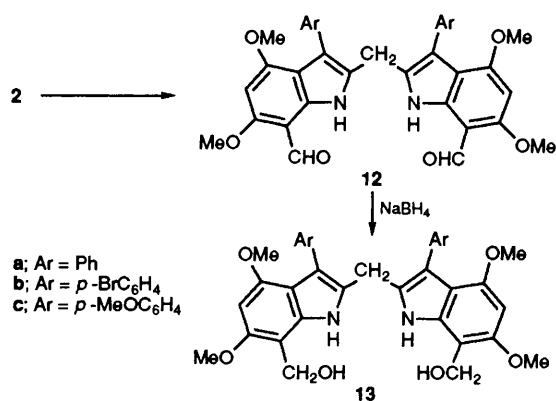


Scheme 3

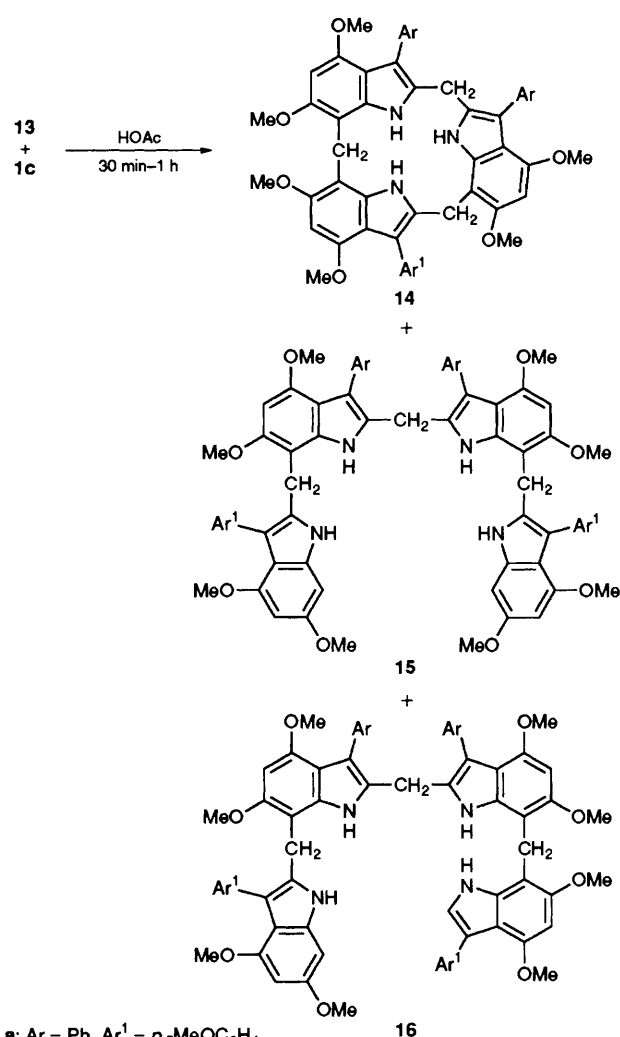


Scheme 4



Scheme 5

The regiochemistry of the above reactions is of considerable significance. Two orientations of addition are possible, one leading to the observed 2,7:2,7:2,7-linkages, the other to a 2,2:7,2:7,7-set of linkages. None of the latter products were observed. We have found that in general, the indoles **1** undergo acid-catalysed addition to benzylic alcohols preferentially at C-2 rather than C-7. Furthermore, the 7-hydroxymethyl compounds **5** are more reactive than the 2-hydroxymethyl compounds **6**. Consequently, in the reaction of **5** with **1**, the initial step would involve combination of the 7-hydroxymethyl group with an indole C-2 position, and this would be followed by a slower combination of a 2-hydroxymethyl group with an indole C-7 position to complete the macrocycle. The initial formation of a 2,7-link thus establishes the regiochemistry. Similar behaviour would occur in the reaction of **9**



Scheme 6

with **7**. The nature of the methylene linkages is clearly shown by NMR spectroscopy. For example, macrocycle **8c** shows three methoxy methyl proton signals, one methylene singlet and one indole 5-H singlet. When different C-3-aryl substituents are introduced, the ¹H NMR spectrum shows different methoxy, methylene and 5-H chemical shifts resulting from the removal of symmetry. The presence of singlet methylene proton resonances shows that these macrocycles are flexible and even at low temperature, no generation of AB systems can be seen. Reaction of **11c** with the *N*-methyl analogue of **1c** gives a macrocycle with an NMR spectrum showing three AB methylene patterns.

Compounds **8** are related to the calix[3]arenes,^{7,8} but with the replacement of an ambident 4-substituted phenol by ambident indoles **1**.[†] Unlike the 4-substituted phenols, indoles **1** do not show orientational symmetry and two isomeric calix[3]indoles are possible.

We also report an efficient method for the synthesis of the isomeric [1.1.1](2,2)(7,2)(7,7)indolophane **14**. The indole-7-carbaldehydes **2** undergo reaction with formaldehyde in acetic acid to give the dialdehydes **12** in quantitative yield.^{9,10} These can be reduced quantitatively with sodium borohydride to the corresponding dialcohols **13** (Scheme 5). Reaction of the dialcohols **13** with the indole **1c** in acetic acid gives the macrocycles **14** in 30–40% yields, together with the linear tetraindolyl oligomers **15** and **16** in yields of 20 and 5%, respectively (Scheme 6). The dialcohol **13c** can be combined

equally effectively with the *N*-methyl analogue of **1c** to give an *N*-methyl-substituted macrocycle in 40% yield.

The ¹H NMR spectrum of **14c** shows nine methoxy proton resonances, three 5-H singlets and three singlets at δ 3.7, 4.15 and 4.38 for the 2,2'-, 2'',7- and 7',7''-linked methylene groups, respectively. This data clearly reflects the unsymmetrical arrangement of indole rings, but also shows that there is enough flexibility for inversion from one conformer to another. However, at lower temperature, the methylene singlets start to broaden, commencing with the 2'',7-linked methylene resonance.

The tetraindolyl oligomers **15** potentially provide excellent starting materials for higher indolylmethylene oligomers.

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References

- 1 D. St. C. Black, N. E. Rothnie and L. C. H. Wong, *Aust. J. Chem.*, 1983, **36**, 2407.
- 2 D. St. C. Black, D. C. Craig and N. Kumar, *J. Chem. Soc., Chem. Commun.*, 1989, 425.
- 3 D. St. C. Black, B. M. K. C. Gatehouse, F. Theobald and L. C. H. Wong, *Aust. J. Chem.*, 1980, **33**, 343.
- 4 D. St. C. Black, N. Kumar and L. C. H. Wong, *Aust. J. Chem.*, 1986, **39**, 15.
- 5 D. St. C. Black, P. A. Keller and N. Kumar, *Aust. J. Chem.*, in the press.
- 6 D. St. C. Black, N. Kumar and L. C. H. Wong, *Synthesis*, 1986, 474.
- 7 A. A. Moshfegh, E. Beladi, L. Radnia, A. S. Hosseini, S. Tofigh and G. H. Hakimelahi, *Helv. Chim. Acta*, 1982, **65**, 1264.
- 8 C. D. Gutsche, *Calixarenes*, RSC, Cambridge, 1989, pp. 43–44.
- 9 D. St. C. Black, *J. Proc. Roy. Soc. N.S.W.*, 1990, 1.
- 10 D. St. C. Black, *Synlett*, 1993, 246.