HETEROCYCLES, Vol. 102, No. 2, 2021, pp. -. © 2021 The Japan Institute of Heterocyclic Chemistry
Received, 15th December, 2020, Accepted, 25th December, 2020, Published online, 8th January, 2021
DOI: 10.3987/COM-20-14397

SYNTHESIS OF SOME (TRIINDOLYL)DIMETHANES AND (TETRAINDOLYL)TRIMETHANES

Kittya Somphol, Naresh Kumar, and David StC. Black*

School of Chemistry, The University of New South Wales, UNSW Sydney, NSW 2052, Australia. Email: d.black@unsw.edu.au

Abstract – Acid catalyzed substitution reactions of 3-substituted-4,6-dimethoxyindole-2,7-dimethanols with 4,6-dimethoxyindoles substituted at C3 and C7 give (triindolyl)dimethanes with 2,2'- and 2,7'-methylene links in good yields. A related example involving a 4,6-dimethoxyindole substituted at C3 and C2 generates the corresponding (triindolyl)dimethane with 2,7'- and 7,7'-methylene links. Similar reactions of 2,7-di(hydroxymethyl)-4,6-dimethoxy-3-methylindole occur with *N*-methylindole and in the case of 1,2-di(indolyl-1-methyl)benzene generate a 16-membered ring compound in high yield. This methodology was also applied to (diindolyl)-dimethanols to afford a range of tetraindolyl trimethanes.

INTRODUCTION

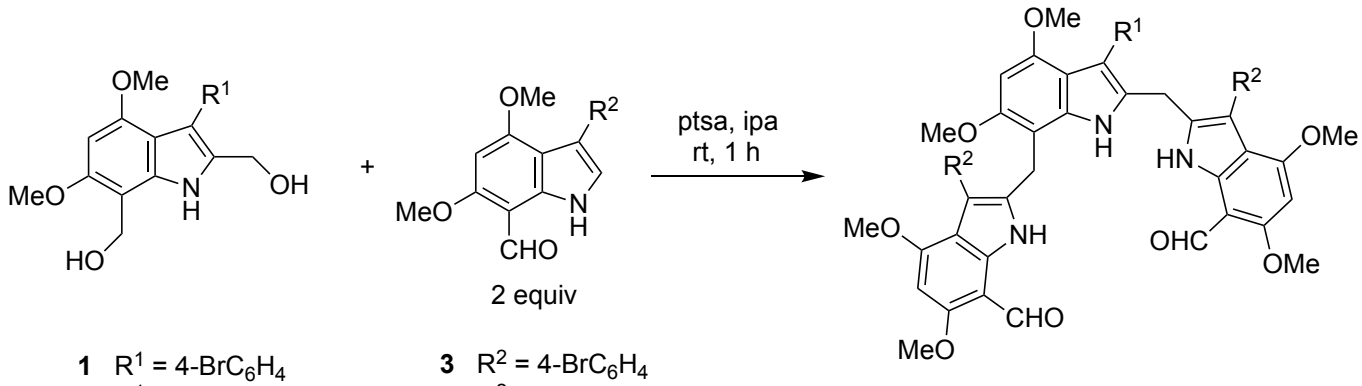
We have previously reported that a variety of (hydroxymethyl)indoles (also named as indole-methanols) can undergo acid-catalysed substitution reactions with other indoles to yield diindolylmethanes.[1-16] Most of this work has focused on reactions of 3-substituted-4,6-dimethoxyindoles with hydroxymethyl substituents at C2 and C7[9-15] but similar behaviour occurs with 4-hydroxymethyl-5,7-dimethoxyindoles.[16] The various nucleophiles have included a range of 3-substituted-4,6-dimethoxyindoles and the acid-catalysed conditions have usually been glacial acetic acid, *p*-toluenesulfonic acid in isopropanol, or hydrochloric acid in methanol. In this paper we initially describe reactions of 2,7-di(hydroxymethyl)-4,6-dimethoxy-3-(4-bromophenyl)indole **1** and the related 3-methyl analog **2** with a range of indole nucleophiles to produce (triindolyl)dimethanes. The di(hydroxymethyl)indoles **1** and **2** were prepared by sodium borohydride reduction of the corresponding indole-2,7-dialdehydes which in turn were obtained by Vilsmeier formylation of the parent 3-substituted-4,6-dimethoxyindoles. Earlier studies[9,13] established that both the C7 and C2 positions of the 3-substituted-4,6-dimethoxyindoles could

behave as nucleophiles in reaction with the (hydroxymethyl)indoles, but product mixtures resulted. In order to achieve clean and selective reactions, we investigated the nucleophilic capacity at C2 of the related and readily available indole-7-aldehydes. The success of this approach led to an effective strategy for the construction of (triindolyl)dimethanes and the subsequent formation of calix[3]indoles in high yield and efficiency.[14] We now describe our further investigations to examine the scope of this synthetic methodology.

RESULTS AND DISCUSSION

Acid catalyzed reactions of indole-2,7-dimethanols with indole-7-aldehydes

We have previously reported[14] that indole-2,7-dimethanol **1** underwent reaction with two equivalents of indole-7-aldehyde **3** in isopropanol with *p*-toluenesulfonic acid to give triindolyl dimethane **5** in 90% yield after 1 hour at room temperature (Scheme 1). Subsequently we investigated the generality of this reaction methodology by combining indole-2,7-dimethanol **2** with 3-methylindole-7-aldehyde **4** in isopropanol and *p*-toluenesulfonic acid and obtained triindolyl dimethane dialdehyde **6** in 96% yield. The combination of indole-2,7-dimethanol **1** with indole-7-aldehyde **4** similarly gave (triindolyl)dimethane dialdehyde **7** in 83% yield (Scheme 1). The proposed mechanism for this reaction has been discussed in our earlier paper.[14]



1 R^1 = 4-BrC_6H_4
2 R^1 = Me

3 R^2 = 4-BrC_6H_4
4 R^2 = Me

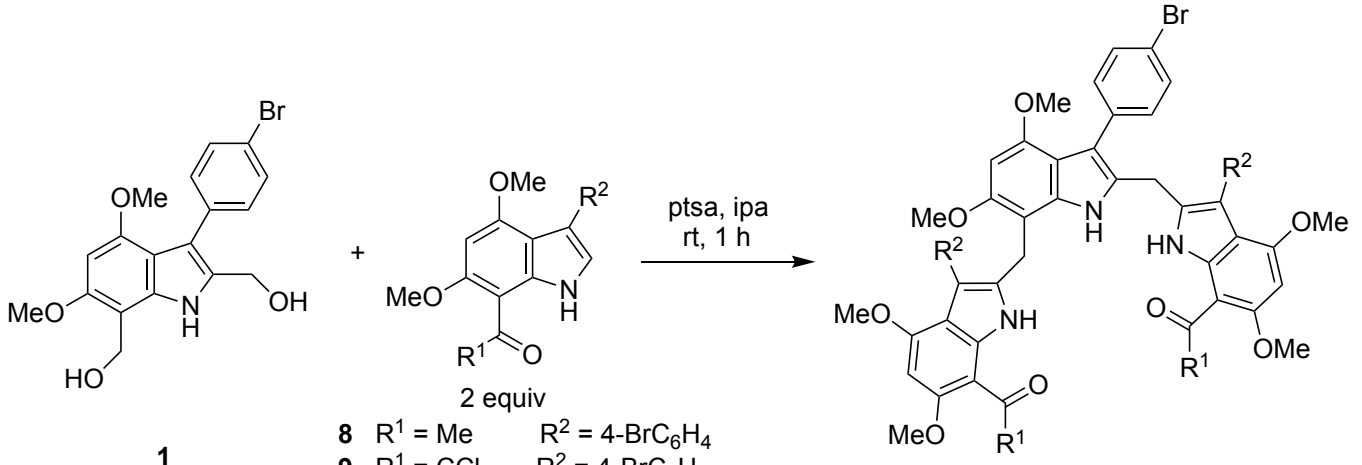
5	R^1 = 4-BrC_6H_4	R^2 = 4-BrC_6H_4	(90%)[6]
6	R^1 = Me	R^2 = Me	(96%)
7	**R^1** = 4-BrC_6H_4	R^2 = Me	(83%)

Scheme 1

Variation of the C7 substituent

Despite the electron withdrawing effect of the 7-aldehyde group in indoles **3** and **4**, the indole C2 position still showed strong nucleophilic character. We therefore investigated the behaviour of the related indole-7-methyl-, 7-trichloromethyl- and 7-benzyl-ketones **8**,[17] **9**[18,19] and **10**[20] respectively, and 7-glyoxylate ester **11**[21] and obtained the corresponding (triindolyl)dimethanes **12-15** in 84-88% yield (Scheme 2). These reaction conditions are important, because low yields and complex product mixtures

