Conformational Mobility of the Bridged Calix[6]arenes with Allyl and Ethyl Groups at the Lower Rim

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The conformational mobility of the bridged calix[6]arenes with allyl and ethyl groups at the lower rim was investigated. Allylation of the tetrahydroxy compounds afforded two isomers: **5a** (cone) and **5b** (1,2,3-alternate), which were separated by silica-gel chromatography. These isomers underwent slow isomerization at room temperature with a half-life time of about 2 weeks. On the other hand, the ethyl derivatives **6–9** were found to exist as mixtures of conformational isomers in solution; they were observed independently on the NMR time-scale but were inseparable on the laboratory time-scale. The ratios of two isomers of **6–9** depended on the functionality on the bridging unit, the effects of which were investigated by molecular mechanics calculations. In the crystalline state, the ethyl derivative **6** with a bromo functionality was found to take the 1,2,3-alternate conformation, while compound **7** with an ethynyl group adopted the cone conformation.

The conformational study has been one of the major aspects in the calixarene chemistry.[1] While calix[4]arenes without capping groups at the lower rim adopt exclusively cone conformations,[2] their alkylated derivatives are known to have four conformational isomers which can be separated on the laboratory time-scale in many cases. There have been a number of reports on their conformational interconversion including the kinetic measurements as well as on the thermodynamic stability of each isomer.[3] On the other hand, the investigation of the conformational behavior of larger class of calixarenes such as calix[6]arenes has often encountered difficulties which are largely due to their conformational mobility.[4] We[5–7] and others[8–11] have reported that introduction of a rigid bridging unit to the calix[6]arene macrocycle can reduce their conformational mobility. During the course of our studies on the synthesis and application of 1,3-phenylenebis(methylene)-bridged calix[6]arenes,[5,6] we found that the uncapped tetrahydroxy compounds **1** adopt a pinched cone conformation[6] while the tetramethoxy derivatives **2** undergo slow conformational interconversion on the NMR time-scale to give broad ^{1}H NMR signals at room temperature.[6a] On the other hand, when the lower rim of **1** is capped with bulkier groups such as benzyl or 4-pyridylmethyl groups, the interconversion was suppressed on the laboratory time-scale and two conformationally frozen isomers (cone and 1,2,3-alternate) of **3** and **4** were isolated by silica-gel chromatography.[7] Their conformational stability was so high that no interconversion was observed even after heating either isomer of **3** at 120 °C for 24 h.[7a] It is expected that middle-sized substituents such as allyl and ethyl groups are appropriate for the investigation of the conformational exchange and equilibrium of the bridged calix[6]arenes of this type. Here we report the relationship between the conformational mobility of the bridged calix[6]arenes (Chart 1) in solution and the bulkiness of the lower-rim substituents. The crystal structures of two tetraethoxy compounds are also presented.

Results and Discussion

The allyl derivative **5** was synthesized under the same conditions as those for the 4-pyridylmethyl derivative **4**[7c] using cesium carbonate as a base in DMF at 70 °C. The crude mixture contained two conformational isomers **5a** (cone) and **5b** (1,2,3-alternate), which were separated by silica-gel chromatography. The ^{1}H NMR spectra of **5a** and **5b** are shown in Fig. 1.

When dissolved in $CDCl_3$, the pure samples of **5a** and **5b** underwent very slow conformational isomerization at room temperature with a half-life time of about 2 weeks. The thermal equilibration starting from both of **5a** and **5b** was monitored by ^{1}H NMR spectroscopy at 100 °C in 1,1,2,2-tetrachloroethane-d_2 (Fig. 2). The isomerization was found to obey an accurate first-order kinetics with a rate constant of 8.2×10^{-4} s^{-1}. The equilibrated molar ratio of **5a** and **5b** was 43 : 57 (**5a** : **5b**) and no other isomer was observed during the isomerization. From these values, the activation free energies for the isomerization are calculated to be 115.8 kJ mol^{-1} (from **5a**) and 116.7 (from **5b**) kJ mol^{-1}, respectively.

These results are in contrast with the benzyl derivative **3** and the 4-pyridylmethyl derivative **4**, in both of which no conformational interconversion was observed upon heating at 120 °C as mentioned above. As expected, the reduced size of the lower rim substituent of **5** in comparison with those of **3** and **4** led to the observation of its slow conformational change on the laboratory time-scale.

It is also important that the 1,2,3-alternate isomer **5b** was obtained in a considerably higher yield (cone : 1,2,3-alternate

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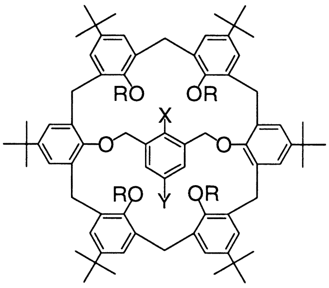
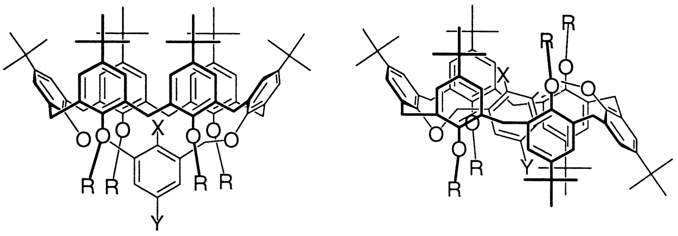
= 49:51) than those of the benzyl or 4-pyridylmethyl derivatives (82:18 for **3**[7a] and 83:17 for **4**[7c]). These results suggest that an equilibrium between **5a** and **5b** was established under the reaction conditions for preparation of **5**.

