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Perchloric acid catalyzed condensation of amine and aldehydes: Synthesis and antibacterial activities of some aryl (*E*)-imines

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A series of Schiff's bases (aryl *E*-imines) have been derived from the perchloric acid catalyzed condensation of aryl amines and substituted benzaldehydes. The yield of the Schiff's bases are more than 80%. The synthesized Schiff's bases are characterized by their physical constants, analytical and spectroscopical data. The antibacterial activities of these Schiff's bases have been studied using Bauer-Kirby method.

Keywords: Schiff's bases, Perchloric acid, IR and NMR spectra, Antibacterial activities.

1. INTRODUCTION

Schiff's bases were first synthesized by Schiff in 1864. Schiff's bases named after Hugo Schiff's formed by the bimolecular condensation products of primary amine with carbonyl compounds. Schiff's bases are characterized by the –N=CH– imine group which find important in elucidating the mechanism of transamination and racemization reaction of biological system [1, 2]. Many reagents have been used for the synthesis of optically active imines like Lewis acids [3], molecular sieves in ionic

liquids [4], solid super acid K-10 montmorillonite [5], Tandam catalyst [6], MnO_2 [7], CaO [8], $ZnCl_2$ [9], $MgSO_4$-PPTS [10], alumina [11], P_2O_5-SiO_2 [12], infrared [13], ultrasound radiation [14] and fly-ash:H_2SO_4 with microwave irradiation. These catalysts were used for the synthesis of chiral imines by condensation of amines [15, 16], with carbonyl compounds [5, 6, 17], alcohols [18] and acid chlorides [3, 19]. The imine starting materials and important intermediates were used for the synthesis of pharmacologically active heterocycles including triazoles, trizolones [20–22]. Optically active imine derivatives possess biological activities such as antimicrobial [23], anticancer [24], antiplasmodic-antihypoxic [25], antitubularcular [26], nematicidal insecticidal [17], anti-inflammatory and lipoxygenase [27]. Hence the authors have taken efforts to synthesis of some imines by perchloric acid catalyzed condensation of aryl amines with various substituted benzaldehydes. The synthesized Schiff's bases have been characterized by their analytical, physical constants and spectroscopic data. These data have been utilized for studying the biological activities of these imine derivatives which have been found out using Bauer-Kirby [28] method.

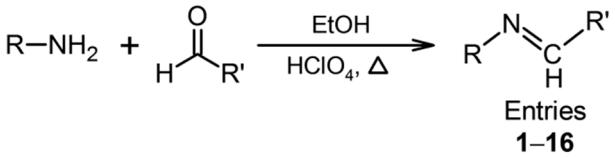
2. EXPERIMENTAL

All chemicals used in this work were purchased from Sigma-Aldrich Chemicals Private Limited. Melting points of all imines have been determined in open glass capillaries on Biom melting point apparatus (Universal Biochemicals Enzyme House, Madurai-3) and are uncorrected. Infrared spectra (KBr, 4000–400 cm^{-1}) have been recorded on Avatar-300 Fourier transform spectrophotometer (Thermo Nicolet, USA). The NMR spectra of all imines were recorded in Bruker AV400 spectrometer (Bruker AXS GmbH, Karlsruhe, Germany), operated 400 MHz frequency for recording ^1H and 100 MHz for ^{13}C NMR spectra in $CDCl_3$ solvent using TMS as internal standard. Electron impact (70 eV) and chemical ionization mode FAB + mass spectra have been recorded in Varian-Saturn 2200 GC-MS spectrometer (Varian 92 Medical Systems, Palo Alto, CA, USA).

2.1. Synthesis of imines

An appropriate equimolar quantity of aryl amines containing electron withdrawing and electron donating substituents (1 mmol), substituted benzaldehydes (1 mmol), perchloric acid (1 mmol) and ethanol (20 mL) were refluxed for about 4 h (Scheme 1). The completion of reaction

was monitored by TLC. After completion of the reaction, the solid product was filtered using filter pump and dried. The crude product was recrystallized from ethanol.



Scheme 1. Synthesis of imines by condensation of aldehydes and amines in presence of perchloric acid.

2.2. Spectral data of entries 6–16

(E)-1-Benzyl-N-benzylidenepiperidin-4-amine (entry 6): Yield 81%; m.p. 64–65°C; IR (KBr, cm^{-1}): ν = 1567.12 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.550 (s, 2H, CH_2), 8.327 (s, 1H, CH), 1.707–3.278 (m, 9H, alicyclic), 7.253–7.741 (m, 10H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.71 (CH_2), 159.16 (CH), 136.50 (C_1), 129.79 (C_2, C_6), 130.50 (C_4), 128.58 (C_3, C_5), 138.71 ($C_{1'}$), 128.21 ($C_{2'}$, $C_{6'}$), 128.13 ($C_{3'}$, $C_{5'}$), 126.25 ($C_{4'}$), 52.51 ($C_{2''}$, $C_{6''}$), 33.53 ($C_{3''}$, $C_{5''}$), 63.21 ($C_{4''}$); MF: $C_{19}H_{22}N_2$; MW: 278.

(E)-1-Benzyl-N-(3-bromobenzylidene)piperidin-4-amine (entry 7): Yield 80%; m.p. 59–60°C; IR (KBr, cm^{-1}): ν = 1565.44 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.510 (s, 2H, CH_2), 8.172 (s, 1H, CH), 7.198–7.888 (m, 9H, Ar), 1.662–3.198 (m, 9H, alicyclic); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.57 (CH_2), 157.54 (CH), 138.51 (C_1), 130.16 (C_2), 122.90 (C_3), 130.64 (C_4), 129.17 (C_5), 127.08 (C_6), 133.34 ($C_{1'}$), 128.28 ($C_{2'}$, $C_{6'}$), 127.05 ($C_{3'}$, $C_{5'}$), 52.01 ($C_{2''}$, $C_{6''}$), 33.46 ($C_{3''}$, $C_{5''}$), 63.20 ($C_{4''}$); MF: $C_{19}H_{21}N_2Br$; MW: 357.

