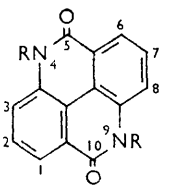
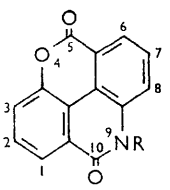
984. *The Peracid Oxidation of 4,9-Diazapyrene.*

By M. Gawlak and R. F. Robbins.

The preparation of 4,9-dihydroxy-4,9-diazapyrene-5,10-dione confirms this as the product of oxidation of 4,9-diazapyrene by peracetic acid. An intermediate oxidation product, the "*C*-hydroxy-compound" of a previous Communication [1] is shown to be 4-hydroxy-4,9-diazapyren-5-one. The lactam resulting from its reduction has been synthesised. A possible mechanism for the formation of hydroxamic acids from 4,9-diazapyrene is discussed. Some examples of intramolecular nucleophilic displacement in 2,2′-disubstituted biphenyls are described and a mechanism suggested for the reaction of 4-hydroxy-4,9-diazapyren-5-one with phosphorus oxychloride.

While 5,10-dimethyl- and 5,10-diphenyl-4,9-diazapyrene give with peracetic acid the corresponding di-*N*-oxides, similar oxidation of 4,9-diazapyrene gives a high-melting product believed to be 4,9-dihydroxy-4,9-diazapyrene-5,10-dione [1] (I; R = OH). The correctness of this formulation is now shown by an independent preparation of the *N*-hydroxy-compound (I; R = OH). Use was made of a method developed by Hey, Leonard, and Rees [2] to prepare 5-hydroxyphenanthridone from 2′-nitrobiphenyl-2-carboxylic acid. When 6,6′-dinitro-2,2′-biphenic acid was warmed with zinc and ammonium chloride in ethanol, and the resulting complex was decomposed with strong acid, the dihydroxamic acid (I; R = OH) appeared in good yield. Hey *et al.* also used boiling tetralin to reduce 2′-nitrobiphenyl-2-carboxylic acid to the corresponding 2-hydroxyamino-compound. Spontaneous cyclodehydration then gave 5-hydroxyphenanthridone. However, with 6,6′-dinitro-2,2′-biphenic acid in boiling tetralin, not only was a hydroxamic acid group formed, but also displacement of one of the nitro-groups introduced a lactone


(I)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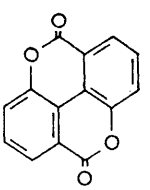
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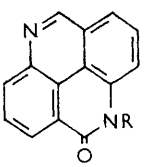

(IV)

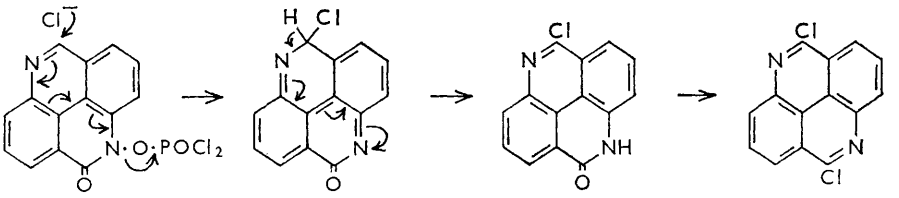
group and so gave the product (II; R = OH). The latter gives a claret colour with ferric chloride in ethanol characteristic of hydroxamic acid, and its infrared absorption curve suggests the presence of both hydroxamic acid and lactone groups. That formation of the lactone (II; R = OH) involves intramolecular nucleophilic attack by $^{-}CO{\cdot}O^{-}$ seems certain, for addition of quinoline to the boiling tetralin improves the yield of the lactone, presumably by base catalysis. In the absence of quinoline, the reaction may be catalysed by the first formed hydroxyamino-derivative produced by reduction of the dinitrobiphenic acid with tetralin. A similar nucleophilic displacement of a nitro-group was noticed when 1-carboxy-10-nitrophenanthridone (obtained by reduction of 6,6′-dinitro-2,2′-biphenic acid with sodium sulphide), was heated in quinoline alone: 9*H*-4-Oxa-9-azapyrene-5,10-dione (II; R = H) was formed. Furthermore, the expulsion of both nitro-groups was observed when 6,6′-dinitro-2,2′-biphenic acid was heated for some time in quinoline: the dilactone (III) was obtained.