The ethyl derivative **6** was also prepared under similar conditions to afford a crude mixture containing two conformational isomers: **6a** and **6b**. Their conformational interconversion was sufficiently slow on the NMR time-scale for them to be observed independently in the ^{1}H NMR spectrum, as shown in Fig. 3. In this case, however, the two isomers can not be separated on the laboratory time-scale. This result seems reasonable because **6** has smaller substituents at the lower rim, to result in a faster rate of isomerization. The half-life time of the isomerization in $CDCl_3$ at room temperature was estimated to



	X	Y	R
1	Br	H	H
2	Br	H	Me
3	Br	H	CH_2Ph
4	Br	H	CH_2-(4-pyridyl)
5	Br	H	$CH_2CH=CH_2$
6	Br	H	Et
7	C≡CH	H	Et
8	OMe	Br	Et
9	H	H	Et



isomer **a** isomer **b**

Chart 1.

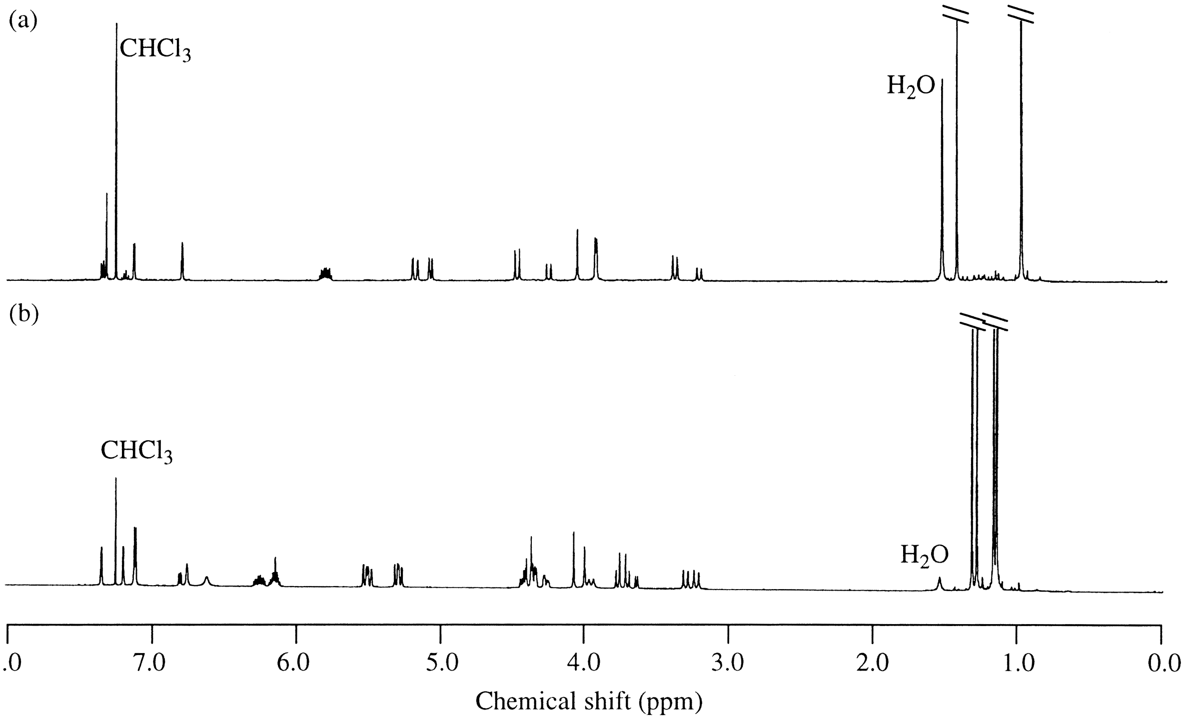


Fig. 1. ^{1}H NMR spectra of the allylated bridged calix[6]arene **5** (500 MHz, $CDCl_3$). (a) cone isomer **5a**. (b) 1,2,3-alternate isomer **5b**.

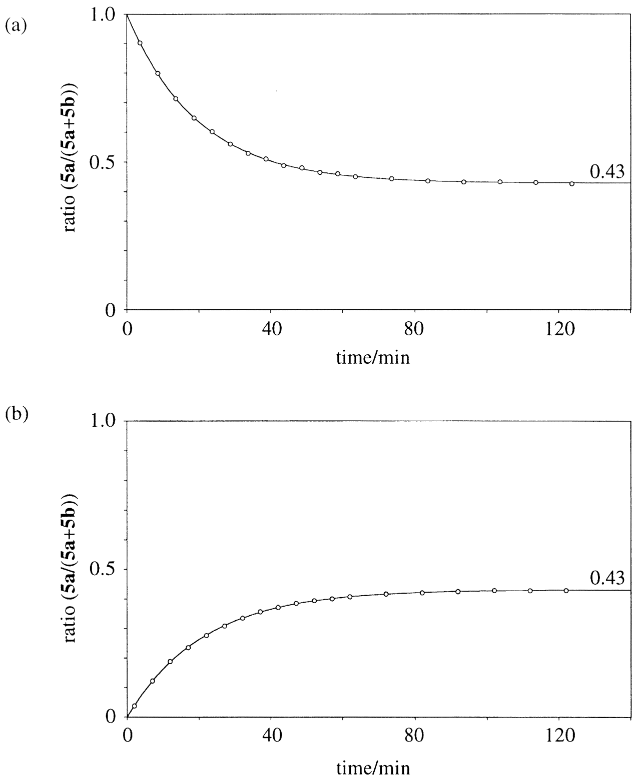


Fig. 2. Thermal equilibration of allylated bridged calix[6]arene **5** in 1,1,2,2-tetrachloroethane-d_2 at 100 °C. (a) From cone isomer **5a**. (b) From 1,2,3-alternate isomer **5b**. Ratios (**5a**/(**5a**+**5b**)) were calculated by the intensity ratio of ^{1}H NMR signals of *t*-butyl groups.

