"Deep-Cavity" Resorcinarenes Dimerize through Hydrogen Bonding and Self-Inclusion

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Abstract: The synthesis of new resorcinarene derivatives featuring extended sides and self-complementary hydrogen-bonding sites is described. Dimerization occurs in solvents such as toluene-d_8, and large cavities result. The dimerization constant $K_D = 1700 \pm 250$ M^{-1} was determined, and the cavity of the dimer was found to encapsulate two heptyl or octyl chains of the subunits. It is proposed that hydrogen bonding and self-inclusion are responsible for the large and compensating thermodynamic parameters for dimerization: $\Delta H = -20.9 \pm 1.3$ kcal mol^{-1} and $\Delta S = -58 \pm 5$ cal mol^{-1} K^{-1}.

Introduction

Self-complementary molecules can dimerize through solvophobic[1] or hydrogen-bonding[2] interactions in apolar media. With structures of appropriate curvature, such self-assembling systems generate cavities and result in encapsulation of smaller guest molecules: "molecule within molecule"[3] complexes are formed. Inside these, reactive intermediates can be stabilized,[4] new forms of stereoisomerism are observed,[5] and even bimolecular reactions can take place.[6] Larger self-assembled cavities of nanoscale dimensions are rare,[7] and in exploring such structures, we have encountered an unusual self-inclusion process that is responsible for their assembly. Below, we describe a synthetic strategy that accesses large and deep supramolecular structures based on expanded resorcinarene building blocks, and the characterization of self-inclusion in their hydrogen bonded dimers.

Results and Discussion

The synthesis of the new structures began with the rigid tetrabromo cavitand **1** prepared earlier by Cram and Reinhoudt.[8] The depth of the cavity was increased by building up the sides through a Suzuki reaction with (*p*-nitrophenyl)boronic acid[9] to afford **2** in 71% yield (Scheme 1). Compound **1** also has been arylated with (*m*-nitrophenyl)boronic acid using the same method in 90% yield. The method provides easy accessibility to a variety of cavitands with deep cavities and functionalized upper rims from the same precursor. Cram and co-workers had previously described the dimerization and self-inclusion of the related **3**, in which the methyl benzoate function of one molecule fills the cavity of another, as in **3·3** (Figure 1).[1b] To encourage the alternative, rim-to-rim dimerization leading to a capsule, we introduced self-complementary hydrogen bond donor and acceptor sites along the rim. Reduction of **2** with Raney nickel/H_2 in toluene to the amine **4** and then acylation with the appropriate acid chlorides gave the amides **5a**−**d**. Yields were 60−70% overall (Scheme 1). The reaction of amine **4** with alkyl isocyanates also proceeded smoothly but gave ureas having lower solubility in solvents friendly to hydrogen bonded aggregation.

The ^{1}H NMR spectra of **5** in DMSO-d_6 clearly showed their monomeric, C_{4v} symmetrical structures. The spectra featured only one set of signals, and the amide NH singlet appeared at ca. 9.8 ppm. In contrast, solutions in toluene-d_8 of compound **5a** bearing an *n*-octanoyl group or **5b** bearing an *n*-nonanoyl group no longer show ^{1}H NMR spectra characteristic of symmetrical or only monomeric species. In particular, four well-resolved and unusually downfield singlets of equal intensity appear between 11 and 9 ppm for the amide NH protons (see

(1) (a) Cram, D. J.; Choi, H.-J.; Bryant, J. A.; Knobler, C. B. *J. Am. Chem. Soc.* **1992**, *114*, 7748−7765. (b) von dem Bussche-Hünnefeld, C.; Helgeson, R. C.; Bühring, D.; Knobler, C. B.; Cram, D. J. *Croat. Chim. Acta* **1996**, *69*, 447−458.

(2) (a) Branda, N.; Wyler, R.; Rebek, J., Jr. *Science* **1994**, *263*, 1267−1268. (b) Chapman, R. G.; Sherman, J. C. *J. Am. Chem. Soc.* **1995**, *117*, 9081−9082. (c) Shimizu, K. D.; Rebek, J., Jr. *Proc. Natl Acad. of Sci. U.S.A.* **1995**, *92*, 12403−12407. (d) Mogck, O.; Böhmer, V.; Vogt, W. *Tetrahedron* **1996**, *52*, 8489−8496. (e) Mogck, O.; Pons, M.; Böhmer, V.; Vogt, W. *J. Am. Chem. Soc.* **1997**, *119*, 5706−5712. (f) Scheerder, J.; van Duynhoven, J. P. M.; Engbersen, J. F. J.; Reinhoudt, D. N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1090−1093. (g)-Arduini, A.; Domiano, L.; Ogliosi, L.; Pochini, A.; Secchi, A.; Ungaro, R. *J. Org. Chem.* **1997**, *62*, 7866−7868. (h) For a recent review see: Conn, M. M.; Rebek, J., Jr. *Chem. Rev.* **1997**, *97*, 1647−1668.

