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Substitution, Oxidation and Addition Reactions at C-7 of Activated Indoles

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Abstract: 4,6-Dimethoxy-2,3-diphenylindole (1) undergoes acylation, bromination, oxidative coupling and acid-catalysed addition to aldehydes at C-7 to produce a range of 7-substituted indoles (3-11), the indolo-isatin (6), the 7,7'-bi-indolyls (14), (16), (18), and the 7,7'-di-indolylmethanes (20-31). Addition to cyclopentanone gave compound (32), while Michael addition to α,β-unsaturated ketones gave compound (33) and the non-benzenoid double adduct (34). Related reactions led to the formation of the ring-fused indoles (39) and (41). Some reactions of the related indole diester (2) are also reported.

Introduction

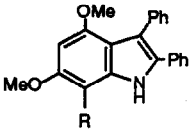
Indoles normally undergo electrophilic substitution and addition reactions at C-3, and if that position is substituted reaction is directed to C-2. We specifically wished to achieve such reactions at C-7, and consequently have investigated the behaviour of several 4,6-dimethoxy substituted indoles. It has already been shown[1,2] that 4,6-dimethoxyindole itself undergoes reaction at C-7 as well as at C-3, as a consequence of the methoxy group activation. Furthermore, we have reported the formylation of the indoles (1) and (2) at C-7, as we required these products for the construction of ligand systems[2,3]. We now record the results of other substitution and addition reactions, carried out for a range of other purposes. Much of the chemistry of the 7-position has been explored using 4,6-dimethoxy-2,3-diphenylindole (1). This indole has its active 2- and 3-positions blocked with phenyl groups leaving the 7-position as the only active site. A variety of reactions can be exclusively undertaken at the 7-position and these include formylation (already recorded) [2,3], acylation, halogenation, oxidative dimerisation and the acid-catalysed addition of aldehydes and α,β-unsaturated ketones [4,5].

Results and Discussion

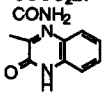
Acylation reactions.

The acetylation and cinnamoylation of the 2,3-diphenyl indole (1) has recently been reported by us [6]. Trifluoroacetic anhydride reacts with the indole (1) in tetrahydrofuran to give a quantitative yield of the trifluoroacetyl derivative (3). This product can usefully be transformed into the 7-carboxylic acid (4), by treatment with base. Acylation can also be effected by oxalyl chloride to give the chloro-oxalyl derivative (5) as the product of mono-substitution. Compound (5) can be quenched with alcohols and amines to give glyoxylic esters and amides respectively. More interestingly, compound (5) undergoes cyclisation on treatment with pyridine to give the isatin derivative (6), as a bright red solid. The infrared spectrum of this compound shows carbonyl stretching frequencies at 1780 and 1730cm^{-1}, indicating a high degree of reactivity. The isatin (6)

consequently reacts readily with alcohols and amines (as exemplified here by methanol, ethanol and ammonia) to give the above glyoxylic esters and amides (7-9). Furthermore, 1,2-diaminobenzene reacts to give the quinoxalinone (10).

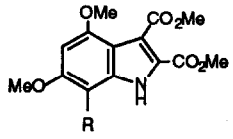


	R
(1)	H
(3)	$COCF_3$
(4)	CO_2H
(5)	COCOCl
(7)	$COCO_2Me$
(8)	$COCO_2Et$
(9)	$CONH_2$

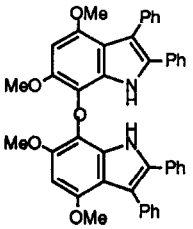


(11) (32)	Br

(33)	
(35)	CH_2CH_2COMe
(37)	CHO
(38)	$CH{=}CHCO_2Et$
(40)	$CH{=}CHCOMe$



	R
(2)	H
(12)	Br
(13)	I



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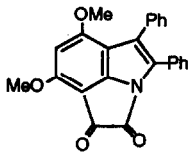
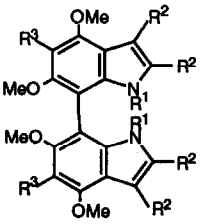


(6)



	R^1	R^2	R^3
(14)	H	Ph	H
(15)	H	CO_2Me	H
(16)	H	Ph	Cl
(18)	Me	Ph	H
(19)	H	4-MeOPh	H

Halogenation

The bromination of the indole (1) to give the 7-bromo compound (11) has already been reported [7]. Similarly, the related 7- bromo-indole (12) can be obtained in high yield. The less reactive indole (2) can indeed be iodinated at C-7 with iodine monochloride in 45% yield, together with the 7,7'-bi-indolyl (15) in 55% yield. This latter compound can be compared with the 7,7'-dimer (14), obtained in a similar reaction from the diphenyl indole (1), from which the 7-iodo compound could not be isolated [7,8]. Attempted chlorination of the indole (1) resulted not only in chlorination at C-5, but also oxidative dimerisation at C-7 to give compound (16), the only example in which C-5 substitution has been observed so far.

Oxidative dimerisation

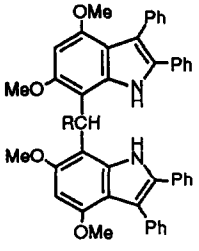
The more general route to 7,7'-bi-indolyls involves the direct oxidation of the indole (1) [8]. Oxidising agents include quinone, chloranil and dichlorodicyanoquinone, which give yields of 100%, 70% and 60% respectively. A small amount of the ether (17) can also be isolated from the chloranil oxidation. The oxidative dimerisation cannot be achieved from the indole (2), nor from the N-methyl analog of indole (1), although the dimer (14) can be readily methylated to give the analog (18). The methoxyphenyl-substituted dimer (19) has also been obtained from the appropriate indole.

The 7,7'-linkage between two indoles has only been reported in few cases. The oxidation of 4-hydroxyindole leads to traces of a compound with this linkage [9]. Two reported alkaloids also have this linkage

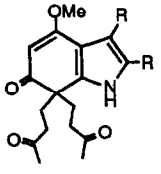
but are yet to be synthesised [10,11]. The parent 7,7'-bi-indolyl has been synthesised in 41% yield by diborane reduction of the corresponding bis-isatin [12].

