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2-AROYLBENZOIC ACIDS. PART VII. SYNTHESIS OF 2-(5'-FLUORO-2'-HYDROXYBENZOYL) BENZOIC ACID

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SUMMARY

The reaction of o-carboxybenzoylation of p-fluorophenol was carried out. As a result of this condensation 2-(5'-fluoro-2'-hydroxybenzoyl)benzoic acid was obtained. The structure of this acid was confirmed by chemical-physical methods.

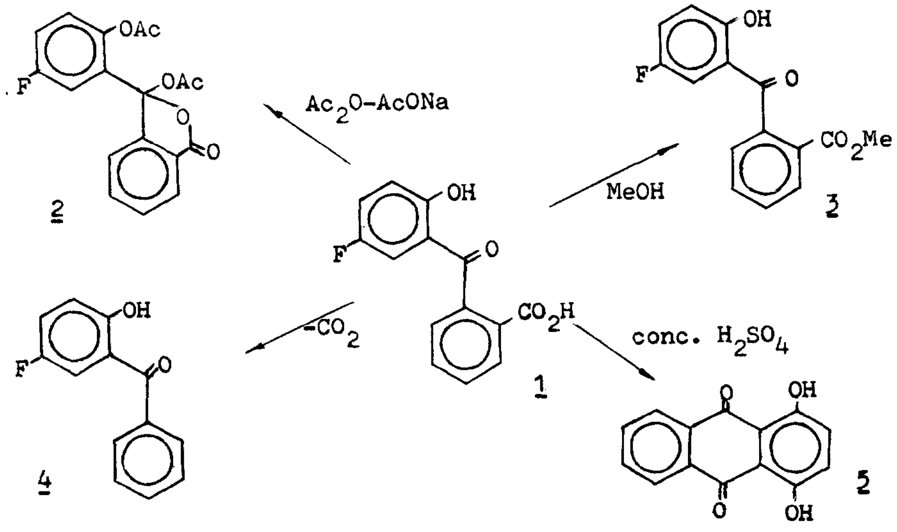
INTRODUCTION

In a previous paper [1] we described the syntheses of two 2-aroylbenzoic acids from o-ethylphenol.

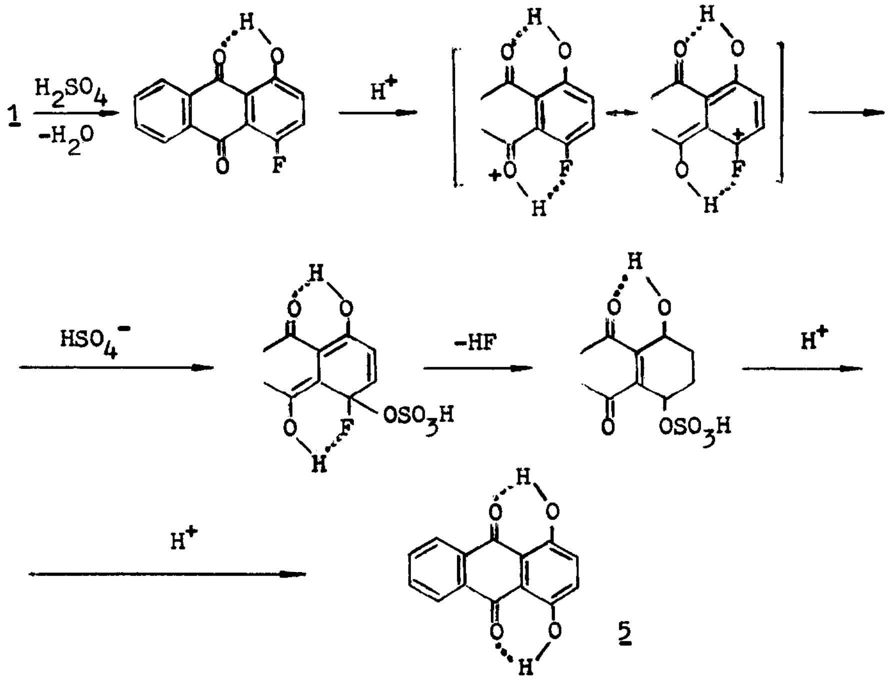
In the course of studing various derivatives of fluoran a need arose for obtaining the new 2-(5'-fluoro-2'-hydroxybenzoyl)-benzoic acid as the intermediate product for future syntheses [2]. The acid, the synthesis of which is reported in this paper, can also be used for the preparation of some phthaleins, the substitution of anthrone, anthracene and anthraquinone.