(E)-1-Benzyl-N-(3-chlorobenzylidene)piperidin-4-amine (entry 8): Yield 83%; m.p. 53–54°C; IR (KBr, cm^{-1}): ν = 1595.71 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.538 (s, 2H, CH_2), 8.236 (s, 1H, CH), 1.689–3.267 (m, 9H, alicyclic), 7.225–7.750 (m, 9H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.66 (CH_2), 157.69 (CH), 138.62 (C_1), 127.05 (C_2), 134.78 (C_3), 130.48 (C_4), 129.87 (C_5), 127.77 (C_6), 138.29 ($C_{1'}$), 128.62 ($C_{2'}$, $C_{6'}$), 128.29 ($C_{3'}$, $C_{5'}$), 126.59 ($C_{6'}$), 52.05 ($C_{2''}$, $C_{6''}$), 33.49 ($C_{3''}$, $C_{5''}$), 63.23 ($C_{4''}$); MF: $C_{19}H_{21}N_2Cl$; MW: 312.

(E)-1-Benzyl-N-(4-chlorobenzylidene)piperidin-4-amine (entry 9): Yield 82%; m.p. 102–103°C; IR (KBr, cm^{-1}): ν = 1592.24 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.543 (s, 2H, CH_2), 8.271 (s, 1H, CH), 1.690–3.234 (m, 9H, alicyclic), 7.251–7.668 (m, 9H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.70 (CH_2), 157.80 (CH), 134.97 (C_1), 129.35 (C_2, C_6), 128.84 (C_3, C_5), 136.39 (C_4), 138.66

($C_{1'}$), 128.39 ($C_{2'}$, $C_{6'}$), 128.24 ($C_{3'}$, $C_{5'}$), 126.99 ($C_{4'}$), 52.10 ($C_{2''}$, $C_{6''}$), 33.50 ($C_{3''}$, $C_{5''}$), 63.23 ($C_{4''}$); MF: $C_{19}H_{21}N_2Cl$; MW: 312.

(E)-1-Benzyl-N-(4-(dimethylamino)benzylidine)piperidin-4-amine (entry 10): Yield 80%; m.p. 57–58°C; IR (KBr, cm^{-1}): ν = 1560.07 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.540 (s, 2H, CH_2), 8.190 (s, 1H, CH), 1.685–3.185 (m, 9H, alicyclic), 6.667–7.749 (m, 9H, Ar), 3.325 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.64 (CH_2), 159.14 (CH), 125.19 (C_1), 124.70 (C_2, C_6), 111.66 (C_3, C_5), 152.00 (C_4), 138.72 ($C_{1'}$), 129.19 ($C_{2'}$, $C_{6'}$), 128.20 ($C_{3'}$, $C_{5'}$), 126.99 ($C_{4'}$), 52.36 ($C_{2''}$, $C_{6''}$), 33.73 ($C_{3''}$, $C_{5''}$), 63.17 ($C_{4''}$), 41.04 (CH_3); MF: $C_{21}H_{27}N_3$; MW: 321.

(E)-1-Benzyl-N-(4-fluorobenzylidine)piperidin-4-amine (entry 11): Yield 80%; m.p. 92–93°C; IR (KBr, cm^{-1}): ν = 1597.18 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.547 (s, 2H, CH_2), 8.282 (s, 1H, CH), 1.729–3.239 (m, 9H, alicyclic), 7.057–7.736 (m, 9H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.56 (CH_2), 157.68 (CH), 132.81 (C_1), 130.03 (C_2, C_6), 115.74 (C_3, C_5), 165.45 (C_4), 138.63 ($C_{1'}$), 129.95 ($C_{2'}$, $C_{6'}$), 128.23 ($C_{3'}$, $C_{5'}$), 126.98 ($C_{4'}$), 52.10 ($C_{2''}$, $C_{6''}$), 33.52 ($C_{3''}$, $C_{5''}$), 63.20 ($C_{4''}$); MF: $C_{19}H_{21}N_2F$; MW: 296.

(E)-1-Benzyl-N-(3-methoxybenzylidine)piperidin-4-amine (entry 12): Yield 86%; m.p. 63–64°C; IR (KBr, cm^{-1}): ν = 1593.42 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.552 (s, 2H, CH_2), 8.294 (s, 1H, CH), 1.708–3.280 (m, 9H, alicyclic), 7.239–7.363 (m, 9H, Ar), 3.851 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.63 (CH_2), 159.88 (CH), 138.66 (C_1), 111.81 (C_2), 159.01 (C_3), 117.09 (C_4), 129.55 (C_5), 121.33 (C_6), 55.41 (3-OMe), 137.98 ($C_{1'}$), 129.14 ($C_{2'}$, $C_{6'}$), 128.21 ($C_{3'}$, $C_{5'}$), 126.96 ($C_{4'}$), 52.14 ($C_{2''}$, $C_{6''}$), 33.49 ($C_{3''}$, $C_{5''}$), 63.19 ($C_{4''}$); MF: $C_{20}H_{24}N_2O$; MW: 308.

(E)-1-Benzyl-N-(4-methoxybenzylidine)piperidin-4-amine (entry 13): Yield 82%; m.p. 49–50°C; IR (KBr, cm^{-1}): ν = 1575.79 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.534 (s, 2H, CH_2), 8.235 (s, 1H, CH), 3.795 (s, 3H, OCH_3), 1.712–3.216 (m, 9H, alicyclic), 6.882–7.672 (m, 9H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.67 (CH_2), 161.52 (CH), 128.95 (C_1), 130.54 (C_2, C_6), 114.38 (C_3, C_5), 164.65 (C_4), 55.38 (4-OCH_3), 138.72 ($C_{1'}$), 128.61 ($C_{2'}$, $C_{6'}$), 128.18 ($C_{3'}$, $C_{5'}$), 126.66 ($C_{4'}$), 52.50 ($C_{2''}$, $C_{6''}$), 33.84 ($C_{3''}$, $C_{5''}$), 63.24 ($C_{4''}$); MF: $C_{20}H_{24}N_2O$; MW: 308.

(E)-1-Benzyl-N-(4-methylbenzylidine)piperidin-4-amine (entry 14): Yield 87%; m.p. 51–52°C; IR (KBr, cm^{-1}): ν = 1573.95 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.547 (s, 1H, CH_2), 8.285 (s, 1H, CH), 1.698–2.249 (m, 9H, alicyclic), 7.187–7.625 (m, 9H, Ar), 2.369 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.70 (CH_2), 159.09 (CH), 133.90 (C_1), 129.29 (C_2, C_6), 129.14 (C_3, C_5), 140.71 (C_4), 138.70 ($C_{1'}$), 128.21 ($C_{2'}$, $C_{6'}$), 128.11 ($C_{3'}$, $C_{5'}$), 126.95 ($C_{4'}$), 52.20 ($C_{2''}$, $C_{6''}$), 33.56 ($C_{3''}$, $C_{5''}$), 63.19 ($C_{4''}$), 21.53 (4-CH_3); MF: $C_{20}H_{24}N_2$; MW: 292.

