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Reactivity of 3-Substituted Indolin-2-ones in Vilsmeier-type Reactions of 4,6-Dimethoxyindoles

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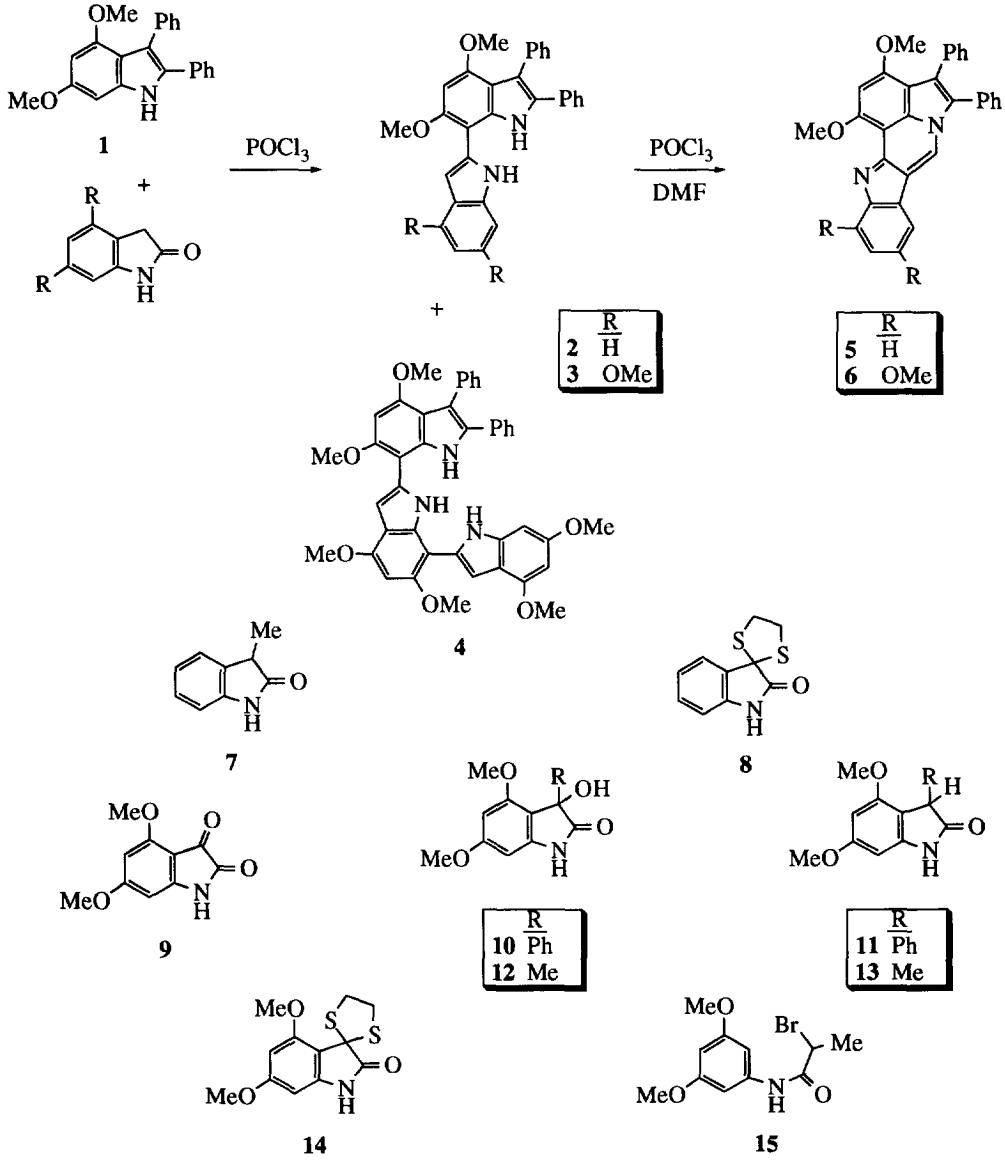
***Abstract*:** 4,6-Dimethoxy-2,3-diphenylindole **1** undergoes reaction with the 3-substituted indolin-2-ones **7,8,11-14** and either phosphoryl chloride or triflic anhydride to give the 2,7'-biindolyl **16**, the 7,7';2,7'-terindolyls **19**, **20** and the 7,7'-biindolyl **23**. Copyright © 1996 Elsevier Science Ltd

