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25,26-Dialkoxycalix[4]arenes. Part 2: 1-Alkoxy-3-benzoyloxy route

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ABSTRACT

Benzoylation of calix[4]arene monoalkyl ethers with benzoyl chloride yielded the corresponding 3-benzoates and/or 2,3-dibenzoates in different reaction conditions. A simple recrystallization process was able to isolate the 3-benzoates in good yield. In the presence of NaH as reaction base, the 1-alkoxy-3-benzoyloxycalixarenes were alkylated with active alkyl halides at proximal position and yielded the corresponding 1,2-dialkoxy derivatives. Basic hydrolysis of compounds afforded the expected 25,26-dialkoxycalix[4]arenes. For the less active alkyl halides, alkylation of 1-alkoxy-3-benzoyloxycalix[4]arenes afforded both the 1,2-dialkoxy derivatives and the benzoyl-migrated 1,3-dialkoxy derivatives. Only the highly symmetrical 1,3-diethoxy-2-benzoyloxycalix[4]arene was able to be isolated upon the deliberate recrystallization process. After basic hydrolysis of the dialkylated crude products, 25,26-dialkoxycalix[4]arenes were chromatographic separated.

1. Introduction

In the literature reported, the calixarene's ether derivatives were prepared either in a one-step process (the tetra-alkyl ethers,[1] the 1,3-dialkyl ethers,[2] and the monoalkyl ethers[3]) or in multi-step procedure (the monoalkyl ethers[4] and the trialkyl ethers[5]). However, the attempt to convert the calix[4]arene's monoalkyl ethers into their 1,2-dialkyl ether derivatives by direct etherification process was shown to be almost impossible. Therefore, a multi-step procedure with an ester protecting group was required for the preparation of calix[4]arene's 1,2-dialkyl ethers.

In our previous report,[6] we had shown that the acetate protecting group was migrated predominant in the etherification reaction when the less active alkyl halides were used. The resulting low productive yield suggested that the proposed 2,3-diacetate synthetic route was not suitable for the preparation of several 1,2-dialkoxycalix[4]arenes. Therefore, a more stable benzoate moiety, which might not migrate as fast as acetate, was selected as the protecting group. In the first section of this paper, we will report a simple synthetic procedure to convert the monoalkoxycalix[4]-arenes into their 3-benzoate derivatives.

It is easy to recognize that both of the available 'lower rim' positions were proximal to the existent alkoxy group in the structure of 1-alkoxy-3-benzoyloxycalix[4]arene. It is also anticipated that the presence of the large steric hindrance benzoate moieties in the 1-alkoxy-3-benzoyloxy's structures might restrict the formation of the fourth 'lower rim' ether linkage and yield only the 1,2-dialkoxy-3-benzoyloxy products. Therefore, the easy accessible 1-alkoxy-3-benzoyloxycalix[4]arenes turned out to be the potential candidates for the preparation of 1,2-dialkoxycalix[4]arenes.

It was then proposed that, as shown in Fig. 1, the 1,2-dialkoxycalix[4]arenes could be prepared by monoetherification of 1-alkoxy-3-benzoyloxycalix[4]arenes following with cleavage of the benzoate-protecting group in basic hydrolysis reaction. This synthetic procedure will be described in the second section of this paper. We will also report a benzoyl-migration phenomena in 1-alkoxy-3-benzoyloxycalix[4]arene systems.

2. Results and discussion

2.1. Benzoylation of calix[4]arene monoalkyl ethers

As reported in the literature[4a], the tribenzoated calix[4]arene monoallyl ether was prepared as a reaction intermediate during the synthesis of calix[4]arene monoallyl ether. It was therefore believed that the calix[4]arene monoalkyl ethers should be able to react with benzoyl chloride to give the corresponding tribenzoated products. However, when calix[4]arene monoalkyl ethers **1**–**5** were treated with benzoyl chloride in a standard acylation conditions, the 3-benzoated products **6**–**10** and/or dibenzoated products **11**–**15** were the only isolated products, as shown in Scheme 1. It was noticed that the tribenzoated products were not detected even with a further increasing of benzoylation period and/or the amount of benzoyl chloride. We believed that, as in previous observed systems,[5–7] the steric hindrance of the benzoate moieties inhibited the introduction of the fourth substituent onto the tri-substituted calix[4]arenes and failed to yield the 1-alkoxy-2,3,4-tribenzoate products.

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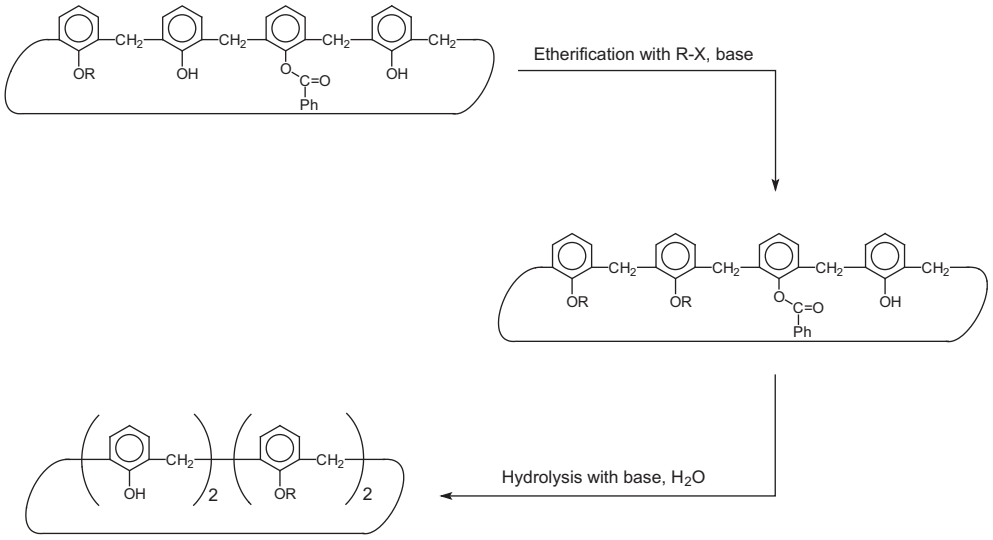
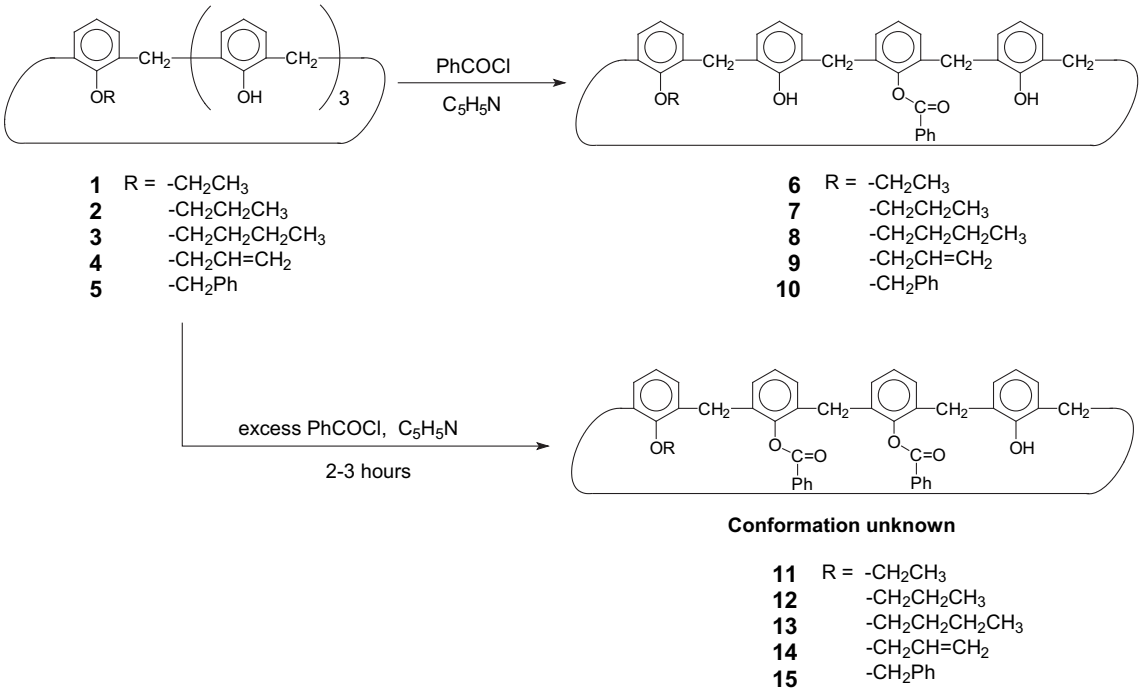


Fig. 1. A proposed synthetic route for the 1,2-dialkoxycalix[4]arenes.



