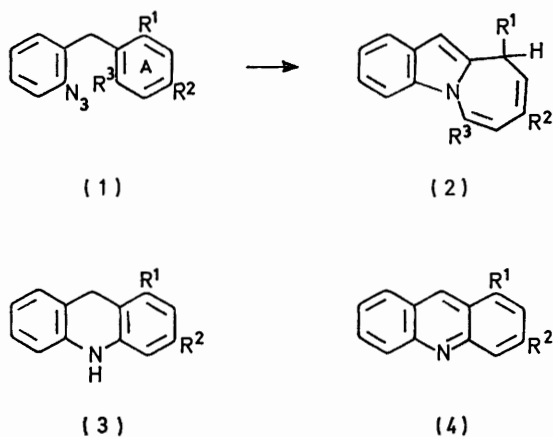


Intramolecular Nitrene Insertions into Aromatic and Hetero-aromatic Systems. Part I. Insertion into Naphthalenes and Tetralins

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Thermal decomposition of 1- and of 2-(2-azidobenzyl)naphthalenes gives, by nitrene insertion, mixtures of benz[*a*]-acridan (10) and benz[*a*]acridine (13), and of benz[*c*]acridan (21) and benz[*c*]acridine (22) respectively. Decomposition of 5-(2-azidobenzyl)tetralin (29) gives predominantly the tetrahydroindolo[2,1-*a*][2]benzazepines (31) and (34), and the tetrahydroindolo[1,2-*a*][1]benzazepine (32); 6-(2-azidobenzyl)tetralin (25) gives the tetrahydroindolo[1,2-*b*][2]benzazepine (26). Minor products from the decomposition of 1-(2-azidobenzyl)naphthalene were indolobenzazepines; minor products from the tetralins were tetrahydro- and hexahydro-benzacridines. The reasons for these contrasting insertion pathways are discussed.

We have reported^{1,2} a number of cases of intramolecular nitrene insertion reactions during decomposition of 2-azidodiphenylmethanes (1), a reaction first reported by Krbeček and Takimoto.³ The usual product of such an insertion is a 10*H*-azepino[1,2-*a*]indole (2) or its 6*H*- or 8*H*-tautomer. In cases where a 2'-methoxy-group was present appreciable quantities of acridan (3)



and acridine (4) were isolated. We are currently investigating the controlling factors in nitrene insertions, and now report investigations in which the ring A in

general formula (1) is part of a naphthalene or tetralin system.

All attempts to cause intra- or inter-molecular nitrene insertion into a naphthalene⁴ or other polycyclic system⁵ with concomitant ring expansion have so far failed. The 2-azidobenzyl naphthalenes (7) and (17) have a geometry ideal for insertion of the nitrene intermediate into the π -system of the naphthalene ring, and we would not expect that the resulting indolobenzazepines would be less stable than the azepinoindoles of type (2). The preparation of 1-(2-aminobenzyl)naphthalene (5) by reduction of the known^{6,7} 1-(2-aminobenzoyl)naphthalene gave an excellent yield, although hydrazone formation was extremely slow. The azide (7) was obtained by treatment of the diazonium salt (6) with sodium azide, and was decomposed in trichlorobenzene at 195°. G.l.c. of a sample of the product showed the presence of two major and three minor products. The major products were identified, after purification, as benz[*a*]acridan (10) (65%) and benz[*a*]acridine (13) (25%) from literature data.^{8,9} The minor products were 1-(2-aminobenzyl)naphthalene (5) (3%) and two isomers, C₁₇H₁₃N. Spectral data showed the isomers to be 7*H*-indolo[1,2-*a*][1]benzazepine (9) (3%) and 7*H*-indolo[2,1-*a*][2]benzazepine (14). In the former, for which 10*H*-azepino[1,2-*a*]indole (2; R¹ = R² = R³ = H) provides² adequate comparison, the absence of extended conjugation (λ_{\max} 263.5 nm), and an n.m.r. spectrum containing a methylene multiplet at δ 3.2–3.5, a 1H doublet at δ 6.45 (J 10 Hz, H-5), and a 1H β -indole

¹ G. R. Cliff and G. Jones, *Chem. Comm.*, 1970, 1705.

² G. R. Cliff and G. Jones, *J. Chem. Soc. (C)*, 1971, 3418.

