Synthesis of Four Generations of Monodisperse Aryl Ester Dendrimers Based on 1,3,5-Benzenetricarboxylic Acid

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ABSTRACT: The convergent synthesis of a series of monodisperse dendrimers based upon symmetrically substituted benzenetricarboxylic acid esters is described. These materials consist of 4, 10, 22, and 46 benzene rings connected symmetrically and have molecular diameters of up to 45 Å. The synthesis proceeds in a stepwise convergent manner, building dendritic arms, three of which are subsequently attached to a molecular core. The critical intermediate for the dendrimer arm synthesis is 5-(*tert*-butyldimethylsiloxy)-isophthaloyl dichloride, obtainable in three steps from 5-hydroxyisophthalic acid. Reaction of the diacid chloride with phenol, followed by removal of the silyl protecting group, gives a new substituted phenol. Two moles of the latter are further reacted with 5-(*tert*-butyldimethylsiloxy)isophthaloyl dichloride. This process is repeated several times. The dendrimer arms formed by these reactions are coupled to 1,3,5-benzenetricarbonyl trichloride yielding dendrimers. Kinetic results suggest that the rate of reaction of the first dendrimer arm with the core is independent of the size of the dendrimer arm. These materials are stable up to 500 °C under N_2 and are highly soluble in typical organic solvents. Possible applications for these materials include molecular weight standards, polymer rheology modifiers, or molecular inclusion hosts.

Introduction

Recently, considerable effort has been expended in the development of polymer systems with architectures other than linear chains. Important examples include ladder, star, and comb polymers which all have some degree of three-dimensional character.[1] The rational synthesis of three-dimensional, ordered polymer systems remains a major challenge. The difficulties in preparing such systems are many, but chief among them are retaining solubility of the growing polymers, preserving regularity and order in the structures, and characterization of products. Despite the difficulties, several laboratories have reported the stepwise synthesis of isotropic, three-dimensional polymer systems in which a large number (approaching all) of the repeat units are also branch sites.[2-12] Materials of this general type have been termed starburst dendrimers,[2] arborols,[5] cascade molecules,[3,5] and dendritic macromolecules.[8]

Two fundamentally different methods have been developed for the stepwise synthesis of dendritic polymers: the divergent approach in which the synthesis is begun at the center of the dendrimer[2-7] and the convergent approach in which the synthesis is begun at the outside of the dendrimer.[8-11] In the former, reaction of a core with 2 or more mol of a reagent containing at least two protected branching sites, followed by removal of the protecting groups and subsequent reaction of the liberated reactive sites, leads to the first generation dendrimer. The process is repeated until a dendrimer of the desired size has been prepared. The disadvantage of this approach is that successive generations require that a geometrically increasing number of reactions be carried out on the growing dendrimer. Circumvention of this problem necessitates large excesses of reactants and forcing conditions and causes difficulty in purification.

We and others have pioneered the alternative convergent approach in which the synthesis begins at what will become the outer surface of the dendrimer.[8-11] Progressively large dendrimer arms are prepared by the attachment of a small number (typically two) of smaller arms to a molecule having two functional groups, X and Y. Each dendrimer arm has a functional group Z which reacts with only one of the two functional groups, e.g. X. The unchanged functional group Y in the new larger arm must then be converted to the functional group Z, permitting further iteration of this process. Finally, the completed dendrimer arms are coupled to a core containing a small number (typically three) of the functional group X. The advantages of the convergent approach have been discussed and include the abilities to precisely control molecular weights and to make materials having functionalities in precise positions and numbers.[8] Our first dendritic system was a series of hydrocarbons consisting of 1,3,5-linked polyphenylenes.[9,10] These materials are thermally stable and highly soluble in common organic solvents. A difficulty with the hydrocarbon system is that as the dendrimers become larger, the coupling chemistry used to assemble them (palladium mediated coupling of an arylboronic acid to an aryl bromide) becomes more sluggish, and side reactions become problematic. In an effort to circumvent this problem and to try to prepare larger molecules, we extended our convergent approach to 1,3,5-benzenetricarboxylic acid esters (Scheme I). We hoped that the ease of formation of ester linkages from an acid chloride and a phenol would minimize side reactions. Secondly, the ester linkage provides two degrees of freedom not present in the hydrocarbon dendrimers, which should permit the preparation of larger molecules. Finally, incorporation of the ester unit makes this series of molecules significantly larger in diameter and molecular weight than the hydrocarbons. The ester series have nominal molecular weights of 438, 1159, 2600, and 5483 with molecular diameters of 19, 30, 37, and 45 Å as estimated from space-filling molecular models, whereas the hydrocarbons have diameters of 15, 20, 25, and 31 Å at the same generation. The greater sizes and higher molecular weights may allow these materials to bind larger numbers of small molecules or modify the properties of other polymers in a blend.

Results and Discussion

Our synthetic strategy to prepare dendritic macromolecules consists of preparing ever larger dendrimer arms or dendrons and coupling several of these to a core. In the present context, the synthesis of the requisite dendrons was based upon a repetitive coupling/deprotection sequence utilizing silyl-protected phenols and acyl chlorides. The exception to this general approach is compound **4**

