Intramolecular Nitrene Insertions into Aromatic and Heteroaromatic Systems. Part 7.[1] Insertions into Electron-deficient Rings

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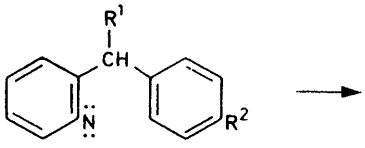
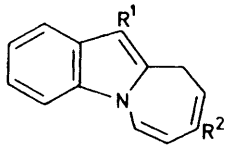
A number of routes to *o*-aminotriphenylmethanes are described, where one benzene ring, or both, carry potential ester groups. The most useful synthon is shown to be the 1,3-dioxan-2-yl substituent, and using this methyl 2-aminodiphenylmethane-4′-carboxylate (18) and dimethyl 2-aminotriphenylmethane-4′,4″-dicarboxylate (28) have been prepared. The azides from these, respectively (19) and (29), on thermolysis at 200 °C gave azepinoindoles (48) and (51), the first examples of ring expansion by an arylnitrene of benzene rings with electron-withdrawing substituents. Also reported are syntheses of 3- and 4-(2-azidobenzyl)pyridines (38) and (39), and of 2-(2-azidobenzyl)thiazole (40); decomposition of these azides gave mainly polymers.

We have reported[2,3] that 2-nitrenodiphenylmethanes (1) give azepinoindoles (2) as principal products, while 2-nitrenotriphenylmethanes (3) give a mixture of azepinoindoles (2) with acridans (4) and acridines (5). Also, the presence of a *p*-methoxy-group on the recipient ring gives a tetracyclic compound (6) in the triphenylmethane series but not in the diphenylmethane series.[3] We have now prepared 2-azidodi- and -tri-phenylmethanes in which a methoxycarbonyl group is present in the recipient ring, together with 2-azidobenzylpyridines and 2-azidobenzylthiazole. The methods of preparation, and the results of thermolysis, are described here.



(1) R^1 = H or Me, R^2 = various
(3) R^1 = Aryl, R^2 = H, OMe, NMe_2



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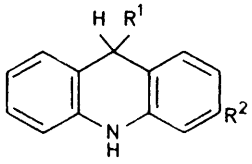

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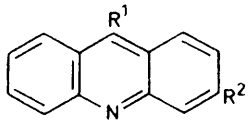

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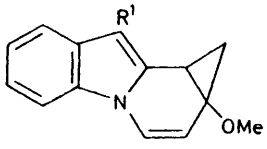
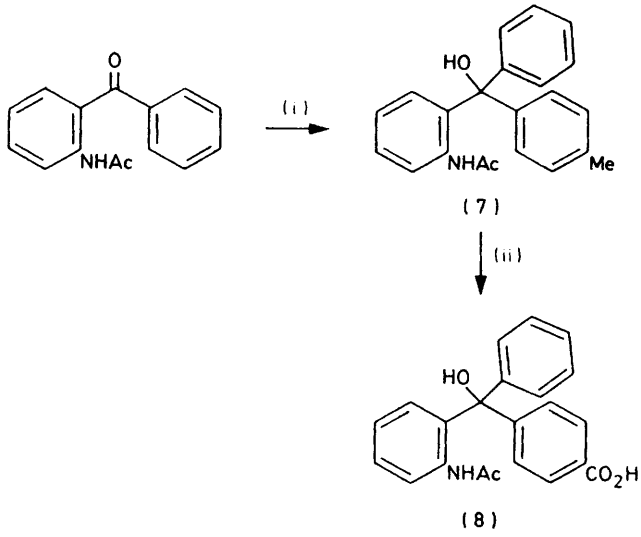


(6) a; R^1 = Ph
b; R^1 = 4-$MeOC_6H_4$

Synthesis.—There are considerable difficulties in the synthesis of a 2-nitro- or 2-amino-diphenylmethane or -triphenylmethane where the second and third rings contain an electron-withdrawing substituent. Our prefered routes have used Grignard reagents,[4] and electron-withdrawing substituents are normally incompatible with Grignard reagents, so that some concealed functionality is required. The most suitable electron-withdrawing substituent appeared to be the alkoxycarbonyl group, and there are a number of satisfactory synthons for the carboxy-group. The simplest of these

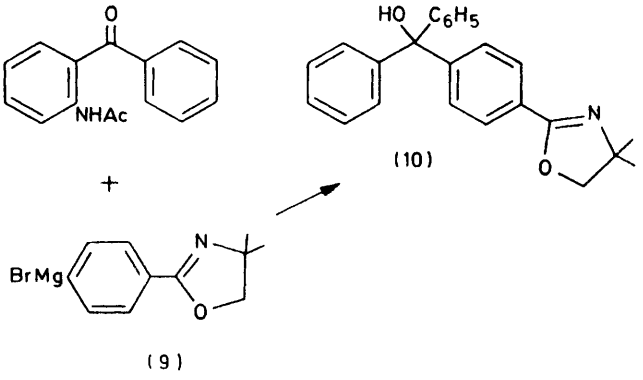


Scheme 1 *Reagents:* (i) *p*-MeC_6H_4MgBr; (ii) $KMnO_4$

is the methyl group which can subsequently be oxidised. The triphenylmethanol (7) was prepared by the reaction of *p*-tolylmagnesium bromide with 2-acetamidobenzophenone. An attempt to oxidise the methyl group in a heterogeneous reaction with aqueous permanganate gave a poor yield of the acid (8). Because of the poor yield and the need for long reaction times and multiple oxidations this route was abandoned without attempts to remove the hydroxy-group.

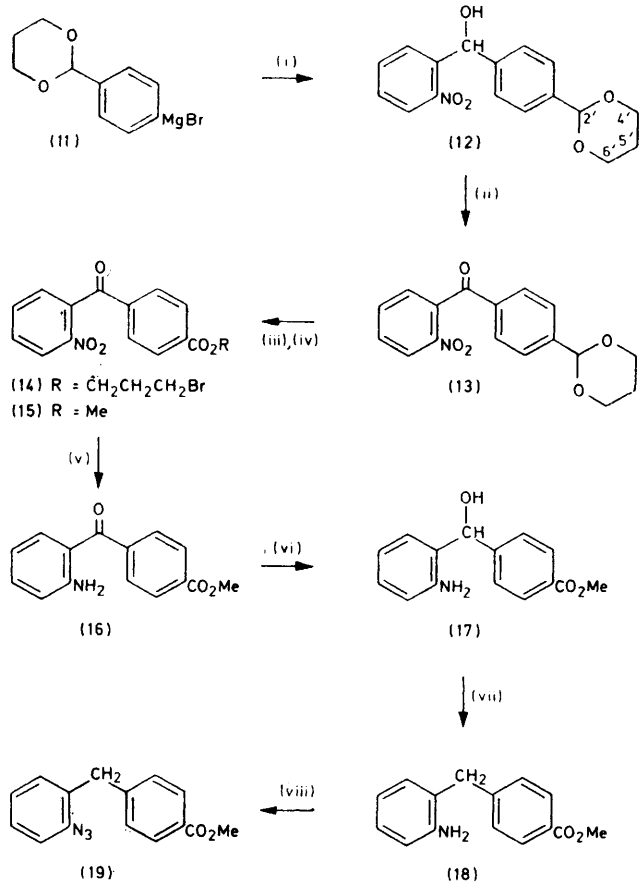
A well-known synthon for the carboxy (or formyl) group is a 4,4-dimethyl-1,3-oxazolin-2-yl substituent[5] and this is known to be unreactive towards Grignard reagents. We treated 2-acetamidobenzophenone with the Grignard reagent (9) and obtained the oxazolinyl-

triphenylmethanol (10). Attempts to reduce the triphenylmethanol to triphenylmethane, for example with formic acid, were unsuccessful. With hindsight,



regeneration of the carboxylic acid with subsequent reduction might have been successful.

We were able to obtain our alkoxycarbonyl-substituted



SCHEME 2 *Reagents:* (i) o-$O_2NC_6H_4CHO$ (A) 1 equiv., −70 °C; (ii) (A), 2 equiv., room temp.; (iii) NBS; (iv) MeOH, HCl; (v) Pd–C, C_6H_{10}; (vi) $NaBH_4$; (vii) Pd–C, H_2, HCl; (viii) HONO, NaN_3

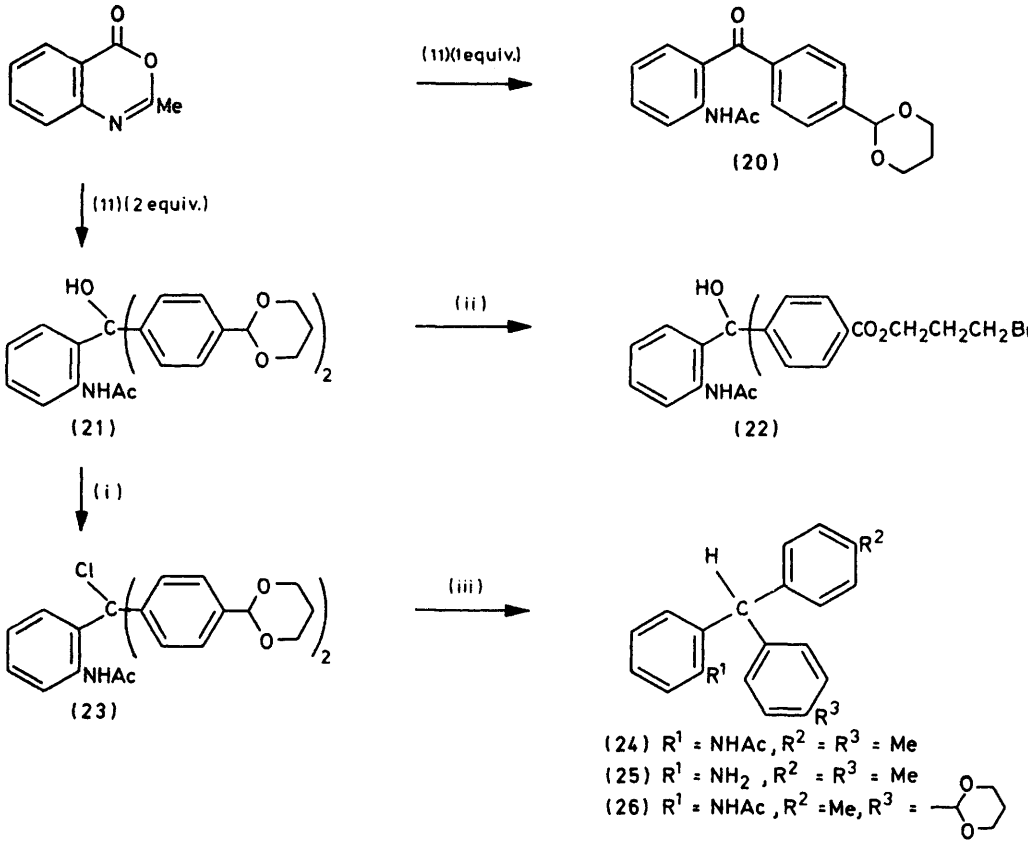
di- and tri-phenylmethanes by using the Grignard reagent (11) from 2-(p-bromophenyl)-1,3-dioxan (Scheme 2). We have established the general use of this versatile formyl and alkoxycarbonyl synthon;[6] the key to its use is its easy and high-yield conversion by N-bromosuccinimide into a 3-bromopropyl ester.[7] The Grignard reagent (11) can only be prepared in the presence of some tetrahydrofuran; at −78 °C it reacted with o-nitrobenzaldehyde to give the diphenylmethanol (12). In the presence of an excess of o-nitrobenzaldehyde, and when allowed to warm to room temperature, the reaction gave the 2-nitrobenzophenone (13). This reaction, reminiscent of the Oppenauer oxidation, has been reported before,[8] but only a few uses in synthesis have been described.[9]

