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Synthesis and characterization of *o*-hydroxyarylalkylketones by using eco-friendly solvent free catalyst in frie's 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 p-toluene sulphonic acid (PTSA). 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 (IR, ^1H NMR Mass) analyses.

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

INTRODUCTION

The Fries rearrangement of aryl esters, a special case of Friedel-Craftacylationprovides an important route for the synthesis of aromatic hydroxyl aryl ketones that find various uses[1]. Lewis acids such asaluminiumchloride[2-3],boron triflouride[3-4], bismuthtriflouride or strong protoic acid such as hydrogen fluoride, methane sulfonic acid[4-9]can be used for this reaction. But theseare corrosive and environment unfriendly catalysts. For example aluminium chloride is too powerful a need to be used in reagent quantities because of itsability to strongly complex Lewis base products[10]. Method for separating thealuminium chloride is by destructive water quench leading to large volume of hazardous wastes. Thus the use ofaluminium chloride 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.

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[11-12].

MATERIALS ANDMETHODS

General: All the chemicals were obtained from E-Merck, India (AR grade) andwere used without further purification. Melting points were taken in an open capillary tube.IRspectra were recorded on a Shimadzu Dr-8031 instrument. 1H NMR spectra of the synthesizedcompounds were recorded on a Bruker-Avance(300MHz) and Varian-Gemini (200MHz)spectrophotometer using CDCl3 solvent and TMS as an 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^{0}C.

Synthesis of Phenyl acetates.Phenyl acetate**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% NaOHsolution 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*-Tolylacetate2b.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**).

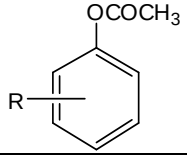
Synthesis of*m*-Tolyl acetate2c.A mixture of m-cresol (54g.1mol) and dry Pyridine (5ml) was placed in a 500 ml beaker. It was kept in ice bath and acetic anhydride (64ml, 1.25mol) was added slowly with constant stirring. The reaction mixture was poured on a mixture of ice (100g) and concentrated hydrochloric acid (50ml) and extracted with carbon tetrachloride (50ml). The extract was washed successively with water, 10% NaOHsolution 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*-Chlorophenylacetate2d.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% NaOHsolution 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*-Chlorophenylacetate2e.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% NaOHsolution and again with water. It

wasdried 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 2.1Phenyl acetates 2a-e



Compd.	R	%Yield	Solubility (NaOH)	B. p ^{0}C
2a	H	70	Insoluble	195
2b	*o*-CH_3	60	Insoluble	180
2c	*m*-CH3	65	Insoluble	185
2d	*o*-Cl	62	Insoluble	175
2e	*p*-Cl	60	Insoluble	172

Fries rearrangement of Phenyl acetate into Hydroxyacetophenone

Synthesis *o*-Hydroxyacetophenone3a.Phenyl acetate **2a**(10g, 0.073mol)was poured in 100 ml round bottom flask containing *p*-toluenesulphonicacid (7g, 0.042mol). The reaction mixture was heated on an oil bath at 100-110^{0}C for 30 minutes. It was poured on ice cold water with vigorous stirring, a mixture of *o*-hydroxyacetophenone (liquid) and*p*-hydroxyacetophenone(solid) was obtained.*o*-Hydroxyacetophenone was isolated by steam distillation. Yield 60%, b.p.213^{0}C.(Table**2.2**). UV:λmax274 mμ,IR (KBr): 3385 cm^{-1},br (-OH); 1650 cm^{-1}str(-CO); 2940 cm^{-1}str (C-H); 3008 cm^{-1}(-CH_3) in methyl.

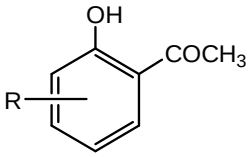
Synthesis of2-Hydroxy-3-methylacetophenone3b.*o*-Tolyl acetate **2b**(10g, 0.066mol)was poured in 100ml round bottom flask containing*p*-toluenesulphonicacid (8g, 0.048mol). The reaction mixture was heated on an oil bath at 90-120^0 C for 30 minutes.It was poured in ice cold water with vigorous stirring, a mixture of 2-hydroxy-3-methylacetophenone (liquid) and 4-hydroxy-3-methylacetophenone (solid) was obtained. *o*-isomer wasisolatedby steam distillation. Yield 75%,b.p.237^{0}C.(Table**2.2**). UV: λmax255 mμ, ^{1}H NMR ($CDCl_3$) ppm: [12.05 (s, 1H)] -OH; [2.24-2.30 (s, 3H)] –CH_3; [2.59-2.63 (s, 3H)] –CH_3;[6.50-8.10 (m,3H)] –Ar-H.

