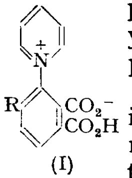
500. *Displacements of Anionoid Substituents in Phthalic Anhydrides by Pyridine and β-Picoline.*

By M. P. Balfe, M. Doughty, and J. Kenyon.

Pyridine and β-picoline react with 3-nitro- and 3 : 6-dichloro-phthalic anhydrides to yield betaines (I). Similar replacements of groups adjacent to electron-attracting substituents by pyridine and other electrophilic molecules are well-known. The reactions now described have two interesting features: First, the carboxyanhydro-group both activates the replacement of the *o*-substituent and, after ring-opening, assumes the negative charge which is required for the formation of the betaine (when a nitro-group is displaced, a betaine is the only product which can be isolated, because the nitrite ion is not sufficiently stable to permit the isolation of a pyridinium nitrite). Secondly, the carboxy-anhydride ring system is particularly effective in activating the *o*-anionoid group. Other evidence is reviewed which shows that electron-attraction by the $\overset{+\longrightarrow}{\mathrm{C—O}}$ dipole is particularly strong when the dipole is held in a ring system coplanar with the nucleus from which a group is to be displaced, which may be because the planar configuration is favourable to polar contributions in the resonance hybrid of the reacting molecule.

When a solution of 3-nitrophthalic anhydride in pyridine is heated, brown nitrous fumes are evolved for about 12 hr., after which the hydrate of 1-(2 : 3-dicarboxyphenyl)-pyridinium betaine (I; R = H) can be isolated from the solution (in 50% yield on the weight of anhydride), the nitro-group having been displaced by pyridine.



(I)

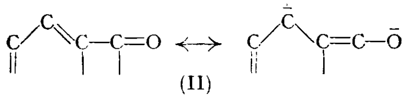
There are many recorded examples of anionoid displacement of groups—including nitro-groups—adjacent to electron-attracting substituents in aromatic nuclei, and fairly numerous examples of replacement of such groups by pyridine: there is one example of the displacement of nitro-groups by pyridine—its reaction with 1 : 8-dinitroanthraquinone (*Chem. Zentr.*, **1903**, ii, 1099).

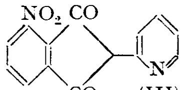
If the displaced group is stable as an anion, then a pyridinium salt is obtained; if the cation contains a group which can assume a negative charge the salt is the salt of a betaine (see, *e.g.*, Zincke, *J. pr. Chem.*, 1910, **82**, 19). The nitro-group is not sufficiently stable as an anion to permit the isolation of a pyridinium nitrite. The reaction product from the displacement of a nitro-group by pyridine can therefore only be identified when the aromatic nucleus contains a group such as carboxyl or hydroxyl capable of assuming a negative charge, thus enabling a betaine to be isolated.

The novel feature of the reaction with 3-nitrophthalic anhydride is that the anhydro-group first activates the displacement of the *o*-nitro-group and then (after ring opening) assumes the negative charge which produces the insoluble betaine. Similarly the carboxy-anhydride group can activate the displacement of *o*-chlorine: 3 : 6-dichlorophthalic anhydride reacts with pyridine and the resulting dibetaine can be isolated from the products of reaction. The anhydro-group does not, of course, activate the *m*-position: 4-chloro- and 4-nitro-phthalic anhydrides do not react with pyridine.

Although many groups retain their electron-attraction in pyridine solution yet they apparently do not facilitate the displacement of an *o*-anionoid group by pyridine: 2-chloro- and 2-nitro-benzoic anhydride, 2-ethyl 1-hydrogen 3-nitrophthalate, 2-ethyl 1-hydrogen 3 : 6-dichlorophthalate, and 5-hydroxy-2-nitrobenzaldehyde do not react with pyridine. In the recorded examples of the entry of pyridine into an aromatic nucleus, the displaced group is usually halogen and two adjacent (2 : 6-)nitro-groups are required to activate it (Borsche and Rautscheff, *Annalen*, 1911, **379**, 152; Zincke *et al.*, *Annalen*, 1904, **330**, 361; **333**, 296). A nitro-group can, however, be activated by one adjacent nitro-group: thus *o*-dinitrobenzene reacts with pyridine evolving brown fumes (betaine formation is impossible and a reaction product cannot be isolated), and 2 : 3-dinitrobenzoic acid reacts similarly, yielding a betaine of the probable structure (I; R = NO_2). Thus it appears that the $\overset{+\longrightarrow}{\mathrm{C{-}O}}$ dipole of the cyclic carboxy-anhydride group is as powerful in *o*-activation as the nitro-group and much more powerful than the $\overset{+\longrightarrow}{\mathrm{C{-}O}}$ dipoles in the linear anhydride group and the aldehyde-group.

