Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
Tetrahedron 62 (2006) 6082–6089

Calix[4]quinones. Part 4: The ClO_2 oxidation of calix[4]arene dialkyl ethers

Yu-Lung Lin, Tzer-Shun Yu, Wen-You Wang and Lee-Gin Lin*

Institute of Applied Chemistry, Chinese Culture University, Taipei 11114, Taiwan, ROC

Received 29 November 2005; revised 31 March 2006; accepted 31 March 2006
Available online 27 April 2006

Abstract—Except for the special case of calix[4]arene diethyl ether **1**, the chlorine dioxide oxidation of dialkyl ethers **2**–**5** yielded only the corresponding calix[4]diquinone dialkyl ethers **8**–**11**. Chlorine dioxide oxidation of calix[4]arene diethyl ether **1** produced two isomeric products **6** and **7**, which were stable enough to be isolated by column chromatography. However, a slow conformational interconversion between isomeric pair **6** and **7** was observed at room temperature, and the equilibrium was reached after 400 h at 18 °C with an amount of 5:3 in favor of *syn*-isomer.
© 2006 Published by Elsevier Ltd.

1. Introduction

Electron transport systems are the vital pathways for energy-producing mechanisms in all living cells, and the quinone and dihydroquinone (*p*-hydroxyphenol) pairs are the key moieties in coenzyme Q for the charge transport process. Based on these known principles, it is rational to propose that the calixquinone and *p*-hydroxycalixarene pairs may serve as an enzyme model to probe the charge transport process.

In the literature, two groups of the calix[4]quinones derivatives, e.g., benzoated calix[4]quinones[1] and etherated calix[4]-quinones,[2,3] were reported. The calix[4]quinone benzoates were synthesized by treating the corresponding calix[4]arene benzoates with chlorine dioxide at room temperature,[1] whereas, the oxidation of calix[4]arene ether derivatives occurred under more severe conditions.[3] Although, a milder chlorine dioxide oxidation condition for calix[4]arene ether derivatives was noted by Gutsche and his co-workers,[2] eventually the oxidation reactions were performed on thallium tris-trifluroacetate in trifluroacetic acid.[3] In this paper, we report on the isolation of calix[4]quinone ether derivatives **6**–**11** from the chlorine dioxide oxidation of the corresponding calix[4]arene ethers **1**–**5**, and also describe primarily the kinetic result of a slow conformational interconversion between isomeric pair **6** and **7**.

Keywords: Calix[4]arene; Calix[4]quinone; Chlorine dioxide oxidation; Conformational interconversion.
* Corresponding author. E-mail: lglin@faculty.pccu.edu.tw

0040–4020/$ - see front matter © 2006 Published by Elsevier Ltd.
doi:10.1016/j.tet.2006.03.110

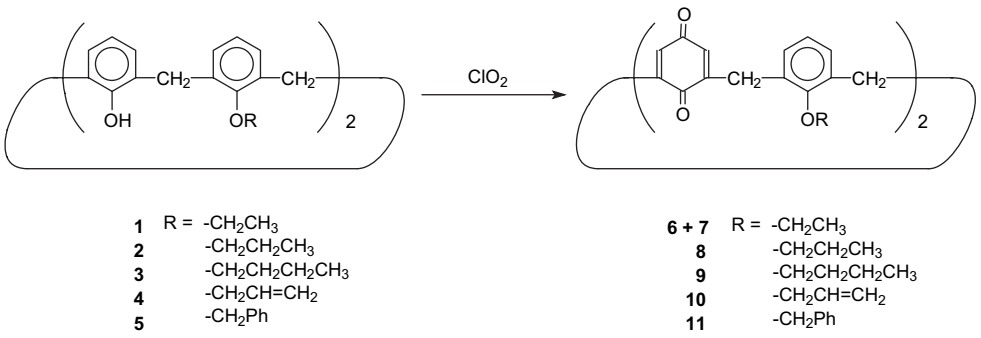
2. Results and discussion

2.1. Calix[4]diquinone dialkyl ethers 6–11

In our earlier work, we have established a standard synthetic procedure for converting the benzoated calix[4]arenes to the corresponding benzoated calix[4]quinones. It would be supportive in calixarenes chemistry if the converting pathway for the calix[4]arene ethers to their corresponding calix[4]-quinones can be established under the same milder reaction conditions.

Due to the conformational flexibility of the calix[4]arene dimethyl ether, five other common calix[4]arene dialkyl ethers (**1**–**5**) were prepared[4] for the study of the chlorine dioxide oxidation as shown in Scheme 1. As in a standard procedure for the oxidation of calix[4]arene benzoated, the calix[4]arene dialkyl ethers **1**–**5** were dissolved in acetonitrile and oxidized with a portion of yellow aqueous chlorine dioxide solution. The reaction mixture was stirred at room temperature, and the reaction was monitored by thin layer chromatography to determine the optimal reaction time for different calix[4]arene dialkyl ethers. Unlike their benzoates counterparts,[1] the oxidization of the calix[4]arene ether derivatives proceeded at various pace, which ranged from 4 h to 96 h. Although the exact solubility of five dialkyl ethers **1**–**5** in acetonitrile was not measured, the solubility, and hence the oxidation rate, seemed to be decreased as the sizes of the substitutent increased.

Large quantities of yellow solids were afforded for all five oxidative reactions after a standard worked up procedure. Except for calix[4]arene diethyl ether, all other oxidation



Scheme 1.

cases produced only one major component. Unfortunately, a simple recrystallization method was not able to isolate the corresponding oxidative products, and therefore, the chromatographic separation was applied for all the oxidation reactions to isolate the corresponding products **6–11**.