(3) This phrase first appeared as the title of a lecture by D. J. Cram at the C. David Gutsche Symposium, Washington University, St. Louis, MO, May 5, 1990; for covalently bonded examples, see: (a) Cram, D. J. *Nature* **1992**, *356*, 29−36. (b) Collet, A.; Dutasta, J. P.; Lozach, B.; Canceill, J. In *Chemistry I-Directed Synthesis and Molecular Recognition*; Weber, E., Ed.; Topics in Current Chemistry, 165; Springer-Verlag: Berlin, 1993; pp 104−129.

(4) Cyclobutadiene in covalently assembled carcerands: Cram, D. J.; Tanner, M. E.; Thomas, R. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1024−1027. Benzyne: Warmuth, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1347−1350. Warmuth, R. *J. Chem. Soc., Chem. Commun.* **1998**, 59−60.

(5) Examples using covalently bonded systems: (a) Sherman, J. C.: Knobler, C. B.; Cram, D. J. *J. Am. Chem. Soc.* **1991**, *113*, 2194−2204. (b) Timmerman, P.; Verboom, W.; van Veggel, F. C. J. M.; van Duynhoven, J. P. M.; Reinhoudt, D. N. *Angew. Chem., Int. Ed. Engl.* **1994**, *34*, 2345−2348.

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(7) MacGillivray, L. R.; Atwood, J. L. *Nature* **1997**, *389*, 469−472.

(8) General synthesis: Cram, D. J.; Karbach, S.; Kim, H.-E.; Knobler, C. B.; Maverick, E. F.; Ericson, J. L.; Helgeson, R. *J. Am. Chem. Soc.* **1988**, *110*, 2229−2237. Specific synthesis of **1**: Timmerman, P.; Boerrigter, H.; Verboom, W.; van Hummel, G. J.; Harkema, S.; Reinhoudt, D. N. *J. Inclusion Phenom.* **1994**, *19*, 167−191.

(9) Hughes, M. P. Ph.D. Thesis, University of Notre Dame, 1997; p 99.

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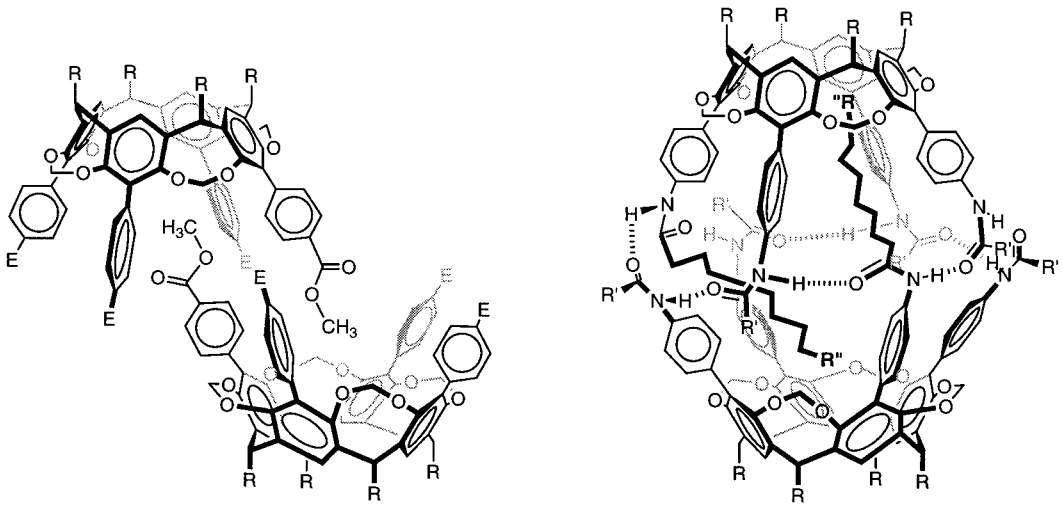
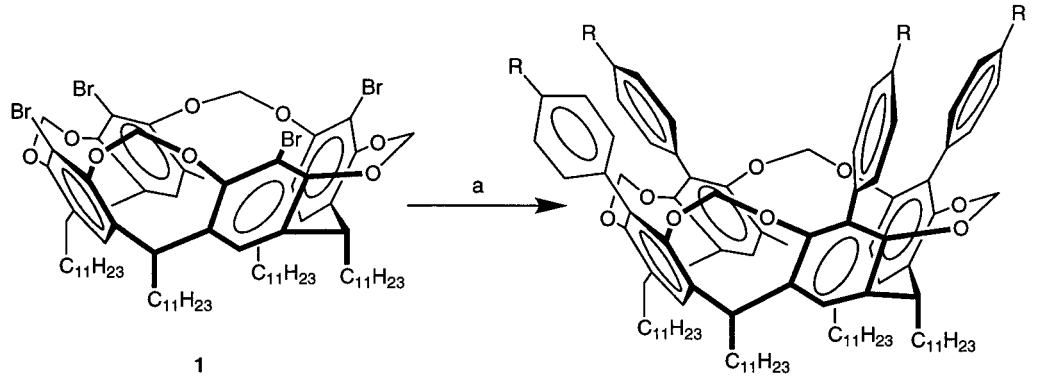


