1140. *Quasi-steroidal Heterocycles. Part III.*[1] *5-Azachrysenes and Related Compounds.*

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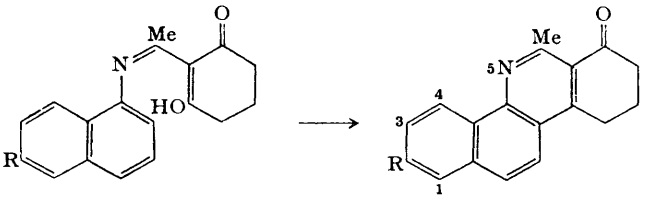
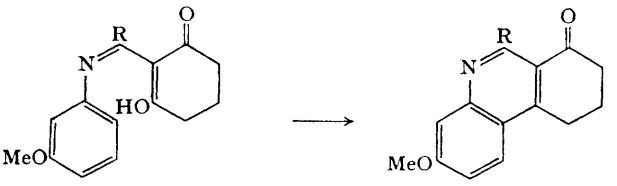
The synthesis of a derivative of 5-azachrysene, with oxygen functions at positions corresponding to 3 and 17 in the steroid nucleus, together with the synthesis of two analogous phenanthridines, is reported. The reduction of both types is also described.

The 7,8,9,10-tetrahydro-5-azachrysene ring system (as in II) has been synthesised by, *inter alia*, Rogers and Smith,[2] who effected ring-closure of the intermediate Schiff's base (I; R = H) with polyphosphoric acid at 170° to give the derivative (II; R = H). We have used this method to prepare the 2-methoxy-compound (II; R = OMe); the presence of the activating methoxy-group causes a decrease of 50° in the optimum temperature for cyclisation of the Schiff's base (I). The 7,8,9,10-tetrahydrophenanthridine (IV; R = Me) was obtained in a similar way. Sodium borohydride reduction of the ketones (II; R = OMe) and (IV; R = Me) gave the corresponding alcohols.



(I) (II)



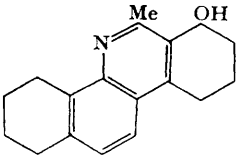
(III) (IV)

The preparation of the tetrahydrophenanthridine (IV; R = H) from the anil (III; R = H) has recently been described in a preliminary account[3] as an intermediate in the synthesis of "6-aza-equilenin." Compounds of this type, with no 6-methyl group (IV; R = H) or activating 3-methoxy-group, could not be obtained from the corresponding anils (as III; R = H) by cyclisation.[2] In our hands the cyclisation of the anil (III; R = H), itself prepared from *NN'*-bis-(*m*-methoxyphenyl)formamidine and cyclohexane-1,3-dione, proceeded smoothly at 135° to give 74% of a product containing 7,8,9,10-tetrahydro-3-methoxy-7-oxophenanthridine (IV; R = H) together with a smaller amount of an isomer, presumably the 1-methoxy-compound. The more abundant isomer was readily obtained pure by crystallisation; its formulation as the 3-methoxy-compound (IV; R = H) was supported by the C–H out-of-plane bending region of its infrared spectrum, which had strong bands at 850 and 822 cm.$^{-1}$, with weaker bands at 788 and 770 cm.$^{-1}$, suggesting a 1,2,4-trisubstituted benzene ring.[4] Weak bands at 760 and 720 cm.$^{-1}$, present in the spectrum of the mixture of isomers, were absent in the pure 3-methoxyphenanthridine (IV; R = H). The minor isomer could

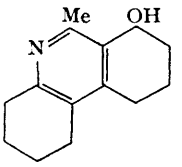
[1] Part II, Emrys R. H. Jones, preceding Paper.
[2] N. A. J. Rogers and H. Smith, *J.*, 1955, 341.
[3] J. H. Burckhalter and H. Watanabe, Abstracts 143rd Amer. Chem. Soc. Meeting, 1963, p. 14A; *Chem. Eng. News*, 1963, **41**, 40.
[4] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, p. 78.

not be isolated by fractional crystallisation. The formation of two isomers in the cyclisation of the anil (III; R = H) is in contrast to the formation of a single product in the cyclisation of the anil (III; R = Me) and similar compounds. That the product from the latter is the expected 3-methoxy-isomer was supported by its infrared spectrum.

