Pergamon

Tetrahedron Letters 42 (2001) 1021–1024

TETRAHEDRON LETTERS

Synthesis, X-ray crystal structure and complexation properties towards metal ions of new thiacalix[4]arenes

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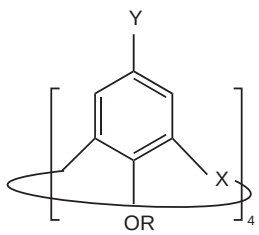
Received 27 July 2000; accepted 3 November 2000

Abstract—*p-tert*-Butyl-tetrakis[(methylcarbonyl)methoxy]tetrathiacalix[4]arene and *p-tert*-butyl-tetrakis[(benzoyl)methoxy]tetrathiacalix[4]arene were prepared and their conformation was established by X-ray crystallography. *p-tert*-Butyl-tetrakis-[(diethylamide)methoxy]tetrathiacalix[4]arene was also synthesized. The ability of these three macrocycles to bind metal ions was investigated via a solvent extraction study. © 2001 Elsevier Science Ltd. All rights reserved.

In the field of supramolecular chemistry, calixarenes have generated increasing interest both in fundamental and applied chemistry.[1] By functionalization of the lower and upper rims, a wide variety of calixarenes has been prepared.[2] These macrocycles have been used for catalysis, molecular recognition or ion separation,[3] as sensors[4] or as nonlinear optical compounds.[5] A new class of macrocycles has been recently reported, derived from calix[4]arenes, and namely thiacalix[4]arenes. They are easily prepared from *p*-alkylphenol and elemental sulfur under basic conditions.[6] NMR studies have indicated that the thiacalixarenes are conformationally much more flexible than ordinary calixarene in solution. The flexibility increases with an increasing number of sulfur bridges.[7] The complexation ability of the thiacalix[4]arenes towards neutral molecules[8] or metal ions has also been investigated.[9,10] As part of our efforts to develop new receptors for molecular or ionic recognition, herein we report the first synthesis and structural determination of two new thiacalix[4]arenes, bearing four ketone groups, and one new thiacalix[4]arene bearing four amido groups on the lower rim. We also describe the metal ion complexing properties of these new macrocycles. The thiacalix[4]arenes **2**, **3** and **4a** (Scheme 1) have been obtained by a method similar to that used for the synthesis of esters of *p-tert*-butylcalixarenes.[11] Compound **5** has been prepared following the procedure given by Hosseini et al.[8] Proton and ^{13}C NMR spectra of compounds **2**,[12] **3**[13] and **4a**[14] in $CDCl_3$ showed the presence of only one conformer. However, it was difficult to determine the conformation of these molecules, due to the absence of methylene bridges, the proton signals of which are used for conformational assignment.



1 X = S, Y = *t*-Bu, R = H
2 X=S, Y = *t*-Bu, R = CH_2COCH_3
3 X=S, Y = *t*-Bu, R = $CH_2COC_6H_5$
4a X=S, Y = *t*-Bu, R = $CH_2CON(CH_2CH_3)_2$
4b X=CH_2, Y = *t*-Bu, R = $CH_2CON(CH_2CH_3)_2$
5 X=S, Y = H, R = H

Scheme 1. Macrocycles tested in complexation.

Keywords: thiacalixarenes; synthesis; conformations; complexation.
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PII: S0040-4039(00)02131-6

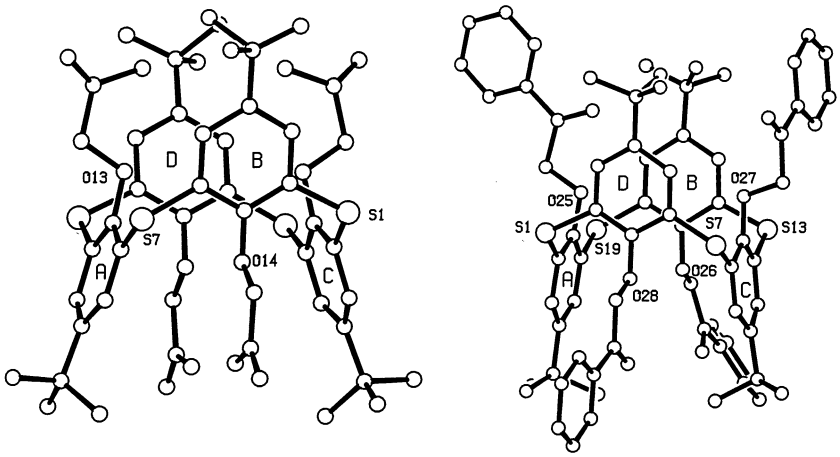

Figure 1. X-Ray structures of **2** and **3**, respectively. H atoms and solvent molecules are omitted.