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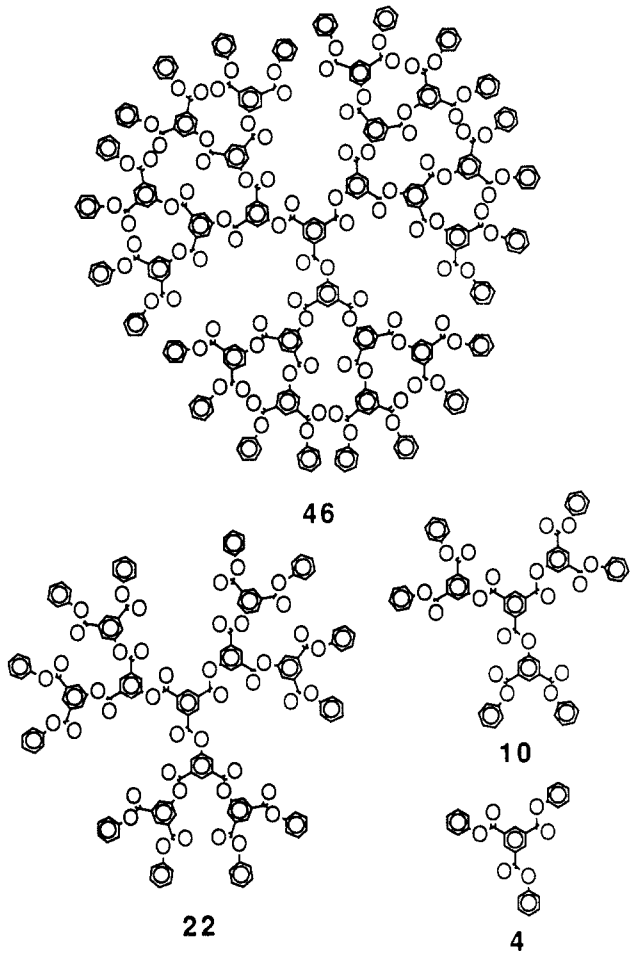
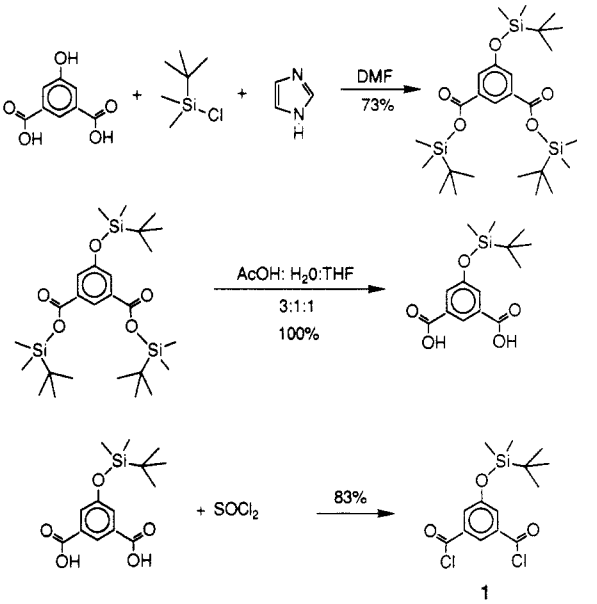
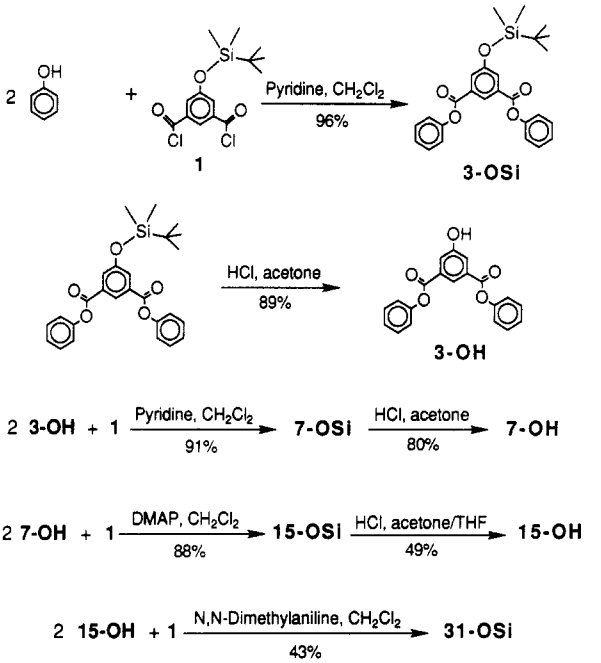
Scheme I



Scheme II



Scheme III

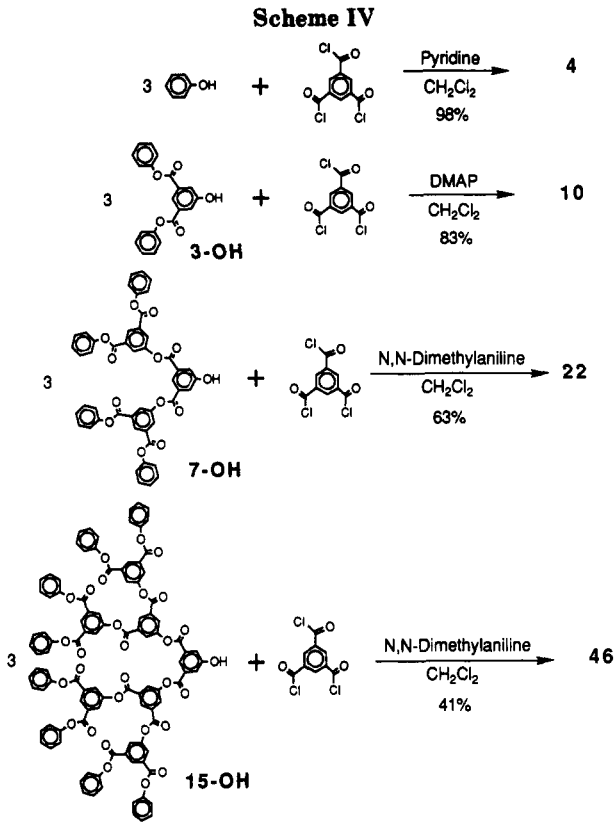


which is prepared simply by the reaction of 3 mol of phenol with 1,3,5-benzenetricarbonyl trichloride. The syntheses of **10**, **22**, and **46**, first required the preparation of the dendrimer arms, **3-OH**, **7-OH**, and **15-OH**. Because of the cumbersome systematic nomenclature for these molecules, we name them by a number referring to the number of benzene rings in the molecule followed by an abbreviation for the reactive functional group. The key intermediate in the syntheses of these is 5-(*tert*-butyldimethylsiloxy)isophthaloyl dichloride, **1**. It was prepared in three steps (Scheme II), in an overall yield of 75–93% beginning with commercially available 5-hydroxyisophthalic acid. The hydroxyl and carboxyl groups of this compound were protected with the *tert*-butyldimethylsilyl group using *tert*-butyldimethylsilyl chloride and imidazole in DMF.[13] The ester groups were then selectively hydrolyzed using acetic acid/water/tetrahydrofuran, and the resulting diacid was converted to the dichloride with $SOCl_2$.

