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Synthesis of Tetraalkylated Calix[4]arenes and Studies of Their Conformational Behaviors

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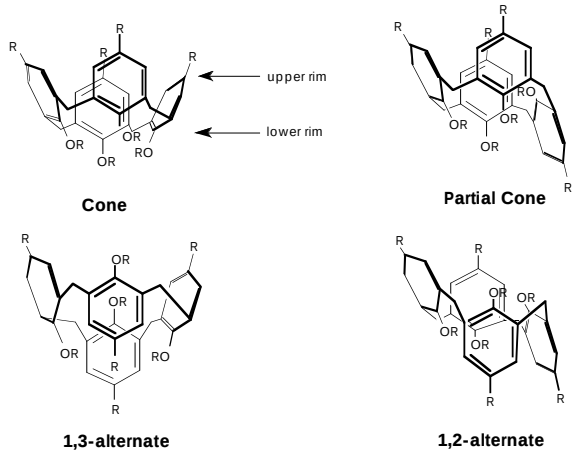
ABSTRACT Three new tetraalkylated calix[4]arenes, 25,27-[*N*,*N'*-di-((2-ethoxy)benzyl)propylene diamine]-26,28-dimethoxy-*p*-*tert*-butylcalix[4]arene dihydrochloride, 7, 25,27-[di(2-ethoxy) nitrobenzene]-26,28-dimethoxy-*p*-*tert*-butylcalix[4]arene, 10, and 25,27-[di(2-ethoxy)azobenzene]-26,28-dimethoxy-*p*-*tert*-butylcalix[4]arene, 11, have been synthesized. These compounds underwent the conformational interconversion of the calix[4]arene unit which could be studied by variable temperature ^{1}H NMR experiments. Rates of conformational interconversion of 7 were determined to be 111.0 s^{-1} and 94.6 s^{-1} in DMSO-d_6 at 50°C and CD_3OD at 27°C, respectively. In $CDCl_3$ at –30°C, compound 10 was found to exist in both cone and partial cone conformations with the ratio of 43:57. Cyclization of 10 by reductive coupling to 11 confined the calix[4]arene unit in cone conformation. The compound 11 in $CDCl_3$ then underwent conformational interconversion upon isomerization of the azobenzene unit leading to mixed conformations of calix[4]arene.

KEYWORDS: calixarene, conformation, interconversion, isomerization, azobenzene.

INTRODUCTION

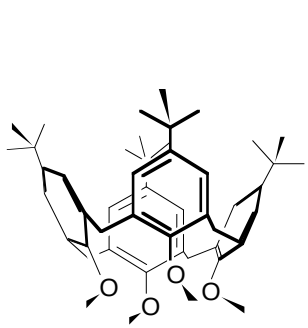
Calix[4]arene is a versatile supramolecular building block.[1-3] The molecule possesses a well preorganized cavity for accommodating guests such as metal ions. Both lower rim and upper rim of the calix[4]arene unit, in particular, can be modified to have useful moieties for complexing cations, anions and organic molecules. Besides these attractive properties, calix[4]arene also has an interesting conformational interconversion which occurred by rotation of the aryl rings through the methylene bridges. The possible conformations of calix[4]arene are cone, partial cone, 1,2-alternate and 1,3-alternate (Scheme 1). The cone conformation is the most favored among these 4 conformations due to the very strong intramolecular hydrogen bonding between the 4 OH groups at the lower rim of the calix.



Scheme 1. Possible conformations of calix[4]arene.

Conformational analysis of tetramethylated calix[4]rene, 1, is one of the most interesting aspects of these supramolecular building blocks. All possible conformations of compound 1 are found by theoretical calculations and NMR studies.[4-7] Shinkai and coworkers reported that upon increasing solvent polarity the concentration of the cone conformation of the calix[4]arene unit in 1 increased.[8] Later Reinhoudt and coworkers have reported the mechanism of conformational interconversion of a series of calix[4]arene derivatives, 2, containing 4 methoxy groups at the lower rim and a bridging group at the upper rim.[9] They found that the conformation of these compounds are confined to cone and partial cone and the movement of the aryl rings depends on the lengths of the bridging groups. Böhmer and colleagues demonstrated that the calix[4]arene unit in a calix[4]arene derivative, 3, tended to be in 1,3-alternate conformation for a shorter bridging chain.[10]

Our group has been working on the synthesis and complexation studies of di- and trisubstituted calix[4]arenes by ^{1}H NMR analysis for a number of years.[11-13] Understanding of the conformational



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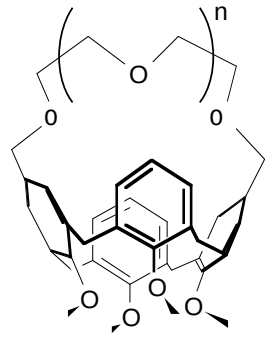

