41. *The Reactions of Acridine and 5-Phenylacridine with Benzyl Radicals.*

By WILLIAM A. WATERS and D. H. WATSON.

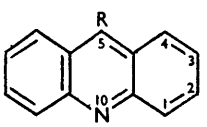
The free-radical reactions of acridine resemble those of anthracene. Benzyl radicals react with acridine to give both 5-benzylacridine and 5 : 10-dibenzylacridan. The major product from 5-phenylacridine is 1-benzyl-5-phenylacridine, the structure of which has been established by an independent synthesis from *o*-benzylphenol and benzanilide, involving a Chapman imidoate rearrangement. Small quantities of 5 : 10-dibenzyl-5-phenylacridan and of an unidentified isomer were also obtained.

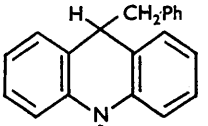
IN a recent paper Beckwith and Waters [1] described a convenient method of generating free benzyl radicals by decomposing *tert.*-butyl peroxide in boiling toluene and showed that the benzyl radicals readily added to the *meso*-positions of anthracene. We have now extended this work to the acridine series and, as we expected from related work,[2] find that similar reactions occur. However, whereas anthracene yields a mixture of 9 : 10-dibenzyl-9 : 10-dihydroanthracene and 9 : 9′-dibenzyl-9 : 9′ : 10 : 10′-tetrahydrodianthryl, acridine gives a mixture of 5-benzylacridine (I; R = $Ph{\cdot}CH_2$) and 5 : 10-dibenzylacridan (III; R = H) but no diacridan. This indicates that the initial addition must be at the *meso*-carbon atom, not the nitrogen atom, to give (II) which must be rather more prone to dehydrogenation to the product (I; R = $Ph{\cdot}CH_2$) than is the analogous benzylanthracene radical. The structures of the products (I; R = $Ph{\cdot}CH_2$) and (III; R =H) were confirmed by independent syntheses.

[1] Beckwith and Waters, *J.*, 1956, 1108.
[2] Turner and Waters, *J.*, 1956, 879.

The reaction of benzyl radicals with 5-phenylacridine proceeds less easily, for there was about 40% recovery of unchanged material. Three pure products have been isolated, of which the two most abundant have been identified. The expected dibenzyl adduct (III; R = Ph), 5 : 10-dibenzyl-5-phenylacridan, was, after purification, obtained in only 2·5% yield and was accompanied by a smaller amount of an isomer which has an ultraviolet spectrum of neither the acridine nor the acridan type. The adduct (III; R = Ph) was also synthesised by treating the sodium adduct of 5-phenylacridine with benzyl chloride.

The major product (10% after purification) of the reaction between benzyl radicals and 5-phenylacridine proved to be a monobenzyl-substituted 5-phenylacridine that was


(I)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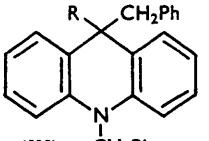
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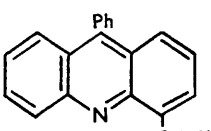
(IV)

oxidised smoothly to a benzoyl-5-phenylacridine and had the typical ultraviolet spectrum and fluorescence of an acridine derivative. Since with aromatic systems of this degree of complexity the diagnosis of the orientation of substituent groups by means of the infrared spectrum is not yet certain it was necessary to establish the exact structure by an independent synthesis. Position 3, *para* to the nitrogen atom, is favoured for electrophilic substitutions of acridine [3,4] and consequently 3-benzyl-5-phenylacridine was first made by condensing *p*-benzylphenol with *N*-phenylbenzimidoyl chloride and thermally rearranging the product, using Chapman's reaction : [5]

$$Ph{\cdot}CH_2{\cdot}C_6H_4{\cdot}O{\cdot}CPh{:}NPh \longrightarrow Ph{\cdot}CH_2{\cdot}C_6H_4{\cdot}NPh{\cdot}CO{\cdot}Ph$$

