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Multicavitands IV : Synthesis of Linear Koilands Obtained by Fusion of Calix[4]arene Derivatives by Silicon Atoms

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Abstract: The synthesis of koilands based on the double fusion of two *p*-methylcalix[4]arenes, two *p*-phenylcalix[4]arenes with two silicon atoms, and of compounds composed of two and three calix[4]arene units fused with one and two silicon atoms, respectively was achieved.

The design and synthesis of large molecular architectures, *i.e.* nanostructures, are under active investigation.[1] An approach to the manufacture of such materials with designed geometry may be based on an iterative assembling process between molecular modules or tectons[2] possessing interaction sites outwardly oriented (exoreceptors).[3] Dealing with the energetics involved between the interaction sites during the self-assembling processes, one may use non-covalent interactions such as electrostatic and H-bonding,[4] coordination bonds[5] or even weaker van der Waals interactions. In the latter case, we prepared koilands[6] which were defined as multicavity receptor molecules composed of at least two cavities arranged in a divergent fashion. Since each individual cavity may form an inclusion complex with a connector molecule, fusing two or more of such cavities, in a rigid framework, may lead in the presence of an appropriate connector to a non-covalently assembled polymeric species which may be called koilate (Figure 1). We have recently achieved the synthesis and x-ray analysis of a linear koilate based on the interconnection of the koiland 9 with hexadiyne (previous contribution in this issue). Koilands based on the fusion of two or three *p*-*tert*-butylcalix[4]arene (**1**)[7] units with two silicon atoms (**9**) were reported (Figure 3).[6] Examples of fused calix[4]arene using titanium(IV),[8a] niobium(V),[8b] aluminium(IV)[8c] have been reported. Two calix[4]arenes has also been interconnected by organic[9] and organometallic bridges.[10]

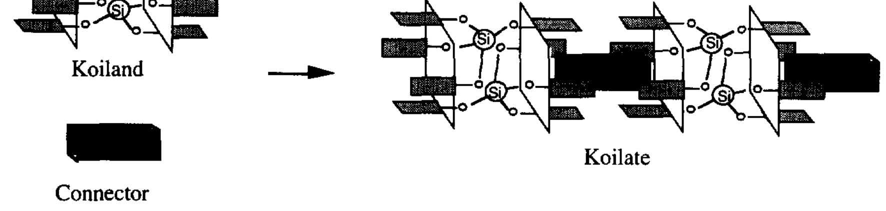

Figure 1: Schematic representation of a koiland (hollow molecular brick) possessing two divergent cavities and of a koilate resulting from the assembling of koilands with a connectors.

Calix[4]arene[7] derivatives are interesting molecules since in their cone conformation they possess both a tuneable preorganised cavity and four hydroxy groups allowing their fusion. Indeed, both the entrance and the depth of the preorganised cavity may be controlled by the nature of the substituent R at the *para* position, *i.e.* H, CH_3, $C(CH_3)_3$, Ph (Figure 2).

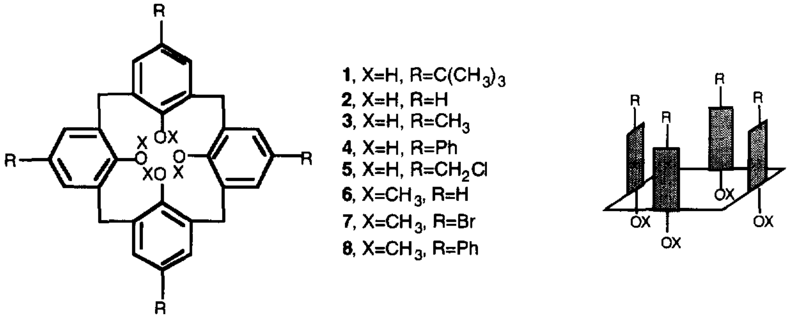

Figure 2: Structures of calix[4]arene derivatives and a schematic representation of their cone conformation.

We report here the first synthesis of koilands based on the double fusion of two *p*-methylcalix[4]arenes **10**, two *p*-phenylcalix[4]arenes **11** with two silicon atoms (Figure 3) as well as the synthesis of compounds **13** and **14** resulting from the mono (**13**) and di (**14**) fusion of two and three calix[4]arene units with one and two silicon atoms respectively (Figure 3).

