Electrophilic Substitution in Indoles. Part 15.[1] The Reaction between Methylenedi-indoles and *p*-Nitrobenzenediazonium Fluoroborate.[2]

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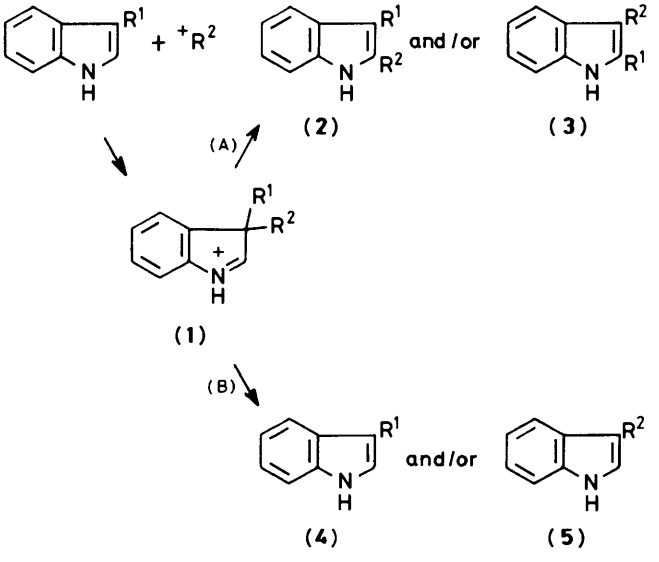
p-Nitrobenzenediazonium fluoroborate (2 mol equiv.) reacts under aqueous conditions with 3,3'-methylenedi-indole (**9a**) and *N,N*-dimethyl-3,3'-methylenedi-indole (**9c**) to give, in each instance, high yields of the corresponding 3-*p*-nitrophenylazoindoles (**13a**) and (**13c**). When 1 mol equiv. of diazonium salt is used, the methylenedi-indole (**9a**) gives <1 mol equiv. of the 3-(*p*-nitrophenylazo)indole (**13a**) and some methylenedi-indole is recovered. In dry acetonitrile, 3,3'-methylenedi-indole gives, with 1 mol equiv. of diazonium salt, a mixture of 3-(*p*-nitrophenylazo)indole (**13a**) (0.45 mol equiv.) and the unstable 3-(*p*-nitrophenylazo)-2,3'-methylenedi-indole (**16a**) (0.42 mol equiv.). The latter was also synthesized from indole-2,3-dione and chloroacetylindole *via* indol-2-yl, indol-3-yl, and 2,3'methylenedi-indole. Essentially similar results were obtained with *N,N*-dimethyl-3,3'-methylenedi-indole (**9c**) and the diazonium salt. The unsymmetrical compounds 3-indol-3-ylmethyl-1,2-dimethylindole (**9d**) and 3-indol-3-ylmethyl-2-methylindole (**9e**), with 2 mol equiv. of diazonium salt in aqueous solution, each give high yields of the two possible 3-*p*-nitrophenylazoindoles. With 1 mol equiv. of the diazonium salt only the 2-methyl-3-*p*-nitrophenylazo derivatives are obtained, together with 3,3'methylenedi-indole. In dry acetonitrile, with either 1 or 2 mol equiv. of diazonium salt, the unsymmetrical methylenedi-indoles each give only the 2-methyl-3-*p*-nitrophenylazoindoles. The displacement of an indolylmethyl residue from methylenedi-indoles by the diazonium salt, and the formation of the azo coupled rearrangement product (**16a**) provides firm evidence that azo coupling of 3-alkylindoles to give the 2,3-disubstituted indoles proceeds by initial attack at the 3-position followed by rearrangement, rather than by direct substitution at the 2-position.

The preceding paper[1] in this series was concerned with the kinetics and mechanism of azo-coupling reactions of indole and its 1-, 2-, and 3-methyl derivatives. The reactions of 3-methylindole differed from those of the other compounds because not only was the product the 2-arylazoindole (rather than a 3-substituted derivative) but the reactions were generally slower, were sensitive to base catalysis, and showed a small deuterium isotope effect (when the rates of substitution were compared with 2-deuterio-3-methylindole). These differences were attributed to a difference in mechanism, *i.e.* that whereas indole and its 1- and 2-methyl derivatives underwent direct electrophilic substitution at the 3-position, followed by rapid proton loss, 3-methylindole was attacked initially at the already substituted 3-position to give an intermediate 3H-indole and the arylazo group then rearranged to the 2-position, followed by loss of proton to give the 2,3-disubstituted indole.

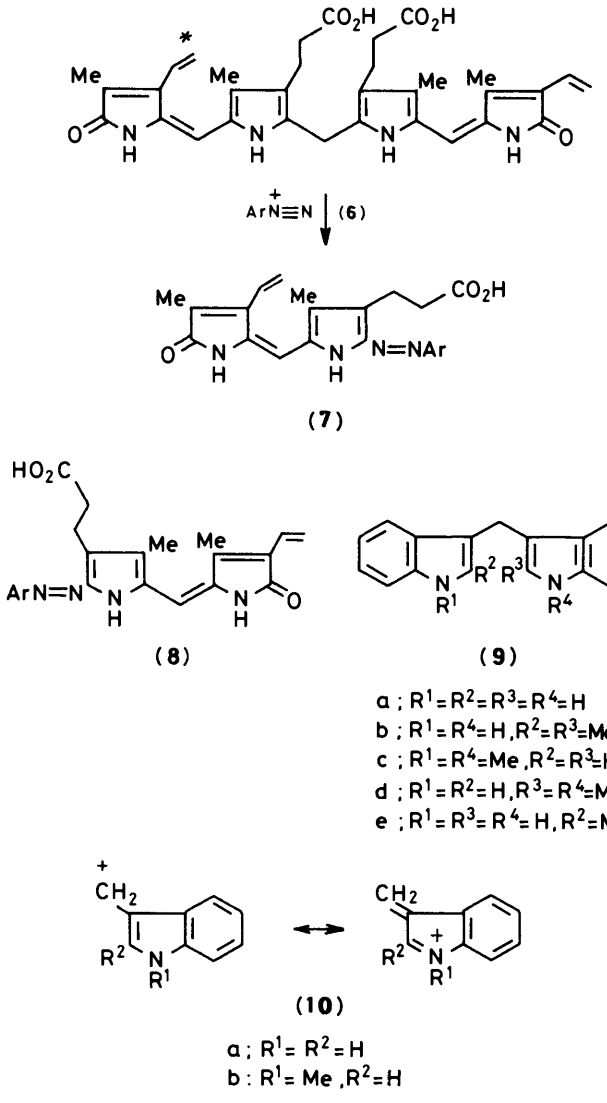
The intermediacy of a 3*H*-indole salt has been inferred from many other electrophilic substitution reactions of 3-alkylindoles and, in some cases, the substituent already present may migrate to the 2-position, leaving the incoming electrophile at the 3-position[3-8] (Scheme 1). Indeed, it has been shown[3,4,9-11] that synthetic 3*H*-indoles, prepared from 3-substituted indolyl Grignard reagents, rearrange in acid to give the 2,3-disubstituted indoles, the substituents in the 3*H*-indoles with the higher migratory aptitudes migrating preferentially. If a 3*H*-indole salt (**1**) is an intermediate in the electrophilic substitution of 3-substituted indoles, there are, in general, two possibilities: path (A), a migration of R^1 or R^2 in the salt (**1**) to give the 2,3-disubstituted indoles (**2**) and (**3**) as discussed above, or path (B), if either of the ions R^{1+} or R^{2+} is particularly stable, it may be eliminated from the intermediate (**1**) without rearrangement which would result in indoles substituted only at the 3-position, *i.e.* (**4**) or (**5**). In either case, the isolation of such products as (**3**) or (**5**) would implicate the intermediate (**1**).