and then condensing the resulting *N*-benzoyl-4-benzyldiphenylamine to 3-benzyl-5-phenylacridine by heating it with zinc chloride. This did not give the desired product, but repetition of the same synthesis starting with *o*-benzylphenol, so as to yield 1-benzyl-5-phenylacridine (IV) gave a substance identical with the product of the free-radical reaction. Comparison of the infrared spectra of the isomers then made evident that in the 9—11 μ region bands indicative of a 1 : 2 : 3-trisubstituted benzene were present in the compound (IV) in addition to bands indicating both 1 : 2-disubstitution and monosubstitution.

Though plausible suggestions as to why attack on 5-phenylacridine might take place at position 1 can be propounded, its extent is surprising, particularly since this reaction product does not appear to be contaminated with isomers.

Experimental

Reaction of Acridine with Benzyl Radicals.—Acridine (12·5 g.), *tert.*-butyl peroxide (17·5 g.), and toluene (500 ml.) were refluxed for 9 days under dry nitrogen. After removal of the solvent under nitrogen a deep yellow gum (25 g.) remained. Part (14 g.) of this was dissolved in *cyclo*hexane and chromatographed through alumina. It gave dibenzyl (50 mg.) and then 5 : 10-*dibenzylacridan* (2·5 g., 18% calc. on acridine) which crystallised from light petroleum in needles, m. p. 143° (Found : C, 89·6; H, 6·3; N, 3·6. $C_{27}H_{23}N$ requires C, 89·7; H, 6·4; N, 3·9%). Its ultraviolet spectrum ($\lambda_{max.}$ 2950 Å; log ε 4·15) was characteristic of the acridan system. Further elution, with *cyclo*hexane–benzene, yielded 5-benzylacridine (1·75 g., 17%), m. p. and mixed m. p. 173°, $\lambda_{max.}$ 2525, 3590 Å (log ε 5·12, 4·01) (Found : C, 89·4; H, 5·8; N, 4·7. Calc. for $C_{20}H_{15}N$: C, 89·3; H, 5·6; N, 5·2%). A little unchanged acridine was also recovered.

For comparison, 5-benzylacridine was synthesised from diphenylamine and phenylacetic acid,[6] and reduced to 5-*benzylacridan* both by boiling with aqueous sodium dithionite in ethanol

[3] Lehmstedt, *Ber.*, 1938, **71**, 808, 1069.
[4] Acheson, Hoult, and Barnard, *J.*, 1954, 4142.
[5] Chapman, *J.*, 1925, **127**, 1992.
[6] Buu-Hoï and Lecoq, *Rec. Trav. chim.*, 1945, **64**, 250.

and by treatment in boiling toluene with sodium and then pentyl alcohol. It crystallised from ethanol and had m. p. 197°, $\lambda_{max.}$ 2850 Å (log ε 4·17) (Found : C, 88·3; H, 6·2; N, 5·1. $C_{20}H_{17}N$ requires C, 88·5; H, 6·3; N, 5·2%). When refluxed for 2 hr. with anhydrous potassium carbonate in an excess of benzyl chloride it gave, after steam-distillation and chromatography, 5 : 10-dibenzylacridan identical in m. p. and spectra with the material described above (Found : C, 89·8; H, 6·7; N, 3·6%).

