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25,26-Dialkoxycalix[4]arenes. Part 1: 25-Alkoxy-26,27-diacetoxy route

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ABSTRACT

Acetylation of calix[4]arene 1,3-dialkyl ethers yielded the corresponding monoacetates. The ^{1}H NMR spectral analysis indicated that the products' alkoxy moieties were 'rotation restricted'. Acylation of calix[4]arene monoalkyl ethers with acetyl chloride yielded monoacetates and/or 2,3-diacetates in different reaction conditions. A simple recrystallization process was able to isolate 2,3-diacetates in good yield. The ^{1}H NMR spectra of the diacetylated products indicated that those compounds also possessed the 'rotation restricted' alkoxy moieties. In the presence of K_2CO_3 as reaction base, alkylation of 2,3-diacetates produced the acetyl-migrated 1,3-dialkyloxy derivatives. Basic hydrolysis of the acetyl-migrated compounds yielded the known 1,3-dialkoxycalix[4]arenes. In the presence of NaH as reaction base, 2,3-diacetates were alkylated with and without the acetyl-migration. For the highly reactive benzyl bromide and allyl bromide, the majority of alkylation proceeded without acetyl-migration. In the other alkyl halides, the products were the acetyl-migrated 1,3-dialkoxy derivatives along with less than one-fourth the amount of non-migrated 1,2-dialkoxy derivatives.

1. Introduction

Calixarenes[1] can be functionalized in either the 'upper rim' or the 'lower rim'. In the lower rim's functionalization, the phenolic hydroxy groups were usually converted into ester or ether moieties. Among them, the ether derivatives were the most studied subjects, and the tetra-alkoxy derivatives were the first 'lower rim' functionalized calix[4]arenes to be prepared.[2] The 1,3-dialkoxy derivatives were later reported by Reinhoudt[3] in a one-step process, whereas, the other alkoxy derivatives, monoalkyl ethers[4] and the trialkyl ethers,[2b,5] were all prepared in multi-step procedures. The calix[4]arene monoalkyl ethers were later found to be achievable in a single step by applying $NaOCH_3$ and/or K_2CO_3 as the reacting base.[6,7] However, to this day, the 1,2-dialkoxy derivatives can only be found in the active alkyl halide cases, e.g., allyl bromide[8] and benzyl bromide,[9] or in the *tert*-butylcalix[4]arene system.[10]

In this paper, we will report a general synthetic procedure to convert the monoalkoxy-calix[4]arenes into their corresponding 2,3-diacetate derivatives. Since the only available position for the further ether linkage was proximal to the existent alkoxy group in the 2,3-diacetate products, it was reasonable to propose that etherification of 25-alkoxy-26,27-diacetoxycalix[4]arenes following with basic hydrolysis would be able to produce the corresponding 25,26-dialkoxycalix[4]arenes. Therefore, We will report a three-step synthetic procedure for the preparation of 25,26-dibenzyloxycalix[4]arene and the acetyl-migration phenomena in 25-alkoxy-26,27-diacetoxycalix[4]arene systems.

2. Results and discussion

2.1. Acetylation of calix[4]arene 1,3-dialkyl ethers

In our earlier research work on the synthesis of calix[4]arene trialkyl ethers, we developed a four-step synthetic procedure with benzoate as a protecting group.[5f] We had noticed that the alkoxy's first methylene hydrogens were always displayed as two sets of multiples with equal intensity after the introducing of the benzoate group. Since the benzoate protecting groups were removed at the final stage of the synthesis, the conformation of the intermediate was only rationally assigned as 'up-down-up'[11] without any further pursued at that time. Recently, some interesting results were observed during the search for the possible synthetic pathways for the calix[4]arene 1,2-dialkyl ethers. Therefore, we decided to investigate the conformation for all the available acylated calix[4]arene alkyl ethers.

When calix[4]arene 1,3-dialkyl ethers **1**–**5** were treated with less hindered acetyl chloride in pyridine at ice bath temperature (Scheme 1), the resulting products **6**–**10** displayed, as their benzoated counterparts, two sets of multiples with equal intensity at δ 3.78 and 3.99 for the alkoxy's first methylene hydrogens. However, when the products were subjected to 2D COSY spectral

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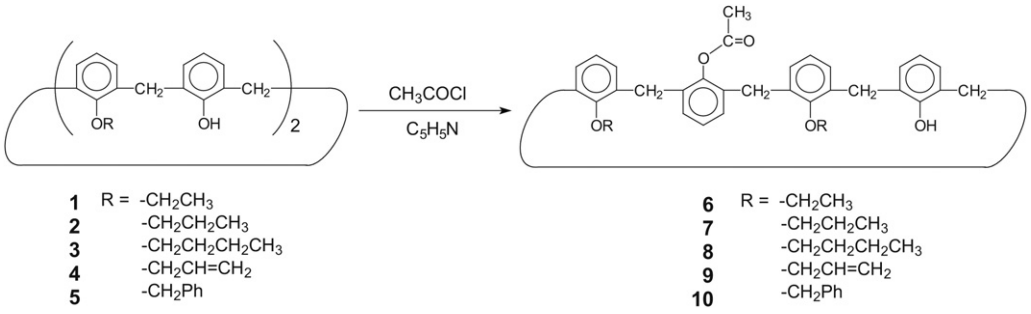


Scheme 1. Synthetic scheme for 1,3-dialkoxy-2-acetoxycalix[4]arenes **6**–**10**.

measurement, to our surprise, the 2D COSY spectrum (Fig. 1) indicated that the two sets of alkoxy's first methylene hydrogen signals actually arose from the protons on the same methylene moieties. This result indicated that the free rotation on the alkoxy C–O single bonds had to have ceased in NMR time scale in order for the creation of two different magnetic environments for the methylene's protons, and hence, to display two multiples with different chemical shifts on the spectrum. Since the acetylated products possessed a sharp melting point and displayed a single spot upon TLC analysis, the same 'up-down-up' conformers were assigned to the products **6**–**10** based on our earlier judgment in the triallyloxycalix[4]arene system.[5f] We will demonstrate that, in Part II of this series, the products **6**–**10** were properly assigned.

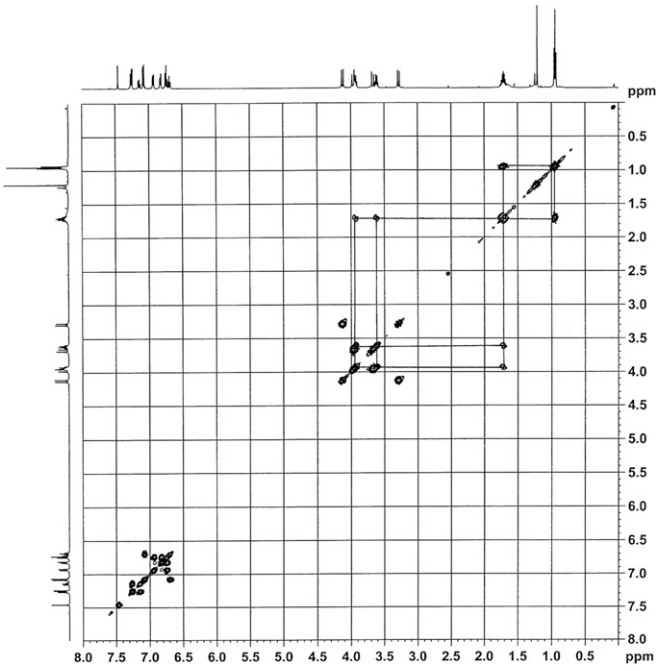


Fig. 1. 2D COSY spectrum of 25-acetoxy-26,28-dipropoxycalix[4]arene (**7**).

A further study indicated that the 1,3-diacetylated products were not produced in more severe reaction conditions, e.g., higher temperature, longer reaction period, and/or larger amounts of acetyl chloride. It was believed that the steric hindrance of the trisubstituent calix[4]arenes prohibited the formation of the fourth 'lower rim' ester linkage in acidic or weaker basic conditions. However, in the later section of this paper, we will demonstrate that the 1,3-diacetylated derivatives could be prepared in a very strange fashion.

2.2. Acetylation of calix[4]arene monoalkyl ethers

As in the previously acetylation cases, when a standard acetylation reaction condition was applied on calix[4]arene monoalkyl ethers **11**–**15**, no trace of tetra-substituent triacetated products were detected even with a further increasing of acetylation period and/or the amount of acetyl chloride. The only isolated products were the corresponding monoacetates **16**–**20** and/or 2,3-diacetates **21**–**25** (Scheme 2). We believed, as in previous systems, that the steric hindrance inhibited the introduction of the fourth substituent onto the tri-substituent calix[4]arenes in the reaction conditions.

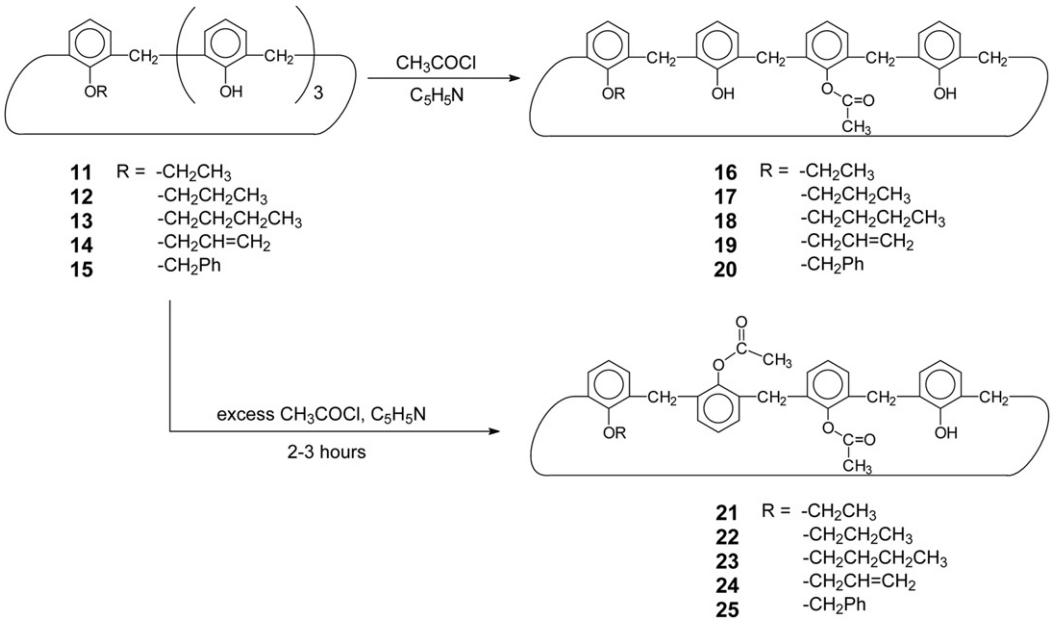
In the acetylation of calix[4]arene monoalkyl ethers **11**–**15**, the monoacetated products **16**–**20** were isolated in over 40% yield when the reaction was performed with a small amount of acetyl chloride for 10 min. Whereas, the 2,3-diacetate products **21**–**25** could be afforded in an easier purification process and higher isolation yield by applying larger amount of acetyl chloride and a longer reaction period upon calix[4]arene monoalkyl ethers **11**–**15**.