Addition to aldehydes and ketones

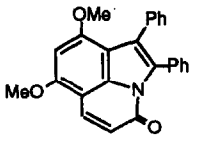
7,7'-Di-indolylmethanes (20-31) have been prepared from the indole (1) and the appropriate aldehydes in yields of 70-100%. The acidic conditions varied from glacial acetic acid in the case of methanal, to hydrochloric acid in either methanol or tetrahydrofuran. The reaction is clearly general and fails only in cases such as propanal, where self condensation of the aldehyde occurs prior to reaction with the indole.



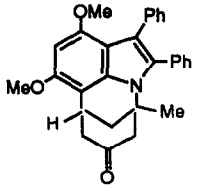
R	
(20)	H
(21)	Me
(22)	n-Pr
(23)	i-Pr
(24)	CH_2Ph
(25)	Ph
(26)	3,4,5-$(MeO)_3$Ph
(27)	2-ClPh
(28)	2-NO_2Ph
(29)	3-NO_2Ph
(30)	4-NO_2Ph
(31)	2-Py



R	
(34)	Ph
(36)	CO_2H



(39)



(41)

Ketones on the other hand proved to be generally unreactive. Acetone, acetophenone and cyclohexanone gave no reaction even after extended periods of reflux. However, the more reactive cyclopentanone reacted with indole (1) to produce the cyclopentene product 32 in 40% yield. This reaction shows that it is possible that the initial addition of indole (1) to a carbonyl compound is reversible and requires a further step such as the elimination of water seen in this example, or attack by a second equivalent of indole, in order to complete an irreversible process.

The above reaction was extended to include an α,β–unsaturated ketone, with combination of indole (1) with cyclohexenone in the presence of acid. This resulted, via a Michael addition, in the formation of the cyclohexanone 33 in 60% yield. In view of this success methyl vinyl ketone (MVK) was reacted with indole (1) in the presence of acid. Unexpectedly, it was found that the indole was alkylated twice at its 7-position with the loss of a methoxy methyl group from the 6-position to give compound (34) in 80% yield. This reaction has now been standardized so that at 0 °C and using only one equivalent of MVK the monoalkylated product (35) can be isolated in 95% yield after chromatography. If this intermediate product is reacted with another equivalent of MVK in the presence of acid, compound (34) can be obtained in 90% yield.

The structure of compound (34) was elucidated by the following spectroscopic data. The mass spectrum indicated a molecular ion at m/z 455 and together with the elemental microanalysis confirmed the molecular composition. This corresponded to the addition of two equivalents of MVK to indole (1) with loss of a methyl

group. The ^1H n.m.r. ($CDCl_3$) spectrum indicated a singlet resonance at 2.07 ppm which integrated for two methyl substituents and four sets of multiplets between 2.1 and 2.5 ppm which corresponded to four CH_2 groups. Furthermore, there was only one signal at 3.83 ppm corresponding to one methoxy group. The ^{13}C n.m.r. ($CDCl_3$) spectrum indicated two ketone resonances at 208.76 and 183.34 ppm, one $\underline{C}$-OCH_3 at 171.32 ppm, only one OCH_3 at 56.26 ppm and an aliphatic quaternary carbon at 45.53 ppm. If product (35) is reacted with acid without MVK present a bright orange compound is formed. Further addition of MVK then gives the dialkylated product (34). The bright orange compound, possibly the chloride salt of an intermediate oxonium cation, could arise from cyclization onto the methoxy group at the 6-position. This could then be followed by loss of the methyl group and subsequent attack of the indole onto another equivalent of MVK to afford the dialkylated product (34).

For comparison, MVK was also reacted in the presence of acid with the indole diester (2). The reaction took 3 days to go to completion and gave product (36) as a white solid in 80% yield. In this case the ester groups on the indole were also hydrolized to carboxyl groups.

It was proposed to synthesize unsaturated compounds related to the MVK addition product (35) by the aldol condensation of the 7-formylindole (37) with suitable activated methylene carbonyl compounds. Initial attempts were directed towards the formation of α,β-unsaturated esters. Thus indole (37) was refluxed in ethyl acetate with sodium ethoxide resulting in the formation of the desired product (38), with the constituent chain at the 7-position, in 10% yield and the cyclic product (39) in 60% yield [13]. This second product was produced from the initial aldol intermediate by cyclization on to the nitrogen atom with loss of ethanol followed by loss of water. This reaction has been shown by other workers in our group to be quite general for the synthesis of pyrroloquinolin-4-ones [13]. It is now reported here that the 2,3-diphenyl-7-formyl indole (37) can undergo the same aldol condensation with ethyl acetate and sodium ethoxide at room temperature to produce compound (38) quantitatively. Furthermore, compound (38) can be cyclized to product (39), by reaction with ethyl acetate and sodium ethoxide at reflux, in 95% yield.

The corresponding reaction of 7-formylindole (37) with acetone and sodium ethoxide gave two products after 3 hours reflux. These were the expected condensation product (40) in 30% yield and an unexpected product (41) in 60% yield. If this reaction is carried out at 0 °C the 7-substituted condensation product (40) can be isolated quantitatively. Further, if product (40) is reacted at reflux in acetone with sodium ethoxide, compound (41) can be isolated after chromatography in 85% yield.

The structure of compound (41) was elucidated by the following spectroscopic data. The mass spectrum clearly indicated a molecular ion at m/z 437 and together with the elemental microanalysis confirmed the molecular composition. This corresponded to the addition of a further equivalent of acetone to compound (40) with loss of water. The infra red spectrum shows no resonances corresponding to a typical indole NH stretching frequency. The ^{13}C n.m.r. spectrum indicated a ketone resonance at 210 ppm, three CH_2 groups at 55, 47 and 38 ppm, an aliphatic CH at 28 ppm, an aliphatic quaternary carbon at 60 ppm, and only one aliphatic CH_3 found at 28.5 ppm. These data obviously indicated a product in which cyclisation had occurred onto the nitrogen atom. The ^1H n.m.r. spectrum also shows distinct splitting patterns from 2-4 ppm., which were elucidated by the aid of a ^1H-^1H COSY and a ^{13}C-^1H correlation experiment. The proton pairs H6a and H6b, and H9a and H9b each show geminal coupling, and also vicinal coupling to H5. H8a and H8b show geminal coupling: H8b also shows long range coupling to H6b and H9b. Compound (40) clearly undergoes further attack from acetone under the basic conditions followed by a ring closure. Subsequent dehydration to a cyclohexenone and Michael addition of the

nitrogen atom under extended basic conditions results in formation of compound (41). The replacement of acetophenone for acetone did not lead to any noticeable reaction.

