144. *The Chemistry of Carcinogenic Nitrogen Compounds. Part II. Further Derivatives of* 1 : 2- *and* 3 : 4-*Benzacridines.*

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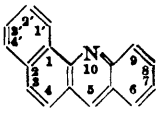
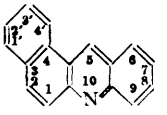
In continuation of earlier work (Buu-Hoï, *J.*, 1946, 792), a large number of new derivatives of 1 : 2- and 3 : 4-benzacridines have been prepared by a set of known methods for the study of their potential carcinogenic, and other physiological properties. The synthesis of these compounds, most of them bearing hydrocarbon substituents of different size and shape in the *meso*-position, involved the preparation of a series of hitherto unknown *N*-arylnaphthylamines.

From the extensive work of Cook and others (Barry, Cook, Haslewood, Hewett, Hieger, and Kennaway, *Proc. Roy. Soc.*, 1935, *B*, **117**, 318; Badger, Cook, Hewett, Kennaway, Kennaway, Martin, and Robinson, *ibid.*, 1940, *B*, **129**, 439; Shear and Leiter, *J. Nat. Cancer Inst.*, 1940, **1**, 303; Lacassagne, Buu-Hoï, Daudel, and Rudali, *Compt. rend.*, 1947, **225**, 238), the relations between carcinogenic power and the nature and position of substituents in the 1 : 2-benzanthracene molecule have become much better understood. In order to obtain similar knowledge in the series of 1 : 2- and 3 : 4-benzacridines (I) and (II), many of which have recently been found to be actively carcinogenic (Lacassagne, Buu-Hoï, Lecocq, and Rudali, *Bull. du Cancer*, 1946, **33**, 48), a number of further new derivatives of these nuclei have now been synthesised for biological testing. Since this work began, the discovery of the sterilising effect of various benzacridines upon the testes of mice (Lacassagne, Buu-Hoï, Rudali, and Lecocq, *ibid.*, 1947, **34**, 28) has provided a new incentive for the synthesising of further compounds of these series.

(I.) 

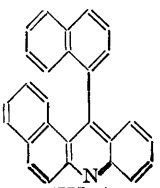
 (II.)

From among 11 possible monomethyl-1 : 2-benzacridines, only 4 have hitherto been prepared. 5-Methyl-1 : 2-benzacridine has been obtained by means of the Bernthsen reaction (Posstowski and Lundin, *Chem. Centr.*, 1940, II, 205; see also Kermack, Slater, and Spragg, *ibid.*, 1931, I, 618), and 7-, 9-, and 2′-methyl-1 : 2-benzacridines *via* the Pfitzinger reaction (von Braun and Wolff, *Ber.*, 1922, **55**, 3685; Buu-Hoï, *loc. cit.*). 6- and 8-*Methyl*-1 : 2-*benzacridines* have now been prepared by the Ullmann–La Torre reaction (*Ber.*, 1904, **37**, 2924) performed upon N-vic.-o-*xylyl*-α-*naphthylamine* and N-p-*xylyl*-α-*naphthylamine*, respectively, both of these new secondary amines having been prepared by heating *vic.*-*o*-xylidine and *p*-xylidine with α-naphthylamine in the presence of some iodine (cf. Knoevenagel, *J. pr. Chem.*, 1914, **89**, 17). The foregoing method is also suitable for the preparation of 9-methyl-1 : 2-benzacridine from N-vic.-m-*xylyl*-α-*naphthylamine*. 7- and 9-Methyl-1 : 2-benzacridines could also be obtained by the interaction of paraformaldehyde with a boiling mixture of α-naphthol and *p*-toluidine and *o*-toluidine, respectively. When a similar reaction was performed upon *m*-toluidine, a complex mixture was obtained, from which only a very small quantity of pure 8-methyl-1 : 2-benzacridine could be isolated.

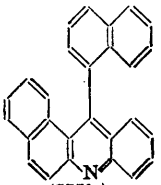
In the 3 : 4-benzacridine series, the 5-, 7-, and 9-methyl derivatives are already known (Posstowski and Lundin, *loc. cit.*; Ullmann, *Chem. Centr.*, 1901, II, 568; Ullmann and Naef, *Ber.*, 1900, **33**, 907). Iodine-catalysed reaction of β-naphthol with *vic.*-*o*-xylidine and *p*-xylidine resulted respectively in N-vic.-o-*xylyl*- and N-p-*xylyl*-β-*naphthylamine*, which gave on heating with lead oxide 6- and 8-*methyl*-3 : 4-*benzacridines*. The latter isomer could more conveniently be prepared from β-naphthol and *m*-toluidine by means of the paraformaldehyde reaction.

