Synthesis of Hexahomotrioxacalix[3]naphthalenes and a Study of Their Alkali-Metal Cation Binding Properties

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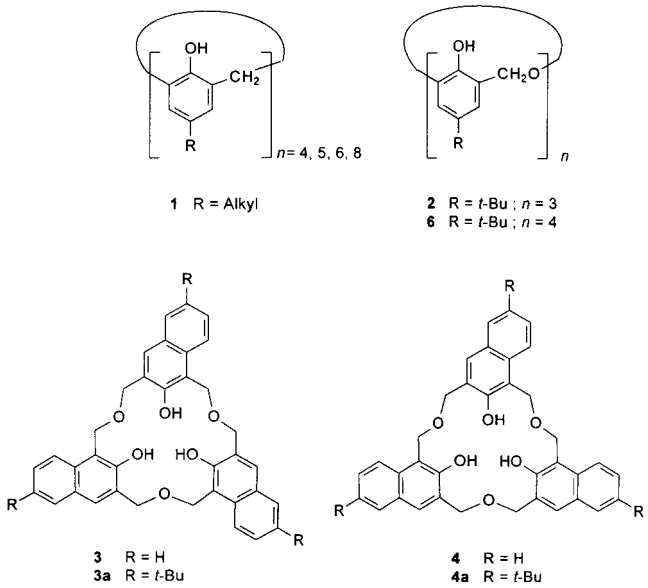
The first syntheses of the C_3-symmetrical and unsymmetrical hexahomotrioxacalix[3]naphthalenes **3** and **4**, respectively, and the corresponding *tert*-butyl hexahomotrioxacalix[3]naphthalene **3a** are reported. A convergent synthesis of the linear hexahomotrimer precursors **19** and **19a** is described, but the direct synthesis of **3** and **3a** can also be achieved from the monomers **20** and **20a**, respectively. A limited study of the binding properties of alkali-metal cations by **3** or **3a** using a picrate−$CHCl_3$ extraction showed only weak abilities to bind with the cations examined.

Introduction

Calixarenes (**1**) and their derivatives continue to be the focus of considerable research activity since they are easily accessible compounds which can show wide-ranging applications as a result of their unique conformational, physicochemical and complexation properties.[1,2] Most of the chemical modifications of the basic calixarenes have been concerned with modifying either their "upper rims" or their "lower rims" (phenolic hydroxyl-bearing) in order to assess and potentially enhance their selectivity toward supramolecular ("host−guest" type) complexation of ionic or neutral species.

A different class of molecules which are closely related to the calixarenes are the homooxacalixarenes, in which the phenolic units are linked by CH_2OCH_2 groups instead of methylene bridges, therefore containing additional methyleneoxy groups in the macrocyclic ring. The best-known example of these compounds is hexahomotrioxacalix[3]arene (**2**), whose synthesis has been reported by Gutsche et al.[3] and Vicens et al.[4] albeit in low yields. More recently, Hampton et al.[5] and Fuji et al.[6,7] have reported different and potentially more useful versatile synthetic routes to **2** and other analogues bearing different alkyl functionalities in their upper rims. Nevertheless, despite the fact that these homoxacalixarenes possess unique structural features and some of their derivatives[8] show ionophoric capabilities, they have received relatively little attention compared with the calixarenes. Among recent studies are notable reports from Shinkai's group in which **2** has been used as a C_3-symmetrical macromolecular host for chiral recognition of α-amino acid derivatives[9] and also as a basic molecular scaffold on which to generate dimeric capsules which have served as a versatile hosts for [60]fullerene.[10]



As part of our ongoing research into developing the chemistry of the calixnaphthalenes,[11] we undertook a

(1) Gutsche, C. D. *Calixarenes Revisited*; Royal Society of Chemistry, Cambridge, **1998**.

(2) *Calixarenes 50th Anniversary*: *Commemorative Issue*; Vicens, J., Asfari, Z., Harrowfield, J. McB., Eds.; Kluwer Academic Publishers: Dordrecht, 1995.

(3) Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, *103*, 3782.

(4) Zerr, P.; Mussrabi, M.; Vicens, J. *Tetrahedron Lett.* **1991**, *32*, 1879.

(5) Hampton, P. D.; Bencze, Z.; Tong, W.; Daitch, C. E. *J. Org. Chem.* **1994**, *59*, 4838.

(6) Tsubaki, K.; Otsubo, T.; Tanaka, K.; Fuji, K.; Kinoshita, T. *J. Org. Chem.* **1998**, *63*, 3260.

(7) Tsubaki, K.; Mukoyoshi, K.; Otsubo, T.; Fuji, K. *Chem. Pharm. Bull.* **2000**, *48*, 882.

(8) Araki, K.; Hayashida, H. *Tetrahedron Lett.* **2000**, *41*, 1807.

(9) Araki, K.; Inada, K.; Shinkai, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 72.

(10) (a) Ikeda, A.; Udzu, H.; Yoshimura, M.; Shinkai, S. *Tetrahedron* **2000**, *56*, 1825. (b) Ikeda, A.; Yoshimura, M.; Udzu, H.; Fukuhara, C.; Shinkai, S. *J. Am. Chem. Soc.* **1999**, *121*, 4296. (c) Ikeda, A.; Yoshimura, M.; Udzu, H.; Fukuhara, C.; Shinkai, S. *Chem. Lett.* **1994**, 587.

(11) Georghiou, P. E.; Ashram, M.; Li, Z.; Chaulk, S. G. *J. Org. Chem.* **1995**, *60*, 7284.

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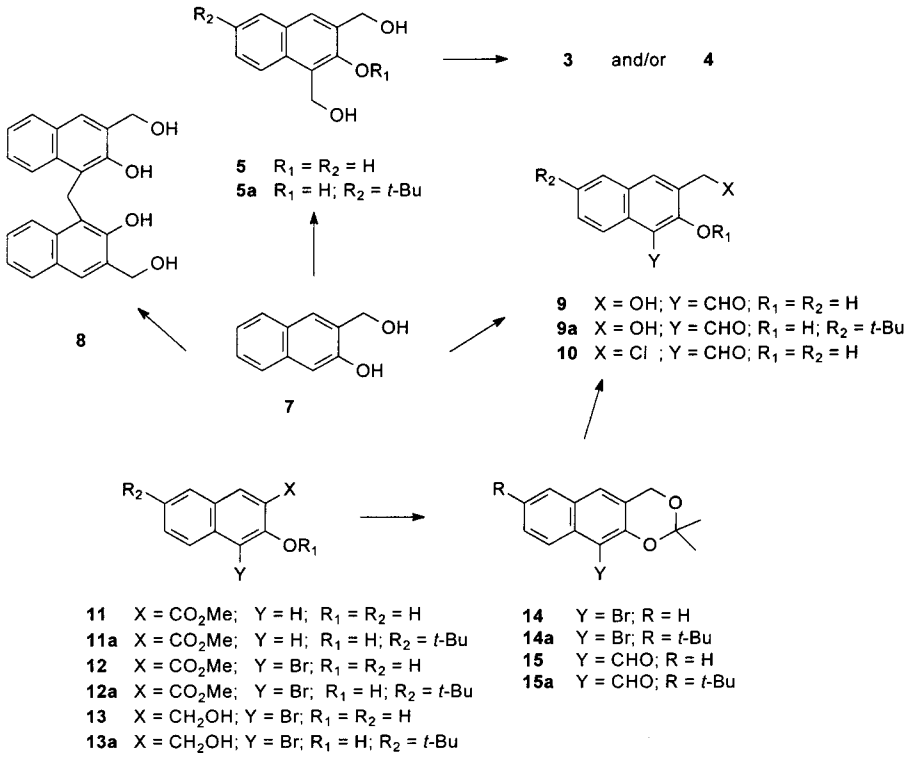
Scheme 1



program to synthesize hexahomotrioxacalix[3]naphthalene (**3**)[12] in order to evaluate its potential as a suitable new inherently chiral supramolecular host or building block. In this paper, we report the first synthesis of both the C_3-symmetrical and unsymmetrical hexahomooxacalix-[3]naphthalenes **3** and **4**, respectively, and also a study of the binding properties of alkali-metal cations by **3**.

