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# New Double-1,2-amide-bridged Calix[4]arenes by Aminolysis of Calix[4]arene Esters

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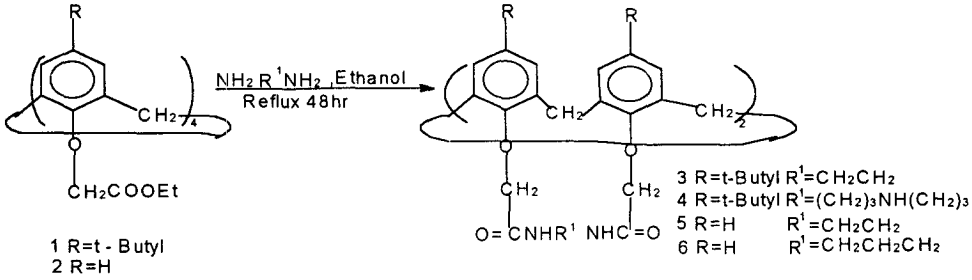
**Abstract:** A new facile method—aminolysis of calix[4]arene esters to obtain lower rim double-1,2-amide-bridged calix[4]arenes is described. We also report the single crystal structure of compound **3** which forms a long chain supramolecule in the solid state *via* intermolecular hydrogen bonding. © 1999 Elsevier Science Ltd. All rights reserved.

Calix[4]arenes are well known for their unique molecular architecture which is extensively used in supramolecular chemistry to build up more complex synthetic receptors for ions[1] and neutral molecules.[2] The complexing ability of these hosts can be tuned either by changing the nature and the number of the binding sites introduced at both rims, or by controlling the conformational properties of the calix[4]arenes. Recently we synthesized a stable endo-cavity complex of a self-assembly calix[4]arene in the solid state with an almost rigid cone conformation. In fact, it has been recently shown that even the cone calix[4]arenes are not completely blocked in solution,[3] but instead the residual conformational mobility lies between the two $C_{2v}$ pinched cone conformations. One of the methods to reduce the conformational mobility and preserve the cone structures is to bridge the calix[4]arenes either at the lower rim by a crown ether[1(b)(c)(d),4] or at the upper rim by an aromatic or other π-donor group.[2(a),5] Here we report on the preparation of new lower rim double-1,2-amide-bridged calix[4]arenes (**3**, **4**, **5** and **6** ) by a new facile method—aminolysis of calix[4]arene esters[6] and the crystal structure of the compound **3**.




1 R=t - Butyl
2 R=H

Recently we have studied the aminolysis of the calix[4]arene esters (**1** and **2**) with many monoamines ($RNH_2$). Now we are interested in the aminolysis of calix[4]arene esters with diamines ($NH_2R_1NH_2$). It was found that the compounds **1** and **2** can be aminolyzed with an excess of a diamine (1:20 molar ratio) in absolute ethanol for two days (scheme 1).[7-10] The aminolysis reaction is dependent on the molar ratio of the calix[4]arene esters and the diamine. For example, according to ESI-MS data, the product of the

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aminolysis of **1** with ethylenediamine (1:20 molar ratio) is a mixture of **3** and a compound in which the four ethyl esters of **1** have all been aminolyzed by three ethylenediamine molecules, one of them forming a cyclic diamide ring , while the other two esters have reacted with one end of the diamine leaving the other amino group free. The aminolysis reaction does not take place when the molar ratio is less than 1:5. For the other three aminolysis reactions(scheme1 compounds **4**, **5** and **6**), the products are all double-1,2-amide-bridged calix[4]arenes when the molar ratio is 1:20.

