3 H), 4.08 (s, 3 H), 3.67 (s, 1 H, OH), 3.50 (m, 3 H), 3.34 (br s, 1 H), 3.24 (m, 1 H), 2.73 (dd, $J$ = 15.7, 5.6 Hz, 1 H), 2.51-2.25 (m, 6 H), 2.32 (s, 3 H), 2.18-1.88 (m, 5 H), 1.77 (dt, $J$ = 2.8, 8.5 Hz, 1 H), 1.23 (at, 6.5 Hz, 6 H), 0.54 (d, $J$ = 6.4 Hz, 3 H); IR ($CHCl_3$) 3600-31—, 3000, 2920, 1725, 1705, 1575, 1450, 1390, 1110, 1100 $cm^{-1}$; UV-vis $\lambda_{max}$ (MeOH) 448 ($\epsilon$ 17 220), 421 (15 773), 397 (9760), 266 (24 283), 241 (25 533).

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# Convergent Functional Groups. 9. Complexation in New Molecular Clefts

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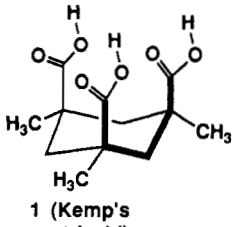
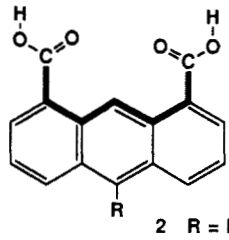
**Abstract:** Two new 2,7-di-*tert*-alkyl-9,9-dimethylxanthene-4,5-dicarboxylic acids are prepared as organic soluble, U-shaped modules for the construction of molecular hosts. Condensation of two diacid units with spacers (e.g., hydroquinone, 4,4'-biphenol, and 2,6-diaminonaphthalene) gives large structures capable of assuming cleftlike shapes that complex sizable guests such as DABCO, quinine, quinidine, and quinoxaline-2,3-dione. The xanthene diacids and their derivatives are shown to contain intramolecular hydrogen bonds that organize the binding sites and modify their chemical properties.

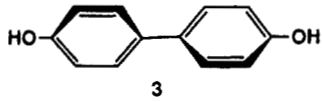
Molecules featuring convergent functional groups in cleftlike shapes have emerged as useful receptors for small molecules.[1] In our own laboratory, structures derived from Kemp's[2] triacid **1** have



**1 (Kemp's triacid)**



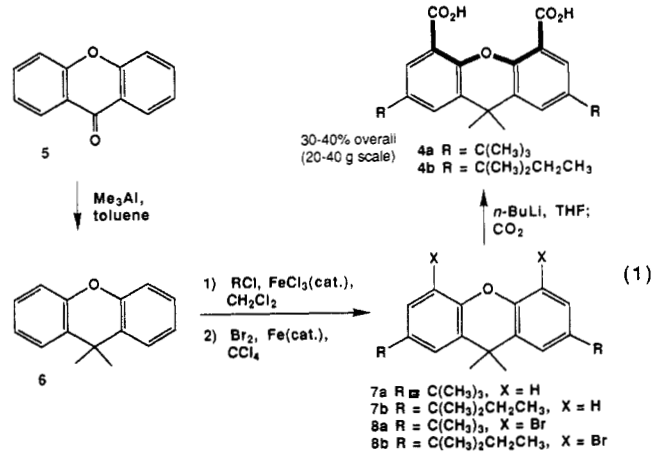
**2** R = H or *n*-octyl



**3**

proven effective probes for studies of molecular recognition. The U-shaped relationship that exists between any two carboxyl functions in **1** in conjunction with spacer elements permits the construction of molecules that fold back upon themselves. We have now explored new modular units based upon xanthene-4,5-dicarboxylic acid derivatives and report here on their advantages for complexation of larger target structures.

Anthracene-4,5-dicarboxylic acids[3] **2** provide U-shaped relationships between functions, but the low solubilities of these compounds and the clefts derived from them with diol or diamine spacers (e.g., biphenol **3**) in most organic solvents thwarted studies of their intermolecular complexes. Systems derived from xanthenes proved tractable. When methyl groups were appended to the 9-position and *tert*-alkyl groups to the 2- and 7-positions of xanthene-4,5-dicarboxylic acid derivatives **4**, highly soluble and readily accessible molecules were at hand. These *tert*-alkylated diacids are prepared from commercially available xanthone (**5**) in four steps (eq 1). Treatment of **5** with $Me_3Al$ in toluene,[4]




(1)

followed by Friedel-Crafts alkylation[5] and bromination, generates compounds **8**. These dibromo compounds were converted to diacids **4** by means of their lithium derivatives. The di-*tert*-amylated compounds (**7b**, **8b**, and **4b**) were each found to contain

(1) For a recent review, see: Rebek, J., Jr. *Angew. Chem.* **1990**, *102*, 261; *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 245.
(2) Kemp, D. S.; Petrakis, K. S. *J. Org. Chem.* **1981**, *46*, 5140. Commercially available from the Aldrich Chemical Co.
(3) For recent uses and leading references, see: Fillers, J. P.; Ravichandran, K. G.; Abdalmuhdi, I.; Tulinsky, A.; Chang, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 417.
(4) Meisters, A.; Mole, T. *Aust. J. Chem.* **1974**, *27*, 1655.
(5) Roberts, R. M.; Khalaf, A. A. *Friedel-Crafts Alkylation Chemistry*; Marcel Dekker: New York, 1984.

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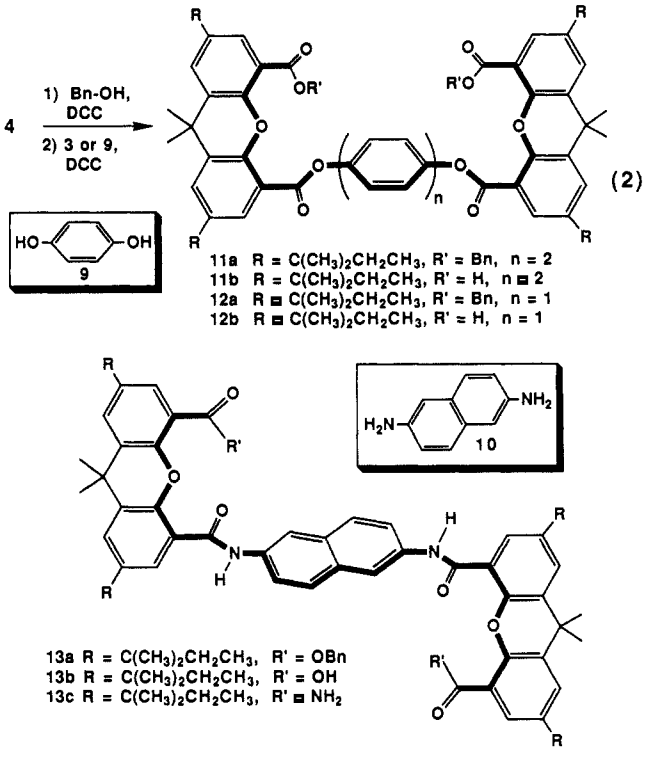
ca. 20% of an impurity in which one of the *tert*-amyl groups was replaced by a *tert*-butyl group. These impurities appear to arise from fragmentation of the *tert*-amyl carbocation during the Friedel–Crafts alkylation step and were not found to have a significant effect upon molecular recognition studies with derivatives of **4b**. The solubility of the di-*tert*-butyl derivative **4a** in $CH_2Cl_2$ at 22 °C is 30 mg/mL, while the di-*tert*-amyl compound **4b** is even more soluble (52 mg/mL). The various host molecules derived from these diacid units were also found to possess excellent solubility in a variety of organic solvents.