3•3
R = C_5H_{11}, E = CO_2CH_3

5a•5a R = $C_{11}H_{23}$, R' = C_7H_{15}, R" = H
5b•5b " R' = C_8H_{17}, R" = CH_3

Figure 1. Structures of Cram's[1b] dimer **3·3** and dimers **5a·5a** and **5b·5b** assembled through hydrogen bonding with self-inclusion.

Scheme 1



a. $Pd(PPh_3)_4$, *p*-$C_6H_4NO_2B(OH)_2$, Na_2CO_3, toluene, 110°C, 26 h, 71%.
b. Raney Ni, H_2, 45 °C, toluene, 16 h, 95%.
c. R'COCl, EtOAc-H_2O, 1:1, K_2CO_3, r.t., 2 h, quantitative yields.

2 R = NO_2
4 R = NH_2
5a R = $NHCO(CH_2)_6CH_3$
b R = $NHCO(CH_2)_7CH_3$
c R = $NHCOCH_2CH_3$
d R = $NHCO(CH_2)_{14}CH_3$

Experimental Section), and they are concentration independent.[10] Unexpectedly, broad multiplets were found in the spectra of **5a** and **5b** at −1.02 and −1.78 ppm, respectively. These upfield signals are characteristic for guests encapsulated in aromatic containers.[2−6] The FTIR spectra of **5a** in toluene-d_8 showed both free (3406 cm^{-1}) and hydrogen-bonded (3337 cm^{-1}) amide NH absorptions; upon dilution, their ratio changes in the manner expected for an aggregate−monomer equilibrium. Further evidence for the aggregation to the dimeric form was obtained from MALDI mass spectrometry (MALDI-MS). For the 5 mM solution of **5a** in toluene-d_8, signals for the monomer and dimer were observed at *m*/*z* of 2024 (100%) and 4047 (40%) Da, respectively (Figure 2a).

Even on the NMR time scale, the exchange rate between the monomeric and the dimeric species is slow in toluene-d_8: two different sets of signals are observed and their ratio changes with concentration and temperature. Dilution experiments in toluene-d_8 were performed at 295 K with compound **5a** at eight different concentrations (20−1 mM). For example, the [dimer]/[monomer] ratio of >3.7 was found at concentrations higher than 20 mM, while only monomer was observed below 0.25 mM. The data obtained fit a simple dimerization model well and yield a dimerization constant K_D of 1700 ± 250 M^{-1}. Additionally, the K_D values were measured at four different temperatures (273−303 K) in toluene-d_8 at 5 mM. The [dimer]/[monomer] ratios of ca. 7, 3, and 1.8 were observed at 273, 283, and 293 K, respectively, and only monomer was observed at >323 K. From the corresponding van't Hoff plot (Figure 3) the values of $\Delta H = -21 \pm 1.3$ kcal mol^{-1} and $\Delta S = -58 \pm 5$ cal mol^{-1} K^{-1} ($\Delta G^0 = -3.8$ kcal mol^{-1} at 295 K) were obtained. These values show the large and compensating effect of dimerization: it is enthalpically favorable and entropically very unfavorable.

