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Synthesis of novel calix[4]arenes containing one and two substituents on the "upper rim"

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Procedures are described for the removal of the *p*-butyl groups from *p-tert*-butylcalix[4]arene and the introduction of benzoyl, nitro, amino and acrylamido groups to yield a series of mono- and bis-substituted compounds on the "upper rim" with potential possibility to polymerized with other monomers. These compounds have been characterized by IR, ^{1}H NMR, elemental analysis and ESI-MS. As the upper rim of the calix[4]arene, which has the site group of polymerization, can be linked into the chains of the polyimides, the ultimate goal of the project is to find a new application for the well established binding properties of calix[4]arene and to develop polyimides that are suitable for the recovery of metal ions from waste water, gas separation and ion-specific electrodes.

Keywords: *p-tert*-Butylcalix[4]arene, upper rim, monomers, polymer

IPC Code: Int Cl.[8] C07C

Calixarenes, which are basket-shaped macrocyclic compounds of potential interest for host-guest complexation studies, were first synthesized by Zinke and Ziegler[1] in 1941 by the base-induced condensation of a *p*-alkylphenol with formaldehyde.

The introduction of functionality into calixarenes continues to be one of the major goals in the rapidly expanding chemistry of these compounds[2]. The methods have been devised for the synthesis of calixarenes contained one and two functional groups on the "upper rim" with potential possibility to polymerized with itself or other monomers in our research.

p-tert-Butylcalix[4]arene **1**, has become one of the most accessible of all of the known macrocyclic cavity-containing compounds, obtainable in greater than 50% yield from the base-induced condensation of *p-tert*-butylphenol and formaldehyde[3], provides a convenient starting material for the preparation of calixarenes carrying a wide variety of groups on both the upper and lower rims[4]. In the present paper, the focus shifts to the upper rim of these compounds, employing the nitro group as precursor to amino group and then acrylamido group which has potential capability to polymerized with itself or other monomers.

Recently, calixarenes and derivatives have become the top topic in supermolecular chemistry research[5-7]. Bonding calixarene to the polymer to get the material with molecular recognition ability affords new approach and theoretical foundation in developing new functional material.

Results and Discussion

p-tert-Butylcalix[4]arene **1** is readily accessible in greater than 50% yield which provides the starting point for the present investigation. The removal of the *p*-butyl groups from **1** has been shown to proceed smoothly to afford calix[4]arene **2** in 78% yield, and this compound would appear to be perfectly adapted to functionalization in the aryl ring at the positions *para* to the hydroxyl groups. Excessive benzoyl chloride in the presence of pyridine reacts with calix[4]arene yields only a tribenzoate **3** with 82% yield which is easily accessed for the selective functionalization of a calixarene. The synthesis of the tribenzoate of calix[4]arene provides the possibility of preparing mono-nitrocalix[4]arene via normal nitration route. Treatment of the tribenzoate with 65% nitric acid gives a 94% yield of pure 5-nitro-25-hydroxy-26, 27, 28-tribenzoyloxycalix[4]arene **4**. The benzoyl groups can be removed to yield the mono-nitrocalixarene **5** with 75% yield. This compound can easily be reduced by $SnCl_2.2H_2O$ to produce the mono-amidocalix[4]arene **6** with 50% yield. Treatment of the mono-amidocalix[4]arene **6** with acrylic chloride in the presence of a small amount triethylamine is a conventional method for producing 5-acrylamido-25,

26, 27, 28-tetrahydroxycalix[4]arene **7** which can be used to polymerized with itself or other monomers to obtain a new kind of material with special functions. 5-Nitro-25-hydroxy-26, 27, 28-tribenzoyloxycalix[4]-arene **4** can be directly reduced to afford 5-amino-25-hydoxy-26, 27 28-tribenzoyloxycalix[4]arene **8** with 63% yield by $SnCl_2.2H_2O$. Treatment of this compound with acrylic chloride produces the mono-acrylamidecalix[4]arene **9** which can also be polymerized with itself or other monomers.

