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Research Article

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Solvent free synthesis of *p*-hydroxyacetophenone in a situ using eco-friendly catalyst in Fries rearrangement

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ABSTRACT

The Fries rearrangement of aromatic esters is usually performed in Lewis acid ($AlCl_3$), we have optimized this reaction with eco-friendly catalyst p-toluene sulphonic acid (PTSA) in situ. It was found to be as efficient new reagent for probing the mechanism of acylation reactions and Fries rearrangement of aromatic esters. PTSA is a strong, stable and biodegradable acid giving high conversion and selectivity (up to 90% of ortho-isomer and 10% of para-isomer at 100% conversion), Further, the conversion was confirmed by elemental and spectral Infra-red , Nuclear Magnetic Resonance, and Mass Spectroscopy (IR, 1H NMR Mass) analyses.

Keywords: Acylation, Fries arrangement, Eco-Friendly Catalyst, *p*-Hydroxyacetophenone

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INTRODUCTION

The Fries rearrangement of aryl esters, a special case of Friedel-Craft acylation provides an important route for the synthesis of aromatic hydroxyl aryl ketones that find various uses [1]. Lewis acids such as aluminium chloride [2-3], boron trifluoride [3-4], bismuth triflouride or strong protoic acid such as hydrogen fluoride, methane sulfonic acid [4-9] can be used for this reaction. But these are corrosive and environment unfriendly catalysts. For example aluminium chloride is too powerful a need to be used in reagent quantities because of its ability to strongly complex Lewis base products [10]. Method for separating the aluminium chloride is by destructive water quench leading to large volume of hazardous wastes. Thus the use of aluminium chloride [11-12] can lead to violations of several principles of green chemistry through the release in the environment of hazardous substances, which pose problem of high toxicity, corrosion and spent acid disposal[13-14]. In view of these disadvantages of the use of Lewis acids it was proposed to achieve the migration of aryl esters to corresponding hydroxyketones with compound other than Lewis acid [15-16].

EXPERIMENTAL SECTION

General Experimental: All the chemicals were obtained from E-Merck, India (AR grade) and were used without further purification. Melting points were taken in an open capillary tube. IR spectra were recorded on a Shimadzu Dr-8031 instrument. 1H NMR spectra of the synthesized compounds were recorded on a Bruker-Avance (300MHz) and Varian-Gemini 200MHz) spectrophotometer using $CDCl_3$ solvent and TMS as the internal standard.

Synthesis of *p*-Toluenesulfonic acid (PTSA).A mixture of pure toluene87g (100ml, 0.95mol) and concentrated sulfuric acid 37g (20ml, 0.35mol) was gently boiled for 1 hour and cooled, the solid *p*-toluenesulfonic acid was precipitated out. It was filtered and dried, yield 35 %, m.p.105^0- 106^0C.

Synthesis of Phenyl acetates(2a). A mixture of phenol (94g, 1mol) and dry pyridine (10ml) was placed in a 500ml beaker. It was kept in ice bath and acetic anhydride (127ml, 1.25mol) was added slowly with constant stirring. The reaction mixture was poured on a mixture of ice cold water and concentrated hydrochloric acid (50ml) and extracted with carbon tetrachloride (100ml). The extract was washed successively with water, 10% NaOH solution and again with water. It was dried over calcium chloride. The solvent was removed by distillation and phenyl acetate was collected at 195 to 197^{0}C, Yield 70 %, (Table**2.1**).

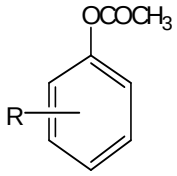
Synthesis of *o*-Tolylacetate (2b).A mixture of *o*-cresol (54g, 1mol) and dry Pyridine (5ml) was placed in a 500ml beaker. It was kept in ice bath and acetic anhydride (64ml, 1.25mol) was added slowly with constant stirring. The reaction mixture was poured on a mixture of ice (100g) and concentrated hydrochloric acid (50ml) and extracted with carbon tetrachloride (50ml). The extract was washed successively with water, 10% NaOH solution and again with water. It was dried over calcium chloride. The solvent was removed by distillation and *o*-tolyl acetate was collected at 175 to 182^{0}C, Yield 60 %,(Table **2.1**).