The high symmetry of **5a** and **5b** is broken by the dimerization process and we propose that self-inclusion is responsible. One of the four alkyl chains from each monomer is encapsulated

(10) The amide NH chemical shift in the model compound *N*-acetanilide appears at 7.0 ppm in toluene-d_8 and is moderately concentration dependent, as is expected for weak, nonspecific aggregation.

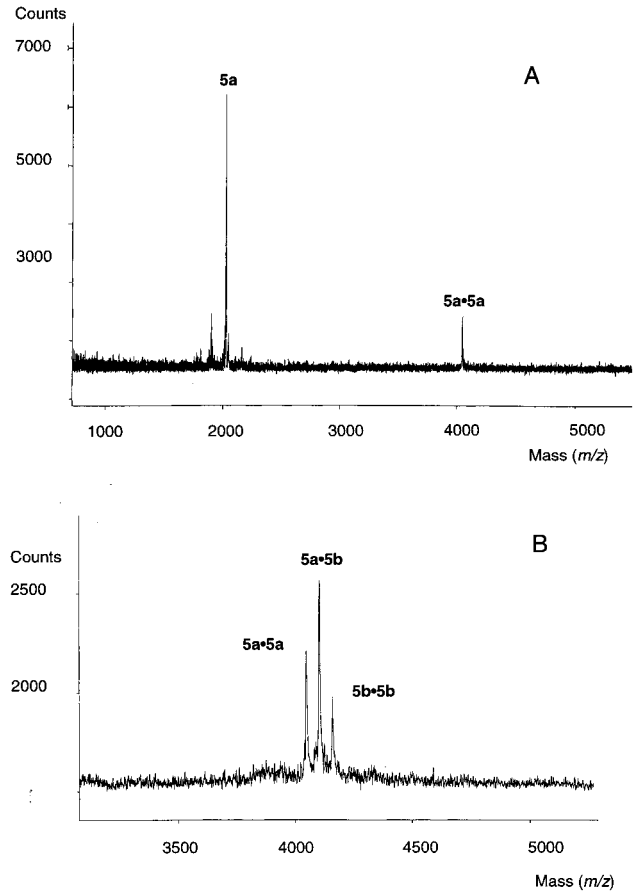


Figure 2. Portion of MALDI mass spectra: (A) compound **5a**; (B) homodimers **5a·5a** and **5b·5b** and heterodimer **5a·5b**.

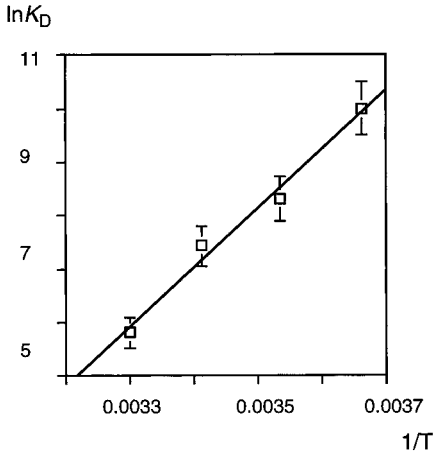


Figure 3. Van't Hoff plot of the ^{1}H NMR data for dimerization of **5a**.

in the dimeric form, with the terminal CH_3 groups positioned in the deepest part of the cavity. This results in the upfield shifts (−1.02 and −1.78 ppm) observed for these methyl groups (Figure 1, right). Similar shifts were observed by Cram for the methyl groups in the dimer of **3·3** (Figure 1, left).[1b]

There are two possible self-inclusion modes, regioisomers on a supramolecular scale.[11] The alkyl substituents inside the cavity are either proximal or distal (Figure 4), and it is difficult to distinguish between the two. Although the distal isomer appears less crowded, either or both could be present. A

