



Synthesis of Hydrazones Schiff Bases and Microbiological Evaluation of Isonicotinoyl Hydrazide with Different Acetophenone

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ABSTRACT

A series of hydrazones Schiff bases compounds have been synthesized by reacting isonicotinoyl hydrazide with 2-hydroxy-5-chloro acetophenone, 2-hydroxy-5-methyl acetophenone, 2-hydroxy-5-carboxy acetophenone, 2,5-dihydroxy acetophenone, 2-hydroxy-5-chloro-4-methyl acetophenone, 2-hydroxy-5-chloro-3-nitro acetophenone, 2-hydroxy-5-methyl-3-nitro acetophenone and 2-hydroxy-5-bromo acetophenone. The Schiff bases have been evaluated for the antifungal and antibacterial activities.

Key words: Schiff bases, Isonicotinoyl hydrazide, Acetophenone, Antibacterial activities.

INTRODUCTION

The Schiff bases play a significant role in the area of Coordination Chemistry. They have widely studied because of their industrial and biological applications. Schiff bases are usually formed by the condensation of aliphatic or aromatic, aldehydes or ketones with primary aliphatic or aromatic amines, hydrazides, etc. The significance of Schiff bases like azomethines, hydrazones, semicarbazones, thiosemicarbazones, etc., lies in the fact that these compounds not only possess antimicrobial activities but also show greater tendency to form complexes. The Schiff bases

prepared by using variety of aldehydes and amines possessed antitubercular, anticancer, antitumor, bacteriostatic, fungicidal, medicinal and agrochemical activities^{1,2}. Along with these their complexes also possesses great utility in pharmacological, agrochemical and biological aspects³.

EXPERIMENTAL

Synthesis of hydrazones Schiff bases ligands

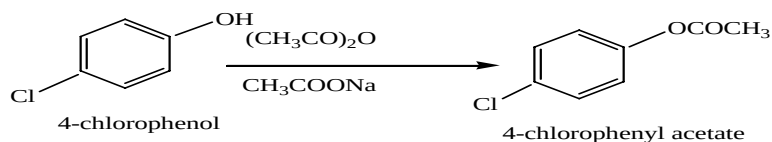
All the hydrazones Schiff bases ligands were synthesized in two steps; In first step the preparation of substituted acetophenone^{4,5,6} and

second step involved the condensation of acetophenone with isonicotinoyl hydrazide^{7,8,9}

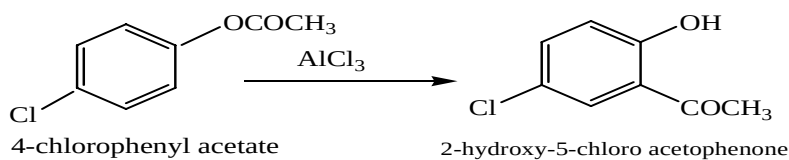
Synthesis of 2-hydroxy-5-chloro acetophenone isonicotinoyl hydrazone[HCAIH]

