Polymerisation of Indole. Part 2.[1] A New Indole Trimer

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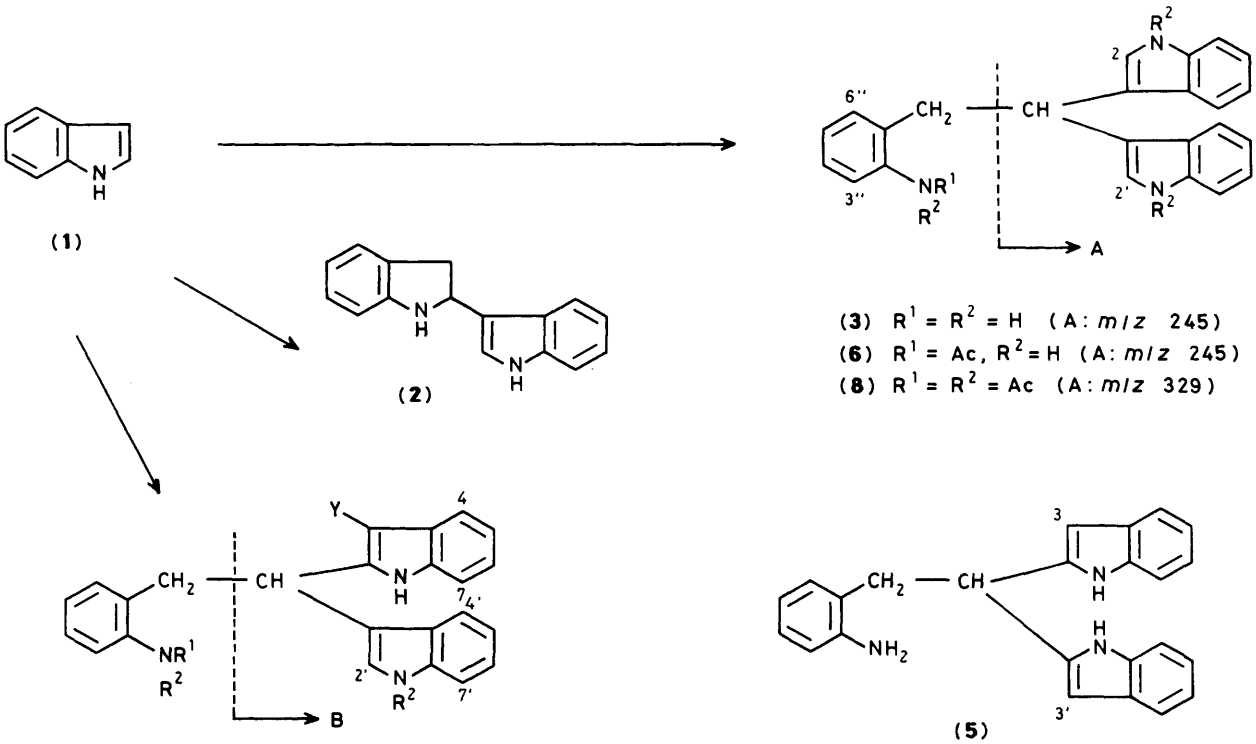
Treatment of indole (**1**) with toluene-*p*-sulphonic acid in benzene provided the 2,3′-indole trimer (**4**), a positional isomer of the well known 3,3′-indole trimer (**3**). The structure of the new trimer (**4**) was established by comparative studies with the trimers (**3**) and (**4**).

It is well known that indole (**1**) itself is easily polymerised under various acid conditions to give 3-(indolin-2-yl)indole[2] (the dimer) (**2**) and/or 3,3′-(*o*-aminophenethylidene)di-indole[2] (the 3,3′-trimer) (**3**). It was formerly believed that the same trimer would be formed on treatment under any acidic conditions, and Smith[3] proposed the generally accepted structure (**3**). However, in the course of our studies on the abnormal Fischer indolisation,[4] we occasionally found that 2,3′-(*o*-aminophenethylidene)di-indole, the 2,3′-trimer (**4**), was produced by treatment of indole (**1**) itself with toluene-*p*-sulphonic acid in benzene.[1] Here we give full details of our experiments on the formation of the 2,3′-trimer (**4**).

Treatment of indole (**1**) with toluene-*p*-sulphonic acid in benzene gave a mixture of dimorphic crystals, m.p. 105—107 °C or 186.5—187.5 °C, in 39.7% yield. The dimorphism of the product (**4**) was confirmed by cross seeding experiments and by comparison of i.r. spectra in solution. The molecular formula was confirmed to be $C_{24}H_{21}N_3$ by the agreement of the elemental analysis with the empirical formula $(C_8H_7N)_n$, and by the appearance of the parent peak in the mass spectrum at *m/z* 351, corresponding to the molecular ion of a trimeric indole. The i.r. spectrum of the new 2,3′-trimer (**4**) is different from that of the known 3,3′-trimer (**3**) in the solid state, but almost the same in solution, even in the fingerprint region, except that the 2,3′-trimer (**4**) shows an additional very small peak at 1 293 cm^{-1}. At the beginning of the study, we wondered whether these crystals might have arisen from polymorphism of the 3,3′-trimer (**3**), which is well known to exhibit dimorphism.[5] However, the difference between compounds (**3**) and (**4**) was confirmed by their R_F



Scheme 1.

values on t.l.c. [diethyl ether–hexane (3:1, v/v)], *ca.* 0.25 for the 3,3′-trimer (**3**) and *ca.* 0.30 for the 2,3′-trimer (**4**), and from their different behaviour on acetylation.

According to the reported procedure,[6] the 3,3′-trimer (**3**) was treated with acetic anhydride at 108 °C for 3 min to give its monoacetyl derivative[6b] (**6**), m.p. 209—212 °C (lit.,[6b] 202 °C); the same treatment of the 2,3′-trimer (**4**) gave another monoacetyl derivative (**7**), m.p. 168.5—171 °C. Moreover, on refluxing with acetic anhydride in the presence of sodium acetate, the 3,3′-trimer (**3**) provided the tetra-acetyl derivative[7] (**8**), m.p. 214.5—218.5 °C (lit.,[7] 210—211 °C), while the 2,3′-trimer (**4**) gave the triacetyl derivative (**9**), m.p. 221.5—224 °C. The triacetyl 2,3′-trimer (**9**) resisted further acetylation even under much stronger acetylating conditions.

Inspection of the ^{1}H n.m.r. spectra of the trimers (**3**) and (**4**) and their monoacetyl derivatives (**6**) and (**7**) disclosed that the two trimers have in common a $CH_2CH<$ group, fourteen aromatic protons, two aromatic amine protons, and two indolic NH groups (Tables 1 and 2). Furthermore, in the mass spectrum, the four compounds (**3**), (**4**), (**6**), and (**7**) all show a base peak at *m/z* 245, assignable to the di-indolylmethyl moiety. In indole chemistry, 2 ⟶ 3 migration of an alkyl or an aryl group under acid conditions is well known (the Plancher rearrangement,[8]); the 2,3′-trimer (**4**) is thus considered to be produced by Plancher rearrangement of the 3,3′-trimer (**3**).

A clue to the structure of the 2,3′-trimer (**4**) came from comparative inspection of the spectral data of the four acetyl derivatives (**6**)—(**9**). In the mass spectrum, the triacetyl 2,3′-trimer (**9**) shows a base peak at *m/z* 287, corresponding to an *N*-monoacetyldi-indolylmethyl cation (B; R^2 = Ac, Y = H); the tetra-acetyl 3,3′-trimer (**8**) peak at *m/z* 329 corresponds to the *N*,*N*′-diacetyldi-indolylmethyl cation (A; R^2 = Ac). These facts suggested that the two indolic nitrogen atoms of the 2,3′-trimer (**4**) are not equivalent; in other words, the 2,3′-trimer (**4**) has both 2- and 3-substituted indole skeletons in its molecule. Moreover, in the ^{1}H n.m.r. spectrum, the monoacetyl 2,3′-trimer (**7**) shows a singlet attributable to 3-H at δ 6.19, but the monoacetyl 3,3′-trimer (**6**) does not. Further, the triacetyl 2,3′-trimer (**9**) shows a diffuse one-proton doublet at δ 6.35, which changes to a sharp singlet on addition of deuterium oxide, indicating that the 2,3′-trimer (**4**) contains a 2-substituted indole nucleus.