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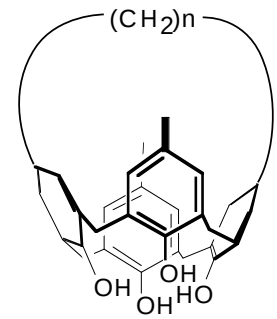

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interconversion of the calix[4]arene conformation is thus an important subject to pursue for better knowledge to control the complexation ability of this superb supramolecular building block. This article describes the synthesis and characterization of 25,27-*N*,*N*´-di((ethoxy)benzyl)propylenediamine-26,28-dimethoxy-*p*-*tert*-butylcalix[4]arene dihydrochloride, 7, 25,27-[di(2-ethoxy) nitrobenzene]-26,28-dimethoxy -*p*-*tert*-butylcalix[4]arene, 10, and 25,27-[di(2-ethoxy)azobenzene]-26,28-dimethoxy-*p*-*tert*-butylcalix[4]arene, 11. Both 7 and 11 contain two methoxy groups and bridging groups with different lengths and rigidity at the lower rim. We have studied effects of solvents and bridging groups towards the conformational interconversion of the calix[4]arene unit in these compounds.

Experimental Section

Materials

All materials were standard analytical grade, purchased from Fluka, JT Baker or Merck, and used without further purification. Commercial grade solvents such as acetone, dichloromethane and methanol were distilled and stored over 4 Å molecular sieves. Acetonitrile was dried according to the standard techniques.[14] Chromatographic separations were performed on silica gel columns (kieselgel 60, 0.063-0.200 mm, Merck). Thin layer chromatography (TLC) was carried out using silica gel plates (kieselgel 60 F_{254}, 1 mm, Merck). 25,27-Di-(2-ethoxy)benzaldehyde-*p*-*tert*-butylcalix[4] arene, 4,[15] and 26,28-dimethoxy-*p*-*tert*-butylcalix[4] arene, 9,[6] were prepared according to methods described in the literature. Unless otherwise noted, all reactions were carried out under nitrogen.

Analytical Instruments

Elemental analyses were carried out on a Perkin Elmer CHON/S analyser (PE2400 series II). Melting points were taken on an Electrothermal 9100 apparatus. UV-visible spectra were recorded on a Spectronic 3000 array spectrophotometer. The ^{1}H-NMR spectra were recorded either on a Bruker ACF 200 MHz or a Bruker AM 400 MHz nuclear magnetic resonance spectrometer. Variable temperature NMR experiments were carried out on a JEOL 500 MHz NMR spectrometer at the Scientific and Technological Research Equipment Center of Chulalongkorn University. Temperatures employed are 120, 100, 50, 27, 0, -15, -25, -35 and -40°C depending on the solvents. In most cases, samples were dissolved in deuterated chloroform and chemical shifts were recorded using a residual chloroform signal as internal reference.

Preparation of 25,27-di-((2-ethoxy)benzaldehyde) -26,28-dimethoxy-p-tert-butylcalix[4]arene, 5. Compound 4 (1.12 g, 1.19 mmol), BaO (0.19 g, 1.21 mmol) and dry THF (80 mL) were placed in a 250 mL two-necked round bottom flask and stirred for 1.5 hours. Then, *t*-BuOK (0.41 g, 3.63 mmol) and CH_3I (0.39 mL, 6.24 mmol) were added to the mixture. The reaction was heated at reflux for 1 hour. After the reaction was cooled to room temperature, THF was evaporated by reduced pressure to dryness. The residue was dissolved in CH_2Cl_2 and washed with 1 M HCl. The organic layer was subsequently separated, dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was chromatographed on a silica gel column using 10% EtOAc in hexane as eluant to separate a crude product of 5 which was further purified by column chromatography using 1% CH_3OH in CH_2Cl_2 as eluent (0.33 g, 28%).

δ_H (200 MHz; $CDCl_3$) 0.79 and 1.04 (9H each, br s, CH_3OAr-*t*-C_4H_9), 1.27 (18H, br s, ROAr-t-C_4H_9), 3.14 (4H, br s, ArCH_2Ar), 3.82 (6H, s, OCH_3), 4.03-4.50 (12H, m, OCH_2CH_2O- and ArCH_2Ar), 6.50 (4H,

br s, CH_3OArH), 6.98-7.05 (8H, m, aromatic and ROAr*H*), 7.52 (2H, t, *J 8.3*, aromatic), 7.82 (2H, d, *J 7.7*, aromatic), 10.44 (2H, br s, C*H*O); Anal. Calc. for $C_{64}H_{76}O_8$: C, 78.98; H, 7.87. Found C, 78.97; H, 7.77.

