516. *Some Derivatives of 4,9-Diazapyrene.*

By R. F. Robbins.

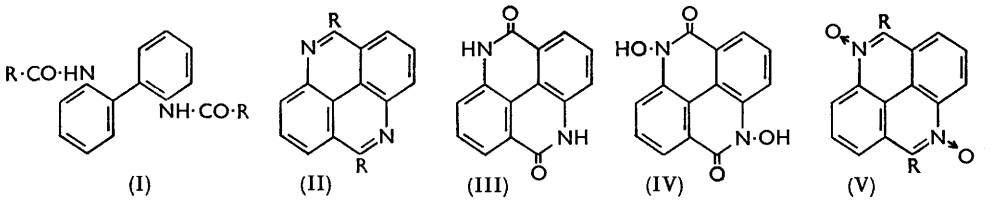
4,9-Diazapyrenes (II; R = H, Me or Ph) have been prepared in good yields and their peracid oxidation has been studied.

Despite their potential chemotherapeutic interest [1] and the use of flavanthrone as a yellow vat dye little is known of the chemistry of 4,9-diazapyrenes (II). This lack of interest has been largely due to the difficulty of synthesis.[2] The preparation of the parent base [2,3] (II; R = H) and the 5,10-dimethyl derivative [2] (II; R = Me) is very recent. Molten aluminium chloride–sodium chloride was used to cyclise 2,2′-diformamido- and 2,2′-diacetamido-biphenyl to the appropriate diazapyrene.

This reagent was used in the present work to prepare these diazapyrenes and, also, 5,10-diphenyl-4,9-diazapyrene (II; R = Ph) from 2,2′-dibenzamidobiphenyl. Optimum yields (~60%) of 4,9-diazapyrene were obtained when the cyclising agent contained a molar excess of aluminium chloride, but the best yields (~40%) of the 5,10-dimethyl and 5,10-diphenyl derivatives resulted only when the sodium chloride was present in excess.

The reaction (I) ⟶ (II) presumably involves two successive ring closures, carbonium-ion formation being followed by intramolecular electrophilic attack.

The resistance of 2,2′-diformamidobiphenyl to cyclisation is understandable. Not only is carbonium-ion formation difficult but formation of the intermediate phenanthridine will be hindered by deactivation of position 6. This will arise both by steric inhibition of the activating power of the other ring and by the $-I$ effect of the group $\cdot N{:}CH^+$ in position 2 of this other ring. The easier carbonium-ion formation when R = Me or Ph presumably explains the milder conditions required to obtain dimethyl- and diphenyl-diazapyrene. The lower yields of these might be due to a greater steric deactivation of position 6 in the biphenyl.



(I) (II) (III) (IV) (V)

5,10-Dimethyl- and 5,10-diphenyl-4,9-diazapyrene were smoothly oxidised to the di-*N*-oxides (V; R = Me or Ph) by peracetic or perphthalic acid. Attempts to prepare the mono-*N*-oxides gave only dioxide and unchanged diazapyrene. The dioxides were reduced by stannous chloride or, better, iron and acetic acid, to the parent diazapyrene.

Oxidation of 4,9-diazapyrene by peracetic acid gave no oxide but instead a high-melting product to which the dihydroxamic acid structure (IV) is assigned. It gives a characteristic claret colour with ferric chloride and a grass-green complex when kept with cupric acetate in ethanol.[4,5] Its alternative formulation as a nitro-aldehyde seems unacceptable since it dissolves in strong alkali, does not form a 2,4-dinitrophenylhydrazone, and is not reduced by iron and acetic acid. The infrared absorption also supports [6] a hydroxamic acid structure.

[1] Fairfull, Peak, Short, and Watkins, *J.*, 1952, 4700.
[2] Mosby, *J. Org. Chem.*, 1957, **22**, 671.
[3] Badger and Sasse, *J.*, 1957, 4.
[4] Hansen and Petrof, *J.*, 1953, 350.
[5] Lott and Shaw, *J. Amer. Chem. Soc.*, 1949, **71**, 67.
[6] Bonnett, Brown, Clark, Sutherland, and Todd, *J.*, 1959 2100; Bonnett, Clark, and Todd, *J.*, 1959, 2104.

