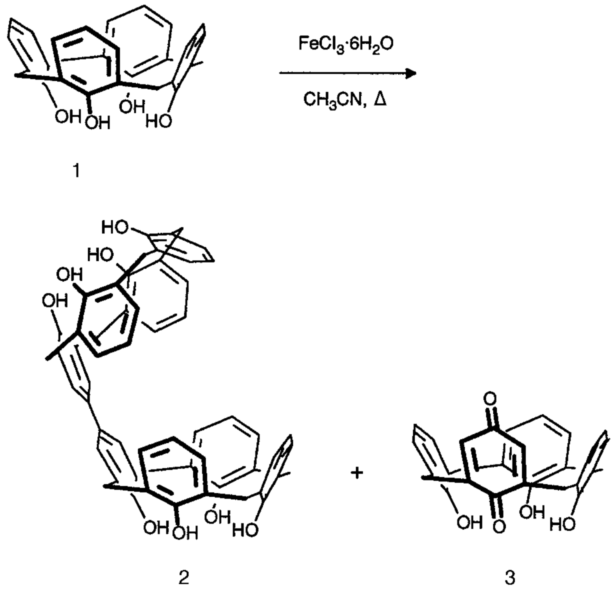
12 Union Road, Cambridge CB21EZ, UK (fax: int. code + (44)1223-336033; e-mail: deposit@ccdc.cam.ac.uk).
[22] J. W. H. M. Uiterwijk, S. Harkema, B. W. van der Waal, F. Göbel, H. T. M. Nibbeling, *J. Chem. Soc. Perkin Trans. II.* **1983**, 1843.
[23] D. L. Clark, S. D. Conradson, S. A. Ekberg, N. J. Hess, M. P. Neu, P. D. Palmer, W. Runde, C. D. Tait, *J. Am. Chem. Soc.* **1996**, *118*, 2089.
[24] J.-M. Combes, C. J. Chisholm-Brause, G. E. Brown, Jr., G. A. Parks, S. D. Conradson, P. G. Eller, I. R. Triay, D. E. Hobart, A. Meijer, *Environ. Sci. Technol.* **1992**, *26*, 376.
[25] C. Nguyen-Trung, G. M. Begun, D. A. Palmer, *Inorg. Chem.* **1992**, *31*, 5280.
[26] C. Madic, G. M. Begun, D. E. Hobart, R. L. Hahn, *Inorg. Chem* **1984**, *23*, 1914.
[27] T. W. Newton, D. E. Hobart, P. D. Palmer, *The Preparation and Stability of Pure Oxidation States of Neptunium, Plutonium, and Americium*, Los Alamos National Laboratory, **1986**, LA-UR-86-967.

5,5′-Bicalix[4]arene: The Bridgeless Prototype of Double Calix[4]arenes of the "Head-to-Head" Type[**]

Placido Neri,* Alessandra Bottino, Francesca Cunsolo, Mario Piattelli, and Enrico Gavuzzo

In the past decade several double (or multiple) calixarenes[1] have been prepared as examples of higher order molecular architectures with new high-level host properties, such as allostery and cooperativity.[2] In these compounds, two (or more) calixarene units are linked at their upper or lower rims[3, 4] through one or more spacer elements. Various structural motifs have been used as spacers, including alkyl, alkenyl, and alkynyl chains, diesters, diamides, metallocenes, ethers and polyethers, sulfides, and diimines.[1, 2, 5] However, to the best of our knowledge, examples of the prototypal compounds with directly coupled (bridgeless) calixarene units have not been reported so far.[6] Here we describe the synthesis, X-ray crystal structure, and derivatization of the first double calixarene of the "head-to-head" type[7] with direct *para-para* linkage, 5,5′-bicalix[4]arene **2**.[8]

