Carcinogenic Nitrogen Compounds. Part LXXIX.[1] A Route to New Condensed Acridines containing a Cyclopent[*kl*]acridine Nucleus

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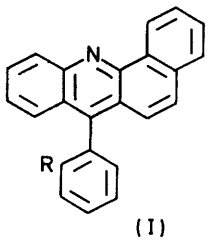
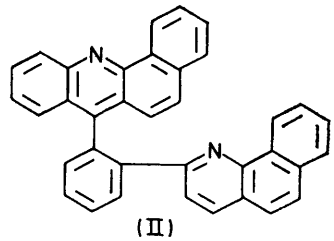
The reaction of 7-*o*-chlorophenylbenz[*c*]acridine with sodium hydroxide in benzo[*h*]quinoline affords a mixture of 7-phenylbenz[*c*]acridine, benz[*c*]indeno[1,3-*kl*]acridine, and benz[*c*]indeno[1,3-*mn*]acridine; a similar cyclisation of 7-*o*-chlorophenyldibenz[*c,h*]acridine leads to dibenz[*c,h*]indeno[1,3-*kl*]acridine, whereas the isomeric 14-*o*-chlorophenyldibenz[*a,h*]acridine gives a mixture of dibenz[*a,h*]acridine and benzo[*h*]phenanthro-[9,10,1-*mna*]acridine.

We have previously[2] shown that 12-(*o*-chlorophenyl)-benz[*a*]acridines readily cyclise to phenanthro[9,10,1-*mna*]acridines under the influence of sodium hydroxide in benzo[*h*]quinoline; this reaction was successfully extended to the preparation of more highly condensed polycyclic systems derived from naphtho[2,1,8-*def*]-quinoline. We expected that similar treatment 7-*o*-chlorophenylbenz[*c*]acridine (I; R = Cl) would cause cyclodehalogenation to give to polycyclic derivatives of the hitherto unknown cyclopent[*kl*]acridine nucleus. We report that the acridine (I; R = Cl), prepared by Bernthsen reaction[3] of *N*-phenyl-α-naphthylamine with *o*-chlorobenzoic acid, afforded a mixture of four components, one of which was 7-phenylbenz[*c*]acridine (I; R = H) resulting from a simple reductive dehalogenation. The mass spectrum and elemental analysis of the second component showed that it resulted from replacement of the halogen in (I; R = Cl) by a benzo[*h*]quinolyl residue; by analogy with other nucleophilic reactions in quinolines,[4] structure (II) is

[1] Part LXXVIII, J. André, N. P. Buu-Hoï, and P. Jacquignon, preceding paper.
[2] N. P. Buu-Hoï, O. Périn-Roussel, and P. Jacquignon, *J.C.S. Perkin I*, 1972, 234.
[3] *Cf.* N. P. Buu-Hoï and J. Lecocq, *Rec. trav. Chim.*, 1945, **64**, 250.
[4] H. Weidel, *Monatsh.*, 1887, **8**, 120; A. Tschitschibabin and Kursanova, *J. Russ. Phys. Chem. Soc.*, 1930, **62**, 1211 (*Chem. Abs.*, 1931, **25**, 2727).

suggested. The other two last components, both of which gave red picrates, were the two expected cyclisation products (III) and (IV); these orange-yellow compounds showed u.v. spectra too similar to each other


