Preparation, Stereochemistry, and Reactions of the Bis(spirodienone) Derivatives of *p-tert*-Butylcalix[4]arene

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The stereochemistry of the spirodienone derivatives of *p-tert*-butylcalix[4]arene (1) is analyzed. Treatment of 1 with base and 2 equiv of phenyltrimethylammonium tribromide resulted in the formation of a mixture of three main products (**4A**, **4A'**, and **4B**) each containing two spirodienone moieties. The molecules slowly mutually interconvert in solution, and in toluene at 80 °C the equilibrium mixture is composed of 10% **4A'**, 65% **4A**, and 25% **4B**. From the NMR data, it is concluded that both **4A** and **4A'** are systems in which the two cyclohexadienone groups are at distal positions (1,3) whereas **4B** has C_s symmetry and the cyclohexadienone rings are at proximal (1,2) positions. Unambiguous structural characterization of the systems was achieved by X-ray crystallography which indicates that **4A'** is the chiral form (C_2 symmetry) while **4A** is the meso (C_i) form. Attempted reduction of **4A** resulted in the regeneration of 1. Reaction of **4A** with HCl results in chloro-de-*tert*-butylation of two rings and rearomatization. Reaction of **4A**, **4A'**, and **4B** with excess benzyne yielded the corresponding Diels-Alder adducts **10A**, **10A'**, and **10B** which do not interconvert in solution. Based on the NMR data it is concluded that for each compound the additions to the two spirodienones occurred with identical diastereofacial discrimination. The Diels-Alder adducts are the first systems in which the phenolic oxygens of a calixarene were converted into nonconjugated ketone groups.

Introduction

Calix[*n*]arenes are macrocyclic compounds in which *n* phenolic and methylene units are arranged in an alternating fashion.[1] Considerable synthetic efforts have been invested in the last years in the modification of the binding groups of the calixarenes (i.e., the OH groups).[1] Two strategies have been used for the preparation of chemically modified calixarenes. The first one is based on the introduction of the functionalities before the cyclization step, by preparation of a suitable precursor with the proper functionalities, which in a later stage is either oligomerized in a stepwise route and cyclized[2] or directly cyclized.[3] The second strategy is based on the chemical transformation of the calixarene; i.e., the modification is carried out after the macrocyclization step. Whereas the first route is in principle more versatile, the second route is more attractive for practical reasons: the optimal conditions for the preparation of *p-tert*-butylcalix[4]arene (1), *p-tert*-butylcalix[6]arene, and *p-tert*-butylcalix[8]arene are now well-known, and these compounds can be prepared in gram quantities.[4] Since the only functional groups present in the calixarene are the OH groups, the second route rests mostly on the chemistry of the phenolic group. Modified calixarenes have been synthesized using reactions characteristic of phenols such as alkylation or acylation of the OH groups,[5] aromatic electrophilic substitution of the phenolic rings,[6] and functionalization via the Claisen rearrangement.[7] In all these cases, the OH functionality either retains its identity or it is converted into ether or ester derivatives. Only a handful of examples are known in which the phenolic OH functional group was transformed into a different group. The OH groups of calixarenes have been totally[8] or partially replaced by hydrogens[9] or amino groups[10] using phosphate esters as intermediates or replaced by SH groups.[9b] In a different modification, the phenol rings of the calixarene derivatives have been oxidized to quinones.[11]

In this paper we report a novel approach for the modification of calixarenes in which the phenolic groups of 1 are oxidized into carbonyl and five-membered cyclic ether functionalities. The procedure results in the conversion of calixarenes into molecules containing stereocenters (which may bestow chirality to the molecule) and a cyclic disposition of carbonyl and ether binding sites like those of a variety of natural ionophores.[12]

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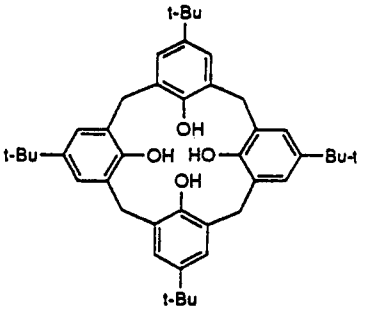

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Results and Discussion

COH/CO Functionality Conversion. The mild oxidation of bis(2-hydroxy-1-naphthyl)methane (2), first examined by Abel,[13] affords a single product in quantitative yield (eq 1) to which a peroxide structure was assigned. Pummerer and Cherbuliez[14] suggested that the product has the spirodienone structure 3 but this assignment was later challenged.[15]

(1)

2 3

Shearing and Smiles explored the chemistry of the product and, based on its reactivity, provided convincing evidence for its spirodienone structure.[16] In addition to the structural studies, they showed that 3 can be conveniently prepared from 2 by reaction with NaOCl/base or with Br_2/HOAc/NaOAc. The oxidative cyclization is not restricted to 2. Other bisphenols can be oxidized in an analogous way.[17,18]

This oxidation of bisphenols is notable since it involves the transformation of the OH groups into two different functional groups (carbonyl and cyclic ether) and the creation of a stereocenter (the spiro carbon). The structural similarity between 2 and 1 (in both systems two phenolic rings are connected to a methylene unit) suggests that a similar reaction may be carried out for the calix[*n*]arenes.

Static Stereochemistry. Since *n* phenolic groups are present in the calix[*n*]arenes several spirodienones derivatives are possible as products of the reaction. These forms arise from two important features of the spirodienone moiety. Firstly, the spiro carbons are stereocenters and therefore can exist in two possible configurations (*R* and *S*). Secondly, since the spirodienone moiety has a nonpalindromic sequence of bonded atoms, a sense of directionality[19] can be associated to it which is independent of the configuration of the stereocenter. Cyclostereoisomerism[20] may result as a consequence of the presence of the two features. The directionality of the spirodienone moiety can be arbitrarily represented by a curved arrow in which the head and tail of the arrow represent the relative locations of the ether and carbonyl moieties, respectively. The arbitrary convention used is shown in Figure 1. Given the convention, for a single spirodienone moiety different "senses" of the curved arrow (clockwise or counterclockwise) simply represent different views of the moiety, i.e., the same moiety "flipped over". If two or more spirodienone units are present in the macrocycle their relative sense (homodirectional or heterodirectional)[21] represents different constitutional isomers. For a bis(spirodienone) derivative of a calix[4]arene two homodirectional arrows represent an alternant arrangement of the enone and ether units of the spirodienone groups along the macrocycle while a tail to tail or head to head arrangement of the arrows represent two cyclohexadienone rings attached to the same methylene group. In the following discussion we will assume that the system is observed under a time scale in which conformational isomerism (e.g., ring inversion) is fast.

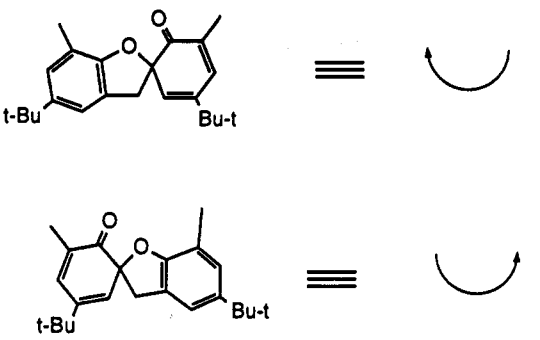

Figure 1. Arbitrary convention for the description of the sense of direction (curved arrow) of a spirodienone moiety.

Inspection of Dreiding models indicates that for a calix[4]arene a spirodienone moiety can be derived only from two proximal phenol rings (i.e., in a 1,2 relationship) since the distance between two distal (1,3) rings is too long to allow the formation of a transannular C–O bond. Two isomeric forms (one pair of enantiomers) should exist for a monospirodienone derivative of 1, and six isomeric forms (two meso forms and two pairs of enantiomers) should exist for a bis(spirodienone) system. The six bis(spirodienone) derivatives of 1 are drawn in Figure 2 together with the maximal symmetry attainable for the systems. These isomers are also shown in a curved arrow and circle representation in Figure 3 in which the sense of each arrow represents the sense of directionality of a given spirodienone moiety and open and filled circles represent the configuration (*R* or *S*) of the stereocenters, respectively.[20] It should be noted that each isomer can be described by an additional representation. For example, isomer i can be represented by two filled circles and two homodirectional arrows either pointing in a clockwise (as shown in Figure 3) or in a counterclockwise direction. None of the enantiomeric pairs qualify as cycloenantiomers, but for larger systems such as a bis(spirodienone) derivative of calix[6]arene cycloenantiomerism is possible.[22]