Table 1. Percent extraction of metal ions by thiacalixarenes

Cations/thiacalix	Li^+	Na^+	K^+	Rb^+	Cs^+	Ca^{2+}	Ba^{2+}	Mg^{2+}	Al^{3+}	Pb^{2+}	Fe^{3+}	Ni^{2+}	Cu^{2+}	Ag^+
1	2.8	1.4	2	1	1	2.4	1.6	0.8	1.1	0.4	4.5	0	1.8	6.6
2	1.1	1.4	0.6	0.6	0.6	1	0.6	0.9	0	1	2.5	1.4	1.3	2.4
3	1.2	2.8	8.6	8.3	3.2	2.4	2.8	3.1	3.9	3.1	8.2	2.7	3.6	35.3
4a	22.9	55	80.1	78	56.4	29.8	24.1	39.7	42.8	32.6	50.9	32.7	40.5	95.9
5	0.8	0.7	0.8	0.7	1.4	0.7	0.3	2.7	3.3	3.6	5.5	3.3	3.9	8.3

In order to gain more information about conformation, these three compounds have been studied by X-ray diffraction methods on suitable monocrystals, which have been obtained from toluene for **2** and **3**, and, from ethyl acetate for **4a**. In all measured cases, these derivatives have adopted the 1,3-alternate conformation.[15] The structures of **2** and of the 2:1 molecular compound of **3** with toluene have been solved. For **4a**, the structure has not been refined anisotropically because the crystals were of bad quality. Compounds **2** and **3** crystallize in centrosymmetric groups. In **2**, one half of the molecule is deduced from the other half by a twofold axis, but **3** shows no internal symmetry. The 1,3-alternate forms of **2** and **3** correspond to similar conformations of the molecules (Fig. 1).

In **2**, the rings make interplanar angles of 106.80(5) and 107.75(5)° with the S plane leading to an enlargement of the cavities on both sides of the molecule. Only Van der Waals contacts are observed between two neighboring molecules. In **3**, the angles of the four aromatic rings A, B, C and D bearing, respectively, O25 (or O13), O26 (or O14), O27 and O28, with the S mean plane are, respectively, 92.3(1), 94.9(9), 95.9(1) and 94.9(9)°. Three out of the four chains have their double bonded oxygen oriented *endo* and a folded shape of their C=O bonds. The toluene molecule is disordered around a center of symmetry and is situated in the interhost space. Steric considerations concerning the accommodation of the solvent molecule may be associated with the specific orientation of the ring connected to C. The shortest distance (3.65(2) Å) between the solvent and the macrocycle occurs between a carbon at the *meta* position of the oxygen in the D ring, and a carbon *meta* to the methyl group in the toluene molecule. In order to evaluate the ability of thiacalix[4]arenes **2**, **3** and **4a** to recognize metal ions, a liquid–liquid extraction[16] of these ions has been carried out. The results are summarized in Table 1. A comparison with *p-tert*-butylthiacalix[4]arene **1**[6] and thiacalix[4]arene **5**[8] is also provided. The amidothiacalix-[4]arene **4a** shows significant complexation of all cations with maximal levels for K^+, Rb^+ and Ag^+. However, its behavior is different from that of the similar calixarene **4b**,[17] which strongly extracts Na^+, K^+, Ca^{++} and Ba^{++}. This is probably because **4b** exists in solution in the cone conformation. For the other compounds, the values of extractability are lower than **4a** and similar calixarenes.[10] On the other hand, for **1**, the results differ from those given in the literature,[9,18] because the extraction is not performed under identical conditions. Thus, for Miyano,[18] the extractabilities are distinctly dependent on pH and are very different at pH 4 and at pH 8 or 10.

In conclusion, from *p-tert*-butylthiacalix[4]arene, three new compounds bearing four ketone or amido groups have been prepared. Complexation studies of these macrocycles show that *p-tert*-butyl-tetrakis[(diethylamide)methoxy]tetrathiacalix[4]arene presents interesting properties for the ionic recognition.

Acknowledgements

The authors wish to thank Professor Marco Ciufolini for correcting the manuscript.

