Intramolecular Ar−O−Ar Bond Formation in Calixarenes

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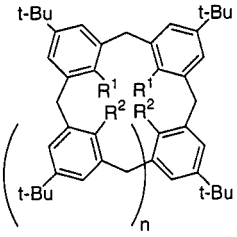
Received April 3, 2001

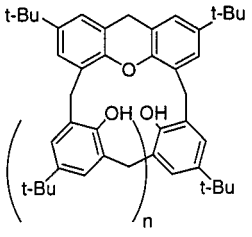
The formal dehydration of two vicinal phenol moieties of *p-tert*-butylcalix[6]arene was achieved in two steps by mild oxidation of the calixarene followed by treatment of the resulting monospirodienone derivative (**9c**) with an ionic hydrogenation mixture (Et_3SiH/CF_3COOH). Reaction of **9c** yielded the unsubstituted xanthenocalix[6]arene **11d**, while treatment of the monospirodienone derivative of a spherand-type calixarene (**13**) with Et_3SiH/CF_3COOH afforded the dibenzofuran derivative **15**. The formation of the latter product indicates that, at least for **13**, the rings forming the Ar−O−Ar bond in the product are not those connected by the spiro bond in the starting material. Methylation of the phenolic hydroxyl groups of **11d** with methyl *p*-toluenesulfonate/K_2CO_3 or dimethyl sulfate/base afforded its dimethyl and tetramethyl ether derivatives. The parent xanthone calix[6]arene derivative **17b** was prepared by *O*-methylation of the phenol groups followed by CrO_3 oxidation of the xanthene methylene group and deprotection of the OH groups. McMurry coupling of calixanthone **17a** afforded the dixanthylene **18**. Calixarenes **11d** and **15** (which possess a xanthene and dibenzofuran group, respectively) were structurally characterized by X-ray crystallography.

Introduction

The calix[*n*]arenes (**1**) are macrocyclic compounds capable of hosting a small molecule in their molecular cavity.[1] Most of the *intra*annular modifications of the calixarenes have been based on the derivatization of the OH groups, and few synthetic transformations have been reported in which the hydroxyl groups have been replaced by another functional group.[2] A transformation of interest involves the dehydration of two adjacent OH groups, resulting in the formation of calixarene xanthene derivatives **2**. These compounds possess structural features of



1a n = 1, $R^1 = R^2$ = OH
1b n = 2, $R^1 = R^2$ = OH
1c n = 3, $R^1 = R^2$ = OH
1d n = 3, R^1 = OH, R^2 = OMe



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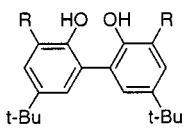
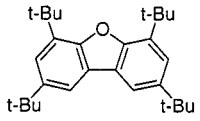
two of the most intensively investigated families of molecular hosts, namely the calixarenes and the crown ethers. Xanthenocalixarenes have been proposed as intermediates in the gas-phase fragmentation of some substituted calix[6]arenes.[3]

The dehydration of 2,2′-dihydroxybiphenyls has been reported in the literature. Dehydration of **3a** may be accomplished by treatment with Nafion-H in boiling xylene.[4,5] Recently, it has been reported that upon reaction with bromine/dioxane or bromine/AcOH[6] **3b** readily undergoes dehydration to afford the tetra-*tert*-butyldibenzofuran **4**.



3a R = H
3b R = t-Bu



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Dean and Locksley reported in 1963 that KBH_4 reduction of the carbonyl group of spironaphthalenone **6** (readily obtained by mild oxidation of the bisnaphthol **5**) followed by treatment of the resulting spiro alcohol **7** with acid yields the dibenzoxanthene derivative **8** (Scheme 1).[7] The complete reaction sequence **5** → **8** results in the formal elimination of a water molecule from the bisnaphthol.

We have shown previously that oxidation of **1a**−**c** with an equimolar amount of a tetraalkylammonium tribro-

(1) For reviews on calixarenes see: (a) Gutsche, C. D. *Calixarenes Revisited*; Royal Society of Chemistry: Cambridge, 1998. (b) Böhmer, V. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713. (c) Gutsche, C. D. *Aldrichimica Acta* **1995**, *28*, 1. (d) Gutsche, C. D. *Calixarenes*; Royal Society of Chemistry: Cambridge, 1989. (e) *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, 2001.

(2) For a review see: Biali, S. E. *Isr. J. Chem.* **1997**, *37*, 131.

(3) See: Neri, P.; Pappalardo, S. *J. Org. Chem.* **1993**, *58*, 1048; Kämmerer, H.; Happel, G.; Caesar, F. *Makromol. Chem.* **1972**, *162*, 179.

(4) Yamato, T.; Hideshima, C.; Prakash, G. K. S.; Olah, G. A. *J. Org. Chem.* **1991**, *56*, 3192.

(5) The attempt to dehydrate *p-tert*-butylcalix[4]arene by treatment with Nafion-H resulted in de-*tert*-butylation, and under harder condition, in fragmentation of the calix skeleton. See: Aleksiuk, O.; Biali, S. E. *Tetrahedron Lett.* **1993**, *34*, 4857. For an additional study of the Nafion-H catalyzed de-*tert*-butylation of calixarenes see: Rha, S. G.; Chang, S.-K. *J. Org. Chem.* **1998**, *63*, 2357.

(6) (a) Vol'eva, V. B.; Belostotskaya, J. S.; Ershov, V. V. *Russ. Chem. Bull.* **1996**, *45*, 744. (b) Belostotskaya, I. S.; Vol'eva, V. B.; Komissarova, N. L.; Ershov, V. V. *Russ. Chem. Bull.* **1996**, *45*, 987.

(7) Dean, F. M.; Locksley, H. D. *J. Chem. Soc.* **1963**, 393.

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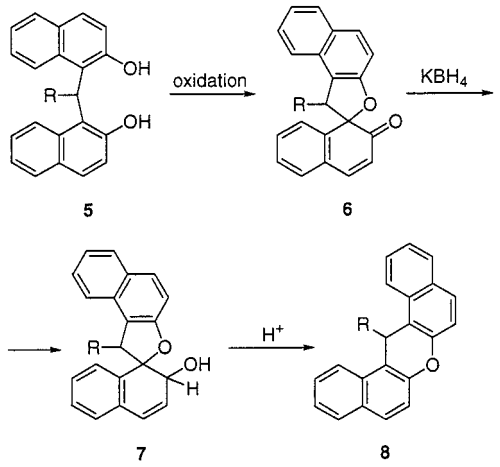
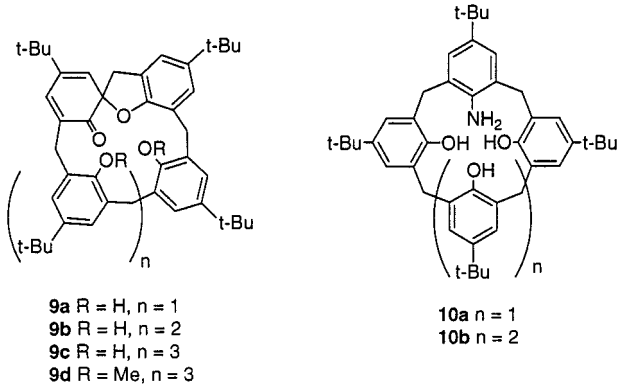
Scheme 1



mide salt yields the monospirodienone calixarene derivatives **9a**−**c**.[8,9,10] These synthetically useful systems have been utilized as key intermediates for the preparation of selectively functionalized calixarenes and, in the case of **9a** and **9b**, for the preparation of the monoaminocalixarenes **10a** and **10b**.[8b,11] Treatment of **9b** and **9c** with

