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Syntheses of Chiral Homoazacalix[4]arenes Incorporating Amino Acid Residues: Molecular Recognition for Racemic Quaternary Ammonium Ions

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Abstract: Chiral calixarene analogues incorporating amino acid residues into the macrocyclic rings were prepared from the cyclization reactions of bis(chloromethyl)phenol−formaldehyde tetramer with amino acid methyl ester in moderate yields. The macrocycles form a chiral concavity, which is induced by the chiral transmission from the point chirality of the amino acid residues to the phenol−formaldehyde tetramer unit. The macrocycles have the cavity π-basic enough to include the quaternary ammonium ion due to the cation−π interaction and can serve as a shift reagent for racemic ammonium ions during ^{1}H NMR analysis.

Modifying calixarenes to provide various properties into the molecules is a field that has great promise. Many studies of the modification of calixarenes have so far been made at the small (lower) and large (upper) rims of the calixarene skeleton.[1] Although some groups have made calixarene analogues,[2] we noticed that the modification of the methylene bridges has not been exploited to any great extent. It occurred to us to make the chiral calixarene analogue, which was constructed by changing from the methylene moiety to a chiral unit. Introduction of a chiral unit into the cyclic array confers chirality on the entire macrocycle, thus providing the possibility for enantiomeric selectivity toward chiral guests. The chiral unit employed in the instance is an amino acid moiety, and the chiral guests are quaternary ammonium ions.

Macrocycles **1** were synthesized from the cyclization reactions of bis(chloromethyl)phenol−formaldehyde tetramers **4** with amino acid methyl esters in 17−67% yields (Scheme 1). The bis(hydroxymethyl)phenol−formaldehyde tetramers **3** were prepared by hydroxymethylation of the corresponding tetramers **2** with 35% formalin in the presence of base at 60 °C in 41% (**3a**) and 39% (**3b**) yields, respectively. Then, **3** was treated with thionyl chloride in dry benzene at room temperature to give **4a** and **4b** in 91 and 92% yields, respectively. They were identified on the basis of IR, mass, 1D and 2D NMR spectral data, and elemental analysis.

The OH phenolic protons of **1** in the ^{1}H NMR spectra were observed at δ 10.0−10.4 ppm as broad singlets. In the IR spectra in chloroform, the OH stretching vibration absorption was observed in the region of 3180−3240 cm^{-1} as broad bands (Table 1[3]). Based on the findings, the intramolecular hydrogen bonding of **1** is compatible with that of calix[4]arene (ν_{OH} 3138 cm^{-1} in CCl_4, δ_{OH} 10.2 ppm in $CDCl_3$).[1a]

The conformation of the macrocycles was determined using NMR spectroscopy. The $ArCH_2Ar$ methylene protons of **1** appeared as three pairs of doublets due to the geminal coupling between H_{exo} and H_{endo} even at 20 °C and did not coalesce in $CDCl_3$ up to 55 °C. The differences between the chemical shifts of the doublets ($\Delta\delta$) of **1** are in the range of 0.67−0.76 ppm, indicating that the adjacent aryl rings adopt a syn orientation (Table 2[3]).[1a] The chemical shifts of the $ArCH_2Ar$ carbon atoms of **1** (δ 31.6−32.7 ppm) provided further support for the all-syn orientation (Table 1[3]).[4] These observations indicate that these calixarene analogues adopt a cone form as the preferred conformation in a solution.

The absence of symmetry in compounds **1a**−**j** is reflected in their very complex ^{1}H and ^{13}C NMR spectra. This chiral character is also manifested in their CD spectra which, interestingly, are more intense in hexane than in methanol, the difference probably being the result of the disruption of the intramolecular hydrogen bonding by the more polar methanol (Figure 1 and Table 3[3]). Since it is known that calixarenes can bind quaternary ammonium ions,[5] we chose α-methylbenzyl trimethylammnoium iodide (**5a**) as a putative guest, measuring the complexation by means of ^{1}H NMR spectroscopy in $CDCl_3$

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(3) Tables 1−4 and Figure 3 are given in the Supporting Information.