The formation of 4,9-dihydroxy-4,9-diazapyrene-5,10-dione (I; R = OH) by oxidation

[1] Robbins, *J.*, 1960, 2553.
[2] Hey, Leonard, and Rees, *J.*, 1962, 4579.

of 4,9-diazapyrene with peracetic acid appears to involve an alkali-soluble intermediate. This "*C*-hydroxy compound" [1] can be prepared by mild (perphthalic acid) oxidation of 4,9-diazapyrene, and its structure has been a matter of conjecture. It is now shown to be 4-hydroxy-4,9-diazapyren-5-one (IV; R = OH). Its infrared absorption shows a wide band at 1675 cm.$^{-1}$, indicative of hydrogen bonding. It dissolves in aqueous alkali hydroxides, but not in sodium hydrogen carbonate, and gives a claret colour with ferric chloride (although the development of a colour is so slow as to have been previously discounted).[1] These observations suggest a hydroxamic acid structure (IV; R = OH), and final proof follows from examination, and synthesis, of its reduction product, which is shown to be 4*H*-4,9-diazapyrene-5-one (IV; R = H). The reduction of 4,9-dihydroxy-4,9-diazapyrene-5,10-dione (I; R = OH) with iron and acetic acid or with Raney nickel and hydrazine gives 4,9-dihydro-4,9-diazapyrene-5,10-dione (I; R = H), whose identity was confirmed by comparison with a sample of the dilactam (I; R = H) prepared by unambiguous synthesis [3] and also by oxidation of 5,10-dimethyl-4,9-diazapyrene.[1] Since this is so, it seems reasonable to suppose that a similar reduction of the hydroxamic acid (IV; R = OH) would give the lactam (IV; R = H). The structure (IV; R = H) of this reduction product follows from the similarity of its ultraviolet absorption spectrum with that of 4*H*-4,10-diazapyrene-5-one [4] and by its preparation from 4,9-diazapyrene by careful oxidation with acid potassium permanganate. The analogous preparation of 1-nitrophenanthridone from 1-nitrophenanthridine has been reported.[5] An alternative synthesis of the lactam (IV; R = H) from 2-acetamido-2′-nitrobiphenyl proved impossible: that only tar resulted in this attempt (with molten aluminium chloride and sodium chloride) accords with the known difficulties of such cyclisations.[6]

Reaction of the 4-hydroxy-4,9-diazapyren-5-one with phosphorus oxychloride in dimethyl- or diethyl-aniline gives 5,10-dichloro-4,9-diazapyrene whose identity was proved by comparison with a sample prepared from 4,9-dihydro-4,9-diazapyrene-5,10-dione (I; R = H) and phosphorus oxychloride and also by converting it into 4,9-diazapyrene through the 5,10-dihydrazino-derivative which was oxidised with copper sulphate. The formation of 5,10-dichloro-4,9-diazapyrene from 4-hydroxy-4,9-diazapyren-5-one may very well involve initial formation of an ester of the hydoxamic acid (IV; R = O·POCl$_2$) and subsequent nucleophilic attack by Cl$^-$ at the suitably activated position 10, thus:

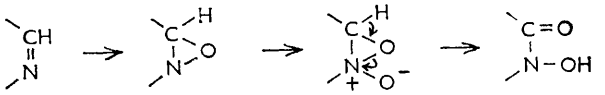


Displacement of the $^-$O·POCl$_2$ group by the appropriate nucleophile could, however, give an *N*-chloroamide. This seems the predominant reaction, because substantial quantities of 4-hydroxy-4,9-diazapyren-5-one are recovered (presumably as a result of the easy hydrolysis during working up of the *N*-chloroamide), while 5,10-dichloro-4,9-diazapyrene is obtained only in small quantity.

