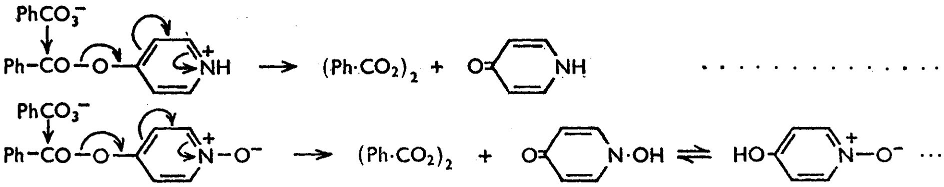
570. *Reactions of Pyridyl Benzoates with Some Perbenzoic Acids.*

By J. I. G. Cadogan.

Whereas 3-pyridyl benzoate with perbenzoic acid in chloroform gives the expected 3-pyridyl benzoate 1-oxide, the 2- and the 4-isomer give dibenzoyl peroxide and no 1-oxide. The mechanisms of the latter and related reactions have been investigated and are discussed.

Although the reactions of peracids with tertiary amines to give the corresponding *N*-oxides are well known for the pyridine series,[1] the reactions of perbenzoic and substituted perbenzoic acids with aromatic esters of the hydroxypyridines have not previously been studied. These reactions were investigated in an attempt to prepare the corresponding *N*-oxides, which were required for another investigation.

When 4-pyridyl benzoate was allowed to react with a large excess of perbenzoic acid in chloroform none of the expected *N*-oxide was isolated or detected, but dibenzoyl peroxide and a mixture of 4-hydroxypyridine and 4-hydroxypyridine 1-oxide were formed. With a slight excess of the peracid, dibenzoyl peroxide and 4-hydroxypyridine 1-oxide appeared; 4-hydroxypyridine was not isolated in this case, but small amounts if present would have been undetected. To account for these products it is considered that the base is first quaternised. This can occur in either or both of two ways: (i) by oxidation of the base to the 1-oxide; (ii) by decomposition of the perbenzoic acid to the stronger benzoic acid, which will protonate the base. Both methods will render the ester liable to nucleophilic attack by perbenzoate anion, as shown. The formation of 4-hydroxypyridine 1-oxide could in theory arise by direct oxidation of 4-hydroxypyridine produced as in (1), but it has been shown, both in this investigation and elsewhere,[2] that such oxidation does not occur under these conditions. Plainly, the relative extents of reactions (1) and (2) will depend on the experimental conditions, and it was conceivable that conditions could be selected which would give 4-pyridyl benzoate 1-oxide. In an attempt to do this, 4-pyridyl benzoate was treated with less than one equivalent of perbenzoic acid in chloroform. The products were dibenzoyl peroxide, 4-hydroxypyridine, and a trace of an unidentified compound. No oxide was detected. Similar results were obtained from experiments with peranisic acid and 4-pyridyl benzoate. A large excess of the acid gave *p*-anisoyl benzoyl peroxide, 4-hydroxypyridine, and 4-hydroxypyridine 1-oxide. A slight excess of the oxidising agent gave the peroxide and 4-hydroxypyridine, while less than one equivalent of the peracid gave 4-hydroxypyridine 1-oxide, 4-hydroxypyridine, and a trace of the peroxide. In no case was the *N*-oxide of the ester isolated, although traces of unidentified solids were obtained in the last two experiments.



. . . . (1)

. . . (2)

The conclusions summarised in the equations are further supported by the results of the following experiments: 2-pyridyl *p*-nitrobenzoate and perbenzoic acid gave benzoyl *p*-nitrobenzoyl peroxide, and 2-pyridyl benzoate gave benzoyl peroxide.

In each of the above cases the high reactivity of the carbonyl-carbon atom towards nucleophilic substitution is a result of favourable polarisation, induced by the quaternary

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[1] Ochiai, *J. Org. Chem.*, 1953, **18**, 534; Katritsky, *Quart. Rev.*, 1956, **10**, 395.

[2] Dr. C. W. Rees, personal communication.

nitrogen atom. Such polarisation can operate only in the 2- and the 4-isomer. If this rationalisation is valid, then the carbonyl-carbon atom in the corresponding 3-isomer should be relatively unreactive towards nucleophilic substitution. This is supported by the isolation of 3-pyridyl benzoate 1-oxide after reactions of perbenzoic acid and of peranisic acid with 3-pyridyl benzoate in chloroform. No diacyl peroxides were isolated or detected.

EXPERIMENTAL

Unless otherwise stated, the light petroleum used had b. p. 60—80°. Perbenzoic and peranisic acid, prepared by standard methods, were stored as approximately 5% solutions in chloroform and were analysed immediately before use.