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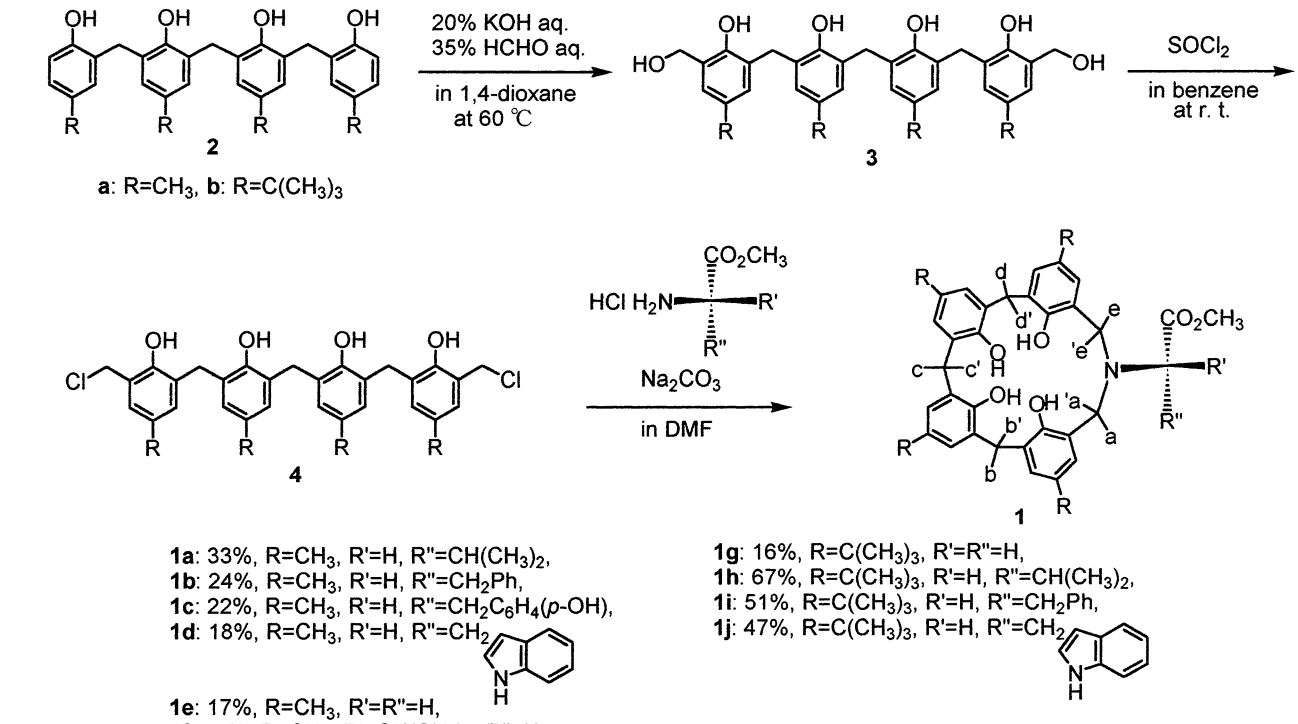
SCHEME 1



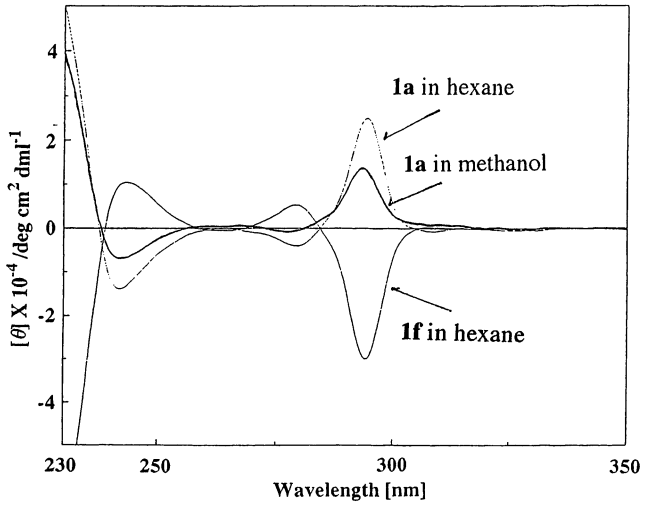


FIGURE 1. CD Spectra of **1a** and **1f**.