(E)-1-Benzyl-N-(3-nitrobenzylidine)piperidin-4-amine (entry 15): Yield 82%; m.p. 60–61°C; IR (KBr, cm^{-1}): ν = 1526.95 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.580 (s, 1H, CH_2), 8.556 (s, 1H, CH), 1.742–3.356 (m, 9H, alicyclic), 7.261–8.390 (m, 9H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.45 (CH_2), 156.51 (CH), 138.35 (C_1), 122.97 (C_2), 148.60 (C_3), 124.92 (C_4), 129.57 (C_5), 133.61 (C_6), 138.18 ($C_{1'}$), 129.20 ($C_{2'}$, $C_{6'}$), 128.26 ($C_{3'}$, $C_{5'}$), 127.08 ($C_{4'}$), 51.83 ($C_{2''}$, $C_{6''}$), 33.31 ($C_{3''}$, $C_{5''}$), 63.13 ($C_{4''}$); MF: $C_{19}H_{21}N_3O_2$; MW: 323.

(E)-1-Benzyl-N-(4-nitrobenzylidine)piperidin-4-amine (entry 16): Yield 85%; m.p. 82–83°C; IR (KBr, cm^{-1}): ν = 1598.42 (C=N); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.559 (s, 2H, CH_2), 8.400 (s, 1H, CH), 1.723–3.362 (m, 9H, alicyclic), 7.260–8.265 (m, 9H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 67.89 (CH_2), 156.81 (CH), 141.99 (C_1), 129.14 (C_2, C_6), 123.86 (C_3, C_5), 148.93 (C_4), 138.55 ($C_{1'}$), 128.82 ($C_{2'}$, $C_{6'}$), 128.25 ($C_{3'}$, $C_{5'}$), 127.03 ($C_{4'}$), 51.92 ($C_{2''}$, $C_{6''}$), 33.37 ($C_{3''}$, $C_{5''}$), 63.21 ($C_{4''}$); MF: $C_{19}H_{21}N_3O_2$, MW: 323.

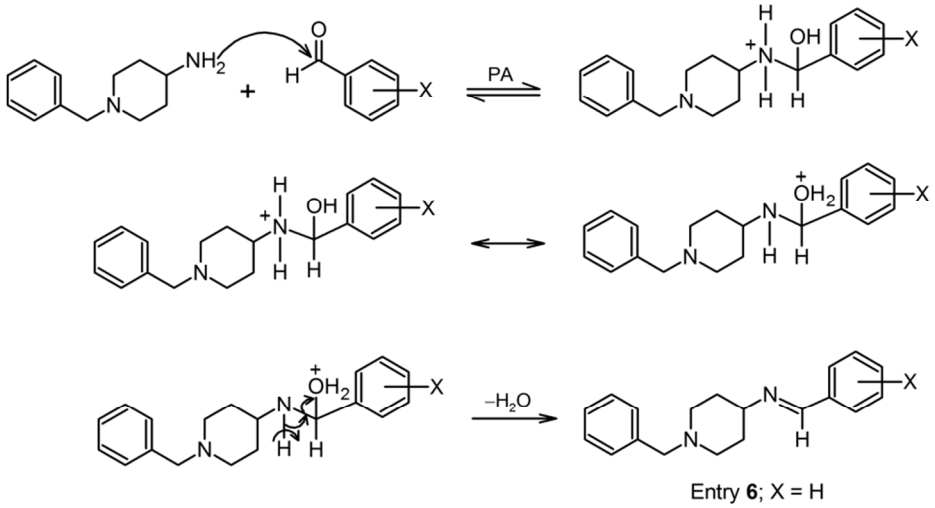
2.3. Antibacterial sensitivity assay

In this present study, antibacterial activities of synthesized imines (entries 6–16) against their respective microbes such as bacterial strains were studied. The antibacterial assays have been performed by using Bauer-Kirby [28] disc diffusion technique. In each petri plate about 0.5 cm^3 of the test bacterial sample has been spread uniformly over the solidified Mueller Hinton agar using sterile glass spreader. Then the discs with 5 mm diameter made from Whatman No. 1 filter paper, impregnated with the solution of the compound have been placed on the medium using sterile forceps. The plates have been incubated for 24 h at 37°C by keeping the plates upside down to prevent the collection of water droplets over the medium. After 24 h, the plates have been visually examined and the diameters of the zone of inhibition were measured. Triplicate results have been recorded by repeating the same procedure.

3. RESULTS AND DISCUSSION

In organic chemistry research laboratory, works have been carried out to synthesize aryl imine derivatives by condensation of aryl amines and various benzaldehydes containing electron withdrawing as well as electron donating substituents. The condensation reaction is feasible with aryl amines and benzaldehydes in the presence of vigorous acidic catalyst like perchloric acid in ethanol except acidic salt or base or its salt in

solution media under reflux condition in atmospheric temperature and pressure. Hence the authors have synthesized the imine derivatives by the condensation reaction between 1 mmol of aryl amines, 1 mmol substituted benzaldehydes, 1 mmol of perchloric acid and 20 cm^3 of ethanol at room temperature (Scheme 1). During the course of this reaction the perchloric acid catalyzes coupling between aryl amines and aldehydes by elimination of water followed by loss of proton forms the imines. The yield of the imines in this reaction is more than 80 %. The proposed general mechanism of this reaction is given in Scheme 2.



Scheme 2. Proposed mechanism of formation of imines by condensation of aldehydes and amines in presence of perchloric acid.

Further, we have also investigated this reaction with equimolar quantities of 4-amino-1-benzylpiperidine and benzaldehyde (entry 6). In this reaction the product yield is 85%. The physical constants, yield and mass spectral data are presented in Table 1. IR and NMR spectroscopic data and mass fragment pattern of selective compounds are given in Table 2 and Schemes 3–6.

Table 1. Physical constants, analytical and mass fragments (m/z) of the imines synthesized by aryl amines and substituted benzaldehydes reaction of the type $R–NH_2 + R'\text{-}CHO \rightarrow R–N=CH–R'$.