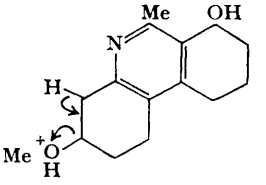
The reduction of the 5-azachrysene and phenanthridine types described above was of interest, and one example of each type was studied. 7,8,9,10-Tetrahydro-6-methyl-7-oxo-5-azachrysene[2] (II; R = H) was reduced by hydrogen and platinum in acetic acid at room temperature to the octahydro-derivative (V). The structure of this compound was established (*a*) by its ultraviolet spectrum, which was closely similar to that of the alcohol derived from the tetrahydrophenanthridine (IV; R = Me), and which had its strongest peak at 240 mμ (ε 42,400), indicating two fused aromatic rings, and (*b*) by its n.m.r. spectrum, which showed a methyl singlet (6·75 τ) and two aromatic protons. Reduction of the benzene ring in quinolines heavily substituted in the heterocyclic ring has been recorded;[5] in the present case the least substituted of the two benzene rings was the preferred site of reduction.



(V)



(VI)



(VII)

Reduction of the tetrahydrophenanthridine (IV; R = Me) under the same conditions also occurred in the benzene ring, as shown by the n.m.r. spectrum of the product, which contained a methyl singlet (7·37 τ), no aromatic protons, no methoxyl protons, and a signal at 5·05 τ (C*H*OH) corresponding to only one proton. The product was, surprisingly, the octahydrophenanthridine (VI), from which the 3-methoxy-group had been eliminated from the presumed intermediate (VII), possibly by the mechanism shown or by a similar one involving proton release from the activated 4-position next to the pyridine ring. The olefin thus produced would be reduced to the fully saturated compound (VI) under the conditions used.

Experimental

Ultraviolet spectra were determined in 0·001% methanolic solution using a Perkin-Elmer 137 spectrometer, infrared spectra in Nujol using a Perkin-Elmer Infracord 137, and n.m.r. spectra at 60 Mc./sec. in a Varian A60 spectrometer using tetramethylsilane as internal standard (τ = 10·00). Solvent extracts were dried over magnesium sulphate.

7,8,9,10-*Tetrahydro-2-methoxy-6-methyl-7-oxo-5-azachrysene* (II; R = OMe).—6-Methoxy-1-naphthylamine (7·2 g.), 2-acetylcyclohexane-1,3-dione (6·5 g.), and ethanol (40 ml.) were boiled together under reflux for 6 hr., and poured into water. The oily product solidified and was crystallised from ethyl acetate–light petroleum (b. p. 60—80°), to give 2-[1-(6-*methoxy*-1-*naphthylimino*)-*ethyl*]*cyclohexane*-1,3-*dione*, m. p. 70—80° (8·0 g., 62%) (Found: C, 73·7; H, 6·3; N, 4·6. $C_{19}H_{19}NO_3$ requires C, 73·8; H, 6·2; N, 4·5%). This Schiff's base (500 mg.) was stirred into polyphosphoric acid (B.D.H., about 80% P_2O_5; 10 ml.) at 110°. The internal temperature was raised to 120° and maintained at 120—125° for 30 min.; the mixture was then poured into ice and aqueous sodium hydroxide. Extraction with ethyl acetate and evaporation of the dried extract gave a residue which was crystallised from light petroleum (b. p. 100—120°), to give 350 mg. (75%) of product, m. p. 159—160°. Further crystallisation from petroleum or benzene gave the pure *product* (II; R = OMe), m. p. 166—168°, dried at 130° *in vacuo* for analysis (Found: C, 78·1; H, 5·7; N, 4·8. $C_{19}H_{17}NO_2$ requires C, 78·3; H, 5·8; N, 4·8%).