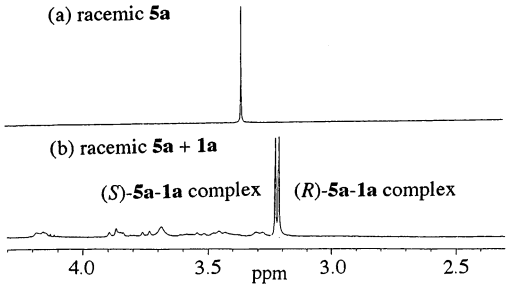


FIGURE 2. Partial ^{1}H NMR spectra of racemic ammonium iodide **5a** in $CDCl_3$: (a) [**5a**] = 1.0×10^{-2} M; (b) [**5a**] = [**1a**] = 1.0×10^{-2} M.

solution. In the presence of **1a**, all protons of the ammonium salt moved to high field due to the ring current effect of the π-cavity of **1a** during the formation of the complex ([**1a**] = [**5a**] = 10 mM, $\Delta\delta = \delta_{obs} - \delta_{free}$, $\Delta\delta N{-}CH_3 = -0.137$ and -0.153 ppm, $\Delta\delta CH = -0.084$ ppm, $\Delta\delta CH_3 = -0.023$ ppm). The higher chemical shifts of the $N{-}CH_3$ protons suggest that the $N{-}CH_3$ group is included in the cavity of **1a**.

Figure 2 shows the trimethyl signal (δ_{N-CH_3} 3.393 ppm) of the racemic **5a** in the ^{1}H NMR spectra. In the presence of **1a**, the trimethyl signal of the racemic ammonium ion was split into two peaks (δ_{N-CH_3} 3.240 and 3.256 ppm) with 1:1 intensity ratio. The ^{1}H NMR spectrum of **1a** with the *R*- or *S*-ammonium ion **5a** showed a single peak (δ_{N-CH_3} 3.240 ppm for the *R*-form, δ_{N-CH_3} 3.256 ppm for the *S*-form). The same phenomena were also observed in the complexes of the racemic **5a** with **1d** (δ_{N-CH_3} 3.240 ppm for the *R*-form, δ_{N-CH_3} 3.234 ppm for the *S*-form).[6] Contrary to this, the similar experiment using the achiral macrocycle **1e** shifted to high field (δ_{N-CH_3} 3.310 ppm) but did not split. In the same experiment using **1j**, the chemical shift of the methyl group (δ_{N-CH_3} 3.385 ppm) of **5a** scarcely changed due to the steric repulsion of the *tert*-butyl group on the phenol ring during the formation of the complex (Table 4[3]). The 1:1 stoichiometry of the complexes (**1**−**5**) was confirmed using Job's method.[7] The association constants (K_a) of **1d** to **5a** were determined

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by a nonlinear least-squares fitting method of a binding curve obtained from the ^{1}H NMR titrations[8] ($K_a = 22 \pm 2$ for **1d**−(*R*)-**5a** complex, $K_a = 20 \pm 2$ for **1d**−(*S*)-**5a**). These results indicate that **1** form the diastereomeric complexes with the racemic ammonium ion **5** through the cation−π interaction.[9]

The synthesis of chiral calixarenes via the insertion of amino acid moieties into the cyclic array has been demonstrated. The ability of these chiral macrocyclic compounds to act as chiral hosts has been measured using quaternary ammonium salts, which are thought to reside in the cavity of the host as the results of π−cation attractions. These chiral calixarenes may serve as chiral shift reagents for racemic quaternary ammonium ions in ^{1}H NMR analyses.[9]

Experimental Section

All chemicals were reagent grade and were used without further purification. Compounds **2a** (lit.[10] mp 173 °C), **2b** (lit.[11] mp 208−209 °C), and **3b** (lit.[12] mp 139−140 °C) were prepared according to the methods reported in the literature.

Synthesis of Bis(hydroxymethyl)phenol−Formaldehyde Tetramer (3). To a mixture of **2a** (4.75 g, 10.2 mmol), 20% potassium hydroxide aqueous solution (20 mL), and 1,4-dioxane (10 mL) was added 35% formalin (80 mL) over 2 h at 0 °C. After the addition was complete, the mixture was heated at 60 °C for 5.5 h under a nitrogen atmosphere. The reaction mixture was cooled to room temperature and acidified by 10% hydrochloride aqueous solution. White precipitates were collected by filtration and dissolved with chloroform. The solution was washed with 10% hydrochloride aqueous solution and dried over anhydrous sodium sulfate. Removal of solvent gave a pale yellow solid, which was subjected to column chromatography on silica gel to give **3a** as colorless crystals.