To our surprise, if the portion of the benzoyl chloride was reduced and the conditions used as stated in **Scheme I**, 25, 27-dibenzoyloxy-26,28-dihydroxy-calix[4]arene **10** was easily yielded from calix[4]arene **2** in 81% yield. This unexpected but easy access to the bisbenzoate affords a means for the synthesis of bis-substitution in the upper rim of a calixarene which was shown in **Scheme II**.

5, 17-Dinitro-26, 28-dibenzoyloxy-25,27-dihydroxycalix[4]arene **11**, 5, 17-dinitro-25, 26, 27, 28-tetrahydroxycalix[4]arene **12**, 5, 17-amino-25, 26, 27, 28-tetrahydroxycalix[4]arene **13**, and 5, 17-diacryl-amido-25, 26, 27, 28-tetrahydroxycalix[4]arene **14** were readily synthesized under the almost same but little modified conditions respectively which were used in **Scheme I** with reasonable yields.

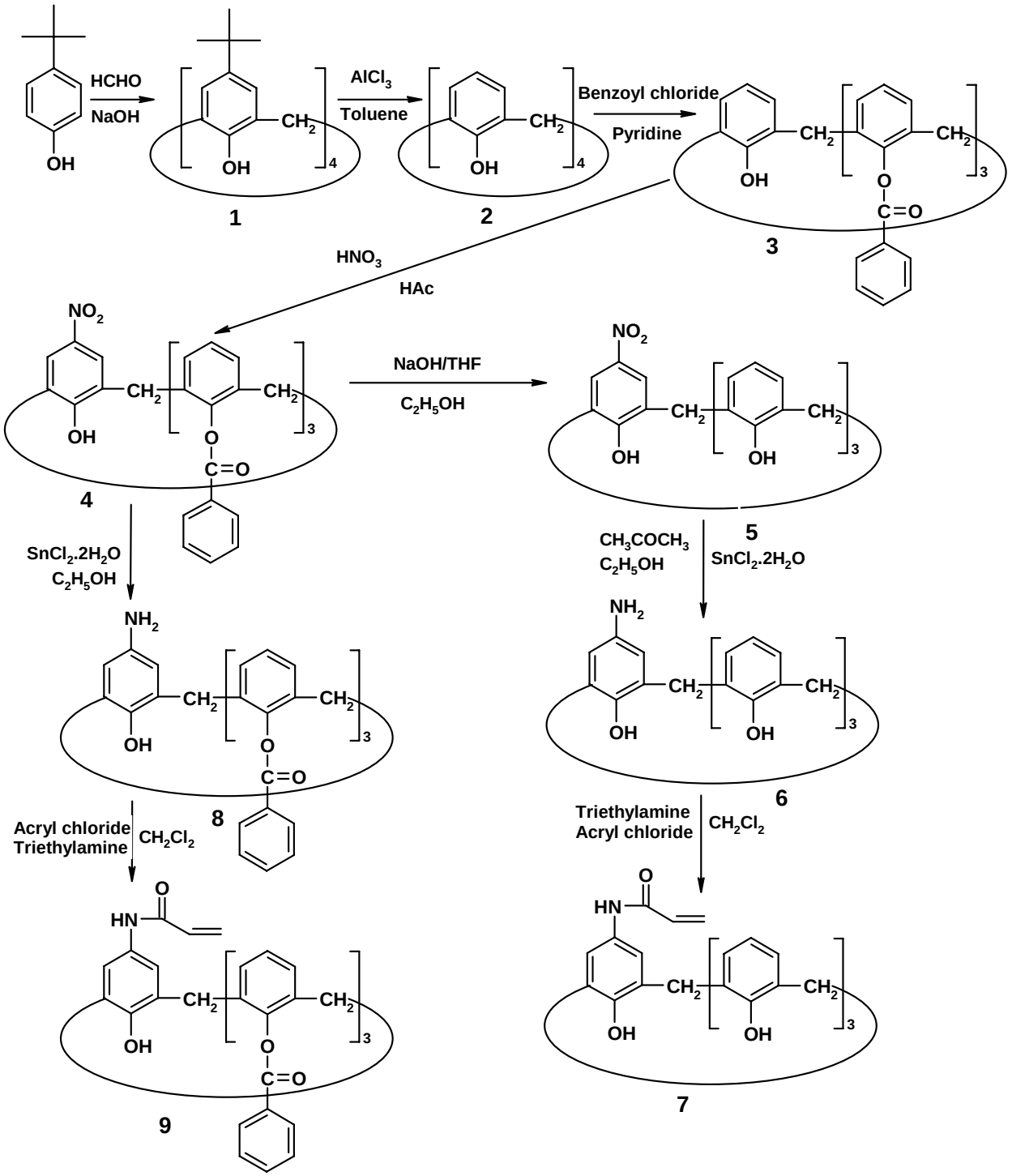
Experimental Section

Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. The melting points of all compounds were measured with a thermal analysis system (Perkin-Elmer 7 Series). The ^{1}H NMR was recorded in $CDCl_3$ on a Bruker Avance 400 instrument at 400 MHz. Elemental analyses were performed on a Perkin-Elmer-240 instrument. Infrared