Results and Discussion

The first synthetic approach investigated toward **3** and/or **4** is outlined in Scheme 1 in which 1,3-bis(hydroxymethyl)-2-hydroxynaphthalene (**5**) was envisioned as being a suitable target precursor compound. This consideration was made by analogy with Hampton's[5] findings that 2,6-bis(hydroxymethyl)-4-substituted phenols self-condensed to form mixtures of oxacalix[3]calixarenes **2** and oxacalix-[4]arenes **6** under high dilution methanesulfonic acid-catalyzed conditions in dimethoxyethane or CH_2Cl_2. However, all attempts at synthesizing **5** directly from 3-hydroxymethyl-2-hydroxynaphthalene (**7**) failed, affording only **8**. An alternative procedure for introducing the hydroxymethyl group at the 1-position of **7** via hydride reduction of **9** which could be produced by formylation of **7** using $TiCl_4/Cl_2CHOCH_3$[13] was not pursued any further since **9** could only be produced in low (18%) yield with an accompanying amount of the chloromethyl product **10** which was formed in 24% yield. A different route to **9** (and its 6-*tert*-butyl derivative **9a**) was evaluated in which methyl 3-hydroxy-2-naphthoate (**11**) (or its 7-*tert*-butyl derivative **11a**)[14] was brominated selectively to afford **12** (or **12a**, respectively), which in turn, was reduced to the hydroxymethylated **13** (or **13a**, respectively). In contrast to **7**, the acetonide **14** (or **14a**) could be formylated (*tert*-butyllithium/DMF) in good yields to give **15** (or **15a**). Deprotection of **15** afforded **9** in good yield; however, subsequent attempted hydride reduction of **9** gave only mixtures of intractable products instead of the desired compound **5**.

Our experience[15] with **7** itself under a variety of acidic conditions has indicated that hetero-Diels−Alder products are formed instead, via *o*-naphthoquinide intermediates. It was concluded therefore that the direct self-condensation approach from **5** (or **5a**) would not likely be successful. During the course of this work, Fuji et al.[6] described a stepwise convergent synthesis of hexahomotrioxacalix[3]arenes having different substituents on their upper rims. Their approach involved cyclization of linear trimers under acidic high-dilution conditions. These trimers, e.g., **16** possessed terminal acetonide-bearing aryl rings and were synthesized via alkylation of **17** with 2 molar equiv of the bromomethylacetonides **18** (Scheme 2). The corresponding analogous alkylation to form linear oxanaphthalene trimers e.g., **19** envisioned reaction of **20** with **21**. Although the hydroxymethyl acetonide **22** (or **22a**) could be obtained in excellent

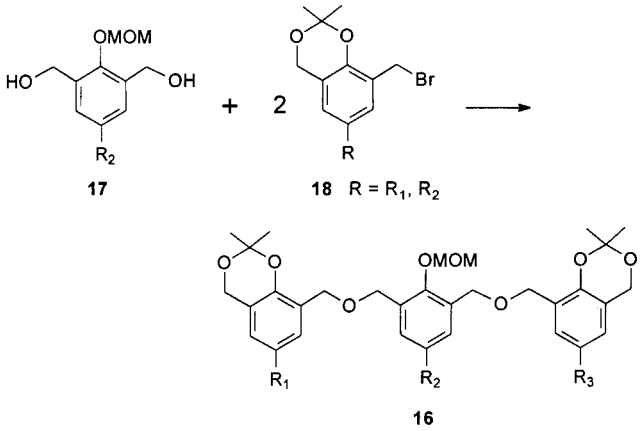
(12) The following names are based upon a "calixarene"-type naming and numbering scheme: *sym*-31,32,33-trihydroxy-2,3,12,13,22,23-hexahomo-3,13,23-trioxacalix[3]naphthalene, for the C_3-symmetrical compound **3**; 31,32,33-trihydroxy-2,3,12,13,22,23-hexahomo-3,13,23-trioxacalix[3]naphthalene for the unsymmetrical compound **4**; *sym*-8,-18,28-tri-*tert*-butyl-31,32,33-trihydroxy-2,3,12,13,22,23-hexahomo-3,-13,23-trioxacalix[3]naphthalene for the C_3-symmetrical compound **3a**. Names based upon the Chemical Abstracts naming system are the following: 16*H*,26*H*,28*H*,-5,29:9,15:19,25-trimetheno-6*H*,8*H*,18*H*-tribenzo[*d*,*l*,*t*][1,9,17]trioxacyclotetracosin-30,31,32-triol for **3**; 16*H*,26*H*,-28*H*-5,29:9,15:19,25-trimetheno-6*H*,8*H*,18*H*-tribenzo[*d*,*l*,*u*][1,9,17]-trioxacyclotetracosin-30,31,32-triol for **4**; 10,10′-[[2-(methoxymethoxy)-1,3-naphthalenediyl]bis(methyleneoxymethylene)]bis[[2,2-dimethyl-4*H*-naphtho[2,3-*d*]-1,3-dioxin for the linear trimer **19**; and 10,10′-[[2-(methoxymethoxy)-1,3-naphthalenediyl]bis(methyleneoxymethylene)]-bis[[2,2-dimethyl-7-(1,1-dimethylethyl)-4*H*-naphtho[2,3-*d*]-1,3-dioxin for the *tert*-butyl linear trimer **19a**.

(13) Vogel, A. I. *Vogel's Textbook of Practical Organic Chemsitry*, 5th ed.; Longman: London, 1989.

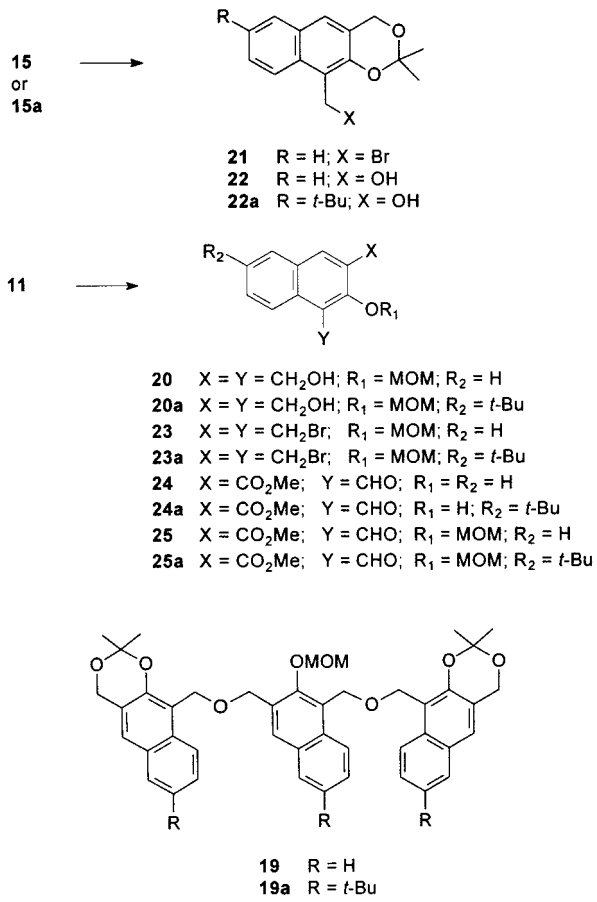
(14) Georghiou, P. E.; Ashram, M.; Clase, H. J.; Bridson, J. N. *J. Org. Chem.* **1998**, *63*, 1819.