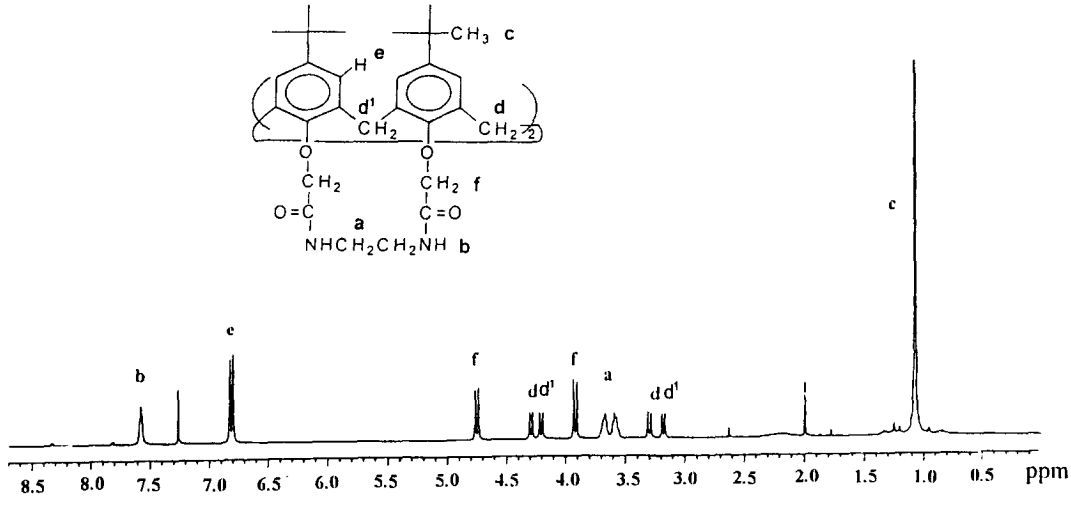


Fig.1 The $^1$H -NMR(500MHz) of the compound **3** in $CDCl_3$ and the assignment according to H-H COSY spectrum.

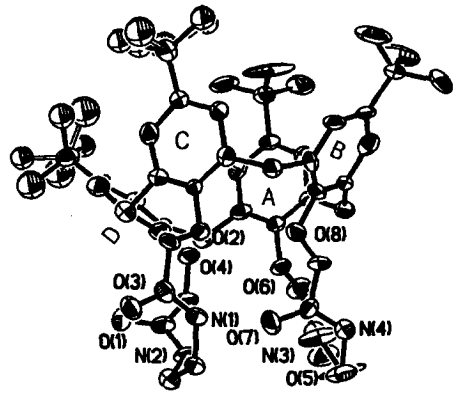


Fig.2 The molecular structure of the compound **3**.

All peaks of the $^1$H-NMR of compound **3** (Fig.1) can be assigned according to the two dimensional H-H COSY spectrum. From Fig.1 a pair of two doublets (**d**) of $ArCH_2Ar$ protons (the pattern is the same as the

1,2-biscrown-calix[4]arene[11]) proves that the compound **3** adopts a cone conformation in solution. From its H-H COSY spectrum , the cross peaks between the pair of doublets of the $OCH_2CO$ protons (**f**) and between the broad doublets of the $NCH_2CH_2N$ protons (**a**) prove that the two hydrogen atoms of the same ethylene (the equatorial and axial) are not in same environment. All these patterns are the same as the 1,2-biscrown-calix[4]arene with a cone conformation.[11] The other three compounds **4**, **5** and **6** also have similar $^1$H-NMR patterns as the compound **3**. So we can deduce the double-bridged calix[4]arenes are 1,2-double-bridged calix[4]arenes which adopt cone conformations in solution. The crystal structure of the compound **3** (Fig.2) provides further evidence for the 1,2-double-bridged structure. Previous studies show that, when the two ethyl esters of compound **2** were aminolyzed by monoamines , $RNH_2$ , the reactions took place on opposite ethyl esters, not on proximal ethyl esters because of steric effects.[4(a)] We think the reaction process might be *via* two steps: first, two opposite ethyl esters are aminolyzed by the two diamine molecules ; then the two residual amino groups of the diamine react with the two residual ethyl esters of the calix[4]arene to obtain the double-1,2-amide-bridged calix[4]arenes.