Of dimethylbenzacridines, from among the very large number of isomers possible in each of the series (I) and (II), only twelve were hitherto known, of which the six bearing a methyl group in the *meso*-position were prepared by Buu-Hoï and Lecocq (*Compt. rend.*, 1944, **218**, 792), and the others by Senier and Compton (*J.*, 1909, **95**, 1627, 1636). The preparation of a number of further isomers has now been undertaken. 8 : 9-*Dimethyl*-1 : 2- and -3 : 4-*benzacridine* have easily been prepared by adding paraformaldehyde to boiling mixtures of 2 : 3-dimethylaniline with α- and β-naphthol, respectively. Replacement of *o*-xylidine by 4-aminodiphenyl in the foregoing reaction yielded 7-*phenyl*-1 : 2- and -3 : 4-*benzacridine*. A Bernthsen reaction performed upon acetic anhydride and N-*phenyl*-4-*methyl*-α-*naphthylamine*, the latter being prepared by heating 4-methyl-α-naphthylamine (synthesised according to Barclay, Burawoy, and Thomson, *J.*, 1944, 109, and Buu-Hoï and Guettier, *Compt. rend.*, 1946, **222**, 665) with aniline in the presence of iodine, resulted in 3 : 5-*dimethyl*-1 : 2-*benzacridine*. N-o-*Tolyl*-4-*methyl*-α-*naphthylamine* similarly obtained from 4-methyl-α-naphthylamine and *o*-toluidine, has been converted into 3 : 5 : 9-*trimethyl*-1 : 2-*benzacridine*. Similar Bernthsen reactions involving acetic anhydride and *N*-*vic*.-*o*-xylyl-, N-o-*xylyl*-, and *N*-*p*-xylyl-α-naphthylamine produced 5 : 8 : 9-, 5 : 7 : 8-, and 5 : 6 : 9-*trimethyl*-1 : 2-*benzacridine*. In the other series, a similar set of reactions carried out with acetic anhydride and *N*-*vic*.-*o*-xylyl-, N-o-*xylyl*-, *N*-*p*-xylyl-, and N-s-m-*xylyl*-β-naphthylamine (the last being prepared in high yield from β-naphthol, *s*-*m*-xylidine, and iodine) gave 5 : 8 : 9-, 5 : 7 : 8-, 5 : 6 : 9-, and 5 : 6 : 8-*trimethyl*-3 : 4-*benzacridine*.

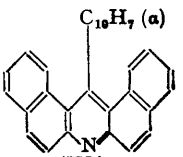
5-Methyl-1 : 2-benzacridine has been found to be strongly carcinogenic (Lacassagne, Buu-Hoï, Lecocq, and Rudali, *loc. cit.*); on the other hand, in the 1 : 2-benzanthracene group, replacement by higher substituents of the methyl radical in favourable positions such as 5 or 10 (Badger, Cook, *et al.*, *loc. cit.*; Shear and Leiter, *loc. cit.*) produces a downward trend in carcinogenicity with the increase in the number of carbon atoms involved. In order to ascertain whether, in the 1 : 2-benzacridine series, similar regularities brought about by changing the size and shape of the *meso*-substituents could be detected, a number of 5-*alkyl*-1 : 2-*benzacridines* have been prepared from *N*-phenyl-α-naphthylamine by extending the Bernthsen reaction to different linear as well as branch-chain homologues of acetic acid. A list of these compounds with their properties is given in Table I, together with those of 5-*phenyl*- and 5-*benzyl*-1 : 2-*benzacridine*, prepared for the study of the influence of aromatic substitution. In Table II, a list appears of 5-*alkyl*-3 : 4-*benzacridines* similarly obtained from *N*-phenyl-β-naphthylamine and a variety of aliphatic acids. 5-*Benzyl*-3 : 4-*benzacridine*, prepared in good yield from phenylacetic acid, was readily oxidised by means of selenium dioxide into 5-*benzoyl*-3 : 4-*benzacridine* according to a convenient procedure devised by Buu-Hoï and Lecocq (*Rec. Trav. chim.*, 1945, **44**, 251). In view of the remarkable results obtained by Kuhn and Moewus (*Ber.*, 1940, **73**, 1086) in inducing mutations in certain species of green algæ by means of 3-ethyl-1-dodecylbenzotriazolium bromide, attention should be specially directed to long-chain compounds such as 5-heptadecyl-1 : 2-benzacridine which gives soapy water-soluble quaternary acridinium salts with dialkyl sulphates and alkyl halogenides. These will form the subject of a separate paper. On the basis of the theory of restricted rotation of aromatic radicals around C–C links due to steric hindrance, and account being paid to the fact that van der Waals forces are likely to be strong in the neighbourhood of *peri*-positions, a molecule such as 5-α-naphthyl-3 : 4-benzacridine might perhaps exist in two optically active forms (III*a*) and (III*b*). Such a compound has now



(III*a*.)



