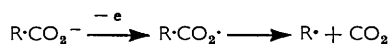


752. *Homolytic Aromatic Substitution. Part XX.* The Phenylation of Pyridine by Electrolysis.*

By P. J. BUNYAN and D. H. HEY.

The electrolysis of benzoic acid in pyridine has been re-investigated, and the proportions in which the three isomeric phenylpyridines are formed have been determined. The results obtained are consistent with the formation of phenyl radicals at the anode.

It is well known that pyridine can be phenylated by a variety of reactions which are all considered to involve the participation of free phenyl radicals. Such reactions have been reviewed by Hey, Stirling, and Williams,¹ who determined the proportions in which the three isomeric phenylpyridines are formed in five such reactions. Fichter and Stenzl² have shown that the electrolysis of benzoic acid in pyridine solution containing diethylamine gives 4-phenylpyridine and possibly 2-phenylpyridine, together with small quantities of biphenyl-4-carboxylic acid, biphenyl, and benzene. On this evidence, together with the observation that the decomposition of benzoyl peroxide in a concentrated solution of benzoic acid in pyridine yields similar products, they concluded that benzoyl peroxide was formed at the anode during electrolysis. The presence of diacyl peroxides at the anode under special conditions and at low temperatures had been previously reported in the electrolysis of aliphatic acids.³ It has been shown recently, however, that the electrolysis of salts of carboxylic acids probably proceeds by direct production of free radicals,⁴ thus:



It is also well established that diaroyl peroxides decompose to give the same intermediates at somewhat higher temperatures than those normally used in the electrolyses:



* Part XIX, preceding paper.

¹ Hey, Stirling, and Williams, *J.*, 1955, 3963.

² Fichter and Stenzl, *Helv. Chim. Acta*, 1939, **22**, 970.

³ Fichter and Zumburn, *Helv. Chim. Acta*, 1927, **10**, 869.

⁴ Lippincott and Wilson, *J. Amer. Chem. Soc.*, 1956, **78**, 4290.

Thus, the analogies drawn by Fichter and Stenzl² have no significance other than that both reactions probably proceed by a common intermediate, namely, the phenyl radical.

In the present work, the phenylation of pyridine by means of the electrolysis of benzoic acid has been re-investigated since, if it proceeds through the formation of a phenyl radical, it should yield all three isomeric phenylpyridines, in proportions comparable with those reported by Hey, Stirling, and Williams.¹ Fichter and Stenzl² themselves isolated only 4-phenylpyridine, which was characterised as the picrate, and possibly 2-phenylpyridine, although Dewar⁵ has erroneously stated that they isolated all three isomers. Fichter and Stenzl's experiment² was repeated, but examination of the infrared spectrum of the basic fraction, from which some 4-phenylpyridine picrate was obtained, showed that it was considerably different from that of an uncontaminated mixture of the three isomeric phenylpyridines. This mixture was therefore not suitable for analysis by the ultraviolet spectrophotometric method used by Hey, Stirling, and Williams.¹ It was further found that the basic fraction could not be readily purified, and that it was not quantitatively converted into a mixture of picrates. Only the very insoluble picrate of 4-phenylpyridine could be recovered from that portion which was so converted. It is considered that these complications arise mainly from the presence of the diethylamine as used by Fichter and Stenzl. Since some salt-forming reagent is necessary to achieve the correct degree of conductivity, and sodium methoxide leads to the formation of deposits on the anode,⁶ it was decided to repeat the electrolysis of benzoic acid in aqueous alkaline pyridine, at the same time using less concentrated solutions, in an attempt to make the electrolysis cleaner and its products less complex. Sandin and Brown⁷ have already reported the phenylation of pyridine by the decomposition of diphenyliodonium chloride in aqueous alkaline pyridine, all three isomeric phenylpyridines being isolated. The infrared spectrum of the somewhat smaller basic fraction obtained under these new conditions also differed from that of an uncontaminated mixture of the three isomeric phenylpyridines in having two additional peaks (3165 and 1672 cm^{-1}), but it was found that these could be introduced and accentuated by the addition of 2-pyridone to a mixture of phenylpyridines. It was estimated that the upper limit of the impurity was 10 moles %. In experiments with a mixture of isomeric phenylpyridines, it was found that 2-pyridone co-distilled with the phenylpyridines, and could not be removed from a chloroform solution by extraction with sodium hydroxide. It was, however, found that a mixture of phenylpyridines could be purified by chromatography on alumina, either directly or after formation of the picrates, but in both cases the isomer ratio of the mixture was altered during the operation. Separation of the isomeric phenylpyridines and 2-pyridone was, however, readily achieved by reaction of the latter with *p*-nitrobenzoyl chloride followed by distillation under reduced pressure.

