

## Selective Acylation and Aminomethylation of Benzoylated Calix[4]arene

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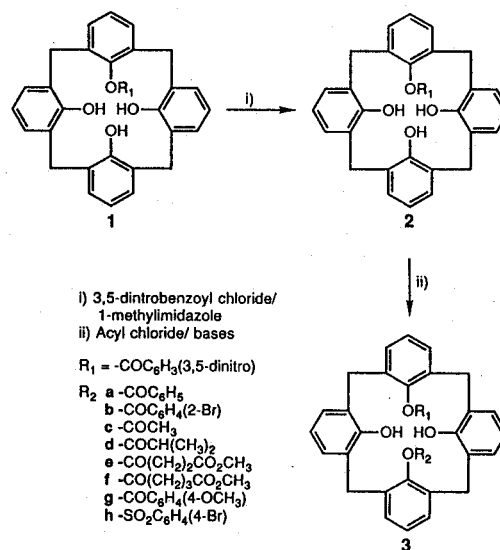
Two different acyl substituents were introduced at the lower rim of calix[4]arene by the two step reactions. Calix[4]arenes (**1**) reacted with 3,5-dinitrobenzoyl chloride to yield monosubstituted calix[4]arene (**2**). Second substitution was achieved by the reaction of **2** with various acyl chlorides. Aminomethylation of monobenzoylated calix[4]arene was conducted successfully in the presence of secondary amine and formaldehyde.

### Introduction

Calixarenes are cavity containing metacyclophanes which are recently utilized as a versatile host molecules.<sup>1,2</sup> Molecular structure of calixarenes could allow the preparation of synthetic macrocycles with a chiral cavity. Most of the chiral calixarenes<sup>3,4</sup> have been prepared as a regioselective functionalization<sup>5,6</sup> at the lower rim of calix[4]arenes. For the purpose of preparation of chiral calixarene we reported monoacylation of calix[4]arene.<sup>7</sup> The acyl groups at the lower rim of calixarene are known as an effective binding sites for the cation.<sup>8</sup> So we extended this functionalization to the regioselective diacylation at the lower rim of calix[4]arenes. Also aminomethylation of benzoylated calix[4]arenes was examined in the presence of secondary amine and formaldehyde to test the reactivity differences of substituted calix[4]arenes. Although diacylation procedures of calix[4]arene were reported<sup>9,10,11</sup> previously, introduction of two different acyl groups at the lower rim of calix[4]arene was not reported yet. Here we report the selective diacylation of calix[4]arene by the two step reaction sequence and the aminomethylation of monobenzoylated calix[4]arene.

### Results and Discussion

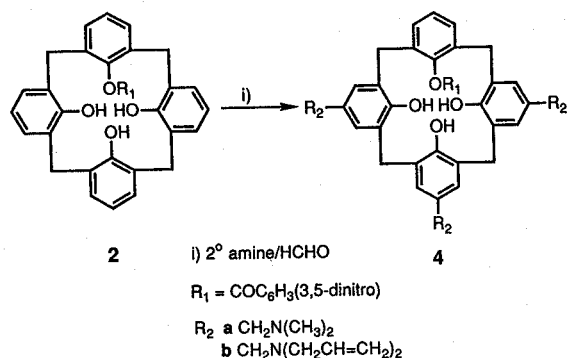
**Diacylation of Calix[4]arene.** Gutche and See<sup>12</sup> reported that *p*-*tert*-butylcalix[4]arene reacted with 3,5-dinitrobenzoyl chloride in the presence of 1-methylimidazole in acetonitrile to yield a monobenzoylated product. We found that calixarene **1** also reacted with 3,5-dinitrobenzoyl chloride in the presence of 1-methylimidazole to give a monobenzoylated calix[4]arene **2** respectively in high yield. The <sup>1</sup>H NMR spectrum of **2** showed two pair of doublets at 3.6-4.0 ppm arising from the methylene protons characteristics of monosubstituted calix[4]arene. Assuming that 3,5-dinitrobenzoyl group might be bulky enough to control the selective second substitution at the lower rim of calixarene, second substitution was carried out with various acyl halides such as benzoyl chloride, acetyl chloride, isobutyryl chloride, 2-bromobenzoyl chloride, 3-methoxycarbonylpropionyl chloride, 4-methoxybenzoyl chloride, and 4-methoxycarbonylbutanoyl chloride in the presence of pyridine as shown in Scheme 1. As expected it turned out that only one substitution was occur-