2.3. Spectral analysis of monoalkoxy-calix[4]arene 2,3-diacetates 21–25

The ^{1}H NMR spectra of the monoacetates **16**–**20** displayed a similar spectral pattern as starting materials **11**–**15** with an extra sharp singlet at δ 2.5 (being a normal chemical shift position for the acetate's methyl hydrogen) for the newly introduced acetate moieties. Since only the 3-monoacetate derivates possessed the same symmetry elements as the starting materials **11**–**15**, therefore, it was easy to assign the structure of the monoacetates **16**–**20** as 25-alkxoy-27-acetoxycalix[4]arenes.

It was known that both the alkoxy and the acetyl groups are able to hinder the 'through-the-annulus' free rotation, and hence, the introduction of the second acetate moieties will then create a chiral plane and greatly reduce the symmetry of the 2,3-diacetate products **21**–**25**. In the lack of any symmetry element in those 2,3-diacetate products, eight sets of doublets for the calixarene's eight methylene hydrogens and two sharp singlets (δ 2.1 and 1.1) for the two different acetate moieties were observed. It was interesting to notice that the second acetate moiety was shifted upfield from their normal position by approximately 1 ppm, and this strong shielding effect could only be arisen from the opposite and/or the adjacent calix[4]arene's phenolic rings. This observation suggested that in order to be shielded by calix[4]arene's aromatic rings the second acetate moiety had to be *anti*- to the other 'lower rim' substituents.

To verify the spatial relationship between three 'lower rim' substituents, a 2D-NOSEY was taken for compound **21**. The spectrum indicated that the two acetate's methyl groups were not space relative, and the ethoxy's methylene hydrogen interacted only with δ 2.1 acetate's signal. This observation implicated that the compound **21** holds the 'up-down-up' arrangement. The chemical shift of the calix[4]arene's methylene carbon (at δ 37.9, 37.8, 31.8, and 31.4) also



Scheme 2. Synthetic scheme for acetylation of 1-alkoxycalix[4]arenes **11**–**15**.

supported the 'up-down-up' structure assignment.[12] Based on those results, the conformation of the compounds **21**–**25** was assigned as 25-alkoxy-*anti*-26-acetoxy-*syn*-27-acetoxycalix[4]arenes. The structure of the compounds **21**–**25** will be further proven on the later section of this paper. The spectra of compounds **21**–**25** also displayed, as in the previous compounds **6**–**10**, two sets of multiples for the alkoxy's first methylene hydrogens (Fig. 2), and a restricted free rotation of the alkoxy C–O single bond was also proposed to clarify the existence of two multiples.

2.4. Etherification of 1-alkoxy-2,3-diacetoxycalix[4]arenes with K_2CO_3

According to our proposed synthetic route, the first step of the synthesis was etherification of 1-alkoxy-2,3-diacetoxycalix[4]arenes **21**–**25**. When compounds **21**–**25** were refluxed with large amounts of NaH and alkyl halides in acetonitrile overnight, a standard procedure for introducing the fourth ether linkage onto the calix[4]arene,[5,6] it was found that all the acetate moieties were removed and tetraalkoxycalix[4]arenes were the only isolated products. A conclusion, which was later found to be inappropriate, was rapidly reached that the strength of the reaction base had to be reduced in order to keep the acetate moieties unaffected. A weaker base, K_2CO_3, was then chosen to replace the NaH in the reaction. When compounds **21**–**25** were refluxed with K_2CO_3 and excess alkyl halides in acetonitrile, over 50% of the yield of the new products **26**–**30** was isolated as colorless crystals (Scheme 3). Not only the ^{1}H NMR spectra of products **26**–**30** displayed two acetate's sharp singlets, which indicated that the reaction conditions did not cleave any acetate moieties; but the spectral integral ratio of the alkoxy's hydrogen also suggested that the second alkoxy moiety was present. Even though the splitting pattern of the calix[4]arene's methylene hydrogens suggested that products **26**–**30** possessed a planar symmetry element, which was not totally in agreement with the 1,2-dialkoxy-3,4-diacetoxy structural arrangement, the products **26**–**30** were still assigned as 1,2-dialkoxy-3,4-diacetoxycalix[4]arenes at this stage. The structure assignment was soon proven to be incorrect when products **26**–**30** were basic hydrolyzed.

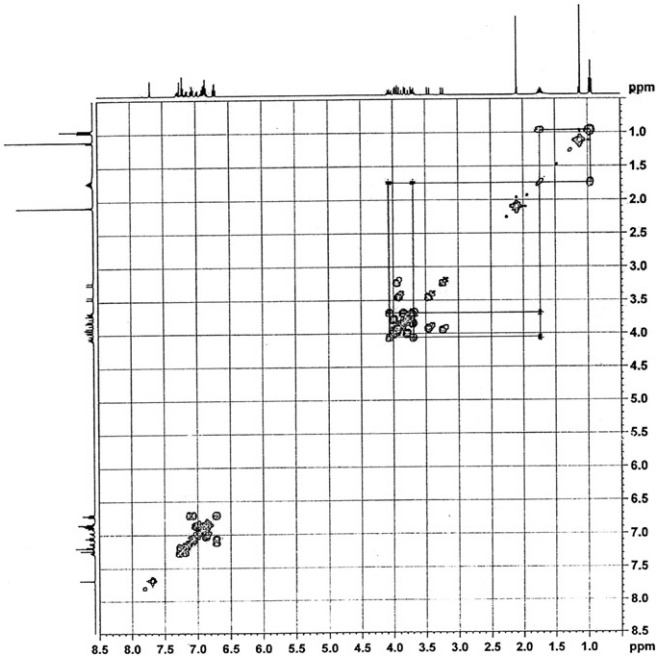
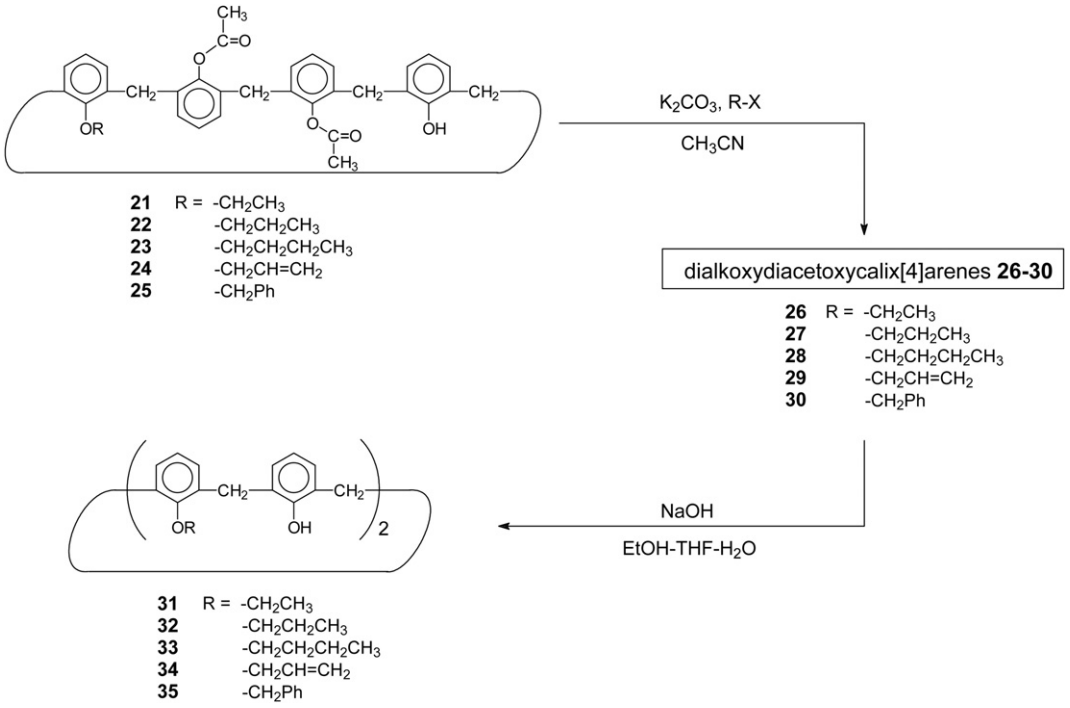


Fig. 2. 2D COSY spectrum of 25,26-diacetoxy-27-propoxy-28-hydroxycalix[4]arene (**22**).

After the introduction of the second ether linkage, compounds **26**–**30** were subjected to basic hydrolysis as in our proposed synthetic route. Instead of isolating the expecting 1,2-dialkoxycalix[4]arenes, it was a surprise to recognize that the hydrolysis products were the known compounds,[3] 1,3-dialkoxycalix[4]arenes **31**–**35**. Since the basic hydrolysis conditions had no effect on the ether linkage, the hydrolysis products had to be derived from 1,3-dialkoxy-2,4-diacetoxycalix[4]arenes. This result suggested that the actual structure of products **26**–**30** were not the expected 1,2-dialkoxy-3,4-diacetoxycalix[4]arenes, but were the acetyl-migrated 1,3-dialkoxy-2,4-diacetoxycalix[4]arenes, as shown in Fig. 3.