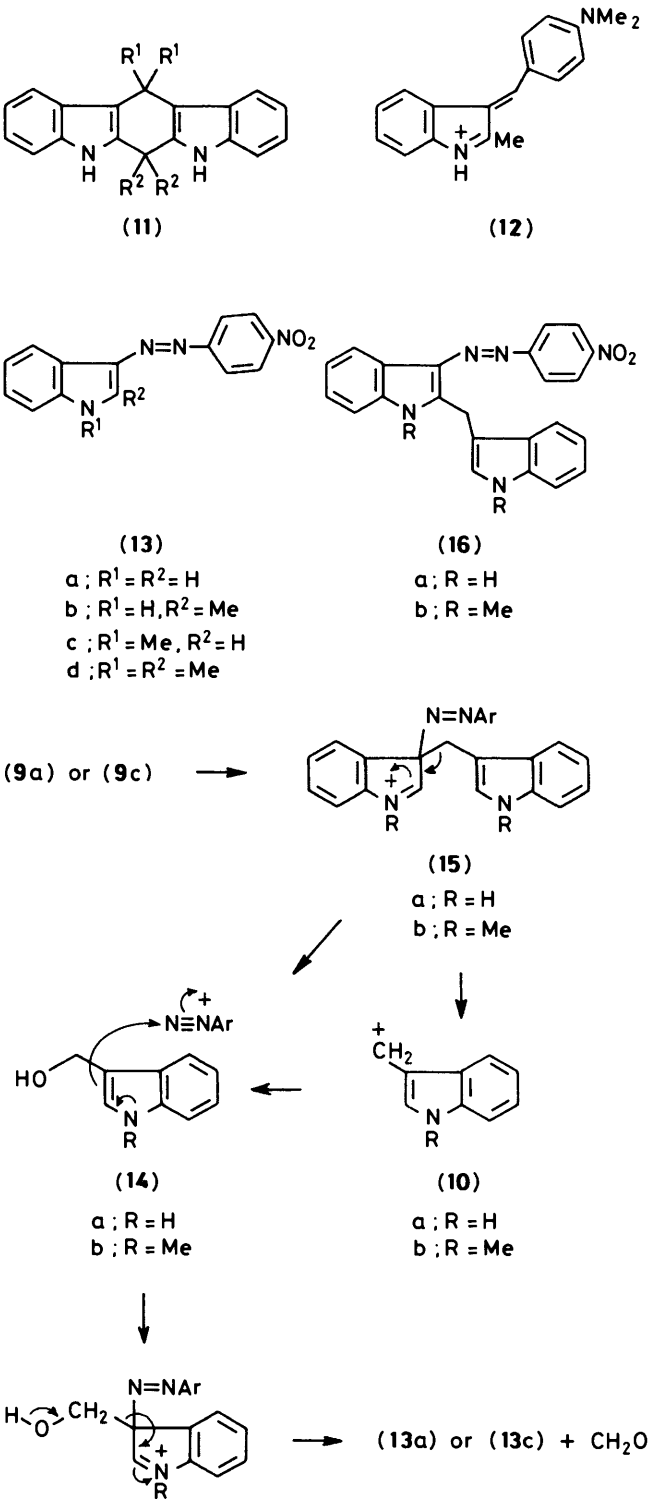
An analogous process to path (B) in the pyrrole field is the Van den Bergh reaction of bilirubin[12] (**6**) with aromatic diazonium ions (usually diazotised sulphanilic acid). The reaction evidently proceeds[13] *via* attack of the diazonium species at the pyrrole 2-position adjacent to the central CH_2 group to give the 2-azo derivatives (**7**) and (**8**) and formaldehyde.[14] Related processes include the condensation of hydroxymethyl- and dialkylaminomethyl-indoles to methylenedi-indoles,[15] and the condensation of aminomethylhalogenomethyl- and acetoxymethyl-pyrroles to dipyrrins (methylenedipyrroles);[16] all these reactions involve *ipso*-attack followed by loss of formaldehyde.



Scheme 1.

Because of the close similarity of pyrroles and indoles in many of their reactions, it occurred to us that methylenedi-indoles





Scheme 2.

might react with diazonium salts in the same way as dipyrrins, *i.e.* by the path (B) shown in Scheme 1. In the event, we have now shown that methylenedi-indoles may react with diazonium salts by both paths (A) and (B) as indicated in our preliminary communication[2] to give products of type (**3**) and (**5**).

p-Nitrophenyldiazonium fluoroborate had proved to be an excellent reagent in the coupling reactions of indole and its simple alkyl derivatives, and we therefore decided to investigate its reactions with the readily available 3,3′-methylenedi-indoles (**9**). Direct coupling of the diazonium salt at the 3 (or 3′) position was expected to result in expulsion of the relatively stable 3-methylene-3*H*-indole cations such as (**10**) with formation of products of types (**5**), and possibly also type (**3**). Indirect evidence that this might happen was also provided by the known reactions[17,18] of 3,3′-methylenedi-indole (**9a**) with aldehydes and ketones to form pentacyclic structures of type (**11**), whereas the 2,2′-dimethyl analogue (**9b**) reacted with *p*-dimethylaminobenzaldehyde to form 2 mol equiv. of the *p*-dimethylaminobenzylidene-3*H*-indole (**12**).[17]

The methylenedi-indoles (**9a**) and (**9c**) were prepared from the appropriate indole and formaldehyde;[19] optimum yields were obtained with acid catalysis at elevated temperatures. 3,3′-Methylenedi-indole (**9a**), on treatment with 2 mol equiv. of *p*-nitrophenyldiazonium tetrafluoroborate in water gave 3-(*p*-nitrophenylazo)indole (**13a**) (1.84 mol equiv.) and formaldehyde, isolated as its dimedone derivative (27%) after careful distillation of the aqueous solution. Similarly, the *N*,*N*-dimethyl analogue (**9c**) gave the corresponding 1-methyl-3-(*p*-nitrophenylazo)indole (**13c**) (1.78 mol equiv.). When only 1 mol equiv. of the diazonium salt was used, 3,3′-methylenedi-indole (**9a**) gave a mixture which on chromatography afforded the azo compound (**13a**) (0.86 mol equiv.) and recovered 3,3-methylenedi-indole (**9a**) (0.3 mol equiv.) These facts can be rationalised formally by attack of the diazonium ion at the 3- or 3′-position of

Table. Effect of water on the rate of azo-coupling of 3,3′-methylenedi-indole (**9a**) in acetonitrile at 30 °C with *p*-nitrobenzenediazonium fluoroborate (in excess)

Water concentration (mol l^{-1})	Pseudo first-order rate constant (s^{-1})
0.35	1.04×10^{-3}
0.69	2.89×10^{-3}
1.04	3.75×10^{-3}
1.38	5.13×10^{-3}
1.73	6.75×10^{-3}

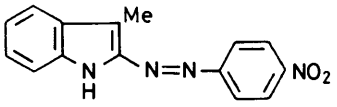
the methylenedi-indole with displacement of the cation (**10a**) or (**10b**) (see Scheme 2). The latter, after conversion into the 3-hydroxymethylindole (**14a**) or (**14b**) would be expected to react again at the 3-position with displacement of formaldehyde. The rate of reaction of the methylenedi-indole is, however, known[20] to be approximately proportional to the water concentration in acetonitrile, in the presence of an excess of *p*-nitrophenyldiazonium ion (see Table) so that direct attack of water on the intermediate (**15a**) or (**15b**) is also likely.

3-Hydroxymethylindole is known[19,21] to transform to methylenedi-indole under mild acidic conditions, and a synthetic sample of the alcohol (**14a**) was shown to react with *p*-nitrobenzenediazonium fluoroborate at *ca.* 7.5×10^3 times as fast as methylenedi-indole (**9a**); failure to detect this intermediate (**14a**) in the reaction mixture was thus not surprising, even when only 1 mol equiv. of diazonium salt was used.

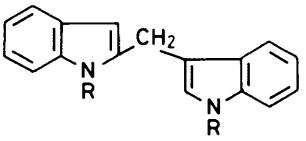
In *dry* acetonitrile, 3,3′-methylenedi-indole (**9a**), with 1 mol equiv. of *p*-nitrobenzenediazonium fluoroborate gave a mixture of two coloured compounds together with small amounts of tarry material. The less polar component, separated by p.l.c. was identified as 3-(*p*-nitrophenylazo)indole (**13a**) (0.45 mol equiv.). The more polar compound (**16a**) (0.42 mol equiv.) was obtained as a thermally unstable, dark red, solid which decomposed rapidly in the solid state to give an intractable material, but which could be kept for several days in dilute solutions of ether or acetone at 0 °C. When the solid was heated above *ca.* 150 °C, *p*-nitroaniline sublimed leaving an extremely complex mixture. The f.d. mass spectrum run at the lowest source temperature (50 °C), gave a single ion at *m/z* 395 corresponding to a monosubstitution product ($C_{23}H_{17}N_5O_2$) of methylenedi-indole (**9a**). On increasing the wire current this ion diminished in intensity and was replaced by two ions at *m/z* 257 and 138. In the electron impact spectrum, the ion of highest mass was at *m/z* 257 and other, intense ions, characteristic of *p*-nitroaniline at *m/z* 138, 108, 92, 80, and 65 were also observed.

