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The Action of Aluminum Chloride on the Diphenyl Ester of Isophthalic, Terephthalic and Naphthalic Acids

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Diphenyl phthalate and aluminum chloride do not yield 2-(4''-hydroxybenzoyl)-4'-hydroxybenzophenone as might be expected; phenolphthalein² and 1-hydroxyanthraquinone³ are produced in this reaction.

We found that diphenyl isophthalate, heated with aluminum chloride, is transformed into 3-(4''-hydroxybenzoyl)-4'-hydroxybenzophenone. The latter compound was obtained also by interaction of isophthalyl chloride, anisole and aluminum chloride; the 3-(4''-methoxybenzoyl)-4'-methoxybenzophenone, produced in this reaction, was demethylated during the preparative process.

Weiss and Chledowski⁴ stated that isophthalyl chloride and anisole react to form not only 3-(4''-methoxybenzoyl)-4'-methoxybenzophenone but also 4-(4''-methoxybenzoyl)-4''-methoxybenzophenone. They attribute the formation of the latter substance to a rearrangement produced by the aluminum chloride. Although these investigators claim that they used pure *m*-xylene from which to prepare the isophthalyl chloride, their *m*-xylene may have contained some of the para isomer.

Diphenyl terephthalate was converted by aluminum chloride into 4-(4''-hydroxybenzoyl)-4'-hydroxybenzophenone. The same benzophenone was obtained by demethylation of the reaction product, 4-(4''-methoxybenzoyl)-4'-

methoxybenzophenone, produced from terephthalyl chloride and anisole.

In view of the general behavior of 1,8-disubstitution products of naphthalene it would be expected that diphenyl naphthalate would react with aluminum chloride similarly to diphenyl phthalate and that phenolnaphthalein would be produced instead of 1,8-di-(*p*-hydroxybenzoyl)-naphthalene. It was found that the phthalein was formed in this reaction in place of the diketone. Jaubert⁵ had obtained this phthalein previously, in an impure state, by condensation of naphthalic anhydride and phenol. We prepared it by a modification of Jaubert's method and also by condensation of 8-(4'-hydroxybenzoyl)-1-naphthoic acid with phenol.

Experimental Part

3-(4''-Hydroxybenzoyl)-4'-hydroxybenzophenone. (a) From Diphenyl Isophthalate and Aluminum Chloride.—Five grams of diphenyl isophthalate,⁶ 6 g. of aluminum chloride and 25 cc. of carbon disulfide were heated on a steam-bath until the carbon disulfide had been removed; the residue was then heated in an oil-bath (185–195°) for twenty-five minutes. The aluminum salt was removed with dilute hydrochloric acid and the mixture extracted with 10% sodium hydroxide solution. The product, obtained by acidification of the alkaline extract, was digested with sodium bicarbonate solution to remove carboxylic acids and the crude hydroxy ketone refluxed with 14 cc. of acetic anhydride for one hour in order to acetylate it. The diacetyl derivative of 3-(4''-hydroxybenzoyl)-4'-hydroxy-

(1) Monsanto-Pfizer Research Associate.

(2) Csanyi, *Ber.*, **52**, 1792 (1919).

(3) Blicke and Weinkauff, *THIS JOURNAL*, **54**, 330 (1932).

(4) Weiss and Chledowski, *Monatsh.*, **65**, 358 (1935).

(5) Jaubert, *Ber.*, **28**, 992 (1895).

(6) Schreder [*ibid.*, **7**, 707 (1874)] reported 120° as the melting point; we found it to be 137–138°.

benzophenone was recrystallized from benzene; m. p. 189–190°.

Anal. Calcd. for $C_{24}H_{18}O_6$: C, 71.62; H, 4.51. Found: C, 71.72; H, 4.59.

Upon hydrolysis of the acetyl derivative with 10% sodium hydroxide solution and recrystallization of the 3-(4"-hydroxybenzoyl)-4'-hydroxybenzophenone several times from dilute alcohol, the latter melted at 207–209°.⁷

The dimethyl ether, obtained by methylation with dimethyl sulfate, melted at 144–146°⁸ after recrystallization from alcohol.

The di-*m*-bromobenzoyl derivative was produced when 2 g. of the dihydroxybenzophenone was heated for three hours with 3.3 g. of *m*-bromobenzoyl chloride at 150–160°. After recrystallization from tetrachloroethane it melted at 234–235°.

Anal. Calcd. for $C_{34}H_{20}O_6Br_2$: Br, 23.36. Found: Br, 23.01.

(b) **From Isophthalyl Chloride, Anisole and Aluminum Chloride.**—Weiss and Chledowski⁸ stirred a mixture of isophthalyl chloride, anisole, aluminum chloride and carbon disulfide, heated it for one hour and isolated 3-(4"-methoxybenzoyl)-4'-methoxybenzophenone. We followed their directions but heated the mixture for three hours on a steam-bath. After removal of the solvent and aluminum salt 20 g. of product, soluble in 10% sodium hydroxide solution, was obtained from 17 g. of isophthalyl chloride. The crude 3-(4"-hydroxybenzoyl)-4'-hydroxybenzophenone was refluxed for one hour with 60 g. of acetic anhydride, the crystalline diacetyl derivative (m. p. 189–190°) hydrolyzed and the benzophenone recrystallized from dilute alcohol; m. p. 207–209°.