Treatment of the dioxan with N-bromosuccinimide in boiling carbon tetrachloride gave an almost quantitative yield of the 3-bromopropyl ester (14), which was transesterified with methanolic hydrogen chloride to the methyl ester (15). Transfer hydrogenation of the nitro-group gave the amine (16) (92% yield), and reduction first with borohydride to give the amino-alcohol (17), then catalytically gave the aminodiphenylmethane (18). Diazotisation and treatment with azide ion gave the azidodiphenylmethane (19).

The synthesis of triphenylmethanes proved much more difficult. The reaction between acetanthranil and the Grignard reagent (11) could be used to make either the 2-acetamidobenzophenone (20) or the triphenylmethanol (21), although the yield of neither was high. Reducing agents suitable for the conversion of triphenylmethanols into triphenylmethanes include zinc dust and acetic acid,[10] anhydrous formic acid,[11] isopropyl alcohol in concentrated sulphuric acid,[12] and boron trifluoride in diethylene glycol.[13] The dioxan ring seemed unlikely to survive any of these, so the compound (21) was treated with N-bromosuccinimide to give the diester (22), and reduction with anhydrous formic acid was attempted, but a tar was obtained. The alcohol (21) was converted into the chloride (23) and this was reduced by the hydridotetracarbonylferrate anion [14] to give a mixture. Dissolving-metal reduction of the chloride (23) also gave a mixture: the products, identified spectroscopically, were the ditolyl amide (24) and the amine (25), and the mono-dioxanyl derivative (26), but the yields were poor.

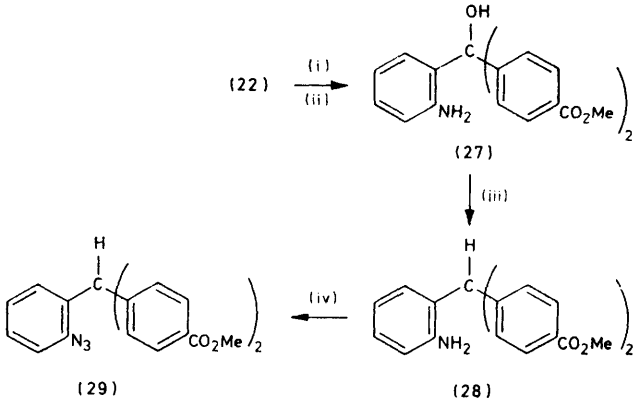
To reduce the number of active sites in our triphenylmethanol to a minimum, we hydrolysed the ester (22), and re-esterified with methanolic hydrogen chloride, giving the amino-ester (27). Removal of the hydroxy-group was not achieved by catalytic reduction, nor with anhydrous formic acid, nor with the 'ionic hydrogenation' reagents, sodium borohydride in trifluoroacetic acid [15] or isopropyl alcohol and sulphuric acid. In the last two cases the problem clearly arose from the lack of ionisation with the three electron-withdrawing substituents. Fortunately red phosphorus and iodine converted the alcohol (27) into the triphenylmethane (28) and formation of the azide (29) was routine, although the yield was poor.

From the reaction at −78 °C between o-nitrobenzaldehyde and 3-pyridyl-lithium or 4-pyridyl-lithium the



SCHEME 3 *Reagents:* (i) MeCOCl; (ii) NBS; (iii) Na, Bu^{t}OH

2-nitrobenzyl alcohols (30) and (31) were obtained. Catalytic reduction of the nitro-compound (30) gave the amino-alcohol (32), which was slowly reduced in an acidic medium to 3-(2-aminobenzyl)pyridine (33). Reduction of compound (31) to 4-(2-aminobenzyl)-pyridine (34) was accomplished in one step. A similar



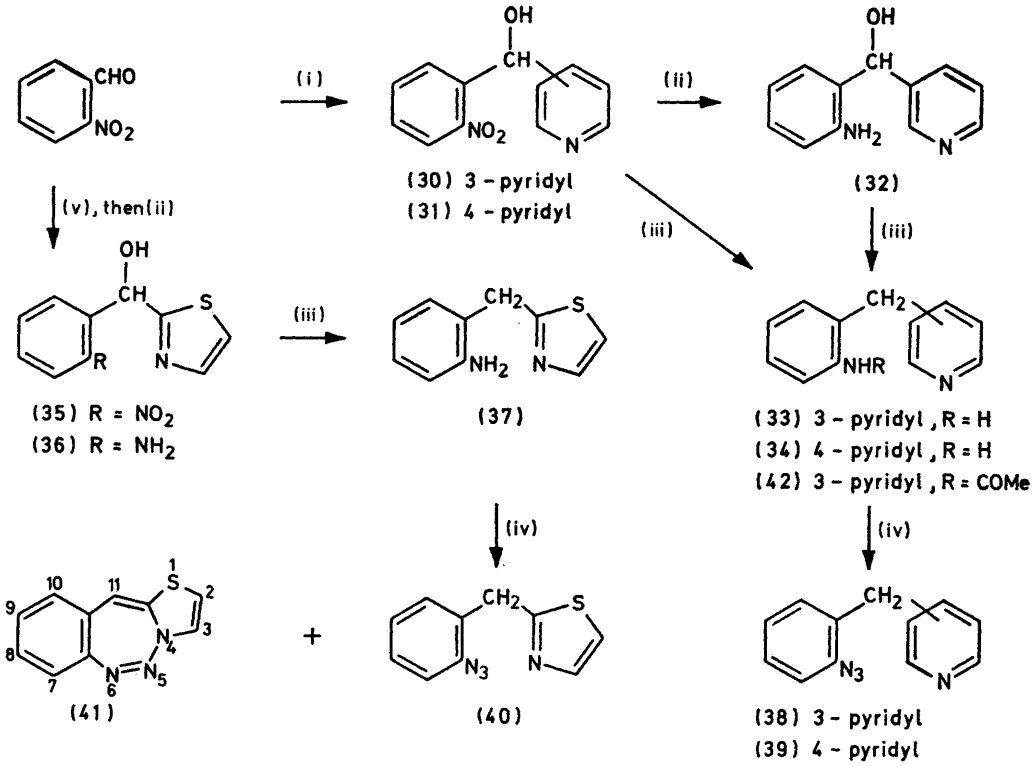
SCHEME 4 *Reagents:* (i) Aq. HCl; (ii) MeOH, HCl; (iii) I_2, red P; (iv) HONO, NaN_3

sequence from thiazol-2-yl-lithium gave the nitro-alcohol (35), the amino-alcohol (36), and thence 3-(2-aminobenzyl)thiazole (37). The three amines (33), (34), and (37) were converted into the azides (38)—(40).

A by-product from the diazotisation of amine (37) was thiazolo[3,2-*c*][1,2,3]benzotriazepine (41). The ^{1}H n.m.r. spectrum of compound (41) showed signals at δ 7.35 and 7.5 (each 1 H, each tr of d, H-8 and -9), 7.6 (1 H, d, H-2, $J_{2,3}$ 3.4 Hz), 7.68 (1 H, s, H-11), 7.73br (1 H, d, H-10), 8.1 (1 H, d, H-3, $J_{2,3}$ 3.4 Hz), and 8.66br (1 H, d, H-7, $J_{7,8}$ 6.8 Hz).

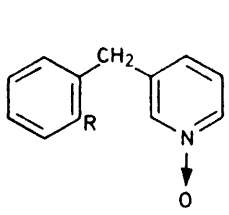
The amine (33) was acetylated to give the *N*-acetyl derivative (42), which was oxidised to the *N*-oxide (43). The amino *N*-oxide (44) was then converted into the azide (45). An attempt to prepare 4-(2-azidobenzyl)-2,6-diphenylpyridine, from *o*-nitrobenzaldehyde and 4-lithio-2,6-diphenylpyridine *via* the alcohol (46) was pursued only as far as the amino-alcohol (47), when the overall yield was too small to continue.

