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Synthesis, characterization and antibacterial screening of some Schiff bases derived from pyrazole and 4-amino antipyrine

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Summary

Some Schiff bases of pyrazole and 4-amino antipyrine have been synthesized. The antibacterial screening of these synthesized compounds was done in dimethyl formamide against four Gram positive bacteria viz. *Bacillus cereus, Staphylococcus aureus, Staphylococcus epidermidids* and *Micrococcus luteus,* and three Gram negative bacteria viz. *Proteus mirabilis, Escherichia coli* and *Klebsiella aerogenes.* It is observed that in comparison to Schiff bases of 4-amino antipyrine, pyrazole Schiff bases are better for inhibition for these selected Gram positive and Gram negative bacterial strains.

Keywords: Pyrazole, 4-amino antipyrine, Schiff bases, dimethyl formamide, antibacterial activity.

Resumen

Síntesis, caracterización y evaluación antibacteriana de algunas bases de Schiff derivadas de pirazol y 4-amino antipirina

Se sintetizaron algunas bases de Schiff a partir de pirazol y 4-amino antipirina. La evaluación de la actividad antibacteriana de estos compuestos en dimetil formamida se realizó frente a cuatro bacterias Gram positivas, *Bacillus cereus, Staphylococcus aureus, Staphylococcus epidermidids* y *Micrococcus luteus,* y frente a tres bacterias Gram negativas, *Proteus mirabilis, Escherichia coli* y *Klebsiella aerogenes.* Se observó

mejor inhibición bacteriana frente a las diferentes cepas para las bases de Schiff basadas en pirazol comparadas con aquellas basadas en 4-amino antipirina.

Palabras clave: Pirazol, 4-amino antipirina, bases de Schiff, dimetil formamida, actividad antibacteriana.

Introduction

Schiff's bases are an important class of organic compounds having a wide variety of applications in many fields such as analytical, biological and inorganic chemistry [1-5]. Some of these compounds act as corrosion inhibitors [6] and are used as catalysts in polymer [7-8] and dyes [9] industries. Further, Schiff bases have gained importance in medicinal and pharmaceutical fields due to a broad spectrum of biological activities like antimicrobial [10-11], antifungal [12-13], antiviral [14], anti-inflammatory [15-16], analgesic [17-18], anticonvulsant [19], antitubercular [20], anticancer [21], antioxidant [22-23], anthelmintic [24], antimalarial [25-26] and so forth.

In continuation of our previous research [27-28], in the present work, some new Schiff bases have been synthesized having pyrazole and 4-amino antipyrine moieties and their structure were confirmed by IR, NMR and mass spectral data. The screening of these compounds was also done to study their antibacterial properties in dimethyl formamide.

Experimental

Synthesis of pyrazole Schiff bases

Synthesis of (1E)-1-(4-nitrophenyl)ethanone phenylhydrazone

Equimolar solution of phenyl hydazine and p-nitro phenyl acetophenone in absolute ethanol was refluxed in water bath for 2 hours using glacial acetic acid as catalysis. The crude product was isolated and was crystallized from absolute alcohol.

Synthesis of 3-(4-nitrophenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde

(1E)-1-(4-nitro phenyl) ethanone phenyl hydrazone (0.01M) was added to Vilsmayer-Haack reagent (prepared by drop wise addition of 3 ml $POCl_3$ in ice cooled 25 ml DMF) and was refluxed for 5 hours. The reaction mixture was poured into ice followed by neutralization using sodium bicarbonate. The crude product was isolated and crystallized from ethanol.

Synthesis of Schiff bases

In an ethanolic solution of 3-(4-nitro phenyl)-5-phenyl-4*H*-pyrazole-4-carbaldehyde and different aromatic amines, 2-3 drops of glacial acetic acid was added and the reaction mixture was refluxed for 10 hours. The resulting solution was cooled to room temperature and was poured in crushed ice with constant stirring. The product was filtered and washed with sodium bisulfate solution to remove the unreacted aldehyde. The crude product was crystallized from methanol and dried.

The synthesized Schiff bases are:

1. SA-1: (E)-3-(4-nitrophenyl)-1-phenyl-4-((2-phenylhydrazono)methyl)-1H-pyrazole
2. SA-2: (E)-4-methyl-N-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)aniline
3. SA-3: (E)-4-nitro-N-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene) aniline
4. SA-4: (E)-4-methoxy-N-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)aniline
5. SA-5: (E)-3-chloro-4-fluoro-N-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)aniline
6. SA-6: (E)-4-chloro-N-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)aniline
7. SA-7: (E)-4-fluoro-N-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)aniline
8. SA-8: (E)-2,5-dichloro-N-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)aniline
9. SA-9: (E)-2-(((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)amino) phenol.

Synthesis of Schiff base from 4-amino antipyrine

Equimolar amount of different aldehydes and 4-amino anti pyridine was dissolved in 30 ml methanol. 0.1 mole of 4-amino antipyrine and few drops of glacial acidic acid were added in this solution and the mixture was refluxed for 12-14 hours at 80 °C-85 °C in water bath.

The resulting solution was cooled to room temperature and then poured in crushed ice with constant stirring. The product was filtered and washed with sodium bisulfate solution to remove the unreacted aldehyde. The crude product was crystallized from methanol and dried.

The following Schiff bases have been synthesized from 4-amino antipyrine:

1. SB-1: (E)-4-((4-(dimethylamino)benzylidene)amino)1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one
2. SB-2: (E)-4-((4-chlorobenzylidene)amino)1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one
3. SB-3: (E)-4-((4-fluorobenzylidene)amino)1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one
4. SB-4: (E)-1,5-dimethyl-4-((2-nitrobenzylidene)amino)-2-phenyl-1H-pyrazol-3(2H)-one
5. SB-5: (E)-1,5-dimethyl-4-((3-nitrobenzylidene)amino)-2-phenyl-1H-pyrazol-3(2H)-one
6. SB-6: (E)-4-((4-hydroxybenzylidene)amino)1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one
7. SB-7: (E)-4-((2-chlorobenzylidene)amino)1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one.