The xanthene diacids were efficiently monoesterified with alcohols such as methanol, phenol, or benzyl alcohol by use of 1,3-dicyclohexylcarbodiimide (DCC) and catalytic 4-(dimethylamino)pyridine.[6] Condensation of the monobenzyl ester of diacid **4b** with the diol spacers **3** and **9** (with DCC) or with diamine **10** (via the monoacid chlorides) generates cleftlike molecules **11a**, **12a**, and **13a**. Mild deprotection of the benzylated

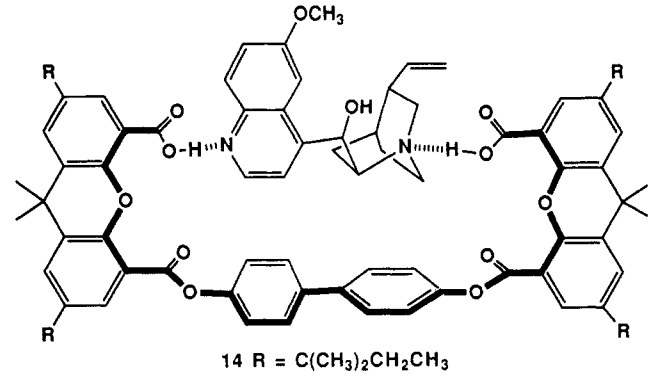


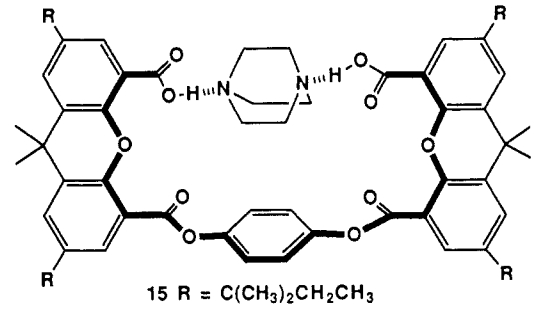

carboxyl groups ($Me_3SiI$ or hydrogenolysis) affords the corresponding diacids **11b–13b**. These diacids can adopt a number of conformations, including the C-shaped convergent one (shown for **11** and **12**) as well as S-shaped ones (shown for **13**).

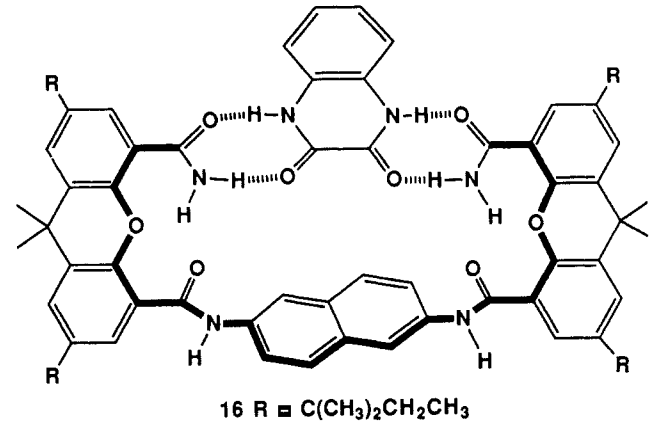
Complexation of sizable molecules bearing divergent amino groups was observed with the new receptors. For example, with quinine or quinidine, a complex with **11b** is formed in $CDCl_3$; a $K_a$ of $2 \times 10^3$ $M^{-1}$ was obtained from NMR titration data. With DABCO, the smaller cleft **12b** derived from hydroquinone showed a $K_a$ of $2.7 \times 10^4$ $M^{-1}$; neither cleft bound other bases of comparable strength, e.g., $Et_3N$, with such high affinity. Structures of these complexes are proposed as **14** and **15**.

Alteration of the chemical lining is easily achieved. For example, the diacid **13b** was treated sequentially with $SOCl_2$ and then $NH_3$ to give the corresponding diamide **13c**. This molecule presents complementary hydrogen bonding and aryl stacking for quinoxaline-2,3-dione; a soluble complex was formed in $CDCl_3$ from this substrate in solid–liquid extraction experiments. The structure proposed in **16** is consistent with the spectroscopic data for the complex.

(6) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522. Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, 4475.