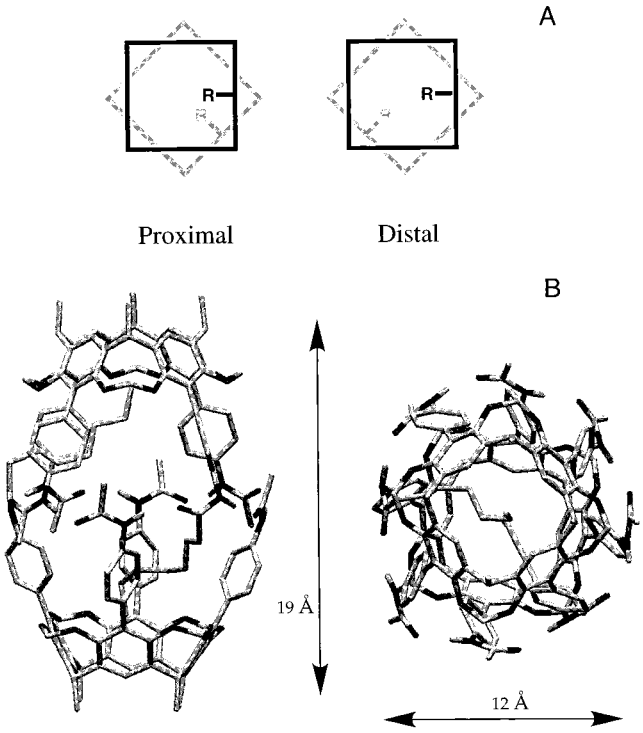


Figure 4. (A) Schematic depiction of proximal and distal regioisomers of dimeric capsule **5a·5a**. (B) Two views on an energy-minimized[12] distal isomer **5a·5a**. Exterior alkyl chains and CH hydrogens are omitted for viewing clarity.

modeling study[12] showed that eight good hydrogen bonds can be formed around the equator of the dimer even when two alkyl chains are tucked inside the cavity, with the alkyl chain of one monomer extended into the cavity of the other (Figure 4). For the enthalpic component, a value of ∼21 kcal mol^{-1} is not unreasonable for eight cooperatively organized hydrogen bonds in toluene.

The dimeric nature of compounds **5a** and **5b** was further supported by a heterodimerization experiment. The downfield shifts of the amide NH for both compounds are different, but mixing the solutions of **5a** and **5b** in a 1:1 ratio at 5 mM gave rise to a new set of (broadened) downfield NH singlets, which reflects the slow formation of a mixed dimer on the NMR time scale. When the same solution was analyzed by MALDI-MS, three dimeric species **5a·5a**, **5b·5b**, and **5a·5b** were clearly observed at 4047, 4159, and 4104 Da, respectively (Figure 2b).

Dimers of **5a** or **5b** possess sizable, egg-shaped cavities of dimensions 12 × 19 Å (Figure 4) and are among the largest reversibly formed cavities synthesized to date. The estimated volume[13] of the internal cavity in the absence of self-inclusion is ∼440 Å^3. Interestingly, all attempts to encapsulate the appropriate guest inside the capsule failed. Thus, suitable size guest molecules such as adamantane, anthracene, bibenzyl, *p*-cyclophane, 2,2′-dimethylbibenzyl, ethylbenzene, 1-phenylheptane, and C_{70} did not show any sign of encapsulation when mixed with **5a·5a** in toluene-d_8. The alkyl chains undoubtedly replace the solvent molecules inside the cavity upon self-inclusion, and this is apparently the more energetically preferred scenario. The residual internal volume, for example, for capsule

(11) This type of isomerism was previously observed in calixarene dimers of reduced symmetry: Castellano, R. K.; Rudkevich, D. M.; Rebek, J., Jr. *Proc. Natl. Acad. Sci. U.S.A.* **1997**, *94*, 7132−7137.

(12) Mohamadi, F.; Richards, N. G.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440−467.

(13) Nicholls, A.; Sharp, K. A.; Honig, B. *Proteins* **1991**, *11*, 281−296. For the internal cavity volume calculations and their application in host−guest chemistry of self-assembled capsules, see ref 14.

5a·5a, thus becomes 190 Å^3. This means that ca. 57% of the cavity is already well filled by self-inclusion, and there is just not enough room to accommodate additional guests or solvent molecules. A recent compilation of occupancy factors or packing coefficients of molecules within molecule complexes in solution indicates that an optimal value is about 55% occupancy.[14] Self-inclusion of this sort has not been observed in the much smaller, calix[4]arene dimers,[2] although evidence of such inclusion in dimers of larger cyclodextrins bearing pyrene functions in aqueous solution was presented by Ueno.[15] The sheer size of the cavities may be responsible for the effect: dimerization takes place when the cavity is well-filled. For example, the short chain *n*-propionylamide derivative **5c** and the long chain palmitoylamide derivative **5d** both exist exclusively in the monomeric state in toluene-d_8. Even though the same pattern of intermolecular hydrogen bonds is possible in their respective dimers, neither side chain is appropriate for self-inclusion. A delicate balance apparently exists between the enthalpic and entropic contributions to molecular recognition by self-inclusion in reversibly formed capsules. The deeper understanding of these factors is our current goal.