spectra were determined on a Nicolet NEXUS-670 spectrometer. In this paper, *p-tert*-butylcalix[4]arene **1**, 25,26,27,28-Tetrahydroxycalix[4]arene **2**, 25, 26, 27-tribenzoyloxy-28-hydroxycalix[4]arene **3** and 5-nitro-25-hydroxy-26, 27, 28-tribenzoyloxycalix[4]arene **4** were synthesized in our laboratory according to methods already reported[8-11].

5-Nitro-25,26,27,28-tetrahydroxycalix[4]arene 5. 5-Nitro-25, 26, 27, 28-tetrahydroxycalix[4]arene **4** (1.56 g, 2 mmole) was dissolved in THF (40 mL), treated with ethanol (40 mL) and NaOH solution (20 mL) containing sodium hydroxide (4 g). The mixture was refluxed for 6 hr at about 70°C. The volatile organic layer was evaporated and the solution was neutralized by HCl until *p*H reaching 2. This mixture was filtrated, washed with water and ether to afford 0.7g (75%) of pure yellow solid powder, yield 75%; m.p.>300°C; IR (KBr): 3427, 2932, 1590, 1451, 1521, 1343, 1278 cm^{-1}; ^{1}H NMR ($CDCl_3$):δ 10.14 (s, 4H, Ar-OH), 7.98 (s, 2H, ArH), 7.12-7.04 (d, 6H, ArH), 6.81-6.71 (t, 3H, ArH), 4.23-3.62 (2s, 8H, Ar-CH_2-Ar); ESI-MS: m/z 470 (M+1); Anal. Calcd for $C_{28}H_{23}NO_6$: C, 71.57; H, 4.90; N, 2.98. Found: C, 71.55; H, 4.87; N, 2.99%.