Compound (40) can be independently synthesised by an acid-catalysed addition of indole (1) to the dimethylacetal of acetyl acetaldehyde.

Experimental

General information : Melting points are uncorrected. Microanalyses were performed by Dr. H. P. Pham of the University of New South Wales. ^{1}H n.m.r. spectra were obtained in the designated solvents on a Bruker CXP 300 (300 MHz), a Bruker AC300F (300 MHz) or a Bruker AM 500 (500 MHz) spectrometer. ^{13}C n.m.r. were obtained in the designated solvents on a Bruker AC300F (300 MHz) or a Bruker AM 500 (500 MHz) spectrometer. Ultraviolet spectra were measured on a Hitachi U-3200 spectrometer and refer to solutions in absolute methanol. Infrared spectra were recorded on a Perkin-Elmer 298 or a Perkin-Elmer 580B spectrometer and refer to paraffin mulls. The E.I. Mass Spectra were recorded on an AEI MS 12 mass spectrometer at 70eV ionising potential and 8000 V accelerating voltage with an ion source temperature of 210°C. FAB spectra were recorded on an AutoSpecQ mass spectrometer. Flash column chromatography was carried out using Merck silica gel 7736 60H, whilst preparative thin layer chromatography was performed on 3 mm plates using Merck silica gel 7730 60GF$_{254}$.

7-Trifluoroacetyl-4,6 dimethoxy-2,3-diphenylindole (3)

Trifluoroacetic anhydride (0.87ml, 0.61mmol) was added to an ice-cold solution of indole (1) in dry tetrahydrofuran (20ml). After stirring for 8h, addition of water gave the product (3) (2.62g,100%) as a bright yellow solid, m.p.164-166 °C (from ethanol). (Found: C, 66.5; H, 3.7; N, 3.2. $C_{24}H_{18}NO_3F_3$ requires C, 66.7; H, 4.2; N, 3.3%). υ_{max} 3419, 1647, 1633, 1598,1550, 1330, 1286, 1251, 1228, 1198, 1148, 1063cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 3.83 and 4.01, s, OCH_3; 6.17, s, H5; 7.23-7.39, m, ArH; 10.73, bs, NH. *m/z* 426 (M+1, 28%), 425 (M, 100), 356 (49), 99 (15), 85 (40), 71 (58), 57 (87).

4,6-Dimethoxy-2,3-diphenylindole-7-carboxylic acid (4)

The trifluoroacetyl compound (3) (2.5g, 6.0mmol) was heated under reflux with potassium hydroxide (1.5g) in aqueous ethanol (50ml, 1:1) for 10 min. After cooling, acification with 10% hydrochloric acid gave the acid (4) (2.2g, 100%), m.p. 190-192 °C. (Found: C, 73.6; H, 4.8; N, 3.5. $C_{23}H_{19}NO_4$ requires C, 74.0; H, 5.1; N, 3.7%). υ_{max} 3340, 1627, 1605, 1592, 1561, 1517, 1502, 1310, 1291, 1269, 1228, 1196cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 3.80 and 4.15, s, OCH_3; 6.3, s, H5; 7.10-7.40, m, ArH; 10.64, bs, NH; 10.89, bs OH. *m/z* 373 (M, 80%), 355 (100), 340 (20), 330 (95), 314 (40), 297 (14).

1,2-Dihydro-6,8-dimethoxy-4,5-diphenylpyrrolo[3.2.1-hi]indole-1,2-dione (6)

Oxalyl chloride (3.0g, 24mmol) was added to the indole (1) (0.32g, 1mmol) in dry benzene (50ml) and the mixture was stirred at room temperature for 45 min. The solution was concentrated to a yellow solid (crude compound (5)), which on further stirring in benzene and pyridine for 24h gave a red solution. This was extracted with chloroform, the extract washed with dilute acid, water and then dried (Na_2SO_4) to give the isatin (6) (0.29g, 84%) as a red solid, m.p. 250-253 °C. υ_{max} 1780, 1730, 1640, 1600cm^{-1}. ^{1}H n.m.r.($CDCl_3$) δ 3.91 and 4.34, s, OCH_3; 7.30-7.50, m, ArH. *m/z* 383 (M, 4%), 356 (40), 355 (100), 340 (15).

Methyl (4,6-dimethoxy-2,3-diphenylindol-7-yl)-glyoxylate (7)

The isatin (6) (0.08g, 0.2mmol) was heated in dry tetrahydrofuran/methanol for 5h. The solution was concentrated to a yellow oil, which was chromatographed (chloroform) to give the ester (7) (0.01g,13%), m.p.

185-188 °C. (Found: C, 72.1; H, 4.9; N, 3.2. $C_{25}H_{21}NO_5$ requires C, 72.3; H, 5.1; N, 3.4%). υ_{max} 3390, 1740, 1690, 1575cm^{-1}. *m/z* 415 (M, 20%), 387 (67), 356 (40), 355 (67), 149 (100).

Ethyl (4,6-dimethoxy-2,3-diphenylindol-7-yl)-glyoxylate (8)

The isatin (6) (0.2g, 0.6mmol) was heated in ethanol for 3h. The solution was concentrated to a yellow solid, which was chromatographed (chloroform/light petroleum) to give the ethyl ester (8) (0.19g,78%) as a yellow solid, m.p. 178-181 °C. (Found: C, 72.5; H, 5.2; N, 3.4. $C_{26}H_{23}NO_5$ requires C, 72.7; H, 5.4; N, 3.3%). υ_{max} 3420, 1735, 1720cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 1.83, t, C-CH_3; 4.23 and 4.37, s, OCH_3; 4.83, q, CH_2; 6.55, s, H5; 7.60-7.79, m, ArH; 11.04, s, NH. *m/z* 429 (M, 50%), 357 (29), 356 (93), 86 (100).

4,6-Dimethoxy-2,3-diphenylindole-7-glyoxylamide (9)

The isatin (6) (0.12g, 0.34mmol) was heated for 2h in dichloromethane containing 15M ammonia. The solution was washed with water, the organic layer dried (Na_2SO_4) and concentrated to give the amide (9) (0.13g, 94%), m.p. 199-202 °C. υ_{max} 3420, 3180, 1685, 1675, 1610cm^{-1}. ^{1}H n.m.r. [$(CD_3)_2SO$ / $CDCl_3$] δ 3.71 and 3.87, s, OCH_3; 6.14, s, H%; 6.50, bs, NH_2; 7.10-7.53, m, ArH; 10.56, s, NH. *m/z* 400 (M, 9%), 356 (15), 189 (100).