1 R = $-CH_2CH_3$
2 $-CH_2CH_2CH_3$
3 $-CH_2CH_2CH_2CH_3$
4 $-CH_2CH{=}CH_2$
5 $-CH_2Ph$

6 R = $-CH_2CH_3$
7 $-CH_2CH_2CH_3$
8 $-CH_2CH_2CH_2CH_3$
9 $-CH_2CH{=}CH_2$
10 $-CH_2Ph$

11 R = $-CH_2CH_3$
12 $-CH_2CH_2CH_3$
13 $-CH_2CH_2CH_2CH_3$
14 $-CH_2CH{=}CH_2$
15 $-CH_2Ph$

Scheme 1. Synthetic scheme for benzoylation of 1-alkoxycalix[4]arenes **1**–**5**.

The 3-benzoates **6**–**10** were easy to prepare by treating monoalkyl ethers **1**–**5** with benzoyl chloride in pyridine for 30 min. A simple recrystallization afforded the monobenzoated products in over 50% yield. Base on pervious 3-acetate cases,[6] it was not too complex to assign the structure of those monobenzoate products as 1-alkoxy-3-benzoates **6**–**10** with an aid from high field NMR and 2D NMR spectrum.

Dibenzoylation of monoalkyl ethers **1**–**5** was achieved by treating with large excess of benzoyl chloride for 2 h. From the previous characterized 3-benzoate products **6**–**10**, it was known that the second benzoate moiety had to link to the 2-position and yielded 1-alkoxy-2,3-dibenzoate products **11**–**15**. Regardless of the structural conformation, the 1-alkoxy-2,3-dibenzoates **11**–**15** possessed no symmetry element, and therefore, very complex ^{1}H NMR spectral patterns were observed. Although it was impossible to assign all the ^{1}H NMR spectral signals, but the increasing of 10 aromatic hydrogens verified the dibenzoate structures. The ^{13}C-chemical shift of the calix[4]arene's methylene carbon seemed to imply that the 1-alkoxy-2,3-dibenzoates **11**–**15** hold the 'up-down-up' conformational arrangement,[8] but all the other available spectral data did not provide solid evidence to establish the exact conformational structure of the products **11**–**15**.

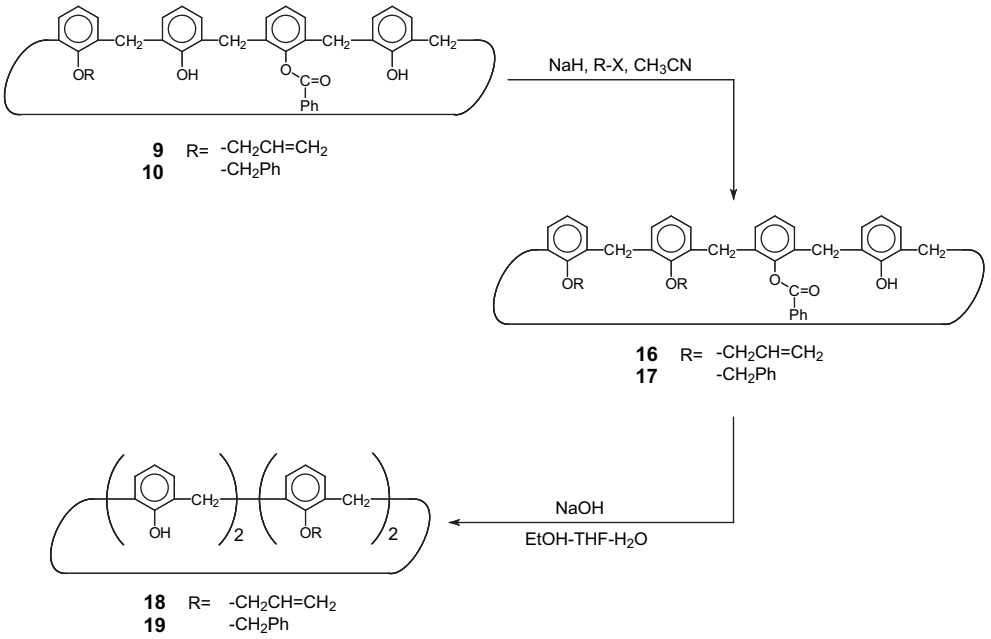
It should be also noted that compounds **11**–**15** seemed to transform slowly into another isomeric forms during the extended reaction period. A further study was required to determine whether the transformed products were either the structural isomer or the conformational isomer of the 1-alkoxy-2,3-dibenzoates **11**–**15**. It is believed that the extended study of the subject will not only reveal the essential of the transformation, but also be able to determine the conformational structure of all the possible 1-alkoxy-2,3-dibenzoate isomers.

2.2. Preparation of 1,2-dialkoxycalix[4]arenes with active alkyl halides

It was reported[6] previously 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 1-dialkoxy-2,3-diacetoxycalix[4]arenes and yielded the expected 1,2-dialkoxy-3,4-diacetoxycalix[4]arenes. Therefore, the same reaction conditions were applied to the 1-alkoxy-3-benzoyloxycalix[4]arene systems. In the two active alkyl halide cases, the benzyl bromide and allyl bromide, the resulting products contained only one major component, and a simple recrystallization was able to isolate the expected 1,2-dialkoxy-3-benzoyloxycalix[4]-arenes **16** and **17**, respectively (Scheme 2).

The integral ratio and the splitting pattern of the methylene hydrogen provided the needed information to confirm the structure of product **17** as 1,2-dibenzyloxy-3-benzoyloxycalix[4]arene. The other etherification product **16** was assigned as 1,2-diallyloxy-3-benzoyloxycalix[4]arene based on the similarity of the spectral feature. The FAB-MS provided further evidences for the existing of the second alkoxy moiety.

After the second alkoxy group was introduced, the 1,2-dialkoxy compounds **16** and **17** were subjected to basic hydrolysis to remove the 'lower rim' benzoate-protecting group as proposed in Fig. 1. One of the hydrolysis product, compound **19**, was identical to the previously synthesis compound, the *syn*-1,2-dibenzyloxycalix[4]-arene.[6] The other hydrolysis product **18** was assigned as *syn*-1,2-



Scheme 2. Synthetic scheme for the 1,2-dialkoxycalix[4]arenes **18** and **19**.

Both products **16** and **17** contained no symmetrical element, and hence, it was uncertain whether the structure of the products could be properly assigned from the ^{1}H NMR spectrum. When the spectrum of product **17** was taken, it was surprised to find that the splitting pattern of the calix[4]arene's methylene and benzyloxy's methylene moieties was well-resolved. A total of 12 doublets were displayed for 12 different methylene hydrogens (eight calix[4]arene's methylene hydrogens and four benzyloxy's methylene hydrogens), as shown in Fig. 2.

diallyloxycalix[4]arene based on the similarity of the spectral feature with the earlier reported 200 MHz NMR spectrum.[9]

2.3. Preparation of 1,2-dialkoxycalix[4]arenes with less active alkyl halides

It was shown previously[6] that two isomeric dialkoxy products were produced in various amounts on the etherification of 1-alkoxy-

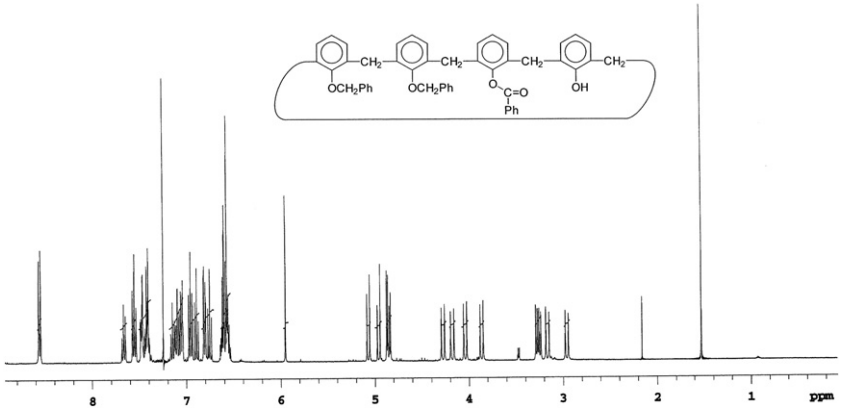
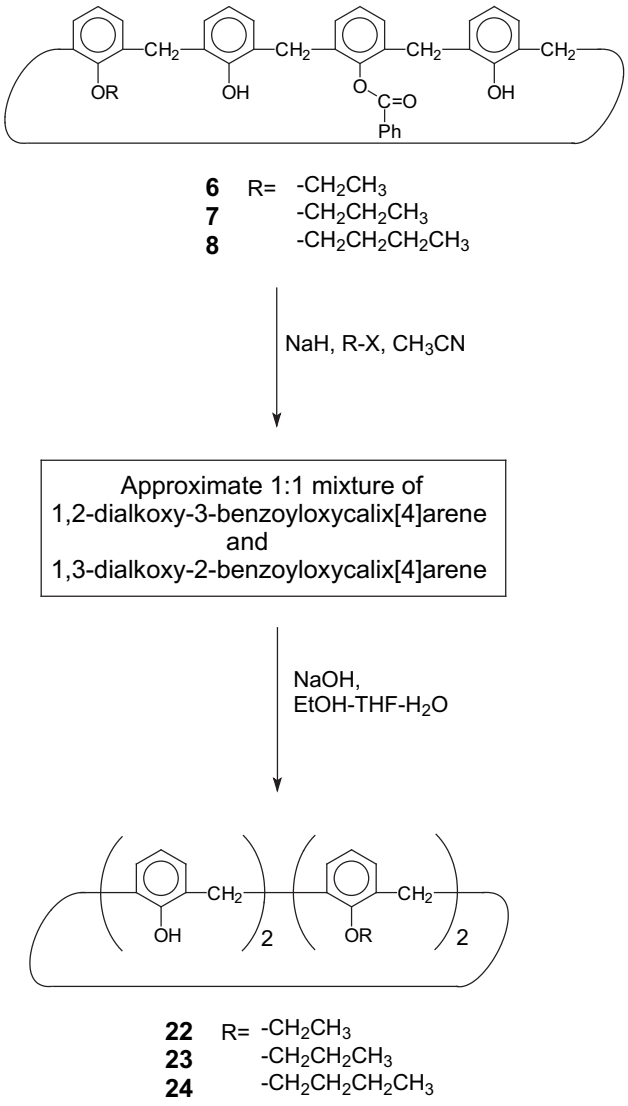