be the order of minutes, which was based on the fact that the ratio was constant (cone: 1,2,3-alternatae = 28:72) even when the spectrum was recorded only 10 minutes after the crystals of the 1,2,3-alaternate isomer **6b** (vide infra) was dissolved. Considering the fact that the methyl derivative **2** showed the averaged broad signal,[6a] ethyl groups are considered to be just on the borderline of ability to slow the conformational interconversion of the bridged calix[6]arenes of this type to the NMR time-scale. These results indicate that, by introduction of ethyl groups at the lower rim of the bridged calix[6]arenes, we can obtain a mixture of the conformational isomers at equilibrium, from which the relative thermodynamic stability of each isomer can be estimated. It was found that the ratio of the isomers depends on the functionality on the bridging unit (Table 1).

Whereas compounds **6** and **7** each existed as a mixture of two isomers, compounds **8**, **9**, and **10**[11b] were found to exist exclusively as the cone isomers (Chart 2).[12] Obviously, the conformational purity of **8**–**10** is not derived from their fixation at the cone conformation but from the predominant thermodynamic stability of the cone isomers.

The relative stability of each isomer of the ethyl derivatives **6** and **8** was investigated by molecular mechanics calculations using MacroModel V5.5 program with the MM3* (GB/SA $CHCl_3$) force field. The lowest energy structures of each isomer are shown in Fig. 4 with their relative energy values. In accordance with the experimental results, the 1,2,3-alternate isomer was found to be the most stable for **6**, while the global minimum structure of **8** adopts the cone conformation. These results can be reasonably explained in terms of the shape of the central functional group on the bridging unit. In compound **8**, the cavity of the cone isomer is large enough to accommodate the methoxy group in the folded shape, whereas there seems to be larger steric repulsion between the functionality and the calix[6]arene macroring in the smaller cavity of the 1,2,3-alternate isomer, which was calculated to be less stable than the cone isomer by 12.23 kJ mol^{-1}. Besides the cone and 1,2,3-alternate isomers, the calculation for **8** gave the third conformational isomer, the partial cone isomer, the relative energy value of which is 3.00 kJ mol^{-1}. This isomer was not observed experimentally, probably because its potential well is not deep enough. In contrast with **8**, the most stable isomer of **6** was found to be the 1,2,3-alternate isomer. This is probably due to the effective stacking of three benzene rings which are almost parallel, with a separation of about 3.5 Å. The spherical shape of the bromo functionality is considered to disturb such an arrangement much less than the folded shape of the methoxy group. The cone isomer of **6** was calculated to be 3.23 kJ mol^{-1} less stable than the 1,2,3-alternate isomer.

As discussed above, in solutions of the ethyl derivatives **6** and **7**, there is an equilibrium between the two conformational isomers, which is fast on the laboratory time-scale. From a chloroform/methanol solution of **6** and a benzene/acetonitrile solution of **7**, we obtained some single crystals of these compounds suitable for X-ray crystallographic analysis. Interestingly, it was found that they crystallized in different conformations; compound **6** with a bromo functionality took the 1,2,3-alternate conformation while **7** with an ethynyl group adopted the cone conformation. The crystal structures of **6** and **7** are shown in Fig. 5. The structure of **6** is in good agreement with the lowest energy structure of 1,2,3-alternate isomer obtained by the molecular mechanics calculations.

These two cases suggest that the conformation in the crystalline state is determined not only by the thermodynamic stability of the cone and 1,2,3-alternate isomers but also by other factors such as crystal packing forces.

Conclusion

The conformational behavior of the bridged calix[6]arenes with allyl or ethyl groups at the lower rim was investigated. Two conformational isomers (cone and 1,2,3-alternate) of the allyl derivative **5** were separable by silica-gel chromatography; they underwent slow conformational isomerization at room temperature with a half-life time of about 2 weeks. On the other hand, the ethyl derivatives **6**–**9** were found to exist as mixtures of conformational isomers in solution which could be observed independently on the NMR time-scale but which were inseparable on the laboratory time-scale. These findings, together with our previous studies on the methyl and arylmethyl derivatives, clearly demonstrate that the conformational mobility of these bridged calix[6]arenes can be finely modulated by appropriate capping of their lower rim.