Preparation of the dendrimer arms used the reiterative sequence of esterification and hydrolysis reactions shown in Scheme III. Reaction of 5-(*tert*-butyldimethylsiloxy)-isophthaloyl dichloride with phenol and pyridine yielded diphenyl 5-(*tert*-butyldimethylsiloxy)isophthalate, **3-OSi**. Typically *tert*-butyldimethylsilyl ethers are cleaved with fluoride ion in THF, and this procedure worked well in the synthesis of **3-OH** but failed to cleanly remove the *tert*-butyldimethylsilyl protecting group from larger phenols.[13] Reaction of **7-OSi** with fluoride ion yielded a mixture of phenols containing substantial amounts of **3-OH** and the unsymmetrical phenol containing five phenyl rings in addition to **7-OH**. We tried numerous reaction conditions containing more or less water, counterions other than tetra-*n*-butylammonium, and adding water buffered to different pH's to effect a clean reaction. All reactions containing fluoride ion gave mixtures. It appeared from TLC of these reaction mixtures as they progressed that silylated phenols, e.g. **3-OSi**, were intermediates in the production of these side products. We then found that reaction of an acetone or THF solution of **7-OSi** with 1 N HCl yielded **7-OH** cleanly and in high yield. Similarly, reaction of **15-OSi** with 1 N HCl yielded **15-OH** cleanly. The reaction of **3-OH** and **7-OH** with **1** proceeded without difficulty. In both of these esterifications, a small excess of the phenol was used which was easily separated from the product by flash chromatography on silica gel.

Reaction of 1,3,5-benzenetricarbonyl trichloride with **3-OH** using either pyridine or the far stronger base and acylation catalyst, (dimethylamino)pyridine (DMAP),[14] gave the dendrimer **10** in good yield (Scheme IV). DMAP improved the yield slightly. Reaction of 1,3,5-benzenetricarbonyl trichloride with **7-OH** and pyridine afforded **22** satisfactorily (28%). We were unsuccessful in preparing **46** cleanly using either pyridine or DMAP. We examined the synthesis of **22** using DMAP instead of pyridine and

Scheme IV



found that **22** was contaminated with materials having slightly higher and lower R_f's on a TLC plate. We isolated these using column chromatography and believe, based on SEC retention times, TLC behavior, and ^1H NMR spectra, that they are unsymmetrical dendrimers containing 18 and 26 phenyl rings. These are obtained by an ester exchange reaction in which **7-OH** replaces a **3-OH**, yielding a compound having four more phenyl rings, and conversely **3-OH** replaces a **7-OH**, yielding a compound having four fewer phenyl rings. Thus, we infer that the impurities obtained in the synthesis of **46** are probably the result of ester exchange. We reasoned that since DMAP caused ester exchange in the synthesis of **22** and both pyridine and DMAP caused ester exchange in the attempted synthesis of **46** we needed a less basic and nucleophilic base than pyridine. We found that reaction of 1,3,5-benzenetricarbonyl trichloride with **15-OH** or **7-OH** and *N,N*-dimethylaniline eliminated ester exchange and afforded **46** and **22** cleanly.

We have tried to extend our syntheses to the next higher generation dendrimer but have not succeeded. Preparation of **31-OSi**, the next protected phenol, proceeded uneventfully, although the yield was somewhat diminished and the reaction took approximately 1 week to reach completion. We have been unable to deprotect **31-OSi** cleanly. Treatment of **31-OSi** with 1 N HCl gave **31-OH** in very low yield, and it was contaminated with **15-OH** and **7-OH**. We assume that hydrolysis of ester linkages is competitive with hydrolysis of the protecting group.

Characterization of the Dendrimers. Because of the high symmetry of these molecules, ^1H NMR spectroscopy is very useful in confirming the structure and assessing the purity of these materials. Spectra for **4**, **10**, **22**, and **46** are shown in Figure 1, and each of the protons even in **46** is well resolved from its neighbor. Protons on the core phenyl ring, ortho and para to phenolic oxygens, and on the terminal phenyl rings each resonate in a specific region. From the number of resonances ortho and para to phenolic oxygens it is quite easy to determine the generation of the

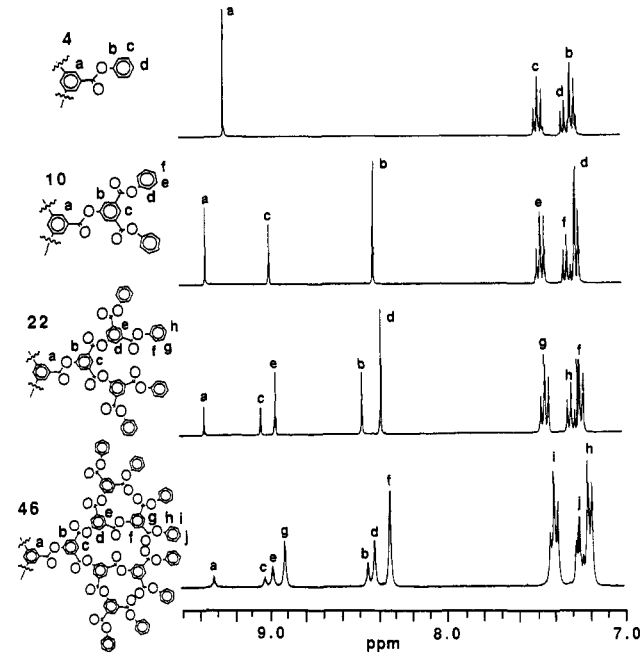


Figure 1. ^1H NMR spectra of dendrimers in $CDCl_3$ at 360 MHz.

