Tuning the Polarity of Hierarchically Assembled Helicates

Miriam Baumert,[a] Markus Albrecht,*[a] Henrik D. F. Winkler,[b] Christoph A. Schalley[b]

[a] Institut für Organische Chemie der RWTH Aachen, Landoltweg 1, 52074 Aachen, Germany
Fax +49(241)8092385; E-mail: Markus.Albrecht@oc.rwth-aachen.de

[b] Institut für Chemie und Biochemie – Organische Chemie, Freie Universität Berlin, Takustr. 3, 14195 Berlin, Germany

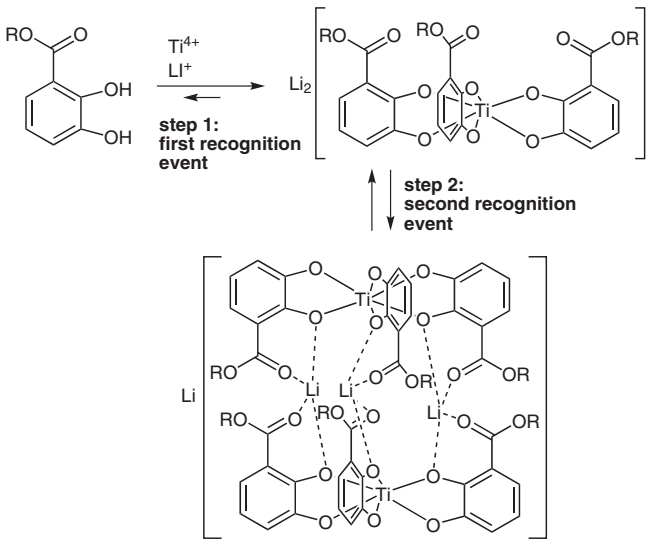
Received 27 August 2009

Abstract: Catechol ligands bearing ester groups in 3-position (**1a**,**b**, **2**) are building blocks for the formation of triply lithium-bridged dinuclear helicate-type complexes $[Li_3(\mathbf{1a},\mathbf{b},\mathbf{2})_6Ti_2]^-$. Attachment of appropriate functionalities at the ester unit allows the fine tuning of the polarity of the compounds to afford solubility in highly nonpolar as well as highly polar solvents. The investigations show that the internal dinuclear core is stable in a broad variety of solvents, even in water.

Key words: helicates, dinuclear complexes, esters, hierarchical self-assembly, templates

The hierarchical formation of highly complex structures is a common process in nature as well as in artificial systems.[1] Examples are proteins[2] or the tobacco mosaic virus.[3] Recently, we described the stepwise assembly of dinuclear double-[4] and triple-stranded helicate-type complexes.[5,6] Catechol building blocks with a carbonyl donor, such as esters, ketones, and aldehydes in 3-position were used to form dinuclear complexes with various coordination centers (Ti^{IV}, $Mo^{VI}O_2$, B^{III}) (Scheme 1).

Common solvents used for study of the 'monomer-dimer' system were methanol, which shifts the equilibrium towards the dinuclear complex and dimethyl sulfoxide favoring the monomer as major product. This preference of monomer versus dimer is due to the ability of the solvent to solubilize lithium cations and to disrupt the dimer. Herein, we extend our studies to the extremes of solvent polarity. First we present complexes, which assemble and are soluble in nonpolar solvents (benzene, chloroform) and in the second part hierarchical helicate formation in water as highly polar reaction medium is described. The aim of this study is to test the stability of the dimeric complexes of ester type ligands in the opposed solvent extremes.



Scheme 1 Hierarchical formation of triply lithium-bridged dinuclear titanium(IV) helicates

Hierarchical Assembly of Highly Hydrophobic Helicates

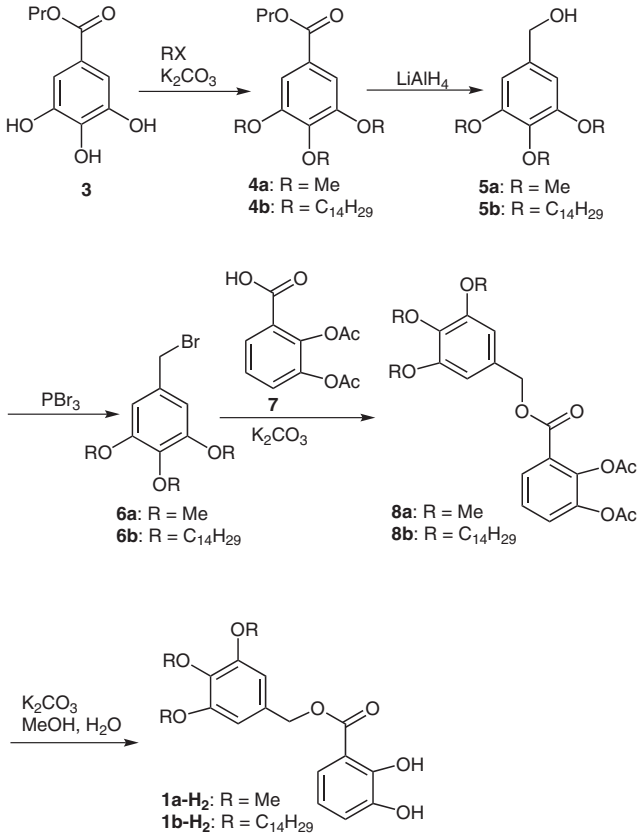
Long alkyl chains were introduced as substituents in ligand $\mathbf{1b\text{-}H_2}$ in order to generate hydrophobicity (Scheme 2). For comparison, the methyl-substituted ligand $\mathbf{1a\text{-}H_2}$ was prepared as well.