Preparation of the Isomeric Pyridyl Benzoates.—The hydroxypyridine (1 mol.), as a 10% solution in chloroform, was boiled under reflux for 30 min. with benzoyl chloride (1 mol.). When cool, the solution was washed with potassium carbonate solution and dried ($MgSO_4$). Evaporation of the filtered solution left the pyridyl benzoate. 2-Pyridyl benzoate was distilled (b. p. 136°/0·4 mm.; m. p. 42°; lit.,[3] m. p. 42°). 3-Pyridyl benzoate had m. p. 51—52° (crystals from light petroleum; lit.,[4] m. p. 51°) (Found: C, 72·5; H, 4·7. Calc. for $C_{12}H_9O_2N$: C, 72·3; H, 4·6%). 4-Pyridyl benzoate had m. p. 79—80° (crystals from light petroleum; lit.,[5] m. p. 81°) (Found: C, 72·3; H, 4·6%). 2-Pyridyl *p*-nitrobenzoate (m. p. 120°, crystals from light petroleum; lit.,[3] m. p. 116°) was prepared similarly.

p-Anisoyl benzoyl peroxide (m. p. 73·5°; crystals from light petroleum) (Found: C, 66·4; H, 4·5. Calc. for $C_{15}H_{12}O_5$: C, 66·2; H, 4·4%) was prepared by shaking an ice-cold solution of peranisic acid in chloroform containing the equivalent amount of benzoyl chloride with an excess of ice-cold 2N-potassium hydroxide. Working up the chloroform solution gave the peroxide. Benzoyl *p*-nitrobenzoyl peroxide (m. p. 115—116°; crystals from light petroleum) (Found: C, 58·2; H, 3·2. Calc. for $C_{14}H_9O_6N$: C, 58·5; H, 3·1%) was similarly prepared from perbenzoic acid and *p*-nitrobenzoyl chloride. 4-Hydroxypyridine 1-oxide was prepared as described by Den Hertog and Combe.[6]

Reaction of Perbenzoic Acid with 3-Pyridyl Benzoate.—3-Pyridyl benzoate (5 g.) was added to a 5% solution of perbenzoic acid in chloroform (85 ml.). The mixture was kept at room temperature for 3 days, then washed with sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation left buff crystals (4·5 g.) which, recrystallised from ethyl acetate followed by light petroleum–benzene, gave *3-pyridyl benzoate 1-oxide* as prisms (3·1 g.), m. p. 127° (Found: C, 66·9; H, 4·1. $C_{12}H_9O_3N$ requires C, 67·0; H, 4·2%).

Reaction of Peranisic Acid with 3-Pyridyl Benzoate.—The procedure was essentially as in the preceding paragraph. The product was 3-pyridyl benzoate 1-oxide, m. p. and mixed m. p. 127°.

Reaction of 2-Pyridyl Benzoate with Perbenzoic Acid.—The ester (2 g.) was left at room temperature in a 5% chloroform solution of perbenzoic acid (40 ml.) for 48 hr. Working up as described in the previous experiment gave dibenzoyl peroxide (1·65 g.), m. p. 97—104° (decomp.), mixed m. p. 102—104° (decomp.), and correct infrared spectrum.

Reaction of 2-Pyridyl p-Nitrobenzoate with Perbenzoic Acid.—The ester (0·3 g.) and 5% perbenzoic acid solution (20 ml.) were caused to react as described above. They gave crude benzoyl *p*-nitrobenzoyl peroxide (0·38 g.), m. p. 100—108°, m. p. undepressed on admixture with authentic material. Recrystallisation from light petroleum gave the pure peroxide (0·3 g.), m. p. and mixed m. p. 115°. The aqueous solution was acidified and the benzoic acid was extracted with methylene chloride. The aqueous solution was evaporated almost to dryness, then the pH was adjusted to 7 and evaporation continued to dryness. The residue was extracted with boiling acetone (3 × 50 ml.). Evaporation of the acetone left a buff solid (0·1 g.) which gave a picrate (0·15 g.), m. p. 165—169° (from acetone), m. p. undepressed on admixture with authentic 2-hydroxypyridine picrate (m. p. 169—170°).

Reactions of 4-Pyridyl Benzoate.—(i) *With perbenzoic acid* (5 *equivalents*). The ester (0·7 g.), with the peracid (5·5%; 45 ml.), was left for 72 hr. at 20°; a gum (0·1 g.) was deposited which proved to be 4-hydroxypyridine 1-oxide (picrate, m. p. and mixed m. p. 165°) admixed with benzoic

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[3] Chichibabin and Szokov, *Ber.*, 1925, **58**, 2650.
[4] Cavallito and Haskell, *J. Amer. Chem. Soc.*, 1944, **66**, 1166.
[5] Arndt and Kalischek, *Ber.*, 1930, **63**, 587.
[6] Den Hertog and Combe, *Rec. Trav. chim.*, 1952, **71**, 752.

acid. The filtered solution was washed with aqueous potassium carbonate and dried ($MgSO_4$). Evaporation of the chloroform solution left dibenzoyl peroxide (0·65 g.), m. p. and mixed m. p. 102° (decomp.). The aqueous portion was acidified and the benzoic acid was extracted with methylene chloride, the aqueous solution was evaporated, and the residue extracted with ethanol. Evaporation of the ethanol left a brown residue which gave a picrate, which on fractional crystallisation from water gave 4-hydroxypyridine picrate (0·28 g.), m. p. and mixed m. p. 235°, and the more soluble 4-hydroxypyridine 1-oxide picrate (0·08 g.), m. p. and mixed m. p. 164°.

