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Selective Synthesis and Isolation of All Possible Conformational Isomers of Proximally Para-Disubstituted Calix[4]arene

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All six possible conformational isomers of the proximally *p*-dibrominated calix[4]arene tetraalkyl ether, **1a**−**f***, were selectively synthesized by appropriate control of stereochemistry during di-*O*-alkylation reactions of 5,11-dibromocalix[4]arene *syn*-dialkyl ethers, namely, 5,11-dibromo-27,28-dihydroxy-25,26-dipropoxy-, 5,11-dibromo-25,26-dihydroxy-27,28-dipropoxy-, 5,11-dibromo-25,28-dihydroxy-26,27-propoxy-, and 5,11-dibromo-26,28-dihydroxy-25,27-dipropoxycalix[4]arenes. Their conformations were confirmed by ^{1}H and ^{13}C NMR spectroscopy and are cone for **1a** (**u**$^{Br}{}_{Pr}$, u$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,u$^{H}{}_{Pr}$), partial cone for **1b*** (**u**$^{Br}{}_{Pr}$, d$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,u$^{H}{}_{Pr}$) and **1d*** (**u**$^{Br}{}_{Pr}$, u$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,d$^{H}{}_{Pr}$), 1,2-alternate for **1c** (**u**$^{Br}{}_{Pr}$, u$^{Br}{}_{Pr}$, d$^{H}{}_{Pr}$,d$^{H}{}_{Pr}$) and **1e*** (**u**$^{Br}{}_{Pr}$, d$^{Br}{}_{Pr}$, d$^{H}{}_{Pr}$,u$^{H}{}_{Pr}$), and 1,3-alternate for **1f*** (**u**$^{Br}{}_{Pr}$, d$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,d$^{H}{}_{Pr}$). Although both **1c** and **1e*** are in the 1,2-alternate conformation, the conformation of **1e*** was found to be strongly distorted and distinct from that of **1c**.

Introduction

A large number of papers have appeared dealing with calixarenes, the third generation of supramolecules after cyclodextrins and crown ethers, especially regarding their structure and functionalization, since they are readily available from cheap starting materials and represent very attractive building blocks for the design of more sophisticated molecules with specific properties.[1] Among the parent compounds, calix[4]arenes have received the most attention due to their unique cavity-shaped architecture. A number of synthetic procedures for the selective functionalization of calix[4]arenes either at the positions of endo hydroxyl groups (endo positions) or at the para positions (exo positions) have been developed during the past two decades, and considerable effort has been directed toward understanding the factors that control the conformational outcome under certain reaction conditions. Consequently, a variety of calix[4]arenes having pair(s) of functional groups on the endo positions and/or on the exo positions with a distal (1,3- or A,C-) regiochemistry have become available and, in some cases, the procedures for the stereoselective synthesis of particular conformers have been well-established.[2]

On the contrary, much less attention has been paid to calix[4]arenes with a proximal (1,2- or A,B-) regiochemistry.[3−6] In particular, only a limited number of 1,2-disubstituted and 1,2-bridged calix[4]arenes at the exo positions have been reported.[5,6,10f,i] For example, 5,11-diphenyl- and 5,11-dimethyl-17,23-di-*tert*-butylcalix[4]arenes can be prepared by a multistep process[5a] and/or a fragment condensation of suitable dimers.[5b] On the other hand, 5,11-dinitrocalix[4]arene tetrapropyl ether,[5c] 5,11-di-*tert*-butyl-17,23-dinitrocalix[4]arene tetrapropyl ether,[5d] and 5,11-diformylcalix[4]arene tetraoctyl ether[5h] are separated from a mixture of their regioisomers. In addition, 5,11-dibromocalix[4]arene tetrapropyl ether[5j] can be prepared by a regioselective bromination, based on differences in reactivity para to the free phenolic

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(1) For representative reviews on calixarenes, see: (a) Gutsche, C. D. *Calixarenes*; Monographs in Supramolecular Chemistry; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, UK, 1989. (b) *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Topics in Inclusion Science 3; Vicens, J., Böhmer, V., Eds.; Kluwer: Dordrecht, The Netherlands, 1991. (c) Shinkai, S. *Tetrahedron* **1993**, *49*, 8933−8968. (d) Takeshita, M.; Shinkai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1088−1097. (e) Böhmer, V. *Angew. Chem.* **1995**, *107*, 785; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713−745. (f) Pochini, A.; Ungaro, R. In *Comprehensive Supramolecular Chemistry*; Vögtle, F., Ed.; Pergamon Press: Oxford, UK, 1996; Vol. 2, pp 103−142. (g) Gutsche, C. D. *Caixarenes Revisited*; Monographs in Supramolecular Chemistry; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, UK, 1998. (h) *Calixarenes in Action*; Mandolini, L., Ungaro, R., Eds.; Imperial College Press: London, UK, 2000. (i) *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer: Dordrecht, The Netherlands, 2001.

(2) For 1,3-disubstituted and bridged calix[4]arenes, see ref 1g, Chapter 5.

(3) For 1,2-disubstituted calix[4]arenes on *endo* positions, see: (a) Bottino, F.; Giunta, L.; Pappalardo, S. *J. Org. Chem.* **1989**, *54*, 5407−5409. (b) Groenen, L. C.; Ruël, B. H. M.; Casnati, A.; Timmerman, P.; Verboom, W.; Harkema, S.; Pochini, A.; Ungaro, R.; Reinhoudt, D. N. *Tetrahedron Lett.* **1991**, *32*, 2675−2678. (c) See: K. A.; Fronczek, F. R.; Waston, W. H.; Kashyap, R. P.; Gutsche, C. D. *J. Org. Chem.* **1991**, *56*, 7256−7268. (d) Gutsche, C. D.; Reddy, P. A. *J. Org. Chem.* **1991**, *56*, 4783−4791. (e) Araki, K.; Iwamoto, K.; Shigematsu, S.; Shinkai, S. *Chem. Lett.* **1992**, 1095−1098. (f) Brunink, J. A. J.; Verboom, W.; Engbersen, J. F. J.; Harkema, S.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1992**, *111*, 511−516. (g) Pappalardo, S.; Giunta, L.; Foti, M.; Ferguson, G.; Gallagher, J. F.; Kaitner, B. *J. Org. Chem.* **1992**, *57*, 2611−2624. (h) Park, Y. J.; Shin, J. M.; Nam, K. C.; Kim, J. M.; Kook, S.-K. *Bull. Korean Chem. Soc.* **1996**, *17*, 643−647. (i) Shu, C.-m.; Yuan, T.-s.; Ku, M.-c.; Ho, Z.-c.; Liu, W.-c.; Tang, F.-s.; Lin, L.-g. *Tetrahedron* **1996**, *52*, 9805−9818. (j) Pappalardo, S. *New. J. Chem.* **1996**, *20*, 465−472. (k) Markovsky, L. N.; Viscotsky, M. A.; Pirozhenko, V. V.; Kalchenko, V. I.; Lipkowski, J.; Yu, A. *Chem. Commun.* **1996**, 69−71. (l) Dieleman, C. B.; Marsol, C.; Matt, D.; Kyritsakas, N.; Harriman, A.; Kintzinger, J.-P. *J. Chem. Soc., Dalton Trans.* **1999**, 4139−4148. (m) Bocheńska, M.; Banach, R.; Zieliñska, A.; Kravtsov, V. Ch. *J. Inclusion Phenom. Macrocycl. Chem.* **2001**, *39*, 219−228.

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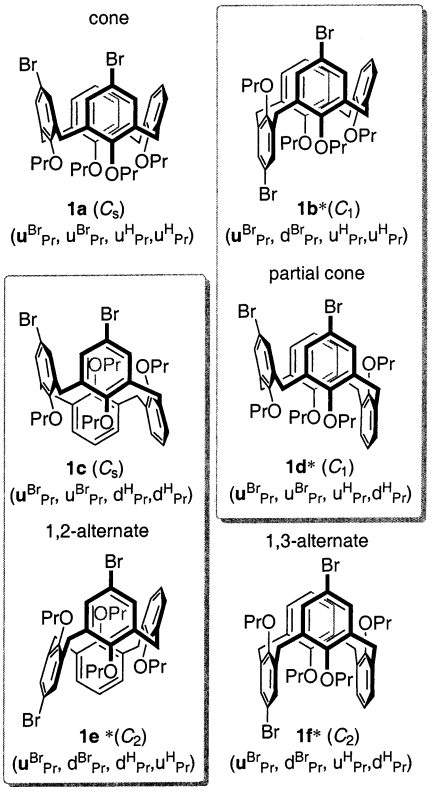
groups versus ethers.[5e,j,7,10f,i] However, no conformational study of calix[4]arenes with a proximal regiochemistry appears to have been conducted, in contrast to those with a distal regiochemistry.

We describe herein the selective synthesis and isolation of all possible conformational isomers of 5,11-dibromocalix-

CHART 1



[4]arene tetrapropyl ether with a proximal regiochemistry, which are one cone ($\mathbf{u}^{Br}_{Pr}$, u^{Br}_{Pr}, u^{H}_{Pr},u^{H}_{Pr}), two partial cone (($\mathbf{u}^{Br}_{Pr}$, d^{Br}_{Pr}, u^{H}_{Pr},u^{H}_{Pr}) and (u^{Br}_{Pr}, u^{Br}_{Pr}, u^{H}_{Pr},d^{H}_{Pr})), two 1,2-alternate (($\mathbf{u}^{Br}_{Pr}$, u^{Br}_{Pr}, d^{H}_{Pr},d^{H}_{Pr}) and ($\mathbf{u}^{Br}_{Pr}$, d^{Br}_{Pr}, d^{H}_{Pr},u^{H}_{Pr})), and one 1,3-alternate ($\mathbf{u}^{Br}_{Pr}$, d^{Br}_{Pr}, u^{H}_{Pr},d^{H}_{Pr}) conformers (Chart 1). It is well-known that *p*-bromocalix[4]arenes are useful intermediates, since bromine-to-lithium exchange reactions proceed selectively and offer a simple route to substituted calix[4]arenes with a variety of functionalities[8] and regiocontrol at the para positions.[9] In addition, the four conformational isomers of 5,11-dibromocalix[4]arene tetrapropyl ether, namely two partial, one 1,2-alternate, and one 1,3-alternate conformers, are inherently chiral.[5i,10] The rest, however, can serve as versatile synthetic precursors to inherently chiral molecules with specific functionalities. Thus, the conformational isomers of 5,11-dibromocalix[4]arene tetraalkyl ether represent very attractive building blocks for the design of synthetic receptors with chiral discrimination ability.