All these compounds were synthesized according to the reaction schemes given in figures 1 and 2.

The physical parameters such as molecular formula, molecular weight, melting point, percentage yields, and R_f values along with the solvent system of all these synthesized compounds are given in tables 1 and 2 respectively.

The IR spectra (KBr pellets) were scanned on IR (SHIMADZU-FTIR-8400) over the frequency range from 4000-400 cm^{-1}. ^1H NMR spectra were scanned on Bruker Spectrometer (400 MHz) by using deuterated DMSO as a solvent. The Mass spectra were scanned on GCMS-SHIMADZU-QP2010.

Antibacterial activity

Test microorganisms

The synthesized compounds were tested for its antibacterial activity against four Gram positive bacteria viz. *Bacillus cereus* ATCC11778, *Staphylococcus aureus* ATCC 29737, *Staphylococcus epidermidids* ATCC 12228 and *Micrococcus luteus* ATCC10240, and three Gram negative bacteria viz. *Proteus mirabilis* NCIM2241, *Escherichia coli* ATCC25922 and *Klebsiella aerogenes* NCTC418. The microorganisms were obtained from National Chemical Laboratory (NCL), Pune, India. Microorganisms were maintained at 4 °C on nutrient agar slants.

Figure 1. Reaction scheme for pyrazole Schiff bases

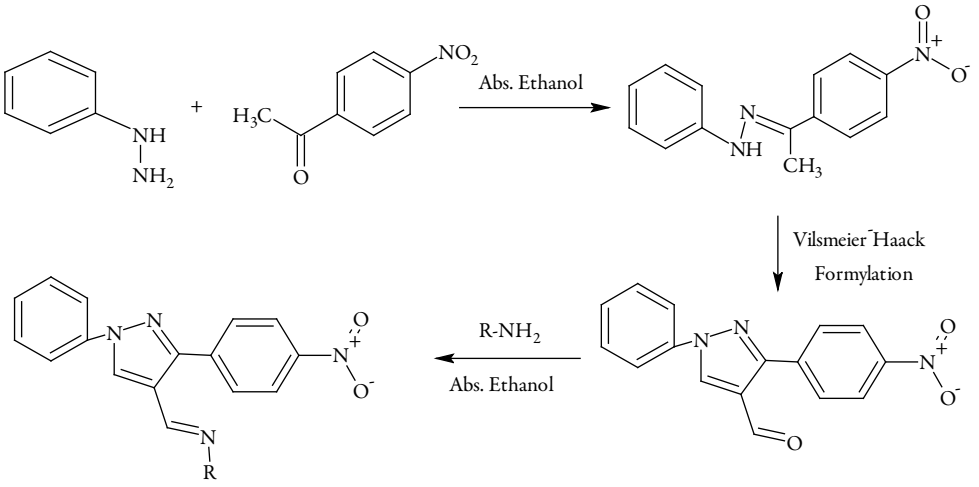


Figure 2. Reaction scheme for 4-amino antipyrine Schiff bases

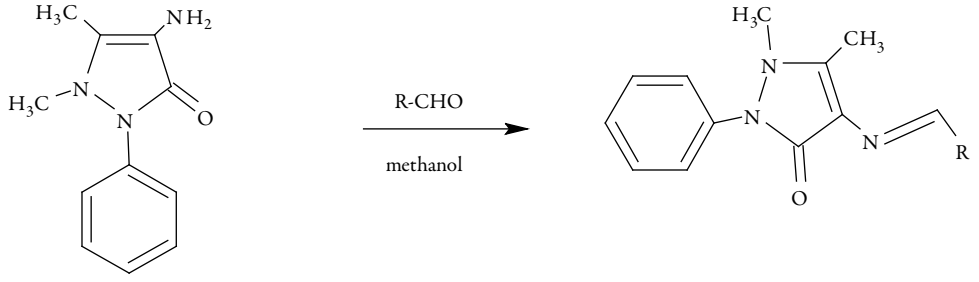


Table 1. Physical constants of pyrazole Schiff bases.

Serial No.	Compound code	R	Molecular formula	Mol. Wt. (g/mol)	R_f* value	M.P. (°C)	Yield (%)
1.	SA-1	-NH-C_6H_5	$C_{22}H_{17}N_5O_2$	383	0.67	266	65
2.	SA-2	4-CH_3-C_6H4	$C_{23}H_{18}N_4O_2$	382	0.54	218	69
3	SA-3	4-NO_2- C_6H_4	$C_{22}H_{15}N_5O_4$	413	0.62	246	65
3.	SA-4	3-OCH_3-C_6H_4	$C_{23}H_{18}N_4O_3$	398	0.54	258	78
4.	SA-5	4-F,3-Cl-C_6H_3	$C_{22}H_{14}ClFN_4O_2$	420	0.47	243	65
5.	SA-6	4-Cl-C_6H_4	$C_{22}H_{15}ClN_4O_2$	402	0.55	198	70
6.	SA-7	4-F-C_6H_4	$C_{22}H_{15}FN_4O_2$	386	0.60	268	72
7.	SA-8	2,5-di Cl-C_6H_3	$C_{22}H_{14}$ $Cl_2N_4O_2$	436	0.46	283	68
8.	SA-9	2-OH-C_6H_4	$C_{22}H_{16}N_4O_3$	384	0.47	256	76

*TLC solvent system: Hexane:Ethyl acetate- 7.0:3.0

Table 2. Physical constants of 4-amino antipyrine Schiff bases.