(15) Georghiou, P. E.; Ashram, M. Unpublished results.

Scheme 2



Scheme 3



yields, its conversion to the corresponding bromide **21** was difficult to achieve in good yields using a variety of conditions. Instead, alkylation of **22** (or **22a**) with the bisbromomethyl compound **23** (or **23a**) derived form **20** (or **20a**) was evaluated (Scheme 3). Synthesis of the MOM-protected **20** (or **20a**) was achieved in comparatively good overall yields (40−45%) using a modified route in which the naphthoate **11**(or **11a**) was formylated to give **24** (or **24a**) which in turn, was *O*-MOM protected to afford **25** (or **25a**). Hydride reduction of **25** (or **25a**) afforded in excellent yields, the desired product(s) which could be converted into the corresponding bisbromomethyl compounds **23** or **23a**, respectively. Alkylation of **23** (or **23a**) with 2 molar equiv of **22** (or **22**a) afforded the linear trioxatrimers **19** (or **19a**).

When **19** was subjected to Fuji's "wet" $CHCl_3-HClO_4$ conditions,[7] two cyclic hexahomotrioxa compounds **3** and **4** were isolated, albeit in low yields (5 and 3%, respectively). The nonsymmetrical cyclic compound **4** was expected by analogy with the mechanism proposed by Fuji et al.[7] for their trioxacalixarenes. Formation of the unexpected C_3-symmetrical **3**, however, can be rationalized by presuming that the linear trimer **19** underwent acid-catalyzed ether cleavage as well as the acid-catalyzed acetonide-deprotection to produce **20** (or possibly the MOM-deprotected **5**) in situ which could subsequently self-condense to form **3**. Alternatively, the MOM-deprotection step could have occurred *after* cyclization.

To test this hypothesis, **20** itself was subjected to the same wet $CHCl_3-HClO_4$ conditions. Hexahomotrioxacalix[3]naphthalene **3** was produced in this single step and could be isolated in 5−6% yields, which although relatively low at this stage has an obvious advantage over the convergent route. Its physical and spectral properties were identical with those of the product obtained from the cyclization of the linear trimer **19**. Since the cyclization could be achieved in a single step, a more convenient direct route to **3** was therefore available, one avoiding the prior formation of the linear trimer, and its immediate precursors. Different acid-catalyzed reaction conditions have been investigated in order to improve the yields of **3** from **20** but thus far have not resulted in any greater improvement in yields. Attempted cyclization of **19** using either Hampton's methanesulfonic acid conditions,[5] or trifluoroacetic acid-$CHCl_3$ conditions in fact failed to produce any discernible amounts of either **3** or **4**. Using the same conditions that were employed for **20**, cyclization of **20a** could also be achieved to form the corresponding "upper-rim" *tert*-butyl analogue **3a** in 5−6% yields.

The ^{1}H NMR spectrum of **3** in $CDCl_3$ or CD_2Cl_2 (Figure 1) is very simple, consistent with its predicted C_3 symmetry. Since the two sets of methylene protons appear as singlets at δ 5.02 and 5.20 ppm, the compound is clearly conformationally highly flexible, indicating rapidly interconverting "cone"-like conformers in which all three hydroxyl groups are on the same face of the 18-membered macrocycle, as opposed to a pair of rapidly interconverting "partial-cone"-like conformers in which one of the hydroxyl group is on the opposite face of the macrocycle to the other two. A VT-^{1}H NMR experiment over the temperature range from 298 to 203 K showed only a broadening of the hydroxyl proton resonance, and no coalescence temperatures could be observed for the methylene protons. The ^{1}H NMR spectrum of **3a** is similar to that of **3** apart from the changes due to the presence of the *tert*-butyl groups. Of course, due to the lack of symmetry of the naphthalene rings, in either **3** or **3a**, the pairs of each of the rapidly interconverting crown conformers is chiral. We have synthesized the lower-rim functionalized di- and tri(ethoxycarbonyl)-methoxy esters which, as with the hexahomocalix[3]-arenes, results in the prevention of interconversion between cone and/or partial cone conformers. The syntheses of these compounds and the study of their conformational and complexation properties with alkali-metal cations and C_{60} will be reported on in due course.

The ability of **3** or **3a** to bind to silver or alkali metal cations was evaluated using a picrate-$CHCl_3$ extraction

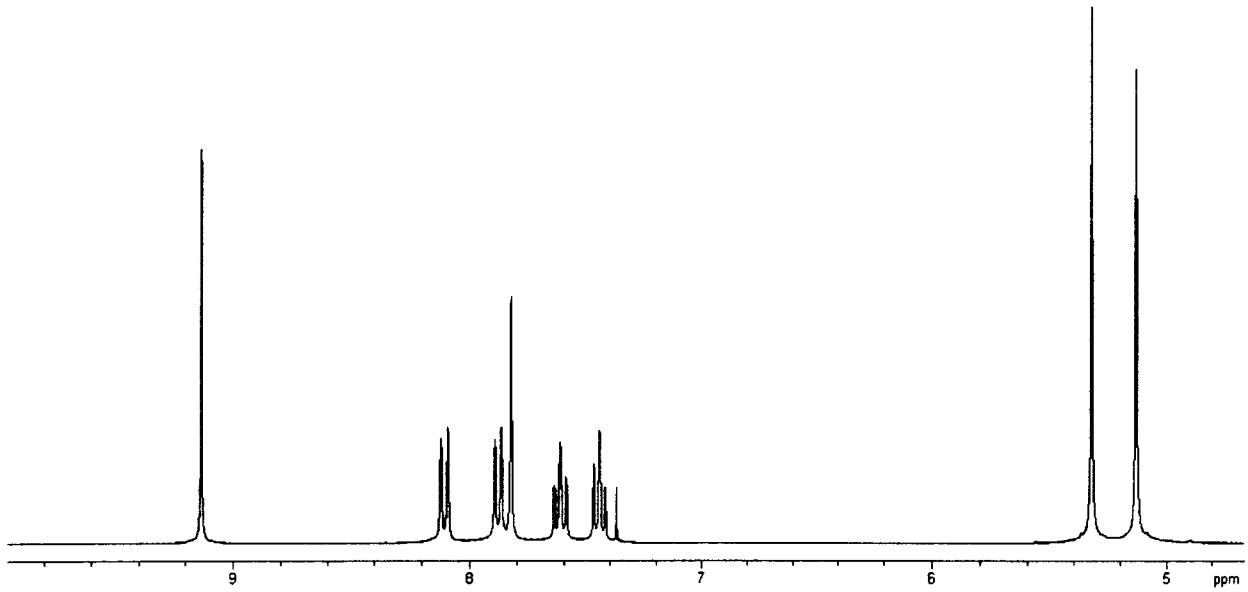


Figure 1.

procedure.[16,17] It was found that both **3** and **3a** showed only weak abilities to bind with the cations investigated. The absorbances determined spectrophotometrically indicated that with the exception Na^+, less that 1% of **3** binds to the other metals, while **3a** showed a higher binding ability for $K^+$and Cs^+ as compared to **3**. These results are consistent with Dutton's reported results with the analogous trioxohexahomocalix[3]arenes in which he found that less than 0.5% of the ligand bound to the alkali metal ion picrates in CH_2Cl_2. These results are similar to those observed with the calix[n]arenes (n = 4, 6, and 8) which also show negligible binding of metal picrates.[17]

Experimental Section

General Methods. For general experimental data see ref 13. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 and 75.47 MHz, respectively, in $CDCl_3$ unless otherwise indicated. All reactions were carried out under Ar or N_2 unless otherwise noted. Chromatography was performed with 60 mesh silica gel and preparative layer (1 mm) chromatography (PLC) with standard thin-layer chromatography (TLC) grade silica gel. HRMS were conducted at the Department of Chemistry, University of Ottawa.

