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P. A. Keller
University of Wollongong, keller@uow.edu.au

N. R. Yepuri
University of Wollongong

M. J. Kelso
University of Wollongong, michael_kelso@uow.edu.au

M. Mariani
University of Wollongong

B. W. Skelton
University of Western Australia

See next page for additional authors

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Abstract
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Keywords
biindole, oxidative dimerisation, thallium oxidative coupling

Disciplines
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Oxidative coupling of indoles using thallium(III) trifluoroacetate

Paul A. Keller,[a*] Nageshwar R. Yepuri,[a] Michael J. Kelso,[a] Michael Mariani,[a] Brian W. Skelton,[b] and Allan H. White[b]

[a]School of Chemistry, University of Wollongong, Wollongong, NSW 2522 Australia

[b]School of Biomedical, Biomolecular and Chemical Sciences, University of Western Australia, WA 6009 Australia

Abstract—The oxidative coupling of polysubstituted electron-rich indoles mediated by thallium trifluoroacetate was found to be a facile, clean, and high yielding reaction. Indolic coupling sites were determined by the nature of the substituents present, with dimerisation at the indole 2-position being the dominant outcome. Indoles bearing two potential reaction sites with similar reactivity were additionally found to undergo heterocoupling.

Introduction

Numerous synthetic methods are available for introducing the biaryl linkage into organic compounds.[1,2] The popular Suzuki reaction and its related organometallic cousins employ specific functionality to direct the sites of reaction and many examples have of course been reported.[3] Also well known are oxidative coupling methods,[4] where biaryl bonds are formed directly at unsubstituted aryl sites which have been activated either by the aryl units themselves or by ring substituents. The clear advantage of oxidative coupling over organometallic methods, particularly for the formation of biaryl dimers, is that it requires no prior functionalisation of the aromatic reaction site(s).[1]

As part of our ongoing investigations into the biological activities of homo- and hetero-dimeric aromatic systems,[5] we wished to identify simple methods for constructing focused libraries of symmetrical and non-symmetrical biindoles incorporating biaryl linkages at the indole 2 and 7 positions. While there have been many syntheses of 2,2′-biindoles,[6] the procedures usually involve numerous steps and are impractical for preparing multiple analogues. In the case of 7,7′-biindoles, very few syntheses have been reported but one notable example[7] describes the oxidative coupling of 4,6-dimethoxy-2,3-diphenylindole in the presence of quinone, chloranil or dichlorodicyanoquinone to yield the homodimeric 7,7′-coupled biindole in 100%, 70% and 60% yields respectively.

Attracted by the simplicity of oxidative coupling methods, we sought to identify a suitable oxidant for preparing our biindole libraries. Thallium (III) trifluoroacetate has previously been used for effecting

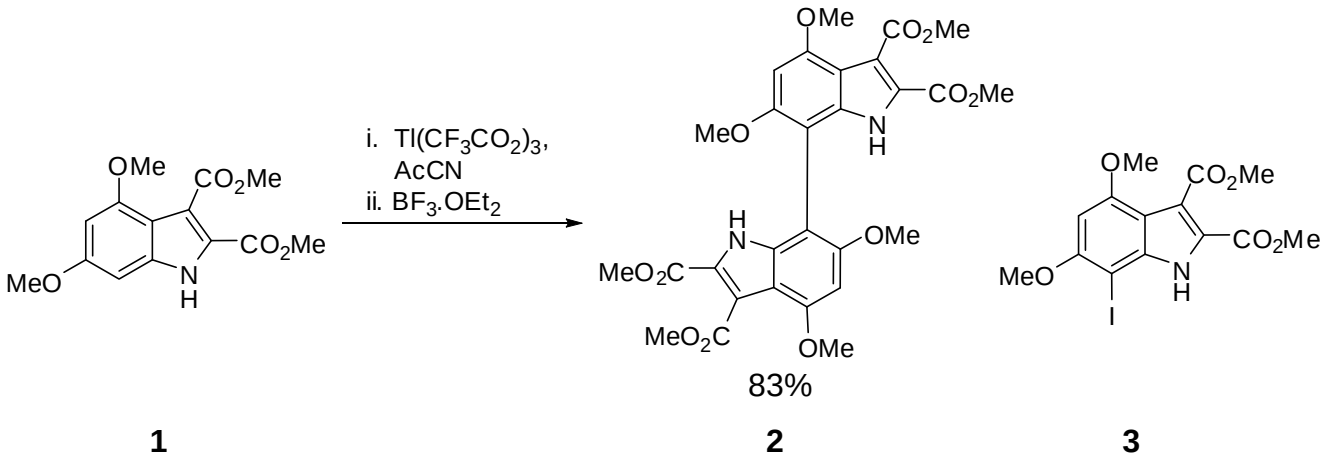
Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

oxidative dimerisations of electron-rich naphthyl compounds,[8] 2-substituted indoles[9] and indolocarbazoles[10] We now wish to report that thallium(III) trifluoroacetate, in combination with $BF_3.Et_2O$, is an effective reagent for the oxidative coupling of electron-rich polysubstituted indoles.

Results and Discussion

Synthesis of 7,7′-biindoles

Our preliminary investigations focussed on the 7,7'- dimerisation of a model compound 2,3-dicarbomethoxy-4,6-dimethoxyindole **1**. This indole monomer had its most reactive positions (C2 and C3) blocked, allowing the two methoxy substituents to activate the C7-position to oxidative dimerisation. The use of thallium trifluoroacetate/$BF_3.Et_2O$ as oxidant afforded the 7,7′-dimer **2** as the sole product in excellent yield (Scheme 1). This rapid and selective reaction was superior to the previously reported oxidation, which employed ICl and produced **2** in 34% yield along with 31% of the iodinated monomer **3**.[7]

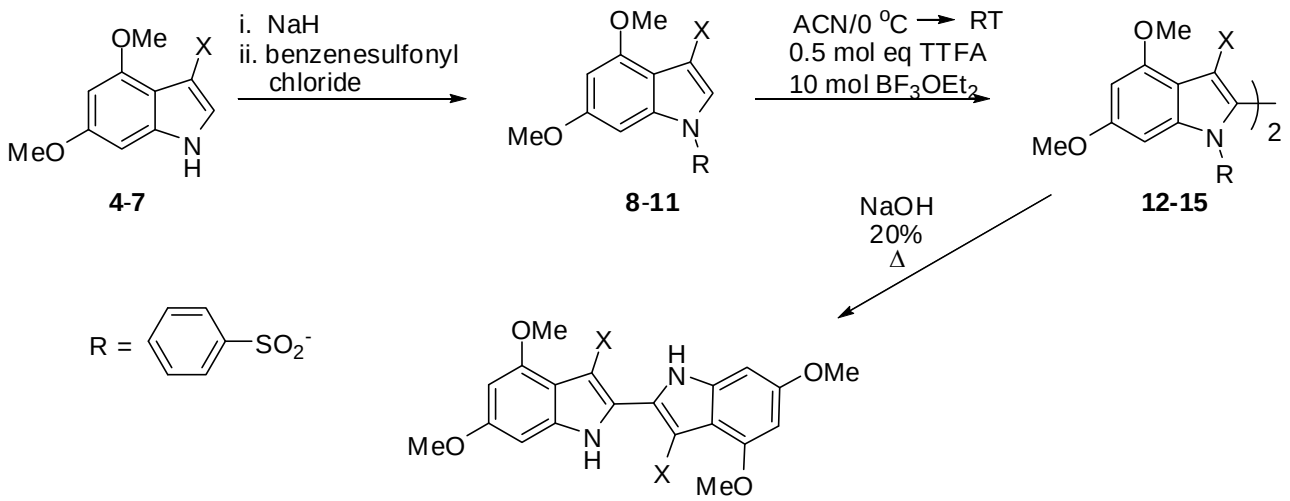


Scheme 1

Synthesis of 2,2′-biindoles

Formation of 2,2′-biindoles by oxidative dimerisation of 3-aryl-4,6-dimethoxyindoles using thallium trifluoroacetate /$BF_3.Et_2O$ was explored next. These monomers had two potential dimerisation sites (C2 and C7) but initial experiments showed that indole N-protection limited dimerisation at the 7-position (data not shown). The substituted indole monomers **4-7**[11] were NH protected using sodium hydride and benzenesulfonyl chloride to give **8-11** after recrystallisation from methanol (Scheme 2). Clean formation of the 2,2′-dimers was achieved by treating an acetonitrile solution of the protected indole monomers with a half-mole equivalent of thallium(III) trifluoroacetate, followed by addition of excess $BF_3.Et_2O$. After one hour of stirring at room temperature, the dimers were isolated and recrystallised from

methanol /dichloromethane. Compound **11** bearing the strongly electron withdrawing p-$NO_2C_6H_4$ at the indole 3-position, did not couple under these conditions, even after prolonged reaction.



X	Yield		
	monomer	dimer	deprotected dimer
p-$MeOC_6H_4$	65% **8**	70% **12**	15% **16**
Ph	70% **9**	70% **13**	15% **17**
p-BrC_6H_4	65% **10**	74% **14**	10% **18**
p-$NO_2C_6H_4$	65% **11**	0% **15**	N/A

Scheme 2

As a representative example, the structure of **12** was supported by analysis of the mass spectrum (ES), which showed a peak at *m/z* 845 assigned as the [M+1] ion. Further support was provided by the ^{1}H NMR spectra, which showed the disappearance of a peak at 7.31 ppm assigned to H2 in **8**. The presence of only 'one set' of peaks in the ^{1}H NMR spectrum was consistent with the formation of a symmetrical dimer. Comparison of the ^{1}H NMR spectrum of **12** with that of the monomer **8** showed a shift in the aromatic peaks assigned to the benzenesulfonyl group from 7.89-7.56 to 7.53-7.30 ppm, and those assigned to the 3-aryl ring from 7.47-6.92 to 7.03-6.65 ppm. The structure of **12** was eventually confirmed by a single crystal X-ray study (Figure 1) which indicated that both phenyl rings are aligned to one side of the molecule, accounting for the downfield shifts of the aromatic signals in the NMR spectra of the dimer **12** relative to the monomer **8**. The 2,2′-dimeric indoles **12-15** can exist as

Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

atropoisomers due to the presence of four *ortho* substituents. Presumably both of these isomers were formed in each of the products as racemic mixtures.