Fig. 2. The ^{1}H NMR spectrum of 1,2-dibenzyloxy-3-benzoyloxycalix[4]arene **17**.

2,3-diacetoxycalix[4]arenes. Similar results were also observed in the less active alkyl halides, and mixtures of products were detected when compounds **6**–**8** were refluxed with 1.5 M equiv of NaH and excess alkyl halides in acetonitrile (Scheme 3). The TLC analysis indicated that the crude product mixtures contained, along with other minor visible components, a small amount of starting material and two new major products. By careful examination of the integral ratio of the alkoxy protons, it was possible to propose that both major compounds were the dialkoxy derivatives.

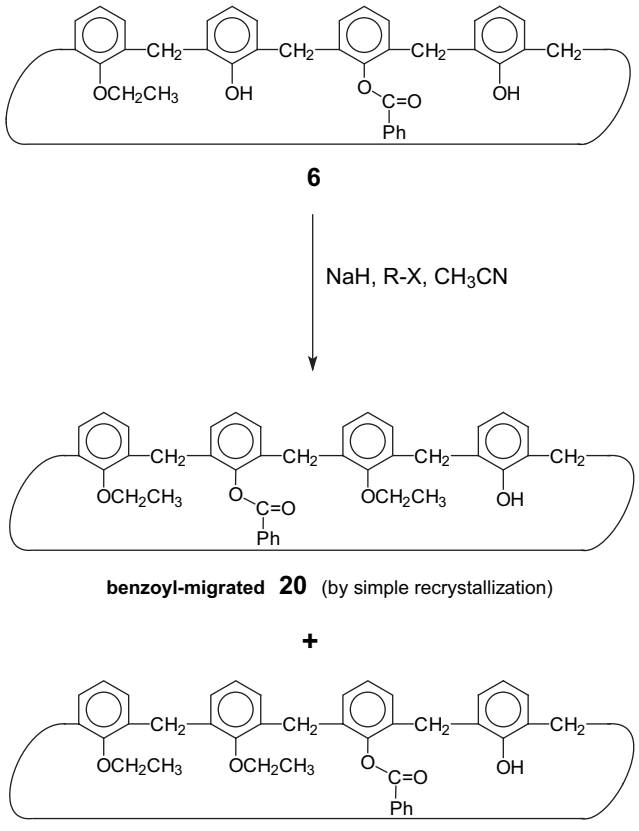


Scheme 3. Synthetic scheme for the 1,2-dialkoxycalix[4]arene **22**–**24**.

Unlike the diacetate cases, the amount of each component could not be evaluated from the acetate's signals. Fortunately, the ^{1}H NMR spectra of these reaction crude products displayed three well-defined triplets for the alkoxy's methyl groups, and the integral ratio of these triplets could be used to replace the non-existent acetate's signal in the estimation procedure. The integral ratio of these triplets displayed in approximate 2:1:1 in all cases, it was soon realized that the two equal intensity triplets arose from the two asymmetrical alkoxy moieties from the 1,2-dialkoxy derivative and the other triplet had to arise from a symmetrical 1,3-dialkoxy product. The 2:1:1 integral ratio also suggested that the two new products were produced in an approximately equal amount. It was then proposed, as in previous diacetate cases, that the benzoate moieties were partially migrated during the etherificaton reaction and produced both the benzoate-migrated 1,3-dialkoxy products and non-migrated 1,2-dialkoxy products.

Although the 50% productive yield of the 1,2-dialkoxycalix[4]-arenes' precursor was higher than quarterly amount in the diacetate cases,[6] but it was easily recognizable that a less-prone-to-migrate protecting group was essential for the preparation of 1,2-dialkoxycalix[4]arenes. Further investigations on the less-prone-to-migrate protecting groups, e.g., silyl ethers,[10] electron-withdrawing benzoates, and electron-releasing benzoates, are under study in our laboratory.

In the most accessible 1,2-diethoxy cases, a simple but very slow recrystallization process was able to crystallize one of the higher symmetrical components, compound **20**, from the product mixture in a small amount (Scheme 4). It should be noted that the crystallized product **20** would be contaminated by the other isomer, if the recrystallization process proceeded too fast and/or too long. The NMR spectral pattern suggested that the molecular structure of product **20** contained a planar symmetry element. It was known clearly that the structure of 1,2-diethoxy-3-benzoyloxycalix[4]arene contained no symmetry elements, therefore, the structure of compound **20** had to be benzoyl-migrated 1,3-diethoxy-2-benzoyloxycalix[4]arene. The integral ratio between ethoxy's protons and aromatic protons supported the structural assignment of product **20**. Further efforts on the purification by recrystallization, unfortunately, failed to isolate any trace of the other isomeric components in pure form.



Scheme 4. Products isolated from ethylation of 1-ethoxy-3-benzoyloxycalix[4]arene **6**.

Although, the structure of product **20** was assigned as 1,3-diethoxy-2-benzoyloxycalix[4]arene, but the spectrum pattern of product **20** was different from the known compounds which were reported earlier by treating 1,3-dialkoxycalix[4]arene with benzoyl chloride in pyridine at ice bath temperature.[5] A noticeable spectral difference between compound **20** and monobenzoated 1,3-dialkoxycalix[4]arene indicated that the two sets of compounds were

isomeric conformers. The exact conformation of product **20** will be discussed in the next section.

After compound **20** was partially crystallized and collected, the mother solution was subjected to column chromatography to retrieve product **21**. The non-migrated 1,2-diethoxy product **21** contained no symmetrical element as compounds **16** and **17**, therefore, a similar ^{1}H NMR spectral feature as previous spectrum (Fig. 2) was able to assign the structure of product **21** as 1,2-diethoxy-3-benzoyloxy-calix[4]arene.

A standard basic hydrolysis was also performed on the similar remained crude materials. When the hydrolysis products were recrystallized from $CHCl_3$ and CH_3OH, rod-like crystals and a small amount of powder solids were collected. The rod-like crystals, which were not adhered on the filter paper, were easy to separate from the powder solid. The crude crystals were then recrystallized again, and the resulting compound **22** was subjected to the ^{1}H NMR spectral analysis.

Similar to the ^{1}H NMR spectrum of product **19**, hydrolysis product **22** also displayed three pairs of doublets with the integral ratio of 1:1:2 for the calix[4]arene's methylene hydrogen. The ethoxy's methylene hydrogens, which also experienced a different magnetic environment, emerged into two sets of multiplets. The existence of two ethoxy moieties was further supported by the MS measurement, therefore, the structure of compound **22** was assigned confidently as 1,2-diethoxycalix[4]arene.

At the meantime, it was found that the benzoyl-migrated 1,3-dialkoxy products were not always crystallized as expected and the quantity of the desired non-migrated 1,2-dialkoxy products was also varied in the mother solution. Therefore, a decision was made to carry out the basic hydrolysis reaction directly without any prior purification on the etherification crude products (Scheme 3). In all three less active alkyl halide cases, all three hydrolyzed crude product mixtures contained different sets of trio-products. The highest R_f components, which existed in a small amount, were shown to be the calix[4]arene monoalkyl ether in all three cases. The other two components, which existed in an approximately equal amount as their benzoated predecessor, were distinguishable on the TLC analysis. Therefore, the hydrolysis crude products were subjected to the chromatographic separation to isolate the 1,2-dialkoxycalix[4]-arenes **22**–**24**. In the chromatographic separation, the 1,2-dialkoxy products **22**–**24** were eluented last following the monoalkoxy and 1,3-dialkoxy products, and the overall isolating yields were in the range of 10%. Whereas, the isolating yields were somewhat higher for their corresponding benzoyl-migrated 1,3-dialkoxy products.