As described in the beginning of this reported, a direct acetylation of 1,3-dialkoxycalix[4]arenes was not able to produce the 2,4-diacetated products. However, this acetyl-migrated etherification provided a strange pathway for the preparation of the tetra-substituent 2,4-diacetated products **26**–**30** in 'partial cone' conformation.

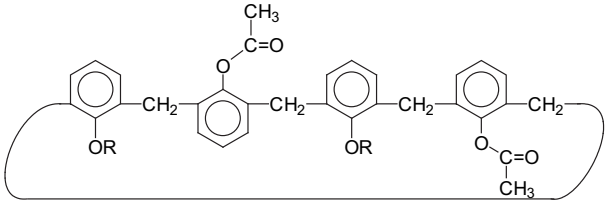


21 R = $-CH_2CH_3$
22 $-CH_2CH_2CH_3$
23 $-CH_2CH_2CH_2CH_3$
24 $-CH_2CH{=}CH_2$
25 $-CH_2Ph$

26 R = $-CH_2CH_3$
27 $-CH_2CH_2CH_3$
28 $-CH_2CH_2CH_2CH_3$
29 $-CH_2CH{=}CH_2$
30 $-CH_2Ph$

31 R = $-CH_2CH_3$
32 $-CH_2CH_2CH_3$
33 $-CH_2CH_2CH_2CH_3$
34 $-CH_2CH{=}CH_2$
35 $-CH_2Ph$

Scheme 3. Etherification of 1-alkoxy-2,3-diacetoxycalix[4]arenes **21**–**25**.



26 R = $-CH_2CH_3$
27 $-CH_2CH_2CH_3$
28 $-CH_2CH_2CH_2CH_3$
29 $-CH_2CH{=}CH_2$
30 $-CH_2Ph$

Fig. 3. Conformational structure of acetyl-migrated 1,3-dialkoxy-2,4-diacetoxycalix[4] arenes **26**–**30**.

2.5. Mechanism for the formation of 1,3-dialkoxy-2,4-diacetoxycalix[4]arenes 26–30

An acetyl-migration proceeding the ether linkage formation was essential for the conversion of 1-alkoxy-2,3-diacetoxycalix[4]arenes **21**–**25** into 1,3-dialkoxy-2,4-diacetoxycalix[4]arenes **26**–**30**. Therefore, we speculated that a cyclic orthoacetate-like anionic intermediate was present during the etherification reaction, as shown in Fig. 4. In such a structural configuration, the alkyl halide substrates would be more favorable to approach the intermediates from the less hindered 3-position side at the final stage and yielded the 1,3-dialkoxy products **26**–**30**. Gutsche and his co-worker had also reported a similar acyl-migrated phenomenon in the calix[4] arene 1,3-dibenzoate system.[13]

The ^{1}H NMR spectra of compounds **26**–**30** indicated that these etherification products belonged to C_v symmetry point group with two different acetate groups. A 'partial cone' conformation with

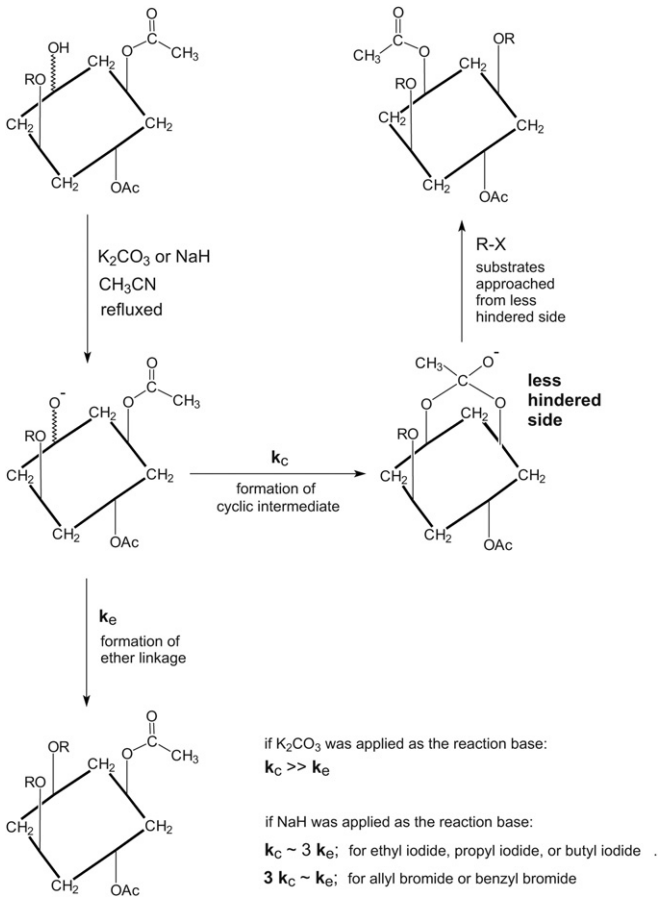


Fig. 4. Proposed mechanism for the formation of 1,3-dialkoxy-2,4-diacetoxycalix[4] arenes.

two acetate moieties '*anti*' to each other was the only reasonable structure for compounds **26**–**30**. It was known that any substituents that were larger than the ethyl group would not be able to rotate through the calix[4]arene's annulus at room temperature.[14] Therefore, the two acetate moieties would also have to be '*anti*' to each other in the structure of starting compounds **21**–**25**. This result was fully agreed with our previous assignment on the structure of 1-alkoxy-2,3-diacetoxycalix[4]arenes **21**–**25**.

It should be noted that all the isolated acetyl-migrated products had two alkoxy groups in *syn* arrangement. The lack of any *anti*-isomer suggested that the breaking of cyclic orthoacetate ring and the formation of ether linkage occurred in a concerted fashion.

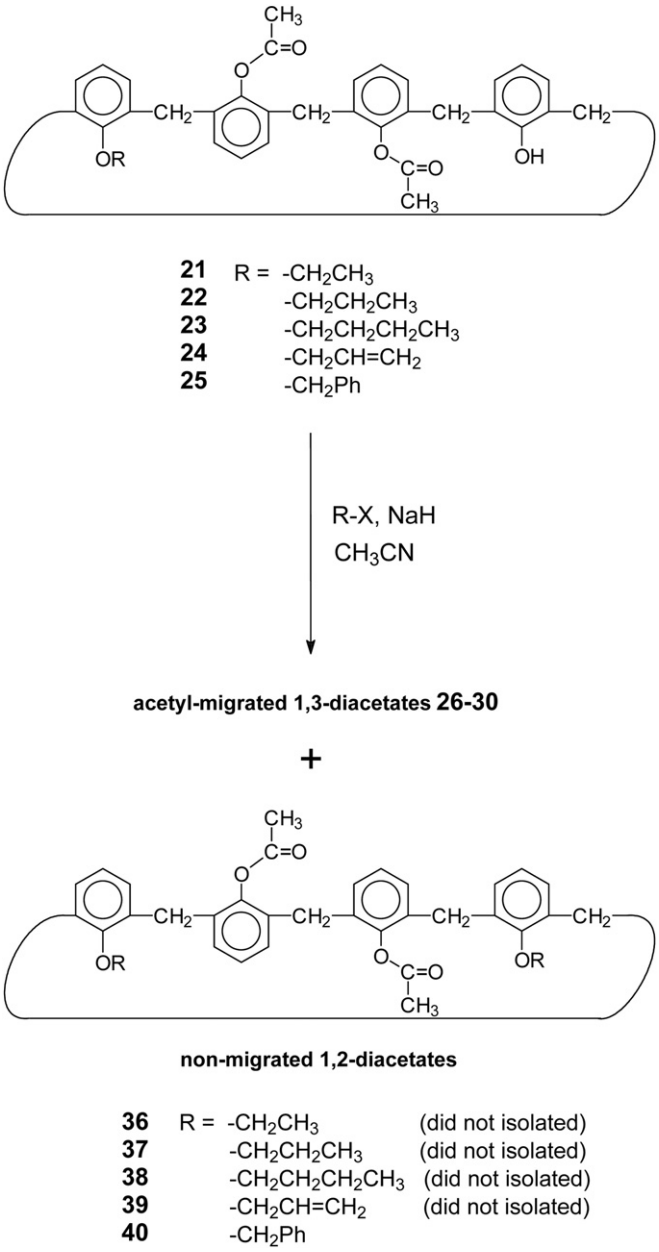
2.6. Formation of 1,2-dialkoxy-3,4-diacetoxycalix[4]arenes

It was shown that the K_2CO_3 reaction conditions failed to yield the expected 1,2-dialkoxy-3,4-diacetoxycalix[4]arenes, and therefore, the direction of the reaction condition adjustment had to shift to the quantity of NaH and reaction periods. After a few trials on the amount of NaH and reaction times, it was found that a refluxing with 1.5 M equiv of NaH and excess alkyl halides in acetonitrile for 14 h was able to introduce the second alkoxy group onto the desired 2-position and yielded the corresponding 1,2-dialkoxy-3,4-diacetoxycalix[4]arenes (Scheme 4).

When compounds **21**–**25** were etherified in the modified reaction conditions, two isomeric dialkoxy derivatives were afforded in various amounts. The ^{1}H NMR spectra of these reaction crude products all displayed two pairs of the acetate's singlets. It was shown previously that the 1,3-dialkoxy products **26**–**30** displayed two sharp singlets at δ 1.5 and 1.9 for the acetate moieties. It was therefore reasonable to assume that the other pair of signals at δ 1.2 and 1.5 arose from the 1,2-dialkoxy products. The integral ratio of those acetate's signals also provided an adequate information to estimate the composition of the crude product. In the two active alkyl halide cases, the allyl bromide and benzyl bromide, the crude products contained approximately a 3 to 1 ratio of 1,2-dialkoxy products and 1,3-dialkoxy products, respectively. In the cases of other less reactive alkyl halides, the opposite results were observed, i.e., the 1,3-dialkoxy products **26**–**28** were afforded in approximately 75% and the amount of the desired 1,2-alkyloxy products **36**–**38** was less than one-fourth.