Entry	R	R′	Product	MW	Yield (%)	m.p. (°C)	Mass (m/z)
1	C_6H_5	C_6H_5	$C_6H_5N=CHC_6H_5$	181	60	52–53 (50–52) [29]	–
2	4-$NO_2C_6H_4$	C_6H_5	4-$NO_2C_6H_4N=CHC_6H_5$	226	75	140–141 (138–140) [29]	–
3	4-$CH_3C_6H_4$	C_6H_5	4-$CH_3C_6H_4N=CHC_6H_5$	195	90	114–115 (112–115) [29]	–
4	4-BrC_6H_4	C_6H_5	4-$BrC_6H_4N=CHC_6H_5$	260	82	62–63 (61–62) [29]	–
5	3-$CH_3OC_6H_4$	C_6H_5	3-$CH_3OC_6H_4N=CHC_6H_5$	211	96	156–157 (154–157) [29]	–
6	$C_{12}H_{16}N$	C_6H_5	$C_{12}H_{16}NN=CHC_6H_5$	278	81	64–65	278 (M^+), 279 (M^{+1}), 265, 212, 201, 187, 152, 113, 102, 94, 81, 69, 52
7	$C_{12}H_{16}N$	3-BrC_6H_4	$C_{12}H_{16}NN=CHC_6H_4Br$ (3)	357	79	59–60	357 (M^+), 359 (M^{+2}), 317, 304, 279, 265, 237, 198, 155, 128, 124, 119, 110, 103, 97, 65, 52

Cont. Table 1.

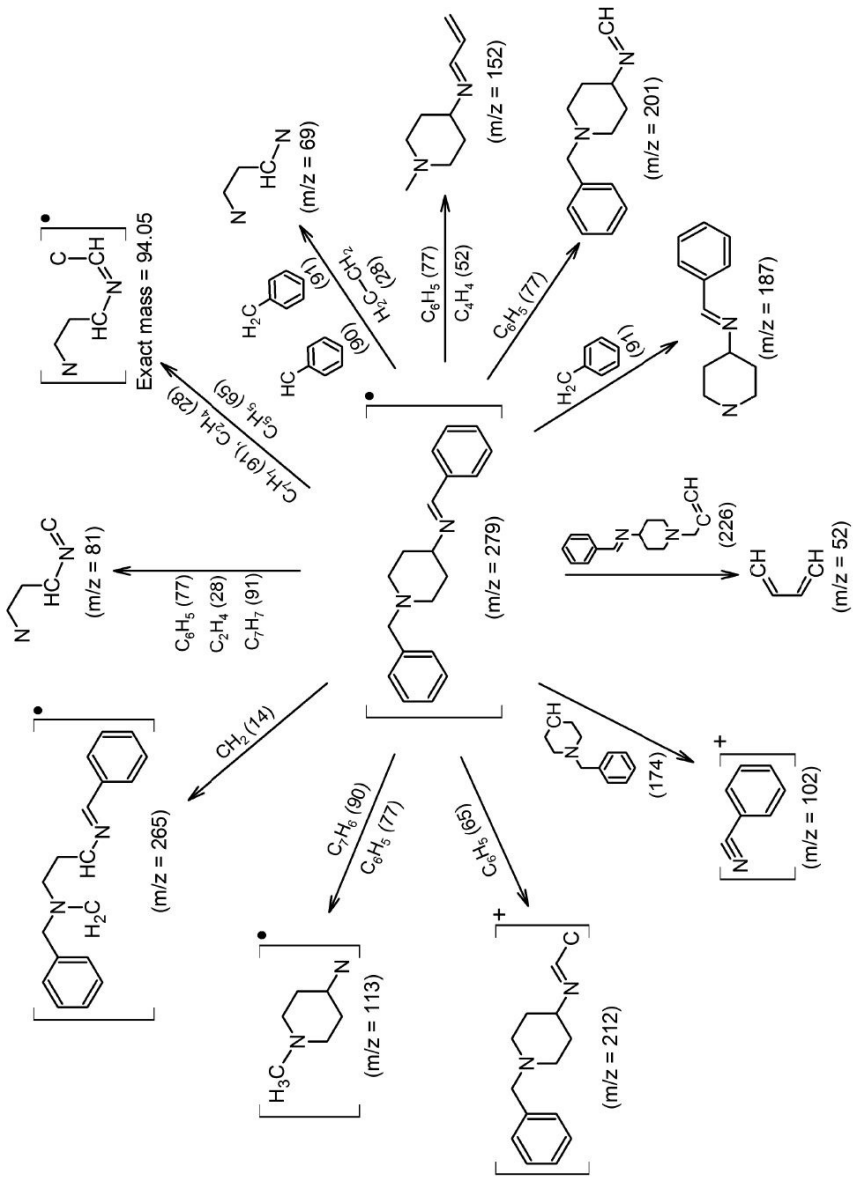
8	$C_{12}H_{16}N$	3-ClC_6H_4	$C_{12}H_{16}NN{=}CHC_6H_4Cl$ (3)	312	83	53–54	312 (M^+), 313 (M^{+1}), 315 (M^{+2}), 299, 282, 260, 235, 179, 138, 111, 105, 86, 65, 52
9	$C_{12}H_{16}N$	4-ClC_6H_4	$C_{12}H_{16}NN{=}CHC_6H_4Cl$ (4)	312	79	102–103	312 (M^+), 313 (M^{+1}), 315 (M^{+2}), 299, 282, 260, 235, 179, 137, 113, 111, 105, 88, 76, 64, 52
10	$C_{12}H_{16}N$	4-$N(CH_3)_2C_6H_4$	$C_{12}H_{16}NN{=}CHC_6H_4N(CH_3)_2$ (4)	321	80	57–58	321 (M^+), 302, 289, 264, 240, 225, 217, 186, 144, 130, 121, 102, 88, 82, 64, 53
11	$C_{12}H_{16}N$	4-FC_6H_4	$C_{12}H_{16}NN{=}CHC_6H_4F$ (4)	296	80	92–93	296 (M^+), 298 (M^{+2}), 282, 270, 244, 226, 219, 205, 179, 163, 135, 122, 108, 105, 95, 69, 53
12	$C_{12}H_{16}N$	3-$CH_3OC_6H_4$	$C_{12}H_{16}NN{=}CHC_6H_4CH_3O$ (3)	308	86	63–64	308 (M^+), 293, 282, 269, 256, 189, 175, 161, 147, 102, 95, 82, 69, 64, 52

Cont. Table 1.