Step-1: Preparation of 2-hydroxy-5-chloro acetophenone

Reaction 1

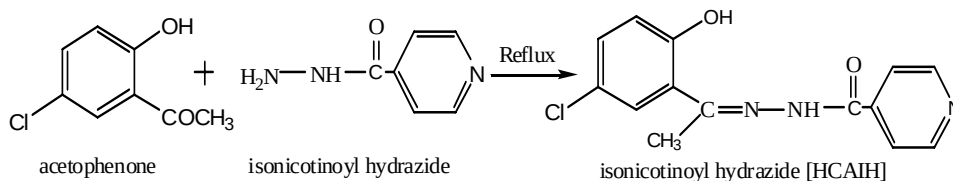


Reaction 2



Step 2: Condensation of acetophenone with isonicotinoyl hydrazide

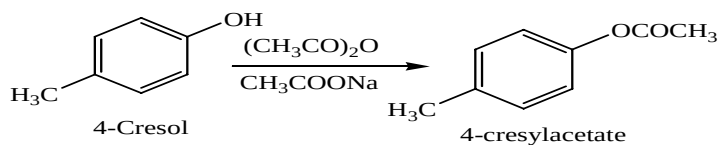
Reaction 1



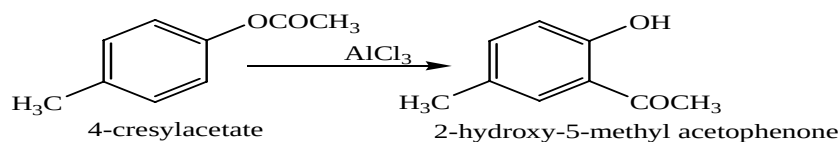
Synthesis of 2-hydroxy-5-methyl acetophenone isonicotinoyl hydrazone[HMAIH]

Step-1 preparation of 2-hydroxy-5-methyl acetophenone

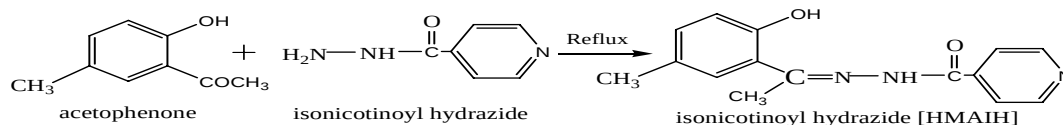
Reaction 1



Reaction 2



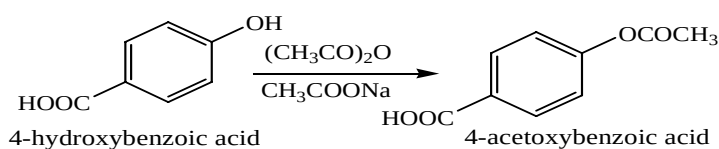
Step-2 Condensation of acetophenone with isonicotinoyl hydrazide



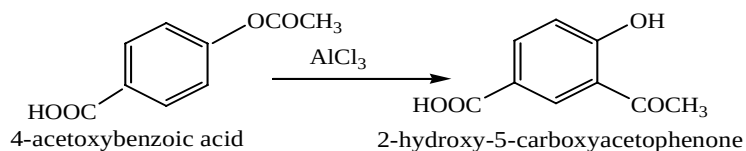
Synthesis of 2-hydroxy-5-carboxy acetophenone isonicotinoyl hydrazone[HCRAIH]

Step 1: Preparation of 2-hydroxy-5-carboxy acetophenone

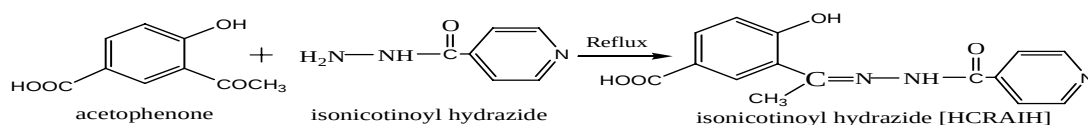
Reaction 1



Reaction 2



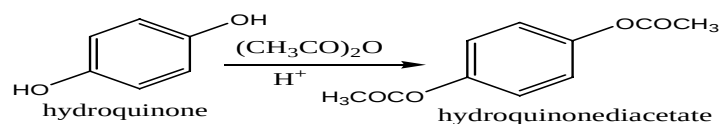
Step-2: Condensation of acetophenone with isonicotinoyl hydrazide



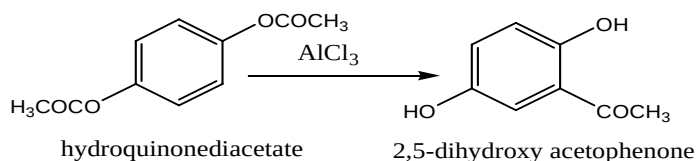
Synthesis of 2,5-dihydroxy acetophenone isonicotinoyl hydrazone[DHAIH]

