548. *Syntheses of Some Derivatives of 2-Phenyl-1-azapyrene.*

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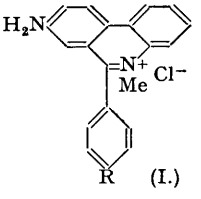
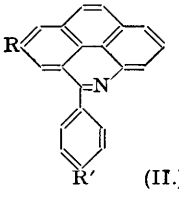
Syntheses of quaternary ammonium salts of 2-phenyl-, 2-*p*-aminophenyl-, 4-carbethoxyamino-2-*p*-nitrophenyl-, and 2-*p*-aminophenyl-4-carbethoxyamino-1-azapyrene are described. Some of these compounds show activity as trypanocides but are inferior, in this respect, to analogous phenanthridinium compounds.

Walls and others (see, *e.g.*, *J. Soc. Chem. Ind.*, 1947, **66**, 182) have shown that marked trypanocidal activity is associated with certain quaternary ammonium salts of 9-phenylphenanthridine containing suitably located substituents such as amino, nitro or methoxyl. An important condition for the development of activity is the presence of at least one such substituent in the phenanthridine ring. Phenidium chloride (I; R = NH_2), which is one of the most active members of the series against *Trypanosoma congolense*, retains activity even if one of its amino-groups is replaced by nitro, to give (I; R = NO_2) (Walls, Browning, Calver, and Leckie, *J.*, 1947, 67). The object of the present work was to prepare similarly substituted derivatives of the analogous ring-system, 2-phenyl-1-azapyrene (II; R = R′ = H) (Cook and Thomson, *J.*, 1945, 395). This polycyclic base readily yielded a quaternary methobromide. Cyclisation of 4-*p*-nitrobenzamidophenanthrene by means of phosphoryl chloride in nitro-



(I.)



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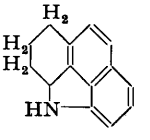

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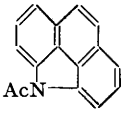

(IV.)

benzene afforded 2-*p*-nitrophenyl-1-azapyrene (II; R = H; R′ = NO_2) which was quaternised and then reduced, etc., to give the methotoluene-*p*-sulphonate of (II; R = H; R′ = NH_2). This amino-quaternary salt had a definite curative action on *T. congolense* infections in mice when administered in doses approaching the maximum tolerated. For the preparation of derivatives of (II) containing an amino-, or substituted amino-, group in the azapyrene part of the molecule, it was considered that the required intermediate 4-amino-*x*-nitrophenanthrene (where *x* is any position other than 5) might be prepared by nitration of 1 : 2 : 3 : 4-tetrahydro-4-ketophenanthrene, followed by application of the Schroeter reaction (*Ber.*, 1930, **63**, 1308) to the oxime of the resulting nitro-ketone. However, under the various conditions tried, a homogeneous mononitro-derivative was readily obtained only by nitration in presence of acetic anhydride. The product, obtained in about 50% yield, must be 1 : 2 : 3 : 4-tetrahydro-4-keto-5-nitrophenanthrene because (*a*) it gave no oxime and (*b*) it gave, on catalytic hydrogenation, 1 : 2 : 3 : 4-tetrahydro-4 : 5-iminophenanthrene (III), which, on acetylation followed by

dehydrogenation, yielded *N*-acetyl-4 : 5-iminophenanthrene (IV). Nitration of 1 : 2 : 3 : 4-tetrahydro-1-ketophenanthrene under similar conditions was then studied in the hope that the nitro-group might likewise enter the 5-position. The product, however, consisted of a 1 : 2 : 3 : 4-tetrahydro-1-keto-*x*-nitrophenanthrene whose structure was determined as follows. Treatment of its oxime with hydrogen chloride in a mixture of acetic acid and acetic anhydride according to Schroeter's method (*loc. cit.*) afforded a 1-amino-nitrophenanthrene which, on diazotisation followed by hypophosphorous acid reduction of its diazonium salt, yielded 9-nitrophenanthrene. If the normal directive effect of a carbonyl group attached to an aromatic system is borne in mind, it is probable that the nitration product is 1 : 2 : 3 : 4-tetrahydro-1-keto-9-nitrophenanthrene, but the possibility of its being the 10-nitro-isomer is not rigidly excluded. The required intermediate was eventually obtained by carbethoxylation of 7-amino-1 : 2 : 3 : 4-tetrahydro-4-ketophenanthrene (Miyasaka, *Chem. Abstr.*, 1940, **34**, 7288), followed by Schroeter treatment of the carbethoxyamino-ketone oxime, which yielded 5-amino-2-carbethoxyaminophenanthrene. Similar treatment of the oxime of 1 : 2 : 3 : 4-tetrahydro-4-keto-7-methoxyphenanthrene yielded 5-amino-2-methoxyphenanthrene. These reactions, involving the conversion of 1 : 2 : 3 : 4-tetrahydro-4-ketophenanthrene oximes into 4-phenanthrylamines, gave yields of the order of 20% and neutral by-products were frequently encountered.