Reaction of 5-Phenylacridine with Benzyl Radicals.—5-Phenylacridine, m. p. 182° (6 g.), prepared from benzoic acid and diphenylamine,[7] *tert.*-butyl peroxide (6 g.), and toluene (300 ml.) were refluxed under nitrogen for 7 days. The orange-red solution on evaporation left a gum (10·9 g.) which was chromatographed in light petroleum through alumina. It gave successively : (i) dibenzyl (1·94 g.), m. p. 52—53°; (ii) a white solid, m. p. 213°, $\lambda_{max.}$ 2950 Å (log ε 3·82), after crystallisation from methanol–methyl acetate, subsequently identified (see below) as 5 : 10-*dibenzyl-5-phenylacridan* (Found : C, 90·1, 90·0; H, 6·2, 6·3; N, 4·0, 3·3. $C_{35}H_{27}N$ requires C, 90·6; H, 6·2; N, 3·2%); (iii) a colourless mixture of the above with some fine needles of an *isomer* (*x*), which after crystallisation from methanol, had m. p. 175°, $\lambda_{max.}$ 2600 Å (log ε 4·80), and thus did not appear to be either an acridine or an acridan (Found : C, 90·1; H, 5·7; N, 3·1%; *M*, in camphor, 361. $C_{33}H_{27}N$ requires *M*, 461); (iv) pale yellow needles which, after crystallisation from methanol, had m. p. 144°, $\lambda_{max.}$ 2575, 3600 Å (log ε 5·11, 3·99), and proved to be 1-*benzyl-5-phenylacridine* (Found : C, 90·1; H, 5·7; N, 4·0. $C_{26}H_{19}N$ requires C, 90·4; H, 5·5; N, 4·1%); and (v) unchanged 5-phenylacridine, m. p. 183°.

Repetition of the reaction with 18 g. of 5-phenylacridine gave 33 g. of gum which was distilled in steam to remove dibenzyl and then extracted with 2N-sulphuric acid to remove basic acridine derivatives, but in fact separated only 5-phenylacridine (7 g., 40%). Chromatography of the less basic residue gave 0·7 g. (2·5%) of 5 : 10-dibenzyl-5-phenylacridan, 0·45 g. of compound (*x*), and 2·5 g. (10·5%) of 1-benzyl-5-phenylacridine.

The following degradation of the benzyl-5-phenylacridine was effected to aid in its identification : Oxidation with an excess of chromium trioxide in acetic acid at 100° gave a 50% yield of 1-*benzoyl-5-phenylacridine* which crystallised from methanol in yellow needles, m. p. 167° (Found : C, 87·4; H, 4·6; N, 3·7. $C_{26}H_{17}ON$ requires C, 86·9; H, 4·8; N, 3·9%). Its infrared spectrum showed strong C=O absorption at 6·025 μ and its ultraviolet spectrum was typical of an acridine derivative ($\lambda_{max.}$ 2550, 3590 Å; log ε 5·03, 4·03). Its oxime, prepared in pyridine, had m. p. 202° and after treatment with phosphorus pentachloride gave a yellow substituted *amide* that crystallised from methanol–methyl acetate in long yellow needles, m. p. 193—194° (Found : C, 83·5; H, 4·9; N, 7·55. $C_{26}H_{18}ON_2$ requires C, 83·4; H, 4·8; N, 7·5%), which could not be identified with any benzamido-phenylacridine already reported in the literature. There was insufficient material for further degradative work.

Synthesis of 10-Benzyl-5-phenylacridan.—5-Phenylacridan,[4] m. p. 170° (1 g.), potassium carbonate (1·5 g.), and benzyl chloride (5 ml.) were heated for 3½ hr. at 180—190°. After steam-distillation the residue was chromatographed and gave 10-*benzyl-5-phenylacridan* which crystallised from methanol–methyl acetate in needles, m. p. 139°, having $\lambda_{max.}$ 2900 Å (log ε 4·17) (Found : C, 89·6; H, 5·9; N, 4·3. $C_{26}H_{21}N$ requires C, 89·9; H, 6·1; N, 4·0%).

Synthesis of 5 : 10-Dibenzyl-5-phenylacridan.—5-Phenylacridine (3 g.), sodium pellets (1·6 g.), and a little broken glass were shaken in dry ether (70 ml.) in a stoppered flask for 24 hr. The intensely violet solution was then treated, under nitrogen, with benzyl chloride, dropwise, until the colour was discharged. Excess of sodium was then removed with ethanol and after being washed with water the product (1·2 g.) was crystallised from methyl acetate, giving material of m. p. 213°, identical with product (ii) described above (Found : C, 90·1; H, 6·5; N, 3·3. Calc. for $C_{33}H_{27}N$: C, 90·6; H, 6·2; N, 3·2%).

