236. *The Chemistry of Carcinogenic Nitrogen Compounds. Part IV. New Substituted Angular Benzacridines and Dibenzacridines.*

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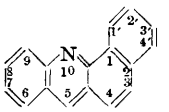
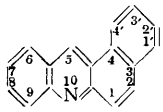
In continuation of earlier investigations (cf. Buu-Hoï, *J.*, 1946, 792; 1949, 670, 2882), numerous new angular benzacridines and dibenzacridines bearing substituents in various positions have been prepared by known methods for examination of their potential carcinogenic or anti-carcinogenic properties. In connection with this work, many new diarylamines and benzphenothiazines are described.

In the 1 : 2-benzanthracene and 1 : 2-benzacridine series, replacement of a methyl group at the *meso*-position by a heavier alkyl group always lowers, or even destroys, the carcinogenic activity (cf. Lacassagne, Buu-Hoï, Lecocq, and Rudali, *Bull. Cancer*, 1946, **33**, 48; 1947, **34**, 22; Shear and Leiter, *J. Nat. Cancer Inst.*, 1940, **1**, 103; Badger, Cook, *et al.*, *Proc. Roy. Soc.*, *B*, 1942, **131**, 170). For instance, 5-ethyl-7-methyl- and 5-ethyl-9-methyl-1 : 2-benzacridine are only slightly active, whereas both 5 : 7- and 5 : 9-dimethyl-1 : 2-benzacridine are extremely powerful carcinogens. Nevertheless, this rule does not necessarily hold when positions other

than the *meso* are involved; thus 6-*iso*propyl-1 : 2-benzanthracene has been found to be more active than the methyl homologue, and both 5-ethyl- and 5-*n*-propyl-1 : 2-benzanthracene also show marked activity (cf. Cook, " Ergebnisse der Vitamin- und Hormonforschung," 1939, Leipzig, p. 237).

(I.)   (II.)

In order to increase the number of substances to be studied from that point of view, many new homologues of 1 : 2- (I) and 3 : 4-benzacridine (II) bearing substituents of various sizes and shapes at the *meso*-position and elsewhere have now been prepared.

The Ullmann–Fettvadjian reaction (condensation of paraformaldehyde with a heated mixture of a naphthol and a primary arylamine; cf. *Ber.*, 1903, **36**, 1029) with *p-tert.*-amylaniline and α- and β-naphthol yielded 7-*tert.*-amyl-1 : 2- and -3 : 4-benzacridine respectively. The same reaction, applied to 2-methyl-5-*iso*propylaniline and β-naphthol, readily gave 9-methyl-6-*iso*propyl-3 : 4-benzacridine. 8-*iso*Propyl-3 : 4-benzacridine, an anologue of the carcinogenic 6-*iso*propyl-1 : 2-benzanthracene, was obtained by thermal cyclodehydration of *N*-cymyl-β-naphthylamine in the presence of lead oxide (cf. Ullmann and La Torre, *Ber.*, 1904, **37**, 2924); this secondary amine was prepared from β-naphthol and 2-methyl-5-*iso*propylaniline by the conventional Knoevenagel method (cf. Knoevenagel, *J. pr. Chem.*, 1914, **89**, 17).

In order to ascertain the effect of ethyl groups in the *meso*-position when several other substituents are also present, a large number of 5-ethyl-1 : 2- and -3 : 4-benzacridines bearing further radicals elsewhere was prepared (see Table I). Their synthesis was readily achieved by the modified Bernthsen reaction (Buu-Hoï and Lecocq, *Compt. rend.*, 1944, **218**, 648; *Rec. Trav. chim.*, 1945, **64**, 251), involving propionic anhydride, zinc chloride, and a series of diversely substituted *N*-arylnaphthylamines. Of these, *N*-3-chloro-2-methylphenyl-α- and -β-naphthylamine, previously unknown, were prepared as usual from 3-chloro-2-methylaniline and the appropriate naphthols, and gave 8-chloro-5 : 9-dimethyl-1 : 2- and -3 : 4-benzacridine. An Ullmann–Fettvadjian reaction could also be performed with 3-chloro-2-methylaniline and β-naphthol, yielding 8-chloro-9-methyl-3 : 4-benzacridine. In these chlorine-containing

TABLE I.

Substituted 5-ethyl-1 : 2-benzacridines.

Substituents.	α-Naphthylamines used.	Crystal form.	M. p.	Formula.	N, %. Found.	Reqd.
7-Methyl	*N-p*-tolyl-	needles	149°	$C_{20}H_{17}N$ [a]	5·0	5·2
8-Methyl	*N-m*-tolyl-	needles	85	$C_{20}H_{17}N$	5·2	5·2
9-Methyl	*N-o*-tolyl-	needles	83	$C_{20}H_{17}N$	5·0	5·2
8-Chloro-9-methyl	*N*-3-chloro-2-methylphenyl-	yellow prisms	134	$C_{20}H_{16}NCl$	4·5	4·6
7 : 8-Dimethyl ...	*N-o*-xylyl-	silky needles	143	$C_{21}H_{19}N$ [b]	4·7	4·9
8 : 9-Dimethyl ...	*N-vic.-o*-xylyl-	needles	95	$C_{21}H_{19}N$	4·6	4·9
6 : 7 : 9-Trimethyl	*N*-ψ-cumyl-	silky needles	125	$C_{23}H_{21}N$ [c]	4·6	4·7

Substituted 5-ethyl-3 : 4-benzacridines.