Cyclisation of 4-benzamidophenanthrenes by means of phosphoric oxide in xylene (Cook and Thomson, *loc. cit.*) proceeded smoothly only in the case of the unsubstituted derivative. In other cases, phosphoryl chloride alone, or preferably in nitrobenzene solution, gave rather better results although it was not invariably successful. For example, 4-*p*-carbethoxyaminobenzamidophenanthrene suffered hydrolysis of the ester grouping as well as cyclisation, a result which is in contrast to the smooth cyclisation of 2-*p*-carbethoxyaminobenzamidodiphenyl derivatives previously reported by Walls (*loc. cit.*; *J.*, 1948, 188). Cyclisation of 2-carbethoxyamino-5-*p*-nitrobenzamidophenanthrene followed by quaternisation yielded the methosulphate of 4-carbethoxyamino-2-*p*-nitrophenyl-1-azapyrene (II; R = $NH{\cdot}CO_2Et$, R′ = NO_2), which, on reduction with iron powder, yielded the methosulphate of 2-*p*-aminophenyl-4-carbethoxyamino-1-azapyrene (II; R = $NH{\cdot}CO_2Et$, R′ = NH_2). The nitro- and amino-quaternary salts showed definite curative actions on *T. congolense* infections in mice but did not show the range of activity possessed by the best of the phenanthridinium compounds. For this reason, and also because of lack of material, attempts were not made to hydrolyse (II; R = $NH{\cdot}CO_2Et$, R′ = NH_2) to a diamine which would be exactly analogous to phenidium chloride.

Experimental.

For the preparation of 1 : 2 : 3 : 4-tetrahydro-4-ketophenanthrene, γ-(β-naphthyl)butyric acid was prepared (on the 100-g. scale) by palladium–charcoal dehydrogenation of methyl γ-(1 : 2 : 3 : 4-tetrahydro-6-naphthyl)butyrate (Newman and Zahm, *J. Amer. Chem. Soc.*, 1943, **65**, 1097). The procedure, recommended by these authors, of dehydrogenation of methyl β-(1 : 2 : 3 : 4-tetrahydro-2-naphthoyl)-propionate, although, in our hands, satisfactory on a small scale (5 g.), was not when applied to larger batches (100 g.) of material. The product then consisted of a mixture containing much β-(β-naphthoyl)-propionic acid and also some not fully aromatised material. γ-(β-Naphthyl)butyric acid was cyclised by means of anhydrous hydrogen fluoride to give 1 : 2 : 3 : 4-tetrahydro-4-ketophenanthrene in 80% yield.

Nitration of 1 : 2 : 3 : 4-*Tetrahydro*-4-*ketophenanthrene*.—A mechanically stirred solution of the ketone (5 g.) in glacial acetic acid (6·4 c.c.) was cooled at 0° and treated dropwise, during 15 minutes, with a cold mixture of acetic anhydride (3·8 c.c.) and nitric acid (98%; 2·5 c.c.). The mixture was kept at 0° for 4 hours. The crystalline product was filtered off, washed with a small quantity of methanol, and then recrystallised from ethanol, giving rhombs (3·0 g., 49%), m. p. 162°, of 1 : 2 : 3 : 4-*tetrahydro*-4-*keto*-5-*nitrophenanthrene* (Found: C, 69·8; H, 4·6; N, 6·0. $C_{14}H_{11}O_3N$ requires C, 69·7; H, 4·6; N, 5·8%). It was recovered unchanged after being boiled under reflux with hydroxylamine hydrochloride in anhydrous pyridine for several hours.