Symmetrical Hexahomotrioxacalix[3]naphthalene (3) and Hexahomotrioxacalix[3]naphthalene (4) from Linear Trioxatrimer 19. To a solution of **19** (200 mg, 0.31 mmol) in wet[6] $CHCl_3$ (40 mL) was added aqueous 60% perchloric acid (0.04 mL). The reaction was stirred at room temperature for 3 h and was then quenched and washed with water until the aqueous layer was neutral to pH paper. The organic layer was dried with anhydrous $MgSO_4$, and the solvent was evaporated on a rotary evaporator to afford a crude product which was subjected to PLC using $CHCl_3$ to give the hexahomotrioxacalix-[3]naphthalene **3** as a colorless solid, (8 mg, 5%): mp 193−195 °C; ^{1}H NMR 5.03 (s, 6H), 5.22 (s, 6H), 7.34 (ddd, J = 8.7, 7.0, 1.0 Hz, 3H), 7.52 (ddd, J = 8.1, 7.0, 1.2 Hz, 3H), 7.72 (s, 3H), 7.78 (d, J = 8.1 Hz, 3H), 8.00 (d, J = 8.7 Hz, 3H), 9.03 (s, 3H); ^{13}C NMR 64.8, 71.8, 115.4, 121.8, 123.3, 125.5, 126.9, 128.2, 128.6, 129.8, 132.8; −EIS MS m/z 558 (M^+), 557. Compound **4** was also obtained as a colorless solid (4 mg, 2%): mp 197−199 °C; ^{1}H NMR 4.87 (s, 2H), 4.99 (s, 2H), 5.04 (s, 4H), 5.16 (s, 2H), 5.33 (s, 2H), 7.44 (m, 3H), 7.62 (m, 2H), 7.73 (s, 1H), 7.89 (m, 3H), 8.04 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 8.7 Hz), 1H), 8.42 (s, 1H), 8.52 (d, J = 8.7 Hz, 1H), 8.81 (s, 1H), 8.95 (s, 1H); +FABMS (m/z) 598, 595, 588, 575, 559, 558 (M^+), 528.

Hexahomotrioxacalix[3]naphthalene 3 from 20. Hexahomotrioxacalix[3]naphthalene **3** was also synthesized directly from **20** (1.00 g, 4.03 mmol) as above to give **3** (30 mg, 5%), whose physical and spectral properties were identical with those of the **3** obtained from linear trimer **19**.

***tert*-Butylhexahomotrioxacalix[3]naphthalene (3a) from 20a.** To a stirred solution of **20a** (1.00 g, 3.29 mmol) in wet[6] $CHCl_3$ (300 mL) was added aqueous 60% $HClO_4$ at room temperature. The reaction mixture was stirred at room temperature for 2−3 h and monitored by TLC. The reaction was then quenched and washed with water until the aqueous layer was neutral to pH paper. The organic layer was dried with anhydrous $MgSO_4$, and the solvent was evaporated on a rotary evaporator to afford a crude product which was subjected to flash chromatography using $CHCl_3$ as solvent to give **3a** as a pale yellow solid (48 mg, 6%): mp 140−142 °C; ^{1}H NMR 1.39 (s, 27H), 5.01 (s, 6H), 5.17 (s, 6H), 7.61 (dd, J = 9.0 and 1.8 Hz, 3H), 7.68 (m, 6H), 7.94 (d, J = 9.0 Hz, 3H), 8.82 (s, 3H); ^{13}C NMR 31.2, 34.5, 64.4, 72.0, 115.2, 121.7, 123.5, 125.3, 125.7, 128.1, 129.6, 131.1, 145.9, 153.7; +FABMS (m/z) calcd for $C_{48}H_{54}O_6$ 726.3920, found 726.4037 (M^+).

2-Hydroxy-3-hydroxymethyl-1-naphthaldehyde (9). $TiCl_4$ (1.50 mL, 14.4 mmol) was added to a stirred solution of 3-hydroxymethyl-2-hydroxynaphthalene (**7**) (1.50 g, 8.62 mmol) in anhydrous CH_2Cl_2 (80 mL) at 0 °C, followed by the addition of Cl_2CHOCH_3 (0 0.70 mL, 8.62 mmol). The mixture was stirred for 5 min at 0 °C and then allowed to warm to room temperature and stirred for a further 45 min. The reaction was quenched by adding cold water (20 mL). The organic layer was separated, and the aqueous layer was extracted with three 20 mL portions of CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$, and the solvent was evaporated on a rotary evaporator. The crude product was separated by PLC using ethyl acetate/hexane (3:7) as the solvent system to afford **9** as a yellow solid (320 mg, 18%): mp 91−92 °C; ^{1}H NMR 2.84 (br, 1H), 4.83 (s, 2H), 7.39 (dd, J = 8.4, 7.2 Hz, 1H), 7.55 (dd, J = 7.8, 7.2 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.94 (s, 1H), 8.20 (d, J = 8.4 Hz, 1H), 10.67 (s,1H); ^{13}C NMR 60.9, 111.0, 118.4, 124.7, 127.3, 128.8, 129.4, 130.0, 132.2, 136.6, 163.2, 193.9; MS m/z 202 (M^+, 45), 185 (13), 184 (73), 157 (8), 156 (63), 129 (12), 128 (100), 127 (42), 115 (22); HRMS calcd for $C_{12}H_{10}O_3$ (M^+) 202.0630, found 202.0639. A second major

(16) (a) Araki, K.; Hashimoto, N.; Otsuka, H.; Shinkai, S. *J. Org. Chem.* **1993**, *58*, 5958. (b) Araki, K.; Inada, K.; Otsuka, H.; Shinkai, S. *Tetrahedron* **1993**, *49*, 9465.

(17) (a) Chang, S.; Cho, I. *J. Chem. Soc., Perkin Trans. 1* **1986**, 211. (b) Iwamato, K.; Shinkai, S. *J. Org. Chem.* **1992**, *57*, 7066.

product isolated was **10** as a yellow solid (450 mg, 24%): mp 87−88 °C; ^{1}H NMR 4.83 (s, 2H), 7.47 (dd, J = 7.5 and 7.1 Hz, 1H), 7.65 (dd, J = 8.5 and 7.1 Hz, 1H), 7.85 (d, J = 7.5 Hz, 1H), 8.13 (s, 1H), 8.35 (d, J = 8.5 Hz, 1H), 10.83 (s, 1H); ^{13}C NMR 37.7, 108.5, 115.6, 122.1, 124.2, 124.6, 126.8, 126.9, 130.3, 136.2, 160.2, 190.9; MS *m*/*z* 223 (4), 222 (26), 221 (11), 220 (M^+, 82), 186 (14), 185 (100), 157 (15), 156 (33), 129 (34), 128 (91), 102 (12); HRMS calcd for $C_{12}H_9ClO_2$ (M^+) 220.0291, found 220.0278.