The foregoing deduction was readily proved by the Vilsmeier-Haack reaction of the monoacetyl 2,3′-trimer (**7**) to give a monoformyl derivative (**10**); the same treatment of the monoacetyl 3,3′-trimer (**6**) resulted in recovery of starting material. In the mass spectrum, the formyl derivative (**10**) shows a base peak at *m/z* 273 attributable to the formylated di-indolylmethyl cation (B; R^2 = H, Y = CHO). Since, generally speaking, Vilsmeier-Haack reaction[2,9] of a 3-unsubstituted indole derivative takes place at C-3, this evidence shows that one of the 3-positions of the two indole units in the 2,3′-trimer (**4**) remains unoccupied. Further, in the ^{1}H n.m.r. spectrum, the formyl derivative (**10**) shows no signal corresponding to 3-H but a one-proton multiplet due to a benzene proton shifted downfield to δ 8.00 and three NH signals. These phenomena can be explained by supposing that 4-H of the formylated indole skeleton is subject to an anisotropic effect[9] of the formyl group at the *peri*-position. These observations established the structure (**10**) of the formyl derivative, and led us to conclude that the new trimer should be assigned structure (**4**).

Recovery of the monoacetyl 3,3′-trimer (**6**) from the Vilsmeier-Haack reaction provided strong confirmation of structure (**3**) for the known 3,3′-trimer.

We note that the *N*-acetyl methyl ^{1}H n.m.r. signals of the monoacetyl 3,3′-trimer (**6**) and the monoacetyl 2,3′-trimer (**7**) in $CDCl_3$ appeared at abnormally high field (δ 1.21 and 1.28). This shows that these methyl groups are subject to the anisotropic effects of the aromatic rings. However, with $(CD_3)_2SO$ as solvent these signals were observed at normal positions (δ 1.92 and δ 1.93), indicating a different steric requirement. We have no explanation for this solvent effect.

In 1954, Smith[3] proposed the generally accepted mechanism for formation of the dimer (**2**) and the 3,3′-trimer (**3**) shown in Scheme 2. As we supposed that the 2,3′-trimer (**4**) was produced by Plancher rearrangement of the 3,3′-trimer (**3**), formed according to Smith's mechanism, under more strongly acidic conditions, we treated the 3,3′-trimer (**3**) with toluene-*p*-sulphonic acid in benzene; this gave the 2,3′-trimer (**4**) and indole (**1**) itself together with recovered 3,3′-trimer (**3**), in 23.1, 19.5, and 3.3% yield, respectively. The formation of indole (**1**) itself in such high yield shows the existence of an equilibrium between the 3,3′-trimer (**3**) and indole (**1**) (Table 3).

Smith's mechanism consists of two steps involving electrophilic attack by two different electrophiles [(**11**) and (**14**)] at C-3 of indole (**1**). The production of indole (**1**) itself in the foregoing experiment made us hesitate to exclude the possibility that one of the two electrophilic attacks on indole (**1**) might take place at C-2 of the indole (**1**) under more strongly acidic conditions. In other words, the Plancher rearrangement process may not be the exclusive pathway for formation of the 2,3′-trimer (**4**).

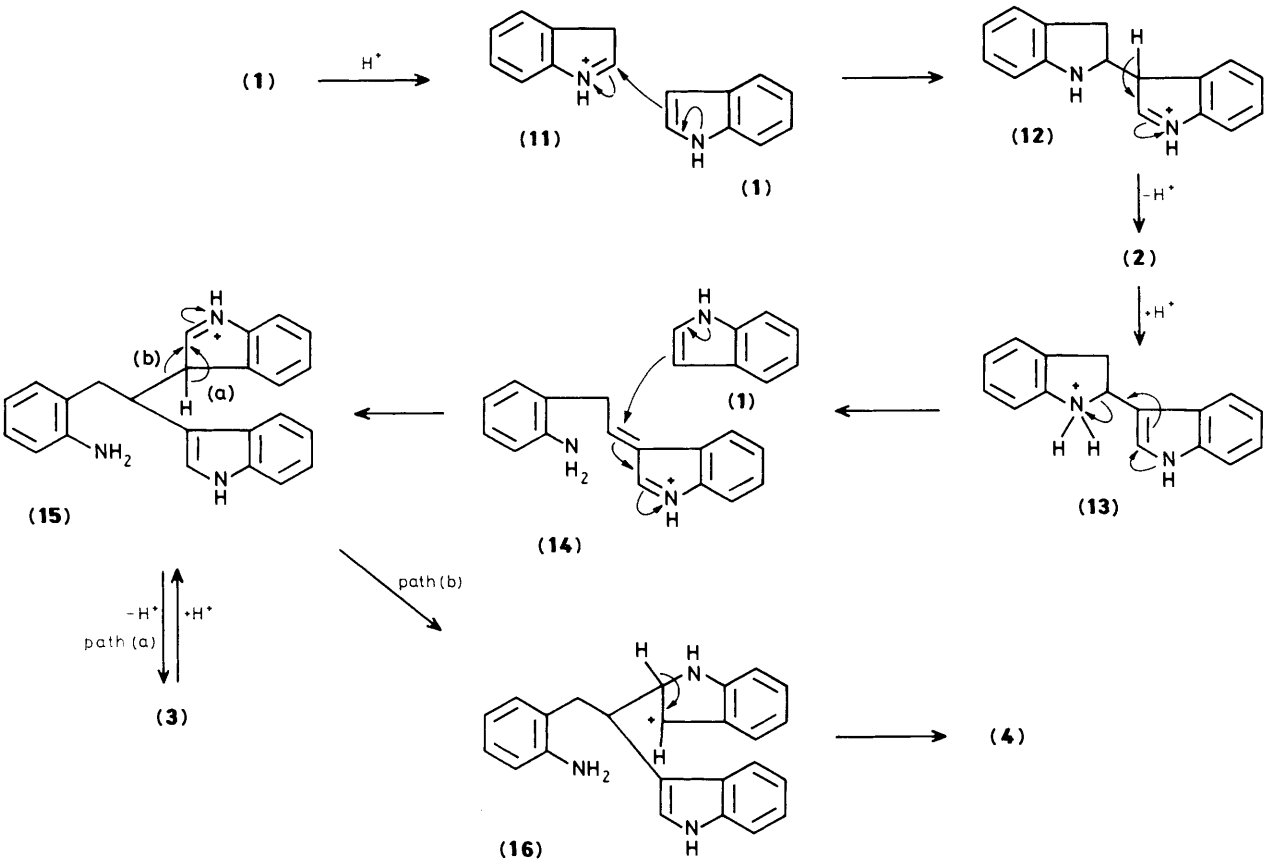
On the other hand, in 1960, Noland *et al.*[10] reported the synthesis of the 3,3′-trimer (**3**) by treatment of *o*-nitrophenyl-

Table 1. ^{1}H N.m.r. spectra of the indole trimers [in $CDCl_3$; δ (100 MHz)]

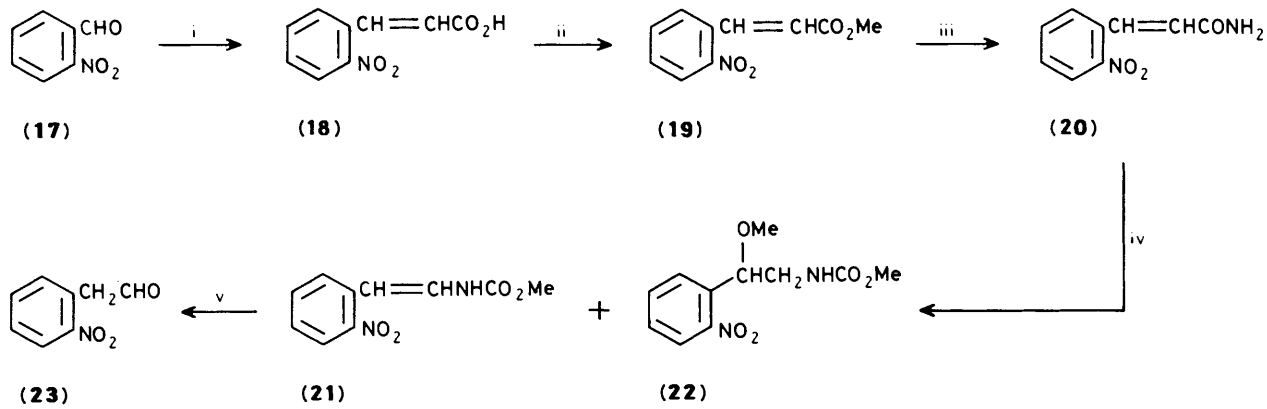
	3,3′-Trimer (**3**)	2,3′-Trimer (**4**)
$-CH_2-CH<$	3.33 (2 H, d, *J* 7.0 Hz)	3.35 (2 H, diffuse d, *J* 7.0 Hz)
$-CH_2-CH<$	4.78 (1 H, t, *J* 7.0 Hz)	4.62 (1 H, t, *J* 7.0 Hz)
ArH	6.38—6.68 (2 H, m),	6.35—6.72 (3 H, m),
	6.76—7.30 (10 H, m),	6.77—7.40 (10 H, m),
	7.41 (2 H, d, *J* 7.8 Hz)	7.43—7.62 (1 H, m)
NH	3.20 (2 H, br s),	2.98 (2 H, br s),
	7.66 (2 H, br s)	7.77 (2 H, br s)

Table 2. ^{1}H N.m.r. spectra of derivatives of the indole trimers [in $(CD_3)_2SO$; δ (100 MHz)]

	Monoacetyl 3,3′-trimer (**6**)	Monoacetyl 2,3′-trimer (**7**)	Monoacetyl monoformyl 2,3′-trimer (**10**)
$-CH_2-CH<$	3.45 (2 H, d, *J* 7.8 Hz)	3.46 (2 H, d, *J* 7.5 Hz)	3.36—3.84 (2 H, m)
$-CH_2-CH<$	4.71 (1 H, t, *J* 7.8 Hz)	4.66 (1 H, t, *J* 7.5 Hz)	5.34 (1 H, diffuse t, *J* 7.5 Hz)
3-H		6.19 (1 H, s)	
	6.68—7.36 (12 H, m)	6.73—7.52 (13 H, m)	6.76—7.50 (12 H, m)
Other ArH	7.46 (2 H, d, *J* 7.5 Hz)		
4-H			8.00 (1 H, m)
NH	8.93 (1 H, s)	9.08 (1 H, s)	9.35 (1 H, s)
	10.60 (2 H, s)	10.72 (2 H, s)	10.91 (1 H, s)
			11.71 (1 H, s)
$COCH_3$	1.88 (3 H, s)	1.96 (3 H, s)	2.04 (3 H, s)
CHO			10.04 (1 H, s)



Scheme 2.



