Synthesis of Polyhydric Phenolic Phenacyl Ethers

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ABSTRACT

Polyhydric phenolic phenacyl ethers are synthesised by micellar mediated reaction with phenacyl and its substituted phenacyl bromide. Biological importance of poly phenacyl ethers are reviewed. Physical data, IR, $^1$HNMR and $^{13}$CNMR are used to characterize the new compounds.

Key words: Phenolic ether, Antimicrobial, Phenacyl bromide.

INTRODUCTION

Phenolic ethers play huge role in medicinal chemistry and some of them are used as adhesives and holt melt. Alkyl phenolic ether prodrugs have been reported where coupling with a hydroxymethylimide using mitsunobu chemistry yielded the product¹. Diphenyl ether like chlornitrofen was widely used in large quantities as a herbicide to control various weeds in rice fields². Polybrominated diphenyl ethers are used as brominated fire retardants. These diphenyl ether had an adverse impact on the structure and function of the soil microbial community and microbial processes³. Polybrominated diphenyl ethers (PBDEs) were applied as polymers for many plastic and electronic products. Due to their ubiquitous distribution in the environment, potential toxicity to human and tendency for bioaccumulation, PBDEs have raised public safety concern⁴. Phenolic ethers are synthesised by various methods with different reactant and also in different environment. This type of reactions are involved in biological and human mechanism. Such kind of mechanism deals with mono hydric phenols and poly ring phenols. These concepts promoted us to prepare such type of phenolic compounds in different environment.

MATERIAL AND METHODS

Trihydric phenols like Pyrogallol (1,2,3 tri hydroxyl benzene), Phloroglucution (1,3,5 tri hydroxyl benzene) and Hydroxyquino (1,2,4 tri hydroxyl benzene) react with phenacyl bromide and methyl, chloro, methoxyl, bromo substituted phenacyl bromide. Here one mole of trihydric phenol is taken for the reaction and 3 moles of phenacyl and appropriately substituted phenacyl bromide. The total reaction was carried out in micellar solution⁵⁶. The micellar medium have both hydrophobic and
hydrophilic region so as to facilitate the reaction to the right path. In this reaction triethylamine was used as cosurfactant. Overall reaction is carried out in room temperature with continuous stirring of 5-10 hrs. Overall reaction solid product was filtered off from the reaction mixture and it was washed several time with water and petroleum ether. Dry product was tested in TLC with ethyl acetate and petroleum ether as the eluent. Synthesis of these 1,2,4 trihydric phenolic phenacyl ethers are given in scheme 1. Similar procedure was adopted for the synthesis of 1,2,3 and 1,3,5 trihydric phenolic phenacyl ethers.

RESULTS AND DISCUSSION

The reaction of trihydric phenols with variously substituted phenacyl bromides in the micellar medium yielded the desired triphenolic

Table 1: Physical data of phenolic phenacyl ethers

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<th>Cmp. No</th>
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<th>m.p. °C</th>
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<th>FW</th>
<th>Found C, H, N Cal. (C,H,N)</th>
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<td>C₆H₃(OCH₂COC₆H₅CH₃)₃</td>
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<td>110-112</td>
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Table 2: IR spectra data of ether compounds

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<th>Compound No</th>
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<th>C-H Aliphatic</th>
<th>C=O</th>
<th>C=C</th>
<th>C-O-C</th>
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(substituted) phenacyl ethers (1-15). The formation of these compounds are revealed by the preliminary laboratory analysis and then the CHN analysis (Table 1). The important group frequencies like aromatic C-H str., aliphatic C-H str., carbonyl str. aromatic C=C str., C-O-C str. (Table 2) showed the formation of the compounds (1-15). The formation and structure of these compounds are further confirmed by the data of $^1$H NMR and $^{13}$NMR spectra (Table 3 and 4).

Table 3: $^1$H NMR data of ether compounds

<table>
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<th>Compound No</th>
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<th>$-\text{O-CH}_2\text{-CO}$</th>
<th>CH$_3$</th>
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<td>7.54-7.91m,7.21-7.45m</td>
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<td>4</td>
<td>7.26-7.98m,6.38-6.92m</td>
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<td>5.15s</td>
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<td>7.29-7.99m,6.93-6.45m</td>
<td>5.58s</td>
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<td>7.60-7.87m,7.26-7.27m</td>
<td>4.40s</td>
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*Data correspond to methoxy methyl group

Table 4: $^{13}$C NMR data of phenolic phenacyl ethers

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<th>Ar-C=O</th>
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</table>

*Data correspond to methoxy methyl group
In the above experiments three types of trihydric phenols have been chosen as the substrate. They are 1,2,3 trihydroxy-, 1,3,5 trihydroxy and 1,2,4 trihydroxy phenols. The significance of these reaction is that in order to increase the yield the reactions were mediated in micellar medium. In this medium the formation of the phenolate ion is stabilized more easily. The novelty of the trihydric phenolic phenacyl ethers are based on its biological activity. The antimicrobial activities of these compounds are presented (Table 5). Microorganisms like Staphylococcus aureus. Escherichia coli are used to determine the antimicrobial studies for the compounds.

Scheme 1: Preparation of 1,2,4 tri phenolic (substituted) phenacyl ethers.
Table 5: Biological activity data of ether compounds

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Standard (Std)-ciprofloxacin 5µg/disc for bacteria solvent control (Sc) - DMSO

REFERENCES