The synthesis consists of five steps, starting with gallic acid propyl ester (**3**), which couples in an S_N-type reaction with iodomethane or 1-bromotetradecane to yield **4a**,**b** (100% **a**, 69% **b**).[7] The following step is the reduction of the ester function with $LiAlH_4$ to afford **5a**,**b**, followed by substitution of the benzylic alcohol by PBr_3 leading to the benzyl bromides **6a**,**b** (yield over two steps: **a**: 69%, **b**: 100%).[8] Compounds **6a**,**b** react with 2,3-diacetoxybenzoic acid (**7**) under basic conditions to yield the protected ligands **8a**,**b**. The ligand precursor selectively is deprotected by mild basic conditions resulting in the ligands **1a**,**b** (yield over two steps: 42% **a**, 29% **b**). Finally, titanium(IV) complexes $Li_2[Ti(\mathbf{1a},\mathbf{b})_3]$ were prepared by dissolving 3 equivalents of the corresponding ligand $\mathbf{1a},\mathbf{b\text{-}H_2}$, 1 equivalent of $TiO(acac)_2$, and 1 equivalent of Li_2CO_3 in chloroform. After stirring overnight, the solvent was removed under reduced pressure to afford the complexes in quantitative yield as red solids.

In earlier studies we have shown that the equilibrium between the mononuclear complex and the dinuclear helicate (see Scheme 1) relies on the polarity of the solvent.[4,5] By dissolving crystals of the dimeric species in different solvents, different equilibrium mixtures of monomer and dimer occur instantaneously.

^{1}H NMR spectrum of the complex $Li[Ti_2(\mathbf{1a})_6Li_3]$ with methyl groups show diasteretopic splitting and – compared to the free ligand – high-field shift of the benzylic

SYNTHESIS 2010, No. 6, pp 0953–0958
Advanced online publication: 24.02.2010
DOI: 10.1055/s-0029-1218684; Art ID: Z18109SS



Scheme 2 Ligand synthesis **1a**,**b**-$\mathbf{H_2}$

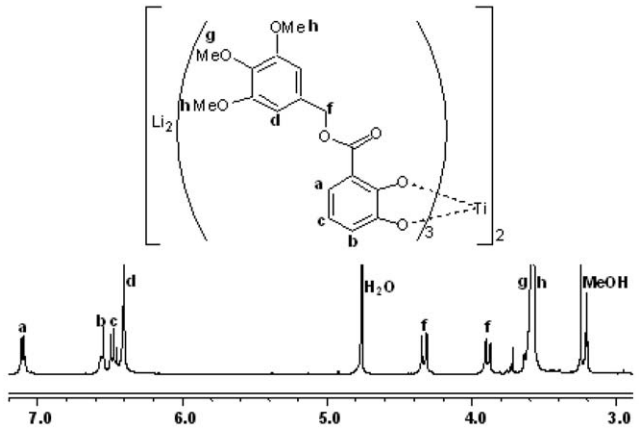


Figure 1 ^{1}H NMR spectrum of dimeric $Li[Ti_2(\mathbf{1a})_6Li_3]$ in CD_3OD

protons **f** at δ = 4.31 (d, *J* = 8.2 Hz, 6 H) and 3.89 (d, *J* = 8.2 Hz, 6 H) (Figure 1), which is typical for the dimeric species.

The monomer-dimer equilibrium of the nonpolar complex $Li_4[Ti_2(\mathbf{1b})_6]$ with long alkyl-substituents was studied in deuterochloroform. To improve the quality of the NMR signals a minute amount of methanol was added. ^{1}H NMR spectroscopy revealed the presence of only one species (Figure 2).

The ^{1}H NMR spectrum shows all relevant signals with some broadening due to aggregation of the complexes in solution (this is suppressed by addition of small amount of

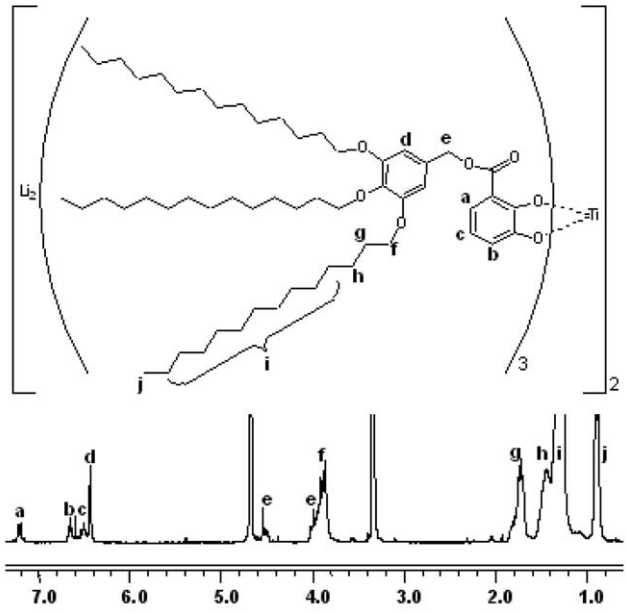


Figure 2 ^{1}H NMR spectrum of dimeric $Li[Ti_2(\mathbf{1b})_6Li_3]$ in $CDCl_3$

methanol). A spectroscopic probe are the diastereotopic protons **e** of the benzylic group at δ = 4.54 (d, *J* = 8.2 Hz, 6 H) and 4.00 (br, 6 H). The latter signal is observed as a 'shoulder' of the multiplet, which is assigned to the methylene groups of the alkyl chains connected to the ether oxygen atoms at δ = 3.88. The observation of diastereotopic behavior of those protons clearly shows the presence of the dimeric species. In the case of the monomer, fast racemization would take place and would result in only one singlet. The lack of this resonance indicates that the dimer-monomer equilibrium is strongly shifted towards the dimer.