Compound **9** can also be prepared from the acetonide **15** in 92% yield: A solution of **15** (300 mg, 1.24 mmol) in a 1:1 mixture of THF/aqueous 1.0 M HCl (5.0 mL) was stirred at room temperature for 24 h. The yellow solution was extracted with $CHCl_3$ (50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, and the solvent was evaporated on a rotary evaporator to afford **9** (230 mg, 92%), which was pure enough (by TLC) to be used in subsequent reactions.

Methyl 4-Bromo-3-hydroxy-2-naphthoate (12). To a solution of methyl 3-hydroxy-2-naphthoate **11** (1.09 g, 5.5 mmol) in dioxane (10 mL) was added a dioxane solution (10 mL) of dioxanedibromide (1.51 g, 5.94 mmol) at room temperature. The reaction was stirred at room temperature for 30 min. Cold water was gradually added until a precipitate formed. The precipitate was separated by filtration and washed with water. The product was air-dried to afford **12** as a yellow solid (1.39 g, 92%):[13] mp 108−109 °C; ^{1}H NMR 4.06 (s, 3H), 7.41 (dd, J = 8.4 Hz, 1H), 7.66 (dd, J = 8.4 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 8.50 (s, 1H); ^{13}C NMR 53.0, 106.8, 113.8, 124.5, 125.6, 127.3, 129.6, 130.4, 131.8, 136.0, 152.9, 169.9; MS *m*/*z* 282 (32), 280 (34), 251 (16), 250 (100), 249 (16), 248 (96), 222 (19), 220 (20), 195 (6), 194 (14); HRMS calcd for $C_{12}H_9BrO_3$ 279.9735 found 279.9774.

Methyl 4-Bromo-7-*tert*-butyl-3-hydroxy-2-naphthoate (12a). Methyl naphthoate **11a** (300 mg, 1.16 mmol) was subjected to the same reaction conditions as **11** to afford **12a** as a yellow solid (355 mg, 91%): mp 111−112 °C; ^{1}H NMR 1.42 (s, 9H), 4.06 (s, 3H), 7.75 (s, 1H), 7.78 (dd, J = 8.7, 1.8 Hz, 1H), 8.13 (dd, J = 8.7, 1.0 Hz, 1H), 8.50 (s, 1H); ^{13}C NMR 30.9, 34.6, 52.9, 106.6, 114.1, 124.5, 125.7, 127.5, 129.7, 131.9, 134.5, 147.3, 152.8, 170.2; MS *m*/*z* 338 (38), 336 (M^+, 39), 323 (16), 321 (17), 307 (19), 306 (99), 305 (21), 304 (100), 292 (10), 291 (65), 290 (12), 289 (66); HRMS calcd for $C_{16}H_{17}BrO_3$ 336.0361, found 336.0348.

1-Bromo-3-hydroxymethyl-2-hydroxynaphthalene (13). To a suspension of LAH (140 mg, 3.58 mmol) in anhydrous THF (10 mL) was added a solution of **12** (500 mg, 1.78 mmol) in anhydrous THF (10 mL) at room temperature. The reaction was quenched after 5 min by adding into wet diethyl ether (30 mL) at 0 °C. The solution was then acidified with aqueous 10% HCl. The organic layer was separated and the aqueous layer was extracted with two 10 mL portions of diethyl ether. The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated on a rotary evaporator to afford **13** as a pale yellow solid (0.45 g, ∼ 95%). After being washed with CH_2Cl_2, the sample was pure enough for use in subsequent reactions. An analytical sample was purified by PLC using ethyl acetate/hexane (3:7) as solvent system to afford **13** as pale yellow crystals: mp 92−93 °C; ^{1}H NMR 2.50 (br, 1H), 4.92 (d, J = 4.8 Hz, 2H), 6.73 (s, 1H), 7.39 (ddd, J = 8.7, 7.5, 1.2 Hz, 1H), 7.55 (ddd, J = 8.1, 7.5, 1.2 Hz, 1H), 7.66 (s, 1H), 7.74 (d, J = 8.1 Hz, 1H), 8.03 (d, J = 8.7 Hz, 1H); ^{13}C NMR 62.9, 106.7, 124.5, 125.3, 127.2, 127.7, 128.1, 128.4, 129.2, 132.0,-149.2; MS *m*/*z* 254 (24), 252 (M^+, 25), 237 (10), 236 (66), 234 (67), 208 (26), 206 (27), 156 (14), 155 (100); HRMS calcd for $C_{11}H_9BrO_2$ 251.9786, found 251.9798.

1-Bromo-6-*tert*-butyl-3-hydroxymethyl-2-hydroxynaphthalene (13a). The naphthoate **12a** (3.42 g, 10.2 mmol) was subjected to the same reaction conditions as **12** to afford **13a** as a colorless solid (1.70 g, 54%): mp 106−107 °C; ^{1}H NMR 1.41 (s, 9H), 2.52 (t, 1H), 4.92 (d, 2H), 6.67 (s, 1H), 7.63−7.69 (m, 3H), 7.97 (d, J = 9.0 Hz, 1H); ^{13}C NMR 31.1, 34.4, 63.2, 106.5, 123.3, 125.4, 126.6, 127.1, 128.3, 129.1, 130.3, 147.2, 148.8; MS *m*/*z* 310 (4), 308 (4), 304 (10), 292 (18), 290 (18), 277 (16), 275 (21), 242 (25), 241 (8), 228 (12), 227 (67), 225 (10), 213 (52), 199(39); HRMS calcd for $C_{15}H_{17}BrO_2$ 308.0412, found 308.0405.

1-Bromonaphthalene Acetonide 14. To a solution of **13** (400 mg, 1.59 mmol) and 2,2-dimethoxypropane (0.68 mL, 5.57 mmol) in acetone (20 mL) was added a catalytic amount of *p*-toluenesulfonic acid. The reaction was stirred at room temperature for 24 h. An excess amount of solid $NaHCO_3$ was added to the reaction mixture, which was then filtered, and the solvent was evaporated on a rotary evaporator. The crude product was dissolved in $CHCl_3$ (20 mL), and the organic layer was washed with two 10 mL portions of water, dried over anhydrous $MgSO_4$, and evaporated on a rotary evaporator to afford **14** as a pale yellow solid (300 mg, 75%) (mp 86−87 °C) which was sufficiently pure enough to use in the subsequent reaction; it can also be purified by flash chromatography using $CHCl_3$/hexane (1:1) as solvent system: ^{1}H NMR 1.67 (s, 6H), 5.08 (s, 2H), 7.40 (dd, J = 8.4, 6.0 Hz, 1H), 7.47 (s, 1H), 7.54 (dd, J = 8.1, 6.0 Hz, 1H), 7.72 (d, J = 8.1 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H); ^{13}C NMR 25.0, 61.0, 101.1, 107.6, 121.6, 122.9, 124.5, 125.9, 127.1, 127.6, 129.1, 132.5, 147.0; MS *m*/*z* 294 (17), 292 (M^+, 18), 237 (14), 236 (98), 235 (15), 234 (97), 208 (24), 206 (25), 156 (12), 155 (100), 127 (74); HRMS calcd for $C_{14}H_{13}$-BrO_2 292.0099, found 292.0120.

