A study of probing the mechanism of acylation reactions and fries rearrangement by polyphosphoric acid (PPA).

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Abstract

[P.sub.2][O.sub.5]/[H.sub.3]P[O.sub.4] (PPA) was found to be an efficient new reagent for probing the mechanism of acylation reactions and Fries rearrangement of acyloxy benzene derivatives and also the direct acylation reactions of phenol derivatives with Carboxylic acids. The reactions proceeded smoothly in the presence of PPA and are highly selective for the preparation of the ortho isomers of hydroxyaryl ketones.

In the same way we have investigated the effects of ortho, meta and para substituents on the acylation reactions of benzoic acid derivatives and also Fries rearrangement in PPA.

Keywords: Polyphosphoric acid (PPA), Acylation reactions, Fries rearrangement, Hydroxyaryl Ketones, Phenol derivatives.

Introduction

Hydroxyaryl ketones are versatile intermediates in the synthesis of biologically active benzoquinone, pesticides, photographic agents, UV absorbents, phenols containing liquid crystal (LC) polymers and low molecular weight mesogens [1-4]. Fries rearrangement is a synthetically useful reaction for the preparation of hydroxyaryl ketones, not only in laboratory but also in industrial processes [5]. Conducted thermally in the presence of friedel-crafts catalysts or photochemically by irradiation with UV such reactions typically give rise to mixtures of ortho- and para- substituted products, the proportion of each is strongly influenced by the reaction media [6]. To overcome this problem, new catalysts such as Hf[(OTf).sub.4] [7], Sc[(OTf).sub.3] [8], Zr[Cl.sub.4] [9], montmorillonite clays [10] and methanesulfonic acid/ phosphorous oxychloride [11] have been developed recently for this reaction. However, most of these catalysts suffer serious drawbacks, which include the use of hazardous and expensive or commercially unavailable reagents, long reaction times, low yields, drastic reaction conditions and tedious workup procedures. On the other hand, an alternative method is direct acylation of phenol derivatives using Al[Cl.sub.3] [12] or HCl[O.sub.4] [13] as a promoter. However, with these catalysts, long reflux time is required and in some cases undesired products are obtained. Therefore, the development of a new catalyst that promotes the direct acylation of phenols or the Fries rearra ngement cleanly and regioselectivety is required.

In this work we probed the mechanism of Fries rearrangement of acyloxy benzene derivatives based on the mechanism which suggested by H. sharghi etal [14] in 1991, they suggested an intermolecular mechanism for the formation of the hydroxybenzophenone D via Fries rearrangement of the ester B (Scheme 1).

[ILLUSTRATION OMITTED]

In addition, we optimized the best conditions to achieve the Fries rearrangement. We also then found that PPA is a novel, mild and efficient reagent to perform this rearrangement.

In the same way, we investigated the effects of ortho- meta- and para- substituents on acylation reactions of benzoic acid derivatives and also Fries rearrangement in PPA (Scheme 2 and Tables 1, 2 and 3)

[ILLUSTRATION OMITTED]

According to Tables 1, 2 and 3 the increase in the substituent's electron donating power, considerably increases the rearrangement from the ester B and vice versa. Therefore, the Fries rearrangement mechanism may be in agreement with the free acylinium ion (Intermolecular rearrangement) mechanism and not related to the [pi]-cmplex (Intermolecular rearrangement) mechanism.

Finally, it could be seen from the above results and with respect to the structure of acylinium ion, that in the presence of electron donating substituents on benzene ring, rearrangement products, increase since stability of acylinium ion is related to the influence of these substituents and vice versa.

In fact, the increase in the electron donating power of substituents on the ortho-, meta- and para-positions of benzene ring notably increases the yields of the ortho-OH(D) isomers and also conversely, the increase in electron withdrawing power of the substituents on the ortho-, meta- and para- positions of benzene ring remarkably affects the rearrangement and ortho-OH(D) isomers are not produced.

In conclusion, considering the above discussion and also G=OH, [NH.sub.2], Cl, Br, N[O.sub.2] and H, it could be clearly seen that the formation of hydroxybenzophenones from Fries rearrangement of the ester (B) occurs via an intermolecular mechanism.

Experimental

Solvents, Reagents and Chemical materials were obtained from the Merck chemical company (West Germany) and Fluka (Switzerland).

Method of calculation for the data reported in the tables

The data reported in the tables were calculated according to the following method. After taking the [sup.1]H-NMR Spectrum of the reaction mixture and drawing a line below the mixture spectrum in the region [delta] (1-3) lengths of the peaks appeaing for the C[H.sub.3] groups which it has measured using a ruler. The lengths of the C[H.sub.3] signals were added up to gether and then the length of each C[H.sub.3] signal was divided by that sum, the resulting value of which was multiplied by 100%. To optain the percentage of each mixture component.

Percent of each component = Length of each C[H.sub.3] peak/Summation of C[H.sub.3] peak lengths x 100%

The expected error of the NMR instrument for this method of calculation was taken to be [+ or -] 0.05%.

General Procedure for the Fries Rearrangement

Representative procedure: A mixture of o-substituted benzoic acid (0.01 mol) and m-cresol (0.01 mol, 1mL) was added to PPA (freshly prepared from 5 mL of [H.sub.3]P[O.sub.4] and 8g of [P.sub.2][O.sub.5]) and heated with stirring 70 [degrees]C for 1hr. Then the reaction mixture was then poured into cold water, extracted with chloroform (200mL), washed with the sodium hydrogen carbonate solution (2 x 150mL) and died with calcium chloride. The solvent was finally evaporated in a, rotary evaporator.

