Selective Hydroxyl Replacement in Calixarenes: Amino-, Azo-, and Xanthenocalixarene Derivatives

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Abstract: The synthesis of monoamino-, azo-, and xanthenocalixarenes and dehydroxylated calixarenes via condensation, reduction, or rearrangement of monospirodienone calixarene derivatives is described. Mild oxidation of *p-tert*-butylcalix[5]arene and *p-tert*-butylcalix[6]arene yielded their corresponding monospirodienone derivatives **4b** and **4c**. Monospirodienone **4b** was characterized by X-ray crystallography. Reaction of **4b** with (2,4-dinitrophenyl)-hydrazine gave a (dinitrophenyl)azo derivative (**8**), which by reaction with HI gave the monoaminotetrahydroxycalix[5]-arene **10**. Reaction of **4b** with hydrazine/base yielded in a Wolff–Kishner-type reaction, the monodehydroxylated calix[5]arene **8**. Reaction of **4b** with a methanolic solution of hydrazine at room temperature yielded a derivative characterized by X-ray crystallography as a system with an azo bridge (**15**). Spirodienone **4b** rearranges in MeOH/H^+, yielding the xanthene derivative **16** as the main product, together with the linear pentamer **17**. The larger spirodienone **4c** rearranges by treatment with MeOH/H^+, yielding the xanthenocalix[6]arene **18.** X-ray diffraction of a crystal of **18** grown in MeCN shows that in the crystal the molecules form intermolecular hydrogen-bonded dimers in which the two molecules mutually include each other; i.e., one of the protuberances of each molecule is located in the V-shaped cavity of its neighboring molecule. Molecules **16** and **18** represent the first examples of calixarene systems incorporating a xanthene moiety.

Introduction

Calixarenes[1] **1** are cyclic phenol–formaldehyde condensation products capable of including small molecules into their molecular cavities.[2] Considerable synthetic efforts have been invested in the modifications of the binding groups of these systems. Although the derivatization of the hydroxyl binding groups (e.g., by alkylation or acylation) is a synthetically simple process, the *replacement* of the hydroxyl oxygens by another atom has been achieved only in a handful of cases; thus, hydroxyl groups of the calixarenes have been totally or partially replaced by thiol groups[3] or hydrogens.[4] Of special interest is the replacement of the hydroxyl binding groups of the calix-arenes by amino groups, since this replacement may bestow basic properties to the systems and drastically alter their binding capabilities. At present, partial aminodehydroxylation has been achieved only for calix[4]arene systems.[5,6]

A synthetic modification as yet unexplored is the formal dehydration of two proximal phenolic OH groups giving a cyclic ether group. This process should yield the hitherto unknown xanthene derivatives of the calixarenes (e.g., **2**) which incorporate structural features of both the calixarenes and the benzo crown ethers.[7] The xanthene group is the "core" of several dyestuffs (e.g., fluorescein, eosin, rhodamine 6G) which have extensive applications, and their introduction into this family of macrocycles may yield systems with novel photophysical properties.[8] Although calixarenes incorporating xanthene moi-eties have been postulated as intermediates in the mass spectral fragmentation of calixarenes, to date no such systems have been prepared and characterized.[9] We have previously attempted the preparation of these compounds by Nafion-H-catalyzed dehy-dration of the *p-tert*-butylcalix[4]arene **1a**, but the reaction resulted in de-*tert*-butylation and, in the presence of diphenyl ether, in the fragmentation of the calixarene skeleton and formation of 9,9′-spirobixanthene (**3**) as the main product.[10] In this paper we describe the *intra*annular incorporation of an amino group, azo group, and hydrogen in a calix[5]arene skeleton by reaction of the monospirodienone derivative of *p-tert*-butylcalix[5]arene with amino nucleophiles. In addition, we report the acid-catalyzed rearrangement of the monospiro-dienone derivative of *p-tert*-butylcalix[5]arene and *p-tert*-

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(2) Böhmer, V. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713.

(3) Gibbs, C. G.; Gutsche, C. D. *J. Am. Chem. Soc.* **1993**, *115*, 5338. Ting, Y.; Verboom, W.; Groenen, L. C.; van Loon, J. D.; Reinhoudt, D. N. *J. Chem. Soc., Chem. Commun.* **1990**, 1435. Delaigue, X.; Hosseini, M. W.; Kyritsakas, N.; de Cian, A.; Fischer, J. *J. Chem. Soc., Chem. Commun.* **1995**, 609.

(4) (a) Goren, Z.; Biali, S. E. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1484. (b) Grynszpan, F.; Goren, Z.; Biali, S. E. *J. Org. Chem.* **1991**, *56*, 532. (c) Grynszpan, F.; Biali, S. E. *Tetrahedron Lett.* **1991**, *32*, 5155. (d) McMurry, J. E. ; Phelan, J. C. *Tetrahedron Lett.* **1991**, *41*, 5655. (e) de Vains, J.-B. R.; Pellet-Rostaing, S.; Lamartine, R. *Tetrahedron Lett.* **1994**, *44*, 8147. (f) Harada, T.; Ohseto, F.; Shinkai, S. *Tetrahedron* **1994**, *50*, 13337. (g) For a recent synthesis of dehydroxylated calix[4]arenes see: Rajca, A.; Padmakumar, R.; Smithisler, D. J.; Desai, S. R.; Ross, C. R., II; Stezowski, J. J. *J. Org. Chem.* **1994**, *59*, 7701.

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(6) (a) Aleksiuk, O.; Grynszpan, F.; Biali, S. E. *J. Org. Chem.* **1993**, *58*, 1994. (b) Grynszpan, F.; Aleksiuk, O.; Biali, S. E. *J. Org. Chem.* **1994**, *59*, 2070.

(7) For a review on crown ethers see: Laidler, D. A.; Stoddart, J. F. In *Updates of the Chemistry of Functional Groups, The Chemistry of Crown Ethers and Analogs*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1989; Chapter 1.

(8) For a review on the photochemistry of xanthene dyes see: Neckers, D. C.; Valdes-Aguilera, O. M. *Adv. Photochem.* **1993**, *18*, 315.

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

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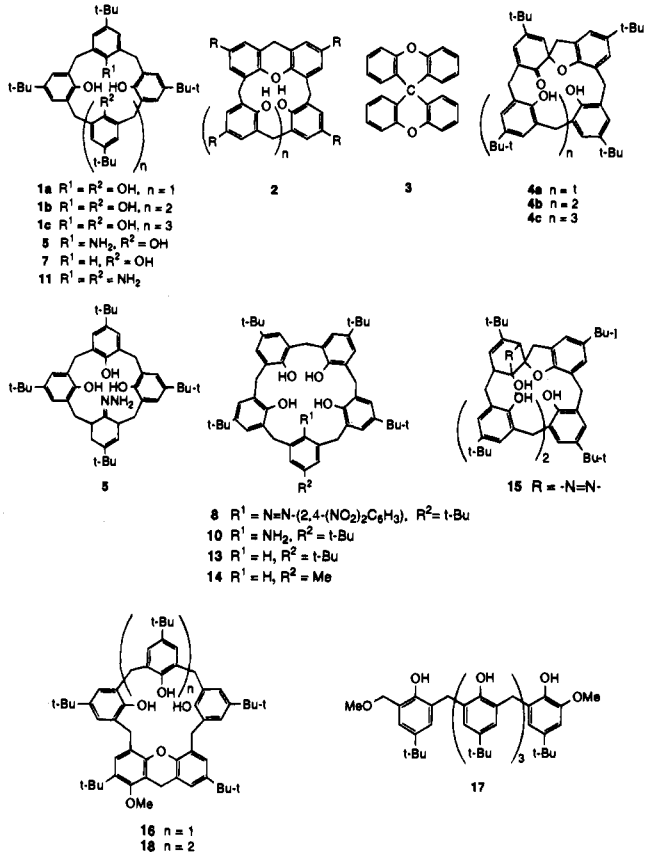
butylcalix[6]arene, which yields calixarene systems incorporating a xanthene unit.



Results and Discussion

Spirodienone Calixarene Derivatives. General Considerations. Spirodienone calixarene derivatives can be obtained by oxidation of the calixarenes with a mild oxidizing agent.[11] An attractive structural feature of a spirodienone moiety, from a synthetic point of view, is the presence of a carbonyl group. In contrast to the rather limited chemistry of the phenolic OH groups, a carbonyl may undergo a wide range of functional group transformations, resulting in the replacement of the carbonyl oxygen (e.g., via its characteristic addition–elimination reactions). Since the spiro C–O bond can be readily cleaved, one can envision the use of the spirodienone calixarene derivatives as synthetic intermediates for the synthesis of calixarenes in which one or more of the former phenolic oxygens are replaced by a different atom. With these considerations in mind we decided to prepare and study the reactions of the monospirodienone derivatives of the calixarenes.

