The First Example of a New Class of Bridged Calixarene

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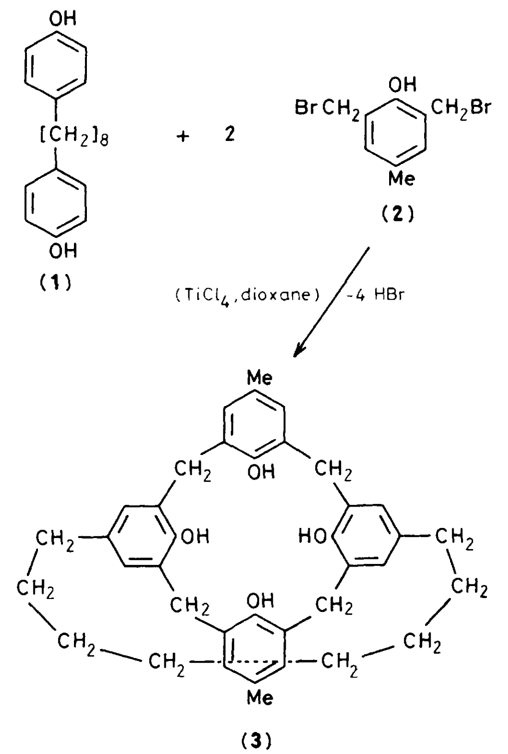
The condensation of 1,8-bis-(*p*-hydroxyphenyl)octane (**1**) and 2,6-bis-(bromomethyl)-*p*-cresol (**2**) in dioxane in the presence of $TiCl_4$ leads to a calix[4]arene (**3**) in which the cone conformation is fixed, since the *para*-positions of two opposite phenolic units are linked by an aliphatic chain.

Cyclic oligonuclear phenolic compounds which Gutsche has designated as calixarenes have attracted appreciable interest in recent years.[1] Owing to their hydrophobic cavity they are able to form 1 : 1[2] or 2 : 1[3] inclusion complexes with aromatic guest molecules in the solid state. On the other hand, because they contain a cyclic array of hydroxy groups they may form complexes with metal ions and act as selective cation carriers in liquid membranes.[4] This complexation ability can be increased if the phenolic hydroxy groups are transformed into open chain[5] or crown like[6] oligoether structures. Further functionalization of calixarenes by reactions involving the *para*-position of the phenolic units was carried out[1,7] in order to obtain enzyme model compounds.[1]

Calix[4]arenes normally exist in the so-called cone confor-



mation as shown by X-ray analysis[2,3] and by dynamic ^{1}H n.m.r. spectroscopy.[8,9] However, above room temperature they are rather flexible and undergo rapid interconversion between different conformations. Introduction of bulky substituents on the hydroxy groups may lead to completely rigid compounds, but then the partial cone[10] or the 1,3-alternate conformation[11] may be fixed instead of the cone conformation.

Another possible means of fixing the cone conformation consists in the connection of two opposite *para*-positions by an aliphatic chain of appropriate length. We report here the first synthesis of such a compound.

The synthesis of (**3**) follows closely the principle which we have described for the preparation of various substituted calix[4]arenes.[12] The condensation of (**1**)[13] with (**2**)[14] requires two intramolecular steps in addition to two intermolecular steps. Consequently we tried this reaction under high dilution conditions. Surprisingly, however, the best results up to now were obtained when (**1**) and (**2**) were heated with $TiCl_4$ (molar ratio 1 : 2 : 4, 30 h at 100 °C) in dioxane without dilution. Up to 20% of pure (**3**)† could be isolated by flash chromatography (silica gel, CH_2Cl_2), in addition to unidentified oligomeric or polymeric condensation products.

Compound (**3**) forms shiny needles from acetone or compact crystals from dimethyl sulphoxide, m.p. 280—282 °C with subsequent decomposition. The 'bicyclic' structure of (**3**)‡ (in comparison with the 'monocyclic' structure of calixarenes) is demonstrated by the electron impact mass spectrum which is dominated by the molecular ion peak (m/z 562, M^+, 100%; m/z 281, M^{2+}, 8%; $< \sim 15\%$ relative intensity for other ions). A similar stability is not found for the corresponding linear phenolic oligomers, not even for similar simple calixarenes. In these cases bond scission at the methylene bridges leads to larger fragments, consisting of two, three, or more phenolic units,[15] which are absent from the spectrum of (**3**) (all other fragments with $m/z > 130$ have intensities lower than 8%).