Preparation of 25,27-[N,N'-di-((2-ethoxy) benzyl)propylenediimine]-26,28-dimethoxy-p-tert-butylcalix[4]arene, 6. Into a stirred solution of compound 5 (0.56 g, 0.58 mmol) in CH_3CN (60 mL) was added dropwise a solution (CH_3OH, 12 mL) of 1,3-diaminopropane (0.08 mL, 0.96 mmol). The reaction was heated at reflux for 24 hours. White solid of 6 precipitated after the reaction mixture was cooled to room temperature. It was isolated by filtration, washed with cold CH_3OH and dried (0.32 g, 55%).

δ_H (200 MHz; $CDCl_3$) 0.79 and 1.03 (9H each, br s, CH_3OAr-*t*-C_4H_9), 1.27 and 1.32 (9H each, br s, ROAr-t-C_4H_9), 1.52-1.70 (1H, m, $NCH_2CH_2CH_2N$), 1.85-2.05 (1H, m, $NCH_2CH_2CH_2N$), 2.80-3.32 (8H, m, NCH_2CH_2 and $ArCH_2Ar$), 3.32-3.61 (3H, br m, OCH_3), 3.74 (3H, br s, OCH_3), 3.90-4.50 (12H, m, OCH_2CH_2O- and $ArCH_2Ar$), 6.43 and 6.50 (4H, br s, CH_3OArH), 6.70-7.10 (8H, m, aromatic and ROAr*H*), 7.27-7.32 (2H, m, aromatic), 7.90 (2H, d, *J 7.2*, aromatic), 8.65 (2H, br s, *H*C=N); Anal. Calc. for $C_{67}H_{82}N_2O_6$: C, 79.57; H, 8.17; N, 2.77. Found C, 79.49; H, 8.03; N, 2.62.

Preparation of 25,27-[N,N'-di-((2-ethoxy) benzyl)propylenediamine]-26,28-dimethoxy-p-tert-butylcalix[4]arene dihydrochloride, 7. Compound 6 (0.47 g, 0.46 mmol) was stirred with suspended $NaBH_4$ (0.48 g, 12.64 mmol) in CH_2Cl_2 (100 mL) for 2 days. Excess $NaBH_4$ was then destroyed by adding a copious amount of water. The organic layer was separated, dried over anhydrous Na_2SO_4 and evaporated to dryness to give a white residue. The residue was added 2% HCl in CH_3OH until pH of the solution became 1. Upon removal of CH_3OH, white solid of 7 precipitated (0.39 g, 77%).

δ_H (500 MHz at 100 °C; DMSO-d_6) 0.95 (18H, s, CH_3OAr-*t*-C_4H_9), 1.30 (18H, br s, ROAr-*t*-C_4H_9), 2.03 (2H, br m, $NCH_2CH_2CH_2N$), 2.84 (4H, br m, $NCH_2CH_2CH_2N$), 3.28 (4H, br m, $ArCH_2Ar$), 3.54 (4H, br s, $ArCH_2N$), 4.11 (6H, br s, OCH_3), 4.16-4.18 (8H, br m, $ArCH_2Ar$ and OCH_2CH_2O), 4.38 (4H, br m, OCH_2CH_2O), 6.65 (4H, br s, CH_3OArH), 7.02 (2H, t, *J 8.3*, aromatic), 7.12 (2H, d, *J 7.2*, aromatic), 7.16 (4H, s, ROAr*H*), 7.38 (2H, t, *J 8.3*, aromatic), 7.59 (2H, d, *J 7.2*, aromatic); MALDI-TOF MS for [M^+]; 1014.2 m/z.

Preparation of 2-(2'-bromoethoxy)nitrobenzene, 8. In a 500 mL two-necked flask equipped with a magnetic bar and a reflux condenser, *o*-nitrophenol (4.45 g, 32.0 mmol), 1,2-dibromoethane (60.11 g, 320.0 mmol) and K_2CO_3 (8.85 g, 64.0 mmol) were mixed in CH_3CN (150 mL). The mixture was refluxed for 24 hours and then allowed to cool to room temperature. The solid was separated by filtration and washed with CH_2Cl_2. The combined solution was then evaporated to dryness to obtain a yellow residue. Methanol was subsequently added to dissolve this residue, and the solution was chilled in an ice bath to precipitate white solid identified as dinitrophenoxy ethylene. The white precipitate was filtered and washed with cold methanol (0.55 g, 7%). The supernatant was evaporated to dryness. The residue was then dissolved in diethyl ether. The desired product, 8, crystallized as a bright yellow solid by adding hexane (5.80 g, 74%).

Melting point: 164-165°C; δ_H (200 MHz; $CDCl_3$) 3.65 (2 H, t, *J* 6.0, $-OCH_2CH_2Br$), 4.40 (2 H, t, *J* 6.0, $-OCH_2CH_2Br$), 7.02-7.10 (2 H, m, aromatic), 7.52 (1 H, t, *J* 8.0, aromatic), 7.81 (1 H, d, *J* 8.0, aromatic); Anal. Calc. for $C_8H_8BrNO_3$: C, 39.05; H, 3.28; N, 5.69. Found C, 39.07; H, 3.21; N, 5.65.