Substituents.	β-Naphthylamines used.	Crystal form.	M. p.	Formula.	N, %. Found.	Reqd.
7-Methyl	*N-p*-tolyl-	needles	134°	$C_{20}H_{17}N$	5·0	5·2
8-Methyl	*N-m*-tolyl-	needles	145	$C_{20}H_{17}N$	5·0	5·2
9-Methyl	*N-o*-tolyl-	needles	138	$C_{20}H_{17}N$ [d]	5·1	5·2
8-Chloro	*N-m*-chlorophenyl-	needles	175	$C_{19}H_{14}NCl$	4·5	4·8
7 : 8-Dimethyl	*N-o*-xylyl-	needles	165	$C_{21}H_{19}N$ [e]	4·8	4·9
7 : 9-Dimethyl	*N-as.-m*-xylyl-	needles	159	$C_{21}H_{19}N$ [f]	4·8	4·9
8 : 9-Dimethyl	*N-vic.-o*-xylyl-	needles	137	$C_{21}H_{19}N$ [g]	4·9	4·9
8-Chloro-9-methyl	*N*-3-chloro-2-methylphenyl-	needles	133	$C_{20}H_{16}NCl$	4·3	4·5
6 : 7 : 9-Trimethyl	*N*-ψ-cumyl-	needles	156	$C_{22}H_{21}N$	4·5	4·7
7-*tert.*-Amyl	*N-p-tert.*-amylphenyl-	oil	[h]	$C_{24}H_{25}N$	4·2	4·3

[a] Found : C, 88·4; H, 6·2. Required : C, 88·5; H, 6·2%. [b] Found : C, 88·2; H, 6·8. Required : C, 88·4; H, 6·6%. [c] Found : C, 88·2; H, 7·2. Required : C, 88·3; H, 7·0%. [d] Found : C, 88·4; H, 6·3. Required : C, 88·5; H, 6·2%. [e] Found : C, 88·4; H, 6·8. Required : C, 88·4; H, 6·6%. [f] Found : C, 88·2; H, 6·7%. [g] Found : C, 88·2; H, 6·8%. [h] B. p. 300—310°/14 mm.

TABLE Ia.

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

Substituents.	Crystal form.[a]	M. p.	Formula.	N, %. Found.	Reqd.
7-Methyl	yellow needles	208—209°	$C_{26}H_{20}O_7N_4$	11·3	11·2
8-Methyl	yellow needles	213—214	$C_{26}H_{20}O_7N_4$	11·0	11·2
9-Methyl	orange needles	146[b]	$C_{26}H_{20}O_7N_4$	10·9	11·2
7 : 8-Dimethyl	yellow needles	212—213	$C_{27}H_{22}O_7N_4$	10·6	10·9
8 : 9-Dimethyl	orange needles	170—171°[b]	$C_{27}H_{22}O_7N_4$	10·8	10·9
6 : 7 : 9-Trimethyl	orange needles	154—156[b]	$C_{28}H_{24}O_7N_4$	10·4	10·6

Picrates of substituted 5-ethyl-3 : 4-benzacridines.

Substituents.	Crystal form.	M. p.	Formula.	N, %. Found.	Reqd.
7-Methyl	yellow needles	244—245°	$C_{26}H_{20}O_7N_4$	11·1	11·2
8-Methyl	orange needles	243—245	$C_{26}H_{20}O_7N_4$	11·0	11·2
9-Methyl	yellow needles	240—241	$C_{26}H_{20}O_7N_4$	11·0	11·2
8-Chloro	yellow needles	dec. >216	$C_{25}H_{17}O_7N_4Cl$	10·4	10·7
7 : 8-Dimethyl	yellow needles	256—258	$C_{27}H_{22}O_7N_4$	11·0	10·9
7 : 9-Dimethyl	yellow needles	dec. >260	$C_{27}H_{22}O_7N_4$	10·8	10·9
8 : 9-Dimethyl	orange needles	237—238	$C_{27}H_{22}O_7N_4$	10·6	10·9
8-Chloro-9-methyl	yellow needles	222—223	$C_{26}H_{19}O_7N_4Cl$	10·6	10·8
6 : 7 : 9-Trimethyl	orange needles	266—267	$C_{28}H_{24}O_7N_4$	10·3	10·6
7-*tert.*-Amyl	yellow prisms	203—204	$C_{30}H_{28}O_7N_4$	9·7	10·0

[a] All *picrates*, except those of 9-methyl-, 8 : 9-dimethyl-, and 6 : 7 : 9-trimethyl-1 : 2-benzacridine (which were readily soluble in ethanol and were recrystallised from that solvent), were recrystallised from a great volume of xylene. [b] These low m. p.s are characteristic of picrates of 1 : 2-benzacridines bearing a methyl group in the 9-position (cf. Buu-Hoï, *J.*, 1949, 670).

substances, the halogen atom occupies a position similar to that in 6-chloro-10-methyl-1 : 2-benzanthracene (Newman and Orchin, *J. Amer. Chem. Soc.*, 1939, **61**, 244). From *N*-*p*-chlorophenyl-β-naphthylamine and acetic anhydride, 7-chloro-5-methyl-3 : 4-benzacridine was prepared, the position of the halogen atom being akin to that in the carcinogenic 7-chloro-10-methyl-1 : 2-benzanthracene (*idem. ibid.*, 1938, **60**, 586).