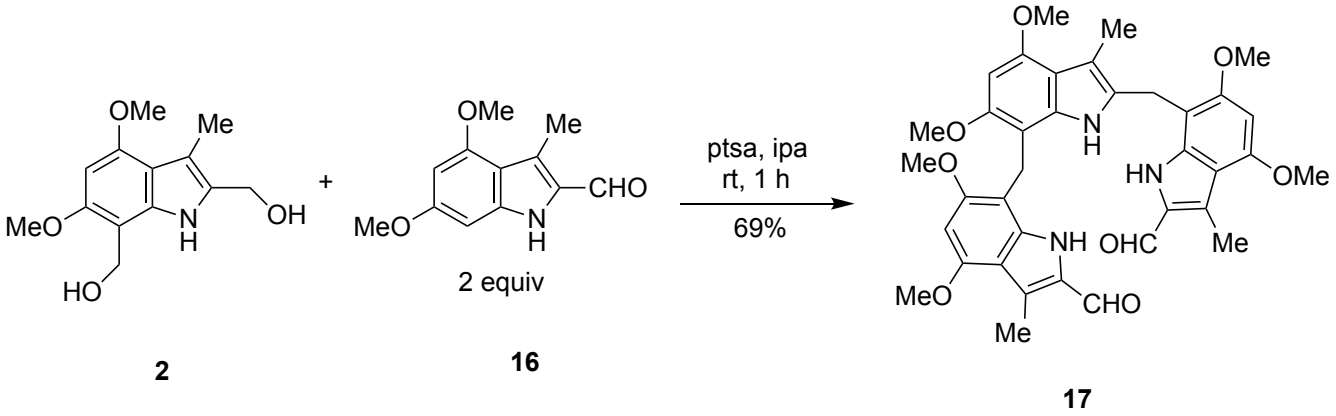
were obtained from reactions in glacial acetic acid, or tetrahydrofuran containing a catalytic amount of concentrated hydrochloric acid. A key feature of the optimized reaction conditions is that the products precipitate directly from the isopropanol, thus promoting high yields and purity. The scope of this reaction appears to be general with respect to the nature of the indole C7 substituent.



Scheme 2

Acid catalyzed reactions of indole-2,7-dimethanol 2 with indole-2-aldehyde 16

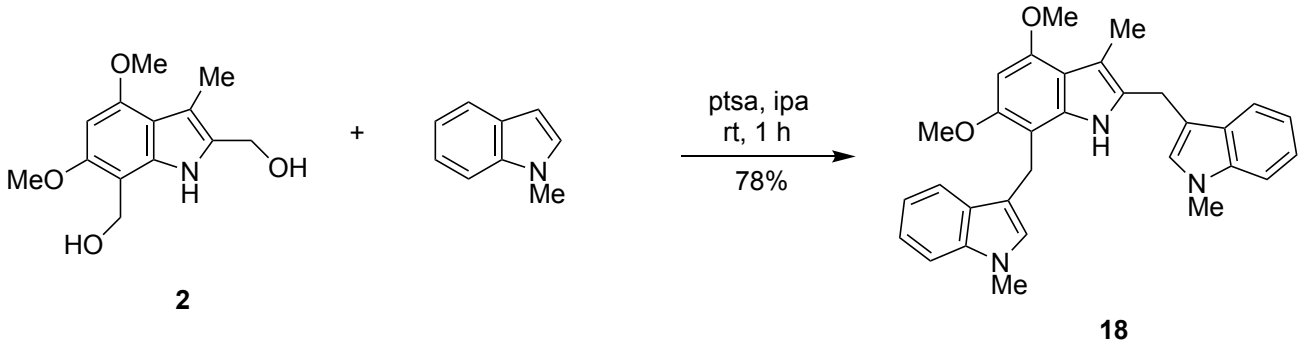
In the formylation of 3-aryl-4,6-dimethoxyindoles the overwhelmingly major product is the 7-aldehyde. However, formylation of 3-methyl-4,6-dimethoxyindole gives both the 7- and 2-aldehydes in almost comparable yields. Thus the readily available indole-2-aldehyde **16** was reacted with indole-2,7-dimethanol **2** in isopropanol containing *p*-toluenesulfonic acid and afforded (triindolyl)-dimethane **17** in 69% yield (Scheme 3). Attempts to react dimethanol **2** with other dimethoxyindoles containing a 2-glyoxylate ester, or a 2-methyl group were unsuccessful and gave complex product mixtures. Compound **17** contains one 2,7'- and one 7,7'-methylene link, whereas the compounds **5**-**7** and **12**-**15** contain one 2,7'- and one 2,2'-methylene link. We have earlier reported the formation of a similar (triindolyl)dimethane, in which the 3-methyl groups of compound **17** are replaced by 4-chlorophenyl substituents, as a trace (2%) product in the reaction of 3-(4-chlorophenyl)-4,6-dimethoxyindole in hot glacial acetic acid with 3-(4-chlorophenyl)-7-hydroxymethyl-4,6-dimethoxyindole.[13] An X-ray crystal determination of this compound revealed a U-shaped structure where the substituent indoles are pendant from the central indole via the two methylene linkages.



Scheme 3

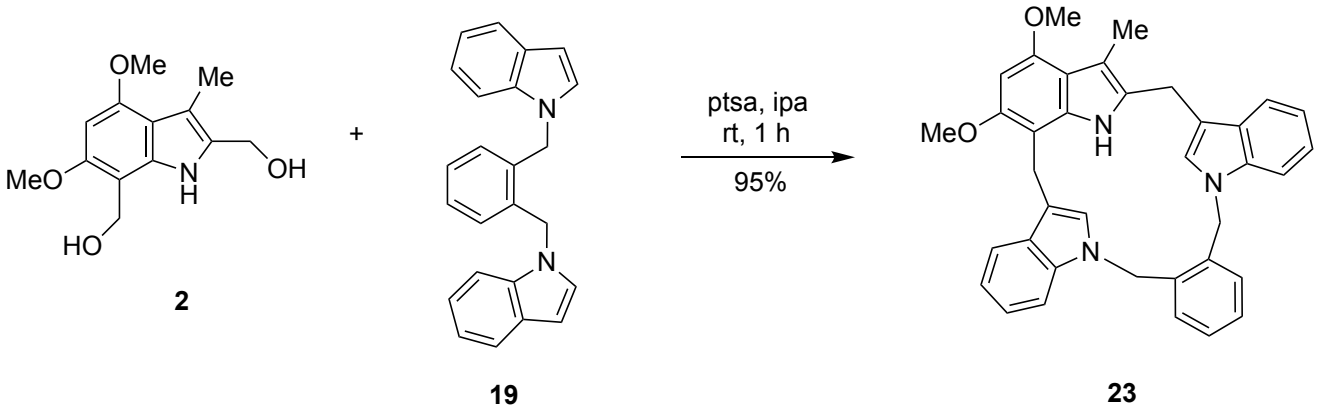
Acid catalyzed reactions of indole-2,7-dimethanol 2 with *N*-alkylindoles

Our investigations of the scope of acid catalyzed substitution reactions of indole-dimethanols next turned to the nature of the nucleophile. So far, the nucleophiles were indoles specially designed for enhanced nucleophilic activity by virtue of the two electron donating methoxy substituents. However, simple indoles are themselves good nucleophiles and it was of interest to establish whether the methoxy groups were essential for the reactions described above. Combination of indole-dimethanol **2** with two equivalents of indole itself using the standard conditions of *p*-toluenesulfonic acid in isopropanol led to a complex polymeric mixture, and a similar result was observed when 2-phenylindole was used as the nucleophile. However, *N*-methylindole reacted smoothly with dimethanol **2** to give (triindolyl)dimethane **18** in 78% yield (Scheme 4).



Scheme 4

This positive result led to an investigation of reactions of dimethanol **2** with one equivalent of diindolyl compounds **19**-**22**, in which the indoles are joined respectively through their nitrogen atoms by *o*-, *m*-, and *p*-xylyl, and simple methylene linkers. Reactions with compounds **20**-**22** gave only polymeric mixtures, but reaction with compound **19** gave a 95% yield of the 16-membered macrocyclic compound **23** (Scheme 5).