RESULTS AND DISCUSSION

The synthesis of 2-(5'-fluoro-2'-hydroxybenzoyl)benzoic acid 1 with the best yield was carried out in sym. tetrachloroethane, at 115-120^{o} for 5 hrs with molar ratio of reagents: p-fluorophenol : phthalic anhydride : $AlCl_3$ = 1 : 1 : 3. The ortho position of the OH and C=O groups in the molecule of this compound was established based on the IR spectrum. The shift of band of aromatic carbonyl vibrations towards the lower frequencies (1640 cm^{-1}) is characteristic for an intramolecular hydrogen bond between an oxygen atom of a C=O group and a hydrogen atom of an OH group in the ortho position. The standard acetylation of 1 with acetate anhydride and sodium acetate gave diacetate 2, so it undoubted indicates the γ-ketoacid structure of the acid 1. The IR spectrum for diacetate 2 shows the typical band for the free carbonyl group of an aromatic lactone (1785 cm^{-1}) and very characteristic bands for C-O-C vibrations of ester (1095 and 1050 cm^{-1}) and C-O-C vibrations of γ-lactone (950 cm^{-1}). The reaction of 1 with methanol gave the methyl ester 3. After decarboxylation of acid 1 in quinoline 5-fluoro-2-hydroxybenzophenone 4 was obtained. This compound was prepared and described by Buu-Hoï et al. [3]. During the cyclization of the acid 1 in concentrated sulphuric acid in the presence of anhydrous $ZnCl_2$, 1,4-dihydroxyanthraquinone 5 is formed. This product was rather unexpected, though Tanabe and Ishikawa [4] described substitution of -F with -OH group in some fluoroanthraquinones in concentrated sulphuric acid solution.



We assume that the mechanism of formation of 5 from the 2-(5'-fluoro-2'-hydroxybenzoyl)benzoic acid 1 in concentrated sulphuric acid is similar of that reported by others [4].



EXPERIMENTAL

Melting points are corrected. IR spectra were measured within the range 650-3600 cm^{-1} on UR-10 (C. Zeiss, Jena) infrared spectrophotometer in Nujol (650-1300 and 1500-2000 cm^{-1}) mulls, νmax data were corrected on the basis of polystyrene spectrum and reported as s - strong, m - medium, w - weak and b - broad bands.

Proton magnetic resonance (NMR) were measured on a Jeol (LNM-4H-100) (80 MHz) spectrometer for deuteriochloroform solution; the internal standard was tetramethylsilane (TMS) (δ= 0.00 ppm), δ max are reported as: s - singlet, m - multiplet, mc - multiplet centre.

Preparation of 2-(5'-fluoro-2'-hydroxybenzoyl)benzoic acid 1 (nc)

Phthalic anhydride (37.0 g) and p-fluorophenol (28.0 g) were melted and then 200 ml of sym. tetrachloroethane was added. The mixture was heated at 60° and portion-wise 100.0 g $AlCl_3$ was added during 1 h. The brown-red solution was heated on an oil bath at 130-140° for 5 hrs, with a constant evolution of HClgas. After cooling, the mass was carefully treated with 200 ml of diluted HCl and then sym. $C_2H_2Cl_4$ was distilled off with steam. A brown solid was decanted, extracted several times with 15% Na_2CO_3 and filtered off. A filtrate was acidified up to pH 2-3 to yield 42.5 g of precipitate. Several crystallizations from acetic acid gave yellowish plates of 1 m.p. 192°. Analysis: Found: C, 64.3; H, 3.7%. $C_{14}H_9O_4F$ requires C, 64.5; H, 3.6%. UV in ethanol: λmax (εmax) 250 (9300), 336 (5350) nm; λmin (εmin) 244 (9000), 210 (1600) nm. IR: νmax 3060 s, 2960 s (OH, dimeric association of COOH); 2500 w, 2350 w (C-F); 2940 w (OH, dimer COOH); 1720 s (C=O, aromatic ketone and COOH); 1640 m (C=O, intramolecular hydrogen bond); 1610 s, 1575 m, 1480 s (C=C, aromatic); 1358 m, 1245 s, 1215 m (OH, phenolic); 1140 m, 1082 m (C-F) cm^{-1}. NMR: δ6.65-7.15 (m, 2; 4,5-H); 7.25 (s, 1; 6-H); 7.4-7.7 (m, 3; 3',4',6'-H); 8.2 (mc, 1; 3-H); 9.2 (s, 2; 2'-OH and 2-COOH) ppm. Mol. wt.: Found: 260 (mass spectrum); calculated: 260.