Scheme 3. *Reagents*: i, Ac_2O, AcONa; ii, conc. HCl, MeOH; iii, conc. NH_4OH, EtOH; iv, aq. NaOCl, MeOH; v, 20% H_2SO_4

acetaldehyde (**23**), prepared from *o*-nitrobenzaldehyde (**17**) (Scheme 3), with a large amount of indole (**1**) in acetic acid, followed by catalytic hydrogenation of the resulting 3,3′-di-indolylmethane (**24**) over Raney nickel. We expected that the 2,3′-di-indolylmethane derivative (**25**) could be prepared if we used more strongly acidic conditions in the condensation step than did Noland.[10] In fact, *o*-nitrophenylacetaldehyde (**23**) in acetic acid gave only one di-indolylmethane derivative (Noland's product) (**24**), which gave the 3,3′-trimer (**3**) on catalytic reduction; however the same acetaldehyde (**23**) treated with anhydrous zinc chloride in acetic acid gave a mixture of two di-indolylmethane derivatives in 15.2 and 33.2% yield, respectively. The minor product was identical with a sample of Noland's product (**24**), prepared according to their procedure in our laboratory. The major product (**25**), obtained as a labile crystalline mass, was isomeric with the 3,3′-di-indolylmethane (**24**) (spectral data; see Experimental section). Since catalytic reduction of the new di-indolylmethane over Raney nickel gave the 2,3′-trimer (**4**), its structure (**25**) was confirmed. Its formation was explained in terms of acid-catalysed rearrangement of the initially formed 3,3′-di-indolylmethane (**24**); treatment of the pure 3,3′-di-indolylmethane (**24**) with anhydrous zinc chloride in acetic acid gave the 2,3′-di-indolylmethane (**25**) together with a trace of starting material (**24**), without formation of indole (**1**) itself. This evidence strongly supports the suggestion of the formation of the 2,3′-trimer (**4**) from the 3,3′-trimer (**3**) by Plancher rearrangement. Release of the *peri*-interaction in the molecule of the 3,3′-trimer (**3**) by formation of

the 2,3′-trimer (**4**), the thermodynamically stable product, would be the driving force.

Since the foregoing result implied that Plancher rearrangement of the 3,3′-trimer (**3**) would take place under other acidic conditions, other reagents were studied (Table 3). The 2,3′-trimer (**4**) could be obtained on treatment with boron trifluoride–ether complex at room temperature and with zinc chloride in acetic acid at 105 °C. However, the desired product (**4**) was not formed at room temperature with the latter reagent. This may be due to poor solubility of the 3,3′-trimer (**3**) in acetic acid at room temperature.

Finally, since we wondered if the reported procedure for preparation of the 3,3′-trimer (**3**) and the dimer (**2**) from indole (**1**) might produce a small amount of the 2,3′-trimer (**4**), we treated indole (**1**) under various acid conditions including the reported procedures (Table 4). The reported method gave no 2,3′-trimer (**4**) at all, as confirmed by detailed t.l.c. examination.

One might ask why the unknown 2,2′-trimer (**5**) could not be formed by a second Plancher rearrangement of the 2,3′-trimer (**4**) under much more strongly acidic conditions. However, since the 2,3′-trimer (**4**) tended to form an insoluble salt in each experiment, it would thus be removed from the reaction system.

Experimental

M.p.s were measured with a micro hot stage (Yanagimoto). I.r. spectra were recorded for Nujol mulls with a Hitachi EPI-G3 spectrometer or a Hitachi 215 spectrometer. U.v. spectra were recorded for solutions in 95% ethanol with a Hitachi EPS-3T spectrometer. N.m.r. spectra (^1H and ^{13}C) were recorded with a JEOL-JNM-FX-270 (270 MHz for ^1H and 67.8 MHz for ^{13}C), and/or a JEOL JNM-4H-100 (100 MHz for ^1H) spectrometer with tetramethylsilane as internal reference. Assignments for those signals due to NH and indolic 2-H and 3-H marked with an asterisk were confirmed by their behaviour on addition of D_2O disappearance of the NH signal and a change of a doublet (or a broad singlet) into a singlet (sharpened) for 2-H and 3-H]. Correlations of ^1H n.m.r. with ^{13}C n.m.r. signals were achieved by selective decoupling experiments. For t.l.c. and preparative t.l.c., silica gel GF_{254} (Merck) was used. Products were identified by i.r. spectroscopy, mixed m.p., and t.l.c.

3,3′-(o-*Aminophenethylidene*)*di-indole* (*the* 3,3′-*Trimer*) (**3**).—A suspension of finely powdered indole (**1**) (2.02 g) in 0.5M hydrochloric acid (200 ml) was stirred at room temperature for 24 h and filtered. The precipitate [the 3,3′-indole trimer (**3**)

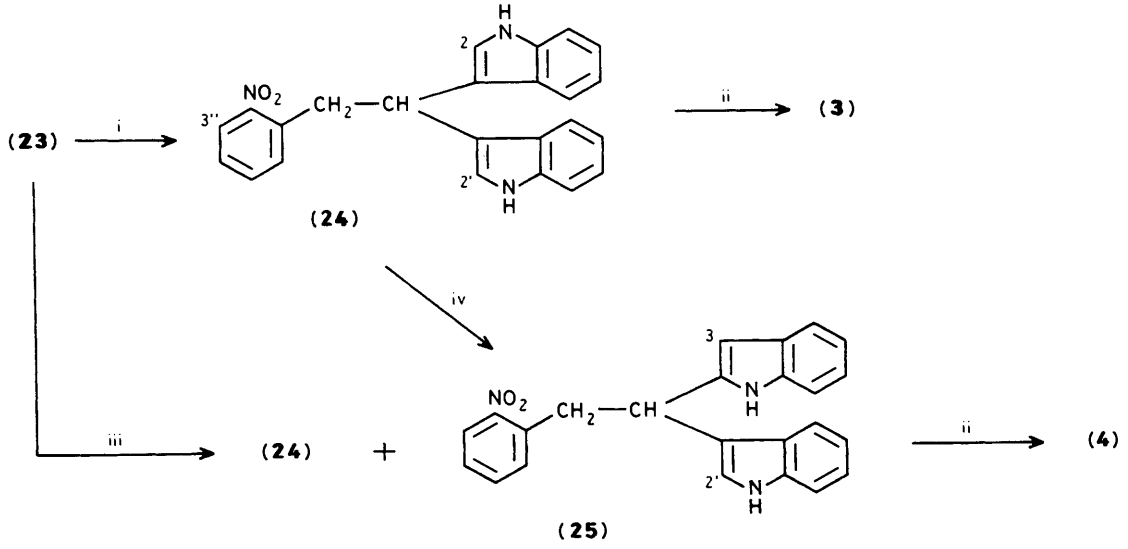
Table 3. Yields of products of treatment of the 3,3′-trimer (**3**) under various acid conditions

Conditions	3,3′-Trimer (3)	Indole (1)	Dimer (2)	2,3′-Trimer (4)
TsOH–PhH, reflux, 8 h	3.3%	19.5%		23.1%
BF_3·Et_2O, room temp. 5 days	9.6%	5.0%	26.9%	33.9%
$ZnCl_2$–AcOH, 105 °C, 4 h	15.3%	4.6%	6.1%	30.7%
$ZnCl_2$–AcOH, room temp., 21 h	92.9%			

Table 4. Yields of polymeric products from indole (**1**) under various acid conditions

Conditions	Indole (1)	Dimer (2)	3,3′-Trimer (3)	2,3′-Trimer (4)	Ref.
HCl gas, PhH, room temp., 1.2 h		98.9%			15
1M HBr room temp., 1.5 h	27.3%	18.7%	44.2%		6*a*
CF_3CO_2H, Et_2O, room temp., 48 h	9.1%	12.2%	68.4%		16
BF_3·Et_2O, room temp., 48 h	2.3%	23.4%	trace	26.7%	
$ZnCl_2$, AcOH, 50 °C, 8.5 h	49.8%	6.3%	34.6%		
$ZnCl_2$, AcOH 100—105 °C, 4 h	4.6%	6.7%	16.9%	34.4%	
0.5M HCl room temp., 24 h			92.8%		6
TsOH–PhH,[a] reflux, 3 h	17.3%			39.7%	

[a] Later, we isolated an indole tetramer from the reaction mixture; we describe this in the following paper.