Linkage of the two calix[4]arene units was accomplished by oxidative coupling of the *p*-H-calix[4]arene **1**[9a] under conditions similar to those of Pummerer's classic binaphthol synthesis[10] (Scheme 1). A solution of **1** in hot CH$_3$CN was treated with solid FeCl$_3\cdot$6H$_2$O, and the suspension was heated at reflux for 4 h. Workup of the reaction mixture and column chromatography of the crude product afforded bicalix[4]arene **2** (10%) and calix[4]monoquinone **3** (6%). The dimeric nature of **2** was indicated by a quasi-molecular ion at $m/z = 847$ in the positive-ion fast-atom-bombardment (FAB) mass spectrum. Correspondingly, the ^{13}C NMR spectrum contains two ArCH$_2$Ar signals, six aromatic CH resonances, three C–OH singlets, and a diagnostic singlet at $\delta = 135.3$ attributable to quaternary carbon atoms involved in bonding of the two halves in **2**.



Scheme 1. Synthesis of 5,5′-bicalix[4]arene **2** by oxidative coupling of *p*-H-calix[4]arene **1**.

Both calixarene moieties are in the *cone* conformation because of the stabilizing cyclic hydrogen bond, as revealed by two broad AX systems for ArCH$_2$Ar protons in the ^{1}H NMR spectrum.[1] These systems sharpen at low temperature, and a Gibbs free energy of activation $\Delta G^{\neq} = 14$ kcal mol^{-1} was estimated from the coalescence temperature for the *cone–cone* conformational interconversion, a value very similar to that reported for the parent monomer **1**.[9b] With respect to the biphenyl moiety, one can presume relatively free rotation around the Ar–Ar bond, with a slight deviation from coplanarity for the two aryl rings. This leads to a *syn* or *anti* orientation of the calix[4]arene units (Figure 1). Energy evaluations (MM2 and MM3) of the two geometries gave very similar values; the *anti* orientation is slightly lower in energy. Therefore, the *syn* and *anti* forms of bicalix[4]arene **2** are expected to be in equilibrium in solution (Figure 1).

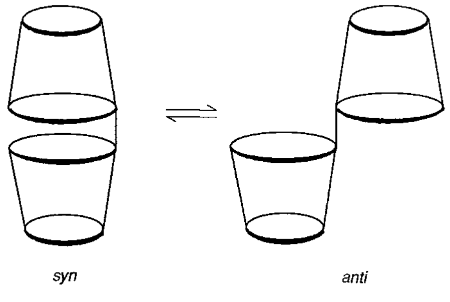


Figure 1. Schematic representation of the proposed equilibrium between the *syn* and *anti* conformations of 5,5′-bicalix[4]arene **2** in solution.

---

[*] Dr. P. Neri, Dr. A. Bottino, Dr. F. Cunsolo, Prof. Dr. M. Piattelli
Istituto per lo Studio delle Sostanze Naturali di Interesse Alimentare e Chimico-Farmaceutico
Consiglio Nazionale delle Ricerche
Via del Santuario 110, I-95028 Valverde, CT (Italy)
Fax: Int. code + (39)95-721-2141
e-mail: neri@issn.ct.cnr.it

Dr. E. Gavuzzo
Istituto di Strutturistica Chimica "G. Giacomello"
C.N.R., Area della Ricerca di Roma, Montelibretti RM (Italy)
Area della Ricerca di Roma, Montelibretti, RM (Italy).

[**] We wish to thank Mr. R. Rapisardi (ICTMP-CNR, Catania) for FAB-MS measurements and Dr. G. Chessari (University of Sheffield) for evaluation of NMR titration data. The institutes cited are associated with the Istituto Nazionale di Coordinamento per la Chimica dei Sistemi Biologici.