Preparation of 25,27-[di(2-ethoxy)nitrobenzene]-26,28-dimethoxy-p-tert-butylcalix[4]arene, 10. In a 250 mL two-necked flask equipped with a magnetic bar and a condenser, 9 (1.37 g, 2.03 mmol), K_2CO_3 (1.12 g, 8.11 mmol), KOH (3-5 pellets) were mixed in CH_3CN (50 mL). After stirring at 35-40°C for 4 hours, 8 (1.00 g, 4.06 mmol) in CH_3CN (40 mL) was then slowly added . The mixture was refluxed for 48 hours and allowed to cool to room temperature. The mixture was filtered and the solid residue was washed with CH_2Cl_2. The filtrate was combined and the solvent was removed to give a brown viscous residue. The residue was dissolved in CH_2Cl_2, washed with saturated NH_4Cl solution and extracted with H_2O (2 x 20 mL). The organic phase was subsequently separated and dried over anhydrous Na_2SO_4. After separation of Na_2SO_4, the solvent was removed to give a dark brown residue. The residue was redissolved in a minimum amount of CH_2Cl_2 and chromatographed on a silica gel column with 10% ethyl acetate in hexane as eluent. The desired product, 10, was crystallized in methanol to give orange needles (0.41 g, 20%).

Melting point: 189-191°C; δ_H (200 MHz; $CDCl_3$) 0.84 and 1.05 (9 H each, br s, CH_3OAr*t-Bu*), 1.28 (18 H each, br s, ROAr*t-Bu*), 3.00-3.40 (4 H, br, $ArCH_2Ar$), 3.47 (6 H, s, $-OCH_3$), 3.60-4.60 (12 H, br, $ArCH_2Ar$ and $-OCH_2CH_2O$-), 6.40-6.69 (4 H, br, CH_3OArH), 6.92-7.30 (8 H, br, nitrobenzene and ROAr*H*), 7.51 (2 H, t, *J* 7.0, nitrobenzene), 7.81 (2 H, d, *J* 8.0,

nitrobenzene); Anal. Calc. for $C_{62}H_{74}N_2O_{10}$: C, 73.93; H, 7.40; N, 2.78. Found C, 73.92; H, 7.46; N, 2.76.

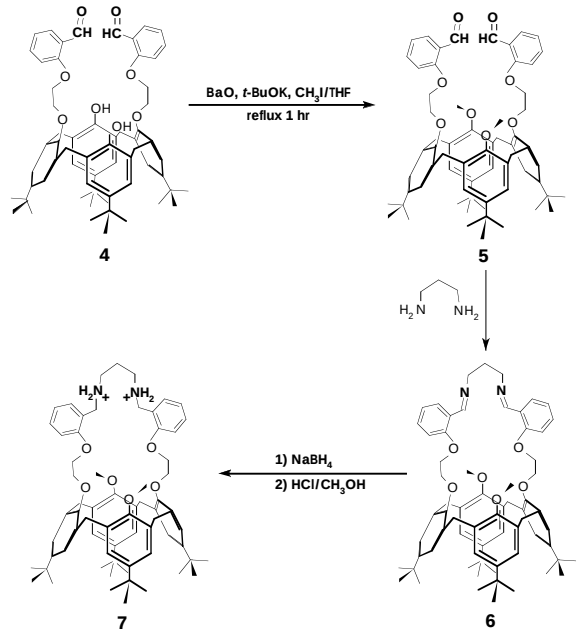
Preparation of 25,27-[di(2-ethoxy)azobenzene]-26,28-dimethoxy-p-tert-butylcalix[4]arene, 11. Compound 10 (0.51 g, 0.50 mmol) in isopropanol (10.0 mL), NaOH (0.20 g, 5.00 mmol) in H_2O (2 mL) and zinc (0.13 g, 2.00 mol) were placed in a 50 mL round-bottom flask. The mixture was refluxed for 2 days and allowed to cool to room temperature. The mixture was filtered and the residue was washed with CH_2Cl_2. The combined filtrate was evaporated to obtain an orange residue. The residue was dissolved in CH_2Cl_2, washed with NH_4Cl and extracted with H_2O (2 x 20 mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The product was then filtered and purified by silica gel column with 5% ethyl acetate in hexane as eluent. It was crystallized in methanol and ethyl acetate to give orange crystals (0.06 g, 12 %).

Melting point: 228-230°C; δ_H (400 MHz; $CDCl_3$) 0.82 and 1.28 (18 H each, s, *t*-Bu protons), 3.10 and 4.23 (4 H each, d, J_{AB} 12.0, ArC*H*$_2$Ar), 3.44 (6 H, s, -OC*H*$_3$), 4.34 and 4.63 (8 H, m, -OC*H*$_2$C*H*$_2$O-), 6.42 (4 H, s, CH_3OAr*H*), 6.94 (2 H, m, azobenzene), 7.01 (4 H, s, ROAr*H*), 7.08 (4 H, m, azobenzene), 7.41 (2 H, m, azobenzene); Anal. Calc. for $C_{62}H_{74}N_2O_6$: C, 78.95; H, 7.91; N, 2.97. Found C, 79.06; H, 7.91; N, 2.97; UV/vis [l (nm), e ($dm^3 \cdot mol^{-1} \cdot cm^{-1}$)]: 334, 19385; 440, 7714.

