The Pattern of Picrate Formation in the Pyridylquinoline Series.

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Diazotised 3-aminoquinoline and pyridine give a mixture of 3-2'- and 3-4'-pyridylquinoline (cf. Coates *et al.*, *J.*, 1943, 401). A possible correlation of distance between ring nitrogen atoms and mono- or di-picrate formation in the pyridylquinoline series is pointed out.

FROM the mixture of 3-pyridylquinolines arising from diazotised 3-aminoquinoline and pyridine Coates, Cook, Heilbron, Hey, Lambert, and Lewis (*J.*, 1943, 401) isolated only two picrates : a major product (A), m. p. 227—229° (free base, m. p. 101·5°), and a minor product (B), m. p. 196° (free base, m. p. 123°). Analogy (cf. Haworth, Heilbron, and Hey, *J.*, 1940, 349, 358; Butterworth, Heilbron, and Hey, *ibid.*, p. 355) suggested that (A) was 3-2'-pyridylquinoline picrate and (B) was regarded as the 3'-isomer. Hey and Williams later (*J.*, 1950, 1678) proved (A) to be the 2'-compound but found an authentic specimen of 3-3'-pyridylquinoline to have m. p. 124° (dipicrate, m. p. 222—223°). On repeating the work of Coates *et al.* they obtained the picrate identical with (A), another, m. p. 214—216°, which did not depress the melting point of an authentic specimen of the 3'-picrate, and a third, m. p. 210° (Williams, Thesis, London, 1949).

The final outcome leads to the conclusion that the second isomeride isolated by Coates *et al.* (*loc. cit.*) could be 3-3'-pyridylquinoline, though no mixed melting-point determinations were carried out with the free bases in spite of the fact that the 3'-base and Coates's unidentified isomer melt at the same temperature. This, however, would be contrary to the theoretical predictions of Wheland (*J. Amer. Chem. Soc.*, 1942, **64**, 900) and Coulson (*J. Chim. phys.*, 1948, **45**, 243), whose calculations showed that the 2'- and the 4'-isomer should be the main products of homolytic aromatic substitution in the pyridine ring. Additional ambiguity is thrown into all these arguments by the possible confusion between monopicrates and dipicrates. Unfortunately, with all the picrates prepared by Coates *et al.* analyses were carried out for nitrogen only and it is not possible to distinguish with certainty between mono- and di-picrates in this manner. The formation of mono- and di-picrates

in substituted quinolines with two basic centre has been discussed by Hey and Williams (*loc. cit.*) and by Schofield and Theobald (*J.*, 1951, 2993). The former found that 4-3'- and 4-4'-pyridylquinaldine gave dipicrates, whilst the three isomeric 2-pyridyl-lepidines and 4-3'-pyridylquinaldine formed monopicrates. Further work was clearly required to resolve these ambiguities.

First, it was found that 3-3'-pyridylquinoline gave a dipicrate which could be obtained in two forms (m. p. 210° and 224—225°). Re-examination of the mixture of 3-pyridyl-quinolines from diazotised 3-aminoquinoline and pyridine then showed it to contain the 2'-isomer (monopicrate, m. p. 227—228°) which would not form a dipicrate, and the 4'-isomer, m. p. 124–125° (depressed on admixture with 3-3'-pyridylquinoline, m. p. 124°), isolable as its dipicrate, m. p. 213—214°. The 3'-isomer could not be detected. These results agree with theoretical predictions. It must be concluded that the picrate (B) of Coates *et al.* (*loc. cit.*) was impure and that Williams's picrates, m. p. 214—216° and 210°, (*loc. cit.*) were both the 4'-picrate, his mixed m. p. observation being without significance. The structure of 3-4'-pyridylquinoline was confirmed by the similarity of its ultra-violet absorption spectrum with those of the 2'- and the 3'-compound.