(III*b*.)



(IV.)

been synthesised in the usual way from α-naphthoic acid and *N*-phenyl-β-naphthylamine; attempts to resolve this and similar substances into enantiomorphic components will be described later. 5-α-*Naphthyl*-3 : 4 : 5 : 6-*dibenzacridine* (IV), a molecule in which the rotation of the *meso*-radical would presumably be still more hindered, was also prepared from ββ-dinaphthylamine; but in this case, considerations of symmetry show that the possibility of optical isomerism must be discarded.

Most of the substances described here (some of which are highly potent carcinogens) are under biological investigation by Professor Lacassagne, and results will be published elsewhere.

Experimental.

N-vic.-o-*Xylyl-α-naphthylamine*.—A mixture of *vic.-o*-xylidine (12 g.), α-naphthylamine (15 g.), and iodine (0·1 g.) was heated under reflux for 26 hours, ammonia being copiously evolved. The dark oil obtained was taken up in toluene, washed with aqueous sodium hydroxide, and dried (Na_2SO_4); after removal of the solvent, the residue was vacuum-fractionated, giving N-vic.-o-*xylyl-α-naphthylamine*, b. p. 242—245°/13 mm. (20 g.), which readily solidified. After recrystallisation from aqueous alcohol, hard large colourless prisms, m. p. 68—69°, were obtained, very soluble in benzene and alcohol, and slowly undergoing oxidation in the air (Found : N, 5·7. $C_{18}H_{17}N$ requires N, 5·6%). With picric acid, a molecular compound crystallising from alcohol in violet-red silky needles, m. p. 128°, was obtained. The higher-boiling fractions contained much αα-dinaphthylamine.

6-*Methyl*-1 : 2-*benzacridine*.—The foregoing amine (5 g.) was heated in a Claisen flask at 350° with finely powdered lead oxide (5 g.) for some minutes, the temperature being subsequently raised to boiling; the distillate was dissolved in hot alcohol, and picric acid added. The *picrate* thereby obtained crystallised from nitrobenzene in silky yellow needles, m. p. 249—251° (decomp.), almost insoluble in alcohol, and only slightly soluble in benzene (Found : N, 12·4. $C_{18}H_{13}N,C_6H_3O_7N_3$ requires N, 12·7%). The free *base* (0·5 g.), obtained on treatment of the picrate with dilute aqueous ammonia, was extracted with chloroform; it crystallised from alcohol in pale yellow needles, m. p. 136° (Found : N, 5·6. $C_{18}H_{13}N$ requires N, 5·7%).

5 : 8 : 9-*Trimethyl*-1 : 2-*benzacridine*.—*N-vic.-o*-Xylyl-α-naphthylamine (5 g.) was heated with acetic anhydride (5 g.) and fused zinc chloride (10 g.) at 200° for one hour, the temperature being subsequently allowed to rise to 250° during some 30 hours. The cooled mixture was thoroughly treated with hot aqueous sodium hydroxide and toluene. The organic layer was separated and dried over potassium hydroxide, the solvent removed, and the dark viscous residue vacuum-distilled. The fraction, b. p. 295—298°/15 mm., was collected, and it solidified upon treatment with alcohol. After two crystallisations from alcohol–benzene, 5 : 8 : 9-*trimethyl*-1 : 2-*benzacridine* (4 g.) was obtained as long, yellow, prismatic needles, m. p. 166° (Found : N, 5·0. $C_{20}H_{17}N$ requires N, 5·2%); the alcoholic solutions gave a strong green fluorescence. The *picrate* crystallised from toluene in long, silky, orange needles, m. p. 162—163°, easily soluble in alcohol and benzene. The low m. p. and high solubility are characteristic of picrates of 1 : 2-benzacridines bearing a methyl group in the 9-position (cf. Buu-Hoï, *loc. cit.*; Senier and Austin, *J.*, 1907, **91**, 1240).

N-p-*Xylyl-α-naphthylamine*.—This *amine* (14 g.), obtained from *p*-xylidine (17 g.), α-naphthylamine (20 g.), and iodine (0·1 g.) in the same manner as was the preceding one, formed a viscous yellow oil, b. p. 242—244°/15 mm., which did not solidify even after many months (Found : N, 5·4. $C_{18}H_{17}N$ requires N, 5·6%). The molecular compound obtained with picric acid crystallised from alcohol in long, silky, violet-red needles, m. p. 109—110°.

8-*Methyl*-1 : 2-*benzacridine*.—(a) *By the Ullmann–La Torre reaction*. Heating of the foregoing amine (10 g.) with lead oxide (100 g.) in the usual manner gave an oil which was converted into a *picrate* (2 g.), crystallising from chlorobenzene in fine orange-yellow needles, m. p. 239—240° (decomp.) (Found : N, 12·6. $C_{18}H_{13}N,C_6H_3O_7N_3$ requires N, 12·7%). The free *base* crystallised from alcohol in pale yellow, elongated prisms, m. p. 148° (Found : N, 5·6. $C_{18}H_{13}N$ requires N, 5·7%).