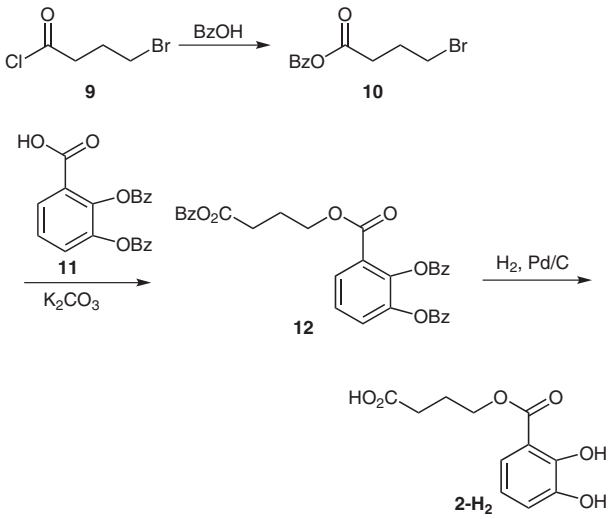
The dimer $Li_3[Ti_2(\mathbf{1b})_6]^-$ is observed as a peak at *m*/*z* = 5392 in ESI FT-ICR-MS studies in THF–methanol.

The model complex $Li_4[Ti_2(\mathbf{1a})_6]$ shows good solubility in a polar solvent like methanol revealing the presence of the dimeric species. Adding nonpolar side chains to obtain $Li_4[Ti_2(\mathbf{1b})_6]$ allows us to dissolve the complex even in chloroform. In this solvent, the lithium cations cannot be solvated and therefore the dimer is further stabilized and seems to be the exclusive species.

Hierarchical Assembly of Highly Hydrophilic Helicates

In order to test the possibilities to tune the polarity of our complexes to the extremes we prepared the carboxylic acid substituted ligand **2**-H_2 (Scheme 3). The synthetic procedure follows a simple basic ester coupling as the key reaction with some additional protective group transformations. Initially the carboxylic acid function of 4-bromobutyryl chloride (**9**) is reacted with benzyl alcohol. Subsequently the protected bromide **10** is coupled in a Williamson ether synthesis[9] with 2,3-dibenzoxybenzoic

acid (**11**) under basic conditions and the resulting ligand precursor **12** is deprotected by hydrogenation in the presence of palladium on charcoal to yield ligand **2-H$_2$** (overall: 79%).



Scheme 3 Synthesis of **2-H$_2$**

The titanium(IV) complex $Li_2[Ti(\mathbf{2})_3]$ was prepared by dissolving 3 equivalents of the corresponding ligand **2-H$_2$**, 1 equivalent $TiO(acac)_2$, and 1 equivalent Li_2CO_3 in methanol. After stirring overnight, the solvent was removed under reduced pressure to give the complex in quantitative yield as red solid.

The complex $Li_4[Ti_2(\mathbf{2})_6]$ is soluble in methanol and even in water. The ^{1}H NMR in D_2O (Figure 3c) reveals the presence of three different species: two coordination compounds and the free ligand. For the major species no diastereotopic splitting and no significant high field shifts are detected as expected for the quickly racemizing monomer. The second, dimeric species shows two diastereotopic protons at $\delta = 3.51$ and 2.88 indicating the dimer to be configuratively stable. The high field shifts of H^d and $H^{d'}$ are typical for helicate formation due to the location of the CH_2 ester protons close to the aromatic unit in the dimer. As additional species traces of free ligand could be detected due to some minor hydrolysis of the complex.

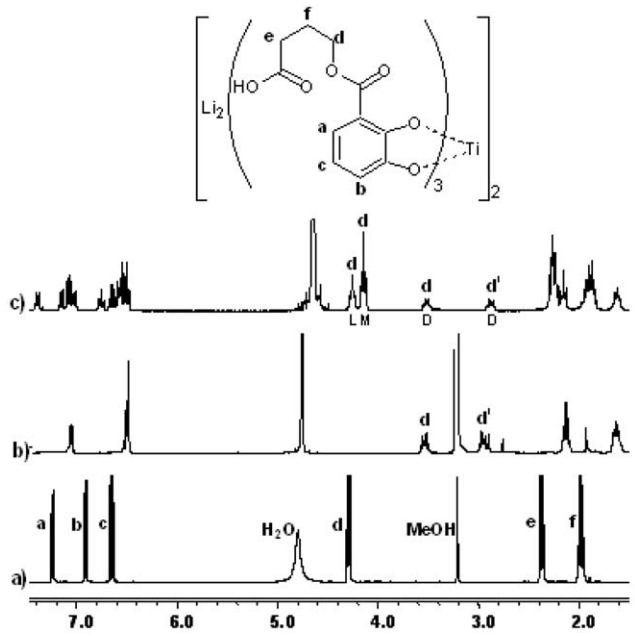


Figure 3 ^{1}H NMR spectra of a) ligand **2-H$_2$** in CD_3OD; b) dimeric $Li[Ti_2(\mathbf{2})_6Li_3]$ in CD_3OD; c) $Li_2[Ti(\mathbf{2})_3]/Li[Ti_2(\mathbf{2})_6Li_3]$ in D_2O; (M = monomer, D = dimer, L = free ligand)

For comparison, we measured the ^{1}H NMR spectrum of $Li_4[Ti_2(\mathbf{2})_6]$ in deuterated methanol (Figure 3b). In this case we only detected the dimeric species, which showed the typical high field shift and two signals for the diastereotopic protons at $\delta = 3.60$ (br, 6 H) and 3.05 (br, 6 H).