Thermolysis of Azides.—Decomposition of the azides (19) and (29) was performed at 200 °C in dilute solution in trichlorobenzene. From azide (19) three products were isolated and characterised and these were the azepinoindole ester (48) (34%), the acridine ester (49) (4%), and the amine (18) (4.8%). The azepinoindole (48) showed in the ^{1}H n.m.r. spectrum the characteristic β-indole proton at δ 6.15 and the 10-H structure was confirmed by the doublet at δ 3.54 (J 6 Hz): H-6 and H-7 formed an AB doublet with J 9.2 Hz. The azepinoindole (48) as first isolated, showed also a small doublet in the ^{1}H n.m.r. spectrum at δ 4.69 which we

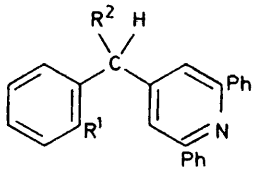


SCHEME 5 *Reagents:* (i) 3- or 4-pyridyl-lithium, −78 °C; (ii) Pd–C, H_2; (iii) Pd–C, HCl, H_2; (iv) $NaNO_2$, HCl, then NaN_3; (v) thiazol-2-yl-lithium

assign to a small percentage (*ca.* 8%) of the 6*H*-isomer (50) Although we were unable to obtain a pure specimen of the 6*H*-isomer, we confirmed its molecular weight by gas-chromatography–mass spectrometry and



(43) R = NHAc
(44) R = NH_2
(45) R = N_3



(46) R^1 = NO_2, R^2 = OH
(47) R^1 = NH_2, R^2 = OH

its breakdown pattern was very similar to that of the 10*H*-isomer, with a major peak at $M - 1$. The important feature to be established for the acridine (49) was the position of the methoxycarbonyl substituent, since we have reported that in one acridine isolated from a nitrene insertion reaction rearrangement has taken place.[3] In the ^{1}H n.m.r. spectrum of compound (49) there was a downfield doublet at δ 8.99 (J 1.2 Hz) which we assign to H-4 (*meta* coupling only, because of the methoxycarbonyl group at C-3). This assignment was confirmed by addition of $Eu(fod)_3$ shift reagent which caused major downfield shifts in this doublet and in another doublet of doublets (H-5).

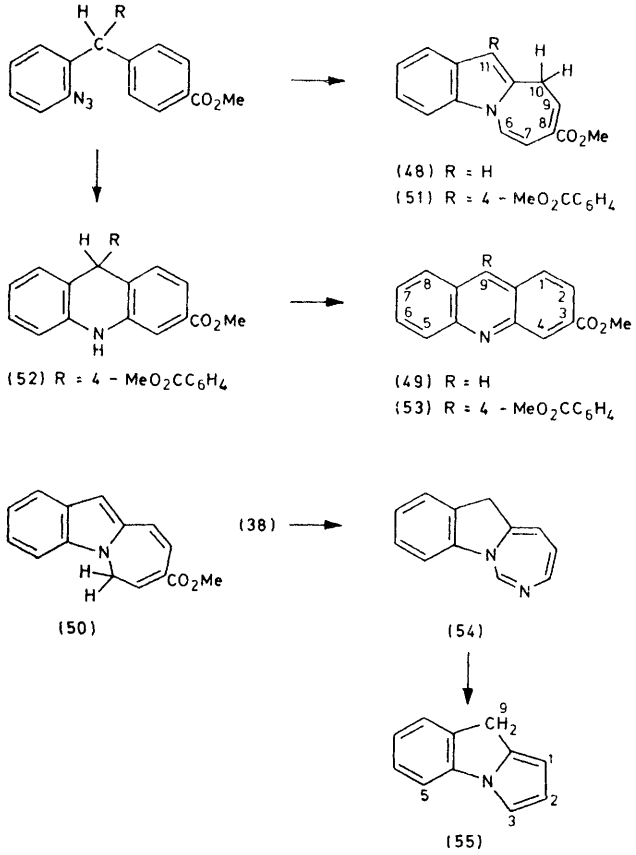
From the azide (29) we isolated three products, identified as the azepinoindole (51) (34%), the acridan (52) (9.8%), which was not fully characterized, and the acridine (53) (5%). The spectra of the azepinoindole (51) were very similar to those of azepinoindole (48); no β-indole hydrogen was present in the ^{1}H n.m.r. but the doublet (H-7) (J 9.4 Hz) at δ 6.39 placed the methoxycarbonyl group at C-8. The acridine (53) was again shown to carry the methoxycarbonyl group at C-3.

Thermolysis of the azides (38), (39), (40), and (45) gave in each case as major product polymeric materials. The only identified products were small amounts of amines (33), (34), and (37), and, from azide (38), a compound of m.p. 90—91 °C and analysing for $C_{11}H_9N$. The ^{1}H n.m.r. spectrum showed signals at δ 3.83 (2 H, s, CH_2), 6.1 (1 H, dd, J 3 and 1.5 Hz), 6.38 (1 H, dd, J 3 and 3 Hz), and 6.99—7.42 (5-H) for which the most likely structure was 9*H*-pyrrolo[1,2-*a*]indole (55).[16] This compound is presumably formed from the diazepinoindole (54). A concerted cyclisation with subsequent elimination of HCN is unlikely; we can advance no evidence for the mechanism of ring contraction.

DISCUSSION

The most important aspect of the nitrene insertions described in this work is the success of the attack by the nitrene on an electron-deficient benzene ring. Methanesulphonylnitrenes have been shown to react with benzenes carrying electron-withdrawing substituents;[17] although the authors present convincing arguments for

a singlet nitrene no ring expansion to azepines was observed (the reaction which we have associated [3] with a singlet nitrene). Azepines have been prepared also by photolysis of *o*-azidobenzoates in methanol: here the suggestion was that the *ortho*-placed electron-withdrawing group made the nitrene more electrophilic, although the effect cannot be simple since *p*-azidobenzoates were converted into azepines much more



slowly.[18] We have felt that the singlet nitrene, thermally generated, should be sufficiently energetic to cause ring expansion even of electron-deficient rings, especially if the attack was intramolecular as in the case of nitrenes generated from *o*-azidobenzylbenzenes, and this view has now been confirmed. Other points to note are the decreased yields of azepinoindole from the azide (19) compared, for example, with those obtained from *o*-azidodiphenylmethane (56%) and the *o*-azido-4′-methoxydiphenylmethane (48%) (not unexpected with the increased energy of activation expected for the attack on an electron-deficient ring); and the decreased proportion of acridine and acridan relative to azepinoindole observed in the decomposition of azide (29). For comparison, *o*-azidotriphenylmethane gave almost equal amounts of azepinoindole and of acridine–acridan mixture, while *o*-azido-4′,4″-dimethoxytriphenylmethane gave the tetracyclic compound (6b) and the acridine–acridan mixture in a ratio 1 : 2. We have suggested [3] that the triphenylmethanes give more acridine–acridan by a hydrogen abstraction, leading to a carbonium ion, less stable (and therefore less accessible) in the diphenylmethane. Our latest results support this suggestion, since electron-withdrawing substituents would lower the stability of the carbonium ion. We have been intrigued by the formation of tetracyclic compounds (6a) and (6b) when a *para*-methoxy-group was present in the original triphenylmethane. We can detect no trace of such a tetracyclic compound from the decomposition of azide (29), which seems to argue that only an electron-donating group can stabilise the tetracyclic compounds of type (6).

We have no explanation for the predominance of polymerisation during the decomposition of azides (38)—(40). We had suspected that the electron-deficient heterocyclic rings inhibited attack by the electrophilic singlet nitrene, thus allowing time for cross-over to triplet, with radical-induced polymerisation. The success of the insertions into the electron-deficient benzene rings makes this suspicion less justified, as does the predominance of polymerisation with the nitrene from azide (45) where the *N*-oxide increases the electron availability in the heterocyclic ring.*

EXPERIMENTAL

Chromatography was performed on alumina (Woelm activity 4 unless otherwise stated) in columns, or silica (Merck PF_{254}) on preparative plates or in medium pressure columns. N.m.r. spectra were run for solutions in $CDCl_3$ unless otherwise stated.

2-Acetamido-4′-methyltriphenylmethanol (7).—A solution of 2-acetamidobenzophenone (48 g) in tetrahydrofuran (THF) (100 ml) was added dropwise to a vigorously stirred, boiling solution of the Grignard reagent from *p*-bromotoluene (103 g) and magnesium (16 g) in dry ether (500 ml). Boiling was continued (4 h) then the cooled mixture treated with a saturated solution of ammonium chloride in ammonia (*d*, 0.880; 500 ml). The ethereal layer was separated, combined with the ethereal washings from the aqueous layer, and the total organic solution was dried ($MgSO_4$), filtered, and evaporated. The residue was triturated with light petroleum (b.p. 60—80 °C), to afford the *triphenylmethanol* (7), which was recrystallized from dichloromethane–light petroleum (b.p. 60—80 °C) (34.4 g, 52%), m.p. 183—185 °C (Found: C, 79.95; H, 6.3; N, 4.0. $C_{22}H_{21}NO_2$ requires C, 79.75; H, 6.4, N, 4.2%); δ 1.51 (3 H, s, $COCH_3$), 2.32 (3 H, s, CH_3), 4.45br (1 H, s, exch. D_2O, OH), 6.5—7.4 (12 H, m), 8.01 (1 H, d), and 9.0br (1 H, s, exch. D_2O, NH); $\nu_{max.}$ (mull) 3 500—3 000 (br), 1 665, and 1 583 cm^{-1}; *m/e* 331 (M^+), 313 (M − 18), 271, and 270 (base peak, loss of H_2O and CH_3CO).

Oxidation of the Triphenylmethanol (7).—A suspension of the triphenylmethanol (7) (10g) in a solution of magnesium sulphate (16 g) in water (450 ml) was vigorously stirred and boiled, during the addition of a solution of potassium permanganate (16 g) in water (50 ml) and for a further 4 h, when the purple colour had disappeared. The mixture was filtered, and the manganese dioxide washed with hot

* *Note added in proof:* Our attention has been drawn to a paper by F. D. Marsh and H. E. Simmons (*J. Am. Chem. Soc.*, 1965, **87**, 3529) in which they reported intermolecular insertion by cyanonitrene into aromatic rings, some bearing electron-withdrawing substituents.

water (500 ml) and then chloroform. From the chloroform washings was recovered starting material (6 g). Acidification of the combined aqueous layers gave 2-*acetamido*-4′-*carboxytriphenylmethanol* (8), m.p. 191—194 °C (from ethyl acetate) (2 g, 55% on unrecovered starting material) (Found: C, 73.15: H, 5.1: N, 3.55. $C_{22}N_{19}NO_4$ requires C, 73.15; H, 5.25; N, 3.9%); δ([$^2H_6$]DMSO) 1.56 (3 H, s, CH_3CO), 3.4br (1 H, s, exch. D_2O, OH), 6.3—8.0 (13 H, m), 9.2br (1 H, s, exch. D_2O, NH), and 11.0—13.5br (1 H, s, exch. D_2O CO_2H) $\nu_{max.}$ (mull) 3 490 (NH), 1 690 (CO_2H), 1 655 (NHCO) cm^{-1} *m/e* 361 (M^+), 301, 300 (base peak, $M - H_2O - CH_3CO$).