Results and Discussion

Synthesis and Characterization

We have synthesized 25,27-*N*,*N*´-di((ethoxy) benzyl) propylenediamine-26,28-dimethoxy-*p*-*tert*-butylcalix[4]arene dihydrochloride, 7, according to the procedure shown in Scheme 2. The preparation of 7 started from methylation of 4 with 2 equiv. of CH_3I in the presence of BaO and *t*-BuOK in THF to obtain the methylated product, 5, in 28%. The product 5 was further reacted with propylene diamine (1:1 stoichiometry) in acetonitrile to precipitate a Schiff base, 6, in 55%. The Schiff base was subsequently reduced with $NaBH_4$ in CH_2Cl_2 and then protonated with 2% v/v HCl/CH_3OH to give the desired product 7 in 76%. ^{1}H NMR spectra of 5, 6 and 7 in $CDCl_3$ at

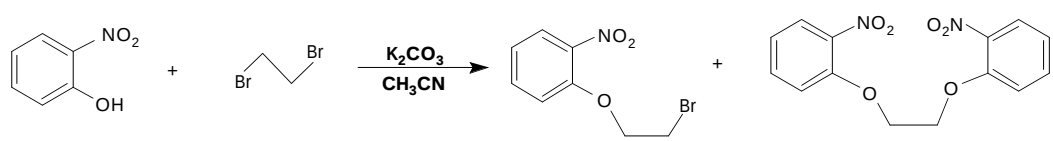


Scheme 2. Synthetic procedure for preparation of 7.

room temperature showed broad signals indicating the conformational interconversion of the calix[4]arene framework due to lack of intramolecular hydrogen bonding. However, elemental analysis results of compounds 5-7 agree with the proposed structures.

We have synthesized other tetrasubstituted calix[4]arenes by attaching two ethoxy nitrobenzene groups into the dimethoxy calix[4]arene (9) framework. Reductive coupling of nitrobenzene groups was then employed to afford the azobenzene crown ether calix[4]arenes. This synthetic procedure started from a nucleophilic substitution reaction between *o*-nitrophenol and excess 1,2-dibromoethane resulting in the isolation of the mono-substituted compound 8 (74%) and disubstituted compound (7%), eq 1. Excess 1,2-dibromoethane was needed in order to produce the monosubstituted product. If the equimolar amount of 1,2-dibromoethane was used, the major product was found to be the disubstituted compound.

Nitrobenzene calix[4]arenes, 10, was synthesized by a nucleophilic substitution reaction between 8 and 9 in the presence of K_2CO_3. Sugar-like crystals



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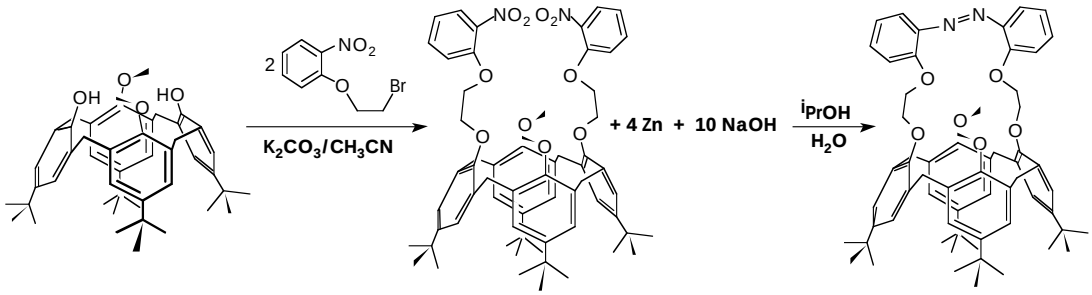

9 **10** **11**

of 10 was obtained in 20% after separation and purification. Reductive coupling of 10 using zinc metal in propanol/water gave the azobenzene, 11, which was crystallized from hot methanol to give orange crystals (12%), eq 2. ^{1}H NMR spectra and microanalysis results of 8, 10 and 11 agree well with the proposed structures.