Scheme 1.

red at the opposite side of lower rim on the 3,5-dinitrobenzoyl group by controlling the reaction conditions. Second acylation of calix[4]arene was successfully conducted in the presence of pyridine by controlling the amount of acyl halide in about 1.2 equivalent. When K<sub>2</sub>CO<sub>3</sub> was used for the second acylation reaction as a base, the several side products were obtained. But reaction of **2** with *p*-bromobenzenesulfonyl chloride gave **3h** in the presence of K<sub>2</sub>CO<sub>3</sub> rather than pyridine as observed in alkylation reaction.

Substitution pattern and conformation of diacylated calix[4]arenes were confirmed by the NMR spectra. The <sup>1</sup>H NMR spectrum of **3a** showed two pair of doublets at 3.5-3.9 ppm arising from the bridged methylene protons and a singlet at 5.10 ppm for the two hydroxy protons, indicating that second substitution was occurred at the opposite side of lower rim of **2** to yield ABCB type calix[4]arene. The <sup>1</sup>H NMR spectrum of **3b** showed the exact same pattern as described above such as two pair of doublets at 3.50-3.83 ppm for the methylene protons and a singlet at 5.0 ppm for the hydroxy protons. The conformation of diacylated calix[4]arenes was deduced from the <sup>13</sup>C NMR chemical shifts<sup>13</sup> of the methylene groups connecting each pair of rings. In



Scheme 2.

a syn orientation (*i.e.* cone conformations), the methylene signals appear around  $\delta$  31 ppm, whereas they appear around  $\delta$  37 ppm when both phenol rings are anti oriented (*i.e.* 1,3-alternate conformation). All of those diacylated calix[4]arenes showed two peaks at about  $\delta$  31 ppm indicating that they exist as a cone conformation.

**Aminomethylation of 3,5-Dinitrobenzoylcalix[4]arene 2.** To examine the influence of lower rim substitution in the reaction of electrophilic substitution of calixarene, several benzoylated calix[4]arenes such as mono, di, and tribenzoylated calixarenes was treated under the aminomethylation reaction condition. When three of the OH groups are substituted by the benzoyl group, aminomethylation was not occurred even under the vigorous reaction conditions. Also when two of the OH groups are substituted by the benzoyl group, aminomethylation was not occurred. Though Reinhoudt reported<sup>15</sup> the success Mannich reaction with 1,3-O-dimethylated calix[4]arene with excess of dimethyl amine and formaldehyde with reflux in dioxane/H<sub>2</sub>O for 3 days, dibenzoylated calix[4]arene which has two free OH and two benzoyl groups at the lower rim of calix[4]arene did not react at all under the same condition applied by Reinhoudt. But when one of the OH group was replaced by 3,5-dinitrobenzoyl group such as **2**, aminomethylation was occurred without any difficulty as shown in Scheme 2. These reactivity difference of the benzoylated calixarenes indicates that two or more large substituents on the lower rim of calix[4]arene prevent the Mannich reaction. This phenomena could be explained by the steric hindrance of the substituents and the acidities of phenols, the phenols in **2** could be more acidic than those in **3** and tribenzoylated calix[4]arene due to the presence of intramolecular hydrogen bonding. Intramolecular hydrogen bonding characteristics of benzoylated calix[4]arene **2** could be seen from IR absorption band of OH group. OH absorption band of **2** was observed at 3,400 cm<sup>-1</sup> as a broad peak due to H-bonding with neighboring OH groups, on the other hand OH absorption bands of di, and tribenzoylated calix[4]arene were observed at 3,530 cm<sup>-1</sup> as a sharp singlet, clearly indicating that di, and tribenzoylated calix[4]arene did not form a intramolecular H-bonding. This aminomethylation reaction sequence of **2** could open up the synthetic route for the selective trifunctionalization of calix[4]arene. Therefore the various functional groups such as cyano, azido, alkylthio, and malonate could be selectively introduced at the upper rim of calix[4]arene.