Oxidation of 1 : 2 : 3 : 4-*Tetrahydro*-4-*keto*-5-*nitrophenanthrene*.—The finely powdered nitro-ketone (0·3 g.) was boiled under reflux with nitric acid (*d* 1·42; 2 c.c.) and water (24 c.c.) for 90 hours. The mixture was cooled and the yellow solid filtered off. It was extracted with warm, 2N-sodium carbonate (5 c.c.). The extract, on acidification with concentrated hydrochloric acid, very slowly deposited crystals which, on recrystallisation from water, formed large, yellow prisms, m. p. 232—234°, of 8-*nitronaphthalene*-1 : 2-*dicarboxylic acid* (Found: C, 54·8; H, 2·9. $C_{12}H_7O_6N$ requires C, 55·1; H, 2·7%).

Catalytic Hydrogenation of 1 : 2 : 3 : 4-*Tetrahydro*-4-*keto*-5-*nitrophenanthrene*.—A suspension of the nitro-ketone (0·5 g.) in absolute ethanol (40 c.c.) was shaken with hydrogen in presence of a 20% palladium–charcoal catalyst (0·2 g.; Newman and Zahm, *loc. cit.*). The mixture rapidly absorbed 3 mols. of hydrogen; hydrogenation was stopped when a further 1·1 mols. had been slowly taken up. The catalyst was filtered off and the filtrate evaporated under reduced pressure. The residual gum, on trituration with ethanol, gave a solid which, on recrystallisation from ethanol, formed white needles (0·1 g.), m. p. 113°, of 1 : 2 : 3 : 4-*tetrahydro*-4 : 5-*iminophenanthrene* (III) (Found: C, 85·8; H, 6·8; N, 6·9. $C_{14}H_{13}N$ requires C, 86·2; H, 6·7; N, 7·2%). Crystals of this substance rapidly darkened on exposure to the atmosphere, and in subsequent experiments it was found preferable to acetylate the

crude hydrogenation product by heating it with acetic anhydride (5 c.c.) on a water-bath for 3 hours. After removal of acetic anhydride under reduced pressure, the residue was recrystallised (charcoal) from methanol, giving prisms (0·26 g.), m. p. 136°, of *N-acetyl*-1 : 2 : 3 : 4-*tetrahydro*-4 : 5-*iminophenanthrene* (Found : C, 80·9; H, 6·1; N, 5·9. $C_{16}H_{15}ON$ requires C, 81·0; H, 6·4; N, 5·9%). Dehydrogenation of this acetyl derivative by heating the substance (100 mg.) with 20% palladium–charcoal (50 mg.) at 180—250° in an atmosphere of carbon dioxide for 1 hour, yielded N-*acetyl*-4 : 5-*iminophenanthrene* (IV), which formed long, white needles (from ethanol), m. p. 174—175° (Found : C, 82·7; H, 5·0; N, 6·0. $C_{16}H_{11}ON$ requires C, 82·4; H, 4·8; N, 6·0%).

Nitration of 1 : 2 : 3 : 4-*Tetrahydro*-1-*ketophenanthrene*.—A solution of the ketone (10 g.) in acetic acid (14 c.c.)–acetic anhydride (4 c.c.) was mechanically stirred and rapidly cooled to 0°. The resulting suspension was treated dropwise, during 30 minutes, with a cold mixture of nitric acid (98%; 5 c.c.) and acetic anhydride (4 c.c.). The mixture was kept at 0° for 3 hours longer. The crystalline product was collected, washed with a small quantity of aqueous ethanol, and then recrystallised from ethanol, giving yellow needles (3·7 g.), m. p. 147—148°, of 1 : 2 : 3 : 4-*tetrahydro*-1-*keto*-9-*nitrophenanthrene* (Found : C, 70·1; H, 4·6; N, 5·8. $C_{14}H_{11}O_3N$ requires C, 69·7; H, 4·6; N, 5·8%).

Catalytic Hydrogenation of 1 : 2 : 3 : 4-*Tetrahydro*-1-*keto*-9-*nitrophenanthrene*.—A suspension of the nitro-ketone (300 mg.) in absolute ethanol (25 c.c.) was hydrogenated in presence of 10% palladium–charcoal (150 mg.). Uptake ceased when 3 mols. of hydrogen had been absorbed. The product consisted of a mixture of a high-melting, neutral solid and a basic fraction which, on treatment with hot 2N-hydrochloric acid, yielded tan-coloured prisms, m. p. 229—231°, of 9-*amino*-1 : 2 : 3 : 4-*tetrahydro*-1-*keto-phenanthrene hydrochloride* (Found : C, 67·6; H, 5·7; N, 5·9. $C_{14}H_{13}ON,HCl$ requires C, 67·8; H, 5·7; N, 5·7%).