Definitive proof of the structure of **2** was obtained through single-crystal X-ray structure analysis.[11] In the crystal the molecule resembles two bowls joined together by the Ar–Ar bond (1.50(1) Å; Figure 2), with the two concavities on opposite sides. The bottom of each bowl is formed by four hydroxy groups. In each bowl an approximate square network of intramolecular hydrogen bonds is created by the four hydroxy groups, each acting once as donor and once as acceptor in two hydrogen bonds. The average length of the eight hydrogen bonds is 2.68 Å [minimum 2.66(1) Å, maximum 2.69(1) Å]. The angles C–O ··· O are all approximately 110°, and the hydroxy hydrogens and one of the two lone pairs from an oxygen atom presumably lie close to the plane formed by the four oxygens of each moiety. The angles O ··· O ··· O are all around 90°. The torsion angle between the Ar moieties is 35(2)°, a typical value for biphenyl systems in which there is very little conjugation between the two aromatic rings.[14] The canting angles between the mean plane of the four methylene carbons and the planes of the phenol rings vary from 51.6° to 61.4° in the two halves. The packing of the host molecules is governed mainly by van der Waals interactions, where the shortest contact is 2.96(1) Å between the O(1) atoms of two centrosymmetric molecules. The crystal contains chloroform, but only three chloroform molecules were identified because of disorder present in the solvent system. Two are included in the pseudocapsules formed by the two opposing bowls of facing centrosymmetric molecules (Figure 3), as a consequence of van der Waals interactions. The third chloroform molecule is outside the capsules, where its acidic hydrogen atom may form a possible hydrogen bond with an OH group (O ··· C = 3.30 Å, O ··· H–C = 166.3°).

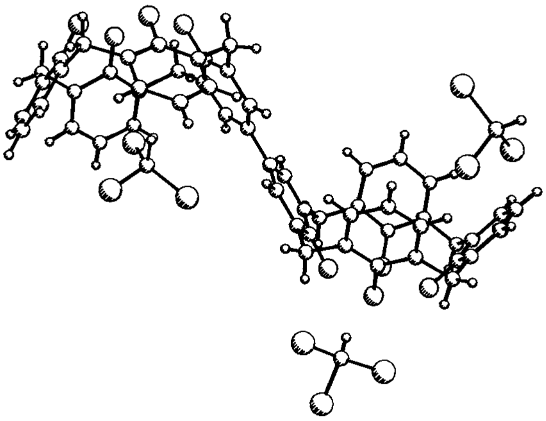


Figure 2. Crystal structure of **2** · 3 $CHCl_3$ (H, C, O, and Cl atoms are drawn as spheres of increasing size).

Each phenol ring of bicalix[4]arene **2** can rotate freely through the 16-membered annulus, leading, in principle, to 21 extreme conformations (apart from enantiomers and *syn*/*anti* alternatives). Blocking this motion by alkylation with groups bulkier than ethyl[15] would then lead to as many atropisomers. Although this appears to be a considerable complication, it at the same time makes **2** a very appealing substrate, provided that conditions can be found for satisfactory stereochemical control of alkylation. To test this potentiality, **2** was treated with 2-(ethoxy)ethyl bromide under conditions (NaH/DMF) known to favor alkylation products in the *cone* conformation.[16] Thus, the octakis[2-(ethoxy)ethoxy] derivative **4** fixed in a double-*cone* conformation was obtained in good yield (55 %) and high stereoselectivity. Further investigation in this direction might similarly lead to the selective preparation of other atropisomers.

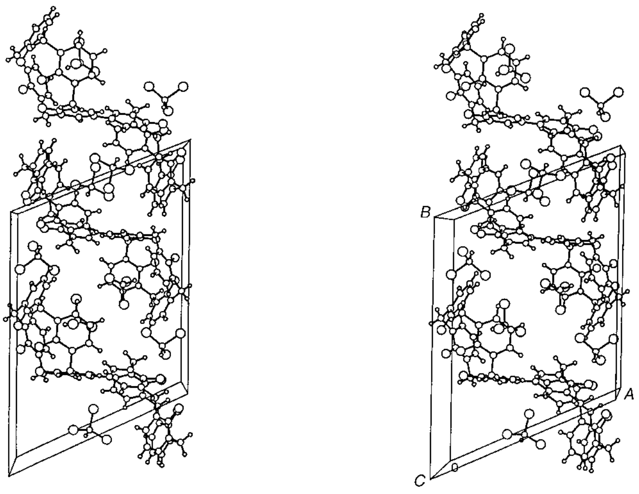
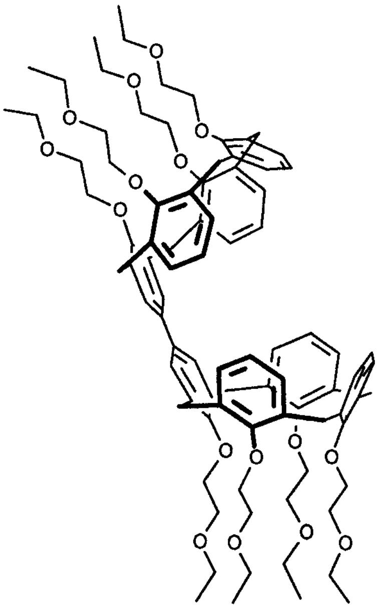
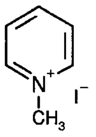