In the chlorine dioxide oxidation conditions, only the free phenol moieties were oxidized into quinones and the alkylated phenol moieties were not affected. Therefore, the oxidated products **6–11** retained the structural C_{2v} symmetry, and the products were easy to identify by their ^{1}H NMR spectrum. Of all the ^{1}H NMR spectra of products **6–11**, a singlet for quinone hydrogens appeared, whereas, the signals for the phenol moieties, which composed one singlet for phenolic hydroxy hydrogens, one triplet for *para*-aromatic hydrogens, and one doublet for *meta*-aromatic hydrogens, vanished. The characteristic signals of the different alkoxy groups, which were also not affected by the chlorine dioxide, were the labels for each oxidative product (**6–11**).

2.2. Conformational interconversion of calix[4]diquinone diethyl ether isomeric pair 6 and 7

As mentioned previously, two major components were observed on the chlorine oxidation of calix[4]arene diethyl ether **1**. Using a TLC analysis, two colored fractions with very different R_f values (0.29 and 0.13) were displayed, and the corresponding products **6** and **7** were easily isolated by column chromatography. The first fraction, compound **6**, displayed a clean ^{1}H NMR spectrum (Fig. 1) for the oxidated structure of calix[4]diquinone diethyl ether, and the FABMS confirmed the molecular weight of the diquinone structure. The second colored fraction, which took a longer period to elute, displayed an overlapping ^{1}H NMR signal (Fig. 2) with a contamination of the first colored fraction material. It was puzzling as a small amount of compound **6** always appeared on the ^{1}H NMR spectrum even with a careful selection of the eluted fractions for the product **7**. The molecular weight determination and the ^{1}H NMR spectral analysis

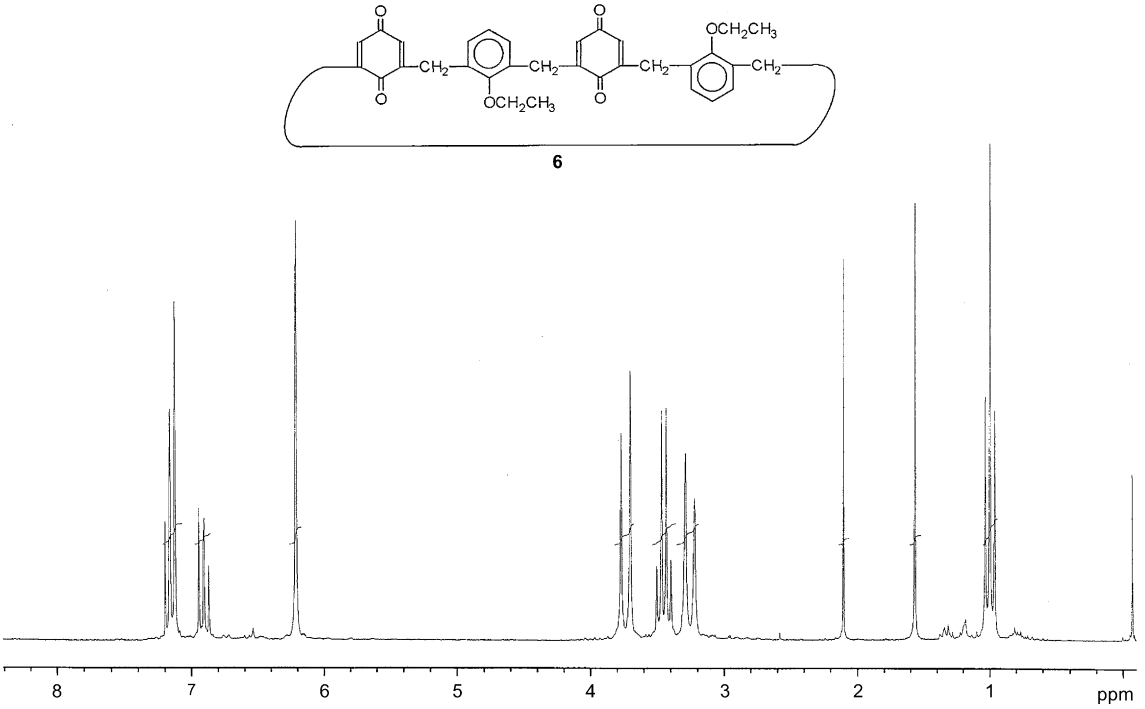


Figure 1. ^{1}H NMR spectrum (200 MHz) of *anti*-25,27-diethoxy-26,28-calix[4]diquinone (**6**).