Synthesis of2-Hydroxy-4-methylacetophenone3c.*m*-Tolyl acetate**2c** (10g, 0.066mol)was poured in 100ml round bottom flask containing *p*-toluenesulphonicacid (8 g, 0.042mol). The reaction mixture was heated on an oil bath at 90-110^0 C for 30 minutes.It was poured in ice cold water with vigorous stirring, a mixture of 2-hydroxy-4-methylacetophenone (liquid) and 4-hydroxy-2-methyl acetophenone (solid) was obtained. 2-Hydroxy-4-methyl acetophenone isomer was isolated by steam distillation method. Yield 60% b.p.242^{0}C(Table**2.2**).UV:λmax270 mμ, IR (KBr): 3410 cm^{-1}, br (-OH); 1770cm^{-1}str (-CO); 2910 cm^{-1}str (C-H); 675-870 cm-1, ben (C-H).

Synthesis of2-Hydroxy -3-chloroacetophenone 3d.*o*-Chlorophenylacetate**2d** (10g, 0.091 mol) was in 100ml round bottom flask containing *p*-toluenesulphonicacid (9 g, 0.052 mol). The reaction mixture was heated on an oil bath at 80-110^0 C for 30 minutes.It was poured in ice cold water with vigorous stirring, a mixture of 2-hydroxy -3-chloro acetophenone(liquid) and 4-hydroxy-3-chloro acetophenone(solid) was obtained. 2-Hydroxy -3-chloro acetophenoneisomer was isolated by steam distillation. Yield 58%b.p. 92^{0}C (Table **2.2**).IR (KBr): 3405cm^{-1},br (-OH); 1630cm^{-1}str (-CO); 2910 cm^{-1}str–(C-H) strin CH_3; 3040 cm^{-1}(Ar-H); 1450 cm^{-1}str (C=C). 800 cm^{-1}str-(C-Cl).

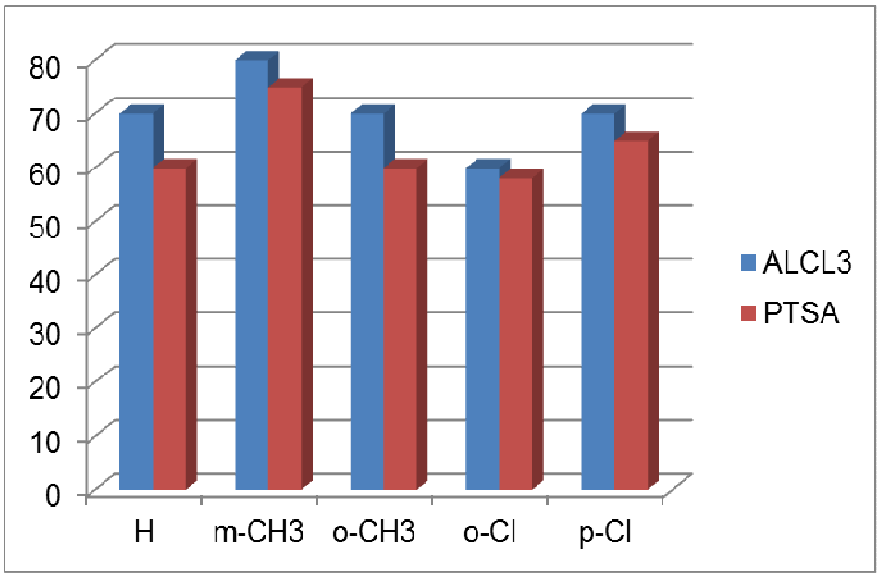
Synthesis of2-Hydroxy-5-chloroacetophenone3e.*p*-Chlorophenyl acetate**2e** (10g, 0.091mol) was in 100 ml round bottom flask containing *p*-toluenesulphonicacid (9 g, 0.052 mol). It was heated on an oil bath at 90-120^{0}C for 30 minutes. The reaction mixture was poured in ice cold water with vigorous stirring, a single compound of 5-chloro-2-hydroxyacetophenone (liquid) was obtained *o*-chlorohydroxyacetophenoneisomer was isolatedby steam distillation.Yield 65%.b.p.128^{0}C (Table **2.2**) IR (KBr): 3405cm^{-1}, br (-OH); 1630cm^{-1}str (-CO); 2910 cm-^{1}str –(C-H) strin CH_3; 3040 cm^{-1}(Ar-H); 1450 cm^{-1}str (C=C) 800 cm-1 str-(C-Cl).

Table**2.2**. *o*-Hydroxyacetophenones**3a-e**



Compd.	R	% Yield $AlCl_3$	% Yield PTSA	$FeCl_3$	B.p^{0}C	Solubility (NaOH)
3a	H	70	60	Violet	213	Soluble
3b	*m*CH_3	80	75	Violet	237	Soluble
3c	*o*-CH_3	70	60	Violet	242	Soluble
3d	*o*-Cl	60	58	Violet	92	Soluble
3e	*p*-Cl	70	65	Violet	128	Soluble

Comparative Chart of formation of Product by Both the Catalyst $AlCl_3$ and PTSA.