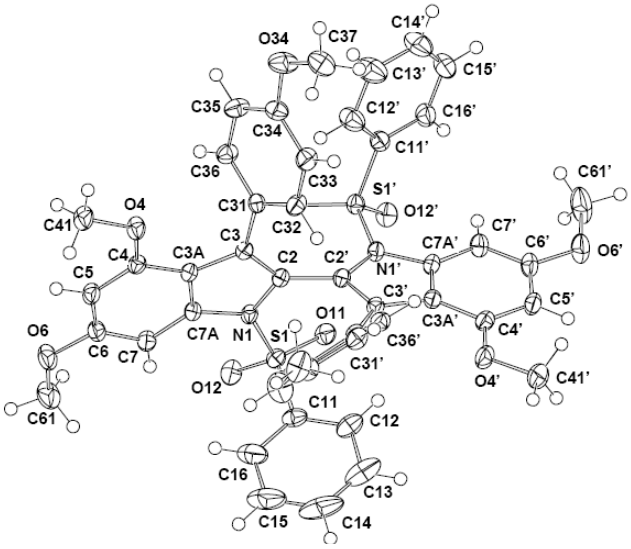
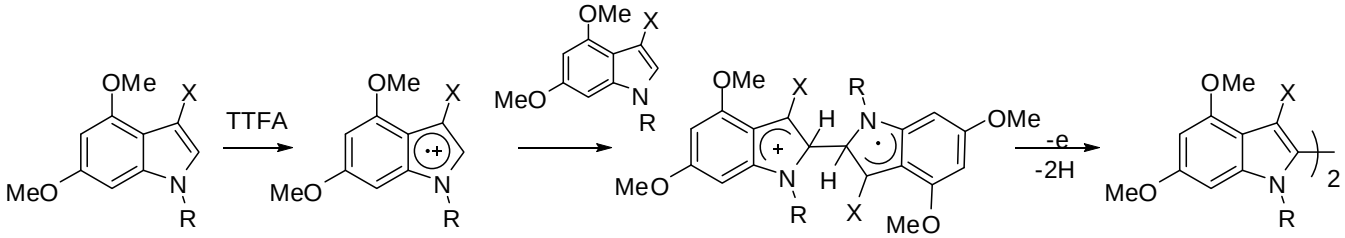


Figure 1. Molecular (ORTEP) projection of **12** down the quasi-two-fold axis.

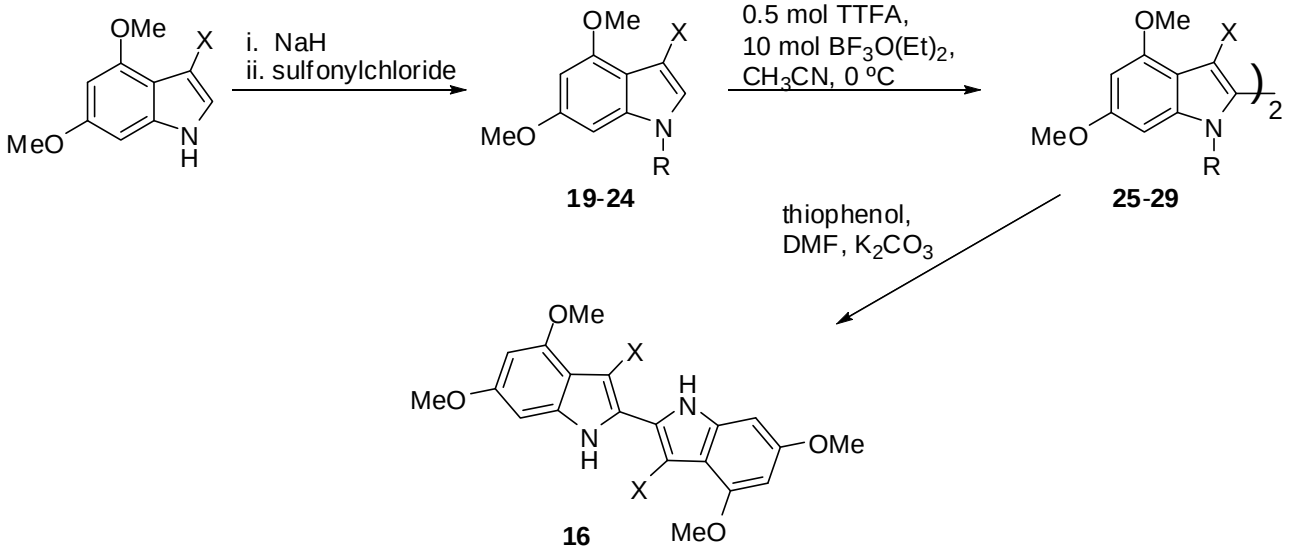
Based on a mechanism previously proposed for thallium(III) promoted oxidative dimerisations[8], we postulate that oxidative 2,2′-dimerisation of these indoles proceeds via an initial one-electron transfer from the electron-rich indole substrate to thallium(III) to form an indole radical cation (Scheme 3). Subsequent electrophilic substitution with a second indole substrate, followed by oxidative aromatization, gives the symmetrical 2,2′-dimers.



Scheme 3

Initial attempts to remove the benzenesulfonyl protecting group from the dimers using thionyl chloride at room temperature yielded complex mixtures. Deprotection was eventually achieved, albeit in disappointing yields of 10-15%, by heating the dimers at reflux for four hours in a 20% solution of sodium hydroxide. Dimer **17** was spectroscopically identical to the reported compound that had previously been synthesised in only 1.5% yield.[12]

The poor outcome in the final deprotection step led us to investigate indole 2,2′-dimerisations using alternative protecting groups. A selection of 3-arylsubstituted indoles were N-protected with various aryl or alkyl sulfonates and then subjected to the dimerisation/deprotection sequence. These results are summarised in Scheme 4. All of the protection and dimerisation reactions proceeded smoothly and in good yield with the exception of *N*-4-nitrobenzenesulfonyl-3-(*p*-nitrophenyl)indole **21**, which produced no dimer and quantitatively returned the starting material even after prolonged reaction times. This was not unexpected given the failure of compound **11** to undergo dimerisation. Confirmation of the structure of **28** was provided from a single crystal X-ray study (Figure 2).



R	X	Yield		
		monomer	dimer	deprotected dimer
p-Me $C_6H_4SO_2$	*p*-BrC_6H_4	70% **19**	70% **25**	Complex mixture
p-NO_2 $C_6H_4SO_2$	*p*-BrC_6H_4	65% **20**	70% **26**	Complex mixture
p-NO_2 $C_6H_4SO_2$	*p*-$NO_2C_6H_4$	65% **21**	NR	-
$MeSO_2$	Ph	75% **22**	70% **27**	Complex mixture
$MeSO_2$	*p*-BrC_6H_4	70% **23**	75% **28**	Complex mixture
$MeSO_2$	*p*-$OMeC_6H_4$	75% **24**	70% **29**	25% **16**

Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

Scheme 4

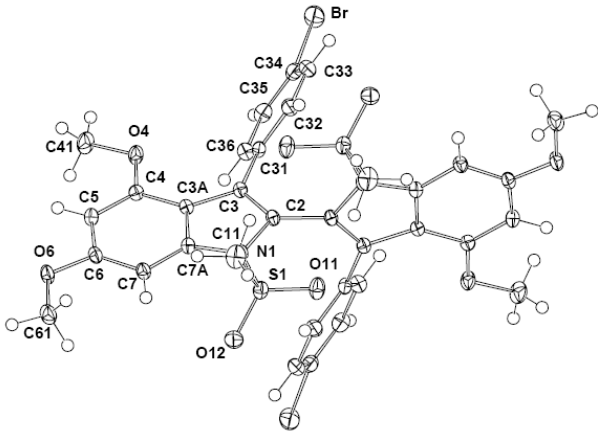


Figure 2: Molecular (ORTEP) projection of **28** down the crystallographic two-fold axis.

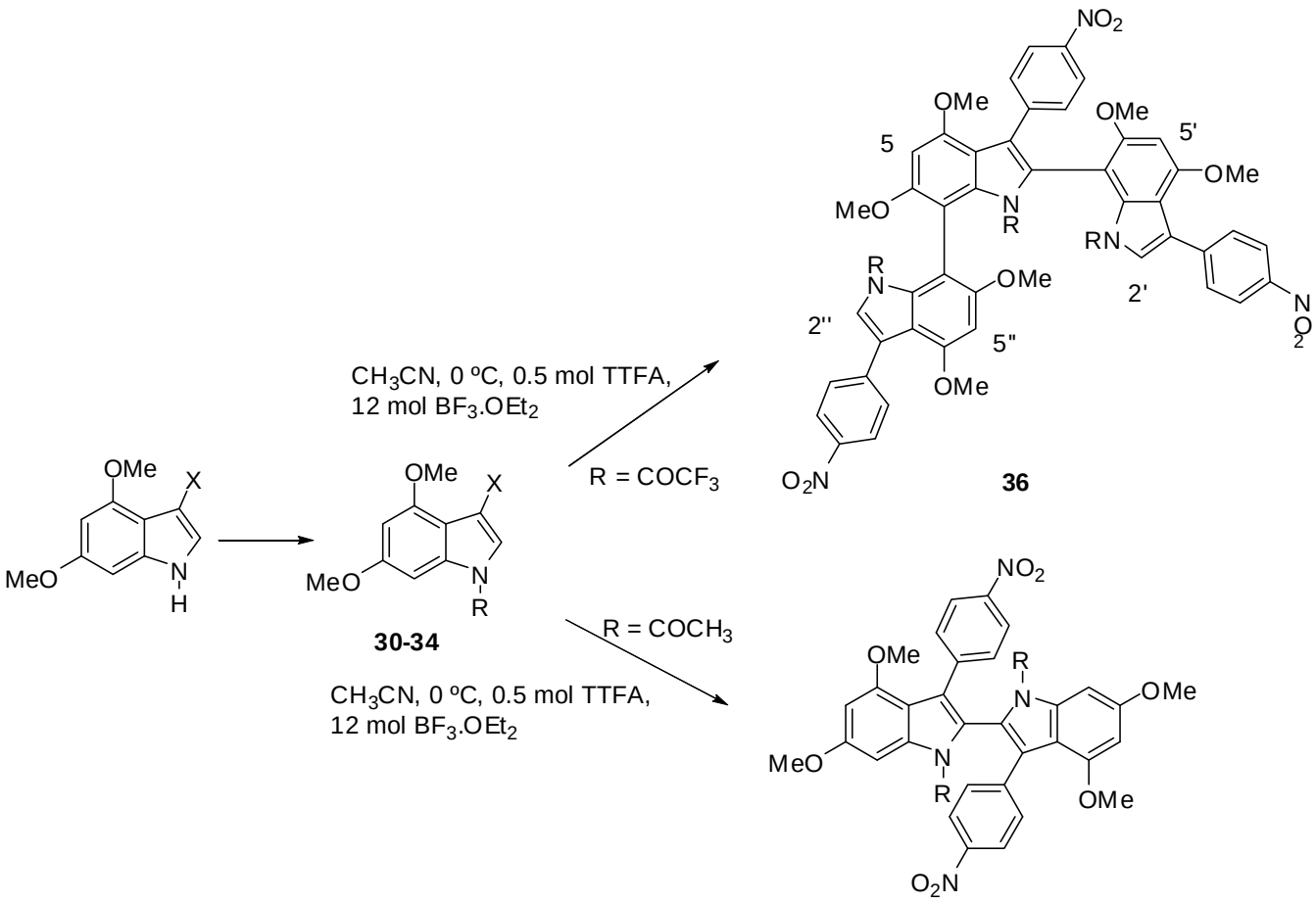
Different reaction conditions were trialled for deprotection of the dimers using thiophenol, DMF and K_2CO_3 at room temperature. Only **29** gave the deprotected 2,2′-biindole **16** in 25% yield, a slight improvement over the 15% obtained from **12** in NaOH ar reflux (Scheme 2). All other deprotection reactions again resulted in complex mixtures.

Oxidative dimerisation with N-acyl protected indoles

The effects of indole N-protection were further explored using acetyl, trifluoroacetyl and Boc groups. The results from the protection, dimerisation and deprotection reactions are summarized in Scheme 5.