Figure 3. Crystal packing of **2** viewed along the *c* axis.

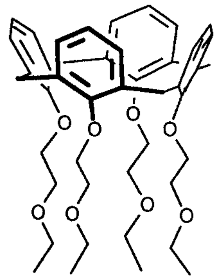
The globular architecture of the *syn* conformation of **2** suggests the potential for cooperation between the two *cone* binding sites in the *endo*-calix complexation of suitable guests. A conformationally blocked double *cone* system like **4** of course appears preferable to this end; indeed, preliminary ^1H NMR experiments (Figure 4) revealed the ability of **4** to include the *N*-methylpyridinium cation **5** (iodide counterion). A value of 153 M^{-1} was estimated for the association constant based on NMR titration,[17a] compared with 6 M^{-1} found for



4



5



6

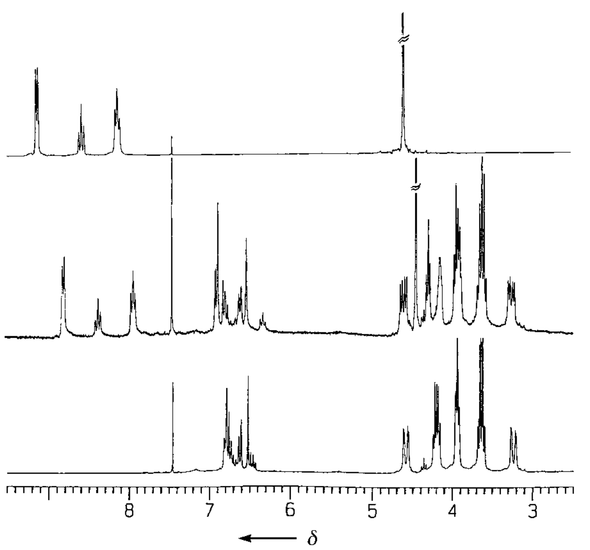


Figure 4. ^{1}H NMR spectra (250 MHz, 295 K, $CDCl_3$/CD_3CN 5/1) of **4** (bottom), *N*-methylpyridinium iodide **5** (top), and a mixture of the two (middle).

the reference compound tetrakis[2-(ethoxy)-ethoxy]calix[4]-arene **6**.[16] This indicates the cooperative action of the two halves in cation inclusion.[17b]