Scheme 4. *Reagents*: i, indole, AcOH; ii, H_2, Raney Ni, AcOH; iii, indole, $ZnCl_2$, AcOH; iv, $ZnCl_2$, AcOH

hydrochloride (2.15 g)], m.p. 175 °C, was dissolved in hot ethanol and made alkaline with aqueous 5% sodium hydroxide (50 ml). After addition of a large quantity of cold water, the resulting precipitate was filtered off. Recrystallisation from aqueous ethanol gave colourless needles (1.88 g), m.p. 173—177 °C (lit.,[6a] 169 °C; lit.,[6b] 167 °C) (Found: C, 82.0; H, 6.1; N, 12.0. Calc. for $C_{24}H_{21}N_3$: C, 82.0; H, 6.0; N, 12.0%); $\nu_{max.}$ (KBr) 3 445, 3 420, and 3 335 cm^{-1}: $\nu_{max.}$($CHCl_3$) 3 480 cm^{-1}; $\lambda_{max.}$ 225, 285, and 292 nm (log ε 4.88, 4.12, and 4.08); for δ_H (100 MHz; $CDCl_3$) see Table 1; δ_H [270 MHz; $(CD_3)_2SO$] 3.35 (2 H, d, *J* 7.6 Hz, CH_2CH), 4.72* (2 H, br s, NH_2), 4.86 (1 H, t, *J* 7.6 Hz, CH_2CH), 6.33 (1 H, dt, *J* 7.6 and 1.1 Hz, 5″-H), 6.57 (1 H, dd, *J* 7.6 and 1.1 Hz, 3″-H), 6.78 (1 H, dt, *J* 7.6 and 1.2 Hz, 4″-H), 6.84 (2 H, t, *J* 7.6 Hz, 5- and 5′-H), 6.88 (1 H, dd, *J* 7.6 and 1.2 Hz, 6″-H), 6.97 (2 H, diffuse t, *J* 7.6 Hz, 6- and 6′-H), 7.26* (2 H, d, *J* 2.0 Hz, 2- and 2′-H), 7.27 (2 H, d, *J* 7.6 Hz, 7- and 7′-H), 7.52 (2 H, d, *J* 7.6 Hz, 4- and 4′-H), and 7.68* (2 H, d, *J* 2.0 Hz, NH × 2); δ_C[$(CD_3)_2SO$] 32.5 (d, CH), 35.9 (t, CH_2), 111.2 (d, C-7 and -7′), 114.8 (d, C-3″), 116.2 (d, C-5″), 117.8 (d, C-5 and -5′), 118.7 (s, C-3 and -3′), 119.0 (d, C-4 and -4′), 120.5 (d, C-6 and -6′), 122.2 (s, C-2 and -2′), 124.7 (s, C-1″), 126.0 (d, C-4″), 126.7 (s, C-3a and -3′a), 129.2 (d, C-6″), 136.4 (s, C-7a and -7′a), and 146.2 (s, C-2″); *m/z* 351 (M^+, 2.8%) and 245 ($C_{17}H_{13}N_2^+$, 100).

2,3′-(o-*Aminophenethylidene*)*di-indole* (*the* 2,3′-*Trimer*) (**4**).—A solution of toluene-*p*-sulphonic acid (monohydrate) (1.30 g) in dry benzene (26 ml) was refluxed for 15 min in a Dean-Stark apparatus. After addition of indole (**1**) (2.00 g), the mixed solution was refluxed for 3 h, was made alkaline with aqueous 5% sodium hydrogen carbonate, and extracted with hot chloroform. The chloroform solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure. The residue was dissolved in cold chloroform, and the insoluble material removed by filtration. The chloroform solution was evaporated to dryness under reduced pressure. The residue was chromatographed with benzene. The starting indole (**1**) (0.346 g) was recovered from the benzene eluate. Elution with ethyl acetate then gave a red-brown oil, which was chromatographed with diethyl ether–hexane (1:1, v/v). Preparative t.l.c. with diethyl ether–hexane (2:1, v/v) then gave a crude material, m.p. 108—180 °C.† Repeated recrystallisation from benzene gave colourless *needles* (0.793 g), m.p. 186.5—187.5 °C (Found: C, 81.8; H, 5.95; N, 11.7. $C_{24}H_{21}N_3$ requires C, 82.0; H, 6.0; N, 12.0%); $\nu_{max.}$(KBr) 3 400 and 3 320 cm^{-1}; $\nu_{max.}$($CHCl_3$) 3 475 and 1 293 cm^{-1}; $\lambda_{max.}$ 222.5, 275sh, 283, and 291 nm (log ε 4.88, 4.19, 4.23, and 4.19); for δ_H (100 MHz; $CDCl_3$) see Table 1; δ_H (270 MHz; $CDCl_3$) 3.28* (2 H, br s, NH_2), 3.36 (1 H, dd, *J* 14.0 and 7.4 Hz, C$H_A$$H_B$CH), 3.45 (1 H, dd, *J* 14.0 and 7.4 Hz, $CH_A$$H_B$CH), 4.70 (1 H, t, *J* 7.4 Hz, CH_2CH), 6.43* (1 H, diffuse s, 3-H), 6.59 (1 H, diffuse d, *J* 7.7 Hz, 3″-H), 6.64 (1 H, diffuse t, *J* 7.7 Hz, 5″-H), 6.90 (1 H, diffuse d, *J* 7.7 Hz, 6″-H), 6.97 (1 H, t, *J* 7.9 Hz, ArH), 7.00 (1 H, t, *J* 7.7 Hz, 4″-H), 7.03* (1 H, d, *J* 2.6 Hz, 2′-H), 7.02—7.20 (5 H, m, ArH), 7.30—7.40 (2 H, m, ArH), 7.80* (1 H, br s, NH), and 8.01* (1 H, br s, NH); δ_C ($CDCl_3$ + few drops of CD_3OD) 36.8 (t, CH_2), 37.3 (d, CH), 99.5 (d, C-3), 110.8 (d, C-7 or -7′), 111.5 (d, C-7′ or -7), 116.4 (d, C-3″), 116.5 (s, C-3′), 119.3 (d × 2), 120.0 (d), 120.9 (d), 121.9 (d), 122.7 (d), 122.9 (d), 125.9 (s), 126.6 (s), 127.3 (d), 128.5 (d), 128.7 (s), 130.8 (d, C-6″), 136.1 (s, C-7a or -7′a), 136.8 (s, C-7′a or -7a), 142.3 (s, C-2), and 144.6 (s, C-2″); *m/z* 351 (M^+, 9.6%) and 245 ($C_{17}H_{13}N_2^+$, 100).