Similar to the ^{1}H NMR spectrum of the earlier isolated hydrolysis product **22**, three pairs of doublets with the integral ratio of 1:1:2 for the calix[4]arene's methylene hydrogen, a distinct spectral feature for 1,2-disubstituted calix[4]arenes, was observed on the spectra of products **23**–**24**. The alkoxy's methylene hydrogens of products **23**–**24**, as in the 1,2-diethoxy case, also emerged into two sets of multiplets. The MS provided further characterization data to support the structural assignment for compounds **23**–**24**.

2.4. Mechanism for the etherification of 1-alkoxy-3-benzoyloxycalix[4]arenes in basic conditions

Based on the results from various etherification conditions, we speculated that a stronger base NaH enhanced the nucleophilicity of the calix[4]arene anion, and achieved the preparation of the 1,2-dialkoxy products. Whereas, a weak base K_2CO_3 preferred the formation of the cyclic orthobenzoate-like anionic intermediates, and hence, yielded the benzoyl-migrated products.

In the cyclic orthobenzoate-like anionic intermediate path, the alkyl halides were probably approached from the less hindered 3-position side, as shown in Fig. 3, and produced the benzoyl-migrated products. It should be noted that the isolated benzoyl-migrated product **20** had two ethoxy groups in *syn* arrangement. The lack of any *anti*-isomer suggested that the breaking of cyclic orthobenzoate ring and the formation of ether linkage were not gone through a stepwise fashion. Therefore, the exact structure of compound **20** was able to assign as in all-*syn* conformation. The earlier prepared monobenzoated 1,3-dialkoxycalix-[4]arene,[5] which was conformational isomer of compound **20**, had to consist of 'up-down-up' arrangement.[11] This 'up-down-up' structure was agreed with our earlier proposed structure.[5]

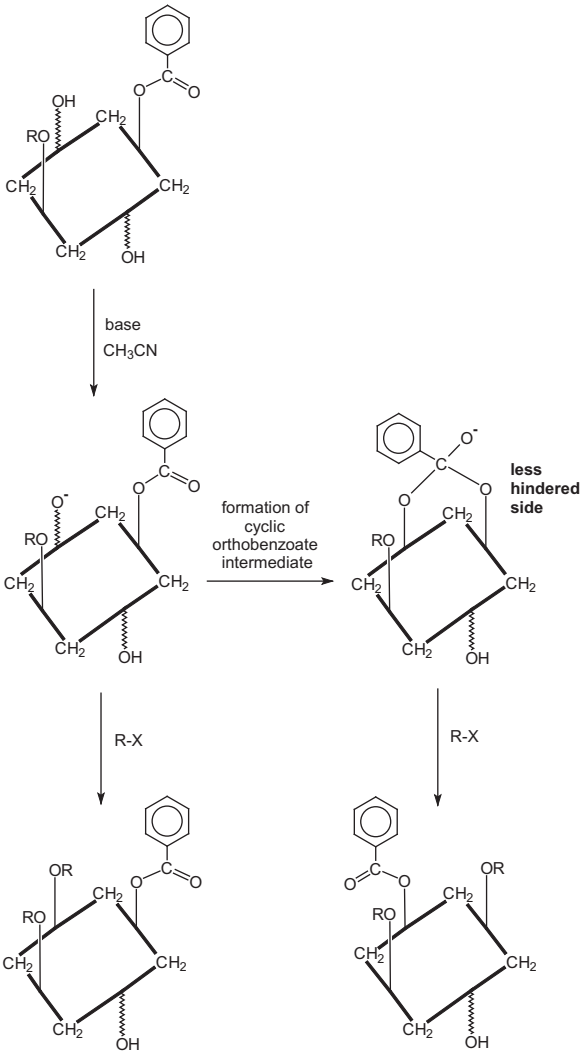


Fig. 3. Proposed mechanism for the intramolecular benzoyl-migration.

Investigation on the benzoyl-migrated behavior of the other 1-alkoxy-3-benzoyloxycalix[4]arenes is under study in this laboratory. It should be point out that such study may shed light on the exact structure of the 1-alkoxy-2,3-dibenzoyloxycalix[4]arenes, a conformational problem, which is unsolved in the first section of this paper. Furthermore, in order to verify the proposed acyl-migrated mechanism, the evaluation of the benzoyl-migration rates on electron-releasing *p*-methoxybenzoate group and electron-withdrawing *p*-nitrobenzoate group are also under examination.

3. Experimental[12]

3.1. General procedure for the monobenzoylation of calix[4]arene monoalkyl ethers

A slurry of 0.50 g of calix[4]arene monoalkyl ethers **1**–**5** was dissolved in 15 mL of pyridine, and 0.5 mL of benzoyl chloride was

then added dropwisely at ice bath temperature. The reaction mixture was stirred for 30 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 1N 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 monobenzoylated products **6**–**10**.

*3.1.1. 25-Benzoyloxy-27-ethoxy-26,28-dihydroxycalix[4]arene (**6**).* An amount of 0.42 g (68%) of colorless fine crystals was collected from 0.50 g (1.11 mmol) of calix[4]arene monoethyl ether **1**: mp 302–304 °C; ^{1}H NMR ($CDCl_3$) δ 8.48–8.50 (dd, 2H, Ar′*H*), 7.63–7.66 (t, *J*=7.6 Hz, 1H, Ar′*H*), 7.50–7.54 (m, 2H, Ar′*H*), 7.17 (s, 1H, ArO*H*), 6.69–7.06 (m, 12H, Ar*H*), 4.19–4.23 (q, *J*=7.0 Hz, 2H, OCH_2CH_3), 4.10–4.14 (d, *J*=13.2 Hz, 2H, $ArCH_2Ar$), 4.08–4.11 (d, *J*=13.6 Hz, 2H, $ArCH_2Ar$), 3.54–3.57 (d, *J*=13.6 Hz, 2H, $ArCH_2Ar$), 3.39–3.42 (d, *J*=13.2 Hz, 2H, $ArCH_2Ar$), 1.82–1.85 (t, *J*=7.0 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 165.6, 152.9, 150.7, 145.4, 133.5, 132.9, 132.5, 130.7, 129.8, 129.6, 129.0, 128.9, 128.6, 128.4, 126.5, 126.4, 126.0, 119.5, 72.7, 32.1, 31.9, 15.3; FAB-MS *m*/*e*: 556 (M^+); HRMS (FAB) *m*/*e*: calcd for $C_{37}H_{32}O_5$: 556.2250; found: 556.2242.

*3.1.2. 25-Benzoyloxy-27-propoxy-26,28-dihydroxycalix[4]arene (**7**).* An amount of 0.48 g (78%) of colorless fine crystals was collected from 0.50 g (1.07 mmol) of calix[4]arene monopropyl ether **2**: mp 256–258 °C; ^{1}H NMR ($CDCl_3$) δ 8.50–8.53 (dd, 2H, Ar′*H*), 7.64–7.69 (m, 1H, Ar′*H*), 7.52–7.56 (m, 2H, Ar′*H*), 6.67–7.16 (m, 14H, Ar*H*, and ArO*H*), 4.07–4.14 (m, 6H, $OCH_2CH_2CH_3$, and $ArCH_2Ar$), 3.50–3.55 (d, *J*=14 Hz, 2H, $ArCH_2Ar$), 3.41–3.37 (d, *J*=13.2 Hz, 2H, $ArCH_2Ar$), 2.18–2.24 (m, $OCH_2CH_2CH_3$), 1.33–1.38 (t, *J*=7.4 Hz, $OCH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$) δ 165.6, 152.9, 150.8, 145.4, 133.5, 132.6, 132.3, 132.2, 130.6, 130.5, 129.7, 129.6, 129.2, 129.1, 128.9, 128.6, 128.4, 128.1, 126.6, 126.2, 126.0, 119.4, 79.0, 32.4, 31.8, 23.4, 11.0; FAB-MS *m*/*e*: 571 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{38}H_{34}O_5$+H^+: 571.2484; found: 571.2493.

*3.1.3. 25-Benzoyloxy-27-butoxy-26,28-dihydroxycalix[4]arene (**8**).* An amount of 0.32 g (52.5%) of colorless fine crystals was collected from 0.50 g (1.04 mmol) of calix[4]arene monobutyl ether **3**: mp 243–245 °C; ^{1}H NMR ($CDCl_3$) δ 8.50–8.53 (dd, 2H, Ar′*H*), 7.62–7.78 (m, 1H, Ar′*H*), 7.52–7.62 (m, 2H, Ar′*H*), 6.67–7.16 (m, 14H, Ar*H* and, ArO*H*), 4.10–4.14 (m, 6H, $OCH_2CH_2CH_2CH_3$, and $ArCH_2Ar$), 3.51–3.54 (d, *J*=13.6 Hz, 2H, $ArCH_2Ar$), 3.36–3.40 (d, *J*=13.2 Hz, 2H, $ArCH_2Ar$), 2.15–2.20 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.70–1.76 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.10–1.15 (t, *J*=7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$) δ 165.6, 152.9, 153.0, 151.0, 145.4, 133.4, 132.7, 132.4, 130.7, 130.5, 129.8, 129.0, 128.9, 128.6, 128.5, 128.4, 126.6, 126.2, 126.0, 119.5, 32.0, 31.8, 19.2, 14.1; FAB-MS *m*/*e*: 585 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{39}H_{36}O_5$+H^+: 585.2641; found: 585.2639.