(b) *By the paraformaldehyde reaction*. To a boiling mixture of α-naphthol (5 g.) and *m*-toluidine (10 g.), paraformaldehyde (1 g.) was cautiously added in small portions; after 10 minutes of further refluxing, vacuum-distillation yielded an orange-yellow oil, b. p. 400°, which was dissolved in alcohol and treated with picric acid. After many crystallisations from nitrobenzene, long, orange-yellow, silky needles, m. p. 240—241°, were obtained. The base (0·5 g.) had m. p. 145—146° undepressed on admixture with a sample prepared as in (a).

5 : 6 : 9-*Trimethyl*-1 : 2-*benzacridine*.—A mixture of the foregoing amine (5 g.), acetic anhydride (5 g.), and zinc chloride (10 g.) was heated at 200—210° for 24 hours, and then at 225—240° for 3 hours. After the routine treatment, the *base* was obtained as large yellow needles (3 g.), m. p. 140° (from alcohol–benzene) (Found : N, 4·9. $C_{20}H_{17}N$ requires N, 5·2%). The picrate crystallised from alcohol–benzene in long silky orange needles, m. p. 165°, which were extremely soluble in benzene.

N-vic.-m-*Xylyl-α-naphthylamine*.—The condensation of *vic.-m*-xylidine with α-naphthylamine in the presence of iodine gave much αα-dinaphthylamine and little of the expected mixed secondary amine. The following procedure gave better yields of the latter compound : a mixture of *vic.-m*-xylidine (10 g.), α-naphthol (15 g.), and iodine (0·1 g.) was heated under reflux for 3 hours and subsequently vacuum-fractionated. The *amine* (10 g.) was obtained as a viscous yellow oil, b. p. 242—244°/13 mm., which did not solidify (Found : N, 5·6. $C_{18}H_{17}N$ requires N, 5·6%). The addition compound with picric acid crystallised from alcohol in long, silky, violet needles, m. p. 102°.

9-*Methyl*-1 : 2-*benzacridine*.—(a) *By the Ullmann–La Torre reaction*. The preceding amine (5 g.), heated at 350—400° with lead oxide (50 g.), yielded an oil which was transformed into a picrate (2 g.) crystallising from alcohol–benzene in short, orange-yellow prisms, m. p. 150—151° after purification from alcohol (cf. von Braun and Wolff, *loc. cit.*).

(b) *By the paraformaldehyde reaction*. α-Naphthol (10 g.), *o*-toluidine (10 g.), and paraformaldehyde (1 g.), brought into reaction as described above, yielded the same picrate (0·2 g.) after crystallisation from alcohol.

7-*Methyl*-1 : 2-*benzacridine*.—The routine reaction between α-naphthol (10 g.), *p*-toluidine (10 g.), and paraformaldehyde (1 g.) gave a picrate (3 g.), m. p. 226—227°; the base had m. p. 131—132° (cf. Buu-Hoï, *loc. cit.*).

N-vic.-o-*Xylyl-β-naphthylamine*.—A mixture of β-naphthol (10 g.), *vic.-o*-xylidine (12 g.), and iodine (0·02 g.) was heated under reflux for 16 hours, then treated with aqueous sodium hydroxide and benzene.

The organic layer was dried (Na_2SO_4), the benzene removed, and the residue vacuum-distilled. The secondary *amine*, b. p. 255—256°/20 mm., solidified immediately, and crystallised from alcohol in colourless prismatic needles (14 g.), m. p. 61—62° (Found : N, 5·4. $C_{18}H_{17}N$ requires N, 5·6%). The substance containing alcohol of crystallisation had m. p. 55°.

6-*Methyl*-3 : 4-*benzacridine*.—The oil resulting from pyrolysis of the above amine (5 g.) over lead oxide (50 g.) yielded a *picrate*, crystallising from nitrobenzene in light, silky, yellow needles, m. p. 276—278° (decomp.), which were almost insoluble in alcohol (Found : N, 12·6. $C_{18}H_{13}N,C_6H_3O_7N_3$ requires N, 12·7%). The *base* crystallised from alcohol in long yellow needles, m. p. 129° (Found : N, 5·6. $C_{18}H_{13}N$ requires N, 5·7%).

5 : 8 : 9-*Trimethyl*-3 : 4-*benzacridine*.—*N*-*vic*.-*o*-Xylyl-β-naphthylamine (4 g.), acetic anhydride (5 g.), and zinc chloride (10 g.) yielded a *base* (2·5 g.) which crystallised from alcohol–benzene in silky yellow needles, m. p. 126°, very soluble in benzene (Found : N, 5·0. $C_{20}H_{17}N$ requires N, 5·2%). The corresponding *picrate* formed long, dark yellow prisms, m. p. 218—220°, from nitrobenzene (Found : N, 11·4. $C_{20}H_{17}N,C_6H_3O_7N_3$ requires N, 11·2%).