3,3′-(o-*Acetamidophenethylidene*)*di-indole* (*the Monoacetyl* 3,3′-*Trimer*) (**6**).—A solution of the 3,3′-trimer (**3**) (0.501 g) in acetic anhydride (1.4 ml) was heated at 108 °C for 3 min, then diluted with a large quantity of water, and the resulting precipitate was separated by filtration. Recrystallisation from ethanol gave colourless prisms (0.515 g), m.p. 209—212 °C (lit.,[6b] 202 °C) (Found: C, 79.35; H, 6.0; N, 10.7. Calc. for $C_{26}H_{23}N_3O$: C, 79.4; H, 5.9; N, 10.7%); $\nu_{max.}$ 3 450, 3 420, 3 350, and 1 680 cm^{-1}; for δ_H [100 MHz; $(CD_3)_2SO$] see Table 2; δ_H [270 MHz; $(CD_3)_2SO$] 1.92 (3 H, s, COMe), 3.48 (2 H, d, *J* 7.6 Hz, CH_2CH), 4.74 (1 H, t, *J* 7.6 Hz, CH_2CH), 6.85 (2 H, diffuse t, *J* 7.5 Hz, 5- and 5′-H), 6.90 (1 H, t, *J* 7.6 Hz, 5″-H), 6.98 (2 H, diffuse t, *J* 7.5 Hz, 6- and 6′-H), 7.02—7.10 (2 H, m, 4″- and 6″-H), 7.16* (2 H, d, *J* 2.1 Hz, 2- and 2′-H), 7.26 (1 H, d, *J* 7.6 Hz, 3″-H), 7.27 (2 H, d, *J* 7.5 Hz, 7- and 7′-H), 7.50 (2 H, d, *J* 7.5 Hz, 4- and 4′-H), 9.11* (1 H, s, NHCO), and 10.70* (2 H, s, NH); δ_H (270 MHz; $CDCl_3$ + few drops of CD_3OD) 1.21 (3 H, s, COMe), 3.52 (2 H, d, *J* 7.1 Hz, CH_2CH), 4.60 (1 H, t, *J* 7.1 Hz, CH_2CH), 6.13 (1 H, br s, NHCO), 6.92—7.00 (2 H, m, ArH), 7.01 (2 H, s, 2-and 2′-H), 7.08—7.19 (4 H, m, ArH), 7.30—7.38 (3 H, m, ArH), 7.42—7.53 (3 H, m, ArH), and 8.59 (2 H, br s, NH); δ_C[$(CD_3)_2SO$] 23.1 (q, Me), 33.7 (d, CH), 36.8 (t, CH_2), 111.3 (d, C-7 and -7′), 117.9 (d, C-5 and -5′), 118.2 (s, C-3 and -3′), 119.0 (d, C-4 and -4′), 120.6 (d, C-6 and -6′), 122.2 (d, C-2 and -2′), 124.9 (d, C-5″), 125.7 (d, C-4″), 126.0 (d, C-3″), 126.5 (s, C-3a and -3a′), 129.9 (d, C-6″), 135.5 (s), 136.2 (s), 136.4 (s, C-7a and -7′a), and 168.3 (s, CO); *m/z* 393 (M^+, 2.4%) and 245 ($C_{17}H_{13}N_2^+$, 100).

2,3′-(o-*Acetamidophenethylidene*)*di-indole* (*the Monoacetyl* 2,3′-*Trimer*) (**7**).—A solution of the 2,3′-trimer (**4**) (0.099 g) in acetic anhydride (0.28 ml) was heated at 100 °C for 3 min, diluted with a large quantity of water, basified with aqueous 10% ammonium hydroxide, and extracted with chloroform. The chloroform solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure. Column chromatography with benzene–ethyl acetate (3:1 v/v) followed by recrystallisation from benzene gave colourless *prisms* (0.078 g), m.p. 168.5—171 °C (Found: C, 79.4; H, 5.9; N, 10.6. $C_{26}H_{23}N_3O$ requires C, 79.4; H, 5.9; N, 10.7%); $\nu_{max.}$ 3 400, 3 350, 3 300, and 1 680 cm^{-1}; for δ_H [100 MHz; $(CD_3)_2SO$] see Table 2; δ_H [270 MHz; $(CD_3)_2SO$] 1.93 (3 H, s, COMe), 3.48 (2 H, d, *J* 7.3 Hz, CH_2CH), 4.69 (1 H, t, *J* 7.3 Hz, CH_2CH), 6.25 (1 H, s, 3′-H), 6.85—7.12 (7 H, m, ArH), 7.15* (1 H, d, *J* 2.1 Hz, 2-H), 7.19—7.42 (4 H, m, ArH), 7.48 (1 H, d, *J* 7.7 Hz, ArH), 9.26* (1 H, br s, NH), 10.82* (1 H, br s, NH), and 10.85* (1 H, br s, NH); δ_H (270 MHz; $CDCl_3$) 1.28 (3 H, s, COMe), 3.46 (1 H, dd, *J* 13.7 and 8.7 Hz, C$H_A$$H_B$CH), 3.54 (1 H, dd, *J* 13.7 and 6.4 Hz, $CH_A$$H_B$CH), 4.47 (1 H, dd, *J* 8.7 and 6.4 Hz, CH_2CH), 5.88* (1 H, br s, NHCO), 6.56* (1 H, br s, 3-H), 6.89* (1 H, d, *J* 2.6 Hz, 2′-H), 6.98 (1 H, t, *J* 7.8 Hz, ArH), 7.05—7.18 (4 H, m, ArH), 7.15—7.23 (2 H, m, ArH), 7.27 (1 H, d, *J* 7.8 Hz, ArH), 7.30 (1 H, d, *J* 7.8 Hz, ArH), 7.40 (1 H, d, *J* 7.8 Hz, ArH), 7.50 (1 H, diffuse d, *J* 7.8 Hz, ArH), 7.57—7.63 (1 H, m, ArH), 7.86* (1 H, br s, NH), and 8.17* (1 H, br s, NH); *m/z* 393 (M^+, 15.3%) and 245 ($C_{17}H_{13}N_2^+$, 100).

1,1′-*Diacetyl*-3,3′-(o-*diacetylaminophenethylidene*)*di-indole* (*the Tetra-acetyl* 3,3′-*Trimer*) (**8**).—A solution of the 3,3′-trimer (**3**) (0.502 g) and anhydrous sodium acetate (0.251 g) in acetic anhydride (2.0 ml) was refluxed for 16 h, poured into a large quantity of water, and extracted with ethyl acetate. The organic layer was washed with water, dried ($MgSO_4$), and evaporated to dryness under reduced pressure. Column chromatography with benzene–ethyl acetate (3:1 v/v) followed by recrystallisation from benzene or ethanol gave colourless needles (0.543 g), m.p. 214.5—218.5 °C (lit.,[7] 210—211 °C) (Found: C, 73.8; H, 5.6; N, 7.8. Calc. for $C_{32}H_{29}N_3O_4$: C, 74.0; H, 5.6; N, 8.1%); $\nu_{max.}$(KBr) 1 708 cm^{-1}; $\nu_{max.}$($CHCl_3$) 1 708 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 2.19 (6 H, s, COMe × 2), 2.53 (6 H, s, COMe × 2),

† Confirmed to be a mixture of two dimorphic forms [m.p. 105—107 °C; $\nu_{max.}$ (KBr) 3 440, 3 395, and 3 315 cm^{-1}; and m.p. 186.5—187.5 °C; $\nu_{max.}$ (KBr) 3 400 and 3 320 cm^{-1}].

3.31 (2 H, d, *J* 7.6 Hz, CH_2CH), 4.85 (1 H, t, *J* 7.6 Hz, CH_2CH), 7.09 (1 H, dd, *J* 7.6 and 1.0 Hz, 3″- or 6″-H), 7.20 (2 H, s, 2- and 2′-H), 7.20 (2 H, dt, *J* 7.7 and 1.1 Hz, 5- and 5′-H), 7.15—7.25 (2 H, m, 5″- and 6″-H, or 3″-and 4″-H), 7.29 (1 H, dt, *J* 7.6 and 2.0 Hz, 4″- or 5″-H), 7.34 (2 H, dt, *J* 7.7 and 1.1 Hz, 6-and 6′-H), 7.44 (2 H, br d, *J* 7.7 Hz, 4- and 4′-H), and 8.42 (2 H, br d, *J* 7.7 Hz, 7- and 7′-H); *m/z* 519 (M^+, 4.2%), 329 ($C_{21}H_{17}N_2O_2^+$, 100), 287 (46.2), and 245 (60.9).

1′-*Acetyl*-2,3′-(o-*diacetylaminophenethylidene*)*di-indole* (*the Triacetyl*-2,3′-*Trimer*) (**9**).—A solution of the 2,3′-trimer (**4**) (0.153 g) and anhydrous sodium acetate (0.077 g) in acetic anhydride (0.6 ml) was refluxed for 16 h, poured into a large quantity of water, basified with saturated aqueous sodium hydrogen carbonate, and extracted with chloroform. The chloroform solution was dried ($MgSO_4$) and evaporated to dryness under reduced pressure. Column chromatography of the residue with benzene–ethyl acetate (10:1 v/v) followed by recrystallisation from methanol–chloroform, gave colourless *prisms* (0.089 g), m.p. 221.5—224 °C (Found: C, 75.2; H, 5.6; N, 8.8. $C_{30}H_{27}N_3O_3$ requires C, 75.45; H, 5.7; N, 8.8%); $\nu_{max.}$ 3 350, 1 715, and 1 680 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 2.13 (3 H, s, COMe), 2.30 (3 H, s, COMe), 2.53 (3 H, s, COMe), 3.30 (1 H, dd, *J* 14.2 and 7.8 Hz, CH_AH_BCH), 3.37 (1 H, dd, *J* 14.2 and 7.8 Hz, CH_AH_BCH), 4.61 (1 H, t, *J* 7.8 Hz, CH_2CH), 6.37* (1 H, diffuse s, 3-H), 6.97 (1 H, dd, *J* 7.8 and 1.4 Hz, ArH), 7.04 (1 H, diffuse t, *J* 7.8 Hz, 5-H), 7.14 (1 H, dt, *J* 7.8 and 1.4 Hz, 5′-H), 7.06—7.20 (4 H, m, ArH), 7.22—7.32 (3 H, m, ArH), 7.32 (1 H, dt, *J* 7.8 and 1.4 Hz, 6′-H), 7.48—7.55 (1 H, m, 4-H), 8.11* (1 H, br s, NH), and 8.41 (1 H, br d, *J* 7.8 Hz, 7′-H); *m/z* 477 (M^+, 22.0%), 287 ($C_{19}H_{15}N_2O^+$, 100), and 245 (74.3).