2- Hydroxy-3(4,6-dimethoxy-2,3-diphenylindol-7-yl)quinoxaline (10)

The indole (1) (0.18g, 0.5mmol) was stirred with oxalyl chloride (3.0g, 0.025mmol) in dry benzene (40ml) at room temperature for 30 min. The solution was concentrated under reduced pressure to give the acid chloride (5). This was dissolved in dichloromethane and treated with dry pyridine (0.07g, 0.9mmol) and 1,2-diaminobenzene (0.06g, 0.51mmol), then heated for 1.5h. The yellow solution was washed , dried (Na_2SO_4) and concentrated to an orange solid, which was chromatographed (chloroform / light petroleum) to give the quinoxaline (10) (0.09g, 40%), m.p. >305 °C, which could not be obtained analytically pure. (Found: C, 73.8; H, 5.0; N, 7.6. $C_{30}H_{23}N_3O_3.H_2O$ requires C, 73.3; H, 5.1; N, 8.6%). υ_{max} 3660-3560, 3460-3380, 1655, 1600cm^{-1}. ^{1}H n.m.r. [$(CD_3)_2SO$ / $CDCl_3$] δ 3.71 and 3.81, s, OCH_3; 6.32, s, H5; 7.09-7.80, m, ArH; 10.44, s, amide NH; 12.19, s, indole NH. *m/z* 473 (M, 100%), 356 (33), 355 (83), 329 (50).

Dimethyl 7-bromo-4,6-dimethoxyindole-2,3-dicarboxylate (12)

Indole (2) (3.0g, 10.2mmol) in tetrahydrofuran (80ml) was stirred with phenyltrimethylammonium tribromide (3.85g, 10.2mmol) for 30 min. The mixture was filtered and the filtrate concentrated to a solid, which on flash chromatography (dichloromethane) gave the bromo compound (12)(3.0g, 78%) as a pale cream powder. m.p 171-172 °C. (Found: C, 45.1; H, 3.7; N, 3.6. $C_{14}H_{14}BrNO_6$ requires C, 45.2; H, 3.8; N, 3.8%). υ_{max} 3473, 1739, 1713, 1646, 1279cm^{-1}. λ_{max} 324nm (ε 10300), 304 (13800), 243 (20200). ^{1}H n.m.r. ($CDCl_3$) δ 3.90 and 3.91, s, ether CH_3; 3.95 and 3.96, s, ester CH_3; 6.30, s, H5; 8.84, bs, NH. ^{13}C n.m.r. ($CDCl_3$) 52.43 and 52.67, ester CH_3; 55.95 and 57.20, ether CH_3; 83.79, C7; 90.45, C5; 111.68 and 115.35, C3a and C7a; 122.66, C3; 135.91, C2; 154.18 and 155.67, C4 and C6; 160.51 and 166.24, CO. *m/z* 373 (M(^{81}Br), 42%), 371 (M(^{79}Br), 42), 342 (27), 341 (100), 340 (28), 339 (100), 326 (27), 324 (25), 298 (22), 296 (23).

Dimethyl 7-iodo-4,6-dimethoxyindole-2,3-dicarboxylate (13) and tetramethyl 7,7'-bi(4,6-dimethoxyindolyl) 2,2',3,3'-tetracarboxylate) (15)

Dimethyl 4,6-dimethoxyindole-2,3-dicarboxylate (2) (1.00g, 3.41mmol) was dissolved in a mixture of dry tetrahydrofuran (40ml) and glacial acetic acid (40ml) in a 250ml conical flask wrapped in aluminium foil to exclude light. To this solution iodine monochloride (0.72g, 4.43mmol) was added. The mixture was left to stir in the dark at room temperature for 18h. After this time water (150ml) was added and the solution brought to neutral by the addition of 2M sodium hydroxide. The tetrahydrofuran was removed under reduced pressure and

the residue was extracted with dichloromethane. The organic layer was collected, dried ($MgSO_4$) and the solvent removed under reduced pressure. Thin layer chromatography (dichloromethane) gave iodo compound (13) (0.44g, 31%) as a white powder and dimer (15) (0.67g 34%) also as a white powder.

Iodo compound (13): m.p. 176-178 °C, (Found: C, 40.3; H, 3.3; N, 3.2. $C_{14}H_{14}INO_6$ requires C, 40.1; H, 3.4; N, 3.3%). υ_{max} 3449, 1734, 1717, 1629, 1559, 1275, 1248, 1217cm^{-1}. λ_{max} 328nm (sh) (ε 5650), 306 (8050), 247 (17200). ^1H n.m.r. ($CDCl_3$) δ 3.91, 3.92, 3.94 and 3.96, s, OCH_3; 6.28, s, H5; 8.73, bs, NH. ^{13}C n.m.r .($CDCl_3$) δ 52.36 and 52.61, ester CH_3; 55.09, C7; 55.86 and 57.18, ether CH_3; 89.83, C5; 111.15 and 115.60, C3a and C7a; 122.10 and 138.70, C2 and C3; 155.42 and 158.42, C4 and C6;160.48, C3CO; 166.40, C2CO. *m/z* 420 (M+1, 14%), 419 (M, 75), 368 (29), 367 (100), 352 (25).

Dimer (15): m.p. 190-192 °C. υ_{max} 3306, 1739, 1715, 1636, 1286cm^{-1}. λ_{max} 304nm (ε 23600), 246 (47700). ^1H n.m.r. ($CDCl_3$) δ 3.90, 3.91, 3.95 and 3.96, s, OCH_3; 6.30, s, H5; 8.94, bs, NH. ^{13}C n.m.r. [$(CD_3)_2SO$] δ 52.42 and 52.52, ester CH_3; 56.44 and 57.35, ether CH_3; 91.24, C5; 95.75, C7; 111.38 and 115.38, C7a and C3a; 123.85, C2; 135.14, C3; 152.99 and 154.37, C4 and C6; 160.39, C3CO; 165.93, C2CO. *m/z* 584 (M, 6%), 292 (40),291 (100), 252 (22).