Experimental

Melting points were determined on a Yanaco micro melting point apparatus. All melting points were uncorrected. Preparative

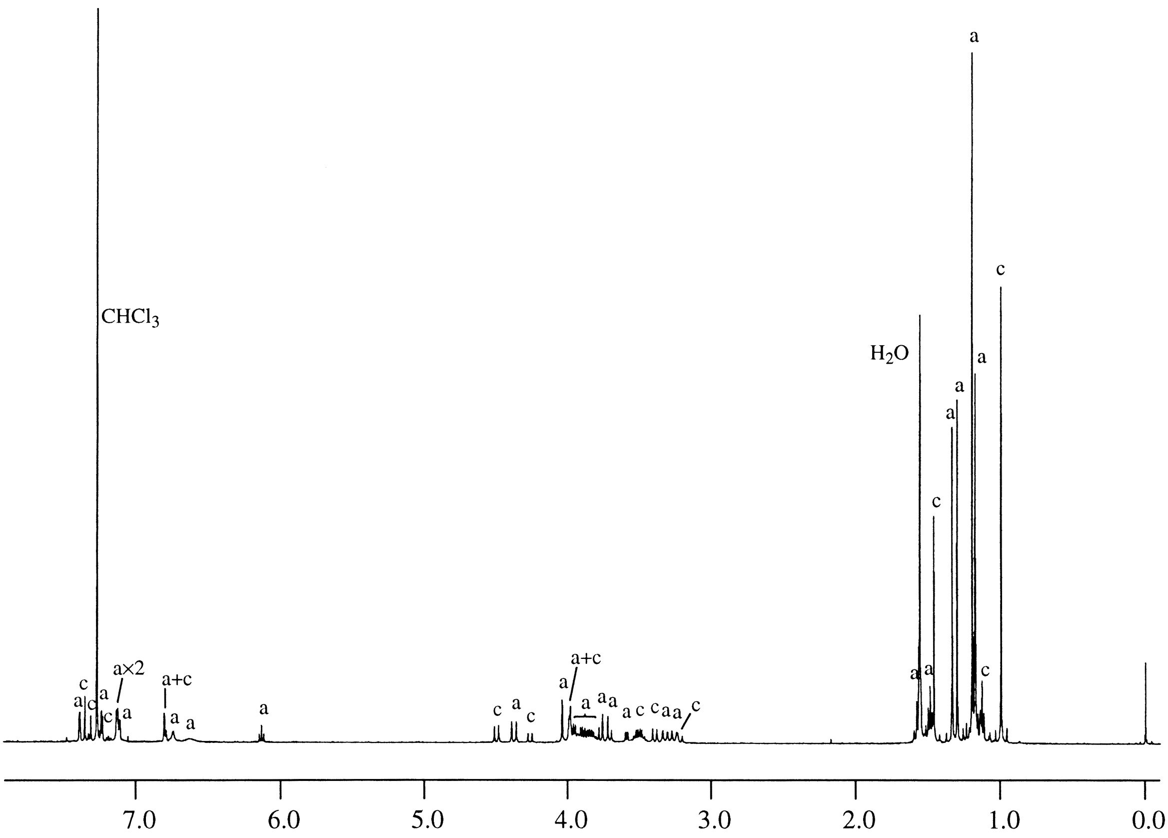
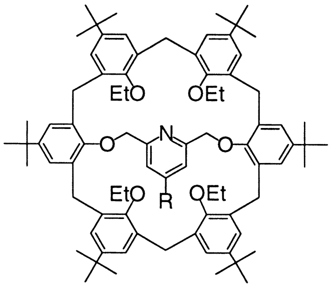


Fig. 3. ^{1}H NMR spectrum of the ethylated bridged calix[6]arene **6** (500 MHz, CDCl$_3$); "c" denotes the signals of cone isomer **6a** and "a" denotes 1,2,3-alternate isomer **6b**.

Table 1. Ratio of the Isomers of the Ethyl Derivatives[a)]

	6	**7**	**8**	**9**	**10**[b)]
Cone	28	40	100	100	100
1,2,3-alternate	72	60	0	0	0

a) Measured in CDCl$_3$ at room temperature. b) Pyridine-bridged calix[6]arene in Ref. 11b.



10 (R = OMe)
11 (R= H)

Chart 2.

TLC was carried out with Merck Kieselgel 60PF254 Art. 7747. ^{1}H NMR spectra were recorded on a Bruker DRX-500 or a JEOL JNM-A500 spectrometer. Assignments of NMR signals were based on 2D-COSY, HMQC, and HMBC spectra. Elemental analyses were performed by the Microanalytical Laboratory of the Department of Chemistry, Faculty of Science, the University of Tokyo.

General Procedure for the Alkylation of the Bridged Calix[6]arenes. To a suspension of bridged calix[6]arene (0.40 mmol) and cesium carbonate (1.57 g, 4.8 mmol) in DMF (40 mL) was added ethyl iodide or allyl bromide (2.4 mmol) and the reaction mixture was stirred at 70 °C for 1 d. After the addition of aq NH$_4$Cl, the mixture was extracted with chloroform, dried over MgSO$_4$, and the solvent was evaporated to dryness. The crude product was purified by recrystallization or silica-gel chromatography.

Synthesis of 38,39,41,42-Tetraallyloxy-37,40-[2-bromo-1,3-phenylenebis(methylenoxy)]-5,11,17,23,29,35-hexa-*t*-butylcalix[6]arene (5). The tetraallyl derivatives **5a** (36%) and **5b** (37%) were obtained after separation by preparative TLC (chloroform : hexane = 1 : 1).