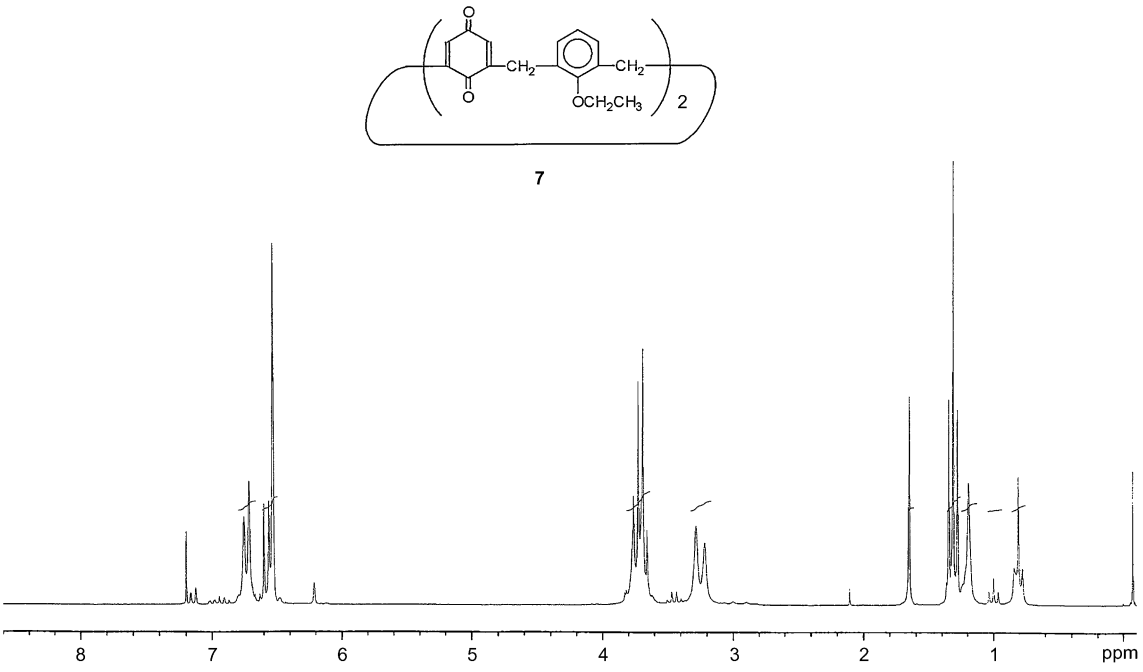


Figure 2. [1]H NMR spectrum (200 MHz) of *syn*-25,27-diethoxy-26,28-calix[4]diquinone (**7**).

indicated that the product **7** also possessed a molecular structure of calix[4]diquinone diethyl ether as the first colored fraction product **6**. The exact structures for each compound were determined by comparing the chemical shift of the quinone hydrogens' singlet. All other *syn*-1,3-dialkylated calix[4]quinones **8–11** displayed a singlet between δ 6.45 and 6.55 for the quinone hydrogens. Based on this observation, a singlet at δ 6.21 was the basis for assigning product **6** as the *anti*-isomer.

The *syn*-1,3-diethylated calix[4]arene (**1**) was not conformational mobile,[5] but an oxidation process with a flexible intermediate was able to explain the formation of the *anti*- and *syn*-isomers (**6** and **7**). However, when products **6** and **7** were sent for a high field NMR spectrum,[6] after a long wait, two identical [1]H NMR spectra were obtained, as shown in Figure 3. It was soon realized that the identical [1]H NMR spectrum resulted from the conformational interconversion between the *anti*- and *syn*-isomers (**6** and **7**) at the ambient temperature, and the earlier flexible intermediate scheme for the formation of the isomeric pairs **6** and **7** was excluded. This 'interconversion' phenomenon was also able to clarify the existence of the 'contamination' during a long elution time for the second colored fraction **7**.

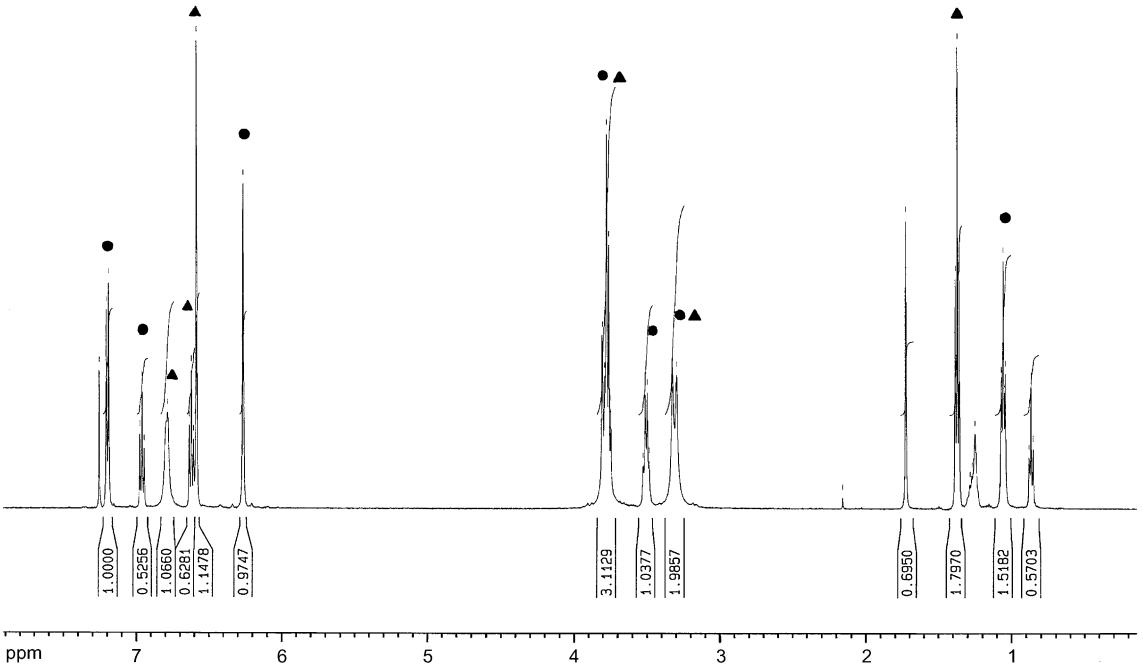


Figure 3. [1]H NMR spectrum (500 MHz) of a mixture of calix[4]diquinones **6** (●) and **7** (▲).