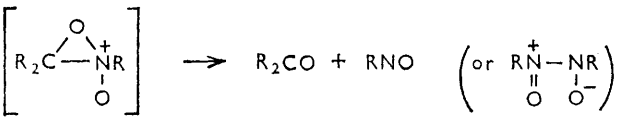
The formation from 4,9-diazapyrene, by treatment with a suitable peracid, of either the mono- (IV; R = OH) or the di-hydroxamic acid (I; R = OH) seems not to take place by the further oxidation of lactam (*e.g.*, I; R = H).[1] Such oxidations are, in any case,

[3] Kenner and Stubbings, *J.*, 1921, 593.
[4] Coffin and Robbins, unpublished observation.
[5] Caldwell and Walls, *J.*, 1952, 2156.
[6] Sasse, in "Current Trends in Heterocyclic Chemistry," ed. Albert, Badger, and Shoppee, Butterworths, London, 1958, p. 83.

rare and give poor yields (*e.g.*, carbostyril with perbenzoic acid gives only 1% of 1-hydroxy-2-quinolone).[7] The formation of the hydroxamic acid (I or IV; R = OH) probably depends on the " anil-like " nature of the 4,5- and 9,10-bonds in 4,9-diazapyrene. Similarly sited bonds in pyrene are well known for their " double-bond " character.[8] Attack by a peracid on either the 4,5- or the 9,10-bond of 4,9-diazapyrene may thus give an oxaziridine whose further oxidation may give an oxaziridine *N*-oxide, which could then rearrange to a hydroxamic acid:



Oxaziridine *N*-oxides have been suggested as intermediates in the formation of nitroso-alkanes (or more usually their dimers) when a suitable imine is treated with two mol. of peracetic acid:[9]



The possibility that the formation of the *N*-hydroxy-compounds (I and IV; R = OH) involves ring opening of an oxaziridine *N*-oxide cannot be excluded. In a nitroso-aldehyde derived from 4,9-diazapyrene, the further reaction of these two very near groups might then very easily occur to give the hydroxamic acid.

Experimental

4,9-*Dihydroxy*-4,9-*diazapyrene*-5,10-*dione*.—To a refluxing solution of 6,6′-dinitro-2,2′-biphenic acid (0·5 g.) and ammonium chloride (0·25 g.) in ethanol (2·5 ml.) and water (0·25 ml.), zinc dust (0·25 g.) was added in 5 min. After 30 min., the precipitated solid and excess of zinc were filtered off. Trituration with hot 2N-hydrochloric acid, washing, and drying, gave a yellow solid (0·127 g.). This was dissolved in concentrated sulphuric acid, and water was added. The precipitate was collected, dried, and sublimed under a vacuum. The resulting pale yellow solid, m. p. >360°, dissolved in concentrated aqueous sodium hydroxide, but not in sodium hydrogen carbonate solution, and gave a claret colour with ferric chloride in ethanol. It was proved to be 4,9-*dihydroxy*-4,9-*diazapyrene*-5,10-*dione* from the similarity of its infrared absorption with that of a sample (Found: C, 62·7; H, 3·1; N, 10·5. $C_{14}H_6N_2O_4$ requires C, 62·7; H, 3·0; N, 10·4% m. p. >350°) prepared by oxidising 4,9-diazapyrene with peracetic acid.[1]

9-*Hydroxy*-4-*Oxa*-9-*azapyrene*-5,10-*dione*.—A solution of 6,6′-dinitro-2,2′-biphenic acid (0·5 g.) in tetralin (10 ml.) and quinoline (2 ml.) was refluxed for 3 hr. and the solvent was removed under a vacuum. Trituration of the residue with methanol gave a product (0·183 g.) whose crystallisation from methylcellosolve and then ethanol–pyridine afforded 9-*hydroxy*-4-*oxa*-9-*azapyrene*-5,10-*dione* (Found: C, 66·1; H, 2·9; N, 5·7. $C_{14}H_7NO_4$ requires C, 66·4; H, 2·8; N, 5·5%), m. p. 315—318° (decomp.).