In the u.v./visible spectrum, besides the indolic bands at $\lambda_{max.}$ 226, 275, 283, and 291 nm, there was a longer wavelength maximum at 430 nm. The latter underwent a bathochromic shift to 554 nm in alkali, in a manner virtually identical with that of 2-methyl-3-(*p*-nitrophenylazo)indole (**13b**)[22] (424→555 nm), but quite distinct from the smaller effect (425→475 nm) shown by 3-methyl-2-(*p*-nitrophenylazo)indole (**17**).[1] In acid solution, the spectrum initially displayed two new maxima at 460 and 582 nm, but the corresponding intermediate was transformed (half-life *ca.* 8 min) into a species with $\lambda_{max.}$ 375 nm. These changes resemble those observed on the addition of an indole to a protonated azoindole[20] and in the present case may be explained by intramolecular attack by the unsubstituted indole nucleus of (**16a**) on the protonated azo group.

The presence of the *p*-nitrophenylazo group at the indolyl 3-position in (**16a**) was also indicated by analysis of the 400 MHz ^{1}H n.m.r. spectrum in [$(CD_3)_2CO$–$(CD_3)_2SO$]. The signal of the 4-proton in the azo-substituted indole system of (**16a**) at δ 8.44 strongly supported a 3-azo substituent; this



(**17**)



(**18**)
a ; R = H
b ; R = Me

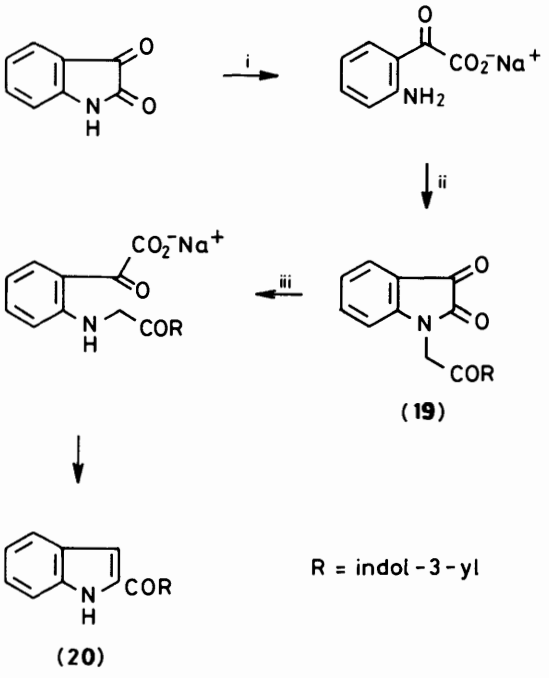
proton resonates at δ 8.44 and 7.74 in the azo derivatives (**13a**) and (**17**) respectively.

Essentially analogous results to those described above were obtained with 1,1′-dimethyl-3,3′-methylenedi-indole (**9c**) and *p*-nitrobenzenediazonium fluoroborate. Thus, in aqueous solution, 1.79 mol equiv. of 1-methyl-3-(*p*-nitrophenylazo)indole (**13c**) were obtained when 2 mol equiv. of the diazonium salt were employed. In non-aqueous solution, use of 1 mol equiv. of diazonium salt gave, by a combination of column chromatography, fractional crystallisations, and h.p.l.c. three components from the reaction mixture. The 1-methylazoindole (**13c**) (0.57 mol equiv.) was accompanied by 1-methyl-2-(1-methylindol-3-ylmethyl)-3-(*p*-nitrophenylazo)indole (**16b**) (0.24 mol equiv.). The ^{1}H n.m.r. spectrum was very similar to that of (**16a**) except that the NH signals were replaced by those of two N–Me groups at δ 3.68 and 3.65. The lowfield indole 4-H resonated at δ 8.63. Also isolated was a small quantity (0.07 mol equiv.) of a non-polar compound of molecular weight 429. From its molecular formula ($C_{30}H_{27}N_3$ by accurate mass measurement), it appeared to be derived from three molecules of the 3-methylene-3H-indole cation (**10b**) and a possible structure is a cyclic trimer with methylene bridges between the 2- and 3-positions of each of the three indole residues; other trace materials of higher molecular weight were detected during the chromatographic separation but were not further investigated.

The significance of the two products (**16a**) and (**16b**) formed by the reaction of the methylenedi-indoles with the diazonium salt made it desirable to confirm their structures by synthesis. The final step of one logical synthesis would involve azo coupling of *p*-nitrobenzenediazonium ion with a 2,3′-methylenedi-indole (**18a**) or (**18b**); it could be predicted that attack at the vacant indolyl 3-position would be much the preferred point of attack by the electrophile. Several attempts were made to synthesize such 2,3′-methylenedi-indoles, but only the successful route is described here.

In 1980, Black and Wong reported[23] that certain 2-acylindoles or 2-acylindolecarboxylic acids could be prepared from indole-2,3-dione as shown in Scheme 3. It was, therefore, expected that 3-chloroacetylindole[24] with indole-2,3-dione under these conditions would give the indolylcarbonylmethyl-indoledione (**19**), basic hydrolysis of which should afford the di-indolyl ketone (**20**).

Reduction of the latter would yield the desired 2,3′-methylenedi-indole (**18a**). In the event, only traces of the indoledione (**19**) were detected when the reaction was attempted under the original conditions. Treatment of indole-2,3-dione with powdered potassium hydroxide in dry dimethylsulphoxide however, followed by the addition of 3-chloroacetylindole at 80 °C in dry dimethyl sulphoxide gave, after chromatography, the required indoledione (**19**) in 20% yield as an orange solid. The mass spectrum gave the molecular ion at *m/z* 304, with the base peak at *m/z* 144, whilst together with other expected signals the ^{1}H n.m.r. spectrum showed the methylene singlet at δ 5.21. Treatment of this product with base gave the di-indolyl ketone (**20**) (81%). Its structure followed from its analytical and spectroscopic properties; in particular the C=O band at 1 620 cm^{-1} in the i.r. was characteristic of an indolyl ketone,[25] and the ^{1}H n.m.r. spectrum showed the disappearance of the original



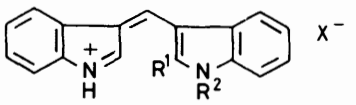
Scheme 3. *Reagents:* i, KOH–DMSO; ii, 3-chloroacetylindole–DMSO; iii, 20% aq. NaOH, reflux

CH_2 signal and the appearance of two broad signals (δ 11.75 and 12.1, each 1 H) corresponding to the indole NH protons. Reduction of this ketone (**20a**) with an excess of lithium aluminium hydride in THF gave the 2,3′-methylenedi-indole (**18a**) as a colourless solid which rapidly turned pink on exposure to light and air. The mass spectrum showed M^+, 246.1151 ($C_{17}H_{14}N_2$) as the base peak and in the ^{1}H n.m.r. spectrum, the methylene singlet at δ 4.18 and the 1 H singlet at δ 6.22 from the indole 3-proton was clearly evident. The u.v. spectrum ($\lambda_{max.}$ 227, 274, 283, and 291 nm) was typically indolic.

The 2,3′-methylenedi-indole (**18a**) was treated with 1 mol equiv. of *p*-nitrobenzenediazonium fluoroborate under the same conditions as had been used for 3,3′-methylenedi-indole (**9a**). The product crystallised from ether at low temperature to give the required 3-(*p*-nitrophenylazo)-2,3′-methylenedi-indole (**16a**) (81%) as dark red crystals. This material was identical in all respects [t.l.c., m.p., mixed m.p., u.v., ^{1}H n.m.r. (90 MHz), and i.r. spectra] with a freshly prepared sample obtained from 3,3′-methylenedi-indole as described above. The ^{1}H n.m.r. spectrum of the 'synthetic' sample was also obtained at 400 MHz which enabled virtually complete assignments of all the proton signals.

Studies[20] on the relative reactivity of various pyrroles and indoles towards the *p*-nitrobenzenediazonium ion have demonstrated a large difference in reactivity at the indolyl 3-position between indoles substituted, and unsubstituted, at the 2-position. In the light of the above results for 3,3′-methylenedi-indole itself, it was interesting to try the diazonium coupling reaction on unsymmetrical methylenedi-indoles type (**9d**) and (**9e**).

