241. *Polynuclear Heterocyclic Systems. Part I. The Synthesis of Condensed Glyoxalinium Salts.*

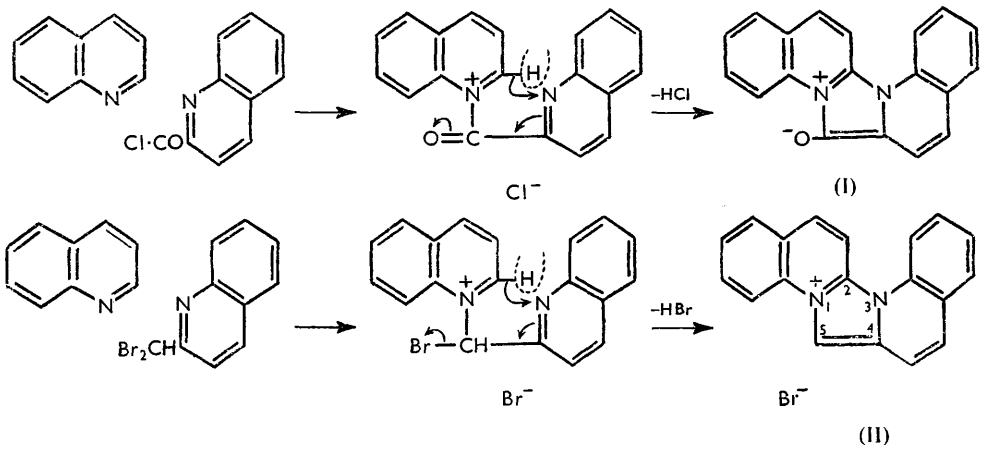
By B. R. Brown and E. H. Wild.

The preparation and properties of pyridino(1′ : 2′-1 : 2)quinolino(1″ : 2″-3 : 4)glyoxalinium, 5-bromopyridino(1′ : 2′-1 : 2)quinolino(1″ : 2″-3 : 4)glyoxalinium, diquinolino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)glyoxalinium (II), and 5-bromoquinolino(1′ : 2′-3 : 4)*iso*quinolino(1″ : 2″-2 : 1)glyoxalinium salts are described. Catalytic reduction of pyridinoquinolinoglyoxalinium bromide has yielded 3′ : 4′ : 5′ : 6′-tetrahydropyridino(1′ : 2′-1 : 2)quinolino(1″ : 2″-3 : 4)glyoxalinium bromide. Evidence for the structures of these compounds and their relation to Besthorn's Red (I) are discussed.

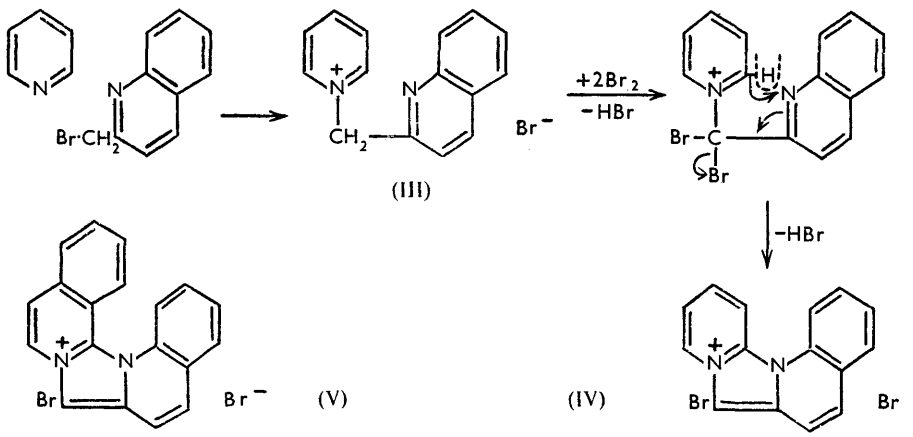
The light-sensitive pigment Besthorn's Red [1,2] is thought to have the mesoionic structure (I).[3,4] The parent heterocyclic skeleton present in this structure, the cationic diquinolino-(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)glyoxalinium (II), has not hitherto been described. The synthesis and study of compounds incorporating this structure would be a valuable step towards a final proof of the structure (I) for Besthorn's Red.

[1] Besthorn and Jaeglé, *Ber.*, 1894, **27**, 907.
[2] Besthorn and Ibele, *Ber.*, 1904, **37**, 1239, 1905, **38**, 2127.
[3] Besthorn, *Ber.*, 1913, **46**, 2762.
[4] Krollpfeiffer and Schneider, *Annalen*, 1937, **530**, 34.