*3.1.4. 25-Benzoyloxy-27-allyloxy-26,28-dihydroxycalix[4]arene (**9**).* An amount of 0.37 g (60%) of colorless fine crystals was collected from 0.50 g (1.08 mmol) of calix[4]arene monoallyl ether **4**: mp 212–214 °C; ^{1}H NMR ($_{CDCl3}$) δ 8.58–8.46 (dd, 2H, Ar′*H*), 7.51–7.79 (m, 3H, Ar′*H*), 6.67–7.21 (m, 14H, Ar*H*, and ArO*H*), 6.29–6.56 (m, 1H, $OCH_2CH{=}CH_2$), 5.71–5.88 (dd, 1H, $OCH_2CH{=}CH_2$), 5.53–5.65 (dd, 1H, $OCH_2CH{=}CH_2$), 4.58–4.76 (m, 2H, $OCH_2CH{=}CH_2$), 4.14–4.18 (d, *J*=14.0 Hz, 2H, $ArCH_2Ar$), 4.12–4.16 (d, *J*=13.2 Hz, 2H, $ArCH_2Ar$), 3.52–3.56 (d, *J*=14.0 Hz, 2H, $ArCH_2Ar$), 3.40–3.44 (d, *J*=13.2 Hz, 2H, $ArCH_2Ar$); ^{13}C NMR ($_{CDCl3}$) δ 165.5, 153.0, 151.0, 145.4, 133.5, 132.8, 132.4, 132.3, 132.1, 130.7, 130.6, 129.6, 129.2, 129.1, 128.9, 128.6, 128.5, 128.1, 126.8, 126.2, 126.1, 119.5, 119.3, 32.5, 32.0, 31.9; FAB-MS *m*/*e*: 568 (M^+); HRMS (FAB) *m*/*e*: calcd for $C_{38}H_{32}O_5$: 568.2250; found: 568.2244.

*3.1.5. 25-Benzoyloxy-27-benzyloxy-26,28-dihydroxycalix[4]arene (**10**).* An amount of 0.39 g (64.5%) of colorless fine crystals was collected from 0.50 g (0.97 mmol) of calix[4]arene monobenzyl ether **5**: mp 238–240 °C; ^{1}H NMR ($CDCl_3$) δ 8.36–8.39 (dd, 2H, Ar′*H*), 7.60–7.70 (m, 3H, Ar′*H*, and Ar″*H*), 7.38–7.50 (m, 5H, Ar′*H*, and Ar″*H*), 6.67–7.08 (m, 12H, Ar*H*, and ArO*H*), 5.12 (s, 2H, OCH_2Ar''), 4.20–4.24 (d, *J*=13.6 Hz, 2H, $ArCH_2Ar$), 4.04–4.01 (d, *J*=13.2 Hz, 2H, $ArCH_2Ar$), 3.45–3.49 (d, *J*=13.6 Hz, 2H, $ArCH_2Ar$), 3.36–3.40 (d, *J*=13.2 Hz, 2H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$) δ 165.4, 153.0, 151.5, 145.2, 136.0, 133.4, 132.7, 132.3, 130.6, 129.5, 129.4, 129.1, 128.9, 128.8, 128.6, 128.5, 127.9, 127.2, 126.2, 126.0, 119.5, 79.0, 31.8; FAB-MS *m*/*e*: 619 (M^++1); HRMS(FAB) *m*/*e*: calcd for $C_{42}H_{34}O_5$+H^+: 619.2484; found: 619.2488.

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

A slurry of 0.50 g of calix[4]arene monoalkyl ethers **1**–**5** was dissolved in 20 mL of pyridine, and 4.0 mL of benzoyl chloride was then added dropwisely at ice bath temperature. The reaction mixture was 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 1N 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 dibenzoylated products **11**–**15**.

*3.2.1. 25,26-Dibenzoyloxy-27-ethoxy-28-hydroxycalix[4]arene (**11**).* An amount of 0.25 g (34%) of colorless fine crystals was collected from 0.50 g (1.11 mmol) of calix[4]arene monoethyl ether **1**: 248–250 °C; ^{1}H NMR ($CDCl_3$) δ 8.00–8.02 (m, 3H, Ar′*H*, and ArO*H*), 7.56–7.60 (t, *J*=7.2 Hz, 1H, Ar′*H*), 7.36–7.40 (t, *J*=7.8 Hz, 2H, Ar′*H*), 6.16–7.25 (m, 17H, Ar*H*, and Ar′*H*), 4.17–4.21 (m, 1H, OCH_2CH_3), 4.07–4.10 (d, *J*=12.8 Hz, 1H, $ArCH_2Ar$), 3.81–3.99 (m, 5H, $ArCH_2Ar$, and OCH_2CH_3), 3.73–3.77 (d, *J*=16.4 Hz, 1H, $ArCH_2Ar$), 3.46–3.50 (d, *J*=14.0 Hz, 1H, $ArCH_2Ar$), 3.25–3.28 (d, *J*=12.8 Hz, 1H, $ArCH_2Ar$), 1.47–1.51 (t, *J*=7.2 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 164.9, 163.3, 153.1, 148.1, 146.6, 133.2, 133.1, 133.0, 132.8, 132.5, 132.3, 131.8, 130.7, 130.1, 130.0, 129.7, 129.6, 129.5, 129.3, 129.3, 128.6, 128.5, 128.2, 128.1, 128.1, 127.9, 127.2, 126.2, 125.3, 125.0, 119.2, 69.4, 37.8, 31.7, 31.2, 15.1; FAB-MS *m*/*e*: 661 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{44}H_{36}O_6$+H^+: 661.2590; found: 661.2599.

*3.2.2. 25,26-Dibenzoyloxy-27-propoxy-28-hydroxycalix[4]arene (**12**).* An amount of 0.33 g (46%) of colorless fine crystals was collected from 0.50 g (1.07 mmol) of calix[4]arene monopropyl ether **2**: mp 254–258 °C; ^{1}H NMR ($CDCl_3$) δ 8.01–8.02 (d, *J*=7.2 Hz, 2H, Ar′*H*), 7.90 (s, 1H, ArO*H*), 7.58–7.62 (t, *J*=7.4 Hz, 1H, Ar′*H*), 7.38–7.41 (t, *J*=7.6 Hz, 2H, Ar′*H*), 6.18–7.25 (m, 17H, Ar*H*, and Ar′*H*), 3.72–4.14 (m, 8H, $ArCH_2Ar$, and $OCH_2CH_2CH_3$), 3.48–3.52 (d, *J*=14.0 Hz, 1H, $ArCH_2Ar$), 3.28–3.31 (d, *J*=12.8 Hz, 1H, $ArCH_2Ar$), 1.95–2.02 (m, 1H, $OCH_2CH_2CH_3$), 1.87–1.94 (m, 1H, $OCH_2CH_2CH_3$), 1.14–1.18 (t, *J*=7.4 Hz, 3H, $OCH_2CH_2CH_3$); ^{13}C NMR ($_{CDCl3}$) δ 164.9, 163.4, 153.1, 152.4, 148.1, 133.2, 133.1, 132.6, 132.5, 132.4, 131.8, 130.2, 129.8, 129.5, 129.4, 129.3, 128.8, 128.6, 128.3, 128.2, 128.1, 127.9, 127.2, 126.2, 125.3, 125.0, 119.2, 37.8, 31.7, 31.1, 23.0, 10.7; FAB-MS *m*/*e*: 674 (M^+); HRMS (FAB) *m*/*e*: calcd for $C_{45}H_{38}O_6$: 674.2668; found: 674.2665.