3-*Formyl*-2,3′-(o-*acetamidophenethylidene*)*di-indole* (*the Acetyl Formyl* 2,3′-*Trimer* (**10**).—Phosphoryl chloride (0.061 ml) was added to *N*,*N*-dimethylformamide (0.5 ml) cooled in ice and the mixture was stirred at room temperature for 30 min. To this cooled solution, a solution of the monoacetyl 2,3′-trimer (**7**) (0.100 g) in *N*,*N*-dimethylformamide (0.5 ml) was added, and the mixture was stirred at room temperature for 19 h, poured into ice–water, and made alkaline with aqueous 10% sodium hydroxide. The resulting mixture was stirred for 1.5 h, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried ($MgSO_4$), and evaporated to dryness under reduced pressure. Column chromatography of the residue with benzene–ethyl acetate (1:1 v/v) gave an oil, which was crystallised by addition of ethanol. The crude mass was washed with benzene and recrystallised from aqueous ethanol to give slightly red *prisms* (0.043 g), m.p. 252—255 °C (Found: C, 76.7; H, 5.55; N, 9.8. $C_{27}H_{23}N_3O_2$ requires C, 76.9; H, 5.5; N, 10.0%); $\nu_{max.}$ 3 370, 3 170, 1 680, and 1 620 cm^{-1}; for δ_H [100 MHz; $(CD_3)_2SO$] see Table 2; δ_H [270 MHz; $(CD_3)_2SO$] 2.04 (3 H, s, COMe), 3.46 (1 H, dd, *J* 14.0 and 9.5 Hz, CH_AH_BCH), 3.68 (1 H, dd, *J* 14.0 and 6.2 Hz, CH_AH_BCH), 5.36 (1 H, dd, *J* 9.5 and 6.2 Hz, CH_2CH), 6.87—6.94 (2 H, m, ArH), 6.97—7.13 (3 H, m, ArH), 7.07—7.14 (1 H, m, 5-H), 7.15 (1 H, dt, *J* 7.2 and 1.5 Hz, 6-H), 7.26 (1 H, d, *J* 7.2 Hz, ArH), 7.33—7.42 (3 H, m, ArH), 7.48* (1 H, d, *J* 1.8 Hz, 2′-H), 7.98 (1 H, dd, *J* 7.2 and 1.5 Hz, 4-H), 9.50* (1 H, s, NH), 10.09 (1 H, s, CHO), 11.07* (1 H, s, NH), and 11.87* (1 H, s, NH); *m/z* 421 (M^+, 10.1%) and 273 ($C_{18}H_{13}N_2O^+$, 100).

o-*Nitrophenylacetaldehyde* (**23**).—(a) o-*Nitrocinnamic acid* (**18**). According to the reported procedure,[11] a suspension of anhydrous sodium acetate (10 g) in acetic anhydride (27.8 ml) containing *o*-nitrobenzaldehyde (**17**) (20.0 g) was heated at 190 °C for 19 h under reflux. After addition of anhydrous sodium acetate (5 g), the mixture was further refluxed for 3 h. Saturated aqueous sodium carbonate [$Na_2CO_3 \cdot 10H_2O$ (40 g)] was added to the cooled mixture, which was refluxed for 1 h and filtered. The filtrate was acidified with concentrated hydrochloric acid. The resulting precipitate was separated and washed with water. Recrystallisation from methanol–chloroform gave pale yellow needles (18.4 g), m.p. 233—244 °C (lit.,[11] 240—241 °C); $\nu_{max.}$ 1 690, 1 515, and 1 340 cm^{-1}.

(b) *Methyl* o-*nitrocinnamate* (**19**). According to the reported procedure,[12] a suspension of *o*-nitrocinnamic acid (**18**) (13.4 g) in anhydrous methanol (178 ml) containing concentrated hydrochloric acid (0.94 ml) was refluxed for 9.5 h and evaporated to dryness under reduced pressure. A large quantity of water was added and the residue was extracted with chloroform. The chloroform solution was washed with aqueous 5% sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated to dryness under reduced pressure. Recrystallisation from methanol gave pale yellow needles (11.9 g), m.p. 72.5—74 °C (lit.,[12] 72 °C); $\nu_{max.}$ 1 700 and 1 325 cm^{-1}.

(c) o-*Nitrocinnamamide* (**20**). According to the reported procedure,[12] aqueous 28% ammonium hydroxide (175 ml) was added to a solution of methyl *o*-nitrocinnamate (6.99 g) (**19**) in ethanol (10.5 ml) at −15 °C. The mixture was heated at 60 °C for 7 h. The resulting precipitate was gathered by filtration. Recrystallization from ethanol gave pale yellow needles (3.51 g), m.p. 187—190 °C (lit.,[12] 185—186 °C; lit.,[13] 182—184 °C); $\nu_{max.}$ 3 475, 3 150, 1 690, and 1 340 cm^{-1}.

Addition of concentrated hydrochloric acid to the filtrate gave *o*-nitrocinnamic acid (2.44 g) as crystals.

(d) *Methyl* o-*nitrostyrylcarbamate* (**21**). According to the reported procedure,[12] an aqueous solution of sodium hypochlorite (0.67 mmol ml^{-1}; 26.4 ml) was added to a solution of *o*-nitrocinnamamide[11,12,13] (**20**) (3.33 g) in methanol (94 ml). The mixture was heated at 85 °C (bath temp.) for 3 min with stirring, then the resulting yellow precipitate was collected by filtration and washed with water. Recrystallisation from methanol gave yellow needles (2.11 g), m.p. 153.5—154.5 °C (lit.,[12,13] 149—150 °C); $\nu_{max.}$ 3 225, 1 700, 1 510, and 1 340 cm^{-1}; δ_H (100 MHz; $CDCl_3$) 3.78 (3 H, s, OMe), 6.55 (1 H, d, *J* 14.0 Hz, CH=C*H*NH), 6.99* (1 H, br s, NH), 7.12—7.64 (4 H, m, ArH and ArC*H*=CH), and 7.88 (1 H, d, *J* 8.0 Hz, 3-H); *m/z* 222 (M^+, 30.0%) and 92 (100).

Methanol was removed from the filtrate by distillation under reduced pressure, and the residue was extracted with chloroform. The extract was dried (K_2CO_3) and evaporated to dryness under reduced pressure. The resulting residue (0.717 g) was combined with the crude material obtained from the mother liquor from recrystallisation of the carbamate (**21**), and chromatographed with benzene–ethyl acetate (20:1, v/v). The first eluate gave more of the desired product (0.300 g); total yield 2.41 g.

(e) *Methyl* β-*methoxy*-o-*nitrophenethylcarbamate* (**22**). The second eluate from the foregoing column chromatography gave colourless *needles* (0.045 g), m.p. 106—115 °C (from ethanol) (Found: C, 51.85; H, 5.6; N, 10.9. $C_{11}H_{14}N_2O_5$ requires C, 52.0; H, 5.55; N, 11.0%); $\nu_{max.}$ 3 325, 1 690, 1 520, and 1 350 cm^{-1}; δ_H (100 MHz; $CDCl_3$) 3.20—3.44 (2 H, m, $CHCH_2$), 3.28 (3 H, s, OMe), 3.56 (3 H, s, OMe), 5.14† (2 H, br s, NH and $CHCH_2$), 7.27—7.64 (3 H, m, ArH), and 7.80—7.96 (1 H, m, 3-H); *m/z* 223 (M^+ − OMe, 15.3%) and 42 (100).

(f) o-*Nitrophenylacetaldehyde* (**23**). According to the reported method,[12] a suspension of finely powdered methyl *o*-nitrostyrylcarbamate (**21**) (0.500 g) in 20% sulphuric acid (10 ml) was refluxed for 1 h, poured into a large quantity of water, and extracted with ether. The ethereal solution was washed with saturated brine, dried ($MgSO_4$), and evaporated to dryness

† On addition of deuterium oxide, the signal changed into a triplet (*J* 3.6 Hz).

under reduced pressure. Column chromatography of the oily residue with benzene gave a brown oil (0.188 g) (lit.,[12] b.p. 134 °C at 5 mmHg); $\nu_{max.}$ (neat) 1 720, 1 520, and 1 345 cm^{-1}; δ_H (100 MHz; $CDCl_3$) 4.12 (2 H, s, CH_2CHO), 7.25—7.75 (3 H, m, ArH), 8.15 (1 H, dd, *J* 8.5 and 2.0 Hz, 3-H), and 9.83 (1 H, s, CH_2CHO).