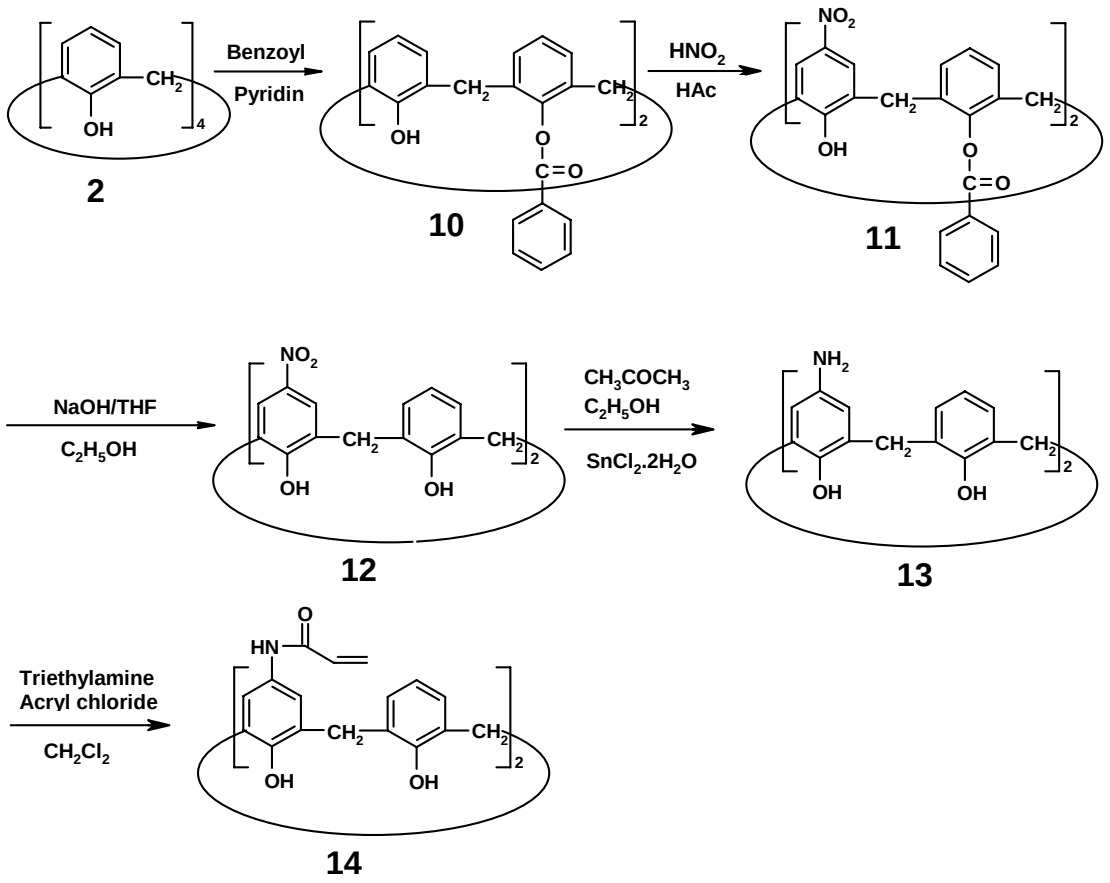
5-Amino-25,26,27,28-tetrahydroxycalix[4]arene 6. A mixture containing 5-nitro-25, 26, 27, 28-tetrahydroxycalix[4]arene **5** (1.1 g) and $SnCl_2.2H_2O$ (6 g) in ethanol (20 mL), acetone (20 mL) and $CHCl_3$ (100 mL) was refluxed at about 70ºC for 18 hr. The reaction was quenched by the addition of ice-water (100 mL). The *p*H value was adjusted to 7 with $NH_3.H_2O$. The slurry was removed by filtration and washed by ethanol and CH_2Cl_2 and the solution was leached by CH_2Cl_2. The organic phase was separated and evaporated to give 0.5 g of blue-green powder, yield 80%; m.p. 117ºC; IR(KBr): 3196, 2944, 1610, 1590, 1467, 1259 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 10.12 (s, 4H, Ar-OH), 7.07-7.01 (m, 6H, ArH), 6.75-6.71 (t, 3H, ArH), 6.39 (s, 2H, ArH), 4.24-4.10, 3.54-3.40 (2s, 8H, Ar-CH_2-Ar), 3.74-3.69 (m, 2H, NH_2); ESI-MS: m/z 440 (M+1); Anal. Calcd for $C_{28}H_{25}NO_4$: C, 76.45; H, 5.69; N, 3.19. Found: C, 76.42; H, 5.67; N, 3.20%.