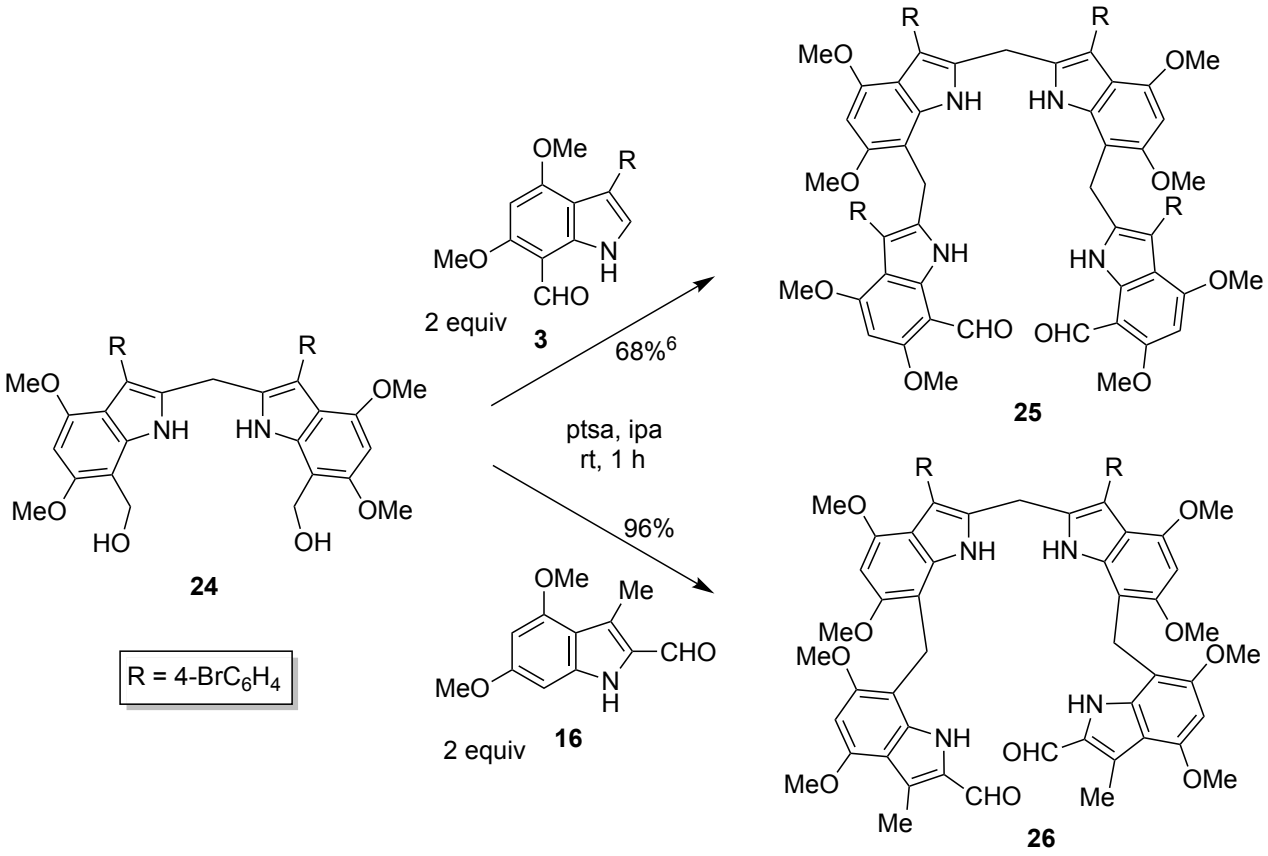


Scheme 5

The structure of macrocycle **23** was clear from its NMR spectroscopic data showing singlet resonances for the methyl, methoxy, and methylene protons, and indicating a flexible structure.

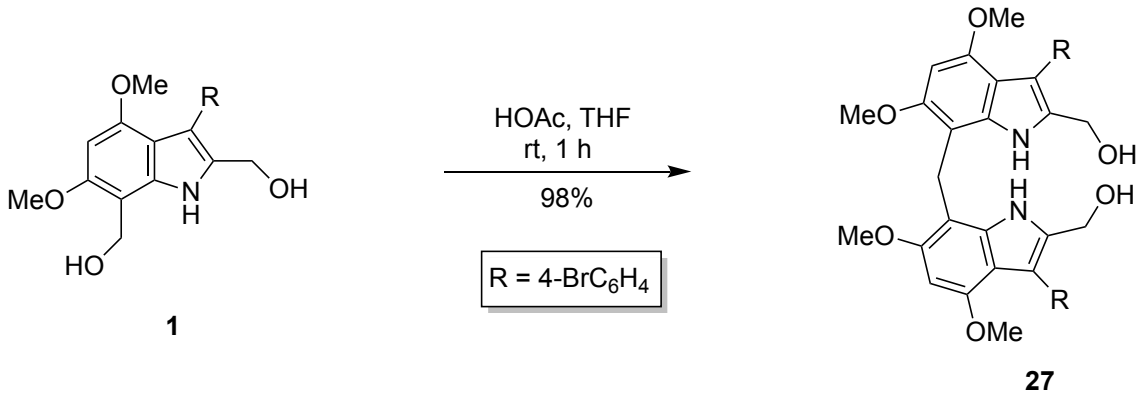
Acid catalyzed reactions of (diindolyl)dimethanols with indole aldehydes

We have previously described[14] the acid catalyzed reaction of 7,7'-di(hydroxymethyl)-2,2'-diindolylmethane **24** with 4,6-dimethoxyindole-7-aldehyde **3** to give (tetraindolyl)trimethane dialdehyde **25** in 68% yield. We now also report that dimethanol **24** also reacts under similar conditions with dimethoxyindole-2-aldehyde **16** to give (tetraindolyl)trimethane dialdehyde **26** in 96% yield (Scheme 6).



Scheme 6

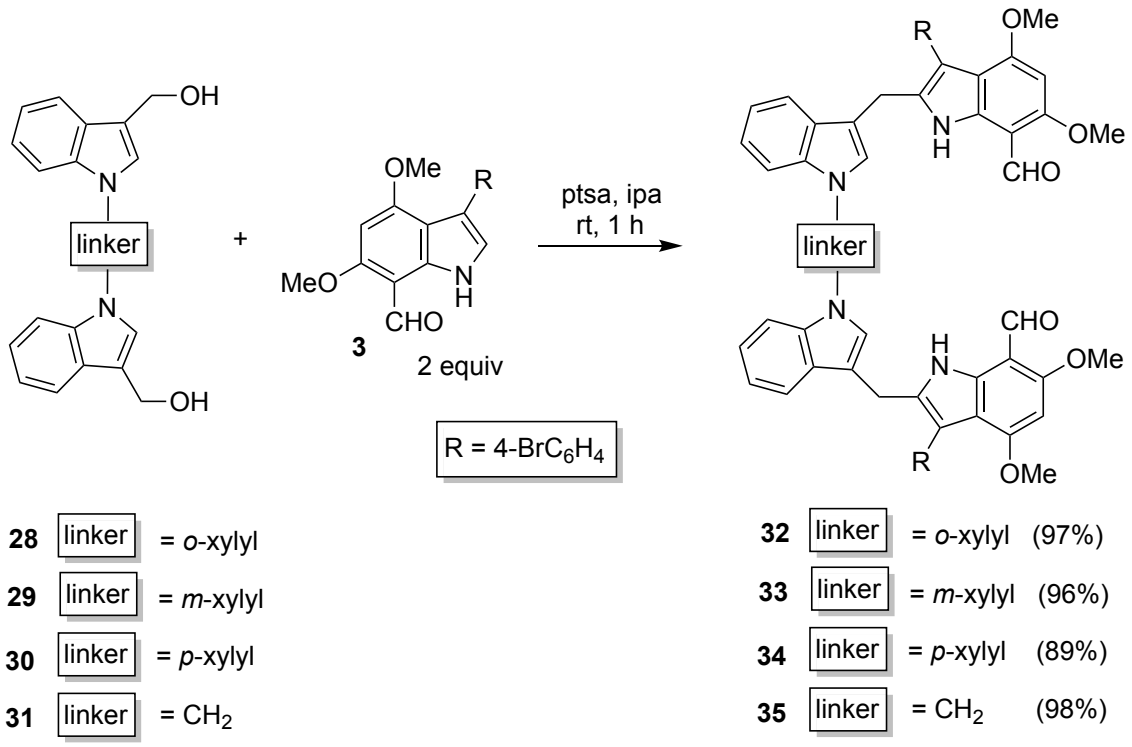
In attempting to extend the scope of this synthetic methodology, we also investigated 2,2'-di(hydroxymethyl)-7,7'-diindolylmethane **27**, which could be obtained in 98% yield from the reaction of indolyl-dimethanol **1** with glacial acetic acid in tetrahydrofuran (Scheme 7). The reaction presumably proceeds via an *ipso* attack of the C7 position of one molecule of indole **1** at the benzylic position of another molecule of indole **1**, followed by loss of formaldehyde in the re-aromatization step. This reaction has been observed for many 4,6-dimethoxyindole-7-methanols,[22,23] but it is interesting to note in this case the preference for this selective reaction at C7 rather than C2. The C7 site is more strongly nucleophilic than the C2 site, and also the C7 methylene carbocation is more readily formed than that at C2. Attempted reactions of dimethanol **27** with two equivalents of either indole-7-aldehyde **3** or indole-2-aldehyde **16** under the standard conditions failed to yield any isolable (tetraindolyl)trimethane products.



1 **27**

Scheme 7

The scope of this general synthetic methodology was extended to include acid catalyzed substitution reactions of the linked di(indolyl-3-methanol) compounds **28-31**[23] with indole-7-aldehyde **3**, which yielded (tetraindolyl)dialdehydes **32-35** in 89-98% yield (Scheme 8).