Synthesis of 3-Benzyl-5-phenylacridine.—*p*-Benzylphenol (35 g.), dissolved in a solution of sodium (5 g.) in dry ethanol (100 ml.), was added to an ether solution of *N*-phenylbenzimidoyl chloride, prepared from benzanilide (37·4 g.) and phosphorus pentachloride (41·7 g.). The mixture was kept overnight, then most of the solvents were removed, and the remainder was poured into water and extracted therefrom into ether. Crystallisation of the product from light petroleum gave 4-*benzylphenyl* N-*phenylbenzimidoate* (51 g.), m. p. 87° (Found : C, 85·5; H, 6·0. $C_{26}H_{21}ON$ requires C, 85·9; H, 5·8%). This substance (18 g.) was heated for 2½ hr. under an air-condenser in a metal-bath at 275°. The product, N-*benzoyl-4-benzyldiphenylamine* (15 g.), when crystallised from ethanol, had m. p. 117° (Found : C, 85·6; H, 5·7; N, 3·9.

[7] Bernthsen, *Ber.*, 1883, **16**, 767.

$C_{26}H_{21}ON$ requires C, 85·9; H, 5·8; N, 3·8%). The latter compound (3·6 g.), benzoic acid (2 g.), and zinc chloride (5 g.) were heated together for 13 hr. under an air-condenser in a metal-bath at 255°. The resulting black solid was extracted with hot acetone, and this solution was poured into concentrated aqueous ammonia and set aside overnight. After addition of water, the precipitate was collected, dried, and extracted with boiling benzene. Chromatography of this through alumina gave a yellow solid which, after crystallisation from methanol–methyl acetate, had m. p. 155°, $\lambda_{max.}$ 2580, 3600 Å (log ε 5·14, 4·05), and so was undoubtedly 3-*benzyl*-5-*phenylacridine* (Found : C, 90·4; H, 5·7; N, 4·0. $C_{26}H_{19}N$ requires C, 90·4; H, 5·5; N, 4·1%).

A similar synthesis of 3-benzoyl-5-phenylacridine was also attempted by ring closure of *N* : 4-dibenzoyldiphenylamine that had been prepared by the procedure of Lippner and Tomlinson.[8] The product however proved to be 5-phenylacridine, m. p. 184°, so the *C*-benzoyl group had evidently been hydrolysed away by the drastic treatment with hot zinc chloride.

Synthesis of 1-*Benzyl*-5-*phenylacridine*.—*o*-Benzylphenol was condensed with *N*-phenylbenzimidoyl chloride, as described above, and gave a 67% yield of 2-*benzylphenyl* N-*phenylbenzimidoate*, m. p. 99° (from light petroleum) (Found : C, 85·5; H, 5·5; N, 4·0%). This, when heated for 2½ hr. at 275°, was transformed in 86% yield into N-*benzoyl*-2-*benzyldiphenylamine*, m. p. 108° (from methanol) (Found : C, 86·1; H, 6·0; N, 4·2%). The last compound (4·2 g.), benzoic acid (2·4 g.), and zinc chloride (6 g.) were heated together at 255° for 16 hr. Extraction of the condensation product by the method described above gave 1·1 g. (22%) of yellow crystals, m. p. 143°, $\lambda_{max.}$ 2570, 3600 Å (log ε 5·02, 3·95), identical by mixed m. p. and infrared spectrum with the product (iv) of the reaction of benzyl radicals and 5-phenylacridine (Found : C, 90·4; H, 5·5; N, 4·1%).

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, August 13th,* 1956.]

[8] Lippner and Tomlinson, *J.*, 1956, 4667.