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A facile synthesis of phenyl phenacyl ethers

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ABSTRACT

Phenyl phenacyl ethers have been synthesised by the micellar catalysed reaction of phenol(s) with equimolar mixture of phenacyl bromide and triethyl amine in 70% methanol-water (v/v) at room temperature. The ethers have been characterised on the basis of the IR and ^{1}H NMR spectral data. This method of synthesis stands as the simple and convenient one, leading to relatively higher yields.

Key words: Phenacyl bromide, Micellar solution, Phenyl phenacyl ethers.

INTRODUCTION

Generally, ethers may be categorised like aryl ether, allyl ether, phenolic ether, phenacyl ether, polyether. They have different structures, depending upon the groups that are connected to the ether oxygen. Crown ethers are special type of cyclic ethers. These ethers are low molecular polyethers.

The compounds containing ether oxygen with phenyl group on one end and aryl, alkyl, benzyl, allyl, vinyl, etc. on the other end are called phenolic ethers or aromatic ethers. These ethers have wide range of applications. The uses of phenolic ethers depend upon the nature of the group attached to the other end of the phenolic oxygen. For example, diphenyl ether and its halo derivatives have agrochemical applications such as herbicides and fungicidies[1,2]. Similarly, phenolic ethers find applications in chemical engineering, pharmaceutical, food, costume and polymer industries.

Various methods have been followed for the preparation of phenyl phenacyl ethers. Aryl phenacyl ethers have been prepared by the micellar mediated reaction of phenacyl bromide with aromatic alcohol and triethylamine [3-5]. Phenacyl phenyl ethers are prepared by the reaction of equal volume of equimolar solutions of phenacyl bromide and phenol, in the presence of sodium carbonate in acetone water mixed media. Phenacyl ethers are prepared by a solution of phenacyl bromide in ethanol with potassium iodide[6].

An elegant approach for the synthesis of these ethers involves micellar as the medium during the reaction. The method is advantageous over the other methods due to comparatively higher yield.

MATERIALS AND METHODS

Phenacyl bromide is obtained by the bromination of acetophenone. Phenols (analytical grade) are purified by distillation or recrystallisation before they are used. Triethylamine (analytical grade) is purified by distillation. Commercial grade sodium lauryl sulphate is used. TLC is carried out on SiO_2 gel and the spots are located by placing the plate in iodine chamber. IR spectra are recorded on a Perkin-elmer FT-IR spectrophotometer and ^1H NMR spectra on a Bruker 200 MHz spectrometer.

Sodium lauryl sulphate (0.6g, 2.08 * 10^{-3} mol dm^3) is dissolved in methanol-water (70-30,v/v) and stirred continuously about two hours. This micellar solution is used as the medium for the reactions.

An equimolar solution of phenacyl bromide, triethyl amine and appropriate phenol are dissolved in minimum amount of methanol . It is then added slowly in required amount of micellar solution. This solution was stirred well for 5-10 hours at room temperature. The solid product is filtered, washed with water and then petroleum ether and dried well. The purity is tested by TLC using cyclohexane, ethylacetate (5:1) as eluent. The solid product is recrystallised from ethylacetate.

RESULTS AND DISCUSSION

Phenyl phenacyl ethers have found relevance in various branches of modern chemical engineering. Hence, attempts have been made to prepare these ethers by simple procedure. It is known that various organic reactions are catalysed by surfactant above their critical micelle concentration (CMC) in aq.organic mixed media[7-9]. In the present work, we have used an anion surfactant in the reaction of phenols with phenacyl bromide in the presence of triethylamine, in attempt to explore on micellar catalysed organic reaction with a view of knowing more effective method for etherification.

The phenyl phenacyl ethers viz., 1,2 – bis (phenacyloxy) benzene **(1)**, 1-3-bis(phenacyloxy) benzene **(2**), 1,4-bis(phenacyloxy) benzene **(3)**, 1,2,3-tris (phenacyloxy) benzene **(4)**, 1,3,5-tris (phenacyloxy) benzene **(5)** and 4-acetyl-3-hydroxy phenyl phenacyl ether **(6)** are prepared (Figure -1) and tested by TLC for their purity and characterised by IR, 1H NMR spectral data (Table.1 and 2). The physical data are presented in Table.3 and the biological activity data of the phenyl phenacyl ethers are given in Table.4.