Experimental Section

General Information. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-300 and a Bruker DRX-600 spectrometers. The chemical shifts were measured relative to residual nondeuterated solvent resonances. Mass spectra were obtained with a VG ZAB-VSE and PerSeptive Biosystems Voyager-Elite mass spectrometer; *m*-nitrobenzyl alcohol (NBA) and 2,5-dihydroxybenzoic acid (DHB) were used as a matrix for FAB-MS and MALDI-MS, respectively. FTIR spectra were recorded on a Perkin-Elmer Paragon 1000 PC FT-IR spectrometer. Silica gel chromatography was performed with Silica Gel 60 (EM Science or Bodman, 230−400 mesh). All experiments with moisture- or air-sensitive compounds were performed in anhydrous solvents under a nitrogen atmosphere. (*p*-Nitrophenyl)boronic acid[9] and compound **1**[8] were prepared in accord with the literature protocols.

Molecular modeling was performed using the Amber* force field in the MacroModel 5.5 program.[12] The program GRASP[13,14] was used to estimate the volume of the internal cavities of the dimers.

2,20:3,19-Dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin,7,11,15,28-Tetrakis-(4-nitrophenyl)-1,21,23,25-tetraundecyl-, Stereoisomer (2). To a stirred solution of tetrabromocavitand **1** (302 mg, 0.206 mmol), Pd(PPh$_3$)$_4$ (104 mg, 0.09 mmol), and (*p*-nitrophenyl)boronic acid (206 mg, 1.23 mmol) in toluene (8.0 mL) was added aqueous Na_2CO_3 (2.0 M, 0.8 mL). After the reaction was heated at 110 °C for 26 h, the mixture was filtered through a pad of Celite, and the solvent was removed under reduced pressure. Column chromatography of the crude residue (toluene) afforded compound **2** (240 mg) as a yellow solid in 71% yield: mp 259−260 °C; FTIR (thin film, cm^{-1}) ν 2925, 2855, 1602, 1519, 1464, 1349, 966, 849, 702. ^{1}H NMR ($CDCl_3$) δ 8.19 (d, J = 8.7 Hz, 8H), 7.41 (s, 4H), 7.24 (d, J = 8.4 Hz, 8H), 5.27 (d, J = 6.7 Hz, 4H), 4.87 (t, J = 8.0 Hz, 4H), 4.26 (d, J = 6.8 Hz, 4H), 2.38 (q, J = 7.0 Hz, 8H), 1.62−1.46 (m, 16H), 1.39−1.26 (m, 64H), 0.90 (t, J = 6.9 Hz, 12H); ^{13}C NMR ($CDCl_3$) δ 152.4, 147.2, 140.8, 138.8, 131.0, 127.5, 123.3, 121.1, 100.5, 36.9, 31.9, 30.2, 29.7, 29.66, 29.63, 29.58, 29.3, 27.8, 22.6, 14.0; MS-FAB *m*/*z* 1769 ([M + Cs]$^+$, calcd for $C_{100}H_{124}N_4O_{16}Cs$ 1769).

2,20:3,19-Dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin, 7,11,15,28-Tetrakis-(4-aminophenyl)-1,21,23,25-tetraundecyl-, Stereoisomer (4). To a suspension of tetranitro compound **2** (198 mg, 0.12 mmol) in toluene (50 mL) was added a catalytic amount of Raney Ni (1 mL slurry solution in H_2O, prewashed with EtOH and toluene two times, respectively) in toluene (1 mL) under H_2 (1 atm), and the reaction mixture was stirred at 45 °C for 16 h. The reaction was cooled to room temperature and filtered through a pad of Celite. The solution was concentrated to give **4** (174 mg) in 95% yield: mp 231−233 °C; FTIR (thin film, cm^{-1}) ν 3463, 3374, 3330, 2924, 2845, 1622, 1520, 1464, 1419, 1155, 1080, 966, 825, 753; ^{1}H NMR ($CDCl_3$) δ 7.24 (s, 4H), 6.85 (d, J = 7.8 Hz, 8H), 6.64 (d, J = 7.8 Hz, 8H), 5.30 (d, J = 6.7 Hz, 4H), 4.84 (t, J = 7.9 Hz, 4H), 4.23 (d, J = 6.7 Hz, 4H), 3.69 (br s, 8H), 2.32 (m, 8H), 1.70−1.27 (m, 76H), 0.91 (t, J = 6.6 Hz, 12H); ^{13}C NMR ($CDCl_3$) δ 152.9, 145.3, 138.3, 131.1, 129.2, 124.0, 119.3, 114.6, 100.6, 37.0, 31.9, 30.0, 29.8, 29.68, 29.65, 29.59, 29.3, 27.9, 22.6, 14.0; HRMS-FAB *m*/*z* 1649.9238 ([M + Cs]$^+$, calcd for $C_{100}H_{132}N_4O_8Cs$ 1649.9100).