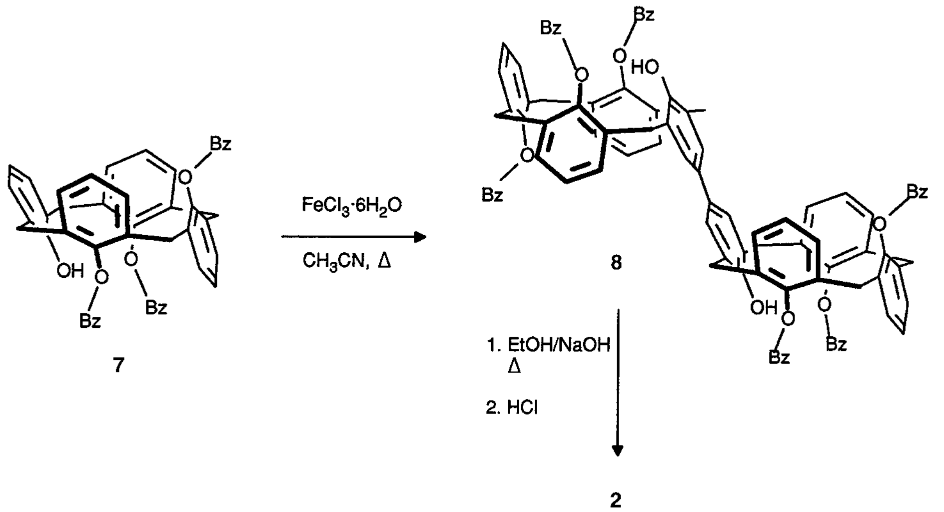
The peculiar structural features of **2** and its high stereochemical potential make it an interesting new building block in host–guest and supramolecular chemistry. For this reason, the availability of larger amounts became imperative, which in turn required improvements in the synthesis. Because the main drawback to direct coupling of **1** seems to be competitive polymerization and/or polyoxidation, we were induced to try an indirect pathway for synthesizing **2** using as starting material a calix[4]arene with a single free phenolic OH group. Therefore, we subjected the readily available tribenzoate **7**, described by Gutsche et al.,[9a, 18] to oxidative coupling with $FeCl_3 \cdot 6H_2O$ (Scheme 2). This led to the dimeric hexabenzoate **8**, which upon alkaline hydrolysis gave 5,5′-bicalixarene **2** in 55–60% overall yield. With this latter procedure the way has become open for a full investigation into the potentialities of bicalixarene building blocks in supramolecular chemistry. An extension of this approach, using different coupling conditions,[20] may result in *para-para*-oligo-calixarenes with novel and interesting architectures. We are currently carrying out work in these directions.

Experimental Section

2: A suspension of **7** (1.5 g, 2.04 mmol) and $FeCl_3 \cdot 6H_2O$ (1.10 g, 4.07 mmol) in CH_3CN (30 mL) was heated at reflux with stirring. After 1.5 h additional $FeCl_3 \cdot 6H_2O$ (1.10 g, 4.07 mmol) was added. The process was repeated several times until the starting material was completely consumed (based on TLC). The solvent was removed by evaporation in vacuo, 3 N HCl added to the residue, and the solid collected by filtration. This crude product was suspended in EtOH (85 mL), and after addition of 15% NaOH (13 mL) the mixture was heated at reflux with stirring for 7 h. Most of the EtOH was subsequently removed by evaporation in vacuo. The resulting suspension was neutralized with 1N HCl, and solid material collected by filtration. This was dissolved in CH_2Cl_2 and again filtered to remove small amounts of insoluble matter. Flash chromatography on silica gel (CH_2Cl_2/petroleum ether, 1/1) led to **2** (0.47 g, 55%). M.p. >360 °C; ^{1}H NMR (250.13 MHz, C_6D_6, 350 K) $\delta = 3.71, 3.76$ (2 × s, 8 H each, $ArCH_2Ar$), 6.43 (t, $J = 7.8$ Hz, 2 H, ArH), 6.47 (t, $J = 7.5$ Hz, 4 H, ArH), 6.69–6.80 (m, 12 H, ArH), 6.87 (s, 4 H, Ar–ArH), 10.01 (brs, 8 H, OH); ^{1}H NMR (250.13 MHz, C_6D_6, 295 K; partial spectrum): $\delta = 3.26, 4.22$ (2 × br, AX, each 8 H, $ArCH_2Ar$); ^{1}H NMR (250.13 MHz, $CDCl_3$, 250 K; partial spectrum): $\delta = 3.55/4.26$ (AX, $J = 13.7$ Hz, 8 H, $ArCH_2Ar$), 3.57/4.26 (AX, $J = 13.7$ Hz, 8 H, $ArCH_2Ar$); ^{13}C NMR (62.9 MHz, $CDCl_3$, 295 K) $\delta = 31.7$, 31.8 (t, $ArCH_2Ar$), 122.2, 122.3, 127.8 (d, $C_{Ar}H$), 128.0, 128.1, 128.2 (s, $\mathit{C}_{Ar}CH_2$), 128.9(2 × C), 129.1 (d, $C_{Ar}H$), 135.3 (s, C_{Ar}–C_{Ar}), 148.0, 148.7, 148.8 (s, $C_{Ar}OH$); positive-ion FAB-MS [*m*-nitrobenzylalcohol (NBA) matrix]: $m/z = 847$ [$M^+ + H$].