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(20) Prelog, V.; Gerlach, H. *Helv. Chim. Acta* **1964**, *47*, 2288. Prelog, V. *Science* **1976**, *193*, 17. See also: Singh, M. D.; Siegel, J.; Biali, S. E.; Mislow, K. *J. Am. Chem. Soc.* **1987**, *109*, 3397.
(21) Biali, S. E.; Buda, A. M.; Mislow, K. *J. Org. Chem.* **1988**, *56*, 1289.
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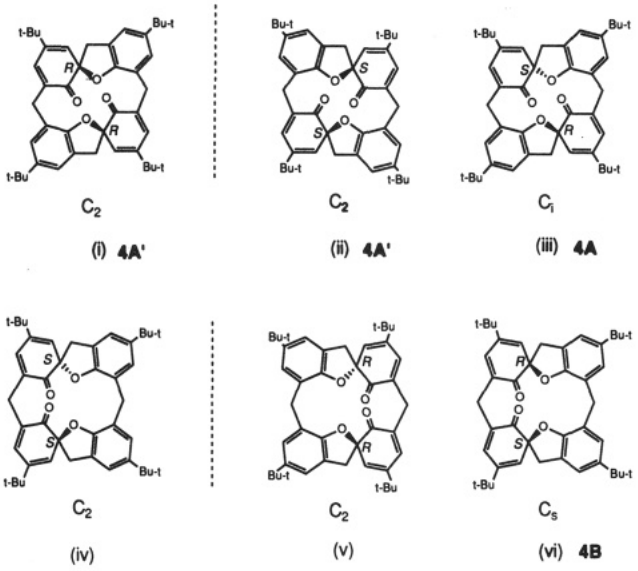


Figure 2. Six isomeric forms (i–vi) of a bis(spirocyclohexadienone) *p-tert*-butylcalix[4]arene derivative. Top: (1,3)-spirodienones. Bottom: (1,2)-spirodienones. The pairs related by a broken line, i.e., i/ii and iv/v represent enantiomers. Pairs of compounds formed by (1,2)- and (1,3)-spirodienones represent constitutional isomers. The absolute configurations are denoted near each stereocenter, point group symmetries under each structure.

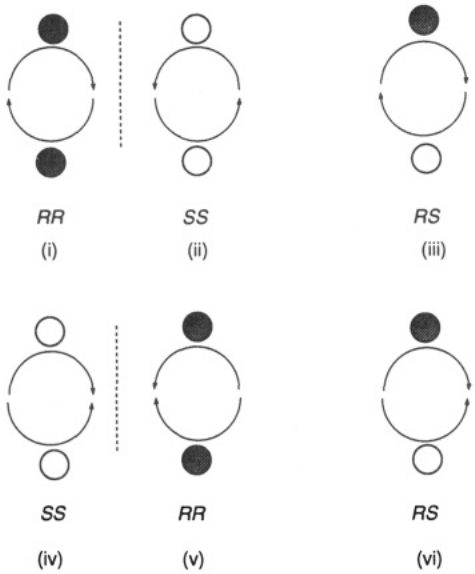
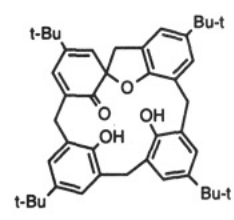


Figure 3. Arrow and circle representation of the six isomeric forms shown in Figure 2. Black and white circles represent the configuration of the stereocenter (*R* or *S*). The sense of the curved arrow represent the directionality of the spirodienone moiety.

Preparation of the Systems. Reaction of 1 or its tetraacetate with the strong oxidant CrO_3 results in the oxidation of the methylenes to carbonyl groups.[23] For the preparation of the bis(spirodienone) derivatives of 1 we treated 1 mol of 1 with 2 mol of either tetrabutylammonium tribromide or phenyltrimethylammonium tribromide in a two-phase basic system (CH_2Cl_2, aqueous NaOH). The latter reagent is somewhat preferable for the reaction since it is completely removed from the reaction mixture by washings with water. Treatment of 1 with the second reagent resulted in the formation of three main products.[24] The three compounds could be separated by liquid chromatography (silica) and are denoted **4A**, **4B**, and **4A'** (in their order of elution). In contrast with 1 which is colorless, these three species all have yellow colors, in agreement with the presence of dienone moieties in each product. As judged by IR spectroscopy the three species contain carbonyl groups ($\nu_{C=O}$ stretching **4A**: 1670 (s); **4A'**: 1670 (s); **4B**: 1690 cm^{-1}) and no OH groups. The formation of the products can be rationalized by assuming that under the reaction conditions the calixarene is deprotonated and the resulting phenolate is brominated yielding, in the first step, an *o*-bromocyclohexadienone derivative, which in a second step undergoes an intramolecular nucleophilic substitution reaction in which the bromine is replaced by the phenoxy group of a neighboring ring resulting in a cyclic five-membered ether. An alternative possibility is that the phenol rings are oxidized by abstraction of the hydrogen atoms from two OH groups yielding two phenoxy radicals which after the C–O spiro bond formation results in the formation of the products.

We have shown previously that treatment of 1 with 1 equiv of the oxidizing agent in the presence of a weak base yields the mono(spirodienone) derivative **5** resulting from the spirocyclization of two proximal rings.[25] In order to check experimentally our assumption that spirodienones can be derived only from proximal phenol rings we reacted the 1,3-didehydroxycalix[4]arene **6**[9] with aqueous $NaOH/CH_2Cl_2/Bu_4N^+Br_3^-$. No reaction took place, which supports our hypothesis that for small ring calixarenes spirodienones can be derived only from the reaction of proximal rings.



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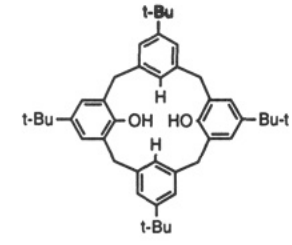

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NMR Spectra of 4A, 4A', and 4B. Spirodienones i–vi should display each two *tert*-butyl signals in the ^1H NMR spectrum. The most indicative region of the NMR for the assignment of the isomers is the methylene region. Precluding accidental isochrony, the enantiomeric pair iv/v should display in an achiral solvent two singlets and two doublets, vi should display six doublets in a 1:1:1:1:2:2 ratio, and i/ii and iii should display four doublets in a 1:1:1:1 ratio. The ^1H NMR spectrum of the methylene region of **4B**, **4A**, and **4A'** (in $CDCl_3$) are displayed in Figure 4. **4B** displays six doublets in a 1:1:2:1:2:1 ratio (δ 4.29 (J = 12.4 Hz), 4.12 (J = 13.1 Hz), 3.72 (J = 15.5 Hz), 3.26 (J = 13.2 Hz), 2.96 (J = 15.5 Hz), and 2.54 ppm (J = 12.4 Hz)) in the methylene region. This is consistent only with a molecule of C_s symmetry in which the mirror plane is bisecting two nonvicinal methylene carbons. In order to accommodate this symmetry, the two cyclohexadienone rings must therefore be located at proximal (1,2)

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(24) In our preliminary communication[12] we reported the formation of only two products. We could isolate a third product (**4A'**) from the reaction mixture by modification of the reaction conditions.

(25) Aleksiuk, O.; Grynszpan, F.; Biali, S. E. *J. Chem. Soc., Chem. Commun.*, in press.

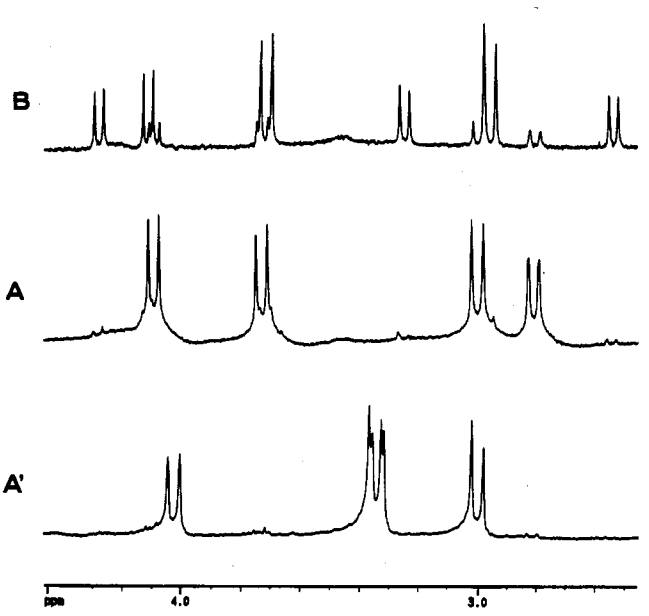
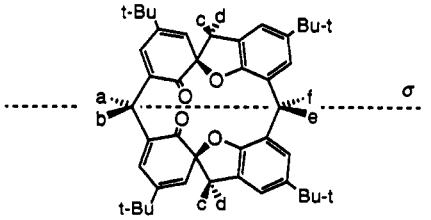