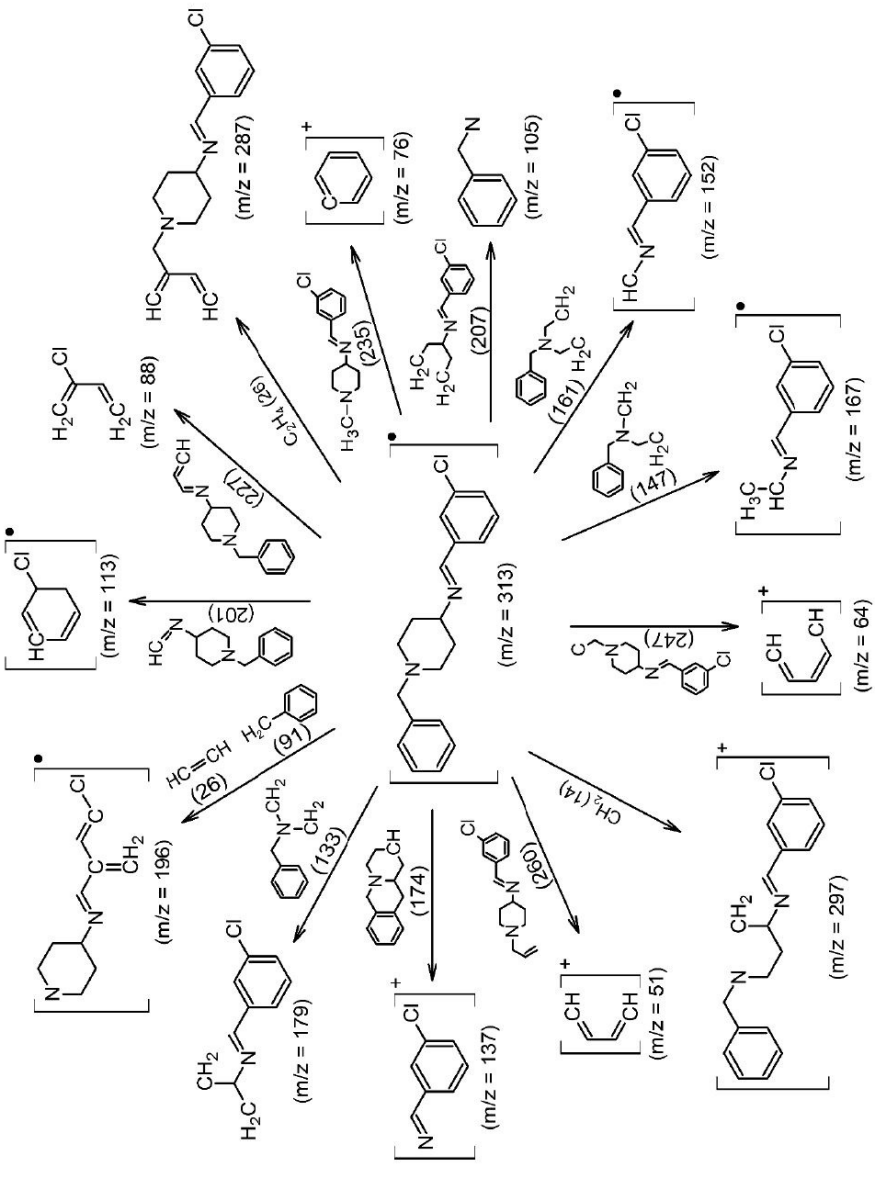
13	$C_{12}H_{16}N$	4-$CH_3OC_6H_4$	$C_{12}H_{16}NN{=}CHC_6H_4CH_3O$ (4)	308	82	49–50	308M^+, 293, 282, 252, 231, 226, 217, 188, 162, 134, 120, 107, 82, 56, 53
14	$C_{12}H_{16}N$	4-$CH_3C_6H_4$	$C_{12}H_{16}NN{=}CHC_6H_4CH_3$ (4)	292	87	51–52	292 (M^+), 293 (M^{+1}), 263, 241, 211, 203, 166, 152, 129, 109, 91, 52
15	$C_{12}H_{16}N$	3-$NO_2C_6H_4$	$C_{12}H_{16}NN{=}CHC_6H_4NO_2$ (3)	323	79	60–61	323 (M^+), 324 (M^{+1}), 295, 285, 267, 253, 247, 222, 119, 110, 85, 63, 53
16	$C_{12}H_{16}N$	4-$NO_2C_6H_4$	$C_{12}H_{16}NN{=}CHC_6H_4NO_2$ (4)	323	85	82–83	323 (M^+), 324 (M^{+1}), 307, 295, 291, 285, 271, 265, 258, 253, 246, 222, 190, 119, 110, 97, 85, 57, 52

Table 2. IR and ^{1}H and ^{13}C NMR spectral data of synthesized imines (entries 6–16).