Serial No.	Compound code	R	Molecular formula	Mol. Wt. (g/mol)	R_f* value	M.P. (°C)	Yield (%)
1.	SB-1	4-$N(CH_3)_2$-C_6H_4	$C_{20}H_{22}N_4O$	334	0.42	218	65
2.	SB-2	4-Cl-C_6H_4	$C_{18}H_{16}$ ClN_3O	325	0.35	258	63
3	SB-3	4-F- C_6H_4	$C_{18}H_{16}FN_3O$	309	0.48	230	64
3.	SB-4	2-NO_2-C_6H_4	$C_{18}H_{16}N_4O_3$	336	0.45	210	73
4.	SB-5	3-NO_2-C_6H_4	$C_{18}H_{16}N_4O_3$	336	0.28	205	68
5.	SB-6	4-OH-C_6H_4	$C_{18}H_{17}N_3O_2$	307	0.34	202	69
6.	SB-7	2-Cl-C_6H_4	$C_{18}H_{16}ClN_3O$	325	0.56	210	78

*TLC solvent system: Hexane:Ethyl acetate- 8.0:2.0

Preparation of the test compound

For all the compounds, solutions were prepared at a concentration of 0.2 mg/ml in DMF.

Preparation of the plates and microbiological assay

The antibacterial evaluation was done by agar well diffusion method [29] using Mueller Hinton agar No. 2 as the nutrient medium. The agar well diffusion method was preferred to be used in this study since it was found to be better than the disc diffusion method as suggested by Essawi *et al.* [30]. The bacterial strains were activated by

inoculating a loop full of test strain in 25 ml of N-broth and the same was incubated for 24 hours in an incubator at 37 °C. 0.2 ml of the activated strain was inoculated in Mueller Hinton agar.

Mueller Hinton agar kept at 45 °C was then poured in the Petri dishes and allowed to solidify. After solidification of the media, 0.85 cm ditch was made in the plates using a sterile cork borer and these were completely filled with the test solution. The plates were incubated for 24 h at 37 °C. The mean value obtained for the three wells was used to calculate the zone of growth inhibition of each sample. The controls were maintained for each bacterial strain. The inhibition zone formed by these compounds against the particular test bacterial strain determined the antibacterial activities of the synthetic compounds. The observed activities are also compared with well known antibiotics.

Results and discussion

The physical parameters all the synthesized compounds are given in tables 1 and 2.

Spectral data

SA-1: (E)-3-(4-nitrophenyl)-1-phenyl-4-((2-phenylhydrazono)methyl)-1H-pyrazole

IR (cm^{-1}, KBr): 1543 (C=C str.), 1598 (C=N str. (Schiff base), 1543 (C=N str., (pyrazole moiety), 1256 (C-N str.), 961 (N-N str.), 1256 (N-O str.).

^{1}H NMR (DMSO-d$_6$) δ(ppm): 6.91- 7.02 (2H, doublet, Ar-H), 7.29- 7.34 (2H, doublet, Ar-H), 7.61-7.62 (2H, multiplet, Ar-H), 7.42-7.59 (9 H, multiplet, Ar-H), 7.63 (1 H, singlet, Ar-H), 8.85 (1H, singlet, -N=CH).
MS: (m/z) = 383

SA-2: (*E*)-4-methyl-*N*-((3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene) aniline

IR (cm^{-1}, KBr): 1537 (C=C str.), 1620 (C=N str. (Schiff base), 1598 (C=N str., (pyrazole moiety), 1256 (C-N str.), 961 (N-N str.), 1288 (N-O str.), 2922 (C-H str. (alkane).

^{1}H NMR (DMSO-d$_6$) δ(ppm): 3.75 (3H, singlet, C-CH_3), 6.86-6.92 (2H, doublet, Ar-H), 7.32- 7.47 (2H, doublet, Ar-H), 7.51-7.63 (9 H, multiplet, Ar-H), 7.74 (1 H, singlet, Ar-H), 8.84 (1H, singlet, -N=CH).

MS: (m/z) = 382

SA-3: (*E*)-4-nitro-*N*-((3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene) aniline

IR (cm^{-1}, KBr): 1508 (C=C str.), 1635 (C=N str. (Schiff base), 1635 (C=N str., (pyrazole moiety), 1242 (C-N str.), 965 (N-N str.), 1339 (N-O str.).

***^{1}H NMR (DMSO-d_6)* δ(ppm):** 6.64-6.71 (2H, doublet, Ar-H), 7.26- 7.32 (2H, doublet, Ar-H), 7.63-7.78 (9 H, multiplet, Ar-H), 7.95 (1 H, singlet, Ar-H), 8.67 (1H, singlet, -N=CH).

MS: (m/z) = 413

SA-4: (*E*)-4-methoxy-*N*-((3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene) aniline

IR (cm^{-1}, KBr): 1504 (C=C str.), 1627 (C=N str. (Schiff base), 1596 (C=N str., (pyrazole moiety), 1242 (C-N str.), 961 (N-N str.), 1338 (N-O str.), 1029 (C-O-C str. Ether).

^{1}H NMR (DMSO-d_6) ***δ(ppm):*** 3.85 (3H, singlet, C-CH_3), 6.94-6.97 (2H, doublet, Ar-H), 7.23- 7.28 (2H, doublet, Ar-H), 7.39-7.55 (9 H, multiplet, Ar-H), 7.56 (1 H, singlet, Ar-H), 8.74 (1H, singlet, -N=CH).

MS: (m/z) = 398

SA-5: (*E*)-3-chloro-4-fluoro-*N*-((3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)aniline

IR (cm^{-1}, KBr): 1502 (C=C str.), 1598 (C=N str. (Schiff base), 1597 (C=N str., (pyrazole moiety), 1226 (C-N str.), 961 (N-N str.), 1340 (N-O str.), 1049 (C-F str.), 754 (C-Cl str.).

^{1}H NMR (DMSO-d_6) δ(ppm): 6.62-6.66 (1H, doublet, Ar-H), 7.07- 7.12 (1 H, triplet, Ar-H), 7.10-8.02 (10 H, multiplet, Ar-H), 8.37 (1 H, singlet, Ar-H), 8.70 (1H, singlet, -N=CH).

MS: (m/z) = 420

SA-6: (*E*)-4-chloro-*N*-((3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene) aniline

IR (cm^{-1}, KBr): 1540 (C=C str.), 1598 (C=N str. (Schiff base), 1635 (C=N str., (pyrazole moiety), 1336 (C-N str.), 960 (N-N str.), 1387 (N-O str.), 754 (C-Cl str.).