We have previously reported that oxidation of *p-tert*-butylcalix[4]arene with trimethylphenylammonium tribromide in a biphasic solvent system (CH_2Cl_2, aqueous $NaHCO_3$) results in the formation of the monospirodienone derivative **4a**.[12] This spirodienone was transformed into the monoaminotrihydroxycalixarene system **5** in a two-step process which involved reaction with hydrazine, yielding the hydrazo derivative **6**, followed by aromatization and N–N cleavage by treatment of **6** with Pd/C in refluxing toluene.[6a] We decided to explore whether a similar transformation can be accomplished for the larger *p-tert*-butylcalix[5]arene **1b** which can be prepared now in reasonable yields thanks to an improved procedure developed by Stewart and Gutsche.[13] The large cavity of **1b** as compared to the rather small one present in **1a** makes the system an attractive potential host for small molecules. We therefore synthesized the monospirodienone derivative of *p-tert*-butylcalix[5]arene (i.e., **4b**) and studied its condensation reactions with hydrazines. In addition, we prepared the monospirodienone derivative of *p-tert*-butylcalix[6]arene[14] **1c** and examined the acid-catalyzed rearrangements of **4b** and **4c**.

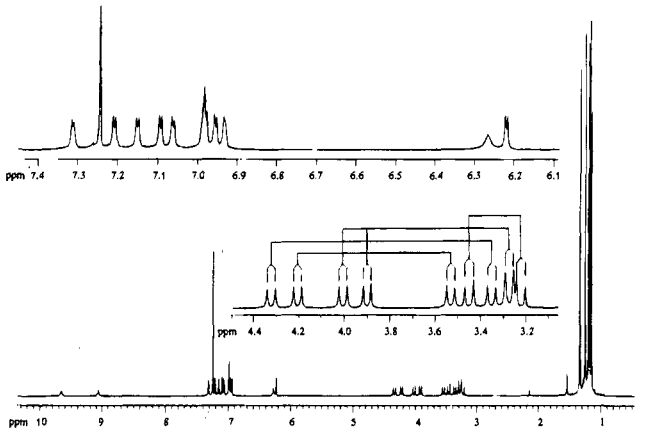


Figure 1. ^1H NMR spectrum (400 MHz, $CDCl_3$) of **4b**.

Preparation and Crystal Structure of 4b. *p-tert*-Butylcalix[5]arene was oxidized to its corresponding monospirodienone derivative **4b** by using reaction conditions ($Me_3N^+Ph\ Br_3^-/NaHCO_3$) similar to those described for the preparation of **4a**.[6a,b] The yellow monospirodienone **4b** displays in the ^1H NMR (400 MHz, $CDCl_3$) five *tert*-butyl signals and five pairs of doublets for the methylene protons (two protons are accidentally isochronous) in agreement with a structure of C_1 symmetry (Figure 1). The presence of a single stereocenter (the spiro atom) renders the molecule asymmetric, and therefore all pairs of geminal methylene protons are symmetry nonequivalent (diastereotopic), as experimentally observed in the ^1H NMR. The elucidation of the coupling pattern of the different protons was accomplished by a DQF COSY 2D NMR spectrum. The methylene pair of doublets which displays the largest ^2J coupling constant (at δ 3.22 and 3.45, J = 15.6 Hz) is assigned to the dihydrofuran ring protons, since as previously shown for the bisspirodienone derivatives of **1a**, these are the protons which display the largest coupling constant.[11]

It seems reasonable to assume, by analogy with other calixarene systems, that in the preferred conformation of the monospirodienone all the phenol groups are identically oriented "above" or "below" the mean macrocyclic plane defined by the methylene carbons, since this arrangement will allow the presence of intramolecular hydrogen bonds between the OH groups. For a given configuration of the spiro carbon (*R* or *S*) two diastereomeric arrangements of the phenol rings should be possible in which the phenol groups are either *syn* or *anti* to the carbonyl group of the spirodienone moiety. These conformations are depicted for a monospirodienone calix[4]arene derivative in Figure 2. A single crystal of **4b** suitable for X-ray crystallography was grown from acetonitrile.[15] The molecule crystallizes with two solvent molecules. The numbering scheme

(11) For studies on polyspirodienone calixarene derivatives see: Litwak, A. M.; Grynszpan, F.; Aleksiuk, O.; Cohen, S.; Biali, S. E. *J. Org. Chem.* **1993**, *58*, 393. Grynszpan, F.; Biali, S. E. *J. Chem. Soc., Chem. Commun.* **1994**, 2545.

(12) Aleksiuk, O.; Grynszpan, F.; Biali, S. E. *J. Chem. Soc., Chem. Commun.* **1993**, 11.

(13) Stewart, D. R.; Gutsche, C. D. *Org. Prep. Proc. Int.* **1993**, *25*, 137.

(14) Gutsche, C. D.; Dhawan, B.; Leonis, M.; Stewart, D. *Org. Synth.* **1989**, *68*, 238.

(15) The authors have deposited atomic coordinates for the structures with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Rd., Cambridge CB2 1EZ, U.K.

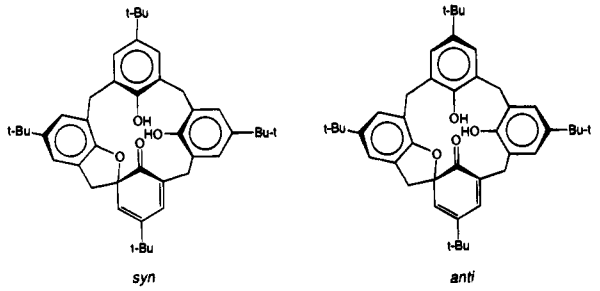


Figure 2. Ideal diastereomeric conformations of a monospirodienone calix[4]arene derivative: left, phenol rings *syn* to the carbonyl group; right, phenol rings *anti* to the carbonyl group.

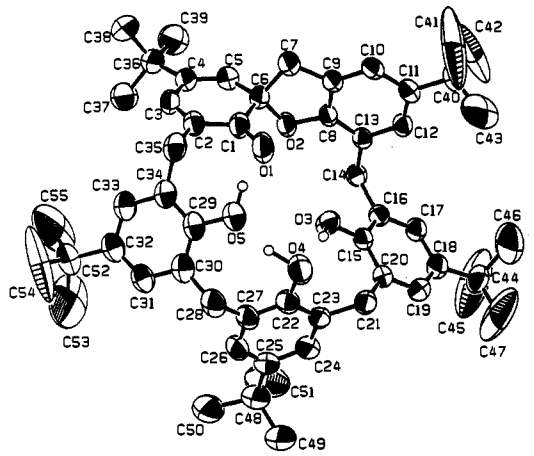


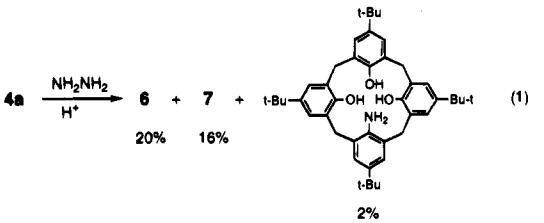
Figure 3. Numbering scheme of the crystal structure of **4b**. The acetonitrile molecules were omitted for clarity.

of the molecule is displayed in Figure 3. The conformation resembles a partial cone with one of the rings somewhat flattened. One of the two acetonitrile molecules is partially included in the calixarene cavity. The crystal structure of **4b** shows that the system adopts a conformation in which the phenol groups are *syn* to the carbonyl group with one hydroxyl group hydrogen bonded to the latter, as judged by the O(1)−O(5) distance (2.67 Å). Oxygen O(5) serves as an acceptor in an additional hydrogen bond (O(4)−O(5) distance 2.67 Å). The spiro C−O bond length is shorter (1.448(5) Å) than the corresponding C−O bond lengths determined for **4a** (1.496(4) Å)[12] or for the bisspirodienone derivatives of **1a** (1.474−1.490 Å).[11] The conformation adopted by **4b** is different from the conformation found for **4a**, where the phenol groups are oriented *anti* to the carbonyl group and one OH group is hydrogen bonded to the ether oxygen.[12] The carbonyl of **4b** resonates in the ^{13}C NMR at a lower field (194.9 ppm) than that of **4a** (203.8 ppm). This suggests that in $CDCl_3$ solution the carbonyl of **4b** is also hydrogen bonded, since hydrogen bonding results in a downfield shift of the resonance signal of carbonyl groups.[16] The molecule displays three signals for the hydroxyl groups at δ 6.27, 9.10, and 9.65. The highest field OH signal is assigned to the proton hydrogen bonded to the carbonyl group.

Preparation of 4c. For the preparation of **4c**, an excess of *p-tert*-butylcalix[6]arene was oxidized by phenyltrimethylammonium tribromide, and the resulting monospirodienone product was purified by chromatography. The compound displays in the ^{13}C NMR a signal at δ 85.33, which is characteristic of the spiro carbon in this family of compounds. In contrast to **4b**, the 400 MHz NMR spectrum ($CDCl_3$) of **4c** displays at room temperature several broad signals for the methylene protons. These signals sharpened at 320 K into 12 partially overlapping doublets. The observed behavior is consistent with the presence of a dynamic process which most likely involves the passage of all rings through the ring annulus and interconverts conformations in which the phenol groups are oriented *syn* or *anti* to the carbonyl group (cf. Figure 2). The ^{13}C chemical shift of the carbonyl group of **4c** in $CDCl_3$ at room temperature (δ 198.75 ppm) is intermediate between the chemical shifts found for **4a** and **4b**, which suggests that both *syn* and *anti* conformations are populated in solution, and rapidly interconvert on the ^{13}C NMR time scale.

