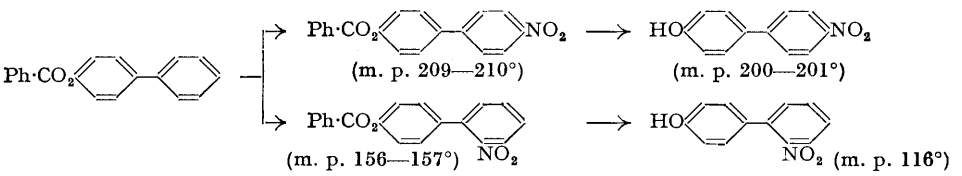
337. *The Nitration of Esters of 4-Hydroxydiphenyl. The Preparation of 4-Hydroxy-4′- and -2′-nitrodiphenyls.*

By Brynmor Jones and (in part) Frank Chapman.

Investigations into the preparation of 4-hydroxy-4′-nitrodiphenyl from 4-hydroxydiphenyl have led to an examination of the nitration in acetic acid solution of the benzoate, benzenesulphonate, toluene-*p*-sulphonate, and acetate of 4-hydroxydiphenyl. It has been established that nitration does not occur exclusively in the 4′-position, but that substantial amounts of the 2′-nitro-esters are formed. An improved method of preparing 4-hydroxy-4′-nitrodiphenyl from the benzoate is described.

Although the literature records a number of investigations of the halogenation of esters of 4-hydroxydiphenyl, their behaviour on nitration has been but little studied. Such information as there is suggests that a single product is formed, and that substitution takes place in the 4′-position. For instance, in the nitration of the toluene-*p*-sulphonate, Bell and Kenyon (*J.*, 1926, 3046) obtained 4′-nitro-4-diphenylyl toluene-*p*-sulphonate. No yield was recorded, but substitution was believed to occur mainly, if not exclusively, in the 4′-position (cf. Waters, " Physical Aspects of Organic Chemistry," 1950, p. 504, where this behaviour is erroneously attributed to the acetate). Later, Hazlet and van Orden (*J. Amer. Chem. Soc.*, 1942, **64**, 2505) nitrated the benzoate and obtained a 40% yield of the unpurified 4′-nitro-4-diphenylyl benzoate. Although this material required several crystallisations before purification was achieved, no other product was isolated, and nitration was stated categorically to occur in one position only. Such a conclusion is at variance with the extensive studies by Le Fèvre and Turner (*J.*, 1928, 247; see Turner, *Rec. Trav. chim.*, 1929, **48**, 821) and by Bell and Kenyon (*J.*, 1926, 2705) on substitution in diphenyl and its derivatives, for not only is the phenyl group itself *op*-directing, but it remains so even when it contains a powerful deactivating substituent, such as a nitro-group.

A careful re-examination of the nitration of the benzoate in acetic acid, in which more precise conditions for the reaction have been worked out, has shown the product to be a mixture of the 4′-nitro- and the 2′-nitro-isomer. A strictly quantitative analysis of the mixture has not been attempted, but it is clear that the 2′-nitro-4-diphenylyl benzoate constitutes at least 25% of the product of nitration. [From 60 g. of the 4-diphenylyl benzoate in two experiments, 31 g. of the 4′- and 17 g. of the 2′-nitro-ester were obtained as pure crystalline products.]



The orientation of this second compound was established by hydrolysis to 4-hydroxy-2′-nitrodiphenyl, followed by oxidation to *o*-nitrobenzoic acid. Its isolation in quantity, together with the principal product, 4′-nitro-4-diphenylyl benzoate, provides a further

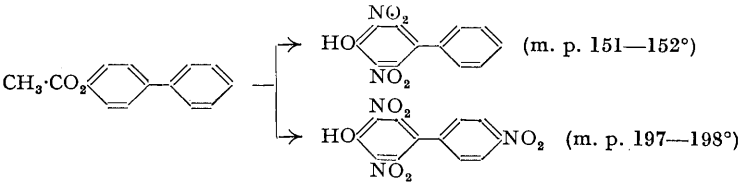
illustration of the *op*-directing influence of a phenyl group containing a deactivating substituent. Benzoylation of the hydroxy-group so reduces its activating influence on the phenyl group to which it is attached that substitution occurs in the other phenyl group.