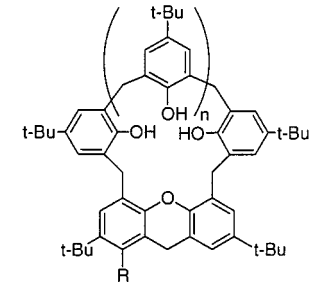


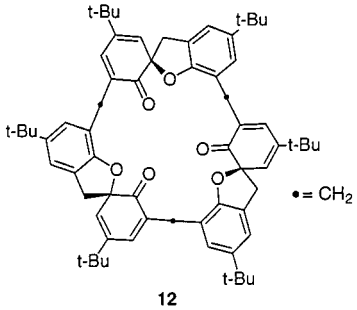
MeOH/H^+ yields the xanthenocalixarene derivatives **11a** and **11b**, respectively, which incorporate a methoxy group (originating from the solvent) in one of the rings of the xanthene unit.[8b,12] The "unsubstituted" (i.e., lacking the *extra*annular methoxy group) xanthenocalix[5]arene **11c** has been obtained by a multistep route which involved conversion of **9b** into the aminotetrahydroxycalix[5]arene **10b**, diazonation of the amino group, and dediazonation of the resulting diazonium salt in the absence of an external nucleophile.[13] However, a simple synthetic route for the preparation of unsubstituted xanthenocalixarenes has been until now unavailable. In this article we report a one-pot direct transformation of the monospirodienone calixarene derivative **9c** into the unsubstituted xanthenocalix[6]arene **11d** and several reactions of the latter compound.

Results and Discussion

The methoxy group in the xanthenocalixarene **11b** originates from the methanol solvent used in the reaction. The incorporation of the methoxy group probably occurs via an acid-catalyzed nucleophilic addition of methanol to the dienone moiety. In principle, if the methanol is replaced by a hydride donor, it could be expected that an unsubstituted xanthenocalixarene will be formed. After several attempts, we found that the combination of trifluoroacetic acid and triethylsilane (used in the "ionic hydrogenation" of double bonds and alcohol functionalities)[14] provides an efficient route for the desired transformation. Xanthenocalix[6]arene **11d** displays in the ^{1}H NMR spectrum (300.133 MHz, $CDCl_3$, rt) three *t*-Bu signals, five doublets for the aromatic protons (a pair of aromatic signals is accidentally isochronous), and two methylene protons singlets (at 4.00 and 3.85 ppm) each integrating for six protons. The NMR spectrum is in agreement with a conformationally flexible system on the NMR time scale possessing bilateral symmetry. The two OH groups, which in the parent calixarene **1c** resonate at 10.53 ppm (in $CDCl_3$), resonate in **11d** at higher fields (δ 8.25 and 7.01 ppm) as expected since no circular array of hydrogen bonds is possible for **11d**. The latter signals are ascribed to the OH groups at phenol rings distal and adjacent to the xanthene group.[15]

Corroboration of the presence of a xanthene subunit in **11d** was obtained by X-ray crystallography (Figure S1, Supporting Information). The molecule adopts a conformation in which two rings are oriented nearly parallel and two rings nearly perpendicularly to the average plane defined by the methylene carbons C14, C42, C35, and C21. The O···O nonbonded distances O2/O3 and O3/O4 are 2.833(5) and 2.758(5) Å, in agreement with





(8) (a) Aleksiuk, O.; Grynszpan, F.; Biali, S. E. *J. Chem. Soc., Chem. Commun.* **1993**, 11. (b) Aleksiuk, O.; Cohen, S.; Biali, S. E. *J. Am. Chem. Soc.* **1995**, *117*, 9645.

(9) For a review on spirodienone calixarene derivatives see: Aleksiuk, O.; Grynszpan, F.; Litwak, M. A.; Biali, S. E. *New J. Chem.* **1996**, *20*, 473. For a review on the oxidation and reduction of calixarenes see: Biali, S. E. in ref 1e, ch. 14, pp 266−279.

(10) For recent studies on spirodienone calixarene derivatives see: Georghiou, P. E.; Ashram, M.; Clase, H. J.; Bridson, J. N. *J. Org. Chem.* **1998**, *63*, 1819. Wang, W.-G.; Zhang, W.-C.; Huang, Z.-T. *J. Chem. Res. Synop.* **1998**, 462.

(11) Aleksiuk, O.; Grynszpan, F.; Biali, S. E. *J. Org. Chem.* **1993**, *58*, 1994.

(12) The reaction failed for **9a** probably because the smaller calixarene cannot accommodate the increase in strain that results from the introduction of the conformationally rigid planar xanthene group.

(13) Van Gelder, J. M.; Aleksiuk, O.; Biali, S. E. *J. Org. Chem.* **1996**, *61*, 8419.

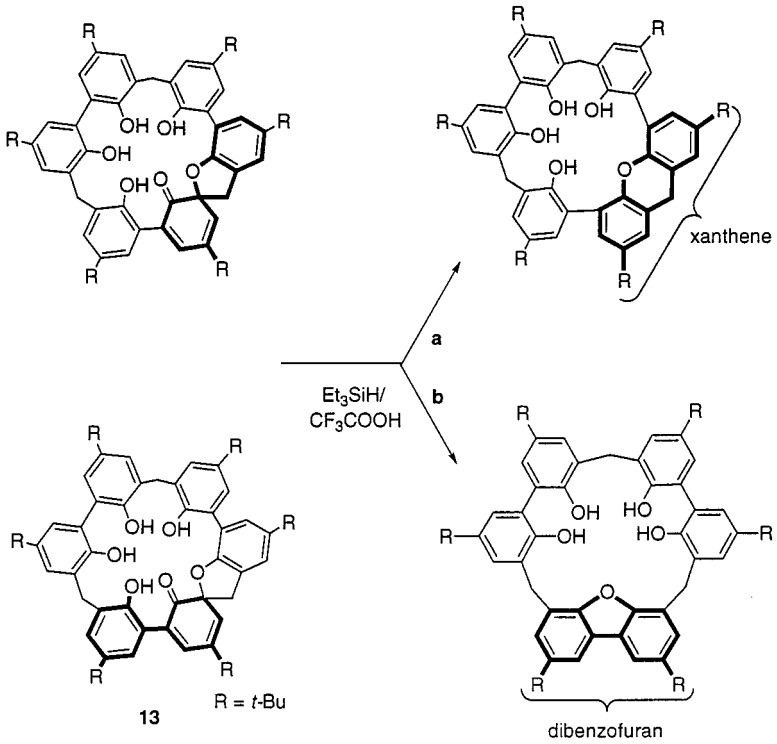


Figure 1. Two possible pathways for the reaction of a spirodienone derivative of a spherand type calixarene (**13**) with the ionic hydrogenation mixture. The reaction involving the cyclohexadienone ring and (a) the ring connected to it by a spiro bond or (b) the phenol ring adjacent to it should afford xanthene and benzofuran derivatives, respectively.

intramolecular hydrogen bonds between the corresponding pairs of vicinal phenol rings.