When refluxed for 6 hr. in tetralin (5 ml.) alone, the dinitrobiphenic acid (0·3 g.) gave 0·13 g. of a yellow solid, which after crystallisation (see above) was shown to be 9-hydroxy-4-oxa-9-azapyrene-5,10-dione by comparison with the foregoing sample (m. p. and mixed m. p. 315—318°, and infrared absorption).

1-*Carboxy*-10-*nitrophenanthridone*.—6,6′-Dinitro-2,2′-biphenic acid (0·5 g.) was dissolved in a minimum of aqueous sodium hydrogen carbonate. To this solution at 100° was added, in 30 min., 1·5 ml. of a solution obtained by adding sulphur (1 g.) to sodium sulphide nonahydrate (0·4 g.) in water (15 ml.). After a further 30 min. at 100° the mixture was made

[7] Lott and Shaw, *J. Amer. Chem. Soc.*, 1949, **71**, 67.
[8] Ref. 6, p. 1.
[9] Emmons, *J. Amer. Chem. Soc.*, 1957, **79**, 6522.

strongly acid and left for 24 hr. The resulting precipitate was collected, washed with water, and extracted with warm aqueous sodium hydrogen carbonate. Acidification by hydrochloric acid of the alkaline extracts gave the crude phenanthridone derivative (0·378 g.). Further purification was effected by trituration with hot ethanol (to remove unchanged dinitrobiphenic acid), dissolution in alkali, and precipitation with hydrochloric acid. Repetition of this process afforded 1-*carboxy*-10-*nitrophenanthridone* (Found: C, 59·4; H, 3·1; N, 9·6. $C_{14}H_8N_2O_5$ requires C, 59·2; H, 2·8; N, 9·9%), melting with decomposition between 260 and 300°.

9H-4-*Oxa*-9-*azapyrene*-5,10-*dione*.—A solution of 1-carboxy-10-nitrophenanthridone (0·15 g.) in quinoline (2 ml.) was refluxed for 30 min., and the mixture was poured into dilute hydrochloric acid. The precipitate was collected and washed with water, and then with methanol, and the resulting dark brown product (0·082 g.) was sublimed at 270°/0·2 mm. Recrystallisation from pyridine of the sublimate afforded the *product* (Found: C, 70·7; H, 3·2. $C_{14}H_7NO_3$ requires C, 70·9; H, 3·0%), m. p. >360°.

4,9-*Dioxapyrene*-5,10-*dione*.—6,6′-Dinitro-2,2′-biphenic acid (0·1 g.) was boiled with quinoline (2 ml.) for 30 min. The dark solution was poured into 5N-hydrochloric acid (10 ml.), and the resulting precipitate was collected. This was washed with dilute hydrochloric acid and with water, and dried; the dry product (0·033 g.) was sublimed at 240—270°/0·5 mm. The buff sublimate crystallised from benzene as white needles of 4,9-dioxapyrene-5,10-dione (Found: C, 70·6; H, 2·6. Calc. for $C_{14}H_6O_4$: C, 70·6; H, 2·5%), m. p. 376° (sublim.) (lit.,[10] >350°; sublim.).

4,9-*Dihydro*-4,9-*diazapyrene*-5,10-*dione*.—A mixture of 4,9-dihydroxy-4,9-diazapyrene-5,10-dione (0·1 g.) and iron powder (0·4 g.) in acetic acid (5 ml.) was heated to 100° for 3 hr. More (0·2 g.) iron powder was then added and heating continued for 1 hr. When the mixture was diluted with water, the organic solid, which separated from the heavy iron powder by flotation, was collected and warmed with 5N-hydrochloric acid. The product was collected and washed with water, dilute aqueous sodium hydroxide, and water, and dried; the dry product (0·08 g.), m. p. 350° (sublim.), was identified [1] by its infrared absorption spectrum as 4,9-dihydro-4,9-diazapyrene-5,10-dione.