Compounds **4b** and **4c** did not display in the CI MS a molecular peak at the expected mass but at two mass units higher. We have shown previously that monospirodienone **4a** shows a great tendency to revert to **1a**, and that this process can be achieved even by simple heating.[12] The behavior observed may indicate that under the mass spectral experimental conditions, the monospirodienones **4b** and **4c** are reduced (or undergo disproportionation), yielding the corresponding calixarene systems.

Reaction of 4a with Hydrazine. As previously reported in our preliminary paper, the main product of the reaction of **4a** with hydrazine dihydrochloride/NaOH/MeOH is the hydrazo derivative **6** which was characterized by X-ray crystallography.[6a] Notably, one of the diene double bonds of the spirodienone is reduced in the product. Reinvestigation of the reaction showed that two additional products are also obtained (eq 1): the



trihydroxy-*p-tert*-butylcalix[4]arene **7** (16% yield), previously prepared by reductive cleavage of a mono(diisopropyl phosphate) ester calixarene derivative,[6b,17] and the monoaminotrihydroxycalixarene **5** (ca. 2%) which can be obtained in a higher yield by treatment of **6** with Pd/C.[6a] The formation of **6** suggests that the reaction of the spirodienone with nucleophiles may be more complex than a simple addition−elimination reaction. The spirodienone (or its hydrazone derivative) seems capable of oxidizing the hydrazine to diimine, which in turn reduces one of the double bonds of the diene. The formation of the monodehydroxylated calixarene **7** in the reaction of **4a** with hydrazine can be rationalized if in the first step the corresponding hydrazone is formed, which under the reaction conditions eliminates nitrogen (a Wolff−Kishner-type process)[18] and undergoes reductive cleavage of the spiro C−O bond.

Aminodehydroxylation of *p-tert*-Butylcalix[5]arene. The mono- and bisspirodienone derivatives of **1a** do not react with the classic derivatizing agent (2,4-dinitrophenyl)hydrazine (DNP). It can be expected that the larger ring size present in **4b** may facilitate the approach of the amino nucleophile, enabling the condensation reaction. We therefore examined the reaction of **4b** with DNP.

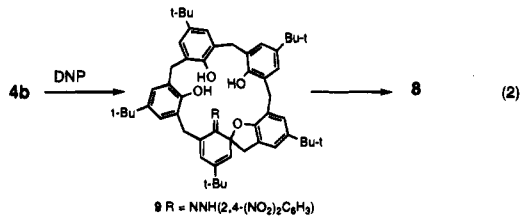
Treating a methanolic solution of **4b** with DNP afforded in good yield (53%, after purification) a red derivative (**8**). The formation of the molecule possibly involves the intermediacy

(16) Breitmaier, E.; Voelter, W. *^{13}C NMR Spectroscopy*, 2nd ed.; Verlag Chemie: Weinheim, New York, 1978; p 77.

(17) The compound we originally described as *p-tert*-butyltrihydroxycalix[4]arene[4b] is indeed a monoaminodihydroxy-*p-tert*-butylcalix[4]arene system.[6b] The "authentic" trihydroxy-*p-tert*-butylcalix[4]arene is described in ref 6b.

(18) Todd, D. *Org. React.* **1948**, *4*, 378.

of the spiro structure **9**, which by hydrogen transfer yields the azocalixarene **8** (eq 2). At present we do not know the



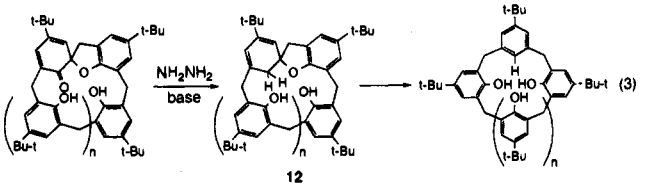
stereochemistry (*E* or *Z*) around the N=N bond, but examination of the reaction mixture by NMR indicates that a single product was formed. On the basis of steric considerations, we believe that this is the less hindered *E* isomer. Azocalixarene **8** displays in the CI MS a molecular peak at two mass units lower than expected (CI MS: *m/z* 987.6 (M − 2H)), a behavior similar to that reported for other azo compounds.[19]

The ^{1}H NMR spectrum of **8** displays three *tert*-butyl signals (in a 2:2:1 ratio), three pairs of doublets (two doublets accidentally overlapping) in a 2:2:1 ratio for the methylene protons, two AB systems and one singlet for the phenol ring aromatic protons, three signals for the dinitrophenyl ring, and two separate OH signals at 7.96 and 8.32 ppm. This is in agreement with a structure of C_s symmetry, in which the cone-to-cone process has been frozen on the NMR time scale. This observation is consistent with the recent findings of Gutsche and co-workers who have shown that the introduction of a single bulky *intra*annular group (a benzyl group) may be sufficient to fix the cone conformation of a calix[5]arene.[20]

We examined the reductive cleavage of the (dinitrophenyl)-azo compound **8** as a potential route for the preparation of monoaminotetrahydroxycalix[5]arenes. The reduction of azo (or hydrazo) groups to amines is considered a reaction "of little preparative interest, there being more direct methods available for the synthesis of amines".[21] However, the facile *intra*annular attachment of a nitrogen-containing group to the calix[5]arene skeleton by reaction of **4b** with DNP suggested that the compound may be used as a precursor of choice for the synthesis of a monoaminocalix[5]arene. We chose HI as the reducing agent, since it was reported that it is capable of reductively cleaving decafluoroazobenzene to pentafluoroaniline.[22] Reaction of **8** with aqueous HI/hexane resulted in a fast reaction, as evidenced by the change in color of the reaction mixture. The main product of the reaction (54% after chromatography) is the monoaminotetrahydroxycalix[5]arene **10** (CI MS: *m/z* 810.7 MH^+). The two-step method **4b** → **8** → **10** represents an excellent method for the *intra*annular introduction on an amino group in a calix[5]arene. Aminocalix[4]arenes have been previously reported by Shinkai[5] and by us,[6] and the isolated compound represents the first introduction of an amino group into a calix[5]arene skeleton.

Protonation of the Aminocalix[5]arene. *p*-Allylcalix[4]-arene protonates *tert*-butylamine, and the resulting ions form an *endo* complex in MeCN solution.[23] The replacement of a hydroxyl by an amino functionality should confer basic properties on the macrocycle. We have previously shown that treatment of a $CDCl_3$ solution of aminocalix[4]arene **5** with solid *p*-toluenesulfonic acid results, as judged by integration of the signals in the ^{1}H NMR, in the formation of the salt **5**H^+TosO$^-$.[6a] The aminocalixarene **10** displays three *tert*-butyl signals in a 2:2:1 ratio, a broad signal for the methylenic protons, and one singlet, one doublet, and several overlapping signals for the aromatic protons, indicating a species of C_s symmetry. Treatment of a $CDCl_3$ solution of **10** with *p*-toluenesulfonic acid resulted, as shown by ^{1}H NMR, in dissolution of an equimolar amount of the acid and the sharpening of the broad methylene signals into three pairs of doublets in a 2:2:1 ratio. This suggests that the resulting tosyl salt is more rigid than the parent aminocalixarene system, as observed for **5**.[6a] The tosylate aromatic protons are shifted to lower field by 0.30 and 0.12 ppm as compared to a $CDCl_3$ solution of *tert*-butylanilinium tosylate. The cone-to-cone inversion barrier was measured for **10** and **10**H^+TosO$^-$ in toluene-d_8 by dynamic NMR. From the chemical shift difference of the methylene protons under slow exchange ($\Delta\nu$ = 219, 186 Hz, J = 13.4 Hz) and the coalescence temperature (T_c = 284.5 K), a barrier of 13.1 ± 0.1 kcal mol^{-1} was calculated for the cone-to-cone ring inversion of **10**. Similarly, a barrier of 16.0 ± 0.1 kcal mol^{-1} was calculated for **10**H^+TosO$^-$.[24] The formation of the tosylate salt increases the rigidity of the system by 2.9 kcal mol^{-1}, probably due to the stronger hydrogen bonds in the salt and the stabilization of the cone by association of the calixarene and tosylate ions. The barrier of **10** (13.1 kcal mol^{-1}) is similar to the barrier determined for **1b** (13.2 kcal mol^{-1}),[25] in contrast to the trend observed for **1a**, in which the formal introduction of amino groups lowers the cone-to-cone inversion barrier (**1a**, $\Delta G_c^{\ddagger}$ = 15.7 kcal mol^{-1} ($CDCl_3$); **7**, $\Delta G_c^{\ddagger}$ = 14.8 kcal mol^{-1} (toluene-d_8, or $CDCl_3$); **11**, $\Delta G_c^{\ddagger}$ = 14.9 kcal mol^{-1} (toluene-d_8), 13.9 kcal mol^{-1} ($CDCl_3$)).[6a,25,26] Apparently, since the intramolecular hydrogen bonding in **1b** is weaker than in **1a** (as evidenced by the lower cone-to-cone inversion barrier of **1b** and its higher OH stretching frequencies in the IR spectrum)[1a] further weakening of the hydrogen bond array in the calix[5]arene by the replacement of an OH by an amino group does not result in an experimentally observable decrease in the rigidity of the system.