These compounds do not appear to have been prepared previously although urorosein perchlorate (**21a**) has been obtained[26] by the condensation of indole-3-carbaldehyde with indole in the presence of perchloric acid. It seemed likely that suitably substituted indole-3-carbaldehydes would lead to unsymmetrically substituted analogues of (**21a**), which could then be reduced to unsymmetrical methylenedi-indoles. In fact, urorosein perchlorate was reduced to methylenedi-indole itself in 70% yield by sodium borohydride in warm ethanol. Reaction

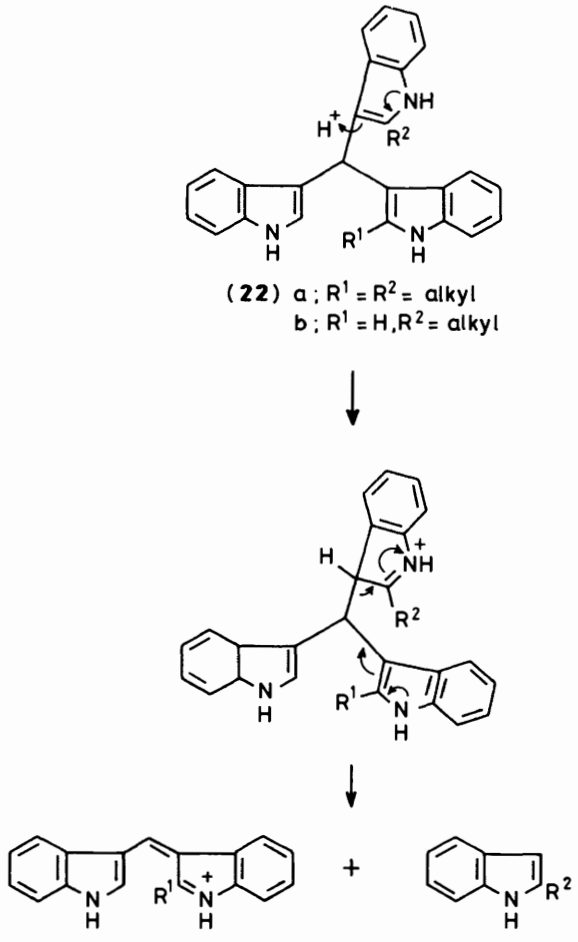


(**21**)

a; $R^1 = R^2 = H$, $X = ClO_4^-$
b; $R^1 = R^2 = Me$, $X = BF_4^-$
c; $R^1 = Me$, $R^2 = H$, $X = BF_4^-$

of indole-3-carbaldehyde with 1,2-dimethylindole and fluoroboric acid in boiling methanol gave the methene salt (**21b**) (94%), reduction of which, as above, gave the crude unsymmetrical methylenedi-indole (**9d**) (83%) as an air- and light-sensitive solid. Its instability precluded elemental analysis but the spectroscopic data obtained with the freshly crystallised sample were fully consistent with its structure. An analogous route afforded the monosubstituted compound (**9e**).

The reaction between indole-3-carbaldehydes and various indoles is probably more complex than appears at first sight. Thus, when 1-methylindole-3-carbaldehyde and indole were treated in methanol with fluoroboric acid, reduction of the intermediate purple solid afforded a complex mixture, in which the symmetrical methylenedi-indoles (**9a**) and (**9c**) were prominent. Similar results were obtained when 1-methylindole and indole-3-carbaldehyde were used as starting materials. These results may be explained by the intermediacy of a methylidynetri-indole of general type (**22**) (Scheme 4).



(**22**) a; $R^1 = R^2$ = alkyl
b; $R^1 = H$, R^2 = alkyl

Scheme 4.

Protonation of an indolylmethylene-3*H*-indole salt will take place preferentially at the 3-position of a 2-alkylindole nucleus in (**22**) leading to unsymmetrical compounds when a 2-alkylindole and indole-3-carbaldehyde are starting materials (**22a**), but to symmetrical products when an unsubstituted indole and a 2-alkylindole-3-carbaldehyde are employed (**22b**).

The methylenedi-indole (**9d**) on treatment with 2 mol equiv. of *p*-nitrobenzenediazonium salt under aqueous conditions gave high yields, after chromatography, of the two possible 3-phenylazoindoles (**13a**) (0.83 mol equiv.) and (**13d**) (0.85 mol equiv.) as expected. When 1 mol equiv. of diazonium salt was used, however, only the 1,2-dimethyl-3-phenylazo derivative (**13d**) (0.85 mol equiv.) together with 0.17 mol equiv. of methylenedi-indole (**9a**) were obtained. A parallel result was obtained with the 2-methyl analogue (**9e**) from which 2-methyl-3-*p*-nitrophenylazoindole (**13b**) (0.8 mol equiv.) and methylenedi-indole (0.13 mol equiv.) were isolated. These results imply initial regiospecific attack by the diazonium ion at the 3-position of the 2-substituted indolyl group of the starting material. The liberated 3-hydroxymethylindole evidently does not compete effectively with starting material for the electrophile—but to some extent undergoes reaction with itself to form 3,3′-methylenedi-indole.[19,20]

When the unsymmetrical methylenedi-indole (**9d**) was treated with 1 or 2 mol equiv. of diazonium ion in dry acetonitrile, only 3-*p*-nitrophenylazo-1,2-dimethylindole (**13d**) was isolated with minute traces of the 3-nitrophenylazoindole analogue (**13a**). Similarly, the 2-methyl derivative (**9e**) gave, under the same conditions, predominantly 3-nitrophenylazo-2-methylindole (**13b**) which was shown to contain $<5\%$ of 3-nitrophenylazoindole (**13a**).

It is clear from the results described above that the pathway taken by the diazo coupling reaction of methylenedi-indoles is dependent on several features—notably the structure of the methylenedi-indole, the presence or absence of water, and the proportions of diazonium salt to methylenedi-indole. In aqueous solution, using 2 mol equiv. of diazonium salt, 3,3′-methylenedi-indoles, like bilirubin, give azo compounds derived from the heterocyclic nuclei on either side of the methylene bridge. If the first attack by the electrophile at the more reactive of the two 3-positions in unsymmetrical cases (that of the indole nucleus with a 2-alkyl substituent) is assumed, the reaction pathway can be represented analogously to that in Scheme 2.

From the observed difference in rates of diazo coupling of indole and 2-methylindole (1:315)[1] at 30 °C, the initial attack on 2-alkyl 3,3′-methylenedi-indoles would be expected to be virtually regiospecific. Hence when only 1 mol equiv. of diazonium ion is employed the reagent is faced with competition between the starting material and 3-hydroxymethylindole. The relative rates[20] of diazo coupling of 2-methylindole, or 1,2-dimethylindole, compared with 3-hydroxymethylindole are at least 7:1 so that for the unsymmetrical cases studied, attack on the unused methylenedi-indole is preferred to that on the displaced hydroxymethylindole and the 2-methyl (or 1,2-dimethyl)-3-nitrophenylazoindole is formed preferentially.

Under non-aqueous conditions, for symmetrical methylenedi-indoles, migration of the indol-3-ylmethylene substituent of the first-formed intermediates (**15a**) or (**15b**) (Scheme 2), occurs directly to give the 2-indol-3-methyl-3-*p*-nitrophenylazoindoles (**16a**) or (**16b**). However, in these reactions, the formation of the 3-*p*-nitrophenylazoindoles is also significant; *i.e.* 0.45 mol equiv. of (**13a**) for (**9a**) and 0.57 mol equiv. of (**13c**) for (**9c**). These products cannot arise from the displaced indolylmethylene group since insufficient water is present to form the 3-hydroxymethylindole. Hence it seems that a simple displacement of the 3-indolylmethyl group from the intermediate (**15a**) or (**15b**) occurs under non-aqueous conditions, at least to some extent. The resulting 3-methylene-3*H*-indole cation (**10a**) or (**10b**) could then form the polymers which always accompany the reaction.

For the unsymmetrical methylenedi-indoles (**9d**) and (**9e**) rearrangement to, or resubstitution at the 2-position under anhydrous conditions is precluded and it is, therefore, not surprising that the yields of 2-methyl-3-*p*-nitrophenylazoindoles are rather higher [0.85 mol equiv. for (**13d**)] than in the cases of the symmetrical compounds. Once again, the greater reactivity of the 2-substituted indole nucleus leads to high regioselectivity, little or no 3-*p*-nitrophenylazoindole being formed.