4: ^{1}H NMR (250.13 MHz, C_6D_6, 295 K) $\delta = 1.17$ (t, $J = 5.7$ Hz, 12 H, CH_3), 1.18 (t, $J = 6.2$ Hz, 12 H, CH_3), 3.18/4.71 (AX, $J = 13.3$ Hz, 8 H, $ArCH_2Ar$), 3.25/4.75 (AX, $J = 13.5$ Hz, 8 H, $ArCH_2Ar$), 3.37–3.49 (m, 16 H, OCH_2), 3.79 (t, $J = 5.5$ Hz, 8 H, CH_2CH_2), 3.88 (q, $J = 5.7$ Hz, 8 H, $\mathit{CH_2}CH_3$), 4.15 (t, $J = 5.5$ Hz, 8 H, $ArOCH_2$), 4.27 (t, $J = 5.6$ Hz, 4 H, $ArOCH_2$), 4.28 (t, $J = 5.8$ Hz, 4 H, $ArOCH_2$), 6.63–6.84 (m, 18 H, ArH), 7.08 (s, 4 H, Ar–ArH); ^{13}C NMR (62.9 MHz, $CDCl_3$, 295 K) $\delta = 15.3$ (q, $OCH_2\mathit{CH_3}$), 30.8, 31.0 (t, $ArCH_2Ar$), 66.4, 69.7, 73.0, 73.2 (t, OCH_2), 122.3, 126.7, 128.1 (d, $C_{Ar}H$), 134.8 (s, $\mathit{C}_{Ar}CH_2$), 135.1 (s, C_{Ar}–C_{Ar}), 155.5, 156.2, 156.4 (s, C_{Ar}–O); positive-ion FAB-MS (NBA): $m/z = 1425$ [$M^+ + H$].

Received: July 8, 1997 [Z10724IE]
German version: *Angew. Chem.* **1998**, *110*, 175–178



Scheme 2. Improved synthesis of **2** through oxidative coupling of two molecules of **7**.

Keywords: biaryls · calixarenes · configuration determination · host–guest chemistry · macrocycles

---

[1] Review on calixarenes: V. Böhmer, *Angew. Chem.* **1995**, *107*, 785; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713.

[2] Review on double calixarenes: Z. Asfari, J. Weiss, J. Vicens, *Synlett* **1993**, 719.

[3] A few exceptions are the double calixarenes bridged at one $ArCH_2Ar$ group: a) O. Aleksiuk, S. E. Biali, *J. Org. Chem.* **1996**, *61*, 5670. b) *Calixarenes: A Versatile Class of Macrocyclic Compounds* (Eds.: J. Vicens, V. Böhmer), Kluwer, Dordrecht, **1991**, p. 60.

[4] Special cases of multiple calixarenes are Böhmer's "annelated"

calixarenes, in which the two macrocycles share two adjacent phenol rings: V. Böhmer, R. Dörrenbächer, M. Frings, M. Heydenreich, D. de Paoli, W. Vogt, G. Ferguson, I. Thondorf, *J. Org. Chem.* **1996**, *61*, 549.

[5] Recent examples not included in ref. [1, 2]: O. Struck, L. A. J. Chrisstoffels, R. J. W. Lugtenberg, W. Verboom, G. J. van Hummel, S. Harkema, D. N. Reinhoudt, *J. Org. Chem.* **1997**, *62*, 2487; J. A. Perez-Adelmar, H. Abraham, C. Sanchez, K. Rissanen, P. Prados, J. de Mendoza, *Angew. Chem.* **1996**, *108*, 1088; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1009; M. A. McKervey, M. Pitarch, *J. Chem. Soc. Chem. Commun.* **1996**, 1689; A. Siepen, A. Zett, F. Vögtle, *Liebigs Ann.* **1996**, 757; P. Lhotak, S. Shinkai, *Tetrahedron Lett.* **1996**, *37*, 645; P. Lhotak, M. Kawaguchi, A. Ikeda, S. Shinkai, *Tetrahedron* **1996**, *52*, 12399; A. Arduini, S. Fanni, G. Manfredi, A. Pochini, R. Ungaro, A. R. Sicuri, F. Ugozzoli, *J. Org. Chem.* **1995**, *60*, 1448; F. Ohseto, S. Shinkai, *J. Chem. Soc. Perkin Trans. 2* **1995**, 1103; H. Ross, U. Lüning, *Angew. Chem.* **1995**, *107*, 2723; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2555.