Scope of the Reaction. To determine the scope of the reaction, several additional spirodienone derivatives were treated with Et_3SiH/CF_3COOH. Treatment of **9b** with this mixture at 0 °C, 25 °C, or 35 °C generated *p-tert*-butylcalix[5]arene (**1b**). Reaction of the tris(spirodienone) calix[6]arene derivative **12**[16] with Et_3SiH/CF_3COOH did not yield a trixanthene derivative but gave the (mono)-xanthene calixarene **11d**. In this case the reaction of two spirodienone subunits of **12** with the ionic hydrogenation reagents regenerated the phenol rings while the third unit reacted in analogy to the spirodienone group of **9c** to form a xanthene group. Alkylation of **9c** with dimethyl sulfate/30% NaOH in the presence of a phase transfer catalyst yielded the tetramethoxy ether derivative **9d**.[17] Reaction of **9d** with Et_3SiH/CF_3COOH did not result in the formation of the xanthene derivative but yielded the known[18] tetramethyl ether calix[6]arene derivative **1d**. Consequently, the ionic hydrogenation mixture reduced the spirodienone unit of **9d** to two phenol rings, with no formation of a xanthene unit.

In the transformation reported by Dean and Locksley[7] (Scheme 1) the dibenzoxanthene moiety necessarily originates from the spirodienone unit. When discussing the mechanism of the reaction **9c** → **11b** we likewise assumed that the two aromatic rings of the substituted xanthene unit originate from the spirodienone subunit, i.e., from the two rings connected by the spiro bond.[8b] The different behavior of **9c** and **9d** can be interpreted as indicating that the reduction of the spirodienone unit of **9d** to phenol moieties is faster than the pathway leading to the xanthene derivative, or alternatively, that a free phenol adjacent to the cyclohexadienone ring is necessary for the formation of the xanthene group. It is possible that the two rings of **9c** which eventually form the xanthene group originate from the cyclohexadienone and the phenol ring adjacent to it and not from the two rings connected by the spiro bond.

Rearrangement of the Monospirodienone Spherand-type Calixarene. To test whether the formation of the ether bond may involve the phenol ring adjacent to the cyclohexadienone ring, we studied the reaction of the monospirodienone derivative **13**.[19] This compound was previously obtained by mild oxidation of the spherand-type calixarene **14**[20] and was fully characterized by spectroscopic methods. The reaction of the spirodienone derivative with the ionic hydrogenation mixture should distinguish between the two routes which should yield different products. If the ether bond is derived from the two rings connected by the spiro bond, the product should be a xanthene derivative, whereas a benzofuran ring should be obtained if the reaction involves the cyclohexadienone and the phenol ring adjacent to it (Figure 1).[21]

(14) Carey, F. A.; Tremper, H. S. *J. Org. Chem.* **1971**, *36*, 758.
(15) The position of the higher field OH signal is concentration dependent.
(16) Grynszpan, F.; Biali, S. E. *J. Org. Chem.* **1996**, *61*, 9512.
(17) For an example of the use of a phase transfer catalyst for the alkylation of *p-tert*-butylcalix[4]arene see: Bitter, I.; Grün, A.; Agai, B.; Toke, L. *Tetrahedron* **1995**, *51*, 7835.
(18) Otsuka, H.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1994**, *59*, 1542.
(19) Agbaria, K.; Aleksiuk, O.; Biali, S. E.; Böhmer, V.; Frings, M.; Thondorf, I. *J. Org. Chem.* **2001**, *66*, 2891.
(20) (a) Yamato, T.; Hasegawa, K.; Saruwatari, Y.; Doamekpor, L. K. *Chem. Ber.* **1993**, *126*, 1435. (b) O'Sullivan, P.; Böhmer, V.; Vogt, W.; Paulus, E. F.; Jakobi, R. A. *Chem. Ber.* **1994**, *127*, 427.
(21) For examples of furan-based calixarenes see: Cafeo, G.; Giannetto, M.; Kohnke, F. H.; La Torre, G. L.; Parisi, M. F.; Menzer, S.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1999**, *5*, 356. For benzofuran-based macrocycles see: Black, D. C., St.; Craig, D. C.; Kumar, N.; Rezaie, R. *Tetrahedron* **1999**, *55*, 4803.

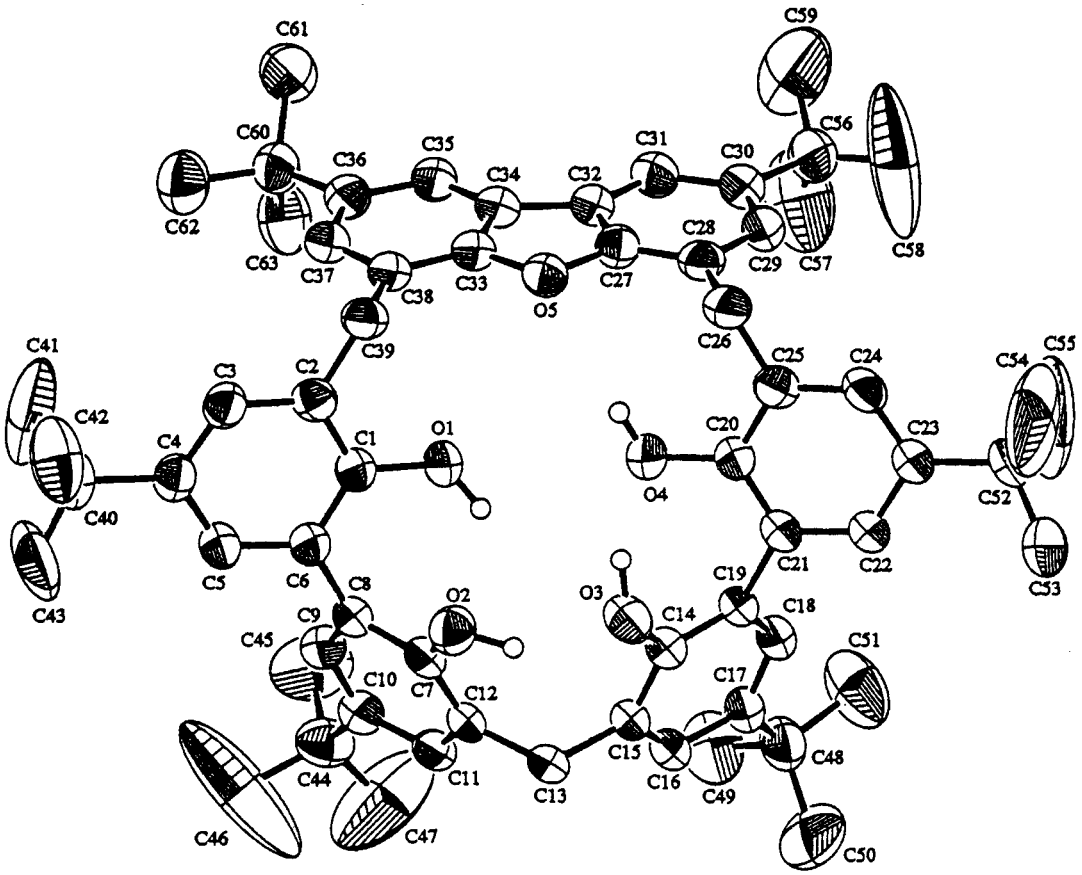
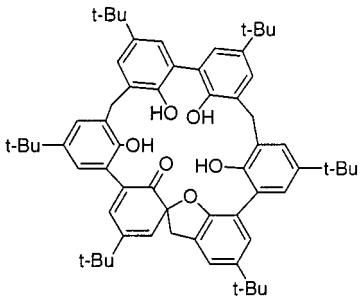


Figure 2. Numbering scheme of the crystal structure of **15**·0.5CH_3CN. The acetonitrile molecules is omitted for clarity.