^{1}H NMR (DMSO-d_6) δ(ppm): 6.52-6.62 (2H, doublet, Ar-H), 7.01- 7.12 (2H, doublet, Ar-H), 7.33-7.52 (9 H, multiplet, Ar-H), 7.82 (1 H, singlet, Ar-H), 8.84 (1H, singlet, -N=CH).

MS: (m/z) = 402

SA-7: (*E*)-4-fluoro-*N*-((3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene) aniline

IR (cm^{-1}, KBr): 1500 (C=C str.), 1599 (C=N str. (Schiff base), 1637 (C=N str., (pyrazole moiety), 1333 (C-N str.), 961 (N-N str.), 1230 (N-O str.), 1079 (C-F str.).

^{1}H NMR (DMSO-d_6) δ(ppm): 6.45-6.53 (2H, doublet, Ar-H), 7.14- 7.26 (2H, doublet, Ar-H), 7.36-7.62 (9 H, multiplet, Ar-H), 7.96 (1 H, singlet, Ar-H), 8.85 (1H, singlet, -N=CH).

MS: (m/z) = 386

SA-8: (*E*)-2,5-dichloro-*N*-((3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)aniline

IR (cm^{-1}, KBr): 1521 (C=C str.), 1590 (C=N str. (Schiff base), 1628 (C=N str., (pyrazole moiety), 1328 (C-N str.), 962 (N-N str.), 1248 (N-O str.), 751 (C-Cl str.).

^{1}H NMR (DMSO-d_6) δ(ppm): 6.43-6.51 (1H, doublet, Ar-H), 7.14- 7.20 (1 H, triplet, Ar-H), 7.35-8.24 (10 H, multiplet, Ar-H), 8.28 (1 H, singlet, Ar-H), 8.96 (1H, singlet, -N=CH).

MS: (m/z) = 436

SA-9: (*E*)-2-(((3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)amino) phenol

IR (cm^{-1}, KBr): 1515 (C=C str.), 1585 (C=N str. (Schiff base), 1634 (C=N str., (pyrazole moiety), 1332 (C-N str.), 960 (N-N str.), 1241 (N-O str.).

^{1}H NMR (DMSO-d_6) δ(ppm): 6.42-6.56 (2H, doublet, Ar-H), 7.08- 7.14 (2H, doublet, Ar-H), 7.25-7.63 (9 H, multiplet, Ar-H), 7.68 (1 H, singlet, Ar-H), 7.92 (1H, singlet, -OH), 8.89 (1H, singlet, -N=CH).

MS: (m/z) = 384

SB-1: (*E*)-4-((4-(dimethylamino)benzylidene)amino)1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2H)-one

IR (cm^{-1}, KBr): 2930 (-C-H str. (asym.)), 2804 (-C-H str. (sym.)), 1582 (C=C str.) 1648 (C=N str.), 1648 (C=O str.), 1582 (C=N str.), 1290 (C-N str.), 973 (N-N str.).

^{1}H NMR (DMSO-d_6) δ(ppm): 2.11-2.35 (6H, singlet, C-CH_3), 2.56 (3H, singlet, C-CH_3), 3.25 (3H, singlet, N-CH_3), 7.05- 7.10 (2H, triplet, Ar-H), 7.35-7.39 (1H, triplet, Ar-H),7.47-7.94 (6H, multiplet, Ar-H), 9.85 (1H, singlet, N=CH-).

MS: (m/z) = 334

SB-2: (*E*)-4-((4-chlorobenzylidene)amino)1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one

IR (cm^{-1}, KBr): 2939 (-C-H str. (asym.)), 2850 (-C-H str. (sym.)), 1571 (C=C str.) 1571 (C=N str.), 1650 (C=O str.), 1593 (C=N str.), 1290 (C-N str.), 739 (C-Cl str.).

^{1}H NMR (DMSO-d_6) δ(ppm): ^{1}H NMR (DMSO-d_6) δ(ppm) : 2.32 (3H, singlet, C-CH_3), 3.22 (3H, singlet, N-CH_3), 6.91- 6.96 (2H, triplet, Ar-H), 7.20-7.29 (1H, triplet, Ar-H),7.35-7.55 (6H, multiplet, Ar-H), 9.74 (1H, singlet, N=CH-).

MS: (m/z) = 325

SB-3: (*E*)-4-((4-fluorobenzylidene)amino)1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one

IR (cm^{-1}, KBr): 2950 (-C-H str. (asym.)), 2830 (-C-H str. (sym.)), 1568 (C=C str.) 1597 (C=N str.), 1651 (C=O str.), 1597 (C=N str.), 1454 (C-H str.), 1221 (C-F str.).

^{1}H NMR (DMSO-d_6) δ(ppm): 2.47 (3H, singlet, C-CH_3), 3.15 (3H, singlet, N-CH_3), 7.07- 7.11 (2H, triplet, Ar-H), 7.30-7.34 (1H, triplet, Ar-H),7.38-7.85 (6H, multiplet, Ar-H), 9.70 (1H, singlet, N=CH-).

MS: (m/z) = 309

SB-4: (*E*)-1,5-dimethyl-4-((2-nitrobenzylidene)amino)-2-phenyl-1*H*-pyrazol-3(2*H*)-one

IR (cm^{-1}, KBr): 2945 (-C-H str. (asym.)), 2835 (-C-H str. (sym.)), 1568 (C=C str.) 1591 (C=N str.), 1647 (C=O str.), 1591 (C=N str.), 1381 (N-O str.).

^{1}H NMR (DMSO-d_6) δ(ppm): 2.48 (3H, singlet, C-CH_3), 3.21 (3H, singlet, N-CH_3), 7.28- 7.32 (2H, triplet, Ar-H), 7.38-7.40 (1H, triplet, Ar-H),7.17-7.46 (6H, multiplet, Ar-H), 9.90 (1H, singlet, N=CH-).

