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Synthesis of an Exo-Ditopic Receptor Based on Calix[4]arene and Catechol

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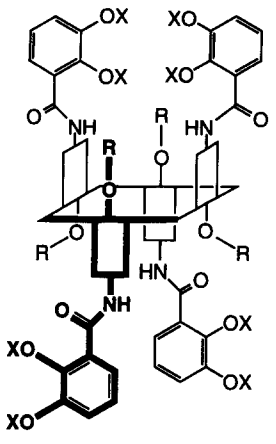
Abstract: The synthesis of a calix[4]arene derivative immobilised in 1,3-alternate conformation by alkylation at the lower rim and bearing four catechoylamide units at the upper rim was achieved. The chelating coordination sites were by construction oriented, in an alternating mode, below and above the main plane of the backbone, thus affording an exo-ditopic ligand.

Although functionalised polymers (complexing polymers), bearing a variety of binding sites capable of binding metal cations are well known since long time, only in recent years much attention has been focused on polymeric species (coordination polymers) in which the metal plays a structural role. This approach presents, at least, two interesting features. The metal, a structural constituent bridging other modules such as organic moieties, presents a large variety of coordination geometry (tetrahedral, octahedral, square planar etc.). Furthermore, due to electronic, redox, photonic and magnetic properties of metal centres , the resulting coordination polymers may also exhibit pre-programmed or unexpected functional features. The preparation of such materials may be envisaged through an iterative assembly of bridging ligands and metals. In this context, the design and synthesis of multisites receptor molecules in which the interaction sites are oriented outwardly (exo-receptors) is of special interest. In this vein, we have already reported the synthesis of exoreceptors based on calixarenes[1,2], amidines[3] and bipyridines.[4]

Molecular units possessing four chelating groups pointing outwards and occupying the apices of a pseudo-tetrahedron may be of interest for construction of one dimensional coordination polymers using lanthanide or actinide metals allowing octacoordination. The design of such a ligand may be based on a preorganised backbone offering the possibility of anchoring four chelating coordination sites in an alternating mode below and above of its main plane. In this regard, *p-tert*-butylcalix[4]arene **1**[5] seems to be the candidate of choice since it may be functionalised at both upper and lower rims. Indeed, one may impose the 1,3-alternate conformation by proper modification at the lower rim through transformation of all four hydroxy groups into ether junctions.[5,6] On the other hand, it has been shown that calix[4]arene may also be functionalised at the upper rim allowing the anchoring of chelating groups.[5]



1 X = H, R = n-Pr

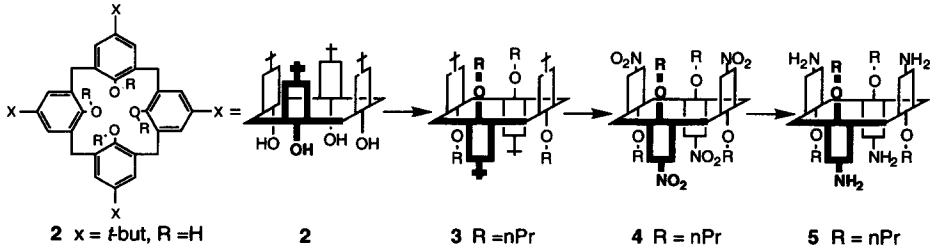
10 X = Bn, R = n-Pr

Our approach to the design of the exo-binucleating ligand **1** was based on the combination of a calix[4]arene framework and four bidentate catecholate moieties. Although calix[4]arene derivatives bearing bidentate bipyridine units at the lower and upper rims have been prepared[7], to our knowledge no example of the combination cited above has been reported. Diaza-[8], Triaza- and tetraaza-macrocycles bearing two, three and four pendant catecholate units have also been previously reported.[9] We report here the first synthesis of a new exo-ditopic ligands **1** composed of a calix[4]arene moiety and four catechol units.

The synthetic strategy for the preparation of **1** was based on the coupling of the acyl chloride derivatives of the protected catechol **9** with the tetraaminocalix[4]arene **5**, followed by deprotection of the benzyl groups.