(g) o-*Nitrophenylacetaldehyde* 2,4-*dinitrophenylhydrazone*. A solution of 2,4-dinitrophenylhydrazine (0.038 g) in aqueous ethanol [water (0.25 ml) and 95% ethanol (0.88 ml)] containing concentrated sulphuric acid (0.19 ml) was added to a solution of *o*-nitrophenylacetaldehyde (**23**) (0.030 g) in a small quantity of 95% ethanol at room temperature with stirring until a precipitate was formed. The precipitate was separated by filtration and purified by column chromatography with chloroform to give red-orange prisms (0.036 g), m.p. 153.5—156 °C (lit.,[14] 150—153 °C) (from ethanol–ethyl acetate) (Found: C, 49.0; H, 3.3; N, 20.2 Calc. for $C_{14}H_{11}N_5O_6$: C, 48.7; H, 3.2; N, 20.3%); $\nu_{max.}$ 3 290, 1 600, and 1 330 cm^{-1}; δ_H (100 MHz; $CDCl_3$) 4.10 (2 H, d, *J* 5.0 Hz, CH_2CH), 7.36—7.80 (4 H, m, ArH), 7.72 (1 H, t, *J* 5.0 Hz, CH_2CH), 8.05 (1 H, dd, *J* 8.0 and 2.0 Hz, 3-H), 8.24 (1 H, dd, *J* 10.0 and 2.7 Hz, 5′-H), 9.02 (1 H, d, *J* 2.7 Hz, 3′-H), and 11.00* (1 H, br s, NH); *m/z* 345 (M^+, 0.8%) and 150 (100).

Condensation of o-*Nitrophenylacetaldehyde* (**23**) *with Indole* (**1**) *in Acetic Acid* [3,3′-(o-*Nitrophenethylidene*)*di-indole* (*the* 3,3′-*Di-indolylmethane*) (**24**)].—A mixed solution of *o*-nitrophenylacetaldehyde (**23**) (0.459 g) and indole (**1**) (0.683 g) in acetic acid (5 ml) was heated at 105 °C for 2 h with stirring and poured into a large quantity of water. The resulting precipitate was separated by filtration. Recrystallisation from benzene gave pale yellow prisms (0.816 g), m.p. 217—218.5 °C (lit.,[10] 208—209 °C) (Found: C, 75.6; H, 4.95; N, 10.6. Calc. for $C_{24}H_{19}N_3O_2$: C, 75.6; H, 5.0; N, 11.0%); $\nu_{max.}$ 3 435, 3 425, 1 520, and 1 350 cm^{-1}; δ_H [270 MHz; $(CD_3)_2SO$] 3.78 (2 H, d, *J* 7.8 Hz, CH_2CH), 4.73 (1 H, t, *J* 7.8 Hz, CH_2CH), 6.84 (2 H, t, *J* 7.6 Hz, 5-and 5′-H), 6.98 (2 H, t, *J* 7.6 Hz, 6- and 6′-H), 7.18 (1 H, br d, *J* 7.6 Hz, 6″-H), 7.20* (2 H, d, *J* 2.1 Hz, 2- and 2′-H), 7.27 (2 H, d, *J* 7.6 Hz, 7- and 7′-H), 7.30 (1 H, dd, *J* 7.6 and 1.6 Hz, 4″-H), 7.36 (1 H, dd, *J* 7.6 and 1.6 Hz, 5″-H), 7.43 (2 H, d, *J* 7.6 Hz, 4- and 4′-H), 7.79 (1 H, dd, *J* 7.6 and 1.6 Hz, 3″-H), and 10.75* (2 H, s, NH × 2); *m/z* 381 (M^+, 2.3%) and 245 ($C_{17}H_{13}N_2^+$, 100).

Condensation of o-*Nitrophenylacetaldehyde* (**23**) *with Indole* (**1**) *in the Presence of Zinc Chloride in Acetic Acid* [2,3′-(o-*Nitrophenethylidene*)*di-indole* (*the* 2,3′-*Di-indolylmethane*) (**25**)].—To a solution of *o*-nitrophenylacetaldehyde (**23**) (0.221 g) and indole (**1**) (0.329 g) in acetic acid (6.3 ml) was added powdered anhydrous zinc chloride (0.055 g). The mixture was heated at 105 °C for 2 h with stirring and poured into a large quantity of water. The aqueous solution was neutralised with aqueous 5% sodium hydrogen carbonate and extracted with ether. The ethereal solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure. The residue was fractionated by column chromatography with diethyl ether–hexane (1:1 v/v) followed by preparative t.l.c. with diethyl ether–hexane (2:3 v/v) to give the following three fractions (in order of elution).

(*a*) Recovered indole (**1**) (0.071 g).

(*b*) The 2,3′-di-indolylmethane (**25**). Preparative t.l.c. with diethyl ether–hexane (1:2 v/v) gave pale brown needles (0.169 g), m.p. 80 °C; $\nu_{max.}$ 3 400, 1 522, and 1 348 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 3.72 (1 H, dd, *J* 13.2 and 8.8 Hz, CH_AH_BCH), 3.92 (1 H, dd, *J* 13.2 and 6.1 Hz, CH_AH_BCH), 4.77 (1 H, dd, *J* 8.8 and 6.1 Hz, CH_2CH), 6.40* (1 H, diffuse s, 3-H), 6.84 (1 H, dd, *J* 7.6 and 1.8 Hz, 6″-H), 6.96* (1 H, d, *J* 2.4 Hz, 2′-H), 6.99 (1 H, diffuse t, *J* 7.3 Hz, 5′- or 6′-H), 7.05 (1 H, diffuse t, *J* 7.3 Hz, 5-H), 7.09 (1 H, dt, *J* 7.3 and 2.1 Hz, 6-H), 7.13—7.25 (2 H, m, 7-H and 6′- or 5′-H), 7.22 (1 H, dt, *J* 7.6 and 1.8 Hz, 5″-H), 7.27 (1 H, dt, *J* 7.6 and 1.8 Hz, 4″-H), 7.36 (1 H, d, *J* 7.3 Hz, 7′- or 4′-H), 7.39 (1 H, d, *J* 7.3, 4′- or 7′-H), 7.53 (1 H, m, 4-H), 7.88 (1 H, dd, *J* 7.6 and 1.8 Hz, 3″-H), 7.92* (1 H, br s, NH), and 8.01* (1 H, br s, NH); *m/z* 381 (M^+, 8.8%) and 245 ($C_{17}H_{13}N_2^+$, 100). All attempts to recrystallise this material failed.

(*c*) The 3,3′-di-indolylmethane (**24**) (0.078 g), m.p. 217—218.5 °C.

Treatment of the 3,3′-*Di-indolylmethane* (**24**) *with Anhydrous Zinc Chloride*.—A mixture of the 3,3′-di-indolylmethane (**24**) (0.101 g) and powdered anhydrous zinc chloride (0.011 g) in acetic acid (1.24 ml) was heated at 105 °C for 8 h with stirring and poured into a large quantity of water. The aqueous solution was neutralised with aqueous 20% sodium hydroxide and extracted with ethyl acetate. The organic layer was washed with aqueous 5% sodium hydrogen carbonate, dried (K_2CO_3), and evaporated to dryness under reduced pressure. Purification by column chromatography with diethyl ether–hexane (1:1, v/v) followed by preparative t.l.c. with diethyl ether–hexane (2:3, v/v) gave the 2,3′-di-indolylmethane (**25**) (0.033 g) and a trace of recovered 3,3′-di-indolylmethane (**24**) (< 0.005 g). The indole (**1**) was not detected by t.l.c. even in the crude material.

Reduction of 3,3′-(o-*Nitrophenethylidene*)*di-indole* (**24**).—A solution of 3,3′-(*o*-nitrophenethylidene)di-indole (**24**) (0.080 g) in methanol (20 ml) was hydrogenated over Raney Nickel (W-7; 0.5 ml wet volume in methanol) at atmospheric pressure and room temperature until absorption of hydrogen ceased. After removal of the catalyst, the solution was evaporated to dryness under reduced pressure. Column chromatography with diethyl ether–hexane (1:1, v/v) gave colourless needles (0.041 g), m.p. 171—172 °C, which were recrystallised from benzene–cyclohexane. This material was identical with a sample of the 3,3′-trimer (**3**) prepared by treatment of indole (**1**) with 0.5M hydrochloric acid.

Reduction of 2,3′-(o-*Nitrophenethylidene*)*di-indole* (**25**).—A solution of 2,3′-(*o*-nitrophenethylidene)di-indole (0.127 g) (**25**) in methanol (20 ml) was hydrogenated over Raney Nickel (W-7; 0.6 ml wet volume in methanol) at atmospheric pressure and room temperature until absorption of hydrogen ceased. After removal of the catalyst, the solution was evaporated to dryness under reduced pressure. Column chromatography with chloroform gave colourless needles (0.053 g), m.p. 183—185 °C, which were recrystallised from benzene. This material was identical with a sample of the 2,3′-trimer (**4**) prepared by treatment of indole (**1**) with anhydrous zinc chloride in acetic acid.