MS: (m/z) = 336

SB-5: (*E*)-1,5-dimethyl-4-((3-nitrobenzylidene)amino)-2-phenyl-1*H*-pyrazol-3(2*H*)-one

IR (cm^{-1}, KBr): 2942 (-C-H str. (asym.)), 2815 (-C-H str. (sym.)), 1584 (C=C str.) 1599 (C=N str.), 1662 (C=O str.), 1590 (C=N str.), 1372 (N-O str.).

^{1}H NMR (DMSO-d_6) δ(ppm): ^{1}H NMR (DMSO-d_6) δ(ppm) : 2.41 (3H, singlet, C-CH_3), 3.07 (3H, singlet, N-CH_3), 6.71- 6.80 (2H, triplet, Ar-H), 7.21-7.39 (1H, triplet, Ar-H),7.52-7.80 (6H, multiplet, Ar-H), 9.99 (1H, singlet, N=CH-).

MS: (m/z) = 336

SB-6: (*E*)-4-((4-hydroxybenzylidene)amino)1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one

IR (cm^{-1}, KBr): 2945 (-C-H str. (asym.)), 2835 (-C-H str. (sym.)), 1584 (C=C str.) 1585 (C=N str.), 1646 (C=O str.), 3350 (O-H str.).

^{1}H NMR (DMSO-d_6) δ(ppm): ^{1}H NMR (DMSO-d_6) δ(ppm) : 2.46 (3H, singlet, C-CH_3), 3.11 (3H, singlet, N-CH_3), 6.85- 6.87 (2H, triplet, Ar-H), 7.30-7.32 (1H, triplet, Ar-H),7.38-7.70 (6H, multiplet, Ar-H), 9.21 (1H, singlet, -OH), 9.85 (1H, singlet, N=CH-).

MS: (m/z) = 307

SB-7: (*E*)-4-((2-chlorobenzylidene)amino)1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one

IR (cm^{-1}, KBr): 2940 (-C-H str. (asym.)), 2835 (-C-H str. (sym.)), 1555 (C=C str.) 1588 (C=N str.), 1650 (C=O str.), 1588 (C=N str.), 750 (C-Cl str.).

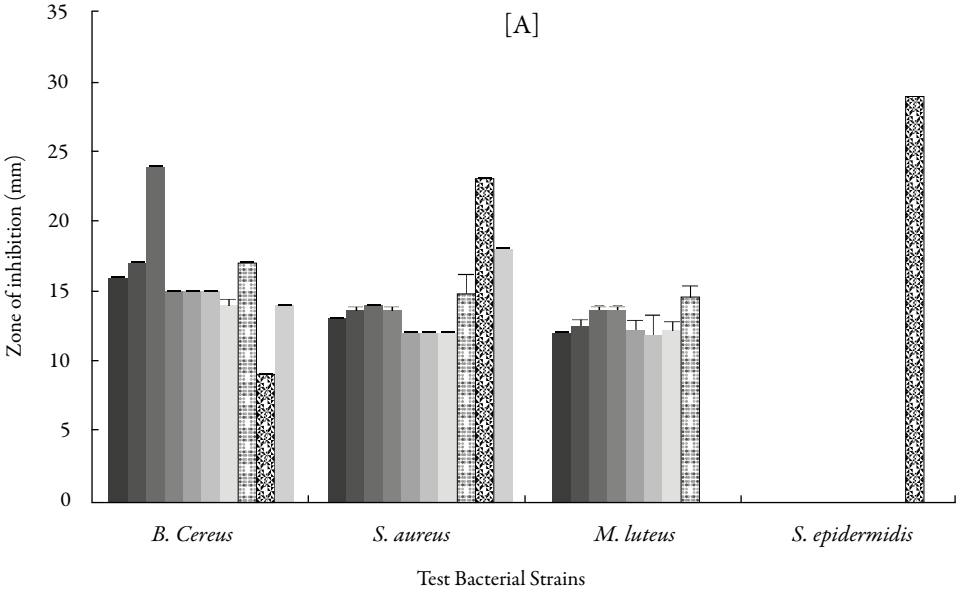
^{1}H NMR (DMSO-d_6) δ(ppm): 2.389 (3H, singlet, -CH_3), 1.713-2.796 (4H, multiplet, C-H), 6.170 (1H, singlet, -CH), 7.196-7.936 (8H, multiplet -CH), 10.201 (1H, singlet, -NH).

MS: (m/z) = 307

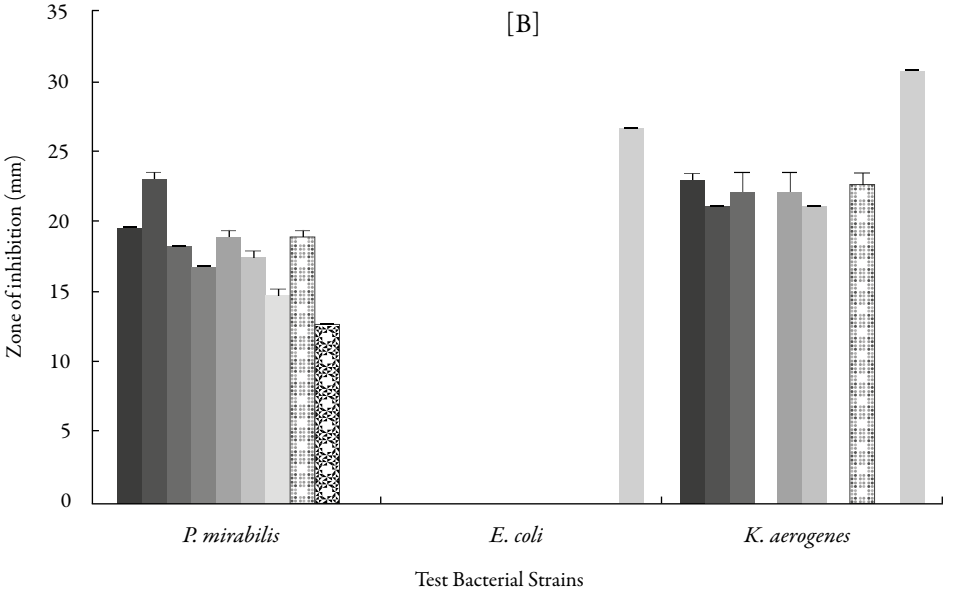
Antibacterial activity

The inhibition zone of pyrazole Schiff bases against different Gram positive and Gram negative bacteria are given in Figure 3.