The *p-tert*-butylcalix[4]arene **2** was prepared according to published procedure.[10]

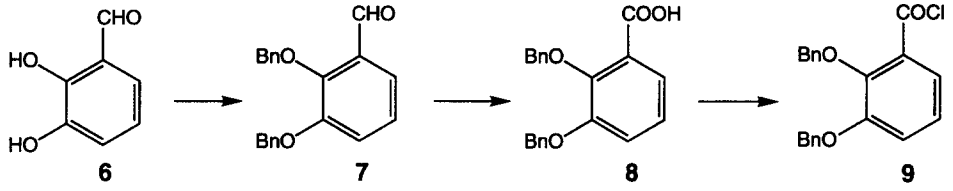
The tetrapropoxy derivative **3** was obtained upon condensation of **2** with propyl iodide in benzene in the presence of *t*-BuOK.[11] This reaction, already reported[11], gave a mixture of partial cone and 1,3-alternate conformers. The desired 1,3-alternate conformer was isolated by crystallisation from CH_2Cl_2/MeOH mixture in 15 % yield. Although it has been shown that the proportion of the desired 1,3-alternate conformer could be enhanced using caesium carbonate[12], nevertheless, because of the high cost of the latter, *t*-BuOK was preferred. The 1,3-alternate conformation of the compound **3** was demonstrated by the observation of a singlet for the CH_2 groups of the calix backbone. Compound **3** was transformed into its tetranitro derivative **4** by the reported ipso nitration using HNO_3/AcOH mixture in CH_2Cl_2.[13] Again, the observation of a singlet for the methylene group of the calix moiety of **4** confirmed that upon ipso nitration, the 1,3-alternate conformation was not altered. Although the reduction of nitro calixarene derivatives using hydrazine and $FeCl_3$[14] or hydrazine and Raney Nickel[15] has been reported, we found that the general procedure developed by Bellamy et al.[16] using $SnCl_2$ and EtOH was the most convenient one. Thus, under these conditions, treatment of **4** afforded the tetraamino compound **5** in 93 % yield.[17] The latter compound has not been reported previously.



2 x = *t*-but, R =H **2** **3** R =nPr **4** R = nPr **5** R = nPr

Although 2,3-dimethoxy-benzoic acid is commercially available, nevertheless, since in our strategy, the calix[4]arene hydroxy groups were blocked by propyl chains, the protection of the catechol was achieved using benzyl group (Bn) which can be deprotected by catalytic hydrogenation. Treatment of the commercially available

2,3-dihydroxy-benzaldehyde **6** with benzyl bromide in EtOH in the presence of K_2CO_3 afforded the protected aldehyde **7** in quantitative yield.[18] The oxidation at r. t. of the latter by $NaClO_2$ in the presence of H_2NSO_3H in a 1/1 acetone/water mixture afforded the acid **8**[18], which was further converted into its acyl chloride **9** by treatment with $(COCl)_2$ in benzene in the presence of a drop of DMF.[18]



6 **7** **8** **9**

The benzyl protected calix[4]arene derivative **10**[19] was obtained in 64 % yield upon condensation of the acyl chloride **9** with the amino calixarene **5** in CH_2Cl_2 in the presence of Et_3N. The desired final compound **1**[20] was generated in 84 % yield by cleavage of the benzyl protecting groups using catalytic hydrogenation (Pd/C). In order to avoid oxidation, the compound **1** was stored in the absence of oxygen. The 1,3-alternate conformation of the precursor **10** and of the final compound **1** was again established by ^1H NMR.

In summary, the synthesis of compound **1** based on a calix[4]arene backbone in the 1,3-alternate conformation bearing four catechoylamide units at its upper rim was achieved in acceptable yields. The binding ability of the latter towards transition metals and lanthanides will be reported elsewhere. The formation of coordination polymers using **1** is under current investigation.

