848. *Carcinogenic Nitrogen Compounds. Part XLVI.*[1] *The Nitration of 2- and 3-Acetamidophenanthrene*

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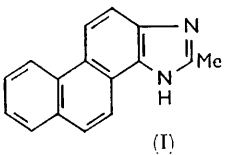
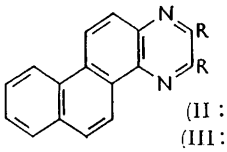
Among the simpler derivatives of phenanthrene, 2- and 3-acetamidophenanthrene are readily accessible; and as they possess versatile carcinogenic activity in rats, eliciting both solid tumours and leukæmias,[2] their chemistry has now been investigated, with a view to their use as starting materials for the preparation of potentially carcinogenic nitrogen-containing molecules.

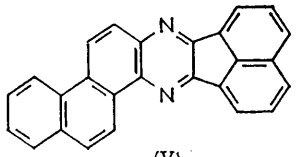
[1] Part XLV, N. P. Buu-Hoï, V. Bellavita, A. Ricci, J. P. Hoeffinger, and D. Balucani, *J.*, 1965, 2646.

[2] E. C. Miller, R. B. Sandin, J. A. Miller, and H. P. Rusch, *Cancer Res.*, 1955, **15**, 188.

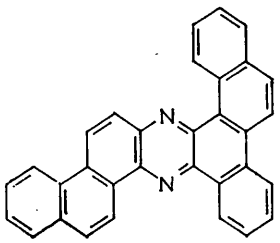
2-Acetamidophenanthrene readily underwent nitration in acetic acid to give 2-acetamido-1-nitrophenanthrene; proof for the structure of the latter was afforded by reduction of its deacetylation product to 1,2-diaminophenanthrene, which had previously been

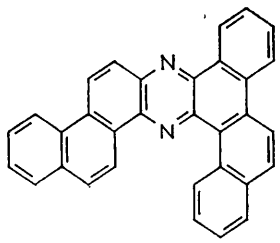

(I)


(II : R = Me)
(III : R = Ph)
(IV : R = MeO·C_6H_4)


(V)

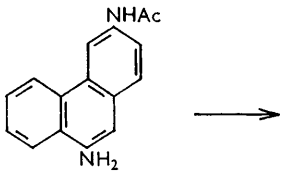
prepared by an unequivocal route.[3] As an *ortho*-diamine, 1,2-diaminophenanthrene gave the imidazole (I) on heating with acetic anhydride, and condensed readily with α-diketones to give condensed quinoxalines or phenazines. 2,3-Dimethyl- (II), 2,3-diphenyl- (III), and 2,3-di-(4-methoxyphenyl)-naphtho[2,1-*f*]quinoxaline (IV) were thus obtained, with dimethylglyoxal, benzil, and anisil, respectively; in view of the carcinogenic activity of simpler compounds of their type,[4] acenaphtho[1,2-*b*]naphtho[2,1-*f*]quinoxaline (V) and benzo[*c*]dinaphtho[1,2-*a*][2,1-*h*]phenazine (VI) were prepared from acenaphthenequinone

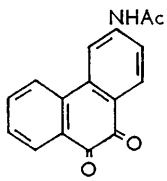

(VI)

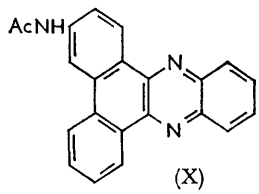

(VII)

and chrysenequinone. In the reaction of 1,2-diaminophenanthrene with the last-named quinone, only one condensation product was obtained, to which we assigned formula (VI), rather than (VII), which represents an overcrowded *cis*-bisangular structure (in the similar case of the condensation of 1,2-diaminonaphthalene with 1,2-naphthoquinone, it is known that the *cis*-bisangular dibenzo[*a*,*j*]phenazine is obtained only as a secondary reaction product [5]).

Mononitration of 3-acetamidophenanthrene, which is more sensitive to this reaction


(VIII)


(IX)


(X)

than the 2-isomer, involved substitution in ring B, as the reaction product was reduced to an amino-3-acetamidophenanthrene which, on sodium dichromate oxidation, afforded

[3] S. V. Bogdanov and L. S. Shibryaeva, *Zhur. Vesesoyuz. Khim. obshch. im. D.I. Mendeleeva*, 1960, **5**, 345.
[4] G. Rudali, H. Chalvet, and F. Winternitz, *Compt. rend.*, 1955, **240**, 1738.
[5] O. N. Witt, *Ber.*, 1886, **19**, 2791; O. Fischer and H. Strauss, *ibid.*, 1908, **41**, 397; cf. G. A. Swan and D. G. I. Felton, " Phenazines," Interscience, New York, 1957, p. 460.

3-acetamido-9,10-phenanthraquinone (IX); in view of the known activation of position 6 in 2-substituted naphthalenes,[6] the most probable structure for the reduction product is (VIII). More energetic nitration conditions led to a 3-acetamidodinitrophenanthrene. Condensation of the quinone (IX) with *o*-phenylenediamine afforded 3-acetamidodibenzo-[*a*,*c*]phenazine (X); methyl- and chloro-substitution-products of (X) were similarly prepared with the appropriate *o*-diamines.

