Comparative reactivity of 5,7-dimethoxyindoles with aldehydes and ketones

Glenn C. Condie, Michelle F. Channon, Donald C. Craig, Mohan Bhadbhade, Naresh Kumar, and David StC. Black*

School of Chemistry, UNSW Sydney, Sydney, NSW 2052, Australia
Email: d.black@unsw.edu.au

Dedicated to Professor Jan Bergman on the occasion of his 80th birthday

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Abstract

This paper describes acid-catalysed reactions of 5,7-dimethoxy-1-methylindole and methyl 5,7-dimethoxyindole-2-carboxylate with a range of aldehydes and ketones. The former indole reacts selectively at C3, whereas the latter reacts preferentially at C4 but also at C3 depending on the reaction conditions. Reactions of indoles with 2,2-dimethoxypropane and triethyl orthoformate are also reported. A range of di- and tri-indolylmethanes are described, together with an indolo-triptycene of novel structure.

Keywords: Tri-indolylmethanes, di-indolylmethanes, indoles, benzindoles, triptycenes

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Introduction

In an attempt to modify the reactivity of indoles to provide diverse substitution in the benzene ring, we have carried out extensive investigations on 4,6-dimethoxyindoles, where the C7 position is strongly nucleophilic, and to a lesser extent on 5,7-dimethoxyindoles, where the C4 position is strongly nucleophilic. The reactivity patterns also depend on the presence of other substituents, and also the fact that the methoxy groups increase the general reactivity of the whole indole framework to the extent that favoured reactivity sites can also be positions C2 and C3. We have previously reported a range of electrophilic substitution reactions on 5,7-dimethoxyindoles: these include formylation, acylation, bromination and nitration. Depending on the structure of the starting indole, reactions can take place at C4 or C3.

We now report a range of acid-catalysed reactions of several 5,7-dimethoxyindoles with aldehydes and ketones, with an emphasis on the comparative behaviour resulting from the structure of the starting material. The two main starting indoles chosen were 5,7-dimethoxy-1-methylindole and methyl 5,7-dimethoxyindole-2-carboxylate: the former in general tends to favour reactions at C3 and the latter at C4. The N-methylindole was chosen ahead of the simpler parent structure because the electron-donating effect of the methyl group confers a more powerful nucleophilic reactivity at C3 (in the same way that N-methylindole is a more effective C3 nucleophile than indole). The presence of the electron-withdrawing carboxylic ester at C2 in indole has the effect of reducing nucleophilic reactivity at C3 and therefore leading to preferential reaction at C4. Some related indoles and indole carbaldehydes participate in some individual reactions (Figure 1). The syntheses of indoles 1 and 5 use different methodology, and all the indoles 1-11 have already been described. The indole was prepared by the reaction of indole with di-t-butyl carbonate. Several aspects of the following work have been mentioned in the report of a conference lecture.

![Figure 1. Selected 5,7-dimethoxyindole starting materials.](image)

Results and Discussion

Reactions with formaldehyde

The N-methylindole 1 failed to react with formaldehyde at room temperature but a complex mixture of products formed when the reaction mixture was heated. However, the less reactive 5,7-dimethoxy-1-methylindole-3-carbaldehyde 7 reacted smoothly with formaldehyde in glacial acetic acid at room temperature to give the 4,4'-diindolylmethane 13 in 66% yield. The N-acetylindole 4 also combined with...
formaldehyde in glacial acetic acid to give the 4,4'-diindolylmethane 14 in 57% yield (Scheme 1). Presumably the C3 position is deactivated by the electron-withdrawing acetyl group. On the other hand, 5,7-dimethoxyindole-4-carbaldehyde 10 and also its N-methyl derivative 9 gave complex mixtures under the same reaction conditions.

Scheme 1. Formation of 4,4'-diindolylmethanes 13 and 14.

The indole-2-carboxylate 5 reacted slowly with formaldehyde in acetic acid over several days to give the 4,4'-diindolylmethane 15 in 85% yield (Scheme 2). An attempt to achieve a faster reaction using methanolic hydrochloric acid gave a yield of only 27%. The structures of the new 4,4'-diindolylmethanes 13, 14 and 15 were clear from their NMR spectra, and the linking methylene protons resonated at 4.99, 4.30 and 4.40 ppm respectively, and the linking carbon atoms resonated at 29.0, 22.4 and 22.6 respectively.

Scheme 2. Formation of 4,4'-diindolylmethanes 15 and 18.
In any acid-catalysed addition of an indole to formaldehyde the initial intermediate would be a hydroxymethyl derivative. Therefore the indole-4-carbaldehyde 10 was reduced by sodium borohydride to give the 4-hydroxymethylindole 16 in 77% yield: treatment of this compound with acetic acid overnight gave a 73% yield of the 4,4′-diindolylmethane 15. The related 1-butyloxycarbonyl-4-hydroxymethylindole 17 was prepared by sodium borohydride reduction of the 1-butyloxycarbonylindole-4-carbaldehyde 12, and in an attempt to convert this by a standard procedure into the related 4-bromomethyl derivative, instead it gave the 1-butyloxycarbonyl-4,4′-diindolylmethane 18 in 75% yield (Scheme 2). The structure was confirmed by almost quantitative conversion of the diindolylmethane 15 into compound 18 by reaction with di-t-butyl carbonate in acetonitrile. The precise mechanism for the formation of the diindolylmethane 18 is not clear. Presumably the intermediate bromomethyl compound undergoes further combination with the indole 17.

However, many cases have been reported where 7-hydroxymethyl-4,6-dimethoxyindoles undergo acid-catalysed ipso-substitution reactions with elimination of formaldehyde to give 7,7′-diindolylmethanes, (e.g. the conversion of indole 16 to diindolylmethane 15) so the two 4-hydroxymethylindoles 16 and 17 were further investigated. When 4-hydroxymethylindole 16 was stirred in methanol with concentrated hydrochloric acid at room temperature, the spiro-dienone 19 precipitated out as a highly pure white solid in 91% yield (Scheme 3).

![Scheme 3](image)

**Scheme 3.** Formation of indolo-spiro-dienones 19 and 20.

A similar reaction with indole 17 gave a mixture of the spiro-dienone 20 (45%), the 4,4′-diindolylmethane 18 (30%), and the 4-methoxymethylindole 21 (12%). The structure of the dienone 19 was established by extensive 1D and 2D NMR spectroscopy: a suitable crystal for X-ray structure determination could not be obtained. The \(^1\)H NMR spectrum showed the presence of two NH resonances and only five methoxy proton resonances, suggesting that the compound contains two indole moieties but that one methoxy group has been lost. The \(^13\)C NMR spectrum showed methoxy carbon resonances between 52 and 58 ppm representing...
the methoxy and ester groups. A resonance for a quaternary carbon at 44.2 ppm indicated the spiro-structure and a resonance for the quinone-type carbonyl carbon appeared at 181.0 ppm. The proposed mechanism for the formation of the dienone 19 initially involves the electrophilic addition of a hydroxymethylene group of one molecule of indole 16 to the substituted C4 position of another molecule of indole 16 to give the C4 disubstituted indole 22. While this intermediate might be expected to lose formaldehyde to give the diindolymethane 15, under these conditions electrophilic substitution occurs at the indole C3 to form the six-membered ring of the product 19. (Scheme 3).

**Reactions with aryl- and heteroaryl-aldehydes**

The 5,7-dimethoxyindoles 1 and 5 react readily with aryl aldehydes under acidic conditions to form diindolymethanes. The most successful conditions involve the use of glacial acetic acid or methanolic hydrochloric acid. Indole 1 combined with a range of benzaldehydes in glacial acetic acid at room temperature to give the aryl-3,3'-diindolymethanes 23-26 in 66-91% yields (Scheme 4).

**Scheme 4.** Formation of aryl-3,3'-diindolymethanes 23-28.

The presence of methoxy groups at C5 and C7 did not change the normal regiochemistry for the formation of diindolymethanes. The bond formation at C3 was established by 1H NMR data showing the meta-coupling between H4 and H6. The diindolymethane 23 was also converted to the 4,4'-dicarbaldehyde 27 under Vilsmeier reaction conditions. Indole 1 also reacted with terephthalaldehyde to yield the tetraindolyldimethane 28 in 71% yield. In contrast, the indole 5 combined with p-chloro- and p-methoxy-benzaldehydes under the improved conditions of concentrated hydrochloric acid in methanol to give the aryl-4,4'-diindolymethanes 29-30, which precipitated out of solution in high yields (Scheme 5). Trace amounts of the more soluble 3,4'-diindolymethane isomers were detected but not isolated and characterized. When indole 5 was reacted with p-chlorobenzaldehyde under the more powerful conditions of phosphoryl chloride in chloroform, a complex mixture of products was formed: after extensive chromatography only the 3,4'-
diindolylmethane 31 could be isolated in 37% yield and characterized. The N-methyl analog 6 of the indole 5 underwent the same reaction to give the 4,4'-diindolylmethane 32 in 93% yield. The diindolylmethane 29 was also converted to the N-Boc derivative 33 by reaction with di-(t-butyl) carbonate (Scheme 5).

Scheme 5. Formation of aryl-4,4'-diindolylmethanes 29, 30, 32, 33 and aryl-3,4'-diindolylmethane 31.

In an attempt to synthesise tri-indolylmethanes, the indoles 1 and 5 were reacted with several indole aldehydes. Indole 1 reacted in glacial acetic acid with indole-3-carbaldehyde 34 to give the 3,3',3'''-triindolylmethane 35 in only 25% yield. Slightly better yields of 37% and 47% were obtained in reactions with the 5,7-dimethoxyindole-4-carbaldehyde 10 and the N-methyl-3-carbaldehyde 7 to give the 3,3',4'''-triindolylmethane 36 and the 3,3',3'''-triindolylmethane 37 respectively. However, since compound 37 is completely symmetrical, its yield was dramatically increased to 88% by the reaction of indole 1 with triethyl orthoformate in methanol in the presence of a catalytic amount of p-toluenesulfonic acid.18-24 This reaction was more generally applied to the NH-indole 2 and the N-benzylindole 3 which yielded the respective 3,3',3'''-triindolylmethanes 38 and 39 in 37% and 77% yields (Scheme 6).
Scheme 6. Formation of 3,3',3'''-triindolylmethanes 35, 37-39 and 3,3',4''-triindolylmethane 36.

Condensation of indole 5 with indole-3-carbaldehyde 34 in methanolic hydrochloric acid gave the 3,3',3'''-triindolylmethane 40 in 46% yield, and the corresponding reaction with the methyl 5,7-dimethoxyindole-4-carbaldehyde 11 gave an 83% yield of a mixture of the 3,3',4''-triindolylmethane 41 and the 3,3',3'''-triindolylmethane 42 in a ratio of 88:12. This result contrasts with the reaction of indole 5 with 4-chlorobenzaldehyde under the same conditions, which showed selective reaction at C4 (see Scheme 5). Presumably the greater steric bulk of the indole aldehydes 34 and 11 could be a factor in directing the reaction away from C4 to the more accessible C3. In comparison, the condensation of indole 5 with triethyl orthoformate gave an 80% yield of a mixture of the 3,3',4''-triindolylmethane 41 and the 3,3',3'''-
triindolymethane 42 in a ratio of 98:2 (Scheme 7). The minor product 42 presumably arises as a result of reversible steps involved in the formation of the triindolymethanes. Several triindolymethanes have been reported as natural products from a marine bacterium and also as products from reactions of indole with N-methylin-2-one or 1,3-dimethylimidazolidin-2-one and phosphoryl chloride.

Scheme 7. Formation of 3,3',4''-triindolymethane 41 and 3,3',3''-triindolymethanes 40 and 42.

Reactions with o-phthalaldehyde

o-Phthalaldehyde represents a special case in reactions of aldehydes with indoles. While terephthalaldehyde behaves normally, o-phthalaldehyde has the possibility to react at two adjacent positions of an indole if they are available. We have previously shown that 1-methyl-4,6-dimethoxyindole reacts regioselectively at C2 and C3 with o-phthalaldehyde to give isomeric indolylbenzocarbazoles depending on the conditions. The indole 1 has positions C2, C3 and C4 available, so it was reacted with o-phthalaldehyde in glacial acetic acid and found to give the 6-(3-indolyl)benzocarbazole 43 in 34% yield (Scheme 8). This is consistent with a slow reaction to give the thermodynamically more stable product, as previously described.
On the other hand, indole 5 only has availability for reaction at C3 and C4: it combined with o-phthalaldehyde in methanolic hydrochloric acid to give a very pure white precipitate of the hetero-triptycene 44 in 90% yield (Scheme 8). Similarly high yields were obtained when the reaction was carried out in either phosphoryl chloride or p-toluenesulfonic acid.

Scheme 8. Formation of indolobenzocarbazole 43 and indolotriptycenes 44 and 46.

The structure of compound 44 was established by extensive NMR spectroscopy and also by an X-ray crystal structure (Figure 2). The $^1$H NMR spectrum showed only one NH, one H6 and three methoxy proton resonances, indicating that the two indole rings were in the same environment. A singlet at 6.90 ppm was assigned to the two bridging methines, thus establishing the presence of two 3,7'-diindolylmethane links, rather than the alternative possibility of one 3,3'-link and one 7,7'-link. The suggested mechanism proceeds via the intermediate 45 as a result of indole C7 attack on each formyl group (Scheme 8). The N-methylindole 6 also reacted with o-phthalaldehyde to give the N-methylated triptycene 46 in 44% yield. The lower yield is thought to be a function of the greater solubility of the product, and no attempt was made to obtain a second crop from the filtrate after collecting the product. The characteristic triptycene structure has been put to use in a variety of applications, including materials chemistry, host-guest chemistry, and molecular motors. 28
Reactions with ketones
Neither indole 1 nor 5 underwent any reaction with a range of acetophenones. The N-methylindole 1 underwent reaction with acetone and acetic anhydride to give the 3,3’-diindolylmethane 47 in a yield of 18%. When glacial acetic acid was used as the solvent an even lower yield (10%) of the benzo[c,d]indole 48 was obtained from a complex mixture. The acid-catalysed condensation of indole and acetone is known to give rise to multiple products.17,29 Indole 5 failed to react with acetone, but it did react when heated in 2,2-dimethoxypropane in the presence of a catalytic amount of p-toluenesulfonic acid to give the benzo[c,d]indole 49 in 34% yield (Scheme 9). The two benzoindoles 48 and 49 show different methyl substitution patterns, indicating that the initial attack for indole 1 takes place from C3, while that for indole 5 takes place from C4. The mechanism appears to be a stepwise intramolecular aldol-type, because neither indole 1 nor 5 showed any reaction with mesityl oxide. The structures of benzindoles 48 and 49 were established by extensive 1D and 2D NMR experiments. Other benz[c,d]indole structures have been reported in similar reactions.30
Scheme 9. Formation of benz[cd]indoles 48 and 49.