The benzene- and toluene-*p*-sulphonates behave similarly, but in these cases the reactions were studied less fully because of the greater difficulty in achieving a clean separation of the products of nitration, and also because the primary objective of this investigation was to find a convenient method of preparing 4-hydroxy-4′-nitrodiphenyl. These three esters of 4-hydroxydiphenyl have a low solubility in cold acetic acid and, since their reactivity towards an electrophilic reagent is also low, nitrations are best carried out at 75—90°. At these temperatures nitration proceeds smoothly, without any noticeable hydrolysis or oxidation.

The benzoate is the least soluble, and its nitration differs from that of the sulphonyl esters in that the main product, 4′-nitro-4-diphenylyl benzoate, is so little soluble that it begins to separate from the hot nitrating mixture. The material which finally crystallised from the cold reaction mixture contained some 2′-nitro-ester, but the greater part of this remained in solution.

The products of nitration of the two sulphonyl esters were more soluble in the mixture of acetic and nitric acids, and separation was accomplished less readily. In the case of the toluene-*p*-sulphonate a substantial part of the 4′-nitro-4-diphenylyl toluene-*p*-sulphonate was obtained when the reaction mixture had been kept in ice for several hours. This ester was comparatively free from the 2′-nitro-isomer. The mixture of nitro-esters formed during nitration of the benzenesulphonate proved even more intractable. No solid separated, and the product obtained after dilution had to be subjected to several fractional crystallisations before the 4′- and the 2′-nitro-ester were obtained pure.

The nitration of 4-diphenylyl acetate, even at 40°, by means of either 98% or 70% nitric acid, was accompanied by hydrolysis, and the product in both cases was a mixture containing 4-hydroxy-di- and -tri-nitrodiphenyls. Two constituents were eventually isolated, and these were shown to be 4-hydroxy-3 : 5-dinitro- and -3 : 5 : 4′-trinitrodiphenyl. The mixture may have contained other hydroxynitrodiphenyls, but their presence was not investigated.



These experiments show that the acetate is not a suitable material for the preparation of 4-hydroxy-4′-nitrodiphenyl, and that the nitration of the two sulphonyl esters gives mixtures of isomers which are obtained pure only with difficulty. On the other hand, nitration of the benzoate provides a reliable and convenient method of preparing 4-hydroxy-2′- and -4′-nitrodiphenyls.

Experimental

(M. p.s are uncorrected. The microanalyses were carried out by Drs. Weiler and Strauss Oxford.)

Nitration of 4-Diphenylyl Benzoate.—To a solution of the ester (40 g.; m. p. 148°) in glacial acetic acid (310 ml.) at 85°, fuming nitric acid (100 ml.) was added, with stirring, at such a rate that the temperature was kept at 85—90° throughout the operation. Under these conditions nitration proceeded smoothly, and, as the last few ml. of nitric acid were added, 4′-nitro-4-diphenylyl benzoate began to separate from solution. After the mixture had cooled slowly to room temperature, the solid deposited was collected, and washed in turn with water and methyl alcohol. It began to soften at 155°, and melted completely at 195° (31·5 g.). At this stage the 4′-nitro-4-diphenylyl benzoate was contaminated with some 2′-nitro-ester, but this was readily removed by a single crystallisation from acetic acid (550 ml.), followed by digestion of the resulting solid with boiling acetic acid (200 ml.). When the solution cooled, pure

4′-nitro-4-diphenylyl benzoate (21 g.), m. p. 209—210°, was obtained. The yield of purified 4′-nitro-ester thus obtained was very consistent, despite the fact that the amount of 2′-nitro-ester which separated with it from the reaction mixture varied appreciably in different experiments. For example, in one experiment 20 g. of 4-diphenylyl benzoate gave only 13·6 g. of unpurified 4′-nitro-4-diphenylyl benzoate, but this on crystallisation yielded 10·5 g. of pure material.

From the acetic acid used to purify the 4′-nitro-4-diphenylyl benzoate some 2′-nitro-4-diphenylyl benzoate was isolated by dilution with water. The main crop, however, was obtained from the acetic acid–nitric mother-liquors by dilution. The material obtained from these two sources was often combined, and purified by crystallisation from acetic acid and alcohol.

In some experiments a small crop of substantially pure 2′-nitro-4-diphenylyl benzoate was obtained by keeping the original mother-liquor for several hours before dilution. In an experiment in which 20 g. of 4-diphenylyl benzoate had been used, and from which the 4′-nitro-4-diphenylyl benzoate had been collected, 2·7 g. of an almost pure *2′-nitro-4-diphenylyl benzoate* were obtained (Found: C, 70·1; H, 4·2; N, 4·5. $C_{19}H_{13}O_4N$ requires C, 70·1; H, 4·1; N, 4·4%).

