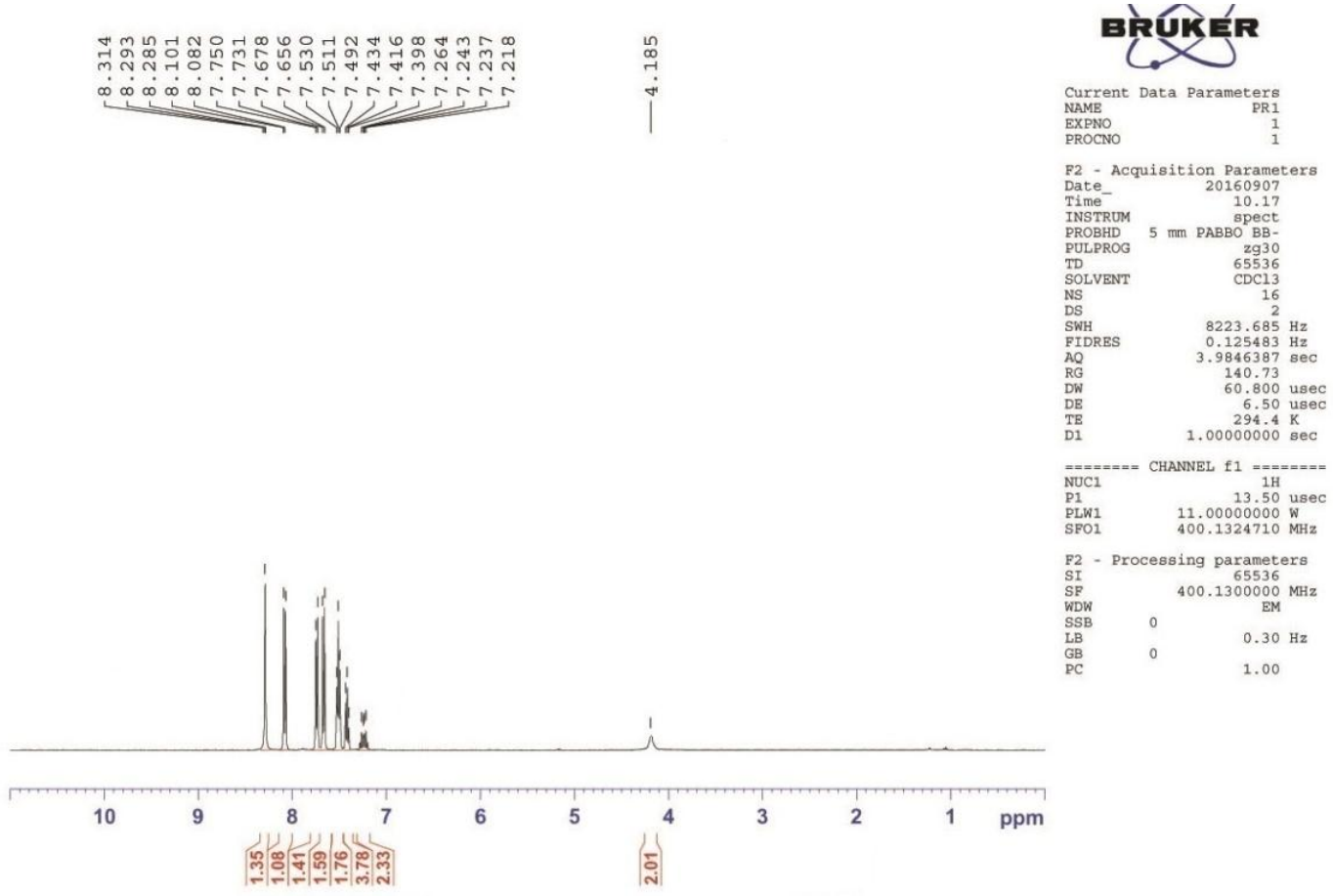


Figure 2. ^{1}H NMR spectrum of compound **1**

Table 3. The chemical shifts of NMR (δ ppm) spectral values of compounds **1-6**

Entry		^{1}H NMR				^{13}C NMR			
		CH_3/ OCH_3	N-**H**	**Ar-H**	N=C**H**	**C=N**	**C*ipso***	**Ar-C**	**CH_3/ OCH_3**
1	H	-	4.19	7.22-8.29	8.31	155.66	142.42	112.33-138.43	-
2	F	-	4.90	7.19-8.44	8.50	155.20	143.88	113.31-139.60	-
3	Cl	-	4.18	7.19-8.45	8.51	155.21	143.89	113.34-139.61	-
4	Br	-	4.25	7.19-8.45	8.51	155.21	143.88	113.31-139.60	-
5	CH_3	2.36	4.07	7.19-8.46	8.52	155.25	143.91	113.33-139.64	27.05
6	OCH_3	3.39	4.08	7.22-8.29	8.31	155.66	149.18	112.33-138.43	52.08

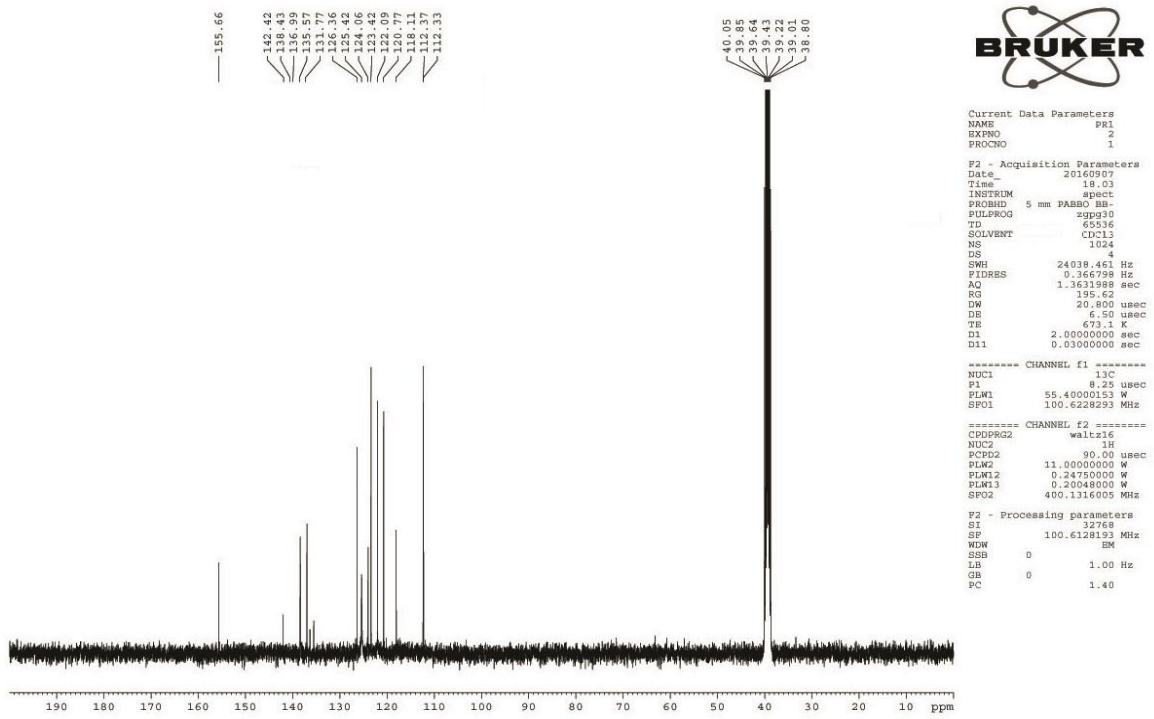


Figure 3. ^{13}C NMR spectrum of compound **1**

The representative ^{13}C NMR spectrum of compound **1** is shown in **Figure 3**. The ^{13}C chemical shifts values of compounds **1-6** are given in **Table 3.** In the ^{13}C NMR spectrum of **1-6**, the weak signal around 155 ppm is due to C=N of Schiff bases. The aromatic carbons could be easily distinguished by their characteristic absorption around 112.33-139.64 ppm. The *ipso* carbons should absorb at higher frequency compared to other aromatic carbons. The *ipso* carbons signal appeared in the interval 142.42-149.18 ppm. Obviously the remaining signals at 27.05 and 52.08 pm are due to methyl and methoxy carbon present in compounds **5** and **6**, respectively.