Step 1: Preparation of 2,5-dihydroxy acetophenone

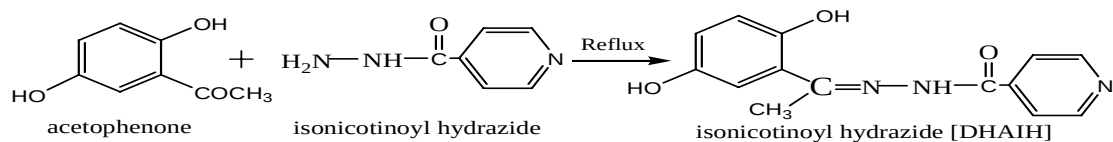
Reaction 1



Reaction 1



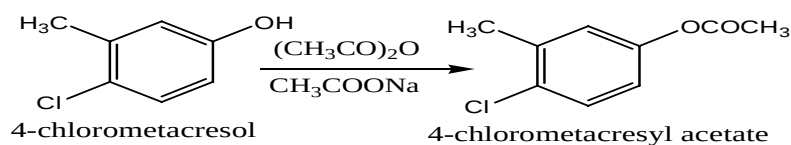
Step 2: Condensation of acetophenone with isonicotinoyl hydrazide



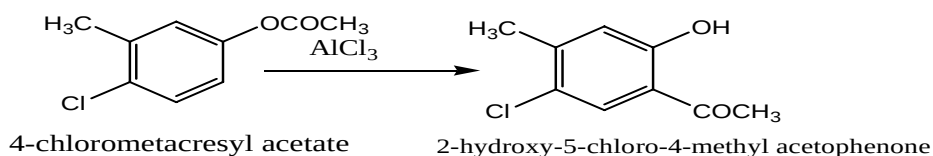
Synthesis of 2-hydroxy-5-chloro-4-methyl acetophenone isonicotinoyl hydrazone [HCMAIH]

Step-1 preparation of 2-hydroxy-5-chloro-4-methyl acetophenone

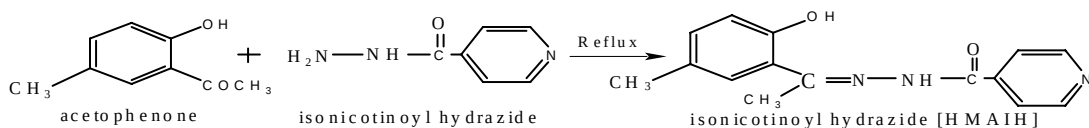
Reaction 1



Reaction 2



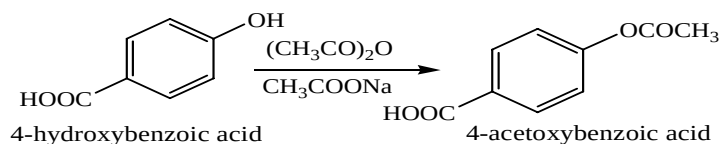
Step 2: Condensation of acetophenone with isonicotinoyl hydrazide



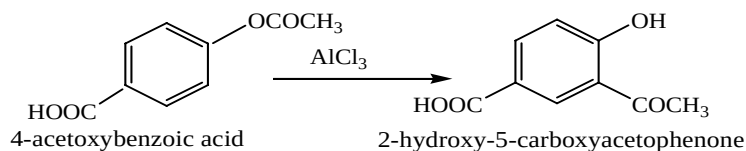
Synthesis of 2-hydroxy-5-chloro-3-nitro acetophenone isonicotinoyl hydrazone [HCNAIH]