The isomer ratio of the purified basic fraction, determined by ultraviolet spectroscopy, was in substantial agreement with the results reported by Hey, Stirling, and Williams for other homolytic phenylations, as shown in the Table. Further, the presence of all three

Ratio of isomers obtained in the phenylation of pyridine.

Method	Isomers (%)			Method	Isomers (%)		
	2-	3-	4-		2-	3-	4-
Benzoyl peroxide	54	32	14	Phenyl iodosobenzoate...	58	28	14
Lead tetrabenzoate	52	32.5	15.5	Electrolysis	56	35	9

isomers was demonstrated beyond doubt by conversion of the mixture of bases into the picrates, fractional crystallisation⁸ of which yielded each isomer as its pure picrate. Some biphenyl-4-carboxylic acid, but no biphenyl, was isolated from the electrolysis. The main product of the electrolysis is an amorphous polymer.

⁵ Dewar, "Electronic Theory of Organic Chemistry," Oxford Univ. Press, Oxford, 1952, p. 256.

⁶ Fichter and Meyer, *Helv. Chim. Acta*, 1934, **17**, 535.

⁷ Sandin and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 2253.

⁸ Haworth, Heilbron, and Hey, *J.*, 1940, 372.

These results support the view that the electrolysis proceeds through the formation of benzyloxy- and phenyl radicals as postulated in the radical theory for the Kolbe electro-synthesis. The 2-pyridone may be considered to arise by the action of benzyloxy-radicals on pyridine to give 2-pyridyl benzoate, which could be hydrolysed to 2-pyridone by the sodium hydroxide used in the working up, or by the attack on pyridine by discharged hydroxyl ions from the water present in the electrolysis.

EXPERIMENTAL

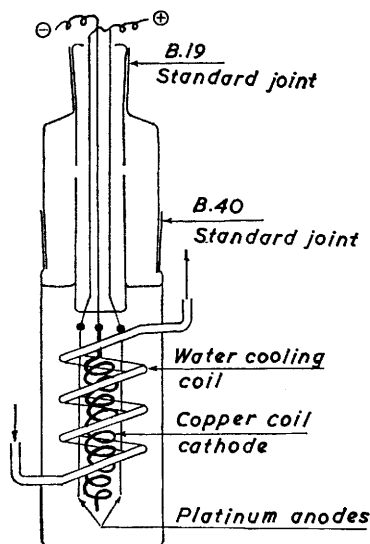
Reagents.—Pyridine (Hopkin and Williams, "AnalaR") was redistilled over potassium hydroxide and collected at 114.5°. Benzoic acid (B.D.H., "AnalaR"), m. p. 123°, was dried for 24 hr. at 70°.

Electrolysis.—Pyridine (44 ml.), benzoic acid (32 g., 0.26 mole) and 2.5*N*-aqueous sodium hydroxide (4 ml., 0.01 mole) were mixed at 70° and electrolysed between two smooth platinum anodes (5.5 × 1.3 cm.) surrounding a copper-coil cathode (2 mm. distant) in the cell illustrated in the Figure, which was suspended in a current of air (15–20°). Water was circulated through the cooling coil. A current of 1 amp. was maintained for 8 hr. by means of a 120 volt D.C. supply unit connected in series with a rheostat. The initial voltage drop across the electrodes (76 v) had to be slowly raised to 120 v during 6 hr. and water (1 ml.) was added at the sixth and the seventh hour to maintain the conductivity. Six such experiments were carried out, and the products combined in two sets of three (A and B). Acidification of the ice-cold solution with 20% hydrochloric acid gave an acid solution C, and a precipitate which was filtered off, washed with cold water, and refluxed with ether (200 ml.). The resulting suspension was filtered, and the residue washed with ether (4 × 50 ml.), and dried at 70°, to give a dark-brown amorphous powder D (from A, 19.3 g.; from B, 18.8 g.). The ethereal filtrate was extracted with 2*N*-aqueous sodium hydroxide (5 × 100 ml.), and the remaining neutral solution E was washed and dried (MgSO₄). Acidification of the alkaline extract with 20% hydrochloric acid gave a light-brown solid F, which was collected and dried *in vacuo* (CaCl₂) (from A, 60.2 g.; from B, 60.8 g.). Removal of the ether from E left a brown liquid (*ca.* 0.5 g.).