Antibacterial studies

In this study, we synthesized new Schiff base and were tested for their ability to inhibit the *in vitro* growth of strains *viz.*, *Staphylococcus aureus, Bacillus subtilis, Streptococcus pyogenes, Klebsiella pneumoniae, E.coli and Pseudomonas aeruginosa* were used for this study. *Chloramphenicol* is used as standard drug for bacterial strain. The Zone of inhibition values of compounds **1-6** along with the standard drug for comparison is furnished in **Table 4** and the statistical bacterial activity column chart was shown in **Figure 4**.

Table 4. Antibacterial activities of compounds **1-6** by disc diffusion method

Pathogens	**Diameter of zone of Inhibition (mm)**						
	Concentration of compound (40µg)						
	1	***2***	***3***	***4***	***5***	***6***	**Chloramphenicol**
Staphylococcus aureus	8	11	8	9	10	13	26
Bacillus subtilis	9	12	9	10	11	18	20
Streptococcus pyogenes	8	10	9	10	8	13	27
Klebsiella pneumoniae	10	12	9	9	8	19	27
E.coli	9	12	10	9	8	18	21
Pseudomonas aeruginosa	10	13	10	9	11	18	24

The antibacterial study showed that most of compounds possess optimum acclivity. The zone of inhibition values of compounds **1-6** are given in **Table 4**, which indicate that all the tested compounds exhibited range 8-12 mm. Compounds **2,5** and **6** showed moderate antibacterial activity against *S. aureus* strain. The Schiff bases **1,3** and **4** showed poor antibacterial activity against *S. aureus* strain within 8-9 mm of zone of inhibition. The compounds **1,3** and **4** show poor activity within 8-9 mm of zone of inhibition. The compound **6** shows excellent activity with 18 mm of zone of inhibition, whereas compound **2** shows satisfactory activity against the Bacillus subtilis strain. The compounds 1 and 3 exhibited moderate against the same strain. The Schiff bases **2, 4** and **6** shows moderate antibacterial activity against *S. pyogenes* strain. The reaming compounds such as **1, 3** and **5** have activity in the inhibition in the region 8-9 mm. The methoxy substituted (Compound **6**) show good activity antibacterial activity against *K. pneumoniae* strain.The remaining compounds **1-5** showed poor activity, when compared to Chloramphenicol. As seen from **Table 4**, *E. coli* bacterial strain showed higher resistance power than our synthetic compounds **1-6**, whereas the standard drug sowed inhibition about 21 mm. The compounds **1-6** show poor activity within 7-8 mm of zone of inhibition, whereas standard drug shows satisfactory activity against the same strain. The methoxy substituent in compound (compound **6**) in the phenyl group gave activity in the inhibition at 18 mm, whereas the reaming compounds **1-5** show acclivity in the interval 9-13 mm.