Figure 4. ^{1}H 400-MHz NMR spectrum of the methylene region of **4B** (top spectrum), **A** (middle spectrum), and **4A'** (bottom spectrum) in $CDCl_3$. The small doublets at δ 2.81, 3.00, 3.73, and 4.00 ppm in the spectrum of **4B** correspond to **4A** and are formed by the slow isomerization of the sample (see text).

positions and therefore structure vi was assigned to **4B**. The rest of the spectra is in full agreement with the proposed structure. In addition to the methylene signals, two *t*-Bu signals (δ 1.24, 1.13 ppm) and four signals at low field (two aromatic signals at δ 7.14, 6.95 ppm and two cyclohexadienone signals at δ 6.80, 5.9 ppm) are observed. Compound **4B** displays in the ^{13}C NMR a single C=O signal ($\delta_{C=O}$ 195.1 ppm), eight signals corresponding to sp^3 carbons (including the spiro carbons), and 10 signals corresponding to C(sp^2) carbons in agreement with the proposed structure. The spiro carbon signal appears at 81.68 ppm which is in the region reported for the spiro carbon signals of **3** and related compounds (82.4–89.3 ppm).[17]

It is interesting to note that the two methylene protons which show the largest geminal coupling constant (15.5 Hz) are the two doublets which integrate for a total of four protons. These signals must correspond to the protons at the five-membered ring (cf. c and d in **4B**) since these are



4B

the only ones which are present in symmetry related pairs. Theoretical considerations indicate that the effect of a π bond on a geminal coupling constant is a function of the angle between the π orbital and the C–H bond, the largest effect is when the two are parallel.[26] The large coupling constant observed for protons c and d is probably the result of the frozen orientation of the methylene moiety which is bisected by the phenyl ring.

(26) Sternhell, S. *Quart. Rev.* **1969**, *23*, 236.

Compounds **4A** and **4A'** display in the ^{1}H NMR spectrum similar patterns for the methylene region, i.e., four doublets in a 1:1:1:1 ratio (Figure 4). This is consistent with either the enantiomeric pair i/ii or with iii, i.e., with structures of either C_2 or C_i symmetry with two distal (1,3) cyclohexadienone rings. **4A** displays in the ^{1}H NMR spectrum (400 MHz, $CDCl_3$) two *t*-Bu signals at δ 0.99 and 1.31, four doublets at δ 2.82 (J = 14.3 Hz), 3.00 (J = 15.4 Hz), 3.73 (J = 15.4 Hz), and 4.10 (J = 14.1 Hz), two aromatic signals at δ 7.08 and 7.00, a doublet at δ 5.81 (J = 2.3 Hz), and a triplet at δ 6.59 which can be assigned to the cyclohexadienone protons. Irradiation of the signal at δ 2.82 resulted in the collapse of the doublet at δ 4.10 and conversion of the triplet at δ 6.58 into a doublet. On the basis of the large coupling constant of the methylene pair at δ 3.00 and 3.73 we assign these signals to the methylene protons which are part of the five-membered rings. The long-range coupling constant between the protons at δ 4.10 and 6.58 indicate that these protons are in spatial proximity. This shows that the signals at δ 6.58 and 5.87 correspond to protons of the dienone ortho and para to the spiro carbon, respectively.

Dienone **4A** displays in the ^{13}C NMR spectrum a carbonyl signal at δ 195.7, 10 signals in the δ 152–119 region corresponding to carbons of sp^2 hybridization, a signal at δ 81.7 which can be ascribed to the spiro carbon, and six aliphatic signals in the δ 38.1–27.9 region. In general, the ^{1}H NMR spectrum of **4A'** is similar to the spectrum of **4A** in the number of signals and their splitting. From the NMR data in $CDCl_3$ one cannot assign the chiral and meso structures to the pair **4A**/**4A'** although from the ^{1}H NMR pattern one can conclude that both **4A** and **4A'** have a cyclic disposition of the carbonyl and ether groups while **4B** has a mirror symmetric disposition.

Molecular Mechanics Calculations. In order to estimate computationally the relative energies and geometries of the structures i, iii, iv, and vi we resorted to molecular mechanics (MM) calculations. For this purpose we used the MM2 force field as implemented by MACROMODEL.[27] According to the calculations the structures iv and vi have identical steric energies, while the chiral form i is 0.6 kcal mol^{-1} lower in energy than iii. The calculated structures of the compounds are shown in Figure 5. Selected calculated parameters of **4A** are collected in Table I. For i, iii, and vi the calculated conformations show small deviations from their ideal C_2, C_i, and C_s symmetry while for vi the conformation markedly departs from the ideal C_2 symmetry. In all the calculated structures the ether oxygens are pointing toward the inner part of the macrocycle while the two carbonyl groups have a nearly parallel or antiparallel disposition and are oriented approximately perpendicular to the macrocyclic plane.

X-ray Structures. In order to find out the solid-state conformations and to assign to **4A** and **4A'** the structures i/ii or iii we grew single crystals of **4B**, **4A**, and **4A'** by slow evaporation of MeCN solutions. **4A** crystallizes without solvent molecules while **4A'** and **4B** crystallize with one and three molecules of MeCN, respectively.[28] The mo-

(27) For a description of the MACROMODEL program see: Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, E.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440.

(28) 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 Road, Cambridge, CB2 1EZ, UK.

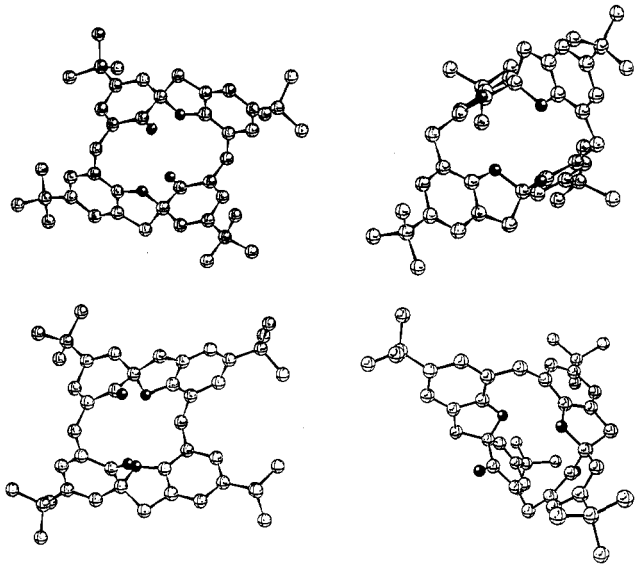


Figure 5. Calculated geometries for the isomers i–vi (cf. Figure 1) of **4**. Oxygen atoms are represented by the black spheres: top left, isomer iii; top right, i; bottom left, vi, bottom right, iv.

Table I. Calculated (MM2) and Experimental (X-ray) Selected Structural Data for 4A[a]

parameter	calcd	exptl	parameter	calcd	exptl
O(1)C(1)	1.21	1.220 (5)	O(2)C(8)	1.36	1.394 (4)
O(2)C(6)	1.42	1.474 (5)	C(7)C(9)C(10)	130.8	130.9 (5)
C(1)C(2)	1.48	1.480 (6)	C(2)C(3)C(4)	124.5	125.8 (4)
C(2)C(3)	1.35	1.319 (6)	C(5)C(6)C(7)	111.2	111.4 (4)
C(2)C(14)	1.52	1.526 (6)	C(6)C(7)C(9)	110.2	102.3 (4)
C(1)C(6)	1.53	1.522 (6)	C(2)C(13)C(14)	108.2	112.8 (4)
C(6)C(7)	1.55	1.556 (6)	O(1)···O(2)	2.95	2.958 (5)
O(2)C(6)	1.42	1.474 (5)	O(1)···O(1′)	4.42	5.031 (7)

[a] Bond lengths and nonbonded distances in Å, angles in deg.

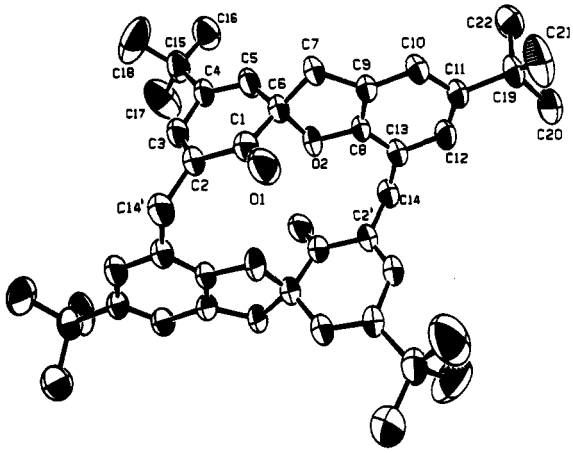


Figure 6. Molecular structure and numbering scheme of **4A**.

lecular structures of **4A**, **4A′** and **4B** are displayed in Figures 6–8. The X-ray data corroborate the NMR assignment that **4B** has a mirror symmetric disposition while **4A** and **4A′** have an alternant disposition of the keto and ether groups and assign to **4A** the meso form iii and to **4A** the chiral form i/ii.[29] This reverts our previous (incorrect) assignment of **4A** as the chiral (C_2) form[12] which was based on the somehow lower calculated steric energy

(29) For examples of chiral calixarenes see: Böhmer, V.; Marschollek, F.; Zetta, L. *J. Org. Chem.* **1987**, *52*, 3200. Casabianca, H.; Royer, J.; Satrallah, A.; Taty-c, A.; Vicens, J. *Tetrahedron Lett.* **1987**, *52*, 6595. Arimura, T.; Shinkai, S. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1896.