Below are tabulated data on picrate formation in the pyridylquinoline series obtained in the present work and by other authors. The Table includes the approximate N–N distances obtained from molecular models and diagrams on the assumption that bond lengths in quinoline are the same as in naphthalene (Robertson, *Proc. Roy. Soc.*, 1933, *A*, **142**, 674; cf. dimensions of benzene and pyridine, Schomaker and Pauling, *J. Amer. Chem. Soc.*, 1939, **61**, 1769) and that the bond between the two nuclei is of the same length as in diphenyl (Dhar, *Indian J. Phys.*, 1932, **7**, 43; *Chem. Abs.*, 1932, **26**, 4517). Where two figures are given in the Table, they represent the approximate minimum and maximum values of the distances between the two ring-nitrogen atoms.

Quinoline derivative	Mono- or di-picrate	N–N distance (Å)	Compound	Mono- or di-picrate	N–N distance (Å)
2-2'-Pyridyl [b]	Mono	3·0—3·7	2-2'-Pyridyl-lepidine [e]...	Mono	3·0—3·7
2-3'-Pyridyl [e]	Mono	4·3—4·95	2-3'-Pyridyl-lepidine [e]...	Mono	4·3—4·95
2-4'-Pyridyl [e]	Mono	5·12	2-4'-Pyridyl-lepidine [e]...	Mono-	5·12
3-2'-Pyridyl [d]	Mono	4·4—5·0	4-2'-Pyridylquinoline [e]	Mono	5·2
3-3'-Pyridyl [d]	Di	5·8—6·25	4-3'-Pyridylquinoline [e]	Di	6·5
3-4'-Pyridyl [d]	Di	6·6	4-4'-Pyridylquinoline [e]	Di	7·1
8-2'-Pyridyl [a]	Mono	2·5—4·2	4-2'-Pyridylquinaldine [e]	Mono	5·2
8-3'-Pyridyl [a]	Mono	3·7—5·1	4-3'-Pyridylquinaldine [e]	Di	6·5
8-4'-Pyridyl [a]	Mono	4·8	4-4'-Pyridylquinaldine [e]	Di	7·1
6-3'-Pyridyl [a]	Di	7·95			

[a] Coates *et al.*, *loc. cit.*   [b] Smirnoff, *Helv. Chim. Acta*, 1921, **4**, 802.   [e] Hey and Williams, *loc. cit.*
[d] Present work.   [e] Schofield and Theobald, *loc. cit.*

There thus appears to be a correlation of picrate formation with the distance between the nitrogen atoms. When this distance is lower than, or equal to, 5·2 Å, monopicrates are formed, whereas if the minimum distance is greater than 5·8 Å, dipicrates are formed. It should be mentioned, however, that 6-methoxy-5(or 7)-2'-pyridylquinoline forms a mono-picrate (Coates *et al.*, *J.*, 1943, 406), as also do some lutidylquinolines (Cook, Heilbron, and Steger, *J.*, 1943, 413), which would be expected to form dipicrates, although these picrates were analysed for nitrogen only so that ambiguities may arise. Steric factors may also be in operation.

EXPERIMENTAL

The spectrophotometric measurements were carried out with a Unicam SP. 500 instrument, absolute ethanolic solutions of the bases (*ca.* 3 mg. per l. of solution) being used.

3-3'-Pyridylquinoline Dipicrates.—3-3'-Pyridylquinoline (λ_{max} 210, 248 mμ; $10^{-3}\varepsilon$ 11·9, 31·7) in acetone was treated with one mol. of picric acid in acetone. Recrystallisation from the same solvent gave 3-3'-*pyridylquinoline dipicrate* as matted yellow needles, m. p. 210° (Found : C, 47·7; H, 2·6; N, 16·5. $C_{14}H_{10}N_2,2C_6H_3O_7N_3$ requires C, 47·5; H, 2·5; N, 16·8%). This was boiled with an excess of picric acid in acetone, whereupon 3-3'-pyridylquinoline dipicrate

separated as small, dark-yellow needles, m. p. 224—225°, after sintering at 180° (Found : C, 47·8; H, 3·1%). Hey and Williams (*loc. cit.*) report m. p. 222—223°, after sintering at 180°, for 3-3'-pyridylquinoline dipicrate.

