Multicavitands II: Synthesis of a Non Centrosymmetric Hollow Molecular Unit (Koiland) Based On Fusion of Two *p-tert*-butylcalix[4]arenes by Both Silicon and Titanium Atoms

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Abstract: The synthesis and NMR structural investigation of a non-centrosymetric koiland (hollow molecular unit) composed of two *p-tert*-butylcalix[4]arenes fused by both silicon and titanium atoms, and of its precursor obtained by fusing two *p-tert*-butylcalix[4]arenes with a silicon atom were achieved.

The chemistry of inclusion complexes, *i.e.* the inclusion of a substrate within the cavity of a receptor molecule is an established area.[1-2] One may extend the concept of inclusion in solution to the construction of new networks in the solid state. For example, a rigid and compact direceptor possessing two divergent cavities with an angle of 180°, considered as a double hollow molecular unit, and a linear connector, possessing two extremities capable each to be included within the cavities of the direceptor, may be assembled in the solid state. The driving force for the assembling process would be non-covalent Van der Walls interactions resulting from the penetration of the connector ends within cavities of the direceptors. In such constructions, the basic hollow molecular unit may be named linear *koiland* (from Greek koilos (κοιλοσ), hollow), and the new plastic (flexible) rode type linear molecular array, obtained by an iterative assembling process, may be called linear *koilate*. (Fig. 1)
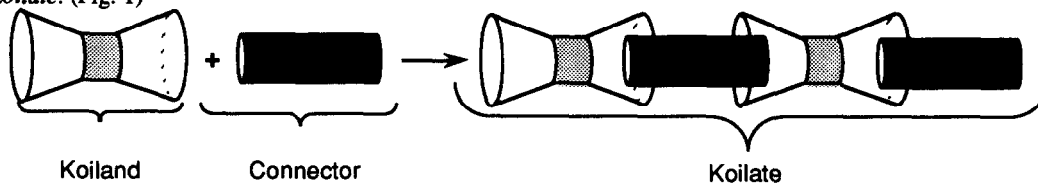

Fig. 1. Schematic representation of linear koilate (see text for definition)

The design of the koiland would obviously be of great importance for the monitoring of the assembling process and the overall geometry of the koilate. Furthermore, whereas in the case of symmetric linear koilands no directionality may be expected for the assembly, with non-centrosymetric koilands in which the left cavity (L) is different from the right cavity (R), one would expect with a symmetric linear connector (C) both the (R-C-L-R-C-L)n and (R-C-L-L-C-R)n type polymers. By fusing two *p-tert*-butylcalix[4]arenes[3,4] with two silicon atoms (Fig. 2), we already succeeded in preparing the centrosymetric linear koiland 1 (Fig.3).[5] Examples of fused *p-tert*-butylcalix[4]arene using titanium(IV),[6] niobium(V),[7] aluminium(IV)[8] have been reported. For the Si,[5] Ti[6]

and Al[7] fused calixarenes X-ray crystallography revealed that these compounds were indeed composed of two divergent hydrophobic cavities interconnected in a linear fashion. Two calix[4]arenes have also been interconnected by organic[8,9] and organometallic bridges.[10] In all examples cited above, the fused or bridged calix[4]arenes, the molecules reported are centrosymetric structures.

We report here the first example of a non centrosymetric and rigid hollow molecular unit composed of two *p-tert*-butylcalix[4]arenes fused simultaneously by both silicon and titanium atoms (Fig. 3). For the design of the koiland, *p-tert*-butylcalix[4]arene (Fig. 2) was again found to be an interesting unit since, in cone conformation, it offers three advantages: i) a preorganized cavity at the "upper rim", ii) possible inclusion of substrates such as toluene,[11] benzene,[12] anisole[13], iii) four aryloxy groups which can be used for interconnecting two calix units. Due to the disposition of the aryloxy groups in cone conformation of the calix, two of these units may be directly fused by two tetra-coordinated atoms leading to a compact and rigid double receptor. Thus the tetrahedron composed of four oxygen atoms around each fusing atom would be made of three oxygen atoms belonging to
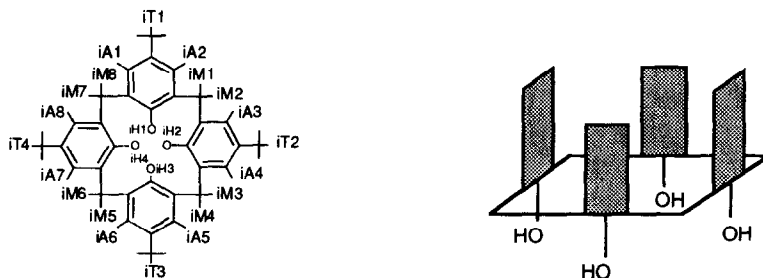