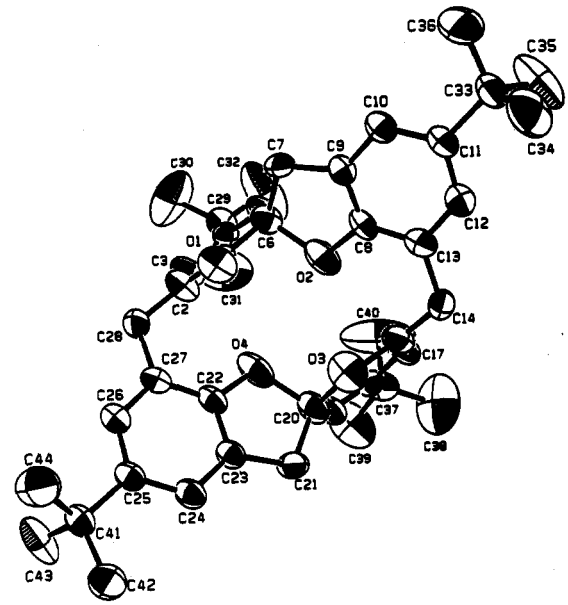


Figure 7. Molecular structure and numbering scheme of **4A′**. MeCN molecules were omitted for clarity.

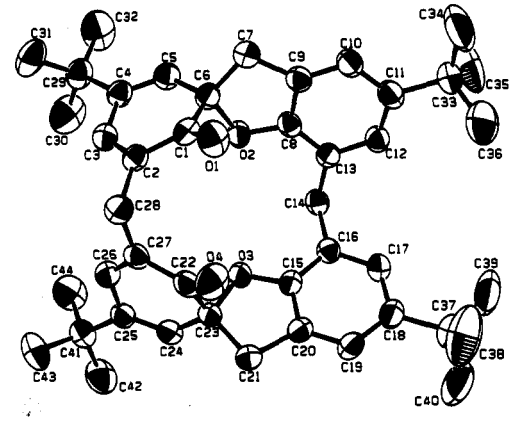


Figure 8. Molecular structure and numbering scheme of **4B**. MeCN molecules were omitted for clarity.

of i/ii over the meso form. The structure of **4A′** could be refined only to a relative high R value, and therefore its structural data are less accurate.

4A crystallizes in the space group $P2_1/c$ with the molecule located in an inversion center. The molecule has crystallographic C_i symmetry in which each pair of carbonyl and ether oxygens are pointing to different directions (up and down) of the mean crystallographic plane. The molecules of **4A′** and **4B** are located in the crystal at general positions, and therefore their crystallographic symmetry is C_1 although the approximately symmetry is C_2 and C_s. The conformations of **4A** and **4B** are reminiscent of the 1,2-alternate conformation, while the conformation of **4A′** is close to a flattened 1,3-alternate form. It can be readily seen by visual inspection of Figures 5 and 6–8 that the MM calculations reproduce quite well the shape and main features of the molecular conformation. A comparison of selected bond lengths, angles, and nonbonded distances is presented in Table I. One feature which is not reproduced by the calculations is the long spiro C(sp^3)–O bonds. The length of these bonds are 1.474 (2) Å for **4A** and 1.486 (3) and 1.490 (3) Å for **4B**, values which are longer than the values of 1.42–1.43 Å calculated for **4A**, **4A′**, and **4B**. The long C–O bond may indicate that this bond is relatively weak and prone to cleavage.

(i) O···O Nonbonded Distances. The carbonyl groups in the spirodienones studied are nearly parallel and point in the same direction both in the case of **4A'** and **4B** and therefore may be suitable for ligation of an ion,[30] while in **4A** the groups are pointing to opposite directions. In all compounds the ether oxygens are pointing to the center of the macrocycle (Figures 6–8). For **4A** the O···O nonbonded distances between oxygens at the carbonyl and ether groups are 2.95 and 3.22 Å. These values are similar for **4A'** (2.87–3.22 Å) while for **4B** the nonbonded distances between oxygens at neighboring rings are 3.46 and 3.72 Å. The distances between oxygens at distal rings are 5.03 (CO/CO) and 5.18 Å (ether/ether) for **4A**, 3.73 (CO/CO) and 3.12 Å (ether/ether) for **4A'**, and 4.67 and 4.71 Å for **4B**. In order to estimate the radius of a spherical cavity defined by the four oxygen atoms (the potential binding groups) the midpoint of the coordinates of the four oxygens must be known. For a symmetrical disposition of oxygens (e.g., a regular tetrahedron) the distance from the midpoint (the tetrahedron center) to any of the oxygen minus the van der Waals radius of an oxygen (1.4 Å) should be equal to the cavity radius. However, for an irregular disposition of oxygens the midpoint is not equidistant to the four oxygens, and in this case the shortest distance to one of the oxygens is used as the estimation of the cavity radius. In the case of **4A** the molecule has C_i symmetry, and therefore the inversion center is the geometric center of the coordinates of the four oxygens and the cavity radius is (3.592/2) − 1.4 = 0.4 Å. For **4A'** and **4B** the calculated cavity radii are 0.44 and 0.88 Å. The cavities of **4A** and **4A'** are too small to encapsulate even the small Li^+, while for **4B** the cavity is larger and Li^+ (and possibly Na^+) may fit in.[31]

(ii) Dienone–MeCN Nonbonded Distances. Crown ethers have been shown by X-ray diffraction to form complexes with molecules containing C–H "acidic" bonds such as nitromethane and dimethyl sulfone in which there are close contacts between the methyl carbon of the guest and the oxygen atoms of the host.[32,33] The close contacts were attributed to CH···O hydrogen bonds, dipole interactions, as well as stabilization of the crystal packing by filling the cavity of the host with the guest.[32,34] For example, for the 1:2 complex of 18-crown-6 with nitromethane the C···O nonbonded distances between the methyl carbon of the NO_2CH_3 and three oxygens located "above" the macrocyclic mean plane are 3.26 (2), 3.25 (2), and 3.32 (2) Å (average 3.28 Å).[34]

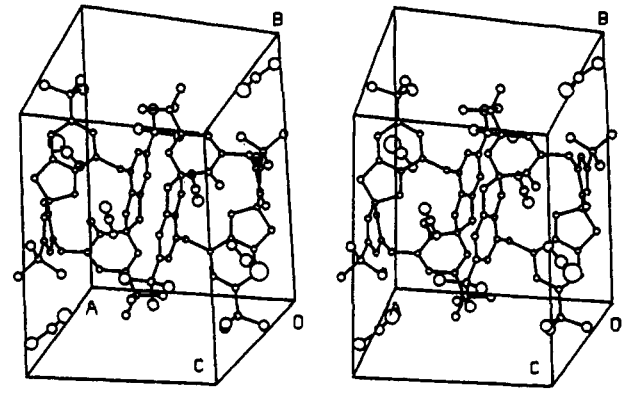


Figure 9. Stereoscopic picture of the unit cell of **4B**·3MeCN. The large circle in the rodlike molecules represents the nitrogen atoms of the MeCN. The two MeCN molecules at opposite corners of the unit cell are the ones which are not within contact distances of the ligand (see text).