Treatment of the 3,3′-*Trimer* (**3**) *under Various Acid Conditions*.—(a) *With toluene*-p-*sulphonic acid in benzene*. A solution of toluene-*p*-sulphonic acid (monohydrate) (0.326 g) in anhydrous benzene (6.5 ml) was refluxed for 15 min in a Dean-Stark apparatus. After addition of the 3,3′-trimer (**3**) (0.500 g), the mixed solution was refluxed for 8 h, then added to a large quantity of water and extracted with chloroform. The chloroform solution was washed with aqueous 5% sodium hydrogen carbonate, dried (K_2CO_3), and evaporated to dryness under reduced pressure. Column chromatography of the residue with diethyl ether–hexane (1:1, v/v) gave three fractions. Preparative t.l.c. with diethyl ether–hexane (2:1, v/v) gave indole (**1**) (0.098 g), the 2,3′-trimer (**4**) (0.115 g), and recovered 3,3′trimer (**3**) (0.017 g).

(b) *With boron trifluoride–ether complex*. A solution of the 3,3′-trimer (**3**) (0.309 g) in boron trifluoride–ether (3.0 ml) was kept at room temperature for 5 days, then added to a large quantity of water, made alkaline with aqueous 5% sodium hydrogen carbonate, and extracted with chloroform. The

chloroform solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure. Column chromatography with diethyl ether–hexane (1:2 to 2:1, v/v) gave four fractions. Preparative t.l.c. with diethyl ether–hexane (2:1, v/v) gave indole (**1**) (0.015 g), the dimer (**2**) (0.083 g), the 2,3′-trimer (**4**) (0.105 g), and recovered 3,3′-trimer (**3**) (0.030 g).

(c) *With anhydrous zinc chloride in acetic acid at* 105 °C. A solution of the 3,3′-trimer (**3**) (0.305 g) and freshly fused zinc chloride (0.405 g) in acetic acid (6 ml) was heated at 105 °C for 4 h, then added to a large quantity of water, made alkaline with aqueous 10% sodium hydroxide, and extracted with chloroform. The chloroform solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure. Column chromatography with diethyl ether–hexane (1:2 to 1:1, v/v) gave four fractions. Preparative t.l.c. with diethyl ether–hexane (2:1, v/v) gave indole (**1**) (0.014 g), the dimer (**2**) (0.019 g), the 2,3′-trimer (**4**) (0.094 g), and recovered 3,3′-trimer (**3**) (0.047 g).

(d) *With anhydrous zinc chloride in acetic acid at room temperature.* The 3,3′-trimer (**3**) (0.030 g) was added to a solution (1.0 ml) of anhydrous zinc chloride in acetic acid (0.013 g ml^{-1}). The mixture was kept at room temperature for 21 h, poured into a large quantity of water, made alkaline with aqueous 10% sodium hydroxide, and extracted with chloroform. The chloroform solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure to give recovered 3,3′-trimer (**3**) (0.027 g).

Treatment of Indole (**1**) *under Various Acid Conditions.*—(a) *Bubbling hydrogen chloride gas in benzene solution.*—According to the reported method,[15] dry hydrogen chloride gas was bubbled into a solution of indole (**1**) (3.00 g) in dry benzene (60 ml) at room temperature for 1.2 h. The resulting precipitate was isolated by filtration and suspended in water (*ca.* 100 ml). After addition of aqueous 10% ammonium hydroxide, the suspension was extracted with diethyl ether. The organic layer was dried (K_2CO_3) and evaporated to dryness to give colourless prisms (2.97 g), m.p. 108—112 °C. Recrystallisation of a portion of this material from benzene gave colourless prisms of the dimer (**2**), m.p. 111.5—113.5 °C (lit.,[6a] 107 °C) (Found: C, 81.9; H, 6.0; N, 11.8. Calc. for $C_{16}H_{14}N_2$: C, 82.0; H, 6.0; N, 12.0%); $\nu_{max.}$ 3 425 and 3 370 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 3.21 (1 H, dd, *J* 15.5 and 8.7 Hz, CH_AH_BCH), 3.48 (1 H, dd, *J* 15.5 and 8.7 Hz, CH_AH_BCH), 4.12* (1 H, br s, NH), 5.26 (1 H, t, *J* 8.7 Hz, CH_2CH), 6.67 (1 H, d, *J* 7.7 Hz, 7′-H), 6.74 (1 H, diffuse t, *J* 7.7 Hz, 5′-H), 7.07 (1 H, t, *J* 7.7 Hz, 6′-H), 7.08 (1 H, diffuse t, *J* 7.6 Hz, 5-H), 7.14 (1 H, d, *J* 7.7 Hz, 4′-H), 7.16* (1 H, d, *J* 2.6 Hz, 2-H), 7.20 (1 H, diffuse t, *J* 7.6 Hz, 6-H), 7.37 (1 H, d, *J* 7.6 Hz, 7-H), 7.59 (1 H, d, *J* 7.6 Hz, 4-H), and 7.98* (1 H, br s, NH); *m/z* 234 (M^+, 87.2%) and 233 (100).

(b) *With* 1M *hydrobromic acid.* According to the reported procedure,[6a] a suspension of finely powdered indole (**1**) (2.00 g) in 1M hydrobromic acid (200 ml) was stirred at room temperature for 1.5 h. The mixture was made alkaline with aqueous 20% sodium hydroxide. The precipitate was collected by filtration and dissolved in a small quantity of hot methanol. The solution was added dropwise to a large quantity of aqueous 5% sodium hydroxide with stirring and extracted with diethyl ether. The ethereal solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure. Column chromatography with diethyl ether–hexane (1:1 v/v) gave recovered indole (**1**) (0.546 g), the dimer (**2**) (0.375 g), and the 3,3′-trimer (**3**) (0.885 g).

(c) *With trifluoroacetic acid in diethyl ether.* According to the reported procedure,[16] trifluoroacetic acid (0.195 ml) was added to a solution of indole (**1**) (0.602 g) in diethyl ether (4.1 ml). The solution was stirred at room temperature for 48 h, methanol (0.5 ml) was added, and the resulting mixture was kept at room temperature for 15 min and evaporated to dryness under reduced pressure. A large quantity of water was added to the residue, and the mixture was made alkaline with aqueous 5% sodium hydrogen carbonate and extracted with diethyl ether. The ethereal solution was washed with aqueous 5% sodium hydrogen carbonate, dried (K_2CO_3), and evaporated to dryness under reduced pressure. Column chromatography with diethyl ether–hexane 2:3, v/v) gave recovered indole (**1**) (0.055 g), the dimer (**2**) (0.074 g), and the 3,3′-trimer (**3**) (0.412 g).

(d) *With boron trifluoride–ether complex.* A solution of indole (**1**) (0.510 g) in boron trifluoride–ether (5.0 ml) was kept at room temperature for 48 h, then added to a large quantity of water, made alkaline with aqueous 5% sodium hydrogen carbonate, and extracted with chloroform. The chloroform solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure. Column chromatography with diethyl ether–hexane (1:4 to 2:1, v/v) gave recovered indole (**1**) (0.012 g), the dimer (**2**) (0.119 g), and the 2,3′-trimer (**4**) (0.136 g).

(e) *With anhydrous zinc chloride in acetic acid at* 50 °C. Indole (**1**) (0.103 g) was added to a solution (3.4 ml) of anhydrous zinc chloride (0.066 g) in acetic acid (5.0 ml). The mixture was stirred at 50 °C for 8.5 h, poured into a large quantity of ice–water, made alkaline with aqueous 10% sodium hydroxide, and extracted with chloroform. The chloroform solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure. Preparative t.l.c. of the residue with diethyl ether–hexane (3:1, v/v) gave recovered indole (**1**) (0.051 g), the dimer (**2**) (0.007 g), and the 3,3′-trimer (**3**) (0.036 g).

(f) *With anhydrous zinc chloride in acetic acid at* 105 °C. A solution of indole (**1**) (0.301 g) and freshly prepared anhydrous zinc chloride (0.391 g) in acetic acid (6 ml) was heated at 105 °C for 4 h. The mixture was added to a large quantity of water, made alkaline with aqueous 10% sodium hydroxide, and extracted with chloroform. The chloroform solution was dried (K_2CO_3) and evaporated to dryness under reduced pressure. Column chromatography with diethyl ether–hexane (1:2 to 2:1, v/v) gave four fractions. Preparative t.l.c. with diethyl ether–hexane (2:1, v/v) gave recovered indole (**1**) (0.014 g), the dimer (**2**) (0.020 g), the 2,3′-trimer (**4**) (0.104 g), and the 3,3′-trimer (**3**) (0.051 g).

Acknowledgements

We thank Professor W. E. Noland, University of Minnesota, for his gift of the 3,3′-trimer and information about it, and Professors Hino and M. Nakagawa, Chiba University, for discussions.

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Received 19*th October* 1987; *Paper* 7/1860