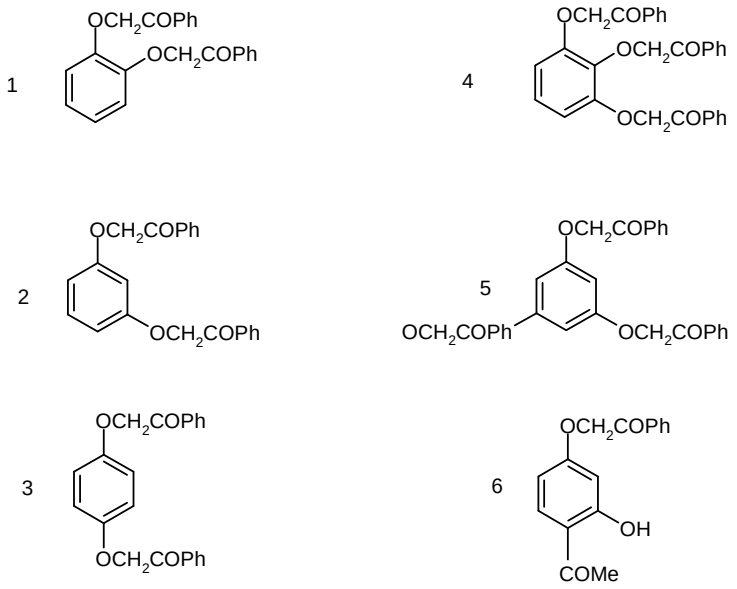


Figure.1 Structure of phenyl phenacyl ethers

Table 1 IR spectral data of phenyl phenacyl ethers(cm^{-1})

Compound No	Aromatic CH	Aliphatic CH	C=O	C=C	C-O-C
1	3108	2940	1606	1524	1226
2	3055	2922	1642	1596	1228
3	3055	2915	1635	1506	1210
4	3065	2956	1696	1585	1226
5	3045	2956	1624	1585	1284
6 *	2920	2855	1702	1577	1284

** υ-OH appeared at 3434 cm^{-1} and υ-CO of acetyl group appeared at 1633 cm^{-1}*

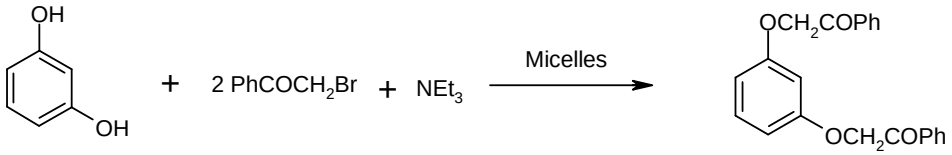
Table 2 ^{1}H NMR spectral data of phenyl phenacyl ethers(ppm)

Compound No	Aliphatic H (-O-CH_2 –CO)	Aromatic H (CO-Ar)	Aromatic H (O-Ar)
1	5.29s	7.12-7.17m	7.55-8.20m
2	5.26s	7.10-7.15m	7.53-8.00m
3	5.22s	6.89-7.50m	7.52-8.00m
4	4.42s	7.86-7.81m	7.64-7.49m
5	4.40s	7.88-7.73m	7.66-7.50m
6*	5.35s	7.27-7.55m	7.27-7.99m

** ν-OH signal appeared at 12.70 ppm as a singlet*

Table 3 Physical data of phenyl phenacyl ethers

Compound No	Yield (%)	m.p(^{o}C)	Molecular Formula	C H O Experimental (Calculated)
1	70	72-74	$C_{22}H_{18}O_4$	76.29 5.24 18.48 (76.40 5.01 18.22)
2	71	125-126	$C_{22}H_{18}O_4$	76.09 5.20 18.24 (76.29 5.24 18.20)
3	77	115-117	$C_{22}H_{18}O_4$	76.41 5.23 18.25 (76.61 5.04 18.48)
4	65	68-70	$C_{30}H_{24}O_6$	74.99 5.03 19.98 (74.71 5.26 19.67)
5	70	84-86	$C_{30}H_{24}O_6$	74.77 5.23 19.82 (74.97 5.01 19.98)
6	73	118-119	$C_{16}H_{14}O_4$	71.10 5.22 23.68 (70.20 5.25 23.56)