Scheme 8

CONCLUSIONS

The ability of a range of dimethoxy activated indoles to act as nucleophiles at C7 and C2 in acid catalyzed substitution reactions with various indole-methanols has been demonstrated. The presence of methoxy substituents is not mandatory for the reactions to proceed, but is mandatory to generate nucleophilicity at C7 and C2. Thus the variety of diindolylmethane links can be expanded from the common 3,3'-diindolylmethanes, to include 2,2'-, 2,3'-, 2,7'-, 3,7'-, and 7,7'-links. Depending on the starting materials, (triindolyl)dimethanes and (tetraindolyl)trimethanes can be produced in high yield. The reaction conditions of *p*-toluenesulfonic acid in isopropanol are critical for the isolation of products in high yield, but do not allow complete generality of scope. The use of indole-aldehyde nucleophiles, especially the indole-7-aldehydes, offers the construction of indolylmethylene oligomers. Once the nucleophilic substitution reaction is complete, the formyl groups can be reduced to generate a new hydroxymethyl substituent, ready for the next substitution reaction to take place. The main challenge we have observed in preliminary experiments to lengthen the oligomeric chain is the issue of solubility, both with respect to solubility of starting materials and relative insolubility of products. Despite these experimental issues, the work offers new developments in the wider field of arylmethylene oligomers and polymers, phenol-formaldehyde polymers, pillarenes and new calixarenes, areas which have been at the basis of many practical applications.

EXPERIMENTAL

Melting points were measured using a Mel-Temp melting point apparatus, and are uncorrected. Microanalyses were performed on a Carlo Erba Elemental Analyser EA 1108 at the Campbell Microanalytical Laboratory, University of Otago, New Zealand. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker DPX300 (300 MHz) spectrometer. Mass spectra were recorded on either a Bruker FT-ICR MS (EI) or a Micromass ZQ2000 (ESI) at UNSW, or a Shimadzu LCMS QP 8000 (ESI) at the University of Otago, New Zealand. Infrared spectra were recorded with a Thermo Nicolet 370 FTIR Spectrometer using KBr discs. Ultraviolet-visible spectra were recorded using a Varian Cary 100 Scan Spectrometer. Column chromatography was carried out using Merck 230-400 mesh ASTM silica gel, whilst preparative thin layer chromatography was performed using Merck silica gel 7730 60GF254.

2',7'';2'',2'''-Tri(4,6-dimethoxy-3-methyl)indolyldimethane-7',7'''-dicarbaldehyde (6). The indole-7-aldehyde **4** (53 mg, 0.24 mmol), indole-2,7-dimethanol **2** (30 mg, 0.12 mmol), and *p*-toluenesulfonic acid monohydrate (2 mg, 0.01 mmol) were stirred together at room temperature in isopropanol (35 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **6** as a bright yellow solid (75 mg, 96%), mp 249-251 ˚C. ν_{max} (KBr): 3424, 3379, 2934, 2843, 1642, 1600, 1568, 1508, 1464, 1433, 1390, 1368, 1353, 1311, 1238, 1212, 1121, 991, 789 cm^{-1}. λ_{max} (CH_2Cl_2): 230 nm (ε 56,600 cm^{-1}M^{-1}), 252 (70,500), 327 (25,000). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.11, 2.31, 2.40 (3s, 9H, Me), 3.89, 3.90, 3.92, 3.98, 4.02, 4.04 (6s, 22H, CH_2, OMe), 5.98, 6.13, 6.28 (3s, 3H, indole H5), 7.24 (s, 1H, centre indole NH), 9.87, 10.17 (2s, 2H, NH), 10.23, 10.29 (2s, 2H, CHO). This compound was not sufficiently soluble for a ^{13}C NMR spectrum to be obtained. Mass Spectrum (+EI): *m/z* (%) 675 ([M+Na]$^{+}$, 100), 654 (M+1, 10). Anal. Calcd for $C_{37}H_{39}N_3O_8$: C, 68.0; H, 6.0; N, 6.4. Found: C, 67.8; H, 6.2; N, 6.2.

2',7'';2'',2'''-(3-(4-Bromophenyl)-4,6-dimethoxyindol-2-yl)(di(4,6-dimethoxy-3-methyl)indol-1,3-yl)-dimethane-7',7'''-dicarbaldehyde (7). The indole-7-aldehyde **4** (0.30 g, 1.37 mmol), indole-2,7-dimethanol **1** (0.27 g, 0.69 mmol), and *p*-toluenesulfonic acid monohydrate (10 mg, 0.05 mmol) were stirred together at room temperature in isopropanol (50 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **7** as a yellow solid (0.46 g, 83%), mp 233-235 ˚C (from CH_2Cl_2/light petroleum). ν_{max} (KBr): 3423, 3346, 1930, 2841, 1639, 1600, 1570, 1507, 1487, 1465, 1434, 1390, 1368, 1237, 1212, 1170, 992, 786 cm^{-1}. λ_{max} (CH_2Cl_2): 246 nm (ε 81,500 cm^{-1}M^{-1}), 320 (31,100). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.09, 2.23 (2s, 6H, Me), 3.71, 3.89, 3.91, 3.96, 4.01, 4.05 (6s, 18H, OMe), 3.98, 3.99 (2s, 4H, CH_2), 5.96, 6.10, 6.34 (3s, 3H, indole H5), 7.31 (d, *J* 8.3 Hz, 2H, aryl H), 7.48 (d, *J* 8.3 Hz, 2H, aryl H), 7.80, 9.86, 10.21 (3s, 3H, NH), 10.21, 10.25 (2s, 2H, CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.0, 10.1 (Me), 20.4, 23.1 (CH_2), 55.2, 55.3, 56.1, 56.3, 56.8 (OMe), 85.7, 86.0, 89.2

(indole C5), 130.3, 132.5 (aryl CH), 101.8, 104.1, 104.3, 104.4, 105.9, 108.7, 109.7, 112.2, 112.6, 113.4, 119.8, 128.7, 130.2, 132.0, 134.5, 136.0, 136.4, 152.7, 153.3, 160.9, 161.2, 162.1, 162.4 (aryl C), 187.8 (2xCHO). Mass Spectrum (+EI): *m/z* (%) 817 ($[M+Na]^+$, 100), 701 (30), 637 (25), 608 (25), 246 (25). Anal. Calcd for $C_{42}H_{40}BrN_3O_8$: C, 63.5; H, 5.0; N, 5.3. Found: C, 63.2; H, 4.9; N, 5.4.

3-(4-Bromophenyl)-4,6-dimethoxy-7-trichloroacetylindole (9). Trichloroacetyl chloride (1.0 mL, 8.96 mmol) was added to a solution of 3-(4-bromophenyl)-4,6-dimethoxyindole (1.0 g, 3.01 mmol) in anhydrous $CHCl_3$ (20 mL). The mixture was heated under reflux overnight in an argon atmosphere. After cooling to room temperature, saturated $NaHCO_3$ was added and the mixture was stirred at room temperature for 30 min. The mixture was extracted with CH_2Cl_2 and the combined extracts were washed with water and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude product was column chromatographed (EtOAc/light petroleum) with the first band yielding 3-(4-bromophenyl)-4,6-dimethoxy-*N*-trichloroacetylindole (0.35 g, 25%) as a bright yellow solid, mp 193-195 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 1717, 1644, 1608, 1594, 1569, 1497, 1420, 1304, 1250, 1211, 1150, 1074, 1010, 845, 811, 755 cm^{-1}. λ_{max} (CH_2Cl_2): 230 nm (ε 19,300 $cm^{-1}M^{-1}$), 266 (25,500), 347 (4,200). ^1H NMR (300 MHz, $CDCl_3$): δ 3.76, 3.91 (2s, 6H, OMe), 6.47 (d, *J* 1.9 Hz, 1H, H5), 7.43, 7.52 (2d, *J* 8.7 Hz, 4H, aryl H), 7.70 (s, 1H, H2), 7.76 (d, *J* 1.9, 1H, H7). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.2, 55.7 (OMe), 93.8 (C5), 97.0 (C7), 121.5 (C2), 130.7, 131.1 (aryl CH), 121.6, 124.6, 132.5, 139.7, 154.3, 157.6, 160.5 (aryl C, C=O). Mass Spectrum (+EI): *m/z* (%) 480 (M+1, $^{35/37/37}Cl^{79}Br$ and $^{35/35/37}Cl^{81}Br$, 13), 478 (M+1, $^{35/35/37}Cl^{79}Br$ and $^{35/35/35}Cl^{81}Br$, 25), 476 (M+1, $^{35/35/35Cl79}Br$, 25), 334 (^{81}Br, 100), 332 (^{79}Br, 80). Anal. Calcd for $C_{18}H_{13}BrCl_3NO_3.0.125C_6H_{14}$: C, 46.1; H, 3.0; N, 2.9. Found: C, 46.1; H, 3.2; N, 2.8.