It was known that the conformational interconversion arose from the 'through-the-annulus-rotation' in the calix[4]arene system, and the rotation could be suppressed by introducing an ethoxy or other larger alkoxy moieties in the 'lower rim'.[5] A simple structure analysis indicated that the oxidation on the diethylated calix[4]arene **1** would not only reduce the size of the 'lower rim' substituents but also remove the 'lower rim' hydrogen bond. The result created a suitable space for the ethoxy moieties to slowly rotate through the 'lower rim' annulus, and produced two stable isomers **6** and **7**. Both isomers were stable enough to be isolated from the reaction mixture, but the slow 'through-the-annulus-rotation' of the ethoxy moieties would enable the two isomers to convert to one another. The rate of the interconversion between two isomers **6** and **7** was in the order of days, and a kinetic study to determine an exact rotation rate would be discussed in next section.

2.3. Kinetic study of the interconversion between calix[4]diquinone diethyl ether isomeric pair 6 and 7

As shown in Figure 3, a sharp singlet at δ 6.21 and a triplet at δ 1.01 were the distinct signals from the *anti*-isomer **6**, whereas a triplet at δ 1.31 arose only from the *syn*-isomer **7**. It was obvious that with an appropriate internal standard, such as methylene chloride, the amount of both *anti*-isomer **6** and *syn*-isomer **7** could be determined by comparing the integral ratio of the selected signals with the sharp methylene chloride's singlet at δ 5.30.

Initially, all the kinetic measurements[7] were carried out in an ice bath temperature; however, the conversion rate was too low to display any significant spectral difference on a week's long study. The measuring temperature was then raised to 18 °C (the temperature of the location of the ^{1}H NMR) to promote the interconversion, but it also created an unexpected problem. Since the NMR sample tube was not flame-sealed, the amount of the CH_2Cl_2, which was added in small amount as an internal standard, was depleted during a several weeks' long measurement. As a result, all the kinetic data were not longer valid with CH_2Cl_2 as an internal standard. A closer examination of the ^{1}H NMR spectrum of isomers **6** and **7**, revealed that only the methylene hydrogens, which included eight calix[4]arene's methylene hydrogens and four ethyl's methylene hydrogens, were displayed in a region between δ 3.0 and 4.0. The integral ratio in that range, therefore, provided a suitable standard to estimate the amount of either isomers **6** and **7** for the kinetic measurement.

The samples for the NMR study were isolated by thick layer chromatography and further purified by recrystallization at low temperature. The samples were dissolved in $CDCl_3$ and subjected to ^{1}H NMR measurement twice a day for a period of two weeks. The amount of each isomer was calculated by comparing the integral ratio of three distinct signals with the integral ratio of the 12 methylene hydrogens' signals, and the result is listed in Table 1. The data were subjected to Computer software Origin to produce a plot as shown in Figure 4. The first order exponential decay fit

Table 1. The composition of *anti*- and *syn*-isomers (**6** and **7**) in the interconversion process

Time	*anti*-Isomer **6** with signal at δ 6.3		*anti*-Isomer **6** with signal at δ 1.1		*syn*-Isomer **7** with signal at δ 1.4	
	Number of proton[a]	Composition in %[a]	Number of proton[a]	Composition in %[a]	Number of proton[a]	Composition in %[a]
0[b]	0.59	9.8	0.39	9.8	5.39	89.8
5	0.68	11.4	0.46	11.5	5.27	87.9
21	0.84	14.0	0.57	14.3	5.01	83.5
28	0.95	15.9	0.64	15.9	4.98	83.0
45	1.18	19.6	0.76	19.1	4.79	79.8
53	1.22	20.3	0.85	21.1	4.72	78.7
69	1.38	23.0	0.90	22.4	4.62	77.0
77	1.40	23.3	0.93	23.1	4.46	74.3
90	1.51	25.2	0.98	24.6	4.39	73.2
93	1.49	24.8	1.01	25.3	4.44	74.0
100	1.50	25.0	1.05	26.4	4.38	73.0
117	1.69	28.1	1.09	27.2	4.24	70.6
124	1.69	28.1	1.12	28.1	4.18	69.6
141	1.74	29.1	1.27	31.7	3.92	65.4
148	1.80	30.1	1.16	29.0	4.05	67.5
165	1.86	31.0	1.28	32.1	3.95	65.8
172	1.89	31.5	1.24	31.0	3.93	65.6
190	1.93	32.2	1.32	32.9	3.81	63.4
197	1.94	32.3	1.29	32.2	3.87	64.5
214	1.99	33.1	1.34	33.4	3.78	63.1
220	2.03	33.9	1.32	33.1	3.83	63.9
236	2.07	34.6	1.33	33.3	3.72	62.0
242	2.20	36.7	1.40	34.9	3.78	63.0
259	2.16	35.8	1.37	34.3	3.72	62.1
267	2.18	36.3	1.39	34.8	3.72	61.9
290	2.18	36.3	1.38	34.6	3.63	60.6
307	2.17	36.2	1.42	35.4	3.61	60.2
333	2.13	35.4	1.49	35.1	3.54	59.1
339	2.19	36.4	1.42	35.7	3.46	57.7
361	2.24	37.3	1.40	35.1	3.40	56.7
405	2.33	38.9	1.45	36.2	3.60	60.1

[a] The integral ratio in the region between δ 3.0 and 4.0 was set as 12 protons, for eight calix[4]arene's methylene hydrogens and four ethyl's methylene hydrogens. The selected signal's integrals were then calculated to estimate the amount and the percentage of the *syn*- and/or *anti*-isomers.

[b] The time '0 h' was set as the time for the first NMR measurement.