3a: mp 143−145 °C (CH_2Cl_2−hexane); FAB−MS *m*/*z* 511 [M − OH]$^+$; IR (KBr) 3381, 3014, 2918, 2852, 1483 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.21 (s, 12H), 3.79 (s, 6H), 4.68 (s, 4H), 6.75 (d, J = 2.0 Hz, 2H), 6.92 (s, 4H), 7.00 (d, J = 2.0 Hz, 2H), 9.18 (bs, 4H); ^{13}C NMR ($CDCl_3$) δ 20.3, 20.4, 30.9, 31.5, 63.6, 125.6, 127.1, 127.2, 127.3, 127.4, 129.5, 129.6, 129.9, 130.5, 130.6, 147.4, 149.7. Anal. Calcd for $C_{33}H_{36}O_6$: C, 74.98; H, 6.06. Found: C, 75.12; H, 5.92.

Synthesis of Bis(chloromethyl)phenol−Formaldehyde Tetramer (4). To a solution of **3** (1.44 mmol) in dry benzene (20 mL) was added a solution of thionyl chloride (1.10 g, 9.1 mmol) in dry benzene (5 mL) over 1 h. After the addition was completed, the mixture was allowed to stir at rt for 5 h. Removal of benzene gave white crystals that were recrystallized from benzene to give **4** as crystals.

4a: mp 200−205 °C (benzene); FAB−MS *m*/*z* 565 [M + 1]$^+$; IR (KBr) 3329, 3012, 2922, 2860, 1483 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.22 (s, 6H), 2.24 (s, 6H), 3.80 (s, 2H), 3.83 (s, 4H), 4.65 (s, 4H), 6.93 (m, 6H), 7.07 (d, 2H, J = 2.0 Hz), 8.51 (bs, 4H); ^{13}C NMR ($CDCl_3$) δ 20.4, 20.5, 31.0, 31.2, 31.6, 43.3, 124.0, 127.0, 127.4, 128.1, 129.2, 129.6, 129.7, 130.6, 131.0, 132.1, 147.2, 149.3. Anal. Calcd for $C_{33}H_{34}Cl_2O_4$: C, 70.07; H, 6.06. Found: C, 69.96; H, 6.15.

4b: mp 180−185 °C (benzene); FAB−MS *m*/*z* 733 [M + 1]$^+$; IR (KBr) 3356, 2960, 2904, 2868, 1487 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 18H), 1.27 (s, 18H), 3.87 (s, 2H), 3.90 (s, 4H), 4.68 (s, 4H), 7.11 (d, 2H, J = 2.0 Hz), 7.16 (s, 4H), 7.31 (d, 2H, J = 2.0 Hz), 8.70 (bs, 4H); ^{13}C NMR ($CDCl_3$) δ 31.4, 31.5, 31.7, 32.2, 34.0, 34.1, 43.8, 123.5, 125.5, 125.9, 126.0, 126.0, 126.9, 127.2, 128.0, 128.6, 144.1, 144.4, 147.1, 149.2. Anal. Calcd for $C_{45}H_{58}Cl_2O_4$: C, 73.65; H, 7.97. Found: C, 73.92; H, 7.66.

General Procedure of the Preparation of Dihomoazacalix[4]arene Derivatives (1). To a solution of bis(chloromethyl)phenol−formaldehyde tetramer (**4**) (1.0 mmol) in dry DMF (24 mL) in the presence of sodium carbonate (0.42 g, 4.0 mmol) was slowly added a solution of amino acid methyl ester monohydrochloride (1.0 mmol) in dry DMF (14 mL) over 1 h. After the addition was completed, the mixture was allowed to react at 30 °C for 2 h. Removal of DMF under reduced pressure a gave yellow oil containing a white powder, which was dissolved in chloroform. The solution was filtered, and evaporation of the solvent gave a yellow oily residue, which was subjected to column chromatography on silica gel using hexane/ethyl acetate 9:1 as an eluent to give macrocyclic compound (**1**) as crystals. Recrystallization from dichloromethane−hexane gave pure **1** as crystals.