7,8,9,10-*Tetrahydro-3-methoxy-6-methyl-7-oxophenanthridine* (IV; R = Me).—*m*-Anisidine (12·3 g.), 2-acetylcyclohexane-1,3-dione (15·4 g.), and ethanol (90 ml.) were boiled under reflux together for 6 hr., and poured into water. The product was crystallised from ethyl acetate–light petroleum (b. p. 60—80°) to give 2-[1-(3-*methoxyphenylimino*)*ethyl*]*cyclohexane*-1,3-*dione*, m. p.

[5] R. C. Elderfield in "Heterocyclic Compounds," ed. Elderfield, Wiley, New York, 1952, vol. IV, p. 282.

123–125° 22·0 g., 85%) (Found: C, 69·2; H, 6·5; N, 5·3. $C_{15}H_{17}NO_3$ requires C, 69·5; H, 6·6; N, 5·4%). This anil (7·5 g.) was stirred into polyphosphoric acid (50 ml.) at 100°; the reaction was exothermic and the internal temperature was maintained at 120–125° for 15 min. The mixture was poured onto ice and aqueos sodium hydroxide, extracted with ethyl acetate, and the extract evaporated. The residue was crystallised from ethyl acetate–light petroleum (b. p. 60—80°) to give the *ketone* (IV; R = Me), m. p. 138—139° (4·3 g.) (Found: C, 74·8; H, 6·4; N, 5·9· $C_{15}H_{15}NO_2$ requires C, 74·4; H, 6·2; N, 5·7%), $\nu_{max.}$ 850s, 829w, 812m, 770w, 720w cm.$^{-1}$. A second crop (0·80 g.), m. p. 128°, made up the total yield to 71%. The corresponding *alcohol* was prepared from the ketone (484 mg.) and sodium borohydride (114 mg.) in ethanol (25 ml.), and was crystallised from light petroleum (b. p. 100—120°), m. p. 154—155° (220 mg.) (Found: C, 73·6; H, 7·2; N, 5·7. $C_{15}H_{17}NO_2$ requires C, 74·1; H, 7·0; N, 5·8%), $\lambda_{max.}$ 215 (ε 29,200) and 240 mμ (45,600).

7,8,9,10-*Tetrahydro*-3-*methoxy*-7-*oxophenanthridine* (IV; R = H).—*m*-Anisidine (112 ml.), ethyl orthoformate (100 ml.), and ethanol (100 ml.) were boiled together under reflux for 18 hr., and cooled. The crystalline product was washed with a little methanol to give NN′-*bis*-(m-*methoxyphenyl*)*formamidine*, m. p. 108—109°, unchanged by recrystallisation from methanol (118 g., 92%) (Found: C, 70·4; H, 6·2; N, 11·0. $C_{15}H_{16}N_2O_2$ requires C, 70·3; H, 6·3; N, 10·9%). This formamidine (5·2 g.) and cyclohexane-1,3-dione (2·0 g.) were heated together at 100° (bath) for 45 min. The product was dissolved in ethyl acetate, the extract was shaken with 5% aqueous hydrochloric acid to remove *m*-anisidine then dried and evaporated, and the residue was crystallised from light petroleum (b. p. 80—100°), to give 2-(3-*methoxyphenyliminomethyl*)*cyclohexane*-1,3-*dione* (3·6 g., 82%), m. p. 65—72°. Further crystallisation raised the m. p. to 78° (Found: C, 68·4; H, 6·1; N, 5·7. $C_{14}H_{15}NO_3$ requires C, 68·6; H, 6·1; N, 5·7%). This anil (9·9 g.) was stirred into polyphosphoric acid (50 ml.) at 110°, the mixture was maintained at an internal temperature of 135° for 30 min., and poured into ice and aqueous sodium hydroxide. The product was extracted into ethyl acetate, the dried extract was evaporated, and the residue was crystallised from benzene–light petroleum (b. p. 60—80°), to give the crude product, m. p. 106—130° (6·8 g., 74%) (Found: C, 73·6; H, 5·5; N, 6·6: Calc. for $C_{14}H_{13}NO_2$ C, 73·9; H, 5·7; N, 6·2%). Thin-layer chromatography on alumina in 25% ethyl acetate–benzene showed the presence of two compounds, R_F 0·76 and 0·67. Crystallisation (twice) of the mixture of isomers from either benzene or methanol gave the pure *product* (IV; R = H), m. p. 147—149° (2·85 g. from 6·45 g. of mixed isomers), R_F 0·67 in the above system (Found: C, 73·9; H, 5·6; N, 6·1%), $\nu_{max.}$ 850s, 822s, 788m, 770w cm.$^{-1}$; weak bands at 760, 720 cm.$^{-1}$ in the spectrum of the crude mixture were absent. Fractionation of the crystallisation mother liquors, using benzene, methanol, and acetone as solvents, failed to provide a pure sample of the second (1-methoxy-) isomer.

