Antimicrobial Activity of a new Series of Bis(isoxazoline), Bis(isoxazole) and their Derivatives

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Abstract

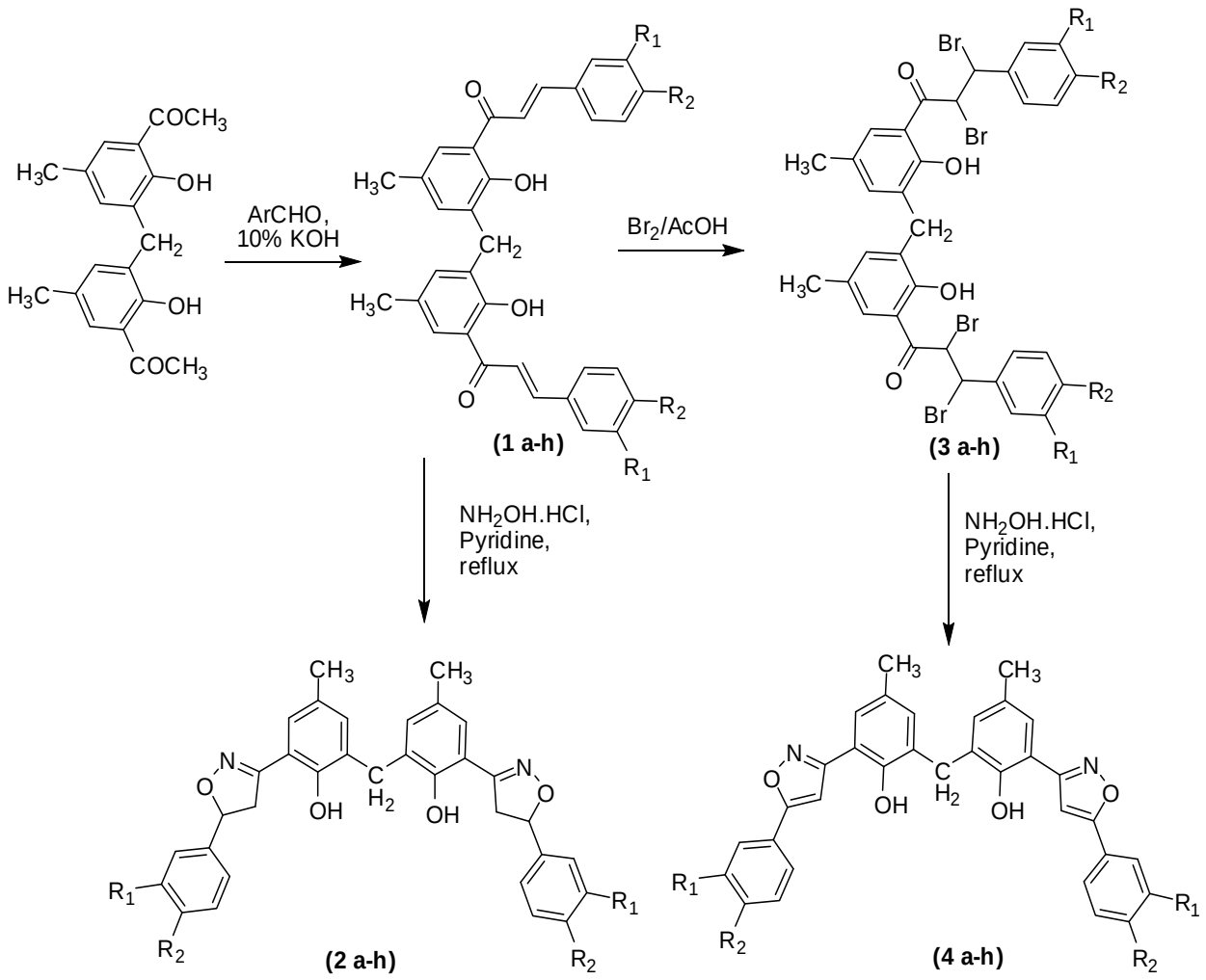
A series of 1,1-bis [2-hydroxy-3-(5'-aryl-isoxazoline-3-yl)-5-methyl phenyl] methane and 1,1-bis [2-hydroxy-3-(5'-aryl-isoxazol-3-yl)-5-methyl phenyl] methane derivatives were evaluated for their antimicrobial activity against some selected pathogenic micro-organisms such as Gram-positive bacteria, Staphylococcus aureus, Citrobacter frundii, Bacillus megatherium and Gram-negative bacteria Staphyloccus aureus, Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Enterobacter aerogenes, Salmonella typhi, Proteus vulgaris.

