420. *The Reactions of Free Benzyl Radicals with* 1 : 2- *and* 3 : 4-*Benzacridine.*

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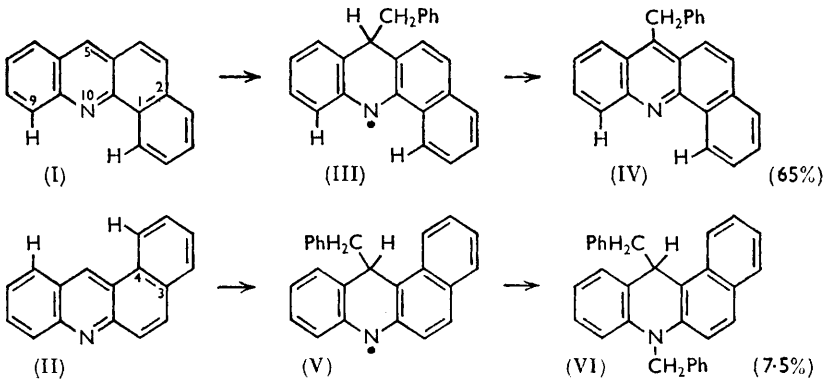
Benzyl radicals have been shown to substitute 1 : 2-benzacridine, in good yield, at the exposed *meso*-position (5) and to a slight extent elsewhere. From the sterically hindered 3 : 4-benzacridine the addition product 5 : 10-dibenzyl-3 : 4-benzacridan was obtained, but only in poor yield. Spatial access of the benzyl radical to the *meso*-position is thus, in both benzacridines, of importance in controlling the courses of reaction.

IN a previous paper [1] we described the reactions of acridine and 5-phenylacridine with benzyl radicals and we now report a similar study with both 1 : 2- and 3 : 4-benzacridine (I and II respectively).

From the reaction of 1 : 2-benzacridine with benzyl radicals a 65% yield of 5-benzyl-1 : 2-benzacridine (IV) was obtained together with a small amount of a dibenzylbenzacridine and 30% of unchanged 1 : 2-benzacridine. From 3 : 4-benzacridine, in contrast, 7·5% of 5 : 10-dibenzyl-3 : 4-benzacridan (VI) was obtained and 75% of unchanged 3 : 4-benzacridine was recovered. In both cases the products found, and possible products which could not be detected in our reaction mixtures, have been synthesised independently by routes that afford conclusive proofs of the structures assigned to them.

Both the reactants yielded considerably more dibenzyl than was obtained in the corresponding reaction with acridine and so must be less reactive radical-acceptors, as would be predicted from approximate calculations of bond localisation energies at the *meso*-carbon centres in the isoconjugate hydrocarbons.[2]



Our previous study with acridine [1] indicated that the initial attack of benzyl radicals on the heterocyclic molecule occurred at the *meso*-carbon atom rather than at the nitrogen

[1] Waters and Watson, *J.*, 1957, 253.
[2] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3357.

atom, and our present results support this conclusion but are of added interest in that they illustrate the significance of steric hindrance to homolytic substitution. In 1 : 2-benzacridine (I) the *meso*-carbon (5) is sterically unhindered, whilst the nitrogen atom is hindered. Consequently radical (III) may easily be formed and its homolytic dehydrogenation (by a second benzyl radical) to (IV) would occur more easily than the addition of a second benzyl radical to the nitrogen. 3 : 4-Benzacridine (II) is of a converse structural type; radical addition to give (V) is difficult, but thereafter the second radical can easily add to yield a benzacridan derivative (VI), though in very low overall yield. Alternatively, compound (VI) might be produced by initial addition of a benzyl radical to the unhindered nitrogen atom of 3 : 4-benzacridine. Evidence that such addition is possible is presented by us in the following paper.

At the inception of this work it was hoped that some evidence of radical attack at the " K " (phenanthrenoid) positions might be discovered, corresponding to the substitution of 5-phenylacridine in the 1-position. The dibenzylacridine isolated from 1 : 2-benzacridine (I) is perhaps formed by a reaction of this type.

Experimental

1 : 2-Benzacridine was prepared from 5-chloro-1 : 2-benzacridine,[3] m. p. 144—145°. This was reduced to 1 : 2-*benzacridan* [Found: C, 88·4; H, 5·7; N, 6·1. $C_{17}H_{13}N$ requires C, 88·2; H, 5·7; N, 6·2%), $\lambda_{max.}$ 2580, 2840, 3500 Å (log ε 4·29, 4·06, 3·97) in ethanol], (yellow plates from aqueous ethanol; m. p. 140°) with hydrogen and Raney nickel in alkaline ethanol.[4] The 1 : 2-benzacridan was then oxidised in boiling water with potassium dichromate and sulphuric acid by the method described by Albert and Willis [5] for the oxidation of 3 : 4-benzacridan. 1 : 2-Benzacridine was thus obtained in 75% yield as lemon-yellow needles (from *cyclo*hexane), m. p. 107—108° (lit.,[6] 108°), $\lambda_{max.}$ in ethanol 2675, 2740, 2850, 3315, 3380, 3415, 3645, 3840 Å (log ε 4·75, 4·90, 4·69, 3·78, 3·78, 3·84, 3·93, 3·96). It was easily reduced to 1 : 2-benzacridan (yield 75%) by treatment with lithium aluminium hydride in boiling tetrahydrofuran (2% solution).