5a: colorless crystals, mp 259 °C (dec); ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.00 (s, 36H), 1.44 (s, 18H), 3.22 (d, J = 14.8 Hz, 2H), 3.39 (d, J = 15.1 Hz, 4H), 3.90–3.96 (m, 8H), 4.07 (s, 4H), 4.26 (d, J = 14.8 Hz, 2H), 4.48 (d, J = 15.1 Hz, 4H), 5.08 (dd, J = 10.6, 1.3 Hz, 4H), 5.19 (dd, J = 17.3, 1.3 Hz, 4H), 5.77–5.85 (m, 4H), 6.79 (d, J = 1.8 Hz, 4H), 7.13 (d, J = 1.8 Hz, 4H), 7.18 (t, J = 7.5 Hz, 1H), 7.32 (s, 4H), 7.35 (d, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 27.12 (t), 30.87 (t), 31.52 (q), 31.74 (q), 34.09 (s), 34.19 (s), 72.58 (t), 74.03 (t), 115.92 (t), 123.96 (s), 124.67 (d), 125.57 (d), 125.62 (d), 126.37 (d), 128.55 (d), 131.82 (s), 131.90 (s), 133.94 (s), 134.68 (d), 137.30 (s), 144.34 (s), 145.06 (s), 152.17 (s), 152.62 (s). Found: C, 78.37; H, 7.92; Br,

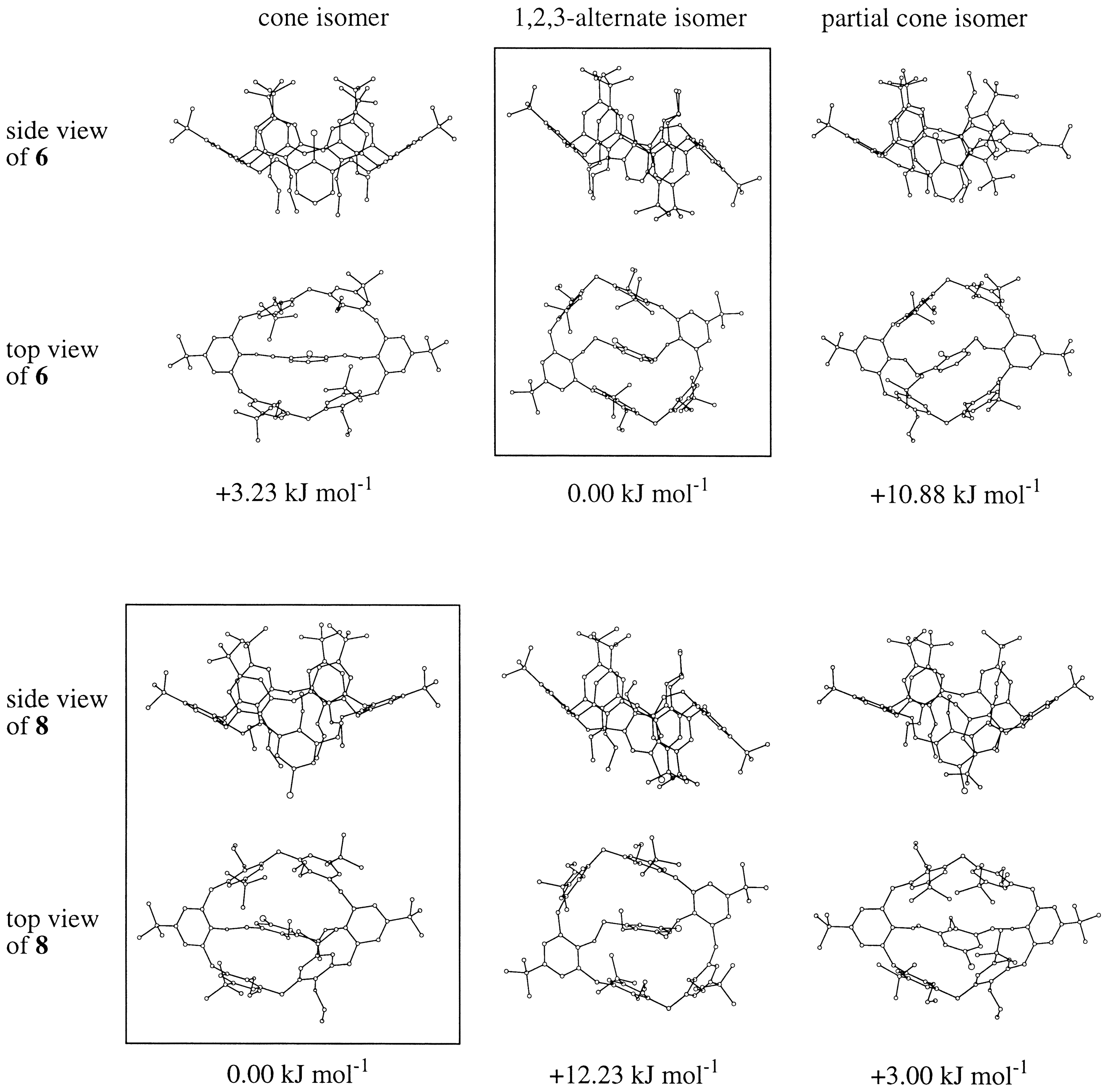
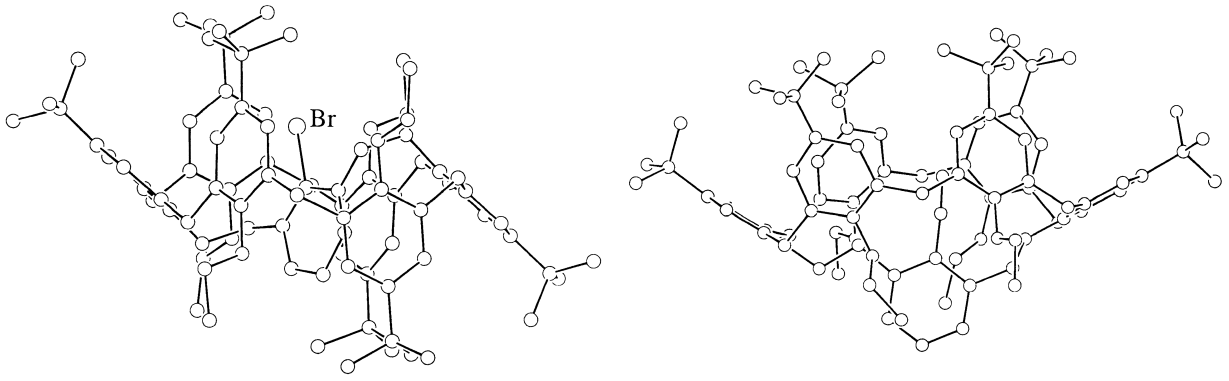