4H-4,9-*Diazapyren*-5-*one*.—(*a*) To a solution of 4,9-diazapyrene (0·5 g.) in 3N-sulphuric acid (10 ml.) at 80° was added potassium permanganate (0·26 g.), portionwise in 15 min. The mixture was cooled and the resulting solid collected. Treatment of this mixture (MnO_2 and the sulphate of the 5-oxo-compound) with 5N-sulphuric acid removed manganese dioxide. From the residue aqueous sodium hydroxide then released the free base which, after being washed with water and dried, was obtained as a pale yellow solid (0·24 g.). Crystallisation from pyridine then afforded 4H-4,9-*diazapyren*-5-*one* (Found: C, 76·2; H, 3·8; N, 12·2. $C_{14}H_8N_2O$ requires C, 76·4; H, 3·7; N, 12·7%), m. p. 366° (decomp.), $\lambda_{max.}$ 243, 253, 273, 306, 317, 344, 358, and 376 mμ (ε 742, 1565, 1612, 3240, 3630, 4600, 3400, and 4360) [cf. 4H-4,10-*diazapyren*-5-*one*,[4] $\lambda_{max.}$ 243, 256, 278, 305, 318, 336, 360, and 376 mμ (ε 1221, 1590, 1762, 3630, 3640, 4120, 4010, and 3720)].

(*b*) To a hot solution of 4-hydroxy-4,9-diazapyren-5-one (0·1 g.; Found: N, 11·6. Calc. for $C_{14}H_6N_2O_2$; N, 11·9%) in acetic acid (3 ml.) was added reduced iron powder (0·5 g.), and the mixture was boiled for 90 min. The hot solution was filtered, diluted with water, and left overnight. A pale yellow solid (0·02 g.) crystallised and after recrystallisation from pyridine gave 4H-4,9-diazapyren-5-one as shown from its m. p. and the similarity of its infrared absorption with the sample from (*a*).

The same lactam (0·012 g.) was obtained by reducing the 4-hydroxy-4,9-diazapyren-5-one (0·1 g.) with hydrazine and Raney nickel in a boiling alcohol solution for 90 min.

5,10-*Dichloro*-4,9-*diazapyrene*.—Dimethyl aniline (10 ml.) containing 4,9-dihydro-4,9-diazapyrene-5,10-dione [1,3] (0·2 g.) and phosphorus oxychloride (20 ml.) was refluxed for 2 hr. and then poured on ice. The *product* (0·202 g.) was collected, washed, dried, and crystallised from chlorobenzene as yellow needles (Found: C, 61·0; H, 2·3; Cl, 25·4; N, 10·5. $C_{14}H_6Cl_2N_2$ requires C, 61·6; H, 2·2; Cl, 26·0; N, 10·3%), which sublime without melting at about 230°.

The same (infrared absorption) dichloro-compound (0·093 g.) was obtained from the reaction (2 hr.) of 4-hydroxy-4,9-diazapyren-5-one (0·3 g.) with phosphorus oxychloride (11 ml.) in boiling diethylaniline (5 ml.). It was isolated by pouring the reaction mixture on ice and subliming the resulting dark brown solid at 250°/10 mm.

4,9-*Diazapyrene*.—A solution of 5,10-dichloro-4,9-diazapyrene (0·2 g.) in ethanol (7 ml.)

[10] Huntress and Seikel, *J. Amer. Chem. Soc.*, 1939, **61**, 1358.

containing 99—100% hydrazine hydrate (3·6 ml.) was boiled for 90 min. and allowed to cool. The impure 5,10-dihydrazino-4,9-diazapyrene (0·185 g.), m. p. >340°, which then crystallised, was filtered off and treated without further purification, with a 10% solution (6 ml.) of cupric sulphate. The mixture was boiled for 10 min. and sodium hydroxide solution then added. All the solid material was collected, washed with water, and dried. The dry product was extracted with benzene, and concentration of the extract gave pale yellow needles m. p. 216—219°. Recrystallisation (methanol) gave 4,9-diazapyrene as shown from its infrared absorption and from its m. p. (220—221°, undepressed on admixture with 4,9-diazapyrene prepared otherwise [1]).

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