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References and notes

1 Delaigue, X., Hosseini, M. W., De Cian, A., Fischer, J., Leize, E., Kieffer, S., Van Dorsselaer, A., *Tetrahedron Lett.*, **1993**, *34*, 3285-3288; Delaigue, X., Hosseini, M. W., Leize, E., Kieffer, S., Van Dorsselaer, A., *Tetrahedron Lett.*, **1993**, *34*, 7561-7564; Delaigue, X., Hosseini, M. W., Graff, R., Kintzinger, J.-P., Raya, J. *Tetrahedron Lett.* **1994**, *35*, 1711-1714; Hajek, F.,Graf, E., Hosseini,M. W.,*Tetrahedron Lett.*, **1996**, *37* 1409-1412; Hajek, F., Graf, E., Hosseini,M. W., Delaigue, X., De Cian, A., Fischer, J., *Tetrahedron Lett.*, **1996**, *37*, 1401-1404.

2 Delaigue, X., Hosseini, M. W. *Tetrahedron Lett.*, **1993**, *34*, 8111-8112; Gibbs, C. G., Gutsche, C. D. *J. Amer. Chem. Soc.*, **1993**, *115*, 5338-5339; Delaigue, X., Harrowfield, J. McB., Hosseini, M. W., De Cian, A., Fischer, J., Kyritsakas, N., *J. Chem. Soc., Chem. Commun.*, **1994**, 1579-1580.

3 Hosseini, M. W., Ruppert, R., Schaeffer, P., De Cian, A., Kyritsakas, N., Fischer, J., *J. Chem. Soc. Chem., Commun.*, **1994**, 2135-2136; Brand, G., Hosseini, M. W., Ruppert, R., De Cian, A., Fischer, J., Kyritsakas, N., *New J. Chem.*, **1995**, *19*, 9-13; Hosseini, M. W., Brand, G., Schaeffer, P., Ruppert, R., De Cian, A., Fischer, J., *Tetrahedron Lett.*, **1996**, *37*, 1405-1408.

4 Kaes, C., Hosseini, M. W., Ruppert, R., De Cian, A., Fischer, J., *Tetrahedron Lett.*, **1994**, *35*, 7233-7236; Delaigue, X., Hosseini, M. W., Kyritsakas, N., De Cian, A., Fischer, J., *J. Chem. Soc., Chem. Commun.*, **1995**, 609-610; Kaes, C., Hosseini, M. W., Ruppert, R., De Cian, A., Fischer, J. *J. Chem. Soc., Chem. Commun.*, **1995**, 1445-1446.

5 C.D. Gutsche,*"Calixarenes"*, Monographs in Supramolecular Chemistry, Ed. J.F. Stoddart, R.S.C., London, 1989; *Calixarenes. A Versatile Class of Macrocyclic Compounds*, Ed. J. Vicens and V. Böhmer, Kluwer Academic Publishers, Dordrecht, 1991; Böhmer, V., *Angew. Chem., Int. Ed. Engl.*, **1995**, *34*, 713-745.

6 Iwamoto, K., Araki, K., Shinkai, S. *Tetrahedron*, **1991**, 47, 4325-4342.

7 Beer, P. D., Martin, J. P., Drew, M. G. B. *Tetrahedron*, **1992**, *48*, 9917-9928; Ulrich, G., Ziessel, R. *Tetrahedron Lett.* **1994**, *35*, 6299-6302; Regnouf de Vains, J.-B., Lamartine, R. *Helv. Chim. Acta*, **1994**, *77*, 1817-1825; Beer, P. D., Chen, Z., Goulden, A. J., Grieve, A., Hesek, D., Szemes, F., Wear, T. *J. Chem. Soc. Chem Comm.* **1994**, 1269-1271, Grigg, R., Holmes, J. M., Jones, S. K;, Amilaprasadh Norbert, W. D. J. *J. Chem. Soc. Chem Comm.* **1994**, 185-187; Casnati, A., Fischer, C.,

Guardigli, M., Isernia, A., Manet, I., Sabbatini, N., Ungaro, R. *J. Chem. Soc. Perkin Trans II* **1996**, 395-399.