TABLE II.

Substituted 1 : 2- and 3 : 4-benzphenothiazines.

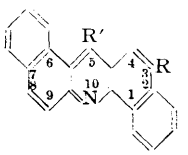
Substituents.	Naphthylamines used.	Crystal form.	M. p.	Formula.	N, %. Found.	Req.
7 : 8-Dimethyl-3 : 4-	*N*-*o*-xylyl-β-	yellowish needles	182°	$C_{18}H_{15}NS$[a]	4·9	5·0
6 : 9-Dimethyl-3 : 4-	*N*-*p*-xylyl-β-	silky needles	170	$C_{18}H_{15}NS$[b]	4·7	5·0
8 : 9-Dimethyl-3 : 4-	*N*-*vic.*-*o*-xylyl-β-	silky needles	182	$C_{18}H_{15}NS$[c]	5·0	5·0
8-Chloro-9-methyl-3 : 4-	*N*-3-chloro-2-methylphenyl-β-	pale yellow prisms	193	$C_{17}H_{12}NSCl$	4·6	4·7
7-*tert.*-Amyl-3 : 4-	*N*-*p*-*tert.*-amylphenyl-β-	pale yellow needles	123	$C_{21}H_{21}NS$[d]	4·2	4·4
7-*sec.*-Amyl-3 : 4-	*N*-*p*-*sec.*-amylphenyl-β-	greenish oil	[f]	$C_{21}H_{21}NS$	4·5	4·4
9-Methyl-6-*iso*propyl-3 : 4-	*N*-cymyl-β-	greenish oil	[g]	$C_{20}H_{19}NS$	4·8	4·6
7-Phenyl-3 : 4-	*N*-4-diphenylyl-β-	yellow needles	226	$C_{22}H_{15}NS$	4·3	4·3
7 : 8-Dimethyl-1 : 2-	*N*-*o*-xylyl-α-	silky needles	176	$C_{18}H_{15}NS$	4·8	5·0
7-Phenyl-1 : 2-	*N*-4-diphenylyl-α-	yellow needles	160	$C_{22}H_{15}NS$[e]	4·1	4·3

[a] Found : S, 12·3. Required : S, 11·9%. [b] Found : S, 12·1%. [c] Found : S, 12·1%. [d] Found : S, 10·3. Required : S, 10·0%. [e] Found : S, 10·0. Required : S, 9·8%. [f] B. p. 310—320°/18 mm. [g] B. p. 311—315°/20 mm.

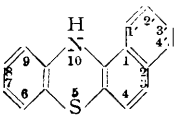
Replacement, in the Bernthsen reaction, of acetic and propionic anhydrides by higher aliphatic acid anhydrides allowed the preparation of further polysubstituted 3 : 4-benzacridines, namely, 7- and 9-methyl-5-*n*-propyl-, 6 : 7 : 9-trimethyl-5-*n*-propyl-, 5-*n*-butyl-6 : 7 : 9-trimethyl-, 5-*iso*butyl-7-methyl-, and 5-*n*-amyl-7-methyl-3 : 4-benzacridine. Aromatic *meso*-substitution is present in 8-methyl-5-phenyl-, 7 : 9-dimethyl-5-phenyl-, and 6 : 7 : 9-trimethyl-5-phenyl-3 : 4-benzacridine, prepared by means of benzoic anhydride and the appropriate secondary amines. The introduction of a phenyl group in other positions was also achieved by performing Bernthsen reactions on *N*-2-diphenylyl-β- and -α-naphthylamine (prepared as usual from *o*- and *p*-aminodiphenyl); 5-methyl-7-phenyl-1 : 2- and 5-methyl-9-phenyl-3 : 4-benzacridine were thus prepared. In view of the carcinogenic activity observed in some phenol

ethers of the 1 : 2-benzanthracene series such as 3-methoxy-, 10-methoxy-, and 10-methyl-3-methoxy-1 : 2-benzanthracene (Fieser and Dietz, *ibid.*, 1929, **51**, 3141; Fieser and Hershberg, *ibid.*, 1937, **59**, 1028), a similar compound in the benzacridine series, 9-methoxy-5-methyl-3 : 4-benzacridine, was prepared from *N*-*o*-methoxyphenyl-β-naphthylamine and acetic anhydride in the usual way.

The relation between carcinogenicity and substitution in the series of dibenzacridines has scarcely been explored as yet, and the preparation of some homologues of bisangular dibenzacridines is therefore recorded here: 3-methyl-1 : 2 : 6 : 7-dibenzacridine (III; R′ = H, R = Me) was obtained by an Ullmann–Fettvadjian reaction between 4-methyl-1-naphthylamine, β-naphthol, and paraformaldehyde; an *x-tert.*-butyl-1 : 2 : 6 : 7-dibenzacridine was similarly obtained from α-naphthylamine and a *tert.*-butyl-2-naphthol of unknown constitution prepared from trimethylcarbinol and β-naphthol (Tschitschibabin, *Bull. Soc. chim.*, 1935, [v], **2**, 497). 5-*n*-Butyl- (III; R = H, R′ = Bu^n), and 5-*iso*butyl-1 : 2 : 6 : 7-dibenzacridine (III; R = H, R′ = Bu^i) were easily prepared from αβ-dinaphthylamine with *n*-valeric and *iso*valeric acid by the Bernthsen reaction.


(III.)


(IV.)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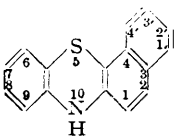
(VI.)

In the 3 : 4 : 6 : 7-dibenzacridine series, 5-ethyl- (IV; R = Et), 5-*iso*propyl- (IV; R = Pr^i), and 5-*iso*butyl-3 : 4 : 6 : 7-dibenzacridine (IV; R = Bu^i) have similarly been obtained from di-β-naphthylamine and propionic, *iso*butyric, and *iso*valeric acid, respectively. It may be mentioned that di-β-naphthylamine was best prepared by heating β-naphthylamine with a little iodine, the Knoevenagel procedure yielding a product which contained *N*-phenyl-β-naphthylamine (cf. Buu-Hoï, *loc. cit.*). It may be recalled in this respect that 5-methyl-3 : 4 : 6 : 7-dibenzacridine has been found to be moderately carcinogenic (Lacassagne, Buu-Hoï, Lecocq, and Rudali, *loc. cit.*), whereas the non-methylated 3 : 4 : 6 : 7-dibenzacridine proved very feebly so (cf. Barry *et al.*, *Proc. Roy. Soc.*, 1935, *B*, **117**, 318).

TABLE III.

5-Substituted acridines.

Substituents.	Acid used.	Crystal form.*	M. p.	Formula.	N, %. Found.	N, %. Reqd.
5-*n*-Amyl	hexoic	needles L	69°	$C_{18}H_{19}N$	5·4	5·6
5-*n*-Octyl	pelargonic	yellowish oil	[a]	$C_{21}H_{25}N$	5·0	4·8
5-*n*-Decyl	*n*-undecoic	needles L	50	$C_{23}H_{29}N$	4·3	4·4
5-*cyclo*Hexyl	hexahydrobenzoic	needles L	85	$C_{19}H_{19}N$	5·2	5·3
5-(2-Phenyl-*n*-butyl)	β-phenylvaleric	prisms L	109	$C_{23}H_{21}N$	4·3	4·9
5-*p*-*n*-Propylphenyl	*p*-propylbenzoic	prisms E	191	$C_{22}H_{19}N$	4·9	4·7
5-α-Naphthyl	α-naphthoic	prisms B	197	$C_{23}H_{15}N$	4·5	4·6
5-β-Naphthyl	β-naphthoic	needles B	248	$C_{23}H_{15}N$	4·3	4·6
5-Benzyl-3 : 7-dimethyl	phenylacetic	needles E	185	$C_{22}H_{19}N$	4·9	4·7
5-α-Naphthyl-3 : 7-dimethyl	α-naphthoic	prisms B	194	$C_{25}H_{19}N$	4·1	4·2

TABLE IIIa.

Picrates of 5-substituted acridines.

Substituents.	Crystal form.*	M. p.	Formula.	N, %. Found.	N, %. Reqd.
5-*n*-Amyl	yellow needles E	207°	$C_{24}H_{22}O_7N_4$	11·6	11·7
5-*n*-Octyl	needles E	194	$C_{27}H_{28}O_7N_4$	10·5	10·7
5-*n*-Decyl	needles E	159	$C_{29}H_{32}O_7N_4$	10·0	10·2
5-*cyclo*Hexyl	needles C	220 [b]	$C_{25}H_{22}O_7N_4$	11·1	11·4
5-*p*-*n*-Propylphenyl	needles C	230—232 [b]	$C_{28}H_{22}O_7N_4$	10·5	10·6
5-(3-Phenyl-*n*-butyl)	needles E	217	$C_{29}H_{24}O_7N_4$	10·1	10·4
5-α-Naphthyl	orange leaflets C	266—268 [b]	$C_{29}H_{18}O_7N_4$	10·3	10·5
5-β-Naphthyl	orange needles C	268 [b]	$C_{29}H_{18}O_7N_4$	10·2	10·5
5-Benzyl-3 : 7-dimethyl	prisms C	223 [b]	$C_{28}H_{22}O_7N_4$	10·4	10·6
3 : 7-Dimethyl-5-α-naphthyl...	orange prisms C	256—260 [b]	$C_{31}H_{22}O_7N_4$	10·8	11·1

* *Solvents:* B benzene; C chlorobenzene; E ethanol; L ligroin. [a] B. p. 220°/0·5 mm. [b] With decomp.

In view of the strong inhibitory effect of certain benzphenothiazines on grafted tumours (Badger *et al.*, *Proc. Roy. Soc.*, 1942, *B*, **130**, 255), and of the structural relation between that kind of compound and the carcinogenic benzacridines and benzcarbazoles, a number of derivatives of 1 : 2- (V) and 3 : 4-benzphenothiazine (VI) was prepared by heating the appropriate diarylamines with sulphur in the presence of iodine (Knoevenagel, *J. pr. Chem.*, 1914, **89**, 23) (see Table II; for similar compounds, see Buu-Hoï *et al.*, *Rev. scientif.*, 1944, **82**, 39; 1945, **83**, 170).

Following the findings of Spear (cited by Cook, *Amer. J. Cancer*, 1940, **39**, 386) concerning the hastening of the carcinogenic action of 3 : 4-benzpyrene by quinaldine and *iso*quinoline, various diversely substituted acridines have been synthesised from diphenylamine and aliphatic and cyclic acids (see Table III). A significant fact observed was the ready formation of cinnamic anhydride in fairly good yield, in the course of an attempt to synthesise 5-styrylacridine by heating cinnamic acid with diphenylamine and zinc chloride. This unexpected route to cinnamic anhydride might be useful for its preparation.

Most of the new substances quoted above have been, or are now, under biological examination by Professor A. Lacassagne in this Institute.

Experimental.

7-tert.-*Amyl*-1 : 2-*benzacridine*.—To a boiling mixture of α-naphthol (5 g.) and *p-tert.*-amylaniline (5 g.), paraformaldehyde (0·5 g.) was cautiously added in small portions; after 10 minutes' further refluxing, vacuum-distillation yielded an orange oil (b. p. *ca.* 300°/18 mm.) which was dissolved in ethanol and treated with picric acid. The crude *picrate* obtained (2·5 g.) was recrystallised twice from xylene, yielding glinting orange-yellow leaflets, m. p. 207—209° (decomp.) (Found: N, 10·7. $C_{28}H_{24}O_7N_4$ requires N, 10·6%). The free *base* obtained on treatment of the picrate with dilute aqueous ammonia was extracted with benzene, and crystallised from ligroin in long almost colourless needles, m. p. 98° (Found: N, 4·7. $C_{22}H_{21}N$ requires N, 4·7%); its hydrochloride formed, from aqueous ethanol, yellow prisms, m. p. 205—215°.

7-tert.-*Amyl*-3 : 4-*benzacridine*.—Similarly obtained from *p-tert.*-amylaniline (10 g.), β-naphthol (10 g.), and paraformaldehyde (1 g.), etc., the *picrate* formed, from nitrobenzene, fine deep-yellow needles, m. p. 254—256° (decomp.) (Found: N, 10·5. $C_{28}H_{24}O_7N_4$ requires N, 10·6%). The *base* (1 g.) crystallised from methanol in pale yellow needles, m. p. 97°, b. p. 295—298°/15 mm. (Found: C, 88·0; H, 7·1; N, 4·6. $C_{22}H_{21}N$ requires C, 88·3; H, 7·0; N, 4·7%); the hydrochloride formed long silky deep-yellow needles, m. p. *ca.* 248—253°, from aqueous ethanol.

9-*Methyl*-6-iso*propyl*-3 : 4-*benzacridine*.—This *compound* (2 g.), obtained from β-naphthol (8 g.), 2-aminocymene (6 g.), and paraformaldehyde (1 g.), formed, from ethanol, long pale yellow needles, m. p. 130—131°, b. p. 295—298°/35 mm. (Found: C, 88·4; H, 6·8; N, 4·6. $C_{21}H_{19}N$ requires C, 88·4; H, 6·6; N, 4·9%); its *picrate* crystallised from xylene in orange-yellow silky needles, m. p. 246—248° (decomp.) (Found: N, 11·0. $C_{27}H_{22}O_7N_4$ requires N, 10·9%).

N-2-*Methyl*-5-iso*propylphenyl*-β-*naphthylamine*.—A mixture of aminocymene (15 g.), β-naphthol 15 g.), and iodine (0·2 g.) was refluxed for 16 hours, and the dark oil formed was taken up in benzene, washed with aqueous sodium hydroxide, and dried (Na_2SO_4); after removal of the solvent, the residue was fractionated in a vacuum, giving 12 g. of a thick yellowish oily *base*, b. p. 256—258°/18 mm., readily autoxidised in the air (Found: N, 5·0. $C_{20}H_{21}N$ requires N, 5·1%).

8-iso*Propyl*-3 : 4-*benzacridine*.—The foregoing amine (2·5 g.) was heated in a Claisen flask at 350° with finely powdered lead oxide (25 g.) for some minutes, the temperature being subsequently raised to the b. p.; the oily yellow distillate was dissolved in hot ethanol, and picric acid added. The *picrate* thereby obtained formed, from nitrobenzene, fine yellow needles, m. p. 276° (Found: N, 11·0. $C_{26}H_{20}O_7N_4$ requires N, 11·2%); the free *base* (0·1 g.) formed, from aqueous methanol, silky almost colourless needles, m. p. 111—112° (Found: C, 88·2; H, 6·4; N, 5·4. $C_{20}H_{17}N$ requires C, 88·5; H, 6·2; N, 5·2%).

N-3-*Chloro*-2-*methylphenyl*-α-*naphthylamine*.—Obtained in the usual way from α-naphthol (15 g.), 3-chloro-2-methylaniline (15 g.), and iodine (0·2 g.) (18 hours' refluxing), this *amine* formed, from ligroin, colourless prisms, m. p. 71°, b. p. 251—253°/18 mm. (Found: N, 5·0. $C_{17}H_{14}NCl$ requires N, 5·2%). The isomeric N-3-*chloro*-2-*methylphenyl*-β-*naphthylamine* (20 g.), similarly obtained from β-naphthol, formed, from ligroin, colourless needles, m. p. 75°, b. p. 259—260°/18 mm. (Found: N, 5·1%).

8-*Chloro*-5 : 9-*dimethyl*-1 : 2-*benzacridine*.—*N*-3-Chloro-2-methylphenyl-α-naphthylamine (4 g.) was heated with acetic anhydride (5 c.c.) and dry zinc chloride (7 g.) at 190—200° for 20 hours. The mixture was treated thoroughly with hot aqueous sodium hydroxide and xylene. The organic layer was separated and dried (KOH), the solvent removed, and the dark viscous residue vacuum-distilled. The sticky orange-yellow distillate (3·5 g.) crystallised from benzene in long silky pale yellow needles, m. p. 173°, sparingly soluble in ethanol (Found: N, 5·0. $C_{19}H_{14}NCl$ requires N, 4·8%).

8-*Chloro*-5 : 9-*dimethyl*-3 : 4-*benzacridine*.—Prepared as above, this *compound* formed, from benzene, pale yellow silky needles, m. p. 186°, also sparingly soluble in ethanol (Found: N, 4·8%); the *picrate* formed, from toluene, silky orange-yellow prisms, m. p. 208—209° (Found: N, 10·4. $C_{25}H_{17}O_7N_4Cl$ requires N, 10·7%).

8-*Chloro*-9-*methyl*-3 : 4-*benzacridine*.—The vacuum-distilled *product* (slight decomp.) obtained from β-naphthol (10 g.), 3-chloro-2-methylaniline (10 g.), and paraformaldehyde (1 g.) crystallised from ethanol in long pale yellow prisms, m. p. 181° (0·5 g.) (Found: C, 77·6; H, 4·4; N, 5·2. $C_{18}H_{12}NCl$ requires

C, 77·8; H, 4·3; N, 5·0%). An attempt to prepare 7-chloro-3 : 4-benzacridine by applying the Ullmann–Fettvadjian reaction to *p*-chloroaniline failed.

7-*Chloro*-5-*methyl*-3 : 4-*benzacridine*.—*N*-*p*-Chlorophenyl-β-naphthylamine (4 g.), heated at 190—200° with acetic anhydride (5 c.c.) and dry zinc chloride (7 g.) for 18 hours, yielded a *base* crystallising from ethanol in long pale yellow needles, m. p. 160° (Found : N, 4·9%); its picrate formed, from xylene, orange-yellow silky needles which charred above 240—245°. For other 1 : 2-benzacridines see Table II.

7-*Methyl*-5-n-*propyl*-3 : 4-*benzacridine*, *etc.*—*N*-*p*-Tolyl-β-naphthylamine (5 g.) was heated with *n*-butyric acid (5 g.) and fused zinc chloride (10 g.) to 200° for 4 hours and then to 210—225° for 20 hours. After the usual treatment, 7-*methyl*-5-n-*propyl*-3 : 4-*benzacridine* was obtained as a yellow viscous resin (4 g.), b. p. 310—315°/70 mm., which crystallised from benzene–ligroin in fine almost colourless needles, m. p. 112°, sparingly soluble in alcohol (Found : N, 5·2. $C_{21}H_{19}N$ requires N, 4·9%); its *picrate* formed deep-yellow prisms, m. p. 254—256°, from nitrobenzene (Found : N, 10·8. $C_{27}H_{22}O_7N_4$ requires N, 10·6%). 9-*Methyl*-5-n-*propyl*-3 : 4-*benzacridine*, similarly prepared from *N*-*o*-tolyl-β-naphthylamine, formed glistening yellowish plates, m. p. 111—112°, from alcohol (Found : C, 88·2; H, 6·6; N, 5·1. $C_{21}H_{19}N$ requires C, 88·4; H, 6·7; N, 4·9%); the *picrate* crystallised from benzene in fine yellow needles, m. p. 211—212° (decomp.) (Found : N, 10·6%). 6 : 7 : 9-*Trimethyl*-5-n-*propyl*-3 : 4-*benzacridine* formed tufts of glinting silky needles, m. p. 135° (Found : C, 88·0; H, 7·3; N, 4·4. $C_{23}H_{23}N$ requires C, 88·1; H, 7·3; N, 4·5%); the *picrate* (fine yellow prisms from benzene) decomposed above 240° (Found : N, 10·4. $C_{29}H_{26}O_7N_4$ requires N, 10·3%). 5-iso*Butyl*-7-*methyl*-3 : 4-*benzacridine*, obtained in 80% yield, had b. p. 270—272°/10 mm., and formed long silky almost colourless needles, m. p. 110—111°, from methanol (Found : N, 4·5. $C_{22}H_{21}N$ requires N, 4·7%); this compound is extremely soluble in benzene and ethanol, and gives a *picrate* separating from benzene in bright yellow prisms, m. p. 230—232° (decomp.) (Found : N, 10·4. $C_{28}H_{24}O_7N_4$ requires N, 10·6%). 5-n-*Amyl*-7-*methyl*-3 : 4-*benzacridine* had b. p. 290—295°/12 mm., and formed unctuous tufts of long silky needles, m. p. 82°, from alcohol (Found : N, 4·4. $C_{23}H_{23}N$ requires N, 4·5%); the *picrate* crystallised from chlorobenzene in yellow prisms, m. p. 233—234° (decomp.) (Found : N, 10·4. $C_{29}H_{26}O_7N_4$ requires N, 10·3%). 5-n-*Butyl*-6 : 7 : 9-*trimethyl*-3 : 4-*benzacridine*, also obtained in good yield, formed long colourless fluffy needles, m. p. 135°, sparingly soluble in alcohol (Found : N, 4·3. $C_{24}H_{25}N$ requires N, 4·2%); its *picrate* formed silky yellow needles (from nitrobenzene), m. p. 257—262° (decomp.) (Found : N, 10·2. $C_{30}H_{28}O_7N_4$ requires N, 10·0%). 8-*Methyl*-5-*phenyl*-3 : 4-*benzacridine* (2 g.), obtained from *N*-*m*-tolyl-β-naphthylamine (2 g.), benzoic anhydride (2 g.), and zinc chloride (5 g.) after 6 hours at 200—210°, formed brilliant, long, pale yellow needles, m. p. 185°, sparingly soluble in alcohol (Found : N, 4·4. $C_{24}H_{17}N$ requires N, 4·4%); the *picrate* crystallised from nitrobenzene in elongated orange-yellow prisms, m. p. 260—262° (decomp.) (Found : N, 10·2. $C_{30}H_{20}O_7N_4$ requires N, 10·2%). 7 : 9-*Dimethyl*-5-*phenyl*-3 : 4-*benzacridine* separated from alcohol–benzene in fine yellowish prisms, m. p. 198° (Found : N, 4·1. $C_{25}H_{19}N$ requires N, 4·2%). 6 : 7 : 9-*Trimethyl*-5-*phenyl*-3 : 4-*benzacridine* crystallised from alcohol–benzene in long, silky, pale yellow needles, m. p. 145° (Found : N, 4·1. $C_{26}H_{21}N$ requires N, 4·0%); its *picrate* formed, from benzene, silky orange-yellow needles which decomposed at 210—213° (Found : N, 9·4. $C_{32}H_{24}O_7N_4$ requires N, 9·7%).

N-2-*Diphenylyl*-β-*naphthylamine*.—From 2-aminodiphenyl (30 g.), β-naphthol (20 g.), and iodine (0·2 g.) (12 hours at 200° and 16 further hours at 240°), this *amine* (35 g.) was obtained as a resinous yellow oil, b. p. 279—280°/14 mm., which crystallised from ethanol or ligroin in large colourless prisms, m. p. 81° (Found : N, 4·7. $C_{22}H_{17}N$ requires N, 4·7%); its picrate formed, from ethanol, silky dark violet needles, m. p. 104°.

5-*Methyl*-9-*phenyl*-3 : 4-*benzacridine*.—This *benzacridine* (1 g.), prepared from the foregoing amine (5 g.), acetic anhydride (5 c.c.), and zinc chloride (7 g.), formed, from ethanol, pale yellow clusters, m. p. 144° (Found : N, 4·2. $C_{24}H_{17}N$ requires N, 4·4%), and the corresponding *picrate* crystallised from nitrobenzene in fine deep-yellow prisms, m. p. 232° (Found : N, 10·2. $C_{30}H_{20}O_7N_4$ requires N, 10·2%).

N-4-*Diphenylyl*-α-*naphthylamine*, *etc.*—Obtained (30 g.) from α-naphthol (20 g.), 4-aminodiphenyl (25 g.), and iodine (0·1 g.), the *compound* crystallised from ethanol in fine colourless prisms, m. p. 149°, b. p. 310—315°/15 mm. (Found : N, 4·6. $C_{22}H_{17}N$ requires N, 4·7%). The isomeric N-4-*diphenylyl*-β-*naphthylamine* (35 g.) formed, from benzene, lustrous colourless leaflets, m. p. 147°, b. p. 305—310°/14 mm. (Found : N, 5·5%). 5-*Methyl*-7-*phenyl*-1 : 2-*benzacridine*, prepared as usual from *N*-4-diphenylyl-α-naphthylamine, formed, from ethanol–benzene, fluffy pale yellow needles, m. p. 197° (Found : C, 90·1; H, 5·5; N, 4·2. $C_{24}H_{17}N$ requires C, 90·3; H, 5·3; N, 4·4%).

9-*Methoxy*-5-*methyl*-3 : 4-*benzacridine*.—Obtained from *N*-*o*-methoxyphenyl-β-naphthylamine (4 g.), acetic anhydride (5 c.c.), and zinc chloride (6 g.), and purified through its *picrate* which formed, from nitrobenzene, golden-yellow silky needles, m. p. 257° (Found : N, 11·0. $C_{25}H_{18}O_8N_4$ requires, N, 11·1%), the *base* (0·5 g.) crystallised from aqueous methanol as silky yellow needles, m. p. 139—140° (the solvated crystals had m. p. <80°), giving with sulphuric acid an orange-yellow colour (Found : N, 5·4. $C_{19}H_{15}ON$ requires N, 5·2%).

3-*Methyl*-1 : 2 : 6 : 7-*dibenzacridine*.—Prepared as usual from 4-methyl-1-naphthylamine (cf. Barclay, Burawoy, and Thompson, *J.*, 1944, 109; Buu-Hoï and Guettier, *Compt. rend.*, 1946, **222**, 665) (4 g.), β-naphthol (5 g.), and paraformaldehyde (0·5 g.), the *base* (1·5 g.) formed, from ethanol–benzene, fine pale yellow needles, m. p. 163° (Found : N, 4·5. $C_{22}H_{15}N$ requires N, 4·7%). The *picrate* crystallised from nitrobenzene in fine orange-yellow prisms, m. p. 268—270° (decomp.) (Found : N, 10·6. $C_{28}H_{18}O_7N_4$ requires N, 10·7%).

x-tert.-*Butyl*-1 : 2 : 6 : 7-*dibenzacridine* formed, from ethanol–benzene, fine pale yellow prisms, m. p. 208° (50%) (Found : C, 89·2; H, 6·0; N, 4·0. $C_{25}H_{21}N$ requires C, 89·5; H, 6·2; N, 4·1%).

5-n-*Butyl*-1 : 2 : 6 : 7-*dibenzacridine*.—This *base* formed, from benzene, pale yellow fluffy needles, m. p. 223—224° (Found : N, 4·2. $C_{25}H_{21}N$ requires N, 4·1%).

The isomeric 5-iso*butyl*-1 : 2 : 6 : 7-*dibenzacridine* crystallised from benzene in silky yellowish needles, m. p. 227° (Found : N, 4·2%).

5-*Ethyl*-3 : 4 : 6 : 7-*dibenzacridine*.—Di-β-naphthylamine (10 g.) was obtained by heating, at 220—250° for some hours, β-naphthylamine (12 g.) with iodine (0·1 g.); the *dibenzacridine* obtained from this

amine (2 g.), propionic anhydride (2 c.c.), and zinc chloride (3 g.) formed, from benzene, silky yellowish needles, m. p. 220° (Found: N, 4·2. $C_{23}H_{17}N$ requires N, 4·5%); its *picrate* formed, from nitrobenzene, fine yellow prisms, m. p. >300° (decomp.) (Found: N, 10·0. $C_{29}H_{30}O_7N_4$ requires N, 10·2%).

5-iso*Propyl*-3 : 4 : 6 : 7-*dibenzacridine* formed, from benzene, pale yellow silky needles, m. p. 219—220° (Found: N, 4·2. $C_{24}H_{19}N$ requires N, 4·3%); 5-iso*butyl*-3 : 4 : 6 : 7-*dibenzacridine* had similar properties and m. p. 219—220° (Found: N, 4·0. $C_{25}H_{21}N$ requires N, 4·1%).

N-p-tert.-*Amylphenyl-β-naphthylamine*.—This *base* (18 g.), obtained from β-naphthol (20 g.), *p-tert.*-amylaniline (25 g.), and iodine (0·2 g.) in the usual way, formed, from methanol, silky glistening colourless needles, m. p. 80°. b. p. 284—285°/20 mm. (Found: N, 4·5. $C_{21}H_{23}N$ requires N, 4·8%).

The isomeric N-p-sec.-*amylphenyl-β-naphthylamine* (13 g.), prepared from *p*-sec.-amylaniline, formed from ligroin colourless needles, m. p. 58°, b. p. 272—276°/20 mm. (Found: N, 4·8. $C_{21}H_{23}N$ requires N, 4·8%). Both amines were readily autoxidised and their ethanolic solutions showed a strong violet fluorescence.

Preparation of Substituted 1 : 2- *and* 3 : 4-*Benzphenothiazines*.—A mixture of the appropriate secondary amine (1 mol.) and sulphur (2 atoms) was heated at *ca.* 180—185° with a little iodine until the evolution of hydrogen sulphide ceased; the dark sticky mass obtained was fractionated in a vacuum or recrystallised several times from benzene or acetone. All the substances obtained (see Table II) gave deep colours with sulphuric acid, ranging from violet-blue to Prussian-blue, and were readily autoxidised to brownish-red insoluble substances.

Preparation of Substituted Acridines (see Table III).—A mixture of diphenylamine and an excess of the appropriate acid was heated with an equal weight of fused zinc chloride at 200° for 12 hours and then at 210—220° for 12 more hours. After treatment with aqueous sodium hydroxide, the acridine was dissolved in toluene or aqueous xylene and vacuum-distilled. When the acid used was cinnamic acid, the only product thus obtained was cinnamic anhydride (m. p. 136°, after crystallisation from ligroin).

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