4-(4"-Hydroxybenzoyl)-4'-hydroxybenzophenone. (a) **From Diphenyl Terephthalate and Aluminum Chloride.**—Diphenyl terephthalate⁹ was treated with aluminum chloride in the same manner as diphenyl isophthalate. The crude hydroxy ketone obtained, after removal of carboxylic acids, was recrystallized from dilute alcohol; m. p. 297–299°. The compound contains solvent of crystallization; for analysis it was dried to constant weight at 115°.

Anal. Calcd. for $C_{20}H_{14}O_4$: C, 75.47; H, 4.40. Found: C, 75.20; H, 4.51.

The diacetyl derivative was prepared and recrystallized from acetic acid; m. p. 249–250°.

Anal. Calcd. for $C_{24}H_{18}O_6$: C, 71.62; H, 4.51. Found: C, 71.50; H, 4.54.

The di-(3-bromobenzoyl) derivative was obtained when 4-(4"-hydroxybenzoyl)-4'-hydroxybenzophenone was heated with 3-bromobenzoyl chloride. It melted at 289–291° after recrystallization from tetrachloroethane.

Anal. Calcd. for $C_{34}H_{20}O_6Br_2$: Br, 23.36. Found: Br, 23.01.

In order to prepare the dioxime 3.7 g. of the hydroxybenzophenone, 200 cc. of methyl alcohol, 5 g. of hydroxylamine hydrochloride and 10 g. of sodium hydroxide were refluxed for eight hours. The oxime was recrystallized from alcohol; m. p. 261–263°.

(7) Weiss and Chledowski [*Monatsh.*, **65**, 363 (1935)] reported 215°.

(8) Weiss and Chledowski [*ibid.*, **65**, 362 (1935)] reported 146–149°.

(9) Schreder, *Ber.*, **7**, 707 (1874).

Anal. Calcd. for $C_{20}H_{14}O_4N_2$: N, 8.04. Found: N, 7.93.

Upon methylation with dimethyl sulfate 4-(4"-methoxybenzoyl)-4'-methoxybenzophenone was obtained; m. p. 225–227°¹⁰ after recrystallization from toluene. Demethylation with constant boiling hydrobromic acid in acetic acid yielded the original hydroxybenzophenone.

(b) **From Terephthalyl Chloride, Anisole and Aluminum Chloride.**—Terephthalyl chloride¹¹ was allowed to react with anisole and aluminum chloride under the same conditions described above in the case of isophthalyl chloride. The hydroxybenzophenone obtained melted at 298–299°.

Phenolnaphthalein. (a) **From Naphthalic Anhydride and Phenol.**—A mixture of 40 g. of naphthalic anhydride, 160 g. of phenol and 100 g. of aluminum chloride was heated for seventy-two hours on a steam-bath, the product decomposed with dilute hydrochloric acid and then steam distilled to remove excess phenol. The material was digested with 10% sodium hydroxide solution, filtered and the filtrate acidified. The red precipitate was dried and dissolved in hot butyl alcohol. When the solution was cooled 5 g. of 8-(4'-hydroxybenzoyl)-1-naphthoic acid was obtained; m. p. 219–220° after several recrystallizations from alcohol.

Anal. Calcd. for $C_{18}H_{12}O_4$: C, 73.95; H, 4.14. Found: C, 73.83; H, 4.14.

The butyl alcoholic mother liquor was steam distilled and the dried, red, amorphous residue refluxed with 100 g. of acetic anhydride for four hours. The solution was concentrated, poured into water and the brown, gummy precipitate covered with alcohol. After twelve hours the mass became crystalline. The product was recrystallized several times from alcohol whereupon the colorless, crystalline diacetyl derivative of phenolnaphthalein was obtained; m. p. 198–199°.¹²

Anal. Calcd. for $C_{28}H_{20}O_6$: C, 74.31; H, 4.46. Found: C, 73.98; H, 4.49.

The diacetyl derivative was refluxed for several hours with dilute aqueous sodium hydroxide and the phthalein obtained recrystallized from dilute alcohol; m. p. 265–266°¹³ with decomposition.

Anal. Calcd. for $C_{24}H_{16}O_4$: C, 78.23; H, 4.38. Found: C, 78.22; H, 4.43.

The color of an alkaline solution of phenolnaphthalein is very similar to that of an alkaline solution of phenolphthalein.

Dr. H. H. Willard found the useful *pH* range to be 8.8–10.8 and the *pK* to be 9.78.

(b) **From 8-(4'-Hydroxybenzoyl)-1-naphthoic Acid.**—A mixture of 5.8 g. of 8-(4'-hydroxybenzoyl)-1-naphthoic acid, 15 g. of phenol and 13.5 g. of aluminum chloride was heated at 150–160° for six hours and then treated with dilute hydrochloric acid. The phthalein was isolated in the manner described above; mixed m. p. 265–266°.