Fig. 2. *p-tert*-butylcalix[4]arene (left) and its schematic representation in cone conformation (right). Protons attribution iA: aromatic, iT: *tert*-butyl, iM: methylene, iH: hydroxy protons; i = 1, 2 for 2 different calix units in the same molecule

one calix (i=1) and the fourth one to the other calix unit (i=2). Compound **3** (Fig. 3) is a koiland possessing two divergent hydrophobic pockets made of two *p-tert*-butylcalix[4]arenes. The non-centrosymetric nature of **3** is based on the difference between the two calix units induced by coordination to two different atoms. Indeed, one of the calix in **3** is triply coordinated to a Si atom whereas the other unit is triply coordinated to a Ti atom.
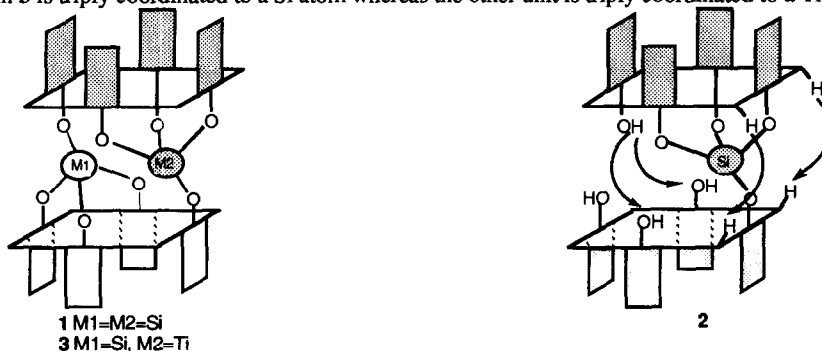

Fig. 3. Schematic representation of **1-3** and observed cross plateaux correlations for **3**.

In order to prepare **3** following a directed strategy, we first explored the synthesis of the monofused compound **2** (Fig. 3).[16] Treatment of *p-tert*-butylcalix[4]arene[15] with 2 eq. of NaH in THF followed by reaction with SiCl4 afforded the compound **2** in 36 % yield. Attempt to increase the yield by varying the different ratio of *p-tert*-butylcalix[4]arene, NaH and SiCl4 failed. Compound **2**, unlike its parent compound *p-tert*-butylcalix[4]arene, was rather soluble in organic solvents such as CHCl3, THF. The structure of **2** was investigated by NMR spectroscopy.[16] Since **1** (Fig. 3) was fully characterised by X-ray crystallography[5] for

comparison purposes, its structure in solution was also studied by two-dimensional NMR techniques. The ^{1}H-NMR spectrum of 1 contained 3 singlets (*tert*-butyl), 4 doublets (methylene), 2 singlets and 2 AB systems for the aromatic protons revealing the centrosymetric nature of 1. A ROESY experiment allowed us to assign all proton in 1 and to confirm the observed structure in the solid state. As expected for a non centrosymetric compound possessing a plane of symmetry, the ^{1}H and ^{13}C spectra clearly indicated that compound 2 was composed of two distinct *p-tert*-butylcalix[4]arenes both in cone conformation (i=1, 2, see Fig. 2). The complete assignment of all protons was based on a ROESY experiment. Due to the possible free rotation around the Si-O bond, one would not expect any preferred rotamer. The ROESY experiment nevertheless showed correlations between 1H$_4$ proton and both 2H$_1$ and 2H$_3$ protons as well as correlations between the equatorial methylene protons 1M$_1$ and 1M$_3$ of the calix unit 1 (i=1) with those, 2M$_1$ and 2M$_3$ of the calix unit 2 (i=2). These observations indicated that, due to possible intra plateau hydrogen bonding between hydroxy groups belonging to both calix units, the face to face (syn) rotamer was the preferred one (Fig. 3). The presence of OH groups was also observed by IR spectroscopy which revealed two broad bands at 3385 cm^{-1} and at 3524 cm^{-1}.