Effects of Solvents and Temperatures towards Conformational Interconversion of 7

Due to the bridge between 2 opposite phenoxy oxygens at the lower rim, the possible conformation of the calix[4] arene framework of 7 are cone, partial cone and 1,3-alternate. We thus studied the conformational behaviors of 7 by ^{1}H NMR spectroscopy. ^{1}H-NMR spectra of 7 in $CDCl_3$, DMSO-d_6 and CD_3OD at room temperature were recorded. The ^{1}H-NMR spectrum in $CDCl_3$, an aprotic solvent, showed complicated lines of *t*-butyl signals and broad lines in the aromatic region. In DMSO-d_6 (Figure 1c), there are three broad singlets appear at 0.81, 0.98 and 1.27 ppm due to CH_3OAr-*t*-C_4H_9 and ROAr-*t*-C_4H_9. The signals in the aromatic region are also complicated and broad. The results show that the conformational interconversion of the calix[4]arene framework occurs in $CDCl_3$ and DMSO-d_6. Interestingly, the ^{1}H NMR spectrum of 7 in CD_3OD (Fig 1b), a polar protic solvent, shows two sharp singlets of *t*-butyl protons at 0.99 and 1.34 ppm and also two broad singlets at 7.21 and 6.71 ppm due to ROAr*H* and CH_3OAr*H*. This signifies the effect of solvents on the rate of the aryl ring interconversion in the calix[4]arene unit.

The temperature dependence of the conformational interconversion in $CDCl_3$, DMSO-d_6 and CD_3OD were then investigated by variable temperature NMR spectroscopy. Unfortunately, the spectra of 7 in $CDCl_3$ showed complicated signals in all regions and the coalescence point cannot be observed. However, upon increasing temperature, the ^{1}H NMR spectra of 7 in DMSO-d_6 became sharper. We have noticed that the singlet at 1.30 ppm was always sharp at various temperatures while the singlet at 0.95 ppm was broad and became more resolved at higher temperature. The signal at 1.30 ppm must belong to $R_{brd}OArC(CH_3)_3$ and the latter is assigned to $CH_3OArC(CH_3)_3$ because the aryl rings of $R_{brd}OArC(CH_3)_3$ cannot move as freely as the rings containing CH_3O- groups. The spectrum recorded at 100 °C is illustrated in Figure 1d. The singlets for CH_3OArH and ROAr*H* appear at 6.65 and 7.16 ppm, respectively. The four aromatic protons of the bridging group become distinct from each other and appear at 7.02, 7.12, 7.38 and 7.59 ppm. The $-OCH_3$ signal appears at 4.11 ppm. We have found that the coalescence temperature was at 50 °C with the line width (at 6.65 ppm) of 50 Hz. The rate of the conformational interconversion was then calculated to be 111.0 s^{-1}.[16]

In addition, studies of the conformational interchange of 7 at lower temperature have been performed in CD_3OD. The spectrum at -40°C (Fig 1a) shows several singlet peaks in the *t*-butyl region and a very complicated signals due to methylene bridge protons suggesting a mixed conformation of the calix[4]arene framework upto 2 conformations in the solution (possibly cone and partial cone). Unfortunately, the spectrum is too complicated to identify the ratio of each conformation. The coalescence temperature was found at 27°C with the line width (at 6.72 ppm) of 43 Hz. The rate of conformational interconversion was calculated to be 94.6 s^{-1} in CD_3OD. However, judging from the coalescence temperature which is lower in CD_3OD, the rate of interconversion seems to be faster in CD_3OD than in DMSO-d_6 or $CDCl_3$ at the same temperature. The presence of the hydrogen bonding in CD_3OD may thus be responsible for increasing the interconversion rate of the aryl rings of calix[4]arene.

In order to examine the effect of conformational interconversion on the complexation ability of 7, the