³ L. Krbeček and H. Takimoto, *J. Org. Chem.*, 1968, **33**, 4286.

⁴ R. Huisgen, D. Vossius, and M. Appl, *Chem. Ber.*, 1958, **91**, 1; R. Huisgen and M. Appl, *ibid.*, p. 12.

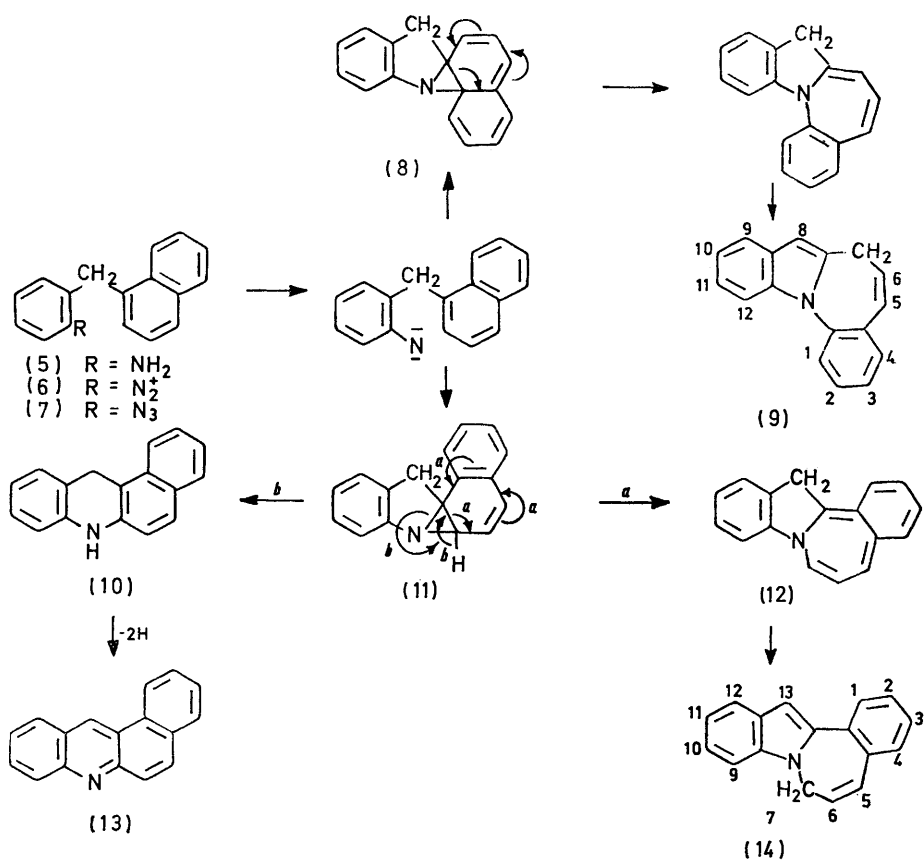
⁵ A. L. J. Beckwith and J. W. Redmond, *Austral. J. Chem.*, 1966, **19**, 1859; *J. Amer. Chem. Soc.*, 1968, **90**, 1351; R. N. Carde and G. Jones, unpublished work on 2-azidobiphenylene.

⁶ W. C. Lothrop and P. A. Goodwin, *J. Amer. Chem. Soc.*, 1943, **65**, 363.

