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Solid phase-promoted greener synthesis and antibacterial activity of novel Schiff bases under catalytically free condition

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ABSTRACT

Non-traditional method (grinding) was used for the preparation of novel schiff bases from 4-amino-3-methyl phenol / 2-amino-4-methyl phenol and several aldehydes and ketones under catalytically free condition. This procedure constitutes an energy efficient, shorter time, higher yield as well as green synthesis approach. Some synthesized products were characterized by IR, NMR and MASS and also tested for antibacterial (*Escherichia coli, Staphylococcus aureus, Bacillus subtilis, and Klebsiella pneumonae*) activities by disc diffusion method

Introduction

Schiff bases and their derivatives, which usually possess diverse biological activities such as antibacterial [1-4], antifungal [4], anti-inflammatory [5], analgesic [6], CNS depressant [6] anticonvulsant [7], anticancer [8], insecticidal [9], plant growth inhibitor [10], antitubercular[11] and antitumor [12-13].

Schiff bases are also used as a starting material in the preparation of number of industrial and biological active compounds via ring closure, cycloaddition and replacement reaction [14]. At present a broad range of methods for synthesizing imines in the presence of catalysts are available: $ZnCl_2$ [15], $TiCl_2$ [16], K-10 [17-18], $MgSO_4$-PPTL [19], $Mg(ClO_4)_2$ [20] and also SiO_2-$NaHSO_4$ (under MW irradiation condition) [21]. More recently, ultrasound irradiation has been used to give rise to the formation of a series of Schiff bases (aryl-aryl and aryl-alkyl), under solvent-free conditions [22] or using SiO_2 as a catalyst in ethanol [23], with short reaction times (10-20 min) and high yields. But, in recent years, environmentally benign synthetic methods have received considerable attention. Verma et al [24] reported synthesis of enamines and imines under microwave irradiation accompanied with solvent less condition. Kaupp et al [25] reported the synthesis of Schiff bases using water as a solvent.

These wide application and biological data prompted us to synthesize new Schiff bases and to ascertain their microbial activity.

Result and discussion

Chemistry:

In this article, we have prepared thirty new Schiff bases under solvent and catalytically free condition (except 27, 28, 29, 30. Table 1). Initially, the mixture of substituted amines and aldehydes was ground in mortar with a pestle at room temperature under neat condition (Table 1, 1-26). The result demonstrated that, completion of reaction in 2-3 min. but, when the mixture of substituted amines and ketones was ground in mortar with a pestle at room temperature under neat condition. The result demonstrated that the need of catalyst. Thus, we chose inexpensive and efficient HOAc as a catalyst for this reaction. HOAc was used in 20 mol % which, leads to excellent yield of the product (Table 1, 27-30).

Anti-bacterial activity:

For the anti-bacterial activities we chose some selected compounds (Table 2). These compounds were evaluated against various pathogenic (Gram-negative and Gram-positive) bacterial strains viz., *Escherichia coli* (*E. coli*), *Staphylococcus aureus* (*S. aureus*), *Bacillus subtilis* (*B. subtilis*) and *Klebsiella pneumonae* (*K. pneumonae*).

The anti-bacterial activities were evaluated by the disc diffusion method. The solvent used for the preparation of compound solution (DMSO) did not show inhibition against the tested organisms (negative control).

The results of anti-bacterial screening of newly synthesized compounds are presented in Table 2. In these compounds 1 and 15 showed good activity (zone of inhibitions 11 and 15 mm at concentration of 250 µg/ml) against *S. aureus.* Compound 6 showed excellent activities (zone of inhibitions 15-19 mm at concentration of 250 µg/ml) against all four bacterial strains. It is interestingly to note that the slight structural difference in 5 and 6 can be observed, but their antibacterial activity is entirely different.

The electric property of the compounds has close relations with biological activity [26, 27] and the weak antibacterial activity of compound 5 compared to compound 6 may be explained by their charge density distribution.

Compound 13 showed good activity (zone of inhibitions 6-16 mm at concentration of 250 µg/ml) against *E. coli, S. aureus and K. pneumonae.* The compound 21 with CH_3 substituent at meta position showed moderate antibacterial activity (zone of inhibitions 11 mm at concentration of 250 µg/ml) against *E. coli.* but the compound 22 with CH_3 substituent at para position did not show any activity against *E. coli, S. aureus, B. subtilis* and *K. pneumonae.*

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