The preparation of Besthorn's Red from quinaldinoyl chloride and quinoline [2,4] probably proceeds by a mechanism of the annexed type. The operation of a similar mechanism should result in the production of cations analogous to that in (II) from the quaternary salts produced by the action of ωω-dibromoquinaldine on pyridine, quinoline, or *iso*-quinoline. By this method the pyridino(1′ : 2′-1 : 2)quinolino(1″ : 2″-3 : 4)glyoxalinium (VI) and the diquinolino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)glyoxalinium (II) salts have been



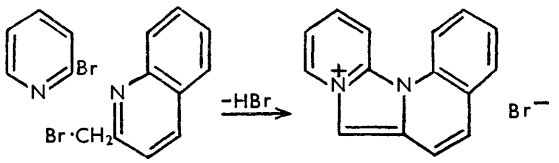
prepared. The use of ω-monobromoquinaldine and pyridine, quinoline, or *iso*quinoline, followed by bromination of the resulting quaternary salts, should yield 5-bromo-derivatives of the glyoxalinium series. This method has yielded 5-bromopyridino(1′ : 2′-1 : 2)quinolino-(1″ : 2″-3 : 4)glyoxalinium (IV) and 5-bromoquinolino(1′ : 2′-3 : 4)*iso*quinolino(1″ : 2″-2 : 1)glyoxalinium (V) salts. The *iso*quinoline compound is formulated thus (V), rather than as 5-bromoquinolino(1′ : 2′-3 : 4)*iso*quinolino(2″ : 3″-1 : 2)glyoxalinium bromide since it is more likely that the 1-position, and not the less reactive 3-position, will be involved in the formation of the glyoxalinium ring. This structure is confirmed by absence of infra-red absorption in the region 860—900 cm.$^{-1}$. This is consistent with the structure (V), but not with the other possible structure which contains isolated aromatic hydrogen atoms.



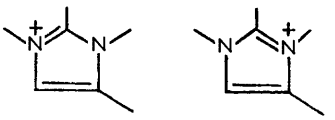
The participation of the α-carbon atom of the pyridine or the second quinoline nucleus in the formation of these compounds has been confirmed by the preparation of the pyridino-(1′ : 2′-1 : 2)quinolino(1″ : 2″-3 : 4)glyoxalinium salt (VI) by an alternative route.

2-Bromopyridine and ω-monobromoquinaldine yielded impure pyridinoquinolinoglyoxalinium bromide, which was converted into the perchlorate and picrate, and their identities were established by infrared comparison with samples of these salt resulting from the reaction between ωω-dibromoquinaldine and pyridine, and by analysis and a mixed melting point of the picrate.

The physical and chemical properties of these compounds are in accord with the condensed glyoxalinium structures deduced from the above methods of synthesis. Thus



(VI)



(VII)

the bromides are typical salts, and the bromide ion can be replaced by other anions (perchlorate or picrate) by treatment with acids. This property is to be expected of a glyoxalinium cation structure in which both nitrogen atoms are involved in resonance of the amidine cation type (VII). For the same reason vigorous treatment with alkylating

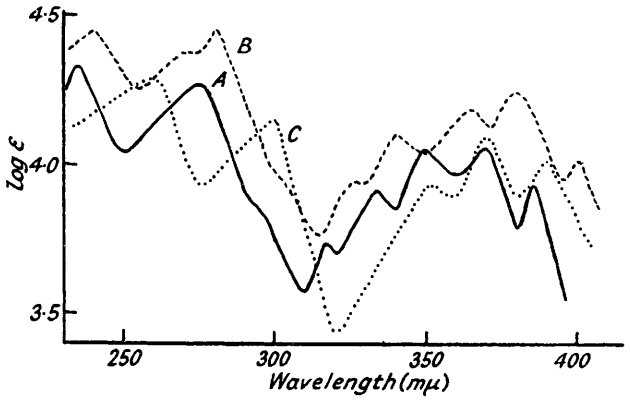


FIG. 1.