Step-1 preparation of 2-hydroxy-5-chloro-3-nitroacetophenone

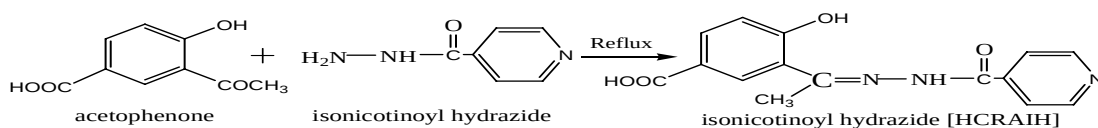
Reaction 1



Reaction 2



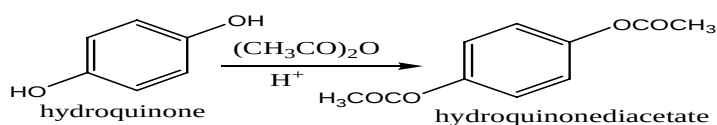
Step 2: Condensation of acetophenone with isonicotinoyl hydrazide



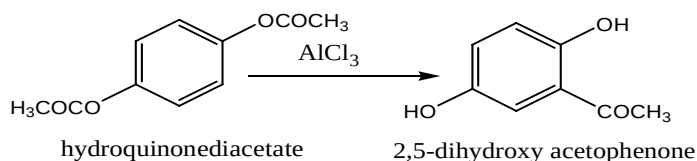
Synthesis of 2,5-dihydroxy acetophenone isonicotinoyl hydrazone [DHAIH]

Step 1: Preparation of 2,5-dihydroxy acetophenone

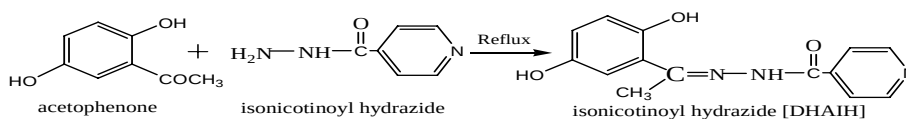
Reaction 1



Reaction 2



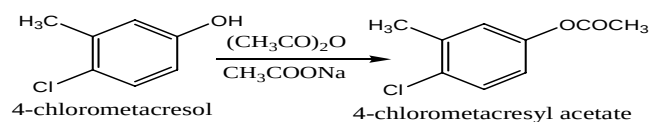
Step 2: Condensation of acetophenone with isonicotinoyl hydrazide



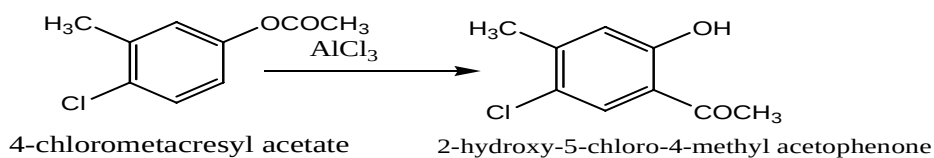
Synthesis of 2-hydroxy-5-chloro-4-methyl acetophenone isonicotinoyl hydrazone [HCMAIH]

Step-1 preparation of 2-hydroxy-5-chloro-4-methyl acetophenone

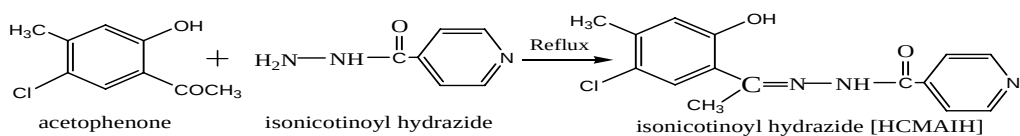
Reaction 1



Reaction 2



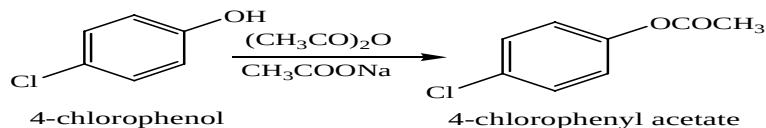
Step 2: Condensation of acetophenone with isonicotinoyl hydrazide