Monodehydroxylated Calixarenes via Wolff–Kishner Reduction of a Spirodienone. One of the classical methods for reducing a carbonyl to a methylene group is the Wolff–Kishner reaction, in which a carbonyl-containing compound is heated with hydrazine hydrate in the presence of base.[18] The mechanism of the reaction involves the formation of a hydrazone as an intermediate. The reduction of the carbonyl of a spirodienone moiety should yield the spirodiene **12**, which by spiro C–O cleavage and hydrogen migration should result in an OH-depleted phenyl ring proximal to a phenol ring (eq 3).



Treatment of **1b** with hydrazine under basic conditions yielded a product which displayed three *tert*-butyl signals and

(19) Tam, S. W. In *The Chemistry of Functional Groups. The Chemistry of the Hydrazo, Azo and Azoxy Groups*; Patai, S., Ed.; Wiley: Chichester, 1975; Chapter 5, p 109.

(20) Stewart, D. R.; Krawieck, M.; Kashyap, R. P.; Watson, W. H.; Gutsche, C. D. *J. Am. Chem. Soc.* **1995**, *117*, 586.

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(24) The barrier was calculated from the exchange rates at the coalescence temperatures according to Kurland, R. J.; Rubin, M. B.; Wise, W. B. *J. Chem. Phys.* **1964**, *40*, 2426.

(25) Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *107*, 6052.

(26) Araki, K.; Murakami, H.; Ohseto, F.; Shinkai, S. *Chem. Lett.* **1992**, 539.

three singlets for the methylene protons in a 2:2:1 ratio, indicating a flexible structure (on the NMR time scale) of C_s symmetry. The aromatic region displayed a somewhat broad triplet at 6.59 ppm, characteristic of the *intra*annular proton of an OH-depleted ring.[4] Two OH signals were observed at very different chemical shifts (δ 6.5 and 8.5 ppm). On the basis of this data, we assign to this product the tetrahydroxycalix[5]arene structure **13**. The related monodehydroxylated calix[5]arene **14** was reported by Fukazawa.[27b] Partially and totally OH-depleted calixarenes were previously obtained by reductive cleavage of calixarene phosphate esters,[4a-f] by reaction of organodilithium reagents with dialdehydes followed by reduction of the resulting diols,[4g] or by a stepwise synthesis.[27]

The ^{1}H NMR spectrum of **13** displayed at 175 K ($CDCl_2F$)[28] a pair of doublets at δ 3.37 and 3.95 ppm (J = 14.2 Hz), and a very broad signal for the methylene protons. Upon raising the temperature, the pair of doublets coalesced at 234 K, indicating a barrier of 10.7 kcal mol^{-1} for the process which exchanges these protons (an inversion process).[24] This barrier is in agreement with the barrier measured by Fukazawa for the monodehydroxylated calix[5]arene **14** in CD_2Cl_2 (ca. 10 kcal mol^{-1})[27b] and is ca. 2.5 kcal mol^{-1} lower than the barrier for the parent **1b** in $CDCl_3$.[25]

We detected in the reaction mixture, analogously as in the reaction of **4a**, traces of the monoaminotetrahydroxycalix[5]-arene **10**. It is likely that this product originates from a Schiff base condensation product, but at present the mechanism of the reaction is unclear.

Reaction of 4b with Hydrazine at rt. In order to see whether the hydrazone derivative of **4b** could be isolated, we examined the reaction of the monospirodienone with hydrazine under mildly acidic conditions at room temperature. The reaction resulted in the formation of three products: the monodehydroxylated calix[5]arene **13**, the aminotetrahydroxycalix[5]arene **10**, and a most unexpected main product (**15**, obtained in 31%). The compound displayed in the ^{1}H NMR spectrum five *tert*-butyl signals, eight methylene signals, an apparent quartet at 5.34, and a doublet at 5.54 ppm. Microanalysis indicated the presence of nitrogen in the system. Compound **15** slowly decomposed in CH_3CN, $CHCl_3$, or EtOH solution. Examination of the ^{1}H NMR spectrum of the decomposition products showed the presence of **13**. Treatment of **15** with refluxing MeOH/NaOH or simple heating gave **1b**.

Crystallization of the compound from acetonitrile afforded material suitable for X-ray crystallography. The numbering scheme of the crystal structure is shown in Figure 4.[15] The molecule displays an azo group (the N−N distance of 1.253 Å is characteristic of a double-bonded unit)[29] bridging the 1 and 3 positions of the spirohexenol ring and a single double bond (between C(31) and C(32)). The molecule exists in a conformation which resembles a flattened partial cone. Two *tert*-butyl groups of the system (C(41)−C(43) and C(49)−C(51)) showed rotational disorder. The phenol group neighboring the azo ring is hydrogen bonded to one of the nitrogens (O(4)−N(1) = 3.03 Å), while two additional hydrogen bonds are formed between neighboring phenol groups (O(3)−O(4) and O(2)−O(3) = 2.81 Å). The formation of **15** probably involves an acid-catalyzed addition of hydrazine to the dienone (Scheme 1). The addition occurs at the less hindered *exo* face of the diene (i.e., *anti* to the ether oxygen).[11] After ketonization of the dienol, an acid-catalyzed intramolecular nucleophilic addition of the free end of the hydrazine takes place. Due to the bicyclic structure of the product, the elimination of water (with the concomitant formation of a hydrazo group) is impossible. The bridging hydrazo group is finally oxidized (most likely by a spirodienone group), yielding **15**.

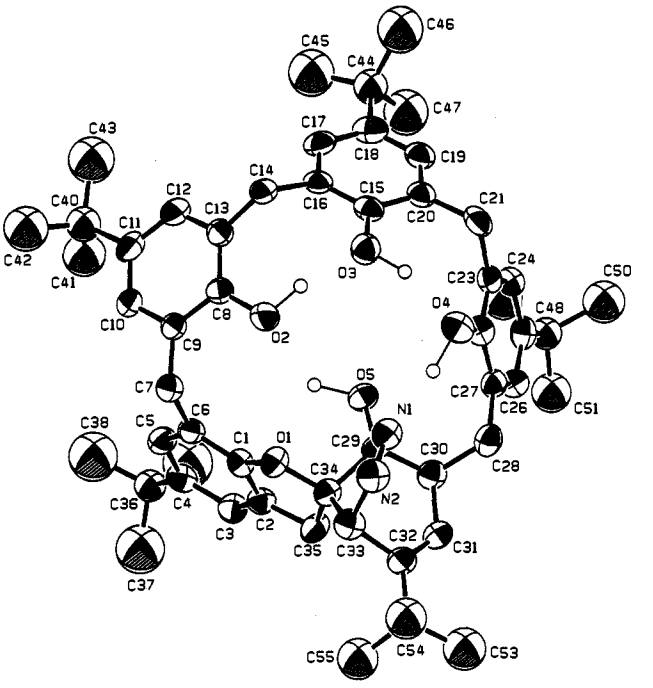
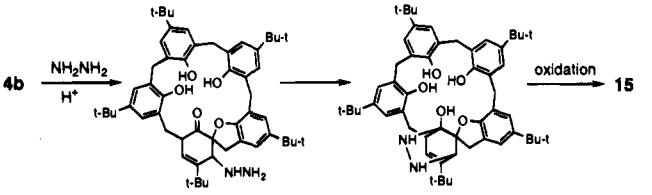
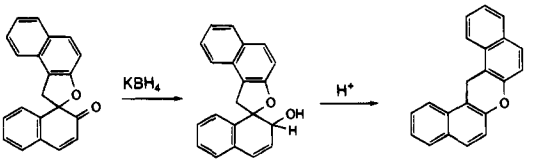


Figure 4. Numbering scheme of the crystal structure of **15**.

Scheme 1



Acid-Catalyzed Rearrangements of the Monospirodienones 4b and 4c. Spironaphthalenones have been reported to undergo several rearrangements. Kasturi and co-workers recently investigated the reactions of these compounds with hydroxylamine, which yield by rearrangement pyrroltropones.[30] Dean and Locksley[31] reported a two-step transformation of a spironaphthalenone to a xanthene structure. Their scheme involved KBH_4 reduction of the spirodienone, followed by acid-catalyzed rearrangement of the resulting spirodienol (eq 4).[31]



(4)

In order to find out whether the monospirodienone **4b** may rearrange to a xanthenocalixarene derivative, we treated a methanolic solution of **4b** with a few drops of H_2SO_4. The

(27) (a) Fukazawa, Y.; Demaya, K.; Usui, S. *Tetrahedron Lett.* **1992**, *33*, 5803. (b) Usui, S.; Deyama, K.; Kinoshita, R.; Odagaki, Y.; Fukazawa, Y. *Tetrahedron Lett.* **1993**, *34*, 8127.