(c) **From Diphenyl Naphthalate and Aluminum Chloride.**—In order to obtain diphenyl naphthalate 39.6 g. of

(10) Weiss and Chledowski [*Monatsh.*, **65**, 358 (1935)] reported 236–239°.

(11) Locher, *Bull. soc. chim.*, [3] **11**, 927 (1894).

(12) Kaufmann [*Z. angew. Chem.*, **40**, 863 (1927)] reported 198–199°.

(13) Jaubert [*Ber.*, **26**, 991 (1895)] stated that the phthalein melted above 200° with charring and the evolution of phenol.

naphthalic anhydride, 80 g. of phosphorus pentachloride and 75 cc. of phosphorus oxychloride were refluxed for twenty hours in an oil-bath, the oxychloride and excess pentachloride removed under diminished pressure and the sirupy, light brown acid chloride¹⁴ mixed, immediately, with 40 g. of phenol. After the vigorous reaction had subsided the mixture was heated for two hours at 140–150°. The product was washed with dilute alkali, with water and then recrystallized from alcohol; m. p. 150–151°.

Anal. Calcd. for $C_{24}H_{16}O_4$: C, 78.23; H, 4.38. Found: C, 78.39; H, 4.41.

A mixture of 4 g. of diphenyl naphthalate, 5 g. of aluminum chloride and 20 cc. of carbon disulfide was heated on a steam-bath until the carbon disulfide had been removed and the solid residue heated for twenty-five minutes in an oil-bath at 155–160°. The mixture was treated with dilute hydrochloric acid and the product then digested with

(14) Mason [*J. Chem. Soc.*, **125**, 2117 (1924)] obtained this acid chloride in crystalline form and Davies and Leeper [*ibid.*, 1125 (1927)] were able to distil the material.

10% sodium hydroxide solution. The solid precipitate, obtained upon acidification of the alkaline solution, was digested with sodium bicarbonate solution and the insoluble portion recrystallized from dilute alcohol; yield of phthalein 1.6 g.; m. p. 264–266°.

Summary

It has been shown that the diphenyl ester of isophthalic acid is converted by aluminum chloride into 3-(4"-hydroxybenzoyl)-4'-hydroxybenzophenone; from diphenyl terephthalate and aluminum chloride there was obtained 4-(4"-hydroxybenzoyl)-4'-hydroxybenzophenone.

Phenolnaphthalein was prepared from diphenyl naphthalate and aluminum chloride and from the hitherto unknown 8-(4'-hydroxybenzoyl)-1-naphthoic acid and phenol.

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Separation and Identification of Amines with 3-Nitrophthalic Anhydride

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While numerous reagents are available for the preparation of derivatives of the three classes of amines, only two, nitrous acid and aryl sulfonyl chlorides, have been used to any considerable extent as a means of separating the different types of amines from each other when they occur in a mixture. Nitrous acid has the disadvantage of destroying completely the identity of the primary amine, often with the formation of a rearranged product. Aryl sulfonyl chlorides have proved to be quite useful on account of the fact that the sulfonamides of the primary amines are generally soluble in aqueous alkali and, consequently, can be separated from the alkali-insoluble sulfonamide of the secondary amine. However, this reagent fails when primary amines of the type $C_6H_5(CH_2)_nNH_2$ are involved because the sulfonamides of these amines are alkali-insoluble.¹ Also, certain ortho-substituted amines, such as *o*-nitroaniline,² can be made to react with aryl sulfonyl chlorides only with considerable difficulty. Finally, recovery of the amines from the sulfonamides is inconvenient, if not difficult, in that hydrolysis of the latter types requires that the reaction be carried out in a sealed tube.

(1) Carothers, Bickford and Hurwitz, *THIS JOURNAL*, **49**, 2908 (1927).

(2) *Cf.* Amundsen, *ibid.*, **59**, 1466 (1937).

In his textbook of qualitative organic analysis, Kamm³ mentions the use of phthalic anhydride as a means of separating the three types of amines. So far as we are aware, there is no other reference in the literature to the general use of this reagent for the separation and identification of amines.⁴ In a private communication to one of us Dr. Kamm stated that he had worked on the phthalic anhydride procedure several years ago while at the University of Illinois but had had little time to use it in practical laboratory work. The use of this reagent depends upon the fact that it does not react with tertiary amines but forms phthalamic acids with both primary and secondary amines. These derivatives are separated by heat which converts the phthalamic acid of the primary amine (I) into an alkali-insoluble N-substituted phthalimide (III) but leaves the phthalamic acid derived from the secondary amine (II) unchanged, and, therefore, alkali soluble.

Attempts to utilize phthalic anhydride for the separation and identification of amines in this Laboratory revealed the following facts: (a)

(3) Kamm, "Qualitative Organic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1932, p. 69.

(4) A few patents [*C. A.*, **22**, 3417 (1928); **23**, 846, 1137 (1929); **28**, 3418 (1934)] covering the separation of certain amines with phthalic anhydride have been issued. Porai-Koshitz in a paper [*C. A.*, **29**, 131 (1935)] describes a rather large scale separation of aniline, methylaniline and dimethylaniline with this reagent.