The acid F was digested in dilute ammonia, treated with aqueous barium chloride (81 g./200 ml.), and filtered in the cold. The residue was twice treated with water (250 ml.) and filtered hot. The filtrates were combined, acidified with 20% hydrochloric acid, filtered, and the solid recrystallised from aqueous alcohol (charcoal) to yield benzoic acid, m. p. and mixed m. p. 121–123° (from A, 57.2 g.; from B, 57.9 g.). The residue from the hot filtration was boiled with 20% hydrochloric acid (30 ml.), filtered, washed, and dried (CaCl₂). Extraction of the residue with boiling benzene (4 × 10 ml.) left a light-brown resinous acid similar in properties to D (from A, 1.25 g.; from B, 1.26 g.), while removal of the benzene, and recrystallisation from aqueous alcohol gave biphenyl-4-carboxylic acid in needles, m. p. and mixed m. p. 223–224° (from A, 0.05 g.; from B, 0.04 g.).

The amorphous residue D was insoluble in most non-basic organic solvents other than dimethylformamide and dimethyl sulphoxide, and was fractionally precipitated from pyridine by methanol. The middle fraction did not melt below 340° (Found: C, 66.2; H, 4.7; N, 3.2%). It was substantially unaffected by prolonged boiling with 10*N*-aqueous sodium hydroxide, concentrated alkaline potassium permanganate, and 70% sulphuric acid, whilst the infrared spectrum (Nujol mull) showed only two very weak bands (1748 and 1626 cm.⁻¹).

Treatment of solution C with concentrated aqueous sodium hydroxide, extraction with ether, and removal of the ether and pyridine from the dried (MgSO₄) extract, left a brown oil which distilled at 64°/0.03 mm., to give a pale green oil (from A, 0.61 g.; from B, 0.60 g.), which partly solidified. The residue weighed (from A) 0.31 g., and (from B) 0.27 g. These fractions



in chloroform (25 ml.) were boiled under reflux for 1 hr. with *p*-nitrobenzoyl chloride (0.6 g.), most of the excess then being removed by shaking with saturated sodium hydrogen carbonate solution (50 ml.) for several hours. Removal of the chloroform from the dried solution (MgSO_4) and subsequent distillation gave a pale green oil, b. p. 140—144°/12 mm. (from A, 0.67 g.; from B, 0.65 g.) and left a small residual yellow oil (*ca.* 0.05 g.), which only distilled at 0.03 mm. with bath-temp. 180°. The main fraction was redissolved in chloroform (25 ml.) and boiled under reflux with 2*N*-aqueous sodium hydroxide (3×50 ml.), the chloroform solution being washed with water between each operation. The dried (MgSO_4) solution was finally redistilled to yield the mixed phenylpyridines as an almost colourless oil (from A, 0.47 g.; from B, 0.42 g.), b. p. 72°/0.05 mm. (Found: N, 9.1. Calc. for $\text{C}_{11}\text{H}_9\text{N}$: N, 9.05%).

The isomer ratio of the mixture of phenylpyridines in this fraction was determined by ultraviolet spectrophotometry with the aid of a " Unicam S.P. 500 " quartz spectrometer. The solvent was ethanol. The calibration spectra of each of the pure isomers used in the calculation were those recorded by Stirling,⁹ using isomers obtained from the pure picrates. The extinction coefficients from the duplicate reactions differed only slightly from one another, and a mean value was used in the calculations. The composition of the mixture thus obtained was 2-, 56%; 3-, 35%; 4-, 9% ($\pm 2\%$).

The phenylpyridine fractions (from A and B) were finally combined and converted into the picrates, fractional crystallisation of which yielded the three pure picrates,⁸ m. p.'s 174—175°, 155—158°, and 196—197° respectively, which were characterised by mixed m. p.'s with authentic specimens.

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⁹ Stirling, Ph.D. Thesis, London, 1955.