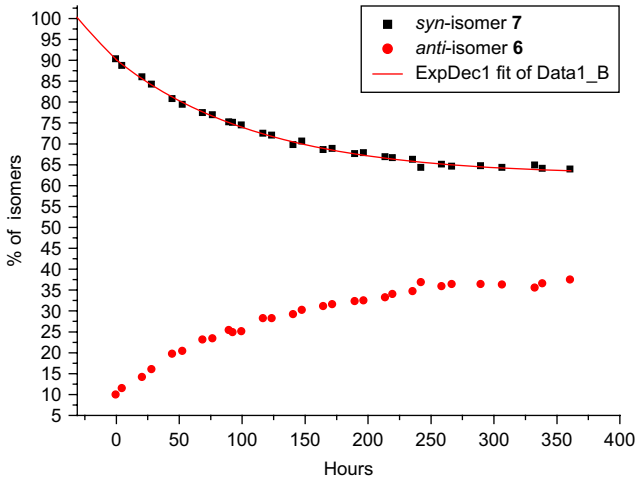


Figure 4. The plot of time versus the composition of *anti*- and *syn*-isomers (**6** and **7**).

indicated that the time elapsed for the purification process; the time between the chromatographic separation and the first NMR measurement was equivalent to 31 h at 18 °C, and the equilibrium was reached after 400 h after the first measurement with the amount of 5:3 in favor of *syn*-isomer **7**. The K_f value was calculated as 9.0×10^{-6} s^{-1} with the aid of Computer software Origin, as shown in Figure 5.

For a practice purpose, the samples were also dissolved in pyridine-d_5 and the spectra were also taken twice a day for a period of two weeks. To our surprise, the conversion rate was faster in the pyridine system. The system took less then 120 h to reach the equilibrium with the amount of 61% *syn*-isomer **7**, and the K_f value was estimated as 2.4×10^{-5} s^{-1}. Although the physical properties between C_5H_5N and $CHCl_3$ were known to be very different, none of them seemed to be able to influence the rate of the interconversion. Therefore, we speculated that the calixarene's cavity might be more suitable for $CHCl_3$ molecule to enter and formed the 'meta-stable' complex, in which the passage for the 'through-the-annulus-rotation' would be blocked and the conversion rate was lengthened. To support this presumption, the system will be further studied with a series of NMR solvents. The results of the different conversion rate may provide an useful information to estimate the calix[4]arene's complexation ability toward the small organic molecules.

3. Experimental[8]

3.1. General procedure

A slurry of 5 mmol of calix[4]arene dialkyl ethers **1**–**5**[4] was dissolved in 150 mL of CH_3CN, and a portion of 100 mL of aqueous ClO_2 solution[9] was then added. The reaction mixture was stirred at room temperature for a specific time, and the organic solvent was removed to leave a yellow and/or orange solid. The solid materials were collected and the purification procedures for the individual product are described separately.

3.1.1. *anti*-25,27-Diethoxy-26,28-calix[4]diquinone (6) and *syn*-25,27-diethoxy-26,28-calix[4]di-quinone (7). The reaction mixture was stirred at room temperature for 6 h, and a yellow solid was collected from a sample of 2.40 g (5.00 mmol) of **1**. Chromatographic separation (eluent: EtOAc/*n*-hexane=1:4) of the first colored fraction (R_f=0.29), which was recrystallized from $CHCl_3$ and CH_3OH, afforded 0.69 g (18.5%) of oxidized product **6** as yellow crystals: mp 125–127 °C; ^{1}H NMR ($CDCl_3$) δ 7.13–7.16 (d, J=7.4 Hz, 4H, Ar*H*), 6.87–6.95 (t, J=7.5 Hz, 2H, Ar*H*), 6.21 (s, 4H, quinone-*H*), 3.70–3.77 (d, J=13.4 Hz, 4H, ArCH_2Ar), 3.40–3.50 (q, J=7.1 Hz, 4H, ArOCH_2CH$_3$), 3.22–3.29 (d, J=13.4 Hz, 4H, ArCH_2Ar), 0.97–1.04 (t, J=7.1 Hz, 6H, ArOCH$_2$CH_3); ^{13}C NMR[10] ($CDCl_3$) δ 188.0, 186.3, 156.3, 147.7, 133.1, 133.0, 131.3, 124.4, 68.6, 32.0, 29.9, 15.4; FABMS *m/z*: 509 (M^++1). Anal.[11] Calcd for $C_{32}H_{28}O_6$: C, 75.59; H, 5.51; for $C_{32}H_{28}O_6\cdot1/4CHCl_3$: C, 71.94; H, 5.25. Found: C, 71.84; H, 5.13.

A second colored fraction (R_f=0.13), which was also recrystallized from $CHCl_3$ and CH_3OH, yielded 0.86 g (42.5%) of yellow crystals of **7**: mp 125–127 °C; ^{1}H NMR ($CDCl_3$)