In other experiments the original reaction mixture of acetic and nitric acid was not allowed to cool to room temperature. Instead, it was cooled to 45—50°, and the 4′-nitro-4-diphenylyl benzoate was then collected. Whichever procedure was adopted, about 11 g. of 2′-nitro-4-diphenylyl benzoate were obtained from 40 g. of 4-diphenylyl benzoate, and with reasonable care it was possible to obtain the two nitro-esters in pure forms in yields which together were 70% of the theoretical.

Attempts to prepare 4′-nitro-4-diphenylyl benzoate, following the rather indefinite instructions given by Hazlet and van Orden (*loc. cit.*), failed: the 4-diphenylyl benzoate was invariably recovered unchanged.

*Nitration of 4-Diphenylyl Toluene-*p*-sulphonate.*—The ester (10 g.), dissolved in glacial acetic acid (75 ml.), was nitrated at 90—95° by gradual addition of nitric acid (98%; 15 ml.). After all the acid had been added, the mixture was stirred for an hour. Unlike the nitration of the benzoate, this reaction did not lead to the immediate separation of any product, but during several hours in a refrigerator some 4′-nitro-4-diphenylyl toluene-*p*-sulphonate (4 g.), m. p. 149—152°, separated from solution. This on crystallisation from benzene–ligroin, and from alcohol, gave 3·7 g. of the pure compound, m. p. 156—157° (Bell and Kenyon, *loc. cit.*, record m. p. 156—158°).

Dilution of the nitric acid–acetic acid mother-liquor with water (100 ml.) gave 2′-nitro-4-diphenylyl toluene-*p*-sulphonate as a thick oil which, after solidifying, was dried and crystallised from benzene–ligroin to give 3·5 g. of a product of m. p. 52—56°. Further purification showed this specimen to contain more than 0·5 g. of the less soluble 4′-nitro-ester (m. p. 156°). This fraction was most easily separated by dissolving the more soluble 2′-nitro-ester in boiling methyl alcohol and decanting the clear liquid, which gave *2′-nitro-4-diphenylyl toluene-*p*-sulphonate* (2 g.) as pale yellow prisms, m. p. 79° (Found: C, 62·1; H, 4·0. $C_{19}H_{15}O_5NS$ requires C, 61·8; H, 4·1%). Further crystallisation from methyl alcohol, ligroin, and acetic acid left the m. p. unchanged.

Nitration of 4-Diphenylyl Benzenesulphonate.—To a solution of the ester (20 g.) in glacial acetic acid (35 ml.) at 90°, fuming nitric acid (35 ml.) was added dropwise at such a rate that the temperature was kept at 85—90°. After all the acid had been added, stirring was continued for an hour, and the solution was then set aside for several hours. When the addition of some 4′-nitro-4-diphenylyl benzenesulphonate failed to induce crystallisation, water (15 ml.) was added, and a dark oil was obtained. This eventually hardened to a solid which after crystallisation from alcohol melted over the range 81—90°. Several crystallisations from acetic acid, and from methyl and ethyl alcohol, were needed before 4′-nitro-4-diphenylyl benzenesulphonate was obtained as pale yellow lustrous plates, m. p. 107°. (The identity of this compound was established by mixed m. p. determination with a specimen of the ester prepared from benzenesulphonyl chloride and 4-hydroxy-4′-nitrodiphenyl in pyridine.) Addition of a further volume of water (25 ml.) to the original reaction mixture yielded a second batch of liquid, which also solidified on storage. This, after three crystallisations from alcohol, gave *2′-nitro-4-diphenylyl benzenesulphonate* as pale yellow lustrous plates, m. p. 106° (Found: C, 61·5; H, 3·6. $C_{18}H_{13}O_5NS$ requires C, 60·9; H, 3·7%).

Because the products of nitration were first obtained as oils, their separation and purification were accompanied by substantial losses. Nevertheless, it was possible to isolate several grams of each of the two isomers in pure form. In view of the similarity of the m. p.s and of the crystalline

forms, particular care was taken to establish their identity. On hydrolysis they gave 4-hydroxy-4′- and -2′-nitrodiphenyls.