8 Graf, E., Hosseini, M. W., Ruppert, R., *Tetrahedron Lett.* **1994**, *35*, 7779-7782; Graf, E., Hosseini, M. W., Ruppert, R., Kyritsakas, N., De cian, A., Fischer, J., Estournès, C., Taulelle, F. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1115-1117; Graf, E., Hosseini, M. W., Ruppert, R., De cian, A., Fischer, J. *J. Chem. Soc., Chem. Comm.* **1995**, 1505-1506.

9 Weitl, F. L. , Raymond, K. N. *J. Am. Chem. Soc.* **1980**, *102*, 2289-2293; Raymond, K. N., Müller, G., Matzanke, B. F. *Topics Current Chem.* **1984**, *123*, 49-102.

10 Gutsche, C. D., Iqbal, M. *Organic Synthesis*, **1989**, *68*, 234.

11 Kelderman, E., Derhaeg, L., Heesink, G. J. T., Verboom, Engbersen, J. F. J., van Hulst, N. E., Persoons, A., Reinhoudt, D. N. *Angew. Chim. Int. Ed. Engl.* **1992**, *31*, 1075-1077.

12 Iwamoto, K;, Araki, K., Shinkai, S. *J. Org. Chem.* **1991**, *56*, 4955-4962.

13 Shinkai, S., Araki, K., Tsubaki, T., Arimura, T., Manabe, O. *J. Chem. Soc. Perkin Trans. I* **1987**, 2297-2299.

14 Shinkai,S., Arimura, T., Araki, K., Kawabata, H., Satoh, H., Tsubaki, T., Manabe, O., Sunamoto, J. *J. Chem. Soc. Perkin Trans. I* **1989**, 2039-2045.

15 vanLoon, J.-D., Janssen, R. G., Verboom, W., Reinhoudt, D. N. *Tetrahedron Lett.* **1992**, *35*, 5125-5128.

16 Bellamy, F. D., Ou, K. *Tetrahedron Lett.* **1984**, *25*, 839-842.

17 A suspension of the tetranitro compound **4**[13] (2.63 g, $3.4x10^{-3}$ mol)and $SnCl_2.2H_2O$ (15.6 g, 0.69 mol) in absolute EtOH (170 ml) was stirred under argon at 70 °C for 2 days.[16] The reaction mixture was allowed to cool to r.t. before it was poured into H_2O (100 ml, pH 8-9/NaOH). The mixture was extracted with CH_2Cl_2 (3x200 ml) and the organic layer dried over $MgSO_4$ affording 2.06 g (93 % yield) of compound **5** as a slightly beige solid which was used in the subsequent reaction without purification; M. p. >300 °C; ^1H (200 MHz, $CDCl_3$, 25 °C): δ (ppm) : 1.05 (t, 12H, J = 7.4 Hz, CH_2CH_3); 1.74 (m., 8H, J = 7.2 Hz, $OCH_2CH_2CH_3$); 2.73 (br.s, 8H, NH_2); 3.41 (s, 8H, $ArCH_2Ar$); 3.54 (t, 8H, J = 7.0 Hz, OCH_2); 6.47 (s, 8H, Ar); ^{13}C (50.32 MHz, $CDCl_3$,, 25 °C): δ (ppm) : 11.02 ($OC_2H_4CH_3$); 23.88 ($OCH_2CH_2CH_3$); 35.82 ($ArCH_2Ar$); 74.56 (OCH_2); 117.66; 134.3; 140.25; 149.5 (Ar).Found: C 70.80, H 8.35, N 8.40; calc. for $C_{40}H_{52}O_4N_4$-H_2O-0.5 EtOH : C 70.97, H 8.28, N 8.07.