Action of Diazotised 3-Aminoquinoline on Pyridine.—The suspension of the hydrochloride from 3-aminoquinoline (18·5 g.), concentrated hydrochloric acid (50 c.c.), and water (25 c.c.) was cooled to 5°, sodium nitrite (9 g.) in water (25 c.c.) added as quickly as possible below 10°, and the solid diazonium salt dissolved by addition of ice and water (400 g.). The solution was introduced during 1 hr. into pyridine (500 c.c.) stirred at 50°. The mixture was made alkaline with ammonia, and pyridine removed in steam. The residual tar was extracted with boiling benzene (charcoal), and the dried (MgSO₄) extract was distilled. The pyridylquinolines, b. p. 145—170°/0·02 mm., formed a golden-yellow oil (10·5 g.) which solidified. The bases (10 g.) in acetone (200 c.c.) were treated with a solution of picric acid (15 g.) in the same solvent (100 c.c.). The picrates were collected and the mother-liquor (A) was preserved. Recrystallisation of the picrates from *cyclo*hexanone gave almost pure 3-2'-pyridylquinoline monopicrate (10·1 g.). On recrystallisation from the same solvent it was obtained as soft yellow needles, m. p. 227—228° (Found : C, 55·1; H, 2·6. Calc. for $C_{14}H_{10}N_2,C_6H_3O_7N_3$: C, 55·2; H, 3·0%). It remained unchanged when boiled with a solution of an excess of picric acid. Decomposition of the picrate with hot 10% aqueous sodium hydroxide, extraction with hot benzene, evaporation of the dried extract, and recrystallisation of the residue from light petroleum (b. p. 60—80°) containing a little benzene, gave 3-2'-pyridylquinoline as stout prisms, m. p. 101·5° ($\lambda_{max.}$ 204, 246 mμ, $10^{-3}\varepsilon$ 9·5, 28·2). Coates *et al.* (*loc. cit.*) give m. p. 227—229° for the picrate and m. p. 101·5° for the free base. The initial *cyclo*hexanone mother-liquor was evaporated under a vacuum on the water-bath. The residual picrate was recrystallised from acetone, giving a product (1·6 g.), m. p. 201—203°. The free base, liberated as before, was recrystallised from light petroleum (b. p. 60—80°) containing a trace of benzene, and was obtained as delicate white plates of 3-4'-*pyridylquinoline* ($\lambda_{max.}$ 206, 252 mμ; $10^{-3}\varepsilon$ 23·4, 38·3), m. p. 124—125° (Found : C, 81·4; H, 4·7. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9%) depressed on admixture with the 2'- or the 3'-base. The *dipicrate* separated from acetone as small yellow needles, m. p. 213—214° (Found : C, 47·5; H, 2·5; N, 16·8. $C_{14}H_{10}N_2,2C_6H_3O_7N_3$ requires C, 47·5; H, 2·5; N, 16·9%). Partial evaporation of the initial acetone mother-liquor (A) gave a further amount (1·3 g.) of 3-4'-pyridylquinoline dipicrate, m. p. 210·5° (free base, m. p. 124—125°, undepressed on admixture with a sample obtained as above).

The initial mixture of bases from the vacuum-distillation (3 g.) was dissolved in a small volume of benzene and chromatographed on a column of alumina (70 g., 6½″ × 1″). Elution with benzene and collection of 25-ml. portions gave 3-2'-pyridylquinoline (0·20 g.), m. p. 94·5—95·5°, undepressed on admixture with an authentic specimen. Further elution with benzene gave a mixture of bases.

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