Since all four hydroxy groups in 2 were disposed in a face to face fashion they could accommodate another atom requiring a tetrahedral mode of coordination. Thus, 2 was used as the precursor for preparing 1 and 3. Indeed, treatment of *p-tert*-butylcalix[4]arene with SiCl$_4$ in THF gave both the homobinuclear compound 1 and the monofused compound 2. Alternatively, the treatment of the isolated 2 with TiCl$_4$ in CH$_2$Cl$_2$ produced a rather high yield (76 %) and almost instantaneous reaction leading to the heterobinuclear compound 3.[17] Whereas the analoguecompound 1 containing two silicon atoms was a colourless solid, 3 was a yellow crystalline solid.

Attempts to confirm the structure of 3 in the solid state failed. Although suitable monocrystals were obtained from chloroform-methanol mixture, we only succeeded in determining the space group and the volume of the unit cell. These values were, as expected, in perfect agreement with the solid state parameters for compound 1.[5] Unfortunately, due to the weak differences between Si and Ti atoms, the disorder in the diffraction pattern was such that accurate structural determination was impossible. The structure of 3 was established by mass spectrometry and by multidimensional NMR experiments.[17] 3 as its analogue 1 and its precursor compound 2 was composed of two calix[4]arene units in their cone conformation. In contrast with 1, the non centrosymetric nature of 3 was revealed by its ^{1}H NMR spectrum which was composed of two sets of signals corresponding to two different calix plateaux (i= 1, 2, Fig. 3). Although a ROESY experiment allowed us to assign all protons in 3, nevertheless, we were unable to localise Si and Ti atoms in 3. Fortunately, in the low field region, the ^{13}C spectra of 3 showed 3 distincts signals with a 1:2:1 ratio. Comparison of the aromatic carbon atoms of all three compounds 1-3 clearly indicated that these signals were those corresponding to carbons connected to the 4 oxygen atoms composing the tetrahedron around the Ti atom. Taking advantage of this observation, using a DEPT-135 sequence followed by a [1]H-^{13}C correlation experiment we first identified all carbon atoms. Using the ROESY data we were able to localise both Si and Ti atoms in 3 and to obtain a complete structural assignment.

Work in the elaboration of networks in the solid state using 3 as a unit is under progress. The precursor compound 2 may also be used for the synthesis of other heterobinuclear compounds. In particular, the synthesis of Si-W, Si-Sn, Si-Pb and Si-V heterobinuclear compounds is under current investigation.

References and notes

1.   Dietrich, B. ; Viout, P. ; Lehn, J.-M. , *Macrocyclic Chemistry*, VCH, Weinheim, **1993**.

2.   Vögtle, F. ; *Supramolecular Chemistry*, Wiley, New York **1991**.

3.   C. D. Gutsche, *Calixarenes* in *Monographs in Supramolecular Chemistry*, The Royal Society of Chemistry, London **1989**.

4.   *Calixarenes. A Versatile Class of Macrocyclic Compounds*, Ed. J. Vicens and V. Böhmer, Kluwer Academic Publishers, Dordrecht, **1991**.

5.   X. Delaigue, M. W. Hosseini, A. De Cian, J. Fischer, E. Leize, S. Kieffer, A. Van Dorsselaer, *Tetrahedron Lett.*, **1993**, *34*, 3285-3288.

6.   Olmstead, M. M. ; Sigel G. ; Hope H. ; Xu, X. ; Power, P. P. , *J. Amer. Chem. Soc.*, **1985**, *107*, 8087-8091.

7.   Corazza, F. ; Floriani, C. ; Chiesti-Villa, A. ; Guastini, C. , *J. Chem. Soc., Chem. Commun.*, **1990**, 1083-1084.

8.   Atwood, J. L. ; Bott, S. G. ; Jones, C. ; Raston, C. L. , *J. Chem. Soc., Chem.Commun.*, **1992**, 1349-1351.

9.   Kraft, D. ; van Loon, J.-D. ; Owens, M. ; Verboom, W. ; Vogt, W. ; McKervey, M. A. ; Böhmer, V. ; Reinhoudt, D. N. , *Tetrahedron Lett.* , **1990**, *31*, 4941-4944.

