
1177. *The Self-quaternisation of 1-4'-Iodobutyl-4-pyridone.*

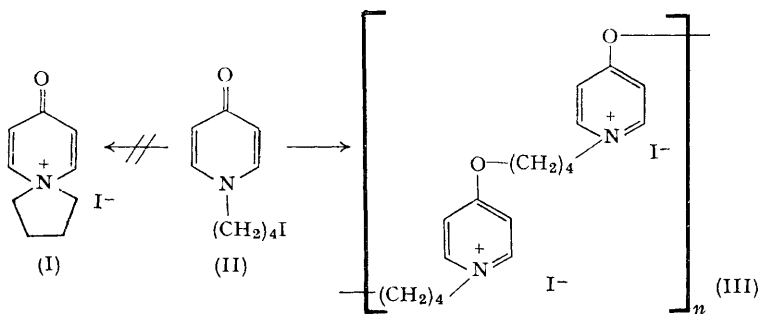
By J. P. BAKER, A. R. KATRITZKY, and T. M. MOYNEHAN.

The title reaction affords a polymeric product (III), as shown by physical and chemical evidence, rather than the spiro-derivative (I).

It is now generally accepted that pyridones are *O*-protonated to yield 2- and 4-hydroxypyridinium cations.¹ The present work was initiated in an attempt to prepare the quaternary

¹ A. R. Katritzky and R. A. Y. Jones, *Chem. and Ind.*, 1961, 722.

spiro-salt (I) which would serve as a model for the *N*-protonated pyridone cations which have been postulated.² 4-Phenoxybutyl bromide and 4-pyridone gave the expected 4'-phenoxybutyl-4-pyridone which was converted by hydriodic acid into the 4'-iodobutyl analogue (II).



However, self-quaternisation of this derivative formed the polymeric iodide (III) rather than the spiro-derivative (I).

The polymeric nature of (III) was shown by cryoscopy in water as compared with potassium iodide and 4-ethoxy-1-methylpyridinium iodide (V). The structure (III) was confirmed by the similarity of the ultraviolet (Fig. 1), infrared, and nuclear magnetic resonance spectra

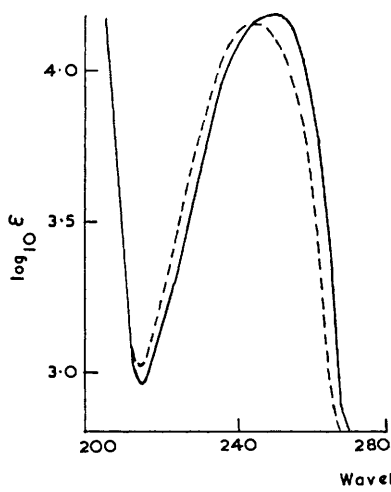


FIG. 1. Ultraviolet spectra, in water, of polymer (III) as chloride (—) and 4-ethoxy-1-methylpyridinium chloride (V) (-----).

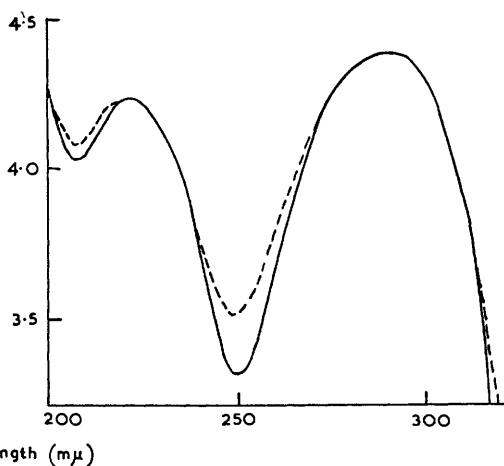
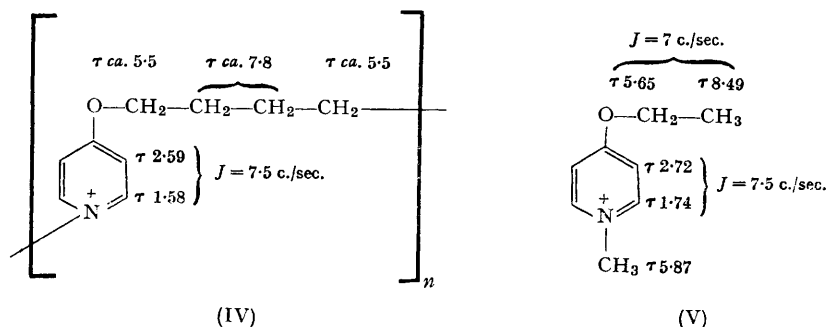


FIG. 2. Ultraviolet spectra, in water, of 1-4'-hydroxybutyl-4-(1-pyrrolidinyl)pyridinium iodide (VI) (—) and 1-ethyl-4-(1-pyrrolidinyl)pyridinium iodide (VII) (-----).