Results and Discussion

Synthesis of Proximally Para-Disubstituted Calix[4]arene Dialkyl Ethers. As a working hypothesis, we assumed that all six possible conformational isomers of the proximally *p*-dibrominated calix[4]arene tetraalkyl ether can be prepared by appropriate stereochemical control during di-*O*-alkylation reactions of 5,11-dibromocalix[4]arene *syn*-dialkyl ethers. We thus synthesized all four possible calix[4]arene *syn*-dipropyl ethers **5**,[5j] **10**, **12***,[11] and **13*** according to Scheme 1. Initially, 25,26-

(4) For 1,2-bridged calix[4]arenes at *endo* positions, see: (a) Arduini, A.; Casnati, A.; Dodi, L.; Pochini, A.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1990**, 1597−1598. (b) van Loon, J.-D.; Kraft, D.; Ankoné, M. J. K.; Verboom, W.; Harkema, S.; Vogt, W.; Böhmer, V.; Reinhoudt, D. N. *J. Org. Chem.* **1990**, *55*, 5176−5179. (c) Yamamoto, H.; Sakaki, T.; Shinkai, S. *Chem. Lett.* **1994**, 469−472. (d) Arduini, A.; Fabbi, M.; Mantovani, M.; Mirone, L.; Pochini, A.; Secchi, A.; Ungaro, R. *J. Org. Chem.* **1995**, *60*, 1454−1457. (e) Pappalardo, S.; Petringa, A.; Parisi, M. F.; Ferguson, G. *Tetrahedron Lett.* **1996**, *37*, 3907−3910. (f) Arduini, A.; McGregor, W. M.; Paganuzzi, D.; Pochini, A.; Secchi, A.; Ugozzoli, F.; Ungaro, R. *J. Chem. Soc., Perkin Trans. 2* **1996**, 839−846. (g) Arnaud-Neu, F.; Caccamese, S.; Fuangswasdi, S.; Pappalardo, S.; Parisi, M. F.; Petringa, A.; Principato, G. *J. Org. Chem.* **1997**, *62*, 8041−8048. (h) Arduini, A.; Domiano, L.; Pochini, A.; Secchi, A.; Ungaro, R.; Ugozzoli, F.; Struck, O.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron* **1997**, *53*, 3767−3776. (i) Arnaud-Neu, F.; Ferguson, G.; Fuangswasdi, S.; Notti, A.; Pappalardo, S.; Parisi, M. F.; Petringa, A. *J. Org. Chem.* **1998**, *63*, 7770−7779. (j) Ferguson, G.; Lough, A. J.; Notti, A.; Pappalardo, S.; Parisi, M. F.; Petringa, A. *J. Org. Chem.* **1998**, *63*, 9703−9710. (k) Ozerov, O. V.; Ladipo, F. T.; Patrik, B. O. *J. Am. Chem. Soc.* **1999**, *121*, 7941−7942. (l) Arduini, A.; Böhmer, V.; Delmau, L.; Desreux, J.-F.; Dozol, J.-F.; Carrera, M. A. G.; Lambert, B.; Musigmann, C.; Pochini, A.; Shivanyuk, A.; Ugozzoli, F. *Chem. Eur. J.* **2000**, *6*, 2135−2144. (m) Narumi, F.; Morohashi, N.; Matsumura, N.; Iki, N.; Kameyama, H.; Miyano, S. *Tetrahedron Lett.* **2002**, *43*, 621−625. (n) Mathieu, A.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **2002**, *43*, 1225−1229.

(5) For 1,2-disubstituted calix[4]arenes on *exo* positions, see: (a) Ho, K. H.; Gutsche, C. D. *J. Org. Chem.* **1982**, *47*, 2713−2719. (b) Böhmer, V.; Merkel, L.; Kunz, U. *J. Chem. Soc., Chem. Commun.* **1987**, 896−897. (c) Kelderman, E.; Derhaeg, L.; Heesink, G. J. T.; Verboom, W.; Engbersen, J. F. J.; van Hulst, N. F.; Persoons, A.; Reinhoudt, D. N. *Angew. Chem.* **1992**, *104*, 1107; *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1075−1077. (d) Verboom, W.; Durie, A.; Egberink, R. J. M.; Asfari, Z.; Reinhoudt, D. N. *J. Org. Chem.* **1992**, *57*, 1313−1316. (e) Pappalardo, S.; Giunta, L.; Foti, M.; Ferguson, G.; Gallagher, J. F.; Kaitner, B. *J. Org. Chem.* **1992**, *57*, 2611−2624. (f) Timmerman, P.; Verboom, W.; van Veggel, F. C. J. M.; van Hoorn, W. P.; Reinhoudt, D. N. *Angew. Chem.* **1994**, *106*, 1313; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1292−1295. (g) Timmerman, P.; Verboom, W.; Reinhoudt, D. N.; Arduini, A.; Grandi, S.; Sicuri, A. R.; Pochini, A.; Ungaro, R. *Synthesis* **1994**, 185−189. (h) Arduini, A.; Fanni, S.; Manfredi, G.; Pochini, A.; Ungaro, R.; Sicuri, A. R.; Ugozzoli, F. *J. Org. Chem.* **1995**, *60*, 1448−1453. (i) Caccamese, S.; Bottino, A.; Cunsolo, F.; Parlato, S.; Neri, P. *Tetrahedron: Asymmetry* **2000**, *11*, 3103−3112. (j) Gagnon, J.; Vézina, M.; Drouin, M.; Harvey, P. D. *Can. J. Chem.* **2001**, *79*, 1439−1446.

(6) For 1,2-bridged calix[4]arenes at *exo* positions, see: Ikeda, A.; Yoshimura, M.; Lhotak, P.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1945−1950.

(7) van Loon, J.-D.; Arduini, A.; Verboom, W.; Ungaro, R.; van Hummel, G. J.; Harkema, S.; Reinhoudt, D. N. *Tetrahedron Lett.* **1989**, *30*, 2681−2684.

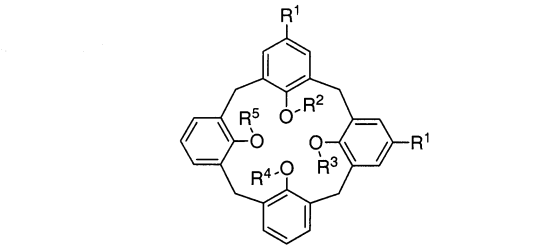
(8) (a) Gutsche, C. D.; Pagoria, P. F. *J. Org. Chem.* **1985**, *50*, 5795−5802. (b) Peak, K.-S.; Kim, H.-J.; Chang, S.-K. *Supramol. Chem.* **1995**, *5*, 83−85. (c) Ohseto, F.; Yamamoto, H.; Matsumoto, H.; Shinkai, S. *Tetrahedron Lett.* **1995**, *36*, 6911−6914. (d) Ihm, H.; Paek, K. *Bull. Korean Chem. Soc.* **1995**, *16*, 71−73. (e) Lhoták, P.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 645−648. (f) Larsen, M.; Jørgensen, M. *J. Org. Chem.* **1997**, *62*, 4171−4173.

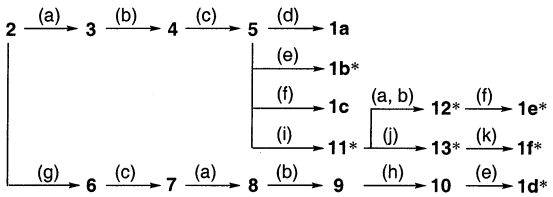
(9) (a) Larsen, M.; Jørgensen, M. *J. Org. Chem.* **1996**, *61*, 6651−6655. (b) see ref 1g, pp 106−107.

(10) For inherently chiral calix[4]arenes with dissymmetry or asymmetry via substitution patters at *exo* and *endo* positions, see: (a) Iwamoto, K.; Shimizu, H.; Araki, K.; Shinkai, S. *J. Am. Chem. Soc.* **1993**, *115*, 3997−4006 (*Corrigendum* **1993**, *115*, 12228) and references therein. (b) Böhmer, V.; Kraft, D.; Vogt, W. *Supramol. Chem.* **1994**, *3*, 299−301. (c) Ferguson, G.; Gallagher, J. F.; Giunta, L.; Neri, P.; Pappalardo, S.; Parisi, M. *J. Org. Chem.* **1994**, *59*, 42−53. (d) González, J. J.; Nieto, P. M.; Prados, P.; Echavarren, A. M.; de Mendoza, J. *J. Org. Chem.* **1995**, *60*, 7419−7423. (e) Reference 4g and references therein. (f) Vysotsky, M. O.; Tairov, M. O.; Pirozhenko, V. V.; Kalchenko, V. I. *Tetrahedron Lett.* **1998**, *39*, 6057−6060. (g) Shu, C.-M.; Chung, W.-S.; Wu, S.-H.; Ho, Z.-C.; Lin, L.-G. *J. Org. Chem.* **1999**, *64*, 2673−2679. (h) Dieleman, C.; Steyer, S.; Jeunesse, C.; Matt, D. *J. Chem. Soc., Dalton Trans.* **2001**, 2508−2517. (i) Tairov, M. A.; Vysotsky, M. O.; Kalchenko, O. I.; Pirozhenko, V. V.; Kalchenko, V. I. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1405−1411.