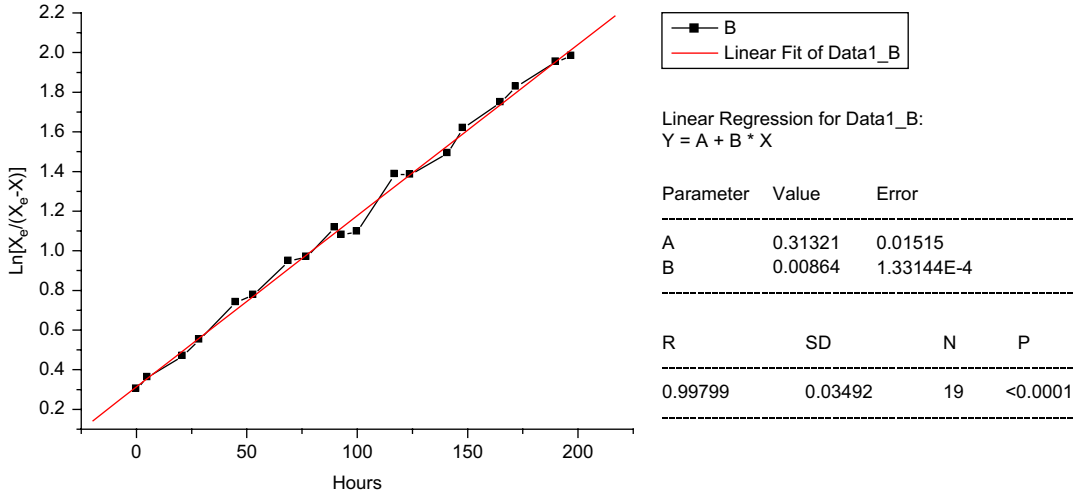


Figure 5. The plot of time versus natural log in the *syn*-**7** to *anti*-**6** interconversion process.

δ 6.72–6.76 (d, J=7.6 Hz, 4H, Ar*H*), 6.54–6.60 (m, 6H, Ar*H* and quinone-*H*), 3.66–3.76 (m, 8H, ArCH_2Ar and ArOCH_2CH$_3$), 3.22–3.29 (d, J=13.2 Hz, 4H, ArCH_2Ar), 1.28–1.35 (t, J=7.0 Hz, 6H, ArOCH$_2$CH_3); ^{13}C NMR (CDCl$_3$) δ 188.6, 186.2, 156.5, 148.1, 132.3, 130.3, 129.8, 123.6, 70.2, 32.1, 16.1; FABMS *m*/*z*: 510 (M^++2). Anal. Calcd for $C_{32}H_{28}O_6$: C, 75.59; H, 5.51; for $C_{32}H_{28}O_6\cdot H_2O$: C, 73.00; H, 5.70. Found: C, 73.03; H, 5.79.

3.1.2. 25,27-Dipropoxy-26,28-calix[4]diquinone (8). The reaction mixture was stirred at room temperature for 36 h, and a yellow solid was collected from a sample of 2.54 g (5.00 mmol) of **2**. Chromatographic separation (eluent: EtOAc/*n*-hexane=1:4) followed by recrystallization from $CHCl_3$ and CH_3OH afforded 1.16 g (43%) of orange color crystals of **8**: mp 178–180 °C; ^{1}H NMR (CDCl$_3$) δ 6.76 (br s, 4H, Ar*H*), 6.57–6.61 (m, 6H, Ar*H* and quinone-*H*), 3.78 (br s, 4H, ArCH_2Ar), 3.60–3.63 (t, J=7.4 Hz, 4H, ArOCH_2CH$_2$CH$_3$), 3.26–3.30 (br d, 4H, ArCH_2Ar), 1.75–1.82 (m, 4H, ArOCH$_2$CH_2CH$_3$), 0.96–0.99 (t, J=7.4 Hz, 6H, ArOCH$_2$CH$_2$CH_3); ^{13}C NMR (CDCl$_3$) δ 188.3, 186.0, 156.4, 148.0, 132.0, 129.9, 129.5, 123.3, 76.3, 31.6, 23.6, 10.6; FABMS *m*/*z*: 537 (M^++1). Anal. Calcd for $C_{34}H_{32}O_6$: C, 76.12; H, 5.97. Found: C, 75.94; H, 5.83.

3.1.3. 25,27-Dibutoxy-26,28-calix[4]diquinone (9). The reaction mixture was stirred at room temperature for 72 h, and an orange solid was collected from a sample of 2.68 g (5.00 mmol) of **3**. Chromatographic separation (eluent: EtOAc/*n*-hexane=1:4) followed by recrystallization from $CHCl_3$ and CH_3OH afforded 1.37 g (48.5%) of orange color crystals of **9**: mp 76–78 °C; ^{1}H NMR (CDCl$_3$) δ 6.76 (br s, 4H, Ar*H*), 6.57–6.61 (m, 6H, Ar*H* and quinone-*H*), 3.79 (br s, 4H, ArCH_2Ar), 3.64–3.67 (t, J=7.0 Hz, 4H, ArOCH_2CH$_2$CH$_2$CH$_3$), 3.29–3.30 (br d, 4H, ArCH_2Ar), 1.72–1.77 (m, 4H, ArOCH$_2$CH_2CH$_2$CH$_3$), 1.38–1.45 (m, 4H, ArOCH$_2$CH$_2$CH_2CH$_3$), 0.92–0.95 (t, J=7.4 Hz, 6H, ArOCH$_2$CH$_2$CH$_2$CH_3); ^{13}C NMR (CDCl$_3$) δ 188.2, 185.9, 156.6, 148.0, 132.0, 129.9, 129.5, 123.3, 74.6, 32.4, 31.7, 19.3, 13.9; FABMS *m*/*z*: 566 (M^++2). Anal. Calcd for $C_{36}H_{36}O_6$: C, 76.60; H, 6.38; for $C_{36}H_{36}O_6\cdot 1/3H_2O$: C, 75.79; H, 6.32. Found: C, 75.72; H, 6.32.