(I)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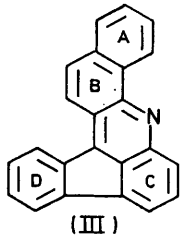
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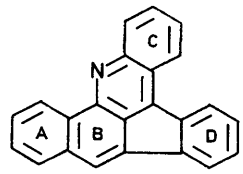
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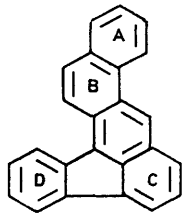
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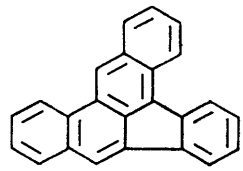
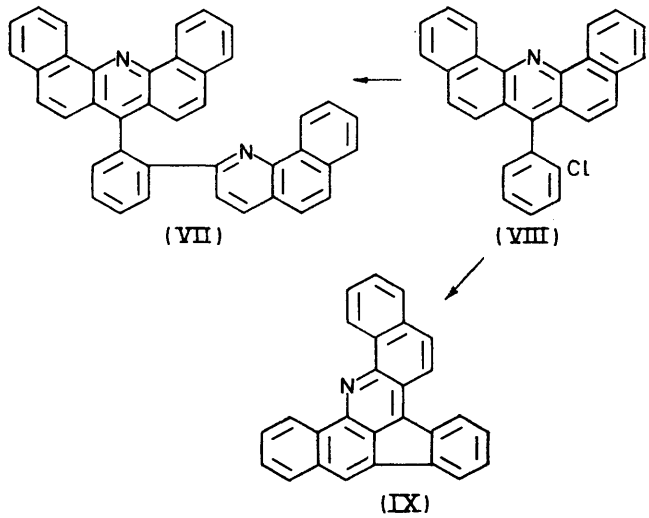

(VI)

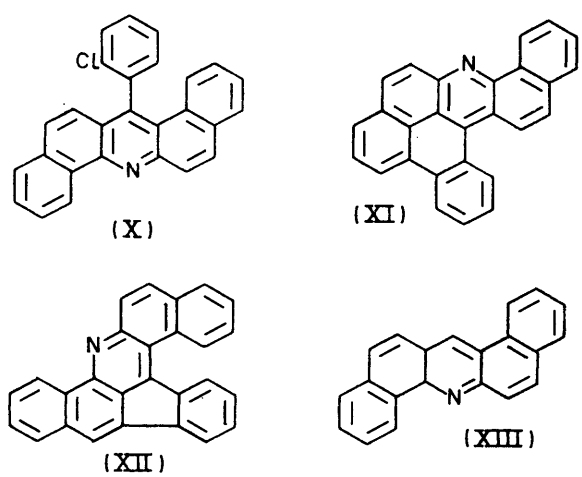
for any conclusion to be drawn as to their respective identities. However, a comparative study of their i.r. spectra (taking into account the out-of-plane C–H vibrations) with those of dibenz[*a*,*j*]aceanthrylene (V) [5] and the isomeric dibenz[*a*,*e*]aceanthrylene (VI),[6] their hydrocarbon counterparts, showed the compound of m.p. 180° (corresponding hydrocarbon, m.p. 181°) to have structure (III), and the compound of m.p. 226° corresponding hydrocarbon, m.p. 232°) to have structure (IV). In the spectrum of compound (III), the 820—550 cm^{-1} region corresponds closely to that found for the hydrocarbon (V): the bands at 750, 738, and 802 cm^{-1} are characteristic of rings A and D (having four vicinal C–H groups) and B (with two vicinal C–H groups), respectively, and the 686 cm^{-1} band and those at *ca.* 750 cm^{-1} can be attributed to ring C (which has three vicinal C–H groups). Likewise, the spectrum of compound (IV) closely resembles that of (VI) (900—490 cm^{-1} region: bands at 764 and 758 cm^{-1} characteristic of rings A, C, and D, which have four vicinal unsubstituted sites, and band at 892 cm^{-1} corresponding to the lone C–H of ring B).

The situation was less complicated in the cyclisation of 7-*o*-chlorophenyldibenz[*c*,*h*]acridine (VIII) (prepared by a Bernthsen reaction of *o*-chlorobenzoic acid and di-α-naphthylamine), as only two products were obtained, a by-product [probably (VII)] resulting from replacement of chlorine by a benzo[*h*]quinolyl group, and the expected dibenz[*c*,*h*]indeno[1,3-*kl*]acridine (IX).