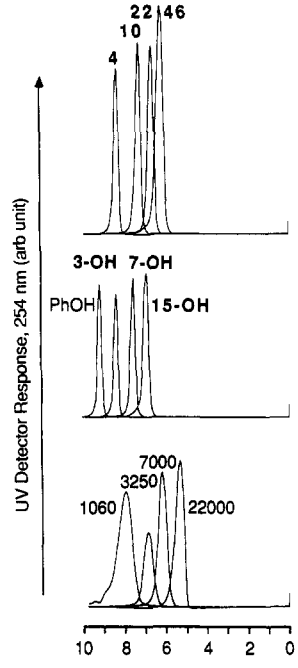


Figure 2. Gel permeation chromatograms of dendrimers (top), dendrons (middle), and polystyrene molecular weight standards (bottom) with a Beckman μ-Spherogel 500-Å column using 1,4-dioxane as the eluant. The polystyrene molecular weight standards have polydispersities of 1.11, 1.04, 1.04, and 1.03 for molecular weights of 1060, 3250, 7000, and 22 000, respectively.

dendrimer. Compound **10** has one set of resonances for protons ortho and para to oxygen, **22** has two sets, and **46** has three. As in the hydrocarbon dendrimers, protons which are closer to the center of the molecule resonate downfield of those further away. We have further characterized the dendrimers by ^{13}C NMR spectroscopy, elemental analyses, and size-exclusion chromatography. Microanalytical data obtained for the compounds are in good agreement with the theoretical values. Size-exclusion chromatograms (Figure 2) of both the symmetrical dendrimers and the dendrons demonstrate the high purity of these materials and the smooth progression of retention times with molecular weight. The traces in Figure 2 demonstrate that the compounds have, as one would expect, significantly narrower molecular weight distribu-

tions than polystyrene molecular weight standards. ^{13}C NMR spectroscopy despite its greater chemical shift dispersion than ^{1}H NMR spectroscopy is less useful in resolving carbon atoms in larger dendrimers.

These materials are all white microcrystalline or glassy solids which are highly soluble in organic solvents such as dichloromethane, chloroform, THF, ethyl acetate, and toluene. The solubility of **46** is 300 g/L in dichloromethane. As with our hydrocarbon dendrimers, the solubilities of these materials are vastly greater than one would expect from comparison to linear analogs. Poly(4-hydroxybenzoic acid) is not appreciably soluble in any organic solvent.[15]

Thermal Properties of the Dendrimers. Compound **46** was found to retain 95% of its mass up to 500 °C at a heating rate of 10 °C/min under N_2. The thermal stability of this material is similar to that of poly(4-hydroxybenzoic acid) and poly(3-hydroxybenzoic acid).[15,16] Differential scanning calorimetric analysis showed that **4** was crystalline, but **10**, **22**, and **46** were glasses having T_g's of 110, 133, and 141 °C. The glass transition temperatures increase with increasing molecular weight and are substantially lower than the T_g's for the hydrocarbon dendrimers having the same number of phenyl rings (126, 190, and 220 °C).[10] The greater flexibility and number of degrees of freedom in the esters lowers the glass transition temperature and the tendency to crystallize present in the hydrocarbon series.

Kinetics of Esterification of Substituted Phenols. We undertook an investigation of the rates of esterification of the series of phenols, **3-OH**, **7-OH**, and **15-OH**. It has been shown experimentally in the synthesis of linear polymers that the reactivity of a functional group at the end of the chain is independent of the length of the chain.[17] This assumption makes it possible to evaluate the kinetics of polymerization reactions. In highly branched dendrons having a single reactive functional group at their "focal point", this assumption must certainly fail at some point. We, therefore, wanted to see if there is a measurable difference in the rates of esterification of our electronically indistinguishable but sterically different phenols. In order for kinetic experiments to be tractable, we examined the rates of reaction with a simple monoacid chloride. Rates of reaction were determined using ^{1}H NMR spectroscopy by following the disappearance of the signals due to protons on the central phenyl ring and the appearance of signals due to the same protons in the product. Kinetic experiments were conducted under pseudo-first-order conditions in the phenol with a minimum of a 6-fold excess of acid chloride and base present. We quickly surveyed the approximate rates of esterification of **3-OH** with several aromatic acid chlorides. The rates of esterification increased with increasingly electron-poor aromatic rings: 3,5-$C_6H_3(NO_2)_2COCl$ > 4-$C_6H_4NO_2COCl$ > C_6F_5COCl > 4-$C_6H_4CH_3COCl$. The rates of reaction of the slowest and fastest were too extreme to be followed conveniently at 20 °C using *N,N*-dimethylaniline as the base. We chose C_6F_5COCl as the model acid chloride because its rate of reaction with **3-OH** was convenient and it simplified the ^{1}H NMR spectra since it has no protons.

The dependence of esterification rates on initial concentrations of **3-OH**, C_6F_5COCl, and $PhNMe_2$ were determined at room temperature. The rates of disappearance of **3-OH** and appearance of **3-O(CO)C_6F_5** were found to be the same, and no intermediates were observable. Rates of esterification increased with increasing concentrations of base and acid chloride and did not depend on the initial concentration of **3-OH** (Table I). The concentration of C_6F_5COCl had the strongest effect on the rate. The rates of esterification were then measured for **7-OH** and **15-OH** and were found to be the same within experimental uncertainty. Apparently, the steric size of **15-OH** is not large enough to affect its rate of reaction with a single acid chloride on an aromatic ring.