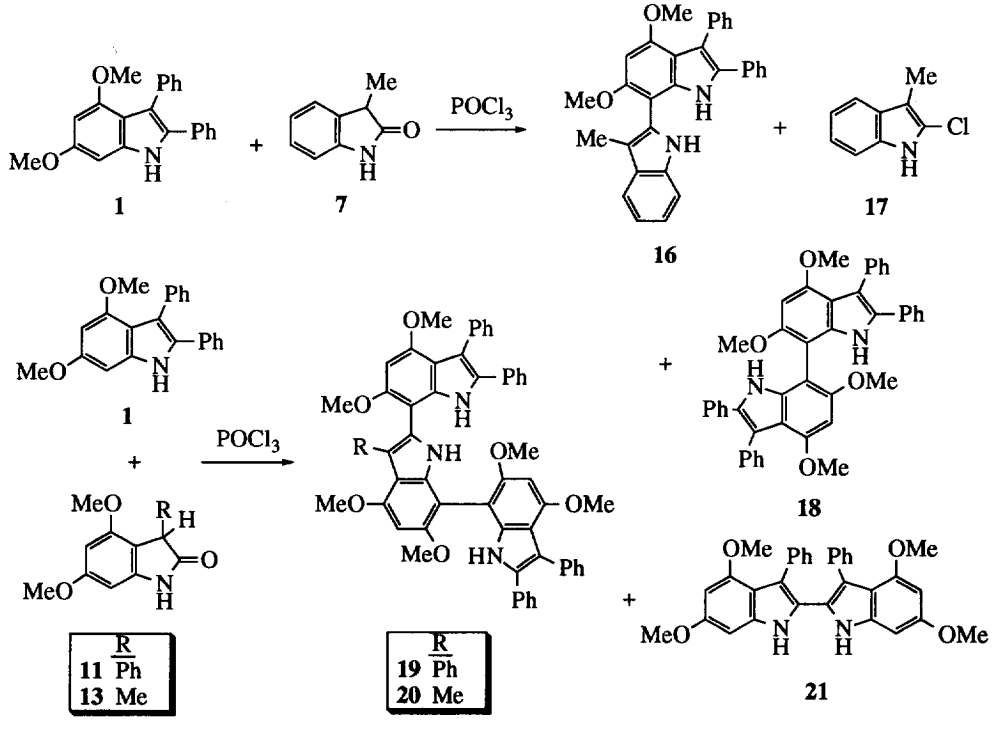
Indolin-2-one and 4,6-dimethoxyindolin-2-one have been shown to undergo reaction with phosphoryl chloride and a range of indoles to yield the related 2-substituted indoles.[1,2] In some cases, further reaction occurred at the unsubstituted 3-position of the 2-indolyl substituent to give terindolyl products. For example, 4,6-dimethoxy-2,3-diphenylindole **1** underwent reaction with indolin-2-one and 4,6-dimethoxyindolin-2-one in the presence of phosphoryl chloride to yield the 2,7'-biindolyls **2** and **3** respectively. Some of the terindolyl **4** was also formed in the latter reaction. In an attempt to control the regioselectivity of reaction of the 2,7'-biindolyl **3**, formylation of it was investigated. Reactions involving one equivalent of phosphoryl chloride in dimethylformamide at 0 °C led to complex mixtures. The use of excess phosphoryl chloride gave better results, but extensive chromatography was still required for product isolation. The use of trifluoromethanesulfonic (triflic) anhydride instead of phosphoryl chloride gave similar results. Formylation at C7 could not be achieved because of preferential reaction at C3, leading ultimately to the fully unsaturated product **6**, after the processes of cyclisation and dehydration had occurred. Similar behaviour was observed with the 2,7'-biindolyl **2**, which afforded the related product **5**. Both bright orange-yellow compounds **5** and **6** were relatively insoluble and difficult to purify, and satisfactory analytical data could not be obtained. However, their structures were established by spectroscopic data. In particular, there were neither carbonyl nor NH stretching frequencies in the infrared spectra, nor were there appropriate aldehyde or NH resonances in the ^{1}H n.m.r. spectra. Mass spectroscopic data were consistent with the proposed structures. In order to overcome the general problem of substitution at C3, the reactivity of 3-substituted indolin-2-ones in the modified Vilsmeier reaction was investigated. The choice of 3-substituted indolin-2-ones was based on several premises. 3-Methylindolin-2-one **7** [3] and the related dithiolan **8** [4] represent model compounds, which would respectively allow the C3 substituent to remain or be removed subsequently by treatment with Raney nickel.[5] In view of the need to continue to functionalise the initial products at C7, 4,6-dimethoxy activation was also desired. Consequently the previously unknown indolin-2-ones **11**, **13** and **14** were prepared from 4,6-dimethoxyisatin **9**, which in turn was derived from 3,5-dimethoxyaniline hydrochloride and oxalyl chloride.[6,7] 4,6-Dimethoxyisatin **9** was reacted initially with phenyl lithium in tetrahydrofuran to produce the

dioxindole **10**, which was reduced by stannous chloride in acetic acid to produce the 3-phenylindolin-2-one **11**. Similarly, isatin **9** was reacted with methylmagnesium chloride to produce the dioxindole **12**, which was converted to the 3-methylindolin-2-one **13**. Furthermore, isatin **9** was reacted with ethane-1,2-dithiol and boron trifluoride etherate in acetic acid to produce the spiro compound **14**. In an alternative approach, the 2-bromoanilide **15**, prepared from 4,6-dimethoxyaniline and 2-bromopropanoyl chloride, could not be cyclised to give the indolin-2-one **13**.



