Sample (1.00 gr) was dissolved and diluted to 100 mL. The final concentration of Cd in solution was adjusted to be 35 ppb. Standard addition method was used rather than the calibration method because it suffered less of matrix interferences and gave better accuracy.[13] The result obtained was 3.7±0.3 ppm which agreed well with the certified value of 3.5±0.4 ppm. To apply this technique to other elements comfortably, further studies on interferences and analytical performances should be done, which are under investigation in our laboratory.

In conclusion, it is demonstrated that on-line direct precipitation preconcentration using hydroxide as a precipitant is feasible to enhance the detection limit of Cd in atomic spectrometry. It is simple, fast, yet efficient for the preconcentration of trace elements and can be applied to other techniques than ICP as well. By selecting a proper precipitant, applications can be extended to specific elements as well as multi-elemental preconcentration.

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Synthesis and Structure Identification of ABCH Type Calix[4]arenes: Two Step Synthesis of Asymmetrically Substituted Calix[4]arenes from Monoalkylcalix[4]arenes

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Several ABCH type chiral calix[4]arenes were prepared from monoalkyl calix[4]arenes by treating with various acyl halide, followed by reacting with benzoyl chloride in pyridine. These asymmetrically substituted ABCH type calix[4]arenes are obtained as racemates mixture which are confirmed by the chiral shift reagent in ^{1}H NMR spectra. The molecular and crystal structure of 5-nitro-26-allyloxy-25-benzoyloxy-28-isobutyryloxy-27-hydroxycalix[4]arene **8a** has been determined by the X-ray diffraction method. Two independent enantiomeric molecules are crystallized in a 1 : 1 racemate mixture. They are in the partial cone conformation in which the benzoyloxy phenyl group is down. There is a bifurcated intramolecular hydrogen bonding involving three functional groups in each molecule.

Introduction

Calixarenes are cavity containing metacyclophanes which are currently utilized as a versatile host molecules.[1-3] One of the most important aspect about host-guest chemistry is molecular recognition.[4,5] Like chiral cyclodextrines, calixarenes are expected to have similar chiral recognition ability because molecular structure of calixarenes could allow the

preparation of synthetic molecule with a chiral cavity.[6] If molecular asymmetry could be originated from the direct calixarene framework, the efficient chiral recognition would be expected.

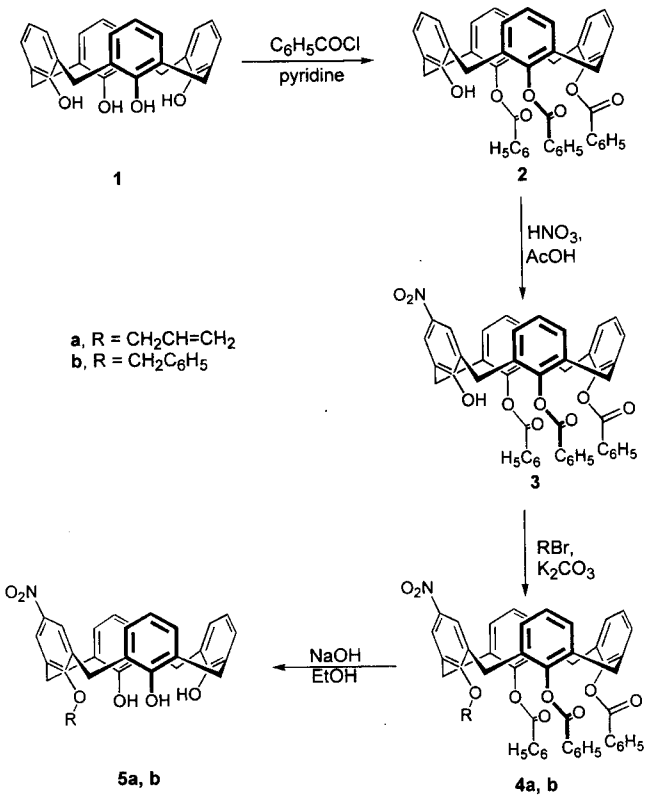
Chiral calixarenes have been prepared by attaching chiral residues to the tetramer.[7] Also the various asymmetric calix[4]arenes were synthesized by the direct introduction of the three or four different substituents at the upper rim[8,9] of calix[4]arenes as well as by the selective alkylation at the lower rim[10,11] of calix[4]arenes. Recently we developed the selective derivatization of calix[4]arene starting from monobenzoylated calix[4]arene.[12,13] For the purpose of developing new synthetic procedure of chiral calixarenes here we report two step synthesis of asymmetrically substituted ABCH type calix[4]arenes from monoalkylcalix[4]arenes.

By introducing three different substituents at the lower rim of calix[4]arenes, not only the various chiral calix[4]arenes are obtained, but also ring inversion is inhibited. Since monoalkylcalix[4]arenes[14,15] are easily available from the selective functionalization, this simple method could provide the efficient synthetic method for the chiral calix[4]arenes.

Results and Discussion

Monoalkylcalix[4]arenes. For the preparation of ABCH type chiral calix[4]arenes, alkyl group was chosen as first substituent to be introduced. Particularly we synthesized *p*-nitroalkylcalix[4]arenes **5**. It was found that alkylation of **3** was much easier than that of **2** and also nitro group would be utilized as a handle for further functionalization. Tribenzoylated calix[4]arene **2** was obtained as following the procedure reported[16] by treating calix[4]arene **1** with excess benzoyl chloride in pyridine. Nitration of **2** with nitric acid and acetic acid in CH_2Cl_2 provide selectively mononitrated calix[4]arene **3**, which was alkylated with allyl bromide as well as benzyl bromide in the presence of K_2CO_3 in THF/DMF solution. Allyl group could be utilized as a handle for further reaction and benzyl was chosen because benzyl group could be removed easily. Benzoyl groups were removed by refluxing **4** in aqueous NaOH solution.