7-*tert*-Butyl-1-bromonaphthalene Acetonide 14a. *tert*-Butyl naphthoate **13a** was subjected (1.70 g, 5.52 mmol) to the same reaction conditions as **13** to afford a crude product that was purified by flash chromatography using ethyl acetate/hexane (1:9) as solvent system to give **14a** as an oily product (1.42 g, 74%): ^{1}H NMR 1.40 (s, 9H), 1.64 (s, 6H), 5.05 (s, 2H), 7.43 (br, 1H), 7.63 (m, 2H), 8.12 (dd, J = 10, 1.0 Hz, 1H); ^{13}C NMR 24.9, 31.1, 34.8, 61.0, 101.0, 107.2, 121.4, 122.6, 122.8, 125.6, 126.1, 128.9, 130.5, 146.4, 147.4; MS *m*/*z* 504 (M − 1 + tosyl, 6), 351 (26), 350 (5), 348 (M^+, 24), 293 (18), 292 (100), 291 (22), 290 (91), 277 (12), 275 (10); HRMS calcd for $C_{18}H_{21}$-BrO_2 348.0725, found 348.0727.

Naphthalenecarboxaldehyde Acetonide (15). *tert*-Butyllithium (8.52 mL, 14.5 mmol) was added dropwise to a solution of bromo compound **14** (3.86 g, 13.2 mmol) in anhydrous THF (150 mL) at −78 °C. The reaction mixture was stirred at −78 °C for a further 1 h, after which time anhydrous dimethylformamide (2.1 mL, 26.4 mmol) was added. The reaction was allowed to warm to room temperature and was stirred for 16 h, after which time it was quenched by adding cold water (20 mL). The reaction mixture was extracted with two 30 mL portions of CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$, and the solvent was evaporated on a rotary evaporator to afford crude **15** as a yellow solid (2.81 g, 87%) which can be further purified by washing with methanol: mp 126−127 °C; ^{1}H NMR 1.69 (s, 6H), 5.10 (s, 2H), 7.42 (dd, J = 8.7, 7.8 Hz, 1H), 7.61 (dd, J = 9.9, 7.8 Hz, 1H), 7.70−7.74 (m, 2H), 9.27 (d, J = 8.7 Hz, 1H) 10.85 (s, 1H); ^{13}C NMR 25.1, 60.6, 101.3, 115.8, 119.9, 122.8, 124.4, 124.8, 124.9, 127.6, 127.8, 129.4, 131.3, 157.4, 191.2; MS *m*/*z* 242 (M^+, 25), 214 (3), 185 (19), 184 (100), 171 (13), 156 (80), 155 (24), 129 (11), 128 (95), 127 (32), 102 (11); HRMS calcd for $C_{15}H_{14}O_3$ 242.0943, found 242.0942.

6-*tert*-Butylnaphthalenecarboxaldehyde Acetonide (15a). *tert*-Butyl bromoacetonide **14a** (1.42 g, 4.08 mmol) was subjected to the same reaction conditions as **14** to afford an viscous oily product (1.10 g, 90%) which was sufficiently pure for the next step. An analytical sample was purified by PLC using ethyl acetate/hexane (1.5:8.5) as solvent system: ^{1}H NMR 1.40 (s, 9H), 1.64 (s, 6H), 5.05 (s, 2H), 7.67 (m, 3H), 9.21 (d, J = 9.3 Hz, 1H), 10.84 (s, 1H); ^{13}C NMR 24.9, 30.9, 34.3, 60.8, 101.2, 115.7, 122.9, 124.6, 127.7, 128.3, 128.9, 131.4, 147.6, 156.8, 191.3; MS *m*/*z* 298 (M^+, 8), 241 (10), 240 (43), 226 (17), 225 (100), 197 (12); HRMS calcd for $C_{19}H_{22}O_3$ 298.1569, found 298.1567.

Linear Trimer (19). To a suspension of NaH (180 mg, 4.84 mmol) in anhydrous THF (35 mL) was added a THF solution consisting both the dibromo **23** (450 mg, 1.21 mmol) and **22** (595 mg, 2.42 mmol) at reflux temperature over 2 h. The reaction was stirred at reflux temperature for 10 h. The reaction mixture was worked up by adding cold water gradually, and the mixture was extracted with two 25 mL portions

of CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_4$ and the solvent evaporated on a rotary evaporator to afford **19** as a solid (767 mg, 98%): mp softness at 53−55 °C, melts at 88−90 °C; ^{1}H NMR 1.56 (s, 6H), 1.60 (s, 6H), 3.40 (s, 3H), 4.80 (s, 2H), 4.90 (s, 2H), 4.98, (s, 2H), 5.06 (d, 2H), 5.08 (br, 2H), 5.11 (s, 2H), 5.20 (s, 2H), 7.29−7.49 (m, 7H), 7.70−7.75 (m, 3H), 7.89 (s, 1H), 7.92−7.95 (m, 1H), 8.10 (d, J = 8.1 Hz, 1H), 8.17 (d, J = 8.7 Hz, 1H); ^{13}C NMR 25.0, 29.7, 57.4, 61.2, 62.9, 62.0, 63.2, 67.7, 101.5, 102.9, 117.4, 117.7, 120.5, 120.6, 123.8, 124.2, 124.3, 124.7, 124.8, 126.2, 126.3, 127.8, 128.1, 128.4, 129.2, 129.3, 130.9, 131.6, 133.0, 133.1, 133.3, 148.3, 148.5, 153.1; +FABMS (NOBA) *m*/*z* 748, 723, 701 (M^+ + 1), 685, 657.

***tert*-Butyl Linear Trimer (19a).** The *tert*-butyl precursor compounds dibromo compound **23a** (250 mg, 0.584 mmol) and **22a** (345 mg, 1.15 mmol) were subjected to the same reaction conditions as **19a** to afford, after PLC using ethyl acetate/hexane (1:4) as solvent system, a colorless solid (151 mg, 31%): mp 90−95 °C; ^{1}H NMR 1.36 (s, 9H), 1.40 (s, 9H), 1.41 (s, 9H), 1.56 (s, 6H), 1.59 (s, 6H), 3.40 (s, 3H), 4.80 (s, 2H), 4.87 (s, 2H), 4.94 (s, 2H), 5.07−5.09 (m, 6H), 5.19 (s, 2H), 7.37−7.68 (m, 9H), 7.85 (d, J = 8.7 Hz, 1H), 7.89 (s, 1H), 8.06 (d, J = 9.3 Hz, 1H), 8.12 (d, J = 9.0 Hz, 1H); ^{13}C NMR 25.0, 31.3, 34.5, 57.4, 61.3, 61.9, 63.0, 67.8, 100.1, 101.7, 117.3, 117.5, 117.6, 120.5, 122.6, 123.1, 123, 6, 123.7, 123.8, 124.2, 124.3, 124.4, 125.1, 125.2, 125.3, 128.4, 129.3, 129.3, 129.4, 130.1, 130.9, 131.2, 131.3, 131.5, 146.4, 146.6, 147.3, 147.8, 148.1, 152.8; +FABMS (NOBA) *m*/*z* 999, 975, 957, 915, 867, 868 (M^+).

