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Fries rearrangement of 3,5-dimethoxyphenyl acetate

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Abstract

3,5-dimethoxyphenyl acetate was studied in the presence of Lewis acid catalyst in different type of solvent (CS_2 , CH_2Cl_2 , C_6H_5Cl and CH_3NO_2) and different temperatures (25^oC and reflux). All the products of the rearrangement were isolated and identified by spectrophotometrically methods. The products were checked by using gas – liquid chromatography and the ortho isomer was the majer one and in many times was the unique.

Key words: Fries rearrangement, 3,5-dimethoxyphenyl acetate,

Introduction :

Phenolic esters [1] can be rearranged by heating with Friedel-Crafts catalysts in a synthetically useful reaction known as the Fries rearrangement [2-5]. Both ortho and para acetylphenols may be produced. The o/p ratio is depended on the temperature, solvents and the amount of catalyst used [6].

The reaction as a whole and specially the catalyst should be anhydrous lewis acid and the ratio of catalyst : ester is important. Though exception that the para product will favour low temperature and the ortho product will favour high temperature.

Many studies were done by using equal moles of ester and catalyst with or without using solvents, the excess of catalyst (2 moles or more) will introduce not only the migration of acyl groupbut also any alkyl group present in the molecule studied [7].

The mechanism of Fries rearrangement till now was unclear, it will be either an intramolecular [3] or intermolecular [8,9] rearrangement . Blatt [10] was proved by cross over experiment that both inter and intramolecular mechanism was found in Fries reaction.

Finally, Fries rearrangement look like Friedel-Crafts reaction due to the presence of unreacted lewis acid which interferes the compounds which are formed from the dissociation of ester to the corresponding phenols or its salt and the acyl chloride.

Experimental

The nuclear magnetic resonance spectra (NMR) were obtained with a Jeol FT-90 spectrometer, using $CDCl_3$, as a solvent. Infrared spectra were determined with a PYE-UNICAM SP3-100 infrared spectrophotometer , using KBr disc and NaCl cell for the solid and liquid unknown on analysis.

g.l.c. data were done by PYE UNICAM Series 304 Gas Chromatography with FID and PV 4810 computing integrator using He as a carrier gas in 250 c with a colum 10% SE 30 on acid washed chromosorb "W" 80-100 mesh stainless steel column $4x\frac{1}{4}$, rate of flowoof He = 3 ml/min. all the chemicals were obtained from FLUKA company.

Prepration of the 3,5-dimethoxyphenyl acetate (1):

To a mixture of 3,5-dimethoxyphenol (7.7 gm , 0.5 mole) and acetic anhydride (11.2 gm , 0.11 mole), concentrated sulphuric acid (0.5 ml) was added. Heat the resulting mixture on a water bath for three hours, cool then pour the mixture on ice/water (200 ml) Extract with diethylether (150 ml), neutralize the ether layer with sodium carbonate solution, then dry it anhydrous sodium sulphate, filterate and evaporation yielded a yellow oily liquid (I). Purification was done by distillation to give a colorless oily liquid, b.p 92 ^oC , υ_{max} =1750 cm^{-1}. The PMR (δ=ppm) = 2.35 (3H,S,-$COCH_3$) ; 3.73 (6H,S,3-OCH_3,S-OCH_3) ; 658 (2H,S,H_2 and H6) ; 6.9 (1H,S,H4).

Results and Discussion :

Table (I), shows the physical data of the two isomers (2 and 3) and Table (II), represents the values of relative retention time for the products corresponding to the reactant.

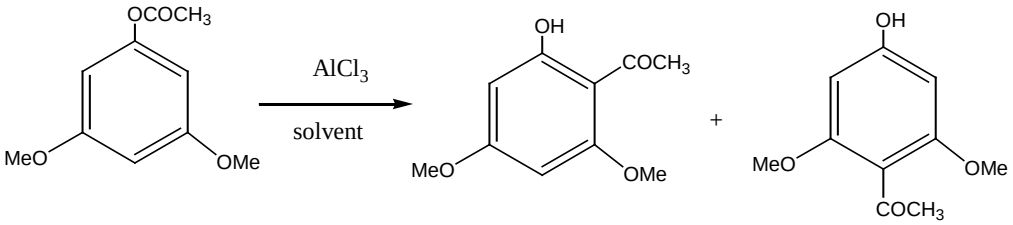
Table (I): physical data of phenols (2 and 3)