The ^{1}H NMR of **4a** showed multiplet at δ 6.06, 5.40 and 4.43 for the five allylic protons and a singlet at δ 3.61 and a pair of doublets at δ 3.80 and 3.65 for the eight bridge methylene protons. The ^{13}C NMR spectrum of **4a** showed one signal at δ 37.05 for the bridge carbons, indicating that **4a** has only *anti* oriented phenol rings[17] which implied **4a** existed as a 1,3-alternate conformation. The ^{1}H NMR spectrum of **5a** appeared as typical monoalkyl calix[4]arene characteristics[18] such as two singlets at δ 9.31 and 8.94 at the ratio of 1 : 2 for the three hydroxy protons and two pairs of doublets at δ 4.40-3.45 for the eight bridge methylene protons. Nitration can be confirmed by a down field shifted singlet of ^{1}H NMR signal for the two nitroaromatic protons, which appeared at δ 7.94. The ^{13}C NMR spectrum of **5a** showed two signals at δ 31.72 and 31.65 for the bridge carbons, indicating that **5a** has only *syn* oriented phenol rings which implied **5a** existed as a cone conformation. The benzyl derivative **5b** also prepared by following the procedure described above for further functionalization by removing benzoyl group selectively. Its NMR spectral data showed the similar characteristics mentioned for **5a**.



Scheme 1. Synthesis of 5-nitro-26-alkyl calix[4]arenes.

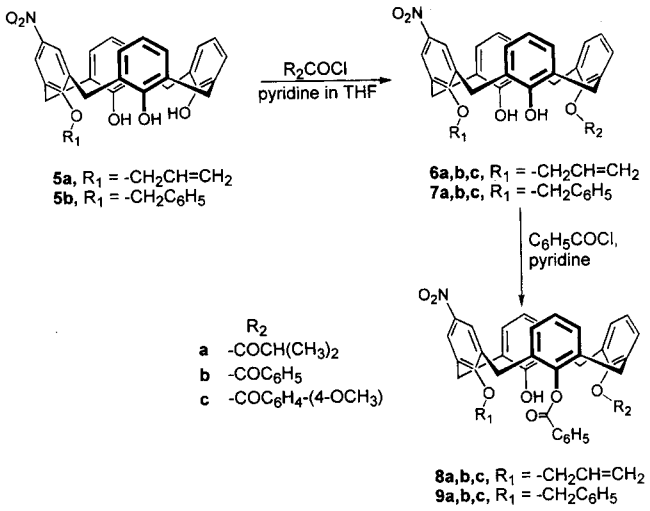
ABCH Type Chiral Calix[4]arenes. Since it is not possible to introduce directly two different acyl groups between the three hydroxy moieties at the lower rim of calix[4]arene, we developed a method to put two different acyl substituents at the lower rim by the two step reactions. Previously, we reported[12,13] that 25-(3,5-dinitrobenzoyloxy)-26,27,28-trihydroxycalix[4]arene and its *p*-*t*-butyl derivative reacted with several acyl chlorides in the presence of pyridine to yield a various AHBH type calix[4]arenes. Following the previous procedure developed by our group, monoallylcalix[4]arene **5a** treated with acyl halides in the presence of pyridine. The AHBH type calix[4]arenes were obtained exclusively when isobutyryl, benzoyl, and 4-methoxybenzoyl chloride were applied. But when acetyl, 4-bromobenzoyl, 3,5-dinitrobenzoyl, and 4-nitrobenzoyl chloride were treated, a mixture of 1,3-disubstituted AHBH type and 1,2-disubstituted ABHH type products was obtained. From this product distribution depending on the acylating agents, it is clear that the more reactive acylating agents such as 3, 5-dinitrobenzoyl, 2-bromobenzoyl, and acetyl chloride produced the mixture of 1,2-and 1,3-product. On the other hand the less reactive acylating agents such as isobutyryl, benzoyl, and 4-methoxybenzoyl chloride produced the exclusive 1,3-product. The less reactive acylating agents obviously could wait more, so the steric effect govern the substitution position. Acylation reaction has been carried out with 2.2 equivalents of acyl chloride in THF in the presence of pyridine. In order to investigate the substituents effect for acylation, benzyl derivative **5b** also was tested with various acyl halides under the same reaction condition described above and obtained the same results as described above for **5a**.

Substitution pattern and conformation of **6** and **7** were confirmed by the NMR spectra. The ^{1}H NMR spectrum of **6a** showed a singlet at δ 7.79 for the two nitroaromatic protons and two pairs of doublets at δ 4.28-3.42 arising from the eight bridge methylene protons, indicating that second substitution was occurred at the opposite side of existing allyl group. The ^{1}H NMR spectrum of other AHBH type calix[4]arenes **6** and **7** showed the similar pattern as described above such as two pairs of doublets at δ 4.40-3.20 for the methylene protons. The IR absorption band of **6a** showed at 3516 cm^{-1} as a sharp singlet for the OH and at 1764 cm^{-1} for the C=O stretching band, indicating that two hydroxy groups are not hydrogen-bonded each other. The IR absorption band of other AHBH type calix[4]arenes **6** and **7** also showed the similar pattern as observed for **6a**. The conformation of 1,3-disubstituted calix[4]arenes **6** and **7** was deduced from the ^{13}C NMR chemical shifts of the bridge methylene carbons. All of those 1,3-disubstituted calix[4]arenes show two peaks at about 32 ppm, indicating that they exist as a cone conformation.