5-Acrylamido-25, 26, 27, 28-tetrahydroxycalix[4]arene 7. 5-Amino-25,26,27,28-tetrahydroxycalix[4]arene **6** (3 g, 6.8 mmole) was dissolved in CH_2Cl_2 (100 mL) and triethylamine (3 mL). Acrylic chloride (15 mL) was added dropwise at ice-temp. to the contents and the solution was stirred for about 1 hr. A portion of water (100 mL) was added to quench the reaction. The solution was washed with diluted NaOH solution, water and CH_2Cl_2 until the *p*H value reached **7**. The CH_2Cl_2 phase was separated and evaporated to afford a kind of deep brown liquid in which acetone and water were added. The water insoluble material was collected by filtration to give milk white power, yield 85%; m.p. 189ºC; IR(KBr): 3448, 1735, 1632 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 10.15 (s, 4H, Ar-OH), 7.18~6.41 (m, 12H, Ar-H), 6.36~6.31 (m, 1H, Ar-NH), 6.18~6.12 (t, 1H, -CH=C-), 5.74-5.72 (d, 2H, -C=CH_2), 4.32-4.28 (2d, 8H, Ar-CH_2-Ar); ESI-MS: m/z 494 (M+1); Anal. Calcd for $C_{31}H_{27}NO_5$: C, 75.37; H, 5.47; N, 2.84. Found: C, 75.25; H, 5.44; N, 2.80%.



Scheme I

5-Amino-25-hydoxy-26, 27, 28-ribenzoyloxy-calix[4]arene 8. 5-Nitro-25-hydroxy-26, 27, 28-tribenzoyloxycalix[4]arene **4** (1.56 g, 2 mmoles) and $SnCl_2.2H_2O$ (4.8 g) in ethanol (50 mL) without water was refluxed for 18 hr and the mixture was poured into ice-water (100 mL) and stirred. $NH_3.H_2O$ was used to adjust the *p*H value to **8** and the compound was filtered and washed with ethanol and CH_2Cl_2. The organic phase was separated and CH_2Cl_2 was evaporated to give pink powder, yield 63%; m.p.



Scheme II

218ºC; IR (KBr): 3438, 2923, 1730, 1267 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.08-6.59 (m, 26H, Ar-H), 6.34 (s, 1H, Ar-OH), 3.79-3.65 (m, 8H, Ar-CH_2-Ar), 3.46-3.42 (m, 2H, NH_2); ESI-MS: m/z 752 (M+1); Anal. Calcd for $C_{49}H_{37}NO_7$: C, 78.21; H, 5.92; N, 1.86. Found: C, 78.16; H, 4.87; N, 1.87%.

5-Acrylamido-25-hydroxy-26, 27, 28-tribenzoyloxycalix[4]arene 9. 5-Amino-25-hydoxy-26,27,28-tribenzoyloxycalix[4]arene **8** (0.38 g, 0.5 mmole) was dissolved in CH_2Cl_2 (20 mL) and triethylamine (0.4 mL), treated with acrylic chloride (0.5 mL) and stirred for 30 min at ice temperature. The mixture was then allowed to slowly warm to room temperature for another 2 hr. A small portion of water was added to quench the reaction and the mixure was washed by diluted HCl, diluted NaOH and CH_2Cl_2 until the *p*H value was **7**. The CH_2Cl_2 phase was separated and evaporated to give deep brown liquid. Upon the addition of petroleum ether, solid powder formed which was recrystallized by CH_2Cl_2/petroleum ether to afford pink powder, yield 87%; m.p. 254°C; IR (KBr): 3531, 3320, 3061, 1730, 1600, 1265 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.08-50 (m, 27H, ArH, CH=C-), 6.14-5.76 (m, 2H, C=CH_2), 5.76-.31 (m, 2H,-OH and –NH), 3.85-3.44 (m, 8H, Ar-CH_2-Ar); ESI MS: m/z 806 (M+1); Anal. Calcd for $C_{52}H_{39}NO_8$: C, 77.50; H, 4.88; N, 1.74. Found: C, 77.45; H, 4.88; N, 1.74%.