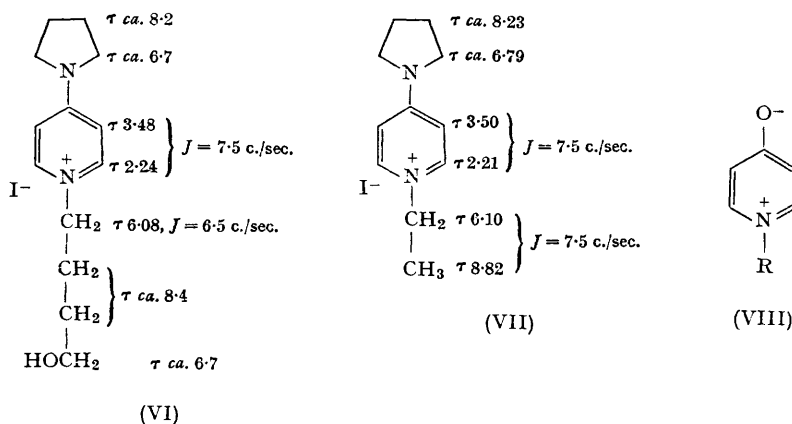
of (IV) and (V) to those of the 4-ethoxy-1-methylpyridinium cation, and by chemical evidence.

Chemical evidence for structure (III) is provided by the reaction with pyrrolidine which formed 1-4'-hydroxybutyl-4-(1-pyrrolidinyl)pyridinium iodide (VI). Spectral comparison of this compound with 1-ethyl-4-(1-pyrrolidinyl)pyridinium iodide (VII) [cf. Fig. 2; formulae (VI) and (VII)] substantiated its structure.

² E. Spinner, *J.*, 1960, 1226, 1232.



The present work emphasises the superior nucleophilicity of the oxygen atoms in 4-pyridones as compared to the nitrogen atoms and thus the importance of the zwitterionic canonical forms, cf. (VIII).



EXPERIMENTAL

1-4'-Phenoxybutyl-4-pyridone.—Ethanolic sodium ethoxide (from 50 c.c. ethanol and 1 g. sodium), 4-pyridone (4.2 g.), and 4-bromobutyl phenyl ether (10.1 g.) were refluxed for 18 hr. with stirring. The filtered solution was evaporated and the residue passed through a short alumina column in chloroform. Evaporation of the eluate gave the *phenoxybutylpyridone* (8.8 g., 82%) as prisms, m. p. 52—55° (from benzene) (Found: C, 74.2; H, 7.2. $C_{15}H_{17}NO_2$ requires C, 74.1; H, 7.0%).

The *picrate* formed plates, m. p. 139—141° (from ethanol) (Found: C, 53.6; H, 4.2. $C_{21}H_{20}N_4O_9$ requires C, 53.4; H, 4.2%).

1-4'-Iodobutyl-4-pyridone Hydriodide.—The phenoxy-pyridone (4.0 g.) and constant-boiling hydriodic acid (30 c.c.) were refluxed for 3 hr. Dilution with water gave 1-4'-*phenoxybutyl-4-pyridone hydriodide* (4.2 g., 69%) as plates, m. p. 149—151° (Found: C, 48.9; H, 4.9. $C_{15}H_{18}INO_2$ requires C, 48.5; H, 4.8%). This salt (2.6 g.) was refluxed with constant-boiling hydriodic acid (10 c.c.) and acetic acid (20 c.c.) for 5 hr. Evaporation at 100°/15 mm. and crystallisation of the residue from ethanol gave the *iodide hydriodide* (2.5 g., 88%) as prisms, m. p. 177—179° (Found: C, 27.2; H, 2.9. $C_9H_{13}I_2NO$ requires C, 26.7; H, 3.2%).

The *picrate* formed plates, m. p. 102—104° (from ethyl acetate) (Found: C, 35.7; H, 2.85. $C_{15}H_{15}IN_4O_8$ requires C, 35.6; H, 3.0%).