Treatment of **13** with Et_3SiH/CF_3COOH yielded a product (**15**), which was crystallized from acetonitrile and submitted to X-ray crystallography (Figure 2). X-ray crystallography conclusively demonstrates that the product formed possesses a dibenzofuran group. This suggests that, at least in the case of **13**, the preferred reaction route involves the cyclohexadienone and the adjacent phenol group. The macrocyclic skeleton of benzofuran **15** adopts a conformation in the crystal of approximated C_s symmetry, with the two chiral 2,2′-dihydroxybiphenyl subunits possessing opposite configurations. The three methylene groups are oriented in the same direction, and the general shape of the conformation, by analogy to cyclotriveratrylene, can be described as "crown".[22] The ^1H NMR spectrum at 215 K (400 MHz, $CDCl_3$) indicates the presence of a major and a minor conformation. The major conformer displays a signal pattern with three *tert*-butyl signals and two pairs of a doublets in a 2:1 ratio for the methylene groups in agreement with a conformation of C_s symmetry.[23]



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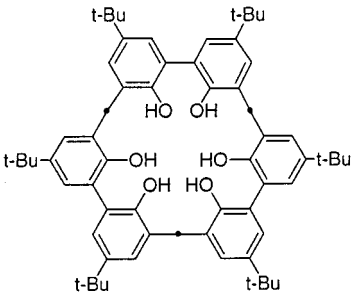

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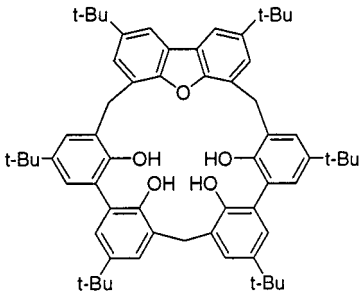
Total and Partial Methylation of the Xanthene Derivative. The *O*-methylation of *p*-*tert*-butylcalix[6]-arene has been extensively studied and all of its methyl ether derivatives have been prepared and characterized.[24] Treatment of the xanthenocalixarene with excess NaH/dimethyl sulfate in THF afforded the corresponding tetramethyl ether derivative **16a**. Upon lowering the temperature of a sample of **16a**, all the methylene, methoxy and *t*-Bu signals extensively broadened in the ^1H NMR spectrum, indicating the presence of an exchange process between the two conformers.

(22) For an analysis of the conformation of the spherand type calixarene see: Agbaria, K.; Biali, S. E.; Böhmer, V.; Brenn, J.; Cohen, S.; Frings, M.; Grynszpan, F.; Harrowfield, J. McB.; Sobolev, A. N.; Thondorf, I. *J. Org. Chem.* **2001**, *66*, 2900.

(23) A detailed computational and experimental study on the conformation and rotational barriers of benzofuran-substituted spherand-type calixarenes will be reported shortly.

(24) (a) Janssen, R. G.; Verboom, W.; Harkema, S.; van Hummel, G. J.; Reinhoudt, D. N.; Pochini, A.; Ungaro, R.; Prados, P.; de Mendoza, J. *J. Chem. Soc., Chem. Commun.* **1993**, 506. (b) Otsuka, H.; Araki, K.; Shinkai, S. *Tetrahedron* **1995**, *51*, 8757.

Methylation of **11d** with methyl *p*-toluenesulfonate using K_2CO_3 as a base afforded a mixture of partially methylated derivatives which were separated by chromatography. From this mixture we isolated a dimethyl ether derivative with a ^{1}H NMR pattern consistent with a structure possessing bilateral symmetry. This compound may be either the bis-1,2 or 3,4 methyl ether derivative. Attempted oxidation of the bis-methyl ether derivative under conditions that oxidize calixarenes with proximal phenol rings to spirodienone derivatives (I_2/KOH) proved unsuccessful, and no signal which could be ascribed to a spirodienone derivative was detected in the ^{1}H and ^{13}C NMR spectra. On this basis we ascribe to the symmetric product the 3,4-substitution pattern **16b**. This assignment was corroborated by a ROESY spectrum (in C_6D_6). NOE cross-peaks were observed between the methoxy signal (δ 3.60 ppm) and two methylene signals at δ 3.83 and 3.82 ppm which were assigned to the methylenes "a" and "b" (cf, **16b**). The 3,4 is kinetically



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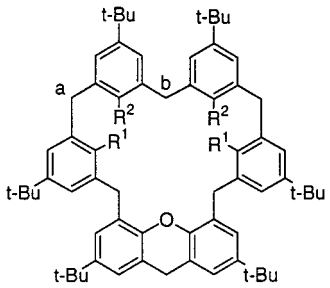


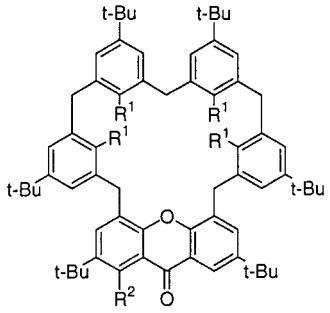
16a $R^1 = R^2 = OMe$
16b R^1 = OH, R^2 = OMe

favored over the 1,2 substitution pattern since probably the first deprotonation (and methylation) step occurs on a distal ring. The OH groups at rings distal to the xanthene group are most likely more acidic than the vicinal phenol since the phenolate derived from a former ring can be stabilized by two hydrogen bonds, while only a single H-bond can stabilize a phenolate on a proximal ring.[25]

Interestingly, the methoxy signals resonate at 3.96 ppm for **16b** while in **16a** they are shifted upfield by 0.6−1 ppm (to 3.37 and 2.94 ppm). This seems to indicate that **16a** adopts a conformation different than the one preferred by **16b**. In the bis-methyl ether derivatives, a pair of vicinal ArOH and ArOMe rings must be oriented syn to allow for an intramolecular hydrogen bond. In the tetrakis methyl ether derivative **16a** lacking OH groups, the rings are most likely oriented anti, and the methoxy groups are therefore located in the shielding region of the neighboring ring(s).

