

PREPARATION OF NITROHYDROXY KETONES BY FRIEDEL-CRAFTS REACTIONS

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Some nitrohydroxy ketones were prepared by FRIEDEL—CRAFTS synthesis from nitrophenols. These processes are compared with the FRIES reaction of the corresponding nitrophenolesters.

1. Introduction

Though nitrohydroxy ketones are synthesized since long by classical methods, the preparation of these compounds by the FRIEDEL—CRAFTS reaction of nitrophenols and acid chlorides is rare. This is doubtlessly due to the retarding effect of the nitro group of the phenyl ring which results in poor yields.

The reaction between phenols and acyl chlorides was studied by ROSEMUND and SCHNURR [1] who found that acylation primarily takes place, instead of the nucleus, actually on the oxygen atom. Similar observations were published later also by other authors [2, 3]. BROWN was the first who succeeded in preparing 3-nitro-4-hydroxy-acetophenone and its homologues in satisfactory yields [33 to 41%] by the FRIEDEL—CRAFTS reaction of the appropriate phenol with acid chloride in the presence of aluminium chloride [4]. Similarly, 5-nitro-2-hydroxy-acetophenone was prepared by the teams of JOSHI [5] and of CHHAYA [6].

As we succeeded earlier [7] in carrying out the FRIES rearrangement of some nitrophenylesters into nitrohydroxy ketones, it appeared to be of interest to compare these FRIES reactions with the corresponding FRIEDEL—CRAFTS reactions.

2. Results and discussion

The reactions between 3-nitrophenol and acetyl chloride, phenyl acetyl chloride, benzoyl chloride, 3-nitrobenzoyl chloride, propionyl chloride, further between 4-nitrophenol and acetyl chloride, 2-nitrophenol and acetyl chloride, respectively, were carried out. The results may be summarized as follows.

The FRIEDEL—CRAFTS and the FRIES reactions yielded in all cases identical products, in accordance with the observations of CULLINANE [8] made with other models. The products were already described earlier by us [7].

At relatively lower temperatures when no substantial FRIES reaction can be observed, the main product of the reaction is nitrophenolester. This temperature limit depends on the nature of the ester, *e. g.* the FRIEDEL—CRAFTS reaction is getting predominant over 80° in the case of 2-nitrophenol and acetyl chloride and over 140° in that of 3-nitrophenol and benzoyl chloride. FRIEDEL—CRAFTS reactions take place at the temperature of the corresponding FRIES reaction, of nitrophenol-esters

In the case of 2-hydroxy ketones, the yields of the FRIEDEL—CRAFTS reaction are but slight lower than those of the FRIES reactions, while in the case of the 4-hydroxy ketone studied the former are appreciably higher. This observation is not in contrast to the presumption that the mechanism of the FRIEDEL—CRAFTS reaction of phenols is in essence similar to the mechanism of the FRIES reaction in the course of which, subsequent to the equilbral splitting of esters, the products of cleavage react with each other giving hydroxy ketones (and esters again) [3]. The favourable yield of 4-hydroxy ketones, in turn, can be explained by the observation of GERECs according to which the *para* rearrangement is promoted by the presence of hydrogen chloride [2]. This can probably be ascribed to the effect of hydrogen chloride on the equilbral splitting of the ester [3]. Obviously in the FRIEDEL—CRAFTS reaction hydrogen chloride is formed as a by-product of the equilbral formation of the ester.

In FRIEDEL—CRAFTS reactions it is necessary to apply at least as many moles of aluminium chloride as the moles of acid chloride used. Of the latter, it is advisable to use 1,5 moles per mole of phenol.

The FRIEDEL—CRAFTS reactions take place in nitrobenzene. However, the use of a solvent is not indispensable because the reactions can be also carried out in melt. Still, the temperature in this latter case should not attain the decomposition temperature of the corresponding nitrophenols in the presence of aluminium chloride [9].

3. Experimental

As examples characteristic of FRIEDEL—CRAFTS reactions, the preparation of 4-nitro-2-hydroxy acetophenone, 4-nitro-2-hydroxy benzophenone and of 4,3'-dinitro-2-hydroxy benzophenone will be described here.

4-nitro-2-hydroxy acetophenone

14,3 ml (15,8 g; 200 mmoles) of acetyl chloride were added to the mixture of 13,9 g (100 mmoles) of 3-nitrophenol and 13,4 g (100 mmoles) of aluminium chloride. The system was kept 3 hours in an oil bath of 125°. On cooling, the complexes were decomposed by a mixture of 30 ml of water and 10 ml of concentrated hydrochloric acid, the obtained turbid aqueous system extracted with 4×25 ml of carbon tetrachloride and 2×25 ml of benzene. The combined organic phases were then subjected to distillation in order to remove the solvents, and the residue made up to 35 ml with methanol. On adding 40 ml of an ethanolic solution of sodium methylate containing 10% of sodium, the system was kept in an ice box when 1,1 g of 4-nitro-2-hydroxy acetophenone sodium precipitated in red brick-coloured crystals (yield 5,5%). Prior to adding sodium ethylate, 9 g of unchanged 3-nitrophenol acetate could be detected in the solution (40% yield).