## Experimental

Melting points of all compounds were recorded on a Mel Temp apparatus without calibration. Infrared (IR) spectra were determined on a Nicolet 520 FT-IR spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian Unity 300 spectrometer. Chemical shifts were recorded as  $\delta$  values in part per million relative to tetramethylsilane as an internal standard. Thin layer chromatography (TLC) analyses were carried out on a silica gel plates.

**25-(3,5-Dinitrobenzoyloxy)-26,27,28-trihydroxycalix[4]arene 2.** Following the procedure reported previously in our lab,<sup>7</sup> 63% of pale yellow crystalline product was obtained by recrystallization from CHCl<sub>3</sub>-MeOH. mp 288 °C dec.

**25-(3,5-Dinitrobenzoyloxy)-27-(benzoyloxy)-26,28-dihydroxycalix[4]arene 3a.** To a solution of 1.0 g (1.6 mmol) of **2**, 0.16 mL of pyridine was added and the solution was stirred until **2** was dissolved completely. 0.23 mL (1.9 mmol) of benzoyl chloride was added slowly and the solution was stirred for 30 min. After TLC analysis the solvents were evaporated and the residue was triturated with methanol. Recrystallization from CHCl<sub>3</sub>-MeOH yielded a 1.03 g (88%) of light yellow crystalline product. mp 282-285 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  9.55 (d, 2H, O<sub>2</sub>NArH), 9.35 (t, 1H, O<sub>2</sub>NArH), 8.25 (d, 2H, COArH), 7.64 (t, 1H, COArH), 7.42 (t, 2H, COArH), 7.08 (t, 4H, ArH), 6.80-7.00 (m, 6H, ArH), 6.78 (t, 2H, ArH), 5.10 (s, 2H, OH), 3.55 and 3.95 (two pairs of d, 8H, ArCH<sub>2</sub>Ar, *J* = 14.6 Hz and 13.9 Hz). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  161.33 (C=O), 152.66, 149.03, 145.58, 145.44, 134.21, 133.08, 132.36, 130.52, 130.25, 129.58, 129.39, 129.26, 129.15, 128.72, 128.51, 128.40, 127.07, 126.72, 123.08 and 120.25 (Ar), 32.62 and 32.38 (-CH<sub>2</sub>-). IR (KBr) 3532 cm<sup>-1</sup> (OH), 1743 cm<sup>-1</sup> (-CO<sub>2</sub>-).

**25-(3,5-Dinitrobenzoyloxy)-27-(2-bromobenzoyloxy)-26,28-dihydroxy-calix[4]arene 3b.** Following the procedure described for **3a** except using 2-bromobenzoyl chloride, 930 mg (70%) of **3b** was obtained from recrystallization of CHCl<sub>3</sub>-MeOH. mp 242 °C dec. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  9.49 (d, 2H, O<sub>2</sub>NArH, *J* = 2.1 Hz), 9.32 (t, 1H, O<sub>2</sub>NArH, *J* = 2.1 Hz), 8.25 (d, 1H, BrArH), 7.80 (d, 1H, BrArH), 7.42 (t, 1H, BrArH), 7.24 (t, 1H, BrArH), 6.78-7.20 (m, 12H, ArH), 5.18 (s, 2H, OH), 3.54-4.07 (two pairs of d, 8H, ArCH<sub>2</sub>Ar). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  161.00 (C=O), 152.60, 148.88, 145.90, 145.33, 135.14, 133.64, 132.13, 131.92, 131.71, 130.16, 129.48, 129.26, 129.14, 128.61, 128.24, 127.21, 126.83, 123.03, and 120.39 (Ar), 32.30 and 32.14 (ArCH<sub>2</sub>Ar). IR (KBr) 3400 cm<sup>-1</sup> (OH), 1730 cm<sup>-1</sup> (-CO<sub>2</sub>-).