(11) Inherently chiral calix[4]arenes are designated with an asterisk (*).

SCHEME 1[a]





compd	R^1	R^2	R^3	R^4	R^5
2	H	H	H	H	H
3	H	H	H	Allyl	Allyl
4	H	H	H	Pr	Pr
5	Br	H	H	Pr	Pr
6	H	H	H	Bn	Bn
7	Br	H	H	Bn	Bn
8	Br	Allyl	Allyl	Bn	Bn
9	Br	Pr	Pr	Bn	Bn
10	Br	Pr	Pr	H	H
11*	Br	H	H	Pr	H
12*	Br	H	H	Pr	Pr	H
13*	Br	Pr	H	Pr	H

[a] Reagents and conditions: (a) allyl bromide, NaH, MeCN, rt; (b) H_2, Pd/C, THF, rt; (c) NBS, MEK, rt; (d) PrBr, NaH, DMF, 0 °C; (e) PrBr, Cs_2CO_3, DMF, 80 °C; (f) PrBr, *t*-BuOK, PhH, reflux; (g) BnBr, NaH, MeCN, rt; (h) $AlCl_3$, PhMe, 0 °C; (i) Me_3SiI, $CHCl_3$, reflux; (j) PrBr, $Ba(OH)_2 \cdot 8H_2O$/BaO, DMF, rt; (k) PrBr, Cs_2CO_3, acetone, reflux.

dihydroxy-27,28-dipropoxycalix[4]arene **4**[5j] in the cone conformation as a precursor to **5**, was obtained in high purity by hydrogenation of 25,26-diallyloxy-27,28-dihydroxycalix[4]arene **3**,[3b,i] prepared according to a modified literature method[3i] in 74% yield. Although the synthetic procedure for the calix[4]arene *syn*-1,2-dipropyl ether **4** via the proximal dipropylation of **2** has recently been described,[5j] the purification of **4** in the cone conformation could not be accomplished by recrystallization in our hands. Proximal dibromination at the exo positions of **4** was achieved through remote control exerted by a functionality on the endo positions to afford **5** in 83% yield. The proximally dibrominated calix[4]arene **5** in the cone conformation exhibited the expected ^{1}H and ^{13}C NMR spectral patterns for dual proximal fuctionalizations at the endo and exo positions. In particular, a set of three AB systems for $ArCH_2Ar$ in the ratio 1:2:1 and three resonances for the pertinent carbons at δ 31.77, 31.26, and 29.90 were observed.[12]

Regioisomer **10**, the calix[4]arene *syn*-dipropyl ether containing two adjacent aryl rings with a bromine atom and an *O*-propyl group, was synthesized via proximally dibenzylated calix[4]arene **6** as a key intermediate. Proximal dibromination at the exo positions of **6**, followed by a *syn*-1,2-diallylation/hydrogenation sequence, afforded **9** as a precursor to the regioisomer **10**. Treatment of **9** with $AlCl_3$ in toluene at 0 °C gave **10** in the cone conformation in 89% yield, which contains two proximally propylated phenol rings bearing bromine atoms at the para position. The ^{1}H NMR spectrum of regioisomer **10** was similar to that of **5** except for the inequivalency in the chemical shift and the signal pattern in the aromatic region. The ^{13}C NMR spectrum showed peaks at δ 31.93, 31.86, and 29.88 for four methylene bridge carbons, all of which indicates that **10** is the regioisomer, and is present in the cone conformation.

The partial depropylation of **5** with trimethylsilyl iodide afforded the inherently chiral 5,11-dibromo-26,27,28-trihydroxy-25-propoxycalix[4]arene **11*** in 94% yield as a precursor to other remaining *syn*-dipropyl ethers **12*** and **13***. The ^{1}H NMR spectrum of **11*** showed four doublets at δ 3.51, 3.42, 3.39, and 3.34, corresponding to the equatorial protons of the methylene bridges, and the ^{13}C NMR spectrum showed peaks at δ 31.71, 31.65, 31.54, and 30.91 for the four pertinent carbons. The values of the ^{13}C NMR chemical shifts[12] and ^{1}H and ^{13}C NMR spectral patterns indicate that **11*** is present in the cone conformation and is inherently chiral. Although treatment of **11*** with allyl bromide under 1,2-di-*O*-alkylation conditions followed by hydrogenation gave a mixture of two regioisomers **5** and **12*** in the ratio of 3:7, the desired *syn*-1,2-dipropyl ether **12*** could be isolated by recrystallization in 20% yield. This ratio indicates that the acidity of the phenol rings substituted with a bromine atom on the para position was enhanced by the inductive effects of the bromine. Treatment of **11*** with propyl bromide under 1,3-di-*O*-alkylation conditions selectively gave the *syn*-1,3-dipropyl ether **13*** in 62% yield. The proximally *p*-dibrominated calix[4]arene *syn*-dipropyl ethers **12*** and **13*** in the cone conformation exhibited the expected ^{1}H and ^{13}C NMR spectral patterns. In particular, a set of four AB systems for $ArCH_2Ar$ in the ratio 1:1:1:1 and four resonances for the pertinent carbons at δ 32.43, 31.75, 31.33, and 29.95, and at δ 31.58, 31.43, 31.34, and 31.26 were observed for the inherently chiral regioisomers **12*** and **13***, respectively.

Alkylations of Proximally Para-Disubstituted Calix[4]arene Dialkyl Ethers. To selectively prepare all possible conformational isomers of the 5,11-dibromocalix[4]arene tetraalkyl ether, di-*O*-alkylations of 5,11-dibromocalix[4]arene dialkyl ethers **5**, **10**, **12***, and **13*** were conducted under a variety of conditions. The results of the reaction of calix[4]arene dialkyl ether **5** with propyl bromide are summarized in Table 1. It is well-known that the conformational outcome is dependent on reaction conditions (temperature, solvent, and base), the para-substituent of calix[4]arene, and the steric demands and reactivity of the derivatizing reagent.[1b,c,e−g] The base in particular can play a pivotal role in the alkylation process. When NaH was used as a base, the cone conformer **1a** was the major product (86−97%) along with the minor partial-cone conformer **1b*** (14−3%) (entries 1−4). Reinhoudt and co-workers previously reported that the tetra-*O*-alkylation of calix[4]arene **2** in DMF using NaH as a base at room temperature proceeds via the *syn*-1,2-dialkylated product,[3b] affording the tetra-*O*-alkylated calix[4]arenes in the cone conformation.[5c] Our results are consistent with these findings, because the use of *syn*-

(12) For a single rule in ^{13}C NMR chemical shifts for determination of calix[4]arene conformations, see: Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P. M.; Sánchez, C. *J. Org. Chem.* **1991**, *56*, 3372−3376.

TABLE 1. Propylation of Calix[4]arene 5[a]

entry	base[b]	solvent	time/h	temp/°C	yield/%	rel. conformer distribution[c]/% cone **1a**	paco **1b***	1,2-alt **1c**
1	NaH	DMF	24	0	96	97	3	0
2	NaH	DMF	6	rt	96	95	5	0
3	NaH	DMF	6	reflux	100	86	14	0
4[d]	NaH	CH_3CN	6	rt	90	97	3	0
5	Cs_2CO_3[e]	DMF	15	80	99	15	85	0
6	*t*-BuOK[f]	C_6H_6	6	reflux	96	0	17	83
7	Na_2CO_3[e]	DMF	15	80	92[g]	(100)[g]	0	0

[a] 7.5 equiv of propyl bromide per OH were used. [b] 7.5 equiv of base per OH were used under standard conditions. [c] The distribution percentage was determined by ^{1}H NMR analysis of the product mixture. [d] Allyl bromide was used as an alkylating reagent, and the products were then hydrogenated with Pd/C and H_2 in THF. [e] 15 equiv of base per OH were used. [f] 2.0 equiv of base per OH were used. [g] Only tri-*O*-alkylated calix[4]arene was formed as a product.

1,2-dialkylated intermediate, that is, calix[4]arene dialkyl ether **5**, as a starting material led to the selective formation of the cone conformation.

The alkylation of **5** in the presence of Cs_2CO_3 selectively gave the partial-cone conformer **1b*** (85%) (entry 5) along with cone conformer **1a** (15%). It has been reported that the alkylation of a *syn*-1,2-diether proceeds through the intermediacy of the tri-*O*-alkylated cone conformer, and that the conformational outcome is determined in the final alkylation step, and is strongly dependent on the cation in the base applied.[3j] Accordingly, the use of Cs_2CO_3 as a base[3j,13] selectively gave the partial-cone conformer. Under the same conditions, the reaction of **10** afforded the other partial-cone conformer **1d*** (73%) along with cone conformer **1a** (27%), for which the selectivity was lower than that of **1b***. In the final alkylation step, Cs^+-induced inversion of the residual phenol ring produces a partial cone phenolate, which is less stable in the latter reaction than in the former reaction due to steric repulsion between cation and para-substituents of the three remaining aromatic rings. The decrease in selectivity is the result of destabilization.