*3.2.3. 25,26-Dibenzoyloxy-27-butoxy-28-hydroxycalix[4]arene (**13**).* An amount of 0.35 g (49%) of colorless fine crystals was collected from 0.50 g (1.04 mmol) of calix[4]arene monobutyl ether **3**: mp 256–258 °C; ^{1}H NMR ($CDCl_3$) δ 8.02–8.04 (d, *J*=7.2 Hz, 2H, Ar′*H*), 7.90

(s, 1H, ArO*H*), 7.60–7.64 (t, *J*=7.6 Hz, 1H, Ar′*H*), 7.40–7.45 (t, *J*=7.8 Hz, 2H, Ar′*H*), 6.21–7.28 (m, 17H, Ar*H*, and Ar′*H*), 3.74–4.14 (m, 8H, ArCH_2Ar, and OCH_2CH_2CH_2CH_3), 3.47–3.51 (d, *J*=13.6 Hz, 1H, ArCH_2Ar), 3.27–3.30 (d, *J*=12.8 Hz, 1H, ArCH_2Ar), 1.92–2.02 (m, 1H, OCH_2CH_2CH_2CH_3), 1.75–1.90 (m, 1H, OCH_2CH_2CH_2CH_3), 1.50–1.57 (m, 2H, OCH_2CH_2CH_2CH_3), 1.05–1.09 (t, *J*=7.4 Hz, 3H, OCH_2CH_2CH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 164.9, 163.4, 153.1, 152.5, 148.1, 146.7, 133.2, 133.2, 133.1, 132.6, 132.5, 132.4, 131.8, 130.7, 130.2, 129.8, 129.6, 129.4, 129.3, 128.8, 128.6, 128.3, 128.2, 128.1, 128.0, 127.2, 126.2, 125.3, 119.2, 74.0, 37.9, 31.7, 31.6, 31.1, 19.0, 14.1; FAB-MS *m*/*e*: 689 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{46}H_{40}O_6$+H^+: 689.2903; found: 689.2902.

*3.2.4. 25,26-Dibenzoyloxy-27-allyloxy-28-hydroxycalix[4]arene (**14**).* An amount of 0.22 g (30%) of colorless fine crystals was collected from 0.50 g (1.08 mmol) of calix[4]arene monoallyl ether **4**: mp 238–240 °C; ^{1}H NMR ($CDCl_3$) δ 8.00–8.02 (d, *J*=8.4 Hz, 2H, Ar′*H*), 7.71 (s, 1H, ArO*H*), 7.59–7.63 (t, *J*=7.4 Hz, 1H, Ar′*H*), 7.40–7.44 (t, *J*=7.6 Hz, 2H, Ar′*H*), 6.21–7.25 (m, 17H, ArH, and Ar'H), 6.05–6.16 (m, 1H, OCH_2C*H*=CH_2), 5.40–5.48 (m, 2H, OCH_2CH=C*H*$_2$), 4.67–4.70 (dd, 1H, OC*H*$_2$CH=CH_2), 4.31–4.36 (dd, 1H, OC*H*$_2$CH=CH_2), 4.08–4.11 (d, *J*=13.2 Hz, 1H, ArC*H*$_2$Ar), 4.02–4.06 (d, *J*=16.4 Hz, 1H, ArC*H*$_2$Ar), 4.00–4.04 (d, *J*=14.0 Hz, 1H, ArC*H*$_2$Ar), 3.90–3.93 (d, *J*=15.6 Hz, 1H, ArC*H*$_2$Ar), 3.84–3.88 (d, *J*=16.4 Hz, 1H, ArC*H*$_2$Ar), 3.75–3.79 (d, *J*=15.6 Hz, 1H, ArC*H*$_2$Ar), 3.48–3.51 (d, *J*=14.0 Hz, 1H, ArC*H*$_2$Ar), 3.27–3.30 (d, *J*=13.2 Hz, 1H, ArC*H*$_2$Ar); ^{13}C NMR ($CDCl_3$) δ 164.9, 163.4, 153.0, 152.3, 148.1, 146.7, 133.2, 133.1, 132.7, 132.6, 132.5, 132.5, 132.4, 131.8, 130.8, 130.2, 130.2, 129.9, 129.5, 129.5, 129.3, 129.0, 128.6, 128.4, 128.2, 128.1, 128.0, 127.3, 126.2, 125.4, 125.3, 125.2, 119.2, 119.2, 75.0, 37.9, 37.8, 31.8, 31.2.

*3.2.5. 25,26-Dibenzoyloxy-27-benzyloxy-28-hydroxycalix[4]arene (**15**).* An amount of 0.20 g (28%) of colorless fine crystals was collected from 0.50 g (0.97 mmol) of calix[4]arene monobenzyl ether **5**: mp 264–268 °C; ^{1}H NMR ($CDCl_3$) δ 7.97–8.01 (dd, 2H, Ar′*H*), 7.59–7.60 (t, 1H, Ar′*H*), 6.22–7.38 (m, 25H, Ar*H*, Ar′*H*, Ar″*H*, and ArO*H*), 5.18–5.21 (d, *J*=11.6 Hz, 1H, OC*H*$_2$Ar″), 4.86–4.89 (d, *J*=11.6 Hz, 1H, OC*H*$_2$Ar″), 4.06–4.10 (d, *J*=12.8 Hz, 1H, ArC*H*$_2$Ar), 4.01–4.05 (d, *J*=16.4 Hz, 1H, ArC*H*$_2$Ar),3.79–3.92 (3d, 3H, ArC*H*$_2$Ar), 3.73–3.77 (d, *J*=16.4 Hz, 1H, ArC*H*$_2$Ar), 3.25–3.31 (2d, 2H, ArC*H*$_2$Ar); ^{13}C NMR ($CDCl_3$) δ 164.9, 163.5, 153.0, 152.7, 148.1, 146.7, 135.8, 133.2, 133.1, 133.0, 132.8, 132.7, 132.5, 132.5, 131.8, 130.7, 130.3, 130.2, 130.2, 129.6, 129.5, 129.3, 129.3, 129.2, 128.8, 128.6, 128.4, 128.1, 127.3, 126.3, 125.3, 125.2, 125.1, 119.2, 38.0, 37.8, 31.7, 31.1; FAB-MS *m*/*e*: 723 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{49}H_{38}O_6$+H^+: 723.2747; found: 723.2740.

3.3. General procedure for the alkylation of 1-alkoxy-3-benzoyloxycalix[4]arenes 9–10 in the present of NaH

A slurry of approximate 0.50 g of 1-alkoxy-3-benzoyloxycalix[4]-arenes **9**–**10**, 0.05 g of 60% NaH, and 4 mol equiv of alkyl halides was refluxed in 50 mL of CH_3CN for 3 h. The solvent was removed by rotory evaporatory and the organic materials were taken up by 30 mL of $CHCl_3$. The organic solution was washed in sequence with 20 mL of 1N HCl and 100 mL of distillated water. The organic solvent was then concentrated and recrystallized from $CHCl_3$ and CH_3OH to afford the corresponding products **16**–**17**.

*3.3.1. 25,26-Diallyloxy-27-benzoyloxy-28-dihydroxycalix[4]arene (**16**).* An amount of 0.21 g (39%) of colorless crystals was afforded form 0.50 g (0.88 mmol) of monoallyloxy compound **9**: mp 166–172 °C; ^{1}H NMR ($CDCl_3$) δ 8.48–8.50 (d, 2H, Ar′*H*),7.62–7.65 (t, 1H, Ar′*H*), 7.52–7.55 (t, 2H, Ar′*H*), 6.55–7.15 (m, 12H, Ar*H*), 6.26–6.33 (m, 1H, OCH_2C*H*=CH_2), 6.10–6.16 (m, 1H, OCH_2C*H*=CH_2), 5.86 (s, 1H, ArO*H*), 5.53–5.57 (d, 1H, OCH_2CH=C*H*$_2$), 5.38–5.41 (d, 1H, OCH_2CH=C*H*$_2$), 4.83–4.93 (m, 2H, OCH_2CH=C*H*$_2$), 4.41–4.63 (m, 5H, OC*H*$_2$CH=CH_2, and ArC*H*$_2$Ar), 4.23–4.30 (2d, 2H, ArC*H*$_2$Ar), 4.08–4.12 (d, *J*=12.8 Hz, 1H, ArC*H*$_2$Ar), 3.44–3.47 (d, *J*=12.8 Hz, 1H, ArC*H*$_2$Ar), 3.26–3.38 (3d, 3H, ArC*H*$_2$Ar); ^{13}C NMR ($CDCl_3$) δ 166.0, 155.1, 153.3, 152.6, 146.0, 136.8, 136.3, 134.7, 134.1, 133.5, 133.3, 132.9, 132.6, 132.1, 131.1, 130.6, 130.0, 129.1, 129.0, 128.9, 128.9, 128.8, 128.5, 128.5, 128.4, 128.0, 127.8, 127.6, 125.0, 124.6, 123.5, 119.5, 118.4, 117.9, 75.2, 31.9, 31.4; FAB-MS *m*/*e*: 609 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{41}H_{36}O_5$+H^+: 609.2641; found: 609.2645.