2-*Acetamido*-4′-(4,4-*dimethyl*-2-*oxazolin*-2-*yl*)*triphenylmethanol* (10).—A solution of 2-acetamidobenzophenone (12 g) in THF (50 ml) was added dropwise to a boiling solution of the Grignard reagent from 2-(4-bromophenyl)-4,4-dimethyloxazoline (25.4 g) [5] and magnesium (2.65 g) in THF (300 ml). Work-up as described for compound (7) gave a red oil; chromatography on alumina (300 g) eluting with benzene, then dichloromethane, gave the *triphenylmethanol* (10), m.p. 103—105 °C [from carbon tetrachloride–light petroleum (b.p. 60—80 °C)] (5.5 g, 27%) (Found: C, 70.5; H, 6.15, N, 6.2. $C_{26}H_{26}N_2O_3 \cdot 1.5H_2O$ requires C, 70.75; H, 6.55; N, 6.3%); δ 1.32 [6 H, s, $(CH_3)_2C$] 1.56 (3 H, s, $COCH_3$), 4.05 (2 H, s, OCH_2), 5.1br (1 H, s, exch. D_2O, OH), 6.5—8.0 (13 H, m), and 8.9br (1 H, s, exch. D_2O, NH); $\nu_{max.}$ (mull) 1 670 and 1 630 cm^{-1}; *m/e* 414 (M^+), 354, 353 (base peak, $M - H_2O - CH_3CO$), 273, and 196.

4-(1,3-*Dioxan*-2-*yl*)-2′-*nitrodiphenylmethanol* (12).—A solution of 4-(1,3-dioxan-2-yl)phenylmagnesium bromide (0.24 mol) in THF (700 ml) was added over 3 h to a cooled (−78 °C) solution of 2-nitrobenzaldehyde (36.2 g, 0.24 mol) in toluene (78 ml). The mixture was stirred at −70 °C (2 h), then allowed to warm to −5 °C over 1 h. After hydrolysis with a saturated solution of ammonium chloride in aqueous ammonia (500 ml), the organic layer was separated, washed with water, saturated sodium metabisulphite solution, and again with water, dried (Na_2SO_4), and evaporated. The residual oil was chromatographed on alumina (1 400 g), elution with dichloromethane giving the *nitrodiphenylmethanol* (12) (30.1 g, 40%), m.p. 98—99 °C (from ethyl acetate) (Found: C, 64.85; H, 5.45; N, 4.35. $C_{17}H_{17}NO_5$ requires C, 64.75; N, 5.4; N, 4.45%); δ 1.35br (1 H, d, $5'_{eq}$) 1.8—2.55 (1 H, m, $5'_{ax}$), 3.5br (1 H, d, exch. D_2O, OH), 3.65—4.35 (4 H, m, H-4′ and -6′), 5.4 (1 H, s, H-2′), and 7.1—7.9 (8 H, m).

4-(1,3-*Dioxan*-2-*yl*)-2′-*nitrobenzophenone* (13).—The reaction was conducted as described for the preparation of the diphenylmethanol (12) except that approximately 2 equivalents of 2-nitrobenzaldehyde were used. The reaction mixture was allowed to warm to room temperature, and kept at this temperature overnight. Work-up as before gave an oil which solidified when triturated with methanol, to give the *benzophenone* (13), m.p. 126—127 °C (46%) (Found: C, 65.35; H, 4.75; N, 4.5. $C_{17}H_{15}NO_5$ requires C, 65.15; H, 4.8; N, 4.5%); δ 1.4 (1 H, d, H-$5'_{eq}$), 1.7—2.5 (1 H, m, H-$5'_{ax}$), 3.6—4.3 (4 H, m, H-4′ and -6′), 5.4 (1 H, s, H-2′), and 7.2—8.15 (8 H, m); $\nu_{max.}$ ($CHCl_3$) 1 675, 1 525, and 1 345 cm^{-1}; *m/e* 313 (M^+), 312, 296 (base peak, $M - 17$), 255, 254, 177, 162, 161, and 160. The brown oil recovered from the methanol solution was chromatographed on alumina, giving 2-nitrobenzyl alcohol and the diphenylmethanol (12) (17%).

Methyl 4-(2-*Nitrobenzoyl*)*benzoate* (15).—(*a*) The benzophenone (13) (10 g) in carbon tetrachloride (100 ml) was treated with *N*-bromosuccinimide (5.7 g) and the mixture was boiled (3 h), then cooled, and filtered. The filtrate was washed with sodium thiosulphate solution, then water, and dried (Na_2SO_4). The solvent was removed *in vacuo* to give a yellow oil (12.4 g, 98%) having δ 2.25 (2 H, q, $CH_2CH_2CH_2$), 3.45 (2 H, t, CH_2Br), 4.4 (2 H, t, CH_2O), 7.3—8.2 (8 H, m); $\nu_{max.}$ (film) 1 725 and 1 690 cm^{-1}.

(*b*) The 3-bromopropyl ester (34.6 g) was dissolved in dry methanol (356 ml) saturated with dry hydrogen chloride. The solution was boiled (18 h), cooled, and concentrated *in vacuo*. The *methyl ester* (15) crystallised (18.6 g, 75%), m.p. 130—132 °C (Found: C, 62.8; H, 3.8; N, 4.95. $C_{15}H_{11}NO_5$ requires C, 63.15; H, 3.85; N, 4.9%); δ 3.9 (3 H, s, OCH_3) and 7.2—8.2 (8 H, m); *m/e* 285 (M^+), 254 ($M - 31$), 163, and 134 (base peak).

Methyl 4-(2-*Aminobenzoyl*)*benzoate* (16).—A solution of the ester (15) (18.6 g) and cyclohexene (111.6 ml) in 95% ethanol (930 ml) with palladium–charcoal (10 g) was boiled (2 h). The filtrate was evaporated to give *methyl aminobenzoylbenzoate* (15.2 g, 92%), m.p. 95—97 °C [from light petroleum (b.p. 60—80 °C)] (Found: C, 70.65, H, 5.15, N, 5.15. $C_{15}H_{13}NO_3$ requires C, 70.6; H, 5.15; N, 5.5%); δ 3.9 (3 H, s), 6.4—6.8 (2 H, m), 7.0—7.3 (2 H, m), 7.6 (2 H, d), and 8.05 (2 H, d).

Methyl 4-[2-*Aminophenyl*(*hydroxy*)*methyl*]*benzoate* (17).—Sodium borohydride (15 pellets) was added to a solution of the ketone (16) (15 g) in methanol (150 ml) and the mixture left with occasional shaking for 2.5 h when reaction was complete (g.l.c.). The mixture was diluted with water, extracted with dichloromethane, and the organic extracts dried (Na_2SO_4) and evaporated to give the virtually pure *alcohol* (17) (14.5 g, 96%), m.p. 134 °C (from benzene) (Found: C, 69.8; H, 5.85; N, 5.65. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.9; N, 5.45%).

Methyl 2-*Aminodiphenylmethane*-4′-*carboxylate* (18).—A solution of the alcohol (17) (13.9 g) in 95% ethanol (500 ml) with palladium–charcoal (7 g) was hydrogenated at room temperature and atmospheric pressure until absorption ceased (1.5 days). Filtration, followed by evaporation of the solvent gave the *diphenylmethane* (10.4 g, 80%), m.p. 101—103 °C [from light petroleum (b.p. 60—80 °C)] (Found: C, 74.75; H, 6.15; N, 5.65. $C_{15}H_{15}NO_2$ requires C, 74.65; H, 6.25; N, 5.8%); δ 3.25br (2 H, s, exch. D_2O, NH_2), 3.80 (3 H, s, OCH_3), 3.85 (2 H, s, CH_2), 6.45—7.2 (6 H, m), and 7.80br (2 H d); $\nu_{max.}$ ($CHCl_3$) 3 380, 3 460, 1 715, 1 280, 1 110, and 1 040 cm^{-1}; $\lambda_{max.}$ 237 and 285 nm (log ε 4.37 and 3.55); *m/e* 241 (base peak, M^+), 182 ($M - 59$).

Methyl 2-*Azidodiphenylmethane*-4′-*carboxylate* (19).—A solution of amine (18) (10.4 g) in 2N-sulphuric acid (215 ml) and dioxan (215 ml) was diazotised at −5 °C with a solution of sodium nitrite (3.02 g) in water (17 ml); stirring was continued at −5 °C (30 min). A solution of sodium azide (3.36 g) in water (17 ml) was added, and the mixture slowly warmed to 30 °C. The organic material was extracted with dichloromethane, the extracts washed with 5% sodium hydroxide solution, dried (Na_2SO_4), and evaporated at 30 °C to give the crude azide (19) as a yellow oil. The oil was purified by chromatography on an alumina column (200 g, foil wrapped to exclude light), eluting with light petroleum (b.p. 40—60 °C)–CH_2Cl_2 (19 : 1 v/v). The *azide* (19) (8.5 g, 77%) had m.p. 69—70 °C [from light petroleum (b.p. 40—60 °C)] (Found: C, 67.15: H, 4.85; N, 15.75. $C_{15}H_{13}N_3O_2$ requires C, 67.4; H, 4.9; N, 15.7%); δ 3.85

(3 H, s, OCH_3) 3.95 (2 H, s, CH_2), 6.95—7.35 (6 H, m), and 7.85br (2 H, d); $\nu_{max.}$ ($CHCl_3$) 2 130, 1 730, 1 280, 1 110, and 1 040, cm^{-1}; $\lambda_{max.}$ 245, 282 (sh), and 292 (sh) nm (log ε 4.41, —, —) *m/e* 267 (M^+), 240, 239 (M − 28), and 180 (base peak).