Negative ESI-MS investigations in H_2O–MeOH show the dimeric species $[Li_3Ti_2(\mathbf{2})_6]^-$ as the only peak at m/z = 1547.

Herein we have described the synthesis of highly nonpolar **1a**,**b-H$_2$** and highly polar ligands **2-H$_2$** as well as the corresponding complexes $Li[Li_3[Ti_2(\mathbf{1a},\mathbf{b}, \mathbf{2})_6]$. The monomer-dimer equilibrium leading to the hierarchical helicate formation is closely connected to the reaction media. By tuning the polarity we increased the band width of the concept to create helicates by hierarchical self-assembly. The combination of nonpolar reaction media with hydrophobic esters as carbonyl donors leads exclusively to the formation of lithium templated dimeric helicates. By using a polar ligand and changing the solvent to water, which is an excellent lithium solvating media, we got the mononuclear complex as major product. Surprisingly we still were able to observe the dimeric complex in significant amounts. This unexpected stability of the helicate type complex is probably due to protonation/deprotonation equilibrium at the carboxylate ester substituents, leading to an enhanced negative charge and stronger electrostatic attraction of the bridging lithium cations. Also, the multivalency effect of the three identical pockets for lithium coordination may play a role: Once the first lithium is bound, the two monomers are much better preorganized for coordination of the second, which again increases preorganization of the complex for the third lithium ion. The results presented here show that we can modify the polarity features of the complexes leading to soluble systems in a broad variety of solvents. This might be of interest for processing of related derivatives, which can have some specific properties.

NMR spectra were recorded with a Varian Mercury 300 or Inova 400 spectrometer. FT-IR spectra were recorded by diffuse reflection (KBr) on a Bruker IFS spectrometer. Mass spectra were measured on a Finnigan SSQ 7000 or a ThermoFisher Scientific LTQ-Orbitrap XL. Elemental analyses were obtained with a Heraeus CHN-O-Rapid analyzer. Melting points: Büchi B-540 (uncorrected). Chemicals were used as received by commercial suppliers.

Alkyl Aryl Ethers 4a,b; General Procedure

Gallic acid propyl ester (**3**; 4.2 g, 20 mmol, 1 equiv), K_2CO_3 (17.4 g, 120 mmol, 6 equiv), and MeI (9.9 g, 70 mmol, 3.5 equiv) or 1-bromotetradecane (19.4 g, 70 mmol, 3.5 equiv) were suspended in

acetone (150 mL) and refluxed for 48 h. Then, H_2O (50 mL) was added. Acetone was removed under reduced pressure and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were dried (Na_2SO_4), the solvent was removed under vacuum, and the residue dried under high vacuum.

3,4,5-Trimethoxybenzoic Acid Propyl Ester (4a)
Yield: 5.1 g (quant); colorless oil.

IR (KBr): 2963, 2839, 1715, 1590, 1502, 1461, 1415, 1335, 1227, 1181, 1126, 1002, 764 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.23 (s, 2 H), 4.20 (t, *J* = 6.9 Hz, 2 H), 3.84 (s, 6 H), 3.82 (s, 3 H), 1.73 (m, 2H), 0.95 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9 (C), 152.9 (C), 142.2 (C), 124.8 (C), 108.0 (CH), 73.5 (CH_2), 66.5 (CH_2), 62.3 (CH_3), 55.1 (CH_3), 10.6 (CH_3).

EI-MS: *m*/*z* = 254 $[M]^+$.

Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.13. Found: C, 61.55; H, 7.28.

3,4,5-Tristetradecyloxybenzoic Acid Propyl Ester (4b)
Yield: 11.1 g (69%); colorless solid; mp 31–33 °C.

IR (KBr): 2924, 2854, 1718, 1588, 1463, 1432, 1334, 1215, 1114, 761 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.26 (s, 2 H), 4.26 (t, *J* = 6.6 Hz, 2 H), 4.01 (t, *J* = 6.6 Hz, 6 H), 1.79 (m, 8 H), 1.46 (m, 6 H), 1.27 (br, 60 H), 1.02 (t, *J* = 6.6 Hz, 6 H), 0.88 (t, *J* = 6.6 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5 (C), 152.8 (C), 142.3 (C), 125.0 (C), 108.0 (CH), 73.5 (CH_2), 69.2 (CH_2), 66.5 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2,), 29.3 (CH_2), 26.1 (CH_2), 22.1 (CH_2), 14.1 (CH_3), 10.5 (CH_3); some CH_2 groups were not observed due to overlap of the resonances.

EI-MS: *m*/*z* = 811 $[M]^+$.