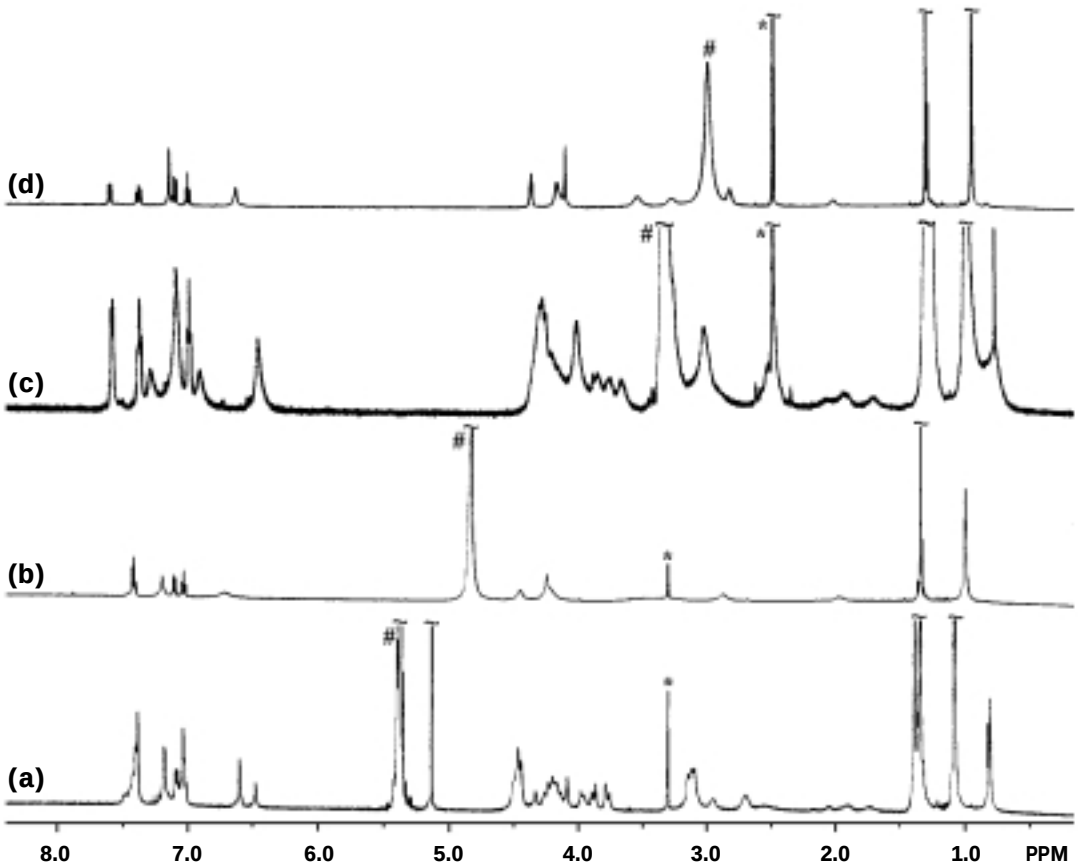

Fig 1. ^{1}H NMR spectra of 7 (a) in CD_3OD at –40°C (b) in CD_3OD at 27°C (c) in DMSO-d_6 at 27°C (d) in DMSO- d_6 at 100°C. * and # denote the trace of water in the solvent and the solvent signal, respectively.

complexation studies of 7 with Zn^{2+} was performed by potentiometric titration.[17] The result showed that 7 did not form a complex with Zn^{2+} as its analogous compound, 25,27-[*N*,*N*'-di-((2-ethoxy)benzyl) propylenediamine]-26,28-dihydroxy-*p*-*tert*-butylcalix[4]arene, did.[12] The conformational interconversion may, therefore, prohibit 7 to form a complex with Zn^{2+}.

Effects of the length and rigidity of the bridging group

In the same manner as 7, the ^{1}H NMR spectrum of 10 in $CDCl_3$ at room temperature (Figure 2a) shows complicated broad signals which indicate the existence of conformation interconversion leading to a mixed conformation of the calix[4]arene framework. However, the ^{1}H NMR spectrum of 10 is more resolved than that of 7 in $CDCl_3$ suggesting the increasing rigidity of calix[4]arene in 10. Upon decreasing temperature, the broad signals became sharper. However, signals due to protons on nitrobenzene rings do not change much when compared to other signals. This implies that the movement of the calix[4]arene unit occurs on the aryl ring containing OCH_3 group. The 500 MHz ^{1}H NMR spectrum of 10 at -30°C (Figure 2b) reveals that in solution ($CDCl_3$) 10 exists as a mixture of two conformers: partial cone and cone conformations. The cone conformation possesses two planes of symmetry. The *t*-butyl protons appear as two singlets at 0.78 and 1.29 ppm. The methoxy protons appear as a singlet at 3.81 ppm. On the other hand, the partial cone conformation has only one plane of symmetry. The *t*-butyl protons appear as three singlets at 1.04, 1.18 and 1.28 ppm (ratio 2:1:1). The methoxy protons appear as two singlets at 3.01 and 3.18 ppm (ratio 1:1). There should be 3 pairs of signals due to methylene bridge protons in the spectrum; however, the signals are superimposed on the glycolic proton signals which appear as 4 sets of multiplets between 4.00-4.50 ppm. The ratio of cone:partial cone can be calculated from the integration ratio of the methyl protons of each conformation to be 43:57.