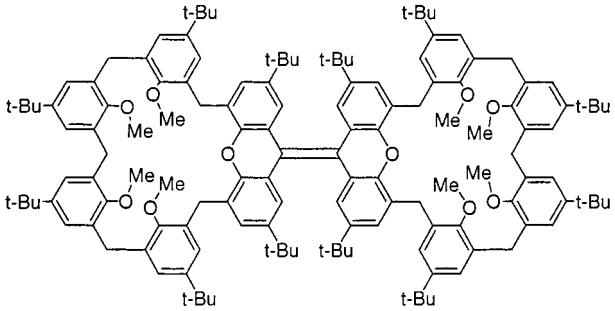
Oxidation of the Xanthene Group. The methylene group of the xanthene subunit of **11b** can be oxidized to a carbonyl by CrO_3 after protection of the phenol groups to their corresponding methyl ethers.[26] The same reaction is effective for the oxidation of **11d** to the xanthonecalix[6]arene **17a**. Compound **17a** displays two methoxy signals at 3.31 and 2.93 ppm. The three methylene groups connecting ArOMe rings are accidentally isochronous and resonate at 3.88 ppm while the methylene groups connecting a ArOMe and the xanthone group resonate at 4.05 ppm. The parent xanthonecalix[6]arene **17b** was prepared by demethylation of **17a** with BBr_3.[27]

Coupling of Calixanthone. We have previously shown that calixanthone **17c** can be reductively dimer-



17a R^1 = OMe, R^2 = H
17b R^1 = OH, R^2 = H
17c R^1 = OMe, R^2 = OMe

ized to the corresponding dixanthylene by reaction with Zn/HCl. However, under these conditions the parent **17a** gave only low yields of the dixanthylene **18**. Two units of calixanthone **17a** were coupled by means of the McMurry coupling reaction[28,29] yielding the dixanthylene **18**. The compound displayed in the ^{1}H NMR spectrum



18

at room temperature in $CDCl_3$ several partially overlapping methylene signals which were difficult to analyze. However, all signals were separated in an aromatic solvent (C_6D_6) at a higher temperature (345 K). Com-

(25) The distance between the oxygen on the two rings connected to the xanthene is too large to allow for an intramolecular hydrogen bond.

(26) Aleksiuk, O.; Biali, S. E. *J. Org. Chem.* **1996**, *61*, 5670.

(27) During the preparation of **11d** we detected after the work up small amounts of **17b**. The reaction probably involves oxidation of the xanthene group by the CF_3COOH, resulting in a radical cation which reacts with molecular oxygen.

(28) For examples of intramolecular and intermolecular McMurry couplings of calix[4]arenes see: Arduini, A.; Fanni, S.; Pochini, A.; Sicuri, A. R.; Ungaro, R. *Tetrahedron* **1995**, *51*, 7951. Lhotak, P.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 645.

(29) For a review on the McMurry coupling reaction see: Furstner, A.; Bogdanovic, B. *Angew. Chem., Int. Ed. Eng.* **1996**, *35*, 2442.

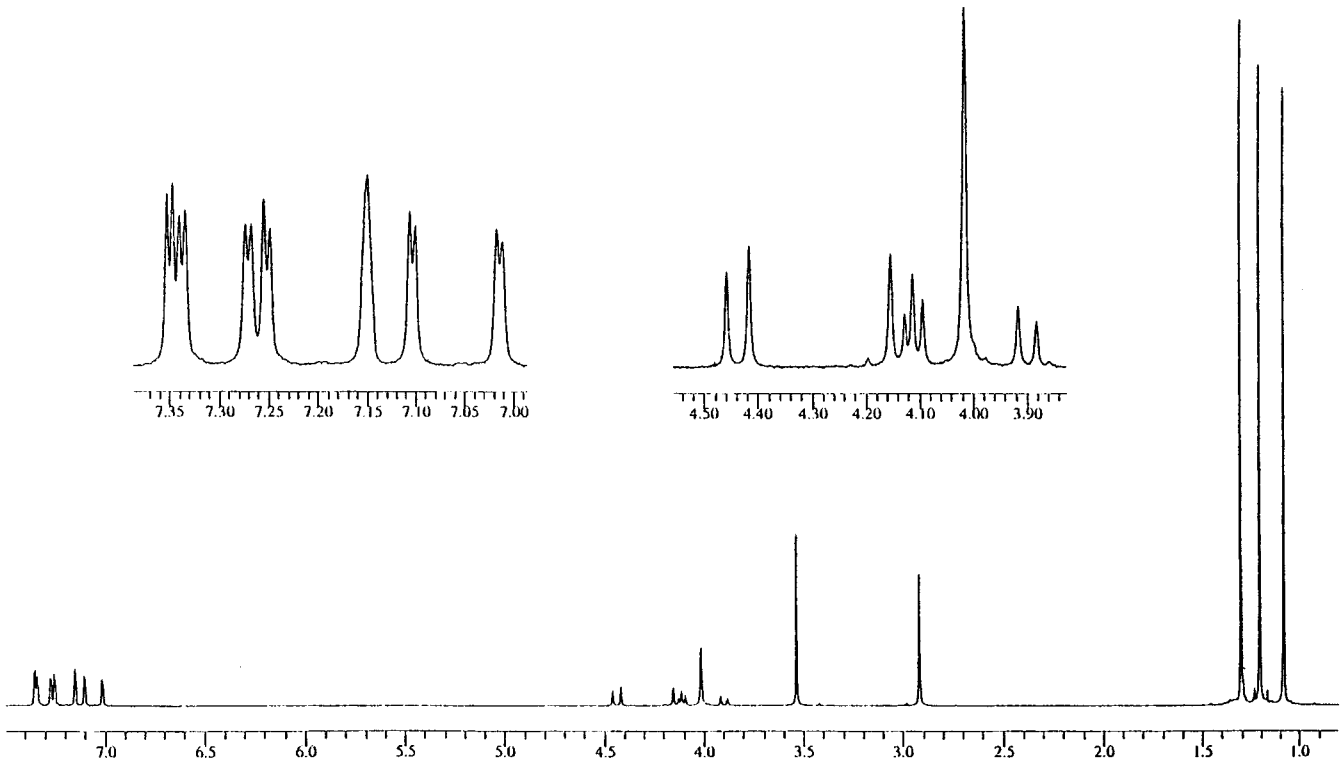


Figure 3. ^{1}H NMR spectrum (400 MHz, C_6D_6, 345 K) of dixanthylene **18** and expansions of the methylene (top left) and aromatic (top right) regions.

pound **18** displayed six aromatic doublets, three *tert*-butyl signals, and two methoxy signals (consistent with a symmetric structure of C_2h symmetry (Figure 3). The methylene region displayed two AB systems (in a 2:1 ratio) and a singlet. The anisochrony of two pairs of methylene protons is due to the nonplanar nature of the central dixanthylene moiety, which renders these protons diastereotopic, even if the rotation through the annulus of all rings is fast on the NMR time scale. The two AB systems are assigned to the methylene protons connected to the xanthene subunit, and to the two methylenes located along the molecular axis. On the basis of a NOESY spectrum, the singlet is assigned to the remaining methylenes which connect two Ar−OMe rings. These methylene protons are also expected to be diastereotopic, and their accidental isochrony under the experimental conditions suggests that they are located in similar magnetic environments. This is in agreement with an anti disposition of the neighboring aryl rings, similarly to that deduced for the parent xanthone derivative on the basis of chemical shift arguments.[30]

Conclusions

The formal dehydration of two OH groups of calixarenes can be achieved via their oxidation to the corresponding mono(spirodienone) derivatives and treatment of the latter compounds with Et_3SiH/CF_3COOH. Starting from *p-tert*-butylcalix[6]arene, this reaction sequence afforded a xanthene derivative, while a dibenzofuran derivative was obtained when the reactions were performed on the spherand-type calixarene **14**.