Fig. 4. The lowest energy structures of the conformational isomers of **6** and **8** calculated with MM3* force field (GB/SA $CHCl_3$) and their relative energies.

5.88%. Calcd for $C_{86}H_{105}BrO_6$: C, 78.57; H, 8.05; Br, 6.08%.

5b: colorless crystals, mp 233–239 °C (dec); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16 (s, 18H), 1.18 (s, 18H), 1.30 (s, 9H), 1.33 (s, 9H), 3.23 (d, J = 15.7 Hz, 2H), 3.31 (d, J = 15.9 Hz, 2H), 3.65 (dd, J = 7.5, 1.5 Hz, 1H), 3.72 (d, J = 12.6 Hz, 2H), 3.78 (d, J = 12.6 Hz, 2H), 3.96 (d, J = 15.7 Hz, 2H), 4.01 (s, 2H), 4.08 (s, 2H), 4.27 (dd, J = 12.6, 4.6 Hz, 2H), 4.33–4.37 (m, 4H), 4.39 (d, J = 15.9 Hz, 2H), 4.43 (dd, J = 12.1, 6.3 Hz, 2H), 5.28 (dd, J = 10.6, 1.3 Hz, 2H), 5.31 (dd, J = 10.4, 1.1 Hz, 2H), 5.50 (dd, J = 17.2, 1.3 Hz, 2H), 5.53 (dd, J = 17.2, 1.1 Hz, 2H), 6.11–6.19 (m, 2H), 6.15 (t, J = 7.5 Hz, 1H), 6.22–6.30 (m, 2H), 6.62 (br, 2H), 6.75 (br, 2H), 6.80 (dd, J = 7.5, 1.5 Hz, 1H), 7.11 (s, 2H), 7.12 (s, 2H), 7.20 (d, J = 2.3 Hz, 2H), 7.35 (d, J = 2.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.84 (t), 29.30 (t), 31.55 (q), 31.60 (q), 31.65 (q × 2), 34.06 (s), 34.16 (s), 34.20 (s), 34.32 (s), 35.12 (t), 71.28 (t), 72.89 (t), 73.18 (t), 73.77 (t), 116.44 (t), 117.39 (t), 123.83 (d), 125.13 (d × 2), 126.74 (s), 127.04 (d), 127.35 (d), 127.82 (d), 128.12 (d), 130.76 (d), 131.31 (d), 131.80 (s), 132.03 (s), 132.25 (s), 132.46 (s), 132.56 (s), 132.76 (s), 133.24 (s), 134.65 (d), 134.74 (d), 136.31 (s), 144.42 (s), 144.45 (s × 2), 144.98 (s), 150.09 (s), 153.74 (s), 154.03 (s), 154.47 (s). Found: C, 77.71; H, 7.88%. Calcd for $C_{86}H_{105}BrO_6 \cdot H_2O$: C, 77.51; H, 8.09%.

Synthesis of 37,40-[2-Bromo-1,3-phenylenebis(methylenoxy)]-5,11,17,23,29,35-hexa-*t*-butyl-38,39,41,42-tetraethoxycalix[6]arene (6). A mixture of conformational isomers (**a**/**b** = 28:72) was obtained in 65% yield after separation by preparative TLC (chloroform:hexane = 1:1).



6 **7**

Fig. 5. Crystal structures of **6** and **7**. Hydrogen atoms, disordered atoms, and the solvent molecules are omitted for clarity.

6: colorless crystals, mp > 300 °C; **6a**: ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.95 (s, 36H), 1.13 (t, J = 7.0 Hz, 12H), 1.46 (s, 18H), 3.21 (d, J = 14.9 Hz, 2H), 3.39 (d, J = 15.0 Hz, 4H), 3.47–3.54 (m, 8H), 3.99 (s, 4H), 4.26 (d, J = 14.9 Hz, 2H), 4.50 (d, J = 15.0 Hz, 4H), 6.80 (d, J = 1.8 Hz, 4H), 7.10 (d, J = 1.8 Hz, 4H), 7.18 (t, J = 7.4 Hz, 1H), 7.31 (d, J = 7.4 Hz, 2H), 7.34 (s, 4H). **6b**: ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.17 (s, 18H), 1.20 (s, 18H), 1.30 (s, 9H), 1.33 (s, 9H), 1.48 (t, J = 7.0 Hz, 6H), 1.56 (t, J = 7.1 Hz, 6H), 3.25 (d, J = 15.9 Hz, 2H), 3.32 (d, J = 15.8 Hz, 2H), 3.59 (dd, J = 7.6, 1.5 Hz, 1H), 3.71 (d, J = 12.5 Hz, 2H), 3.76 (d, J = 12.5 Hz, 2H), 3.81–3.96 (m, 10H), 3.98 (s, 2H), 4.04 (s, 2H), 4.37 (d, J = 15.8 Hz, 2H), 6.12 (t, J = 7.6 Hz, 1H), 6.62 (brs, 2H), 6.73 (brs, 2H), 6.79 (dd, J = 7.6, 1.5 Hz, 1H), 7.12 (s, 2H), 7.13 (s, 2H), 7.23 (d, J = 2.3 Hz, 2H), 7.38 (d, J = 2.4 Hz, 2H). Found: C, 75.03; H, 7.99; Br, 5.83; Cl, 3.18%. Calcd for C$_{82}$H$_{105}$BrO$_6$·0.4CHCl$_3$: C, 75.30; H, 8.08; Br, 6.08; Cl, 3.24%.

