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RESEARCH ARTICLE

Microwave-Assisted Synthesis of Pyrimidinethione Derivatives

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ABSTRACT

In the present article a few pyrimidinethione derivatives are synthesized in a two step procedure using microwave radiation. The compounds are screened for antibacterial activity against four bacterial species. The results revealed that the compounds are obtained in good yields as compared to the conventional method of synthesis and the time required for the completion of the reaction was considerably less. All the compounds exhibited antibacterial potential against the gram negative and gram positive bacteria tested .

Keywords: Pyrmidinethione, antimicrobial, microwave assisted synthesis, chalcone

Introduction

The chemistry of pyrimidinones has received considerable attention in the recent times due to their wide range of biological activities, like antimicrobials, antithrombotic, antihypertensive, antimalarial, antiviral, anti-inflammatory.[1]

The combination of solvents and long reaction time periods, poor yield makes the conventional method of synthesis of these compounds quite inefficient. Thus a simple, general and efficient procedure for the synthesis of this important heterocyclic system is required. Hence the present work of microwave-assisted synthesis of pyrimidinethiones was undertaken.

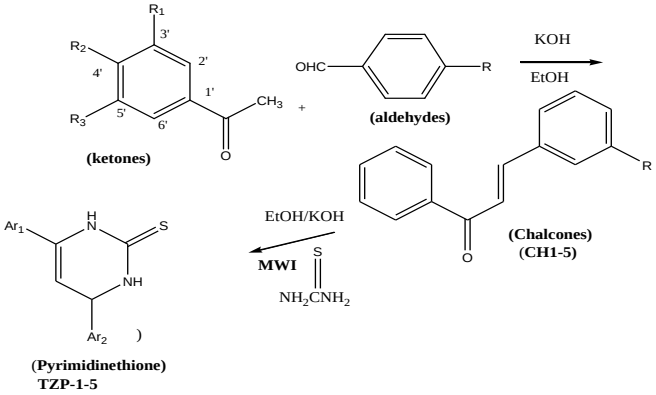
The application of microwave irradiation (MWI) to organic synthesis has been the focus of considerable attention in recent years and is becoming an increasingly popular technology. The salient features of the microwave approach are rapid reaction rates, cleaner reaction conditions and enhancements in chemical yields.

Under the framework of "green chemistry" we have developed an environmentally benign synthesis of pyrimidinethiones.

Further attractions of this method are that it allows reaction in open vessels (this avoiding risk of high pressure development) and synthesis on preparative scales.

Materials and Methods

A series of pyrimidinethione derivative was synthesized by using different arylmethylene acetophenone derivatives. The steps adapted in the synthesis of pyrimidinethione derivative are obtained from literature reported by Salma et al.[2]



Following steps are involved in the synthesis of pyrimidinethione derivatives:

Step-1: Synthesis of arylmethylene derivatives/chalcones derivatives.

A series of chalcone derivatives were synthesized using different substituted ketone and different substituted benzaldehyde using Claisen-Schimidt condensation. A solution of different acetophenone and aromatic aldehydes were dissolved in ethanol (15 ml), under stirring, and aqueous KOH (50%, 12 ml) was added dropwise. The reaction mixture was stirred at room temperature and kept overnight. After 14-16 hr, the reaction mixture was diluted with H_2O and acidified with HCl (10%). The separated solid was filtered and washed with ice-cold water till the

washings were neutral to litmus. Recrystallised from methanol. The list of chalcone prepared is given in the Table 1.

Step-2: Microwave assisted synthesis of pyrimidinethione derivatives.

A mixture of aryl methylene derivatives/chalcones, thiourea and KOH in ethanol (50 ml) was kept in microwave oven for sufficient time and heat. Ethanol was evaporated to its half and the mixture was left overnight. Ethanol was distilled off and water was added to the precipitate, filtered, washed the product with water until free from alkali. The product was recrystallized from ethanol.

The reaction time for the synthesis of different pyrimidinethiones is given in table 2.

The synthesized pyrimidine derivatives are pale yellow to off white crystals, with no characteristic odour. These derivatives are soluble in chloroform, ethanol, slightly soluble in methanol and practically insoluble in benzene. The melting points were determined by open capillary method and are uncorrected. The anti microbial activity of the synthesized pyrimidine-2-thione derivatives was performed on different gram positive and gram-negative bacteria and also on fungi. Different methods of isolation of the bacteria are reported in the literature. Different methods for screening of the compounds for anti microbial activity are also reported. The results of antibacterial screening are reported in table 3.

Results and Discussions

The yield of all the synthesized compounds is found to be significant. All the synthesized pyrimidine-2-thione derivatives show anti bacterial activity against both gram positive and gram-negative bacteria. The compounds were found to be active against the gram positive bacteria in comparatively lower dose than that required for the activity against the gram negative bacteria in most of the cases.

All the synthesized compounds possessed anti bacterial activity. By visualizing activity data, it could be observed that compound TZP-1 and TZP-2 exhibit significant activity against *P. aerugenosa.* Compound TZP-1, TZP-2, TZP-3 and

TZP-4 and TZP-5 showed remarkable activity against *S. aureus*. In case of *B. substillis* compounds TZP-4 and TZP-5 showed good activity. Promising activity was observed in case of compounds TZP-1, TZP-2, TZP-3, and TZP-4 against *Proteus mirabilis*

The results indicate that the 4, 6 position of the pyrimidine-2-thione does play an important role in the anti microbial activity of the compounds. In addition to the phenyl ring with dimethyl amino substitution on the 4 position of the pyrimidine, is vital for the activity.

The result also indicates that the substitution on the phenyl ring of 6 positions with hydroxyl group leads to a more potent anti microbial agent as compared to non-substituted phenyl ring.

As envisaged from the literature review it could be concluded that the microwave assisted synthesis more efficient than the conventional means. The use of such nonconventional reaction condition reveals several features like a short reaction time as compared to the conventional heating, ease of work up, selectivity and improvement in yield.

Table 1:- List of Chalcone Prepared

Compound r	Ketones	Aldehydes	Yie
CH-1	Acetophenone	Benzaldehyde	91%
CH-2	Acetophenone	p-dimethylaminobenza	87%
CH-3	2-hydroxyacetop	p-dimethylaminobenza	94%
CH-4	2-4-dihydroaceto	p-dimethylaminobenza	79%
CH-5	2-hydroxyacetop	benzaldehyde	85%

Table 2:- The Yield and Reaction Time for the synthesis of Pyrimidinethiones

Compound r	Chalcone us	MWI	Time (mi	Yield %
TZP-1	CH-1	20	2	85
TZP-2	CH-2	20	3.4	94
TZP-3	CH-3	40	3.5	87
TZP-4	CH-4	40	2.6	79
TZP-5	CH-5	20	4	86

Table 3: Antibacterial activity of the synthesized compounds

Compound	MIC (μg/ml)			
	Proteus mirabilis	Pseudomonas aeruginosa	Staphylococus aureus	Bacillus subtilis
Tzp-1	75	97	84	46
Tzp-2	82	107	90	75
Tzp-3	109	91	56	78
Tzp-4	104	84	43	92
Tzp-5	76	90	90	85
Norfloxacin	08	07	03	09

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