[6] The shortest spacer used so far is a single CH_2 group: K. Araki, K. Hisaichi, T. Kanai, S. Shinkai, *Chem. Lett.* **1995**, 569.

[7] The *para* positions (upper rim) of a calixarene system are commonly considered as the "head," while the OH groups (lower rim) represent the "tail": W. Wasikievicz, G. Rokicki, J. Kielkiewicz, V. Böhmer, *Angew. Chem.*, **1994**, *106*, 230; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 214.

[8] The complete IUPAC name for this compound is 5,5′-bicalix[4]arene-25,25′,26,26′,27,27′,28,28′-octol.

[9] a) C. D. Gutsche, L.-G. Lin, *Tetrahedron* **1986**, *42*, 1633; b) C. D. Gutsche, L. J. Bauer, *J. Am. Chem. Soc.* **1985**, *107*, 6052.

[10] R. Pummerer, E. Prell, A. Rieche, *Ber. Dtsch. Chem. Ges. B* **1926**, *59*, 2159.

[11] Crystal structure analysis of **2**: $C_{56}H_{46}O_8 \cdot 3\,CHCl_3$, $M_r = 1205.11$, triclinic, space group $P\bar{1}$ (no. 2), $a = 15.389(3)$, $b = 19.630(4)$, $c = 10.790(2)$ Å, $\alpha = 90.45(2)$, $\beta = 108.78(1)$, $\gamma = 67.71(1)^\circ$, $V = 2831(1)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.41$ g cm^{-3}, colorless crystals from $CHCl_3$/EtOH, crystal dimensions $0.25 \times 0.30 \times 0.45$ mm^3, θ-2θ scan ($2\theta_{max} = 124.2^\circ$), $F(000) = 1240$, room temperature. Of 9285 measured reflections, 8908 were independent ($R_{int} = 0.068$). Data were collected with a Rigaku AFC5R diffractometer with graphite-monochromated $Cu_{K\alpha}$ radiation and a 12 kW rotating anode generator. The data were corrected for Lorentzian and polarization effects, and an empirical absorption correction was applied to intensities based on azimuthal scans of several reflections; $\mu(Cu_{K\alpha}) = 45.27$ cm^{-1}, no decay correction. The structure was solved by direct methods with the program SIR 92.[12] Non-hydrogen atoms were refined anisotropically[13] except for one solvent molecule refined isotropically because of disorder. All hydrogen atoms (apart from OH) were positioned geometrically (riding model). Final refinements were carried out according to the full-matrix least-squares method based on 4189 observed reflections with $F_o > 10\,\sigma(F_o)$ and 665 variable parameters. $R = 0.117$, $R_w = 0.121$, $w = (\sin\theta/\lambda)^2$, $S = 1.38$. Maximum and minimum peaks of the final difference Fourier map: 2.20 and -1.03 e Å^{-3}; these residual electron densities could not be assigned to any chemically sensible moiety. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100536. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: int. code + (44) 1223-336033; e-mail: deposit@chemcrys.cam.ac.uk).

[12] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, *J. Appl. Crystallogr.* **1994**, *27*, 435.

[13] M. Camalli, R. Spagna, *J. Appl. Crystallogr.* **1994**, *27*, 861.

[14] E. G. Boonstra, *Acta Crystallogr.* **1963**, *16*, 816.

[15] K. Iwamoto, K. Araki, S. Shinkai, *J. Org. Chem.* **1991**, *56*, 4955.