2-Acetamido-4′-(1,3-dioxan-2-yl)benzophenone (20) *and 2-Acetamido-4′,4″-bis-(1,3-dioxan-2-yl)triphenylmethanol* (21).—(*a*) The Grignard reagent from 1-(1,3-dioxan-2-yl)-4-bromobenzene (9 g) in anhydrous tetrahydrofuran (100 ml) was added slowly (0.5 h) to a vigorously stirred solution of freshly distilled 2-methyl-3,1-benzoxazin-4-one (6.44 g) in a mixture of anhydrous toluene (100 ml) and dry ether (50 ml) at −5 °C. Stirring was continued at 0 °C (2 h) and overnight at room temperature. The yellow complex was hydrolysed (aqueous ammonia, *d* 0.880, 100 ml), the organic layer separated, and the aqueous phase extracted with ether (3 × 50 ml). The combined organic solutions were washed with saturated sodium chloride solution, dried ($MgSO_4$), concentrated, and adsorbed on alumina. Column chromatography (Al_2O_3, 250 g) gave the benzophenone (20) (2.1 g, 17.5%) and the triphenylmethanol (21) (1.7 g, 11.6%). The *benzophenone* (20) had m.p. 121—121.5 °C (from methanol) (Found: C, 70.55; H, 5.75; N, 4.5. $C_{19}H_{19}NO_4$ requires C, 70.15; H, 5.9; N, 4.3%); δ 1.2—1.5 (1 H, m, H-5′$_{eq}$), 1.7—2.5 (4 H, m, CH_3 and H-5′$_{ax}$), 3.6—4.3 (4 H, m, H-4′ and -6′), 5.4 (1 H, s, H-2′), 6.5—7.6 (8 H, m), and 8.5br (1 H, d, H 6); *m/e* 325 (M^+, 23%), 324 (81), 283 (27, M − C_2H_2O), 282 (26, M − CH_3CO), 266 (100) 225 (41), and 197 (43). *2-Acetamido-4′,4″-bis-(1,3-dioxan-2-yl)triphenylmethanol* (21) had m.p. 176—177 °C (from dichloromethane) (Found: C, 71.0; H, 6.55; N, 2.7. $C_{29}H_{31}NO_6$ requires C, 71.15; H, 6.4; N, 2.85%); δ 1.25—1.45 (5 H, CH_3 and H-5′$_{eq}$), 1.75—2.5 (2 H, m, 5′$_{ax}$), 3.6—4.4 (8 H, m, H-4′ and -6′) 4.9br (1 H, s, OH, exch. D_2O), 5.4 (2 H, s, H-2′), 6.4—7.4 (11 H, m), 7.95br (1 H, d, H 6), and 9.0br (1 H, s, NH); *m/e* 489 (M^+, 6%).

(*b*) By using two equivalents of the Grignard reagent the triphenylmethanol (21) was obtained in 45% yield. A substantial proportion of this was obtained as a solid by trituration of the crude reaction product with methanol.

Bis-(3-bromopropyl) 2-Acetamido-α-hydroxytriphenylmethane-4′,4″-dicarboxylate (22).—*N*-Bromosuccinimide (3.2 g) was added to a solution of the triphenylmethanol (21) (4.6 g) in carbon tetrachloride (25 ml). The mixture was boiled under reflux (2 h), cooled, filtered, and the filtrate evaporated. The *diester* (22) (4.56 g, 78%) had m.p. 69—72 °C [from light petroleum (b.p. 40—60 °C)]; $\nu_{max.}$ 3 590, 3 400, and 1 725 cm^{-1}; δ 1.5 (3 H, s), 2.35 (4 H, m, *J* 6 Hz, $OCH_2CH_2CH_2$), 3.55 (4 H, t, CH_2O), 4.45 (4 H, t, CH_2Br), 6.05br (1 H, s, exch. D_2O, OH), 6.5—8.0 (12 H, m), and 9.0br (1 H, s, exch. D_2O, NH).

2-Acetamido-4′,4″-bis-(1,3-dioxan-2-yl)triphenylmethyl Chloride (23).—The triphenylmethanol (21) (2.9 g) in anhydrous benzene (5.8 ml) was treated with acetyl chloride (0.44 ml) and the solution gently warmed to boiling. The solution was then allowed to stand for 5 days at room temperature, during which time a pale yellow solid precipitated. The solid *chloride* was filtered off, washed with a little benzene containing acetyl chloride, and dried at 0.05 mmHg and 70 °C (2.1 g, 69%); it had m.p. 176—179 °C (Found: C, 68.45; H, 6.1; N, 2.85. $C_{29}H_{30}ClNO_5$ requires C, 68.55; H, 5.9; N, 2.75%); $\nu_{max.}$ 3 300, 1 660, and 1 510 cm^{-1}; δ 1.45br (2 H, d, H-5′$_{eq}$), 1.75—2.5 (5 H, m, CH_3 and H-5′$_{ax}$), 3.5—4.4 (8 H, m, H-4′ and -6′), 5.5 (2 H, s, H-2′), and 6.6—8.0 (13 H, m).

Reduction of the Triphenylmethyl Chloride (23).—Small pieces of sodium metal (total weight 0.45 g) were added to a solution of the chloride (23) in tetrahydrofuran (3.4 ml) containing anhydrous t-butyl alcohol (0.8 ml), under nitrogen. The mixture was boiled under reflux (18 h), cooled, and treated with an excess of methanol. The solution was poured into water (25 ml) and extracted with ether (3 × 10 ml). The ethereal extracts were dried ($MgSO_4$) and evaporated; the solid residue showed five components on t.l.c. Preparative t.l.c. (eluant toluene–ethyl acetate, 3 : 1 v/v) gave three major components A, B, and C. Component A was 2-acetamido-4′,4″-dimethyltriphenylmethane (24), *m/e* 329; δ 1.9 (3 H, s, CH_3CO), 2.3 (6 H, s, CH_3), 5.45 (1 H, s, methine), and 6.8—7.8 (13 H, m). Component B was 2-amino-4′,4″-dimethyltriphenylmethane (25), *m/e* 287; δ 2.3 (6 H, s, CH_3), 5.35 (1 H, s, methine), and 6.6—7.2 (14 H, m, aromatic and NH_2). Component C was 2-acetamido-4′-(1,3-dioxan-2-yl)-4″-methyltriphenylmethane (26), *m/e* 401; δ 1.2—1.5 (1 H, m, H-5′$_{eq}$), 1.8—2.5 (1 H, m, H-5′$_{ax}$), 1.9 (3 H, s, CH_3CO), 2.3 (3 H, s, CH_3), 3.6—4.3 (4 H, m, H-4′, and -6′), 5.45br (2 H, s, H-2′ and methine), and 6.6—7.8 (13 H, m).

Dimethyl 2-Amino-α-hydroxytriphenylmethane-4′,4″-dicarboxylate (27).—A solution of the bis-(3-bromopropyl) ester (22) (10.3 g) in 95% ethanol (32 ml) containing concentrated hydrochloric acid (8 ml) was boiled under reflux (3 h). The green solution was evaporation (finally at 0.05 mmHg), and the green solid residue dissolved in anhydrous methanol (400 ml) saturated with dry hydrogen chloride; the solution was boiled (18 h). Evaporation gave a green tar which was shaken with saturated aqueous sodium hydrogencarbonate (100 ml) and dichloromethane (2 × 150 ml). The organic phase was separated, dried (Na_2SO_4), and evaporated to give a green solid, largely the amino-diester (27). A sample was purified by preparative t.l.c. (eluant toluene–ethyl acetate, 9 : 1 v/v) and had m.p. 93—95 °C [from light petroleum (b.p. 60—80 °C)], yellow needles $\nu_{max.}$ 3 420, 1 725, 1 280, 1 100, and 1 010, cm^{-1}; δ 3.8 (6 H, s), 4.3br (3 H, s, exch. D_2O), 6.3—6.8 (2 H, m), 6.9—7.4 (6 H, m), and 7.9 (4 H, d, *J* 8 Hz); *m/e* 374 (35%, M − 17), 367 (50%), and 354 (100).

Dimethyl 2-Aminotriphenylmethane-4′,4″-dicarboxylate, (28).—A mixture of red phosphorus (10.1 g) and iodine (4.7 g) in glacial acetic acid (337 ml) was kept at room temperature (20 min). Water (34 ml) and the hydroxyamine (27) (13.5 g) were added and the mixture boiled under reflux (4 h). The warm mixture was filtered and the filtrate was poured slowly into a solution of sodium metabisulphite (70 g) in water (200 ml). The cooled solution was basified with ammonia with external cooling, the aqueous phase extracted with dichloromethane (2 × 250 ml), and the organic phases were combined, dried, (Na_2SO_4), and evaporated. The residual fawn solid was substantially pure amine (28) (11.9 g, 92%): A sample was purified by preparative t.l.c. The *N-benzoyl derivative* had m.p. 130—132 °C (from cyclohexane) (Found: C, 75.4; H, 5.4; N, 2.35. $C_{30}H_{25}NO_5$ requires C, 75.15; H, 5.25; N, 2.9%). The free amine (28) had $\nu_{max.}$ 3 430, 3 390, 1 720, 1 280, 1 110, and 1 040 cm^{-1}; δ 3.3br (s, 2 H, exch. D_2O, NH_2), 3.85 (6 H, s, CO_2CH_3), 5.5br (1 H, s), 6.5—7.1 (4 H, m), 7.1 (4 H d, *J* 8 Hz), and 7.9 (4 H, d, *J* 8 Hz); *m/e* 375 (M^+, 100), 360 (16, M − 15), 344 (16), 316 (24), and 240 (20).