A, Pyridino(1′ : 2′-1 : 2)*quinolino*(1″ : 2″-3 : 4)*glyoxalinium bromide* (VI) *in water.*

B, 5-Bromopyridino(1′ : 2′-1 : 2)*quinolino*(1″ : 2″-3 : 4)*glyoxalinium bromide* (IV) *in water.*

C, Diquinolino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)*-glyoxalinium bromide* (II) *in methanol.*

agents (methyl or ethyl halides) does not yield quaternary salts. Further, the salts are not acid salts of amines, since the anhydrous salts (the bromides of the 5-bromo-compounds and the picrates and perchlorates) do not show the infrared absorption expected of the NH group, and treatment of the salts with alkali yields, not free amines, but solutions which have ultraviolet spectra identical with those of the original salts, indicating that they contain the ionised glyoxalinium hydroxides. The stability of the aromatic glyoxalinium nucleus is shown by the substantial stability of 5-bromopyridinoquinolinoglyoxalinium bromide in hot concentrated sulphuric acid; only a slight amount of sulphonation occurred.

The bromides of the 5-bromo-compounds, prepared as outlined above, are isolated from the reaction as perbromides (Br_3^-), from which the bromides of the cations are obtained by dissolution in pyridine. The presence of the extra bromine molecule as a perbromide is evident from this easy decomposition with cold pyridine, and from the ready regeneration of the perbromide by treatment of the bromide with bromine in aqueous acetic acid. Further, the perbromides instantaneously liberate iodine from acidified potassium iodide solution, and the action of heat in a dry tube liberates free bromine. The formulation of these compounds as perbromides is confirmed by our failure to prepare them in the absence of the bromide ion.

The ultraviolet spectra and the fluorescent properties of the salts strongly suggest a polycyclic aromatic structure. The close similarity between the spectra of the compounds (Fig. 1) indicates a common structure, and the change from the non-fluorescent

N-2-quinolylmethylpyridinium bromide (III) with a final absorption band at 320 mμ to the fluorescent product of its bromination, 5-bromopyridino(1′ : 2′-1 : 2)quinolino(1″ : 2″-3 : 4)glyoxalinium bromide (IV), with a final absorption band at 400 mμ is analogous to the similar differences found between benzene or naphthalene and 1 : 2-benzanthracene.

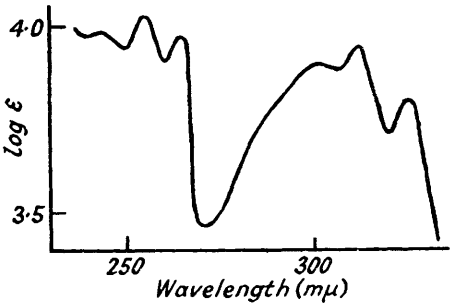
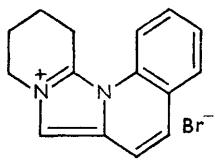


FIG. 2.
3′ : 4′ : 5′ : 6′-*Tetrahydropyridino*(1′ : 2′-1 : 2)*quinolino*-(1″ : 2″-3 : 4)*glyoxalinium bromide* (VIII) *in ethanol.*

The strong absorption of the compounds in the region 310—400 mμ (Fig. 1) is best accounted for by structures of the condensed glyoxalinium type.

The behaviour of the compounds towards hydrogenation also supports the polynuclear structures. Pyridinoquinolinoglyoxalinium bromide yielded a 3′ : 4′ : 5′ : 6′-tetrahydro-derivative whose glyoxalinium structure (VIII) is based upon the ready conversion into a perchlorate and a picrate, and upon the fact that aqueous sodium hydroxide causes no visible change, so that the substance is unlikely to be the hydrobromide of an amine. Also, its ultraviolet spectrum (Fig. 2) is intermediate between those of quinolinium and pyridinoquinolinoglyoxalinium salts. This retention of the glyoxalinium structure is not surprising in view of the know reluctance of glyoxalines to undergo hydrogenation.



(VIII)