1a: mp 183−186 °C; $[\alpha]^{20}_D = +58$ (c = 0.1, $CHCl_3$); FAB−MS *m*/*z* 624 [M + 1]$^+$; ^{1}H NMR ($CDCl_3$) δ 0.88 (d, J = 6.5 Hz, 3H), 1.35 (br s, 6H), 2.17 (s, 3H), 2.18 (s, 9H), 2.41 (m, 1H), 3.03 (d, J = 14.5 Hz, 1H), 3.07 (d, J = 10.5 Hz, 1H), 3.39 (d, J = 13.5 Hz, 1H), 3.42 (d, J = 13.5 Hz, 1H), 3.43 (d, J = 13.5 Hz, 1H), 3.44 (d, J = 12.2 Hz, 1H), 3.75 (s, 3H), 3.97 (d, J = 14.5 Hz, 1H), 4.06 (d, J = 13.5 Hz, 1H), 4.17 (d, J = 13.5 Hz, 1H), 4.18 (d, J = 13.5 Hz, 1H), 4.39 (d, J = 12.2 Hz, 1H), 6.52 (d, J = 2.0 Hz, 1H), 6.72 (d, J = 2.0 Hz, 1H), 6.85 (d, J = 2.0 Hz, 1H), 6.91 (d, J = 2.0 Hz, 1H), 6.94 (d, J = 2.0 Hz, 1H), 6.96 (d, J = 2.0 Hz, 1H), 6.97 (d, J = 2.0 Hz, 1H), 7.02 (d, J = 2.0 Hz, 1H), 10.32 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 19.3, 20.2, 20.5, 27.5, 31.6, 32.1, 50.0, 50.8, 54.1, 69.0, 120.6, 122.4, 126.8, 127.2, 127.8, 128.1, 128.3, 128.8, 129.1, 129.1, 129.2, 129.2, 129.4, 129.6, 129.8, 130.5, 131.1, 131.5, 132.2, 146.9, 147.4, 150.1, 151.3, 171.4. Anal. Calcd for $C_{39}H_{45}NO_6$: C, 75.09; H, 7.27; N, 2.25. Found: C, 75.11; H, 7.31; N, 2.12.

1b: mp 232−236 °C; $[\alpha]^{20}_D = +37$ (c = 0.1, $CHCl_3$); FAB−MS *m*/*z* 672 [M+ 1]$^+$; ^{1}H NMR ($CDCl_3$ at −60 °C) δ 2.20 (s, 3H), 2.23 (s, 3H), 2.24 (s, 3H), 2.28 (s, 3H), 3.11 (d, 1H), 3.29 (dd, J = 5.5, 13.8 Hz, 1H), 3.39 (d, J = 13.5 Hz, 1H), 3.41 (d, J = 13.5 Hz, 1H), 3.47 (d, J = 13.5 Hz, 1H), 3.49 (d, J = 13.5 Hz, 1H), 3.70 (dd, J = 5.5, 8.0 Hz, 1H), 3.77 (s, 3H), 3.88 (d, J = 13.5 Hz, 1H), 3.91 (d, J = 13.5 Hz, 1H), 3.93 (dd, J = 8.0, 13.8 Hz, 1H), 4.20 (d, J = 13.5 Hz, 2H), 4.58 (d, J = 12.0 Hz, 1H), 6.57 (br s, 1H), 6.79 (br s, 1H), 6.89 (br s, 1H), 6.97 (br s, 2H), 7.01 (br s, 1H), 7.05 (br s, 1H), 7.09 (br s, 1H), 7.30−7.50 (m, 5H), 8.98 (br s, 1H), 9.88 (br s, 1H), 10.05 (br s, 1H), 11.95 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.3, 20.4, 20.5, 31.5, 32.0, 34.8, 51.4, 53.5, 63.5, 120.7, 122.2, 126.7, 127.1, 127.5, 127.6, 127.7, 128.1, 128.3, 128.6, 128.7, 128.9, 129.2, 129.2, 129.3, 129.4, 129.5, 130.2, 130.6, 131.0, 131.2, 131.4, 138.1, 146.9, 147.4, 150.5, 151.2, 170.8. Anal. Calcd for $C_{43}H_{45}NO_6$: C, 76.88; H, 6.75; N, 2.08. Found: C, 76.84; H, 6.94; N, 1.96.