1,3-Bis(hydroxymethyl)-2-*O*-methoxymethylnaphthalene (20). To a suspension of LAH (792 mg, 20.8 mmol) in anhydrous THF (100 mL) was added a THF solution of **25** (1.89 g, 6.90 mmol) at room temperature. After 5 min, the reaction was quenched by pouring into wet diethyl ether (100 mL) at 0 °C. The reaction mixture was then slowly acidified with aqueous 5% HCl until the aqueous layer become slightly acidic. The organic layer was separated, and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated on a rotary evaporator to give **20** as a colorless solid (1.60 g, 94%): mp 87−88 °C; ^{1}H NMR 2.98 (d, 2H), 3.63 (s, 3H), 4.73 (s, 2H), 5.02 (s, 4H), 7.45 (ddd, J = 8.1, 7.5, 1.2 Hz, 1H), 7.54 (ddd, J = 8.4, 7.5, 1.2 Hz, 1H), 7.79 (s, 1H), 7.78 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.1 Hz, 1H); ^{13}C NMR 55.9, 56.0, 57.6, 61.8, 100.7, 123.4, 124.0, 125.5, 127.0, 128.4, 129.5, 131.3, 132.8, 133.4; MS *m*/*z* 248 (M^+, 2), 216 (7), 187 (5), 186 (35), 185 (16), 158 (27), 157 (27), 141 (10), 130 (6), 129 (21), 128 (26), 127 (17); HRMS calcd for $C_{14}H_{16}O_4$ 248.1049, found 248.1041.

6-*tert*-Butyl-1,3-bis(hydroxymethyl)-2-*O*-methoxymethylnaphthalene (20a). Carboxaldehyde **25a** (1.68 g, 5.10 mmol) was subjected to the same reaction conditions as **20** to afford **20a** after PLC purification, as a viscous yellow oil (1.22 mg, 79%): ^{1}H NMR 1.41 (s, 9H), 2.92 (br, 2H), 3.64 (s, 3H), 4.75 (s, 2H), 5.04 (s, 4H), 7.65 (dd, J = 9.0, 2.1 Hz, 1H), 7.75 (d, J = 2.1 Hz, 1H), 7.81 (s, 1H), 8.13 (d, J = 9.0 Hz, 1H); ^{13}C NMR 31.1, 34.6, 56.0, 57.4, 61.8, 100.7, 123.4, 123.7, 125.9, 127.8, 129.5, 130.7, 131.3, 133.2, 148.2, 152.7; MS *m*/*z* 304 (M^+, 4), 272 (4), 242 (16), 228 (7), 227 (39), 213 (17), 199 (11); HRMS calcd for $C_{18}H_{24}O_4$ 304.1674, found 304.1670.

1-Bromomethylnaphthalene Acetonide 21. To a solution of alcohol **22** (180 mg, 0.74 mmol) and CBr_4 (370 mg, 1.11 mmol) in anhydrous THF (40 mL) at 0 °C was added a THF solution (10 mL) of Ph_3P (390 mg, 1.48 mmol). The reaction was stirred and allowed to gradually warm to room temperature. After 6 h, the reaction was worked up by filtering off the colorless precipitate and evaporating the solvent. The residue was purified by PLC using $CHCl_3$ petroleum ether (1:1) to afford **21** as a colorless solid (35 mg, 15%): mp 86−87 °C (decomposes upon standing); ^{1}H NMR 1.55 (solvent), 1.64 (s, 6H), 4.66 (s, 2H), 5.20 (s, 2H), 7.30−7.76 (m, 5H); ^{13}C NMR 24.4, 28.5, 59.6, 61.1, 120.66, 124.0, 127.2, 128.7, 129.2; MS *m*/*z* 308 (3), 306 (M^+, 3), 250 (5), 248 (5), 170 (13), 169 (100), 142 (4), 141 (28), 140 (4), 139 (11).

Hydroxymethyl Acetonide 22. $NaBH_4$ (35 mg, 0.91 mmol) was added to a solution of aldehyde **15** (220 mg, 0.91 mmol) in a mixture of MeOH/THF (5 mL:1 mL) at 0 °C. The reaction was stirred for a further 1 h at 0 °C. The reaction mixture was quenched by adding cold water (5 mL) and was then extracted with two 10 mL portions of $CHCl_3$. The combined organic extracts were dried over anhydrous $MgSO_4$, and the solvent was evaporated on a rotary evaporator to afford **22** as a colorless solid (160 mg, 72%), mp 153−154 °C. For a larger scale sample, the product can be purified by washing with diethyl ether: ^{1}H NMR 1.63 (s, 6H), 1.92 (t, J = 6.3 Hz, 1H), 5.07 (s, 2H), 5.15 (d, J = 6.3 Hz, 2H), 7.35 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.47 (brs, 1H), 7.49 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H); ^{13}C NMR (acetone-d_6) 25.4, 54.5, 61.8, 101.0, 122.3, 124.5, 124.7, 124.9, 126.8, 128.9, 129.7, 133.9, 148.6; MS *m*/*z* 244 (M^+, 15), 187 (6), 186 (52), 185 (15), 159 (11), 158 (100), 157 (79), 141 (10), 130 (16), 129 (34), 128 (27), 115 (21); HRMS calcd for $C_{15}H_{16}O_3$ 244.1099, found 244.1098.

6-*tert*-Butylhydroxymethyl Acetonide 22a. The *tert*-butyl aldehyde **15a** (970 mg, 3.24 mmol) was subjected to the same reaction conditions as **15**. The crude product was purified by flash chromatography using ethyl acetate/hexane (3:7) as solvent system to afford **22a** as a colorless semisolid (496 mg, 51%): ^{1}H NMR 1.41 (s, 9H), 1.62 (s, 6H), 2.02 (br, 1H), 5.06 (s, 2H), 5.15 (br, 2H), 7.45 (brs, 1H), 7.60 (dd, J = 9.0, 2.1 Hz, 1H), 7.66 (d, J = 2.1 Hz, 1H), 8.05 (d, J = 9.0 Hz, 1H); ^{13}C NMR 25.0, 31.1, 34.6, 55.4, 61.2, 100.1, 120.3, 120.6, 122.7, 122.9, 123.9, 125.5, 128.4, 130.1, 146.5, 147.4; MS *m*/*z* 300 (M^+, 17), 243 (16), 242 (88), 227 (36), 214 (48), 213 (100), 200 (11), 199 (73); HRMS calcd for $C_{19}H_{24}O_3$ 300.1725, found 300.1700.

1,3-Bis(bromomethyl)-2-*O*-methoxymethylnaphthalene (23). To a mixture of **20** (1.55 g, 6.27 mmol) and Ph_3P (6.59 g, 25.0 mmol) in anhydrous CH_2Cl_2 (100 mL) was added CBr_4 (8.24 g, 25.0 mmol) in small portions over 10 min. The reaction was stirred for an additional 10 min and then quenched by adding cold aqueous 10% $NaHCO_3$ solution until the aqueous layer became basic. The organic layer was separated and then washed with several portions of cold water until the aqueous layer was neutral. Drying over anhydrous $MgSO_4$ and then evaporating the solvent afforded a viscous product which was purified by flash chromatography using ethyl acetate/hexane (1:9) as the solvent to give **23** as a colorless solid (1.01 g, 43%) (mp 114−115 °C) and which decomposes on standing at room temperature for any length of time: ^{1}H NMR 3.76 (s, 3H), 4.80 (s, 2H), 5.10 (s, 2H), 5.38 (s, 2H), 7.52 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.66 (ddd, J = 8.4, 6.9, 1.2 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.96 (s, 1H), 8.12 (d, J = 8.4 Hz, 1H); ^{13}C NMR 25.1, 29.2, 30.4, 57.8, 100.4, 122.5, 123.7, 124.7, 125.9, 127.6, 128.0, 128.7, 131.2, 132.4, 153.0; MS *m*/*z* 376 (0.1), 374 (0.5), 280 (1), 278 (1), 250 (6), 248 (6), 182 (2), 172 (2), 171 (13), 170 (19), 169 (100), 142 (11), 141 (41), 115 (25); HRMS calcd for $C_{14}H_{14}Br_2O_2$ 371.9361, found 371.9350.