Figure 3. Antibacterial activity of pyrazole Schiff bases against [A] Gram positive [B] Gram negative bacteria.



(■:SA-1;■: SA-2;■: SA-3;■: SA-4;■: SA-5;■: SA-6;■: SA-7;▦:SA-8;▩: ampicillin;■: chloramphenicol).



(■:SA-1;■: SA-2;■: SA-3;■: SA-4;■: SA-5;■: SA-6;■: SA-7;▦:SA-8;▩: ampicillin;■: chloramphenicol).

It is evident from figure 3 [A] that SA-3 and SA-8 exhibited maximum inhibition against all the selected Gram positive bacteria except *S. epidermidis.* Against *B. cereus*, minimum inhibition is exhibited by SA-7 while other compounds show almost equal inhibition. Against *S. aureus*, SA-3 and SA-8 shows maximum inhibition followed by SA-2 and SA-4. Minimum inhibition is exhibited by SA-1, SA-5, SA-6 and SA-7. Against *M. luteus* also, SA-8 showed maximum inhibition followed by SA-3 and SA-4. SA-6 exhibited minimum inhibition. For *S. epidermidis*, not a single compound showed inhibition. Thus, *S. epidermidis* is the most resistant strain.

Thus, for the studied Gram positive bacteria, different compounds behave differently. All the compounds have the same common moiety but different substituents as side chain as shown in table 1. SA-3 and SA-8, which exhibited maximum inhibition, contain 4-nitro and 2, 5-dichloro aniline respectively as side chain. Thus, these two groups are the most effective substituent groups for the selected Gram positive bacteria.

Figure 3 [B] shows that against *P. mirabilis*, SA-2 shows maximum inhibition followed by SA-1, SA-5 and SA-8 and SA-7 shows minimum activity. SA-2 contains 4-methyl aniline side chain, which is found to enhance the inhibition whereas 4-fluoro aniline (as in SA-7) is least effective. Against *E. coli*, none of the compound exhibited activity indicating thereby that it is the most resistant bacteria strain.

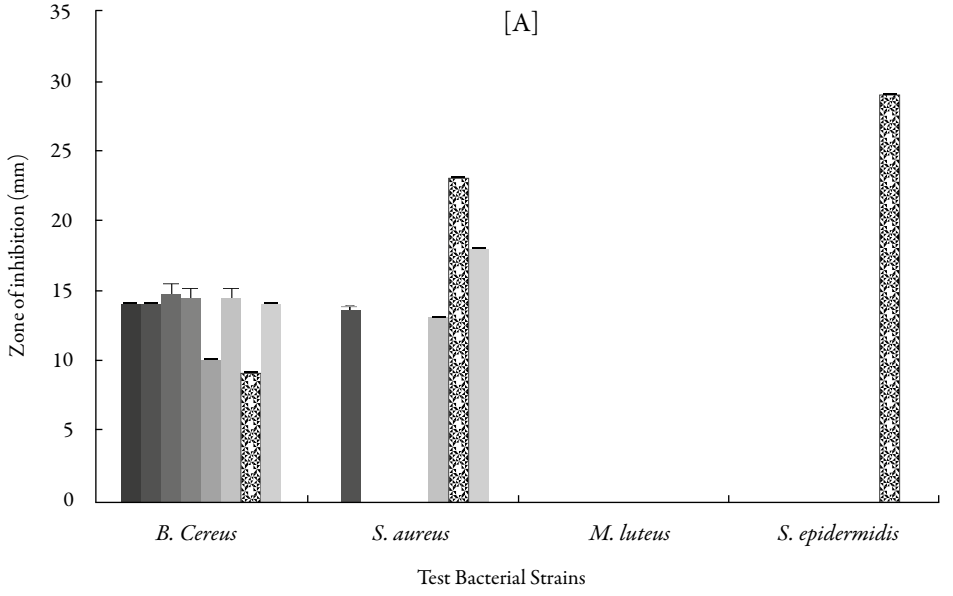
Against *K. aerogenes*, SA-1 showed maximum inhibition which contains phenyl hydrazine. This is followed by SA-8 containing 2, 5-dichloro aniline while SA-4 and SA-7 showed no inhibition at all. Thus, the presence of 4-methoxy (as in SA-4) and 4-fluoro (as in SA-7) had no effect on these selected bacterial strains

The inhibition zone of 4-amino antipyrine Schiff bases against different Gram positive and Gram negative bacteria are given in Figure 4.