When *t*-BuOK was used as a base, the alkylation of **5** in benzene at reflux preferentially gave the 1,2-alternate conformer **1c** (83%) along with minor partial-cone conformer **1b*** (17%) (entry 6). Moreover, the reaction of **12*** under the same conditions afforded less selectively the other 1,2-alternate conformer **1e*** (70%) along with two partial-cone conformers **1b*** and **1d*** (30%). Although several studies dealing with fixed 1,2-alternate conformers have appeared,[4e,h−k,m,14] only a limited number of tetra-*O*-substituted calix[4]arenes in the fixed 1,2-alternate conformation without intramolecular bridge are known.[14a−d]

From the alkylation of calix[4]arene *syn*-1,3-dipropyl ether **13*** in the presence of Cs_2CO_3, the 1,3-alternate conformer **1f*** was obtained as the major product (85%) along with three other conformers **1a**, **1b***, and **1d*** (15%). Often calix[4]arene derivatives in the fixed 1,3-alternate conformation can be selectively produced, when the di-*O*-alkylation of calix[4]arene *syn*-1,3-diethers[14b,15] and tetra-*O*-alkylation of parent calix[4]arenes[13,14c] are conducted with Cs_2CO_3 in THF/DMF, DMF, CH_3CN, or acetone. In the reaction of **13***, a relatively high selectivity (85%) of the desired 1,3-alternate conformer was observed. This result is consistent with the generalization that small para-substituents in the calix[4]arenes favor 1,3-alternate conformers.[14c,15a]

Conformational Features of Proximally Para-Disubstituted Calix[4]arene Tetraalkyl Ethers. The conformational isomers of proximally para-disubstituted 5,11-dibromocalix[4]arene tetrapropyl ether, **1a**−**f***, exhibited the expected ^{1}H and ^{13}C NMR spectral patterns for proximal fuctionalizations at the exo positions in each conformation. De Mendoza and co-workers reported that the resonance arising from the bridge methylene carbon is near δ 31 when two adjacent aryl groups are in the syn orientation, and near δ 37 when they are in the anti orientation.[12] Indeed, the resonances for the bridge methylene carbons are observed at δ 31.11, 31.01, and 30.83 for **1a**, at δ 35.48, 35.13, 30.69, and 30.62 for **1b***, at δ 37.79, 28.95, and 28.81 for **1c**, at δ 35.59, 35.33, 30.59, and 30.44 for **1d***, at δ 38.46, 37.22, and 28.91 for **1e***, and at δ 35.45, 35.11, and 34.71 for **1f***. These findings are in full agreement with those expected on the basis of symmetry considerations, substantiating each conformation.

Although the ^{1}H NMR spectrum of the partial-cone conformer **1d*** is very similar to that of partial-cone conformer **1b***, the resonance for the methyl protons in the *O*-propyl groups substituted on the rotated aryl ring of **1d*** appeared at slightly higher field (δ 0.70) than that (δ 0.83) of **1b***. This indicates that the hydrophobic cavity contained by the remaining three aryl rings of **1d*** is deeper than that of **1b*** due to the two bromine substituents on the para positions, and, as a result, the methyl group is entrapped in the hydrophobic cavity in solution.

In the case of the 1,2-alternate conformers, marked differences were observed between the ^{1}H NMR signals of **1c** and **1e***. In particular, strong upfield shifts for all the methyl and methylene protons in the *O*-propyl groups were observed for **1c**. The reason for this is that all the protons are exposed to the diamagnetic shielding effects

(13) Iwamoto, K.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1991**, *56*, 4955−4962.

(14) For calix[4]arenes in 1,2-alternate conformation, see: (a) Groenen, L. C.; van Loon, J.-D.; Verboom, W.; Harkema, S.; Casnati, A.; Ungaro, R.; Pochini, A.; Ugozzoli, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 2385−2392. (b) Iwamoto, K.; Araki, K.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1611−1613. (c) Iwamoto, K.; Shinkai, S. *J. Org. Chem.* **1992**, *57*, 7066−7073. (d) No, K.; Park, Y. J.; Kim, K. H.; Shin, J. M. *Bull. Korean Chem. Soc.* **1996**, *17*, 447−452. (e) Mathieu, A.; Asfari, Z.; Thuery, P.; Nierlich, M.; Faure, S.; Vicens, J. *J. Inclusion Phenom. Macrocycl. Chem.* **2001**, *40*, 173−181.

(15) (a) Verboom, W.; Datta, S.; Asfari, Z.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1992**, *57*, 5394−5398. (b) Fujimoto, K.; Nishiyama, N.; Tsuzuki, H.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 2* **1992**, 643−648. (c) Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing, M.-J.; Egberink, R. J. M.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767−2777.

of the two pairs of aryl rings (one above and one below the mean plane containing the four bridging methylenes).[4e,j] That is to say, two *O*-propyl groups located on the same side of the mean plane appear to alternate in filling the pockets created by the two facing aryl rings, which takes place on both sides of the mean plane. Totally, all the protons in the four *O*-propyl groups of **1c** display strong upfield shifts. On the other hand, no strong upfield shifts are seen for protons in the two *O*-propyl groups of **1e***. This suggests that, in the 1,2-altenate conformer **1e***, one of the two facing aryl rings is splayed outward and close to the mean methylene-containing plane, leading one of the two *O*-propyl groups located on the same side to exclusively fill the pocket. For the entire molecule, only two propyl groups are entrapped in the hydrophobic pockets. A similar conformational feature has been reported for 1,2;3,4-calix[4]arene-crown-5;crown-6, in which the rings closer to the mean plane are adjacent, and not the alternate ones.[14e] Consequently, the conformation of **1e*** even in solution appears to be strongly distorted and distinct from that of **1c**, although both are in the 1,2-alternate conformation.

Conclusion

All possible conformational isomers of the proximally *p*-dibrominated calix[4]arene tetraalkyl ether, **1a**−**f***, could be prepared successfully by using the proper bases and starting materials, 5,11-dibromocalix[4]arene *syn*-dialkyl ethers. Their conformations were confirmed by ^{1}H and ^{13}C NMR spectra to be cone for **1a** (**u**$^{Br}{}_{Pr}$, u$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,u$^{H}{}_{Pr}$), partial cone for **1b*** (**u**$^{Br}{}_{Pr}$, d$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,u$^{H}{}_{Pr}$) and **1d*** (**u**$^{Br}{}_{Pr}$, u$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,d$^{H}{}_{Pr}$), 1,2-alternate for **1c** (**u**$^{Br}{}_{Pr}$, u$^{Br}{}_{Pr}$, d$^{H}{}_{Pr}$,d$^{H}{}_{Pr}$) and **1e*** (**u**$^{Br}{}_{Pr}$, d$^{Br}{}_{Pr}$, d$^{H}{}_{Pr}$,u$^{H}{}_{Pr}$), and 1,3-alternate for **1f*** (**u**$^{Br}{}_{Pr}$, d$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,d$^{H}{}_{Pr}$). Consequently, it appears that the hydrophobic cavity produced by the three aryl rings of the partial-cone conformer **1d*** is deeper than that of the other partial-cone conformer **1b*** due to the two bromine substituents on the para positions, and that, although both of the conformational isomers **1c** and **1e*** are in the 1,2-alternate conformation, the conformation of **1e*** in solution is distinct from that of **1c**. These conformational isomers of 5,11-dibromocalix[4]arene tetraalkyl ether represent very attractive building blocks for the design of synthetic receptors with chiral discrimination ability, since the bromine substituents are readily and selectively converted to other substituents.

Experimental Section

General Remarks. ^{1}H and ^{13}C NMR spectra were obtained at the indicated frequency as dilute solutions in $CDCl_3$ at room temperature. Recycling preparative gel-permeation chromatography (GPC) and high-performance liquid chromatography (HPLC) were performed with a liquid chromatograph, using JAIGEL-1H and 2H columns and two YMC-pack SIL SH-043-10 columns, respectively. Analytical thin-layer chromatography (TLC) and column chromatography were carried out on precoated silica gel 60 F_{254} plastic sheets (E. Merck) and with silica gel 60 (spherical 0.040−0.100 mm, Kanto), respectively. Tetrahydrofuran (THF) was freshly distilled from Na-benzophenone. Acetonitrile and chloroform used in reactions as a solvent were distilled from CaH_2 and P_2O_5, respectively. *p-tert*-Butylcalix[4]arene,[16] calix[4]arene **2**,[17] and calix[4]arene 1,2-diallyl ether **3**[3b,i] were prepared according to literature methods and a modified method. Unless otherwise noted, starting materials and substrates were commercially available materials and were used without further purification.