Initially it was found that the reaction between 4,6-dimethoxy-2,3-diphenylindole **1** and 3-methylindolin-2-one **7** with phosphoryl chloride produced the 2,7'-biindolyl **16** in 71% yield, together with a trace of 2-chloro-3-methylindole **17**. The fact that the latter compound **17** was detected shows that it is somewhat reluctant to undergo further reaction, because of the presence of the 3-methyl group. Under similar conditions the spiro-indolin-2-one **8** proved to be unreactive and after 12 hours reflux, the only observed product was the 7,7'-biindolyl **18**. This compound clearly arises from the oxidative dimerisation of the indole **1**, and has been observed in trace amounts in similar previous reactions. It has been synthesised quantitatively by the oxidative dimerisation of indole **1** using either a variety of quinones or iodine monochloride.[8,9]

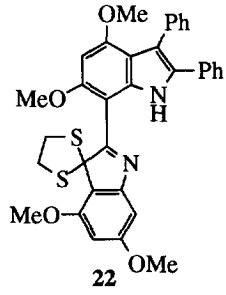
Indolin-2-ones **11** and **13** were each reacted with indole **1** and phosphoryl chloride and predominantly formed the 7,7'; 2,7'-terindolyl compounds **19** (45%) and **20** (38%) respectively. Clearly the indolin-2-ones **11** and **13** underwent initial reaction with indole **1** to produce the desired 2,7'-bi-indolyl system, which then combined with a further equivalent of indole **1**. Once again in each reaction the formation of small amounts of the 7,7'-biindolyl **18** was observed. Although it could be seen from ^{1}H n.m.r. spectra of partially purified reaction mixtures that traces of quater- and poly-indolyl systems were also produced, the only other product that could be isolated was the 2,2'-bi-indolyl **21** in a 5% yield from the reaction of indolin-2-one **11**. The isolation of this 2,2'-biindolyl **21** would seem to indicate that the intermediate 2-chloroindole resulting from the reaction of indolin-2-one **11** and phosphoryl chloride undergoes a coupling reaction of some type.



Therefore, this would substantiate the hypothesis that the phosphoryl chloride in these reactions could chlorinate indole **1** at C7 to give a product which then could undergo a similar kind of coupling. Furthermore, terindolyls **19** and **20** could then be obtained by the same type of reaction. Replacement of phosphoryl chloride with triflic anhydride led to cleaner reactions and higher yields of the terindolyls **19** and **20** (60% and 50% respectively). Again, small amounts of the 7,7'-biindolyl **18** were observed.

In contrast to the spiro-indolin-2-one **8**, the dimethoxy analog **14** did react with indole **1** and phosphoryl chloride, demonstrating the activating influence of those groups. However, the product was not the expected 2,7'-biindolyl **22**, but a 7,7'-biindolyl type of compound, which was shown to have the unusual structure **23**. A trace of the 7,7'-biindolyl **18** was also observed in this reaction.

The structure of compound **23** was elucidated from ^{1}H and ^{13}C n.m.r. spectroscopic data. The ^{1}H n.m.r. spectrum showed two distinct signals near 10.3 ppm corresponding to two NH resonances which both disappeared during a D_2O exchange experiment. Also there were two distinct singlets near 6.4 ppm corresponding to H6 and H5' (note carbazole numbering). If the expected product **22** had been formed, the spectrum should contain only one NH signal, a singlet for H5' at ≈6.0 ppm and a set of two meta coupled doublets for H5 and H7 at 6.0–6.5 ppm. The ^{13}C n.m.r. spectrum also indicates two CH signals at 90.6 and 89.6 ppm which correspond to C6 and C5' of structure **23**. Again if product **22** were formed, three CH signals at ≈90 ppm corresponding to C5', C5 and C7 would be expected. Also the characteristic C3 spiro carbon signal, which is usually located at 60–65 ppm, is missing from the ^{13}C n.m.r. spectrum. Furthermore, the infrared spectrum shows two clear resonances at 3463 and 3373 cm^{-1} corresponding to two NH stretching frequencies.



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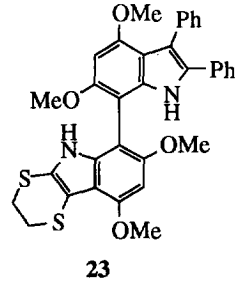


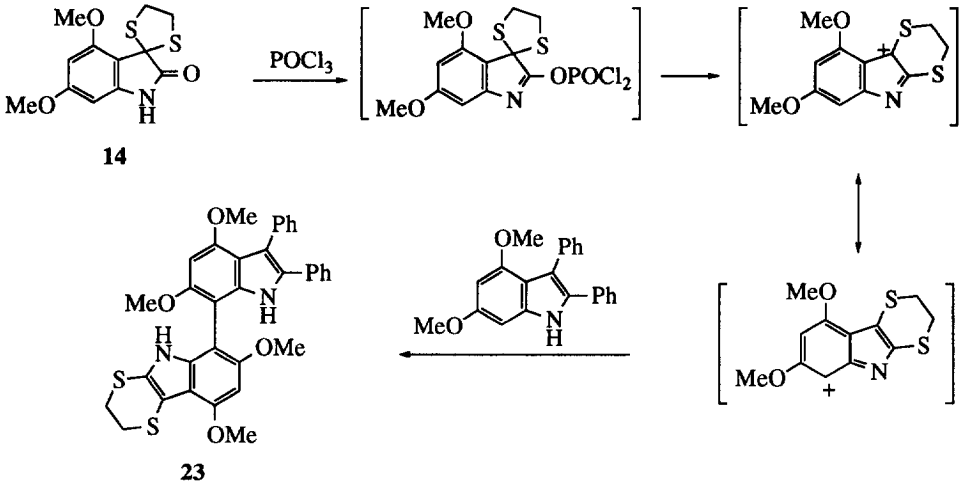
23

Previously, it has been found that 1,3-dithiolanes formed on a carbon attached directly to an aromatic ring undergo a rapid, high-yield rearrangement to dihydro-1,4-dithiin derivatives, provided that a methyl or methylene group is available in the other α-position.[10,11]