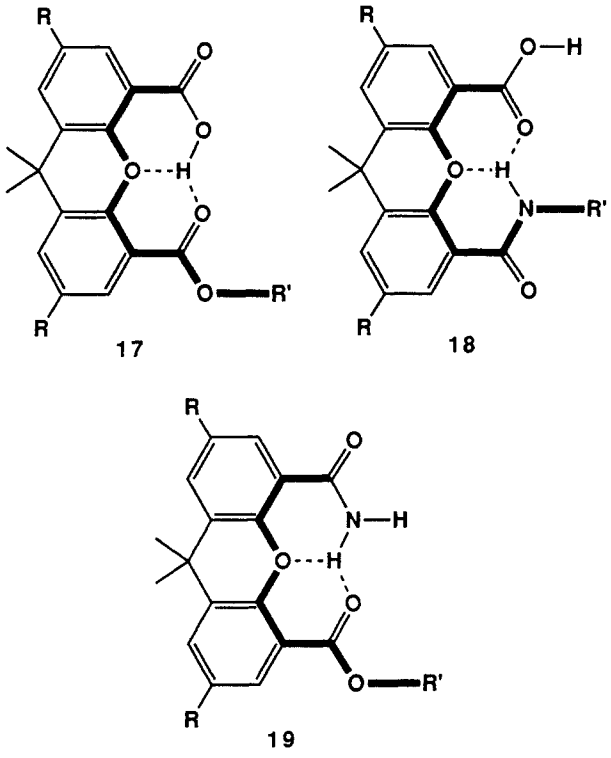



Spectroscopic studies of ester and amide derivatives of diacids **4a** and **4b** indicate the presence of intramolecular hydrogen bonding between the substituents at the 4- and 5-positions. The bonding patterns observed in acid–ester derivatives (e.g., **11b** and **12b**) and in the acid–amide derivatives (e.g., **13b**) are represented by structures **17** and **18**. In the $^1H$ NMR spectra of $CDCl_3$ solutions of the acid–ester derivatives, the carboxyl protons appear as relatively sharp peaks of concentration-invariant chemical shift. In contrast, the carboxyl protons of the acid–amide derivatives are generally not observed, and the aromatic and amide protons of some of these derivatives exhibit concentration-dependent chemical shifts. In the infrared spectra of 0.05 M $CHCl_3$ solutions of the acid–esters, the OH group appears as a single band at 3335 $cm^{-1}$ (ca. 100 $cm^{-1}$ wide at half intensity). In the acid–amides, it appears as a broad band (2500–3500 $cm^{-1}$), typical of *intermolecularly* hydrogen-bonded carboxylic acids. Together, these spectroscopic data suggest that the acid–ester derivatives do not self-associate, whereas the acid–amide derivatives are considerably more "sticky".

Intramolecular hydrogen bonding endows the 4,5-xanthenedicarboxylic acid system with unique structural features. The acid–amide derivatives **18** are preorganized, providing protons with enhanced acidity in an appropriate position for binding. Cleftlike structures containing acid–amide units are relatively shallow, since the aryl spacer group is held close to the binding site. In contrast, the acid–ester derivatives **17** are preorganized in a conformation in which the carboxyl proton is unable to participate efficiently




in intermolecular hydrogen bonding. Cleftlike structures containing these units should be able to adopt relatively deep conformations. Amide–ester compounds of the form **19** were found to exist in the preorganized, deep conformation shown. 4,5-Xanthenedicarboxamide derivatives should be able to exist in two intramolecularly hydrogen-bonded conformations. $^1$H NMR data suggest that both of these conformations are present, and in rapid equilibrium, in amide–amide **13c**.

The structural differences between the acid–esters and acid–amides are also reflected in their chemical properties. Whereas the acid–ester derivatives associate only weakly with triethylamine ($K_a = 10^2$ M$^{-1}$), the acid–amides associate strongly ($K_a = 10^4$–$10^5$ M$^{-1}$). The large difference in acidity between free s-trans and intramolecularly hydrogen bonded s-cis carboxyl groups is also reflected in the reactivity of the 4,5-xanthenedicarboxylic acids **4a** and **4b** and is responsible for their selectivity toward monoesterification (vide supra).

In summary, the two new 2,7-di-*tert*-alkyl-9,9-dimethylxanthene-4,5-dicarboxylic acids are easily prepared in quantity as highly soluble, U-shaped building blocks for molecular hosts. The relatively large distance between the carboxyl groups (4.6 Å,[7] compared to 2.5–4.1 Å in Kemp's triacid[8]) should facilitate the design and synthesis of cleftlike structures containing suitably located functionalized or chiral spacer groups. Furthermore, we anticipate that the novel structural and chemical features provided by intramolecular hydrogen bonding within the 4,5-xanthenedicarboxylic acid building blocks should prove useful in the development of catalysts as well as additional hosts.

## Experimental Section

**Instrumentation.** Infrared spectra were obtained by use of a Mattson Cygnus 100 FT IR spectrophotometer. $^1$H NMR spectra were measured with Bruker WM-250 (250-MHz) and AC-250 (250-MHz) and Varian XL-300 (300-MHz) and GE-300 (300-MHz) spectrometers. $^{13}$C NMR spectra were determined on Varian XL-300 (75-MHz) and GE-300 (75-MHz) spectrometers. Chemical shifts are expressed in parts per million ($\delta$) downfield from tetramethylsilane. High-resolution electron ionization mass spectra (HRMS) were determined on a Finnegan MAT 8200 instrument. Elemental analyses were performed by Robertson Laboratory, Inc., Madison, NJ.

**Materials.** Commercial-grade reagents and solvents were used without further purification except as indicated. Dichloromethane, benzyl alcohol, and pyridine were distilled from calcium hydride. Tetrahydrofuran and toluene were distilled from sodium benzophenone ketyl.

**Titrations.** Typically, a 2 mM solution of host in dry $CDCl_3$ was prepared, a 500-$\mu$L aliquot was transferred to a 5-mm NMR tube, and a spectrum was recorded. Aliquots of a 20 mM $CDCl_3$ solution of guest were added, and a spectrum was recorded after each addition. The addition of guest was continued until the chemical shift of the host signals remained constant (typically after the addition of ca. 20 aliquots). Association constants were obtained by nonlinear least-squares fit of the saturation plot to the 1:1 binding isotherm.[9]

**Extractions. Solubilization of Quinoxaline-2,3-dione.** Quinoxaline-2,3-dione (8 mg) was added to a 2 mM solution of receptor **13c** in 1 mL of dry $CDCl_3$. The mixture was sonicated for 10 min at room temperature and filtered. The amount of quinoxaline-2,3-dione dissolved was calculated by integration of the appropriate $^1$H NMR signals of the filtrate.

**9,9-Dimethylxanthene (6).**[4] A 1-L, three-necked, round-bottomed flask equipped with an argon inlet adapter, an addition funnel, a rubber septum, and a magnetic stirring bar was charged with a suspension of 9-xanthone (50.0 g, 0.255 mol) in 300 mL of toluene. The apparatus was evacuated and filled with argon three times and then cooled in an ice bath while trimethylaluminum solution (2.0 M in toluene, 320 mL, 0.640 mol) was added over 50 min. The resulting solution was allowed to warm to room temperature over ca. 3 h and stirred further for 14 h. The reaction mixture was transferred via cannula into a manually stirred mixture of 250 mL of concentrated HCl and 4 L of ice. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation to afford 51.5 g (96%) of **6** as a yellow oil, which was used without further purification.