Indole acetylation was achieved using tetrabutylammonium hexafluorophosphate with potassium hydroxide and CH_2Cl_2 under phase transfer conditions. Trifluoroacetyl protection of the indoles was carried out using a modified literature protocol.[13] Oxidative dimerisation was attempted on compounds **30**-**34** using the conditions described above. In stark contrast to monomers **8** and **24** (which contain 3-*p*-methoxyphenyl indolic substituents and N-phenylsulfonyl and N-methylsulfonyl groups respectively) the analogous N-acetyl and N-trifluoroacetyl-protected indoles **30** and **32** yielded no 2,2′-biindoles. Inexplicably, the corresponding N-Boc derivative **34** produced a complex mixture of products. Furthermore, given that compounds **11** and **21** (which carry 3-*p*-nitrophenyl indolic substituents) failed to undergo dimerisation, it was very surprising to find that the N-acetyl protected 3-(*p*-nitrophenyl)indole **31** dimerised to **35** in 30% yield! What was perhaps even more surprising was the finding that the 3-(*p*-nitrophenyl)indole **33** gave no trace of the 2,2-dimer but instead produced the

2,7′,7,7″-terindole **36** in 35% yield (Scheme 5). The remaining mass was identified as the starting indole **33** and its N-deprotected precursor.



R	X	Yield		
		monomer	dimer	trimer
$COCH_3$	*p*-OMePh	65% **30**	NR	NR
$COCH_3$	*p*-NO_2Ph	57% **31**	2,2′-dimer 30% **35**	-
$COCF_3$	*p*-OMePh	60% **32**	NR	NR
$COCF_3$	*p*-NO_2Ph	60% **33**	-	2,7′,7,7″-trimer 35% **36**
Boc	*p*-OMePh	99% **34**	-	-

Scheme 5

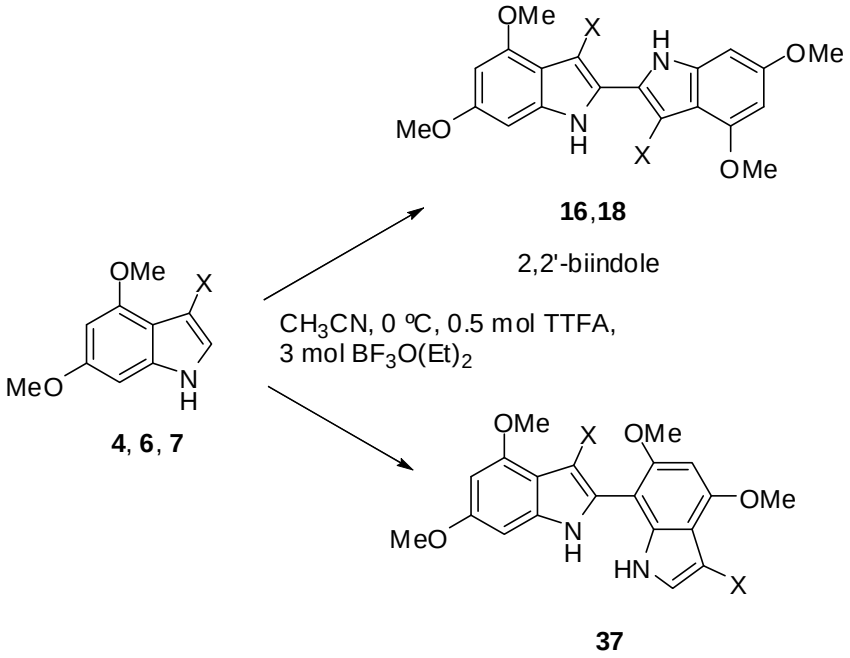
Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

Support for the structure of the trimer **36** was provided by its mass spectrum (ES) which showed a peak at 1179 corresponding to the M+1 ion. Analysis of the ^{1}H NMR spectrum showed singlet peaks at 6.73, 6.66, and 6.44 ppm corresponding to the H5′, H5 and H5″ protons. These three protons showed no *meta*-coupling to their respective H7 protons (usually observed), suggesting the molecule contains 2,7′- and 7,7″-linkages. Additionally, one H2 signal was absent from the ^{1}H NMR spectrum while there were clearly two other singlets at 7.21 and 6.95 ppm corresponding to the H2′ and H2″ protons. The proposed structure was fully supported by gHMBC, gCOSY and NOESY correlations.

The mechanism for the formation of **36** is not clear, although on the basis of current knowledge about TTFA promoted oxidations and dimerisation of indoles,[8,14] it may be due to the *p*-nitro group and trifluoroacetate group at the N1 position not activating the 2-position to the same level as occurs in the examples that underwent coupling. This would allow reaction at the C7 position to become a significant process. The 2,7′-dimer could then undergo further oxidative coupling between the 7 and 7′ positions yielding the 2,7′,7,7″-trimer **36**.

2.4. Thallium(III) trifluoroacetate mediated coupling of 4,6-dimethoxy-3-aryl indoles without N-protection

The oxidative dimerisation of indoles **4**, **6** and **7** using thallium (III) trifluoroacetate was attempted in the absence of NH protecting groups. After preliminary optimisation reactions, it was found that 3 to 5 equivalents of the Lewis acid were best added at 0 ºC before continued stirring at room temperature for three hours. The results are summarised in Scheme 6. Indole **4** gave the 2,2′-dimer **16** in 35% yield, the remainder being starting material and other baseline products. Indole **6** gave 20% of 2,2′-dimer **18** with 50% of the starting material recovered. Interestingly, 4,6-dimethoxy-3-(*p*-nitrophenyl)indole **6** gave only the 2,7′-dimer **38** (20%) with no traces of formation of 2,2′-dimer.



X	Yield	
	2,2′-dimer	2,7′-dimer
p-OMePh	35% **16**	-
p-BrPh	20% **18**	-
p-NO_2Ph	-	15% **37**

Scheme 6

For all oxidative coupling reactions attempted without *N*-protecting groups the reactions took longer and returned significant quantities of starting material, suggesting that dimerisation is facilitated by N-protection. The results also suggest that the alkyl or arylsulfonyl groups may help in the regiospecificity of the 2,2′-dimerisation provided the 3-aryl substituent is mildly electron-withdrawing or electron-donating.

Conclusions

Oxidative coupling of indoles with thallium(III) trifluoroacetate provides good to excellent yields of 2,2′-dimers. Protecting groups such as benzenesulfonyl, tosyl or methanesulfonyl aid formation of the 2,2′-dimer, provided that the *para* substituent on the 3-aryl ring is mildly deactivating or an electron-donating group. When the 3-aryl ring bears a *para* substituent which is a strong electron-withdrawing group, e.g. NO_2, no reaction is observed unless an N-acetyl protecting group is present which leads to

Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

2,7′-dimerisation. Changing the indole N-protecting group to a trifluoroacetate group deactivates C2 and activates C7 such that trimeric-indoles are formed.

Experimental

Melting point determinations were carried out on a Gallenkamp melting point apparatus. Chemical ionization (CI) and electron impact (EI) mass spectra were obtained on a Shimadzu QP-5000 mass spectrometer by a direct insertion technique with an electron beam energy of 70 eV. Electrospray (ESI) mass spectra were obtained on a VG Autospec spectrometer. High-resolution mass spectra (HRMS) were determined on a micromass QTof2 spectrometer using polyethylene glycol or polypropylene glycol as the internal standard. The *m/z* values are stated with their peak intensity as a percentage in parentheses. Proton and carbon nuclear magnetic resonance (NMR) spectra were obtained as specified on a Varian Mercury 300 MHz or Varian Inova 500 MHz spectrometer. Spectra were recorded in the specified deuterated solvent, and referenced to the residual non-deuterated solvent signal. Chemical shifts (δ) in ppm were measured relative to the internal standard. Analytical thin layer chromatography (TLC) was carried out on Merck silica gel 60 F254 pre-coated aluminium plates with a thickness of 0.2 mm. All column chromatography was performed under 'flash' conditions on Merck silica gel 60 (230-400 mesh). Chromatography solvent mixtures were measured by volume. Sodium hydride was used as a dispersion in oil. Organic solvent extracts were dried with anhydrous magnesium sulfate. All compounds were judged to be of greater than 95% purity based upon 1H NMR and TLC analysis.

*7,7'-Bi(4,6-dimethoxyindolyl)-2,2',3,3'-tetracarboxylate) (**2**)*

To a solution of dimethyl 4,6-dimethoxyindole-2,3-dicarboxylate **1** (460 mg, 1.57 mmol) and thallium trifluoroacetate (432 mg, 0.79 mmol) in dry acetonitrile (40 mL) was added $BF_3.(CH_3CH_2)_2O$ (785 μL, 0.79 mmol) and the reaction allowed to stir at rt for 40 min. The reaction was then extracted with water (100 mL) and CH_2Cl_2 (4 x 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated and the residue subjected to flash silica gel column chromatography (5:1 CH_2Cl_2:EtOAc) to yield the dimer **2** (420 mg, 83%) as a pale yellow powder which was spectroscopically identical to that reported.[7]

General procedure (A) for the synthesis of protected indole starting materials:

To a stirred solution of 4,6-dimethoxy-3-phenylindole (1 mol) in CH_2Cl_2 under a nitrogen atmosphere, was added sodium hydride (1 mol, 60% dispersion in oil) and the reaction then stirred for 25 min. The

sulfonyl chloride (1 mol) was then added and the reaction left to stir at 25 °C for an additional 2 h. The solvent was then removed under reduced pressure and the resultant residue was suspended in water (50 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The organic fractions were combined, dried ($MgSO_4$), concentrated under reduced pressure and the residue recrystallised from methanol yielding the corresponding protected indole.

*N-Benzenesulfonyl-4,6-dimethoxy-3-(4-methoxyphenyl)indole (**8**)*

This was prepared by general procedure (**A**) using 4,6-dimethoxy-3-(4-methoxyphenyl)indole **4** (2.00 g, 7.0 mmol), sodium hydride (0.28 g, 7.0 mmol in 60% oil dispersion) and benzenesulfonyl chloride (1.23 g, 7.0 mmol) to give the indole **8** (2.11 g, 73%) as a white solid, mp 131-133 °C. ^{1}H NMR δ: 7.89 (2H, d, J = 7.5 Hz, sulfonyl ArH2″ and 6″), 7.59-7.41 (3H, m, sulfonyl ArH3″, 4″, and 5″), 7.47 (2H, d, J = 8.7 Hz, ArH2′ and 6′), 7.31 (1H, s, H2), 7.20 (1H, d, J = 1.8 Hz, H7), 6.92 (2H, d, J = 8.7 Hz, ArH3′ and 5′), 6.32 (1H, d, J = 1.8 Hz, H5), 3.88 (3H, s, C4 OCH_3), 3.84 (3H, s, C6 OCH_3), 3.71 (3H, s, ArC4 OCH_3). ^{13}C NMR δ: 159.5 (ArC4′), 159.0 (C6), 155.0 (C4), 138.5 (C7a), 137.5 (sulfonyl ArC1″), 134.0 (sulfonyl ArC4″), 130.8 (sulfonyl ArC2″ and 6″), 129.4, (sulfonyl ArC3″ and 5″), 126.9 (C3), 124.4 (ArC1′), 121.1 (C2), 113.3 (ArC3′ and 5′), 110.0 (C3a), 96.0 (C7), 90.0 (C5), 55.5 (C4 O<u>C</u>H_3), 54.5 (C6 O<u>C</u>H_3), 54.3 (ArC4 O<u>C</u>H_3). CI-MS *m/z*: 424 ([M+1]$^+$, 10%), 391 (15), 340 (10), 284 (30), 149 (20), 125 (15), 113 (50), 97 (70), 85 (100); ES-HRMS *m/z*: calcd for [M+1]$^+$ $C_{23}H_{22}NO_5S$ 424.1219; found 424.1230.

