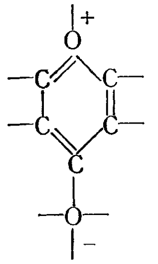
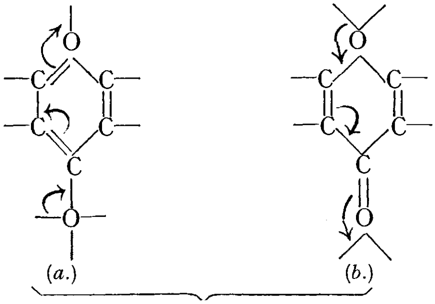
310. *An Example of Anhydronium Base Formation in the Quinoline Series.*

By H. Lempert and Robert Robinson.

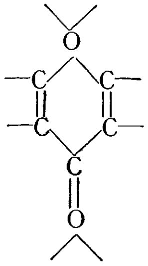
The exigencies of constitution frequently permit the intramolecular reversible dehydration of an -onium hydroxide, and such anhydro-derivatives may assume one of two extreme forms or occupy an intermediate position between these limits. For instance, the γ-pyrones are the anhydrides of 4-hydroxypyrylium hydroxides and might be full dipoles (I) or as electrically neutralised as possible (III); actually, it is postulated that a compromise (II) is the rule, and that it is an equilibrium position resulting from the opposition of the forces favouring an aromatic system (I) and those leading to the neutralisation of charges (III). In (II) the formulæ (*a*) and (*b*) are identical, and the arrows represent the transfer of an unknown fraction of the duplet only; it is immaterial for the present purpose whether this be envisaged statically or dynamically, instantaneously or statistically over a finite period of time.



(I.)



(II.)



(III.)

We may describe form (I) as betaine-like, (III) as quinonoid, and the forms (II) have been termed *anhydronium* bases (Armit and Robinson, J., 1925, **127**, 1604; cf. Kermack, Perkin, and Robinson, J., 1922, **121**, 1877; Robinson and Robinson, J., 1924, **125**, 832), and the question of their existence must be studied in each case by comparison with recognised types of the forms (I) and (III).

The arguments in the case of the γ-pyrones are well known, and their formulation as (II) serves to explain the chief characteristics of the group, *viz.*, (i) dipole moments smaller than would be expected from (I) and yet greater than (III) would suggest (cf. Hunter and Partington, J., 1933, 87), (ii) intermediate volatility, fusibility, and solubility, (iii) decreased carbonyl reactivity on comparison with ordinary unsaturated ketones, (iv) ready transformation into kations of pyrylium salts by means of protons or kationoid alkyl groups, (v) specific absorption spectra and fluorescence phenomena.

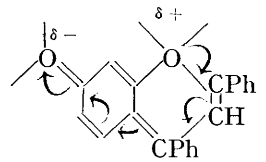
The 7-hydroxybenzopyrylium hydroxides, with a somewhat longer conjugated system, are entirely analogous to the 4-hydroxypyrylium hydroxides and, *e.g.*, 7-hydroxy-2 : 4-

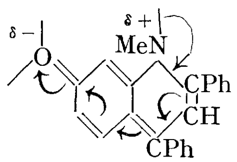
diphenylbenzopyrylium chloride gives the anhydronium base (IV) when sodium acetate is added to its aqueous solution. It is not supposed that an oxonium hydroxide is produced and that this loses water; the anhydronium bases may be directly obtained by deprotonation of the -onium kations (cf. Irvine and Robinson, J., 1927, 2086). (IV) is regarded as an anhydronium base on account of its colour (contrasting with that of the related pyrylium salt) and its solubility in organic solvents, which exclude the full betaine formula and, on the other hand, the direct methylation of the oxygen in position 7 which is not compatible with the full quinonoid type of formula. Armit and Robinson (*loc. cit.*) effected this methylation by treating the anhydronium base with methyl sulphate (*loc. cit.*); their work was overlooked by Kehrmann and Rieder (*Helv. Chim. Acta*, 1926, **9**, 491), who later described the same process.

The present work was undertaken in order to determine whether the analogy between pyrone and pyridone could be extended so as to embrace benzopyrylium and quinoline derivatives, and to this end we investigated the behaviour of the methohydroxides of 7-hydroxyquinolines.