**2,7-Bis(1,1-dimethylethyl)-9,9-dimethylxanthene (7a).** An ice-cooled, 1-L, three-necked, round-bottomed flask equipped with a drying tube, an addition funnel, a glass stopper, and a magnetic stirring bar was charged with 9,9-dimethylxanthene (**6**) (51.5 g, 0.245 mol), 500 mL of $CH_2Cl_2$, and $FeCl_3$ (2.0 g, 0.012 mol). *tert*-Butyl chloride (65 mL, 0.60 mol) was added over 50 min. The reaction mixture was allowed to warm to room temperature over ca. 3 h and stirred further for 15 h. The reaction mixture was extracted with 1 L of $H_2O$, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation to afford a gray-green solid. The solid was suspended in 400 mL of absolute EtOH, and the mixture was boiled, allowed to cool, and filtered to afford 41.9 g (53%) of **7a** as a white solid. Concentration of the filtrate afforded an additional 3.9 g (5%) of **7a**: mp 191–192 °C; IR ($CHCl_3$) 3009, 2967, 2908, 2871, 1489, 1407, 1365, 1295, 1268, 1134, 1122, 1088, 849, 826, 753 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 7.40 (d, $J$ = 2.4 Hz, 2 H), 7.21 (dd, $J$ = 8.6, 2.3 Hz, 2 H) 6.96 (d, $J$ = 8.5 H, 2 H), 1.65 (s, 6 H), and 1.33 (s, 18 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 148.3, 145.4, 129.2, 124.3, 122.7, 115.6, 34.4, 34.3, 32.5, 31.6; HRMS $m/e$ for $C_{23}H_{30}O$, calcd 322.2297, found 322.2298.

**2,7-Bis(1,1-dimethylpropyl)-9,9-dimethylxanthene (7b).** An ice-cooled, 2-L, three-necked, round-bottomed flask equipped with a gas inlet adapter connected to a mineral oil bubbler, a glass stopper, and a mechanical stirrer was charged with 9,9-dimethylxanthene (**6**), (52.2 g, 0.248 mol), 500 mL of $CH_2Cl_2$, and 2-chloro-2-methylbutane (92 mL, 0.75 mol). $FeCl_3$ (4.0 g, 0.025 mol) was added in several portions over 30 min, and then the reaction mixture was allowed to warm to room temperature over ca. 3 h and stirred further for 14 h. $FeCl_3$ (4.0 g, 0.025 mol) was then added in one portion, and the reaction mixture was stirred for an additional 6 h. The reaction mixture was extracted with 1 L of $H_2O$, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation to afford 88.2 (101%) of impure **7b** as a yellow-black semisolid. An analytical sample of **7b** was prepared by recrystallization two times from EtOH: mp 130–131 °C; IR ($CHCl_3$) 3008, 2968, 2932, 2879, 1488, 1467, 1407, 1387, 1379, 1364, 1293, 1260, 1133, 1088, 843, 825, 767, 759 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 7.34 (d, $J$ = 2.3 Hz, 2 H), 7.14 (dd, $J$ = 8.5, 2.4 Hz, 2 H), 6.95 (d, $J$ = 8.5 Hz, 2 H), 1.64 (s, 6 H), 1.63 (q, $J$ = 7.4 Hz, 4 H), 1.29 (s, 12 H), 0.69 (t, $J$ = 7.4 Hz, 6 H); HRMS $m/e$ for $C_{25}H_{34}O$, calcd 350.2610, found 350.2607.

**4,5-Dibromo-2,7-bis(1,1-dimethylethyl)-9,9-dimethylxanthene (8a).** An ice-cooled, 1-L, three-necked, round-bottomed flask equipped with a gas inlet adapter connected to a mineral oil bubbler, an addition funnel, and a mechanical stirrer was charged with a solution of 2,7-bis(1,1-dimethylethyl)-9,9-dimethylxanthene (**7a**) (45.4 g, 0.141 mol) in 500 mL of $CCl_4$. Bromine (16 mL, 0.31 mol) was added dropwise over 25 min, and the reaction mixture was allowed to warm to room temperature over ca. 3 h and stirred further for 23 h.[10] Fe powder (0.39 g, 0.007 mol)

(7) Value determined by use of MM2 calculations.

(8) Value determined by X-ray crystallography. Rebek, J., Jr.; Marshall, L.; Wolak, R.; Parris, K.; Kolloran, M.; Askew, B.; Nemeth, D.; Islam, N. *J. Am. Chem. Soc.* **1985**, *107*, 7476.

(9) For a discussion of this method, see: Tjivikua, T.; Deslongchamps, G.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1990**, *112*, in press.

was then added in one portion, and the reaction mixture was stirred for an additional 16 h. Bromine (5 mL, 0.10 mol) was then added, and the reaction mixture was stirred for an additional 10 h. The reaction mixture was diluted with 1 L of $CH_2Cl_2$ and extracted with 500 mL of $H_2O$. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated to afford a yellow solid. Recrystallization from THF–EtOH afforded 56.7 g (84%) of **8a** as two crops of white crystals: mp 259–260 °C; IR ($CHCl_3$) 3011, 2969, 2909, 2872, 1588, 1479, 1448, 1404, 1366, 1301, 1276, 1186, 1099, 875, 866, 752 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.48 (d, $J$ = 2.0 Hz, 2 H), 7.34 (d, $J$ = 2.3 Hz, 2 H), 1.63 (s, 6 H), 1.32 (s, 18 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 147.5, 145.5, 131.3, 128.7, 121.7, 110.5, 35.6, 34.4, 31.7, 31.2. Anal. Calcd for $C_{23}H_{28}Br_2O$: C, 57.52; H, 5.88. Found: C, 57.28; H, 5.75.

**4,5-Dibromo-2,7-bis(1,1-dimethylpropyl)-9,9-dimethylxanthene (8b).** An ice-cooled, 2-L, three-necked, round-bottomed flask equipped with a gas inlet adapter connected to a mineral oil bubbler, an addition funnel, and a mechanical stirrer was charged with a solution of crude 2,7-bis-(1,1-dimethylpropyl)-9,9-dimethylxanthene (**7b**) (88.2 g, 0.252 mol) in 500 mL of $CCl_4$. Bromine (32 mL, 0.62 mol) was added dropwise over 30 min, and the reaction mixture was allowed to warm to room temperature over ca. 4 h and stirred further for 8 h.[10] Fe powder (1.38 g, 0.025 mol) was then added in one portion, and the reaction mixture was stirred for an additional 11 h and then poured into 1 L of $H_2O$. The aqueous phase was separated and extracted with a 100- and a 20-mL portion of $CH_2Cl_2$, and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated to afford 152.7 g of dark gray-green semisolid. Recrystallization three times from absolute EtOH afforded 34.8 g (28%) of **8b** as white crystals. Concentration of the second and third mother liquors, followed by recrystallization three times from absolute EtOH, afforded a second crop of 5.4 g (4%) of **8b** as a tan solid: mp 177–178 °C; IR ($CHCl_3$) 3011, 2969, 2938, 2931, 2880, 1587, 1451, 1405, 1388, 1380, 1365, 1309, 1274, 1188, 1099, 874, 864 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.42 (d, $J$ = 2.1 Hz, 2 H), 7.27 (d, $J$ = 2.0 Hz, 2 H), 1.63 (q, $J$ = 7.5 Hz, 4 H), 1.62 (s, 6 H), 1.28 (s, 12 H), 0.69 (t, $J$ = 7.4 Hz, 6 H); HRMS $m/e$ for $C_{25}H_{32}{}^{79}Br_2O$, calcd 506.0821, found 506.0817.