7,7'-Bi(4,6-dimethoxy-2,3-diphenyl)indolyl (14)

Indole (1) (0.5g, 1.52mmol) was dissolved in tetrahydrofuran(40ml) containing hydrochloric acid (4ml) and 1,4-benzoquinone (0.16g). After vigorous stirring for 3h, water was added and the product obtained by extraction with dichloromethane as a white solid (0.5g, 100%), m.p. 290-294 °C (from dichloromethane / petroleum ether). (Found: C, 80.7; H, 5.3; N, 4.3. $C_{44}H_{36}N_2O_4$ requires C, 80.5; H, 5.5; N, 4.3%). λ_{max} 316nm (ε 35000). υ_{max} 3433, 1603, 1332, 1205, 701 cm^{-1}. ^1H n.m.r. ($CDCl_3$): δ 3.80 and 3.84, s, OCH_3; 6.49, s H5; 7.20-7.45, m, ArH; 8.01, s, NH. *m/z* 657 (M+1, 52), 656 (100), 610 (32), 575 (23), 328 (53), 127 (41), 113 (76).

Yields of 70% and 60% were obtained using chloranil and dichlorodicyanoquinone respectively. Use of chloranil gave in addition the ether (17).

7,7'-Di(4,6-dimethoxy-2,3-diphenylindolyl)ether (17)

This was obtained as a yellow solid (0.05g, 10%), m.p. 262-263 °C (from dichloromethane / petroleum ether) . λmax 251nm (ε 9000), 323 (5300). υ_{max} 3412, 1601, 1546, 1345, 1207, 701 cm^{-1}. ^1H n.m.r. ($CDCl_3$): δ 3.76, 3.79, 3.82 and 3.91, s, OCH_3; 6.43 and 6.50, s, H5; 7.12-7.48, m, ArH; 7.96 and 7.98, s, NH. *m/z* 673 (M+1, 30), 672 (M, 63), 656 (23), 250 (50), 248 (100), 246 (80).

7,7'-Bi(4,6-dimethoxy-1-methyl-2,3-diphenylindolyl) (18)

The dimer (14) was methylated using methyl iodide and potassium hydroxide in dimethylsulfoxide. Compound (18) (87%) could not be obtained analytically pure. m.p. >300 °C. *m/z* 684 (M, 100%).

7,7'-Bi(5-chloro-4,6-dimethoxy-2,3-diphenylindolyl) (16)

Indole (1) (0.5g, 1.52mmol) was added to a stirred suspension of anhydrous cupric chloride (0.6g, 4.5mmol) in acetonitrile (20ml). After stirring overnight at room temperature, the solvent was evaporated and the residue chromatographed in dichloromethane to give the biindolyl (160 as a white powder (0.33g, 60%), m.p. 303-305 °C. ^1H n.m.r. ($CDCl_3$): δ 3.29 and 3.66, s, OCH_3; 7.21-7.51, m, ArH; 8.34, bs, NH. *m/z* 726 (M ($^{37,35}Cl$), 66%), 724 (M (^{35}Cl),100).

General method for reaction of indole (1) with aldehydes.

Indole (1) (0.5g, 1.52mmol) was reacted with the aldehyde (0.75mmol) in tetrahydrofuran (40ml) containing concentrated hydrochloric acid (4ml). After 3 h of vigorous stirring, water was added to precipitate

the product, which was collected and recrystallised. Reaction with methanal was carried out in glacial acetic acid and with benzaldehyde in methanol, and in each case the product precipitated out directly.

Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)methane (20)

(0.51g, 100%), m.p. 293-295 °C (from dichloromethane / petroleum ether). (Found: C, 80.4; H, 5.6; N, 4.0. $C_{45}H_{38}N_2O_4$ requires C, 80.6; H, 5.7; N, 4.2%). λ_{max} 261nm (ε 10000), 315 (6200). υ_{max} 3348, 1604, 1353, 1162, 1125, 1004, 755, 698cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 3.65 and 4.12, s, OCH_3; 4.39, s, CH_2; 6.32, s, H5; 7.21-7.37, m, ArH; 10.15, s, NH. *m/z* 671.(M+1, 37%), 670 (M, 75), 343 (37), 342 (87), 329 (100).

1,1-Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)ethane (21)

(9.42g, 80%), m.p. 175-177 °C (from dichloromethane / petroleum ether). (Found: C, 80.5; H, 5.7; N, 4.0. $C_{46}H_{40}N_2O_4$ requires C, 80.7; H, 5.9; N, 4.1%). λ_{max} 263nm (ε 9800), 323 (4400). υ_{max} 3304, 1604, 1506, 1201, 1160, 1133, 699cm^{-1}. ^{1}H n.m.r.($CDCl_3$) δ 2.05, d, *J* 7.5 Hz, CH_3 ; 3.65 and 4.12, s, OCH_3; 5.30, q, *J* 7.5 Hz, CH; 6.33, s, H5; 7.22-7.37, m, ArH; 10.22, bs, NH. ^{13}C n.m.r. ($CDCl_3$) δ 58.25 and 55.56, OCH_3; 28.49, CH; 18.49, CH_3. *m/z* 685 (M+1, 35%), 684 (M, 67), 357 (28), 356 (100), 355 (83), 340(24), 329 (48).

1,1-Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)butane (22)

(0.38g, 70%), m.p. 168-169 °C (from dichloromethane / petroleum ether). (Found: C, 81.1; H, 6.2; N, 3.8. $C_{48}H_{44}N_2O_4$ requires C, 80.9; H, 6.2; N, 3.9%). λ_{max} 263nm (ε 55100), 316 (32300). υ_{max} 3347, 3330, 1604, 1294, 1157, 1133, 998, 700cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 1.06, t, CH_3; 1.45, m, CH_2; 2.52, m, CH_2; 3.66 and 4.12, s, OCH_3; 5.51, t, CH; 6.33, s, H5; 7.21-7.38, m, ArH; 9.95, bs, NH; 10.52, bs, NH. *m/z* 383 (100), 329 (90), 384 (35), 368 (25), 314 (38).