The crystal structure analysis was used to probe the solid-state conformation. The single crystal of compound **3**, which is obtained by slow evaporation of the acetonitrile solution for about 15 days, contains water of solvation (not shown) and is unstable in air. The crystal structure of the compound **3**[7] reveals a pinched cone conformation. The angles between the plane of the aromatic rings (A, B, C and D) and the plane of four $CH_2$ moieties which link the aromatic rings (mean deviation from the best plane 0.091) are 96.0, 134.0, 92.2 and 130.9°, respectively. Two opposite rings (A and C) are almost parallel with interplanar angle (8.2°), while phenolic rings B and D are tilted away from the calixarene cavity. This conformation leads to O...O separations 5.66Å between O(2) and O(6) and 3.92Å between O(4) and O(8). The O...O distances between adjacent phenolic oxygens O(2) and O(4); O(6) and O(8) are 3.53Å and 3.65Å respectively. The separation of the *tert*-butyl carbon atoms of ring B and D and ring A and C are 11.74Å and 5.98Å respectively. The conformation thus adopted by the compound **3** creates a smaller cavity, which effectively precludes a solvent molecule ($CH_3CN$) being encapsulated in the cavity and this is what we observe. In accord with this, the water of solvation, which is hydrogen bonded to the carbonyl oxygens O(5) and O(3), is *exo* to the calixarene cavity. The main conformation-determining features in this molecule are the presence of two hydrogen bonds: one intramolecular hydrogen bond N(1)—H(1A).....O(7) (bond length 3.004Å, bond angle 133.7°), the other intermolecular hydrogen bond N(4)—H(4A).....O(1) (2.926Å, 161.2°). These are between the carbonyl oxygens and the amide nitrogen of the diamide functional groups. The intermolecular hydrogen bond makes the compound **3** form a long chain supramolecule in the solid state. The double-1,2-amide-bridge calix[4]arenes are calixcryptands with hydrophilic cavities on the lower rim in addition to the hydrophobic cavities composed of

four benzene rings on the upper rim. Their receptor properties are under investigation.

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## References and Notes.