Synthesis of *m*-Tolyl acetate (2c).A mixture of m-cresol (54g.1mol) and dry Pyridine (5ml) was placed in a 500 ml beaker. It was kept in ice bath and acetic anhydride (64ml, 1.25mol) was added slowly with constant stirring. The reaction mixture was poured on a mixture of ice (100g) and concentrated hydrochloric acid (50ml) and extracted with carbon tetrachloride (50ml). The extract was washed successively with water, 10% NaOH solution and again with water. It was dried over calcium chloride. The solvent was removed by distillation and*m*-tolyl acetate was collected at 180 to 187^{0}C, Yield 65.1%,(Table **2.1**).

Synthesis of *o*-Chlorophenylacetate (2d).A mixture of *o*-chloro phenol (80g, 1mol) and dry Pyridine (5ml) was placed in a 500 ml beaker. It was kept in ice bath and acetic anhydride (64ml, 1.25mol) was added slowly with constant stirring. The reaction mixture was poured on a mixture of ice (100g) and concentrated hydrochloric acid (50ml) and extracted with carbon tetrachloride (50ml). The extract was washed successively with water, 10% NaOH solution and again with water. It was dried over calcium chloride. The solvent was removed by distillation and *o*-chlorophenyl acetate was collected at 175 to 182^{0}C, Yield 62.38 %,(Table**2.1**).

Synthesis of *p*-Chlorophenylacetate (2e).A mixture of *p*-chloro phenol (80g, 1mol) and dry Pyridine (5ml) was placed in a 500 ml beaker. It was kept in ice bath and acetic anhydride (64ml, 1.25mol) was added slowly with constant stirring. It was poured on a mixture of ice (100g) and concentrated hydrochloric acid (50ml) and extracted with carbon tetrachloride (50ml). The extract was washed successively with water, 10% NaOH solution and again with water. It was dried over calcium chloride. The solvent was removed by distillation and*p*-chloro phenyl acetate was collected at 175 to 182^{0}C, Yield 60%, (Table**2.1**).

Table 1. Phenyl acetates 2a-e



Compd.	R	%Yield	Solubility (NaOH)	B. p ^{0}C
2a	H	70	Insoluble	195
2b	*o*-CH_3	60	Insoluble	206
2c	*m*-CH3	65	Insoluble	216
2d	*o*-Cl	62	Insoluble	175
2e	*p*-Cl	60	Insoluble	160

Fries rearrangement of Phenyl acetate into*para*-Hydroxyacetophenone

***p*-Hydroxyacetophenone(4a)**.The white solid residue obtained during the isolation of *o*-hydroxyacetophenone above (Expt.7) was crystallized in petroleum ether. Yield 30%, m.p.110^{0}C. (Table **2.3**) UV: λmax 275 mμ, IR (KBr): 3300 cm^{-1}, br (-OH); 1650 cm^{-1}str (-CO); 3000 cm^{-1}str (C-H); 2910 cm^{-1} (-CH_3) in methyl.

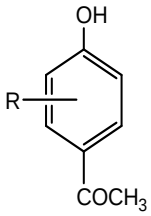
4-Hydroxy-3-methylacetophenone(4b). The white solid residue obtained during the isolation of 2-hydroxy-3-methyl acetophenone above (Expt.9) was crystallized with petroleum ether. Yield 30%, m.p.109^{0}C. (Table **2.3**). UV: λmax 280 mμ, ^{1}H NMR ($CDCl_3$) ppm[2.30(s, 3H)]–CH_3; [2.57 (s, 3H)] –CH_3; [6.80-7.82 (m,3H)] –Ar-H.

4-Hydroxy-2-methylacetophenone(4c).The off white solid residue obtained during the isolation of 2-hydroxy-6-methyl acetophenone above (Expt.11) was crystallized it with petroleum ether. %Yield = 30m.p. 135^{0}C. (Table

2.3).UV: λmax 264 mμ, IR (KBr): 3180 cm^{-1}, br (-OH); 1680cm^{-1}str (-CO); 2990 cm^{-1}str (C-H); 600-870 cm-1, ben (C-H).

4-Hydroxy-3-chloroacetophenone(4d). The white solid residue obtained during the isolation of 2-hydroxy -3-chloro acetophenone above (Expt.13) was crystallized it with petroleum ether. Yield 30% m.p. 147^0C.(Table **2.3**). IR (KBr): 3405cm^{-1}, br (-OH); 1630cm^{-1}str (-CO); 2910 cm^{-1}str –(C-H) str in CH_3; 3040 cm^{-1}(Ar-H); 1450 cm^{-1}str (C=C). 800 cm^{-1}str -(C-Cl).