We speculated that after the weak base, K_2CO_3, neutralized the calix[4]arene's phenolic hydroxy moieties into an anion form, the resulting weak nucleophile could only attack the adjacent acetate group and produced the cyclic intermediate. Whereas, the stronger base, NaH, was able to convert the calix[4]arene into a better nucleophile, and hence, increased the rate of the ether formation. As the composition of the crude products might suggest, the rate of the ether formation k_e was approximately three times faster than the rate of the cyclic intermediate formation k_c in the cases of active alkyl halides. However, the reaction rate seemed to be reversed in the less reactive alkyl halide cases, and the production of the desired 1,2-dialkoxy products was less than one-quarter. The productive yield, not the isolating yield, of less than 25% clearly indicated that the proposed synthetic route was not acceptable for the preparation of 1,2-dialkoxycalix[4]arenes. Therefore, a new approach was developed and will be illustrated in Part II of this series.

For the allyl bromide and benzyl bromide cases, the crude products contained approximately three quarters of the desired 1,2-dialkoxy products **39** and **40**. Hence, the recrystallization process was applied to purify the desired products. During the recrystallization process, it was noticed that the more symmetrical 1,3-dialkoxy side products were always crystallized first. In the benzyl bromide case, the 1,3-dibenzyloxy product **30** was crystallized as the first crop, and further concentrations of the mother solution yielded 1,2-dibenzyloxy-3,4-diacetoxycalix[4]arene **40**. In the allyl bromide case, the two diallyloxy isomeric pairs **29** and **39**



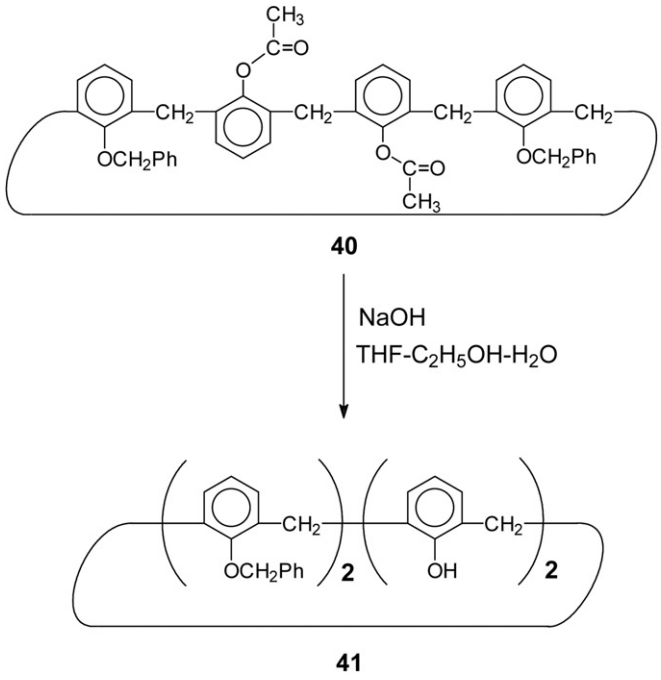
Scheme 4. Synthetic scheme for 1,2-dialkoxy-3,4-diacetoxycalix[4]arenes **36**–**40**.

were always crystallized together and the isolation of product **39** was not achieved. Fortunately, a new approach that will be illustrated in Part II of this series eliminated the necessity of the chromatographic separation.

2.7. Basic hydrolysis of 1,2-dibenzyloxy-3,4-diacetoxycalix[4]arenes

After the isolation of 1,2-dibenzyloxy **40** was achieved, product **40** was subjected to basic hydrolysis to remove the 'lower rim' acetate protecting groups as shown in Scheme 5.

The hydrolysis product, *syn*-1,2-dibenzyloxycalix[4]arene (**41**), also possessed a symmetrical plane as its isomeric 1,3-dibenzyloxy countpart **35**. However, the symmetrical plane bisected the two isomeric dibenzyloxy compounds differently, and the ^{1}H NMR spectrum of 1,2-dibenzyloxy **41** was expected to be very different from its isomeric 1,3-dibenzyloxy countpart **35**. The ^{1}H NMR spectrum of the *syn*-1,3-dibenzyloxycalix[4]arene **35** displayed one



Scheme 5. Synthetic scheme for 1,2-dibenzyloxycalix[4]arene **41**.

pair of doublets for the calix[4]arene's methylene hydrogen and one sharp singlet for the benzyloxy's methylene hydrogen. Whereas, the ^{1}H NMR spectrum of *syn*-1,2-dibenzyloxycalix[4]arene displayed (as shown in Fig. 5) three pairs of doublets with an integral ratio of 1:1:2 for the same calix[4]arene's methylene hydrogen. The benzyloxy's methylene hydrogens, which experienced a different magnetic environment, also emerged as a predictive pair of doublets. The FAB-MS provided a strong support for the existing of the two benzyloxy moieties of the compound **41**. An alternate synthetic approach for the preparation of 1,2-dibenzyloxycalix[4]arene (**41**) will also be described in Part II of this series.

3. Experimental[15]

3.1. General procedure for the monoacetylation of calix[4]arene dialkyl ethers

A slurry of approximate 3.50 mmol of calix[4]arene dialkyl ethers **1**–**5** was dissolved in 20 mL of pyridine, and 5.0 mL of acetyl chloride was then added dropwisely at room temperature. The reaction mixtures were stirred for 24 h, and the solvent was removed by rotory evaporatory to leave an oily residue. The organic materials were taken up by 50 mL of $CHCl_3$, and washed with 20 mL of 1 N HCl twice followed with 100 mL of saturated $NaHCO_3$ solution and 100 mL of distillated water. The organic solvent was removed to leave a pale yellow solid. Chromatographic separation (eluent: EtOAc/*n*-hexane = 1:4), following by recrystallization from $CHCl_3$ and CH_3OH yielded the corresponding monoacetylated products **6**–**10**.

*3.1.1. 25-Acetoxy-26,28-diethoxycalix[4]arene (**6**).* An amount of 0.24 g (13%) of colorless fine crystals was collected from 1.68 g (3.50 mmol) of calix[4]arene diethyl ether **1**: mp 230–231 °C; ^{1}H NMR ($CDCl_3$) δ 7.28 (d, J=7.6 Hz, 2H, Ar*H*), 7.21 (s, 1H, ArO*H*), 7.16 (t, J=7.6 Hz, 1H, Ar*H*), 7.07 (d, J=7.5 Hz, 2H, Ar*H*), 6.90 (d, J=7.5 Hz, 2H, Ar*H*), 6.82 (d, J=6.6 Hz, 2H, Ar*H*), 6.73 (t, J=7.5 Hz, 2H, Ar*H*), 6.69 (t, J=7.5 Hz, 1H, Ar*H*), 4.10 (d, J=13.1 Hz, 2H, ArCH_2Ar), 3.97–4.01 (m, 2H, OCH_2CH$_3$), 3.94 (d, J=15.7 Hz, 2H, ArCH_2Ar), 3.74–3.82 (m, 2H, OCH_2CH$_3$), 3.64 (d, J=15.7 Hz, 2H, ArCH_2Ar), 3.28 (d, J=13.2 Hz, 2H, ArCH_2Ar), 1.34 (s, 3H, COCH_3), 1.27 (t, J=7 Hz, 6H, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 168.7, 154.4, 153.1, 148.1, 134.1, 133.0, 132.9, 132.8, 129.6, 129.5, 129.0, 128.7, 128.5, 128.1, 127.6, 124.9, 123.5, 118.8, 69.2, 37.9, 31.2, 20.4, 15.1; FAB-MS m/e: 522 (M^+); HRMS (FAB) m/e: calcd for $C_{34}H_{34}O_5$: 522.2406; found: 522.2394.

*3.1.2. 25-Acetoxy-26,28-dipropoxycalix[4]arene (**7**).* An amount of 0.22 g (11%) of colorless fine crystals was collected from 1.79 g (3.52 mmol) of calix[4]arene dipropyl ether **2**: mp 238–239 °C; ^{1}H NMR ($CDCl_3$) δ 7.43 (s, 1H, ArO*H*), 7.26 (d, J=7.6 Hz, 2H, Ar*H*), 7.14 (t, J=7.6 Hz, 1H, Ar*H*), 7.08 (d, J=7.5 Hz, 2H, Ar*H*), 6.93 (d, J=7.6 Hz, 2H, Ar*H*), 6.82 (d, J=6.4 Hz, 2H, Ar*H*), 6.75 (t, J=7.5 Hz, 2H, Ar*H*), 6.69 (t, J=7.4 Hz, 1H, Ar*H*), 4.12 (d, J=13.2 Hz, 2H, ArCH_2Ar), 3.90–3.98 (m, 4H, ArCH_2Ar and OCH_2CH$_2$CH$_3$), 3.58–3.69 (m, 4H, ArCH_2Ar and OCH_2CH$_2$CH$_3$), 3.28 (d, J=13.2 Hz, 2H, ArCH_2Ar), 1.65–1.74 (m, 4H, OCH$_2$CH_2CH$_3$), 1.20 (s, 3H, COCH_3), 0.94 (t, J=7.4 Hz, 6H, OCH$_2$CH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 168.8, 154.6, 153.4, 148.0, 133.9, 133.0, 132.8, 129.6, 129.5, 128.6, 128.3, 128.0, 125.0, 123.5, 118.6, 75.1, 37.9, 31.2, 23.2, 20.3, 10.5.