Table I
Rates of Esterification of Aryl-OH with C_6F_5COCl

run	substrate	[aryl-OH], M	[C_6F_5COCl], M	[DMA], M	rate × 10^4, M s^{-1}
1	**3-OH**	0.01	0.20	0.20	1.5
2	**3-OH**	0.02	0.20	0.20	1.4
3	**3-OH**	0.03	0.20	0.20	1.2
4	**3-OH**	0.01	0.10	0.20	0.88
5	**3-OH**	0.01	0.40	0.20	3.2
6	**3-OH**	0.01	0.20	0.10	1.1
7	**3-OH**	0.01	0.20	0.40	2.3
8	**3-OH**	0.02	0.20	0.40	2.2
9	**7-OH**	0.02	0.20	0.20	1.7
10	**15-OH**	0.02	0.20	0.20	1.7

Conclusion

This work describes the rational syntheses of a series of symmetrical, monodisperse aryl ester dendrimers possessing high thermal stability and solubility in organic solvents. With the present deprotecting and coupling chemistries, it appears unlikely that larger dendrimers in this series can be prepared. Ester exchange is a synthetic difficulty but can be overcome by judicious choice of reaction conditions. The rates of reaction with a simple acid chloride of phenols having 3, 7, and 15 phenyl rings are the same within our experimental uncertainty. These materials are of interest as models for isotropic high polymers and may themselves have utility as plasticizers for conventional organic polymers.

Experimental Section

General Procedures. All reactions were performed under an atmosphere of dry argon unless otherwise stated. All reagents and solvents unless otherwise specified were obtained from Aldrich Chemical Co. and were used without further purification. Dichloromethane, dimethylformamide, and pyridine were Aldrich anhydrous grade. Melting points were obtained on a Mel-Temp melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 360 spectrometer at 360.1 and 90.5 MHz, respectively, in $CDCl_3$ unless stated otherwise and were referenced to TMS or $CHCl_3$. Analytical TLCs were run on commercial Merck plates coated with silica gel GF254 (0.25 mm thick). Analytical GPC analyses were obtained using a Beckman solvent delivery system (1 mL/min), a 500-Å μ-Spherogel column, and an adjustable-wavelength UV/vis detector usually operated at 254 nm using *p*-dioxane (Aldrich, HPLC grade) as the eluant.

Thermal gravimetric analyses were carried out under nitrogen in a Perkin-Elmer TGA-7 using a heating rate of 10 °C/min. The calorimetric data were obtained on a Perkin-Elmer DSC-7 at a scanning rate of 15 °C/min under a flow (20 mL/min) of nitrogen. The temperature scale was calibrated using the melting points of indium and zinc and is accurate to ±0.1 °C. Samples typically weighed 3–4 mg, and aluminum containers were used.

1,3,5-Benzenetricarbonyl Trichloride. This compound was recrystallized from warm hexanes, yielding fine white needles which were filtered quickly and dried in vacuo (mp 34.5–36 °C).

Triphenyl 1,3,5-Benzenetricarboxylate (4). A 100-mL Schlenk flask equipped with a magnetic stirring bar and an Ar inlet was charged with phenol (2.14 g, 22.7 mmol) and pyridine (60 mL). A solution of benzenetricarbonyl trichloride (1.81 g, 6.78 mmol) in CH_2Cl_2 (20 mL) was slowly added, and the mixture was allowed to stir overnight. The colorless solution was diluted with CH_2Cl_2, extracted with 1 N HCl several times, washed with brine, and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The white solid was recrystallized from EtOAc/

EtOH, yielding fine white needles (2.19 g, 74%). Mp: 176–178 °C. Anal. Calcd for $C_{27}H_{18}O_6$: C, 74.00; H, 4.14; O, 21.86. Found: C, 73.64; H, 4.07; O, 22.17. ^{1}H NMR: δ 9.25 (s, 3 H), 7.47 (t, J = 8 Hz, 6 H), 7.32 (t, J = 8 Hz, 3 H), 7.29 (d, J = 8 Hz, 6 H). ^{13}C NMR: δ 163.38, 150.55, 136.07, 131.22, 129.67, 126.36, 121.51.

Bis(*tert*-butyldimethylsilyl) 5-(*tert*-Butyldimethylsiloxy)isophthalate. A 1-L Schlenk flask equipped with a magnetic stirring bar and an Ar inlet was charged with 3-hydroxyisophthalic acid (18.24 g, 100.1 mmol), *tert*-butyldimethylsilyl chloride (61.1 g, 405 mmol), imidazole (40.9 g, 601 mmol), and DMF (500 mL). The reaction vessel was flushed with Ar for 5 min, and the reaction mixture was warmed to 57 °C and stirred overnight. The reaction mixture was a yellow solution with white needles on the side of the flask. It was diluted with H_2O to a total volume of 1 L and extracted with hexanes (4 × 250 mL). The organic solutions were combined, washed with brine, and dried over $MgSO_4$. The volatiles were removed under reduced pressure, yielding a white solid (50.1 g, 95%). ^{1}H NMR: δ 8.27 (t, J = 2 Hz, 1 H), 7.70 (d, J = 2 Hz, 2 H), 1.03 (s, 18 H), 0.993 (s, 9 H), 0.385 (s, 12 H), 0.228 (s, 6 H).

5-(*tert*-Butyldimethylsiloxy)isophthalic Acid. A 1-L round-bottomed flask equipped with a magnetic stirring bar was charged with bis(*tert*-butyldimethylsilyl) 5-(*tert*-butyldimethylsiloxy)isophthalate (25.5 g, 48.6 mmol). THF (100 mL), glacial acetic acid (300 mL), and distilled water (100 mL) were added sequentially, and the reaction mixture was stirred for 3 h under air. The reaction mixture was diluted with cold H_2O and cooled to 0 °C in an ice bath, yielding a fine white precipitate which was filtered and dried in vacuo (14.4 g, 100%). Mp: 43–46 °C. ^{1}H NMR (DMSO-d_6): δ 13.37 (bs, 2 H), 8.15 (t, J = 2 Hz, 1 H), 7.61 (d, J = 2 Hz, 2 H), 1.01 (s, 9 H), 0.267 (s, 6 H).