Preparations of 3 : 4-benzacridine by the reactions of Ullmann and Fetvadjian [7] and of Buu-Hoï [8] gave variable and uncertain yields. A much more certain route was that of ring closure of *N*-2′-naphthylanthranilic acid [9] to 5-chloro-3 : 4-benzacridine,[3] reduction of this to 3 : 4-benzacridan, m. p. 166—168°, $\lambda_{max.}$ in ethanol, 2680, 2780, 3160, 3675 Å (log ε 4·34, 4·40, 4·09, 3·57), with hydrogen and Raney nickel, as described by Badger, Seidler, and Thomson,[4] and oxidation of the latter in boiling water with potassium dichromate and sulphuric acid as described by Albert and Willis.[5] The 3 : 4-benzacridine crystallised from *cyclo*hexane in white needles, m. p. 131° (lit., 131°), $\lambda_{max.}$ in ethanol 2765, 2850, 3365, 3465, 3635, 3835 Å (log ε 4·76, 4·73, 3·77, 3·88, 4·00, 4·03).

Reaction of 1 : 2-*Benzacridine with Benzyl Radicals.*—1 : 2-Benzacridine (4·5 g.) in dry toluene (400 ml.) was refluxed under nitrogen with *tert.*-butyl peroxide (8·2 g.) for 76 hr. After evaporation of the solvent the residual gum (9 g.), in light petroleum (200 ml.), was chromatographed on alumina (600 g.) with light petroleum–benzene. It gave (*a*) dibenzyl(1·6 g.), (*b*) 1 : 2-benzacridine (1·4 g., 31%), yellow needles (from *cyclo*hexane), m. p. and mixed m. p. 107°, (*c*) 5-benzyl-1 : 2-benzacridine (4·0 g., 64%) which crystallised from *cyclo*hexane in pale yellow needles, m. p. and mixed m. p. (see below) 144° (Found: C, 89·8; H, 5·2; N, 4·6. Calc. for $C_{24}H_{17}N$: C, 90·2; H, 5·4; N, 4·4%), $\lambda_{max.}$ in ethanol 2680, 2780, 2885, 3350, 3490, 3670, 3865 Å (log ε 4·79, 4·97, 4·94, 3·89, 3·99, 4·05, 4·03), and (*d*) a gum (0·75 g.) which after extraction with 2N-sulphuric acid, basification, and further chromatography gave a *dibenzyl*-1 : 2-*benzacridine* (80 mg., 1%) which crystallised from *cyclo*hexane in pale yellow needles, m. p. 177·5—179° (corr.) (Found: C, 90·8; H, 5·7; N, 3·7. $C_{31}H_{23}N$ requires C, 90·9; H, 5·7; N, 3·4%). The infrared absorption of the

[3] Bachmann and Picha, *J. Amer. Chem. Soc.*, 1946, **68**, 1599.
[4] Cf. Badger, Seidler, and Thomson, *J.*, 1951, 3207.
[5] Albert and Willis, *J. Soc. Chem. Ind.*, 1946, **65**, 26.
[6] Ullmann and La Torre, *Ber.*, 1904, **37**, 2922.
[7] Ullmann and Fetvadjian, *Ber.*, 1903, **36**, 1029.
[8] Buu-Hoï, *J.*, 1949, 670.
[9] Ullmann, *Annalen*, 1907, **355**, 350. (This is best prepared by a Chapman reaction; cf. ref. 1.)

last compound at 698, 709, and 753 cm.$^{-1}$ indicates the presence of phenyl and its absorption in chloroform [$\lambda_{max.}$ 2740, 2840, 2950, 3380, 3435, 3540, 3715, 3920 Å (log ε 4·54, 4·72, 4·75, 3·76, 3·76, 3·80, 3·87, 3·76)] indicates that it is a substituted 1 : 2-benzacridine. A trace of a colourless benzyl-1 : 2-benzacridine (structure inferred from light absorption), m. p. 194—197°, was also obtained.

Reaction of 3 : 4-*Benzacridine with Benzyl Radicals.*—3 : 4-Benzacridine (6 g.), toluene (300 ml.), and *tert.*-butyl peroxide (6·7 g.) were refluxed under nitrogen for 9 days. Investigation of the product, as described above, established the presence of dibenzyl (5 g.), 3 : 4-benzacridine (4·2 g., 70%), and 5 : 10-*dibenzyl*-3 : 4-*benzacridan* (0·81 g., 7·5%). The last crystallised from methanol–methyl acetate in white needles, m. p. and mixed m. p. 157—159° (Found: C, 90·3; H, 6·0; N, 3·2. $C_{31}H_{25}N$ requires C, 90·5; H, 6·1; N, 3·4%), $\lambda_{max.}$ 2765, 3165, 3600 Å (log ε 4·56, 4·18, 3·64), inflexions at 2675, 3060 Å (log ε 4·47, 4·11) (*i.e.*, absorption of acridan type).