*N-Benzenesulfonyl-4,6-dimethoxy-3-phenylindole (**9**)*

This was prepared by general procedure (**A**) using 4,6-dimethoxy-3-phenylindole **5** (2.00 g, 7.9 mmol), sodium hydride (0.32 g, 8.0 mmol) and benzenesulfonyl chloride (1.40 g, 7.9 mmol) to give the indole **9** (2.14 g, 69%) as a white solid, mp 125-128 °C. ^{1}H NMR δ: 7.90-7.54 (5H, m, sulfonyl ArH″), 7.46-7.36 (5H, m, ArH′), 7.36 (1H, s, H2), 7.20 (1H, d, J = 3.0 Hz, H7), 6.33 (1H, d, J = 3.0 Hz, H5), 3.95 (1H, s, C4 OCH_3), 3.65 (1H, s, C6 OCH_3). ^{13}C NMR δ: 159.5 (C6), 154.5 (C4), 139.0 (C7a), 138.0 (ArC4′), 134.0 (sulfonylArC4″), 129.5 (sulfonylArC2″ and 6″), 129.2 (sulfonylArC1″), 129.0 (sulfonylArC3″ and 5″), 128.0 (ArC4′), 127.5 (ArC2′ and 6′), 127.0 (ArC3′ and 5′), 124.7 (C3) 122.0 (C2), 112.5 (C3a), 95.0 (C7), 90.0 (C5), 56.0 (C4 OCH_3), 55.7 (C6 OCH_3). ES-MS *m/z*: 394 ([M+1]$^+$, 80%), 310, (25), 254, (100), 187, (50), 141, (20); ES-HRMS *m/z*: calcd for [M+1]$^+$ $C_{22}H_{20}NO_4S$ 394.1113; found 394.1108.

Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

*N-Benzenesulfonyl-3-(4-bromophenyl)-4,6-dimethoxyindole (**10**)*

This was prepared by general procedure (**A**) using 4,6-dimethoxy-3-(4-bromophenyl)indole **6** (2.50 g, 7.5 mmol), sodium hydride (0.30 g, 7.5 mmol, 60% dispersion in oil) and benzenesulfonyl chloride (1.33 g, 7.5 mmol) to give the indole **10** (2.49 g, 70%) as a white solid, mp 137-139 °C. ^{1}H NMR δ: 7.96 (2H, d, J = 8.7 Hz, sulfonyl ArH2″ and 6″), 7.56 (2H, m, sulfonyl ArH3″ and 5″), 7.49-7.54 (4H, m, ArH2′ 3′ 5′ and 6′), 7.25-7.48 (1H, m, sulfonyl ArH4″), 7.34 (1H, s, H2), 7.19 (1H, d, J = 1.8 Hz, H7), 6.33 (1H, d, J = 1.8 Hz, H5), 3.88 (3H, s, C4 OCH_3), 3.71 (3H, s, C6 OCH_3). ^{13}C NMR δ: 160.0 (C6), 154.0 (C4), 138.3 (C7a), 138.0 (ArC4′), 134.0 (sulfonyl ArC1″), 133.0 (sulfonyl ArC4″), 131.3 (ArC2′ and 6′), 130.9 (ArC3′ and 5′), 129.5 (sulfonyl ArC2″ and 6″), 127.0 (sulfonyl ArC3″ and 5″), 123.7 (ArC1″), 121.7 (C2), 121.4 (C3), 112.9 (C3a), 96.0 (C7), 90.0 (C5), 58.5 (C4 O$\underline{C}H_3$), 58.0 (C6 O$\underline{C}H_3$). CI-MS *m/z*: 474 ([M+1]$^{+}$ ^{81}Br 20%), 332 (15), 173 (30), 159 (75), 143 (100); EI-HRMS *m/z*: calcd for $C_{22}H_{18}NO_4S^{79}Br$ 471.0139; found 471.0126.

*N-Benzenesulfonyl-4,6-dimethoxy-3-(4-nitrophenyl)indole (**11**)*

This was prepared by general procedure (**A**) using 4,6-dimethoxy-3-(4-nitrophenyl)indole **7** (2.00 g, 6.7 mmol), sodium hydride (0.27 g 6.7 mmol) and benzenesulfonyl chloride (1.18 g, 6.7 mmol) to give the the indole **10** (1.78 g, 61%) as a white solid, mp 150-152 °C. ^{1}H NMR δ: 8.22 (2H, d, J = 9.0 Hz, ArH2′ and 6′), 7.93 (2H, d, J = 9.0 Hz, ArH3′ and 5′), 7.69 (2H, d, J = 8.7 Hz, sulfonyl ArH2″ and 6″), 7.59-7.45 (2H, m, sulfonyl ArH3″, 4″, and 5″), 7.19 (1H, d, J = 2.1 Hz, H7), 6.36 (1H, d, J = 2.1 Hz, H5), 3.90 (3H, s, C4 OCH_3), 3.79 (3H, s, C6 OCH_3); ^{13}C NMR δ: 159.8 (C6), 154.6 (C4), 146.9 (sulfonylArC1″), 141.1 (sulfonylArC1″), 138.1 (C7a) 137.7 (ArC4), 134.4 (sulfonylArC4″), 130.3 (ArC2′ and 6′), 129.6, (sulfonylArC3′ and 5′), 127.1 (ArC3′ and 5′), 123.1 (sulfonylArC2″ and 6″), 122.7 (C2), 112.3 (C3a), 95.6 (C7), 89.9 (C5), 56.6 (C4 O$\underline{C}H_3$), 55.4 (C6 O$\underline{C}H_3$). ES-MS *m/z* 439 ([M+1]$^{+}$, 100%); EI-HRMS *m/z*: calcd for $C_{22}H_{18}N_2O_6S$ 438.0885; found 438.0907.

*3-(4-Bromophenyl)-4,6-dimethoxy-N-(4'-methylphenylsulfonyl)indole (**19**)*

This was prepared by general procedure (**A**) using 4,6-dimethoxy-3-(4-bromophenyl)indole **6** (2.00 g, 6.0 mmol), sodium hydride (0.24 g, 6.0 mmol) and *p*-toluenesulfonyl chloride (0.19 g, 6.0 mmol) to give the indole **19** (2.20 g, 76%) as white solid, mp 138-140 °C. ^{1}H NMR δ: 7.78 (2H, d, J = 7.8 Hz, ArH2′ and H6′), 7.49 (2H, d, J = 9.0 Hz, tosylArH3″ and 5″), 7.39 (2H, d, J = 9.0 Hz, tosylArH2″ and 6″), 7.34 (1H, s, H2), 7.25 (2H, d, J = 7.8 Hz, Ar3H′ and 5′), 7.18 (1H, d, J = 1.8 Hz, H7), 6.32 (1H, d, J = 1.8 Hz, H5), 3.88 (3H, s, C4 OCH_3), 3.70 (3H, s, C6 OCH_3), 2.35 (3H, s, CH_3). ^{13}C NMR δ: 159.4 (C6), 154.6

(C4), 145.2 (tosylC1″), 137.5 (C7a), 135.1 (ArC4′), 133.0 (ArC4′), 131.3 (ArC2′ and 6′), 130.9 (ArC3′ and 5′), 130.1 (tosyl ArC2″ and 6″), 127.0 (tosyl ArC3″ and 5″), 125.0 (tosyl ArC4″), 123.4 (C3), 121.3 (ArC1′), 121.7 (C2), 112.8 (C3a), 95.4 (C7), 90.0 (C5), 56.1 (C4 OCH_3), 55.5, (C-6 OCH_3), 22.0 CH_3. EI-HRMS *m/z*: calcd for $C_{23}H_{20}NO_4S^{79}Br$ 485.0296; found 485.0293.

*3-(4-Bromophenyl)-4,6-dimethoxy-N-(p-nitrobenzenesulfonyl)indole (**20**)*

This was prepared by general procedure (**A**) using 4,6-dimethoxy-3-(4-bromophenyl)indole **6** (2.00 g, 6.0 mmol), sodium hydride (0.29 g, 6.0 mmol, 50% dispersion in oil) and *p*-nitrobenzenesulfonyl chloride (1.33 g, 6.0 mmol) to give the indole **20** (2.25 g, 73%) as yellow solid, mp 220-222 °C. ^{1}H NMR δ: 8.29 (2H, d, J = 8.7 Hz, Ar2H′ and 6′), 8.05 2H, d, J = 8.7 Hz, ArH3′ and 5′), 7.49 (2H, d, J = 6.6 Hz, sulfonylArH3″ and 5″), 7.37 (2H, d, J = 6.6 Hz, sulfonylAr2H″and 6″), 7.3 (1H, s, H2), 7.17 (1H, d, J = 1.8 Hz, H7), 6.36 (1H, d, J = 1.8 Hz, H5), 3.89 (3H, s, C4 OCH_3), 3.71 (3H, s, C6 OCH_3). ^{13}C NMR δ: 160.0 (C6), 155.0 (C4), 151.5 (sulfonylArC1″) 143.5 (ArC4′), 138.0 (C7a), 133.0 (ArC1′), 131.3 (ArC2′ and 6′), 131.0 (ArC3′ and 5′), 128.2 (sulfonylArC2″ and 6″), 125.0, (sulfonylArC4″), 124.8 (sulfonylArC3″ and 5″), 122.0 (C3), 121.1 (C2), 113.4 (C3a), 95.9 (C7), 90.1 (C5), 56.1 (C4 OCH_3), 55.4 (C4 OCH_3). CI-MS *m/z*: 519 ($[M+1]^+$, ^{81}Br, 100%), 455 (10), 332 (50), 236 (10); EI-HRMS *m/z*: calcd for $C_{22}H_{17}{}^{79}BrN_2O_6S$ 515.9990; found 515.9982.

*4,6-Dimethoxy-N-(p-nitrobenzenesulfonyl)-3-(4-nitrophenyl)indole (**21**)*

This was prepared by general procedure (**A**) using 4,6-dimethoxy-3-(4′-nitrophenyl)indole **7** (2.00 g, 6.7 mmol) sodium hydride (0.32 g, 6.7 mmol) and *p*-nitrobenzenesulfonyl chloride (1.48 g, 6.7 mmol) to give the indole **21** (2.17 g, 67%) as a pale yellow solid, mp190-193 °C. ^{1}H NMR δ: 8.34 (2H, d, J = 9.0 Hz, ArH2 and 6), 8.24 (2H, d, J = 8.7 Hz, sulfonylArH3 and 5), 8.10 (2H, d, J = 9.0 Hz, ArH3 and 5), 7.68 (2H, d, J = 8.7 Hz, sulfonylArH2 and 6), 7.26 (1H, s, H2), 7.18 (1H, d, J = 1.8 Hz, H7), 6.39 (1H, d, J = 1.8 Hz, H5), 3.91 (3H, s, C4 OCH_3), 3.73 (3H, s, C6 OCH_3). ^{13}C NMR δ: 160.1 (C6), 156.0 (C4), 146.1 (ArC4), 144.0 (ArC1), 141.0 (C7a), 148.0 (sulfonylArC4), 131.0 (ArC2 and 60, 128.1 (sulfonylArC2 and 6), 125.5 (ArC3 and 5), 125.0 (sulfonylArC1), 123.0 (C2), 122.0 (ArC2 and 6), 121.0 (C3), 113.0 (C3a), 96.0 (C7), 90.0 (C5), 58.0 (C4 OCH_3), 56.0 (C6 OCH_3). CI-MS *m/z* 484.0, ($[M+1]^+$, 100%), 420 (10), 299 (30); EI-HRMS *m/z*: calcd for $C_{22}H_{17}N_3O_8S$ 483.0736; found 483.0746.

Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

*N-Methanesulfonyl-4,6-dimethoxy-3-phenylindole (**22**)*

This was prepared by general procedure (**A**) using 4,6-dimethoxy-3-phenylindole **5** (2.00 g, 7.9 mmol) sodium hydride (0.32 g, 8.0 mmol) and methanesulfonyl chloride (0.90 g, 7.9 mmol) to give the indole **23** (1.96 g, 75%) as white solid, mp 140-142 °C. ^{1}H NMR δ: 7.57 (2H, d, J = 8.4 Hz, ArH2′ and 6′), 7.38-7.34 (3H, m, ArH3′, 4′, and 5′), 7.23 (1H, s, H2), 7.10 (1H, d, J = 2.1 Hz, H5), 6.41 (1H, d, J = 2.1 Hz, H7), 3.89 (3H, s, C4 O$\underline{C}H_3$), 3.76, (3H, s, C6 O$\underline{C}H_3$), 3.11 (3H, s, CH_3). ^{13}C NMR δ: 160.0 (C6), 155.0 (C4), 138.0 (C7a), 134.0 (ArC1′) 130.0 (ArC2′ and 6′), 128.0 (ArC3′ and 5′), 127.6 (ArC4′), 125.0 (C3), 122.0 (C2), 113.0 (C3a), 96.0, (C7), 90.0 (C5), 56.0, (C4 O$\underline{C}$H3), 55.6 (C6 O$\underline{C}H_3$), 40.0, $\underline{C}H_3$. CI-MS *m/z*: 332 ([M+1]$^+$, 45%), 270 (15), 132 (15), 103 (20), 71 (100); ES-HRMS *m/z*: calcd for [M+1]$^+$ $C_{17}H_{18}NO_4S$ 332.0957 found; 332.0959.

*3-(4-Bromophenyl)-N-methanesulfonyl-4,6-dimethoxyindole (**23**)*

This was prepared by general procedure (**A**) using 4,6-diemthoxy-3-(4′-bromophenyl)indole **6** (2.00 g, 6.0 mmol), sodium hydride (0.24 g, 6.0 mmol) and methanesulfonyl chloride (0.69 g, 6.0 mmol) to give the the indole **25** (1.72 g, 70%) as a white solid, mp 147-150 °C. ^{1}H NMR δ: 7.51 (2H, d, J = 9.0 Hz, ArH2′ and 4′), 7.43 (2H, d, J = 9.0 ArH3′ and 5′), 7.22 (1H, s, H2), 7.02, (1H, d, J = 2.1 Hz, H7), 6.40 (1H, d, J = 2.1 Hz, H5), 3.89 (3H, s, C4 OCH_3), 3.77, (3H, s, C6 OCH_3), 3.13, (s, Me). ^{13}C NMR δ: 160.0 (C6), 156.5 (C4), 138.0 (C7a), 134.0 (ArC4′) 130.5 (ArC2′ and 6′), 130.0 (ArC3′ and 5′), 124.0 (ArC1′), 123.0 (C3), 122.0 (C2), 112.0 (C3a), 96.0 (C7), 90.0 (C5), 55.0 (C4 O$\underline{C}H_3$), 54.5 (C6 O$\underline{C}H_3$), 42.0 CH_3. CI-MS *m/z*: 412 ([M+1]$^+$, ^{81}Br, 20%), 332 (15), 254(10), 113 (25), 97(30), 81 (100); ES-HRMS *m/z*: calcd for [M+1]$^+$ $C_{17}H_{17}NO_4S^{79}Br$ 410.0062; found 410.0061.

*N-Methanesulfonyl-4,6-dimethoxy-3-(4-methoxyphenyl)indole (**24**)*

This was prepared by general procedure (**A**) using 4,6-dimethoxy-3-(4′-methoxyphenyl)indole **4** (2.00 g, 7.0 mmol), sodium hydride (0.28 g, 7.0 mmol) and methane sulfonyl chloride (0.81 g, 7.1 mmol) to give the indole **27** (1.99 g, 79%) as white solid, mp 145-148 °C. ^{1}H NMR δ: 7.50 (2H, d, J = 9.0 Hz, ArH2′ and 6′), 7.17 (1H, s, H2), 7.10 (1H, d, J = 2.1 Hz, H5), 6.93 (2H, d, J = 9.0 Hz, ArH3′ and 5′), 6.40 (1H, d, J = 2.1 Hz, H7), 3.88 (3H, s, C4 OCH_3), 3.85 (3H, s, C6 OCH_3), 3.77, (3H, s, ArC4 OCH_3), 3.09 (3H, s, CH_3). ^{13}C NMR δ: 159.9 (ArC4′), 158.5 (C6), 155.0 (C4), 138.0 (C7a), 132.0 (ArC2′ and 6′) 126.0 (ArC1′) 124.0 (C3), 121.0 (C2), 114.0 (ArC3′ and 5′), 110.0 (C3a) 96.0 (C7), 90.0 (C5), 56.0 (C4 O$\underline{C}H_3$), 55.6 (C6 O$\underline{C}H_3$) 55.7, (ArC4 O$\underline{C}H_3$), 40.0, ($\underline{C}H_3$). CI-MS *m/z*: 362 ([M+1]$^+$, 90%), 340 (15),

284 (30), 149 (15), 113 (20), 97 (25), 81 (100); EI-HRMS *m/z*: calcd for $C_{18}H_{19}NO_5S$ 361.0983; found 361.0989.

*N-Acetyl-4,6-dimethoxy-3-(4-methoxyphenyl)indole (**30**)*

To a solution of 4,6-dimethoxy-3-(4-methoxyphenyl)indole **4** (0.50g, 1.80 mmol), acetyl chloride (0.14 g, 1.80 mmol), and potassium hydroxide (0.10 g, 1.80 mmol) in CH_2Cl_2 (15 mL), was added a catalytic amount of the phase transfer catalyst tetrabutylammonium hexafluorophosphate (20 mol%) in CH_2Cl_2 (25 mL) under a nitrogen atmosphere. The reaction mixture was stirred for 12 h before water (30 mL) was added and the organic layer separated. The solvent was then removed under reduced pressure, and the oily liquid subjected to flash chromatography (ethyl acetate:hexane 2:8) to yield the indole **31** (0.37 g, 65%) as a white solid, mp 145-158 °C. ^{1}H NMR δ: 7.77 (1H, d, J = 1.8 Hz, H7), 7.51 (2H, d, J = 9.0 Hz, Ar2′ and 6′), 7.10 (1H, s, H2), 6.94, (2H, d, J = 9.0 Hz, Ar3′ and 5′), 6.40 (1H, d, J = 1.8 Hz, H5), (3.89, 3.85, and 3.75, 3 x OCH_3), 2.61 (3H, s, $COCH_3$). ^{13}C NMR δ: 169.1 (C=O), 159.8 (ArC4′), 159.0 (C6), 154.4 (C4), 138.4 (C7a), 130.7 (ArC2′ and 6′) 127.0 (ArC1′),124.2 (C3), 120.4 (C2) 113.3 (ArC3′ and 5′), 112.8 (C3a) 95.9 (C7) 93.1 (C5), (55.9, 55.5, and 55.4 3 x OCH_3), 24.4 (CO<u>C</u>H_3). CI-MS *m/z*: 326 ([M+1]$^+$, 100%), 283 (20), 268 (10). EI-HRMS *m/z*: calcd for $C_{19}H_{19}NO_4$ 325.1314; found 325.1398.

*N-Acetyl-4,6-dimethoxy-3-(4′-nitrophenyl)indole (**31**)*

To a solution of 4,6-dimethoxy-3-(4-nitrophenyl)indole **7** (0.50 g, 1.70 mmol), acetyl chloride (0.13 g, 1.70 mmol), and potassium hydroxide (0.10 g, 1.8mmol) in CH_2Cl_2 (15 mL) was added a catalytic amount of phase transfer catalyst tetrabutylammonium hexafluorophosphate (20 mol%) in CH_2Cl_2 (25 mL) under a nitrogen atmosphere. The reaction mixture was stirred for 12 h. To the reaction mixture water was added, and the organic layer separated. The solvent was removed under reduced pressure, and the oily liquid then purified by flash chromatography (ethylacetate:hexane, 2:8) to yield the indole **32** (0.32 g, 57%) as a white solid, mp 180-182 °C. ^{1}H NMR δ: 8.27 (2H, d, J = 9.0 Hz, ArH2′ and 6′), 7.87 (2H, d, J = 9.0 Hz, ArH3′ and 5′), (1H, s, H2), 7.70 (1H, d, J = 1.8 Hz, H7), 6.53 (1H, d, J = 1.8 Hz, H5), 3.84 (3H, s, C4 OCH_3), 3.79 (3H, s, C6 OCH_3), 2.68 (3H, s, acetyl CH_3). ^{13}C NMR δ: 160.0 (C6), 154.0 (C4), 149.0 (C=O), 142.0 (ArC4′), 139.0 (C7a), 131.0 (ArC2′ and 6′), 123.0 (ArC3′ and 5′), 122.0 (C2), 121.8 (C3), 112.0 (C3a), 97.0 (C7), 93.0 (C5), 56.0 (C4 OCH_3), 55.0 (C6 OCH_3), 26.0 (CO<u>C</u>H_3). CI-MS *m/z*: 341 ([M+1]$^+$, 100%); EI-HRMS *m/z*: calcd for $C_{18}H_{16}N_2O_5$ 340.1059; found 340.1072.

Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

*N-tert-Butylcarbamate-4,6-dimethoxy-3-(4-methoxyphenyl)indole (**34**)*

To a solution of 4,6-dimethoxy-3-(4′-methoxyphenyl)indole **4** (0.50 g, 1.80 mmol) and di-*tert*-butyldicarbonate (0.37 g, 1.80 mmol) in CH_2Cl_2 (25 mL) was added a catalytic amount of DMAP and the reaction stirred under a nitrogen atmosphere for thirty min. To the reaction mixture was added water, the organic layer separated, the solvent removed under reduced pressure, and the solid then recrystallised from methanol to yield the indole **35** (0.68 g, 99%), as a white solid, mp 151-153 °C. ^{1}H NMR δ: 8.22 (1H, d, J = 1.8 Hz, H7), 7.51 (2H, d, J = 9.0 Hz, ArH2′ and 6′), 6.92 (2H, d, J = 9.0 Hz, ArH3′ and 5′), 6.47 (1H, d, J = 1.8 Hz, H5), 6.35 (d, J = 2.1 Hz), 3.88 (3H, s, ArC4 OC$\underline{H}_3$), 3.83 (3H, s, C4 OC$\underline{H}_3$), 3.74 (3H, s, C6 OC$\underline{H}_3$). ^{13}C NMR δ: 159.9 (C=O), 159.8 (C6), 154.3 (C4), 150.0 (C7a), 130.8 (ArC2′ and 6′), 127.4 (ArC1′), 121.1 (C2), 113.2 (ArC3′ and 5′), 106.8 (C3a), 95.0 (C7), 91.7 (C5), 84.0 ($CO_2\underline{C}(CH_3)$), (55.8, 55.4, and 55.4, 3 x O$\underline{C}H_3$), 28.4, (3 x C, *t*-BOC). CI-MS *m/z*: 383 ($[M^+]^+$, 90%), 370 (15), 327 (100), 283 (30), 268 (10); ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{22}H_{26}NO_5$ 384.1811; found 384.1807.