The indole 5 underwent reaction with two reactive ketones, ninhydrin and 1-pentanoylisatin. When indole 5 and ninhydrin were heated together in methanol with concentrated hydrochloric acid a yellow precipitate of the 1:1 adduct 50 was obtained in 91% yield, regardless of the stoichiometry. However, when

Scheme 10. Formation of 2-(4-indolyl)indane-1,3-dione 50 and 2,2-di(4-indolyl)indane-1,3-dione 51.
two equivalents of indole 5 and one of ninhydrin were heated together in toluene with a catalytic amount of
p-toluenesulfonic acid, initial formation of the adduct 50 was observed, but continued heating for two days
showed that this was converted into the 4,4'-diindolylmethane 51 in 98% yield (Scheme 10).

Indole 5 failed to undergo any reaction with isatin but it reacted with the more reactive 1-pentanoylisatin
52 when heated in methanol with concentrated hydrochloric acid to give the 4,4'-diindolylmethane 53 in 75%
yield (Scheme 11). Under these conditions it is known\textsuperscript{31,32} that the 1-pentanoylisatin could undergo ring-
opening following attack at C2 by methanol to give the related methyl glyoxylate 54, which could then react
with the indole 5. Subsequent hydrolysis of the amide and cyclisation, for which there is precedent,\textsuperscript{33} would
then generate the observed product 53. This possibility was checked and it was found that compound 53 was
obtained in 79% yield when indole 5 and the methyl glyoxylate 54 were reacted together under the same
conditions (Scheme 11). Some 3,3-diindolylindolin-2-ones are known where the indoles are linked through C3
and also C2: these compounds show interesting biological activity.\textsuperscript{34}

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{H} \quad \text{N} \quad \text{NH} \quad \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]
\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{H} \quad \text{C} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{O} \quad \text{Me} \]
\[ \text{O} \quad \text{Me} \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]

\[ \text{MeO} \quad \text{MeO} \quad \text{CO}_2\text{Me} \]
\[ \text{HN} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O} \quad \text{Bu}^n \]
General. \(^1\)H and \(^{13}\)C NMR spectra were recorded on a Bruker AC300F (\(^1\)H: 300MHz, \(^{13}\)C: 75.5 MHz) or a Bruker AM500 spectrometer. The chemical shifts (\(\delta\)) and coupling constants (\(J\)) are expressed in ppm and hertz respectively. Carbon attribution C, CH, CH2 and CH3 were determined by \(^{13}\)C, DEPT and HMQC experiments. Infrared (IR) spectra were recorded on a Mattson Genesis Series FTIR spectrometer using potassium bromide disks, except where specified. Ultraviolet and visible (UV/Vis) spectra were recorded in tetrahydrofuran or methanol using a Carey 100 spectrometer. Mass spectra were recorded on a VG Quattro MS (EI) or a Finnigan MAT (MALDI). High resolution mass spectrometry (HRMS) was carried out at the Research School of Chemistry, Australian National University. Melting points were measured using a Mel–Temp melting point apparatus. Microanalyses were performed at the Campbell Microanalytical Laboratory, University of Otago, New Zealand. Column chromatography was carried out using Merck 230-400 mesh silica gel or Merck 70-230 mesh silica gel, whilst preparative TLC was performed using Merck 60GF254 silica gel. X-ray crystallography was conducted with a suitable single crystal and crystallographic data excluding structure factors have been deposited with the Cambridge Crystallographic Data Centre: Compound 44 – Deposition Number 2004528

Methyl 1-(tert-butylxycarbonyl)-4-formyl-5,7-dimethoxyindole-2-carboxylate (12). A suspension of methyl 4-formyl-5,7-dimethoxyindole-2-carboxylate (11) (0.49 g, 1.85 mmol), di-tert-butyl dicarbonate (0.79 g, 3.62 mmol) and N,N-dimethylaminopyridine (48 mg) in anhydrous acetonitrile (12.0 mL) was stirred at room temperature, under nitrogen, for 70 min. The solvent was then evaporated in vacuo and the remaining residue purified via suction column chromatography (dichloromethane) to give the title compound (0.66 g, 98%) as a colourless syrup that solidified upon standing, mp 164-166 °C. IR (\(\nu_{\text{max}}, \text{cm}^{-1}\)): 1755, 1714, 1661, 1585, 1399, 1367, 1233, 1156, 1108. UV/Vis (\(\lambda_{\text{max}}, \text{nm}, \epsilon, \text{cm}^{-1}\text{M}^{-1}\)): 242 (21,600), 267 (12,000), 321 (18,500), 354 (11,700), 368 (8,300); \(^1\)H NMR (300 MHz, CDCl3): \(\delta\)H 1.64 (9H, s, CMe3), 3.90, 3.94, 3.99 (each 3H, s, OMe), 6.42 (1H, s, H6), 7.98 (1H, s, H3), 10.49 (1H, s, CHO). \(^{13}\)C NMR (75 MHz, CDCl3): \(\delta\)C 27.8 (CMe3), 52.5, 57.4, 56.2 (OMe), 85.6 (CMe3), 93.2 (C6), 112.0 (C3), 111.1, 123.3, 126.4, 130.5, 150.6, 153.2 (aryl C), 162.8 and 161.4 (CO and CO2Me), 188.8 (CHO). MS (+EI, m/z, %): 363 (M, 5), 290 (14), 264 (12), 263 (100), 232 (33), 231 (97), 230 (32), 214 (13), 204 (17), 203 (11), 202 (63), 188 (13), 174 (22), 160 (17), 144 (11). Anal. calcd for C\(_{18}\)H\(_{21}\)NO\(_5\): C, 59.5; H, 5.8; N, 3.8. Found: C, 59.5; H, 5.8; N, 3.6.

4,4'-Bis(5,7-dimethoxy-1-methylindolyl)methane-3,3'-dicarbaldehyde (13). 5,7-Dimethoxy-1-methylindole-3-carbaldehyde (7) (0.15 g, 0.69 mmol) was dissolved in glacial acetic acid (3 mL) and the reaction mixture was put under an inert gas atmosphere. Aqueous formaldehyde solution (37%, 0.4 mL, 0.54 mmol) was added, and the reaction mixture was stirred at room temperature for 6 h. The resulting precipitate was filtered, washed with water and dried, affording 4,4'-di(5,7-dimethoxy-1-methylindolyl)methane-3,3'-dicarbaldehyde 13 (0.10 g, 66%) as a white solid, mp 294-295 °C. IR (\(\nu_{\text{max}}, \text{cm}^{-1}\)): 1643, 1584, 1528, 1496, 1453, 1415, 1315, 1245, 1210, 1119, 1062. UV/Vis (\(\lambda_{\text{max}}, \text{nm}, \epsilon, \text{cm}^{-1}\text{M}^{-1}\)): 257 (24,000), 270 (19,000), 314 (13,000), 333 (14,000). \(^1\)H NMR (300 MHz, CDCl3): \(\delta\)H 3.43, 3.84 and 4.04 (18H, s, OMe and NMe), 4.99 (2H, s, CH2), 6.34 (2H, s, H6), 7.72 (2H, s, H2), 10.36 (2H, s, CHO). \(^{13}\)C NMR (75 MHz, CDCl3): \(\delta\)C 29.0 (CH2), 37.9 (C x 2, NMe), 55.6 and 57.1 (C x 4, OMe), 93.7 (C x 2, aryl CH), 115.9, 119.5, 123.1, 128.8, (C x 8, aryl C), 139.2 (C x 2, aryl CH), 146.2 and 154.6 (C x 4, aryl C), 185.8 (C x 2, CHO). MS (+EI, m/z, %): 450 (M, 13), 419 (11), 232 (33), 231 (49), 216 (45), 203 (100). Anal. calcd for C\(_{25}\)H\(_{26}\)N\(_2\)O\(_6\): C, 66.7; H, 5.8; N, 6.2. Found: C, 66.7; H, 5.5; N, 6.0.

4,4'-Bis(1-acetyl-5,7-dimethoxyindolyl)methane (14). 1-Acetyl-5,7-dimethoxyindole 4 (0.10 g, 0.46 mmol), 37% aqueous formaldehyde solution (0.03 mL, 0.40 mmol) and glacial acetic acid (2 mL) were combined and stirred at room temperature for 2 d under an inert gas atmosphere. The solution was diluted with water and...
the resulting turbid mixture was allowed to stand overnight before being filtered. The filtered material was washed with water and dried, affording 4,4'-di(1-acetyl-5,7-dimethoxyindolyl)methane 14 (23 mg, 22%) as a grey powder. Radial chromatography using 1:39 methanol : dichloromethane gave a colourless oil which solidified to yield a white solid, mp 157-159 °C. IR (v_max cm⁻¹): 1692, 1599, 1371, 1328, 1268, 1246, 1221, 1199, 1110, 1101. UV/Vis (λ_max nm, ε, cm⁻¹ M⁻¹): 325 (17,000). ¹H NMR (300 MHz, CDCl₃): δ_H 2.58 (6H, s, COMe), 3.88 and 3.92 (12H, s, OMe), 4.30 (2H, s, CH₂), 6.53 (2H, s, H6), 6.66 (2H, d, J 3.8 Hz, H3), 7.47 (2H, d, J 3.8 Hz, H2). ¹³C NMR (75 MHz, CDCl₃): δ_C 22.4 (CH₂), 25.7 (C x 2, COMe), 56.0 and 57.0 (C x 4, OMe), 94.7 and 107.5 (C x 4, aryl CH), 114.1 and 119.7 (C x 4, aryl C), 127.8 (C x 2, aryl CH), 134.7, 146.5 and 153.9 (C x 6, aryl C), 169.4 (C x 2, COMe). MS (+EI, m/z, %): 451 (M+1, 24), 450 (M, 100), 408 (45), 335 (38), 190 (47), 189 (52), 160 (86). HRMS (m/z): Calculated for C₂₅H₂₄N₈O₆ [M+Na]⁺: 473.1683. Found: 473.1656.

The filtrate was extracted with dichloromethane, and the organic phase was washed with water and saturated NaHCO₃ solution, dried (Na₂SO₄), and the solvent removed under reduced pressure affording 4,4'-di(1-acetyl-5,7-dimethoxyindolyl)methane 14 (36 mg, 35%) as an off-white powder. This product was confirmed by comparison with the other product obtained from this reaction using thin layer chromatography and ¹H NMR spectroscopy.

**Dimethyl 4,4'-methylenebis[5,7-dimethoxy-1H-indole]-2,2'-dicarboxylate (15).** **Method A.** A solution of methyl 4-hydroxymethyl-5,7-dimethoxyindole-2-carboxylate 16 (50 mg, 0.19 mmol) in glacial acetic acid (2.0 mL) was stirred at room temperature for 5 d. The resulting precipitate was filtered through a frit, washed twice with acetic acid (1 mL), then with water, and dried to give the title compound (33 mg, 73%) as a white powder, mp 292-294 °C. IR (v_max cm⁻¹): 3321, 1690, 1599, 1351, 1330, 1253, 1211, 1094. UV/Vis (λ_max nm, ε, cm⁻¹ M⁻¹): 241 (54,700), 276 (16,800, sh), 297 (53,200), 337 (8,620). ¹H NMR (300 MHz, CDCl₃): δ_H 3.87, 3.88, 3.94 and (each 6H, s, OMe), 4.40 (2H, s, bridging CH₂), 6.55 (2H, s, H6), 7.26 (2H, d, J 2.3 Hz, H3), 8.79 (2H, bs, NH). ¹³C NMR (75 MHz, CDCl₃): δ_C 22.6 (bridging CH₂), 51.6, 55.4, 58.2 (OMe), 62.2 (CO₂Me), 95.5 (C6), 108.7 (C3), 114.7, 124.2, 126.6, 128.8, 144.8, 151.2 (aryl C). MS (MALDI, m/z, %): 482 (M, 36), 481 (M-1, 100). Anal. calcd for C₃₂H₂₄N₄O₈: C, 62.2; H, 5.4; N, 5.81. Found: C, 62.0; H, 5.5; N, 5.8%.

**Method B.** A solution of methyl 5,7-dimethoxyindole-2-carboxylate 5 (50 mg, 0.21 mmol) and 4-hydroxymethyl-5,7-dimethoxyindole-2-carboxylate 16 (56 mg, 0.21 mmol) in glacial acetic acid (2.0 mL) was stirred at room temperature for 75 min. The resulting precipitate was filtered through a frit, washed successively with a little acetic acid, water, saturated NaHCO₃ solution, water, and then dried to give the title compound (71 mg, 70%) as a white powder.

**Method C.** A mixture of methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.25 g, 1.06 mmol) and formaldehyde (0.2 mL) in anhydrous methanol (7 mL) was stirred at room temperature with concentrated HCl (1 drop) for 19 h. The resulting precipitate was filtered through a frit, washed with water, and dried to give the title compound (70 mg, 27%) as a white powder.

**Method D.** A mixture of methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.25 g, 1.06 mmol) and 40% aqueous formaldehyde (10 drops) in glacial acetic acid (4.0 mL) was stirred at room temperature for 3 d. The resulting precipitate was filtered through a frit, washed with water, and dried to give the title compound (0.22 g, 85%) as a white powder.