1c: mp 172−177 °C; $[\alpha]^{20}_D = +54$ (c = 0.1, $CHCl_3$); FAB−MS *m*/*z* 688 [M + 1]$^+$; ^{1}H NMR ($CDCl_3$ at −60 °C) δ 2.16 (s, 3H), 2.17 (s, 3H), 2.18 (s, 3H), 2.20 (s, 3H), 3.19 (br s, 1H), 3.26 (br s, 1H), 3.29 (br s, 1H), 3.36 (d, J = 13.5 Hz, 1H), 3.43 (d, J = 13.5 Hz, 1H), 3.45 (d, J = 12.5 Hz, 1H), 3.52 (d, J = 13.5 Hz, 1H), 3.64 (br s, 1H), 3.70 (br s, 3H), 3.83 (d, J = 12.5 Hz, 1H), 3.91 (d, J = 13.5 Hz, 1H), 4.14 (br s, 2H), 4.39 (br s, 1H), 6.57 (d, J = 2.0 Hz, 1H), 6.71 (d, J = 2.0 Hz, 1H), 6.78 (m, 2H), 6.82 (d, J = 2.0 Hz, 1H), 6.90 (d, J = 2.0 Hz, 1H), 6.91 (br s, 2H), 6.95 (d, J = 2.0 Hz, 1H), 7.02 (d, J = 2.0 Hz, 1H), 7.08 (m, 2H), 10.03 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 20.3, 20.5, 31.6, 32.0, 33.9, 51.2, 51.4, 53.5, 63.7, 115.4, 120.5, 122.0, 127.1, 127.5, 127.7, 127.8, 128.1, 128.6, 128.8, 128.9, 129.1, 129.3, 129.5, 129.8, 130.2, 130.6, 131.0, 131.3, 131.4, 147.0, 147.4, 150.5, 151.5, 154.5, 171.0. Anal. Calcd for $C_{43}H_{45}NO_7$ E1/2(H_2O): C, 74.12; H, 6.65; N, 2.01. Found: C, 74.09; H, 6.59; N, 1.93.

1d: mp 216−220 °C; $[\alpha]^{20}_D = +60$ (c = 0.1, $CHCl_3$); FAB−MS *m*/*z* 711 [M + 1]$^+$; ^{1}H NMR ($CDCl_3$) δ 2.14 (s, 3H), 2.19 (s, 3H), 2.21 (s, 3H), 2.22 (s, 3H), 3.31 (d, J = 13.5 Hz, 2H), 3.44 (d, J = 13.5 Hz, 1H), 3.46 (d, J = 13.5 Hz, 1H), 3.47 (dd, J = 5.2, 12.5 Hz, 1H), 3.54 (d, J = 14.0 Hz, 1H), 3.61 (dd, J = 8.1, 12.5 Hz, 1H), 3.70 (s, 3H), 3.77 (d, J = 13.5 Hz, 1H), 3.87 (dd, J = 5.2, 8.1 Hz, 1H), 3.90 (d, J = 14.0 Hz, 1H), 4.18 (d, J = 13.5 Hz,

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2H), 4.52 (d, J = 11.5 Hz, 1H), 6.55 (d, J = 2.0 Hz, 1H), 6.75 (d, J = 2.0 Hz, 1H), 6.85 (d, J = 2.0 Hz, 1H), 6.89 (d, J = 2.0 Hz, 1H), 6.94 (d, J = 2.0 Hz, 1H), 6.96 (d, J = 2.0 Hz, 1H), 6.98 (d, J = 2.0 Hz, 1H), 7.02 (dd, J = 7.0, 8.0 Hz, 1H), 7.04 (d, J = 2.0 Hz, 1H), 7.15 (br s, 1H), 7.16 (dd, J = 7.0, 8.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 2.0 Hz, 1H), 7.15 (br s, 1H), 7.16 (dd, J = 7.0, 8.0 Hz,1H), 7.36 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 8.00 (br s, 1H), 10.27 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 20.3, 20.4, 20.5, 24.9, 31.3, 31.6, 32.1, 51.0, 51.3, 53.5, 61.7, 111.1, 111.3, 118.5, 119.1, 120.6, 121.8, 122.3, 123.6, 127.2, 127.3, 127.5, 127.7, 127.8, 128.1, 128.5, 128.8, 128.9, 129.2, 129.2, 129.3, 129.5, 130.0, 130.6, 131.0, 131.4, 131.4, 136.2, 147.0, 147.4, 150.5, 151.1, 171.0. Anal. Calcd for $C_{45}H_{46}N_2O_6$: C, 76.03; H, 6.52; N, 3.93. Found: C, 76.01; H, 6.79; N, 3.71.