Preparations of Reference Compounds.—5-Benzyl-1 : 2-benzacridine, prepared by fusion of *N*-phenyl-1-naphthylamine and phenylacetic acid with zinc chloride,[8] had m. p. 143—144° [picrate, m. p. 225—256° (decomp.)]. 5-*Benzyl*-1 : 2-*benzacridan*, obtained by reduction of this compound with lithium aluminium hydride in tetrahydrofuran, crystallised from light petroleum in needles, m. p. 125° (Found: C, 89·7; H, 6·0; N, 4·7. $C_{24}H_{19}N$ requires C, 89·7; H, 6·0; N, 4·4%), $\lambda_{max.}$ in ethanol 2600, 3465 Å (log ε 4·32, 3·98).

5-Benzyl-1 : 2-benzacridan (0·18 g.) was added with stirring to a solution of potassamide (from 0·13 g. of potassium and a trace of ferric nitrate) in liquid ammonia (130 ml.). After 30 min. the dark colour of the solution was discharged by dropwise addition of benzyl chloride and, after evaporation of the ammonia, the excess of benzyl chloride was removed in steam. The residue was taken up in light petroleum–benzene (1 : 1) and filtered through alumina. After recrystallisation from methanol–methyl acetate the 5 : 10-*dibenzyl*-1 : 2-*benzacridine* (0·12 g.) formed needles, m. p. 123—124° (Found: C, 90·8; H, 6·1; N, 3·4. $C_{31}H_{25}N$ requires C, 90·5; H, 6·1; N, 3·4%), $\lambda_{max.}$ in ethanol 2545, 3375 Å (log ε 4·31, 3·89).

5-Benzyl-3 : 4-benzacridine,[8] prepared by fusion at 215—240° of *N*-phenyl-2-naphthylamine,[10] phenylacetic acid, and zinc chloride, had m. p. 143° (from light petroleum) (Found: C, 90·2; H, 5·2; N, 4·2. Calc. for $C_{24}H_{17}N$: C, 90·2; H, 5·4; N, 4·4%), $\lambda_{max.}$ in ethanol 2480, 2780, 2850, 3510, 3685, 3880 Å (log ε 4·41, 4·83, 4·81, 3·93, 4·01, 3·97).

5-Benzyl-3 : 4-benzacridine (2·15 g.) in boiling toluene (100 ml.) was treated with sodium (10·5 g.), and pentanol (100 ml.) was gradually added. When the sodium had dissolved the solution was cooled, washed with water, and evaporated. Crystallisation of the residue from methanol gave 5-*benzyl*-1′ : 2′ : 3′ : 4′-*tetrahydro*-3 : 4-*benzacridan*, m. p. 156—157° (1 g.) (Found: C, 88·6; H, 7·2; N, 4·3. $C_{24}H_{23}N$ requires C, 88·6; H, 7·1; N, 4·3%). Its light absorption in ethanol, $\lambda_{max.}$ 2830 Å (log ε 4·15), indicates that it contains an acridan and not a benzacridan system. The same compound was obtained (yield 95%; m. p. 156—157°) by reducing 5-benzyl-3 : 4-benzacridine with excess of sodium in liquid ammonia. Oxidation of this substance (50 mg.) in aqueous alcohol with ferric chloride at 100° gave yellow needles, m. p. 117—119°, $\lambda_{max.}$ in ethanol 2565, 3575 Å (log ε 5·34, 4·15) (indicative of 5-benzyl-1′ : 2′ : 3′ : 4′-tetrahydro-3 : 4-benzacridine).

5-*Benzyl*-3 : 4-*benzacridan* was obtained by reducing 5-benzyl-3 : 4-benzacridine (1·0 g.) with lithium aluminium hydride (0·4 g.) in refluxing tetrahydrofuran (30 ml.) for 14 hr. and then decomposing the excess of reducing agent with ethyl acetate. It crystallised from methanol–methyl acetate in needles, m. p. 138—140° (0·75 g.) (Found: C, 89·7; H, 5·9; N, 4·1. $C_{24}H_{19}N$ requires C, 89·7; H, 6·0; N, 4·4%), $\lambda_{max.}$ in ethanol 2735, 3080, 3635, 3815 Å (log ε 4·56, 4·06, 3·63, 3·53). Benzylation of this in liquid ammonia, with potassamide and benzyl chloride as described above, gave 5 : 10-dibenzyl-3 : 4-benzacridan, wich crystallised from methanol in needles, m. p. 161—163° (Found: C, 90·4; H, 5·9; N, 3·8. Calc. for $C_{31}H_{25}N$: C, 90·5; H, 6·1; N, 3·4%), $\lambda_{max.}$ in ethanol 2680, 2770, 3065, 3160, 3600 Å (log ε 4·47, 4·56, 4·11, 4·18, 3·64).

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[10] Knoevenagel, *J. prakt. Chem.*, 1914, **89**, 17.