In order to introduce third substituent selectively, disubstituted calix[4]arene **6a** was treated with excess benzoyl chloride in pyridine, assuming that hydroxy groups at the lower rim of calix[4]arene substituted with benzoyl groups until the third substitution occurred. As expected, **6a** reacted with only one benzoyl chloride to yield ABCH type calix[4] arenes **8a** exclusively. The characteristics of asymmetrically substituted calix[4]arene **8a** can be observed from ^{1}H NMR spectrum, which showed two peaks at δ 7.62 and 7.39 with a long range coupled signal (J=2.7 Hz), and four pairs of doublets at δ 4.4-3.3 for the eight bridge methylene protons. The ^{1}H NMR spectrum of other ABCH type calix[4]arenes **8** and **9** also showed the typical chiral calix[4]arene characteristics such as four pairs of doublets at 4.60-3.20 ppm for the eight methylene protons and very complicated aromatic signals. The IR absorption bands of **8a** showed at 3377 cm^{-1} as a broad peak for the OH and two peaks at 1740 cm^{-1} and 1726 cm^{-1} for the ester carbonyl stretching band, indicating that hydroxy group formed intramolecular hydrogen bond with one of ester groups. The similar asymmetric properties were observed with benzyl derivatives **9** in ^{1}H NMR spectrum.

The conformation of ABCH type chiral calix[4]arenes **8** and **9** was deduced from the ^{13}C NMR chemical shifts of the bridge methylene carbons. All of those asymmetrically trisubstituted calix[4]arenes **8** and **9** show four peaks between δ 31-38, two at around δ 38 and two at around δ 32, indicating that they are chiral and exist as a partial cone or 1,2-alternate conformation. X-ray structure analysis showed that **8a** exist as a partial cone conformation. In order to confirm that the asymmetrically substituted compounds **8** and **9** consist of a pair of enantiomers, we measured their ^{1}H NMR spectra in the presence of chiral shift reagents as shown in Figure 1. It was found that Pirkle's reagent[19] ((S)-2,2,2-trifluoro-1-(9-anthryl)ethanol) is very effective. In all six asymmetric compounds peaks shifted slightly upfield and split into more complicated pattern due to doubling even at 25 °C.

X-ray Structure Analysis. All of the crystal data, data collection and refinements of **8a** are summarized in Table 1. The structure was solved by direct method and refined by the full-matrix least-squares using the program



Scheme 2. Synthesis of the ABCH type calix[4]arenes.

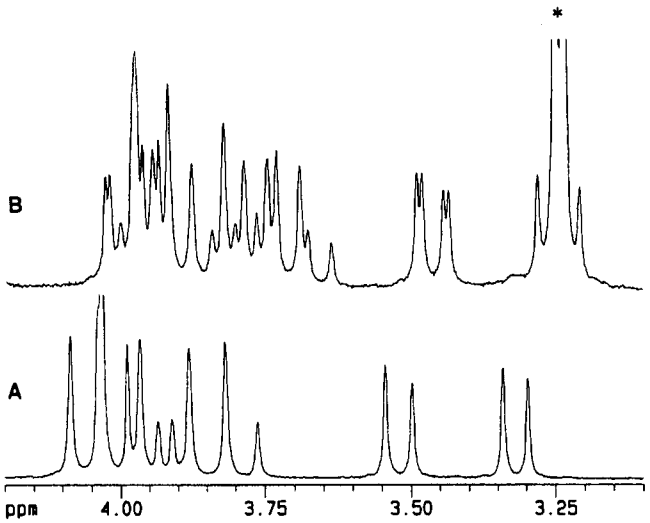


Figure 1. Partial ^{1}H NMR spectra of compound **8a** in $CDCl_3$: (A) in the absence of Pirkle's reagent; (B) in the presence of Pirkle's reagent (3 equiv). *Peak from Pirkle's reagent.

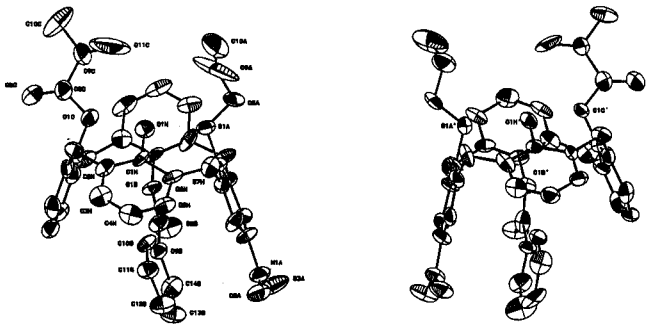
Shelxl-97.[21]

The asymmetric unit is comprised of two independent enantiomeric molecules (1 and 2) in the partial cone conformation in which the benzoyl phenyl group is down as shown in Figure 2 and 3. This conformation is often described with reference to the plane of the macrocyclic ring CH_2 groups. The dihedral angles with the planes of the four phenyl rings are: ring A 65.9, ring B 60.9, ring C 105.7, and ring H 132.8° for molecule 2.

The H atom bonded to the unsubstituted phenol O atom was not located. It is notable, however, the intramolecular distances to the neighboring ether O atoms are likely to be the bifurcated hydrogen bonded: O(1H)···O(1A) 2.706 and O(1H)···O(1C) 2.918 Å for the molecule 1 and O(1H)···O (1A) 2.729 and O(1H)···O(1C) 2.899 Å for molecule 2. These intramolecular hydrogen bonding involving three functional group, hydroxy, allyloxy, and isobutyryloxy could be due to the partial cone conformation. Only the benzoyloxy group for each molecule did not involve the hydro-

Table 1. Summary of Crystal Data

Crystal data	
$C_{42}H_{37}NO_8$	D=1.295 (calc.) gcm^{-3}
Mw=683.73 amu	Mo-Kα Radiation
Monoclinic	λ=0.7107 Å
$P2_1/a$	Cell parameters from 19 reflections
a=19.698 (4) Å	2θ=12°-25°
b=16.874 (4) Å	μ=0.90 mm^{-1}
c=21.994 (4) Å	T=293(2) K
β=106.410(10)°	0.3×0.2×0.6 mm
V=7013.0 (3) Å^3	Pale yellow
Z=8	
Data collection	
Enraf-Nonius CAD-4 Diffractometer	θ_{max}=20°
$\omega/2\theta$ Scan type	h=0→18
Absorption correction: none	k=0→16
6501 independent reflections	l=−21→20
1695 observed reflections [I>2σ(I)]	3 standard reflections monitored every one hour
	intensity variation: none
Refinement	
Refinement on F^2	
R(F)=0.084	$\Delta\rho_{max}$=0.29 eÅ^{-3}
wR(F^2)=0.202	$\Delta\rho_{min}$=-0.31 eÅ^{-3}
S=0.980	Extinction correction: none
6501 reflections	Atomic scattering factors from *International Tables for Crystallography*[22]
991 parameters	
Calculated weights $w=1/[\sigma^2(F_o^2)+(0.1280P)^2+0.00P]$ where $P=(F_o^2+2F_c^2)/3$	



(A) (B)

Figure 2. Molecular conformation of **8a** with atomic numbering: (A) Molecule 1; (B) Molecule 2.

gen bond.