1 : 2 : 3 : 4-*Tetrahydro*-1-*keto*-9-*nitrophenanthrene Oxime*.—The ketone (3·1 g.) was heated under reflux on a water-bath with hydroxylamine hydrochloride (1·9 g.), ethanol (50 c.c.), and pyridine (20 c.c.) for 2·5 hours. The solvents were removed under reduced pressure. The residue was triturated with water, to give a solid (3·2 g.; m. p. 194—196°) which, on recrystallisation from ethanol, formed yellow rhombs, m. p. 202—203° (Found : N, 10·8. $C_{14}H_{12}O_3N_2$ requires N, 10·9%).

1-*Amino*-9-*nitrophenanthrene*.—A suspension of the foregoing oxime (2·25 g.) in acetic acid (34 c.c.)–acetic anhydride (4·5 c.c.) was heated on a water-bath and treated with a stream of anhydrous hydrogen chloride during 8 hours. The resulting solution was cooled and set aside at room temperature for 3 days. The crystalline material (1·9 g.) which separated was collected and extracted with boiling 2N-hydrochloric acid (1500 c.c.). The insoluble residue (0·5 g.) was extracted with boiling benzene (150 c.c.). The extract was cooled and then percolated through a short column of activated alumina. The column was washed with benzene. Evaporation of the benzene filtrates furnished a crystalline solid (0·2 g.) which, on recrystallisation from ethanol, formed pale buff-coloured needles, m. p. 208—210°, of a *substance* (Found : C, 63·1; H, 4·7; N, 5·6. $C_{13}H_{11}O_4N$ requires C, 63·6; H, 4·5; N, 5·7%). Basification, with concentrated ammonia solution, of the hydrochloric acid extract gave a precipitate (1 g.) which was collected, washed with water, and purified by chromatography from benzene solution on alumina. The adsorbed base was eluted by means of 0·2% methanol–benzene. It formed crimson needles (0·7 g.) (from ethanol), m. p. 171—173°, of 1-*amino*-9-*nitrophenanthrene* (Found : C, 70·2; H, 4·1; N, 11·9. $C_{14}H_{10}O_2N_2$ requires C, 70·6; H, 4·2; N, 11·8%).

Deamination of 1-*Amino*-9-*nitrophenanthrene*.—A solution of nitrosylsulphuric acid, prepared by

stirring, with methyl sulphate (50 g.). The mixture was heated to 80° for a further hour, cooled, diluted with water (700 c.c.), and then set aside for 12 hours. The sparingly soluble sodium salt which separated was filtered off. Acidification of the filtrate with concentrated hydrochloric acid gave a precipitate (29 g.) which was distilled at 206—215°/0·2 mm. The distillate was recrystallised from acetone to give crystals (20·5 g.), m. p. 129—132°, of γ-(6-methoxy-2-naphthyl)butyric acid. A further quantity (12·5 g.) of pure material, m. p. 134—136°, was obtained by acidification of the above-mentioned sodium salt.

1 : 2 : 3 : 4-*Tetrahydro*-4-*keto*-7-*methoxyphenanthrene* (cf. Miyasaka, *Chem. Abstr.*, 1940, **34**, 1012).—A solution of γ-(6-methoxy-2-naphthyl)buytric acid (10 g.) in anhydrous benzene (150 c.c.) was treated portionwise with phosphoric oxide (50 g.). The mixture was boiled under reflux on a water-bath for 3 hours. It was cooled and then decomposed with crushed ice (250 g.). Sodium chloride (30 g.) and ether (150 c.c.) were added. The organic layer was separated, washed with brine, filtered, and evaporated. The residual gum was dissolved in ether (100 c.c.). The crystalline solid which separated slowly, was filtered off and recrystallised from benzene, to give clusters of needles (0·8 g.), m. p. 130—132°, of γ-(6-*methoxy*-2-*naphthyl*)*butyric anhydride* (Found: C, 76·4; H, 6·5; OMe, 13·2. $C_{30}H_{30}O_5$ requires C, 76·6; H, 6·4; OMe, 13·2%). The residue obtained by evaporation of the filtrate distilled as a pale-yellow oil, b. p. 172—175°/0·3 mm., which crystallised on cooling to give prisms (6·0 g.), m. p. 52°, of 1 : 2 : 3 : 4-tetrahydro-4-keto-7-methoxyphenanthrene (Found: C, 79·3; H, 6·2. Calc. for $C_{15}H_{14}O_2$: C, 79·6; H, 6·2%). This was also obtained (yield, 81%) by anhydrous hydrogen fluoride treatment of γ-(6-methoxy-2-naphthyl)buytric acid. With hydroxylamine hydrochloride in boiling pyridine it gave an *oxime* which separated from ethanol in rhombs, m. p. 174° (Found: N, 5·8. $C_{15}H_{15}O_2N$ requires N, 5·8%).

