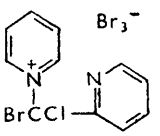
410. *Polynuclear Heterocyclic Systems. Part III.*[1] *The Synthesis of Dipyridinoglyoxalinium and Related Salts.*

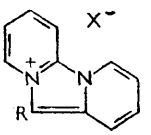
By B. R. Brown and J. Humphreys.

Dipyridino(1′ : 2′-1: 2, 1″ : 2″-3 : 4)-, 5-bromodipyridino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)-, 5-bromodipyridino(1″ : 2″-3 : 4)**quinolino**(1′ : 2′-1 : 2)-, and 5-bromopyridino(1″ : 2″-3 : 4)*iso***quinolino**(2′ : 1′-1 : 2)-glyoxalinium salts have been prepared from ω-bromo-α-picoline.

It has not been possible, by using the methods previously described,[1,2] to obtain glyoxalinium salts from ωω-dichloro-α-picoline.[3] This compound formed a quaternary salt, not a glyoxalinium salt, with pyridine. Bromination of the quaternary salt gave the bromo-quaternary salt (I) without cyclisation.



(I)



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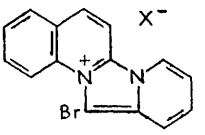
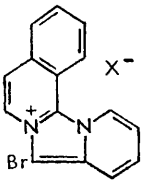


(III)

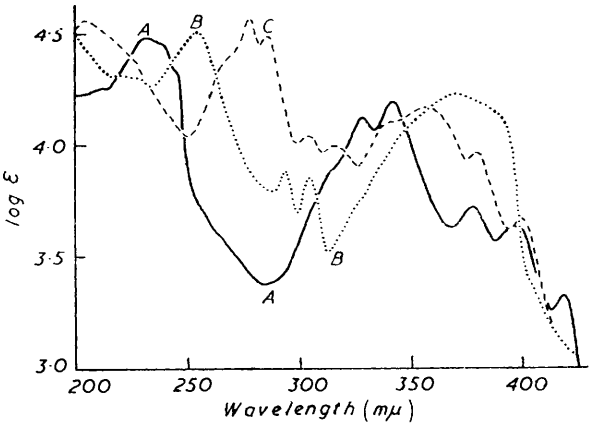


(IV)

It is not possible to brominate α-picoline directly.[4] It is unchanged after treatment with bromine at 90° for several days in acetic acid containing sodium acetate; the acetic acid is preferentially brominated and bromoform can be isolated. Attempts to brominate picoline 1-oxide and ω-bromo-α-picoline were unsuccessful.

[1] Part II, Brown and White, *J.*, 1957, 1589.
[2] Brown and Wild, *J.*, 1956, 1158.
[3] Dyson and Hammick, *J.*, 1939, 781.
[4] Brown, Hammick, and Thewlis, *J.*, 1951, 1145.

ω-Bromo-α-picoline [5] has been obtained in quantity by conversion of α-picoline 1-oxide into 2-hydroxymethylpyridine [6] and direct reaction of this with aqueous hydrobromic acid. Reaction of the crude ω-bromo-α-picoline with pyridine, quinoline, and *iso*quinoline yielded the quaternary bromides which were characterised as dipicrates. Bromination of these bromides and spontaneous ring closure yielded the corresponding glyoxalinium salts (II, R = Br; III; and IV), the characteristic absorption spectra of which are illustrated.



Ultraviolet spectra in ethanol: (*A*) 5-*Bromodipyridino*(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)*glyoxalinium bromide* (II; R = Br); (*B*) 5-*bromopyridino*(1″ : 2″-3 : 4)*quinolino*(1′ : 2′-1 : 2)*glyoxalinium bromide* (III); and (*C*) 5-*bromopyridino*(1″ : 2″-3 : 4)iso*quinolino*(2′ : 1′-1 : 2)*glyoxalinium bromide* (IV).

Dipyridino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)glyoxalinium salts (II; R = H) have been prepared from ω-bromo-α-picoline and 2-bromopyridine. This method is less efficient than the others available for glyoxalinium salts [2] but, as ωω-dibromo-α-picoline is not available, it is the most convenient way to obtain the parent compound of the series.