**Methyl 4-hydroxymethyl-5,7-dimethoxyindole-2-carboxylate (16).** Sodium borohydride (1.44 g, 38 mmol) was added portionwise to a stirred suspension of methyl 4-formyl-5,7-dimethoxyindole-2-carboxylate 11 (1.00 g, 3.80 mmol) in methanol (100 mL) and stirring was continued at room temperature for 5.5 h. The mixture was then diluted with water and extracted with ethyl acetate. The organic extract was dried (MgSO₄) and the solvent evaporated in vacuo to give the title compound (0.78 g, 77%) as a white powder, mp 148-151 °C. IR (v_max cm⁻¹): 3477, 3177, 1717, 1698, 1594, 1538, 1455, 1432, 1327, 1260, 1217, 1199, 1175, 1148, 1122, 1094,
1. (tert-butylxycarbonyl)-4-hydroxymethyl-5,7-dimethoxyindole-2-carboxylate (17). Sodium borohydride (0.12 g, 3.2 mmol) was added portionwise, over 15 min, to a stirred suspension of methyl 1-(tert-butylxycarbonyl)-4-formyl-5,7-dimethoxyindole-2-carboxylate 12 (0.30 g, 0.83 mmol) in methanol (20 mL). After stirring for 15 min further at room temperature, the solvent was evaporated in vacuo and the remaining residue suspended in 1M NaOH and extracted with ethyl acetate. The organic extract was washed twice with 1M NaOH, then twice with brine, dried (MgSO₄), and the solvent evaporated in vacuo to give the title compound (0.273 g, 90%) as a colourless crystalline solid, mp 138-141 °C. IR (νmax, cm⁻¹): 3559, 1765, 1704, 1592, 1542, 1437, 1253, 1158, 1144, 1089, 999. UV/Vis (λmax, nm, ε, cm⁻³M⁻¹): 241 (27,800), 294 (17,600), 334 (4,580). ¹H NMR (300 MHz, CDCl₃): δ H 1.64 (9H, s, CMe₃), 2.05 (1H, bs, CH₂), 3.93, 3.90, 3.89 (each 3H, s, OMe), 4.87 (2H, s, CH₂OH), 6.55 (1H, s, H6), 7.28 (1H, s, H3). ¹³C NMR (75 MHz, CDCl₃): δ C 27.3 (CMe₃), 51.9, 55.6, 57.5 (OMe), 57.5 (CH₂OH), 84.6 (CMe₃), 95.3 (C6), 109.1 (C3), 161.0 (CO₂Me), 112.8, 123.2, 127.6, 128.3, 146.9, 150.5, 153.0 (aryl C). MS (+EI, m/z, %): 365 (M, 6), 292 (10), 265 (77), 248 (20), 234 (13), 233 (100), 216 (36), 204 (22), 149 (22). Anal. calcd for C₁₃H₁₅NO₃: C, 59.2; H, 6.3; N, 3.8. Found: C, 59.0; H, 6.4; N, 3.8%.

Method B. Method B. A solution of bromine (27 mg, 0.17 mmol) in carbon tetrachloride (1.5 mL) was added dropwise to a stirred suspension of triphenylphosphine (40 mg, 0.15 mmol) in carbon tetrachloride (1.0 mL). The resulting yellow suspension was stirred further for 25 min, under nitrogen, at room temperature before triethylamine (17 mg, 0.17 mmol) in carbon tetrachloride (1.0 mL) was added and stirring continued for 20 min. A solution of methyl 1-(tert-butylxycarbonyl)-4-hydroxymethyl-5,7-dimethoxyindole-2-carboxylate 17 (0.56 mg, 0.15 mmol) in carbon tetrachloride (4 mL) was then added dropwise and stirring continued for 2 d. The solvent was then evaporated in vacuo and the remaining residue purified via gravity column chromatography (2% MeOH/CH₂Cl₂ to give the title compound (39 mg, 75%) as a colourless crystalline solid, mp 179-180 °C. IR (νmax, cm⁻¹): 1771, 1720, 1590, 1396, 1371, 1258, 1234, 1157, 1083. UV/Vis (λmax, nm, ε, cm⁻³M⁻¹): 241 (54,000), 294 (33,800), 344 (10,000). ¹H NMR (300 MHz, CDCl₃): δ H 1.60 (18H, s, CMe₃), 3.86 (12H, s, OMe), 3.89 (6H, s, OMe), 4.32 (2H, s, bridging CH₂), 6.56 (2H, s, H6), 7.37 (2H, s, H3). ¹³C NMR (75 MHz, CDCl₃): δ C 22.3 (bridging CH₂), 27.3 (CMe₃), 51.7, 55.5, 57.5 (OMe), 84.2 (CMe₃), 96.2 (C6), 111.1 (C3), 114.2, 123.5, 127.3, 128.3, 145.4, 150.8, 151.7 (CO and aryl C), 161.2 (CO₂Me). MS (MALDI, m/z, %): 682 (M, 42), 582 (18), 482 (100), 248 (69). Anal. calcd for C₃₅H₄₂N₂O₁₂: C, 61.6; H, 6.2; N, 4.1. Found: C, 61.5; H, 6.3; N, 4.0%.

Method B. A suspension of dimethyl 4,4'-methylenebis[5,7-dimethoxy-1H-indole]-2,2'-dicarboxylate 15 (50 mg, 0.10 mmol) and di-(t-butyl)carbonate (125 mg, 0.57 mmol) in acetonitrile (3.0 mL) was stirred at room temperature, under nitrogen, with a catalytic quantity of 4-dimethylaminopyridine for 23 h. The solvent was then evaporated in vacuo and the remaining residue purified via suction column chromatography (1% MeOH/CH₂Cl₂ to give compound 18 (67 mg, 95%) as a white solid.

Dimethyl [1,3,4,5-tetrahydro-6,8-dimethoxybenz[c,d]indole]-4-spiro-4',1,4,7-trihydro-5',7'-methoxyindol-7-one]-2,2'-dicarboxylate (19). Methyl 4-hydroxymethyl-5,7-dimethoxyindole-2-carboxylate 16 (77 mg, 0.30 mmol) in methanol (15 mL) was stirred at room temperature with concentrated HCl (1 drop) for 3 h. The resulting precipitate was filtered through a frit, washed with water, and dried to give the title compound (66
Acid catalyzed reaction of methyl 1-(tert-butyloxycarbonyl)-4-hydroxymethyl-5,7-dimethoxyindole-2-carboxylate (17). Methyl 1-(tert-butyloxycarbonyl)-4-hydroxymethyl-5,7-dimethoxyindole-2-carboxylate 17 (50 mg, 0.14 mmol) in methanol (1.5 mL) was stirred at room temperature with concentrated HCl (1 drop) for 40 min. The resulting precipitate was filtered through a frit, washed sequentially with a little methanol and water, and dried to give the diindolylmethane 18 (8 mg, 17%) as a white powder. The reaction filtrate and methanolic washings were combined and stirred for a further 4 d. The solvent was then evaporated *in vacuo* and the remaining residue purified via gravity column chromatography (1% MeOH/CH₂Cl₂) to give the three following products:

**Dimethyl 4,4'-methylenebis[1-(tert-butyloxycarbonyl)-5,7-dimethoxy-1H-indole]-2,2'-dicarboxylate (18)** (6 mg, 13%) was obtained as a white powder.

**Dimethyl 1-[1-(tert-butyloxycarbonyl)-1,3,4,5-tetrahydro-6,8-dimethoxybenz[c,d]indole]-4-spiro-4'-[1-(tert-butyloxycarbonyl)-1,4,7-trihydro-5'-methoxyindol-7-one]-2,2'-dicarboxylate (20).** (21 mg, 45%) was obtained as a white powder, mp 153-157 °C. IR (νmax, cm⁻¹): 1779, 1727, 1696, 1641, 1464, 1334, 1278, 1254, 1229. UV/Vis (λmax nm, ε, cm⁻¹M⁻¹): 244 (41,000), 287 (24,000), 299 (34,500), 312 (21,700), 347 (7,300). ¹H NMR (300 MHz, CDCl₃): δH 2.88 (1H, d, J 15.8 Hz, CH₂), 3.08 (1H, d, J 16.6 Hz, CH₂), 3.44 (1H, d, J 15.8 Hz, CH₂), 3.61 (1H, d, J 16.6 Hz, CH₂), 3.71, 3.78, 3.85, 3.89, 4.01 (each 3H, s, OMe), 5.37 (1H, d, J 2.3 Hz, H3'), 5.81 (1H, s, H6'), 6.55 (1H, s, H6), 8.74, 9.58 (2H, bs, NH). ¹³C NMR (75 MHz, CDCl₃): δC 32.5, 33.3 (CH₂), 44.2 (alkyl C), 52.1, 56.1, 57.0, 58.4 (OMe), 97.1 (C₆), 102.8 (C₆'), 112.9 (C₃'), 123.6, 126.0, 128.2, 128.3, 128.6, 145.6, 151.1 (aryl C), 161.4, 162.9 (CO₂Me), 178.3 and 181.0 (C₅ and quinone CO). MS (MALDI, m/z, %): 503 (M+Na, 10), 480 (M, 52), 479 (100); MS (+El, m/z, %): 481 (23), 480 (M, 100), 449 (27), 448 (37), 421 (41), 417 (16), 416 (13), 389 (43), 345 (13), 167 (22), 149 (50). HRMS (m/z): Calcd for C₂₅H₂₄N₂O₈ [M]⁺ 480.1533. Found: 480.1528. Anal. calcd for C₂₅H₂₄N₂O₈·0.5 H₂O: C, 61.3; H, 5.1; N, 5.7. Found: C, 61.2; H, 4.9; N, 5.8%.

3,3'-Bis(5,7-dimethoxy-1-methylindolyl)phenylmethane (23). 5,7-Dimethoxy-1-methylindole 1 (0.10 g, 0.53 mmol), benzaldehyde (0.05 mL, 0.53 mmol) and glacial acetic acid (2 mL) were combined and stirred at room temperature for 3 h. The resulting precipitate was filtered, washed with water and dried to give 3,3'-bis-(5,7-dimethoxy-1-methylindolyl)phenylmethane 23 (94 mg, 76%) as a white powder, mp 195 °C. IR (νmax cm⁻¹): 1582, 1497, 1458, 1414, 1279, 1205, 1147, 1117, 1047, 809. UV/Vis (λmax nm, ε, cm⁻¹M⁻¹): 213 (49,000), 229 (54,000), 266 (12,000), 273 (11,000), 299 (11,000), 307 (10,000). ¹H NMR (300 MHz, CDCl₃): δH 3.66 (6H, s, NMe), 3.88 (12H, s, OMe), 5.64 (1H, br s, CH), 6.28 (2H, d, J 2.0 Hz, H6), 6.33 (2H, d, J 2.0 Hz, H4), 6.37 (2H,
3,3'-Bis(5,7-dimethoxy-1-methylindolyl)-4-chlorophenylmethane (24). 5,7-Dimethoxy-1-methylindole 1 (0.20 g, 1.05 mmol), 4-chlorobenzaldehyde (0.15 g, 1.05 mmol) and glacial acetic acid (4 mL) were combined and stirred at room temperature for 3 h. The resulting precipitate was filtered, washed with water and dried to give 3,3’-di(5,7-dimethoxy-1-methylindolyl)-4-chlorophenylmethane 24 (0.22 g, 83%) as an off-white powder. Recrystallisation from dichloromethane and petroleum ether afforded a white powder, mp 194 °C. IR (ν_max, cm⁻¹): 1582, 1500, 1454, 1413, 1280, 1203, 1148, 1118, 1049, 804. UV/Vis (λ_max, nm, ε, cm⁻¹M⁻¹): 262 (12,000), 299 (9,300), 308 (8,300). ¹H NMR (300 MHz, CDCl₃): δ_H 3.68, 3.88 and 3.88 (18H, s, OMe and NMe), 5.61 (1H, br s, CH), 6.29 (4H, m, aryl H), 6.34 (2H, d, J 0.85 Hz, H6), 7.23 (2H, d, J 0.85 Hz, H4), 7.23 (2H, s, H2). ¹³C NMR (75 MHz, CDCl₃): δ_C 36.1 (2C, NMe), 39.5 (CH), 55.3 and 55.8 (4C, OMe), 93.1 and 94.3 (4C, aryl CH), 117.3 and 122.5 (4C, aryl C), 128.2 (2C, phenyl CH), 128.9 (2C, aryl C), 129.6 (2C, aryl C), 130.0 (2C, phenyl CH), 131.5 and 143.1 (aryl C), 148.0 and 154.0 (4C, aryl C). MS (+El, m/z, %): 507 (M, 37 Cl isotope, 11), 506 (37 Cl isotope, 36), 505 (M, 35 Cl isotope, 35), 504 (35 Cl isotope, 100), 503 (15), 489 (32), 393 (68). HRMS (m/z): Calcd for C₂₉H₂₉Cl₂N₂NaO₄ [M+Na]^⁺, 527.1708. Found: 527.1734. Anal. calcd for C₂₉H₂₉Cl₂N₂O₄: C, 69.0; H, 5.8; N, 5.5. Found: C, 68.7; H, 5.7; N, 5.1 5%. 3,3'-Bis(5,7-dimethoxy-1-methylindolyl)-4-hydroxyphenylmethane (25). 5,7-Dimethoxy-1-methylindole 1 (0.25 g, 1.31 mmol), 4-hydroxybenzaldehyde (0.12 g, 0.99 mmol) and glacial acetic acid (5 mL) were combined and stirred at room temperature for 5 h. The resulting precipitate was filtered, washed with water and dried to give 3,3’-di(5,7-dimethoxy-1-methylindolyl)-4-hydroxyphenylmethane 25 (0.29 g, 91%) as a white powder, mp 227 °C. IR (ν_max, cm⁻¹): 3396, 1582, 1511, 1498, 1455, 1280, 1205, 1148, 1117, 1044 cm. UV/Vis (λ_max, nm, ε, cm⁻¹M⁻¹): 217 (43,000), 230 (48,000), 267 (12,000), 272 (12,000), 299 (11,000), 307 (9,700). ¹H NMR (300 MHz, CDCl₃): δ_H 3.67, 3.87 and 3.88 (18H, s, OMe and NMe), 5.58 (1H, br s, CH), 6.28 (2H, d, J 2.0 Hz, H4), 6.33 (2H, d, J 2.0 Hz, H6), 6.35 (2H, s, H2), 6.72 and 7.17 (4H, m, aryl H). ¹³C NMR (75 MHz, CDCl₃): δ_C 36.1 (2C, NMe), 39.2 (CH), 55.3 and 55.8 (4C, OMe), 93.4, 94.2 and 114.9 (6C, aryl CH), 118.1, 122.5 and 129.1 (6C, aryl C), 129.6 and 129.7 (4C, aryl CH), 136.9 (aryl C), 147.9 (2C, aryl C), 153.6 (aryl C), 153.9 (2C, aryl C). MS (+El, m/z, %): 487 (M, 29), 486 (100), 485 (23), 471 (44), 393 (49), 295 (16), 243 (19), 191 (28). HRMS (m/z): Calcd for C₂₉H₂₉Cl₂N₂O₄ [M+Na]^⁺, 509.2047. Found: 509.2020. 3,3'-Bis(5,7-dimethoxy-1-methylindolyl)-4-nitrophenylmethane (26). 5,7-Dimethoxy-1-methylindole 1 (0.20 g, 1.05 mmol), 4-nitrobenzaldehyde (0.16 g, 1.05 mmol) and glacial acetic acid (4 mL) were combined and stirred at room temperature for 5 h. The resulting precipitate was filtered, washed with water and dried to give 3,3’-di(5,7-dimethoxy-1-methylindolyl)-4-nitrophenylmethane 26 (0.18 g, 66%) as a yellow powder. Recrystallisation from dichloromethane and petroleum ether afforded a fibrous yellow solid, mp 221-222 °C. IR (ν_max, cm⁻¹): 1583, 1514, 1491, 1455, 1341, 1280, 1208, 1148, 1118, 991. UV/Vis (λ_max, nm, ε, cm⁻¹M⁻¹): 216 (49,000), 228 (54,000), 272 (22,000), 295 (17,000), 306 (14,000). ¹H NMR (300 MHz, CDCl₃): δ_H 3.67 (6H, s, NMe), 3.89 (12H, s, OMe), 5.74 (1H, br s, CH), 6.26 and 6.30 (4H, d, J 2.0 Hz, H6 and H4), 6.35 (2H, s, H2), 7.46 and 8.13 (4H, m, aryl H). ¹³C NMR (75 MHz, CDCl₃): δ_C 36.2 (2C, NMe), 40.0 (CH), 55.4 and 55.7 (4C, OMe), 92.7 and 94.4 (4C, aryl CH), 116.1 and 122.5 (4C, aryl C), 123.5 (2C, aryl CH), 128.6 (2C, aryl C), 129.4 and 129.6 (4C, aryl CH), 146.3 (aryl C), 148.1 (2C, aryl C), 152.5 (aryl C), 154.2 (2C, aryl C). MS (+El, m/z, %): 516 (M, 31), 1203 (75), 1044 (9)
3,3'-Bis(5,7-dimethoxy-1-methylindolyl)phenylmethane-4,4'-dicarbaldehyde (27). Phosphoryl chloride (0.10 mL, 1.07 mmol) was added to an ice-cold solution of 3,3'-di[5,7-dimethoxy-1-methylindolyl]phenylmethane 23 (0.10 g, 0.21 mmol) in dry N,N-dimethylformamide (3 mL) with stirring and cooling in ice, and the reaction mixture was heated with stirring at 70 °C for 15 min. After cooling, the reaction mixture was poured over ice and basified using 10% aqueous sodium hydroxide solution. After standing overnight, the precipitate was filtered, washed with water and dried to give 3,3'-di[5,7-dimethoxy-1-methylindolyl]phenylmethane-4,4'-dicarbaldehyde 27 (93 mg, 83%) as a brown powder. Recrystallisation from dichloromethane and petroleum ether afforded dark cream needles, mp 158-159 °C. IR (ν_max, cm⁻¹): 1656, 1650, 1597, 1567, 1402, 1332, 1216, 1119, 1052. UV/Vis (λ_max, nm, ε, cm⁻¹ M⁻¹): 259 (25,000), 362 (23,000). ¹H NMR (300 MHz, d₆-DMSO): δH 3.81, 3.84 and 3.99 (18H, 3s, OMe and NMe), 6.32 (2H, s, H6), 6.53 (2H, s, H2), 6.72 (1H, br s, CH), 6.96 (2H, m, aryl H), 7.15 (3H, m, aryl H), 10.26 (2H, s, CHO). ¹³C NMR (75 MHz, d₆-DMSO): δC 36.3 (2C, NMe), 43.0 (CH), 56.0 and 57.0 (4C, OMe), 90.8 (2C, aryl CH), 111.6, 118.9 and 122.4 (aryl C), 125.6 (aryl CH), 126.9 (aryl C), 127.8 and 128.8 (4C, phenyl CH), 133.7 (2C, aryl CH), 145.2, 152.7 and 159.3 (aryl C), 187.8 (2C, CHO). MS (+EI, m/z, %): 527 (M, 11), 526 (31), 498 (13), 497 (29), 493 (21), 292 (88), 278 (96), 249 (47), 219 (54), 105 (63). HRMS (m/z): Calcd for C₃₁H₃₀N₄O₈ [M+Na]^+: 549.1966. Found: 549.1985.