**2,7-Bis(1,1-dimethylethyl)-9,9-dimethylxanthene-4,5-dicarboxylic Acid (4a).** A 2-L, three-necked, round-bottomed flask equipped with an argon inlet adapter, an addition funnel, and a mechanical stirrer was charged with a solution of 4,5-dibromo-2,7-bis(1,1-dimethylethyl)-9,9-dimethylxanthene (**8a**) (56.3 g, 0.117 mol) in 1.4 L of THF. The flask was cooled with a dry ice–acetone bath (−78 °C), *n*-BuLi solution (2.5 M in hexanes, 140 mL, 0.350 mol) was added over 15 min, and the resulting suspension was stirred for an additional 30 min. The addition funnel was replaced by a gas inlet tube, and dry $CO_2$ (61 g, 1.39 mol) was bubbled into the reaction mixture.[11] The clear solution was allowed to warm to room temperature and then poured into a mixture of 300 mL of ice, 100 mL of concentrated aqueous HCl, and 500 mL of diethyl ether. The organic phase was separated and extracted with 200 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to afford an oily white solid. The solid was washed with ca. 500 mL of hexanes and dried at 1 mmHg to yield 44.2 g (92%) of **4a** as a white solid: mp 307–309 °C; IR ($CHCl_3$) 2500–3600, 3320 (br), 3029, 2969, 2910, 2874, 1715, 1693, 1615, 1446, 1398, 1367, 1336, 1303, 1267, 1217, 1122, 898, 856, 766, 750, 713 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 11.86 (br s, 2 H), 8.19 (d, $J$ = 2.5 Hz, 2 H), 7.73 (d, $J$ = 2.5 Hz, 2 H), 1.71 (s, 6 H), 1.39 (s, 18 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.1, 147.6, 147.0, 130.5, 129.1, 128.8, 116.5, 34.5, 34.3, 32.3, 31.1. Anal. Calcd for $C_{25}H_{30}O_5$: C, 73.15; H, 7.30. Found: C, 73.13; H, 7.30.

**2,7-Bis(1,1-dimethylpropyl)-9,9-dimethylxanthene-4,5-dicarboxylic Acid (4b).** A 2-L, three-necked, round-bottomed flask equipped with an argon inlet adapter, a rubber septum, and a mechanical stirrer was charged with a solution of 4,5-dibromo-2,7-bis(1,1-dimethylpropyl)-9,9-dimethylxanthene (**8b**) (26.0 g, 0.0511 mol) in 500 mL of THF. The flask was cooled with a dry ice–acetone bath (−78 °C), *n*-BuLi solution (1.6 M in hexanes, 96 mL, 0.154 mol) was added by syringe over 6 min, and the resulting clear solution was stirred for an additional 30 min. The septum was replaced by a gas inlet tube, and dry $CO_2$ (44 g, 1.00 mol) was bubbled into the reaction mixture.[11] The clear solution was allowed to warm to 5 °C, quenched with 200 mL of 1 M HCl solution, and partitioned between 300 mL of diethyl ether and 1 L of $H_2O$. The organic phase was separated and extracted with 1 L of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to afford an oily, pale yellow solid. The solid was washed with 200 mL of hexanes and dried at 1 mmHg to yield 20.9 g (93%) of **4b** as a cream-colored solid: mp 255–256 °C; IR ($CHCl_3$) 2400–3500, 3320 (br), 3029, 2969, 2938, 2880, 1714, 1694, 1615, 1446, 1390, 1366, 1339, 1331, 1303, 1258, 1246, 1217, 1121, 757, 753 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 12.10 (br s, 2 H), 8.13 (d, $J$ = 2.4 Hz, 2 H), 7.66 (d, $J$ = 2.4 Hz, 2 H), 1.70 (q, $J$ = 7.4 Hz, 4 H), 1.70 (s, 6 H), 1.36 (s, 12 H), 0.72 (t, $J$ = 7.4 Hz, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 168.7, 147.2, 145.1, 130.2, 129.5, 129.3, 116.3, 37.9, 36.7, 34.4, 32.4, 28.4, 9.1. Anal. Calcd for $C_{27}H_{34}O_5$: C, 73.95; H, 7.81. Found: C, 73.65; H, 7.61.

**Dibenzyl 2,2′,7,7′-Tetrakis(1,1-dimethylpropyl)-9,9,9′,9′-tetramethyl-5,5′-[4,4′-biphenylenebis(oxycarbonyl)]di-4-xanthenecarboxylate (11a).** A 25-mL, two-necked, round-bottomed flask equipped with an argon inlet adapter and a rubber septum was charged with 2,7-bis(1,1-dimethylpropyl)-9,9-dimethylxanthene-4,5-dicarboxylic acid (**4b**) (0.379 g, 0.864 mmol), 4-(dimethylamino)pyridine (0.010 g, 0.082 mmol), 10 mL of $CH_2Cl_2$, and benzyl alcohol (0.090 mL, 0.869 mol). The flask was cooled in an ice bath, and dicyclohexylcarbodiimide (0.178 g, 0.863 mmol) was added in one portion. After 5 min, the ice bath was removed, and the resulting white suspension was stirred for 5 h. 4,4′-Biphenol (0.080 g, 0.430 mmol) and dicyclohexylcarbodiimide (0.194 g, 0.940 mmol) were then added sequentially, and the reaction mixture was stirred further for 15 h. The suspension was filtered, and the filtrate was concentrated by rotary evaporation to afford 0.585 g of pale yellow, foamy solid. Column chromatography on silica gel (gradient elution with ethyl acetate–hexanes) afforded 0.313 g (60%) of **11a** as a white, foamy solid: mp 182–186 °C; IR ($CHCl_3$) 3031, 3014, 2969, 2938, 2880, 1724, 1613, 1493, 1446, 1389, 1380, 1365, 1320, 1275, 1225, 1216, 1196, 1165, 1137, 1101, 1084, 1009, 769, 753, 698 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.82 (d, $J$ = 2.4 Hz, 2 H), 7.60 (d, $J$ = 2.4 Hz, 2 H), 7.59 (appar d, $J$ = 8.7 Hz, 4 H), 7.53 (d, AB pattern, $J$ = 2.4 Hz, 2 H), 7.51 (d, AB pattern, $J$ = 2.4 Hz, 2 H), 7.36 (appar d, $J$ = 8.7 Hz, 4 H), 7.24–7.31 (m, 10 H), 5.15 (s, 4 H), 1.69 (q, $J$ = 7.5 Hz, 4 H), 1.69 (s, 12 H), 1.64 (q, $J$ = 7.4 Hz, 4 H), 1.35 (s, 12 H), 1.29 (s, 12 H), 0.73 (t, $J$ = 7.4 Hz, 6 H), 0.69 (t, $J$ = 7.4 Hz, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 166.8, 165.1, 150.9, 147.9, 146.9, 144.2, 144.1, 138.2, 136.5, 131.0, 130.4, 128.5, 128.1, 128.0, 127.5, 126.6, 126.3, 122.5, 120.7, 118.9, 111.5, 66.5, 37.7, 37.6, 36.7, 36.6, 34.6, 31.9, 31.2, 28.2, 8.8; HRMS $m/e$ for $C_{80}H_{85}O_{10}$ ([M − H]$^+$), calcd 1205.6142, found 1205.6147.