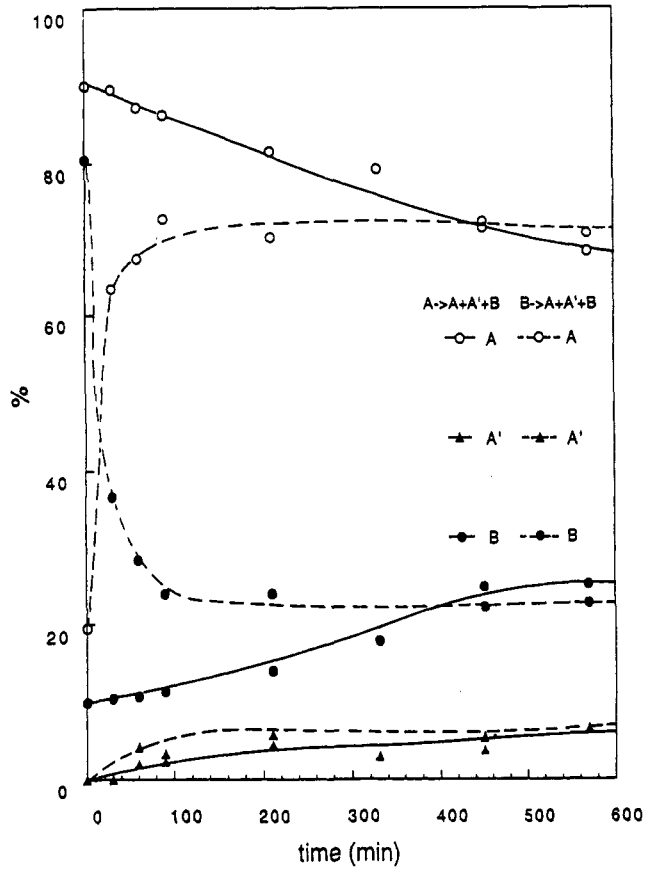


Figure 10. Isomerization of samples of original composition of 80% **4B**, 20% **4A** (dotted line) and 90% **4A**, 10% **4B** (plain line) in toluene at 80 °C as a function of time.

In compound **4A'** the single MeCN molecule is located outside the molecular cavity with its molecular axis oriented approximately perpendicular to the cyclohexadienone plane. Unfortunately, the poor *R* factor of the structure makes a discussion of the fine structural details of the complex unwarranted.

One of the three MeCN molecules in the crystal of **4B** is not within contact distance of the macrocycle and lies in between the molecules of **4B** while the two remaining MeCN are in proximity to either the carbonyl or ether oxygens (Figure 9). The MeCN molecule associated to the carbonyl oxygens shows two short C···O nonbonded distances (3.309 (5) Å, (O(4)···C(46)≡N), and 3.289(4) Å,

(30) Seebach, D.; Müller, H.-M.; Bürger, H. M.; Plattner, D. A. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 434.

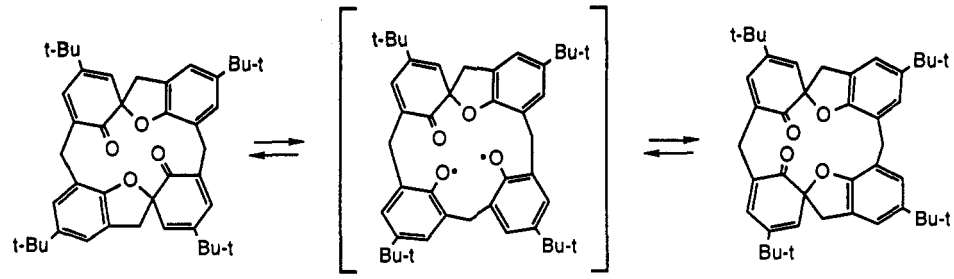
(31) In order to estimate qualitatively whether **4A**, **4A'**, and **4B** are capable of binding cations, we determined the ^1H NMR spectrum of the systems in $CDCl_3/CD_3OH$ (9:1 v/v) (see: Shinkai, S.; Fujimoto, K.; Otsuka, T.; Ammon, H. L. *J. Org. Chem.* **1992**, *57*, 1516) in the absence and in the presence of excess $MClO_4$ (M = Li, Na, K). The interaction of none of the cations with **4A** resulted in any appreciable shift, while for **4A'** the addition of Na^+ resulted in small shifts of the aromatic and cyclohexadienone protons ($\Delta\delta$ = 0.022–0.05 ppm). For compound **4B** small shifts were observed for both Li^+ and Na^+ ions, the largest shift being observed for Na^+ ($\Delta\delta$ = 0.02–0.07 ppm).

(32) For a review see: Vögtle, F.; Müller, W. M.; Watson, W. H. *Top. Curr. Chem.* **1984**, *125*, 131.

(33) The van der Waals radii of a methyl and an oxygen are 2.0 and 1.4 Å, respectively (Gordon, A. J.; Ford, R. A. *The Chemist Companion*; Wiley: New York, 1972; p 109). Distances shorter than 3.4 Å are considered "contact distances". For a discussion on the crystallographic evidence on C–H···O bonds see: Taylor, R.; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 5063.

(34) de Boer, J. A. A.; Reinhoudt, D. N.; Harkema, S.; van Hummel, G. J.; de Jong, F. *J. Am. Chem. Soc.* **1982**, *104*, 4073. van Zon, A.; de Jong, F.; Reinhoudt, D. N.; Torni, G. J.; Onwezen, Y. *Rec. Trav. Chim. Pays Bas* **1981**, *100*, 453.

Scheme I



(O(2)···C(46)=N)), while one contact distance is observed for the MeCN associated to the ether oxygens (3.236 (4) Å, (O(2)···C(45)—C(46)=N). It seems likely that whereas the short distances between the oxygens and the methyl group of the MeCN reflect CH···O hydrogen bonds the contact with the nitrile carbon reflects an electrostatic interaction between the ether and nitrile dipoles.

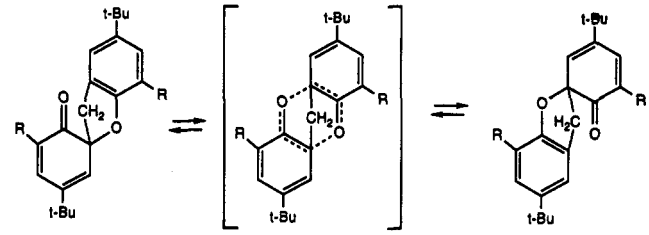
Solution Isomerization. During the determination of the solution NMR spectra of **4** in $CDCl_3$ we noticed that the compounds mutually interconvert in solution (cf. Figure 4). The isomerization process is slow on the NMR time scale. Heating a sample of **4A** in nitrobenzene-d_5 did not result in any broadening of the NMR signals and resulted only in equilibration.

In order to determine the equilibrium constant between the three forms and qualitatively estimate the isomerization rates, solutions of **4A**, **4A'**, and **4B** in toluene were prepared and the isomerization was followed at 80 °C. The starting compositions of the solutions were (i) 90% **4A**, 10% **4B**; (ii) 89% **4A'**, 3.9% **4B**, 7.1% **4A**, and (iii) 80.5% **4B**, 19.5% **4A**. The composition of the mixture at different time intervals was determined by integration of the cyclohexadienone protons in the ^1H NMR spectrum. For the three mixtures the equilibration was followed until identical compositions were found. Under the conditions described the equilibrium mixture is composed of 65% **4A**, 10% **4A'**, and 25% **4B**. The free energy difference ($\Delta G°$) between **4A** and **4B** is 0.67 kcal mol^{-1} and between **4A** and **4A'** is 1.32 kcal mol^{-1}. Under the experimental conditions, the relative stabilities of **4A** and **4A'** are opposite to the prediction of the MM2 calculations.

The equilibration data starting either from **4A** or **4B** are shown in Figure 10. In the equilibration starting from **4A** the ratio **4A'**/**4B** is not constant as the isomerization proceeds, but slowly increases until it reaches the equilibrium value. A similar behavior was observed in the equilibrations starting from **4B**: the ratio **4A'**/**4A** increases during the progress of the equilibration until the equilibrium value is achieved. This suggests that the **4A** ⇌ **4B** equilibration is faster than the equilibration of either **4A** or **4B** with **4A'**. Dienone **4A'**, the least stable isomer thermodynamically, is the isomer which is most stable kinetically. This conclusion is supported by the equilibration data. The compound for which the longest time is necessary to achieve 50% conversion is **4A'** (9 h). It should be noted that in the case of **4A'** the isomerization should lead to the racemization of an optically active sample.

Two simple mechanisms can be envisioned for the isomerization of **4** (Scheme I). The simplest one involves the cleavage of the C(sp^3)–O bond of the spirodienone moiety leading to two phenoxy radicals. Regeneration of the C–O bond could occur with inversion or retention of the configuration of the spiro carbon, and with retention

Scheme II



or reversal of the directionality of the spirodienone moiety. The second mechanism (Cope rearrangement) involves the concerted cleavage and formation of spiro bonds (Scheme II). This rearrangement should be stereospecific, and as inspection of molecular models shows, the new stereocenter created should have a configuration identical to the one distroyed. The **4A** ⇌ **4A'** and **4B** ⇌ **4A'** isomerizations which involve the change in configuration of one stereocenter cannot proceed through the concerted process and therefore the biradical route must be at least partially responsible for the isomerization process.