1,1-Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)-2-methylpropane (23)

(0.38g, 70%), m.p. 188-189 °C (from dichloromethane / petroleum ether). (Found: C, 78.0; H, 6.0; N, 3.6. $C_{48}H_{44}N_2O_4.1.5\ H_2O$ requires C, 77.9; H, 6.4; N, 3.8%). λ_{max} 263nm (ε 34600), 316 (19800). υ_{max} 3317, 1603, 1507,1159, 1131, 998, 700cm^{-1}. ^{1}H n.m.r .($CDCl_3$) δ 0.87 and 1.14, d, CH_3; 3.37, m, H2; 3.65 and 4.11, bs, OCH_3; 4.60, bd, H1; 6.30, s, H5'; 7.21-7.36, m, ArH; 9.95 and 10.54, bs, NH. *m/z* 713 (M+1, 25%), 712 (M, 40), 672 (62), 671 (100), 384 (25), 383 (61).

1,1-Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)-2-phenylethane (24)

(0.40g, 70%), m.p. 222-223 °C (from dichloromethane / petroleum ether). (Found: C, 82.4; H, 5.6; N, 3.6. $C_{52}H_{44}N_2O_4$ requires C, 80.1; H,5.8; N, 3.7%). λ_{max} 247nm (ε 56200), 328(34700). υ_{max} 3460, 1604, 1588,1262, 1113, 698cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 2.69, bs, H2; 3.74 and 3.96, s, OCH_3; 5.23, bt, H1; 6.33, s, H5'; 7.21-7.46, m, ArH; 9.85 and 10.11, s, NH. *m/z* 760 (M, 1%), 431 (100), 408 (32), 329 (60), 314 (44), 120 (80), 105 (60).

1,1-Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)phenylmethane (25)

(0.57g, 100%), m.p. 270-271 °C (from dichloromethane / petroleum ether). (Found: C, 81.9; H, 5.5; N, 3.6. $C_{51}H_{42}N_2O_4$ requires C, 82.0; H, 5.7; N, 3.8%). λ_{max} 261nm (ε 6500), 315 (4000). υ_{max} 3375, 3302, 3058, 1624, 1604, 1125, 995, 785, 699cm^{-1}. ^{1}H n.m.r.($CDCl_3$) δ 3.70 and 3.80, s, OCH_3; 6.60, s, H5; 6.82, s, CH; 7.21-7.45, m, ArH. *m/z* 747 (M+1, 3%), 746 (M, 7), 419 (100), 414 (90), 329 (44).

(3,4,5,-Trimethoxyphenyl)-di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)methane (26)

(0.57g, 90%), m.p. 160-161 °C (from dichloromethane / petroleum ether). (Found: C, 77.5; H, 6.2; N, 3.0. $C_{54}H_{48}N_2O_7$ requires C, 77.5; H, 5.8; N, 3.3%). λ_{max} 260nm (ε 57600), 316 (31300). υ_{max} 3329,

1604, 1509, 1330, 1156, 1131, 1000, 700cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 3.65, 3.67 and 3.81, s, each 6H, OCH_3; 3.87, s, 3H, OCH_3; 6.30, s, H5; 6.45, s, ArH; 6.66, s, CH. *m/z* 837 (M+1, 30%), 836 (M, 60), 509 (45), 508 (100), 477 (35), 476 (90), 418 (40), 329 (35).

(2-Chlorophenyl)-di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)methane (27)

(0.53g, 90%), m.p. 230-234 °C (from dichloromethane / petroleum ether). (Found: C, 78.2; H, 5.1; N, 3.3. $C_{51}H_{41}ClN_2O_4$ requires C, 78.4; H, 5.3; N, 3.6%). λ_{max} 260nm (ε 32100), 318 (18800). υ_{max} 3388, 3308, 1605, 1160, 1149, 998, 756, 701cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 3.66 and 3.70, s, OCH_3; 6.29, s, H5; 6.67, s, CH; 7.16-7.43, m, ArH; 9.78, bs, NH. *m/z* 744 (60%), 743 (100), 697 (10), 682 (18).

Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)(2-nitrophenyl)methane (28)

(0.60g, 100%), m.p. 282-284 °C (from chloroform / ethanol). (Found: C, 77.6; H, 5.2; N, 5.2. $C_{51}H_{41}N_3O_6$ requires C, 77.4; H, 5.2; N, 5.3%). λ_{max} 260nm (ε 22000), 313 (14000). υ_{max} 3384, 3299, 1605, 1359, 1156, 1127, 999, 701, 701cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 3.66 and 3.82, s, OCH_3; 6.25, bs, H5; 6.67, s, CH; 7.16-7.78, m, ArH; 9.82, bs, NH. *m/z* 792 (M+1, 55%), 791 (M, 100), 742 (42), 740(78), 739 (50), 462 (30).

Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)(3-nitrophenyl)methane (29)

(0.60g, 100%), m.p. 188-190 °C (from chloroform / ethanol). (Found: C, 77.1; H, 4.9; N, 5.1. $C_{51}H_{41}N_3O_6$ requires C, 77.4; H, 5.2; N, 5.3%). λ_{max} 261nm (ε 45600), 314 (25600). υ_{max} 3388, 3291, 1604, 1528, 1355, 1120, 996, 701cm^{-1}. ^{1}H n.m.r.($CDCl_3$) δ 3.69 and 3.79, s, OCH_3; 6.32, s, H5; 6.72, s, CH; 7.17-8.21, m, ArH; 9.95, bs, NH. *m/z* 792 (M+1, 40%), 791 (M, 75), 477 (22), 462 (80), 392 (100), 316 (38).

Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)(4-nitrophenyl)methane (30)

(0.60g, 100%), m.p. 180-181 °C (from chloroform / ethanol). (Found: C, 77.7; H, 5.3; N, 5.3. $C_{51}H_{41}N_3O_6$ requires C, 77.4; H, 5.2; N, 5.3%). λ_{max} 263nm (ε 43500), 310 (28000). υ_{max} 3390, 3307, 1604, 1520, 1347, 1155, 997, 759, 701cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 3.70 and 3.81, s, OCH_3; 6.34, s, H5; 6.74, s, CH; 7.19-8.18, m, ArH; 9.98, bs, NH. *m/z* 792 (M+1, 55%), 791 (M, 100), 462 (66), 328 (43).

Di-(4,6-dimethoxy-2,3-diphenylindol-7-yl)(2-pyridyl)methane (31)

(0.43g, 75%), m.p. 218-220 °C (from dichloromethane / petroleum ether). (Found: C, 80.3; H, 5.5; N, 5.4. $C_{50}H_{41}N_3O_4$ requires C, 80.3; H, 5.5; N, 5.6%). λ_{max} 261nm (ε 47900), 315 (28000). υ_{max} 3366, 3282, 1603, 1294, 1158, 1119, 996, 701cm^{-1}. ^{1}H n.m.r.($CDCl_3$) δ 3.66 and 3.78, s, OCH_3; 6.31, s, H5; 6.80, s, CH; 7.16-7.36, m, ArH; 9.93, bs, NH. *m/z* 748 (M+1, 18%), 747 (M, 32), 716 (62), 715 (44), 420 (62), 419 (47), 389 (31), 357 (43), 329 (100).