1,4-Bis[di(5',7'-dimethoxy-1'-methylindol-3'-yl)methyl]benzene (28). 5,7-Dimethoxy-1-methylindole 1 (0.20 g, 0.15 mmol), terephthalaldehyde (50 mg, 0.37 mmol) and glacial acetic acid (4 mL) were combined and stirred at room temperature for 5.5 h. The resulting precipitate was filtered, washed with water and dried to afford 1,4-bis[di(5',7'-dimethoxy-1'-methylindol-3'-yl)methyl]benzene 28 (0.16 g, 71%) as an off-white solid. Recrystallisation from acetone and petroleum ether yielded colourless crystals, mp 271-273 °C. IR (ν_max, cm⁻¹): 1584, 1497, 1455, 1412, 1281, 1207, 1148, 1117, 1050. UV/Vis (λ_max, nm, ε, cm⁻¹ M⁻¹): 265 (31,000), 302 (22,000), 306 (21,000). ¹H NMR (300 MHz, CDC³): δH 3.61, 3.86 and 3.87 (36H, s, OMe and NMe), 5.60 (2H, br s, CH), 6.27 and 6.33 (8H, d, J 2.1 Hz, H6 and H4), 6.35 (4H, s, H2), 7.23 (4H, s, aryl H). ¹³C NMR (75 MHz, CDC³): δC 36.1 (4C, NMe), 39.9 (2C, CH), 55.3 and 55.6 (8C, OMe), 93.2 and 94.1 (8C, aryl CH), 118.1 and 122.4 (8C, aryl C), 128.5 (4C, phenyl CH), 129.1 (4C, aryl C), 129.6 (4C, aryl CH), 141.9 (2C, phenyl C), 147.9 and 153.9 (8C, aryl C). MS (+EI, m/z, %): 863 (M, 0.01), 217 (16), 161 (37), 121 (90). HRMS (m/z): Calcd for C₅₉H₄₈N₄O₈ [M+Na]^+: 885.3834. Found: 885.3790.

Dimethyl 4,4'-(4-chlorophenyl)methylene]bis[5,7-dimethoxyindole]-2,2'-dicarboxylate (29). A solution of methyl 5,7-dimethoxyindole-2-carboxylic acid 5 (0.15 g, 0.64 mmol) and p-chlorobenzaldehyde (90 mg, 0.64 mmol) in anhydrous methanol (10.0 mL) was stirred at room temperature with concentrated HCl (3 drops) for 5 h. The resulting precipitate was filtered through a frit, washed with water, and dried to give the title compound (0.16 g, 84%) as a white powder, mp 265-268 °C. IR (ν_max, cm⁻¹): 3441, 3278, 1721, 1702, 1590, 1550, 1440, 1319, 1244, 1222, 1155, 986, 749. UV/Vis (λ_max, nm, ε, cm⁻¹ M⁻¹): 242 (53,700), 278 (20,200), 297 (34,900), 336 (9,600). ¹H NMR (300 MHz, CDC³): δH 3.48, 3.83 and 3.94 (each 6 H, s, OMe), 6.51 (2H, s, H6), 6.56 (1H, s, bridging CH), 6.68 (2H, d, J 2.3 Hz, H3), 7.07 and 7.18 (each 2H, d, J 8.3 Hz, p-chlorophenyl), 8.84 (2H, bs, NH). ¹³C NMR (75 MHz, CDC³): δC 41.6 (bridging CH), 51.7, 55.4 and 58.1 (Ome), 95.8 (C6), 109.2 (C3), 127.8 and 130.2 (p-chlorophenyl CH), 116.9, 124.4, 126.6, 128.6, 131.1, 142.3, 145.4 and 152.2 (aryl C), 162.1 (CO₂Me). MS (+EI, m/z, %): 595 (M+1, 37Cl, 11), 594 (M, 37Cl, 37), 593 (M+1, 35Cl, 33), 592 (M, 35Cl, 100), 563 (24), 562 (20), 561 (61), 327 (26), 326 (30), 325 (60). Anal. calcd for C₃₁H₂₉Cl₂N₂O₅: C, 62.8; H, 4.9; N, 4.7. Found: C, 62.9; H, 4.7; N, 4.8%.

Dimethyl 4,4'-(4-methoxyphenyl)methylene]bis[5,7-dimethoxyindole]-2,2'-dicarboxylate (30). A mixture of methyl 5,7-dimethoxyindole-2-carboxylic acid 5 (0.34 g, 1.45 mmol) and p-methoxybenzaldehyde (99 mg, 0.73...
mmol) in anhydrous methanol (5.0 mL) was stirred at room temperature with concentrated HCl (1 drop) for 2 h. The resulting precipitate was filtered through a frit, washed with a little methanol, then water, and dried to give the title compound (0.39 g, 88%) as a white powder, m.p. 256-259 °C (methanol). IR (v_{\text{max}}, \text{cm}^{-1}): 3443, 1710, 1588, 1538, 1509, 1438, 1319, 1246, 1206, 1088, 984. UV/Vis (λ_{\text{max}}, nm, ε, cm^{-1} M^{-1}): 242 (55,500), 298 (35,100), 338 (9,930). 1H NMR (300 MHz, CDCl3): δH 3.44 (6H, s, OMe), 3.78 (3H, s, OMe), 3.81 and 3.94 (each 6H, s, OMe), 6.51 (2H, s, H6), 6.55 (1H, s, bridging CH), 6.61 (2H, d, J 2.3 Hz, H3), 6.78 and 7.06 (each 2H, d, J 8.3 Hz, p-methoxyphenyl), 8.81 (2H, bs, NH). 13C NMR (75 MHz, CDCl3): δC 41.9 (bridging CH), 52.1 (OMe), 55.8 (p-methoxyphenyl OMe), 55.9 and 58.9 (OMe), 96.7 (C6), 110.0 (C3), 113.9 and 130.4 (p-methoxyphenyl CH), 118.8, 125.0, 126.9, 129.2, 136.2, 145.6, 152.7 and 158.2 (aryl C), 162.7 (CO2Me). MS (MALDI, m/z, %): 588 (M, 54), 587 (100). Anal. calcd for C32H32N2O9: C, 65.3; H, 5.5; N, 4.8. Found: C, 65.3; H, 5.6; N, 4.8%.  

**Dimethyl 3,4’-[[4-chlorophenyl]methylene]bis[5,7-dimethoxyindole]-2,2'-dicarboxylate (31).** A solution of methyl 5,7-dimethoxyindole-2-carboxylate 1 (0.15 g, 0.64 mmol) and p-chlorobenzaldehyde (46 mg, 0.33 mmol) in anhydrous chloroform (15 mL) was heated at reflux with phosphoryl chloride (0.1 mL, 1 mmol) for 2 h. The resulting solution was washed sequentially with iced water and dilute NaOH, and dried (MgSO4). The solvent was then evaporated in vacuo and the remaining residue was purified via gravity column chromatography (CH2Cl2) to give the title compound (70 mg, 37%) as a white powder, mp 221-224 °C. IR (v_{\text{max}}, \text{cm}^{-1}): 3418, 3347, 1698, 1584, 1536, 1440, 1436, 1323, 1251, 1201, 1155. UV/Vis (λ_{\text{max}}, nm, ε, cm^{-1} M^{-1}): 241 (48,000), 273 (18,000), 298 (34,000), 339 (10,000). 1H NMR (300 MHz, CDCl3): δH 3.31, 3.45, 3.79, 3.82, 3.89 and 3.95 (each 3H, s, OMe), 6.29 and 5.83 (each 1H, d, J 1.9 Hz H6 and H4 respectively), 6.52 (1H, s, H6’), 6.56 (1H, d, J 2.3 Hz, H3’), 6.99 (1H, s, bridging CH), 7.16 (4H, m, p-chlorophenyl), 8.88 and 8.90 (each 1H, bs, NH and NH’). 13C NMR (75 MHz, CDCl3): δC 40.9 (bridging CH), 52.0, 52.2, 55.4, 55.8, 55.9 and 58.6 (OMe), 95.2, 96.4 and 97.5 (C4, C6, and C6’), 109.2 (C3’), 128.5 and 130.9 (p-chlorophenyl CH), 162.5 and 162.45 (CO2Me), 117.1, 123.4, 123.9, 124.9, 125.4, 127.3, 128.6, 128.9, 132.0, 142.8, 146.0, 147.0, 153.1 and 154.9 (aryl C). MS (+EI, m/z, %): 595 (37Cl, 9), 594 (M, 37Cl, 29), 593 (28), 592 (M, 35Cl, 67), 591 (12), 561 (14), 560 (9), 536 (12), 535 (40), 534 (37), 533 (100), 532 (20), 531 (17), 530 (17). Anal. calcd for C31H29ClN2O8: C, 62.8; H, 4.9; N, 4.7. Found: C, 62.8; H, 4.9; N, 4.9%.  