The second band eluted from the column yielded 7- trichloroacetyl indole **9** (0.37 g, 27%) as an orange solid, mp 190-192 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 3385, 1643, 1579, 1558, 1538, 1465, 1348, 1216, 1183, 1164, 1122, 1097, 1068, 1010, 980 cm^{-1}. λ_{max} (CH_2Cl_2): 234 nm (ε 22,100 $cm^{-1}M^{-1}$), 267 (18,800), 346 (9,600). ^1H NMR (300 MHz, $CDCl_3$): δ 3.93, 3.99 (2s, 6H, OMe), 6.23 (s, 1H, H5), 7.08 (d, *J* 2.6 Hz, 1H, H2), 7.41 (d, *J* 8.6 Hz, 2H, aryl H), 7.49 (d, *J* 8.3 Hz, 2H, aryl H), 10.29 (br s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.4, 55.6 (OMe), 87.6 (C5), 121.4 (C2), 130.7, 131.0 (aryl CH), 60.3, 110.0, 110.7, 118.5, 120.1, 134.2, 139.7, 160.3, 161.3 (aryl C, CCl_3), 182.3 (C=O). Mass Spectrum (+EI): *m/z* (%) 482 (M+1, $^{37/37/37}Cl^{79}Br$ and $^{35/37/37}Cl^{81}Br$, 60), 480 (M+1, $^{35/37/37}Cl^{79}Br$ and $^{35/35/37}Cl^{81}Br$, 60), 478 (M+1, $^{35/35/37}Cl^{79}Br$ and $^{35/35/35}Cl^{81}Br$, 100), 476 (M+1, $^{35/35/35}Cl^{79}Br$, 75). Anal. Calcd for $C_{18}H_{13}BrCl_3NO_3.0.5CH_2Cl_2$: C, 42.7; H, 2.7; N, 2.7. Found: C, 43.1; H, 2.7; N, 2.7.

7',7'''-Diacetyl-2',7'';2'',2'''-tri(3-(4-bromophenyl)-4,6-dimethoxy)indolyldimethane (12). The 7-acetyl indole **8** (95 mg, 0.25 mmol), indole-2,7-dimethanol **1** (50 mg, 0.13 mmol), and *p*-toluenesulfonic acid monohydrate (6 mg, 0.03 mmol) were stirred together at room temperature in

isopropanol (30 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **12** as a yellow solid (124 mg, 85%), mp 176-178 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 3390, 2934, 1624, 1585, 1560, 1487, 1464, 1433, 1377, 1353, 1264, 1212, 1195, 996 cm^{-1}. λ_{max} (CH_2Cl_2): 233 nm (ε 66,600 $cm^{-1}M^{-1}$), 289 (30,300). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.62, 2.64 (2s, 6H, Me), 3.66 (s, 6H, 2xOMe), 3.81, 3.98, 4.03, 4.05 (4s, 12H, OMe), 3.82, 4.18 (2s, 4H, CH_2), 6.93 (d, *J* 8.3 Hz, 2H, aryl H), 6.09, 6.22, 6.31 (3s, 3H, indole H5), 6.98 (s, 1H, centre indole NH), 7.06-7.18 (m, 4H, aryl H), 7.23-7.31 (m, 4H, aryl H), 7.40 (d, *J* 8.3 Hz, 2H, aryl H), 10.49, 10.95 (2s, 2H, NH). ^{13}C NMR (75 MHz, $(CD_3)_2SO_4$): δ 21.6, 21.8 (CH_2), 33.1 (Me), 55.5, 55.8, 56.9, 57.0, 57.7 (OMe), 88.6, 88.8 (indole C5), 130.2, 130.3, 132.8, 133.1 (aryl CH), 101.1, 104.4, 112.0, 113.4, 119.2, 119.4, 130.3, 130.5, 131.4, 131.8, 132.8, 132.9, 133.1, 133.7, 134.9, 136.7, 137.1, 153.0, 153.3, 158.9 (aryl C), 197.1, 199.0 (C=O). Mass Spectrum (+EI): *m/z* (%) 1106 (M+1, $^{79/81/81}$Br, 15), 1104 (M+1, $^{79/79/81}$Br, 17%), 373 (100), 402 (30), 386 (60), 346 (30), 282 (75). Anal. Calcd for $C_{54}H_{46}Br_3N_3O_8.0.25C_6H_{14}$: C, 59.2; H, 4.4; N, 3.7. Found: C, 59.3; H, 4.5; N, 3.6.

7',7'''-Di(trichloroacetyl)-2',7'';2'',2'''-tri(3-(4-bromophenyl)-4,6-dimethoxy)indolyldimethane (13). The 7-trichloroacetylindole **9** (110 mg, 0.24 mmol), indole-2,7-dimethanol **1** (46 mg, 0.12 mmol), and *p*-toluenesulfonic acid monohydrate (6 mg, 0.03 mmol) were stirred together at room temperature in isopropanol (30 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **13** as a yellow-green solid (139 mg, 88%), mp 197 ˚C (dec.) (from CH_2Cl_2/hexane). ν_{max} (KBr): 3421, 2936, 2838, 1624, 1585, 1559, 1487, 1465, 1373, 1355, 1243, 1219, 1200, 1162, 1134, 994, 820, 796 cm^{-1}. λ_{max} (CH_2Cl_2): 232 nm (ε 104,800 $cm^{-1}M^{-1}$), 256 (62,300), 343 (21,800). ^{1}H NMR (300 MHz, $(CD_3)_2SO_4$): δ 3.59, 3.65, 3.73, 3.75, 3.90, 3.92 (6s, 18H, OMe), 4.09, 4.17 (2s, 4H, CH_2), 6.26, 6.38, 6.41 (3s, 3H, indole H5), 6.98-7.08 (m, 6H, aryl H), 7.19-7.32 (m, 6H, aryl H), 10.44, 10.69, 10.82 (3s, 3H, NH). ^{13}C NMR (75 MHz, $(CD_3)_2SO_4$): δ 22.1, 23.0 (CH_2), 55.6, 56.1, 56.4, 56.8 (OMe), 88.9, 89.9 (C5), 129.8, 130.0, 130.2, 132.7, 132.9 (aryl CH), 97.8, 98.0, 98.1, 100.9, 111.5, 111.7, 112.0, 112.8, 113.1, 113.4, 119.3, 130.2, 131.2, 132.2, 132.7, 133.9, 134.0, 134.5, 134.9, 136.8, 136.9, 137.0, 152.9, 153.6, 159.3, 160.3, 182.1, 182.4, 183.2 (aryl C, CCl_3, C=O). Mass Spectrum (+EI): *m/z* (%) 1310 (M, $^{79/79/81}$Br, 12), 607 (50), 490 (100), 362 (40), 346 (45). Anal. Calcd for $C_{54}H_{40}Br_3Cl_6N_3O_8.0.75C_6H_{14}$: C, 51.1; H, 3.7; N, 3.1. Found: C, 51.0; H, 3.4; N, 3.2.

2',7'';2'',2'''(3-(4-Bromophenyl)-4,6-dimethoxyindol-2-yl)(di(3-(4-chlorophenyl)-4,6-dimethoxy)-indol-1,3-yl)dimethane-7',7'''-di(2-phenylethanone) (14). The indole-7-(2-phenylethanone) **10** (50 mg, 0.123 mmol), indole-2,7-dimethanol **1** (24 mg, 0.06 mmol), and *p*-toluenesulfonic acid monohydrate (2 mg, 0.01 mmol) were stirred together at room temperature in isopropanol (20 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **7** as a yellow solid (62 mg, 85%), mp 146.5-148 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 3408, 2936, 2841, 1624, 1586, 1520, 1489, 1464, 1452,

1433, 1347, 1351, 1213, 1195, 996, 834, 794 cm^{-1}. λ_{max} (CH_2Cl_2): 234 nm (ε 78,800 $cm^{-1}M^{-1}$), 316 (36,300). ^1H NMR (300 MHz, $CDCl_3$): δ 3.57, 3.65, 3.80, 3.95, 3.97, 4.05 (6s, 18H, OMe), 4.01, 4.13 (2s, 4H, bridging CH_2), 4.38, 4.39 (2s, 4H, C$\underline{H}_2$Ph), 6.05, 6.24, 6.25 (3s, 3H, indole H5), 6.82 (d, *J* 2.6 Hz, 2H, aryl H), 6.85 (d, *J* 2.6 Hz, 2H, aryl H), 6.96 (d, *J* 3.0 Hz, 2H, aryl H), 6.99 (d, *J* 3.0 Hz, 2H, aryl H), 7.07 (d, *J* 8.3 Hz, 2H, aryl H), 7.10 (s, 1H, NH), 7.21-7.31 (m, 14H, aryl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.8, 23.6 (bridging CH_2), 50.7, 50.8 (C$\underline{H}_2$Ph), 54.8, 55.0, 55.4, 55.9, 56.0, 56.1 (OMe), 87.3, 87.4, 89.5 (indole C5), 126.2, 126.3, 127.2, 127.3, 128.1, 128.2, 129.5, 129.6, 129.9, 131.6, 132.0, 132.4, (aryl CH), 101.0, 104.2, 111.4, 111.7, 112.3, 114.1, 114.2, 119.6, 127.8, 129.2, 130.1, 130.4, 131.3, 131.5, 132.3, 132.5, 133.7, 133.8, 134.2, 136.2, 136.3, 136.4, 152.5, 152.8, 153.3, 158.7, 158.9, 160.0, 160.3 (aryl C), 171.0, 172.8 (C=O). Mass Spectrum (+EI): *m/z* (%) 1165 (M, $^{35/35}Cl^{79}Br$, 15), 762 (100). Anal. Calcd for $C_{66}H_{54}BrCl_2N_3O_8.0.25C_6H_{14}$: C, 68.2; H, 4.9; N, 3.5. Found: C, 68.2; H, 5.1; N, 3.5.