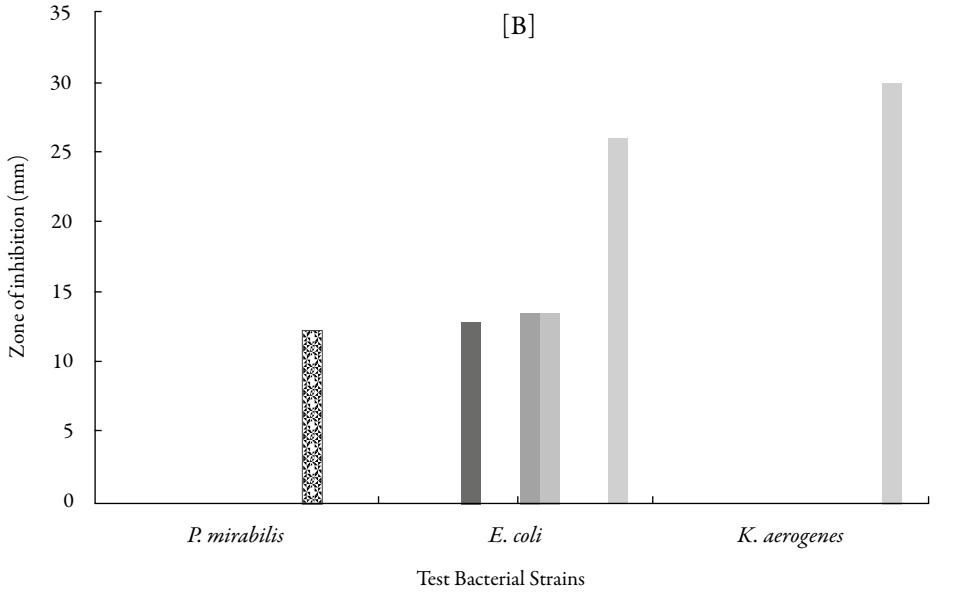
It is evident from Figure 4 [A] that against *B. cereus*, all the compounds except SB-7 exhibited inhibition and maximum inhibition is for SB-3 which is followed by SB-6. SB-5 showed minimum inhibition. Against *S. aureus*, only SB-2 and SB-6 exhibited inhibition. Other compounds had no effect on this strain. For *M. luteus* and *S. epidermidis,* none of the compounds showed inhibition. Thus, these two strains are most resistant for these compounds.

Accordingly, again different compounds behave differently for different bacteria. The compounds have the same common moiety but different substituents as side chain which is given in table 2. SB-3 contains 4-fluoro phenyl whereas SB-6 is having 4-hydroxy phenyl. Thus, these two groups are more effective against *B. cereus* than other substitution groups. 2-chloro phenyl present in SB-7 is not effective at all against

Figure 4. Antibacterial activity of 4-amino antipyrin Schiff bases against [A] Gram positive [B] Gram negative bacteria.



(■:SA-1;■: SA-2;■: SA-3;■: SA-4;■: SA-5;■: SA-6;■: SA-7;▦:SA-8;▩: ampicillin;■: chloramphenicol).



(■:SA-1;■: SA-2;■: SA-3;■: SA-4;■: SA-5;■: SA-6;■: SA-7;▦:SA-8;▩: ampicillin;■: chloramphenicol).

this bacterial strain. Against *S. aureus*, only 4-chloro phenyl (as in SB-2) and 4-hydroxy phenyl (as in SB-6) are effective. However, when chloro group is at 2nd position (as in SB-7), there is no inhibition. This suggests that position plays an important role in inhibition. Thus, out of four selected Gram positive bacterial strains, *M. luteus* and *S. epidermidis* are the most resistant Gram positive bacterial strain.

Figure 4 [B] shows that only compounds, SB-3, SB-5 and SB-6 could inhibit *E. coli*. Other compounds had no effect against this bacterial strain. This suggests that 4-fluoro phenyl, 3-nitro phenyl and 4-hydroxy phenyl are effective against this strain. SB-4 also contains nitro group but at 2nd position but there is no effect of this compound on *E. coli*. Thus, the presence of group at this position is not effective. Not a single compound could inhibit *P. mirabilis* and *K. aerogenes*. Thus, *P. mirabilis* and *K. aerogenes* are the most resistant Gram positive bacterial strain.

Comparison of inhibition exhibited by Schiff bases of these two different moieties shows that most of the pyrazole Schiff bases showed inhibition. Schiff bases are not effective against *S. epidermidis*. Further, the extent of inhibition is higher for pyrazole Schiff bases. Thus, pyrazole Schiff bases are better for inhibition for these selected Gram positive and Gram negative bacterial strains.

Conclusion

It is concluded that the inhibition depends on the type and position of substitutions of the compounds. The effect of different substitution group is different when attached to different moiety. The pyrazole Schiff bases are better for inhibition for these selected Gram positive and Gram negative bacterial strains in comparison to 4-amino antipyrine. Overall, *B. cereus* is the most susceptible bacteria.

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Disclosure statement

No potential conflict of interest was reported by the authors.

References

1. N.R. Bader, Applications of Schiff's bases chelates in quantitative analysis: a review, *Rasayan J. Chem.*, **3**(4), 660-670 (2010).

2. S. Çakır, E. Biçer, Synthesis, spectroscopic and electrochemical characteristics of a novel Schiff-base from saccharin and tryptophan, *J. Iran. Chem. Soc.*, **7**(2), 394-404 (2010).

3. S. Kumar, D.N. Dahr, P.N. Saxena, Applications of metal complexes of Schiff bases. A review, *J. Sci. Ind. Res.*, **68**, 181-187 (2009).

4. P. Przybylski, A. Huczyński, K. Pyta, B. Brzezinski, F. Bartl, Biological properties of Schiff bases and azo derivatives of phenol, *Curr. Org. Chem.*, ***13***, 124-148 (2009).

5. C. Chandramouli, M.R. Shivanand, T.B. Nayanbhai, B. Bheemachari, R.H. Udupi, Synthesis and biological screening of certain new triazole Schiff bases and their derivatives bearing substituted benzothiazole moiety, *J. Chem. Pharm. Res.*, **4**(2), 1151-1159 (2012).

6. S.S. Abd Rehim, M.A.M. Ibrahim, K.F. Khalid, The inhibition of 4-(2- amino-5-methyl phenylazo)antipyrine on corrosion of mild steel in HCl solution, *Mater. Chem. Phys.,* **70**, 268-273 (2001).

7. E. Yousif, N. Salih, J. Salimon, Improvement of photo stabilisation of PVC in the presence of 2N-salisylidine-5-(substituted)-1,3,4-triadiazole, *J. Appl. Polym. Sci.*, **120**, 2207-2214 (2011).

8. E. Yousif, J. Salimon, N. Salih, New stabilizer for polystyrene based on 2N-salisylidine-5-(substituted)-1,3,4-triadiazole compounds, *J. Saudi Chem. Soc.*, **16**, 299-306 (2012).