**Dimethyl 4,4'-[[4-chlorophenyl]methylene]bis[5,7-dimethoxy-N-methylindole]-2,2'-dicarboxylate (32).** A mixture of methyl 5,7-dimethoxy-N-methyl-indole-2-carboxylate 6 (0.26 g, 1.05 mmol) and p-chlorobenzaldehyde (148 mg, 1.05 mmol) in anhydrous methanol (3 mL) was stirred at room temperature with concentrated HCl (1 drop) for 1.5 h. The resulting precipitate was filtered through a frit, washed with water, and dried to give the title compound (0.304 g, 93%) as a white powder, mp 178-183 °C. IR (v_{\text{max}}, \text{cm}^{-1}): 1711, 1583, 1458, 1325, 1240, 1204, 1175, 1089, 991. UV/Vis (λ_{\text{max}}, nm, ε, cm^{-1} M^{-1}): 244 (57,700), 280 (21,600), 300 (33,800), 347 (11,200). 1H NMR (300 MHz, CDCl3): δH 3.48, 3.78 and 3.91 (each 6H, s, OMe), 4.28 (6H, s, NMe), 6.48 (2H, s, H6), 6.53 (1H, s, bridging CH), 6.88 (2H, s, H3), 7.05 and 7.17 (each 2H, d, J 8.3 Hz, p-chlorophenyl). 13C NMR (75 MHz, CDCl3): δC 34.9 (NMe), 41.9 (bridging CH), 51.8, 56.0 and 58.4 (OMe), 97.0 (C6), 111.5 (C3), 128.2 and 130.6 (p-chlorophenyl CH), 116.8, 127.0, 128.4, 128.6, 131.4, 143.0, 147.8 and 152.1 (aryl C), 163.0 (CO2Me). MS (+EI, m/z, %): 621 (M, 4), 464 (13), 453 (14), 440 (68), 426 (100), 371 (22), 332 (13), 321 (18), 266 (29), 252 (42), 228 (79). Anal. calcd for C33H33ClN2O8: C, 63.8; H, 5.4; N, 4.5. Found: C, 63.6; H, 5.2; N, 4.6%.  

**Dimethyl 4,4’-[[4-chlorophenyl]methylene]bis[1-tert-butoxy carbonyl-5,7-dimethoxyindole]-2,2'-dicarboxylate (33).** A mixture of dimethyl p-chlorophenyl-4,4’-di(5,7-dimethoxyindol)methylene-2,2'-dicarboxylate 29 (0.76 mg, 0.13 mmol), di-(t-butyl)carbonate (121 mg, 0.55 mmol) in anhydrous acetonitrile (5 mL) was stirred at room temperature with a catalytic quantity of N,N-dimethylaminopyridine for 2.5 h. The solvent was then evaporated in vacuo and the remaining yellow syrup purified via suction column chromatography (CH2Cl2) to give the title compound (65 mg, 64%) as a white powder, mp >133 °C (decomp.). IR (v_{\text{max}}, cm^{-1}): 1770, 1721,
1589, 1546, 1488, 1437, 1394, 1371, 1336, 1257, 1231\(\nu\), 1157, 1081. UV/Vis (\(\lambda_{\text{max}}, \text{nm}, \epsilon, \text{cm}^{-1}\text{M}^{-1}\))：243 (50,900), 296 (31,200), 343 (11,100). \(^1\)H NMR (300 MHz, CDCl\(_3\))：\(\delta_H\) 1.64 (18H, s, CMe\(_3\)), 3.50, 3.81, and 3.90 (each 6H, s, OMe), 6.51 (1H, s, bridging CH), 6.54 (2H, s, H6), 6.78 (2H, s, H3), 7.02 (2H, d, J 8.3 Hz, p-chlorophenyl), 7.19 (2H, d, J 8.7 Hz, p-chlorophenyl). \(^{13}\)C NMR (75 MHz, CDCl\(_3\))：\(\delta_C\) 41.9 (bridging CH), 27.8 (CMe\(_3\)), 52.3, 56.0 and 58.0 (OMe), 84.9 (CMe\(_3\)), 97.1 (C6), 112.0 (C3), 128.4 and 130.6 (p-chlorophenyl CH), 116.7, 124.3, 127.7, 128.7, 131.7, 142.2, 146.4 and 153.3 (aryl C), 151.4 (CO), 161.6 (CO\(_2\)Me). MS (MALDI, m/z, %)：790 (26), 691 (M-Boc, 14), 592 (M-2 x Boc, 100). Anal. calcd for C\(_{41}\)H\(_{45}\)ClN\(_2\)O\(_{12}\)：C, 62.1; H, 5.7; N, 3.5. Found：C, 61.8; H, 5.9; N, 3.56%.

**Indol-3-yl)-bis(5',7'-dimethoxy-1'-methylindol-3'-yl)methane (35).** 5,7-Dimethoxy-1-methylindole 1 (0.20 g, 1.05 mmol), indole-3-carbaldehyde 34 (0.11 g, 0.79 mmol) and glacial acetic acid (4 mL) were combined and stirred at room temperature for 4 h under an inert gas atmosphere. The resulting precipitate was filtered, washed with water and dried, yielding (indol-3-yl)-di(5',7'-dimethoxy-1'-methylindol-3'-yl)methane 35 (67 mg, 25%) as an off-white solid. Recrystallisation from dichloromethane and petroleum ether afforded a white solid which turned pink on exposure to air, mp 224-225 °C. IR (\(\nu_{\text{max}}, \text{cm}^{-1}\))：3411, 3343, 1584, 1495, 1456, 1413, 1281, 1204, 1147, 1117, 1044. UV/Vis (\(\lambda_{\text{max}}, \text{nm}, \epsilon, \text{cm}^{-1}\text{M}^{-1}\))：274 (21,000), 293 (19,000), 303 (17,000). \(^1\)H NMR (300 MHz, CDCl\(_3\))：\(\delta_H\) 3.68, 3.85 and 3.88 (18H, 3 x s, OMe and NMe), 5.92 (1H, br s, CH), 6.29 (2H, d, J 2.0 Hz, H6'), 6.46 (2H, s, H2'), 6.48 (2H, d, J 2.0 Hz, H4'), 6.76 (1H, d, J 2.0 Hz, H2), 6.99 (1H, m, H5), 7.16 (1H, m, H6), 7.35 (1H, d, J 8.2 Hz, H4'), 7.47 (1H, d, J 7.7 Hz, H7), 7.87 (1H, br s, NH). \(^{13}\)C NMR (75 MHz, CDCl\(_3\))：\(\delta_C\) 30.9 (CH), 36.1 (2C, NMe), 55.3 and 55.8 (4C, OMe), 93.3 and 94.0 (4C, aryl CH), 110.8 (aryl CH), 117.6 (2C, aryl C), 118.8 (aryl CH), 119.7 (aryl C), 120.2 and 121.5 (aryl CH), 122.4 (2C, aryl C), 123.3 (aryl CH), 127.2 (aryl C), 129.1 (2C, aryl C), 129.4 (2C, aryl CH), 136.7 (aryl C), 147.9 and 153.7 (4C, aryl C). MS (+EI, m/z, %)：510 (M, 19), 509 (100), 494 (46), 391 (17), 317 (38), 191 (90), 176 (73). HRMS (m/z)：Calcd for C\(_{31}\)H\(_{33}\)N\(_3\)NaO\(_4\) [M+Na]*，532.2207. Found：532.2206.

**5,7-Dimethoxyindol-4-yl)-bis(5',7'-dimethoxy-1'-methylindol-3'-yl)methane (36).** 5,7-Dimethoxy-1-methylindole 1 (0.20 g, 1.05 mmol), 5,7-dimethoxyindole-4-carbaldehyde 10 (0.16 g, 0.79 mmol) and glacial acetic acid (4 mL) were combined and stirred at room temperature overnight. The resulting precipitate was filtered, washed with water and dried, yielding an off-white powder (0.19 g). \(^1\)H NMR spectroscopy showed that the powder contained 5,7-dimethoxyindol-4-yl)-di(5',7'-dimethoxy-1'-methylindol-3'-yl)methane 36 in 53% yield and unreacted 5,7-dimethoxyindole-4-carbaldehyde 10 (18% of the original amount). Radial chromatography using dichloromethane afforded 5,7-dimethoxyindol-4-yl)-di(5',7'-dimethoxy-1'-methylindol-3'-yl)methane 36 (0.11 g, 37%) as a purple glass. Recrystallisation from dichloromethane and petroleum ether gave purple crystals, mp 270-271 °C. IR (\(\nu_{\text{max}}, \text{cm}^{-1}\))：3406, 1583, 1493, 1457, 1412, 1314, 1282, 1205, 1145, 1114, 1047. UV/Vis (\(\lambda_{\text{max}}, \text{nm}, \epsilon, \text{cm}^{-1}\text{M}^{-1}\))：269 (13,000), 299 (12,000), 304 (11,000). \(^1\)H NMR (300 MHz, CDCl\(_3\))：\(\delta_H\) 3.65 (6H, s, OMe or NMe), 3.77 (3H, s, OMe), 3.85 (12H, s, NMe and/or OMe), 3.95 (3H, s, OMe), 6.23 (2H, d, J 2.1 Hz, H6'), 6.34 (1H, dd, J 2.3, 3.0 Hz, H3), 6.37 (1H, t, J 1.1 Hz, CH), 6.44 (2H, d, J 2.1 Hz, H4'), 6.51 (1H, s, H6), 6.54 (2H, d, J 1.1 Hz, H2'), 6.90 (1H, m, H2), 8.07 (1H, m, NH). \(^{13}\)C NMR (75 MHz, CDCl\(_3\))：\(\delta_C\) 31.2 (CH), 36.1 (2C, NMe), 55.3 (2C, OMe), 55.3 (OMe), 55.6 (2C, OMe), 59.5 (OMe), 93.3 (aryl CH), 93.5 and 93.8 (4C, aryl CH), 103.8 (aryl CH), 117.5 (2C, aryl C), 117.5 (aryl C), 122.2 (2C, aryl C), 123.0 (aryl C), 123.2 (aryl CH), 128.7 (aryl C), 129.5 (2C, aryl CH), 129.7 (2C, aryl C), 144.5 (aryl C), 147.7 (2C, aryl C), 150.7 (aryl C), 153.5 (2C, aryl C). MS (+EI, m/z, %)：570 (M, 15), 569 (51), 554 (34), 391 (63), 191 (80), 176 (94), 148 (74). HRMS (m/z)：Calcd for C\(_{32}\)H\(_{34}\)N\(_4\)NaO\(_6\) [M+Na]*，592.2418. Found：592.2453.

**3,3',3''-Tris(5,7-dimethoxy-1-methylindolyl)methane (37).** Method 1. 5,7-Dimethoxy-1-methylindole 1 (0.20 g, 1.05 mmol), 5,7-dimethoxy-1-methylindole-3-carbaldehyde 7 (0.17 g, 0.79 mmol) and glacial acetic acid (4 mL) were combined and stirred at room temperature overnight. The resulting precipitate was filtered,
washed with water and dried, yielding 3,3',3''-tri(5,7-dimethoxy-1-methylindolyl)methane 37 (0.14 g, 47%) as a pale pink solid. Recrystallisation from dichloromethane and petroleum ether afforded a white powder, mp 245-246 °C. IR (νmax cm⁻¹): 1584, 1488, 1456, 1412, 1281, 1205, 1147, 1116, 1048, 810. UV/Vis (λmax nm, ε, cm⁻³ M⁻¹): 266 (16,000), 273 (15,000), 300 (17,000), 307 (16,000). ¹H NMR (300 MHz, CDCl₃): δH 3.68, 3.86 and 3.88 (27H, 3s, OMe and NMe), 5.78 (1H, br s, CH), 6.28 (3H, d, J 2.0 Hz, H6), 6.46 (3H, s, H2), 6.46 (3H, d, J 2.0 Hz, H4). ¹³C NMR (75 MHz, CDCl₃): δC 30.9 (CH), 36.1 (3C, NMe), 55.3 and 55.8 (6C, OMe, 93.6 and 93.9 (6C, aryl CH), 117.8, 122.5 and 129.3 (9C, aryl C), 129.5 (3C, aryl CH), 147.9 and 153.7 (6C, aryl C). MS (+EI, m/z, %): 584 (M, 27), 583 (79), 568 (68), 392 (55), 391 (100), 192 (80), 191 (84), 176 (71). Anal. calcd for C₃₆H₃₇N₃O₆: C, 70.0; H, 6.4; N, 7.2. Found: C, 69.7; H, 6.5; N, 7.0.

**Method 2.** 5,7-Dimethoxy-1-methylindole 1 (0.20 g, 1.05 mmol) was dissolved in AR grade methanol (7 mL). Triethyl orthoformate (0.58 mL, 3.49 mmol) was added, followed by a trace amount of 4-toluenesulfonic acid, and the reaction mixture was heated at reflux for 30 min. After cooling, the resulting precipitate was filtered, washed with 10% aqueous ammonia solution followed by water and dried, affording 3,3',3''-tri(5,7-dimethoxy-1-methylindolyl)methane 37 (0.18 g, 88%) as a white solid.

3,3',3''-Tris(5,7-dimethoxyindolyl)methane 38. 5,7-Dimethoxyindole 2 (0.20 g, 1.13 mmol) was dissolved in AR grade methanol (5 mL). Triethyl orthoformate (1.24 mL, excess) was added, followed by a trace amount of 4-toluenesulfonic acid, and the reaction mixture was heated at reflux for 1 h. After cooling, the resulting precipitate was filtered, washed with 10% aqueous ammonia solution followed by water and dried, affording 3,3',3''-tri(5,7-dimethoxyindolyl)methane 38 (75 mg, 37%) as a pale orange solid, mp 205-206 °C. IR (νmax cm⁻¹): 3323, 1571, 1494, 1455, 1317, 1201, 1145, 1130, 1049, 937, 814. UV/Vis (λmax nm, ε, cm⁻³ M⁻¹): 267 (17,000), 293 (14,000), 302 (12,000). ¹H NMR (300 MHz, CDCl₃): δH 3.68 and 3.91 (18H, 2s, OMe), 5.91 (1H, m, CH), 6.32 (3H, d, J 2.1 Hz, H6), 6.50 (1H, m, H4), 6.71 (3H, m, H2), 7.97 (3H, br m, NH). ¹³C NMR (75 MHz, CDCl₃): δC 31.5 (CH), 53.5 and 53.9 (6C, OMe), 93.6 and 93.8 (6C, aryl CH), 119.6 and 122.5 (6C, aryl C), 123.3 (3C, aryl CH), 127.8, 146.3 and 154.3 (9C, aryl C). MS (+EI, m/z, %): 542 (M, 2), 363 (11), 177 (45), 162 (49), 134 (100), 119 (95). HRMS (m/z): Calcd for C₃₁H₂₃N₃NaO₆ [M+Na]+, 564.2105. Found: 564.2074.