(28) Siegel, J.; Anet, F. A. L. *J. Org. Chem.* **1988**, *53*, 2629.

(29) Allmann, R. In *The Chemistry of Functional Groups. The Chemistry of the Hydrazo, Azo and Azoxy Groups*; Patai, S., Ed.; Wiley: Chichester, 1975; Chapter 2.

(30) Kasturi, T. R.; Jayaram, S. K.; Pragnacharyulu, P. V. P.; Sattigeri, J. A.; Reddy, G. M.; Kumar, K. A. *Tetrahedron* **1993**, *49*, 113. Kasturi, T. R.; Kumar, K. A.; Pragnacharyulu, P. V. P. *Tetrahedron* **1993**, *49*, 125. Kasturi, T. R.; Kumar, K. A.; Pragnacharyulu, P. V. P.; Srivedi, G. *Tetrahedron* **1993**, *49*, 135.

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

main product **16** displayed a signal in the ^{13}C NMR at δ 61.12 ppm which can be assigned to a methoxy group. The compound displayed in the ^1H NMR spectrum four *tert*-butyl signals (one signal of double intensity), indicating that all rings are symmetry unequivalent, and several broad signals which become sharper upon raising the temperature for the methylene protons, in agreement with a structure which is undergoing a dynamic process on the NMR time scale. On the basis of the NMR and the mass spectral data (CI MS: *m/z* 823 (MH^+)), and by analogy with the product isolated in the acid-catalyzed rearrangement of **4c** (see below), we assign to this product the xanthenocalix[5]-arene structure **16**.

Xanthene **16** is obtained in conjunction with an additional product which displays in the ^1H NMR five OH signals, several singlets for the methylene protons (indicating free rotation of the rings on the NMR time scale), and two methoxy groups. The compound displays in the ^{13}C NMR spectrum a signal at δ 73.43 characteristic of a C_{sp^3}–O carbon. On the basis of these data, we assign to the product the linear pentameric structure **17**.[32] Compound **17** displays in the CI MS a molecular peak at *m/z* 872 and fragments at *m/z* 678 and 516 resulting from the cleavage of phenolic units from the linear chain, a behavior usually observed for the linear oligomers.[1] The formation of **17** can be rationalized as the result of the acid-catalyzed cleavage of the C–O and $C-CH_2$ bonds to the spiro carbon.

The attempted rearrangement of **4c** by treatment with MeOH/H^+ gave, as judged by ^1H NMR, almost quantitatively the xanthenocalix[6]arene **18** (CI MS: *m/z* 985.8 (MH^+)). The lack of ring opening products suggests that the macrocyclic ring of **4c** is less strained than that of **4b**. The ^1H NMR spectrum of **18** (400 MHz, C_6D_6, rt) displays, in addition to the aromatic signals, six signals for the *tert*-butyl groups, a methoxy signal at δ 3.39, and six singlets in the δ 3.78–3.96 ppm region for the methylene groups, indicating that the structure is flexible at room temperature on the NMR time scale.

In order to characterize the system, we submitted the molecule to X-ray crystallography. The compound crystallizes from MeCN as a 1:1 complex in the $P\bar{1}$ space group with two molecules in the unit cell related by an inversion center.[15] The methoxy group and the MeCN molecule are disordered, and they were refined with half occupancy at two positions. The numbering scheme of the crystal structure is displayed in Figure 5. The molecule exists in the crystal in a conformation in which the two phenol rings adjacent to the xanthene moiety are nearly coplanar, while the two remaining phenol rings and the xanthene moiety are oriented in different directions.[33] The molecule can be seen to have two "V"-shaped cavities located at different faces of the macrocycle. The MeCN molecule is included in the cavity delimited by the four phenol rings.

Examination of the O···O nonbonded distances revealed that the pairs O(4)–O(3) and O(3)–O(2) are within hydrogen bond distances (2.884(4) and 2.765(4) Å, respectively). Interestingly, whereas the intramolecular distance between O(1) and O(2) is 4.336(4) Å, these atoms are *inter*molecularly hydrogen bonded as indicated by their short mutual distance (2.839 Å).[34] This led us to examine the packing of the molecule in the crystal. The two molecules related by the inversion center are connected

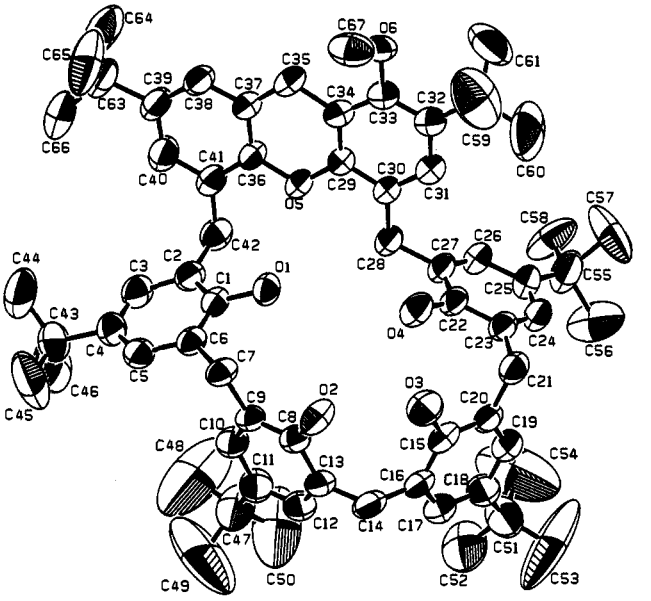


Figure 5. Numbering scheme of the crystal structure of **18**. The MeCN molecule was omitted for clarity. The large ellipsoids of the *tert*-butyl groups are due to disorder.

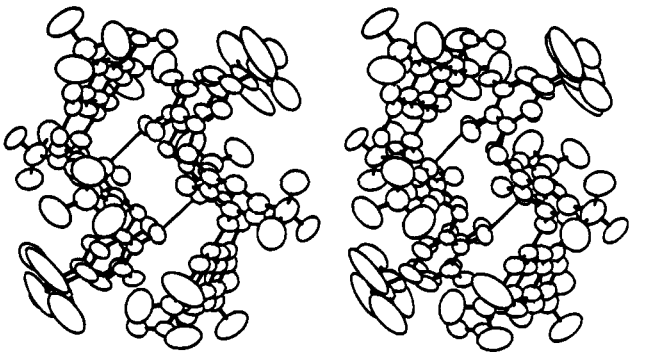


Figure 6. Stereoscopic side view of the dimer of **18**. The intramolecular hydrogen bonds are represented by lines. MeCN molecules were omitted for clarity.

by two hydrogen bonds. The two molecules in the dimer are complementary in shape and mutually inclusive; i.e., one of the protuberances of each molecule is located in the V-shaped cavity of its neighboring molecule (Figure 6). Each xanthene ring lies above one of the hydrogen-bonded rings (C(8)–C(13)). The mutual inclusion observed in the crystal structure of **18** may be the result of the conformation adopted and is most likely forced by the hydrogen bonds. In addition to serving as a host to the MeCN, each molecule can be viewed as serving as both a host and a guest of its neighboring calixarene molecule.

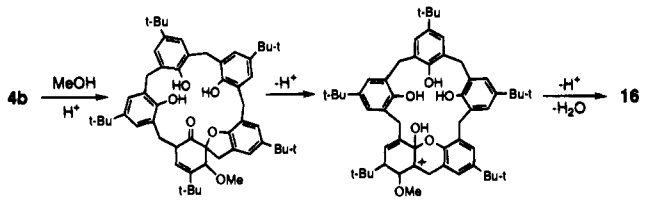
Mechanism of the Formation of the Xanthenocalixarenes. The methoxy group incorporated into the xanthene skeleton originates from the solvent; replacement of the MeOH by EtOH in the rearrangement of **4c** resulted in the formation of the corresponding ethoxy-substituted xanthenocalixarene. On the basis of these observations, we propose, tentatively, the mechanism depicted in Scheme 2, which involves activation of the diene to nucleophilic addition of a methanol molecule, ketonization of the resulting dienol, and acid-catalyzed ring expansion followed by elimination of water. The first steps in the proposed

(32) For stepwise syntesis of phenol–formaldehyde pentamers see: Zinke, A.; Kretz, R.; Leggewie, E.; Hössinger, K. *Monatsh. Chem.* **1952**, *83*, 1213. Casraghi, G.; Cornia, M.; Ricci, G.; Balduzzi, G.; Casnati, G.; Andreetti, G. D. *Makromol. Chem.* **1983**, *184*, 1363.