*3.1.3. 25-Acetoxy-26,28-dibutoxycalix[4]arene (**8**).* An amount of 0.36 g (17.5%) of colorless fine crystals was collected from 1.87 g (3.49 mmol) of calix[4]arene dibutyl ether **3**: mp 194–195 °C; ^{1}H NMR ($CDCl_3$) δ 7.43 (s, 1H, ArO*H*), 7.26 (d, J=7.6 Hz, 2H, Ar*H*), 7.14 (t, J=7.8 Hz, 1H, Ar*H*), 7.07 (d, J=7.2 Hz, 2H, Ar*H*), 6.92 (d, J=7.6 Hz, 2H, Ar*H*), 6.82 (d, J=7.2 Hz, 2H, Ar*H*), 6.73 (t, J=7.8 Hz, 2H, Ar*H*), 6.69 (t, J=7.4 Hz, 1H, Ar*H*), 4.11 (d, J=13.2 Hz, 2H, ArCH_2Ar), 3.92–3.98 (m, 4H, ArCH_2Ar

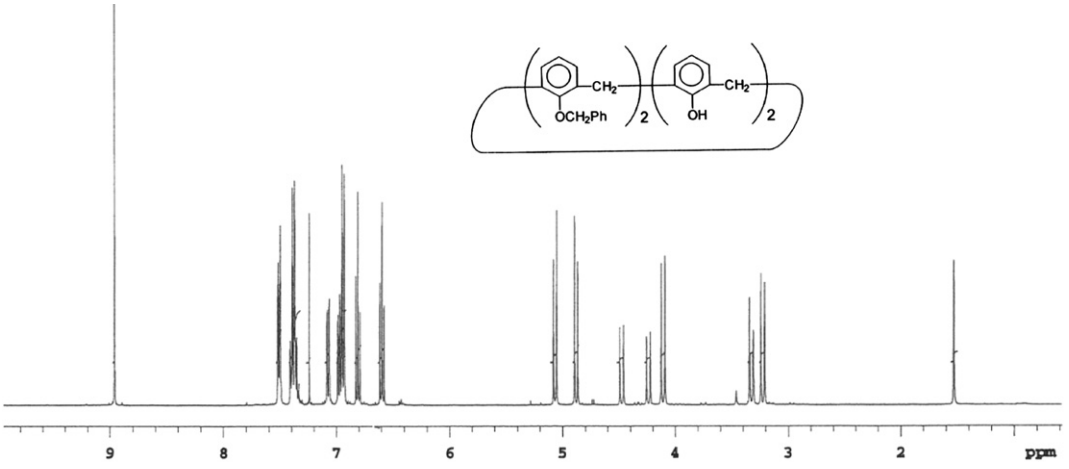


Fig. 5. The ^{1}H NMR spectrum of the *syn*-1,2-dibenzyloxycalix[4]arene **41**.

and $OCH_2CH_2CH_2CH_3$), 3.62–3.69 (m, 4H, $ArCH_2Ar$ and $OCH_2CH_2CH_2CH_3$), 3.28 (d, J=13.2 Hz, 2H, $ArCH_2Ar$), 1.57–1.75 (2m, 4H, $OCH_2CH_2CH_2CH_3$), 1.35–1.48 (m, 4H, $OCH_2CH_2CH_2CH_3$), 1.22 (s, 3H, $COCH_3$), 0.95 (t, J=7.2 Hz, 6H, $OCH_2CH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$) δ 168.8, 154.6, 153.4, 148.0, 133.9, 133.0, 132.8, 129.6, 129.5, 128.6, 128.3, 128.0, 124.9, 123.5, 118.7, 73.4, 37.9, 32.0, 31.2, 20.3, 19.2, 14.1.

*3.1.4. 25-Acetoxy-26,28-diallyloxycalix[4]arene (**9**).* An amount of 0.30 g (15.5%) of colorless fine crystals was collected from 1.76 g (3.49 mmol) of calix[4]arene diallyl ether **4**: mp 218–219 °C; ^{1}H NMR ($CDCl_3$) δ 7.25 (d, J=6.9 Hz, 2H, Ar*H*), 7.13 (s, 1H, ArO*H*), 7.10 (t, J=7.9 Hz, 1H, Ar*H*), 7.07 (d, J=7.5 Hz, 2H, Ar*H*), 6.92 (d, J=7.0 Hz, 2H, Ar*H*), 6.84 (d, J=7.2 Hz, 2H, Ar*H*), 6.76 (t, J=7.5 Hz, 2H, Ar*H*), 6.69 (t, J=7.5 Hz, 1H, Ar*H*), 5.92–5.99 (m, 1H, $OCH_2CH{=}CH_2$), 5.26 (dd, J=17.2, 1.6 Hz, 2H, $OCH_2CH{=}CH_2$), 5.18 (dd, J=10.6, 1.3 Hz, 2H, $OCH_2CH{=}CH_2$), 4.47–4.50 (m, 2H, $OCH_2CH{=}CH_2$), 4.22 (dd, J=5.3, 12.9 Hz, 2H, $OCH_2CH{=}CH_2$), 4.08 (d, J=13.2 Hz, 2H, $ArCH_2Ar$), 3.94 (d, J=15.6 Hz, 2H, $ArCH_2Ar$), 3.66 (d, J=15.7 Hz, 2H, $ArCH_2Ar$), 3.27 (d, J=13.2 Hz, 2H, $ArCH_2Ar$), 1.41 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$) δ 168.7, 154.1, 153.2, 147.9, 134.0, 132.9, 132.8, 130.0, 129.6, 128.7, 128.1, 128.0, 125.1, 123.7, 118.7, 117.2, 73.9, 37.8, 31.1, 20.5; FAB-MS m/e: 546 (M^+).

*3.1.5. 25-Acetoxy-26,28-dibenzyloxycalix[4]arene (**10**).* An amount of 0.28 g (14.5%) of colorless fine crystals was collected from 1.81 g (3.14 mmol) of calix[4]arene dibenzyl ether **5**: mp 205–206 °C; ^{1}H NMR (CDCl3) δ 7.25–7.35 (m, 10H, Ar′*H*), 7.09 (s, 1H, ArO*H*), 7.04 (d, J=7.4 Hz, 4H, Ar*H*), 6.94 (d, J=7.5 Hz, 2H, Ar*H*), 6.88 (d, J=6.5 Hz, 2H, Ar*H*), 6.84 (t, J=7.6 Hz, 1H, Ar*H*), 6.79 (t, J=7.5 Hz, 2H, Ar*H*), 6.67 (t, J=7.4 Hz, 1H, Ar*H*), 5.08 (d, J=12 Hz, 2H, $ArOCH_2Ar'$), 4.78 (d, J=12.0 Hz, 2H, $ArOCH_2Ar'$), 4.04 (d, J=13.2 Hz, 2H, $ArCH_2Ar$), 3.92 (d, J=15.5 Hz, 2H, $ArCH_2Ar$), 3.67 (d, J=15.5 Hz, 2H, $ArCH_2Ar$), 3.21 (d, J=13.3 Hz, 2H, $ArCH_2Ar$), 1.44 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$) δ 168.7, 154.4, 153.4, 147.9, 137.0, 133.9, 133.0, 132.9, 129.9, 129.8, 128.8, 128.3, 128.1, 127.9, 127.6, 127.2, 127.1, 125.1, 123.9, 118.6, 75.2, 37.9, 31.1, 20.6; FAB-MS m/e: 646 (M^+); HRMS (FAB) m/e: calcd for $C_{44}H_{38}O_5$: 646.2720; found: 646.2730.

3.2. General procedure for the monoacetylation of calix[4] arene monoalkyl ethers

A slurry of 0.50 g of calix[4]arene monoalkyl ethers **11**–**15** was dissolved in 10 mL of pyridine, and 0.2 mL of acetyl chloride was then added dropwisely at ice bath temperature. The reaction mixtures were stirred for 10 min, and the solvent was removed by rotory evaporatory to leave an oily residue. The organic materials were taken up by 50 mL of $CHCl_3$, and washed with 20 mL of 1 N HCl twice followed with 100 mL of saturated $NaHCO_3$ solution and 100 mL of distillated water. The organic solvent was then removed from the organic portion to leave an off white residue. Recrystallized from $CHCl_3$ and CH_3OH yielded the corresponding monoacetylated products **16**–**10**.

*3.2.1. 25-Acetoxy-27-ethoxy-26,28-dihydroxycalix[4]arene (**16**).* An amount of 0.28 g (51%) of colorless fine crystals was collected from 0.50 g (1.11 mmol) of calix[4]arene monoethyl ether **11**: mp 241–243 °C; ^{1}H NMR ($CDCl_3$) δ 7.01–7.19 (m, 6H, Ar*H* and ArO*H*), 6.93–6.97 (d, J=7.2 Hz, 2H, Ar*H*), 6.85–6.88 (d, J=7.6 Hz, 2H, Ar*H*), 6.68–6.81 (m, 4H, Ar*H*), 4.10–4.18 (m, 4H, $ArCH_2Ar$ and OCH_2CH_3), 4.03–4.06 (d, J=13.2 Hz, 2H, $ArCH_2Ar$), 3.48–3.52 (d, J=14.0 Hz, 2H, $ArCH_2Ar$), 3.37–3.41 (d, J=14.0 Hz, 2H, $ArCH_2Ar$), 2.53 (s, 3H, $COCH_3$), 1.65–1.69 (t, J=7.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 169.7, 152.6, 151.1, 144.0, 133.1, 132.5, 129.4, 128.9, 128.8, 128.6, 128.4, 127.3, 126.2, 126.1, 119.7, 72.6, 31.8, 20.8, 15.1; FAB-MS m/e: 494 (M^+); HRMS (FAB) m/e: calcd for $C_{32}H_{30}O_5$: 494.2093; found: 494.2094.