5-(*tert*-Butyldimethylsiloxy)isophthaloyl Dichloride (1). A 300-mL round-bottomed flask equipped with a magnetic stirring bar, a condensor, and an Ar inlet, was charged with 5-(*tert*-butyldimethylsiloxy)isophthalic acid (19.5 g, 65.6 mmol) and thionyl chloride (150 mL). The suspension was heated to 110 °C and stirred overnight. The thionyl chloride was distilled, leaving a brown, crystalline solid. Purification was carried out using Kugelrohr distillation (110 °C, 20 mTorr), yielding a white crystalline solid (17.6 g, 83%) which was stored in an Ar-filled glovebox. Mp: 43.4–45.6 °C. Anal. Calcd for $C_{14}H_{18}O_3SiCl_2$: C, 50.45; H, 5.44; O, 14.40; Cl, 21.27. Found: C, 50.38; H, 5.40; O, 13.97; Cl, 21.40. ^{1}H NMR: δ 8.46 (t, J = 2 Hz, 1 H), 7.82 (d, J = 2 Hz, 2 H), 1.02 (s, 9 H), 0.286 (s, 6 H).

3-OSi. Procedure A. A 1-L Schlenk flask equipped with a magnetic stirring bar and an Ar inlet was charged with phenol (11.4 g, 121 mmol), CH_2Cl_2 (350 mL), and pyridine (100 mL). Compound 1 (16.7 g, 50.1 mmol) was brought out of the glovebox in a pear-shaped flask sealed with a rubber septum, dissolved in the minimum quantity of CH_2Cl_2 (ca. 40 mL), and transferred dropwise via cannula to the stirred solution. The reaction mixture was stirred overnight and concentrated under reduced pressure. The resulting brown slush was dissolved in CH_2Cl_2, extracted with 1 N NaOH, 1 N HCl, and brine, and dried over $MgSO_4$. The CH_2Cl_2 was removed under reduced pressure, yielding a light tan solid (21.5 g, 96%). Mp: 108–110 °C. Anal. Calcd for $C_{26}H_{28}O_5Si$: C, 69.61; H, 6.29; O, 17.83. Found: C, 69.10; H, 6.25; O, 17.41. ^{1}H NMR: δ 8.63 (t, J = 3 Hz, 1 H), 7.89 (d, J = 3 Hz, 2 H), 7.45 (t, J = 8 Hz, 4 H), 7.30 (t, J = 8 Hz, 2 H), 7.25 (d, J = 8 Hz, 4 H), 1.03 (s, 9 H), 0.286 (s, 6 H).

3-OH. Procedure B. A 1-L round-bottomed flask equipped with a magnetic stirring bar was charged with **3-OSi** (21.2 g, 47.3 mmol), acetone (500 mL), and 1 N HCl (70 mL) and heated to 50 °C under air. The reaction was monitored by TLC and was complete in 24 h. Acetone and water were removed under reduced pressure, and the resulting slush was dissolved in ca. 1 L of CH_2Cl_2. This mixture was extracted with water and brine and dried over $MgSO_4$. The solvent and *tert*-butyldimethylsiloxane were removed under reduced pressure initially and then dried under high vacuum (10^{-2} Torr). The crude solid was recrystallized from hot toluene, yielding a fluffy white solid (14.0 g, 89%). Mp: 181–183 °C. Anal. Calcd for $C_{20}H_{14}O_5$: C, 71.85; H, 4.22; O, 23.93. Found: C, 71.60; H, 4.09; O, 23.59. ^{1}H NMR: δ 8.59 (t, J = 2 Hz, 1 H), 7.94 (d, J = 2 Hz, 2 H), 7.45 (t, J = 8 Hz, 4 H), 7.30 (t, J = 8 Hz, 2 H), 7.24 (d, J = 8 Hz, 4 H).

10. Procedure C. A 50-mL Schlenk flask equipped with magnetic stirring bar and Ar inlet was charged with **3-OH** (4.08 g, 12.2 mmol) and (dimethylamino)pyridine (2.54 g, 20.8 mmol). The solids were dissolved in 25 mL of CH_2Cl_2. Benzenetricarbonyl trichloride was placed in a 25-mL pear-shaped flask sealed with a rubber septum, placed under Ar, and dissolved in 10 mL of CH_2Cl_2. This solution was added slowly via syringe to the stirred contents of the Schlenk flask, and the reaction mixture was allowed to stir overnight. The cloudy, tan solution was diluted to 60 mL with CH_2Cl_2, extracted with 1 N HCl, washed with brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure. The crude white solid was chromatographed on 75 g of silica gel using CH_2Cl_2 as the eluant. The white, glassy solid was recrystallized from EtOAc/EtOH, yielding a soapy, white solid (3.36 g, 82.7%). Anal. Calcd for $C_{69}H_{42}O_{18}$: C, 71.50; H, 3.65; O, 24.85. Found: C, 71.26; H, 3.83; O, 25.11. ^{1}H NMR: δ 9.36 (s, 3 H), 8.99 (t, J = 2 Hz, 3 H), 8.40 (d, J = 2 Hz, 6 H), 7.46 (t, J = 8 Hz, 12 H), 7.31 (t, J = 8 Hz, 6 H), 7.26 (d, J = 8 Hz, 12 H). ^{13}C NMR: δ 163.23, 162.69, 150.73, 150.55, 136.66, 132.09, 130.78, 129.63, 128.21, 126.32, 121.48.

7-OSi. This compound was synthesized via procedure A using 8.19 g (24.6 mmol) of 1, 19.5 g (58.3 mmol) of **3-OH**, and 75 mL of pyridine in 200 mL of CH_2Cl_2 for 20 h. Workup was the same as in procedure A except that the reaction mixture was not extracted with 1 N NaOH. The crude product was chromatographed on 250 g of silica gel using CH_2Cl_2 as the eluant, and excess **3-OH** was eluted from the column after **7-OSi** using 10% EtOAc in CH_2Cl_2. The purified glassy, white solid weighed 20.79 g (91%). Mp: 113–118 °C. Anal. Calcd for $C_{54}H_{44}O_{13}Si$: C, 69.81; H, 4.77; O, 22.39. Found: C, 69.64; H, 4.59; O, 22.06. ^{1}H NMR: δ 8.96 (t, J = 2 Hz, 2 H), 8.69 (t, J = 2 Hz, 1 H), 8.36 (d, J = 2 Hz, 4 H), 7.95 (d, J = 2 Hz, 2 H), 7.46 (t, J = 8 Hz, 8 H), 7.31 (t, J = 8 Hz, 4 H), 7.26 (d, J = 8 Hz, 8 H), 1.04 (s, 9 H), 0.313 (s, 6 H).