25, 27-Dibenzoyloxy-26, 28-dihydroxycalix[4]arene 10. 25, 26, 27, 28-Tetrahydroxycalix[4]arene **2** (1.7g, 4 mmoles) was dissolved in pyridine (60 mL) and benzoyl chloride (1.5 mL) was added at ice-bath. The mixture was stirred at 0°C for 2 hr and allowed to slowly warm to room temperature for another 2 hr. A portion of water (3000 mL) was added, and the water insoluble material was collected by filtration. Recrystallization from MeOH-$CHCl_3$ afforded thin, colorless plates, yield 47%; m.p. 280°C; IR (KBr): 3523, 1742 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.39-6.70 (m, 22H, ArH), 5.52 (s, 2H, ArOH), 4.02-3.98 (d, 4H, Ar-CH_2-Ar), 3.55-3.51 (d, 4H, Ar-CH_2-Ar); ESI-MS: m/z 633 (M+1); Anal. Calcd for $C_{42}H_{32}O_6$: C, 79.73; H, 5.10. Found: C, 79.70; H, 5.09%.

5, 17-Dinitro-26, 28-dibenzoyloxy-25, 27-dihydroxycalix[4]arene 11. 25,27-Dibenzoyloxy-26, 28-dihydroxycalix[4]arene **10** (1.1g, 1.7 mmole) was dissolved in $CHCl_3$ (60 mL) and acetic acid (2 mL) and 65% HNO_3 (0.5 mL) were added at room temperature. The mixure was stirred for 1 hr. When the reaction was completed the organic phase was separated and washed by NaOH solution, H_2O and $CHCl_3$, respectively. The $CHCl_3$ was evaporated to yield yellow crude product. Recrystallization from MeOH-$CHCl_3$ afforded thin, yellow plates, yield 81%; m.p. 256°C; IR (KBr): 3481, 3065, 1601, 1452, 2926, 1735, 1522, 1340, 1657, 1266 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.34~7.53 (m, 20H, ArH), 6.34 (s, 2H, ArOH), 4.02-3.94 (d, 4H, Ar-CH_2-Ar), 3.71-3.65 (d, 4H, Ar-CH_2-Ar); ESI-MS: m/z 724 (M+1); Anal. Calcd for $C_{42}H_{32}N_2O_{10}$: C, 69.80; H, 4.18; N, 3.88. Found: C, 69.75; H, 4.17; N, 3.87%.

5, 17-Dinitro-25, 26, 27, 28-tetrahydroxycalix[4]arene 12. 5, 17-Dinitro-26, 28-dibenzoyloxy-25, 27-dihydroxycalix[4]arene **11** (2.9 g, 4 mmoles) was dissolved in THF (80 mL), treated with ethanol (80 mL) and NaOH solution (40 mL) containing sodium hydroxide (8 g). The mixture was refluxed for 6 hr at about 70°C. The volatile organic layer was evaporated and the solution was neutralized by HCl until *p*H reaching 2. This mixture was filtrated and washed with water and ether to afford pure yellow solid powder, yield 24%; m.p.>256ºC; IR (KBr): 3418, 3088, 1595, 1454, 1519, 1344, 1269 cm^{-1}; ^1H NMR ($CDCl_3$): δ 10.13 (s, 4H, Ar-OH), 7.99 (s, 4H, ArH), 7.18-7.17 (d, 4H, ArH), 6.89-6.85 (t, 3H, ArH), 4.29-3.47 (2s, 8H, Ar-CH_2-Ar); ESI-MS: m/z 515 (M+1); Anal. Calcd for $C_{28}H_{22}N_2O_8$: C, 65.37; H, 4.31; N, 5.44. Found: C, 65.35; H, 4.27; N, 5.47%.