2',7'';2'',2'''(3-(4-Bromophenyl)-4,6-dimethoxyindol-2-yl)(di(3-(4-chlorophenyl)-4,6-dimethoxy-indol-1,3-yl))dimethane-7',7'''-digyloxylate (15). The indole-7-glyoxylate **11** (99 mg, 0.26 mmol), indole-2,7-dimethanol **1** (50 mg, 0.13 mmol), and *p*-toluenesulfonic acid monohydrate (4 mg, 0.02 mmol) were stirred together at room temperature in isopropanol (30 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **15** as a yellow solid (124 mg, 84%), mp 200-201 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 3413, 2938, 2839, 1739, 1623, 1587, 1564, 1510, 1489, 1363, 1313, 1213, 1174, 1158, 1131, 1091, 1074, 993, 800 cm^{-1}. λ_{max} (CH_2Cl_2): 230 nm (ε 85,600 $cm^{-1}M^{-1}$), 258 (74,100), 331 (31,200). ^1H NMR (300 MHz, $CDCl_3$): δ 1.39 (t, *J* 7.2 Hz, 6H, OC$H_2\underline{Me}$), 3.64, 3.74, 3.82, 3.88, 3.92, 4.08 (6s, 18H, OMe), 4.82, 4.16 (2s, 4H, bridging CH_2), 4.38 (q, *J* 7.0 Hz, 4H, OC$\underline{H}_2$Me), 6.06, 6.13, 6.29 (3s, 3H, indole H5), 6.83 (s, 1H, centre indole NH), 7.03 (d, *J* 8.7 Hz, 2H, aryl H), 7.46 (d, *J* 8.7, 2H, aryl H), 7.17-7.31 (m, 8H, aryl H), 10.01, 10.73 (2s, 2H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (OC$H_2\underline{Me}$), 25.2 (bridging CH_2), 55.3, 55.1, 56.7, 56.8, 56.9 (OMe), 61.3 (O$\underline{C}H_2$Me), 87.2, 87.4, 89.2 (indole C5), 127.4, 127.8, 130.0, 131.8, 132.1, 132.3 (aryl CH), 100.6, 101.3, 111.9, 112.1, 113.6, 119.8, 128.8, 130.8, 131.9, 132.9, 133.9, 134.0, 134.8, 136.2, 137.0, 137.1, 153.0, 153.3, 161.2, 161.4, 161.5 (aryl C), 165.9, 184.8 (C=O). Mass Spectrum (+EI): *m/z* (%) 1130 (M+1, $^{35/35}Cl^{79}Br$, 15), 744 (100). Anal. Calcd for $C_{58}H_{50}BrCl_2N_3O_{12}.0.25C_6H_{14}$: C, 62.0; H, 4.7; N, 3.6. Found: C, 62.2; H, 4.6; N, 3.8.

7',7'';2'',7'''-Tri(4,6-dimethoxy-3-methyl)indolylmethane-7',7'''-dicarbaldehyde (17). The indole-2-aldehyde **16** (0.88 g, 4.02 mmol), indole-2,7-dimethanol **2** (0.50 g, 1.99 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg, 0.05 mmol) were stirred together at room temperature in isopropanol (50 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **17** as a bright yellow solid (0.90 g, 69%), mp 283-284 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 3348, 2935, 1840, 1643, 1620, 1526, 1450, 1437, 1369, 1346, 1333, 1260, 1217, 1169, 1150, 1111, 1013, 992 cm^{-1}. λ_{max} (CH_2Cl_2): 258 nm (ε 56,200 $cm^{-1}M^{-1}$), 324 (54,900). ^1H NMR (300 MHz, $CDCl_3$): δ 2.42, 2.62, 2.65

(3s, 9H, Me), 3.08, 3.68 (2s, 6H, OMe), 3.89 (s, 5H, CH_2, OMe), 3.91, 4.24 (2s, 6H, OMe), 4.26 (s, 5H, CH_2, OMe), 5.61, 6.23, 6.31 (3s, 3H, indole H5), 8.89, 10.08, 10.24 (3s, 3H, NH), 9.82, 9.84 (2s, 2H, CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.3, 10.6 (Me), 18.0, 18.1 (CH_2), 54.8, 55.2, 55.4, 56.4, 56.8, 56.8 (OMe), 87.1, 87.6, 88.2 (indole C5), 102.6, 102.8, 103.8, 108.2, 114.0, 114.1, 126.1, 126.4, 126.5, 128.8, 131.5, 131.6, 137.0, 139.5, 139.6, 150.8, 153.2, 155.3, 156.0, 156.4 (aryl C), 178.8, 178.9 (CHO). Mass Spectrum (MALDI): *m/z* (%) 676 ($[M+Na]^+$, 20), 653 (M, 35), 473 (25), 450 (100), 435 (45), 232 (45). Anal. Calcd for $C_{37}H_{39}N_3O_8$: C, 68.0; H, 6.0; N, 6.4. Found: C, 67.8; H, 6.1; N, 6.5.

3',7'';2'',3'''(4,6-Dimethoxy-3-methylindol-2-yl)(di(1-methylindol-1,3-yl)dimethane (18). *N*-Methylindole (52 mg, 0.40 mmol), indole-2,7-dimethanol **2** (50 mg, 0.20 mmol), and *p*-toluenesulfonic acid monohydrate (2 mg, 0.01 mmol) were stirred together at room temperature in isopropanol (10 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **18** as a yellow solid (70 mg, 78%), mp 119-120 ˚C (from EtOAc/hexane). ν_{max} (KBr): 3353, 2927, 1622, 1601, 1518, 1465, 1449, 1342, 1327, 1200, 1153, 1137, 1012, 991 cm^{-1}. λ_{max} (CH_2Cl_2): 230 nm (ε 19,900 $cm^{-1}M^{-1}$), 286 (3,300). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.62 (s, 3H, Me), 3.54, 3.71, 3.72, 3.86 (4s, 12H, OMe, NMe), 4.12, 4.24 (2s, 4H, CH_2), 6.03 (s, 1H, centre indole H5), 6.66, 6.81 (2s, 2H, outer indole H2), 7.08-7.34 (m, 6H, aryl H), 7.57-7.66 (m, 2H, aryl H), 9.38 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.6 (Me), 20.8, 21.8 (CH_2), 32.5, 32.5 (NMe), 55.4, 57.5 (OMe), 88.5 (centre indole C5), 108.9, 109.0, 118.5, 118.8, 119.0, 119.2, 121.3, 121.5, 126.9, 127.1 (aryl CH), 104.5, 106.6, 112.5, 114.3, 118.8, 121.3, 127.9, 131.3, 136.5, 137.0, 137.1, 150.4, 152.9 (aryl C). Mass Spectrum (+EI): *m/z* (%) 478 (M+1, 11), 413 (15) 347 (100), 220 (20), 144 (15). Anal. Calcd for $C_{31}H_{31}N_3O_2.0.5EtOAc$: C, 76.0; H, 6.8; N, 8.1. Found: C, 75.9; H, 6.8; N, 7.9.

29,31-Dimethoxy-33-methyl-10,19,37-triazaoctacyclo[26.5.2.1^{3,10}.1^{19,26}.0^{4,9}.0^{12,17}.0^{20,25}.0^{32,36}]hepta-triaconta-1(33),3(34),4(9),5,7,12(17),13,15,20(25),21,23, 26(35),28,30,32(36) (23). The diindolylxylene **19** (67 mg, 0.20 mmol), indole-2,7-dimethanol **2** (50 mg, 0.20 mmol), and *p*-toluenesulfonic acid monohydrate (2 mg, 0.01 mmol) were stirred together at room temperature in isopropanol (20 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **23** as a yellow solid (105 mg, 95%), mp 184-186 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 3425, 2929, 1622, 1516, 1463, 1342, 1237, 1212, 1154, 1131, 1101, 1014, 993 cm^{-1}. λ_{max} (CH_2Cl_2): 279 nm (ε 10,000 $cm^{-1}M^{-1}$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.38 (s, 3H, Me), 3.89 (s, 3H, OMe), 3.93 (s, 5H, OMe, bridging CH_2), 4.13 (s, 2H, bridging CH_2), 5.14, 5.28 (2s, 4H, CH_2N), 6.26 (s, 1H, NH), 6.33 (d, *J* 3.0 Hz, 2H, aryl H), 6.91-7.58 (m, 13H, aryl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.4 (Me), 20.1, 21.0 (bridging CH_2), 46.2, 47.3 (CH_2N), 55.3, 58.0 (OMe), 89.1 (C5), 108.7, 108.9, 119.0, 119.2, 119.4, 119.6, 121.8, 122.1, 123.2, 124.0, 129.01, 129.2, 131.9, 132.1, (aryl CH), 103.1, 106.0, 113.2, 113.9, 114.4, 127.7, 128.0, 129.4, 130.2, 134.8, 135.1, 136.7, 137.5, 152.2, 152.9 (aryl C). Mass Spectrum (+EI): *m/z* (%) 607 ($[M+K]^+$, 30), 552 (M+1, 100).