There is a considerable body of evidence that an anionoid group attached to an aromatic nucleus is particularly easy to replace when there is in the *o*-position a carbonyl group which forms part of a ring system; *e.g.*, in substituted phthalic anhydrides (Pratt and Perkins, *J. Amer. Chem. Soc.*, 1918, **40**, 198, 219; Marriott and Robinson, *J.*, 1939, 134; and the present experiments), anthraquinones (Barnett, "Anthracene and Anthraquinone," Baillière, Tindall, and Cox, London, 1928, p. 199), 1-chloroxanthone (Dhar, *J.*, 1917, **117**, 1068), and 1-chloro-4-nitroacridone (Nisbet and Goodlet, *J.*, 1932, 2772). In all these examples the activating carbonyl group is held in a ring system which is coplanar with the aromatic nucleus from which a group is displaced; presumably the coplanarity increases the activation because it favours the contribution of the structure (II) in the resonance hybrid.


(II)


(III)

β-Picoline reacts with 3-nitrophthalic anhydride, yielding the β-methyl betaine analogous to (I). α-Picoline yields 4-nitro-2-2′-pyridylindane-1 : 3-dione (III) in accordance with the known reactivity of its methyl group. Quinoline, and nicotinic and α-picolinic acid, reacted with 3-nitrophthalic anhydride with the evolution of brown fumes but no definite products could be isolated. Hot triethylamine does not dissolve 3-nitrophthalic anhydride or react with it in solvents (dilution with dioxan prevents the reaction of pyridine with the anhydride).

EXPERIMENTAL

Interaction of 3-*Nitrophthalic Anhydride and Pyridine: Formation of* 1-(2 : 3-*Dicarboxyphenyl*)*pyridinium Betaine Hydrate*.—A mixture of 3-nitrophthalic anhydride (10 g.) and pyridine (30 c.c.; b. p. range 0·6°) contained in a flask fitted with a narrow air-condenser (30″) was heated in an oil-bath at 105—110°. The initially clear yellow solution became deep brown within 15 min. and brown fumes of oxides of nitrogen appeared. After an hour a yellowish-brown crystalline cake was being deposited on the sides of the flask: with continued heating the deposit blackened and increased in amount and after 12 hr. evolution of brown fumes ceased. The cooled product was filtered off and the crystalline material washed with light petroleum, crushed, and dried (6·8 g.); after two crystallisations from aqueous alcohol (33%) (norite), it formed slightly yellow prisms (1·9 g.). It darkens at 120° and decomposes to a black mass at 270—280° [Found: C, 60·1; H, 4·3; N, 5·0%; *M* (by titration with NaOH), 261·5. $C_{13}H_9O_4N,H_2O$ requires C, 59·8; H, 4·2; N, 5·35%; *M*, 261·2].

The following salts were readily prepared from the betaine: 1-(2 : 3-*dicarboxyphenyl*)-*pyridinium chloride*, yellow prisms (from aqueous alcohol), m. p. 185—190° (decomp.) (Found: N, 4·45; Cl, 11·8. $C_{13}H_9O_4N,HCl,H_2O$ requires N, 4·7; Cl, 12·0%), *acetate*, prisms (from acetic acid), m. p. 199—200° (Found: C, 59·6; H, 4·4; N, 5·0. $C_{15}H_{13}O_6N$ requires C, 59·4; H, 4·3; N, 4·6%), and *picrate*, yellow needles (from methanol), m. p. 184—185° (Found: C, 49·5; H, 2·6; N, 11·9. $C_{19}H_{12}O_{10}N_4$ requires C, 50·0; H, 2·65; N, 12·2%).

Non-interaction of 3-*Nitrophthalic Anhydride and Pyridine in Dioxan.*—A solution of the anhydride (5 g.) in dry dioxan (20 c.c.) and pyridine (10 c.c.) was kept at 100° for 12 hr.; the solution darkened but slightly, evolved no brown fumes and, by evaporation, yielded unchanged anhydride, m. p. 160—163°.