5, 17-Amino-25, 26, 27, 28-tetrahydroxycalix[4]arene 13. 5, 17-Dinitro-25, 26, 27, 28-tetrahydroxycalix[4]arene **12** (1.2 g, 2 mmoles) and $SnCl_2.2H_2O$ (14 g) in ethanol (40 mL), acetone (40 mL) and $CHCl_3$ (100 mL) was refluxed at about 70° for 18 hr. The reaction was quenched by the addition of ice water (100 mL). The *p*H value was adjusted to 7 with $NH_3.H_2O$. The slurry was removed by filtration and washed by ethanol and $CHCl_3$ and the solution was extracted with $CHCl_3$. The organic phase was separated and evaporated to give blue-green powder, yield 61%; m.p. 123°C; IR (KBr): 3176, 2958, 1600, 1590, 1463, 1272 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.56 (br, 4H, Ar-OH), 7.53~7.51 (d, 4H, ArH), 7.44 (s, 4H, ArH), 6.65 (t, 2H, ArH), 4.24~4.10, 3.54~3.40 (2s, 8H, Ar-CH_2-Ar); ESI-MS: m/z 455 (M+1); Anal. Calcd for $C_{28}H_{26}N_2O_4$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.93; H, 5.74; N, 6.18%.

5, 17-Diacrylamido-25, 26, 27, 28-tetrahydroxycalix[4]arene 14. 5-Amino-25, 26, 27, 28-tetrahydroxycalix[4]arene **6** (3.1 g, 6.8 mmoles) was dissolved in $CHCl_3$ (100 mL) and triethylamine (3 mL). Acrylic chloride (30 mL) was added at ice temp. to the contents and the solution was stirred for about 1 hr. Water (100 mL) was added to quench the reaction. The solution was washed with diluted NaOH solution, water and $CHCl_3$ until the *p*H value reached 7. The CH_2Cl_2 phase was separated and evaporated to afford deep brown liquid in which acetone and water were added, and the water insoluble material was collected by filtration to give milk white powder, yield 60%; m.p. 191ºC; IR (KBr): 3458, 1736, 1632 cm^{-1}; ^1H NMR ($CDCl_3$): δ 10.18 (s, 4H, Ar-OH), 7.18~6.41 (m, 10H, Ar-H), 6.36-6.31 (m, 2H, Ar-NH), 6.18-6.12 (t, 2H, -CH=C-), 5.74-5.72 (d, 4H, -C=CH_2), 4.32-4.28 (2d, 8H, Ar-CH_2-Ar); ESI-MS: m/z 563 (M+1); Anal. Calcd for $C_{34}H_{30}N_2O_6$: C, 72.58; H, 5.32; N, 4.99. Found: C, 72.55; H, 5.32; N, 4.99%.

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References

1 Zinke A & Ziegler E, *Ber*, 74, **1941**, 1979.
2 Bohmer V, *Angew Chem Int Ed Engl*, 34, **1995**, 713.
3 Gutsche C D, Iqbal M & Stewart D, *J Org Chem*, 51, **1986**, 742.
4 Kumar S & Gutsche C D, *J Org Chem*, 64, **1999**, 998.
5 Harris S J, Barrett G & Mckervey M A, *J Chem Soc Chem Commun*, **1991**, 1224.
6 Shinkai S, Kawaguchi H & Manbe O, *J Polym Sci Polym Lett*, 26, **1988**, 391.
7 Klok H A, Eibeck P, Moller M & Reinhoudt D, *Macromolecules*, 30, **1997**, 795.
8 Gutsche C D & Iqbal M, *Org Synth*, 68, **1990**, 243.
9 Gutsche C D, Levine J A & Sujeeth P K, *J Org Chem*, 50, **1985**, 5802.
10 Gutsche C D & Lin L G, *Tetrahedron*, 42, **1986**, 1633.
11 Loon J D, Arduini A, Coppi L, Verboom W, Pochin A, Unggaro R, Harkema S & Reinhoudt D N, *J Org Chem*, 55, **1990**, 5639.