5,11-Dibromo-25,26,27,28-tetrapropoxycalix[4]arene (u$^{Br}{}_{Pr}$, u$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,u$^{H}{}_{Pr}$) (1a). To a mixture of **5** (0.50 g, 0.75 mmol) and dry NaH (0.27 g, 11 mmol) in CH_3CN (30 mL) was added allyl bromide (1.36 g, 11.2 mmol), and the reaction mixture was stirred at room temperature for 6 h. Aqueous HCl (1 N, 20 mL) was then added dropwise, and most of the organic solvent was evaporated. The diallylation product was extracted with $CHCl_3$ (4 × 30 mL). The combined organic layer was dried over $MgSO_4$ and concentrated. The residue (0.56 g), which contained the cone and partial cone conformers in a ratio of 97:3, was purified by preparative TLC (SiO_2; hexanes/$CHCl_3$ 1:1; R_f 0.79) to give the cone conformer (0.43 g) as a white solid.[18] The intermediate product was dissolved in THF (50 mL), and 5% palladium on carbon (0.20 g) was added to the solution. The mixture was stirred under a hydrogen atmosphere (1 atm), with hydrogen bubbling through the mixture, at room temperature for 6 h. The catalyst was removed by filtration and the solution was concentrated under reduced pressure. The residue was purified by passing it through a short column (SiO_2; $CHCl_3$) to give pure cone conformer **1a** (0.39 g, 0.52 mmol, 69%) as a white solid. Mp 124−125 °C (lit.[5j] mp 117−119 °C). R_f 0.77 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.76−6.70 (m, 6H), 6.66−6.60 (m, 4H), 4.47 (d, J = 13.6 Hz, 1H, ArCH_2Ar), 4.42 (d, J = 13.6 Hz, 2H, ArCH_2Ar), 4.37 (d, J = 13.6 Hz, 1H, ArCH_2Ar), 3.90−3.77 (m, 8H), 3.20 (d, J = 13.6 Hz, 1H, ArCH_2Ar), 3.13 (d, J = 13.6 Hz, 2H, ArCH_2Ar), 3.06 (d, J = 13.6 Hz, 1H, ArCH_2Ar), 1.908 (sextet, J = 7.3 Hz, 4H), 1.890 (sextet, J = 7.3 Hz, 4H), 1.004 (t, J = 7.5 Hz, 3H), 0.998 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.65, 155.93, 137.79, 136.72, 135.37, 134.35, 131.21, 130.60, 128.63, 128.12, 122.41, 114.82, 76.84, 76.82, 31.11 (Ar*C*H$_2$Ar), 31.01 (Ar*C*H$_2$Ar), 30.83 (Ar*C*H$_2$Ar), 23.36, 23.26, 10.45, 10.39. IR (KBr) ν 3061, 2963, 2933, 2875, 1573, 1450, 1385, 1249, 1210, 1005, 964, 853, 764 cm^{-1}. Anal. Calcd for $C_{40}H_{46}Br_2O_4$: C, 64.01; H, 6.18. Found: C, 64.04; H, 6.17.

5,11-Dibromo-25,26,27,28-tetrapropoxycalix[4]arene (u$^{Br}{}_{Pr}$, d$^{Br}{}_{Pr}$, u$^{H}{}_{Pr}$,u$^{H}{}_{Pr}$) (1b*). To a mixture of **5** (0.50 g, 0.75 mmol) and Cs_2CO_3 (3.67 g, 11.3 mmol) in DMF (30 mL) was added propyl bromide (1.38 g, 11.2 mmol), and the reaction mixture was stirred at 80 °C for 15 h. Aqueous HCl (1 N, 20 mL) was then added, and the resulting solution was extracted with $CHCl_3$ (4 × 30 mL). The combined organic layer was dried over $MgSO_4$, concentrated, and filtered through a short column (SiO_2; $CHCl_3$). The filtrate was evaporated, and the residue (0.56 g), which contained the two conformers **1a** and **1b*** in a ratio of 15:85, was recrystallized from $CHCl_3$−MeOH to give the pure partial cone conformer **1b*** (0.28 g, 0.37 mmol, 49%) as a white solid. Mp 175−177 °C. R_f 0.76 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.31 (m, 2H), 7.14−6.91 (m, 5H), 6.59 (t, J = 5.1 Hz, 1H), 6.31−6.26 (m, 2H), 4.10 (d, J = 13.4 Hz, 1H, ArCH_2Ar), 4.03 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 3.82−3.66 (m, 4H), 3.61 (s, 2H, ArCH_2Ar), 3.60−3.54 (m, 2H), 3.53 (s, 2H, ArCH_2Ar), 3.37−3.33 (m, 2H), 3.09 (d, J = 13.4 Hz, 1H, ArCH_2Ar), 3.01 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 1.98 (sextet, J = 7.3 Hz, 2H), 1.896 (sextet, J = 7.2 Hz, 2H), 1.878 (sextet, J = 7.2 Hz, 2H), 1.54−1.46 (m, 2H), 1.16−1.11 (m, 9H), 0.83 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.05, 156.60, 155.55, 154.80, 137.39, 136.37, 136.27, 136.22, 135.22, 133.70, 133.33, 133.23, 132.64, 132.05, 131.19, 131.15, 129.52, 129.31, 128.99, 128.92, 122.59, 121.95, 114.92, 114.49, 76.46, 76.26, 75.97, 75.13, 35.48 (Ar*C*H$_2$Ar), 35.13

(16) (a) Gutsche, C. D.; Iqbal, M. *Org. Synth.* **1989**, *68*, 234−237. (b) For spectral data, see: Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, *103*, 3782−3792.

(17) Gutsche, C. D.; Lin, L.-G. *Tetrahedron* **1986**, *42*, 1633−1640.

(18) Isolation of the cone conformer from the conformational mixture of 5,11-diromono-27,28-diallyloxy-25,26-dipropoxycalix[4]arene was much easier than that from the mixture of 5,11-diromono-25,26,27,28-tetrapropoxycalix[4]arene. The route via this diallyl ether intermediate was therefore adopted for preparing the cone conformer **5** in high purity.

(ArCH_2Ar), 30.69 (ArCH_2Ar), 30.62 (ArCH_2Ar), 24.28, 24.02, 23.93, 22.48, 11.11, 11.05, 10.97, 10.09. IR (KBr) ν 3066, 2963, 2932, 2873, 1574, 1453, 1384, 1251, 1195, 1006, 963, 855, 763 cm^{-1}. Anal. Calcd for $C_{40}H_{46}Br_2O_4$: C, 64.01; H, 6.18. Found: C, 64.04; H, 6.14.

5,11-Dibromo-25,26,27,28-tetrapropoxycalix[4]arene (u^{Br}_{Pr}, u^{Br}_{Pr}, d^{H}_{Pr},d^{H}_{Pr}) (1c). To a solution of **5** (0.50 g, 0.75 mmol) and potassium *tert*-butoxide (0.34 g, 3.0 mmol) in benzene (30 mL) was added propyl bromide (1.38 g, 11.2 mmol), and the reaction mixture was heated under reflux for 6 h. Aqueous HCl (1 N, 20 mL) was then added, and the resulting solution was extracted with $CHCl_3$ (4 × 30 mL). The combined organic layer was dried over $MgSO_4$, concentrated, and filtered through a short column (SiO_2; $CHCl_3$). The filtrate was evaporated, and the residue (0.54 g), which contained the two conformers **1b*** and **1c** in a ratio of 17:83, was recrystallized from $CHCl_3$−MeOH to give pure 1,2-alternate conformer **1c** (0.25 g, 0.33 mmol, 44%) as a white solid. Mp 193−194 °C. R_f 0.75 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.22 (d, J = 2.5 Hz, 2H), 7.15 (d, J = 2.5 Hz, 2H), 7.09 (dd, J = 7.6, 1.5 Hz, 2H), 7.01 (dd, J = 7.5, 1.4 Hz, 2H), 6.83 (t, J = 7.5 Hz, 2H), 4.19 (d, J = 12.6 Hz, 1H, ArCH_2Ar), 4.09 (d, J = 12.8 Hz, 1H, ArCH_2Ar), 3.83 (s, 4H, ArCH_2Ar), 3.43−3.26 (m, 8H), 3.18 (d, J = 12.6 Hz, 1H, ArCH_2Ar), 3.06 (d, J = 12.8 Hz, 1H, ArCH_2Ar), 1.41−1.29 (m, 2H), 1.23−1.11 (m, 2H), 1.08−0.96 (m, 2H), 0.95−0.83 (m, 2H), 0.73 (t, J = 7.5 Hz, 6H), 0.60 (t, J = 7.5 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 156.53, 155.82, 136.01, 135.40, 134.75, 132.44, 132.15, 131.25, 129.32, 129.29, 122.19, 114.78, 75.10, 75.08, 37.79 (ArCH_2Ar), 28.95 (ArCH_2-Ar), 28.81 (ArCH_2Ar), 23.10, 22.79, 10.38, 10.34. IR (KBr) ν 3063, 2962, 2932, 2875, 1575, 1465, 1385, 1251, 1196, 1009, 964, 853, 764 cm^{-1}. Anal. Calcd for $C_{40}H_{46}Br_2O_4$: C, 64.01; H, 6.18. Found: C, 64.14; H, 6.19.

5,11-Dibromo-25,26,27,28-tetrapropoxycalix[4]arene (u^{Br}_{Pr}, u^{Br}_{Pr}, u^{H}_{Pr},d^{H}_{Pr}) (1d*). To a mixture of **10** (0.50 g, 0.75 mmol) and Cs_2CO_3 (3.67 g, 11.3 mmol) in DMF (30 mL) was added propyl bromide (1.38 g, 11.2 mmol), and the reaction mixture was heated at 80 °C for 15 h. Aqueous HCl (1 N, 20 mL) was then added, and the reaction mixture was extracted with $CHCl_3$ (4 × 30 mL). The combined organic layer was dried over $MgSO_4$, concentrated, and filtered through a short column (SiO_2; $CHCl_3$). The filtrate was evaporated, and the residue (0.56 g), which contained the two conformers **1a** and **1d*** in a ratio of 27:73, was subjected to recycling preparative HPLC (SiO_2; $CHCl_3$/hexane 1:5) to give pure partial cone conformer **1d*** (0.31 g, 0.41 mmol, 55%) as a white solid. Mp 148−150 °C. R_f 0.78 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27−7.15 (m, 5H), 7.06 (dd, J = 7.4, 1.3 Hz, 1H), 6.87 (t, J = 7.5 Hz, 1H), 6.66 (t, J = 7.6 Hz, 1H), 6.30−6.26 (m, 2H), 4.06 (d, J = 13.6 Hz, 1H, ArCH_2Ar), 3.99 (d, J = 13.7 Hz, 1H, ArCH_2Ar), 3.86−3.70 (m, 4H), 3.68 (s, 2H, ArCH_2Ar), 3.60 (s, 2H, ArCH_2Ar), 3.58−3.49 (m, 2H), 3.27−3.22 (m, 2H), 3.04 (d, J = 13.6 Hz, 1H, ArCH_2Ar), 2.96 (d, J = 13.7 Hz, 1H, ArCH_2-Ar), 2.02 (sextet, J = 7.4 Hz, 2H), 1.91−1.82 (m, 4H), 1.40−1.28 (m, 2H), 1.17 (t, J = 7.4 Hz, 3H), 1.11 (t, J = 7.4 Hz, 3H), 1.10 (t, J = 7.4 Hz, 3H), 0.70 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.52, 156.42, 155.58, 154.85, 139.49, 138.41, 135.16, 134.34, 134.25, 133.30, 132.67, 132.57, 132.11, 131.97, 131.40, 130.73, 130.58, 130.16, 129.77, 128.44, 122.06, 121.94, 114.74, 114.60, 76.45, 76.26, 75.69, 75.01, 35.59 (ArCH_2Ar), 35.33 (ArCH_2Ar), 30.59 (ArCH_2Ar), 30.44 (ArCH_2-Ar), 24.34, 23.99, 23.90, 22.38, 11.08, 11.05, 11.02, 9.40. IR (KBr) ν 3070, 2962, 2932, 2874, 1576, 1456, 1386, 1250, 1195, 1002, 965, 854, 761 cm^{-1}. Anal. Calcd for $C_{40}H_{46}Br_2O_4$: C, 64.01; H, 6.18. Found: C, 64.08; H, 6.21.