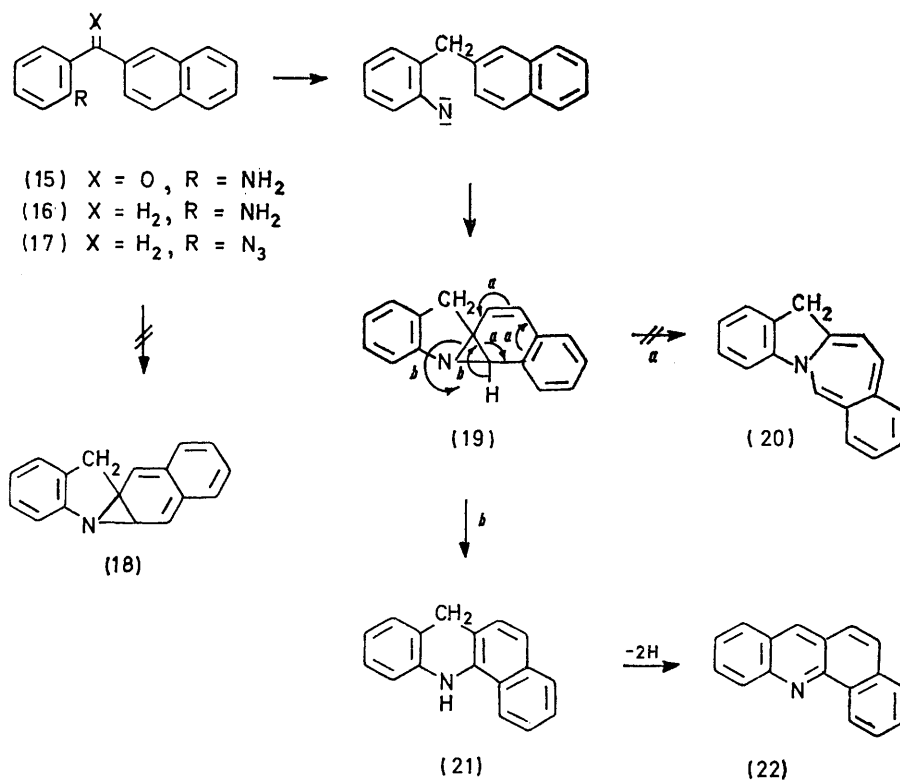
⁷ C. Graebe, *Ber.*, 1896, **29**, 827.

⁸ R. Huisgen and W. D. Zahler, *Chem. Ber.*, 1963, **96**, 736.

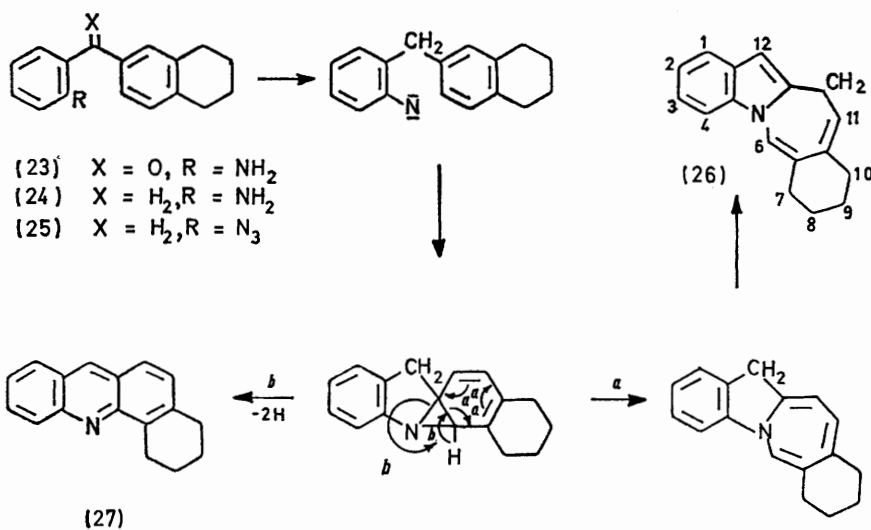
⁹ G. T. Morgan, F. M. G. Micklethwait, and H. B. Winfield, *J. Chem. Soc.*, 1904, **85**, 745.