(33) Related conformations (e.g., a "double partial cone") were observed for other calix[6]arene systems. See for example: Rizzoli, C.; Andreetti, G. D.; Ungaro, R.; Pochini, A. *J. Mol. Struct.* **1982**, *82*, 133. Atwood, J. L.; Clark, D. L.; Juneja, R. K.; Orr, G. W.; Robinson, K. D.; Vincent, R. L. *J. Am. Chem. Soc.* **1992**, *114*, 7559.

(34) Several dimeric associations of calixarenes in the solid state were reported by Atwood and co-workers (Atwood, J. L.; Orr, G. W.; Juneja, R. K.; Bott, S. G.; Hamada, F. *Pure Appl. Chem.* **1993**, *65*, 1471), but in these structures no self-inclusion of the calixarene skeletons was observed. Fukazawa and co-workers have presented evidence that a trihydroxycalix[4]-arene forms hydrogen-bonded dimers in solution (ref 27a).

Scheme 2



mechanisms for the formation of **15** (Scheme 1) and **16** (Scheme 2) are identical (nucleophilic addition to a meta position). However, if the nucleophile is monodentate (as in the case of MeOH), the intramolecular nucleophilic addition to the carbonyl cannot take place and the rearrangement pathway is the preferred one.

Conclusions. Monospirodienone derivatives can be used as intermediates in the preparation of monoamino and monodehydroxylated systems, as well as of the hitherto unknown azo- and xanthenocalixarenes.

Experimental Section

Crystallography. The X-ray diffraction data were measured with a PW1100/20 Philips four circle computer-controlled diffractometer or an ENRAF-NONIUS CAD-4 automatic diffractometer. Mo Kα (λ = 0.710 69 Å) or C_u Kα (λ = 1.541 78 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.

Crystal data for **4b**: $C_{55}H_{66}O_5 \cdot 2CH_3CN$, FW = 889.24 g mol^{-1}, space group *C2/c*, a = 27.725(7) Å, b =14.546(3) Å, c = 29.215(7) Å, β = 106.35(2)°; V = 11306(9) Å^3, z = 8, ϱ_{calc} = 1.05 g cm^{-3}, μ(Cu Kα) = 4.82 cm^{-1}, no. of unique reflections 8270, no. of reflections with $I \geq 3\sigma_I$ = 5576, R = 0.081, R_w = 0.108. Crystal data for **15**: $C_{55}H_{70}N_2O_5$, FW = 839.18 g mol^{-1}, space group *C2/c*, a = 27.709(3) Å, b = 26.518(4) Å, c = 19.258(3) Å, β = 113.79(2)°; V = 10612(1) Å^3, z = 8, ϱ_{calc} = 1.05 g cm^{-3}, μ(Mo Kα) = 0.62 cm^{-1}, no. of unique reflections 7110, no. of reflections with $I \geq 3\sigma_I$ = 4118, R = 0.083, R_w = 0.100. Crystal data for **18**: $C_{67}H_{84}O_6 \cdot CH_3CN$, FW = 1026.47 g mol^{-1}, space group $P\bar{1}$, a = 16.608(4) Å, b = 17.596(2) Å, c = 12.993(3) Å, α = 97.87(1)°, β = 108.67(3), γ = 62.99(1)°; V = 3191(2) Å^3, z = 2, ϱ_{calc} = 1.07 g cm^{-3}, μ(Cu Kα) = 4.88 cm^{-1}, no. of unique reflections 9360, no. of reflections with $I \geq 3\sigma_I$ = 6422, R = 0.080, R_w = 0.112.

General Methods. Melting points were obtained with a Melt-Temp II apparatus and are uncorrected. Phenyltrimethylammonium tribromide was purchased from Aldrich. All column chromatographies were performed using silica gel, 230–400 mesh, purchased from Merck.

Monospirodienone *p-tert*-Butylcalix[5]arene Derivative 4b. A 1.0 g sample of *p-tert*-butylcalix[5]arene **1b**[13] (1.23 mmol) was dissolved in 150 mL of CH_2Cl_2, and a solution of 0.35 g (0.94 mmol) of phenyltrimethylammonium tribromide in 50 mL of CH_2Cl_2 was slowly added to the stirred solution during a 0.5 h period. After the addition was complete, the mixture was stirred for an additional 1 h. To the solution was added 200 mL of saturated aqueous $NaHCO_3$. After stirring for 12 h, the organic phase was separated, washed several times with water and evaporated. Column chromatography of the residue (eluent CH_2Cl_2/petroleum ether, 2:3) gave yellow **4b** (0.47 g, 0.58 mmol, 63% based on the tribromide), mp 185–190 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 1.15 (s, *t*-Bu, 9H), 1.17 (s, *t*-Bu, 9H), 1.20 (s, *t*-Bu, 9H), 1.25 (s, *t*-Bu, 9H), 1.33 (s, *t*-Bu, 9H), 3.22 (d, 1H, J = 15.7 Hz), 3.27 (d, 2H, J = 14.8 Hz), 3.35 (d, 1H, J = 14.4 Hz), 3.45 (d, 1H, J = 15.5 Hz), 3.53 (d, 1H, J = 14.0 Hz), 3.90 (d, 1H, J = 13.7 Hz), 4.01 (d, 1H, J = 14.4 Hz), 4.20 (d, 1H, J = 13.9 Hz), 4.32 (d, 1H, J = 14.3 Hz), 6.22 (d, 1H, J = 2.4 Hz), 6.27 (br s, 1H, OH), 6.93 (br, 1H), 6.95 (d, 1H, J = 2.3 Hz), 6.98 (d, 2H, J = 2.6 Hz), 7.06 (d, 1H, J = 2.4 Hz), 7.09 (d, 1H, J = 2.4 Hz), 7.15 (d, 1H, J = 2.4 Hz), 7.20 (d, 1H, J = 2.4 Hz), 7.30 (d, 1H, J = 2.3 Hz), 9.10 (s, OH), 9.65 (s, OH). ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 28.46, 31.28, 31.46, 31.48, 31.54, 31.57, 31.71, 31.74, 32.91, 33.87, 34.01, 34.13, 34.27, 42.01, 84.65 (spiro C–O), 119.79, 121.93, 122.77, 125.07, 125.24, 125.29, 125.96,125.98, 126.06, 126.15, 126.25, 126.49, 126.54, 126.90, 127.15, 129.06, 132.20, 134.58, 141.07, 141.36, 141.95, 142.95, 144.14, 144.25, 147.92, 148.47, 150.83, 154.86, 203.77 (C=O). IR: ν_{CO} 1620 cm^{-1}. CI MS: *m/z* 811.7 (M + 3H)$^+$. Anal. Calcd for $C_{55}H_{68}O_5$: C, 81.64; H; 8.47. Found: C, 81.61; H, 8.65.

Monospirodienone *p-tert*-Butylcalix[6]arene Derivative 4c. To a stirred solution of 15 g (15 mmol) of **1c**[14] dissolved in 1.5 L of CH_2Cl_2 was slowly added during 1 h a solution of 2.88 g (7.7 mmol) of phenyltrimethylammonium tribromide dissolved in 150 mL of CH_2Cl_2, and the mixture was stirred for an additional 2 h. To the solution was added 1 L of saturated $NaHCO_3$, and the mixture was stirred overnight. The organic phase was separated, filtrated, and washed several times with water. After evaporation of the solvent, the residue was treated with 80 mL of MeCN and the undissolved white solid (unreacted **1c**) separated by filtration. The filtrate was evaporated, yielding 5.1 g of yellow **4c** of >90% purity (by NMR). Further purification was achieved by column chromatography (eluent $CHCl_3$), yielding 3.9 g (4.0 mmol) **4c** (52% based on the tribromide), mp 235–240 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 1.08 (s, 9H, *t*-Bu), 1.24 (s, 9H, *t*-Bu), 1.25 (s, 18H, *t*-Bu), 1.27 (s, 9H, *t*-Bu), 1.28 (s, 9H, *t*-Bu), 3.17 (d, J = 15.6 Hz, 1H, CH_2), 3.22 (br d, J = 16.7 Hz, 1H, CH_2), 3.56 (d, J = 13.9 Hz, 1H, CH_2), 3.64 (d, J = 15.2 Hz, 1H, CH_2), 3.67 (d, J = 13.3 Hz, 1H, CH_2), 3.68 (d, J = 13.9 Hz, 1H, CH_2), 3.69 (d, J = 14 Hz, 1H, CH_2), 3.89 (d, 1H, CH_2), 3.93 (d, J = 13.9 Hz, 1H, CH_2), 3.97 (d, J = 14 Hz, 1H, CH_2), 4.04 (br d, 1H, CH_2), 4.07 (d, J = 16.4 Hz, 1H, CH_2), 6.11 (d, J = 2.1 Hz, 1H, C=CH), 6.78 (br s, 1H, C=CH), 6.99 (d, J = 2.3 Hz, 1H, Ar-H), 7.03 (br, 1H, Ar-H), 7.06 (d, J = 2.4 Hz, 1H, Ar-H), 7.09 (m, 3H, Ar-H), 7.14 (m, 4H, Ar-H), 7.91(br, OH), 8.39 (br, OH), 9.15 (br, OH), 9.29 (br, OH). ^{13}C NMR ($CDCl_3$): δ 14.13, 22.65, 28.46, 30.14, 31.46, 31.50, 31.56, 31.59, 31.65, 31.67, 32.60, 33.89, 33.93, 33.97, 34.05, 34.35, 34.39, 40.37, 85.33, 120.46, 122.08, 124.73, 125.20, 125.68, 125.79, 125.87, 125.92, 126.19, 126.37, 126.53, 126.64, 127.11, 127.17, 127.35, 128.01, 128.36, 128.95, 135.20, 138.08, 141.98, 143.66, 143.96, 144.45, 144.90, 145.52, 146.65, 147.35, 148.06, 150.28, 152.34, 198.75. IR: ν_{CO} 1670 cm^{-1}. CI MS: *m/z* 973.8 (M + 3H)$^+$. Anal. Calcd for $C_{66}H_{82}O_6$: C, 81.61; H; 8.51. Found: C, 81.26; H, 8.69.