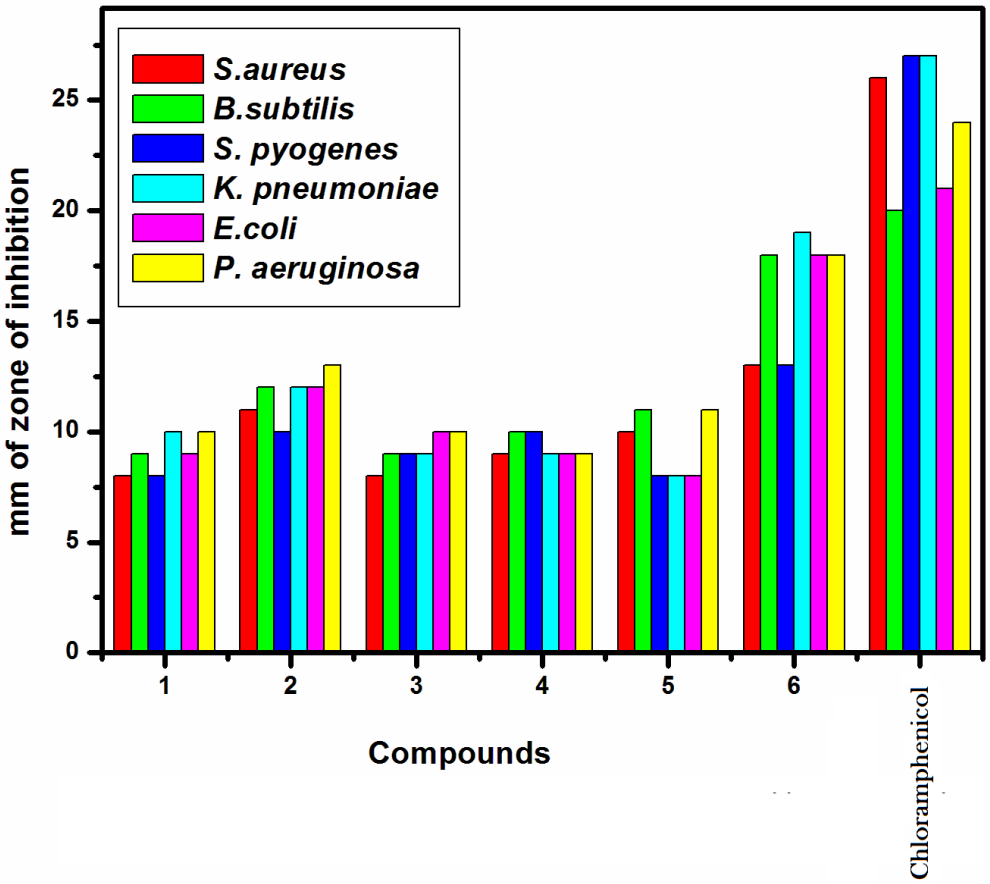


Figure 4. The chart representation of the antibacterial activity of compounds 1-6

CONCLUSION

In this work, we have disclosed the synthesis for (*E*)-4,6-dibromo-N^1-(4-substituted benzylidene)benzene-1,2-diamine. Using readily available 2-amino-4,6 dibromobenzaldehyde, 4-substituted aniline and ethanol as solvent. For all these compounds, elemental analysis, FT-IR, ^{1}H and ^{13}C NMR spectra have been recorded. All the compounds were screened for their preliminary antibacterial activity by disc diffusion method. Compound **6** was found good active against *Klebsiella pneumoniae* bacterial strains used for present study. This compound **6** will be utilized in further work to design more potent molecules.