**2,2′,7,7′-Tetrakis(1,1-dimethylpropyl)-9,9,9′,9′-tetramethyl-5,5′-[4,4′-biphenylenebis(oxycarbonyl)]di-4-xanthenecarboxylic Acid (11b).** A solution of dibenzyl ester **11a** (0.174 g, 0.144 mmol) and iodotrimethylsilane (0.164 mL, 1.15 mmol) in 10 mL of $CH_2Cl_2$ was stirred under argon for 4 h. The reaction mixture was extracted with 10 mL of 1 M HCl solution, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation to afford a pale yellow oil. The oil was triturated with three 1-mL portions of hexanes and recrystallized from diethyl ether to afford 0.116 g (78%) of **11b** as a white solid: mp 265–266 °C; IR ($CHCl_3$) 3335 (br), 3029, 3014, 2969, 2939, 2933, 1726, 1616, 1494, 1445, 1390, 1366, 1322, 1303, 1289, 1263, 1234, 1216, 1195, 1165, 1112, 1093, 1009, 969, 847, 760, 752 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 11.81 (s, 2 H), 8.20 (d, $J$ = 2.5 Hz, 2 H), 8.19 (d, $J$ = 2.4 Hz, 2 H), 7.74 (d, $J$ = 2.4 Hz, 2 H), 7.67 (appar d, $J$ = 8.5 Hz, 4 H), 7.63 (d, $J$ = 2.5 Hz, 2 H), 7.37 (appar d, $J$ = 8.6 Hz, 4 H), 1.74 (q, $J$ = 7.4 Hz, 4 H), 1.72 (s, 12 H), 1.68 (q, $J$ = 7.4 Hz, 4 H), 1.40 (s, 12 H), 1.34 (s, 12 H), 0.77 (t, $J$ = 7.4 Hz, 6 H), 0.69 (t, $J$ = 7.4 Hz, 6 H). Anal. Calcd for $C_{66}H_{74}O_{10}$: C, 77.17; H, 7.26. Found: C, 76.76; H, 7.29.

**Dibenzyl 2,2′,7,7′-Tetrakis(1,1-dimethylpropyl)-9,9,9′,9′-tetramethyl-5,5′-[1,4-phenylenebis(oxycarbonyl)]di-4-xanthenecarboxylate (12a).** Reaction of diacid **4b** (0.300 g, 0.684 mmol), 4-(dimethylamino)pyridine (0.010 g, 0.082 mmol), benzyl alcohol (0.071 mL, 0.686 mol), dicyclohexylcarbodiimide (0.141 g, 0.683 mmol), hydroquinone (0.038 g, 0.345 mmol), and dicyclohexylcarbodiimide (0.155 g, 0.751 mmol) according to the procedure used for the preparation and purification of **11a** afforded 0.125 g (32%) of **12a** as a white solid: mp 230–232 °C; IR ($CHCl_3$) 3032, 3013, 2969, 2939, 2880, 1725, 1613, 1502, 1446, 1389, 1380, 1365, 1320, 1274, 1226, 1218, 1201, 1173, 1138, 1100, 1083, 698 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 2.3 Hz, 2 H), 7.58 (d, $J$ = 2.3 Hz, 2 H), 7.52 (d, $J$ = 2.2 Hz, 2 H), 7.48 (d, $J$ = 2.2 Hz, 2 H), 7.22–7.35 (m, 10 H), 7.30 (s, 4 H), 5.16 (s, 4 H), 1.69 (q, $J$ = 7.3 Hz, 4 H), 1.67

(10) It is critical that the 2,7-di-*tert*-alkyl-9,9-dimethylxanthenes **7a** and **7b** be converted to the corresponding 4-bromo-2,7-di-*tert*-alkyl-9,9-dimethylxanthenes *prior* to the addition of the Fe catalyst. That complete conversion has occurred is best determined by examination of an aliquot by $^1H$ NMR spectroscopy in $CDCl_3$. The resonances of the $H_1$ and $H_8$ protons of **7a** and **7b**, which occur at $\delta$ 6.96 (d, $J$ = 8.5 Hz, 2 H), are replaced by the resonance of the $H_8$ protons of the monobrominated intermediates at $\delta$ 7.08 (d, $J$ = 8.5 Hz, 1 H). Significant quantities of the 4,5-dibromo-2,7-di-*tert*-alkyl-9,9-dimethylxanthenes **8a** and **8b** may also form prior to the addition of the catalyst. The formation of these products prior to the addition of the Fe catalyst does not adversely affect the yield of the reaction. It was sometimes necessary to employ prolonged reaction times or elevated reaction temperatures to effect complete monobromination. Addition of the Fe catalyst prior to monobromination of the 2,7-di-*tert*-alkyl-9,9-dimethylxanthenes appeared to generate products arising from ipso substitution at the 2- or 7-positions.

(11) Gaseous $CO_2$ was generated from dry ice in a one-necked flask equipped with a drying tube filled with silica gel dessiccant.

(s, 12 H), 1.64 (q, $J$ = 7.4 Hz, 4 H), 1.34 (s, 12 H), 1.29 (s, 12 H), 0.72 (t, $J$ = 7.4 Hz, 6 H), 0.68 (t, $J$ = 7.4 Hz, 6 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.5, 164.4, 148.5, 147.7, 146.6, 143.9, 143.8, 136.4, 130.8, 130.2, 128.4, 128.0, 127.8, 127.7, 127.3, 126.4, 126.2, 122.7, 120.5, 118.7, 66.6, 37.82, 37.75, 36.8, 34.7, 32.0, 28.4, 9.1; HRMS $m/e$ for $C_{74}H_{82}O_{10}$, calcd 1130.5908, found 1130.5906.