EXPERIMENTAL

Pyridino(1′ : 2′-1 : 2)*quinolino*(1″ : 2″-3 : 4)*glyoxalinium Series* (VI).—(a) *From* ωω-*dibromoquinaldine and pyridine.* ωω-Dibromoquinaldine (5·0 g.) and pyridine (50 ml.) were boiled under reflux for 2½ hr. The solid which had separated was washed with pyridine, then with ether, and dried. The crude solid (3·4 g.) was treated in aqueous solution with charcoal, then filtered, the filtrate evaporated to dryness, and the solid recrystallised from ethanol–ether. *Pyridino*(1′ : 2′-1 : 2)*quinolino*(1″ : 2″-3 : 4)*glyoxalinium bromide hemihydrate* separated as fawn-coloured plates (Found, in material dried at room temperature and pressure : C, 58·3; H, 3·9; N, 8·9. $C_{15}H_{11}N_2Br,\frac{1}{2}H_2O$ requires C, 58·4; H, 3·9; N, 9·1%). The infrared spectrum contains a band at 3450 cm.$^{-1}$ characteristic of the hydroxyl group of the solvent of crystallisation. Light absorption in H_2O : max. at 235, 275, 317, 334, 350, 370, and 386 mμ (log ε 4·33, 4·28, 3·73, 3·92, 4·05, 4·07, and 3·94); min. at 250, 310, 320, 340, 360, and 380 mμ (log ε 4·04, 3·58, 3·70, 3·85, 3·96, and 3·79). The anhydrous *bromide* was obtained when the hemihydrate was dried at 100°/0·1 mm. (Found : Br, 27·2. $C_{15}H_{11}N_2Br$ requires Br, 26·8%). The compound is very soluble in water, slightly less soluble in methanol or ethanol, and insoluble in ether or in pyridine. The aqueous solution precipitates silver bromide from aqueous silver nitrate.

Treatment of the bromide in methanol with aqueous perchloric acid yielded the *perchlorate* which separated from methanol as pale yellow needles (Found, in material dried at 100°/0·1 mm. : C, 56·0; H, 3·5. $C_{15}H_{11}O_4N_2Cl$ requires C, 56·5; H, 3·45%).

Prepared from the bromide in ethanol, the *picrate* separated from acetone as yellow plates, m. p. 238—239° (Found : C, 56·8; H, 3·1; N, 15·6. $C_{21}H_{13}O_7N_5$ requires C, 56·4; H, 2·9; N, 15·7%).

(b) *From* ω-*monobromoquinaldine and* 2-*bromopyridine.* ω-Monobromoquinaldine (50 mg.), 2-bromopyridine (1·0 g.), and benzene (10 ml.) were boiled under reflux for 30 min. The resulting dark crystals were washed with ether and boiled in aqueous solution with charcoal. Evaporation of the filtrate and crystallisation of the residue from ethanol–ether gave a mixture

of light brown crystals (50 mg.) which could not be separated by further crystallisation. This was probably a mixture of the required bromide with the hydrobromide of α-bromopyridine, the other reaction product. Conversion into the perchlorate, followed by three recrystallisations from methanol, yielded buff needles, which by infrared comparison were proved to be identical with the pyridinoquinolinoglyoxalinium perchlorate prepared as described above. Conversion of this perchlorate into the picrate and crystallisation from acetone yielded yellow plates, m. p. 238—239°, unchanged on admixture with the picrate prepared as described above (Found : C, 56·1; H, 2·7%). The infrared curves of the two picrates were identical.

3′ : 4′ : 5′ : 6′-*Tetrahydropyridino*(1′ : 2′-1 : 2)*quinolino*(1″ : 2″-3 : 4)*glyoxalinium Series* (VIII).—Pyridinoquinolinoglyoxalinium bromide (1·0 g.) was hydrogenated for 12 hr. in the presence of Raney nickel at 110—120°/100 atm. The resulting pale yellow solution was filtered and evaporated to small bulk, yielding colourless crystals. Two crystallisations from ethanol gave the *tetrahydro-compound* (0·25 g.) as colourless needles (Found : C, 58·55; H, 5·4; N, 8·4; Br, 24·7. $C_{15}H_{15}N_2Br,\frac{1}{2}C_2H_6O$ requires C, 58·9; H, 5·5; N, 8·6; Br, 24·55%). The presence of alcohol of crystallisation is confirmed by the infrared spectrum (hydroxyl band at 3450 cm.$^{-1}$). The compound is very soluble in water and in polar solvents generally, but is insoluble in non-polar solvents. Silver nitrate precipitates silver bromide from an aqueous solution of the compound. Aqueous sodium hydroxide has no visible action on the salt. Light absorption in EtOH : max. at 245, 255, 265, 300, 312, and 326 mμ (log ε 3·99, 4·03, 3·97, 3·90, 3·94, and 3·80); min. at 240, 250, 260, 270, 308, and 320 mμ (log ε 3·98, 3·94, 3·90, 3·46, 3·88, and 3·71).