General procedure (B) for the synthesis of bisindoles: oxidative dimerisation:

Solid thallium(III) trifluoroacetate (0.53 mmol) was mixed with the solid protected indole (1.06 mmol) under a nitrogen atmosphere. Dry acetonitrile (7 mL) was added and the resultant mixture cooled to 0 °C. Boron trifluoride diethyletherate (8.0 mmol) was then added slowly into the reaction mixture, and allowed to stir for 1h. The reaction mixture was poured into water and extracted with CH_2Cl_2 (5 x 50 mL). The combined organic layers were concentrated to give a dark residue.

*2,2′-Bi-[N-benzenesulfonyl-4,6-dimethoxy-3-(4-methoxyphenyl)]indole (**12**)*

This was prepared by general procedure (**B**) using *N*-benzenesulfonyl-3-(4-methoxyphenyl)-4,6-dimethoxyindole **8** (0.50 g, 1.18 mmol), thallium(III) trifluoroacetate (0.32 g, 0.55 mmol) and boron trifluoride diethyletherate (1.12 g, 7.9 mmol) The residue was recrystallised from CH_2Cl_2/ methanol to give the indole **12** (0.35 g, 70%) as a white solid, mp 242-246 °C. ^{1}H NMR δ: 7.53 (2H, d, J = 6.0 Hz, sulfonylArH2″ and 6″), 7.46 (1H, t, sulfonylArH4″) 7.30 (2H, t, sulfonylArH3″ and 5″), 7.03 (2H, d, J = 12.0 Hz, ArH2′ and 6′), 7.02 (1H, d, J = 1.8 Hz, H7), 6.65 (2H, d, J = 12.0 Hz, ArH3′ and 5′), 6.25 (1H, d, J = 1.8 Hz, H5), 3.76 (3H, s, C4 OCH_3), 3.75 (3H, s, C6 OCH_3), 3.56 (1H, s, ArC4 OCH_3). ^{13}C NMR δ: 159.3 (ArC4′), 159.0 (C6), 154.5 (C4), 139.9 (C7a), 139.0 (sulfonylArC1″), 133.9 (ArC4), 131.8 (sulfonylArC2″ and 6″), 129.5 (sulfonylArC3″ and 5″), 127.0 (C2), 126.7 (ArC2′ and 6′), 126.3 (C3), 126.5 (ArC1′), 124.0 (C3a), 122.0 (C2), 112.5 (C3a), 112.0 (ArC3′ and 5′), 94.5 (C5), 92.0 (C7), 56.0

(C4 OCH_3), 55.0 (C6 OCH_3). ES-MS *m/z*: 845 ($[M+1]^+$, 35%), 797.2 (10), 704.2 (15), 625 (5), 552.3 (15), 475.4 (10), 411.2 (15), 332.3 (50%), 304.3 (100), 272.3 (50), 244.2 (80), 214.0 (40), 157.9 (75), 141.8 (45), 105.9 (90); ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{46}H_{41}N_2O_{10}S_2$ 845.2203; found 845.2209.

*2,2′-Bi-(N-benzenesulfonyl-4,6-dimethoxy-3-phenyl)indole (**13**)*

This was prepared by general procedure (**B**) using *N*-benzenesulfonyl-3-phenyl-4,6-dimethoxyindole **9** (0.50 g, 1.3 mmol), thallium(III) trifluoroacetate (0.35 g, 0.65 mmol) and boron trifluoride diethyletherate (1.12 g, 7.9 mmol). Recrystallisation from CH_2Cl_2/ methanol gave the indole **13** (0.34 g, 69% yield) as a white solid, mp 224-226 °C. ^{1}H NMR δ: 7.57-7.01 (10H, m, sulfonylArH2″, 3″, 4″ and 6″, and ArH2′, 3′, 4′, 5′, and 6′), 7.00 (1H, d, J = 1.8 Hz, H7), 6.22 (1H, d, J = 1.8 Hz, H5), 3.76 (3H, s, C4 OCH_3), 3.53 (3H, s, C6 OCH_3). ^{13}C NMR δ: 159.3 (C6), 154.9 (C4), 139.0 (C7a), 139.5 (sulfonylArC1″), 133.8 (C3), 133.4 (sulfonylArC4″), 130.7 (sulfonylArC2″ and 6″), 129.1 (sulfonylArC3″ and 5″), 129.0 (ArC4′), 128.5 (ArC4′), 128.0 (C2), 127.5 (ArC2′ and 6′), 127.2 (ArC3′ and 5′), 126.9 (ArC1′), 122.3 (C3a), 95.5 (C7), 90.8 (C5), 55.9 (C4 OCH_3), 55.4 (C6 OCH_3). ES-MS *m/z*: 785.0 ($[M^+]^+$, 30%), 746.2 (20), 649.4 (25), 552.2 (20), 413, 304, 272, 244 (100%); ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{44}H_{37}N_2O_8S_2$ 785.1991; found 785.1978.

*2,2′-Bi-[N-benzenesulfonyl-3-(4-bromophenyl)-4,6-dimethoxy]indole (**14**)*

This was prepared using general procedure (**B**) using thallium(III) trifluoroacetate (0.29 g, 0.53 mmol), *N*-benzenesulfonyl-3-(4-bromophenyl)-4,6-dimethoxyindole **10** (0.50 g, 1.06 mmol) and boron trifluoride diethyletherate (1.12, 7.90 mmol). The residue was recrystallised from CH_2Cl_2/methanol to give the indole **14** (0.37 g, 74%) as a white solid, mp 263-265 °C. ^{1}H NMR δ: 7.90 (2H, d, J = 9.0 Hz, sulfonylArH2″ and 6″), 7.55-7.34 (7H, m, sulfonylArH3″ and 4″, 5″ and ArH2′, 3′, 5′, and 6′), 7.19 (1H, d, J = 1.8 Hz, H7), 6.34 (1H, d, J = 1.8 Hz, H5), 3.88 (3H, s, C4 OCH_3), 3.72 (3H, s, C6 OCH_3). ^{13}C NMR δ: 159.3 (C6), 154.5 (C4), 137.8 (C7a), 137.4 (ArC4′), 134.1 (sulfonylArC4′), 132.8 (C2), 131.2 (sulfonylArC2″ and 6″), 130.7 (sulfonylArC3″ and 5″), 129.9 (ArC1′), 129.4 (ArC1′), 129.2 (ArC2′ and 6′), 126.8 (ArC3′ and 5′), 123.5 (C3), 113.0 (C3a), 95.3 (C7), 89.9 (C5), 56.0 (C4 OCH_3), 55.3 (C6 OCH_3). ES-MS *m/z*: 942.7 ($[M+1]^+$, ^{81}Br, 30%), 761.3 (10), 488.0 (20), 392.2 (30), 338.4 (30), 316.3 (35), 314.2 (70), 288.3 (60), 270.2 (50), 244.2 (45), 174.8 (30), 166.9 (40), 144.9 (70), 125.8 (80), 103.9 (100); ES-HRMS *m/z*: calc for $[M+1]^+$ $C_{44}H_{35}N_2O_8{}^{79}Br_2S_2$ 941.0202; found 941.0254.

Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

*2,2′-Bi-[4,6-dimethoxy-3-(4-methoxyphenyl)]indole (**16**)*

A solution of 2,2′-bi[*N*-benzenesulfonyl-4,6-dimethoxy-3-(4-methoxyphenyl)]indole **12** (0.30 g, 0.3 mmol) in dioxane (20 mL) with 20% aqueous sodium hydroxide (5 mL) was heated at reflux for 4 h. The reaction mixture was poured onto cold water (60 mL) and partitioned with CH_2Cl_2 (3 x 50 mL). The solvent was evaporated under vacuum and the residue recrystallised from CH_2Cl_2/methanol to give the indole **16** (0.03 g, 15%) as a pale yellow solid, mp 197-200 °C. ^{1}H NMR δ: 11.2 (1H, s, NH), 6.93 (2H, d, J = 9.0 Hz, ArH2′ and 6′), 6.59 (2H, d, J = 9.0 Hz, ArH3′ and 5′), 6.41 (1H, d, J = 1.8 Hz, H5), 6.10 (1H, d, J = 1.8 Hz, H7), 3.74 (3H, s, C4 OCH_3), 3.66 (3H, s, C6 OCH_3), 3.60 (3H, s, ArC4′ OCH_3). ^{13}C NMR (DMSO d_6) δ: 158.3 (ArC4′), 158.2 (C6′), 154.3 (C4′), 138.0 (C7a), 132.0 (ArC2′ and 6′), 128.5 (ArC1′), 124.6 (C2), 116.3 (C3), 112.2 (ArC3′ and 5′), 112.0 (C3a), 92.0 (C5), 87.2 (C7), 55.9 (C4 O$\underline{C}H_3$), 55.6 (C6 O$\underline{C}H_3$), 55.4 (ArC4 O$\underline{C}H_3$); CI-MS *m/z*: 564([M+1]$^+$, 60%), 338 (100), 285 (10), 197 (5), 153 (10), 137 (25), 121 (30), 97 (30); ES-HRMS *m/z*: calcd [M+1]$^+$ $C_{34}H_{33}N_2O_6$ 564.2260; found 564.2259.

*2,2′-Bi-(4,6-dimethoxy-3-phenyl)indole (**17**)*

A solution of 2,2′-bi-(*N*-benzenesulfonyl-4,6-dimethoxy-3-phenyl)indole **13** (0.30 g, 0.4 mmol) in dioxane (20 mL) with 20% aqueous sodium hydroxide (5 mL) was heated at reflux for 4 h. The reaction mixture was poured into cold water and partitioned with CH_2Cl_2 (3 x 50 mL). The solvent was evaporated and the residue recrystallised from CH_2Cl_2/ methanol yielding the indole **17** (0.03 g, 15%) as a pale yellow solid mp 174-178 °C. ^{1}H NMR δ: 10.00 (1H, s, NH), 7.21-7.18 (2H, m, ArH2′ and 6′), 7.09-7.06 (3H, m, ArH3′, 4′, and 5′), 6.49 (1H, d, J = 3.0 Hz, H7), 6.18 (1H, d, J = 3.0 Hz, H5), 3.77 (3H, s, C4 OC$\underline{H}_3$), 3.66 (3H, s, C6 OCH_3); ^{13}C NMR δ: 158.0 (C6), 155.0 (C4), 138.0 (C7a), 136.0 (C3), 131.0 (ArC4′), 126.7 (ArC2′ and 6′), 125.2 (ArC3′ and 5′), 125.0 (ArC1′), 118.0 (C2), 112.0 (C3a), 92.0 (C7), 86.2 (C5) 55.0 (C4 OCH_3), 54.5 (C6 OCH_3). ES-MS *m/z*: 504.2 ([M+1]$^+$, 60%), 338.4 (25), 144.9 (20), 105.9 (45), 103.9 (100), 71.0 (25); ES-HRMS *m/z*: calcd for [M+1]$^+$ $C_{32}H_{29}N_2O_4$ 504.2049; found 504.2054.