N-p-*Xylyl*-β-*naphthylamine*.—From *p*-xylidine (25 g.), β-naphthol (20 g.), and iodine (0·1 g.) this *amine* (29 g.) was obtained as a pale yellow, viscous oil which reddened rapidly in the air, and set into a crystalline mass, m. p. *ca.* 40°, after some weeks (Found : N, 5·4. $C_{18}H_{17}N$ requires N, 5·5%).

8-*Methyl*-3 : 4-*benzacridine*.—Obtained from β-naphthol (10 g.), *m*-toluidine (10 g.), and paraformaldehyde (1 g.), this *base* formed fine, pale yellow needles (3 g.), m. p. 143° (from methanol), very soluble in benzene and alcohol (Found : N, 5·6. $C_{18}H_{13}N$ requires N, 5·7%). The *picrate* formed short, silky, orange-yellow needles, m. p. 262—263° (decomp. and sublim.) from nitrobenzene (Found : N, 12·5. $C_{18}H_{13}N,C_6H_3O_7N_3$ requires N, 12·7%). The same substance was obtained in good yield by heating *N*-*p*-xylyl-β-naphthylamine with lead oxide at 350—380°.

5 : 6 : 9-*Trimethyl*-3 : 4-*benzacridine*.—*N*-*p*-Xylyl-β-naphthylamine (5 g.) was heated at 220° for 24 hours with acetic anhydride (5 g.) and zinc chloride (10 g.), and the resulting product treated in the ordinary way. The *base* (2·5 g.) was obtained in yellow prisms (from alcohol), m. p. 131—132° (Found : N, 5·2. $C_{20}H_{17}N$ requires N, 5·2%). The *picrate* crystallised from nitrobenzene in fine, silky, orange-yellow needles, m. p. 266—267° (decomp.) (Found : N, 11·1. $C_{20}H_{17}N,C_6H_3O_7N_3$ requires N, 11·2%).

8 : 9-*Dimethyl*-1 : 2-*benzacridine*.—The product obtained from α-naphthol (10 g.), *vic*.-*o*-xylidine (10 g.), and paraformaldehyde (1 g.) was a converted into a *picrate* (4 g.), which crystallised from chlorobenzene in long, silky, orange-yellow needles, m. p. 160°, soluble in alcohol and benzene (Found : N, 11·6. $C_{19}H_{15}N,C_6H_3O_7N_3$ requires N, 11·5%). The *base* formed yellow, silky leaflets, m. p. 96—97°, very easily soluble in alcohol (Found : N, 5·5. $C_{19}H_{15}N$ requires N, 5·4%).

8 : 9-*Dimethyl*-3 : 4-*benzacridine*.—This *base* was obtained in a similar manner, but in better yield, from β-naphthol, *vic*.-*o*-xylidine, and paraformaldehyde. It crystallised from alcohol–benzene in long, silky, yellow needles, m. p. 148° (Found : N, 5·2. $C_{19}H_{15}N$ requires N, 5·4%). Its *picrate* formed silky, orange-yellow prisms, m. p. 266—267° (with decomp. and sublim.) from chlorobenzene (Found : N, 11·4. $C_{19}H_{15}N,C_6H_3O_7N_3$ requires N, 11·5%).

7-*Phenyl*-1 : 2-*benzacridine*.—Similarly obtained from α-naphthol (5 g.), *p*-aminodiphenyl (5 g.), and paraformaldehyde (0·5 g.), this formed a *picrate* (1·5 g.), short, orange-yellow needles, m. p. 250—251°, (decomp.), from nitrobenzene (Found : N, 10·6. $C_{23}H_{15}N,C_6H_3O_7N_3$ requires N, 10·4%). The free *base* crystallised from alcohol–benzene in long, pale yellow prisms, m. p. 163° (Found : N, 4·4. $C_{23}H_{15}N$ requires N, 4·5%). It distilled without decomposition above 450° at atmospheric pressure.

7-*Phenyl*-3 : 4-*benzacridine*.—The *base* obtained from β-naphthol (5 g.), *p*-aminodiphenyl (5 g.), and paraformaldehyde (1 g.) crystallised from alcohol in long, pale yellow, silky prisms (0·5 g.), m. p. 116°, very soluble in benzene and in hot alcohol (Found : N, 4·6. $C_{23}H_{15}N$ requires N, 4·5%). The *picrate* formed orange-yellow needles, m. p. 309—310° (decomp.), from nitrobenzene (Found : N, 10·8. $C_{23}H_{15}N,C_6H_3O_7N_3$ requires N, 10·4%). The hydrobromide crystallised from alcohol in tufts of silky yellow needles.