3,3',3''-Tris(1-benzyl-5,7-dimethoxyindolyl)methane 39. 1-Benzyl-5,7-dimethoxyindole 3 (0.20 g, 0.75 mmol) was dissolved in AR grade methanol (17 mL). Triethyl orthoformate (0.88 mL, excess) was added, followed by a trace amount of 4-toluenesulfonic acid, and the reaction mixture was heated at reflux for 1.5 h. After cooling, the resulting precipitate was filtered, washed with 10% aqueous ammonia solution followed by water and dried, affording 3,3',3''-tri(1-benzyl-5,7-dimethoxy-indolyl)methane 39 (0.16 g, 77%) as a white solid. Recrystallisation from dichloromethane and petroleum ether yielded a white powder, mp 262-263 °C. IR (νmax cm⁻¹): 1615, 1585, 1493, 1453, 1426, 1282, 1204, 1165, 1149, 1049, 812, 700. UV/Vis (λmax nm, ε, cm⁻³ M⁻¹): 266 (19,000), 274 (17,000), 301 (18,000), 307 (18,000). ¹H NMR (300 MHz, CDCl₃): δH 3.56 and 3.76 (18H, 2s, OMe), 5.40 (6H, s, CH₃), 5.86 (1H, br s, CH), 6.25 (3H, d, J 2.0 Hz, H6), 6.47 (d, J 2.0 Hz, H4), 6.62 (3H, s, H2), 6.98 (6H, m, aryl H), 7.18 (9H, m, aryl H). ¹³C NMR (75 MHz, CDCl₃): δC 31.5 (CH), 52.1 (3C, CH₃), 55.2 and 55.6 (6C, OMe), 93.5 and 94.5 (6C, aryl CH), 118.2 and 122.0 (6C, aryl C), 126.3 (6C, aryl CH), 126.7 (3C, aryl CH), 128.2 (6C, aryl CH), 129.0 (3C, aryl CH), 129.5, 140.1, 147.7 and 153.9 (12C, aryl C). MS (+EI, m/z, %): 812 (M, 13), 811 (24), 796 (10). HRMS (m/z): Calcd for C₃₂H₄₉N₃NaO₆ [M+Na]+, 834.3513. Found: 834.3458.

**Dimethyl 3,3'-[indol-3-ylmethylene]bis[5,7-dimethoxyindole]-2,2'-dicarboxylate 40.** A solution of methyl 5,7-dimethoxyindole-2-carboxylate 2 (0.10 g, 0.43 mmol) and indole-3-carbaldehyde 34 (62 mg, 0.43 mmol) in anhydrous methanol (3 mL) was stirred at room temperature with concentrated HCl (1 drop) for 24 h. The resulting precipitate was filtered through a frit, washed with water, and dried to give the title compound (58 mg, 46%) as a white powder, mp 220-223 °C. IR (νmax cm⁻¹): 3454, 3434, 3379, 3316, 1702, 1590, 1543, 1456, 1438, 1323, 1312, 1245, 1197, 1156. UV/Vis (λmax nm, ε, cm⁻³ M⁻¹): 239 (49,400), 273 (21,300), 293 (31,600),
336 (10,400). 1H NMR (300 MHz, CDCl3): δH 3.87, 3.82, and 3.11 (each 6H, s, OMe), 5.94 (2H, bs, H4 and H4'), 6.23 (2H, d, J 1.9 Hz, H6 and H6'), 6.67 (1H, d, J 1.1 Hz, H2' ), 7.10 and 6.90 (each 1H, dt, J 1.1, 7.9 Hz, H5' and H6''), 7.33 (2H, dt, J 1.1, 7.9 Hz, H4'' and H7''), 7.49 (1H, d, J 1.5 Hz, bridging CH), 7.90 (1H, bs, NH''), 8.90 (2H, bs, NH and NH'). The signals at 8.90 and 7.90 ppm exchanged with D2O. 13C NMR (300 MHz, CDCl3): δC 39.5, 39.2, and 31.9 (bridging CH), 51.8, 51.9, and 52.0, 55.2, 55.3, and 55.4 (OMe), 94.5 (C4 and C4'), 96.7 (C6 and C6'), 116.6, 118.6, 119.3, 121.3 and 123.6 (indolyl CH), 117.9, 123.2, 124.0, 125.3, 127.9, 128.3, 137.0, 147.3 and 154.0 (aryl C), 162.0 (CO2Me). MS (+EI, m/z, %): 598 (25), 597 (M, 71), 539 (33), 538 (100), 507 (16), 506 (49), 502 (21), 235 (45), 203 (48), 174 (27), 144 (23), 117 (21). Anal. calcd for C33H33N3O8: C, 66.3; H, 5.2; N, 7.0. Found: C, 66.3; H, 5.1; N, 7.0%.

Reacction of methyl 5,7-dimethoxyindole-2-carboxylate (5) with methyl 4-formyl-5,7-dimethoxyindole-2-carboxylate (11). A mixture of methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.180 g, 0.765 mmol) and methyl 4-formyl-5,7-dimethoxyindole-2-carboxylate 11 (0.106 g, 0.403 mmol) in anhydrous methanol (4 mL) was heated at reflux with concentrated HCl (2 drops) for 3.5 h. The resulting precipitate was filtered, washed with a little methanol, then water, and dried to give an isomeric mixture (0.227 g, 83%) of the 3,3',4'-triphenylmethane 41 and the 3,3',3''-tridindomethane 42 in a 88:12 ratio, as a white powder, mp 244-247 °C. IR (vmax, cm⁻¹): 3468, 3335, 1716, 1589, 1539, 1451, 1437, 1329, 1310, 1247, 1199, 1156. UV/Vis (λmax, nm, ε, cm⁻²M⁻¹): 241 (66,800), 279 (27,600), 297 (46,400), 338 (14,400). MS (MALDI, m/z, %): 715 (M, 47), 714 (100). Anal. calcd for C34H33N3O12·0.5H2O: C, 61.3; H, 5.3; N, 5.8. Found: C, 61.1; H, 5.0; N, 5.7%.

Purification of the isomeric mixture via preparative thin layer chromatography led to the isolation and characterisation of compound 41, and recovery of a trace amount of compound 42.

Trimethyl 3',4'-methylidynetris[5,7-dimethoxyindole]-2,2',2''-tricarboxylate (41). 1H NMR (300 MHz, CDCl3): δH 3.02 (3H, s, OMe), 3.16 and 3.39 (each 3H, bs, OMe), 3.71 (3H, s, OMe), 3.75 (6H, s, OMe), 3.85, 3.87, 3.92 (each 3H, s, OMe), 5.78 and 5.95 (each 1H, bs, H4 and H4'), 6.23 and 6.27 (each 1H, d, J 1.9 Hz, H3' and H6''), 6.52 (2H, s, H6 and H6'), 7.73 (1H, s, bridging CH), 8.87 (2H, bs, NH and NH'), 8.94 (1H, bs, NH''). 13C NMR (75 MHz, CDCl3): δC 34.6 (bridging CH), 51.8, 51.9, 52.0, 52.1, 55.0, 55.2, 55.8, 55.9 and 59.1 (OMe), 94.9 and 95.3 (C4), 97.1, 97.3, and 97.4 (C6), 109.4 (C3), 118.8, 123.1, 123.3, 123.8, 124.1, 125.0, 126.2, 127.2, 127.3, 129.2, 129.5, 145.7, 146.9, 147.0, 153.1, 154.7, 155.1 (aryl C), 162.4, 162.5 and 162.9 (CO2Me).

Trimethyl 3',3''-methylidynetris[5,7-dimethoxyindole]-2,2',2''-tricarboxylate (42). IR (vmax, cm⁻¹): 3468, 1714, 1652, 1634, 1455, 1248, 1199, 1158; 1H NMR (300 MHz, CDCl3): δH 3.87, 3.78, and 2.98 (each 6H, s, OMe), 5.95 (3H, d, J 1.9 Hz, H4), 6.24 (3H, d, J 1.9 Hz, H6), 8.15 (1H, s, bridging CH), 8.94 (3H, bs, NH). 13C NMR (75 MHz, CDCl3): δC 32.4 (bridging CH), 51.4, 54.5, and 55.4 (OMe), 94.2 (C4), 96.7 (C6), 122.5, 123.8, 125.3, 128.7, 146.6 and 154.7 (aryl C), 162.1 (CO2Me).

Reaction of methyl 5,7-dimethoxyindole-2-carboxylate (5) with triethyl orthoformate: formation of compounds 41 and 42. A mixture of methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.250 g, 1.06 mmol) and triethyl orthoformate (0.10 mL, 0.60 mmol) in anhydrous methanol (3 mL) was heated at reflux with a catalytic quantity of 6-toluenesulfonic acid, for 24 h. The resulting precipitate was filtered through a frit, washed with a little methanol, then water, and dried to give a 98:2 isomeric mixture (0.202 g, 80%) of the 3,3',4'-tridindomethane 41 and 3,3',3''-tridindomethane 42 as a white powder.

2,4-Dimethoxy-5-methyl-6-(5',7'-dimethoxy-1'-methylindol-3'-yl)benzo[1,2-b]carbazole (43). 5,7-Dimethoxy-1-methylindole 1 (0.20 g, 1.05 mmol), phthalaldehyde (70 mg, 0.52 mmol) and glacial acetic acid (4 mL) were combined and stirred at room temperature for 4.5 h. The resulting precipitate was filtered, washed with
water and dried, yielding 2,4-dimethoxy-5-methyl-6-(5',7'-dimethoxy-1'-methylindol-3'-yl)benzo[1,2-
b]carbazole 43 as a bright yellow powder (87 mg, 34%). Recrystallisation from ethyl acetate and petroleum ether afforded bright yellow crystals, mp 191-192 °C. IR (ν_{max} cm\(^{-1}\)): 1589, 1498, 1457, 1302, 1278, 1207, 1151, 1116, 1057. UV/Vis (λ_{max} nm, ε, cm\(^{-1}\)M\(^{-1}\)): 278 (47,000), 287 (59,000), 307 (14,000), 322 (7,500), 337 (4,000), 407 (5,600), 419 (5,600). \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ \(_H\) 3.53 (3H, br s, 5-NMe), 3.58 (3H, s, 5'-Ome), 3.90 (3H, s, 4-Ome), 3.98 (6H, s, 2-Ome and 7'-Ome), 4.16 (3H, s, 1'-NMe), 6.20 (1H, d, J 2.1 Hz, H4'), 6.38 (1H, d, J 2.1 Hz, H6'), 6.66 (1H, d, J 2.1 Hz, H3), 7.02 (1H, s, H2'), 7.30 (1H, m, H8), 7.35 (1H, d, J 2.1 Hz, H1), 7.36 (1H, m, H9), 7.82 (1H, d, J 8.4 Hz, H7), 8.05 (1H, dd, J 1.4, 8.2 Hz, H10), 8.54 (1H, s, H11). \(^13\)C NMR (75 MHz, CDCl\(_3\)): δ \(_C\) 34.6 and 36.5 (NMe), 55.4, 55.7, 55.8 and 56.0 (Ome), 93.3, 94.9, 95.0 and 100.0 (aryl CH), 111.1 and 112.0 (aryl C), 117.7 (aryl CH), 121.8 (aryl C), 122.4 (aryl CH), 124.5 (aryl C), 124.6 and 125.8 (aryl CH), 126.4 and 128.0 (aryl CH), 128.2 (aryl CH), 129.4 (aryl C), 130.8 (aryl CH), 132.1, 133.7, 141.9, 147.5, 148.1, 154.4 and 154.9 (aryl C). MS (+El, m/z, %): 481 (M, 28), 480 (85), 465 (15). Anal. calcd for C\(_{38}\)H\(_{28}\)N\(_2\)O\(_2\): C, 75.0; H, 5.9; N, 5.8. Found: C, 74.8; H, 5.9; N, 5.6 %.

**Dimethyl 2,6,8,12-tetrahydro-3,5,9,11-tetramethoxy-6,12-o-benzeno-diindolo[4,4a,3-bc:4',4a',3'-fg]cyclooctene-1,7-dicarboxylate (44).** Method A. A stirred solution of methyl 5,7-dimethoxyindole-2-carboxylate 5 (1.75 g, 7.46 mmol) and phthalaldialdehyde (0.50 g, 3.73 mmol) in anhydrous methanol (15 mL) was heated at reflux with concentrated HCl (2 drops) for 3 h. After cooling to room temperature the resulting precipitate was filtered through a frit, washed with a little methanol, then water, and dried to give the title compound (1.92 g, 90%) as a white powder, mp 316-319 °C. IR (ν_{max} cm\(^{-1}\)): 3468, 3334, 1687, 1590, 1538, 1456, 1436, 1392, 1354, 1298, 1254, 1204, 1111, 1000. UV/Vis (λ_{max} nm, ε, cm\(^{-1}\)M\(^{-1}\)): 245 (49,000), 279 (18,000), 301 (21,000), 345 (11,000). \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ \(_H\) 3.85, 3.94 and 4.08 (each 6H, s, OMe), 6.46 (2H, s, H6), 6.90 (2H, s, bridging CH), 7.12 (2H, m, aryl CH), 7.48 (2H, m, aryl CH), 8.66 (2H, bs, NH). \(^13\)C NMR (75 MHz, CDCl\(_3\)): δ \(_C\) 40.0 (bridging CH), 52.1, 56.0 and 60.0 (Ome), 97.3 (C6), 127.5 and 130.3 (aryl CH), 117.9, 121.6, 124.2, 125.9, 127.1, 142.5, 145.6 and 150.0 (aryl C), 163.2 (CO2Me). MS (MALDI, m/z, %): 568 (M, 100). Anal. calcd for C\(_{32}\)H\(_{28}\)N\(_2\)O\(_2\): C, 67.6; H, 5.0; N, 4.9. Found: C, 67.9; H, 5.0; N, 4.9 %.