Anal. Calcd for $C_{37}H_{33}N_3O_2.0.25H_2O$: C, 79.9; H, 6.1; N, 7.6. Found: C, 79.8; H, 6.4; N, 7.3.

7',7'';2'',2''';7''',7''''-Di(3-(4-bromophenyl)-4,6-dimethoxyindol-2,3-indol-yl)(di(4,6-dimethoxy-3-methylindol-1,4-yl)trimethane-7',7''''-dicarbaldehyde (26). The indole-2-aldehyde **16** (59 mg, 0.27 mmol), diindolyl-dimethanol **24** (100 mg, 0.135 mmol), and *p*-toluenesulfonic acid monohydrate (2 mg, 0.01 mmol) were stirred together at room temperature in isopropanol (20 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **26** as a pale yellow solid (145 mg, 96%), mp 239-240 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 3341, 2935, 2838, 1645, 1620, 1594, 1547, 1523, 1488, 1463, 1450, 1435, 1372, 1344, 1332, 1256, 1216, 1163, 1149, 1114, 1172, 1001, 837, 821, 791 cm^{-1}. λ_{max} (CH_2Cl_2): 238 (ε 91,300 $cm^{-1}M^{-1}$), 361 (66,000). ^1H NMR (300 MHz, $CDCl_3$): δ 2.62 (s, 6H, Me), 2.96, 3.72, 3.76, 4.27 (4s, 24H, OMe), 3.92 (s, 4H, 7,7'- CH_2 link), 4.13 (s, 2H, 2,2'- CH_2 link), 5.62, 6.39 (2s, 4H, índole H5), 7.28 (d, *J* 8.7 Hz, 4H, aryl H), 7.45 (d, *J* 8.7 Hz, 4H, aryl H), 9.37, 10.15 (2s, 4H, NH), 9.82 (s, 2H, CHO). The compound was not sufficiently soluble for a ^{13}C NMR spectrum to be obtained. Mass Spectrum (+EI): *m/z* (%) 1137 (M-3, $^{81/81}Br$, 60), 1135 (M-3, $^{79/81}Br$, 100), 1133 (M-3, $^{79/79}Br$, 85). Anal. Calcd for $C_{59}H_{54}Br_2N_4O_{10}.0.5H_2O$: C, 61.7; H, 4.8; N, 4.9. Found: C, 61.7; H, 4.6; N, 4.8.

Di(3-(4-bromophenyl)-4,6-dimethoxyindol-7-yl)methane-2',2''-dimethanol (27). The índole-2,7-dimethanol **1** (0.50 g, 1.27 mmol) in THF (20 mL) was stirred at room temperature with glacial acetic acid (20 mL) for 1 h. Water was added and the resulting precipitate was filtered off, washed with water, and dried to yield compound **27** as a yellow solid (0.46 g, 98%), mp 219-221 ˚C. ν_{max} (KBr): 3339, 2934, 2837, 1622, 1595, 1565, 1520, 1489, 1449, 1435, 1339, 1262, 1216, 1155, 1118, 1072, 1000, 837, 812, 789 cm^{-1}. λ_{max} (CH_2Cl_2): 234 nm (ε 50,700 $cm^{-1}M^{-1}$), 285 (22,200). ^1H NMR (300 MHz, $(CD_3)_2SO_4$): δ 3.69, 4.09 (2s, 12H, OMe), 4.19 (s, 2H, CH_2), 4.54 (d, *J* 4.5 Hz, 4H, C<u>H</u>$_2$OH), 5.45 (t, *J* 4.9 Hz, 2H, CH_2O<u>H</u>), 6.44 (s, 2H, H5), 7.23 (d, *J* 5.3 Hz, 4H, aryl H), 7.47 (d, *J* 5.7 Hz, 4H, aryl H), 10.18 (s, 2H, NH). ^{13}C NMR (75 MHz, $(CD_3)_2SO_4$): δ 18.5 (bridging CH_2), 55.5, 57.26 (OMe), 55.6 (CH_2OH), 89.1 (índole C5), 130.3, 132.7 (aryl CH), 103.3, 111.2, 111.5, 118.9, 135.0, 136.5, 151.4, 152.8 (aryl C). Mass Spectrum (+EI): *m/z* (%) 721 (M-OH, $^{81/81}Br$, 65), 719 (M-OH, $^{79/81}Br$, 100), 374 (M-OH, $^{79/79}Br$, 70). Anal. Calcd for $C_{35}H_{32}Br_2N_2O_6.0.5CH_3COOH$: C, 56.4; H, 4.5; N, 3.7. Found: C, 56.6; H, 4.3; N, 3.6.

1,2-Di(indol-1-ylmethyl)benzene-3',3''-di(3-(4-bromophenyl)-4,6-dimethoxy-7-formylindol-2-yl)-methane (32). The indole-7-aldehyde **3** (0.19 g, 0.52 mmol), diindolyl-dimethanol **28** (0.10 g, 0.26 mmol), and *p*-toluenesulfonic acid monohydrate (10 mg, 0.05 mmol) were stirred together at room temperature in isopropanol (20 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **32** as a pale yellow solid (0.27 g, 97%), mp 275.5-277 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 3412, 3308, 3934, 3846, 1644, 1590, 1562, 1509, 1486, 1456, 1435, 1393, 1354, 1252, 1213, 1192, 1170, 1119, 994 cm^{-1}. λ_{max} (CH_2Cl_2): 293 (ε 23,100 $cm^{-1}M^{-1}$), 330 (11,900). ^1H NMR (300 MHz, $CDCl_3$): δ

3.83, 3.94 (2s, 12H, OMe), 4.13 (s, 4H, CH_2), 5.17 (s, 4H, CH_2N), 6.12 (s, 2H, dimethoxyíndole H5), 6.78 (s, 2H, índole H2), 6.82-6.85 (m, 2H, aryl H), 6.99-7.08 (m, 6H, aryl H), 7.20-7.23 (m, 2H, aryl H), 7.31-7.34 (m, 6H, aryl H), 7.46 (d, *J* 8.3 Hz, 4H, aryl H), 10.25 (s, 2H, NH), 10.26 (s, 2H, CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 2.2 (bridging CH_2), 47.4 (CH_2N), 55.3, 56.3 (OMe), 86.6 (dimethoxyindole C5), 109.6, 118.9, 119.4, 122.2, 126.1, 128.0, 128.3, 130.4, 132.4 (aryl CH), 104.2, 111.2, 112.6, 112.7, 119.9, 127.5, 133.6, 134.3, 134.5, 136.2, 136.7, 160.5, 162.3 (aryl C), 188.1 (CHO). Mass Spectrum (+EI): *m/z* (%) 580 (M-$C_{27}H_{22}BrN_2O_3$, 100), 349 (15), 220 (10). Anal. Calcd for $C_{60}H_{48}Br_2N_4O_6.1.5H_2O$: C, 65.1; H, 4.6; N, 5.1. Found: C, 65.0; H, 4.6; N, 5.0.

1,3-Di(indol-1-ylmethyl)benzene-3',3''-di(3-(4-bromophenyl)-4,6-dimethoxy-7-formylindol-2-yl)-methane (33). The indole-7-aldehyde **3** (0.19 g, 0.52 mmol), diindolyl-dimethanol **29** (0.10 g, 0.26 mmol), and *p*-toluenesulfonic acid monohydrate (10 mg, 0.05 mmol) were stirred together at room temperature in isopropanol (20 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **33** as a pale yellow solid (0.27 g, 96%), mp 142-145 ˚C (from CH_2Cl_2/hexane). ν_{max} (KBr): 3411, 2931, 2847, 1643, 1591, 1562, 1465, 1393, 1353, 1327, 1247, 1213, 1191, 1170, 1119, 994 cm^{-1}. λ_{max} (CH_2Cl_2): 255 (ε 19,900 $cm^{-1}M^{-1}$), 294 (12,700). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.83, 3.93 (2s, 12H, OMe), 4.13 (s, 4H, CH_2), 5.20 (s, 4H, CH_2N), 6.11 (s, 2H, dimethoxyindole H5), 6.91-7.49 (m, 22H, aryl H, índole H2), 10.26 (s, 2H, NH), 10.28 (s, 2H, CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.3 (bridging CH_2), 49.7 (CH_2N), 55.3, 56.29 (OMe), 86.6 (dimethoxyindole C5), 109.8, 118.8, 119.2, 122.0, 125.9, 126.4, 130.4, 132.4 (aryl CH), 104.3, 111.3, 112.2, 112.7, 119.9, 127.6, 133.7, 134.4, 136.3, 136.7, 138.2, 160.5, 162.3 (aryl C), 188.1 (CHO). Mass Spectrum (+EI): *m/z* (%) 1083 (M+1, $^{81/81}$Br, 25), 722 (100), 362 (55). HRMS (+ESI): $C_{60}H_{48}Br_2N_4O_6$ requires 1083.1978 ($^{81/81}$Br), 1081.1998 ($^{79/81}$Br), 1079.2019 ($^{79/79}$Br), found 1083.2029 ($^{81/81}$Br), 1081.2030 ($^{79/81}$Br), 1079.1997 ($^{79/79}$Br). Satisfactory elemental microanalysis could not be obtained for this compound $C_{60}H_{48}Br_2N_4O_6$.