1-(4,6-Dimethoxy-2,3-diphenylindol-7-yl)cyclopentene (32)

This was prepared as above in tetrahydrofuran with a 6 h reaction time. (0.24g, 40%), m.p.199-200 °C (from dichloromethane /petroleum ether). (Found: C, 81.9; H,6.2; N, 3.8. $C_{29}H_{23}NO_2$ requires C, 82.0; H 6.4; N, 3.5%). λ_{max} 322nm (ε 16400). υ_{max} 3458, 1605, 1262, 1135, 998, 702cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 2.06, m, CH_2; 2.61 and 2.85, bt, CH_2; 3.71 and 3.89, s, OCH_3; 6.31, s, H5; 7.24-7.40, m, ArH and CH 8.30, s, NH. *m/z* 396 (M+1, 31%), 395 (M, 100), 370 (25), 352 (13).

3-(4,6-Dimethoxy-2,3-diphenylindol-7-yl)cyclohexanone (33)

This was prepared as above with 2-cyclohexenone in tetrahydrofuran with a 6 h reaction time. (0.39g, 60%), m.p. 285-288 °C (from dichloromethane). (Found: C, 79.2; H, 6.2; N, 3.1. $C_{28}H_{27}NO_3$ requires C, 79.0; H, 6.4; N, 3.3%). λ_{max} 247nm (ε 25000), 323 (13500). υ_{max} 3375, 1706, 1605, 1344, 1126, 994,

741, 703cm^{-1}. ^{1}H n.m.r. [$(CD_3)_2SO$] δ 1.73-3.23, m, CH_2; 3.61 and 3.84, s, OCH_3; 3.71, m, CH; 6.39, s, H5; 7.18-7.27, m, ArH; 10.87, s, NH. *m/z* 426 (M+1, 38%), 425 (M, 100), 410 (19), 382 (15), 355 (16).

1-(4,6-Dimethoxy-2,3-diphenylindol-7-yl)butan-3-one (35)

Indole (1) (0.5g, 1.52mmol) was added to a stirred and ice cooled solution of methyl vinyl ketone (0.11g, 1.52mmol) in dry tetrahydrofuran (40ml) and concentrated hydrochloric acid (4ml). After 3h of stirring water was added to the solution and the product separated with dichloromethane and concentrated. The product was then column chromatographed (dichloromethane) to give the butanone as a white solid (0.49g, 80%), mp 147-148 °C (from dichloromethane / petroleum ether). (Found: C, 78.6; H, 6.3; N, 3.4. $C_{26}H_{25}NO_3$ requires C, 78.2; H, 6.3; N, 3.5%). λ_{max} 248nm (ε 31250), 326(18100). ν_{max} 3407, 1702, 1605, 1334, 1232, 1122, 794, 702 cm^{-1}. ^{1}H n.m.r. ($CDCl_3$): δ 2.14 , s, CH_3; 2.89 and 3.09, t, *J* 6.0Hz, CH_2; 3.66 and 3.89, s, OCH_3; 6.27, s, H5'; 7.18-7.45, m, ArH; 9.38, bs, NH. ^{13}C n.m.r. ($CDCl_3$) δ 17.57 and 44.20, CH_2; 30.20, CH_3; 55.68 and 56.93, OCH_3; 89.70, C5'; 125.61, 126.60, 127.30, 127.86, 128.45 and 131.45, ArCH; 104.75, 113.52, 114.65, 133.01, 133.20, 136.41 and 137.31, ArC; 153.50 and 153.77, C-OCH_3; 210.92, C=O. *m/z* 401(M+2, 26%), 400(M+1, 31), 399(M, 100), 327(39), 375(10), 342(9), 312(15).

6,7-Dihydro-7,7-di(3-oxobut-1-yl)-2,3-diphenyl-4-methoxyindol-6(H)-one (34)

Indole (1) (0.5g, 1.52mmol) was added to a stirred and ice cooled solution of methyl vinyl ketone (0.22g, 3.04mmol) in dry tetrahydrofuran (40ml) and concentrated hydrochloric acid (4ml). After 3h of stirring water was added to the solution and the product separated with dichloromethane and concentrated. The product was then column chromatographed (chloroform/methanol (95:5)) to give the product as a white solid (0.55g, 80%), mp 230-231 °C (from dichloromethane / petroleum ether). (Found: C, 76.7; H, 6.7; N, 3.0. $C_{29}H_{29}NO_4$ requires C, 76.5; H, 6.4; N, 3.1). λ_{max} 229nm (ε 50600), 275(38300), 325(11100). ν_{max} 3257, 1721, 1704, 1645, 1619, 1237, 1181, 1009, 841, 697 cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 2.07 s, CH_3; 2.15 - 2.48, m, CH_2; 3.83, s, OCH_3; 5.74, s, H5; 7.23-7.45, m, ArH; 9.69, s, NH. ^{13}C n.m.r. ($CDCl_3$) δ 30.22, CH_3; 32.48 and 38.56, CH_2; 45.53, C; 56.26, OCH_3; 106.02, C5; 126.47, 126.93, 127.64, 127.83, 128.27 and 130.91, ArCH; 119.20, 119.37, 131.19, 132.06, 134.25 and 141.27, ArC; 171.32, C-OCH_3; 183.34, C6; 208.76, C=O. *m/z* 457(M+2, 3%), 456(M+1, 13), 455(M, 41), 385(69), 384(100), 329(69), 328(47), 314(31).