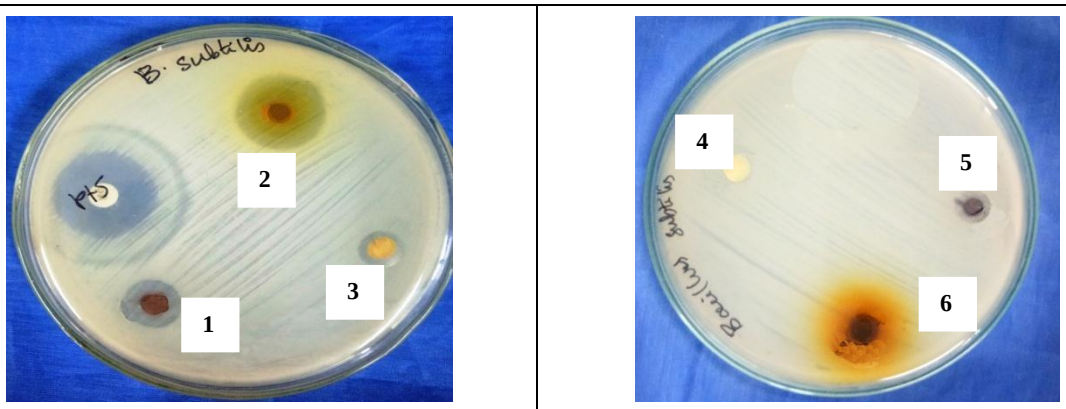


Figure 5. Zone of inhibition of compounds **1-6** against *B. subtilis.*

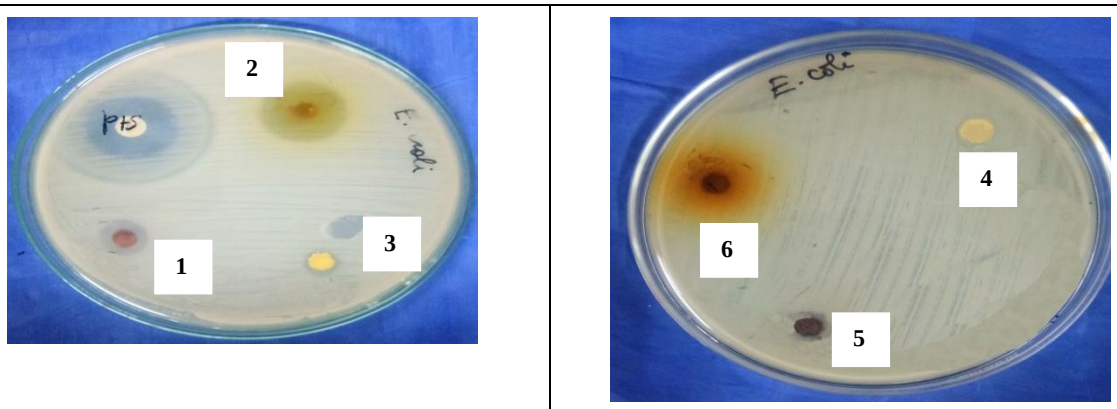


Figure 6. Zone of inhibition of compounds **1-6** against *E. coli*

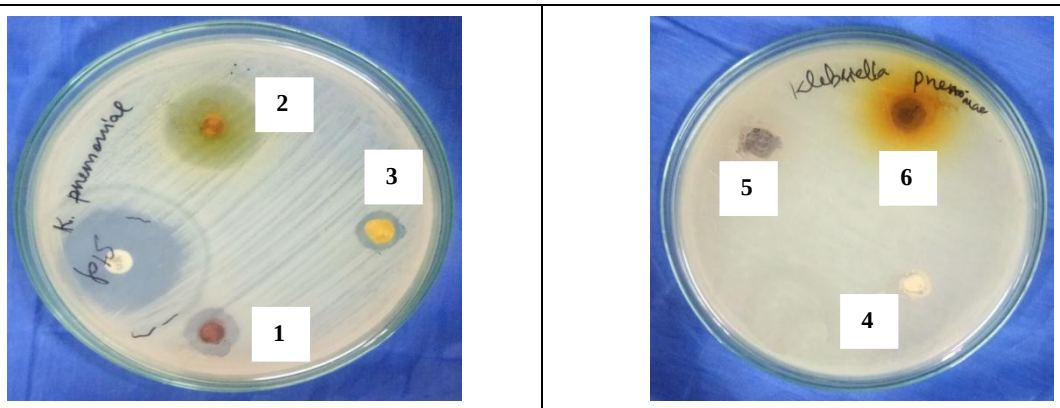


Figure 7. Zone of inhibition of compounds **1-6** against *K. pneumonia.*

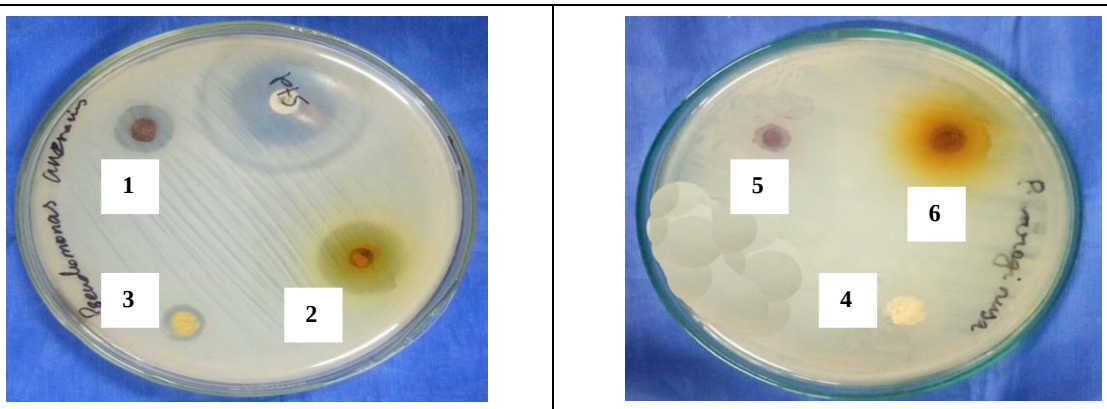