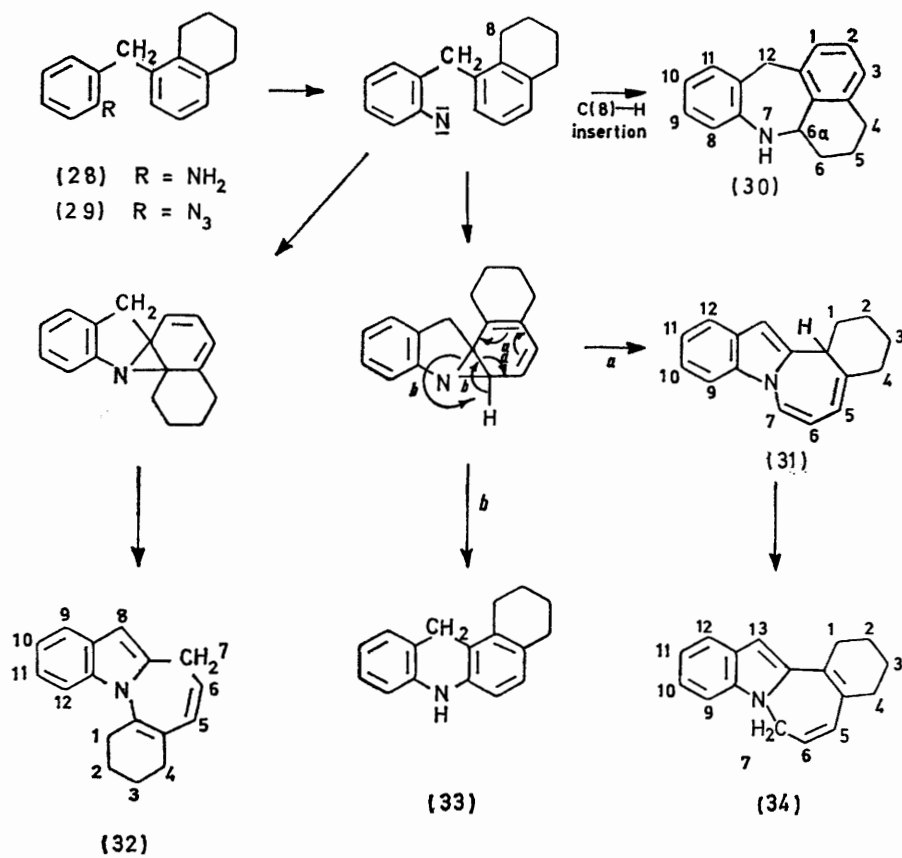
SCHEME 1



SCHEME 2



SCHEME 3



SCHEME 4

singlet at δ 6.21 are in good accord with the proposed structure (9). In the latter, extended conjugation (λ_{\max} 275.5 and 312 nm) and n.m.r. absorptions at δ 4.56 (2H, d, J 6 Hz, H-7), 6.80 (1H, d, J 9 Hz, H-5), and 6.71 (1H, s, H-13) can be compared with the spectra of 6,8,10-trimethyl-6*H*-azepino[1,2-*a*]indole.² The mass spectra of compounds (9) and (14) both show the molecular ion as base peak, again characteristic of the various α *H*-azepino[1,2-*a*]indoles. The products are summarised in Scheme 1.

The preparation of 2-(2-azidobenzyl)naphthalene (17) followed a route similar to that used for azide (7). The reaction between 2-methyl-3,1-benzoxazin-4-one and 2-naphthylmagnesium bromide reported⁶ to give only 8% of 2-(2-aminobenzoyl)naphthalene (15) gave in our hands a 30% yield. Huang-Minlon reduction gave 2-(2-aminobenzyl)naphthalene (16), which was converted *via* the diazonium salt into the azide (17). Decomposition of the azide (17) at 180° gave a mixture of benz[*c*]acridan (21) (38.5%), benz[*c*]acridine (22) (36%), and 2-(2-aminobenzyl)naphthalene (16) (3.5%) (Scheme 2).

For comparison, the products from decomposition of the corresponding tetralin azides (25) and (29) were examined. Friedel-Crafts arylation of tetralin with 2-nitrobenzoyl chloride gave a poor yield of 6-(2-nitrobenzoyl)-1,2,3,4-tetrahydronaphthalene; sequential catalytic and Huang-Minlon reduction gave first the amine (23) and then 6-(2-aminobenzyl)tetralin (24), from which the azide (25) was prepared. Decomposition of the azide (25) gave one major and a number of minor products. The major product (70%) was identified as 8,9,10,12-tetrahydro-7*H*-indolo[1,2-*b*][2-benzazepine (26). The u.v. spectrum showed the absence of extended conjugation (λ_{\max} 270 nm), and the n.m.r. spectrum showed a β -indole singlet at δ 6.07, a methylene multiplet at δ 3.26 (J 7 Hz), and a 1H triplet at δ 5.63 (H-11); all spectral data agree well with those of the 10*H*-azepinoindoles (2). The only other identified product was 1,2,3,4-tetrahydrobenz[*c*]acridine (27) (1–2%) (Scheme 3).