Experimental

1-(α-*Chloro*-α-2-*pyridylmethyl*)*pyridinium Chloride*.—A solution of ωω-dichloro-α-picoline [3] (Found: C, 44·8; H, 3·3. Calc. for $C_6H_5NCl_2$: C, 44·5; H, 3·1%) (5·0 g.) in pyridine (30 ml.) was boiled under reflux for 2 hr. Decantation of pyridine left hygroscopic crystals (1·5 g.) which were crystallised several times from methanol–ether to give the *chloride hemihydrate* as colourless needles (Found: C, 52·75; H, 4·7; N, 11·1; Cl, 28·5. $C_{11}H_{10}N_2Cl_2,\frac{1}{2}H_2O$ requires C, 52·8; H, 4·4; N, 11·2; Cl, 28·4%). The ultraviolet spectrum in ethanol showed the compound to be a simple pyridine derivative.

1-(α-*Bromo*-α-*chloro*-α-2-*pyridylmethyl*)*pyridinium Perbromide*.—A mixture of the above pyridinium chloride (0·5 g.), glacial acetic acid (10 ml.), fused sodium acetate (0·5 g.), and bromine (0·8 ml.) was boiled under reflux for 2 hr. The precipitate (0·3 g.) crystallised from acetic acid as brown needles of the *perbromide* (Found: C, 25·5; H, 1·3; Hal, 69·3. $C_{11}H_9N_2ClBr_4$ requires C, 25·2; H, 1·7; Hal, 67·8%).

ω-*Bromo*-α-*picoline*.[5]—To ice-cold acetic anhydride (250 ml.) was added 48% hydrobromic acid (63 ml.) and 2-hydroxymethylpyridine acetate [6] (7·7 g.), and the mixture was heated at 100° for 4 hr. Evaporation under reduced pressure gave the crude ω-bromo-α-picoline hydrobromide which was dissolved in water and treated with aqueous sodium hydroxide; the liberated ω-bromo-α-picoline was taken up in benzene and dried. No attempt was made to purify the ω-bromopicoline as it is known to be unstable.[5] Evaporation of the benzene solution left a yellow lachrymatory oil.

Dipyridino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)*glyoxalinium Salts* (II; R = H).—A solution of ω-bromopicoline (4·0 g.) and 2-bromopyridine (4·0 g.) in benzene (70 ml.) was boiled under reflux for 4 days. The deposit of brown crystals was washed several times with benzene, dissolved in water (30 ml.), boiled with charcoal, and filtered off. The filtrate was made just alkaline with aqueous sodium hydroxide at 0° and extracted several times with ether to remove unchanged starting materials.

[5] Cf. Šorm and Šedivý, *Coll. Czech. Chem. Comm.*, 1948, **13**, 289.
[6] Boekelheide and Linn, *J. Amer. Chem. Soc.*, 1954, **76**, 1286.

Half of the resulting aqueous solution was treated with excess of 60% perchloric acid, and the precipitated *perchlorate* was separated, washed with water, and crystallised several times from methanol to afford pale brown plates (0·80 g.) (Found: C, 49·5; H, 3·3; N, 10·85; Cl, 13·9. $C_{11}H_{19}O_4N_2Cl$ requires C, 49·2; H, 3·35; N, 10·4; Cl, 13·2%), $\lambda_{max.}$ in ethanol 227, 236, 272, 284, 319, 334, 364, 381, and 402 mμ (log ε 4·52, 4·49, 3·37, 3·32, 4·09, 4·18, 3·68, 3·60, and 3·31), $\lambda_{min.}$ 234, 267, 279, 286, 325, 355, 374, and 395 mμ (log ε 4·46, 3·36, 3·28, 3·31, 3·99, 3·57, 3·46, and 3·13).

The other half of the solution was acidified with aqueous hydrobromic acid and treated with excess of hot aqueous picric acid. The precipitated *picrate* was crystallised several times from acetic acid to give yellow needles (0·70 g.), m. p. 200—210° (decomp.) (Found: C, 51·65; H, 2·8; N, 17·7. $C_{17}H_{11}O_7N_5$ requires C, 51·4; H, 2·8; N, 17·6%).

1-(2-*Pyridylmethyl*)*pyridinium Bromide*.—Pyridine (10 ml.) was added to a solution of ω-bromopicoline (4·0 g.) in benzene (50 ml.) and the mixture was boiled for 15 min. Next day the benzene was decanted and the solid crystallised from ethanol–ether to yield colourless, hygroscopic needles (2·0 g.). The derived *dipicrate* separated from aqueous methanol as orange plates, m. p. 158° (Found: C, 44·0; H, 2·6; N, 17·8. $C_{23}H_{16}O_{14}N_8$ requires C, 43·95; H, 2·55; N, 17·8%).