Dimethyl 2-Azidotriphenylmethane-4′,4″-dicarboxylate (29).—A solution of the amino-diester (28) (11.6 g) in 2N-sulphuric acid (150 ml) with 1,4-dioxan (150 ml) was diazo-

tised at −5 °C using sodium nitrite (2.21 g) in water (15 ml), then the solution was stirred at −5 °C (30 min). A solution of sodium azide (2.41 g) in water (15 ml) was added in one portion at −5 °C, and the mixture slowly warmed to 30 °C. Extraction with dichloromethane (2 × 100 ml), washing with 5% aqueous sodium hydroxide (100 ml), drying (Na_2SO_4), and evaporation gave a red oil (14 g). Chromatography on alumina (250 g) on a foil-wrapped column, gave on elution with light petroleum (b.p. 40—60 °C)–dichloromethane (19 : 1 v/v) the *azide* (29) as a yellow oil (2.6 g, 21%) (Found: C, 67.71; H, 4.9; N, 10.05. $C_{23}H_{19}N_3O_4$ requires C, 63.8; H, 4.75; N, 10.45%); $\nu_{max.}$ 2 130, 1 720, 1 110, and 1 040 cm^{-1}; δ 3.8 (6 H, s, CO_2CH_3), 5.8br (1 H, s), 6.7—7.3 (8 H, m), and 7.85 (4 H, d, *J* 8 Hz); *m/e* 401 (M^+, 2%), 473 (40, *M* − 28), and 443 (50).

2-*Nitrophenyl*-(3-*pyridyl*)*methanol* (30).—A solution of 3-bromopyridine [19] (15 g) in dry ether (45 ml) was added over 15 min to a cooled (−70 to −80 °C), stirred solution of n-butyl-lithium (50 ml of a 15% w/w solution in hexane, with 50 ml ether) under nitrogen. The yellow mixture was stirred (15 min) after addition was complete, and then a solution of *o*-nitrobenzaldehyde (14.5 g) in dry ether (100 ml) was added dropwise over 30 min. Stirring was continued at −70 °C (2 h) then at room temperature (2 h). The reaction mixture was poured into ice–water saturated with salt and sodium metabisulphite. The ethereal layer was separated, and the aqueous phase further extracted with ether (8 × 200 ml). In some cases the product crystallised as a solid; more often the combined ether extracts were evaporated and the residue steam-distilled The non-volatile material was salted out, extracted with ether (6 × 50 ml), and the dried (Na_2SO_4) extracts evaporated. The yield of the *nitro-alcohol* (30) was 14—17 g (64—75%), m.p. 105.5—106.5 °C (from carbon tetrachloride) (Found: C, 62.25; H, 4.3; N, 12.2. $C_{12}H_{10}N_2O_3$ requires C, 62.6; H, 4.4; N, 12.15%); $\nu_{max.}$ 3 300 (br) cm^{-1}; δ 4.9br (1 H, s, exch. D_2O, OH), 6.4 (1 H, s), 7.1—8.0 (6 H, m), and 8.35 (2 H, d, *J* 2 Hz, overlying d, *J* 7 Hz, α-pyridine H); *m/e* 2.3 (*M* − 16).

2-*Nitrophenyl*-(4-*pyridyl*)*methanol* (31).—Compound (31) was prepared as described for compound (30) from 4-bromopyridine.[20] Some alcohol (31) precipitated from the ether extracts; the rest of the ether soluble material was chromatographed on alumina. Total yield of *nitro-alcohol* (31) was 60%, m.p. 169—170 °C (from ethyl acetate) (Found: C, 62.9; H, 4.4; N, 12.05. $C_{12}H_{10}N_2O_3$ requires C, 62.6; H, 4.4; N, 12.15%); $\nu_{max.}$ (DMSO) 3 200 (br) cm^{-1}; δ 6.2 (1 H, d, *J* 5 Hz; singlet after addition of D_2O), 6.5 (d, 1 H, *J* 5 Hz, exch. D_2O, OH), 7.2—8.0 (6 H, m), and 8.4 (2 H, dd, *J* 2 and 6 Hz, pyridine α-H); *m/e* 214, 213 (*M* − 17), 197 (*M* − 33, 50%), 196 (*M* − 34, 100), 182 (38), 168 (66), 155 (38), 140 (22), 128 (56), and 127 (96).

2-*Nitrophenyl*(*thiazol*-2-*yl*)*methanol* (35).—This compound was prepared as described by Sternbach *et al.*,[21] from 2-bromothiazole.[22]

2-*Aminophenyl*-(3-*pyridyl*)*methanol* (32).—The nitro-alcohol (30) (2.3 g) was hydrogenated in 95% ethanol (50 ml) over palladium–charcoal (10%; 0.5 g) until three equivalents of hydrogen were absorbed. The mixture was filtered, and the filtrate evaporated to give the crude amino-alcohol (32) as a yellow oil (1.96 g, 98%), which solidified when triturated with light petroleum. Recrystallized from benzene, the *amino-alcohol* had m.p. 143—144 °C (Found: C, 71.5; H, 6.05; N, 13.6. $C_{12}N_{12}N_2O$ requires C, 72.0; H, 6.05; N, 14.0%); $\nu_{max.}$ 3 450, 3 380, 1 640, 1 590, 1 575, 1 455, 1 295, 1 000, 870, and 860 cm^{-1}; δ 4.35br (3 H, s, exch. D_2O, NH_2 and OH), 5.75 (1 H, s), 6.5—7.3 (5 H, m), 7.6br (1 H, d, *J* 7 Hz), and 8.3 (2 H, overlapping d, *J* 8 and 2 Hz, pyridine α-H); *m/e* 201 (9), 200 (M^+, 33), 182 (*M* − 18, 27%), and 181 (*M* − 19, 100%).

2-*Aminophenyl*(*thiazol*-2-*yl*)*methanol* (36).—Reduction as described above gave from the nitro-alcohol (35) the *amino-alcohol* (36) (98%), m.p. 97.5—98 °C (from ethyl acetate) (Found: C, 58.15; H, 4.8; N, 13.6. $C_{10}H_{10}N_2OS$ requires C, 58.25; H, 4.85; N, 13.6%); δ ([$^2H_6$]DMSO) 4.7br (3 H, s, NH_2 and OH), 6.0 (1 H, s), and 6.4—7.5 (6 H, m); *m/e* 206 (M^+, 58%), 187 (*M* − 19, 33), 98 (48), and 86 (100%).

3-(2-*Aminobenzyl*)*pyridine* (33).—A solution of the amino-alcohol (32) (1 g) in ethanol (34 ml) with concentrated hydrochloric acid (1.2 ml) and palladium–charcoal (0.5 g, 10%) was hydrogenated at atmospheric temperature and pressure until one equivalent of hydrogen had been taken up (*ca.* 20 h). The solution was filtered and the filtrate basified (ammonia, *d* 0.88) and evaporated. The residue was extracted with dichloromethane and the solution was dried (Na_2SO_4) and evaporated to give the *aminobenzylpyridine* (33) as an oil which solidified (0.8 g, 86%), m.p. 84—85 °C (from cyclohexane) (Found: C, 78.4; H, 6.6; N, 15.4. $C_{12}H_{12}N_2$ requires C, 78.2; H, 6.6; N, 15.2%). $\nu_{max.}$ 3 440 and 3 380 cm^{-1}; δ 3.5br (2 H, s, exch. D_2O, NH_2), 3.8 (2 H, s, CH_2), 6.6—7.5 (6 H, m), and 8.5 (2 H, overlapping d, pyridine α-H), *m/e* 184 (100%, M^+), 183 (96), 168 (91, *M* − NH_2), 167 (91, *M* − NH_3), and 166 (87%).

4-(2-*Aminobenzyl*)*pyridine* (34).—A solution of the nitro-alcohol (31) (6.5 g) in 95% ethanol (195 ml) containing concentrated hydrochloric acid (7.5 ml) was hydrogenated at atmospheric temperature and pressure over 10% Pd–C (3 g) (*ca.* 43 h). Work-up as described for compound (33) was followed by distillation to give the *aminobenzylpyridine* (34), (3.7 g, 71%), b.p. 134—140 °C at 0.06 mmHg. Recrystallised from cyclohexane the amine had m.p. 96—98 °C (Found: C, 78.5; H, 6.85; N, 15.2. $C_{12}H_{12}N_2$ requires C, 78.2; H, 6.6; N, 15.2%); $\nu_{max.}$ 3 460 and 3 390 cm^{-1}; δ 3.5br (2 H, s, NH_2), 3.8 (2 H, s, CH_2), 6.4—7.1 (6 H, m), and 8.3 (2 H, dd, *J* 6 and 1 Hz, pyridine α-H); *m/e* 184 (M^+, 64%), 169 (22), 167 (16), and 106 (98).

2-(2-*Aminobenzyl*)*thiazole* (37).—Hydrogenation of the amino-alcohol (36) (7.2 g) in 95% ethanol (400 ml) with concentrated HCl (3 ml) over Pd–C (3 g, 10%) was incomplete after 7 days. Further catalyst was added (3 g) and after a further 7 days the mixture was worked up as described above. The crude oil was triturated with ethyl acetate–hexane (1 : 3 v/v), and the solid *aminobenzylthiazole* (37) (2.96 g) filtered off. The filtrate was evaporated; medium pressure chromatography of the residue (hexane–ethyl acetate; 7 : 3 v/v) gave a further quantity of amine (37), total 4.46 g (38%). The amine had m.p. 49—49.5 °C (from cyclohexane) (Found: C, 63.15; H, 5.3; N, 14.85. $C_{10}H_{10}N_2S$ requires C, 63.15; H, 5.25; N, 14.75%); δ 4.05br (2 H, s, exch. D_2O, NH_2), 4.1 (2 H, s, CH_2), and 6.4—7.5 (6 H, m); *m/e* 190 (M^+, 100%), 157 (44), 130 (38), and 117 (35).