10. van Loon, J.-D. ; Kraft, D. ; Ankoné, M. J. K. ; Verboom, W. ; Harkema, S. ; Böhmer, V. ; Reinhoudt, D. N. , *J. Org. Chem.* , **1990**, *55*, 5176-5179.

11. Beer, P. D. ; Keefe, A. D. ; Slawin, A. M. Z. ; Williams, D. J. , *J. Chem Soc. Dalton Trans.* , **1990**, 3675-3682.

12. Andreetti, G. D. ; Ungaro, R. ; Pochini, A. , *J. Chem. Soc., Chem. Commun.*, **1979**, 1005-1007.

13. Coruzzi, M. ; Andreetti, G. D. ; Bocchi, V. ; Pochini, A. ; Ungaro, R. , *J. Chem. Soc. , Perkin Trans. II*, **1982**, 1133-1138.

14. Ungaro, R. ; Pochini, A. ; Andreetti, G. D. ; Domiano, P. , *J. Chem. Soc. , Perkin Trans. II*, **1985**, 197-201.

15. Gutsche, C. D. ; Iqbal, M. , *Organic Syntheses*, **1989**, *68*, 234-237.

16. To a suspension of *p-tert*-butylcalix[4]arene[15] (2 g, 2.70 mmol) in dry THF (50 ml), NaH (260 mg, 10.82 mmol) was added under argon and the mixture was stirred at room temp. over a period of 17 h. To the slurry $SiCl_4$ (0.2 ml, 1.7 mmol) was added and the mixture further stirred for another 3 h. THF was removed and the pure compound **2** (0.652 g, 36% yield) was obtained as a white solid after chromatography (SiO_2, Eluent CH_2Cl_2/hexane 10/90), m. p. 315-316°C; ^{1}H NMR ($CDCl_3$, 400 MHz, 25°C) δ 1.18 (s, 9H, $1T_4$), 1.20 (s, 9H, $2T_2$), 1.24 (s, 9H, $1T_2$), 1.25 (s, 18H, $2T_1$-$2T_3$), 1.27 (s, 9H, $2T_4$), 1.29 (s, 18H, $1T_1$-$1T_3$), 3.41 (d, J= 13.2 Hz, 2H, $1M_2$-$1M_4$), 3.44 (d, J= 11.4 Hz, 2H, $2M_2$-$2M_4$), 3.51 (d, J= 13.8 Hz, 2H, $2M_6$-$2M_8$), 3.53 (d, J= 13.2 Hz, 2H, $1M_6$-$1M_8$), 4.36 (d, J= 13.7 Hz, 2H, $2M_5$-$2M_7$), 4.43 (d, J= 13.4 Hz, 2H, $1M_1$-$1M_3$), 4.75 (d, J= 13 Hz, 2H, $2M_1$-$2M_3$), 4.78 (d, J= 13.5 Hz, 2H, $2M_5$-$2M_7$), 6.97 (s, 2H, $1A_7$-$1A_8$), 7.05 (AB, 2.2 Hz, 2H, $2A_1$-$2A_6$), 7.07 (AB, 2.4 Hz, 2H, $1A_2$-$1A_5$), 7.09 (s, 2H, $2A_3$-$2A_4$), 7.10 (s, 2H, $2A_7$-$2A_8$), 7.12 (AB, 2.4 Hz, 2H, $2A_2$-$2A_5$), 7.13 (s, 2H, $1A_3$-$1A_4$), 7.20 (AB, 2.5 Hz, 2H, $1A_1$-$1A_6$), 7.59 (s, 1H, $1H_1$), 9.69 (s, 2H, $2H_1$-$2H_3$), 10.33 (s, 1H, $2H_4$); ^{13}C NMR ($CDCl_3$, 100.62 MHz, 25°C) δ 31.25, 31.39, 31.41, 31.47, 31.50, 31.55 (CH_3), 31.92, 33.13, 33.62 (CH_2), 33.84, 33.93, 34.00, 34.08, 34.13, 34.34 (C), 34.74 (CH_2), 124.58, 124.92, 125.05, 125.71, 125.82, 126.23, 126.25, 126.68, 127.31, 128.40, 128.44, 129.12, 130.32, 131.32, 132.61 (CH_2, CH, arom.), 142.06, 143.39, 143.64, 144.22, 144.25, 145.39, 146.69, 146.88, 147.41, 147.64, 148.38, 148.58 (C-C(CH_3), C-O, arom.); ^{29}Si NMR ($CDCl_3$, 79.49 MHz, 25°C) δ -107.58; IR (KBr) 3385, 3524 cm^{-1} (OH str.); UV 280nm (14900 lmol[-1]cm^{-1}); positive ion FAB m/z 1320.4 (M.[+], 45%); Found: H 8.10, C 80.02; calcd for $C_{88}H_{108}O_8Si$: H 8.24, C 79.95%.