Nitration of 4-Diphenylyl Acetate.—The acetate was prepared by Hazlet and Kornberg's method (*J. Amer. Chem. Soc.*, 1939, **61**, 3037). The following experiment is typical of several carried out in an attempt to nitrate it.

The acetate (20 g.; m. p. 87°) was dissolved in glacial acetic acid (100 ml.) at 40°, and nitric acid (70%; 40 ml.) was added at such a rate that the temperature was kept at this value. After all the acid had been added, the solution was kept at 40° for a further 30 minutes. In some experiments the product, a mixture of hydroxy-di- and -tri-nitrodiphenyls (19·5 g.; m. p. 143—152°) separated from the warm solution. In others, the product was obtained on cooling (98% nitric acid gave the same product).

From this mixture two hydroxynitrodiphenyls were finally isolated in pure form: the 3 : 5-dinitro-, m. p. 151—152°, and the 3 : 5 : 4′-trinitro-compound, m. p. 197—198°. No easy method of separation was found and, as a result of losses during purification, no estimate can be made of the amount of these two compounds in the original mixture.

A first rough separation was achieved by treating the dry mixture with boiling chloroform, which dissolved the more soluble dinitro-compound, leaving the greater part of the 3 : 5 : 4′-trinitro-compound. This, after many crystallisations from glacial acetic acid, was obtained as pale yellow needles, m. p. 197—198° (Found: C, 47·5; H, 2·5; N, 13·4. Calc. for $C_{12}H_7O_7N_3$: C, 47·1; H, 2·3; N, 13·8%). Evaporation of the chloroform extract gave a product, m. p. 136—140°, which, after crystallisation from acetic acid, gave eventually 4-hydroxy-3 : 5-dinitrodiphenyl as pale yellow plates, m. p. 151—152° (Found: C, 55·6; H, 3·1; N, 11·2. Calc. for $C_{12}H_8O_5N_2$: C, 55·4; H, 3·1; N, 10·8%). The m. p.s of these two compounds were not depressed on their admixture with pure specimens of the compounds prepared respectively by careful nitration of 4-hydroxy-4′-nitrodiphenyl and 4-hydroxydiphenyl.

Hydrolysis of 4′-Nitro- and 2′-Nitro-4-diphenylyl Benzoate.—A suspension of the 4′-nitro-ester (30 g.) in ethyl alcohol (150 ml.) was heated under reflux and hydrolysed by careful addition of a solution of potassium hydroxide (20 g. in 50 ml. of water). The immediate deep red coloration showed that hydrolysis was rapid, but, to ensure that it was complete, the mixture was heated for 15 minutes. On cooling, the potassium salt of 4-hydroxy-4′-nitrodiphenyl separated in deep blue lustrous plates (24 g.). These were dissolved in the minimum volume of hot water and acidified, 4-hydroxy-4′-nitrodiphenyl being precipitated as a bright yellow solid, m. p. 200—201° (18 g.) (Bell and Kenyon, *loc. cit.*, gave m. p. 203°). It gave a methyl ether, m. p. 111°.

2′-Nitro-4-diphenylyl benzoate (15 g.), dissolved in alcohol–acetone (150 ml.), was hydrolysed in a similar manner, but in this case the potassium salt of 4-hydroxy-2′-nitrodiphenyl was not deposited, and on acidification benzoic acid was precipitated. When this had been collected, the filtrate was diluted with water (500 ml.) and a brown oil separated. After several hours, this solidified and, after being dried, it was crystallised from ether–ligroin (b. p. 40—60°). Further crystallisation from carbon tetrachloride gave the 4-hydroxy-2′-nitrodiphenyl as elongated prisms (2·1 g.), m. p. 116° (Found: N, 6·4. Calc. for $C_{12}H_9O_3N$: N, 6·5%). Its methyl ether, m. p. 64°, crystallised from methyl alcohol in the same form.

To a portion of 4-hydroxy-2′-nitrodiphenyl dissolved in aqueous alkali at 40° was added a solution of potassium permanganate until no further decolorisation occurred. The mixture was then heated on a water-bath for an hour. The cold solution was decolorised with sulphur dioxide, and extracted with ether. After removal of the ether, the solid remaining was crystallised from water and gave *o*-nitrobenzoic acid, m. p. 143° (unchanged when the sample was mixed with an authentic specimen).

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University College, Hull.
The University, Sheffield.

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