1e: mp 237−241 °C; FAB−MS m/z 582 $[M + 1]^+$; ^{1}H NMR ($CDCl_3$) δ 2.19 (s, 12H), 3.10−4.10 (m, 12H), 6.66 (d, J = 2.4 Hz, 2H), 6.90 (d, J = 2.4 Hz, 2H), 6.93 (d, J = 2.4 Hz, 2H), 7.00 (d, J = 2.4 Hz, 2H), 10.28 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 20.3, 20.5, 31.6, 32.1, 51.2, 55.3, 121.6, 127.5, 127.9, 128.1, 129.0, 129.4, 129.5, 129.6, 130.8, 130.9, 147.3, 151.2, 170.0. Anal. Calcd for $C_{45}H_{46}N_2O_6$: C, 76.03; H, 6.52; N, 3.94. Found: C, 76.01; H, 6.79; N, 3.71.

1f: mp 176−180 °C; $[\alpha]^{20}_D$ = −60 (c = 0.1, $CHCl_3$); FAB−MS m/z 624 $[M + 1]^+$. Anal. Calcd for $C_{39}H_{45}NO_6$: C, 75.09; H, 7.27; N, 2.25. Found: C, 74.98; H, 7.31; N, 2.40.

1g: mp 160−165 °C; EI−MS (70 eV) 749 M^+; ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 12H), 3.00−4.30 (m, H), 6.84 (d, J = 2.4 Hz, 2H), 7.13 (s, 4H), 7.23 (d, J = 2.4 Hz, 2H), 10.44 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 31.4, 31.5, 32.1, 32.7, 33.8, 34.0, 51.4, 53.4, 55.2, 120.9, 125.5, 125.7, 125.8, 127.2, 127.4, 127.7, 127.8, 142.6, 144.1, 147.2, 151.1, 170.3. Anal. Calcd for $C_{48}H_{63}NO_6$: C, 76.87; H, 8.47; N, 1.87. Found: C, 76.60; H, 8.72; N, 1.80.

1h: mp 232−235 °C; $[\alpha]^{20}_D$ = +57 (c = 0.1, $CHCl_3$); FAB−MS m/z 792 $[M + 1]^+$; ^{1}H NMR ($CDCl_3$) δ 0.90 (d, J = 5.5 Hz, 3H), 1.23 (s, 27H), 1.24 (s, 9H), 1.40 (d, J = 5.5 Hz, 3H), 2.43 (m, 1H), 3.03 (d, J = 14.5 Hz, 1H), 3.11 (d, J = 10.5 Hz, 1H), 3.44 (d, J = 13.6 Hz, 2H), 3.47 (d, J = 13.6 Hz, 1H), 3.50 (d, J = 12.2 Hz, 1H), 3.72 (s, 3H), 4.00 (d, J = 14.5 Hz, 1H), 4.14 (d, J = 13.6 Hz, 1H), 4.19 (d, J = 13.6 Hz, 1H), 4.21 (d, J = 13.6 Hz, 1H), 4.42 (d, J = 12.2 Hz, 1H), 6.65 (d, J = 2.0 Hz, 1H), 6.83 (d, J = 2.0 Hz, 1H), 7.00 (d, J = 2.0 Hz, 1H), 7.01 (d, J = 2.0 Hz, 1H), 7.11 (d, J = 2.0 Hz, 1H), 7.13 (d, J = 2.0 Hz, 1H), 7.14 (d, J = 2.0 Hz, 1H), 7.16 (d, J = 2.0 Hz, 1H), 10.33 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 19.3, 20.2, 27.5, 31.4, 31.5, 31.9, 32.1, 32.7, 33.8, 33.9, 34.0, 50.1, 50.7, 54.3, 68.9, 120.1, 121.8, 128.4, 129.2, 142.4, 142.9, 143.9, 144.4, 146.9, 147.3, 150.0, 151.1, 171.8. Anal. Calcd for $C_{51}H_{69}NO_6$: C, 77.33; H, 8.78; N, 1.77. Found: C, 77.39; H, 9.01; N, 1.67.