Experimental

M.p.s were determined with a Kofler hot-stage apparatus and are corrected. N.m.r. spectra were measured in $CDCl_3$ with a Perkin-Elmer R-32 instrument at 90 MHz unless otherwise stated. I.r. spectra were recorded on a Unicam SP 200 grating spectrophotometer and u.v. spectra were recorded in absolute ethanol on either a Cary 17 or a Unicam SP 800 spectrophotometer. Mass spectra were obtained with a Varian CH5-D instrument by electron impact—direct insertion probe at 70 eV and 50/uA. Light petroleum refers to that of boiling range 40—60 °C. Organic solutions were dried over magnesium sulphate; thin layer chromatography was performed using plates coated with Merck silica gel HF254. Preparative thin layer chromatography was carried out using 20 × 20 cm^2 plates coated with Merck silica gel PF254. Merck (Kieselgel 60) silica was used for column chromatography. Acetonitrile was distilled over phosphorus pentaoxide under nitrogen, the fraction b.p. 82 °C being collected and kept over molecular sieve type 4A.

3,3′-*Methylenedi-indole* (**9a**).—Formaldehyde (40% aqueous solution; 4 ml) was added dropwise to indole (11.7 g, 0.1 mol) suspended in a mixture of glacial acetic acid (3 g, 0.05 mol) in water (250 ml). The mixture was vigorously stirred under nitrogen at 90 °C for 5 h in the dark after which it was cooled and the solid product filtered off, washed with water, and recrystallised from aqueous ethanol to give colourless needles, m.p. 165—166 °C (lit.,[19] m.p. 166 °C) (12 g, 98%).

1,1′-*Dimethyl*-3,3′-*methylenedi-indole* (**9c**).—This compound was prepared as above using 1-methylindole (13.1 g) in place of indole. The crude product separated as a red gum which was extracted with ethyl acetate (3 × 100 ml); the combined extracts were washed with saturated aqueous sodium hydrogencarbonate (2 × 100 ml) and water (2 × 100 ml), dried ($MgSO_4$), and evaporated. The residue was recrystallised from ethanol to give the title compound (10 g, 73%) as colourless plates, m.p. 110—112 °C (lit.,[19] m.p. 112—113 °C), δ 3.61 (6 H, s, 2 × N–CH_3), 4.20 (2 H, s, CH_2), 6.74 (2 H, s, 2 × 2-H), 7.30—6.97 (6 H, m, 2 × 5-, 6-, and 7-H), and 7.62 (2 H, d, *J* 7 Hz, 2 × 4-H).

p-*Nitrobenzenediazonium Tetrafluoroborate*.[27]—A solution of sodium nitrite (0.85 g, 12.5 mmol) in water (2 ml) was added dropwise with vigorous stirring to an ice-cooled mixture of *p*-nitroaniline (1.7 g, 12.5 mmol) and 40% fluoroboric acid solution (5.5 ml, 7.2 g). When all the nitrite had been added, the cooling bath was removed and the suspension stirred for a further 10 min. The stiff paste was filtered successively with ice-cold fluoroboric acid, ethanol, and ether and dried *in vacuo* to give the crude diazonium salt as a cream powder (2.9 g, 98%) which was sufficiently pure for use in synthetic reactions. Material for kinetic runs was recrystallised from acetone–light petroleum as almost colourless, very fine needles.

3-(p-*Nitrophenylazo*)*indole* (**13a**).—A solution of indole (117 mg, mmol) in ethanol (5 ml) was added in one portion with vigorous stirring to *p*-nitrobenzenediazonium tetrafluoroborate[27] (238 mg, 1 mmol) in water (100 ml). The mixture was

stirred for 10 min at 20 °C after which the precipitated solid was filtered off, washed with water, and recrystallised from aqueous ethanol to give the title compound as bright orange needles (250 mg, 95%), m.p. 220—222 °C (lit.,[28] m.p. 195—197 °C) (Found: C, 63.0; H, 3.7. Calc. for $C_{14}H_{10}N_4O_2$: C, 63.1; H, 3.8%).

1-*Methyl*-3-(p-*nitrophenylazo*)*indole* (**13c**).—(a) *From* 1-*methylindole*. The reaction of 1-methylindole (131 mg, 1 mmol) with the *p*-nitrobenzenediazonium salt as above afforded the title compound (**13c**) as red needles (230 mg, 82%) from aqueous dioxane, m.p. 189—191 °C (lit.,[1] m.p. 188—191 °C) (Found: C, 64.6; H, 4.1. Calc. for $C_{15}H_{12}N_4O_2$: C, 64.3; H, 4.3%).

(b) *From* 3-(p-*nitrophenylazoindole*). Anhydrous potassium carbonate (200 mg) was added to a solution of 3-(*p*-nitrophenylazo)indole (**13a**) (50 mg) in anhydrous acetone (10 ml). Carbon dioxide was evolved and a clear blue-purple solution obtained. Methyl iodide (100 mg) was added and the mixture was maintained at 30—35 °C for 2 h before being poured into water. The orange precipitate was filtered off and recrystallised from aqueous dioxane to give the title compound (**13c**) (50 mg, 89%), m.p. 189—191 °C undepressed on mixing with an equal quantity of material prepared by method (a).

2-*Methyl*-3-(p-*nitrophenylazo*)*indole* (**13b**).—This compound was prepared from 2-methylindole (131 mg, 1 mmol) and the *p*-nitrobenzenediazonium salt as red microneedles, m.p. 225—227 °C (decomp.) (lit.,[1] m.p. 228—230 °C decomp.) from aqueous ethanol (250 mg, 89%) (Found: C, 64.4; H, 4.2. Calc. for $C_{15}H_{12}N_4O_2$: C, 64.3; H, 4.3%).

3-*Methyl*-2-(p-*nitrophenylazo*)*indole* (**17**).—This compound was prepared from 3-methylindole (131 mg, 1 mmol) and the *p*-nitrobenzenediazonium salt as dark red crystals, m.p. 220—222 °C (decomp.) (lit.,[1] m.p. 217—220 °C) from aqueous ethanol (200 mg, 71%).

1,2-*Dimethyl*-3-(p-*nitrophenylazo*)*indole* (**13d**).—This compound was prepared by the action of *p*-nitrobenzenediazonium salt on 1,2-dimethylindole (145 mg, 1 mmol). Recrystallisation of the crude product from aqueous dioxane afforded the title compound (**13d**) as dark red needles, m.p. 209—210 °C (decomp.) (270 mg, 90%) (Found: C, 65.5: H, 4.7. $C_{16}H_{14}N_4O_2$ requires C, 65.3; H, 4.8%).

This compound was also prepared from 2-methyl-3-(*p*-nitrophenylazo)indole by method (b) for the preparation of 1-methyl-(3-*p*-nitrophenylazo)indole in 88% yield. The material was identical by chromatography, i.r. and mixed m.p. with the material prepared above.

Reaction of 3,3′-*Methylenedi-indole* (**9a**) *with Aqueous* p-*Nitrobenzenediazonium Tetrafluoroborate*.—(*a*) A solution of 3,3′-methylenedi-indole (246 mg, 1 mmol) in ethanol (10 ml) was added to a stirred solution of *p*-nitrobenzenediazonium fluoroborate (475 mg, 2 mmol) in water (300 ml). The reaction vessel was closed and the mixture stirred at 20 °C for 3 h. The reaction mixture was then immersed in an oil-bath at 130—140 °C and the aqueous distillate was collected. The residue was crystallised from aqueous ethanol to afford 3-(*p*-nitrophenylazo)indole (490 mg, 92%) identical (t.l.c., i.r., and mixed m.p.) with authentic material.

The aqueous distillate from the above reaction was treated with 5,5-dimethylcyclohexane-1,3-dione (dimedone) (1 g) in ethanol (20 ml) and stirred at 20 °C for 1 h. The mixture was then concentrated to *ca.* 30 ml by distillation under reduced pressure and kept at 0 °C overnight. The crystalline product (150 mg) was filtered off and recrystallised from aqueous ethanol (×3) to give the dimedone derivative of formaldehyde (80 mg; equivalent to 8.2 mg, 27%, of formaldehyde), m.p. 189—191 °C (lit.,[29] m.p. 189 °C) identical (mixed m.p. and i.r.) with an authentic specimen.