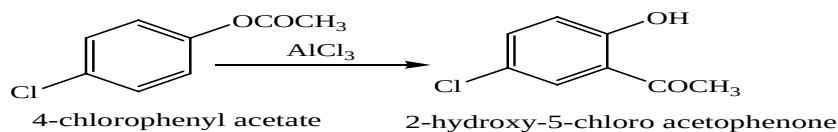
Synthesis of 2-hydroxy-5-chloro-3-nitro acetophenone isonicotinoyl hydrazone [HCNAIH]

Step-1 preparation of 2-hydroxy-5-chloro-3-nitroacetophenone

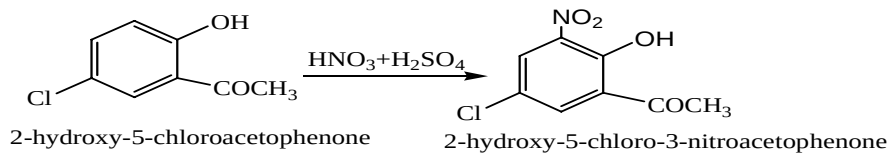
Reaction 1



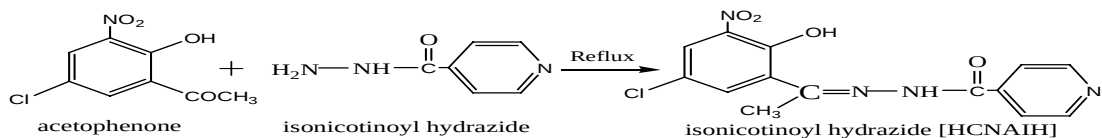
Reaction 2



Reaction 3



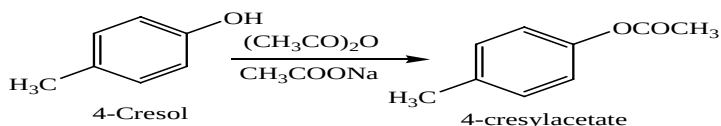
Step 2: Condensation of acetophenone with isonicotinoyl hydrazide



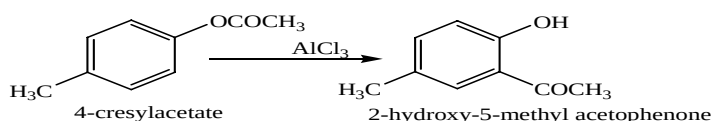
Synthesis of 2-hydroxy-5-methyl-3-nitro acetophenone isonicotinoyl hydrazone [HMNAIH]

Step 1: Preparation of 2-hydroxy-5-methyl-3-nitroacetophenone

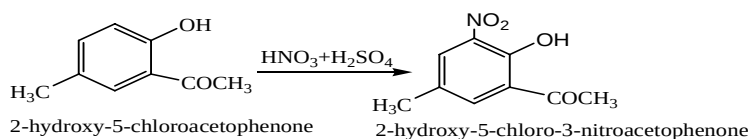
Reaction 1



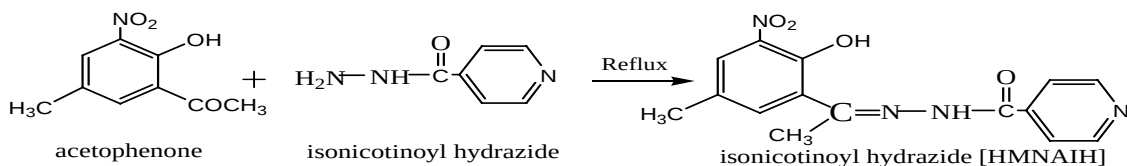
Reaction 2



Reaction 3



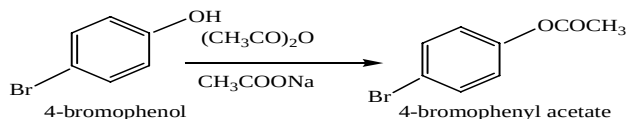
Step 2: Condensation of acetophenone with isonicotinoyl hydrazide