Formation of the cyclic hydroxamic acid (IV) might be supposed to take place by the further oxidation of an intermediate dilactam (III) or its tautomer (II; R = OH). This reaction bears a formal resemblance to the oxidation of carbostyril to 1-hydroxy-2-quinolone by perbenzoic acid.[5] The dilactam (III), previously prepared by the cyclisation of 6,6′-diacetamidobiphenic acid,[7] was obtained by the chromic acid oxidation of 5,10-dimethyl-4,9-diazapyrene. This reaction is analogous to the oxidation of 9-methylphenanthridine to phenanthridone [8] and illustrates the reactivity of the methyl groups in the diazapyrene. The dilactam (III) was insoluble in peracetic acid and was apparently unaffected by prolonged reaction at 70°, thus making it an unlikely intermediate in the formation of the hydroxamic acid (IV).

With perphthalic acid 4,9-diazapyrene gave a product whose properties,[9] infrared absorption,[10] and nitrogen analysis * suggested a *C*-hydroxy-compound, possibly (II; R = OH). Its further oxidation by peracetic acid gave the hydroxamic acid (IV). Structure (II; R = OH) is, however, suspect, for the tautomeric dilactam (III) could not be isolated when the " *C*-hydroxy-compound " was boiled for a long time with alkali or pyridine, or kept in concentrated sulphuric acid.

Experimental

4,9-Diazapyrene.—2,2′-Diformamidobiphenyl [2] (5 g.) was added, portionwise, to a melt of aluminium chloride (89 g.) and sodium chloride (19 g.) at 100°. After 8 hr. at 250° the mixture was poured on ice, basified with sodium hydroxide, and filtered. After being washed with water, the product was dried and extracted with benzene. Treatment of the extract with charcoal, filtration, removal of the solvent, and crystallisation from methanol gave 4,9-diazapyrene (2·55 g., 60%) as yellow needles, m. p. 220—221° (Found: C, 82·5; H, 3·8; N, 13·8. Calc. for $C_{14}H_8N_2$: C, 82·3; H, 3·9; N, 13·7%.) Mosby [2] gives m. p. 220—220·7°, Badger [3] m. p. 209—210°. The foregoing compound (0·25 g.) and boiling methyl iodide (10 ml.) gave in 30 min. a *monomethiodide* (0·42 g., 70%) as orange needles (from methanol), decomp. 230—240° (Found: N, 8·1. $C_{15}H_{11}IN_2$ requires N, 8·1%).

5,10-Dimethyl-4,9-diazapyrene.—2,2′-Diacetamidobiphenyl [2] (5 g.), aluminium chloride (25 g.), and sodium chloride (15 g.) after 8 hr. at 250°, with working up as in the previous experiment, gave 5,10-dimethyl-4,9-diazapyrene (1·8 g., 43%) as yellow needles, m. p. 261—262° (from methanol) (lit.,[2] 260—261·4°) (Found: C, 82·5; H, 5·2; N, 12·0. Calc. for $C_{11}H_{12}N_2$: C, 82·7; H, 5·2; N, 12·1%).

5,10-Diphenyl-4,9-diazapyrene.—2,2′-Dibenzamidobiphenyl [11] (2 g.), aluminium chloride (10 g.), and sodium chloride (6 g.) were heated for 8 hr. at 250°. The crude product obtained as above was triturated with ethanol and then extracted (Soxhlet) with chlorobenzene, affording 5,10-diphenyl-4,9-diazapyrene (0·77 g., 42%), m. p. 320—321° (Found: C, 87·6; H, 4·6; N, 8·1. Calc. for $C_{26}H_{16}N_2$: C, 87·6; H, 4·5; N, 7·9%), as needles from chlorobenzene. It gave a picrate, m. p. 203—205°. Fairfull *et al.*[1] give m. p. 320—321°, picrate, m. p. 205—206°.