Interaction of 3-*Nitrophthalic Anhydride and Quinoline.*—A solution of the anhydride (5 g.) in freshly distilled dry quinoline (20 c.c.) after being kept at 105—106° for 30 min. began to evolve nitrous fumes and continued doing so for 24 hr. The main product was a black tar which yielded no crystalline material.

Interaction of 3-*Nitrophthalic Anhydride and* β-*Picoline: Formation of* 1-(2 : 3-*Dicarboxyphenyl*)*picolinium Betaine Hydrate.*—A solution of the anhydride (10 g.) in purified β-picoline (15 c.c.) was slowly heated to 110°: brown fumes were evolved and a rather vigorous reaction ensued during which dark brown crystals began to separate. After 12 hr. at 110° the mixture was filtered and the solid (2·35 g.) washed with light petroleum. After two crystallisations from aqueous alcohol (norite) the *betaine monohydrate* was obtained as buff-coloured clusters of prisms which decomposed with blackening at 215—217° [Found: C, 61·0; H, 4·9%; *M* (by titration with NaOH), 277. $C_{14}H_{11}O_4N,H_2O$ requires C, 61·1; H, 4·8%; *M*, 275·3].

Interaction of 3 : 6-*Dichlorophthalic Anhydride and Pyridine: Formation of* 2 : 3-*Dicarboxyphenylene*-1 : 4-*bispyridinium Dibetaine.*—A solution of the anhydride (7·5 g.) in pyridine (15 c.c.) was kept at 110°: within 20 min. crystals began to separate and after 2 hr. the product became a brown sludge. This was diluted with light petroleum and filtered, the separated solid being washed with light petroleum until free from pyridine. This crude material (8·8 g.) after two crystallisations from aqueous acetone yielded the *pentahydrate* of the dibetaine as long colourless needles which darkened at 180° but did not melt below 330° [Found: C, 53·0; H, 5·6; N, 6·45; H_2O (loss at 105°), 21·0. $C_{18}H_{12}O_4N_2,5H_2O$ requires C, 52·7; H, 5·4; N, 6·8; H_2O, 20·9%].

Interaction of 2 : 3-*Dinitrobenzoic Acid and Pyridine: Isolation of* 1-(6-*Carboxy*-2-*nitrophenyl*)*pyridinium Picrate.*—A solution of 2 : 3-dinitrobenzoic acid (m. p. 201—202°; 1·5 g.) in pyridine (10 c.c.), kept at 110° for 2 hr., slowly darkened and evolved brown fumes: the solution was then heated under gentle reflux for 8 hr. The crystalline precipitate (0·36 g.) after two crystallisations from aqueous acetone yielded the betaine, as buff-coloured stout rods which darkened at 170° and decomposed at 225°. This betaine was characterised as the derived *picrate* (formed in aqueous methanol), bright yellow needles (from methanol), m. p. 191° (Found: C, 45·4; H, 2·2; N, 14·8. $C_{18}H_{11}O_{11}N_5$ requires C, 45·7; H, 2·3; N, 14·4%).

The following pairs of compounds when kept at 110—115° for 6—8 hr. readily evolved oxides of nitrogen; the other products of the reactions were generally dark amorphous solids or tars from which no crystalline material could be isolated: (i) *o*-dinitrobenzene and pyridine; (ii) *o*-dinitrobenzene and picolinic acid. Tetrachlorophthalic anhydride and pyridine yielded non-crystalline products.

Compounds which are Stable to Hot Pyridine.—When solutions, in an excess of pyridine, of each of the following compounds were kept at 110° for 8—20 hr., the compounds were recovered unchanged: 3-nitrophthalic acid, m. p. 215—216°; 2-ethyl 1-hydrogen 3-nitrophthalate, m. p. 156—157°; 4-nitrophthalic anhydride, m. p. 117—119°; 3-nitrophthalimide, m. p. 214—215°: 3-iodophthalimide, m. p. 237—239°; 5-hydroxy-2-nitrobenzaldehyde, m. p. 166—167°; *o*-nitrobenzoic anhydride, m. p. 134—135°; *o*-chlorobenzoic anhydride, m. p. 79—81°; *p*-dinitrobenzene, m. p. 171—172°; 4-chlorophthalic anhydride, m. p. 95—96°.

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