**Method B.** A stirred solution of methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.11 g, 0.48 mmol) and phthalaldialdehyde (32 mg, 0.24 mmol) in chloroform (4 mL) was treated with phosphoric chloride (0.02 mL, 0.2 mmol). The darkened solution was stirred at room temperature for 3 days before it was basified with 2M NaOH and extracted with dichloromethane. The organic extract was washed with water, dried (MgSO\(_4\)), and the solvent evaporated in vacuo to give the title compound (0.13 g, 93%) as a white powder.

**Method C.** A mixture of methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.19 g, 0.79 mmol) and phthalaldialdehyde (53 mg, 0.24 mmol) in anhydrous methanol (7 mL), was stirred with p-toluenesulfonic acid (10 mg), under nitrogen, for 4 d. The resulting precipitate was filtered through a frit, washed with a little methanol, then water, and dried to give the title compound (150 mg, 100%) as a white powder.

**Dimethyl 2,6,8,12-tetrahydro-3,5,9,11-tetramethoxy-2,8-dimethyl-6,12-o-benzenodiindolo[4,4a,3-bc:4',4a',3'-fg]cyclooctene-1,7-dicarboxylate (46).** A stirred solution of methyl 5,7-dimethoxy-N-methylindole-2-carboxylate (6) (0.230 g, 0.923 mmol) and phthalaldialdehyde (80 mg, 0.60 mmol) in anhydrous methanol (5 mL) was stirred at ambient temperature with concentrated HCl (1 drop) for 4 h. The resulting precipitate was filtered through a frit, washed with water, and dried to give the title compound (0.12 g, 44%) as a white powder, mp 356-358 °C. IR (ν_{max} cm\(^{-1}\)): 1713, 1586, 1457, 1394, 1320, 1288, 1227, 1202, 1116. UV/Vis (λ_{max} nm, ε, cm\(^{-1}\)M\(^{-1}\)): 247 (46,500), 277 (15,500), 300 (17,000), 356 (11,500). \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ \(_H\) 3.80, 3.89 and 4.05 (each 6H, s, OMe), 4.14 (6H, s, OMe), 6.40 (2H, s, H6), 6.73 (2H, bs, bridging CH), 7.13 (2H, dd, J 3.4, 5.6 Hz, aryl H), 7.45 (2H, dd, J 3.4, 5.7 Hz, aryl H). \(^13\)C NMR (75 MHz, CDCl\(_3\)): δ \(_C\) 34.7 (NMe), 39.7 (bridging CH), 52.0, 56.2, and 59.2 (Ome), 97.0 (C6), 127.5 and 130.0 (aryl CH), 163.8 (CO2Me), 117.4, 125.0, 125.2,
2,2-Bis(5',7'-dimethoxy-1'-methylindol-3'-yl)propane (47). 5,7-Dimethoxy-1-methylindole 1 (0.10 g, 0.53 mmol), AR grade acetone (1 mL, excess) and acetic anhydride (4 mL) were combined and heated at reflux in an inert gas atmosphere for 6 h. No precipitate was formed so the reaction mixture was diluted with water and allowed to stand overnight. The resulting precipitate was filtered, washed with water and dried, affording a white solid. Radial chromatography using 50:50 dichloromethane: petroleum ether yielded 2,2-bis(5',7'-dimethoxy-1'-methylindol-3'-yl)propane 47 (20 mg, 18%) as pale tan crystals, mp 168-169 °C. IR (v_{\text{max}}, \text{cm}^{-1}): 1580, 1495, 1456, 1413, 1305, 1258, 1212, 1149, 1116, 1045. UV/Vis (\lambda_{\text{max}} nm, \epsilon, \text{cm}^{-1}\text{M}^{-1}): 221 (42,000), 229 (43,000), 266 (10,000), 272 (10,000), 300 (11,000), 307 (10,000). ^1H NMR (300 MHz, CDCl_3): δ H 1.83 (6H, s, Me), 3.65, 3.85 and 3.93 (18H, 3s, OMe and NMe), 6.22 (2H, d, J 2.3 Hz, H6), 6.44 (2H, d, J 2.3 Hz, H4), 6.71 (2H, s, H2). ^13C NMR (75 MHz, d_6-DMSO): δ C 29.8 (2C, Me), 34.1 (C), 36.1 (2C, NMe), 55.3 and 55.8 (4C, OMe), 95.3 and 95.9 (4C, aryl CH), 122.6 and 122.9 (4C, aryl C), 127.2 (2C, aryl CH), 128.4, 147.8 and 152.9 (6C, aryl C). MS (+El, m/z, %): 423 (M, 4), 422 (14), 407 (39), 216 (13). HRMS (m/z): Calcd for C_{25}H_{30}N_{2}O_{4} [M+Na]^+: 445.2098. Found: 445.2091.

6,8-Dimethoxy-1,3,3,5-tetramethyl-1,3-dihydrobenz[c]dijlindole (48). 5,7-Dimethoxy-1-methylindole 1 (0.20 g, 1.05 mmol), AR grade acetone (2 mL, excess) and glacial acetic acid (4 mL) were combined and refluxed under an inert gas atmosphere for 7 h. No precipitate was formed so the reaction mixture was diluted with water and allowed to stand overnight. The resulting colloidal solution was extracted with dichloromethane, and the organic phase was dried (Na_2SO_4) and the solvent removed under reduced pressure yielding a brown oil. Radial chromatography using 50:50 dichloromethane: petroleum ether afforded 6,8-dimethoxy-1,3,3,5-tetramethyl-1,3-dihydrobenz[c]dijlindole 48 (28 mg, 10%) as a cream solid, mp 123-125 °C. IR (v_{\text{max}}, \text{cm}^{-1}): 1605, 1513, 1464, 1409, 1283, 1234, 1214, 1116, 1089, 1053, 1023. UV/Vis (\lambda_{\text{max}} nm, \epsilon, \text{cm}^{-1}\text{M}^{-1}): 234 (19,000), 249 (22,000), 300 (4,800), 314 (6,800), 328 (9,300), 342 (9,500), 355 (4,700). ^1H NMR (300 MHz, CDCl_3): δ H 1.28 (6H, s, Me), 2.28 (3H, d, J 1.1 Hz, Me), 3.83 (3H, s, 6-OMe), 3.90 (3H, s, 8-OMe), 3.94 (3H, s, NMe), 5.24 (1H, br d, J 1.1 Hz, H4), 6.26 (1H, s, H7), 6.68 (1H, s, H2). ^13C NMR (75 MHz, CDCl_3): δ C 22.5 (5-Me), 33.6 (2C, 3-Me), 33.9 (C3), 35.5 (NMe), 55.5 (8-OMe), 59.4 (6-OMe), 94.8 (C7), 109.5 (C5a), 119.9 (C8a), 121.9 (C2a), 123.8 (C2), 127.3 (C5), 127.3 (C8b), 134.6 (C4), 147.3 (C8), 149.4 (C6). MS (+El, m/z, %): 271 (M, 22), 256 (100), 241 (20). HRMS (m/z): Calcd for C_{17}H_{21}NNaO_2 [M+Na]^+: 294.1464. Found: 294.1457. Anal. calcd for C_{17}H_{21}NO_2: C, 75.2; H, 7.8; N, 5.2. Found: C, 74.7; H, 8.0; N, 4.7 %.

Methyl 1,5-dihydro-6,8-dimethoxy-3,5,5-trimethylbenz[c]dijlindole-2-carboxylate (49). A mixture of methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.15 g, 0.64 mmol) in 2,2-dimethoxypropane (2 mL) was heated at reflux with a catalytic quantity of p-toluenesulfonic acid for 16 h. Water was then added and the resulting gum decanted from the solute, dissolved in ethyl acetate, washed sequentially with water and brine, dried (MgSO_4), and then the solvent evaporated in vacuo. The remaining red residue was purified via gravity column chromatography (2% MeOH/CH_2Cl_2) to give the title compound (55 mg, 34%) as a yellow powder, mp (softens at 174 °C) 183-187 °C. IR (v_{\text{max}}, \text{cm}^{-1}): 3349, 1686, 1536, 1456, 1391, 1336, 1272, 1253, 1172, 997. UV/Vis (\lambda_{\text{max}} nm, \epsilon, \text{cm}^{-1}\text{M}^{-1}): 245 (15,000), 273 (11,000), 301 (13,000), 312 (12,000), 366 (6,100). ^1H NMR (300 MHz, CDCl_3): δ H 1.46 (6H, s, Me), 2.30 (3H, d, J 1.1 Hz, Me), 3.86, 3.89, and 3.94 (each 3H, s, OMe), 5.45 (1H, d, J 1.5 Hz, H4), 6.54 (1H, s, H7), 8.46 (1H, bs, NH). ^13C NMR (75 MHz, CDCl_3): δ C 22.3 and 28.5 (Me), 38.0 (C5), 51.4, 55.5, and 57.6 (OMe), 97.0 (C7), 141.0 (C4), 118.6, 120.1, 120.3, 120.5, 123.7, 127.7, 143.9 and 151.5 (aryl C), 161.9 (CO_2Me). MS (+El, m/z, %): 315 (M, 16), 300 (67), 269 (17), 268 (100), 182 (20), 134 (15),...
112 (15). HRMS (m/z): Calcd for C_{18}H_{22}NO_{4} [M]^+ 315.1471. Found: 315.1473. Anal. calcd for C_{18}H_{22}NO_{4}: 0.25H_{2}O: C, 66.7; H, 6.8; N, 4.3. Found: C, 66.9; H, 6.7; N, 4.0 %.

**Methyl 4-(2-hydroxy-2'-indane-1',3'-dionyl)-5,7-dimethoxyindole-2-carboxylate (50).** A stirred suspension of methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.25 g, 1.1 mmol) and ninhydrin (0.19 g, 1.1 mmol) in anhydrous methanol (4 mL) was heated at reflux with concentrated HCl (3 drops) for 1.5 h. After cooling to room temperature, the resulting precipitate was filtered through a frit, washed with water, and dried to give the title compound (0.38 g, 91%) as a yellow powder, mp 238-241 °C. IR (v_{\text{max}}, \text{cm}^{-1}): 3412, 3323, 1744, 1698, 1584, 1536, 1438, 1326, 1246, 1216, 1145, 973. UV/Vis (λ_{\text{max}} nm, ε, cm^{-1}M^{-1}): 241 (42,500), 282 (14,300), 297 (17,300), 329 (5,600). ^1H NMR (300 MHz, CDCl₃): δ 3.45, 3.90, and 3.95 (each 3H, s, OMe), 6.28 (1H, s, H6), 7.86 (2H, m, ninhydrinyl), 7.90 (1H, d, J 2.3 Hz, H3), 8.03 (2H, m, ninhydrinyl), 9.01 (1H, bs, NH). ^13C NMR (300 MHz, d₆-DMSO): δ 3.25, 3.84, and 3.87 (each 3H, s, OMe), 6.52 (1H, s, H6), 6.89 (1H, s, OH), 7.74 (1H, s, H3), 7.98 (4H, s, ninhydrinyl), 11.68 (1H, bs, NH). The signals at 6.89 and 11.68 ppm exchanged with D₂O. ^11C NMR (75 MHz, d₆-DMSO): δ C 51.9, 56.1 and 57.5 (OMe), 78.3 (COH), 95.4 (C6), 111.6 (C3), 123.6 and 136.5 (ninhydrinyl CH), 111.2, 125.9, 127.2, 127.7, 140.4, 147.7, 150.0 (aryl C), 161.9 (CO₂Me), 199.3 (CO). MS (+EI, m/z, %): 395 (M, 96), 363 (19), 320 (20), 304 (18), 265 (13), 262 (14), 235 (54), 230 (52), 204 (16), 203 (100), 144 (23), 105 (13), 104 (54). Anal. calcd for C_{21}H_{17}NO_{5}: C, 63.8; H, 4.3; N, 3.5. Found: C, 63.9; H, 4.4; N, 3.6 %.

**Dimethyl 2,2-bis(5,7-dimethoxyindol-4-yl)indane-1,3-dione-2',2'-dicarboxylate (51).** Methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.25 g, 1.1 mmol) and ninhydrin (95 mg, 0.53 mmol) in anhydrous toluene (50 mL) was heated at reflux with a catalytic quantity of p-toluenesulfonic acid for 2 d using a Dean-Stark apparatus. After cooling to room temperature, the resulting precipitate was filtered through a frit, washed with a little toluene, then light petroleum (the combined filtrate was kept aside, see below), and dried to give the title compound (0.32 g, 98%) as a yellow powder, mp 238-240 °C (chloroform/light petroleum). IR (v_{\text{max}}, \text{cm}^{-1}): 3457, 3343, 1704, 1322, 1253, 1210, UV/Vis (λ_{\text{max}} nm, ε, cm^{-1}M^{-1}): 243 (60,600), 277 (19,300), 298 (29,700), 334 (8,850). ^1H NMR (300 MHz, CDCl₃): δ 3.51, 3.74 and 3.95 (each 6H, s, OMe), 6.34 (2H, d, J 2.3 Hz, H3' and H3''), 6.44 (2H, s, H6' and H6''), 7.76 and 7.98 (each 2H, m, ninhydrinyl), 8.75 (2H, bs, NH). ^13C NMR (75 MHz, CDCl₃): δ C 52.0, 58.6, 56.0 (OMe), 63.2 (bridging C), 96.6 (C6' and C6''), 111.3 (C3' and C3''), 123.5 and 134.6 (ninhydrinyl CH), 113.4, 124.7, 127.0, 129.1, 142.3, 147.4, 152.1 (aryl C), 162.4 (CO₂Me), 197.7 (CO). MS (+EI, m/z, %): 612 (M, 18), 577 (17), 551 (20), 369 (17), 368 (40), 367 (22), 353 (16), 339 (37), 313 (66), 299 (25), 285 (22), 265 (27), 264 (68), 262 (58), 239 (82), 238 (37), 236 (100). HRMS (m/z): Calcd for C_{33}H_{28}N_{2}O_{10}: [M]^+, 612.1744. Found: 612.1748.