In conclusion, the present paper describes the synthetic pathway for the preparation of ten ABCH type chiral calix [4]arenes. They were synthesized by the two step reaction from monoalkylcalix[4]arenes. All of these asymmetrically substituted ABCH type compounds exist as a partial cone conformation and their racemates were confirmed by the chiral shift reagent in ^{1}H NMR spectra.

Experimental

25,26,27-Tribenzoyloxy-28-hydroxycalix[4]arene

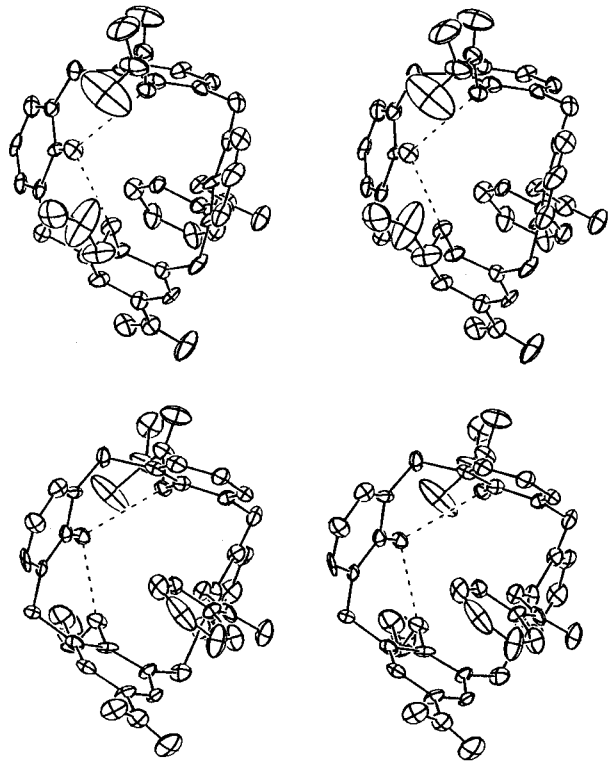


Figure 3. Stereo view of the molecules. The dotted lines are indicated the hydrogen bond. Top: Molecule 1, bottom: Molecule 2.

2 was prepared by the known procedure.[16] mp 274-276 °C (*lit.*[16] 276-277 °C).

5-Nitro-26-hydroxy-25,27,28-tribenzoyloxycalix [4]arene 3 was prepared by the known procedure.[20] mp > 267 °C, dec. (*lit.*[20] 267-268 °C, dec.).

5-Nitro-26-allyloxy-25,27,28-tribenzoyloxycalix [4]arene 4a. A mixture of **3** (4.0 g, 5.12 mmol), K_2CO_3 (2.16 g, 15.4 mmol), and allyl bromide (4.52 mL, 51.2 mmol) in THF (150 mL)/DMF (30 mL) was refluxed for 4 h. The solvents were removed and the residue was acidified and treated with $CHCl_3$ and H_2O. The organic layer separated and removed the solvents. The residue was triturated with methanol. The crude product was recrystallized from $CHCl_3$-MeOH to give 3.0 g (73%) of slight yellowish fine crystals. mp >264 °C, dec. ^{1}H NMR ($CDCl_3$) δ 7.80-6.60 (m, 26H, ArH), 6.06 (m, 1H, -CH=), 5.40 (m, 2H, =CH_2), 4.43 (d, 2H -OCH_2-, J=5.0 Hz), 3.80 and 3.65 (a pair of d, 4H, $ArCH_2Ar$, J=15.1 Hz), 3.61 (s, 4H, $ArCH_2Ar$). ^{13}C NMR ($CDCl_3$) δ 164.26, 163.84, 161.90, 148.16, 147.16, 142.34, 135.76, 134.03, 133.62, 133.45, 133.29, 132.78, 132.04, 131.88, 131.25, 130.89, 130.69, 130.55, 128.53, 128.24, 128.12, 127.63, 126.22, 125.11, 124.84, and 117.56 (-CO_2-, Ar, and -CH=CH_2), 72.14 (-OCH_2-), 37.05 ($ArCH_2$-Ar). IR (KBr, cm^{-1}) 1731 (-CO_2-), 1518 and 1341 (-NO_2).

5-Nitro-26-benzyloxy-25,27,28-tribenzoyloxy-calix[4]arene 4b. Following the procedure described for **4a**, 3.50 g (78%) of **4b** was obtained after recrystallization from $CHCl_3$-MeOH. mp >295 °C, dec. ^{1}H NMR ($CDCl_3$) δ 7.85-6.55 (m, 31H, ArH), 5.01 (s, 2H, -OCH_2-), 3.68 and 3.63 (a pair of d, 4H, $ArCH_2Ar$, J=14.9 Hz), 3.59 (s, 4H, $ArCH_2Ar$). ^{13}C NMR ($CDCl_3$) δ 164.28, 163.98, 162.36, 148.14, 147.85, 142.29, 136.32, 135.78, 134.13, 133.77,

133.45, 133.26, 131.99, 131.87, 131.40, 130.90, 130.84, 130.67, 128.68, 128.56, 128.49, 128.46, 128.19, 127.81, 127.64, 126.40, 124.93, and 124.81 (-CO_2- and Ar), 73.99 (-OCH_2-), 36.97 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 1729 (-CO_2-), 1518 and 1340 (-NO_2).