Figure 8. Zone of inhibition of compounds **1-6** against *P. aeruginosa.*

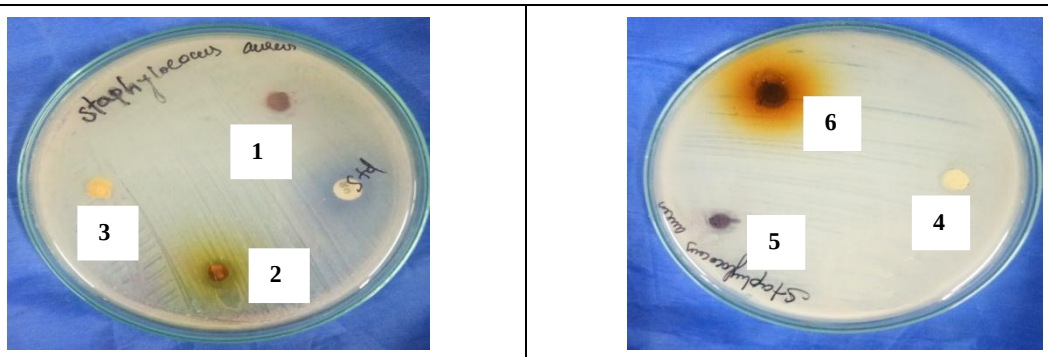


Figure 9. Zone of inhibition of compounds **1-6** against *S. aureus.*

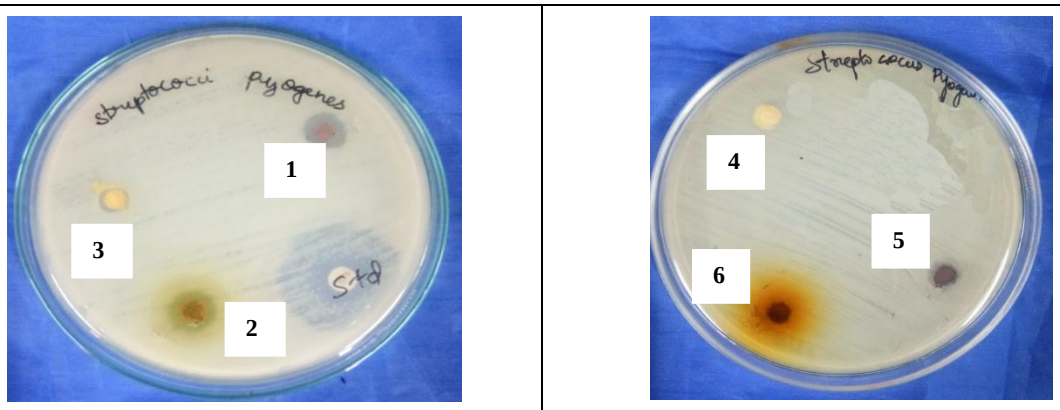


Figure 10. Zone of inhibition of compounds **1-6** against *S. pyogenes.*

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