Table 2.*p*-Hydroxyacetophenones4a-d



		% Yield Conventional Method		% Yield MW Process				Solubility (NaOH)
Compd.	R	AlCl3	PTSA	ALCl3	PTSA	FeCl3	m.p. ^{0}c	
4a	H	40	45	42	46	Voilet	109	Soluble
4b	*m*-CH3	35	42	39	44	Voilet	130	Soluble
4c	*o*-CH3	38	42	40	44	Voilet	107	Soluble
4d	*0*-Cl	40	44	41	45	Voilet	140	Soluble

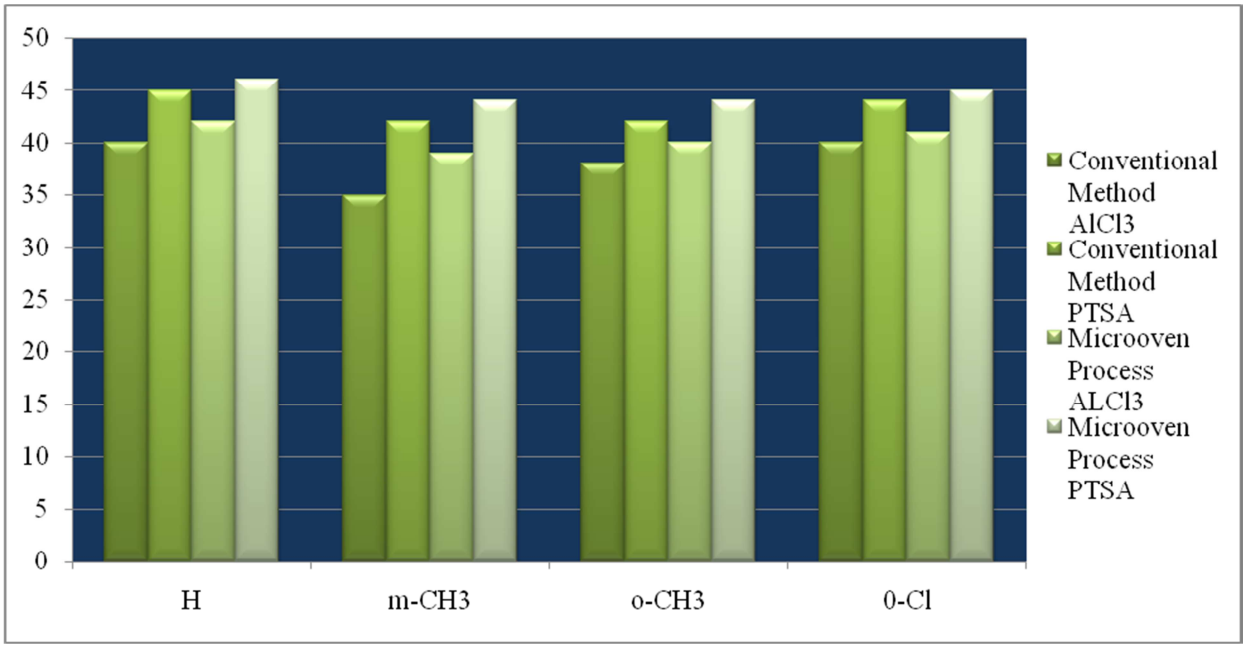
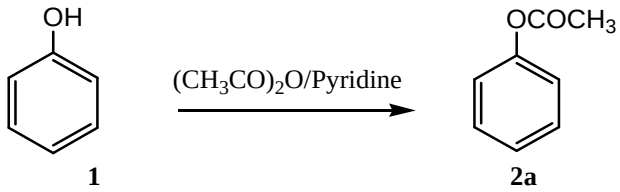


Figure 1.Comparative chart of synthesized *p*-Hydroxyacetopheneone by conventional and micro oven method using $AlCl_3$ and eco-friendly catalyst (PTSA)