*3.2.2. 25-Acetoxy-27-propoxy-26,28-dihydroxycalix[4]arene (**17**).* An amount of 0.26 g (47.5%) of colorless fine crystals was collected from 0.50 g (1.07 mmol) of calix[4]arene monopropyl ether **12**: mp 282–284 °C; ^{1}H NMR ($CDCl_3$) δ 6.98–7.19 (m, 6H, Ar*H* and ArO*H*), 6.85–6.88 (d, J=7.6 Hz, 2H, Ar*H*), 6.77–6.80 (d, J=7.6 Hz, 2H, Ar*H*), 6.61–6.80 (m, 4H, Ar*H*), 4.06–4.10 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 3.94–4.01 (m, 4, $ArCH_2Ar$ and $OCH_2CH_2CH_3$), 3.40–3.44 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 3.30–3.34 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 2.45 (s, 3H, $COCH_3$), 2.00–2.06 (m, 2H, $OCH_2CH_2CH_3$), 1.21–1.25 (t, J=7.4 Hz, $OCH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$) δ 169.6, 152.8, 151.2, 144.9, 133.0, 132.4, 129.4, 128.7, 128.6, 128.5, 127.2, 126.2, 126.0, 119.6, 31.81, 31.7, 23.3, 21.7, 10.6; FAB-MS m/e: 508 (M^+); HRMS (FAB) m/e: calcd for $C_{33}H_{32}O_5$: 508.2250; found: 508.2263.

*3.2.3. 25-Acetoxy-27-butoxy-26,28-dihydroxycalix[4]arene (**18**).* An amount of 0.25 g (46%) of colorless fine crystals was collected from 0.50 g (1.04 mmol) of calix[4]arene monobutyl ether **13**: mp 262–264 °C; ^{1}H NMR ($CDCl_3$) δ 7.08–7.20 (m, 6H, Ar*H* and ArO*H*), 6.90–6.92 (d, J=7.6 Hz, 2H, Ar*H*), 6.83–6.86 (d, J=7.6 Hz, 2H, Ar*H*), 6.68–6.78 (m, 4H, Ar*H*), 4.04–4.18 (m, 6H, $ArCH_2Ar$ and $OCH_2CH_2CH_2CH_3$), 3.49–3.53 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 3.39–3.43 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 2.54 (s, 3H, $COCH_3$), 2.06–2.08 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.80–1.82 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.10–1.15 (t, J=7.3 Hz, $OCH_2CH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$) δ 169.5, 152.8, 151.1, 144.9, 132.9, 132.3, 129.4, 128.7, 128.6, 128.5, 127.1, 126.2, 125.9, 119.5, 32.1, 31.8, 31.7, 20.6, 19.3, 14.0; FAB-MS m/e: 522 (M^+); HRMS (FAB) m/e: calcd for $C_{34}H_{34}O_5$: 522.2406; found: 522.2410.

*3.2.4. 25-Acetoxy-27-allyloxy-26,28-dihydroxycalix[4]arene (**19**).* An amount of 0.22 g (40%) of colorless fine crystals was collected from 0.50 g (1.08 mmol) of calix[4]arene monoallyl ether **14**: mp 222–224 °C; ^{1}H NMR ($CDCl_3$) δ 7.08–7.18 (m, 6H, Ar*H* and ArO*H*), 6.91–6.93 (d, J=7.6 Hz, 2H, Ar*H*), 6.84–6.86 (d, J=7.6 Hz, 2H, Ar*H*), 6.70–6.79 (m, 4H, Ar*H*), 6.15–6.35 (m, 1H, $OCH_2CH{=}CH_2$), 5.69–5.74 (dd, 1H, $OCH_2CH{=}CH_2$), 5.43–5.46 (dd, 1H, $OCH_2CH{=}CH_2$), 4.55–4.60 (m, 2H, $OCH_2CH{=}CH_2$), 4.15–4.18 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 3.95–4.03 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 3.47–4.50 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 3.38–3.42 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 2.53 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$) δ 169.5, 152.7, 151.1, 144.9, 133.0, 132.4, 132.1, 129.4, 128.8, 128.7, 128.6, 128.5, 127.4, 126.3, 126.0, 119.6, 118.7, 31.9, 31.8, 20.8; FAB-MS m/e: 506 (M^+); HRMS (FAB) m/e: calcd for $C_{33}H_{30}O_5$: 506.2093; found: 506.2094.

*3.2.5. 25-Acetoxy-27-benzyloxy-26,28-dihydroxycalix[4]arene (**20**).* An amount of 0.24 g (44%) of colorless fine crystals was collected from 0.50 g (0.97 mmol) of calix[4]arene monobenzyl ether **15**: mp 264–266 °C; ^{1}H NMR ($CDCl_3$) δ 7.67–7.70 (m, 2H, Ar′*H*), 7.38–7.5 (m, 3H, Ar′*H*), 7.05–7.12 (m, 6H, Ar*H* and ArO*H*), 6.95–6.98 (d, J=7.6 Hz, 2H, Ar*H*), 6.86–6.88 (d, J=7.6 Hz, 2H, Ar*H*), 6.65–6.85 (m, 4H, Ar*H*), 5.09 (s, 2H, OCH_2Ar'), 4.21–4.25 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 4.21–4.25 (d, J=13.6 Hz, 2H, $ArCH_2Ar$), 3.92–3.96 (d, J=13.2 Hz, 2H, $ArCH_2Ar$), 3.45–3.49 (d, J=12.4 Hz, 2H, $ArCH_2Ar$), 3.35–3.89 (d, J=13.2 Hz, 2H, $ArCH_2Ar$), 2.36 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$) δ 169.3, 152.7, 151.1, 144.6, 135.8, 133.2, 132.4, 129.5, 128.8, 128.7, 128.5, 128.4, 128.2, 127.5, 126.5, 126.2, 119.7, 78.7, 31.9, 31.8, 20.56; FAB-MS m/e: 557 (M^++1); HRMS (FAB) m/e: calcd for $C_{37}H_{32}O_5$+H^+: 557.2328; found: 557.2321.

3.3. General procedure for the diacetylation of calix[4]arene monoalkyl ethers

A slurry of 0.50 g of calix[4]arene monoalkyl ethers **11**–**15** was dissolved in 20 mL of pyridine, and 2.0 mL of acetyl chloride was then added dropwisely at ice bath temperature. The reaction mixtures were stirred for 2 h, and the solvent was removed by rotory evaporatory to leave an oily residue. The organic materials were taken up by 50 mL of $CHCl_3$, and washed with 20 mL of 1 N HCl twice followed with 100 mL of saturated $NaHCO_3$ solution and

100 mL of distillated water. The organic solvent was then removed from the organic portion to leave an off white residue. Recrystallized from $CHCl_3$ and CH_3OH yielded the corresponding diacetylated products **21**–**25**.

*3.3.1. 25,26-Diacetoxy-27-ethoxy-28-hydroxycalix[4]arene (**21**).* An amount of 0.40 g (67.5%) of colorless fine crystals was collected from 0.50 g (1.11 mmol) of calix[4]arene monoethyl ether **11**: mp 257–259 °C; ^{1}H NMR ($CDCl_3$) δ 7.73 (s, 1H, ArO*H*), 6.68–7.28 (m, 12H, Ar*H*), 3.68–4.14 (m, 8H, ArCH_2Ar and OCH_2CH$_3$), 3.45 (d, *J*=14.0 Hz, 1H, ArCH_2Ar), 3.25 (d, *J*=12.8 Hz, 1H, ArCH_2Ar), 2.09 (s, 3H, COCH_3), 1.28 (t, *J*=7.0 Hz, 3H, OCH$_2$CH_3), 1.10 (s, 3H, COCH_3); ^{13}C NMR ($CDCl_3$) δ 169.5, 168.4, 152.9, 152.5, 148.2, 146.8, 133.8, 133.7, 133.1, 132.9, 132.7, 131.8, 129.6, 129.5, 129.4, 129.2, 128.9, 128.3, 128.0, 127.9, 126.6, 125.2, 125.1, 119.3, 69.0, 37.9, 37.8, 31.8, 31.4, 20.6, 19.9, 14.6; FAB-MS *m*/*e*: 537 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{34}H_{32}O_6$+H^+: 537.2277; found: 537.2279.

*3.3.2. 25,26-Diacetoxy-27-propoxy-28-hydroxycalix[4]arene (**22**).* An amount of 0.25 g (42%) of colorless fine crystals was collected from 0.50 g (1.07 mmol) of calix[4]arene monopropyl ether **12**: mp 234–236 °C; ^{1}H NMR ($CDCl_3$) δ 7.69 (s, 1H, ArO*H*), 6.69–7.27 (m, 12H, Ar*H*), 3.67–4.07 (m, 8H, ArCH_2Ar and OCH_2CH$_2$CH$_3$), 3.45 (d, *J*=13.6 Hz, 1H, ArCH_2Ar), 3.24 (d, *J*=12.8 Hz, 1H, ArCH_2Ar), 2.09 (s, 3H, COCH_3), 1.71–1.75 (m, 2H, OCH$_2$CH_2CH$_3$), 1.10 (s, 3H, COCH_3), 0.95 (t, *J*=7.6 Hz, OCH$_2$CH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 169.5, 168.5, 153.0, 152.7, 148.2, 146.8, 133.7, 133.5, 133.2, 133.0, 132.8, 131.8, 129.7, 129.5, 129.4, 129.3, 129.1, 128.3, 128.0, 127.9, 126.3, 125.2, 125.1, 125.0, 119.1, 75.3, 37.9, 37.8, 31.8, 31.3, 22.8, 20.6, 20.0, 10.4; FAB-MS *m*/*e*: 551 (M^++1); HRMS (FAB) calcd for $C_{35}H_{34}O_6$+H^+: 551.2434; found: 551.2432.