17. To a solution of **2** (0.1 g, 0.076 mmol.) in dry CH_2Cl_2 (20 ml) a 10% solution of $TiCl_4$ (0.1 ml, 0.087mmol) in dry CH_2Cl_2 was added yielding an orange-brown solution. The mixture was further stirred for 1 h. before Et_3N (0.4 ml) was added and the mixture evaporated to dryness. The pure compound **3** (79 mg, 76%) was obtained as a yellow solid after chromatography (SiO_2, CH_2Cl_2); m. p. >380 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, 25°C) δ 1.09 (s, 9H, $2T_2$), 1.16 (s, 9H, $1T_4$), 1.18 (s, 9H, $2T_3$), 1.19 (s, 9H, $1T_2$), 1.24 (s, 18H, $1T_1$-$1T_3$), 1.30 (s, 18H, $2T_1$-$2T_3$), 3.22 (d, J= 13.7 Hz, 2H, $1M_5$-$1M_7$), 3.33 (d, J= 12.8 Hz, 2H, $1M_1$-$1M_3$), 3.41 (d, J= 13.9 Hz, 2H, $2M_5$-$2M_7$), 3.50 (d, J= 13.6 Hz, 2H, $2M_1$-$2M_3$), 4.38 (d, J= 12.6 Hz, 2H, $2M_6$-$2M_8$), 4.46 (d, J= 12.3 Hz, 2H, $1M_6$-$1M_8$), 4.74 (d, J= 12.6 Hz, 2H, $1M_2$-$1M_4$), 5.06 (d, J= 13.5 Hz, 2H, $2M_2$-$2M_4$), 6.87 (s, 2H, $2A_3$-$2A_4$), 6.99 (AB, 2.5 Hz, $1A_1$-$1A_6$), 7.01 (s, 2H, $1A_7$-$1A_8$), 7.05 (s, 2H, $1A_3$-$1A_4$), 7.05 (AB, 2.5 Hz, 2H, $2A_6$-$2A_1$), 7.08 (s, 2H, $2A_7$-$2A_8$), 7.09 (AB, 2.5 Hz, 2H, $1A_5$-$1A_2$), 7.16 (AB, 2.5 Hz, 2H, $2A_2$-$2A_5$); ^{13}C NMR ($CDCl_3$, 100.62 MHz, 25°C) δ 31.20, 31.24, 31.36, 31.41, 31.50, 31.67 (CH_3), 32.63 (C), 33.01, 33.50, 33.61 (CH_2), 34.05, 34.07, 34.10, 34.17, 34.32 (C), 34.66 (CH_2), 123.69, 124.37, 124.66, 125.27, 125.38, 125.95, 126.17, 126.77, 126.86, 128.94, 129.03, 129.92, 130.07, 130.31, 131.08, 132.80, (C-H, C-CH_2, arom.) 144.10, 144.40, 144.48, 144.62, 145.32, 145.35, 147.23, 147.26, 147.71, 157.37, 160.69, 161.74, 147.23, 147.26, 147.71, 157.37, 160.69, 161.74 (C-C($CH_3)_3$, C-O, arom.); ^{29}Si NMR ($CDCl_3$, 79.49 MHz, 26°C) δ -112.32; UV 280 nm (21900 lmol[-1]cm^{-1}), 273 nm (22400 lmol[-1]cm^{-1}) Positive ion FAB m/z= 1364.6 (M.[+], 100%); Found: H 7.97, C 77.19, calcd for $C_{88}H_{104}O_8SiTi$: H 7.68, C 77.39.