5-Nitro-26-allyloxy-25,27,28-trihydroxycalix[4]arene 5a. A mixture of **4a** (5.0 g, 6.20 mmol), NaOH (10 g) in THF (120 mL), EtOH (60 mL), and H_2O (50 mL) was refluxed for 12 h. After neutralization, the mixture was extracted with $CHCl_3$ (200 mL), evaporated the solvents, and the crude product was recrystallized in $CHCl_3$-MeOH to give 2.40 g (76%) of pale yellow needles **5a**. mp >175 °C, dec. ^1H NMR ($CDCl_3$) δ 9.31 (s, 1H, OH), 8.94 (s, 2H, OH), 7.94 (s, 2H, O_2NArH), 7.10 (d, 2H, ArH, J=7.5 Hz), 7.06 (d, 2H, ArH), 6.97 (d, 2H, ArH), 6.73 (t, 2H, ArH), 6.67 (t, 1H, ArH), 6.50-6.30 (m, 1H, -CH=), 5.80-5.50 (m, 2H, =CH_2), 4.74 (d, 2H, -OCH_2-), 4.40, 4.22, 3.53, and 3.46 (two pairs of d, 8H, $ArCH_2Ar$, J=13.2 Hz and 13.8 Hz). ^{13}C NMR ($CDCl_3$) δ 156.40, 150.88, 148.67, 145.01, 135.90, 131.36, 129.39, 128.84, 128.49, 128.37, 126.59, 124.87, 122.29, and 121.26 (Ar and -CH=CH_2), 78.24 (-OCH_2-), 31.72 and 31.65 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3372 and 3175 (-OH), 1525 and 1346 (-NO_2).

5-Nitro-26-benzyloxy-25,27,28-trihydroxycalix[4]arene 5b. Following the procedure described for **5a**, 3.2 g (98%) of **5b** was obtained after recrystallization from $CHCl_3$-MeOH. mp 245-247 °C. ^1H NMR ($CDCl_3$) δ 9.22 (s, 1H, OH), 8.88 (s, 2H, OH), 7.98 (s, 2H, O_2NArH), 7.70-6.60 (m, 16H, ArH), 5.26 (s, 2H, -OCH_2-), 4.32, 4.18, 3.48, and 3.43 (two pairs of d, 8H, $ArCH_2Ar$, J=13.2 Hz and 13.8 Hz). ^{13}C NMR ($CDCl_3$) δ 156.46, 150.93, 148.64, 145.04, 136.01, 134.60, 129.53, 129.37, 129.19, 129.00, 128.85, 128.48, 128.38, 128.32, 126.56, 124.94, 122.28, and 121.22 (Ar), 79.90 (-OCH_2-), 31.72 and 31.69 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3308 (-OH), 1525 and 1348 (-NO_2).

5-Nitro-26-allyloxy-28-isobutyryloxy-25,27-dihydroxycalix[4]arene 6a. To a solution of **5a** (0.30 g, 0.59 mmol) in dry THF (40 mL), pyridine (0.12 mL) and isobutyryl chloride (0.16 mL) was added slowly. After 1 h, the solvents were removed and the residue was triturated with MeOH. The crude products were recrystallized from $CHCl_3$-MeOH to give 0.15 g (44%) of **6a**. mp >225 °C, dec. ^1H NMR ($CDCl_3$) δ 7.79 (s, 2H, O_2NArH), 7.11 (d, 4H, ArH), 6.94-6.70 (m, 11H, ArH and OH), 6.32-6.16 (m, 1H, -CH=), 5.71 and 5.44 (m, 2H, =CH_2), 4.58 (d, 2H, -OCH_2-), 4.28, 3.92, 3.49, and 3.41 (two pairs of d, 8H, $ArCH_2Ar$, J= 13.5 Hz and 13.8 Hz), 3.09 (septet, 1H, -CH-), 1.53 (d, 6H, -CH_3, J=7.2 Hz). ^{13}C NMR ($CDCl_3$) δ 174.78 (-CO_2-), 156. 83, 152.78, 144.82, 144.05, 134.89, 132.04, 131.68, 129.31, 128.96, 128.82, 127.93, 126.80, 126.22, 124.74, 120.04, and 119.12 (Ar and -CH=CH_2), 77.30 (-OCH_2-), 34.64 (-CH-), 31.71 and 31.63 ($ArCH_2Ar$), 19.15 (-CH_3). IR (KBr, cm^{-1}) 3516 and 3417 (-OH), 1764 (-CO_2-), 1525 and 1344 (-NO_2).

5-Nitro-26-allyloxy-28-benzoyloxy-25,27-dihydroxycalix[4]arene 6b. Following the procedure described for **6a**, 0.20 g (56%) of **6b** was obtained after recrystallization from $CHCl_3$-MeOH. mp 215 °C, dec. ^1H NMR ($CDCl_3$) δ 8.46-6.71 (m, 16H, ArH), 6.71 (s, 2H, OH), 6.30 (m, 1H, -CH=), 5.83 and 5.57 (m, 2H, -CH_2=), 4.61 (d, 2H, -OCH_2-), 4.27, 4.01, 3.54, and 3.45 (two pairs of d, 8H, $ArCH_2Ar$, J=13.6 Hz, 13.7 Hz, and 13.9 Hz). ^{13}C NMR ($CDCl_3$) δ 164.95 (-CO_2-), 156.93, 152.84, 144.78, 134.88, 133.92, 132.24, 131.83, 130.64, 129.45, 129.04, 128.86, 128.75, 128.01, 126.92, 126.04, 124.85, 120.07, and 119.38 (Ar and -CH=CH_2), 32.02 and 31.95 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3541 and 3431 (-OH), 1731 (-CO_2-), 1523 and 1342 (-NO_2).