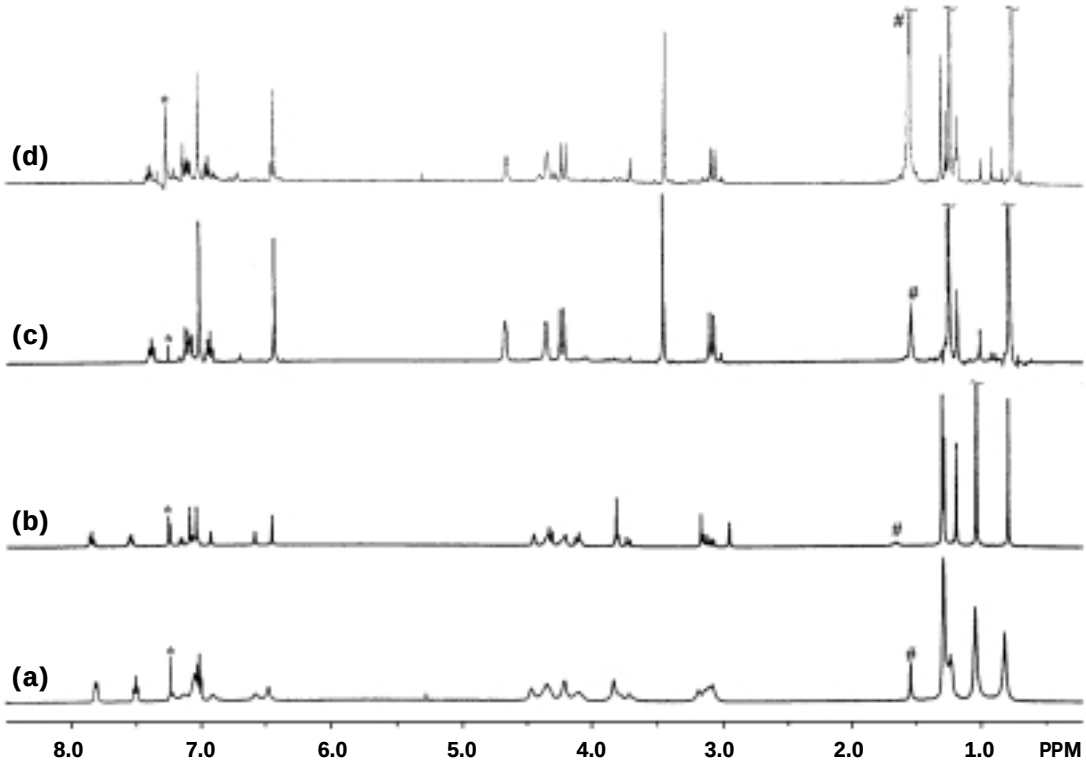

Fig 2. ^{1}H NMR spectra ($CDCl_3$) of (a) 10 at 27°C (b) 10 at -30°C (c) 11 at 25°C (d) 11 at 25°C after isomerization. * and # denote the trace of water in the solvent and the solvent signal, respectively.

The ^{1}H NMR spectrum of the coupling product ($CDCl_3$, room temperature), 11, is quite well resolved (Figure 2c), compared to that of 10. The spectrum suggests that 11 exists in a cone conformation which represents by one pair (AB system) of methylene bridge protons at 3.10 and 4.23 ppm (J = 12 Hz) and two singlets at 6.24 and 7.01 ppm corresponding to the *meta*-protons on the phenyl rings of calix[4]arene. The *t*-butyl protons appear as two sharp singlets at 0.82 and 1.28 ppm. The result shows that the bridging group of 11 (ethoxyazobenzene) can enhance the rigidity of the calix[4]arene framework probably by squeezing the two connected aryl rings together, which makes it harder for the methoxy groups to swing through the calixarene annulas.

It is well known that azobenzene exists in two isomers: *cis* and *trans*.[18] These two isomers can be switched by light. Upon standing in the day light for several hours, the ^{1}H NMR spectrum of 11 changed dramatically. In Fig 2d, there are many singlets due to *t*-butyl protons between 0.7-1.4 ppm. The region of the methylene and aromatic protons becomes very complicated. Another singlet probably due to methoxy protons appears at 3.72 ppm. The results suggest the occurrence of mixed conformations in the NMR time scale and also show that the conformational interconversion of the calix[4]arene unit takes place upon isomerization of the azobenzene unit which acts as a bridging group. Compared to the results obtained by Reinhoudt et al,[9] compound 2 containing shortest glycolic chain (n = 1) still showed conformational interconversion. The length of the bridging chains may not be the only one factor in controlling the conformational interconversion. The rigidity or inflexibility of the bridging group must also be accounted for governing the conformational behavior of calix[4]arene. Recently, Okada and colleagues have discovered that using the proper bridging groups between aryl rings at the *ortho* and *para* positions (with respect to the hydroxy groups) resulted in rigid calix[4]arene frameworks.[19,20]

Conclusion

The calix[4]arene unit in 7 containing a benzo propylenediamine bridging group was found to undergo conformational interconversion at different rates depending on solvents. In a protic solvent like

CD_3OD, the conformational interconversion seemed to be faster than in aprotic solvents such as $CDCl_3$ and DMSO-d_6 at the same temperature. Changing two substituents to ethoxy nitrobenzene in 10 increased the rigidity of calix[4]arene. Compound 10 existed in both cone and partial cone conformation (43:57) in $CDCl_3$ at –30 °C. Reductive coupling of nitrobenzene to azobenzene in 11 allowed the calix[4]arene unit to exist in cone conformation. Reducing rigidity upon isomerization of the azobenzene group caused the conformational interconversion to occur and resulted in mixed conformations of calix[4]arene. We have thus demonstrated that temperature, solvent, length and rigidity of bridging groups have strong effects on conformational behaviors of the calix[4]arene unit.

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