14-*o*-Chlorophenyldibenz[*a*,*h*]acridine (X), which in theory could cyclise either to the benzophenanthroacridine derivative (XI) or to the isomeric dibenzindenoacridine derivative (XII), afforded in fact only the


(VII) (VIII) (IX)

former (XI), together with dibenz[*a*,*h*]acridine (XIII) [engendered by cleavage of the *meso*-aryl group in (X)]. Assignment of structure (XI) was based on the u.v. absorption spectrum, halochromism in sulphuric acid, and colour of the picrate, all of which resembled data previously recorded for the isomeric benzo[*j*]phenanthro-

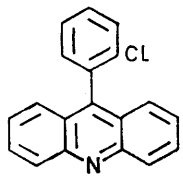

(X) (XI) (XII) (XIII)

[9,10,1-*mna*]acridine; [2] that compound (XI) was formed rather than (XII) could be due either to the particularly sterically crowded structure of (XII), or to the less ready formation of an azafluoranthene nucleus than an azapyrene one. In favour of this assumption was our

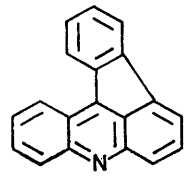
[5] L. F. Fieser and A. M. Seligman, *J. Amer. Chem. Soc.*, 1935, **57**, 2174.

[6] D. Lavit-Lamy and N. P. Buu-Hoï, *Chem. Comm.*, 1966, 92; *Bull. Soc. chim. France*, 1966, 2613, 2619.

inability to cyclise 9-*o*-chlorophenylacridine (XIV) to indeno[1,3-*kl*]acridine (XV), even under drastic conditions.



(XIV)



(XV)

Compounds (III), (IV), (IX), and (XI) are undergoing tests for carcinogenic activity in mice [(III) and (IV) are aza-analogues of, respectively, the hydrocarbons (V) and (VI), already found to be carcinogenic].[7,8]

EXPERIMENTAL

I.r. spectra were taken with a Perkin-Elmer instrument for potassium bromide discs (1·5 mg sample in 0·6 g).

7-o-*Chlorophenylbenz*[c]*acridine* (I; R = Cl).—A mixture of *N*-phenyl-α-naphthylamine (5 g), *o*-chlorobenzoic acid (4 g), and anhydrous zinc chloride (7 g) was heated at *ca.* 200—220° for 4 h, and the cooled product was triturated with aqueous 20% sodium hydroxide in the presence of toluene. The toluene layer was washed with water and dried (Na_2SO_4), the solvent was removed, and the residue was fractionated *in vacuo*; the portion of b.p. 315—320° at 20 mmHg (5 g) crystallised as pale yellow leaflets, m.p. 64—65° (from ethanol) (Found: C, 81·4; H, 4·3; N, 3·9. $C_{23}H_{14}ClN$ requires C, 81·3; H, 4·2; N, 4·1%); *picrate*, deep yellow prisms, m.p. 213° (from chlorobenzene) (Found: N, 9·7. $C_{29}H_{17}ClN_4O_7$ requires N, 9·9%).