3-(2-*Azidobenzyl*)*pyridine* (38).—A solution of sodium nitrite (6.25 g) in water (140 ml) was added dropwise to a stirred cooled (0 °C) solution of the amine (33) (14.8 g) in a mixture of water (38 ml), concentrated HCl (38 ml), and dioxan (100 ml). After addition was complete the solution

was stirred (30 min), then rapidly filtered into a solution of sodium azide (6.25 g) and sodium acetate (62.5 g) in water (280 ml) also at 0 °C. The mixture was stirred at 0 °C (30 min) and extracted with dichloromethane (2 × 250 ml), and the dichloromethane solution was dried (Na_2SO_4), and evaporated at 30 °C. The crude azide (38) was purified by chromatography on a foil-wrapped column (500 g alumina), eluting with light petroleum (b.p. 40—60 °C)–benzene (1 : 4 v/v). The pure *azide* (38) was a yellow oil (11.6 g, 69%) (Found: C, 68.5; H, 4.95; N, 25.7. $C_{12}H_{10}N_4$ requires C, 68.55; H, 4.8; N, 26.65%); $\nu_{max.}$ 2 100 cm^{-1}; δ 3.85 (2 H, s, CH_2), 6.9—7.5 (6 H, m), and 8.3—8.4 (2 H, m, pyridine α-H); *m/e* 185 (24%), 184 (52), 183 (96), 182 (100, *M* − 28), 181 (96), 179 (37), 167 (24), 163 (43), 156 (50), and 155 (96).

4-(2-*Azidobenzyl*)*pyridine* (39).—Prepared as described for compound (38) in 80% yield the *azide* (39) had m.p. 54.5—55 °C [from light petroleum (b.p. 40—60 °C)] (Found: C, 67.9; H, 4.7; N, 26.35. $C_{12}H_{10}N_4$ requires C, 68.55; H, 4.8; N, 26.65%); $\nu_{max.}$ 2 120 cm^{-1}, δ 3.8 (2 H, s), 6.85—7.3 (6 H, m), and 8.35 (2 H, d, *J* 6 Hz); *m/e* 210 (M^+, 10%), 183 (30), and 182 (100, *M* − 28).

2-(2-*Azidobenzyl*)*thiazole* (40) *and Thiazolo*[3,2-c][1,2,3]-*benzotriazepine* (41).—In the diazotisation of the amine (37), by the method described above, a yellow precipitate was observed. Chromatography on alumina (eluant light petroleum–benzene, 1 : 4 v/v) gave the *azide* (40) (35%) (Found: C, 55.4; H, 3.6; N, 25.75. $C_{10}H_8N_4S$ requires C, 55.55; H, 3.7; N, 25.95%); $\nu_{max.}$ 2 120 cm^{-1}; δ 4.25 (2 H, s) and 7.0—7.6 (6 H, m); Elution with dichloromethane gave the *thiazolobenzotriazepine* (41) (21%) m.p. 176—177.5 °C (Found: C, 59.55; H, 3.5; N, 20.85. $C_{10}H_7N_2S$ requires C, 59.7; H, 3.5; N, 20.9%); ^1H n.m.r. data given in Discussion; *m/e* 201 (M^+, 33%) and 160 (35); $\lambda_{max.}$ 219, 255, and 325 nm ($\log_{10}\varepsilon$ 3.28, 2.9, and 3.2); $\lambda_{max.}$ (95% EtOH + conc. HCl) 259, 327, and 340 nm ($\log_{10}\varepsilon$ 3.24, 2.93, and 3.14).

3-(2-*Acetamidobenzyl*)*pyridine* (42).—A stirred suspension of the amine (33) (17.4 g) in water (112 ml) was treated dropwise at 0 °C with acetic anhydride (38 ml); stirring was continued until all solid had dissolved. The mixture was basified (ammonia) to pH 8—9 and the solid *amide* (42) filtered off, washed with cold water, and dried in a vacuum at 100 °C (17.3 g, 81%), m.p. 140—141 °C (from benzene) (Found: C, 74.2; H, 6.1; N, 12.5. $C_{14}H_{14}N_2O$ requires C, 74.3; H, 6.25; N, 12.4%); $\nu_{max.}$ 3 430, 1 660, 1 580, and 1 540 cm^{-1}; δ 2.0 (3 H, s), 3.9 (2 H, s), 7.0—7.5 (6 H, m), 7.75br (1 H, s, exch. D_2O), and 8.35 (2 H, m, pyridine α-H); *m/e* 226 (100%, M^+), 184 (100, *M* − 42).

3-(2-*Acetamidobenzyl*)*pyridine* N-*oxide* (43).—A solution of the amide (42) (34.4 g) in glacial acetic acid (250 ml) with 30% hydrogen peroxide (50 ml) was heated at 55—60 °C for 2 h. A further 25 ml of hydrogen peroxide was added, and heating continued (15 h) at 75—80 °C. Evaporation, addition of water, and re-evaporation gave an oil which was dissolved in chloroform and treated with a stiff aqueous paste of potassium carbonate. The chloroform solution was filtered, dried (Na_2SO_4), and evaporated to give an oil which solidified. Medium pressure chromatography gave the N-*oxide* (43) (eluted with methanol–ethyl acetate, (3 : 7 v/v) (24.1 g, 66%), m.p. 157—158 °C (from acetone) (Found: C, 69.05; H, 5.65; N, 11.5. $C_{14}H_{14}N_2O$ requires C, 69.4; H, 5.85; N, 11.55%); $\nu_{max.}$ (DMSO) 3 450, 1 675, 1 600, 1 580, 1 520, 1 480, 1 360, 1 265, 1 155, and 755 cm^{-1}; δ 2.0 (3 H, s), 3.9 (2 H, s), 7.0—7.4 (6 H, m), 7.9 (2 H, m), and 9.3br (1 H, s, exch. D_2O); *m/e* 242 (5%, M^+), 226 (93%, *M* − 16), 184 (100%, *M* − 16 − 42).

3-(2-*Aminobenzyl*)*pyridine* N-*Oxide* (44).—A suspension of the amide (43) (24.1 g) in 10% aqueous sodium hydroxide (550 ml) was boiled under reflux (4 h). The solution was evaporated, the residue extracted with chloroform (*ca.* 400 ml), and the filtered chloroform extract dried (Na_2SO_4) and evaporated. The N-*oxide* (44) (17 g, 85%) had m.p. 126—127 °C (from benzene) (Found: C, 72.0; H, 6.0; N, 13.8. $C_{12}H_{12}N_2O$ requires C, 72.0; H, 6.05; N, 14.0%); $\nu_{max.}$ (DMSO) 3 430, 3 340, and 3 215 cm^{-1}; δ 3.8 (2 H, s), 4.8br (2 H, br s, exch. D_2O, NH_2), 6.4—6.8 (2 H, m), 6.8—7.3 (4 H, m), and 8.0 (2 H, m); *m/e* 200 (M^+), 185 (61), 184 (100, *M* − 16).

3-(2-*Azidobenzyl*)*pyridine* N-*Oxide* (45).—The amine (44) (16 g) was diazotised as described above, but no dioxan was necessary as solvent. The aqueous mixture, after treatment with sodium azide, was extracted with dichloromethane (2 × 250 ml), and the organic layers were dried and evaporated, giving a red oil (24.8 g). Chromatography on alumina (300 g) with ether gave the deoxygenated azide (38) (1.6 g, 6.7%). Elution with dichloromethane–ether gave the *azide* (45) (4 g, 21%), m.p. 96 °C (from cyclohexane) (Found: C, 63.75; H, 4.25; N, 25.1. $C_{12}H_{10}N_4O$ requires C, 63.7; H, 4.45; N, 24.75%); $\nu_{max.}$ 2 120 cm^{-1}; δ 3.8 (2 H, s), 6.9—7.4 (6 H, m), and 7.95 (2 H, m); *m/e* 226 (39%, M^+), 198 (44, *M* − 28), 182 (100, *M* − 28 − 16).

2,6-*Diphenylpyridine* N-*Oxide*.—A solution of 2,6-diphenylpyridine [23] (46.2 g) in glacial acetic acid (240 ml) with 30% hydrogen peroxide (20 ml) was boiled under reflux (2 h). Further quantities of hydrogen peroxide (8 × 20 ml) were added at intervals over five days to the boiling solution. After this time no further reaction occurred although starting material was still present. Sulphur dioxide was passed through the cooled solution to remove the excess of peroxide (15 min). Work-up was as for the *N*-oxide (43). The crude oil (41 g) was purified by medium pressure chromatography; elution with toluene gave unchanged 2,6-diphenylpyridine (22.6 g). Elution with toluene–ethyl acetate (3 : 1 v/v) gave the *N*-oxide (17.7 g, 37%; 71% based on unrecovered starting material), m.p. 126—127 °C [from chloroform–light petroleum (b.p. 40—60 °C)] (lit.,[14] 125—126 °C) (Found: C, 82.6; H, 5.1; N, 6.05. Calc. for $C_{17}H_{13}NO$: C, 82.55; H, 5.3; N, 5.65%); *m/e* 247 (M^+), 231 (*M* − 16).

4-*Bromo*-2,6-*diphenylpyridine*.—Phosphoryl bromide (43 g) was added to a solution of 2,6-diphenylpyridine *N*-oxide (12.3 g) in dry toluene (100 ml), and the solution was boiled under reflux (2.5 h). The cooled mixture was poured into ice–water (250 ml), basified with ammonia to pH 10, and extracted with dichloromethane (2 × 200 ml). The dried (Na_2SO_4) solution was evaporated to give a red oil (16 g). Medium-pressure chromatography gave, on elution with light petroleum (b.p. 40—60 °C)–toluene (3 : 1 v/v), the *bromopyridine* (5.8 g). Trituration with ethanol gave almost pure bromo-compound (3.4 g, 22%), m.p. 90 °C (from absolute ethanol) (Found: C, 65.65; H, 3.7; N, 4.65. $C_{17}H_{12}BrN$ requires C, 65.8; H, 3.9; N, 4.5%); δ 7.35 (6 H, m), 7.7 (2 H, s, pyridine β-H), and 8.0 (4 H, m, *ortho* protons on phenyl rings); *m/e* 311 (97%), 309 (100, M^+), 230 (79, *M* − Br); $\lambda_{max.}$ 255, 293, and 310 nm ($\log_{10}\varepsilon$ 4.35, —, 3.85). Further elution gave 2,6-diphenylpyridine (6 g, 52%).