It is possible that the resulting intermediate from the reaction of indolin-2-one **14** with phosphoryl chloride could undergo a concerted rearrangement in the presence of acid to give a stabilized carbocation, which could then undergo nucleophilic attack from indole **1** followed by aromatization to give compound **23.** This rearrangement must occur reasonably quickly as the desired product **22** was not observed: such a hypothesis is consistent with previous reports[10,11].

The reaction of the spiro-indolin-2-one **14** with phosphoryl chloride on its own yielded no isolable products. After an extended period of reflux the reaction mixture contained multiple products in very small

yields. Similar behaviour was shown by the other 3-substituted indolin-2-ones **11** and **13** and contrasts with that shown by 4,6-dimethoxyindolin-2-one itself.[2]



14

23

EXPERIMENTAL

General Information

^{1}H n.m.r. spectra were recorded at 300 MHz with a Bruker CXP-300 or at 500 MHz with a Bruker AM-500 spectrometer, and refer to deuterochloroform solutions with chloroform (7.26 ppm) as an internal standard. Signals due to exchangeable protons (NH) were identified by exchange with deuterium oxide. The usual notational conventions are used. ^{13}C n.m.r. spectra were recorded at 125.77 MHz with a Brucker AM-500 spectrometer, and refer to deuterochloroform solutions with chloroform (77.0 ppm) as an internal standards. Low resolution mass spectra were obtained on an A.E.I. MS12 spectrometer at 70eV and 8000V accelerating potential at 210 °C ion source temperature. Infrared spectra were recorded with a Perkin Elmer 580B and refer to paraffin mulls or KBr disks of solids. Ultraviolet spectra were measured using a Hitachi UV-3200 spectrophotometer. Microanalyses were performed by Dr. H.P. Pham of the UNSW Microanalytical Unit.

10,12-Dimethoxy-1,2-diphenylindolo[3,2-e]pyrrolo[3,2,1,-i,j]quinoline (5)

To a stirred and ice cooled solution of 2,7'-bi-indolyl **2** (0.2g, 0.45mmol) in dimethylformamide (2ml) was added dropwise an ice cold solution of phosphoryl chloride (0.16g, 0.10ml, 1.08mmol) in dimethylformamide (1ml). The solution was allowed to come to room temperature and then was made strongly basic with sodium hydroxide solution (20%). The resulting orange-yellow precipitate was collected, washed with water and dried. This solid was then column chromatographed using chloroform/methanol 9:1 as the eluent to give compound **5** (0.08g, 40%), m.p. 184-189 °C. ^{1}H n.m.r. ($CDCl_3$): δ 4.01 and 4.40, 2s, OMe; 6.83, s, H11;

7.28-7.53, m, 12H, ArH; 7.94, d, J8.1Hz, 1H, ArH; 8.15, d, J8.1Hz, 1H, ArH; 8.84, s, H4. Mass spectrum: *m/z* 454(M, 100%), 440(60), 439(50), 425(55), 409(20).

5,7,10,12-Tetramethoxy-1,2-diphenylindolo[3,2-e]pyrrolo[3,2,1,-i,j] quinoline (6)

In a similar manner to the synthesis of compound **5**, 2,7'-bi-indolyl **3** (0.2g, 0.40mmol) gave the orange-yellow compound **6** (0.02g, 10%), m.p. 184-189 °C. ^{1}H n.m.r. ($CDCl_3$): δ 3.88, 3.92, 4.08 and 4.37, 4s, OMe; 6.60, 6.70 and 7.17, 3s, H5, H7, H11; 7.36, s, 5H, ArH; 7.57-7.62, m, 5H, ArH; 8.95, s, H4. Mass spectrum: *m/z* 514(M, 75%), 515(100), 499(39), 498(38), 431(58).

4,6-Dimethoxyisatin (9)

3,5-Dimethoxyaniline hydrochloride (17g, 0.09mol) was thoroughly mixed with oxalyl chloride (17ml, 0.2mol) in a 500 ml open flask and heated to 165-170 °C for 1h. On cooling methanol was added and the mixture refluxed and filtered while hot. The resulting dark green solid was dissolved in a 5% sodium hydroxide solution and left to stand for 5 min. The dark red solution obtained was then acidified to pH4 with formic acid and left to stand for 1h. The resulting brown yellow precipitate was then collected, washed with water and dried. This solid was then placed into a Soxhlet thimble and extracted with dichloromethane over a period of two weeks to give the isatin as a bright yellow solid (14.9g, 80%), m.p. 296-299 °C, (lit[7] m.p. 292-295 °C).