5,10-Dimethyl-4,9-diazapyrene 4,9-*Dioxide.*—(*a*) 5,10-Dimethyl-4,9-diazapyrene (0·5 g.) in acetic acid (15 ml.) was treated with 30% hydrogen peroxide (5 ml.). After 2 hr. at 70° the mixture was neutralised with ammonia solution, and the tan-coloured powder filtered off (0·4 g.). Recrystallisation from pyridine gave 5,10-*dimethyl*-4,9-*diazapyrene* 4,9-*dioxide* (Found: C, 72·7; H, 4·8; N, 10·4. $C_{16}H_{12}N_2O_2$ requires C, 72·7; H, 4·6; N, 10·6%) as yellow needles which darken at 280° and decompose at 284—286° (heating at 8° per min.).

(*b*) 5,10-Dimethyl-4,9-diazapyrene (0·5 g.) in chloroform (25 ml.) was treated with ethereal perphthalic acid (15 ml.; 2·2 atom-equiv. of oxygen). After 48 hr. at 0—5° the solvent was removed in a vacuum, the residue basified with ammonia, and the product filtered off and washed with water and a little ethanol. Recrystallisation from pyridine gave the dioxide (0·21 g., 37%), m. p. and mixed m. p. 284—286 (decomp. from 280°) (Found: N, 10·7%).

* Poor carbon analyses seem characteristic of compounds of this type (cf. ref. 7).

[7] Kenner and Stubbings, *J.*, 1921, 593.
[8] Walls, *J.*, 1935, 1405.
[9] Landquist, *J.*, 1956, 1885.
[10] Bellamy, " The Infra-Red Spectra of Complex Molecules," Methuen, London, 2nd edn., 1958, p. 96.
[11] Wittig, Jesaitis, and Glos, *Annalen*, 1952, **577**, 5.

The dioxide gave no colour reaction with ferric chloride or cupric acetate in ethanol, nor did it liberate iodine from acid potassium iodide. It (0·05 g.) was heated with acetic acid (1·5 ml.) and reduced iron powder (0·1 g.) on the water-bath for 45 min., then filtered and basified with sodium hydroxide. The product was filtered off and washed with water. Extraction of the dry material with benzene followed by evaporation of the extract to small volume gave, on cooling, yellow needles (0·02 g., 46%), m. p. 261—262°, undepressed on admixture with 5,10-dimethyl-4,9-diazapyrene.

5,10-*Diphenyl*-4,9-*diazapyrene* 4,9-*Dioxide*.—(*a*) 5,10-Diphenyl-4,9-diazapyrene (0·5 g.) in acetic acid (50 ml.) containing 30% hydrogen peroxide (4 ml.) was kept at 70° for 21 hr. Dilution with water and filtration gave the crude dioxide (0·43 g., 79%) which from chlorobenzene formed yellow needles, m. p. 320—321° (decomp.), of *dioxide* (Found: N, 7·2. $C_{26}H_{16}N_2O_2$ requires N, 7·2%).

(*b*) 5,10-Diphenyl-4,9-diazapyrene (0·1 g.) in chloroform (20 ml.) was treated with ethereal perphthalic acid (3 ml.; 2·8 g.-equiv. of oxygen). After 5 days at 0—5° and working up as before, crystallisation from chlorobenzene gave the dioxide (0·5 g., 46%). From pyridine it formed yellow needles, m. p. and mixed m. p. 320—321° (Found: C, 80·8; H, 3·9; N, 7·4. $C_{26}H_{16}N_2O_2$ requires C, 80·4; H, 4·1; N, 7·2%).

(*c*) 5,10-Diphenyl-4,9-diazapyrene (0·1 g.) with perphthalic acid (1 mol.) gave after 24 hr. at 0—5° the dioxide (0·04 g.) as yellow needles (from pyridine), m. p. and mixed m. p. 320—321°. Unchanged diazapyrene was recovered from the crystallisation residues.

This dioxide had the same properties as its analogue and on reduction gave 5,10-diphenyl-4,9-diazapyrene (27%) identified by mixed m. p. The use of stannous chloride and concentrated hydrochloric acid gave a less pure product.