1. (a) Bohmor, V. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713-745. (b) Ungaro, R.; Casnati, A.; Ugozzoli, F.; Pochini, A.; Dozol, J.-F.; Hill, C.; Rouquette, H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1506-1509. (c) Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing M.-J.; Egberink, R. J. M.; de Jong, F.; Reinhoudt, D. N. J. *Am. Chem. Soc.* **1995**, *117*, 2767-2777. (d) Aeungaitrepirom, W.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **1997**, 38, 1907-1910.
2. (a) Arduini, A.; M$^c$Gregor, W. M.; Pochini, A.; Secchi, A.; Ugozzoli, F.; Ungaro, R. *J. Org. Chem.* **1996**, *61*, 6881-6887. (b) Jung, Y. E.; Song, B. M.; Chang, S.-K. *J. Chem. Soc. Perkin Trans.2* **1995**, 2031-2034.
3. (a) Scheerder, J.; Vreekamp, R. H.; Engbersen, J. F. J.; Verboom, W.; van Duynhoven, J. P. M.; Reinhoudt,D. N. *J. Org. Chem.* **1996**, *61*, 3476-3481. (b) Conner, M.; Janout, V.; Regen, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 9670-9671.
4. (a) Arduini, A.; Domiano, L.; Pochini, A.; Secchi, A.; Ungaro, R.; Ugozzoli, F.; Struck, O.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron* **1997**, *53*, 3767-3776. (b) Pulpoka, B.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **1996**, *37*, 6315-6318.
5. (a) Lhotak, P.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 645-648. (b) Kanamathareddy, S.; Gutsche, C. D *J.Org. Chem.* **1995**, *60*, 6070-6075.
6. (a) Bitter,I.; Grun, A.; Toth, G.; Balazs,B.; and Toke, L.; *Tetrahedron.* **1997**, 53, 9799-9812 (b)Bitter,I.; Grun,A.; Toth, G.; Balazs,B.; Horvath, G.; and Toke, L.; *Tetrahedron.* **1998**, 54, 3857-3870.-9812
7. Analytical data of compound **3**: column chromatography ($SiO_2$; $CH_3COOH$) *ESI-MS(+)*: 929.7 [M+H$^+$/z] *$^1$H-NMR* (500MHz, $CDCl_3$): δ(ppm) 1.08 (s, 36H, t-butyl) 3.18 (d, 2H, J=12.5Hz, $ArCH_2Ar$) 3.30 (d, 2H, J=13.0Hz, $ArCH_2Ar$) 3.50-3.60 (broad m, 4H, $NCH_2CH_2N$) 3.60-3.70 (broad m, 4H, $NCH_2CH_2N$) 3.92 (d, 4H, J=13.5Hz, $OCH_2CO$) 4.19-4.22 (d, 2H, J=13.0Hz, $ArCH_2Ar$) 4.28-4.30 (d, 2H, J=13.0Hz, $ArCH_2Ar$) 4.74-4.77 (d, 4H, $OCH_2CO$) 6.80 6.83 (s, 8H, ArH) 7.58 (s, 4H, NH). Crystal data of compound **1a**: colorless crystal, dimensions 0.4×0.3×0.3 mm, monoclinic, space group $P2_1/n$, with a = 19.273(4), b = 17.208(5), c = 19.897(5)Å, α = 90°, β = 114.19°, γ = 90°, V = 6019(3)Å$^3$, Dc = 1.045 mg /cm$^3$, Z = 4, Final R indices [I>2σ (I)]: R1=0.1070, WR2=0.1937.
8. Analytical data of compound **4**: *ESI-MS(+)*: 1093.8 [M+Na$^+$/z]; 1071.8 [M+H$^+$/z]; 536.5 [(M+2H$^+$)/$_{2z}$] *$^1$H-NMR* (500MHz, $CDCl_3$): δ(ppm) 1.07 (s, 36H, t-butyl) 2.57-2.68 2.68-2.80 ( broad m, 8H, $NCH_2\underline{CH_2}CH_2N$) 3.45-3.65 (broad m, 16H, $NCH_2$) 3.24 (d, 2H, J=13.0Hz, $ArCH_2Ar$) 3.34 (d, 2H, J=13.5Hz, $ArCH_2Ar$) 4.46-4.64 (m, 8H, $ArCH_2Ar$ + $OCH_2CO$) 4.69 (d, 4H, J=14.5Hz, $OCH_2CO$) 6.77 (s, 8H, ArH) 7.93 (s, 6H, NH).
9. Analytical data of compound **5**: *ESI-MS(−)*: 704.1 [M−H$^+$/z] *$^1$H-NMR* (500MHz, $CDCl_3$): δ(ppm) 3.21 (d, 2H, J=13.0Hz, $ArCH_2Ar$) 3.33 (d, 2H, J=14.0Hz, $ArCH_2Ar$) 3.54-3.67 (width m, 4H, $NCH_2CH_2N$) 3.67-3.80 (width m, 4H, $NCH_2CH_2N$) 4.03 (d, 4H, J=13.5Hz, $OCH_2CO$) 4.27 (d, 2H, J=14.0Hz, $ArCH_2Ar$) 4.38 (d, 2H, J=13.0Hz, $ArCH_2Ar$) 4.79 (d, 4H, J=13.5Hz, $OCH_2CO$) 6.66 (s, 12H, ArH) 7.43 (s, 4H, NH).
10. Analytical data of compound **6**: *ESI-MS(+)*: 755.6 [M+Na$^+$/z] *$^1$H-NMR* (500MHz, $CDCl_3$): δ(ppm) 3.22 (d, 2H, J=13.5Hz, $ArCH_2Ar$) 3.35 (d, 2H, J=14.5Hz, $ArCH_2Ar$) 3.50-3.70 (broad m, 8H, $NCH_2$) 4.17 (d, 4H, J=14.0Hz, $OCH_2CO$) 4.26 (d, 2H, J=14.5Hz, $ArCH_2Ar$) 4.51 (d, 2H, J=13.5Hz, $ArCH_2Ar$) 4.71 (d, 4H, J=14.0Hz, $OCH_2CO$) 6.64 6.60 (2s, 12H, ArH) 7.56 (s, 4H, NH).
11. (a) Arduini, A.; McGregor, W. M.; Paganuzzi, D.; Pochini, A.; Secchi, A.; Ugozzoli, F.; Ungaro, R. *J. Chem. Soc., Perkin Trans.2* **1996**, 839-846. (b) Arduini, A.; Fabbi, M.; Mantovani, M.; Mirone, L.; Pochini, A.; Secchi, A.; Ungaro, R. *J. Org. Chem.* **1995**, *60*, 1454-1457.