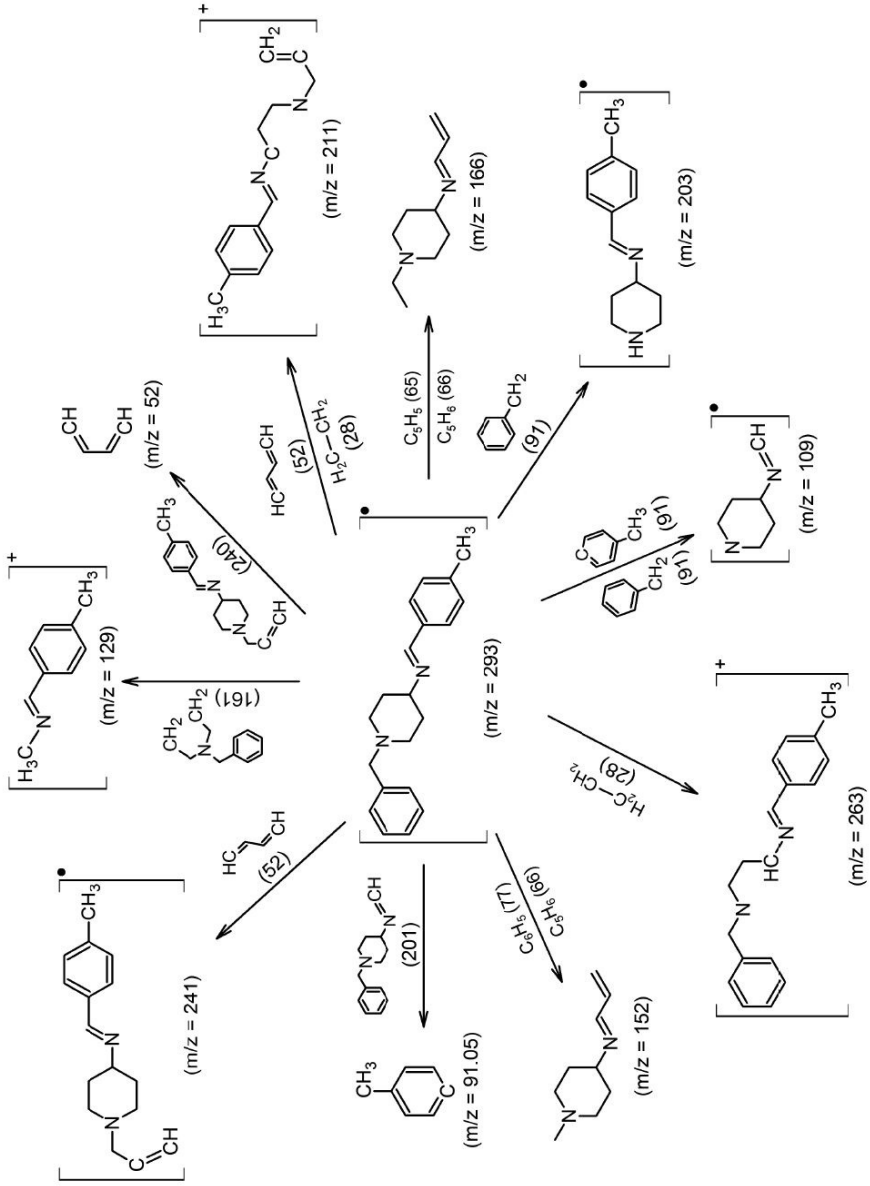
Entry	X	IR (ν, cm^{-1})	^{1}H NMR (δ, ppm)		^{13}C NMR (δ, ppm)		
		CN	CH_2	CH=N	C=N	CH_2	C_{ipso}
6	H	1567.12	3.550	8.327	159.16	67.71	130.50
7	3-Br	1565.44	3.510	8.172	157.54	67.57	122.90
8	3-Cl	1595.71	3.538	8.236	157.69	67.66	134.78
9	4-Cl	1592.24	3.543	8.271	157.80	67.70	136.39
10	4-$N(CH_3)_2$	1560.70	3.540	8.190	159.14	67.64	152.00
11	4-F	1597.18	3.547	8.282	157.68	67.56	165.45
12	3-OCH_3	1593.45	3.552	8.294	159.88	67.63	159.01
13	4-OCH_3	1575.79	3.534	8.235	161.52	67.67	164.65
14	4-CH_3	1573.95	3.547	8.285	159.09	67.70	140.71
15	3-NO_2	1526.95	3.580	8.556	156.51	67.45	148.60
16	4-NO_2	1598.42	3.559	8.400	156.81	67.89	148.93



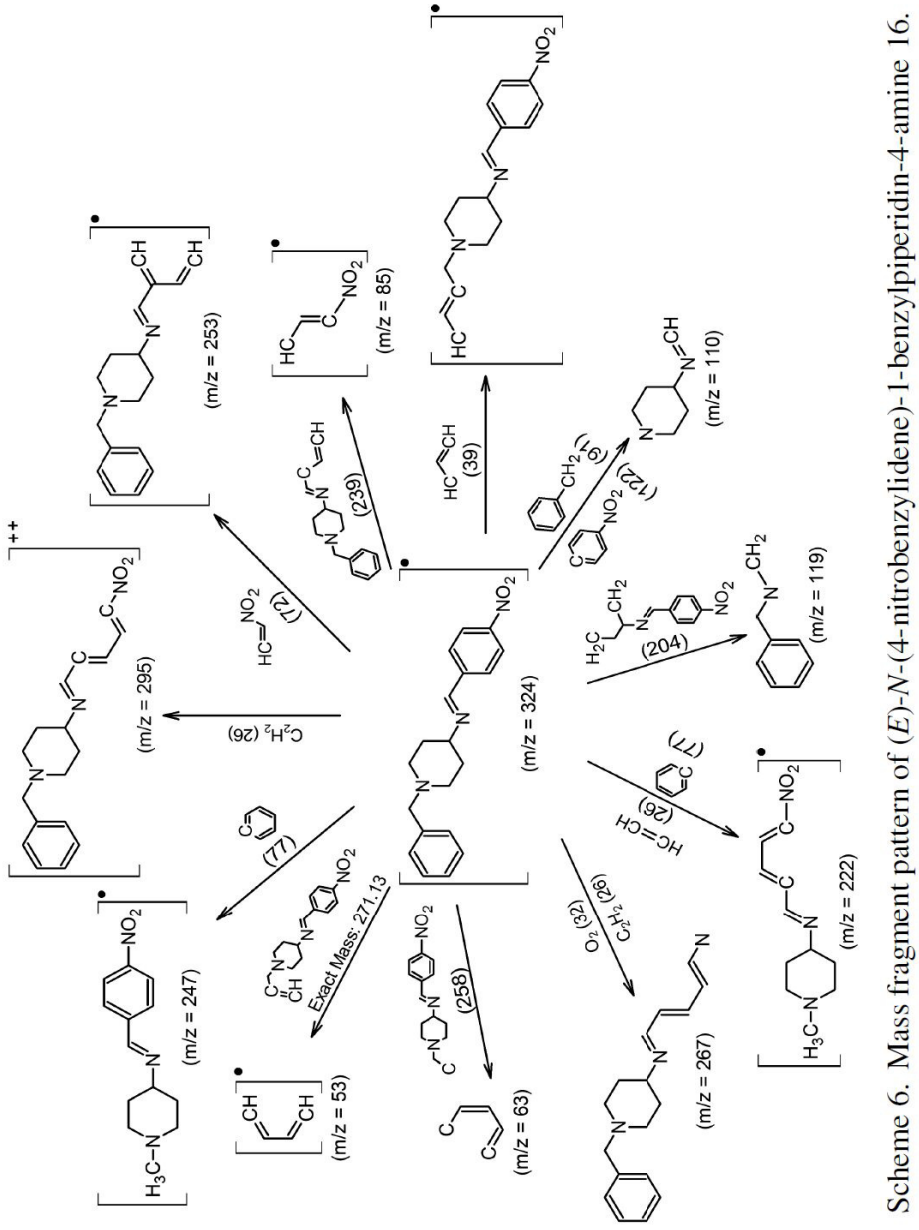
Scheme 3. Mass fragment pattern of (*E*)-1-benzyl-*N*-benzylidenepiperidin-4-amine 6.