When treated with alkalis, neither 7-hydroxyquinoline nor 7-*hydroxy*-2 : 4-*dimethylquinoline metho*-salts gave any indication of the formation of bases soluble in ether or benzene, but 7-hydroxy-2 : 4-diphenylquinoline methosulphate furnished a base (V), which dissolves in benzene to a red solution and is changed by methyl iodide into 7-*methoxy*-2 : 4-*diphenylquinoline methiodide.* Thus, this anhydronium base is the analogue of (IV) in properties and reactions. It appears that the tendency towards the formation of the quinonoid structure is suppressed in the non-arylated 7-hydroxyquinolines, probably because the nitrogen atom has too great an affinity for its charge. This is diminished, as always, by phenyl substitution. In the pyrylium series of much less stable oxonium kations, even the 2 : 4-dimethyl derivatives yield coloured anhydronium bases.

(IV.)





(V.)

The Skraup reaction does not appear to have been previously applied to *m*-anisidine; the product is 7-*methoxyquinoline.* Fischer (*Ber.*, 1882, **15**, 1979) methylated the hydroxyl group of 7-hydroxyquinoline, but no analyses or m.p.'s of derivatives were recorded. The orientation of our base was established by conversion into the known 7-hydroxyquinoline methiodide. In the ring closure of the anil from *m*-anisidine and acetylacetone by means of phosphoryl chloride, two substances were obtained, although one of them greatly preponderated. The higher-melting of the two isomerides is assumed to be the 7-derivative, the justification being based on the following quinoline derivatives: 5-Nitro-, m. p. 72°; 7-nitro-, m. p. 132—133°; 5-amino-, m. p. 110°; 7-amino-, m. p. 188—190°; 5-chloro-, m. p. 31—32°; 7-chloro-, m. p. 45°; 5-hydroxy-, m. p. 224—228°; 7-hydroxy-, m. p. 235—238°. The allocation based on these comparisons agreed with the fact that the 7-isomeride was the one produced in larger relative amount.

EXPERIMENTAL.

m-*Anisidine.*—The reduction of *m*-nitroanisole (35 g.) was conveniently effected by West's method (J., 1925, **127**, 494) using alcohol (110 c.c.), concentrated hydrochloric acid (7·5 c.c.), and iron filings (42 g.) carefully added during 1 hour. The mixture was mechanically stirred and heated on the steam-bath for 5 hours, then worked up by known methods; the yield was 80% (23·2 g., b. p. 125°/13 mm.).

Phenyl β-m-*Methoxyanilinostyryl Ketone.*—A mixture of dibenzoylmethane (19 g.), *m*-anisidine (10 g.), and acetic acid (10 c.c.) was gently refluxed for 10 minutes and then kept for 4 days. The sticky mass was distilled in nitrogen under diminished pressure, yielding successively *m*-anisidine, dibenzoylmethane, and a reddish-brown oil, b. p. 250—258°/1—2 mm., which partly crystallised on keeping. It was dissolved in the minimum of hot methyl alcohol, and on cooling two layers separated, the lower of which ultimately crystallised to a yellow mass (yield, 13 g.) (Found : N, 3·9. $C_{22}H_{19}O_2N$ requires N, 4·3%). The *substance* crystallised from alcohol–light petroleum in pale yellow needles, m. p. 75—76°; negative ferric reaction.

7-*Methoxy*-2 : 4-*diphenylquinoline*.—Dry hydrogen chloride was passed through a solution of the above anil (13 g.) in acetic acid (12 c.c.) for 24 hours at 0°; the mixture was then kept for 24 hours in the ice-chest. Addition of ether precipitated a crystalline, bright yellow hydrochloride (11 g.) which was collected and dried in a vacuum. This salt (24·5 g.) was triturated with aqueous ammonia, and the base was ultimately crystallised by mulching the treacly mass with a little ether; the resulting white paste was then filtered off, and the substance crystallised by rapid evaporation (air-blast) of a benzene solution, being obtained in colourless plates parallelogram-shaped, m. p. 102° (10 g.) (Found : C, 84·8; H, 5·6; N, 4·7. $C_{22}H_{17}ON$ requires C, 84·9; H, 5·5; N, 4·5%). The neutral solutions of this *base* exhibit violet fluorescence, and the yellow solution in sulphuric acid has a blue fluorescence; the sparingly soluble sulphate is precipitated on the addition of water. The picrate, prepared in alcoholic solution, crystallised from acetone in yellow prisms, m. p. 200°.

The *methosulphate*, prepared from the dry components in benzene solution (steam-bath), crystallised from acetone in yellow fibrous needles, m. p. 230—235° (Found : S, 7·4. $C_{24}H_{23}O_5NS$ requires S, 7·3%). The aqueous and alcoholic solutions of this salt exhibit a violet-blue fluorescence.