(2,6-*Diphenyl*-4-*pyridyl*)-(2-*nitrophenyl*)*methanol* (46).—Prepared as described for the alcohol (30) from 4-bromo-2,6-diphenylpyridine (1.55 g), the crude product (1.9 g)

was chromatographed on alumina (100 g). Elution with light petroleum (b.p. 40—60 °C)–benzene (3 : 1 v/v) gave unchanged bromide (0.2 g, 12%). Elution with benzene gave the *pyridylmethanol* (46) (1.4 g, 73%), which solidified on trituration with light petroleum, m.p. 160 °C (from benzene) (Found: C, 75.6; H, 4.6; N, 7.45. $C_{24}H_{18}N_2O_3$ requires C, 75.4; H, 4.75; N, 7.35%); $\nu_{max.}$ 3 400 cm^{-1}; δ($CDCl_3$–[$^2H_6$]acetone) 5.2br (1 H, d, *J* 5 Hz, exch. D_2O, OH), 6.5 (1 H, d, *J* 5 Hz; singlet when D_2O added), 7.2—7.8 (10 H, m), 7.7 (2 H, s, pyridine β-H), and 7.8—8.1 (4 H, m); *m/e* 382 (M^+) and 381 (100).

(2-*Aminophenyl*)-(2,6-*diphenyl*-4-*pyridyl*)*methanol* (47).—The nitro-compound (46) (0.48 g) was hydrogenated in 95% ethanol (20 ml) with concentrated HCl (0.75 ml) over Pd–C (0.25 g) until uptake of hydrogen ceased. Work-up, as described previously, gave a yellow solid (0.44 g) which was purified by preparative t.l.c., eluting with ethyl acetate–toluene (9 : 1 v/v) to give the *amine* (47) (0.3 g, 68%), m.p. 216—217 °C (from chloroform) (Found: C, 80.75; H, 5.6; N, 7.85. $C_{24}H_{20}N_2O$ requires C, 81.82; H, 5.7; N, 7.95%); δ([$^2H_6$]DMSO) 3.1br (3 H, s, exch. D_2O, NH_2 and OH), 5.85 (1 H, s), 6.5—7.0 (4 H, m), 7.2—7.5 (6 H, m), 7.6 (2 H, s), and 8.0 (4 H, m); *m/e* 352 (M^+, 100%), 337 (33), 336 (28), 335 (52, M — 17), and 334 (61, M — 18).

Thermal Decomposition of the Azide (19).—A solution of the azide (19) (8.1 g) in anhydrous 1,2,4-trichlorobenzene (100 ml) was added dropwise over 1 h to vigorously stirred trichlorobenzene (1 l) under dry nitrogen at 200 °C. The solution was further heated at 200 °C for 4 h after which time no azide could be detected (i.r.). The solvent was evaporated off at 0.3 mmHg giving a red oil (8.9 g) which was chromatographed on alumina (300 g). Elution with light petroleum (b.p. 40—60 °C) gave trichlorobenzene (1.5 g). Elution with light petroleum–benzene (3 : 1 v/v) gave *methyl* 10H-*azepino*[1,2-a]*indole*-8-*carboxylate* (48) (2.4 g, 34%), as yellow prisms from light petroleum (b.p. 60—80 °C), m.p. 106—108 °C (Found: C, 75.65; H, 5.45; N, 5.85. $C_{15}H_{13}NO_2$ requires C, 75.3; H, 5.5; N, 5.85%); $\nu_{max.}$ 1 720, 1 640, 1 610, 1 080, and 1 040 cm^{-1}; $\lambda_{max.}$ 222(sh), 249, 277, 292 (sh), and 330 nm ($\log_{10}\varepsilon$, —, 4.18, 4.02, —, and 3.43); δ 3.54 (2 H, d, *J* 6 Hz), 3.75 (3 H, s, CO_2CH_3), 6.15 (1 H, s, H-11), 6.24 (1 H, d, *J* 9.2 Hz, H-7), 7.03br (1 H, t, *J* 6 Hz), 7.35 (1 H, d, *J* 9.2 Hz, H-6), and 7.1—7.6 (4 H m); *m/e* 239 (91%, M^+), 238 (72), 224 (22, M — 15), 180 (100, M — CH_3CO_2). Further elution from the column, using benzene–light petroleum (1 : 1 v/v) gave a mixture, separated by preparative t.l.c. into the amine (18) (0.5 g, 4.2%) and *methyl acridine*-3-*carboxylate* (49) (0.4 g, 4%), m.p. 153.5—155.5 °C [from light petroleum (b.p. 60—80 °C)] (Found: C, 75.25; H, 4.45; N, 6.15. $C_{15}H_{11}NO_2$ requires C, 75.95; H, 4.65; N, 5.9%); $\nu_{max.}$ 1 730, 1 615, 1 605, 1 270, and 1 090 cm^{-1}; $\lambda_{max.}$ 238(sh), 255(sh), 264, 337(sh), 344(sh), and 356 nm ($\log_{10}\varepsilon$ —, —, 4.76, —, —, 3.69); δ 4.02 (3 H, s, CO_2CH_3), 7.57 (1 H, d of t, H-7), 7.83 (1 H, d of t, H-6), 8.0 (1 H, subsplit d, *J* 8.5 Hz, H-8), 8.06 (2 H, d of d, H-1 and -2), 8.27 (1 H, subsplit d, *J* 9 Hz, H-5), 8.78br (1 H, s, H-9), and 8.99 (1 H, d, *J* 1.2 Hz, H-4). Addition of Eu(fod)$_3$ caused major shifts in the signals at δ 8.27 (H-5) and 8.99 (H-4), and revealed H-2 as a broadened doublet (*J* 8.8 Hz). Decoupling of the signal at δ 8.27 simplified the signal at δ 7.83, establishing this as due to H-6; *m/e* 237 (M^+, 96%), 206 (100, M — 31), and 178 (67%, M — 59). Other bands from preparative t.l.c. and other fractions from the column were not identified.

Thermal Decomposition of the Azide (29).—A solution of the azide (29) (2.2 g) in anhydrous trichlorobenzene (50 ml) was added dropwise (30 min) to vigorously stirred trichlorobenzene (250 ml) at 190 °C under nitrogen. Stirring and heating were continued for 4 h, then the solvent was removed at 0.1 mmHg, and the residual yellow oil (2 g) chromatographed (medium pressure; eluant light petroleum–ethyl acetate, 3 : 1 v/v). Early fractions contained trichlorobenzene (0.5 g). Next eluted was *methyl* 11-(p-*methoxycarbonylphenyl*)-10H-*azepino*[1,2-a]*indole*-8-*carboxylate* (51) (0.7 g, 34%), m.p. 157—160 °C (from cyclohexane) (Found: C, 73.8; H, 5.2; N, 3.5. $C_{23}H_{19}NO_4$ requires C, 74.0; H, 5.15; N, 3.75%); $\nu_{max.}$ 1 720, 1 640, 1 610, 1 270, and 1 100 cm^{-1}; δ 3.65 (2 H, d, *J* 6.8 Hz, H-10), 3.79 (3 H, s, CO_2CH_3), 3.96 (3 H, s, CO_2CH_3), 6.39 (1 H, d, *J* 9.4 Hz, H-7), 7.09 (1 H, t, *J* 6.8 Hz, H-9), 7.49 (1 H, d, *J* 9.4 Hz, H-6), 7.54 (2 H, d, *J* 8.6 Hz, H-2′ and -6′), 7.2—7.9 (4 H, m), and 8.15 (2 H, d, *J* 8.6 Hz, H-3′ and -5′); $\lambda_{max.}$ 225 (sh), 243, 356 (sh), 325, 350 (sh) nm ($\log_{10}\varepsilon$ —, 4.58, —, 4.3, —); *m/e* 373 (M^+, 100%), 372 (30), 358 (18), 314 (60), and 163 (78). Later fractions contained a mixture of the acridan (52) and the acridine (53), which were separated by preparative t.l.c. (eluant light petroleum–ethyl acetate, 3 : 1 v/v, multiple elutions). The acridan (52) gave inconsistent analyses (0.2 g, 9.8%); δ 5.3 (1 H, br s), 6.6—8.0 (15 H, m), 8.2 (2 H, d, *J* 8 Hz), and 8.8 (1 H, s). *Methyl* 9-(p-*methoxycarbonylphenyl*)*acridine*-3-*carboxylate* (53), yellow crystals from cyclohexane, had m.p. 189—192 °C (0.1 g, 4.9%) (Found: C, 74.1; H, 4.5; N, 4.25. $C_{23}H_{17}NO_4$ requires C, 74.4; H, 4.6; N, 3.75%); $\nu_{max.}$ 1 720, 1 610, 1 570, 1 280, 1 245, 1 110, and 1 090 cm^{-1}; $\lambda_{max.}$ 232, 263, 347 (sh), 363, and 383 (sh) nm ($\log_{10}\varepsilon$ 4.64, 4.88, —, 3.9, —); δ 4.02 (6 H, s, CO_2CH_3), 7.53 (2 H, d, *J* 8 Hz, H-6), 8.3 (3 H, m), and 9.04 (1 H, dd, *J* 1.6 and 0.8 Hz, H-4). Addition of Eu(fod)$_3$ caused downfield shifts in the signals at δ 7.9 and 9.04 and a doublet from the signal at δ 8.3 (*J* 8.5 Hz, H-2); *m/e* 371 (M^+, 100%), 340 (63), 312 (50), and 169 (72).

Thermolysis of the Azides (38), (39), *and* (40).—A solution of the azide (38) (11.2 g) in 1,2,4-trichlorobenzene (100 ml) was added dropwise over 1 h to trichlorobenzene (1 l) at 185° C with vigorous stirring, under nitrogen. Heating was continued for 4 h, when all azide had been decomposed (i.r.). Evaporation gave a black tar (17.5 g). Chromatography on on alumina (530 g) gave trichlorobenzene (7.6 g); further elution with light petroleum (b.p. 40—60 °C) gave the pyrroloindole (55), (0.2 g, 2.4%), m.p 90—91 °C (from absolute ethanol) (lit.,[24] 90—91 °C) (Found: C, 85.0; H, 5.85; N, 9.1. Calc. for $C_{11}H_9N$: C, 85.1; H, 5.85; N, 9.0%). Further elution with benzene gave 3-(2-aminobenzyl)pyridine (33) (0.25 g, 2.5%). The majority of the material required highly polar solvents for elution, and appeared to be polymeric.

Azides (39) and (40) were similarly decomposed, and similarly gave mainly polymer. In the former case a 24% yield of amine (34) was recovered.

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