Scheme 4. Mass fragment pattern of (*E*)-*N*-(3-chlorobenzylidene)-1-benzylpiperidin-4-amine 8.



Scheme 5. Mass fragment pattern of (*E*)-*N*-(4-methylbenzylidene)-1-benzylpiperidin-4-amine 14.



Scheme 6. Mass fragment pattern of (*E*)-*N*-(4-nitrobenzylidene)-1-benzylpiperidin-4-amine 16.

We have studied the effect of solvent for this condensation of amines and benzaldehydes by observing the yield of the products. The solvents like formic acid, acetic acid, dioxane, methanol, dichloromethane, dimethylformamide (DMF), tetrahydrofuran (THF) and toluene have been used for this reaction with 4-amino-1-benzylpiperidine and benzaldehyde. The percentage of products with various solvents is shown in Table 3 and the statistical diagram is shown in Fig. 1. Carrying out this condensation reaction with above solvents the observed yields are 73%, 68%, 65%, 69%, 75%, 70%, 78% and 71%, respectively. Here the authors have observed the good yield of imines in this synthetic method by condensation of amine and aldehydes in presence of perchloric acid at reflux condition.

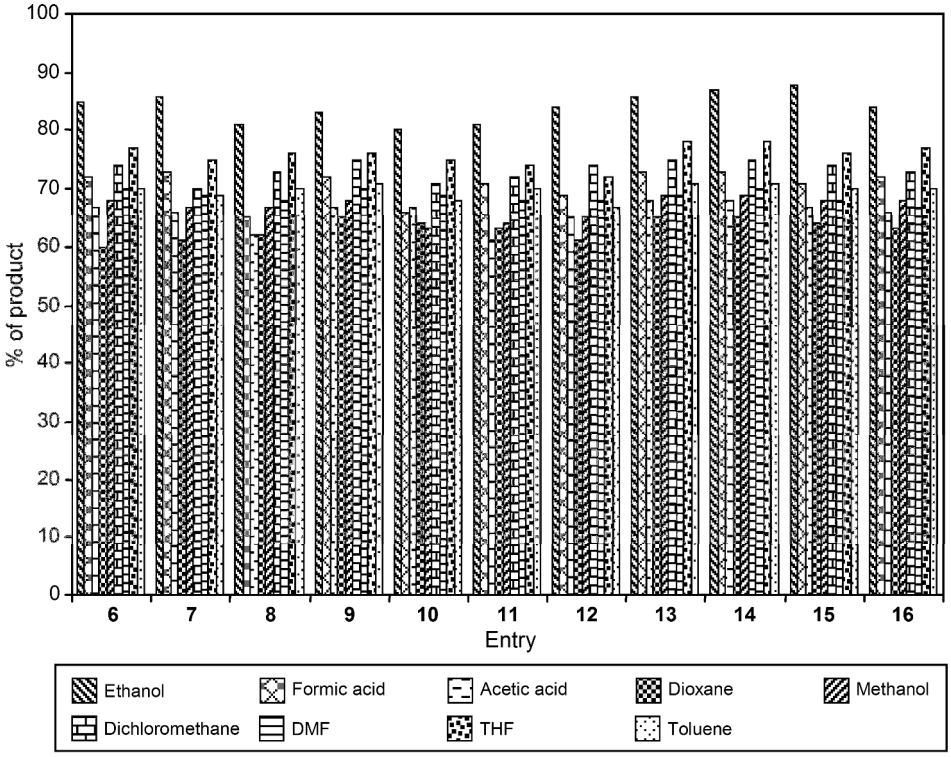


Fig. 1. The effect of solvents for synthesis of Schiff's bases by perchloric acid catalyzed condensation of aryl amines and benzaldehydes-clustered column chart (entries 6–16).

Table 3. The effect of solvent on the yield of imines from the condensation of amines and aldehydes (entries 6–16).

Entry	Ethanol	Formic acid	Acetic acid	Dioxane	Methanol	Dichloromethane	DMF	THF	Toluene
6	85	72	67	60	68	74	70	77	70
7	86	73	66	61	67	70	69	75	69
8	81	65	62	62	67	73	68	76	70
9	83	72	67	65	68	75	70	76	71
10	80	66	67	64	63	71	69	75	68
11	81	71	61	63	64	72	68	74	70
12	84	69	65	61	65	74	68	72	67
13	86	73	68	65	69	75	69	78	71
14	87	73	68	65	69	75	70	78	71
15	88	71	67	64	68	74	68	76	70
16	84	72	66	63	68	73	67	77	70

DMF – Dimethylformamide; THF – Tetrahydrofuran.

3.1. Antibacterial activities

The antibacterial screening effect of synthesized Schiff's bases are shown in Fig. 2(A–E).