5-Nitro-26-allyloxy-28-(4-methoxybenzoyloxy)-25,27-dihydroxycalix[4]arene 6c. Following the procedure described for **6a**, 0.23 g (61%) of 6c was obtained after recrystallization from $CHCl_3$-MeOH. mp >226 °C, dec. ^1H NMR ($CDCl_3$) δ 8.39-6.75 (m, 17H, ArH and OH), 6.40-6.26 (m, 1H, -CH=), 5.78 and 5.54 (two d, 2H, =CH_2), 4.62 (d, 2H, -OCH_2-), 4.28, 4.00, 3.54, and 3.44 (two pairs of d, 8H, $ArCH_2Ar$, J=13.8 Hz and 13.5 Hz), 3.94 (s, 3H, -OCH_3). ^{13}C NMR ($CDCl_3$) δ 164.61, 164.21, 156.99, 152.84, 144.88, 144.71, 134.88, 132.82, 132.34, 131.99, 129.44, 128.99, 128.83, 128.00, 126.85, 126.06, 124.85, 121.16, 120.05, 119.25, and 114.08 (Ar, -CO_2-, and -CH=CH_2), 77.32 (-OCH_2-), 55.55 (-OCH_3), 31.98 and 31.93 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3517 and 3421 (-OH), 1735 (-CO_2-), 1524 and 1343 (-NO_2).

5-Nitro-26-benzyloxy-28-isobutyryloxy-25,27-dihydroxycalix[4]arene 7a. To a solution of **5b** (0.30 g, 0.537 mmol) in dry THF (30 mL), pyridine (0.11 mL) and isobutyryl chloride (0.073 mL) was added slowly at room temperature. After 2 h, removed the solvents and the crude products were recrystallized $CHCl_3$-MeOH to give 0.17 g (53%) of white cotton type crystalline **7a**. mp 275-277 °C. ^1H NMR ($CDCl_3$) δ 7.64 (s, 2H, O_2NArH), 7.70-6.73 (m, 16H, ArH and OH), 5.09 (s, 2H, -OCH_2-), 4.33, 3.87, 3.48, and 3.38 (two pairs of d, 8H, $ArCH_2Ar$, J=13.4 Hz and 13.6 Hz), 2.95 (septet, 1H, -CH-), 1.43 (d, 6H, -CH_3, J=7.0 Hz). ^{13}C NMR ($CDCl_3$) δ 174.74 (-CO_2-), 156.81, 152.83, 144.97, 144.00, 135.29, 135.02, 132.05, 129.33, 128.95, 128.93, 128.87, 128.82, 128.14, 127.95, 126.79, 126.27, 124.83, and 120.07 (Ar), 79.07 (-OCH_2-), 34.60 (-CH- from isobutyryl), 31.76 and 31.62 ($ArCH_2Ar$), 19.16 (-CH_3). IR (KBr, cm^{-1}) 3487 and 3358 (-OH), 1760 (-CO_2-), 1525 and 1349 (-NO_2).

5-Nitro-26-benzyloxy-28-benzoyloxy-25,27-dihydroxycalix[4]arene 7b. Following the procedure described for **7a**, 0.20 g (56%) of **7b** was obtained as colorless crystals. mp >261 °C, dec. ^1H NMR ($CDCl_3$) δ 8.40-6.60 (m, 21H, ArH), 6.56 (s, 2H, OH), 5.13 (s, 2H, -OCH_2-), 4.30, 3.99, 3.47, and 3.42 (two pairs of d, 8H, $ArCH_2Ar$, J= 13.4 Hz and 13.6 Hz). ^{13}C NMR ($CDCl_3$) δ 164.97 (-CO_2-), 157.15, 152.82, 144.83, 144.65, 135.40, 134.85, 133.79, 132.10, 130.48, 129.45, 129.13, 128.99, 128.88, 128.85, 128.81, 127.99, 126.88, 126.22, 124.83, 120.07, and 98.93 (Ar), 79.13 (-OCH_2-), 31.84 and 31.76 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3516 and 3422 (-OH), 1750 (-CO_2-), 1522 and 1348 (-NO_2).

5-Nitro-26-benzyloxy-28-(4-methoxybenzoyloxy)-25,27-dihydroxycalix[4]arene 7c. Following the procedure described for **7a**, 0.18 g (49%) of **7c** was obtained as colorless crystals. mp 284-286 °C. ^1H NMR ($CDCl_3$) δ 8.30 (d, 2H, ArH, J=8.8 Hz), 7.80 (s, 2H, O_2NArH), 7.66-6.72 (m, 16H, ArH), 6.66 (s, 2H, OH), 5.13 (s, 2H, -OCH_2-), 4.34, 3.99, 3.49, and 3.42 (two pairs of d, 8H, $ArCH_2Ar$, J=13.6 Hz, 13.7 Hz, 13.7 Hz, and 13.8 Hz), 3.91 (s, 3H, -CH_3). ^{13}C

NMR ($CDCl_3$) δ 164.62, 164.14, 157.20, 152.86, 144.87, 144.68 ,135.58, 134.88, 135.58, 134.88, 132.66, 132.21, 129. 46, 129.13, 128.94, 128.83, 128.78, 126.78, 126.26, 121.04, 120.06, and 114.25 (-CO_2- and Ar), 79.06 (-OCH_2-), 55.58 (-OCH_3), 31.82 and 31.76 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3526 (-OH), 1736 (-CO_2-), 1523 and 1352 (-NO_2).