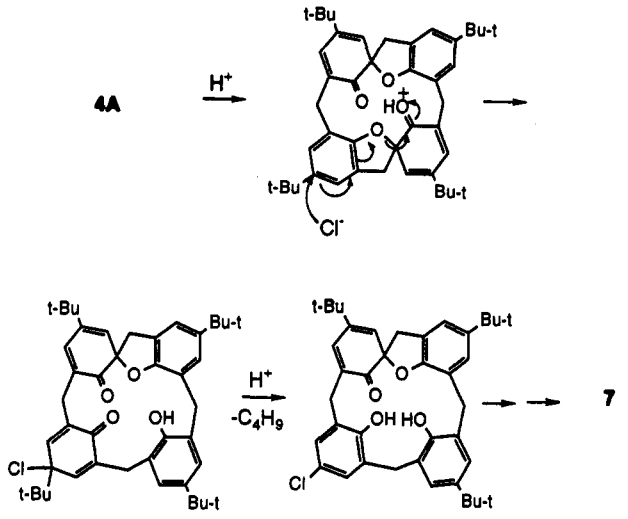
Reactions. Spirodienone **3** does not react with acetic anhydride or acetyl chloride. Reduction with Zn/AcOH regenerates **2**.[16] Attempted selective reduction of the carbonyl with $Et_3SiH/(Ph_3P)_3RhCl$[35] or reduction of **4A** with $LiAlH_4$, $NaBH_4$, or $H_2/Rh/Al_2O_3$ regenerates **1**. Attempted complexation of **4** with $Fe(CO)_5$ or melting of the samples of the spirodienones regenerates **1**.

(a) Selective Extraannular Modification. During our attempts to react the carbonyl group of **4** with amine nucleophiles we treated a solution of **4A** in MeCN with hydrazine and added concentrated HCl as catalyst. The only product isolated from the reaction in addition to a large amount of an insoluble compound formed by self-condensation of the MeCN was the 11,23-di-*tert*-butyl-5,17-dichlorocalix[4]arene **7**;[36a] i.e., the reaction resulted in aromatization of two cyclohexadienones and chloro-de-*tert*-butylation of two distal rings. The same product was obtained in the absence of hydrazine. Prolonged reflux of a solution of **4A** in MeCN in the presence of Bu_4N^+ Cl^- without acid catalyst resulted in isomerization of **4A**, i.e., in a mixture of **4A** + **4A'** + **4B**. Addition of a small amount of acetic acid did not result in a change in the outcome of the reaction, indicating that both a strong acid and the Cl^- are needed for the chloro-de-*tert*-butylation. No reaction was observed when **1** was treated with concentrated HCl in MeCN. Treatment of a solution of **4A** in MeCN with concd HBr or HI resulted in the formation of **1**. In order

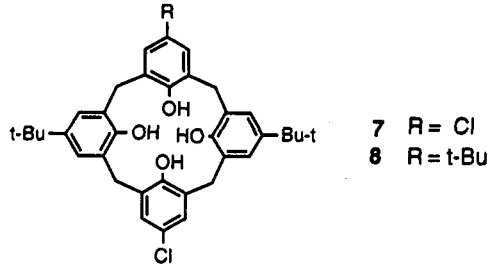
(35) Ojima, I.; Nihonyanagi, M.; Kogure, T.; Kumagai, M.; Horiuchi, S.; Nakatsugawa, K. *J. Organomet. Chem.* **1975**, *94*, 449.

(36) (a) This compound has been previously prepared in a multistep synthesis: de Mendoza, J.; Nieto, P. M.; Prados, P.; Sanchez, C. *Tetrahedron* **1990**, *46*, 671. (b) Böhmer, V.; Chhim, P.; Kämmerer, H. *Makromol. Chem.* **1979**, *180*, 2503.

Scheme III

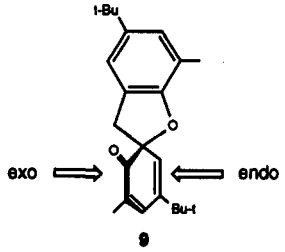


to explore the scope of the reaction the mono(spirodienone) calix[4]arene **5**[25] was reacted under similar conditions. The isolated product was the 11,17,23-tri-*tert*-butyl-5-chlorocalix[4]arene **8**. This compound has been previously prepared (in 2% yield) by condensation of a trisphenol with 2,6-bis(bromomethyl)-4-chlorophenol.[36b] When the reaction was carried out using DCl, no deuterium incorporation was observed judged by the aromatic signal of the product and the integration of the NMR signals. Based on this observation the mechanism shown in Scheme III is suggested.



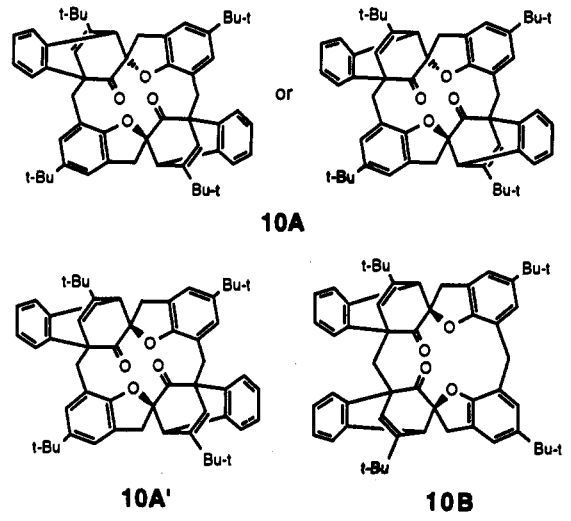
7 R = Cl
8 R = t-Bu

(b) Diels–Alder Reaction. The dienone moieties of the cyclohexadienone rings in compounds **4A**, **4A′**, and **4B** are in principle capable of adding benzyne, yielding the corresponding Diels–Alder adducts. Since in each compound the two faces of a given diene are diastereotopic several products are possible for the reaction. The two faces can be designated exo or endo depending on whether the face is on a syn or anti relationship to the methylene group (cf. **9**).



9

Treatment of either **4A**, **4A′**, or **4B** with benzyne (generated from benzenediazonium-2-carboxylate hydrochloride)[37] in the presence of propylene glycol yielded the colorless Diels–Alder bis adducts **10A**, **10A′**, and **10B**, respectively. **10A** is of very low solubility in most organic



10A

10A′ **10B**

solvents. Each bis adduct displays two *t*-Bu signals, two signals for the aromatic protons of the phenol rings, and a pair of doublets for the bridgehead and vinylic protons. The patterns of the methylene protons are identical to the starting material and appear as two pairs of doublets for **10A**, six doublets (in a 1:1:1:1:2:2 ratio) for **10B**, and a pair of doublets and an AB quartet for **10A′**. The fact that the symmetry of the starting bis(spirodienones) is retained in the adducts indicates that in each case both benzyne additions occurred with the same diastereofacial discrimination; i.e., the addition took place either in an exo–exo or endo–endo fashion.

For assigning the stereochemistry of the bis-adducts formed we compared the ^{1}H NMR spectra of the compounds. The largest difference in the chemical shifts was observed for the vinylic protons. The vinyl proton signal is at a "normal" chemical shift for **10A′** (δ 6.06 (J = 2.2 Hz)), shifted upfield for **10A** (δ 4.97 (J = 2.3 Hz)), and downfield for **10B** (δ 6.83 (J = 2.2 Hz)). This difference in chemical shifts probably reflects the different environments of the vinylic protons in each compound and may be used for assigning the stereochemistry of each bis-adduct obtained, provided that the conformation and geometric parameters of the exo–exo and endo–endo forms are known. In order to obtain this structural information we resorted to MACROMODEL MM2 calculations. According to the latter the exo–exo bis-adducts of **4B** and **4A** are more stable than their corresponding endo–endo forms by 14.1 and 5.1 kcal mol^{-1}, respectively, while for **4A′** the endo–endo form is more stable by 7.6 kcal mol^{-1} than the exo–exo form. Examination of the calculated geometries for the bis-adducts of **4B** shows that only the exo–exo form can explain the upfield resonance of the vinylic proton observed for **10B**. In this conformation the two vinylic protons are pushed toward each other (calculated H/H distance 2.0 Å) and this should result in van der Waals deshielding of these protons.[38] According to the calculated geometries of the adducts of **4A′** in the exo–exo form the vinylic protons are located above a neighboring phenoxy ring, whereas in the endo–endo form they are at a "normal" environment. Since the NMR spectrum shows a very marked shielding of the vinylic protons, it can be concluded that the stereochemistry of **10A′** is exo–exo. In the case of **4A** both endo–endo and

(37) Adams, R.; Johnson, J. R.; Wilcox, C. F., Jr. *Laboratory Experiments in Organic Chemistry*; Macmillan: New York, 1970; p 452.
(38) Günther, H. *NMR Spectroscopy*; Wiley: Chichester, 1980; p 88.

exo–exo adducts should display vinylic protons at "normal" environments, and therefore we cannot assign the stereochemistry (endo–endo or exo–exo) of **10A**.