RESULTS AND DISCUSSION

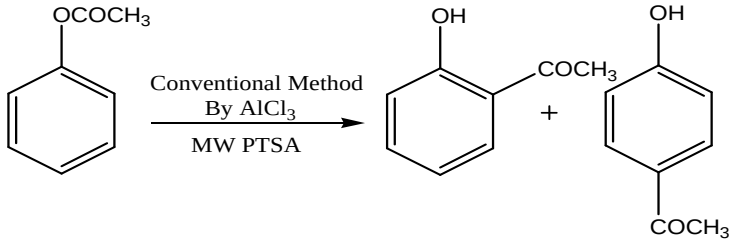
The Fries rearrangement was performed at 90^0-160^0C without any solvent using catalytic amount of *p*-toluenesulfonicacid. The yields of products were obtained near about same as that of with aluminium chloride ($AlCl_3$). The reaction time was also importance, 98% conversion of phenyl acetates **2a** was achieved within 30 min.at 90^0-160^0C.The ortho/para ratio **3a/4a** was always in favour of the desired compound **3a** and decreased during the conversion of phenyl acetates. The reaction may be carried out under optimized temperature, low temperature favours the formation para product and high temperature favours the formation ortho product. The synthesized

compounds have been confirmed on the basis of elemental analysis and spectral data. It was found to be very important to use an anhydrous*p*-toluenesulfonic acid, as traces of water hydrolyse phenyl acetate **2a** to phenol and acetic acid. The comparative chart of synthesized *p*-Hydroxyacetopheneone by conventional and micro oven method using $AlCl_3$ and eco-friendly catalyst (PTSA) have presented in Figure **1**.



1 **2a**

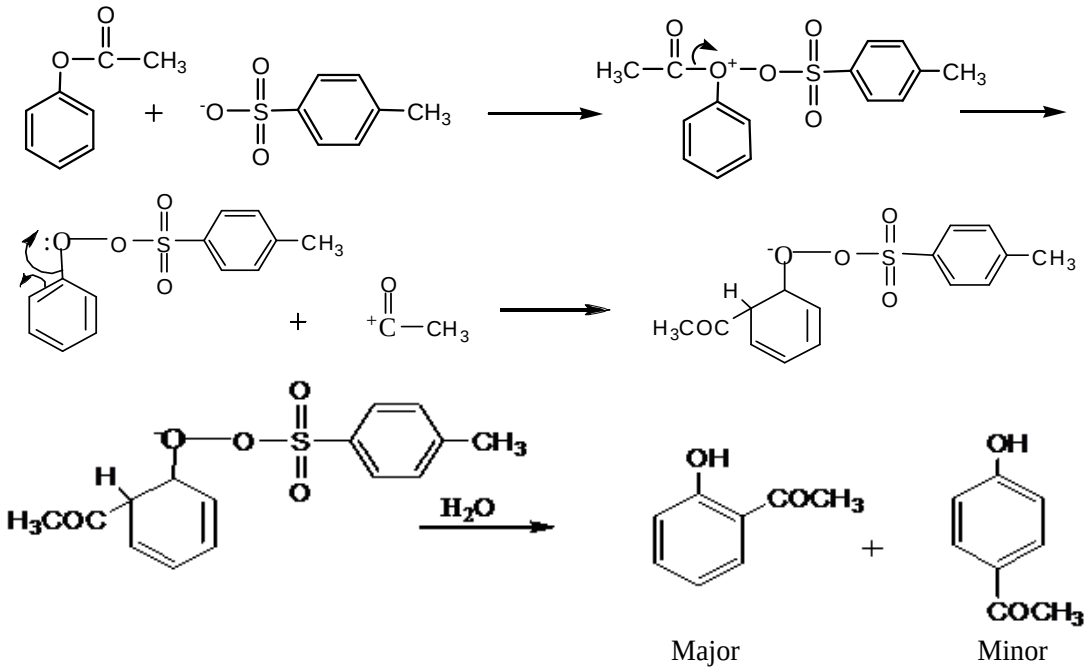
Scheme 1: Synthesized the Phenyl acetate from Phenol



2a **3a** **4**

Scheme 2: Fries of Phenyl acetate into Ortho/Para Hydroxyacetopnenone

MECHANISM



Major Minor

CONCLUSION

p-Toluenesulfonicacid a biodegradable white solid, was used in the Fries rearrangement of phenyl acetate to*o*-hydroxyacetophenone and *p*-hydroxyacetophenone with very good conversion of around 98% and very good yield of the ortho product. To obtain such performances, a molar ratio of *p*-toluenesulfonic acid is not necessary. Hydroxyketones were easily separated from the aqueous solution by extraction with organic solvents.*P*-Toluenesulfonic acid is a biodegradable and easy to handle. It performances are similar to aluminium chloride (yield, conversion, selectivity) and has lower impact on the environment.

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