4,6-Dimethoxy-3-hydroxy-3-phenylindolin-2-one (10)

Phenyl lithium (10ml, 20%) was added to a stirred and ice cooled solution of isatin **9** (5g, 24.0mmol) in anhydrous tetrahydrofuran (250ml). The mixture was brought to room temperature for 20 min then neutralised with a solution of ammonium chloride. The product was separated using dichloromethane and evaporated to dryness. Dichloromethane was added and the mixture refluxed and filtered while hot to afford the product **10** as a white solid (5.6g, 81%), m.p. 206-208 °C. (Found: C, 67.4; H, 5.2; N, 4.9. $C_{16}H_{15}NO_4$ requires C, 67.4; H, 5.3; N, 4.9%). λ_{max} 230nm(ε 18660), 284(2120). ν_{max} 3420, 3171, 2924, 1714, 1635, 1518, 1471, 1359, 1315, 1230, 1153, 989, 893, 844, 800 cm^{-1}. ^{1}H n.m.r. [$(CD_3)_2SO$]: δ 3.41, bs, OH; 3.58 and 3.77, 2s, OMe; 6.13, d, J2.0Hz, H5; 6.17, d, J2.0Hz, H7; 7.19-7.28, m, ArH; 10.28, bs, NH. ^{13}C n.m.r. [$(CD_3)_2SO$]: δ 55.55 and 55.69, OMe; 89.71 and 92.71, C5 and C7; 125.81, 127.33 and 128.02, ArCH; 77.47, C3; 111.13, C3a; 141.16, C1'; 144.43, C7a; 157.47 and 162.40, C-OMe; 179.17, C=O. Mass spectrum: *m/z* 285(M, 65%), 269(75), 256(100), 240(35), 180(25).

4,6-Dimethoxy-3-phenylindolin-2-one (11)

Stannous chloride (3.79g, 20mmol) in acetic acid (100ml) and hydrochloric acid (10ml) were added to a solution of dioxindole **10** (5.0g, 17.5mmol) in acetic acid (20ml) and heated to 80-90 °C for 0.5h. The solution was then poured into ice water, the resulting white precipitate collected and dried. The crude product was placed in a Soxhlet thimble, extracted with dichloromethane and evaporated to dryness to give a white solid (4.6g, 98%), m.p. 236-238 °C. (Found: C, 71.4; H, 5.6; N, 5.2. $C_{16}H_{15}NO_3$ requires C, 71.4; H, 5.6; N, 5.2%). λ_{max} 224nm (ε 24800), 262(2790). ν_{max} 3158, 1709, 1605, 1452, 1348, 1149, 1112, 814, 709 cm^{-1}. ^{1}H n.m.r. [$(CD_3)_2SO$]: δ 3.59 and 3.77, 2s, OMe; 4.53, s, H3; 6.17, d, J2.0Hz, H5; 6.21, d, J2.1Hz, H7; 7.07-7.46, m, ArH; 10.41, s, NH. ^{13}C n.m.r. [$(CD_3)_2SO$]: δ 50.20, CH; 55.55 and 55.64, OMe; 89.55 and 92.44, C5 and C7; 127.06, 128.11 and 128.59, ArCH; 107.41, C3a; 137.56, C1'; 144.98, C7a; 156.61 and 161.66, C-OMe; 177.83, C=O. Mass spectrum : *m/z* 270(M+1, 15%), 269(M, 100), 254(50), 240(40).

4,6-Dimethoxy-3-hydroxy-3-methylindolin-2-one (12)

Methyl magnesium chloride (3ml, 20% solution) was added to a stirred and ice cooled solution of isatin **9** (1.0g, 4.8mmol) in dry tetrahydrofuran (50ml). The mixture was brought to room temperature for 20 min then neutralized with a solution of ammonium chloride. The product was separated using dichloromethane and recrystallised from dichloromethane and petroleum ether to give the dioxindole **12** as a pale cream solid (0.8g, 74%), m.p. 195-198 °C. (Found: C, 59.4; H, 5.9; N, 6.5. $C_{11}H_{13}N0_4$ requires C, 59.2; H, 5.9; N, 6.3%). λ_{max} 224nm (ε 24957), 266 (2456). ν_{max} 3275, 3223, 1712, 1631, 1611, 1520, 1368, 1345, 1234, 1159, 819 cm^{-1}. ^1H n.m.r. [$(CD_3)_2SO$]: δ 1.39, s, Me; 3.73 and 3.76, 2s, OMe; 5.48, s, OH; 6.00, d, J2.1Hz, H5; 6.14, d, J2.0Hz, H7; 10.08, s, NH. ^{13}C n.m.r. [$(CD_3)_2SO$]: δ 22.53, Me; 55.59 and 55.65, OMe; 89.65 and 82.39, C5 and C7; 72.93, C3; 111.07, C3a; 143.60, C7a; 157.71 and 161.95, C-OMe; 180.42, C=O. Mass spectrum : *m/z* 223(M, 38%): 208(100), 180(70).