In contrast with the parent system **4**, the adducts **10** do not isomerize in solution. For example, reflux of a solution of **10A'** in toluene for 66 h did not result in any appreciable isomerization as judged by NMR. The increased kinetic stability of **10A'** as compared to **4A'** is probably the result that the homolytic cleavage of the spiro bonds in **10** does not result in the aromatization of the enone. It should be noted also that the isomerization **10A** ⇌ **10B** (or **10A'** ⇌ **10B**) requires, in addition to the cleavage of the spiro C–O bonds, the additional cleavage and formation of two C–C bonds.

Conclusions. The mild oxidation of *p-tert*-butylcalix[4]arene (**1**) results in the formation of a mixture of **4A** + **4A'** + **4B** in which the binding OH groups were transformed into carbonyl and ether groups. These compounds which easily revert to **1** undergo Diels–Alder addition and chloro-de-*tert*-butylation. Compounds **4** and **10** represent the first examples in which the hydroxylic oxygen groups of a calixarene have been converted into nonquinonic carbonyl oxygens.

Experimental Section

NMR spectra were recorded on a Bruker WP-200- and AMX-400-MHz pulsed FT spectrometers. Melting points were determined on a Mel-Temp apparatus and are uncorrected.

Molecular Mechanics Calculations. For the calculations of the structures we used the MM2 force field as implemented in MACROMODEL V 3.0. Structures were minimized using the block-diagonal Newton Raphson procedure. All structures were characterized as minima (no negative eigenvalues in the second-derivative matrix).

X-ray Crystal Structural Analysis. Data were measured on a ENRAF-NONIUS CAD-4 automatic diffractometer. Cu K_α (λ = 1.54178 Å) radiation with a graphite crystal monochromator in the incident beam was used. Intensities were corrected for Lorenz and polarization effects. All non-hydrogen atoms were found by using the results of the SHELXS-86 direct method analysis. After several cycles of refinement[39] the positions of the hydrogen atoms were calculated and added to the refinement process. The crystallographic data for **4A**, **4A'**, and **4B** are collected in Table I (supplementary material).

2,8,13,19-Tetrakis(1,1-dimethylethyl)-11*H*,22*H*-4,6:6,10:15,17:17,21-tetramethanodibenzo[*b*,*k*][1,10]dioxacyclooctadecin-23,25-dione (4A). To a solution of 10.12 g of **1** (15.6 mmol) in 400 mL of CH_2Cl_2 was dropped with stirring 11.73 g of phenyltrimethylammonium tribromide (31.2 mmol) dissolved in 150 mL of CH_2Cl_2 during 1 h, and then 505 g of a 28% aqueous NaOH solution was dropped during 30 min. The solution was refluxed under stirring for 4 h. The solution was cooled to rt, 50 mL of CH_2Cl_2 and 50 mL water were added, and after phase separation the organic phase was washed with brine, water, and then dried ($MgSO_4$). After the organic solvent was evaporated, the residue was chromatographed (silica, eluent: chloroform) and the compounds isolated were recrystallized from MeCN yielding 2.72 g of **4A** (4.2 mmol, 27%), mp 270 °C, 0.92 g of **4A'** (1.42 mmol, 9.1%), mp 254–256 °C dec, and 0.90 g of **4B** (1.4 mmol, 9%), mp 270 °C.

4A: ^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 1.00 (s, *t*-Bu, 18 H), 1.31 (s, *t*-Bu, 18 H), 2.81 (d, ^3J = 14.3 Hz, ^4J = 1.4 Hz, CH_2, 2 H), 3.00 (d, J = 15.4 Hz, CH_2, 2 H), 3.73 (d, J = 15.4 Hz, CH_2, 2H), 4.10 (d, J = 14.1 Hz, CH_2, 2 H), 5.82 (d, J = 2.3 Hz, C=CH, 2H), 6.59 (t, J = 2.1 Hz, C=CH, 2 H), 7.00 (d, J = 1.5 Hz, ArH, 2 H), 7.07 (s, ArH, 2 H); ^{13}C NMR ($CDCl_3$, rt) δ 27.96, 28.43 (C*Me*$_3$), 31.87 (C*Me*$_3$), 34.11, 34.27, 38.07, 81.73 (C(sp^3)O), 119.94, 122.69, 125.47, 126.19, 127.18, 134.77, 138.49, 143.32, 144.54, 153.58, 195.66 (C=O); IR ν_{CO} = 1670 cm^{-1} (s) 1650 cm^{-1} (w); UV (CH_2Cl_2) (λ_{max} = 230.7 nm ϵ = 21 800); MS (CI, methane) *m/z* 645 (B, MH$^+$) 589 (40, M – (*t*-Bu). Anal. Calcd for $C_{44}H_{52}O_4$: C, 81.95; H, 8.13. Found: C, 78.84; H, 8.52.[40]

4A': ^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 1.09 (s, *t*-Bu, 18 H), 1.26 (s, *t*-Bu, 18 H), 3.01 (d, J = 15.2 Hz, CH_2, 2 H), 3.36 (d, J = 16.4 Hz, CH_2, 4 H), 4.04 (d, J = 16.0 Hz, CH_2, 2 H), 5.88 (d, J = 2.0 Hz, C=CH, 2 H), 6.83 (d, 2 H), 6.95 (s, ArH, 2 H), 6.98 (s, ArH, 2 H); ^{13}C NMR ($CDCl_3$, rt) δ 28.56 (C*Me*$_3$), 31.73 (C*Me*$_3$), 33.05, 34.03, 34.12, 40.20, 80.94 (C(sp^3)O), 119.27, 119.41, 125.33, 127.83, 128.01, 133.81, 136.08, 142.83, 143.26, 153.42, 197.47 (C=O); IR ν_{CO} = 1670 (s), 1640 (sh) cm^{-1}.

4B: ^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 1.13 (s, *t*-Bu, 18 H), 1.24 (s, *t*-Bu, 18 H), 2.54 (d, J = 12.5 Hz, CH_2, 1 H), 2.96 (d, J = 15.5 Hz, CH_2, 2 H), 3.26 (d, J = 13.2 Hz, CH_2, 1 H), 3.72 (d, J = 15.5 Hz, CH_2, 2 H), 4.12 (d, J = 13.1 Hz, CH_2, 1 H), 4.29 (d, J = 12.3 Hz, CH_2, 1 H), 5.91 (d, J = 2.3 Hz, C=CH, 2 H), 6.80 (d, J = 2.2 Hz, C=CH, 2 H), 6.95 (s, ArH, 2 H), 7.14 (s, ArH, 2 H); ^{13}C NMR ($CDCl_3$, rt), δ 28.37 (C*Me*$_3$), 29.12, 31.76 (C*Me*$_3$), 31.87, 34.18, 34.31, 37.69, 81.68 (C(sp^3)O), 119.59, 122.57, 125.60, 126.49, 127.46, 135.54, 135.91, 143.67, 145.44, 152.73, 195.07 (C=O); IR ν_{CO} = 1690 cm^{-1}; MS (CI) (isobutane) *m/z* 645.30 (MH$^+$, 100), 589.50, 19.

2,15,28,32-Tetrakis(1,1-dimethylethyl)-7*H*,13*H*,20*H*,26*H*-7,12:20,25-dietheno-4,6:6,12:17,19:25-tetramethanotetrabenzo[*b*,*f*,*k*,*o*]dioxacyclooctadecin-29,33-dione (10A). To a solution of **4A** (50 mg, 0.077 mmol) in 5 mL of 1,2-dichloroethane were added benzenediazonium-2-carboxylate (50 mg, 0.27 mmol) and, dropwise, 3 mL of propylene oxide. After 1 h of reflux, the mixture was cooled and the solid obtained (**10A**) was filtered.

10A: ^{1}H NMR (400 MHz, $CDCl_3$, rt), δ 0.96 (s, *t*-Bu, 18 H), 1.26 (s, *t*-Bu, 18 H), 2.84 (d, J = 17.0 Hz, CH_2, 2 H), 2.98 (d, J = 15.8 Hz, CH_2, 2 H), 3.11 (d, J = 14.5 Hz, CH_2, 2 H), 4.08 (d, J = 2.3 Hz, C_q-H, 2 H), 4.29 (d, J = 14.1 Hz, CH_2, 2 H), 4.97 (d, J = 2.4 Hz, C_q-H, 2 H), 6.97 (s, ArH, 2 H), 7.00 (s, ArH, 2 H), 7.18–7.34 (m, PhH, 8 H); ^{13}C NMR ($CDCl_3$, rt) δ 27.53 (C*Me*$_3$), 27.90, 31.87 (C*Me*$_3$), 34.22, 34.52, 39.38, 51.96, 57.16, 80.36 (C(sp^3)O), 119.89, 119.93, 120.06, 121.85, 125.77, 126.95, 127.16, 127.64, 141.29, 143.79, 152.92, 155.47, 197.0 (C=O); IR ν_{CO} = 1725 cm^{-1}; MS (CI) (methane) *m/z* 797.08 (MH$^+$, 14), (769.0, B); mp >450 °C. Anal. Calcd for $C_{56}H_{60}O_4$: C, 84.38; H, 7.59. Found: C, 77.97; H, 7.97.