1 : 2 : 3 : 4-*Tetrahydro*-7-*hydroxy*-4-*ketophenanthrene*.—A solution of the foregoing methoxy-ketone (15·5 g.) in anhydrous benzene (160 c.c.) was boiled under reflux with powdered, anhydrous aluminium chloride (24 g.) for 4 hours. The mixture was cooled and then poured into a mixture of crushed ice and hydrochloric acid. The precipitate was filtered off, washed with dilute hydrochloric acid and water, and then dissolved in 2N-sodium hydroxide. The solution was clarified by extraction with a small quantity of ether and then acidified with concentrated hydrochloric acid. The precipitated hydroxy-ketone (13·6 g.; m. p. 182—186°) was sufficiently pure for the next stage. A sample crystallised from methanol in elongated prisms, m. p. 186—187° (Found: C, 79·4; H, 5·7. Calc. for $C_{14}H_{12}O_2$: C, 79·2; H, 5·7%) (Miyasaka, *loc. cit.*, is quoted to give m. p. 117°). The hydroxy-ketone was also obtained directly by cyclisation of γ-(6-hydroxy-2-naphthyl)butyric acid with anhydrous hydrogen fluoride.

7-*Amino*-1 : 2 : 3 : 4-*tetrahydro*-4-*ketophenanthrene* (cf. Miyasaka, *loc. cit.*, p. 7288).—A mixture of the aforesaid hydroxy-ketone (2 g.), dioxan (4 c.c.), and saturated sodium hydrogen sulphite solution (6 c.c.) was treated dropwise with concentrated ammonia solution (*d* 0·88; 8 c.c.) and then heated for 19 hours at 180—190° in a sealed tube. The contents of four such tubes were poured into water. The precipitate was filtered off, washed with water, and dissolved in chloroform (200 c.c.). The solution was extracted twice with 2N-sodium hydroxide. Acidification of the extracts gave 1·3 g. of somewhat tarry starting material. The chloroform solution was washed with water and then evaporated. The residue was extracted with boiling N-hydrochloric acid (1500 c.c.). Basification of the extract with concentrated ammonia solution gave a yellow precipitate (3·7 g.) of practically pure amino-ketone, m. p. 153—155°.

7-*Carbethoxyamino*-1 : 2 : 3 : 4-*tetrahydro*-4-*ketophenanthrene*.—A solution of 7-amino-1 : 2 : 3 : 4-tetrahydro-4-ketophenanthrene (3·94 g.) in a mixture of ethanol (80 c.c.) and diethylaniline (3·3 c.c.) was treated dropwise with ethyl chloroformate (1·96 c.c.), boiled under reflux for 30 minutes, and then concentrated on a water-bath to small bulk. The practically pure product (4·56 g.) crystallised on cooling. A further quantity (0·3 g.) was obtained by evaporation of the filtrate and treatment of the residue with dilute hydrochloric acid, followed by recrystallisation of the residue from ethanol. The *carbethoxy-amino-ketone* formed clusters of stout needles (from ethanol), m. p. 182—183° (Found: C, 72·3; H, 6·1; N, 4·9. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·1; N, 5·0%). With hydroxylamine hydrochloride in boiling pyridine it yielded an *oxime* which formed colourless rhombs (from ethanol), m. p. 167° (Found: N, 9·5. $C_{17}H_{18}O_3N_2$ requires N, 9·4%).