4,6-Dimethoxy-3-methylindolin-2-one (13)

Stannous chloride (1.0g, 4.4mmol) in acetic acid (20ml) and hydrochloric acid (1ml) was added to a solution of dioxindole (48) (0.5g, 2.2mmol) in acetic acid (10ml) and heated to 80-90 °C for 0.5h. The solution was cooled and the product separated using dichloromethane and recrystallised from dichloromethane and petroleum ether to give the indolin-2-one **13** as a pale cream solid (0.39g, 85%), m.p. 135-137 °C. (Found: C, 63.9; H, 6.4; N, 7.0. $C_{11}H_{13}NO_3$ requires C, 63.8; H, 6.3; N, 6.8%). λ_{max} 231nm(ε 10129), 256(3607). ν_{max} 3136, 3060, 1710, 1639, 1619, 1597, 1522, 1220, 1207, 1154, 1120, 810, cm^{-1}. ^1H n.m.r. ($CDCl_3$): δ 1.49, d, J7.6Hz, Me; 3.45, q, J7.6Hz, H3; 3.78 and 3.80, 2s, OMe; 6.14, d, J2.1Hz, H5; 6.17, d, J2.0Hz, H7; 9.13, s, NH. ^{13}C n.m.r. ($CDCl_3$): δ 14.41, Me; 39.89, CH; 55.18 and 55.54, OMe; 89.24 and 92.66, C5 and C7; 109.51, C3a; 143.04, C7a; 156.66 and 161.26, C-OMe; 163.08, C=O. Mass spectrum: *m/z* 207(M, 60%), 192(100).

4,6-Dimethoxy-3-spiro(1',3'-dithiolan-2'-indolin)2-one (14)

To a solution of isatin **9** (2.07g 0.01mol) in acetic acid (60ml) at 60 °C was added ethane-1,2-dithiol (1ml, 0.01mol) followed by slow addition of boron trifluoride etherate (2ml, 0.02 mol). The solution was kept at 60 °C for 20 min then cooled, water added, and the resulting pale brown precipitate filtered off and washed with water to give the indolin-2-one **14** (3.4g, 80%), m.p. 228 °C (from ethyl acetate). (Found: C, 50.7; H, 4.6; N, 5.2. $C_{12}H_{13}NO_3S_2$ requires C, 50.9; H, 4.6; N, 4.9%). λ_{max} 237nm (ε 21388), 290(3241). ν_{max} 3143, 3062, 1716, 1619, 1517, 1345, 1281, 1204, 1159, 1121, 811 cm^{-1}. ^1H n.m.r. [$(CD_3)_2SO$]: δ 3.63, m, CH_2; 3.75 and 3.79, 2s, OMe; 6.04, d, J2.1Hz, H5; 6.19, d, J2.1Hz, H7; 10.50, bs, NH. ^{13}C n.m.r. [$(CD_3)_2SO$]: δ 40.07, CH_2; 55.78 and 56.00, OMe; 89.73 and 93.04, C5 and C7; 62.13, C3; 104.87, C3a; 143.39, C7a; 157.55 and 162.72, C-OMe; 178.98, C=O. Mass spectrum: *m/z* 283(M, 85%), 255(65), 244(50), 223(100), 222(80), 194(55).

N-(3,5-Dimethoxyphenyl)-2-bromopropanamide (15)

2-Bromopropanoyl chloride (0.7ml, 6.6mmol) in dry tetrahydrofuran (5ml) was added dropwise to a stirred and ice-cooled solution of 3,5-dimethoxyaniline (1.01g, 6.6mmol) and dry pyridine (0.54ml, 6.6mmol) in dry tetrahydrofuran (20ml). The solution was brought to room temperature and stirred for 1h. The solution was then evaporated to dryness and the product separated from the crude mixture by column chromatography using dichloromethane as eluent to give the product **15** (1.23g, 65%), m.p. 81-82 °C (from dichloromethane and petroleum ether). (Found: C, 46.2; H, 5.2; N, 4.8. $C_{11}H_{14}BrN0_3$ requires C, 45.9; H, 4.9; N,4.9%). λ_{max} 264nm(ε 8139). ν_{max} 3286, 3232, 3175, 3120, 1671, 1631, 1610, 1568, 1209, 1072 cm^{-1}. ^1H n.m.r.

($CDCl_3$): δ 1.91, d, J7.0Hz, Me; 3.75, s, OMe; 4.51, q, J7.0HZ, H2; 6.24, t, J2.3Hz, 1H, ArH; 6.77, d, J2.2Hz, 2H, ArH; 8.22, s, NH. ^{13}C n.m.r. ($CDCl_3$): δ 22.37, Me; 44.60, CH; 55.29, OMe; 97.35 and 98.39, ArCH; 138.67, ArC; 160.94, C-OMe; 167.87, C=O. Mass spectrum: *m/z* 289(M, ^{81}Br, 41%), 287(M, ^{79}Br, 39%), 208(100), 180(45), 153(35).