Polymeric Hydriodide (III).—The iodide hydriodide (2 g.), suspended in water, was treated with potassium carbonate (10% excess). The mixture was shaken and extracted with chloroform. The dried ($MgSO_4$) extract was refluxed for 18 hr.; on standing, an oil precipitated and finally crystallised. The *polymer* (1.0 g., 73%) separated from methanol as a microcrystalline powder, m. p. 210—212° (Found: C, 38.5; H, 4.5; I, 44.9; N, 5.3. $C_9H_{12}INO$ requires C, 39.0; H, 4.3; I, 45.8; N, 5.1%).

1-4'-Bromobutyl-4-pyridone Hydrobromide.—The phenoxy-pyridone (3.0 g.), in hydrobromic acid (48% ; 40 c.c.), was refluxed for 4 hr. After evaporation at 100°/15 mm. the residue crystallised from ethanol-ethyl acetate to give the *hydrobromide* (2.2 g., 57%) as needles, m. p. 132—134.5° (Found: C, 35.1; H, 4.1. C₉H₁₃Br₂NO requires C, 34.7; H, 4.2%).

The *picrate* formed prisms, m. p. 112—113.5° (from ethanol) (Found: C, 38.8; H, 3.5. C₁₅H₁₅BrN₄O₈ requires C, 39.2; H, 3.3%).

The polymer bromide (cf. III) was obtained only in an amorphous form, but this gave the polymer iodide (III), m. p. and mixed m. p. 209—211°, on treatment with sodium iodide.

1-4'-Phenoxybutyl-2-pyridone.—4-Bromobutyl phenyl ether (9.0 g.) and pyridine (7.0 g.) were heated at 100° for 2 hr. The resultant oil was washed with dry ether, and added in water (50 c.c.) dropwise to potassium ferrocyanide (26 g.) and sodium hydroxide (20 g.) in water (150 c.c.) at 0°. The mixture was then warmed to 50° for 2 hr. Extraction with chloroform, and distillation of the dried (MgSO₄) extracts, gave the *phenoxy-pyridone* (3.7 g., 39%) b. p. 180—182°/0.8 mm. (Found: C, 73.7; H, 7.1; N, 6.1. C₁₅H₁₇NO₂ requires C, 74.1; H, 7.0; N, 5.8%).

The *picrate* formed prisms, m. p. 86—88° (from benzene) (Found: C, 53.5; H, 4.3. C₂₁H₂₀N₄O₉ requires C, 53.4; H, 4.2%).

4-Ethoxy-1-methylpyridinium Iodide.—4-Ethoxypyridine [picrate, m. p. 127°, lit.,³ 129—130°], prepared by reduction of the *N*-oxide with iron (cf. ref. 3), with methyl iodide in ether gave the *methiodide* as prisms, m. p. 125° (from Cellosolve) (Found: C, 36.3; H, 4.3; N, 5.3. C₈H₁₂INO requires C, 36.2; H, 4.5; N, 5.3%).

4-(1-Pyrrolidinyl)pyridine Ethiodide.—4-Chloropyridine 1-oxide⁴ (5 g.) was heated with pyrrolidine (10 c.c.) and water (15 c.c.) at 160° for 18 hr. (sealed tube). The product and potassium carbonate (5 g.) were evaporated at 100°/15 mm. The residue was extracted with ethyl acetate, and the extracts run through a short alumina column. Evaporation gave 4-(1-pyrrolidinyl)pyridine (1.0 g., 25%) as hygroscopic plates, m. p. 31—33° [from light petroleum (b. p. 40—80°)].

The *ethiodide*, prepared at 20° in ether, formed hygroscopic needles, m. p. 134° (from ethanol-ether) (Found: C, 43.3; H, 5.4; I, 41.0. C₁₁H₁₇IN₂ requires C, 43.4; H, 5.6; I, 41.8%).

Nuclear magnetic resonance spectra were measured on a Perkin-Elmer spectrometer operating at 40 Mc./sec. Compound (III) and 4-ethoxypyridine methiodide (V) were measured in deuterium oxide with methyl cyanide as standard, and in (CF₂Cl)₂CO(D₂O)_{5/2} with tetramethylsilane as standard. 1-4'-Hydroxybutyl-4-(1-pyrrolidinyl)pyridinium iodide (VI) and 1-ethyl-4-(1-pyrrolidinyl)pyridinium iodide (VII) were measured in deuterium oxide with methyl cyanide as standard.

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³ H. J. den Hertog and W. P. Combe, *Rec. Trav. chim.*, 1951, **70**, 589.

⁴ A. R. Katritzky, E. W. Randall, and L. E. Sutton, *J.*, 1957, 1769.