**25-(3,5-dinitrobenzoyloxy)-27-(acetyloxy)-26,28-dihydroxycalix[4]arene 3c.** Following the procedure described for **3a** except using acetyl chloride, 830 mg (80%) of **3c** was obtained from recrystallization of CHCl<sub>3</sub>-MeOH. mp 275 °C dec. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  9.33 (s, 3H, O<sub>2</sub>NArH), 6.70-7.10 (m, 12H, ArH), 5.00 (s, 2H, OH), 3.50-3.83 (two pairs of d, 8H, ArCH<sub>2</sub>Ar, *J* = 13.9 Hz and 14.7 Hz), 2.45 (s, 3H, CH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  168.47 and 161.06 (-CO<sub>2</sub>-), 152.74, 148.81, 145.98, 145.33, 132.98, 132.26, 130.25, 129.50, 129.34, 129.18, 127.84, 127.55, 126.99, 123.11, and 119.90 (Ar), 33.42 and 33.37 (ArCH<sub>2</sub>Ar), 20.64 (-CH<sub>3</sub>). IR (KBr) 3540 cm<sup>-1</sup> (OH), 1750 and 1740 cm<sup>-1</sup> (-CO<sub>2</sub>-).

**25-(3,5-dinitrobenzoyloxy)-27-(isobutyroyloxy)-26,28-dihydroxy-calix[4]arene 3d.** Following the proce-

cedure described for **3a** except using isobutyryl chloride, 830 mg (75%) of **3d** was obtained from recrystallization of  $\text{CHCl}_3$ -MeOH. mp 250 °C dec.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.41 and 9.35 (d and t, 3H,  $\text{O}_2\text{NArH}$ ), 6.78-7.12 (m, 12H, ArH), 5.18 (s, 2H, OH), 3.50-3.90 (two pairs of d, 8H,  $\text{ArCH}_2\text{Ar}$ ,  $J=13.9$  Hz and 14.7 Hz), 3.14 (m, 1H,  $-\text{CH}-$ ), 1.43 (d, 6H,  $-\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  174.98 and 161.36 ( $-\text{CO}_2-$ ), 152.75, 149.02, 145.52, 144.96, 133.09, 132.07, 132.02, 130.15, 129.32, 129.18, 128.29, 128.00, 127.01, 126.77, 123.17, and 120.16 (Ar), 77.23 ( $-\text{CH}-$ ), 34.10 and 32.62 ( $\text{ArCH}_2\text{Ar}$ ), 19.30 ( $-\text{CH}_3$ ). IR (KBr)  $3500\text{ cm}^{-1}$  (OH),  $1750\text{ cm}^{-1}$  ( $-\text{CO}_2-$ ).

**25-(3,5-dinitrobenzoyloxy)-27-(3-methoxycarbonylpropionyloxy)-26,28-dihydroxycalix[4]arene 3e.** Following the procedure described for **3a** except using 3-methoxycarbonylpropionyl chloride, 500 mg (43%) of **3e** was obtained from recrystallization of  $\text{CHCl}_3$ -MeOH. mp 238-241 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.38 and 9.10 (d and t, 3H,  $\text{O}_2\text{NArH}$ ), 6.70-7.20 (m, 12H, ArH), 5.10 (s, 2H, OH), 3.54-3.90 (two pairs of d, 8H,  $\text{ArCH}_2\text{Ar}$ ,  $J=13.9$  Hz and 14.7 Hz), 3.70 (s, 3H,  $-\text{OCH}_3$ ), 3.10 and 2.80 (two t, 4H,  $-\text{CH}_2\text{CH}_2-$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  172.56, 170.38 and 161.12 ( $-\text{CO}_2-$ ), 152.75, 148.79, 145.97, 145.28, 132.38, 132.28, 130.27, 130.10, 129.50, 129.39, 129.12, 127.85, 127.63, 127.01, 123.13, and 119.90 (Ar), 52.05 ( $-\text{OCH}_3$ ), 33.46 and 33.29 ( $\text{ArCH}_2\text{Ar}$ ), 28.72 and 28.61 ( $-\text{CH}_2\text{CH}_2-$ ). IR (KBr)  $3450\text{ cm}^{-1}$  (OH),  $1740\text{ cm}^{-1}$  ( $-\text{CO}_2-$ ).