1,4-Di(indol-1-ylmethyl)benzene-3',3''-di(3-(4-bromophenyl)-4,6-dimethoxy-7-formylindol-2-yl)-methane (34). The indole-7-aldehyde **3** (0.27 g, 0.76 mmol), diindolyl-dimethanol **30** (150 mg, 0.38 mmol), and *p*-toluenesulfonic acid monohydrate (10 mg, 0.05 mmol) were stirred together at room temperature in isopropanol (30 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **34** as a pale yellow solid (0.37 g, 89%), mp 274-276 ˚C (from CH_2Cl_2). ν_{max} (KBr): 3407, 2933, 2845, 1640, 1591, 1562, 1509, 1486, 1466, 1393, 1353, 1324, 1245, 1213, 1186, 1165, 1119, 993 cm^{-1}. λ_{max} (CH_2Cl_2): 231 nm (ε 90,700 $cm^{-1}M^{-1}$), 254 (54,400), 293 (30,300), 325 (22,300). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84, 3.95 (2s, 12H, OMe), 4.15 (s, 4H, CH_2), 5.20 (s, 4H, CH_2N), 6.13 (s, 2H, dimethoxyindole H5), 6.87 (s, 2H, índole H2), 7.00 (s, 4H, xylyl H), 7.02-7.05 (m, 2H, aryl H), 7.10-7.20 (m, 4H, aryl H), 7.31-7.37 (m, 6H, aryl H), 7.47 (d, *J* 8.3 Hz, 4H, aryl H), 10.23 (s, 2H, NH), 10.29 (s, 2H, CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.3 (bridging CH_2), 49.5 (CH_2N), 55.3, 56.30 (OMe), 86.5 (C5''),

109.7, 118.8, 119.23, 122.0, 126.3, 127.0, 130.4, 132.4 (aryl CH), 104.2, 111.2, 112.3, 112.8, 119.9, 127.5, 133.6, 134.3, 136.3, 136.7, 136.8, 160.5, 162.3 (aryl C), 188.1 (CHO). HRMS (+ESI): $C_{60}H_{48}Br_2N_4O_6$ $[M+Na]^+$ 1103.1820 ($^{81/81}$Br), found 1103.1848 ($^{81/81}$Br). Anal. Calcd for $C_{60}H_{48}Br_2N_4O_6.1.5CH_2Cl_2$: C, 61.1; H, 4.3; N, 4.6. Found: C, 61.2; H, 4.1; N, 4.3.

Di(indol-1-ylmethyl)methane-3',3''-di(3-(4-bromophenyl)-4,6-dimethoxy-7-formylindol-2-yl)-methane (35). The indole-7-aldehyde **3** (0.24 g, 0.67 mmol), diindolyl-dimethanol **31** (0.10 g, 0.33 mmol), and *p*-toluenesulfonic acid monohydrate (10 mg, 0.05 mmol) were stirred together at room temperature in isopropanol (20 mL) for 1 h, and the resulting precipitate was filtered off and dried to give compound **35** as a pale yellow solid (0.32 g, 98%), mp 275-276 ˚C. ν_{max} (KBr): 3411, 2935, 2846, 1640, 1591, 1562, 1510, 1486, 1461, 1394, 1353, 1245, 1213, 1190, 1157, 1119, 993, 794, 743 cm^{-1}. λ_{max} (CH_2Cl_2): 230 nm (ε 70,800 $cm^{-1}M^{-1}$), 256 (44,600), 325 (18,800). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84, 3.96 (2s, 12H, OMe), 4.10 (s, 4H, CH_2), 6.13 (s, 2H, CH_2), 6.21 (s, 2H, dimethoxyindole H5), 6.96 (s, 2H, H2), 7.04, 7.18 (2t, *J* 7.5 Hz, 4H, H4, H7), 7.28-7.35 (m, 8H, aryl H), 7.43 (d, *J* 8.3 Hz, 4H, aryl H), 10.27 (s, 2H, CHO), 10.29 (s, 2H, NH). The compound was not sufficiently soluble for a ^{13}C NMR spectrum to be obtained. Mass Spectrum (+EI): *m/z* (%) 991 (M+1, $^{79/81}$Br, 40), 633 (65), 503 (100), 374 (85), 338 (60). Anal. Calcd for $C_{53}H_{42}Br_2N_4O_6$: C, 64.3; H, 4.3; N, 5.7. Found: C, 64.0; H, 4.5; N, 5.4.

ACKNOWLEDGEMENTS

Financial support from the Australian Research Council is gratefully acknowledged.

REFERENCES

1. D. E. Ames, R. E. Bowman, D. D. Evans, and W. A. Jones, *J. Chem. Soc*., 1956, 1984.
2. E. E. Leete, *J. Am. Chem. Soc*., 1959, **81**, 6023.
3. J. Bergman, S. Högberg, and O. J. Lindström, *Tetrahedron*, 1970, **26**, 3347.
4. A. R. Mattocks, *J. Chem. Soc., Perkin Trans. I*, 1978, 896.
5. C. A. Harrison, R. Leineweber, C. J. Moody, and J. M. J. Williams, *J. Chem. Soc., Perkin Trans I*, 1995, 1131.
6. D. L. Boger, A. Santillan, M. Searcey, and Q. Jin, *J. Am. Chem. Soc*., 1998, **120**, 11554.
7. W.-R. Chao, D. Yean, K. Amin, C. Green, and L. Jong, *J. Med. Chem*., 2007, **50**, 3412.
8. M. S. C. Pedras and V. K. Sarma-Mamillapalle, *Bioorg. Med. Chem*., 2012, **20**, 3991.
9. D. StC. Black, M. C. Bowyer, N. Kumar, and P. S. R. Mitchell, *J. Chem. Soc., Chem. Commun.*, 1993, 819.
10. D. StC. Black, D. C. Craig, and N. Kumar, *Tetrahedron Lett.*, 1995, **36**, 8075.
11. D. StC. Black, D. C. Craig, N. Kumar, and D. B. McConnell, *Tetrahedron Lett.*, 1996, **37**, 241.

12. D. StC. Black, N. Kumar, and D. B. McConnell, *Tetrahedron*, 2000, **56**, 8513.
13. P. K. Bowyer, D. StC. Black, and D. C. Craig, *Tetrahedron*, 2005, **61**, 10781.
14. K. Somphol, R. Chen, M. Bhadbhade, N. Kumar, and D. StC. Black, *Synlett,* 2013, **24**, 24.
15. R. Chen, K. Somphol, M. Bhadbhade, N. Kumar, and D. StC. Black, *Synlett*, 2013, **24**, 1497.
16. M. Bingul, B. B. Cheung, N. Kumar, and D. StC. Black, *Tetrahedron*, 2014, **70**, 7363.
17. M. Mielczarek, R. V. Thomas, C. Ma, H. Kandemir, X. Yang, M. Bhadbhade, D. StC. Black, R. Griffith, P. J. Lewis, and N. Kumar, *Bioorg. Med. Chem*., 2015, **23**, 1763.
18. K. Wood, D. StC. Black, and N. Kumar, *Tetrahedron*, 2011, **67**, 4093.
19. M. Mielczarek, R. V. Devakaram, C. Ma, X. Yang, H. Kandemir, B. Purwono, D. StC. Black, R. Griffith, P. J. Lewis, and N. Kumar, *Org. Biomol. Chem*., 2014, **12**, 2882.
20. D. StC. Black, N. Kumar, and T. D. Wahyuningsih, *ARKIVOC*, 2008, **vi**, 42.
21. T. D. Wahyuningsih, N. Kumar, and D. StC. Black, *Tetrahedron*, 2007, **63**, 6713.
22. D. StC. Black, M. C. Bowyer, M. M. Catalano, A. J. Ivory, P. A. Keller, N. Kumar, and S. J. Nugent, *Tetrahedron*, 1994, **50**, 10497.
23. J. C. Dobrowolski, K. Somphol, M. Santoso, H. Duong, C. R. Gardner, N. Kumar, and D. StC. Black, *Aust. J. Chem*., 2017, **70**, 1188.