*3.3.2. 25,26-Dibenzyloxy-27-benzoyloxy-28-dihydroxycalix[4]arene (**17**).* An amount of 0.20 g (35%) of colorless crystals was afforded form 0.50 g (0.81 mmol) of monobenzyloxy compound **10**: mp 244–246 °C; ^{1}H NMR (CDCl3) δ 8.54–8.56 (d, 2H, Ar′*H*), 7.64–7.66 (t, 1H, Ar′*H*), 7.53–7.57 (t, 2H, Ar′*H*), 6.52–7.48 (m, 22H, Ar*H*, and Ar″*H*), 5.94 (s, 1H, ArO*H*), 5.05–5.08 (d, *J*=12.8 Hz, 1H, OC*H*$_2$Ar″), 4.94–4.97 (d, *J*=12.8 Hz, 1H, OC*H*$_2$Ar″), 4.83–4.87 (2d, 2H, OC*H*$_2$Ar″), 4.25–4.29 (d, *J*=12.8 Hz, 1H, ArC*H*$_2$Ar), 4.16–4.19 (d, *J*=12.8 Hz, 1H, ArC*H*$_2$Ar), 4.02–4.05 (d, *J*=12.8 Hz, 1H, ArC*H*$_2$Ar), 3.84–3.88 (d, *J*=12.8 Hz, 1H, ArC*H*$_2$Ar), 3.23–3.28 (2d, 2H, ArC*H*$_2$Ar), 3.18–3.20 (d, *J*=12.8 Hz, 1H, ArC*H*$_2$Ar), 2.95–2.98 (d, *J*=12.8 Hz, 1H, ArC*H*$_2$Ar); ^{13}C NMR($CDCl_3$) δ 166.0, 154.2, 153.3, 152.4, 146.0, 136.8, 136.6, 136.4, 134.3, 133.4, 133.0, 132.6, 132.3, 131.5, 130.7, 130.3, 130.1, 129.2, 129.1, 128.9, 128.7, 128.7, 128.6, 128.6, 128.4, 127.9, 127.8, 127.6, 127.6, 126.4, 125.0, 124.6, 123.4, 119.6, 78.1, 31.7, 31.4, 31.3, 31.0; FAB-MS *m*/*e*: 709 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{49}H_{40}O_5$: 708.2877; found: 708.2867.

3.4. General procedure for the basic hydrolysis of 1,2-dialkoxy-3-benzoyloxycalix[4]arenes 16–17

A slurry of approximate 0.20 g of 1,2-dialkoxy-3-benzoyloxycalix[4]arenes **16**–**17** and 2.00 g of 25% NaOH was refluxed in a mixture of 10 mL of C_2H_5OH and 30 mL of THF for 24 h. The solvent was removed by rotory evaporatory and the organic materials were taking 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 hydrolysis products **18**–**19**.

*3.4.1. 25,26-Diallyloxy-27,28-dihydroxycalix[4]arene (**18**).* An amount of 0.09 g (49%) of colorless crystals was afforded form 0.22 g (0.36 mmol) of diallyloxy compound **16**: mp 155–160 °C; ^{1}H NMR ($CDCl_3$) δ 8.72 (s, 2H, ArO*H*), 6.59–7.06 (m, 12H, ArCH_2Ar), 6.34–6.43 (m, 2H, OCH_2C*H*=CH_2), 5.57–5.60 (dd, *J*=16.4, 0.8 Hz, 2H, OCH_2CH=C*H*$_2$), 5.39–5.43 (dd, *J*=11.2, 0.8 Hz, 2H, OCH_2CH=C*H*$_2$), 4.66–4.67 (m, 2H, OC*H*$_2$CH=CH_2), 4.49–4.53 (m, 3H, OC*H*$_2$CH=CH_2, and ArC*H*$_2$Ar), 4.32–4.36 (d, *J*=13.2 Hz, 3H, ArC*H*$_2$Ar), 3.34–3.43 (m, 4H, ArC*H*$_2$Ar); ^{13}C NMR ($CDCl_3$) δ 153.1, 151.0, 134.6, 134.3, 133.5, 129.2, 129.1, 129.0, 128.7, 128.7, 128.0, 124.9, 120.6, 119.1, 77.3, 31.9, 31.7, 30.4.

*3.4.2. 25,26-Dibenzyloxy-27,28-dihydroxycalix[4]arene (**19**).* An amount of 0.08 g (41%) of colorless crystals was afforded form 0.23 g (0.32 mmol) of dibenzyloxy compound **17**: mp 230–232 °C; ^{1}H NMR ($CDCl_3$) δ 8.93 (s, 2H, ArO*H*), 6.56–7.51 (m, 22H, Ar*H*, and Ar′*H*), 5.05–5.08 (d, *J*=11.2 Hz, 2H, OC*H*$_2$Ar'), 4.87–4.90 (d, *J*=11.2 Hz, 2H, OC*H*$_2$Ar'), 4.47–4.50 (d, *J*=12.4 Hz, 1H, ArC*H*$_2$Ar), 4.23–4.26 (d, *J*=13.2 Hz, 1H, ArC*H*$_2$Ar), 4.10–4.13 (d, *J*=12.8 Hz, 2H, ArC*H*$_2$Ar), 3.33–3.36 (d, *J*=13.2 Hz, 2H, ArC*H*$_2$Ar), 3.22–3.25 (d, *J*=12.8 Hz, 2H, ArC*H*$_2$Ar); ^{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.

*3.4.3. 25,27-Diethoxy-26-benzoyloxy-28-hydroxycalix[4]arene (**20**).* A slurry of 0.46 g (0.83 mmol) of 1-ethoxy-3-benzoyloxycalix-

[4]arenes (**6**), 0.07 g of 60% NaH, and 0.59 g (3.78 mmol) of ethyl iodide was refluxed in 50 mL of CH_3CN for 16 h. The solvent was removed by rotory evaporatory and the organic materials were taken up by 30 mL of $CHCl_3$. The organic solution was washed in sequence with 20 mL of 1N HCl and 100 mL of distillated water. The organic solvent was then concentrated and slow recrystallized from $CHCl_3$ and CH_3OH to afford 0.05 g (10%) of colorless crystals **20**: mp 258–260 °C; ^{1}H NMR ($CDCl_3$) δ 8.91–8.93 (d, 2H, Ar′*H*), 7.63–7.66 (t, 1H, Ar′*H*), 7.58–7.61 (t, 2H, Ar′*H*), 7.41 (s, 1H, ArO*H*), 6.57–7.27 (m, 12H, Ar*H*), 4.28–4.32 (d, *J*=13.2 Hz, 2H, ArCH_2Ar), 4.17–4.20 (d, *J*=12.8 Hz, 2H, OCH_2CH$_3$), 3.61–3.63 (m, 4H, OCH_2CH$_3$), 3.34–3.37 (d, *J*=12.8 Hz, 4H, ArCH_2Ar), 0.82–0.85 (t, *J*=7.2 Hz, 6H, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 167.4, 153.4, 152.9, 146.8, 135.6, 133.3, 133.1, 132.9, 132.8, 129.5, 128.7, 128.5, 128.4, 128.2, 128.1, 127.9, 126.1, 124.0, 118.7, 72.0, 31.2, 30.4, 14.9; FAB-MS *m*/*e*: 584 (M^+); HRMS (FAB) *m*/*e*: calcd for $C_{39}H_{36}O_5$: 584.2563; found: 584.2553.

*3.4.4. 25,26-Diethoxy-27-benzoyloxy-28-hydroxycalix[4]arene (**21**).* The mother solution of the pervious recrystallization procedure was concentrated to leave a pale yellow solid material. Chromatographic separation (eluent: EtOAc/*n*-hexane = 1 : 7) following by recrystallization from $CHCl_3$ and CH_3OH afforded 0.10 g (20.5%) of colorless crystals **21**: mp 196–200 °C; ^{1}H NMR ($CDCl_3$) δ 8.48–8.50 (d, 2H, Ar′*H*), 7.63–7.66 (t, 1H, Ar′*H*), 7.52–7.56 (t, 2H, Ar′*H*), 7.24 (s, 1H, ArO*H*), 6.52–7.17 (m, 12H, Ar*H*), 4.42–4.45 (d, *J*=13.2 Hz, 1H, ArCH_2Ar), 4.22–4.27 (2d, 2H, ArCH_2Ar), 4.08–4.11 (d, *J*=13.6 Hz, 1H, ArCH_2Ar), 3.95–4.06 (m, 4H, OCH_2CH$_3$), 3.41–3.45 (d, *J*=13.6 Hz, 1H, ArCH_2Ar), 3.31–3.35 (d, *J*=13.6 Hz, 1H, ArCH_2Ar), 3.24–3.28 (2d, 2H, ArCH_2Ar), 1.59–1.62 (t, *J*=7.0 Hz, 3H, OCH$_2$CH_3), 1.36–1.39 (t, *J*=7.2 Hz, 3H, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 166.1, 155.9, 153.3, 152.9, 146.1, 136.7, 136.4, 134.3, 133.4, 133.1, 132.8, 132.1, 131.3, 130.6, 130.0, 129.4, 129.3, 129.2, 129.0, 128.8, 128.7, 128.5, 128.4, 127.7, 127.5, 124.9, 124.4, 123.3, 119.6, 71.8, 69.8, 31.5, 31.4, 31.2, 30.8, 15.6, 15.5; FAB-MS *m*/*e*: 585 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{39}H_{36}O_5$+H^+: 585.2641; found: 585.2651.