*2′,2-Bi-[3-(4-bromophenyl)-4,6-dimethoxy]indole (**18**)*

This was prepared by general procedure (**B**) using 4,6-dimethoxy-3-(4-bromophenyl)indole **6** (0.20 g, 0.6 mmol), thallium(III) trifluroacetate (0.16 g, 0.3 mmol) and boron trifluoride diethyletherate (0.43 g, 3.0 mmol). The residue was subjected to flash silica gel column chromatography (50:50 hexane:ethyl acetate) yielding the indole **18** (0.04 g, 20%) as a pale yellow solid, mp 195-197 °C. ^{1}H NMR δ: 7.85

(2H, d, J = 7.5 Hz, ArH3′ and 5′), 7.21 (2H, d, J = 7.5 Hz, ArH2′ and 6′), 7.28 (1H, d, J = 1.8 Hz, H7), 6.32 (1H, s, H5), 3.84 (3H, s, C4 OCH_3), 3.49 (3H, s, C6 OCH_3). ^{13}C NMR ($CDCl_3$) δ: 153.5 (C-6 and C-4), 140.0 (C-7a), 133.0 (C-2), 132.8 (C-3), 130.4 (ArC-4′), 128.0 (ArC2′ and 6′), 127.8 (ArC2′ and 5′), 126.0 (C-3a), 121.6 (ArC1′), 94.3 (C-7), 92.0 (C-5), 57.8 (C-4-O$\underline{C}H_3$), 56.0 (C-6-O$\underline{C}H_3$). ES-MS *m/z*: 663 ($[M+1]^+$, ^{80}Br 60%), 607 (10), 468.5 (15), 332 (40), 316 (50), 304 (50), 288 (70) 244 (100); ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{32}H_{27}N_2O_4{}^{79}Br_2$ 661.0338; found 661.0331.

*2,2′-Bi-[3-(4-bromophenyl)-(N-p-methylbenzenesulfonyl)-4,6-dimethoxy-]indole (**25**)*

This was prepared by general procedure (**B**) using *N*-(4-methylphenylsulfonyl)-3-(4-bromophenyl)-4,6-dimethoxyindole **19** (0.50 g, 1.0 mmol), thallium(III) trifluoroacetate (0.28 g 0.50 mmol) and boron trifluoride diethyletherate (1.12 g, 7.9 mmol). Recrystallisation from CH_2Cl_2/ methanol gave the indole **25** (0.36 g 73%) as a yellow solid, mp 219 °C. ^1H NMR δ: 7.45 (2H, d, J = 8.4 Hz, sulfonylArH3″ and 5″), 7.17 (2H, d, J = 8.7 Hz, ArH2′ and 6′), 7.14, (2H, d, J = 8.7 Hz, ArH3′ and 5′), 7.04 (1H, d, J = 2.1 Hz, H7), 6.86, (2H, d, J = 8.4 Hz, sulfonylArH2″ and 6″), 6.26 (1H, d, J = 2.1 Hz, H5), 3.79 (3H, s, C6 OCH_3), 3.57 (3H, s, C4 OCH_3), 2.36 (3H, s, CH_3). ^{13}C NMR δ: 159.6 (C6), 154.8 (C4), 144.7 (sulfonylArC4′), 138.7 (C7a), 136.7 (ArC4′), 132.9 (ArC1′), 132.2 (sulfonylArC2″ and 6″), 130.1 (ArC2′ and 6′), 129.8 (ArC3′ and 5′), 127.2 (sulfonylArC3″ and 5″), 126.0 (sulfonylArC1′), 124.0 (C2), 121.4 (C3), 112.3 (C3a), 95.4 (C7), 90.8 (C5), 55.8 (C4 OCH_3), 55.3 (C6 OCH_3), 21.8 (Me). ES-MS *m/z*: 970.7 ($[M^+1]^+$, ^{81}Br, 20%), 501.7 (20), 304.3 (30), 288.2 (35), 272.2 (40), 244.3 (100), 225.1 (45), 103.7 (80). ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{46}H_{37}N_2O_2S_2{}^{79}Br_2$ 969.0515; found 969.0524.

*2,2′-Bi-[3-(4-bromophenyl)-4,6-dimethoxy-(N-p-nitrobenzenesulfonyl)]indole (**26**)*

This was prepared by general procedure (**B**) using *N*-(*p*-nitrobenzenesulfonyl)-3-(4-bromophenyl)-4,6-dimethoxyindole **20** (0.50 g, 1.1 mmol), thallium(III) trifluoroacetate (0.30 g, 0.55 mmol), and boron trifluoride diethyletherate (1.12 g, 7.9 mmol). Recrystallisation from CH_2Cl_2/methanol gave the indole **26** (0.33 g, 67%) as a yellow solid, mp 232-235 °C. ^1H NMR δ: 8.14 (2H, d, J=8.7 Hz, ArH3 and 5), 7.48 (2H, d, J=9.0 Hz, ArH2 and 6), 7.20 (2H, d, J = 8.7 Hz, sulfonylArH2″ and 6″), 7.02 (1H, d, J = 1.8 Hz, 7H), 7.03 (2H, d, J=9.0 Hz, sulfonylArH3″ and 5″), 6.39 (1H, d, J = 1.8 Hz, H4), 3.82 (3H, s, C4 OCH_3), 3.63 (s, C6 OCH_3); ^{13}C NMR δ: 160.6 (C6), 155.2 (C4), 150.3 (sulfonylArC4), 144.4 (sulfonylArC1), 139.1 (C7a), 132.3 (ArC1), 132.2 (sulfonyl ArC3and 5), 130.4 (ArC2 and 6), 130.0 (C2), 127.9 (sulfonylArC2 and 6), 124.51 (ArC3 and 50, 122.9 (ArC4), 122.0 (C30, 112.4 (C3a), 96.0 (C7), 90.8 (C5), 56.0 (C4 OCH_3), 55.4 (C6 OCH_3 and ArC4 OCH_3). ES-MS *m/z*: 1031 ($[M+1]^+$, ^{81}Br,

Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

100%) 887.3 (10), 757.9 (30), 705.9 (60), 662.0 (50), 629.8, (50), 585.9 (80), 564.0 (95), 498.8 (70), 451.6, (45), 391.6 (100); ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{44}H_{33}N_4O_{12}S_2{}^{79}Br_2$ 1030.9903; found 1030.9919.

*2,2′-Bi-(N-methanesulfonyl-4,6-dimethoxy-3-phenyl)indole (**27**)*

This was prepared by general procedure (**B**) using *N*-methanesulfonyl-3-phenyl-4,6-dimethoxyindole **22** (0.50 g, 1.5 mmol) thallium(III) trifluoroacetate (0.41 g, 0.75 mmol) and boron trifluoride diethyletherate (1.12 g, 7.9 mmol). Recrystallisation from CH_2Cl_2/ methanol gave the indole **27** (0.33 g, 67%) as a white solid, mp 229-231 °C. ^{1}H NMR δ: 7.25-7.16 (4H, m, ArH2′, 3′, 4′, 5′, and 6′), 7.11 (1H, d, J = 3.0 Hz, H5), 6.32 (1H, d, J = 3.0 Hz, H7), 3.87 (3H, s, C4 OCH_3), 3.59 (3H, s, C6 OCH_3), 2.90 (3H, s, CH3). ^{13}C NMR δ: 160.0 (C7), 155.0 (C4), 148.0 (C7a), 134.0 (ArC1′), 130.0 (ArC2′ and 6′), 127.3 (C3), 127.1 (ArC3′ and 5′), 127.0 (C2), 126.5 (ArC4′), 113.0 (C3a), 95.0 (C7), 90.0 (C5), 56.0 (C4 OCH_3), 55.6 (C6 OCH_3), 40.0 (Me). ES-MS *m/z* 661.1 ($[M+1]^+$, 50%), 348.1 (20), 132.8 (18), 105.9 (30), 103.9 (40), 71.0 (100); ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{34}H_{33}N_2O_8S_2$ 661.1678; found 661.1674.

*2,2′-Bi-[3-(4-bromophenyl)-N-methanesulfonyl-4,6-dimethoxy]indole (**28**)*

This was prepared by general procedure (**B**) using *N*-methanesulfonyl-3-(4-bromophenyl)-4,6-dimethoxyindole **23** (0.50 g, 1.2 mmol), thallium(III) trifluoroacetate (0.33 g, 0.6 mmol) and boron trifluoride diethyletherate) (1.12 g, 7.9 mmol). Recrystallisation from CH_2Cl_2/ methanol gave the indole **28** (0.40 g, 80%) as a white solid, mp 179-182 °C. ^{1}H NMR δ: 7.31 (2H, d, J = 9.0 Hz, ArH2 and 6), 7.08 (1H, d, J = 3.0 Hz, H5), 7.02 (2H, d, J = 9.0 Hz, ArH3 and 5), 6.33 (1H, d, J = 3.0 Hz, H7), 3.89 (3H, s, C4 OCH_3), 3.61 (3H, s, C6 OCH_3), 3.06 (3H, s, CH_3). ^{13}C NMR δ: 160.2 (C6), 155.0 (C4), 138.0 (C7a), 132.7 (ArC4′), 132.0 (ArC3′ and 5′), 130.3 (ArC2′ and 6′), 126.3 (ArC1′), 123.3 (C2), 121.4 (C3), 112.6 (C3a), 95.6 (C7), 89.9 (C5), 56.8 (C4 O$\underline{C}H_3$), 56.0 (C6 O$\underline{C}H_3$), 40.0 ($\underline{C}H_3$). ES-MS *m/z*: 817.9 ($[M+1]^+$, ^{81}Br, 15%), 466.8 (25), 464.7 (10), 343.8 (10), 341.4 (15), 338.4 (30), 275.9 (15), 204.9 (20), 144.9 (20), 132.8 (25), 105.9 (40), 103.9 (100),71.0 (35), 60.1 (50); ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{34}H_{31}N_2O_8S_2{}^{79}Br_2$ 816.9889; found 816.9863.

*2,2′-Bi-[N-methanesulfonyl-4,6-dimethoxy-(4-methoxyphenyl)]indole (**29**)*

This was prepared by general procedure (**B**) using *N*-methanesulfonyl-3-(4-methoxyphenyl)-4,6-dimethoxyindole **24** (0.50 g, 1.3 mmol), thallium(III) trifluoroacetate (0.36 g 0.65 mmol), boron trifluoride diethyletherate (1.12 g, 7.9 mmol). Recrystallisation from CH_2Cl_2/methanol gave the indole

29 (0.38 g, 76%) as a white solid, mp 219-222 °C. ^{1}H NMR δ: 7.18 (2H, d, J = 9.0 Hz, ArH2′ and 6′), 7.12 (1H, d, J = 1.8 Hz, H7), 6.74, (2H, d, J = 9.0 Hz, ArH3′ and 5′), 6.33, (1H, d, J = 1.8 Hz, H5), 3.88 (3H, s, C4 OCH_3), 3.74 (3H, s, C6 OCH_3), 3.62 (3H, s, ArC4 OCH_3), 2.93 (3H, s, CH_3); ^{13}C NMR δ: 159.9 (ArC4′), 158.5 (C6), 155.0 (C4), 138.0 (C7a), 132.0 (ArC2′ and 6′), 126.0 (ArC1′), 123.8 (C3), 123.4 (C2), 113.5 (C3a), 113.0 (Ar3′ and 5′), 96.0 (C7), 90.0 (C5), 56.0 (C4 O$\underline{C}H_3$), 55.7 (C6 O$\underline{C}H_3$), 55.6 (ArC4 O$\underline{C}H_3$), 40.0 ($\underline{C}H_3$); ES-MS *m/z*: 721.2 ([M+1]$^+$, 40%), 547.4 (15), 503.9 (10), 376.1 (20), 360.4 (25), 338.4 (70), 304.2, 244.1, 103.9, (50), 71.0 (50), 60.1 (100); ES-HRMS *m/z*: calcd for [M+1]$^+$ $C_{36}H_{37}N_2O_{10}S_2$ 721.1889; found 721.1883.