Anhydronium Base of 7-*Hydroxy*-2 : 4-*diphenylquinoline Methohydroxide* (V).—7-Hydroxy-2 : 4-diphenylquinoline was prepared by the method of Bülow and Issler (*Ber.*, 1903, **36**, 4013) (11·5 g. of *m*-aminophenol and 23·5 g. of dibenzoylmethane gave 24 g. of the anil, m. p. 172°; 18 g. of the anil gave 16 g. of the quinoline, m. p. 272°) (Found : C, 84·5; H, 5·2. Calc. for $C_{21}H_{15}ON$: C, 84·8; H, 5·1%). The greenish-yellow solution in hydrochloric acid is not fluorescent, but the golden-yellow solution in sulphuric acid exhibits a blue fluorescence. The oily methosulphate, prepared in boiling xylene solution, was well washed and then treated with aqueous potassium hydroxide and benzene, which immediately became red. The benzene layer was separated, dried over solid potash, concentrated to a small bulk, and mixed with about 10 vols. of light petroleum. The brick-red precipitate was quickly collected and dried over calcium chloride under diminished pressure of nitrogen (Found : C, 78·0, 78·2; H, 5·8, 6·0. $C_{22}H_{17}ON,1·5H_2O$ requires C, 78·1; H, 5·9%). The yellow aqueous solution of this *base* exhibits a blue fluorescence, and both colour and fluorescence are destroyed on the addition of hydrochloric acid, returning on neutralisation. On heating, the substance gradually decomposes but at the room temperature the water is held tenaciously.

Action of Methyl Iodide on the Anhydronium Base.—The base (0·6 g.) was dried over phosphoric oxide in a high vacuum for 2 weeks, at 50°, and then dissolved as far as possible in pure benzene (100 c.c.) in an atmosphere of nitrogen. Methyl iodide (10 c.c.) was added, and the solution refluxed until the red colour had disappeared. Partial separation of the methiodide occurred, and the sticky, yellow, partly solid mass was collected and triturated with a small volume of alcohol containing a trace of sulphur dioxide. The solid, recrystallised from alcohol–ether, formed yellow prismatic needles (Found : C, 60·6; H, 4·5; MeO, 6·5. $C_{23}H_{20}ONI$ requires C, 60·9; H, 4·4; 1MeO, 6·9%). The neutral solutions of this 7-*methoxy*-2 : 4-*diphenylquinoline methiodide* exhibit a violet-blue fluorescence; attempts to prepare the substance directly from 7-methoxy-2 : 4-diphenylquinoline and methyl iodide were unsuccessful.

7-*Methoxyquinoline*.—A mixture of *m*-anisidine (15 g.), *m*-nitroanisole (9·4 g.), dry glycerol (4·8 c.c.), and sulphuric acid (13·5 c.c.) was heated to 150° (oil-bath), and then to a higher temperature with great caution. Each time a reaction appeared to be imminent the flask was shaken; at 158° the flask was removed from the source of heat, and a few seconds later a very vigorous reaction set in. When this had subsided, the mixture was refluxed for 2 hours, sulphuric acid (5 c.c.) added, and the whole refluxed for a further 5 hours. The base was isolated as usual by eventual steam-distillation, the distillate acidified with hydrochloric acid and concentrated, and the sparingly soluble chromate precipitated by the addition of potassium dichromate (30 g.); unchanged *m*-anisidine then suffered oxidation. The free *base*, obtained in the known manner from the chromate, had b. p. 145—147°/12 mm. (7 g.) (Found : C, 75·0; H, 6·0. $C_{10}H_9ON$ requires C, 75·4; H, 5·7%). The bright yellow solution in hydrochloric acid exhibits a violet fluorescence, and the yellow solution in concentrated sulphuric acid fluoresces green and violet on the addition of water. The platinichloride is a buff precipitate, and the *picrate*, yellow prismatic needles from alcohol, has m. p. 216° (Found : C, 50·0; H, 3·6. $C_{10}H_9ON,C_6H_3O_7N_3$ requires C, 49·6; H, 3·1%).

The *methiodide*, prepared in methyl-alcoholic solution, crystallised from alcohol in bright yellow needles that darkened at 190° and finally melted at 204° (decomp.) (Found, by titration : I, 42·0. $C_{11}H_{12}ONI$ requires I, 42·2%). The colourless aqueous solution of this salt exhibited a bright blue fluorescence. It (2·6 g.) was demethylated by means of hydriodic acid (25 c.c., b. p. 125°) and phenol (1 g.) during 1 hour (oil-bath at 140°) in an atmosphere of carbon dioxide. Ether (50 c.c.) was added after cooling, and the yellow crystalline precipitate was recrystallised from alcohol, forming pale yellow, flat needles, m. p. 245° (decomp.) (1·5 g.) (Found : I, 44·1. Calc. for $C_{20}H_{20}ONI$: I, 44·2%). The aqueous solution of this 7-hydroxyquinoline methiodide exhibited a bright green fluorescence.