General Procedure for the Preparation of Tetraamides (5a−d). To a solution of **4** in EtOAc:H_2O (1:1) was added 10 equiv of the appropriate acid chloride and 25 equiv of K_2CO_3. The solution was vigorously stirred at rt for 2 h, and the organic layer was separated. The aqueous layer was extracted with EtOAc, and the combined organic solution was washed with brine and dried over $MgSO_4$. The solution was concentrated in vacuo, and the resulting solid was washed with hexanes to give the desired tetraamide in quantitative yield.

2,20:3,19-Dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin, 7,11,15,28-Tetrakis-(4-*n*-octanoylamidophenyl)-1,21,23,25-tetraundecyl-, Stereoisomer (5a): mp 232−235 °C; FTIR (thin film, cm^{-1}) ν 3304, 2925, 2846, 1666, 1595, 1531, 1458, 1159, 1084, 969, 833; ^{1}H NMR (DMSO-d_6) δ 9.85 (s, 4H), 7.74 (s, 4H), 7.53 (d, J = 8.6 Hz, 8H), 6.97 (d, J = 8.5 Hz, 8H), 5.18 (d, J = 7.0 Hz, 4H), 4.65 (t, J = 7.7 Hz, 4H), 4.27 (d, J = 6.5 Hz, 4H), 2.46 (m, 8H), 2.26 (t, J = 7.2 Hz, 8H), 1.56−1.24 (m, 120H), 0.85 (m, 24H), 0.90 (t, J = 7.1 Hz, 12H); ^{1}H NMR (toluene-d_8, 330 K) δ 7.73 (s, 4H), 7.39 (d, J = 7.9 Hz, 8H), 6.91 (d, J = 8.1 Hz, 8H), 6.67 (s, 4H), 5.32 (m, 8H), 4.51 (d, J = 6.8 Hz, 4H), 2.55 (m, 8H), 1.95 (t, J = 7.5 Hz, 8H), 1.56−1.24 (m, 132H), 0.95 (t, J = 7.0 Hz, 12H), 0.86 (t, J = 7.0 Hz, 12H); ^{1}H NMR (downfield and upfield portions in toluene-d_8, 295 K) δ 11.01, 9.62, 9.19, 9.09 (4 × s, 8H, NH), −1.02 (br m, 6H, CH_3); ^{13}C NMR ($CDCl_3$) δ 171.9, 152.7, 138.4, 137.2, 130.4, 129.7, 129.1, 119.8, 119.3, 100.4, 37.7, 37.0, 31.8, 31.7, 30.2, 29.8, 29.7, 29.6, 29.3, 29.1, 28.99, 28.92, 28.8, 27.9, 25.6, 22.6, 14.0, 13.6; MALDI MS *m*/*z* 2024 (M), 4047 (2M); HRMS-FAB *m*/*z* 2154.3469 ([M + Cs]$^+$, calcd for $C_{132}H_{188}N_4O_{12}Cs$ 2154.3278).