*3.3.3. 25,26-Diacetoxy-27-butoxy-28-hydroxycalix[4]arene (**23**).* An amount of 0.36 g (61%) of colorless fine crystals was collected from 0.50 g (1.04 mmol) of calix[4]arene monobutyl ether **13**: mp 201–203 °C; ^{1}H NMR ($CDCl_3$) δ 7.69 (s, 1H, ArO*H*), 6.70–7.28 (m, 12H, Ar*H*), 3.68–4.15 (m, 8H, ArCH_2Ar and OCH_2CH$_2$CH$_2$CH$_3$), 3.45 (d, *J*=13.6 Hz, 1H, ArCH_2Ar), 3.24 (d, *J*=12.8 Hz, 1H, ArCH_2Ar), 2.09 (s, 3H, COCH_3), 1.71–1.79 (m, 1H, OCH$_2$CH_2CH$_2$CH$_3$), 1.61–1.70 (m, 1H, OCH$_2$CH_2CH$_2$CH$_3$), 1.38–1.45 (m, 2H, OCH$_2$CH$_2$CH_2CH$_3$), 1.13 (s, 3H, COCH_3), 0.94 (t, *J*=7.4 Hz, 3H, OCH$_2$CH$_2$CH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 169.4, 168.4, 153.0, 152.8, 148.2, 146.8, 133.7, 133.5, 133.2, 133.0, 132.8, 131.8, 129.7, 129.5, 129.4, 129.3, 129.1, 128.3, 128.0, 127.8, 126.3, 125.2, 125.1, 125.0, 119.1, 73.7, 37.9, 37.8, 31.8, 31.6, 31.3, 20.5, 20.0, 19.0, 14.0; FAB-MS *m*/*e*: 565 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{36}H_{36}O_6$+H^+: 565.2590; found: 565.2599.

*3.3.4. 25,26-Diacetoxy-27-allyloxy-28-hydroxycalix[4]arene (**24**).* An amount of 0.23 g (39%) of colorless fine crystals was collected from 0.50 g (1.08 mmol) of calix[4]arene monoallyl ether **14**: mp 206–208 °C; ^{1}H NMR ($CDCl_3$) δ 7.44 (s, 1H, ArO*H*),6.68–7.28 (m, 12H, Ar*H*), 5.83–5.96 (m, 1H, OCH$_2$C*H*=CH$_2$), 5.15–5.24 (m, 2H, OCH$_2$CH=CH_2), 4.53–4.61 (m, 1H, OCH_2CH=CH$_2$), 4.21–4.28 (m, 1H, OCH_2CH=CH$_2$), 3.67–4.03 (m, 6H, ArCH_2Ar), 3.44 (d, *J*=13.6 Hz, 1H, ArCH_2Ar), 3.24 (d, *J*=13.2 Hz, 1H, ArCH_2Ar), 2.11 (s, 3H, COCH_3), 1.18 (s, 3H, COCH_3); ^{13}C NMR ($CDCl_3$) δ 169.5, 168.5, 153.0, 152.4, 148.2, 146.9, 133.7, 133.6, 133.1, 132.8, 131.9, 131.6, 129.8, 129.6, 129.5, 129.4, 129.3, 128.4, 128.0, 126.3, 125.4, 125.3, 125.2, 119.3, 118.1, 73.84, 37.9, 37.8, 35.1, 31.7, 31.4, 20.7, 20.4, 20.1; FAB-MS *m*/*e*: 549 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{35}H_{32}O_6$+H^+: 549.2277; found: 549.2274.

*3.3.5. 25,26-Diacetoxy-27-benzyloxy-28-hydroxycalix[4]arene (**25**).* An amount of 0.26 g (45%) of colorless fine crystals was collected from 0.50 g (0.97 mmol) of calix[4]arene monobenzyl ether **15**: mp 225–227 °C; ^{1}H NMR ($CDCl_3$) δ 6.70–7.45 (m, 18H, ArO*H*, Ar*H*, and Ar′*H*), 5.22 (d, *J*=11.2 Hz, 1H, OCH_2Ar′), 4.82 (d, *J*=11.6 Hz, 1H, OCH_2Ar′), 4.08 (d, *J*=16.4 Hz, 1H, ArCH_2Ar), 3.82–4.00 (m, 4H, ArCH_2Ar), 3.75 (d, *J*=16.0 Hz, 1H, ArCH_2Ar), 3.47 (d, *J*=14.0 Hz, 1H, ArCH_2Ar), 3.26 (d, *J*=12.8 Hz, 1H, ArCH_2Ar), 2.10 (s, 3H, COCH_3), 1.23 (s, 3H, COCH_3); ^{13}C NMR ($CDCl_3$) δ 169.5, 168.5, 153.1, 152.8, 148.2, 146.9, 135.7, 133.7, 133.6, 133.3, 132.9, 131.9, 130.0, 129.6, 129.5, 129.4, 129.1, 128.5, 128.4, 128.3, 128.1, 128.0, 127.6, 126.2, 125.4, 125.2, 119.2, 75.6, 38.0, 37.9, 31.8, 31.4, 20.7, 20.2; FAB-MS *m*/*e*: 599 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{39}H_{34}O_6$+H^+: 599.2434; found: 599.2436.

3.4. General procedure for the alkylation of 1-monoalkoxy-2,3-diacetoxycalix[4]arenes 21–25 in the present of K_2CO_3

A slurry of approximate 0.50 g of 1-monoalkoxy-2,3-diacetoxycalix[4]arenes **21**–**25**, 1.00 g of K_2CO_3, and 2 mL of alkyl halide was refluxed in 50 mL of CH_3CN for 24 h. The solvent was removed and the organic materials were taken up by 50 mL of $CHCl_3$. The solution was washed in sequence with 20 mL of 1 N HCl and 100 mL of distillated water, and the solvent was then removed to leave a colorless solid. Recrystallization from $CHCl_3$ and CH_3OH yielded the corresponding dialkoxy products **26**–**30**.

*3.4.1. 25,27-Diethoxy-26,28-diacetoxycalix[4]arene (**26**).* An amount of 0.37 g (71%) of colorless crystals was afforded from 0.50 g (0.93 mmol) of monoethoxy compound **21**: mp>300 °C (dec); ^{1}H NMR ($CDCl_3$) δ 6.62–7.29 (m, 12H, Ar*H*), 3.85–3.89 (m, 6H, ArCH_2Ar and OCH_2CH$_3$), 3.64–3.69 (m, 2H, OCH_2CH$_3$), 3.53–3.57 (d, *J*=14.8 Hz, 2H, ArCH_2Ar), 3.18–3.21 (d, *J*=14.8 Hz, 2H, ArCH_2Ar), 1.91 (s, 3H, COCH_3), 1.56 (s, 3H, COCH_3), 1.35–1.37 (t, *J*=7.2 Hz, 6H, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 171.9, 168.7, 155.2, 148.8, 148.1, 135.5, 134.0, 133.3, 132.4, 130.4, 129.4, 129.3, 128.5, 125.5, 125.0, 122.3, 69.9, 37.6, 30.6, 21.8, 21.4, 15.77; FAB-MS *m*/*e*: 565 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{36}H_{36}O_6$+H^+: 565.2590; found: 565.2588.

*3.4.2. 25,27-Dipropoxy-26,28-diacetoxycalix[4]arene (**27**).* An amount of 0.37 g (69%) of colorless crystals was afforded from 0.50 (0.91 mmol) g of monopropoxy compound **22**: mp 216–218 °C; ^{1}H NMR ($CDCl_3$) δ 6.63–7.31 (m, 12H, Ar*H*), 3.88–3.92 (d, *J*=13.6 Hz, 4H, ArCH_2Ar), 3.73–3.78 (m, 2H, OCH_2CH$_2$CH$_3$), 3.50–3.59 (m, 4H, ArCH_2Ar and OCH_2CH$_2$CH$_3$), 3.20–3.23 (d, *J*=13.2 Hz, 2H, ArCH_2Ar), 1.94 (s, 3H, COCH_3), 1.79–1.85 (m, 4H, OCH$_2$CH_2CH$_3$), 1.56 (s, 3H, COCH_3), 0.95–1.02 (t, *J*=7.2 Hz, 6H, OCH$_2$CH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 171.9, 168.7, 155.4, 148.9, 148.1, 135.5, 134.0, 133.2, 132.2, 130.4, 129.5, 129.4, 128.5, 125.5, 125.0, 122.2, 77.3, 77.0, 76.7, 76.6, 37.5, 30.6, 23.4, 21.5, 21.5, 10.6; FAB-MS *m*/*e*: 593 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{38}H_{40}O_6$+H^+: 593.2903; found: 593.2906.

*3.4.3. 25,27-Dibutoxy-26,28-diacetoxycalix[4]arene (**28**).* An amount of 0.25 g (45%) of colorless crystals was afforded from 0.50 g (0.88 mmol) of monobutoxy compound **23**: mp 178–180 °C; ^{1}H NMR ($CDCl_3$) δ 6.64–7.29 (m, 12H, Ar*H*), 3.86–3.91 (2d, *J*=13.4 Hz, 4H, ArCH_2Ar), 3.73–3.81 (m, 2H, OCH_2CH$_2$CH$_2$CH$_3$), 3.53–3.59 (m, 4H, ArCH_2Ar and OCH_2CH$_2$CH$_2$CH$_3$), 3.19–3.22 (d, *J*=13.2 Hz, 2H, ArCH_2Ar), 1.93 (s, 3H, COCH_3), 1.75–1.78 (m, 4H, OCH$_2$CH_2CH$_2$CH$_3$), 1.54 (s, 3H, COCH_3), 1.38–1.44 (m, 4H, OCH$_2$CH$_2$CH_2CH$_3$), 0.94–0.98 (t, *J*=7.2 Hz, 3H, OCH$_2$CH$_2$CH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 172.9, 168.7, 155.4, 148.8, 148.1, 135.5, 134.0, 133.2, 132.2, 130.4, 129.5, 129.4, 128.5, 125.5, 125.0, 122.2, 74.7, 37.5, 32.2, 30.6, 21.5, 19.3, 13.9.