(*b*) A solution of 3,3′-methylenedi-indole (**9a**) (246 mg, 1 mmol) in ethanol (20 ml) was added to *p*-nitrobenzenediazonium tetrafluoroborate (238 mg, 1 mmol) in water (150 ml). After 1 h, the mixture was extracted with ether (3 × 100 ml) and the combined extracts dried (Na_2SO_4) and evaporated to afford a red solid (400 mg). This solid was chromatographed on silica (50 g) using ether–light petroleum mixtures of increasing ether content as eluant. Two main fractions were collected: (i) colourless crystals, m.p. 163—165 °C (75 mg, 30%), identified as starting material (**9a**) by comparison with an authentic specimen; (ii) orange needles from aqueous ethanol, m.p. 220—222 °C (230 mg, 86%) identified as 3-(*p*-nitrophenylazo)indole (**13a**).

Reaction of 1,1′-*Dimethyl*-3,3′-*methylenedi-indole* (**9c**) *with* p-*Nitrobenzenediazonium Tetrafluoroborate in Aqueous Solution*.—1,1′-Dimethyl-3,3′-methylenedi-indole (**9c**) (274 mg, 1 mmol) was dissolved in ethanol (20 ml) and added in one portion to a solution of *p*-nitrobenzenediazonium tetrafluoroborate (475 mg, 2 mmol) in water (300 ml). The mixture was left at 20 °C for 1 h to give a red precipitate which was filtered off, washed with water, and recrystallised from aqueous dioxane. This afforded red needles (500 mg, 89%), m.p. 189—191 °C identical (mixed m.p., t.l.c., and i.r.) with an authentic specimen of 1-methyl-3-(*p*-nitrophenylazo)indole.

Reaction of 3-*Hydroxymethylindole* (**14a**) *with* p-*Nitrobenzenediazonium Tetrafluoroborate*.—3-Hydroxymethylindole (**14a**) (147 mg, 1 mmol) in ethanol (10 ml) was added to *p*-nitrobenzenediazonium tetrafluoroborate (238 mg, 1 mmol) in water (150 ml). An orange precipitate immediately separated and was filtered off and recrystallised from aqueous ethanol to give orange needles, m.p. 220—222 °C (decomp.) (250 mg, 94%) identical (mixed m.p., i.r., and t.l.c.) with an authentic specimen of 3-(*p*-nitrophenylazo)indole.

Reaction of 3,3′-*Methylenedi-indole* (**9a**) *with* p-*Nitrobenzenediazonium Tetrafluoroborate in Acetonitrile Solution*.—3,3′-Methylenedi-indole (**9a**) (246 mg, 1 mmol) in dry acetonitrile (25 ml) was treated with *p*-nitrobenzenediazonium tetrafluoroborate (238 mg, 1 mmol). After 5 min the red solution was poured into a mixture of saturated aqueous sodium hydrogencarbonate (50 ml) and water (50 ml) and the resulting suspension extracted with ether (4 × 50 ml). The combined extracts were washed with water (3 × 50 ml), dried ($MgSO_4$), and evaporated to give a dark red oil (415 mg). This oil was dissolved in acetone (5 ml) and chromatographed on silica gel thick-layer plates using ether–light petroleum (7:3) as eluant. Two main bands were separated and these were scraped from the plates and the adsorbed organic material extracted by stirring with dry acetone before evaporation: (i) R_F 0.70 gave orange needles, m.p. 220—222 °C (decomp.) (120 mg, 45%) identified by comparison with authentic material as 3-(*p*-nitrophenylazo)indole; (ii) R_F 0.55 gave 3-(*p*-nitrophenylazo)-2,3′-methylenedi-indole (**16a**) as a dark red solid, decomposing without melting at *ca.* 150 °C (165 mg, 39%); *m/z* (%) 257 (17), 138 (100), 108 (32), 92 (41), 80 (12), and 65 (85). For full spectroscopic details see synthesis and preparation below. A dark brown band, R_F 0.0—0.1 was not investigated further.

Pyrolysis of the Azo Derivative (**16a**) *of* 3,3′-*Methylenedi-indole*.—The azo compound (**16a**) (12 mg) was placed in the sealed end of a long glass tube and the tube evacuated on a water pump. The sealed end of the tube was immersed in a silicone oil-bath at 150 °C. After 10 min the temperature was gradually raised to 230 °C and maintained at the latter

temperature for 10 min before allowing the tube to cool to 20 °C and disconnecting the water pump. Yellow crystals, m.p. 148—149 °C (2 mg, 48%) were removed from the upper parts of the tube and found to be identical (mixed m.p., u.v.) with a specimen of *p*-nitroaniline. The residue at the bottom of the tube was analysed by t.l.c. and found to contain a complex mixture of highly coloured compounds.

Reaction of 1,1′-*Dimethyl*-3,3′-*methylenedi-indole* (**9c**) *with* p-*Nitrobenzenediazonium Tetrafluoroborate in Acetonitrile.*—1,1′-Dimethyl-3,3′-methylenedi-indole (**9c**) (274 mg, 1 mmol) in dry acetonitrile (20 ml) was treated portionwise with *p*-nitrobenzenediazonium tetrafluoroborate (238 mg, 1 mmol). After being stirred at 20 °C for 2 min the dark red solution was poured into a mixture of saturated aqueous sodium hydrogencarbonate (50 ml) and water (50 ml). The precipitate was collected, washed well with water, and dried to give the crude product as a dark red solid (430 mg). This was dissolved in chloroform (5 ml) and chromatographed on silica (50 ml), using ether–light petroleum mixture of increasing ether content as eluant. Two main fractions were collected: (i) pale yellow solid, m.p. 150—155 °C (decomp.) (30 mg); *m/z* (%) 430 (6), 429 (21, M^+), 414 (6), 399 (4), 286 (33), 285 (100), 284 (49), 271 (6), 270 (22), 269 (15), 144 (34), 143 (20), 142 (20), 135 (11), 128 (8), 127 (7), and 65 (7) (Found: *M*, 429.2189. $C_{30}H_{27}N_3$ requires *M*, 429.2205). The structure of the compound could not be determined; (ii) Red crystals (310 mg). This material appeared as a single spot on t.l.c. in all solvent systems but on h.p.l.c. using 5% dioxane in light petroleum (b.p. 60—80 °C) two bands (R_t 15 and 21 min) were apparent. The crude mixture was dissolved in boiling dioxane (2 ml) and the mixture allowed to cool slowly to 15 °C. Orange-red crystals separated and were identified as 1-methyl-3-(*p*-nitrophenylazo)indole (**13c**) (110 mg), m.p. 186—188 °C by m.p., i.r., and h.p.l.c. The dioxane mother liquors were separated by preparative high pressure liquid chromatography using 8% ethyl acetate in cyclohexane as eluant. Two main products were isolated: (*a*) R_t 50min, red crystals (50 mg), m.p. 186—188 °C identified as 1-methyl-3-(*p*-nitrophenylazo)indole (**13c**). (*b*) R_t 62 min, dark red crystals of 1-methyl-2-(1′-methylindol-3′-ylmethyl)-3-(*p*-nitrophenylazo)indole (**16b**) (100 mg, 24%) decomposing without melting at *ca.* 150 °C; δ[$(CD_3)_2CO$; 220 MHz] 3.65 (3 H, s, N–CH_3), 3.68 (3 H, s, N–CH_3), 4.78 (2 H, s, CH_2), 6.71 (1 H, s, 2′-H), 7.45—7.10 (6 H, m, 6 × Indole-H), 7.66 (1 H, m, 4′-H), 7.96 (2 H, d, *J* 9 Hz, 2-and 6-ArH), 8.29 (2 H, d, *J* 9 Hz, 3- and 5-ArH), 8.64 (1 H, m, 4-H) [Found: *M* (field desorption m.s.), 423. $C_{25}H_{21}N_5O_2$ requires *M*, 423]. (*c*) Late h.p.l.c. fractions afforded a mixture of the above compound and a component (6 mg) having *M* (from field desorption m.s.) 566 ($C_{35}H_{30}N_6O_2$ requires *M*, 566).