*3.4.5. 25,26-Diethoxy-27,28-dihydroxycalix[4]arene (**22**) by recrystallization.* The mother solution of the recrystallization procedure for compound **20** was concentrated to leave a pale yellow solid material. The solid material was then refluxed with 2.00 g of 25% NaOH in a mixture of 10 mL of C_2H_5OH and 30 mL of THF for 24 h. The solvent was removed and the organic materials were dissolved in 50 mL of $CHCl_3$. The solution was washed with 20 mL of 1N HCl and 100 mL of distillated water, and the organic solvent was then removed to leave a colorless solid. Recrystallization from $CHCl_3$ and CH_3OH precipitated a mixture of rod-like crystals and powder solids. The rod-like crystals were collected and recrystallized from $CHCl_3$ and CH_3OH to give 0.11 g (27.5%) of colorless crystals **22**: mp 185–190 °C; ^{1}H NMR ($CDCl_3$) δ 8.86 (s, 2H, ArO*H*), 6.59–7.04 (m, 12H, ArH), 4.50–4.53 (d, *J*=12.4 Hz, 1H, ArCH_2Ar), 4.35–4.38 (d, *J*=13.2 Hz, 1H, ArCH_2Ar), 4.31–4.34 (d, *J*=12.8 Hz, 2H, ArCH_2Ar), 4.19–4.23 (m, 2H OCH_2CH$_3$), 4.04–4.10 (m, 2H, OCH_2CH$_3$), 3.37–3.42 (d, *J*=13.2 Hz, 2H, ArCH_2Ar), 3.34–3.38 (d, *J*=12.8 Hz, 2H, ArCH_2Ar), 1.68–1.72 (t, *J*=13.2 Hz, 6H, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 153.2, 151.2, 134.7, 134.3, 129.4, 129.3, 129.1, 128.7, 128.0, 124.8, 120.6, 71.8, 31.9, 31.8, 30.2, 15.5; FAB-MS *m*/*e*: 480 (M^+); HRMS (FAB) *m*/*e*: calcd for $C_{32}H_{32}O_4$: 480.2301; found: 480.2293.

3.5. General procedure for 1,2-dialkoxycalix[4]arene 22–24 by chromatographic separation

A slurry of approximate 0.50 g of 1-alkoxy-3-benzoyloxycalix[4]-arenes **6**–**8**, 0.05 g of 60% NaH, and 4 mol equiv of alkyl halides was refluxed in 50 mL of CH_3CN for 14 h. The solvent was removed by rotory evaporatory and the organic materials were taken up by 30 mL of $CHCl_3$. The organic solution was washed with 100 mL of distillated water, and the solvent was removed to leave a pale yellow solid.

The pale yellow solid material was then refluxed with 2.00 g of 25% NaOH in a mixture of 10 mL of C_2H_5OH and 30 mL of THF for 24 h to remove the benzoate moieties. The solvent was removed and the organic materials were taken up with 50 mL of $CHCl_3$. The organic solution was washed with 20 mL of 1N HCl and 100 mL of distillated water, and the organic solvent was removed to leave a colorless solid. Chromatographic separation, following by recrystallization from $CHCl_3$ and CH_3OH yielded the corresponding hydrolysis products **22**–**24**.

*3.5.1. 25,26-Diethoxy-27,28-dihydroxycalix[4]arene (**22**) by chromatographic separation.* An amount of 0.49 g of etherification crude products was collected from 0.54 g (0.97 mmol) of compound **6**. Chromatographic separation (eluent: EtOAc/*n*-hexane = 1:15) of the crude product afforded 0.12 g (26%) of colorless crystals in second fraction which was shown to be identical to the previous known 1,3-diethoxycalix[4]arene. An amount of 0.06 g (13%) of colorless fine crystals was collected in the third section. The melting point and the spectral feature of the colorless crystals were identical to the previous prepared product **22**.

*3.5.2. 25,26-Dipropoxy-27,28-dihydroxycalix[4]arene (**23**) by chromatographic separation.* An amount of 0.49 g of etherification crude products was collected from 0.50 g (0.88 mmol) of compound **7**. Chromatographic separation (eluent: EtOAc/*n*-hexane = 1 : 20) of the crude product afforded 0.10 g (22%) of colorless crystals in second fraction which was shown to be identical to the previous known 1,3-dipropoxycalix[4]arene. An amount of 0.07 g (15.5%) of off-white crystals was collected as compound **23**: mp 197–198 °C; ^{1}H NMR ($CDCl_3$) δ 8.96 (s, 2H, ArO*H*), 7.02–7.04 (d, *J*=7.6 Hz, 2H, Ar*H*), 6.93–6.98 (m, 6H, Ar*H*), 6.74–6.78 (t, *J*=7.6 Hz, 2H, Ar*H*), 6.58–6.62 (t, *J*=7.6 Hz, 2H, Ar*H*), 4.52–4.55 (d, *J*=12.0 Hz, 1H, ArCH_2Ar), 4.31–4.35 (d, *J*=13.2 Hz, 3H, ArCH_2Ar), 4.05–4.11 (m, 2H, OCH_2CH$_2$CH$_3$), 3.85–3.92 (m, 2H, OCH_2CH$_2$CH$_3$), 3.33–42 (3d, 4H, ArCH_2Ar), 2.12–2.18 (m, 4H, OCH$_2$CH_2CH$_3$), 1.15–1.19 (t, *J*=7.4 Hz, 6H, OCH$_2$CH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 153.4, 151.2, 134.6, 134.1, 129.4, 129.1, 129.0, 128.8, 128.7, 128.0, 124.7, 120.1, 78.3, 31.9, 31.8, 29.9, 23.2, 10.3; FAB-MS *m*/*e*: 509 (M^++1); HRMS (FAB) *m*/*e*: calcd for $C_{34}H_{36}O_4$+H^+: 509.2692; found: 509.2687.

*3.5.3. 25,26-Dibutoxy-27,28-dihydroxycalix[4]arene (**24**) by chromatographic separation.* An amount of 0.58 g of etherification crude products was collected from 0.50 g (0.86 mmol) of compound **8**. Chromatographic separation (eluent: EtOAc/*n*-hexane = 1:20) of the crude product afforded 0.07 g (15%) of colorless crystals in second fraction which was shown to be identical to the previous known 1,3-dibutoxycalix[4]arene. An amount of 0.05 g (10.5%) of colorless fine crystals was collected as compound **24**: mp 168–170 °C; ^{1}H NMR ($CDCl_3$) δ 8.92 (s, 2H, ArO*H*), 7.02–7.04 (d, *J*=7.6 Hz, 2H, Ar*H*), 6.95–6.96 (m, 6H, Ar*H*), 6.74–6.78 (t, *J*=7.6 Hz, 2H, Ar*H*), 6.58–6.62 (t, *J*=7.6 Hz, 2H, Ar*H*), 4.51–4.54 (d, *J*=12.4 Hz, 1H, ArCH_2Ar), 4.33–4.36 (d, *J*=13.2 Hz, 1H, ArCH_2Ar), 4.31–4.34 (d, *J*=12.8 Hz, 2H, ArCH_2Ar), 4.07–4.13 (m, 2H, OCH_2CH$_2$CH$_2$CH$_3$), 3.90–3.96 (m, 2H, OCH_2CH$_2$CH$_2$CH$_3$), 3.26–3.42 (3d, 4H, ArCH_2Ar), 2.09–2.15 (m, 4H, OCH$_2$CH_2CH$_2$CH$_3$), 1.56–1.64 (m, 4H, OCH$_2$CH$_2$CH_2CH$_3$), 1.07–1.11 (t, *J*=7.2 Hz, 6H, OCH$_2$CH$_2$CH$_2$CH_3); ^{13}C NMR ($CDCl_3$) δ 152.6, 150.34, 134.1, 133.6, 128.9, 128.6, 128.3, 127.5, 124.3, 120.2, 33.1, 33.0, 32.9, 31.1, 20.5, 15.5; FAB-MS *m*/*e*: 536 (M^+); HRMS (FAB) *m*/*e*: calcd for $C_{36}H_{40}O_4$: 536.2927; found: 536.2914.

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Supplementary data

Copies of ^{1}H and ^{13}C NMR spectra of compounds **1**–**24** are available. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.03.048. These data include MOL files and InChIKeys of the most important compounds described in this article.

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11. The conformational assignment is based on the relative position of the phenolic O-substitutents. Due to the 'through-the-annulus' free rotation of the phenolic hydroxy groups, the relative position of the free phenolic OH moieties are not assigned.
12. 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 spectra are recorded on Varian 400-MR 400 MHz FT NMR spectrometer and chemical shifts are reported as δ values in ppm relative to TMS (δ=0.00). FAB-MS and HRMS (FAB) spectra were taken on a Finnigan/Thermo Quest MAT 95XL 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 (absorbant thickness 0.2 mm).