Preparation of 3-acetoxy-3-(2'-acetoxy-5'-fluorophenyl)phthalide 2 (nc)

A mixture of acid 1 (2.0 g), acetic anhydride (20 ml) and sodium acetate (2.0 g) was refluxed for 3 hrs at 120° and then poured on ice water giving 2.5 g of crude diacetate 2. After several crystallizations from aqueous acetic acid, colourless crystals were obtained m.p. 145°. Analysis: Found: C, 61.5; H, 3.6%. $C_{18}H_{13}O_6F$ requires C, 61.6; H, 3.8%. IR: νmax 1785 s (C=O, conjugated aromatic γ-lactone); 1375 (CH_3, acetate); 1270 m, 1218 s, 1170 s (C-O, acetate); 1050 s, 1050 s (C-O-C vibrations of ester), 950 s (C-O-C vibrations of γ-lactone) cm^{-1}. NMR: δ2.1 (s, 6; 2-$OCOCH_3$ and 3-$OCOCH_3$); 7.0-7.25 (m, 2; 5,6-H); 7.5-7.65 (m, 4; 4,3',4',6'-H); 7.9 (mc, 1; 7-H) ppm.

Methyl 2-(5'-fluoro-2'-hydroxybenzoyl)benzoate 3 (nc)

The acid (1.0 g) and methanol (80 ml) containing sulphuric cid (3 ml) were refluxed for 5 hrs. The product was poured on water and collected (0.85 g). Several crystallizations from ethanol yielded colourless crystals m.p. 66°. Analysis: Found: C, 65.8; H, 4.3%. $C_{15}H_{11}O_4F$ requires C, 65.7; H, 4.0%. IR: ν_{max} 1740 s (C=O, methyl ester of $COOCH_3$) ; 1642 s (C=O, aromatic ketone, intramolecular hydrogen bond); 1310 s, 1240 w, 1218 s (OH, phenolic); 940 m, 860 m, 760 m (C-H, 1,2- and 1,2,4-trisubstituted aromatic) cm^{-1}.

Preperation of 2-hydroxy-5-fluorobenzophenone 4

The acid (2.0 g) and freshly distilled quinoline (5 ml) were placed in a flask (fitted with a side neck and air condenser) and heated on a Wood bath at 254° for 4 minutes, when 0.03 g $Cu(CH_3COO)_2 \cdot H_2O$ was added. The temp. 254° was maintained for 40 minutes. After cooling the product was extracted with ethyl ether (20 ml). The ether layer was separated and dried ($MgSO_4$). Evaporation of the ether and recrystallization of the residual (1.4 g) from ethanol afforded needles m.p. 76.5° (cited [3] 77°). Analysis: Found: C, 72.4; H, 4.2%. $C_{13}H_9O_2F$ requires C, 72.2; H, 4.2%. IR: ν_{max} 3300 s (OH, association polim.) ; 1640 s (C=O, aromatic ketone); 1595 s, 1577 s, 1505 m (C=C, aromatic); 1280 s, 1120 s (OH, phenolic); 860 m, 842 m, 800 s (C-H, aromatic, 1,2,4-trisubstituted) cm^{-1}.

Preparation of 1,4-dihydroxyanthraquinone 5

A mixture of acid 1 (2.6 g), conc. sulphuric acid (26 ml) and anhydrous $ZnCl_2$ (2.6 g) was heated 4 hrs at 80°. After cooling the mixture was carefully poured on 250 g of ice and coagulated. The product was filtered and dissolved in 10% NaOH. The alkaline solution was acidified to pH 2-3 yielding 2.0 g of red-brown crude anthraquinone 5. Purification by sublimation under reduced pressure (2 Torr) at 180-190° gave red needles m.p. 202° (cited [3] 197-199°), identical with authentic samoles of 1,4-dihydroxyanthraquinone (IR spectra).

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