5-*Amino*-2-*carbethoxyaminophenanthrene*.—A solution of 7-carbethoxyamino-1 : 2 : 3 : 4-tetrahydro-4-ketophenanthrene oxime (6·16 g.) in hot glacial acetic acid (37 c.c.) was treated with acetic anhydride (6 c.c.). It was then heated in an oil-bath at 95—100° and treated with a slow stream of anhydrous hydrogen chloride, passed over the surface of the liquid, during 6 hours. The dark mixture was set aside for 3 days and then filtered. The residue was extracted with boiling 0·5N-hydrochloric acid (1200 c.c.). The residue (1·23 g.; m. p. 153—156°), on repeated recrystallisation (charcoal) from ethanol, formed clumps of white needles, m. p. 166°, of a *substance* which has not been identified (Found: C, 70·6; H, 6·0; N, 8·4. $C_{19}H_{18}O_3N_2$ requires C, 70·8; H, 5·6; N, 8·7%). The hydrochloric acid extract, on basification with concentrated ammonia solution, gave a precipitate which was purified by means of chromatography of a benzene solution on alumina followed by elution of the adsorbed base with 0·1% methanol–benzene. The purified *amine* (1·09 g., 19%) formed tan-coloured prisms (from ethanol), m. p. 164° (Found: N, 9·6. $C_{17}H_{16}O_2N_2$ requires N, 9·9%). Addition of acetic anhydride (0·1 c.c.) to a solution of the amine (50 mg.) in boiling ethanol (2 c.c.) yielded the *acetyl* derivative which formed minute, colourless rhombs (from ethanol), m. p. 241° with previous shrinking (Found: C, 70·6; H, 5·8; N, 9·0. $C_{19}H_{18}O_3N_2$ requires C, 70·8; H, 5·6; N, 8·7%).

5-*Amino*-2-*methoxyphenanthrene*.—Treatment of 1 : 2 : 3 : 4-tetrahydro-4-keto-7-methoxyphenanthrene oxime (3·7 g.) in acetic acid (19 c.c.)–acetic anhydride (3·7 c.c.) with anhydrous hydrogen chloride at 95—100° for 6 hours, followed by isolation as described above for 5-amino-2-carbethoxyaminophenanthrene, furnished 5-*amino*-2-*methoxyphenanthrene* which formed red rhombs (yield, 13%) (from ethanol), m. p. 106° (Found: C, 80·3; H, 6·0; N, 6·1. $C_{15}H_{13}ON$ requires C, 80·7; H, 5·8; N, 6·3%).

Derivatives of 4-Benzamidophenanthrene.—These were prepared by portionwise addition of a slight excess of the substituted benzoyl chloride to a solution, cooled at 0°, of the appropriate 4-aminophenanthrene in anhydrous pyridine. After being set aside at room temperature for 24 hours, the pyridine solutions were poured into water and the precipitated amides purified by recrystallisation. 4-p-*Nitrobenzamidophenanthrene* formed pale-yellow needles (from ethanol), m. p. 234° (Found : C, 73·9; H, 4·5; N, 7·9. $C_{21}H_{14}O_3N_2$ requires C, 73·7; H, 4·1; N, 8·2%), 4-p-*carbethoxyaminobenzamidophenanthrene*, needles (from ethanol), m. p. 222° (Found : N, 7·5. $C_{24}H_{20}O_3N_2$ requires N, 7·3%), 2-*methoxy*-5-p-*nitrobenzamidophenanthrene*, pale yellow needles (from acetic acid), m. p. 231—232° (Found : C, 70·8; H, 4·4; N, 7·2. $C_{22}H_{16}O_4N_2$ requires C, 70·9; H, 4·3; N, 7·5%), 2-*carbethoxyamino*-5-p-*nitrobenzamidophenanthrene*, pale-yellow needles (from acetic acid), m. p. 247° (Found : C, 66·7; H, 4·6; N, 9·8. $C_{24}H_{19}O_5N_3$ requires C, 67·1; H, 4·5; N, 9·8%), and 2-*carbethoxyamino*-5-p-*carbethoxyaminobenzamidophenanthrene*, minute rhombs (from acetic acid), m. p. 222° (Found : C, 68·5; H, 5·4; N, 9·0. $C_{27}H_{25}O_5N_3$ requires C, 68·8; H, 5·3; N, 8·9%).

Cyclisation Experiments.