Catalytic Reductions.—(*a*) 7,8,9,10-*Tetrahydro*-6-*methyl*-7-*oxo*-5-*azachrysene*.[2] This compound (854 mg.) was dissolved in acetic acid (40 ml.) and water (10 ml.), Adams catalyst (400 mg.) was added, and the mixture was shaken under hydrogen (1 atm.) at room temperature until absorption ceased (6 hr.). After removal of catalyst by filtration, the filtrate was basified (NaOH) and extracted with ethyl acetate. The dried extract was evaporated, and the residue crystallised from light petroleum (b. p. 100—120°) to give a *hemihydrate* of the product, m. p. 166—168° (340 mg.) (Found: C, 78·4; H, 8·0; N, 5·1. $C_{18}H_{21}NO,\frac{1}{2}H_2O$ requires C, 78·3; H, 8·0; N, 5·1%). Drying *in vacuo* at 130° over P_2O_5 gave the anhydrous 1,2,3,4,7,8,9,10-*octahydro*-7-*hydroxy*-6-*methyl*-5-*azachrysene* (V), m. p. unchanged (Found: C, 80·6; H, 7·9; N, 5·2. $C_{18}H_{21}NO$ requires C, 81·0; H, 7·9; N, 5·2%), $\lambda_{max.}$ 215 (ε 28,900) and 240 mμ (42,400); the n.m.r. spectrum in trifluoroacetic acid showed a methyl singlet (6·75 τ) and two aromatic protons.

(*b*) 7,8,9,10-*Tetrahydro*-3-*methoxy*-6-*methyl*-7-*oxophenanthridine*. This ketone (1·00 g.) was reduced under the above conditions. Removal of ethyl acetate from the dried extract left a gum, which was crystallised from ether by concentration of an ether solution at 0° to give the product, m. p. 68—69° (600 mg.). After drying (P_2O_5) at room temperature for 5 days, 1,2,3,4,7,8,9,10-*octahydro*-7-*hydroxy*-6-*methylphenanthridine hemihydrate* was obtained (Found: C, 74·3; H, 8·7; N, 6·3. $C_{14}H_{19}NO,\frac{1}{2}H_2O$ requires C, 74·3; H, 8·8; N, 6·2%). Drying for shorter periods (3 hr.) gave the *hydrate* (Found: C, 71·2; H, 8·8; N, 6·0. $C_{14}H_{19}NO,H_2O$ requires C, 71·5; H, 8·9; N, 6·0%). τ (in deuterochloroform) 5·05 (C*H*OH), 7·37 (C*H*$_3$, singlet), 7·0—8·4 (14—15*H* in addition to the methyl protons); no aromatic protons and no methoxyl protons.

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