**25-(3,5-dinitrobenzoyloxy)-27-(4-methoxycarbonylbutyryloxy)-26,28-dihydroxycalix[4]arene 3f.** Following the procedure described for **3a** except using 4-methoxycarbonylbutanoyl chloride, 230 mg (64%) of **3f** was obtained from recrystallization of  $\text{CHCl}_3$ -MeOH. mp 195-198 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.38 (s, 3H,  $\text{O}_2\text{NArH}$ ), 7.08 (d, 2H, ArH), 6.80-7.00 (m, 8H, ArH), 6.69 (t, 2H, ArH), 5.05 (s, 2H, OH), 3.50, 3.55 and 3.75, 3.78 (two pairs of d, 8H,  $\text{ArCH}_2\text{Ar}$ ,  $J=13.9$  Hz and 14.7 Hz), 2.87 and 2.55 (two t, 4H,  $-\text{CH}_2-$ ), 2.14 (m, 2H,  $-\text{CH}_2-$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  173.22, 170.70 and 161.07 ( $-\text{CO}_2-$ ), 152.67, 148.79, 145.74, 145.09, 132.87, 132.12, 132.09, 130.17, 129.41, 129.38, 129.28, 129.15, 127.85, 127.55, 126.97, 126.90, 123.03, and 119.92 (Ar), 51.55 ( $-\text{OCH}_3$ ), 33.17 and 33.15 ( $\text{ArCH}_2\text{Ar}$ ), 32.56, 32.41, 19.74 ( $-\text{CH}_2-$ ). IR (KBr)  $3450\text{ cm}^{-1}$  (OH),  $1740\text{ cm}^{-1}$  ( $-\text{CO}_2-$ ).

**25-(3,5-dinitrobenzoyloxy)-27-(p-methoxybenzoyloxy)-26,28-dihydroxycalix[4]arene 3g.** Following the procedure described for **3a** except using p-methoxybenzoyl chloride, 830 mg (80%) of **3g** was obtained from recrystallization of  $\text{CHCl}_3$ -MeOH. mp 270 °C dec.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.55 and 9.36 (d and t, 3H,  $\text{O}_2\text{NArH}$ ), 8.18 (d, 2H, ArH from p-methoxybenzoyl), 6.70-7.20 (m, 14H, ArH), 5.10 (s, 2H, OH), 3.54, 3.55 and 3.90, 3.94 (two pairs of d, 8H,  $\text{ArCH}_2\text{Ar}$ ,  $J=13.9$  Hz and 14.7 Hz), 3.93 (s, 3H,  $-\text{OCH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  164.34, 163.88, 161.92 ( $-\text{CO}_2-$ ), 152.88, 148.58, 146.31, 146.09, 132.88, 132.80, 132.72, 132.68, 132.59, 132.39, 130.27, 129.50, 129.35, 128.99, 128.73, 125.32, 125.05, 123.06, 120.65, 119.11, 114.31, and 114.17 (Ar), 55.65 ( $-\text{OCH}_3$ ), 32.82, 32.66 ( $\text{ArCH}_2\text{Ar}$ ). IR (KBr)  $3500\text{ cm}^{-1}$  (OH),  $1745\text{ cm}^{-1}$  ( $-\text{CO}_2-$ ).

**25-(3,5-dinitrobenzoyloxy)-27-(p-bromobenzenesulfonyloxy)-26,28-dihydroxycalix[4]arene 3h.** To a solution of 300 mg (0.485 mmol) of **2** in 50 mL of THF, 340 mg (2.4 mmol) of  $\text{K}_2\text{CO}_3$  and 1.22 g (4.8 mmol) of p-bromobenzenesulfonyl chloride was added and refluxed for **2h**. The solvents were evaporated and the residue was triturated with