Anal. Calcd for $C_{52}H_{96}O_5 \cdot H_2O$: C, 76.13; H, 12.16. Found: C, 76.43; H, 11.67.

Reduction of the Esters 4a,b to Benzyl Alcohols 5a,b; General Procedure
Compound **4** (**4a**: 2.5 g, **4b**: 8.1 g, 10 mmol, 1 equiv) was dissolved in Et_2O (100 mL). $LiAlH_4$ (1 equiv) was added slowly and stirred for 4 h. H_2O (10 mL) was added, the solution neutralized with H_2SO_4 (10%), and the phases were separated. The organic layer was washed with brine (30 mL), dried (Na_2SO_4), and the solvent was removed under vacuum.

3,4,5-Trimethoxybenzyl Alcohol (5a)
Yield: 1.7 g (86%); lightly yellow oil.

IR (KBr): 3401, 2942, 1594, 1505, 1460, 1424, 1331, 1237, 1128, 1058, 1009, 830 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.61 (s, 2 H), 4.57 (s, 2 H), 3.79 (s, 6 H), 3.76 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.1 (C), 137.0 (C), 136.9 (C), 103.6 (CH), 65.0 (CH_2), 60.8 (CH_3), 56.0 (CH_3).

EI-MS: *m*/*z* = 198 $[M]^+$.

3,4,5-Tristetradecyloxybenzyl Alcohol (5b)
Yield: 7.4 g (quant); colorless solid; mp 50–51 °C.

IR (KBr): 2922, 2852, 1593, 1509, 1466, 1438, 1341, 1230, 1129, 726 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.49 (s, 2 H), 4.52 (s, 2 H), 3.89 (m, 6 H), 1.74 (m, 6 H), 1.22 (br, 66 H), 0.81 (t, *J* = 6.6 Hz, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.2 (C), 136.0 (C), 15.3 (CH), 69.1 (CH_2), 65.7 (CH_2), 32.0 (CH_3), 29.9 (CH_2), 29.8 (CH_2), 29.7 29.9 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 26.2 (CH_2), 22.8 (CH_2), 14.2 (CH_3).

EI-MS: *m*/*z* = 745 $[M]^+$.

Anal. Calcd for $C_{49}H_{92}O_4$: C, 78.97; H, 12.44. Found: C, 78.89; H, 11.48.

Bromination of the Alcohol Function; General Procedure
Compound **5** (**5a**: 2.0 g, **5b**: 7.4 g, 10 mmol, 3 equiv) was dissolved in Et_2O (20 mL) and pyridine (2 equiv) was added. The solution was cooled to –20 °C, PBr_3 (1 equiv) was added, and the suspension was stirred overnight. H_2O (10 mL) was added, the phases were separated, the organic layer was dried (Na_2SO_4), and the solvent removed under reduced pressure.

3,4,5-Trimethoxybenzyl Bromide (6a)
Yield: 2.1 g (80%); colorless solid; mp 76 °C.

IR (KBr): 2940, 2837, 1589, 1506, 1463, 1424, 1329, 1244, 1207, 1125, 989, 830, 780, 664, 596, 545 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.54 (s, 2 H), 4.39 (s, 2 H), 3.80 (s, 6 H), 3.77 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.2 (C), 138.1 (C), 133.1 (C), 106.1 (CH), 60.9 (CH_3), 56.2 (CH_3), 34.4 (CH_2).

EI-MS: *m*/*z* = 262 $[M + H]^+$, 181 $[M - Br]^+$.

Anal. Calcd for $C_{10}H_{13}BrO_3$: C, 46.00; H, 5.02. Found: C, 46.48; H, 4.94.

3,4,5-Tristetradecyloxybenzyl Bromide (6b)
Yield: 8.0 g (quant); colorless solid; mp 49–50 °C.

IR (KBr): 2923, 2853, 1591, 1503, 1462, 1335, 1243, 1121, 724 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.50 (s, 2 H), 4.36 (s, 2 H), 3.90 (m, 6 H), 1.78 (m, 6 H), 1.37 (br, 6 H), 1.20 (br, 60 H), 0.81 (t, *J* = 6.6 Hz, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.1 (C), 138.3 (C), 132.5 (C), 107.5 (CH), 69.1 (CH_2), 34.7 (CH_2), 33.0 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 26.2 (CH_2), 22.8 (CH_2), 14.2 (CH_3); some groups were not observed due to overlap of the resonances.

EI-MS: *m*/*z* = 808 $[M]^+$.

Anal. Calcd for $C_{49}H_{91}BrO_3$: C, 72.82; H, 11.35. Found: C, 71.57; H, 10.87.

Ester Formation and Cleavage of the Protective Groups; General Procedure
The bromide **6** (**6a**: 0.5 g, **6b**: 1.6 g, 2 mmol, 1 equiv), K_2CO_3 (1.7 g, 12 mmol, 6 equiv), and 2,3-diacetoxybenzoic acid (**7**; 0.3 g, 2 mmol, 1 equiv) were suspended in acetone (30 mL) and refluxed for 2 h. H_2O (10 mL) was added and the mixture extracted with CH_2Cl_2 (2 × 15 mL). The combined organic layers were dried (Na_2SO_4) and the solvent was removed. The crude product was purified by flash chromatography (**8a**: CH_2Cl_2, **8b**: *n*-pentane–CH_2Cl_2, gradient 4:1 to 2:1). Compound **8** (1 equiv) and K_2CO_3 (1 equiv) were refluxed for 2 h in H_2O–acetone (1:10) mixture. The suspension was filtered and the crude product was purified by flash chromatography in the case of **1a-H$_2$** (CH_2Cl_2). CH_2Cl_2–pentane (4:1) was used as eluent for **1b-H$_2$**.