7-OH. This compound was prepared via procedure B using 27.3 g (29.4 mmol) of **7-OSi** and 210 mL of 1 N HCl in 1.5 L of acetone heated to 53 °C for 42 h in air. The white solid was recrystallized from hot toluene, yielding 19.24 g (80%) of a glassy, white solid. Mp: 207–211 °C. Anal. Calcd for $C_{48}H_{30}O_{13}$: C, 70.76; H, 3.71; O, 25.53. Found: C, 70.65; H, 3.56; O, 25.56. ^{1}H NMR: δ 8.63 (t, J = 2 Hz, 2 H), 8.61 (t, J = 2 Hz, 1 H), 8.33 (d, J = 2 Hz, 4 H), 7.23 (d, J = 2 Hz, 2 H), 7.44 (t, J = 8 Hz, 8 H), 7.29 (t, J = 8 Hz, 4 H), 7.24 (d, J = 8 Hz, 8 H), 6.32 (bs, 1 H).

22. This compound was prepared via procedure C using benzenetricarbonyl trichloride (0.512 g, 1.93 mmol), **7-OH** (5.64 g, 6.93 mmol), *N*,*N*-dimethylaniline (1.10 mL, 8.68 mmol) as the base, and CH_2Cl_2 (25 mL). Upon addition of benzenetricarbonyl trichloride, the solution became clear, bright green and eventually turned deep blue overnight. The crude product was dissolved in the minimum quantity of CH_2Cl_2 and chromatographed on 200 g of silica gel using 1% EtOAc in CH_2Cl_2 as the eluant. The product was recrystallized in EtOAc/EtOH, yielding a fine, white powder (3.19 g, 63%). Anal. Calcd for $C_{153}H_{90}O_{42}$: C, 70.67; H, 3.49; O, 25.84. Found: C, 70.32; H, 3.73; O, 26.09. ^{1}H NMR: δ 9.35 (s, 3 H), 9.03 (t, J = 2 Hz, 3 H), 8.95 (t, J = 2 Hz, 6 H), 8.46 (d, J = 2 Hz, 6 H), 8.35 (d, J = 2 Hz, 12 H), 7.45 (t, J = 8 Hz, 24 H), 7.28 (t, J = 8 Hz, 12 H), 7.24 (d, J = 8 Hz, 24 H). ^{13}C NMR: δ 163.21, 162.70, 162.51, 150.91, 150.72, 150.51, 132.01, 131.33, 130.66, 129.62, 128.85, 128.19, 126.30, 121.47.

Synthesis of 22 Accompanied by Ester Interchange. Procedure C was followed using **7-OH** (5.0 g, 6.6 mmol), (dimethylamino)pyridine (1.32 g, 10.8 mmol), benzenetricarbonyl trichloride (0.476 g, 1.79 mmol), and CH_2Cl_2 (35 mL). The reaction was worked up 16 h later as described in procedure C. A fraction of the white solid (1.0 g) was chromatographed on silica gel (100 g) starting with 0.25% EtOAc/CH_2Cl_2, and then gradually increasing to 1% EtOAc/CH_2Cl_2. TLC in 1% EtOAc/CH_2Cl_2 of the fractions showed two spots in addition to the spot for **22**: one above and one below. Size-exclusion chromatography of the three compounds showed that their retention times were 6.0, 6.2, and 6.3 min for the first, second, and third materials off the columns, respectively. First compound: ^{1}H NMR: δ 9.37 (m, 3 H), 9.06 (t, J = 2 Hz, 2 H), 8.99 (t, J = 2 Hz, 1 H), 8.97 (t, J = 2 Hz, 4 H), 8.49 (d, J = 2 Hz, 4 H), 8.40 (d, J = 2 Hz, 2 H), 8.37 (d, J = 2 Hz, 8 H), 7.45 (t, J = 8 Hz, 20 H), 7.30 (t, J = 8 Hz, 10 H), 7.26 (d, J = 8 Hz, 20 H). The second material off of

the column was shown by SEC retention time, R_f, on a TLC plate and ^{1}H NMR spectroscopy to be **22**. Third compound: ^{1}H NMR: δ 9.38 (m, 3 H), 9.05 (m, 3 H), 9.04 (t, J = 3 Hz, 1 H), 8.97 (m, 7 H), 8.48 (m, 6 H), 8.46 (d, J = 3 Hz, 2 H), 8.37 (m, 14 h), 7.49 (t, J = 8 Hz, 28 H), 7.29 (t, J = 8 Hz, 14 H), 7.25 (d, J = 8 Hz, 28 H).

15-OSi. This compound was prepared via procedure A using **7-OH** (14.27 g, 17.52 mmol), DMAP (3.67 g, 30.0 mmol), and CH_2Cl_2 (250 mL). Compound **1** (2.47 g, 7.41 mmol) was dissolved in CH_2Cl_2 (10 mL) and the solution transferred to the reaction mixture slowly via syringe. The reaction mixture was allowed to stir overnight and worked up as described above. The resulting white solid was chromatographed on silica gel (150 g) using CH_2Cl_2 as the eluant. The product was a white glassy solid weighing 12.4 g (88% yield). Mp: 161–164 °C. Anal. Calcd for $C_{110}H_{76}O_{29}Si$: C, 69.91; H, 4.05; O, 24.55. Found: C, 69.80; H, 4.01; O, 24.09. ^{1}H NMR: δ 9.03 (t, J = 2 Hz, 2 H), 8.97 (t, J = 2 Hz, 4 H), 8.71 (t, J = 2 Hz, 1 H), 8.44 (d, J = 2 Hz, 4 H), 8.37 (d, J = 2 Hz, 8 H), 7.97 (d, J = 2 Hz, 2 H), 7.45 (t, J = 8 Hz, 16 H), 7.30 (t, J = 8 Hz, 8 H), 7.26 (d, J = 8 Hz, 16 H), 1.04 (s, 9 H), 0.32 (s, 6 H).