MeOH. Recrystallization from  $\text{CHCl}_3$ -MeOH yielded 200 mg (53%) of **3h**. mp 240 °C dec.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.50 and 9.25 (d and t, 3H,  $\text{O}_2\text{NArH}$ ,  $J=2.1$  Hz), 7.75 and 7.90 (pair of d, 4H, ArH from brosyl,  $J=9.7$  Hz), 6.60-7.15 (m, 12H, ArH), 5.00 (s, 2H, OH), 3.00-4.00 (two pairs of d, 8H,  $\text{ArCH}_2\text{Ar}$ ,  $J=14.1$  Hz and 14.4 Hz).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  161.84 ( $-\text{CO}_2-$ ), 152.41, 150.13, 148.89, 145.15, 133.86, 132.91, 132.81, 131.79, 130.35, 130.00, 129.84, 129.49, 129.31, 129.20, 128.29, 128.00, 127.76, 127.55, 127.38, 123.29, and 120.35 (Ar), 32.12 ( $\text{ArCH}_2\text{Ar}$ ). IR (KBr)  $3500\text{ cm}^{-1}$  (OH),  $1740\text{ cm}^{-1}$  ( $-\text{CO}_2-$ ).

**11,17,23-Tris(dimethylamino)methyl-25-(3,5-dinitrobenzoyloxy)-26,27,28-trihydroxycalix[4]arene 4a.**

To a solution of 300 mg (0.485 mmol) of **2** in 30 mL THF, 0.12 mL of formaldehyde (35%) and 0.12 mL of dimethylamine (50%) were added and the solution stirred for **3h**. The solvents were evaporated and the residue triturated with methanol to give 300 mg (83%) of **4a**. mp 270 °C dec.  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  14.20 (br s, 3H, OH), 9.75 and 9.16 (d and t, 3H,  $\text{O}_2\text{NArH}$ ), 7.19-6.87 (m, 9H, ArH), 4.09-3.16 (two pairs of d, 8H,  $\text{ArCH}_2\text{Ar}$ ), 3.35 (br s, 6H,  $\text{ArCH}_2\text{N}$ ), 2.30 (br s, 18H,  $-\text{N}(\text{CH}_3)_2$ ).  $^{13}\text{C}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  162.47 ( $-\text{CO}_2-$ ), 155.46, 148.76, 148.03, 145.35 ( $\text{O}_2\text{NAr}$ ), 133.75, 133.07, 130.42, 130.21, 129.72, 129.48, 128.69, 128.39, 127.65, 127.13, 123.12, and 117.48 (Ar), 67.28, 41.71, 33.86, 31.46 ( $\text{ArCH}_2\text{Ar}$ ), 25.38 ( $-\text{CH}_3$ ). IR (KBr)  $3400\text{ cm}^{-1}$  (OH),  $1750\text{ cm}^{-1}$  ( $\text{C}=\text{O}$ ), 1547 and  $1344\text{ cm}^{-1}$  ( $\text{NO}_2$ ).

**11,17,23-Tris(diallylamino)methyl-25-(3,5-dinitrobenzoyloxy)-26,27,28-trihydroxycalix[4]arene 4b.**

Following the procedure described for **4a** except using diallylamine and formaldehyde, 360 mg (78%) of **4b** was obtained from recrystallization of  $\text{CHCl}_3$ -Hexane. mp 130-133 °C.  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  14.30 (br s, 3H, OH), 9.73 and 9.16 (d and t, 3H,  $\text{O}_2\text{NArH}$ ), 7.03-6.80 (m, 9H, ArH), 5.86 (m, 3H,  $=\text{CH}-$ ), 5.42-5.24 (m, 6H,  $=\text{CH}_2$ ), 4.06-3.21 (two pairs of d, 8H,  $\text{ArCH}_2\text{Ar}$ ), 3.40 (br s, 6H,  $\text{ArCH}_2\text{N}$ ), 3.89-2.90 (m, 6H,  $-\text{N}-\text{CH}=\text{}$ ).  $^{13}\text{C}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  162.39 ( $\text{C}=\text{O}$ ), 155.19, 148.83, 148.10, 145.34, 133.69, 133.03, 130.42, 129.90, 129.33, 128.74, 128.31, 127.78, 125.72, 123.28, 122.60, and 120.10 (Ar), 56.49, 54.96, 54.37 ( $-\text{CH}_2-$  from allyl), 48.29 ( $\text{ArCH}_2-\text{N}-$ ), 33.94, 31.47 ( $\text{ArCH}_2\text{Ar}$ ). IR (KBr)  $3400\text{ cm}^{-1}$  (OH),  $1760\text{ cm}^{-1}$  ( $\text{C}=\text{O}$ ), 1547 and  $1344\text{ cm}^{-1}$  ( $\text{NO}_2$ ).