General procedure for the reaction of indole 1 with either phosphoryl chloride or triflic anhydride

To a stirred solution of indole **1** (1.52mmol) and an indolin-2-one (1.52mmol) in anhydrous chloroform (30ml) was added either phosphoryl chloride or triflic anhydride (3.04mmol). After either refluxing for 4-12h, or stirring for 30 min at room temperature respectively, the mixture was cooled and made strongly basic with sodium hydroxide solution (10%). The mixture was extracted with chloroform, dried, concentrated and chromatographed on silica gel using dichloromethane as the eluent to yield the product.

Reaction of indole 1 and indolin-2-one 7 with phosphoryl chloride

Indole **1** (0.5g, 1.52mmol) and indolin-2-one **7** (0.23g, 1.52mmol) gave two products.

(i) **4,6-Dimethoxy-7-(3'-methylindol-2'-yl)-2,3-diphenylindole (16)**

(0.49g, 71%), R_f 0.65, m.p. 215 °C (from dichloromethane and petroleum ether). (Found: C, 81.2; H, 5.5; N, 6.1. $C_{31}H_{26}N_2O_2$ requires C, 81.2; H, 5.7; N, 6.1%). λ_{max} 245nm(ε 21743), 319(15140). ν_{max} 3440, 3422, 3405, 1624, 1607, 1340, 1140, 749 cm^{-1}. ^1H n.m.r. [$(CD_3)_2SO$]: δ 2.15, s, Me; 3.72 and 3.79, 2s, OMe; 6.51, s, H5; 6.98-7.52, m, ArH; 10.72, s, NH; 10.80, s, NH. Mass spectrum: *m/z* 459(M+1, 38%), 458(M, 100%), 443(45), 329(15), 229(15).

(ii) **2-Chloro-3-methylindole (17)**

(0.007g, 1%), R_f 0.75, m.p. 125 °C (from dichloromethane and petroleum ether). ^1H n.m.r. [$(CD_3)_2SO$]: δ 2.19, s, Me; 7.02, t, J7.5Hz, 1H, ArH; 7.10, t, J7.6Hz, 1H, ArH; 7.27, d, J8.1Hz, 1H, ArH; 7.43, d, J7.9Hz, 1H, ArH; 11.55, s, NH. Mass spectrum: *m/z* 167(M, ^{37}Cl, 30%), 166(40), 165(M, ^{35}Cl, 100%), 164(95), 140(80), 138(40).

Reaction of indole 1 and indolin-2-one 11 with phosphoryl chloride

Indole **1** (0.5g, 1.52mmol) and indolin-2-one **11** (0.41g, 1.53mmol) gave two products.

(i) **4,6-Dimethoxy-7-[4',6'-dimethoxy-3'-phenyl-7'-(4'',6''-dimethoxy-2'',3''-diphenylindol-7''-yl)indol-2'-yl]2,3-diphenylindole (19)**

(0.31g, 45%), R_f 0.75, m.p. 180-186 °C. (Found: C, 79.6; H, 5.7; N, 4.4. $C_{60}H_{49}N_3O_6$ requires C,79.4; H, 5.4; N, 4.6%). λ_{max} 244nm(ε 59630), 321(29960). ν_{max} 3445, 1599, 1464, 1331,1139, 993, 697 cm^{-1}. ^1H n.m.r. ($CDCl_3$): δ 3.64, 3.72 , 3.80, 3.84, 3.91 and 3.94, 6s, OMe; 6.30, 6.48 and 6.59, 3s, H5, H5' and H5''; 6.92-6.96, m, 2H, ArH; 7.16-7.37, m, 19H, ArH; 7.46-7.49, m, 2H, ArH; 7.61-7.63, m, 2H, ArH; 7.84, 8.06 and 8.36, 3s, NH. ^{13}C n.m.r. ($CDCl_3$): δ 55.24, 55.41, 57.07, 57.72 and 57.80, OMe; 89.99, 90.35 and 90.84, C5, C5' and C5''; 125.83, 126.76, 126.87, 127.19, 127.29, 127.62, 127.84, 128.05, 128.32, 130.34, 131.41 and 131.51, ArCH; 97.98, 98.51 and 98.70, C3, C3' and C3''; 111.97, 113.18, 113.51, 113.95, 114.89 and 115.31, C3a, C3'a, C3''a, C7a, C7'a and C7''a; 132.53, 132.63, 132.75, 132.98, 135.55, 135.83, 136.12, 136.97 and 137.38, ArC; 154.15, 154.34, 154.49, 154.76, and 155.05, C-OMe. Mass spectrum: *m/z* 909(M+2, 25%), 908(M+1, 65), 907(M, 100).

(ii) **2,2'-Bi-(4,6-dimethoxy-3-phenyl)indolyl (21)**

(0.02g, 1.5%), R_f 0.65, m.p. 275-279 °C. (Found: C, 76.2; H, 5.8; N, 5.5. $C_{32}H_{28}N_2O_4$ requires C, 76.2; H, 5.6; N, 5.6%). λ_{max} 230nm(ε 43570), 278(23570), 330(12860). ν_{max} 3368, 1619, 1519, 1462, 1377, 1314, 1199, 1133, 899 cm^{-1}. ^1H n.m.r. [$(CD_3)_2SO$]: δ 3.60 and 3.76, 2s, OMe; 6.14, d, J2.0Hz, H5, H5'; 6.43, d, J2.0Hz, H7, H7'; 6.94-7.03, m, ArH; 11.28, s, NH. ^{13}C n.m.r. [$(CD_3)_2SO$]: δ 55.06 and 55.47, OMe; 87.00, C5; 91.92, C7; 125.05, 126.75 and 130.48, ArCH; 110.93, 116.95, 135.81, 137.63 and 137.78, ArC; 154.41 and 157.04, C-OMe. Mass spectrum: *m/z* 505(M+1, 10%), 504(M, 30), 489(10), 252(15), 149(30).