5,11-Dibromo-25,26,27,28-tetrapropoxycalix[4]arene (u^{Br}_{Pr}, d^{Br}_{Pr}, d^{H}_{Pr},u^{H}_{Pr}) (1e*). To a solution of **12*** (0.50 g, 0.75 mmol) and potassium *tert*-butoxide (0.34 g, 3.0 mmol) in benzene (30 mL) was added propyl bromide (1.38 g, 11.2 mmol), and the reaction mixture was heated under reflux for 6 h. Aqueous HCl (1 N, 20 mL) was then added, and the resulting solution was extracted with $CHCl_3$ (4 × 30 mL). The combined organic layer was dried over $MgSO_4$, concentrated, and filtered through a short column (SiO_2; $CHCl_3$). The filtrate was evaporated, and the residue (0.54 g), which contained the 1,2-alternate conformer **1e*** (70%) and two other conformers **1b*** and **1d***, was subjected to recycling preparative HPLC (SiO_2; $CHCl_3$/hexane 1:5) to give pure 1,2-alternate conformer **1e*** (0.28 g, 0.37 mmol, 49%) as a white solid. Mp 123−126 °C. R_f 0.80 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.21 (d, J = 2.5 Hz, 2H), 7.16 (dd, J = 7.4, 1.6 Hz, 2H), 7.06 (d, J = 2.3 Hz, 2H), 7.01 (dd, J = 7.5, 1.4 Hz, 2H), 6.93 (t, J = 7.4 Hz, 2H), 4.14 (d, J = 12.7 Hz, 2H, ArCH_2Ar), 3.96 (s, 2H, ArCH_2Ar), 3.70 (s, 2H, ArCH_2Ar), 3.68−3.62 (m, 2H), 3.49−3.43 (m, 2H), 3.25−3.19 (m, 2H), 3.12 (d, J = 12.7 Hz, 2H, ArCH_2Ar), 3.09−3.03 (m, 2H), 1.73−1.59 (m, 4H), 0.95 (t, J = 7.5 Hz, 6H), 0.92−0.83 (m, 2H), 0.44 (t, J = 7.5 Hz, 6H), 0.30−0.17 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.07, 155.24, 136.23, 135.07, 134.66, 132.42, 132.26, 131.88, 129.44, 128.91, 122.58, 114.88, 76.02, 74.17, 38.46 (ArCH_2Ar), 37.22 (ArCH_2-Ar), 28.91 (ArCH_2Ar), 23.50, 22.45, 10.78, 9.98. IR (KBr) ν 3061, 2962, 2936, 2877, 1573, 1458, 1385, 1250, 1219, 1198, 1010, 956, 856, 767 cm^{-1}. Anal. Calcd for $C_{40}H_{46}Br_2O_4$·0.04 $CHCl_3$: C, 63.27; H, 6.10. Found: C, 63.33; H, 6.00.

5,11-Dibromo-25,26,27,28-tetrapropoxycalix[4]arene (u^{Br}_{Pr}, d^{Br}_{Pr}, u^{H}_{Pr},d^{H}_{Pr}) (1f*). To a mixture of **13*** (0.50 g, 0.75 mmol) and Cs_2CO_3 (3.67 g, 11.3 mmol) in acetone (30 mL) was added propyl bromide (1.38 g, 11.2 mmol), and the reaction mixture was heated under reflux for 15 h. Aqueous HCl (1 N, 20 mL) was added, and the resulting solution was extracted with $CHCl_3$ (4 × 30 mL). The combined organic layer was dried over $MgSO_4$, concentrated, and filtered through a short column (SiO_2; $CHCl_3$). The filtrate was evaporated, and the residue (0.53 g), which contained the 1,3-alternate conformer **1f*** (85%) and three other conformers **1a**, **1b***, and **1d***, was recrystallized from $CHCl_3$−MeOH to give pure 1,3-alternate conformer **1f*** (0.23 g, 0.31 mmol, 41%) as a white solid. Mp 183−185 °C. R_f 0.59 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.17−7.01 (m, 8H), 6.82 (t, J = 7.5 Hz, 2H), 3.70−3.58 (m, 8H), 3.56 (s, 2H, ArCH_2Ar), 3.51 (s, 4H, ArCH_2Ar), 3.43 (s, 2H, ArCH_2Ar), 1.85−1.76 (m, 8H), 1.08 (t, J = 7.4 Hz, 12H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.08, 155.26, 135.93, 134.96, 133.74, 132.79, 132.44, 131.92, 130.07, 129.54, 122.18, 114.56, 74.84, 74.56, 35.45 (ArCH_2Ar), 35.11 (ArCH_2Ar), 34.71 (ArCH_2-Ar), 23.96, 10.93. IR (KBr) ν 3070, 2962, 2935, 2867, 1576, 1450, 1383, 1252, 1196, 1067, 1009, 963, 854, 759 cm^{-1}. Anal. Calcd for $C_{40}H_{46}Br_2O_4$: C, 64.01; H, 6.18. Found: C, 63.79; H, 6.13.

25,26-Dihydroxy-27,28-dipropoxycalix[4]arene (4). To a solution of calix[4]arene 1,2-diallyl ether **3** (5.00 g, 9.90 mmol) in THF (200 mL) was added 5% palladium on carbon (1.00 g). The mixture was stirred under a hydrogen atmosphere (1 atm), with hydrogen bubbling through the mixture, at room temperature for 12 h. After filtration and evaporation of the solvent, the residue was recrystallized from $CHCl_3$−MeOH to give **4** (4.99 g, 9.81 mmol, 99%) as a white solid. Mp 190−191 °C (lit.[5j] mp 195−196 °C). R_f 0.47 ($CHCl_3$/hexane 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.99 (s, 2H), 7.06 (dd, J = 7.6, 1.5 Hz, 2H), 6.99−6.97 (m, 6H), 6.79 (t, J = 7.6 Hz, 2H), 6.63 (t, J = 7.5 Hz, 2H), 4.55 (d, J = 12.4 Hz, 1H, ArCH_2Ar), 4.34 (d, J = 13.0 Hz, 2H, ArCH_2Ar), 4.34 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 4.12−4.06 (m, 2H), 3.93−3.86 (m, 2H), 3.41 (d, J = 12.4 Hz, 1H, ArCH_2Ar), 3.39 (d, J = 13.0 Hz, 2H, ArCH_2Ar), 3.35 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 2.20−2.07 (m, 4H), 1.16 (t, J = 7.5 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.46, 151.19, 134.66, 134.12, 129.42, 129.11, 129.05, 128.78, 128.77, 128.02, 124.71, 120.53, 78.29, 31.91 (ArCH_2Ar), 31.78 (ArCH_2-Ar), 29.98 (ArCH_2Ar), 23.27, 10.34. IR (KBr) ν 3323, 3081, 2927, 1591, 1465, 1246, 1197, 1094, 980, 756 cm^{-1}. Anal. Calcd for $C_{34}H_{36}O_4$: C, 80.28; H, 7.13. Found: C, 79.88; H, 7.16.

5,11-Dibromo-27,28-dihydroxy-25,26-dipropoxycalix-[4]arene (5). To a solution of **4** (7.95 g, 15.6 mmol) in 2-butanone (250 mL) was added *N*-bromosuccinimide (5.56 g, 31.2 mmol), and the yellow solution was stirred at room

temperature for 24 h. After evaporation of the solvent, trituration of the solid residue with MeOH gave **5** (8.60 g, 12.9 mmol, 83%) as a white solid. Mp 260−262 °C dec (lit.[5j] mp >200 °C dec). R_f 0.29 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.89 (s, 2H), 7.11−7.06 (m, 6H), 6.98 (dd, J = 7.6, 1.5 Hz, 2H), 6.84 (t, J = 7.6 Hz, 2H), 4.51 (d, J = 12.4 Hz, 1H, ArCH_2Ar), 4.30 (d, J = 13.4 Hz, 1H, ArCH_2Ar), 4.27 (d, J = 13.1 Hz, 2H, ArCH_2Ar), 4.11−4.05 (m, 2H), 3.91−3.84 (m, 2H), 3.43 (d, J = 12.4 Hz, 1H, ArCH_2Ar), 3.36 (d, J = 13.1 Hz, 2H, ArCH_2Ar), 3.22 (d, J = 13.4 Hz, 1H, ArCH_2Ar), 2.18−2.06 (m, 4H), 1.15 (t, J = 7.5 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.26, 150.52, 134.64, 133.17, 131.55, 131.22, 130.74, 130.52, 129.22, 129.17, 125.09, 112.18, 78.45, 31.77 (ArCH$_2$Ar), 31.26 (ArCH$_2$Ar), 29.90 (ArCH$_2$Ar), 23.23, 10.29. IR (KBr) ν 3449, 3073, 2966, 2929, 2874, 1586, 1467, 1211, 1193, 1088, 997, 769 cm^{-1}. Anal. Calcd for $C_{34}H_{34}Br_2O_4$: C, 61.28; H, 5.14. Found: C, 60.91; H, 5.17.