3.1.4. 25,27-Dibenzyloxy-26,28-calix[4]diquinone (10). The reaction mixture was stirred at room temperature for 96 h, and a yellow solid was collected from a sample of 3.02 g (5.00 mmol) of **4**. Chromatographic separation (eluent: EtOAc/*n*-hexane=1:4) followed by recrystallization from $CHCl_3$ and CH_3OH afforded 1.96 g (62%) of yellow crystals of **10**: mp 234–235 °C; ^{1}H NMR (CDCl$_3$) δ 7.33–7.34 (m, 6H, Ar′*H*), 7.26–7.28 (m, 4H, Ar′*H*), 6.77 (br s, 4H, Ar*H*), 6.62–6.65 (t, J=7.5 Hz, 2H, Ar*H*), 6.44 (s, 4H, quinone-*H*), 4.77 (s, 4H, OCH_2Ar′), 3.63 (br d, 4H, ArCH_2Ar), 3.14 (br s, 4H, ArCH_2Ar); ^{13}C NMR (CDCl$_3$) δ 188.1, 185.9, 155.8, 147.8, 136.6, 132.1, 130.2, 129.6, 128.6, 128.5, 128.3, 128.2, 123.6, 76.3, 31.7, 31.5; FABMS *m*/*z*: 634 (M^++2). Anal. Calcd for $C_{42}H_{32}O_6$: C, 79.75; H, 5.06; for $C_{42}H_{32}O_6\cdot 1/2H_2O$: C, 78.63; H, 5.15. Found: C, 78.69; H, 4.81.

The yellow crude product can also be purified by recrystallizing four times from $CHCl_3$ and CH_3OH to afford 1.35 g (42.5%) of the yellow powder of **10**. The physical and the spectral properties of this yellow powder were identical to the product, which was purified from the chromatographic method.

3.1.5. 25,27-Diallyloxy-26,28-calix[4]diquinone (11). The reaction mixture was stirred at room temperature for 4 h, and an orange solid was collected from a sample of 2.52 g (5.00 mmol) of **5**. Chromatographic separation (eluent: EtOAc/*n*-hexane=1:4) followed by recrystallization from $CHCl_3$ and CH_3OH afforded 1.82 g (67.5%) of orange color crystals of **11**: mp 186–188 °C; ^{1}H NMR (CDCl$_3$) δ 6.82–6.83 (br d, 4H, Ar*H*), 6.63–6.66 (t, J=7.6 Hz, 2H, Ar*H*), 6.55 (s, 4H, quinone-*H*), 5.99–6.07 (m, 2H, ArOCH$_2$C*H*=CH$_2$), 5.30–5.34 (dd, J=17.1, 1.3 Hz, 2H, ArOCH$_2$CH=CH_2), 5.23–5.25 (dd, J=10.4, 0.9 Hz, 2H, ArOCH$_2$CH=CH_2), 4.22–4.23 (d, J=5.5 Hz, 4H, ArOCH_2CH=CH$_2$), 3.69 (br s, 4H, ArCH_2Ar), 3.33–3.34 (br d, 4H, ArCH_2Ar); ^{13}C NMR (CDCl$_3$) δ 188.2, 186.1, 156.0, 147.6, 133.4, 132.2, 130.1, 130.0, 123.6, 118.0, 74.6, 32.2; FABMS *m*/*z*: 533 (M^++1). Anal. Calcd for $C_{34}H_{28}O_6$: C, 76.69; H, 5.26. Found: C, 76.62; H, 5.04.

Acknowledgements

Financial support of this work from the National Science Council of the Republic of China (Grant NSC-92-2113-M034-001) is gratefully acknowledged.

References and notes

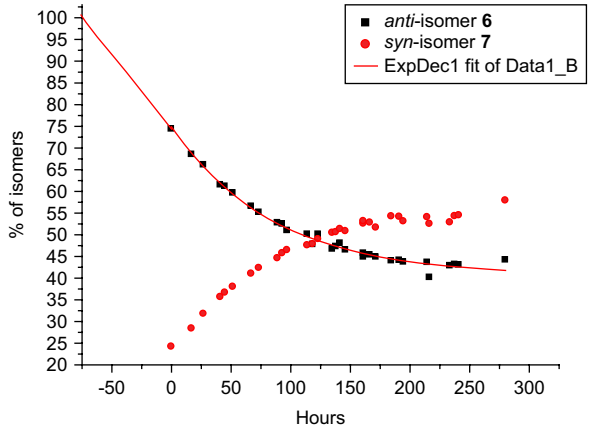
1. (a) Lee, M.-D.; Yang, K.-M.; Tsoo, C.-Y.; Shu, C.-M.; Lin, L.-G. *Tetrahedron* **2001**, *57*, 8095; (b) Yang, K.-M.; Lee, M.-D.; Chen, R.-F.; Chen, Y.-L.; Lin, L.-G. *Tetrahedron* **2001**, *57*, 8101.
2. Reddy, P. A.; Kashyap, R. P.; Watson, W. H.; Gutsche, C. D. *Isr. J. Chem.* **1992**, *32*, 89.
3. (a) Kim, N. Y.; Chang, S.-K. *J. Org. Chem.* **1998**, *63*, 2362; (b) Beer, P. D.; Chen, Z.; Gale, P. A.; Heath, J. A.; Knubley, R. J.; Ogden, M. I.; Drew, M. B. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1994**, *19*, 343; (c) Beer, P. D.; Chen, Z.; Gale, P. A. *Tetrahedron* **1994**, *50*, 931; (d) Reddy, P. A.; Gutsche, C. D. *J. Org. Chem.* **1993**, *58*, 3245.
4. Van Loon, J.-D.; Arduini, A.; Coppi, L.; Verboom, W.; Pochini, A.; Ungaro, R.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1990**, *55*, 5639.
5. Iwamoto, K.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1991**, *56*, 4955.
6. We thank Ms. S.-L. Huang of NSC Instrumental Center in Taipei for taking all the high field NMR measurements.
7. All the kinetic studies were preformed on JOEL DMX-200 WB spectrometer. Based on the data from Table 1, the error in the true value of each integral ratio was estimated to be less than 3%. Hence, the inaccuracy of the *K* calcd. value was estimated to be less than 6%.
8. All reagents were obtained from Commercial Chemical Companies and used without further purification. Melting points were taken in capillary tubes on a Mel-Temp apparatus (Laboratory Devices, Cambridge, MA) and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra are recorded on Burker DMX-500 SB spectrometer and chemical shifts are reported as δ values in parts per million. FABMS spectra were taken on a JOEL