Prepared in aqueous methanol and crystallised from methanol the *perchlorate* separated as colourless prismatic needles (Found : C, 55·7; H, 4·8. $C_{15}H_{15}O_4N_2Cl$ requires C, 55·8; H, 4·65%).

Treatment of the bromide in water with picric acid and crystallisation from acetone gave the *picrate* as yellow needles, m. p. 186—187° (Found : C, 55·9; H, 4·15. $C_{21}H_{17}O_7N_5$ requires C, 55·9; H, 3·8%).

5-*Bromopyridino*(1′ : 2′-1 : 2)*quinolino*(1″ : 2″-3 : 4)*glyoxalinium Series* (IV).—A mixture of *N*-2-quinolylmethylpyridinium bromide[5] (2·1 g.), water (10 ml.), acetic acid (50 ml.), and sodium acetate (4·0 g.) was treated at 90° during 10 min. with bromine (3·9 g.) in acetic acid (20 ml.). The yellow crystalline product was separated from the cold mixture, washed with acetic acid, and crystallised from acetic acid, in which it is sparingly soluble, to yield 5-*bromopyridinoquinolinoglyoxalinium perbromide* (3·0 g.) as yellow plates, m. p. 340—350° to a red melt (Found : C, 33·8; H, 1·7; Br, 59·4. $C_{15}H_{10}N_2Br_4$ requires C, 33·5; H, 1·85; Br, 59·4%). The product is not very soluble in organic solvents in general, and is only slightly soluble in water from which silver bromide is precipitated by aqueous silver nitrate. A solution of the perbromide in ethanol immediately liberates iodine from acidified starch–potassium iodide paper. The action of heat on the compound liberates free bromine.

The perbromide (1·3 g.) was dissolved in cold pyridine (12 ml.). After a short time a yellow crystalline compound began to be precipitated. When precipitation was complete (several hours) the solid was separated, washed with ether, and crystallised from methanol, to yield yellow needles (0·85 g.) of *5-bromopyridinoquinolinoglyoxalinium bromide*, m. p. 338—345° to a red melt (Found : C, 47·8; H, 2·7; N, 7·3, 7·5; total Br, 42·4, 42·8; Br^-, 22·6. $C_{15}H_{10}N_2Br_2$ requires C, 47·6; H, 2·6; N, 7·4; Br, 42·3; Br^-, 21·2%). Treatment of the bromide with bromine in aqueous acetic acid regenerated the perbromide whose identity was established by infrared examination. Light absorption in H_2O : max. at 240, 270, 280, 325, 340, 365, 380, and 400 mμ (log ε 4·45, 4·38, 4·45, 3·94, 4·10, 4·19, 4·25, and 4·02); min. at 255, 275, 315, 330, 350, 370, and 395 mμ (log ε 4·25, 4·37, 3·76, 3·92, 4·03, 4·12, and 3·95).

Prepared in methanol and crystallised from ethanol the *perchlorate* was obtained as lemon-yellow crystals (Found : C, 45·55; H, 2·6. $C_{15}H_{10}O_4N_2ClBr$ requires C, 45·3; H, 2·5; Hal, 29·1%). Treatment of the perchlorate with bromine and recrystallisation from aqueous acetic acid left the compound unchanged (Found : C, 45·1; H, 2·7; Hal, 29·7%).

Prepared in ethanol and crystallised from ethanol–acetone the *picrate* was obtained as orange-yellow plates, m. p. 214° (Found : C, 47·7; H, 2·3. $C_{21}H_{12}O_7N_5Br$ requires C, 47·9; H, 2·3%).

Action of concentrated sulphuric acid on 5-bromopyridinoquinolinoglyoxalinium bromide. The bromide (0·5 g.) was heated at 100° with concentrated sulphuric acid (2·0 ml.) for 7 hr. Dilution with water (10 ml.) and treatment with hot aqueous picric acid (0·35 g.) yielded an orange solid (0·6 g.), which was washed with water, and alcohol, and dried. A solution of the solid in acetone

[5] Brown, Hammick, and Thewlis, *J.*, 1951, 1145.

was poured on a column of alumina and eluted with acetone (250 ml.), methanol (400 ml.), and finally chloroform (100 ml.). The yellow acetone solution was evaporated and the solid (40 mg.) crystallised from acetone, to yield yellow needles, m. p. 226° (Found : C, 42·0; H, 2·1; N, 11·2. $C_{21}H_{12}O_{10}N_5BrS$ requires C, 41·6; H, 2·0; N, 11·6%). This *picrate* is readily soluble in aqueous sodium carbonate, suggesting that it is a sulphonic acid derivative of the 5-bromopyridinoquinolinoglyoxalinium nucleus.