2,3-Dihydroxybenzoic Acid 3,4,5-Trimethoxybenzyl Ester (1a-H$_2$)
Yield: 0.3 g (42%); colorless solid; mp 136 °C.

IR (KBr): 3430, 2942, 2840, 1737, 1669, 1595, 1509, 1464, 1425, 1333, 1307, 1238, 1129, 1007, 822, 758 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.21 (dd, *J* = 8.0, 1.7 Hz, 1 H), 6.93 (dd, *J* = 8.0, 1.7 Hz, 1 H), 6.70 (s, 2 H), 6.65 (t, *J* = 8.0 Hz, 1 H), 5.23 (s, 2 H), 3.78 (s, 6 H), 3.67 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1 (C), 153.4 (C), 149.0 (C), 145.1 (C), 138.3 (C), 132.4 (C), 120.6 (CH), 120.0 (CH), 119.3 (CH), 112.4 (C), 105.7 (CH), 67.4 (CH_2), 60.9 (CH_3), 56.2 (CH_3).

EI-MS: *m*/*z* = 334 $[M]^+$.

Anal. Calcd for $C_{17}H_{18}O_7 \cdot 0.5H_2O$: C, 59.48; H, 5.58. Found: C, 59.88; H, 6.23.

2,3-Dihydroxybenzoic Acid 3,4,5-Tristetradecyloxybenzoyl Ester (1b-H_2)

Yield: 0.5 g (29%); colorless solid; mp 39–44 °C.

IR (KBr): 3565, 2921, 2851, 1672, 1593, 1469, 1438, 1383, 1302, 1236, 1121, 968, 752, 723 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 10.84 (s, 1 H, OH), 7.39 (dd, *J* = 8.0, 1.4 Hz, 1 H), 7.10 (dd, *J* = 8.0, 1.4 Hz, 1 H), 6.79 (t, *J* = 8.0 Hz, 1 H), 6.61 (s, 2 H), 5.64 (s, 1 H, OH), 5.27 (s, 2 H), 3.97 (m, 6 H), 1.78 (m, 6 H), 1.46 (br, 6 H), 1.26 (br, 60 H), 0.88 (t, *J* = 8.0 Hz, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.1 (C), 153.3 (C), 148.9 (C), 145.1 (C), 138.6 (C), 130.0 (C), 120.7 (CH), 119.9 (CH), 119.2 (CH), 112.5 (C), 107.2 (CH), 69.2 (CH_2), 31.9 (CH_2), 30.3 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 26.2 (CH_2), 22.7 (CH_2), 14.1 (CH_3); some groups are not observed due to overlap of the resonances.

ESI-MS (+, MeOH): *m*/*z* = 905 $[M + Na]^+$.

Anal. Calcd for $C_{56}H_{96}O_7 \cdot H_2O$: C, 74.79; H, 10.98. Found: C, 74.74; H, 11.07.

4-Bromobutyric Acid Benzyl Ester (10)

To a solution of 4-bromobutyryl chloride (**9**; 0.4 g, 2 mmol, 1 equiv) in $CHCl_3$ (10 mL) were added benzylic alcohol (0.2 g, 1 equiv) and Et_3N (0.2 g, 1 equiv), and the mixture was stirred overnight. H_2O (2 mL) was added, the $CHCl_3$ layer was dried (Na_2SO_4), and the solvent removed under reduced pressure to give the crude product as colorless oil; yield: 0.5 g (89%).

IR (KBr): 3443, 3033, 2920, 2850, 1735, 1450, 1383, 1309, 1269, 1173, 1125, 991, 746, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.35 (m, 5 H), 5.13 (s, 2 H), 3.45 (t, *J* = 6.4 Hz, 2 H), 2.55 (t, *J* = 6.4 Hz, 2 H), 2.19 (ps q, *J* = 6.4 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.4 (C), 135.8 (C), 128.6 (CH), 128.3 (CH), 128.2 (CH), 66.7 (CH_2), 32.7 (CH_2), 32.5 (CH_2), 27.8 (CH_2).

EI-MS: *m*/*z* = 258 $[M + H]^+$.

2,3-Bisbenzyloxybenzoic Acid 3-Benzyloxycarbonylpropyl Ester (12)

Bromide **10** (0.3 g, 1 mmol, 1 equiv), 2,3-dibenzoxybenzoic acid (**11**; 0.2 g, 1 equiv), and K_2CO_3 (0.4 g, 3 equiv) were suspended in acetone (10 mL) and the mixture refluxed for 3 h. The salts were filtered off, the solvent removed under reduced pressure, and the crude product purified by flash chromatography (CH_2Cl_2) to give the desired product as a colorless oil; yield: 0.5 g (89%).