Compound name and number	m.p	υ_{max} cm^{-1}	nmr data s(ppm)
2,4-dimethoxy-6-hydroxy-acetophenone (2)	139^{o}C	1648 (CO) 3122 (OH)	2.41 (3H,S,-$COCH_3$) 3.70 (3H,S,4-OCH_3) 3.81 (3H,S,2-OCH_3) 6.70(1H,S,H3) 6.75(1H,S,H5) 12.81(1H,S,OH)
2,6-dimethoxy-4-hydroxy-acetophenone (3)	171^{o}C	1662 (CO) 3449 (OH)	2.21 (3H,S,-$COCH_3$) 3.65 (6H,S,2-a6-OCH_3) 6.78 (2H,S,H3 and H5) 10.1(1H,S,OH)

Table (II): Gas liquid chromatography analysis for the relative relation time (R.R.T) for compounds 1,2 and 3 corresponding to the 3,5-dimethoxy phenols

Compound name and number	R.T cm*	R.R.T
3,5-dimethoxy phenol	2.1	1.0
3,5-dimethoxyphenyl acetate (1)	4.3	2.4
2,4-dimethoxy-6-hydroxy-acetophenone (2)	8.1	4.0
2,6-dimethoxy-4-hydroxy-acetophenone (3)	7.2	3.4

* speed of chromatogram = 350 cm/min



First of all, there is no rearrangement happened in the absence of lewis acid in highly temperature and in the presence of solvents (nitromethane, chlorobenzene….etc.) or without using solvent .

Fries reaction is a really catalytic rearrangement and irreversible (proved by heating the acetylphenol in the same solvents dose not give the ester). The check was done by g.l.c. technique.

Table (III) shows that always the migration of the acyl group to the ortho position except for the nitromethane also the yield of the ketone increase with temperature except for carbondisulfide (there was a heterogenous solution because of weak ability of CS_2 to dissolve the aluminum chloride complex, when the scission of ester, Acetyl chloride (high volatile) will not have the requird time to form the acylating complex, then it will be volatile so that it explained the highly percentage of phenol (34.4).

Table (III) : Gas-liquid chromatographic analysis of Fries reaction of 3,5-dimethoxyphenyl acetate (1) by using 1:1 molar ratio (ester : $AlCl_3$) for two hours.

Solvent (20 ml)	Temp.°C	% phenol	% ketone	Isomer distrib	
				o-	p-
CS_2	25 reflux	18.83 34.4	23 2.4	100 100	- -
CH_2Cl_2	25 reflux	28.4 14.86	20.7 25.7	100 100	- -
C_6H_5Cl	25 reflux	23 14	12 85	100 100	- -
CH_3NO_2**	25 reflux	29.32 27	3 57	96.7 99.05	3.7 0.34

** compounds 2 and 3 were isolated by using column chromatography (silicagel 230-240 mesh, eluent was bezene : petroleum ether 1:3) then the products werea crystallized from ethanol

The percentage of ortho isomer except for nitromethane always 100% that means the mechanism of rearrangement is intramolecular (forming a cyclic chelating complex between the catalyst and ester, its stability increased with highly temperature).

On the other hand we cannot ignored the intermolecular rearrangement which formed from the complex (CH_3COCl : $AlCl_3$) and this complex explained the low yield of the para isomer in nitromethane , this solvent have the ability to react with the complex (CH_3COCl : $AlCl_3$) , then partial ionization formed free acetylating agent with low concentration to formed the para isomer (highly steric hinderance isomer).

To prove the intermolecular reaction, Table (IV) shows the using of reactive molecule as a competiting reagent ; like mesitylene in the presence of AlCl3 , from glc data acetyl mestiylene were presented . when we duplicated the moles of catalyst ; the yield of acyl mestiylene increased , this

mean that CH_3CO^+ becomes free in the medium and reacted with $AlCl_3$ to form the complex which attack the mestiylene . Figure (I) shows the mechanism proposed. Finally, $AlCl_3$ was the effective lewis acid than $ZnCl_2$ and $FeCl_3$, due to high yield.