Reaction of 4a with Hydrazine. To a solution of 2.0 g of **4a** (3.09 mmol) in 150 mL of MeOH was added 10 g (95 mmol) of hydrazine dihydrochloride. The mixture was heated to reflux, and a solution of NaOH (7.6 g, 190 mmol) in 200 mL of MeOH was added slowly during 1.5 h. After the addition was complete, the mixture was stirred for an additional 30 min. The precipitate was removed by filtration, and the filtrate evaporated. The residue was dissolved in CH_2Cl_2 and washed with water. The organic phase was evaporated and the residue chromatographed (eluent $CHCl_3$), yielding 452 mg (20%) of **6**, 325 mg (16%) of **7**, and 43 mg (2%) of **5**. The spectroscopic data for these compounds are described in refs 6a (supporting information) and 6b.

5,11,17,23,29-Penta-*tert*-butyl-31-[(2,4-dinitrophenyl)azo]-32,33,34,35-tetrahydroxycalix[5]arene (8). A mixture of 1 g of **4b** and 1 g of (2,4-dinitrophenyl)hydrazine was dissolved in 100 mL of MeOH, 8 drops of concentrated H_2SO_4 were added, and the mixture was refluxed for 2 h. After evaporation of the solvent the residue was dissolved in $CHCl_3$ and the precipitate removed by filtration. The $CHCl_3$ was evaporated, and the residue was purified by chromatography (eluent $CHCl_3$), yielding 650 mg (53%) of **8** as a red powder, mp 175–177 °C. Alternatively, **8** can be isolated from the reaction mixture by adding 200 mL of petroleum ether, 40–60 °C, filtration, and evaporation of the filtrate, giving 0.80 g (65%) of **8**, essentially pure by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 1.12 (s, 9H, *t*-Bu), 1.23 (s, 18H, *t*-Bu), 1.33 (s, 18H, *t*-Bu), 3.43 (d, 2H, J = 14.0 Hz), 3.44 (d, 1H, J = 14.1 Hz), 3.61 (d, 2H, J = 14.0 Hz), 4.07 (d, 3H, J = 13.9 Hz), 4.71 (d, 2H, J = 13.9 Hz), 7.19 (d, 2H, J = 2.6 Hz), 7.20 (d, 2H, J = 2.7 Hz); 7.24 (d, 2H, J = 2.7 Hz), 7.25 (d, 2H, J = 2.5 Hz), 7.27(s, 2H), 7.96 (s, 2H), 8.15 (d, 1H, ^3J = 8.7 Hz), 8.32 (s, 2H), 8.71 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.4 Hz), 9.02 (d, 1H, ^4J = 2.3 Hz); ^{13}C NMR (100.62, $CDCl_3$, rt): δ 30.66, 31.22, 31.38, 31.60, 32.59, 33.83, 33.90, 34.85, 120.84, 123.50, 125.33, 125.64, 125.80, 126.08, 126.27, 126.45, 126.73, 126.83, 126.99, 129.00, 134.43, 143.12, 143.75, 145.12, 145.82, 147.64, 147.71, 149.19, 149.61, 155.46; CI MS: *m/z* 987.6 (B, M – 2H), 810.6 (**10**H$^+$). Anal. Calcd for $C_{61}H_{74}O_8N_4$: C, 73.91; H, 7.52; N, 5.65. Found: C, 73.62; H, 7.43; N, 5.39.

5,11,17,23,29-Penta-*tert*-butyl-31-amino-32,33,34,35-tetrahydroxycalix[5]arene (10). A solution of 0.8 g of **8** in 100 mL of petroleum ether (40−60 °C) was shaken with 15 mL of concentrated aqueous HI (64%) for 1 h. The organic phase was separated, washed with sodium thiosulfate, and evaporated. Column chromatography of the residue (eluent CH_2Cl_2) afforded 0.35 g (54%) of **10**, mp 195−198 °C.[35] ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 1.20 (s, 9H, *t*-Bu), 1.22 (s, 18H, *t*-Bu), 1.24 (s, 18H, *t*-Bu), 3.80 (br, 10H, CH_2), 7.17 (m, 6H, Ar-H), 7.21 (d, J = 2.4 Hz, 2H, Ar-H), 7.26 (s, 2H, Ar-H). ^{13}C NMR (100.62 MHz, $CDCl_3$, rt): δ 31.25, 31.42, 31.48, 31.80, 33.47, 33.84, 33.85, 34.07, 125.12, 125.37, 125.48, 125.63, 126.29, 126.50, 126.65, 126.75, 134.00, 134.50, 143.13, 143.82, 147.38, 147.71, 148.63. CI MS: *m/z* 810.6 (MH^+).

Data for $10H^+Tos^-$ (mp > 189 °C, dec). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 1.16 (s, 18H, *t*-Bu), 1.18 (s, 9H, *t*-Bu), 1.21 (s, 18H, *t*-Bu), 2.32 (s, 3H, Me), 3.25 (d, J = 14.3 Hz, 2H, CH_2), 3.42 (d, J = 14.5 Hz, 1H, CH_2), 3.48 (d, J = 14.5 Hz, 2H, CH_2), 4.01 (d, J = 14.4 Hz, 2H, CH_2), 4.19 (d, J = 14.6 Hz, 1H, CH_2), 4.25 (d, J = 14.2 Hz, 2H, CH_2), 7.05 (d, J = 2.2 Hz, 2H, Ar-H), 7.07 (d, J = 2.3 Hz, 2H, Ar-H), 7.10 (part hidden d, 2H, Ar-H (Tos)), 7.11 (br s, 4H, Ar-H), 7.22 (s, 2H, Ar-H), 7.86 (d, J = 8.1 Hz, 2H, Ar-H (Tos)). ^{13}C NMR (100.62 MHz, $CDCl_3$, rt): δ 14.12, 21.43, 22.66, 31.02, 31.27, 31.40, 31.47, 31.59, 32.51, 32.82, 34.29, 123.71, 125.22, 125.58, 125.81, 126.13, 126.20, 126.24, 126.51, 128.98, 134.74, 140.65, 140.74, 143.36, 143.47, 147.50, 147.84, 151.38.

5,11,17,23,29-Penta-*tert*-butyl-31,32,33,34-tetrahydroxycalix[5]arene (13). To a stirred solution of 0.4 g of **1b** in 50 mL of MeOH was added 2 mL of hydrazine hydrate and 0.10 g of NaOH. The solution was refluxed for 3 h, and the MeOH was evaporated. The residue was dissolved in 100 mL of $CHCl_3$ and washed with 10% aqueous HCl followed by brine. The organic phase was evaporated and the residue chromatographed (eluent CH_2Cl_2), yielding 0.16 g (41%) of **13**, mp 164−167 °C. ^{1}H NMR (400 MHz, $CDCl_3$, rt)): δ 1.24 (s, *t*-Bu, 9H), 1.26 (s, *t*-Bu, 18H), 1.29 (s, *t*-Bu, 18H), 3.76 (s, 4H, CH_2), 3.78 (s, 2H, CH_2), 3.91 (s, 4H, CH_2), 6.59 (br t, 1H, Ar-H_a), 6.67 (s, 2H, OH), 7.02 (d, J = 2.5 Hz, 2H, Ar-H), 7.17 (s, 6H, Ar-H), 7.24 (d, J = 2.5 Hz, 2H, Ar-H), 8.41 (s, OH). ^{13}C NMR (100.62 MHz, $CDCl_3$, rt): δ 31.31, 31.46, 31.56, 31.98, 32.50, 33.97, 33.98, 34.68, 37.98, 124.20, 124.53, 125.30, 125.72, 125.97, 126.13, 126.65, 127.01, 127.16, 127.28, 140.40, 143.40, 144.14, 147.65, 149.70, 152.74. CI MS: *m/z* 810.7 (MH^+). Anal. Calcd for $C_{55}H_{70}O_4$·EtOH: C, 81.38; H, 9.11. Found: C, 81.10; H, 9.09.