IR (KBr): 3033, 2951, 1730, 1581, 1464, 1379, 1264, 1157, 1088, 1044, 979, 911, 737, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.33 (m, 16 H), 7.13 (dd, *J* = 8.2, 1.7 Hz, 1 H), 7.96 (t, *J* = 8.2 Hz, 1 H), 5.13 (s, 2 H), 5.10 (s, 2 H), 5.08 (s, 2 H), 4.29 (t, *J* = 6.3 Hz, 2 H), 2.45 (t, *J* = 6.3 Hz, 2 H), 2.03 (ps q, *J* = 6.3 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.7 (C), 166.2 (C), 152.8 (C), 148.3 (C), 137.5 (C), 136.6 (C), 135.9 (C), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH, double int.), 128.1 (CH), 127.9 (CH), 127.6 (CH), 127.0 (C), 124.0 (CH), 122.8 (CH), 118.0 (CH), 75.7 (CH_2), 71.3 (CH_2), 66.4 (CH_2), 64.1 (CH_2), 30.9 (CH_2), 24.1 (CH_2).

ESI-MS (+, $CHCl_3$): *m*/*z* = 517 $[M + Li]^+$.

2,3-Dihydroxybenzoic Acid 3-Carboxypropyl Ester (2-H_2)

Ligand precursor **12** (0.3 g, 0.5 mmol, 1 equiv) was dissolved in EtOAc (50 mL), 10% Pd/C catalyst (30 mg) was added, and the mixture stirred for 12 h under H_2 atmosphere (10 bar). The catalyst was filtered off and the solvent removed under reduced pressure to give the product as a colorless solid; yield: 120 mg (quant); mp 51 °C.

IR (KBr): 3465, 3101, 3039, 2965, 2363, 2339, 1729, 1668, 1470, 1408, 1311, 1273, 1159, 1067, 994, 761, 591 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.22 (dd, *J* = 8.0, 1.4 Hz, 1 H), 6.90 (dd, *J* = 8.0, 1.4 Hz, 1 H), 6.65 (t, *J* = 8.0 Hz, 1 H), 4.29 (t, *J* = 6.3 Hz, 2 H), 2.37 (t, *J* = 6.3 Hz, 2 H), 1.98 (ps q, *J* = 6.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.1 (C), 170.2 (C), 149.8 (C), 145.6 (C), 120.3 (CH), 119.8 (CH), 118.6 (CH), 112.4 (C), 64.4 (CH_2), 30.2 (CH_2), 23.9 (CH_2).

EI-MS: *m*/*z* = 240 $[M]^+$.

Anal. Calcd for $C_{11}H_{12}O_6$: C, 55.00; H, 5.04. Found: C, 55.26; H, 5.24.

Titanium(IV) Complexes of Ligands 1 and 2; General Procedure

Catechol ligand **1a**,**b**-H_2, **2**-H_2 (**1a**-H_2: 33 mg, **1b**-H_2: 82 mg, **2**-H_2: 24 mg, 0.1 mmol, 3 equiv), titanyl bis(acetylacetonate) (8.7 mg, 1 equiv), and Li_2CO_3 (2.5 mg, 1 equiv) were dissolved in $CHCl_3$ or MeOH (10 ml), and the mixture was stirred overnight. The solvent was removed and the residue dried under vacuum to afford the ligands as red solids in quantitative yield.

$Li_4[Ti_2(1a)_6]$

Yield: 35 mg.

IR (KBr): 3433, 2944, 1681, 1594, 1508, 1449, 1382, 1336, 1296, 1254, 1218, 1125, 1007, 817, 748, 691, 577, 535 cm^{-1}.

^1H NMR (400 MHz; CD_3OD): δ = 7.09 (dd, *J* = 8.2, 1.7 Hz, 6 H), 6.55 (dd, *J* = 8.2, 1.7 Hz, 6 H), 6.47 (t, *J* = 8.2 Hz, 6 H), 6.41 (s, 12 H), 4.31 (d, *J* = 8.2 Hz, 6 H), 3.89 (d, *J* = 8.2 Hz, 6 H), 3.59 (s, 36 H), 3.58 (s, 18 H).

ESI-MS (–, $CHCl_3$–MeOH): *m*/*z* = 2148 $[Li_4Ti_2(\mathbf{1a})_6CH_3O]^-$.

ESI-MS (+, $CHCl_3$–MeOH): *m*/*z* = 1065 $[Li_3Ti(\mathbf{1a})_3]^+$.

Anal. Calcd for $C_{102}H_{96}Li_4O_{42}Ti_2 \cdot 5H_2O$: C, 55.48; H, 4.84. Found: C, 55.68; H, 5.34.

$Li_4[Ti_2(1b)_6]$

Yield: 90 mg.

IR (KBr): 2924, 2853, 1679, 1593, 1447, 1382, 1334, 1295, 1257, 1220, 1116, 996, 820, 747, 695, 543 cm^{-1}.

^1H NMR (300 MHz, CD_3OD–$CDCl_3$, 1:2): δ = 7.21 (d, *J* = 8.2 Hz, 6 H), 6.66 (d, *J* = 8.2 Hz, 6 H), 6.14 (t, *J* = 8.2 Hz, 6 H), 6.44 (s, 12 H), 4.54 (d, *J* = 8.2 Hz, 6 H), 4.00 (br, 6 H), 3.88 (m, 36 H), 1.74 (m, 36 H), 1.44 (br, 36 H), 1.28 (br, 36 H), 0.89 (m, 54 H).

ESI-MS (–, THF–MeOH): *m*/*z* = 5392 $[Li_3Ti_2(\mathbf{1b})_6]^-$.

Anal. Calcd for $C_{168}H_{282}Li_2O_{21}Ti·6H_2O$: C, 71.86; H, 10.69. Found: C, 71.90; H, 10.40.

$Li_4[Ti_2(2)_6]$
Yield: 26 mg.