Table (IV): Gas-liquid chromatographic analysis of Fries reaction of (1) in the presence of mesitylene in chloroform solvent for 2 hours

Temp. ^oC	Molar ratio acetate:mestiylene: $AlCl_3$	% acyl mestiylene	% ketone	Isomer distrib	
				o-	p-
35	1:1:1	0.1	0.4	100	-
reflux	1:1:1	1.3	30.4	100	-
35	1:1:2	8.1	9.9	100	-
reflux	1:1:2	1.24	97.1	100	-

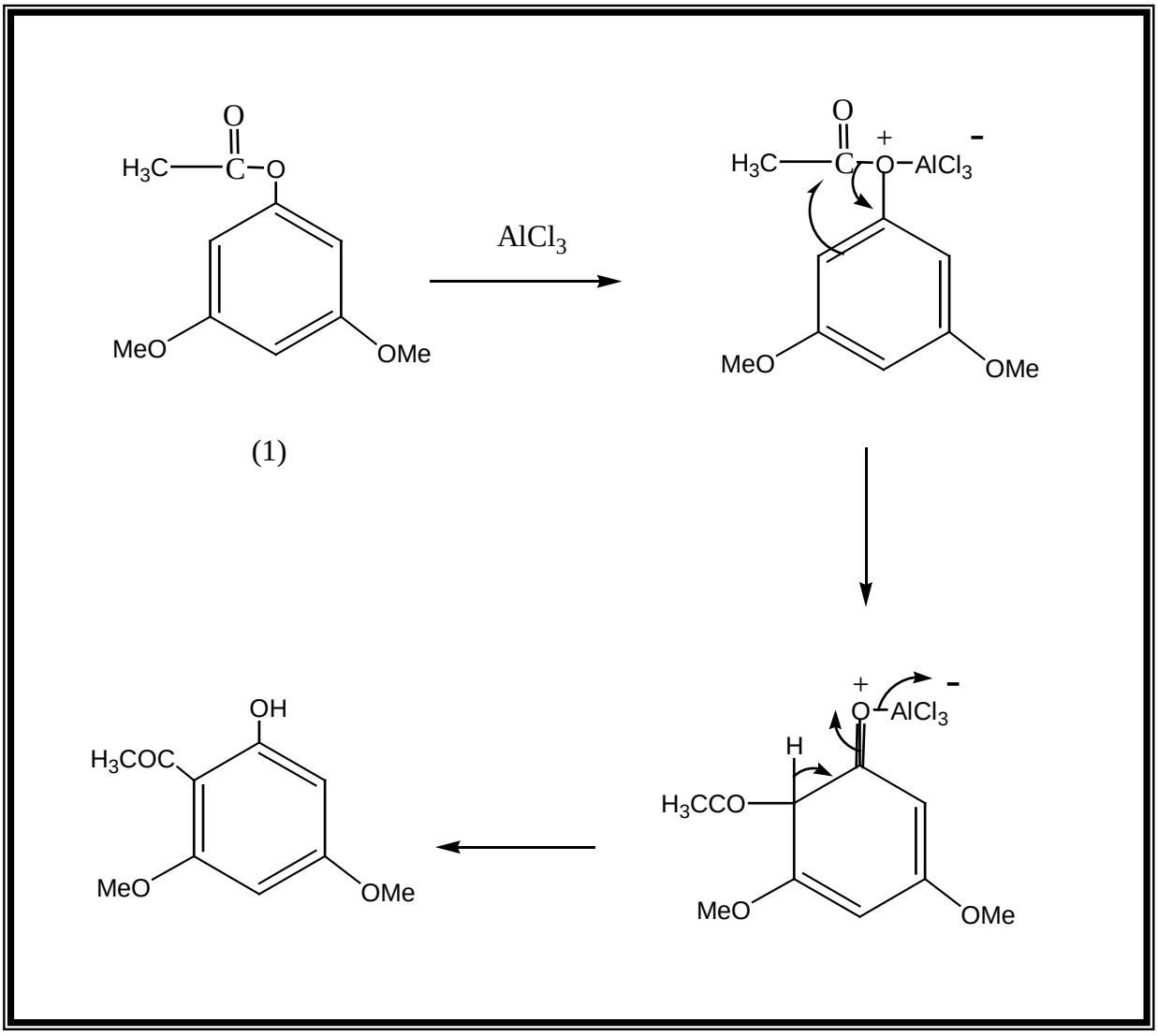


Figure (1) : mechanism of the migration of acyl group

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