Reaction of 4b with Hydrazine. A mixture of 0.158 g of **4b**, 2.0 g of hydrazine dihydrochloride, and 0.9 g of NaOH in 50 mL of MeOH was stirred at rt for 1.5 h. During that time the yellow color of the solution disappeared. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2/H_2O, the phases were separated, and the organic phase was washed with water several times. After evaporation of the CH_2Cl_2, the products were purified by column chromatography (eluent $CHCl_3$). The last fraction obtained was chromatographed a second time (eluent $CHCl_3$/EtOH, 20:1), yielding 51.1 mg of **15** (31%), mp 208−212 °C dec[35] together with 26.8 mg (17%) of **13** and 4.3 mg of **10** (3%), mp 195−198 °C.

Data for 15. ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 1.16 (s, 9H, *t*-Bu), 1.22 (s, 9H, *t*-Bu), 1.24 (s, 9H, *t*-Bu), 1.27 (s, 9H, *t*-Bu), 1.32 (s, 9H, *t*-Bu), 2.44 (dd, J = 14.2, 2.7 Hz, 1H), 2.82 (app t, 1H), 2.93 (dt, J = 14.7, 0.9 Hz), 3.05 (d, J = 16.8 Hz, 1H, CH_2), 3.23 (d, J = 13.3 Hz, 1H, CH_2), 3.28 (d, J = 16.8 Hz, 1H, CH_2), 3.45 (d, J = 14.4 Hz, 1H, CH_2), 3.53 (d, J = 14.0 Hz, 1H, CH_2), 4.18 (d, J = 14.3 Hz, 1H, CH_2), 4.23 (s, 1H, OH), 4.30 (d, J = 13.0 Hz, 1H, CH_2), 4.31 (d, J = 13.9 Hz, 1H, CH_2), 5.34 (q, J = 1.5 Hz, 1H, NCH), 5.54 (d, J = 1.5 Hz, 1H, C=CH), 6.82 (d, J = 1.4 Hz, 1H), 6.99 (d, J = 2.5 Hz, 1H), 7.16 (m, 3H, Ar-H), 7.20 (d, J = 2.5 Hz, 1H, Ar-H), 7.21 (d, J = 2.4 Hz, 1H, Ar-H), 7.24 (partially hidden d, 1H, ArH), 8.03 (OH), 8.77 (OH), 9.34 (OH). ^{13}C NMR: δ 28.07, 28.35, 28.69, 30.79, 31.46, 31.48, 31.54, 31.59, 31.90, 33.79, 33.88, 33.95, 34.16, 34.92, 43.13, 85.81, 93.27, 111.15, 118.88, 121.51, 123.94, 124.90, 125.31, 125.56, 125.58, 125.66, 125.67, 125.75, 125.76, 125.88, 126.01, 126.35, 126.50, 126.72, 127.05, 142.33, 143.45, 143.91, 144.49, 145.20, 147.89, 148.46, 149.91, 153.56.

Rearrangement of the Monospirodienone 4b. To a solution of 0.5 g of **4b** in 20 mL of EtOH was added 3 drops of concentrated H_2SO_4, and the mixture was refluxed for 4 h. The MeOH was evaporated and the residue chromatographed (eluent CH_2Cl_2), giving 0.245 g (48%) of the xanthene **16**, mp >195 °C dec,[35] and 0.115 g (21%) of the linear pentamer **17**, mp > 115 °C dec.

Data for Xanthenocalix[5]arene 16. ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 1.16 (s, 9H, *t*-Bu), 1.27 (s, 18H, *t*-Bu), 1.28 (s, 9H, *t*-Bu), 1.34 (s, 9H, *t*-Bu), 3.82 (br, 4H, CH_2), 3.85 (s, 3H, OMe), 3.99 (br, 4H, CH_2), 4.02 (br, 4H, CH_2), 4.06 (s, 2H, CH_2), 6.97 (d, 2H, J = 2.5 Hz, Ar-H), 6.99 (d, 2H, J = 2.5 Hz, Ar-H), 7.05 (s, 1H, Ar-H), 7.11 (d, 1H, J = 2.4 Hz, Ar-H), 7.14 (d, J = 2.5 Hz, 3H, Ar-H), 7.24 (br, OH), 7.39 (br, OH), 8.21 (br, OH). ^{13}C NMR (100.62, $CDCl_3$, rt): δ 25.47, 30.38, 30.64, 31.04, 31.32, 31.49, 31.57, 31.60, 32.42, 32.45, 33.95, 34.02, 34.21, 34.62, 61.12 (OMe), 116.78, 120.88, 121.08, 123.68, 125.45, 125.50, 125.53, 126.08, 126.16, 126.19, 126.22, 127.00, 127.28, 127.29, 127.43, 127.66, 136.93, 142.86, 143.04, 144.60, 145.71, 146.00, 147.93, 149.26, 149.40, 149.64, 155.84. CI MS: *m/z* 823.5 (MH^+).

Data for Linear Pentamer 17. ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 1.22 (s, 9H, *t*-Bu), 1.235 (s, 9H, *t*-Bu), 1.237 (s, 9H, *t*-Bu), 1.25 (s, 9H, *t*-Bu), 1.26 (s, 9H, *t*-Bu), 3.49 (s, 3H, OMe), 3.848 (s, 3H, OMe), 3.853 (s, 4H, CH_2), 3.89 (s, 2H, CH_2), 3.91 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 6.74 (d, 1H, J = 2.1 Hz), 6.88 (d, 1H, J = 2.2 Hz), 6.90 (1H, OH), 7.11 (m, 6H), 7.24 (d, 1H), 8.63 (s, 1H, OH), 8.66 (s, 1H, OH), 8.99 (s, 1H, OH), 9.09 (s, 1H, OH). ^{13}C NMR (100.62, $CDCl_3$, rt): δ 31.19, 31.47, 31.52, 31.56, 32.17, 32.25, 33.93, 33.94, 33.95, 33.99, 34.38, 56.05, 58.47, 73.43, 106.76, 119.19, 122.35, 123.56, 125.68, 125.71, 125.78, 126.16, 127.11, 127.20, 127.29, 127.38, 127.39, 127.42, 127.50, 127.57, 139.90, 143.25, 143.42, 143.65, 143.85, 143.90, 146.38, 147.50, 147.53, 147.94, 149.70. CI MS: *m/z* 873.5 (MH^+), 678.3, 516.3. Anal. Calcd for $C_{57}H_{76}O_7$: C, 78.40; H, 8.77. Found: C, 78.10; H, 8.71.

Xanthenocalix[6]arene 18. To a solution of 2 g of **4c** in 100 mL of MeOH was added 0.5 mL of concentrated H_2SO_4, and the mixture was refluxed for 1 h. After cooling to rt, the precipitate was filtrated, washed with MeOH, and dried under suction, yielding 1.23 g (61%) of **18**, mp 217−222 °C dec.[35] ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 1.15 (s, 9H, *t*-Bu),1.17 (s, 9H, *t*-Bu), 1.218 (s, 9H, *t*-Bu), 1.224 (s, 9H, *t*-Bu), 1.23 (s, 9H, *t*-Bu), 1.28 (s, 9H, *t*-Bu), 3.82 (s, 2H, CH_2), 3.83 (s, 2H, CH_2), 3.84 (s, 2H, CH_2), 3.85 (s, 3H, OMe), 3.96 (s, 2H, CH_2), 3.97 (s, 2H, CH_2), 4.00 (s, 2H, CH_2), 6.87 (s, 1H, Ar-H), 6.91 (d, J = 2.2 Hz, 1H, Ar-H), 6.92 (d, J = 2.4 Hz, 1H, Ar-H), 6.95 (d, J = 2.3 Hz, 1H, Ar-H), 7.11 (m, 4H, Ar-H), 7.13 (d, J = 2.4 Hz, 1H, Ar-H), 7.15 (m, 2H, Ar-H). ^{13}C NMR ($CDCl_3$, rt): δ 25.6, 30.1, 30.2, 31.0, 31.43, 31.46, 31.6, 32.34, 33.91, 33.93, 33.97, 34.7, 61.6 (OMe), 117.5, 121.6, 121.9, 123.5, 124.9, 125.1, 125.2, 125.71, 125.73, 125.77, 125.92, 125.99, 126.03, 126.70, 126.77, 126.79, 126.94, 126.97, 126.99, 127.04, 137.10, 143.2, 144.1, 146.1, 147.4, 148.62, 148.67, 148.70, 150.0, 155.8. CI MS: *m/z* 985.8 (MH^+).

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Supporting Information Available: Tables of positional and thermal parameters for **4b**, **15**, and **18** (20 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(35) We were unable to obtain satisfactory microanalytical data for compounds **10**, **15**, **16**, and **18**, probably due to to incomplete combustion. See: Böhmer, V.; Schön, M.; Wolff, A. *J. Org. Chem.* **1992**, *57*, 790.