Cyclisation of the Chlorophenylbenzacridine (I; R = Cl).—A mixture of the foregoing acridine (2 g) and potassium hydroxide (10 g) in benzo[*h*]quinoline (14 g) was heated at 360° for 4 h, and the cooled product was treated with water and chloroform; the chloroform and benzo[*h*]quinoline were distilled off *in vacuo* and the brown residue was dissolved in chloroform and purified by chromatography on a silica column. Elution with benzene afforded (*a*) 7-phenylbenz[*c*]acridine, pale yellow prisms (0·1 g), m.p. and mixed m.p.[9] 140—141° (Found: M^+, 305. Calc. *M*, 305); (*b*) *benz*[c]*indeno*[1,3-kl]*acridine* (III), which was purified *via* its *picrate*, red needles, m.p. (with pre-heating) 245° (decomp. >220°) (from *o*-dichlorobenzene) (Found: N, 10·8. $C_{29}H_{16}N_4O_7$ requires N, 10·5%); the free *base* formed orange-yellow needles (50 mg), m.p. 180° (from cyclohexane), whose solutions in sulphuric acid were orange-red (Found: C, 91·7; H, 4·6; N, 4·3%; M^+, 303. $C_{23}H_{13}N$ requires C, 91·9; H, 4·3; N, 4·6%; *M*, 303); $\lambda_{max.}$ (cyclohexane) 218 (log ε 4·6), 226 (4·81), 241 (4·42), 252 (4·52), 268 (4·45), 280 (4·53), 290 (4·66), 300 (4·77), 330 (3·17), 353 (3·62), 380 (4·04), 398 (4·22), 412 (4·07), 422 (4·2), 430 (3·99), and 435 nm (3·78); (*c*) 7-(o-*benzo*[h]*quinolin*-2-*ylphenyl*)*benz*[c]*acridine* (II), pale yellow leaflets (0·2 g), m.p. 210—211° (from cyclohexane) (Found: C, 89·3; H, 4·5; N, 5·8%; M^+, 482. $C_{36}H_{22}N_2$ requires C, 89·6; H, 4·6; N, 5·8%; *M*, 482); and (*d*) *benz*[c]*indeno*[1,3-mn]-*acridine* (IV), purified *via* its *picrate*, bright red prisms, m.p. (with pre-heating) 268° (decomp. >230°) (from benzene) (Found: N, 10·4. $C_{29}H_{16}N_4O_7$ requires N, 10·5%); free *base*, bright yellow needles (0·1 g), m.p. 226° (from benzene; intense greenish yellow fluorescence), whose solutions in sulphuric acid were orange-red (Found: C, 91·0; H, 4·5; N, 4·7%; M^+, 303. $C_{23}H_{13}N$ requires C, 91·1; H, 4·3; N, 4·6%; *M*, 303); $\lambda_{max.}$ 219 (log ε 4·63), 227 (4·54), 237 (4·62), 242 (4·62), 255 (4·72), 259 (4·71), 268 (4·45), 280 (4·57), 287 (4·5), 293 (4·61), 300 (4·5), 305 (4·6), 326 (3·6), 337 (3·41), 370 (4·02), 374 (4·04), 391 (4·27), 401 (4·18), 412 (4·31), and 430 nm (3·45).

7-o-*Chlorophenyldibenz*[c,h]*acridine* (VIII).—Prepared as for compound (I; R = Cl) from di-α-naphthylamine, this *acridine* (50% yield), b.p. 326—330° at 12 mmHg, formed pale yellow needles, m.p. 279—280° (from toluene) (Found: C, 82·8; H, 4·4; N, 3·4. $C_{27}H_{16}ClN$ requires C, 83·2; H, 4·2; N, 3·6%); it gave no picrate.

Cyclisation of the Acridine (VIII).—A mixture of the acridine (2 g), sodium hydroxide (10 g), and benzo[*h*]-quinoline (12 g) was heated at 360° for 4 h, and the product was worked up as before; chromatography on silica [eluants cyclohexane, then cyclohexane–benzene (3 : 2)] afforded (*a*) *dibenz*[c,h]*indeno*[1,3-kl]*acridine* (IX), bright yellow needles (0·1 g), m.p. 245° (from benzene), whose solutions in sulphuric acid were orange-red (Found: C, 91·9; H, 4·5; N, 3·9. $C_{27}H_{15}N$ requires C, 91·7; H, 4·3; N, 4·0%); *picrate*, orange-red prisms, m.p. (with pre-heating) 196° (decomp. >175°) (from ethanol–benzene) (Found: N, 9·5. $C_{33}H_{18}N_4O_7$ requires N, 9·6%); and (*b*)7-(o-*benzo*[h]*quinolin*-2-*ylphenyl*)*dibenz*[c,h]*acridine*(VII), prisms (0·2 g), m.p. 286° (from benzene) (Found: C, 90·4; H, 4·7; N, 5·1%; M^+, 532. $C_{40}H_{24}N_2$ requires C, 90·3; H, 4·6; N, 5·3%; *M*, 532).