The ^{1}H n.m.r. spectra of (**3**) were recorded over a large temperature range in $CDCl_3$ (−60 to 70 °C), [$^{2}H_5$]pyridine (−40 to 100 °C), and [$^{2}H_6$]dimethyl sulphoxide (80 to 170 °C). For all solvents and all temperatures an AB-type pattern (J_{AB} 13.8 Hz) was found for the methylene protons, as is typical for calix[4]arenes in the cone conformation. Only slight changes in chemical shift are observed in $CDCl_3$ (δ 4.18 to 4.16 and 3.40 to 3.32) and [$^{2}H_5$]pyridine (δ 4.66 to 4.39 and 3.59 to 3.39) when the temperature is increased, while the chemical shift remains constant in $(CD_3)_2SO$ (δ 4.15 and 3.16). This means that a basket-like conformation corresponding to the cone conformation of calixarenes is fixed or predominant, even at the higher temperatures. On the other hand, the signal for the OH protons of (**3**) in $CDCl_3$ (δ 9.05 at 25 °C) splits into two singlets at low temperature (δ 9.26 and 9.14 at −60 °C), which is not observed for the corresponding compound with an aliphatic chain of 10 carbon atoms. We therefore conclude that the molecular skeleton of (**3**) has an energy minimum which requires two pairs of different hydroxy groups, and that the cyclic array of four equivalent hydroxy groups is formed only if the intramolecular mobility is slightly increased.

Variation of the length of the chain connecting the opposite phenolic units obviously will lead to definite variations in the cone conformation of the calixarene ring. Thus, higher specifity and selectivity in complexation behaviour may be expected for compounds of this bridged calixarene type.

Received, 3rd December 1984; Com. 1700

References

1 For recent reviews see: C. D. Gutsche, *Acc. Chem. Res.*, 1983, **16**, 161; *Top. Curr. Chem.*, 1984, **123**, 1.
2 G. D. Andreetti, R. Ungaro, and A. Pochini, *J. Chem. Soc., Chem. Commun.*, 1979, 1005.
3 R. Ungaro, A. Pochini, G. D. Andreetti, and P. Domiano, *J. Chem. Soc., Perkin Trans. 2*, 1985, 197.
4 R. M. Izatt, J. D. Lamb, R. T. Hawkins, P. R. Brown, S. R. Izatt, and J. R. Christensen, *J. Am. Chem. Soc.*, 1983, **105**, 1782.
5 V. Bocchi, D. Foina, A. Pochini, R. Ungaro, and G. D. Andreetti, *Tetrahedron*, 1982, **38**, 373.
6 C. Alfieri, E. Dradi, A. Pochini, R. Ungaro, and G. D. Andreetti, *J. Chem. Soc., Chem. Commun.*, 1983, 1075.
7 C. D. Gutsche and J. A. Levine, *J. Am. Chem. Soc.*, 1982, **104**, 2652.
8 G. Happel, B. Mathiasch, and H. Kämmerer, *Makromol. Chem.*, 1975, **176**, 3317; H. Kämmerer, G. Happel, and B. Mathiasch, *ibid.*, 1981, **182**, 1685.
9 C. D. Gutsche and L. J. Bauer, *Tetrahedron Lett.*, 1981, **22**, 4763.
10 C. Rizzoli, G. D. Andreetti, R. Ungaro, and A. Pochini, *J. Mol. Struct.*, 1982, **82**, 133.
11 C. D. Gutsche, B. Dhawam, J. A. Levine, K. H. No, and L. J. Bauer, *Tetrahedron*, 1983, **39**, 409.
12 V. Böhmer, Ph. Chhim, and H. Kämmerer, *Makromol. Chem.*, 1979, **180**, 2539.
13 Yu. E. Doroshenko and V. A. Segeev, *J. Org. Chem. USSR*, 1965, **1**, 1602.
14 W. M. Bright and P. Cammarata, *J. Am. Chem. Soc.*, 1952, **74**, 3690.
15 *E.g.* H. Kämmerer and G. Happel, *Monatsh. Chem.*, 1981, **112**, 759; *Makromol. Chem.*, 1978, **179**, 1199.
16 E. Paulus, H. Goldmann, and V. Böhmer, unpublished results.

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† Satisfactory elemental analyses were obtained for (**3**); i.r. (KBr): 3250 (ν_{OH}); 3010, 2920, and 2850 (ν_{CH}); 1610 ($\nu_{C=C}$); 1485 and 1460 cm^{-1} (δ_{CH}); ^{1}H n.m.r. (90 MHz, $CDCl_3$, Me_4Si) δ 9.06 (s, 4H, OH), 6.88 (s, 4H, ArH), 6.61 (s, 4H, ArH), 4.16 (d, 4H, J_{AB} 13.8 Hz, $ArCH_AH_BAr$), 3.35 (d, 4H, J_{AB} 13.8 Hz, $ArCH_AH_BAr$), 2.22 (s, 6H, Me), and *ca.* 2.25, 1.15, and 0.50 (m, br., 16H total, $[CH_2]_8$).

‡ The result of a single crystal X-ray analysis is in accordance with the proposed structure.[16]