Experimental.—Melting points were taken on a Maquenne block. 2- and 3-Acetylphenanthrene were prepared by acetylation of phenanthrene and fractional crystallisation of the ketone mixture, according to Mosettig and Van de Kamp;[7] Beckmann rearrangement of the oximes was effected with phosphorus pentachloride in ether.

2-Amino-1-nitrophenanthrene. To a supersaturated solution of 2-acetamidophenanthrene (19 g.) in acetic acid (420 c.c.), fuming nitric acid (*d* 1·49) (18 c.c., dissolved in 20 c.c. acetic acid) was added dropwise at 43—45°, with stirring; after a further 30 minutes' stirring, the yellow precipitate which formed was collected, washed with water, then with methanol, and recrystallised first from acetic acid, then from benzene, to give *2-acetamido-1-nitrophenanthrene*, golden-yellow prisms (15·5 g.), m. p. 195° (Found: C, 68·4; H, 4·5; N, 10·0. $C_{16}H_{12}N_2O_3$ requires C, 68·5; H, 4·3; N, 10·0%). Deacetylation, effected by refluxing the acetyl compound (3 g.) for 2 hr. with hydrochloric acid (20 c.c.) in ethanol (50 c.c.), and basification with aqueous sodium hydroxide, afforded *2-amino-1-nitrophenanthrene*, crystallising as copper-red leaflets (1·7 g.), m. p. 209°, from benzene (Found: C, 70·7; H, 4·4; N, 11·5. $C_{14}H_{10}N_2O_2$ requires C, 70·6; H, 4·2; N, 11·7%).

2-Acetamido-1-aminophenanthrene. This was prepared from 2-acetamido-1-nitrophenanthrene (6 g., in 210 c.c. ethanol) by 3 hours' refluxing with 95% hydrazine hydrate (40 g.) and Raney nickel (1 g.), and gave colourless needles (3·8 g.), m. p. 250° (decomp. >237°), from ethanol (Found: C, 76·8; H, 5·8; N, 11·3. $C_{16}H_{14}N_2O$ requires C, 76·8; H, 5·6; N, 11·2%).

1,2-Diaminophenanthrene. This was best prepared by reduction of 2-amino-1-nitrophenanthrene (1·3 g.) with hydrazine hydrate (10 c.c.) and Raney nickel (0·5 g.) in ethanol (110 c.c.), and formed shiny, colourless leaflets (0·8 g.), m. p. 185°, from ethanol (Found: C, 80·5; H, 6·0; N, 13·5. Calc. for $C_{14}H_{12}N_2$: C, 80·8; H, 5·8; N, 13·5%). This compound was identical with a sample of 1,2-diaminophenanthrene prepared from 1-nitroso-2-hydroxyphenanthrene (the structure of which was established by oxidation to the corresponding phenanthrofuroxan) by Bogdanov and Shibryaeva.[3] The identity was confirmed by conversion (*a*) into phenanthro-[1,2-*c*][1,2,5]selenadiazole, m. p. 190° (from isopentanol; brownish-red halochromy in sulphuric acid) (lit.,[3] m. p. 189·8—190°); and (*b*) into dibenzo[*a*,*c*]naphtho[2,1-*h*]phenazine (with phenanthraquinone), m. p. 300° (from benzene; deep blue halochromy in sulphuric acid) (lit.,[3] m. p. 299·5—300°). New azopolycycles prepared from 1,2-diaminophenanthrene included: *2-methylphenanthro*[1,2-d]*imidazole* (I), colourless prisms, m. p. 276°, from ethanol (Found: C, 82·7; H, 5·4; N, 12·1. $C_{16}H_{12}N_2$ requires C, 82·7; H, 5·2; N, 12·0%), *picrate*, greenish-yellow prisms, m. p. 307° (decomp. >286°), from nitrobenzene (Found: N, 15·3. $C_{22}H_{15}N_5O_7$ requires N, 15·2%); *2,3-dimethylnaphtho*[2,1-f]*quinoxaline* (II), colourless needles (0·2 g.), m. p. 194°, from ethanol, b. p. 230—235°/0·5 mm. (Found: C, 83·6; H, 5·6; N, 10·8. $C_{18}H_{14}N_2$ requires C, 83·7; H, 5·5; N, 10·8%), *picrate*, lemon-yellow prisms, m. p. 232° (decomp. >196°), from benzene (Found: N, 14·7. $C_{24}H_{17}N_5O_7$ requires N, 14·4%); *2,3-diphenylnaphtho*[2,1-f]*quinoxaline* (III), pale yellow needles, m. p. 245°, from isopentanol (violet halochromy in sulphuric acid) (Found: C, 87·7; H, 4·7; N, 7·3. $C_{28}H_{18}N_2$ requires C, 87·9; H, 4·8; N, 7·3%); *2,3-di-(4-methoxyphenyl)naphtho*[2,1-f]*quinoxaline* (IV), pale yellow needles, m. p. 251°, from acetic acid (deep blue halochromy in sulphuric aid) (Found: C, 81·4; H, 5·0; N, 6·6. $C_{30}H_{22}N_2O_2$ requires C, 81·4; H, 5·0; N, 6·3%), *picrate*, orange-yellow prisms, m. p. 226° (decomp.), from xylene (Found: N, 10·5. $C_{36}H_{25}N_5O_9$ requires N, 10·4%); *acenaphtho*[1,2-b]*naphtho*[2,1-f]-*quinoxaline* (V), orange-yellow needles, m. p. 309°, from xylene (deep red halochromy in sulphuric acid) (Found: C, 88·0; H, 4·0; N, 7·7. $C_{26}H_{14}N_2$ requires C, 88·1; H, 4·0; N, 7·9%); *benzo*[c]*dinaphtho*[1,2-a][2,1-h]*phenazine* (VI), lemon-yellow prisms, m. p. 292°, from toluene (ultramarine halochromy in sulphuric acid) (Found: C, 89·0; H, 4·5. $C_{32}H_{18}N_2$ requires C, 89·3; H, 4·2%); no isomer could be isolated from the mother-liquors.