Condensation of o-methoxybenzoic Acid and m-cresol

A mixture of o-methoxy benzoic acid (0.01 mol 1.25g and m-cresol (0.01 mol, 1mL) was added to PPA (freshly prepared from 5mL) [H.sub.3]P[O.sub.4] and 8g [P.sub.2][O.sub.5]) heated with stirring at 70[degrees] C for 1hr., after which time it was poured into cold water, extracted with dichloromethane (200 mL) and washed with the sodium hydrogen carbonate solution (2 x 150 mL) and the resulting solvent dried with calcium chloride and them evaporated the solvent on the rotary evaporator.

The resulting mixture was chromatographed over silicagel. Elution with hexane-CH[Cl.sub.3] (1:1) gave 2'-methoxy-4-hydroxy-2-methylbenzophenone (C , 20%) as white crystal is (m.p: 105-110 [degrees]C). Further elution with CH[Cl.sub.3]-C[H.sub.3]OH (5:1) yielded 2'-methoxy-2-hydroxy-4-methylbenzophenone (D,30%) as orange needles (m.p:75-80[degrees] C).

2'-methoxy-2-hydroxy-4-metylbenzophenone (D) [sup.1]HNMR, CD[Cl.sub.3], [delta], 2.35 (s, 3H, C[H.sub.3]), 3.7 (s, 3H, OC[H.sub.3]), 6.4 (d, 1H, J=4Hz), 6.75 (d, 1H, J=4Hz), 6.95-7.5 (Multiplet, 5H), 12(s 1H, OH). IR, [v.sub.max] (KBr); 3700-3000 (b), 2940 (w), 1650 (w), 1600 (s), 1560 (w), 1490 (m), 1450 (m), 1430(m), 1300 (s), 1250 (s), 1100 (m), 750 (s), 700 (w), 620 (m) UV [[lambda].sub.max] (dioxane) 269, 330 nm.

2'-methoxy-4-hydroxy-2-metylbenzophenone (C)

This compound was obtaind when the above reaction was carried out at 70 [degrees]C for 6 hr. and recristalised in 1:1 ratio of hexane/C[H.sub.2][Cl.sub.2] (793 mg, 70%).

[sup.1]HNMR, CD[Cl.sub.3], [delta],2.45(s,3H, C[H.sub.3]), 3.6(s, 3H, OC[H.sub.3]),6.5-7.5 (Multiplet, 7H): IR [v.sub.max] (KBr); 3500-3000(b), 3000 (w), 2040 (m), 1950 (m), 1900 (m), 1780 (m), 1650-1430 (b), 1390 (m), 1330-1200 (b), 1100 (s), 1020 (s), 910 (s), 870 (s), 830 (s), 750 (s), 700 (m), 620 (s): UV [[lambda].sub.max] (dioxane), 280 nm.

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Table 1: The effect of ortho-substituents on acylation reactions and Fries rearrangement in [P.sub.2][O.sub.5]-[H.sub.3]P[O.sub.4] mixtures.

No.	G	Comp (A)%	Comp. (B)%	Comp. (C)%
1	H	0	100	0
2	OC[H.sub.3]	45	1	21
3	C[H.sub.3]	30	36	15
4	OH	52	48	0
5	N[H.sub.2]	100	0	0
6	Cl	5	63	9
7	Br	5	59	0
8	N[O.sub.2]	42	46	0

No.	Comp. (D)%	Comp. (E)%	Comp. (F)%	Rearrangement from ester (B)%
1	0	0	0	0
2	33	0	0	98
3	19	0	0	49
4	0	0	0	0
5	0	0	0	0
6	13	10	0	35
7	16	20	0	38
8	12	0	0	21

Table 2: The effect of metha-substituents on acylation reactions and Fries rearrangement in [P.sub.2][O.sub.5]-[H.sub.3]P[O.sub.4]

mixtures.

No.	G	Comp (A)%	Comp (B)%	Comp. (C)%
1	H	0	100	0
2	OC[H.sub.3]	15	55	13
3	C[H.sub.3]	_	_	_
4	OH	30	63	7
5	N[H.sub.2]	100	0	0
6	Cl	82	18	9
7	Br	39	61	0
8	N[O.sub.2]	100	0	0

No.	Comp. (D)%	Comp. (E)%	Comp. (F)%	Rearrangement from ester (B)%
1	0	0	0	0
2	17	0	0	35
3	_	_	_	_
4	0	0	0	10
5	0	0	0	0
6	0	0	0	0
7	0	0	0	0
8	0	0	0	0

Table 3: The effect of p-substituents on acylation reactions and Fries rearrangement in [P.sub.2][O.sub.5]-[H.sub.3]P[O.sub.4] mixtures.

No.	G	Comp (A)%	Comp . (B)%	Comp. (C)%
1	H	0	100	0
2	OC[H.sub.3]	28	42	0
3	C[H.sub.3]	31	50	3
4	OH	43	49	8
5	N[H.sub.2]	82	18	0
6	Cl	64	36	9
7	Br	62	38	0
8	N[O.sub.2]	100	0	0

No.	Comp. (D)%	Comp. (E)%	Comp. (F)%	Rearrangement from ester (B)%
1	0	0	0	0
2	30	0	0	42
3	14	0	0	25
4	0	0	0	14
5	0	0	0	0
6	0	0	0	0
7	0	0	0	0
8	0	0	0	0