2,20:3,19-Dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin, 7,11,15,28-Tetrakis-(4-*n*-nonanoylamidophenyl)-1,21,23,25-tetraundecyl-, Stereoisomer (5b): mp 242−244 °C; FTIR (thin film, cm^{-1}) ν 3306, 2923, 2846, 1668, 1599, 1538, 1464, 1086, 967, 756; ^{1}H NMR (DMSO-d_6) δ 9.85 (s, 4H), 7.74 (s, 4H), 7.53 (d, J = 8.3 Hz, 8H), 6.97 (d, J = 8.3 Hz, 8H), 5.17 (d, J = 6.6 Hz, 4H), 4.66 (t, J = 7.7 Hz, 4H), 4.27 (d, J = 6.3 Hz, 4H), 2.27 (t, J = 7.1 Hz, 8H), 1.54−0.67 (m, 152H); ^{1}H NMR (downfield and upfield portions in toluene-d_8, 295 K) δ 10.74, 9.77, 9.36, 9.14 (4 × s, 8H, NH), −1.78 (br m, 6H, CH_3); ^{13}C NMR ($CDCl_3$) δ 170.2, 153.1, 138.7, 137.6, 130.7, 130.1, 129.5, 120.2, 119.6, 100.7, 38.0, 37.4, 35.6, 32.23, 32.16, 32.0, 30.7, 30.2, 30.1, 30.02, 30.00, 29.8, 29.7, 29.6, 29.49, 29.46, 29.40, 29.3, 29.1, 28.3, 25.9, 24.5, 23.1, 23.0, 22.9, 14.4, 14.3, 14.0; MALDI MS *m*/*z* 2080 (M), 4159 (2M); HRMS-FAB *m*/*z* 2210.3701 ([M + Cs]$^+$, calcd for $C_{136}H_{196}N_4O_{12}Cs$ 2210.3904).

2,20:3,19-Dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin, 7,11,15,28-Tetrakis-(4-*n*-propionylamidophenyl)-1,21,23,25-tetraundecyl-, Stereoisomer (5c): mp >260 °C; FTIR (thin film, cm^{-1}) ν 3304, 2923, 2846, 1671, 1522, 1463, 1080, 1018, 964, 798; ^{1}H NMR ($CDCl_3$) δ 7.49 (d, J = 7.7 Hz, 8H), 7.46 (br s, 4H), 7.30 (s, 4H), 6.98 (d, J = 8.0 Hz, 8H), 5.20 (d, J = 6.5 Hz, 4H), 4.84 (t, J = 7.9 Hz, 4H), 4.19 (d, J = 6.7 Hz, 4H), 2.34 (m, 16H), 1.56−1.21 (m, 80H), 1.82 (t, J = 7.3 Hz, 12H), 0.90 (t, J = 7.1 Hz, 12H); ^{13}C NMR ($CDCl_3$) δ 173.2, 153.5, 139.1, 137.9, 131.2, 130.4, 129.8, 120.6, 112.0, 101.2, 37.8, 32.6, 31.4, 31.1, 30.6, 30.45, 30.40, 30.39, 30.1, 28.7, 23.3, 14.8, 10.3; HRMS−FAB *m*/*z* 1764.0869 ([M + Na]$^+$, calcd for $C_{112}H_{148}N_4O_{12}Na$ 1764.0991).

2,20:3,19-Dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin, 7,11,15,28-Tetrakis-

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(4-palmitoylamidophenyl)-1,21,23,25-tetraundecyl-, Stereoisomer (5d). FTIR ($CHCl_3$, cm^{-1}) ν 3434, 3030, 2933, 2855, 1707, 1519, 1465, 1205, 1086, 969, 754; ^1H NMR ($CDCl_3$) δ 7.48 (d, $J = 7.5$ Hz, 8H), 7.33 (br s, 4H), 7.29 (s, 4H), 6.97 (d, $J = 7.9$ Hz, 8H), 5.21 (d, $J = 5.6$ Hz, 4H), 4.83 (t, $J = 7.9$ Hz, 4H), 4.19 (d, $J = 6.1$ Hz, 4H), 2.31 (m, 16H), 1.64−1.27 (m, 176H), 0.88 (m, 24H); ^{13}C NMR ($CDCl_3$) δ 172.2, 153.1, 138.7, 138.6, 137.5, 130.8, 130.0, 129.4, 120.1, 119.6, 100.8, 38.1, 37.4, 35.6, 34.3, 32.21, 32.19, 30.02, 30.01, 29.93, 29.91, 29.8, 29.7, 29.64, 29.62, 29.5, 25.9, 24.9, 22.95, 22.94, 14.4, 14.3; MS−FAB *m*/*z* 2494 ($[M + Na]^+$, calcd for $C_{100}H_{124}N_4O_{16}Na$ 2494).

^{1}H NMR Dimerization Experiments. The dimerization constant K_D values for **5a·5a** were determined at eight different concentrations (1−20 mM) by integration of the corresponding monomer and dimer signals at 295 K according to the known equations;[1a] good reproducibility (±15%) was obtained.

For the van't Hoff analysis, the dimerization constant K_D values were measured in toluene-d_8 at four different temperatures (273−303 K) at 5 mM. The data are reproducible within a 5% error.

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