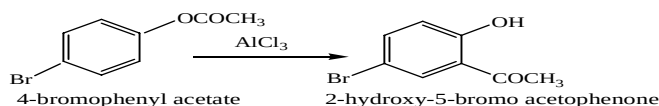
Synthesis of 2-hydroxy-5-bromo acetophenone isonicotinoyl hydrazone [HBAIH]

Step 1: Preparation of 2-hydroxy-5-bromo acetophenone

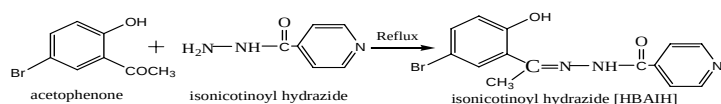
Reaction 1



Reaction 2



Step 2: Condensation of acetophenone with isonicotinoyl hydrazide



RESULTS AND DISCUSSION

¹H NMR and IR spectral data of the Schiff bases ligand^{10,11,12,13}

HCAIH: δ 12.90,(1H, S, Phenolic OH); 11.40 (1H, S, imino OH); 9.10 and 8.15,(4H, d, isonicotine); 7.76, 7.23 and 7.07,(3H, m, phenyl) and 3.43 ppm,(3H, S, methyl) HMAIH: δ 12.70,(1H, S, Phenolic OH); 11.20(1H, S, imino OH); 9.00 and 8.00, (4H, d, isonicotine); 7.80, 7.30 and 7.10,(3H, m, phenyl); 3.25 (3H, S, methyl) and 2.20 ppm, (3H, S, Ar-methyl) HCRAIH: δ 14.90,(1H, S, Ar-COOH); 12.75(1H, S, Phenolic OH); 11.30(1H, S, imino); 8.93 and 7.90,(4H, d, isonicotine); 7.78,7.35 and 7.18,(3H, m, phenyl); 3.15 ppm (3H, S, methyl) DHAIH: δ 12.85,(1H, S, Phenolic C₂-OH); 11.35 (1H, S, imino); 10.44,(1H, S, Phenolic C₂-OH); 8.84 and

7.88,(4H, d, isonicotine); 7.38, 7.26 and 7.17,(3H, m, phenyl) and 3.25 ppm (3H, S, methyl) HCMAIH: δ 12.95,(1H, s, Phenolic OH); 11.4 ,(1H, s, imino) 8.75 and 7.98,(4H, d, isonicotine); 7.8 and 6.82 (2H, m, phenyl); 3.1 (3H, s, methyl) and 2.25 ppm, (3H, S, Ar-methyl) HCNAIH: δ 12.95, (1H, s, Phenolic OH); 11.34 ,(1H, s, imino) 9.05 and 9.08,(4H, d, isonicotine); 8.15 and 7.35 (2H, m, phenyl); and 3.25 ppm (3H, s, methyl) HMNAIH: δ 12.63, (1H, s, Phenolic OH); 11.18 ,(1H, s, imino); 8.98 and 7.95,(4H, d, isonicotine); 8.07 and 7.27 (2H, m, phenyl); 3.24 (3H, s, methyl) and 2.46 ppm, (3H, s, Ar-methyl) HBAIH: δ 12.80, (1H, S, Phenolic OH); 11.45 (1H, S, imino OH); 9.15 and 8.10,(4H, d, isonicotine); 7.75, 7.25 and 7.06, (3H, m, phenyl) and 3.45 ppm, (3H, S, methyl).