**2,2′,7,7′-Tetrakis(1,1-dimethylpropyl)-9,9,9′,9′-tetramethyl-5,5′-[1,4-phenylenebis(oxycarbonyl)]di-4-xanthenecarboxylic Acid (12b).** A 25-mL, one-necked, round-bottomed flask equipped with a magnetic stirring bar and fitted with an argon inlet adapter equipped with a cold-finger condenser was charged with dibenzyl ester **12a** (0.097 g, 0.086 mmol), 5 mL of absolute EtOH, 5 mL of THF, 1,4-cyclohexadiene (0.081 mL, 0.86 mmol), and 0.025 g of 10% Pd/C. The mixture was heated at reflux for 3 h, allowed to cool to room temperature, filtered through Celite, and concentrated to afford 0.078 g of a light gray solid. Recrystallization from $CH_2Cl_2$–$Et_2O$ followed by drying (80 °C, 1 mmHg) afforded 0.068 g (83%) of **12b** as a white solid: mp 288–291 °C dec; IR ($CHCl_3$) 3335 (br), 3029, 2969, 2939, 2933, 2880, 1725, 1615, 1503, 1445, 1390, 1366, 1330, 1322, 1303, 1263, 1235, 1175, 1156, 1112, 1092, 1017, 969, 848 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 11.8 (br s, 2 H), 8.19 (d, $J$ = 2.4 Hz, 2 H), 8.17 (d, $J$ = 2.4 Hz, 2 H), 7.73 (d, $J$ = 2.4 Hz, 2 H), 7.62 (d, $J$ = 2.4 Hz, 2 H), 7.34 (s, 4 H), 1.74 (q, $J$ = 7.4 Hz, 4 H), 1.71 (s, 12 H), 1.68 (q, $J$ = 7.5 Hz, 4 H), 1.40 (s, 12 H), 1.33 (s, 12 H), 0.77 (t, $J$ = 7.4 Hz, 6 H), 0.69 (t, $J$ = 7.4 Hz, 6 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 164.9, 164.0, 148.1, 147.8, 146.5, 145.3, 145.2, 130.9, 130.3, 129.9, 129.6, 128.7, 128.3, 122.8, 116.9, 115.6, 38.0, 37.9, 36.8, 36.7, 34.4, 32.5, 31.3, 28.3, 9.1, 9.0. Anal. Calcd for $C_{60}H_{70}O_{10}$: C, 75.76; H, 7.42. Found: C, 75.51; H, 7.22.

**5-(Benzyloxycarbonyl)-2,7-bis(1,1-dimethylpropyl)-9,9-dimethylxanthene-4-carboxylic Acid.** A 25-mL, two-necked, round-bottomed flask equipped with an argon inlet adaptor, a magnetic stirring bar, and a rubber septum was charged with 2,7-bis(1,1-dimethylpropyl)-9,9-dimethylxanthene-4,5-dicarboxylic acid (**4b**) (1.00 g, 2.28 mmol), 4-(dimethylamino)pyridine (0.027 g, 0.22 mmol), 25 mL of $CH_2Cl_2$, and benzyl alcohol (0.240 g, 2.31 mmol). The flask was cooled in an ice bath, and dicyclohexylcarbodiimide (0.470 g, 2.28 mmol) was added in one portion. After 10 min, the ice bath was removed and the reaction was stirred at room temperature for 3 h. The mixture was diluted with 50 mL of hexanes, filtered, and concentrated by rotary evaporation to a colorless syrup. Column chromatography on silica gel (elution with ethyl acetate–hexanes) afforded 0.826 g (68%) of 5-(benzyloxycarbonyl)-2,7-bis(1,1-dimethylpropyl)-9,9-dimethylxanthene-4-carboxylic acid as a colorless liquid that crystallized upon standing: mp 96–98 °C; IR (KBr) 3355, 3351, 2962, 1712, 1388, 1236, 1103, 785 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 12.00 (s, 1 H), 8.19 (d, $J$ = 1.5 Hz, 1 H), 7.94 (d, $J$ = 1.5 Hz, 1 H), 7.62 (d, $J$ = 1.5 Hz, 1 H), 7.59 (d, $J$ = 1.5 Hz, 1 H), 7.50 (d, $J$ = 6.6 Hz, 2 H), 7.37 (m, 3 H), 5.46 (s, 2 H), 1.64 (s, 6 H), 1.59 (m, 4 H), 1.32 (s, 6 H), 1.31 (s, 6 H), 0.69 (t, $J$ = 6 Hz, 3 H), 0.68 (t, $J$ = 6 Hz, 3 H); HRMS $m/e$ for $C_{34}H_{40}O_5$, calcd 528.2872, found 528.2875.

**5-(Benzyloxycarbonyl)-2,7-bis(1,1-dimethylpropyl)-9,9-dimethylxanthene-4-carbonyl Chloride.** 5-(Benzyloxycarbonyl)-2,7-bis(1,1-dimethylpropyl)-9,9-dimethylxanthene-4-carboxylic acid (0.575 g, 1.05 mmol) was dissolved in a mixture of 20 mL of $CH_2Cl_2$ and 1 mL of $SOCl_2$. The resulting solution was refluxed for 2 h under an argon atmosphere. The mixture was concentrated in vacuo to afford the acid chloride as a syrup: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 7.85 (d, $J$ = 2.2 Hz, 1 H), 7.60 (d, $J$ = 2.3 Hz, 1 H), 7.56 (d, $J$ = 2.3 Hz, 1 H), 7.52 (d, $J$ = 6.6 Hz, 2 H), 7.45 (d, $J$ = 2.3 Hz, 1 H), 7.35 (m, 3 H), 5.50 (s, 2 H), 1.68 (m, 4 H), 1.63 (s, 6 H), 1.32 (s, 6 H), 1.28 (s, 6 H), 0.69 (q, $J$ = 7.8 Hz, 6 H).