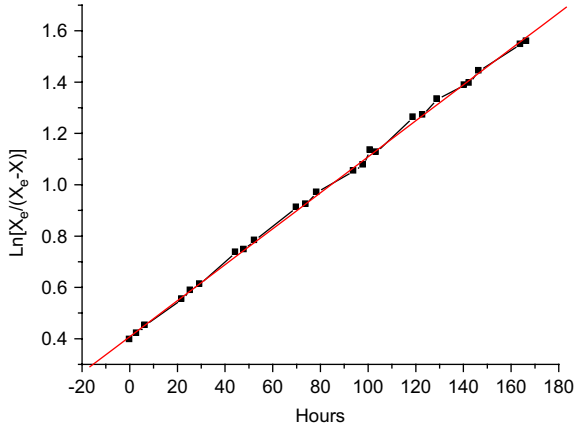
JMS-HX 102 spectrometer and elemental analyses were performed on a Perkin–Elmer 240C analyzer. The kinetic studies were performed on JOEL DMX-200 WB spectrometer. Chromatographic separations were performed with Merck silica gel (230–400 mesh ASTM) on columns of 25 mm diameter filled to height of 150 mm. TLC analyses were carried out on Macherey–Nagel aluminum back silica gel 60 F_{254} plates (absorbent thickness 0.2 mm).

9. Aqueous chlorine dioxide solution was prepared by mixing equal volume of sodium chlorite solution ($NaClO_2 \cdot 2H_2O$, 31.60 g, 0.25 mol in 500 mL of deionized water) and sodium persulfate solution ($Na_2S_2O_8$, 29.70 g, 0.25 mol in 500 mL of deionized water). The solution was then stored in a brown bottle at 0 °C prior to being used.
10. The pure compounds of **6** and **7** will convert into an equilibrium mixture or partial converted mixture during the purification process and/or NMR measurement. Therefore, the ^{13}C NMR spectrum for either compound **6** or **7** consisted spectral signals from the original compound and the converted compound in a minor amount. To properly assign the ^{13}C NMR spectrum for compounds **6** and **7**, the task was achieved by marking all the identical signals from both spectra, and then assigning the lower intensity peaks as the signal arose from the converted compound.
11. All the new compounds, which were submitted for Elemental Analysis (EA), were dried at 120 °C under vacuum for 48 h prior to the analysis. If the analysis value was different from the calculated value, the sample was dried at 140 °C under vacuum for 48 h prior to another analysis. The drying period will be increased further, if the sample still received a different EA value from the theoretical value. The procedure was continued until a constant EA value was attained.

Appendix 1

The results of the kinetic studied for *anti*-**6** to *syn*-**7** conversion in $CHCl_3$.





B
Linear Fit of Data1_B

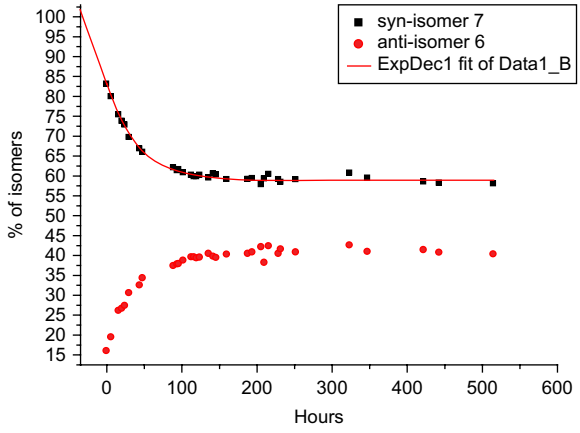
Linear Regression for Data1_B:
Y = A + B * X

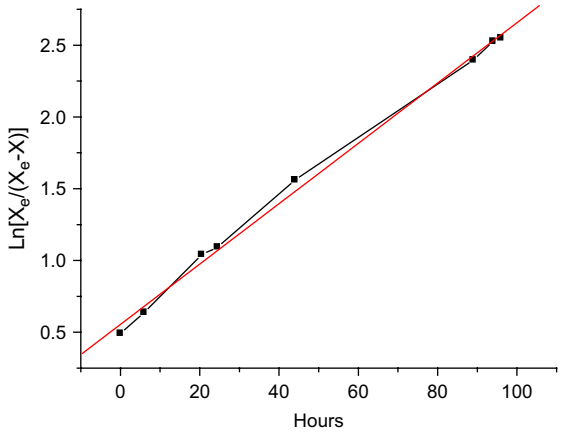
Parameter	Value	Error
A	0.40793	0.00475
B	0.00701	4.88789E-5

R	SD	N	P
0.99947	0.01231	24	<0.0001

Appendix 2

The results of the kinetic studied for *syn*-**7** to *anti*-**6** conversion in C_5H_5N.





B
Linear Fit of Data1_B

Linear Regression for Data1_B:
Y = A + B * X

Parameter	Value	Error
A	0.55468	0.03033
B	0.02102	5.0406E-4

R	SD	N	P
0.99828	0.05401	24	<0.0001