1-(*Indol*-3-*ylcarbonylmethyl*)*indole*-2,3-*dione* (**19**).—Indole-2,3-dione (4.0 g, 27 mmol) in dry DMSO (20 ml) was added dropwise to a vigorously stirred suspension of potassium hydroxide (crushed pellets; 0.5 g, 27 mmol) in dry DMSO (20 ml) under nitrogen. The mixture was stirred at room temperature for 1.5 h and then the temperature was raised to 80 °C. To the resulting reddish solution a solution of 3-chloroacetylindole (m.p. 232—233 °C, lit.,[24] 230—232 °C) (5.2 g) in dry DMSO (15 ml) was added dropwise and the mixture was stirred at this temperature for 1 h before cooling to 20 °C. The resulting dark orange solution was poured into ice–10% hydrochloric acid (50 ml), to give an orange solid which was filtered off, washed with water until the washings were neutral, and air dried. Chromatography over silica gel (500 g) using chloroform as eluant gave the *title compound* (**19**) as orange needles after crystallisation from acetone (1.7 h, 20%), m.p. 282—284 °C; δ[$(CD_3)_2SO$] 5.21 (2 H, s, CH_2), 6.95—7.4 (4 H, m), 7.4—7.76 (3 H, m), 8.11 (1 H, m, 4-H), 8.64 (1 H, s, 2-*H*), and 12.18 (1 H br s, NH); $\nu_{max.}$(Nujol) 3 200 (NH) 1 650, and 1 720 cm^{-1} (C=O); $\lambda_{max.}$ 226 (ε 9 100), 249 (19 700), 251sh (14 800), 263sh (7 300), 272 (5 100), and 300 nm (9 700); *m/z* (%) 305 (M^+ + 1, 1.4), 304 (M^+, 6), 145 (12), 144 (100), and 116 (8) (Found: C, 71.0; H, 4.12; N, 9.26. $C_{18}H_{12}N_2O_3$ requires C, 71.0; H, 3.98; N, 9.21%).

Indol-2-*yl Indol*-3′-*yl Ketone* (**20**).—The indoledione (**19**) (0.9 g, 3.3 mmol) in 20% aqueous sodium hydroxide (55 ml) was refluxed for 12 h and then cooled to 20 °C. The resulting off-white precipitate was filtered off, washed with water until the washings were neutral, and then air dried. Afrer crystallisation from methanol the pure title compound (**20**) was obtained as off-white crystals (0.62 g, 81%), m.p. 260—261 °C; δ[$(CD_3)_2SO$] 6.98—8.0 (8 H, m), 8.34 (1 H, m, 4′-H), 8.40 (1 H, s, 2′-H), 11.75 (1 H, br s, NH), and 12.1 (1 H, br s, N′-H); $\nu_{max.}$(Nujol) 3 380 (NH) and 1 620 cm^{-1} (C=O); $\lambda_{max.}$ 237 (ε 6 900), 251 (8 600), 264sh (6 600), 274sh (6 300), 281 (5 800), 300sh (8 100), and 344 cm^{-1} (14 000); *m/z* (%) 261 (M^+ + 1, 22), 260 (M^+, 100), 259 (19), 144 (66), 143 (26), 117 (67), 116 (16), 115 (12), and 89 (16) (Found: C, 78.3; H, 4.93; N, 10.7. $C_{17}H_{12}N_2O$ requires C, 78.4; H, 4.65; N, 10.8%).

2,3′-*Methylenedi-indole* (**18a**).—A solution of the ketone (**20**) (0.55 g, 2 mmol) in dry THF (5 ml) was added to a stirred suspension of lithium aluminium hydride (0.45 g, 12 mmol) in dry THF (10 ml) under nitrogen in the dark. The mixture was heated under reflux for 1 h before being cooled to 20 °C. Excess of lithium aluminium hydride was decomposed by dropwise addition of saturated aqueous Rochelle salt. The tetrahydrofuran solution was decanted off and the aluminium salts were washed with ether (5 × 15 ml). The ether and the tetrahydrofuran solutions were combined, washed with water (3 × 15 ml), dried, and evaporated under reduced pressure to leave an off-white solid (0.42 g) which was crystallised from 95% ethanol to give the *title compound* (**18a**) as a colourless solid (0.38 g, 73%), m.p. 141—142 °C. The compound turned pink in contact with light and air; δ[$CDCl_3$–$(CD_3)_2SO$] 4.18 (2 H, s, CH_2), 6.22 (1 H, s, 3-H), 6.8—7.6 (9 H, m), 10.08 (1 H, br s, NH), and 10.11 (1 H, br s, NH); $\nu_{max.}$(Nujol) 3 430 cm^{-1} (NH); $\lambda_{max.}$ 227 (ε 29 900), 274sh (8 400), 283 (8 700), and 291sh nm (7 500); *m/z* (%) 247 (M^+ + 1, 16), 246 (M^+, 100), 245 (79), 244 (9), 243 (13), 130 (28), and 117 (17) (Found: *M*, 246.1151. $C_{17}H_{14}N_2$ requires *M*, 246.1157).

3-(p-*Nitrophenylazo*)-2,3′-*methylenedi-indole* (**16a**) *from* 2,3′-*Methylenedi-indole* (**18a**).—A solution of 2,3′-methylenedi-indole (**18a**) (0.246 g, 1 mmol) in dry acetonitrile (25 ml) was treated at 20 °C for 4-nitrobenzenediazonium tetrafluoroborate (0.238 g, 1 mmol). After 5 min the resultant dark red solution was poured into saturated aqueous sodium hydrogencarbonate (50 ml)–water (50 ml). The mixture was extracted with ether (4 × 50 ml), and the combined extracts were washed with water (3 × 50 ml), dried, and evaporated under reduced pressure at low temperature. The residual dark red solid was crystallised from ether to give the required 3-(*p*-nitrophenylazo)-2,3′-methylenedi-indole (**16a**) as dark red crystals (0.32 g, 81%), m.p. 166 °C (decomp.); δ[$(CD_3)_2CO$] 4.8 (2 H, s, CH_2), 6.81—7.6 (9 H, m), 8.05 (2 H, d, *J* 9 Hz, ArH *meta* to NO_2), 8.33 (2 H, d, *J* 9 Hz, ArH *ortho* to NO_2), 8.51 (1 H, m, 4-H), 10.1 (1 H, br s, NH), and 10.95 (1 H, br s, NH); δ[$(CD_3)_2CO$–$(CD_3)_2SO$ (1:1); 400 MHz] 4.76 (2 H, s, CH_2), 6.91 (1 H, m, 5′-H), 7.05 (1 H, m, 5-H), 7.23 (2 H, m, 6-H and 6′-H), 7.37 (1 H, m, 2′-H), 7.41 (2 H, m, 7-H and 7′-H), 7.58 (1 H, m, 4′-H), 8.09 (2 H, d, *J* 9 Hz, ArH *meta* to NO_2), 8.39 (2 H, d, *J* 9 Hz, ArH *ortho* to NO_2), 8.44 (1 H, m, 4-H), 10.45 (1 H, br, N′H), and 10.96 (1 H, br, NH); $\nu_{max.}$(Nujol) 3 400, 1 602, and 1 580 cm^{-1}; $\lambda_{max.}$ 226 (ε 30 300), 275sh (11 100),

283sh (12 300), 291sh (11 500), and 430 (17 100); *m/z* (%) (f.d.) 397 (M^+ + 2, 6.5), 396 (M^+ + 1, 29), and 395 (M^+, 100).

3-(p-*Nitrophenylazo*)-2,3′-*Methylenedi-indole* (**16a**) *from* 3,3′-*Methylenedi-indole* (**9a**).—The above azo compound (**16a**) was prepared as described for the synthesis from 2,3′-methylenedi-indole using the same relative molar concentration of 3,3′-methylenedi-indole (**9a**) and *p*-nitrobenzenediazonium tetrafluoroborate. The crude products (0.4 g) were subjected to preparative layer chromatography [silica gel, ether–light petroleum (7:3) as developing solvent] and the product band (R_F 0.55) was removed and extracted into dry acetone. Solvent was removed under reduced pressure at low temperature and the residual dark red solid was crystallised from ether to give the required title compound (**16a**) as dark red crystals (0.09 g, 22%), m.p. 164 °C, mixed m.p. 163.5 °C (decomp.) with an authentic sample prepared as above. The u.v., i.r., and n.m.r. spectra were identical with those of the product from the reaction of 2,3′-methylenedi-indole with *p*-nitrobenzenediazonium tetrafluoroborate.