Synthesis of 5,11,17,23,29,35-hexa-*t*-butyl-38,39,41,42-tetraethoxy-37,40-[2-ethynyl-1,3-phenylenebis(methylenoxy)]calix[6]arene (7): Obtained as an inseparable mixture of conformational isomers (**a**/**b** = 40:60) in 58% yield after separation by preparative TLC (chloroform:hexane = 1:1).

7: colorless crystals, mp > 300 °C; **7a**: ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.46 (s, 1H), 1.01 (s, 36H), 1.14 (t, J = 6.8 Hz, 12H), 1.41 (s, 18H), 3.22 (d, J = 15.0 Hz, 2H), 3.40 (d, J = 14.6 Hz, 4H), 3.44–3.48 (m, 4H), 3.54–3.58 (m, 4H), 4.02 (s, 4H), 4.35 (d, J = 15.0 Hz, 2H), 4.48 (d, J = 14.6 Hz, 4H), 6.74 (d, J = 1.8 Hz, 4H), 7.12 (d, J = 1.8 Hz, 4H), 7.18 (t, J = 7.5 Hz, 1H), 7.27 (s, 4H), 7.35 (d, J = 7.5 Hz, 2H). **7b**: ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.18 (s, 18H), 1.22 (s, 18H), 1.28 (s, 9H), 1.32 (s, 9H), 1.48 (t, J = 6.9 Hz, 6H), 1.54 (t, J = 7.0 Hz, 6H), 2.17 (s, 1H), 3.22 (d, J = 14.0 Hz, 2H), 3.30 (d, J = 15.9 Hz, 2H), 3.55 (dd, J = 7.7, 1.5 Hz, 1H), 3.71 (d, J = 12.7 Hz, 2H), 3.76 (d, J = 12.7 Hz, 2H), 3.80–3.96 (m, 12H), 3.98 (s, 2H), 4.37 (d, J = 15.9 Hz, 2H), 6.20 (t, J = 7.7 Hz, 1H), 6.62 (brs, 2H), 6.78 (brs, 2H), 6.82 (dd, J = 7.7, 1.5 Hz, 1H), 7.10 (s, 2H), 7.12 (s, 2H), 7.22 (d, J = 2.6 Hz, 2H), 7.30 (d, J = 2.3 Hz, 2H). Found: C, 82.96; H, 8.78%. Calcd for C$_{84}$H$_{106}$O$_6$: C, 83.26; H, 8.82%.

Synthesis of 37,40-[5-bromo-2-methoxy-1,3-phenylenebis(methylenoxy)]-5,11,17,23,29,35-hexa-*t*-butyl-38,39,41,42-tetraethoxycalix[6]arene (8): Obtained in 72% yield after recrystallization from chloroform/methanol.

8: colorless crystals, mp > 300 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.90 (s, 3H), 0.98 (s, 36H), 1.24 (t, J = 6.9 Hz, 12H), 1.45 (s, 18H), 3.21 (d, J = 14.3 Hz, 2H), 3.39 (d, J = 15.0 Hz, 4H), 3.64–3.74 (m, 8H), 4.15 (s, 4H), 4.42 (d, J = 14.3 Hz, 2H), 4.49 (d, J = 15.0 Hz, 4H), 6.70 (d, J = 1.7 Hz, 4H), 7.08 (d, J = 1.7 Hz, 4H), 7.33 (s, 4H), 7.38 (s, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 15.51 (q), 27.19 (t), 30.73 (t), 31.47 (q), 31.71 (q), 34.00 (s), 34.24 (s), 60.31 (q), 68.45 (t), 68.66 (t), 114.28 (s), 123.81 (d), 125.17 (d), 128.11 (d), 128.65 (d), 132.27 (s), 133.19 (s), 133.67 (s), 134.76 (s), 144.60 (s), 145.12 (s), 152.39 (s), 152.76 (s), 155.83 (s). Found: C, 76.20; H, 8.19; Br, 6.16%. Calcd for C$_{83}$H$_{107}$BrO$_7$·0.5H$_2$O: C, 76.35; H, 8.34; Br, 6.12%.

Synthesis of 5,11,17,23,29,35-hexa-*t*-butyl-38,39,41,42-tetraethoxy-37,40-[1,3-phenylenebis(methylenoxy)]calix[6]arene (9): Obtained in 57% yield after recrystallization from chloroform/methanol.