N-*Phenyl*-4-*methyl*-α-*naphthylamine*.—Obtained from 4-methyl-α-naphthylamine (10 g.), aniline (15 g.), and iodine (0·1 g.) in the ordinary manner, this *base* formed a viscous yellow oil (15 g.), b. p. 230—240°/15 mm., which set to a crystalline mass on standing (Found : N, 6·1. $C_{17}H_{15}N$ requires N, 6·0%).

3 : 5-*Dimethyl*-1 : 2-*benzacridine*.—The *base* (2 g.), obtained from the foregoing amine (5 g.), acetic anhydride (5 g.), and zinc chloride (8 g.), crystallised from alcohol–benzene in long, pale yellow, silky needles, m. p. 167° (Found : N, 5·6. $C_{19}H_{15}N$ requires N, 5·4%). The *picrate* formed orange-yellow prisms, m. p. 240—241° (decomp. above 225°), from chlorobenzene (Found : N, 11·2. $C_{19}H_{15}N,C_6H_3O_7N_3$ requires N, 11·5%).

N-o-*Tolyl*-4-*methyl*-α-*naphthylamine*.—This *base* was a viscous yellow oil, b. p. 240—250°/13 mm., which darkened rapidly on exposure to the air and did not solidify even after 2 years (Found : N, 5·4. $C_{18}H_{17}N$ requires N, 5·6%).

3 : 5 : 9-*Trimethyl*-1 : 2-*benzacridine*.—The *picrate* of this base crystallised from alcohol–benzene in orange-yellow prisms, m. p. 225—226° (Found : N, 11·4. $C_{20}H_{17}N,C_6H_3O_7N_3$ requires N, 11·2%). The free *base* formed long, silky, yellow needles, m. p. 127—128° (Found : N, 5·4. $C_{20}H_{17}N$ requires N, 5·2%).

N-o-*Xylyl*-α-*naphthylamine*.—This *amine* (21 g.) was obtained from 3 : 4-dimethylaniline (15 g.), α-naphthylamine (18 g.), and iodine (0·1 g.) in the form of a viscous yellow oil, b. p. 241—243°/12 mm. (Found : N, 5·6. $C_{18}H_{17}N$ requires N, 5·6%). The addition compound with picric acid crystallised from alcohol in long, silky, dark violet needles, m. p. 121°.

5 : 7 : 8-*Trimethyl*-1 : 2-*benzacridine*.—The *base* (2·5 g.) obtained on heating the foregoing amine (5 g.) with acetic anhydride (5 g.) and zinc chloride (7 g.) at 220—225° for 4 hours formed long, silky, pale yellow needles, m. p. 144°, from alcohol–benzene (Found : N, 5·3. $C_{20}H_{17}N$ requires N, 5·2%). The *picrate* separated from chlorobenzene in orange-yellow prisms, m. p. 255—256° (decomp.) (Found : N, 11·2. $C_{20}H_{17}N,C_6H_3O_7N_3$ requires N, 11·2%).

N-o-*Xylyl*-β-*naphthylamine*.—This *amine* (22 g.), obtained from 3 : 4-dimethylaniline (20 g.), β-naphthol (20 g.), and iodine (0·1 g.), formed long colourless prisms from alcohol, m. p. 116°, b. p.

256—257°/15 mm. (Found : N, 5·4. $C_{18}H_{17}N$ requires N, 5·6%). This amine is much less soluble in the ordinary solvents than are its isomers described above.

5 : 7 : 8-*Trimethyl* 3 : 4-*benzacridine*.—The *base* formed faintly yellow needles from alcohol, m. p. 176—177° (Found : N, 5·2. $C_{20}H_{17}N$ requires N, 5·2%), and the *picrate* fine orange-yellow needles from nitrobenzene, m. p. above 285° (decomp.), very slightly soluble in chlorobenzene (Found : N, 11·4. $C_{20}H_{17}N,C_6H_3O_7N_3$ requires N, 11·2%).

N-s-m-*Xylyl*-β-*naphthylamine*.—From *s*-*m*-xylidine (10 g.), β-naphthol (10 g.), and iodine (0·01 g.), was obtained an *amine* (5 g.), b. p. 238—245°/15 mm., which crystallised from alcohol in long, glistening, colourless needles, m. p. 94°, extremely soluble in benzene (Found : N, 5·6. $C_{18}H_{17}N$ requires N, 5·6%).

TABLE I.

5-Substituted 1 : 2-*benzacridines*.