1,3-Bis(bromomethyl)-6-*tert*-butyl-2-*O*-methoxymethylnaphthalene (23a). The *tert*-butyl diol **20a** (1.14 g, 3.74 mmol) was subjected to the same reaction conditions as **20** to afford after chromatography **23a** as a pale yellow oil (669 mg, 42%): ^{1}H NMR 1.44 (s, 9H), 3.75 (s, 3H), 4.80 (s, 2H), 5.10 (s, 2H), 5.37 (s, 2H), 7.74−7.80 (m, 2H), 7.94 (s, 1H), 8.06 (d, J = 9.0 Hz, 1H); ^{13}C NMR 24.8, 25.5, 29.6, 31.1, 34.7, 57.8, 100.3, 122.3, 123.4, 123.7, 123.8, 125.2, 126.6, 126.9, 130.5, 131.0, 131.2, 132.4, 132.5, 148.7, 152.3; MS *m*/*z* 350 (3), 348 (4), 306 (4), 304 (3), 293 (18), 292 (100), 291 (20), 290 (98), 277 (22), 275 (22), 249 (6), 225 (52), 211 (52), 196 (13); HRMS calcd for $C_{18}H_{22}Br_2O_2$ 427.9986, found 427.9996.

Methyl 4-Formyl-3-hydroxy-2-naphthoate (24). To a solution of the methyl ester **11** (9.2 g, 45.5 mmol) in anhydrous CH_2Cl_2 (185 mL) was added $TiCl_4$ (8.28 mL, 76.2 mmol) at room temperature, followed by Cl_2CHOCH_3 (12.9 mL, 138 mmol). The reaction mixture was refluxed for 2 h and then quenched by slowly adding cold water while the reaction mixture was cooled at 0 °C. The mixture was diluted with 50 mL of CH_2Cl_2. The organic layer was separated, dried, and concentrated on a rotary evaporator. The crude product was dissolved in 20 mL of $CHCL_3$ and boiled with charcoal. The filtrate was evaporated to give **24** as a yellow solid (8.10 g, 77%): mp 140−141 °C; ^{1}H NMR 4.06 (s, 3H), 7.43 (ddd, J =

8.1, 6.9, 1.2 Hz, 1H), 7.70 (ddd, J = 8.6, 6.9, 1.5 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 8.69 (s, 1H), 9.11 (d, J = 8.7, 1H), 10.94 (s, 1H), 12.03 (br, 1H); ^{13}C NMR 52.9, 123.9, 125.1, 126.4, 130.3, 132.5, 134.5, 140.5, 163.8, 191.9; MS m/z 230 (M^+, 37), 202 (27), 197 (11), 171 (13), 170 (100), 142 (43), 114 (30), 113 (25); HRMS calcd for $C_{13}H_{10}O_4$ 230.0579, found 230.0576.

Methyl 6-*tert*-Butyl-4-formyl-3-hydroxy-2-naphthoate (24a). *tert*-Butyl methyl ester **15a** (1.00 g, 3.88 mmol)[14] was subjected to the same reaction conditions as **15** to afford, after PLC purification, **24a** as a dark yellow solid (747 mg, 67%): mp 220−221 °C; ^{1}H NMR 1.40 (s, 9H), 4.05 (s, 3H), 7.75 (d, J = 1.8 Hz, 1H), 7.80 (dd, J = 9.3, 2.1 Hz, 1H), 8.68 (s, 1H), 9.04 (d, J = 9.0 Hz, 1H), 10.91 (s, 1H), 11.92 (br, 1H); ^{13}C NMR 30.9, 34.4, 52.7, 114.6, 123.4, 125.1, 126.4, 131.5, 132.8, 140.6, 147.9, 163.3, 169.1, 191.7; MS m/z 286 (M^+, 52), 272 (9), 271 (51), 258 (12), 239 (55), 226 (100), 211 (16); HRMS calcd for $C_{17}H_{18}O_4$ 286.1205, found 286.1199.

Methyl 4-Formyl-3-*O*-methoxymethyl-2-naphthoate (25). To a solution of ester **24** (100 mg, 0.435 mmol) in anhydrous CH_2Cl_2 (10 mL) at room temperature was added MOMCl (0.10 mL, 1.305 mmol) followed by 0.33 mL (1.74 mmol) of diisopropylethylamine. The mixture was refluxed for 30 min and cooled to room temperature, and then the organic layer was washed gradually with portions of aqueous 1% HCl until the aqeous layers became acidic. Drying and evaporating the solvent afforded **25** as a yellow solid (110 mg, 85%): mp 63−64 °C; ^{1}H NMR 3.61 (s, 3H), 3.98 (s, 3H), 5.23 (s, 2H), 7.57 (ddd, J = 8.1, 6.9, 1.5 Hz, 1H), 7.75 (ddd, J = 8.7, 6.9, 1.5 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 8.67 (s, 1H), 9.23 (d, J = 8.7 Hz, 1H), 10.84 (s, 1H); ^{13}C NMR 52.6, 58.2, 102.6, 123.44, 125.22, 126.7, 129.3, 131.5, 132.6, 139.8, 160.9, 165.5, 193.3; MS m/z 274 (M^+, 2), 243 (5), 242 (7), 229 (8), 198 (2), 197 (12), 170 (14), 45 (100); HRMS calcd for $C_{15}H_{14}O_5$ 274.0841, found 274.0832.

Methyl 7-*tert*-Butyl-4-formyl-3-*O*-methoxymethyl-2-naphthoate (25a). *tert*-Butyl methyl ester **24a** was subjected to the same reaction conditions as **24** to afford, after PLC purification, **25a** as an oily yellow product (297 mg, 90%): ^{1}H NMR 1.39 (s, 9H), 3.60 (s, 3H), 3.98 (s, 3H), 5.21 (s, 2H), 7.81 (s, 1H), 7.83 (dd, J = 9.0, 1.2 Hz, 1H), 8.66 (s,1H), 9.15 (d, J = 9.0 Hz, 1H), 10.83 (s, 1H); ^{13}C NMR 30.8, 34.6, 52.5, 58.0, 102.6, 123.2, 124.3, 124.8, 129.8, 130.7, 140.1, 149.4, 165.5, 193.2; MS m/z 330 (M^+, 10), 299 (8), 285 (25), 284 (23), 269 (20), 255 (8), 253 (21),226 (44); HRMS calcd for $C_{19}H_{22}O_5$ 330.1467, found 330.1486.

Metal Picrate Binding Studies. Extractions of metal picrates from deionized water into chloroform (spectrograde) were performed according to the following typical procedure: 5 mL of an aqueous 1.0×10^{-4} M solution of the metal picrate and 5 mL of a chloroform 1.0×10^{-4} M solution of **3** or **3a** in $CHCl_3$ were mechanically shaken in a Teflon-lined stoppered glass tube for 24 h. The mixture was then equilibrated in a thermostated water bath at 25.0 ± 0.1 °C for 2 h in order to achieve good phase separation. The absorbance of the metal picrate remaining in the aqueous phase was then determined spectrophotometrically at 358 nm on a HP 8452A diode array UV−vis spectrophotometer. Percentage extraction (%E) is calculated from the expression $\%E = 100(A_o - A)/A_o$, where A_o is the absorbance of the aqueous solution without **3** or **3a**.

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Supporting Information Available: Copies of high-resolution ^{1}H and ^{13}C NMR spectra and mass spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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