1i: mp 169−171 °C; $[\alpha]^{20}_D$ = +30 (c = 0.1, $CHCl_3$); EI−MS (70 eV) 839 M^+; ^{1}H NMR ($CDCl_3$) δ 1.16 (s, 27H), 1.17 (s, 9H), 3.21 (dd, J = 5.4, 11.9 Hz, 1H), 3.33 (dd, J = 7.3, 11.9 Hz, 1H), 3.47 (d, J = 14.0 Hz, 1H), 3.49 (d, J = 14.0 Hz, 2H), 3.55 (d, J = 12.0 Hz, 1H), 3.57 (s, 3H), 3.61 (d, J = 14.0 Hz, 1H), 3.68 (dd, J = 5.4, 7.3 Hz, 1H), 3.81 (d, J = 12.0 Hz, 1H), 3.99 (d, J = 14.0 Hz, 1H), 4.13 (d, J = 14.0 Hz, 2H), 4.28 (d, J = 14.0 Hz, 1H), 6.69 (d, J = 2.0 Hz, 1H), 6.81 (d, J = 2.0 Hz, 1H), 7.01−7.23 (m, 12H), 10.44 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 31.4, 31.5, 32.1, 32.8, 33.9, 34.0, 51.3, 53.7, 63.8, 120.3, 121.6, 12.5,1 125.4, 125.5, 125.7, 126.7, 127.2, 127.3, 127.6, 127.7, 127.9, 128.4, 128.6, 129.5, 138.3, 142.7, 144.1, 144.4, 147.1, 150.6, 151.1, 171.0. Anal. Calcd for $C_{55}H_{69}NO_6 \cdot {}^1/_2(C_6H_{12})$: C, 78.96; H, 8.57; N, 1.59. Found: C, 78.75; H, 8.87; N, 1.54.

1j: mp 188−190 °C; $[\alpha]^{20}_D$ = +22 (c = 0.1, $CHCl_3$); EI−MS (70 eV) 878 M^+; ^{1}H NMR ($CDCl_3$) δ 1.14 (s, 9H), 1.19 (s, 9H), 1.22 (s, 9H), 1.24 (s, 9H), 2.94 (d, J = 14.0 Hz, 1H), 3.31 (d, J = 14.0 Hz, 1H), 3.46 (d, J = 14.0 Hz, 1H), 3.52 (d, J = 14.0 Hz, 1H), 3.55 (dd, J = 12.2, 13.0 Hz, 1H), 3.74 (dd, J = 1.0, 13.0 Hz, 1H), 3.86 (d, J = 14.0 Hz, 1H), 4.07 (d, J = 14.0 Hz, 1H), 4.33 (d, J = 11.5 Hz, 1H), 4.35 (dd, J = 1.0, 12.2 Hz, 2H), 4.46 (d, J = 14.0 Hz, 1H), 4.70 (d, J = 14.0 Hz, 1H), 5.02 (d, J = 11.5 Hz, 1H), 6.64 (d, J = 2.0 Hz, 1H), 6.76 (d, J = 2.0 Hz, 1H), 6.91 (dd, J = 7.3, 7.6 Hz, 1H), 6.96 (d, J = 2.0 Hz, 1H), 7.01 (d, J = 2.0 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 7.10 (d, J = 2.0 Hz, 1H), 7.13 (d, J = 2.0 Hz, 1H), 7.15 (d, J = 2.0 Hz, 1H), 7.21 (dd, J = 7.3, 7.8 Hz, 1H), 7.37 (d, J = 2.0 Hz, 1H), 7.72 (s, 1H), 7.85 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 31.4, 31.5, 31.9, 32.0, 32.7, 33.8, 34.0, 51.4, 53.7, 62.0, 110.9, 111.3, 118.5, 119.2, 119.8, 121.2, 121.9, 123.8, 124.7, 125.3, 125.5, 125.6, 125.7, 126.6, 127.1, 127.3, 127.4, 127.5, 127.6, 127.9, 128.0, 128.8, 136.6, 142.6, 142.8, 144.0, 144.4, 147.0, 147.2, 150.4, 151.0, 170.9. Anal. Calcd for $C_{57}H_{70}N_2O_6 \cdot H_2O$: C, 76.31; H, 8.09; N, 3.12. Found: C, 76.29; H, 8.22; N, 3.06.

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Supporting Information Available: Tables 1−4 and Figure 3. This material is available free of charge via the Internet at http://pubs.acs.org.

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