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12. General: Acetone and toluene were freshly distilled. Other reagents were reagent grade and were used without further purification. Column chromatography was performed with silica 60 (0.040–0.063 mm) from E. Merck. All reactions were carried out under nitrogen. Melting points: Electrothermal 9100 point apparatus. ^{1}H NMR spectra were recorded in $CDCl_3$ solution, at 25°C, using a Bruker AM 300 NMR spectrometer operating at 300 and 75 MHz for ^{1}H and ^{13}C, respectively. UV measurements were recorded on a Shimadzu UV-2401 PC spectrophotometer. Mass spectra were obtained by electrospray technique (HP 5989/MS engine, S.C.A., CNRS, Solaize, France). Elemental analyses were performed at S.C.A., CNRS, Solaize, France. *p-tert*-Butyltetrakis[(methylcarbonyl)methoxy]tetrathiacalix[4]arene **2**: To a suspension of chloroacetone (0.33 ml, 5.2 mmol) and NaI (0.77 g, 5.2 mmol) in acetone (25 ml) stirred during 20 min at room temperature, were added *p-tert*-butylthiacalix[4]arene **1** (0.5 g, 0.693 mmol), K_2CO_3 (0.86 g, 6.23 mmol) and acetone (100 ml). The mixture was refluxed for 3 days, cooled at room temperature and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with H_2O, sat. solution of $Na_2S_2O_3$, then H_2O. After evaporation of the solvent, a yellow powder was obtained and washed with EtOH. After filtration the solid product was purified by column chromatography (SiO_2, CH_2Cl_2) to afford pure product in 53% yield (347 mg). Mp 314–315°C. ^{1}H NMR: δ=7.34 (s, 8H, Ar*H*), 4.47 (s, 8H, OCH_2CO), 1.5 (s, 12H, CH_2COCH_3), 1.23 (s, 36H, C(CH_3)$_3$). ^{13}C NMR: δ= 205.79 (CH_2COCH_3), 156.1, 148.16, 129.81, 129.04 (*C*Ar), 74.08 (CH_2COCH_3), 34.79 (*C*(CH$_3$)$_3$), 31.5 (C(*C*H$_3$)$_3$), 27.99 (CH_2CO*C*H$_3$). EI MS; *m*/*z*: 967.3 [M+Na]$^+$ (calcd 967.7). $C_{52}H_{64}O_8S_4$: calcd C, 66.07; H, 6.82; found: C, 65.96; H, 6.87.
13. *p - tert* - Butyl - tetrakis[(benzoyl)methoxy]tetrathiacalix[4]-arene **3**: To a suspension of chlorophenylketone (0.85 g, 5.73 mmol) and NaI (0.86 g, 5.73 mmol) in acetone (50 ml) stirred during 3 h at room temperature were added *p-tert*-butylthiacalix[4]arene **1** (0.5 g, 0.693 mmol) and K_2CO_3 (0.9 g, 6.5 mmol). The mixture was refluxed for 2 days, cooled at room temperature and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with a solution of $NaHSO_3$ (1N), then H_2O. After evaporation of the solvent, MeOH was added in an orange oil; a yellow powder was obtained and was precipitated from CH_2Cl_2/EtOH to give a white powder in 15% yield (124 mg). Mp 225–226°C. ^{1}H NMR: δ= 7.85–7.90 (m, 8H, Ar*H*), 7.57–7.20 (m, 20H, benzyl *H*), 5.31 (s, 8H, OCH_2CO), 1.35–0.95 (m, 36H, C(CH_3)$_3$). ^{13}C NMR: δ=157.36, 146.80, 132.61, 128.14 (*C*Ar), 135.86, 132.61, 129.01, 128.39 (*C*benzyl), 72.83 (O*C*H$_2$CO), 34.54 (*C*(CH$_3$)$_3$), 31.38 (C(*C*H$_3$)$_3$). EI MS; *m*/*z*: 1215.4 [M+Na]$^+$ (calcd 1215.9). $C_{72}H_{72}O_8S_4$+EtOH (1238.9): calcd C, 71.73; H, 6.30; O, 11.62; found: C, 71.82; H, 6.20; O, 11.60.
14. *p - tert* - Butyl - tetrakis[(diethylamide)methoxy]tetrathiacalix[4]arene **4a**: To a suspension of α-chloro-*N*,*N*-diethylacetamide (0.95 ml, 6.93 mmol) and NaI (1.04 g, 6.93 mmol) in acetone (10 ml) stirred during 1 h at room temperature were added *p-tert*-butylthiacalix[4]arene **1** (0.5 g, 0.693 mmol) and K_2CO_3 (0.96 g, 6.93 mmol) and acetone (40 ml). The mixture was refluxed for 2 days, cooled at room temperature and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with solution of 1N HCl (40 ml), sat. solution of $Na_2S_2O_3$, then H_2O. After evaporation of the solvent, acetonitrile was added in a yellow viscous precipitate; a yellow powder was obtained in 41% yield (333 mg). Mp 292.5–293°C. ^{1}H NMR: δ=7.53 (s, 8H, Ar*H*), 4.68 (s, 8H, OCH_2CO), 3.42, 3.40, 3.37, 3.35 (q, 8H, -NCH_2CH$_3$); 3.31, 3.29, 3.27, 3.24 (q, 8H, -NCH_2CH$_3$), 1.25 (s, 36H, C(CH_3)$_3$), 1 (t, 12H, NCH$_2$CH_3), 0.88 (t, 12H, -NCH$_2$CH_3). ^{13}C NMR: δ=167 ($CH_2CON(Et)_2$), 158.02, 146.17, 133.43, 128.16 (*C*Ar), 69.66 (O*C*H$_2$CO), 41.94 (-N*C*H$_2$CH$_3$), 40.38 (N*C*H$_2$CH$_3$), 34.60 (*C*(CH$_3$)$_3$), 31.63 (C(*C*H$_3$)$_3$), 14.88 (-NCH$_2$*C*H$_3$), 13.45 (-NCH$_2$-*C*H$_3$). EI MS; *m*/*z*: 1173.6 [M+H]$^+$ (calcd 1173.9). $C_{64}H_{92}O_8N_4S_4$: calcd C, 65.49; H, 7.90; found: C, 64.99; H, 8.08.
15. X-Ray data for **2**: $C_{52}H_{64}O_8S_4$, *M*=944.7, monoclinic, *a*=10.306(2), *b*=12.705(3), *c*=19.548(4) Å, β= 102.19(3)°, *U*=2502.0(9) Å^3, space group *P*2/*n*, *Z*=2, D_c=1.255 Mg m^{-3}, μ(Mo Kα)=0.242 mm^{-1}. Crystal size 0.4×0.22×0.18 mm. Data were measured at 203 K. *R*= 0.0516, R_w=0.127 for 4912 independent observed reflections with [*I*>2σ(*I*)]. X-Ray data for the 2:1 complex between **3** and toluene: $C_{72}H_{72}O_8S_4$+1/2(C_7H_8), *M*= 1235.57, triclinic, *a*=11.526(2), *b*=15.296(3), *c*= 21.494(4) Å, α=101.11(3), β=92.38(3), γ=111.85(3)°, *U*=3424.5(12) Å^3, space group *P*-1, *Z*=2, D_c=1.198 Mg m^{-3}, μ(Mo Kα)=0.193 mm^{-1}. Crystal size 0.3×0.25×0.2 mm. Data were measured at 203 K. *R*=0.069, R_w=0.161 for 5613 independent observed reflections with [*I*>2σ(*I*)]. X-Ray data for **4a**: $C_{64}H_{92}O_8N_4S_4$, *M*=1172.9, orthorhombic, *a*=19.389(4), *b*=12.539(2), *c*=27.586(5) Å,