(30) At 600 MHz ($CDCl_3$, rt) the accidental isochrony is removed and these protons appear as a closely spaced pair of doublets. We thank Dr. Hugo Gottlieb and Dr. Vered Marks for conducting this determination.

Experimental Section

Crystallography. Crystal data for **9d**, formula: $C_{63}H_{82}O_5 \cdot CH_3CN$, space group $P\bar{1}$, a = 16.687(7) Å, b =17.48(1) Å, c = 12.274(3) Å, α = 97.86(3)°, β = 103.63(3)°, γ = 61.90(4)°, V = 3069(3) Å^3, Z = 2, D_c = 1.08 Mg m^{-3}, μ(Cu Kα) = 5.13 cm^{-1}, no. of unique reflections = 8989, no. of reflections with $I \geq 3\sigma_I$ = 6208, R_1= 0.088, R_w = 0.132. Crystal data for **15** formula: $C_{63}H_{76}O_5 \cdot 0.5\ CH_3CN$, space group $P\bar{1}$, a = 17.101(6) Å, b =18.021(6) Å, c = 10.568(2) Å, α = 90.58(2)°, β = 93.88(3)°, γ = 117.92(4)°, V = 2868(2) Å^3, Z = 2, D_c = 1.08 Mg m^{-3}, μ(Cu Kα) = 5.18 cm^{-1}, T = 293(2) K, no. of unique reflections = 9509, no. of reflections with $I \geq 3\sigma_I$ = 6226, R_1 = 0.098, R_w = 0.145, Data were measured on an ENRAF-Nonius CAD-4 computer-controlled diffractometer. Cu Kα (λ = 1.54178 Å) radiation with a graphite crystal monochromator in the incident beam was used. All crystallographic computing was done on a VAX 9000 computer using the TEXSAN structure analysis software.

General Methods. Melting points were obtained with a Melt-Temp II apparatus and are uncorrected. Et_3SiH and CF_3COOH were purchased from Aldrich. All column chromatographies were performed using silica gel 230−400 mesh purchased from Merck.

Preparation of 11d. To a solution of 1 g (1 mmol) of **9c** in 30 mL CH_2Cl_2 was added at room temperature 4 mL CF_3COOH. After stirring the reaction mixture for 3 min, 7 mL of Et_3SiH was added and the mixture was refluxed for 3 h. After evaporating the solvent, the residue was treated with 40 mL petroleum ether and the undissolved material (*p-tert*-butylcalix[6]arene) was filtered. The solvent was evaporated and the residue was treated with 20 mL MeOH and stirred for 1 h. The undissolved solid was filtered and purified by chromatography (eluent $CHCl_3$/hexane 3:1) yielding 0.3 g (35%) pure **11d** mp 257 °C. ^{1}H NMR (400.133 MHz, $CDCl_3$, RT) δ 8.30 (s, 2H, OH), 7.16 (d, J = 2.4 Hz, 2H, Ar−H), 7.13 (d, J = 1.8 Hz, 2H, Ar−H), 7.12 (d, J = 2.4 Hz, 2H, Ar−H), 7.09 (d, J = 2.4 Hz, 2H, Ar−H), 7.01 (br s, 2H, OH), 6.97 (d, J = 1.8 Hz, 2H, Ar−H), 6.96 (d, J = 2.4 Hz, 2H, Ar−H), 4.00 (s, 6H, CH_2), 3.85 (s, 6H, CH_2), 1.251 (s, 18H, *t*-Bu), 1.248 (s, 18H, *t*-Bu), 1.17 (s,

18H, *t*-Bu). ^{13}C NMR (100.61 MHz, $CDCl_3$, RT) δ 148.78, 148.57, 147.42, 145.99, 144.15, 143.19, 127.09, 127.00, 126.83, 126.70, 125.98, 125.79, 125.75, 125.25, 125.02, 123.50, 122.01, 34.29, 34.02, 33.96, 32.41, 31.50, 30.44, 29.88 ppm. CI MS (−DCI) *m*/*z* 954.8 (M^-).

Reaction of the Tris(spirodienone) Derivative of *p*-*tert*-Butylcalix[6]arene with Et_3SiH/CF_3COOH. To a solution of 1 g of the tris(spirodienone) derivative **12** in 30 mL CH_2Cl_2 was added 6 mL of CF_3COOH. After stirring for 5 min, 10 mL of Et_3SiH was added and the mixture was refluxed for 4 h. After cooling to RT, the solvent was evaporated and 15 mL of MeOH was added. The precipitate was filtrated, washed with 4 mL MeOH and dried under suction yielding 0.6 g (68%) **11d**.

Preparation of 15. To a solution of 0.5 g (0.53 mmol) monospirodienone **13** dissolved in 15 mL of CH_2Cl_2 was added at room temperature 3 mL of CF_3COOH. After stirring the reaction mixture for 3 min, 5 mL of Et_3SiH was added and the mixture was refluxed for 3h. The solvent was evaporated and 20 mL of CH_3CN was added. The precipitate that formed was filtrated. Chromatography of the crude product (eluent: benzene−hexane 4:1) afforded 0.24 g (49%) **15**, mp 395−400 (dec) °C. ^{1}H NMR (400.13 MHz, $CDCl_3$, 215 K) δ (major conformer) 8.07 (s, 2H, OH), 7.65 (s, 2H, Ar−H), 7.55 (d, J = 2 Hz, 2H, Ar−H), 7.30 (d, J = 2 Hz, 2H, Ar−H), 7.24 (s, 2H, Ar−H), 7.20 (d, J = 2 Hz, 2H, Ar−H), 7.02 (d, J = 2 Hz, 2H, Ar−H), 6.42 (s, 2H, OH), 4.88 (d, J = 13.9 Hz, 2H, CH_2), 4.38 (d, J = 13.9 Hz, 1H, CH_2), 3.85 (d, J = 14.2 Hz, 2H, CH_2), 3.68 (d, J = 13.6 Hz, 1H, CH_2), 1.40 (s, 18H, *t*-Bu), 1.29 (s, 18H, *t*-Bu), 1.21 (s, 18H, *t*-Bu). ^{13}C NMR (100.61 MHz, $CDCl_3$, RT) δ 152.55, 148.58, 146.68, 146.59, 145.13, 144.53, 128.55, 128.23, 127.74, 127.57, 127.29, 127.07, 126.65, 126.18, 125.58, 124.76, 123.42, 114.97, 34.87, 34.35, 34.24, 32.41, 32.00, 31.86, 31.68, 30.60 ppm. −DCI MS *m*/*z* 954.8 (M^-).