**Dibenzyl 2,2′,7,7′-Tetrakis(1,1-dimethylpropyl)-9,9,9′,9′-tetramethyl-5,5′-[2,6-bis(aminocarbonyl)naphthalenediyl]di-4-xanthenecarboxylate (13a).** A 25-mL, two-necked, round-bottomed flask equipped with an argon inlet adaptor, a magnetic stirring bar, and a rubber septum was charged with 5-(benzyloxycarbonyl)-2,7-bis(1,1-dimethylpropyl)-9,9-dimethylxanthene-4-carbonyl chloride (obtained previously), 5 mL of pyridine, and 2,6-diaminonaphthalene (0.096 g, 0.46 mmol). The reaction mixture was stirred overnight. The solvent was evaporated in vacuo, and the residue was dissolved in 60 mL of $CH_2Cl_2$. The organic solution was washed with 1 M HCl solution, dried over $Na_2SO_4$, filtered, and evaporated to yield a brown liquid. Column chromatography on silica gel (elution with ethyl acetate–hexanes) afforded 0.310 g (56%) of **13a** as a pale yellow solid: mp 136–138 °C; IR (KBr) 3329, 2963, 1717, 1662, 1653, 1533, 1437, 1223, 1112, 1099 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 10.74 (s, 2 H), 8.44 (s, 2 H), 8.34 (d, $J$ = 2.4 Hz, 2 H), 7.85 (s, 4 H), 7.82 (d, $J$ = 2.3 Hz, 2 H), 7.61 (d, $J$ = 2.3 Hz, 2 H), 7.54 (d, $J$ = 2.4 Hz, 2 H), 7.21 (m, 10 H), 5.11 (s, 4 H), 1.69 (m, 8 H), 1.65 (s, 12 H), 1.35 (s, 12 H), 1.32 (s, 12 H), and 0.70 (t, $J$ = 7.4 Hz, 12 H); HRMS $m/e$ for $C_{78}H_{86}N_2O_8$, calcd 1178.6384, found 1178.6384.

**2,2′,7,7′-Tetrakis(1,1-dimethylpropyl)-9,9,9′,9′-tetramethyl-5,5′-[2,6-bis(aminocarbonyl)naphthalenediyl]di-4-xanthenecarboxylic Acid (13b).** A Parr flask was charged with 0.1 g of 10% Pd/C and a solution of dibenzyl 2,2′,7,7′-tetrakis(1,1-dimethylpropyl)-9,9,9′,9′-tetramethyl-5,5′-[2,6-bis(aminocarbonyl)naphthalenediyl]di-4-xanthenecarboxylate (**13a**) (0.200 g, 0.17 mmol) in 6 mL of $CH_2Cl_2$ and 50 mL of EtOH. The mixture was shaken under a hydrogen atmosphere (30 psig) for 12 h, diluted with $CH_2Cl_2$ (in order to dissolve all the solid formed during the reaction), and filtered. The filtrate was evaporated, yielding a white solid 0.165 g (97%) of the pure diacid–diamide **13b**: mp 300 °C (dec); IR (KBr) 3284, 3136, 2934, 1717, 1605, 1476, 1441, 1225, 1116 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 11.25 (br s, 2 H), 8.92 (s, 2 H), 8.45 (d, $J$ = 2.4 Hz, 2 H), 8.23 (d, $J$ = 2.3 Hz, 2 H), 7.73 (d, $J$ = 2.4 Hz, 2 H), 7.67 (d, $J$ = 2.3 Hz, 2 H), 7.32 (d, $J$ = 8.2 Hz, 2 H), 7.24 (d, $J$ = 8.2 Hz, 2 H), 1.70 (m, 8 H), 1.69 (s, 12 H), 1.46 (s, 12 H), 1.40 (s, 12 H), 0.89 (m, 12 H); HRMS $m/e$ for $C_{64}H_{74}N_2O_8$, calcd 998.5437, found 998.5445.

**2,2′,7,7′-Tetrakis(1,1-dimethylpropyl)-9,9,9′,9′-tetramethyl-5,5′-[2,6-bis(aminocarbonyl)naphthalenediyl]di-4-xanthenecarbonyl Chloride.** The diacid–diamide **13b** (0.100 g, 0.1 mmol) was dissolved in a mixture of 30 mL of $CH_2Cl_2$ and 0.2 mL of $SOCl_2$. The resulting clear solution was refluxed for 2 h under an argon atmosphere. The solvent was evaporated in vacuo affording a yellowish solid of the diacid chloride–diamide, which was used in the next step without further purification: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 9.94 (s, 2 H), 8.45 (s, 2 H), 8.32 (d, $J$ = 2 Hz, 2 H), 8.09 (d, $J$ = 1.9 Hz, 2 H), 7.91 (d, $J$ = 8.7 Hz, 2 H), 7.77 (d, $J$ = 8.7 Hz, 2 H), 7.74 (d, $J$ = 1.9 Hz, 2 H), 7.55 (d, $J$ = 1.9 Hz, 2 H), 1.71 (s, 12 H), 1.69 (m, 8 H), 1.36 (s, 12 H), 1.35 (s, 12 H), 0.72 (m, 12 H).

**2,2′,7,7′-Tetrakis(1,1-dimethylpropyl)-9,9,9′,9′-tetramethyl-5,5′-[2,6-bis(aminocarbonyl)naphthalenediyl]di-4-xanthenecarboxamide (13c).** The diacid chloride–diamide (obtained previously) was dissolved in 40 mL of $CH_2Cl_2$ and the resulting solution cooled to 0 °C. Ammonia gas was bubbled into the solution for 4 min, and then the reaction mixture was stirred at 0 °C for 1 h. The solution was diluted with 50 mL of $CH_2Cl_2$ and washed with 1 M HCl solution, dried over $Na_2SO_4$, filtered, and concentrated in vacuo to afford a solid. Trituration with a mixture of ethyl acetate and hexanes (2:1) yielded 0.07 g (70%) of the pure tetraamide **13c** as a white powder: mp >325 °C; IR (KBr) 3412, 3190, 2963, 1652, 1610, 1442, 1255, 1115 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 8.66 (s, 2 H), 8.35 (s, 2 H), 7.88 (d, $J$ = 2.2 Hz, 2 H), 7.84 (d, $J$ = 8.7 Hz, 2 H), 7.75 (d, $J$ = 1.8 Hz, 2 H), 7.62 (d, $J$ = 8.7 Hz, 2 H), 7.55 (s, 2 H), 7.55 (d, $J$ = 2.2 Hz, 2 H), 7.52 (d, $J$ = 2.3 Hz, 2 H), 5.66 (s, 2 H), 1.07 (s, 12 H), 1.65 (s, 8 H), 1.36 (s, 12 H), 1.32 (s, 12 H), 0.72 (m, 12 H); HRMS $m/e$ for $C_{64}H_{76}N_4O_6$, calcd 996.5764, found 996.5762. An analytical sample of **13c** was prepared by recrystallization from ethyl acetate–hexanes. Anal. Calcd for $C_{64}H_{76}N_4O_6$: C, 77.10, H, 7.63; N, 5.62. Found: C, 77.23; H, 7.64; N, 5.58.

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