5-Nitro-26-allyloxy-25-benzoyloxy-28-isobutyryloxy-27-hydroxycalix[4]arene 8a. To a solution of **6a** (0.30 g, 0.518 mmol) in pyridine (40 mL), benzoyl chloride (1.8 mL) was added slowly at room temperature. The reaction mixture was stirred for 12 h, and then 50 mL of $CHCl_3$ was added. The organic layer washed with water, separated, and evaporated. The residue was triturated with MeOH, filtered, and dried. Recrystallization of crude products from $CHCl_3$-MeOH gave 0.24 g (68%) of pale yellowish needles **8a**. mp >230 °C, dec. ^{1}H NMR ($CDCl_3$) δ 7.62 (d, 1H, O_2NArH, J=2.7 Hz), 7.39 (d, 1H, O_2NArH, J= 2.7 Hz), 7.25-7.18 (m, 7H, ArH), 7.12 (t, 1H, ArH, J=7.5 Hz), 6.90-6.22 (m, 7H, ArH and OH), 6.00-5.84 (m, 1H, -CH=), 5.30 (m, 2H, =CH_2), 4.60-4.31 (m, 2H, -OCH_2-), 4.09, 4.08, 3.99, 3.97, 3.88, 3.77, 3.51, and 3.03 (four fairs of d, 8H, $ArCH_2Ar$, J=16.5 Hz, 13.8 Hz, 12.6 Hz, and 16.8 Hz), 2.59 (septet, 1H, -CH-), 1.29, 1.27, 1.26, and 1.24 (a pair of d, 6H, -CH_3, J=7.2 Hz). ^{13}C NMR ($CDCl_3$) δ 174.99, 162.98 (-CO_2-), 157.54, 152.74, 148.14, 146.56, 143.69, 134.61, 134.16, 133.36, 133.01, 132.88, 131.71, 131.22, 131.01, 129.95, 129.63, 129.49, 129.35, 129.18, 129.09, 128.39, 128.36, 127.30, 125.76, 125.70, 125.15, 125.06, 124.66, 120.01, and 119.81 (Ar and -CH=CH_2), 74.80 (-OCH_2-), 37.99, 37.87, 31.70, and 31.19 ($ArCH_2Ar$), 34.15, 19.22, and 18.61 (-$CH(CH_3)_2$). IR (KBr, cm^{-1}) 3377 (-OH), 1740 and 1726 (-CO_2-), 1522 and 1343 (-NO_2).

5-Nitro-26-allyloxy-25,28-bisbenzoyloxy-27-hydroxycalix[4]arene 8b. Following the procedure described for **8a**, 0.24 g (60%) of **8b** was obtained as pale yellow crystals. mp >210 °C, dec. ^{1}H NMR ($CDCl_3$) δ 7.92 (d, 2H, ArH), 7.68 and 7.40 (two d, 2H, O_2NArH, J=2.7 Hz), 7.63 (t, 1H, ArH, J=7.5 Hz), 7.42 (t, 2H, ArH, J=7.5 Hz), 7.30-6.40 (m, 14H, ArH and OH), 6.32 (t, 1H, ArH), 6.10 (m, 1H, -CH=), 5.48 and 5.45 (two d, 2H, =CH_2), 4.74-4.36 (m, 2H, -OCH_2-), 4.07, 4.05, 4.04, 3.97, 3.91, 3.77, 3.54, and 3.34 (four pairs of d, 8H, $ArCH_2Ar$, J=16.2 Hz, 15.9 Hz, 14.1 Hz, and 12.9 Hz). ^{13}C NMR ($CDCl_3$) δ 164.58, 162.98 (-CO_2-), 157.75, 152.71, 147.93, 146.53, 143.75, 134.61, 134.41, 133.28, 133.16, 132.96, 131.98, 131.59, 131.06, 130.65, 130.53, 129.68, 129.37, 129.29, 129.26, 129.22, 129.00, 128.51, 128.42, 128.07, 127.39, 127.34, 125.87, 125.70, 125.16, 124.89, 124.77, 120.56, and 119.96 (Ar and -CH=CH_2), 75.42 (-OCH_2-), 37.79, 31.84, and 31.27 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3411 (-OH), 1724 (-CO_2-), 1524 and 1343 (-NO_2).

5-Nitro-26-allyloxy-25-benzoyloxy-28-(4-methoxybenzoyloxy)-27-hydroxy-calix[4]arene 8c. Following the procedure described for **8a**, 0.16 g (70%) of **8c** was obtained as colorless crystals. mp 234-237 °C, dec. ^{1}H NMR ($CDCl_3$) δ 7.83 (d, 2H, ArH, J=8.88 Hz), 7.67 and 7.40 (two d, 2H, O_2NArH, J=2.7 Hz), 7.30-6.80 (m, 12H, ArH), 6.63-6.45 (m, 4H, ArH and OH), 6.32 (t, 1H, ArH), 6.00-6.20 (m, 1H, -CH=), 5.47 (two d, 2H, =CH_2), 4.69-4.39 (m, 2H, -OCH_2-), 4.10, 4.07, 4.00, 3.96, 3.90, 3.80, 3.56, and 3.37 (four pairs of d, 8H, $ArCH_2Ar$, J=13.2 Hz, 13.9 Hz, 15.1 Hz, and 16.1 Hz), 3.92 (s, 3H, -OCH_3). ^{13}C NMR ($CDCl_3$) δ 164.28, 163.69, 163.05, 158.01, 152.74, 147.98, 146.58, 143.74, 134.71, 134.45, 133.37, 133.19, 133.00, 132.82, 132.15, 131.86, 131.14, 130.57, 129.73, 129.34, 129.28, 129.22, 129.05, 128.56, 128.43, 127.44, 125.84, 125.76, 125.23, 125.13, 124.77, 121.60, 120.04, and 119.99 (-CO_2-, Ar, and -CH=CH_2), 75.42 (-OCH_2-), 55.46 (-OCH_3), 37.83, 31.86, and 31.33 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3385 (-OH), 1728 (-CO_2-), 1532 and 1342 (-NO_2).