Preparation of 10B. To a solution of **4B** (20 mg, 0.3 mmol) in 5 mL of 1,2-dichloroethane were added benzendiazonium-2 carboxylate hydrochloride (20 mg, 0.1 mmol) and, dropwise, 3 mL of propylene oxide. After 1 h of reflux under stirring the mixture was cooled and filtered and the filtrate evaporated. The residue obtained was triturated with 3 mL of petroleum ether. The solid obtained (**10A**) was filtered and the filtrate evaporated to yield 20 mg (82%) of **11B**. The compound was recrystallized from dichloromethane, mp 275–280 °C: ^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 1.10 (s, *t*-Bu, 18 H), 1.18 (s, *t*-Bu, 18 H), 2.79 (d, J = 13.7 Hz, CH_2, H), 2.88 (d, J = 15.8 Hz, CH_2, H), 3.04 (d, J = 15.8 Hz, CH_2, H), 3.26 (d, J = 13.2 Hz, CH_2, H), 3.99 (d, J = 13.1 Hz, CH_2, H), 4.01 (d, J = 13.6 Hz, CH_2, H), 4.13 (d, J = 2.0 Hz, C_q-H, 2 H), 6.78 (d, J = 1.8 Hz, C=CH, 2 H), 6.83 (d, J = 2.2 Hz, 2 H), 7.02 (d, J = 1.8 Hz, 2 H), 7.15–7.44 (m, ArH, 8 H); ^{13}C NMR ($CDCl_3$, rt) δ 25.36, 26.91, 28.12 (C*Me*$_3$), 31.74 (C*Me*$_3$), 34.13, 34.97, 37.33, 52.75, 59.32, 80.47 (C(sp^3)O), 119.48, 120.91, 122.18, 124.01, 125.24, 125.75, 126.45, 126.52, 127.55, 141.54, 143.28, 144.19, 153.41, 154.5, 194.56 (C=O); IR ν_{CO} = 1735 cm^{-1}; MS (CI) *m/z* 797.1 (MH$^+$, B), 711.3 (58). Anal. Calcd for $C_{56}H_{60}O_4$: C, 84.38; H, 7.59. Found: C, 83.19; H, 8.29.

Preparation of 10A'. The compound was prepared according to the procedure described for **10A** and was recrystallized from acetonitrile, mp 367 °C: ^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 1.21 (s, *t*-Bu, 18 H), 1.24 (s, *t*-Bu, 18 H), 2.80 (d, J = 15.6 Hz, CH_2, 2 H), 2.86 (d, J = 15.6 Hz, CH_2, 2 H), 3.45 (d, J = 16.6 Hz, CH_2, 2 H), 3.83 (d, J = 16.6 Hz, CH_2, 2 H), 4.13 (d, J = 2.1 Hz, CH, 2 H), 6.06 (d, J = 2.1 Hz, C=CH, 2 H), 6.85 (s, 2 H, ArH), 7.04 (s, 2 H, ArH), 7.18–7.30 (m, ArH, 6 H, C_6H_4), 7.56 (d, J = 8 Hz, C_6H_4); ^{13}C NMR ($CDCl_3$, rt) δ 28.39 (C*Me*$_3$), 31.83 (C*Me*$_3$), 34.09,

(39) All crystallographic computing was done on a VAX computer using the TEXAN structure analysis package.

(40) We could not get satisfactory microanalytical data for **4** and **10**. This seems to be a property for several calixarene systems. See: Böhmer, V.; Jung, K.; Schön, M.; Wolff, A. *J. Org. Chem.* **1992**, *57*, 790.

34.83, 38.90, 53.20, 56.23, 81.61 (C(sp^3)O), 119.55, 120.03, 121.65, 125.27, 125.34, 126.23, 126.80, 127.23, 128.87, 141.13, 142.51, 143.12, 153.88, 155.58, 194.99 (C=O); IR ν_{CO} = 1720 cm^{-1}; MS (CI) *m/z* 797.1 (MH^+, B).

Reaction of 4A with $NaBH_3CN$. A mixture of **4A** (30 mg, 0.046 mmol), ammonium acetate (28.7 mg, 0.372 mmol), and $NaCNBH_3$ (1.63 mg, 0.026 mmol) in 3 mL of methanol was stirred at rt for 18 h, and a solution of concd HCl was dropped into the mixture until a pH < 2 was reached. The ^1H NMR spectrum of the residue indicates that it is composed of a mixture of **4A** and **1**.

Attempted Oxidation of 5. The reaction was carried out in conditions similar to the ones used for the preparation of **4**. To a solution of 30 mg (0.047 mmol) of **5** in 10 mL of CH_2Cl_2 were added 45.7 mg (0.095 mmol) tetrabutylammonium tribromide and 10 g of a 28% solution of NaOH. After the usual workup the residue was analyzed by ^1H NMR which showed the exclusive presence of the starting material.

11,23-Di-*tert*-butyl-5,17-dichloro-25,26,27,28-tetrahydroxycalix[4]arene (7). **4A** (0.1 g, 0.155 mmol) was dissolved in 200 mL MeCN, and to the solution was added 7 mL of concd HCl. After the mixture was refluxed for 40 min, the solvent was evaporated yielding a large amount of solid material. The solid was treated with $CHCl_3$ and the material filtered. Evaporation of the filtrate yielded a solid which was recrystallized from MeCN/$CHCl_3$ (3:1) yielding 50 mg (0.08 mmol, 53%) **7**, mp 355–360 °C (lit.[36] mp > 300 °C): ^{13}C NMR ($CDCl_3$) δ 31.44, 31.94, 34.15, 126.09, 126.53, 126.80, 128.64, 129.89, 145.23, 147.29.

Reaction of **5**[25] under similar conditions yielded 11,17,23-tri-*tert*-butyl-5-chloro-25,26,27,28-tetrahydroxycalix[4]arene (**8**) in 60% yield, mp (MeCN) 339–342 °C (lit.[36] mp 354–355 °C): ^1H NMR (400 MHz, $CDCl_3$, rt) δ 1.18 (s, *t*-Bu, 9 H), 1.22 (s, *t*-Bu, 18 H), 3.45 (d (broad), CH_2, 2 H), 3.48 (d(broad), CH_2, 2 H), 4.22 (d (broad), CH_2, 4 H), 7.00 (s, ArH 2 H), 7.01 (d, J = 2.4 Hz, ArH, 2 H), 7.03 (s, ArH, 2 H), 7.09 (d, J = 2.4 Hz, ArH, 2 H) (lit.[36] δ 1.16, 1.18, 3.84, ~7.16 ppm); ^{13}C NMR ($CDCl_3$) δ 31.36, 31.42, 32.09, 32.40, 33.98, 34.08, 125.64, 125.88, 126.16, 126.31, 126.59, 127.47, 128.08, 128.54, 130.11, 144.68, 144.82, 146.18, 146.55, 147.78.

Reduction of 4A with $Et_3SiH/RhCl(PPh_3)_3$. To 10 mL of dry benzene were added 97.8 mg of **4B**, 0.022 mg of $RhCl(PPh_3)_3$, and 0.6 mL of Et_3SiH, and the mixture was kept at 60–70 °C for 4 h. After filtration through a small amount of silica the solvent was evaporated. Chromatography (silica, eluent: $CHCl_3$/hexane (3:1)) yielded 50% of **1** which was identified by its spectral properties. When a similar reaction was carried out with **4A**, **1** was obtained in 45% yield.

Reaction of 5 with Acids. To 25 mL of toluene were added 100 mg of a mixture of **4A** and **4B** and 100 mg of tosylic acid, and the mixture was refluxed for 90 min. The solvent was evaporated to half the volume and the solution decanted from the oil which was formed. Evaporation of the liquid gave **1** as shown by NMR.

Catalytic Hydrogenation of 4A. To a 1-L hydrogenation bomb were added a solution of 200 mg of **4A** in 15 mL of ethanol and 20 mg of Rh/Al_2O_3. The mixture was shaken for 4 h at 80 °C under 55 psi H_2. Evaporation of the solvent gave, as shown by NMR, a mixture of **4A** and **1**.

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Supplementary Material Available: Summary of X-ray diffraction data for compounds **4A**, **4A'**, and **4B** (1 page). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.