Reduction of 3-*Indol*-3-*ylmethylene*-3H-*indol*-3-*ium* (*Urorosein*) *Perchlorate*.—The title perchlorate (**21a**) (1 g), prepared by the method of Smith,[26] was dissolved in hot methanol (40 ml) and treated with sodium borohydride (0.5 g) in methanol (10 ml) made alkaline with a few drops of aqueous sodium hydroxide. After 10 min, the mixture was poured into water (100 ml) and the precipitate collected, and recrystallised from aqueous ethanol to give 3,3′-methylenedi-indole (**9a**) (0.5 g, 70%), m.p. 165—167 °C, undepressed on admixture with an authentic specimen.

3-(1,2-*Dimethylindol*-3-*ylmethylene*)-3H-*indol*-3-*ium Fluoroborate* (**21b**).—1,2-Dimethylindole (1 g) and indole-3-carbaldehyde (1 g) were dissolved in boiling methanol (20 ml). Fluoroboric acid (40% aqueous solution; 2.20 g) was added in one portion and the deep red solution formed allowed to cool. Crystallisation commenced rapidly the reaction mixture becoming almost solid. After being cooled the crystalline paste was filtered, and the crystals recrystallised from dry methanol to give a deep red crystalline powder with brilliant green iridescence (2.4 g, 94%). The title compound (**21b**) had no definite melting point but changed on heating above *ca.* 100 °C (Found: C, 63.2; H, 4.6; N, 7.85. $C_{19}H_{16}N_2 \cdot HBF_4$ requires C, 63.3; H, 4.8; N, 7.8%).

3-(2-*Methylindol*-3-*ylmethylene*)-3H-*indol*-3-*ium Fluoroborate* (**21c**).—This compound was prepared as above using 1 equiv. of 2-methylindole in place of 1,2-dimethylindole. The *salt* (**21c**) formed dark red iridescent crystals similar in appearance to those of the 1,2-dimethyl compound (Found: C, 62.5; H, 4.4; N, 7.9. $C_{18}H_{14}N_2HBF_4$ requires C, 62.4; H, 4.4; N, 8.1%).

3-(*Indol*-3-*ylmethyl*)-1,2-*dimethylindole* (**9d**).—The salt (**21b**) (2.0 g) dissolved in methanol (150 ml) when heated and the deep red solution was treated portionwise with solid sodium borohydride (2.0 g). The colour was rapidly discharged, and the straw coloured solution was kept at 20 °C under nitrogen for a further 15 min. Water (200 ml) was added and the resulting suspension was kept under nitrogen in the dark for 2 h. The pinkish precipitate was filtered off to give the crude methylenedi-indole (**9d**) (1.3 g, 83%). The product was extremely sensitive to air and light and was purified immediately before use by chromatography on silica gel under nitrogen using ether as eluant, followed by crystallisation from aqueous ethanol; it formed colourless needles, m.p. 138—139 °C. Owing to its high sensitivity a satisfactory elemental analysis could not be obtained, but its spectral data were fully consistent with the proposed structure: δ 2.32 (3 H, s, C-CH_3), 3.59 (3 H, s, N-CH_3), 4.15 (2 H, s, CH_2), 6.65 (1 H, br s, 2-H), 7.25—6.95 (6 H, m, 2 × 5-, 6-, and 7-H), 7.48 (2 H, m, 2 × 4-H), 7.68 (1 H, br s, NH); $\lambda_{max.}$ 275sh (ε 4 300), 283 (4 600), and 290sh nm (4 000); *m/z* (%) 275 (M^+ + 1, 17), 274 (M^+, 100), 273 (33), 260 (11), 259 (55), 158 (19), 157 (39), 144 (10), 137 (M^{2+}, 17), 130 (14), and 129 (23).

3-(*Indol*-3-*ylmethyl*)-2-*methylindole* (**9e**).—By using the above method and the same relative proportions of the salt (**21c**) and sodium borohydride the methylenedi-indole (**9e**) was obtained as colourless, air-sensitive crystals (1 g, 81%), m.p. 164—165 °C; δ 2.23 (3 H, s, C-CH_3), 4.10 (2 H, s, CH_2), 6.52 (1 H, br s, 2-H), and 7.68—6.98 (10 H, m, 2 × 1-, 4-, 5-, 6-, and 7-H); *m/z* (%) 261 (M^+ + 1, 15), 260 (100), 259 (25), 144 (20), 143 (38), 130 (15), and 129 (25).

Reaction of 3-(*Indol*-3-*ylmethyl*)-2-*methylindole* (**9e**) *with* p-*Nitrobenzenediazonium Tetrafluoroborate*.—The methylenedi-indole (**9e**) was treated with *p*-nitrobenzenediazonium fluoroborate (1 equiv.) in acetonitrile solution as described above. The crude product contained in addition to tarry polymeric material only a single coloured band on examination by t.l.c. and h.p.l.c. in several solvent systems. A sample was purified by chromatography on thick layer silica plates using ether–light petroleum (1:1) to give orange crystals, m.p. 223—225 °C (decomp.). The n.m.r. spectrum of this compound was identical with that of 2-methyl-3-(*p*-nitrophenylazo)indole (**13b**). Comparison of the size of the methyl signal with those of the aromatic signals showed that 3-(*p*-nitrophenylazo)indole was present in less than 5% of the concentration of the 2-methyl analogue.

The above reaction was also performed in aqueous solution. After similar chromatographic separation, 2-methyl-3-(*p*-nitrophenylazo)indole (**13b**) (80%) and 3,3′-methylenedi-indole (**9a**) (26%) were the only crystalline compounds isolated. 3-(*p*-Nitrophenylazo)indole (**13a**) and 2-methyl-3-(*p*-nitrophenylazo)indole (**13b**) could not be separated by t.l.c. or h.p.l.c.

Reaction of 3-(*Indol*-3-*ylmethyl*)-1,2-*dimethylindole* (**9d**) *with* p-*Nitrobenzenediazonium Tetrafluoroborate*.—The methylenedi-indole (**9d**) (274 mg, 1 mmol) in ethanol (10 ml) was added to a solution of *p*-nitrobenzenediazonium tetrafluoroborate (475 mg, 2 mmol) in water (300 ml). A red precipitate separated immediately and this was filtered off, washed with water, and dried (550 mg). A sample of the crude product (55 mg) was dissolved in acetone (2 ml) and separated on thick layer silica plates using ether–light petroleum (1:1) as eluant. The two coloured bands were each removed and extracted with acetone. Removal of the acetone afforded the products. Band (i) R_F 0.65 gave red needles (25 mg, 85%), m.p. 207—209 °C (decomp.) identified as 1,2-dimethyl-3-(*p*-nitrophenylazo)indole (**13d**) by comparison (mixed m.p., t.l.c., and i.r.) with an authentic specimen. Band (ii) R_F 0.45 gave orange needles (22 mg, 83%), m.p. 220—222 °C (decomp.) identified as 3-(*p*-nitrophenylazo)indole (**13a**) by comparison (mixed m.p., t.l.c., and i.r.) with an authentic specimen.

The above reaction was carried out under the same conditions except that only 1 mmol of the diazonium salt was used. The crude product was chromatographed on thick layer silica plates using ether–light petroleum (3:7) as eluant. Two bands were extracted. Band (i) R_F 0.80 gave colourless crystals, m.p. 164—166 °C (34%) identical with an authentic specimen of 3,3′-methylenedi-indole (**9a**) (i.r., mixed m.p.). Band (ii) R_F 0.55 gave red crystals, m.p. 207—209 °C (decomp.) (85%) identical, (i.r., t.l.c., and mixed m.p.) with authentic 1,2-dimethyl-3-(*p*-nitrophenylazo)indole (**13d**). No 3-(*p*-nitrophenylazo)indole could be detected under these conditions.

The methylenedi-indole (**9d**) (274 mg, 1 mmol) in acetonitrile

(25 ml) was treated with *p*-nitrobenzenediazonium tetrafluoroborate (238 mg, 1 mmol) and left at 20 °C for 5 min. The dark red solution was poured into water (50 ml) and saturated aqueous sodium hydrogencarbonate (50 ml) and the resulting precipitate was filtered off and crystallised from aqueous dioxane to afford dark red needles (250 mg, 85%), m.p. 207—209 °C identical (mixed m.p., i.r., and t.l.c.) with an authentic specimen of 1,2-dimethyl-3-(*p*-nitrophenylazo)indole (**13d**).

The above reaction in acetonitrile was repeated using 0.002 mol equiv. of the diazonium salt. Essentially identical results were obtained; only minute traces of 3-(*p*-nitrophenylazo)indole could be detected by t.l.c.

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