The same dipicrate, m. p. and mixed m. p. 158° (Found: C, 44·0; H, 2·7; N, 17·5%), was obtained by treating the product from ω-monochloro-α-picoline and pyridine with picric acid.

5-*Bromodipyridino*(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)*glyoxalinium Salts* (II; R = Br).—Bromination of 1-(2-pyridylmethyl)pyridinium bromide (1·5 g.) as described previously for similar quaternary salts [1] yielded the *glyoxalinum perbromide* (2·4 g.) as orange needles from acetic acid (Found: C, 27·0; H, 1·7; N, 5·5; Br, 65·7. $C_{11}H_8N_2Br_4$ requires C, 27·1; H, 1·65; N, 5·7; Br, 65·5%). Treatment of the perbromide (1·3 g.) with pyridine gave the *bromodipyridinoglyoxalinium bromide* (0·8 g.) which separated from methanol as pale yellow needles (Found: C, 40·0; H, 2·4; N, 8·7; Br, 48·9. $C_{11}H_8N_2Br_2$ requires C, 40·2; H, 2·5; N, 8·5; Br, 48·8%). The *picrate* separated from acetone as slender yellow needles, m. p. 208° (Found: C, 43·1; H, 2·1. $C_{17}H_{10}O_7N_5Br$ requires C, 42·95; H, 2·1%).

1-(2-*Pyridylmethyl*)*quinolinium Bromide*.—ω-Bromopicoline (3 g.) and quinoline (7 ml.) in boiling benzene (25 ml.) gave an oily quaternary salt. The derived *dipicrate* separated from ethanol as orange needles, m. p. 173° (Found: C, 48·1; H, 2·6; N, 16·4. $C_{27}H_{18}O_{14}N_8$ requires C, 47·8; H, 2·65; N, 16·5%).

5-*Bromopyridino*(1″ : 2″-3 : 4)*quinolino*(1′ : 2′-1 : 2)*glyoxalinium Salts* (III).—Bromination of the crude pyridylmethylquinolinium bromide (2·2 g.) and treatment with pyridine yielded the *pyridinoquinolinoglyoxalinium bromide hydrate* (1·1 g.) which separated from methanol–ether as yellow needles (Found: C, 45·7; H, 3·2; N, 7·2; Br, 40·0. $C_{15}H_{10}N_2Br_2,H_2O$ requires C, 45·5; H, 3·0; N, 7·1; Br, 40·4%). The infrared spectrum in Nujol contains a band at 3450 cm.$^{-1}$. The derived *perchlorate* separated from methanol as pale brown needles (Found: C, 45·4; H, 2·6; N, 7·35. $C_{15}H_{10}O_4N_2ClBr$ requires C, 45·3; H, 2·5; N, 7·1%). The *picrate* separated from acetone as yellow needles, m. p. 231° (Found: C, 48·0; H, 2·4. $C_{21}H_{12}O_7N_5Br$ requires C, 48·0; H, 2·3%).

2-(2-*Pyridylmethyl*)iso*quinolinium Bromide*.—*iso*Quinoline (5·0 g.) and ω-bromopicoline (2 g.) in boiling benzene (25 ml.) gave a red solid quaternary bromide (2·5 g.). The derived *dipicrate* separated from methanol–acetone as yellow plates, m. p. 188° (Found: C, 48·2; H, 2·7; N, 16·9. $C_{27}H_{18}O_{14}N_8$ requires C, 47·8; H, 2·65; N, 16·5%).

5-*Bromopyridino*(1″ : 2″-3 : 4)iso*quinolino*(2′ : 1′-1 : 2)*glyoxalinium Salts* (IV).—The above crude quaternary salt (2·1 g.) was brominated, and the product treated with pyridine to yield the *glyoxaliniuim bromide monohydrate* (1·6 g.) which separated from methanol–ether as pale brown needles (Found: C, 45·2; H, 2·8; Br, 40·3. $C_{15}H_{10}N_2Br_2,H_2O$ requires C, 45·5; H, 3·0; Br, 40·4%). The infrared spectrum in Nujol contains a band at 3450 cm.$^{-1}$. The derived *perchlorate* separated from methanol as colourless needles (Found: C, 45·5; H, 2·7; N, 6·7. $C_{15}H_{10}O_4N_2ClBr$ requires C, 45·3; H, 2·5; N, 7·1%).

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