Substituent.	Acid used in prepn.	Crystal form.	M. p. (and b. p.).	Formula.	N, %, found.	N, %, required.
n-Propyl	*n*-Butyric	Yellow prisms	87° (280—282°/2 mm.)	$C_{20}H_{17}N$	5·0	5·2
*iso*Butyl	*iso*Valeric	Glistening yellow prisms	107	$C_{21}H_{19}N$	5·1	4·9
n-Amyl.....	Hexoic	Silky glistening needles	84	$C_{22}H_{21}N$	4·6	4·7
n-Heptyl	*n*-Octoic	Almost colourless needles	60	$C_{24}H_{25}N$	4·4	4·2
4-Heptyl	Di-*n*-propylacetic	Soft silky needles	79 (295—300°/10 mm.)	$C_{24}H_{25}N$	4·2	4·2
n-Octyl.....	Nonoic	Soft needles	48	$C_{25}H_{27}N$	4·3	4·1
n-Nonyl	Decoic	Long soft needles	51	$C_{26}H_{29}N$	4·0	3·9
n-Heptadecyl	Stearic	Silky colourless needles	82 (370—372°/20 mm.)	$C_{34}H_{45}N$	3·0	2·9
Phenyl	Benzoic	Silky pale yellow prisms	140 (320—325°/18 mm.)	$C_{23}H_{15}N$	4·3	4·5
Benzyl	Phenylacetic	Silky yellow needles	145° (300°/10 mm.)	$C_{24}H_{17}N$	4·4	4·3

TABLE I(*a*).

Picrates of 5-substituted 1 : 2-*benzacridines*.

Substituent.	Crystal form.*	M. p.†	Formula.	N, %, found.	N, %, required.
n-Propyl	Yellow needles	237° †	$C_{26}H_{20}O_7N_4$	11·4	11·2
*iso*Butyl	Brilliant yellow leaflets	230—231 †	$C_{27}H_{22}O_7N_4$	11·2	10·9
n-Amyl	Yellow needles	187—188 †	$C_{28}H_{24}O_7N_4$	10·8	10·6
n-Heptyl	Silky yellow needles (C_6H_6)	194—196 †	$C_{30}H_{28}O_7N_4$	10·3	10·0
4-Heptyl	Orange-yellow needles	200—202 †	$C_{30}H_{28}O_7N_4$	10·2	10·0
n-Octyl	Silky yellow needles (C_6H_6)	176	$C_{31}H_{30}O_7N_4$	10·1	9·8
n-Nonyl	Silky yellow needles (C_6H_6)	155—156	$C_{32}H_{32}O_7N_4$	9·4	9·6
n-Heptadecyl	Long soft needles (C_6H_6)	108	$C_{40}H_{48}O_7N_4$	8·2	8·0
Phenyl	Dark yellow prisms	(Decomp. at 204—205°)	$C_{29}H_{18}O_7N_4$	10·8	10·5
Benzyl	Orange-yellow needles	(Decomp. at 220—222°)	$C_{30}H_{20}O_7N_4$	10·5	10·2

* All crystallised from nitrobenzene except where benzene is specified in parentheses.
† M. p.s marked thus are with decomposition.

5 : 6 : 8-*Trimethyl*-3 : 4-*benzacridine*.—The *base* (3 g.) obtained from the preceding amine (5 g.), acetic anhydride (5 g.), and zinc chloride (10 g.) crystallised from hot alcohol (very easily soluble) in beautiful pale yellow needles, m. p. 159—160° (Found : N, 5·3. $C_{20}H_{17}N$ requires N, 5·2%). The *picrate* formed silky, orange-yellow needles from nitrobenzene, which decomposed on being heated above 290° without having a definite m. p. up to 310° (Found : N, 11·4. $C_{20}H_{17}N,C_6H_3O_7N_3$ requires N, 11·2%).

Preparation of 5-*Substituted* 1 : 2- *and* 3 : 4-*Benzacridines*.—The standard procedure employed in the preparation of the *benzacridines* listed in Tables I and II consisted in heating in a metal-bath *N*-phenyl-α-naphthylamine or the β-isomer with a large excess of the required acid and freshly-fused powdered zinc chloride. The duration (generally 24—36 hours) and the temperature (220—250°) of heating depend

upon the nature of the acid used, and are greater for long-chain aliphatic than for aromatic acids. The procedure for the treatment of the dark sticky mass obtained was the ordinary one, and vacuum-distillation was extensively used for separation. In most cases, purification through the *picrate* was necessary to obtain the solid base. Crystallisations were made from alcohol or alcohol–benzene, most of the benzacridines being very soluble in the latter.

Oxidation of 5-Benzyl-3 : 4-benzacridine.—A mixture of this benzacridine (2 g.), selenium dioxide (1 g.), and dry xylene (20 c.c.) was heated under reflux for 6 hours; after filtration from the precipitated selenium, the solvent was removed in a vacuum, and the brown semi-solid residue dissolved in hot alcohol. The solid (0·5 g.) obtained on cooling was recrystallised from the same solvent, giving *5-benzoyl-3 : 4-benzacridine* in microscopic bright yellow needles (Found : N, 4·5. $C_{24}H_{15}ON$ requires N, 4·2%),

TABLE II.