4,9-*Dihydroxy*-5,10-*dioxo*-4,9-*diazapyrene*.—4,9-Diazapyrene (0·35 g.) in glacial acetic acid (10 ml.) containing 30% hydrogen peroxide (2 ml.) was kept at 70° for 22 hr., then diluted with water, and the product was filtered off and washed with water and hot ethanol. The product (0·27 g.) formed, from pyridine, yellow needles, m. p. >360°, of 4,9-*dihydroxy*-5,10-*dioxo*-4,9-*diazapyrene* (Found: C, 62·7; H, 3·1; N, 10·5. $C_{14}H_8N_2O_4$ requires C, 62·7; H, 3·0; N, 10·4%), soluble in concentrated acid or alkali but not in dilute sodium hydrogen carbonate solution. It gave a claret colour with ferric chloride in ethanol and a grass-green precipitate with cupric acetate in ethanol. It gave no iodine with acid potassium iodide nor did it form a 2,4-dinitrophenylhydrazone with Brady's reagent. Iron and acetic acid appeared not to affect it (colour reactions unchanged). It had $\nu_{max.}$ (KBr disc) 3750, 3250, 2850, 1655, and 1595 cm.$^{-1}$.

The " C-*Hydroxy-compound."*—4,9-Diazapyrene (0·5 g.) in chloroform (37·5 ml.) was treated with perphthalic acid in ether (15·75 ml., 2 atom-equiv. of oxygen). After 30 min. at room temperature the solvent was removed in a vacuum, water (50 ml.) added, and the mixture steam-distilled. Evaporation of the water in a vacuum gave a gum which on trituration with methanol deposited a yellow powder (0·415 g.), m. p. 286—291°. Recrystallisation from pyridine gave the "C-*hydroxy-compound*" (Found: N, 11·8. $C_{14}H_8N_2O_2$ requires N, 11·9%) as yellow needles, m. p. >360° (decomp.), $\nu_{max.}$ (KBr disc) 3700, 1485, and 1260 cm.$^{-1}$. This was soluble in dilute sodium hydroxide but not in sodium hydrogen carbonate solution or common organic solvents. It gave no colour with ferric chloride or with cupric acetate, and no iodine with acid potassium iodide. It was unchanged on treatment with iron and acetic acid. When it had been dissolved in concentrated sulphuric acid and left for several days the addition of water precipitated no dilactam. It was unaltered when boiled for 12 hr. with pyridine, as shown by the similarity of the infrared absorption curves. After it had been refluxed for 2 hr. with 4N-sodium hydroxide, acidification precipitated a pale yellow solid which did not give the blue fluorescence with concentrated sulphuric acid characteristic of the dilactam.

The "*C*-hydroxy-compound" (0·2 g.) in acetic acid (6 ml.) containing 30% hydrogen peroxide (1 ml.) was kept at 70° for 10 hr. The precipitated solid was filtered off and washed with hot aqueous ethanol. The product (0·135 g.) formed, from pyridine, yellow needles, m. p. >360°, shown by their infrared absorption curve to be 4,9-dihydroxy-5,10-dioxo-4,9-diazapyrene.

4,9-*Dihydro*-5,10-*dioxo*-4,9-*diazapyrene*.—5,10-Dimethyl-4,9-diazapyrene (0·2 g.) in glacial acetic acid (5 ml.) containing sodium dichromate (0·9 g.) was refluxed for 1 hr. The mixture was poured into water, and the precipitate filtered off and washed. Sublimation (at 300—320°/0·5—1 mm.) gave crude 4,9-dihydro-5,10-dioxo-4,9-diazapyrene (Found: C, 72·3; H, 3·6; N, 11·7. Calc. for $C_{14}H_8N_2O_2$: C, 71·2; H, 3·4; N, 11·9%) as a yellow powder, m. p.

>360° (decomp.), $\nu_{max.}$ (KBr disc) 3100, 1670, 1615, 1575, 1435, 1365, 743, and 650 cm.$^{-1}$. It was insoluble in all the usual organic solvents, dilute acid, and alkali. It dissolved in alcoholic alkali and gave a blue fluorescent solution with concentrated sulphuric acid.

I am indebted to Drs. Catchpole and Elliott and their associates for determination of infrared spectra.

NOTTINGHAM & DISTRICT TECHNICAL COLLEGE. [*Received, December 7th*, 1959.]