25,26-Dibenzyloxy-27,28-dihydroxycalix[4]arene (6). To a slurry of calix[4]arene **2** (5.00 g, 11.8 mmol) and NaH (2.83 g of a 60% dispersion in paraffin liquid, 71 mmol) in CH_3CN (250 mL) was added benzyl bromide (3.08 mL, 25.9 mmol), and the reaction mixture was stirred at room temperature for 30 min to produce a light purple solution. Aqueous HCl (1 N, 30 mL) was then added dropwise, and most of the organic solvent was evaporated. After addition of water (40 mL), the product was extracted with $CHCl_3$ (80 mL). The combined organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by passing it through a short column (SiO_2; hexane, then $CHCl_3$) to give **6** (4.29 g, 7.09 mmol, 60%) as a white solid. Mp 224−227 °C. R_f 0.75 ($CHCl_3$). ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.97 (s, 2H), 7.53−7.35 (m, 10H), 7.09−6.93 (m, 8H), 6.81 (t, J = 7.6 Hz, 2H), 6.59 (t, J = 7.6 Hz, 2H), 5.06 (d, J = 11.2 Hz, 2H), 4.88 (d, J = 11.2 Hz, 2H), 4.47 (d, J = 12.4 Hz, 1H, ArCH_2Ar), 4.24 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 4.10 (d, J = 12.7 Hz, 2H, ArCH_2Ar), 3.33 (d, J = 13.2 Hz, 2H, ArCH_2Ar), 3.22 (d, J = 13.0 Hz, 2H, ArCH_2Ar). ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 153.31, 151.23, 136.71, 134.81, 134.54, 129.32, 129.09, 129.00, 128.84, 128.75, 128.70, 128.62, 128.16, 125.05, 120.57, 78.56, 31.99 (ArCH$_2$Ar), 30.66 (ArCH$_2$Ar). IR (KBr) ν 3404, 3332, 3035, 2934, 2857, 1591, 1465, 1215, 1182, 1092, 973, 915, 759, 698 cm^{-1}. Anal. Calcd for $C_{42}H_{36}O_4$: C, 83.42; H, 6.00. Found: C, 82.95; H, 6.18.

5,11-Dibromo-25,26-dibenzyloxy-27,28-dihydroxycalix[4]arene (7). To a solution of **6** (3.80 g, 6.28 mmol) in 2-butanone (100 mL) was added *N*-bromosuccinimide (2.24 g, 12.6 mmol), and the yellow solution was stirred at room temperature for 24 h. After evaporation of the solvent, the residue was recrystallized from $CHCl_3$−MeOH to give **7** (4.31 g, 5.65 mmol, 90%) as a white solid. Mp 113−116 °C. R_f 0.74 ($CHCl_3$). ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.90 (s, 2H), 7.49−7.37 (m, 10H), 7.13−6.96 (m, 8H), 6.86 (t, J = 7.6 Hz, 2H), 5.05 (d, J = 11.3 Hz, 2H), 4.85 (d, J = 11.3 Hz, 2H), 4.45 (d, J = 12.6 Hz, 1H, ArCH_2Ar), 4.16 (d, J = 13.8 Hz, 1H, ArCH_2Ar), 4.02 (d, J = 13.0 Hz, 2H, ArCH_2Ar), 3.35 (d, J = 12.6 Hz, 1H, ArCH_2Ar), 3.19 (d, J = 13.8 Hz, 1H, ArCH_2Ar), 3.17 (d, J = 13.0 Hz, 2H, ArCH_2Ar). ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 153.21, 150.53, 136.42, 134.84, 133.64, 131.55, 131.28, 130.92, 130.10, 129.45, 129.36, 129.15, 128.86, 125.39, 112.24, 78.76, 31.84 (ArCH$_2$Ar), 31.52 (ArCH$_2$Ar), 30.64 (ArCH$_2$Ar). IR (KBr) ν 3312, 3063, 2929, 2876, 1458, 1219, 1186, 975, 764, 700 cm^{-1}. Anal. Calcd for $C_{42}H_{34}Br_2O_4$: C, 66.16; H, 4.49. Found: C, 66.04; H, 4.69.

5,11-Dibromo-27,28-diallyloxy-25,26-dibenzyloxycalix[4]arene (8). To a mixture of **7** (3.00 g, 3.93 mmol) and NaH (2.36 g of a 60% dispersion in paraffin liquid, 59 mmol) in CH_3CN (100 mL) was added allyl bromide (5.1 mL, 59 mmol), and the reaction mixture was stirred at room temperature for 6 h. Aqueous HCl (1 N, 60 mL) was then added dropwise, and most of the organic solvent was evaporated. The product was extracted with $CHCl_3$ (100 mL), and the organic layer was dried over $MgSO_4$ and concentrated. The residue was recrystallized from $CHCl_3$−MeOH to give **8** (2.78 g, 3.30 mmol, 84%) as a plate-shaped crystal. Mp 155−158 °C. R_f 0.67 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.32−7.23 (m, 10H), 6.74−6.54 (m, 10H), 6.29−6.14 (m, 2H), 5.20−5.12 (m, 4H), 4.92 (d, J = 11.6 Hz, 2H), 4.83 (d, J = 11.6 Hz, 2H), 4.38 (d, J = 6.5 Hz, 4H), 4.30 (d, J = 13.9 Hz, 1H, ArCH_2Ar), 4.25 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 4.18 (d, J = 13.9 Hz, 2H, ArCH_2Ar), 3.05 (d, J = 13.9 Hz, 1H, ArCH_2Ar), 3.04 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 2.96 (d, J = 13.9 Hz, 2H, ArCH_2Ar). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 155.45, 155.14, 137.99, 137.64, 137.06, 135.48, 135.01, 134.76, 131.28, 130.62, 129.68, 128.80, 128.21, 128.16, 128.10, 122.85, 117.86, 115.25, 76.80, 76.00, 31.34 (ArCH$_2$Ar), 31.29 (ArCH$_2$Ar), 31.25 (ArCH$_2$Ar). IR (KBr) ν 3062, 3039, 2922, 2859, 1572, 1459, 1196, 992, 754, 699 cm^{-1}. Anal. Calcd for $C_{48}H_{42}Br_2O_4$: C, 68.42; H, 5.02. Found: C, 68.73; H, 5.20.

5,11-Dibromo-25,26-dibenzyloxy-27,28-dipropoxycalix[4]arene (9). To a solution of **8** (3.70 g, 4.39 mmol) in THF (200 mL) was added 5% palladium on carbon (0.70 g). The mixture was stirred under a hydrogen atmosphere (1 atm), with hydrogen bubbling through the mixture, at room temperature for 3 h. After filtration and evaporation of the solvent, the residue was purified by passing it through a short column (SiO_2; $CHCl_3$) to give **9** (3.50 g, 4.13 mmol, 94%) as a white solid. Mp 140−143 °C. R_f 0.67 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.40−7.22 (m, 10H), 6.77−6.68 (m, 6H), 6.61−6.54 (m, 4H), 4.88 (d, J = 11.5 Hz, 2H), 4.83 (d, J = 11.5 Hz, 2H), 4.36 (d, J = 13.8 Hz, 1H, ArCH_2Ar), 4.25 (d, J = 13.5 Hz, 2H, ArCH_2Ar), 4.17 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 3.89−3.74 (m, 4H), 3.05 (d, J = 14.3 Hz, 1H, ArCH_2Ar), 2.99 (d, J = 14.0 Hz, 3H, ArCH_2Ar), 1.85 (sextet, J = 7.5 Hz, 4H), 0.92 (t, J = 7.5 Hz, 6H). ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 156.20, 155.71, 138.12, 138.05, 137.14, 135.88, 134.97, 131.63, 130.98, 129.84, 129.08, 128.48, 128.32, 123.16, 115.18, 78.91, 76.06, 31.58 (ArCH$_2$Ar), 31.47 (ArCH$_2$Ar), 31.31 (ArCH$_2$Ar), 23.60, 10.69. IR (KBr) ν 3030, 2924, 2874, 1572, 1457, 1210, 1194, 966, 764, 699 cm^{-1}. Anal. Calcd for $C_{48}H_{46}Br_2O_4$: C, 68.09; H, 5.48. Found: C, 68.23; H, 5.54.