The 5-(2-azidobenzyl)tetralin (29) was obtained from 5-(2-aminobenzyl)tetralin (28), prepared by the standard procedure. The azide (29) decomposed at 183° (6 h) to give a complex mixture. The major products were the tetrahydroindolobenzazepines (31), (32), and (34); of these compound (31) was unstable, and its structure was assigned on limited spectral data (Tables 1 and 2). Also characterised were 1,2,3,4,7,12-hexahydrobenz[*a*]acridine (33), and a compound C₁₇H₁₇N, assigned the structure (30), assumed to be formed by nitrene C-H insertion into the *peri*-methylene group (Scheme 4).

DISCUSSION

The experiments described above suggest explanations for the failure of naphthalene derivatives to undergo ring expansion after nitrene insertion. The experiments using tetralins leave no doubt that the geometry of the systems (7) and (17) is suitable for π -bond insertion,*

and the preferred route with the tetralins leads to ring expansion. If the nitrene insertion into the naphthalenes leads to the aziridines (11) and (19) (Schemes 1 and 2) the resonance energy of one benzene ring is retained; formation of the aziridines (8) and (18) is correspondingly disfavoured. However, if the intermediates (11) or (19) proceed to the necessary precursors (12) and (20) for indolobenzazepine formation (arrows *a*) the system again loses all the naphthalene resonance energy, and hence opening to give a benzacridan (arrows *b*) is favoured. Direct opening of the aziridine ring as shown in Schemes 1 and 2 leads to an intermediate which must undergo a hydrogen shift to produce the final product. The nature of this hydrogen shift is under investigation.

EXPERIMENTAL

Column chromatography was performed on Woelm alumina, activity IV. Preparative layer chromatography (p.l.c.) was performed with 40 cm plates coated with Merck silica gel PF₂₅₄. G.l.c. was carried out on a Pye series 104, 1.5 m \times 4 mm glass column, stationary phase OV17. All u.v. spectra were determined in solution in 95% ethanol. Mass spectra were measured on a Hitachi-Perkin-Elmer RMU-6 machine, using a heated inlet.

1-(2-Aminobenzoyl)naphthalene.—The Grignard reagent from 1-bromonaphthalene (41.6 g) and magnesium (5.24 g) in dry tetrahydrofuran (200 ml) was added (0.5 h) to a cold (–5°), vigorously stirred solution of freshly distilled 2-methyl-3,1-benzoxazin-4-one (32.2 g) in dry toluene (500 ml) and dry ether (250 ml). Stirring was continued at 0° (2 h) and at room temperature (4 h). Addition of 10% hydrochloric acid (750 ml), separation of the organic layer, ether extraction of the aqueous layer, and combination of the organic extracts, gave, after evaporation of the organic solvents, a residue, which was hydrolysed by a boiling mixture of 10*N*-hydrochloric acid (200 ml) and 95% ethanol (500 ml) (4 h). The cooled mixture was washed (aq. NaOH), and extracted with ether; the combined ethereal extracts were dried (MgSO₄), evaporated, and the residue chromatographed on alumina (250 g) in toluene. The isolated 1-(2-aminobenzoyl)naphthalene (26.2 g, 53%) crystallised from ethanol (95%), m.p. 138–140° (lit.,⁶ 138°; lit.,⁷ 140.5°).

2-(2-Aminobenzoyl)naphthalene (15).—This was prepared as described above in 30% yield, m.p. 109–110° (from 95% ethanol) (lit.,⁸ yield 8.3%, m.p. 106°; lit.,⁸ m.p. 110–111°).

5-(2-Aminobenzoyl)-1,2,3,4-tetrahydronaphthalene.—This was prepared as described above from 5-bromo-1,2,3,4-tetrahydronaphthalene.⁹ The pale yellow *tetralin* had m.p. 121–122° (from 95% ethanol) (31%) (Found: C, 81.0; H, 6.6; N, 5.5. C₁₇H₁₇NO requires C, 81.25; H, 6.8; N, 5.55%), ν_{\max} (mull) 3430, 3320, 1625, and 1610 cm⁻¹, λ_{\max} 220, 233.5, 261.5, and 374 nm (log ϵ 4.29, 4.32, 3.90, and 3.80), δ (CDCl₃) 1.5–1.9 (4H, m), 2.4–2.9 (4H, m), 6.1–6.7 (4H, m; 2H exch. with D₂O), and 6.8–7.4 (5H, m).