*2,2′-Bi[N-acetyl-4,6-dimethoxy-3-(4-nitrophenyl)indole (**35**)*

This was prepared by general procedure (**B**) using *N*-acetyl-4,6-dimethoxy-3-(4-nitrophenyl)indole **32** (0.20 g, 0.6 mmol), thallium(III) trifluroacetate (0.16 g, 0.3 mmol) and boron trifluoride diethyletherate (1.02 mL, 7.2 mmol). The residue was subjected to flash silica gel column chromatography (70:30 hexane:ethylacetate) yielding the indole **36** (0.06 g, 30%) as a pale yellow solid, mp 179-181 °C. ^{1}H NMR δ: 8.20 (2H, d, J = 9.0Hz, ArH3′ and 5′), 7.61 (1H, d, J = 2.1Hz, H7), 7.57 (1H, d, J = 9.0 Hz, ArH2′ and 6′), 6.36 (1H, d, J = 2.1 Hz, H5), 3.89 (3H, s, C4 OCH_3), 3.70 (3H, s, C6 OCH_3), 2.59 (3H, s, acetyl). ^{13}C NMR δ: 171.0 (C=O), 163.9 (C6), 157.8 (C4), 147.5 (ArC1′), 146.1 (ArC4′), 142.3 (C7a), 126.3 (ArC2′ and 6′), 124.0 (ArC3′ and C5′), 122.5 (C2), 104.0 (C3a), 96.5 (C7), 96.0 (C5), 56.0 (C6 OCH_3), 55.7 (C4 OCH_3), 26.7 (CO$\underline{C}H_3$). EI-MS *m/z* 689 ([M+1]$^+$, 7%), 663 (100).

*2-(4,6-Dimethoxy-3-(4-nitrophenyl)-N-trifluoroacetyl-1H-indol-7-yl)-4,4′,6,6′-tetramethoxy-3,3′-bi(4-nitrophenyl)-N,N′-di(trifluoroacetyl)-1H,1′H-7,7′-biindole (**36**)*

This was prepared by general procedure (**B**) using thallium(III) trifluoroacetate (0.14 g, 0.25 mmol), *N*-trifluoro-4,6-dimethoxy-3-(4′-nitrophenyl)-1-trifluoroacetateindole **34** (0.20 g, 0.50 mmol) and boron trifluoride diethyletherate (0.29 g, 2.0 mmol). The residue was subjected to flash silica gel column chromatography (60:40 hexane:ethyl acetate) yielding the trimer **37** (0.70 g, 35%) as a yellow solid, mp 165-168 °C. ^{1}H NMR δ: 8.24 (2H, d, J = 5.1 Hz, ArH2′ and 6′), 8.21 (2H, d, J = 5.1 Hz, ArH2″ and 6″), 7.94 (2H, d, J = 5.1 Hz, ArH2 and 6), 7.66 (2H, d, J = 4.8 Hz, ArH3′ and 5′) 7.55 (2H, d, J = 4.8 Hz, ArH3″ and 5″), 7.21 (1H, s, H2″), 7.12 (2H, d, J = 4.8 Hz, ArH3 and 5), 6.95 (1H, s, H2′), 6.73, (1H, s, H5″), 6.66 (1H, s, H5), 6.44 (1H, s, H5′), 3.95 (C4 OCH_3″), 3.92 (C4 OCH_3), 3.84 (C6 OCH_3″), 3.81 (C4 OCH_3′) 3.79 (C6 OCH_3), 3.72 (C6 OCH_3′). ^{13}C NMR δ: 160.2 (C6′), 157.4 (C6″), 156.8 (C6), 156.6 (C4′), 154.8 (C4″), 154.0 (C4), 147.4 (ArC4′), 147.3 (ArC4″), 146.4 (ArC4), 142.0 (ArC1′), 141.1

Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

(ArC1″), 140.0 (ArC1), 137.2 (C7a″), 137.2 (C7a), 137.0 (C7a′), 130.4 (ArC2′ and 6′, ArC2′ and 6″, and ArC2 and 6), 128.0 (C2), 124.6 (C3″), 124.3 (C3′), 123.0 (ArC3′ and 5′ and ArC3″ and 5″), 122.4 (ArC3 and 5), 121.9 (C2″), 121.3 (C2′), 121.0 (C3), 114.2 (C3a″), 113.1 (C3a′), 112.8 (C3a), 106.2 (C7″), 105.5 (C7), 100.2 (C7′), 94.5 (C5″), 92.6 (C5), 91.8 (C5′), 57.2 (C4 O$\underline{C}H_3$″), 57.1 (C4 O$\underline{C}H_3$), 56.0 (C6 O$\underline{C}H_3$′), 55.6 (C4 O$\underline{C}H_3$′), 55.5 (C6 O$\underline{C}H_3$″), 55.3 (C6 O$\underline{C}H_3$). ES-MS *m/z*: 1179.2 ($[M+1]^+$, 25%), 1082.3 (20), 986.3 (30), 416.2 (20), 400.3 (20), 338.4 (30), 313.2 (10), 218.9 (30), 179.0 (50), 104.0 (100); ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{54}H_{36}N_6O_{15}F_9$ 1179.2095; found 1179.2089.

*4,6-Dimethoxy-2-[4′,6′-dimethoxy-3′-(4-nitrophenylindol)-7′-yl]-3-[(4-nitrophenyl)indole (**37**)*

This was prepared by general procedure (**B**) using 4,6-dimethoxy-3-(4′-nitrophenyl)indole **6** (0.20 g, 0.67 mmol), thallium(III) trifluoroacetate (0.18 g, 0.34 mmol), and boron trifluoride diethyletherate (0.47 g, 3.3 mmol). The crude residue was subjected to flash silica gel column chromatography (70:30, hexane:ethylacetate) to give the indole **38** (0.04 g, 20%) as a yellow solid, mp 245-248 °C. ^{1}H NMR δ: 8.56 (1H, s, NH), 8.18 (2H, d, J = 5.1 Hz, Ar3H″ and 5″), 8.02 (2H, d, J = 5.4 Hz, ArH3′ and 5′), 7.94 (1H, s, NH′), 7.67 (2H, d, J = 5.1 Hz, Ar2H″ and 6″), 7.55 (2H, d, J = 5.4 Hz, Ar2H′ and 6′), 6.88 (1H, s, H2′) 6.57 (1H, d, J = 1.8 Hz, H7), 6.41 (1H, s, H5′), 6.32 (1H, d, J = 1.8 Hz, H5), 3.91 (3H, s, C6 OCH_3), 3.88 (3H, s, C6′ OCH_3), 3.79 (3H, s, C4 OCH_3), 3.75 (3H, s, C4′ OCH_3). ^{13}C NMR δ: 158.3 (C6), 155.6 (C6′), 154.5 (C4), 155.3 (C4′), 145.7 (ArC1″), 145.4 (ArC1′), 144.9 (ArC4′), 143.7 (ArC4″), 138.2 (C7a), 137.7 (C7a′), 130.9 (ArC2′ and 6′), 129.8 (ArC2″ and 6″), 127.5 (C3), 122.8 (ArC3′ and 5′), 123.3 (ArC3″ and 5″), 122.9 (C2′), 117.3 (C3′), 114.9 (C2), 111.2 (C3a), 110.1 (C3a′), 97.1 (C7), 92.7 (C5), 89.7 (C5′), 86.9 (C7), 55.0 (C4 O$\underline{C}H_3$), 53.5 (C4′ O$\underline{C}H_3$), 53.1 (C6′ O$\underline{C}H_3$), 52.0 C6. ES-MS *m/z*: 594.2 $[M+1]^+$, (15%), 338.5 (50), 336.2 (100), 147.1 (90). ES-HRMS *m/z*: calcd for $[M+1]^+$ $C_{32}H_{26}N_4O_8$ 595.1829; found 595.1832.

Structure determinations

Full spheres of CCD diffractometer data were measured (monochromatic Mo Kα radiation, $\lambda = 0.7107_3$ Å; ω-scans; T ca. 153 K) yielding $N_{t(otal)}$ reflections, these merging to N unique (R_{int} cited) after 'empirical'/multiscan absorption correction (proprietary software), N_o with $F > 4\sigma(F)$ being considered 'observed'. All were used in the full matrix least squares refinement on F^2, refining anisotropic displacement parameters for the non-hydrogen atoms, hydrogen atom treatment following a riding model; reflection weights were $(\sigma^2(F^2) + (aP)^2)^{-1}$ ($P = (F_o^2 + 2F_c^2)/3$). Neutral atom complex scattering factors were used within the SHELXL 97 program.[15] Pertinent results are given in Figures 1, 2 and reference

16; full .cif depositions (without structure factor amplitudes) are deposited with the Cambridge Crystallographic Data Centre, CCDC 680107, 680108.

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Corresponding author. Paul Keller, Tel.: +61 2 4221 4692; fax: +61 4221 4287; e-mail: Keller@uow.edu.au

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15. **12.** $C_{46}H_{40}N_2O_{10}S_2$, M = 845.0. Monoclinic, space group $P2_1/n$, a = 12.725(1), b = 17.671(1), c = 18.158(1) Å, β = 91.449(2)°, V = 4082 Å^3. D_c (Z = 4) = 1.37$_5$ g cm^{-3}. μ_{Mo} = 0.19 mm^{-1}; specimen: 0.10 x 0.09 x 0.08 mm; $'T'_{min/max}$ = 0.82. $2\theta_{max}$ = 70°; N_t = 67457, N = 18054 (R_{int} = 0.077), N_o = 8927; $R1$ = 0.055, $wR2$ = 0.14 (a = 0.067). $|\Delta\rho_{max}|$ = 1.38 e Å^{-3}. **28.** $C_{34}H_{30}Br_2N_2O_8S_2{\cdot}2(CH_3)_2CO$, M = 934.7. Monoclinic, space group $C2/c$, a = 20.766(2), b = 9.7298(8), c = 22.543(2) Å, β = 117.101(2)°, V = 4055 Å^3. D_c (Z = 4) = 1.53$_1$ g cm^{-3}. μ_{Mo} = 2.2 mm^{-1}; specimen: 0.28 x 0.15 x 0.12 mm; $'T'_{min/max}$ = 0.72. $2\theta_{max}$ = 75°; N_t = 42853, N = 10294 (R_{int} = 0.045), N_o = 5440; $R1$ = 0.037, $wR2$ = 0.077 (a = 0.034). $|\Delta\rho_{max}|$ = 0.95 e Å^{-3}