15-OH. This compound was prepared via procedure B, using **15-OSi** (12.4 g, 6.55 mmol), acetone (500 mL), THF (115 mL), and 1 N HCl (90 mL). The reaction mixture was heated to 60 °C for 3 days and worked up as described above. The resulting tan solid was recrystallized from toluene/EtOH, yielding 5.59 g (49%) of a fine white powder. Mp: 169–172 °C. Anal. Calcd for $C_{104}H_{62}O_{29}$: C, 70.35; H, 3.52; O, 26.13. Found: C, 69.93; H, 3.43; O, 25.89. ^{1}H NMR: δ 8.93 (t, J = 2 Hz, 2 H), 8.91 (t, J = 2 Hz, 4 H), 8.54 (t, J = 2 Hz, 1 H), 8.35 (d, J = 2 Hz, 4 H), 8.32 (d, J = 2 Hz, 8 H), 7.87 (d, J = 2 Hz, 2 H), 7.40 (t, J = 8 Hz, 16 H), 7.25 (t, J = 8 Hz, 8 H), 7.21 (d, J = 8 Hz, 16 H).

46. This compound was prepared by following procedure C using benzenetricarbonyl trichloride (0.0804 g, 0.303 mmol), **15-OH** (1.78 g, 1.00 mmol), CH_2Cl_2 (10 mL), and *N,N*-dimethylaniline (0.175 mL, 1.38 mmol). The reaction mixture was allowed to stir for 4 days and was monitored by TLC. It turned deep blue and was worked up as described above, yielding 1.78 g of a blue solid. The solid was chromatographed on 100 g of silica gel, beginning with 1% EtOAc in CH_2Cl_2 as the eluant and gradually changing to 2% EtOAc in CH_2Cl_2. The white, glassy product weighed 0.683 g (41%). Anal. Calcd for $C_{321}H_{186}O_{90}$: C, 70.32; H, 3.42; O, 26.26. Found: C, 70.02; H, 3.31; O, 26.12. ^{1}H NMR: δ 9.26 (bs, 3 h), 8.98 (bs, 3 H), 8.94 (bs, 6 H), 8.88 (bs, 12 H), 8.41 (bs, 6 H), 8.38 (bs, 12 H), 8.29 (bs, 24 H), 7.37 (t, J = 8 Hz, 48 H), 7.23 (t, J = 8 Hz, 24 H), 7.18 (d, J = 8 Hz, 48 H). ^{13}C NMR: δ 163.09, 162.58, 162.44, 150.84, 150.66, 150.49, 131.89, 131.16, 130.54, 129.84, 129.52, 129.33, 128.71, 128.10, 126.20, 121.43.

31-OSi. This compound was prepared via procedure A using **1** (0.16 g, 0.47 mmol), **15-OH** (2.03 g, 1.15 mmol), *N,N*-dimethylaniline (0.25 mL, 1.9 mmol), and CH_2Cl_2 (25 mL). The reaction mixture was followed by SEC for 7 days. The solution was worked up as described above, yielding 2.1 g of a blue solid. This solid was chromatographed on silica gel (100 g) using 1% EtOAc/CH_2Cl_2 as the eluant. The fractions were combined, and the solvent was removed under reduced pressure, yielding a white solid (0.78 g, 43%). Anal. Calcd for $C_{222}H_{140}O_{61}Si$: C, 69.96; H, 3.70; O, 25.60. Found: C, 70.06; H, 3.54; O, 25.84. ^{1}H NMR: δ 9.05 (t, J = 3 Hz, 2 H), 9.03 (t, J = 3 Hz, 4 H), 8.96 (t, J = 3 Hz, 8 H), 8.69 (t, J = 3 Hz, 1 H), 8.45 (m, 12 H), 8.36 (d, J = 3 Hz, 16 H), 7.96 (d, J = 3 Hz, 2 H), 7.44 (t, J = 8 Hz, 32 H), 7.29 (t, J = 8 Hz, 16 H), 7.25 (d, J = 8 Hz, 32 H), 1.03 (s, 9 H), 0.30 (s, 6 H).

Kinetics. Rates of reaction were measured by following the concentrations of starting material and product using ^{1}H NMR spectroscopy. The time of base addition was taken as t = 0; the temperature of the probe was 293 K; and spectra were acquired with 16 scans, an acquisition time of 1.90 s, a pulse width of 5 ms, and a relaxation delay of 1 s. Ratios of peak areas were used in calculating the amount of phenol remaining. The resonances used were δ 7.94, which is due to the two protons ortho to the phenolic oxygen, and δ 8.34 which is the corresponding protons on the pentafluorobenzoyl ester. For runs 9 and 10, the amount of substrate remaining was calculated from the ratio of the areas for the resonances at 7.94 and for CH_2Cl_2, and then normalizing it to the ratio obtained before base was added. The details are given for a typical kinetic experiment (run 1). A 2-mL volumetric flask was charged with **3-OH** (0.01348 g, 0.0403 mmol), C_6F_5COCl (115 μL, 0.800 mmol), and CH_2Cl_2 (1.3 μL) and diluted with $CDCl_3$. A 1-mL volumetric flask was charged with 102 μL (0.805 mmol) of *N,N*-dimethylaniline and diluted with $CDCl_3$. An NMR tube was charged with 400 μL of the first solution, and a spectrum was taken. The second solution (400 μL) was added to the NMR tube, it was left in the spectrometer for the duration of the experiment, and spectra were recorded at appropriate time intervals. Runs 2–8 were carried out similarly using solutions containing various concentrations of reactants, and in runs 9 and 10 carefully purified samples of **7-OH** and **15-OH** were used.

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