IR (KBr): 3364, 2954, 2320, 1729, 1676, 1592, 1563, 1442, 1296, 1253, 1214, 1156, 1064, 1012, 987, 806, 746, 680 cm^{-1}.

^1H NMR (300 MHz, CD_3OD): δ = 7.09 (m, 6 H), 6.57 (m, 12 H), 3.60 (br, 6 H), 3.05 (br, 6 H), 2.28 (t, *J* = 7.2 Hz, 12 H), 1.72 (ps q, *J* = 7.2 Hz, 12 H).

^1H NMR (300 MHz, D_2O): δ [dimer (minor species)] = 7.38 (d, *J* = 8.1 Hz, 6 H), 7.15 (d, *J* = 8.1 Hz, 6 H), 6.75 (t, *J* = 8.1 Hz, 6 H), 3.51 (m, 6 H), 2.88 (m, 6 H), 2.15 (t, *J* = 7.4 Hz, 12 H), 1.82 (ps q, *J* = 7.4 Hz, 12 H); δ [monomer (major species)] = 7.07 (d, *J* = 7.9 Hz, 3 H), 6.55 (m, 6 H), 4.14 (t, *J* = 6.3 Hz, 6 H), 2.27 (t, *J* = 6.3 Hz, 6 H), 1.88 (ps q, *J* = 6.3 Hz, 6 H).

ESI-MS (+, H_2O–MeOH): *m*/*z* = 1547 $[Li_5Ti_2(\mathbf{2})_6]^+$.

Anal. Calcd for $C_{33}H_{27}O_{18}Li_2Ti·3H_2O$: C, 47.51; H, 3.99. Found: C, 47.64; H, 4.51.

Acknowledgment

Financial support by the Deutsche Forschungsgemeinschaft (DFG) and the Fonds der Chemischen Industrie is gratefully acknowledged.

References

(1) (a) Lehn, J. M. *Supramolecular Chemistry, Concepts and Perspectives*; VCH: Weinheim, **1996**. (b) Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry*; Wiley-VCH: Weinheim, **2002**.

(2) (a) Abedin, M. J.; Liepold, L.; Suci, P.; Young, M.; Douglas, T. *J. Am. Chem. Soc.* **2009**, *131*, 4346. (b) Yu, T.-B.; Bai, J. Z.; Guan, Z. *Angew. Chem. Int. Ed.* **2009**, *48*, 1097; *Angew. Chem.* **2009**, *121*, 1117. (c) Pradeep, C. P.; Long, D.-L.; Newton, G. N.; Song, Y.-F.; Cronin, L. *Angew. Chem. Int. Ed.* **2008**, *47*, 4388; *Angew. Chem.* **2008**, *120*, 4460. (d) Cheglakov, Z.; Weizmann, Y.; Braunschweig, A. B.; Wilner, O. I.; Willner, I. *Angew. Chem. Int. Ed.* **2008**, *47*, 126; *Angew. Chem.* **2008**, *120*, 132. (e) Matsuura, K.; Murasato, K.; Kimizuka, N. *J. Am. Chem. Soc.* **2005**, *127*, 10148.

(3) (a) Klug, A. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 565; *Angew. Chem.* **1983**, *95*, 579. (b) Tan, W. S.; Lewis, C. L.; Horelik, N. E.; Pregibon, D. C.; Doyle, P. S.; Yi, H. *Langmuir* **2008**, *24*, 12483.

(4) (a) Albrecht, M.; Baumert, M.; Klankermayer, J.; Kogej, M.; Schalley, C. A.; Fröhlich, R. *Dalton Trans.* **2006**, 4395. (b) Albrecht, M.; Fiege, M.; Baumert, M.; de Groot, M.; Fröhlich, R.; Russo, L.; Rissanen, K. *Eur. J. Inorg. Chem.* **2007**, 609.

(5) Albrecht, M.; Mirtschin, S.; de Groot, M.; Janser, I.; Runsink, J.; Raabe, G.; Kogej, M.; Schalley, C. A.; Fröhlich, R. *J. Am. Chem. Soc.* **2005**, *127*, 10371.

(6) Reviews on helicates: (a) Piguet, C.; Bernardinelli, G.; Hopfgartner, G. *Chem. Rev.* **1997**, *97*, 2005. (b) Albrecht, M. *Chem. Rev.* **2001**, *101*, 3457. (c) Hannon, M. J.; Childs, L. J. *Supramol. Chem.* **2004**, *16*, 7. (d) Albrecht, M. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 797.

(7) Terazzi, E.; Torelli, S.; Bernardenielli, G.; Rivera, J.-P.; Benech, J.-M.; Bourgogne, C.; Donnio, B.; Guillon, D.; Imbert, D. G.; Bünzli, J.-C.; Pinto, A.; Jeannerat, D.; Piguet, C. *J. Am. Chem. Soc.* **2005**, *127*, 888.

(8) Tanabe, K.; Yasuda, K.; Yoshio, M.; Kato, T. *Org. Lett.* **2007**, *9*, 4271.

(9) (a) Williamson, W. *Liebigs Ann. Chem.* **1851**, *77*, 37. (b) Feuer, H.; Hooz, J. In *The Chemistry of the Ether Linkage*; Patai, S., Ed.; Wiley: New York, **1967**, 445–498. (c) Okuro, K.; Kinbara, K.; Tsumoto, K.; Ishii, N.; Aida, T. *J. Am. Chem. Soc.* **2009**, *131*, 1626.