9. K.M. Abuamer, A.A. Maihub, M.M. El-Ajaily, A.M. Etorki, M.M. Abou-Krisha, A. Almagani, The role of aromatic Schiff bases in the dyes techniques, *Int. J. Org. Chem*., **4**, 7-15 (2014).

10. S. Mallad, A.M. Isloor, S. Isloor, D.S. Akhila, H.K. Fun, Synthesis, characterization and antibacterial activity of some new pyrazole based Schiff basas, *Arab. J. Chem.*, **6**(3), 335-340 (2013).

11. S.A. Patil, C .T. Prabhakar, B.M. Halasangi, S.S. Toragalmathand, P.S. Badami, DNA cleavage, antibacterial, antifungal anthelmintic studies of Co (II), Ni (II) and Cu (II) complexes of coumarin Schiff bases: synthesis and spectral approach, *Spectrochim. Acta A Mol. Biomol. Spectrosc.*, **137***,* 641-651 (2014).

12. Z. Guo, R. Xing, S. Liu, Z. Zhong, X. Ji, L. Wang, Antifungal properties of Schiff bases of chitosan N-substituted chitosan and quaternized chitosan, *Carbohydr. Res.*, **42**(10), 1329-1332 (2007).

13. N. Raman, S. Thalamuthu, J. Dhaveethuraja, M.A. Neelakandan, S. Banerjee, DNA cleavage and antimicrobial activity studies on transition metal (ii) complexes of 4-amino antipyrine derivative, *J. Chil. Chem. Soc.*, **53**(1), 1450-1454 (2008).

14. K.S. Kumar, S. Ganguly, R. Veerasamy, E. de Clercq, Synthesis, antiviral activity and cytotoxic evolution, *Eur. J. Med. Chem.*, **45**(11), 5474-5479 (2010).

15. M.S. Alam, J.H. Choi, D.U. Lee, Synthesis of novel Schiff base analogues of 4-amino-1,5-dimethyl-2-phenylpyrazol-3-one and their evaluation for antioxidant and anti-inflammatory activity, *Bioorg. Med. Chem.,* **20**, 4103-4108 (2012).

16. B.S. Sathe, E. Jaychandran, V.A. Jagtap, G.M. Sreenivasa, Synthesis characterization and anti-inflamatory evolution of new benzofluorothiazole Schiff's bases, *Int. J. Pharm. Res. Dev.*, **3**(3), 164-169 (2011).

17. A. Pandey, D. Dewangan, S. Verma, A. Mishra, R.D. Dubey, Synthesis of Schiff bases of 2-amino-5-aryl-1,3,4-thiadiazole and its analgesic, antiinflammatory, antibacterial and anti-tubercular activity, *Int. J. ChemTech Res.*, **3**(1), 178-184 (2011).

18. R.P. Chinnasamy, R. Sundararajan, S. Govindaraj, Synthesis, characterization, and analgesic activity novel schiff base of isatin derivatives, *J. Adv. Pharm. Tech. Res.*, **1**(3), 342-347 (2010).

19. G.S. Kurdekar, M.P. Sathishma, S. Budagumpi, 4-Amino antipyrine-based Schiff-base transition metal complexes as potent anticonvulsant agents, *Med. Chem. Res.*, **21**, 2273-2279 (2012).

20. T. Aboul-Fadl, F.A. Mohammed, E.A. Hassan, Synthesis, antitubercular activity and pharmacokinetic studies of some schiff bases derived from 1- alkylisatin and isonicotinic acid hydrazide, *Arch. Pharm. Res.*, **26**(10), 778-784 (2003).

21. S.M.M. Ali, M.A. Azad, M. Jesmin, *In vivo* anticancer activity of vanillin semicarbazone, *Asian Pacific J. Tropical Biomed.*, **2**(6), 438-442 (2012).

22. N.M. Aburas, N.R. Stevanović, M. Milčić, A.Đ. Lolić, M.M. Natić, Ž.L. Tešić, R.M. Baošić, Influence of the structure on the antioxidant activity of tetradentate Schiff bases and their copper(II) complexes: Possible mechanisms, *J. Braz. Chem. Soc.*, **24**(8), 1322-1328 (2013).

23. Z. Guo, R. Xing, S. Liu, H. Yu, P. Wang, C. Li, P. Li, The synthesis and antioxidant activity of the Schiff bases of chitosan and carboxymethyl chitosan, *Bioorg. Med. Chem. Lett.*, **15**(20), 4600-4603 (2005).

24. T. Singh, D. Khobragade, Synthesis of thiazolidine-4-one for their anthelmintic activity, *Unique J. Pharma. Biol. Sci.*, **2**(1), 13-15 (2014).

25. Y. Li, Z. S. Yang, H. Zhang, B.J. Cao, F.D. Wang, Artemisinin derivatives bearing Mannich base group: synthesis and antimalarial activity, *Bioorg. Med. Chem.*, **11**, 4363-4368 (2003).

26. M.S. Alam, D.U. Lee, M.L. Bari, Antibacterial and cytotoxic activities of Schiff base analogues of 4-aminoantipyrine, *J. Korean Soc. Appl. Biol. Chem.*, **57**(5), 613-619 (2014).

27. S. Baluja, S. Chanda, N. Godvani, Synthesis and antibacterial studies of some metal chelates of 1,2,4-triazole Schiff bases, *Pharm. Chem. J.*, **48**(12), 795-799 (2015).

28. D. Menpara, K. Nandha, S. Baluja, S. Chanda, Antimicrobial activity of some quinazoline heterocycles, *World J. Pharm. Sci.*, **2**(8), 860-865 (2014).

29. J. Parekh, P. Inamdar, R. Nair, S. Baluja, S. Chanda, Synthesis and antibacterial activity of some Schiff bases derived from 4-amino benzoic acid, *J. Serb. Chem. Soc.*, **70**, 1155-1162 (2005).

30. T. Essawi, M. Srour, Screening of some Palestinian medicinal plants for antibacterial activity, *J. Ethnopharmacol.*, **70**, 343-349 (2000).

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