2-*Phenyl*-1-*azapyrene Methobromide.*—Treatment of 4-benzamidophenanthrene with phosphoric oxide in boiling xylene (Cook and Thomson, *loc. cit.*) smoothly afforded 2-phenyl-1-azapyrene in 70% yield. A solution of the base (0·36 g.) in anhydrous nitrobenzene (1·5 c.c.) was heated to 150—160° and then treated with methyl sulphate (0·24 c.c.). The mixture was heated at 150—160° for 5 minutes, cooled, and then diluted with anhydrous ether. The crystalline product was collected and dissolved in warm water (5 c.c.). The solution was filtered and then treated with saturated potassium bromide solution. The precipitate, on recrystallisation from water, formed clusters of yellow needles (0·38 g.), m. p. 227° (decomp.), of 2-*phenyl*-1-*azapyrene methobromide dihydrate* (Found : C, 64·6; H, 5·2; N, 3·6. $C_{22}H_{16}NBr,2H_2O$ requires C, 64·4; H, 4·9; N, 3·4%). 4-Carbethoxyaminobenzamido-, 4-*p*-nitrobenzamido-, and 2-methoxy-5-*p*-nitrobenzamido-phenanthrene were largely unaffected by similar treatment with phosphoric oxide in boiling xylene. In the case of the last named, a very low yield of 4-*methoxy*-2-p-*nitrophenyl*-1-*azapyrene* (II; R = OMe; R′ = NO_2), minute, yellow crystals (from acetic acid), m. p. 259—260° (Found : N, 7·9. $C_{22}H_{14}O_3N_2$ requires N, 7·9%), was isolated. The carbethoxyamino-compound was also largely unchanged on treatment with phosphoric oxide in syrupy phosphoric acid according to Bailey and Robinson's method (*J.*, 1950, 1375). Attempts to cyclise derivatives of 4-benzamidophenanthrene with phosphoryl chloride alone also met with little success.

Action of Phosphoryl Chloride on 2-Methoxy-5-p-*nitrobenzamidophenanthrene.*—The amide (100 mg.) was heated under reflux on a water-bath with phosphoryl chloride (1 c.c.) for 2 hours. The resulting solution was evaporated at 40° under reduced pressure. The residue was treated with ice and dilute ammonia solution. The resulting orange, heterogeneous solid (100 mg.) was dissolved in warm acetone. Addition of an acetone solution of picric acid gave a precipitate (20 mg.), which, on repeated recrystallisation from acetone, formed minute, orange prisms, m. p. 243—246° (decomp.), of 4-*methoxy*-2-p-*nitrophenyl*-1-*azapyrene picrate* (Found : C, 57·4; H, 3·3; N, 11·6. $C_{22}H_{14}O_3N_2,C_6H_3O_7N_3$ requires C, 57·6; H, 3·0; N, 12·0%).

Action of Phosphoryl Chloride on 4-Carbethoxyaminobenzamidophenanthrene.—(i) A solution of the amide (200 mg.), in phosphoryl chloride (2 c.c.), was boiled under reflux on an oil-bath for 60 minutes. It was then evaporated at 40° under reduced pressure. The residual yellow syrup, on trituration with ice-water, yielded an orange, sticky solid which on treatment with ice-cold, N-ammonia largely dissolved. The solution was filtered and then cautiously acidified with dilute hydrochloric acid. The precipitate (120 mg.; m. p. 125—140°) was extracted with warm ethanol. The extract was concentrated under reduced pressure and then diluted with water. The yellow precipitate (40 mg.), on repeated recrystallisation from methanol, formed sheaves of pale yellow prisms, m. p. 96—98° (decomp.), of an unidentified *substance* whose analytical data approached those of 2-*p*-carboxyaminophenyl-1-azapyrene (Found : C, 77·5; H, 4·4; N, 8·0. $C_{22}H_{14}O_2N_2$ requires C, 78·0; H, 4·2; N, 8·3%).

(ii) The amide (630 mg.) was boiled under reflux (oil-bath) with phosphoryl chloride (3·1 c.c.) for 6 hours. Excess of phosphoryl chloride was removed at 40° under reduced pressure and the residue treated with crushed ice. The mixture was filtered. Basification of the aqueous filtrate with dilute aqueous ammonia gave a yellow precipitate (0·28 g.; m. p. 120—130°), which was extracted with boiling ethanol. Concentration of the extract, followed by treatment of it with ethanolic picric acid, yielded a precipitate (0·4 g.) which, on repeated recrystallisation from ethanol, formed microscopic, orange prisms, m. p. 216—219° (decomp.), of 2-p-*aminophenyl*-1-*azapyrene picrate* (Found : C, 61·7; H, 3·3; N, 13·0. $C_{21}H_{14}N_2,C_6H_3O_7N_3$ requires C, 62·0; H, 3·3; N, 13·4%). The picrate was decomposed by treatment with dilute ammonia solution and the base extracted into chloroform. The extract was evaporated and the residual gum purified by adsorption on a column of alumina from benzene solution. The pale yellow band formed was eluted by 0·2% methanol–benzene and, on repeated recrystallisation from methanol, then yielded minute, yellow rhombs, m. p. 124—125°, of 2-p-*aminophenyl*-1-*azapyrene monohydrate* (II; R = H; R′ = NH_2) (Found : C; 81·3; H, 4·9; N, 9·2. $C_{21}H_{14}N_2,H_2O$ requires C, 80·7; H, 5·2; N, 9·0%). No uniform material could be isolated from the hydrochloric acid-insoluble products of the reaction.