* Similar arguments could be advanced on the basis of a spirodiene intermediate, as proposed by Cadogan.¹⁰

¹⁰ J. I. G. Cadogan, *Accounts. Chem. Res.*, 1972, 5, 303.

1,2,3,4-Tetrahydro-6-(2-nitrobenzoyl)naphthalene.— Anhydrous aluminium chloride (133 g) was added to a cold (−5°) mixture of 2-nitrobenzoyl chloride (93 g) and dry tetralin (66 g) in dry carbon disulphide (300 ml). When evolution of hydrogen chloride ceased, the mixture was boiled (2 h). The cooled mixture was hydrolysed by dilute hydrochloric acid, the organic layer removed, and the aqueous layer extracted with chloroform. The combined organic extracts were evaporated to give a black tar; column chromatography (alumina, 400 g) in chloroform gave a mixture of product and tetralin. Further chromatography (alumina, 150 g) in petroleum (b.p. 60–80°) gave the tetralin (13.6 g, 10%), crystallised from methanol as yellow plates, m.p. 140.5–141° (Found: C, 72.8; H, 5.4; N, 4.9. $C_{17}H_{15}NO_3$ requires C, 72.6; H, 5.35; N, 4.9%), ν_{\max} (mull) 1660, 1528, and 1355 cm^{-1} , λ_{\max} 266 nm (log ϵ 4.34), δ (CDCl₃) 1.7–2.0 (4H, m), 2.7–3.0 (4H, m), and 7.0–8.4 (7H, m).

6-(2-Aminobenzoyl)-1,2,3,4-tetrahydronaphthalene (23).— A solution of the foregoing nitro-compound (9.3 g) in ethanol (95%) with Pd-C (0.5 g) was hydrogenated (60 lb in⁻²) until absorption ceased. Evaporation of the filtered solution gave, after column chromatography in petroleum (b.p. 60–80°), the 2-aminobenzoyltetralin (23) as an oil, b.p. 155–160° at 0.3 mmHg (7.5 g, 86%) (Found: C, 81.7; H, 7.05; N, 5.2. $C_{17}H_{17}NO$ requires C, 81.25; H, 6.8; N, 5.55%), ν_{\max} (CCl₄) 3490, 3350, 1635, and 1615 cm^{-1} , λ_{\max} 230.5, 268, and 376 nm (log ϵ 4.21, 4.10, and 3.62), δ (CDCl₃) 1.5–2.1 (4H, m), 2.4–3.0 (4H, m), 5.95br (2H, s, exch. D₂O), and 6.4–7.6 (7H, m).

1-(2-Aminobenzyl)naphthalene (5).—A solution of 1-(2-aminobenzoyl)naphthalene (15 g) and hydrazine hydrate (12 ml) in dry ethylene glycol (250 ml) was maintained at 150° until hydrazone formation was complete (g.l.c., 24 h). Potassium hydroxide (20 g) was added slowly, and the temperature raised until distillation of water and hydrazine ceased, then maintained at 180° (4 h). The cooled, diluted mixture was extracted with ether, the ethereal extracts dried (MgSO₄) and evaporated, and the residue crystallised from petroleum (b.p. 60–80°) to give the aminobenzyl-naphthalene (5), m.p. 101.5–102.5° (12.8 g, 91%) (Found: C, 87.6; H, 6.6; N, 6.2. $C_{17}H_{15}N$ requires C, 87.5; H, 6.5; N, 6.0%), ν_{\max} (film) 3450, 3370, and 1620 cm^{-1} , λ_{\max} 225 (log ϵ 4.28), 263sh, 274sh, 283 (4.0), and 292sh nm.

2-(2-Aminobenzyl)naphthalene (16).—Similarly prepared from 2-(2-aminobenzoyl)naphthalene, in 90% yield, this had b.p. 160–170° at 0.05 mmHg (lit.,⁸ 150–160° at 0.001 mmHg).