Table 1: Analytical data of compound synthesized

S.No.	Compound	Molecular formula	Colour	m.p.(°c)	Compound
1	HCAIH	C ₁₄ H ₁₂ N ₃ O ₂ Cl	Yellow	218	
2	HMAIH	C ₁₅ H ₁₅ N ₃ O ₂	Yellow	230	
3	HCRAIH	C ₁₅ H ₁₃ N ₃ O ₄	Yellow	277	
4	DHAIH	C ₁₄ H ₁₃ N ₃ O ₃	Yellow	310	
5	HCMAIH	C ₁₅ H ₁₄ N ₃ O ₂ Cl	Yellow	254	
6	HCNAIH	C ₁₄ H ₁₁ N ₄ O ₄ Cl	Yellow	280	
7	HMNAIH	C ₁₅ H ₁₄ N ₄ O ₄	Yellow	286	
8	HBAIH	C ₁₄ H ₁₂ N ₃ O ₂ Br	Yellow	275	

Table 2: Antimicrobial activity¹⁴

S. No	Compound	Zone of inhibition (in mm)						
		<i>E.coli</i> (mm)	<i>S.typhi</i> (mm)	<i>A.aerogenes</i> (mm)	<i>B.subtilis</i> (mm)	<i>B.megatherium</i> (mm)	<i>P.vulgaris</i> (mm)	<i>S.aureus</i> (mm)
1	HCAIH	R	R	R	R	R	S ₁₁	S ₁₈
2	HMAIH	S ₁₆	R	S ₉	S ₁₁	S ₉	S ₉	S ₂₄
3	HCRAIH	R	R	S ₁₄	R	R	S ₁₄	S ₁₇
4	DHAIH	S ₁₇	S ₁₂	S ₁₂	S ₁₆	S ₉	S ₁₀	S ₁₁
5	HCMAIH	S ₁₉	S ₁₁	R	R	S ₉	S ₂₂	S ₁₄
6	HCNAIH	R	R	R	R	R	S ₉	S ₁₅
7	HMNAIH	S ₁₃	R	R	S ₉	R	R	S ₁₈
8	HBAIH	S ₉	R	S ₁₁	S ₇	R	S ₈	R

R-Resistant

S-Sensitivity

IR spectra of all ligand shows (C=N) peaks at range 1603-1617 cm⁻¹ and absence of (C=O) peaks at around 1666 – 1685 cm⁻¹ indicates the Schiff base formation. IR spectra of all Schiff bases ligand HCAIH: 3220cm⁻¹ (N-H), 2945cm⁻¹ (O-H), 1669cm⁻¹ (C=O), 1607cm⁻¹ (C=N), 1480 cm⁻¹ (C-O); HMAIH: 3200cm⁻¹ (N-H), 2941cm⁻¹ (O-H), 1666cm⁻¹ (C=O), 1611cm⁻¹ (C=N), 1481cm⁻¹ (C-O); HCRAIH: 3290cm⁻¹ (N-H), 2944cm⁻¹ (O-H), 1666 cm⁻¹ (C=O), 1611cm⁻¹ (C=N), 1490cm⁻¹ (C-O); DHAIH 3240cm⁻¹ (N-H), 2952cm⁻¹ (O-H), 1668cm⁻¹ (C=O), 1603cm⁻¹ (C=N), 1485cm⁻¹ (C-O); HCMAIH: 3199cm⁻¹ (N-H), 2950cm⁻¹ (O-H), 1679cm⁻¹ (C=O), 1606cm⁻¹ (C=N), 1484cm⁻¹ (C-O); HCNAIH:

3182cm⁻¹ (N-H), 2991cm⁻¹ (O-H), 1685cm⁻¹ (C=O), 1617cm⁻¹ (C=N), 1531cm⁻¹ (C-O); HMNAIH: 3211cm⁻¹ (N-H), 2803cm⁻¹ (O-H), 1684cm⁻¹ (C=O), 1612cm⁻¹ (C=N), 1526cm⁻¹ (C-O); HBAIH: 3225 cm⁻¹ (N-H), 2950cm⁻¹ (O-H), 1670cm⁻¹ (C=O), 1610cm⁻¹ (C=N), 1485cm⁻¹ (C-O);

CONCLUSIONS

All the Schiff bases ligands shows more activity towards *S. aureus* and least activity towards *S. typhi*. The structural changes have marked effect on the sensitivity and sensitivity varies with organisms.

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