On altering the reaction period to 8 hours, the temperature to 130°, and the mole ratios of phenol-aluminium chloride-acetyl chloride to 1:1,5:1,5, the yield increased consecutively to 16,5–18,0%.¹ The free ketone could be liberated from its sodium salt by shaking at 60–70° with a 1,0*N* solution of sulphuric acid. M. p. of the product: 63°, on recrystallization from ethanol: m. p. 67°.

4-nitro-2-hydroxy benzophenone

23 ml (28,1 g = 200 mmoles) of benzoyl chloride was added to a mixture of 13,9 g (100 mmoles) of 3-nitrophenol and 13,4 g (100 mmoles) of aluminium chloride, the system kept 2 hours in a 170° oil bath. On cooling, the melt was decomposed with a mixture of 15 ml of concentrated hydrochloric acid and 100 g of ice, affording a brownish aqueous emulsion and a dark sticky paste. On decanting the aqueous emulsion, it was shaken with 2 × 30 ml of carbon tetrachloride. The paste residual on the bottom of the flask was treated with 40 ml of ethanol, and the solvent removed by distillation in order to obtain waterfree residue. The combined organic phases obtained from the above described extraction were dried (Na₂SO₄), poured on the anhydrous paste, and the system refluxed for 12 hours, and extracted with 4 × 40 ml of a 4% solution of sodium hydroxide in order to separate the phenols from the ester. The combined alkaline extracts were acidified with concentrated hydrochloric acid, shaken with 4 × 40 ml of carbon tetrachloride, the combined extracts dried (Na₂SO₄), and the solvent removed. On cooling, the residue solidified to a brown mass which was extracted with 6 × 10 ml of boiling petroleum ether. Removal of petroleum ether gave 5,3 g of a yellow substance which was recrystallized from ethanol to give 2,4 g of crude ketone (9,9% yield)² which melted at 90–104°. On recrystallization from ethanol and ligroin m. p. was 108°. The product was identical with that prepared from 4-nitrosalicylic chloride and benzene [10].

When the mole ratio was altered to 1:1,5:1,5 for phenol- aluminium chloride- acyl haloid, the reaction period to 3 hours and the temperature to 125–130°, the amount of crude 3-nitrophenol benzoate crystallizing after decomposition ranged 22,4 g (92% yield) m. p. 80–93° and no ketonic product could be obtained.

When the mole ratio of the last experiment was maintained, and the system was heated 2 hours at 170°, the yield referred to crude ketone was 7,5%.

4,3'-dinitro-2-hydroxy benzophenone

Mode of preparation as in preceding experiment with a mole ratio of 1:1,5:1,5 of 3-nitrophenol (13,9 g = 100 mmoles)- aluminium chloride- 3-nitrobenzoyl chloride, at 175–180° for 2,5 hours. On cooling, a partially blistered melt was obtained. This was treated with 170 ml of ethanol, shaken till it almost completely dissolved, then a mixture of 20 ml of concentrated hydrochloric acid and 1000 ml of water was poured to the system. On allowing the reaction mixture to stand overnight, the aqueous solution was decanted and shaken with 4 × 100 ml of carbon tetrachlo-

¹ The corresponding FRIES reaction under similar conditions gave around 20% yield [7].

² The FRIES reaction of 3-nitrophenyl benzoate in the presence of equimolar AlCl₃ gave 11% yield of crude ketone [10].

ride, and with 6×100 ml of benzene. Subsequently 3×50 ml of ethanol was poured on the black tar-like mass, the solvent removed by distillation to make it water free, and the combined mixture of tetrachloromentane and benzene previously dried (Na_2SO_4) poured on the residual mass. On refluxing the system 12 hours and filtering the mixture hot, the filtrate was evaporated to dryness, the residue boiled with 3×100 ml of petroleum ether and then with 4×15 ml of ligroin, the combined extract evaporated, and the residual crystals recrystallized from ethanol: yield 0,15 g, m. p. $150-152^\circ$. On recrystallization it melted at $157-158^\circ$.

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ПОЛУЧЕНИЕ НИТРОГИДРОКСИКЕТОНОВ РЕАКЦИЕЙ ФРИДЕЛЬ-КРАФТСА

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Были получены некоторые нитрогидроксикетоны из нитрофенолов путём синтеза Фридель—Крафтса. Процессы сопоставляются с реакцией Фриза соответствующих сложных эфиров нитрофенола.