9: colorless crystals, mp 291–296 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.91 (s, 36H), 1.26 (t, J = 7.0 Hz, 12H), 1.45 (s, 18H), 3.24 (d, J = 14.2 Hz, 2H), 3.44 (d, J = 15.5 Hz, 4H), 3.54–3.63 (m, 8H), 4.22 (s, 4H), 4.33 (d, J = 14.2 Hz, 2H), 4.46 (d, J = 15.5 Hz, 4H), 5.35 (s, 1H), 6.82 (d, J = 1.7 Hz, 4H), 6.89 (d, J = 1.7 Hz, 4H), 7.17 (s, 2H), 7.35 (s, 4H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 15.48 (q), 28.72 (t), 30.16 (t), 31.23 (q), 31.69 (q), 33.99 (s), 34.28 (s), 68.69 (t), 71.67 (t), 122.04 (d), 122.45 (d), 124.06 (d), 125.01 (d), 126.46 (d), 128.02 (d), 132.71 (s), 132.83 (s), 133.40 (s), 138.19 (s), 144.94 (s), 145.82 (s), 152.22 (s), 152.66 (s). Found: C, 81.76; H, 8.74%. Calcd for C$_{82}$H$_{106}$O$_6$·H$_2$O: C, 81.68; H, 9.03%.

Kinetic Measurements. A pure isomer of bridged calix[6]arene (**5a** or **5b**) dissolved in tetrachloroethane-d_2 was heated at 100 °C in NMR (270 MHz) probe. Molar ratios of **5a**/**5b**, calculated from the integral intensity of signals of *t*-butyl groups (1.00 ppm for **5a** and 1.16 and 1.18 ppm for **5b**), were monitored for two hours (19 points). A non-linear least square fit for the experimental data gave the rate constant $k_+ + k_-$ (8.5×10^{-4} s^{-1} for the experiment started from **5a** and 7.9×10^{-4} s^{-1} for **5b**) and equilibrated ratio of isomers (cone isomer/total isomer = 0.43 for both experiments) along with the time needed to adjust the temperature. The averaged value (8.2×10^{-4} s^{-1}) was used for the calculation of activation free energy.

Molecular Mechanics Calculations. All calculations were carried out with the MacroModel software package (version 5.5)[13] running on an O2 Silicon Graphics workstation. The energy was minimized using the MM3* force field after setting the solvent option to chloroform. Monte Carlo multiple-minimum conformational searches on **6** and **8** (4000 steps) were performed starting from the 1,2,3-alternate conformation to afford the 1,2,3-alternate (for **6**) and cone (for **8**) conformation as the global energy minimum structure, respectively. The energies of other isomers are those of the local minimum structures found in the conformational searches.

X-ray Crystallographic Analysis of 6 and 7. Single crystals of **6**·2CHCl$_3$ and **7**·2C$_6$H$_6$ were grown in chloroform/methanol and benzene/acetonitrile solutions, respectively. The intensity data were collected at 120 K on a MAC Science DIP-2030 imaging plate area detector with Mo$K\alpha$ radiation (λ = 0.71069 Å); such data were corrected for Lorentz and polarization factors, and for absorption using the multi-scan method. Crystallographic and experimental data were listed in Table 2. The structures were solved by the direct method and refined by full-matrix least squares on F^2 using SHELXL 97.[14] The non-hydrogen atoms were refined anisotropically except for the disordered benzene rings of **6**, one of which was refined using the rigid group model. Hydrogen atoms were idealized by using the riding model. The structure of **6** was also solved in the centrosymmetric space group $P2_1/n$ where the molecule of **6** possesses an inversion center resulted from a disorder of the bridging unit (50:50). The reflection data, however, showed no systematic absence in $h0l$ zone to exclude the possibility of $P2_1/n$, which was also supported by its higher $R1$ value (0.10). The ratio of the two disordered orientations of the bridging unit in space group $P2_1$ was finally refined to be 0.68:0.32. Lists of final atomic coordinates, bond lengths and angles, thermal parameters and torsion angles have been deposited as Document No 74055 at the Office of the Editor of Bull. Chem. Soc. Jpn. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition numbers 169225 and 169226.

Table 2. Crystallographic Data for **6**·2CHCl$_3$ and **7**·2C$_6$H$_6$

	6·2CHCl$_3$	**7**·2C$_6$H$_6$
Formula	C$_{84}$H$_{107}$BrCl$_6$O$_6$	C$_{96}$H$_{118}$O$_6$
Temperature/K	120	120
Crystal system	monoclinic	triclinic
Space group	$P2_1$	$P\bar{1}$
a/Å	13.321(1)	12.392(1)
b/Å	14.721(1)	17.180(1)
c/Å	20.678(1)	20.161(1)
α/deg		72.785(3)
β/deg	93.106(2)	82.023(2)
γ/deg		86.782(3)
V/Å	4049.0(5)	4059.7(5)
Z	2	2
Calculated density/g cm^{-3}	1.235	1.119
Reflections collected	26509	24635
Unique	14458	13606
R_{int}	0.018	0.013
F_{000}	1592	1484
Limiting indices	$-16 \le h \le 16$	$0 \le h \le 15$
	$-17 \le k \le 17$	$-20 \le k \le 21$
	$-25 \le l \le 25$	$-23 \le l \le 24$
Restraints/parameters	12/964	24/966
Goodness of fit (F^2)	1.026	1.033
R indices ($I > 2\sigma(I)$)	$R1 = 0.0515$	$R1 = 0.0599$
	$wR2 = 0.1420$	$wR2 = 0.1556$
R indices (all data)	$R1 = 0.0536$	$R1 = 0.0662$
	$wR2 = 0.1441$	$wR2 = 0.1633$

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