Claus and Masson (*J. pr. chem.*, 1892, **45**, 237; 1893, **48**, 176) obtained the methiodides of 7-hydroxyquinoline, m. p. 251°, and 5-hydroxyquinoline, m. p. 224°, by direct combination of the hydroxyquinolines with methyl iodide.

Methyl β-m-*Methoxyanilino-α-propenyl Ketone.*—After a range of trials the following conditions were selected. A mixture of *m*-anisidine (16 g.), acetylacetone (15 g.), and anhydrous calcium chloride (3·5 g.) was heated in a nitrogen atmosphere (oil-bath at 140°) for 70 minutes. On addition of ether to the cooled, yellow, viscous mass, an abundant white crystalline precipitate formed (microscopic bunches of needles) and this was doubtless a calcium chloride adduct. On addition of water, it was decomposed, and a yellow oil passed into the ethereal solution. This was isolated as usual, but an atmosphere of nitrogen was maintained at all stages; a bright yellow oil, b. p. 170—178°/10 mm., was obtained (yield, 23·8 g.) (Found : C, 70·0; H, 7·4. $C_{12}H_{15}O_2N$ requires C, 70·2; H, 7·3%).

7-*Methoxy*-2 : 4-*dimethylquinoline.*—The action of sulphuric acid on the above anil gave unsatisfactory results. (A) Ring closure of the anil (12 g.) by means of hydrogen chloride in acetic acid solution at 0°, as described above for the diphenyl analogue, afforded a *hydrochloride* (10 g.), precipitated by ether, which was crystallised from alcohol (Found: N, 6·1. $C_{12}H_{13}ON,HCl$ requires N, 6·3%). The free *base* was a thick yellow oil (6 g.), b. p. 180—185°/25 mm. (Found : C, 76·9; H, 6·7. $C_{12}H_{13}ON$ requires C, 77·0; H, 6·9%). The fluorescence of the yellow solution in hydrochloric acid was blue, and that in concentrated sulphuric acid was violet-blue; picrate, m. p. 215°.

The *methiodide* was prepared from its generators in cold concentrated methyl-alcoholic solution; it crystallised from alcohol in yellow needles, m. p. 238° (decomp.) with earlier darkening (Found, by titration : I, 38·3. $C_{13}H_{16}ONI$ requires I, 38·6%). The aqueous solution exhibited a violet fluorescence. On demethylation, as described above, 7-*hydroxy*-2 : 4-*dimethylquinoline methiodide* was obtained; it crystallised from alcohol as brownish-yellow feathery needles, m. p. 265° (decomp.) after darkening from 256° (Found : C, 45·2; H, 4·6; I, by titration, 40·0, 40·6. $C_{12}H_{14}ONI$ requires C, 45·7; H, 4·4; I, 40·3%). The aqueous solution exhibited a green fluorescence. The action of alkalis on this salt in aqueous solution afforded no benzene- or ether-soluble anhydronium base, but only the quaternary hydroxide or oxidation products.

(B) The anil (23·8 g.) was carefully added to phosphoryl chloride (85 c.c.) and, after the initial reaction had subsided, the red liquid was gently refluxed for 1½ hours. Crystals separated on cooling, but the whole product was treated with dilute aqueous ammonia, and the base collected by means of ether. The oil was distilled in nitrogen, b. p. 135—160°/10 mm. (10·6 g.). This specimen proved to be a mixture of bases, but it could not be directly separated into its constituents. The mixed methiodides obtained from the oil were triturated with warm alcohol, and the residue, after many crystallisations, was obtained in long yellow needles, m. p. 230° (decomp.) (Found : I, 38·2, 38·4%). As was confirmed by direct comparison, this salt evidently consisted of nearly pure 7-methoxy-2 : 4-dimethylquinoline methiodide.

The alcoholic filtrate was concentrated, and the salt precipitated with ether was crystallised from alcohol; it was much more readily soluble than the isomeride, and afforded ultimately, small brownish-yellow needles which sintered at 160°, darkened at 165°, and melted at 180° (decomp.) (Found, by titration : I, 38·1%). We consider that this substance must be 5-*methoxy*-2 : 4-*dimethylquinoline methiodide*; its aqueous solution exhibits a violet fluorescence.

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