[6] Cf. N. P. Buu-Hoï and R. Daudel, *Rec. Trav. chim.*, 1946, **65**, 731.
[7] E. Mosettig and J. Van de Kamp, *J. Amer. Chem. Soc.*, 1930, **52**, 3704; 1933, **55**, 3442.

3-Acetamido-9(or 10)-nitrophenanthrene. A solution of 3-acetamidophenanthrene (18 g.) in acetic acid (90 c.c.) was treated dropwise at 12—15° with fuming nitric acid (12 c.c.) dissolved in acetic acid (60 c.c.). The precipitate which formed after 30 min. at room temperature was washed with water, then with methanol, and recrystallised from acetic acid, giving yellow prisms (11·5 g.), m. p. 250° (Found: C, 68·5; H, 4·4; N, 9·9%). When more nitrating agent or a higher temperature was used, the mononitro-product was accompanied by 30—35% of a 3-acetamido-9(or 10),x-dinitrophenanthrene, which crystallised as golden-yellow needles, m. p. 263° (from acetic acid) (Found: C, 58·9; H, 3·3; N, 12·9. Calc. for $C_{16}H_{11}N_3O_5$: C, 59·1; H, 3·4; N, 12·9%).

3-Acetamido-9(or 10)-aminophenanthrene (VIII or isomer). 3-Acetamido-9(or 10)-nitrophenanthrene (8 g.) in ethanol (250 c.c.) was treated with hydrazine hydrate (53 c.c.) and Raney nickel (1 g.) as above; the reduction product formed colourless needles (5·8 g.), m. p. 204°, from ethanol (Found: C, 76·6; H, 5·8; N, 11·1%). 3,9(or 10)-Diacetaminophenanthrene, prepared with acetic anhydride in acetic acid at 100°, formed prisms, m. p. 319°, from acetic acid (Found: C, 74·1; H, 5·4; N, 9·7. Calc. for $C_{18}H_{16}N_2O_2$: C, 74·0; H, 5·5; N, 9·6%). 3,9(or 10)-Diaminophenanthrene, obtained by deacetylation of compound (VIII) with hydrochloric acid in boiling ethanol and basification of the dihydrochloride obtained, formed colourless prisms darkening rapidly in the air, m. p. 153°, from cyclohexane (Found: C, 80·8; H, 5·9%).

3-Acetamido-9,10-phenanthraquinone (IX). A mixture of 3,9(or 10)-diacetamidophenanthrene (0·5 g.), sodium dichromate (3 g.), and acetic acid (15 c.c.) was refluxed for 30 min. and left overnight at room temperature; the precipitate formed was washed with water and recrystallised from acetic acid, then nitrobenzene, giving the *quinone* as orange needles (0·25 g.), m. p. 311° (Found: C, 72·2; H, 4·2; N, 5·1. $C_{16}H_{11}NO_2$ requires C, 72·5; H, 4·2; N, 5·3%). Condensation with *o*-phenylenediamine gave *3-acetaminodibenzo*[a,c]*phenazine* (X), lemon-yellow needles, m. p. 346°, from isopentanol (brick-red halochromy in sulphuric acid) (Found: C, 77·9; H, 4·6; N, 12·6. $C_{22}H_{15}N_3O$ requires C, 78·3; H, 4·5; N, 12·5%); 3-acetamido-11(or 12)-methyldibenzo[*a,c*]phenazine, pale yellow needles, m. p. 337°, from acetic acid (blood-red halochromy in sulphuric acid) (Found: C, 78·5; H, 5·0. Calc. for $C_{23}H_{17}N_3O$: C, 78·6; 4·9%); 3-acetamido-11(or 12)-chlorodibenzo[*a,c*]phenazine, yellow prisms, m. p. 331°, from *o*-dichlorobenzene (deep red halochromy in sulphuric acid) (Found: C, 70·7; H, 4·0. Calc. for $C_{22}H_{14}ClN_3O$: C, 71·1; H, 3·8%).

Results of biological tests will be reported elsewhere.

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