[16] J.-D. van Loon, J. F. Heida, W. Verboom, D. N. Reinhoudt, *Recl. Trav. Chim. Pays-Bas* **1992**, *111*, 353.

[17] a) NMR titrations (250 MHz, 295 K) were carried out in $CDCl_3$/CD_3CN (5/1). The association constants were determined with a nonlinear fitting program using the concentration-dependent shifts of the NMe group while the concentration of the host (**4** or **6**) was held constant. b) A similar cooperative action in the complexation of *N*-methylpyridinium iodide was found by Shinkai et al. for a CH_2-bridged double calix[4]arene.[6]

[18] For the "up-down-up" stereochemical assignment of **7**: C.-M. Shu, W.-C. Liu, M.-C. Ku, F.-S. Tang, M.-L. Yeh, L.-G. Lin, *J. Org. Chem.* **1994**, *59*, 3730.

[19] Further examples of biaryl coupling: M. Larsen, M. Jørgensen, *J. Org. Chem.* **1997**, *62*, 4171; S. Zhang, D. Zhang, L. S. Liebeskind, *ibid.* **1997**, *62*, 2312; N. G. Andersen, S. P. Maddaford, B. A. Keay, *ibid.* **1996**, *61*, 9556; N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457; G. Sartori, R. Maggi, F. Bigi, M. Grandi, *J. Org. Chem.* **1994**, *59*, 3701; D. A. Whiting in *Comprehensive Organic Synthesis, Vol. 3* (Eds.: B. M. Trost, I. Fleming), Pergamon, New York, **1991**, p. 659; J. K. Stille, *Angew. Chem.* **1986**, *98*, 504; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 508; E. Negishi, *Acc. Chem. Res.* **1982**, *15*, 340.

Lanthanide-Assisted Self-Assembly of an Inert, Metal-Containing Nonadentate Tripodal Receptor[**]

Stéphane Rigault, Claude Piguet,[*]
Gérald Bernardinelli, and Gérard Hopfgartner

Recent fascinating applications of lanthanide, Ln^{III}, complexes as contrast agents for medical resonance imagining (MRI), luminescent stains for fluoroimmunoassays, and catalysts for the selective cleavage of RNA and DNA require close and tunable control of the coordination sphere to enhance specific structural and electronic properties.[1] The development of tailored receptors for Ln^{III} remains a challenge for synthetic chemists, since Ln^{III} ions do not display pronounced stereochemical preferences for particular bonding modes.[2] Highly preorganized macrobicyclic cryptands allow only partial control of the coordination of Ln^{III} ions,[3] and their tedious preparation has encouraged the development of Ln^{III}-assisted template syntheses of macrocyclic Shiff base complexes.[4] However, the nondirectional Ln–ligand bonds and the high sensitivity of Ln^{III} to basic conditions severely limit their use as template ions in the preparation of macrobicycles[5] and self-assembled metal-containing supramolecular compounds.[6]

A recent approach uses the segmental ligands L^1 and L^2, which are predisposed for the selective recognition of f-block metal ions. The self-assembled homotopic triple-stranded helicates $[Ln_2(L^1)_3]^{6+}$ result from the reaction of L^1 with $Ln(ClO_4)_3$,[7] while equimolar mixtures of $Ln(ClO_4)_3$ and $M(ClO_4)_2$ (M = Zn, Fe) produce head-to-head heterotopic

---

[*] Dr. C. Piguet, S. Rigault
Department of Inorganic, Analytical and Applied Chemistry
University of Geneva
30 quai E. Ansermet, CH-1211 Geneva 48 (Switzerland)
Fax: Int. code + (41) 22-702 6069
e-mail: claude.piguet@chiam.unige.ch.

Dr. G. Bernardinelli
Laboratory of X-ray Crystallography, University of Geneva

Dr. G. Hopfgartner
Pharmaceuticals Division, Department of Drug Metabolism and Kinetics
F. Hoffmann-La Roche Ltd, Basel (Switzerland)

[**] This work was supported by the Swiss National Science Foundation and the Werner Foundation.