14-o-*Chlorophenyldibenz*[a,h]*acridine* (X).—This *acridine*, b.p. 340—350° at 15 mmHg, prepared from *N*-β-naphthyl-α-naphthylamine, formed pale yellow prisms (50%), m.p. 196° (from cyclohexane) (Found: C, 83·6; H, 4·3; N, 3·5%); *picrate*, bright yellow prisms, m.p. (with pre-heating) 246° (from benzene) (Found: N, 9·4. $C_{33}H_{19}ClN_4O_7$ requires N, 9·1%).

Cyclisation of the Acridine (X).—This, effected as before, afforded a product which, purified by chromatography on silica, furnished (*a*) *x*,*x*′-bi(benzo[*h*]quinolyl), sublimable microprisms (0·3 g), m.p. 286° (from benzene) (Found: N, 7·7%; M^+, 356. Calc. for $C_{26}H_{16}N_2$: N, 7·9%; *M*, 356); (*b*) traces of dibenz[*a*,*h*]acridine, pale yellow needles, m.p. *ca.* 220°, identified by its n.m.r. spectrum[10] (Found: C, 90·5; H, 4·5; N, 4·9%; M^+, 279. Calc. for $C_{21}H_{13}N$: C, 90·3; H, 4·7; N, 5·0%; *M*, 279); and (*c*) *benzo*[h]*phenanthro*[9,10,1-mna]*acridine* (XI), deep yellow needles (0·2 g), m.p. 203° (from benzene), whose solutions in sulphuric acid were red (Found: C, 91·5; H, 4·4; N, 3·7. $C_{27}H_{15}N$ requires C, 91·7; H, 4·3; N, 4·0%); *picrate*, orange-yellow prisms, m.p. 220° (from benzene) (Found: N, 9·4. $C_{33}H_{18}N_4O_7$ requires N, 9·6%). The u.v. absorption spectrum was very similar to that of dibenzo[*a*,*l*]pyrene;[11] $\lambda_{max.}$ 216 (log ε 4·83), 232 (4·67), 257 (4·55), 268 (4·58), 302 (4·86), 310 (4·9), 367 (4·34), 380 (4·45), 399 (4·17), and 422 nm (4·56).

[7] *Cf.* A. Lacassagne, N. P. Buu-Hoï, F. Zajdela, and F. A. Vingiello, *Naturwiss.*, 1968, **55**, 43; A. Lacassagne, N. P. Buu-Hoï, F. Zajdela, and D. Lavit-Lamy, *Compt. rend.*, 1963, **256**, 2728.

[8] M. Shear, *Amer. J. Cancer*, 1936, **28**, 334.

[9] N. P. Buu-Hoï, *J. Chem. Soc.*, 1949, 670.

[10] J. André, P. Jacquignon, F. Périn, and N. P. Buu-Hoï, *Bull. Soc. chim. France*, 1970, 3909.

[11] *Cf.* W. Carruthers, *J. Chem. Soc.*, 1967, 1525.

9-o-*Chlorophenylacridine* (XIV).—Prepared from diphenylamine, this *acridine* (60% yield), b.p. 285—290° at 15 mmHg, formed pale yellow needles, m.p. 231° (from benzene) (Found: C, 79·1; H, 4·4; N, 4·8. $C_{19}H_{12}ClN$ requires C, 78·8; H, 4·2; N, 4·8%); *picrate*, lemon yellow prisms, m.p. (with pre-heating) 230° (decomp. >205°) (from chlorobenzene) (Found: N, 10·8. $C_{25}H_{15}ClN_4O_7$ requires N, 10·8%). This acridine was not cyclised on heating (12 h) with sodium hydroxide either in benzo[*h*]-quinoline or alone.

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