Scheme 1 Synthesis of phenyl phenacyl ether

The Scheme 1 shows the representation for the phenyl phenacyl ether synthesis. The –$COCH_2Br$ part of the $PhCOCH_2Br$ and OH group of PhOH (s) may be highly exposed in the hydrophilic region, whereas aromatic part of the reactants may be populated in the hydrophobic region of the micelles. In this mechanism triethylamine acts as co-surfactant [10]. The reaction may be facilitated at the interface of the micelles. The method proposed in this

investigation has advantages over other methods in terms of facile manner of preparation, use of a simple organic base(NEt_3), use of polyhydric phenols, ease of isolation of products and milder reaction conditions. Similar methods of synthesis are followed with other di and trihydric phenols. Here, one mole of trihyrdic phenol reacts with three moles of phenacyl bromide and with three mole of triethyl amine base. The stirring time of the reaction is varied corresponds to di, trihydric phenols.

IR absorption at 1284-1210 cm^{-1} indicates C-O-C ether linkage in the compounds **1-6** in Table.1. Phenyl phenacyl ether shows this band at 1220 cm^{-1}[3]. The slight increase in the frequency may be attributed to the shortening of the C-O-C bond, especially in compound **6** the presence of electron withdrawing $-COCH_3$ group causes the effect. The carbonyl absorption frequency of phenacyl ethers (**1-6**) occurs at 1606-1702 cm^{-1}. This observed value is less than that of the saturated aliphatic ketone (1715 cm^{-1}). The decrease in the value may be due to the conjugation of the carbonyl group with aromatic ring which lengthens the carbonyl bond.

The ^1H NMR spectra data of compounds **1-6** are given in Table.2. The singlet in the range 5.35- 4.40 ppm correspond to methylene protons ($-O-CH_2-CO-$) of the compounds **1-6**. This signal moves down field(5.69 ppm) in the compound (**6**). This is due to the presence of electron with drawing group $-COCH_3$ at para position. There is a free OH group in compound **6**. This is known from the NMR signal at 12.70 ppm. It is also supported by IR frequency at 3434 cm^{-1}.

Table 4 Biological data of phenyl phenacyl ethers(1-6)

Compound No	Zone of inhibition	*Staphylococcus Aureus* (Gram + ve)	*Bacillus subtilis* (Gram + ve)	*Shigella shigal* (Gram – ve)	*Pseudomonas aruginosa* (Gram – ve)
1	50mg	11	11	14	12
	150mg	12	14	17	15
	250mg	20	16	18	15
2	50mg	11	10	9	12
	150mg	22	12	15	10
	250mg	25	18	18	15
3	50mg	21	11	10	13
	150mg	23	13	16	11
	250mg	25	19	19	16
4	50 mg	11	11	14	12
	150mg	12	14	17	15
	250mg	20	16	18	15
5	50mg	10	10	13	11
	150mg	11	13	16	14
	250mg	21	15	17	15
6	50mg	12	11	10	13
	150mg	23	13	16	11
	250mg	26	19	18	15

The biological studies on compounds **1-6** reveal that they are generally active against the gram positive and gram negative micro-organisms under consideration (Table.4). Further, it has been planned to do an indepth study on the biological activities of the above compounds.

CONCLUSION

In view of the importance of ether compounds, it has been planned to prepare new phenyl phenacyl ethers from polyhydric phenols. The reactions may be facilitated at the interface of the micelles. The micelles environment has both hydrophilic and hydrophobic region. The use of organic base triethylamine acts as co-surfactant in this procedure. The method proposed in the investigation has advantage over the other methods in terms of facile manner of preparation and isolation of product. The anti- bacterial properties of these phenyl phenacyl ethers prompt to give much more attention towards the synthesis of such series of compounds.

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