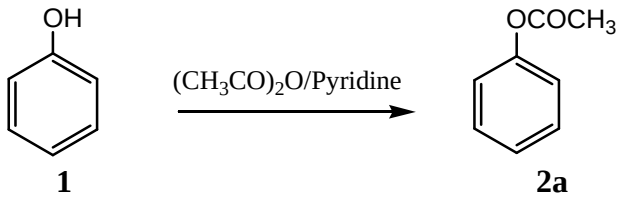


RESULTS AND DISCUSSION

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

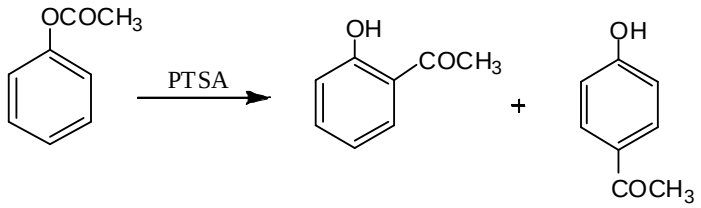
synthesized compounds have been confirmed on the basis of elemental analysis and spectral data. It was found to be veryimportantto use an anhydrous*p*-toluenesulfonic acid, as traces of waterhydrolysephenyl acetate**2a**to phenol and acetic acid.

Scheme 1: Synthesized of Phenyl acetate from Phenol.



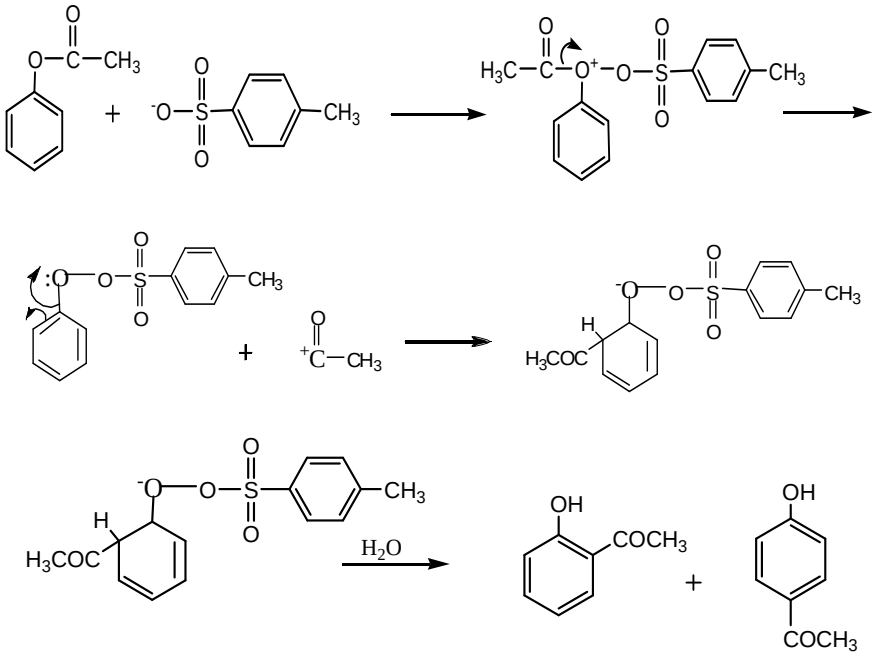
1 **2a**

Scheme 2: FriesofPhenyl acetate into Ortho/Para Hydroxyacetophenone.



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

Mechanism of reaction



CONCLUSION

p-Toluenesulfoni cacid a biodegradable white solid, was used in the Fries rearrangement of phenyl acetate too-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 acidis a biodegradable and easy to handle. It performances are similar toaluminium chloride (yield, conversion, selectivity) and has lower impact on the environment.

REFERENCES

[1]F. J. Waller, R. W. Van Scoyoc, *Chem. Tech.*,**1987**, *17*, 438.
[2]B.B. Ramesh, IN **1993**,171,970 ShasunChemicals(m) Ltd., India
[3]M.B. Hocking, J.Chem.Technol.Biotechnol.**1980**, 30,626.
[4]J.L. Boyer, J.Org.Chem.**2000**,65,4712.
[5]P.A.Staniland, EP**1982,**57, 503, Imperial ChemicalIndustries PLC, UK.
[6] M. Kusuda, JP**1987**, 62, 234Asahi ChemicalIndustry Co., Ltd., Japan.
[7] A. Behr, DE**1998**, 19, 736, Henkel K.-G.a.A.,Germany.
[8] H. Sharghi, J.Chem.Res., Synop. **1998**,10, 628.
[9]B.Kaboudin, Tetrahedron**1999**,55 12865.
[10]W. B. Jensen, **1980**.*The Lewisacid-baseconcepts: an overview*.New York: Wiley.
[11]Yamamoto,Hisashi**1999**.*Lewisacidreagents: a practical approach*. New York: