948. *Carcinogenic Nitrogen Compounds. Part XIII.* Benzacridines, Benzocarbazoles, and Related Compounds bearing Ethyl and Propyl Groups.*

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In continuation of earlier work (Buu-Hoï, *J.*, 1946, 792; 1949, 670; 1950, 1146), several benzacridines, dibenzacridines, benzocarbazoles, dibenzocarbazoles, and benzophenarsazines bearing ethyl or propyl groups have been prepared for biological examination as potential carcinogens.

In the 1 : 2-benzanthracene and 3 : 4-benzophenanthrene series, several hydrocarbons bearing ethyl or propyl groups are active carcinogens (Badger, Cook, Hewett, Kennaway, and Martin, *Proc. Roy. Soc.*, 1942, *B*, **131**, 170; Shear and Leiter, *J. Nat. Cancer Inst.*, 1940, **1**, 103) or inhibitors of tumour growth (Badger, Elson, Haddow, Hewett, and Robinson, *Proc. Roy. Soc.*, 1942, *B*, **130**, 255); in some cases, the biological activity of the ethyl or *iso*propyl compounds surpasses that of the corresponding methyl compounds. A large number of benzacridines, dibenzacridines, benzocarbazoles, dibenzocarbazoles, and benzophenarsazines bearing ethyl, *n*-propyl, or *iso*propyl radicals has therefore been prepared by standard methods.

3″-Ethyl-1 : 2-6 : 7-dibenzacridine is moderately carcinogenic on the skin in mice and 7-ethyl-5-methyl-1 : 2-benzacridine fairly active.

Experimental (with M. Hubert-Habart)

Preparation of 6-*Ethyl*-2-*naphthol.*—6-Acetyl-2-methoxynaphthalene (Haworth and Sheldrick, *J.*, 1934, 865) was reduced by the Clemmensen method, and the product (38 g.) demethylated with pyridine hydrochloride. Reaction of 6-ethyl-2-naphthol, aromatic aldehydes, and hydrogen chloride in acetic acid gave the following 3 : 4-6 : 7-dibenzoxanthens (Claisen, *Annalen*, 1887, **237**, 265) : 5-*p*-chlorophenyl-2′ : 3″-diethyl- (from *p*-chlorobenzaldehyde), long, shiny needles (from acetic acid), m. p. 202—203° (Found : C, 82·6; H, 5·8. Calc. for $C_{31}H_{25}OCl$: C, 82·9; H, 5·6%); 5-(3 : 4-dichlorophenyl)-2′ : 3″-diethyl-3 : 4-6 : 7-dibenzoxanthen (from 3 : 4-dichlorobenzaldehyde), shiny leaflets (from acetic acid), m. p. 218° (Found : C, 77·1; H, 5·0. Calc. for $C_{31}H_{24}OCl_2$: C, 77·0; H, 4·9%).

2′-*Ethyl*-3 : 4-*benzocarbazole.*—6-Ethyl-2-naphthol (5 g.) and phenylhydrazine hydrogen sulphite (50 c.c. of a saturated aqueous solution) were refluxed for 48 hours; the carbazole, in benzene, was washed with dilute hydrochloric acid, and then vacuum-distilled (b. p. 300—310°/24 mm.); it formed needles (from methanol) (1 g.), m. p. 131° (Found : C, 88·0; H, 6·0. $C_{18}H_{15}N$ requires C, 88·2; H, 6·1%), giving a violet-red picrate.

2′-iso*Propyl*-1 : 2-5 : 6-*dibenzocarbazole.*—7-*iso*Propyl-1-tetralone β-naphthylhydrazone, heated for 5 minutes with a saturated solution of hydrogen chloride in acetic acid, gave 3 : 4-*dihydro*-2′-iso*propyl*-1 : 2-5 : 6-*dibenzocarbazole* (95%), needles (from benzene), m. p. 194°, which

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formed a deep red sulphuric acid solution (Found: N, 4·3. $C_{23}H_{21}N$ requires N, 4·5%); a solution of this compound (2 g.) in xylene, refluxed for 2 hours with chloranil (2·4 g.), yielded 2′-iso*propyl*-1 : 2-5 : 6-*dibenzocarbazole*, as shiny leaflets (from benzene), m. p. 203° (Found: C, 89·0; H, 6·2. $C_{23}H_{19}N$ requires C, 89·3; H, 6·1%), giving a deep red sulphuric acid solution, and a deep violet picrate. The Grignard derivative of this carbazole with methyl sulphate gave 9-*methyl*-2′-iso*propyl*-1 : 2-5 : 6-*dibenzocarbazole*, shiny leaflets (from methanol), m. p. 173° (Found: C, 89·0; H, 6·4. $C_{24}H_{21}N$ requires C, 89·2; H, 6·5%).

Amines derived from Ethylanilines.—*p*-Ethylaniline (15 g.) [*toluene*-p-*sulphonyl* derivative, long silky needles (from ligroin), m. p. 91° (Found: N, 5·0. $C_{15}H_{17}O_2NS$ requires N, 5·1%)], and α-naphthylamine (17 g.) were refluxed for 24 hours with iodine (0·5 g.); N-p-*ethylphenyl*-α-*naphthylamine* (12 g.) formed a pale yellow, viscous oil, b. p. 260°/21 mm. (Found: C, 87·2; H, 6·8. $C_{18}H_{17}N$ requires C, 87·4; H, 6·9%). Similarly prepared were: N-p-*ethylphenyl*-β-

(a) *Substituted* 1 : 2-*benzacridines.*

Substituent	M. p.	Formula	Found, %: C	Found, %: H	Reqd., %: C	Reqd., %: H
7-Ethyl-5-methyl	110°	$C_{20}H_{17}N$	88·4	6·5	88·6	6·3
6-Ethyl-9-methyl [a]	82	$C_{20}H_{17}N$	88·3	6·3	88·6	6·3
5 : 6-Diethyl-9-methyl [b]	86	$C_{22}H_{21}N$	87·9	6·8	88·3	7·0
8-Chloro-9-methyl-5-*iso*propyl	159	$C_{21}H_{18}NCl$	78·7	5·8	78·9	5·6

[a] The picrate formed from ethanol orange-brown needles, m.p. 144°. [b] The picrate formed from ethanol orange needles, m. p. 127° [the low m. p. of the two picrates is characteristic of picrates of 1 : 2-benzacridines bearing an alkyl group in the 9-position (cf. Buu-Hoï, *J.*, 1949, 670; 1950, 1146; Senier and Austin, *J.*, 1907, **91**, 1240)].

(b) *Substituted* 3 : 4-*benzacridines and their derivatives.*

Substituent	M. p. (or b. p./mm.)	Formula	Found, %: C	Found, %: H	Reqd., %: * C	Reqd., %: * H
7-Ethyl-5-methyl [a]	295—300°/20	$C_{20}H_{17}N$	—	—	—	—
Picrate	236 (dec. >210)	$C_{26}H_{20}O_7N_4$	11·5		11·2	
Hydrobromide	219	$C_{20}H_{18}NBr$	67·8	5·2	68·2	5·1
5 : 7-Diethyl	300/18	$C_{21}H_{19}N$	88·5	6·9	88·4	6·7
Picrate	236 (dec. >205)	$C_{27}H_{22}O_7N_4$	10·6		10·9	
Hydrobromide	218—220	$C_{21}H_{20}NBr$	68·5	5·5	68·9	5·5
6-Ethyl-9-methyl	140	$C_{20}H_{17}N$	88·3	6·5	88·6	6·3
Picrate	265 (dec. >255)	$C_{26}H_{20}O_7N_4$	11·5		11·2	
9-Methyl-6-*n*-propyl	117	$C_{21}H_{19}N$	88·2	6·5	88·4	6·7
Picrate	257 (dec. >240)	$C_{27}H_{22}O_7N_4$	11·2		10·9	
9-Ethyl-6-*n*-propyl	93	$C_{22}H_{21}N$	88·0	7·3	88·3	7·0
Picrate	240 (sec. >225)	$C_{28}H_{24}O_7N_4$	10·4		10·6	
6-Ethyl-5 : 9-dimethyl	134	$C_{21}H_{19}N$	88·2	6·6	88·4	6·7
Picrate	217	$C_{27}H_{22}O_7N_4$	10·6		10·9	
5 : 6-Diethyl-9-methyl	135	$C_{22}H_{21}N$	87·9	6·8	88·3	7·0
Picrate	dec. >230	$C_{28}H_{24}O_7N_4$	10·5		10·6	
5-*iso*Propyl	169	$C_{20}H_{17}N$	88·5	6·1	88·6	6·3
Picrate	238 (dec. >220)	$C_{26}H_{20}O_7N_4$	10·8		11·2	
7-Methyl-5-*iso*propyl	156	$C_{21}H_{19}N$	88·1	6·5	88·4	6·7
Picrate	274 (dec. >260)	$C_{27}H_{22}O_7N_4$	10·6		10·9	
7-Ethyl-5-*iso*propyl	145	$C_{22}H_{21}N$	88·0	6·9	88·3	7·0
Picrate	dec. >252	$C_{28}H_{24}O_7N_4$	10·8		10·6	
9-Methyl-5-*iso*propyl	144	$C_{21}H_{19}N$	88·1	6·8	88·4	6·7
Picrate	200	$C_{27}H_{22}O_7N_4$	10·6		10·9	
9-Phenyl-5-*iso*propyl	131	$C_{26}H_{21}N$	90·7	6·2	89·9	6·1
Picrate	237—238	$C_{32}H_{24}O_7N_4$	9·4		9·7	
6 : 7-Dimethyl-5-*iso*propyl	183	$C_{22}H_{21}N$	88·5	7·0	88·3	7·0
Picrate	275	$C_{28}H_{24}O_7N_4$	10·9		10·6	
8 : 9-Dimethyl-5-*iso*propyl	142	$C_{22}H_{21}N$	88·1	7·2	88·3	7·0
Picrate	247 (dec. >232)	$C_{28}H_{24}O_7N_4$	10·4		10·6	
2′-*tert.*-Butyl-7-methyl-5-*iso*propyl	138	$C_{25}H_{27}N$	87·9	8·0	88·0	7·9
Picrate	222	$C_{31}H_{30}O_7N_4$	9·6		9·8	
8-Chloro-9-methyl-5-*iso*propyl	158	$C_{21}H_{18}NCl$	78·6	5·6	78·9	5·6
Picrate	235	$C_{27}H_{21}O_7N_4Cl$	10·0		10·2	

* Lone values relate to nitrogen (for picrates).

[a] The acridines were recrystallised from methanol or ethanol, their picrates from xylene or nitrobenzene, and their hydrobromides from dilute ethanol.

naphthylamine, shiny prisms (from methanol), m. p. 64° (Found: C, 87·1; H, 7·1%); N-(5-*ethyl*-2-*methylphenyl*)-α-*naphthylamine*, a thick yellow oil, b. p. 263—264°/16 mm. (Found:

C, 87·1; H, 7·2. $C_{19}H_{19}N$ requires C, 87·4; H, 7·3%); and the β-*naphthyl* analogue, a viscous yellow oil, b. p. 265—268°/16 mm. (Found: C, 87·3; H, 7·5%).

Amines derived from 6-*Ethyl*-2-*naphthol.*—6-*Ethyl*-N-*phenyl*-2-*naphthylamine* (7 g.), prepared similarly, had b. p. 250—255°/16 mm., and formed silky needles (from methanol), m. p. 100° (Found: C, 87·1; H, 7·1. $C_{18}H_{17}N$ requires C, 87·4; H, 6·9%); the p-*tolyl* analogue formed shiny leaflets (from ethanol), m. p. 101° (Found: C, 87·1; H, 7·1. $C_{19}H_{19}N$ requires C, 87·4; H, 7·3%). 6-n-*Propyl*-N-*phenyl*-2-*naphthylamine* was a pale yellow, viscous oil, b. p. 270—272°/16 mm. (Found: C, 87·2; H, 7·5. $C_{19}H_{19}N$ requires C, 87·4; H, 7·3%), and the p-*tolyl* analogue silky needles (from light petroleum), m. p. 76—77° (Found: C, 87·0; H, 7·3. $C_{20}H_{21}N$ requires C, 87·3; H, 7·6%).

10-*Chloro*-8-*ethyl*-5 : 10-*dihydro*-1 : 2-*benzophenarsazine.*—A solution of *N*-*p*-ethylphenyl-β-naphthylamine (3·5 g.) and arsenic trichloride (3 g.) in *o*-dichlorobenzene (20 c.c.) was refluxed for 3 hours; the solid *arsazine* obtained on cooling gave silky, orange-yellow needles (4·5 g.), m. p. 241° (decomp. >225°), from nitrobenzene; these gave an orange-red sulphuric acid solution (Found: C, 60·6; H, 4·0. $C_{18}H_{15}NClAs$ requires C, 60·8; H, 4·2%); the isomeric 3′-*ethyl* compound formed shiny, orange-yellow leaflets (from nitrobenzene), m. p. 220° (decomp. >212°) (Found: C, 60·4; H, 4·1%).

10-*Chloro*-8-*ethyl*-5 : 10-*dihydro*-3 : 4-*benzophenarsazine.*—This *compound* formed from *o*-dichlorobenzene silky, golden-yellow prisms, m. p. 210° (decomp. >196°) (Found: C, 60·5; H, 4·1%), and, when it (1·2 g.) was treated with an ethereal solution of methylmagnesium iodide in excess, yielded 8-*ethyl*-5 : 10-*dihydro*-10-*methyl*-3 : 4-*benzophenarsazine* (1 g.), shiny needles (from ligroin), m. p. 109—110°, giving with sulphuric acid an orange colour (Found: C, 68·0; H, 5·1. $C_{19}H_{18}NAs$ requires C, 68·1; H, 5·4%).

10-*Chloro*-9-*ethyl*-5 : 10-*dihydro*-6-*methyl*-1 : 2-*benzophenarsazine* formed from toluene silky, yellow needles, decomposing above 245° (Found: C, 61·4; H, 4·4. $C_{19}H_{17}NClAs$ requires C, 61·7; H, 4·6%); the isomeric 3′-*ethyl*-8-*methyl* compound crystallised from nitrobenzene as silky, golden-yellow prisms, m. p. 275° (decomp. >270°) (Found: C, 61·4; H, 4·3%). 10-*Chloro*-9-*ethyl*-5 : 10-*dihydro*-6-*methyl*-3 : 4-*benzophenarsazine* crystallised from toluene as long, silky, lemon-yellow needles, m. p. 205° (decomp. >188°) (Found: C, 61·3; H, 4·4%).

5-*Ethylisatin.*—To a mixture of chloral hydrate (54 g.) and sodium sulphate (750 g.) in water (800 c.c.), a solution of *p*-ethylaniline (30 g.) in 10% hydrochloric acid (220 c.c.) and then an aqueous solution of hydroxylamine hydrochloride (60 g.) were added; after a brief boiling, the mixture was cooled, and the precipitated *iso*nitroso-compound collected, dried, and treated with sulphuric acid (360 g.) below 80°. The *isatin* obtained after decomposition with ice crystallised from methanol as long, silky, orange needles, m. p. 135° (Found: C, 68·4; H, 5·2. $C_{10}H_9O_2N$ requires C, 68·6; H, 5·1%); the *indophenazine* obtained with *o*-phenylenediamine formed from ethanol silky, yellow needles, m. p. 227—228° (Found: N, 16·7. $C_{16}H_{13}N_3$ requires N, 17·0%); 5-ethylisatin *N*′-phenylhydrazone crystallised from ethanol as bright yellow plates, m. p. 200°.

3″-*Ethyl*-1 : 2-6 : 7-*dibenzacridine.*—A mixture of 6-ethyl-2-naphthol (2 g.) and α-naphthylamine (2 g.) was cautiously treated at 250° with paraformaldehyde (1 g.) in small portions; the acridine was subsequently boiled for 5 minutes, and purified by vacuum-distillation. The *picrate*, crystallised from nitrobenzene as fine, orange-yellow prisms, m. p. 276—277° (decomp. >240°) (Found: N, 10·0. $C_{23}H_{17}N,C_6H_3O_7N$ requires N, 10·4%); its decomposition with aqueous ammonia yielded the *base*, fine, pale yellow needles (from ethanol), m. p. 154° (Found: C, 89·6; H, 5·6. $C_{23}H_{17}N$ requires C, 89·9; H, 5·5%).

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