*3.4.4. 25,27-Diallyloxy-26,28-diacetoxycalix[4]arene (**29**).* An amount of 0.29g (54%) of colorless crystals was afforded from 0.50 g (0.91 mmol) of monoalloxy compound **24**: mp 210–212 °C; ^{1}H NMR ($CDCl_3$) δ 6.64–7.29 (m, 12H, Ar*H*), 6.05–6.17 (m, 2H, OCH$_2$C*H*=CH$_2$), 5.24–5.34 (2d, 4H, OCH$_2$CH=CH_2), 4.26–4.32 (m, 2H, OCH_2CH=CH$_2$), 4.12–4.18 (m, 2H, OCH_2CH=CH$_2$), 3.87–3.91 (d, *J*=13.2 Hz, 4H,

ArCH_2Ar), 3.54–3.59 (d, J=13.2 Hz, 2H, ArCH_2Ar), 3.19–3.23 (d, J=13.2 Hz, 2H, ArCH_2Ar), 1.89 (s, 3H, COCH_3), 1.52 (s, 3H, COCH_3); ^{13}C NMR ($CDCl_3$) δ 171.8, 168.6, 154.9, 148.7, 148.1, 135.4, 133.9, 133.8, 133.3, 132.5, 130.5, 129.5, 129.3, 128.5, 125.5, 125.0, 122.6, 118.8, 75.7, 37.6, 30.8, 21.9, 21.4; FAB-MS m/e: 589 (M^++1); HRMS (FAB) m/e: calcd for $C_{38}H_{36}O_6$+H^+: 589.2590; found: 589.2597.

*3.4.5. 25,27-Dibenzyloxy-26,28-diacetoxycalix[4]arene (**30**).* An amount of 0.34 g (59%) of colorless crystals was afforded from 0.50 g (0.83 mmol) of monobenzyloxy compound **25**: mp 222–224 °C; ^{1}H NMR ($CDCl_3$) δ 6.66-7.36 (m, 22H, ArH and Ar′H), 4.69–4.72 (d, J=10.4 Hz, 2H, OCH_2Ar′), 4.62–4.65 (d, J=10.4 Hz, 2H, OCH_2Ar′), 3.83–3.86 (d, J=13.6 Hz, 2H, ArCH_2Ar), 3.75–3.79 (d, J=14.6 Hz, 2H, ArCH_2Ar), 3.49–3.53 (d, J=14.6 Hz, 2H, ArCH_2Ar), 3.09–3.12 (d, J=13.6 Hz, 2H, ArCH_2Ar), 1.93 (s, 3H, COCH_3), 1.09 (s, 3H, COCH_3); ^{13}C NMR ($CDCl_3$) δ 172.0, 169.0, 155.1, 149.0, 148.4, 136.6, 135.7, 133.9, 133.8, 132.8, 130.7, 129.9, 129.8, 129.7, 128.8, 128.7, 125.8, 125.1, 122.8, 77.9, 77.4, 77.3, 76.6, 37.8, 31.0, 21.7, 21.4; FAB-MS m/e: 689 (M^++1); HRMS (FAB) m/e: calcd for $C_{46}H_{40}O_6$+H^+: 689.2903; found: 689.2901.

3.5. General procedure for the basic hydrolysis of dialkoxy-diacetoxycalix[4]arene 26–30

A slurry of dialkoxy-diacetoxycalix[4]arene ethers **26**–**30** and 2.00 g of NaOH was refluxed in a mixture of 10 mL of C_2H_5OH and 50 mL of THF for 24 h. The solvent was removed by rotory evaporatory and the organic materials were taken up by 50 mL of $CHCl_3$. The solution was washed in sequence with 20 mL of 1N HCl and 100 mL of distillated water, and the solvent was then removed to leave a colorless solid. Recrystallization from $CHCl_3$ and CH_3OH yielded the corresponding 1,3-dialkoxycalix[4]arenes **31**–**35**.

*3.5.1. 25,27-Diethoxy-26,28-dihydroxycalix[4]arene (**31**).* An amount of 0.15 g (38%) of colorless fine crystals was collected from 0.47 g (0.83 mmol) of compound **26**: mp 254–256 °C. The ^{1}H NMR was identical to the known compound.

*3.5.2. 25,27-Dipropoxy-26,28-dihydroxycalix[4]arene (**32**).* An amount of 0.14 g (75%) of colorless fine crystals was collected from 0.22 g (0.37 mmol) of compound **27**: mp 256–258 °C. The ^{1}H NMR was identical to the known compound.

*3.5.3. 25,27-Dibutoxy-26,28-dihydroxycalix[4]arene (**33**).* An amount of 0.10 g (64%) of colorless fine crystals was collected from 0.18 g (0.29 mmol) of compound **28**: mp 212–216 °C. The ^{1}H NMR was identical to the known compound.

*3.5.4. 25,27-Diallyloxy-26,28-dihydroxycalix[4]arene (**34**).* An amount of 0.22 g (76%) of colorless fine crystals was collected from 0.34 g (0.58 mmol) of compound **29**: mp 208–210 °C. The ^{1}H NMR was identical to the known compound.

*3.5.5. 25,27-Dibenzyloxy-26,28-dihydroxycalix[4]arene (**35**).* An amount of 0.15 g (45%) of colorless fine crystals was collected from 0.38 g (0.55 mmol) of compound **30**: mp 230–232 °C. The ^{1}H NMR was identical to the known compound.

3.6. General procedure for the alkylation of 1-monoalkoxy-2,3-diacetoxycalix[4]arenes 21–25 in the present of NaH

A slurry of approximate 0.50 g of 1-monoalkoxy-2,3-diacetoxycalix[4]arenes **21**–**25**, 0.05 g of 60% NaH, and 1 mL of alkyl halide was refluxed in 50 mL of CH_3CN for 14 h. The solvent was removed and the organic materials were taken up by 50 mL of $CHCl_3$. The organic solution was washed in sequence with 20 mL of 1 N HCl and 100 mL of distillated water. The organic solvent was then concentrated and recrystallized from $CHCl_3$ and CH_3OH to afford the mixture of acetyl-migrated 1,3-dialkoxy **26**–**30** and non-migrated 1,2-alkoxy **36**–**40**, respectively, in various amount. Product **40** was the only compound, which could be purified by a simple crystallization procedure.

*3.6.1. 25,26-Dibenzyloxy-27,28-diacetoxycalix[4]arene (**40**).* A slurry of 0.50 g (0.83 mmol) of compound **25**, 0.05 g of 60% NaH, and 0.28 g (1.67 mmol) of benzyl bromide was refluxed in 50 mL of CH_3CN for 14 h. The solvent was removed and the organic materials were taken up by 50 mL of $CHCl_3$. The solution was washed with 20 mL of 1 N HCl and 100 mL of distillated water twice, and the solvent was then removed to leave a colorless solid. Recrystallization from $CHCl_3$ and CH_3OH afforded the first crops as 1,3-dialkoxy products **30**. The mother solution was further concentration to precipitate second crops of solid. Further recrystallization from $CHCl_3$ and CH_3OH yielded 0.22 g (28%) of colorless crystals **40**: mp 240–245 °C; ^{1}H NMR ($CDCl_3$) δ 6.89–7.30 (m, 22H, ArH and Ar′H), 4.65 (s, 2H, OCH_2Ar′), 4.61–4.64 (d, J=11.8 Hz, 1H, OCH_2Ar′), 4.55–4.58 (d, J=11.8 Hz, 1H, OCH_2Ar′), 4.04–4.07 (d, J=12.8 Hz, 1H, ArCH_2Ar), 3.82–3.85 (d, J=12.8 Hz, 1H, ArCH_2Ar), 3.51–3.65 (m, 3H, ArCH_2Ar), 3.48–3.52 (d, J=15.6 Hz, 1H, ArCH_2Ar), 3.14–3.17 (d, J=12.8 Hz, 1H, ArCH_2Ar), 2.96–2.99 (d, J=12.8 Hz, 1H, ArCH_2Ar), 1.50 (s, 3H, COCH_3), 1.23 (s, 3H, COCH_3); ^{13}C NMR ($CDCl_3$) δ 170.2, 168.5, 155.2, 155.0, 148.6, 146.3, 137.5, 137.0, 135.8, 135.0, 134.9, 134.3, 133.7, 132.7, 132.4, 131.6, 130.1, 129.4, 129.3, 129.1, 128.9, 128.8, 128.6, 128.5, 128.5, 128.1, 128.1, 128.0, 127.3, 125.0, 124.8, 123.6, 122.7, 76.1, 37.9, 37.6, 30.6, 30.1, 20.2, 20.0; FAB-MS m/e: 689 (M^++1); HRMS (FAB) m/e: calcd for $C_{46}H_{40}O_6$+H^+: 689.2903; found: 689.2890.

*3.6.2. 25,26-Dibenzyloxy-27,28-dihydroxycalix[4]arene (**41**).* A slurry of0.38 g (0.69 mmol) of 1,2-dibenzyloxy compound **40** and 8.00 g of 25% NaOH was refluxed in a mixture of 10 mL of C_2H_5OH and 50 mL of THF for 24 h. The solvent was removed by rotory evaporatory and the organic materials were taken up by 50 mL of $CHCl_3$. The solution was washed with 20 mL of 1 N HCl and 100 mL of distillated water twice, and the solvent was then removed to leave a colorless solid. Recrystallization from $CHCl_3$ and CH_3OH yielded 0.22 g (65%) of colorless crystals **41**: mp 230–232 °C; ^{1}H NMR ($CDCl_3$) δ 8.93 (s, 2H, ArOH), 6.56–7.51 (m, 22H, ArH and Ar′H), 5.05–5.08 (d, J=11.2 Hz, 2H, OCH_2Ar′), 4.87–4.90 (d, J=11.2 Hz, 2H, OCH_2Ar′), 4.47–4.50 (d, J=12.4 Hz, 1H, ArCH_2Ar), 4.23–4.26 (d, J=13.2 Hz, 1H, ArCH_2Ar), 4.10–4.13 (d, J=12.8 Hz, 2H, ArCH_2Ar), 3.33–3.36 (d, J=13.2 Hz, 2H, ArCH_2Ar), 3.22–3.25 (d, J=12.8 Hz, 2H, ArCH_2Ar); ^{13}C NMR ($CDCl_3$) δ 153.1, 151.0, 136.5, 134.6, 134.4, 129.2, 129.1, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.0, 124.9, 120.4, 78.4, 31.8, 30.5; FAB-MS m/e: 605 (M^++1); HRMS (FAB) m/e: calcd for $C_{42}H_{36}O_4$+H^+: 605.2692; found: 605.2708.

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Supplementary data

Copies of ^{1}H and ^{13}C NMR spectra of compounds **6**–**35**, **40** and **41** are available. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.03.010.

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