5-(2-Aminobenzyl)-1,2,3,4-tetrahydronaphthalene (28).— Similarly prepared from 5-(2-aminobenzoyl)tetralin, in 83% yield, the pale yellow aminobenzyltetralin (28) crystallised from petroleum (b.p. 40–60°), m.p. 68.5–69° (Found: C, 86.4; H, 8.26; N, 5.8. $C_{17}H_{19}N$ requires C, 86.05; H, 8.05; N, 5.9%), ν_{\max} (CHCl₃) 3450, 3375, and 1619 cm^{-1} , λ_{\max} 219sh, 234sh, and 285 nm (log ϵ 3.37), δ (CDCl₃) 1.6–2.0 (4H, m), 2.5–3.0 (4H, m), 3.4br (2H, exch. D₂O), 3.73 (2H, s), and 6.5–7.1 (7H, m).

6-(2-Aminobenzyl)-1,2,3,4-tetrahydronaphthalene (24).— Similarly prepared from 6-(2-aminobenzoyl)tetralin, in 94% yield, the 6-aminobenzyltetralin (24) was a pale yellow oil, b.p. 165–170° at 0.45 mmHg (Found: C, 85.9; H, 7.75; N, 5.8. $C_{17}H_{19}N$ requires C, 86.05; H, 8.05; N, 5.9%), ν_{\max} (film) 3440, 3360, and 1620 cm^{-1} , λ_{\max} 224sh, 237sh,

273sh, 280.5 (log ϵ 3.8), and 289sh nm, δ (CDCl₃) 1.6–1.9 (4H, m), 2.5–2.9 (4H, m), 3.39 (2H, s, exch. D₂O), 3.78 (2H, s), and 6.4–7.2 (7H, m).

1-(2-Azidobenzyl)naphthalene (7).—A solution of 1-(2-aminobenzyl)naphthalene (5) (11.7 g) in a mixture of 4N-sulphuric acid (250 ml) and 1,4-dioxan (250 ml) was treated at −5° with sodium nitrite (3.8 g) in water (50 ml). After 15 min a solution of sodium azide (3.6 g) in water (50 ml) was added, and the mixture warmed to 30°. The cooled mixture was extracted with ether, and the ethereal extracts dried (MgSO₄) and evaporated (reduced pressure, ambient temperature). The residual oil was percolated through alumina (200 g) in petroleum (b.p. 60–80°), and the eluted azide (7) (10.8 g, 84%) was a pale yellow oil (Found: C, 78.5; H, 5.1; N, 15.9. $C_{17}H_{13}N_3$ requires C, 78.75; H, 5.05; N, 16.2%), ν_{\max} (film) 2125 and 1285 cm^{-1} , λ_{\max} 221.5 (log ϵ 4.92), 253 (4.08), 260sh, 271sh, and 281 nm (4.01), δ (CCl₄) 4.23 (2H, s) and 6.6–8.0 (11H, m).

2-(2-Azidobenzyl)naphthalene (17).—Similarly prepared, in 56% yield, from 2-(2-aminobenzyl)naphthalene (16), the azide (17) was a yellow oil (Found: C, 79.6; H, 5.65; N, 15.1. $C_{17}H_{13}N_3$ requires C, 78.75; H, 5.05; N, 16.2%), ν_{\max} (film) 2125 and 1290 cm^{-1} , λ_{\max} 228 (log ϵ 4.93), 253 (4.15), 275sh, and 285sh nm, δ (CDCl₃) 3.98 (2H, s) and 6.9–7.8 (11H, m).

5-(2-Azidobenzyl)-1,2,3,4-tetrahydronaphthalene (29).— Similarly prepared, in 90% yield, the azide (29) gave crystals, m.p. 48–50° from petroleum (b.p. 40–60°) (Found: C, 78.1; H, 6.85; N, 15.6. $C_{17}H_{17}N_3$ requires C, 77.55; H, 6.5; N, 15.95%), ν_{\max} (film) 2130 and 1290 cm^{-1} , λ_{\max} 251.5 (log ϵ 3.99), 278sh, and 288sh nm, δ (CDCl₃) 1.5–1.9 (4H, m), 2.3–2.9 (4H, m), 3.81 (2H, s), and 6.6–7.2 (7H, m).