$U=6706.0(1)$ Å^3, space group $Pna2_1$, $Z=4$, μ(Mo Kα) = 0.19 mm^{-1}. Data were measured at 203 K. For all structures, intensities were measured by a Nonius Kappa CCD diffractometer using Mo Kα radiation ($\lambda=0.71073$ Å). The structure was solved by direct methods and refinements with full matrix least-squares were calculated using SHELX97.[19] Crystallographic data (excluding structure factors) for the structure of compounds **2** and **3** were deposited at the Cambridge Crystallographic Data Centre. (CCDC numbers 149388 and 149389, respectively.)

16. Determination of extraction data: The alkali picrates were prepared by pHmetry from aqueous picric acid solution and aqueous solution of metal hydroxide (LiOH, NaOH, KOH, RbOH, CsOH, $Ca(OH)_2$, $Ba(OH)_2$) or metal nitrate (Fe^{3+}, Ni^{2+}, Cu^{2+}, Mg^{2+}, Al^{3+}, Pb^{2+}, Ag^{+}); in these cases, the solutions are weakly acidic pH 4). Deionized water was used for all aqueous solutions. Aqueous picrate solution (3 ml, 2.32×10^{-4} M) and 3 ml of a 2.32×10^{-4} M solution of thiacalixarene in CH_2Cl_2 (HPLC grade) were shaken by hand and were then kept for 2 h in a glass tube immersed in a thermostated water bath at 23°C. The absorbances A_i of the aqueous phase after extraction, and, A_0 of the aqueous phase before extraction, were measured at 355 nm (the wavelength of maximum absorption of the picrate ion, $\lambda_{max}=355$ nm). The percentage cation extracted was calculated as the ratio $100\times(A_0-A_i)/A_0$.
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