In a similar experiment 4-pyridyl benzoate (1·4 g.) was treated with slightly less perbenzoic acid (5%; 70 ml.). In this case 4-hydroxypyridine 1-oxide (0·55 g.; m. p. and mixed m. p. 238—240°) separated as pale yellow crystals, uncontaminated with benzoic acid. The chloroform solution gave dibenzoyl peroxide [1·48 g.; m. p. and mixed m. p. 99—103° (decomp.)].

(ii) *With perbenzoic acid* (1·45 *equivalents*). The ester (0·7 g.) and the acid (5·5%; 13 ml.) were caused to react in the usual way. 4-Hydroxypyridine 1-oxide (0·1 g.; m. p. and mixed m. p. 239—240°) was precipitated. Dibenzoyl peroxide [0·25 g.; m. p. and mixed m. p. 100° (decomp.)] and 4-hydroxypyridine 1-oxide picrate (0·5 g.; m. p. and mixed m. p. 165°) were also isolated.

(iii) *With perbenzoic acid* (0·72 *equivalent*). The ester (1·32 g.) and acid (5·5%; 13 ml.) were allowed to react in the usual way. No solid was precipitated. The chloroform solution was extracted with aqueous potassium carbonate and then with 2N-hydrochloric acid. Evaporation of the chloroform solution left dibenzoyl peroxide [0·18 g.; m. p. and mixed m. p. 104—105° (decomp.)]. Basification and extraction of the acidic washings gave the ester and a trace of an unidentified colourless solid, m. p. 70—105°. Working up the alkaline washings in the usual way gave 4-hydroxypyridine picrate (0·35 g.; m. p. and mixed m. p. 232°).

(iv) *With peranisic acid* (5 *equivalents*). The ester (0·7 g.) was treated with 5·4% peranisic acid solution (55 ml.) in the usual way. The colourless solid (1·95 g.) which was deposited was treated with water and filtered off. The residue (1·6 g.) was *p*-anisic acid, m. p. and mixed m. p. 180°. The filtrate gave 4-hydroxypyridine picrate (0·2 g.), m. p. and mixed m. p. 238°. Concentration of the mother-liquors gave another picrate (0·35 g.; m. p. 140—160°) which, on recrystallisation from water gave 4-hydroxypyridine 1-oxide picrate, m. p. and mixed m. p. 158—161°. The chloroform solution gave yellow *p*-anisoyl benzoyl peroxide (0·6 g.), m. p. 67—72°; recrystallisation from light petroleum gave the pure peroxide.

In a similar experiment involving the ester (1·4 g.) and less peranisic acid in more dilute solution (2%; 100 ml.), 4-hydroxypyridine 1-oxide (0·62 g.; m. p. and mixed m. p. 238—241°) was deposited. Crude anisoyl benzoyl peroxide (1·4 g.), m. p. 64—69° (m. p. and mixed m. p. 71—74° after recrystallisation from light petroleum), was also isolated.

(v) *With peranisic acid* (1·45 *equivalents*). The ester (0·7 g.) with the acid (5·4%; 16 ml.) gave a solid (0·48 g.; m. p. 145°) which was a mixture of *p*-anisic acid and 4-hydroxypyridine 1-oxide (picrate, m. p. and mixed m. p. 161—165°). The chloroform solution on evaporation left a gum which, on extraction with light petroleum, gave colourless crystals (0·1 g.; m. p. 70—90°). Repeated recrystallisation gave a solid, m. p. 114—115°, which could not be identified. Evaporation of the light petroleum mother-liquors left anisoyl benzoyl peroxide (0·2 g.), m. p. and mixed m. p. 69°.

(vi) *With peranisic acid* (0·72 *equivalent*). The ester (0·7 g.) with the acid (5·4%; 8 ml.) deposited no solid. Working up as described in (v) gave a trace of anisoyl benzoyl peroxide, an unidentified solid, m. p. 130—150° (trace), unchanged ester, 4-hydroxypyridine picrate (0·12 g., m. p. and mixed m. p. 235°), and 4-hydroxypyridine 1-oxide picrate (50 mg.; m. p. and mixed m. p. 167—168°).

Reaction of 4-Hydroxypyridine with Perbenzoic Acid.—4-Hydroxypyridine (0·5 g.) and perbenzoic acid in chloroform (5% solution; 40 ml.) were kept at room temperature for 48 hr. No solid had been precipitated in this time and 4-hydroxypyridine was recovered almost quantitatively from the solution as the picrate, m. p. and mixed m. p. 238—239°.

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