6,7-Dihydro-7,7-di(3-oxobut-1-yl)-4-methoxy-6-oxo-indole-2,3-dicarboxylic acid (36)

Indole (2) (0.5g, 1.3mmol) was added to a stirred and ice cooled solution of methyl vinyl ketone (0.22g, 3.04mmol) in dry tetrahydrofuran (40ml) and concentrated hydrochloric acid (4ml). After three days of stirring water was added to the solution and the product separated as a white solid (0.53g, 80%), mp 187-188 °C (from dichloromethane). (Found: C, 57.0; H, 5.1; N, 3.4. $C_{19}H_{21}NO_8.H_2O$ requires C, 57.0; H, 5.5; N, 3.5%). λ_{max} 252nm (ε 14700), 281(10800), 314(9400). ν_{max} 3190, 1735, 1720, 1704, 1379, 1244, 1209, 1001, 781, 761 cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 1.76-2.58, m, CH_2; 1.92, s, CH_3; 3.91, s, OCH_3; 6.06, s, H5; 9.95, s, NH, 13.56, s, CO_2H. *m/z* 392(M+1, 12%), 391(100), 346(19), 320(30), 250(86), 243(30).

Reaction of 7-formyl indole (37) with ethylacetate

A solution of sodium ethoxide (5ml) in ethylacetate (4ml) was added dropwise with stirring to a solution of 7-formyl-indole (37) (0.5g, 1.40mmol) in ethylacetate (40ml) under reflux. After 3h the solution was allowed to cool, diluted with water (100ml) and acidified with 10% hydrochloric acid. The ethylacetate was then evaporated off, the crude mixture filtered and the solid separated by radial chromatography using dichloromethane as the eluent. This gave two products, product (38) as a bright yellow powder and product (39) as a white solid.

Ethyl 3-(4,6-dimethoxy-2,3-diphenylindol-7-yl)propenoic acid (38)

(0.06g, 10%), m.p. 240-243 °C (from dichloromethane / petroleum ether). (Found: C, 75.8; H, 6.1. N, 3.2. $C_{27}H_{25}NO_4$ requires C, 75.9; H, 5.9; N, 3.3%). ^{1}H n.m.r. ($CDCl_3$) δ 1.36, t, CH_3; 3.76 and 3.98, s, OCH_3; 4.28, q, CH_2; 6.28, s, H5; 6.56, d, 1H, alkenyl; 7.24-7.38, m, ArH; 8.20, d, alkenyl; 8.60, s, NH. *m/z* 428(M+1, 25%), 427(M, 100), 382(20), 339(20).

7,9-Dimethoxy-1,2-diphenyl-4-oxo-4H-pyrrolo[3,2,1-i,j]quinoline (39)

(0.32g, 60%), m.p. 246-248 °C, (lit[13] m.p. 246-247 °C) (from dichloromethane / petroleum ether). (Found: C, 79.0; H, 4.7; N, 3.8. $C_{25}H_{19}NO_3$ requires C, 78.7; H, 5.0; N, 3.7%). λ_{max} 254nm(ε 10800), 366(13100). ν_{max} 1678, 1608, 1245, 814, 701 cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 3.84 and 4.03, s, OCH_3; 6.40, s, H7; 6.40, d, alkenyl; 7.21-7.35, m, ArH; 7.99, d, alkenyl. *m/z* 382(M+1, 38%), 381(M, 100), 380(39), 366(28).

Reaction of 7-formyl indole (37) and acetone.

A solution of sodium ethoxide (5ml) in acetone (4ml) was added dropwise with stirring to a solution of 7-formyl-indole (37) (0.5g, 1.40mmol) in acetone (40ml) under reflux. After 3h the solution was allowed to cool, diluted with water (100ml) and acidified with 10% hydrochloric acid. The acetone was then evaporated off, the crude mixture filtered and the solid separated by column chromatography using dichloromethane as the eluent. This gave product (40) as a bright yellow powder and product (41) as a white solid.

1-(4,6-Dimethoxy-2,3-diphenylindol-7-yl)but-1-en-3-one (40)

(0.17g, 30%), m.p. 255 °C. (Found: C, 78.9; H, 5.7; N, 3.5. $C_{26}H_{23}NO_3$ requires C, 78.6; H, 5.8; N, 3.5%). λ_{max} 246nm(ε 38950), 335(29550). ν_{max} 3397, 1631, 1581, 1557, 1428, 1366, 1322, 1241, 1164, 1111, 982, 698 cm^{-1}. ^{1}H n.m.r. ($CDCl_3$) δ 2.38, s, CH_3; 3.72 and 3.97, s, OCH_3; 6.46, s, H5'; 7.08, d, alkenyl; 7.21-7.31, m, ArH; 8.12, d,alkenyl; 11.49, s, NH. *m/z* 398(M+1, 22%), 397(M, 81), 383(25), 382(100), 380(39), 366(23).

1-Methyl-4',6'-dimethoxy-2',3'-diphenylindolo[4,3,2-h,i]-azabicyclo [3.3.1.]nonan-7-one (41)

(0.38g, 60%), m.p. 242-244 °C. (Found: C, 79.7; H, 6.3; N, 3.3. $C_{29}H_{27}NO_3$ requires C, 79.6; H, 6.2; N, 3.2%). λ_{max} 227nm(ε 19400), 298(6900). ν_{max} 3410, 1717, 1608, 1518, 1207, 1107, 703 cm^{-1}. ^{1}H n.m.r.[$(CD_3)_2SO$] δ 2.22-2.26, m, H6b and H9b; 2.46, dd, H6a; 2.63, m, H8b; 2.80, d, H8a; 2.86, dd, H9a; 3.65, s, OCH_3; 3.73, m, H5; 3.85, s, OCH_3; 6.38, s, H5'; 7.01-7.43, m, ArH. ^{13}C n.m.r. [$(CD_3)_2SO$] d 27.87, aliphatic CH; 28.17, CH_3; 40.09, 47.13 and 55.12, CH_2; 55.56 and 56.76, OCH_3; 59.92, aliphatic C; 89.79, H5'; 125.33, 126.78, 128.02, 128.15, 128.49, 131.17, 131.99 and 132.32, ArCH; 104.71, 109.17, 115.73, 134.29, 134.41, 134.73 and 135.45, ArC; 150.91 and 152.66, C-OCH_3; 209.29, C=O. *m/z* 438(M+1, 30%), 437(M, 100), 422(25), 380(20).

Reaction of indole (1) with acetylaldehyde dimethylacetal

To a mixture of indole (1) (0.996g, 3.03 mmol) in acetylacetaldehyde dimethyl acetal (10 mL) was added hydrochloric acid (32%, 2.0 ml) dropwise and the mixture stirred for 1 h at room temperature. Water (100 mL) was added to precipitate the indole (40) (0.70g, 58%), identical with the authentic compound described above.

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