5-Substituted 3 : 4-benzacridines.

Substituent.	Acid used in prepn.	Crystal form.	M. p. (and b. p.).	Formula.	N, %, found.	N, %, required.
n-Propyl	*n*-Butyric	Almost colourless needles	108°	$C_{20}H_{17}N$	5·1	5·2
*iso*Butyl	*iso*Valeric	Glistening yellow leaflets	115 (285—290°/12 mm.)	$C_{21}H_{19}N$	5·2	5·0
n-Amyl.....	Hexoic	Long silky needles	93 (305—310°/16 mm.)	$C_{22}H_{21}N$	4·4	4·7
3-Pentyl	Diethylacetic	Long silky needles	120	$C_{22}H_{21}N$	4·6	4·7
n-Heptyl	Octoic	Soft almost colourless needles	105	$C_{24}H_{25}N$	4·3	4·2
4-Hepyl	Di-*n*-propylacetic	Long soft needles	74—75	$C_{24}H_{25}N$	4·2	4·2
n-Octyl.....	Nonoic	Long silky needles	101 (322°/20 mm.)	$C_{25}H_{27}N$	4·2	4·1
n-Nonyl	Decoic	Long silky colourless needles	74—75	$C_{26}H_{29}N$	4·1	3·9
Benzoyl	Phenylacetic	Almost colourless tufts	143	$C_{24}H_{17}N$	4·3	4·6
α-Naphthyl ...	α-Naphthoic	Yellow microcrystals	209	$C_{27}H_{17}N$	4·1	3·9

TABLE II(*a*).

Picrates of 5-substituted 3 : 4-benzacridines.

Substituent.	Crystal form.*	M. p.†	Formula.	N, %, found.	N, %, required.
n-Propyl	Golden-yellow leaflets	244—245° †	$C_{26}H_{20}O_7N_4$	11·3	11·2
*iso*Butyl	Glistening yellow needles	213—214 †	$C_{27}H_{22}O_7N_4$	11·0	10·9
n-Amyl.....	Fine yellow needles	225 †	$C_{28}H_{24}O_7N_4$	10·4	10·6
3-Pentyl	Fine yellow needles (C_6H_6)	188—189	—	—	—
n-Heptyl	Silky golden-yellow needles	182—183	$C_{30}H_{28}O_7N_4$	10·3	10·0
4-Heptyl	Fine yellow needles	213—214 †	$C_{30}H_{28}O_7N_4$	10·2	10·0
n-Octyl.....	Fine yellow needles	192 †	$C_{31}H_{30}O_7N_4$	9·7	9·8
n-Nonyl	Glistening yellow leaflets	180—181	$C_{32}H_{32}O_7N_4$	9·9	9·6
Benzyl	Dark yellow needles	214—216 †	$C_{30}H_{20}O_7N_4$	10·1	10·2
α-Naphthyl	Bright yellow prisms (C_6H_6)	241—242 †	$C_{33}H_{20}O_7N_4$	9·0	9·5

* All crystallised from nitrobenzene except where benzene is specified in parentheses.
† M. p.s marked thus are with decomposition.

m. p. 220—221° (decomp.), easily soluble in benzene; the substance darkened on exposure to the air, and gave an intense greenish-yellow fluorescence with sulphuric acid. The *picrate* formed glistening yellow plates from nitrobenzene, m. p. 257—259° (decomp.) (Found : N, 10·1. $C_{30}H_{18}O_8N_4$ requires N, 9·9%).

5-α-Naphthyl-3 . 4 : 5 : 6-dibenzacridine.—A mixture of ββ-dinaphthylamine (2 g.) (Benz, *Ber.*, 1883, **16**, 17), α-naphthoic acid (2 g.), and zinc chloride (1 g.) was heated at 200—215° for 4 hours, during which much of the α-naphthoic acid lost carbon dioxide, giving a sublimate of naphthalene. The usual treatment with aqueous sodium hydroxide and toluene left a yellow residue. This *base* (0·2 g.) crystallised from xylene to give yellowish plates, m. p. 282° (with sublimation), almost insoluble in alcohol (Found : N, 3·5. $C_{31}H_{19}N$ requires N, 3·4%). The *picrate* formed dark yellow needles from chlorobenzene, m. p. 280—281° (decomp.) (Found : N, 9·1. $C_{37}H_{22}O_7N_4$ requires N, 8·8%).

Note.—Many acridines very strongly retain traces of the solvents used for their crystallisation, and the analytical data in this series of papers therefore relate to vacuum-distilled samples.

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