18 Rastetter, W. H., Erickson, T. J., Venuti, M. C. *J. Org. Chem.* **1981**, *46*, 3579-3590.

19 To a stirred solution of **5** (620 mg, $9.5x10^{-4}$ mol) and freshly distilled Et_3N (1 ml, $7.2x10^{-3}$ mol) in dry CH_2Cl_2 (30 ml), a solution of the acylchloride derivative of the benzyl protected catechol **9**[18] (2.08 g, 5.9x10-3 mol) in dry CH_2Cl_2 (30 ml) was added dropwise under argon and the mixture further stirred at r. t. for 2 days. The reaction mixture was evaporated to dryness before it was taken up in CH_2Cl_2 (30 ml) and washed with water (3x15 ml). The organic layer was dried over $MgSO_4$. The pure compound **10** (1.2 g, 64 % yield) was obtained by crystallisation from CH_2Cl_2/MeOH. M. p. 114-116 °C; ^1H (300 MHz, $CDCl_3$, 25 °C): δ (ppm) : 0.43 (t, 12H, J = 7.2 Hz, $OC_2H_4CH_3$); 0.97 (m., 8H, J = 7.2 Hz, $OCH_2CH_2CH_3$); 3.13 (t, 8H, J = 7.2 Hz, $OCH_2C_2H_5$); 3.54 (s, 8H, $ArCH_2Ar$); 5.16 (s, 8H, OCH_2Ph); 5.17 (s, 8H, OCH_2Ph); 6.90-7.86 (m, 45H, Ar.); 9.81 (s, 4H, H-amid); ^{13}C (75.48 MHz, $CDCl_3$, 25 °C): δ(ppm): 9.82 ($OC_2H_4CH_3$); 22.45 ($OCH_2CH_2CH_3$); 38.16 ($ArCH_2Ar$); 71.42, 71.83, 76.32 (OCH_2); 117.17, 120.85, 123.69, 124.48, 127.60, 128.23, 128.55, 128.66, 128.80, 129.06, 132.15, 134.05, 136.14, 136.41, 146.52, 151.76, 153.33 (Ar); 162,07 (*C*=O)

20 To a solution of the functionalised calix derivative **10** (250 mg, $1.30x10^{-4}$ mol) in AcOEt (20 ml), EtOH (40 ml) and Pd/C (100 mg) was added and the mixture degassed before H_2 (1 atm) was introduced. The reaction was monitored by thin layer chromatography which revealed that it was completed after 8h. To the mixture, a drop of conc. HCl was added before it was filtered. The solid was washed with boiling EtOH (100 ml), the filtrate and the wash were combined and filtered over celite (100 mg). The removal of the solvent left the pure compound **1** as a slightly beige solid (131 mg, 84 % yield). In order to avoid oxidation, the compound **1** was stored in the absence of oxygen. M. p. 183-185 °C, decomp.; ^1H (300 MHz, CD_3OD, 25 °C): δ (ppm) : 0.78 (t, 12H, J = 7.2 Hz, $OC_2H_4CH_3$); 1.50(m., 8H, J = 7.2 Hz, $OCH_2CH_2CH_3$); 3.46 (t, 8H, J = 7.2 Hz, $OCH_2C_2H_5$); 3.82 (s, 8H, $ArCH_2Ar$); 6.71 (t, 4H, J = 8.0 Hz, Ar); 6.93 (dd, 4H, ^1J = 7.8 Hz, ^2J = 1.4 Hz, Ar); 7.43 (dd, 4H, ^1J = 8.0 Hz, ^2J = 1.2 Hz, Ar); 7.45 (s, 8H, Ar); ^{13}C (50.32 MHz, CD_3OD, 25 °C): δ (ppm) : 11.85 ($OC_2H_4CH_3$); 25.35 ($OCH_2CH_2CH_3$); 40.09 ($ArCH_2Ar$); 75.27 ($OCH_2C_2H_5$); 119.42, 120.88, 121.06, 125.03, 134.33, 136.68; 148.39, 150.56; 156.49 (Ar); 170,13 (*C*=O); FAB $^+$ (*meta*-nitrobenzylalcohol matrix) m/z 1197.5 (MH^+); Found: C 65.30, H 5.34; calc. for $C_{68}H_{68}O_{16}N_4$-$3H_2O$: C 65.27, H 5.96.

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