Preparation of Tetramethoxyxanthenocalix[6]arene. To a solution of 1.5 g of **11d** (1.5 mmol) in 120 mL of dry THF was added 0.25 g of NaH (10.4 mmol). The mixture was heated to reflux, a solution of 1.3 g of dimethyl sulfate (10.3 mmol) in 10 mL of dry THF was added, and the reflux was continued for 90 min. The excess of NaH was neutralized with EtOH, 100 mL of CH_2Cl_2 was added and the mixture was washed with water. After phase separation the organic layer was evaporated. Recrystallization of the residue from MeOH afforded 1 g (63%) of tetramethoxyxanthenocalix[6]arene (**16a**) mp 233 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$, RT) δ 7.18 (d, J = 2.4 Hz, 2H, Ar−H), 7.07 (d, J = 2.6 Hz, 2H, Ar−H), 7.06 (d, J = 2.4 Hz, 2H, Ar−H), 7.00 (d, J = 2.3 Hz, 2H, Ar−H), 6.90 (d, J = 2.3 Hz, 2H, Ar−H), 6.74 (d, J = 2.4 Hz, 2H, Ar−H), 4.08 (s, 2 H, CH_2), 3.95 (br s, 2H, CH_2), 3.91 (br s, 4H, CH_2), 3.88 (s, 4H, CH_2), 3.47 (s, 6H, OMe), 2.80 (s, 6H, OMe), 1.23 (s, 18H, *t*-Bu), 1.22 (s, 18H, *t*-Bu), 1.05 (s, 18H, *t*-Bu) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$, rt) δ 154.26, 154.21, 148.65, 145.56, 145.46, 145.14, 133.91, 133.68, 133.67, 132.15, 127.00, 126.30, 126.16, 125.55, 124.76, 123.36, 120.07, 60.37, 59.64, 34.23, 34.16, 32.40, 31.97, 31.54, 31.43, 29.39, 29.31 ppm. CI MS *m*/*z* 1011.8 (MH^+).

Preparation of Tetramethoxyxanthonecalix[6]arene. To a solution of 0.8 g of **16a** (7.9 mmol) in 80 mL of acetic acid was added 3.2 g of $K_2Cr_2O_7$ and the mixture was stirred overnight at room temperature. Water was added until the excess of the dichromate was dissolved completely (600 mL). A white precipitate was formed which was filtrated and washed with water. Purification of the compound was achieved by chromatography (eluent: CH_2Cl_2 followed by CH_2Cl_2/MeOH 20:1) yielding 0.48 g of (59%) **17a**, mp 243 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$, RT) δ 8.22 (d, J = 2.4 Hz, 2H, Ar−H), 7.44 (d, J = 2.3 Hz, 2H, Ar−H), 7.18 (d, J = 2.3 Hz, 2H, Ar−H), 7.06 (d, J = 2.2 Hz, 2H, Ar−H), 6.99 (d, J = 2.1 Hz, 2H, Ar−H), 6.69 (d, J = 2.1 Hz, 2H, Ar−H), 4.05 (s, 4H, CH_2), 3.88 (s, 6H, CH_2), 3.37 (s, 6, OMe), 2.94 (s, 6H, OMe), 1.30 (s, 18H, *t*-Bu), 1.22 (s, 18H, *t*-Bu), 1.02 (s, 18 H, *t*-Bu) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$, RT) δ 178.37 (C═O), 154.16, 154.10, 152.53, 146.32, 145.83, 145.49, 134.09, 133.92, 133.84, 133.18, 130.95, 128.86, 126.19, 126.12, 126.08, 124.30, 120.84, 120.56, 60.33, 59.59, 34.68, 34.09, 34.07, 32.72, 31.46, 31.39, 31.32, 30.92, 29.66 ppm. CI MS 1025.6 *m*/*z* (MH^+).

Demethylation of 17a. To a solution of 0.4 g (0.39 mmol) of **17a** in 15 mL of dry CH_2Cl_2 was added during 10 min under an inert atmosphere 15 mL of a 1 N CH_2Cl_2 solution of BBr_3 and the mixture was stirred at room temperature for 6 days. The excess of BBr_3 was quenched with water (30 mL), and 20 mL of CH_2Cl_2 was added. After phase separation the organic phase was washed with water and evaporated. Purification of the compound was achieved by chromatography (eluent, $CHCl_3$:hexane 3:1) yielding 0.25 g (66%) **17b**, mp 250−255 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$, RT) δ 8.23 (d, J = 2.4 Hz, 2H, Ar−H), 8.18 (s, 2H, OH), 7.53 (d, J = 2.4 Hz, 2H, Ar−H), 7.19 (d, J = 2.2 Hz, 2H, Ar−H), 7.12 (br s, 4H, J = 2.4 Hz, Ar−H), 7.04 (d, J = 2.1 Hz, 2H, Ar−H), 6.70 (s, 2H, OH), 4.19 (s, 4H, CH_2), 3.85 (s, 6H, CH_2), 1.33 (s, 18H, *t*-Bu), 1.25 (s, 18H, *t*-Bu), 1.17 (s, 18H, *t*-Bu). ^{13}C NMR (100.61 MHz, $CDCl_3$, RT) δ 178.28 (C═O), 152.05, 148.99, 147.58, 146.66, 144.26, 143.58, 132.79, 128.54, 127.08, 126.98, 126.39, 126.19, 126.02, 125.95, 124.31, 121.10, 120.96, 34.82, 34.06, 34.02, 32.20, 31.71, 31.51, 31.40, 30.18. CI MS (DCI) *m*/*z* 968.8 (M^-).

Partial Methylation of 11d. To a suspension of 0.6 g (0.62 mmol) of **11d** and 89 mg of (0.64 mmol) K_2CO_3 in 15 mL of CH_3CN was added 0.24 g of (0.2 mL, 1.29 mmol) methyl *p*-toluenesulfonate and the mixture was refluxed for 24 h. After evaporation of the solvent, the mixture was dissolved in 50 mL of CH_2Cl_2 and washed with water. The organic layer was separated and the solvent was evaporated. The dimethyl ether derivative was purified by column chromatography (eluent: $CHCl_3$/hexane 4:1) yielding 0.12 g of (19%) **16b**, mp 236 °C. ^{1}H NMR (400.133 MHz, $CDCl_3$, RT) δ 7.26 (s, 2H, OH), 7.08 (d, J = 2.4 Hz, 2H, Ar−H), 7.03 (d, 2H, Ar−H), 7.01 (d, 2H, Ar−H), 7.00 (d, J = 2.6 Hz, 2H, Ar−H), 6.92 (d, J = 2.4 Hz, 2H, Ar−H), 6.64 (d, J = 2.3 Hz, 2H, Ar−H), 3.96 (s, 6H, OMe), 3.94 (br s, 2H, CH_2), 3.89 (br s, 2H, CH_2), 3.80 (br s, 8H, CH_2), 1.26 (s, 18H, *t*-Bu), 1.11 (s, 18H, *t*-Bu), 1.03 (s, 18H, *t*-Bu). ^{13}C NMR (100.62 MHz, $CDCl_3$, RT) δ 152.02, 149.92, 149.27, 147.40, 145.05, 141.36, 133.68, 132.88, 128.08, 127.29, 126.13, 126.10, 126.03, 125.51, 124.71, 124.45, 122.65, 121.54, 62.36 (OMe), 34.11, 33.74, 32.27, 31.55, 31.37, 31.21, 30.86, 29.96, 29.53 ppm. CI MS (−DCI) *m*/*z* 981.0 ($[M(-H)]^-$).