Keywords: Bis-isoxazoline, Bis-isoxazole, antimicrobial activity

Introduction

Five-membered heterocycles, isoxazolines represent a class of compounds of great biological importance. For instance, isoxazolines posses a broad spectrum of biological activity[1,2] (insecticidal, antibacterial, antibiotic, antitumor, antifungal, etc). Isoxazoline also serves as an important building block for the synthesis of biologically active molecules[2] and serves as a prodrug for an antiarthritic agent.[3]

Synthesis of 1,1-bis [2-hydroxy-3-(5'-aryl-isoxazoline-3-yl)-5-methyl phenyl] methanes and 1,1-bis [2-hydroxy-3-(5'-aryl-isoxazol-3-yl)-5-methyl phenyl] methanes derivatives were carried out and well established on the basis of their spectral analysis and elemental analysis **Scheme 1**.[4,5] Literature survey shows that the title compound have lot of biological importance therefore, thought that to study their antimicrobial activity.



Scheme 1: Synthesis of bis(isoxazoline), bis(isoxazole) and their derivatives[4,5]

Results and Discussion

The compounds **2a-h and 4a-h** were tested for antimicrobial activity against *Staphylococcus aureus, Citrobacter frundii, Bacillus megatherium*(Gram-positive bacteria) and *Staphyloccus aureus, Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Enterobacter aerogenes, Salmonella typhi, Proteus vulgaris* (Gram-negative bacteria) using agar disc-diffusion method[2] at a concentration 25 µg/mL in DMF as a solvent. After 24 h of inhibition at 34 ºC the zones of inhibition were measured in mm. These values were recorded in **Tables 1** and **2**

Table 1: Antibacterial activity of
1,1-bis [2-hydroxy-3-(5'-aryl-isoxazoline-3-yl)-5-methyl phenyl] methane 2a-h

Organism	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**
S.aureus	++	++	++	+++	+++	++	++	+++
C. frundii	+++	++	++	++	++	--	--	++
B. megatherium	++++	++++	++++	+++	+++	--	++	--
E. coli	++	+++	+++	++	+++	++	++	++
P.mirabilis	+++	+++	++	++	++	++	++	+++
P.aeruginosa	++	+++	++++	+++	+++	++	+++	++
E.aerogenes	++	+++	++	++	+++	++	++	++
S.typhi	--	--	--	--	--	--	--	--
p. vulgaris	++	++	++	+++	++	+++	+++	++

Table 2: Antibacterial activity of
1,1-bis [2-hydroxy-3-(5'-aryl-isoxazol-3-yl)-5-methyl phenyl] methane 4a-h

Organism	**4a**	**4b**	**4c**	**4d**	**4e**	**4f**	**4g**	**4h**
S.aureus	++	+++	++	+++	+++	++	++	+++
C. frundii	++	--	+++	++	--	--	++	--
B. megatherium	+++	++	++	++	++	++	--	--
E. coli	++	+++	+++	++	+++	++	++	++
P.mirabilis	++	+++	++	++	+++	++	++	++
P.aeruginosa	+++	+++	+++	+++	+++	+++	++	++
E.aerogenes	+++	++	++	++	++	+++	+++	+++
S.typhi	--	--	--	--	--	--	--	--
p. vulgaris	++	++	+++	++	++	++	+++	+++

Antimicrobial activities of compounds **2-4** were tested by Sterile agar discs (2 mm diameter) moistened with the compound solution in DMF of specific concentration 100 µg /disc were carefully placed on the agar culture plates that had been previously inoculated separately with the microorganisms. The plates were incubated at 34 ºC and the diameter of the growth inhibition zones were measured after

24 h. After incubation degree of sensitivity to drugs is determined by measuring the visible clear of growth of zone inhibition.

The results of the compounds for antibacterial testing shown in Table 1 and 2 revealed that, in general, the inhibitory activity against the Gram-positive bacteria was higher than that of the Gram-negative bacteria in Table 1and opposite in Table 2.

From **Table 1**, The compounds **2a**, **2b** and **2c** showed excellent activity against *B. meaatherium* bacteria (inhibitory zone = 12 mm) and good activity against *E. coli, P.mirabilis, P. aeruginasa* (inhibitory zone 8-12 mm). Compound 2d and 2e moderate acitivity and compound 2f-h are weak activity against *S.aureus, B. megatherium, P.aeruginasa*. Compound 2f inactive against *C. frundii, B. megatherium* and all compounds displayed inactivity against *S. typhi* bacteria.

From **Table 2**, The compounds **4b, 4c** and **4e showed** good activity against *S.aureus, P.mirabilis P. aeruginasa* (inhibitory zone 8-12 mm). *B. meaatherium* bacteria (inhibitory zone = 12 mm). Compound **4d** and **4e** moderate activity against *S.aureus, B. megatherium*, *P.aeruginasa* and compound **4f-h** are weak activity. Compound **4b, 4e, 4f, 4h** inactive against *C.frundii*, and **4g, 4h** inactive against *B. megatherium*, and all compounds displayed inactivity against S. typhi bacteria. All the test compounds exhibited moderate (**2d-f** and **4b, 4c, 4e**) to high (**2a-c**) inhibitory effect towards tested fungi (**Table 1 and 2**).

Conclusion

A new series of bis(isoxazoline), bis(isoxazole) and their derivatives tested for antimicrobial activity by disc diffusion methods, showing moderate to potent inhibition.

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