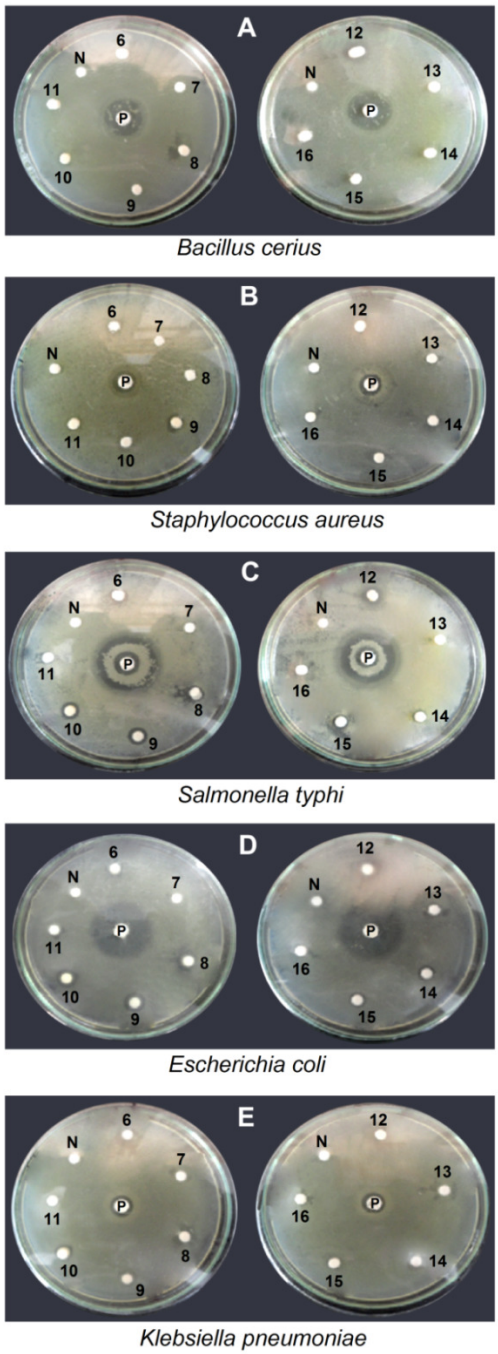


Fig. 2(A–E). Antibacterial activities of imines petri-dishes (entries 6–16). N – Control (DMSO); P – Standard drug (Ampicillin).

The antibacterial activities of all the synthesized imines have been studied against three Gram-positive pathogenic strains *Bacillus cereus*, *Staphylococcus aureus, Salmonella typhi and* two Gram-negative strains *Escherichia coli* and *Klebsiella pneumoniae* species. The disc diffusion technique was followed using the Bauer-Kirby [28] method, at a concentration of 250 μg/cm^3 with Ampicillin used as the standard. The zone of inhibition is compared using Table 4 and the corresponding clustered column chart is shown in Fig. 3. A good antibacterial activity has been possessed by all compounds on the microorganisms in general. The imines having substituents H, 3-Cl, 4-$N(CH_3)_2$, 4-F and 4-OCH_3 showed good activity against *B. cereus* strains. The H, 3-Br, 4-$N(CH_3)_2$, 4-F, 4-OCH_3, 4-CH_3 and 3-NO_2 substituted imines shows good activity against *S. aureus* strains. All imines showed good antibacterial activity against *S. typhi* except 3-OCH_3 and 4-Cl substituted imines. Similarly all compounds showed good activities on *E. coli* and *K. pneumoniae* species except 4-Cl and 4-CH_3 substituted imines. DMSO was not produced any zone inhibition against the bacterial strains tested.

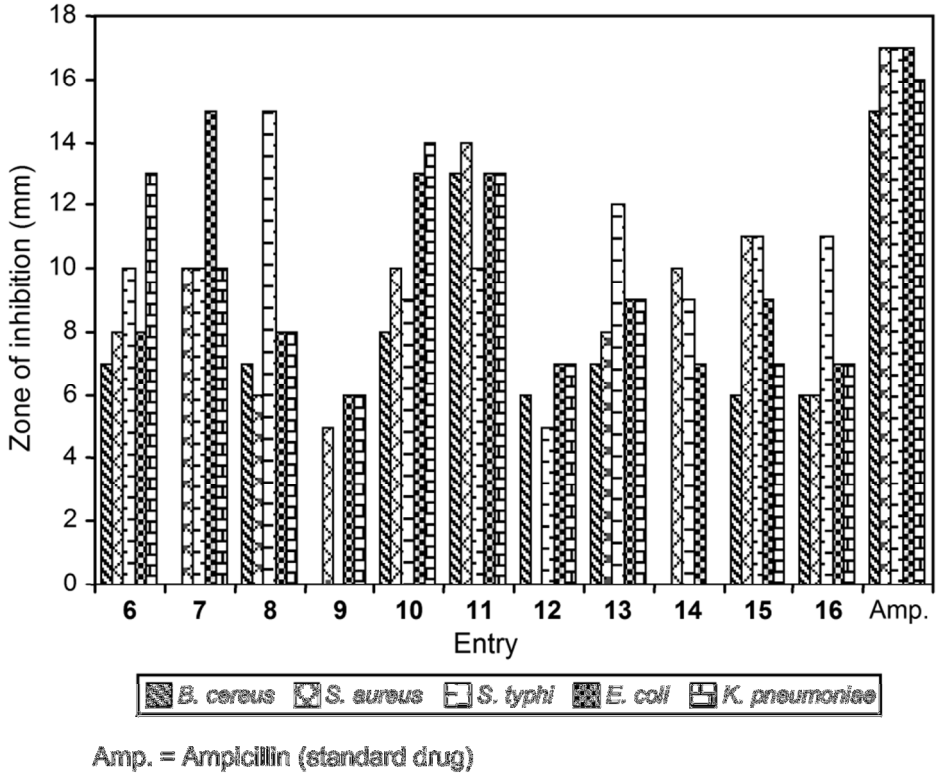


Fig. 3. Antibacterial activities of imines clustered column chart (entries 6–16).

Table 4. Antibacterial activities of imines (entries 6–16).

Entry	Substituent	Zone of inhibition (mm)				
		B. cerus	*S. aureus*	*S. typhi*	*E. coli*	*K. pneumoniae*
6	H	7	8	10	8	13
7	3-Br	–	10	10	15	10
8	3-Cl	7	6	15	8	8
9	4-Cl	–	5	–	6	6
10	4-$N(CH_3)_2$	8	10	9	13	14
11	4-F	13	14	10	13	13
12	3-OCH_3	6	–	5	7	7
13	4-OCH_3	7	8	12	9	9
14	4-CH_3	–	10	9	7	–
15	3-NO_2	6	11	11	9	7
16	4-NO_2	6	6	11	7	7
Standard drug	Ampicillin	15	17	17	17	16

4. CONCLUSIONS

A series of aryl imines have been synthesized by condensation of aryl amines and substituted benzaldehydes using perchloric acid under the reflux condition. This reaction protocol offers a simple, easier work-up procedure and high yield. These imines were characterized by their physical constants, spectral data. The UV, IR, NMR spectral data of these imines has been correlated with Hammett substituent constants, F and R parameters. From the results of statistical analyses, the effects of the substituents on the spectral data have been studied. The antibacterial activities of all synthesized imines have been studied using Bauer-Kirby method.

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