5,11-Dibromo-25,26-dihydroxy-27,28-dipropoxycalix[4]arene (10). To a stirred solution of **9** (2.74 g, 3.24 mmol) in toluene (300 mL) at 0 °C was added anhydrous $AlCl_3$ (0.86 g, 6.4 mmol), and the reaction mixture was stirred at 0 °C for 1 h. The reaction was then quenched with diluted HCl (50 mL). The organic layer was separated, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (SiO_2; $CHCl_3$/hexane 4:1) to give **10** (1.92 g, 2.88 mmol, 89%) as a white solid. Mp 266−269 °C. R_f 0.58 ($CHCl_3$/hexane 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.87 (s, 2H), 7.13 (s, 4H), 7.02 (dd, J = 7.5, 1.3 Hz, 2H), 6.98 (dd, J = 7.5, 1.3 Hz, 2H), 6.68 (t, J = 7.5 Hz, 2H), 4.46 (d, J = 12.5 Hz, 1H, ArCH_2Ar), 4.30 (d, J = 13.0 Hz, 2H, ArCH_2Ar), 4.28 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 4.06−4.00 (m, 2H), 3.89−3.83 (m, 2H), 3.39 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 3.35 (d, J = 13.0 Hz, 2H, ArCH_2Ar), 3.30 (d, J = 12.5 Hz, 1H, ArCH_2Ar), 2.17−2.05 (m, 4H), 1.15 (t, J = 7.4 Hz, 6H). ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 153.03, 151.18, 136.66, 136.14, 132.42, 131.54, 129.29, 129.00, 128.55, 128.28, 121.04, 117.32, 78.65, 31.93 (ArCH$_2$Ar), 31.86 (ArCH$_2$Ar), 29.88 (ArCH$_2$Ar), 23.36, 10.42. IR (KBr) ν 3301, 2964, 2936, 2878, 1572, 1466, 1197, 979, 755 cm^{-1}. Anal. Calcd for $C_{34}H_{34}Br_2O_4$: C, 61.28; H, 5.14. Found: C, 60.89; H, 5.15.

5,11-Dibromo-26,27,28-trihydroxy-25-propoxycalix[4]arene (11*). To a stirred solution of **5** (5.00 g, 7.50 mmol) in $CHCl_3$ (250 mL) was added dropwise trimethylsilyl iodide (3.04 mL, 21.4 mmol), and the mixture was heated under reflux for 24 h. After addition of water (100 mL), the organic layer was separated, washed with water, dried over $MgSO_4$, and concentrated. The residue was purified through a short column (SiO_2; $CHCl_3$) to give **11*** (4.40 g, 7.05 mmol, 94%). Mp 164−166 °C. R_f 0.49 ($CHCl_3$/hexane 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.69 (s, 1H), 9.46 (s, 1H), 9.18 (s, 1H), 7.20 (d, J = 2.4 Hz, 1H), 7.12−7.07 (m, 6H), 7.03 (dd, J = 7.5, 1.4 Hz, 1H), 6.92 (t, J = 7.6 Hz, 1H), 6.73 (t, J = 7.5 Hz, 1H), 4.41 (d, J = 12.8 Hz, 1H, ArCH_2Ar), 4.23 (d, J = 13.4 Hz, 1H, ArCH_2Ar), 4.20 (d, J

= 13.9 Hz, 2H, ArCH_2Ar), 4.16−4.05 (m, 2H), 3.51 (d, J = 13.4 Hz, 1H, ArCH_2Ar), 3.42 (d, J = 13.9 Hz, 1H, ArCH_2Ar), 3.39 (d, J = 12.8 Hz, 1H, ArCH_2Ar), 3.34 (d, J = 13.9 Hz, 1H, ArCH_2Ar), 2.24−2.11 (m, 2H), 1.27 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.34, 150.41, 150.32, 148.52, 133.77, 133.73, 131.58, 131.29, 131.13, 131.07, 131.06, 130.78, 130.42, 129.66, 129.42, 129.05, 128.90, 127.92, 127.42, 126.39, 121.46, 113.69, 112.23, 79.18, 31.71 (ArCH$_2$Ar), 31.65 (ArCH$_2$Ar), 31.54 (ArCH$_2$Ar), 30.91 (ArCH$_2$Ar), 23.26, 10.65. IR (KBr) ν 3334, 2936, 2875, 1591, 1466, 1216, 1083, 956, 758 cm^{-1}. Anal. Calcd for $C_{31}H_{28}Br_2O_4$: C, 59.63; H, 4.52. Found: C, 59.42; H, 4.63.

5,11-Dibromo-25,28-dihydroxy-26,27-dipropoxycalix[4]-arene (12*). To a mixture of **11*** (1.47 g, 2.35 mmol) and NaH (0.28 g of a 60% dispersion in paraffin liquid, 7.0 mmol) in CH_3CN (50 mL) was added allyl bromide (0.23 mL, 2.7 mmol), and the reaction mixture was stirred at room temperature for 20 min to produce a light purple solution. Aqueous HCl (1 N, 30 mL) was then added dropwise, and most of the organic solvent was evaporated. The allylation product was extracted with $CHCl_3$ (3 × 40 mL). The combined organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by passing it through a short column (SiO_2; hexane, then $CHCl_3$). The intermediate product was dissolved in THF (50 mL), and 5% palladium on carbon (0.30 g) was added to the solution. The mixture was stirred under a hydrogen atmosphere (1 atm), with hydrogen bubbling through the mixture, at room temperature for 1 h. After filtration and evaporation of the solvent, the residue (1.42 g) was subjected to recycling preparative GPC ($CHCl_3$). The first eluate was concentrated, and the residue that contained the two isomers **5** and **12*** in a ratio of 3:7 (0.92 g) was recrystallized from $CHCl_3$−MeOH to give **12*** (0.32 g, 0.48 mmol, 20%) as a white solid. Mp 250−252 °C. R_f 0.64 ($CHCl_3$/hexane 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.31 (s, 1H), 8.76 (s, 1H), 7.14−7.00 (m, 8H), 6.92 (t, J = 7.5 Hz, 1H), 6.70 (t, J = 7.5 Hz, 1H), 4.49 (d, J = 12.5 Hz, 1H, ArCH_2Ar), 4.43 (d, J = 12.6 Hz, 1H, ArCH_2Ar), 4.27 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 4.21−4.15 (m, 1H), 4.16 (d, J = 13.5 Hz, 1H, ArCH_2-Ar), 3.97−3.89 (m, 2H), 3.85−3.79 (m, 1H), 3.50 (d, J = 13.5 Hz, 1H, ArCH_2Ar), 3.37 (d, J = 12.5 Hz, 1H, ArCH_2Ar), 3.32 (d, J = 13.6 Hz, 1H, ArCH_2Ar), 3.22 (d, J = 12.6 Hz, 1H, ArCH_2Ar), 2.27−1.96 (m, 4H), 1.17 (t, J = 7.4 Hz, 3H), 1.14 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.75, 152.77, 151.39, 150.46, 136.38, 136.05, 134.68, 133.78, 132.13, 131.81, 131.51, 131.35, 130.82, 130.49, 129.55, 129.48, 129.30, 128.76, 128.53, 128.37, 125.89, 121.43, 116.61, 111.91, 78.78, 78.43, 32.43 (ArCH$_2$Ar), 31.75 (ArCH$_2$Ar), 31.33 (ArCH$_2$Ar), 29.95 (ArCH$_2$Ar), 23.51, 23.22, 10.56, 10.35. IR (KBr) ν 3235, 2967, 2928, 2875, 1574, 1468, 1205, 979, 859, 762 cm^{-1}. Anal. Calcd for $C_{34}H_{34}Br_2O_4$: C, 61.28; H, 5.14. Found: C, 60.90; H, 5.15.

5,11-Dibromo-26,28-dihydroxy-25,27-dipropoxycalix-[4]arene (13*). To a mixture of **11*** (1.00 g, 1.60 mmol), BaO (1.43 g, 9.33 mmol), and $Ba(OH)_2$·$8H_2O$ (1.51 g, 4.79 mmol) in DMF (50 mL) was added propyl bromide (0.72 mL, 7.9 mmol), and the reaction mixture was stirred at room temperature for 24 h. Aqueous HCl (1 N, 50 mL) was then added, and the resulting solution was extracted with $CHCl_3$ (3 × 50 mL). The combined organic layer was washed with 10% aqueous $Na_2S_2O_3$ (50 mL), dried over $MgSO_4$, and concentrated. The residue was recrystallized from $CHCl_3$−MeOH to give **13*** (0.66 g, 0.99 mmol, 62%) as a white solid. Mp 315−317 °C. R_f 0.65 ($CHCl_3$/hexane 2:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.37 (s, 1H), 8.17 (s, 1H), 7.19 (d, J = 2.4 Hz, 1H), 7.13 (d, J = 2.4 Hz, 1H), 7.09−6.93 (m, 6H), 6.82 (t, J = 7.5 Hz, 1H), 6.66 (t, J = 7.5 Hz, 1H), 4.28 (d, J = 13.1 Hz, 1H, ArCH_2Ar), 4.27 (d, J = 12.9 Hz, 1H, ArCH_2Ar), 4.25 (d, J = 13.1 Hz, 1H, ArCH_2Ar), 4.21 (d, J = 13.0 Hz, 1H, ArCH_2Ar), 3.98−3.91 (m, 4H), 3.40 (d, J = 13.1 Hz, 1H, ArCH_2Ar), 3.34 (d, J = 12.9 Hz, 1H, ArCH_2-Ar), 3.33 (d, J = 13.1 Hz, 1H, ArCH_2Ar), 3.29 (d, J = 13.1 Hz, 1H, ArCH_2Ar), 2.08−2.00 (m, 4H), 1.301 (t, J = 7.4 Hz, 3H), 1.296 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.43, 152.79, 151.97, 151.37, 135.96, 134.90, 133.59, 132.63, 132.38, 131.89, 131.19, 130.88, 130.37, 129.53, 129.29, 129.16, 128.91, 128.67, 128.10, 127.22, 125.69, 119.43, 117.91, 110.63, 78.76, 78.56, 31.58 (ArCH$_2$Ar), 31.43 (ArCH$_2$Ar), 31.34 (ArCH$_2$Ar), 31.26 (ArCH$_2$Ar), 23.62, 23.58, 11.04, 11.00. IR (KBr) ν 3275, 2960, 2932, 2875, 1575, 1467, 1219, 1197, 1061, 957, 760 cm^{-1}. Anal. Calcd for $C_{34}H_{34}Br_2O_4$: C, 61.28; H, 5.14. Found: C, 61.04; H, 5.20.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of conformational isomers **1a**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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