2-p-*Nitrophenyl*-1-*azapyrene* (II; R = H; R′ = NO_2).—4-*p*-Nitrobenzamidophenanthrene (0·7 g.) was heated under reflux with phosphoryl chloride (2 c.c.) and anhydrous nitrobenzene (5 c.c.) in an oil-bath at 155—160° for 2 hours. The mixture was cooled, decomposed with crushed ice, and then distilled in steam. The residual solid was collected and recrystallised from ethanol (charcoal), followed by acetic acid, to give the *azapyrene* as yellow needles (0·4 g.), m. p. 241° (Found : N, 8·4. $C_{21}H_{12}O_2N_2$ requires N, 8·6%).

2-p-*Aminophenyl*-1-*azapyrene Methotoluene*-p-*sulphonate.*—A solution of the foregoing nitro-azapyrene (0·35 g.) in anhydrous nitrobenzene was heated to 180° and then treated portionwise with methyl toluene-*p*-

sulphonate (0·4 g.). The mixture was heated at 200° for 15 minutes. The crystalline material which separated on cooling was filtered off, washed with ether, and recrystallised from water to give long, yellow needles (0·32 g.), m. p. 245—250°. These were heated under reflux on a water-bath with " reduced " iron powder (0·35 g.), 0·1N-hydrochloric acid (1 c.c.), and ethanol (10 c.c.) for 1·5 hours. The mixture was treated with 0·1N-sodium hydroxide (0·8 c.c.) and ethanol (15 c.c.), and filtered while hot. Concentration of the filtrate gave the amino-quaternary *salt* in crimson plates (0·2 g.), m. p. 268—270° (decomp.) (Found : C, 72·8; H, 5·0; N, 6·0. $C_{29}H_{24}O_3N_2S$ requires C, 72·5; H, 5·0; N, 5·8%).

4-*Carbethoxyamino*-2-p-*nitrophenyl*-1-*azapyrene Methosulphate*.—2-Carbethoxyamino-5-*p*-nitrobenzamidophenanthrene (1·32 g.) was heated under reflux with anhydrous nitrobenzene (12 c.c.) at 135—140° (bath-temp.) and treated dropwise with phosphoryl chloride (2·6 c.c.). The mixture was heated at 135—140° for 1 hour, cooled, poured into water, basified with concentrated ammonia solution, and then distilled in steam. The residual solid was best purified at the next stage. It was heated with anhydrous nitrobenzene (6 c.c.) at 155—165° and treated with methyl sulphate (0·6 c.c.). The mixture was heated at 160—165° for 8 minutes, cooled, poured into water, and then distilled in steam. The residue was concentrated to approx. 80 c.c and then filtered while hot. The *methosulphate sesquihydrate* separated from the filtrate in minute, yellow prisms (0·58 g.), m. p. 230—232° (decomp.) (Found : C, 55·3; H, 4·8; N, 7·3. $C_{26}H_{23}O_8N_3S,1\frac{1}{2}H_2O$ requires C, 55·3; H, 4·6; N, 7·4%).

2-p-*Aminophenyl*-4-*carbethoxyamino*-1-*azapyrene Methosulphate*.—The foregoing nitro-quaternary salt (280 mg.) was added, in portions, to a mixture of " reduced " iron powder (300 mg.), 0·05N-sulphuric acid (2 c.c.), and ethanol (6 c.c.), heated under reflux on a water-bath. The mixture was boiled under reflux for 2 hours, treated with 0·1N-sodium hydroxide (0·9 c.c.), then filtered while hot. The residue was extracted with several portions of boiling ethanol. The combined filtrates were concentrated to approx. 5 c.c. and set aside for several hours. The red solution was decanted from dark red gum and evaporated. The residue, on being rubbed with a small quantity of methanol, yielded a solid which, on repeated recrystallisation from methanol, formed long, scarlet needles (80 mg.), m. p. 225° (decomp.), of the amino-quaternary salt *monohydrate* (Found : C, 59·3; H, 5·4; N, 7·6. $C_{26}H_{25}O_6N_3S,H_2O$ requires C, 59·4; H, 5·2; N, 8·0%).

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