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## Synthesis of Several Diester Group-Containing Calix[4]arenes

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Several ester group-containing calix[4]arenes were synthesized by the reaction of calix[4]arene and various acyl chlorides. Two or four ethyl succinyl units could be introduced into the calix[4]arene lower rim depending on the reaction conditions. But the mixture of three and four ethyl malonyl substituted calix[4]arenes were obtained and only three ethyl oxalyl units were introduced at the lower rim of calix[4]arene. Interestingly when calix[4]arene was treated with ethyl oxalyl chloride in the presence of aluminum chloride, two ethyl oxalyl units were introduced at the upper rim of calix[4]arene. The conformation of those ester-containing calix[4]arenes was presented based on the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra.

### Introduction

Since the modern discovery of calixarene by Gutsche<sup>1</sup> it has been developed as a variety of purpose such as host-guest chemistry,<sup>2-4</sup> inclusion compounds,<sup>5,6</sup> organic catalysts<sup>7,8</sup> and certain metal ionophores.<sup>9</sup> Recently a series<sup>10,11</sup> of metal ionophores based on calixarenes were synthesized and utilized as a metal ion sensors. Most notable calixarene ionophores were prepared by McKervey *et al.*<sup>12</sup> They synthesized polyfunctional esters and ketones capable of showing ionophoric activity. The tetramer esters and ketones display peak selectivity for the sodium ion, and the hexaesters extract  $\text{K}^+$  better than  $\text{Na}^+$ . The octamers are the least effective ionophores. In that calixarene, the ethereal oxygen and the carbonyl oxygen are involved in the complex with the alkali metal.

We, however, focused more on the two oxygens in the diester groups than on the ethereal oxygen. For the purpose of developing effective metal ion ionophores we synthesized the several ester group-containing calix[4]arenes. Ethyl succinyl, ethyl malonyl, and ethyl oxalyl chloride were used as an ester group precursor. The conformation of the ester group-containing calix[4]arenes was discussed based on NMR spectra.

### Results and Discussion

#### Reaction with Ethyl Succinyl Chloride. Calix[4]

arene **1a**, **1b** were treated with ethyl succinyl chloride in the presence of bases (Table 1). By controlled the amount of ethyl succinyl chloride, two or four ethyl succinyl groups were introduced at the lower rim of calix[4]arene. Figure 1 shows several O-acylation products prepared by the reaction of calixarene and acyl halides. Tetrasubstitution was occurred in the presence of excess ethyl succinyl chloride. Depending on the para substituents of calix[4]arene the conformation<sup>13,14</sup> of tetraesters varied. If there are no para substituents, 1,3-alternate conformation products were obtained. On the other hand If there are bulky para substituents such as *p-t*-butyl group, cone conformation products were obtained. The conformation of calix[4]arenes **2a** and **2b** was confirmed by the NMR spectrum. The  $^1\text{H}$  NMR spectrum of **2a** shows a multiplet at 7.0-7.2 ppm for the aromatic protons, and a quartet at 4.16 and a triplet at 1.28 ppm for the ethoxy protons, a singlet at 3.75 for the bridged methylene protons, and two triplets at 1.98 and 2.50 ppm for the two succinyl methylene protons. A singlet for the bridge methylene protons is characteristic for the 1,3-alternate conformation. The only one bridge methylene carbon peak appears at 37.4 ppm, indicating that the four phenol rings are all anti orientated.<sup>15</sup> Therefore it is 1,3-alternate conformation. But, the  $^1\text{H}$  NMR spectrum of **2b** shows a singlet at 6.95 ppm for the aromatic protons, a quartet at 4.17 ppm and a triplet at 1.28 ppm for the ethoxy protons, a pair of doublets at 4.00 and 3.28 ppm for the bridged methylene protons, two triplets at 3.20 and 2.74 ppm for the succinyl methylene protons, and a sing-