**1-Pentanoyl-2,3-dihydroindole-2,3-dione (52).** Valeryl chloride (10.30 g, 85.4 mmol) was added dropwise over 10 min to a stirred suspension of isatin (12.0 g, 81.6 mmol) and pyridine (8 mL) in dichloromethane (140 mL) at room temperature. The mixture was heated at reflux for 1 h and then allowed to cool before the resulting red solution was washed briefly with dilute hydrochloric acid and dried (MgSO₄). The solvent was then removed in vacuo to approximately 50 mL before light petroleum was added to effect the precipitation of the product, which was then filtered and washed with light petroleum. Recrystallization from cyclohexane gave the title compound (15.8 g, 84%) as a bright yellow powder, mp 96-99 °C. IR (v_{\text{max}}, \text{cm}^{-1}): 1783, 1757, 1708, 1609, 1466, 1331, 1169. UV/Vis (λ_{\text{max}} nm, ε, cm^{-1}M^{-1}): 239 (18,600), 295 (4,100). ^1H NMR (300 MHz, CDCl₃): δ H 0.97 (3H, t, J 7.2 Hz, Me), 1.44 and 1.74 (each 2H, m, CH₂), 3.10 (2H, t, J 7.5 Hz, CH₂), 7.32 and 7.71 (each 1H, t, J 7.5 Hz, phenyl), 7.78 and 8.43 (each 1H, d, J 7.5 Hz, phenyl). ^13C NMR (75 MHz, CDCl₃): δ C 13.7 (Me), 22.1, 26.1 and 37.9 (CH₂), 118.2, 125.2, 125.9 and 138.8 (aryl CH), 119.2 and 148.8 (aryl C), 157.7 and 173.0 (CONHCO), 180.2 (CO). MS (+EI, m/z, %): 231 (M, 4), 146 (100), 90 (28), 85 (44), 57 (52). Anal. calcd for C_{13}H_{13}NO_{3}: C, 67.5; H, 5.7; N, 6.1. Found: C, 67.5; H, 5.8; N, 6.2 %.
Dimethyl 5,5\"",7,7\""-tetramethoxy-2\'-oxo-[3,3\':3\''(2'H),3\''-ter-1H-indole]-2,2\""-dicarboxylate (53). Method A. A solution of methyl 5,7-dimethoxyindole-2-carboxylate 5 (0.25 g, 1.1 mmol) and N-pentanoylisatin 52 (0.25 g, 1.1 mmol) in anhydrous methanol (25 mL) was heated at reflux with concentrated HCl (10 drops) for 7 h. The resulting precipitate was filtered through a frit, washed with water, and dried to give the title compound (0.24 g, 75\%) as a white powder, mp 299-301 °C. IR (ν_max, cm\(^{-1}\)): 3629, 3449, 3386, 1715, 1692, 1587, 1540, 1316, 1249, 1236, 1216. UV/Vis (λ_max nm, ε, cm\(^{-1}\)M\(^{-1}\)): 242 (57,200), 298 (37,400), 338 (10,200). \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ_H 3.44, 3.46, 3.76 and 3.77 (each 3H, s, OMe), 3.94 (6H, s, OMe), 5.79 (1H, bs, H3\""), 6.46 (1H, s, H3), 6.50 (2H, s, H6 and H6\""), 6.81 (1H, t, J 7.5 Hz, indolonyl), 6.87 and 7.12 (each 1H, d, J 7.5 Hz, indolonyl H4\' and H7\'), 7.16 (1H, t, J 7.5 Hz, indolonyl), 7.40 (1H, bs, NH\'), 8.77 and 8.79 (each 1H, bs, NH and NH\""). \(^1\)H NMR (300 MHz, d_6-DMSO): δ_H 3.24 and 3.41 (each 3H, s, OMe), 3.65 and 3.89 (each 6H, s, OMe), 5.87 and 6.43 (each 1H, s, H3 and H3\""), 6.56 and 6.61 (each 1H, s, H6 and H6\""), 6.67 (1H, t, J 7.5 Hz, indolonyl), 6.77 and 6.92 (each 1H, d, J 7.5 Hz, indolonyl), 7.04 (1H, t, J 7.5 Hz, indolonyl), 10.14 (1H, bs, NH\'), 11.35 and 11.48 (each 1H, bs, NH and NH\""). \(^1\)C NMR (75 MHz, d_6-DMSO): δ_C 56.9 (bridging C, C\''), 51.7, 51.8, 55.9, 56.0, 58.4 and 58.8 (OMe), 97.8 and 98.1 (C6 and C6\''), 108.7 and 109.4 (C3 and C3\'''), 120.7, 124.6, 126.8 (indolonyl CH), 111.7, 116.4, 125.7, 125.8, 126.2, 127.1, 128.1, 136.6, 141.5, 146.2, 151.4 (aryl C), 161.6 and 161.7 (CO_2Me), 178.6 (CONH). MS (MALDI, m/z, %): 599 (M, 48), 598 (100). Anal. calcd for C_{32}H_{29}O_{3}H_{2}O: C, 62.2; H, 5.1; N, 6.8. Found: C, 62.5; H, 4.8; N, 6.8.%

Method B. A mixture of methyl 5,7-dimethoxyindole-2-carboxylate 2 (0.16 g, 0.70 mmol) and methyl N-butyli-2\'-acetamidophenylglyoxylic ester 54 (0.10 g, 0.39 mmol) in anhydrous methanol (2 mL) was heated at reflux with concentrated HCl (1 drop) for 3 h. The resulting precipitate was filtered through a frit, washed with a little methanol, then water, and dried to give the title compound (0.17 g, 79\%) as a white powder.

Methyl 2\'-\{(n-butylamido)phenylglyoxylic ester (54). A mixture of N-pentanoylisatin 52 (1.00 g, 4.32 mmol) in anhydrous methanol (2 mL) was heated at reflux with concentrated HCl (1 drop) for 2 h. The solvent was then evaporated and the remaining residue was purified via suction column chromatography (dichloromethane) to give the title compound (0.64 g, 56\%) as a bright yellow syrup. IR (ν_max, cm\(^{-1}\)): 3323, 1742, 1704, 1655, 1608, 1584, 1530, 1450, 1204, 1161, 1000, 753. UV/Vis (λ_max nm, ε, cm\(^{-1}\)M\(^{-1}\)): 240 (19,000), 266 (8,000), 349 (4,000). \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ_H 0.95 (3H, t, J 7.2 Hz, Me), 1.42 and 1.74 (each 2H, m, CH\(_2\)), 2.46 (2H, t, J 7.2 Hz, CH\(_2\)), 3.99 (3H, s, OMe), 7.13 (1H, dt, J 1.1, 7.5 Hz, phenyl), 7.65 (2H, m, phenyl), 8.82 (1H, dd, J 1.1, 8.6 Hz, phenyl), 11.07 (1H, bs, NHCO). \(^13\)C NMR (75 MHz, CDCl\(_3\)): δ_C 13.6 (Me), 22.2, 27.4 and 38.3 (CH\(_2\)), 52.9 (CO_2Me), 120.8, 122.5, 133.5 and 137.1 (aryl CH), 117.0 and 142.6 (aryl C), 163.8 (CO_2Me), 173.0 (CONH), 190.2 (CO). MS (+EI, m/z, %): 263 (M, 2), 204 (64), 146 (24), 120 (100), 92 (31), 90 (22), 85 (23), 57 (63). HRMS (m/z): Calcd for C_{14}H_{17}NO_{4} [M]^+, 263.1158. Found: 263.1159.

Supplementary Material

A check cif file (compound 44) is available as Supplementary Data. Graphical NMR spectroscopic data are also presented for compounds 5, 15, 19, 44, 49, and 53.

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References

1. Black, D. StC.; Kumar, N.; Wong, L. C. H. *Aust. J. Chem.* **1986**, *39*, 15-20.  
   https://doi.org/10.1071/CH860015
2. Black, D. StC. *Synlett* **1993**, 246-252.  
   https://doi.org/10.1055/s-1993-22420
3. Black, D. StC.; Bowyer, M. C.; Kumar, N.; Mitchell, P. S. R. *J. Chem.Soc., Chem. Commun.* **1993**, 819-821.  
   https://doi.org/10.1039/c39930000819
4. Black, D. StC.; Bowyer, M. C.; Catalano, M. M.; Ivory, A. J.; Keller, P. A.; Kumar, N.; Nugent, S. J. *Tetrahedron* **1994**, *50*, 10497-10508.  
   https://doi.org/10.1016/S0040-4020(01)89590-9
5. Black, D. StC.; Bowyer, M. C.; Bowyer, P. K.; Ivory, A. J.; Kim, M.; Kumar, N.; McConnell, D. B.; Popiolek, M. *Aust. J. Chem.* **1994**, *47*, 1741-1750.  
   https://doi.org/10.1071/CH9941741
6. Black, D. StC.; Craig, D. C.; Kumar, N. *Aust. J. Chem.* **1996**, *49*, 311-318.  
   https://doi.org/10.1071/CH9960311
7. Chen, R.; Bhadbhade, M.; Kumar, N.; Black, D. StC. *Tetrahedron Lett.* **2012**, *53*, 3337-3341.  
   https://doi.org/10.1016/j.tetlet.2012.04.082
8. Somphol, K.; Chen, R.; Bhadbhade, M.; Kumar, N.; Black, D. StC. *Synlett* **2013**, 24-28.  
   https://doi.org/10.1055/s-0033-1338688
9. Chen, R.; Somphol, K.; Bhadbhade, M.; Kumar, N.; Black, D. StC. *Synlett* **2013**, 1497-1500.  
   http://doi.org/10.1055/s-0033-1338688
10. Condie, G. C.; Channon, M. F.; Ivory, A. J.; Kumar, N.; Black, D. StC. *Tetrahedron* **2005**, *61*, 4989-5004.  
    https://doi.org/10.1016/j.tet.2005.03.048
11. Black, D. StC.; Craig, D. C.; Kumar, N. *Tetrahedron Lett.* **1991**, *32*, 1587-1590.  
   https://doi.org/10.1016/0040-4020(91)90747-1
12. Black, D. StC.; Channon, M. F.; Clayton, K. A.; Condie, G. C.; Harper, J. B.; Kumar, N.; Pchalek, K.; Wahyuningsih, T. D.; *Arkivoc* **2006**, *(vii)*, 67-75.  
    https://doi.org/10.3998/ark.5550190.0007.707
13. Schöllkopf, U.; Lonsky, R.; Lehr, P. *Liebigs Ann. Chem.* **1985**, 413-417.  
   https://doi.org/10.1002/jlac.198519850217
14. Oliveira, D. d. J.; Coelho, F. *Synth. Commun.* **2000**, *30*, 2143-2159.  
   https://doi.org/10.1080/00397910008087393
15. Dobrowolski, J.; Somphol, K.; Santosso, M.; Duong, H.; Gardner, C. R.; Kumar, N.; Black, D. StC. *Aust. J. Chem.* **2017**, *70*, 1188-1195.  
   https://doi.org/10.1071/CH17257
16. Joule, J. A. in *Science of Synthesis*; Thomas, E. J. Ed.; Georg Thieme Verlag: Stuttgart, 2000, Vol. 10, pp 361-652.  
   http://doi.org/10.1055/sos-SD-110-00001
17. Trofimov, B. A.; Nedolya, N. A. in *Comprehensive Heterocyclic Chemistry III*; Jones, G. A.; Ramsden, C. A. Eds.; Elsevier: Oxford, 2008, Vol. 3, pp 45-267.  
   https://doi.org/10.1016/B978-008044992-0.00302-3
18. Clezy, P. S.; Fookes, C. J. R.; Liepa, A. J. *Aust. J. Chem.* **1972**, *25*, 1979-1990.  
   https://doi.org/10.1071/CH721979
19. Akgün, E.; Pindur, U.; Müller, J. J. Heterocycl. Chem. 1983, 20, 1303-1305. https://doi.org/10.1002/jhet.5570200530
20. Schiffl, E.; Pindur, U. J. Heterocycl. Chem. 1986, 23, 651-656. https://doi.org/10.1002/jhet.5570230303
21. Pindur, U.; Müller, J. J. Heterocycl. Chem. 1987, 24, 289-290. https://doi.org/10.1002/jhet.5570240156
22. Witzel, H.; Pindur, U. J. Heterocycl. Chem. 1988, 25, 907-910. https://doi.org/10.1002/jhet.5570250339
23. Gmeiner, P.; Kraxner, J.; Bollinger, B. Synthesis 1996, 1196-1198. https://doi.org/10.1055/s-1996-4356
24. Kraxner, J.; Arlt, M.; Gmeiner, P. Synlett 2000, 125-127. https://doi.org/10.1055/s-2000-6439
25. Rodrigues, A. M. S.; Rohée, C.; Fabre, T.; Batailler, N.; Sautel, F.; Carletti, I.; Nogues, S.; Suzuki, M. T.; Stien, D. Tetrahedron Lett. 2017, 58, 3172-3173. https://doi.org/10.1016/j.tetlet.2017.07.005
26. Aghazadeh, M. Arkivoc 2019, (vi), 141-148. https://doi.org/10.24820/ark.5550190.p011.012
27. Black, D. StC.; Craig, D. C.; Santoso, M. Tetrahedron Lett. 1999, 40, 6653-6656. https://doi.org/10.1016/S0040-4039(99)01268-X
28. Zhao, L.; Li, Z.; Wirth, T. Chem. Lett. 2010, 39, 658-667. https://doi.org/10.1246/cl.2010.658
29. Bergman, J.; Norrby, P. O.; Tilstam, U.; Venemalm, L. Tetrahedron 1989, 45, 5549-5564, and references cited therein. https://doi.org/10.1016/S0040-4020(01)89501-6
30. Sakagami, M.; Muratake, H.; Natsume, M. Chem. Pharm. Bull. Japan 1994, 42, 1393-1398. https://doi.org/10.1248/cpb.42.1393
31. Black, D. StC.; Moss, G. I.; Wong, L. C. H. Tetrahedron Lett. 1978, 2837-2838.
32. Cheah, W. C; Wood, K.; Black, D. StC.; Kumar, N. Tetrahedron 2011, 67, 7603-7610. https://doi.org/10.1016/j.tet.2011.07.036
33. Hewawasam, P.; Meanwell, N. A. Tetrahedron Lett. 1994, 35, 7303-7306. https://doi.org/10.1016/0040-4039(94)85299-5
34. Liu, J-X.; Zhu, Z-Q.; Yu, L.; Du, B-X.; Mei, G-J.; Shi, F. Synthesis 2018, 50, 3436-3444, and references cited therein. https://doi.org/10.1055/s-0037-1609732

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