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Synthesis of a mixture of Dichalconated derivatives of tautomers of Thio Benzimidazole and evaluation of their Antibacterial and Antifungal activity

Sheena Mathew*, Mary Mathew
Department of Pharmaceutical Chemistry, College of Pharmaceutical Sciences, Medical College, Trivandrum, Kerala – 695011
Corresponding Author:Sheena Mathew

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ABSTRACT: Chalcones have been prepared by Claisen-Schimidt condensation of thiobenzimidazole ketone at two sites with different aromatic aldehydes to give a mixture of two dichalcones of thiobenzimidazole. A mixture of chalcones are obtained due to the occurrence of tautomerism of thiobenzimidazole which possess an interesting profile of anti-bacterial and anti-fungal activities.

KEYWORDS: Thiobenzimidazole, Chalcones, tautomers, antibacterial activity, antifungal activity

I. INTRODUCTION

Benzimidazole derivatives play a vital role in biological fields such as antimicrobial, antiviral, antidiabetic, antispasmodic, and anticancer activities. Thiobenzimidazole derivatives have also been found to be biologically potent. Chalcones represent an essential group of natural as well as synthetic products and some of them possess wide range of pharmacological activity such as antibacterial, antitumour, anticancer, antitubercular,anti-inflammatory, antioxidant, antimalarial, antileishmanial etc. The presence of reactive α, β- unsaturated keto group in chalcones is found to be responsible for their biological activity.

II. EXPERIMENTAL METHODS

Synthetic method for preparation of dichalcones of thiobenzimidazole:

Step-1: A mixture of orthophenylenediamine (0.4mol), carbon disulphide (0.6mol) and alcoholic KOH (0.6mol) was taken in a clean and dry R.B. flask and refluxed for 2 hrs using an electrical heating mantle. The reaction mixture was cooled to room temperature and poured into 750 ml of ice cold water and mixed thoroughly. To this concentrated HCl was added drop wise until the product precipitated out. The precipitate was collected by filtration. The product was recrystalized from suitable solvent of m.p. 285-300°C.

Step-2: A mixture of thiobenzimidazole (0.30 mol) and acetyl chloride (0.30 mol) with K_2CO_3 (6.168 g) in ethanol (250 ml) was kept overnight at room temperature. The reaction mixture was refluxed on a steam bath for about 3 hrs. It was cooled filtered and solvent was distilled off under reduced pressure and the product was obtained and was recrystallised with ethanol. Yield 82%, m.p. 94.5ºC

Step-3: A solution of thiobenzimidazole (0.01 mol) and appropriately substituted aldehyde (0.02 mol) in ethanol were taken in a beaker. Potassium hydroxide(2%, 5 mL) was added in to it. The reaction mixture was refluxed for 5 hrs and then the solvent was removed by vacuum distillation and then it was poured into crushed ice and acidified with HCl. The solid separated was filtered and recrystallised from ethanol.

III. RESULTS AND DISCUSSION

Chemistry:

Dichalcones of thiobenzimidazole were synthesized after obtaining thiobenzimidazole from orthophenylenediamine and CS_2. Thiobenzimidazole shows tautomerism and on Claisen-Schimidt condensation with substituted aromatic aldehydes it gives a mixture of two products which are derived from the tautomers thiobenzimidazole.

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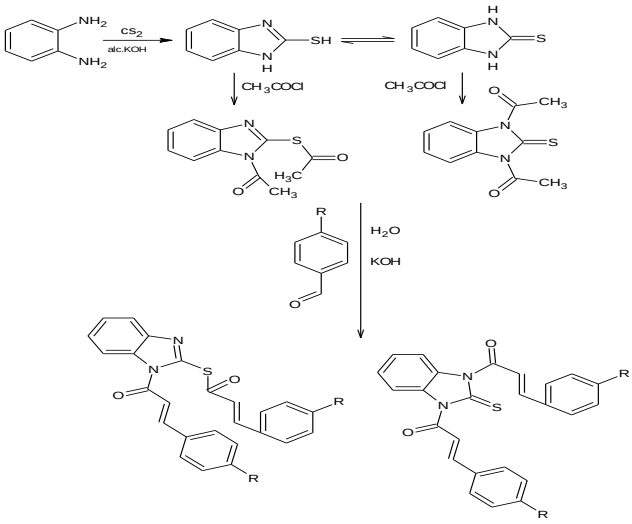

Antibacterial & Antifungal activity

Cylinder bore method was employed to study in-vitro anti-microbial activity of dichalcone mixtures (Ta-Tg) against E.coli, S.aureus and C.albicans. The preparation of the nutrient broth, subculture, nutrient agar medium and Sabouraud Dextrose Agar medium was done as per the standard procedure. Each test compounds (5mg) was dissolved in 5ml of dimethyl sulfoxide(1000µg/ml). Nutrient agar medium was used for anti-bacterial activity where Gentamycin was used as reference drug and DMS as a control which did not reveal any inhibition. Sabouraud Dextrose Agar medium was employed to test anti-fungal activity where Griseofulvin was used as reference drug and DMS as a control which revealed no inhibition.

		Zone of inhibition (mm)		
	R	E.coli	S.aureus	C.albicans
Ta	-H	12	09	11
Tb	-4-NO_2	16	13	12
Tc	-4-NH_2	11	08	13
Td	-4-F	10	10	06
Te	-2-OH	10	09	10
Tf	-2,4-$(OH)_2$	09	08	09
Tg	-2,4-$(CH_3)_2$	16	12	14
Gentamycin	-	21	25	Not done
Griseofulvin	-	Not done	Not done	22
DMS	-	00	00	00

IV. CONCLUSION

A novel series of a mixture of dichalcones of thioimidazole tautomers were synthesized and screened for antibacterial and antifungal activity. Among the tested compounds Tb & Tg exhibited considerable anti-bacterial activity and compounds Tb, Tc & Tg showed significant anti-fungal activity. The compounds with electron releasing groups at various positions shown to have better activity.

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