Reaction of indole 1 and indolin-2-one 11 with triflic anhydride

Indole **1** (0.5g, 1.52mmol) and indolin-2-one **11** (0.41g, 1.53mmol) gave the terindolyl **19** (0.41g, 60%), R_f 0.75, m.p. 180-186 °C.

Reaction of indole 1 and indolin-2-one 13 with phosphoryl chloride

Indole **1** (0.5g, 1.52mmol) and indolin-2-one **13** (0.32g, 1.54mmol) gave **4,6-dimethoxy-7-[4',6'-dimethoxy-3'-methyl-7'-(4'',6''-dimethoxy-2'',3''-diphenylindol-7''-yl)indol-2'-yl]2,3-diphenylindole 20** (0.32g, 50%) m.p. 142-144 °C. (Found: C, 77.8; H, 5.9; N, 4.7. $C_{55}H_{47}N_3O_6$ requires C,78.1; H, 5.6; N, 5.0%). λ_{max} 245nm(ε 59300), 324(28270). ν_{max} 3419, 1599, 1457, 1377, 1328, 1258, 1204, 1138, 996 cm^{-1}. ^1H n.m.r. ($CDCl_3$): δ 2.45, s, Me; 3.65, 3.85 and 4.05, 3s, OMe; 3.70, s, 9H, OMe; 6.40, 6.45 and 6.50, 3s, H5, H5' and H5"; 7.20-7.45, 20H, ArH; 7.85, 8.05 and 8.20, 3s, NH. ^{13}C n.m.r. ($CDCl_3$): δ 12.29, Me; 55.45 , 57.00 and 57.91, OMe; 89.60, 89.98 and 91.11, C5, C5' and C5"; 125.80, 125.92, 126.84, 127.04, 127.26, 127.31, 128.05, 128.30, 128.35, 131.45 and 131.51, ArCH; 97.61, 98.84 and 99.23, C3, C3' and C3"; 110.29, 113.01, 113.62, 114.18, 114.84 and 114.88, C3a, C3'a, C3"a, C7a, C7'a and C7"a; 132.73, 132.75, 132.79, 133.04, 135.86, 136.15, 136.93 and 137.47, ArC; 153.97, 154.23, 154.69, 154.75, 155.01 and 155.09, C-OMe. Mass spectrum: *m/z* 847(M+2, 20%), 846(M+1, 65), 845(M, 100), 830(15), 656(20), 532(20).

Reaction of indole 1 and indolin-2-one 13 with triflic anhydride

Indole **1** (0.5g, 1.52mmol) and indolin-2-one **13** (0.32g, 1.54mmol) gave the terindolyl **20** (0.32g, 50%) m.p. 142-144 °C.

5,7-Dimethoxy-8-(4',6'-dimethoxy-2',3'-diphenylindol-7'-yl)-1,4-dithia-1,2,3,4-tetrahydrocarbazole (23)

Reaction of indole **1** (0.5g, 1.52mmol) and indolin-2-one **14** (0.43g, 1.52 mmol) with phosphoryl chloride (0.28ml, 3.04mmol) after 6h reflux gave the biindolyl **23** (0.45g, 50%), m.p. 258-260 °C (from dichloromethane and petroleum ether). (Found: C, 68.8; H, 5.0; N, 4.9. $C_{34}H_{30}N_2O_4S_2$ requires C, 68.7; H, 5.1; N, 4.7%). λ_{max} 248nm(ε 35892), 319(20649). ν_{max} 3463, 3373, 1594, 1507, 1329, 1206, 1140, 994, 699 cm^{-1}. ^1H n.m.r. [$(CD_3)_2SO$]: δ 3.20-3.35, m, CH_2; 3.66, 3.68, 3.70 and 3.88, 4s, OMe; 6.40 and 6.46, 2s, H6 and H5'; 7.14-7.26, m, ArH; 10.25, s, NH; 10.31, s, NH. ^{13}C n.m.r. [$(CD_3)_2SO$]: δ 26.81 and 27.56, CH_2; 55.44, 57.73, 56.82 and 56.88, OMe; 89.65 and 90.56, C5 and C5'; 125.79, 126.79, 127.42, 127.94, 129.26 and 131.53, ArCH; 96.58, 99.26, 99.51, 111.96, 112.74, 113.78, 118.17, 132.92, 133.24, 136.89, 137.20 and 137.86, ArC; 151.91, 153.90, 154.10 and 154.43, COMe. Mass spectrum: *m/z* 597(M+2, 20%), 596(M+1, 40%), 595(M, 100%), 567(25).

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