The starting material for the synthesis of all compounds reported was the *p*-*tert*-butylcalix[4]arene **1** prepared according to the published procedure.[11] The calix[4]arene **2** was obtained by aluminium chloride de-*tert*-butylation of **1**.[12] The latter was the common starting material for the synthesis of both *p*-methylcalix[4]arene **3** and *p*-phenylcalix[4]arene **4**. Although the synthesis of **3** was first reported by Gutsche *et al.*,[13a] the procedure by Ungaro *et al.*[13b] was found to be more convenient. In the latter case we found that the same procedure leading to the chloromethyl compound **5** may be applied using chloromethyl-ethyl ether (96 % yield) which costs half the price of the chloromethyl-n-octyl ether previously used. Furthermore, in the $LiAlH_4$ reduction step of **5** affording the desired compound **3**, we found that quenching the excess of $LiAlH_4$ with 10% H_2SO_4 instead of dilute HCl was much more convenient since it allowed an easy separation of the supernatant. Finally the desired compound **3** could be crystallised from toluene, thus avoiding the purification by chromatography. Although the synthesis of compound **4** was again initially reported by Gutsche *et al*,[14a,b] the recent preparation reported by Atwood *et al*[14c] appeared to be more efficient. Compound **2** was first protected to its tetramethyl ether derivative **6** before it was converted to the *p*-bromo compound **7**.[15] The latter was converted to the *p*-phenyl derivative **8** using a palladium-catalysed coupling reaction with phenylboronic acid.[14c] Finally, the desired compound **4** was obtained after deprotection using BBr_3 in CH_2Cl_2.

Whereas for both compounds **2** [16] and **4** [14c] the cone conformation was established in the solid state by X-ray analysis, to our knowledge, for compound **3** no X-ray data is available so far. Upon treatment of **3** by 4.4 eq. of NaH in dry THF over a period of 18 h at r.t., followed by addition at once of 1.1 eq. of neat $SiCl_4$ and further stirring at r.t. for 2 h, the doubly fused compound **10** was obtained in 42% yield after chromatography (SiO_2, CH_2Cl_2/hexane:1/1). Compound **11** was obtained from compound **4** in 17% yield using the same procedure (4.4 eq. NaH, 6h, r. t., 1.2 eq. $SiCl_4$, 1h, r. t.).

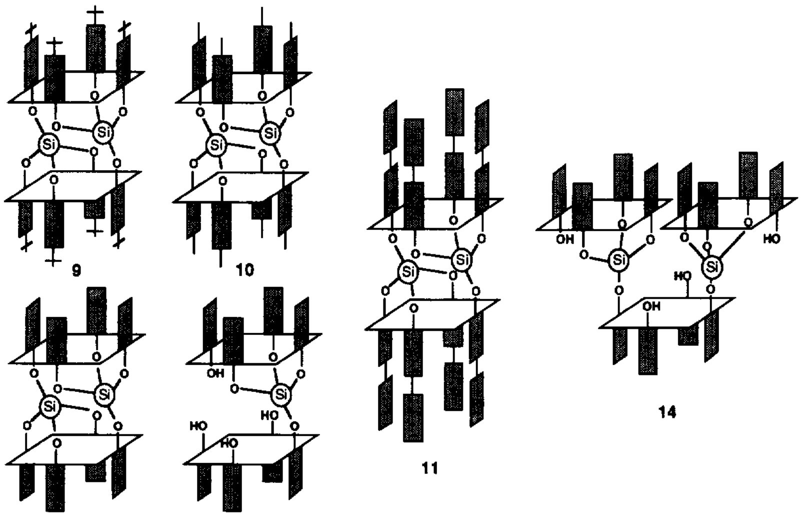

Figure 3: Schematic representation of doubly fused two *p-tert*-butylcalix[4]arenes (**9**), *p*-methylcalix[4]arenes (**10**), *p*-phenylcalix[4]arenes (**11**) and calix[4]arenes (**12**) by two silicon atoms, mono fused two calix[4]arenes (**13**) with one Si atom and of three calix[4]arenes (**14**) fused by two silicon atoms.[17]

With compound **12**, under the conditions mentioned above, we were not able to isolate the doubly fused compound. Nevertheless, treatment of **2** with 4.4 eq. of NaH under reflux for 2h followed by addition at once of 1.1 eq. of SiCl4 at r. t. and further stirring for 2h, afforded the mono fused compound **13** (10% yield) and the trimer **14** composed of three calixarene units fused by two Si atoms in 6% yield. Whereas compound **13** could be isolated by precipitation from CHCl3, compound 14 was obtained after chromatography (SiO2, CH2Cl2/hexane: 1/1). The yield of **14** was further increased to 42% by dropwise addition of a 10% solution of SiCl4 in dry THF followed by further stirring for 2h at r. t. . We have previously demonstrated that the same type of structures may be obtained with *p-tert*-butylcalix[4]arene.[1,6b,c] The proposed structures for both **13** and **14** (Figure 3) were in agreement with the detailed one- and two-dimensional NMR analyses reported for the similar compounds based on **1**.[6b,c]

In conclusion, we were able to fuse two *p*-methylcalix[4]arenes and two *p*-phenylcalix[4]arenes with two Si atoms. The fusion of two calix[4]arenes with one silicon and of three calix[4]arenes with two silicon atoms was also achieved. Attempts to prepare koilates based on these new modules and linear connectors are under investigation.

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17 All new compounds reported were fully analysed by NMR spectroscopy and by Mass spectrometry and gave satisfactory elemental analysis.

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