Methylation of the Monospirodienone 9c. A total of 1 g (1.03 mmol) of **9c** and 1 g of tetrabutylammonium bromide were dissolved in 100 mL of CH_2Cl_2, and 10 mL of dimethyl sulfate (34.2 mmol) was added. A total of 100 mL of a 30% NaOH solution was added and the mixture was stirred for 48 h while refluxing. After 24 h another 0.5 g of tetrabutylammonium bromide and 5 mL of dimethyl sufate were added. After cooling to room temperature, 150 mL of water was added, and the organic phase was separated and washed several times with water. The solvent was evaporated and the residue was chromatrographed (eluent: $CHCl_3$) yielding 0.63 g of **9d** (61%), mp 233 °C. ^{1}H NMR (400.133 MHz, $CDCl_3$, RT) δ 7.20 (d, J = 2.4 Hz, 1H, Ar−H), 7.17 (d, J = 2.4 Hz, 1H, Ar−H), 7.09 (d, J = 2.4 Hz, 1H, Ar−H)), 7.00 (d, J = 2.4 Hz, 1H, Ar−H), 6.98−6.95 (overlapping d, 4H, Ar−H), 6.91 (broad s, 1H, Ar−H), 6.88 (d, J = 2.4 Hz, 1H, Ar−H), 6.84 (d, J = 2.4 Hz, 1H, Ar−H), 6.07 (d, J = 2.3 Hz, 1H, Ar−H), 4.23 (d, J = 15.1 Hz, 1H, CH_2), 4.09 (d, J = 15.2 Hz, 1H, CH_2), 4.02 (d, J = 14.3 Hz, 1H, CH_2), 3.98 (d, J = 15.8 Hz, 1H, CH_2), 3.97 (d, J = 15.9 Hz, 1H, CH_2), 3.92 (d, J = 14.1 Hz, 1H, CH_2), 3.73 (d, J = 15.2 Hz, 1H, CH_2), 3.67 (d, J = 15.1 Hz, 1H, CH_2), 3.47 (d, J = 15.8, 1H, CH_2), 3.42 (d, J = 15.5 Hz, 1H, CH_2), 3.33 (s, 3H, OMe), 3.15 (d, J = 16.1 Hz, 1H, CH_2), 3.11 (d, J = 15.6 Hz, 1H, CH_2), 3.07 (s, 3H, OMe), 3.03 (s, 3H, OMe), 2.75 (s, 3H, OMe), 1.25 (s, 9H, *t*-Bu), 1.22 (s, 9H, *t*-Bu), 1.20 (s, 9H, *t*-Bu), 1.15 (s, 9H, *t*-Bu), 1.13 (s, 9H, *t*-Bu), 1.10 (s, 9H, *t*-Bu). ^{13}C NMR 197.91 (C═O), 155.01, 154.63, 154.47, 154.26, 153.91, 145.78, 145.61, 145.48, 143.64, 142.42, 139.14, 134.26, 134.22, 134.17, 134.08, 133.80, 133.78, 133.14, 132.40, 131.10, 129.82, 126.44, 126.36, 126.00, 125.93, 125.84, 124.73, 121.35, 119.67, 84.17, 60.64 (OMe), 60.23−60.21 (3 OMe), 34.28, 34.23, 34.20, 34.18, 32.78, 31.78, 31.56, 31.54, 31.45, 31.25, 29.36, 29.04, 28.52 ppm. CI MS (−DCI) *m*/*z* 1026.8 (M^-).

Reaction of 9d with H^+/MeOH. To a solution of 0.5 g (0.48 mmol) of **9d** in 40 mL of MeOH was added 0.6 mL of concentrated H_2SO_4, and the mixture was refluxed for 1.5 h.

After cooling to room temperature, the precipitate was filtrated, washed with MeOH, and dried under suction yielding 0.39 g (76%) of the known[17] 5,11,17,23,29,35-hexa-*tert*-butyl-37,38,39,40-tetramethoxy-41,42-dihydroxycalix[6]arene **1d**, mp 230−235 °C.

Dixanthylenocalix[6]arene 18. *Procedure A.* A total of 0.5 mL of $TiCl_4$ was dissolved in 30 mL of dry THF at 0 °C. A total of 1.14 g $LiAlH_4$ was added in portions, and the mixture was gradually heated to room temperature and stirred for 40 min. To the resulting suspension was added dropwise a solution of 0.4 g (0.38 mmol) of **17a** in 10 mL dry THF with stirring. The mixture was stirred for 2 h at room temperature and refluxed for 24 h. After treatment with 20 mL of HCl 5 N and 50 mL of CH_2Cl_2, the organic phase was filtered and washed several times with water. After evaporation of the solvent the residue was chromatographed (eluent: $CHCl_3$/hexane 4:1) yielding 0.11 g (28%) dixanthylenocalix[6]arene. *Procedure B.* To a solution of 0.2 g of **17a** (0.19 mmol) in 70 mL of acetic acid was added 6 g of zinc dust. The solution was heated to 100 °C and 20 mL of conc HCl was added during a 90 min period. After stirring overnight at 100 °C, the solid ($ZnCl_2$) was filtered, 100 mL $CHCl_3$ was added to the filtrate, and the resulting solution was washed several times with water. The organic phase was evaporated and the residue purified by column chromatography ($CHCl_3$/hexane 3:1) yielding 36 mg (18%) of **18**, mp 382 °C. ^{1}H NMR (400.133 MHz, C_6D_6, 345 K), δ 7.35 (d, J = 2.4 Hz, 4H, Ar−H), 7.34 (d, J = 2.4 Hz, 4H, Ar−H), 7.27 (d, J = 2.4 Hz, 4H, Ar−H), 7.25 (d, J = 2.4 Hz, 4H, Ar−H), 7.10 (d, J = 2.3 Hz, 4H, Ar−H), 7.01 (d, J = 2.4 Hz, 4H, Ar−H), 4.44 (d, J = 16.7 Hz, 4H, CH_2), 4.13 (d, J = 16.6 Hz, 4H, CH_2), 4.11 (d, J = 13.6 Hz, 2H, CH_2), 4.02 (s, 8H, CH_2), 3.90 (d, J = 13.6 Hz, 2H, CH_2), 3.54 (s, 12H, OMe), 2.92 (s, 12H, OMe), 1.30 (s, 36H, *t*-Bu), 1.21 (s, 36H, *t*-Bu), 1.09 (s, 36H, *t*-Bu) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$, rt) δ 154.25, 154.19, 152.54, 145.50, 145.35, 144.66, 133.93, 133.79, 133.58, 132.54, 128.14, 127.09, 126.41, 126.31, 125.50, 125.20, 124.72, 122.87, 122.34, 60.29, 59.53, 34.08, 34.05, 31.85, 31.47, 31.35, 31.25, 29.12 ppm, CI MS m/z 2018.8 (MH^+).

Acknowledgment. We thank Dr. Joel M. van Gelder for preliminary experiments, Dr. Michael Frings and Dr. Volker Böhmer (Mainz) for providing us with samples of **14**, and Dr. Shmuel Cohen for the crystal structure determinations.

Supporting Information Available: ^{1}H NMR spectra of **9d**, **11d**, **15** (at 215 and 298 K), **16a**, **16b** and **17a**, crystallographic tables for **11d** and **15**, and ORTEP diagram of the crystal structure of **11d**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0103468