5-Nitro-26-benzyloxy-25-benzoyloxy-28-isobutyryloxy-27-hydroxycalix[4]arene 9a. To a solution of **7a** (0.30 g, 0.50 mmol) in pyridine (60 mL), benzoyl chloride (1.4 mL) was added slowly at room temperature. After 12 h, followed the procedure for **8a** and 0.34 g (74%) of **9a** was obtained as yellow crystals. mp >255 °C, dec. ^{1}H NMR ($CDCl_3$) δ 7.62 (d, 1H, O_2NArH), 7.44-6.17 (m, 21H, ArH and OH), 5.14 and 4.80 (a pair of d, 2H, -OCH_2-, J= 10.8 Hz), 4.11-3.26 (four pairs of d, 8H, $ArCH^2Ar$), 2,49 (septet, 1H, -CH-), 1.21 and 1.18 (two d, 6H, -CH_3). ^{13}C NMR ($CDCl_3$) δ 174.85, 162.97 (-CO_2-), 158.09, 152.76, 148.19, 146.45, 143.70, 134.83, 134.66, 134.29, 133.36, 133.00, 132.70, 131.73, 131.35, 130.63, 129.89, 129.52, 129.39, 129.27, 129.24, 129.16, 128.94, 128.71, 128.39, 128.34, 128.29, 128.21, 127.58, 127.29, 125.69, 125.66, 125.28, 124.72, and 119.94 (Ar), 34.02 (-CH-), 37.95, 31.70, and 31.11 (ArCH2Ar), 19.30 and 18.54 (-CH_3). IR (KBr, cm^{-1}) 3377 (-OH), 1743 and 1726 (-CO_2-), 1525 and 1348 (-CO_2-).

5-Nitro-26-benzyloxy-25,28-bisbenzoyloxy-27-hydroxycalix[4]arene 9b. Following the procedure described for **8a** and 0.25 g (60%) of **9b** was obtained as colorless crystals. mp >260 °C, dec. ^{1}H NMR ($CDCl_3$) δ 7.95 (d, 4H, ArH), 7.60 (t, 2H, ArH), 7.50-6.20 (m, 22H, ArH and OH), 5.18 and 4.86 (a pair of d, 2H, -OCH_2-, J=11.7 Hz), 4.04, 4.11, 3.86, 3.82, 3.77, 3.71, 3.28, and 3.24 (four pairs of d, 8H, $ArCH_2Ar$, J=12.9 Hz, 15.9 Hz, and 15.6 Hz). ^{13}C NMR ($CDCl_3$) δ 164.94, 163.55 (-CO_2-), 153.05, 152.68, 148.12, 146.72, 135.81, 133.16, 133.14, 133.05, 132.81, 132.71, 132.59, 132.47, 131.80, 130.73, 130.36, 130.30, 130.22, 129.66, 129.46, 129.35, 129.30, 129.25, 128.89, 128.68, 128.64, 128.47, 128.41, 128.14, 127.32, 126.32, 125.34, 125.26, 125.18, and 119.18 (Ar), 77.34 (-OCH_2-), 38.01, 37.80, 31.70, and 31.11 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3448 (-OH), 1733 and 1722 (-CO_2-), 1521 and 1348 (-NO_2).

5-Nitro-26-benzyloxy-25-benzoyloxy-28-(4-methoxybenzoyloxy)-27-hydroxy-calix[4]arene 9c. Following the procedure described for **8a** and 0.29 g (84%) of **9c** was obtained as yellow crystals. mp >255 °C, dec. ^{1}H NMR ($CDCl_3$) δ 7.80 (d, 2H, ArH), 7.64 (d, 1H, O_2NArH), 7.44-6.28 (m, 22H, ArH and OH), 5.20 and 4.94 (a pair of d, 2H, -OCH_2-, J=11.4 Hz), 4.05-3.30 (four pairs of d, 8H, $ArCH_2Ar$), 3.90 (s, 3H, -CH_3). ^{13}C NMR ($CDCl_3$) δ 164.15, 163.73, 163.10, 158.61, 152.72, 148.07, 146.48, 143.61, 135.24, 134.90, 134.45, 133.32, 133.20, 132.85, 132.76, 132.21, 131.22, 130.54, 129.79, 129.27, 129.24, 129.04, 128.81, 128.70, 128.48, 128.42, 127.45, 125.89, 125.68, 125.60, 125.33, 124.91, 121.41, 119.97, and 113.54 (-CO_2- and Ar), 77.12 (-OCH_2-), 55.51 (-OCH_3), 37.94, 37.79, 31.78, and 31.29 ($ArCH_2Ar$). IR (KBr, cm^{-1}) 3370 (-OH), 1747 and 1726 (-CO_2-), 1521 and 1347 (-NO_2).

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A Mechanistic Study on Addition Reactions of Alicyclic Amines to 3-Butyn-2-one

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Second-order rate constants have been measured spectrophotometrically for the addition reaction of a series of alicyclic amines to 3-butyn-2-one to yield their respective enamines at 25.0 °C. The reactivity of the amines increases with increasing the basicity of the amines. However, the Brönsted-type plot obtained exhibits a downward curvature as the basicity of the amines increases, *i.e.* β_{nuc} decreases from 0.3 for low basic amines ($pK_a <$ 9) and to 0.1 for highly basic amines ($pK_a > 9$). Such a curvature in the Brönsted-type plot is clearly indicative of a change in the reaction mechanism or transition state structure. From the corresponding reactions run in D_2O, the magnitude of kinetic isotope effect (KIE) has been calculated to be about 0.8 for highly basic amines and 1.21 for weakly basic amines. The difference in the magnitude of KIE also supports a change in the reaction mechanism or transition state structure upon changing the basicity of the amines. Furthermore, the small KIE clearly suggests that H^+ transfer is not involved in the rate-determining step, *i.e.* the addition reaction is considered to proceed via a stepwise mechanism in which the attack of the amines to the acetylene is the rate-determining step. The curvature in the Brönsted-type plot has been attributed to a change in the degree of bond formation between the amine and the acetylene.

Introduction

Nucleophilic additions to carbon carbon triple bonds have been widely investigated due to synthetic interests.[1-5] Particularly, additions of nitrogenous nucleophiles to acetylenes with electron withdrawing groups such as COR, CO_2R, CN and SO_2R have been frequently employed as a route to a variety of heterocyclic compounds.[5] The types of het-