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ORIGINAL ARTICLE

Synthesis and antimicrobial evaluation of fatty chain substituted 2,5-dimethyl pyrrole and 1,3-benzoxazin-4-one derivatives

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KEYWORDS

Condensation;
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Structure activity relationship

Abstract Fatty acids themselves have a number of biological properties and its easy intake by the human body will focus to the synthesis of many heterocyclic moiety substituted with fatty acid residue, to make more gradual intake of heterocycles in the human body. 2,5-Dimethyl pyrrole **2**(**a**–**e**) and 1,3-benzoxazin-4-one **4**(**b**–**e**) derivatives were synthesized, from cyclization of fatty acid hydrazide **1**(**a**–**e**) with acetonyl acetone and from the reaction of fatty esters **3**(**b**–**e**) with anthranilic acid in the presence of $POCl_3$, respectively. All these compounds were characterized with the help of IR, ^1H NMR, ^{13}C NMR and mass spectra. The synthesized compounds were screened for antimicrobial evaluation against gram-positive (*Staphylococcus aureus* SA 22, *Bacillus subtilis* MTCC 121), gram-negative (*Escherichia coli* K12, *Klebsiella pneumoniae*) and fungal strains (*Candida albicans* IOA-109) and were found to be good antimicrobial agents.

1. Introduction

The pyrrole ring is a part of many biological compounds such as the enzyme catalase, the bile pigment bilirubin and the mould pigment prodigiosin; it is also a significant part of macrocyclic porphyrin ring system of chlorophyll and hemin [1,2]. Apart from these properties pyrrole and its derivative possess a number of biological activities such as antiallergic, antitumor [3], antibacterial, antifungal [4], antiinflammatory, analgesic [5], anticonvulsant [6], antimycobacterial [7] antitubercular, anticancer [8] and anti HIV [9]. Substituted dimethyl pyrroles can be synthesized from the widely used Knorr pyrrole synthesis [10]. Other methods are also known for the synthesis of 2,5-dimethyl pyrrole derivatives [11,12]. Sometimes for the synthesis of substituted pyrroles, photochemical reactions are also used, which involves the use of other pyrrole precursor including the migration of group from one nitrogen atom to the ring carbon atom [13]. Despite the biological use of substituted dimethyl pyrroles they have been synthetically

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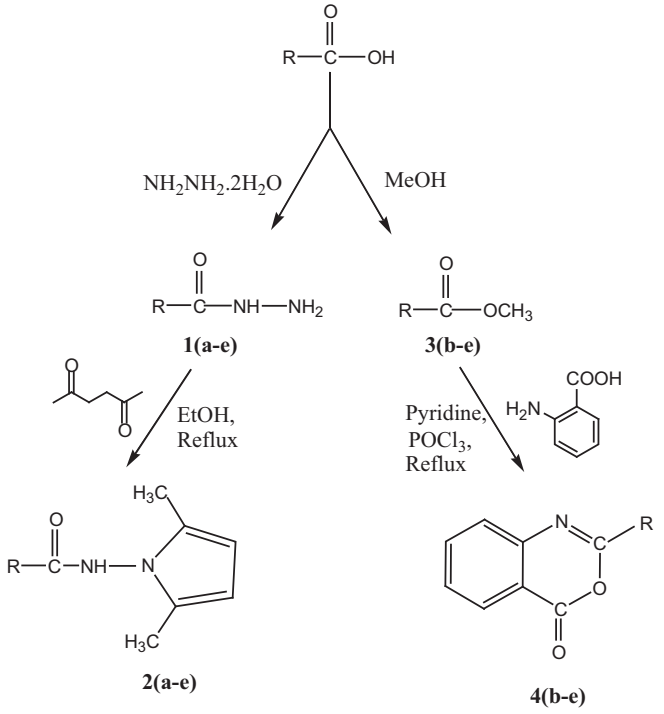

Compound	R
1a, 2a	CH_3-$(CH_2)_{14}$-
1b, 2b, 3b, 4b	H_E, H_Z C=CH-$(CH_2)_8$-
1c, 2c, 3c, 4c	CH_3-$(CH_2)_7$-CH=CH-$(CH_2)_7$-
1d, 2d, 3d, 4d	CH_3-$(CH_2)_5$-CH(OH)-CH_2-CH=CH-$(CH_2)_7$-
1e, 2e, 3e, 4e	CH_3-$(CH_2)_4$-CH=CH-CH_2-CH_2-CH(OH)-$(CH_2)_7$-

Scheme 1 Synthetic pathway for the synthesis of a series of N-fatty acid derivative substituted 2,5-dimethyl pyrrole and 2-alkenyl/hydroxyalkenyl chain substituted-benz-1,3-oxazin-4-one.

very useful compounds. In the solid phase synthesis 2,5-dimethyl pyrroles can be used as a good protecting group for protecting the terminal amines. Solid supported 2,5-dimethyl pyrrole was obtained in pure form and quantitative yield by microwave irradiation using dimethyl pyridine (DMP) as solvent. The microwave irradiation speeds up the reaction rate and solid supported pyrrole derivative was obtained only in five minutes [14]. These 2,5-dimethyl pyrroles, undergo reductive condensation (did not undergo self condensation) with acetonyl acetone to form 1,3-diphenyl-4,7-dimethyl isoindoline [1,2]. Various methods are known for the synthesis of dimethyl pyrrole derivatives using different reagents and substrates, these derivatives were found very useful in the field of chemistry as well as in biology [15–20]. Preliminary data on the synthesis of substituted pyrrole derivative of saturated fatty acid (stearic acid) have been already reported [21], but the unsaturated fatty acid amide substitution on 2,5-disubstituted pyrrole has not been reported yet.

On the other hand, 1,3-benzoxazin-4-one derivatives are biologically very useful compounds [22]. These are used either directly or indirectly in many fields such as industries [23], research field and in clinical work [24]. Clinically used 4-quinazolone derivatives were synthesized from benzoxazinone starting material [25]. Vinyl and phosphate group substituted benzoxazinone derivatives were used as hypnotic drug [26], antiphlogistic drug [27] and possessed antimuscular contraction properties [28]. These derivatives are very useful in natural product chemistry, because they were found in the form of acetal glycosides in plant of different taxonomic positions [29]. Nitrogen atom of these derivatives is a part of the aglyconic cyclo hemiacetal unit, therefore it can act as a plant's own resistance factor towards pests, insects, fungi and other microbial diseases. A conjugate base benzoxazine kanamycin can be used as a suitable fluorescent nucleus (probe) for detecting the mycoplasmas in cell culture [30]. These derivatives also proved to be neuropeptide Y Y5 receptor antagonists through quantitative structure activity relationship (QSAR) studies [31] and also as factor Xa (FXa) inhibitor (it is a trypsin like protease, helps in blood coagulation) [32]. The 1,3-benzoxazin-4-one undergoes nucleophilic ring opening reaction with Ruppert's