6-(2-Azidobenzyl)-1,2,3,4-tetrahydronaphthalene (25).— Similarly prepared from 6-(2-aminobenzyl)tetralin (24), in 62% yield, the azide (25) crystallised from 95% ethanol as pale yellow needles, m.p. 44–45° (Found: C, 78.1; H, 6.75; N, 15.9. $C_{17}H_{17}N_3$ requires C, 77.55; H, 6.5; N, 15.95%), ν_{\max} (mull) 2118 and 1288 cm^{-1} , λ_{\max} 251.5 (log ϵ 3.99), 279sh, and 289sh nm, δ (CDCl₃) 1.6–1.9 (4H, m), 2.5–2.9 (4H, m), 3.83 (2H, s), and 6.8–7.2 (7H, m).

Thermal Decomposition of Azides: Typical Procedure.—A solution of the azide (7) (9.5 g) in 1,2,4-trichlorobenzene (100 ml) was added dropwise over 45 min to vigorously stirred trichlorobenzene (1.5 l) at 195° and the mixture was maintained at this temperature (4 h) while dry nitrogen was passed through the solution. Removal of the solvent at 1 mmHg produced a pale yellow solid: g.l.c. (245°; N₂ 50 ml min⁻¹) showed five peaks. Peaks 4 and 5 (in increasing retention time) made up the bulk of the material. Acid washing of an ethereal solution of the mixed products removed product 4; basification of the acid extracts gave a solid, crystallising from petroleum (b.p. 60–80°), identified as benz[*a*]acridine (13), m.p. 130.5–131° (lit.,¹¹ 131°). Evaporation of the ethereal solution, after removal of product 4, gave a residue; product 5 crystallised from petroleum (b.p. 60–80°), and was identified as benz[*a*]acridin (10), m.p. 166–168° (lit.,¹² 166–168°). Column chromatography of the crude mixture (4 g) (alumina, 300 g; toluene) gave four major fractions; the third of these gave pure 1-(2-aminobenzyl)naphthalene (5), m.p. 101–102°. From the first fraction by p.l.c. (toluene), followed by further column chromatography of the band of highest *R*_F

¹¹ N. G. Buu-Hoi, R. Royer, and M. Hubert-Habart, *J. Chem. Soc.*, 1955, 1082.

¹² W. A. Waters and D. H. Watson, *J. Chem. Soc.*, 1959, 2082.

86.2; H, 6.95; N, 5.7%), ν_{\max} (film) 3490 and 1604 cm^{-1} , λ_{\max} 260 ($\log \epsilon$ 3.91) and 235 nm (3.44), δ (CDCl_3 ; 220 MHz) 1.7—2.2 (4H, m), 2.68—2.85 (2H, m), 3.3br (NH, exch. D_2O), 3.36 (1H, d, J 15.2 Hz, H-12), 4.92 (1H, d, J 15.2 Hz, H-12), 5.1—5.2 (1H, m, H-6a), 6.36 (1H, d, J 8 Hz), 6.54 (1H, t, J 8 Hz), and 6.8—7.2 p.p.m. (5H, m), m/e 236 (13%, M^+), 235 (85), 234 (65), 233 (13), 218 (13), 208 (18), 207 (100), 206 (30), and 204 (13). Fraction (E) crystallised from petroleum (b.p. 60—80°) to give 1,2,3,4,7,12-hexahydrobenz[*a*]acridine (33), m.p. 168—170°, δ (CDCl_3) 1.6—2.0 (4H, m), 2.5—2.9 (4H, m), 3.94 (2H, s, H-12), 5.72br (NH, exch. D_2O), and 6.3—7.2 (6H, m). The hexahydro-

benzacridine (33) was rapidly oxidised and was characterised as its oxidation product 1,2,3,4-tetrahydrobenz[*a*]acridine, m.p. 119.5—120.5° [from petroleum (b.p. 60—80°)] (Found: C, 87.3; H, 6.25; N, 6.0. $\text{C}_{17}\text{H}_{15}\text{N}$ requires C, 87.5; H, 6.5; N, 6.0%), ν_{\max} (mull) 1625 cm^{-1} , λ_{\max} 250sh, 256 ($\log \epsilon$ 5.15), and 355 (3.97) nm, δ (CDCl_3) 1.6—2.0 (4H, m), 2.6—3.0 (4H, m), 6.9—8.3 (6H, m), and 8.42 (1H, s).

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