The orange-yellow methanol eluate was evaporated, and the solid residue (250 mg.) crystallised several times from methanol, and finally from acetone, to yield yellow needles, m. p. 214°, unchanged on admixture with 5-bromopyridinoquinolinoglyoxalinium picrate (Found : C, 47·2; H, 2·6%). The infrared curves of the two picrates were identical.

The eluted chloroform was colourless and yielded no solid on evaporation even though the column remained orange-yellow.

Diquinolino(1′ : 2′-1 : 2, 1″ : 2″-3 : 4)*glyoxalinium Series* (II).—ωω-Dibromoquinaldine (4·0 g.) and quinoline (56 ml.) were heated together for 9 hr. just below the b. p. The dark insoluble crystalline solid was separated from the cold mixture, washed with ether, and then with a few drops of methanol–water. The brown solid was heated in aqueous solution with charcoal, and the solution filtered and evaporated to dryness. Crystallisation of the resulting solid from ethanol–ether gave pale yellow prisms (0·8 g.) of *diquinolinoglyoxalinium bromide monohydrate* (Found : C, 61·8; H, 4·2; N, 7·4; Br, 21·8. $C_{19}H_{13}N_2Br,H_2O$ requires C, 62·1; H, 4·1; N, 7·6; Br, 21·8%). The infrared spectrum of the compound shows a band at 3380 $cm.^{-1}$, confirming its formulation as a hydrate. Crystallisation of the compound from water yielded a different *hydrate* as pale yellow needles (Found : C, 55·8, 55·6; H, 5·1, 5·1. $C_{19}H_{13}N_2Br,3\frac{1}{2}H_2O$ requires C, 55·4; H, 4·85%).

Solutions of the salt in polar solvents have a strong blue fluorescence. Light absorption in MeOH : max. at 225, 260, 300, 350, 370, and 390 mμ (log ε 4·12, 4·30, 4·15, 3·94, 4·09, and 4·02); min. at 230, 275, 320, 360, and 380 mμ (log ε 4·11, 3·93, 3·44, 3·88, and 3·89).

The *perchlorate*, prepared in aqueous solution, separated from methanol as yellow needles (Found : C, 61·5; H, 3·6; N, 7·7. $C_{19}H_{13}O_4N_2Cl$ requires C, 61·9; H, 3·6; N, 7·6%).

Prepared in, and crystallised from, ethanol, the *picrate* was obtained as yellow needles, m. p. 261—262° (Found : C, 60·4; H, 3·4. $C_{25}H_{15}O_7N_5$ requires C, 60·4; H, 3·0%).

5-*Bromoquinolino*(1′ : 2′-3 : 4)iso*quinolino*(1″ : 2″-2 : 1)*glyoxalinium Series* (V).—N-2-*Quinolylmethyl*isoquinolinium *bromide*. ω-Monobromoquinaldine (0·3 g.), *iso*quinoline (8·5 ml.), and benzene (10 ml.) were warmed together to effect dissolution. The crystalline solid which separated was washed with ether and crystallised from methanol–ether, yielding the *quaternary salt* (0·5 g.) as colourless plates (Found : Br, 22·0. $C_{19}H_{15}N_2Br,H_2O$ requires Br, 21·7%). The compound is extremely deliquescent.

Perbromide. *N*-2-Quinolylmethyl*iso*quinolinium bromide (0·5 g.), acetic acid (2 ml.), water (5 ml.), and sodium acetate (1·0 g.) were heated at 90° and treated dropwise with bromine in acetic acid until no further precipitation was observed. The crystalline solid was separated from the cold mixture, washed with aqueous methanol, then with ether, and crystallised from methanol–ether. 5-*Bromoquinolino*(1′ : 2′-3 : 4)iso*quinolino*(1″ : 2″-2 : 1)*glyoxalinium perbromide* (50 mg.) separated as yellow plates (Found : Br, 54·5. $C_{19}H_{12}N_2Br_4$ requires Br, 54·4%). A solution of the compound in methanol immediately liberates iodine from acidified starch–iodide paper. Light absorption in H_2O : max. at 285, 300, 315, and 370 mμ (log ε 4·21, 4·19 3·97, and 3·91); min. at 295, 310, and 330 mμ (log ε 4·15, 3·94, and 3·55).

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